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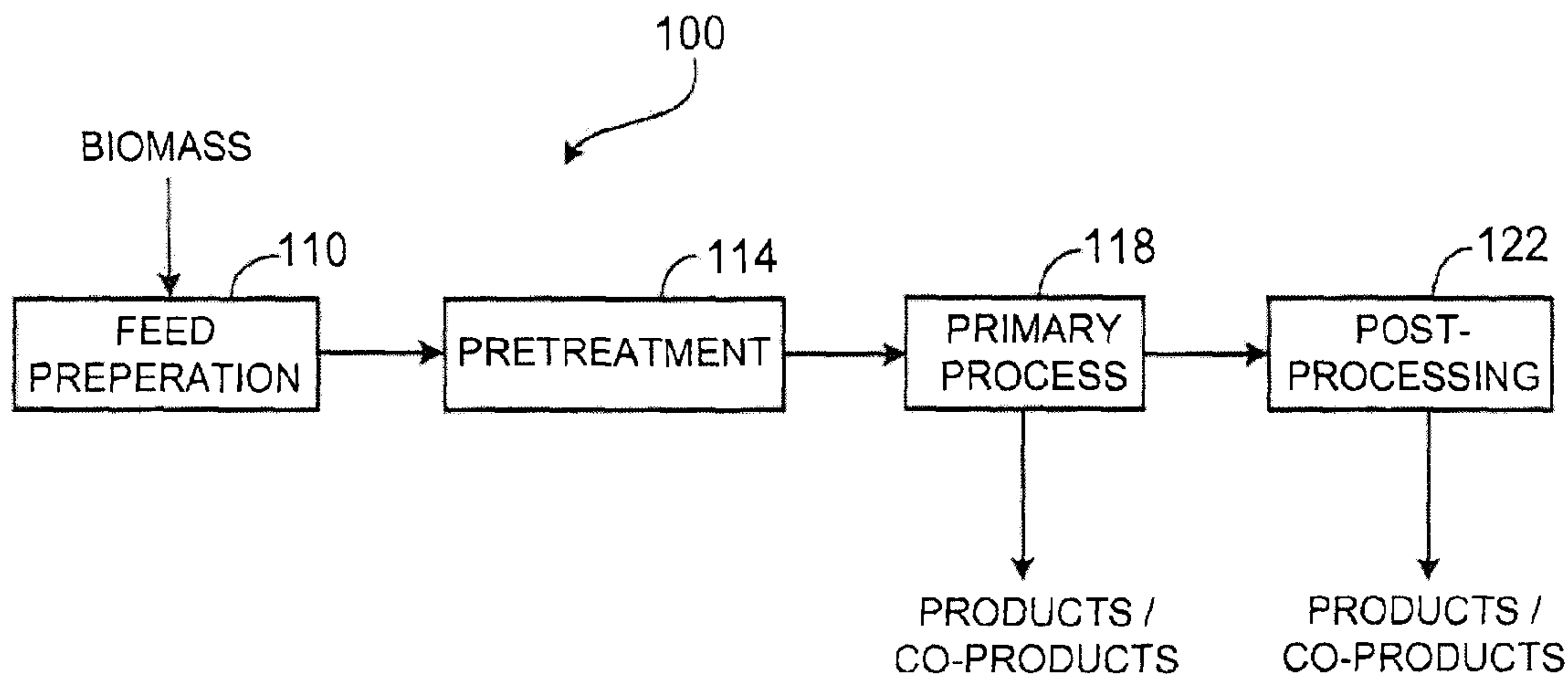
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(54) Titre : TRANSFORMATION DE BIOMASSE

(54) Title: PROCESSING BIOMASS



(57) Abrégé/Abstract:

Biomass (e.g., plant biomass, animal biomass, and municipal waste biomass) is processed to produce useful products, such as fuels. For example, systems can use feedstock materials, such as cellulosic and/or lignocellulosic materials and/or starchy or sugary materials, to produce ethanol and/or butanol, e.g., by fermentation.

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ABSTRACT

Biomass (e.g., plant biomass, animal biomass, and municipal waste biomass) is processed to produce useful products, such as fuels. For example, systems can use feedstock materials, such as cellulosic and/or lignocellulosic materials and/or starchy or sugary materials, to produce ethanol and/or butanol, e.g., by fermentation.

5

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JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
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PROCESSING BIOMASS

This application is a division of Canadian Application Serial No. 2,722,601 (parent application), filed April 28, 2009.

5 It should be understood that the expression “the present invention” or the like used in this specification may encompass not only the subject matter of this divisional application, but that of the parent application also.

TECHNICAL FIELD

This invention relates to processing biomass, such as methods and systems for processing biomass.

10 BACKGROUND

Various carbohydrates, such as cellulosic and lignocellulosic materials, e.g., in fibrous form, are produced, processed, and used in large quantities in a number of applications. Often such materials are used once, and then discarded as waste, or are simply considered to be waste materials, e.g., sewage, bagasse, sawdust, and stover.

15 SUMMARY

Biomass can be processed to alter its structure at one or more levels. The processed biomass can then be used, for example as a source of materials and/or fuel.

20 In general, the invention pertains to methods of changing a molecular and/or a supramolecular structure of a biomass feedstock. As will be discussed below, in some implementations, the methods include irradiating and quenching the biomass feedstock. In other implementations, the methods include irradiating the feedstock, cooling the feedstock, and again irradiating the feedstock.

The invention as claimed relates to:

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- a method of making a sucrose solution, the method comprising: irradiating crystalline sucrose, wherein the total dose of radiation is from 30 Mrad to 70 Mrad; and wherein irradiating is performed at a dose rate greater than 0.15 Mrad per second combining the irradiated sucrose with water under conditions that allow the sucrose to dissolve; thereby

5 making a sucrose solution; and

- a method of making amorphous sucrose, the method comprising: irradiating crystalline sucrose, wherein the total dose of radiation is from 30 Mrad to 70 Mrad; and wherein irradiating is performed at a dose rate greater than 0.15 Mrad per second thereby making amorphous sucrose.

10 Carbohydrate-containing materials (e.g., biomass materials or biomass-derived materials, such as starchy materials, cellulosic materials, lignocellulosic materials, or biomass materials that are or that include significant amounts of low molecular weight sugars (e.g., monosaccharides, disaccharides, or trisaccharides), can be processed to change their structure, and products can be made from the structurally changed materials.

15 For example, many of the methods described herein can provide cellulosic and/or lignocellulosic materials that have a lower molecular weight and/or crystallinity relative to a native material. Many of the methods provide materials that can be more readily utilized by a variety of microorganisms to produce useful products, such as hydrogen, alcohols (e.g., ethanol or butanol), organic acids (e.g., acetic acid), hydrocarbons, co-products

20 (e.g., proteins) or mixtures of any of these. Many of the products obtained, such

as ethanol or n-butanol, can be utilized as a fuel for powering cars, trucks, tractors, ships or trains, e.g., as an internal combustion fuel or as a fuel cell feedstock. Many of the products obtained can also be utilized to power aircraft, such as planes, e.g., having jet engines or helicopters. In addition, the products described herein can be utilized for electrical power generation, e.g., in a conventional steam generating plant or in a fuel cell plant.

In one aspect, the invention features methods that include quenching a biomass feedstock that has been irradiated to ionize the biomass feedstock so that the feedstock has a first level of radicals which are detectable with an electron spin resonance spectrometer, to an extent that the radicals are at a second level lower than the first level.

In another aspect, the invention features methods that include irradiating a biomass feedstock to ionize the biomass feedstock so that the feedstock has a first level of radicals which are detectable with an electron spin resonance spectrometer, and quenching the irradiated biomass feedstock to an extent that the radicals are at a second level, lower than the first level, in the quenched biomass feedstock.

Some methods further include processing the irradiated and quenched biomass feedstock to produce a product.

Some implementations include one or more of the following features.

Quenching can include quenching the radicals to a level that is no longer detectable with the electron spin resonance spectrometer, e.g., less than about 10^{14} spins. Quenching can include applying pressure to the biomass, e.g., a pressure of greater than about 1000 psi. Pressure can be applied together with the application of heat. Quenching can include contacting the biomass with a gas capable of reacting with the radicals, e.g., contacting the biomass with a fluid capable of penetrating into the biomass and reacting with the radicals. Quenching can also, or alternatively, include contacting the biomass with an antioxidant. In some cases, the biomass feedstock includes an antioxidant dispersed therein, and quenching includes contacting the antioxidant dispersed in the biomass feedstock with the radicals.

In another aspect, the invention features a method including irradiating a biomass feedstock that has been prepared by reducing one or more dimensions of individual pieces of the biomass feedstock, using an apparatus comprising an accelerator configured

to accelerate particles, such as electrons or ions, wherein the apparatus is capable of processing greater than 1,000 tons of biomass material per year, e.g., greater than 10,000, 25,000, 50,000, 100,000, or even greater than 1,000,000 tons of biomass per year.

5 In a further aspect, the invention features irradiating a biomass feedstock, e.g., with ionizing radiation of electrons or ions, to change a molecular and/or supramolecular structure of the biomass feedstock, cooling the biomass feedstock, and then re-irradiating the biomass feedstock. The two applications of radiation can be the same or different, e.g., the same kind, such as electrons at the same level.

10 The invention also features products formed by these methods, and systems for performing the methods.

Some implementations of these methods include one or more of the following features.

15 The biomass feedstock can be cooled to an extent that after cooling the biomass is at a temperature below its initial temperature prior to irradiation. Cooling of the biomass can include contacting the biomass with a fluid at a temperature below the initial temperature of the biomass or below the temperature of the biomass after irradiation.

20 Each irradiation of the biomass feedstock can be performed as the biomass feedstock is being pneumatically conveyed in a fluid. Radiation can be applied as the biomass feedstock falls under the influence of gravity. For example, the biomass can be conveyed from a first belt at a first height and captured by a second belt at a second level, lower than the first level, the trailing edge of the first belt and the leading edge of the second belt defining a gap, and ionizing radiation can be applied to the biomass feedstock in the defined gap. During irradiation the biomass can be conveyed past a particle gun and through a beam of charged particles. The biomass feedstock may have a bulk density
25 of less than about 0.25 g/cm^3 in a region under and/or above the beam.

30 In another aspect, the invention features methods of changing a molecular structure and/or a supramolecular structure of a starchy material or of a low molecular weight sugar, such as sucrose, in a biomass feedstock comprising at least about 10 percent by weight of the low molecular weight sugar. The methods include processing a treated biomass feedstock to produce a product, the treated biomass feedstock having been prepared by pretreating a biomass feedstock using a pretreatment method that

changes the molecular structure and/or supramolecular structure of the starchy material or of the low molecular weight sugar portion, selected from radiation, sonication, pyrolysis, and oxidation.

5 In another aspect, the invention features methods of treating a biomass feedstock including a starchy material to change the molecular structure and/or supramolecular structure of the starchy material, with at least one method selected from the group consisting of radiation, sonication, pyrolysis, and oxidation.

Any of the above aspects of the invention can, in some implementations, include one or more of the following features.

10 The method can further include treating the biomass feedstock with one or more other pretreatment methods, wherein the other pretreatment methods are selected from sonication, pyrolysis, and oxidation.

Radiation can be in the form of an electron beam, which can be applied, for example, at a total dosage of between about 10 MRad and about 50 MRad. The radiation
15 can be ionizing radiation.

Processing can include making a combustible fuel. In some cases, processing includes converting the irradiated material utilizing a microorganism having the ability to convert at least about 1 percent by weight of the biomass to the fuel.

In some implementations, processing comprises fermenting the feedstock,
20 aerobically or anaerobically, to produce a product such as a fuel, e.g., ethanol. For example, processing may comprise contacting the feedstock with a microorganism having the ability to convert at least a portion, e.g., at least about 1 percent by weight, of the feedstock to the product. The microorganism can be a natural microorganism or an engineered microorganism. For example, the microorganism can be a bacterium, e.g., a
25 cellulolytic bacterium, a fungus, e.g., a yeast, a plant or a protist, e.g., an algae, a protozoa or a fungus-like protist, e.g., a slime mold. When the organisms are compatible, mixtures may be utilized.

The product can include one or more of hydrogen, organic acids, proteins, hydrocarbons, and alcohols, e.g., ethanol, n-propanol, isopropanol, n-butanol, and
30 mixtures thereof. Other examples of products that may be produced by the methods disclosed herein include mono- and polyfunctional C1-C6 alkyl alcohols, mono- and

poly-functional carboxylic acids, C1-C6 hydrocarbons, and combinations thereof. Other examples of alcohols include methanol, ethylene glycol, propylene glycol, 1,4-butane diol, glycerin, and combinations thereof. Carboxylic acids include formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, palmitic acid, stearic acid, oxalic acid, malonic acid, succinic acid, glutaric acid, oleic acid, linoleic acid, glycolic acid, lactic acid, γ -hydroxybutyric acid, and combinations thereof. Hydrocarbons include methane, ethane, propane, pentane, n-hexane, and combinations thereof. Many of these products may be used as fuels.

The method can further include preparing the biomass feedstock by reducing one or more dimensions of individual pieces of the biomass feedstock.

In some cases, the biomass feedstock has internal fibers, and the biomass feedstock has been sheared to an extent that its internal fibers are substantially exposed. The biomass feedstock can in some cases include or be made up of discrete fibers and/or particles having a maximum dimension of not more than about 0.5 mm.

The biomass feedstock can be prepared and then pretreated, or pretreated and then prepared. The pretreatment method can be selected from, e.g., radiation, such as radiation from a beam of electrons or ions, sonication, pyrolysis, and oxidation. In some embodiments, at least one of the pretreatment methods, e.g., radiation, is performed on the biomass feedstock while the biomass feedstock is exposed to air, nitrogen, oxygen, helium, or argon. In some embodiments, pretreatment can include pretreating the biomass feedstock with steam explosion.

In some embodiments, the biomass is prepared by reducing one or more dimensions of individual pieces of biomass includes shearing, wet or dry grinding, cutting, squeezing, compressing or mixtures of any of these processes. For example, shearing can be performed with a rotary knife cutter. The shearing can produce fibers having an average length-to-diameter ratio of greater than 5/1. In some embodiments, the prepared biomass can have a BET surface area of greater than 0.25 m²/g. The biomass can be sheared to an extent that internal fibers of the biomass are substantially exposed. The biomass can be sheared to an extent that it has a bulk density of less than about 0.35 g/cm³.

In some embodiments, two or more pretreatment methods can be applied to the biomass feedstock, for example radiation and sonication, radiation and oxidation, radiation and pyrolyzation, sonication and oxidation, sonication and pyrolyzation, or oxidation and pyrolyzation. The two or more processes can be performed in any order or
5 at or about the same time.

In some embodiments, the change in molecular structure and/or change in supramolecular structure of the biomass, e.g., the cellulosic or lignocellulosic material or low molecular weight sugar or starchy material, can include a change in any one or more of an average molecular weight, average crystallinity, surface area, degree of
10 polymerization, porosity, branching, grafting, domain size or number, a change in kind or number of chemical functional groups, and a change in formula weight. For example, the change in molecular structure and/or supramolecular structure can include a decrease in either one or both of an average molecular weight and average crystallinity or an increase in either one or both of surface area and porosity.

15 In some instances, functionalized biomass (biomass in which the number and/or kind of functional groups has been changed) is more soluble and more readily utilized by microorganisms in comparison to un-functionalized biomass. In addition, many of the functionalized materials described herein are less prone to oxidation and can have enhanced long-term stability under ambient conditions.

20 In some embodiments, at least one pretreatment method can be performed on biomass in which less than about 25 percent by weight of the biomass is in a swollen state, the swollen state being characterized as having a volume of more than about 2.5 percent higher than an unswollen state. In other embodiments, the biomass is mixed with or includes a swelling agent. For example, in any method described herein, the biomass
25 can be mixed with or and include a swelling agent, and the biomass can receive a dose of less than about 10 Mrad of radiation.

The pretreated biomass material can further include, optionally, a buffer, such as sodium bicarbonate or ammonium chloride, an electrolyte, such as potassium chloride or sodium chloride, a growth factor, such as biotin, and/or a base pair such as uracil, a
30 surfactant, a mineral, or a chelating agent.

In some cases, pretreatment is performed while the biomass feedstock is exposed to air, nitrogen, oxygen, helium or argon. Pretreatment may be performed under pressure, e.g., under a pressure of greater than about 2.5 atmospheres. The methods described herein may further include oxidizing the biomass prior to pretreatment.

5 The biomass feedstock may include, for example, paper, paper products, paper waste, wood, particle board, sawdust, agricultural waste, sewage, silage, grasses, rice hulls, bagasse, cotton, jute, hemp, flax, bamboo, sisal, abaca, straw, corn cobs, corn stover, switchgrass, alfalfa, hay, rice hulls, coconut hair, cotton, synthetic celluloses, seaweed, algae, and mixtures thereof. The biomass may in some cases include a
10 synthetic material.

 The biomass can in some cases include a carbohydrate that includes one or more β -1,4-linkages and has a number average molecular weight between about 3,000 and 50,000.

 In some implementations, the biomass material includes a starch, e.g., corn starch,
15 wheat starch, potato starch or rice starch, a derivative of starch, or a material that includes starch, such as an edible food product or a crop. For example the starchy material can be arracacha, buckwheat, banana, barley, cassava, kudzu, oca, sago, sorghum, regular household potatoes, sweet potato, taro, yams, or one or more beans, such as fava beans, lentils, or peas.

20 In other implementations, the biomass material is or includes a low molecular weight sugar. For example, the biomass materials can include at least about 0.5 percent by weight of a low molecular weight sugar, e.g., at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 12.5, 25, 35, 50, 60, 70, 80, 90 or even at least about 95 percent by weight of the low molecular weight sugar. In some instances, the biomass is composed substantially of the
25 low molecular weight sugar, e.g., greater than 95 percent by weight, such as 96, 97, 98, 99 or substantially 100 percent by weight of the low molecular weight sugar. Biomass materials that include low molecular weight sugars can be agricultural products or food products, such as sugarcane and sugar beets, or an extract therefrom, e.g., juice from sugarcane or sugar beets. Specific examples of low molecular weight sugars include
30 cellobiose, lactose, sucrose, glucose and xylose, along with derivatives thereof.

Processing low molecular weight sugars by any of the methods described herein can make the resulting products more soluble and/or easier to utilize by microbes.

In one aspect, a method of converting an intermediate to a product includes treating an irradiated intermediate product with a microorganism, the intermediate having
5 been prepared by irradiating a starchy material and treating the starchy material with an enzyme.

In another aspect, a method of converting an intermediate to a product includes preparing an intermediate by irradiating a starchy material and treating the starchy material with an enzyme, and treating the irradiated intermediate product with a
10 microorganism.

Another aspect includes a product produced by any one of the above methods.

In one aspect, a biomass feedstock processing system includes an irradiating device configured to ionize a biomass feedstock so that the feedstock has a first level of radicals detectable with an electron spin resonance spectrometer; and a quenching device
15 configured to quench the ionized biomass feedstock to an extent that the radicals are at a second level lower than the first level.

In another aspect, a biomass feedstock processing system includes one or more irradiating devices configured to irradiate a biomass feedstock with at least two separate doses of radiation; and a cooling device configured to cool the biomass feedstock
20 between doses of radiation.

In some implementations, a system also includes a biomass feedstock positioned to be ionized by the irradiating device(s).

In any of the methods or systems disclosed herein, radiation may be applied from a device that is in a vault.

25 The term "fibrous material," as used herein, is a material that includes numerous loose, discrete and separable fibers. For example, a fibrous material can be prepared from a bleached Kraft paper fiber source by shearing, e.g., with a rotary knife cutter.

The term "screen," as used herein, means a member capable of sieving material according to size. Examples of screens include a perforated plate, cylinder or the like, or
30 a wire mesh or cloth fabric.

The term “pyrolysis,” as used herein, means to break bonds in a material by the application of heat energy. Pyrolysis can occur while the subject material is under vacuum, or immersed in a gaseous material, such as an oxidizing gas, e.g., air or oxygen, or a reducing gas, such as hydrogen.

5 Oxygen content is measured by elemental analysis by pyrolyzing a sample in a furnace operating at 1300 °C or above.

 The terms “biomass” refers to any non-fossilized, i.e., renewable, organic matter. The various types of biomass include plant biomass (defined below), microbial biomass, animal biomass (any animal by-product, animal waste, etc.) and municipal waste biomass
10 (residential and light commercial refuse with recyclables such as metal and glass removed).

 The term “plant biomass” and “lignocellulosic biomass” refer to virtually any plant-derived organic matter (woody or non-woody). Plant biomass can include, but is not limited to, agricultural or food crops (e.g., sugarcane, sugar beets or corn kernels) or
15 an extract therefrom (e.g., sugar from sugarcane and corn starch from corn), agricultural crop wastes and residues such as corn stover, wheat straw, rice straw, sugar cane bagasse, and the like. Plant biomass further includes, but is not limited to, trees, woody energy crops, wood wastes and residues such as softwood forest thinnings, barky wastes, sawdust, paper and pulp industry waste streams, wood fiber, and the like. Additionally,
20 grass crops, such as switchgrass and the like have potential to be produced on a large-scale as another plant biomass source. For urban areas, the best potential plant biomass feedstock includes yard waste (e.g., grass clippings, leaves, tree clippings, and brush) and vegetable processing waste.

 “Lignocellulosic feedstock,” is any type of plant biomass such as, but not limited
25 to, non-woody plant biomass, cultivated crops, such as, but not limited to, grasses, for example, but not limited to, C4 grasses, such as switchgrass, cord grass, rye grass, miscanthus, reed canary grass, or a combination thereof, or sugar processing residues such as bagasse, or beet pulp, agricultural residues, for example, soybean stover, corn stover, rice straw, rice hulls, barley straw, corn cobs, wheat straw, canola straw, rice
30 straw, oat straw, oat hulls, corn fiber, recycled wood pulp fiber, sawdust, hardwood, for example aspen wood and sawdust, softwood, or a combination thereof. Further, the

lignocellulosic feedstock may include cellulosic waste material such as, but not limited to, newsprint, cardboard, sawdust, and the like.

Lignocellulosic feedstock may include one species of fiber or alternatively, lignocellulosic feedstock may include a mixture of fibers that originate from different lignocellulosic feedstocks. Furthermore, the lignocellulosic feedstock may comprise fresh lignocellulosic feedstock, partially dried lignocellulosic feedstock, fully dried lignocellulosic feedstock or a combination thereof.

For the purposes of this disclosure, carbohydrates are materials that are composed entirely of one or more saccharide units or that include one or more saccharide units. The saccharide units can be functionalized about the ring with one or more functional groups, such as carboxylic acid groups, amino groups, nitro groups, nitroso groups or nitrile groups and still be considered carbohydrates. Carbohydrates can be polymeric (e.g., equal to or greater than 10-mer, 100-mer, 1,000-mer, 10,000-mer, or 100,000-mer), oligomeric (e.g., equal to or greater than a 4-mer, 5-mer, 6-mer, 7-mer, 8-mer, 9-mer or 10-mer), trimeric, dimeric, or monomeric. When the carbohydrates are formed of more than a single repeat unit, each repeat unit can be the same or different.

Examples of polymeric carbohydrates include cellulose, xylan, pectin, and starch, while cellobiose and lactose are examples of dimeric carbohydrates. Examples of monomeric carbohydrates include glucose and xylose.

Carbohydrates can be part of a supramolecular structure, e.g., covalently bonded into the structure. Examples of such materials include lignocellulosic materials, such as those found in wood.

A starchy material is one that is or includes significant amounts of starch or a starch derivative, such as greater than about 5 percent by weight starch or starch derivative. For purposes of this disclosure, a starch is a material that is or includes an amylose, an amylopectin, or a physical and/or chemical mixture thereof, e.g., a 20:80 or 30:70 percent by weight mixture of amylose to amylopectin. For example, rice, corn, and mixtures thereof are starchy materials. Starch derivatives include, e.g., maltodextrin, acid-modified starch, base-modified starch, bleached starch, oxidized starch, acetylated starch, acetylated and oxidized starch, phosphate-modified starch, genetically-modified starch and starch that is resistant to digestion.

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For purposes of this disclosure, a low molecular weight sugar is a carbohydrate or a derivative thereof that has a formula weight (excluding moisture) that is less than about 2,000, e.g., less than about 1,800, 1,600, less than about 1,000, less than about 500, less than about 350 or less than about 250. For example, the low molecular weight sugar can be a monosaccharide, e.g., glucose or xylose, a disaccharide, e.g., cellobiose or sucrose, or a trisaccharide.

A combustible fuel is a material capable of burning in the presence of oxygen. Examples of combustible fuels include ethanol, n-propanol, n-butanol, hydrogen and mixtures of any two or more of these.

Swelling agents as used herein are materials that cause a discernable swelling, e.g., a 2.5 percent increase in volume over an unswollen state of cellulosic and/or lignocellulosic materials, when applied to such materials as a solution, e.g., a water solution. Examples include alkaline substances, such as sodium hydroxide, potassium hydroxide, lithium hydroxide and ammonium hydroxides, acidifying agents, such as mineral acids (e.g., sulfuric acid, hydrochloric acid and phosphoric acid), salts, such as zinc chloride, calcium carbonate, sodium carbonate, benzyltrimethylammonium sulfate, and basic organic amines, such as ethylene diamine.

A "sheared material," as used herein, is a material that includes discrete fibers in which at least about 50% of the discrete fibers have a length/diameter (L/D) ratio of at least about 5, and that has an uncompressed bulk density of less than about 0.6 g/cm³. A sheared material is thus different from a material that has been cut, chopped or ground.

Changing a molecular structure of a biomass feedstock, as used herein, means to change the chemical bonding arrangement, such as the type and quantity of functional groups, or conformation of the structure. For example, the change in the molecular structure can include changing the supramolecular structure of the material, oxidation of the material, changing an average molecular weight, changing an average crystallinity, changing a surface area, changing a degree of polymerization, changing a porosity, changing a degree of branching, grafting on other materials, changing a crystalline domain size, or an changing an overall domain size.

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Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable
5 methods and materials are described below. All publications, Appendices, patent applications, patents, and other references mentioned herein or attached hereto are incorporated by reference in their entirety for all that they contain. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

10 Other features and advantages of the invention will be apparent from the following detailed description, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1 is a block diagram illustrating conversion of biomass into products and co-
15 products.

FIG. 2 is block diagram illustrating conversion of a fiber source into a first and second fibrous material.

FIG. 3 is a cross-sectional view of a rotary knife cutter.

FIG. 4 is block diagram illustrating conversion of a fiber source into a first,
20 second and third fibrous material.

FIG. 5 is block diagram illustrating densification of a material.

FIG. 6 is a perspective view of a pellet mill.

FIG. 7A is a densified fibrous material in pellet form.

FIG. 7B is a transverse cross-section of a hollow pellet in which a center of the hollow is in-line with a center of the pellet.

5 FIG. 7C is a transverse cross-section of a hollow pellet in which a center of the hollow is out of line with the center of the pellet.

FIG. 7D is a transverse cross-section of a tri-lobal pellet.

FIG. 8 is a block diagram illustrating a treatment sequence for processing feedstock.

10 FIG. 9 is a perspective, cut-away view of a gamma irradiator housed in a concrete vault.

FIG. 10 is an enlarged perspective view of region R of FIG. 9.

FIG. 11 is a block diagram illustrating an electron beam irradiation feedstock pretreatment sequence.

15 FIG. 11A is a schematic representation of biomass being ionized, and then oxidized or quenched.

FIG. 11B is a schematic side view of a system for irradiating a low bulk density material, while FIG. 11C is cross-sectional of the system taken along 11C-11C.

20 FIG. 11D is a schematic cross-sectional view of a fluidized bed system for irradiating a low bulk density material.

FIG. 11E is a schematic side-view of another system for irradiating a low bulk density material.

FIG. 12 is a schematic view of a system for sonicating a process stream of cellulosic material in a liquid medium.

25 FIG. 13 is a schematic view of a sonicator having two transducers coupled to a single horn.

FIG. 14 is a block diagram illustrating a pyrolytic feedstock pretreatment system.

FIG. 15 is a cross-sectional side view of a pyrolysis chamber.

FIG. 16 is a cross-sectional side view of a pyrolysis chamber.

30 FIG. 17 is a cross-sectional side view of a pyrolyzer that includes a heated filament.

FIG. 18 is a schematic cross-sectional side view of a Curie-Point pyrolyzer.

FIG. 19 is a schematic cross-sectional side view of a furnace pyrolyzer.

FIG. 20 is a schematic cross-sectional top view of a laser pyrolysis apparatus.

FIG. 21 is a schematic cross-sectional top view of a tungsten filament flash
5 pyrolyzer.

FIG. 22 is a block diagram illustrating an oxidative feedstock pretreatment system.

FIG. 23 is block diagram illustrating a general overview of the process of converting a fiber source into a product, e.g., ethanol.

10 FIG. 24 is a cross-sectional view of a steam explosion apparatus.

FIG. 25 is a schematic cross-sectional side view of a hybrid electron beam/sonication device.

FIG. 26 is a block diagram illustrating a dry milling process for corn kernels.

FIG. 27 is a block diagram illustrating a wet milling process for corn kernels.

15 FIG. 28 is a scanning electron micrograph of a fibrous material produced from polycoated paper at 25 X magnification. The fibrous material was produced on a rotary knife cutter utilizing a screen with 1/8 inch openings.

FIG. 29 is a scanning electron micrograph of a fibrous material produced from bleached Kraft board paper at 25 X magnification. The fibrous material was produced on
20 a rotary knife cutter utilizing a screen with 1/8 inch openings.

FIG. 30 is a scanning electron micrograph of a fibrous material produced from bleached Kraft board paper at 25 X magnification. The fibrous material was twice sheared on a rotary knife cutter utilizing a screen with 1/16 inch openings during each shearing.

25 FIG. 31 is a scanning electron micrograph of a fibrous material produced from bleached Kraft board paper at 25 X magnification. The fibrous material was thrice sheared on a rotary knife cutter. During the first shearing, a 1/8 inch screen was used; during the second shearing, a 1/16 inch screen was used, and during the third shearing a 1/32 inch screen was used.

30 FIG. 32 is a schematic side view of a sonication apparatus, while FIG. 33 is a cross-sectional view through the processing cell of FIG. 32.

FIG. 34 is a scanning electron micrograph at 1000 X magnification of a fibrous material produced from shearing switchgrass on a rotary knife cutter, and then passing the sheared material through a 1/32 inch screen.

FIGS. 35 and 36 are scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 10 Mrad and 100 Mrad gamma rays, respectively, at 1000 X magnification.

FIG. 37 is a scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 10 Mrad and sonication at 1000 X magnification.

FIG. 38 is a scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 100 Mrad and sonication at 1000 X magnification.

FIG. 39 is an infrared spectrum of Kraft board paper sheared on a rotary knife cutter.

FIG. 40 is an infrared spectrum of the Kraft paper of FIG. 39 after irradiation with 100 Mrad of gamma radiation.

FIG. 41 is a schematic view of a process for biomass conversion.

FIG. 42 is schematic view of another process for biomass conversion.

DETAILED DESCRIPTION

Systems and processes are described herein that can use various biomass materials, such as cellulosic materials, lignocellulosic materials, starchy materials or materials that are or that include low molecular weight sugars, as feedstock materials. Such materials are often readily available, but can be difficult to process, e.g., by fermentation, or can gives sub-optimal yields at a slow rate. In some cases, the difficulty in processing stems at least in part from the recalcitrance of the feedstock. Processing steps are described herein that can reduce this recalcitrance and thereby facilitate conversion of the biomass feedstock to a desired product.

In the processes described herein, feedstock materials are first physically prepared for processing, often by size reduction of raw feedstock materials. Physically prepared feedstock can then be pretreated or processed using one or more of radiation (which may in some cases be under controlled thermal conditions), sonication, oxidation, pyrolysis, and steam explosion. The various pretreatment systems and methods can be used in

combinations of two, three, or even four of these technologies. Other techniques which may be used to enhance the processing of the feedstock are described herein, for example cooling the feedstock between irradiating steps and quenching the biomass feedstock after irradiation.

5 Functionalized materials are also disclosed herein, having desired types and amounts of functionality, such as carboxylic acid groups, enol groups, aldehyde groups, ketone groups, nitrile groups, nitro groups, or nitroso groups, which can be prepared using the methods described herein. Such functionalized materials can be, e.g., more soluble, easier to utilize by various microorganisms or can be more stable over the long
10 term, e.g., less prone to oxidation.

 In some cases, the feedstock can include low molecular weight sugars or starchy materials, as will be discussed in detail herein.

TYPES OF BIOMASS

 Generally, any biomass material that is or includes carbohydrates composed
15 entirely of one or more saccharide units or that include one or more saccharide units can be processed by any of the methods described herein. For example, the biomass material can be cellulosic or lignocellulosic materials, starchy materials, such as kernels of corn, grains of rice or other foods, or materials that are or that include one or more low
 molecular weight sugars, such as sucrose or cellobiose.

20 For example, such materials can include paper, paper products, wood, wood-related materials, particle board, grasses, rice hulls, bagasse, cotton, jute, hemp, flax, bamboo, sisal, abaca, straw, corn cobs, rice hulls, coconut hair, algae, seaweed, cotton, synthetic celluloses, or mixtures of any of these. Suitable materials include those listed in the Summary section, above.

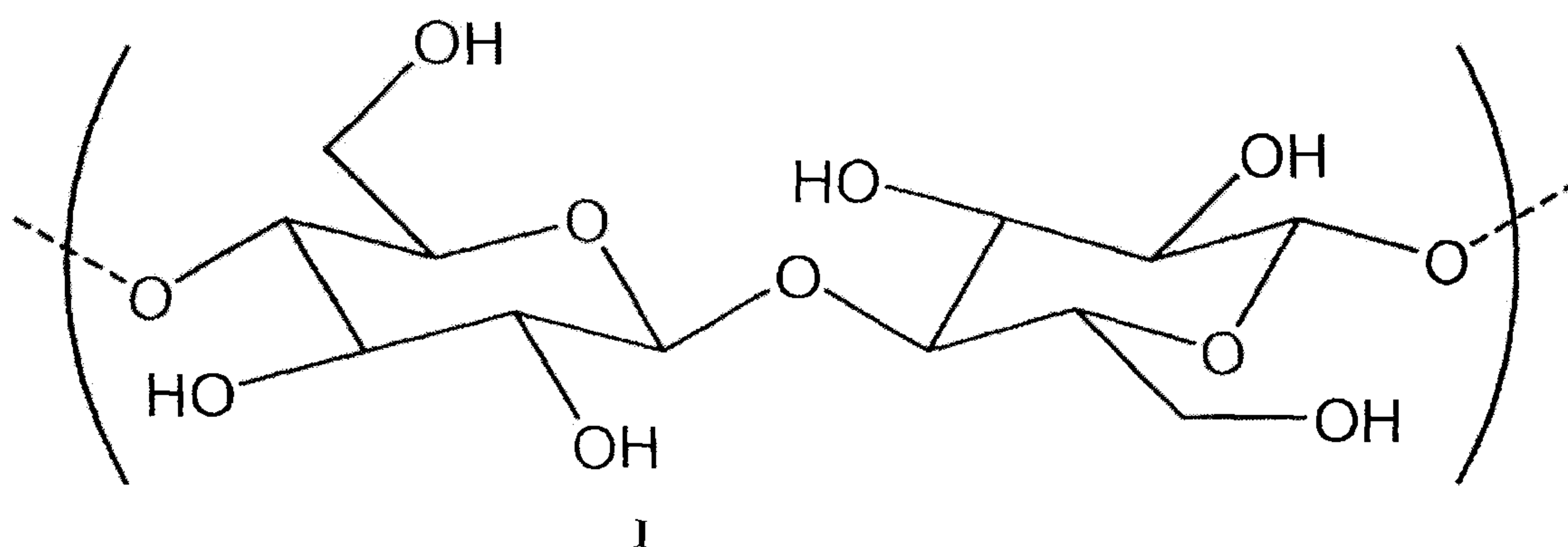
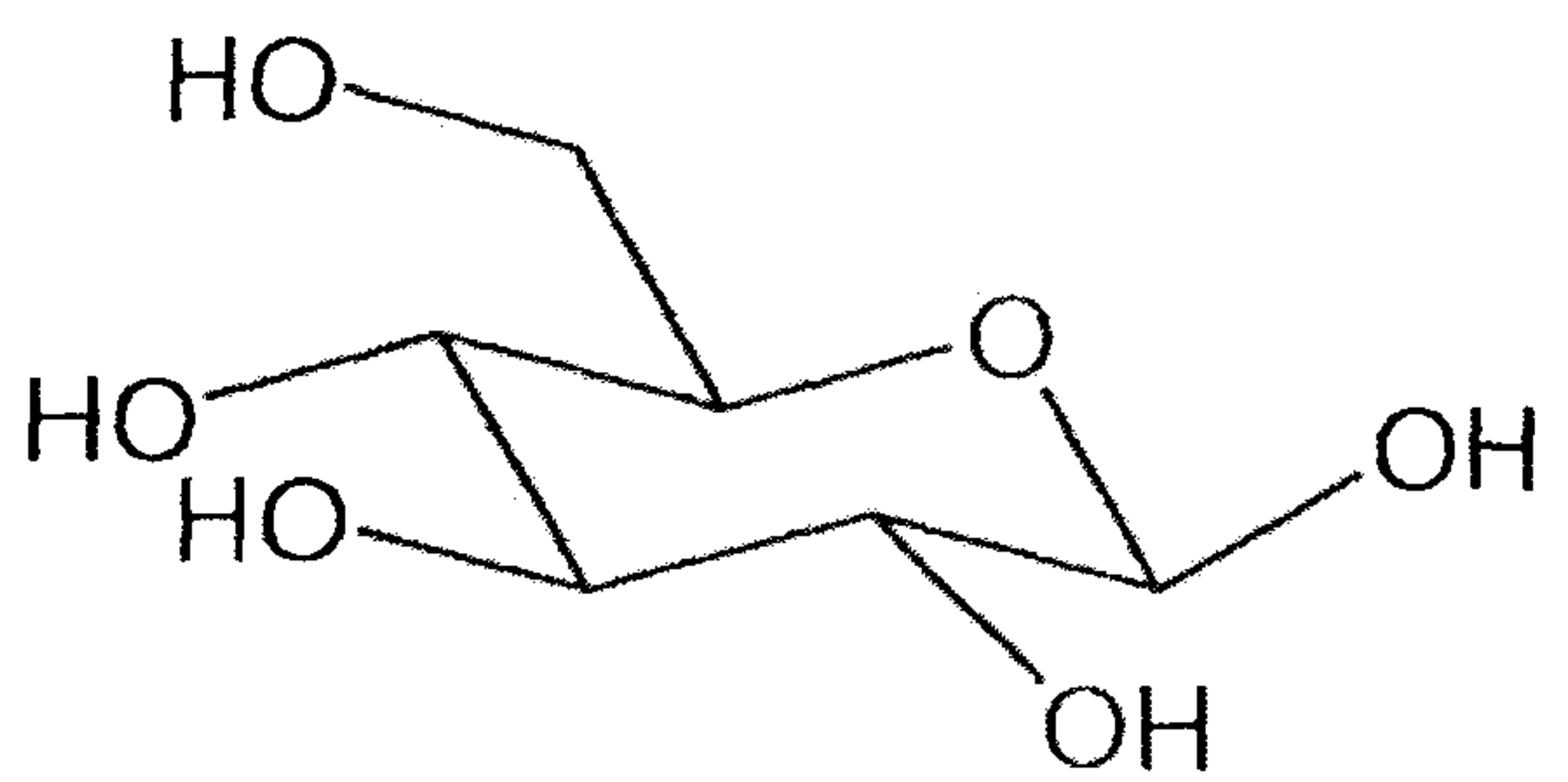
25 Fiber sources include cellulosic fiber sources, including paper and paper products (e.g., polycoated paper and Kraft paper), and lignocellulosic fiber sources, including wood, and wood-related materials, e.g., particle board. Other suitable fiber sources include natural fiber sources, e.g., grasses, rice hulls, bagasse, cotton, jute, hemp, flax, bamboo, sisal, abaca, straw, corn cobs, rice hulls, coconut hair; fiber sources high in α -
30 cellulose content, e.g., cotton; and synthetic fiber sources, e.g., extruded yarn (oriented

yarn or un-oriented yarn). Natural or synthetic fiber sources can be obtained from virgin scrap textile materials, e.g., remnants or they can be post consumer waste, e.g., rags. When paper products are used as fiber sources, they can be virgin materials, e.g., scrap virgin materials, or they can be post-consumer waste. Aside from virgin raw materials, post-consumer, industrial (e.g., offal), and processing waste (e.g., effluent from paper processing) can also be used as fiber sources. Also, the fiber source can be obtained or derived from human (e.g., sewage), animal or plant wastes. Additional fiber sources have been described in U.S. Patent Nos. 6,448,307, 6,258,876, 6,207,729, 5,973,035 and 5,952,105.

Microbial biomass includes biomass derived from naturally occurring or genetically modified unicellular organisms and/or multicellular organisms, e.g., organisms from the ocean, lakes, bodies of water, e.g., salt water or fresh water, or on land, and that contains a source of carbohydrate (e.g., cellulose). Microbial biomass can include, but is not limited to, for example protists (e.g., animal (e.g., protozoa such as flagellates, amoeboids, ciliates, and sporozoa) and plant (e.g., algae such as alveolates, chlorarachniophytes, cryptomonads, euglenids, glaucophytes, haptophytes, red algae, stramenopiles, and viridiaeplantae)), seaweed, plankton (e.g., macroplankton, mesoplankton, microplankton, nanoplankton, picoplankton, and femtoplankton), phytoplankton, bacteria (e.g., gram positive bacteria, gram negative bacteria, and extremophiles), yeast and/or mixtures of these. In some instances, microbial biomass can be obtained from natural sources, e.g., the ocean, lakes, bodies of water, e.g., salt water or fresh water, or on land. Alternatively or in addition, microbial biomass can be obtained from culture systems, e.g., large scale dry and wet culture systems.

Animal biomass includes any organic waste material such as animal-derived waste material or excrement or human waste material or excrement (e.g., manure and sewage).

In some embodiments, the carbohydrate is or includes a material having one or more β -1,4-linkages and having a number average molecular weight between about 3,000 and 50,000. Such a carbohydrate is or includes cellulose (I), which is derived from (β -glucose 1) through condensation of $\beta(1\rightarrow4)$ -glycosidic bonds. This linkage contrasts itself with that for $\alpha(1\rightarrow4)$ -glycosidic bonds present in starch and other carbohydrates.



5

Starchy Materials

Starchy materials include starch itself, e.g., corn starch, wheat starch, potato starch or rice starch, a derivative of starch, or a material that includes starch, such as an edible food product or a crop. For example, the starchy material can be arracacha, buckwheat, banana, barley, cassava, kudzu, oca, sago, sorghum, regular household potatoes, sweet potato, taro, yams, or one or more beans, such as favas, lentils or peas. A blend of any two or more starchy materials is also a starchy material. Starch sources include, e.g., wheat, barley, corn and potatoes. In particular embodiments, the starchy material is derived from corn. Various corn starches and derivatives are described in "Corn Starch," Corn Refiners Association (11th Edition, 2006), which is attached hereto as Appendix A.

A starch (e.g., CAS# 9005-25-8 and chemical formula $(C_6H_{10}O_5)_n$) generally comprises a mixture of amylose and amylopectin (usually in 20:80 or 30:70 ratios) and generally exists as a homopolymer of repeating anhydroglucose units joined by an α -

glucosidic on the next starch unit through hemiacetal linkages. Starch molecules typically are made up of 1,4-linkages are referred to as amylose while 1,6-linkages serve as the branching point in branched starch molecules called amylopectin.

5 Granular Structure

Table 1. Granule Size of Various Starches

Starch Species	Granule Size Range (μm) (Coulter Counter)	Average size (μm)
Waxy Rice	2-13	5.5
High Amylose Corn	4-22	9.8
Corn	5-25	14.3
Cassava	3-28	14
Sorghum	3-27	16
Wheat	3-34	6.5, 19.5
Sweet Potato	4-40	18.5
Arrowroot	9-40	23
Sago	15-50	33
Potato	10-70	36
Canna (Aust. Arrowroot)	22-85	53

Plants store starch within specialized organelles called amyloplasts where they are deposited to form granules. These granules are comprised of newly-synthesized starch layered around a hilum nucleus, and vary in diameter from 2 to 130 microns. The size and shape of the granule is characteristic of the plant's origin and serves as a way of identifying the source of a particular starch (Table 1). The structure of the granule of grain is crystalline with the starch molecules orienting in such a way as to form radially oriented crystals giving rise to the phenomenon of birefringence. When a beam of polarized light is directed through a starch granule, the granule is divided by dark lines into four wedge-shaped sections. This cross-hatching or cross is characteristic of spherocrystalline structures.

Amylose

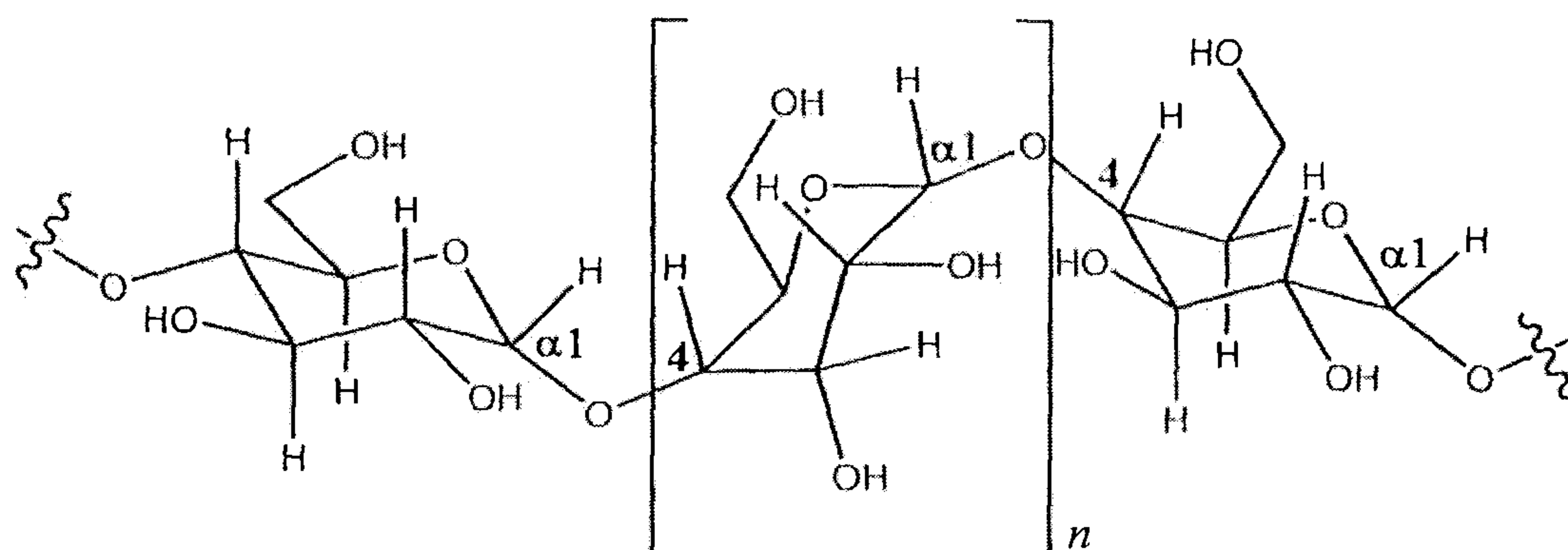


Figure 2. Representative Partial Structure of Amylose

Amylose molecules consist of single mostly-unbranched chains with 500-20,000
 5 α-(1,4)-D-glucose units depending on the source. The α(1,4) bonds promote the
 formation of a helix structure. The structural formula of amylose is pictured in Figure 2
 where the number of repeated glucose subunits (n) can be many thousands (usually in the
 range of 300 to 3000). Amylose starch is less readily digested than amylopectin;
 however, it takes up less space so is preferred for storage in plants. Amylose makes up
 10 about 30% of the stored starch in plants. The digestive enzyme amylase works on the
 ends of the starch molecule, breaking it down into sugars.

Amylose molecules contribute to gel formation because the linear chains can
 orient parallel to each other, moving close enough together to bond. Probably due to the
 ease with which amylose molecules slip past each other in the cooked paste, they do not
 15 contribute significantly to viscosity.

Amylopectin

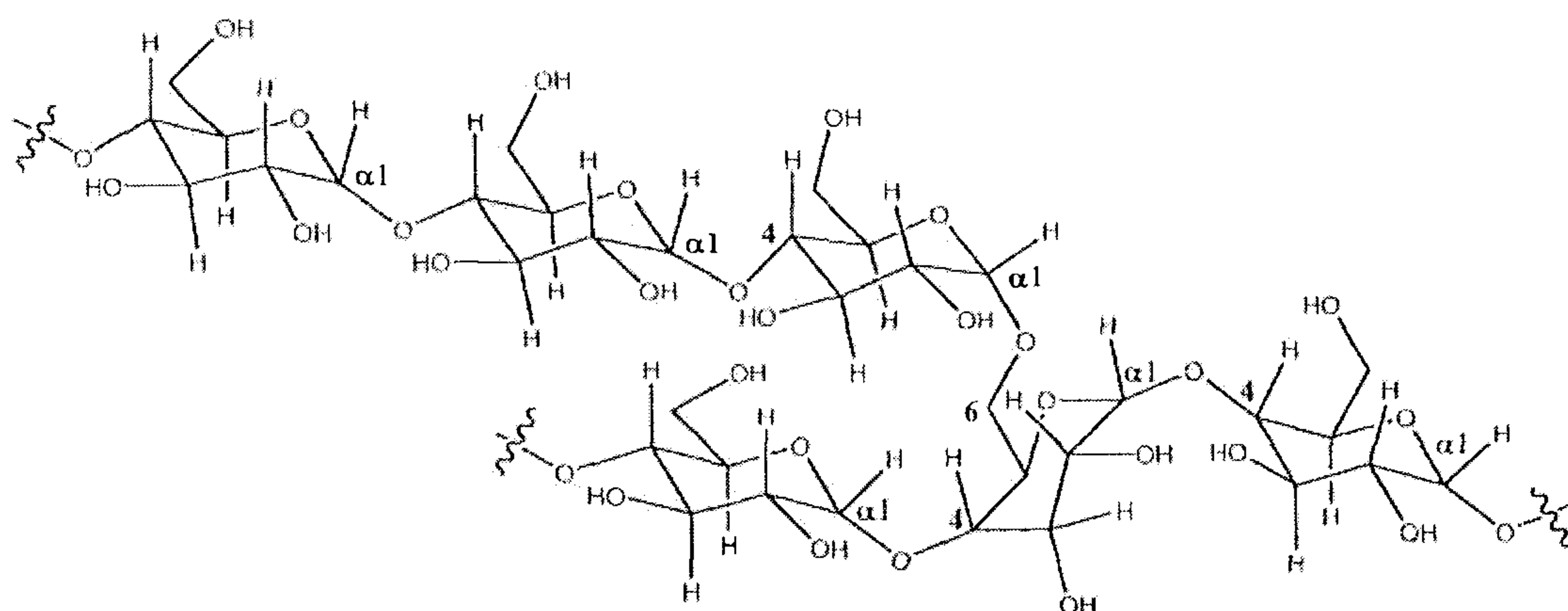


Figure 3. Representative partial structure of amylopectin

Amylopectin is formed by non-random α -(1,6)-branching of the amylose-type α -(1,4)-D-glucose structure. As can be seen in Figure 3, glucose units are linked in a linear way with α (1,4) bonds. Branching takes place with α (1,6) bonds occurring every 24 to 30 glucose units and is determined by branching enzymes. Each amylopectin molecule contains a million or so residues, about 5% of which form the branch points.

The branched amylopectin molecules give viscosity to the cooked paste due to the role it serves in maintaining the swollen granule. Their side chains and bulky shape keep amylopectin molecules from orienting closely enough to hydrogen bond together, so they do not usually contribute to gel formation.

Source

Plants hydrolyze starch releasing the glucose subunits when energy is required. By far the largest source of starch is corn (maize) with other commonly used sources being wheat, potato, tapioca and rice. The relative proportions of amylose to amylopectin and 1,6-linkage branch-points are established genetically and are relatively constant for each species of starch. For example, amylomaizes contain over 50% amylose, whereas “waxy” maize has almost none (~3%).

Unprocessed Starch

Starch that is produced by the corn wet milling process and then dried is referred to as common, regular, or unmodified corn starch. Various forms of corn starch exist

including, fine or coarse powders, flakes, pearls or even larger particles. Unmodified starch can be minimally processed by adjusting the pH, by mild heat treatment, or by adding small quantities of chemicals or adjuvants before or after drying in order to optimize performance. As an example, enzyme conversion of starch to sugars can be accelerated by adjusting the pH of the starch.

By far the most consumed polysaccharide in the human diet is starch. Starch (in particular cornstarch) is used in cooking for thickening foods such as sauces. In industry, it is used in the manufacturing of adhesives, paper, textiles, and as a mold in the manufacture of sweets such as wine gums and jelly beans. Papermaking is the largest non-food application for starches globally, consuming millions of metric tons annually. In a typical sheet of copy paper for example, the starch content may be as high as 8%. Both chemically modified and unmodified starches are used in papermaking.

The chemical composition of starch, highly oxygenated carbon molecules, makes starch an excellent product for use as a chemical feedstock.

Genetically Modified Starch

Genetically modified starch, which refers to starch from genetically engineered plants, has been modified to reduce the need for chemical processing (reducing cost, toxicity, or environmentally hazardous processes), or in order to produce novel carbohydrates which might not naturally occur in the plant species being harvested. The modification in this sense refers to the genetic engineering of the plant DNA, and not the later processing or treatment of the starch or starch granules.

Genetically modified starch is of particular interest in the manufacture of biodegradable polymers and non-cellulose feedstock in the paper industry, as well as the creation of new food additives. For example, waxy maize was studied extensively in the 1950's for its desirable properties. Waxy maize starch, which is essentially 100% amylopectin, yields pastes that are almost clear when cool, non-congealing, and when dried in thin films, yields a translucent, water-soluble coating often used for thickening a wide variety of prepared foods. Genetic modification of this starch to try and increase the amylose content could potentially result in an excellent film former and might be spun into a fiber. Research in this area resulted in the commercial development of two corn

hybrids, one containing about 55%, the other about 70% amylose, and recently research has resulted in developing a starch with 80% amylose.

Modified Starch

5 Modified starch is a food additive which is prepared by treating starch or starch granules, causing the starch to be partially degraded. Modified starch is used as a thickening agent, stabilizer, or an emulsifier. Apart from food products, modified starch is also found in pharmaceuticals. Starches are modified for a number of reasons including, to increase their stability to excessive heat, acid, and freezing; to change their
10 texture; or to lengthen or shorten gelatinization time.

Acid-Modified Starch

 Acid-treated starch, usually simply referred to as "modified starch", is prepared by treating starch or starch granules with inorganic acids. The primary reaction taking place
15 during acid treatment is hydrolysis of glucosidic bonds in starch molecules. Acid modification reduces the chain length of the starch, but does not substantially change the molecular configuration. In this method, a starch-water suspension is agitated while being subjected to mild treatment with dilute mineral acid at temperatures elevated but below the starch gelatinization temperature. Upon achieving the desired viscosity, the
20 acid is neutralized with sodium carbonate and the starch is filtered, washed, and dried.

Oxidized Corn Starch

 Another method for reducing viscosity is oxidation. Although oxidizing agents such as chlorine, hydrogen peroxide and potassium permanganate can be used, oxidized
25 starches produced by the wet milling process are almost always made using sodium hypochlorite as the oxidizing agent. Aqueous starch suspensions under agitation are treated with dilute sodium hypochlorite containing a small excess of sodium hydroxide (NaOH) and heated to 120 °F. When the desired viscosity is achieved, the oxidized starch slurry is treated with a reducing agent such as sodium bisulfite to remove excess
30 hypochlorite, the pH is adjusted, and the starch is filtered, washed and finally dried. Treatment of starch with an oxidizing agent randomly converts hydroxyl groups to

carboxyl or carbonyl groups, which results in the cleavage of the adjacent glucosidic bond. Oxidized starches are used in batters and breading as they adhere quite well to meats.

5 **Dextrins**

Dextrins are a group of low molecular weight carbohydrates produced by the dry heating or roasting of unmodified starch, with or without an acid or alkaline catalyst. Other dextrinization methods utilize a fluid bed, in which unmodified starch is placed in a reactor and suspended or "fluidized" in a stream of heated air. The starch is then
10 acidified and heated until the desired end product is obtained. During dextrinization, the granule is not destroyed but granule integrity is disrupted. When dextrins are suspended in water and heated, the granules swell and separate into layers that eventually break free and disperse. Dextrins are mixtures of linear α -(1,4)-linked D-glucose polymers starting with an α -(1,6) bond. Industrial production is, in general, performed by acidic hydrolysis
15 of potato starch. Dextrins are water-soluble, white to slightly yellow solids that are optically active. Under analysis, dextrins can be detected with iodine solution, giving a red coloration.

There are three major types of dextrins: white, yellow, and British gums. White dextrins have a white color and have reduced viscosities, and cold water solubilities
20 ranging from 5 to over 90%. White dextrins are used to make very soft gels. Yellow dextrins (produced with less acid, higher temperatures, and more time) are yellow in color and have higher water solubility. Yellow dextrins are used for making high solids pastes that are very tacky and, when applied in thin films, dry rapidly. Finally, British gums are produced by adding little or no acid to very dry starch and then roasting while
25 gradually increasing the temperature. They are tan to light brown in color and are used to prepare nearly solid gels through very soft gels to viscous liquids.

Cyclodextrins

Cyclodextrins are non-reducing cyclic glucose oligosaccharides resulting from the cyclomaltodextrin glucanotransferase catalyzed degradation of starch. There are three
30 common cyclodextrins with 6, 7 or 8 D-glucopyranonsyl residues (α -, β -, and γ -

cyclodextrin, respectively) linked by α -1,4 glycosidic bonds (Figure 4). All three cyclodextrins have similar structures (bond lengths and orientations) apart from the structural necessities of accommodating a different number of glucose residues. They present a bottomless bowl-shaped (truncated cone) molecule stiffened by hydrogen
5 bonding between the 3-OH and 2-OH groups around the outer rim. Cyclodextrins are used for encapsulation for controlled flavor release, masking odors and tastes, stabilizing emulsions, increasing foaming power, and controlling or masking color.

Starch Derivatives (Crosslinked and Stabilization)

10 Starch can be chemically derivatized at the primary and secondary hydroxyl positions, which imparts different properties than those found in the parent starch. This is presumably due to disruption of hydrogen bonds. Two types of derivatives are prepared commercially, crosslinked/inhibited and stabilization. Crosslinked starches, sometimes referred to as inhibited starches, are made by reacting hydroxyl groups on two different
15 molecules within a granule with a bifunctional agent. Reagents such as phosphorus oxychloride or sodium trimetaphosphate may be used as crosslinking agents. Very small amounts of these agents can exert a marked effect on the behavior of the cooked starch.

Starch can be stabilized against gelling using monofunctional reagents. These reagents react with hydroxyl groups on the starch to introduce substituent groups that
20 interfere with hydrogen bonding effects thereby increasing their water combining capacity or viscosity, or imparting a positive charge to the starch molecule. Reagents used in the stabilization of starch through disruption of hydrogen bonding include, ethylene oxide to produce hydroxyethyl starch, acetic anhydride to produce starch acetates, succinic anhydride to produce starch succinates, monosodium orthophosphate or
25 sodium tripolyphosphate to produce starch phosphates, and propylene oxide to produce hydroxypropyl starches. Reagents that impart a positive charge to the starch molecule include tertiary or quaternary amines to produce cationic starches.

Pregelatinized Starch

30 Suspensions of many starches and starch derivatives can be gelatinized and dried to yield a broad variety of pregelatinized starches. This is done on a single drum dryer

with applicator rolls. The starch slurry is heated to gelatinize it, instantaneously dried and ground to desired granulation requirement. Pregelatinized starch is used to thicken instant desserts such as puddings, allowing the food to thicken with the addition of cold water or milk. Similarly, cheese sauce granules (such as in Macaroni and Cheese or lasagna) or gravy granules may be thickened with boiling water without the product going lumpy. Commercial pizza toppings containing modified starch will thicken when heated in the oven, keeping them on top of the pizza, and then become runny when cooled.

10 **Bleached Starches**

Bleaching by very light oxidation is carried out using sodium hypochlorite, sodium chlorite, hydrogen peroxide, potassium permanganate, peracetic acid, or ammonium persulfate with sulfur dioxide. Interaction with the starch molecules must be very small since no change occurs in the physical properties of the starch or its solution except in its color. Theoretically, there will be production of a few aldehyde or carboxyl groups. Only trace amounts of sodium chloride, sodium sulfate or sodium acetate remain in the final product. The bleached starch is recovered on continuous filters or centrifuges using copious amounts of water to remove trace amounts of inorganic salts formed from the bleaching agent, dried and packaged.

20

Low Molecular Weight Sugars

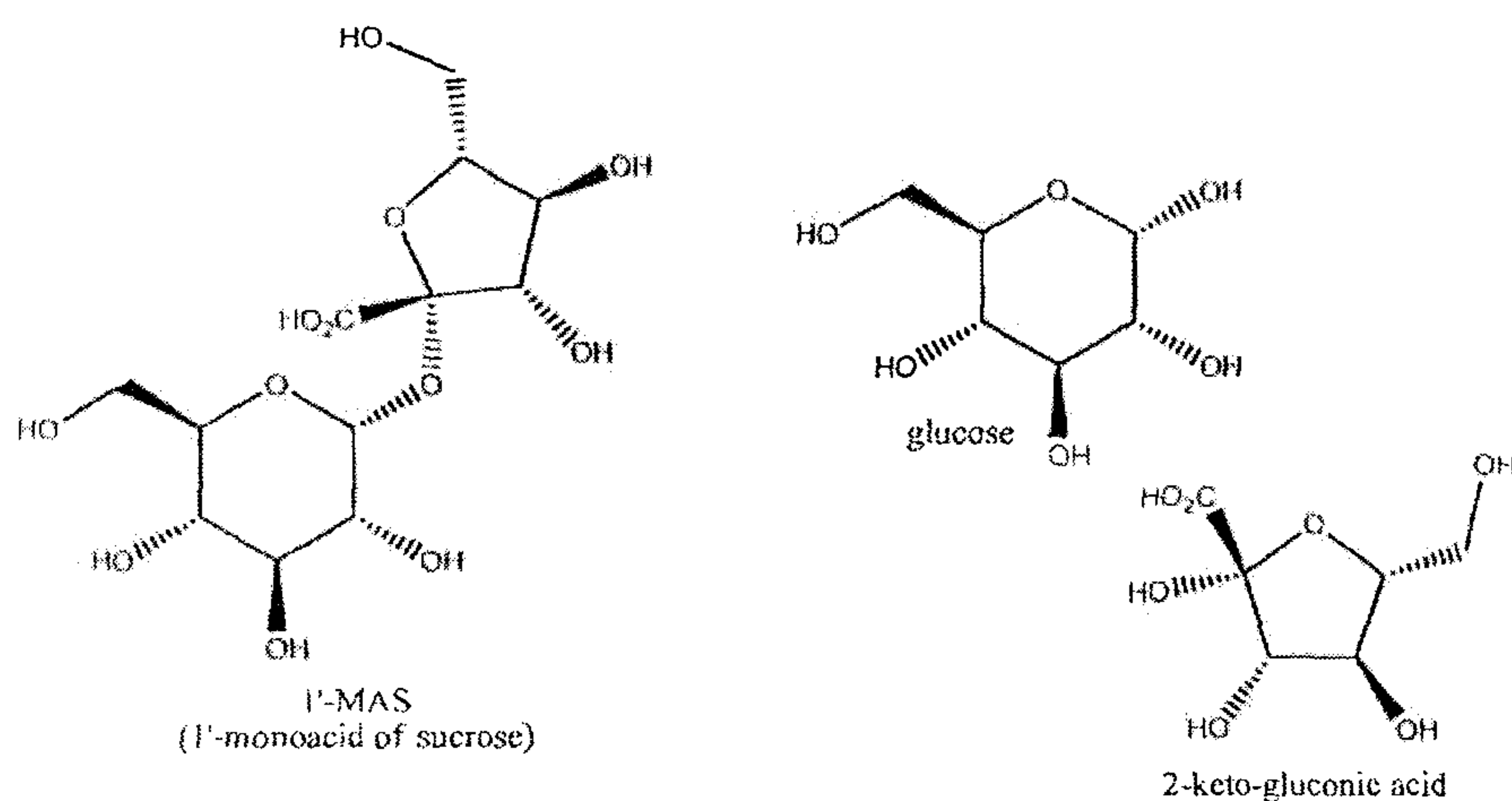
Biomass materials that include low molecular weight sugars can, e.g., include at least about 0.5 percent by weight of the low molecular sugar, e.g., at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 12.5, 25, 35, 50, 60, 70, 80, 90 or even at least about 95 percent by weight of the low molecular weight sugar. In some instances, the biomass is composed substantially of the low molecular weight sugar, e.g., greater than 95 percent by weight, such as 96, 97, 98, 99 or substantially 100 percent by weight of the low molecular weight sugar.

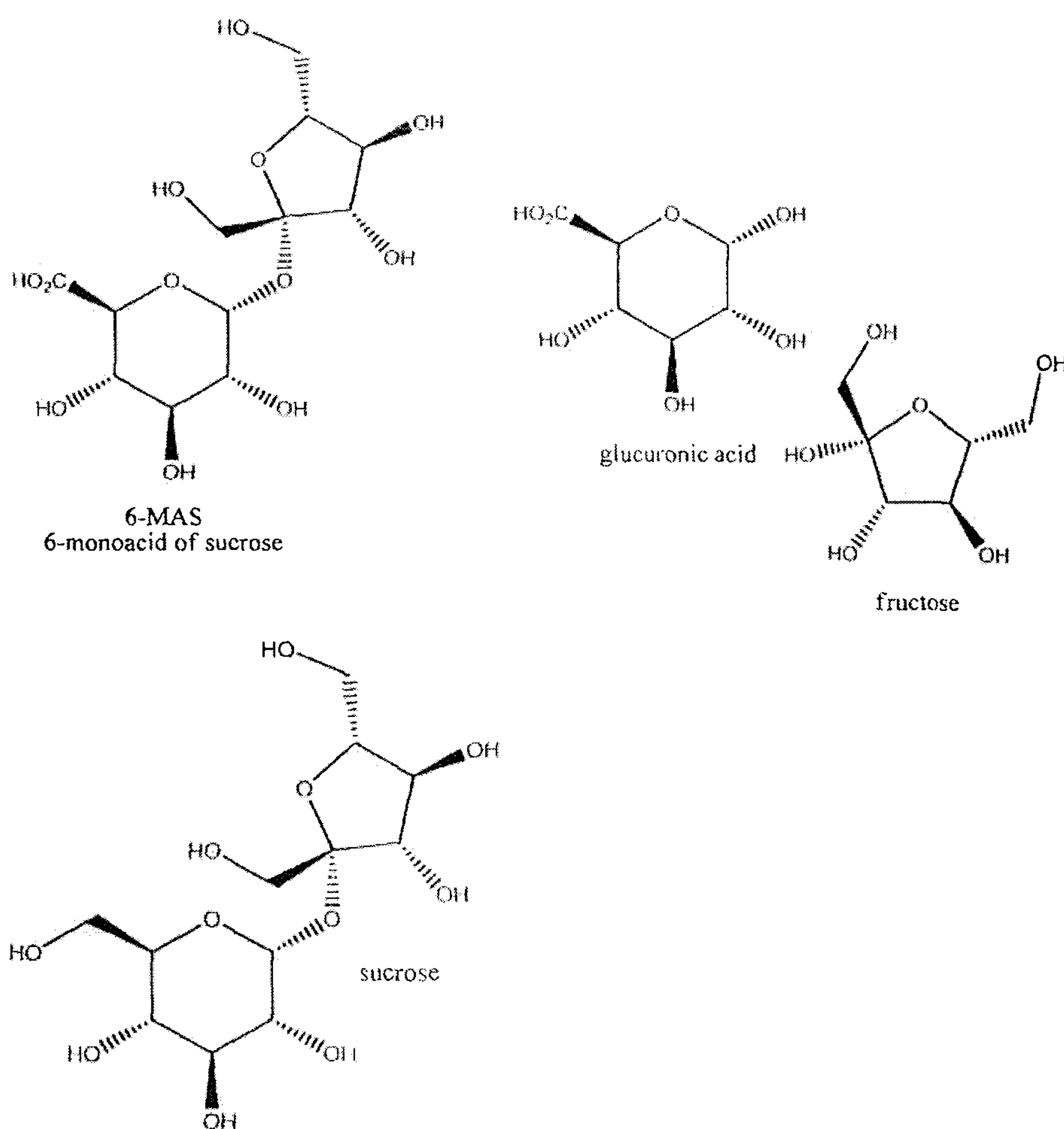
Biomass materials that include low molecular weight sugars can be agricultural products or food products, such as sugarcane and sugar beets or an extract therefrom, e.g., juice from sugarcane, or juice from sugar beets. Biomass materials that include low

30

molecular weight sugars can be substantially pure extracts, such as raw or crystallized table sugar (sucrose). Low molecular weight sugars include sugar derivatives. For example, the low molecular weight sugars can be oligomeric (e.g., equal to or greater than a 4-mer, 5-mer, 6-mer, 7-mer, 8-mer, 9-mer or 10-mer), trimeric, dimeric, or
 5 monomeric. When the carbohydrates are formed of more than a single repeat unit, each repeat unit can be the same or different.

Specific examples of low molecular weight sugars include cellobiose, lactose, sucrose, glucose and xylose, along with derivatives thereof. In some instances, sugar derivatives are more rapidly dissolved in solution or utilized by microbes to provide a
 10 useful material, such as ethanol or butanol. Several such sugars and sugar derivatives are shown below.





5 Ethanol from Low Molecular Weight Sugars

More than half of world ethanol production is produced from sugar and sugar byproducts, with Brazil being by far the world leader. Currently, there is no commercial production of ethanol from sugarcane or sugar beets in the United States, where 97 percent of ethanol is produced from corn.

10 Technologically, the process of producing ethanol from sugar is simpler than converting corn into ethanol. Converting corn into ethanol requires additional cooking (wet milling process) and the application of enzymes, whereas the conversion of sugar requires only a yeast fermentation process. The energy requirement for converting sugar into ethanol is about half that for corn. However, the technology and direct energy costs

are but one of several factors that determine the feasibility of ethanol production. Other factors include relative production costs (including feedstocks), conversion rates, proximity to processing facilities, alternative prices and government policies, facility construction and processing costs. As other countries have shown that it can be economically feasible to produce ethanol from sugar and other new feedstocks are researched, interest in the United States in ethanol production from sugar has increased.

In response to the growing interest around sugar and ethanol, USDA released a study in July 2006 titled: "The Economic Feasibility of Ethanol Production from Sugar in the United States" which is incorporated herein by reference in its entirety. The report found that at the current market prices for ethanol, converting sugarcane, sugar beets and molasses to ethanol would be profitable (see Table 1).

Table 1. Current Market Prices for Ethanol

Feedstock	Total Costs*	Processing Costs*
Corn (wet milling/dry milling):	\$ 1.03/1.05	\$ 0.63/0.52
Raw Sugarcane	\$ 2.40	\$ 0.92
Raw Sugar beets	\$ 2.35	\$ 0.77
Molasses**	\$ 1.27	\$ 0.36
Raw Sugar**	\$ 3.48	\$ 0.36
Refined sugar**	\$ 3.97	\$ 0.36

*Per gallon

**Excludes transportation costs

Sugar Beets

Sugar beets are an annual crop grown in 11 states across a variety of climatic conditions, from the hot climate of the Imperial Valley of California to the colder climates of Montana and North Dakota. Sugar beet byproducts include beet pulp, which can be sold for animal feed, and molasses, which is also sold for animal feed or further processed to extract more sugar.

Sugar beet processing facilities convert raw sugar beets directly into refined sugar in a 1-step process. While planted sugar beet acreage has fallen slightly since the 1990s, sugar production actually increased due to investments in new processing equipment, the adoption of new technologies, improved crop varieties and enhanced technologies for the de-sugaring of molasses. Sugar beets are very bulky and relatively expensive to transport

or 0.051 tons of sugarcane per gallon of ethanol produced

Sugar beets:

15.58% refined sugar recovery rate, plus 40.0 pounds of sucrose from beet molasses
 5 1 ton of sugar beets = 311.6 pounds of sucrose from refined sugar
 and 40.0 pounds of sucrose from beet molasses
 = 351.6 pounds (0.1758 tons) of sucrose
 = 24.8 gallons of ethanol
 10 or 0.040 tons of sugar beets per gallon of ethanol produced

Molasses:

49.2% total sugars as sucrose
 1 ton of molasses = 984 pounds (0.492 tons) of sucrose
 15 = 69.4 gallons of ethanol
 or 28.8 pounds of molasses per gallon of ethanol produced
 or 2.45 gallons of molasses per gallon of ethanol produced
 (using a conversion of 1.0 gallon of molasses = 11.74 pounds of weight)
 20

Raw sugar:

96.0% totals sugars as sucrose
 1 ton of raw sugar = 1920 pounds (0.96 tons) of sucrose
 = 135.4 gallons of ethanol
 25 or 14.77 pounds of raw sugar per gallon of ethanol produced

Refined beet sugar:

100.0% total sugars as sucrose
 1 ton of refined sugar = 2000 pounds (1.0 ton) of sucrose
 30 = 141.0 gallons of ethanol
 or 14.18 pounds of refined sugar per gallon of ethanol produced

Results from this study have several important implications concerning the production of ethanol from sugar crops in the United States. First, under existing
 35 fermentation technology, corn is currently the cheapest feedstock available for use in the production of ethanol in the United States. Second, given current and future projected sugar and ethanol market prices, it appears that the production of sugar is the most profitable use of sugarcane or sugar beets. Third, cellulosic conversion of biomass into ethanol offers the potential for a wide variety of feedstocks to be used in ethanol
 40 production.

Systems and processes are described herein that can utilize these low molecular weight to produce ethanol more rapidly and more cost effectively.

5 Blends of any biomass materials described herein can be utilized for making any of the products described herein, such as ethanol. For example, blends of cellulosic materials and starchy materials can be utilized for making any product described herein.

SYSTEMS FOR TREATING BIOMASS

FIG. 1 shows a system 100 for converting biomass, particularly biomass with significant cellulosic and lignocellulosic components and/or starchy components, into useful products and co-products. System 100 includes a feed preparation subsystem 110, a pretreatment subsystem 114, a primary process subsystem 118, and a post-processing subsystem 122. Feed preparation subsystem 110 receives biomass in its raw form, physically prepares the biomass for use as feedstock by downstream processes (e.g., reduces the size of and homogenizes the biomass), and stores the biomass both in its raw and feedstock forms. Biomass feedstock with significant cellulosic and/or lignocellulosic components, or starchy components can have a high average molecular weight and crystallinity that can make processing the feedstock into useful products (e.g., fermenting the feedstock to produce ethanol) difficult. For example, others have used acids, bases and enzymes to process cellulosic, lignocellulosic or starchy feedstocks. As described herein, in some embodiments, such treatments are unnecessary, or are necessary only in small or catalytic amounts.

Pretreatment subsystem 114 receives feedstock from the feed preparation subsystem 110 and prepares the feedstock for use in primary production processes by, for example, reducing the average molecular weight and crystallinity of the feedstock. Primary process subsystem 118 receives pretreated feedstock from pretreatment subsystem 114 and produces useful products (e.g., ethanol, other alcohols, pharmaceuticals, and/or food products). In some cases, the output of primary process subsystem 118 is directly useful but, in other cases, requires further processing provided by post-processing subsystem 122. Post-processing subsystem 122 provides further processing to product streams from primary process system 118 which require it (e.g., distillation and denaturation of ethanol) as well as

treatment for waste streams from the other subsystems. In some cases, the co-products of subsystems 114, 118, 122 can also be directly or indirectly useful as secondary products and/or in increasing the overall efficiency of system 100. For example, post-processing subsystem 122 can produce treated water to be recycled for use as process water in other subsystems and/or can produce burnable waste which can be used as fuel for boilers producing steam and/or electricity.

The optimum size for biomass conversion plants is affected by factors including economies of scale and the type and availability of biomass used as feedstock. Increasing plant size tends to increase economies of scale associated with plant processes. However, increasing plant size also tends to increase the costs (e.g., transportation costs) per unit of feedstock. Studies analyzing these factors suggest that the appropriate size for biomass conversion plants can range from 1000 to 10,000 or more dried tons of feedstock per day depending at least in part on the type of feedstock used. The type of feedstock can also impact plant storage requirements with plants designed primarily for processing feedstock whose availability varies seasonally (e.g., corn stover) requiring more on- or of-site feedstock storage than plants designed to process feedstock whose availability is relatively steady (e.g., waste paper).

PHYSICAL PREPARATION

In some cases, methods of processing begin with a physical preparation of the feedstock, e.g., size reduction of raw feedstock materials, such as by cutting, grinding, shearing, ball milling, nip-roll processing, or chopping. In some cases, the material can be reduced into particles using a hammermill, disk-refiner, or flaker. In some cases, loose feedstock (e.g., recycled paper, starchy materials, or switchgrass) is prepared by shearing or shredding. Screens and/or magnets can be used to remove oversized or undesirable objects such as, for example, rocks or nails from the feed stream.

Feed preparation systems can be configured to produce feed streams with specific characteristics such as, for example, specific maximum sizes, specific length-to-width, or specific surface areas ratios. As a part of feed preparation, the bulk density of feedstocks can be controlled (e.g., increased or decreased).

Size Reduction

In some embodiments, the material to be processed is in the form of a fibrous material that includes fibers provided by shearing a fiber source. For example, the shearing can be performed with a rotary knife cutter.

5 For example, and by reference to FIG. 2, a fiber source 210 is sheared, e.g., in a rotary knife cutter, to provide a first fibrous material 212. The first fibrous material 212 is passed through a first screen 214 having an average opening size of 1.59 mm or less (1/16 inch, 0.0625 inch) to provide a second fibrous material 216. If desired, fiber source can be cut prior to the shearing, e.g., with a shredder. For example, when a paper is used
10 as the fiber source, the paper can be first cut into strips that are, e.g., 1/4- to 1/2-inch wide, using a shredder, e.g., a counter-rotating screw shredder, such as those manufactured by Munson (Utica, N.Y.). As an alternative to shredding, the paper can be reduced in size by cutting to a desired size using a guillotine cutter. For example, the guillotine cutter can be used to cut the paper into sheets that are, e.g., 10 inches wide by
15 12 inches long.

In some embodiments, the shearing of the fiber source and the passing of the resulting first fibrous material through the first screen are performed concurrently. The shearing and the passing can also be performed sequentially, e.g., in a batch-type process.

For example, a rotary knife cutter can be used to concurrently shear the fiber
20 source and screen the first fibrous material. Referring to FIG. 3, a rotary knife cutter 220 includes a hopper 222 that can be loaded with a shredded fiber source 224 prepared by shredding the fiber source. Shredded fiber source is sheared between stationary blades 230 and rotating blades 232 to provide a first fibrous material 240. First fibrous material 240 passes through screen 242, and the resulting second fibrous material 244 is captured
25 in bin 250. To aid in the collection of the second fibrous material, the bin can have a pressure below nominal atmospheric pressure, e.g., at least 10 percent below nominal atmospheric pressure, e.g., at least 25 percent below nominal atmospheric pressure, at least 50 percent below nominal atmospheric pressure, or at least 75 percent below nominal atmospheric pressure. In some embodiments, a vacuum source 252 is utilized to
30 maintain the bin below nominal atmospheric pressure.

Shearing can be advantageous for “opening up,” “stressing,” or even reducing the molecular weight of the fibrous materials, making the cellulose of the materials more susceptible to chain scission and/or reduction of crystallinity. The open materials can also be more susceptible to oxidation when irradiated.

5 The fiber source can be sheared in a dry state, a hydrated state (e.g., having up to ten percent by weight absorbed water), or in a wet state, e.g., having between about 10 percent and about 75 percent by weight water. The fiber source can even be sheared while partially or fully submerged under a liquid, such as water, ethanol, or isopropanol.

10 The fiber source can also be sheared in a gas (such as a stream or atmosphere of gas other than air), e.g., oxygen or nitrogen, or steam.

Other methods of making the fibrous materials include, e.g., stone grinding, mechanical ripping or tearing, pin grinding, ball milling, nip-roll processing, or air attrition milling.

15 If desired, the fibrous materials can be separated, e.g., continuously or in batches, into fractions according to their length, width, density, material type, or some combination of these attributes.

For example, ferrous materials can be separated from any of the fibrous materials by passing a fibrous material that includes a ferrous material past a magnet, e.g., an electromagnet, and then passing the resulting fibrous material through a series of screens, each screen having different sized apertures.

20 The fibrous materials can also be separated, e.g., by using a high velocity gas, e.g., air. In such an approach, the fibrous materials are separated by drawing off different fractions, which can be characterized photonically, if desired. Such a separation apparatus is discussed, e.g., in Lindsey et al, U.S. Patent No. 6,883,667.

25 The fibrous materials can have a low moisture content, e.g., less than about 7.5, 5, 3, 2.5, 2, 1.5, 1, or 0.5% by weight before processing. This material can be irradiated with a beam of particles, such as electrons or protons. The irradiation can be immediately following preparation of the material, or after a moisture reduction step, e.g., drying at approximately 105 °C for 4-18 hours, so that the moisture content is, e.g., less
30 than about 0.5% before use.

If desired, lignin can be removed from any of the fibrous materials that include lignin. Also, to aid in the breakdown of the materials that include the cellulose, the material can be treated prior to irradiation with heat, a chemical (e.g., mineral acid, base or a strong oxidizer such as sodium hypochlorite) and/or an enzyme.

5 In some embodiments, the average opening size of the first screen is less than 0.79 mm (1/32 inch, 0.03125 inch), e.g., less than 0.51 mm (1/50 inch, 0.02000 inch), less than 0.40 mm (1/64 inch, 0.015625 inch), less than 0.23 mm (0.009 inch), less than 0.20 mm (1/128 inch, 0.0078125 inch), less than 0.18 mm (0.007 inch), less than 0.13 mm (0.005 inch), or even less than less than 0.10 mm (1/256 inch, 0.00390625 inch).

10 The screen is prepared by interweaving monofilaments having an appropriate diameter to give the desired opening size. For example, the monofilaments can be made of a metal, e.g., stainless steel. As the opening sizes get smaller, structural demands on the monofilaments may become greater. For example, for opening sizes less than 0.40 mm, it can be advantageous to make the screens from monofilaments made from a material
15 other than stainless steel, e.g., titanium, titanium alloys, amorphous metals, nickel, tungsten, rhodium, rhenium, ceramics, or glass. In some embodiments, the screen is made from a plate, e.g., a metal plate, having apertures, e.g., cut into the plate using a laser. In some embodiments, the open area of the mesh is less than 52%, e.g., less than 41%, less than 36%, less than 31%, less than 30%.

20 In some embodiments, the second fibrous material is sheared and passed through the first screen, or a different sized screen. In some embodiments, the second fibrous material is passed through a second screen having an average opening size equal to or less than that of first screen.

Referring to FIG. 4, a third fibrous material 220 can be prepared from the second
25 fibrous material 216 by shearing the second fibrous material 216 and passing the resulting material through a second screen 222 having an average opening size less than the first screen 214.

Generally, the fibers of the fibrous materials can have a relatively large average length-to-diameter ratio (e.g., greater than 20-to-1), even if they have been sheared more
30 than once. In addition, the fibers of the fibrous materials described herein may have a relatively narrow length and/or length-to-diameter ratio distribution.

As used herein, average fiber widths (i.e., diameters) are those determined optically by randomly selecting approximately 5,000 fibers. Average fiber lengths are corrected length-weighted lengths. BET (Brunauer, Emmet and Teller) surface areas are multi-point surface areas, and porosities are those determined by mercury porosimetry.

5 The average length-to-diameter ratio of the second fibrous material 14 can be, e.g., greater than 8/1, 10/1, 15/1, 20/1, 25/1, or even greater than 50/1. An average length of the second fibrous material 14 can be, e.g., between about 0.5 mm and 2.5 mm, e.g., between about 0.75 mm and 1.0 mm, and an average width (i.e., diameter) of the second fibrous material 14 can be, e.g., between about 5 μm and 50 μm , e.g., between about 10
10 μm and 30 μm .

In some embodiments, a standard deviation of the length of the second fibrous material 14 is less than 60 percent of an average length of the second fibrous material 14, e.g., less than 50 percent of the average length, less than 40 percent of the average length, less than 25 percent of the average length, less than 10 percent of the average length, less
15 than 5 percent of the average length, or even less than 1 percent of the average length.

In some embodiments, a BET surface area of the second fibrous material is greater than 0.1 m^2/g , e.g., greater than 0.25 m^2/g , greater than 0.5 m^2/g , greater than 1.0 m^2/g , greater than 1.5 m^2/g , greater than 1.75 m^2/g , greater than 5.0 m^2/g , greater than 10 m^2/g , greater than 25 m^2/g , greater than 35 m^2/g , greater than 50 m^2/g , greater than 60
20 m^2/g , greater than 75 m^2/g , greater than 100 m^2/g , greater than 150 m^2/g , greater than 200 m^2/g , or even greater than 250 m^2/g . A porosity of the second fibrous material 14 can be, e.g., greater than 20 percent, greater than 25 percent, greater than 35 percent, greater than 50 percent, greater than 60 percent, greater than 70 percent, e.g., greater than 80 percent, greater than 85 percent, greater than 90 percent, greater than 92 percent, greater than 94
25 percent, greater than 95 percent, greater than 97.5 percent, greater than 99 percent, or even greater than 99.5 percent.

In some embodiments, a ratio of the average length-to-diameter ratio of the first fibrous material to the average length-to-diameter ratio of the second fibrous material is, e.g., less than 1.5, e.g., less than 1.4, less than 1.25, less than 1.1, less than 1.075, less
30 than 1.05, less than 1.025, or even substantially equal to 1.

In particular embodiments, the second fibrous material is sheared again and the resulting fibrous material passed through a second screen having an average opening size less than the first screen to provide a third fibrous material. In such instances, a ratio of the average length-to-diameter ratio of the second fibrous material to the average length-to-diameter ratio of the third fibrous material can be, e.g., less than 1.5, e.g., less than 1.4, less than 1.25, or even less than 1.1.

In some embodiments, the third fibrous material is passed through a third screen to produce a fourth fibrous material. The fourth fibrous material can be, e.g., passed through a fourth screen to produce a fifth material. Similar screening processes can be repeated as many times as desired to produce the desired fibrous material having the desired properties.

Densification

Densified materials can be processed by any of the methods described herein, or any material described herein, e.g., any fibrous material described herein, can be processed by any one or more methods described herein, and then densified as described herein.

A material, e.g., a fibrous material, having a low bulk density can be densified to a product having a higher bulk density. For example, a material composition having a bulk density of 0.05 g/cm^3 can be densified by sealing the fibrous material in a relatively gas impermeable structure, e.g., a bag made of polyethylene or a bag made of alternating layers of polyethylene and a nylon, and then evacuating the entrapped gas, e.g., air, from the structure. After evacuation of the air from the structure, the fibrous material can have, e.g., a bulk density of greater than 0.3 g/cm^3 , e.g., 0.5 g/cm^3 , 0.6 g/cm^3 , 0.7 g/cm^3 or more, e.g., 0.85 g/cm^3 . After densification, the product can be processed by any of the methods described herein, e.g., irradiated, e.g., with gamma radiation. This can be advantageous when it is desirable to transport the material to another location, e.g., a remote manufacturing plant, where the fibrous material composition can be added to a solution, e.g., to produce ethanol. After piercing the substantially gas impermeable structure, the densified fibrous material can revert to nearly its initial bulk density, e.g., greater than 60 percent of its initial bulk density, e.g., 70 percent, 80 percent, 85 percent

or more, e.g., 95 percent of its initial bulk density. To reduce static electricity in the fibrous material, an anti-static agent can be added to the material.

In some embodiments, the structure, e.g., bag, is formed of a material that dissolves in a liquid, such as water. For example, the structure can be formed from a polyvinyl alcohol so that it dissolves when in contact with a water-based system. Such
5 embodiments allow densified structures to be added directly to solutions that include a microorganism, without first releasing the contents of the structure, e.g., by cutting.

Referring to FIG. 5, a biomass material can be combined with any desired additives and a binder, and subsequently densified by application of pressure, e.g., by
10 passing the material through a nip defined between counter-rotating pressure rolls or by passing the material through a pellet mill. During the application of pressure, heat can optionally be applied to aid in the densification of the fibrous material. The densified material can then be irradiated.

In some embodiments, the material prior to densification has a bulk density of less
15 than 0.25 g/cm³, e.g., 0.20 g/cm³, 0.15 g/cm³, 0.10 g/cm³, 0.05 g/cm³ or less, e.g., 0.025 g/cm³. Bulk density is determined using ASTM D1895B. Briefly, the method involves filling a measuring cylinder of known volume with a sample and obtaining a weight of the sample. The bulk density is calculated by dividing the weight of the sample in grams by the known volume of the cylinder in cubic centimeters.

20 The preferred binders include binders that are soluble in water, swollen by water, or that has a glass transition temperature of less 25 °C, as determined by differential scanning calorimetry. By water-soluble binders, we mean binders having a solubility of at least about 0.05 weight percent in water. By water swellable binders, we mean binders that increase in volume by more than 0.5 percent upon exposure to water.

25 In some embodiments, the binders that are soluble or swollen by water include a functional group that is capable of forming a bond, e.g., a hydrogen bond, with the fibers of the fibrous material, e.g., cellulosic fibrous material. For example, the functional group can be a carboxylic acid group, a carboxylate group, a carbonyl group, e.g., of an aldehyde or a ketone, a sulfonic acid group, a sulfonate group, a phosphoric acid group, a
30 phosphate group, an amide group, an amine group, a hydroxyl group, e.g., of an alcohol, and combinations of these groups, e.g., a carboxylic acid group and a hydroxyl group.

Specific monomeric examples include glycerin, glyoxal, ascorbic acid, urea, glycine, pentaerythritol, a monosaccharide or a disaccharide, citric acid, and tartaric acid.

Suitable saccharides include glucose, sucrose, lactose, ribose, fructose, mannose, arabinose and erythrose. Polymeric examples include polyglycols, polyethylene oxide, polycarboxylic acids, polyamides, polyamines and polysulfonic acids polysulfonates.

Specific polymeric examples include polypropylene glycol (PPG), polyethylene glycol (PEG), polyethylene oxide, e.g., POLYOX[®], copolymers of ethylene oxide and propylene oxide, polyacrylic acid (PAA), polyacrylamide, polypeptides, polyethylenimine, polyvinylpyridine, poly(sodium-4-styrenesulfonate) and poly(2-acrylamido-methyl-1-propanesulfonic acid).

In some embodiments, the binder includes a polymer that has a glass transition temperature less than 25 °C. Examples of such polymers include thermoplastic elastomers (TPEs). Examples of TPEs include polyether block amides, such as those available under the tradename PEBAX[®], polyester elastomers, such as those available under the tradename HYTREL[®], and styrenic block copolymers, such as those available under the tradename KRATON[®]. Other suitable polymers having a glass transition temperature less than 25 °C include ethylene vinyl acetate copolymer (EVA), polyolefins, e.g., polyethylene, polypropylene, ethylene-propylene copolymers, and copolymers of ethylene and alpha olefins, e.g., 1-octene, such as those available under the tradename ENGAGE[®]. In some embodiments, e.g., when the material is a fiberized polycoated paper, the material is densified without the addition of a separate low glass transition temperature polymer.

In a particular embodiment, the binder is a lignin, e.g., a natural or synthetically modified lignin.

A suitable amount of binder added to the material, calculated on a dry weight basis, is, e.g., from about 0.01 percent to about 50 percent, e.g., 0.03 percent, 0.05 percent, 0.1 percent, 0.25 percent, 0.5 percent, 1.0 percent, 5 percent, 10 percent or more, e.g., 25 percent, based on a total weight of the densified material. The binder can be added to the material as a neat, pure liquid, as a liquid having the binder dissolved therein, as a dry powder of the binder, or as pellets of the binder.

The densified fibrous material can be made in a pellet mill. Referring to FIG. 6, a pellet mill 300 has a hopper 301 for holding undensified material 310 that includes carbohydrate-containing materials, such as cellulose. The hopper communicates with an auger 312 that is driven by variable speed motor 314 so that undensified material can be transported to a conditioner 320 that stirs the undensified material with paddles 322 that are rotated by conditioner motor 330. Other ingredients, e.g., any of the additives and/or fillers described herein, can be added at inlet 332. If desired, heat may be added while the fibrous material is in the conditioner. After being conditioned, the material passes from the conditioner through a dump chute 340, and to another auger 342. The dump chute, as controlled by actuator 344, allows for unobstructed passage of the material from conditioner to auger. Auger is rotated by motor 346, and controls the feeding of the fibrous material into die and roller assembly 350. Specifically, the material is introduced into a hollow, cylindrical die 352, which rotates about a horizontal axis and which has radially extending die holes 250. Die 352 is rotated about the axis by motor 360, which includes a horsepower gauge, indicating total power consumed by the motor. Densified material 370, e.g., in the form of pellets, drops from chute 372 and are captured and processed, such as by irradiation.

The material, after densification, can be conveniently in the form of pellets or chips having a variety of shapes. The pellets can then be irradiated. In some embodiments, the pellets or chips are cylindrical in shape, e.g., having a maximum transverse dimension of, e.g., 1 mm or more, e.g., 2 mm, 3 mm, 5 mm, 8 mm, 10 mm, 15 mm or more, e.g., 25 mm. Other convenient shapes include pellets or chips that are plate-like in form, e.g., having a thickness of 1 mm or more, e.g., 2 mm, 3 mm, 5 mm, 8 mm, 10 mm or more, e.g., 25 mm; a width of, e.g., 5 mm or more, e.g., 10 mm, 15 mm, 25 mm, 30 mm or more, e.g., 50 mm; and a length of 5 mm or more, e.g., 10 mm, 15 mm, 25 mm, 30 mm or more, e.g., 50 mm.

Referring now FIG. 7A-7D, pellets can be made so that they have a hollow inside. As shown, the hollow can be generally in-line with the center of the pellet (FIG. 7B), or out of line with the center of the pellet (FIG. 7C). Making the pellet hollow inside can increase the rate of dissolution in a liquid after irradiation.

Referring now to FIG. 7D, the pellet can have, e.g., a transverse shape that is multi-lobal, e.g., tri-lobal as shown, or tetra-lobal, penta-lobal, hexa-lobal or deca-lobal. Making the pellets in such transverse shapes can also increase the rate of dissolution in a solution after irradiation.

5 Alternatively, the densified material can be in any other desired form, e.g., the densified material can be in the form of a mat, roll or bale.

Examples

In one example, half-gallon juice cartons made of un-printed white Kraft board having a bulk density of 20 lb/ft³ can be used as a feedstock. Cartons can be folded flat
10 and then fed into a shredder to produce a confetti-like material having a width of between 0.1 inch and 0.5 inch, a length of between 0.25 inch and 1 inch and a thickness equivalent to that of the starting material (about 0.075 inch). The confetti-like material can be fed to a rotary knife cutter, which shears the confetti-like pieces, tearing the pieces apart and releasing fibrous material.

15 In some cases, multiple shredder-shearer trains can be arranged in series with output. In one embodiment, two shredder-shearer trains can be arranged in series with output from the first shearer fed as input to the second shredder. In another embodiment, three shredder-shearer trains can be arranged in series with output from the first shearer fed as input to the second shredder and output from the second shearer fed as input to the
20 third shredder. Multiple passes through shredder-shearer trains are anticipated to decrease particle size and increase overall surface area within the feedstream.

In another example, fibrous material produced from shredding and shearing juice cartons can be treated to increase its bulk density. In some cases, the fibrous material can be sprayed with water or a dilute stock solution of POLYOXTM WSR N10 (polyethylene
25 oxide) prepared in water. The wetted fibrous material can then be processed through a pellet mill operating at room temperature. The pellet mill can increase the bulk density of the feedstream by more than an order of magnitude.

PRETREATMENT

Physically prepared feedstock can be pretreated for use in primary production processes by, for example, reducing the average molecular weight and crystallinity of the feedstock and/or increasing the surface area and/or porosity of the feedstock.

5 In some embodiments, the cellulosic and/or lignocellulosic material includes a first cellulose having a first number average molecular weight and the resulting carbohydrate includes a second cellulose having a second number average molecular weight lower than the first number average molecular weight. For example, the second number average molecular weight is lower than the first number average molecular
10 weight by more than about twenty-five percent, e.g., 2x, 3x, 5x, 7x, 10x, 25x, even 100x reduction.

In some embodiments, the first cellulose has a first crystallinity and the second cellulose has a second crystallinity lower than the first crystallinity, such as lower than about two, three, five, ten, fifteen or twenty-five percent lower.

15 In some embodiments, the first cellulose has a first level of oxidation and the second cellulose has a second level of oxidation higher than the first level of oxidation, such as two, three, four, five, ten or even twenty-five percent higher.

Pretreatment processes can include one or more of irradiation, sonication, oxidation, pyrolysis, and steam explosion. The various pretreatment systems and
20 methods can be used in combinations of two, three, or even four of these technologies.

Pretreatment Combinations

In some embodiments, biomass can be processed by applying two or more of any of the processes described herein, such as two, three, four or more of radiation, sonication (or any other disruption technique described herein, e.g., treatment with a rotor-stator
25 disruptor), oxidation, pyrolysis, and steam explosion either with or without prior, intermediate, or subsequent feedstock preparation as described herein. The processes can be applied to the biomass in any order or concurrently. For example, a carbohydrate can be prepared by applying radiation, sonication, oxidation, pyrolysis, and, optionally, steam explosion to a cellulosic and/or lignocellulosic material (in any order or concurrently).
30 The provided carbohydrate-containing material can then be converted by one or more microorganisms, such as bacteria, yeast, or mixtures of yeast and bacteria, to a number of

desirable products, as described herein. Multiple processes can provide materials that can be more readily utilized by a variety of microorganisms because of their lower molecular weight, lower crystallinity, and/or enhanced solubility. Multiple processes can provide synergies and can reduce overall energy input required in comparison to any single
5 process.

For example, in some embodiments, feedstocks are provided that include a carbohydrate that is produced by a process that includes irradiating and sonicating, irradiating and oxidizing, irradiating and pyrolyzing, or irradiating and steam-exploding (in either order or concurrently) a cellulosic and/or a lignocellulosic material. The
10 provided feedstock can then be contacted with a microorganism having the ability to convert at least a portion, e.g., at least about 1 percent by weight, of the feedstock to the product, such as the combustible fuel.

Pretreatment Conditions

15 In some embodiments, the process does not include hydrolyzing the cellulosic and/or lignocellulosic material, such as with an acid, e.g., a mineral acid, such as hydrochloric or sulfuric acid, an enzyme or a base. If desired, some or none of the feedstock can include a hydrolyzed material. For example, in some embodiments, at least about seventy percent by weight of the feedstock is an unhydrolyzed material, e.g., at
20 least at 95 percent by weight of the feedstock is an unhydrolyzed material. In some embodiments, substantially all of the feedstock is an unhydrolyzed material. For example, treatment with alkali can be avoided.

Any feedstock or any reactor or fermentor charged with a feedstock can include a buffer, such as sodium bicarbonate, ammonium chloride or Tris; an electrolyte, such as
25 potassium chloride, sodium chloride, or calcium chloride; a growth factor, such as biotin and/or a base pair such as uracil or an equivalent thereof; a surfactant, such as Tween[®] or polyethylene glycol; a mineral, such as such as calcium, chromium, copper, iodine, iron, selenium, or zinc; or a chelating agent, such as ethylene diamine, ethylene diamine tetraacetic acid (EDTA) (or its salt form, e.g., sodium or potassium EDTA), or
30 dimercaprol.

When radiation is utilized, it can be applied to any sample that is dry or wet, or even dispersed in a liquid, such as water. For example, irradiation can be performed on cellulosic and/or lignocellulosic material in which less than about 25 percent by weight of the cellulosic and/or lignocellulosic material has surfaces wetted with a liquid, such as water. In some embodiments, irradiating is performed on cellulosic and/or lignocellulosic material in which substantially none of the cellulosic and/or lignocellulosic material is wetted with a liquid, such as water.

In some embodiments, any processing described herein occurs with the cellulosic and/or lignocellulosic material remaining dry as acquired or after the material has been dried, e.g., using heat and/or reduced pressure. For example, in some embodiments, the cellulosic and/or lignocellulosic material has less than about five percent by weight retained water, measured at 25°C and at fifty percent relative humidity.

The feedstock can be treated so that it has a low moisture content, e.g., less than about 7.5, 5, 3, 2.5, 2, 1.5, 1, or 0.5% by weight. This material can be irradiated with a beam of particles, such as electrons or protons. The irradiation can be immediately following preparation of the material or after a moisture reduction step, e.g., drying at approximately 105 °C for 4-18 hours.

If desired, a swelling agent, as defined herein, can be utilized in any process described herein. In some embodiments, when a cellulosic and/or lignocellulosic material is processed using radiation, less than about 25 percent by weight of the cellulosic and/or lignocellulosic material is in a swollen state, the swollen state being characterized as having a volume of more than about 2.5 percent higher than an unswollen state, e.g., more than 5.0, 7.5, 10, or 15 percent higher than the unswollen state. In specific embodiments when radiation is utilized, the cellulosic and/or lignocellulosic material includes a swelling agent, and swollen cellulosic and/or lignocellulosic receives a dose of less than about 10 Mrad. In other embodiments, when radiation is utilized on a cellulosic and/or lignocellulosic material, substantially none of the cellulosic and/or lignocellulosic material is in a swollen state.

In some embodiments, no chemicals, e.g., no swelling agents, are added to the biomass prior to irradiation. For example, in some of these embodiments no alkaline substances (such as sodium hydroxide, potassium hydroxide, lithium hydroxide and

ammonium hydroxides), acidifying agents (such as mineral acids (e.g., sulfuric acid, hydrochloric acid and phosphoric acid)), salts, such as zinc chloride, calcium carbonate, sodium carbonate, benzyltrimethylammonium sulfate, or basic organic amines, such as ethylene diamine, are added prior to irradiation or other processing. In some cases, no
5 additional water is added. For example, the biomass prior to processing can have less than 0.5 percent by weight added chemicals, e.g., less than 0.4, 0.25, 0.15 or 0.1 percent by weight added chemicals. In some instances, the biomass has no more than a trace, e.g., less than 0.05 percent by weight added chemicals, prior to irradiation. In other instances, the biomass prior to irradiation has substantially no added chemicals or
10 swelling agents. Avoiding the use of such chemicals can also be extended throughout processing, e.g., at all times prior to fermentation, or at all times.

When radiation is utilized in any process, it can be applied while the cellulosic and/or lignocellulosic is exposed to air, oxygen-enriched air, or even oxygen itself, or blanketed by an inert gas such as nitrogen, argon, or helium. When maximum oxidation
15 is desired, an oxidizing environment is utilized, such as air or oxygen. The distance from the radiation source can also be optimized to maximize reactive gas formation, e.g., ozone and/or oxides of nitrogen.

When radiation is utilized, it may be applied to biomass, such as cellulosic and/or lignocellulosic material, under a pressure of greater than about 2.5 atmospheres, such as
20 greater than 5, 10, 15, 20 or even greater than about 50 atmospheres.

When the process includes radiation, the irradiating can be performed utilizing an ionizing radiation, such as gamma rays, x-rays, energetic ultraviolet radiation, such as ultraviolet C radiation having a wavelength of from about 100 nm to about 280 nm, a beam of particles, such as a beam of electrons, slow neutrons or alpha particles. In some
25 embodiments, irradiating includes two or more radiation sources, such as gamma rays and a beam of electrons, which can be applied in either order or concurrently.

Any processing technique described herein can be used at a pressure above or below normal, earth-bound atmospheric pressure. For example, any process that utilizes radiation, sonication, oxidation, pyrolysis, steam explosion, or combinations of any of
30 these processes to provide materials that include a carbohydrate can be performed under high pressure, which can increase reaction rates. For example, any process or

combination of processes can be performed at a pressure greater than about normal atmospheric pressure, e.g., at a pressure of greater than about 25 MPa, e.g., greater than 50 MPa, 75 MPa, 100 MPa, 150 MPa, 200 MPa, 250 MPa, 350 MPa, 500 MPa, 750 MPa, 1,000 MPa, or greater than 1,500 MPa.

5 **Radiation Treatment**

One or more irradiation processing sequences can be used to process raw feedstock from a wide variety of different sources to extract useful substances from the feedstock, and to provide partially degraded organic material which functions as input to further processing steps and/or sequences. Irradiation can reduce the molecular weight
10 and/or crystallinity of feedstock. In some embodiments, energy deposited in a material that releases an electron from its atomic orbital is used to irradiate the materials. The radiation may be provided by 1) heavy charged particles, such as alpha particles or protons, 2) electrons, produced, for example, in beta decay or electron beam accelerators, or 3) electromagnetic radiation, for example, gamma rays, x rays, or ultraviolet rays. In
15 one approach, radiation produced by radioactive substances can be used to irradiate the feedstock. In some embodiments, any combination in any order or concurrently of (1) through (3) may be utilized. In another approach, electromagnetic radiation (e.g., produced using electron beam emitters) can be used to irradiate the feedstock. The doses applied depend on the desired effect and the particular feedstock. For example, high
20 doses of radiation can break chemical bonds within feedstock components and low doses of radiation can increase chemical bonding (e.g., cross-linking) within feedstock components. In some instances when chain scission is desirable and/or polymer chain functionalization is desirable, particles heavier than electrons, such as protons, helium nuclei, argon ions, silicon ions, neon ions carbon ions, phosphorus ions, oxygen ions or
25 nitrogen ions can be utilized. When ring-opening chain scission is desired, positively charged particles can be utilized for their Lewis acid properties for enhanced ring-opening chain scission. For example, when oxygen-containing functional groups are desired, irradiation in the presence of oxygen or even irradiation with oxygen ions can be performed. For example, when nitrogen-containing functional groups are desirable,
30 irradiation in the presence of nitrogen or even irradiation with nitrogen ions can be performed.

Referring to FIG. 8, in one method, a first material 2 that is or includes cellulose having a first number average molecular weight ($^T M_{N1}$) is irradiated, e.g., by treatment with ionizing radiation (e.g., in the form of gamma radiation, X-ray radiation, 100 nm to 280 nm ultraviolet (UV) light, a beam of electrons or other charged particles) to provide a
 5 second material 3 that includes cellulose having a second number average molecular weight ($^T M_{N2}$) lower than the first number average molecular weight. The second material (or the first and second material) can be combined with a microorganism (e.g., a bacterium or a yeast) that can utilize the second and/or first material to produce a product, e.g., a fuel 5 that is or includes hydrogen, an alcohol (e.g., ethanol or butanol, such as n-,
 10 sec- or t-butanol), an organic acid, a hydrocarbon or mixtures of any of these.

Since the second material 3 has cellulose having a reduced molecular weight relative to the first material, and in some instances, a reduced crystallinity as well, the second material is generally more dispersible, swellable and/or soluble in a solution containing a microorganism. These properties make the second material 3 more
 15 susceptible to chemical, enzymatic and/or biological attack relative to the first material 2, which can greatly improve the production rate and/or production level of a desired product, e.g., ethanol. Radiation can also sterilize the materials.

In some embodiments, the second number average molecular weight (M_{N2}) is lower than the first number average molecular weight ($^T M_{N1}$) by more than about 10
 20 percent, e.g., 15, 20, 25, 30, 35, 40, 50 percent, 60 percent, or even more than about 75 percent.

In some instances, the second material has cellulose that has as crystallinity ($^T C_2$) that is lower than the crystallinity ($^T C_1$) of the cellulose of the first material. For example, ($^T C_2$) can be lower than ($^T C_1$) by more than about 10 percent, e.g., 15, 20, 25,
 25 30, 35, 40, or even more than about 50 percent.

In some embodiments, the starting crystallinity index (prior to irradiation) is from about 40 to about 87.5 percent, e.g., from about 50 to about 75 percent or from about 60 to about 70 percent, and the crystallinity index after irradiation is from about 10 to about 50 percent, e.g., from about 15 to about 45 percent or from about 20 to about 40 percent.
 30 However, in some embodiments, e.g., after extensive irradiation, it is possible to have a

crystallinity index of lower than 5 percent. In some embodiments, the material after irradiation is substantially amorphous.

In some embodiments, the starting number average molecular weight (prior to irradiation) is from about 200,000 to about 3,200,000, e.g., from about 250,000 to about 1,000,000 or from about 250,000 to about 700,000, and the number average molecular weight after irradiation is from about 50,000 to about 200,000, e.g., from about 60,000 to about 150,000 or from about 70,000 to about 125,000. However, in some embodiments, e.g., after extensive irradiation, it is possible to have a number average molecular weight of less than about 10,000 or even less than about 5,000.

In some embodiments, the second material can have a level of oxidation ($^T\text{O}_2$) that is higher than the level of oxidation ($^T\text{O}_1$) of the first material. A higher level of oxidation of the material can aid in its dispersibility, swellability and/or solubility, further enhancing the materials susceptibility to chemical, enzymatic or biological attack. In some embodiments, to increase the level of the oxidation of the second material relative to the first material, the irradiation is performed under an oxidizing environment, e.g., under a blanket of air or oxygen, producing a second material that is more oxidized than the first material. For example, the second material can have more hydroxyl groups, aldehyde groups, ketone groups, ester groups or carboxylic acid groups, which can increase its hydrophilicity.

Ionizing Radiation

Each form of radiation ionizes the biomass via particular interactions, as determined by the energy of the radiation. Heavy charged particles primarily ionize matter via Coulomb scattering; furthermore, these interactions produce energetic electrons that may further ionize matter. Alpha particles are identical to the nucleus of a helium atom and are produced by the alpha decay of various radioactive nuclei, such as isotopes of bismuth, polonium, astatine, radon, francium, radium, several actinides, such as actinium, thorium, uranium, neptunium, curium, californium, americium, and plutonium.

When particles are utilized, they can be neutral (uncharged), positively charged or negatively charged. When charged, the charged particles can bear a single positive or negative charge, or multiple charges, e.g., one, two, three or even four or more charges.

In instances in which chain scission is desired, positively charged particles may be desirable, in part, due to their acidic nature. When particles are utilized, the particles can have the mass of a resting electron, or greater, e.g., 500, 1000, 1500, or 2000 or more times the mass of a resting electron. For example, the particles can have a mass of from
5 about 1 atomic unit to about 150 atomic units, e.g., from about 1 atomic unit to about 50 atomic units, or from about 1 to about 25, e.g., 1, 2, 3, 4, 5, 10, 12 or 15 amu.

Accelerators used to accelerate the particles can be electrostatic DC, electrodynamic DC, RF linear, magnetic induction linear or continuous wave. For example, cyclotron type accelerators are available from IBA, Belgium, such as the Rhodotron® system, while DC
10 type accelerators are available from RDI, now IBA Industrial, such as the Dynamitron®. Ions and ion accelerators are discussed in Introductory Nuclear Physics, Kenneth S. Krane, John Wiley & Sons, Inc. (1988), Krsto Prelec, FIZIKA B 6 (1997) 4, 177–206, a copy of which is attached hereto as Appendix B, Chu, William T., “Overview of Light-Ion Beam Therapy”, Columbus-Ohio, ICRU-IAEA Meeting, 18-20 March 2006, a copy
15 of which is attached hereto as Appendix C, Iwata, Y. et al., “Alternating-Phase-Focused IH-DTL for Heavy-Ion Medical Accelerators”, Proceedings of EPAC 2006, Edinburgh, Scotland, a copy of which is attached hereto as Appendix D, and Leitner, C.M. et al., “Status of the Superconducting ECR Ion Source Venus”, Proceedings of EPAC 2000, Vienna, Austria, a copy of which is attached hereto as Appendix E.

20 Electrons interact via Coulomb scattering and bremsstrahlung radiation produced by changes in the velocity of electrons. Electrons may be produced by radioactive nuclei that undergo beta decay, such as isotopes of iodine, cesium, technetium, and iridium. Alternatively, an electron gun can be used as an electron source via thermionic emission.

 Electromagnetic radiation interacts via three processes: photoelectric absorption,
25 Compton scattering, and pair production. The dominating interaction is determined by the energy of the incident radiation and the atomic number of the material. The summation of interactions contributing to the absorbed radiation in cellulosic material can be expressed by the mass absorption coefficient.

 Electromagnetic radiation is subclassified as gamma rays, x rays, ultraviolet rays,
30 infrared rays, microwaves, or radiowaves, depending on its wavelength.

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For example, gamma radiation can be employed to irradiate the materials. Referring to FIGS. 9 and 10 (an enlarged view of region R), a gamma irradiator 10 includes gamma radiation sources 408, e.g., ^{60}Co pellets, a working table 14 for holding the materials to be irradiated and storage 16, e.g., made of a plurality iron plates, all of which are housed in a concrete containment chamber (vault) 20 that includes a maze entranceway 22 beyond a lead-lined door 26. Storage 16 includes a plurality of channels 30, e.g., sixteen or more channels, allowing the gamma radiation sources to pass through storage on their way proximate the working table.

In operation, the sample to be irradiated is placed on a working table. The irradiator is configured to deliver the desired dose rate and monitoring equipment is connected to an experimental block 31. The operator then leaves the containment chamber, passing through the maze entranceway and through the lead-lined door. The operator mans a control panel 32, instructing a computer 33 to lift the radiation sources 12 into working position using cylinder 36 attached to a hydraulic pump 40.

Gamma radiation has the advantage of a significant penetration depth into a variety of material in the sample. Sources of gamma rays include radioactive nuclei, such as isotopes of cobalt, calcium, technicium, chromium, gallium, indium, iodine, iron, krypton, samarium, selenium, sodium, thalium, and xenon.

Sources of x rays include electron beam collision with metal targets, such as tungsten or molybdenum or alloys, or compact light sources, such as those produced commercially by Lyncean.

Sources for ultraviolet radiation include deuterium or cadmium lamps.

Sources for infrared radiation include sapphire, zinc, or selenide window ceramic lamps.

Sources for microwaves include klystrons, Slevin type RF sources, or atom beam sources that employ hydrogen, oxygen, or nitrogen gases.

Various other irradiating devices may be used in the methods disclosed herein, including field ionization sources, electrostatic ion separators, field ionization generators, thermionic emission sources, microwave discharge ion sources, recirculating or static accelerators, dynamic linear accelerators, van de Graaff accelerators, and folded tandem accelerators. Such devices are disclosed, for example, in International Publication Nos. WO 2009/154876 and WO 2009/134745.

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Electron Beam

In some embodiments, a beam of electrons is used as the radiation source. A beam of electrons has the advantages of high dose rates (e.g., 1, 5, or even 10 Mrad per second), high throughput, less containment, and less confinement equipment. Electron beams can also have up to 80 percent electrical efficiency, allowing for a low energy usage, which can translate into a low cost of operation and low greenhouse gas emissions corresponding to the small amount of energy used. Electrons can also be more efficient at causing chain scission. In addition, electrons having energies of 4-10 MeV can have a penetration depth of 5 to 30 mm or more, such as 40 mm. In low bulk density materials, such as many of the materials described herein, e.g., materials having a bulk density of less than about 0.5 g/cm³, electrons having energies in the 4-10 MeV range can penetrate 4-8 inches or even more.

Electron beams can be generated, e.g., by electrostatic generators, cascade generators, transformer generators, low energy accelerators with a scanning system, low energy accelerators with a linear cathode, linear accelerators, and pulsed accelerators. Electrons as an ionizing radiation source can be useful, e.g., for relatively thin piles of materials, e.g., less than 0.5 inch, e.g., less than 0.4 inch, 0.3 inch, 0.2 inch, or less than 0.1 inch. In some embodiments, the energy of each electron of the electron beam is from about 0.3 MeV to about 2.0 MeV (million electron volts), e.g., from about 0.5 MeV to about 1.5 MeV, or from about 0.7 MeV to about 1.25 MeV.

FIG. 11 shows a process flow diagram 3000 that includes various steps in an electron beam irradiation feedstock pretreatment sequence. In first step 3010, a supply of dry feedstock is received from a feed source. As discussed above, the dry feedstock from the feed source may be pre-processed prior to delivery to the electron beam irradiation devices. For example, if the feedstock is derived from plant sources, certain portions of the plant material may be removed prior to collection of the plant material and/or before the plant material is delivered by the feedstock transport device. Alternatively, or in addition, as expressed in optional step 3020, the biomass feedstock can be subjected to

mechanical processing (e.g., to reduce the average length of fibers in the feedstock) prior to delivery to the electron beam irradiation devices.

In step 3030, the dry feedstock is transferred to a feedstock transport device (e.g., a conveyor belt) and is distributed over the cross-sectional width of the feedstock transport device approximately uniformly by volume. This can be accomplished, for example, manually or by inducing a localized vibration motion at some point in the feedstock transport device prior to the electron beam irradiation processing.

In some embodiments, a mixing system introduces a chemical agent 3045 into the feedstock in an optional process 3040 that produces a slurry. Combining water with the processed feedstock in mixing step 3040 creates an aqueous feedstock slurry that may be transported through, for example, piping rather than using, for example, a conveyor belt.

The next step 3050 is a loop that encompasses exposing the feedstock (in dry or slurry form) to electron beam radiation via one or more (say, N) electron beam irradiation devices. The feedstock slurry is moved through each of the N "showers" of electron beams at step 3052. The movement may either be at a continuous speed through and between the showers, or there may be a pause through each shower, followed by a sudden movement to the next shower. A small slice of the feedstock slurry is exposed to each shower for some predetermined exposure time at step 3053.

Electron beam irradiation devices may be procured commercially from Ion Beam Applications, Louvain-la-Neuve, Belgium or the Titan Corporation, San Diego, CA. Typical electron energies can be 1 MeV, 2 MeV, 4.5 MeV, 7.5 MeV, or 10 MeV. Typical electron beam irradiation device power can be 1 kW, 5 kW, 10 kW, 20 kW, 50 kW, 100 kW, 250 kW, or 500 kW. Effectiveness of depolymerization of the feedstock slurry depends on the electron energy used and the dose applied, while exposure time depends on the power and dose. Typical doses may take values of 1 kGy, 5 kGy, 10 kGy, 20 kGy, 50 kGy, 100 kGy, or 200 kGy.

Tradeoffs in considering electron beam irradiation device power specifications include cost to operate, capital costs, depreciation, and device footprint. Tradeoffs in considering exposure dose levels of electron beam irradiation would be energy costs and environment, safety, and health (ESH) concerns. Typically, generators are housed in a vault, e.g., of lead or concrete. Tradeoffs in considering electron energies include energy

costs; here, a lower electron energy may be advantageous in encouraging depolymerization of certain feedstock slurry (see, for example, Bouchard, et al, Cellulose (2006) 13: 601-610).

5 It may be advantageous to provide a double-pass of electron beam irradiation in order to provide a more effective depolymerization process. For example, the feedstock transport device could direct the feedstock (in dry or slurry form) underneath and in a reverse direction to its initial transport direction. Double-pass systems can allow thicker feedstock slurries to be processed and can provide a more uniform depolymerization through the thickness of the feedstock slurry.

10 The electron beam irradiation device can produce either a fixed beam or a scanning beam. A scanning beam may be advantageous with large scan sweep length and high scan speeds, as this would effectively replace a large, fixed beam width. Further, available sweep widths of 0.5 m, 1m, 2 m or more are available.

15 Once a portion of feedstock slurry has been transported through the *N* electron beam irradiation devices, it may be necessary in some embodiments, as in step 3060, to mechanically separate the liquid and solid components of the feedstock slurry. In these embodiments, a liquid portion of the feedstock slurry is filtered for residual solid particles and recycled back to the slurry preparation step 3040. A solid portion of the feedstock slurry is then advanced on to the next processing step 3070 via the feedstock transport
20 device. In other embodiments, the feedstock is maintained in slurry form for further processing.

Heavy Ion Particle Beams

25 Particles heavier than electrons can be utilized to irradiate carbohydrates or materials that include carbohydrates, e.g., cellulosic materials, lignocellulosic materials, starchy materials, or mixtures of any of these and others described herein. For example, protons, helium nuclei, argon ions, silicon ions, neon ions carbon ions, phosphorus ions, oxygen ions or nitrogen ions can be utilized. In some embodiments, particles heavier than electrons can induce higher amounts of chain scission. In some instances, positively
30 charged particles can induce higher amounts of chain scission than negatively charged particles due to their acidity.

Heavier particle beams can be generated, e.g., using linear accelerators or cyclotrons. In some embodiments, the energy of each particle of the beam is from about 1.0 MeV/atomic unit to about 6,000 MeV/atomic unit, e.g., from about 3 MeV/ atomic unit to about 4,800 MeV/atomic unit, or from about 10 MeV/atomic unit to about 1,000 MeV/atomic unit.

Electromagnetic Radiation

In embodiments in which the irradiating is performed with electromagnetic radiation, the electromagnetic radiation can have, e.g., energy per photon (in electron volts) of greater than 10^2 eV, e.g., greater than 10^3 , 10^4 , 10^5 , 10^6 , or even greater than 10^7 eV. In some embodiments, the electromagnetic radiation has energy per photon of between 10^4 and 10^7 , e.g., between 10^5 and 10^6 eV. The electromagnetic radiation can have a frequency of, e.g., greater than 10^{16} hz, greater than 10^{17} hz, 10^{18} , 10^{19} , 10^{20} , or even greater than 10^{21} hz. In some embodiments, the electromagnetic radiation has a frequency of between 10^{18} and 10^{22} hz, e.g., between 10^{19} to 10^{21} hz.

Doses

In some embodiments, the irradiating (with any radiation source or a combination of sources) is performed until the material receives a dose of at least 0.05 Mrad, e.g., at least 0.1, 0.25, 1.0, 2.5, 5.0, or 10.0 Mrad. In some embodiments, the irradiating is performed until the material receives a dose of between 1.0 Mrad and 6.0 Mrad, e.g., between 1.5 Mrad and 4.0 Mrad. In other embodiments, irradiating is performed at a dose between about 0.1 MRad and about 10 MRad, e.g., between about 0.25 MRad and about 9 MRad, between about 0.5 MRad and about 7.5 MRad or between about 0.75 MRad and about 5 MRad.

In some embodiments, the irradiating is performed at a dose rate of between 5.0 and 1500.0 kilorads/hour, e.g., between 10.0 and 750.0 kilorads/hour or between 50.0 and 350.0 kilorads/hours.

In some embodiments, two or more radiation sources are used, such as two or more ionizing radiations. For example, samples can be treated, in any order, with a beam of electrons, followed by gamma radiation and UV light having wavelengths from about

100 nm to about 280 nm. In some embodiments, samples are treated with three ionizing radiation sources, such as a beam of electrons, gamma radiation, and energetic UV light.

In one example of the use of radiation as a pretreatment, half-gallon juice cartons made of un-printed polycoated white Kraft board having a bulk density of 20 lb/ft³ are
5 used as a feedstock. Cartons are folded flat and then fed into a sequence of three shredder-shearer trains arranged in series with output from the first shearer fed as input to the second shredder, and output from the second shearer fed as input to the third shredder. The fibrous material produced by the shredder-shearer train can be sprayed with water and processed through a pellet mill operating at room temperature. The densified pellets
10 can be placed in a glass ampoule which is evacuated under high vacuum and then back-filled with argon gas. The ampoule is sealed under argon. Alternatively, in another example, the ampoule is sealed under an atmosphere of air. The pellets in the ampoule are irradiated with gamma radiation for about 3 hours at a dose rate of about 1 Mrad per hour to provide an irradiated material in which the cellulose has a lower molecular weight
15 than the starting material.

Additives to Enhance Molecular Weight Breakdown During Irradiation

In some embodiments, prior to irradiation, various materials, e.g., solids or liquids, can be added to the biomass to enhance molecular weight reduction. In those
20 instances in which a liquid is utilized, the liquid can be in contact with outer surfaces of the biomass and/or the liquid can be in interior portions of the biomass, e.g., infused into the biomass.

For example, the material can be a neutral weak base, such as alanine, ammonia, ammonia/water mixture, e.g., 25 percent by weight ammonia in water, water, methyl
25 amine, dimethyl amine, trimethyl amine, pyridine, or a anionic base, such as a salt of acetic acid (e.g., sodium acetate), sodium carbonate, sodium bicarbonate or a salt of an ion of hydrogen sulfide (e.g., sodium hydrosulfide).

Alternatively, the material can be a neutral weak acid, such as formic acid, acetic acid, trichloroacetic acid, water, hydrogen sulfide or a cationic acid, such as an
30 ammonium salt.

Quenching and Controlled Functionalization of Biomass

After treatment with one or more ionizing radiations, such as photonic radiation (e.g., X-rays or gamma-rays), e-beam radiation or particles heavier than electrons that are positively or negatively charged (e.g., protons or carbon ions), any of the carbohydrate-containing materials or mixtures described herein become ionized; that is, they include radicals at levels that are detectable with an electron spin resonance spectrometer. The current limit of detection of the radicals is about 10^{14} spins at room temperature. After ionization, any biomass material that has been ionized can be quenched to reduce the level of radicals in the ionized biomass, e.g., such that the radicals are no longer detectable with the electron spin resonance spectrometer. For example, the radicals can be quenched by the application of a sufficient pressure to the biomass and/or by utilizing a fluid in contact with the ionized biomass, such as a gas or liquid, that reacts with (quenches) the radicals. Using a gas or liquid to at least aid in the quenching of the radicals can be used to functionalize the ionized biomass with a desired amount and kind of functional groups, such as carboxylic acid groups, enol groups, aldehyde groups, nitro groups, nitrile groups, amino groups, alkyl amino groups, alkyl groups, chloroalkyl groups or chlorofluoroalkyl groups. In some instances, such quenching can improve the stability of some of the ionized biomass materials. For example, quenching can improve the resistance of the biomass to oxidation. Functionalization by quenching can also improve the solubility of any biomass described herein, can improve its thermal stability, and can improve material utilization by various microorganisms. For example, the functional groups imparted to the biomass material by the quenching can act as receptor sites for attachment by microorganisms, e.g., to enhance cellulose hydrolysis by various microorganisms.

FIG. 11A illustrates changing a molecular and/or a supramolecular structure of a biomass feedstock by pretreating the biomass feedstock with ionizing radiation, such as with electrons or ions of sufficient energy to ionize the biomass feedstock, to provide a first level of radicals. As shown in FIG. 11A, if ionized biomass remains in the atmosphere, it will be oxidized, such as to an extent that carboxylic acid groups are generated by reacting with the atmospheric oxygen. In some instances with some materials, such oxidation is desired because it can aid in the further breakdown in

molecular weight of the carbohydrate-containing biomass, and the oxidation groups, e.g., carboxylic acid groups can be helpful for solubility and microorganism utilization in some instances. However, since the radicals can “live” for some time after irradiation, e.g., longer than 1 day, 5 days, 30 days, 3 months, 6 months or even longer than 1 year, materials properties can continue to change over time, which in some instances, can be undesirable. Detecting radicals in irradiated samples by electron spin resonance spectroscopy and radical lifetimes in such samples is discussed in Bartolotta et al., Physics in Medicine and Biology, 46 (2001), 461-471 and in Bartolotta et al., Radiation Protection Dosimetry, Vol. 84, Nos. 1-4, pp. 293-296 (1999) which are attached hereto as Appendix F and Appendix G, respectively. As shown in FIG. 11A, the ionized biomass can be quenched to functionalize and/or to stabilize the ionized biomass. At any point, e.g., when the material is “alive”, “partially alive” or fully quenched, the pretreated biomass can be converted into a product, e.g., a fuel, a food, or a composite.

In some embodiments, the quenching includes an application of pressure to the biomass, such as by mechanically deforming the biomass, e.g., directly mechanically compressing the biomass in one, two, or three dimensions, or applying pressure to a fluid in which the biomass is immersed, e.g., isostatic pressing. In such instances, the deformation of the material itself brings radicals, which are often trapped in crystalline domains, in close enough proximity so that the radicals can recombine, or react with another group. In some instances, the pressure is applied together with the application of heat, such as a sufficient quantity of heat to elevate the temperature of the biomass to above a melting point or softening point of a component of the biomass, such as lignin, cellulose or hemicellulose. Heat can improve molecular mobility in the polymeric material, which can aid in the quenching of the radicals. When pressure is utilized to quench, the pressure can be greater than about 1000 psi, such as greater than about 1250 psi, 1450 psi, 3625 psi, 5075 psi, 7250 psi, 10000 psi or even greater than 15000 psi.

In some embodiments, quenching includes contacting the biomass with a fluid, such as a liquid or gas, e.g., a gas capable of reacting with the radicals, such as acetylene or a mixture of acetylene in nitrogen, ethylene, chlorinated ethylenes or chlorofluoroethylenes, propylene or mixtures of these gases. In other particular embodiments, quenching includes contacting the biomass with a liquid, e.g., a liquid

soluble in, or at least capable of penetrating into the biomass and reacting with the radicals, such as a diene, such as 1,5-cyclooctadiene. In some specific embodiments, the quenching includes contacting the biomass with an antioxidant, such as Vitamin E. If desired, the biomass feedstock can include an antioxidant dispersed therein, and the quenching can come from contacting the antioxidant dispersed in the biomass feedstock with the radicals.

Other methods for quenching are possible. For example, any method for quenching radicals in polymeric materials described in Muratoglu et al., U.S. Patent Application Publication No. 2008/0067724 and Muratoglu et al., U.S. Patent No. 7,166,650, which are attached as Appendix H and Appendix I, respectively, can be utilized for quenching any ionized biomass material described herein. Furthermore any quenching agent (described as a "sensitizing agent" in the above-noted Muratoglu disclosures) and/or any antioxidant described in either Muratoglu reference can be utilized to quench any ionized biomass material.

Functionalization can be enhanced by utilizing heavy charged ions, such as any of the heavier ions described herein. For example, if it is desired to enhance oxidation, charged oxygen ions can be utilized for the irradiation. If nitrogen functional groups are desired, nitrogen ions or anions that includes nitrogen can be utilized. Likewise, if sulfur or phosphorus groups are desired, sulfur or phosphorus ions can be used in the irradiation.

In some embodiments, after quenching any of the quenched ionized materials described herein can be further treated with one or more of radiation, such as ionizing or non-ionizing radiation, sonication, pyrolysis, and oxidation for additional molecular and/or supramolecular structure change.

25

Particle Beam Exposure in Fluids

In some cases, the cellulosic or lignocellulosic materials can be exposed to a particle beam in the presence of one or more additional fluids (e.g., gases and/or liquids). Exposure of a material to a particle beam in the presence of one or more additional fluids can increase the efficiency of the treatment.

30

In some embodiments, the material is exposed to a particle beam in the presence of a fluid such as air. Particles accelerated in any one or more of the types of accelerators disclosed herein (or another type of accelerator) are coupled out of the accelerator via an output port (e.g., a thin membrane such as a metal foil), pass through a volume of space occupied by the fluid, and are then incident on the material. In addition to directly treating the material, some of the particles generate additional chemical species by interacting with fluid particles (e.g., ions and/or radicals generated from various constituents of air, such as ozone and oxides of nitrogen). These generated chemical species can also interact with the material, and can act as initiators for a variety of different chemical bond-breaking reactions in the material. For example, any oxidant produced can oxidize the material, which can result in molecular weight reduction.

In certain embodiments, additional fluids can be selectively introduced into the path of a particle beam before the beam is incident on the material. As discussed above, reactions between the particles of the beam and the particles of the introduced fluids can generate additional chemical species, which react with the material and can assist in functionalizing the material, and/or otherwise selectively altering certain properties of the material. The one or more additional fluids can be directed into the path of the beam from a supply tube, for example. The direction and flow rate of the fluid(s) that is/are introduced can be selected according to a desired exposure rate and/or direction to control the efficiency of the overall treatment, including effects that result from both particle-based treatment and effects that are due to the interaction of dynamically generated species from the introduced fluid with the material. In addition to air, exemplary fluids that can be introduced into the ion beam include oxygen, nitrogen, one or more noble gases, one or more halogens, and hydrogen.

Irradiating Low Bulk Density Biomass Materials and Cooling Irradiated Biomass

During treatment of biomass materials with ionizing radiation, especially at high dose rates, such as at rates greater than 0.15 Mrad per second, e.g., 0.25 Mrad/s, 0.35 Mrad/s, 0.5 Mrad/s, 0.75 Mrad/s or even greater than 1 Mrad/sec, biomass materials can retain significant quantities of heat so that the temperature of the biomass materials becomes elevated. While higher temperatures can, in some embodiments, be

advantageous, e.g., when a faster reaction rate is desired, it is advantageous to control the heating of the biomass to retain control over the chemical reactions initiated by the ionizing radiation, such as crosslinking, chain scission and/or grafting, e.g., to maintain process control. Low bulk density materials, such as those having a bulk density of less than about 0.4 g/cm³, e.g., less than about 0.35, 0.25 or less about 0.15 g/cm³, especially when combined with materials that have thin cross-sections, such as fibers having small transverse dimensions, are generally easier to cool. In addition, photons and particles can generally penetrate further into and through materials having a relatively low bulk density, which can allow for the processing of larger volumes of materials at higher rates, and can allow for the use of photons and particles that having lower energies, e.g., 0.25 MeV, 0.5 MeV, 0.75 MeV or 1.0 MeV, which can reduce safety shielding requirements. Many of the biomass materials described herein can be processed in one or more of the systems shown in FIGS. 11B, 11C, 11D and 11E, which are described below. The systems shown allow one or more types of ionizing radiation, such as relativistic electrons or electrons in combination with X-rays, to be applied to low bulk density biomass materials at high dose rates, such as at a rate greater than 1.0, 1.5, 2.5 Mrad/s or even greater than about 5.0 Mrad/s, and then to allow for cooling of the biomass prior to applying radiation for a second, third, fourth, fifth, sixth, seventh, eighth, ninth or even a tenth time.

For example, in one method of changing a molecular and/or a supramolecular structure of a biomass feedstock, the biomass is pretreated at a first temperature with ionizing radiation, such as photons, electrons or ions (e.g., singularly or multiply charged cations or anions), for a sufficient time and/or a sufficient dose to elevate the biomass feedstock to a second temperature higher than the first temperature. The pretreated biomass is then cooled to a third temperature below the second temperature. Finally, if desired, the cooled biomass can be treated one or more times with radiation, e.g., with ionizing radiation. If desired, cooling can be applied to the biomass after and/or during each radiation treatment.

The biomass feedstock can be physically prepared as discussed above, e.g., by reducing one or more dimensions of individual pieces of the biomass feedstock so that

the feedstock can be more efficiently processed, e.g., more easily cooled and/or more easily penetrated by an ionizing radiation.

In some implementations, the ionizing radiation is applied at a total dose of less than 25 Mrad or less than 10 Mrad, such as less than 5 Mrad or less than 2.5 Mrad, and at
5 a rate of more than 0.25 Mrad per second, such as more than 0.5, 0.75 or greater than 1.0 Mrad/s, prior to cooling the biomass.

The pretreating of the biomass feedstock with ionizing radiation can be performed as the biomass feedstock is being pneumatically conveyed in a fluid, such as a gas, e.g., nitrogen or air. To aid in molecular weight breakdown and/or functionalization of
10 the materials, the gas can be saturated with any swelling agent described herein and/or water vapor. For example, acidic water vapor can be utilized. To aid in molecular weight breakdown, the water can be acidified with an organic acid, such as formic, or acetic acid, or a mineral acid, such as sulfuric or hydrochloric acid.

The pretreating of the biomass feedstock with ionizing radiation can be performed
15 as the biomass feedstock falls under the influence of gravity. This procedure can effectively reduce the bulk density of the biomass feedstock as it is being processed and can aid in the cooling of the biomass feedstock. For example, the biomass can be conveyed from a first belt at a first height above the ground and then can be captured by a second belt at a second level above the ground lower than the first level. For example, in
20 some embodiments, the trailing edge of the first belt and the leading edge of the second belt define a gap. Advantageously, the ionizing radiation, such as a beam of electrons, protons, or other ions, can be applied at the gap to prevent damage to the biomass conveyance system.

Cooling of the biomass can include contacting the biomass with a fluid, such as a
25 gas, at a temperature below the first or second temperature, such as gaseous nitrogen at or about 77 K. Even water, such as water at a temperature below nominal room temperature (e.g., 25 degrees Celsius) can be utilized.

Often advantageously, the biomass feedstock has internal fibers, and prior to irradiation with the ionizing radiation, the biomass feedstock has been sheared to an
30 extent that its internal fibers are substantially exposed. This shearing can provide a low bulk density material having small cross-sectional dimensions, which can aid in the

breakdown and/or functionalization of the biomass. For example, in some embodiments, the biomass is or includes discrete fibers and/or particles having a maximum dimension of not more than about 0.5 mm, such as not more than about 0.25 mm, not more than about 0.1 mm or not more than about 0.05 mm.

5 In some embodiments, the biomass feedstock to which the ionizing radiation is applied has a bulk density of less than about 0.35 g/cm^3 , such as less than about 0.3, 0.25, 0.20, or less than about 0.15 g/cm^3 during the application of the ionizing radiation. In such embodiments, the biomass feedstock can be cooled, and then ionizing radiation can be applied to the cooled biomass. In some advantageous embodiments, the biomass
10 feedstock is or includes discrete fibers and/or particles having a maximum dimension of not more than about 0.5 mm, such as not more than about 0.25 mm, not more than about 0.1 mm, not more than about 0.05 mm, or not more than about 0.025 mm.

FIGS. 11B and 11C show a fibrous material generating, treating, conveying and irradiating device 1170 (shielding not illustrated in the drawings). In operation, paper
15 sheet 1173, e.g., scrap bleached Kraft paper sheet, is supplied from a roll 1172 and delivered to a fiberizing apparatus 1174, such as a rotary shearer. The sheet 1173 is converted into fibrous material 1112 and is delivered to a fiber-loading zone 1180 by conveyer 1178. If desired, the fibers of the fibrous material can be separated, e.g., by screening, into fractions having different L/D ratios. In some embodiments, the fibrous
20 material 1112 of generally a low bulk density and advantageously thin cross-section, is delivered continuously to zone 1180; in other embodiments, the fibrous material is delivered in batches. A blower 1182 in loop 1184 is positioned adjacent to the fiber-loading zone 1180 and is capable of moving a fluid medium, e.g., air, at a velocity and volume sufficient to pneumatically circulate the fibrous material 1112 in a direction
25 indicated by arrow 1188 through loop 1184.

In some embodiments, the velocity of air traveling in the loop is sufficient to uniformly disperse and transport the fibrous material around the entire loop 1184. In some embodiments, the velocity of flow is greater than 2,500 feet/minute, e.g., 5,000 feet/minute, 6,000 feet/minute or more, e.g., 7,500 feet/minute or 8,500 feet/minute.

30 The entrained fibrous material 1112 traversing the loop passes an application zone 1190, which forms part of loop 1184. Here, any desired additives described herein are

applied, such as a liquid, such as water, which may be acidified or made basic. In operation, application zone 1190 applies an additive, such as a liquid solution 1196, to the circulating fibrous material via nozzles 98, 99 and 11100. When a liquid is applied, the nozzles produce an atomized spray or mist, which impacts the fibers as the fibers pass in
5 proximity to the nozzles. Valve 11102 is operated to control the flow of liquid to the respective nozzles 1198, 1199, and 11100. After a desired quantity of additive is applied, the valve 11102 is closed.

In some embodiments, the application zone 1190 is two to one hundred feet long or more, e.g., 125 feet, 150 feet, 250 feet long or more, e.g., 500 feet long. Longer
10 application zones allow for application of liquid over a longer period of time during passage of fibrous material through application zone 1190. In some embodiments, the nozzles are spaced apart, e.g., by from about three to about four feet, along the length of loop 1184.

As the fibrous material moves in loop 1184 and through the irradiating portion of
15 the loop 11107 that includes a horn 11109 for delivering ionizing radiation, ionizing radiation is applied to the fibrous material (shielding is not shown).

As the irradiated fibrous material moves around loop 1184, it cools by the action of gases, such as air, circulating at high speeds in the loop. The material is bathed in reactive gases, such as ozone and/or oxides of nitrogen, that are produced from the action
20 of the ionizing radiation on the circulating gases, such as air. After passing through the irradiating portion 11107, a cooling fluid, such as a liquid (e.g., water) or a gas, such as liquid nitrogen at 77 K, can be injected into loop 1184 to aid in the cooling of the fibrous material. This process can be repeated more than one time if desired, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 times or more, e.g., 15 times, to deliver the desired dose to the fibrous material.
25 While, as shown, the long axis of the horn is along the direction of flow, in some implementations, the long axis of the horn is transverse to the direction of the flow. In some implementations, a beam of electrons is utilized as a principal ionizing radiation source and X-rays as a secondary ionizing radiation source. X-rays can be generated by having a metal target, such as a tantalum target 11111, on the inside of loop 1184 such
30 that when electrons strike the target, X-rays are emitted.

After a desired dose is delivered to the fibrous material, the fibrous material can be removed from loop 1184 via a separator 11112, which is selectively connected to loop 1184 by section 11114 and gate valve 11116. When valve 11116 is opened, another valve is also opened to allow air to enter the loop 1184 to compensate for air exiting through separator 11112.

FIG. 11D shows a fluidized bed fibrous irradiating device 11121 with shielding. Fibrous material in a fluid, such as a gas, such as air under pressure, is delivered to a shielded containment vessel 11123 via piping 11125 and into a shielded fluidized bed portion 11127. Counter-current streams 11131 of fluid, such as a gas, and transverse streams 11133 of fluid, such as a gas, that can be the same as or different from the fluid delivered counter-currently, combine to cause turbulence in the bed portion. Ionizing radiation is applied to the fluidized bed portion as the fibrous material is conveyed through the bed portion. For example, as shown, three beams of electrons from three Rhodotron® machines 11135, 11136 and 11137 can be utilized. Advantageously, each beam can penetrate into the fluidized bed a different depth and/or each beam can emit electrons of a different energy, such as 1, 3, and 5 MeV. As the irradiated fibrous material moves through the system, it cools by the action of gases, such as air, circulating at high speeds in the system and it is bathed in reactive gases, such as ozone and/or oxides of nitrogen, that are produced from the action of the ionizing radiation on the circulating gases, such as air. If desired, the process can be repeated a desired number of times until the fibrous material has received a desired dose. While the fluidized bed has been illustrated such that its long axis is horizontal with the ground, in other implementations, the long axis of the bed is perpendicular to the ground so that the fibrous material falls under the influence of gravity.

FIG. 11E shows another fibrous material conveying and irradiating device 11140 without shielding. Fibrous material 11144 is delivered from a bin 11142 to a first conveyer 11150 at a first level above the ground and then the material is transferred to a second conveyer 11152 at a lower height than the first conveyer. The trailing edge 11160 of the first conveyer and the leading edge 11161 of the second conveyer 11152 define a gap with a spacing S. For example, the spacing S can be between 4 inches and about 24 inches. Material 11144 has enough momentum to free fall under gravity and then to be

captured by the second conveyer 11152 without falling into the gap. During the free fall, ionizing radiation is applied to the material. This arrangement can be advantageous in that the ionizing radiation is less likely to damage the conveying system because the conveying system is not directly contacted by the radiation.

5 After the material passes through the irradiating portion, a cooling fluid, such as a liquid (e.g., water) or a gas, such as liquid nitrogen at 77 K, can be applied to the material to aid in the cooling of the fibrous material. This process can be repeated more than one time if desired, e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10 times or more, e.g., 15 times, to deliver the desired dose to the fibrous material. While, as shown, the long axis of the horn is
10 transverse to the direction of the material flow, other beam arrangements are possible. In some implementations, a beam of electrons is utilized as a principal ionizing radiation source and X-rays as a secondary ionizing radiation source. X-rays can be generated by having a metal target, such as a tantalum target, in the gap on the opposite side of the material, such that as the electrons that pass through the material they strike the target,
15 generating X-rays.

Sonication and other Biomass Disruption Processes

One or more sonication processing sequences can be used to process raw feedstock from a wide variety of different sources to extract useful substances from the feedstock, and to provide partially degraded organic material which functions as input to
20 further processing steps and/or sequences. Sonication can reduce the molecular weight and/or crystallinity of feedstock, such as one or more of any of the biomass materials described herein, e.g., one or more carbohydrate sources, such as cellulosic or lignocellulosic materials, or starchy materials.

Referring again to FIG. 8, in one method, a first material 2 that includes cellulose
25 having a first number average molecular weight ($\overline{M}_{N1}$) is dispersed in a medium, such as water, and sonicated and/or otherwise cavitated, to provide a second material 3 that includes cellulose having a second number average molecular weight ($\overline{M}_{N2}$) lower than the first number average molecular weight. The second material (or the first and second material in certain embodiments) can be combined with a microorganism (e.g., a
30 bacterium or a yeast) that can utilize the second and/or first material to produce a fuel 5

that is or includes hydrogen, an alcohol, an organic acid, a hydrocarbon or mixtures of any of these.

Since the second material has cellulose having a reduced molecular weight relative to the first material, and in some instances, a reduced crystallinity as well, the second material is generally more dispersible, swellable, and/or soluble in a solution containing the microorganism, e.g., at a concentration of greater than 10^6 microorganisms/mL. These properties make the second material more susceptible to chemical, enzymatic, and/or microbial attack relative to the first material 2, which can greatly improve the production rate and/or production level of a desired product, e.g., ethanol. Sonication can also sterilize the materials, but should not be used while the microorganisms are supposed to be alive.

In some embodiments, the second number average molecular weight ($^T M_{N2}$) is lower than the first number average molecular weight ($^T M_{N1}$) by more than about 10 percent, e.g., 15, 20, 25, 30, 35, 40, 50 percent, 60 percent, or even more than about 75 percent.

In some instances, the second material has cellulose that has as crystallinity ($^T C_2$) that is lower than the crystallinity ($^T C_1$) of the cellulose of the first material. For example, ($^T C_2$) can be lower than ($^T C_1$) by more than about 10 percent, e.g., 15, 20, 25, 30, 35, 40, or even more than about 50 percent.

In some embodiments, the starting crystallinity index (prior to sonication) is from about 40 to about 87.5 percent, e.g., from about 50 to about 75 percent or from about 60 to about 70 percent, and the crystallinity index after sonication is from about 10 to about 50 percent, e.g., from about 15 to about 45 percent or from about 20 to about 40 percent. However, in certain embodiments, e.g., after extensive sonication, it is possible to have a crystallinity index of lower than 5 percent. In some embodiments, the material after sonication is substantially amorphous.

In some embodiments, the starting number average molecular weight (prior to sonication) is from about 200,000 to about 3,200,000, e.g., from about 250,000 to about 1,000,000 or from about 250,000 to about 700,000, and the number average molecular weight after sonication is from about 50,000 to about 200,000, e.g., from about 60,000 to about 150,000 or from about 70,000 to about 125,000. However, in some embodiments,

e.g., after extensive sonication, it is possible to have a number average molecular weight of less than about 10,000 or even less than about 5,000.

In some embodiments, the second material can have a level of oxidation ($^T\text{O}_2$) that is higher than the level of oxidation ($^T\text{O}_1$) of the first material. A higher level of oxidation of the material can aid in its dispersibility, swellability and/or solubility, further enhancing the materials susceptibility to chemical, enzymatic or microbial attack. In some embodiments, to increase the level of the oxidation of the second material relative to the first material, the sonication is performed in an oxidizing medium, producing a second material that is more oxidized than the first material. For example, the second material can have more hydroxyl groups, aldehyde groups, ketone groups, ester groups or carboxylic acid groups, which can increase its hydrophilicity.

In some embodiments, the sonication medium is an aqueous medium. If desired, the medium can include an oxidant, such as a peroxide (e.g., hydrogen peroxide), a dispersing agent and/or a buffer. Examples of dispersing agents include ionic dispersing agents, e.g., sodium lauryl sulfate, and non-ionic dispersing agents, e.g., poly(ethylene glycol).

In other embodiments, the sonication medium is non-aqueous. For example, the sonication can be performed in a hydrocarbon, e.g., toluene or heptane, an ether, e.g., diethyl ether or tetrahydrofuran, or even in a liquefied gas such as argon, xenon, or nitrogen.

Without wishing to be bound by any particular theory, it is believed that sonication breaks bonds in the cellulose by creating bubbles in the medium containing the cellulose, which grow and then violently collapse. During the collapse of the bubble, which can take place in less than a nanosecond, the implosive force raises the local temperature within the bubble to about 5100 K (even higher in some instance; see, e.g., Suslick et al., Nature 434, 52-55) and generates pressures of from a few hundred atmospheres to over 1000 atmospheres or more. It is these high temperatures and pressures that break the bonds. In addition, without wishing to be bound by any particular theory, it is believed that reduced crystallinity arises, at least in part, from the extremely high cooling rates during collapse of the bubbles, which can be greater than about 10^{11} K/second. The high cooling rates generally do not allow the cellulose to

organize and crystallize, resulting in materials that have reduced crystallinity. Ultrasonic systems and sonochemistry are discussed in, e.g., Olli et al., U.S. Patent No. 5,766,764; Roberts, U.S. Patent No. 5,828,156; Mason, Chemistry with Ultrasound, Elsevier, Oxford, (1990); Suslick (editor), Ultrasound: its Chemical, Physical and Biological Effects, VCH, Weinheim, (1988); Price, "Current Trends in Sonochemistry" Royal Society of Chemistry, Cambridge, (1992); Suslick et al., Ann. Rev. Mater. Sci. 29, 295, (1999); Suslick et al., Nature 353, 414 (1991); Hiller et al., Phys. Rev. Lett. 69, 1182 (1992); Barber et al., Nature, 352, 414 (1991); Suslick et al., J. Am. Chem. Soc., 108, 5641 (1986); Tang et al., Chem. Comm., 2119 (2000); Wang et al., Advanced Mater., 12, 1137 (2000); Landau et al., J. of Catalysis, 201, 22 (2001); Perkash et al., Chem. Comm., 988 (2001); Nikitenko et al., Angew. Chem. Inter. Ed. (December 2001); Shafi et al., J. Phys. Chem B 103, 3358 (1999); Avivi et al., J. Amer. Chem. Soc. 121, 4196 (1999); and Avivi et al., J. Amer. Chem. Soc. 122, 4331 (2000).

Sonication Systems

FIG. 12 shows a general system in which a cellulosic material stream 1210 is mixed with a water stream 1212 in a reservoir 1214 to form a process stream 1216. A first pump 1218 draws process stream 1216 from reservoir 1214 and toward a flow cell 1224. Ultrasonic transducer 1226 transmits ultrasonic energy into process stream 1216 as the process stream flows through flow cell 1224. A second pump 1230 draws process stream 1216 from flow cell 1224 and toward subsequent processing.

Reservoir 1214 includes a first intake 1232 and a second intake 1234 in fluid communication with a volume 1236. A conveyor (not shown) delivers cellulosic material stream 1210 to reservoir 1214 through first intake 1232. Water stream 1212 enters reservoir 1214 through second intake 1234. In some embodiments, water stream 1212 enters volume 1236 along a tangent establishing a swirling flow within volume 1236. In certain embodiments, cellulosic material stream 1210 and water stream 1212 can be introduced into volume 1236 along opposing axes to enhance mixing within the volume.

Valve 1238 controls the flow of water stream 1212 through second intake 1232 to produce a desired ratio of cellulosic material to water (e.g., approximately 10% cellulosic material, weight by volume). For example, 2000 tons/day of cellulosic material can be

combined with 1 million to 1.5 million gallons/day, e.g., 1.25 million gallons/day, of water.

Mixing of cellulosic material and water in reservoir 1214 is controlled by the size of volume 1236 and the flow rates of cellulosic material and water into the volume. In some embodiments, volume 1236 is sized to create a minimum mixing residence time for the cellulosic material and water. For example, when 2000 tons/day of cellulosic material and 1.25 million gallons/day of water are flowing through reservoir 1214, volume 1236 can be about 32,000 gallons to produce a minimum mixing residence time of about 15 minutes.

Reservoir 1214 includes a mixer 1240 in fluid communication with volume 1236. Mixer 1240 agitates the contents of volume 1236 to disperse cellulosic material throughout the water in the volume. For example, mixer 1240 can be a rotating vane disposed in reservoir 1214. In some embodiments, mixer 1240 disperses the cellulosic material substantially uniformly throughout the water.

Reservoir 1214 further includes an exit 1242 in fluid communication with volume 1236 and process stream 1216. The mixture of cellulosic material and water in volume 1236 flows out of reservoir 1214 via exit 1242. Exit 1242 is arranged near the bottom of reservoir 1214 to allow gravity to pull the mixture of cellulosic material and water out of reservoir 1214 and into process stream 1216.

First pump 1218 (e.g., any of several recessed impeller vortex pumps made by Essco Pumps & Controls, Los Angeles, California) moves the contents of process stream 1216 toward flow cell 1224. In some embodiments, first pump 1218 agitates the contents of process stream 1216 such that the mixture of cellulosic material and water is substantially uniform at inlet 1220 of flow cell 1224. For example, first pump 1218 agitates process stream 1216 to create a turbulent flow that persists along the process stream between the first pump and inlet 1220 of flow cell 1224.

Flow cell 1224 includes a reactor volume 1244 in fluid communication with inlet 1220 and outlet 1222. In some embodiments, reactor volume 1244 is a stainless steel tube capable of withstanding elevated pressures (e.g., 10 bars). In addition or in the alternative, reactor volume 1244 includes a rectangular cross section.

Flow cell 1224 further includes a heat exchanger 1246 in thermal communication with at least a portion of reactor volume 1244. Cooling fluid 1248 (e.g., water) flows into heat exchanger 1246 and absorbs heat generated when process stream 1216 is sonicated in reactor volume 1244. In some embodiments, the flow rate and/or the temperature of cooling fluid 1248 into heat exchanger 1246 is controlled to maintain an approximately constant temperature in reactor volume 1244. In some embodiments, the temperature of reactor volume 1244 is maintained at 20 to 50 °C, e.g., 25, 30, 35, 40, or 45 °C. Additionally or alternatively, heat transferred to cooling fluid 1248 from reactor volume 1244 can be used in other parts of the overall process.

An adapter section 1226 creates fluid communication between reactor volume 1244 and a booster 1250 coupled (e.g., mechanically coupled using a flange) to ultrasonic transducer 1226. For example, adapter section 1226 can include a flange and O-ring assembly arranged to create a leak tight connection between reactor volume 1244 and booster 1250. In some embodiments, ultrasonic transducer 1226 is a high-powered ultrasonic transducer made by Hielscher Ultrasonics of Teltow, Germany.

In operation, a generator 1252 delivers electricity to ultrasonic transducer 1252. Ultrasonic transducer 1226 includes a piezoelectric element that converts the electrical energy into sound in the ultrasonic range. In some embodiments, the materials are sonicated using sound having a frequency of from about 16 kHz to about 110 kHz, e.g., from about 18 kHz to about 75 kHz or from about 20 kHz to about 40 kHz. (e.g., sound having a frequency of 20 kHz to 40 kHz). In some implementations, sonication is performed, for example, at a frequency of between about 15 kHz and about 25 kHz, such as between about 18 kHz and 22 kHz. In specific embodiments, sonicating can be performed utilizing a 1 KW or larger horn, e.g., a 2, 3, 4, 5, or even a 10 KW horn.

The ultrasonic energy is then delivered to the working medium through booster 1248. The ultrasonic energy traveling through booster 1248 in reactor volume 1244 creates a series of compressions and rarefactions in process stream 1216 with an intensity sufficient to create cavitation in process stream 1216. Cavitation disaggregates the cellulosic material dispersed in process stream 1216. Cavitation also produces free radicals in the water of process stream 1216. These free radicals act to further break down the cellulosic material in process stream 1216.

In general, 5 to 4000 MJ/m³, e.g., 10, 25, 50, 100, 250, 500, 750, 1000, 2000, or 3000 MJ/m³, of ultrasonic energy is applied to process stream 16 flowing at a rate of about 0.2 m³/s (about 3200 gallons/min). After exposure to ultrasonic energy in reactor volume 1244, process stream 1216 exits flow cell 1224 through outlet 1222. Second pump 1230 moves process stream 1216 to subsequent processing (e.g., any of several recessed impeller vortex pumps made by Essco Pumps & Controls, Los Angeles, California).

While certain embodiments have been described, other embodiments are possible.

As an example, while process stream 1216 has been described as a single flow path, other arrangements are possible. In some embodiments for example, process stream 1216 includes multiple parallel flow paths (e.g., flowing at a rate of 10 gallon/min). In addition or in the alternative, the multiple parallel flow paths of process stream 1216 flow into separate flow cells and are sonicated in parallel (e.g., using a plurality of 16 kW ultrasonic transducers).

As another example, while a single ultrasonic transducer 1226 has been described as being coupled to flow cell 1224, other arrangements are possible. In some embodiments, a plurality of ultrasonic transducers 1226 are arranged in flow cell 1224 (e.g., ten ultrasonic transducers can be arranged in a flow cell 1224). In some embodiments, the sound waves generated by each of the plurality of ultrasonic transducers 1226 are timed (e.g., synchronized out of phase with one another) to enhance the cavitation acting upon process stream 1216.

As another example, while a single flow cell 1224 has been described, other arrangements are possible. In some embodiments, second pump 1230 moves process stream to a second flow cell where a second booster and ultrasonic transducer further sonicate process stream 1216.

As still another example, while reactor volume 1244 has been described as a closed volume, reactor volume 1244 is open to ambient conditions in certain embodiments. In such embodiments, sonication pretreatment can be performed substantially simultaneously with other pretreatment techniques. For example, ultrasonic energy can be applied to process stream 1216 in reactor volume 1244 while electron beams are simultaneously introduced into process stream 1216.

As another example, while a flow-through process has been described, other arrangements are possible. In some embodiments, sonication can be performed in a batch process. For example, a volume can be filled with a 10% (weight by volume) mixture of cellulosic material in water and exposed to sound with intensity from about 50 W/cm² to about 600 W/cm², e.g., from about 75 W/cm² to about 300 W/cm² or from about 95 W/cm² to about 200 W/cm². Additionally or alternatively, the mixture in the volume can be sonicated from about 1 hour to about 24 hours, e.g., from about 1.5 hours to about 12 hours, or from about 2 hours to about 10 hours. In certain embodiments, the material is sonicated for a pre-determined time, and then allowed to stand for a second pre-determined time before sonicating again.

Referring now to FIG. 13, in some embodiments, two electroacoustic transducers are mechanically coupled to a single horn. As shown, a pair of piezoelectric transducers 60 and 62 is coupled to a slotted bar horn 64 by respective intermediate coupling horns 70 and 72, the latter also being known as booster horns. The mechanical vibrations provided by the transducers, responsive to high frequency electrical energy applied thereto, are transmitted to the respective coupling horns, which may be constructed to provide a mechanical gain, such as a ratio of 1 to 1.2. The horns are provided with a respective mounting flange 74 and 76 for supporting the transducer and horn assembly in a stationary housing.

The vibrations transmitted from the transducers through the coupling or booster horns are coupled to the input surface 78 of the horn and are transmitted through the horn to the oppositely disposed output surface 80, which, during operation, is in forced engagement with a workpiece (not shown) to which the vibrations are applied.

The high frequency electrical energy provided by the power supply 82 is fed to each of the transducers, electrically connected in parallel, via a balancing transformer 84 and a respective series connected capacitor 86 and 90, one capacitor connected in series with the electrical connection to each of the transducers. The balancing transformer is known also as "balun" standing for "balancing unit." The balancing transformer includes a magnetic core 92 and a pair of identical windings 94 and 96, also termed the primary winding and secondary winding, respectively.

In some embodiments, the transducers include commercially available piezoelectric transducers, such as Branson Ultrasonics Corporation models 105 or 502, each designed for operation at 20 kHz and a maximum power rating of 3 kW. The energizing voltage for providing maximum motional excursion at the output surface of the transducer is 930 volt rms. The current flow through a transducer may vary between zero and 3.5 ampere depending on the load impedance. At 930 volt rms the output motion is approximately 20 microns. The maximum difference in terminal voltage for the same motional amplitude, therefore, can be 186 volt. Such a voltage difference can give rise to large circulating currents flowing between the transducers. The balancing unit 430 assures a balanced condition by providing equal current flow through the transducers, hence eliminating the possibility of circulating currents. The wire size of the windings must be selected for the full load current noted above and the maximum voltage appearing across a winding input is 93 volt.

While ultrasonic transducer 1226 has been described as including one or more piezoelectric active elements to create ultrasonic energy, other arrangements are possible. In some embodiments, ultrasonic transducer 1226 includes active elements made of other types of magnetostrictive materials (e.g., ferrous metals). Design and operation of such a high-powered ultrasonic transducer is discussed in Hansen et al., U.S. Patent No. 6,624,539. In some embodiments, ultrasonic energy is transferred to process stream 16 through an electrohydraulic system.

While ultrasonic transducer 1226 has been described as using the electromagnetic response of magnetostrictive materials to produce ultrasonic energy, other arrangements are possible. In some embodiments, acoustic energy in the form of an intense shock wave can be applied directly to process stream 16 using an underwater spark. In some embodiments, ultrasonic energy is transferred to process stream 16 through a thermohydraulic system. For example, acoustic waves of high energy density can be produced by applying power across an enclosed volume of electrolyte, thereby heating the enclosed volume and producing a pressure rise that is subsequently transmitted through a sound propagation medium (e.g., process stream 1216). Design and operation of such a thermohydraulic transducer is discussed in Hartmann et al., U.S. Patent 6,383,152.

Some embodiments use a high frequency, rotor-stator device. This type of device produces high-shear, microcavitation forces, which can disintegrate biomass in contact with such forces. Two commercially available high-frequency, rotor-stator dispersion devices are the SupratonTM devices manufactured by Krupp Industrietechnik GmbH and marketed by Dorr-Oliver Deutschland GmbH of Connecticut, and the DispaxTM devices
5 manufactured and marketed by Ika-Works, Inc. of Cincinnati, Ohio. Operation of such a microcavitation device is discussed in Stuart, U.S. Patent No. 5,370,999.

In another biomass disruption technique, microwave or radiowave energy is applied to a treated or untreated biomass material, such as a lignocellulosic material, in a
10 manner that water within the biomass material is vaporized, but overall the biomass material undergoes little bulk heating. For example, a frequency of from about 10 MHz to about 300,000 MHz can be applied to the biomass material. In some instances the microwave or radiowave energy is applied in short pulses, e.g., having a duration of less than 0.1 seconds, e.g., less than 0.05 seconds, less than 0.03 seconds, less than 0.01
15 seconds or even less, e.g., 0.005 seconds. Without wishing to be bound by any particular theory, it is believed when the microwave or radiowave energy is applied in this manner, water is vaporized within the biomass material with explosive force, which disrupts the lignin and "peels" it away from the cellulose. At the same time, since application of such energy does not heat the bulk material, the lignin does not tend to re-apply onto the
20 cellulose, which could block access to the cellulose, e.g., by an enzyme or microbe. Many of the properties of lignin are described Carter Fox in a thesis entitled "Chemical and Thermal Characterization of Three Industrial Lignin and Their Corresponding Esters (May 2006, University of Idaho).

In another biomass disruption technique, treated (e.g., using any treatment method
25 described herein) or untreated biomass material is subjected to a hot, compressed fluid, such as water. In such a method, the biomass is placed in a pressure vessel containing a fluid, such as water, at an elevated temperature, e.g., above 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, or above 180 °C. The pressure vessel is placed under gas pressure, such as under argon, nitrogen or air, and then stirred, e.g., with a two blade
30 turbine propeller for a period of time, e.g., 10 minutes, 20 minutes, 30 minutes, 45 minutes, 60 minutes or 90 minutes. In some embodiments, the pressure is between about

500 psig and 2000 psig, e.g., between about 650 psig and about 1500 psig or between about 700 psig and about 1200 psig. In some embodiments, the temperature is at or 5 or 10 °C above a glass transition temperature for the lignin. Without wishing to be bound by any particular theory, it is believed that when the temperature is above the glass transition temperature of the lignin, the conditions in the pressure vessel cause the lignin to “peel” away from the cellulose, making the cellulose more exposed for breakdown, e.g., by an enzyme.

In another biomass disruption technique, treated, e.g., irradiated, or untreated biomass material is delivered to a nip defined between two counter rotating pressure rolls, which can be optionally heated. Pressure in the nip can be adjusted by the amount of biomass material fed into the nip and the spacing between the pressure rolls. In some embodiments, the pressure in the nip can be greater than 1,000 psi per linear inch, e.g., greater than 2,500 psi, greater than 5,000 psi, greater than 7,500 psi, greater than 10,000 psi, or even greater than 15,000 psi per linear inch. In some embodiments, the pressure rolls are operated at an elevated temperature, e.g., above 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, or above 180 °C. In some embodiments, the rolls are operated at a temperature above a glass transition temperature of the lignin. Without wishing to be bound by any particular theory, it is believed that the pressure and heat in the nip can disrupt any lignin of the biomass material, making the cellulose more accessible and available to an enzyme.

Pyrolysis

One or more pyrolysis processing sequences can be used to process raw feedstock from a wide variety of different sources to extract useful substances from the feedstock, and to provide partially degraded organic material which functions as input to further processing steps and/or sequences.

Referring again to the general schematic in FIG. 8, a first material 2 that includes cellulose having a first number average molecular weight ($\overline{M}_{N1}$) is pyrolyzed, e.g., by heating the first material in a tube furnace, to provide a second material 3 that includes cellulose having a second number average molecular weight ($\overline{M}_{N2}$) lower than the first

number average molecular weight. The second material (or the first and second material in certain embodiments) is/are combined with a microorganism (e.g., a bacterium or a yeast) that can utilize the second and/or first material to produce a fuel 5 that is or includes hydrogen, an alcohol (e.g., ethanol or butanol, such as n-, sec or t-butanol), an organic acid, a hydrocarbon or mixtures of any of these.

Since the second material has cellulose having a reduced molecular weight relative to the first material, and in some instances, a reduced crystallinity as well, the second material is generally more dispersible, swellable and/or soluble in a solution containing the microorganism, e.g., at a concentration of greater than 10^6 10 microorganisms/mL. These properties make the second material 3 more susceptible to chemical, enzymatic and/or microbial attack relative to the first material 2, which can greatly improve the production rate and/or production level of a desired product, e.g., ethanol. Pyrolysis can also sterilize the first and second materials.

In some embodiments, the second number average molecular weight ($^T M_{N2}$) is 15 lower than the first number average molecular weight ($^T M_{N1}$) by more than about 10 percent, e.g., 15, 20, 25, 30, 35, 40, 50 percent, 60 percent, or even more than about 75 percent.

In some instances, the second material has cellulose that has as crystallinity ($^T C_2$) that is lower than the crystallinity ($^T C_1$) of the cellulose of the first material. For 20 example, ($^T C_2$) can be lower than ($^T C_1$) by more than about 10 percent, e.g., 15, 20, 25, 30, 35, 40, or even more than about 50 percent.

In some embodiments, the starting crystallinity (prior to pyrolysis) is from about 40 to about 87.5 percent, e.g., from about 50 to about 75 percent or from about 60 to about 70 percent, and the crystallinity index after pyrolysis is from about 10 to about 50 25 percent, e.g., from about 15 to about 45 percent or from about 20 to about 40 percent. However, in certain embodiments, e.g., after extensive pyrolysis, it is possible to have a crystallinity index of lower than 5 percent. In some embodiments, the material after pyrolysis is substantially amorphous.

In some embodiments, the starting number average molecular weight (prior to 30 pyrolysis) is from about 200,000 to about 3,200,000, e.g., from about 250,000 to about 1,000,000 or from about 250,000 to about 700,000, and the number average molecular

weight after pyrolysis is from about 50,000 to about 200,000, e.g., from about 60,000 to about 150,000 or from about 70,000 to about 125,000. However, in some embodiments, e.g., after extensive pyrolysis, it is possible to have a number average molecular weight of less than about 10,000 or even less than about 5,000.

5 In some embodiments, the second material can have a level of oxidation ($^T\text{O}_2$) that is higher than the level of oxidation ($^T\text{O}_1$) of the first material. A higher level of oxidation of the material can aid in its dispersibility, swellability and/or solubility, further enhancing the materials susceptibility to chemical, enzymatic or microbial attack. In some embodiments, to increase the level of the oxidation of the second material relative
10 to the first material, the pyrolysis is performed in an oxidizing environment, producing a second material that is more oxidized than the first material. For example, the second material can have more hydroxyl groups, aldehyde groups, ketone groups, ester groups or carboxylic acid groups, which can increase its hydrophilicity.

 In some embodiments, the pyrolysis of the materials is continuous. In other
15 embodiments, the material is pyrolyzed for a pre-determined time, and then allowed to cool for a second pre-determined time before pyrolyzing again.

Pyrolysis Systems

 FIG. 14 shows a process flow diagram 6000 that includes various steps in a pyrolytic feedstock pretreatment system. In first step 6010, a supply of dry feedstock is
20 received from a feed source.

 As described above, the dry feedstock from the feed source may be pre-processed prior to delivery to the pyrolysis chamber. For example, if the feedstock is derived from plant sources, certain portions of the plant material may be removed prior to collection of the plant material and/or before the plant material is delivered by the feedstock transport
25 device. Alternatively, or in addition, the biomass feedstock can be subjected to mechanical processing 6020 (e.g., to reduce the average length of fibers in the feedstock) prior to delivery to the pyrolysis chamber.

 Following mechanical processing, the feedstock undergoes a moisture adjustment step 6030. The nature of the moisture adjustment step depends upon the moisture content
30 of the mechanically processed feedstock. Typically, pyrolysis of feedstock occurs most efficiently when the moisture content of the feedstock is between about 10% and about

30% (e.g., between 15% and 25%) by weight of the feedstock. If the moisture content of the feedstock is larger than about 40% by weight, the extra thermal load presented by the water content of the feedstock increases the energy consumption of subsequent pyrolysis steps.

5 In some embodiments, if the feedstock has a moisture content which is larger than about 30% by weight, drier feedstock material 6220, which has a low moisture content, can be blended in, creating a feedstock mixture in step 6030 with an average moisture content that is within the limits discussed above. In certain embodiments, feedstock with a high moisture content can simply be dried by dispersing the feedstock material on a
10 moving conveyor that cycles the feedstock through an in-line heating unit. The heating unit evaporates a portion of the water present in the feedstock.

 In some embodiments, if the feedstock from step 6020 has a moisture content which is too low (e.g., lower than about 10% by weight), the mechanically processed feedstock can be combined with wetter feedstock material 6230 with a higher moisture
15 content, such as sewage sludge. Alternatively, or in addition, water 6240 can be added to the dry feedstock from step 6020 to increase its moisture content.

 In step 6040, the feedstock – now with its moisture content adjusted to fall within suitable limits – can be preheated in an optional preheating step 6040. Preheating step 6040 can be used to increase the temperature of the feedstock to between 75 °C and 150
20 °C in preparation for subsequent pyrolysis of the feedstock. Depending upon the nature of the feedstock and the particular design of the pyrolysis chamber, preheating the feedstock can ensure that heat distribution within the feedstock remains more uniform during pyrolysis, and can reduce the thermal load on the pyrolysis chamber.

 The feedstock is then transported to a pyrolysis chamber to undergo pyrolysis in
25 step 6050. In some embodiments, transport of the feedstock is assisted by adding one or more pressurized gases 6210 to the feedstock stream. The gases create a pressure gradient in a feedstock transport conduit, propelling the feedstock into the pyrolysis chamber (and even through the pyrolysis chamber). In certain embodiments, transport of the feedstock occurs mechanically; that is, a transport system that includes a conveyor
30 such as an auger transports the feedstock to the pyrolysis chamber.

Other gases 6210 can also be added to the feedstock prior to the pyrolysis chamber. In some embodiments, for example, one or more catalyst gases can be added to the feedstock to assist decomposition of the feedstock during pyrolysis. In certain embodiments, one or more scavenging agents can be added to the feedstock to trap
5 volatile materials released during pyrolysis. For example, various sulfur-based compounds such as sulfides can be liberated during pyrolysis, and an agent such as hydrogen gas can be added to the feedstock to cause desulfurization of the pyrolysis products. Hydrogen combines with sulfides to form hydrogen sulfide gas, which can be removed from the pyrolyzed feedstock.

10 Pyrolysis of the feedstock within the chamber can include heating the feedstock to relatively high temperatures to cause partial decomposition of the feedstock. Typically, the feedstock is heated to a temperature in a range from 150 °C to 1100 °C. The temperature to which the feedstock is heated depends upon a number of factors, including the composition of the feedstock, the feedstock average particle size, the moisture
15 content, and the desired pyrolysis products. For many types of biomass feedstock, for example, pyrolysis temperatures between 300 °C and 550 °C are used.

The residence time of the feedstock within the pyrolysis chamber generally depends upon a number of factors, including the pyrolysis temperature, the composition of the feedstock, the feedstock average particle size, the moisture content, and the desired
20 pyrolysis products. In some embodiments, feedstock materials are pyrolyzed at a temperature just above the decomposition temperature for the material in an inert atmosphere, e.g., from about 2 °C above to about 10 °C above the decomposition temperature or from about 3 °C above to about 7 °C above the decomposition temperature. In such embodiments, the material is generally kept at this temperature for
25 greater than 0.5 hours, e.g., greater than 1.0 hour or greater than about 2.0 hours. In other embodiments, the materials are pyrolyzed at a temperature well above the decomposition temperature for the material in an inert atmosphere, e.g., from about 75 °C above to about 175 °C above the decomposition temperature or from about 85 °C above to about 150 °C above the decomposition temperature. In such embodiments, the material is generally
30 kept at this temperature for less than 0.5 hour, e.g., less 20 minutes, less than 10 minutes, less than 5 minutes or less than 2 minutes. In still other embodiments, the materials are

pyrolyzed at an extreme temperature, e.g., from about 200 °C above to about 500 °C above the decomposition temperature of the material in an inert environment or from about 250 °C above to about 400 °C above the decomposition temperature. In such embodiments, the material is generally kept at this temperature for less than 1 minute, e.g., less than 30 seconds, 15 seconds, 10 seconds, 5 seconds, 1 second or less than 500 ms. Such embodiments are typically referred to as flash pyrolysis.

In some embodiments, the feedstock is heated relatively rapidly to the selected pyrolysis temperature within the chamber. For example, the chamber can be designed to heat the feedstock at a rate of between 500 °C/s and 11,000 °C/s, for example from 500 °C/s to 1000 °C/s.

A turbulent flow of feedstock material within the pyrolysis chamber is usually advantageous, as it ensures relatively efficient heat transfer to the feedstock material from the heating sub-system. Turbulent flow can be achieved, for example, by blowing the feedstock material through the chamber using one or more injected carrier gases. In general, the carrier gases are relatively inert towards the feedstock material, even at the high temperatures in the pyrolysis chamber. Exemplary carrier gases include, for example, nitrogen, argon, methane, carbon monoxide, and carbon dioxide. Alternatively, or in addition, mechanical transport systems such as augers can transport and circulate the feedstock within the pyrolysis chamber to create a turbulent feedstock flow.

In some embodiments, pyrolysis of the feedstock occurs substantially in the absence of oxygen and other reactive gases. Oxygen can be removed from the pyrolysis chamber by periodic purging of the chamber with high pressure nitrogen (e.g., at nitrogen pressures of 2 bar or more). Following purging of the chamber, a gas mixture present in the pyrolysis chamber (e.g., during pyrolysis of the feedstock) can include less than 4 mole% oxygen (e.g., less than 1 mole% oxygen, and even less than 0.5 mole% oxygen). The absence of oxygen ensures that ignition of the feedstock does not occur at the elevated pyrolysis temperatures.

In certain embodiments, relatively small amounts of oxygen can be introduced into the feedstock and are present during pyrolysis. This technique is referred to as oxidative pyrolysis. Typically, oxidative pyrolysis occurs in multiple heating stages. For example, in a first heating stage, the feedstock is heated in the presence of oxygen to

cause partial oxidation of the feedstock. This stage consumes the available oxygen in the pyrolysis chamber. Then, in subsequent heating stages, the feedstock temperature is further elevated. With all of the oxygen in the chamber consumed, however, feedstock combustion does not occur, and combustion-free pyrolytic decomposition of the feedstock (e.g., to generate hydrocarbon products) occurs. In general, the process of heating feedstock in the pyrolysis chamber to initiate decomposition is endothermic. However, in oxidative pyrolysis, formation of carbon dioxide by oxidation of the feedstock is an exothermic process. The heat released from carbon dioxide formation can assist further pyrolysis heating stages, thereby lessening the thermal load presented by the feedstock.

In some embodiments, pyrolysis occurs in an inert environment, such as while feedstock materials are bathed in argon or nitrogen gas. In certain embodiments, pyrolysis can occur in an oxidizing environment, such as in air or argon enriched in air. In some embodiments, pyrolysis can take place in a reducing environment, such as while feedstock materials are bathed in hydrogen gas. To aid pyrolysis, various chemical agents, such as oxidants, reductants, acids or bases can be added to the material prior to or during pyrolysis. For example, sulfuric acid can be added, or a peroxide (e.g., benzoyl peroxide) can be added.

As discussed above, a variety of different processing conditions can be used, depending upon factors such as the feedstock composition and the desired pyrolysis products. For example, for cellulose-containing feedstock material, relatively mild pyrolysis conditions can be employed, including flash pyrolysis temperatures between 375 °C and 450 °C, and residence times of less than 1 second. As another example, for organic solid waste material such as sewage sludge, flash pyrolysis temperatures between 500 °C and 650 °C are typically used, with residence times of between 0.5 and 3 seconds. In general, many of the pyrolysis process parameters, including residence time, pyrolysis temperature, feedstock turbulence, moisture content, feedstock composition, pyrolysis product composition, and additive gas composition can be regulated automatically by a system of regulators and an automated control system.

Following pyrolysis step 6050, the pyrolysis products undergo a quenching step 6250 to reduce the temperature of the products prior to further processing. Typically,

quenching step 6250 includes spraying the pyrolysis products with streams of cooling water 6260. The cooling water also forms a slurry that includes solid, undissolved product material and various dissolved products. Also present in the product stream is a mixture that includes various gases, including product gases, carrier gases, and other
5 types of process gases.

The product stream is transported via in-line piping to a gas separator that performs a gas separation step 6060, in which product gases and other gases are separated from the slurry formed by quenching the pyrolysis products. The separated gas mixture is optionally directed to a blower 6130, which increases the gas pressure by blowing air
10 into the mixture. The gas mixture can be subjected to a filtration step 6140, in which the gas mixture passes through one or more filters (e.g., activated charcoal filters) to remove particulates and other impurities. In a subsequent step 6150, the filtered gas can be compressed and stored for further use. Alternatively, the filtered gas can be subjected to further processing steps 6160. For example, in some embodiments, the filtered gas can
15 be condensed to separate different gaseous compounds within the gas mixture. The different compounds can include, for example, various hydrocarbon products (e.g., alcohols, alkanes, alkenes, alkynes, ethers) produced during pyrolysis. In certain embodiments, the filtered gas containing a mixture of hydrocarbon components can be combined with steam gas 6170 (e.g., a mixture of water vapor and oxygen) and subjected
20 to a cracking process to reduce molecular weights of the hydrocarbon components.

In some embodiments, the pyrolysis chamber includes heat sources that burn hydrocarbon gases such as methane, propane, and/or butane to heat the feedstock. A portion 6270 of the separated gases can be recirculated into the pyrolysis chamber for combustion, to generate process heat to sustain the pyrolysis process.

25 In certain embodiments, the pyrolysis chamber can receive process heat that can be used to increase the temperature of feedstock materials. For example, irradiating feedstock with radiation (e.g., gamma radiation, electron beam radiation, or other types of radiation) can heat the feedstock materials to relatively high temperatures. The heated feedstock materials can be cooled by a heat exchange system that removes some of the
30 excess heat from the irradiated feedstock. The heat exchange system can be configured

to transport some of the heat energy to the pyrolysis chamber to heat (or pre-heat) feedstock material, thereby reducing energy cost for the pyrolysis process.

The slurry containing liquid and solid pyrolysis products can undergo an optional de-watering step 6070, in which excess water can be removed from the slurry via
5 processes such as mechanical pressing and evaporation. The excess water 6280 can be filtered and then recirculated for further use in quenching the pyrolysis decomposition products in step 6250.

The de-watered slurry then undergoes a mechanical separation step 6080, in which solid product material 6110 is separated from liquid product material 6090 by a
10 series of increasingly fine filters. In step 6100, the liquid product material 6090 can then be condensed (e.g., via evaporation) to remove waste water 6190, and purified by processes such as extraction. Extraction can include the addition of one or more organic solvents 6180, for example, to separate products such as oils from products such as alcohols. Suitable organic solvents include, for example, various hydrocarbons and halo-
15 hydrocarbons. The purified liquid products 6200 can then be subjected to further processing steps. Waste water 6190 can be filtered if necessary, and recirculated for further use in quenching the pyrolysis decomposition products in step 6250.

After separation in step 6080, the solid product material 6110 is optionally subjected to a drying step 6120 that can include evaporation of water. Solid material
20 6110 can then be stored for later use, or subjected to further processing steps, as appropriate.

The pyrolysis process parameters discussed above are exemplary. In general, values of these parameters can vary widely according to the nature of the feedstock and the desired products. Moreover, a wide variety of different pyrolysis techniques,
25 including using heat sources such as hydrocarbon flames and/or furnaces, infrared lasers, microwave heaters, induction heaters, resistive heaters, and other heating devices and configurations can be used.

A wide variety of different pyrolysis chambers can be used to decompose the feedstock. In some embodiments, for example, pyrolyzing feedstock can include heating
30 the material using a resistive heating member, such as a metal filament or metal ribbon.

The heating can occur by direct contact between the resistive heating member and the material.

5 In certain embodiments, pyrolyzing can include heating the material by induction, such as by using a Curie-Point pyrolyzer. In some embodiments, pyrolyzing can include heating the material by the application of radiation, such as infrared radiation. The radiation can be generated by a laser, such as an infrared laser.

10 In certain embodiments, pyrolyzing can include heating the material with a convective heat. The convective heat can be generated by a flowing stream of heated gas. The heated gas can be maintained at a temperature of less than about 1200 °C, such as less than 1000 °C, less than 750 °C, less than 600 °C, less than 400 °C or even less than 300 °C. The heated gas can be maintained at a temperature of greater than about 250 °C. The convective heat can be generated by a hot body surrounding the first material, such as in a furnace.

15 In some embodiments, pyrolyzing can include heating the material with steam at a temperature above about 250 °C.

20 An embodiment of a pyrolysis chamber is shown in FIG. 15. Chamber 6500 includes an insulated chamber wall 6510 with a vent 6600 for exhaust gases, a plurality of burners 6520 that generate heat for the pyrolysis process, a transport duct 6530 for transporting the feedstock through chamber 6500, augers 6590 for moving the feedstock through duct 6530 in a turbulent flow, and a quenching system 6540 that includes an auger 6610 for moving the pyrolysis products, water jets 6550 for spraying the pyrolysis products with cooling water, and a gas separator for separating gaseous products 6580 from a slurry 6570 containing solid and liquid products.

25 Another embodiment of a pyrolysis chamber is shown in FIG. 16. Chamber 6700 includes an insulated chamber wall 6710, a feedstock supply duct 6720, a sloped inner chamber wall 6730, burners 6740 that generate heat for the pyrolysis process, a vent 6750 for exhaust gases, and a gas separator 6760 for separating gaseous products 6770 from liquid and solid products 6780. Chamber 6700 is configured to rotate in the direction shown by arrow 6790 to ensure adequate mixing and turbulent flow of the feedstock within the chamber.

30

A further embodiment of a pyrolysis chamber is shown in FIG. 17. Filament pyrolyzer 1712 includes a sample holder 1713 with resistive heating element 1714 in the form of a wire winding through the open space defined by the sample holder 1713. Optionally, the heated element can be spun about axis 1715 (as indicated by arrow 1716) to tumble the material that includes the cellulosic material in sample holder 1713. The space 1718 defined by enclosure 1719 is maintained at a temperature above room temperature, e.g., 200 to 250 °C. In a typical usage, a carrier gas, e.g., an inert gas, or an oxidizing or reducing gas, traverses through the sample holder 1713 while the resistive heating element is rotated and heated to a desired temperature, e.g., 325 °C. After an appropriate time, e.g., 5 to 10 minutes, the pyrolyzed material is emptied from the sample holder. The system shown in FIG. 17 can be scaled and made continuous. For example, rather than a wire as the heating member, the heating member can be an auger screw. Material can continuously fall into the sample holder, striking a heated screw that pyrolyzes the material. At the same time, the screw can push the pyrolyzed material out of the sample holder to allow for the entry of fresh, unpyrolyzed material.

Another embodiment of a pyrolysis chamber is shown in FIG. 18, which features a Curie-Point pyrolyzer 1820 that includes a sample chamber 1821 housing a ferromagnetic foil 1822. Surrounding the sample chamber 1821 is an RF coil 1823. The space 1824 defined by enclosure 1825 is maintained at a temperature above room temperature, e.g., 200 to 250 °C. In a typical usage, a carrier gas traverses through the sample chamber 1821 while the foil 1822 is inductively heated by an applied RF field to pyrolyze the material at a desired temperature.

Yet another embodiment of a pyrolysis chamber is shown in FIG. 19. Furnace pyrolyzer 130 includes a movable sample holder 131 and a furnace 132. In a typical usage, the sample is lowered (as indicated by arrow 137) into a hot zone 135 of furnace 132, while a carrier gas fills the housing 136 and traverses through the sample holder 131. The sample is heated to the desired temperature for a desired time to provide a pyrolyzed product. The pyrolyzed product is removed from the pyrolyzer by raising the sample holder (as indicated by arrow 134).

In certain embodiments, as shown in FIG. 20, a cellulosic target 140 can be pyrolyzed by treating the target, which is housed in a vacuum chamber 141, with laser

light, e.g., light having a wavelength of from about 225 nm to about 1500 nm. For example, the target can be ablated at 266 nm, using the fourth harmonic of a Nd-YAG laser (Spectra Physics, GCR170, San Jose, Calif.). The optical configuration shown allows the nearly monochromatic light 143 generated by the laser 142 to be directed using mirrors 144 and 145 onto the target after passing through a lens 146 in the vacuum chamber 141. Typically, the pressure in the vacuum chamber is maintained at less than about 10^{-6} mm Hg. In some embodiments, infrared radiation is used, e.g., 1.06 micron radiation from an Nd-YAG laser. In such embodiments, an infrared sensitive dye can be combined with the cellulosic material to produce a cellulosic target. The infrared dye can enhance the heating of the cellulosic material. Laser ablation is described by Blanchet-Fincher et al., in U.S. Patent No. 5,942,649.

Referring to FIG. 21, in some embodiments, a cellulosic material can be flash pyrolyzed by coating a tungsten filament 150, such as a 5 to 25 mil tungsten filament, with the desired cellulosic material while the material is housed in a vacuum chamber 151. To affect pyrolysis, current is passed through the filament, which causes a rapid heating of the filament for a desired time. Typically, the heating is continued for seconds before allowing the filament to cool. In some embodiments, the heating is performed a number of times to effect the desired amount of pyrolysis.

In certain embodiments, carbohydrate-containing biomass material can be heated in an absence of oxygen in a fluidized bed reactor. If desired, the carbohydrate containing biomass can have relatively thin cross-sections, and can include any of the fibrous materials described herein, for efficient heat transfer. The material can be heated by thermal transfer from a hot metal or ceramic, such as glass beads or sand in the reactor, and the resulting pyrolysis liquid or oil can be transported to a central refinery for making combustible fuels or other useful products.

In some embodiments, irradiating the biomass material, e.g., with a beam of particles, such as electrons, prior to pyrolysis can lower the pyrolysis temperature, resulting in less energy being consumed during pyrolysis.

Oxidation

One or more oxidative processing sequences can be used to process raw feedstock from a wide variety of different sources to extract useful substances from the feedstock,

and to provide partially degraded organic material which functions as input to further processing steps and/or sequences.

Referring again to FIG. 8, a first material 2 that includes cellulose having a first number average molecular weight ($^T M_{N1}$) and having a first oxygen content ($^T O_1$) is oxidized, e.g., by heating the first material in a tube furnace in stream of air or oxygen-enriched air, to provide a second material 3 that includes cellulose having a second number average molecular weight ($^T M_{N2}$) and having a second oxygen content ($^T O_2$) higher than the first oxygen content ($^T O_1$). The second material (or the first and second material in certain embodiments) can be, e.g., combined with a resin, such as a molten thermoplastic resin or a microorganism, to provide a composite 4 having desirable mechanical properties, or a fuel 5

Such materials can also be combined with a solid and/or a liquid. For example, the liquid can be in the form of a solution and the solid can be particulate in form. The liquid and/or solid can include a microorganism, e.g., a bacterium, and/or an enzyme. For example, the bacterium and/or enzyme can work on the cellulosic or lignocellulosic material to produce a fuel, such as ethanol, or a coproduct, such as a protein. Fuels and coproducts are described in "FIBROUS MATERIALS AND COMPOSITES," USSN 11/453,951, filed June 15, 2006. The entire contents of each of the foregoing applications are incorporated herein by reference.

In some embodiments, the second number average molecular weight is not more than 97 percent lower than the first number average molecular weight, e.g., not more than 95 percent, 90, 85, 80, 75, 70, 65, 60, 55, 50, 45, 40, 30, 20, 12.5, 10.0, 7.5, 5.0, 4.0, 3.0, 2.5, 2.0 or not more than 1.0 percent lower than the first number average molecular weight. The amount of reduction of molecular weight will depend upon the application.

In some embodiments in which the materials are used to make a fuel or a coproduct, the starting number average molecular weight (prior to oxidation) is from about 200,000 to about 3,200,000, e.g., from about 250,000 to about 1,000,000 or from about 250,000 to about 700,000, and the number average molecular weight after oxidation is from about 50,000 to about 200,000, e.g., from about 60,000 to about 150,000 or from about 70,000 to about 125,000. However, in some embodiments, e.g.,

after extensive oxidation, it is possible to have a number average molecular weight of less than about 10,000 or even less than about 5,000.

In some embodiments, the second oxygen content is at least about five percent higher than the first oxygen content, e.g., 7.5 percent higher, 10.0 percent higher, 12.5 percent higher, 15.0 percent higher or 17.5 percent higher. In some preferred embodiments, the second oxygen content is at least about 20.0 percent higher than the oxygen content of the first material. Oxygen content is measured by elemental analysis by pyrolyzing a sample in a furnace operating 1300 °C or higher. A suitable elemental analyzer is the LECO CHNS-932 analyzer with a VTF-900 high temperature pyrolysis furnace.

In some embodiments, oxidation of first material 200 does not result in a substantial change in the crystallinity of the cellulose. However, in some instances, e.g., after extreme oxidation, the second material has cellulose that has as crystallinity (T_{C2}) that is lower than the crystallinity (T_{C1}) of the cellulose of the first material. For example, (T_{C2}) can be lower than (T_{C1}) by more than about 5 percent, e.g., 10, 15, 20, or even 25 percent. This can be desirable to enhance solubility of the materials in a liquid, such as a liquid that includes a bacterium and/or an enzyme.

In some embodiments, the starting crystallinity index (prior to oxidation) is from about 40 to about 87.5 percent, e.g., from about 50 to about 75 percent or from about 60 to about 70 percent, and the crystallinity index after oxidation is from about 30 to about 75.0 percent, e.g., from about 35.0 to about 70.0 percent or from about 37.5 to about 65.0 percent. However, in certain embodiments, e.g., after extensive oxidation, it is possible to have a crystallinity index of lower than 5 percent. In some embodiments, the material after oxidation is substantially amorphous.

Without wishing to be bound by any particular theory, it is believed that oxidation increases the number of hydrogen-bonding groups on the cellulose, such as hydroxyl groups, aldehyde groups, ketone groups carboxylic acid groups or anhydride groups, which can increase its dispersibility and/or its solubility (e.g., in a liquid). To further improve dispersibility in a resin, the resin can include a component that includes hydrogen-bonding groups, such as one or more anhydride groups, carboxylic acid groups, hydroxyl groups, amide groups, amine groups or mixtures of any of these groups. In

some preferred embodiments, the component includes a polymer copolymerized with and/or grafted with maleic anhydride. Such materials are available from Dupont under the tradename FUSABOND®.

Generally, oxidation of first material 200 occurs in an oxidizing environment. For example, the oxidation can be effected or aided by pyrolysis in an oxidizing environment, such as in air or argon enriched in air. To aid in the oxidation, various chemical agents, such as oxidants, acids or bases can be added to the material prior to or during oxidation. For example, a peroxide (e.g., benzoyl peroxide) can be added prior to oxidation.

Oxidation Systems

FIG. 22 shows a process flow diagram 5000 that includes various steps in an oxidative feedstock pretreatment system. In first step 5010, a supply of dry feedstock is received from a feed source. The feed source can include, for example, a storage bed or container that is connected to an in-line oxidation reactor via a conveyor belt or another feedstock transport device.

As described above, the dry feedstock from the feed source may be pre-processed prior to delivery to the oxidation reactor. For example, if the feedstock is derived from plant sources, certain portions of the plant material may be removed prior to collection of the plant material and/or before the plant material is delivered by the feedstock transport device. Alternatively, or in addition, the biomass feedstock can be subjected to mechanical processing (e.g., to reduce the average length of fibers in the feedstock) prior to delivery to the oxidation reactor.

Following mechanical processing 5020, feedstock 5030 is transported to a mixing system which introduces water 5150 into the feedstock in a mechanical mixing process. Combining water with the processed feedstock in mixing step 5040 creates an aqueous feedstock slurry 5050, which can then be treated with one or more oxidizing agents.

Typically, one liter of water is added to the mixture for every 0.02 kg to 1.0 kg of dry feedstock. The ratio of feedstock to water in the mixture depends upon the source of the feedstock and the specific oxidizing agents used further downstream in the overall process. For example, in typical industrial processing sequences for lignocellulosic biomass, aqueous feedstock slurry 5050 includes from about 0.5 kg to about 1.0 kg of dry biomass per liter of water.

In some embodiments, one or more fiber-protecting additives 5170 can also be added to the feedstock slurry in feedstock mixing step 5040. Fiber-protecting additives help to reduce degradation of certain types of biomass fibers (e.g., cellulose fibers) during oxidation of the feedstock. Fiber-protecting additives can be used, for example, if a
5 desired product from processing a lignocellulosic feedstock includes cellulose fibers. Exemplary fiber-protecting additives include magnesium compounds such as magnesium hydroxide. Concentrations of fiber-protecting additives in feedstock slurry 5050 can be from 0.1% to 0.4% of the dry weight of the biomass feedstock, for example.

In certain embodiments, aqueous feedstock slurry 5050 can be subjected to an
10 optional extraction 5180 with an organic solvent to remove water-insoluble substances from the slurry. For example, extraction of slurry 5050 with one or more organic solvents yields a purified slurry and an organic waste stream 5210 that includes water-insoluble materials such as fats, oils, and other non-polar, hydrocarbon-based substances. Suitable solvents for performing extraction of slurry 5050 include various alcohols,
15 hydrocarbons, and halo-hydrocarbons, for example.

In some embodiments, aqueous feedstock slurry 5050 can be subjected to an optional thermal treatment 5190 to further prepare the feedstock for oxidation. An example of a thermal treatment includes heating the feedstock slurry in the presence of pressurized steam. In fibrous biomass feedstock, the pressurized steam swells the fibers,
20 exposing a larger fraction of fiber surfaces to the aqueous solvent and to oxidizing agents that are introduced in subsequent processing steps.

In certain embodiments, aqueous feedstock slurry 5050 can be subjected to an optional treatment with basic agents 5200. Treatment with one or more basic agents can help to separate lignin from cellulose in lignocellulosic biomass feedstock, thereby
25 improving subsequent oxidation of the feedstock. Exemplary basic agents include alkali and alkaline earth hydroxides such as sodium hydroxide, potassium hydroxide, and calcium hydroxide. In general, a variety of basic agents can be used, typically in concentrations from about 0.01% to about 0.5% of the dry weight of the feedstock.

Aqueous feedstock slurry 5050 is transported (e.g., by an in-line piping system) to
30 a chamber, which can be an oxidation preprocessing chamber or an oxidation reactor. In oxidation preprocessing step 5060, one or more oxidizing agents 5160 are added to

feedstock slurry 5050 to form an oxidizing medium. In some embodiments, for example, oxidizing agents 5160 can include hydrogen peroxide. Hydrogen peroxide can be added to slurry 5050 as an aqueous solution, and in proportions ranging from 3% to between 30% and 35% by weight of slurry 5050. Hydrogen peroxide has a number of advantages as an oxidizing agent. For example, aqueous hydrogen peroxide solution is relatively inexpensive, is relatively chemically stable, and is not particularly hazardous relative to other oxidizing agents (and therefore does not require burdensome handling procedures and expensive safety equipment). Moreover, hydrogen peroxide decomposes to form water during oxidation of feedstock, so that waste stream cleanup is relatively straightforward and inexpensive.

In certain embodiments, oxidizing agents 5160 can include oxygen (e.g., oxygen gas) either alone, or in combination with hydrogen peroxide. Oxygen gas can be bubbled into slurry 5050 in proportions ranging from 0.5% to 10% by weight of slurry 5050. Alternatively, or in addition, oxygen gas can also be introduced into a gaseous phase in equilibrium with slurry 5050 (e.g., a vapor head above slurry 5050). The oxygen gas can be introduced into either an oxidation preprocessing chamber or into an oxidation reactor (or into both), depending upon the configuration of the oxidative processing system. Typically, for example, the partial pressure of oxygen in the vapor above slurry 5050 is larger than the ambient pressure of oxygen, and ranges from 0.5 bar to 35 bar, depending upon the nature of the feedstock.

The oxygen gas can be introduced in pure form, or can be mixed with one or more carrier gases. For example, in some embodiments, high-pressure air provides the oxygen in the vapor. In certain embodiments, oxygen gas can be supplied continuously to the vapor phase to ensure that a concentration of oxygen in the vapor remains within certain predetermined limits during processing of the feedstock. In some embodiments, oxygen gas can be introduced initially in sufficient concentration to oxidize the feedstock, and then the feedstock can be transported to a closed, pressurized vessel (e.g., an oxidation reactor) for processing.

In certain embodiments, oxidizing agents 5160 can include nascent oxygen (e.g., oxygen radicals). Typically, nascent oxygen is produced as needed in an oxidation reactor or in a chamber in fluid communication with an oxidation reactor by one or more

decomposition reactions. For example, in some embodiments, nascent oxygen can be produced from a reaction between NO and O₂ in a gas mixture or in solution. In certain embodiments, nascent oxygen can be produced from decomposition of HOCl in solution. Other methods by which nascent oxygen can be produced include via electrochemical generation in electrolyte solution, for example.

In general, nascent oxygen is an efficient oxidizing agent due to the relatively high reactivity of the oxygen radical. However, nascent oxygen can also be a relatively selective oxidizing agent. For example, when lignocellulosic feedstock is treated with nascent oxygen, selective oxidation of lignin occurs in preference to the other components of the feedstock such as cellulose. As a result, oxidation of feedstock with nascent oxygen provides a method for selective removal of the lignin fraction in certain feedstocks. Typically, nascent oxygen concentrations of between about 0.5% and 5% of the dry weight of the feedstock are used to effect efficient oxidation.

Without wishing to be bound by theory, it is believed that nascent oxygen reacts with lignocellulosic feedstock according to at least two different mechanisms. In a first mechanism, nascent oxygen undergoes an addition reaction with the lignin, resulting in partial oxidation of the lignin, which solubilizes the lignin in aqueous solution. As a result, the solubilized lignin can be removed from the rest of the feedstock via washing. In a second mechanism, nascent oxygen disrupts butane cross-links and/or opens aromatic rings that are connected via the butane cross-links. As a result, solubility of the lignin in aqueous solution increases, facilitating separation of the lignin fraction from the remainder of the feedstock via washing.

In some embodiments, oxidizing agents include ozone (O₃). The use of ozone can introduce several chemical handling considerations in the oxidation processing sequence. If heated too vigorously, an aqueous solution of ozone can decompose violently, with potentially adverse consequences for both human system operators and system equipment. Accordingly, ozone is typically generated in a thermally isolated, thick-walled vessel separate from the vessel that contains the feedstock slurry, and transported thereto at the appropriate process stage.

Without wishing to be bound by theory, it is believed that ozone decomposes into oxygen and oxygen radicals, and that the oxygen radicals (e.g., nascent oxygen) are

responsible for the oxidizing properties of ozone in the manner discussed above. Ozone typically preferentially oxidizes the lignin fraction in lignocellulosic materials, leaving the cellulose fraction relatively undisturbed.

Conditions for ozone-based oxidation of biomass feedstock generally depend upon the nature of the biomass. For example, for cellulosic and/or lignocellulosic feedstocks, ozone concentrations of from 0.1 g/m³ to 20 g/m³ of dry feedstock provide for efficient feedstock oxidation. Typically, the water content in slurry 5050 is between 10% by weight and 80% by weight (e.g., between 40% by weight and 60% by weight). During ozone-based oxidation, the temperature of slurry 5050 can be maintained between 0 °C and 100 °C to avoid violent decomposition of the ozone.

In some embodiments, feedstock slurry 5050 can be treated with an aqueous, alkaline solution that includes one or more alkali and alkaline earth hydroxides such as sodium hydroxide, potassium hydroxide, and calcium hydroxide, and then treated thereafter with an ozone-containing gas in an oxidation reactor. This process has been observed to significantly increase decomposition of the biomass in slurry 5050. Typically, for example, a concentration of hydroxide ions in the alkaline solution is between 0.001% and 10% by weight of slurry 5050. After the feedstock has been wetted via contact with the alkaline solution, the ozone-containing gas is introduced into the oxidation reactor, where it contacts and oxidizes the feedstock.

Oxidizing agents 5160 can also include other substances. In some embodiments, for example, halogen-based oxidizing agents such as chlorine and oxychlorine agents (e.g., hypochlorite) can be introduced into slurry 5050. In certain embodiments, nitrogen-containing oxidizing substances can be introduced into slurry 5050. Exemplary nitrogen-containing oxidizing substances include NO and NO₂, for example. Nitrogen-containing agents can also be combined with oxygen in slurry 5050 to create additional oxidizing agents. For example, NO and NO₂ both combine with oxygen in slurry 5050 to form nitrate compounds, which are effective oxidizing agents for biomass feedstock. Halogen- and nitrogen-based oxidizing agents can, in some embodiments, cause bleaching of the biomass feedstock, depending upon the nature of the feedstock. The bleaching may be desirable for certain biomass-derived products that are extracted in subsequent processing steps.

Other oxidizing agents can include, for example, various peroxyacids, peroxyacetic acids, persulfates, percarbonates, permanganates, osmium tetroxide, and chromium oxides.

Following oxidation preprocessing step 5060, feedstock slurry 5050 is oxidized in step 5070. If oxidizing agents 5160 were added to slurry 5050 in an oxidation reactor, then oxidation proceeds in the same reactor. Alternatively, if oxidizing agents 5160 were added to slurry 5050 in a preprocessing chamber, then slurry 5050 is transported to an oxidation reactor via an in-line piping system. Once inside the oxidation reactor, oxidation of the biomass feedstock proceeds under a controlled set of environmental conditions. Typically, for example, the oxidation reactor is a cylindrical vessel that is closed to the external environment and pressurized. Both batch and continuous operation is possible, although environmental conditions are typically easier to control in in-line batch processing operations.

Oxidation of feedstock slurry 5050 typically occurs at elevated temperatures in the oxidation reactor. For example, the temperature of slurry 5050 in the oxidation reactor is typically maintained above 100 °C, e.g., in a range from 120 °C to 240 °C. For many types of biomass feedstock, oxidation is particularly efficient if the temperature of slurry 5050 is maintained between 150 °C and 220 °C. Slurry 5050 can be heated using a variety of thermal transfer devices. For example, in some embodiments, the oxidation reactor contacts a heating bath that includes oil or molten salts. In certain embodiments, a series of heat exchange pipes surround and contact the oxidation reactor, and circulation of hot fluid within the pipes heats slurry 5050 in the reactor. Other heating devices that can be used to heat slurry 5050 include resistive heating elements, induction heaters, and microwave sources, for example.

The residence time of feedstock slurry 5050 in the oxidation reactor can be varied as desired to process the feedstock. Typically, slurry 5050 spends from 1 minute to 60 minutes undergoing oxidation in the reactor. For relatively soft biomass material such as lignocellulosic matter, the residence time in the oxidation reactor can be from 5 minutes to 30 minutes, for example, at an oxygen pressure of between 3 and 12 bars in the reactor, and at a slurry temperature of between 160 °C and 210 °C. For other types of feedstock, however, residence times in the oxidation reactor can be longer, e.g., as long as 48 hours.

To determine appropriate residence times for slurry 5050 in the oxidation reactor, aliquots of the slurry can be extracted from the reactor at specific intervals and analyzed to determine concentrations of particular products of interest such as complex saccharides. Information about the increase in concentrations of certain products in
5 slurry 5050 as a function of time can be used to determine residence times for particular classes of feedstock material.

In some embodiments, during oxidation of feedstock slurry 5050, adjustment of the slurry pH may be performed by introducing one or more chemical agents into the oxidation reactor. For example, in certain embodiments, oxidation occurs most
10 efficiently in a pH range of about 9-11. To maintain a pH in this range, agents such as alkali and alkaline earth hydroxides, carbonates, ammonia, and alkaline buffer solutions can be introduced into the oxidation reactor.

Circulation of slurry 5050 during oxidation can be important to ensure sufficient contact between oxidizing agents 5160 and the feedstock. Circulation of the slurry can
15 be achieved using a variety of techniques. For example, in some embodiments, a mechanical stirring apparatus that includes impeller blades or a paddle wheel can be implemented in the oxidation reactor. In certain embodiments, the oxidation reactor can be a loop reactor, in which the aqueous solvent in which the feedstock is suspended is simultaneously drained from the bottom of the reactor and recirculated into the top of the
20 reactor via pumping, thereby ensuring that the slurry is continually re-mixed and does not stagnate within the reactor.

After oxidation of the feedstock is complete, the slurry is transported to a separation apparatus where a mechanical separation step 5080 occurs. Typically, mechanical separation step 5080 includes one or more stages of increasingly fine filtering
25 of the slurry to mechanically separate the solid and liquid constituents.

Liquid phase 5090 is separated from solid phase 5100, and the two phases are processed independently thereafter. Solid phase 5100 can optionally undergo a drying step 5120 in a drying apparatus, for example. Drying step 5120 can include, for example, mechanically dispersing the solid material onto a drying surface, and evaporating water
30 from solid phase 5100 by gentle heating of the solid material. Following drying step

5120 (or, alternatively, without undergoing drying step 5120), solid phase 5100 is transported for further processing steps 5140.

Liquid phase 5090 can optionally undergo a drying step 5110 to reduce the concentration of water in the liquid phase. In some embodiments, for example, drying
5 step 5110 can include evaporation and/or distillation and/or extraction of water from liquid phase 5090 by gentle heating of the liquid. Alternatively, or in addition, one or more chemical drying agents can be used to remove water from liquid phase 5090. Following drying step 5110 (or alternatively, without undergoing drying step 5110), liquid phase 5090 is transported for further processing steps 5130, which can include a
10 variety of chemical and biological treatment steps such as chemical and/or enzymatic hydrolysis.

Drying step 5110 creates waste stream 5220, an aqueous solution that can include dissolved chemical agents such as acids and bases in relatively low concentrations. Treatment of waste stream 5220 can include, for example, pH neutralization with one or
15 more mineral acids or bases. Depending upon the concentration of dissolved salts in waste stream 5220, the solution may be partially de-ionized (e.g., by passing the waste stream through an ion exchange system). Then, the waste stream – which includes primarily water – can be re-circulated into the overall process (e.g., as water 5150), diverted to another process, or discharged.

20 Typically, for lignocellulosic biomass feedstocks following separation step 5070, liquid phase 5090 includes a variety of soluble poly- and oligosaccharides, which can then be separated and/or reduced to smaller-chain saccharides via further processing steps. Solid phase 5100 typically includes primarily cellulose, for example, with smaller amounts of hemicellulose- and lignin-derived products.

25 In some embodiments, oxidation can be carried out at elevated temperature in a reactor such as a pyrolysis chamber. For example, referring again to FIG. 17, feedstock materials can be oxidized in filament pyrolyzer 1712. In a typical usage, an oxidizing carrier gas, e.g., air or an air/argon blend, traverses through the sample holder 1713 while the resistive heating element is rotated and heated to a desired temperature, e.g., 325 °C.
30 After an appropriate time, e.g., 5 to 10 minutes, the oxidized material is emptied from the sample holder. The system shown in FIG. 17 can be scaled and made continuous. For

example, rather than a wire as the heating member, the heating member can be an auger screw. Material can continuously fall into the sample holder, striking a heated screw that pyrolyzes the material. At the same time, the screw can push the oxidized material out of the sample holder to allow for the entry of fresh, unoxidized material.

5 Feedstock materials can also be oxidized in any of the pyrolysis systems shown in FIGS. 18-20 and described above in the Pyrolysis Systems section.

 Referring again to FIG. 21, feedstock materials can be rapidly oxidized by coating a tungsten filament 150, together with an oxidant, such as a peroxide, with the desired cellulosic material while the material is housed in a vacuum chamber 151. To affect
10 oxidation, current is passed through the filament, which causes a rapid heating of the filament for a desired time. Typically, the heating is continued for seconds before allowing the filament to cool. In some embodiments, the heating is performed a number of times to effect the desired amount of oxidation.

 Referring again to FIG. 12, in some embodiments, feedstock materials can be
15 oxidized with the aid of sound and/or cavitation. Generally, to effect oxidation, the materials are sonicated in an oxidizing environment, such as water saturated with oxygen or another chemical oxidant, such as hydrogen peroxide.

 Referring again to FIGS. 9 and 10, in certain embodiments, ionizing radiation is used to aid in the oxidation of feedstock materials. Generally, to effect oxidation, the
20 materials are irradiated in an oxidizing environment, such as air or oxygen. For example, gamma radiation and/or electron beam radiation can be employed to irradiate the materials.

Other Processes

 Steam explosion can be used alone without any of the processes described herein,
25 or in combination with any one or more of the processes described herein.

 FIG. 23 shows an overview of the entire process of converting a fiber source or feedstock 400 into a product 450, such as ethanol, by a process that includes shearing and steam explosion to produce a fibrous material 401, which is then hydrolyzed and converted, e.g., fermented, to produce the product. The fiber source can be transformed
30 into the fibrous material 401 through a number of possible methods, including at least one shearing process and at least one steam explosion process.

For example, one option includes shearing the fiber source, followed by optional screening step(s) and optional additional shearing step(s) to produce a sheared fiber source 402, which can then be steam exploded to produce the fibrous material 401. The steam explosion process is optionally followed by a fiber recovery process to remove liquids or the "liquor" 404, resulting from the steam exploding process. The material resulting from steam exploding the sheared fiber source may be further sheared by optional additional shearing step(s) and/or optional screening step(s).

In another method, the fibrous material 401 is first steam exploded to produce a steam exploded fiber source 410. The resulting steam exploded fiber source is then subjected to an optional fiber recovery process to remove liquids, or the liquor. The resulting steam exploded fiber source can then be sheared to produce the fibrous material. The steam exploded fiber source can also be subject to one or more optional screening steps and/or one or more optional additional shearing steps. The process of shearing and steam exploding the fiber source to produce the sheared and steam exploded fibrous material will be further discussed below.

The fiber source can be cut into pieces or strips of confetti material prior to shearing or steam explosion. The shearing processes can take place with the material in a dry state (e.g., having less than 0.25 percent by weight absorbed water), a hydrated state, or even while the material is partially or fully submerged in a liquid, such as water or isopropanol. The process can also optimally include steps of drying the output after steam exploding or shearing to allow for additional steps of dry shearing or steam exploding. The steps of shearing, screening, and steam explosion can take place with or without the presence of various chemical solutions.

In a steam explosion process, the fiber source or the sheared fiber source is contacted with steam under high pressure, and the steam diffuses into the structures of the fiber source (e.g., the lignocellulosic structures). The steam then condenses under high pressure thereby "wetting" the fiber source. The moisture in the fiber source can hydrolyze any acetyl groups in the fiber source (e.g., the acetyl groups in the hemicellulose fractions), forming organic acids such as acetic and uronic acids. The acids, in turn, can catalyze the depolymerization of hemicellulose, releasing xylan and limited amounts of glucan. The "wet" fiber source (or sheared fiber source, etc.) is then

“exploded” when the pressure is released. The condensed moisture instantaneously evaporates due to the sudden decrease in pressure and the expansion of the water vapor exerts a shear force upon the fiber source (or sheared fiber source, etc.). A sufficient shear force will cause the mechanical breakdown of the internal structures (e.g., the lignocellulosic structures) of the fiber source.

The sheared and steam exploded fibrous material is then converted into a useful product, such as ethanol. In some embodiments, the fibrous material is converted into a fuel. One method of converting the fibrous material into a fuel is by hydrolysis to produce fermentable sugars, 412, which are then fermented to produce the product. Other methods of converting fibrous materials into fuels may also be used.

In some embodiments, prior to combining with the microorganism, the sheared and steam exploded fibrous material 401 is sterilized to kill any competing microorganisms that may be on the fibrous material. For example, the fibrous material can be sterilized by exposing the fibrous material to radiation, such as infrared radiation, ultraviolet radiation, or an ionizing radiation, such as gamma radiation. The microorganisms can also be killed using chemical sterilants, such as bleach (e.g., sodium hypochlorite), chlorhexidine, or ethylene oxide.

One method to hydrolyze the sheared and steam exploded fibrous material is by the use of cellulases. Cellulases are a group of enzymes that act synergistically to hydrolyze cellulose. Commercially available Accellerase® 1000 enzyme complex, which contains a complex of enzymes that reduces lignocellulosic biomass into fermentable sugars, can also be used.

According to current understanding, the components of cellulase include endoglucanases, exoglucanases (cellobiohydrolases), and b-glucosidases (cellobiases). Synergism between the cellulase components exists when hydrolysis by a combination of two or more components exceeds the sum of the activities expressed by the individual components. The generally accepted mechanism of action of a cellulase system (particularly of *T. longibrachiatum*) on crystalline cellulose is that endoglucanase hydrolyzes internal β -1,4-glycosidic bonds of the amorphous regions, thereby increasing the number of exposed non-reducing ends. Exoglucanases then cleave off cellobiose units from the non-reducing ends, which in turn are hydrolyzed to individual glucose

units by b-glucosidases. There are several configurations of both endo- and exo-glucanases differing in stereospecificities. In general, the synergistic action of the components in various configurations is required for optimum cellulose hydrolysis. Cellulases, however, are more inclined to hydrolyze the amorphous regions of cellulose. A linear relationship between crystallinity and hydrolysis rates exists whereby higher crystallinity indices correspond to slower enzyme hydrolysis rates. Amorphous regions of cellulose hydrolyze at twice the rate of crystalline regions. The hydrolysis of the sheared and steam exploded fibrous material may be performed by any hydrolyzing biomass process.

Steam explosion of biomass sometimes causes the formation of by-products, e.g., toxicants, that are inhibitory to microbial and enzymatic activities. The process of converting the sheared and steam exploded fibrous material into a fuel can therefore optionally include an overliming step prior to fermentation to precipitate some of the toxicants. For example, the pH of the sheared and steam exploded fibrous material may be raised to exceed the pH of 10 by adding calcium hydroxide ($\text{Ca}(\text{OH})_2$) followed by a step of lowering the pH to about 5 by adding H_2SO_4 . The overlimed fibrous material may then be used as is without the removal of precipitates. As shown in FIG. 23, the optional overliming step occurs just prior to the step of hydrolysis of the sheared and steam exploded fibrous material, but it is also contemplated to perform the overliming step after the hydrolysis step and prior to the fermenting step.

FIG. 24 depicts an example of a steam explosion apparatus 460. The steam explosion apparatus 460 includes a reaction chamber 462, in which the fiber source and/or the fibrous material is placed through a fiber source inlet 464. The reaction chamber is sealed by closing fiber source inlet valve 465. The reaction chamber further includes a pressurized steam inlet 466 that includes a steam valve 467. The reaction chamber further includes an explosive depressurization outlet 468 that includes an outlet valve 469 in communication with the cyclone 470 through the connecting pipe 472. Once the reaction chamber contains the fiber source and/or sheared fiber source and is sealed by closing valves 465, 467 and 469, steam is delivered into the reaction chamber 462 by opening the steam inlet valve 467 allowing steam to travel through steam inlet 466. Once the reaction chamber reaches target temperature, which can take about 20 - 60

seconds, the holding time begins. The reaction chamber is held at the target temperature for the desired holding time, which typically lasts from about 10 seconds to 5 minutes. At the end of the holding time period, outlet valve is opened to allow for explosive depressurization to occur. The process of explosive depressurization propels the contents of the reaction chamber 462 out of the explosive depressurization outlet 468, through the connecting pipe 472, and into the cyclone 470. The steam exploded fiber source or fibrous material then exits the cyclone in a sludge form into the collection bin 474 as much of the remaining steam exits the cyclone into the atmosphere through vent 476. The steam explosion apparatus further includes wash outlet 478 with wash outlet valve 479 in communication with connecting pipe 472. The wash outlet valve 479 is closed during the use of the steam explosion apparatus 460 for steam explosion, but opened during the washing of the reaction chamber 462.

The target temperature of the reaction chamber 462 is preferably between 180 and 240 degrees Celsius or between 200 and 220 degrees Celsius. The holding time is preferably between 10 seconds and 30 minutes, or between 30 seconds and 10 minutes, or between 1 minute and 5 minutes.

Because the steam explosion process results in a sludge of steam exploded fibrous material, the steam exploded fibrous material may optionally include a fiber recovery process where the "liquor" is separated from the steam exploded fibrous material. This fiber recovery step is helpful in that it enables further shearing and/or screening processes and can allow for the conversion of the fibrous material into fuel. The fiber recovery process occurs through the use of a mesh cloth to separate the fibers from the liquor. Further drying processes can also be included to prepare the fibrous material or steam exploded fiber source for subsequent processing.

Combined Irradiating, Pyrolyzing, Sonicating, and/or Oxidizing Devices

In some embodiments, it may be advantageous to combine two or more separate irradiation, sonication, pyrolyzation, and/or oxidation devices into a single hybrid machine. Using such a hybrid machine, multiple processes may be performed in close juxtaposition or even simultaneously, with the benefit of increasing pretreatment throughput and potential cost savings.

For example, consider the electron beam irradiation and sonication processes. Each separate process is effective in lowering the mean molecular weight of cellulosic material by an order of magnitude or more, and by several orders of magnitude when performed serially.

5 Both irradiation and sonication processes can be applied using a hybrid electron beam/sonication device as is illustrated in FIG. 25. Hybrid electron beam/sonication device 2500 is pictured above a shallow pool (depth ~ 3-5 cm) of a slurry of cellulosic material 2550 dispersed in an aqueous, oxidant medium, such as hydrogen peroxide or carbamide peroxide. Hybrid device 2500 has an energy source 2510, which powers both
10 electron beam emitter 2540 and sonication horns 2530.

Electron beam emitter 2540 generates electron beams, which pass through an electron beam aiming device 2545 to impact the slurry 2550 containing cellulosic material. The electron beam aiming device can be a scanner that sweeps a beam over a range of up to about 6 feet in a direction approximately parallel to the surface of the
15 slurry 2550.

On either side of the electron beam emitter 2540 are sonication horns 2530, which deliver ultrasonic wave energy to the slurry 2550. The sonication horns 2530 end in a detachable endpiece 2535 that is in contact with the slurry 2550.

The sonication horns 2530 are at risk of damage from long-term residual exposure
20 to the electron beam radiation. Thus, the horns can be protected with a standard shield 2520, e.g., made of lead or a heavy-metal-containing alloy such as Lipowitz metal, which is impervious to electron beam radiation. Precautions must be taken, however, to ensure that the ultrasonic energy is not affected by the presence of the shield. The detachable endpieces 2535, which are constructed of the same material and attached to the horns
25 2530, are in contact with the cellulosic material 2550 during processing and are expected to be damaged. Accordingly, the detachable endpieces 2535 are constructed to be easily replaceable.

A further benefit of such a simultaneous electron beam and ultrasound process is that the two processes have complementary results. With electron beam irradiation alone,
30 an insufficient dose may result in cross-linking of some of the polymers in the cellulosic material, which lowers the efficiency of the overall depolymerization process. Lower

doses of electron beam irradiation and/or ultrasound radiation may also be used to achieve a similar degree of depolymerization as that achieved using electron beam irradiation and sonication separately. An electron beam device can also be combined with one or more of high frequency, rotor-stator devices, which can be used as an
5 alternative to ultrasonic sonication devices.

Further combinations of devices are also possible. For example, an ionizing radiation device that produces gamma radiation emitted from, e.g., ^{60}Co pellets, can be combined with an electron beam source and/or an ultrasonic wave source. Shielding requirements may be more stringent in this case.

10 The radiation devices for pretreating biomass discussed above can also be combined with one or more devices that perform one or more pyrolysis processing sequences. Such a combination may again have the advantage of higher throughput. Nevertheless, caution must be observed, as there may be conflicting requirements between some radiation processes and pyrolysis. For example, ultrasonic radiation
15 devices may require the feedstock be immersed in a liquid oxidizing medium. On the other hand, as discussed previously, it may be advantageous for a sample of feedstock undergoing pyrolysis to be of a particular moisture content. In this case, the new systems automatically measure and monitor for a particular moisture content and regulate the same. Further, some or all of the above devices, especially the pyrolysis device, can be
20 combined with an oxidation device as discussed previously.

PRIMARY PROCESSES

Fermentation

Generally, various microorganisms can produce a number of useful products, such as a fuel, by operating on, e.g., fermenting the pretreated biomass materials. For
25 example, alcohols, organic acids, hydrocarbons, hydrogen, proteins or mixtures of any of these materials can be produced by fermentation or other processes.

The microorganism can be a natural microorganism or an engineered microorganism. For example, the microorganism can be a bacterium, e.g., a cellulolytic bacterium, a fungus, e.g., a yeast, a plant or a protist, e.g., an algae, a protozoa or a

fungus-like protist, e.g., a slime mold. When the organisms are compatible, mixtures of organisms can be utilized.

To aid in the breakdown of the materials that include the cellulose, one or more enzymes, e.g., a cellulolytic enzyme can be utilized. In some embodiments, the materials
 5 that include the cellulose are first treated with the enzyme, e.g., by combining the material and the enzyme in an aqueous solution. This material can then be combined with the microorganism. In other embodiments, the materials that include the cellulose, the one or more enzymes and the microorganism are combined at the concurrently, e.g., by combining in an aqueous solution.

10 Also, to aid in the breakdown of the materials that include the cellulose, the materials can be treated post irradiation with heat, a chemical (e.g., mineral acid, base or a strong oxidizer such as sodium hypochlorite), and/or an enzyme.

During the fermentation, sugars released from cellulolytic hydrolysis or the saccharification step, are fermented to, e.g., ethanol, by a fermenting microorganism such
 15 as yeast. Suitable fermenting microorganisms have the ability to convert carbohydrates, such as glucose, xylose, arabinose, mannose, galactose, oligosaccharides or polysaccharides into fermentation products. Fermenting microorganisms include strains of the genus *Saccharomyces spp.* e.g., *Saccharomyces cerevisiae* (baker's yeast), *Saccharomyces distaticus*, *Saccharomyces uvarum*; the genus *Kluyveromyces*, e.g.,
 20 species *Kluyveromyces marxianus*, *Kluyveromyces fragilis*; the genus *Candida*, e.g., *Candida pseudotropicalis*, and *Candida brassicae*, *Pichia stipitis* (a relative of *Candida shehatae*, the genus *Clavispora*, e.g., species *Clavispora lusitaniae* and *Clavispora opuntiae* the genus *Pachysolen*, e.g., species *Pachysolen tannophilus*, the genus *Bretannomyces*, e.g., species *Bretannomyces clausenii* (Philippidis, G. P., 1996,
 25 Cellulose bioconversion technology, in Handbook on Bioethanol: Production and Utilization, Wyman, C.E., ed., Taylor & Francis, Washington, DC, 179-212). In particular embodiments, such as when xylose is present, *Pichia stipitis* (ATCC 66278) is utilized in fermentation.

Commercially available yeast include, for example, Red Star®/Lesaffre Ethanol
 30 Red (available from Red Star/Lesaffre, USA) FALI® (available from Fleischmann's Yeast, a division of Burns Philip Food Inc., USA), SUPERSTART® (available from

Alltech, now Lallemand), GERT STRAND[®] (available from Gert Strand AB, Sweden) and FERMOL[®] (available from DSM Specialties).

Bacteria that can ferment biomass to ethanol and other products include, e.g., *Zymomonas mobilis* and *Clostridium thermocellum* (Philippidis, 1996, *supra*). Leschine et al. (*International Journal of Systematic and Evolutionary Microbiology* 2002, **52**, 1155-1160) isolated an anaerobic, mesophilic, cellulolytic bacterium from forest soil, *Clostridium phytofermentans* sp. nov., which converts cellulose to ethanol.

Fermentation of biomass to ethanol and other products may be carried out using certain types of thermophilic or genetically engineered microorganisms, such as Thermoanaerobacter species, including *T. mathranii*, and yeast species such as *Pichia* species. An example of a strain of *T. mathranii* is A3M4 described in Sonne-Hansen et al. (*Applied Microbiology and Biotechnology* 1993, **38**, 537-541) or Ahring et al. (*Arch. Microbiol.* 1997, **168**, 114-119). Other genetically engineered microorganisms are discussed in U.S. Patent No 7,192,772.

Yeast and *Zymomonas* bacteria can be used for fermentation or conversion. The optimum pH for yeast is from about pH 4 to 5, while the optimum pH for *Zymomonas* is from about pH 5 to 6. Typical fermentation times are about 24 to 96 hours with temperatures in the range of 26 °C to 40 °C, however thermophilic microorganisms prefer higher temperatures.

Enzymes which break down biomass, such as cellulose, to lower molecular weight carbohydrate-containing materials, such as glucose, during saccharification are referred to as cellulolytic enzymes or cellulase. These enzymes may be a complex of enzymes that act synergistically to degrade crystalline cellulose. Examples of cellulolytic enzymes include: endoglucanases, cellobiohydrolases, and cellobiases (β -glucosidases). A cellulosic substrate is initially hydrolyzed by endoglucanases at random locations producing oligomeric intermediates. These intermediates are then substrates for exo-splitting glucanases such as cellobiohydrolase to produce cellobiose from the ends of the cellulose polymer. Cellobiose is a water-soluble β -1,4-linked dimer of glucose. Finally cellobiase cleaves cellobiose to yield glucose.

A cellulase is capable of degrading biomass and may be of fungal or bacterial origin. Suitable enzymes include cellulases from the genera *Bacillus*, *Pseudomonas*,

Humicola, *Fusarium*, *Thielavia*, *Acremonium*, *Chrysosporium* and *Trichoderma*, and include species of *Humicola*, *Coprinus*, *Thielavia*, *Fusarium*, *Myceliophthora*, *Acremonium*, *Cephalosporium*, *Scytalidium*, *Penicillium* or *Aspergillus* (see, e.g., EP 458162), especially those produced by a strain selected from the species *Humicola insolens* (reclassified as *Scytalidium thermophilum*, see, e.g., U.S. Patent No. 4,435,307), *Coprinus cinereus*, *Fusarium oxysporum*, *Myceliophthora thermophila*, *Meripilus giganteus*, *Thielavia terrestris*, *Acremonium* sp., *Acremonium persicinum*, *Acremonium acremonium*, *Acremonium brachypenum*, *Acremonium dichromosporum*, *Acremonium obclavatum*, *Acremonium pinkertoniae*, *Acremonium roseogriseum*, *Acremonium incoloratum*, and *Acremonium furatum*; preferably from the species *Humicola insolens* DSM 1800, *Fusarium oxysporum* DSM 2672, *Myceliophthora thermophila* CBS 117.65, *Cephalosporium* sp. RYM-202, *Acremonium* sp. CBS 478.94, *Acremonium* sp. CBS 265.95, *Acremonium persicinum* CBS 169.65, *Acremonium acremonium* AHU 9519, *Cephalosporium* sp. CBS 535.71, *Acremonium brachypenum* CBS 866.73, *Acremonium dichromosporum* CBS 683.73, *Acremonium obclavatum* CBS 311.74, *Acremonium pinkertoniae* CBS 157.70, *Acremonium roseogriseum* CBS 134.56, *Acremonium incoloratum* CBS 146.62, and *Acremonium furatum* CBS 299.70H. Cellulolytic enzymes may also be obtained from *Chrysosporium*, preferably a strain of *Chrysosporium lucknowense*. Additionally, *Trichoderma* (particularly *Trichoderma viride*, *Trichoderma reesei*, and *Trichoderma koningii*), alkalophilic *Bacillus* (see, for example, U.S. Patent No. 3,844,890 and EP 458162), and *Streptomyces* (see, e.g., EP 458162) may be used. The bacterium, *Saccharophagus degradans*, produces a mixture of enzymes capable of degrading a range of cellulosic materials and may also be used in this process.

Anaerobic cellulolytic bacteria have also been isolated from soil, e.g., a novel cellulolytic species of *Clostridium*, *Clostridium phytofermentans* sp. nov. (see Leschine et. al, *International Journal of Systematic and Evolutionary Microbiology* (2002), 52, 1155-1160).

Cellulolytic enzymes using recombinant technology can also be used (see, e.g., WO 2007/071818 and WO 2006/110891).

Other enzyme and enzyme formulations that can be used are discussed in Published U.S. Patent Application Nos. 2006/0008885 and 2006/0068475, and in PCT Application No. WO 2006/128304.

5 The cellulolytic enzymes used can be produced by fermentation of the above-noted microbial strains on a nutrient medium containing suitable carbon and nitrogen sources and inorganic salts, using procedures known in the art (see, e.g., Bennett, J.W. and LaSure, L. (eds.), *More Gene Manipulations in Fungi*, Academic Press, CA 1991). Suitable media are available from commercial suppliers or may be prepared according to published compositions (e.g., in catalogues of the American Type Culture Collection).
10 Temperature ranges and other conditions suitable for growth and cellulase production are known in the art (see, e.g., Bailey, J.E., and Ollis, D.F., *Biochemical Engineering Fundamentals*, McGraw-Hill Book Company, NY, 1986).

Treatment of cellulose with cellulase is usually carried out at temperatures between 30 °C and 65 °C. Cellulases are active over a range of pH of about 3 to 7. A
15 saccharification step may last up to 120 hours. The cellulase enzyme dosage achieves a sufficiently high level of cellulose conversion. For example, an appropriate cellulase dosage is typically between 5.0 and 50 Filter Paper Units (FPU or IU) per gram of cellulose. The FPU is a standard measurement and is defined and measured according to Ghose (1987, *Pure and Appl. Chem.* 59:257-268).

20 In particular embodiments, ACCELERASE® 1000 enzyme complex (Genencor) is utilized as the enzyme system at a loading of 0.25 mL per gram of substrate. ACCELERASE® 1000 enzyme complex is a multiple enzyme cocktail with multiple activities, mainly exoglucanase, endoglucanase, hemicellulase and beta-glucosidase. The cocktail has a minimum endoglucanase activity of 2500 CMC U/g and
25 a minimum beta-glucosidase activity of 400 pNPG U/g. The pH of the cocktail is from about 4.8 to about 5.2. In other particular embodiments, the enzyme system utilized is a blend of CELLUCLAST® 1.5L and Novozyme 188. For example, 0.5 mL of CELLUCLAST® 1.5L and 0.1 mL of Novozyme 188 can be used for each gram of substrate. When a higher hemicellulase (xylanase) activity is desired, OPTIMASH™ BG
30 can be utilized.

Mobile fermentors can be utilized, as described in U.S. Provisional Patent Application Serial 60/832,735, now Published International Application No. WO 2008/011598.

5 **Ethanol Fermentation**

Ethanol is a product of fermentation. Fermentation is a sequence of reactions which release energy from organic molecules in the absence of oxygen. In this application of fermentation, energy is obtained when sugar is changed to ethanol and carbon dioxide. All beverage ethanol, and more than half of industrial ethanol, is made
10 by this process. Changing corn to ethanol by fermentation takes many steps. Starch in corn must be broken down into simple sugars before fermentation can occur. This can be achieved, for example, by cooking the corn and adding the enzymes alpha amylase and gluco amylase. These enzymes function as catalysts to speed up the chemical changes. Once a simple sugar is obtained, yeast is added. Yeast is a single-celled fungus, which
15 feeds on the sugar and causes the fermentation. As the fungi feeds on the sugar, it produces alcohol (ethanol) and carbon dioxide. In fermentation, the ethanol retains much of the energy that was originally in the sugar, which explains why ethanol is an excellent fuel.

The fermentation reaction is represented by the simple equation:

20



Ethanol can be made from a wide variety of available feedstocks. Fuel ethanol can be made from crops which contain starch such as feed grains, food grains, such as
25 corn, and tubers, such as potatoes and sweet potatoes. Crops containing sugar, such as sugar beets, sugarcane, and sweet sorghum also could be used for the production of ethanol. In addition, food processing byproducts, such as molasses, cheese whey, and cellulosic materials including grass and wood, as well as agricultural and forestry residues, can be processed to ethanol. As discussed above, these and other feedstocks
30 can be treated as discussed herein to facilitate production of ethanol.

Conversion of Starchy Materials

FIGS. 26 and 27 show block diagrams for a dry and wet milling process, respectively, and illustrate the conversion, e.g., fermentation, of corn kernels to ethanol and other valuable co-products.

Referring particularly now to FIG. 26, in some implementations, a dry milling process for the conversion of corn kernels to ethanol, e.g., anhydrous ethanol, that can be utilized as a fuel, e.g., automobile or aviation fuel, can begin with pretreating the dried corn kernels with any one or more pretreatments described herein, such as radiation, e.g., any one or more types of radiation described herein (e.g., a beam of electrons in which each electron has an energy of about 5 MeV or a beam of protons in which the energy of each proton is about 3-100 MeV). After pre-treatment, the corn kernels can be ground and/or sheared into a powder. Although any one or more pretreatments described herein can be applied after grinding and/or at any time during the dry milling process outlined in FIG. 26, pretreating prior to grinding and/or shearing can be advantageous in that the kernels are generally more brittle after pretreatment and, as a result, are easier and can require less energy to grind and/or shear. In some embodiments, a selected pretreatment can be applied more than once during conversion, e.g., prior to milling and then after milling.

After grinding and/or shearing, the milled, dry kernels can be optionally hydrated by adding the milled material to a vessel containing water and, optionally, hydrating agents, such as surfactants. Optionally, this reaction vessel can also include one or more enzymes, such as amylase, to aid in further breakdown of starchy biomass, or the reaction vessel may contain one or more acids, such as a mineral acid, e.g., dilute sulfuric acid. If a hydration vessel is utilized, its contents are emptied into a conversion vessel, e.g., a fermentation vessel, which includes one or more conversion microbes, such as one or more yeasts, bacteria or mixtures of yeasts and/or bacteria. If a hydration vessel is not utilized, the milled material can be directly charged to the conversion vessel, e.g., for fermentation.

After conversion, the remaining solids are removed and dried to give distillers dry grains (DDG), while the ethanol is distilled off. In some embodiments, a thermophilic

microbe is utilized for the conversion and the ethanol is continuously removed by evaporation as it is produced. If desired, the distilled ethanol can be fully dehydrated, such as by passing the wet ethanol through a zeolite bed, or distilling with benzene.

Referring particularly now to FIG. 27, in some implementations, the wet milling process for the conversion of corn kernels to anhydrous ethanol begins with pretreating the dried corn kernels with any one or more pretreatments described herein, such as radiation, e.g., any one or more types of radiation described herein (e.g., a beam of electrons in which each electron has an energy of about 5 MeV). After pre-treatment, the corn kernels are steeped in dilute sulfuric acid and gently stirred to break the corn kernels into its constituents. After steeping, the fiber, oil and germ portions are fractionated and dried, and then combined with any solids remaining after distillation to give corn gluten feed (CGF). After removing germ and fiber, in some embodiments, the gluten is separated to give corn gluten meal (CGM). The remaining starch can be pretreated again (or for the first time) by any pretreatment described herein, e.g., to reduce its molecular weight and/or to functionalize the starch so that it is more soluble. In some embodiments, the starch is then charged to a reaction vessel containing water and, optionally, hydrating agents, such as surfactants. Optionally, this reaction vessel can also include one or more enzymes, such as amylase, to aid in further breakdown of starch, or the reaction vessel may contain one or more acids, such as a mineral acid, e.g., dilute sulfuric acid. As shown, saccharification can occur in several vessels and then the contents of the final vessel can be emptied into a conversion vessel, e.g., a fermentation vessel, which includes one or more conversion microbes, such as one or more yeasts or bacteria.

After conversion, the ethanol is distilled off. In some embodiments, a thermophilic microbe is utilized for the conversion and the ethanol is continuously removed by evaporation as it is produced. If desired, the distilled ethanol can be fully dehydrated, such as by passing the wet ethanol through a zeolite bed.

Gasification

In addition to using pyrolysis for pre-treatment of feedstock, pyrolysis can also be used to process pre-treated feedstock to extract useful materials. In particular, a form of pyrolysis known as gasification can be employed to generate fuel gases along with

various other gaseous, liquid, and solid products. To perform gasification, the pre-treated feedstock is introduced into a pyrolysis chamber and heated to a high temperature, typically 700 °C or more. The temperature used depends upon a number of factors, including the nature of the feedstock and the desired products.

5 Quantities of oxygen (e.g., as pure oxygen gas and/or as air) and steam (e.g., superheated steam) are also added to the pyrolysis chamber to facilitate gasification. These compounds react with carbon-containing feedstock material in a multiple-step reaction to generate a gas mixture called synthesis gas (or "syngas"). Essentially, during gasification, a limited amount of oxygen is introduced into the pyrolysis chamber to
10 allow some feedstock material to combust to form carbon monoxide and generate process heat. The process heat can then be used to promote a second reaction that converts additional feedstock material to hydrogen and carbon monoxide.

 In a first step of the overall reaction, heating the feedstock material produces a char that can include a wide variety of different hydrocarbon-based species. Certain
15 volatile materials can be produced (e.g., certain gaseous hydrocarbon materials), resulting in a reduction of the overall weight of the feedstock material. Then, in a second step of the reaction, some of the volatile material that is produced in the first step reacts with oxygen in a combustion reaction to produce both carbon monoxide and carbon dioxide. The combustion reaction releases heat, which promotes the third step of the reaction. In
20 the third step, carbon dioxide and steam (e.g., water) react with the char generated in the first step to form carbon monoxide and hydrogen gas. Carbon monoxide can also react with steam, in a water gas shift reaction, to form carbon dioxide and further hydrogen gas.

 Gasification can be used as a primary process to generate products directly from
25 pre-treated feedstock for subsequent transport and/or sale, for example. Alternatively, or in addition, gasification can be used as an auxiliary process for generating fuel for an overall processing system. The hydrogen-rich syngas that is generated via the gasification process can be burned, for example, to generate electricity and/or process heat that can be directed for use at other locations in the processing system. As a result,
30 the overall processing system can be at least partially self-sustaining. A number of other products, including pyrolysis oils and gaseous hydrocarbon-based substances, can also be

obtained during and/or following gasification; these can be separated and stored or transported as desired.

A variety of different pyrolysis chambers are suitable for gasification of pre-treated feedstock, including the pyrolysis chambers disclosed herein. In particular, fluidized bed reactor systems, in which the pre-treated feedstock is fluidized in steam and oxygen/air, provide relatively high throughput and straightforward recovery of products. Solid char that remains following gasification in a fluidized bed system (or in other pyrolysis chambers) can be burned to generate additional process heat to promote subsequent gasification reactions.

Syngas can be reformed using a Fischer-Tropsch process, which is a catalyzed chemical reaction in which the synthesis gas is converted into liquid alcohols and hydrocarbons. The most common catalysts are based on iron and cobalt, although nickel and ruthenium have also been used.

In an alternative process, a biofilm can be used to reform the syngas to produce the liquid fuel instead of a chemical catalyst. Such a process has been described by Coskata, Inc. Any of the biomass materials described herein can be used in Coskata's process.

In some embodiments, irradiating the biomass material, e.g., with a beam of particles, such as electrons, prior to gasification can lower the gasification temperature, resulting in less energy being consumed during gasification, and can result in less char and tar formation, resulting in enhanced syngas yield.

POST-PROCESSING

Distillation

After fermentation, the resulting fluids can be distilled using, for example, a "beer column" to separate ethanol and other alcohols from the majority of water and residual solids. The vapor exiting the beer column can be, e.g., 35% by weight ethanol, and can be fed to a rectification column. A mixture of nearly azeotropic (92.5%) ethanol and water from the rectification column can be purified to pure (99.5%) ethanol using vapor-phase molecular sieves. The beer column bottoms can be sent to the first effect of a three-effect evaporator. The rectification column reflux condenser can provide heat for

this first effect. After the first effect, solids can be separated using a centrifuge and dried in a rotary dryer. A portion (25%) of the centrifuge effluent can be recycled to fermentation and the rest sent to the second and third evaporator effects. Most of the evaporator condensate can be returned to the process as fairly clean condensate with a small portion split off to waste water treatment to prevent build-up of low-boiling compounds.

Waste water treatment

Wastewater treatment is used to minimize makeup water requirements of the plant by treating process water for reuse within the plant. Wastewater treatment can also produce fuel (e.g., sludge and biogas) that can be used to improve the overall efficiency of the ethanol production process. For example, as described in further detail below, sludge and biogas can be used to create steam and electricity that can be used in various plant processes.

Wastewater is initially pumped through a screen (e.g., a bar screen) to remove large particles, which are collected in a hopper. In some embodiments, the large particles are sent to a landfill. Additionally or alternatively, the large particles are burned to create steam and/or electricity as described in further detail below. In general, the spacing on the bar screen is between 1/4 inch to 1 inch spacing (e.g., 1/2 inch spacing).

The wastewater then flows to an equalization tank, where the organic concentration of the wastewater is equalized during a retention time. In general, the retention time is between 8 hours and 36 hours (e.g., 24 hours). A mixer is disposed within the tank to stir the contents of the tank. In some embodiments, mixers disposed throughout the tank are used to stir the contents of the tank. In certain embodiments, the mixer substantially mixes the contents of the equalization tank such that conditions (e.g., wastewater concentration and temperature) throughout the tank are uniform.

A first pump moves water from the equalization tank through a liquid-to-liquid heat exchanger. The heat exchanger is controlled (e.g., by controlling the flow rate of fluid through the heat exchanger) such that wastewater exiting the heat exchanger is at a desired temperature for anaerobic treatment. For example, the desired temperature for anaerobic treatment can be between 40 °C to 60 °C.

After exiting the heat exchanger, the wastewater enters one or more anaerobic reactors. In some embodiments, the concentration of sludge in each anaerobic reactor is the same as the overall concentration of sludge in the wastewater. In other embodiments, the anaerobic reactor has a higher concentration of sludge than the overall concentration
5 of sludge in the wastewater.

A nutrient solution containing nitrogen and phosphorus is metered into each anaerobic reactor containing wastewater. The nutrient solution reacts with the sludge in the anaerobic reactor to produce biogas which can contain 50% methane and have a heating value of approximately 12,000 British thermal units, or Btu, per pound). The
10 biogas exits each anaerobic reactor through a vent and flows into a manifold, where several biogas streams are combined into a single stream. A compressor moves the stream of biogas to a boiler or a combustion engine as described in further detail below. In some embodiments, the compressor also moves the single stream of biogas through a desulphurization catalyst. Additionally or alternatively, the compressor can move the
15 single stream of biogas through a sediment trap.

A second pump moves anaerobic effluent from the anaerobic reactors to one or more aerobic reactors (e.g., activated sludge reactors). An aerator is disposed within each aerobic reactor to mix the anaerobic effluent, sludge, and oxygen (e.g., oxygen contained in air). Within each aerobic reactor, oxidation of cellular material in the anaerobic
20 effluent produces carbon dioxide, water, and ammonia.

Aerobic effluent moves (e.g., via gravity) to a separator, where sludge is separated from treated water. Some of the sludge is returned to the one or more aerobic reactors to create an elevated sludge concentration in the aerobic reactors, thereby facilitating the aerobic breakdown of cellular material in the wastewater. A conveyor removes excess
25 sludge from the separator. As described in further detail below, the excess sludge is used as fuel to create steam and/or electricity.

The treated water is pumped from the separator to a settling tank. Solids dispersed throughout the treated water settle to the bottom of the settling tank and are subsequently removed. After a settling period, treated water is pumped from the settling
30 tank through a fine filter to remove any additional solids remaining in the water. In some embodiments, chlorine is added to the treated water to kill pathogenic bacteria. In some

embodiments, one or more physical-chemical separation techniques are used to further purify the treated water. For example, treated water can be pumped through a carbon adsorption reactor. As another example, treated water can be pumped through a reverse osmosis reactor.

5 In the processes disclosed herein, whenever water is used in any process, it may be grey water, e.g., municipal grey water, or black water. In some embodiments, the grey or black water is sterilized prior to use. Sterilization may be accomplished by any desired technique, for example by irradiation, steam, or chemical sterilization.

10 **Waste combustion**

 The production of alcohol from biomass can result in the production of various by-product streams useful for generating steam and electricity to be used in other parts of the plant. For example, steam generated from burning by-product streams can be used in the distillation process. As another example, electricity generated from burning by-product streams can be used to power electron beam generators and ultrasonic
15 transducers used in pretreatment.

 The by-products used to generate steam and electricity are derived from a number of sources throughout the process. For example, anaerobic digestion of wastewater produces a biogas high in methane and a small amount of waste biomass (sludge). As
20 another example, post-distillate solids (e.g., unconverted lignin, cellulose, and hemicellulose remaining from the pretreatment and primary processes) can be used as a fuel.

 The biogas is diverted to a combustion engine connected to an electric generator to produce electricity. For example, the biogas can be used as a fuel source for a spark-
25 ignited natural gas engine. As another example, the biogas can be used as a fuel source for a direct-injection natural gas engine. As another example, the biogas can be used as a fuel source for a combustion turbine. Additionally or alternatively, the combustion engine can be configured in a cogeneration configuration. For example, waste heat from the combustion engines can be used to provide hot water or steam throughout the plant.

30 The sludge, and post-distillate solids are burned to heat water flowing through a heat exchanger. In some embodiments, the water flowing through the heat exchanger is

evaporated and superheated to steam. In certain embodiments, the steam is used in the pretreatment reactor and in heat exchange in the distillation and evaporation processes. Additionally or alternatively, the steam expands to power a multi-stage steam turbine connected to an electric generator. Steam exiting the steam turbine is condensed with
5 cooling water and returned to the heat exchanger for reheating to steam. In some embodiments, the flow rate of water through the heat exchanger is controlled to obtain a target electricity output from the steam turbine connected to an electric generator. For example, water can be added to the heat exchanger to ensure that the steam turbine is operating above a threshold condition (e.g., the turbine is spinning fast enough to turn the
10 electric generator).

While certain embodiments have been described, other embodiments are possible.

As an example, while the biogas is described as being diverted to a combustion engine connected to an electric generator, in certain embodiments, the biogas can be passed through a fuel reformer to produce hydrogen. The hydrogen is then converted to
15 electricity through a fuel cell.

As another example, while the biogas is described as being burned apart from the sludge and post-distillate solids, in certain embodiments, all of the waste by-products can be burned together to produce steam.

PRODUCTS / CO-PRODUCTS

Alcohols

The alcohol produced can be a monohydroxy alcohol, e.g., ethanol, or a polyhydroxy alcohol, e.g., ethylene glycol or glycerin. Examples of alcohols that can be produced include methanol, ethanol, propanol, isopropanol, butanol, e.g., n-, sec- or t-butanol, ethylene glycol, propylene glycol, 1, 4-butane diol, glycerin or mixtures of these
25 alcohols.

Each of the alcohols produced by the plant have commercial value as industrial feedstock. For example, ethanol can be used in the manufacture of varnishes and perfume. As another example, methanol can be used as a solvent used as a component in windshield wiper fluid. As still another example, butanol can be used in plasticizers,
30 resins, lacquers, and brake fluids.

Bioethanol produced by the plant is valuable as an ingredient used in the food and beverage industry. For example, the ethanol produced by the plant can be purified to food grade alcohol and used as a primary ingredient in the alcoholic beverages.

5 Bioethanol produced by the plant also has commercial value as a transportation fuel. The use of ethanol as a transportation fuel can be implemented with relatively little capital investment from spark ignition engine manufacturers and owners (e.g., changes to injection timing, fuel-to-air ratio, and components of the fuel injection system). Many automotive manufacturers currently offer flex-fuel vehicles capable of operation on ethanol/gasoline blends up to 85% ethanol by volume (e.g., standard equipment on a
10 Chevy Tahoe 4 x 4).

Bioethanol produced by this plant can be used as an engine fuel to improve environmental and economic conditions beyond the location of the plant. For example, ethanol produced by this plant and used as a fuel can reduce greenhouse gas emissions from manmade sources (e.g., transportation sources). As another example, ethanol
15 produced by this plant and used as an engine fuel can also displace consumption of gasoline refined from oil.

Bioethanol has a greater octane number than conventional gasoline and, thus, can be used to improve the performance (e.g., allow for higher compression ratios) of spark ignition engines. For example, small amounts (e.g., 10% by volume) of ethanol can be
20 blended with gasoline to act as an octane enhancer for fuels used in spark ignition engines. As another example, larger amounts (e.g., 85% by volume) of ethanol can be blended with gasoline to further increase the fuel octane number and displace larger volumes of gasoline.

Bioethanol strategies are discussed, e.g., by DiPardo in *Journal of Outlook for*
25 *Biomass Ethanol Production and Demand (EIA Forecasts)*, 2002; Sheehan in *Biotechnology Progress*, 15:8179, 1999; Martin in *Enzyme Microbes Technology*, 31:274, 2002; Greer in *BioCycle*, 61-65, April 2005; Lynd in *Microbiology and Molecular Biology Reviews*, 66:3, 506-577, 2002; Ljungdahl et al., in U.S. Patent No. 4,292,406; and Bellamy, in U.S. Patent No. 4,094,742.

Organic acids

The organic acids produced can include monocarboxylic acids or polycarboxylic acids. Examples of organic acids include formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic, palmitic acid, stearic acid, oxalic acid, malonic acid, succinic acid, glutaric acid, oleic acid, linoleic acid, glycolic acid, lactic acid, γ -hydroxybutyric acid or mixtures of these acids.

Co-Products***Lignin Residue***

As described above, lignin-containing residues from primary and pretreatment processes has value as a high/medium energy fuel and can be used to generate power and steam for use in plant processes. However, such lignin residues are a new type of solids fuel and there is little demand for it outside of the plant boundaries, and the costs of drying it for transportation only subtract from its potential value. In some cases, gasification of the lignin residues can convert it to a higher-value product with lower cost.

Other Co-Products

Cell matter, furfural, and acetic acid have been identified as potential co-products of biomass-to-fuel processing facilities. Interstitial cell matter could be valuable, but might require significant purification. Markets for furfural and acetic acid are in place, although it is unlikely that they are large enough to consume the output of a fully commercialized lignocellulose-to-ethanol industry.

EXAMPLES

The following Examples are intended to illustrate, and do not limit the teachings of this disclosure.

Example 1 – Preparation Of Fibrous Material From Polycoated Paper

A 1500 pound skid of virgin, half-gallon juice cartons made of un-printed polycoated white Kraft board having a bulk density of 20 lb/ft³ was obtained from

International Paper. Each carton was folded flat, and then fed into a 3 hp Flinch Baugh shredder at a rate of approximately 15 to 20 pounds per hour. The shredder was equipped with two 12 inch rotary blades, two fixed blades and a 0.30 inch discharge screen. The gap between the rotary and fixed blades was adjusted to 0.10 inch. The output from the shredder resembled confetti having a width of between 0.1 inch and 0.5 inch, a length of between 0.25 inch and 1 inch and a thickness equivalent to that of the starting material (about 0.075 inch).

The confetti-like material was fed to a Munson rotary knife cutter, Model SC30. Model SC30 is equipped with four rotary blades, four fixed blades, and a discharge screen having 1/8 inch openings. The gap between the rotary and fixed blades was set to approximately 0.020 inch. The rotary knife cutter sheared the confetti-like pieces across the knife-edges, tearing the pieces apart and releasing a fibrous material at a rate of about one pound per hour. The fibrous material had a BET surface area of $0.9748 \text{ m}^2/\text{g} \pm 0.0167 \text{ m}^2/\text{g}$, a porosity of 89.0437 percent and a bulk density (@0.53 psia) of 0.1260 g/mL. An average length of the fibers was 1.141 mm and an average width of the fibers was 0.027 mm, giving an average L/D of 42:1. A scanning electron micrograph of the fibrous material is shown in FIG. 28 at 25 X magnification.

Example 2 – Preparation Of Fibrous Material From Bleached Kraft Board

A 1500 pound skid of virgin bleached white Kraft board having a bulk density of 30 lb/ft³ was obtained from International Paper. The material was folded flat, and then fed into a 3 hp Flinch Baugh shredder at a rate of approximately 15 to 20 pounds per hour. The shredder was equipped with two 12 inch rotary blades, two fixed blades and a 0.30 inch discharge screen. The gap between the rotary and fixed blades was adjusted to 0.10 inch. The output from the shredder resembled confetti having a width of between 0.1 inch and 0.5 inch, a length of between 0.25 inch and 1 inch and a thickness equivalent to that of the starting material (about 0.075 inch). The confetti-like material was fed to a Munson rotary knife cutter, Model SC30. The discharge screen had 1/8 inch openings. The gap between the rotary and fixed blades was set to approximately 0.020 inch. The rotary knife cutter sheared the confetti-like pieces, releasing a fibrous material at a rate of about one pound per hour. The fibrous material had a BET surface area of $1.1316 \text{ m}^2/\text{g} \pm 0.0103 \text{ m}^2/\text{g}$, a porosity of 88.3285 percent and a bulk density (@0.53 psia) of 0.1497

g/mL. An average length of the fibers was 1.063 mm and an average width of the fibers was 0.0245 mm, giving an average L/D of 43:1. A scanning electron micrograph of the fibrous material is shown in FIG. 29 at 25 X magnification.

Example 3 – Preparation Of Twice Sheared Fibrous Material From Bleached Kraft Board

5 A 1500 pound skid of virgin bleached white Kraft board having a bulk density of 30 lb/ft³ was obtained from International Paper. The material was folded flat, and then fed into a 3 hp Flinch Baugh shredder at a rate of approximately 15 to 20 pounds per hour. The shredder was equipped with two 12 inch rotary blades, two fixed blades and a 0.30 inch discharge screen. The gap between the rotary and fixed blades was adjusted to 0.10 inch. The output from the shredder resembled confetti (as above). The confetti-like material was fed to a Munson rotary knife cutter, Model SC30. The discharge screen had 1/16 inch openings. The gap between the rotary and fixed blades was set to approximately 0.020 inch. The rotary knife cutter the confetti-like pieces, releasing a fibrous material at a rate of about one pound per hour. The material resulting from the first shearing was fed back into the same setup described above and sheared again. The resulting fibrous material had a BET surface area of 1.4408 m²/g +/- 0.0156 m²/g, a porosity of 90.8998 percent and a bulk density (@0.53 psia) of 0.1298 g/mL. An average length of the fibers was 0.891 mm and an average width of the fibers was 0.026 mm, giving an average L/D of 34:1. A scanning electron micrograph of the fibrous material is shown in FIG. 30 at 25 X magnification.

Example 4 – Preparation Of Thrice Sheared Fibrous Material From Bleached Kraft Board

A 1500 pound skid of virgin bleached white Kraft board having a bulk density of 30 lb/ft³ was obtained from International Paper. The material was folded flat, and then fed into a 3 hp Flinch Baugh shredder at a rate of approximately 15 to 20 pounds per hour. The shredder was equipped with two 12 inch rotary blades, two fixed blades and a 0.30 inch discharge screen. The gap between the rotary and fixed blades was adjusted to 0.10 inch. The output from the shredder resembled confetti (as above). The confetti-like material was fed to a Munson rotary knife cutter, Model SC30. The discharge screen had 1/8 inch openings. The gap between the rotary and fixed blades was set to approximately 0.020 inch. The rotary knife cutter sheared the confetti-like pieces across the knife-

edges. The material resulting from the first shearing was fed back into the same setup and the screen was replaced with a 1/16 inch screen. This material was sheared. The material resulting from the second shearing was fed back into the same setup and the screen was replaced with a 1/32 inch screen. This material was sheared. The resulting fibrous material had a BET surface area of $1.6897 \text{ m}^2/\text{g} \pm 0.0155 \text{ m}^2/\text{g}$, a porosity of 87.7163 percent and a bulk density (@0.53 psia) of 0.1448 g/mL . An average length of the fibers was 0.824 mm and an average width of the fibers was 0.0262 mm, giving an average L/D of 32:1. A scanning electron micrograph of the fibrous material is shown in FIG. 31 at 25 X magnification.

10 **Example 5 – Preparation Of Densified Fibrous Material From Bleached Kraft Board Without Added Binder**

Fibrous material was prepared according to Example 2. Approximately 1 lb of water was sprayed onto each 10 lb of fibrous material. The fibrous material was densified using a California Pellet Mill 1100 operating at 75°C . Pellets were obtained having a bulk density ranging from about 7 lb/ft^3 to about 15 lb/ft^3 .

Example 6 – Preparation Of Densified Fibrous Material From Bleached Kraft Board With Binder

Fibrous material was prepared according to Example 2.

A 2 weight percent stock solution of POLYOXTM WSR N10 (polyethylene oxide) was prepared in water.

Approximately 1 lb of the stock solution was sprayed onto each 10 lb of fibrous material. The fibrous material was densified using a California Pellet Mill 1100 operating at 75°C . Pellets were obtained having a bulk density ranging from about 15 lb/ft^3 to about 40 lb/ft^3 .

25 **Example 7 – Reducing the Molecular Weight of Cellulose in Fibrous Kraft Paper by Gamma Radiation with Minimum Oxidation**

Fibrous material is prepared according to Example 4. The fibrous Kraft paper is densified according to Example 5.

The densified pellets are placed in a glass ampoule having a maximum capacity of 250 mL. The glass ampoule is evacuated under high vacuum (10^{-5} torr) for 30 minutes,

and then back-filled with argon gas. The ampoule is sealed under argon. The pellets in the ampoule are irradiated with gamma radiation for about 3 hours at a dose rate of about 1 Mrad per hour to provide an irradiated material in which the cellulose has a lower molecular weight than the fibrous Kraft starting material.

5 **Example 8 – Reducing the Molecular Weight of Cellulose in Fibrous Kraft Paper by Gamma Radiation with Maximum Oxidation**

Fibrous material is prepared according to Example 4. The fibrous Kraft paper is densified according to Example 5.

10 The densified pellets are placed in a glass ampoule having a maximum capacity of 250 mL. The glass ampoule is sealed under an atmosphere of air. The pellets in the ampoule are irradiated with gamma radiation for about 3 hours at a dose rate of about 1 Mrad per hour to provide an irradiated material in which the cellulose has a lower molecular weight than the fibrous Kraft starting material.

15 **Example 9 - Methods of Determining Molecular Weight of Cellulosic and Lignocellulosic Materials by Gel Permeation Chromatography**

Cellulosic and lignocellulosic materials for analysis were treated according to Example 4. Sample materials presented in the following tables include Kraft paper (P), wheat straw (WS), alfalfa (A), and switchgrass (SG). The number “132” of the Sample ID refers to the particle size of the material after shearing through a 1/32 inch screen.
20 The number after the dash refers to the dosage of radiation (MRad) and “US” refers to ultrasonic treatment. For example, a sample ID “P132-10” refers to Kraft paper that has been sheared to a particle size of 132 mesh and has been irradiated with 10 MRad.

Table 1. Peak Average Molecular Weight of Irradiated Kraft Paper

Sample Source	Sample ID	Dosage ¹ (MRad)	Ultrasound ²	Average MW ± Std Dev.
Kraft Paper	P132	0	No	32853±10006
	P132-10	10	“	61398 ± 2468**
	P132-100	100	“	8444 ± 580
	P132-181	181	“	6668 ± 77
	P132-US	0	Yes	3095 ± 1013

25 **Low doses of radiation appear to increase the molecular weight of some materials

¹Dosage Rate = 1MRad/hour

²Treatment for 30 minutes with 20kHz ultrasound using a 1000W horn under re-circulating conditions with the material dispersed in water.

Table 2. Peak Average Molecular Weight of Irradiated Materials

Sample ID	Peak #	Dosage ¹ (MRad)	Ultrasound ²	Average MW $\pm$ Std Dev.
WS132	1	0	No	1407411 $\pm$ 175191
	2	"	"	39145 $\pm$ 3425
	3	"	"	2886 $\pm$ 177
WS132-10*	1	10	"	26040 $\pm$ 3240
WS132-100*	1	100	"	23620 $\pm$ 453
A132	1	0	"	1604886 $\pm$ 151701
	2	"	"	37525 $\pm$ 3751
	3	"	"	2853 $\pm$ 490
A132-10*	1	10	"	50853 $\pm$ 1665
	2	"	"	2461 $\pm$ 17
A132-100*	1	100	"	38291 $\pm$ 2235
	2	"	"	2487 $\pm$ 15
SG132	1	0	"	1557360 $\pm$ 83693
	2	"	"	42594 $\pm$ 4414
	3	"	"	3268 $\pm$ 249
SG132-10*	1	10	"	60888 $\pm$ 9131
SG132-100*	1	100	"	22345 $\pm$ 3797
SG132-10-US	1	10	Yes	86086 $\pm$ 43518
	2	"	"	2247 $\pm$ 468
SG132-100-US	1	100	"	4696 $\pm$ 1465

*Peaks coalesce after treatment

**Low doses of radiation appear to increase the molecular weight of some materials

¹Dosage Rate = 1MRad/hour

²Treatment for 30 minutes with 20kHz ultrasound using a 1000W horn under re-circulating conditions with the material dispersed in water.

Gel Permeation Chromatography (GPC) is used to determine the molecular weight distribution of polymers. During GPC analysis, a solution of the polymer sample is passed through a column packed with a porous gel trapping small molecules. The sample is separated based on molecular size with larger molecules eluting sooner than smaller molecules. The retention time of each component is most often detected by refractive index (RI), evaporative light scattering (ELS), or ultraviolet (UV) and compared to a calibration curve. The resulting data is then used to calculate the molecular weight distribution for the sample.

A distribution of molecular weights rather than a unique molecular weight is used to characterize synthetic polymers. To characterize this distribution, statistical averages are utilized. The most common of these averages are the "number average molecular weight" (M_n) and the "weight average molecular weight" (M_w). Methods of calculating these values are described in the art, e.g., in Example 9 of WO 2008/073186.

The polydispersity index or PI is defined as the ratio of M_w/M_n . The larger the PI, the broader or more disperse the distribution. The lowest value that a PI can be is 1. This represents a monodisperse sample; that is, a polymer with all of the molecules in the distribution being the same molecular weight.

5 The peak molecular weight value (M_p) is another descriptor defined as the mode of the molecular weight distribution. It signifies the molecular weight that is most abundant in the distribution. This value also gives insight to the molecular weight distribution.

10 Most GPC measurements are made relative to a different polymer standard. The accuracy of the results depends on how closely the characteristics of the polymer being analyzed match those of the standard used. The expected error in reproducibility between different series of determinations, calibrated separately, is ca. 5-10% and is characteristic to the limited precision of GPC determinations. Therefore, GPC results are most useful when a comparison between the molecular weight distributions of different samples is
15 made during the same series of determinations.

 The lignocellulosic samples required sample preparation prior to GPC analysis. First, a saturated solution (8.4% by weight) of lithium chloride (LiCl) was prepared in dimethyl acetamide (DMAc). Approximately 100 mg of each sample was added to approximately 10 g of a freshly prepared saturated LiCl/DMAc solution, and each
20 mixture was heated to approximately 150°C-170°C with stirring for 1 hour. The resulting solutions were generally light- to dark-yellow in color. The temperature of the solutions was decreased to approximately 100°C and the solutions were heated for an additional 2 hours. The temperature of the solutions was then decreased to approximately 50°C and each sample solution was heated for approximately 48 to 60 hours. Of note,
25 samples irradiated at 100 MRad were more easily solubilized as compared to their untreated counterpart. Additionally, the sheared samples (denoted by the number 132) had slightly lower average molecular weights as compared with uncut samples.

 The resulting sample solutions were diluted 1:1 using DMAc as solvent and were filtered through a 0.45 μ m PTFE filter. The filtered sample solutions were then analyzed
30 by GPC. The peak average molecular weight (M_p) of the samples, as determined by Gel Permeation Chromatography (GPC), are summarized in Tables 1 and 2. Each sample was

prepared in duplicate and each preparation of the sample was analyzed in duplicate (two injections) for a total of four injections per sample. The EasiCal polystyrene standards PS1A and PS1B were used to generate a calibration curve for the molecular weight scale from about 580 to 7,500,00 Daltons.

5

Table 3. GPC Analysis Conditions

Instrument:	Waters Alliance GPC 2000
	Plgel 10 μ Mixed-B
Columns (3):	S/N's: 10M-MB-148-83; 10M-MB-148-84; 10M-MB-174-129
Mobile Phase (solvent):	0.5% LiCl in DMAc (1.0 mL/min.)
Column/Detector Temperature:	70 °C
Injector Temperature:	70 °C
Sample Loop Size:	323.5 μ L

Example 10- Determining Crystallinity of Irradiated Material by X-Ray Diffraction

X-ray diffraction (XRD) is a method by which a crystalline sample is irradiated with monoenergetic x-rays. The interaction of the lattice structure of the sample with these x-rays is recorded and provides information about the crystalline structure being irradiated. The resulting characteristic "fingerprint" allows for the identification of the crystalline compounds present in the sample. Using a whole-pattern fitting analysis (the Rietvelt Refinement), it is possible to perform quantitative analyses on samples containing more than one crystalline compound.

15

Table 4. XRD Data Including Domain Size and % Crystallinity

Sample ID	Domain Size (Å)	% Crystallinity
P132	55	55
P132-10	46	58
P132-100	50	55
P132-181	48	52
P132-US	26	40
A132	28	42
A132-10	26	40
A132-100	28	35
WS132	30	36
WS132-10	27	37
WS132-100	30	41
SG132	29	40
SG132-10	28	38

SG132-100	28	37
SG132-10-US	25	42
SG132-100-US	21	34

Each sample was placed on a zero background holder and placed in a Phillips PW1800 diffractometer using Cu radiation. Scans were then run over the range of 5° to 50° with a step size of 0.05° and a counting time of 2 hours each.

5 Once the diffraction patterns were obtained, the phases were identified with the aid of the Powder Diffraction File published by the International Centre for Diffraction Data. In all samples the crystalline phase identified was cellulose – Ia, which has a triclinic structure.

10 The distinguishing feature among the 20 samples is the peak breadth, which is related to the crystallite domain size. The experimental peak breadth was used to compute the domain size and percent crystallinity, which are reported in Table 4.

Percent crystallinity (X_c %) is measured as a ratio of the crystalline area to the total area under the x-ray diffraction peaks,

15
$$X_c \% = \frac{A_c}{\{A_a + A_c\}} \times 100\%$$

where,

A_c = Area of crystalline phase

A_a = Area of amorphous phase

X_c = Percent of crystallinity

20 To determine the percent crystallinity for each sample it was necessary to first extract the amount of the amorphous phase. This is done by estimating the area of each diffraction pattern that can be attributed to the crystalline phase (represented by the

sharper peaks) and the non-crystalline phase (represented by the broad humps beneath the pattern and centered at 22° and 38°).

A systematic process was used to minimize error in these calculations due to broad crystalline peaks as well as high background intensity. First, a linear background was applied and then removed. Second, two Gaussian peaks centered at 22° and 38° with widths of 10-12° each were fitted to the humps beneath the crystalline peaks. Third, the area beneath the two broad Gaussian peaks and the rest of the pattern were determined. Finally, percent crystallinity was calculated by dividing the area beneath the crystalline peak by the total intensity (after background subtraction). Domain size and % crystallinity of the samples as determined by X-ray diffraction (XRD) are presented in Table 4.

Example 11 - Porosimetry Analysis of Irradiated Materials

Mercury pore size and pore volume analysis (Table 5) is based on forcing mercury (a non-wetting liquid) into a porous structure under tightly controlled pressures. Since mercury does not wet most substances and will not spontaneously penetrate pores by capillary action, it must be forced into the voids of the sample by applying external pressure. The pressure required to fill the voids is inversely proportional to the size of the pores. Only a small amount of force or pressure is required to fill large voids, whereas much greater pressure is required to fill voids of very small pores.

Table 5. Pore Size and Volume Distribution by Mercury Porosimetry

Sample ID	Total Intrusion Volume (mL/g)	Total Pore Area (m ² /g)	Median Pore Diameter (Volume) (μm)	Median Pore Diameter (Area) (μm)	Average Pore Diameter (4V/A) (μm)	Bulk Density @ 0.50 psia (g/mL)	Apparent (skeletal) Density (g/mL)	Porosity (%)
P132	6.0594	1.228	36.2250	13.7278	19.7415	0.1448	1.1785	87.7163
P132-10	5.5436	1.211	46.3463	4.5646	18.3106	0.1614	1.5355	89.4875
P132-100	5.3985	0.998	34.5235	18.2005	21.6422	0.1612	1.2413	87.0151
P132-181	3.2866	0.868	25.3448	12.2410	15.1509	0.2497	1.3916	82.0577
P132-US	6.0005	14.787	98.3459	0.0055	1.6231	0.1404	0.8894	84.2199
A132	2.0037	11.759	64.6308	0.0113	0.6816	0.3683	1.4058	73.7990
A132-10	1.9514	10.326	53.2706	0.0105	0.7560	0.3768	1.4231	73.5241
A132-100	1.9394	10.205	43.8966	0.0118	0.7602	0.3760	1.3889	72.9264
SG132	2.5267	8.265	57.6958	0.0141	1.2229	0.3119	1.4708	78.7961
SG132-10	2.1414	8.643	26.4666	0.0103	0.9910	0.3457	1.3315	74.0340
SG132-100	2.5142	10.766	32.7118	0.0098	0.9342	0.3077	1.3590	77.3593
SG132-10-US	4.4043	1.722	71.5734	1.1016	10.2319	0.1930	1.2883	85.0169

SG132-100-US	4.9665	7.358	24.8462	0.0089	2.6998	0.1695	1.0731	84.2010
WS132	2.9920	5.447	76.3675	0.0516	2.1971	0.2773	1.6279	82.9664
WS132-10	3.1138	2.901	57.4727	0.3630	4.2940	0.2763	1.9808	86.0484
WS132-100	3.2077	3.114	52.3284	0.2876	4.1199	0.2599	1.5611	83.3538

The AutoPore 9520 can attain a maximum pressure of 414 MPa or 60,000 psia. There are four low-pressure stations for sample preparation and collection of macropore data from 0.2 psia to 50 psia. There are two high-pressure chambers, which collect data from 25 psia to 60,000 psia. The sample is placed in a bowl-like apparatus called a penetrometer, which is bonded to a glass capillary stem with a metal coating. As mercury invades the voids in and around the sample, it moves down the capillary stem. The loss of mercury from the capillary stem results in a change in the electrical capacitance. The change in capacitance during the experiment is converted to volume of mercury by knowing the stem volume of the penetrometer in use. A variety of penetrometers with different bowl (sample) sizes and capillaries are available to accommodate most sample sizes and configurations. Table 6 below defines some of the key parameters calculated for each sample.

Table 6. Definition of Parameters

Parameter	Description
Total Intrusion Volume:	The total volume of mercury intruded during an experiment. This can include interstitial filling between small particles, porosity of sample, and compression volume of sample.
Total Pore Area:	The total intrusion volume converted to an area assuming cylindrical shaped pores.
Median Pore Diameter (volume):	The size at the 50 th percentile on the cumulative volume graph.
Median Pore Diameter (area):	The size at the 50 th percentile on the cumulative area graph.
Average Pore Diameter:	The total pore volume divided by the total pore area (4V/A).
Bulk Density:	The mass of the sample divided by the bulk volume. Bulk volume is determined at the filling pressure, typically 0.5 psia.
Apparent Density:	The mass of sample divided by the volume of sample measured at highest pressure, typically 60,000 psia.
Porosity:	(Bulk Density/ Apparent Density) x 100%

Example 12 - Particle Size Analysis of Irradiated Materials

The technique of particle sizing by static light scattering is based on Mie theory (which also encompasses Fraunhofer theory). Mie theory predicts the intensity vs. angle relationship as a function of the size for spherical scattering particles provided that other system variables are known and held constant. These variables are the wavelength of incident light and the relative refractive index of the sample material. Application of Mie theory provides the detailed particle size information. Table 7 summarizes particle size using median diameter, mean diameter, and modal diameter as parameters.

Table 7. Particle Size by Laser Light Scattering (Dry Sample Dispersion)

Sample ID	Median Diameter (μm)	Mean Diameter (μm)	Modal Diameter (μm)
A132	380.695	418.778	442.258
A132-10	321.742	366.231	410.156
A132-100	301.786	348.633	444.169
SG132	369.400	411.790	455.508
SG132-10	278.793	325.497	426.717
SG132-100	242.757	298.686	390.097
WS132	407.335	445.618	467.978
WS132-10	194.237	226.604	297.941
WS132-100	201.975	236.037	307.304

Particle size was determined by Laser Light Scattering (Dry Sample Dispersion) using a Malvern Mastersizer 2000 using the following conditions:

Feed Rate: 35%
 Disperser Pressure: 4 Bar
 Optical Model: (2.610, 1.000i), 1.000

An appropriate amount of sample was introduced onto a vibratory tray. The feed rate and air pressure were adjusted to ensure that the particles were properly dispersed. The key component is selecting an air pressure that will break up agglomerations, but does not compromise the sample integrity. The amount of sample needed varies

depending on the size of the particles. In general, samples with fine particles require less material than samples with coarse particles.

Example 13 - Surface Area Analysis of Irradiated Materials

Table 8. Summary of Surface Area by Gas Adsorption

5 Surface area of each sample was analyzed using a Micromeritics ASAP 2420 Accelerated Surface Area and Porosimetry System. The samples were prepared by first degassing for 16 hours at 40 °C. Next, free space (both warm and cold) with helium is calculated and then the sample tube is evacuated again to remove the helium. Data collection begins after this second evacuation and consists of defining target pressures, 10 which controls how much gas is dosed onto the sample. At each target pressure, the quantity of gas adsorbed and the actual pressure are determined and recorded. The pressure inside the sample tube is measured with a pressure transducer. Additional doses of gas will continue until the target pressure is achieved and allowed to equilibrate. The quantity of gas adsorbed is determined by summing multiple doses onto the sample. The 15 pressure and quantity define a gas adsorption isotherm and are used to calculate a number of parameters, including BET surface area (Table 8).

Sample ID	Single point surface area (m ² /g)	BET Surface Area (m ² /g)
P132	@ P/P ₀ = 0.250387771 1.5253	1.6897
P132-10	@ P/P ₀ = 0.239496722 1.0212	1.2782
P132-100	@ P/P ₀ = 0.240538100 1.0338	1.2622
P132-181	@ P/P ₀ = 0.239166091 0.5102	0.6448
P132-US	@ P/P ₀ = 0.217359072 1.0983	1.6793
A132	@ P/P ₀ = 0.240040610 0.5400	0.7614
A132-10	@ P/P ₀ = 0.211218936 0.5383	0.7212
A132-100	@ P/P ₀ = 0.238791097 0.4258	0.5538
SG132	@ P/P ₀ = 0.237989353 0.6359	0.8350
SG132-10	@ P/P ₀ = 0.238576905 0.6794	0.8689
SG132-100	@ P/P ₀ = 0.241960361 0.5518	0.7034
SG132-10-US	@ P/P ₀ = 0.225692889 0.5693	0.7510
SG132-100-US	@ P/P ₀ = 0.225935246 1.0983	1.4963
WS132	@ P/P ₀ = 0.237823664 0.6582	0.8663
WS132-10	@ P/P ₀ = 0.238612476 0.6191	0.7912
WS132-100	@ P/P ₀ = 0.238398832 0.6255	0.8143

20 The BET model for isotherms is a widely used theory for calculating the specific surface area. The analysis involves determining the monolayer capacity of the sample

surface by calculating the amount required to cover the entire surface with a single densely packed layer of krypton. The monolayer capacity is multiplied by the cross sectional area of a molecule of probe gas to determine the total surface area. Specific surface area is the surface area of the sample aliquot divided by the mass of the sample.

5 **Example 14 - Fiber Length Determination of Irradiated Materials**

Fiber length distribution testing was performed in triplicate on the samples submitted using the Techpap MorFi LB01 system. The average length and width are reported in Table 9.

10 **Table 9. Summary of Lignocellulosic Fiber Length and Width Data**

Sample ID	Arithmetic Average (mm)	Average Length Weighted in Length (mm)	Statistically Corrected Average Length Weighted in Length (mm)	Width (micrometers) (μm)
P132-10	0.484	0.615	0.773	24.7
P132-100	0.369	0.423	0.496	23.8
P132-181	0.312	0.342	0.392	24.4
A132-10	0.382	0.423	0.650	43.2
A132-100	0.362	0.435	0.592	29.9
SG132-10	0.328	0.363	0.521	44.0
SG132-100	0.325	0.351	0.466	43.8
WS132-10	0.353	0.381	0.565	44.7
WS132-100	0.354	0.371	0.536	45.4

Example 15 - Ultrasonic Treatment of Irradiated and Un-irradiated Switchgrass

Switchgrass was sheared according to Example 4. The switchgrass was treated by ultrasound alone or irradiation with 10 Mrad or 100 Mrad of gamma rays, and then
 15 sonicated. The resulting materials correspond to G132-BR (un-irradiated), G132-10-BR (10 Mrad and sonication) and G132-100-BR (100 Mrad and sonication), as presented in Table 1. Sonication was performed on each sample for 30 minutes using 20kHz ultrasound from a 1000W horn under re-circulating conditions. Each sample was dispersed in water at a concentration of about 0.10 g/mL.

20 FIGS. 32 and 33 show the apparatus used for sonication. Apparatus 500 includes a converter 502 connected to booster 504 communicating with a horn 506 fabricated from titanium or an alloy of titanium. The horn, which has a seal 510 made from VITON[®] about its perimeter on its processing side, forms a liquid tight seal with a processing cell

508. The processing side of the horn is immersed in a liquid, such as water, that has dispersed therein the sample to be sonicated. Pressure in the cell is monitored with a pressure gauge 512. In operation, each sample is moved by pump 517 from tank 516 through the processing cell and is sonicated. After, sonication, the sample is captured in tank 520. The process can be reversed in that the contents of tank 520 can be sent through the processing cell and captured in tank 516. This process can be repeated a number of times until a desired level of processing is delivered to the sample.

Example 16 - Scanning Electron Micrographs of Un-irradiated Switchgrass in Comparison to Irradiated and Irradiated and Sonicated Switchgrass

Switchgrass samples for the scanning electron micrographs were applied to carbon tape and gold sputter coated (70 seconds). Images were taken with a JEOL 6500 field emission scanning electron microscope.

FIG. 34 is a scanning electron micrograph at 1000 X magnification of a fibrous material produced from shearing switchgrass on a rotary knife cutter, and then passing the sheared material through a 1/32 inch screen.

FIGS. 35 and 36 are scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 10 Mrad and 100 Mrad gamma rays, respectively, at 1000 X magnification.

FIG. 37 is a scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 10 Mrad and sonication at 1000 X magnification.

FIG. 38 is a scanning electron micrographs of the fibrous material of FIG. 34 after irradiation with 100 Mrad and sonication at 1000 X magnification.

Example 17 - Infrared Spectrum of Irradiated Kraft Paper in Comparison to Un-irradiated Kraft Paper

The FT-IR analysis was performed on a Nicolet/Impact 400. The results indicate that all samples reported in Table 1 are consistent with a cellulose-based material.

FIG. 39 is an infrared spectrum of Kraft board paper sheared according to Example 4, while FIG. 40 is an infrared spectrum of the Kraft paper of FIG. 39 after irradiation with 100 Mrad of gamma radiation. The irradiated sample shows an additional peak in region A (centered about 1730 cm^{-1}) that is not found in the un-irradiated material.

Example 18 - Combination of Electron Beam and Sonication Pretreatment

Switchgrass is used as the feedstock and is sheared with a Munson rotary knife cutter into a fibrous material. The fibrous material is then evenly distributed onto an open tray composed of tin with an area of greater than about 500 in². The fibrous material is distributed so that it has a depth of about 1 – 2 inches in the open tray. The fibrous material may be distributed in plastic bags at lower doses of irradiation (under 10 MRad), and left uncovered on the metal tray at higher doses of radiation.

Separate samples of the fibrous material are then exposed to successive doses of electron beam radiation to achieve a total dose of 1 Mrad, 2 Mrad, 3, Mrad, 5 Mrad, 10 Mrad, 50 Mrad, and 100 Mrad. Some samples are maintained under the same conditions as the remaining samples, but are not irradiated, to serve as controls. After cooling, the irradiated fibrous material is sent on for further processing through a sonication device.

The sonication device includes a converter connected to booster communicating with a horn fabricated from titanium or an alloy of titanium. The horn, which has a seal made from VITON® about its perimeter on its processing side, forms a liquid tight seal with a processing cell. The processing side of the horn is immersed in a liquid, such as water, into which the irradiated fibrous material to be sonicated is immersed. Pressure in the cell is monitored with a pressure gauge. In operation, each sample is moved by pump through the processing cell and is sonicated.

To prepare the irradiated fibrous material for sonication, the irradiated fibrous material is removed from any container (e.g., plastic bags) and is dispersed in water at a concentration of about 0.10 g/mL. Sonication is performed on each sample for 30 minutes using 20 kHz ultrasound from a 1000 W horn under re-circulating conditions. After sonication, the irradiated fibrous material is captured in a tank. This process can be repeated a number of times until a desired level of processing is achieved based on monitoring the structural changes in the switchgrass. Again, some irradiated samples are kept under the same conditions as the remaining samples, but are not sonicated, to serve as controls. In addition, some samples that were not irradiated are sonicated, again to serve as controls. Thus, some controls are not processed, some are only irradiated, and some are only sonicated.

Example 19 – Microbial Testing of Pretreated Biomass

Specific lignocellulosic materials pretreated as described herein are analyzed for toxicity to common strains of yeast and bacteria used in the biofuel industry for the fermentation step in ethanol production. Additionally, sugar content and compatibility with cellulase enzymes are examined to determine the viability of the treatment process. Testing of the pretreated materials is carried out in two phases as follows.

I. Toxicity and Sugar Content

Toxicity of the pretreated grasses and paper feedstocks is measured in yeast *Saccharomyces cerevisiae* (wine yeast) and *Pichia stipitis* (ATCC 66278) as well as the bacteria *Zymomonas mobilis* (ATCC 31821) and *Clostridium thermocellum* (ATCC 31924). A growth study is performed with each of the organisms to determine the optimal time of incubation and sampling.

Each of the feedstocks is then incubated, in duplicate, with *S. cerevisiae*, *P. stipitis*, *Z. mobilis*, and *C. thermocellum* in a standard microbiological medium for each organism. YM broth is used for the two yeast strains, *S. cerevisiae* and *P. stipitis*. RM medium is used for *Z. mobilis* and CM4 medium for *C. thermocellum*. A positive control, with pure sugar added, but no feedstock, is used for comparison. During the incubation, a total of five samples is taken over a 12 hour period at time 0, 3, 6, 9, and 12 hours and analyzed for viability (plate counts for *Z. mobilis* and direct counts for *S. cerevisiae*) and ethanol concentration.

Sugar content of the feedstocks is measured using High Performance Liquid Chromatography (HPLC) equipped with either a Shodex® sugar SP0810 or Biorad Aminex® HPX-87P column. Each of the feedstocks (approx. 5 g) is mixed with reverse osmosis (RO) water for 1 hour. The liquid portion of the mixture is removed and analyzed for glucose, galactose, xylose, mannose, arabinose, and cellobiose content. The analysis is performed according to National Bioenergy Center protocol *Determination of Structural Carbohydrates and Lignin in Biomass*.

II. Cellulase Compatibility

Feedstocks are tested, in duplicate, with commercially available Accellerase® 1000 enzyme complex, which contains a complex of enzymes that reduces lignocellulosic

biomass into fermentable sugars, at the recommended temperature and concentration in an Erlenmeyer flask. The flasks are incubated with moderate shaking at around 200 rpm for 12 hours. During that time, samples are taken every three hours at time 0, 3, 6, 9, and 12 hours to determine the concentration of reducing sugars (Hope and Dean, *Biotech J.*, 1974, 144:403) in the liquid portion of the flasks.

Example 20 - Alcohol Production Using Irradiation-Sonation Pretreatment

The optimum size for biomass conversion plants is affected by factors including economies of scale and the type and availability of biomass used as feedstock. Increasing plant size tends to increase economies of scale associated with plant processes. However, increasing plant size also tends to increase the costs (e.g., transportation costs) per unit of biomass feedstock. Studies analyzing these factors suggest that the appropriate size for biomass conversion plants can range from 2000 to 10,000 dried tons of biomass feedstock per day. The plant described below is sized to process 2000 tons of dry biomass feedstock per day.

FIG. 41 shows a process schematic of a biomass conversion system configured to process switchgrass. The feed preparation subsystem processes raw biomass feedstock to remove foreign objects and provide consistently sized particles for further processing. The pretreatment subsystem changes the molecular structure (e.g., reduces the average molecular weight and the crystallinity) of the biomass feedstock by irradiating the biomass feedstock, mixing the irradiated the biomass feedstock with water to form a slurry, and applying ultrasonic energy to the slurry. The irradiation and sonication convert the cellulosic and lignocellulosic components of the biomass feedstock into fermentable materials. The primary process subsystem ferments the glucose and other low weight sugars present after pretreatment to form alcohols.

Example 21- Electron Beam Processing of table sugar (sucrose)

Sucrose was treated with a beam of electrons using a vaulted Rhodotron® TT200 continuous wave accelerator delivering 5 MeV electrons at 80 kW output power. The table below describes the nominal parameters for the TT200. The nominal doses (in MRad) and actual doses (in kGy) delivered to the samples are also given below.

Rhodotron® TT 200 Parameters

Beam	
Beam Produced:	Accelerated electrons
Beam energy:	Nominal (maximum): 10 MeV (+0 keV–250 keV)
Energy dispersion at 10 MeV:	Full width half maximum (FWHM) 300 keV
Beam power at 10 MeV:	Guaranteed Operating Range 1 to 80 kW
Power Consumption	
Stand-by condition (vacuum and cooling ON):	<15 kW
At 50 kW beam power:	<210 kW
At 80 kW beam power:	<260 kW
RF System	
Frequency:	107.5 ± 1 MHz
Tetrode type:	Thomson TH781
Scanning Horn	
Nominal Scanning Length (measured at 25-35 cm from window):	120 cm
Scanning Range:	From 30% to 100% of Nominal Scanning Length
Nominal Scanning Frequency (at max. scanning length):	100 Hz ± 5%
Scanning Uniformity (across 90% of Nominal Scanning Length)	± 5%

Dosages Delivered to the Sucrose Samples

Total Dosage (MRad) (Number Associated with Sample ID)	Delivered Dose (kgy) ¹
1	9.9
3	29.0
5	50.4
7	69.2
10	100.0
15	150.3
20	198.3
30	330.9
50	529.0
70	695.9
100	993.6

¹For example, 9.9kgy was delivered in 11 seconds at a beam current of 5mA and a line speed of 12.9 feet/minute. Cool time between 1 MRad treatments was about 2 minutes.

5

The solubility of the sucrose samples treated above 30 Mrad was enhanced, and at or above 30 Mrad, the sucrose appeared visually to be devoid of crystallinity. Above 70 Mrad, the sucrose was converted into a solid mass of material.

10

Feed preparation

The selected design feed rate for the plant is 2,000 dry tons per day of switchgrass biomass. The design feed is chopped and/or sheared switchgrass.

Biomass feedstock, in the form of bales of switchgrass, is received by the plant on truck trailers. As the trucks are received, they are weighed and unloaded by forklifts. Some bales are sent to on-site storage while others are taken directly to the conveyors. From there, the bales are conveyed to an automatic unwrapping system that cuts away the plastic wrapping and/or net surrounding the bales. The biomass feedstock is then
5 conveyed past a magnetic separator to remove tramp metal, after which it is introduced to shredder-shearer trains where the material is reduced in size. Finally, the biomass feedstock is conveyed to the pretreatment subsystem.

In some cases, the switchgrass bales are wrapped with plastic net to ensure they
10 don't break apart when handled, and may also be wrapped in plastic film to protect the bale from weather. The bales are either square or round. The bales are received at the plant from off-site storage on large truck trailers.

Since switchgrass is only seasonally available, long-term storage is required to provide feed to the plant year-round. Long-term storage will likely consist of 400-500
15 acres of uncovered piled rows of bales at a location (or multiple locations) reasonably close to the ethanol plant. On-site short-term storage is provided equivalent to 72 hours of production at an outside storage area. Bales and surrounding access ways as well as the transport conveyors will be on a concrete slab. A concrete slab is used because of the volume of traffic required to deliver the large amount of biomass feedstock required. A
20 concrete slab will minimize the amount of standing water in the storage area, as well as reduce the biomass feedstock's exposure to dirt. The stored material provides a short-term supply for weekends, holidays, and when normal direct delivery of material into the process is interrupted.

The bales are off-loaded by forklifts and are placed directly onto bale transport
25 conveyors or in the short-term storage area. Bales are also reclaimed from short-term storage by forklifts and loaded onto the bale transport conveyors.

Bales travel to one of two bale unwrapping stations. Unwrapped bales are broken up using a spreader bar and then discharged onto a conveyor that passes a magnetic separator to remove metal prior to shredding. A tramp iron magnet is provided to catch
30 stray magnetic metal and a scalping screen removes gross oversize and foreign material ahead of multiple shredder-shearer trains, which reduce the biomass feedstock to the

proper size for pretreatment. The shredder-shearer trains include shredders and rotary knife cutters. The shredders reduce the size of the raw biomass feedstock and feed the resulting material to the rotary knife cutters. The rotary knife cutters concurrently shear the biomass feedstock and screen the resulting material.

5 Three storage silos are provided to limit overall system downtime due to required maintenance on and/or breakdowns of feed preparation subsystem equipment. Each silo can hold approximately 55,000 cubic feet of biomass feedstock (~3 hours of plant operation).

Pretreatment

10 A conveyor belt carries the biomass feedstock from the feed preparation subsystem 110 to the pretreatment subsystem 114. As shown in FIG. 42, in the pretreatment subsystem 114, the biomass feedstock is irradiated using electron beam emitters, mixed with water to form a slurry, and subjected to the application of ultrasonic energy. As discussed above, irradiation of the biomass feedstock changes the molecular
15 structure (e.g., reduces the average molecular weight and the crystallinity) of the biomass feedstock. Mixing the irradiated biomass feedstock into a slurry and applying ultrasonic energy to the slurry further changes the molecular structure of the biomass feedstock. Application of the radiation and sonication in sequence may have synergistic effects in that the combination of techniques appears to achieve greater changes to the molecular
20 structure (e.g., reduces the average molecular weight and the crystallinity) than either technique can efficiently achieve on its own. Without wishing to be bound by theory, in addition to reducing the polymerization of the biomass feedstock by breaking intramolecular bonds between segments of cellulosic and lignocellulosic components of the biomass feedstock, the irradiation may make the overall physical structure of the
25 biomass feedstock more brittle. After the brittle biomass feedstock is mixed into a slurry, the application of ultrasonic energy further changes the molecular structure (e.g., reduces the average molecular weight and the crystallinity) and also can reduce the size of biomass feedstock particles.

Electron Beam Irradiation

30 The conveyor belt 491 carrying the biomass feedstock into the pretreatment subsystem distributes the biomass feedstock into multiple feed streams (e.g., 50 feed

streams) each leading to separate electron beam emitters 492. In this embodiment, the biomass feedstock is irradiated while it is dry. Each feed stream is carried on a separate conveyor belt to an associated electron beam emitter. Each irradiation feed conveyor belt can be approximately one meter wide. Before reaching the electron beam emitter, a
5 localized vibration is induced in each conveyor belt to evenly distribute the dry biomass feedstock over the cross-sectional width of the conveyor belt.

Electron beam emitter 492 (e.g., electron beam irradiation devices commercially available from Titan Corporation, San Diego, CA) are configured to apply a 100 kilo-Gray dose of electrons applied at a power of 300 kW. The electron beam emitters are
10 scanning beam devices with a sweep width of 1 meter to correspond to the width of the conveyor belt. In some embodiments, electron beam emitters with large, fixed beam widths are used. Factors including belt/beam width, desired dose, biomass feedstock density, and power applied govern the number of electron beam emitters required for the plant to process 2,000 tons per day of dry feed.

15 Sonication

The irradiated biomass feedstock is mixed with water to form a slurry before ultrasonic energy is applied. There can be a separate sonication system associated with each electron beam feed stream or several electron beam streams can be aggregated as feed for a single sonication system.

20 In each sonication system, the irradiated biomass feedstock is fed into a reservoir 1214 through a first intake 1232 and water is fed into the reservoir 1214 through second intake 1234. Appropriate valves (manual or automated) control the flow of biomass feedstock and the flow of water to produce a desired ratio of biomass feedstock to water (e.g., 10% cellulosic material, weight by volume). Each reservoir 1214 includes a mixer
25 1240 to agitate the contents of volume 1236 and disperse biomass feedstock throughout the water.

In each sonication system, the slurry is pumped (e.g., using a recessed impeller vortex pump 1218) from reservoir 1214 to and through a flow cell 1224 including an ultrasonic transducer 1226. In some embodiments, pump 1218 is configured to agitate
30 the slurry 1216 such that the mixture of biomass feedstock and water is substantially uniform at inlet 1220 of the flow cell 1224. For example, the pump 1218 can agitate the

slurry 1216 to create a turbulent flow that persists throughout the piping between the first pump and inlet 1220 of flow cell 1224.

Within the flow cell 1224, ultrasonic transducer 1226 transmits ultrasonic energy into slurry 1216 as the slurry flows through flow cell 1224. Ultrasonic transducer 1226
5 converts electrical energy into high frequency mechanical energy (e.g., ultrasonic energy), which is then delivered to the slurry through booster 48. Ultrasonic transducers are commercially available (e.g., from Hielscher USA, Inc. of Ringwood, New Jersey) that are capable of delivering a continuous power of 16 kilowatts.

The ultrasonic energy traveling through booster 1248 in reactor volume 1244
10 creates a series of compressions and rarefactions in process stream 1216 with an intensity sufficient to create cavitation in process stream 1216. Cavitation disaggregates components of the biomass feedstock including, for example, cellulosic and lignocellulosic material dispersed in process stream 1216 (e.g., slurry). Cavitation also produces free radicals in the water of process stream 1216 (e.g., slurry). These free
15 radicals act to further break down the cellulosic material in process stream 1216. In general, about 250 MJ/m^3 of ultrasonic energy is applied to process stream 1216 containing fragments of poplar chips. Other levels of ultrasonic energy (between about 5 and about 4000 MJ/m^3 , e.g., 10, 25, 50, 100, 250, 500, 750, 1000, 2000, or 3000) can be applied to other biomass feedstocks. After exposure to ultrasonic energy in reactor
20 volume 1244, process stream 1216 exits flow cell 24 through outlet 1222.

Flow cell 1224 also includes a heat exchanger 1246 in thermal communication with at least a portion of reactor volume 1244. Cooling fluid 1248 (e.g., water) flows into heat exchanger 1246 and absorbs heat generated when process stream 1216 (e.g., slurry) is sonicated in reactor volume 1244. In some embodiments, the flow of cooling fluid
25 1248 into heat exchanger 1246 is controlled to maintain an approximately constant temperature in reactor volume 1244. In addition or in the alternative, the temperature of cooling fluid 1248 flowing into heat exchanger 1246 is controlled to maintain an approximately constant temperature in reactor volume 1244.

The outlet 1242 of flow cell 1224 is arranged near the bottom of reservoir 1214 to
30 induce a gravity feed of process stream 1216 (e.g., slurry) out of reservoir 1214 towards

the inlet of a second pump 1230 which pumps process stream 1216 (e.g., slurry) towards the primary process subsystem.

Sonication systems can include a single flow path (as described above) or multiple parallel flow paths each with an associated individual sonication unit. Multiple sonication units can also be arranged to series to increase the amount of sonic energy applied to the slurry.

Primary Processes

A vacuum rotary drum type filter removes solids from the slurry before fermentation. Liquid from the filter is pumped cooled prior to entering the fermentors. Filtered solids are passed to the post-processing subsystem for further processing.

The fermentation tanks are large, low pressure, stainless steel vessels with conical bottoms and slow speed agitators. Multiple first stage fermentation tanks can be arranged in series. The temperature in the first stage fermentation tanks is controlled to 30 degrees centigrade using external heat exchangers. Yeast is added to the first stage fermentation tank at the head of each series of tanks and carries through to the other tanks in the series.

Second stage fermentation consists of two continuous fermentors in series. Both fermentors are continuously agitated with slow speed mechanical mixers. Temperature is controlled with chilled water in external exchangers with continuous recirculation. Recirculation pumps are of the progressive cavity type because of the high solids concentration.

Off gas from the fermentation tanks and fermentors is combined and washed in a counter-current water column before being vented to the atmosphere. The off gas is washed to recover ethanol rather than for air emissions control.

Post-Processing

Distillation

Distillation and molecular sieve adsorption are used to recover ethanol from the raw fermentation beer and produce 99.5% ethanol. Distillation is accomplished in two columns—the first, called the beer column, removes the dissolved CO₂ and most of the water, and the second concentrates the ethanol to a near azeotropic composition.

All the water from the nearly azeotropic mixture is removed by vapor phase molecular sieve adsorption. Regeneration of the adsorption columns requires that an ethanol water mixture be recycled to distillation for recovery.

5 Fermentation vents (containing mostly CO₂, but also some ethanol) as well as the beer column vent are scrubbed in a water scrubber, recovering nearly all of the ethanol. The scrubber effluent is fed to the first distillation column along with the fermentation beer.

10 The bottoms from the first distillation contain all the unconverted insoluble and dissolved solids. The insoluble solids are dewatered by a pressure filter and sent to a combustor. The liquid from the pressure filter that is not recycled is concentrated in a multiple effect evaporator using waste heat from the distillation. The concentrated syrup from the evaporator is mixed with the solids being sent to the combustor, and the evaporated condensate is used as relatively clean recycle water to the process.

15 Because the amount of stillage water that can be recycled is limited, an evaporator is included in the process. The total amount of the water from the pressure filter that is directly recycled is set at 25%. Organic salts like ammonium acetate or lactate, steep liquor components not utilized by the organism, or inorganic compounds in the biomass end up in this stream. Recycling too much of this material can result in levels of ionic strength and osmotic pressures that can be detrimental to the fermenting organism's efficiency. For the water that is not recycled, the evaporator concentrates the dissolved 20 solids into a syrup that can be sent to the combustor, minimizing the load to wastewater treatment.

Wastewater Treatment

25 The wastewater treatment section treats process water for reuse to reduce plant makeup water requirements. Wastewater is initially screened to remove large particles, which are collected in a hopper and sent to a landfill. Screening is followed by anaerobic digestion and aerobic digestion to digest organic matter in the stream. Anaerobic digestion produces a biogas stream that is rich in methane that is fed to the combustor. Aerobic digestion produces a relatively clean water stream for reuse in the process as 30 well as a sludge that is primarily composed of cell mass. The sludge is also burned in the combustor. This screening / anaerobic digestion / aerobic digestion scheme is standard

933-16(S)

within the current ethanol industry and facilities in the 1-5 million gallons per day range can be obtained as "off-the-shelf" units from vendors.

Combustor, Boiler, and Turbogenerator

5 The purpose of the combustor, boiler, and turbogenerator subsystem is to burn various by-product streams for steam and electricity generation. For example, some lignin, cellulose, and hemicellulose remains unconverted through the pretreatment and primary processes. The majority of wastewater from the process is concentrated to a syrup high in soluble solids. Anaerobic digestion of the remaining wastewater produces a biogas high in methane. Aerobic digestion produces a small amount of waste biomass
10 (sludge). Burning these by-product streams to generate steam and electricity allows the plant to be self sufficient in energy, reduces solid waste disposal costs, and generates additional revenue through sales of excess electricity.

Three primary fuel streams (post-distillate solids, biogas, and evaporator syrup) are fed to a circulating fluidized bed combustor. The small amount of waste biomass
15 (sludge) from wastewater treatment is also sent to the combustor. A fan moves air into the combustion chamber. Treated water enters the heat exchanger circuit in the combustor and is evaporated and superheated to 510°C (950°F) and 86 atm (1265 psia) steam. Flue gas from the combustor preheats the entering combustion air then enters a baghouse to remove particulates, which are landfilled. The gas is exhausted through a
20 stack.

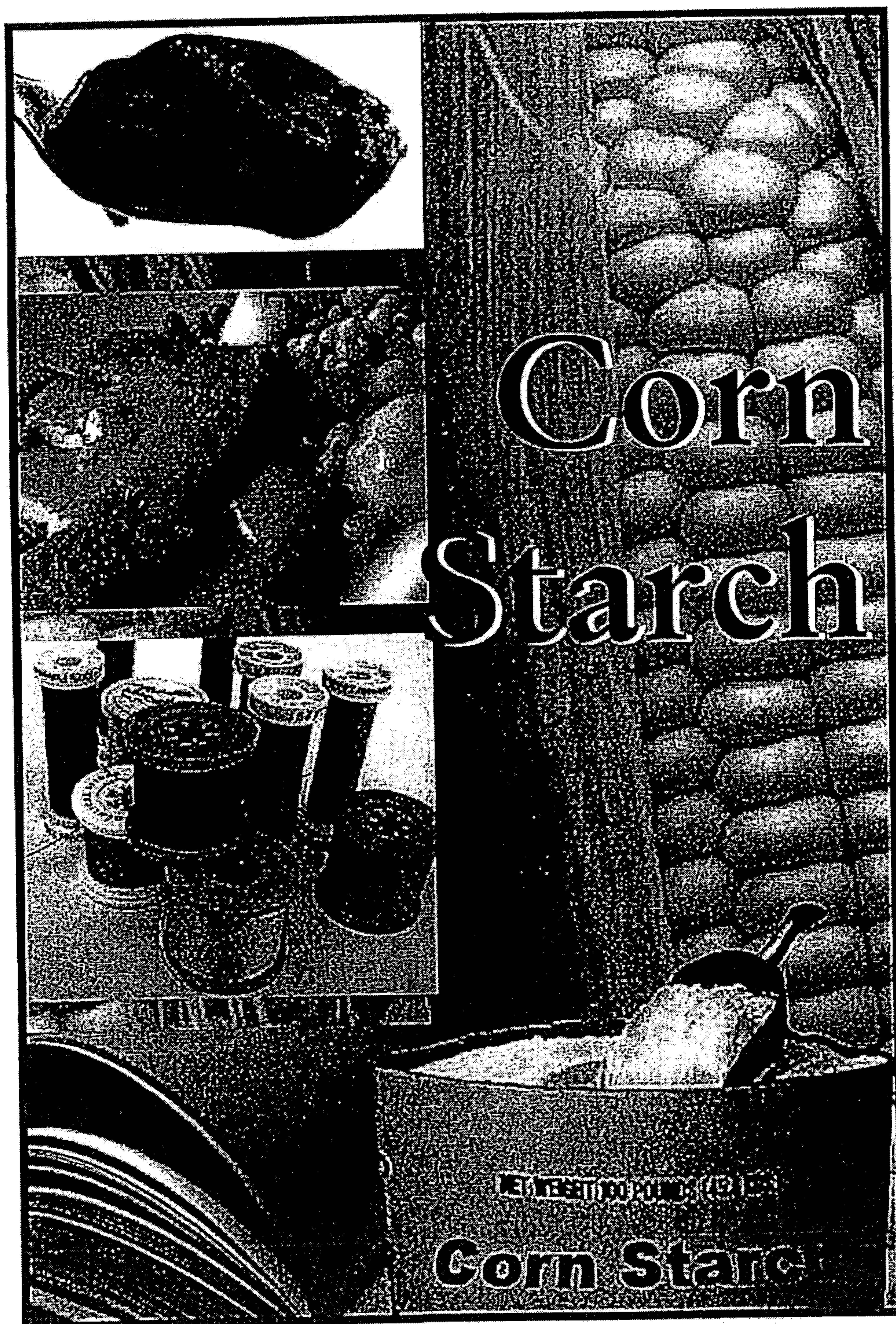
A multistage turbine and generator are used to generate electricity. Steam is extracted from the turbine at three different conditions for injection into the pretreatment reactor and heat exchange in distillation and evaporation. The remaining steam is condensed with cooling water and returned to the boiler feedwater system along with
25 condensate from the various heat exchangers in the process. Treated well water is used as makeup to replace steam used in direct injection.

33-16(S)

OTHER EMBODIMENTS

The scope of the claims should not be limited by the preferred embodiments set forth in the examples, but should be given the broadest interpretation consistent with the description as a whole.

APPENDIX A



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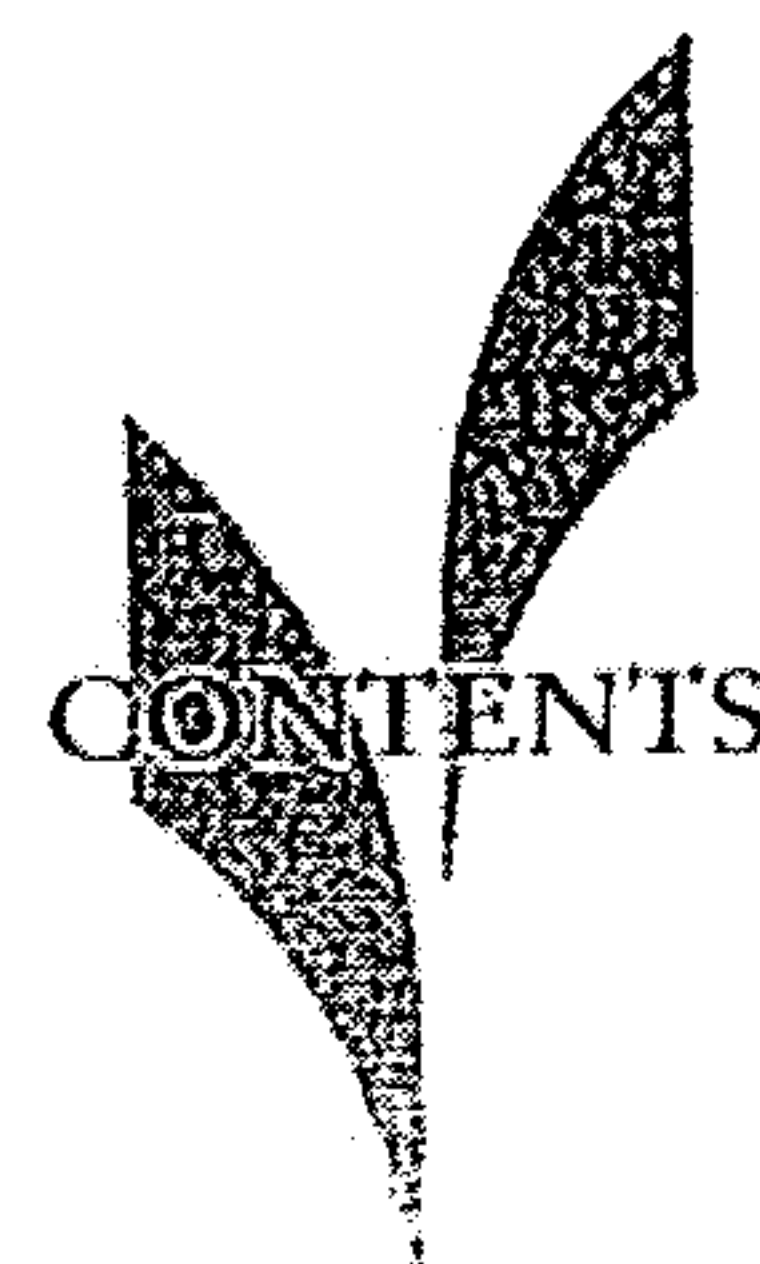
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P.O. Box 1470
Decatur, Illinois 62525

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P.O. Box 5662/MS62
Minneapolis, Minnesota 55440-5662

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5 Westbrook Corporate Center
Westchester, Illinois 60154

National Starch and Chemical Company
10 Finderne Avenue
Bridgewater, New Jersey 08807-0500

Penford Products Co.
(A company of Penford Corporation)
P.O. Box 428
Cedar Rapids, Iowa 52406-0428

Roquette America, Inc.
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Tate & Lyle Ingredients Americas, Inc.
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PLANT LOCATIONS

Plants:

Cedar Rapids, Iowa 52404
Clinton, Iowa 52732
Columbus, Nebraska 68601
Decatur, Illinois 62525
Marshall, Minnesota 56258-2744

Plants:

Blair, Nebraska 68008-2649
Cedar Rapids, Iowa 52406-2638
Dayton, Ohio 45413-8001
Decatur, Alabama 35601
Eddyville, Iowa 52553-5000
Hammond, Indiana 46320-1094
Memphis, Tennessee 38113-0368
Wahpeton, North Dakota 58075

Plants:

Bedford Park, Illinois 60501-1933
Stockton, California 95206-0129
Winton-Salem, North Carolina 27107

Plants:

Indianapolis, Indiana 46221
North Kansas City, Missouri 64116

Plant:

Cedar Rapids, Iowa 52404-2175

Plant:

Keokuk, Iowa 52632-6647

Plants:

Decatur, Illinois 62521
Lafayette, Indiana 47902
Lafayette, Indiana 47905
Loudon, Tennessee 37774

Each day of the year, in some manner or another, every American's life is touched by one of our most abundant renewable resources, corn starch. From the clothing we wear to the food on our table, corn starch is a component of tens of thousands of manufactured products that define our modern lifestyle.



The use of starch is chronicled in records of the early Egyptians, who manufactured papyrus using a starch coating. Roman records indicate that those early innovators found uses for starch in foods, medicine, cosmetics and fabrics. It was not until the middle of the nineteenth century, however, that the process for large-scale efficient extraction of starch from corn was developed. The development and continual improvement of this process has enabled the corn refining industry to offer American consumers abundant supplies of starch tailored to meet the most exacting needs of individual customers.

Our tenth edition of *Corn Starch* reviews the chemistry of the starch granule, describes how corn refiners extract starch from the corn kernel, how it is treated to produce special products and reviews handling and analytical procedures for starches. We hope that you will find this guide useful and will not hesitate to contact the Corn Refiners Association, if we can provide you with further information on starch and its products.

A handwritten signature in cursive script, reading "Audrae Erickson".

Audrae Erickson
President
Corn Refiners Association

Readers are advised that the information and suggestions contained herein are general in nature and that specific technical questions should be referred to the Association or member companies. Questions as to the price and/or availability of the products described should be directed to individual Association members.

INTRODUCTION

The corn plant (*Zea mays*) is a high-capacity, factory for efficiently converting large amounts of radiant energy from the sun into stable chemical energy. This energy is stored as cellulose, oil and starch in the corn plant and in the corn kernel.

The corn plant is also one of nature's greatest multipliers. Approximately four months after planting, a single kernel of corn weighing about one one-hundredth of an ounce will yield 800 kernels weighing eight ounces. In comparison to this 800-fold seed multiplication in corn, wheat will produce a 50-fold yield per seed planted.

By careful genetic control, corn has been developed which can grow in the temperate and semi-tropical areas throughout the world. With annual production of corn topping 10 billion bushels, the United States ranks as the world's largest grower of corn. Since the corn grain averages about 70-72% starch (dry basis) this enormous quantity of corn provides an almost unlimited raw mate-

rial supply from which starch may be produced.

In 1844, Colgate & Co. built small corn starch factories at Jersey City, New Jersey, and Columbus, Ohio. In 1848, the much larger Kingsford Cornstarch Plant was built in Oswego, New York. Since that time, starch technology has steadily improved and production has increased many-fold. Today, corn starch dominates the world's industrial and food starch markets.

This booklet presents a brief, simplified description of the manufacture of starch by the corn refining (wet milling) process, a summary of the physicochemical properties of starch that make it of such great value to mankind and general information about how starch is used in food and industrial applications. We hope you find this information useful. If you wish further information on starch, corn or corn refining, please contact the Corn Refiners Association or its member companies.

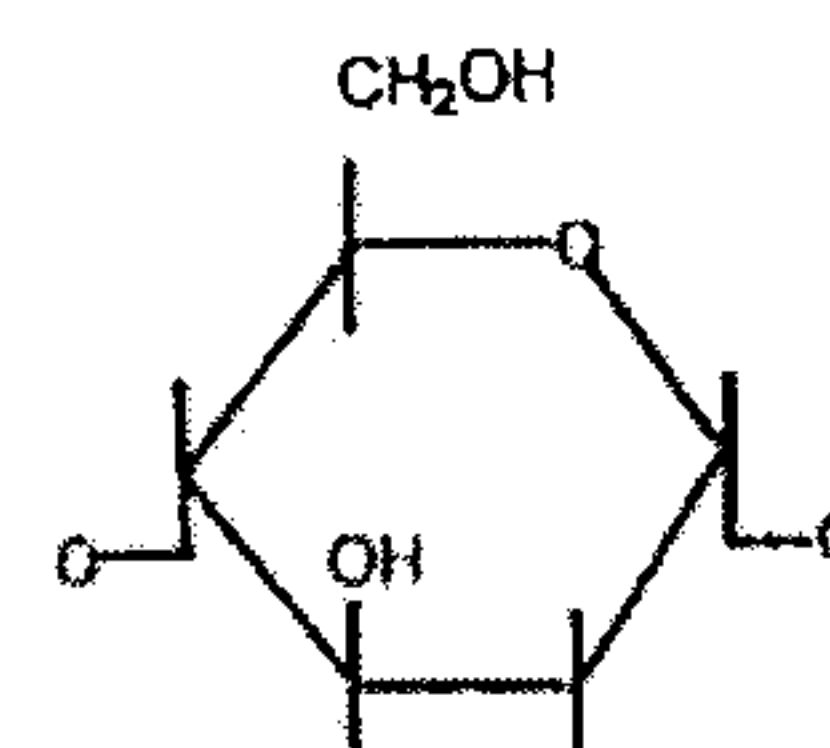
Starch exists as a major carbohydrate storage product in all plants containing chlorophyll. In the process known as photosynthesis, green plants extract energy from sunlight to form glucose from carbon dioxide and water. Glucose fuels plant growth processes and is the primary building material for plant support structures such as cellulose and hemicellulose. When the plant reaches maturity, the reproduction cycle begins, culminating in pollination and formation of the starch- and oil-rich seed embryo. Starch and oil exist in the corn kernel to supply energy to the germinating seed. Starch is a carbohydrate polymer made by the linking of glucose units end-to-end into very long chains, similar to the stringing together of pearls in the making of a pearl necklace.

Newly-synthesized starch is layered around a hilum nucleus within the plant cell, in structures called granules (Figure 1). Starch granules vary in size and shape, characteristic of specific plant sources. Figure 2 shows the comparative sizes and shapes of granules from six common starches. Starch molecules are oriented within granules in specific crystalline patterns. This is

illustrated in Figure 3, showing the Maltese cross pattern characteristic of these crystal structures, viewed in aqueous suspension under polarized light.

The highly structured nature of the starch granule is demonstrated by its great strength. After all the pulverizing, pumping, centrifugal circulation and physical attrition in the wet phases of the corn wet milling operation, followed by drying, grinding and mechanical or air transportation of the dry starch, practically all of the granules remain intact. Granule integrity also persists in both modified and derivatized starches.

Isolated starch is typically a dry, soft, white powder. It is insoluble in cold water, alcohol, ether and most organic solvents. Starch, if kept dry, is stable in storage for indefinite periods. Though starch granules are physically durable, they can be disrupted quite easily. If granules in water suspension are gradually heated, they begin to absorb water. The granules hydrate, increase in size and finally lose their structural integrity. This results in loss of characteristic birefringence and opacity, an increase in viscosity, and the eventual formation of a paste



α -D-glucopyranose unit



Figure 1
Layers of starch formed around the hilum

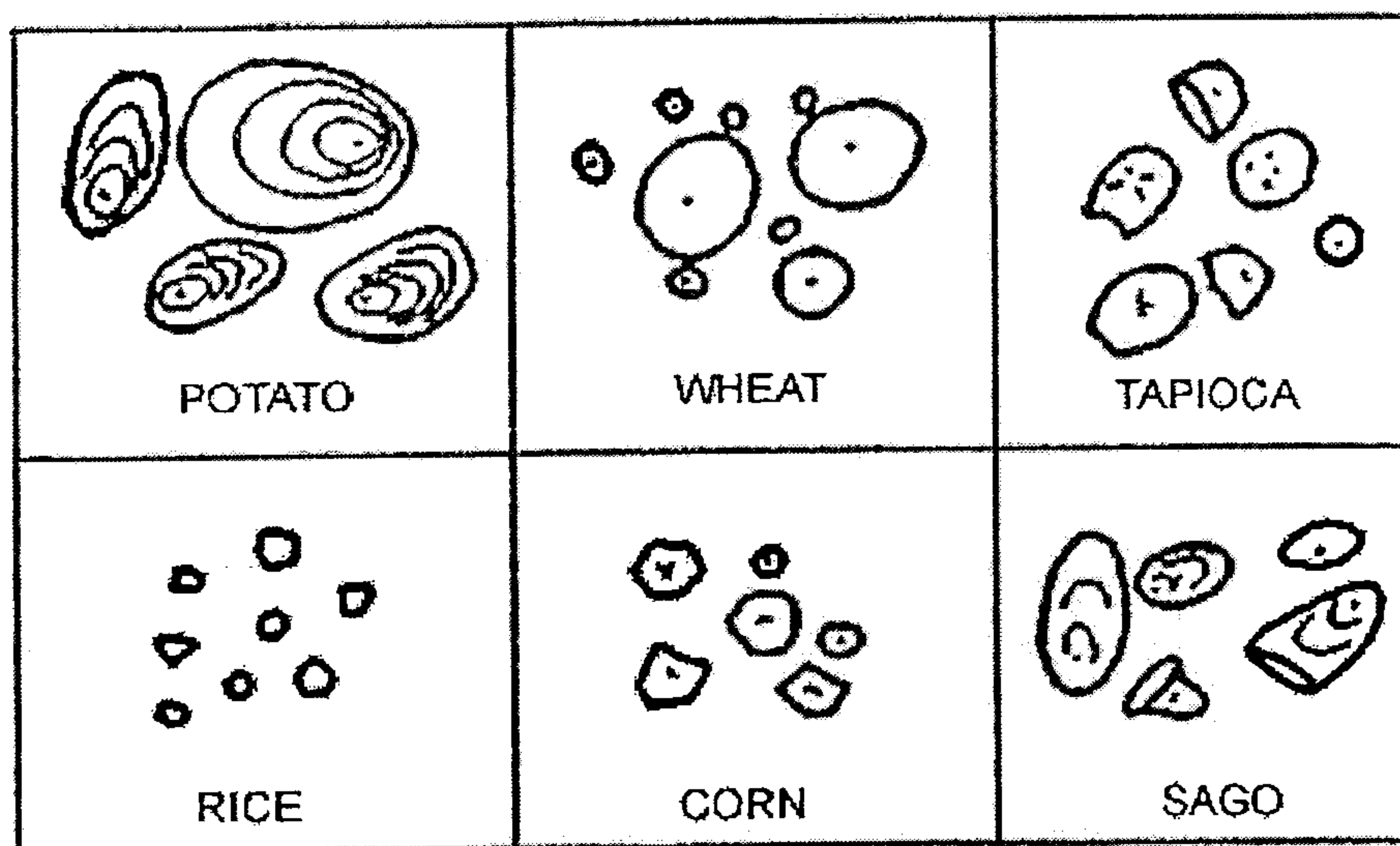


Figure 2
Shape of six common
starch granules

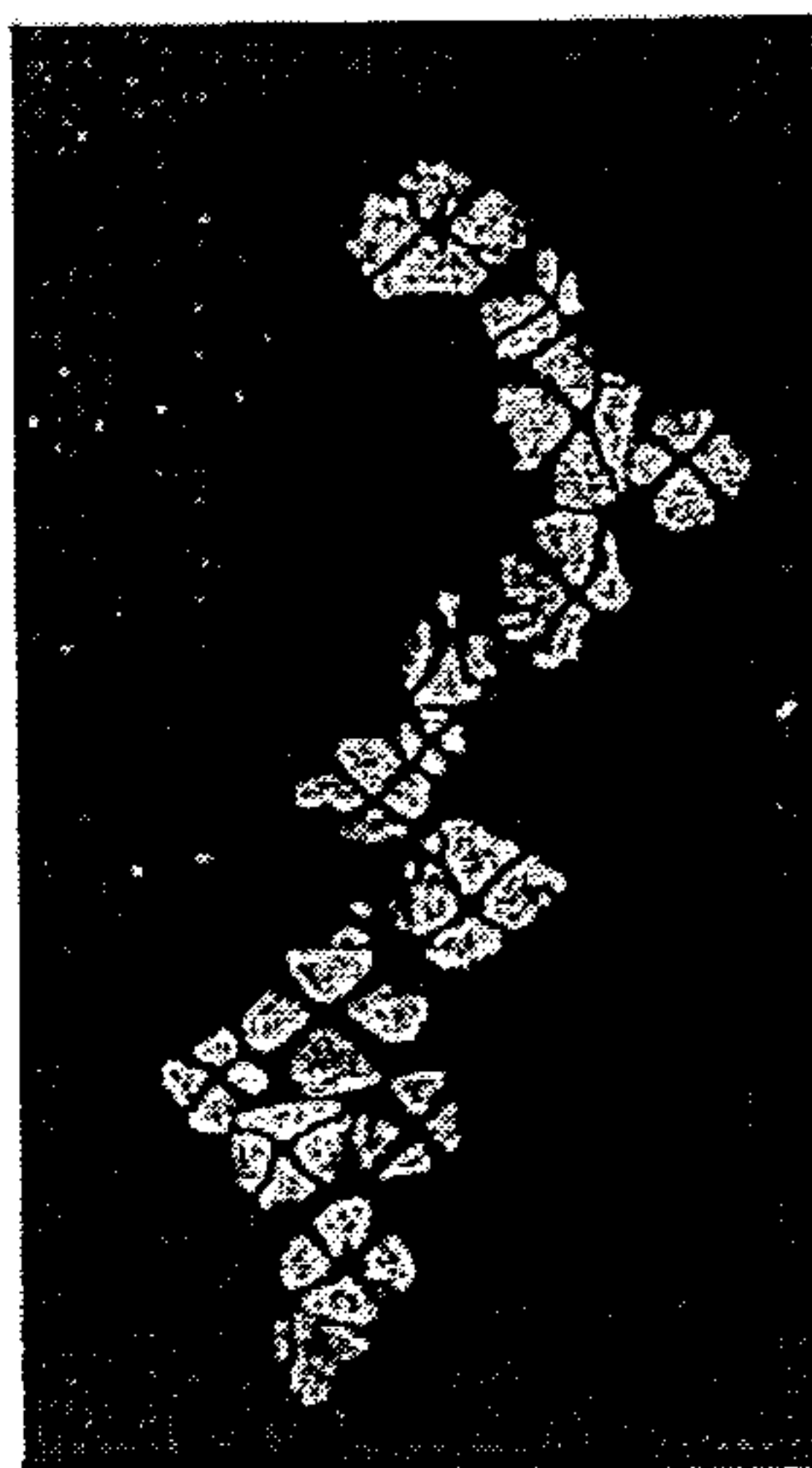


Figure 3
Corn starch photographed
under polarized light. Note
typical "Maltese cross"
pattern

or gel. This process is referred to as starch *pasting* or *gelatinization*. The temperature at the which gelatinization of a starch occurs — the *gelatinization temperature* — is dependent upon such factors as starch concentration, pH of the suspension, rate of heating, the presence of certain salts, and the specific procedure being followed. Under well-defined conditions, starches can be classified using gelatinization temperature as a means for differentiation.

The properties of the starch granule are dependent upon the arrangement of the bonds which link glucose units to one-another within the starch molecule itself. The starch molecule is a homopolymer of repeating

anhydroglucose units joined by an alpha-glucosidic linkage, the aldehyde group of one unit being chemically bound to a hydroxyl group on the next unit through hemiacetal linkages. In most starches the alpha-1,4-linkage predominates, with only occasional 1,6-linkages. The 1,4-linkages yield straight chain starch molecules called *amylose*, while the 1,6-linkages serve as the branching point in branched-chain starch molecules called *amylopectin* (Figure 6). The proportions of these two types of starch molecules are established genetically and are relatively constant for each species of starch. For example, corn starch contains 27% of the linear amylose polymer, potato starch 20%, and tapi-

oca starch 17%.

Plant geneticists have learned to manipulate genetic controls in corn and have developed commercial varieties of corn that contain all branched-chain starch amylopectin molecules are called *waxy maize*. At the other extreme, a variety containing as high as 70% straight chain amylose molecules is grown commercially, and is called *high amylose* corn. 82% and higher amylose hybrids have recently been announced. The granules of waxy maize gelatinize much like normal corn starch. High amylose corn, on the other hand, will not gelatinize even in boiling water, but must be pressure cooked or hydrated by treatment with dilute sodium hydroxide. More detailed discussion of the effect of these variations in molecular structure is presented later.

The inherent properties of the starch granule can be altered by mild chemical treatment and/or derivatization. Oxidation with sodium hypochlorite, for example, decreases the gelatinization point in direct proportion to the quantity of chemical used. Similar effects are observed when starch is derivatized with ethylene oxide or

other reagents. In contrast, starch derivatives can be made in which the granule will not gelatinize at all when exposed to the severe conditions of moist heat and pressure.

The granular structure of starch, one of nature's fascinating architectural forms, is a vital element in the flexibility of commercial starches to fill specific product needs.

Corn kernels have three main parts: the seed coat or pericarp, the starchy endosperm, and the embryo, commonly called the germ (Figure 4). The pericarp is the outer skin or hull of the kernel which serves to protect the seed. The endosperm, the main energy reserve, makes up about 80% of the total weight of the kernel. It is about 90% starch and 7% gluten protein, with the remainder consisting of small amounts of oil, minerals and trace constituents. The embryonic germ contains a miniature plant made up of a root-like portion and five or six embryonic leaves. In addition, large quantities of high energy oil are present to feed the tiny plant when it starts to grow, as

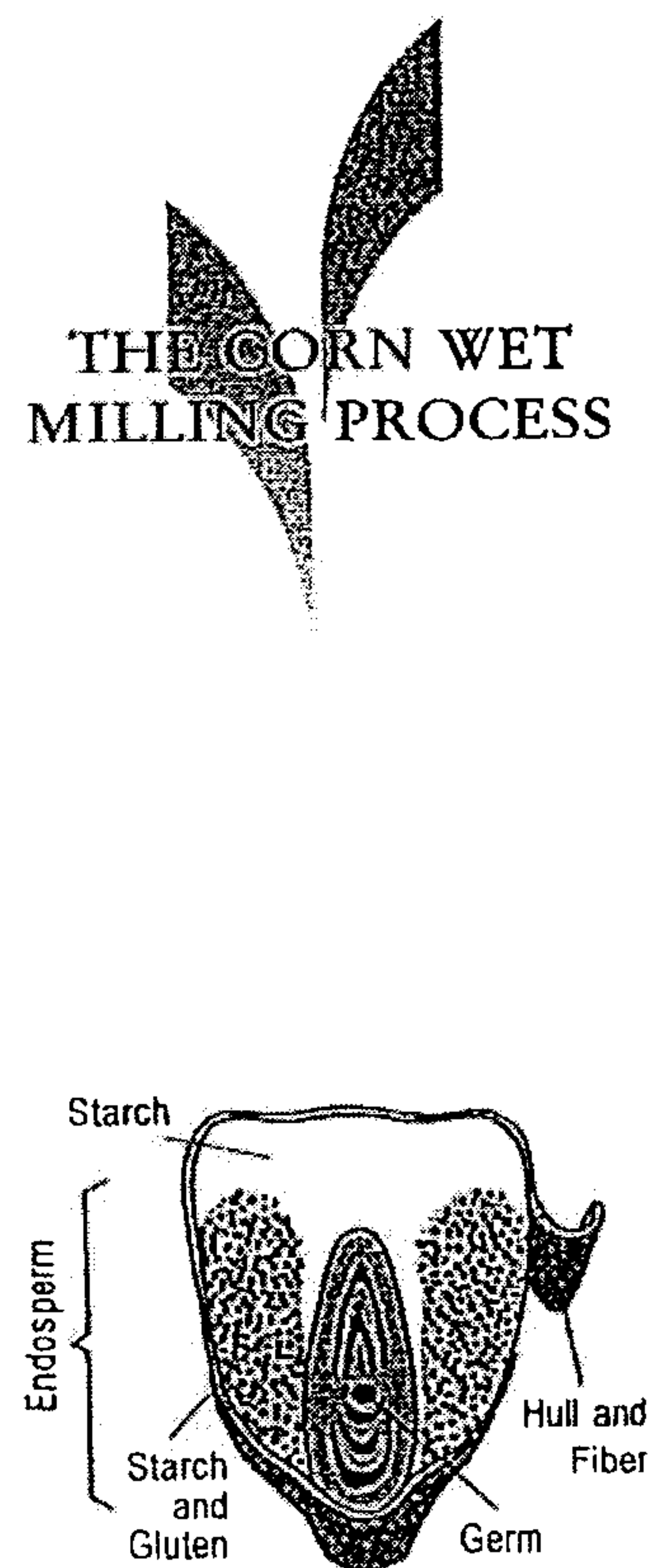


Figure 4
A kernel of corn

along with many substances required during germination and early development.

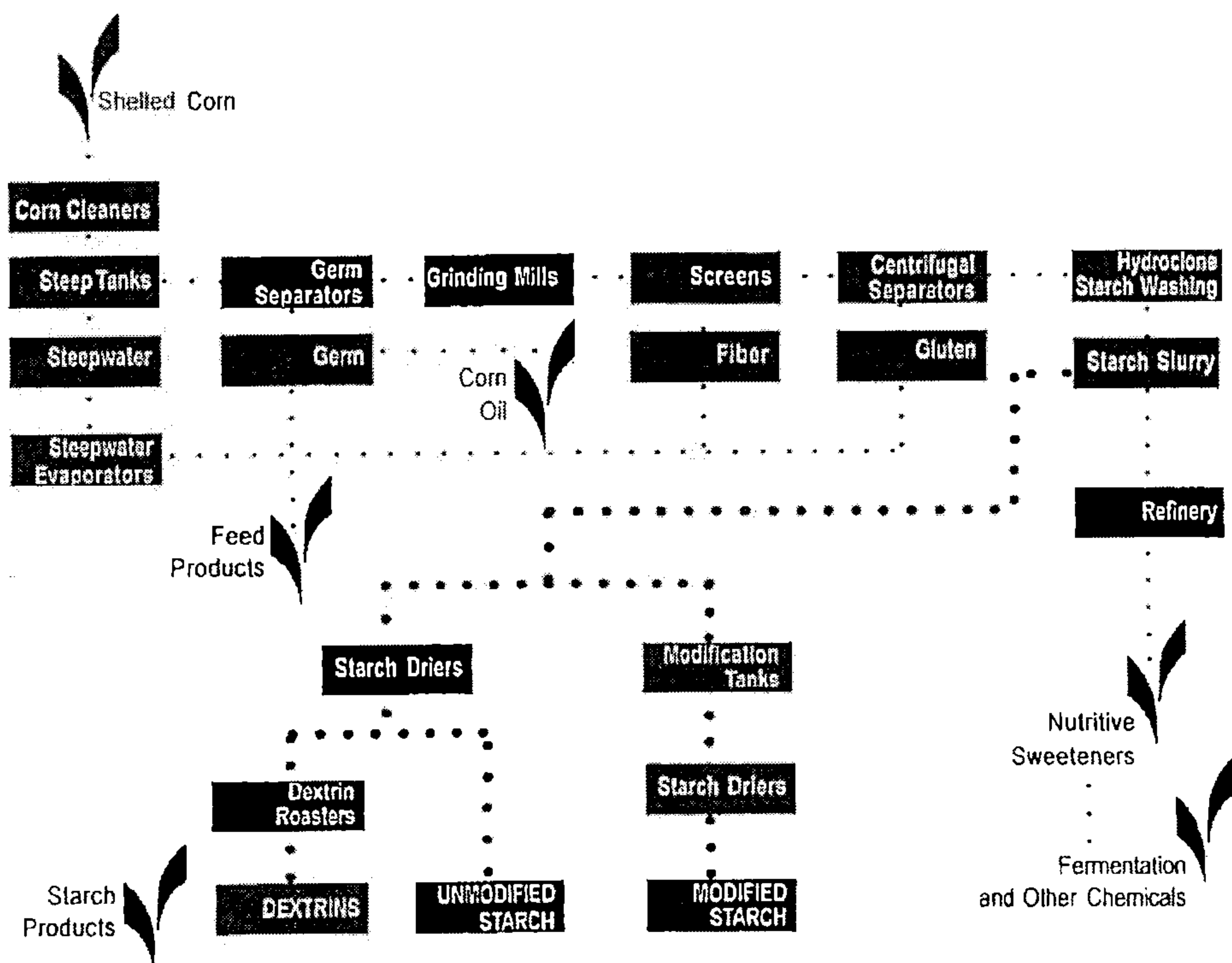
The corn wet milling process is illustrated in Figure 5, in which the kernel is separated into its component parts, and those parts are then further subdivided and refined.

Corn wet millers buy shelled corn that is delivered to the plant by truck, barge or rail car. Normally #2 grade corn is purchased, based on USDA standards.

Incoming corn is cleaned to remove extraneous material such as pieces of cob, foreign seeds, stray metal, and fine grit. It then is conveyed to storage silos, holding up to 350,000 bushels, until ready to go to the refinery.

Cleaned corn is transported to large tanks called *steeps*. Warm water (125°-130°F) containing small quantities of dissolved sulfur dioxide is circulated through the steeps for approximately 24-48 hours to soften the kernel. Sulfur dioxide and water

Figure 5
The corn wet milling process



react during steeping to form sulfurous acid, which controls undesirable fermentation and assists in separation of starch and protein. During steeping, the soluble components are extracted from the intact kernel. At the conclusion of steeping, water is drained from the kernels and concentrated in multiple effect evaporators to yield concentrated *steepwater*. This protein-rich extract may be used as a nutrient for microorganisms in the production of enzymes, antibiotics and other fermentation products. Most steepwater, however, is combined with fiber and gluten in the production of animal feed ingredients. Further information on feed products produced by corn wet millers may be found in the booklet *Corn Wet Milled Feed Products*, available on the Corn Refiners Association website, www.corn.org.

Softened corn kernels next pass through mild attrition mills to loosen the hull and free the germ from the starch-rich endosperm. Water is added to the attrition mills and a thick slurry of macerated kernels and whole germ results. Because the germ at this stage contains 40-50% oil, it is lighter than the endosperm and hull. Centrifugal force is

used to isolate the germ.

Clean, separated germ is dried and the crude oil is removed by mechanical presses and/or solvent extraction. The crude oil may be refined to yield a fine quality salad and cooking oil or a raw material for the preparation of corn oil margarine. Extracted germ meal is used in animal feed. Further information on production and use of corn oil may be found in the booklet *Corn Oil*, available on the Corn Refiners Association website, www.corn.org.

The remaining mixture of hull and endosperm then passes through a series of grinding and screening operations. Large hull particles are retained on screens and removed, while finer protein and starch particles pass through. The hull is added to animal feed or washed and milled in the production of refined corn fiber (bran).

The water slurry of starch and gluten protein is next separated by centrifugation. Because starch and gluten differ widely in buoyant density, nearly complete separation is obtained. Typical operations yield a gluten stream containing over 60% protein, while the starch stream is over 99% starch.

The gluten is dried and sold as gluten meal (60% protein).

The white, nearly-pure starch slurry is further washed to remove small quantities of solubles. At this stage the starch slurry may be further processed to make any common (unmodified) corn starch or converted to make sweeteners or fermentation products. Various modified or derivatized starches may be produced by treating the slurry of washed starch with chemicals or enzymes. After treatment, the products are recovered by filtration or centrifugation and the starch is dried.



PHYSICO-CHEMICAL PROPERTIES OF STARCH

What is starch? Starch is a highly functional carbohydrate in its unmodified state. It is also a highly reactive carbohydrate, which may be modified physically, chemically or enzymatically to meet specific needs.

Starches have four major physicochemical properties that make them useful in food and industrial applications. Both types of starch molecules—amylose and amylopectin (Figure 6)—are polyhydroxy compounds and hydrate when heated in water, combining with indi-

vidual water molecules. As the molecules hydrate, they increase in size, immobilize much of the water present, thicken the aqueous system and form a paste. The first useful physicochemical property, thickening, gives many food products such as puddings, gravies, sauces and pie fillings their desired physical characteristics. This property is also useful in many industrial starch applications.

The second useful physicochemical property is the ability of the starch paste to disperse and suspend other ingredients or particulate matter. In many foods, fats and proteins are suspended and/or emulsified in starch pastes. In coatings for paper and in some adhesives, clay particles are suspended in thick starch pastes.

When starch pastes are allowed to cool, they thicken and can congeal into a semi-solid gel. The third useful physicochemical property, gel formation, provides the body typical of starch-based puddings, salad dressings and some types of adhesives.

The fourth useful physicochemical property of starch paste is its ability to produce strong adhesive films when

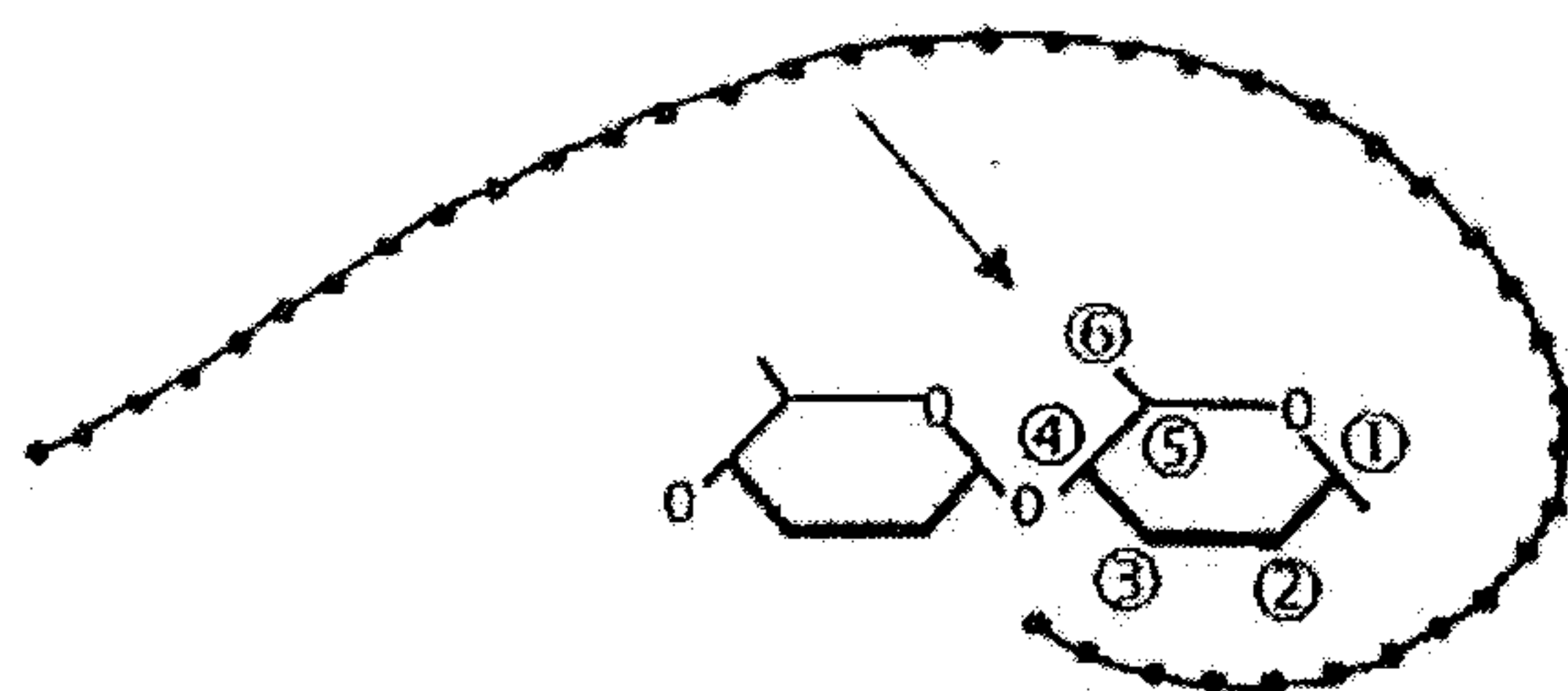
spread on smooth surfaces and dried. The major industrial uses of starch, such as paper coating and sizing, textile sizing, corrugated board manufacture and all adhesive applications utilize this property.

These four important properties vary in degree from one starch source to another. When the structures of linear and branched starches were elucidated and methods were

developed for detecting and quantifying the two types of molecules, their functional properties were finally explained.

Straight chain amylose molecules tend to line up parallel to each other in solution. As the solution cools, there is less energy available to keep the molecules apart. The hydroxyl groups on parallel amylose

Amylose



Amylopectin

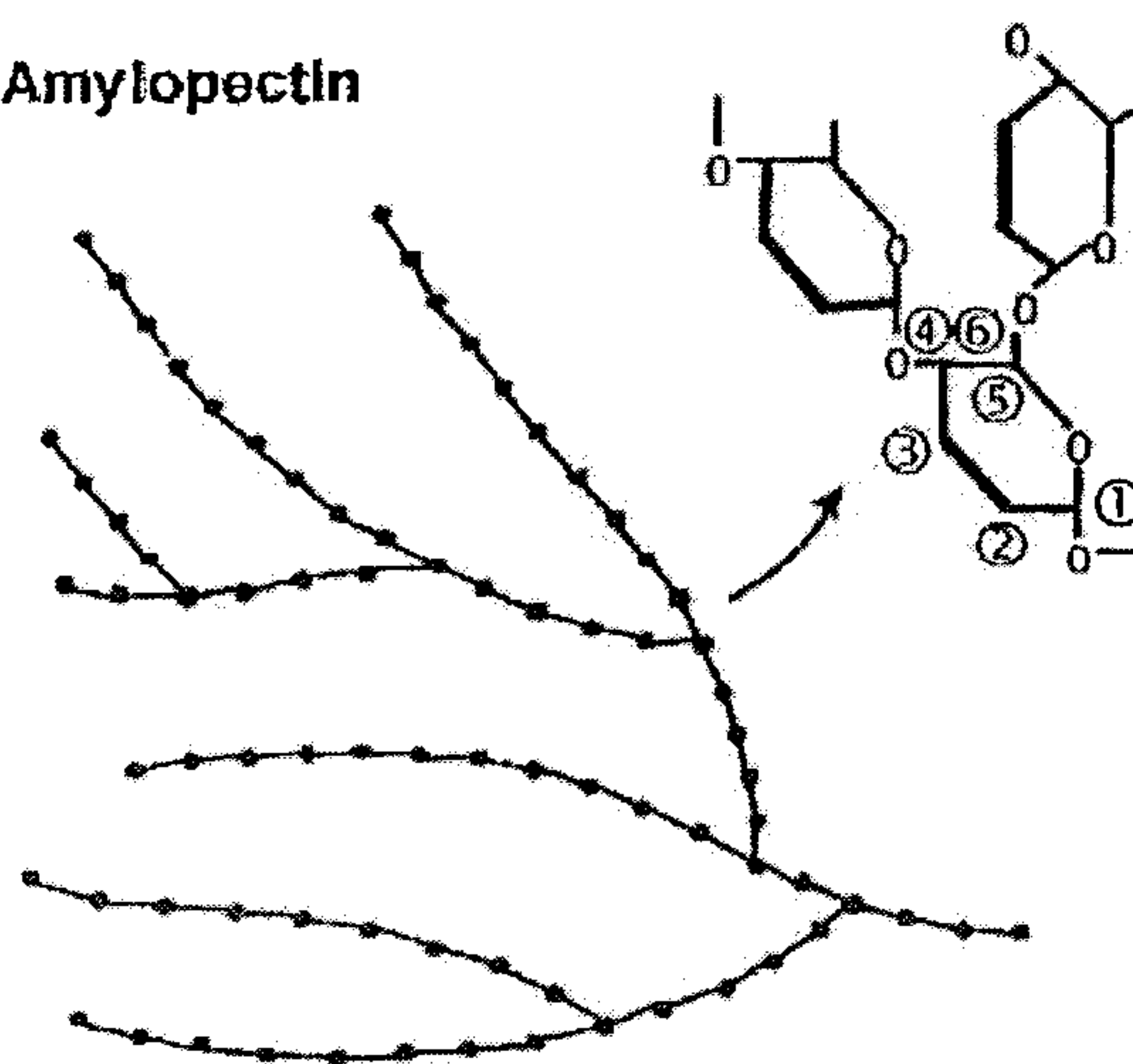
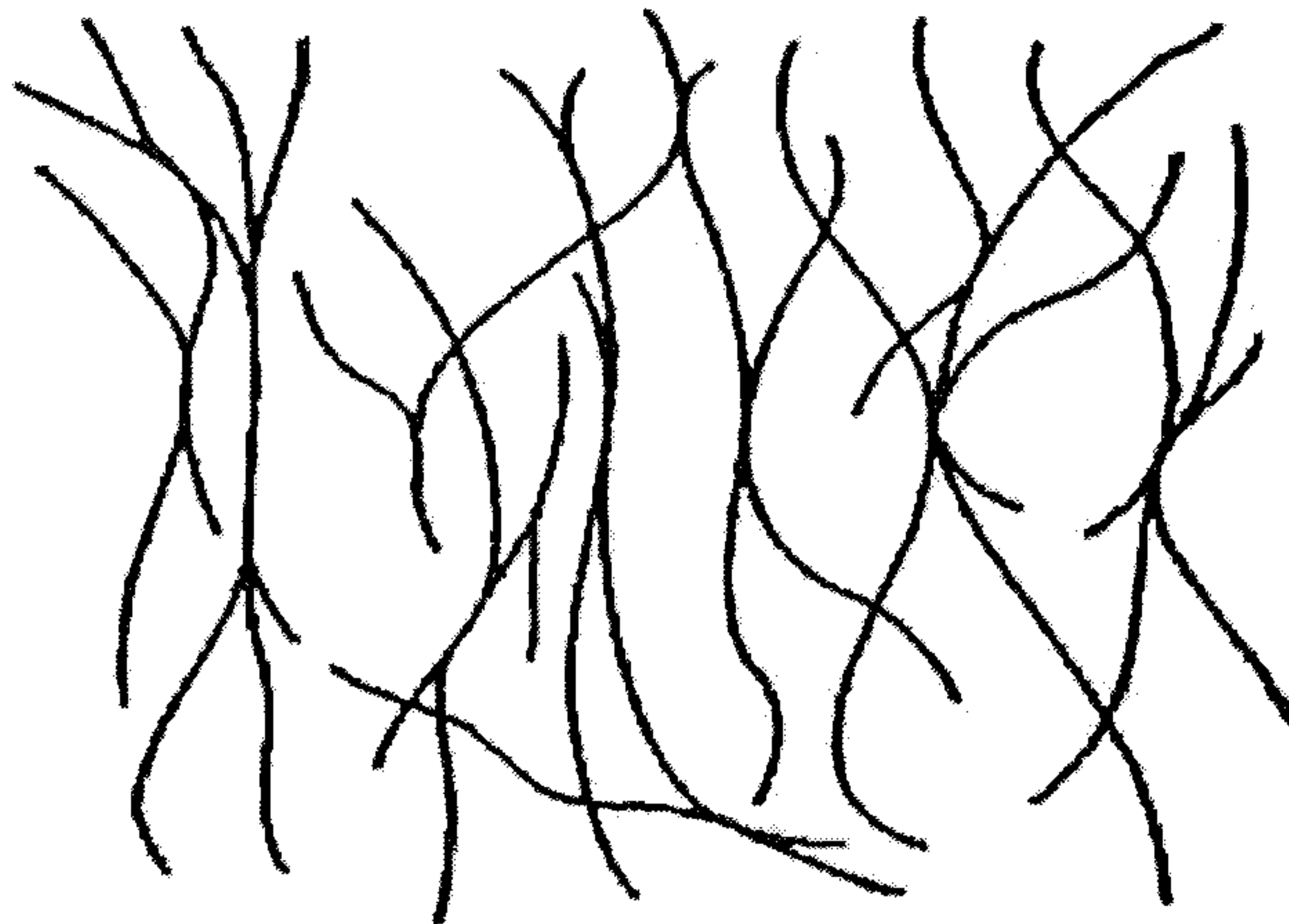


Figure 6
Amylose (top) and
Amylopectin (bottom)
molecules

Figure 7
Micelle formation in
amylose molecules



molecules exert attractive forces and the molecules are pulled together. This phenomenon, illustrated in Figure 7, is often referred to as retrogradation. The overall result is a gelled paste. The oriented areas are called micelles. Starches with a high percentage of amylose are difficult to gelatinize because of the extra energy needed to hydrate and disintegrate the firmly-bonded, crystalline aggregates of amylose. After gelatinization such starches form firm gels and when properly prepared, yield strong, tough films.

At the opposite end of the functional spectrum are the

waxy starches, which are nearly 100% amylopectin. They gelatinize easily and yield nearly-transparent, viscous pastes that retrograde slowly to weak gels. Between these extremes is found a wide range of natural starches as well as many starch modifications and derivatives. Based on the behavioral diversities of native starches, the starch chemist, by selection of the proper raw material, followed by application of selected modification or derivatization techniques, can devise products with a broad range of functional characteristics.

UNMODIFIED, REGULAR, NATIVE OR COMMON CORN STARCH

If the starch produced by the corn wet milling process is simply dried, it is called a common, regular or unmodified corn starch. It is available in various physical forms: corn starches may be sold as fine or coarse powders, as flakes, as pearls or be agglomerated to larger particles.

Slight variations can be introduced into unmodified starch by adjusting pH, by mild heat treatment, or by adding small quantities of chemicals or adjuvants before or after drying. Such starches will then perform more effectively in specific applications. For example, common starch intended for enzyme conversion may be adjusted to a specific pH and small amounts of inorganic salts that facilitate enzyme action may be added. Starches for food use are also often pH adjusted.

More unmodified corn starch is sold than any other type. It is used in the manufacture of corrugated board, coated and sized paper, paperboard, adhesives, salad dressings, beer, canned foods, dry food mixes (such as puddings, cakes, baking

powder, etc.), molding starch, laundry starch, etc.

Unmodified corn starch, when cooked, has such great thickening power that pastes containing more than 4-5% solids are too thick to handle. Further, such pastes gel very rapidly when cooled. For many uses higher solids-containing pastes with reduced tendency to thicken or with the ability to form softer gels are required.

The chemical composition of starch — highly oxygenated carbon compounds — make starch an excellent product for use as a chemical feedstock. Many industrial products, which today are derived from petrochemical feedstocks, are increasingly being synthesized from starch or cellulosic feedstocks. Examples of current commercial products of this type include the use of corn starch in the production of biodegradable plastics.

GENETIC VARIATIONS OF CORN STARCH

Many applications require starches in which properties other than viscosity have been modified. For many years, tapioca starch was the choice for puddings, fruit fillings and certain types of



hard biscuits. When the supply of tapioca became short during the late 1930's, and later became unavailable, intensive research was begun to develop a genetic variety of corn that contained starch with properties similar to tapioca starch. A type of corn first found in China in 1908 and maintained as a genetic curiosity was called waxy corn because of its waxy appearance. The starch in this corn had properties similar to starch from tapioca.

An active breeding program was begun in 1956-57 to develop a commercial variety of corn that retained the waxy maize characteristics. By 1944, sufficient waxy maize was grown to demonstrate that it could be processed by the wet milling method to yield a starch that was a satisfactory replacement for tapioca.

Waxy maize starch, which is essentially 100% amylopectin, yields pastes that are almost clear when cool, non-congealing, and when dried in thin films, yields a translucent, water-soluble coating. Waxy starches are used for thickening a wide variety of prepared foods. Most commercial waxy starches are modified by crosslinking and/or derivatization to

further enhance their advantageous properties.

The development of waxy maize encouraged geneticists to look for a mutant that might yield a starch with a much higher amylose content than regular corn. Such a starch, it was postulated, should be an excellent film former and might be spinnable into a fiber. Genetic research ultimately resulted in the commercial development of two corn hybrids, one containing about 55%, the other about 70% amylose. Recent research has resulted in developing starches with greater than 80% amylose. The ultimate goal is to have native hybrid corn starch with 100% amylose.

High-amylose granules are smaller than those from regular or waxy maize corn and they often have unusual shapes. Some granules do not gelatinize or lose their birefringence even when boiled for a long time. However, they will gelatinize in dilute alkali or alkaline salts, or when heated in water under pressure at elevated temperatures. The solutions must be kept hot or the amylose quickly gels and retrogrades. High amylose starches are used to produce sizes for textiles

and to produce quick-setting confectionery gums. High amylose starches appear to be resistant to human digestion (hence, "resistant starches") and may find application in reduced-calorie food products.

Active research programs are now being conducted into new methods to alter the genetic makeup of corn to produce starches which have the characteristics and functionality of the starch derivatives discussed below. Several are now commercially available. The genetically engineered starches allow processors to use fewer chemicals in their production, and to claim "native" labeling in addition to their unique functionality and their contribution to the development of new foods.

MODIFIED STARCH

Native starches have certain inherent features for use in the development of foods, pharmaceuticals and industrial products. Among other advantages, they are readily available, generally low in price, and yield a simple, consumer-friendly label when listed in an ingredient panel.

However, the advent of more sophisticated process-

ing systems made it apparent that the natural properties of raw starches could not meet the demanding processing requirements of increasingly sophisticated product formulations.

In order to meet such manufacturing requirements, starch chemists developed modified starches. The techniques and chemicals used to manufacture food and industrial modified starches have been thoroughly researched and tested to ensure safety and functionality. Modified food starches are strictly defined and regulated by the United States Food and Drug Administration (FDA) in 21 CFR Chapter 1, paragraph 172.892, and industrial modified starches are covered by 21 CFR Chapter 1, paragraph 178.3520.

Acid-modified corn starch

The first method used commercially to reduce the viscosity of starch pastes was the acid-modification process patented by Duryea in 1899. In this method, a starch-watersuspension is agitated while being subjected to mild treatment with dilute mineral acid at temperatures elevated but below the starch gelatinization temperature, for varying

periods of time. When tests show the desired viscosity has been reached, the acid is neutralized with sodium carbonate and the starch is filtered, washed and dried. In this manner a series of starches yielding pastes of decreasing viscosity are produced.

The primary reaction taking place during acid-modification is hydrolysis of glucosidic bonds in starch molecules. This limited and controlled hydrolysis produces two important consequences. First, since the starch molecule is so large, only a small amount of cleavage is needed to markedly reduce viscosity. Second, disruption of bonds within the granule weakens the granule structure. Like the parent starch, all acid-modified starch pastes have reduced viscosities when warm, yet have a strong tendency to gel when cooled. This suggests that acid-modification reduces chain length but does not substantially change the molecular configuration. When starch fragments reorient, the cooled pastes can and will set to firm gels. These so-called acid-modified or thin boiling starches are used in large quantities in textile warp sizes, especially for cottons and cotton polyester blends.

The starch pastes, applied to warp yarns and dried, serve as an adhesive to bind the fibers in the warp giving increased strength and resistance to abrasion needed in the loom during weaving. The lower viscosity acid-modified starches are also used in calendar and size press applications in the paper industry to enhance printability and abrasion resistance of the paper surface. This ability to form firm gels is utilized by the confectioner in the manufacture of starch-based gum candies.

Oxidized corn starch

A second method for reducing the viscosity and altering the properties of starch is oxidation. Although oxidizing agents such as chlorine, hydrogen peroxide and potassium permanganate can be used, oxidized starches produced by the corn wet milling industry are almost exclusively made using sodium hypochlorite as the oxidizing agent.

As in the case of acid-modification, aqueous starch suspensions under continuous agitation are treated with dilute sodium hypochlorite containing a small excess of caustic soda (NaOH). The reagent solution is added slowly to the starch suspen-

sion in a reactor which is maintained at about 120°F. Cooling water in the reactor jacket or external heat exchangers remove heat generated during the oxidation reaction. When the correct amount of reagent has been added and sufficient time for reaction has elapsed, the viscosity of the starch is determined. When the desired degree of oxidation is reached, the starch slurry is treated with a reducing agent such as sodium bisulfite to remove excess hypochlorite, adjusted to the desired pH, filtered, washed and dried. Products with a wide range of modification can be produced.

Oxidized starch retains its original granule structure and is still insoluble in cold water. It is extremely white due to the bleaching action of the sodium hypochlorite. In addition to having decreased viscosity, oxidized starch pastes are relatively clear and show a reduced tendency to thicken or set back when cooled. When dried, oxidized starch films are clear and tough. Because the highly oxidized starches give relatively clear pastes at high solids, they are sometimes referred to as gums.

Treatment of starch with sodium hypochlorite brings about a random oxidation of a limited number of hydroxyl groups to carboxyl or carbonyl

groups, with the resulting rupture of the adjacent glucosidic bond. Since the oxidation occurs in the presence of excess sodium hydroxide, the carboxyl groups are neutralized, resulting in a sodium salt. Since the sodium salt of the carboxyl group is bulkier than the parent hydroxyl group, it is postulated that the tendency of the amylose molecules to associate and retrograde into gels is reduced. The major uses for oxidized starches are in the paper industry as tub, size press and calendar sizes; in the textile industry as warp sizes and as components in adhesives. They are used in food applications where high solids, low viscosity and a creamy body are desired, such as in bakery fillings. Oxidized starches perform well in batters and breading due to good adhesion to meat products.

Dextrins

Dextrins are produced from starch by dry heating or roasting unmodified starch with or without an acid or alkaline catalyst.

In this process, unmodified starch, dried to about 5-7% moisture, is usually acidified with very small amounts of mineral acid

and placed in heated, agitated vessels called reactors or roasters. The temperature is increased at a controlled rate and then maintained at a maximum temperature for varying lengths of time. The resulting product is cooled, blended and sometimes aged. Another dextrinization method utilizes a fluid bed, in which unmodified starch is placed in a reactor and suspended or "fluidized" in a stream of heated air. The starch is then acidified and, as in the conventional or "roaster" process, heated under controlled conditions of time and temperature until the desired end product is attained. With several degrees of freedom possible in such processes, a range of dextrans with widely varying properties is produced.

During dextrinization, the granule is not destroyed but granule integrity is disrupted. When dextrans are suspended in water and heated, the granules swell and then undergo a "peeling" action, separating into layers that eventually break free and disperse. The extent of occurrence of this behavior varies with the degree of conversion of the dextrin.

Dextrans differ from other modified starches in that,

not only are they reduced in viscosity, but they also have appreciable cold water solubility, reduced tendency to gel and increased reducing power. High solids solutions of some of the more highly converted dextrans produce tacky, quick-setting adhesives used in making all types of paper products (bags, laminates, paper boxes, paper tubes and envelopes).

There are several theories regarding what takes place during the dextrinization process. The process reduces the strength of the chemical bonds, which give the starch granule its integrity and brings about generalized molecular scissions that both reduce molecular size and alter molecular arrangement. In those cases where acids are present, simple hydrolytic cleavage is believed to occur. A combination of hydrolysis, recombination and formation of new glucosidic linkages likely accounts for altered paste viscosities and congealing characteristics.

There are three major types of dextrans: white, yellow and British gums. Depending on the processing conditions involved, there may be many subtypes.

White Dextrins

The first type, white dextrins, have a white color similar to original corn starch, but have reduced viscosities, and cold water solubilities ranging from 5 to over 90%. White dextrins produce light colored pastes that set to soft but definite gels. The lower solubility products yield pastes similar to the most highly acid-modified thin-boiling starches. The higher solubility white dextrins (40-90%) can be used at much higher concentrations to yield very soft gels.

Yellow Dextrins

Yellow or canary dextrins are the second type. By using less acid, higher temperatures and more time, dextrins with high water solubility and a distinct yellow color can be produced. The yellow dextrins are used to produce high solids pastes (40-60%) that are very tacky and, when applied in thin films, dry rapidly. They make excellent adhesives, especially for paper products.

British Gums

British gums, the third type, are produced by adding little or no acid to very dry starch and then roasting a long time with slowly increasing temperature. They are tan to

light brown in color and have a distinct caramelized odor. A range of products results, varying from low to high solubility. The pastes prepared from these dextrins vary from nearly solid gels through very soft gels to viscous liquids.

Cyclodextrins

Although similar in name to dextrins, cyclodextrins are produced through quite different processes and have different uses. Cyclodextrins are produced through treatment of starch with a glucosyltransferase enzyme. The resulting water-soluble product takes the physical shape of a hollow cone, with an interior cavity of different sizes depending on the production method. A unique property of the interior of the cone is its hydrophobic nature, enabling cyclodextrins to be used to encapsulate a wide variety of compounds.

Uses for cyclodextrins include encapsulation for controlled flavor release, masking odors and tastes, stabilizing emulsions, increasing foaming power, and controlling or masking color. These properties are finding increasing applications in chemical, pharmaceutical and food markets.

Starch derivatives

Since the starch molecule contains many primary and secondary hydroxyl groups, it can be modified by chemical derivatization.

Unlike the modifications thus far discussed, derivatization may or may not reduce the viscosity of the parent starch. Derivatization is used to impart different properties to the derivative than those of the parent starch. This allows the derivative to meet more effectively the requirements of specific end uses. Countless starch derivatives have been described in technical literature and in patents, but only a limited number are manufactured and used commercially.

The derivatization of starch differs from most chemical modifications of polymers in that the changes in properties are attained with very slight changes in the molecule itself. In fact, all commercial derivatives are prepared under such mild conditions (usually in aqueous suspensions) that the starch granules retain their integrity. This allows the products to be handled in processing and application in much the same manner as the common starches previously discussed.

Starch derivatives are usually prepared by adding the desired reagent to an agitated suspension of corn starch in water. By adjusting the pH of the slurry with an alkali, and sometimes with a catalyst, the mild reactions proceed on the ungelatinized starch at only slightly elevated temperatures. After sufficient reaction time, the derivatives are recovered by filtration or centrifugation, washed with water, dried and packaged.

Two basic types of derivatives are prepared commercially:

Crosslinked/inhibited

Crosslinked starches, sometimes referred to as inhibited starches, are made to overcome the sensitivity of starch sols to shear and processing conditions. This is accomplished by treating starch in the granule state with trace amounts of bifunctional agents capable of reacting with hydroxyl groups on two different molecules within the granule.

Reagents such as phosphorus oxychloride or sodium trimetaphosphate may be used as crosslinking agents. Very small amounts of these agents can exert a marked effect on the behavior of the cooked starch. The de-

gree of crosslinking controls the rate and extent to which starch swells on cooking. Crosslinking decreases the sensitivity of starch sols to temperature, agitation and acids, improving resistance to loss in viscosity.

Stabilization

Starch is stabilized against gelling by using monofunctional reagents. These reagents react with hydroxyl groups on the starch to introduce substituent groups that interfere with intermolecular association between starch molecules. Certain reagents may also introduce specific functionality into starches, e.g., increasing their water combining capacity or viscosity, or imparting a positive charge to the starch molecule.

Hydroxyethyl starches—To produce hydroxyethyl starch, a starch slurry is adjusted to an alkaline pH and a salt is added to suppress the tendency of the starch to gelatinize. Ethylene oxide in varying quantities is added slowly to the agitated slurry and allowed to react for the proper time. Most hydroxyethyl starches are also acid-modified to reduce their viscosity. The hydroxyethylated starch is recovered by filtration, washed and dried. The intro-

duction of the hydroxyethyl group reduces the gelatinization temperature of the starch and results in clear, stable pastes. Hydroxyethyl starches are widely used in surface sizing and coating paper.

Cationic starches—Reaction of corn starch with tertiary or quaternary amines yields quaternary ammonium or amino alkyl starches. When dispersed, these starches exhibit positively charged particles that are strongly adsorbed by negatively charged cellulose fibers in the manufacture of paper. Less starch is used; but, more importantly, nearly all of the cationic starch in solution is adsorbed by the paper, leaving very little in the effluent going to the waste disposal system. This greatly reduces the biological oxygen demand (BOD) load. In addition, cationic starch promotes the retention of filters and pigments in the sheet while reducing the loss of very fine paper fibers. The additional retained fiber and the ability of the starch to bond the cellulose fibers together give greatly increased internal strength to the sheet. This substantive characteristic of cationic starches makes them useful also as surface sizes and as an adhesive in pigmented

coatings. With the growing use of recycled paper stock in the manufacture of paper, more highly treated cationic starches are necessary to give strength and fiber retention properties. Computer printer paper requires higher cation treated starches to yield properties needed to function properly.

Starch acetates—Corn starch can be acetylated with acetic anhydride or vinyl acetate under carefully controlled conditions of pH, temperature and time. After reaction, the starch is isolated by filtration, washed and dried. Sufficient acetyl groups are introduced to prevent retrogradation of the starch paste. Acetylated starches are used to size textile warps, yielding tough, yet flexible yarns. The reduced tendency to congeal makes starch acetates easy to pump and to apply at the slasher.

Starch acetates are also used as food starches. For example, waxy maize starch can be crosslinked with phosphorus oxychloride and then acetylated with acetic anhydride or vinyl acetate to produce an excellent thickener, texturizer or stabilizer used in preparing a wide variety of products.

Starch succinates—The use of

succinic anhydride instead of acetic anhydride yields starch succinates, which are also used as thickening agents for foods. The 1-octenyl succinic ester is also prepared and has affinity for fats and oils superior to that of other derivatives. These starches act as emulsifiers in such products as salad dressing, flavors and beverages.

Starch phosphates—Starch can be esterified with monosodium orthophosphate or sodium tripolyphosphate to yield starch phosphates which produce gels that are more stable than those produced from the parent starch. The phosphated starches are used mainly in preparing food products.

Hydroxypropyl starches—Propylene oxide added to an alkaline starch suspension reacts with the starch to yield hydroxypropyl derivatives. When made in accordance with 21 CFR 172.892, hydroxypropyl starches are used in food products where low temperature or frozen stability is needed.

Hydroxyethyl starch can only be used in food packaging and industrial applications.

Other starch derivatives—Starch can be etherified by treatment with acrolein.

Such ethers may then be esterified with either acetic or succinic anhydride. Starches are also esterified with phosphorus oxychloride and then etherified with propylene oxide.

Pregelatinized starches

Suspensions of most starches and starch derivatives can be gelatinized and dried to yield a broad variety of pregelatinized starches. This is normally done on a single drum dryer with applicator rolls. The starch slurry is heated to gelatinize it, instantaneously dried and ground to desired granulation requirement. These products can be dispersed in cold water with agitation to yield pastes comparable to those obtained by cooking the raw starch. The pregelatinized starches make possible the production of many unique food and industrial products that do not require heat for preparation. "Instant" adhesives and "Instant" starch-based puddings are examples of these types of products. New types of cold-water soluble (CWS) starches are made using aqueous/alcohol reaction, which causes the granule to swell and retain its structure without being ruptured. Such starches yield easier to use, smoother bodied products. Newer mechanical

processes being used are spray drying and extrusion. Often these procedures involve the application of several treatments.

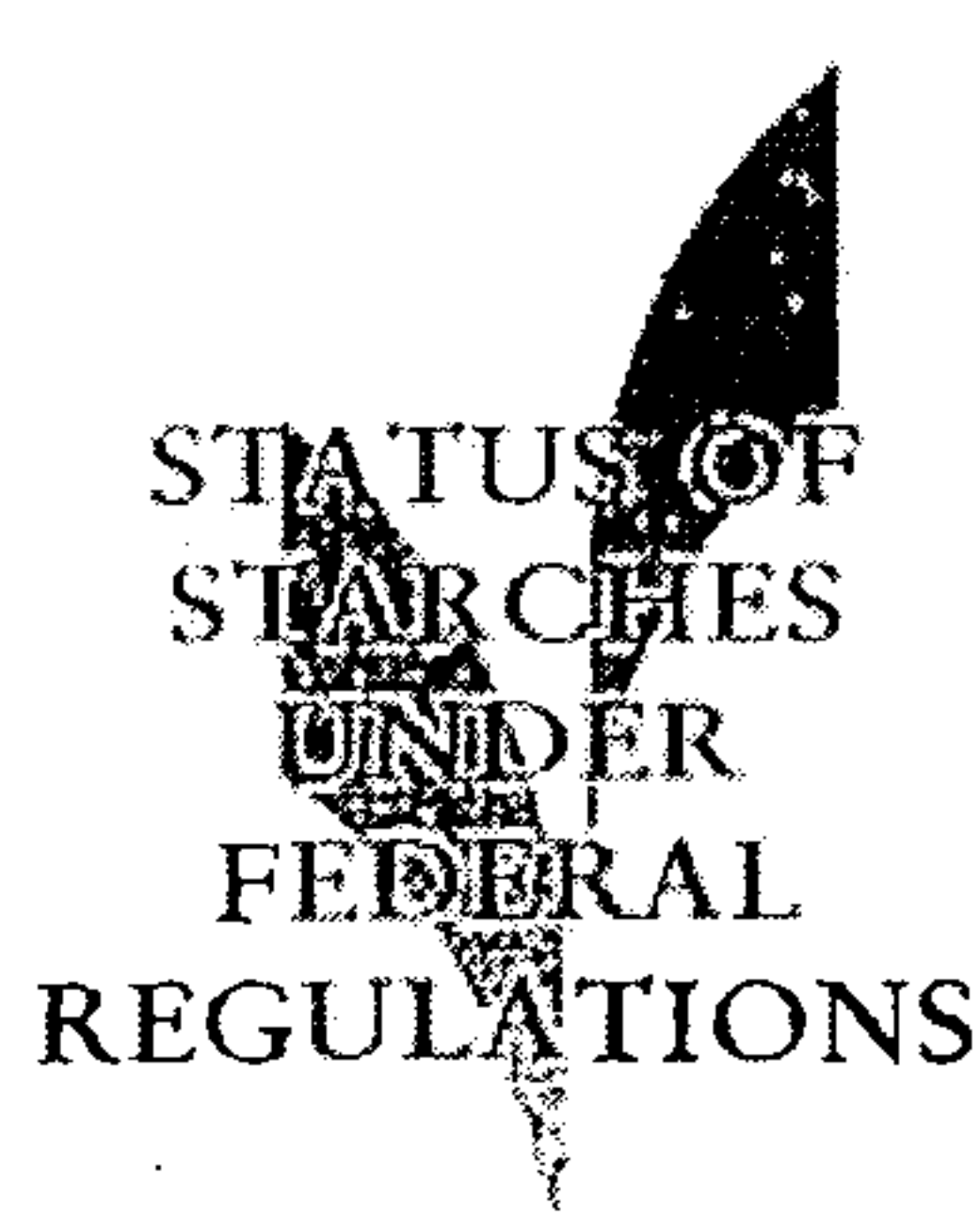
Bleached starches

Even though starches are quite white, certain uses require starches that are stark white. Such products are manufactured from starches by treating them with small amounts of such agents as hydrogen peroxide, peracetic acid, ammonium persulfate, potassium permanganate, sodium chlorite or sodium hypochlorite. The conditions of application are designed to whiten without producing any detectable chemical change in the starch. The bleached starch is recovered on continuous filters or centrifuges, washed with copious amounts of water to remove traces of inorganic salts formed from the bleaching agent, dried and packaged.

Bleached starches perform functionally in the same manner as the parent starch but are lower in microbiological population due to the bleaching agents used. They are used in the manufacture of pills and body powders.



Corn starch photographed at 3000x.



STATUS OF STARCHES UNDER FEDERAL REGULATIONS

The Food and Drug Administration has proposed to affirm the "generally recognized as safe" (GRAS) status of food grade unmodified or common starches as well as pregelatinized starches. In addition, the same regulations proposed affirming the GRAS status of unmodified starches with differing amylose/amylopectin contents, such as high amylose and waxy corn starches. These proposals are found in 50 FR 12821-12825. Corn starches have been affirmed as GRAS for use in food contact surfaces in 21 CFR 182.70 and 182.90. Dextrins have also been affirmed as GRAS by the Food and Drug Administration. Regulations covering dextrins may be found in 21 CFR 184.1277.

Two specific regulations promulgated by FDA cover the bleached, the modified and the derivatized starches approved for use in foods and in food packaging. These regulations specify the treatment approved, set limits for either the quantity of modifying agent used in preparing the product and/or the amount introduced into the starch. They also specify the names to be used for modified starch in ingredients lists. In the ingredi-

ents list on the label of a finished food, the name is, "food starch- modified." The two regulations are: Food starch-modified — 21 CFR 172.892; and Industrial starch-modified — 21 CFR 178.3520.

For food starch-modified, these regulations cover acid-modified, bleached, oxidized, esterified and etherified starches, and starches treated with various combinations of these treatments.

For industrial starch-modified, the regulations cover starches treated by similar methods, as well as irradiated starches and starches treated with specific surface-active agents. Industrial starch-modified regulations specify the use of these products as a component of articles for food packaging, processing and storage.

In addition to regulatory actions by the Food and Drug Administration, various groups such as the *Food Chemicals Codex*, *U.S. Pharmacopeia* and the *National Formulary* have issued guidelines and specifications for starches, modified starches and dextrins intended for specific uses.

Dry starches are available in multiwall paper bags and in rail car or bulk truck shipments. Other containers such as paper drums, metal and rubber containers of various sizes, and corrugated boxes can be used but require special arrangements between user and supplier. Bulk bags up to 2000 pounds may be useful for industrial users, while smaller bags (25 and 50 lb.) are available for retail customers. Bulk installations vary in size from those with capacity for a few thousand pounds to those with capacity to handle several bulk rail hopper cars of starch at one time.

Because starch is a finely divided organic material, handling conditions that create dust may increase the risk of explosion. Explosion prevention measures include the use of non-sparking metals, explosion proof electrical motors and eliminating sparks, flames and hot surfaces in starch handling areas. Compliance with OSHA, EPA and local safety and health regulations is required.

Starch from a dry bulk handling station can be transported to points of use throughout a plant by properly designed air, vacuum and mechanical systems. Dry starches can also be slurried in water and pumped to the point of use. Because starch settles rapidly from water, continuous agitation or recirculation is necessary to maintain a suspension. Proper design of both dry and wet starch handling systems is necessary. Starch manufacturers will supply engineering assistance in designing such systems.

Starch is very stable and can be stored for long periods if kept dry. Like many other organic materials, however, it will degrade and decompose if allowed to become damp. Because starches are somewhat hygroscopic, they will vary in moisture content depending upon the humidity of the atmosphere in which they have been stored. Storage should avoid areas where aromatic products are stored, as starches can readily pick up flavors.



SHIPPING AND HANDLING DRY STARCHES



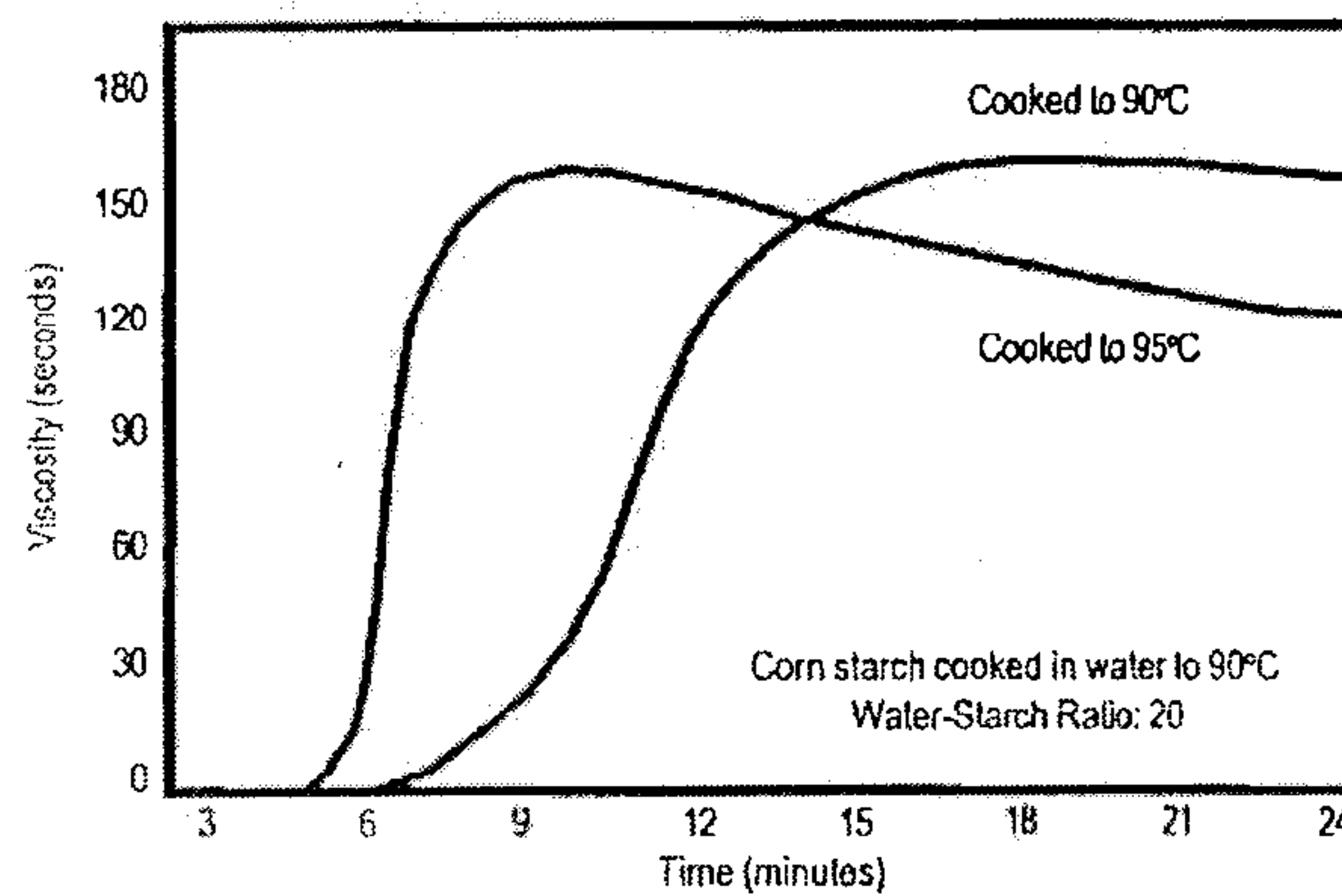
Most applications for starches require that they be suspended in water and then heated above the gelatinization temperature. The viscosity of the resulting paste is dependent on many variables, such as starch type, solids concentration, pH, amount of agitation during cooking, rate of heating, maximum temperature reached, time held at that temperature and the presence of other ingredients in the suspension.

As pointed out earlier, gelatinization temperature will vary with the type of starch selected for use. Further, the observed gelatinization temperature of a specific starch may vary with the physical conditions imposed upon the system. As shown in Figure 8, if starch under certain specific conditions of concentration, pH and agitation is heated in a water

bath maintained at 90°C, the observed gelatinization temperature and the resulting viscosities are not the same as with the bath maintained at 95°C. The 90°C cook reaches its maximum viscosity in about 18 minutes and then remains relatively constant. The 95°C cook, on the other hand, reaches its maximum in just over 9 minutes, but then gradually decreases in viscosity. The granules subjected to the more rapid temperature rise reach their maximum expansion and then begin to rupture with a resulting loss of viscosity. Adverse starch breakdown can be reduced or prevented by using a low level of crosslinking.

The effect of agitation on the gelatinization and breakdown of corn starch is shown in Figure 9. In this experiment a 5% starch suspension at room tempera-

Figure 8
Effect of temperature on gelatinization



ture was placed in a water bath maintained at 90°C and agitated at two different speeds. The solid line shows that the paste agitated at 100 rpm required approximately 18 minutes to reach its maximum viscosity and then remained constant for the last three minutes. In contrast, the suspension agitated at 200 rpm reached a maximum viscosity after 6 minutes, followed by a rapid viscosity decrease and then a continued, but much slower, viscosity decrease. In the 200 rpm cook, improved heat transfer caused the temperature to rise at a faster rate and the granules to gelatinize more rapidly. The mechanical action of the 200 rpm agitator, however, ruptured the swollen granules resulting in a sharp drop in viscosity. Continued agitation brought about only slight viscosity decrease after the granules were me-

chanically ruptured. Crosslinking reduces viscosity loss due to shearing of the granule by use of agitators, pumps and homogenizers.

The effect of pH on corn starch gelatinization and breakdown is demonstrated in Figure 10. The reference sample at pH 4.0 yields a typical cooking curve for normal corn starch. Increasing the pH to 7.0 caused more rapid gelatinization, but yielded a comparable viscosity in the cooked paste. Increasing the pH from 4.0 to 7.0 increased the ability of the starch granule to hydrate and gelatinize, but did not provide sufficient alkalinity to produce appreciable viscosity breakdown after gelatinization. However, when the pH was increased to 10.0 with alkali, gelatinization occurred in a much shorter time due to an

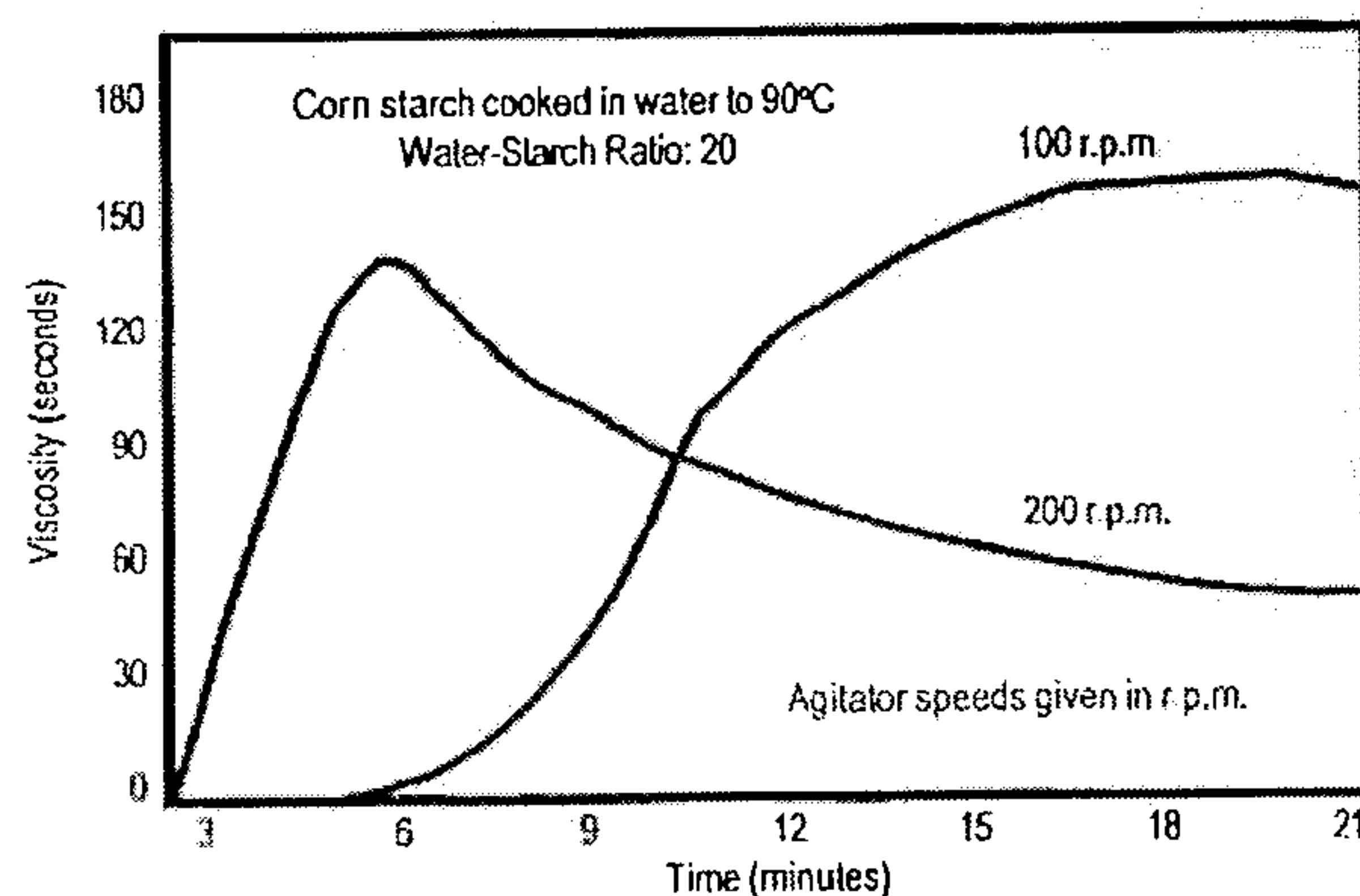


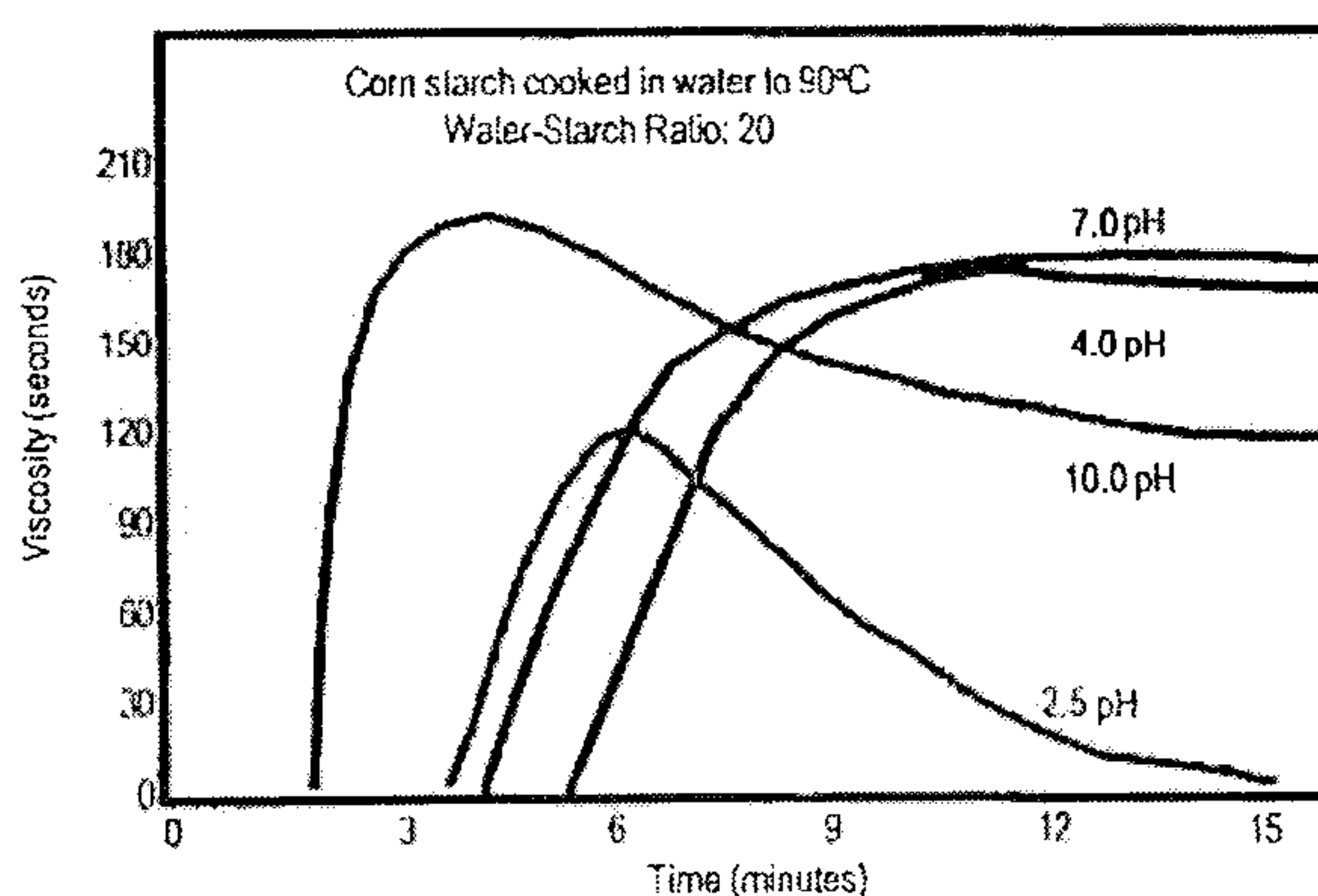
Figure 9
Effect of agitation on gelatinization

increased rate of hydration of the starch molecules. The higher alkalinity also ruptured some of the swollen granules with a resulting loss of viscosity. Although not shown in Figure 10, if the starch had been dispersed in 2% sodium hydroxide solution, it would have gelatinized without any added heat to a relatively stable, but less viscous paste than that produced by heating at pH 10.0.

The final curve on Figure 10 shows the viscosity behavior of a starch suspension adjusted to pH 2.5. Gelatinization began much like the suspension at pH 7.0, but the paste attained a lower maximum viscosity and then underwent a rapid and continuing loss of viscosity. At pH 2.5 and at temperatures approaching 80°C the starch molecules probably undergo

glucosidic cleavage, weakening the entire granular structure, which ultimately disintegrates yielding water-dispersible fragments of lower molecular weight. The effects of other materials in the solution on the rate of gelatinization of starch and the characteristics of the resulting pastes also can be observed. For example, when cooked in 10% sucrose solutions, starches gelatinize less rapidly and form less viscous pastes, since sucrose binds water so that less is available for granule gelatinization. When the diastatic enzyme alpha-amylase is present, marked decreases in viscosity occur. If beta-amylase is present, the viscosity drops and up to 60% of the starch may be converted to maltose. If glucoamylase is present, the starch may be converted to over 95% glucose.

Figure 10
Effect of pH on
gelatinization



Another method for preparing starch pastes involves continuous pressure cooking, often referred to as jet cooking. In this process the starch suspension is mixed with steam and then injected into a pressure vessel, where it is held for a very short period of time at temperatures over 100°C and at pressures higher than atmospheric. The paste is then flashed down to atmospheric pressure, with resultant evaporative cooling and concentration. If desired, some modification of the starch may be obtained by adding small quantities of specific chemicals to the starch slurry before injection into the cooker. This allows the user to alter the properties of the starch paste in a continuous process to meet the requirements of his specific use, but it does mean that the user must assume responsibility for controlling the degree of modification accomplished.

Since starch properties can also be altered by derivatization and modification, almost unlimited variations can be obtained. This versatility has made possible the development of many specialty starch products designed for specific fields of application. It is impossible to discuss the

many products commercially available in this brief discussion. Typical applications for food and industrial starches, and dextrins are included at the end of this booklet. Any reader wishing assistance with these products is encouraged to contact individual member companies of the Corn Refiners Association. They would be pleased to offer assistance in selecting the correct product and in recommending proper methods of application.

Cooked starches may be used hot, at room temperature or chilled. The proper conditions for altering the temperature must be applied to the hot paste if the desired results are to be obtained. Conditions are often designed for a specific application, but some general guidelines follow:

1. Hot starch pastes continue to lose viscosity if maintained near boiling temperatures. They should be cooled to the temperature at which they are to be used immediately after cooking.
2. Starch pastes lose viscosity in direct proportion to the force of agitation. If viscosity is to be maintained, gentle



but thorough agitation should be used after cooking.

3. Starch pastes increase in viscosity as they are cooled. The amount of agitation applied during cooling affects the physical characteristics of the cooled paste. Continuous agitation during cooling yields pastes smoother in texture and with fewer tendencies to gel than those not stirred. Conversely, maximum gelling demands that no agitation be applied during cooling.

4. Undercooked starch pastes yield gels that release water upon standing. Though often referred to as "weeping," as the more correct term is *syneresis*. Selection of the proper starch product, thorough cooking and proper cooling eliminates syneresis.

5. Dilute starch pastes, particularly those of unmodified and acid-modified starches, may develop a distinct cloudiness. This cloud is the result of *retrogradation*

of the amylose polymer in the starch. Retrogradation is the process of molecular alignment and dehydration that produces large, loosely bound molecular aggregates. Given sufficient time and no agitation, these aggregates may precipitate (settle). Clouding and precipitation can be prevented by keeping starch pastes at a temperature of about 170°F with gentle, continuous agitation. Oxidized, certain derivatized and most dextrinized starches have reduced tendency to retrograde. Waxy starches do not exhibit this retrogradation phenomenon to any marked degree.

6. Due to the ready accessibility of sugars, starch pastes are excellent media for the growth of many airborne microorganisms. If stored at or near room temperature for more than 24 hours, preservatives must be added to prevent fermentation, loss of viscosity and eventual spoilage.

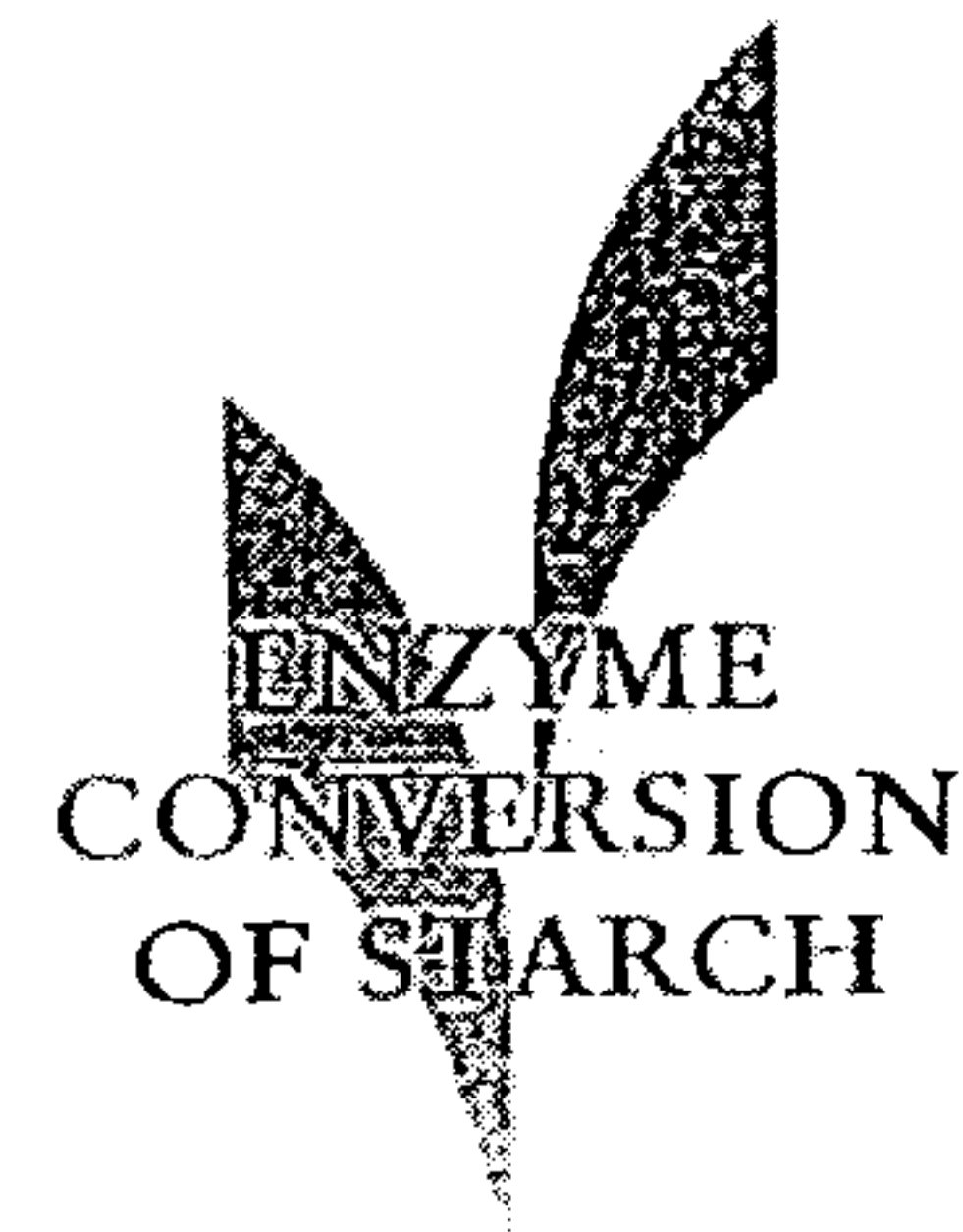
Starch pastes of all types are susceptible to hydrolysis by amylolytic enzymes resulting in shorter polymer chain lengths and sharply reduced viscosities. Enzyme hydrolysis is widely used, particularly in the textile and paper industry and in the preparation of corn syrups and dextrose.

Cotton warp yarns are commonly sized with starches to give them the needed strength for proper weaving. However, the starch must be removed from the woven cloth before it is dyed. A diastatic enzyme (alpha-amylase) that rapidly hydrolyzes starch to short, water soluble fragments is used for this purpose. The enzyme is applied to wet cloth, allowed to stand for the correct period of time to permit the enzyme to act on the starch, and the solubilized hydrolysates are then washed from the cloth with warm water.

Paper manufacturers use large quantities of starch that is enzyme converted in the paper mill. The enzyme conversion process allows the papermaker to replace the modified or derivatized starches with unmodified starch for some applications. It also allows the papermaker to custom convert

starch to the viscosity required for specific applications. In a typical paper or textile mill, bulk starch is automatically scaled into converting equipment, where it is slurried in water at the correct concentration (35-40% starch suspensions for high solids conversions). The starch slurry is adjusted to the desired pH, alpha-amylase is added and a programmed heat cycle is set in operation. In a typical conversion cycle, steam is applied to a closed, jacketed, agitated vessel heating the starch suspension to 80°C in 15 minutes. This swells the starch and initiates rapid enzyme conversion. The conversion is held at 80°C for 45 minutes and then heated to about 105°C in 15 minutes. The elevated temperature is maintained for 30 minutes to inactivate the enzyme and thoroughly disperse the starch.

At the conclusion of the 105°C holding period, the starch is cooled to the temperature at which it is to be used by one of several means. If it is intended for use as a tub size or for application at the size press on a paper machine, it will quite likely be cooled by dilution with cold water. Pigments or other chemical aids may be added simultaneously with



the dilution water.

If the conversion is intended for use in preparation of a pigmented coating for paper, it is cooled by adding it to a "clay slip" which is a high solids mixture of clay or other pigments with dispersing agents, dyes and other chemical aids. Since paper coating is accomplished at very high speeds, the rheological properties of the starch-clay-chemical mix (coating color) must be carefully controlled.

Primary control of the final viscosity of enzyme-converted starch is achieved by varying the quantity of enzyme utilized, but variation of the physical conditions imposed upon the system also affects the characteristics of the converted starch. Batch systems are often employed, but continuous systems are also in use commercially.

Generally, starches used for enzyme conversion are unmodified and are specially

prepared for this use. They are usually pH adjusted and buffered; small quantities of various adjuvants are incorporated in the slurry before drying and special drying techniques may be used.

The major use for enzyme-converted starch occurs right in the wet milling plant, where each year billions of pounds of starch are converted to nutritive carbohydrate sweeteners. These processes utilize alpha-amylase, beta-amylase, glucoamylase, debranching enzymes and isomerases. They are discussed in a booklet entitled *Nutritive Sweeteners from Corn*, available on the Corn Refiners Association website, www.corn.org.

Enzyme treatment today is frequently used to prepare starch for subsequent derivatization and processing steps, which result in the creation of products with unique physical and functional properties.

The chemical literature contains descriptions of countless methods for determining the chemical and physical properties of starch.

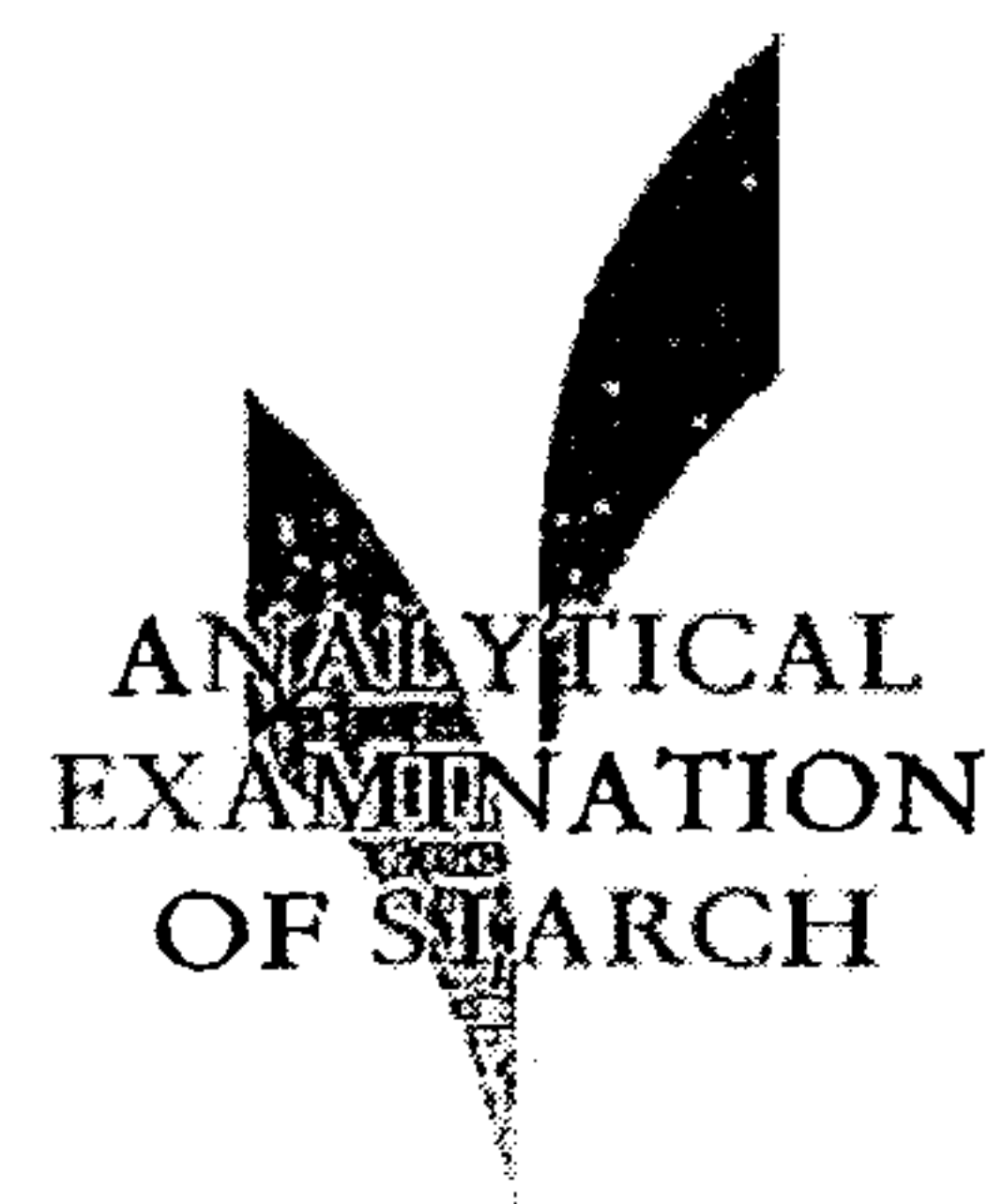
The Corn Refiners Association, through its Technical Affairs Committee, has spent many years developing and standardizing analytical procedures for starch and starch derived products which are practical and effective. The committee actively continues its work on standardization of analytical procedures today.

As a result of this extensive work, the Corn Refiners Association publishes these analytical procedures and

makes them available to the public. These methods are published in *Analytical Methods of the Member Companies*, available from the Association's website, www.corn.org.

By cooperation with the Association of Official Analytical Chemists many of these methods are available through that organization's reference publications as well.

The Corn Refiners Association has published many analytical procedures applicable to unmodified and modified starches and dextrans, sweeteners and corn byproducts.



CORN REFINING INDUSTRY PRODUCT USE

	Unmodified starch	Modified starch	Dextrins		Unmodified starch	Modified starch	Dextrins
ALCOHOLIC BEVERAGES, BREWING				Vinegar	*		
Beer, liquor		*		Worcestershire sauce		*	
BEVERAGES, NON-ALCOHOLIC				CONFECTIONERY & GUM			
Carbonated		*		Chewing gum	*	*	*
Protein drinks			*	Chocolates	*		
Fruit drinks & juices		*	*	Confectionery	*	*	*
Powdered mixes	*	*	*	Licorice	*	*	*
BAKING, SNACK FOODS				Marshmallows	*	*	*
Baking powder	*	*		Nougats	*	*	*
Bars, energy & snack		*		FATS AND OILS			
Biscuits	*	*	*	Margarine	*	*	*
Breads & rolls	*	*	*	Pan coatings	*		
Cakes	*	*	*	FORMULATED DAIRY PRODUCTS			
Cookies	*	*	*	Cheese spreads & foods	*	*	*
Crackers	*	*	*	Coffee whitener	*	*	*
Doughnuts	*	*	*	Condensed milk			*
Extracts and flavors		*	*	Frozen cream	*	*	*
Food coloring			*	Yogurt		*	
Frosting, icing, glazes	*	*	*	ICE CREAM & FROZEN DESSERTS			
Pies	*	*	*	Frozen puddings/custards	*	*	*
Potato chips		*	*	Ice cream or milk	*	*	*
Powdered sugar	*	*		Powdered mixes	*	*	*
Pretzels	*	*	*	Sherberts, water ices	*	*	*
Spices			*	JAMS, JELLIES, PRESERVES			
Yeast	*			Fruit butters	*	*	*
CANNED FRUITS & VEGETABLES				Jams		*	*
Fruits & berries	*	*		Jellies		*	*
Fruit fillings	*	*		Marmalade		*	*
Soups	*	*	*	Preserves			*
Tomato sauces	*	*	*	MEAT PRODUCTS			
Vegetables	*	*		Bologna	*	*	*
CEREALS				Breakfast meals		*	
Cereals	*	*	*	Chicken products		*	
Cereal bars	*	*	*	Dried meals		*	
CONDIMENTS				Fish, seafood	*	*	
Catsup	*	*		Hotdogs		*	
Gravies	*	*	*	Mincemeat	*	*	*
Mayonnaise	*	*		Sausages	*	*	
Mustard	*	*		Surimi	*	*	
Oriental sauces	*	*	*	MIXES, PREPARED			
Pickles, pickle products		*		Cake mixes	*	*	*
Relishes		*		Cookie, brownie mixes	*	*	*
Salad dressings	*	*	*	Dessert mixes	*	*	*
Sauce mixes	*	*	*	Dried foods	*	*	*

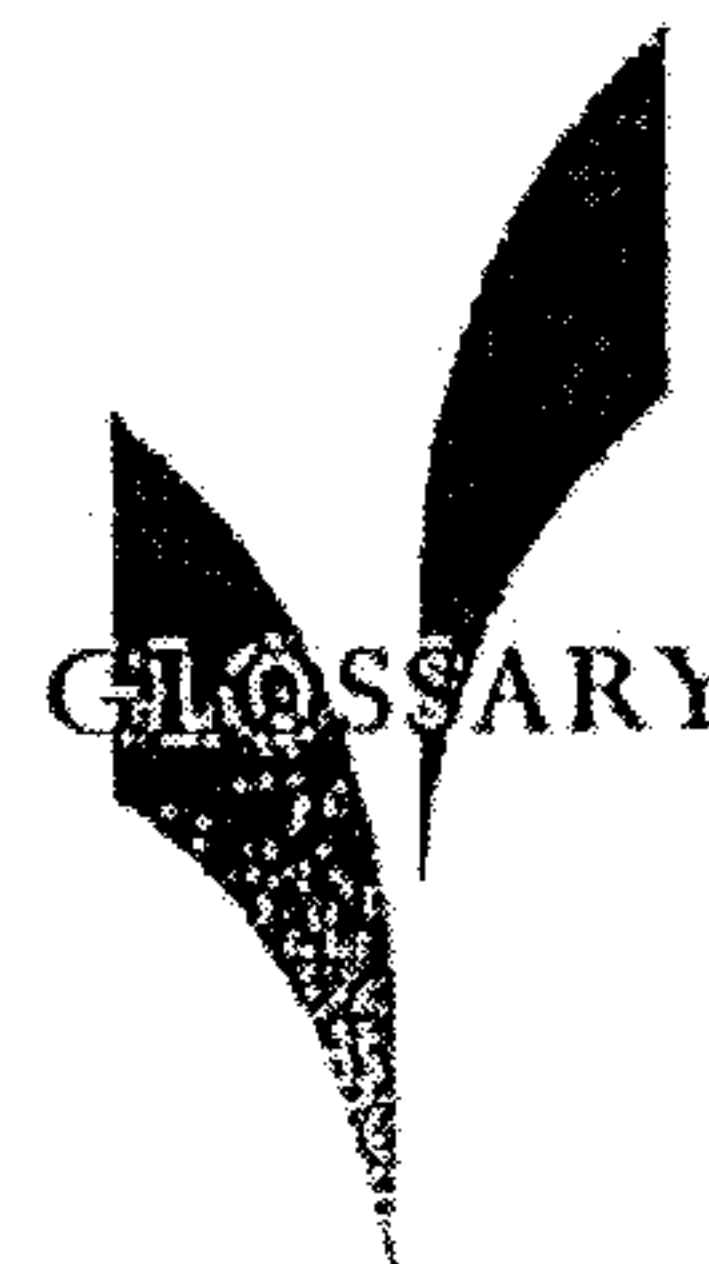
CORN REFINING INDUSTRY PRODUCT USE

	Unmodified starch	Modified starch	Dextrins		Unmodified starch	Modified starch	Dextrins
Eggs, frozen or dried	*	*	*	Coatings (food & drug)	*	*	*
Frosting, icing mixes	*	*	*	Cough drops	*	*	*
Gelatin mixes		*	*	Drugs	*	*	*
Gravy mixes	*	*	*	Medicinal syrups	*	*	*
Instant breakfast foods	*	*	*	Pharmaceuticals	*	*	
Instant tea		*	*	TOBACCO			
Pancake, waffle mixes	*	*	*	Tobacco		*	*
Quickbread mixes	*	*	*	ANIMAL FEED			
Seasoning mixes	*	*	*	Cat	*	*	*
Soups, dried	*	*	*	Cattle	*	*	
SYRUPS & SWEETENERS				Dog	*	*	*
Chocolate, cocoa	*	*	*	Fish	*	*	*
Dessert toppings	*	*	*	Swine	*		
Fruit and table	*	*	*	CHEMICALS			
Low calorie sweeteners		*	*	Acetic Acid	*		
Soda fountain	*	*	*	Agrochemicals	*	*	
MISC. FOODS				Dispersing agents	*	*	
Baby Food	*	*	*	Enzymes	*	*	
Desserts (puddings/custards)	*	*	*	Fermentation processes	*	*	*
Dietetic preparations	*	*	*	Food acids	*	*	
Invalid feedings	*	*	*	Industrial alcohol	*	*	
Peanut butter			*	Insecticides	*	*	
Precooked frozen meals	*	*		Organic solvents	*	*	*
Rice & coffee polish	*		*	Pharmaceuticals	*	*	
HOUSEHOLD NEEDS				PAPER, PAPER RELATED PRODUCTS			
Air freshener		*		Abrasive paper & cloth	*	*	*
Batteries		*		Bookbinding	*	*	*
Briquettes	*	*	*	Envelopes	*	*	*
Cleaners		*		Glassine	*	*	*
Crayons & chalk		*	*	Labels	*	*	*
Diapers	*	*		Paper	*	*	*
Laundry care		*		Parchment	*	*	*
Matches		*	*	Printing inks	*	*	*
Metal cleaner	*			Straws	*	*	*
Trash bags	*	*		Wallpaper	*	*	*
Twine, cord, string	*	*		PASTE, ADHESIVES			
PERSONAL CARE				Adhesives	*	*	*
Cosmetics	*	*	*	Binders, binding agents	*	*	*
Deodorant		*		Glues	*	*	*
Hair styling products		*		Gums	*	*	*
Surgical dressings	*	*		Mucilages	*	*	*
PHARMACEUTICALS				Pastes	*	*	*
Antibiotics	*		*	TEXTILE			
Aspirin	*	*		Cord polishing	*	*	

CORN REFINING INDUSTRY PRODUCT USE

	Unmodified starch	Modified starch	Dextrins		Unmodified starch	Modified starch	Dextrins
TEXTILES cont.				MINING/METALLURGY			
Dyes & dyeing	*	*	*	Electroplating		*	
Oilcloth	*	*		Galvanizing		*	
Printing	*	*	*	Metal plating		*	
Sizing materials	*	*	*	Ore refining, separation	*	*	*
Textile	*	*		MISC. INDUSTRIAL			
Window shades, shade cloth	*	*	*	Boiler compounds		*	
BUILDING MATERIALS				Explosives	*	*	*
Cardboard	*	*		Filters	*	*	
Ceramics	*	*	*	Fireworks	*	*	*
Coatings (wood, metal)	*	*		Leather tanning		*	
Cork products	*	*		Lubricating agents		*	
Fiberglass	*	*		Oil-well drilling	*	*	
Fiberboard, plywood	*	*	*	Plastics, incl. degradable	*	*	
Glass or rock wool	*	*		Protective colloids		*	*
Laminated	*	*	*	Refractories		*	
Linoleum	*	*		Rubber (cold process)	*		
Paints and varnishes	*	*		Shoes		*	
Tile, ceiling	*	*	*	Tires (rubber)	*		
Wall treatment compound		*		Water recovery (Industrial)		*	
Wallboard	*	*	*				

To aid in the understanding of industry-specific information in this booklet, technical terms are explained in the text at the points where they are first used. For reader convenience, definitions of some of the more difficult terms and of terms having special meanings in the corn refining industry are listed here.



Amylose – A starch molecule made up of glucose units chemically arranged in long straight chains.

Amylopectin – A starch molecule made up of glucose units chemically arranged into branched chains.

Anhydroglucose units – The basic $C_6H_{10}O_5$ unit that occurs repeatedly in all starch molecules.

Aqueous – Containing water.

BOD – Biological oxygen demand, the measure of the amount of oxygen in a body of water used over a period of time through bacteria and plankton activity to stabilize decomposable organic waste.

Brabender – Amylo-viscograph unit used to measure viscosity.

Carbohydrate – A chemical compound composed of carbon, hydrogen and oxygen (starch, sugar and cellulose are three of the most common examples).

Congel – To change from a liquid to a semi- solid, non-fluid mass.

Convert – To change to a lower molecular weight form, as by dextrinization, hydrolysis, etc.

Corn – The seed from commercially grown maize (*Zea mays*) used primarily for animal feed and corn-derived food and industrial products; not sweet corn.

Derivative – A product obtained by reacting starch with a chemical compound, resulting in unique physical and functional properties.

Enzyme – Any of a class of protein molecules that catalyze specific biochemical transformations, as in the conversion of starch to glucose.

Fluidity – Reciprocal of viscosity.

Fractions – The two types of molecules found in starches—linear and branched; amylose and amylopectin.

Gel – A firm, semi-rigid, cooled starch paste resembling a jelly; to form a gel.

Gelatinize – To cook starch in aqueous suspension to the point at which swelling of the granules take place, forming a viscous sol.

Genetics – A branch of biology dealing with hereditary variations in plants and animals. As an applied science, it is used to improve corn by breeding desired characteristics into new varieties.

Glucosidic cleavage – The hydrolysis of a glucose polymer whereby water is the agent, which, under acid or enzyme catalysis, acts to split apart the glucosidic bond holding adjacent glucose units together and regenerates an hydroxyl group on each glucose component.

Granule – The small, grain-like storage particle produced in plants, consisting of starch molecules arranged in characteristic patterns.

High amylose starch – A starch containing over 50% amylose (usually 55-70%).

Hydrate – A molecular-water association.

Hydrolysis – Process of splitting a molecule into smaller parts by chemical reaction with water.

Hydroxyl (OH) group – A chemical radical consisting of one oxygen and one hydrogen atom.

Hygroscopic – Readily absorbing and retaining moisture.

Kernel – A whole grain or seed of a cereal, especially corn.

Linkage – The specific bonding arrangement by which molecules are joined to form larger molecules.

Micelles – The tight bundles into which linear starch molecules and the linear segments of the branched molecules are drawn together.

Molecule – A unit of matter; the smallest portion of a compound that retains chemical identity with the substance in mass.

Mutant – An offspring different from its parent in some well-marked characteristic.

Oxidation – The act of oxidizing which is brought about by increasing the number of positive charges on an atom or the loss of negative charges.

pH – A measure of the acidity or alkalinity of a solution, pH 7 being neutral, lower values acid and higher values being alkaline.

Polymer – A very large, complex molecule formed by chemically joining a large number of identical smaller units (or monomers) in a repeating pattern.

Retrogradation – Dehydration and reversion of cooked starch from a paste to a condition of insolubility.

Slurry – Suspension of starch in water, with or without other components of corn.

Stable – Term indicates that the starch paste does not change appreciably in viscosity, clarity or texture with age.

Starch paste – The thick, viscous, smooth suspension formed by cooking starch in a water suspension to a point above its gelatinization temperature.

Steepwater – Water containing dissolved protein, minerals and other substances in which corn has been soaked or "steeped" during the initial stages of the corn refining process.

Suspension – A heterogeneous mixture of an insoluble granular or powdered material with a fluid.

Synthesize – To build up a compound by the union of simpler compounds or of its elements.

Viscosity – Term used to indicate the resistance of liquids to flow; often used to describe the thickness of a starch paste.

Waxy maize – A variety of corn, the starch content of which consists solely of branched molecules.

Wet milling – A process for separating corn into its component parts using a water-sulfur dioxide system.

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APPENDIX B

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CODEN FIZBE7

IONS AND ION ACCELERATORS FOR CANCER TREATMENT

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A scientific review paper

Energetic ions in the mass range up to neon may have important advantages in cancer treatment when compared to other, conventional types of radiation. This review will first consider radiobiological properties of several types of radiation (photons, electrons, protons and ions), pointing out to the relevant characteristics of ions compared to other types. Parameters of ion beams as required for cancer treatment will then be defined, followed by the review of the status of proton and ion therapy and clinical trials, and a description of operating and planned facilities. Finally, on the basis of existing experience and desired future performance, a possible design of such a facility will be suggested.

1. Introduction

Radiation therapy has become one of the most important modalities in the treatment of cancer. It is estimated that a person has one out of three chance to be confronted with the disease during his or her lifetime and that less than half of them will be cured. While the surgery is still the most successful treatment, radiation therapy either alone or in combination with other modalities contributes to about 40% of the overall cure rates. It is interesting to note that chemotherapy alone results in a rather small part of cancer cures; it

PRELEC: IONS AND ION ACCELERATORS FOR CANCER TREATMENT

is used mostly as an adjuvant therapy. All other modalities contribute only a few percent to the cure rates.

Ideally, the objective of any cancer treatment method is to remove or destroy the tumor while preserving at the same time the healthy tissue as much as possible. It was with this idea in mind that almost a hundred years ago low-energy X-rays began to be used for this purpose, although their penetration was poor and therapeutic effect debatable. In early 1920's, radium units came into use, producing deeper penetrating gamma rays; this was followed by electron accelerators providing higher energy X-rays. Nuclear reactors made radioactive cobalt sources available and they became a standard gamma-ray source for radiotherapy, used until the present (e.g., gamma knife). Most modern and very widely used machines for X-ray therapy are compact linear accelerators and it is estimated that there are up to 4000 of them around the world. Over the years, this technique has been constantly improved, the machines have been adapted to the hospital environment and the delivery of the radiation to the tumor has become more and more accurate, trying at the same time to spare the healthy tissues. However, there are still many cases where it is not possible to avoid irradiation of critical organs in the vicinity of the tumor; the maximum dose allowed for critical organs would in such cases limit the dose given to the tumor, leading to a possible failure of the local control.

About fifty years ago, R. Wilson remarked that the Bragg peak of monoenergetic protons (and other, heavier ions) would allow the radiation dose to be preferentially delivered at the end of their path, in the tumor itself where most damage has to be done. By modulating the proton (or ion) energy it would, in principle, be possible to irradiate the whole volume of the tumor with a uniform and sufficient dose, while keeping the dose delivered to other organs at a lower value. This characteristic, together with a high lateral beam accuracy, is the basis of conformal treatment of tumors, which is an important step toward the ideal method. Since this first proposal, there were a number of proton machines either adapted or specifically built for tumor treatment.

The most recent and quite promising introduction into the range of types of radiation for cancer treatment have been energetic ions in the mass range from carbon to neon. They will be referred to as light ions, although in the medical literature they are usually called heavy ions. In addition to the advantage of showing a Bragg peak which has a similar characteristic of protons, and an even better lateral beam accuracy than protons, ions have other characteristics which could make them more suitable for treatment of some types of tumors than any other radiation. The linear energy transfer (LET) or the rate of energy deposition along the path of a particle is higher for light ions (fast neutrons have a similar property) than it is for conventional radiation, including protons; the relative biological effectiveness (RBE) tends to be higher if LET values are higher. Furthermore, some tumors cells are anoxic and as such are more resistant to conventional radiation due to the oxygen effect, characterized by the oxygen enhancement ratio (OER). There are also indications that the effects of light ion radiation in the tumor do not depend as much on the cell cycle as they do for conventional radiation.

However, possible advantages of light ions compared to conventional radiation result in a more complex system for beam production and, especially, for beam delivery to the patient. With high LET particles and with a large part of their energy delivered at the end of the track, in the Bragg peak, it becomes extremely important to properly adjust not only

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the shape of the beam but its energy and the time spent irradiating a certain part of the tumor as well; otherwise, healthy tissues may be exposed unnecessarily while the tumor may not get the required dose. The proper utilization of light ions requires a state-of-art application of medical diagnostics (CT, MRI, PET) to determine the exact shape and location of the tumor, a full computer control of the accelerator and beam delivery system and a fast and accurate measurement of the beam dose delivered at any instant to the patient. Until very recently, this complexity of the system has been one of the reasons why light ions have found a very limited use in medicine, particularly in the treatment of cancer, so that at present there is just one dedicated facility in the operation (Chiba, Japan). Another reason for the lack of interest was the fact that in the past the few accelerators capable of producing light ion beams with parameters adequate for medical applications were designed for a totally different purpose (nuclear and particle physics), with energies and intensities not matched to the needs of patient treatment, complicated to use and expensive to operate. Compared to light ion accelerators, electron linacs for photon production have enjoyed a long history of development and present designs are well adapted to a hospital environment.

This review will try to address several issues, such as possible advantages of light ion therapy compared to protons and conventional radiation, the complexity of such a system and its possible adaptation to a hospital environment, and the question of cost-effectiveness compared to other modalities for cancer treatment.

2. *Characteristics and effects of radiation*

The objective of any cancer treatment is the control or, possibly, permanent elimination of the tumor. As this process involves and results in cell destruction, the success of the treatment will always depend on the degree of discrimination between healthy tissues and tumor itself. Conventional types of radiation, which include gamma-rays from radioactive isotopes, brehmsstrahlung photons and electrons, have been used widely and routinely for treatment of human cancer since the earliest days (the word "conventional" is used because of historical reasons, without implying limitations or a lower quality). It is a common property of conventional radiation that the dose delivered to the body is the highest in the entrance region and decreases as the radiation penetrates the body (Fig. 1). For gamma-rays and photons, the decrease has an exponential character, which means that after passing through the target, the radiation dose decreases further but healthy tissues and possibly critical organs beyond the tumor are still being irradiated. The effect of radiation on healthy tissues both in front and behind the tumor may, therefore, limit the dose delivered to the tumor. The photon energy is transferred to the tissue through stochastic processes, such as inelastic scattering or photoelectric processes. Therefore, a photon beam is subject to strong scattering as it penetrates the body and this leads to a lateral beam spreading which has to be taken into consideration. Photons and gamma-rays are called indirectly ionizing because the biological effect is due to the action of fast electrons produced in tissues. High-energy electrons are directly ionizing particles; the dose delivered is decreasing even faster with depth than for photons but they have a finite range if the energy is properly selected (Fig. 1). They also show the effects of a strong scattering, resulting in a lateral

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spreading of the beam as it penetrates the body. The delivery of conventional radiation can be substantially improved if the tumor is irradiated from several directions, by rotating the beam around the patient and aiming it toward the isocentre. Although this complicates the beam delivery system, the result is a more favourable ratio of the doses in the tumor and outside. In the case of gamma rays from radioactive cobalt, application of this method has led to the creation of the so called "gamma knife" where the rays from more than a hundred sources are collimated and directed toward the tumor enabling its destruction. Compared to other types of radiation, the conventional radiation is at present by far the most widely used type, contributing almost exclusively to a substantial part of cancer cure rates. Their most efficient use is in the case of fast growing tumors because those cells divide frequently and photons act especially on cells during their division.

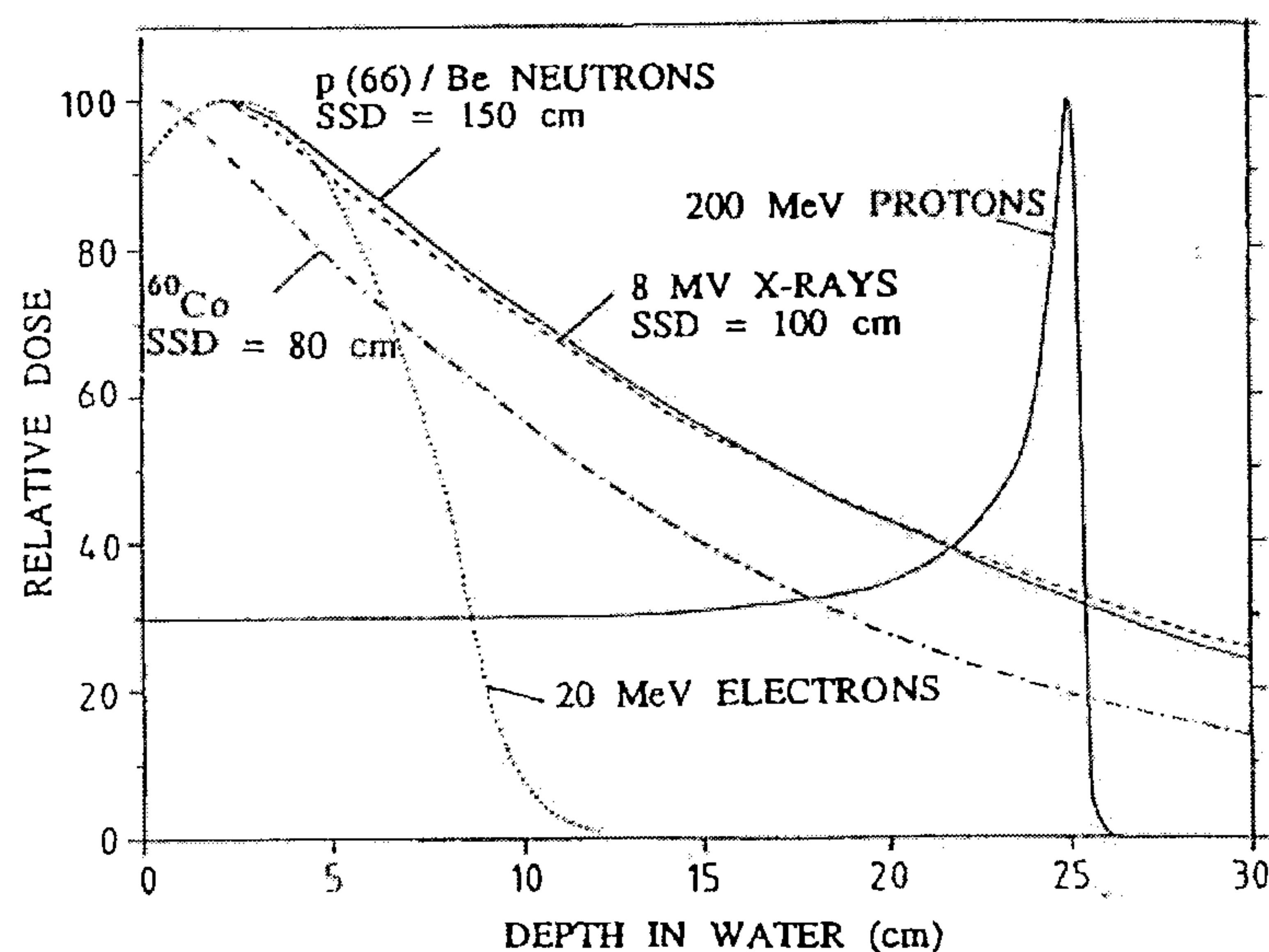


Fig. 1. Depth-dose curves for several types of radiation [1].

In spite of the successes of conventional radiotherapy, either alone or in combination with other modalities (surgery, chemotherapy), about 17% of patients diagnosed with a local cancer (absence of metastases) die due to the failure of the local control; the local recurrence is frequent in sites such as upper digestive tract, brain, skull base, in gynecological tumors and in some tumors with high metastatic rates [2,3]. These patients could mostly benefit from an improvement in radiation therapy. There are two approaches to achieve such an improvement, one through a better dose delivery of conventional radiation, and the other through the introduction of new types of radiation for therapy. There are, however, limits to the first approach, one of them being the mentioned depthwise distribution of the physical dose.

Charged particles heavier than electrons (protons, ions) have properties that make them more attractive for treatment of some tumors [2,4a,5]. Their interaction with matter is

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predominantly through processes involving electrons in target atoms. Because of their much larger mass compared to electrons, they suffer significantly less lateral scattering and less beam spreading; this difference becomes more pronounced with the increasing mass of ions. As a heavy charged particle penetrates into the tissue, it loses its energy in inelastic processes and its velocity is decreasing. The energy deposition rate is a function of energy, and as the particle is slowing down the rate at first increases slowly (Fig. 2; dotted curves); this region

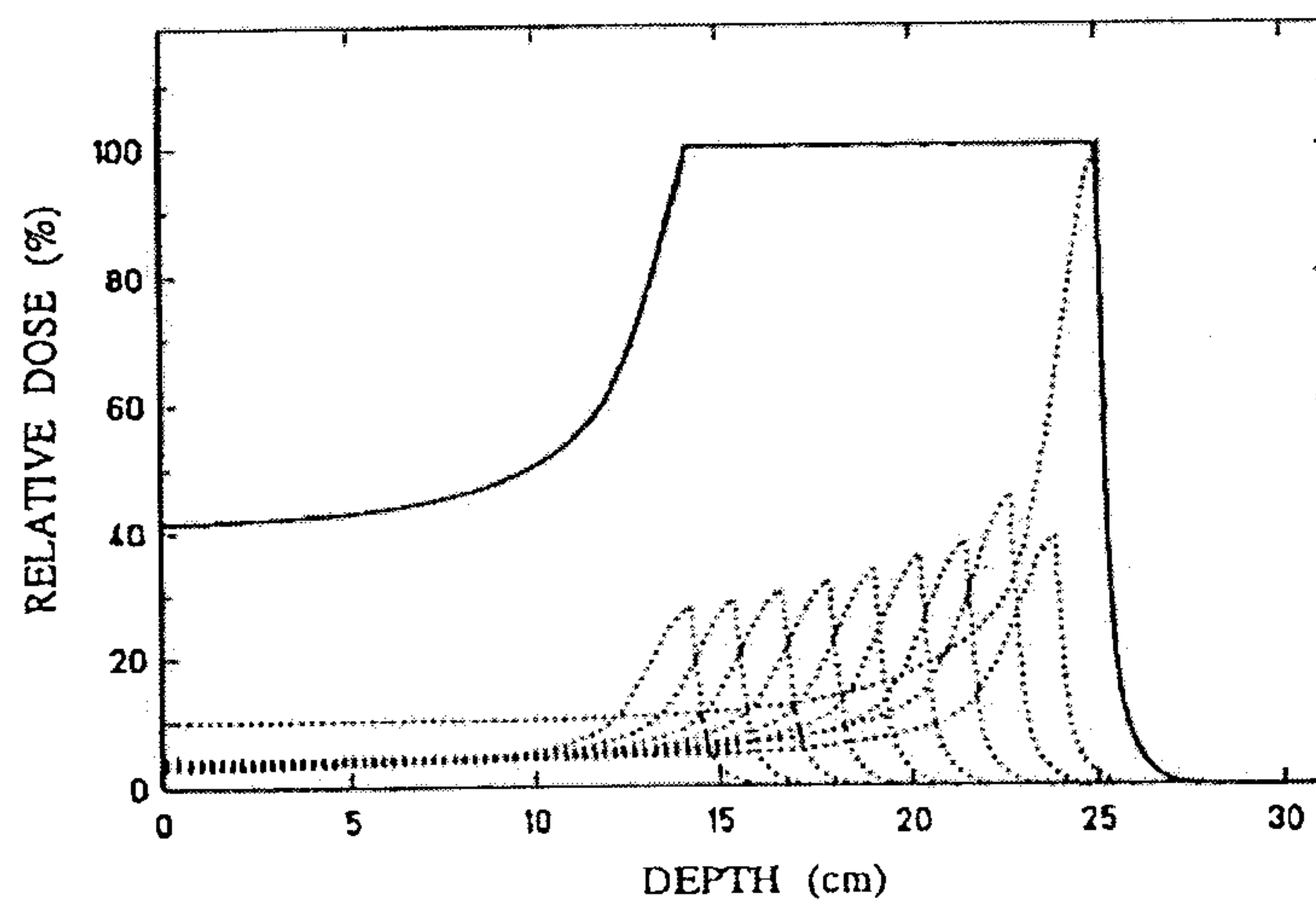


Fig. 2. Spread-out-Bragg-peak (SOBP) [1].

is usually called a plateau. Toward the end of the path, the particle experiences a steep rise in the energy loss rate, just before it is fully stopped (the Bragg peak). The position of the Bragg peak depends on the mass and energy of the particle and on the stopping power of the target. These two effects, a less pronounced lateral scattering and the Bragg peak at the end of the path, led to the first proposal to use protons in radiotherapy about fifty years ago. For tumors with a thickness comparable to the width of the Bragg peak, a charged particle beam with the energy selected such that the peak coincides with the tumor, should in principle be capable to deposit a large part of its energy into the tumor itself, minimizing the damage to the organs in the entrance channel and avoiding fully any irradiation beyond the tumor. Many tumors, however, have a thickness larger than the width of the Bragg peak, and the target has to be irradiated in several steps, each time with beams of different energy, covering thus the whole volume (Fig. 2; solid curve). This method of the spread-out Bragg peak leads to the tumor conform treatment, applicable in principle to any tumor shape, and representing the closest approach to the ideal procedure.

Another parameter relevant for estimating and describing effects of radiation is the linear energy transfer or LET, usually expressed in units $\text{keV}/\mu\text{m}$. Values of this parameter depend on the charge and energy of the particle and, therefore, change as particles penetrate the tissues. For an ideal monoenergetic beam, LET values are meaningful, but for a real beam they are always average values, depending on the way the average has been

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calculated. Still, this parameter is useful as an indication of the biological effectiveness of radiation and different types are described as being low-LET (photons, protons) or high-LET (neutrons, light ions). The order of magnitude of LET values in $\text{keV}/\mu\text{m}$ is around 1 for photons, between 10 and 100 for protons and up to 1000 for light ions.

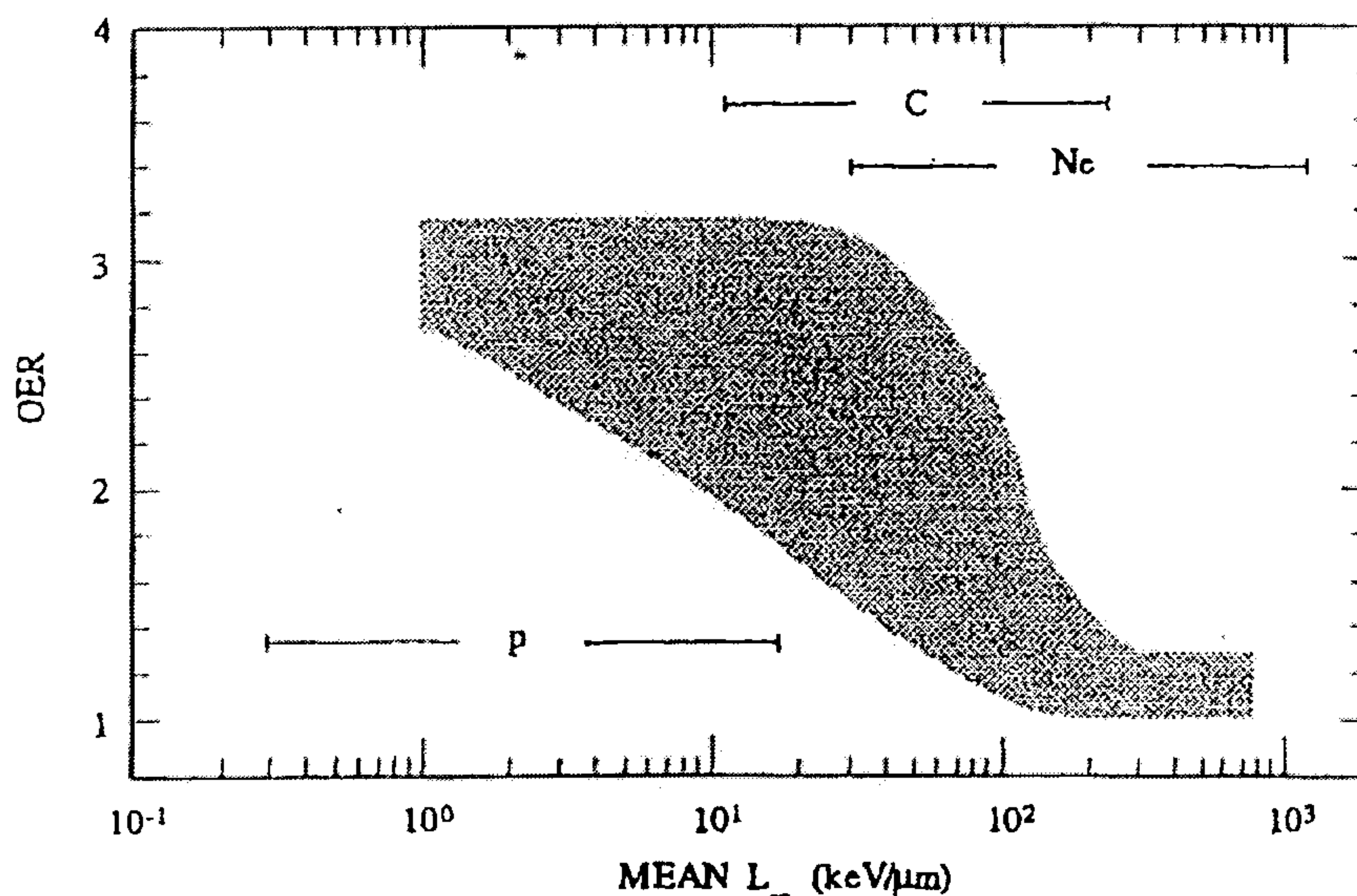


Fig. 3. Range of measured oxygen-enhancement ratio (OER) values for different types of radiation and cell lines [1].

The failure of the local control of tumors treated with conventional radiation is in some cases caused by a higher radiation resistance of anoxic cells present in the core of the tumor [1,4a,6]. Oxygen enhancement ratio (OER) is a parameter describing this effect; it is defined as the ratio of the absorbed dose of a given radiation to produce a certain biological effect in an anoxic cell population to the dose that would be needed to achieve the same effect in normally oxygenated cell population. OER values for conventional radiation have been found to be as high as 3, which may indicate the difficulty in delivering a sufficiently high dose to the (anoxic) cells in the core of the tumor, without causing an irreparable damage to the surrounding healthy tissues or critical organs. The oxygen enhancement ratio decreases with increasing LET and for particles with LET values above a few hundred $\text{keV}/\mu\text{m}$, it may even approach 1 (Fig. 3). Reduced values of OER have been considered as an important argument for the use of high-LET particles although the clinical studies have not fully confirmed its significance and expectations.

Another phenomenon of importance for radiobiological effectiveness is the sensitivity of cells to radiation as function of the phase in the cell cycle [4a,6]. For conventional radiation, cells are most sensitive during the dividing phase, while they are more resistant in the DNA synthesis phase. This difference can be very substantial. For light ions, however,

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the dependence of the sensitivity on the phase in the cell cycle seems to be greatly reduced, especially for LET values above a few hundred keV/ μ m.

While the linear energy transfer (LET) describes the energy deposition (i.e., loss) of a particle along its path, the radiation dose is a measure of energy absorbed per unit mass of tissue; the dose is measured in units of Gray or rad (1 Gy = 100 rad). This is one of the most important measurable quantities in radiotherapy and it is usually quoted when reporting biological experiments or clinical trials [6,7a]. However, equal doses of different types of radiation do not always produce equal biological effects, resulting in different values of the relative biological effectiveness (RBE). The RBE is formally defined as the ratio of the dose of 250 keV X-rays to the dose of some other type of radiation, both resulting in the same biological effect. The response of cells, cell populations and tumors in patients to radiation will vary greatly and a general comparison of RBE values is not very relevant unless all the conditions of the experiment or clinical trial are specified. Still, the general conclusion that the RBE is higher for higher LET (and lower OER) types of radiation remains valid, for the range of interest for light ion therapy (Fig. 4).

In summary, protons and light ions have several properties that distinguish them from conventional radiation and offer new possibilities in cancer treatment. For protons, the advantages are a better distribution of the delivered dose due to a reduced lateral scattering and due to the existence of the Bragg peak. Light ions experience even less lateral scattering and they have additional characteristics, distinguishing them from both, conventional radiation and protons. While the latter are low-LET types of radiation, light ions are high-LET particles and as such show a reduced oxygen effect, their effects are less dependent on the cell cycle and they have a higher relative biological effectiveness. Therefore, light ions could be of benefit in treating slowly growing, well defined tumors. However, they also have a tendency to fragment after a nuclear collision; lighter fragmented particles may have an energy giving them a deeper penetration than the original ion and causing some irradiation of tissues beyond the distal peak. There are also some questions about an increased tumorigenic potential of light ions compared to other types of radiation. It is because of these new effects that the mass range of light ions presently considered for and used in tumor treatment is limited to those below neon; at both facilities where light ions are now used (Chiba, GSI), carbon ions are the species of the choice.

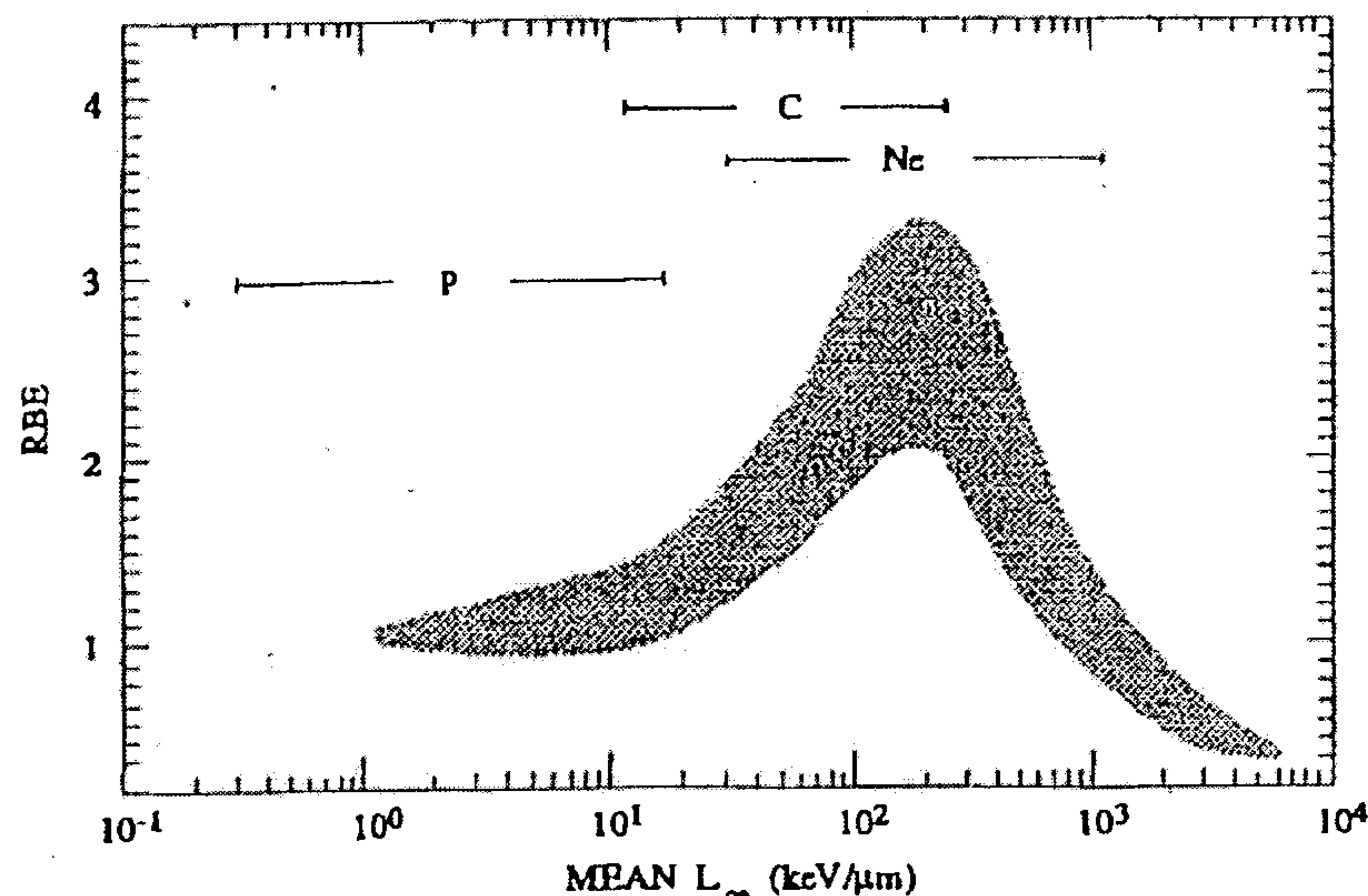
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 Fig. 4. Range of experimental data for the relative biological effectiveness (RBE) factor as a function of linear energy transfer (LET) values [1].

3. Requirements and parameters of ion beams for cancer treatment

3.1. Ion species and energy

At the Chiba facility, most of the research of the effects of light ions on cells and almost all clinical trials have been done with ions up to neon, although the their facility has been designed for ions up to argon. There is a general agreement that carbon ions offer a very good compromise between advantages in the treatment (a very favourable ratio of

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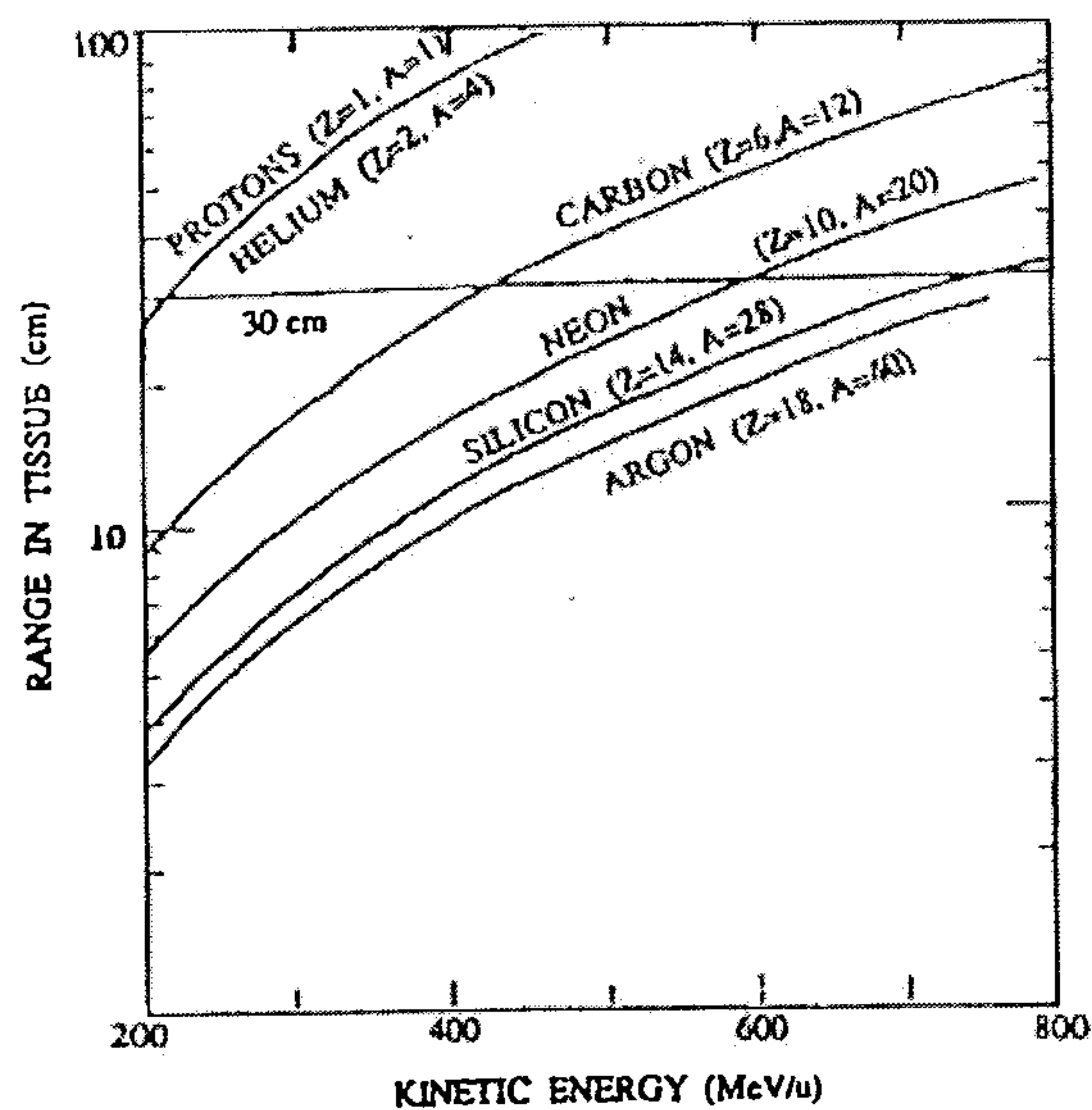


the dose delivered to the tumor and the entrance dose, good radiobiological properties) and disadvantages that should be minimized (fragmentation, distal dose). For a certain desired penetration depth (or position of the Bragg peak), the energy of ions delivered to the patient will depend on the ion species (Fig. 5); the ion energy will then determine the size of the machine and its cost. While for protons an energy of 250 MeV is sufficient for irradiation of tumors seated up to a depth of 30 cm (water equivalent), light ions require a higher energy for the same penetration. Carbon ions with an energy of 290 MeV/u will penetrate only 15 cm deep and for 30 cm an energy above 400 MeV/u would be required. For even heavier ions, such as neon, energies about 650 MeV/u are needed. Once the range of ion species has been selected, the top energy of the heaviest ion will determine the size of the machine and its cost. There are some trade-offs available in considering these parameters: a machine designed for a certain ion species and the full penetration depth (highest energy envisaged) is capable of delivering even heavier ions at the similar or somewhat lower energy per nucleon (the maximum energy will depend on the charge to mass ratio of ions); although for heavier ions

Fig. 5. Range-energy curves for several ion species of interest in cancer therapy [1].

the penetration would not be as deep, they could still be used for treatment of those tumors located closer to the surface of the body. For comparison, at an energy of 400 MeV/u carbon ions would have a penetration depth of 28 cm, oxygen ions 20 cm and neon ions only 17 cm. Ions like neon and heavier have a relatively higher plateau (dose delivered between the entrance and the tumor) and are preferred for shallow tumor locations to limit the damage to healthy tissues (Fig. 6); a lower energy per nucleon may, therefore, still be satisfactory. Should a deeper range be required, the machine should be designed for a higher energy. There will be additional requirements on the precision of the desired beam energy (position of the Bragg peak) and on the allowed energy spread of the beam

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(broadening of the Bragg peak); it is possible to reduce these two effects by using energy defining collimators in the transport line, but this necessarily results in the loss of beam intensity. However, modern accelerators have already achieved the desired accuracy in energy setting and control (0.1% or better); the beam energy spread is also within the limits required for treatment. The knowledge of the properties of tissues in the path of the beam is more critical because this will affect the range (or position of the Bragg peak) and will have to be included into the planning of the treatment.

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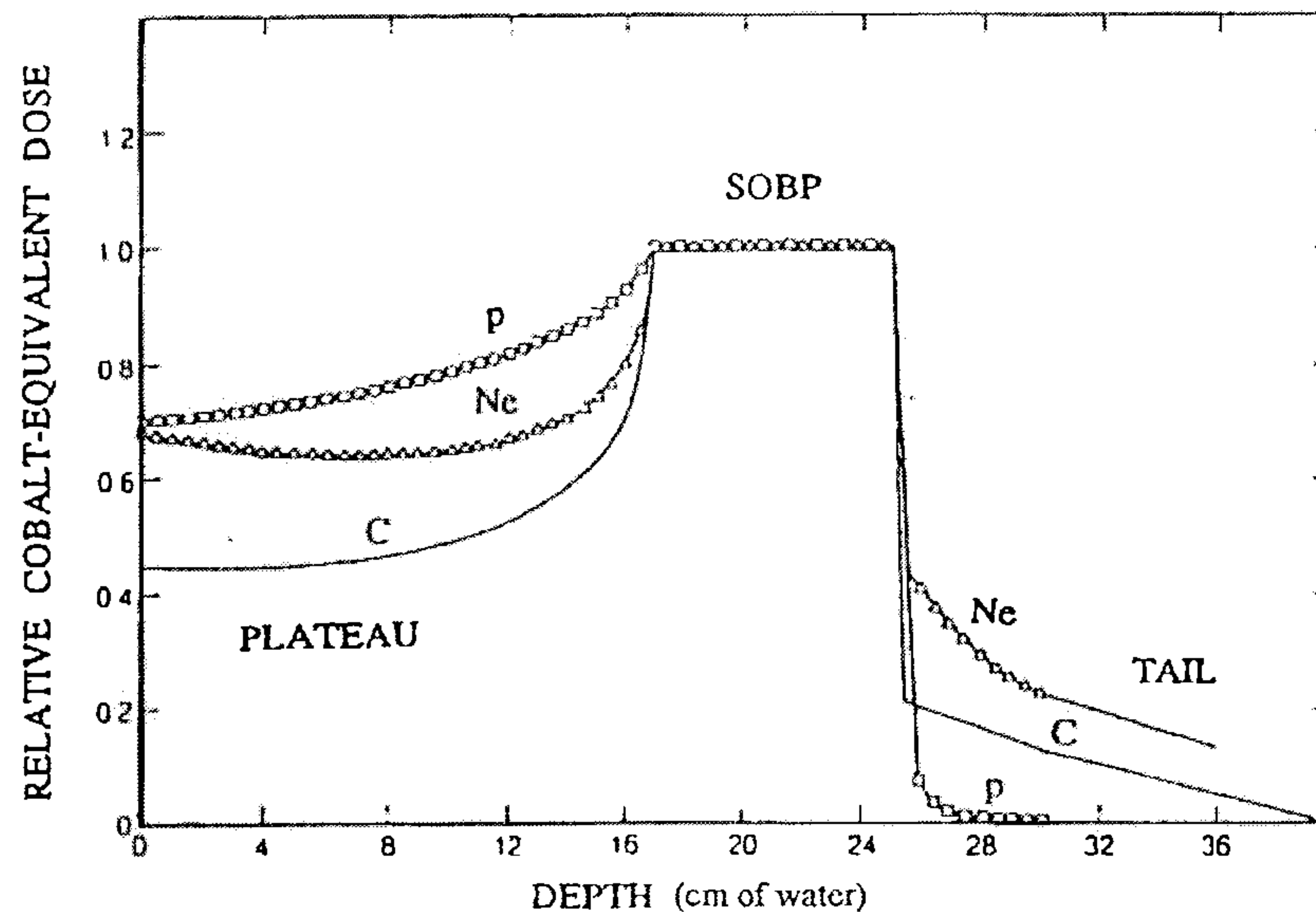


Fig. 6. Spread-out Bragg peak for several ion species, showing relative heights of the plateau and tail regions [1].

The treatment of larger volume tumors with protons or light ions requires scanning of the volume with ions of varying energy, to achieve a spread-out Bragg peak [8]. There are two methods to achieve the modulation of beam energy, one utilizes a fixed output energy from the accelerator (or, possibly, a few energies at large steps) when the changes of the beam energy are accomplished by energy degraders in the treatment room (passive systems), while the other is based on the energy modulation of the accelerator itself (active scanning). The first method, exclusively used at present, does not pose any additional requirement on the accelerator and the beam transfer line except for a fixed and steady output energy, but it does need very carefully designed energy degraders as well as elements for collimation; it may, however, result in a deterioration of the beam quality when passing through the degrader (scattering, fragmentation) and in additional background radiation in the treatment room. For some types of accelerators this is the only method applicable. The other method, by modulating the output energy of the accelerator itself, moves the burden of complexity from the final part of the transfer line to the machine itself. Modern designs of some accelerators, such as, e.g., a synchrotron, and beam transfer lines have reached a stage where it is possible to change the output energy of the machine and necessary transfer line parameters on a pulse-to-pulse basis, which may take only a second or less. This method allows the tumor volume to be scanned a small element by a small element (voxel), always with an appropriate energy and intensity. In spite of the additional complexity of the active scanning, further developments of the accelerator and beam transport control systems will soon make possible the introduction of this method for tests and patient treatment.

Finally, in order to accurately deliver the required dose throughout the tumor, the ac-

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celerator has to provide the desired ion species with very little contamination. In the case of light ions, accelerators may not be able to distinguish between different species having the same charge-to-mass ratio and the selection will have to be done in the injector stage.

3.2. *Beam intensity*

Beam intensity (or flux), required from the accelerator, is determined by several factors, among them the desired duration of the treatment, prescribed dose, method of beam energy modulation and size and location of the target. To minimize the effects of the motion of the patient during the irradiation it is desirable that treatment times be no longer than at most few minutes (in some cases it may be even necessary to synchronize the radiation pulses with breathing or heart beats). There is some flexibility in the choice of the length of the treatment time; one may e.g. ask for a dose of 5 Gy/min to be delivered to a target volume of 2 liters, at the full beam energy. Corresponding values of light ion beam intensities for such a rate of irradiation are of the order of 10^9 particles per second, less for heavier ion species because of their higher relative biological efficiency. The intensity of the beam at the exit of the accelerator will have to be higher because of losses in beam handling and transport from the machine to the patient. Passive systems in principle will have higher losses, possibly up to 80%, but one cannot expect a transport efficiency much better than 50% even with active scanning systems. The latter systems, however, have the advantage that the fraction of the beam, which is not delivered to the patient, is dumped outside the treatment room without contributing to the background radiation. The accelerator, together with the ion source and the injector stage, should be designed for the required output beam intensities over the whole range of ion species. For a certain machine design, the beam output will be lower for heavier ions, but so will be the required target beam intensity. Beam intensities given in Table 1 should be considered as upper limits; even lower values could be acceptable if this would lead to a simpler and less costly design or to a better beam quality because many tumors are smaller than two liters or a longer irradiation time could be allowed.

TABLE 1. *Values of the beam intensities required for the treatment of patients.*

Ion	C	N	O	Ne	Ar
Beam intensity on target (particles/second)	1×10^9	9×10^8	7×10^8	5×10^8	2×10^8

3.3. *Time structure of the beam on the target*

An accurate dose delivery over the volume of the tumor requires a well defined time structure of the beam from the accelerator. If a passive beam delivery system is used, the target is irradiated slice by slice with a broad beam and the time structure is less critical as long as it is possible to monitor and control the time a slice is exposed to the beam. An active beam scanning system poses stricter requirements on the time structure unless there is an on-line beam detection system to accurately measure the dose delivered to any volume element and to deliver a signal to move the beam to the next element once the appropriate dose has been reached. Without such an on-line system, the extracted beam

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from the accelerator should be as steady as possible, with intensity fluctuations within a few percent only, which leads to very tight tolerances on accelerator and beam line elements and their power supplies.

In addition to the stability of the beam, there are other considerations. Regardless of the type of the machine, whether it is a cyclotron, linac or synchrotron, the beam will have an inherent intensity structure related to the rf accelerating voltage; depending on the type of the machine the beam may be available with a macroscopic duty factor less than 100%. A cyclotron operates with a duty factor of 100% and there is an rf structure corresponding to the frequency of the accelerating voltage; the beam intensity control is done best at the low energy end, ion source or ion injector. A linac usually has a very low duty factor, with pulses of a few milliseconds duration, but a high intensity and, again, showing an rf structure corresponding to the accelerating voltage. The low duty factor makes linacs less suitable for ion delivery systems. Finally, a synchrotron with a slow extraction system can have a duty factor up to 50% and its rf structure can in principle be removed by debunching the beam although there are no special advantages in doing this. A synchrotron, as a pulsed device, is well matched to both, passive and active beam delivery systems. The length of the extracted beam pulse could be made to correspond to the time needed to fully or partially irradiate a slice of the target, and the energy can then easily be changed for the next slice. However, the extracted beam intensity in a synchrotron is quite susceptible to any fluctuations or noise in magnet power supplies and efforts have to be made to address this problem.

4. Status of proton and light-ion cancer therapy, clinical trials

4.1. Facilities and number of potential patients

Statistics of the incidence of cancer and its cure rates indicate that there is room for a substantial improvement. Conventional surgery has reached a high level of safety and further improvements can be expected through the introduction of less traumatic procedures (laser surgery, laparotomies) and a broader use of reconstructive surgery. Chemotherapy is much less frequently chosen and justified as a single modality; patients benefit by its use as an adjuvant treatment. For the local control, most important part of cancer treatment, it is the radiation therapy that contributes greatly to the cure rates and which is still open to new methods of application and to new types of radiation. Even conventional new radiation techniques, such as stereotactic radiosurgery and conformal therapy, contribute to an increase of the dose delivered to the tumor without exceeding the allowed dose to healthy tissues. Protons and light ions, however, offer a further improvement in the treatment of certain tumor sites where conventional radiation may often fail. As mentioned earlier, the sites where proton and light ion beams could most benefit the patient are those where their characteristics (physical selectivity, radiobiological effects) can be fully utilized; the preferred sites would be those in a close vicinity of vital organs or those showing resistance to conventional radiation. Experience with proton beams (good physical selectivity), with neutrons (high-LET radiation) and with light ions (good physical selectivity, high-LET radiation) has shown that for a number of tumors substantially better results can be achieved,

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both in the local control and in the long term survival. On the basis of these characteristics and supported by an limited experience, estimates have been made for the number of potential cases that could benefit from proton and light ion therapy [1,9,10,11a,12]. For the Metropolitan New York area, with a population of 20 million, it has been estimated that out of 100 000 new cancer cases per year, about 15 000 would benefit from proton therapy; an estimate done for Italy has shown that about 7 000 patients per year would benefit from light ion therapy, in a population of about 60 million. In a dedicated facility, it should be possible to treat about 1 000 to 2 000 patients a year. Hence, a proton facility could be fully utilized in any population of about ten million, while a light ion facility would be justified for agglomerations of several tens of million.

The real situation with proton and ion facilities is quite different. Although the use of protons has been suggested fifty years ago, at present there are less than twenty facilities in operation, with less than 20 000 patients treated so far. For light ions less experience has been gained: fewer than 3 000 patients have been treated so far, among them about 2 500 in the Berkeley facility which was closed in 1993. Presently, there is just one facility dedicated for light-ion cancer treatments, in Chiba (Japan), while clinical trials are about to begin in the nuclear laboratory at GSI (Germany). There are three proton facilities projected to be put into operation within a few years; another ion facility in Japan (Hyogo) is projected for the operation in the year 2001 and there are two European projects (TERA and CERN-AUSTRON-TERA-GSI collaboration) in the design stage. This reluctance in embarking with more vigor on clinical applications of light ions stems not only from the need for a substantial initial investment, but also from the uncertainty expressed by clinicians that anticipated benefits of light ions in comparison with other types of radiation may not be fully realized in clinical trials.

4.2. *Clinical trials with protons*

Although not the first facility to use protons for tumor treatment, the Harvard Cyclotron Laboratory (HCL), in collaboration with the Massachusetts General Hospital (MGH), has treated the largest number of patients (more than 7000 so far) and gained most experience in the field [5,4b,7b,7c,13,14,11b,11c]. Results have been so encouraging that a new machine, again a cyclotron but with a higher energy, will be put into operation at the MGH, in 1998. Pathologies treated with proton beams fall into several categories in a certain order of priorities, starting with those close to highly critical structures where advantages of protons have been clearly demonstrated and no additional studies are needed; in the second group are pathologies characterized by a prevalently local evolution where local control will lead to a greater probability of cure than by using conventional radiation. Finally protons can be used for palliative treatment of locally advanced tumors with very poor prognosis. At HCL/MGH, the largest group of patients has been those treated for ocular tumors, especially uveal melanomas. Treatments have been highly successful with respect to local control, eye retention and visual preservation. A large number of patients with cervical spine and skull base chordomas and chordosarcomas have been treated as well. While the outcome, when using conventional radiotherapy and/or surgery for those tumors was very often fatal, a combined photon/proton treatment has resulted in a high local control rate and very good long-term survival rates. Similar encouraging results were

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achieved with a combined photon/proton treatment of prostate cancer, while the treatment of some intracranial tumors was much less successful.

The other important center in U.S.A. for cancer treatment with protons is situated in Loma Linda, as a fully dedicated facility [11d]. It is a 250 MeV synchrotron, put into operation in 1990 where more than 2000 patients have been treated. Anatomic regions treated include brain, head and neck, spine, posterior abdomen and pelvis. The majority of patients were diagnosed with prostate cancer. Together with the MGH facility, Loma Linda synchrotron with its three gantries and one fixed beam will for a long time be in the forefront of proton beam applications in cancer treatment.

At the Paul Scherrer Institute (PSI) in Villigen, Switzerland more than 2000 patients have been treated so far with protons, most of them for ocular tumors with a 72 MeV cyclotron beam [2,7d,11e,11f]. Results were excellent, comparable to the treatment by enucleation but with the advantage of preserving the eye and a reasonable visual acuity, even in unfavourable cases of large tumors. There are plans to broaden the application of proton beams by using the 590 MeV cyclotron at PSI; the energy will have to be reduced to match the required range even for treatment of deep seated tumors. It is envisaged that the tumor volume will be scanned in three dimensions, moving the Bragg peak longitudinally by using a number of range shifters, sweeping magnetically the beam in one perpendicular direction and slowly moving the patient in the other.

The Proton Medical Research Center at Tsukuba, Japan [4c] has concentrated its efforts on treatment of thoraco-abdominal tumors, a different emphasis from other similar centers. About 500 patients have been treated thus far, using the 500 MeV synchrotron beam, degraded to 250 MeV. Due to a relatively small number of cases per type of tumor, the results are not conclusive but there are indications that primary malignancies of the esophagus, lung and liver may benefit from the improved physical dose distribution of proton beams, when applied either alone or in combination with photons.

There has been an active program of proton therapy in Russia since 1969, mostly at the Institute for Theoretical and Experimental Physics (ITEP) in Moscow [4d,11g]. Close to 3000 patients have been treated for a large variety of tumor sites, many of them in an inoperable stage, by using the 70 - 200 MeV proton beam from the ITEP synchrotron. Although the number of cases per site has been rather small and therefore the statistics are not reliable, results for some tumors have been very encouraging, in a good agreement with clinical trials at other centers. The main difficulty for the clinical work in Russia has been the lack of dedicated facilities; medical applications usually have had a much lower priority in scheduling the time on the machine. The prospects for the recently prepared program to develop a hospital-based facility are, however, not very good because of the present economic situation in Russia.

4.3. *Clinical trials with light ions*

In spite of the expected benefits of light ion radiation, due to their better physical selectivity and to the additional radiobiological effects, there have been very few clinical trials worldwide, with a very limited number of patients. If the trials with helium nuclei are excluded from consideration (helium nuclei have characteristics similar to protons, i.e. they are low LET radiation), there were only about 500 patients treated so far, with either neon or carbon ions. The pioneering work was done at the Lawrence Berkeley Laboratory, in

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the period between 1979 and 1992 when about 300 patients were irradiated with neon ions from the Bevatron facility; the facility was closed soon thereafter and no further trials were done [15,16,7e,4e,4f,11h]. The most commonly used energy of neon ions was 585 MeV/u, sufficient to penetrate to the deepest tumors. Most patients were selected for neon ion treatment because conventional modalities were ineffective (inoperable tumors, tumors not responding to conventional radiation). This fact makes a comparison more difficult because easily treatable cases, with a more favourable outcome, were excluded. The objective of those trials was to develop techniques for therapy planning and delivery, study the response for a variety of tumors and evaluate the acute and late toxicity of neon irradiation. The list of treated tumor types is long and, therefore, the number of patients was too small for good statistics. Still, neon ions appear to offer potentially improved local control and survival rates for a number of tumor types; results agree well with those obtained with other high-LET radiation such as neutrons. Improved control and survival rates were achieved for patients with paranasal sinus tumors, some salivary gland tumors, bile duct carcinomas, some soft tissue and bone sarcomas, and advanced prostate carcinomas; in some cases the rates were twice as high as with photons. The outcome of treatment of other types of tumors, such as some brain tumors, melanomas, advanced head and neck tumors, lung, esophageal, gastric and pancreatic malignancies, was not better than with conventional therapy, which usually meant that it was not favourable. The conclusion of the LBL trials was that neon ion radiotherapy offers a clinically feasible modality for several selected human cancers, with improved results when compared to conventional photon therapy. It is expected that better results, with fewer side effects, could be obtained with a better, more conformal system of beam delivery than used at LBL.

Although all patients treated at the LBL with light ions (excluding helium) received neon ion therapy, this choice does not seem to be the best. Carbon ions have radiobiological dose distribution features which have advantages compared to both protons and neon ions. While the physical selectivity is similar for all those particles, carbon ions have high-LET characteristics, and compared to neon ions, a lower dose in the plateau region and a smaller fragmentation tail beyond the target. The two facilities where light ions are used (or soon will be) have decided to concentrate the trials on carbon ions although the range of available species is much broader. The first facility is at Chiba, where clinical trials have been in progress since 1994 and about 200 patients have been treated with carbon ions [7f,17,18a,11i]. A wide variety of tumors have been and will be treated, including some deep-seated tumors which did not respond well to neon beams. Patients are carefully selected according to a number of criteria to determine the tumor response and the toxicity for normal tissues; locally advanced and/or inoperable localized carcinomas have been chosen. For head and neck sites locally advanced, recurrent or radioresistant tumors not treatable with other modalities are selected; brain tumors selected for treatment are malignant glioma and astrocytoma, while other sites include inoperable lung tumors, primary liver tumors, cervical cancer, prostate cancer, esophageal cancer and inoperable sarcomas of the bone and soft tissue. In the first phase, it is intended to use conservative doses, below those tolerated by healthy tissues; later on, the dose will be increased in small increments. This approach is justified because of the need to establish proper protocols for the treatment and because of high values of the factor RBE for some tissues such as the central nervous system which have to be spared as much as possible. Preliminary results show that

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there were no major healthy tissue morbidities and that carbon ion therapy is a promising modality for cancer treatment. Trials are planned to continue, expanding eventually the range of ion species to silicon or argon (for tumors located closer to the surface), with the hope to determine the appropriate role of ions in radiotherapy.

At the GSI heavy-ion research complex in Darmstadt (Germany), an experimental cancer treatment program is underway, to continue for five years and to include about 350 patients [18b,11j]. The main objective of the program is to test a novel, most advanced method of beam delivery by using two-dimensional magnetic raster scanning coupled with an active accelerator energy modulation. An ionization chamber in front of the patient measures the number of ions at a specific point in the tumor volume and controls the speed of scanning. After the successful conclusion of the clinical trials the plan is to design and build a hospital based facility.

5. Types of accelerators for light ion therapy

5.1. Cyclotrons

Cyclotrons are machines with a constant magnetic field and a fixed frequency of the accelerating voltage. The injection of the beam from the ion source, its acceleration in the machine and ejection are a continuous process; the extracted beam has a fixed energy and its intensity can also be continuous which can have advantages when scanning the tumor. While cyclotrons delivering proton beams with energies up to 230 MeV have already been developed by industry to operate in a hospital environment, their application as accelerators for light ion therapy is not very feasible. The energy per nucleon needed for the same penetration depth is higher, also the charge to mass ratio of ions compared to protons is lower; because of these factors, a standard-design light-ion cyclotron for cancer treatment would have a prohibitively large magnet. The only cyclotron even considered for light ions was part of the now abandoned European Light Ion Medical Accelerator (EULIMA) Project. In order to reduce the large size and weight of a standard magnet, a superconducting single coil design was considered and developed for EULIMA, having an external radius of only 2.32 m. However, the cyclotron was not the preferred choice for this facility because the required superconducting technology was very sophisticated, not justifying other advantages of a cyclotron.

5.2. Linear accelerators

Conventional linear accelerators are usually very low duty-factor machines, delivering high ion beam currents in short pulses (of about a millisecond duration), often for injection into the next stage accelerator such as a synchrotron. They can accept and accelerate ions having a certain ratio of the charge to mass and deliver a beam with an energy fixed or, at best, variable in large steps. Although the extraction efficiency is close to 100%, there are presently no linear accelerators used for either proton or light ion therapy (there was a proposal to use a small fraction of the proton beam from the Brookhaven National Laboratory's 200 MeV linear accelerator for cancer treatment but it was decided not to proceed). Linear accelerators are machines requiring a large space, they are expensive to build and to

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maintain and beam characteristics are not most favourable for radiotherapy. Improved performance (broader spectrum of ion species, a higher duty factor, some flexibility in output energy, reduced size) can be achieved by using superconducting cavities but this is again a sophisticated technology which is not very suitable for a hospital environment.

5.3. *Synchrotrons*

A synchrotron is a pulsed accelerator, with particles moving on a closed, approximately circular trajectory where the magnetic field and the frequency of the accelerating voltage vary in time as the energy of particles increases. The pulse rate of a synchrotron is of the order of 1 per second or less except for very large machines, and the duty factor can be as high as 50%. The energy of the extracted beam depends on the final value of the magnetic field and can be changed on a pulse-to-pulse basis, which makes this type of a machine very well matched to the depth scanning by beam energy modulation. Although the extracted beam intensity is lower than from either a cyclotron or a linear accelerator, by a proper design it can be made sufficiently high for any ion species and for treatment of tumors at any depth. Other extracted beam parameters, such as emittance, energy spread or time structure, can also be matched to the needs of the beam delivery system. Due to its advantages, flexibility in output energy and ion species, a sufficient intensity, a reliable operation and a moderate size and cost, a synchrotron is the machine of choice in all projects for light ion treatment of cancer.

6. *Light ion facilities, existing and future*

6.1. *History: BEVALAC Program*

Although the first acceleration of ions heavier than helium was accomplished in 1971, clinical trials had to wait until 1975 for the completion of the BEVALAC complex consisting of the synchrotron Bevatron and the linear accelerator SuperHILAC serving as its injector. The beam resources of this facility were shared between the nuclear physics research and biomedical studies. There were two treatment rooms, both utilizing horizontal beams. Initially a scattering system with two foils was used to spread the beam but uniform fields larger than 20 cm diameter were difficult to achieve without a significant deterioration of beam properties. In 1983, a magnetic wobbler system was installed consisting of two orthogonal dipole magnets and delivering the beam in a set of concentric circles, their radii controlled by the amplitude of the magnet coil currents. A more advanced raster scanning system was subsequently developed and commissioned just before the shutting down of the facility in 1993. In the retrospect, the main drawbacks of the BEVALAC program were the difficulties in running a machine for two different programs, with different requirements, rather high operating costs, beam characteristics not optimized for medical applications and a relatively high incidence of breakdowns which is not acceptable for routine radiotherapy.

6.2. *Loma Linda proton synchrotron*

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Although this machine was not designed for light ions, the review of existing facilities will begin with the proton synchrotron at the University at Loma Linda because it is the first synchrotron built for a hospital and used exclusively for medical applications [4g,11k]. The engineering design and fabrication of the accelerator and beam transport systems were done by the Fermi National Accelerator Laboratory (Fermilab), beginning mid-1986. The maximum energy has been chosen to be 250 MeV, sufficient to treat even the deepest tumors. A duoplasmatron proton source feeds a 2 MeV radio frequency quadrupole (RFQ) which serves as an injector into the synchrotron. The machine is weak focusing, which made it simpler but it may have limited the intensity. In the year 1990, the first patient was treated, and since then the facility has been fully commissioned to include three gantry rooms and one fixed (horizontal) beam room. The operation of the machine itself has been very satisfactory, it was stable, reliable and reproducible. It will be very interesting to compare the experience with this facility with the MGH new cyclotron facility, soon to become operational, to see whether a single approach in the design of a proton facility is sufficient or whether both should be pursued. As a reference, it can be mentioned that Loma Linda synchrotron could accelerate heavier particles, such as fully stripped ions from helium up to possibly neon, but with a much lower intensity and a final energy just below 70 MeV/u, which is barely sufficient to irradiate even tumors very close to the surface.

6.3. HIMAC facility (Chiba)

The Heavy Ion Medical Accelerator in Chiba (HIMAC) is the first and only light ion accelerator in the world which has been designed specifically for medical and radiobiological applications [7g,7h,7i,19,18c]. The parameters of the machine were defined broadly enough to cover possible future requirements for heavier ion species and a higher maximum energy. The range of available ions goes thus from helium to argon, and the maximum energy was chosen to be 800 MeV/u for silicon, sufficient for a penetration depth of 30 cm (for argon ions the maximum energy is 700 MeV/u, which is sufficient for their optimal application, treatment of tumors close to the surface). The required beam intensity was determined on the basis of the dose rate of 5 Gy/min, for a field size of 22 cm diameter. This dose rate requires intensities ranging from 2.7×10^8 particles per second (pps) for argon to 1.2×10^{10} pps for helium; for carbon, which is presently used for clinical trials, the required intensity is 2×10^9 pps. Synchrotron is the only accelerator capable to satisfy the requirements for such a broad range of ion species, beam intensities and energy. In order to achieve such a flexibility and increase the reliability of the facility, it was decided to build two synchrotron rings, one on top of the other. The upper ring was designed for a somewhat lower energy, 600 MeV/u maximum, and it delivers a vertical beam to two treatment rooms and a horizontal beam to a room for radiobiological studies. The lower ring delivers a horizontal beam at the full energy of 800 MeV/u to two treatment rooms as well as a beam for general studies. Because of a much higher rigidity of light ions to be used in therapy compared to protons (for the same magnetic field the radius of curvature has to be larger by a factor of about 4 for heaviest ions and highest energy) gantries for light ions would have to be larger by a similar factor and most often are not considered for use in light ion facilities.

The detailed design and arrangement of the elements of the injector were determined

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by the beam parameters of available ion sources. There are two ion sources used in the injector, a Penning source with a hot cathode suitable for ions from helium to neon and an electron cyclotron resonance (ECR) ion source for elements up to argon. Installation of an upgraded ECR ion source is underway, to provide the facility with even heavier ions, such as Fe. The two selected sources do not produce fully stripped ions, which is a requirement for acceleration in the HIMAC synchrotron; ions have to be first accelerated to an energy high enough to achieve an efficient stripping to bare nuclei. The first stage of acceleration is done in a radiofrequency quadrupole (RFQ) accelerator, designed to accept ions in a low charge state (relative charge to mass ratio $q/m > 1/7$); such a low value of the ratio q/m dictates that the RFQ has to be very long ($l = 7.3$ m) which complicates the design. The output energy of the RFQ is still not high enough to achieve a full stripping, and ions are fed into a 24 m long Alvarez type linear accelerator where their energy is raised to 6 MeV/u; this is sufficient to achieve a high fraction of bare nuclei when the beam passes through a thin carbon stripping foil. The size of the ring is primarily determined by the final, maximum ion energy and at HIMAC the circumference is 130 m. The focusing is strong, of the separated function type. The maximum dipole magnetic field is 1.5 T, with a rise time up to 2 T s^{-1} . Repetition rate can be varied between 0.3 and 1.5 Hz, with a flat top of up to 400 ms. For acceleration of heavier ions (Fe), the two rings could be operated in cascade.

The beam delivery system is standard, with two orthogonal wobbler dipole magnets to cover the required target field, a scatterer to achieve a smoother transverse dose distribution, a ridge filter to broaden the momentum spread and thus the Bragg peak, and a range shifter to change the beam energy. Although the synchrotron energy can in principle be varied on a pulse-to-pulse basis, the necessary instrumentation and controls have not yet been installed and the energy is varied by means of range shifters. The maximum field size is $15 \times 22 \text{ cm}^2$.

The Chiba facility is part of the national program to combat cancer, developed in 1984. The construction started in 1988, machines were commissioned in 1993 and clinical trials started the following year. The cost of the facility was high, more than 300 million dollars (M\$), with yearly operating costs of 45 M\$. The whole system operates well, reliably and reproducibly; at present, the most important improvement project deals with removing ripples and fluctuations in the extracted beam.

6.4. GSI facility

The use of light ions from the GSI synchrotron SIS in radiotherapy was considered at the time of the proposal for the machine itself, but its realization had to wait until early 1990's [18b,4h,20a,18d]. At that time, there was already some experience gained at LBL with its BEVALAC facility, showing better results in treatment of several tumors compared to conventional radiation. Although light ions, which are high-LET radiation, should have certain advantages with respect to low-LET protons, clinical results from LBL did not fully confirm that; as one possible explanation, it was suggested that the dose delivery system at LBL has permitted an essential part of this high-LET radiation to be deposited outside the tumor, thus limiting the dose to the tumor itself. The objective of the GSI program has been to develop the best possible conform dose delivery system and to test the effects of light ions under such conditions. The machine itself has not been designed

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with medical applications in mind, but for production of all ions up to uranium for nuclear physics studies. The ring is rather large, and the maximum energy reaches 2 GeV/u for particles with $q/m = 0.5$ or 1 GeV/u for uranium. The ion beam spill may be as long as 1 to 2 seconds. Recent upgrades had as the objective an increase of intensity to the space charge limit of the ring but the original light-ion intensity was already sufficient for tumor treatment. The linear accelerator UNILAC serves as the injector into the ring; this was a logical solution because UNILAC was already available and in operation.

Of the two basic approaches in the design of the beam delivery system, the active beam spreading method was selected. The other approach, a passive system, has the disadvantage of irradiating a substantial fraction of healthy tissues around the tumor with potentially lethal high-LET ions. In the passive system, the ratio of the doses to the tumor and surrounding tissues can be improved by a careful design of a number of beam shaping modules for each patient, depending on the shape of the tumor and energy of the beam for a particular slice of the target; this process is demanding and costly. A great deal of effort was devoted to studies of active systems at GSI. In principle, this is a simple system: the treatment volume is dissected into slices of equal thickness and each slice is irradiated separately by moving the beam across its cross-section. The shapes of consecutive slices will be quite different one from the other. Therefore, using the active beam delivery it should be possible to treat tumors of any shape. The control of beam energy to match the depth of a slice is done by modulating the accelerator and beam transfer line parameters.

To scan the beam laterally, across a slice, two different methods have been considered, raster and voxel scanning. In the raster scanning, the beam is moved continuously over the slice, and the writing speed is adjusted according to the required dose for the particular spot. In the voxel scanning, the beam stays at a spot long enough to deliver the required dose, then it is turned off and moved to the next spot. In the practical realization, there are no fundamental differences between the two methods and they both are capable of creating the proper dose distribution. While the motion of the beam across the slice is in principle a matter of controlling the elements of the beam transfer line to match the shape of the slice, it is much more complex to properly deliver the needed dose to each volume element. First, the beam with its energy adjusted to place the Bragg peak into the distal slice will deliver a dose, although lower, to all slices closer to the surface. The dose to be delivered to any subsequent slice has to take into account what has been previously deposited. Second, light ions are subject to fragmentation when passing through the matter and those lighter fragments may have a deeper penetration, delivering a certain dose beyond the Bragg peak, i.e. in the healthy tissue beyond the tumor (Fig. 6). Third, the relative radiobiological efficiency will be a very complex function of many parameters, such as particle energy, nuclear fragmentation, and properties of different tissues; it will have to be estimated in the best possible way to determine what dose to deliver to each volume element and then properly instruct the beam delivery system. The last problem remaining is to measure on-line the dose that has been delivered to a certain spot and then give the signal to move the beam; fast on-line ionization chambers are used for that purpose. On-line control of the dose distribution has an additional advantage: the system will be much less sensitive to ripple or fluctuations in the extracted beam intensity which was of primary concern for passive systems.

The extracted beam energy is changed by varying the parameters of the machine; a

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large number of fixed energy values have been selected and corresponding machine settings stored in a computer, to enable a pulse-to-pulse change of energies. The approach selected by the GSI is evidently the most advanced and should be capable of adjusting the delivered dose to the shape of the tumor with the minimum damage to the healthy tissues. In a few years, when the first results are known, it will be possible to compare not only the passive method as used at the HIMAC with the GSI active method, but also to determine whether a better dose delivery will prove expected advantages of light ions.

A few years ago, as an exercise, a medical synchrotron for light ions was designed at GSI. The maximum energy was 480 MeV/u, for all species up to neon; the intensity was chosen rather low, 10^8 neon ions per second, resulting in a smaller vacuum chamber. The size of the machine was also relatively small, about 50 m in circumference.

6.5. COSY facility

The cooler synchrotron and storage ring COSY, recently put into operation at Jülich, Germany, has also been considered for medical applications [20b,111]. Although primarily a proton machine intended for nuclear physics, it should be capable to accelerate light ions up to neon. At the maximum magnetic field, the energy of light ions would be similar to that of the HIMAC facility but substantial modifications of the injector would be required to expand the range from protons to light ions. There are several areas of studies covered by the proposed medical program, among them comparison of active and passive beam spreading systems, treatments with a fixed horizontal line vs. a rotating gantry, and as a long range objective, the comparison of protons and light ions. As this facility will remain primarily a nuclear physics center, the number of patients will be limited to about 100 per year if at some future time clinical trials begin.

6.6. TERA project

The TERA project is an ambitious study by a large collaboration of Italian institutions, universities and hospitals with the goal of establishing an Italian centre for hadrontherapy [1,21,11m]. The initial goal has been later broadened to form a whole network of facilities for hadron cancer treatment, called RITA. This network would consist of the oncological hadrontherapy center, linked with several centers devoted to proton therapy and with other hospitals. For the oncological center, the study concluded that the best option would be a synchrotron serving for acceleration of H^- and light ions. Protons within an energy range of 60 to 250 MeV would be generated at extraction, by stripping of accelerated H^- ions. The same ring could be upgraded in the future to accelerate fully stripped light ions up to oxygen, at energies between 120 and 400 MeV/u. When operating with H^- ions, the ion source will be followed by an RFQ with the output energy of 2 MeV; the beam will then be further accelerated in a linear accelerator up to an energy of 11 MeV and injected into the synchrotron. For light ions, the choice of the ion source is of crucial importance for the design of the injector itself. Two ion sources have been considered, a Penning ion source delivering high ion currents but in low charge states, and an ECR ion source with a lower yield but with higher charge states. The first injector design was based on a Penning source delivering O^{2+} ions; this would be followed by an RFQ to raise the energy to 250 keV/u. The final stage, a synchrotron, needs fully stripped ions for injection and low charge

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state oxygen ions have to be pre-accelerated to an energy high enough to achieve the full stripping. For the TERA project, the process of raising the charge state would proceed in two steps. After the initial acceleration in the linear accelerator to an energy of 850 keV/u, the optimum charge state after stripping is O^{6+} ; this will be followed by further acceleration to 3 MeV/u, sufficient for a good yield of fully stripped oxygen ions. This is a rather complex scheme and not very efficient because it requires a two-section linear accelerator, with one stripping foil inserted between the sections and one after the second section. Although the yield of the optimum charge state after the stripping foil is much lower than the beam intensity before the foil, it is expected that the synchrotron output would be sufficient to deliver the required dose to the patient. Both injectors, H^- for proton therapy and the light ion injector, would require about the same injection magnetic field which simplifies the operation. The design value of the maximum magnetic field needed for acceleration of fully stripped oxygen ions to an energy of 400 MeV/u is 1.4 T; for the maximum energy of H^- ions of 250 MeV the field is only 0.537 T which allows an efficient acceleration with very small losses due to stripping of H^- ions in the magnetic field. The proposed lattice is of the strong focusing, separated function type, with a circumference of about 60 m. The repetition rate is 2 Hz for H^- operation and 1 Hz for light ion operation; the flat top is 0.3 s.

The oncological center has been designed to have five treatment rooms, two with proton gantries capable of handling 250 MeV beams, one room with full energy horizontal and vertical proton beams, one room with two lower energy horizontal beams for treatment of eye, head and neck tumors, and one room devoted to future light ion therapy; there will also be an experimental room for protons and light ions. When fully in operation, about 1000 patients could be treated per year. At this stage of the project, both passive and active beam delivery systems are under consideration. It should be mentioned that as part of the TERA project, other options for proton acceleration have also been considered, such as a compact synchrotron and a compact high frequency linear accelerator.

6.7. Hyogo project

In addition to the HIMAC facility, which has been put into operation a few years ago, there is another proton/light ion facility under construction in Japan. This is the Heavy Ion Medical Accelerator Project by Hyogo Prefecture Government [7j], planned for initial operation in the year 2001. The facility will use protons, helium and carbon ions, with energies up to 230 MeV/u for protons and helium and up to 320 MeV/u for carbon. Beam intensities have been determined from the requirement for a dose rate of 5 Gy/min delivered to a target volume of 15 cm diameter and a fully extended spread-out Bragg peak. Ion beam energies will allow a penetration depth of 30 cm for protons and helium ions and 20 cm for carbon ions. The repetition rate of the synchrotron is 1 Hz for protons and 0.5 Hz for other ions, with a spill length of 0.4 s. There will be five beam lines, three for helium and carbon ions (one horizontal, one vertical and one 45° oblique line) and two proton lines with gantries. For the initial operation, a passive beam delivery system is envisaged.

6.8. Med-AUSTRON initiative

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The initiative Med-AUSTRON was established in 1995 with the objective to study the feasibility for a proton and ion cancer research center in Austria. Studies are ongoing, in collaboration with the TERA Foundation, CERN and GSI, and the results will be presented at a meeting scheduled for October 1997. Preliminary parameters of the ring are slightly different than in the original TERA proposal, although the machine is still designed for protons and light ions. The light ion species considered in this study is carbon (as presently used at Chiba and GSI facilities), with a maximum energy of 425 MeV/u. The ring has a larger circumference, 71 m, but this increase in size would add very little to the overall cost of the facility. In addition to the studies of slow beam extraction from the synchrotron, there are a number of related issues to be covered as well, such as beam stability during the spill and passive and active beam delivery options.

6.9. BNL booster

At Brookhaven National Laboratory, Upton, U.S.A., there is a 200 MeV H^- linear accelerator; it was recently proposed to use a small part of the beam for proton therapy but the plan was abandoned because of difficulties in scheduling the two applications, high energy physics and medical, without one interfering with the other [10]. Another accelerator, a booster synchrotron, was designed and constructed to serve as injector of any ion species (protons to uranium ions) into the Alternating Gradient Synchrotron (AGS). The maximum energy as well as beam intensities have been determined by the needs of the AGS ring, and further, of the Relativistic Heavy Ion Collider (RHIC), presently under construction, and are more than sufficient for any medical application. For light ions such as carbon or oxygen the AGS Booster is capable, using the existing tandem van de Graaff injector, to provide a sufficient beam intensity at any energy required for tumor treatment. Other ion species (nitrogen, neon) would need a new ion source and injector to replace the tandem. There is a proposal to utilize the Booster beam for radiobiological studies of interest to NASA with ions up to iron, but patient treatment has not been included in the proposal. By adding a new ion source and injector, it would be possible to extend the range of parameters of the Booster (ion species, energy, intensity) and change them on a pulse-to-pulse basis. The interference with the principal mode of operation of the Booster, which is acceleration of ions for injection into the AGS, would be minimal because AGS and RHIC will need the beam only part of the time.

7. A dedicated light ion facility for cancer treatment

7.1. Accelerator

The analysis of light ion beam parameters, required for tumor treatment, has shown that of the three types of accelerators considered in this report, it is only a synchrotron that is capable to deliver beams of different species, with an energy variable on a pulse-to-pulse basis and a duty factor of the extracted beam well matched to either the passive or active mode of beam delivery [4i,4j]. A cyclotron is a machine designed for a fixed energy and range shifters have to be used if lower energies are needed; this may result in a deterioration of beam properties, one of the most important characteristics of light ions. Conventional cyclotron designs, when extended to light ions, lead to very large and

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massive machines. Therefore, superconducting magnets have to be considered. Even this technology requires large units and a very sophisticated design which is not very suitable for a hospital environment. A linear accelerator for ion energies of interest in tumor therapy is a very long and expensive machine; although it is in principle possible to design a linear accelerator for handling different ion species and even to modulate its final energy, there are other disadvantages that preclude this option. On the other hand, a number of synchrotrons have been constructed so far, at an acceptable cost, for different purposes and a broad range of parameters (ion species, energy, duty factor, duration of the flat top). They perform well, reliably and with a good reproducibility and they are accelerators of choice for light ion tumor therapy.

The synchrotron lattice designs have been perfected to a high degree and at present it is possible to find a design close to the optimum for given beam parameters. The expertise for a proper design exists at many laboratories around the world, and industry may be willing to participate in the construction, in collaboration with one or more laboratories. Existing designs, such as TERA or Med-AUSTRON, can serve as the basis for any new light ion facility.

7.2. Ion sources

There is, however, one element of the accelerator with some room for improvement. This is the preceding stage, the injector. Several considerations require that only fully stripped ions be injected into the synchrotron. First, the acceleration efficiency depends on the charge state of ions, therefore the size of the machine, its cost and time for ions to reach the final energy will also depend on the charge state; this is why the injector into the synchrotron has to produce fully stripped ions (bare nuclei). The same rule applies to the injector itself: a higher charge state of ions produced in the source will result in a more efficient acceleration and a smaller, simpler and less costly injector. The design of the Chiba facility illustrates this point: the beam from the ion source is accelerated in a 7.3 m long RFQ, followed by a 24 m long linear accelerator, all in order to give partially stripped ions enough energy for an efficient full stripping at injection into the synchrotron. The second, also important consideration are losses of ions in collisions with molecules of the residual gas in the vacuum chamber; they will be lowest for fully stripped ions.

7.2.1. Low charge state ion sources

A typical representative of low charge state ion sources and also one still frequently used in accelerators, is the Penning or PIG (from Philips Ionization Gauge) ion source. It is very simple in principle, consisting of two cathodes placed at each end of a hollow, cylindrical anode; the electrode structure is immersed in a magnetic field. Electrons emitted from either cathode are accelerated by the cathode electric field into the hollow anode where they are trapped and forced to make many oscillations along the magnetic field lines before they are lost to the anode. Electrons with a sufficient energy will ionize particles in the source volume and a plasma will be created there. Penning sources are capable of producing copious ion currents of any element, but in a rather low ionization state and with a broad charge state distribution; the reason for the former is a relatively low cathode to anode voltage that the plasma in the source can sustain.

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The standard approach in the design of a high energy ion accelerator (such as for cancer treatment), based on a low charge state ion source, is to select a charge state with a sufficient intensity, then preaccelerate the ions to an intermediate level and pass them through a thin stripping target. At the exit of the stripper, charge states of ions will be higher than before but their spectrum will be broader; the price to pay is the fact that unwanted states will have to be rejected, resulting in a substantial loss of intensity. In some cases the process has to be repeated once more, by further acceleration and final stripping before injection into the synchrotron, as was proposed for the first TERA project. It is evident that this scheme, although based on a simple inexpensive ion source, could be more costly concerning the overall acceleration process itself.

7.3. *Intermediate charge state ion sources - ECR*

An electron cyclotron resonance (ECR) ion source is again a magnetic electron trap, where a plasma is created and maintained in a weak magnetic field. Ionization is performed by fast electrons in a step-by-step process, resulting in an increase of the average charge state of ions. Electrons are heated by high frequency electromagnetic waves introduced into the plasma; there is a region in the plasma where the wave frequency is in resonance with the magnetic field. ECR ion sources have been in a wide use for several decades, they are reliable and easy to operate, although much more expensive than, e.g., a Penning source. They are capable of producing intermediate charge states of many elements, up to uranium, but their performance with light ions is what is relevant for medical applications. The best yields of carbon or oxygen ions of modern ECR ion sources is in the helium-like state, with two electrons remaining, while for heavier ions, the optimum charge state is lower. Still, an ECR ion source for use in a medical accelerator would require just one stripping stage to produce bare nuclei, with the final yield not much different from a Penning source. This type of ion sources is being used or proposed as an alternative to Penning sources, e.g., at Chiba or in the TERA proposal. The work on improving ECR sources is going on at many laboratories, but it is doubtful that enough progress will be made to produce a high enough yield of fully stripped light ions in a foreseeable future.

7.4. *High charge state ion sources - EBIS*

An electron beam ion source (EBIS) is a device where electrons and ions are confined in a combination of electrostatic and magnetic fields. The magnetic field is solenoidal, serving to compress and confine a high-current-density electron beam. The negative space charge of electrons confines the ions radially while a system of coaxial electrodes confines them axially via properly selected potentials. The process of ionization is again step-by-step, in collisions between fast electrons in the beam and confined ions. An EBIS is in principle a pulsed device, where the process starts with the injection of neutral particles or very low charge state ions of the desired species. During the confinement time, which can be chosen at will, the charge state distribution of confined ions moves from lower to higher values; the final distribution depends on the electron beam current density and the confinement time. These two parameters can be easily adjusted so that the source is able to produce any ion species in any charge state (e.g., fully stripped uranium). For light ions up to neon, satisfactory yields of bare nuclei have already been achieved, while for

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heavier ions such as argon, yields are still too low. The comparison of performances of an ECR source with an EBIS is not straightforward: an ECR source is in principle a device delivering a certain current, while an EBIS delivers a certain positive charge depending on the electron beam parameters and size of the device. Thus the ion current from an EBIS will depend also on the selected value of the ion pulse length, which is adjustable within a certain range. The latter property of an EBIS makes this source very suitable for injection into a synchrotron because a very high current can be injected into the ring during a short interval. At present, the work on EBIS development is proceeding at several laboratories and within a few years, a simple, room-temperature device should become available delivering ion intensities needed for medical synchrotrons. The main advantage of an EBIS is its possibility of producing fully stripped ions, up to neon with a sufficient intensity, eliminating thus the need for any stripping before injection into the synchrotron and making the injector short, simple and less expensive. Any source of fully stripped light ions has to be extremely clean, to avoid any contamination of the extracted beam with ions of unwanted species having the same charge-to-mass ratio.

7.5. *Injector*

The simplest design of an injector results if the source can deliver fully stripped ions. At present, it is only an EBIS that is capable of delivering sufficient intensities of fully stripped ions, but should an ECR be developed in the future with the similar performance, the choice will be between these two types, with other characteristics deciding which one to use. In any case, the only accelerator stage between the source and the synchrotron ring will be just a short RFQ, with an energy high enough to accelerate and inject the required number of ions. Elimination of stripping foils will make the design simpler, more reliable and easier to operate.

7.6. *Beam delivery system*

The only beam delivery system presently in use on proton and light ion accelerators for tumor treatment is of the passive type. The active-type systems, with accelerator energy modulation and beam raster or voxel scanning, will be tested in the near future at the GSI facility. Although active systems seem to be more complex, once the required technology is developed (accelerator controls, beam intensity monitoring and controls, interface between the beam delivery system and patient) the most important element will be to determine the exact location, shape and properties of the tumor, as well as properties of tissues ahead of the tumor. The knowledge of the properties of healthy tissues is of crucial importance, not only because they will determine what will happen to the beam when passing toward the tumor, but because it will serve to estimate the dose delivered to healthy organs. However, the design of the accelerator should be such as to satisfy the requirements of either a passive or an active beam delivery system.

8. *Cost effectiveness of light-ion cancer therapy*

There are two issues to consider when estimating the cost effectiveness of light ion cancer therapy: costs of treatment of a patient as compared with other modalities having

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similar prospects for cure of cancer and costs of treatment of a patient for whom there are no other (or better) modalities for cure compared to costs of other life-saving procedures. While the first issue is the question of economics - how to find the most cost-effective treatment if several modalities with similar outcomes are available, the second issue borders with the question how to determine whose life should be saved.

One of the most thorough analyses of costs of a proton/light-ion facility has been done for the TERA project [21]; estimates are available for a few other projects as well [2,3,10]. The Phase I of the TERA project would be limited to production and use of protons only, while the addition of light ions up to oxygen has been considered as an upgrade. The total cost of the facility has been estimated at about \$M 50, with the light-ion upgrade adding about \$M 7.5; this includes management, installation and commissioning costs and 15% contingency. It is interesting to note that the accelerator itself contributes less than 20% to the total construction cost of the facility. To estimate the cost of the treatment per patient, several assumptions had to be made in the proposal; the first was about the number of patients that could be treated per year. After an initial period of two years, and operation in two shifts, about 1 000 patients could be treated per year (this number could be increased by adding more treatment rooms or by operating in three shifts which is a standard mode of operation at nuclear or high energy physics machines). Assuming a 25 year amortization and including the operating costs, the estimated cost per patient was about \$ 15 000 for proton therapy; light-ion therapy would be more expensive by about 20%. A somewhat lower estimate has been arrived at for a German project. If, instead, 1 500 patients are treated per year, the cost would be reduced correspondingly. There are two major proton therapy facilities in the United States, Loma Linda and Harvard Cyclotron Laboratory; their charges have been quoted in a wide range, from \$ 10 000 to \$ 60 000, depending on the number of sessions. At present, there are no light-ion facilities either existing or proposed to be built in the United States.

It is not easy to compare these costs with other modalities for cancer treatment, again because of a broad range of costs, from one country to another and depending on the extent of the disease. In Germany, the average cost of conventional radiotherapy amounts to about \$ 5 000, but the modern conformal radiation treatment would be more expensive; oncological surgery is more expensive, on the average about \$ 10 000, and chemotherapy even more, up to \$ 40 000. In USA, the structure of costs is different, so that e.g. an oncological surgery may easily cost \$ 25 000. From these data, it would follow that a proton therapy treatment is about twice as expensive as conventional radiotherapy, while the light-ion treatment may be up to three times more expensive. Average costs of proton therapy are comparable to oncological surgery, but lower than for chemotherapy. However, there are other factors to be taken into account, such as the length of the stay in the hospital (which in some cases is the major contribution to the total cost), overall treatment time, quality of life and socio-economic disruption of life, and acute and long-term morbidity. When all these factors are included, it may well be that a somewhat more expensive modality, such as radiotherapy with protons or even with light ions, would be preferable.

Finally, addressing the second issue, one should consider costs of other socially and economically acceptable treatments, such as bone marrow transplantation which may cost up to \$100 000, and heart transplantation which may cost up to \$ 140 000 for the surgery alone and further several hundred thousand for hospital and drug costs. The latter proce-

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ture, long term life-saving, is presently, in about 60% of cases, limited not by the costs of the treatment itself but by the number of available organs. However, this issue is beyond the scope of this report.

9. Conclusions

Light ions have several distinct characteristics that seem to offer a more promising treatment of some types of cancer than other types of radiation. Their physical selectivity in the dose delivery is very good, with lower scattering and enhanced energy deposition at the end of the track. Radiobiological properties, such as a reduced sensitivity to the phase in the cell cycle, a lower oxygen enhancement ratio and higher values of factors LET and RBE also seem attractive and advantageous for cancer treatment. Analyses performed for several projects have shown that there are a number of types of cancer where light ions may offer a much better or the only prospect for cure and, therefore, can not be considered to compete with established methods but to complement them. Still, the number of patients treated so far has been relatively very small and limited to just two facilities, Berkeley and Chiba. There are several reasons for the reluctance to introduce this new type of radiation as a modality in cancer treatment and we shall try to address them.

It is a fact that, except for the dedicated Chiba facility, all other accelerators capable of producing energetic light ions were built for a different purpose and with different characteristics than needed for the therapy. The range of their parameters (ion species, energy, intensity) is usually much broader and the construction and operating costs much higher than acceptable for medical applications; the facilities tend to be complex and not reliable enough. Because tumor treatment is not their primary purpose, the time available for radiobiological studies and trials is limited. The Chiba facility, once in full operation, will be able to supply the needed ion beams and in a few years valuable experience will be gained about the effectiveness and advantages of light ions. The new Hyogo facility should be in operation by the year 2001 and add more data to the statistics. With these two facilities, Japan has taken a leading role in exploring the merits of light ions. European efforts, although very important for the progress of the field, are concentrated on limited clinical studies at the GSI and on TERA Project and Med-AUSTRON initiative. If these efforts result in the construction of a dedicated light-ion facility in Europe, this will be again an important step in determining the feasibility of light-ion use in cancer treatment. In the United States, at present there is no ongoing effort, after the closing of the Bevalac facility. The only accelerator capable of producing light ions for cancer treatment is the Booster at Brookhaven National Laboratory, but presently there are no plans to use its beams in medicine, although it is likely to be used for radiobiological research.

Characteristics of light ions that make them attractive for cancer treatment, are also the reason that their application is much more critical and complex. Tumor diagnostics and beam delivery systems become very sophisticated, and so do the accelerator controls. However, after the initial investment into the development of the hardware and software of a prototype facility, the next generation should become simple enough to be operated in a hospital environment. Results from GSI studies in accelerator control and active beam delivery systems will be very important for further developments.

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Progress in the use of conventional types of radiation, including protons, has been substantial and the beam delivery has moved closer to the ideal, conform treatment. This has been mentioned as an argument against the introduction of new types of radiation in tumor treatment. However, light ions were never supposed to replace the methods which have already achieved excellent results but to try to treat those cases for which other modalities offer little or no hope. To prove or disprove the expectations, based on physical and radiobiological properties, it is necessary to broaden the studies and clinical trials to get better statistics.

Finally, there is the question of cost-effectiveness compared to other modalities. Again, it may be true that conventional radiation treatments are less costly than one with light ions, but here the argument is the same as before: if light ion treatment is a much better or the only modality available for certain tumor sites, then the cost should be of secondary importance, considering other more expensive, but life saving procedures.

To conclude, for such a universal medical problem as cancer, it is important to explore all avenues to accomplish a cure. Radiation with light ions offers a possibility to improve existing methods, but the number of patients is still far too small to reach the judgement about its benefits and advantages. In the present situation, one cannot expect that funds would become available to start construction of new facilities above those mentioned before. It is, therefore, important that the facilities already existing, including those built for other purpose, are utilized as much as possible for radiobiological studies and clinical trials of a limited number of tumor sites where other methods fail or are not very successful; an international cooperation will be indispensable to achieve the desired results.

Acknowledgements

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IONI I IONSKI UBRZIVAČI ZA LIJEČENJE RAKA

Upotreba iona visoke energije te mase do neona pruža značajne prednosti prema uobičajenim metodama zračenja u liječenju nekih vrsta raka. U ovom preglednom radu izlažu se radiobiološke značajke više vrsta zračenja (fotona, elektrona, protona i iona), s naglaskom na usporedbe učinaka brzih iona i drugih vrsta zračenja. Nadalje, utvrđuju se parametri ionskih snopova za liječenje raka, daje pregled dosadašnjeg rada u ionskoj terapiji i kliničkim ispitivanjima s protonima i brzim ionima, te opisuju sustavi koji su u upotrebi i koji se planiraju. Na kraju, na osnovi poznatih iskustava i budućih potreba, predlaže se najpovoljniji sustav ionskog ubrzivača za liječenje raka.

APPENDIX C

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Overview of Light-Ion Beam Therapy

William T. Chu

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Overview of Light-Ion Beam Therapy

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History of Hadron Therapy

In 1930, Ernest Orlando Lawrence at the University of California at Berkeley invented the cyclotron. One of his students, M. Stanley Livingston, constructed a 13-cm diameter model that had all the features of early cyclotrons, accelerating protons to 80 keV using less than 1 kV on a semi-circular accelerating electrode, now called the "dee."¹ Soon after, Lawrence constructed the first two-dee 27-Inch (69-cm) Cyclotron, which produced protons and deuterons of 4.8 MeV. In 1939, Lawrence constructed the 60-Inch (150-cm) Cyclotron, which accelerated deuterons to 19 MeV. Just before WWII, Lawrence designed a 184-inch cyclotron, but the war prevented the building of this machine. Immediately after the war ended, the Veksler-McMillan principle of phase stability was put forward, which enabled the transformation of conventional cyclotrons to successful synchrocyclotrons. When completed, the 184-Inch Synchrocyclotron produced 340-MeV protons. Following it, more modern synchrocyclotrons were built around the globe, and the synchrocyclotrons in Berkeley and Uppsala, together with the Harvard cyclotron, would perform pioneering work in treatment of human cancer using accelerated hadrons (protons and light ions).

When the 184-Inch Synchrocyclotron was built, Lawrence asked Robert Wilson, one of his former graduate students, to look into the shielding requirements for of the new accelerator. Wilson soon realized that the 184-Inch would produce a copious number of protons and other light ions that had enough energy to penetrate human body, and could be used for treatment of deep-seated diseases. Realizing the advantages of delivering a larger dose in the Bragg peak² when placed inside deep-seated tumors, he published in a medical journal a seminal paper on the rationale to use accelerated protons and light ions for treatment of human cancer.³ The precise dose localization provided by protons and light ions means lower doses to normal tissues adjacent to the treatment volume compared to those in conventional (photon) treatments.

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¹ E.O. Lawrence and M.S. Livingstone, Phys. Rev 37: 1707 (1931); and M.S. Livingston, "The Production of High-Velocity Hydrogen Ions Without the Use of High Voltages," PhD thesis, University of California, Berkeley (1931).

² W.H. Bragg and R. Kleeman, "On the ionization curves of radium." Philosophical Magazine, 8: 726-738 (1904).

³ R.R. Wilson, "Radiological use of fast protons," Radiol. 47, 487-491 (1946).

Wilson wrote his personal account of this pioneering work in 1997.⁴

In 1954 Cornelius Tobias and John Lawrence at the Radiation Laboratory (former E.O. Lawrence Berkeley National Laboratory) of the University of California, Berkeley performed the first therapeutic exposure of human patients to hadron (deuteron and helium ion) beams at the 184-Inch Synchrocyclotron.⁵ By 1984, or 30 years after the first proton treatment at Berkeley, programs of proton radiation treatments had opened at: University of Uppsala, Sweden, 1957⁶; the Massachusetts General Hospital-Harvard Cyclotron Laboratory (MGH/HCL), USA, 1961⁷; Dubna (1967), Moscow (1969) and St Petersburg (1975) in Russia⁸; Chiba (1979) and Tsukuba (1983) in Japan; and Villigen, Switzerland, 1984. These centers used the accelerators originally constructed for nuclear physics research. The experience at these centers has confirmed the efficacy of protons and light ions in increasing the tumor dose relative to normal tissue dose, with significant improvements in local control and patient survival for several tumor sites. M.R. Raju reviewed the early clinical studies.⁹

In 1990, the Loma Linda University Medical Center in California heralded in the age of *dedicated* medical accelerators when it commissioned its proton therapy facility with a 250-MeV synchrotron.¹⁰ Since then there has been a relatively rapid increase in the number of hospital-based proton treatment centers around the world, and by 2006 there are more than a dozen commercially-built facilities in use, five new facilities under construction, and more in planning stages.

Light-Ion Beam Therapy

In the 1950s larger synchrotrons were built in the GeV region at Brookhaven (3-GeV Cosmotron) and at Berkeley (6-GeV Bevatron), and today most of the world's largest accelerators are synchrotrons. With advances in accelerator design in the early 1970s, synchrotrons at Berkeley¹¹ and Princeton¹² accelerated ions with atomic numbers between 6 and 18, at energies that permitted the initiation of several biological studies.¹³ It is worth noting that when the Bevatron was converted to accelerate light ions, the main push came from biomedical users who wanted to use high-LET radiation for treating human cancer.

⁴ R.R. Wilson, "Foreword to the Second International Symposium on Hadrontherapy," in *Advances in Hadrontherapy*, (U. Amaldi, B. Larsson, and Y. Lemoigne, editors), Excerpta Medica, Elsevier, International Congress Series **1144**: ix-xiii (1997).

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Physical Characteristics of Light-Ion Beams

Bragg Peak and Spread-Out Bragg Peak

When energetic light ions enter an absorbing medium, they are slowed down by losing their kinetic energy mainly through ionizing the medium. The energy loss per unit mass for unit area of the absorber, or specific ionization (usually expressed in keV/ μm in water) increases with decreasing particle velocity, giving rise to a sharp maximum in ionization near the end of the range, known as the Bragg peak. When a beam of monoenergetic heavy charged particles enters the patient body, the depth-dose distribution is characterized by a relatively low dose in the entrance region (plateau) near the skin and a sharply elevated dose at the end of the range (Bragg peak), viz., Fig. 1(a). A pristine beam with a narrow Bragg peak makes it possible to irradiate a very small, localized region within the body with an entrance dose lower than that in the peak region.¹⁴ To treat an extended target, the Bragg peak is spread out to cover volume by modulating the energy of the particles to form a spread-out Bragg peak (SOBP), viz., Fig. 1(b).

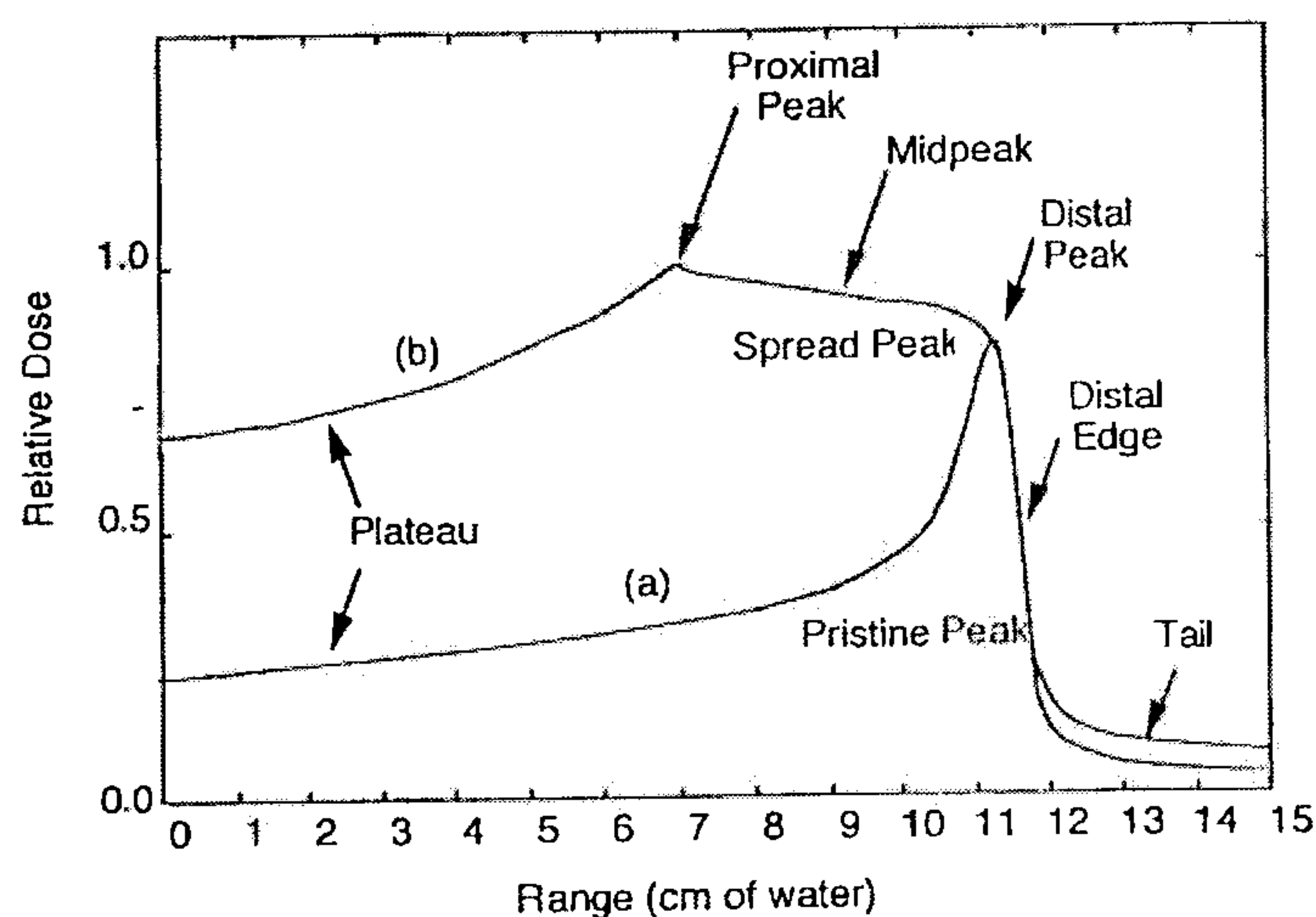


Fig. 1. (a) Bragg curve of an ion beam. (b) SOBP curve, which has several regions referred to as the plateau, the proximal peak, the midpeak, the distal peak regions, the distal dose-falloff edge, and the tail. A uniform biological dose distribution within the SOBP region is obtained by compensating for the variation in RBE of the radiation as a function of penetrating depth.

Examples of SOBP ionization curves, adjusted with RBE, of several ion beams are shown in Fig. 2. For the light-ion beams, the radiation dose abruptly decreases beyond the Bragg peak, sparing any critical organs and healthy tissues located downstream of the target volume from unwanted radiation. The entrance dose, the dose upstream of the target, is also low compared with the peak dose.

¹⁴ C. A. Tobias, H. O. Anger and J. H. Lawrence, Am. J. Roentgenol. 67: 1-27 (1952).

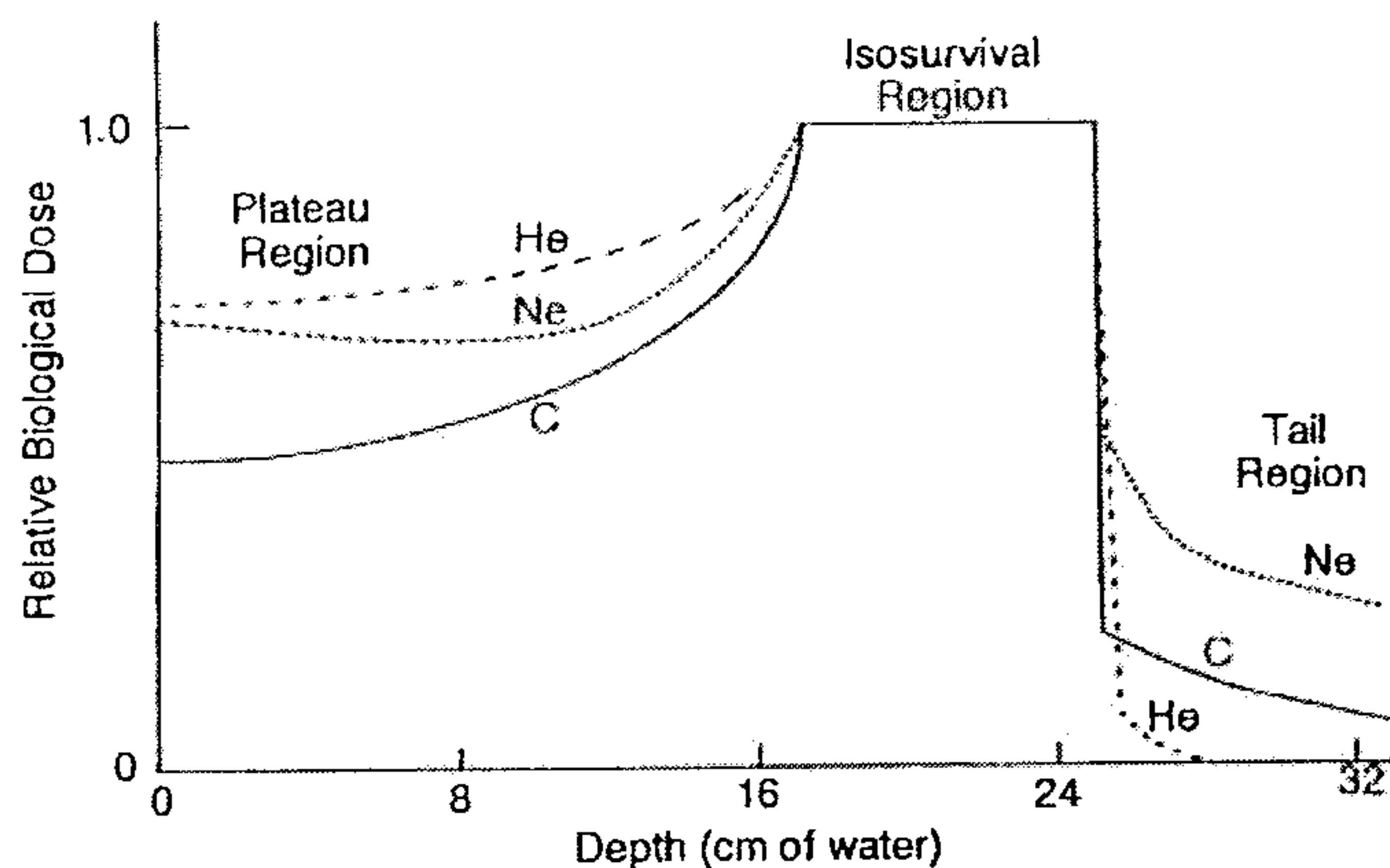


Fig. 2. The relative biological doses of SOBPs of helium, carbon, and neon ion beams as a function of penetrating depth in water are shown for comparison. The doses are normalized at the isosurvival region and the figure shows the different relative entrance, plateau, and tail doses for these beams.

Multiple Scattering and Range Straggling

Multiple scattering of an incident ion stems from the small angle deflection of it due to collisions with the nuclei of the traversed material. Numerous small angle deflections in an ion beam lead to lateral spreading of the incident ions away from the central trajectory resulting in larger divergence of the beam. Elastic Coulomb scattering dominates this process with a small strong-interaction scattering correction. The angular distribution of the scattered particles is roughly Gaussian for small deflection angles, and the mean beam deflection is approximately proportional to the penetration depth (Fig. 3(B))

Range straggling is the dispersion of the path length of a particle beam due to statistical fluctuations in the energy-loss process. The end result is to produce a smearing of the range of the stopping particle beam. For a particle traveling in a direction x , with energy E and mean range R , the distribution of ranges, $S(x)$, is Gaussian,¹⁵

$$S(x) = \frac{1}{\sqrt{2\pi}\sigma_x} e^{-(x-R)^2/2\sigma_x^2}$$

In the region where this formula is valid ($2 < R < 40$ cm), σ_x is almost proportional to range, R , and inversely proportional to the square root of the particle mass number, A .

Multiple scattering and range straggling effects for ion beams vary approximately inversely to the square-root of the mass of the particle. Interactions of several light ions penetrating absorbing material is characterized in Fig. 3, showing σ for range straggling (A) and mean beam deflections due to multiple scattering (B). Removing material from the beam line could minimize the range straggling and multiple scattering. For example magnetic deflection can eliminate the material needed to spread the beam in a scattering system, or changing the accelerator energy can eliminate material degraders used to change the energy of the beam.

¹⁵ H. W. Lewis, Phys. Rev. 85: 20 (1952).

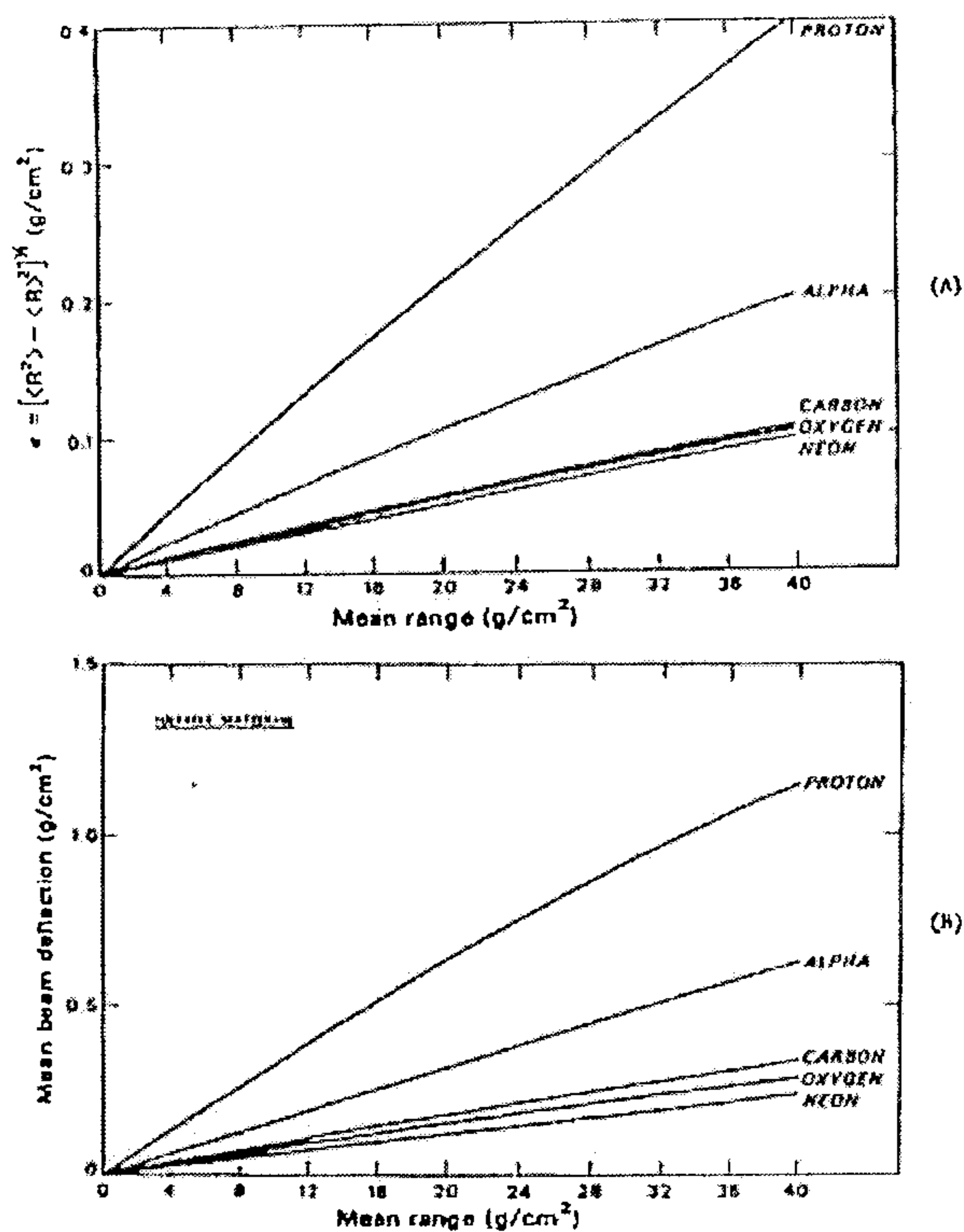


Fig. 3. Interactions of light ions penetrating absorbing material are characterized by σ for range straggling (A) and for multiple scattering (B). For example, the σ values for range straggling in 20-cm of water are: 2.0, 1.0, 0.6, and 0.5 mm for protons, helium, carbon, and neon ions, respectively.

The sharpness of the lateral dose falloff, often called the *apparent* penumbra, is of clinical importance because the radiation exposure of the normal tissues adjacent to the target volume often limits the therapy dose. Heavier ion beams exhibit sharper lateral dose falloffs at the field boundary than for the lighter ions: viz., Fig. 4 that compares the penumbrae of proton and carbon beams. The penumbra width increases essentially linearly with the penetration depth of the beam. For low-Z ions, such as protons, sharpest dose falloffs are obtained when the final collimator is at the surface of the patient. For higher-Z ion beams, such as carbon ion beams, scanning narrow pencil beams without collimations will produce narrow penumbrae.

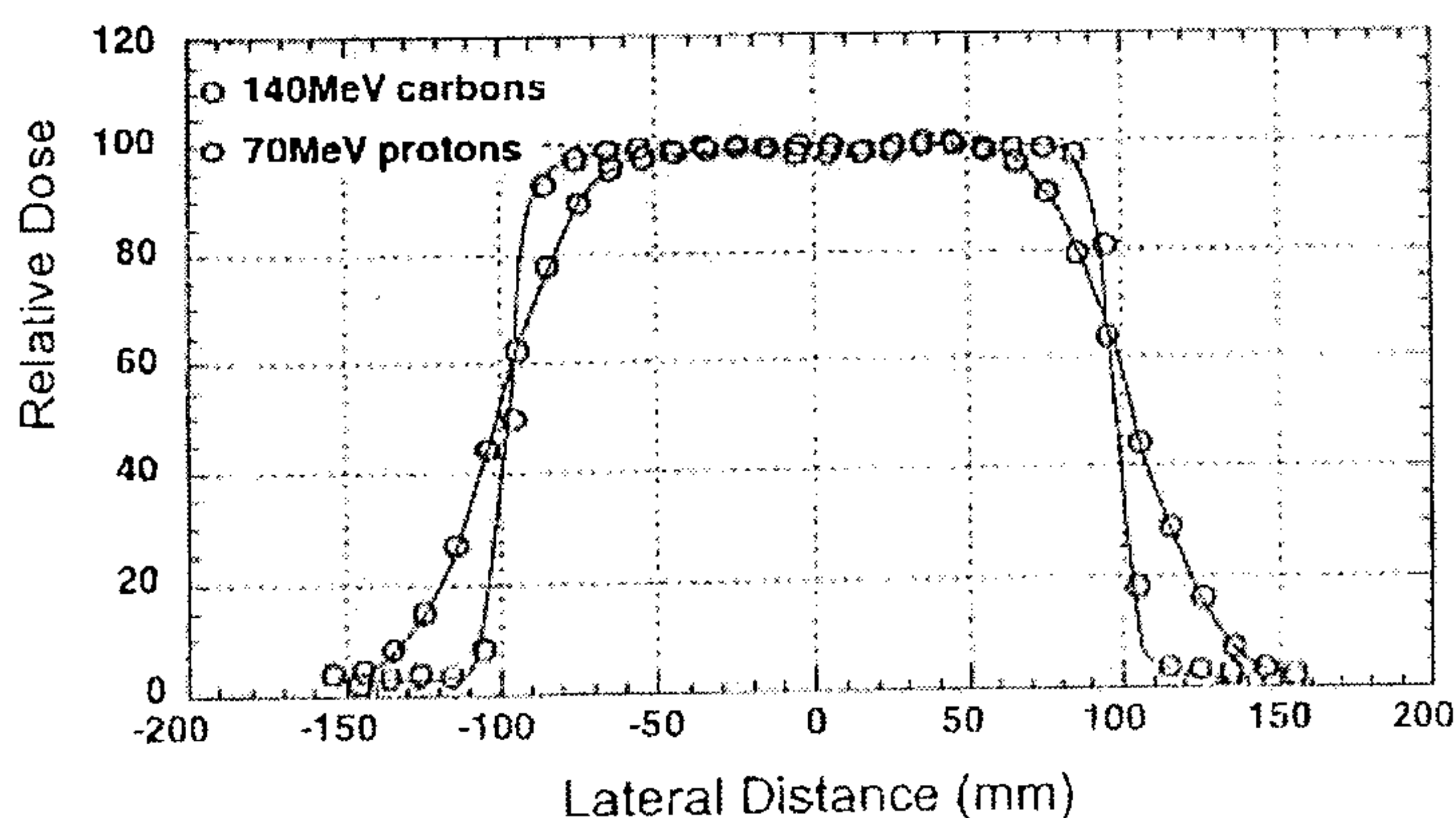


Fig. 4. The penumbra of a carbon beam is much sharper than that of a proton beam of the comparable range. (Based on the paper presented by H. Tsuji, at the 39th meeting of PTCOG, San Francisco, October 2002.)

The effect of multiple scattering becomes more pronounced for small size beams as indicated in Fig. 5, which examines depth-dose curves of proton and carbon-ion beams of comparable range for an uncollimated beam and a 1-cm diameter collimated beam. The Bragg peaks appear almost unchanged for the two carbon-ion beams; whereas, the Bragg peak is much suppressed for the collimated proton beam (Fig. 5(a)). Lateral dose distributions of the collimated 1-cm diameter proton beam exhibits broader penumbra, especially at the end of its range and wider range straggling. The collimated carbon-ion beam shows much smaller beam scattering and straggling. For treating small targets, where the sharpness of the lateral dose falloff is essential, the choice of the heavier ion beam becomes important.¹⁶

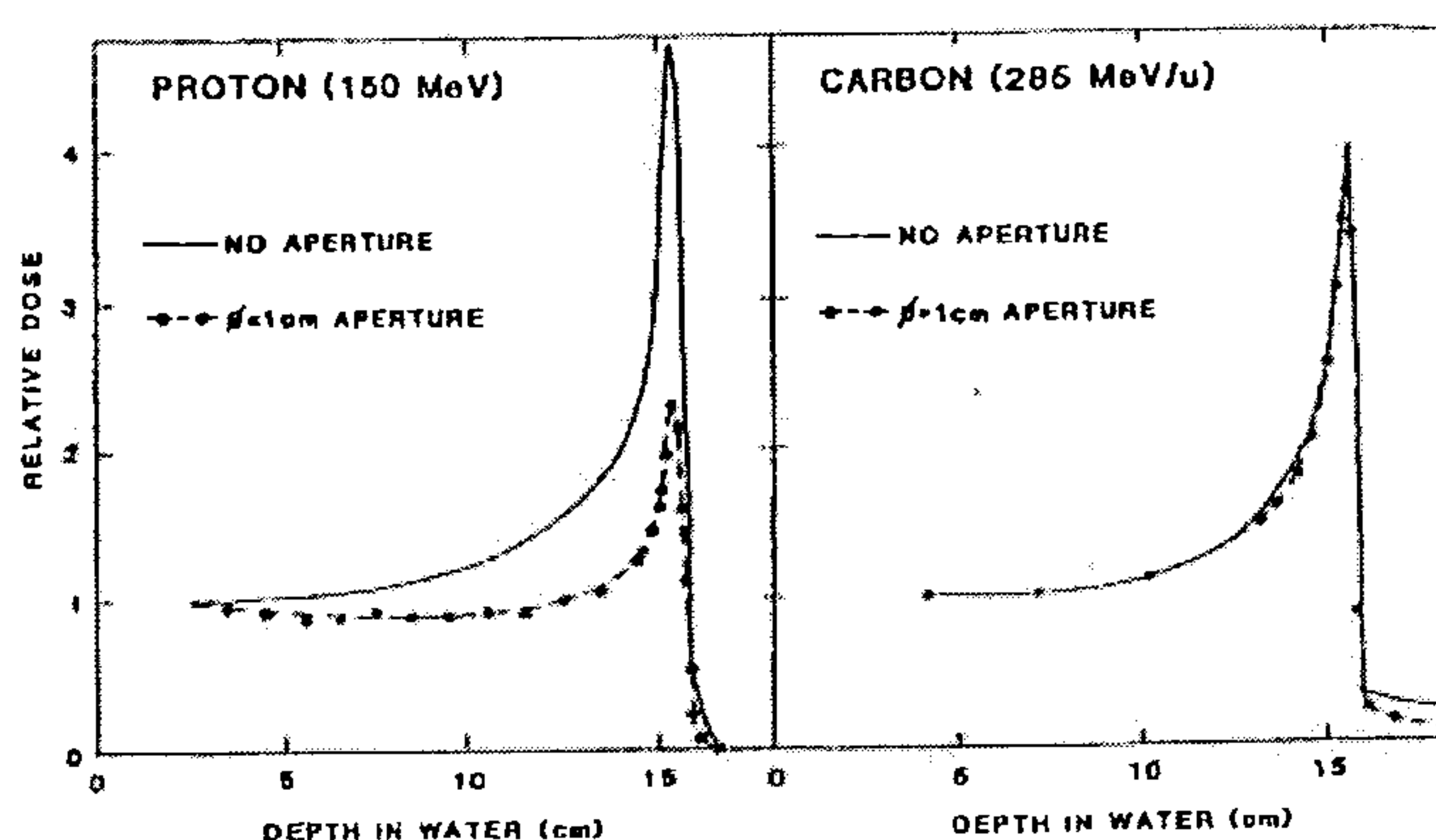


Fig. 5(a). Depth-dose curves of proton and carbon-ion beams of comparable range are compared. For each ion, uncollimated and collimated 1-cm diameter beams are examined. Bragg peaks appear almost unchanged for the two carbon-ion beams; whereas, the Bragg peak is much suppressed for the collimated proton beam.

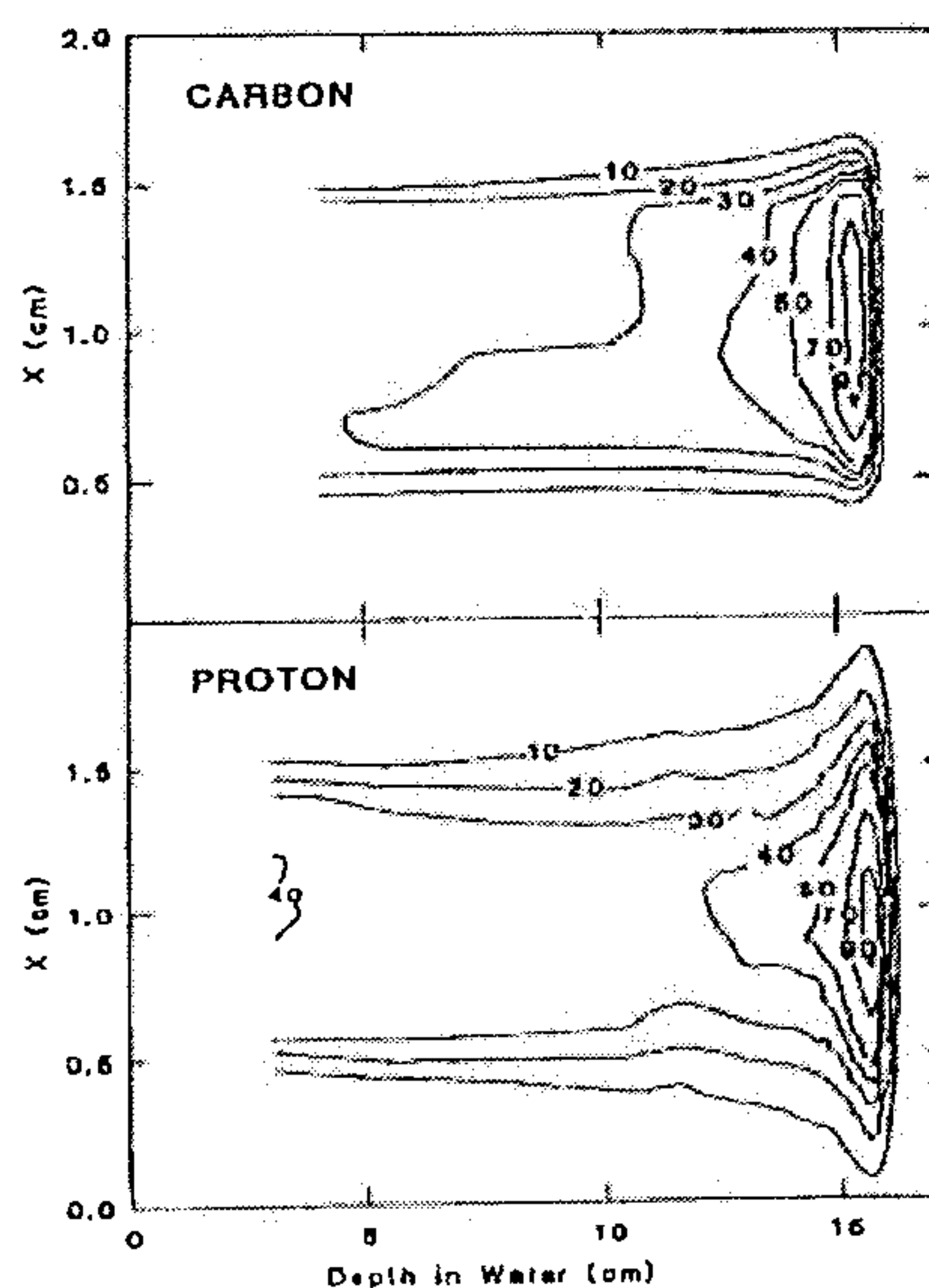


Fig. 5(b). Dose distributions in the plane that includes the central ray of proton and carbon-ion beams are shown. Both beams are collimated to a 1-cm diameter.

¹⁶ M.H. Phillips, K.A. Frankel, J.T. Lyman, J.I. Fabrikant and R.P. Levy, *Int. J. Radiat. Oncol. Biol. Phys.* 8: 211-220 (1990).

Beam Fragmentation

As a particle beam penetrates through matter, the primary particles suffer fragmentation collisions, which decrease the number of primaries with the corresponding increase of lighter fragments along the penetration path.¹⁷ Fragmentation refers to the process where the projectile nucleus, after suffering a nuclear collision with a target nucleus, is broken apart into several daughter particles. The remnants of the projectile nucleus emerge from the absorbing material with similar speeds as that of the original projectile nucleus. The target nucleus may also break apart, but these fragments have relatively low energy and do not travel with the beam.

Fig. 6 shows the measured fragment number and dose contribution as a function of the particle charge for a neon-ion beam after traversing 16 cm of water. The measurement was made with BERKLET. The instrument consists of a 300- μm thick Si detector and a 5.5-cm thick Ge detector, which when operated in coincidence, measures the dE/dx and the total energy of the particle, respectively.¹⁸

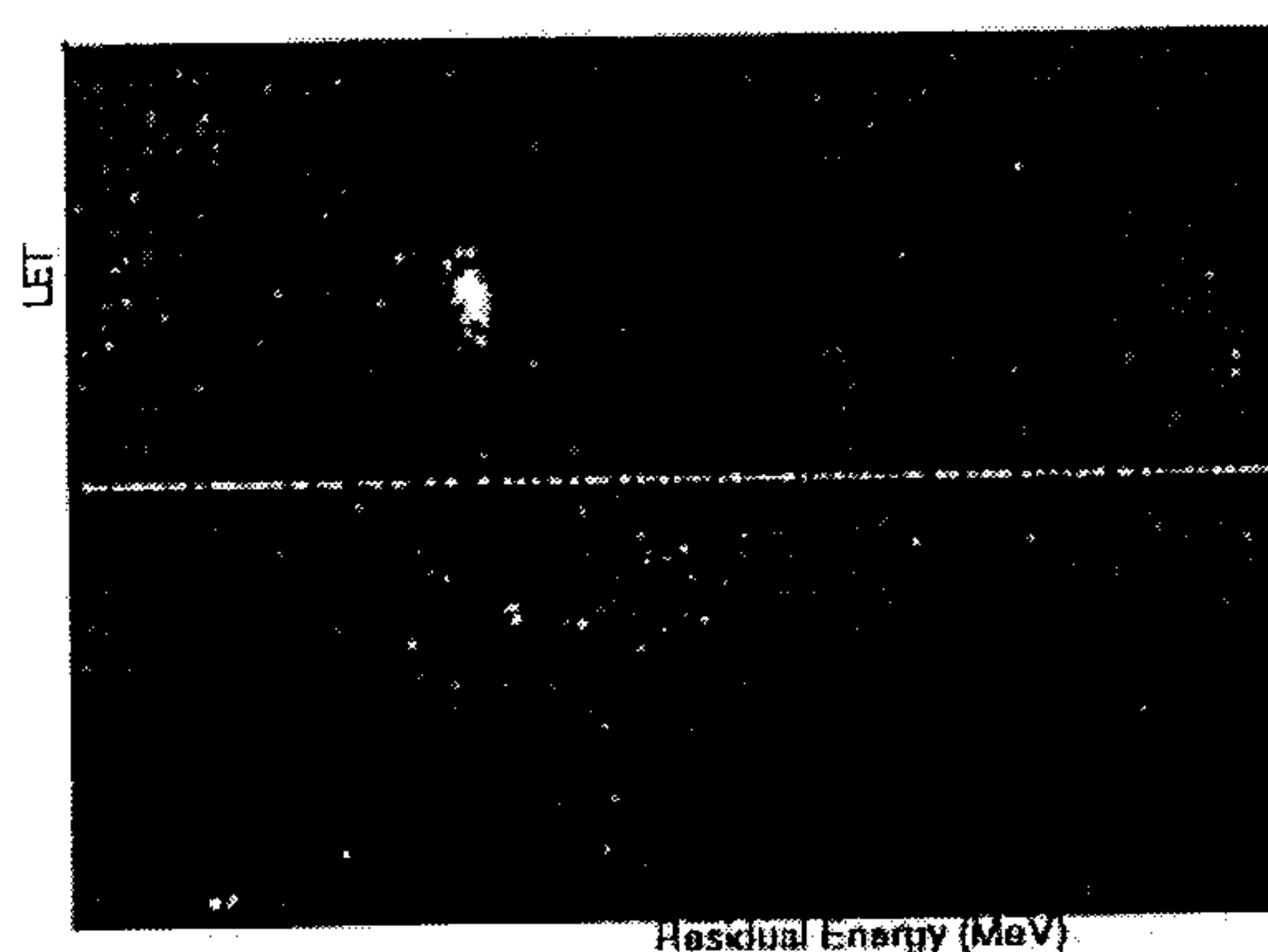


Fig. 6(a). Scatter plot of fragments on the residual energy versus LET (or dE/dx). The brightest spot is the primary beam particles. The bands are particles of a given charge. (CBB 875-4105)

¹⁷ A.S. Goldhaber and H.H. Heckman, *Ann. Rev. Nucl. Part. Sci.* **28**: 161-205 (1978).

¹⁸ J. Llacer, J.B. Schmidt and C.A. Tobias, *Med. Phys.* **17**: 158-162 (1990); and J. Llacer and H.W. Kraner, *Nucl. Instrum. and Methods* **98**: 467-475 (1972).

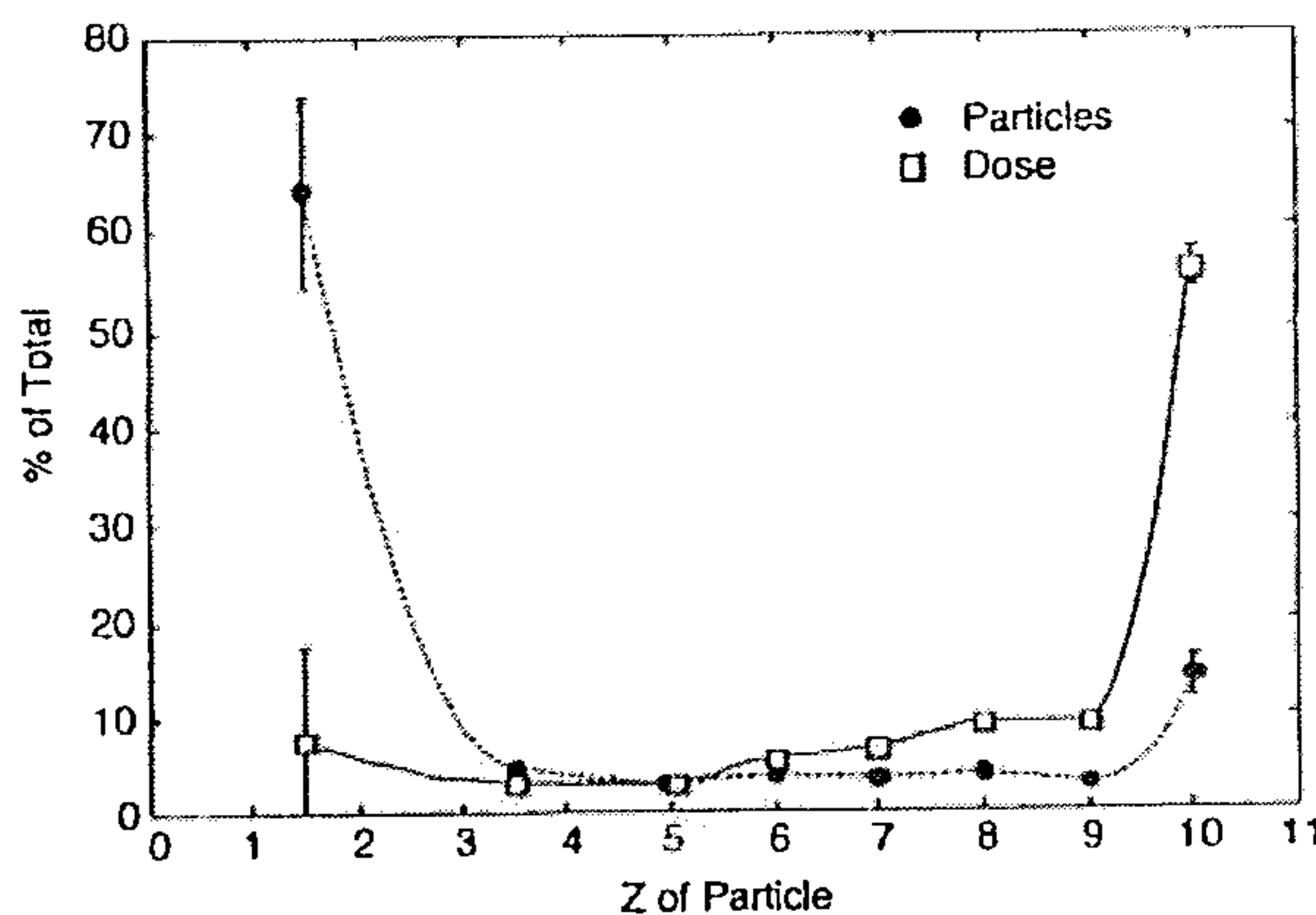


Fig. 6(b). Two sets of data show contributions of different atomic charges to the total particle number and the total dose delivered. Fragments are from neon ions in the proximal peak region of a 12-cm spread out Bragg peak with a residual range of 28 cm in water. It corresponds to the beam traversing 16 cm of water. The data for low Z values (1-2 and 3-4) are lumped together.

For protons colliding with a water-like target material (e.g., soft tissue), knocked-out neutrons from the target nuclei are the dominant interaction products. These neutrons contribute to the dose delivered beyond the stopping region of the primary projectile. Light ions also produce such a neutron background. Even after accounting for the higher RBE of the neutrons produced, they contribute less than 0.5 % of the biological dose delivered to the patient.¹⁹ Their contribution would be larger in cases where the range of the beam is severely degraded upstream of the patient, such as by a double scattering method, then whole body exposure could become an issue.

As discussed above, carbon and neon ions fragment into a larger number of nuclear species. These fragments lead to a significant dose beyond the actual stopping range of the primary particles, and contribute significantly to the dose within the spread-out Bragg peak. In general, the heavier the nuclear projectile, the larger the dose delivered in the region beyond the Bragg peak when normalized to the dose delivered by primary ions at the proximal peak of the SOBP.

An additional complication is that a fragmented beam has a radiobiological effect different from that of the primary beam. The LET distribution of the fragmented beam becomes quite complex as more of the primary beam fragments²⁰; hence, RBE, which is a function of the LET of the beam, is a function of the depth of the material penetrated. For SOBP, the composition of the beam and its biological effect is also a function of depth and must be accounted by adjusting the physical depth-dose distribution to obtain a uniform biological dose distribution.

Biological Rationale for Clinical Use of Light Ions

By the late 1980s, radiobiological research with light-ion beams, essential concomitant to a successful and safe clinical research program, had three major aspects. First was determining the optimal strategies for tumor treatment by analysis of the biological responses of tumor tissue to different ions, delivered at various doses and at various intervals. Second, determining tolerance doses and the risks of carcinogenesis and cell transformation for normal tissues. Thirdly, fundamental radiobiological understanding and characterizing physical phenomena

¹⁹ J.B. McCaslin, P.R. LaPlant, A.R. Smith, W.P. Swanson and R.H. Thomas, IEEE Trans. Nucl. Sci. NS-32: 3104-3106 (1985).

²⁰ J. Llacer, C.A. Tobias, W.R. Holley and T. Kanai, Med. Phys. 11: 266-278 (1984).

such as ion fragmentation and biological effects such as DNA damage and repair. Knowledge gained from basic research influenced the choices of ion, energy, beam delivery system, and treatment schedule. At the same time, the emerging picture of the processes by which radiation causes genetic damage, and by which the DNA attempts to recover from the insult, enhanced our understanding of the risks posed by radiation exposure in general, including exposure associated with radiation accidents and space exploration, as well as radiotherapy.

These early studies are sometimes called "classical" cellular radiobiology to distinguish it from "new" molecular radiobiology that was developed in more recent years.²¹ We will describe here some of the significant results that have emerged from early radiobiological research at Berkeley, especially as they relate to then ongoing cancer therapy trials.

LET, OER and RBE

The higher relative biological effectiveness (RBE) values of higher-Z ion beams indicated a high likelihood of an enhanced therapeutic potential when compared with lower-Z particle beams, such as protons.²² The RBE of each ion has been studied in some detail with a variety of biological endpoints showed that the RBE of an ion beam is not a simple function of LET even though LET is usually used to describe of the differences in radiation damage by various light ions (Fig. 7(a)).²³ RBE also depends on the endpoint of measurements, such as the survival level, the kinds of ions and types of cells and tissues used in the experiments (Fig. 7(b)). In general, the values of RBE and the degrees of dose localization increases with the Z values from protons to silicon ions, and at LET values higher than approximately 200 keV/ μ m, the RBE values decline.

Another important point is that the failures in local control of tumors treated with low-LET radiation (conventional and proton radiation) are often due to its inability to completely eradicate anoxic tumor cells which are resistant to such radiation. High-LET radiation exhibits the biological advantages of lower oxygen effect (lower OER values), as indicated in Fig. 8. The OER value is defined as the ratio of the dose needed to render the same end-point for anoxic cells to that for well-oxygenated cells.

²¹ J. Yarnold, "Molecular and cellular responses to radiotherapy," in *Advances in Hadrontherapy*, (U. Amaldi, B. Larsson, and Y. Lemoigne, editors), Excerpta Medica, Elsevier, International Congress Series 1144: 3-11 (1997).

²² *PART III. "Particles and Radiation Therapy, Third International Conference,"* Int. J. Radiat. Oncol. Biol. Phys., 8 (1982).

²³ E. A. Blakely, F. Q. H. Ngo, S. B. Curtis and C. A. Tobias, *Adv. Radiat. Biol.* 11: 295- 389 (1984).

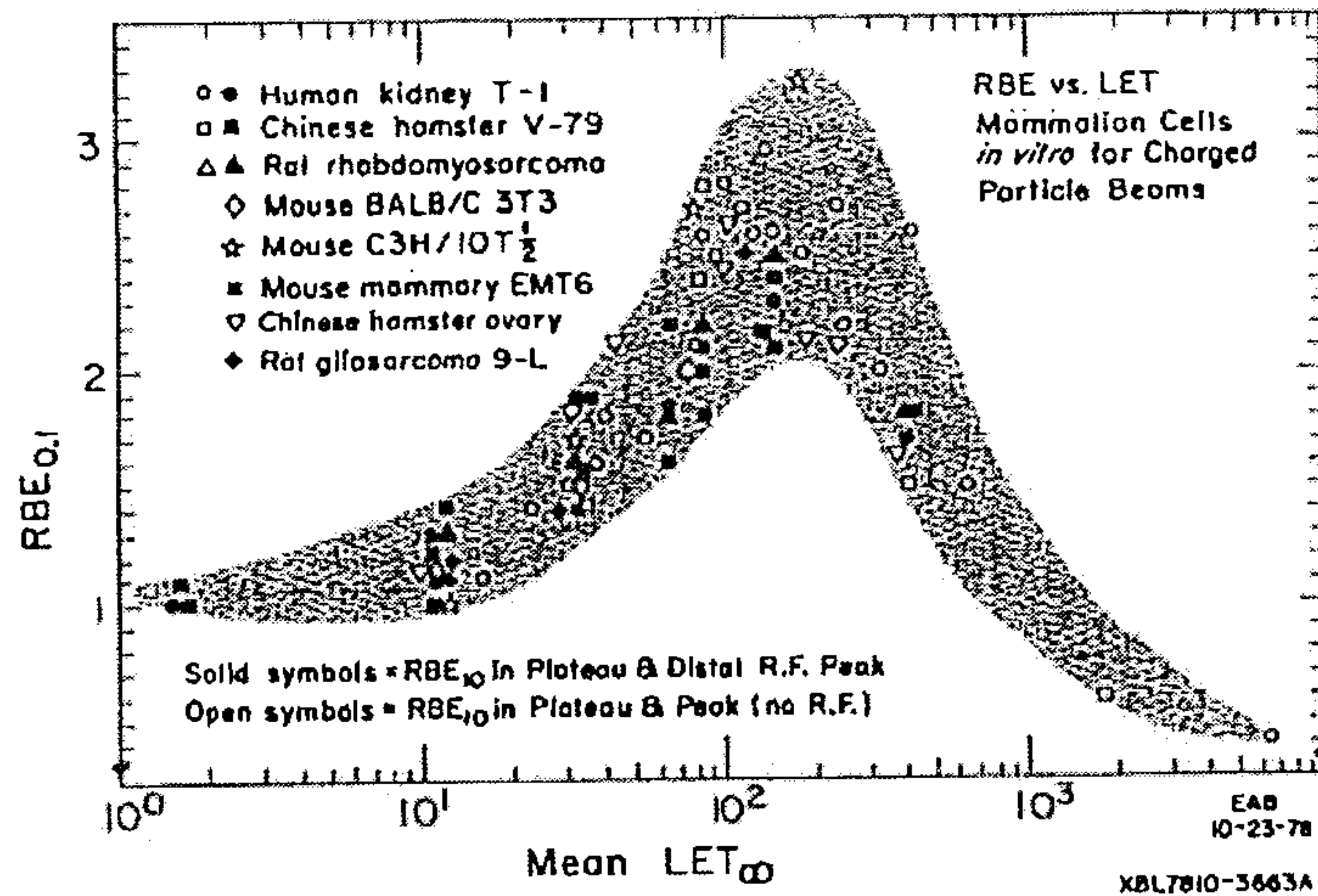


Fig. 7(a). RBE vs. LET. The data is from a number of experiments using a number of ions, energies and cell types. The shaded area shows the general trend of the data.

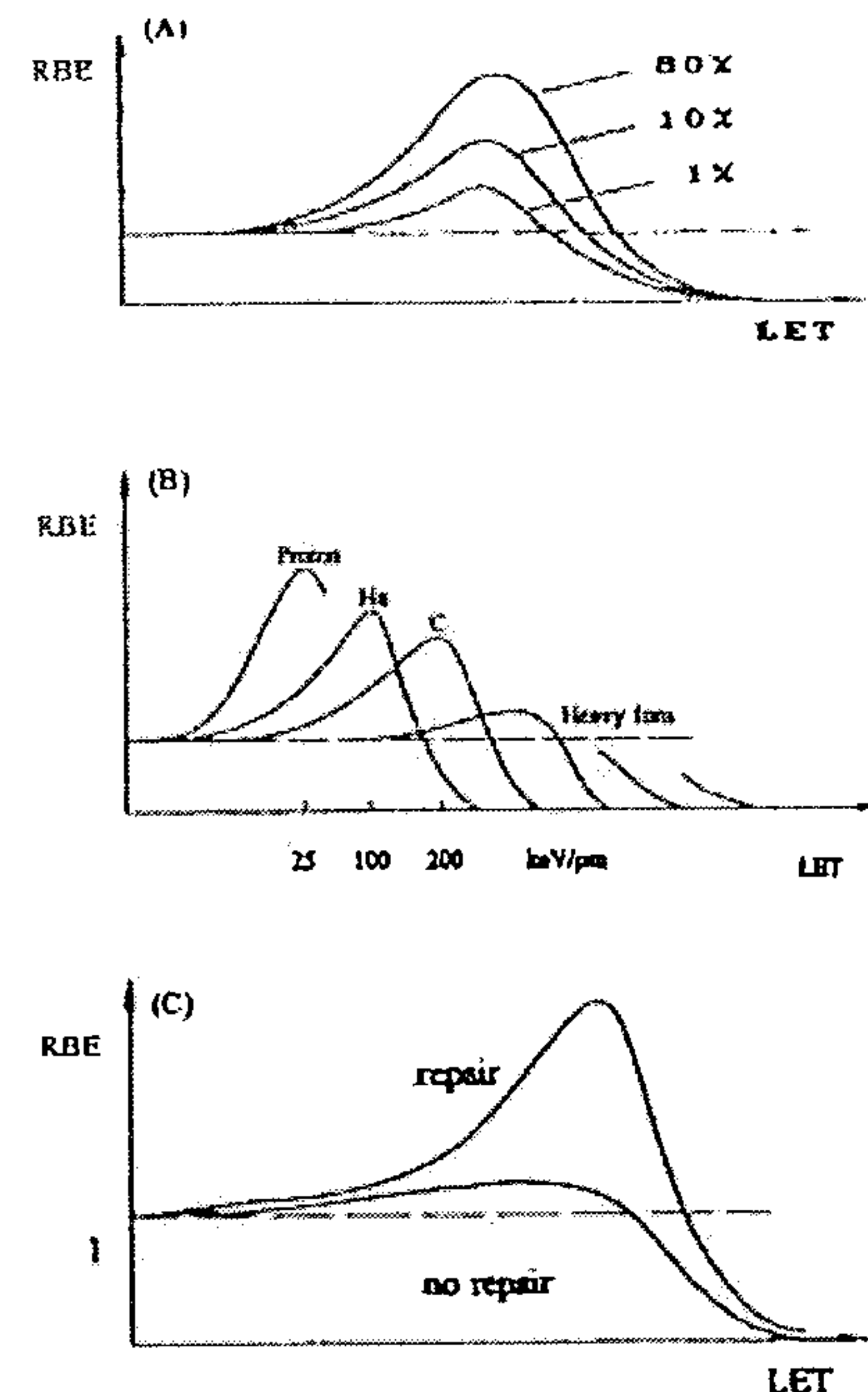


Fig. 7(b). The relationship between RBE vs. LET is a function of (A) the endpoint of measurements, e.g., survival, (B) kinds of ions, and (C) type of cells or tissues.

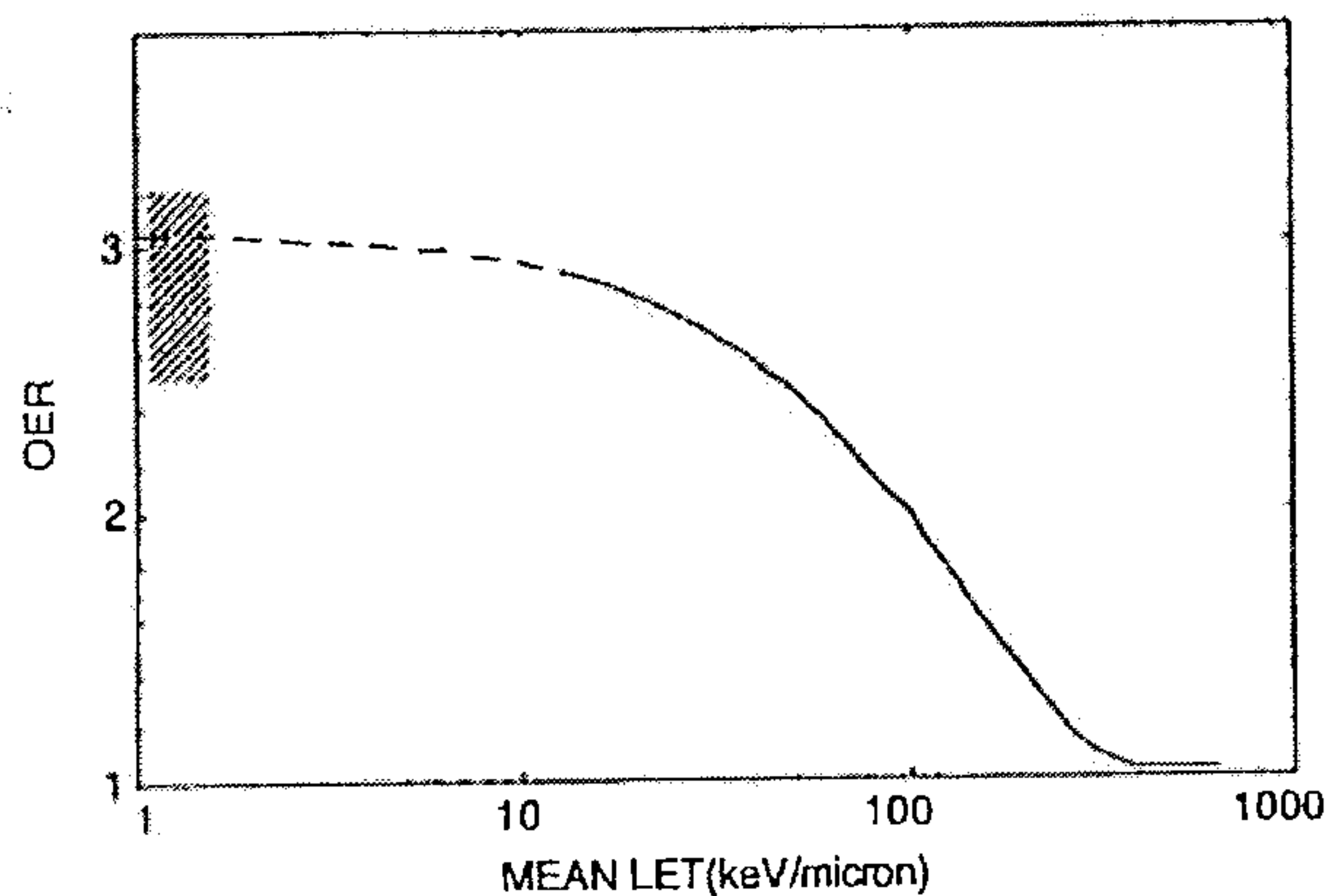


Fig. 8(a). OER vs. LET. The shaded area represents the measured OER for x rays. The curve is a generalized fit to data using various ions and energies.

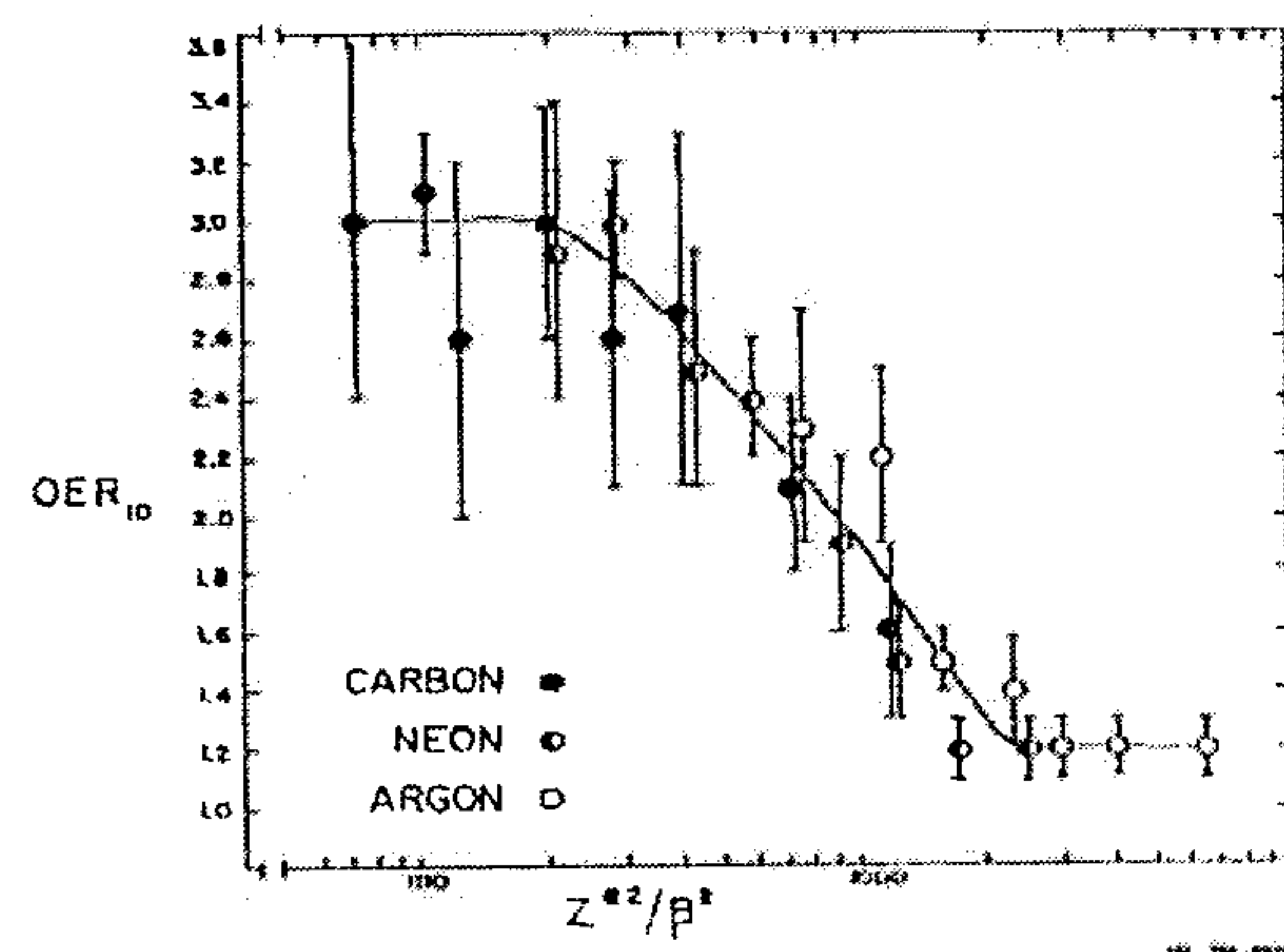


Fig. 8(b). Measured data of OER vs. Z^2/β^2 for carbon, neon and argon ion beams.

In 1967, Tobias and Todd gave the scientific justification for utilizing light-ion beams combining the characteristics of light-ion beams in LET, RBE and OER.²⁴ In 1980 LBNL published a report compiling the results of research in physics, biology and medicine about light-ion therapy.²⁵ The conjecture was that, referring to Fig. 9, the most advantageous species of ions for cancer treatment are located at higher values of "oxygen gain factor," which is a parameter proportional to the inverse of OER, and at the same time at higher values of RBE. For the smaller and shallower targets (upper panel), it appeared that carbon and neon-ion beams are superior to other ions. For larger and deeper targets (lower panel), the relative placement of each of the therapy modalities is altered, and proton, helium and carbon-ion beams are quite similar.

One has to carefully interpret the meanings of Fig. 9 under other clinical considerations. Simple mindedly, we may take RBE not crucial on the assumption that the low RBE may be readily compensated with higher physical doses; whereas, the oxygen gain factor is biologically important factor that is intrinsic properties of the ion species. However, the gain in oxygen effect must be weighed against the increased mutagenesis and carcinogenesis of the higher-Z ions. It was generally agreed that ions of atomic numbers between carbon and silicon are the most interesting high-LET ions for clinical use.^{26,27} Today, carbon ion beams are chosen for therapy as the carbon ion has both biological and dose localization advantages superior to those of lighter ions such as protons, yet avoids some complications with higher-Z ions. For carbon ion beams, enough high LET is present to provide significant differences in DNA damage, and suppression of radiation repair. The use of heavier ions such as neon and silicon leads to complexity in treatment planning because of the high LET in the entrance region and the fragment tail. Normal tissues in these regions need to be carefully assessed and treatment plans designed which avoid significant late effects, especially in CNS.

The radiobiological rationale for using these high-Z ions for therapy,^{28,29} as understood then, can be summarized as follows: (a) The high resistance of hypoxic cells relative to oxic cells is reduced when irradiated with high-LET radiation. (b) Slowly proliferating cells (in G₀ or long G₁ phase in cell cycle) show a similar increase in sensitivity, if irradiated with high-LET radiation. (c) Overall treatment time with high-LET radiation can be shortened since fewer fractions of larger doses may be used instead of multiple fractions of small doses when the surrounding normal tissue damage in a fewer fraction can be kept comparable to that of a standard low-LET fraction. The last point squarely contrasts against the rationale that there is an

²⁴ C. A. Tobias and P. W. Todd, Radiobiology and Radiotherapy, Natl. Cancer Inst. Monogr. 24: 1-21 (1967).

²⁵ "Biological and Medical Research with Accelerated Heavy Ions at the Bevalac, 1977-1980," (M.C. Pirruccello and C.A. Tobias, eds.), Lawrence Berkeley Laboratory, LBL-11220, pp. 423 (1980).

²⁶ E.A. Blakely, C.A. Tobias, B.A. Ludewigt, and W.T. Chu, "Some Physical and Biological Properties of Light Ions," *Proc. of the Fifth PTCOG Meeting and the International Workshop on Biomedical Accelerators, December 1986* (ed. by W. T. Chu), Lawrence Berkeley Laboratory, Berkeley, CA, LBL-22962, 19-41 (1987).

²⁷ P.K. Lillis-Hearne, J.R. Castro, "Indications for Heavy Ions- Lessons from Berkeley," in *Ion Beams in Tumour Therapy* (V. Linz, ed.), Chapman & Hall, 133-141 (1995).

²⁸ J.F. Fowler, *Nuclear Particles in Cancer Treatment*, Medical Physics Handbook, No. 8, Adam Higler Press, Bristol, England (1981).

²⁹ E. J. Hall, *Int. J. Radiat. Oncol. Biol. Phys.* 8: 2137-2140 (1982).

advantage in using multiple, small fractions of low-LET radiation for sparing late damage.³⁰ Cutting down the number of ion-beam treatments would benefit individual patients as well as the management of the clinic.

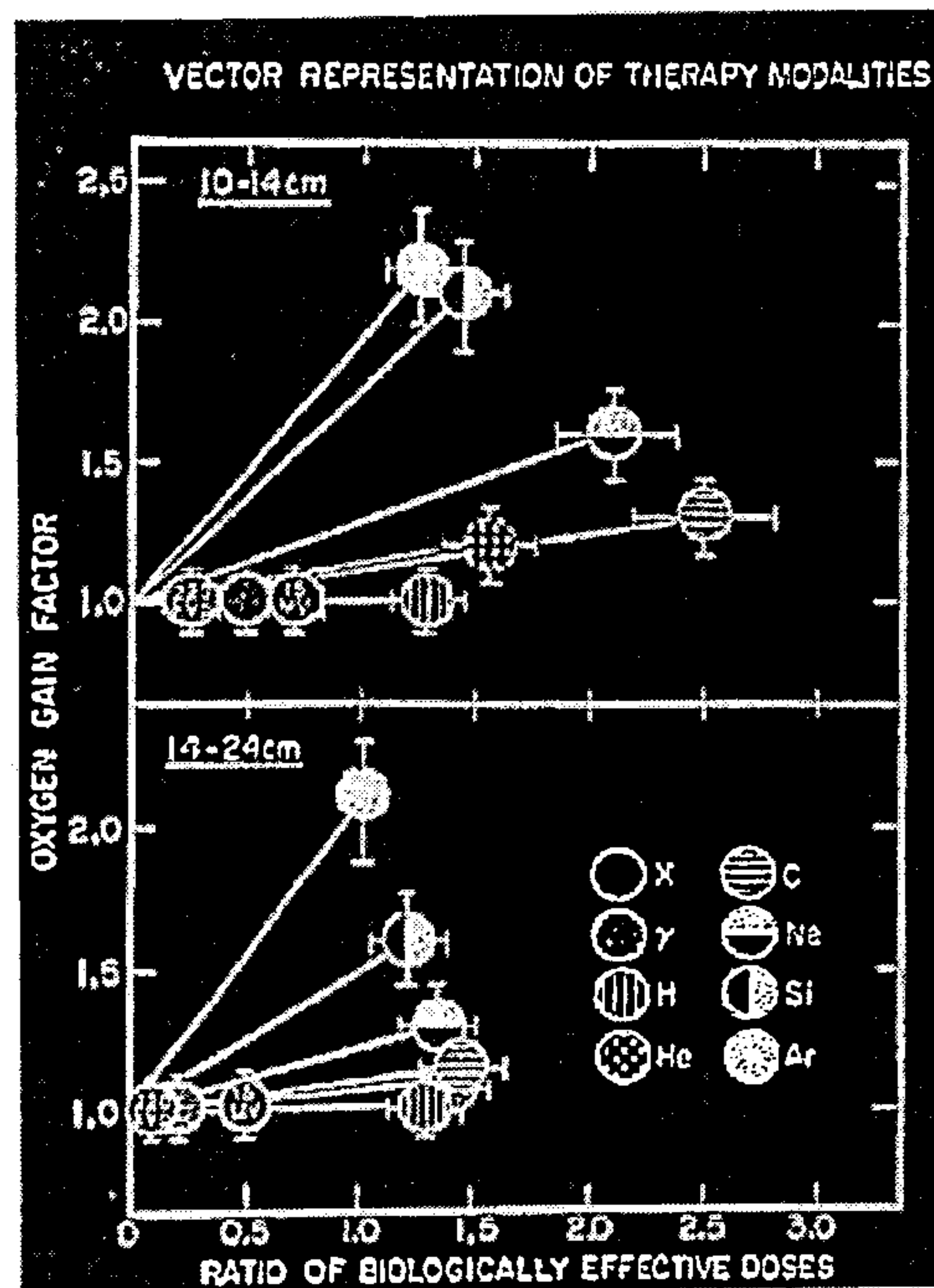


Fig. 9. "Vector representation" of therapy modalities for treatment of: small shallow targets (upper panel) and large deep targets (lower panel). The "oxygen gain factor" is a parameter proportional to the inverse of OER, and the "ratio of biologically effective doses" represent RBEs of the ions in question. (XBL 808-36238)

Physical Parameters of Clinical Beams

Protocols for heavy charged-particle beam dosimetry have been established by the American Association of Physicists in Medicine for protons and heavier ions.³¹ They describe the methods of calculating the dose based on measurements using various dosimeters. Discussions of these methods are reviewed in other publications.³²

RBE and LET Distributions

The main function of the treatment planning and delivery is to create a radiation field that produces uniform cell killing or a uniform biological response. Changes in the primary

³⁰ H.D. Suit, M. Goitein, J.E. Munzenrider, L. Verhey, P. Blitzer, E. Gragoudas, A.M. Koehler, M. Urie, R. Gentry, W. Shipley, M. Urano, J. Duttenhaver and M. Wagner, *Int. J. Radiat. Oncol. Biol. Phys.* 8: 2199-2205 (1982).

³¹ *American Association of Physicists in Medicine, Protocols for Heavy Charged Particle Beam Dosimetry, A Report of Task Group 20, Radiation Therapy Committee, American Institute of Physics, New York, AAPM Report No. 16 (1986).*

³² J. J. Broerse, J. T. Lyman and J. Zoetelief, "Dosimetry of External Beams of Nuclear Particles," in *The Dosimetry of Ionizing Radiation* (ed. by K. R. Kase, B. E. Bjärngard and F. H. Attix), Academic Press, Orlando, FL, Vol. I: 230-290 (1985).

particle beam from fragmentation lead to changes in the biological effectiveness of the radiation. Fig. 10 shows a measurement of RBE as a function of depth. Dose-averaged LET, L_D , is defined as:

$$L_D = \frac{\int L D(L) dL}{\int D(L) dL}$$

where $D(L)$ is the dose contributed by particles of a given LET, L , and $\Phi(L)$ is the fluence of particles with the given L , and

$$D(L) = \frac{1.6 \times 10^7 \Phi L}{\rho},$$

where ρ is the material density in g/cm³, L is measured in keV/μm and Φ in particles/cm².

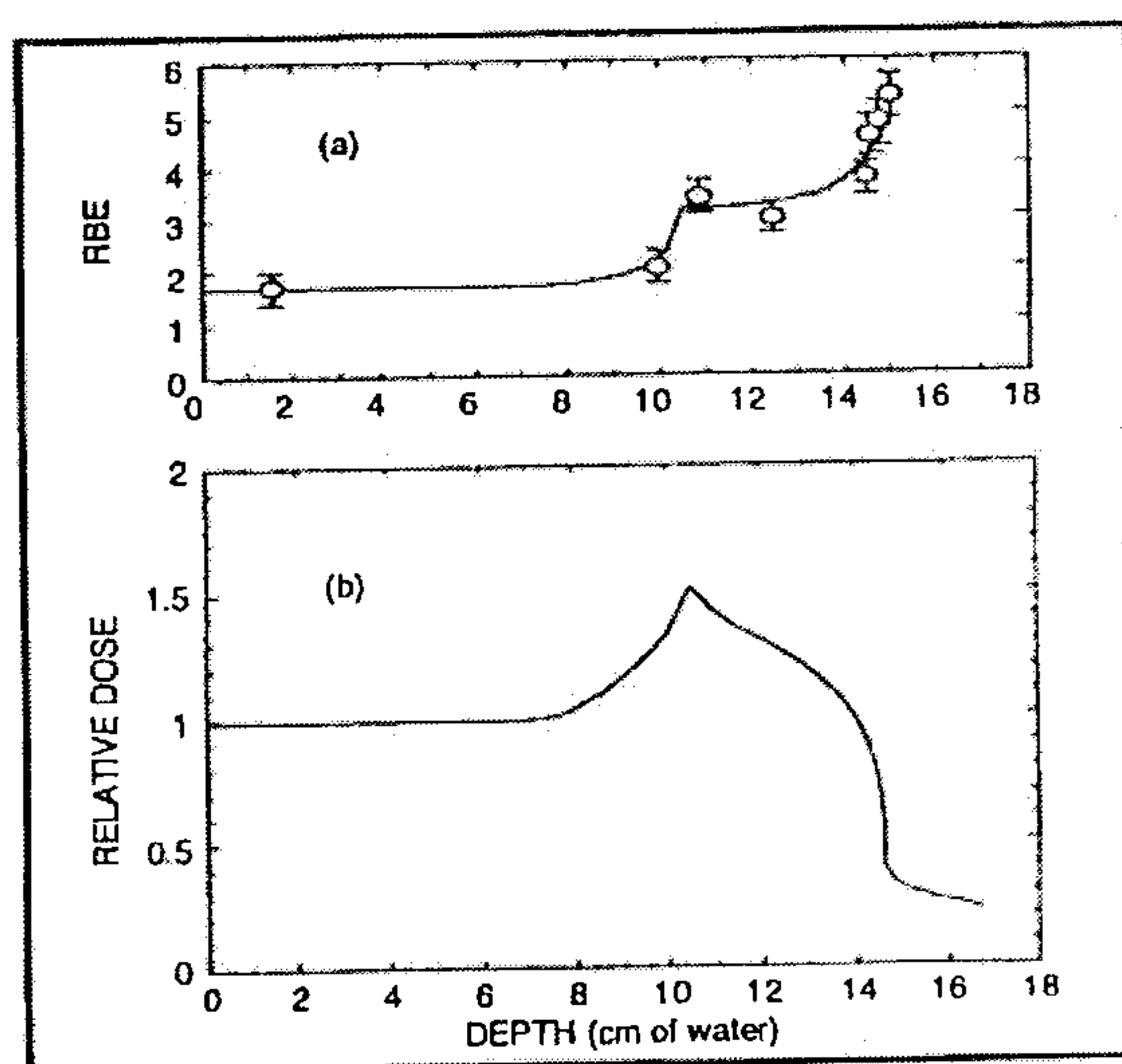


Fig. 10(a) Measured RBE data at various depths in water of a range-modulated beam. The solid line is to guide the eye.

(b) The associated physical dose distribution, which would render an isosurvival region in SOBP when the physical dose is multiplied by RBE at each depth.

The tail region of the depth-dose curve is a complex mix of particles; its RBE is important in predicting the response of tissue beyond the Bragg peak where critical structures might be found. Tail doses are typically one tenth of the dose in the proximal peak, and biological measurements in the tail region are difficult due to the large dose need at the proximal peak in order to measure reliably cell responses in the tail. Measurements of dose-averaged LET in this region are simpler to make, but not very straightforward in predicting the biological effects.

Verification of Treatment planning and Delivery Using Radioactive Beams

Treatment plans and delivery usually rely on xCT data, where the CT numbers are calibrated for ion beam stopping power in various types of tissues (see Fig. 11).³³ Such treatment plans

³³ G. T. Y. Chen, "CT in high LET therapy planning," *Proc. of the Symposium on Computed Tomography in Radiotherapy, September 1981* (ed. by C. C. Ling and R. Morton), Washington, DC, Raven Press, New York, 221-228 (1983).

could render errors as large as ± 5 mm in a 10 cm range.³⁴ For ion-beam treatment, the penalty paid for a small range inaccuracy is much more severe than for photon treatment as schematically illustrated in Fig. 12. By substituting a radioactive beam to deliver a "treatment" according to a therapy plan, and imaging the actual treatment volume, the conformation of the delivered dose with the target volume can be verified.^{35,36}

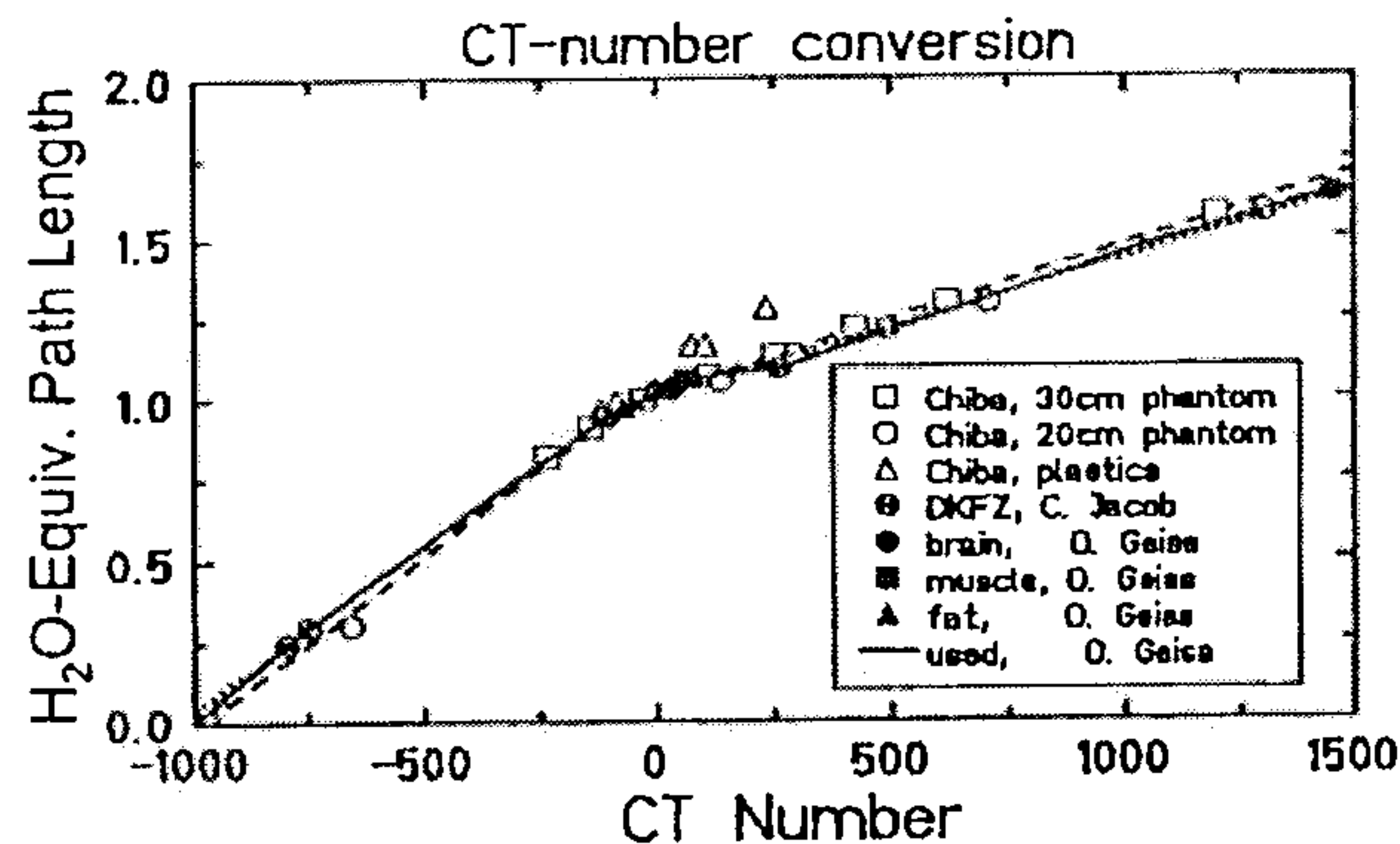


Fig. 11. Conversion of the CT numbers of tissues to water-equivalent path lengths for ion-beam treatment planning.

When a stable nucleus of an ion beam collides with a nucleus of the target material, the two nuclei knock off pieces (nucleons) of one another in peripheral collisions. Projectile ions may emerge, with one or two neutrons knocked out, with approximately the same velocity. The radioactive secondaries can be separated from the primary ion beam by magnetic momentum analysis and collected, and transported from the production target to the treatment room, and into the patient body. Production and collection of radioactive beams such as ^{19}Ne produced from ^{20}Ne and ^{11}C and ^{10}C from ^{12}C have been investigated at LBNL.³⁷ The most interesting isotope is ^{10}C (positron emitter, 19 second half life) as it is suitable for PET imaging. If the Bragg peak of a ^{10}C beam of known momentum were aligned to the distal edge of a target volume inside the patient body, one can deliver with confidence a ^{12}C beam into the same target.

³⁴ E. L. Alpen, W. Saunders, A. Chatterjee, J. Llacer, G. T. Chen and J. Scherer, *Brit. J. Radiol.* **58**: 542-548 (1985).

³⁵ J. Llacer, *Nucl. Sci. Applications* **3**: 111 (1988)

³⁶ S. D. Henderson, M. Collier, T. Renner, A. Chatterjee and J. Llacer, *Med. Phys.* **14**: 468 (1987).

³⁷ J. R. Alonso, B. Feinberg, J. G. Kalnins, G. F. Krebs, M. A. McMahan and I. Tanihata, "Radioactive beam production at the Bevalac," *Proc. of the First International Conference on Radioactive Nuclear Beams, Berkeley, CA, October 16-18, 1989* (ed. by W. D. Myers, J. M. Mischke and E. B. Norman), World Scientific Publishing Co., Teaneck, NJ, 112 (1990).

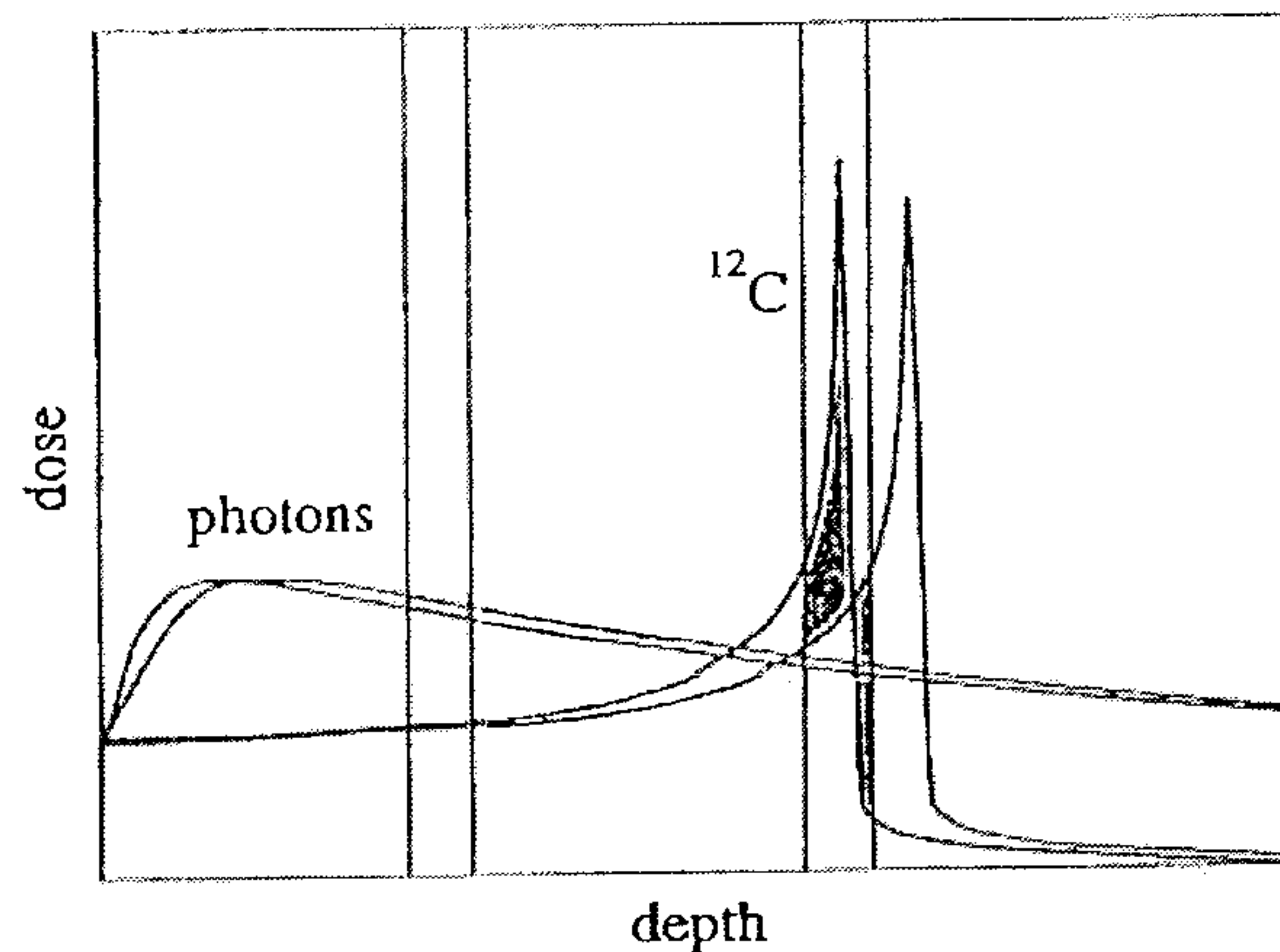


Fig. 12. For photon treatment, an error in target depth, indicated by two red lines at left, results in small dose error (red area). Whereas, for light ions, a similar error in range determination, shown in displaced Bragg peaks, would result in much more severe dose error as indicated by red areas (a big under-dose under the peak, and an overdose beyond the dose falloff region).

A schematic drawing of a specially-developed PET detector, called "Positron Emitting Beam Analyzer (PEBA) is shown in Fig. 13(a). It illustrates how PEBA localizes a stopping radioactive (positron-emitting) nucleus by measuring the annihilation photons of the positron emitted by the decay of ^{10}C nucleus. The transverse dimension of the stopping region of the ^{10}C nuclei and distance between the stopping nucleus and the point of annihilation are greatly exaggerated in Fig. 13(a). A PET image of stopping ^{19}Ne in a phantom is shown in Fig. 13(b). One can determine the location of the Bragg peak within <0.5 mm using sophisticated PET systems.

In a similar vein, GSI has implemented a PET system for in-beam in-situ therapy control, i.e., during ion beam treatment by assessing the radioactive isotopes produced by the ^{12}C beams.³⁸

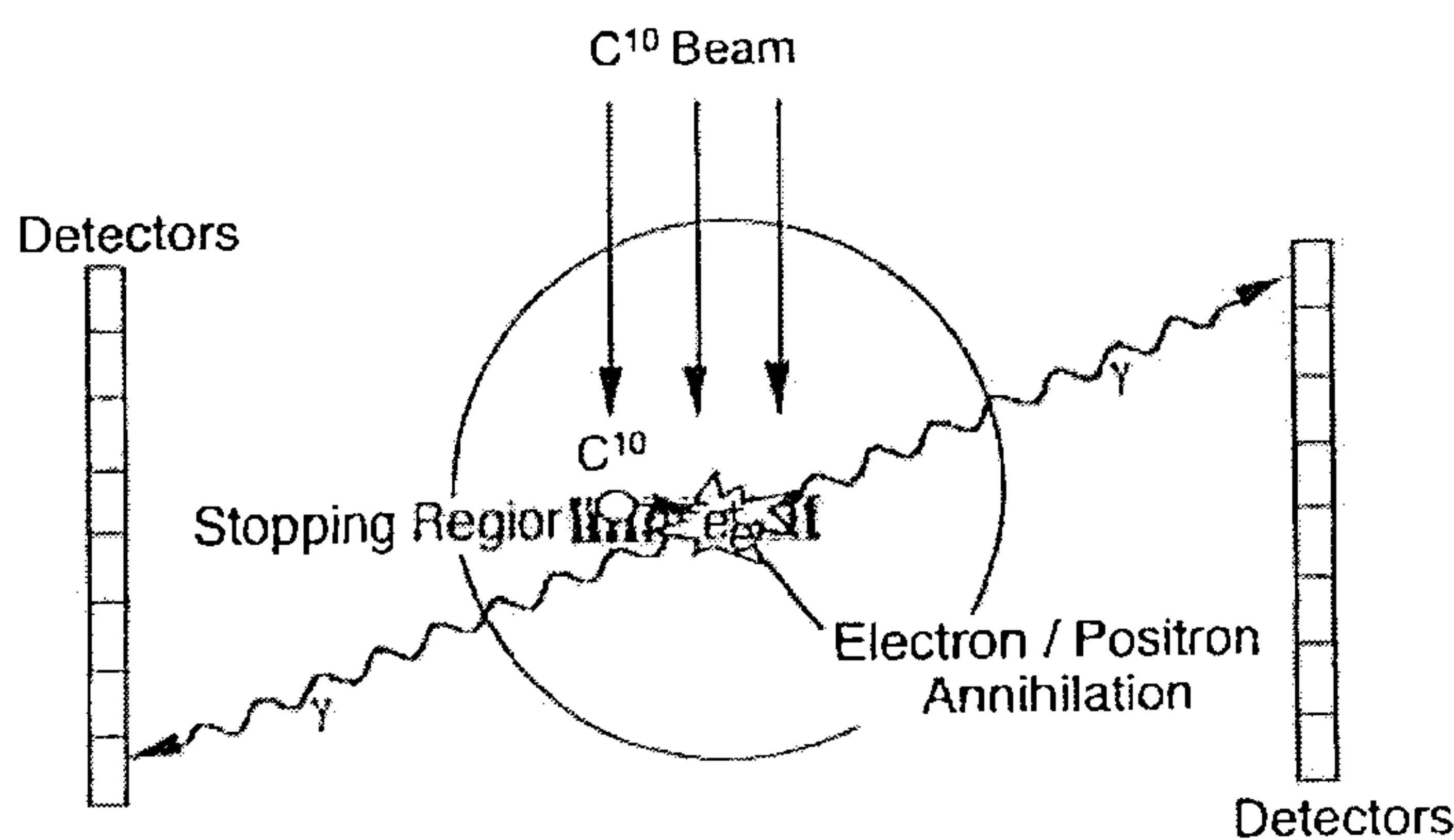


Fig. 13(a). A schematic drawing of PEBA.

³⁸ W. Enghardt, J. Debus, T. Haberer, B.G. Hasch, R. Hinz, O. Jakel, M. Kramer, K. Lauckner, J. Pawelke, "The application of PET to quality assurance of heavy-ion tumor therapy," *Strahlenther Onkol.* **175 Suppl. 2:** 33-36 (1999)

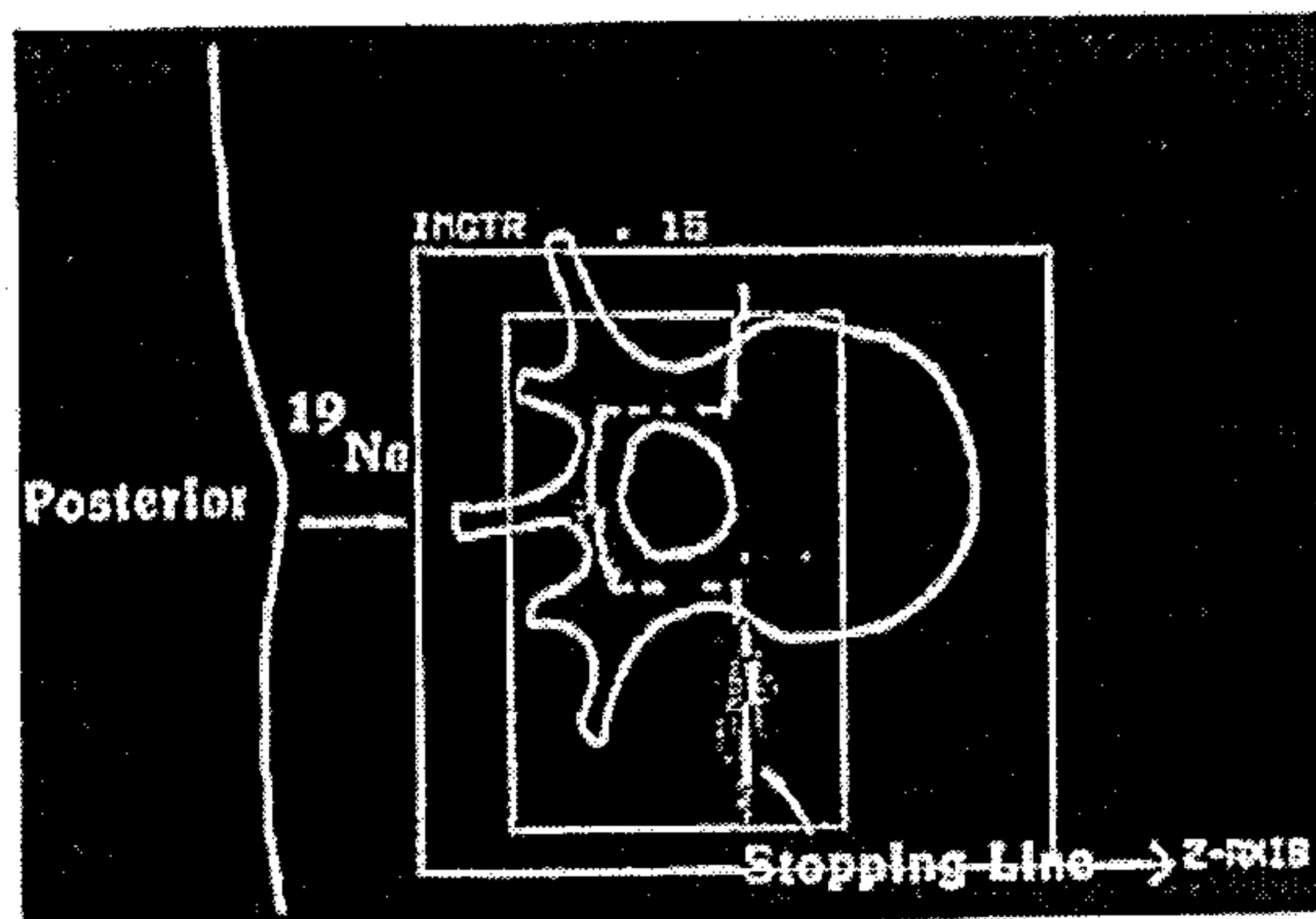


Fig. 13(b). An image of the stopping region of ^{19}Ne . The beam was created by a compensator to exclude the spinal cord region of a patient (phantom) from the Bragg peak radiation. (XBC 865-4162)

Ion Beam Research for Space Biology

Beyond the protection of the Earth's magnetic shield, the abundance of galactic cosmic rays, both light and heavy ions, is such that during a three-year trip to Mars 30% of the cell nuclei in an astronaut's body would be traversed by one or more heavily ionizing particles ($10 \leq Z \leq 28$), assuming shielding typical of today's spacecraft. Iron nuclei are the major contributor to these radiation effects, but their consequences must be understood. Radiobiology research in light-ion therapy naturally extended into space biology research program, first at the Bevalac at LBNL and now at the Booster Accelerator Facility of the Relativistic Heavy Ion Collider (RHIC) at the Brookhaven National Laboratory. It focuses on the effects of both iron-ion beams and the secondary particles produced by fragmentation in absorbing materials.³⁹ Experiments are in progress to determine their effects on cell inactivation and neoplastic cell transformation and to calculate the cross sections for cell transformation by low- and high-LET radiation. Preliminary results indicate that, compared with the cross section for cell inactivation or death, the cross section for cell transformation is about 10,000 times smaller. Such a difference implies that only a very few genes are involved in radiation-induced cell transformation. Life shortening, cataract formation, and tumorigenesis in animals irradiated with iron-ion beams are also under investigation. Early results on cataract expression suggest a shortened latency for iron-ion exposure, compared with low-LET radiation.

Clinical Trials Using Light Ions

The construction of the Bevalac accelerator complex at LBNL, in which the SuperHILAC injected ion beams into the Bevatron, expanded the opportunity for medical studies with light ion beams.⁴⁰ J.R. Castro and his team conducted clinical trials for treating human cancer using light ion beams at the 184-Inch Synchrocyclotron and the Bevalac from 1977 to 1992, when the

³⁹ TASK GROUP ON THE BIOLOGICAL EFFECTS OF SPACE RADIATION. *Radiation Hazards to Crews of Interplanetary Missions: Biological Issues and Research Strategies*. Washington, DC. Space Studies Board Commission on Physical Sciences, Mathematics and Applications, National Research Council. National Academy Press (1996).

⁴⁰ A. Ghiorso, H. A. Grunder, W. Hartsough, G. Lambertson, E. Lofgren, K. Lou, R. Main, R. Mobley, R. Morgado, W. Salsig and F. Selph, IEEE Trans. Nucl. Sci. NS-20: 155 (1973).

accelerators were closed.⁴¹ Ions of interest ranged from ^4He to ^{28}Si . ^{20}Ne ions with energies per nucleon of 450 and 585 MeV have been most commonly used. The numbers of patients treated were 2054 patients with helium ion beams and 433 patients with neon ion beams. The patients treated with helium ions included primary skull base tumors: chondrosarcomas, chordomas, meningiomas, etc. The patient treated during 1987-1992 showed increased local control, representing the influence of improved immobilization, treatment planning and delivery, and availability of MRI. Using ^{20}Ne ions, they also treated, and obtained excellent 5-year local control of, carcinomatous lesions arising from paranasal sinuses, nasopharynx or salivary glands, and extending into the skull base. Complications observed were mainly cranial nerve injuries including optic nerves, and radiation injury in the brain stem or temporal lobes.⁴²

Since the end of 1997, clinical trials at the Gesellschaft für Schwerionenforschung (GSI), Darmstadt, have treated with carbon-ion beams relatively radioresistant tumors such as chordomas and low-grade chondrosarcomas of the skull base, adenoid cystic carcinomas and malignant meningiomas.^{43,44} These tumors in the head region, which have not been treatable with conventional therapy methods. The new therapy led to a significant reduction of the tumor in all patients without any signs of relapse; local control rates achieved were comparable to neutron therapy but with less toxicity. By June 2005, about 250 patients have been treated successfully at GSI. Based on the studies at GSI, a therapy centre in Heidelberg is being built where up to 1,000 patients per year could be treated.

In 1994 the National Institute of Radiological Sciences (NIRS) in Chiba, Japan, commissioned its Heavy Ion Medical Accelerator in Chiba (HIMAC), which has two synchrotrons and produces ion beams from ^4He to ^{40}Ar up to a maximum energy per nucleon of 800 MeV. The HIMAC houses two treatment rooms, one with both a horizontal and a vertical beam, and the other with a vertical beam only. There are also a secondary (radioactive) beam room, a biology experimental room, and a physics experimental room, all equipped with horizontal beam lines. All beam lines are of the fixed beam type, in contrast to rotating gantries. Currently, their clinical trials use carbon ions, and they have successfully treated 1796 patients by February 2004. Currently, Phase I and II clinical trials are under way. They have demonstrated safety and efficacy of carbon ions to a great extent. In the near future they plan to establish an optimum irradiation method, identify the sites and histological types in which carbon ions are particularly effective, and clarify differences in indication from low-LET radiation. In 2004 HIMAC has obtained for the carbon-ion treatment the Japanese government

⁴¹ J.R. Castro, J.M. Quivey, J.T. Lyman, G.T. Chen, T.L. Phillips, C.A. Tobias, and E.L. Alpen, "Current status of clinical particle radiotherapy at Lawrence Berkeley Laboratory," *Cancer* **46**: 633-641 (1980); J. Castro, *Progress in Radio-Oncology* (Ed. D Kogelnik), 643-648 (1995); J.R. Castro, "Clinical programmes: a review of past and existing hadron protocols," in *Advances in Hadrontherapy*, (U. Amaldi, B. Larsson, and Y. Lemoigne, editors), Excerpta Medica, Elsevier, International Congress Series **1144**: 79-94 (1997).

⁴² J.R. Castro, D.E. Linstadt, J.P. Bahary, et al., "Experience in charged particle irradiation of tumours of the skull base: 1977-1992," *Int. J. Radia. Oncol. Biol. Phys.* **29**: 647 (1994).

⁴³ H. Eickhoff, T. Haberer, G. Kraft, U. Krause, M. Richter, R. Steiner, J. Debus, "The GSI Cancer Therapy Project," *Strahlenther. Onkol.* **175** (Suppl.2): 21-24 (1999).

⁴⁴ D. Schulz-Ertner, A. Nikoghosyan, C. Thilmann, Th. Haberer, O. Jäkel, C. Karger, G. Kraft, M. Wannenmacher, J. Debus, "Results of carbon ion radiotherapy in 152 patients," *Int. J. Rad. Oncol. Biol. Phys.* **58**: 631 - 640 (2004).

approval as “highly advanced medical technology,” which is comparable to the US FDA approval.

In 2001 at Harima Science Garden City, Japan, the Hyogo Ion Beam Medical Center (HIBMC) was commissioned as the first hospital-based facility in the world to provide both proton and carbon-ion beam therapy, which provides protons of maximum energy of 230 MeV and carbon ions of maximum energy per nucleon of 320 MeV. Six therapy rooms are available with seven treatment ports. Three rooms are dedicated to carbon ion beams: one with a vertical beam line, one with a horizontal and one with a 45 degree oblique beam line. Two proton treatment rooms are equipped with commercially designed rotating gantries. By the end of 2005, HIBMC has treated 825 patients using protons and 53 patients with carbon-ion beams.

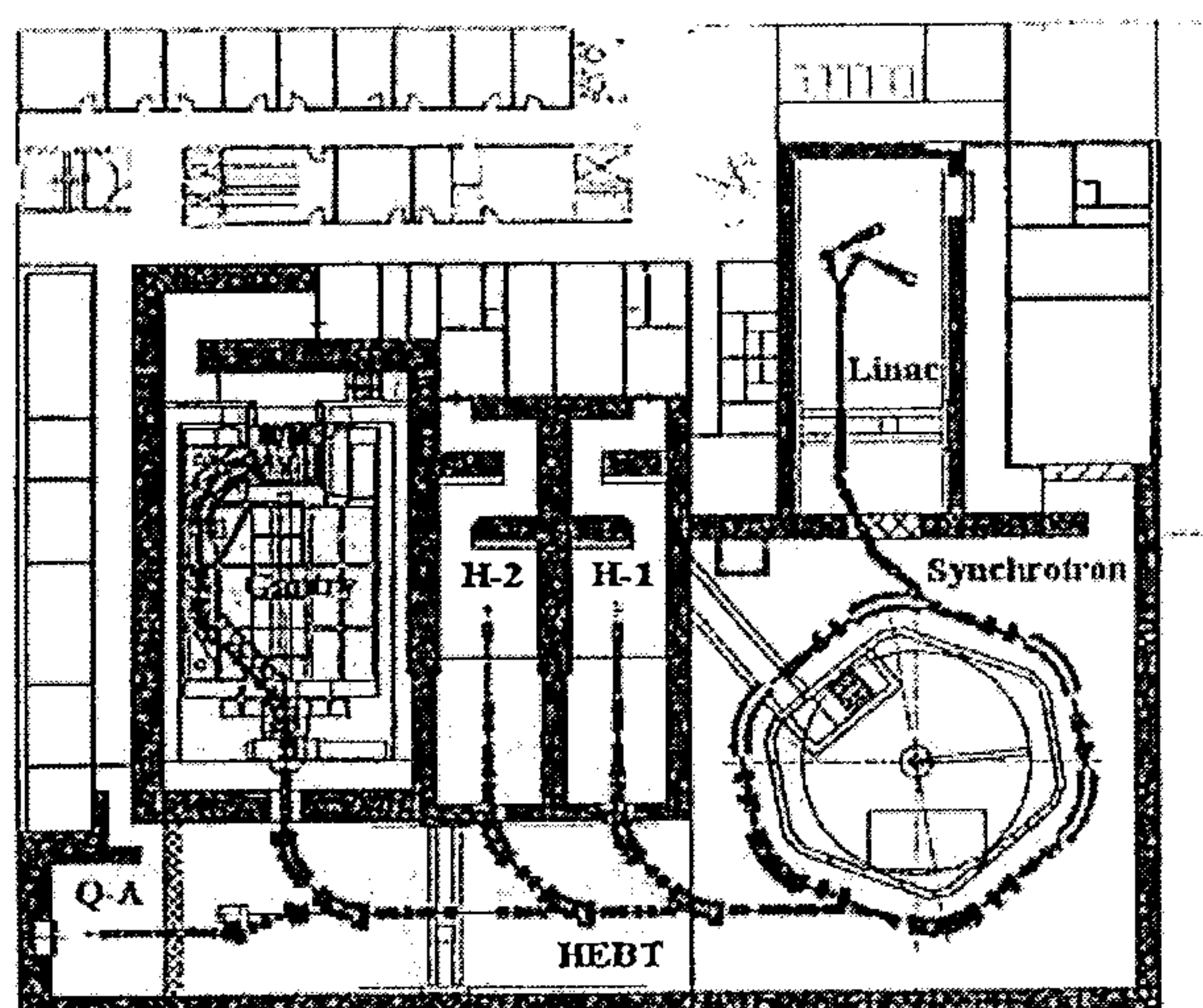


Fig. 14. Plan view of the Ion Therapy Unit under construction in Heidelberg.

The Heidelberg Ion Beam Therapy Center (HIT) is constructing the Ion Therapy Unit in Heidelberg, Germany. It is a joint project of the University Clinic Heidelberg, the German Cancer Research Center (DKFZ), the Gesellschaft für Schwerionenforschung (GSI) and the Research Center Rossendorf (FZR). As shown in Fig. 14, two ion sources feed the synchrotron via a linear accelerator. It houses three treatment rooms: two with a horizontal beam (H-1 and H-2) and one with a rotating gantry, which makes it possible to aim the beam at the patient from all directions. This system, which will be capable of treating tumors with both carbon ions and protons, is expected to begin treating patients in 2007.

European Network for LIGHT ion Therapy (ENLIGHT) plans for four national centers: Heidelberg Ion Therapy (HIT); the Centro Nazionale di Adroterapia Oncologica (CNAO) in Pavia; MedAustron in Wiener Neustadt; and ETOILE in Lyon. There is an increasing interest in further initiatives and more countries are expressing interest in creating national projects, in particular Sweden, the Netherlands, Belgium, Spain and the UK. There are other initiatives for light-ion facilities in several locations in the US and Japan, in Lanzhou, China, in Busan, Korea, and elsewhere.

Relation between the present report and other IAEA and ICRU reports

The present report will be on “Dose and volume specification for prescribing, recording and reporting ion-beam therapy” —

- to help accurately administer treatments
 - for individual patient treatment
 - for therapy planning
 - for data management with DICOM compliance (IMPAC)
- to standardize the treatment reporting
- to facilitate meaningful inter-comparison of treatment results among carbon ion centers
 - also inter-comparison with conventional therapy

Issues to consider including in the present report:

Prescribe and report doses to volumes rather than to discrete points

- Justifications for it for carbon-ion treatment

The location/volume of the dose specification in treatment plan

- The dose should be specified at the point where the dose changes least for small errors in determining ion beam path due to the uncertainties in integrated stopping power.
 - Mid-peak of the SOBP
 - Not at the proximal peak of the SOBP.
- The dose should be specified at the point where the dose changes most rapidly for small errors in determining ion beam path due to the uncertainties in integrated stopping power.
 - Mid-point of the distal dose falloff
- Dose-volume histogram

Units of dose specified and reported

- “Physical dose and RBE” vs. “biological dose” in “Gray-equivalent (GyE)” (dose-weighting factors)

Should one specify the errors in treatment plans?

- Errors help assess the under-dosing within the treatment volume, and over-dosing the adjacent normal tissues.⁴⁵
- (Corollary) Should one present the upper and lower limits of dose delivered within a certain volume?

Are the radioactive beam measurements of dose delivery important?

- It improves the accuracy of treatment planning and delivery.

Dose verification of treatment delivery

- For scanned beam delivery, a measurement requires a complete scan of the entire field.
 - In case when a treatment is accomplished by assembling several non-uniform dose distributions, each dose measurement for verification requires complete scans. A very time- and accelerator resource-consuming process.
 - Multiple detectorss

Dosimetry standardization for inter-comparisons among ion-beam centers

- Dosimeter calibrations
- Do you compare physical or biological doses?
 - What units for biological doses?
- Will it be practical, or feasible or even advisable, to agree on a “standard” ion beam setup with comparable beam quality? Weighting of absorbed dose implies the selection of reference treatment conditions.⁴⁶

⁴⁵ M. Goitein, “Calculation of the uncertainty in the dose delivered in radiation therapy,” *Med. Phys.* 12: 608-612 (1985).

⁴⁶ A.Wambersie, R.Gahbauer and H.G.Menzel, “RBE and weighting of absorbed dose in ion-beam therapy,” *Radiotherapy and Oncology*, **73 (Suppl.2)**, 40-49, and 176-182 (2004); and A.Wambersie, H.G.Menzel, R.A.Gahbauer, D.T.L.Jones, B.D.Michael, H.Paretzke, “Biological weighting of absorbed dose in radiation therapy,” *Radiation Protection Dosimetry*, **99**: 445-452 (2002).

APPENDIX D

ALTERNATING-PHASE-FOCUSED IH-DTL FOR HEAVY-ION MEDICAL ACCELERATORS

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Abstract

Compact linacs, consisted of a Radio-Frequency-Quadrupole (RFQ) linac and Interdigital H-mode Drift-Tube-Linac (IH-DTL) having the same operating frequency of 200 MHz, were designed for an injector of heavy-ion medical accelerators. For beam focusing of IH-DTL, the method of Alternating-Phase-Focusing (APF) was applied. The total length of the RFQ linac and APF IH-DTL is approximately 6 m. With the two linacs, carbon ions produced by an ECR Ion-Source (ECRIS) could be accelerated up to 4.0 MeV/u. The compact linacs were constructed and installed in NIRS. We have succeeded to accelerate carbon ions with the APF linac for the first time. The present status of the compact linacs as well as results of acceleration tests was presented.

INTRODUCTION

At the National Institute of Radiological Sciences (NIRS), cancer therapy using high-energy carbon ions from the Heavy Ion Medical Accelerator in Chiba (HIMAC) has been carried out since June 1994[1]. Until now, more than 2,600 patients have been treated in NIRS. Due to the successful clinical results over more than ten years, a number of projects on construction of these accelerator complexes dedicated to the cancer therapy have been proposed over the world. Since these existing accelerator complexes are costly and large in size, the development of cost-effective and compact accelerators for a hospital-based complex is needed for the increased use of the heavy-ion therapy.

In the development of the hospital-based accelerator complex, the design of an injector plays a key role, because the existing heavy-ion linacs are quite large. The size of the injector would affect the total size of the

complex as well as total costs of construction. Therefore, we developed the compact injector for the heavy-ion medical accelerators.

The compact injector consisted of ECRIS and two linacs, which are the RFQ linac and IH-DTL having the same operating frequency of 200 MHz. For beam focusing of IH-DTL, the method of APF was applied. Injection and extraction energies of the two linacs were summarized in Table 1. In the following sections, the present status of the compact injector and results of beam acceleration tests were described.

COMPACT INJECTOR

A schematic drawing of the compact injector was shown in Fig. 1. For an ion source, permanent-magnet 10 GHz ECRIS was employed[2]. Use of the permanent magnets to produce all the required magnetic field allowed us to design considerably simple and cost-effective ion-source, because it would not require any power supply as well as cumbersome cooling system. ECRIS was first manufactured and tested in NIRS. As a result, we found that ECRIS can produce $^{12}\text{C}^{4+}$ of more than 400 μA under an extraction voltage of 30 kV, corresponding to the ion energy of 10 keV/u.

Ions produced by ECRIS were analyzed with a Low-Energy-Beam-Transport (LEBT) line, and carbon ions of $^{12}\text{C}^{4+}$ having 10 keV/u were selected. The analyzed carbon ion were transported through the LEBT line and then injected to the RFQ linac. Transverse phase-space matching to the linac was accomplished by adjusting focusing elements, such as an electrostatic quadrupole triplet and magnetic solenoid, installed in the LEBT line. Transverse emittances of carbon ions from ECRIS were measured using the LEBT line in prior to installation of the linacs. Beam transmission through the LEBT line was better than 90%.

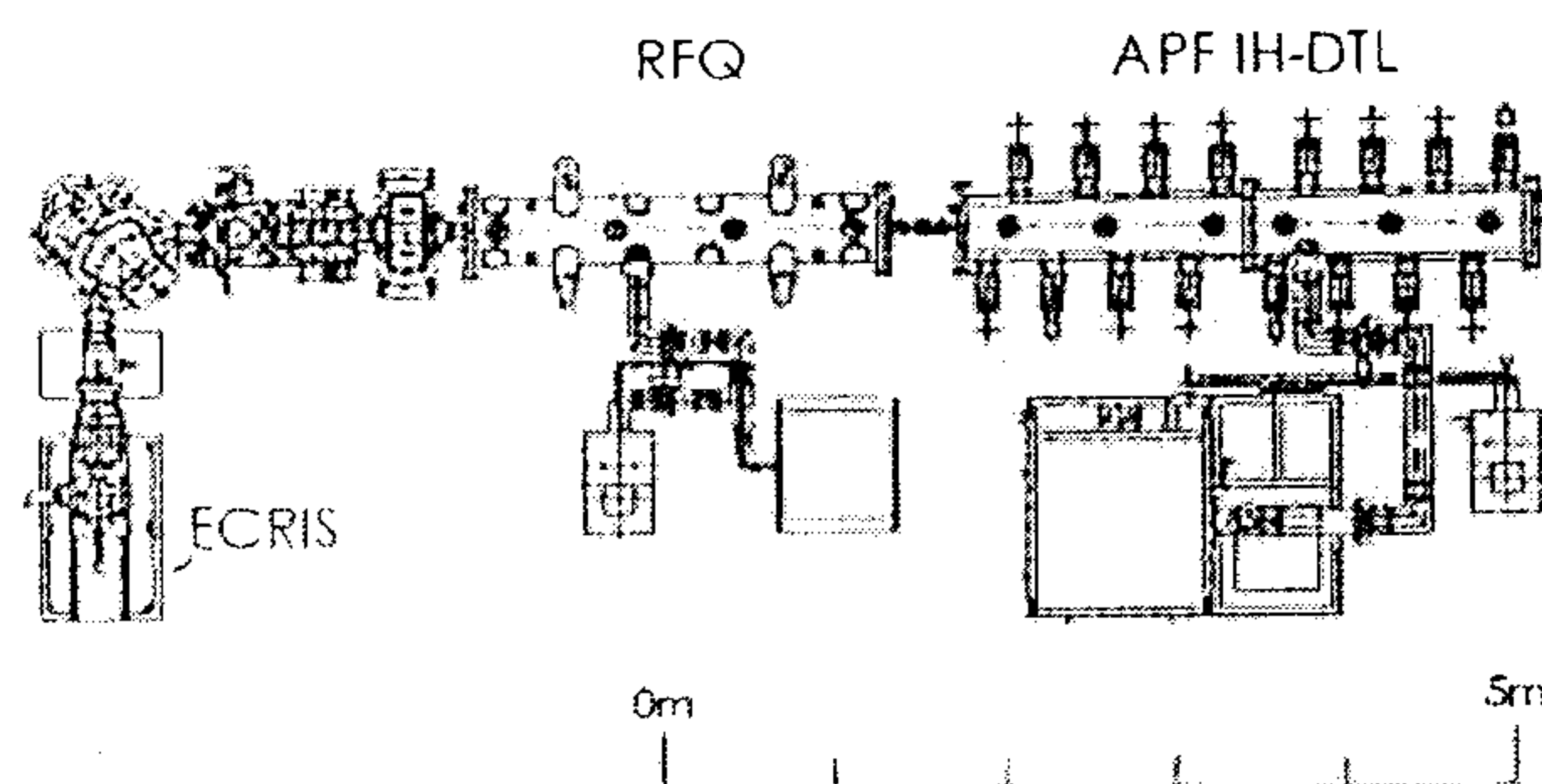


Figure 1: A schematic drawing of the compact injector.

Table 1: Major parameters of the compact linacs

Parameters	RFQ	IH-DTL	Units
Injection energy	0.01	0.61	MeV/u
Extraction energy	0.61	4.0	MeV/u
Operating frequency	200	200	MHz
q/m	1/3	1/3	-
Cavity length	2.5	3.4	m
Cavity outer diameter	0.42	0.44	m

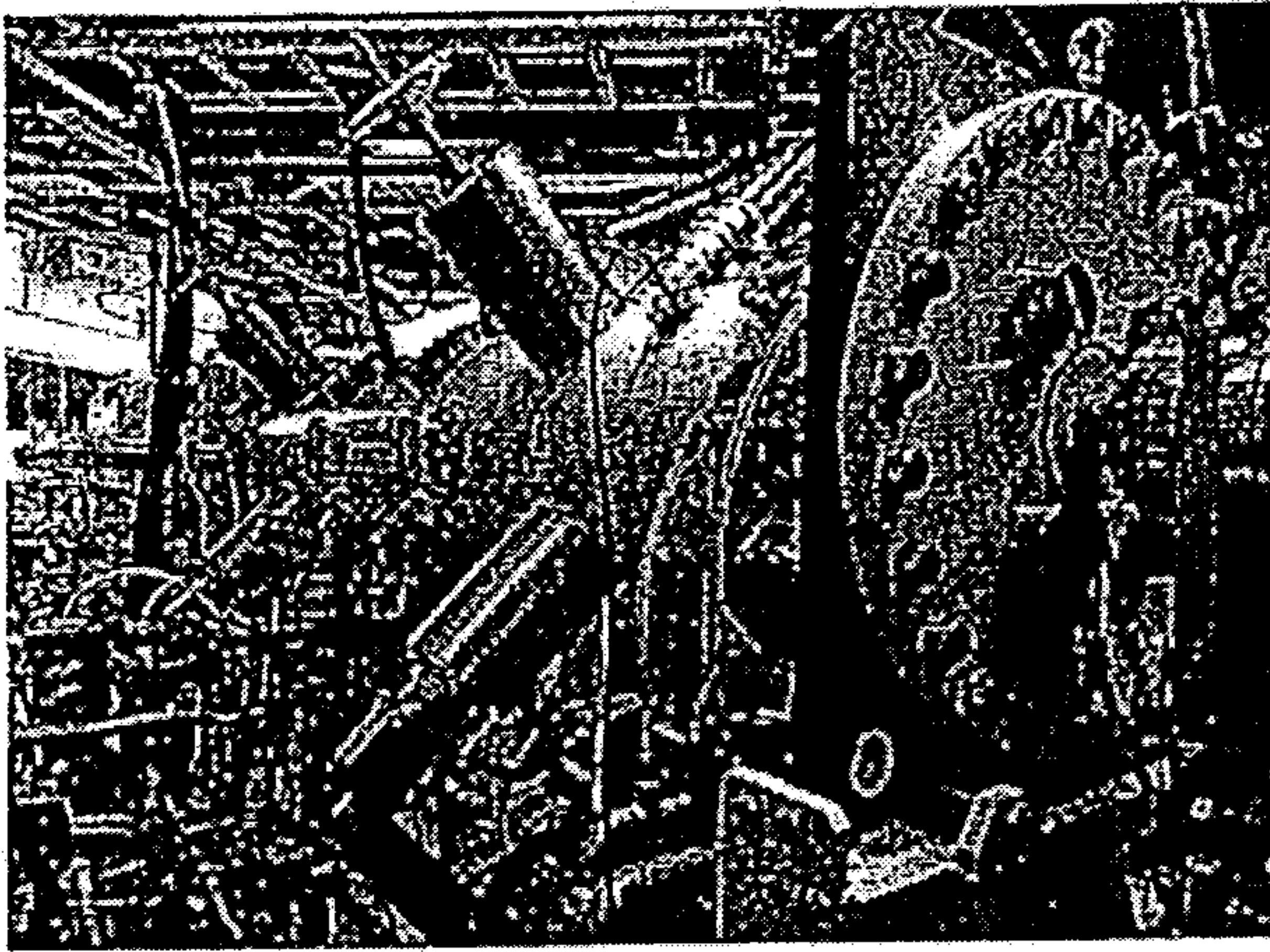


Fig. 2 A picture of the compact RFQ linac (a view from upstream).

The RFQ linac has a conventional four-vane structure. It can accelerate carbon ions up to 610 keV/u. By optimizing cell parameters for acceleration of carbon ions and using the rather high operating-frequency of 200 MHz, we could design the compact cavity; length and outer diameter of the cavity are 2.5 m and 0.42 m, respectively. The construction of the RFQ linac was completed in July 2005 and installed in NIRS. A picture of the RFQ linac is presented in Fig. 2.

For IH-DTL, the APF method was adopted to focus accelerating ions. The method utilizes focusing and defocusing strengths provided with the rf acceleration field by choosing the positive and negative synchronous phases alternately at each gap. By analogy with the principle of strong focusing, both longitudinal and transverse stability of motion would be obtained. Hence, no additional focusing element has to be installed in the cavity making the cavity structure significantly simple. This also indicates that drift tubes can be fabricated smaller and shorter and therefore allowed us to employ higher operating frequency and lower injection energy than ever before with conventional DTLs, such as the Alvarez structure. Although the method has such the attractive features, it has never been practically used since it was first proposed in 50s.

Table 2: Parameters calculated for APF IH-DTL

Parameters	Value	Units
Number of unit cells	72	-
Normalized 90% transverse emittance of the injected beam	0.68	$\pi \cdot \text{mm} \cdot \text{mrad}$
Normalized 90% transverse emittance of the extracted beam	0.86	$\pi \cdot \text{mm} \cdot \text{mrad}$
Normalized 90% longitudinal emittance of the injected beam	1.3	$\pi \cdot \text{ns} \cdot \text{keV/u}$
Normalized 90% longitudinal emittance of the extracted beam	1.6	$\pi \cdot \text{ns} \cdot \text{keV/u}$
Energy spread ($\Delta E/E$)	± 0.4	%
Transmission	99.6	%

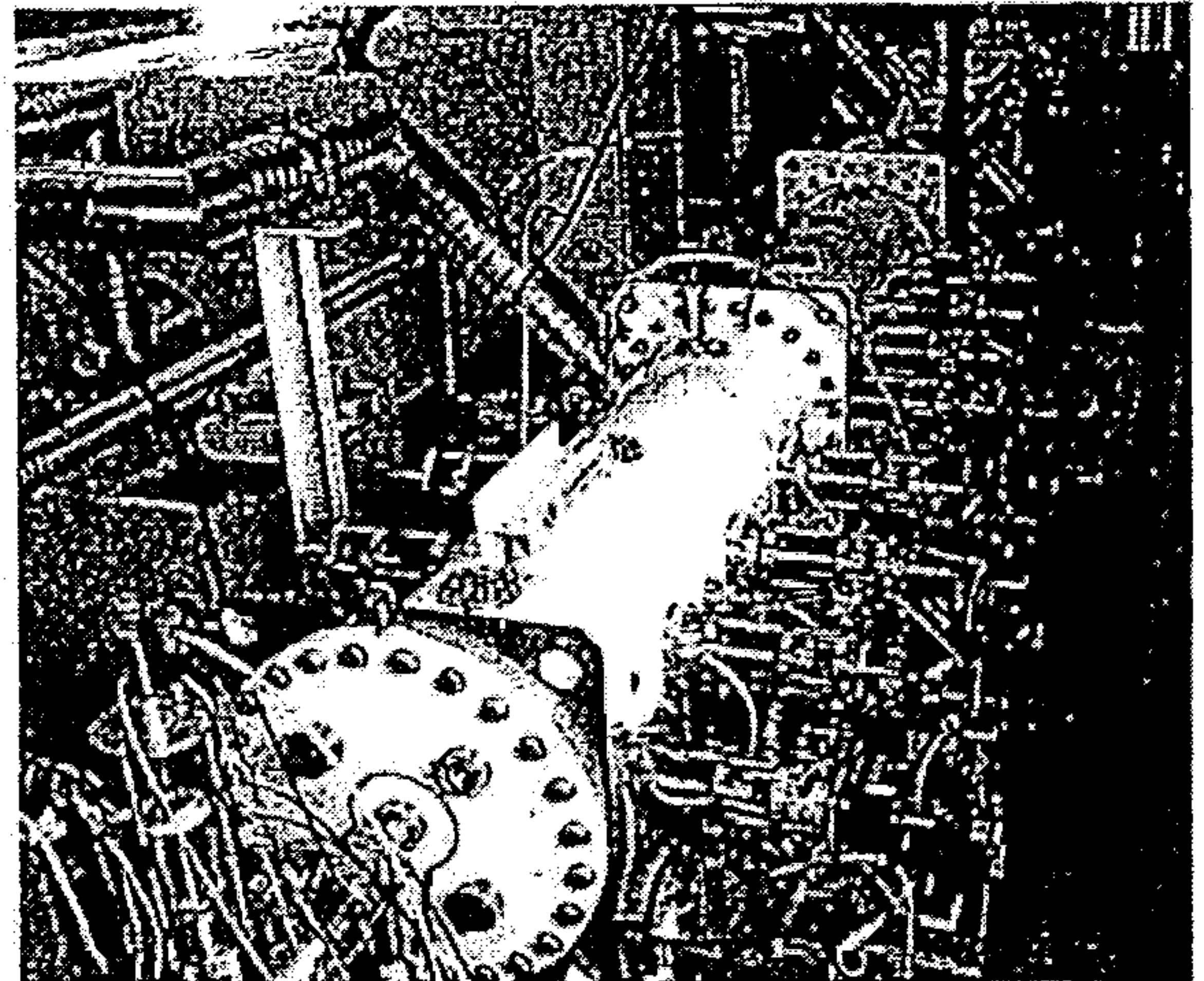


Fig. 3 A picture of APF IH-DTL (a view from the downstream).

Due to the nature of the method, focusing strengths provided by the rf acceleration field are rather weak as compared with these of magnetically focused DTLs. Moreover, beam motion for the APF linac depends strongly on a choice of the alternating synchronous phases, and it is generally difficult to optimize an array of the synchronous phases to obtain sufficient acceptances as well as low emittances of extracted beam.

By using a sinusoidal function to describe the phase array and performing beam dynamics simulations iteratively, we succeeded to optimize the phase array as described in refs. [3,4]. The calculated transmission was reached to as high as 99.6% indicating the sufficient acceptance of this APF structure. Parameters calculated for APF IH-DTL are summarized in Table 2.

The IH structure was used for the cavity of APF IH-DTL. An idea of the IH structure was first proposed in 50s. Although the structure was known to provide better shunt impedance than that of conventional DTLs, IH-DTL has not been used for many decades. A major reason for this is that an electromagnetic (EM) field distribution could not be calculated with existing two-dimensional EM field solvers, because the field distribution in the IH cavity depends strongly on its total structure of the cavity. Therefore, lengthy and costly model studies had been required to determine the final structure of the cavity. With recent development of three-dimensional EM field solvers, it became possible to calculate the EM field in the IH cavity directly. Although these solvers were recently applied to design IH-DTL, accuracy of these solvers was not confirmed. To verify the accuracy of the solver and tuning capability of our inductive tuners, we constructed a full-scale model cavity of APF IH-DTL[4]. Electric field distribution of the model cavity was measured by using the perturbation method and compared with the designed distribution. The result of the comparison indicated that the gap voltages over the model cavity could be controlled with excellent accuracy, while maintaining the desired cavity

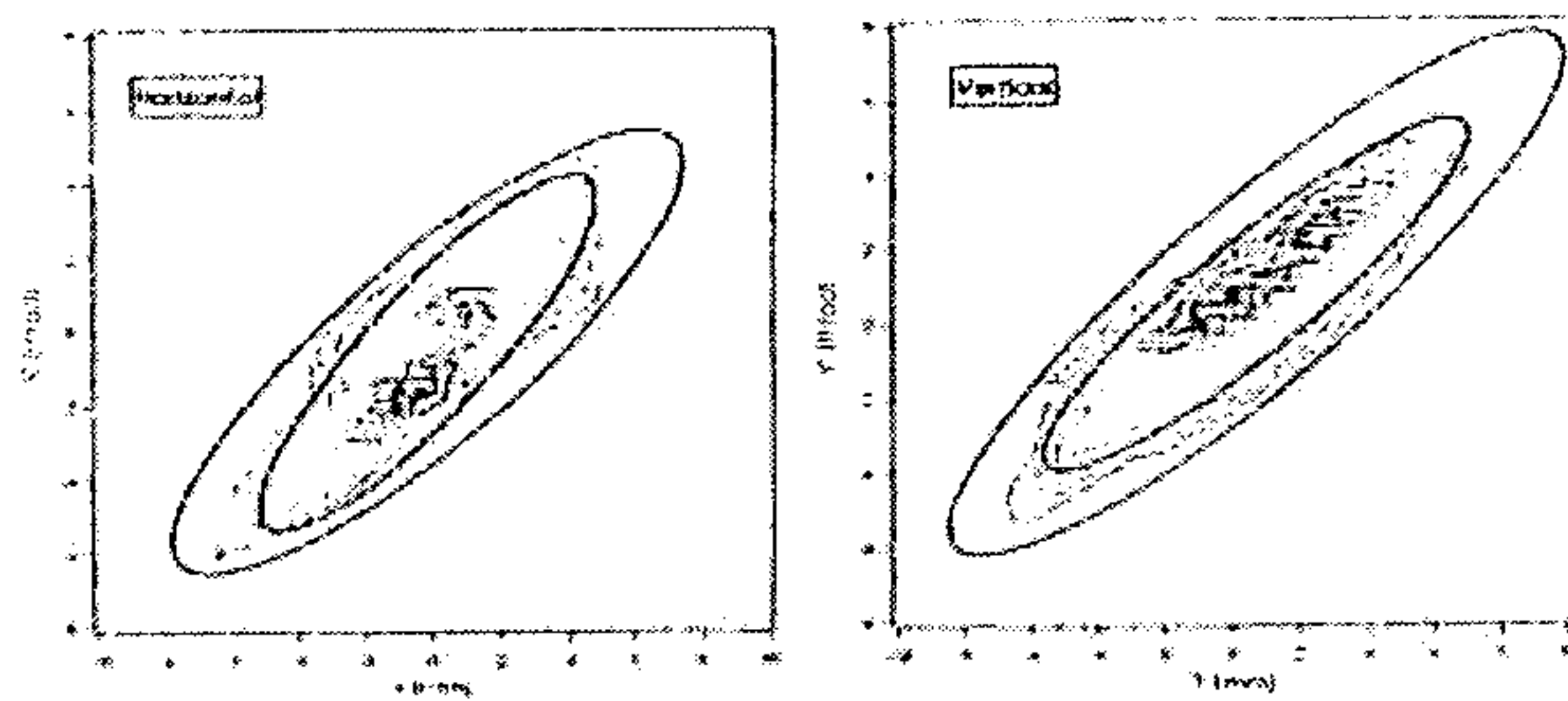


Figure 4: Measured transverse phase-space distributions of carbon ions ($^{12}\text{C}^{4+}$) extracted from APF IH-DTL. Solid and dotted curves show results of the 100% and 90% emittance fits.

frequency, once tuning with the inductive tuners has been performed.

Based on the model cavity, the design of the high-power cavity for APF IH-DTL has been developed. The construction of APF IH-DTL and rf amplifiers has completed in February 2006. A picture of APF IH-DTL is shown in Fig. 3. The electric field was measured and tuned with the inductive tuners. After the tuning, most of the gap voltages were tuned to the designed voltages within a few percent of accuracy. The quality factor was measured to be 12,000 corresponding 80% of the calculated value ($Q_c=15,000$). The required rf power was estimated to be 360 kW assuming 80% of Q_c .

BEAM ACCELERATION TESTS

The RFQ linac was first constructed and installed in conjunction with ECRIS. In prior to installation of APF IH-DTL, beam acceleration tests only with ECRIS and the RFQ linac were performed. Energy and phase space distributions of the extracted carbon beam having the energy of 610 keV/u were measured and compared with those calculated with the PARMTEQ code. As a result, we found the measured distributions were fairly well reproduced with the calculated distributions.

After the beam acceleration tests of the RFQ linac, APF IH-DTL was installed downstream of the RFQ linac. In between the RFQ linac and APF IH-DTL, a magnetic quadrupole triplet was installed for matching of transverse phase space. The total length of the triplet was approximately 38 cm. Matched beam would be injected to APF IH-DTL and finally accelerated up to 4.0 MeV/u.

After commissioning of the entire compact injector system completed in March 2006, an rf power, generated by the three rf amplifiers having maximum output of 500 kW, was delivered to the cavity of APF IH-DTL. After a few days of conditioning, the designed power of 360 kW was successfully fed into the cavity without any problem.

The beam acceleration tests were subsequently performed, and we have succeeded to accelerate carbon ions. Extracted beam was measured with a beam analyzing line located downstream of APF IH-DTL. Beam intensity of $^{12}\text{C}^{4+}$ ions extracted from APF IH-DTL was measured to be as high as 390 pA, which would be twice as much as that required for the treatments.

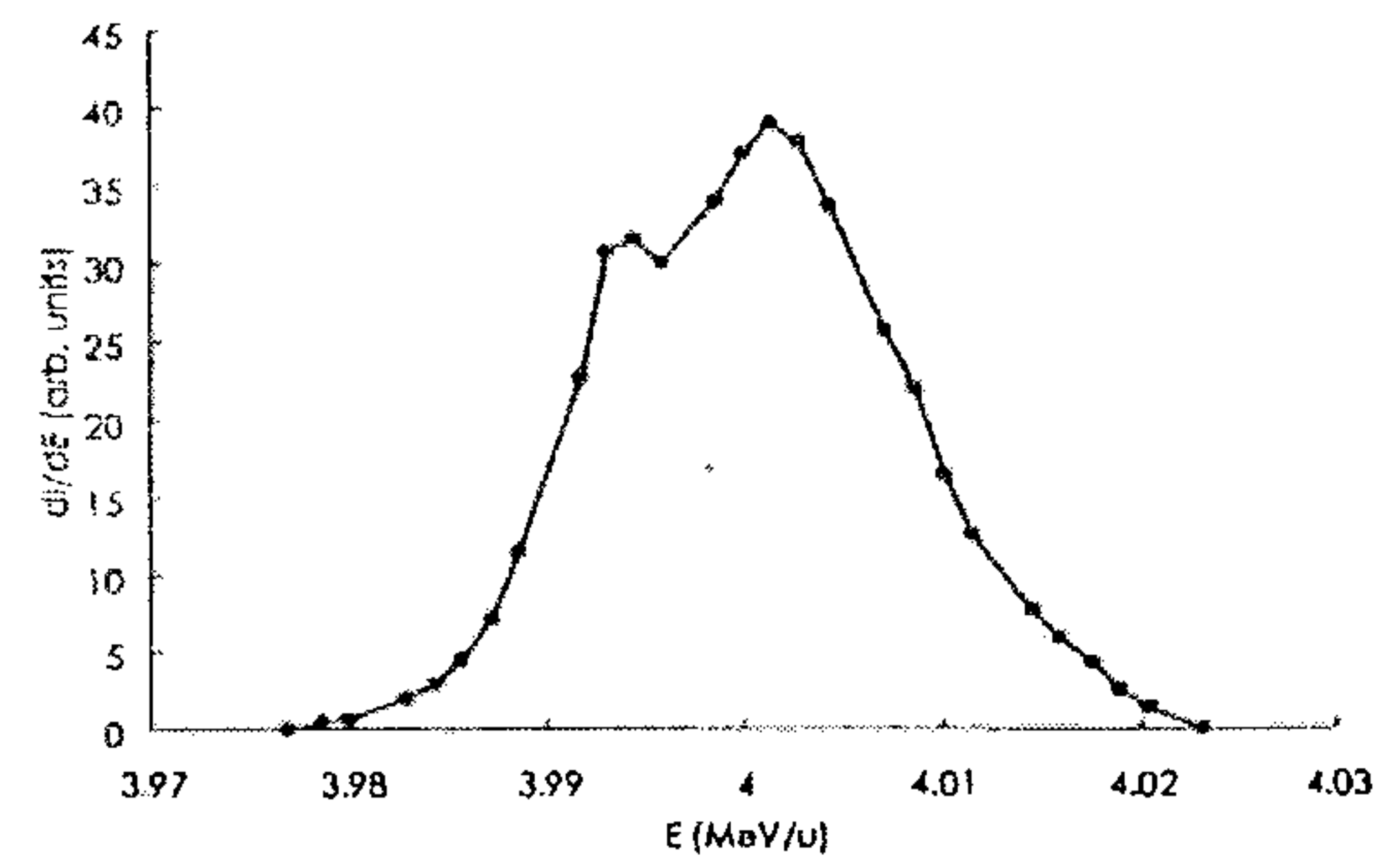


Fig. 5 A measured energy distribution of $^{12}\text{C}^{4+}$.

The beam transmission of the entire injector system, including LEBT, the RFQ linac and APF IH-DTL, was reached up to 79%. With the known transmission of LEBT and the RFQ linac, the transmission through APF IH-DTL was estimated to be almost 100%.

Transverse phase-space distributions were measured with a pair of a slit and profile monitor installed in the beam analyzing line. The results were presented in Fig. 4. The distributions were fitted with an elliptical function as shown by the curves in Fig. 4. The normalized 90% emittances for the both coordinates were estimated by the fit to be approximately $1.0 \pi \cdot \text{mm} \cdot \text{mrad}$, which was slightly higher than the calculated value given in Table 2. The energy distribution of accelerated $^{12}\text{C}^{4+}$ ions was measured as shown in Fig. 5. The average energy and spread were roughly $E_{\text{ave}}=4.0 \text{ MeV/u}$ and $\Delta E/E=\pm 0.4\%$, respectively, which were reproduced well with those calculated. We note here that these measured parameters would suffice requirements given by our design of the synchrotron ring.

SUMMARY

The compact injector, consisting of ECRIS and two linacs, which are the RFQ and APF IH-DTL, was designed and constructed. The acceleration tests were performed, and we have succeeded to accelerate carbon ions with the APF linac for the first time. The results of the tests further demonstrated its excellent performance.

The total length of the two linacs was reduced to approximately 6 m, which is considerably shorter than that of the existing heavy-ion linacs. With this successful result, the final design and construction of the hospital-based complex have been started.

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- * Corresponding author. E-mail: y_iwata@nirs.go.jp
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- [2] M. Muramatsu *et al.*, Rev. of Sci. Instrum., 76, 113304 (2005).
- [3] Y. Iwata *et al.*, Proceedings of EPAC04, Lucerne, Switzerland, 2631 (2004).
- [4] Y. Iwata *et al.*, Nucl. Instrum. and Meth. in Phys. Res. A (submitted).

APPENDIX E

STATUS OF THE SUPERCONDUCTING ECR ION SOURCE *VENUS*

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Abstract

A new, very high magnetic field superconducting ECR ion source, *VENUS*, is under development at the LBNL 88-Inch Cyclotron. It will boost the maximum energies and intensities for heavy ions from the cyclotron particularly for ions with mass greater than 60. It will also serve as R&D ion source for the proposed Rare Isotope Accelerator (RIA) project in the US, which requires up to 10 pμA of U^{30+} . The superconducting magnet structure consists of three solenoids and six racetrack coils with iron poles forming the sextupole. The coils are designed to generate a 4T axial mirror field at injection and 3T at extraction and a radial sextupole field of 2.4 T at the plasma chamber wall. Test results of the magnet coils, which exceeded design requirements with minimum training, are presented. The magnet assembly with its cryostat will be enclosed by an iron shield and therefore must be designed to withstand any possible forces between coils and iron, which can be as high as 35,000 kg-force. The low energy beam transport line (LEBT) and mass analyzing system of the ion source is designed to

transport a proton-equivalent current of 25mA at 20kV extraction voltage. The design of the ion source and LEBT will be discussed.

1 INTRODUCTION

The superconducting ECR ion source (ECRIS) *VENUS*, whose R&D progress has been previously documented [1, 2], is presently beginning its construction phase. The *VENUS* project aims for following significant improvements for ECRIS:

1. Reach the highest magnetic fields so far obtained in an ECRIS to improve plasma confinement.
2. Utilize a commercially available 10kW-CW 28 GHz gyrotron amplifier to take advantage of the high magnetic fields and the large plasma volume.
3. Develop new clamping schemes for the superconducting coils in order to withstand the strong magnetic forces.
4. Use state of the art cryogenic equipment, utilizing cryocoolers and High Tc leads, to eliminate the need of a liquid-He filling system.

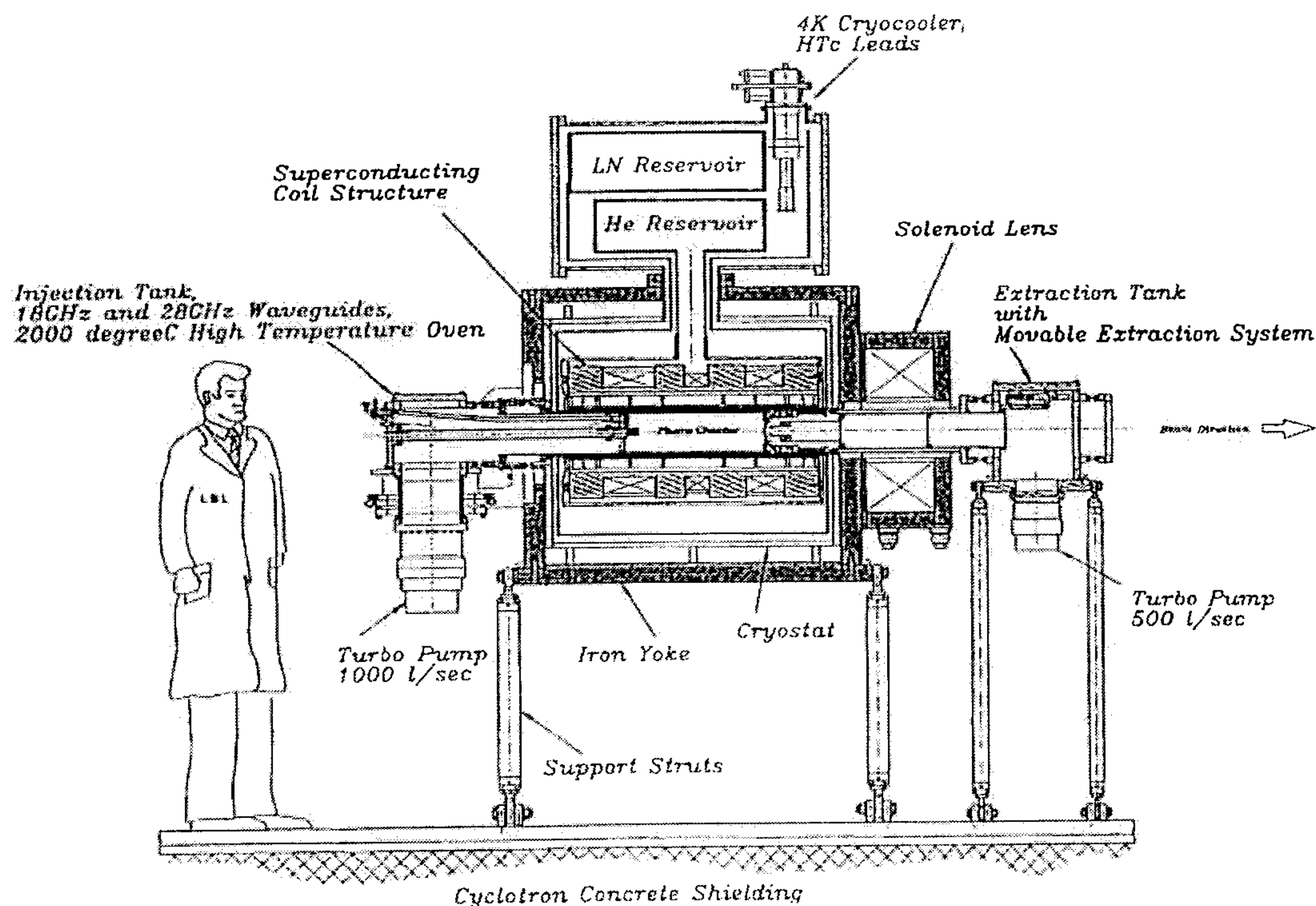


Figure 1: Section view of the *VENUS* ion source.

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

53983-16D3

CLAIMS:

1. A method of making a sucrose solution, the method comprising:

irradiating crystalline sucrose, wherein the total dose of radiation is from 30 Mrad to 70 Mrad; and wherein irradiating is performed at a dose rate greater than 0.15 Mrad per second

5 combining the irradiated sucrose with water under conditions that allow the sucrose to dissolve;

thereby making a sucrose solution.

2. The method of claim 1, wherein irradiating comprises exposing the crystalline sucrose to an electron beam.

10 3. The method of claim 2, wherein irradiating comprises irradiating the sucrose with more than one electron beam device.

4. The method of claim 1, wherein the irradiated sucrose has a crystallinity that is at least 10 percent lower than the crystalline sucrose prior to irradiation.

15 5. The method of claim 1, wherein the crystalline sucrose has a crystallinity index prior to irradiation of from about 40 to about 87.5 percent, and the irradiated sucrose has a crystallinity index of from about 10 to about 50 percent.

6. A method of making amorphous sucrose, the method comprising:

irradiating crystalline sucrose, wherein the total dose of radiation is from 30 Mrad to 70 Mrad; and wherein irradiating is performed at a dose rate greater than 0.15 Mrad per second

20 thereby making amorphous sucrose.

7. The method of claim 6, wherein irradiating comprises exposing the crystalline sucrose to an electron beam.

8. The method of claim 7, wherein irradiating comprises irradiating the sucrose with more than one electron beam device.

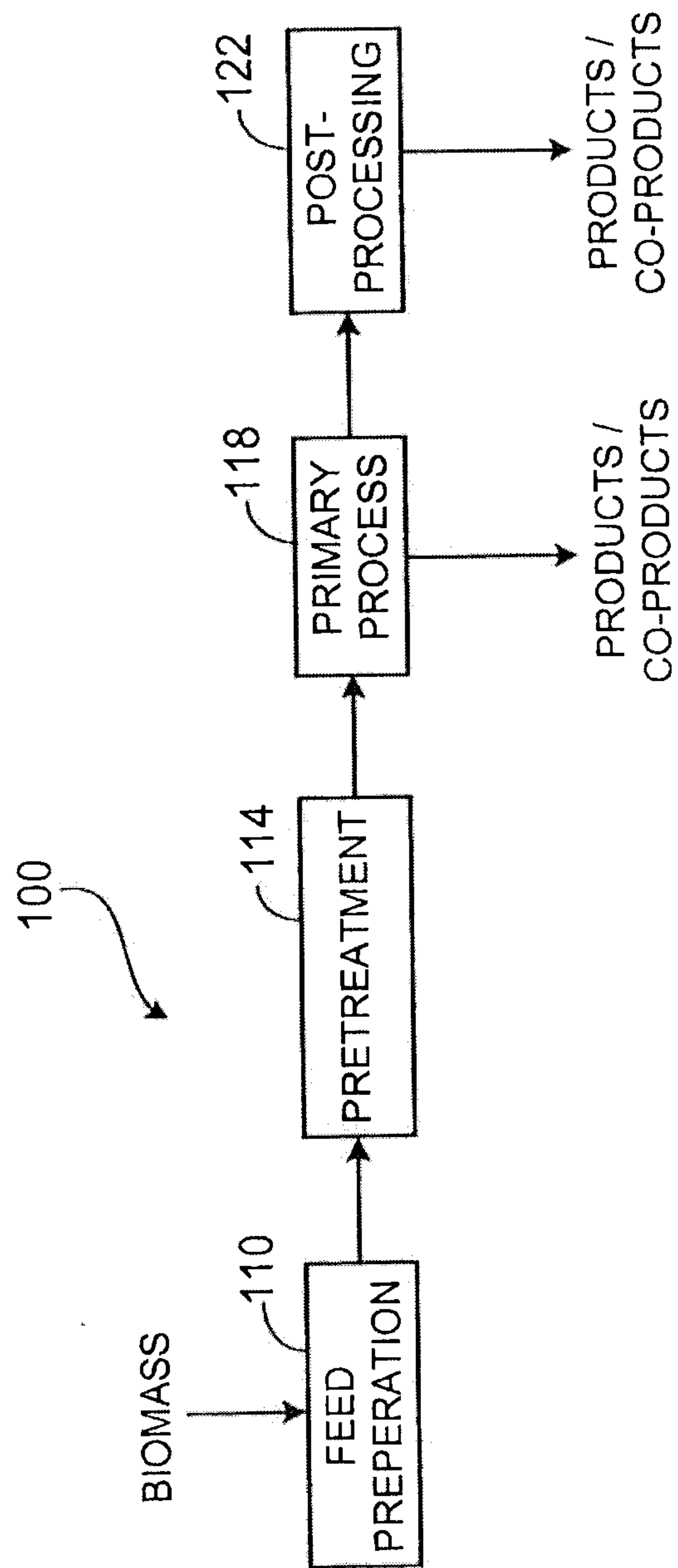


FIG. 1

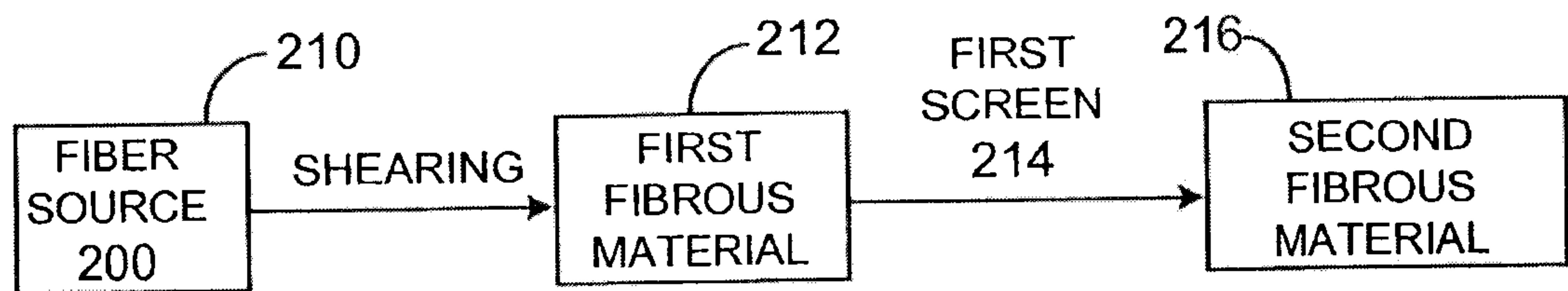
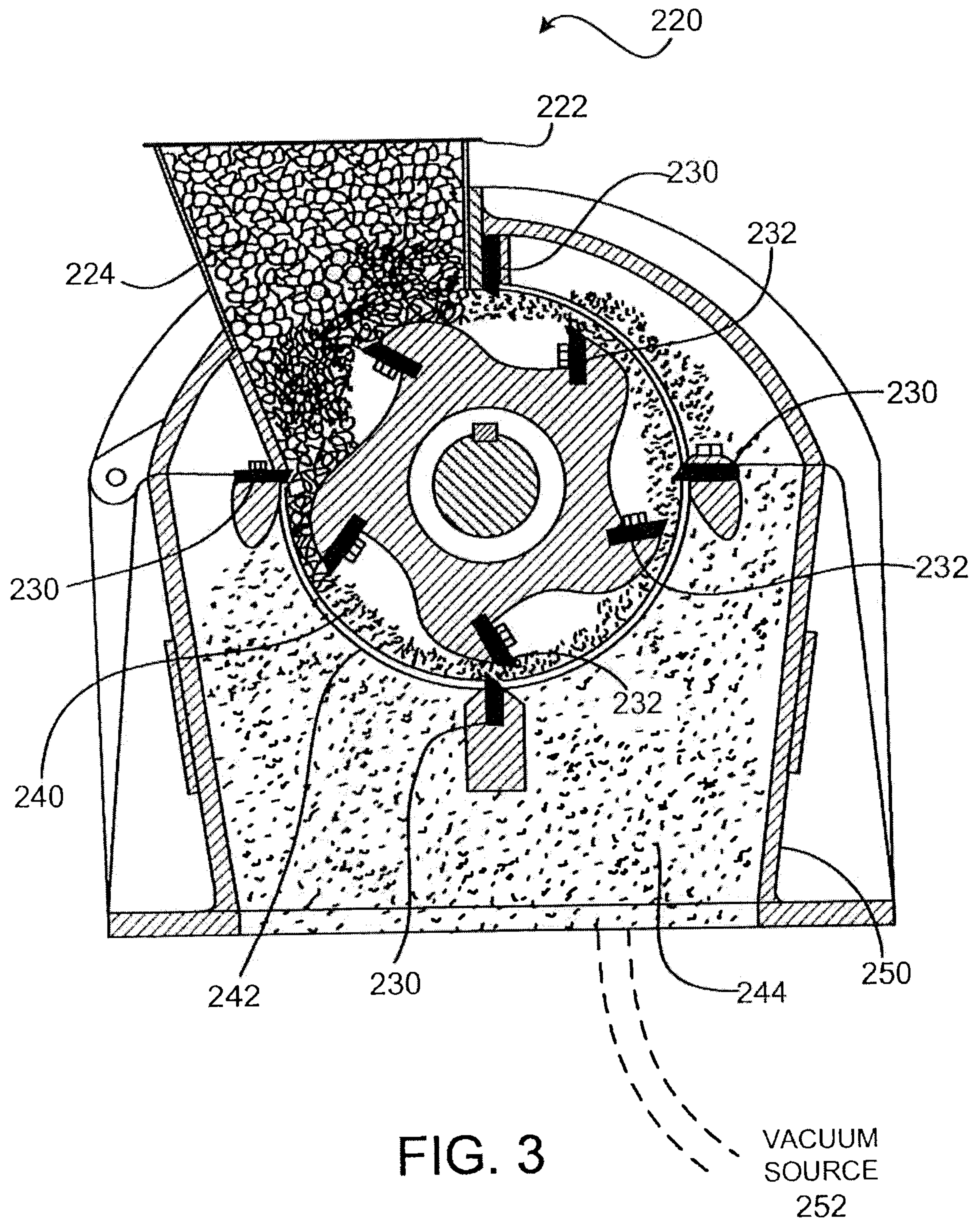
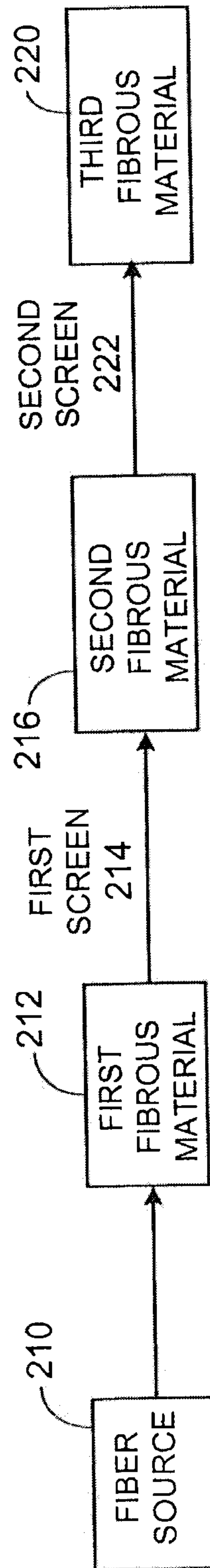


FIG. 2



**FIG. 4**

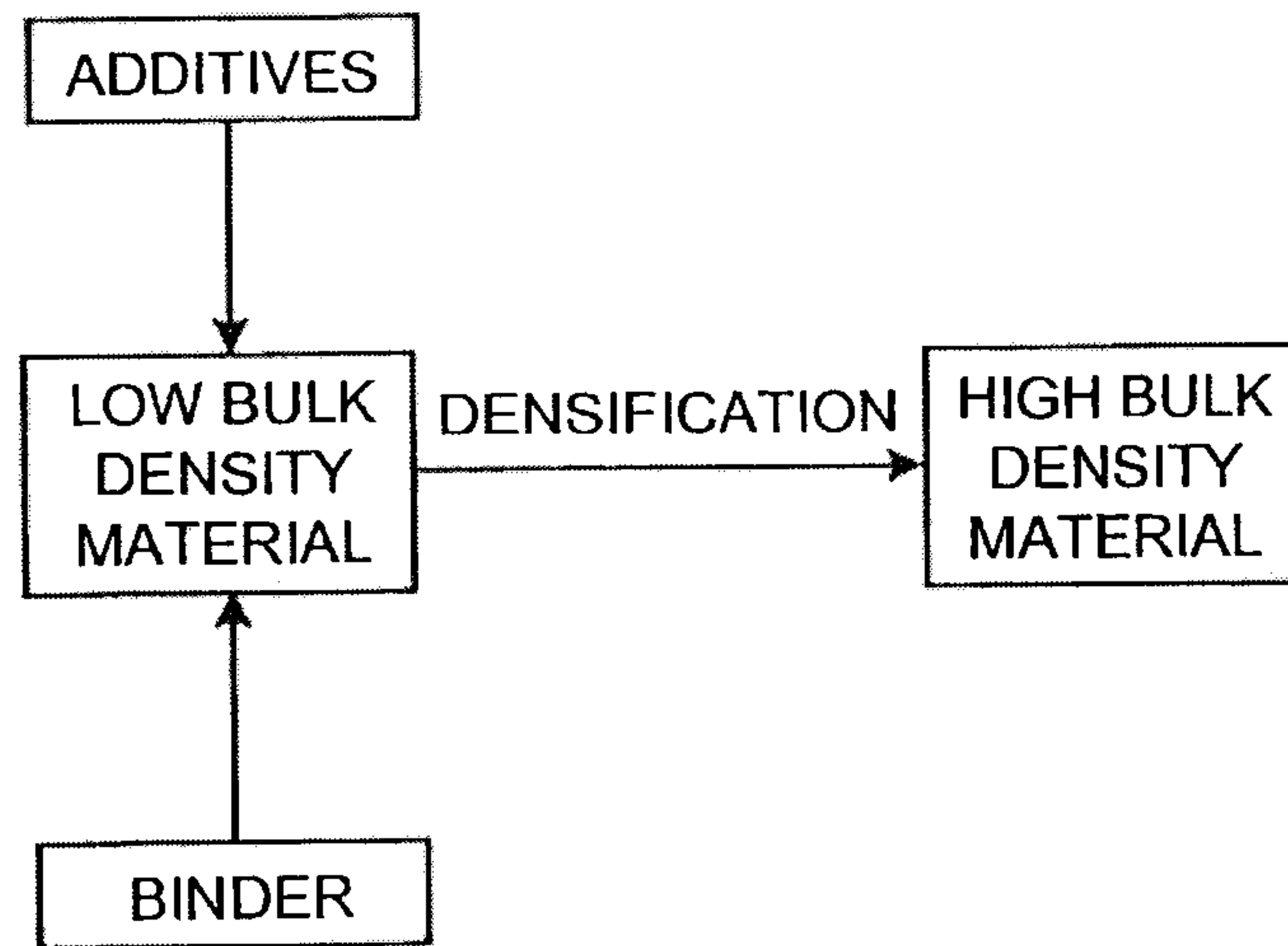


FIG. 5

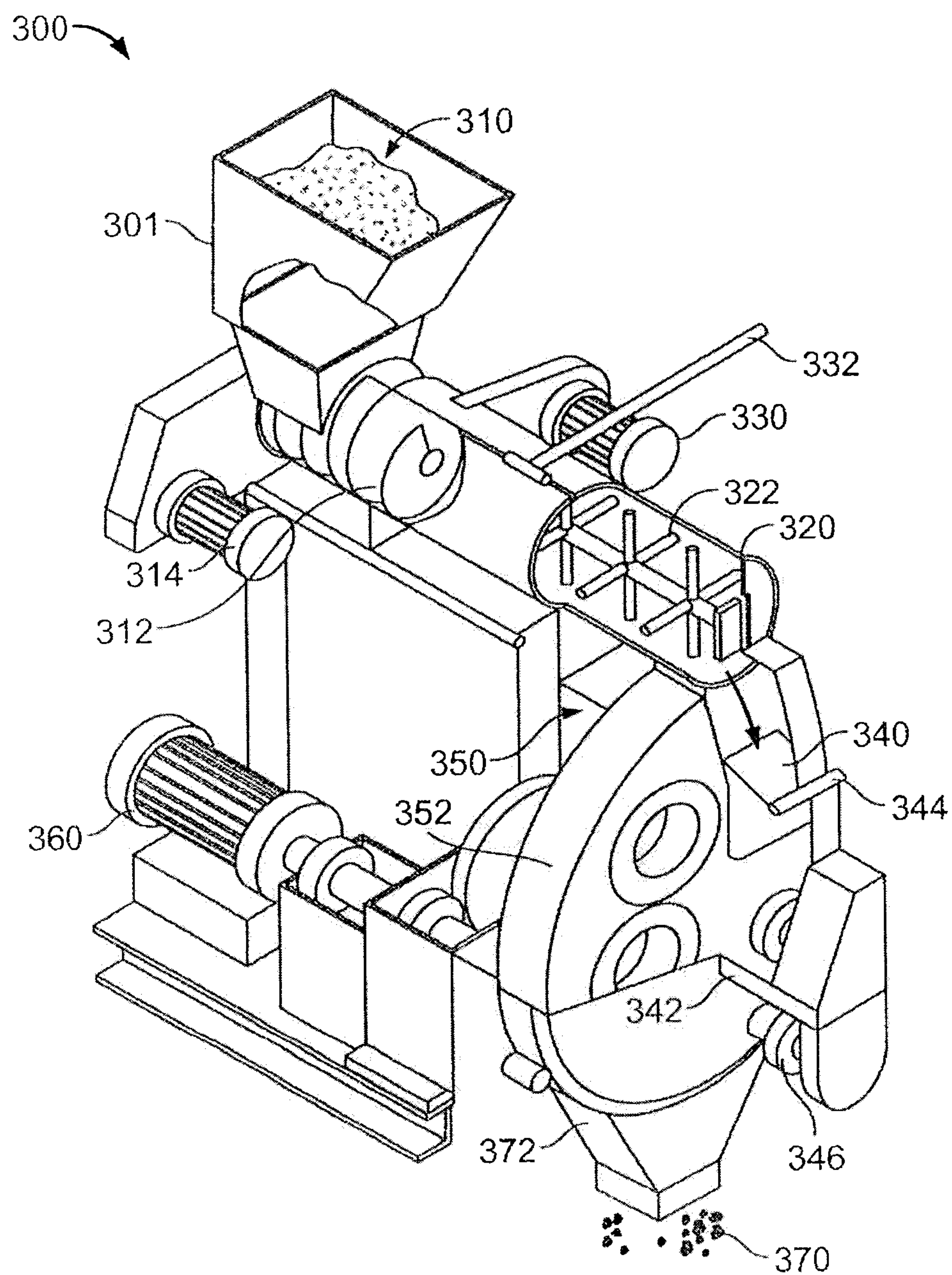


FIG. 6

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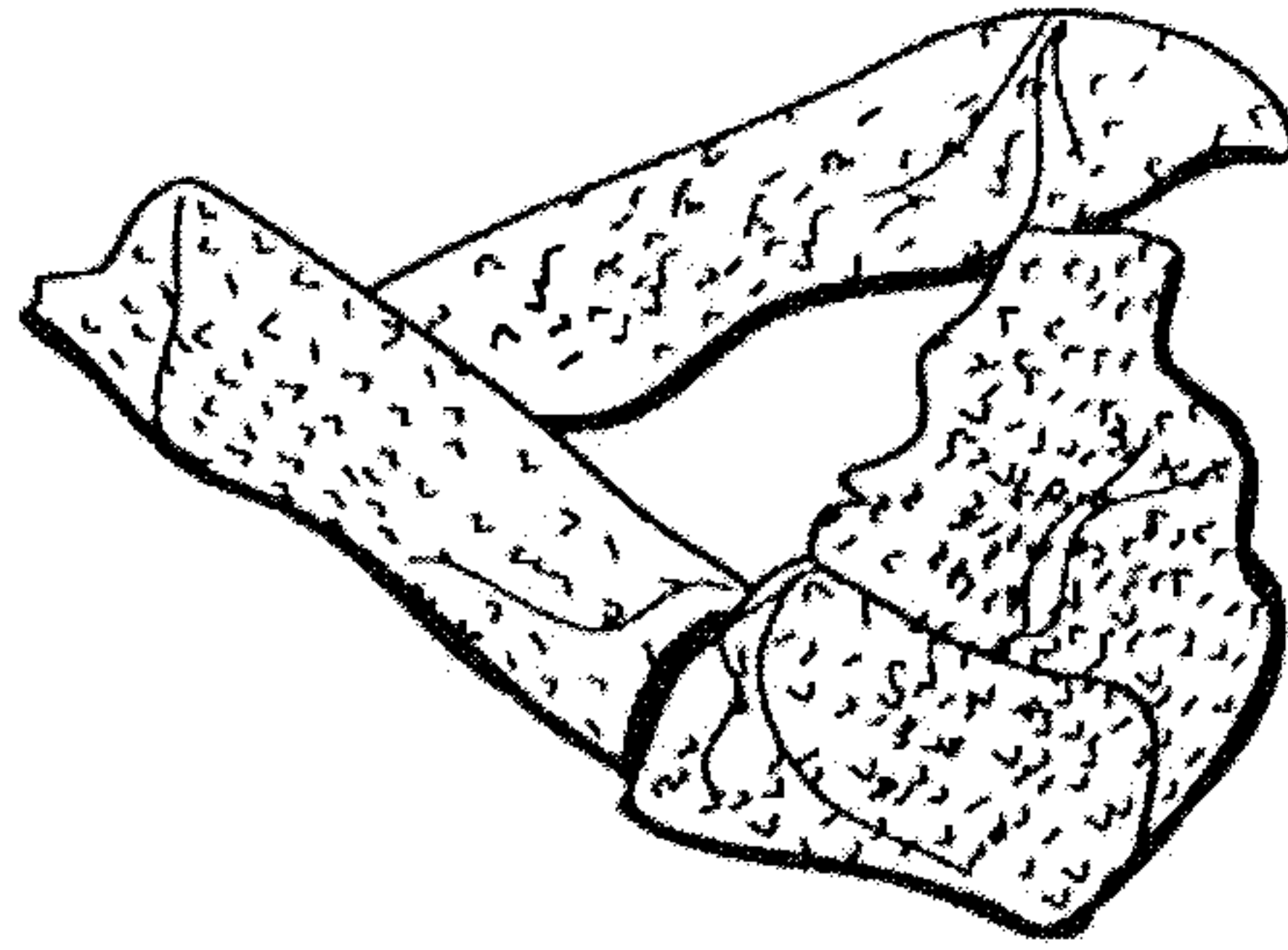


FIG. 7A

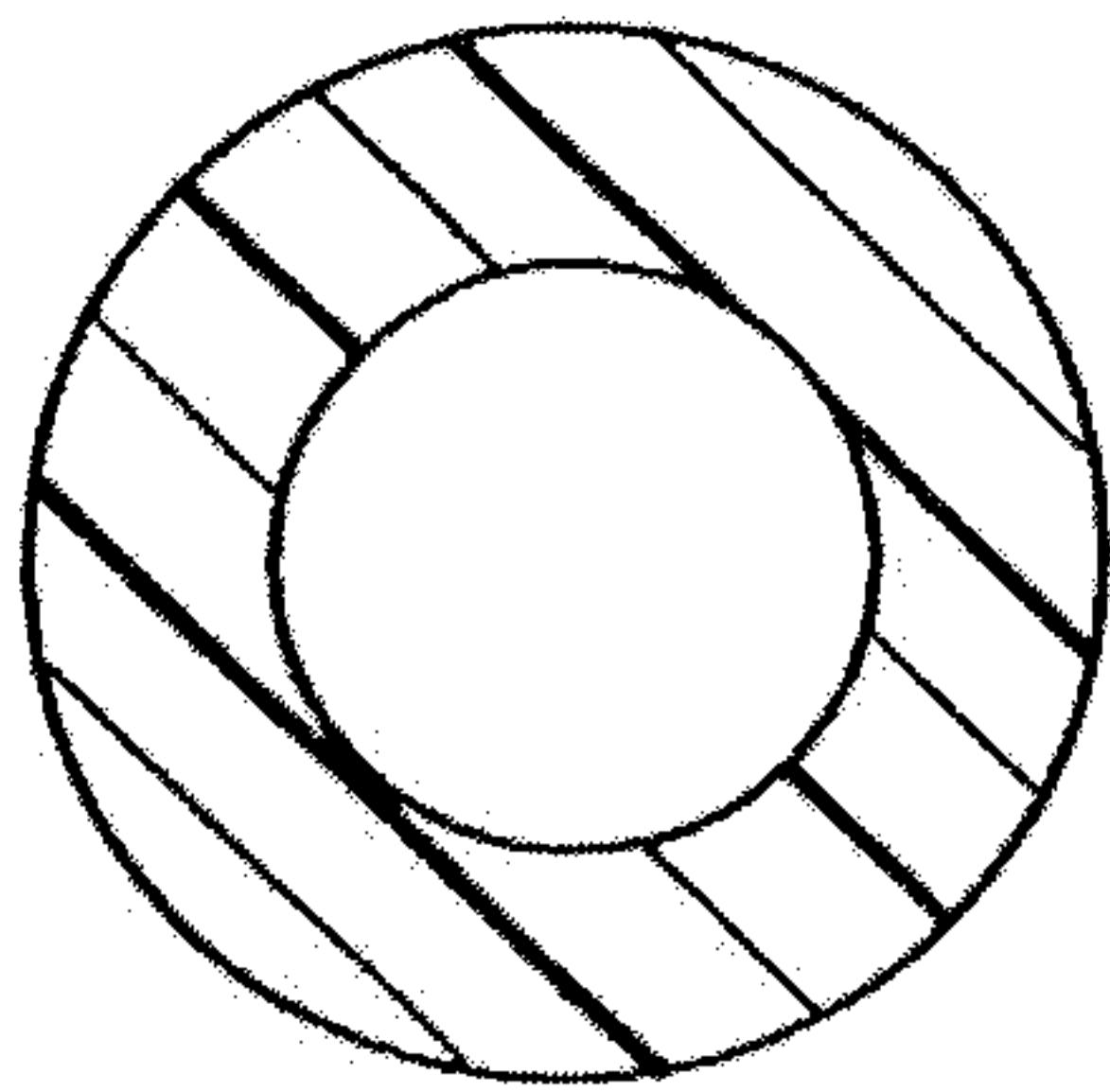


FIG. 7B

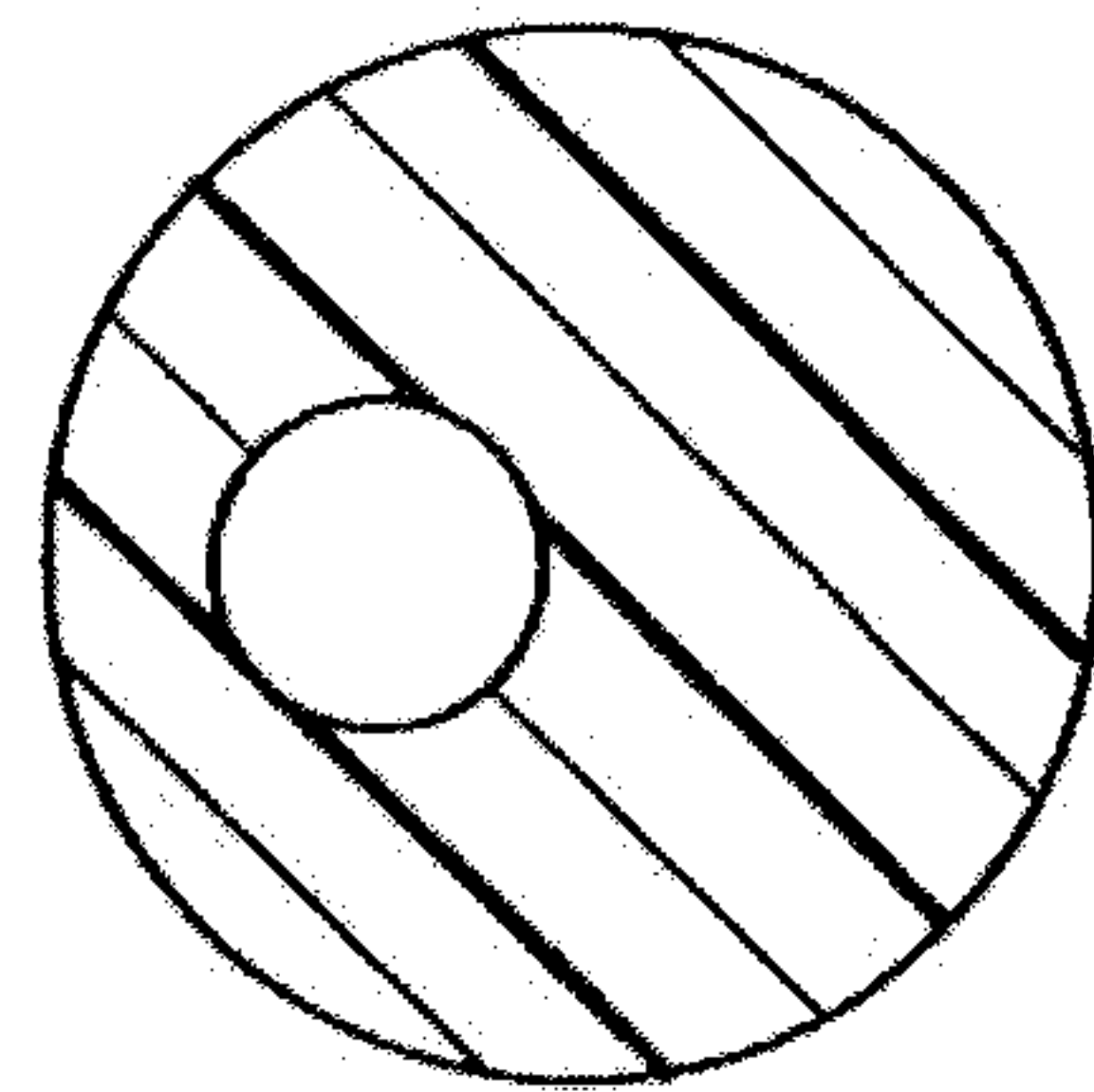


FIG. 7C

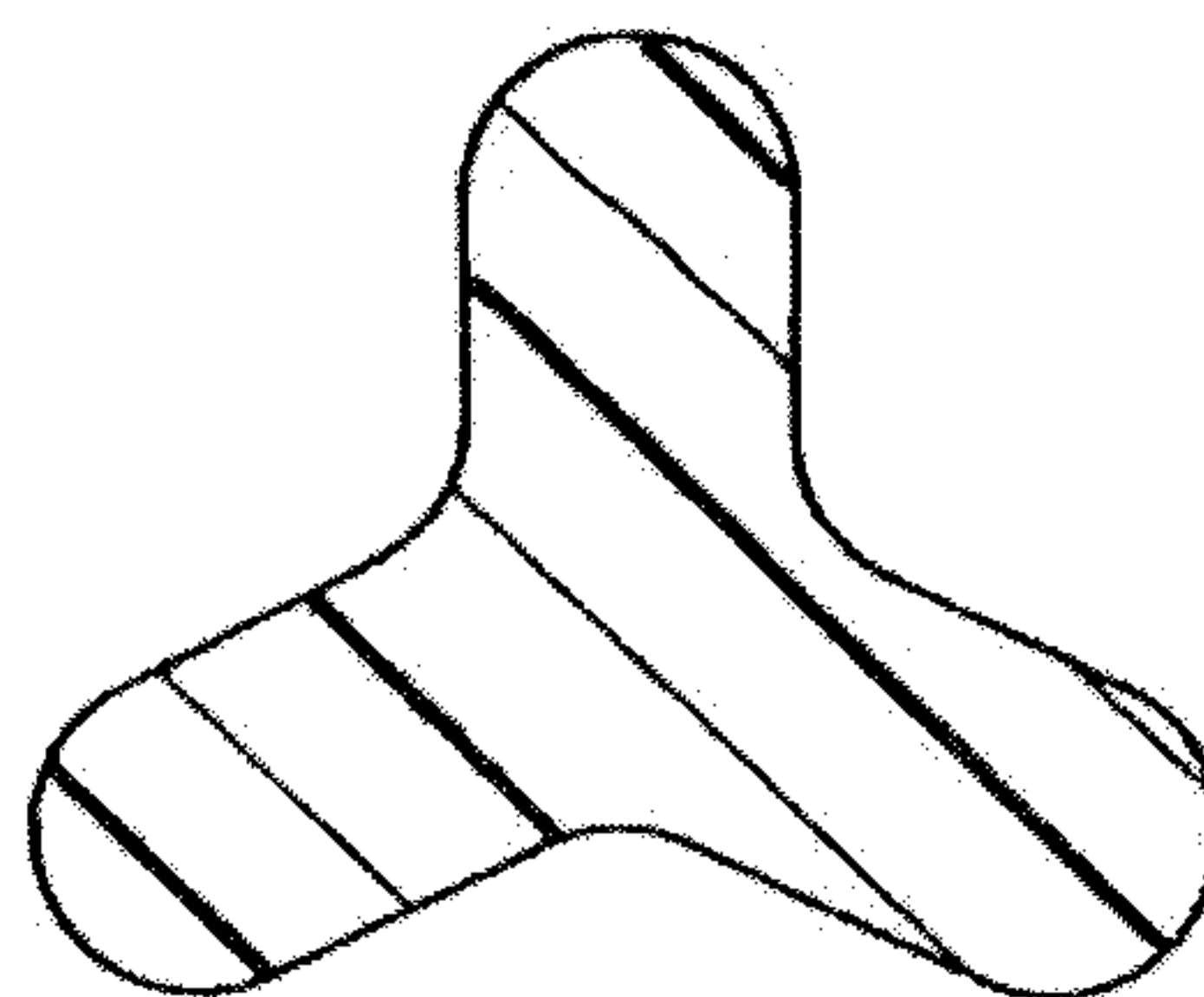


FIG. 7D

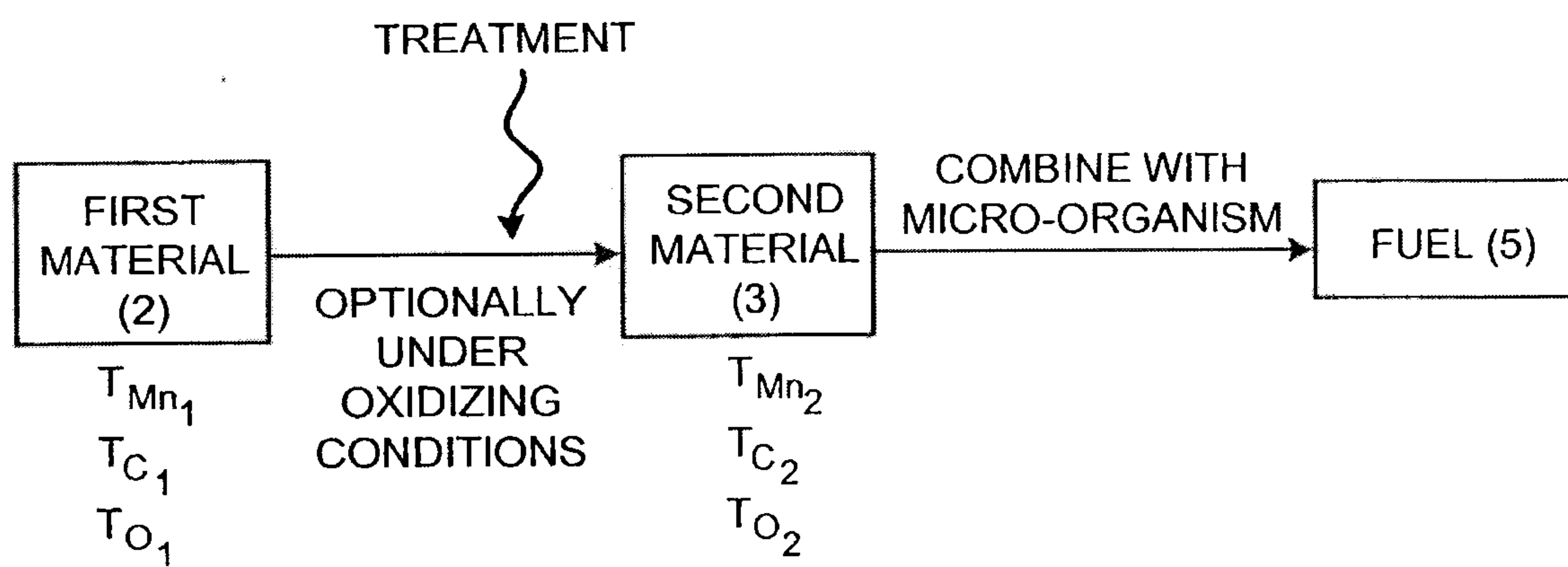


FIG. 8

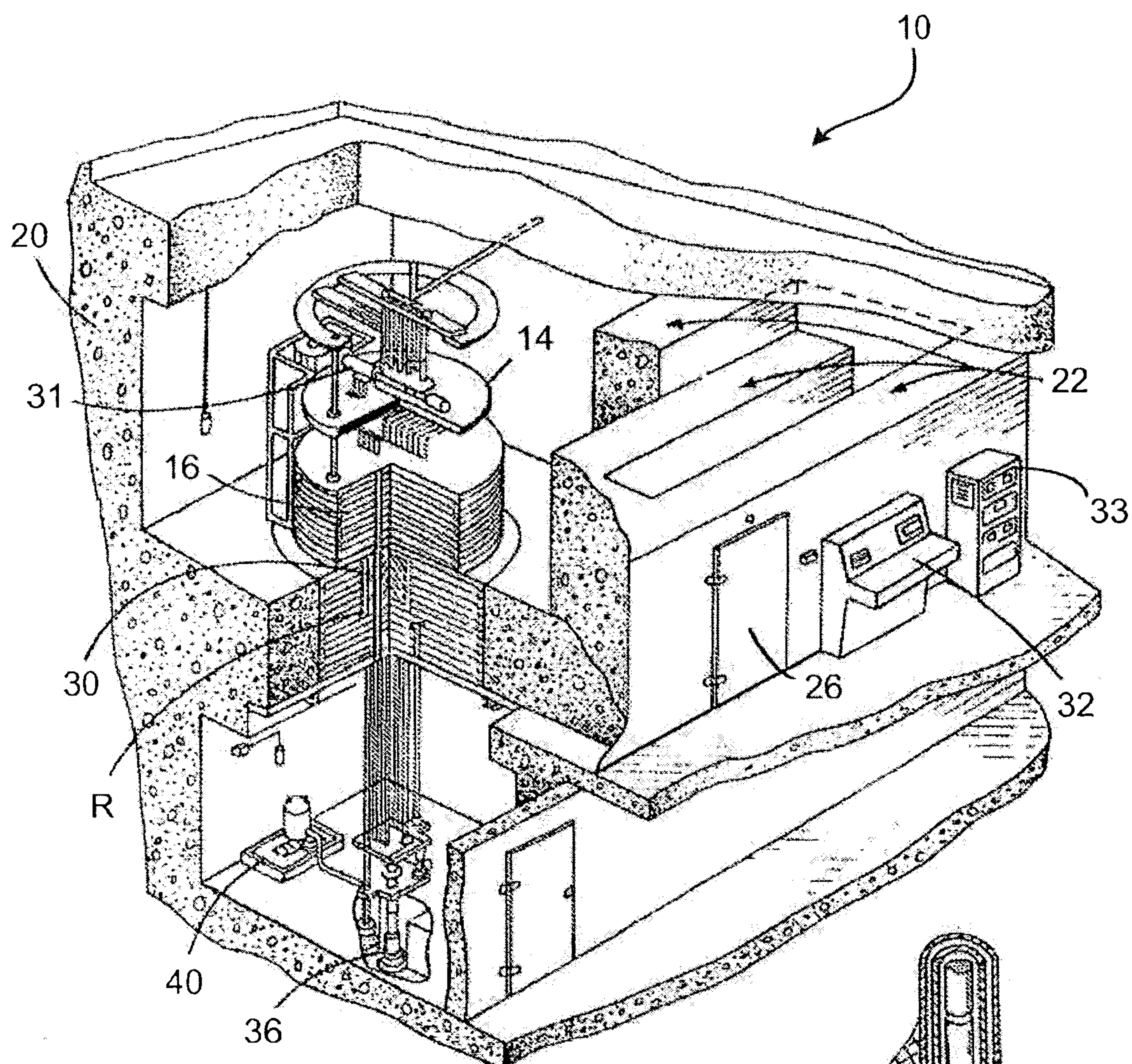


FIG. 9

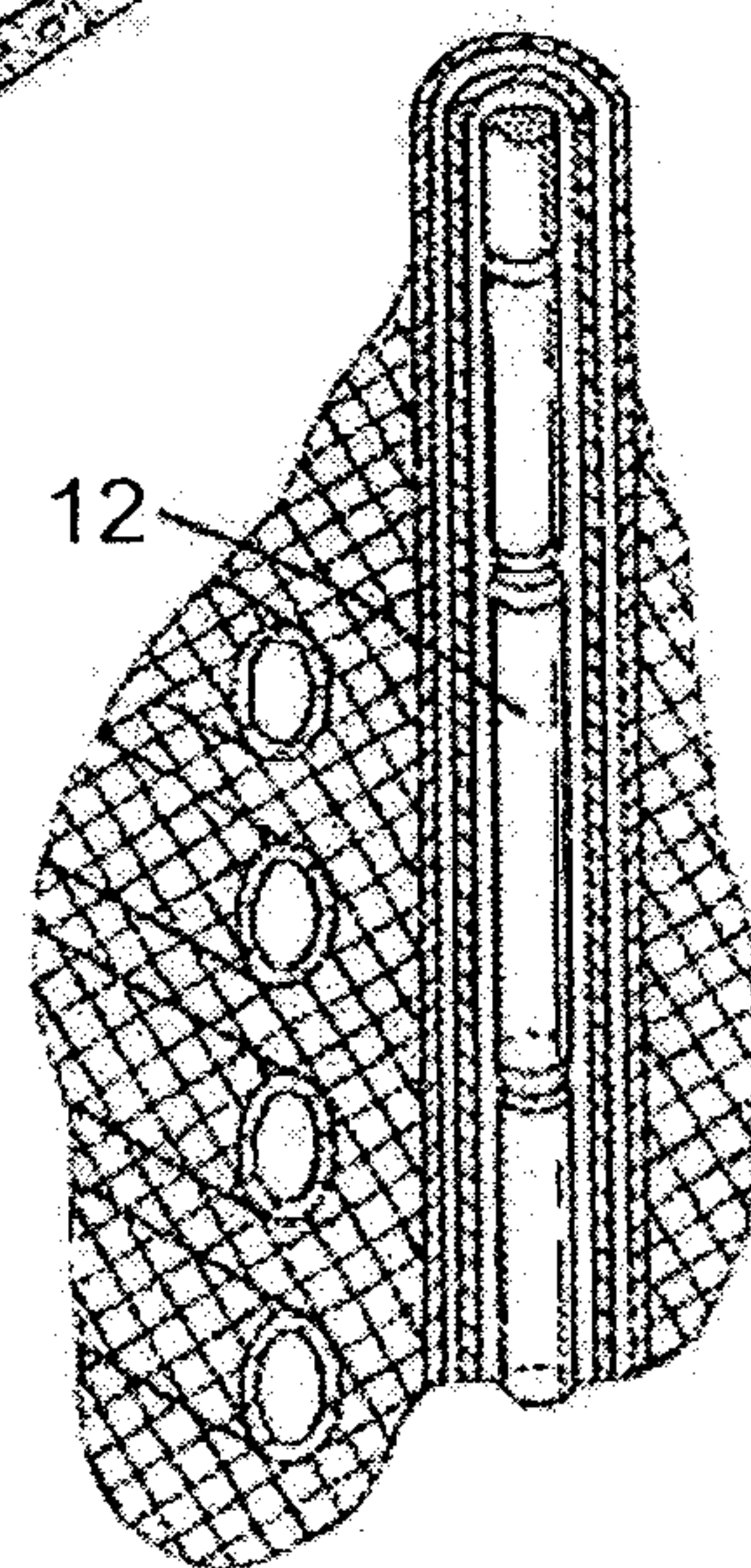


FIG. 10

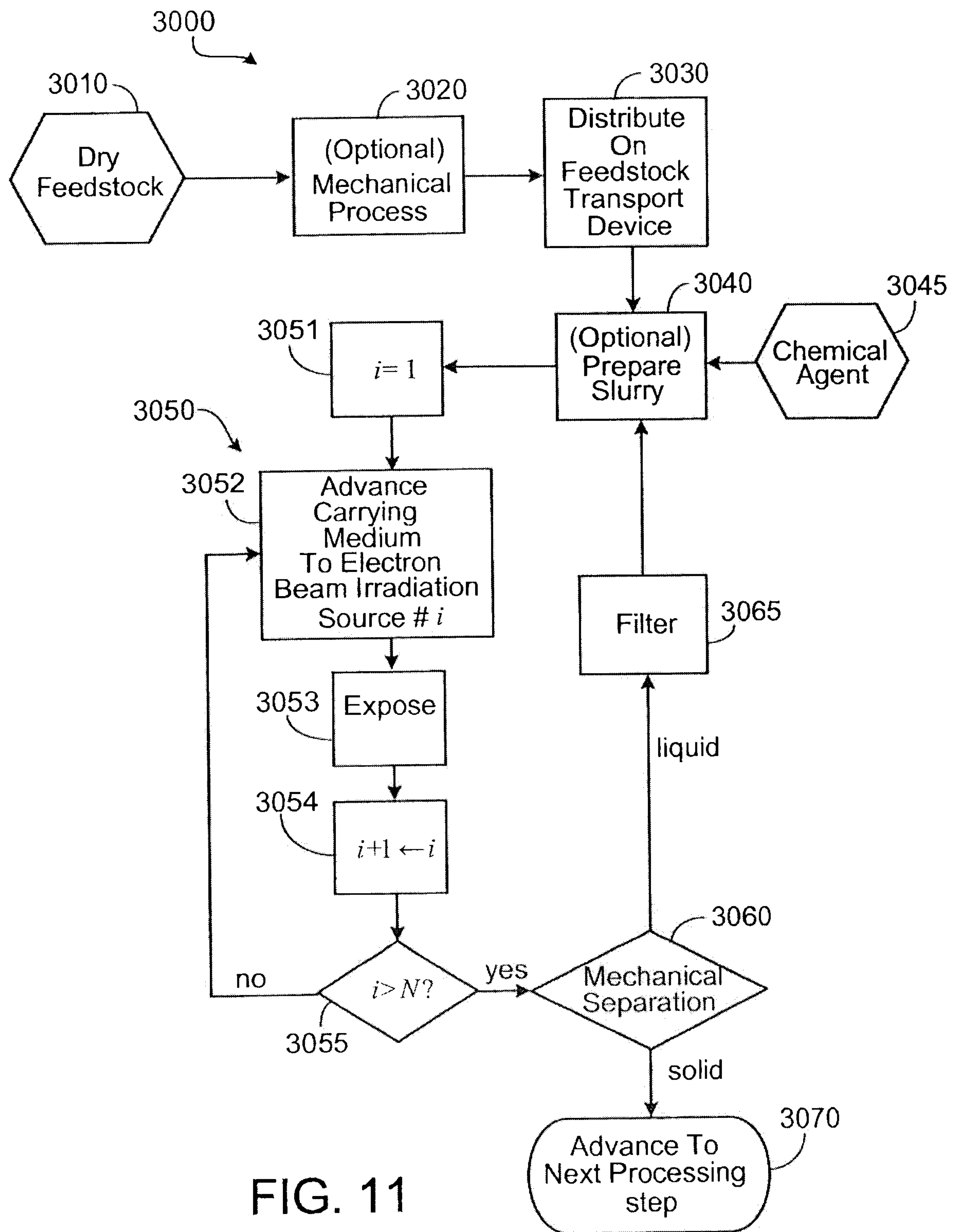


FIG. 11

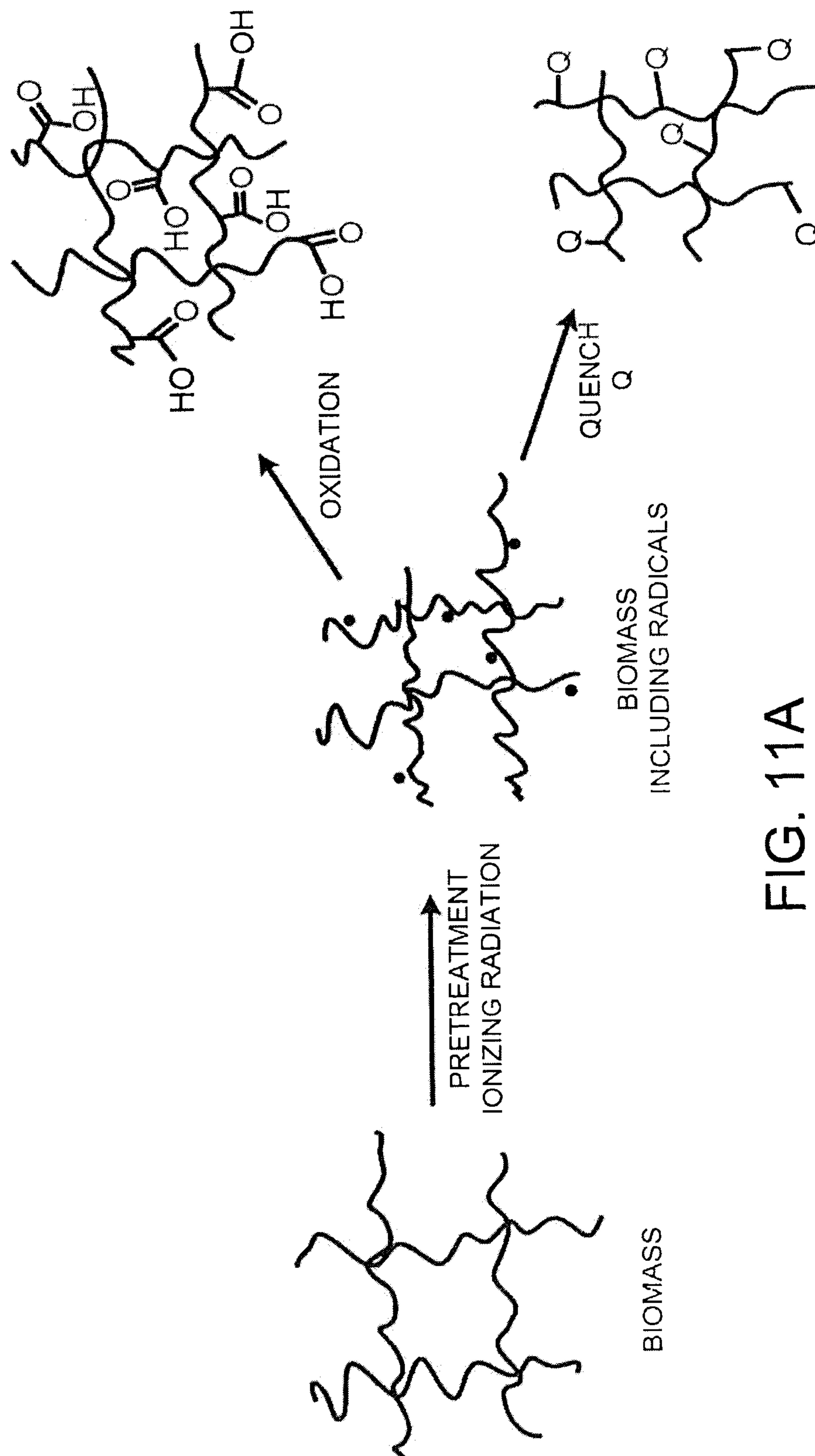
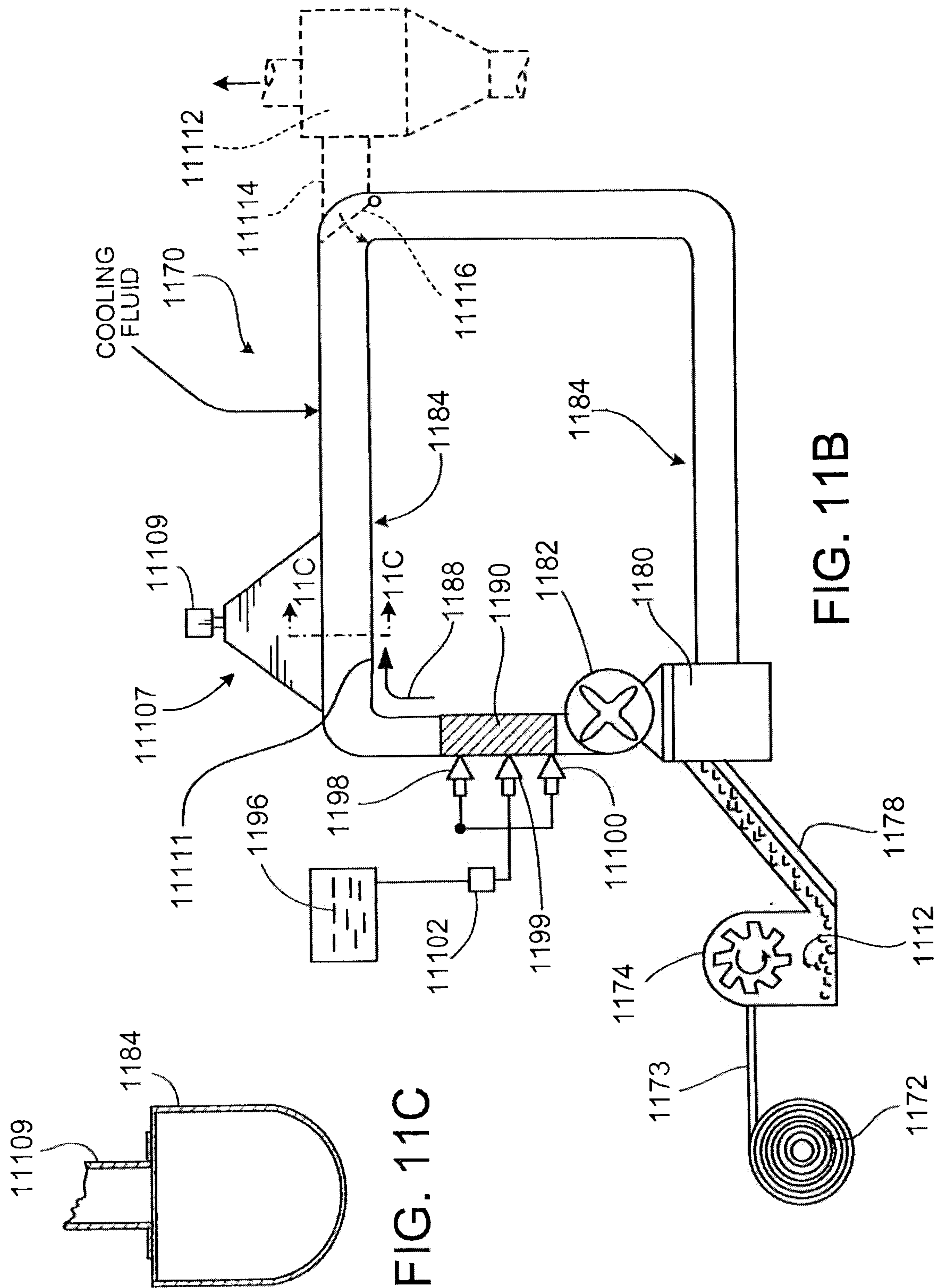


FIG. 11A

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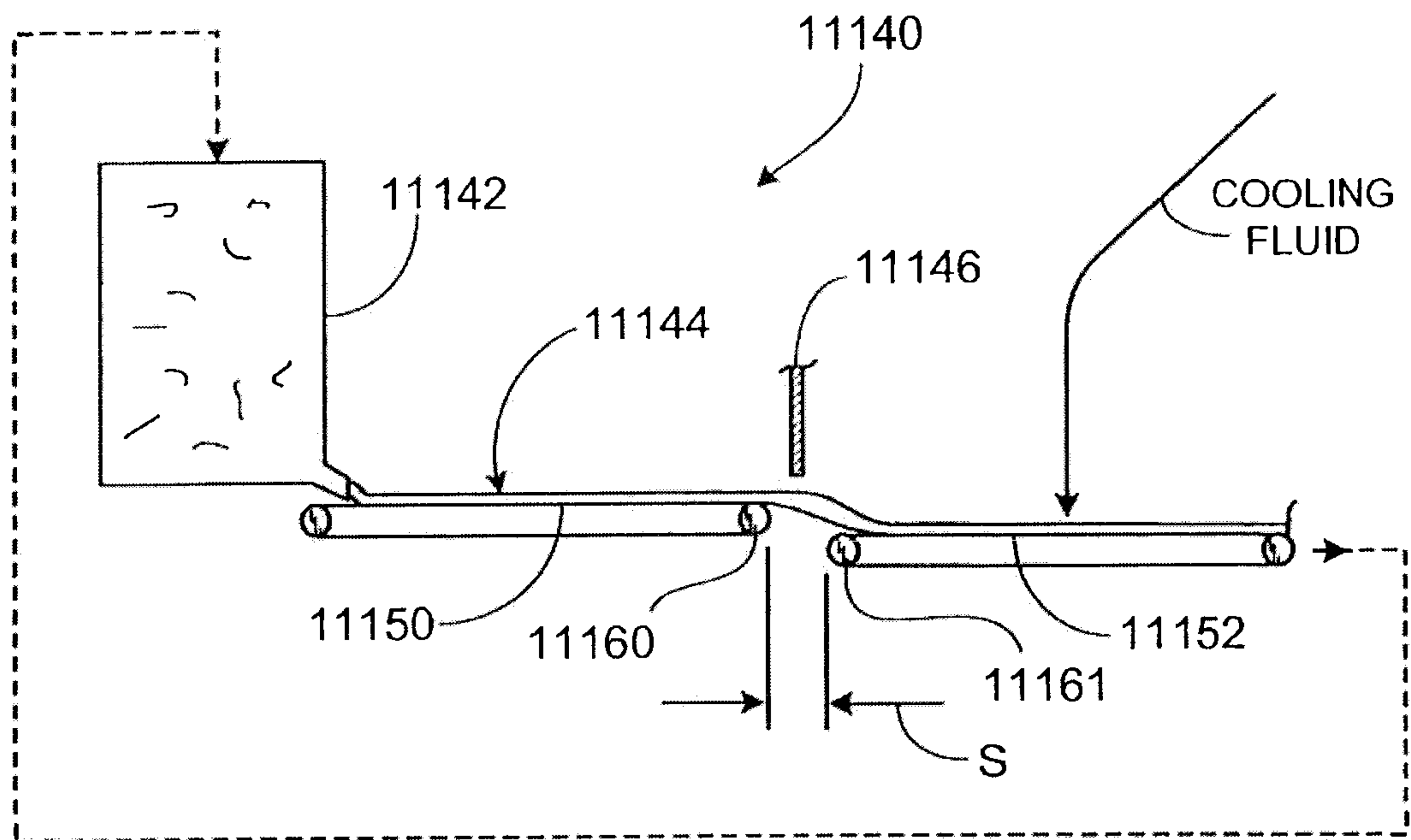


FIG. 11E

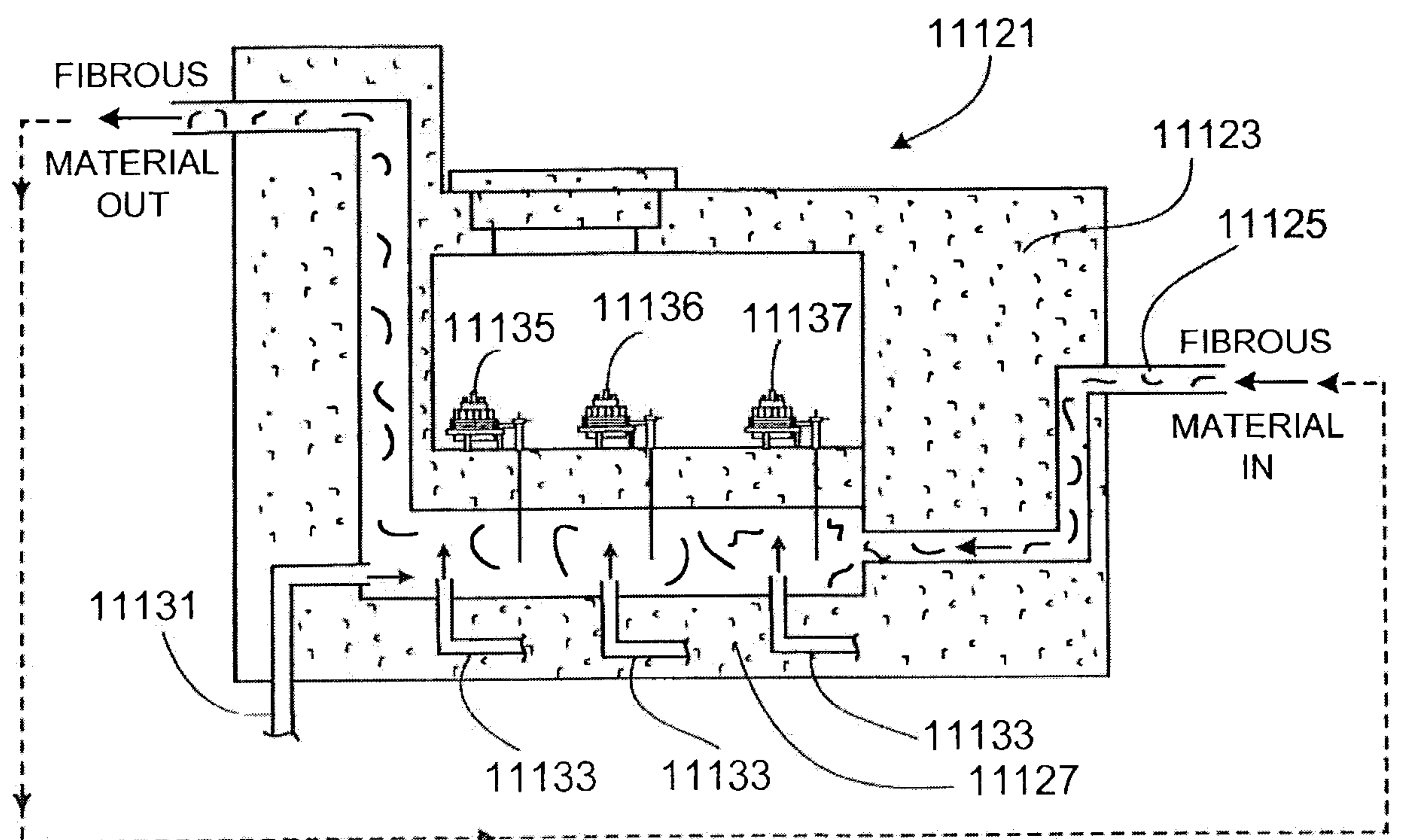


FIG. 11D

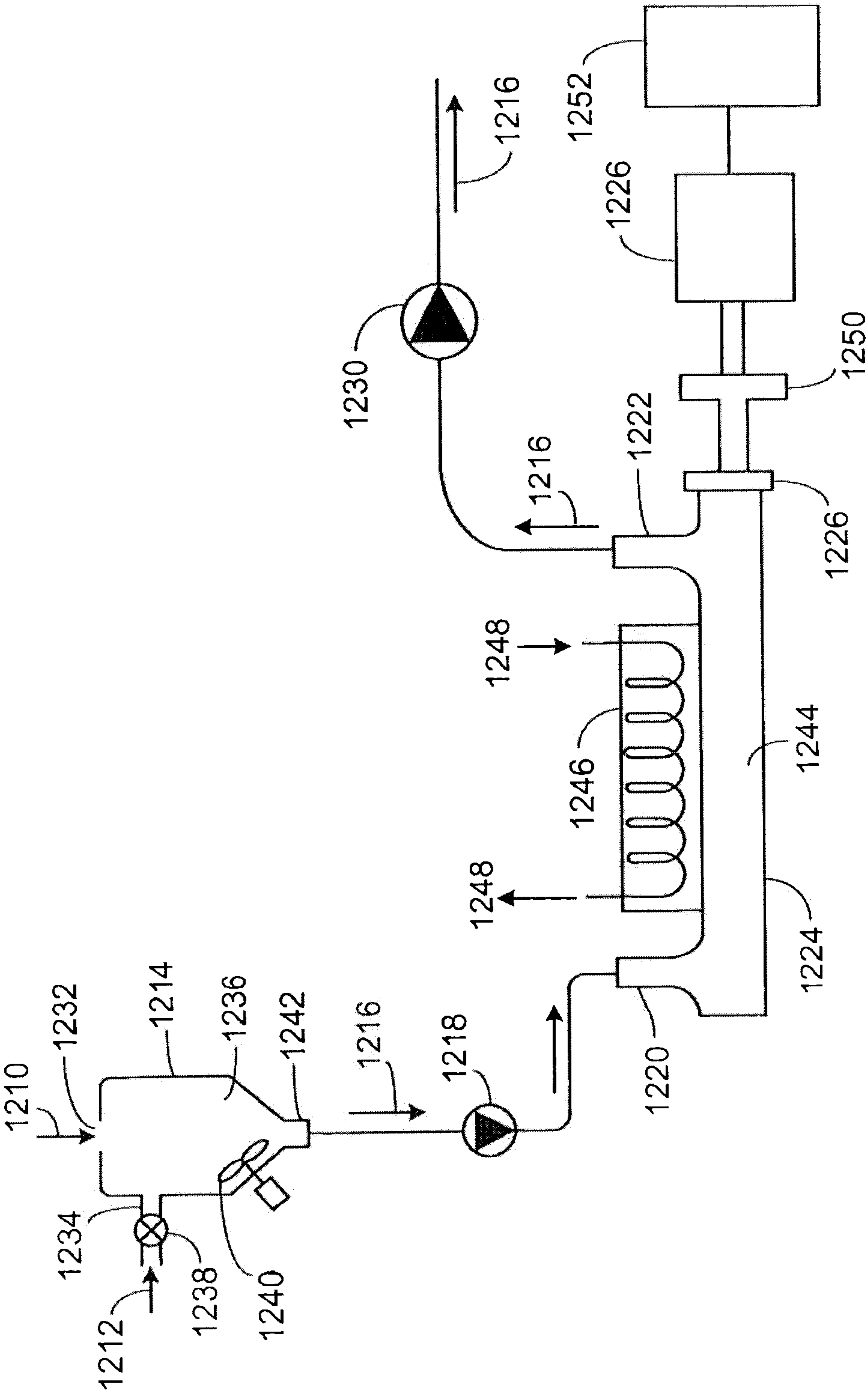


FIG. 12

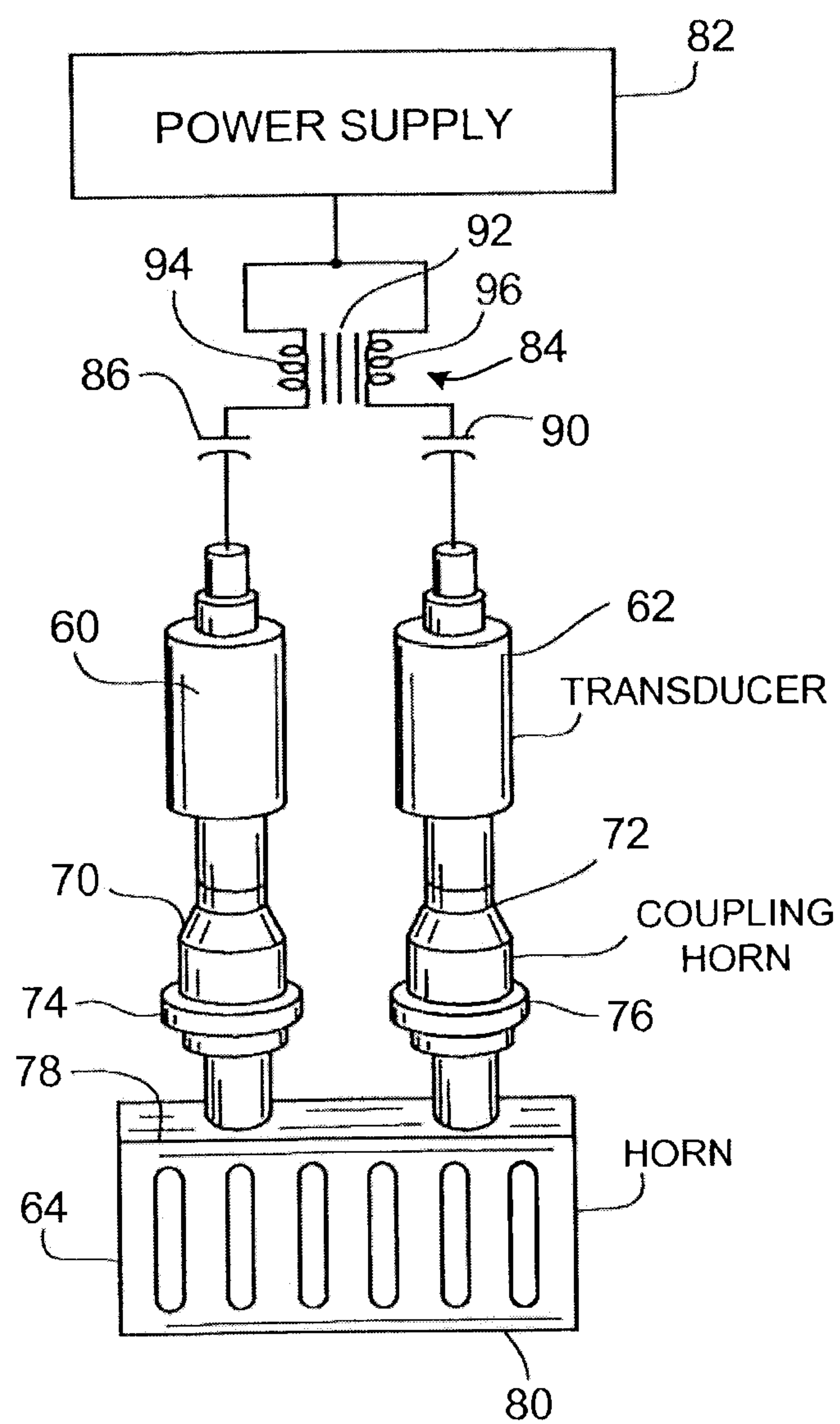
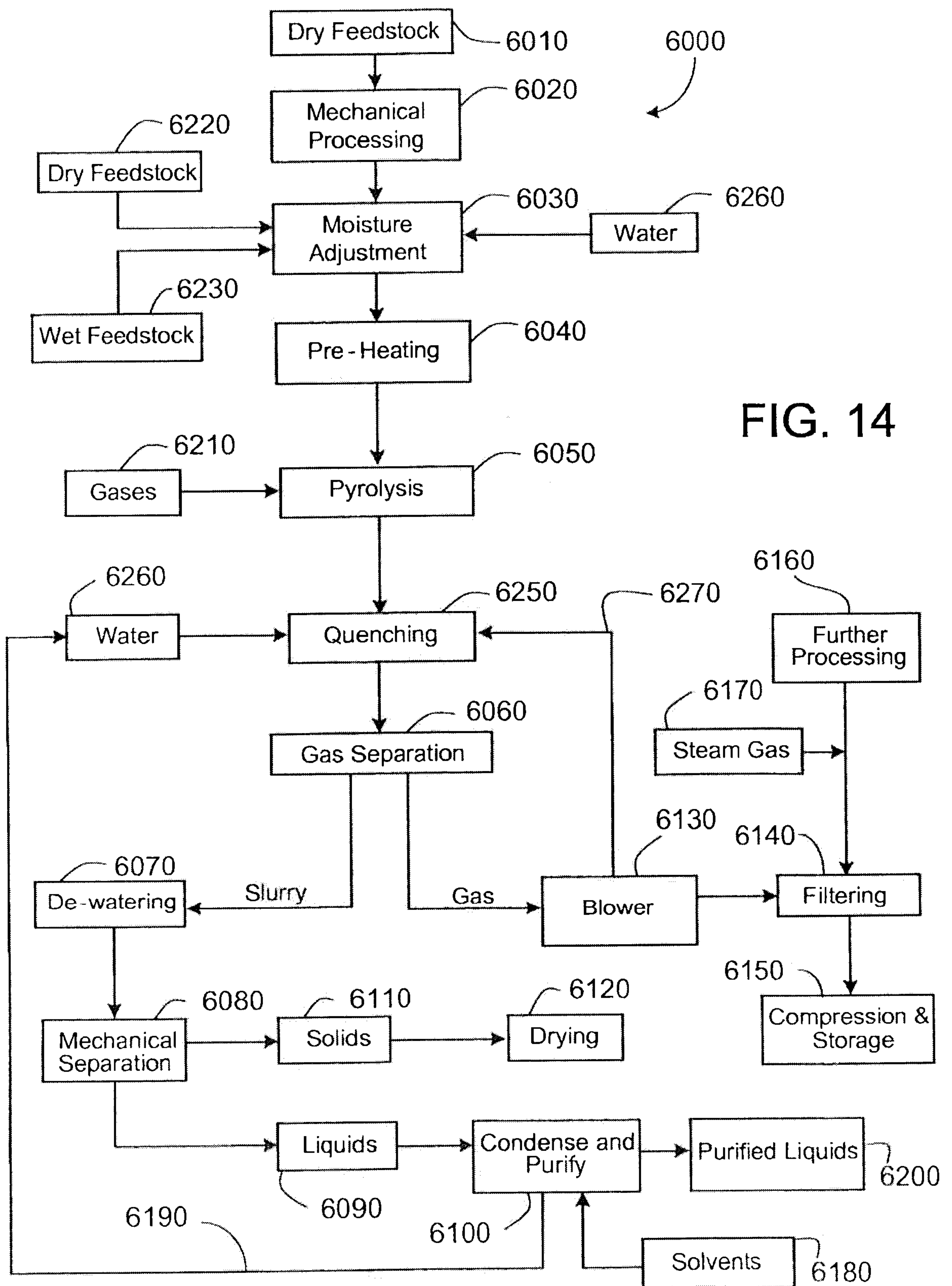
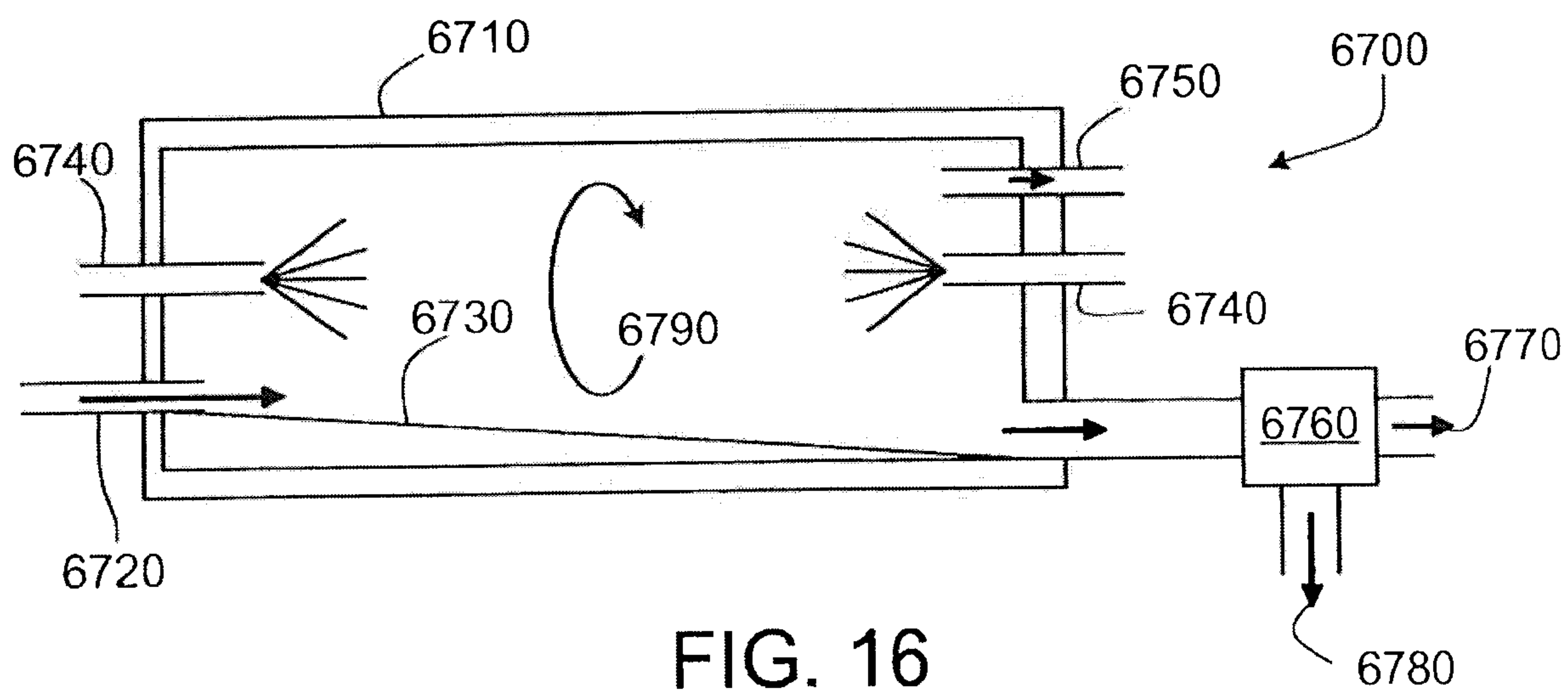
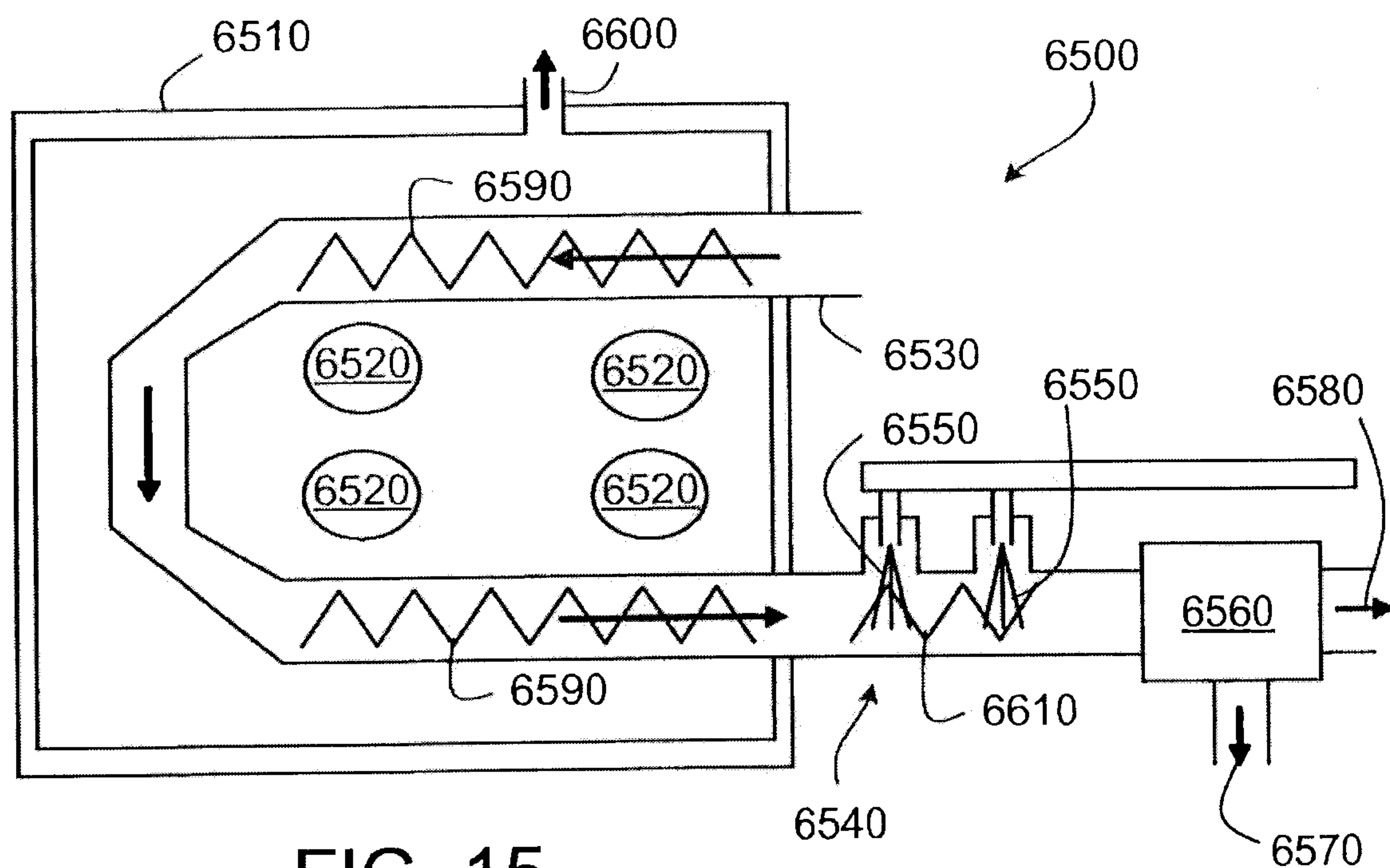


FIG. 13





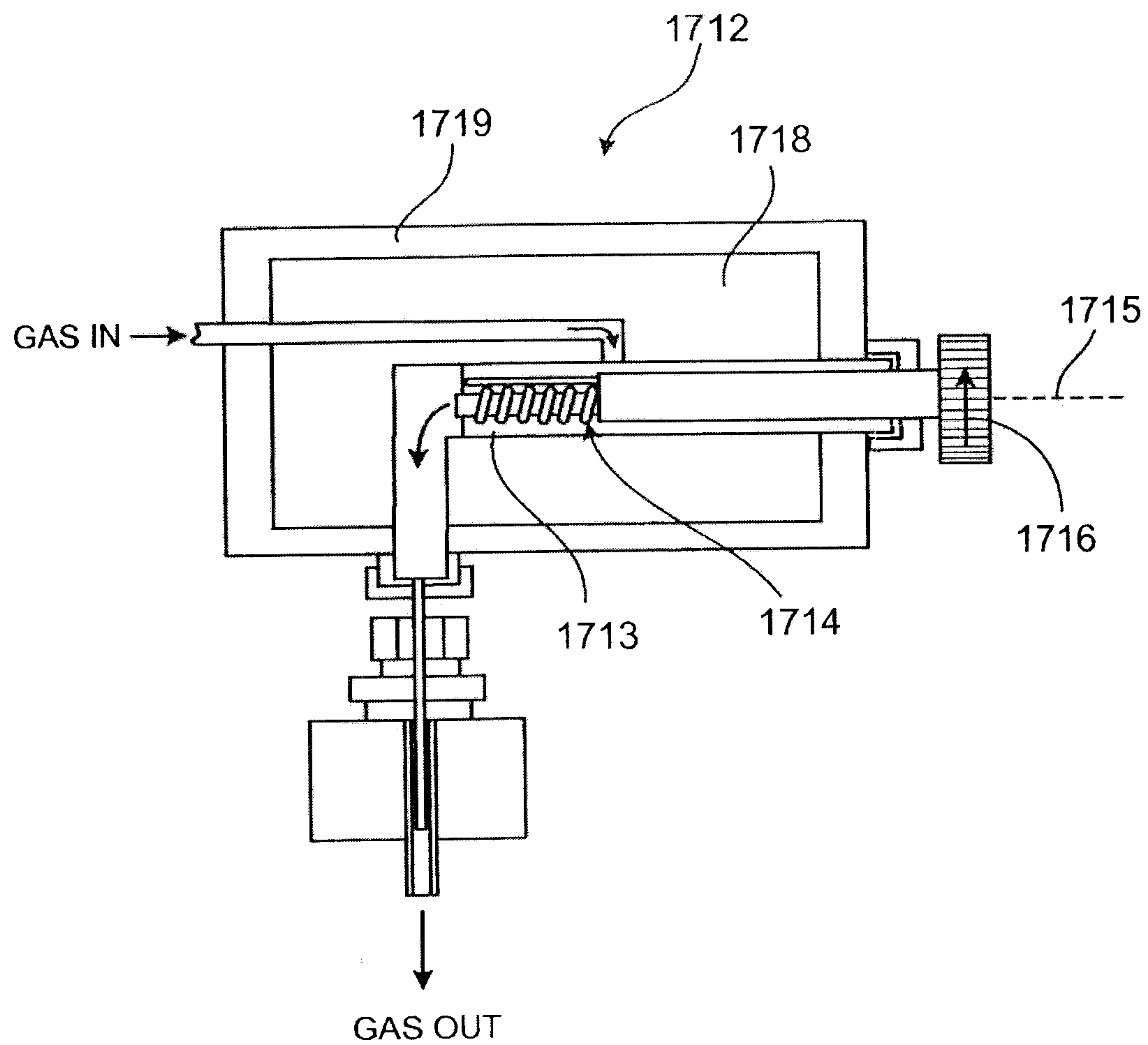


FIG. 17

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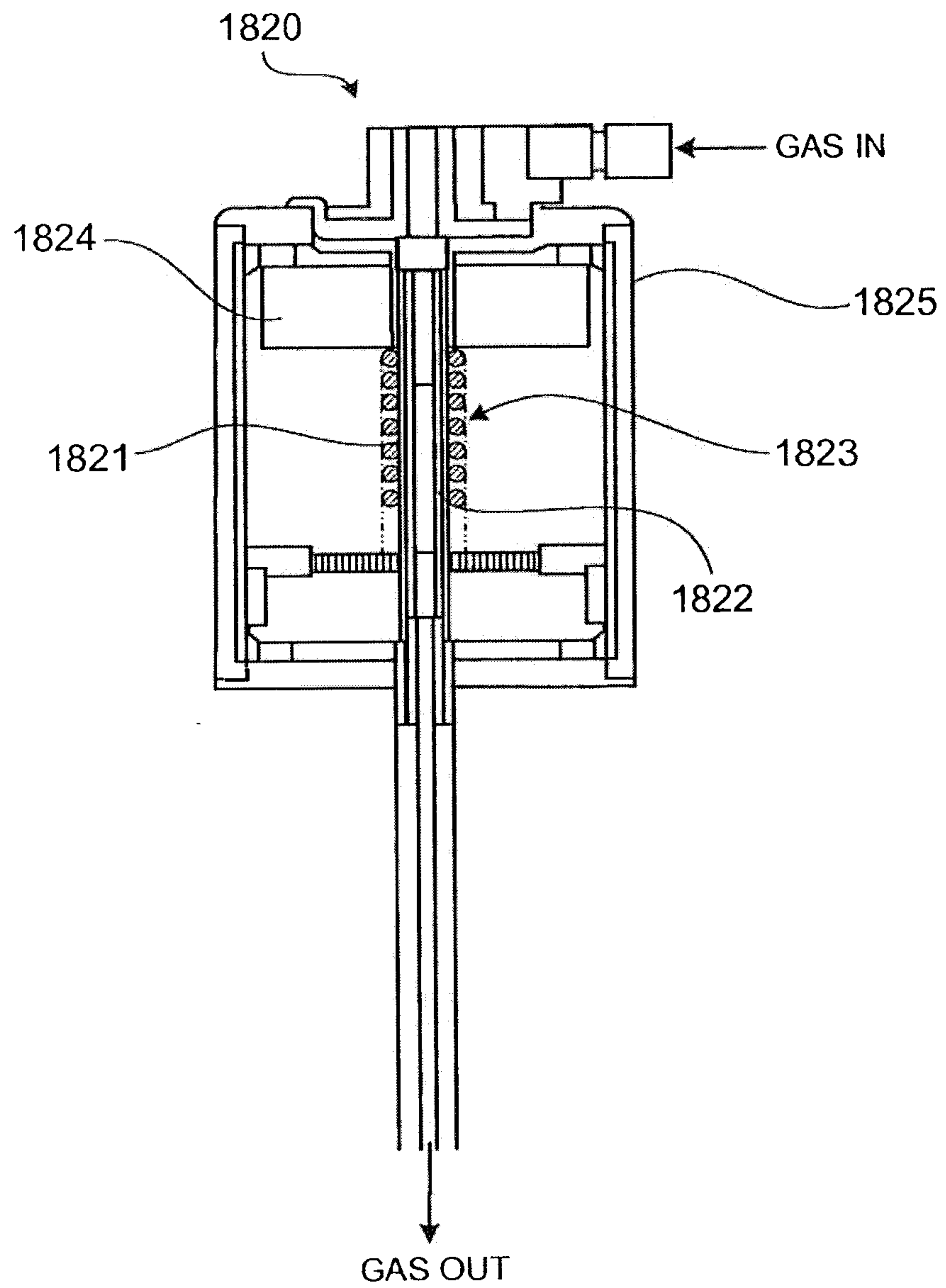


FIG. 18

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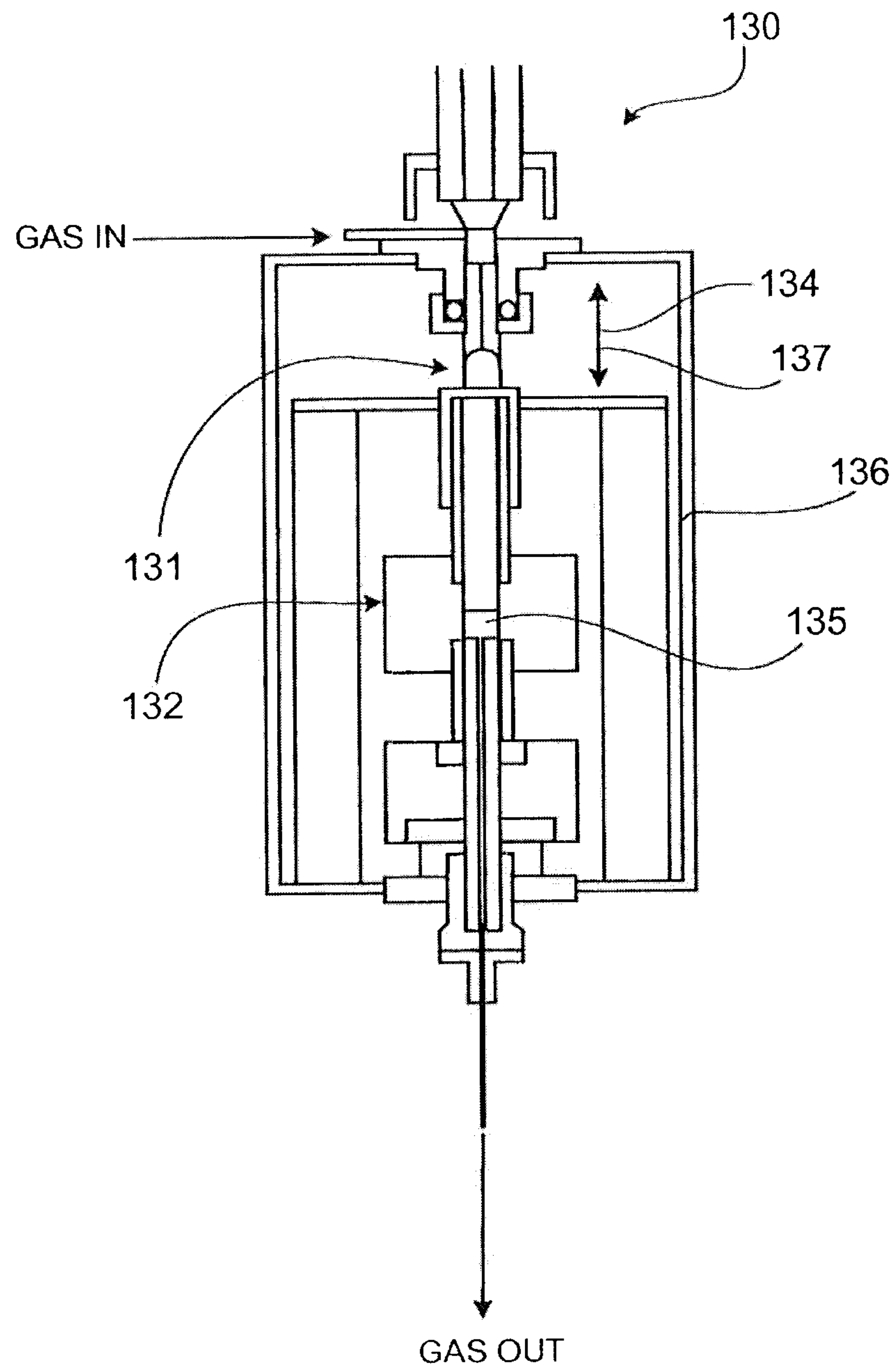


FIG. 19

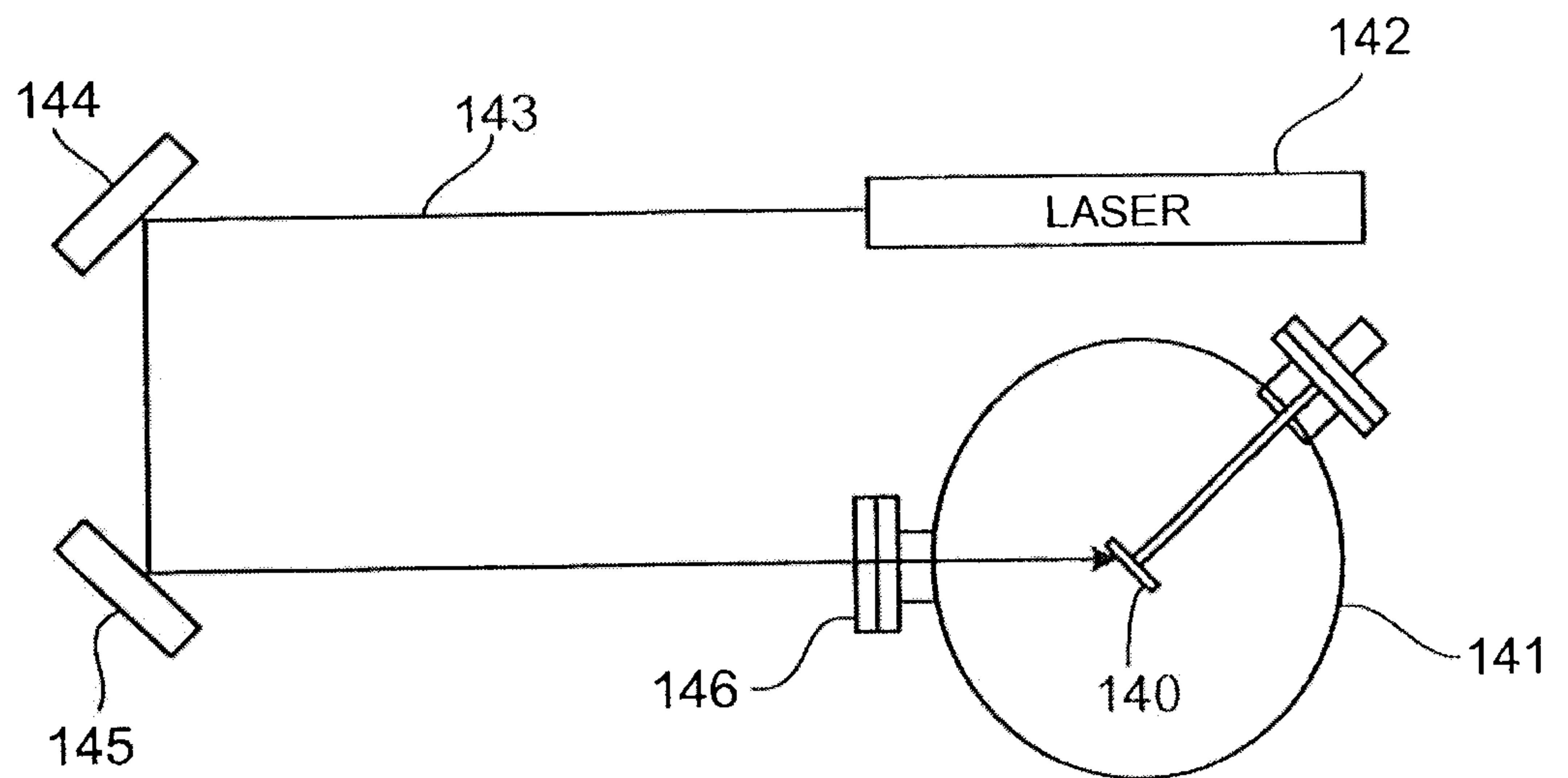


FIG. 20

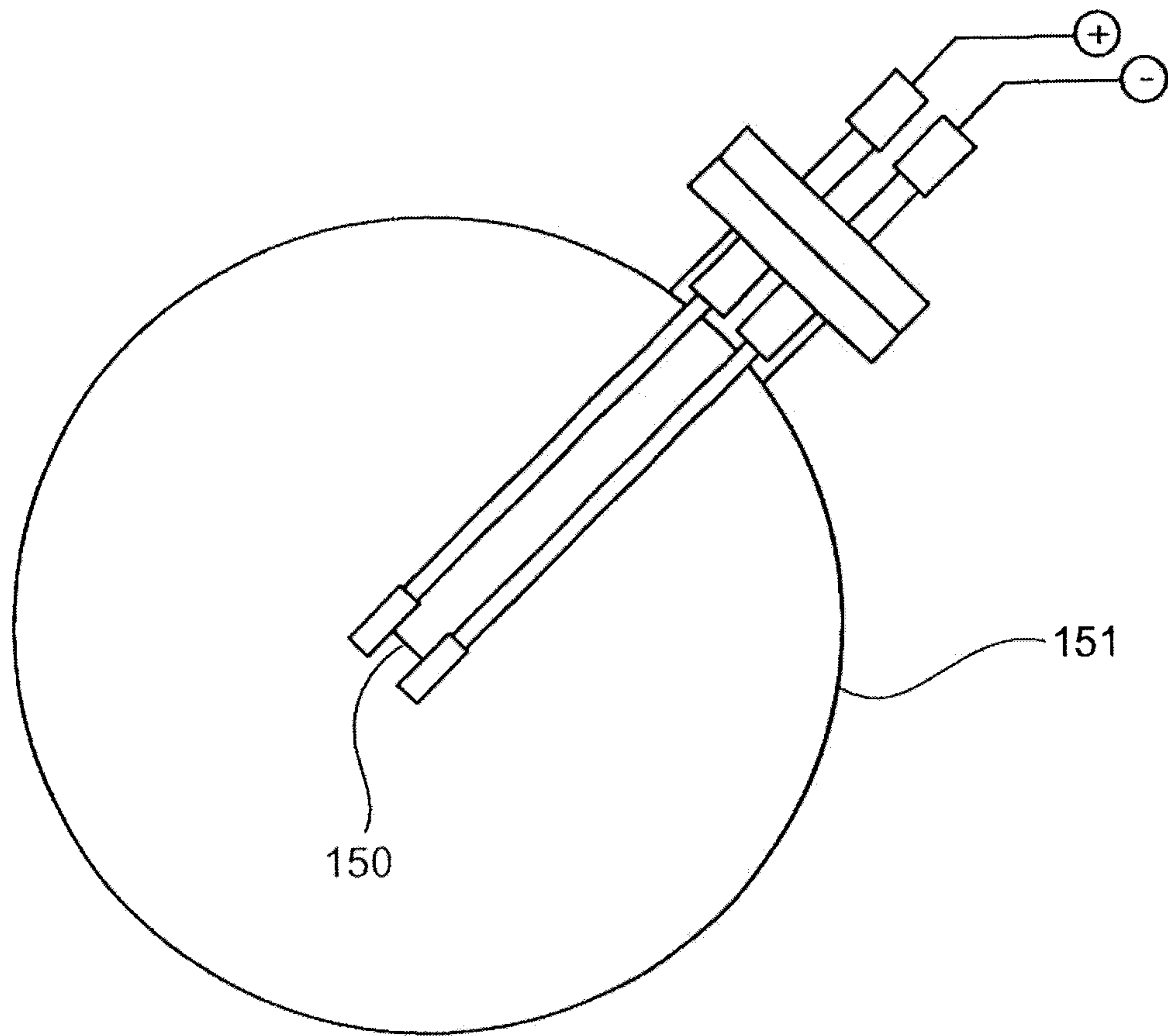
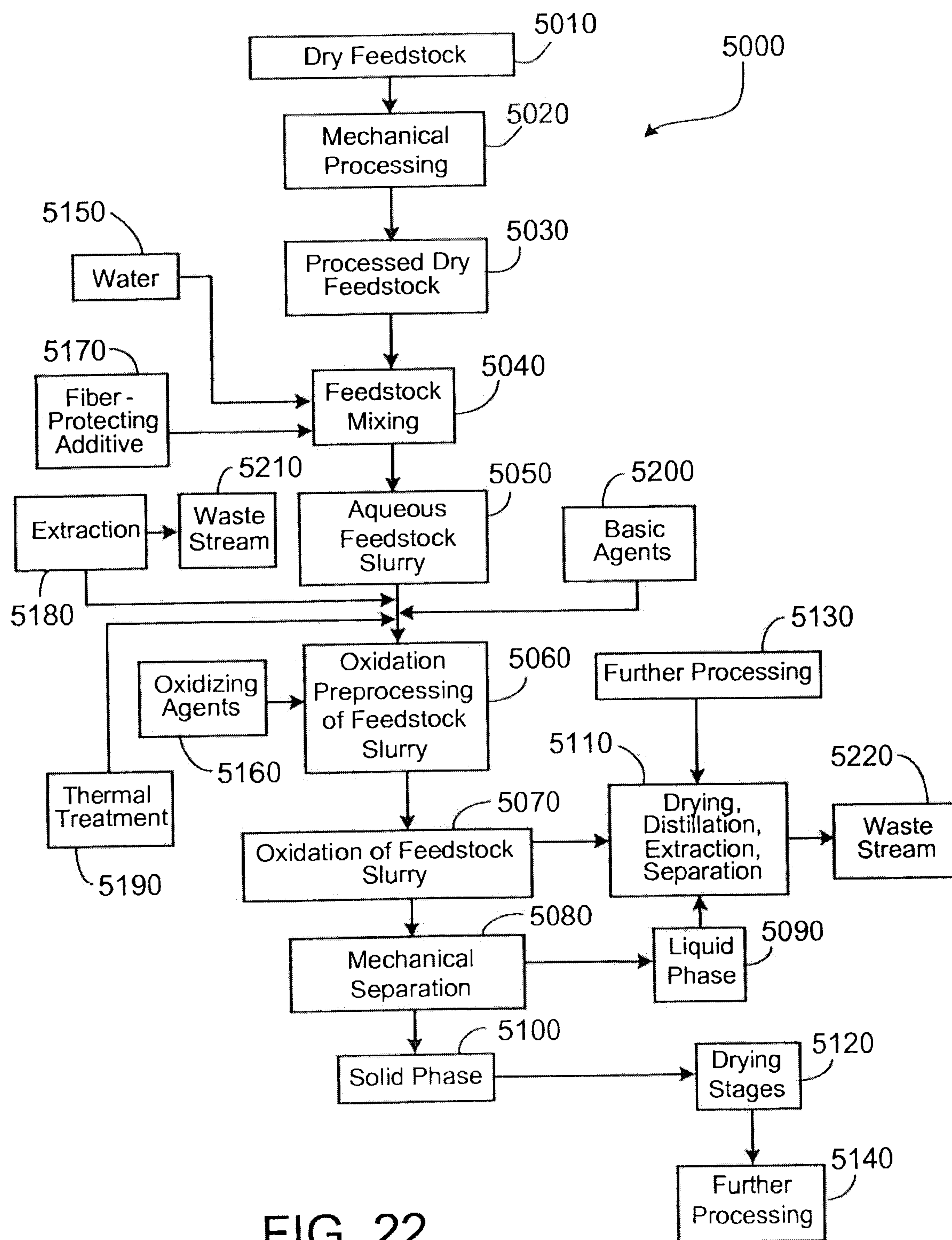
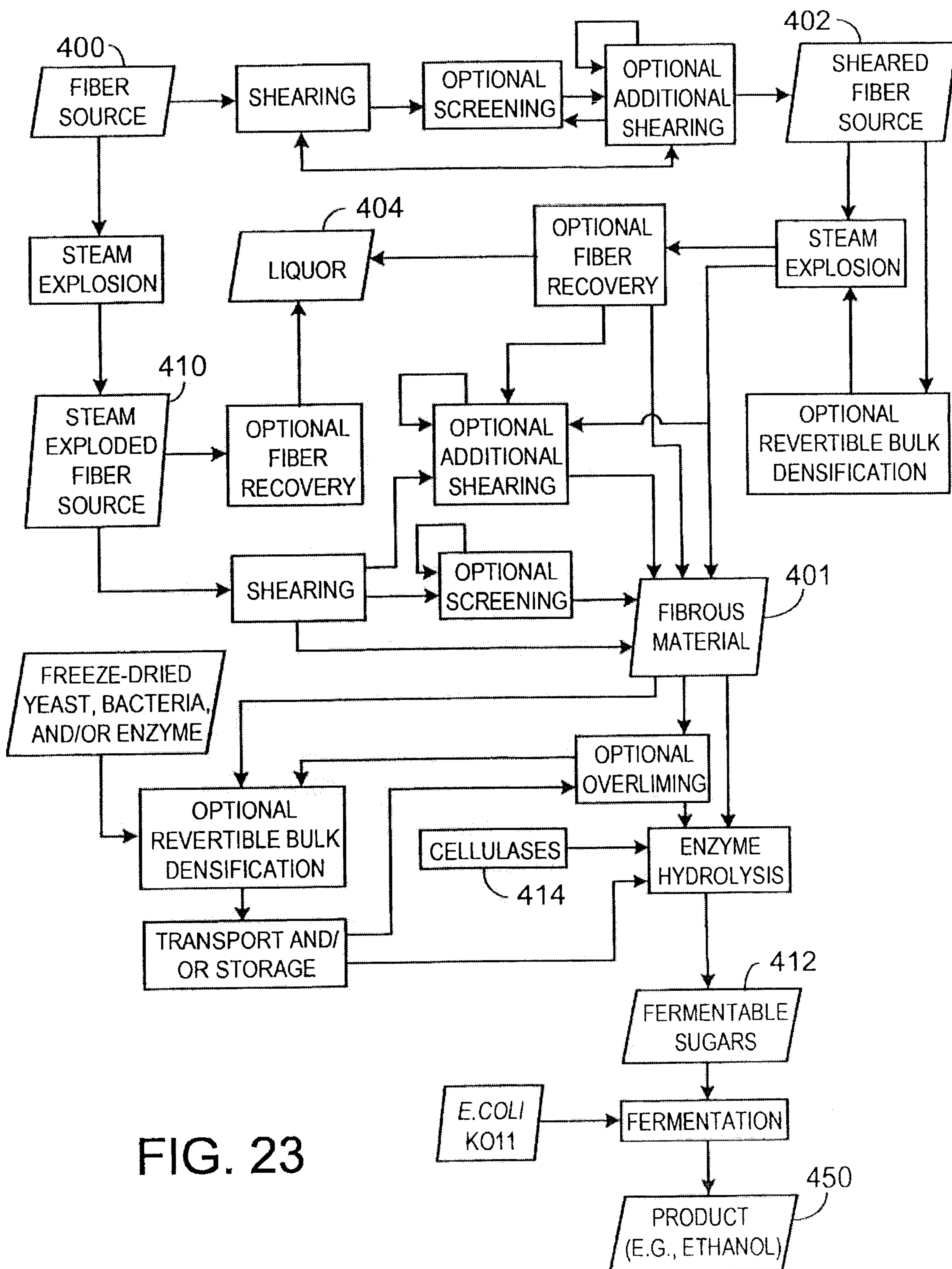


FIG. 21





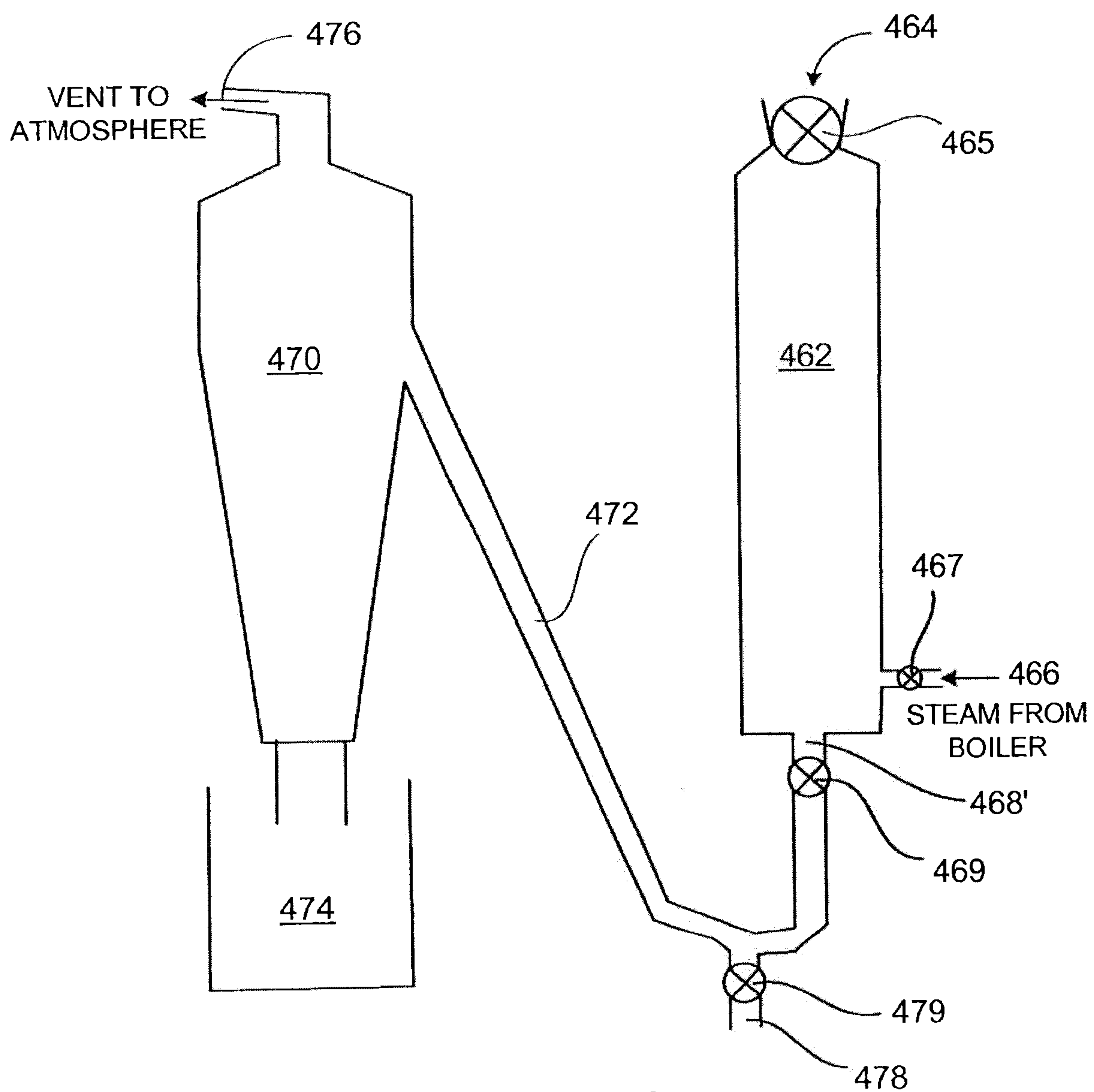


FIG. 24

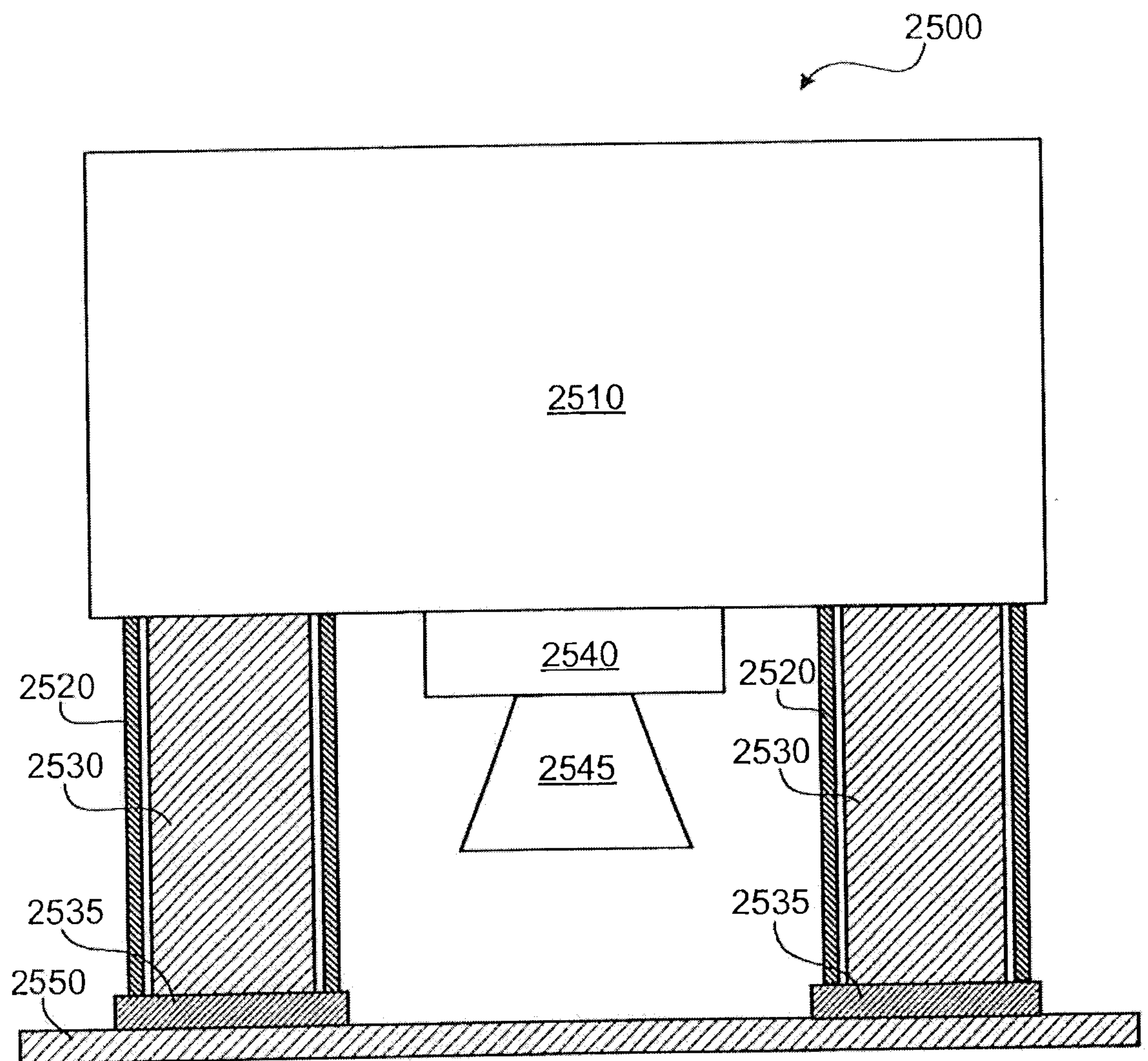


FIG. 25

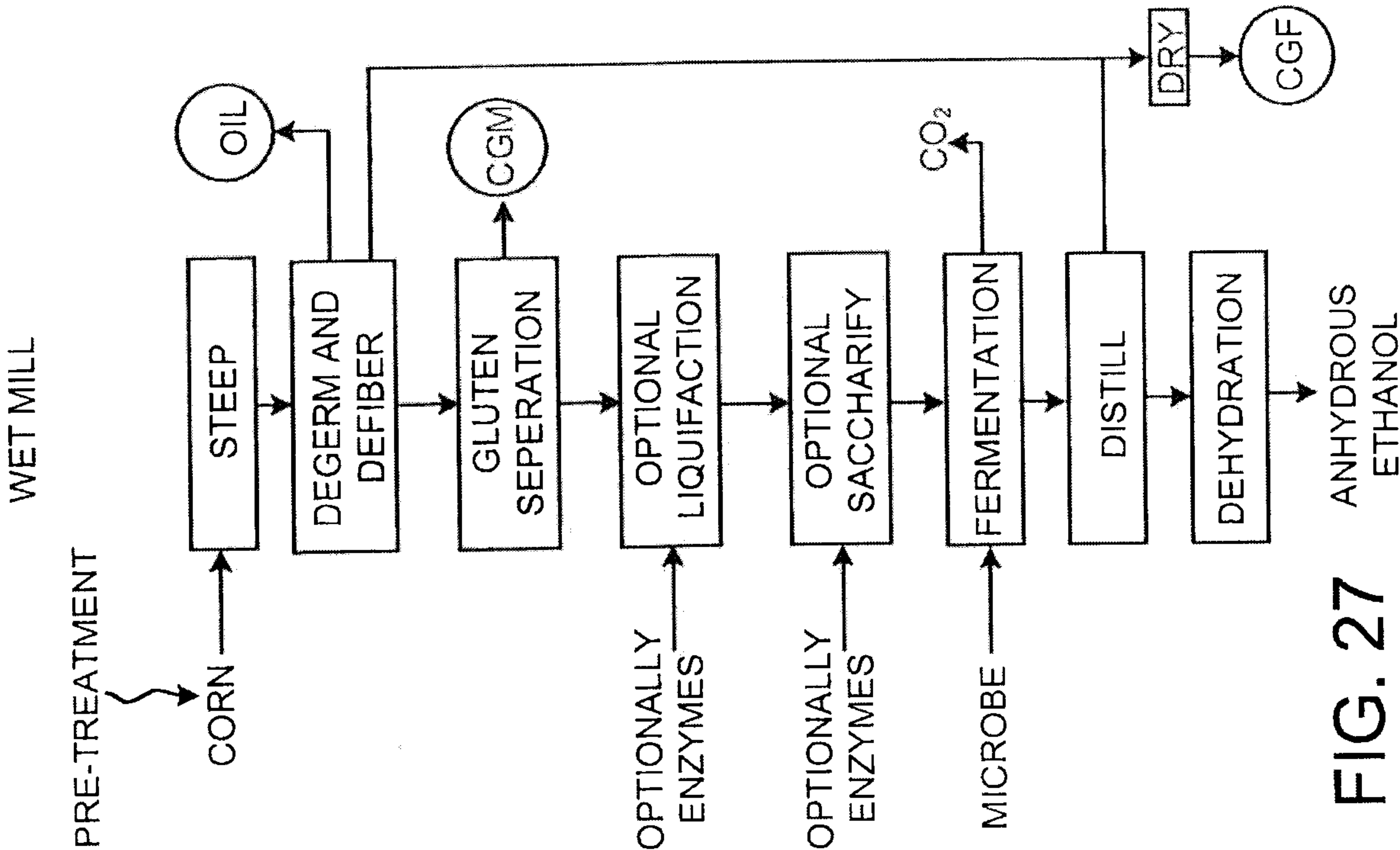


FIG. 27

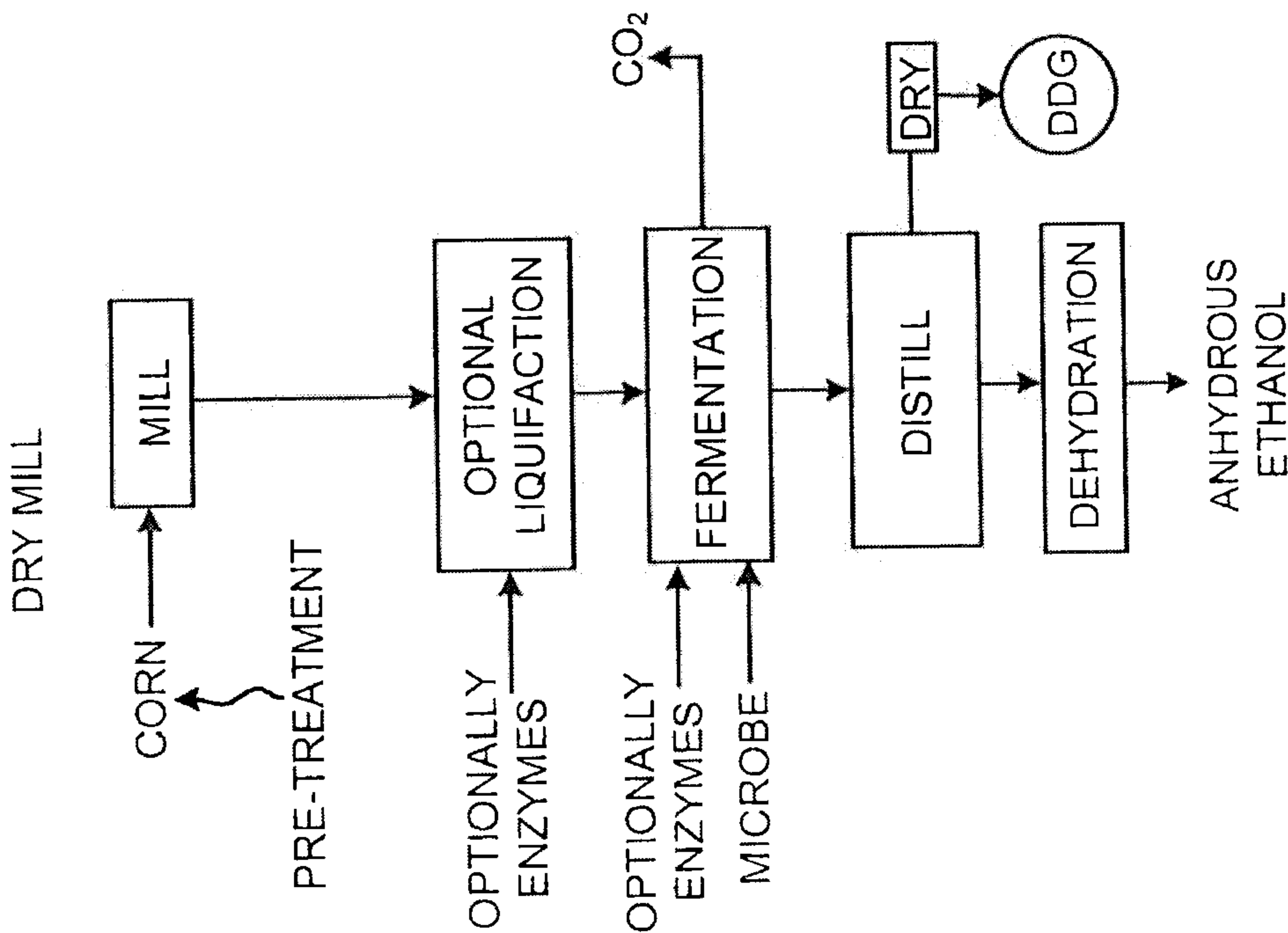


FIG. 26



X25 1mm

FIG. 28

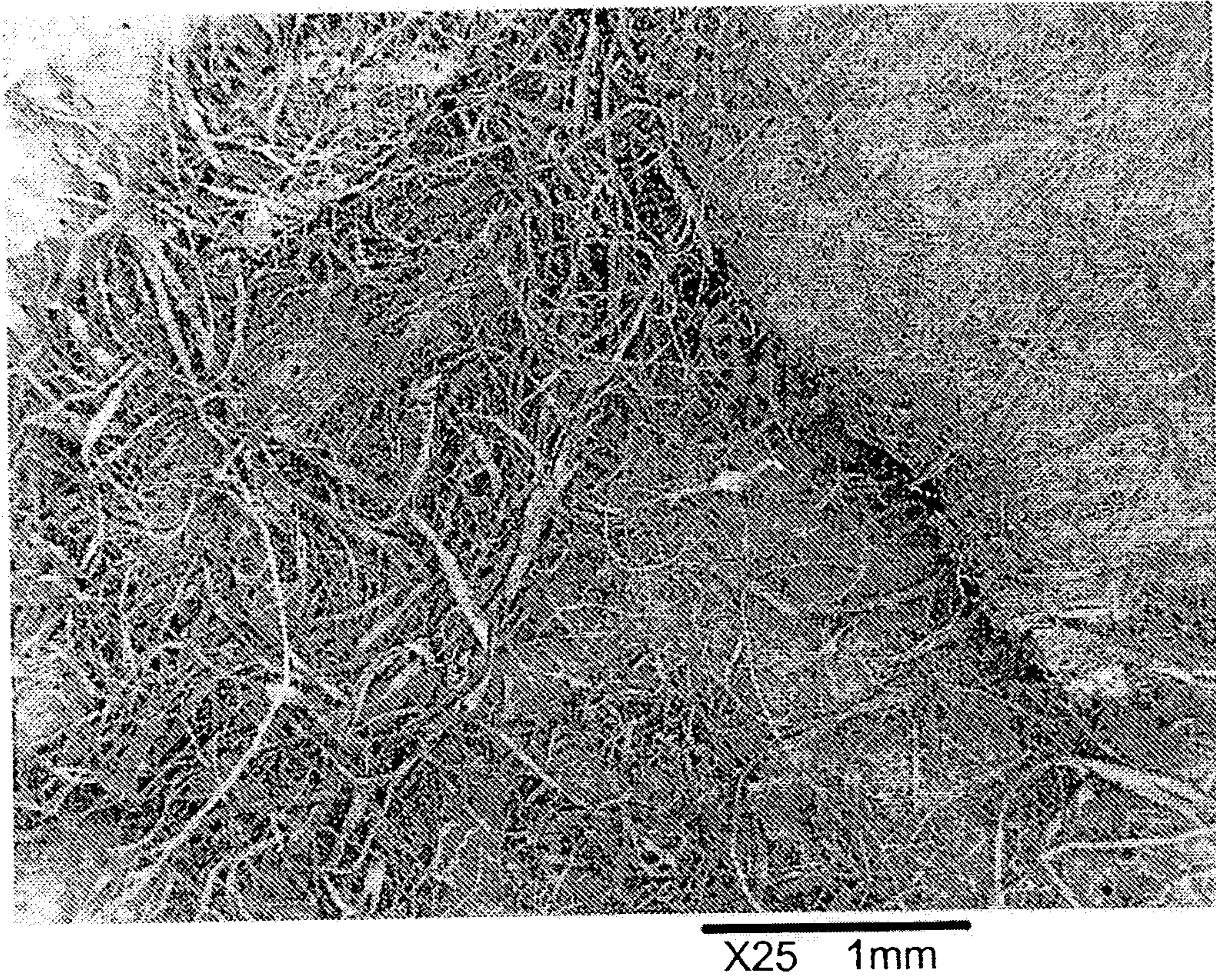


FIG. 29



X25 1mm

FIG. 30

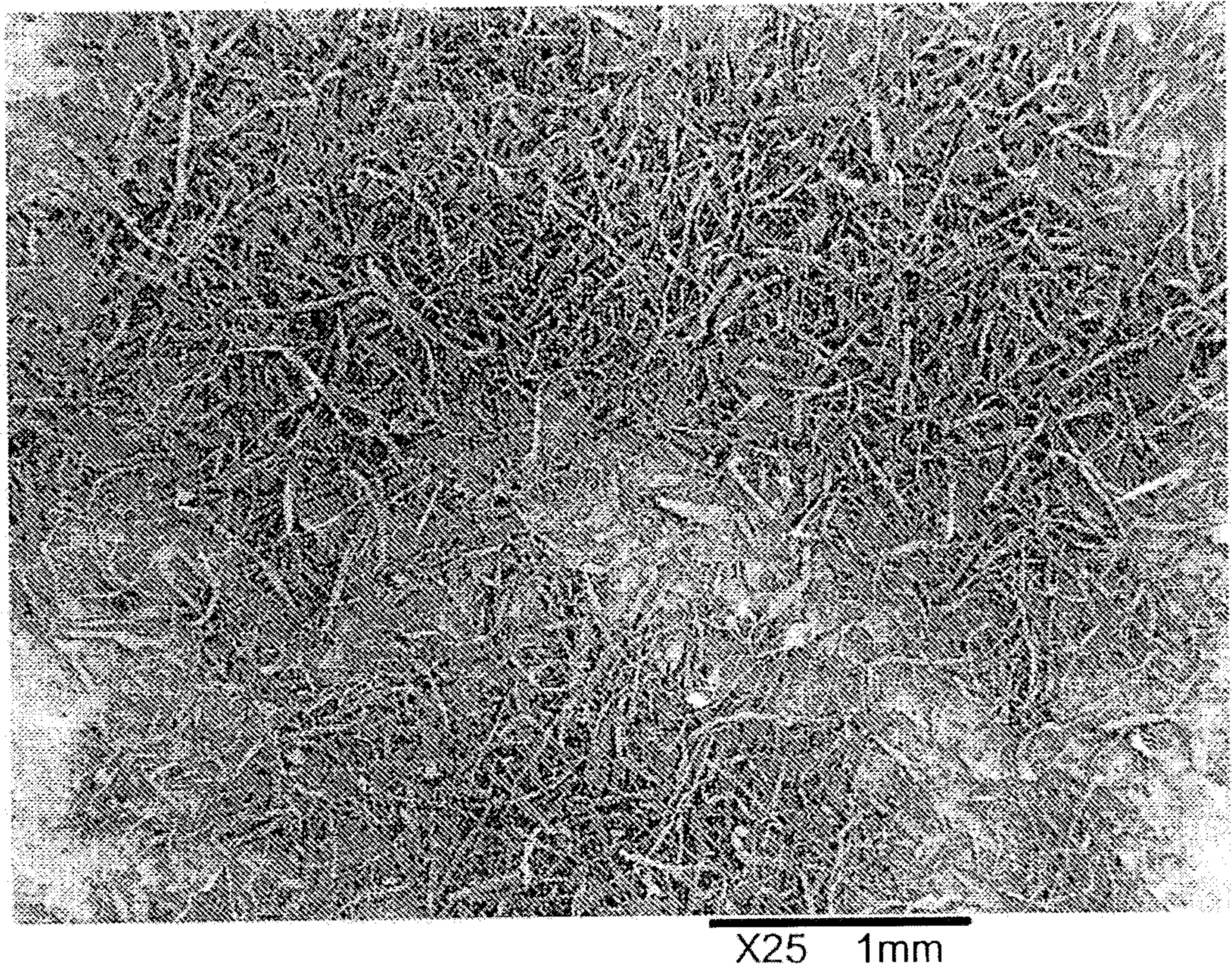


FIG. 31

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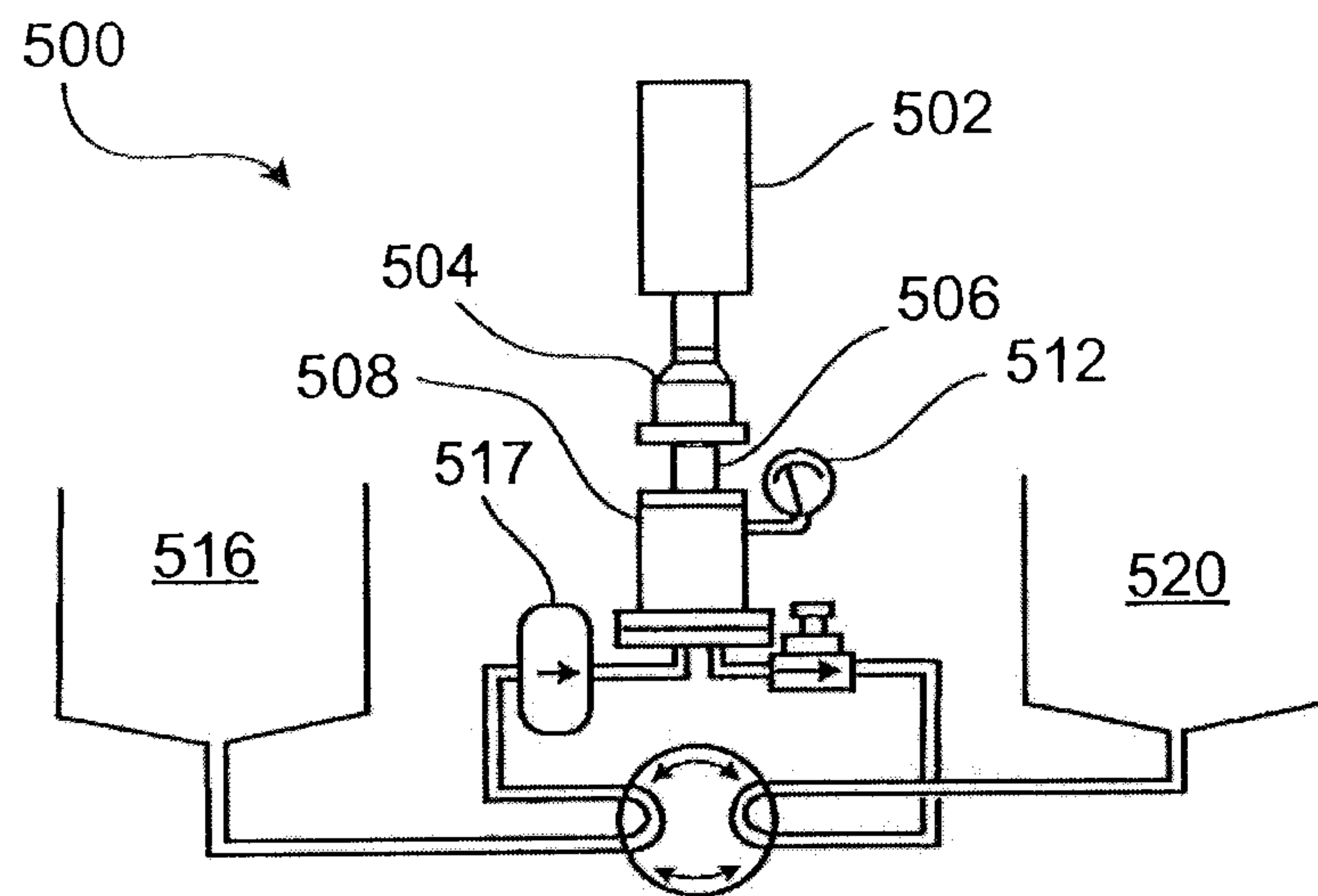


FIG. 32

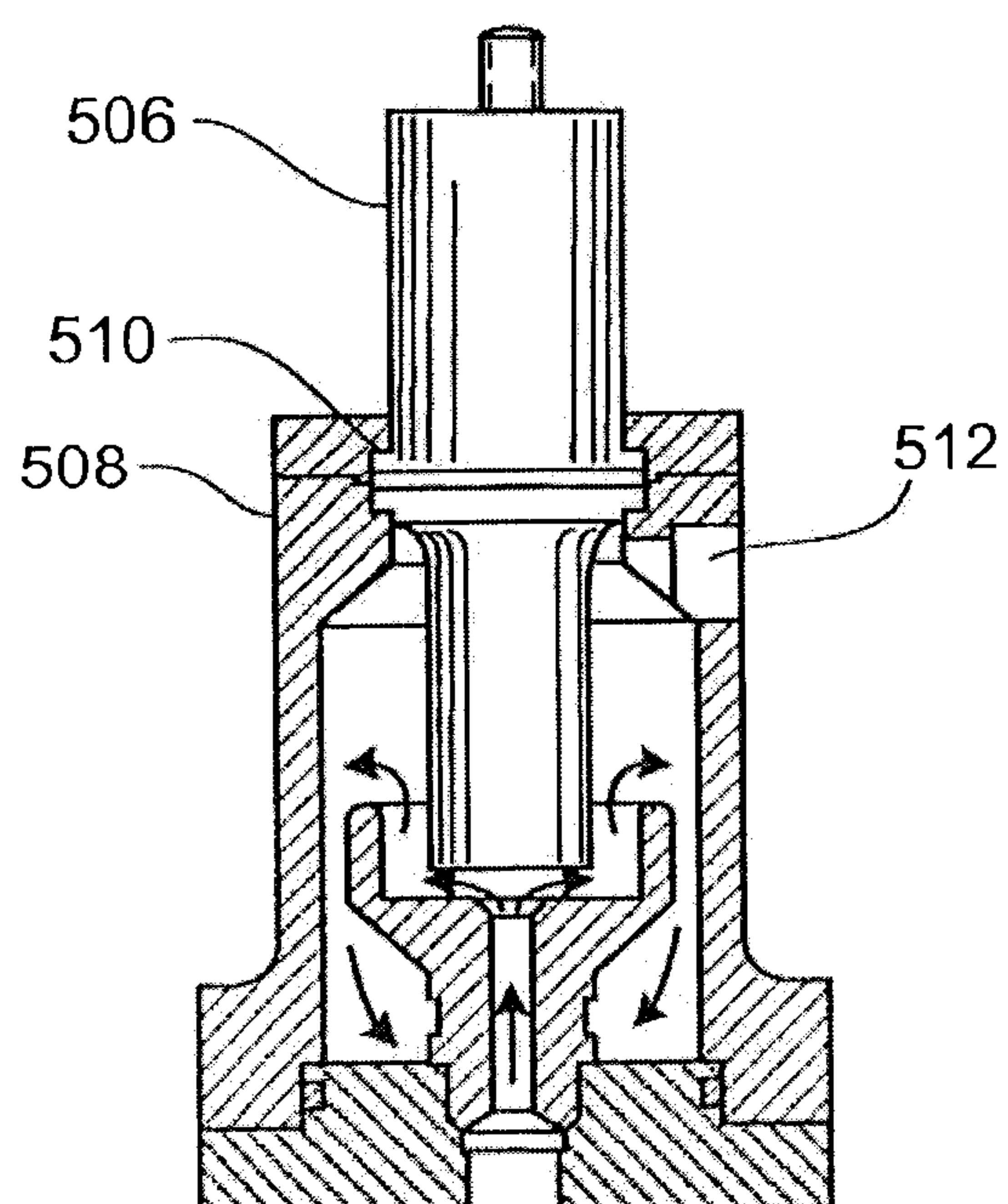


FIG. 33

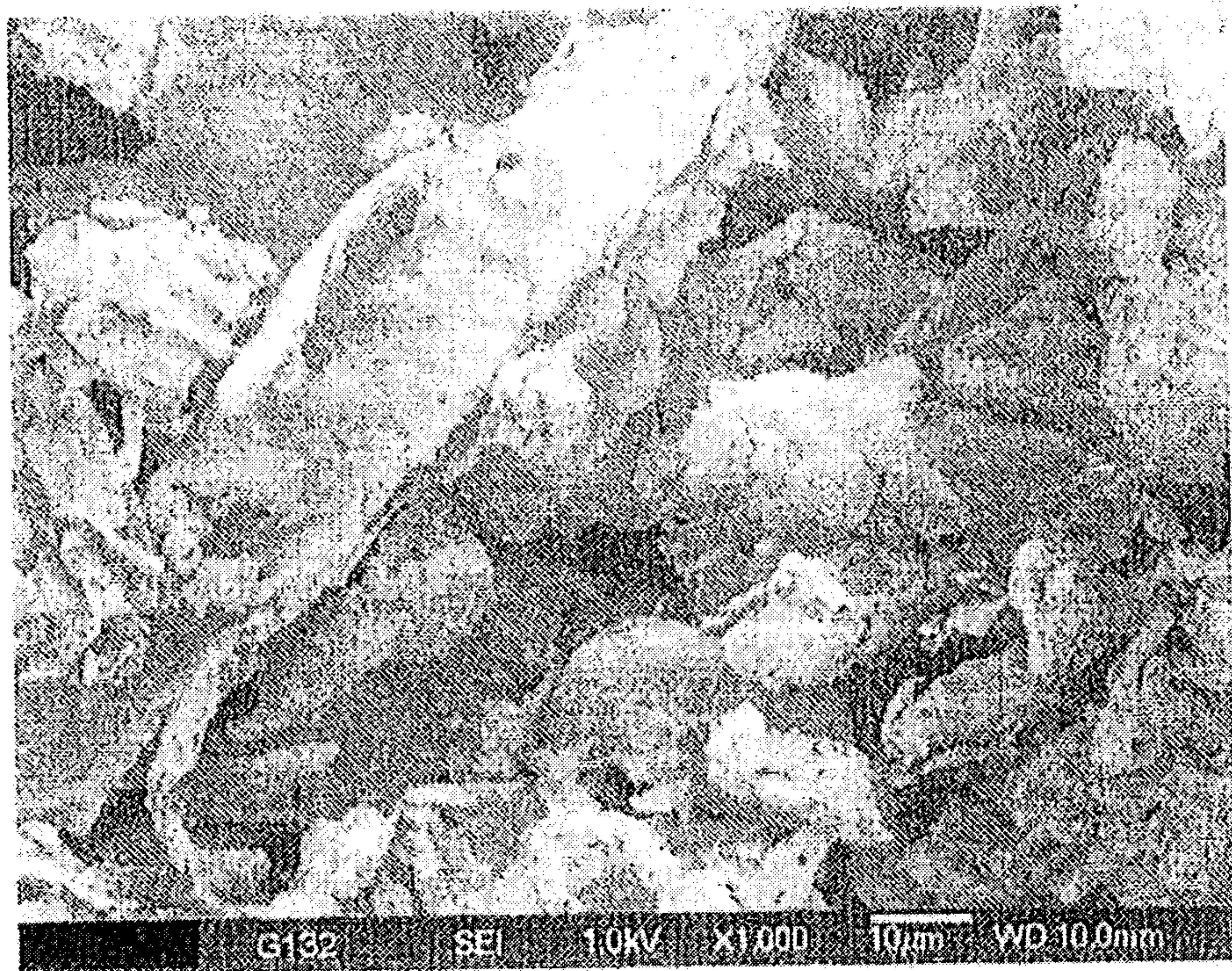


FIG. 34

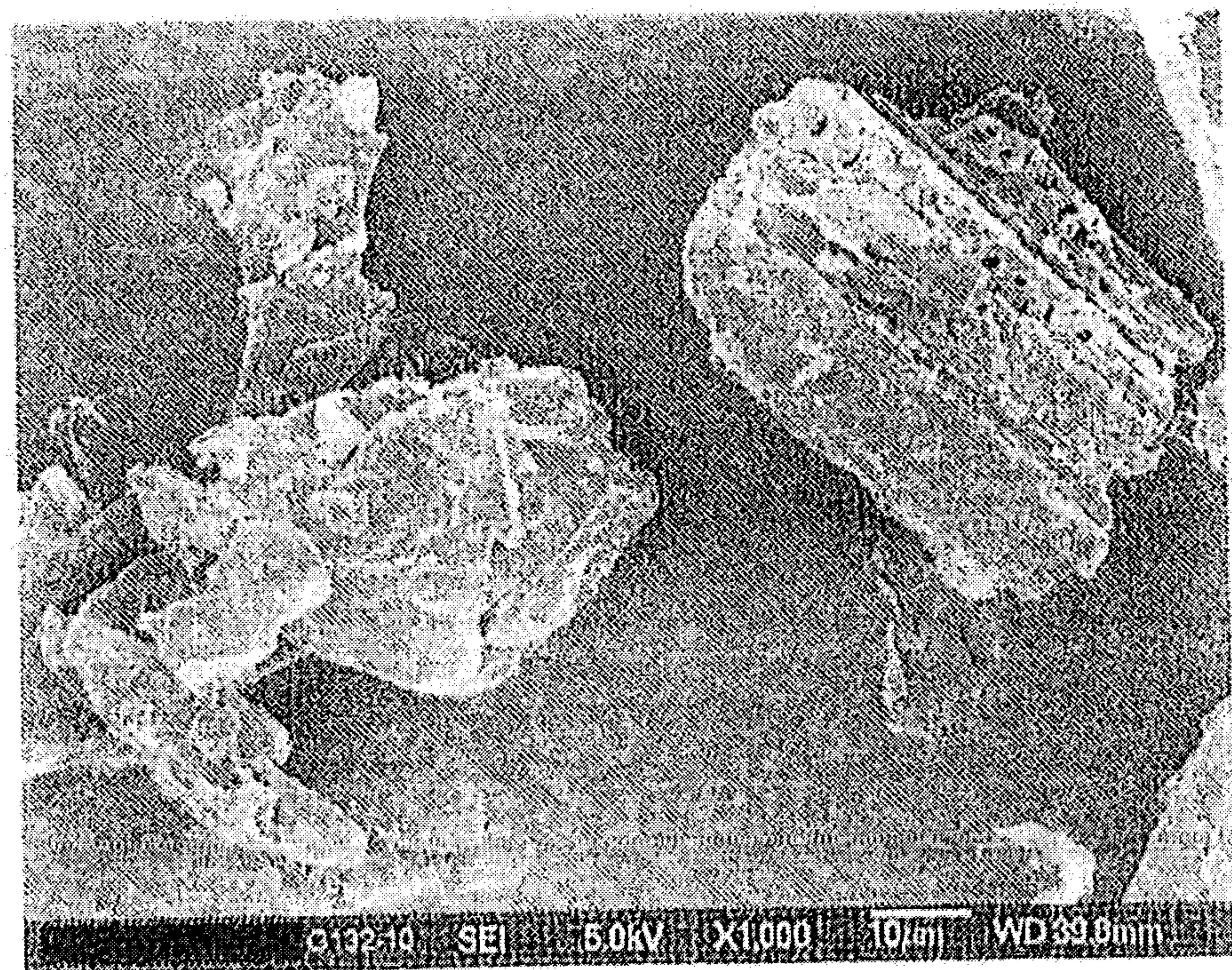


FIG. 35

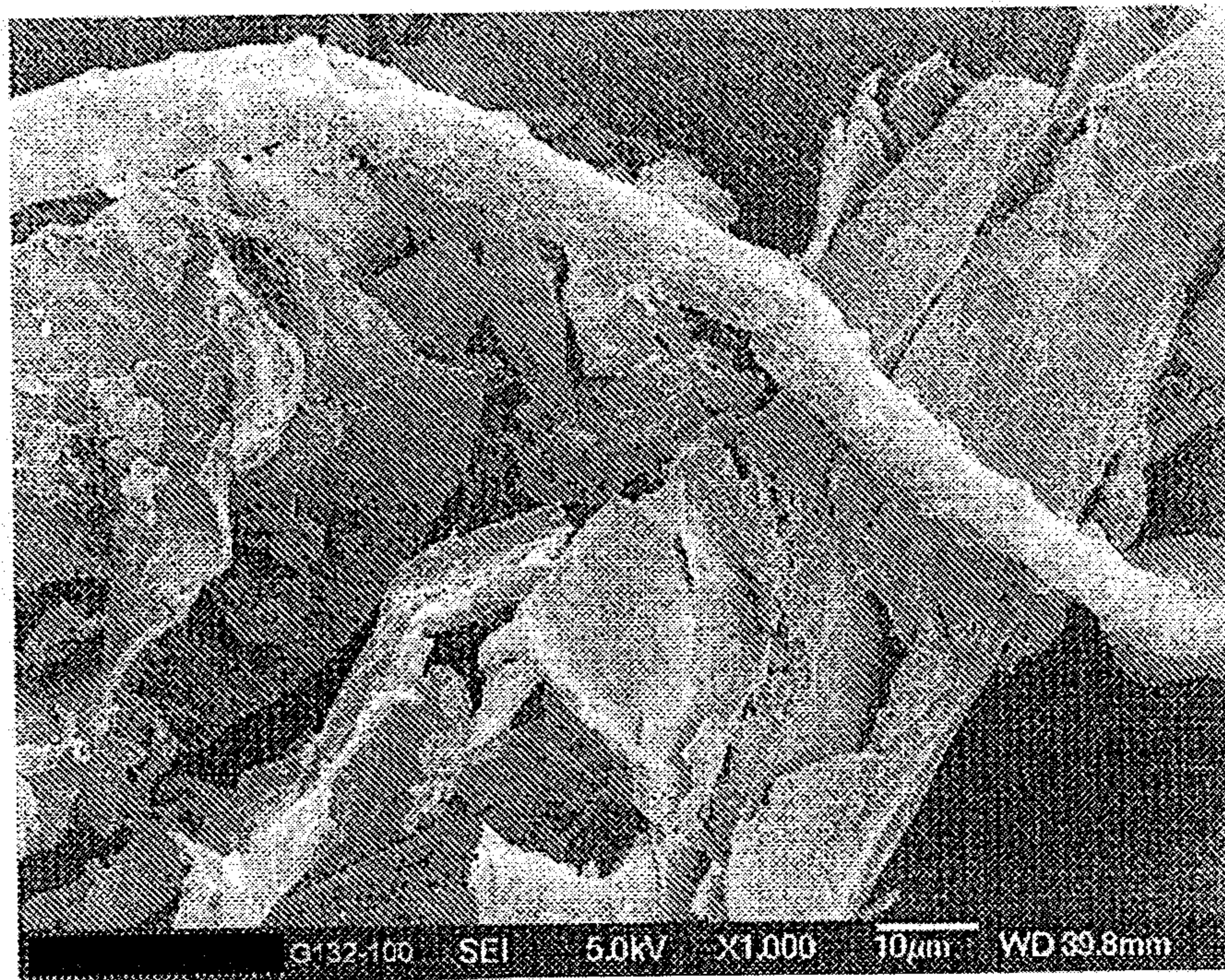


FIG. 36

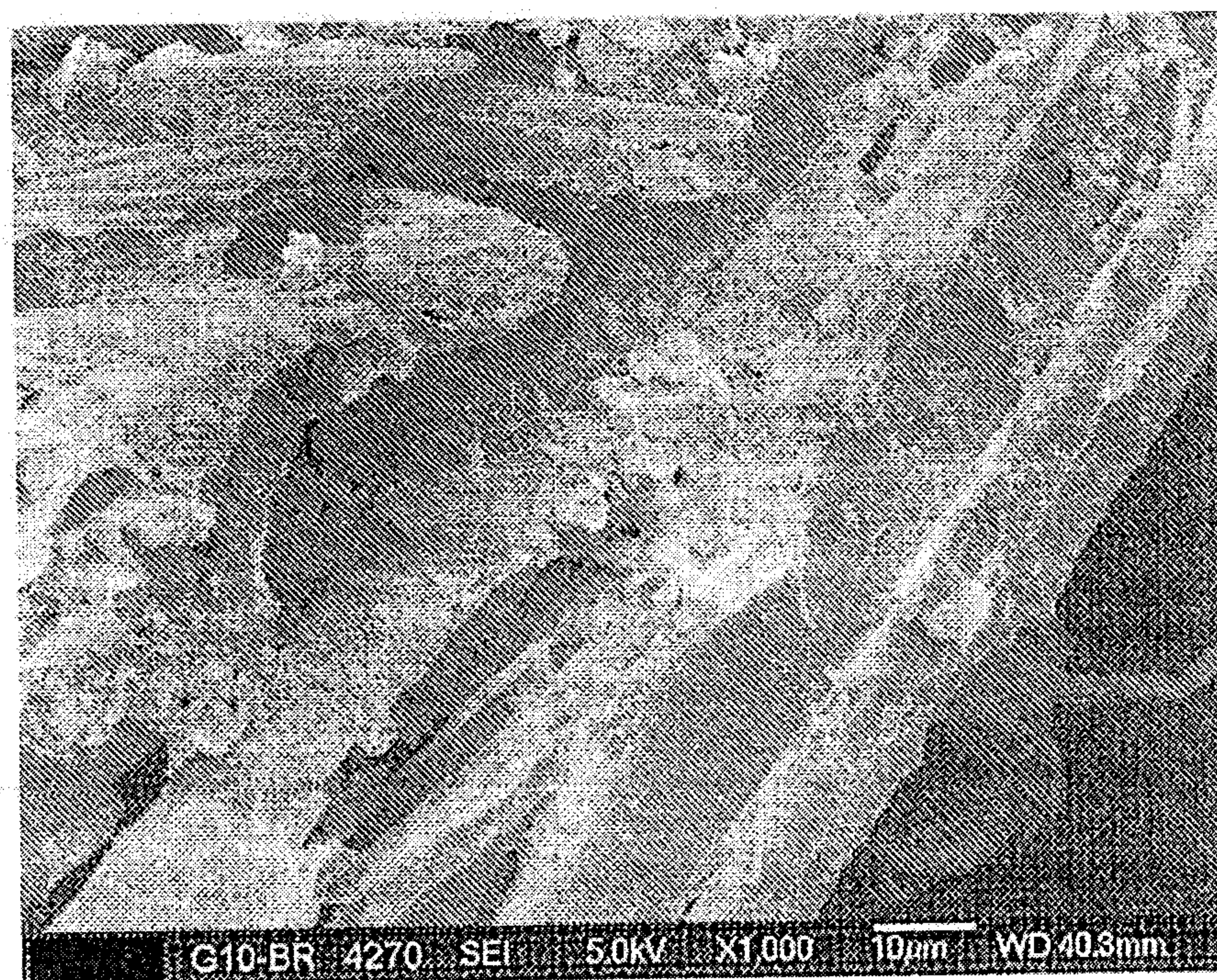


FIG. 37

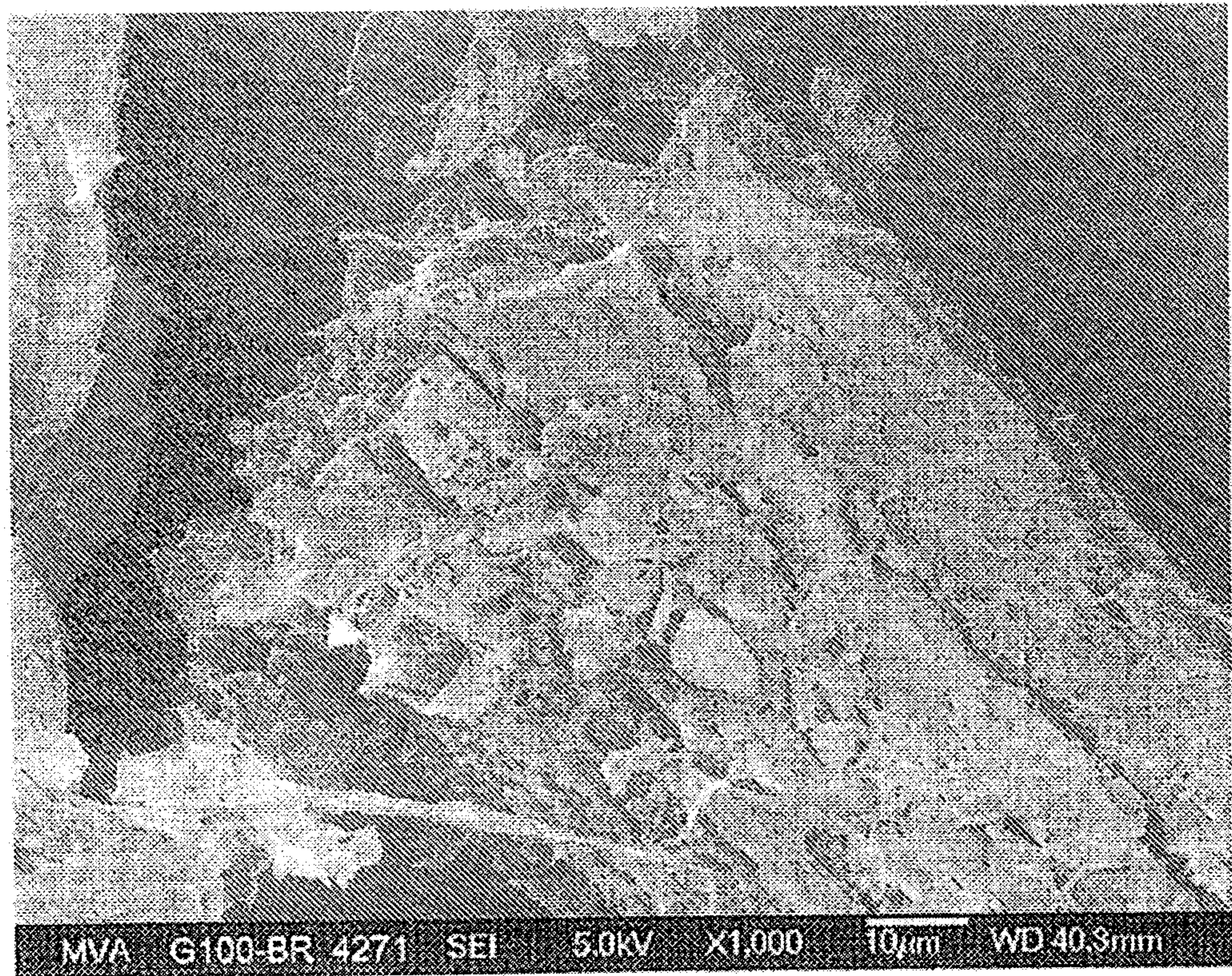


FIG. 38

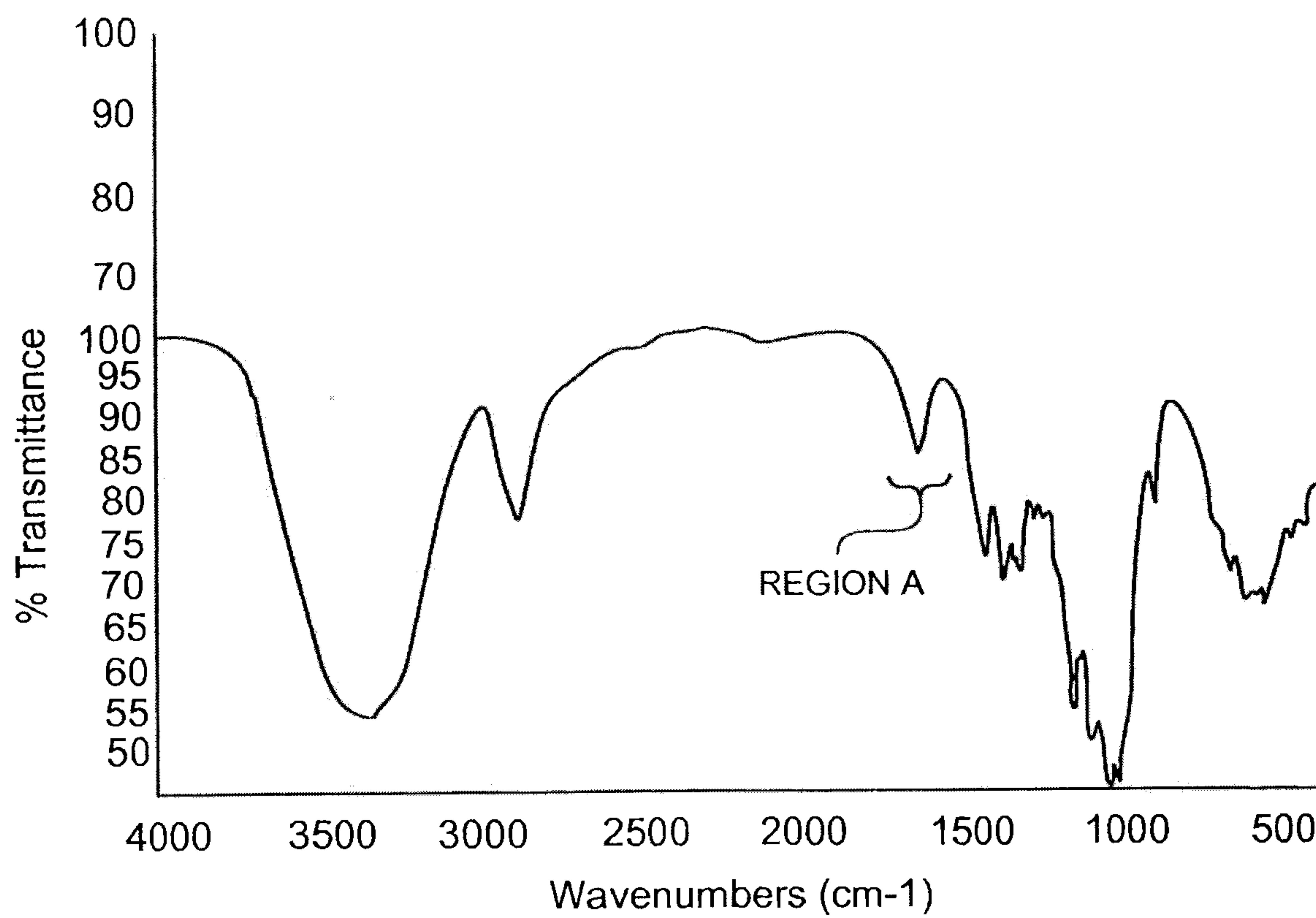
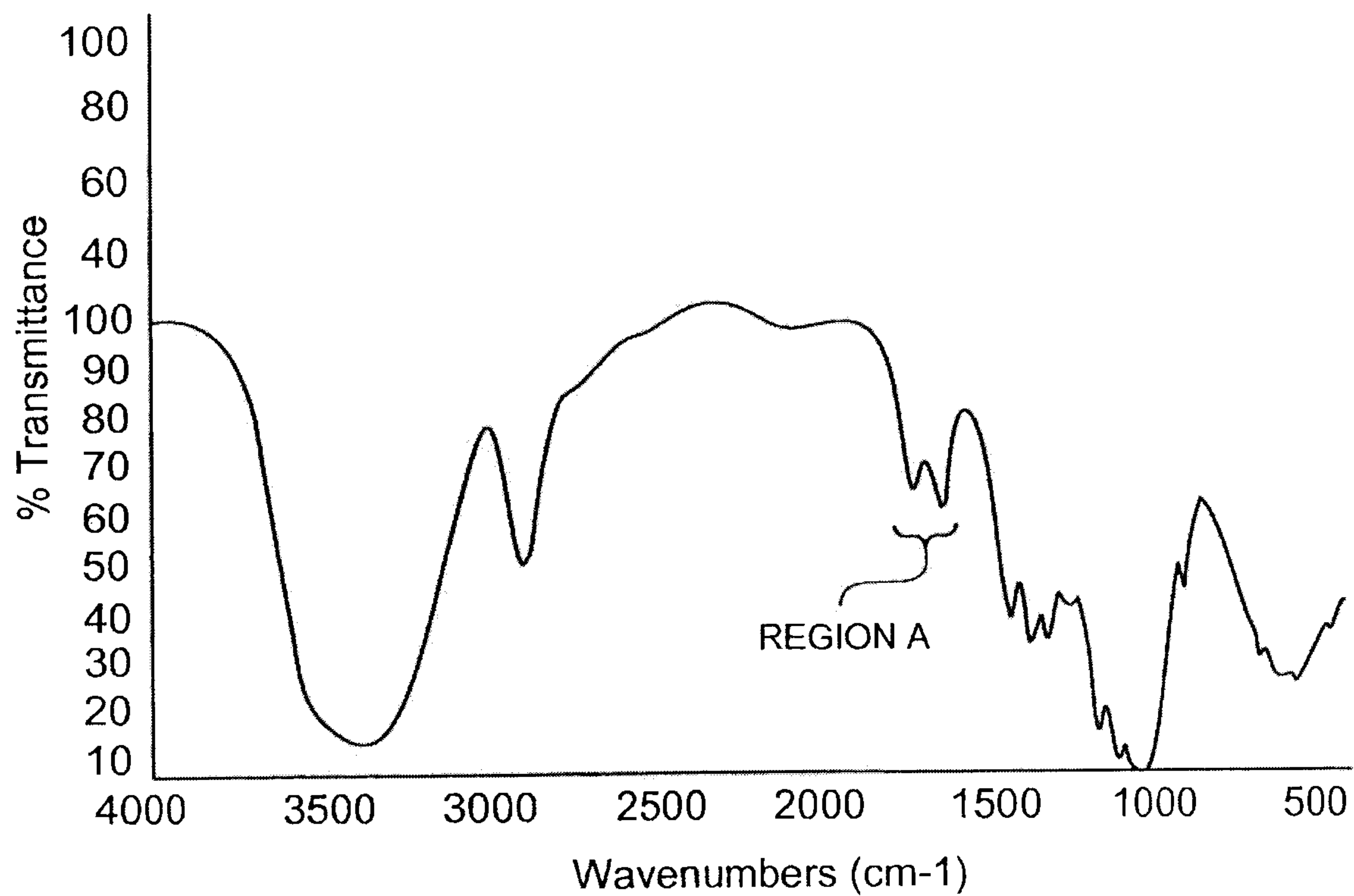


FIG. 39

**FIG. 40**

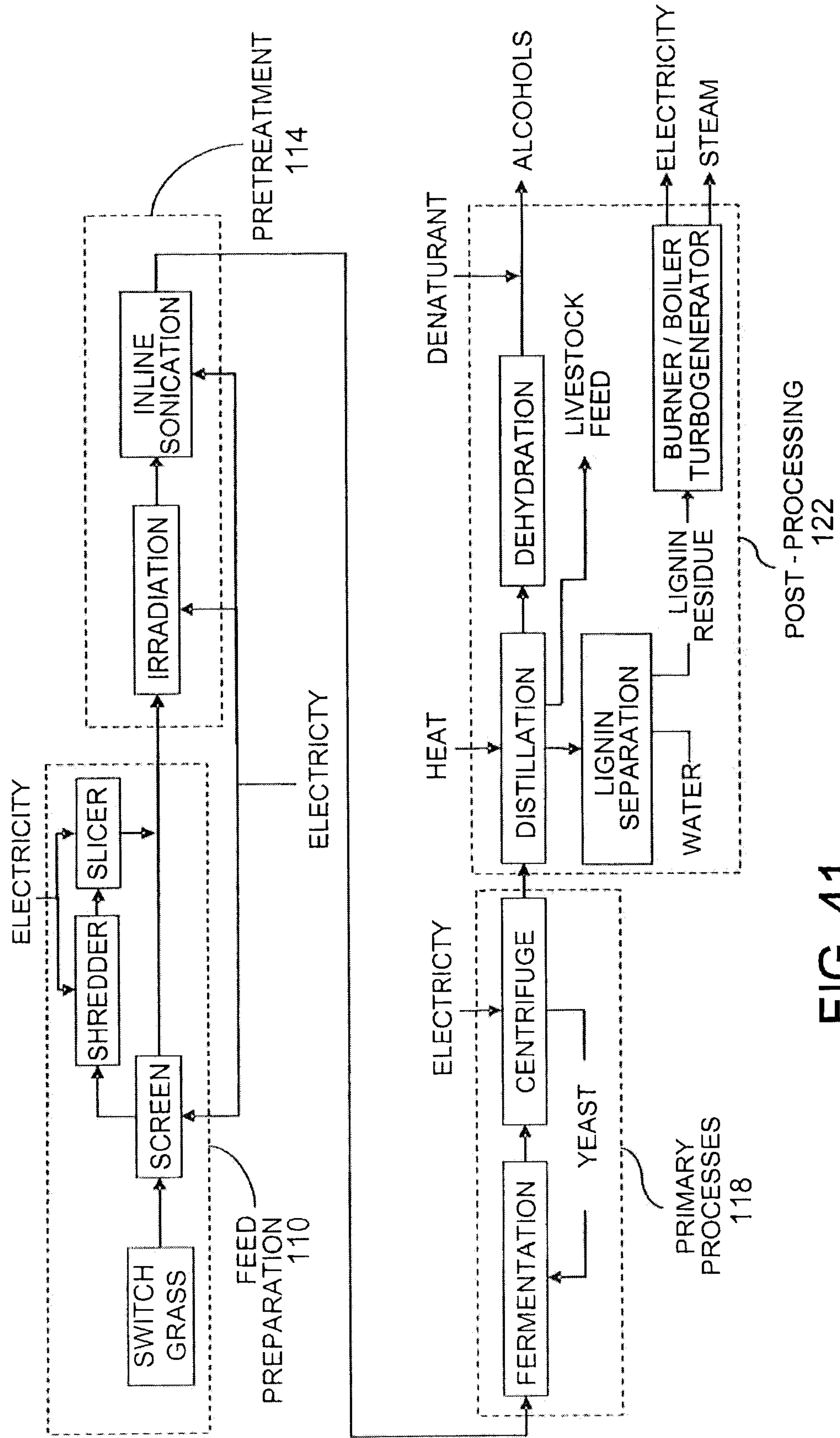


FIG. 41

