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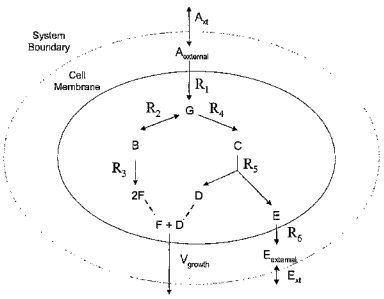
(54) **Title:** MULTICELLULAR METABOLIC MODELS AND METHODS



(57) **Abstract:** The invention provides a computer readable medium or media, having: (a) a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (d) a constraint set for said plurality of reactions for said first, second and third data structures, and (e) commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells. The first, second and third data structures also can include a plurality of data structures. Additionally provided is a method for predicting a physiological function of a multicellular organism. The method includes: (a) providing a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) providing a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) providing a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (d) providing a constraint set for said plurality of reactions for said first, second and third data structures; (e) providing an objective function, and (f) determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

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MULTICELLULAR METABOLIC MODELS AND METHODS

BACKGROUND OF THE INVENTION

This invention relates generally to analysis of the activity of chemical reaction networks and, more specifically, to computational methods for simulating and predicting the activity of multiple interacting reaction networks.

Therapeutic agents, including drugs and gene-based agents, are being rapidly developed by the pharmaceutical industry with the goal of preventing or treating human disease. Dietary supplements, including herbal products, vitamins and amino acids, are also being developed and marketed by the nutraceutical industry. Because of the complexity of the biochemical reaction networks in and between human cells, even relatively minor perturbations caused by a therapeutic agent or a dietary component in the abundance or activity of a particular target, such as a metabolite, gene or protein, can affect hundreds of biochemical reactions. These perturbations can lead to desirable therapeutic effects, such as cell stasis or cell death in the case of cancer cells or other pathologically hyperproliferative cells. However, these perturbations can also lead to undesirable side effects, such as production of toxic byproducts, if the systemic effects of the perturbations are not taken into account.

Current approaches to drug and nutraceutical development do not take into account the effect of a perturbation in a molecular target on systemic cellular behavior. In order to design effective methods of repairing, engineering or disabling cellular activities, it is essential to understand human cellular behavior from an integrated perspective.

Cellular metabolism, which is an example of a process involving a highly integrated network of biochemical reactions, is fundamental to all normal cellular or physiological processes, including homeostatis, proliferation, differentiation, programmed cell death (apoptosis) and motility. Alterations in cellular metabolism characterize a vast number of human diseases. For example, tissue injury is often characterized by increased catabolism of glucose, fatty acids and amino acids, which, if persistent, can lead to organ dysfunction. Conditions of low oxygen supply (hypoxia) and nutrient supply, such as occur in solid tumors, result in a myriad of adaptive metabolic changes including activation of glycolysis and neovascularization. Metabolic dysfunctions also contribute

to neurodegenerative diseases, cardiovascular disease, neuromuscular diseases, obesity and diabetes. Currently, despite the importance of cellular metabolism to normal and pathological processes, a detailed systemic understanding of cellular metabolism in human cells is currently lacking.

Thus, there exists a need for models that describe interacting reaction networks within and between cells, including core metabolic reaction networks and metabolic reaction networks in specialized cell types, which can be used to simulate different aspects of multicellular behavior under physiological, pathological and therapeutic conditions. The present invention satisfies this need, and provides related advantages as well.

SUMMARY OF THE INVENTION

The invention provides a computer readable medium or media, having: (a) a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (d) a constraint set for said plurality of reactions for said first, second and third data structures, and (e) commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells. The first, second and third data structures also can include a plurality of data structures. Additionally provided is a method for predicting a physiological function of a multicellular organism. The method includes: (a) providing a first data structure relating a plurality of reactants to a plurality

of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) providing a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) providing a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (d) providing a constraint set for said plurality of reactions for said first, second and third data structures; (e) providing an objective function, and (f) determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a schematic representation of a hypothetical metabolic network.

Figure 2 shows mass balance constraints and flux constraints (reversibility constraints) that can be placed on the hypothetical metabolic network shown in Figure 1.

Figure 3 shows the stoichiometric matrix (S) for the hypothetical metabolic network shown in Figure 1.

Figure 4 shows, in Panel A, an exemplary biochemical reaction network and in Panel B, an exemplary regulatory control structure for the reaction network in panel A.

Figure 5 shows a metabolic network of central human metabolism.

Figure 6 shows an example of a gene-protein-reaction association for triosphosphate isomerase.

Figure 7 shows a metabolic network of adipocyte metabolism.

Figure 8 shows muscle contraction in a myocyte metabolic model.

Figure 9 shows a metabolic network of myocyte metabolism.

Figure 10 shows a metabolic network of coupled adipoctye-myocyte metabolism.

Figure 11 shows triacylglycerol degradation in an adipocyte model.

Figure 12 shows the impairment of muscle contraction as a result of lactate accumulation during anaerobic exercise. Time is in arbitrary unit. Concentration and yield of lactate (Y_{Lac}) production are in mol/mol glucose.

Figure 13 shows glycogen utilization versus (highlighted on the left) glucose utilization (highlighted on the right) in myocyte.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides *in silico* models that describe the interconnections between genes in the *Homo sapiens* genome and their associated reactions and reactants. The invention also provides *in silico* models that describe interconnections between different biochemical networks within a cell as well as between cells. The interconnections among different biochemical networks between cells can describe interactions between, for example, groups of cells including cells within different locations, tissues, organs or between cells carrying out different functions of a multicellular organism. Therefore, the models can be used to simulate different aspects of the cellular behavior of a cell derived from a multicellular organism, including a human cell, as well as be used to simulate different aspects of cellular behavioral interactions of groups of cells. Such groups of cells include, for example, eukaryotic cells, such as those of the same tissue type or colonies of prokaryotic cells, or different types of eukaryotic cells derived from the same or different tissue types from a multicellular organism. The different aspects of cellular behavior, including cellular behavioral interactions, can be simulated under different normal, pathological and therapeutic conditions, thereby providing valuable information for therapeutic, diagnostic

and research applications. One advantage of the models of the invention is that they provide a holistic approach to simulating and predicting the activity of multicellular organisms, cellular interactions and individual cells, including the activity of *Homo sapiens* cells. Therefore, the models and methods can be used to simulate the activity of multiple interacting cells, including organs, physiological systems and whole body metabolism for practical diagnostic and therapeutic purposes.

In one embodiment, the invention is exemplified by reference to a metabolic model of a *Homo sapien* cell. This *in silico* model of an eukaryotic cell describes the cellular behavior resulting from two or more interacting networks because it can contain metabolic, regulatory and other network interactions, as described below. The models and methods of the invention applicable to the production and use of a cellular model containing two or more interacting networks also are applicable to the production and use of a multi-network model where the two or more networks are separated between compartments such as cells or tissues of a multicellular organism. Therefore, a *Homo sapien* or other eukaryotic cell model of the invention exemplifies application of the models and methods of the invention to models that describe the interaction of multiple biochemical networks between and among cells of a tissue, organ, physiological system or whole organism.

In another embodiment, the *Homo sapiens* metabolic models of the invention can be used to determine the effects of changes from aerobic to anaerobic conditions, such as occurs in skeletal muscles during exercise or in tumors, or to determine the effect of various dietary changes. The *Homo sapiens* metabolic models can also be used to determine the consequences of genetic defects, such as deficiencies in metabolic enzymes such as phosphofructokinase, phosphoglycerate kinase, phosphoglycerate mutase, lactate dehydrogenase and adenosine deaminase.

In a further embodiment, the invention provides a model of multicellular interactions that includes the network reconstruction, characteristics and simulation performance of an integrated two cell model of human adipocyte and myocyte cells. This multicellular model also included an intra-system biochemical network for extracellular physiological systems. The model was generated by reconstructing each of the component biochemical networks within the cells and combining them together with the

addition of the intra-system biochemical network and achieved accurate predictive performance of the two cell types under different physiological conditions. Such multicellular metabolic models can be employed for the same determinations as described above for the *Homo sapiens* metabolic models. The determinations can be performed at the cellular, tissue, physiological system or organism level.

The multicellular and *Homo sapiens* metabolic models also can be used to choose appropriate targets for drug design. Such targets include genes, proteins or reactants, which when modulated positively or negatively in a simulation produce a desired therapeutic result. The models and methods of the invention can also be used to predict the effects of a therapeutic agent or dietary supplement on a cellular function of interest. Likewise, the models and methods can be used to predict both desirable and undesirable side effects of the therapeutic agent on an interrelated cellular function in the target cell, as well as the desirable and undesirable effects that may occur in other cell types. Thus, the models and methods of the invention can make the drug development process more rapid and cost effective than is currently possible.

The multicellular and *Homo sapiens* metabolic models also can be used to predict or validate the assignment of particular biochemical reactions to the enzyme-encoding genes found in the genome, and to identify the presence of reactions or pathways not indicated by current genomic data. Thus, the models can be used to guide the research and discovery process, potentially leading to the identification of new enzymes, medicines or metabolites of clinical importance.

The models of the invention are based on a data structure relating a plurality of reactants to a plurality of reactions, wherein each of the reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product. The reactions included in the data structure can be those that are common to all or most cells or to a particular type or species of cell, including *Homo sapiens* cells, such as core metabolic reactions, or reactions specific for one or more given cell type.

As used herein, the term "reaction" is intended to mean a conversion that consumes a substrate or forms a product that occurs in or by a cell. The term can include

a conversion that occurs due to the activity of one or more enzymes that are genetically encoded by a genome of the cell. The term can also include a conversion that occurs spontaneously in a cell. When used in reference to a *Homo sapiens* reaction, the term is intended to mean a conversion that consumes a substrate or forms a product that occurs in or by a *Homo sapiens* cell. Conversions included in the term include, for example, changes in chemical composition such as those due to nucleophilic or electrophilic addition, nucleophilic or electrophilic substitution, elimination, isomerization, deamination, phosphorylation, methylation, reduction, oxidation or changes in location such as those that occur due to a transport reaction that moves a reactant from one cellular compartment to another. In the case of a transport reaction, the substrate and product of the reaction can be chemically the same and the substrate and product can be differentiated according to location in a particular cellular compartment. Thus, a reaction that transports a chemically unchanged reactant from a first compartment to a second compartment has as its substrate the reactant in the first compartment and as its product the reactant in the second compartment. It will be understood that when used in reference to an *in silico* model or data structure, a reaction is intended to be a representation of a chemical conversion that consumes a substrate or produces a product.

As used herein, the term "reactant" is intended to mean a chemical that is a substrate or a product of a reaction that occurs in or by a cell. The term can include substrates or products of reactions performed by one or more enzymes encoded by a genome, reactions occurring in cells or organisms that are performed by one or more non-genetically encoded macromolecule, protein or enzyme, or reactions that occur spontaneously in a cell. When used in reference to a *Homo sapiens* reactant, the term is intended to mean a chemical that is a substrate or product of a reaction that occurs in or by a *Homo sapiens* cell. Metabolites are understood to be reactants within the meaning of the term. It will be understood that when used in reference to an *in silico* model or data structure, a reactant is intended to be a representation of a chemical that is a substrate or a product of a reaction that occurs in or by a cell.

As used herein the term "substrate" is intended to mean a reactant that can be converted to one or more products by a reaction. The term can include, for example, a reactant that is to be chemically changed due to nucleophilic or electrophilic addition, nucleophilic or electrophilic substitution, elimination, isomerization, deamination,

phosphorylation, methylation, reduction, oxidation or that is to change location such as by being transported across a membrane or to a different compartment.

As used herein, the term "product" is intended to mean a reactant that results from a reaction with one or more substrates. The term can include, for example, a reactant that has been chemically changed due to nucleophilic or electrophilic addition, nucleophilic or electrophilic substitution, elimination, isomerization, deamination, phosphorylation, methylation, reduction or oxidation or that has changed location such as by being transported across a membrane or to a different compartment.

As used herein, the term "stoichiometric coefficient" is intended to mean a numerical constant correlating the number of one or more reactants and the number of one or more products in a chemical reaction. Typically, the numbers are integers as they denote the number of molecules of each reactant in an elementally balanced chemical equation that describes the corresponding conversion. However, in some cases the numbers can take on non-integer values, for example, when used in a lumped reaction or to reflect empirical data.

As used herein, the term "plurality," when used in reference to reactions or reactants including *Homo sapiens* reactions or reactants, is intended to mean at least 2 reactions or reactants. The term can include any number of reactions or reactants in the range from 2 to the number of naturally occurring reactants or reactions for a particular of cell or cells. Thus, the term can include, for example, at least 10, 20, 30, 50, 100, 150, 200, 300, 400, 500, 600 or more reactions or reactants. The number of reactions or reactants can be expressed as a portion of the total number of naturally occurring reactions for a particular cell or cells including a *Homo sapiens* cell or cells, such as at least 20%, 30%, 50%, 60%, 75%, 90%, 95% or 98% of the total number of naturally occurring reactions that occur in a particular *Homo sapiens* cell.

Similarly, the term "plurality," when used in reference to data structures, is intended to mean at least 2 data structures. The term can include any number of data structures in the range from 2 to the number of naturally occurring biochemical networks for a particular subsystem, system, intracellular system, cellular compartment, organelle, extra-cellular space, cytosol, mitochondrion, nucleus, endoplasmic reticulum, group of

cells, tissue, organ or organism. Therefore, the term can include, for example, at least about 3, 4, 5, 6, 7, 8, 9, 10, 25, 20, 25, 50, 100 or more biochemical networks. The term also can be expressed as a portion of the total number of naturally occurring networks for any of the particular categories above occurring in prokaryotic or eukaryotic cells including *Homo sapiens*.

As used herein, the term "data structure" is intended to mean a physical or logical relationship among data elements, designed to support specific data manipulation functions. The term can include, for example, a list of data elements that can be added combined or otherwise manipulated such as a list of representations for reactions from which reactants can be related in a matrix or network. The term can also include a matrix that correlates data elements from two or more lists of information such as a matrix that correlates reactants to reactions. Information included in the term can represent, for example, a substrate or product of a chemical reaction, a chemical reaction relating one or more substrates to one or more products, a constraint placed on a reaction, or a stoichiometric coefficient.

As used herein, the term "constraint" is intended to mean an upper or lower boundary for a reaction. A boundary can specify a minimum or maximum flow of mass, electrons or energy through a reaction. A boundary can further specify directionality of a reaction. A boundary can be a constant value such as zero, infinity, or a numerical value such as an integer. Alternatively, a boundary can be a variable boundary value as set forth below.

As used herein, the term "variable," when used in reference to a constraint is intended to mean capable of assuming any of a set of values in response to being acted upon by a constraint function. The term "function," when used in the context of a constraint, is intended to be consistent with the meaning of the term as it is understood in the computer and mathematical arts. A function can be binary such that changes correspond to a reaction being off or on. Alternatively, continuous functions can be used such that changes in boundary values correspond to increases or decreases in activity. Such increases or decreases can also be binned or effectively digitized by a function capable of converting sets of values to discreet integer values. A function included in the term can correlate a boundary value with the presence, absence or amount of a

biochemical reaction network participant such as a reactant, reaction, enzyme or gene. A function included in the term can correlate a boundary value with an outcome of at least one reaction in a reaction network that includes the reaction that is constrained by the boundary limit. A function included in the term can also correlate a boundary value with an environmental condition such as time, pH, temperature or redox potential.

As used herein, the term "activity," when used in reference to a reaction, is intended to mean the amount of product produced by the reaction, the amount of substrate consumed by the reaction or the rate at which a product is produced or a substrate is consumed. The amount of product produced by the reaction, the amount of substrate consumed by the reaction or the rate at which a product is produced or a substrate is consumed can also be referred to as the flux for the reaction.

As used herein, the term "activity," when used in reference to a *Homo sapiens* cell or a multicellular interaction, is intended to mean the magnitude or rate of a change from an initial state to a final state. The term can include, for example, the amount of a chemical consumed or produced by a cell, the rate at which a chemical is consumed or produced by a cell, the amount or rate of growth of a cell or the amount of or rate at which energy, mass or electrons flow through a particular subset of reactions.

The invention provides a computer readable medium, having a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product.

Also provided is a computer readable medium or media, having: (a) a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) a third data

structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) a constraint set for said plurality of reactions for said first, second and third data structures, and (d) commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

Depending on the application, the plurality of reactions for any of a multicellular, multi-network or single cell model or method of the invention, including a *Homo sapiens* cell model or method, can include reactions selected from core metabolic reactions or peripheral metabolic reactions. As used herein, the term "core," when used in reference to a metabolic pathway, is intended to mean a metabolic pathway selected from glycolysis/gluconeogenesis, the pentose phosphate pathway (PPP), the tricarboxylic acid (TCA) cycle, glycogen storage, electron transfer system (ETS), the malate/aspartate shuttle, the glycerol phosphate shuttle, and plasma and mitochondrial membrane transporters. As used herein, the term "peripheral," when used in reference to a metabolic pathway, is intended to mean a metabolic pathway that includes one or more reactions that are not a part of a core metabolic pathway.

A plurality of reactants can be related to a plurality of reactions in any data structure that represents, for each reactant, the reactions by which it is consumed or produced. Thus, the data structure, which is referred to herein as a "reaction network data structure," serves as a representation of a biological reaction network or system. An example of a reaction network that can be represented in a reaction network data structure of the invention is the collection of reactions that constitute the core metabolic reactions of *Homo sapiens*, or the metabolic reactions of a skeletal muscle cell, as shown in the Examples. Further examples of reaction networks that can be represented in a reaction network data structure of the invention are the collection of reactions that constitute the core metabolic reactions and the triacylglycerol (TAG) biosynthetic pathways of an adipocyte cell; the core metabolic reactions and the energy and contractile reactions of a myocyte cell, and the intra-system reactions that supply buffering functions of the kidney.

The choice of reactions to include in a particular reaction network data structure, from among all the possible reactions that can occur in multicellular organisms or among multicellular interactions, including human cells, depends on the cell type or types and the physiological, pathological or therapeutic condition being modeled, and can be determined experimentally or from the literature, as described further below.

The reactions to be included in a particular network data structure of a multicellular interaction can be determined experimentally using, for example, gene or protein expression profiles, where the molecular characteristics of the cell can be correlated to the expression levels. The expression or lack of expression of genes or proteins in a cell type can be used in determining whether a reaction is included in the model by association to the expressed gene(s) and or protein(s). Thus, it is possible to use experimental technologies to determine which genes and/or proteins are expressed in a specific cell type, and to further use this information to determine which reactions are present in the cell type of interest. In this way a subset of reactions from all of those reactions that can occur in human cells are selected to comprise the set of reactions that represent a specific cell type. cDNA expression profiles have been demonstrated to be useful, for example, for classification of breast cancer cells (Sorlie et al., Proc. Natl. Acad. Sci. U.S.A. 98(19):10869-10874 (2001)).

The methods and models of the invention can be applied to any multicellular interaction as well as to any *Homo sapiens* cell type at any stage of differentiation, including, for example, embryonic stem cells, hematopoietic stem cells, differentiated hematopoietic cells, skeletal muscle cells, cardiac muscle cells, smooth muscle cells, skin cells, nerve cells, kidney cells, pulmonary cells, liver cells, adipocytes and endocrine cells (e.g. beta islet cells of the pancreas, mammary gland cells, adrenal cells, and other specialized hormone secreting cells). Similarly, the methods and models of the invention can be applied to any interaction between any of these cell types, including two or more of the same cell type or two or more different cell types. Described below in Example IV is an example of the interactions that occur between myocyte cells and adipocyte cells during different physiological conditions.

The methods and models of the invention can be applied to normal cells, pathological cells as well as to combinations of interactions between normal cells,

interactions between pathological cells or interactions between normal and pathological cells. Normal cells that exhibit a variety of physiological activities of interest, including homeostasis, proliferation, differentiation, apoptosis, contraction and motility, can be modeled. Pathological cells can also be modeled, including cells that reflect genetic or developmental abnormalities, nutritional deficiencies, environmental assaults, infection (such as by bacteria, viral, protozoan or fungal agents), neoplasia, aging, altered immune or endocrine function, tissue damage, or any combination of these factors. The pathological cells can be representative of any type of pathology, such as a human pathology, including, for example, various metabolic disorders of carbohydrate, lipid or protein metabolism, obesity, diabetes, cardiovascular disease, fibrosis, various cancers, kidney failure, immune pathologies, neurodegenerative diseases, and various monogenetic metabolic diseases described in the Online Mendelian Inheritance in Man database (Center for Medical Genetics, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD)).

The methods and models of the invention can also be applied to cells or organisms undergoing therapeutic perturbations, such as cells treated with drugs that target participants in a reaction network or cause an effect on an interactive reaction network, cells or tissues treated with gene-based therapeutics that increase or decrease expression of an encoded protein, and cells or tissues treated with radiation. As used herein, the term "drug" refers to a compound of any molecular nature with a known or proposed therapeutic function, including, for example, small molecule compounds, peptides and other macromolecules, peptidomimetics and antibodies, any of which can optionally be tagged with cytostatic, targeting or detectable moieties. The term "gene-based therapeutic" refers to nucleic acid therapeutics, including, for example, expressible genes with normal or altered protein activity, antisense compounds, ribozymes, DNAzymes, RNA interference compounds (RNAi) and the like. The therapeutics can target any reaction network participant, in any cellular location, including participants in extracellular, cell surface, cytoplasmic, mitochondrial and nuclear locations. Experimental data that are gathered on the response of cells, tissues, or interactions thereof, to therapeutic treatment, such as alterations in gene or protein expression profiles,

can be used to tailor a network or a combination of networks for a pathological state of a particular cell type.

The methods and models of the invention can be applied to cells, tissues and physiological systems, including *Homo sapiens* cells, tissues and physiological systems, as they exist in any form, such as in primary cell isolates or in established cell lines, or in the whole body, in intact organs or in tissue explants. Accordingly, the methods and models can take into account intercellular communications and/or inter-organ communications, the effect of adhesion to a substrate or neighboring cells (such as a stem cell interacting with mesenchymal cells or a cancer cell interacting with its tissue microenvironment, or beta-islet cells without normal stroma), and other interactions relevant to multicellular systems.

The reactants to be used in a reaction network data structure of the invention can be obtained from or stored in a compound database. As used herein, the term "compound database" is intended to mean a computer readable medium or media containing a plurality of molecules that includes substrates and products of biological reactions. The plurality of molecules can include molecules found in multiple organisms, thereby constituting a universal compound database. Alternatively, the plurality of molecules can be limited to those that occur in a particular organism, thereby constituting an organism-specific compound database. Each reactant in a compound database can be identified according to the chemical species and the cellular compartment in which it is present. Thus, for example, a distinction can be made between glucose in the extracellular compartment versus glucose in the cytosol. Additionally each of the reactants can be specified as a metabolite of a primary or secondary metabolic pathway. Although identification of a reactant as a metabolite of a primary or secondary metabolic pathway does not indicate any chemical distinction between the reactants in a reaction, such a designation can assist in visual representations of large networks of reactions.

As used herein, the term "compartment" is intended to mean a subdivided region containing at least one reactant, such that the reactant is separated from at least one other reactant in a second region. A subdivided region included in the term can be correlated with a subdivided region of a cell. Thus, a subdivided region included in the term can be, for example, the intracellular space of a cell; the extracellular space around a

cell; the periplasmic space, the interior space of an organelle such as a mitochondrium, endoplasmic reticulum, Golgi apparatus, vacuole or nucleus; or any subcellular space that is separated from another by a membrane or other physical barrier. For example, a mitochondrial compartment is a subdivided region of the intracellular space of a cell, which in turn, is a subdivided region of a cell or tissue. A subdivided region also can include, for example, different regions or systems of a tissue, organ or physiological system of an organism. Subdivided regions can also be made in order to create virtual boundaries in a reaction network that are not correlated with physical barriers. Virtual boundaries can be made for the purpose of segmenting the reactions in a network into different compartments or substructures.

As used herein, the term "substructure" is intended to mean a portion of the information in a data structure that is separated from other information in the data structure such that the portion of information can be separately manipulated or analyzed. The term can include portions subdivided according to a biological function including, for example, information relevant to a particular metabolic pathway such as an internal flux pathway, exchange flux pathway, central metabolic pathway, peripheral metabolic pathway, or secondary metabolic pathway. The term can include portions subdivided according to computational or mathematical principles that allow for a particular type of analysis or manipulation of the data structure.

The reactions included in a reaction network data structure can be obtained from a metabolic reaction database that includes the substrates, products, and stoichiometry of a plurality of metabolic reactions of *Homo sapiens*, other multicellular organisms or single cell organisms that exhibit biochemical or physiological interactions. The reactants in a reaction network data structure can be designated as either substrates or products of a particular reaction, each with a stoichiometric coefficient assigned to it to describe the chemical conversion taking place in the reaction. Each reaction is also described as occurring in either a reversible or irreversible direction. Reversible reactions can either be represented as one reaction that operates in both the forward and reverse direction or be decomposed into two irreversible reactions, one corresponding to the forward reaction and the other corresponding to the backward reaction.

Reactions included in a reaction network data structure can include intra-system or exchange reactions. Intra-system reactions are the chemically and electrically balanced interconversions of chemical species and transport processes, which serve to replenish or drain the relative amounts of certain metabolites. These intra-system reactions can be classified as either being transformations or translocations. A transformation is a reaction that contains distinct sets of compounds as substrates and products, while a translocation contains reactants located in different compartments. Thus a reaction that simply transports a metabolite from the extracellular environment to the cytosol, without changing its chemical composition is solely classified as a translocation, while a reaction that takes an extracellular substrate and converts it into a cytosolic product is both a translocation and a transformation. Further, intra-system reactions can include reactions representing one or more biochemical or physiological functions of an independent cell, tissue, organ or physiological system. For example, the buffering function of the kidneys for the hematopoietic system and intra-cellular environments can be represented as intra-system reactions and be included in a multicellular interaction model either as an independent reaction network or merged with one or more reaction networks of the constituent cells.

Exchange reactions are those which constitute sources and sinks, allowing the passage of metabolites into and out of a compartment or across a hypothetical system boundary. These reactions are included in a model for simulation purposes and represent the metabolic demands placed on *Homo sapiens*. While they may be chemically balanced in certain cases, they are typically not balanced and can often have only a single substrate or product. As a matter of convention the exchange reactions are further classified into demand exchange and input/output exchange reactions.

The metabolic demands placed on a multicellular or *Homo sapiens* metabolic reaction network can be readily determined from the dry weight composition of the cell, cells, tissue, organ or organism which is available in the published literature or which can be determined experimentally. The uptake rates and maintenance requirements for *Homo sapiens* cells can also be obtained from the published literature or determined experimentally.

Input/output exchange reactions are used to allow extracellular reactants to enter or exit the reaction network represented by a model of the invention. For each of the extracellular metabolites a corresponding input/output exchange reaction can be created. These reactions are always reversible with the metabolite indicated as a substrate with a stoichiometric coefficient of one and no products produced by the reaction. This particular convention is adopted to allow the reaction to take on a positive flux value (activity level) when the metabolite is being produced or removed from the reaction network and a negative flux value when the metabolite is being consumed or introduced into the reaction network. These reactions will be further constrained during the course of a simulation to specify exactly which metabolites are available to the cell and which can be excreted by the cell.

A demand exchange reaction is always specified as an irreversible reaction containing at least one substrate. These reactions are typically formulated to represent the production of an intracellular metabolite by the metabolic network or the aggregate production of many reactants in balanced ratios such as in the representation of a reaction that leads to biomass formation, also referred to as growth.

A demand exchange reactions can be introduced for any metabolite in a model of the invention. Most commonly these reactions are introduced for metabolites that are required to be produced by the cell for the purposes of creating a new cell such as amino acids, nucleotides, phospholipids, and other biomass constituents, or metabolites that are to be produced for alternative purposes. Once these metabolites are identified, a demand exchange reaction that is irreversible and specifies the metabolite as a substrate with a stoichiometric coefficient of unity can be created. With these specifications, if the reaction is active it leads to the net production of the metabolite by the system meeting potential production demands. Examples of processes that can be represented as a demand exchange reaction in a reaction network data structure and analyzed by the methods of the invention include, for example, production or secretion of an individual protein; production or secretion of an individual metabolite such as an amino acid, vitamin, nucleoside, antibiotic or surfactant; production of ATP for extraneous energy requiring processes such as locomotion or muscle contraction; or formation of biomass constituents.

In addition to these demand exchange reactions that are placed on individual metabolites, demand exchange reactions that utilize multiple metabolites in defined stoichiometric ratios can be introduced. These reactions are referred to as aggregate demand exchange reactions. An example of an aggregate demand reaction is a reaction used to simulate the concurrent growth demands or production requirements associated with cell growth that are placed on a cell, for example, by simulating the formation of multiple biomass constituents simultaneously at a particular cellular or organismic growth rate.

A specific reaction network is provided in Figure 1 to exemplify the above-described reactions and their interactions. The reactions can be represented in the exemplary data structure shown in Figure 3 as set forth below. The reaction network, shown in Figure 1, includes intra-system reactions that occur entirely within the compartment indicated by the shaded oval such as reversible reaction R_2 which acts on reactants B and G and reaction R_3 which converts one equivalent of B to 2 equivalents of F. The reaction network shown in Figure 1 also contains exchange reactions such as input/output exchange reactions A_{xt} and E_{xt}, and the demand exchange reaction, V_{growth}, which represents growth in response to the one equivalent of D and one equivalent of F. Other intra-system reactions include R_1 which is a translocation and transformation reaction that translocates reactant A into the compartment and transforms it to reactant G and reaction R_6 which is a transport reaction that translocates reactant E out of the compartment.

A reaction network can be represented as a set of linear algebraic equations which can be presented as a stoichiometric matrix S, with S being an m x n matrix where m corresponds to the number of reactants or metabolites and n corresponds to the number of reactions taking place in the network. An example of a stoichiometric matrix representing the reaction network of Figure 1 is shown in Figure 3. As shown in Figure 3, each column in the matrix corresponds to a particular reaction n, each row corresponds to a particular reactant m, and each S_{mn} element corresponds to the stoichiometric coefficient of the reactant m in the reaction denoted n. The stoichiometric matrix includes intra-system reactions such as R_2 and R_3 which are related to reactants that participate in the respective reactions according to a stoichiometric coefficient having a sign indicative of whether the reactant is a substrate or product of the reaction and a

value correlated with the number of equivalents of the reactant consumed or produced by the reaction. Exchange reactions such as $-E_{xt}$ and $-A_{xt}$ are similarly correlated with a stoichiometric coefficient. As exemplified by reactant E, the same compound can be treated separately as an internal reactant (E) and an external reactant ($E_{external}$) such that an exchange reaction (R_6) exporting the compound is correlated by stoichiometric coefficients of -1 and 1, respectively. However, because the compound is treated as a separate reactant by virtue of its compartmental location, a reaction, such as R_5, which produces the internal reactant (E) but does not act on the external reactant ($E_{external}$) is correlated by stoichiometric coefficients of 1 and 0, respectively. Demand reactions such as V_{growth} can also be included in the stoichiometric matrix being correlated with substrates by an appropriate stoichiometric coefficient.

As set forth in further detail below, a stoichiometric matrix provides a convenient format for representing and analyzing a reaction network because it can be readily manipulated and used to compute network properties, for example, by using linear programming or general convex analysis. A reaction network data structure can take on a variety of formats so long as it is capable of relating reactants and reactions in the manner exemplified above for a stoichiometric matrix and in a manner that can be manipulated to determine an activity of one or more reactions using methods such as those exemplified below. Other examples of reaction network data structures that are useful in the invention include a connected graph, list of chemical reactions or a table of reaction equations.

A reaction network data structure can be constructed to include all reactions that are involved in metabolism occurring during the interaction of two or more cells, *Homo sapiens* cell metabolism or any portion thereof. A portion of an organisms metabolic reactions that can be included in a reaction network data structure of the invention includes, for example, a central metabolic pathway such as glycolysis, the TCA cycle, the PPP or ETS; or a peripheral metabolic pathway such as amino acid biosynthesis, amino acid degradation, purine biosynthesis, pyrimidine biosynthesis, lipid biosynthesis, fatty acid metabolism, vitamin or cofactor biosynthesis, transport processes and alternative carbon source catabolism. Examples of individual pathways within the peripheral pathways are set forth in Table 1. Other examples of portions of metabolic reactions that can be included in a reaction network data structure of the invention include, for example, TAG biosynthesis, muscle contraction requirements, bicarbonate

buffer system and/or ammonia buffer system. Specific examples of these and other reactions are described further below and in the Examples.

Depending upon a particular application, a reaction network data structure can include a plurality of *Homo sapiens* reactions including any or all of the reactions listed in Table 1. Similarly, a reaction network data structure also can include the reactions set forth in Examples I-IV and include, for example, single reaction networks, multiple reaction networks that interact within a cell as well as multiple reaction networks that interact between cells or physiological systems.

For some applications, it can be advantageous to use a reaction network data structure that includes a minimal number of reactions to achieve a particular *Homo sapiens* activity or activity of a multicellular interaction under a particular set of environmental conditions. A reaction network data structure having a minimal number of reactions can be identified by performing the simulation methods described below in an iterative fashion where different reactions or sets of reactions are systematically removed and the effects observed. Accordingly, the invention provides a computer readable medium, containing a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein the plurality of *Homo sapiens* reactions contains at least 65 reactions. For example, the core metabolic reaction database shown in Tables 2 and 3 contains 65 reactions, and is sufficient to simulate aerobic and anaerobic metabolism on a number of carbon sources, including glucose. Similarly, the invention provides a computer readable medium containing a data structure relating a plurality of reactants of multicellular interactions to a plurality of reactions from multicellular interactions, wherein the reactions contain at least 430 for a two cell interaction. Such reactions between multicellular interactions are exemplified in Table 11, for example.

Depending upon the particular cell type or types, the physiological, pathological or therapeutic conditions being tested, the desired activity and the number of cellular interactions of a model or method of the invention, a reaction network data structure can contain smaller numbers of reactions such as at least 200, 150, 100 or 50 reactions. A reaction network data structure having relatively few reactions can provide the advantage of reducing computation time and resources required to perform a

simulation. When desired, a reaction network data structure having a particular subset of reactions can be made or used in which reactions that are not relevant to the particular simulation are omitted. Alternatively, larger numbers of reactions can be included in order to increase the accuracy or molecular detail of the methods of the invention or to suit a particular application. Thus, a reaction network data structure can contain at least 300, 350, 400, 450, 500, 550, 600 or more reactions up to the number of reactions that occur in or by multicellular interactions, including *Homo sapiens*, or that are desired to simulate the activity of the full set of reactions occurring in multicellular interactions, including *Homo sapiens*. A reaction network data structure that is substantially complete with respect to the metabolic reactions of a multicellular organism, including *Homo sapiens*, provides an advantage of being relevant to a wide range of conditions to be simulated, whereas those with smaller numbers of metabolic reactions are specific to a particular subset of conditions to be simulated.

A *Homo sapiens* reaction network data structure can include one or more reactions that occur in or by *Homo sapiens* and that do not occur, either naturally or following manipulation, in or by another organism, such as *Saccharomyces cerevisiae*. It is understood that a *Homo sapiens* reaction network data structure of a particular cell type can also include one or more reactions that occur in another cell type. Addition of such heterologous reactions to a reaction network data structure of the invention can be used in methods to predict the consequences of heterologous gene transfer and protein expression, for example, when designing *in vivo* and *ex vivo* gene therapy approaches. Similarly, reaction networks for a multicellular interactions also can include one or more reactions that occur entirely within the species of origin of the cellular interactions or can contain one or more heterologous reactions from one or more different species.

The reactions included in a reaction network data structure of the invention can be metabolic reactions. A reaction network data structure can also be constructed to include other types of reactions such as regulatory reactions, signal transduction reactions, cell cycle reactions, reactions controlling developmental processes, reactions involved in apoptosis, reactions involved in responses to hypoxia, reactions involved in responses to cell-cell or cell-substrate interactions, reactions involved in protein synthesis and regulation thereof, reactions involved in gene transcription and translation, and

regulation thereof, and reactions involved in assembly of a cell and its subcellular components.

A reaction network data structure or index of reactions used in the data structure such as that available in a metabolic reaction database, as described above, can be annotated to include information about a particular reaction. A reaction can be annotated to indicate, for example, assignment of the reaction to a protein, macromolecule or enzyme that performs the reaction, assignment of a gene(s) that codes for the protein, macromolecule or enzyme, the Enzyme Commission (EC) number of the particular metabolic reaction, a subset of reactions to which the reaction belongs, citations to references from which information was obtained, or a level of confidence with which a reaction is believed to occur in *Homo sapiens* or other organism. A computer readable medium or media of the invention can include a gene database containing annotated reactions. Such information can be obtained during the course of building a metabolic reaction database or model of the invention as described below.

As used herein, the term "gene database" is intended to mean a computer readable medium or media that contains at least one reaction that is annotated to assign a reaction to one or more macromolecules that perform the reaction or to assign one or more nucleic acid that encodes the one or more macromolecules that perform the reaction. A gene database can contain a plurality of reactions, some or all of which are annotated. An annotation can include, for example, a name for a macromolecule; assignment of a function to a macromolecule; assignment of an organism that contains the macromolecule or produces the macromolecule; assignment of a subcellular location for the macromolecule; assignment of conditions under which a macromolecule is regulated with respect to performing a reaction, being expressed or being degraded; assignment of a cellular component that regulates a macromolecule; an amino acid or nucleotide sequence for the macromolecule; a mRNA isoform, enzyme isoform, or any other desirable annotation or annotation found for a macromolecule in a genome database such as those that can be found in Genbank, a site maintained by the NCBI (ncbi.nlm.gov), the Kyoto Encyclopedia of Genes and Genomes (KEGG) (www.genome.ad.jp/kegg/), the protein database SWISS-PROT (ca.expasy.org/sprot/), the LocusLink database maintained by the NCBI (www.ncbi.nlm.nih.gov/LocusLink/), the Enzyme Nomenclature database

maintained by G.P. Moss of Queen Mary and Westfield College in the United Kingdom (www.chem.qmw.ac.uk/iubmb/enzyme/).

A gene database of the invention can include a substantially complete collection of genes or open reading frames in a multicellular organism, including *Homo sapiens*, or a substantially complete collection of the macromolecules encoded by the organism's genome. Alternatively, a gene database can include a portion of genes or open reading frames in an organism or a portion of the macromolecules encoded by the organism's genome, such as the portion that includes substantially all metabolic genes or macromolecules. The portion can be at least 10%, 15%, 20%, 25%, 50%, 75%, 90% or 95% of the genes or open reading frames encoded by the organism's genome, or the macromolecules encoded therein. A gene database can also include macromolecules encoded by at least a portion of the nucleotide sequence for the organism's genome such as at least 10%, 15%, 20%, 25%, 50%, 75%, 90% or 95% of the organism's genome. Accordingly, a computer readable medium or media of the invention can include at least one reaction for each macromolecule encoded by a portion of an organism's genome, including a *Homo sapiens* genome.

An *in silico* model of multicellular interactions, including a *Homo sapiens* model, of the invention can be built by an iterative process which includes gathering information regarding particular reactions to be added to a model, representing the reactions in a reaction network data structure, and performing preliminary simulations wherein a set of constraints is placed on the reaction network and the output evaluated to identify errors in the network. Errors in the network such as gaps that lead to non-natural accumulation or consumption of a particular metabolite can be identified as described below and simulations repeated until a desired performance of the model is attained. An exemplary method for iterative model construction is provided in Example I. For multicellular interactions, an iterative process includes producing one or more component reaction networks followed by combining the components into a higher order multi-network system, as described in Example IV. For example, components can include the central metabolism reaction network and the cell specific reaction networks such as TAG biosynthesis for adipocytes or muscle contraction for myocytes. Combination of the central metabolism and the cell specific reaction networks into a single model produces, for example, a cell specific reaction network. Components also can include the individual

cell types, tissues, physiological systems or intra-system reaction networks that are constituents of the larger multicellular system. Combining these components into a larger model produces, for example, a model describing the relationships and interactions of the multicellular system together with its various interactions.

Thus, the invention provides a method for making a data structure relating a plurality of reactants to a plurality of reactions in a computer readable medium or media. The method includes the steps of: (a) identifying a plurality of reactions and a plurality of reactants that are substrates and products of the reactions; (b) relating the plurality of reactants to the plurality of *Homo sapiens* reactions in a data structure, wherein each of the reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product; (c) making a constraint set for the plurality of reactions; (d) providing an objective function; (e) determining at least one flux distribution that minimizes or maximizes the objective function when the constraint set is applied to the data structure, and (f) if the at least one flux distribution is not predictive of physiology, then adding a reaction to or deleting a reaction from the data structure and repeating step (e), if the at least one flux distribution is predictive of physiology, then storing the data structure in a computer readable medium or media. The method can be applied to multicellular interactions within or among single or multicullar organisms, including *Homo sapiens*.

Information to be included in a data structure of the invention can be gathered from a variety of sources including, for example, annotated genome sequence information and biochemical literature.

Sources of annotated human genome sequence information include, for example, KEGG, SWISS-PROT, LocusLink, the Enzyme Nomenclature database, the International Human Genome Sequencing Consortium and commercial databases. KEGG contains a broad range of information, including a substantial amount of metabolic reconstruction. The genomes of 304 organisms can be accessed here, with gene products grouped by coordinated functions, often represented by a map (e.g., the enzymes involved in glycolysis would be grouped together). The maps are biochemical pathway templates which show enzymes connecting metabolites for various parts of metabolism. These

general pathway templates are customized for a given organism by highlighting enzymes on a given template which have been identified in the genome of the organism. Enzymes and metabolites are active and yield useful information about stoichiometry, structure, alternative names and the like, when accessed.

SWISS-PROT contains detailed information about protein function. Accessible information includes alternate gene and gene product names, function, structure and sequence information, relevant literature references, and the like.

LocusLink contains general information about the locus where the gene is located and, of relevance, tissue specificity, cellular location, and implication of the gene product in various disease states.

The Enzyme Nomenclature database can be used to compare the gene products of two organisms. Often the gene names for genes with similar functions in two or more organisms are unrelated. When this is the case, the E.C. (Enzyme Commission) numbers can be used as unambiguous indicators of gene product function. The information in the Enzyme Nomenclature database is also published in Enzyme Nomenclature (Academic Press, San Diego, California, 1992) with 5 supplements to date, all found in the European Journal of Biochemistry (Blackwell Science, Malden, MA).

Sources of biochemical information include, for example, general resources relating to metabolism, resources relating specifically to human metabolism, and resources relating to the biochemistry, physiology and pathology of specific human cell types.

Sources of general information relating to metabolism, which were used to generate the human reaction databases and models described herein, were J.G. Salway, *Metabolism at a Glance*, 2nd ed., Blackwell Science, Malden, MA (1999) and T.M. Devlin, ed., *Textbook of Biochemistry with Clinical Correlations*, 4th ed., John Wiley and Sons, New York, NY (1997). Human metabolism-specific resources included J.R. Bronk, *Human Metabolism: Functional Diversity and Integration*, Addison Wesley Longman, Essex, England (1999).

The literature used in conjunction with the skeletal muscle metabolic models and simulations described herein included R. Maughan et al., *Biochemistry of Exercise and Training*, Oxford University Press, Oxford, England (1997), as well as references on muscle pathology such as S. Carpenter et al., *Pathology of Skeletal Muscle*, 2nd ed., Oxford University Press, Oxford, England (2001), and more specific articles on muscle metabolism as may be found in the Journal of Physiology (Cambridge University Press, Cambridge, England).

In the course of developing an *in silico* model of metabolism during or for multicellular interactions, the types of data that can be considered include, for example, biochemical information which is information related to the experimental characterization of a chemical reaction, often directly indicating a protein(s) associated with a reaction and the stoichiometry of the reaction or indirectly demonstrating the existence of a reaction occurring within a cellular extract; genetic information, which is information related to the experimental identification and genetic characterization of a gene(s) shown to code for a particular protein(s) implicated in carrying out a biochemical event; genomic information, which is information related to the identification of an open reading frame and functional assignment, through computational sequence analysis, that is then linked to a protein performing a biochemical event; physiological information, which is information related to overall cellular physiology, fitness characteristics, substrate utilization, and phenotyping results, which provide evidence of the assimilation or dissimilation of a compound used to infer the presence of specific biochemical event (in particular translocations); and modeling information, which is information generated through the course of simulating activity of cells, tissues or physiological systems using methods such as those described herein which lead to predictions regarding the status of a reaction such as whether or not the reaction is required to fulfill certain demands placed on a metabolic network. Additional information relevant to multicellular organisms that can be considered includes, for example, cell type-specific or condition-specific gene expression information, which can be determined experimentally, such as by gene array analysis or from expressed sequence tag (EST) analysis, or obtained from the biochemical and physiological literature.

The majority of the reactions occurring in a multicellular organism's reaction networks are catalyzed by enzymes/proteins, which are created through the

transcription and translation of the genes found within the chromosome in the cell. The remaining reactions occur either spontaneously or through non-enzymatic processes. Furthermore, a reaction network data structure can contain reactions that add or delete steps to or from a particular reaction pathway. For example, reactions can be added to optimize or improve performance of a model for multicellular interactions in view of empirically observed activity. Alternatively, reactions can be deleted to remove intermediate steps in a pathway when the intermediate steps are not necessary to model flux through the pathway. For example, if a pathway contains 3 nonbranched steps, the reactions can be combined or added together to give a net reaction, thereby reducing memory required to store the reaction network data structure and the computational resources required for manipulation of the data structure.

The reactions that occur due to the activity of gene-encoded enzymes can be obtained from a genome database which lists genes identified from genome sequencing and subsequent genome annotation. Genome annotation consists of the locations of open reading frames and assignment of function from homology to other known genes or empirically determined activity. Such a genome database can be acquired through public or private databases containing annotated nucleic acid or protein sequences, including *Homo sapiens* sequences. If desired, a model developer can perform a network reconstruction and establish the model content associations between the genes, proteins, and reactions as described, for example, in Covert et al. *Trends in Biochemical Sciences* 26:179-186 (2001) and Palsson, WO 00/46405.

As reactions are added to a reaction network data structure or metabolic reaction database, those having known or putative associations to the proteins/enzymes which enable/catalyze the reaction and the associated genes that code for these proteins can be identified by annotation. Accordingly, the appropriate associations for all of the reactions to their related proteins or genes or both can be assigned. These associations can be used to capture the non-linear relationship between the genes and proteins as well as between proteins and reactions. In some cases one gene codes for one protein which then perform one reaction. However, often there are multiple genes which are required to create an active enzyme complex and often there are multiple reactions that can be carried out by one protein or multiple proteins that can carry out the same reaction. These associations capture the logic (i.e. AND or OR relationships) within the associations.

Annotating a metabolic reaction database with these associations can allow the methods to be used to determine the effects of adding or eliminating a particular reaction not only at the reaction level, but at the genetic or protein level in the context of running a simulation or predicting a multicellular interaction activity, including *Homo sapiens* activity.

A reaction network data structure of the invention can be used to determine the activity of one or more reactions in a plurality of reactions occurring from multicellular interactions, including a plurality of *Homo sapiens* reactions, independent of any knowledge or annotation of the identity of the protein that performs the reaction or the gene encoding the protein. A model that is annotated with gene or protein identities can include reactions for which a protein or encoding gene is not assigned. While a large portion of the reactions in a cellular metabolic network are associated with genes in the organism's genome, there are also a substantial number of reactions included in a model for which there are no known genetic associations. Such reactions can be added to a reaction database based upon other information that is not necessarily related to genetics such as biochemical or cell based measurements or theoretical considerations based on observed biochemical or cellular activity. For example, there are many reactions that can either occur spontaneously or are not protein-enabled reactions. Furthermore, the occurrence of a particular reaction in a cell for which no associated proteins or genetics have been currently identified can be indicated during the course of model building by the iterative model building methods of the invention.

The reactions in a reaction network data structure or reaction database can be assigned to subsystems by annotation, if desired. The reactions can be subdivided according to biological criteria, such as according to traditionally identified metabolic pathways (glycolysis, amino acid metabolism and the like) or according to mathematical or computational criteria that facilitate manipulation of a model that incorporates or manipulates the reactions. Methods and criteria for subdviding a reaction database are described in further detail in Schilling et al., *J. Theor. Biol.* 203:249-283 (2000), and in Schuster et al., *Bioinformatics* 18:351-361 (2002). The use of subsystems can be advantageous for a number of analysis methods, such as extreme pathway analysis, and can make the management of model content easier. Although assigning reactions to subsystems can be achieved without affecting the use of the entire model for simulation,

assigning reactions to subsystems can allow a user to search for reactions in a particular subsystem which may be useful in performing various types of analyses. Therefore, a reaction network data structure can include any number of desired subsystems including, for example, 2 or more subsystems, 5 or more subsystems, 10 or more subsystems, 25 or more subsystems or 50 or more subsystems.

The reactions in a reaction network data structure or metabolic reaction database can be annotated with a value indicating the confidence with which the reaction is believed to occur in one or more cells of a multicellular interaction or in one or more reaction networks within a cell such as a *Homo sapiens* cell. The level of confidence can be, for example, a function of the amount and form of supporting data that is available. This data can come in various forms including published literature, documented experimental results, or results of computational analyses. Furthermore, the data can provide direct or indirect evidence for the existence of a chemical reaction in a cell based on genetic, biochemical, and/or physiological data.

The invention further provides a computer readable medium, containing (a) a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product, and (b) a constraint set for the plurality of *Homo sapiens* reactions. Similarly, the computer readable medium or media can relate a plurality of reactions to a plurality of reactions within first and second cells and for an intra-system between first and second interacting cells.

Constraints can be placed on the value of any of the fluxes in the metabolic network using a constraint set. These constraints can be representative of a minimum or maximum allowable flux through a given reaction, possibly resulting from a limited amount of an enzyme present. Additionally, the constraints can determine the direction or reversibility of any of the reactions or transport fluxes in the reaction network data structure. Based on the *in vivo* environment where multiple cells interact, such as in a human organism, the metabolic resources available to the cell for biosynthesis of essential molecules for can be determined. Allowing the corresponding transport fluxes to be

active provides the *in silico* interaction between cells with inputs and outputs for substrates and by-products produced by the metabolic network.

Returning to the hypothetical reaction network shown in Figure 1, constraints can be placed on each reaction in the exemplary format shown in Figure 2, as follows. The constraints are provided in a format that can be used to constrain the reactions of the stoichiometric matrix shown in Figure 3. The format for the constraints used for a matrix or in linear programming can be conveniently represented as a linear inequality such as

$$bj \leq vj \leq aj : j = 1....n \qquad \text{(Eq. 1)}$$

where v_j is the metabolic flux vector, b_j is the minimum flux value and a_j is the maximum flux value. Thus, a_j can take on a finite value representing a maximum allowable flux through a given reaction or b_j can take on a finite value representing minimum allowable flux through a given reaction. Additionally, if one chooses to leave certain reversible reactions or transport fluxes to operate in a forward and reverse manner the flux may remain unconstrained by setting b_j to negative infinity and a_j to positive infinity as shown for reaction R_2 in Figure 2. If reactions proceed only in the forward reaction b_j is set to zero while a_j is set to positive infinity as shown for reactions R_1, R_3, R_4, R_5, and R_6 in Figure 2. As an example, to simulate the event of a genetic deletion or non-expression of a particular protein, the flux through all of the corresponding metabolic reactions related to the gene or protein in question are reduced to zero by setting a_j and b_j to be zero. Furthermore, if one wishes to simulate the absence of a particular growth substrate one can simply constrain the corresponding transport fluxes that allow the metabolite to enter the cell to be zero by setting a_j and b_j to be zero. On the other hand if a substrate is only allowed to enter or exit the cell via transport mechanisms, the corresponding fluxes can be properly constrained to reflect this scenario.

The ability of a reaction to be actively occurring is dependent on a large number of additional factors beyond just the availability of substrates. These factors, which can be represented as variable constraints in the models and methods of the invention include, for example, the presence of cofactors necessary to stabilize the protein/enzyme, the presence or absence of enzymatic inhibition and activation factors,

the active formation of the protein/enzyme through translation of the corresponding mRNA transcript, the transcription of the associated gene(s) or the presence of chemical signals and/or proteins that assist in controlling these processes that ultimately determine whether a chemical reaction is capable of being carried out within an organism. Of particular importance in the regulation of human cell types is the implementation of paracrine and endocrine signaling pathways to control cellular activities. In these cases a cell secretes signaling molecules that may be carried far afield to act on distant targets (endocrine signaling), or act as local mediators (paracrine signaling). Examples of endocrine signaling molecules include hormones such as insulin, while examples of paracrine signaling molecules include neurotransmitters such as acetylcholine. These molecules induce cellular responses through signaling cascades that affect the activity of biochemical reactions in the cell. Regulation can be represented in an *in silico Homo sapiens* model by providing a variable constraint as set forth below.

Thus, the invention provides a computer readable medium or media, including (a) a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product, and wherein at least one of the reactions is a regulated reaction; and (b) a constraint set for the plurality of reactions, wherein the constraint set includes a variable constraint for the regulated reaction. Additionally, the invention provides a computer readable medium or media including data structures for two or more cells and for an intra-system and a constraint set for the plurality of reactions within the data structures that includes a variable constraint for a regulated reaction.

As used herein, the term "regulated," when used in reference to a reaction in a data structure, is intended to mean a reaction that experiences an altered flux due to a change in the value of a constraint or a reaction that has a variable constraint.

As used herein, the term "regulatory reaction" is intended to mean a chemical conversion or interaction that alters the activity of a protein, macromolecule or enzyme. A chemical conversion or interaction can directly alter the activity of a protein, macromolecule or enzyme such as occurs when the protein, macromolecule or enzyme is

post-translationally modified or can indirectly alter the activity of a protein, macromolecule or enzyme such as occurs when a chemical conversion or binding event leads to altered expression of the protein, macromolecule or enzyme. Thus, transcriptional or translational regulatory pathways can indirectly alter a protein, macromolecule or enzyme or an associated reaction. Similarly, indirect regulatory reactions can include reactions that occur due to downstream components or participants in a regulatory reaction network. When used in reference to a data structure or *in silico Homo sapiens* model, for example, the term is intended to mean a first reaction that is related to a second reaction by a function that alters the flux through the second reaction by changing the value of a constraint on the second reaction.

As used herein, the term "regulatory data structure" is intended to mean a representation of an event, reaction or network of reactions that activate or inhibit a reaction, the representation being in a format that can be manipulated or analyzed. An event that activates a reaction can be an event that initiates the reaction or an event that increases the rate or level of activity for the reaction. An event that inhibits a reaction can be an event that stops the reaction or an event that decreases the rate or level of activity for the reaction. Reactions that can be represented in a regulatory data structure include, for example, reactions that control expression of a macromolecule that in turn, performs a reaction such as transcription and translation reactions, reactions that lead to post translational modification of a protein or enzyme such as phophorylation, dephosphorylation, prenylation, methylation, oxidation or covalent modification, reactions that process a protein or enzyme such as removal of a pre- or pro-sequence, reactions that degrade a protein or enzyme or reactions that lead to assembly of a protein or enzyme.

As used herein, the term "regulatory event" is intended to mean a modifier of the flux through a reaction that is independent of the amount of reactants available to the reaction. A modification included in the term can be a change in the presence, absence, or amount of an enzyme that performs a reaction. A modifier included in the term can be a regulatory reaction such as a signal transduction reaction or an environmental condition such as a change in pH, temperature, redox potential or time. It will be understood that when used in reference to an *in silico Homo sapiens* model or data structure, or when used in reference to a model or data structure for a multicellular

interaction, a regulatory event is intended to be a representation of a modifier of the flux through a *Homo sapiens* reaction or reaction occurring in one or more cells in a multicellular interaction that is independent of the amount of reactants available to the reaction.

The effects of regulation on one or more reactions that occur in *Homo sapiens* can be predicted using an *in silico Homo sapiens* model or multicellular model of the invention. Regulation can be taken into consideration in the context of a particular condition being examined by providing a variable constraint for the reaction in an *in silico Homo sapiens* model or multicellular model. Such constraints constitute condition-dependent constraints. A data structure can represent regulatory reactions as Boolean logic statements (Reg-reaction). The variable takes on a value of 1 when the reaction is available for use in the reaction network and will take on a value of 0 if the reaction is restrained due to some regulatory feature. A series of Boolean statements can then be introduced to mathematically represent the regulatory network as described for example in Covert et al. *J. Theor. Biol.* 213:73-88 (2001). For example, in the case of a transport reaction (A_in) that imports metabolite A, where metabolite A inhibits reaction R2 as shown in Figure 4, a Boolean rule can state that:

$$\text{Reg-R2} = \text{IF NOT(A\_in)}. \qquad \text{(Eq. 2)}$$

This statement indicates that reaction R2 can occur if reaction A_in is not occurring (i.e. if metabolite A is not present). Similarly, it is possible to assign the regulation to a variable A which would indicate an amount of A above or below a threshold that leads to the inhibition of reaction R2. Any function that provides values for variables corresponding to each of the reactions in the biochemical reaction network can be used to represent a regulatory reaction or set of regulatory reactions in a regulatory data structure. Such functions can include, for example, fuzzy logic, heuristic rule-based descriptions, differential equations or kinetic equations detailing system dynamics.

A reaction constraint placed on a reaction can be incorporated into an *in silico Homo sapiens* model or mulicellular model of interacting cells using the following general equation:

$$(\text{Reg-Reaction}) * b_j \leq v_j \leq a_j * (\text{Reg-Reaction}), \forall$$

$j = 1....n$ (Eq. 3)

For the example of reaction R2 this equation is written as follows:

$(0)*\text{Reg-R2} \leq R2 \leq (\infty)*\text{Reg-R2}.$ (Eq. 4)

Thus, during the course of a simulation, depending upon the presence or absence of metabolite A in the interior of the cell where reaction R2 occurs, the value for the upper boundary of flux for reaction R2 will change from 0 to infinity, respectively.

With the effects of a regulatory event or network taken into consideration by a constraint function and the condition-dependent constraints set to an initial relevant value, the behavior of the *Homo sapiens* reaction network or one or more reaction networks of a multicellular interaction can be simulated for the conditions considered as set forth below.

Although regulation has been exemplified above for the case where a variable constraint is dependent upon the outcome of a reaction in the data structure, a plurality of variable constraints can be included in an *in silico Homo sapiens* model or other model of multicellular interactions to represent regulation of a plurality of reactions. Furthermore, in the exemplary case set forth above, the regulatory structure includes a general control stating that a reaction is inhibited by a particular environmental condition. Using a general control of this type, it is possible to incorporate molecular mechanisms and additional detail into the regulatory structure that is responsible for determining the active nature of a particular chemical reaction within an organism.

Regulation can also be simulated by a model of the invention and used to predict a *Homo sapiens* physiological function without knowledge of the precise molecular mechanisms involved in the reaction network being modeled. Thus, the model can be used to predict, *in silico*, overall regulatory events or causal relationships that are not apparent from *in vivo* observation of any one reaction in a network or whose *in vivo* effects on a particular reaction are not known. Such overall regulatory effects can include those that result from overall environmental conditions such as changes in pH, temperature, redox potential, or the passage of time.

As described previously and further below, the models and method of the invention are applicable to a wide range of multicellular interactions. The multicellular interactions include, for example, interactions between prokaryotic cells such as colony growth and chemotaxis. The multicellular interactions include, for example, interactions between two or more eukaryotic cells such as the concerted action of two or more cells of the same or different cell type. A specific example of the concerted action of the same cell type includes the combined output of the contractile activity of myocytes. A specific example of the concerted action of different cell types includes the energy production of adipocyte cells and the contractile activity of myocyte cells based on the consumption of energy available from the adipocyte cells. Multicellular interactions also can include, for example, interactions between host cells and a pathogen, such as a bacteria, virus or worm, as well as symbiotic interactions between host cells and microbes, for example. A symbiotic microbe can include, for example, *E. coli*. Further examples of host and microbe interactions include bacterial communities that reside in the skin and mouth and the vagina flora, providing the host with a defense against infections. Moreover, the models and methods of the invention also can be used to reconstruction the reaction networks between a plurality of dynamic multicellular interactions including, for example, interactions between host cells or tissues, pathogen and symbiotic microbe.

Multicellular interactions also include, for example, interactions between cells of different tissues, different organs and/or physiological systems as well as interactions between some or all cells, tissues organs and/or physiological systems within a multicellular organism. Specific examples of such interactions include organismic homeostasis, signal transduction, the endocrine system, the exocrine system, sensory transduction, secretion, the hematopoietic system, the immune system, cell migration, cell adherence, cell invasion and neuronal and synaptic transduction. Numerous other multicellular interactions are well known in the art and can similarly be reconstructed and simulated to predict an activity thereof using the models and methods of the invention.

Given the teachings and guidance provided herein with respect to the construction and use of multiple reaction networks including, for example, the regulated and metabolic reaction networks of a *Homo sapiens* cell, those skilled in the art will know how to employ the models and methods of the invention for the construction and use of any multicellular interaction. Specific examples of such multicellular interactions are

described above. Other examples of multicellular interactions include, for example, all interactions occurring between two or more cells such as those cells set forth in Table 5 below. Such multicellular interactions can occur between cells within the same or different physiological category or functional characterization. Similarly, such multicellular interactions also can occur between cells within the same and between different physiological categories or functional characterizations. The number and types of different cellular interactions will be determined by the multicellular model being produced using the methods of the invention.

Models of multicellular interactions also can include, for example, interactions between cells of one or more tissues and organs. The models and methods of the invention are applicable to predict the activity of interactions between some or all cell types of a tissue or organ. The models and methods of the invention also can include reaction networks that include interactions between some or all cell types of two or more tissues or organs. Specific examples of tissues or organs and their respective cell types and functions are shown below in Table 6. The models and methods of the invention can include, for example, some or all of these interactions to predict their respective activities.. Similarly, Table 7 exemplifies the cell types of a liver. Given the teachings and guidance provided herein, the models and methods of the invention can be used to construct an *in silico* reconstruction of the reaction networks for some or all of these cell types to predict some or all of the activities of the liver. Further, an *in silico* reconstruction of reaction networks for some or all multicellular interactions exemplified in Tables 5-7, including those within and between tissues and organs, can be produced that can be used to predict some or all activities of one or more tissues or of an organism. Therefore, the invention provides for the *in silico* reconstruction of whole organisms, including human organisms, tissues, cells and physical or physiological functions performed by such cellular systems.

The invention also provides for the *in silico* reconstruction of a plurality of reaction networks that interact to perform the same or different activity. The plurality can be a small, medium or large plurality and can reside within the same cell, different cells or in different tissues or organisms. Specific examples of such pluralities residing within the same cell include the reaction networks exemplified below in Example IV for a myocyte or for an adipocyte. Specific examples of such pluralities residing in different

cells or tissues include the reaction networks exemplified below in Example IV for coupled adipocyte-myocyte metabolism. Another example of interactions between different reaction networks within different networks includes interactions between pathogen and host cells.

Briefly, and as described previously, a computer readable medium or media can be produced that includes a plurality of data structures each relating a plurality of reactants to a plurality of reactions from each cell within the multicellular interaction. The reactions include a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and said product In a two cell interaction, including populations of two cell types, the plurality of data structures can include a first data structure and a second data structure corresponding to the reactions within the two cells or populations of two cell types. The data structures will describe the reaction networks for each cell.

For optimization of the multicellular interaction containing two cells, a third data structure is particularly useful for relating a plurality of intra-system reactants to a plurality of intra-system reactions between the first and second cells. Each of the intra-system reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and said product. The inta-system data structure can be included in the reconstruction as an independent data structure or as a component of one or more data structures for either or both cells within such a two cell interaction model. A specific example of intra-system reactions represented by a third data structure is shown in Figure 10 for the bicarbonate and ammonia buffer systems employed in the two cell model describing adipocyte and myocyte interactions.

As with the models and methods of the invention described above and below, a computer readable medium or media describing a multicellular interaction also will contain a constraint set for the plurality of reactions for each of the first, second and third data structures as well as commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures. The objective function can be, for example, those objective functions exemplified previously, those exemplified below or in the Examples

as well as various other object functions well known to those skilled in the art given the teachings and guidance provided herein. Solving the optimization problem by determining one or more flux distribution will predict a physiological function of occurring as a result of the interaction between the first and second cells of the model.

Each of the first, second or third data structures can include one or more reaction networks. For example, and with reference to Figures 5-10, a reaction network for each of the cells exemplified therein can be defined as the different networks within each cell such as central metabolism and the cell specific reactions. Applying this view, the adipocyte and myocyte cells each contain at least two reaction networks. When combined together with the intra-cellular reaction network and the exchange reactions, the interactions of the two cells exemplified in Figure 6 can be described by at least five different reaction networks. The interactions of this two cell model can therefore be described using at least five data structures. Alternatively, a reaction network can be defined as all the networks within each cell. When combined together with the intra-cellular reaction network and the exchange reactions, the interactions of the exemplified adipocyte and myocyte cells can be described by at least three different reaction networks. One reaction network for each cell and one reaction network for the intra-system reactions. Therefore, each of the first, second or third data structures can consist of a plurality of two or more reaction networks including, for example, 2, 3, 4, 5, 10, 20 or 25 or more as well as all integer numbers between and above these exemplary numbers. Similarly, given the teachings and guidance provided herein, the models and methods of the invention can be generated and used to predict an activity and/or physiological function of the intercellular network interactions or the intracellular network interaction. The latter interactions, for example, also predict an activity and/or a physiological function of the interactions between two or more cells including cells of different tissues, organs of a multicellular organism or of a whole organism.

As with the number of reaction networks within a data structure, the models and methods of the invention also can employ greater than three data structures as exemplified above. For example, the models and method of the invention can comprise one or more fourth data structures having one or more fourth constraint sets where each fourth data structure relates a plurality of reactants to a plurality of reactions from a cell already included in the model or from one or more third cells within the multicellular

interaction. Use of one or more fourth data structures is particularly useful when reconstructing a interactions between three or more interacting cells including a large plurality of cells such as the cells within a tissue, organ, physiological system or organism. Each of the reactions within such fourth data structures include a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and said product.

The number of fourth data structures can correspond to the number of cells greater than the first and second cells of the multicellular interaction and include, for example, a plurality of data structures. As with the specific embodiment of a two cell interaction, the plurality of data structures for three or more interacting cells can correspond to different cells within the cellular interaction as well as correspond to different cell types within the cellular interaction. The number of cells can include, for example, at least 4 cells, 5 cells, 6 cells, 7 cells, 8 cells, 9 cells, 10 cells, 100 cells, 1000 cells, 5000 cells, 10,000 cells or more. Therefore, the number of cells within a multicellular interaction model or used in a method of predicting a behavior of such multicellular interactions can include some or all cells which constitute a group of interacting cells, a tissue, organ, physiological system or whole organism. The multicellular interaction models and methods of the invention also can include some or all cells which constitute a group of interacting cells of different types or from different tissues, organs, physiological systems or organisms. The organism can be single cell prokaryotic or eukaryotic organism or multicellular eukaryotic organisms. Specific examples of different cell types include a mammary gland cell, hepatocyte, white fat cell, brown fat cell, liver lipocyte, red skeletal muscle cell, white skeletal muscle cell, intermediate skeletal muscle cell, smooth muscle cell, red blood cell, adipocyte, monocyte, reticulocyte, fibroblast, neuronal cell epithelial cell or one or more cells set forth in Table 5. Specific examples of physiological functions resulting from multicellular interactions that can be predicted include metabolite yield, ATP yield, biomass demand, growth, triacylglycerol storage, muscle contraction, milk secretion and oxygen transport capacity.

Intra-system reactions of a multicellular interaction model or method of the invention has been exemplified above and below with reference to the extracellular *in vivo* environment and, in particular, with reference to buffering this environment by

supplying functions of the renal system. Given the teachings and guidance provided herein, those skilled in the art will understand that any extracellular reaction, plurality of reactions, function of the extracellular space or function supplied into the extracellular space by another cell, tissue or physiological system can be employed as an intra-system reaction network. Such reactions or activities can represent normal or pathological conditions or both conditions occurring within this intra-system environment. Specific examples of intra-system reactions include one or more reactions performed in the hematopoietic system, urine, connective tissue, contractile tissue or cells, lymphatic system, respiratory system or renal system. Reactions or reactants included in one or more intra-system data structures can be, for example, bicarbonate buffer system, an ammonia buffer system, a hormone, a signaling molecule, a vitamin, a mineral or a combination thereof.

The *in silico* models of multicellular or multi-network interactions, including *Homo sapiens* model and methods, described herein can be implemented on any conventional host computer system, such as those based on Intel.RTM. microprocessors and running Microsoft Windows operating systems. Other systems, such as those using the UNIX or LINUX operating system and based on IBM.RTM., DEC.RTM. or Motorola.RTM. microprocessors are also contemplated. The systems and methods described herein can also be implemented to run on client-server systems and wide-area networks, such as the Internet.

Software to implement a method or model of the invention can be written in any well-known computer language, such as Java, C, C++, Visual Basic, FORTRAN or COBOL and compiled using any well-known compatible compiler. The software of the invention normally runs from instructions stored in a memory on a host computer system. A memory or computer readable medium can be a hard disk, floppy disc, compact disc, magneto-optical disc, Random Access Memory, Read Only Memory or Flash Memory. The memory or computer readable medium used in the invention can be contained within a single computer or distributed in a network. A network can be any of a number of conventional network systems known in the art such as a local area network (LAN) or a wide area network (WAN). Client-server environments, database servers and networks that can be used in the invention are well known in the art. For example, the database server can run on an operating system such as UNIX, running a relational database

management system, a World Wide Web application and a World Wide Web server. Other types of memories and computer readable media are also contemplated to function within the scope of the invention.

A database or data structure of the invention can be represented in a markup language format including, for example, Standard Generalized Markup Language (SGML), Hypertext markup language (HTML) or Extensible Markup language (XML). Markup languages can be used to tag the information stored in a database or data structure of the invention, thereby providing convenient annotation and transfer of data between databases and data structures. In particular, an XML format can be useful for structuring the data representation of reactions, reactants and their annotations; for exchanging database contents, for example, over a network or internet; for updating individual elements using the document object model; or for providing differential access to multiple users for different information content of a data base or data structure of the invention. XML programming methods and editors for writing XML code are known in the art as described, for example, in Ray, "Learning XML" O'Reilly and Associates, Sebastopol, CA (2001).

A set of constraints can be applied to a reaction network data structure to simulate the flux of mass through the reaction network under a particular set of environmental conditions specified by a constraints set. Because the time constants characterizing metabolic transients and/or metabolic reactions are typically very rapid, on the order of milli-seconds to seconds, compared to the time constants of cell growth on the order of hours to days, the transient mass balances can be simplified to only consider the steady state behavior. Referring now to an example where the reaction network data structure is a stoichiometric matrix, the steady state mass balances can be applied using the following system of linear equations

$$S \cdot v = 0 \qquad \text{(Eq. 5)}$$

where S is the stoichiometric matrix as defined above and v is the flux vector. This equation defines the mass, energy, and redox potential constraints placed on the metabolic network as a result of stoichiometry. Together Equations 1 and 5 representing the reaction constraints and mass balances, respectively, effectively define the capabilities

and constraints of the metabolic genotype and the organism's metabolic potential. All vectors, v, that satisfy Equation 5 are said to occur in the mathematical nullspace of S. Thus, the null space defines steady-state metabolic flux distributions that do not violate the mass, energy, or redox balance constraints. Typically, the number of fluxes is greater than the number of mass balance constraints, thus a plurality of flux distributions satisfy the mass balance constraints and occupy the null space. The null space, which defines the feasible set of metabolic flux distributions, is further reduced in size by applying the reaction constraints set forth in Equation 1 leading to a defined solution space. A point in this space represents a flux distribution and hence a metabolic phenotype for the network. An optimal solution within the set of all solutions can be determined using mathematical optimization methods when provided with a stated objective and a constraint set. The calculation of any solution constitutes a simulation of the model.

Objectives for activity of a human cell can be chosen. While the overall objective of a multi-cellular organism may be growth or reproduction, individual human cell types generally have much more complex objectives, even to the seemingly extreme objective of apoptosis (programmed cell death), which may benefit the organism but certainly not the individual cell. For example, certain cell types may have the objective of maximizing energy production, while others have the objective of maximizing the production of a particular hormone, extracellular matrix component, or a mechanical property such as contractile force. In cases where cell reproduction is slow, such as human skeletal muscle, growth and its effects need not be taken into account. In other cases, biomass composition and growth rate could be incorporated into a "maintenance" type of flux, where rather than optimizing for growth, production of precursors is set at a level consistent with experimental knowledge and a different objective is optimized.

Certain cell types, including cancer cells, can be viewed as having an objective of maximizing cell growth. Growth can be defined in terms of biosynthetic requirements based on literature values of biomass composition or experimentally determined values such as those obtained as described above. Thus, biomass generation can be defined as an exchange reaction that removes intermediate metabolites in the appropriate ratios and represented as an objective function. In addition to draining intermediate metabolites this reaction flux can be formed to utilize energy molecules such as ATP, NADH and NADPH so as to incorporate any maintenance requirement that must

be met. This new reaction flux then becomes another constraint/balance equation that the system must satisfy as the objective function. Using the stoichiometric matrix of Figure 3 as an example, adding such a constraint is analogous to adding the additional column V_{growth} to the stoichiometric matrix to represent fluxes to describe the production demands placed on the metabolic system. Setting this new flux as the objective function and asking the system to maximize the value of this flux for a given set of constraints on all the other fluxes is then a method to simulate the growth of the organism.

Continuing with the example of the stoichiometric matrix applying a constraint set to a reaction network data structure can be illustrated as follows. The solution to equation 5 can be formulated as an optimization problem, in which the flux distribution that minimizes a particular objective is found. Mathematically, this optimization problem can be stated as:

Minimize Z (Eq. 6)

where $z = \sum c_i \cdot v_i$ (Eq. 7)

where Z is the objective which is represented as a linear combination of metabolic fluxes v_i using the weights c_i in this linear combination. The optimization problem can also be stated as the equivalent maximization problem; i.e. by changing the sign on Z. Any commands for solving the optimazation problem can be used including, for example, linear programming commands.

A computer system of the invention can further include a user interface capable of receiving a representation of one or more reactions. A user interface of the invention can also be capable of sending at least one command for modifying the data structure, the constraint set or the commands for applying the constraint set to the data representation, or a combination thereof. The interface can be a graphic user interface having graphical means for making selections such as menus or dialog boxes. The interface can be arranged with layered screens accessible by making selections from a main screen. The user interface can provide access to other databases useful in the invention such as a metabolic reaction database or links to other databases having information relevant to the reactions or reactants in the reaction network data structure or

to a multicellular organism's physiology, including *Homo sapiens* physiology. Also, the user interface can display a graphical representation of a reaction network or the results of a simulation using a model of the invention.

Once an initial reaction network data structure and set of constraints has been created, this model can be tested by preliminary simulation. During preliminary simulation, gaps in the network or "dead-ends" in which a metabolite can be produced but not consumed or where a metabolite can be consumed but not produced can be identified. Based on the results of preliminary simulations areas of the metabolic reconstruction that require an additional reaction can be identified. The determination of these gaps can be readily calculated through appropriate queries of the reaction network data structure and need not require the use of simulation strategies, however, simulation would be an alternative approach to locating such gaps.

In the preliminary simulation testing and model content refinement stage the existing model is subjected to a series of functional tests to determine if it can perform basic requirements such as the ability to produce the required biomass constituents and generate predictions concerning the basic physiological characteristics of the particular cell type being modeled. The more preliminary testing that is conducted the higher the quality of the model that will be generated. Typically, the majority of the simulations used in this stage of development will be single optimizations. A single optimization can be used to calculate a single flux distribution demonstrating how metabolic resources are routed determined from the solution to one optimization problem. An optimization problem can be solved using linear programming as demonstrated in the Examples below. The result can be viewed as a display of a flux distribution on a reaction map. Temporary reactions can be added to the network to determine if they should be included into the model based on modeling/simulation requirements.

Once a model of the invention is sufficiently complete with respect to the content of the reaction network data structure according to the criteria set forth above, the model can be used to simulate activity of one or more reactions in a reaction network. The results of a simulation can be displayed in a variety of formats including, for example, a table, graph, reaction network, flux distribution map or a phenotypic phase plane graph.

Thus, the invention provides a method for predicting a *Homo sapiens* physiological function. The method includes the steps of (a) providing a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) providing a constraint set for the plurality of *Homo sapiens* reactions; (c) providing an objective function, and (d) determining at least one flux distribution that minimizes or maximizes the objective function when the constraint set is applied to the data structure, thereby predicting a *Homo sapiens* physiological function.

A method for predicting a *Homo sapiens* physiological function can include the steps of (a) providing a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product, and wherein at least one of the reactions is a regulated reaction; (b) providing a constraint set for the plurality of reactions, wherein the constraint set includes a variable constraint for the regulated reaction; (c) providing a condition-dependent value to the variable constraint; (d) providing an objective function, and (e) determining at least one flux distribution that minimizes or maximizes the objective function when the constraint set is applied to the data structure, thereby predicting a *Homo sapiens* physiological function.

Further, a method for predicting a physiological function of a multicellular organism also is provided. The method includes: (a) providing a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) providing a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (c) providing a third data structure relating a plurality of intra-system reactants to a plurality

of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (d) providing a constraint set for said plurality of reactions for said first, second and third data structures; (e) providing an objective function, and (f) determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

As used herein, the term "physiological function," when used in reference to *Homo sapiens*, is intended to mean an activity of an organism as a whole, including a multicellular organism and/or a *Homo sapiens* organism or cell as a whole. An activity included in the term can be the magnitude or rate of a change from an initial state of, for example, two or more interacting cells or a *Homo sapiens* cell to a final state of the two or more interacting cells or the *Homo sapiens* cell. An activity included in the term can be, for example, growth, energy production, redox equivalent production, biomass production, development, or consumption of carbon nitrogen, sulfur, phosphate, hydrogen or oxygen. An activity can also be an output of a particular reaction that is determined or predicted in the context of substantially all of the reactions that affect the particular reaction in two or more interacting cells or a *Homo sapiens* cell, for example, or substantially all of the reactions that occur in a plurality of interacting cells such as a tissue, organ or organism, or substantially all of the reactions that occur in a *Homo sapiens* cell (e.g. muscle contraction). Examples of a particular reaction included in the term are production of biomass precursors, production of a protein, production of an amino acid, production of a purine, production of a pyrimidine, production of a lipid, production of a fatty acid, production of a cofactor or transport of a metabolite. A physiological function can include an emergent property which emerges from the whole but not from the sum of parts where the parts are observed in isolation (see for example, Palsson, *Nat. Biotech* 18:1147-1150 (2000)).

A physiological function of reactions within two or more interacting cells, including *Homo sapiens* reactions, can be determined using phase plane analysis of flux distributions. Phase planes are representations of the feasible set which can be presented

in two or three dimensions. As an example, two parameters that describe the growth conditions such as substrate and oxygen uptake rates can be defined as two axes of a two-dimensional space. The optimal flux distribution can be calculated from a reaction network data structure and a set of constraints as set forth above for all points in this plane by repeatedly solving the linear programming problem while adjusting the exchange fluxes defining the two-dimensional space. A finite number of qualitatively different metabolic pathway utilization patterns can be identified in such a plane, and lines can be drawn to demarcate these regions. The demarcations defining the regions can be determined using shadow prices of linear optimization as described, for example in Chvatal, *Linear Programming* New York, W.H. Freeman and Co. (1983). The regions are referred to as regions of constant shadow price structure. The shadow prices define the intrinsic value of each reactant toward the objective function as a number that is either negative, zero, or positive and are graphed according to the uptake rates represented by the x and y axes. When the shadow prices become zero as the value of the uptake rates are changed there is a qualitative shift in the optimal reaction network.

One demarcation line in the phenotype phase plane is defined as the line of optimality (LO). This line represents the optimal relation between respective metabolic fluxes. The LO can be identified by varying the x-axis flux and calculating the optimal y-axis flux with the objective function defined as the growth flux . From the phenotype phase plane analysis the conditions under which a desired activity is optimal can be determined. The maximal uptake rates lead to the definition of a finite area of the plot that is the predicted outcome of a reaction network within the environmental conditions represented by the constraint set. Similar analyses can be performed in multiple dimensions where each dimension on the plot corresponds to a different uptake rate. These and other methods for using phase plane analysis, such as those described in Edwards et al., *Biotech Bioeng.* 77:27-36(2002), can be used to analyze the results of a simulation using an *in silico Homo sapiens* model of the invention.

A physiological function of *Homo sapiens* can also be determined using a reaction map to display a flux distribution. A reaction map of *Homo sapiens* can be used to view reaction networks at a variety of levels. In the case of a cellular metabolic reaction network a reaction map can contain the entire reaction complement representing a global perspective. Alternatively, a reaction map can focus on a particular region of

metabolism such as a region corresponding to a reaction subsystem described above or even on an individual pathway or reaction.

Thus, the invention provides an apparatus that produces a representation of a *Homo sapiens* physiological function, wherein the representation is produced by a process including the steps of: (a) providing a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product; (b) providing a constraint set for the plurality of *Homo sapiens* reactions; (c) providing an objective function; (d) determining at least one flux distribution that minimizes or maximizes the objective function when the constraint set is applied to the data structure, thereby predicting a *Homo sapiens* physiological function, and (e) producing a representation of the activity of the one or more *Homo sapiens* reactions. Similarly, the invention provides an apparatus that produces a representation of two or more interacting cells, including a tissue, organ, physiological system or whole organism wherein data structures are provided relating a plurality of reactants to a plurality of reactions for each type of interacting cell and for one or more intra-system functions. A constraint set is provided for the plurality of reactions for the plurality of data structures as well as an objective function that minimizes or maximizes an objective function when the constraint set is applied to predict a physiological function of the two or more interacting cells. The apparatus produces a representation of the activity of one more reactions of the two or more interacting cells.

The methods of the invention can be used to determine the activity of a plurality of *Homo sapiens* reactions including, for example, biosynthesis of an amino acid, degradation of an amino acid, biosynthesis of a purine, biosynthesis of a pyrimidine, biosynthesis of a lipid, metabolism of a fatty acid, biosynthesis of a cofactor, transport of a metabolite and metabolism of an alternative carbon source. In addition, the methods can be used to determine the activity of one or more of the reactions described above or listed in Table 1.

The methods of the invention can be used to determine a phenotype of a *Homo sapiens* mutant or aberrant cellular interaction between two or more cells. The

activity of one or more reactions can be determined using the methods described above, wherein the reaction network data structure lacks one or more gene-associated reactions that occur in *Homo sapiens* or in a multicellular organism or multicellular interaction. Alternatively, the methods can be used to determine the activity of one or more reactions when a reaction that does not naturally occur in the model of multicellular interactions or in *Homo sapiens*, for example, is added to the reaction network data structure. Deletion of a gene can also be represented in a model of the invention by constraining the flux through the reaction to zero, thereby allowing the reaction to remain within the data structure. Thus, simulations can be made to predict the effects of adding or removing genes to or from one or more cells within a multicellular interaction, including *Homo sapiens* and/or a *Homo sapiens* cell. The methods can be particularly useful for determining the effects of adding or deleting a gene that encodes for a gene product that performs a reaction in a peripheral metabolic pathway.

A drug target or target for any other agent that affects a function of a multicellular interaction, including a *Homo sapiens* function can be predicted using the methods of the invention. Such predictions can be made by removing a reaction to simulate total inhibition or prevention by a drug or agent. Alternatively, partial inhibition or reduction in the activity a particular reaction can be predicted by performing the methods with altered constraints. For example, reduced activity can be introduced into a model of the invention by altering the a_j or b_j values for the metabolic flux vector of a target reaction to reflect a finite maximum or minimum flux value corresponding to the level of inhibition. Similarly, the effects of activating a reaction, by initiating or increasing the activity of the reaction, can be predicted by performing the methods with a reaction network data structure lacking a particular reaction or by altering the a_j or b_j values for the metabolic flux vector of a target reaction to reflect a maximum or minimum flux value corresponding to the level of activation. The methods can be particularly useful for identifying a target in a peripheral metabolic pathway.

Once a reaction has been identified for which activation or inhibition produces a desired effect on a function of a multicellular interaction, including a *Homo sapiens* function, an enzyme or macromolecule that performs the reaction in the multicellular system or a gene that expresses the enzyme or macromolecule can be identified as a target for a drug or other agent. A candidate compound for a target

identified by the methods of the invention can be isolated or synthesized using known methods. Such methods for isolating or synthesizing compounds can include, for example, rational design based on known properties of the target (see, for example, DeCamp et al., *Protein Engineering Principles and Practice*, Ed. Cleland and Craik, Wiley-Liss, New York, pp. 467-506 (1996)), screening the target against combinatorial libraries of compounds (see for example, Houghten *et al.*, *Nature*, 354, 84-86 (1991); Dooley *et al.*, *Science*, 266, 2019-2022 (1994), which describe an iterative approach, or R. Houghten et al. PCT/US91/08694 and U.S. Patent 5,556,762 which describe the positional-scanning approach), or a combination of both to obtain focused libraries. Those skilled in the art will know or will be able to routinely determine assay conditions to be used in a screen based on properties of the target or activity assays known in the art.

A candidate drug or agent, whether identified by the methods described above or by other methods known in the art, can be validated using an *in silico* model or method of multicellular interactions, including a *Homo sapiens* model or method of the invention. The effect of a candidate drug or agent on physiological function can be predicted based on the activity for a target in the presence of the candidate drug or agent measured *in vitro* or *in vivo*. This activity can be represented in an *in silico* model of the multicellular system by adding a reaction to the model, removing a reaction from the model or adjusting a constraint for a reaction in the model to reflect the measured effect of the candidate drug or agent on the activity of the reaction. By running a simulation under these conditions the holistic effect of the candidate drug or agent on the physiological function of the multicellular system, including *Homo sapiens* physiological function can be predicted.

The methods of the invention can be used to determine the effects of one or more environmental components or conditions on an activity of, for example, a multicellular interaction, a tissue, organ, physiological function or a *Homo sapiens* cell. As set forth above an exchange reaction can be added to a reaction network data structure corresponding to uptake of an environmental component, release of a component to the environment, or other environmental demand. The effect of the environmental component or condition can be further investigated by running simulations with adjusted a_j or b_j values for the metabolic flux vector of the exchange reaction target reaction to reflect a finite maximum or minimum flux value corresponding to the effect of the

environmental component or condition. The environmental component can be, for example an alternative carbon source or a metabolite that when added to the environment of a multicellular system, organism or *Homo sapiens* cell can be taken up and metabolized. The environmental component can also be a combination of components present for example in a minimal medium composition. Thus, the methods can be used to determine an optimal or minimal medium composition that is capable of supporting a particular activity of a multicellular interaction or system, including a particular activity of *Homo sapiens*.

The invention further provides a method for determining a set of environmental components to achieve a desired activity for *Homo sapiens*. The method includes the steps of (a) providing a data structure relating a plurality of *Homo sapiens* reactants to a plurality of *Homo sapiens* reactions, wherein each of the *Homo sapiens* reactions includes a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating the substrate and the product; (b)providing a constraint set for the plurality of *Homo sapiens* reactions; (c) applying the constraint set to the data representation, thereby determining the activity of one or more *Homo sapiens* reactions (d) determining the activity of one or more *Homo sapiens* reactions according to steps (a) through (c), wherein the constraint set includes an upper or lower bound on the amount of an environmental component and (e) repeating steps (a) through (c) with a changed constraint set, wherein the activity determined in step (e) is improved compared to the activity determined in step (d). Similarly, a method for determining a set of environmental components to achieve a desired activity for a multicellular interaction also is provided. The method includes providing a plurality of data structures relating a plurality of reactants to a plurality of reactions for each type of interacting cell and for one or more intra-system functions; providing a constraint set for the plurality of reactions for the plurality of data structures as well as providing an objective function that minimizes or maximizes an objective function when the constraint set is applied to predict a physiological function of the two or more interacting cells; determining the activity of one or more reactions within two or more interacting cells using a constraint set having an upper or lower bound on the amount of an environmental component and repeating these steps until the activity is improved.

It is understood that modifications which do not substantially affect the activity of the various embodiments of this invention are also included within the definition of the invention provided herein. Accordingly, the following examples are intended to illustrate but not limit the present invention.

EXAMPLE I

This example shows the construction of a universal *Homo sapiens* metabolic reaction database, a *Homo sapiens* core metabolic reaction database and a *Homo sapiens* muscle cell metabolic reaction database. This example also shows the iterative model building process used to generate a *Homo sapiens* core metabolic model and a *Homo sapiens* muscle cell metabolic model.

A universal *Homo sapiens* reaction database was prepared from the genome databases and biochemical literature. The reaction database shown in Table 1 contains the following information:

Locus ID - the locus number of the gene found in the LocusLink website.

Gene Ab. - various abbreviations which are used for the gene.

Reaction Stoichiometry - includes all metabolites and direction of the reaction, as well as reversibility.

E.C. - The Enzyme Commission number.

Additional information included in the universal reaction database, although not shown in Table 1, included the chapter of Salway, supra (1999), where relevant reactions were found; the cellular location, if the reaction primarily occurs in a given compartment; the SWISS PROT identifier, which can be used to locate the gene record in SWISS PROT; the full name of the gene at the given locus; the chromosomal location of the gene; the Mendelian Inheritance in Man (MIM) data associated with the gene; and the tissue type, if the gene is primarily expressed in a certain tissue. Overall, 1130 metabolic enzyme- or transporter-encoding genes were included in the universal reaction database.

Fifty-nine reactions in the universal reaction database were identified and included based on biological data as found in Salway supra (1999), currently without genome annotation. Ten additional reactions, not described in the biochemical literature or genome annotation, were subsequently included in the reaction database following preliminary simulation testing and model content refinement. These 69 reactions are shown at the end of Table 1.

From the universal *Homo sapiens* reaction database shown in Table 1, a core metabolic reaction database was established, which included core metabolic reactions as well as some amino acid and fatty acid metabolic reactions, as described in Chapters 1, 3, 4, 7, 9, 10, 13, 17, 18 and 44 of J.G. Salway, Metabolism at a Glance, 2nd ed., Blackwell Science, Malden, MA (1999). The core metabolic reaction database included 211 unique reactions, accounting for 737 genes in the *Homo sapiens* genome. The core metabolic reaction database was used, although not in its entirety, to create the core metabolic model described in Example II.

To allow for the modeling of muscle cells, the core reaction database was expanded to include 446 unique reactions, accounting for 889 genes in the *Homo sapiens* genome. This skeletal muscle metabolic reaction database was used to create the skeletal muscle metabolic model described in Example II.

Once the core and muscle cell metabolic reaction databases were compiled, the reactions were represented as a metabolic network data structure, or "stoichiometric input file." For example, the core metabolic network data structure shown in Table 2 contains 33 reversible reactions, 31 non-reversible reactions, 97 matrix columns and 52 unique enzymes. Each reaction in Table 2 is represented so as to indicate the substrate or substrates (a negative number) and the product or products (a positive number); the stoichiometry; the name of each reaction (the term following the zero); and whether the reaction is reversible (an R following the reaction name). A metabolite that appears in the mitochondria is indicated by an "m," and a metabolite that appears in the extracellular space is indicated by an "ex."

To perform a preliminary simulation or to simulate a physiological condition, a set of inputs and outputs has to be defined and the network objective function

specified. To calculate the maximum ATP production of the *Homo sapiens* core metabolic network using glucose as a carbon source, a non-zero uptake value for glucose was assigned and ATP production was maximized as the objective function, using the representation shown in Table 2. The network's performance was examined by optimizing for the given objective function and the set of constraints defined in the input file, using flux balance analysis methods. The model was refined in an iterative manner by examining the results of the simulation and implementing the appropriate changes.

Using this iterative procedure, two metabolic reaction networks were generated, representing human core metabolism and human skeletal muscle cell metabolism.

EXAMPLE II

This example shows how human metabolism can be accurately simulated using a *Homo sapiens* core metabolic model.

The human core metabolic reaction database shown in Table 3 was used in simulations of human core metabolism. This reaction database contains a total of 65 reactions, covering the classic biochemical pathways of glycolysis, the pentose phosphate pathway, the tricitric acid cycle, oxidative phosphorylation, glycogen storage, the malate/aspartate shuttle, the glycerol phosphate shuttle, and plasma and mitochondrial membrane transporters. The reaction network was divided into three compartments: the cytosol, mitochondria, and the extracellular space. The total number of metabolites in the network is 50, of which 35 also appear in the mitochondria. This core metabolic network accounts for 250 human genes.

To perform simulations using the core metabolic network, network properties such as the P/O ratio were specified using Salway, supra (1999) as a reference. Oxidation of NADH through the Electron Transport System (ETS) was set to generate 2.5 ATP molecules (i.e. a P/O ratio of 2.5 for NADH), and that of $FADH_2$ was set to 1.5 ATP molecules (i.e. a P/O ratio of 1.5 for $FADH_2$).

Using the core metabolic network, aerobic and anaerobic metabolisms were simulated *in silico*. Secretion of metabolic by-products was in agreement with the known physiological parameters. Maximum yield of all 12 precursor-metabolites

(glucose-6-phosphate, fructose-6-phosphate, ribose-5-phosphate, erythrose-4-phosphate, triose phosphate, 3-phosphoglycerate, phosphoenolpyruvate, pyruvate, acetyl CoA, α-ketoglutarate, succinyl CoA, and oxaloacetate) was examined and none found to exceed the values of its theoretical yield.

Maximum ATP yield was also examined in the cytosol and mitochondria. Salway, supra (1999) reports that in the absence of membrane proton-coupled transport systems, the energy yield is 38 ATP molecules per molecule of glucose and otherwise 31 ATP molecules per molecule of glucose. The core metabolic model demonstrated the same values as described by Salway supra (1999). Energy yield in the mitochondria was determined to be 38 molecules of ATP per glucose molecule. This is equivalent to production of energy in the absence of proton-couple transporters across mitochondrial membrane since all the protons were utilized only in oxidative phosphorylation. In the cytosol, energy yield was calculated to be 30.5 molecules of ATP per glucose molecule. This value reflects the cost of metabolite exchange across the mitochondrial membrane as described by Salway, supra (1999).

EXAMPLE III

This example shows how human muscle cell metabolism can be accurately simulated under various physiological and pathological conditions using a *Homo sapiens* muscle cell metabolic model.

As described in Example I, the core metabolic model was extended to also include all the major reactions occurring in the skeletal muscle cell, adding new functions to the classical metabolic pathways found in the core model, such as fatty acid synthesis and β-oxidation, triacylglycerol and phospholipid formation, and amino acid metabolism. Simulations were performed using the muscle cell reaction database shown in Table 4. The biochemical reactions were again compartmentalized into cytosolic and mitochondrial compartments.

To simulate physiological behavior of human skeletal muscle cells, an objective function had to be defined. Growth of muscle cells occurs in time scales of several hours to days. The time scale of interest in the simulation, however, was in the order of several to tens of minutes, reflecting the time period of metabolic changes during

exercise. Thus, contraction (defined as, and related to energy production) was chosen to be the objective function, and no additional constraints were imposed to represent growth demands in the cell.

To study and test the behavior of the network, twelve physiological cases (Table 8) and five disease cases (Table 9) were examined. The input and output of metabolites were specified as indicated in Table 8, and maximum energy production and metabolite secretions were calculated and taken into account.

Table 8

Metabolite Exchange	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Glucose	I	I	-	-	I	I	-	-	-	-	-	-
O2	I	-	I	-	I	-	I	-	I	-	I	-
Palmitate	I	I	-	-	-	-	-	-	I	I	-	-
Glycogen	I	I	I	I	-	-	-	-	-	-	-	-
Phosphocreatine	I	I	-	-	-	-	-	-	-	-	I	I
Triacylglycerol	I	I	-	-	-	-	I	I	-	-	-	-
Isoleucine	I	I	-	-	-	-	-	-	-	-	-	-
Valine	I	I	-	-	-	-	-	-	-	-	-	-
Hydroxybutyrate	-	-	-	-	-	-	-	-	-	-	-	-
Pyruvate	O	O	O	O	O	O	O	O	O	O	O	O
Lactate	O	O	O	O	O	O	O	O	O	O	O	O
Albumin	O	O	O	O	O	O	O	O	O	O	O	O

Table 9

Disease	Enzyme Deficiency	Reaction Constrained
McArdle's disease	phosphorylase	GBE1
Tarui's disease	phosphofructokianse	PFKL
Phosphoglycerate kinase deficiency	phosphoglycerate kinase	PGK1R
Phosphoglycerate mutase deficiency	phosphoglycerate mutase	PGAM3R
Lactate dehydrogenase deficiency	Lactate dehyrogenase	LDHAR

The skeletal muscle model was tested for utilization of various carbon sources available during various stages of exercise and food starvation (Table 8). The by-product secretion of the network in an aerobic to anaerobic shift was qualitatively compared to physiological outcome of exercise and found to exhibit the same general features such as secretion of fermentative by-products and lowered energy yield.

The network behavior was also examined for five disease cases (Table 9). The test cases were chosen based on their physiological relevance to the model's predictive capabilities. In brief, McArdle's disease is marked by the impairment of glycogen breakdown. Tarui's disease is characterized by a deficiency in phosphofructokinase. The remaining diseases examined are marked by a deficiency of metabolic enzymes phosphoglycerate kinase, phosphoglycerate mutase, and lactate dehydrogenase. In each case, the changes in flux and by-product secretion of metabolites were examined for an aerobic to anaerobic metabolic shift with glycogen and phosphocreatine as the sole carbon sources to the network and pyruvate, lactate, and albumin as the only metabolic by-products allowed to leave the system. To simulate the disease cases, the corresponding deficient enzyme was constrained to zero. In all cases, a severe reduction in energy production was demonstrated during exercise, representing the state of the disease as seen in clinical cases.

EXAMPLE IV

This Example shows the construction and simulation of a multi-cellular model demonstrating the interactions between human adipocytes and monocytes.

The specific examples described above demonstrate the use a constraint-based approach in modeling metabolism in microbial organisms including prokaryotes such as *E. coli* and eukaryotes such as *S. cerevisiae* as well as for complex multicellular organisms requiring regulatory interactions such as humans. Described below is the modeling procedure, network content, and simulation results including network characteristics and metabolic performance of an integrated two-cell model of human adipocyte (fatty cell) and myocyte (muscle cell) using the compositions and methods of the invention. Simulations were performed to exemplify the coupled function of the two cell types during distinct physiological conditions corresponding to the coupled function of adipocyes and myocytes during sprint and marathon physiological conditions.

A human metabolic network model was reconstructed using biochemical, physiological, and genomic data as described previously. Briefly, the central metabolic network was used as a template for the construction of cell-specific models by adding biochemical reactions known to occur in specific cell-types of interest based on genomic, biochemical, and/or physiological information. Other methods for reconstructing the cell-specific models included reconstructing all the biochemical pathways and biochemical reactions that occur in the human metabolism regardless of their tissue specificity and location within the cell in a database and then reconstructing cell-, tissue-, organ-specific models by separating reactions that occur in specified cells, tissues, and/or organs based on genomic, physiological, biochemical, and/or high throughput data such as gene expression, proteomics, metabolomics, and other types of "omic" data. In this latter approach, in addition to the cell-, tissue-, and/or organ-specific reactions, reactions can be added to balance metabolites and represent the biochemistry, physiology, and genetics of the cells, tissues, organs, and/or whole human body. In the approach described below, the initial reconstruction of a central metabolic network followed by development of cell-specific models, the reconstruction of a generic central metabolic network is not a necessary step in reconstructing and modeling human metabolism. Rather, it is performed to accelerate the reconstruction process.

Implementation of the multi-cellular adipocyte-myocyte model is described below with reference to the reconstruction of the constituent components. In this regard, the reconstruction of a central human metabolic network is described first followed by the reconstruction procedures for fatty cell and muscle cell specific networks. The reconstruction procedure by which the two cell-specific models were combined to generate a multi-cellular model for human metabolism is then described.

Metabolic Network of Central Human Metabolism

The metabolic network of the central human metabolism was constructed as a template and a starting point for reconstructing more specific cell models. To construct a central metabolic network for human metabolism, a compendium of 1557 annotated human genes obtained from Kyoto Encyclopedia of Genes and Genomes KEGG, National Center for Biotechnology Information or NCBI, and the Universal Protein Resource or UniProt databases was used. In addition to the genomic and proteomic data, several primary textbooks and publications on the biochemistry of human metabolism also were used and includedthe *Human Metabolism: Functional Diversity and Integration*, Ed. by J.R. Bronk, Harlow, Addison, Wesley, Longman (1999); *Textbook of Biochemistry with Clinical Correlations*, Ed. by Thomas M. Devlin, New York, Wiley-Liss (2002), and *Metabolism at a Glance*, Ed. by J.G. Salway, Oxford, Malden, MA, Blackwell Science (1999). The network reconstruction of human central metabolism included metabolic pathways for glycolysis, gluconeogenesis, citrate cycle (TCA cycle), pentose phosphate pathway, galactose, malonyl-CoA, lactate, and pyruvate metabolism. The methods described previously were similarly used for this reconstruction as well as those described below. Metabolic reactions were compartmentalized into extra-cellular space, cytosol, mitochondrion, and endoplasmic reticulum. In addition to the biochemical pathways, exchange reactions were included based on biochemical literature and physiological evidence to provide the transport of metabolites across different organelles and cytosolic membrane.

The completed central metabolic network for human metabolism is shown in Figure 5 where dashed lines indicate organelle, cell, or system boundary. The large dashed rectangle (black) represents the cytosolic membrane. The large dashed circle (red) represents the mitochondrial membrane and small dashed circle (green) represents

the endoplasmic reticulum membrane. The human central metabolic network contains 80 reactions of which 25 are transporters and 60 unique metabolites 5. A representative example of a gene-protein-reaction association is shown in Figure 6 where the open reading frame or ORF (7167) is associated to an mRNA transcript (TPI1). The transcript is then associated to a translated protein (Tpi1) that catalyzes a corresponding reaction (TPI).

Adipocyte Metabolic Network

Adipocytes are specialized cells for synthesizing and storing triacylglycerol. Triacylglycerols (TAG's) are synthesized from dihydroxyacetone phosphate and fatty acids in white adipose tissue. Triacylglycerol synthesized in adipocytes can be hydrolyzed (or degraded) into fatty acids and glycerol via specialized pathways in the fat cells. The fatty acids that are released from triacylglycerol leave the cell and are transported to other cell types such as myocytes for energy production. The fatty acid composition of triacylglycerol in human mammary adipose tissue has been experimentally measured (Raclot et al., 324:911-5 (1997)) and includes essential, non-essential, saturated, unsaturated, even-, and odd-chain fatty acids (Table 10).

Table 10. Fatty acid composition of fat cell TAG in human, NEFA released by these cells *in vitro*, and relative mobilization (% NEFA/% TAG) of fatty acids.

Fatty acid	TAG (weight %)	NEFA (weight %)	Relative mobilization	Fatty acid	TAG (weight %)	NEFA (weight %)	Relative mobilization
$C_{12:0}$	0.50±0.07	0.45±0.06	0.88±0.02	$C_{20:1,n-11}$	0.17±0.01	0.11±0.01***	0.66±0.03
$C_{14:0}$	3.08±0.13	2.94±0.15	0.94±0.01	$C_{20:1,n-9}$	0.84±0.02	0.53±0.02***	0.62±0.01
$C_{14:1,n-7}$	0.03±0.00	0.03±0.00	1.07±0.14	$C_{20:1,n-7}$	0.03±0.00	0.02±0.00*	0.67±0.03
$C_{14:1,n-5}$	0.20±0.01	0.19±0.02	0.96±0.03	$C_{20:2,n-9}$	0.04±0.00	0.02±0.00**	0.63±0.06
$C_{15:0}$	0.33±0.02	0.35±0.02	1.05±0.02	$C_{20:2,n-6}$	0.31±0.02	0.26±0.01*	0.82±0.04
$C_{16:0}$	22.79±0.56	23.51±0.74	1.02±0.01	$C_{20:3,n-6}$	0.26±0.03	0.24±0.03	0.90±0.05
$C_{16:1,n-9}$	0.54±0.01	0.42±0.02***	0.77±0.01	$C_{20:3,n-3}$	0.03±0.00	0.03±0.00	0.90±0.06
$C_{16:1,n-7}$	2.77±0.21	3.69±0.34*	1.31±0.02	$C_{20:4,n-6}$	0.35±0.03	0.57±0.04***	1.60±0.04
$C_{17:1,n-8}$	0.29±0.02	0.36±0.02*	1.21±0.03	$C_{20:4,n-3}$	0.03±0.01	0.04±0.01	1.13±0.16
$C_{18:0}$	6.67±0.35	6.41±1.39	0.95±0.06	$C_{20:5,n-3}$	0.04±0.01	0.10±0.01***	2.25±0.08
$C_{18:1,n-9}$	40.79±0.52	39.77±0.57	0.96±0.01	$C_{22:0}$	0.04±0.01	0.02±0.01*	0.42±0.05
$C_{18:1,n-7}$	1.90±0.05	2.12±0.10	1.10±0.03	$C_{22:1,n-11}$	0.03±0.01	0.01±0.00*	0.37±0.02
$C_{18:1,n-5}$	0.27±0.01	0.31±0.03	1.12±0.04	$C_{22:1,n-9}$	0.07±0.01	0.03±0.00**	0.45±0.03
$C_{18:2,n-6}$	16.23±0.86	16.21±0.62	0.99±0.01	$C_{22:4,n-6}$	0.17±0.02	0.10±0.01**	0.58±0.03
$C_{18:3,n-6}$	0.04±0.00	0.05±0.01	1.27±0.07	$C_{22:5,n-6}$	0.02±0.01	0.01±0.00	0.59±0.05
$C_{18:3,n-3}$	0.51±0.02	0.75±0.03***	1.43±0.03	$C_{22:5,n-3}$	0.20±0.03	0.11±0.01**	0.55±0.02
$C_{20:0}$	0.21±0.02	0.10±0.01***	0.47±0.04	$C_{22:6,n-3}$	0.21±0.04	0.14±0.02*	0.65±0.04

*P<0.05; **P<0.01; ***P<0.001

The adipocyte metabolic model was constructed by adding the non-essential saturated, unsaturated, even- and odd-chain fatty acid biosynthetic pathways to the central metabolic network for 21 of the fatty acids listed in Table 10. The remaining 13 essential fatty acids were supplied to the cell via the extra-cellular space, representing the nutritional intake from the environment. Pathway for biosynthesis of triacylglycerol (TAG) from all 34 fatty acids was included to account for the formation and storage of TAG in adipocytes. Reactions for hydrolysis of TAG into fatty acids were also included to represent TAG degradation. In addition to fatty acid synthesis and TAG biosynthesis and degradation, transport reactions were included to allow for the release of fatty acids from intra-cellular space to the environment.

The metabolic model of an adipocyte cell contains a total of 198 reactions of which 63 are transporters. The adipocyte cell model is shown in Figure 7 where dashed lines indicate organelle, cell, or system boundary. The large dashed rectangle

(yellow) represents the adipocyte cytosolic membrane. The two large dashed circles (red) represent the mitochondrial membrane and the small dashed circle at the top (green) represents the endoplasmic reticulum membrane. As shown, metabolic reactions were compartmentalized into extra-cellular, cytosolic, mitochondrial, and endoplasmic reticulum. As described above, the extra-cellular space represents the environment outside the cell, which can include the space outside the body, connective tissues, and interstitial space between cells.

Myocyte Metabolic Network

The energy required for muscle contraction is generally supplied by glucose, stored glycogen, phosphocreatine, and fatty acids. The myocyte model was constructed by adding phosphocreatine kinase reaction, myosin-actin activation mechanism, and β-oxidation pathway to the central metabolic network. Muscle contraction was represented by a sequential conversion of myoactin to myosin-ATP, myosin-ATP to myosin-ADP-P, myosin-ADP-P to myosin-actin-ADP-P complex, myosin-actin-ADP-P to myoactin, and subsequently the formation of muscle contraction as shown in Figure 8.

The conversion of myoactin to myosin-actin-ADP-P complex and muscle contraction results in a net conversion of ATP and H_2O to ADP, H^+, and P_i.

The complete reconstructed metabolic model for myocyte cell metabolism is shown in Figure 9 where dashed lines indicate organelle, cell, or system boundary. The large dashed rectangle (brown) represents the myocyte cytosolic membrane. The two large dashed circles (red) represent the mitochondrial membrane. The medium sized dashed circle (purple) represents the peroxisomal membrane and the small dashed circle (green) represents the endoplasmic reticulum membrane. The myocyte network contains a total of 205 reactions of which 46 are transport reactions. Reactions for utilizing phosphcreatine as well as selected pathways for β-oxidation of saturated, unsaturated, even- and odd-chain fatty acids and their intermediates were also included in the model and are shown in Figure 9. As with the previous network models, metabolic reactions were compartmentalized into extra-cellular, cytosolic, mitochondrial, peroxisomal, and endoplasmic reticulum.

Multi-cellular Adipocyte-Myocyte Reconstruction

To generate a multi-cellular model for human metabolism, the metabolic function of the two models of adipocyte and myocyte were integrated by reconstructing a model that includes all the metabolic reactions in the two individual cell types. The interaction of the two cell types were then represented within an "intra-system" space, which represents the connective tissues such as blood, urine, and interstitial space, and an outside environment or "extra-system" space. To represent the uptake of metabolites and essential fatty acids from the environment, appropriate transport reactions were added to exchange metabolites across the extra-system boundary. Additional reactions also were added to balance metabolites in the intra-system space by including the bicarbonate and ammonia buffer systems as they function in the kidneys. These reactions were initially omitted but were added to improve the model once the requirement for the integrated system to buffer extracellular protons in the interstitial space became apparent once simulation testing began. The combined adipocyte-myocyte model contains 430 reactions and 240 unique metabolites. The complete reconstruction is shown in Figure 10 and a summary of the reactions is set forth in Table 11. A substantially complete listing of all the reactions set forth in Figure 10 is set forth below in Table 15.

Table 11. Network properties of central metabolic network, adipocyte, myocyte, and multi-cell adipocyte-myocyte models.

Model	Reactions	Transporters	Compounds
Central Metabolism	80	25	60
Adipocyte	198	63	150
Myocyte	205	46	167
Adipocyte-Myocyte	430	135	240

In Figure 10, dashed lines again indicate organelle, cell, or system boundaries. The outer most large dashed rectangle (black) separates the environment inside and outside the human body. The two interior dashed rectangles represents the adipocyte cytosolic membrane (top, yellow) and the myocyte cytosolic membrane (bottom, brown). The pair of larger dashed circles within the adipocyte and myocyte cytosol (red) represent the mitochondrial membrane. The medium sized dashed circle in

the myocyte cytosol (purple) represents the peroxisomal membrane and small dashed circle within the adipocyte and myocyte cytosol (green) represent the endoplasmic reticulum membrane.

METABOLIC SIMULATIONS

The computational and infrastructure requirements for producing the integrated multi-cellular model were assessed by examining the network properties of first, the cell-specific models, and then the integrated multi-cellular reconstruction.

Metabolic Model of Central Human Metabolism

The metabolic capabilities of the central human model was determined through computation of maximum yield of the 12 precursor metabolites per glucose. The results are shown in Table 12. In all cases, the network's yield was less or equal to the maximum theoretical values except for succinyl-CoA. In the case of succinyl-CoA, a higher yield was possible by incorporating CO_2 via pyruvate carboxylase reaction, PCm. In addition to precursor metabolite yields, the maximum ATP yield per mole of glucose was computed in the network. The maximum ATP yield for the central human metabolism was computed to be 31.5 mol ATP/mol glucose, which is consistent with previously calculated values (Vo et al., *J. Biol. Chem.* 279:39532-40. (2004)).

Table 12. Maximum theoretical and central human metabolic network yields for the precursor metabolites per glucose. Units are in mol/mol glucose.

Precursor Metabolites	Theoretical	Central Metabolism
Glucose 6-P	1	0.94
Fructose 6-P	1	0.94
Ribose 5-P	1.2	1.115
Erythrose 4-P	1.5	1.37
Glyceraldehyde 3-P	2	1.775
3-P Glycerate	2	2
Phosphoenolpyruvate	2	2
Pyruvate	2	2
Oxaloacetate, mitochondrial	2	1.969
Acetyl-CoA, mitochondrial	2	2
aKeto-glutarate, mitochondrial	1	1
Succinyl-CoA, mitochondrial	1	1.595

The biomass demand in living cells is a requirement for the production of biosynthetic components such as amino acids, lipids and other molecules that are needed to provide cell integrity, maintenance, and growth. All the biosynthetic components were made from the 12 precursor metabolites in the central metabolism shown in Table 12. The rate of growth and biomass maintenance in mammalian cells however is typically much lower than the rate of metabolic activities. Thus to represent the cells' biosynthetic requirement, a small flux demand was imposed for the production of the 12 precursor metabolites while maximizing for ATP. In the absence of experimental measurements, the capability of the network to meet the biosynthetic requirements was examined by constructing a reaction in which all the precursor metabolites were made simultaneously with stoichiometric coefficients of one as set forth in the reaction below:

Precursor Demand: $3pg[c] + accoa[m] + akg[m] + e4p[c] + f6p[c] + g3p[c] + g6p[c] + oaa[m] + pep[c] + pyr[c] + r5p[c] + succoa[m] \rightarrow (2)\ coa[m]$

In the absence of quantitative measurement, the above reaction serves to demonstrate the ability of the network to meet both biomass and energy requirements in the cell simultaneously. The maximum ATP yield for the central metabolism with a demand of 0.01 mmol/gDW of precursor metabolites was computed to be 29.0, demonstrating that the energy and carbon requirements for precursor metabolite

generation, as expected, reduce the maximum energy production in the cell and this amount can be quantified using the reconstructed model.

Triacylglycerol Storage and Utilization in Adipocyte Tissue

As described previously, a main function of adipocyte is to synthesize, store, and hydrolyze triacylglycerols. The stored TAG can be used to generate ATP during starvation or under high-energy demand conditions. TAG hydrolysis results in the formation of fatty acids and glycerol in adipocyte. Fatty acids are transported to other tissues such as the muscle tissue where they can be utilized to generate energy. Glycerol is utilized further by the liver and other tissues where it is converted into glycerol phosphate and enters glycolytic pathway.

To simulate the storage of triacylglycerol from glucose in adipocyte, TAG synthesis was simulated by maximizing an internal demand for cytosolic triacylglycerol. The maximum yield of triacylglycerol per glucose was computed to be 0.06 mol TAG/mol glucose, without any biomass demand. To demonstrate how the stored TAG can be reutilized to produce fatty acids, the influx of all other carbon sources including glucose was constrained to zero and glycerol secretion, which is assumed to be taken up by the liver, was maximized. When 2 mol of cytosolic proton was allowed to leave the system, a glycerol yield of 1 mol glycerol/mol TAG or 100% was computed. The excess two protons were formed in TAG degradation pathway. As shown in Figure 11, degradation of TAG was performed in the following three steps: (1) TRIGH_ac_HS_ub; (2) 12DGRH_ac_HS_ub, and (3) MGLYCH_ac_HS_ub). Glycerol generated as an end product of this pathway was transported out of the cell via a proton-coupled symport mechanism. TAG was hydrolyzed completely to fatty acids and glycerol in three steps and in each step one proton is released. Glycerol transport was coupled to one proton. Thus, a net amount of two protons were generated per mol TAG degraded.

To balance protons, an ATPase reaction across the cytosolic membrane was used. However, since the β-oxidative pathways were not included in this adipocyte model, this network is unable to use membrane bound ATPase to balance the internal protons. When β-oxidative pathways are added to the adipocyte model, the model can completely balance protons.

In addition to triacylglycerol synthesis and hydrolysis, the maximum ATP yield on glucose (YATP/glucose) was computed in the adipocyte model. As for the central human metabolic network, YATP/glucose was 31.5 mol ATP/mol glucose.

Muscle Contraction During Aerobic and Anaerobic Exercise

The required energy in muscle tissue is generally supplied by glucose, stored glycogen, and phosphocreatine. During anaerobic exercise such as a sprint, for example, the blood vessels in the muscle tissue are compressed and the cells are isolated from the rest of the body (Devlin, *supra*). This compression restricts the oxygen supply to the tissue and enforces anaerobic energy metabolism in the cell. As a result, lactate is generated to balance the redox potential and must be secreted out of the cell. In the liver, lactate is converted into glucose. However, rapid muscle contraction and decreased blood flow to the muscle tissue cause lactate accumulation during anaerobic exercise and quickly impairs muscle contraction. During starvation or under high-energy demands, the glucose and glycogen storage of the muscle tissue quickly depletes and the energy storage in triacylglycerol molecules supplied by fatty cells is used to generate ATP.

To simulate the muscle physiology at steady state, phosphocreatine kinase reaction, myosin-actin activation mechanism, and β-oxidation pathway were included in the central metabolic network. The physiological function of muscle tissue was simulated by determining the maximum amount of contraction that is generated from the energy supplied by glucose, stored glycogen, phosphocreatine, and supplied fatty acids.

The metabolic capabilities of the myocyte model were assessed by first computing the maximum ATP yield on glucose. As for the central human metabolic network, YATP/glucose was 31.5 mol ATP/mol glucose. The muscle contraction was also examined with glucose as the sole carbon source. Maximum muscle contraction with glucose was computed to be 31.5 mol/mol glucose in aerobic and 2 mol/mol glucose in anaerobic condition. Lactate was secreted as a byproduct during anaerobic contraction ($Yield_{lactate/glucose}$ = 2 mol/mol).

As lactate accumulates during anaerobic metabolism, its secretion rate quickly fails to meet the demand to release lactate into the blood. To simulation the impairment of muscle contraction in anaerobic exercise, the maximum lactate secretion

rate was constrained to 75%, 50%, 25%, and 0% of its maximum value under anaerobic condition. The results using these different constraints are shown in Figure 12 where the time is shown as an arbitrary unit, rate of contraction and lactate secretion are in mols per cell mass per unit time, r corresponds to rate and lac corresponds to lactate. The results show that as more lactate accumulates in anaerobic metabolism, the maximum allowable lactate secretion decreases and maximum muscle contraction decreased proportionally.

The muscle contraction was simulated also with stored glycogen and phosphocreatine as the energy source. The maximum contraction for glycogen was computed to be 32.5 mol/mol glycogen in aerobic and 3 mol/mol glycogen in anaerobic condition. The observed difference between the maximum contraction generated by glycogen in comparison to glucose arises from the absence of the phosphorylation or glucokinase step in the first step of glycolysis. The results of glycogen versus glucose utilization are illustrated in Figure 13 where the glycogen utilization pathway is shown as the thick bent arrow on the left (red) and the glucose utilization pathway is shown as the thick straight arrow on the right (blue). The dashed circle (green) represents the endoplasmic reticulum membrane. The maximum contraction from phosphocreatine under both aerobic and anaerobic conditions was computed to be 1 mol/mol phosphocreatine. The energy generated from phosphocreatine is independent of the energy produced through oxidative phosphorylation and thus was computed to be the same in both aerobic and anaerobic conditions.

In addition, β-oxidative pathways in the myocyte tissue were examined by supplying the network with eicosanoate (n-C20:0), octadecenoate (C18:1, n-9), and pentadecanoate (C15:0) as examples of fatty acid oxidation of odd- and even-chain, and saturated and unsaturated fatty acids. The results are shown in Table 13 and demonstrate that maximum contraction in the myocyte model was 134 mol/mol for eicosanoate, 118.5 mol/mol for octadecenoate, and 98.5 mol/mol for pentadecanoate. The results also show that on a carbon-mole basis, all the fatty acids yielded approximately the same contraction, which was equivalent to ATP yield. Contraction was observed to be larger in terms of carbon yield than that generated from glucose (i.e. ~6.6 mol ATP/C-mol fatty acid in comparison to 5.3 mol ATP/C-mol glucose). The maximum ATP yield for palmitate (C16:0) was also computed to be 106 mol ATP/mol palmitate, which was

consistent with the previously calculated values (Vo et al, *supra*). One mol of cytosolic protons per mol of fatty acid was supplied to the network for fatty acid oxidation.

Table 13. Maximum contraction in the myocyte model given different fatty acids

Fatty Acid	Abbreviation*	Maximum Contraction (mol/mol fatty acid)	Maximum Contraction (mol/C-mol)
Eicosanoate	C20:0	134	6.7
Octadecenoate	C18:1, n-9	118.5	6.6
Palmitate	C16:0	106	6.6
Pentadecanoate	C15:0	98.5	6.6

*Abbreviation indicates: number of carbons in the fatty acid, number of double bonds, carbon number where the 1st double bond appears if the fatty acid is unsaturated.

A unit of proton per fatty acid is required in the network to balance fatty acyl CoA formation in the cell as illustrated in the following reaction:

Fatty Acid CoA Ligase:	Fatty Acid + ATP + CoA → Fatty Acyl-CoA + AMP + PPi
Adenylate Kinase:	AMP + ATP ↔ (2) ADP
Inorganic Diphosphatase:	PPi + H_2O → H^+ + (2) Pi
Net:	Fatty Acid + CoA + (2) ATP + H_2O → Fatty Acyl-CoA + (2)O ADP + (2) Pi + H^+

With respect to ATP balance (i.e. ATP + H_2O → ADP + P_i + H^+), the net reaction has one mol less H_2O and H^+. Water can freely diffuse through the membrane. However, cell membrane is impermeable to free protons and thus protons were balanced in all compartments. The proton requirement in the cell can be fulfilled with a proton-coupled fatty acid transporter. It has been observed that the proton electrochemical gradient across the inner membrane plays a crucial role in energizing the long-chain fatty acid transport apparatus in *E. coli* and the proton electrochemical gradient across the inner membrane is required for optimal fatty acid transport (DiRusso et al., *Mol. Cell. Biochem.* 192:41-52 (1999)). Fatty acid transporters in *S. cerevisiae* have also been studied, however, no evidence is currently available on the mechanism of transport. When a

proton coupled fatty acid transporter was used in the model, the requirement for supplying a mol of proton to the system was eliminated.

Adipocyte-Myoctye Coupled Functions

Muscle cells largely rely on their stored glycogen and phosphocreatine content. During aerobic exercise, however, glucose, glycogen, and phosphcreatine storage of muscle cells are depleted and energy generation in myocytes is achieved by fatty acid oxidation. Lipolysis or lipid degradation proceeds in muscle cells following the transfer of fatty acids from adipocytes to myocytes via blood.

Modeling of multi-cellular metabolism was performed using a constraint-based approach as described herein where the metabolic networks of adipocyte and myocyte were combined into a multi-cellular metabolic model as shown in Figure 10. The integrated model was assessed by computing the network energy requirements during anaerobic exercise such as that corresponding to a sprint and aerobic exercise such as that corresponding to a marathon. From a purely additive perspective, combining all of the reactions from the adipocyte model with those from the myocyte model was initially performed as a sufficient indicator for the combined network to compute integrated physiological results. However, with the two models strictly combined in this manner they were deficient at computing integrated functions such as those described below and, in particular, the results described in the "Muscle Contraction in a Marathon" section below. Addition of buffer systems for bicarbonate and ammonia allowed the combined model to function more efficiently and predictably. In retrospect, the inclusion of intra-system reactions is consistent with the role that, for example, the kidney plays in integrated metabolic physiology.

Simulation of an Integrated Model for Muscle Contraction During a Sprint: The energy requirements of myocytes in a sprint are extremely high and supplied primarily from the fuel present in the muscle. In addition, oxygen cannot be transported to the cells fast enough to trigger an aerobic metabolism. It has been estimated that only 5% of the energy in a sprint is supplied via oxidative phosphorylation and the remaining ATP is generated from anaerobic metabolism from stored glycogen and phosphocreatine

(*Biochemical and Physiological Aspects of Human Nutrition,* Philadelphia, Ed. by M.H. Stipanuk, W.B. Saunders, (2000)).

To simulate the metabolic activity of the muscle in a sprint, the maximum muscle contraction in an aerobic condition was computed by supplying the multi-cellular model with glucose, glycogen, and phosphocreatine as shown in Table 14. In addition, muscle contraction was simulated under anaerobic condition by constraining the oxygen supply to zero. Maximum contraction was computed to be the same as in the isolated myocyte model, as expected, demonstrating that the integrated model retains the functionalities observed in the single-cell model.

Table 14. Simulation results in the adipocyte-myocyte integrated model.[1]

Carbon Source	**Objective (Cell Type)**	**Aerobic mol/mol carbon source**	**Anaerobic**
Glucose	Contraction (M)	31.5	2
Glycogen	Contraction (M)	32.5	3
Phosphocreatine	Contraction (M)	1	1
Glucose	ATP synthesis (A)	32.5	-
Glucose	TAG synthesis (A)	0.06	-
TAG	Glycerol (I)	1*	-
TAG supplying C12:0, C14:0, C15:0, C16:0, C18:0, C18:1 n-9, and C20:0	Contraction (M)	253.9	-

* Two protons were allowed to leave the cytosol (see section "Triacylglycerol Storage and Utilization in Adipocyte Tissue")
- Not relevant
[1]M, myocyte; A, adipocyte; I, intra-system; TAG, triacylglycerol; C12:0, dodecanoate; C14:0, tetradecanoate; C15:0, pentadecanoate; C16:0, palmitate, C18:0, octadecanoate; C18:1 n-9, octadecenoate; C20:0, eicosanoate

Simulation of an Integrated Model for Muscle Contraction During a Marathon: The total energy expenditure in a marathon is about 12,000 kJ or 2868 kcal, which is equivalent to burning about 750 g of carbohydrate or 330 g of fat (Stipanuk, *supra*). Since the total stored carbohydrate in the body is only about 400 to 900 g, the mobilized fatty acids from adipose tissue provide an important part of the supplied energy to the muscle cells in an aerobic metabolism and especially in a marathon.

To simulate the aerobic oxidation of fatty acid in the muscle cells, the integrated model was first demonstrated to be able to synthesize and store triacylglycerol in the adipocyte compartment when supplied by glucose. As for the single cell model, the

integrated adipocyte-myocyte network was able to store TAG in adipocyte compartment. The results are shown in Table 14. In addition, TAG degradation and fatty acid mobilization to the blood was simulated by maximizing glycerol secretion in the intra-system space generated from the stored TAG in adipocyte. As with the single cell model, TAG hydrolysis was simulated with the integrated adipocyte-myocyte model and maximum glycerol secretion rate was shown to be the same.

To demonstrate the coupled function of the two cell types, muscle contraction in an aerobic exercise was simulated by constraining all other alternative carbon sources including glucose, stored glycogen, and phosphocreatine to zero and supplying adipocyte with stored triacylglycerol as an energy source. Exchange fluxes were included to ensure the proper transfer of fatty acids between the two models. The maximum muscle contraction in the network that contains β-oxidative pathways for fatty acids C12:0, C14:0, C15:0, C16:0, C18:0, C18:1 n-9, and C20:0 was simulated and computed to be 253.9 mol/mol TAG. The total contraction in this simulation is the sum of maximum contraction that is generated if the model was supplied with each fatty acid individually. The results from using the integrated model demonstrated that energy generated in the muscle cell from triacylglycerol is produced in an additive fashion and metabolite balance in the two cell types does not reduce the energy production in the cell.

These studies further demonstrate the the application of a constraint-based approach to modeling multi-cellular integrated metabolic models. The results also indicate that modeling multi-cellular networks can be optimized by incorporating intra-system reactions such as the bicarbonate and ammonia buffer systems into the integrated adipocyte-myocyte model. The reconstructed models and simulation results also demonstrated that metabolic functions of various cell types can be studied, understood and reproduced using the methods of the invention. Furthermore, coupling of the functions of multiple cell types in a system was demonstrated through the transport of various metabolites and the coupled function of different cell types were studied by imposing biologically appropriate objective function. Finally, the ability to predict further network modifications, such as the transport mechanism of fatty acids into myocyte, using the reconstructed models also was demonstrated. These results also indicate that multi-cellular modeling can be extended to the modeling of more than two cells and which correspond to various cell types including the same specie or among

multiple different species, tissues, organs, and whole body by including additional genomic, biochemical, physiological, and high throughput datasets.

Throughout this application various publications have been referenced within parentheses. The disclosures of these publications in their entireties are hereby incorporated by reference in this application in order to more fully describe the state of the art to which this invention pertains.

Although the invention has been described with reference to the disclosed embodiments, those skilled in the art will readily appreciate that the specific examples and studies detailed above are only illustrative of the invention. It should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

Table 1

Locus ID	Gene Ab.	Reaction Stoichiometry	E.C.
1. Carbohydrate Metabolism			
1.1 Glycolysis / Gluconeogenesis [PATH:hsa00010]			
3098	HK1	GLC + ATP -> G6P + ADP	2.7.1.1
3099	HK2	GLC + ATP -> G6P + ADP	2.7.1.1
3101	HK3	GLC + ATP -> G6P + ADP	2.7.1.1
2645	GCK, HK4, MODY2, NIDDM	GLC + ATP -> G6P + ADP	2.7.1.2
2538	G6PC, G6PT	G6P + H2O -> GLC + PI	3.1.3.9
2821	GPI	G6P <-> F6P	5.3.1.9
5211	PFKL	F6P + ATP -> FDP + ADP	2.7.1.11
5213	PFKM	F6P + ATP -> FDP + ADP	2.7.1.11
5214	PFKP, PFK-C	F6P + ATP -> FDP + ADP	2.7.1.11
5215	PFKX	F6P + ATP -> FDP + ADP	2.7.1.11
2203	FBP1, FBP	FDP + H2O -> F6P + PI	3.1.3.11
8789	FBP2	FDP + H2O -> F6P + PI	3.1.3.11
226	ALDOA	FDP <-> T3P2 + T3P1	4.1.2.13
229	ALDOB	FDP <-> T3P2 + T3P1	4.1.2.13
230	ALDOC	FDP <-> T3P2 + T3P1	4.1.2.13
7167	TPI1	T3P2 <-> T3P1	5.3.1.1
2597	GAPD, GAPDH	T3P1 + PI + NAD <-> NADH + 13PDG	1.2.1.12
26330	GAPDS, GAPDH-2	T3P1 + PI + NAD <-> NADH + 13PDG	1.2.1.12
5230	PGK1, PGKA	13PDG + ADP <-> 3PG + ATP	2.7.2.3
5233	PGK2	13PDG + ADP <-> 3PG + ATP	2.7.2.3
5223	PGAM1, PGAMA	13PDG -> 23PDG	5.4.2.4
		23PDG + H2O -> 3PG + PI	3.1.3.13
		3PG <-> 2PG	5.4.2.1
5224	PGAM2, PGAMM	13PDG <-> 23PDG	5.4.2.4
		23PDG + H2O -> 3PG + PI	3.1.3.13
		3PG <-> 2PG	5.4.2.1
669	BPGM	13PDG <-> 23PDG	5.4.2.4
		23PDG + H2O <-> 3PG + PI	3.1.3.13
		3PG <-> 2PG	5.4.2.1
2023	ENO1, PPH, ENO1L1	2PG <-> PEP + H2O	4.2.1.11
2026	ENO2	2PG <-> PEP + H2O	4.2.1.11
2027	ENO3	2PG <-> PEP + H2O	4.2.1.11
26237	ENO1B	2PG <-> PEP + H2O	4.2.1.11
5313	PKLR, PK1	PEP + ADP -> PYR + ATP	2.7.1.40
5315	PKM2, PK3, THBP1, OIP3	PEP + ADP -> PYR + ATP	2.7.1.40
5160	PDHA1, PHE1A, PDHA	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	1.2.4.1
5161	PDHA2, PDHAL	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	1.2.4.1
5162	PDHB	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	1.2.4.1
1737	DLAT, DLTA, PDC-E2	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	2.3.1.12
8050	PDX1, E3BP	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	2.3.1.12
3939	LDHA, LDH1	NAD + LAC <-> PYR + NADH	1.1.1.27
3945	LDHB	NAD + LAC <-> PYR + NADH	1.1.1.27
3948	LDHC, LDH3	NAD + LAC <-> PYR + NADH	1.1.1.27
5236	PGM1	G1P <-> G6P	5.4.2.2
5237	PGM2	G1P <-> G6P	5.4.2.2
5238	PGM3	G1P <-> G6P	5.4.2.2
1738	DLD, LAD, PHE3, DLDH, E3	DLIPOm + FADm <-> LIPOm + FADH2m	1.8.1.4
124	ADH1	ETH + NAD <-> ACAL + NADH	1.1.1.1
125	ADH2	ETH + NAD <-> ACAL + NADH	1.1.1.1
126	ADH3	ETH + NAD <-> ACAL + NADH	1.1.1.1
127	ADH4	ETH + NAD <-> ACAL + NADH	1.1.1.1
128	ADH5	FALD + RGT + NAD <-> FGT + NADH	1.2.1.1
		ETH + NAD <-> ACAL + NADH	1.1.1.1
130	ADH6	ETH + NAD <-> ACAL + NADH	1.1.1.1
131	ADH7	ETH + NAD <-> ACAL + NADH	1.1.1.1
10327	AKR1A1, ALR, ALDR1		1.1.1.2
97	ACYP1		3.6.1.7

98 ACYP2		3.6.1.7
1.2 Citrate cycle (TCA cycle) PATH:hsa00020		
1431 CS	ACCOAm + OAm + H2Om -> COAm + CITm	4.1.3.7
48 ACO1, IREB1, IRP1	CIT <-> ICIT	4.2.1.3
50 ACO2	CITm <-> ICITm	4.2.1.3
3417 IDH1	ICIT + NADP -> NADPH + CO2 + AKG	1.1.1.42
3418 IDH2	ICITm + NADPm -> NADPHm + CO2m + AKGm	1.1.1.42
3419 IDH3A	ICITm + NADm -> CO2m + NADHm + AKGm	1.1.1.41
3420 IDH3B	ICITm + NADm -> CO2m + NADHm + AKGm	1.1.1.41
3421 IDH3G	ICITm + NADm -> CO2m + NADHm + AKGm	1.1.1.41
4967 OGDH	AKGm + NADm + COAm -> CO2m + NADHm + SUCCOAm	1.2.4.2
1743 DLST, DLTS	AKGm + NADm + COAm -> CO2m + NADHm + SUCCOAm	2.3.1.61
8802 SUCLG1, SUCLA1	GTPm + SUCCm + COAm <-> GDPm + Plm + SUCCOAm	6.2.1.4
8803 SUCLA2	ATPm + SUCCm + COAm <-> ADPm + Plm + SUCCOAm	6.2.1.4
2271 FH	FUMm + H2Om <-> MALm	4.2.1.2
4190 MDH1	MAL + NAD <-> NADH + OA	1.1.1.37
4191 MDH2	MALm + NADm <-> NADHm + OAm	1.1.1.37
5091 PC, PCB	PYRm + ATPm + CO2m -> ADPm + OAm + Plm	6.4.1.1
47 ACLY, ATPCL, CLATP	ATP + CIT + COA + H2O -> ADP + PI + ACCOA + OA	4.1.3.8
3657		
5105 PCK1	OA + GTP -> PEP + GDP + CO2	4.1.1.32
5106 PCK2, PEPCK	OAm + GTPm -> PEPm + GDPm + CO2m	4.1.1.32
1.3 Pentose phosphate cycle PATH:hsa00030		
2539 G6PD, G6PD1	G6P + NADP <-> D6PGL + NADPH	1.1.1.49
9563 H6PD		1.1.1.47
	D6PGL + H2O -> D6PGC	3.1.1.31
25796 PGLS, 6PGL	D6PGL + H2O -> D6PGC	3.1.1.31
5226 PGD	D6PGC + NADP -> NADPH + CO2 + RL5P	1.1.1.44
6120 RPE	RL5P <-> X5P	5.1.3.1
7086 TKT	R5P + X5P <-> T3P1 + S7P	2.2.1.1
	X5P + E4P <-> F6P + T3P1	
8277 TKTL1, TKR, TKT2	R5P + X5P <-> T3P1 + S7P	2.2.1.1
	X5P + E4P <-> F6P + T3P1	
6888 TALDO1	T3P1 + S7P <-> E4P + F6P	2.2.1.2
5631 PRPS1, PRS I, PRS, I	R5P + ATP <-> PRPP + AMP	2.7.6.1
5634 PRPS2, PRS II, PRS, II	R5P + ATP <-> PRPP + AMP	2.7.6.1
2663 GDH		1.1.1.47
1.4 Pentose and glucuronate interconversions PATH:hsa00040		
231 AKR1B1, AR, ALDR1, ADR		1.1.1.21
7359 UGP1	G1P + UTP -> UDPG + PPI	2.7.7.9
7360 UGP2, UGPP2	G1P + UTP -> UDPG + PPI	2.7.7.9
7358 UGDH, UDPGDH		1.1.1.22
10720 UGT2B11		2.4.1.17
54658 UGT1A1, UGT1A, GNT1, UGT1		2.4.1.17
7361 UGT1A, UGT1, UGT1A		2.4.1.17
7362 UGT2B, UGT2, UGT2B		2.4.1.17
7363 UGT2B4, UGT2B11		2.4.1.17
7364 UGT2B7, UGT2B9		2.4.1.17
7365 UGT2B10		2.4.1.17
7366 UGT2B15, UGT2B8		2.4.1.17
7367 UGT2B17		2.4.1.17
13 AADAC, DAC		3.1.1.-
3991 LIPE, LHS, HSL		3.1.1.-
1.5 Fructose and mannose metabolism PATH:hsa00051		
4351 MPI, PMI1	MAN6P <-> F6P	5.3.1.8
5372 PMM1	MAN6P <-> MAN1P	5.4.2.8
5373 PMM2, CDG1, CDGS	MAN6P <-> MAN1P	5.4.2.8
2762 GMDS		4.2.1.47
8790 FPGT, GFPP		2.7.7.30
5207 PFKFB1, PFRX	ATP + F6P -> ADP + F26P	2.7.1.105
	F26P -> F6P + PI	3.1.3.46

5208 PFKFB2	ATP + F6P -> ADP + F26P	2.7.1.105
	F26P -> F6P + PI	3.1.3.46
5209 PFKFB3	ATP + F6P -> ADP + F26P	2.7.1.105
	F26P -> F6P + PI	3.1.3.46
5210 PFKFB4	ATP + F6P -> ADP + F26P	2.7.1.105
	F26P -> F6P + PI	3.1.3.46
3795 KHK		2.7.1.3
6652 SORD	DSOT + NAD -> FRU + NADH	1.1.1.14
2526 FUT4, FCT3A, FUC-TIV		2.4.1.-
2529 FUT7		2.4.1.-
3036 HAS1, HAS		2.4.1.-
3037 HAS2		2.4.1.-
8473 OGT, O-GLCNAC		2.4.1.-
51144 LOC51144		1.1.1.-
1.6 Galactose metabolism PATH:hsa00052		
2584 GALK1, GALK	GLAC + ATP -> GAL1P + ADP	2.7.1.6
2585 GALK2, GK2	GLAC + ATP -> GAL1P + ADP	2.7.1.6
2592 GALT	UTP + GAL1P <-> PPI + UDPGAL	2.7.7.10
2582 GALE	UDPGAL <-> UDPG	5.1.3.2
2720 GLB1		3.2.1.23
3938 LCT, LAC		3.2.1.62
		3.2.1.108
2683 B4GALT1, GGTB2, BETA4GAL-T1, GT1, GTB		2.4.1.90
		2.4.1.38
		2.4.1.22
3906 LALBA		2.4.1.22
2717 GLA, GALA	MELI -> GLC + GLAC	3.2.1.22
2548 GAA	MLT -> 2 GLC	3.2.1.20
	6DGLC -> GLAC + GLC	
2594 GANAB	MLT -> 2 GLC	3.2.1.20
	6DGLC -> GLAC + GLC	
2595 GANC	MLT -> 2 GLC	3.2.1.20
	6DGLC -> GLAC + GLC	
8972 MGAM, MG, MGA	MLT -> 2 GLC	3.2.1.20
	6DGLC -> GLAC + GLC	
		3.2.1.3
1.7 Ascorbate and aldarate metabolism PATH:hsa00053		
216 ALDH1, PUMB1	ACAL + NAD -> NADH + AC	1.2.1.3
217 ALDH2	ACALm + NADm -> NADHm + ACm	1.2.1.3
219 ALDH5, ALDHX		1.2.1.3
223 ALDH9, E3		1.2.1.3
		1.2.1.19
224 ALDH10, FALDH, SLS		1.2.1.3
8854 RALDH2		1.2.1.3
1591 CYP24		1.14.-.-
1592 CYP26A1, P450RAI		1.14.-.-
1593 CYP27A1, CTX, CYP27		1.14.-.-
1594 CYP27B1, PDDR, VDD1, VDR, CYP1, VDDR, I, P450C1		1.14.-.-
1.8 Pyruvate metabolism PATH:hsa00620		
54988 FLJ20581	ATP + AC + COA -> AMP + PPI + ACCOA	6.2.1.1
31 ACACA, ACAC, ACC	ACCOA + ATP + CO2 <-> MALCOA + ADP + PI + H	6.4.1.2
		6.3.4.14
32 ACACB, ACCB, HACC275, ACC2	ACCOA + ATP + CO2 <-> MALCOA + ADP + PI + H	6.4.1.2
		6.3.4.14
2739 GLO1, GLYI	RGT + MTHGXL <-> LGT	4.4.1.5
3029 HAGH, GLO2	LGT -> RGT + LAC	3.1.2.6
2223 FDH	FALD + RGT + NAD <-> FGT + NADH	1.2.1.1
9380 GRHPR, GLXR		1.1.1.79
4200 ME2	MALm + NADm -> CO2m + NADHm + PYRm	1.1.1.38

10873 ME3	MALm + NADPm -> CO2m + NADPHm + PYRm	1.1.1.40
29897 HUMNDME	MAL + NADP -> CO2 + NADPH + PYR	1.1.1.40
4199 ME1	MAL + NADP -> CO2 + NADPH + PYR	1.1.1.40
38 ACAT1, ACAT, T2, THIL, MAT	2 ACCOAm <-> COAm + AACCOAm	2.3.1.9
39 ACAT2	2 ACCOAm <-> COAm + AACCOAm	2.3.1.9
1.9 Glyoxylate and dicarboxylate metabolism PATH:hsa00630		
5240 PGP		3.1.3.18
2758 GLYD	3HPm + NADHm -> NADm + GLYAm	1.1.1.29
10797 MTHFD2, NMDMC	METHF <-> FTHF	3.5.4.9
	METTHF + NAD -> METHF + NADH	1.5.1.15
4522 MTHFD1	METTHF + NADP <-> METHF + NADPH	1.5.1.15
	METHF <-> FTHF	3.5.4.9
	THF + FOR + ATP -> ADP + PI + FTHF	6.3.4.3
1.10 Propanoate metabolism PATH:hsa00640		
34 ACADM, MCAD	MBCOAm + FADm -> MCCOAm + FADH2m	1.3.99.3
	IBCOAm + FADm -> MACOAm + FADH2m	
	IVCOAm + FADm -> MCRCOAm + FADH2m	
36 ACADSB	MBCOAm + FADm -> MCCOAm + FADH2m	1.3.99.3
	IBCOAm + FADm -> MACOAm + FADH2m	
	IVCOAm + FADm -> MCRCOAm + FADH2m	
1892 ECHS1, SCEH	MACOAm + H2Om -> HIBCOAm	4.2.1.17
	MCCOAm + H2Om -> MHVCOAm	
1962 EHHADH	MHVCOAm + NADm -> MAACOAm + NADHm	1.1.1.35
	HIBm + NADm -> MMAm + NADHm	
	MACOAm + H2Om -> HIBCOAm	4.2.1.17
	MCCOAm + H2Om -> MHVCOAm	
3030 HADHA, MTPA, GBP	MHVCOAm + NADm -> MAACOAm + NADHm	1.1.1.35
	HIBm + NADm -> MMAm + NADHm	
	MACOAm + H2Om -> HIBCOAm	4.2.1.17
	MCCOAm + H2Om -> MHVCOAm	
	C160CARm + COAm + FADm + NADm -> FADH2m + NADHm + C140COAm + ACCOAm	1.1.1.35 4.2.1.17
23417 MLYCD, MCD		4.1.1.9
18 ABAT, GABAT	GABA + AKG -> SUCCSAL + GLU	2.6.1.19
5095 PCCA	PROPCOAm + CO2m + ATPm -> ADPm + Plm + DMMCOAm	6.4.1.3
5096 PCCB	PROPCOAm + CO2m + ATPm -> ADPm + Plm + DMMCOAm	6.4.1.3
4594 MUT, MCM	LMMCOAm -> SUCCOAm	5.4.99.2
4329 MMSDH	MMAm + COAm + NADm -> NADHm + CO2m + PROPCOAm	1.2.1.27
8523 FACVL1, VLCS, VLACS		6.2.1.-
1.11 Butanoate metabolism PATH:hsa00650		
3028 HADH2, ERAB	C140COAm + 7 COAm + 7 FADm + 7 NADm -> 7 FADH2m + 7 NADHm + 7 ACCOAm	1.1.1.35
3033 HADHSC, SCHAD		1.1.1.35
35 ACADS, SCAD	MBCOAm + FADm -> MCCOAm + FADH2m	1.3.99.2
	IBCOAm + FADm -> MACOAm + FADH2m	
7915 ALDH5A1, SSADH, SSDH		1.2.1.24
2571 GAD1, GAD, GAD67, GAD25	GLU -> GABA + CO2	4.1.1.15
2572 GAD2	GLU -> GABA + CO2	4.1.1.15
2573 GAD3	GLU -> GABA + CO2	4.1.1.15
3157 HMGCS1, HMGCS	H3MCOA + COA <-> ACCOA + AACCOA	4.1.3.5
3158 HMGCS2	H3MCOA + COA <-> ACCOA + AACCOA	4.1.3.5
3155 HMGCL, HL	H3MCOAm -> ACCOAm + ACTACm	4.1.3.4
5019 OXCT		2.8.3.5
622 BDH	3HBm + NADm -> NADHm + Hm + ACTACm	1.1.1.30
1629 DBT, BCATE2	OMVALm + COAm + NADm -> MBCOAm + NADHm + CO2m	2.3.1.-
	OIVALm + COAm + NADm -> IBCOAm + NADHm + CO2m	
	OICAPm + COAm + NADHm -> IVCOAm + NADHm + CO2m	
1.13 Inositol metabolism PATH:hsa00031		
2. Energy Metabolism		
2.1 Oxidative phosphorylation PATH:hsa00190		
4535 MTND1	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3

4536 MTND2	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4537 MTND3	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4538 MTND4	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4539 MTND4L	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4540 MTND5	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4541 MTND6	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4694 NDUFA1, MWFE	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4695 NDUFA2, B8	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4696 NDUFA3, B9	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4697 NDUFA4, MLRQ	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4698 NDUFA5, UQOR13, B13	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4700 NDUFA6, B14	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4701 NDUFA7, B14.5a, B14.5A	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4702 NDUFA8, PGIV	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4704 NDUFA9, NDUFS2L	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4705 NDUFA10	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4706 NDUFAB1, SDAP	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4707 NDUFB1, MNLL, CI-SGDH	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4708 NDUFB2, AGGG	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4709 NDUFB3, B12	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4710 NDUFB4, B15	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4711 NDUFB5, SGDH	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4712 NDUFB6, B17	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4713 NDUFB7, B18	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4714 NDUFB8, ASHI	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4715 NDUFB9, UQOR22, B22	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4716 NDUFB10, PDSW	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4717 NDUFC1, KFYI	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4718 NDUFC2, B14.5b, B14.5B	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4724 NDUFS4, AQDQ	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4725 NDUFS5	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4726 NDUFS6	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4731 NDUFV3	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4727 NDUFS7, PSST	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4722 NDUFS3	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3

	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4720 NDUFS2	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4729 NDUFV2	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4723 NDUFV1, UQOR1	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
4719 NDUFS1, PRO1304	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
4728 NDUFS8	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.5.3
	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	1.6.99.3
6391 SDHC	SUCCm + FADm <-> FUMm + FADH2m FADH2m + Qm <-> FADm + QH2m	1.3.5.1
6392 SDHD, CBT1, PGL, PGL1	SUCCm + FADm <-> FUMm + FADH2m FADH2m + Qm <-> FADm + QH2m	1.3.5.1
6389 SDHA, SDH2, SDHF, FP	SUCCm + FADm <-> FUMm + FADH2m FADH2m + Qm <-> FADm + QH2m	1.3.5.1
6390 SDHB, SDH1, IP, SDH	SUCCm + FADm <-> FUMm + FADH2m FADH2m + Qm <-> FADm + QH2m	1.3.5.1
7386 UQCRFS1, RIS1	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
4519 MTCYB	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
1537 CYC1	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
7384 UQCRC1, D3S3191	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
7385 UQCRC2	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
7388 UQCRH	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
7381 UQCRB, QPC, UQBP, QP-C	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
27089 QP-C	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
10975 UQCR	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	1.10.2.2
1333 COX5BL4	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
4514 MTCO3	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
4512 MTCO1	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
4513 MTCO2	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1329 COX5B	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1327 COX4	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1337 COX6A1, COX6A	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1339 COX6A2	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1340 COX6B	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1345 COX6C	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
9377 COX5A, COX, VA, COX-VA	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1346 COX7A1, COX7AM, COX7A	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1347 COX7A2, COX VIIa-L	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1348 COX7A3	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1349 COX7B	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
9167 COX7A2L, COX7RP, EB1	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1350 COX7C	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
1351 COX8, COX VIII	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	1.9.3.1
4508 MTATP6	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
4509 MTATP8	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
499 ATP5A2	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
507 ATP5BL1, ATPSBL1	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
508 ATP5BL2, ATPSBL2	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
519 ATP5H	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
537 ATP6S1, ORF, VATPS1, XAP-3	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
514 ATP5E	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
513 ATP5D	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
506 ATP5B, ATPSB	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
509 ATP5C1, ATP5C	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
498 ATP5A1, ATP5A, ATPM, OMR, HATP1	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
539 ATP5O, ATPO, OSCP	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
516 ATP5G1, ATP5G	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
517 ATP5G2	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34

518 ATP5G3	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
515 ATP5F1	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
521 ATP5I	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
522 ATP5J, ATP5A, ATPM, ATP5	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
9551 ATP5J2, ATP5JL, F1FO-ATPASE	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
10476 ATP5JD	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
10632 ATP5JG	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
9296 ATP6S14	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
528 ATP6D	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
523 ATP6A1, VPP2	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
524 ATP6A2, VPP2	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
525 ATP6B1, VPP3, VATB	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
526 ATP6B2, VPP3	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
529 ATP6E	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
527 ATP6C, ATPL	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
533 ATP6F	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
10312 TCIRG1, TIRC7, OC-116, OC-116kDa, OC-116KDA, ATP6N1C	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
23545 TJ6	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
50617 ATP6N1B	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
535 ATP6N1	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
51382 VATD	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
8992 ATP6H	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
9550 ATP6J	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
51606 LOC51606	ADPm + Pim + 3 H -> ATPm + 3 Hm + H2Om	3.6.1.34
495 ATP4A, ATP6A	ATP + H + Kxt + H2O <-> ADP + PI + Hext + K	3.6.1.36
496 ATP4B, ATP6B	ATP + H + Kxt + H2O <-> ADP + PI + Hext + K	3.6.1.36
476 ATP1A1	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
477 ATP1A2	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
478 ATP1A3	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
479 ATP1AL1	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
23439 ATP1B4	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
481 ATP1B1, ATP1B	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
482 ATP1B2, AMOG	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
483 ATP1B3	ATP + 3 NA + 2 Kxt + H2O <-> ADP + 3 NAxt + 2 K + PI	3.6.1.37
27032 ATP2C1, ATP2C1A, PMR1	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
487 ATP2A1, SERCA1, ATP2A	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
488 ATP2A2, ATP2B, SERCA2, DAR, DD	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
489 ATP2A3, SERCA3	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
490 ATP2B1, PMCA1	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
491 ATP2B2, PMCA2	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
492 ATP2B3, PMCA3	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
493 ATP2B4, ATP2B2, PMCA4	ATP + 2 CA + H2O <-> ADP + PI + 2 CAxt	3.6.1.38
538 ATP7A, MK, MNK, OHS	ATP + H2O + Cu2 -> ADP + PI + Cu2xt	3.6.3.4
540 ATP7B, WND	ATP + H2O + Cu2 -> ADP + PI + Cu2xt	3.6.3.4
5464 PP, SID6-8061	PPI -> 2 PI	3.6.1.1
2.2 Photosynthesis PATH:hsa00195		
2.3 Carbon fixation PATH:hsa00710		
2805 GOT1	OAm + GLUm <-> ASPm + AKGm	2.6.1.1
2806 GOT2	OA + GLU <-> ASP + AKG	2.6.1.1
2875 GPT	PYR + GLU <-> AKG + ALA	2.6.1.2
2.4 Reductive carboxylate cycle (CO2 fixation) PATH:hsa00720		
2.5 Methane metabolism PATH:hsa00680		
847 CAT	2 H2O2 -> O2	1.11.1.6
4025 LPO, SPO		1.11.1.7
4353 MPO		1.11.1.7
8288 EPX, EPX-PEN, EPO, EPP		1.11.1.7
9588 KIAA0106, AOP2		1.11.1.7
6470 SHMT1, CSHMT	THF + SER <-> GLY + METTHF	2.1.2.1
6472 SHMT2, GLYA, SHMT	THFm + SERm <-> GLYm + METTHFm	2.1.2.1

51004 LOC51004	2OPMPm + O2m -> 2OPMBm 2OPMMBm + O2m -> 2OMHMBm	1.14.13.-
9420 CYP7B1	2OPMPm + O2m -> 2OPMBm 2OPMMBm + O2m -> 2OMHMBm	1.14.13.-
2.6 Nitrogen metabolism PATH:hsa00910		
11238 CA5B		4.2.1.1
23632 CA14		4.2.1.1
759 CA1		4.2.1.1
760 CA2		4.2.1.1
761 CA3, CAIII		4.2.1.1
762 CA4, CAIV		4.2.1.1
763 CA5A, CA5, CAV, CAVA		4.2.1.1
765 CA6		4.2.1.1
766 CA7		4.2.1.1
767 CA8, CALS, CARP		4.2.1.1
768 CA9, MN		4.2.1.1
770 CA11, CARP2		4.2.1.1
771 CA12		4.2.1.1
1373 CPS1	GLUm + CO2m + 2 ATPm -> 2 ADPm + 2 Plm + CAPm	6.3.4.16
275 AMT	GLYm + THFm + NADm <-> METTHFm + NADHm + CO2m + NH3m	2.1.2.10
3034 HAL, HSTD, HIS	HIS -> NH3 + URO	4.3.1.3
2746 GLUD1, GLUD	AKGm + NADHm + NH3m <-> NADm + H2Om + GLUm AKGm + NADPHm + NH3m <-> NADPm + H2Om + GLUm	1.4.1.3
8307 GLUD2	AKGm + NADHm + NH3m <-> NADm + H2Om + GLUm AKGm + NADPHm + NH3m <-> NADPm + H2Om + GLUm	1.4.1.3
2752 GLUL, GLNS	GLUm + NH3m + ATPm -> GLNm + ADPm + Pim	6.3.1.2
22842 KIAA0838	GLN -> GLU + NH3	3.5.1.2
27165 GA	GLN -> GLU + NH3	3.5.1.2
2744 GLS	GLNm -> GLUm + NH3m	3.5.1.2
440 ASNS	ASPm + ATPm + GLNm -> GLUm + ASNm + AMPm + PPIm	6.3.5.4
1491 CTH	LLCT + H2O -> CYS + HSER	4.4.1.1
	OBUT + NH3 <-> HSER	4.4.1.1
2.7 Sulfur metabolism PATH:hsa00920		
9060 PAPSS2, ATPSK2, SK2	APS + ATP -> ADP + PAPS	2.7.1.25
	SLF + ATP -> PPI + APS	2.7.7.4
9061 PAPSS1, ATPSK1, SK1	APS + ATP -> ADP + PAPS	2.7.1.25
	SLF + ATP -> PPI + APS	2.7.7.4
10380 BPNT1	PAP -> AMP + PI	3.1.3.7
6799 SULT1A2		2.8.2.1
6817 SULT1A1, STP1		2.8.2.1
6818 SULT1A3, STM		2.8.2.1
6822 SULT2A1, STD		2.8.2.2
6783 STE, EST		2.8.2.4
6821 SUOX		1.8.3.1
3. Lipid Metabolism		
3.1 Fatty acid biosynthesis (path 1) PATH:hsa00061		
2194 FASN		2.3.1.85
3.2 Fatty acid biosynthesis (path 2) PATH:hsa00062		
10449 ACAA2, DSAEC	MAACOAm -> ACCOAm + PROPCOAm	2.3.1.16
30 ACAA1, ACAA	MAACOA -> ACCOA + PROPCOA	2.3.1.16
3032 HADHB	MAACOA -> ACCOA + PROPCOA	2.3.1.16
3.3 Fatty acid metabolism PATH:hsa00071		
51 ACOX1, ACOX		1.3.3.6
33 ACADL, LCAD		1.3.99.13
2639 GCDH		1.3.99.7
2179 FACL1, LACS	ATP + LCCA + COA <-> AMP + PPI + ACOA	6.2.1.3
2180 FACL2, FACL1, LACS2	ATP + LCCA + COA <-> AMP + PPI + ACOA	6.2.1.3
2182 FACL4, ACS4	ATP + LCCA + COA <-> AMP + PPI + ACOA	6.2.1.3
1374 CPT1A, CPT1, CPT1-L		2.3.1.21
1375 CPT1B, CPT1-M		2.3.1.21

1376 CPT2, CPT1, CPTASE		2.3.1.21
1632 DCI		5.3.3.8
11283 CYP4F8		1.14.14.1
1543 CYP1A1, CYP1		1.14.14.1
1544 CYP1A2		1.14.14.1
1545 CYP1B1, GLC3A		1.14.14.1
1548 CYP2A6, CYP2A3		1.14.14.1
1549 CYP2A7		1.14.14.1
1551 CYP3A7		1.14.14.1
1553 CYP2A13		1.14.14.1
1554 CYP2B		1.14.14.1
1555 CYP2B6		1.14.14.1
1557 CYP2C19, CYP2C, P450IIC19		1.14.14.1
1558 CYP2C8		1.14.14.1
1559 CYP2C9, P450IIC9, CYP2C10		1.14.14.1
1562 CYP2C18, P450IIC17, CYP2C17		1.14.14.1
1565 CYP2D6		1.14.14.1
1571 CYP2E, CYP2E1, P450C2E		1.14.14.1
1572 CYP2F1, CYP2F		1.14.14.1
1573 CYP2J2		1.14.14.1
1575 CYP3A3		1.14.14.1
1576 CYP3A4		1.14.14.1
1577 CYP3A5, PCN3		1.14.14.1
1580 CYP4B1		1.14.14.1
1588 CYP19, ARO		1.14.14.1
1595 CYP51		1.14.14.1
194 AHHR, AHH		1.14.14.1
3.4 Synthesis and degradation of ketone bodies PATH:hsa00072		
3.5 Sterol biosynthesis PATH:hsa00100		
3156 HMGCR	MVL + COA + 2 NADP <-> H3MCOA + 2 NADPH	1.1.1.34
4598 MVK, MVLK	ATP + MVL -> ADP + PMVL	2.7.1.36
	CTP + MVL -> CDP + PMVL	
	GTP + MVL -> GDP + PMVL	
	UTP + MVL -> UDP + PMVL	
10654 PMVK, PMKASE, PMK, HUMPMKI	ATP + PMVL -> ADP + PPMVL	2.7.4.2
4597 MVD, MPD	ATP + PPMVL -> ADP + PI + IPPP + CO2	4.1.1.33
3422 IDI1	IPPP <-> DMPP	5.3.3.2
2224 FDPS	GPP + IPPP -> FPP + PPI	2.5.1.10
	DMPP + IPPP -> GPP + PPI	2.5.1.1
9453 GGPS1, GGPPS	DMPP + IPPP -> GPP + PPI	2.5.1.1
	GPP + IPPP -> FPP + PPI	2.5.1.10
		2.5.1.29
2222 FDFT1, DGPT	2 FPP + NADPH -> NADP + SQL	2.5.1.21
6713 SQLE	SQL + O2 + NADP -> S23E + NADPH	1.14.99.7
4047 LSS, OSC	S23E -> LNST	5.4.99.7
1728 DIA4, NMOR1, NQO1, NMORI		1.6.99.2
4835 NMOR2, NQO2		1.6.99.2
37 ACADVL, VLCAD, LCACD		1.3.99.-
3.6 Bile acid biosynthesis PATH:hsa00120		
1056 CEL, BSSL, BAL		3.1.1.3
		3.1.1.13
3988 LIPA, LAL		3.1.1.13
6646 SOAT1, ACAT, STAT, SOAT, ACAT1, ACACT		2.3.1.26
1581 CYP7A1, CYP7		1.14.13.17
6715 SRD5A1		1.3.99.5
6716 SRD5A2		1.3.99.5
6718 AKR1D1, SRD5B1, 3o5bred		1.3.99.6
570 BAAT, BAT		2.3.1.65
3.7 C21-Steroid hormone metabolism PATH:hsa00140		
1583 CYP11A, P450SCC		1.14.15.6

3283 HSD3B1, HSD3B, HSDB3	IMZYMST -> IIMZYMST + CO2 IMZYMST -> IIZYMST + CO2	5.3.3.1 1.1.1.145
3284 HSD3B2	IMZYMST -> IIMZYMST + CO2 IMZYMST -> IIZYMST + CO2	5.3.3.1 1.1.1.145
1589 CYP21A2, CYP21, P450C21B, CA21H, CYP21B, P450c21B		1.14.99.10
1586 CYP17, P450C17		1.14.99.9
1584 CYP11B1, P450C11, CYP11B		1.14.15.4
1585 CYP11B2, CYP11B		1.14.15.4
3290 HSD11B1, HSD11, HSD11L, HSD11B		1.1.1.146
3291 HSD11B2, HSD11K		1.1.1.146
3.8 Androgen and estrogen metabolism PATH:hsa00150		
3292 HSD17B1, EDH17B2, EDHB17, HSD17		1.1.1.62
3293 HSD17B3, EDH17B3		1.1.1.62
3294 HSD17B2, EDH17B2		1.1.1.62
3295 HSD17B4		1.1.1.62
3296 HSD17BP1, EDH17B1, EDHB17, HSD17		1.1.1.62
51478 HSD17B7, PRAP		1.1.1.62
412 STS, ARSC, ARSC1, SSDD		3.1.6.2
414 ARSD		3.1.6.1
415 ARSE, CDPX1, CDPXR, CDPX		3.1.6.1
11185 INMT		2.1.1.-
24140 JM23		2.1.1.-
29104 N6AMT1, PRED28		2.1.1.-
29960 FJH1		2.1.1.-
3276 HRMT1L2, HCP1, PRMT1		2.1.1.-
51628 LOC51628		2.1.1.-
54743 HASJ4442		2.1.1.-
27292 HSA9761		2.1.1.-
4. Nucleotide Metabolism		
4.1 Purine metabolism PATH:hsa00230		
11164 NUDT5, HYSAH1, YSA1H		3.6.1.13
5471 PPAT, GPAT	PRPP + GLN -> PPI + GLU + PRAM	2.4.2.14
2618 GART, PGFT, PRGS	PRAM + ATP + GLY <-> ADP + PI + GAR	6.3.4.13
	FGAM + ATP -> ADP + PI + AIR	6.3.3.1
	GAR + FTHF -> THF + FGAR	2.1.2.2
5198 PFAS, FGARAT, KIAA0361, PURL	FGAR + ATP + GLN -> GLU + ADP + PI + FGAM	6.3.5.3
10606 ADE2H1	CAIR + ATP + ASP <-> ADP + PI + SAICAR	6.3.2.6
	CAIR <-> AIR + CO2	4.1.1.21
5059 PAICS, AIRC, PAIS	CAIR + ATP + ASP <-> ADP + PI + SAICAR	6.3.2.6
158 ADSL	ASUC <-> FUM + AMP	4.3.2.2
471 ATIC, PURH	AICAR + FTHF <-> THF + PRFICA	2.1.2.3
	PRFICA <-> IMP	3.5.4.10
3251 HPRT1, HPRT, HGPRT	HYXAN + PRPP -> PPI + IMP	2.4.2.8
	GN + PRPP -> PPI + GMP	
3614 IMPDH1	IMP + NAD -> NADH + XMP	1.1.1.205
3615 IMPDH2	IMP + NAD -> NADH + XMP	1.1.1.205
8833 GMPS		6.3.5.2
14923		
2987 GUK1	GMP + ATP <-> GDP + ADP DGMP + ATP <-> DGDP + ADP GMP + DATP <-> GDP + DADP	2.7.4.8
2988 GUK2	GMP + ATP <-> GDP + ADP DGMP + ATP <-> DGDP + ADP GMP + DATP <-> GDP + DADP	2.7.4.8
10621 RPC39		2.7.7.6

10622 RPC32		2.7.7.6
10623 RPC62		2.7.7.6
11128 RPC155		2.7.7.6
25885 DKFZP586M0122		2.7.7.6
30834 ZNRD1		2.7.7.6
51082 LOC51082		2.7.7.6
51728 LOC51728		2.7.7.6
5430 POLR2A, RPOL2, POLR2, POLRA		2.7.7.6
5431 POLR2B, POL2RB		2.7.7.6
5432 POLR2C		2.7.7.6
5433 POLR2D, HSRBP4, HSRPB4		2.7.7.6
5434 POLR2E, RPB5, XAP4		2.7.7.6
5435 POLR2F, RPB6, HRBP14.4		2.7.7.6
5436 POLR2G, RPB7		2.7.7.6
5437 POLR2H, RPB8, RPB17		2.7.7.6
5438 POLR2I		2.7.7.6
5439 POLR2J		2.7.7.6
5440 POLR2K, RPB7.0		2.7.7.6
5441 POLR2L, RPB7.6, RPB10		2.7.7.6
5442 POLRMT, APOLMT		2.7.7.6
54479 FLJ10816, Rpo1-2		2.7.7.6
55703 FLJ10388		2.7.7.6
661 BN51T		2.7.7.6
9533 RPA40, RPA39		2.7.7.6
10721 POLQ		2.7.7.7
11232 POLG2, MTPOLB, HP55, POLB		2.7.7.7
23649 POLA2		2.7.7.7
5422 POLA		2.7.7.7
5423 POLB		2.7.7.7
5424 POLD1, POLD		2.7.7.7
5425 POLD2		2.7.7.7
5426 POLE		2.7.7.7
5427 POLE2		2.7.7.7
5428 POLG		2.7.7.7
5980 REV3L, POLZ, REV3		2.7.7.7
7498 XDH		1.1.3.22
		1.1.1.204
9615 GDA, KIAA1258, CYPIN, NEDASIN		3.5.4.3
2766 GMPR		1.6.6.8
51292 LOC51292		1.6.6.8
7377 UOX		1.7.3.3
6240 RRM1	ADP + RTHIO -> DADP + OTHIO	1.17.4.1
	GDP + RTHIO -> DGDP + OTHIO	
	CDP + RTHIO -> DCDP + OTHIO	
	UDP + RTHIO -> DUDP + OTHIO	
6241 RRM2	ADP + RTHIO -> DADP + OTHIO	1.17.4.1
	GDP + RTHIO -> DGDP + OTHIO	
	CDP + RTHIO -> DCDP + OTHIO	
	UDP + RTHIO -> DUDP + OTHIO	
4860 NP, PNP	AND + PI <-> AD + R1P	2.4.2.1
	GSN + PI <-> GN + R1P	
	DA + PI <-> AD + R1P	
	DG + PI <-> GN + R1P	
	DIN + PI <-> HYXAN + R1P	
	INS + PI <-> HYXAN + R1P	
	XTSINE + PI <-> XAN + R1P	
1890 ECGF1, hPD-ECGF	DU + PI <-> URA + DR1P	2.4.2.4
	DT + PI <-> THY + DR1P	
353 APRT	AD + PRPP -> PPI + AMP	2.4.2.7
132 ADK	ADN + ATP -> AMP + ADP	2.7.1.20
1633 DCK		2.7.1.74

1716 DGUOK		2.7.1.113
203 AK1	ATP + AMP <-> 2 ADP	2.7.4.3
	GTP + AMP <-> ADP + GDP	
	ITP + AMP <-> ADP + IDP	
204 AK2	ATP + AMP <-> 2 ADP	2.7.4.3
	GTP + AMP <-> ADP + GDP	
	ITP + AMP <-> ADP + IDP	
205 AK3	ATP + AMP <-> 2 ADP	2.7.4.3
	GTP + AMP <-> ADP + GDP	
	ITP + AMP <-> ADP + IDP	
26289 AK5	ATP + AMP <-> 2 ADP	2.7.4.3
	GTP + AMP <-> ADP + GDP	
	ITP + AMP <-> ADP + IDP	
4830 NME1, NM23, NM23-H1	UDP + ATP <-> UTP + ADP	2.7.4.6
	CDP + ATP <-> CTP + ADP	
	GDP + ATP <-> GTP + ADP	
	IDP + ATP <-> ITP + IDP	
	DGDP + ATP <-> DGTP + ADP	
	DUDP + ATP <-> DUTP + ADP	
	DCDP + ATP <-> DCTP + ADP	
	DTDP + ATP <-> DTTP + ADP	
	DADP + ATP <-> DATP + ADP	
4831 NME2, NM23-H2	UDP + ATP <-> UTP + ADP	2.7.4.6
	CDP + ATP <-> CTP + ADP	
	GDP + ATP <-> GTP + ADP	
	IDP + ATP <-> ITP + IDP	
	DGDP + ATP <-> DGTP + ADP	
	DUDP + ATP <-> DUTP + ADP	
	DCDP + ATP <-> DCTP + ADP	
	DTDP + ATP <-> DTTP + ADP	
	DADP + ATP <-> DATP + ADP	
4832 NME3, DR-nm23, DR-NM23	UDP + ATP <-> UTP + ADP	2.7.4.6
	CDP + ATP <-> CTP + ADP	
	GDP + ATP <-> GTP + ADP	
	IDP + ATP <-> ITP + IDP	
	DGDP + ATP <-> DGTP + ADP	
	DUDP + ATP <-> DUTP + ADP	
	DCDP + ATP <-> DCTP + ADP	
	DTDP + ATP <-> DTTP + ADP	
	DADP + ATP <-> DATP + ADP	
4833 NME4	UDPm + ATPm <-> UTPm + ADPm	2.7.4.6
	CDPm + ATPm <-> CTPm + ADPm	
	GDPm + ATPm <-> GTPm + ADPm	
	IDPm + ATPm <-> ITPm + IDPm	
	DGDPm + ATPm <-> DGTPm + ADPm	
	DUDPm + ATPm <-> DUTPm + ADPm	
	DCDPm + ATPm <-> DCTPm + ADPm	
	DTDPm + ATPm <-> DTTPm + ADPm	
	DADPm + ATPm <-> DATPm + ADPm	
22978 NT5B, PNT5, NT5B-PENDING	AMP + H2O -> PI + ADN	3.1.3.5
	GMP -> PI + GSN	
	CMP -> CYTD + PI	
	UMP -> PI + URI	
	IMP -> PI + INS	
	DUMP -> DU + PI	
	DTMP -> DT + PI	
	DAMP -> DA + PI	
	DGMP -> DG + PI	
	DCMP -> DC + PI	
	XMP -> PI + XTSINE	
4877 NT3	AMP -> PI + ADN	3.1.3.5

	GMP -> PI + GSN CMP -> CYTD + PI UMP -> PI + URI IMP -> PI + INS DUMP -> DU + PI DTMP -> DT + PI DAMP -> DA + PI DGMP -> DG + PI DCMP -> DC + PI XMP -> PI + XTSINE	
4907 NT5, CD73	AMP -> PI + ADN GMP -> PI + GSN CMP -> CYTD + PI UMP -> PI + URI IMP -> PI + INS DUMP -> DU + PI DTMP -> DT + PI DAMP -> DA + PI DGMP -> DG + PI DCMP -> DC + PI XMP -> PI + XTSINE	3.1.3.5
7370 UMPH2	AMP -> PI + ADN GMP -> PI + GSN CMP -> CYTD + PI UMP -> PI + URI IMP -> PI + INS DUMP -> DU + PI DTMP -> DT + PI DAMP -> DA + PI DGMP -> DG + PI DCMP -> DC + PI XMP -> PI + XTSINE	3.1.3.5
10846 PDE10A	cAMP -> AMP cAMP -> AMP cdAMP -> dAMP cIMP -> IMP cGMP -> GMP cCMP -> CMP	3.1.4.17
27115 PDE7B	cAMP -> AMP cAMP -> AMP cdAMP -> dAMP cIMP -> IMP cGMP -> GMP cCMP -> CMP	3.1.4.17
5136 PDE1A	cAMP -> AMP cAMP -> AMP cdAMP -> dAMP cIMP -> IMP cGMP -> GMP cCMP -> CMP	3.1.4.17
5137 PDE1C, HCAM3	cAMP -> AMP cAMP -> AMP cdAMP -> dAMP cIMP -> IMP cGMP -> GMP cCMP -> CMP	3.1.4.17
5138 PDE2A	cAMP -> AMP cAMP -> AMP cdAMP -> dAMP cIMP -> IMP cGMP -> GMP	3.1.4.17

	cCMP -> CMP	
5139 PDE3A, CGI-PDE	cAMP -> AMP	3.1.4.17
	cAMP -> AMP	
	cdAMP -> dAMP	
	cIMP -> IMP	
	cGMP -> GMP	
	cCMP -> CMP	
5140 PDE3B	cAMP -> AMP	3.1.4.17
	cAMP -> AMP	
	cdAMP -> dAMP	
	cIMP -> IMP	
	cGMP -> GMP	
	cCMP -> CMP	
5141 PDE4A, DPDE2	cAMP -> AMP	3.1.4.17
5142 PDE4B, DPDE4, PDEIVB	cAMP -> AMP	3.1.4.17
5143 PDE4C, DPDE1	cAMP -> AMP	3.1.4.17
5144 PDE4D, DPDE3	cAMP -> AMP	3.1.4.17
5145 PDE6A, PDEA, CGPR-A	cGMP -> GMP	3.1.4.17
5146 PDE6C, PDEA2	cGMP -> GMP	3.1.4.17
5147 PDE6D	cGMP -> GMP	3.1.4.17
5148 PDE6G, PDEG	cGMP -> GMP	3.1.4.17
5149 PDE6H	cGMP -> GMP	3.1.4.17
5152 PDE9A	cAMP -> AMP	3.1.4.17
	cAMP -> AMP	
	cdAMP -> dAMP	
	cIMP -> IMP	
	cGMP -> GMP	
	cCMP -> CMP	
5153 PDES1B	cAMP -> AMP	3.1.4.17
	cAMP -> AMP	
	cdAMP -> dAMP	
	cIMP -> IMP	
	cGMP -> GMP	
	cCMP -> CMP	
5158 PDE6B, CSNB3, PDEB	cGMP -> GMP	3.1.4.17
8654 PDE5A	cGMP -> GMP	3.1.4.17
100 ADA	ADN -> INS + NH3	3.5.4.4
	DA -> DIN + NH3	
270 AMPD1, MADA	AMP -> IMP + NH3	3.5.4.6
271 AMPD2	AMP -> IMP + NH3	3.5.4.6
272 AMPD3	AMP -> IMP + NH3	3.5.4.6
953 ENTPD1, CD39		3.6.1.5
3704 ITPA		3.6.1.19
107 ADCY1	ATP -> cAMP + PPI	4.6.1.1
108 ADCY2, HBAC2	ATP -> cAMP + PPI	4.6.1.1
109 ADCY3, AC3, KIAA0511	ATP -> cAMP + PPI	4.6.1.1
110 ADCY4	ATP -> cAMP + PPI	4.6.1.1
111 ADCY5	ATP -> cAMP + PPI	4.6.1.1
112 ADCY6	ATP -> cAMP + PPI	4.6.1.1
113 ADCY7, KIAA0037	ATP -> cAMP + PPI	4.6.1.1
114 ADCY8, ADCY3, HBAC1	ATP -> cAMP + PPI	4.6.1.1
115 ADCY9	ATP -> cAMP + PPI	4.6.1.1
2977 GUCY1A2, GUC1A2, GC-SA2		4.6.1.2
2982 GUCY1A3, GUC1A3, GUCSA3, GC-SA3		4.6.1.2
2983 GUCY1B3, GUC1B3, GUCSB3, GC-SB3		4.6.1.2
2984 GUCY2C, GUC2C, STAR		4.6.1.2
2986 GUCY2F, GUC2F, GC-F, GUC2DL, RETGC-2		4.6.1.2

3000 GUCY2D, CORD6, GUC2D, LCA1, GUC1A4, LCA, retGC		4.6.1.2
4881 NPR1, ANPRA, GUC2A, NPRA		4.6.1.2
4882 NPR2, ANPRB, GUC2B, NPRB, NPRBi		4.6.1.2
159 ADSS	IMP + GTP + ASP -> GDP + PI + ASUC	6.3.4.4
318 NUDT2, APAH1		3.6.1.17
5167 ENPP1, M6S1, NPPS, PCA1, PC-1, PDNP1		3.6.1.9
5168 ENPP2, ATX, PD-IALPHA, PDNP2		3.6.1.9
5169 ENPP3, PD-IBETA, PDNP3		3.6.1.9
		3.1.4.1
2272 FHIT		3.6.1.29
4.2 Pyrimidine metabolism PATH:hsa00240		
790 CAD	GLN + 2 ATP + CO2 -> GLU + CAP + 2 ADP + PI	6.3.5.5
	CAP + ASP -> CAASP + PI	2.1.3.2
	CAASP <-> DOROA	3.5.2.3
1723 DHODH	DOROA + O2 <-> H2O2 + OROA	1.3.3.1
7372 UMPS, OPRT	OMP -> CO2 + UMP	4.1.1.23
	OROA + PRPP <-> PPI + OMP	2.4.2.10
51727 LOC51727	ATP + UMP <-> ADP + UDP	2.7.4.14
	CMP + ATP <-> ADP + CDP	
	DCMP + ATP <-> ADP + DCDP	
50808 AKL3L		2.7.4.10
1503 CTPS	UTP + GLN + ATP -> GLU + CTP + ADP + PI	6.3.4.2
	ATP + UTP + NH3 -> ADP + PI + CTP	
7371 UMPK, TSA903	URI + ATP -> ADP + UMP	2.7.1.48
	URI + GTP -> UMP + GDP	
	CYTD + GTP -> GDP + CMP	
7378 UP	URI + PI <-> URA + R1P	2.4.2.3
1806 DPYD, DPD		1.3.1.2
1807 DPYS, DHPase, DHPASE, DHP		3.5.2.2
51733 LOC51733		3.5.1.6
7296 TXNRD1, TXNR	OTHIO + NADPH -> NADP + RTHIO	1.6.4.5
1854 DUT	DUTP -> PPI + DUMP	3.6.1.23
7298 TYMS, TMS, TS	DUMP + METTHF -> DHF + DTMP	2.1.1.45
978 CDA, CDD	CYTD -> URI + NH3	3.5.4.5
	DC -> NH3 + DU	
1635 DCTD	DCMP <-> DUMP + NH3	3.5.4.12
7083 TK1	DU + ATP -> DUMP + ADP	2.7.1.21
	DT + ATP -> ADP + DTMP	
7084 TK2	DUm + ATPm -> DUMPm + ADPm	2.7.1.21
	DTm + ATPm -> ADPm + DTMPm	
1841 DTYMK, TYMK, CDC8	DTMP + ATP <-> ADP + DTDP	2.7.4.9
4.3 Nucleotide sugars metabolism PATH:hsa00520		
23483 TDPGD		4.2.1.46
1486 CTBS, CTB		3.2.1.-
5. Amino Acid Metabolism		
5.1 Glutamate metabolism PATH:hsa00251		
8659 ALDH4, P5CDH	P5C + NAD + H2O -> NADH + GLU	1.5.1.12
2058 EPRS, QARS, QPRS	GLU + ATP -> GTRNA + AMP + PPI	6.1.1.17
		6.1.1.15
2673 GFPT1, GFA, GFAT, GFPT	F6P + GLN -> GLU + GA6P	2.6.1.16
9945 GFPT2, GFAT2	F6P + GLN -> GLU + GA6P	2.6.1.16
5859 QARS		6.1.1.18
2729 GLCLC, GCS, GLCL	CYS + GLU + ATP -> GC + PI + ADP	6.3.2.2
2730 GLCLR	CYS + GLU + ATP -> GC + PI + ADP	6.3.2.2
2937 GSS, GSHS	GLY + GC + ATP -> RGT + PI + ADP	6.3.2.3
2936 GSR	NADPH + OGT -> NADP + RGT	1.6.4.2
5188 PET112L, PET112		6.3.5.-
5.2 Alanine and aspartate metabolism PATH:hsa00252		

4677 NARS, ASNRS	ATP + ASP + TRNA -> AMP + PPI + ASPTRNA	6.1.1.22
435 ASL	ARGSUCC -> FUM + ARG	4.3.2.1
189 AGXT, SPAT	SERm + PYRm <-> ALAm + 3HPm	2.6.1.51
	ALA + GLX <-> PYR + GLY	2.6.1.44
16 AARS		6.1.1.7
1615 DARS		6.1.1.12
445 ASS, CTLN1, ASS1	CITR + ASP + ATP <-> AMP + PPI + ARGSUCC	6.3.4.5
443 ASPA, ASP, ACY2		3.5.1.15
1384 CRAT, CAT1		2.3.1.7
	ACCOA + CAR -> COA + ACAR	
8528 DDO		1.4.3.1
5.3 Glycine, serine and threonine metabolism PATH:hsa00260		
5723 PSPH, PSP	3PSER + H2O -> PI + SER	3.1.3.3
29968 PSA	PHP + GLU <-> AKG + 3PSER	2.6.1.52
	OHB + GLU <-> PHT + AKG	
26227 PHGDH, SERA, PGDH, PGD, PGAD	3PG + NAD <-> NADH + PHP	1.1.1.95
23464 GCAT, KBL		2.3.1.29
211 ALAS1, ALAS	SUCCOA + GLY -> ALAV + COA + CO2	2.3.1.37
212 ALAS2, ANH1, ASB	SUCCOA + GLY -> ALAV + COA + CO2	2.3.1.37
4128 MAOA	AMA + H2O + FAD -> NH3 + FADH2 + MTHGXL	1.4.3.4
4129 MAOB	AMA + H2O + FAD -> NH3 + FADH2 + MTHGXL	1.4.3.4
26 ABP1, AOC1, DAO		1.4.3.6
314 AOC2, DAO2, RAO		1.4.3.6
8639 AOC3, VAP-1, VAP1, HPAO		1.4.3.6
2731 GLDC	GLY + LIPO <-> SAP + CO2	1.4.4.2
1610 DAO, DAMOX		1.4.3.3
2617 GARS		6.1.1.14
2628 GATM		2.1.4.1
2593 GAMT		2.1.1.2
PISD, PSSC, DKFZP566G2246, 23761 DJ858B16	PS -> PE + CO2	4.1.1.65
635 BHMT		2.1.1.5
29958 DMGDH		1.5.99.2
875 CBS	SER + HCYS -> LLCT + H2O	4.2.1.22
6301 SARS, SERS		6.1.1.11
10993 SDS, SDH	SER -> PYR + NH3 + H2O	4.2.1.13
6897 TARS		6.1.1.3
5.4 Methionine metabolism PATH:hsa00271		
4143 MAT1A, MATA1, SAMS1, MAT, SAMS	MET + ATP + H2O -> PPI + PI + SAM	2.5.1.6
4144 MAT2A, MATA2, SAMS2, MATII	MET + ATP + H2O -> PPI + PI + SAM	2.5.1.6
1786 DNMT1, MCMT, DNMT	SAM + DNA -> SAH + DNA5MC	2.1.1.37
10768 AHCYL1, XPVKONA	SAH + H2O -> HCYS + ADN	3.3.1.1
191 AHCY, SAHH	SAH + H2O -> HCYS + ADN	3.3.1.1
4141 MARS, METRS, MTRNS		6.1.1.10
4548 MTR	HCYS + MTHF -> THF + MET	2.1.1.13
5.5 Cysteine metabolism PATH:hsa00272		
833 CARS		6.1.1.16
1036 CDO1	CYS + O2 <-> CYSS	1.13.11.20
8509 NDST2, HSST2, NST2		2.8.2.-
5.6 Valine, leucine and isoleucine degradation PATH:hsa00280		
586 BCAT1, BCT1, ECA39, MECA39	AKG + ILE -> OMVAL + GLU	2.6.1.42
	AKG + VAL -> OIVAL + GLU	
	AKG + LEU -> OICAP + GLU	
587 BCAT2, BCT2	OICAPm + GLUm <-> AKGm + LEUm	2.6.1.42
	OMVALm + GLUm <-> AKGm + ILEm	
5014 OVD1A		1.2.4.4
593 BCKDHA, MSUD1	OMVALm + COAm + NADm -> MBCOAm + NADHm + CO2m	1.2.4.4
	OIVALm + COAm + NADm -> IBCOAm + NADHm + CO2m	
	OICAPm + COAm + NADm -> IVCOAm + NADHm + CO2m	
594 BCKDHB, E1B	OMVALm + COAm + NADm -> MBCOAm + NADHm + CO2m	1.2.4.4

	OIVALm + COAm + NADm -> IBCOAm + NADHm + CO2m OICAPm + COAm + NADH -> IVCOAm + NADHm + CO2m	
3712 IVD	IVCOAm + FADm -> MCRCOAm + FADH2m	1.3.99.10
316 AOX1, AO		1.2.3.1
4164 MCCC1	MCRCOAm + ATPm + CO2m + H2Om -> MGCOAm + ADPm + Pim	6.4.1.4
4165 MCCC2	MCRCOAm + ATPm + CO2m + H2Om -> MGCOAm + ADPm + Pim	6.4.1.4
5.7 Valine, leucine and isoleucine biosynthesis PATH:hsa00290		
23395 KIAA0028, LARS2		6.4.1.4
3926 LARS		6.4.1.4
3376 IARS, ILRS		6.1.1.5
7406 VARS1, VARS		6.1.1.9
7407 VARS2, G7A		6.1.1.9
5.8 Lysine biosynthesis PATH:hsa00300		
3735 KARS, KIAA0070	ATP + LYS + LTRNA -> AMP + PPI + LLTRNA	6.1.1.6
5.9 Lysine degradation PATH:hsa00310		
8424 BBOX, BBH, GAMMA-BBH, G-BBH		1.14.11.1
5351 PLOD, LLH		1.14.11.4
5352 PLOD2		1.14.11.4
8985 PLOD3, LH3		1.14.11.4
10157 LKR/SDH, AASS	LYS + NADPH + AKG -> NADP + H2O + SAC SAC + H2O + NAD -> GLU + NADH + AASA	1.5.1.9
5.10 Arginine and proline metabolism PATH:hsa00330		
5009 OTC	ORNm + CAPm -> CITRm + Pim + Hm	2.1.3.3
383 ARG1	ARG -> ORN + UREA	3.5.3.1
384 ARG2	ARG -> ORN + UREA	3.5.3.1
4842 NOS1, NOS		1.14.13.39
4843 NOS2A, NOS2		1.14.13.39
4846 NOS3, ECNOS		1.14.13.39
4942 OAT	ORN + AKG <-> GLUGSAL + GLU	2.6.1.13
5831 PYCR1, P5C, PYCR	P5C + NADPH -> PRO + NADP P5C + NADH -> PRO + NAD PHC + NADPH -> HPRO + NADP PHC + NADH -> HPRO + NAD	1.5.1.2
5033 P4HA1, P4HA		1.14.11.2
5917 RARS	ATP + ARG + ATRNA -> AMP + PPI + ALTRNA	6.1.1.19
1152 CKB, CKBB	PCRE + ADP -> CRE + ATP	2.7.3.2
1156 CKBE		2.7.3.2
1158 CKM, CKMM		2.7.3.2
1159 CKMT1, CKMT, UMTCK		2.7.3.2
1160 CKMT2, SMTCK		2.7.3.2
6723 SRM, SPS1, SRML1	PTRSC + SAM -> SPRMD + 5MTA	2.5.1.16
262 AMD1, ADOMETDC	SAM <-> DSAM + CO2	4.1.1.50
263 AMDP1, AMD, AMD2	SAM <-> DSAM + CO2	4.1.1.50
1725 DHPS	SPRMD + Qm -> DAPRP + QH2m	1.5.99.6
6611 SMS	DSAM + SPRMD -> 5MTA + SPRM	2.5.1.22
4953 ODC1	ORN -> PTRSC + CO2	4.1.1.17
6303 SAT, SSAT		2.3.1.57
5.11 Histidine metabolism PATH:hsa00340		
10841 FTCD	FIGLU + THF -> NFTHF + GLU	2.1.2.5 4.3.1.4
3067 HDC		4.1.1.22
1644 DDC, AADC		4.1.1.28
3176 HNMT		2.1.1.8
218 ALDH3	ACAL + NAD -> NADH + AC	1.2.1.5
220 ALDH6	ACAL + NAD -> NADH + AC	1.2.1.5
221 ALDH7, ALDH4	ACAL + NAD -> NADH + AC	1.2.1.5
222 ALDH8	ACAL + NAD -> NADH + AC	1.2.1.5
3035 HARS	ATP + HIS + HTRNA -> AMP + PPI + HHTRNA	6.1.1.21
5.12 Tyrosine metabolism PATH:hsa00350		

6898	TAT	AKG + TYR -> HPHPYR + GLU	2.6.1.5
3242	HPD, PPD	HPHPYR + O2 -> HGTS + CO2	1.13.11.27
3081	HGD, AKU, HGO	HGTS + O2 -> MACA	1.13.11.5
2954	GSTZ1, MAAI	MACA -> FACA	5.2.1.2
			2.5.1.18
2184	FAH	FACA + H2O -> FUM + ACA	3.7.1.2
7299	TYR, OCAIA		1.14.18.1
7054	TH, TYH		1.14.16.2
1621	DBH		1.14.17.1
5409	PNMT, PENT		2.1.1.28
1312	COMT		2.1.1.6
7173	TPO, TPX		1.11.1.8
5.13 Phenylalanine metabolism PATH:hsa00360			
501	ATQ1		1.2.1.-
5.14 Tryptophan metabolism PATH:hsa00380			
6999	TDO2, TPH2, TRPO, TDO	TRP + O2 -> FKYN	1.13.11.11
8564	KMO	KYN + NADPH + O2 -> HKYN + NADP + H2O	1.14.13.9
8942	KYNU	KYN -> ALA + AN	3.7.1.3
		HKYN + H2O -> HAN + ALA	
23498	HAAO, HAO, 3-HAO	HAN + O2 -> CMUSA	1.13.11.6
7166	TPH, TPRH		1.14.16.4
438	ASMT, HIOMT, ASMTY		2.1.1.4
15	AANAT, SNAT		2.3.1.87
3620	INDO, IDO		1.13.11.42
10352	WARS2	ATPm + TRPm + TRNAm -> AMPm + PPIm + TRPTRNAm	6.1.1.2
7453	WARS, IFP53, IFI53, GAMMA-2	ATP + TRP + TRNA -> AMP + PPI + TRPTRNA	6.1.1.2
4734	NEDD4, KIAA0093		6.3.2.-
5.15 Phenylalanine, tyrosine and tryptophan biosynthesis PATH:hsa00400			
5053	PAH, PKU1	PHE + THBP + O2 -> TYR + DHBP + H2O	1.14.16.1
10667	FARS1		6.1.1.20
2193	FARSL, CML33		6.1.1.20
10056	PheHB		6.1.1.20
8565	YARS, TYRRS, YTS, YRS		6.1.1.1
5.16 Urea cycle and metabolism of amino groups PATH:hsa00220			
5832	PYCS		2.7.2.11
		GLUP + NADH -> NAD + PI + GLUGSAL	1.2.1.41
		GLUP + NADPH -> NADP + PI + GLUGSAL	
95	ACY1		3.5.1.14
6. Metabolism of Other Amino Acids			
6.1 beta-Alanine metabolism PATH:hsa00410			
6.2 Taurine and hypotaurine metabolism PATH:hsa00430			
2678	GGT1, GTG, D22S672, D22S732, GGT	RGT + ALA -> CGLY + ALAGLY	2.3.2.2
2679	GGT2, GGT	RGT + ALA -> CGLY + ALAGLY	2.3.2.2
2680	GGT3	RGT + ALA -> CGLY + ALAGLY	2.3.2.2
2687	GGTLA1, GGT-REL, DKFZP566O011	RGT + ALA -> CGLY + ALAGLY	2.3.2.2
6.3 Aminophosphonate metabolism PATH:hsa00440			
5130	PCYT1A, CTPCT, CT, PCYT1	PCHO + CTP -> CDPCHO + PPI	2.7.7.15
9791	PTDSS1, KIAA0024, PSSA	CDPDG + SER <-> CMP + PS	2.7.8.-
6.4 Selenoamino acid metabolism PATH:hsa00450			
22928	SPS2		2.7.9.3
22929	SPS, SELD		2.7.9.3
6.5 Cyanoamino acid metabolism PATH:hsa00460			
6.6 D-Glutamine and D-glutamate metabolism PATH:hsa00471			
6.7 D-Arginine and D-ornithine metabolism PATH:hsa00472			
6.9 Glutathione metabolism PATH:hsa00480			
5182	PEPB		3.4.11.4
2655	GCTG		2.3.2.4
2876	GPX1, GSHPX1	2 RGT + H2O2 <-> OGT	1.11.1.9
2877	GPX2, GSHPX-GI	2 RGT + H2O2 <-> OGT	1.11.1.9

2878	GPX3	2 RGT + H2O2 <-> OGT	1.11.1.9
2879	GPX4	2 RGT + H2O2 <-> OGT	1.11.1.9
2880	GPX5	2 RGT + H2O2 <-> OGT	1.11.1.9
2881	GPX6	2 RGT + H2O2 <-> OGT	1.11.1.9
2938	GSTA1		2.5.1.18
2939	GSTA2, GST2		2.5.1.18
2940	GSTA3		2.5.1.18
2941	GSTA4		2.5.1.18
2944	GSTM1, GST1, MU		2.5.1.18
2946	GSTM2, GST4		2.5.1.18
2947	GSTM3, GST5		2.5.1.18
2948	GSTM4		2.5.1.18
2949	GSTM5		2.5.1.18
2950	GSTP1, FAEES3, DFN7, GST3, PI		2.5.1.18
2952	GSTT1		2.5.1.18
2953	GSTT2		2.5.1.18
4257	MGST1, GST12, MGST, MGST-I		2.5.1.18
4258	MGST2, GST2, MGST-II		2.5.1.18
4259	MGST3, GST-III		2.5.1.18
7. Metabolism of Complex Carbohydrates			
7.1 Starch and sucrose metabolism PATH:hsa00500			
6476	SI		3.2.1.10
			3.2.1.48
11181	TREH, TRE, TREA	TRE -> 2 GLC	3.2.1.28
2990	GUSB		3.2.1.31
2632	GBE1	GLYCOGEN + PI -> G1P	2.4.1.18
5834	PYGB	GLYCOGEN + PI -> G1P	2.4.1.1
5836	PYGL	GLYCOGEN + PI -> G1P	2.4.1.1
5837	PYGM	GLYCOGEN + PI -> G1P	2.4.1.1
2997	GYS1, GYS	UDPG -> UDP + GLYCOGEN	2.4.1.11
2998	GYS2	UDPG -> UDP + GLYCOGEN	2.4.1.11
276	AMY1A, AMY1		3.2.1.1
277	AMY1B, AMY1		3.2.1.1
278	AMY1C, AMY1		3.2.1.1
279	AMY2A, AMY2		3.2.1.1
280	AMY2B, AMY2		3.2.1.1
178	AGL, GDE		2.4.1.25
			3.2.1.33
10000	AKT3, PKBG, RAC-GAMMA, PRKBG		2.7.1.-
1017	CDK2		2.7.1.-
1018	CDK3		2.7.1.-
1019	CDK4, PSK-J3		2.7.1.-
1020	CDK5, PSSALRE		2.7.1.-
1021	CDK6, PLSTIRE		2.7.1.-
1022	CDK7, CAK1, STK1, CDKN7		2.7.1.-
1024	CDK8, K35		2.7.1.-
1025	CDK9, PITALRE, CDC2L4		2.7.1.-
10298	PAK4		2.7.1.-
10746	MAP3K2, MEKK2		2.7.1.-
1111	CHEK1, CHK1		2.7.1.-
11200	RAD53, CHK2, CDS1, HUCDS1		2.7.1.-
1195	CLK1, CLK		2.7.1.-
1326	MAP3K8, COT, EST, ESTF, TPL-2		2.7.1.-
1432	MAPK14, CSBP2, CSPB1, PRKM14, PRKM15, CSBP1, P38, MXI2		2.7.1.-
1452	CSNK1A1		2.7.1.-
1453	CSNK1D, HCKID		2.7.1.-
1454	CSNK1E, HCKIE		2.7.1.-
1455	CSNK1G2		2.7.1.-
1456	CSNK1G3		2.7.1.-

		2.7.1.-
1612	DAPK1, DAPK	2.7.1.-
1760	DMPK, DM, DMK, DM1	2.7.1.-
1859	DYRK1A, DYRK1, DYRK, MNB, MNBH	2.7.1.-
208	AKT2, RAC-BETA, PRKBB, PKBBETA	2.7.1.-
269	AMHR2, AMHR	2.7.1.-
27330	RPS6KA6, RSK4	2.7.1.-
2868	GPRK2L, GPRK4	2.7.1.-
2869	GPRK5, GRK5	2.7.1.-
2870	GPRK6, GRK6	2.7.1.-
29904	HSU93850	2.7.1.-
30811	HUNK	2.7.1.-
3611	ILK, P59	2.7.1.-
3654	IRAK1, IRAK	2.7.1.-
369	ARAF1, PKS2, RAFA1	2.7.1.-
370	ARAF2P, PKS1, ARAF2	2.7.1.-
3984	LIMK1, LIMK	2.7.1.-
3985	LIMK2	2.7.1.-
4117	MAK	2.7.1.-
4140	MARK3, KP78	2.7.1.-
4215	MAP3K3, MAPKKK3, MEKK3	2.7.1.-
4216	MAP3K4, MAPKKK4, MTK1, MEKK4, KIAA0213	2.7.1.-
4217	MAP3K5, ASK1, MAPKKK5, MEKK5	2.7.1.-
4293	MAP3K9, PRKE1, MLK1	2.7.1.-
4294	MAP3K10, MLK2, MST	2.7.1.-
4342	MOS	2.7.1.-
4751	NEK2, NLK1	2.7.1.-
4752	NEK3	2.7.1.-
5058	PAK1, PAKalpha	2.7.1.-
5062	PAK2, PAK65, PAKgamma	2.7.1.-
5063	PAK3, MRX30, PAK3beta	2.7.1.-
5127	PCTK1, PCTGAIRE	2.7.1.-
5128	PCTK2	2.7.1.-
5129	PCTK3, PCTAIRE	2.7.1.-
5292	PIM1, PIM	2.7.1.-
5347	PLK, PLK1	2.7.1.-
5562	PRKAA1	2.7.1.-
5563	PRKAA2, AMPK, PRKAA	2.7.1.-
5578	PRKCA, PKCA	2.7.1.-
5579	PRKCB1, PKCB, PRKCB, PRKCB2	2.7.1.-
5580	PRKCD	2.7.1.-
5581	PRKCE	2.7.1.-
5582	PRKCG, PKCC, PKCG	2.7.1.-
5583	PRKCH, PKC-L, PRKCL	2.7.1.-
5584	PRKCI, DXS1179E, PKCI	2.7.1.-
5585	PRKCL1, PAK1, PRK1, DBK, PKN	2.7.1.-
5586	PRKCL2, PRK2	2.7.1.-
5588	PRKCQ	2.7.1.-
5590	PRKCZ	2.7.1.-
5594	MAPK1, PRKM1, P41MAPK, P42MAPK, ERK2, ERK, MAPK2, PRKM2	2.7.1.-
5595	MAPK3, ERK1, PRKM3, P44ERK1, P44MAPK	2.7.1.-
5597	MAPK6, PRKM6, P97MAPK, ERK3	2.7.1.-
5598	MAPK7, BMK1, ERK5, PRKM7	2.7.1.-
5599	MAPK8, JNK, JNK1, SAPK1, PRKM8, JNK1A2	2.7.1.-

5601	MAPK9, JNK2, PRKM9, P54ASAPK, JUNKINASE	2.7.1.-
5602	MAPK10, JNK3, PRKM10, P493F12, P54BSAPK	2.7.1.-
5603	MAPK13, SAPK4, PRKM13, P38DELTA	2.7.1.-
5604	MAP2K1, MAPKK1, MEK1, MKK1, PRKMK1	2.7.1.-
5605	MAP2K2, MEK2, PRKMK2	2.7.1.-
5606	MAP2K3, MEK3, MKK3, PRKMK3	2.7.1.-
5607	MAP2K5, MEK5, PRKMK5	2.7.1.-
5608	MAP2K6, MEK6, MKK6, SAPKK3, PRKMK6	2.7.1.-
5609	MAP2K7, MAPKK7, MKK7, PRKMK7, JNKK2	2.7.1.-
5610	PRKR, EIF2AK1, PKR	2.7.1.-
5613	PRKX, PKX1	2.7.1.-
5894	RAF1	2.7.1.-
613	BCR, CML, PHL, BCR1, D22S11, D22S662	2.7.1.-
6195	RPS6KA1, HU-1, RSK, RSK1, MAPKAPK1A	2.7.1.-
6196	RPS6KA2, HU-2, MAPKAPK1C, RSK, RSK3	2.7.1.-
6197	RPS6KA3, RSK2, HU-2, HU-3, RSK, MAPKAPK1B, ISPK-1	2.7.1.-
6198	RPS6KB1, STK14A	2.7.1.-
6199	RPS6KB2, P70-BETA, P70S6KB	2.7.1.-
6300	MAPK12, ERK6, PRKM12, SAPK3, P38GAMMA, SAPK-3	2.7.1.-
6416	MAP2K4, JNKK1, MEK4, PRKMK4, SERK1, MKK4	2.7.1.-
6446	SGK	2.7.1.-
658	BMPR1B, ALK-6, ALK6	2.7.1.-
659	BMPR2, BMPR-II, BMPR3, BRK-3	2.7.1.-
673	BRAF	2.7.1.-
6792	STK9	2.7.1.-
6794	STK11, LKB1, PJS	2.7.1.-
6885	MAP3K7, TAK1	2.7.1.-
699	BUB1	2.7.1.-
701	BUB1B, BUBR1, MAD3L	2.7.1.-
7016	TESK1	2.7.1.-
7272	TTK, MPS1L1	2.7.1.-
7867	MAPKAPK3, 3PK, MAPKAP3	2.7.1.-
8408	ULK1	2.7.1.-
8558	CDK10, PISSLRE	2.7.1.-
8621	CDC2L5, CDC2L, CHED	2.7.1.-
8737	RIPK1, RIP	2.7.1.-
8814	CDKL1, KKIALRE	2.7.1.-
8899	PRP4, PR4H	2.7.1.-
9064	MAP3K6, MAPKKK6	2.7.1.-
9149	DYRK1B	2.7.1.-
92	ACVR2, ACTRII	2.7.1.-
9201	DCAMKL1, KIAA0369	2.7.1.-
93	ACVR2B	2.7.1.-
983	CDC2	2.7.1.-
984	CDC2L1	2.7.1.-
5205	FIC1, BRIC, PFIC1, PFIC, ATP8B1	3.6.1.-

DHPP -> DHP + PI
GTP -> GSN + 3 PI
DGTP -> DG + 3 PI

7.2 Glycoprotein biosynthesis PATH:hsa00510			
1798	DPAGT1, DPAGT, UGAT, UAGT, D11S366, DGPT, DPAGT2, GPT		2.7.8.15
29880	ALG5		2.4.1.117
8813	DPM1	GDPMAN + DOLP -> GDP + DOLMANP	2.4.1.83
1650	DDOST, OST, OST48, KIAA0115		2.4.1.119
6184	RPN1		2.4.1.119
6185	RPN2		2.4.1.119
10130	P5		5.3.4.1
10954	PDIR		5.3.4.1
11008	PDI		5.3.4.1
2923	GRP58, ERp57, ERp60, ERp61, GRP57, P58, PI-PLC, ERP57, ERP60, ERP61		5.3.4.1
5034	P4HB, PROHB, PO4DB, ERBA2L		5.3.4.1
7841	GCS1		3.2.1.106
4121	MAN1A1, MAN9, HUMM9		3.2.1.113
4245	MGAT1, GLYT1, GLCNAC-TI, GNT-I, MGAT		2.4.1.101
4122	MAN2A2, MANA2X		3.2.1.114
4124	MAN2A1, MANA2		3.2.1.114
4247	MGAT2, CDGS2, GNT-II, GLCNACTII, GNT2		2.4.1.143
4248	MGAT3, GNT-III		2.4.1.144
6487	SIAT6, ST3GALII		2.4.99.6
6480	SIAT1		2.4.99.1
2339	FNTA, FPTA, PGGT1A		2.5.1.-
2342	FNTB, FPTB		2.5.1.-
5229	PGGT1B, BGGI, GGTI		2.5.1.-
5875	RABGGTA		2.5.1.-
5876	RABGGTB		2.5.1.-
1352	COX10		2.5.1.-
7.3 Glycoprotein degradation PATH:hsa00511			
4758	NEU1, NEU		3.2.1.18
3073	HEXA, TSD		3.2.1.52
3074	HEXB		3.2.1.52
4123	MAN2C1, MANA, MANA1, MAN6A8		3.2.1.24
4125	MAN2B1, MANB, LAMAN		3.2.1.24
4126	MANBA, MANB1		3.2.1.25
2517	FUCA1		3.2.1.51
2519	FUCA2		3.2.1.51
175	AGA, AGU		3.5.1.26
7.4 Aminosugars metabolism PATH:hsa00530			
6675	UAP1, SPAG2, AGX1	UTP + NAGA1P <-> UDPNAG + PPI	2.7.7.23
10020	GNE, GLCNE		5.1.3.14
22951	CMAS		2.7.7.43
1727	DIA1		1.6.2.2
4669	NAGLU, NAG		3.2.1.50
7.5 Lipopolysaccharide biosynthesis PATH:hsa00540			
6485	SIAT5, SAT3, STZ		2.4.99.-
7903	SIAT8D, PST, PST1, ST8SIA-IV		2.4.99.-
8128	SIAT8B, STX, ST8SIA-II		2.4.99.-
7.7 Glycosaminoglycan degradation PATH:hsa00531			
3423	IDS, MPS2, SIDS		3.1.6.13
3425	IDUA, IDA		3.2.1.76
411	ARSB		3.1.6.12
2799	GNS, G6S		3.1.6.14
2588	GALNS, MPS4A, GALNAC6S, GAS		3.1.6.4
8. Metabolism of Complex Lipids			
8.1 Glycerolipid metabolism PATH:hsa00561			

10554 AGPAT1, LPAAT-ALPHA, G15	AGL3P + 0.017 C100ACP + 0.062 C120ACP + 0.100 C140ACP + 0.270 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> PA + ACP	2.3.1.51
10555 AGPAT2, LPAAT-BETA	AGL3P + 0.017 C100ACP + 0.062 C120ACP + 0.100 C140ACP + 0.270 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> PA + ACP	2.3.1.51
1606 DGKA, DAGK, DAGK1		2.7.1.107
1608 DGKG, DAGK3		2.7.1.107
1609 DGKQ, DAGK4		2.7.1.107
8525 DGKZ, DAGK5, HDGKZETA		2.7.1.107
8526 DGKE, DAGK6, DGK		2.7.1.107
8527 DGKD, DGKDELTA, KIAA0145		2.7.1.107
1120 CHKL	ATP + CHO -> ADP + PCHO	2.7.1.32
EKI1	ATP + ETHM -> ADP + PETHM	2.7.1.82
1119 CHK, CKI	ATP + CHO -> ADP + PCHO	2.7.1.32
43 ACHE, YT		3.1.1.7
1103 CHAT		2.3.1.6
5337 PLD1		3.1.4.4
26279 PLA2G2D, SPLA2S		3.1.1.4
30814 PLA2G2E		3.1.1.4
5319 PLA2G1B, PLA2, PLA2A, PPLA2		3.1.1.4
5320 PLA2G2A, MOM1, PLA2B, PLA2L		3.1.1.4
5322 PLA2G5		3.1.1.4
8398 PLA2G6, IPLA2		3.1.1.4
8399 PLA2G10, SPLA2		3.1.1.4
1040 CDS1	PA + CTP <-> CDPDG + PPI	2.7.7.41
10423 PIS	CDPDG + MYOI -> CMP + PINS	2.7.8.11
2710 GK	GL + ATP -> GL3P + ADP	2.7.1.30
2820 GPD2	GL3Pm + FADm -> T3P2m + FADH2m	1.1.99.5
2819 GPD1	T3P2 + NADH <-> GL3P + NAD	1.1.1.8
248 ALPI	AHTD -> DHP + 3 PI	3.1.3.1
249 ALPL, HOPS, TNSALP	AHTD -> DHP + 3 PI	3.1.3.1
250 ALPP	AHTD -> DHP + 3 PI	3.1.3.1
251 ALPPL2	AHTD -> DHP + 3 PI	3.1.3.1
439 ASNA1, ARSA-I		3.6.1.16
8694 DGAT, ARGP1	DAGLY + 0.017 C100ACP + 0.062 C120ACP + 0.100 C140ACP + 0.270 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> TAGLY + ACP	2.3.1.20
3989 LIPB		3.1.1.3
3990 LIPC, HL		3.1.1.3
5406 PNLIP		3.1.1.3
5407 PNLIPRP1, PLRP1		3.1.1.3
5408 PNLIPRP2, PLRP2		3.1.1.3
8513 LIPF, HGL, HLAL		3.1.1.3
4023 LPL, LIPD		3.1.1.34
8443 GNPAT, DHAPAT, DAP-AT		2.3.1.42
8540 AGPS, ADAP-S, ADAS, ADHAPS, ADPS, ALDHPSY		2.5.1.26
4186 MDCR, MDS, LIS1		3.1.1.47
5048 PAFAH1B1, LIS1, MDCR, PAFAH		3.1.1.47
5049 PAFAH1B2		3.1.1.47
5050 PAFAH1B3		3.1.1.47
5051 PAFAH2, HSD-PLA2		3.1.1.47
7941 PLA2G7, PAFAH, LDL-PLA2		3.1.1.47
8.2 Inositol phosphate metabolism PATH:hsa00562		
5290 PIK3CA	ATP + PINS -> ADP + PINSP	2.7.1.137
5291 PIK3CB, PIK3C1	ATP + PINS -> ADP + PINSP	2.7.1.137
5293 PIK3CD	ATP + PINS -> ADP + PINSP	2.7.1.137
5294 PIK3CG	ATP + PINS -> ADP + PINSP	2.7.1.137
5297 PIK4CA, PI4K-ALPHA	ATP + PINS -> ADP + PINS4P	2.7.1.67

5305	PIP5K2A	PINS4P + ATP -> D45PI + ADP	2.7.1.68
5330	PLCB2	D45PI -> TPI + DAGLY	3.1.4.11
5331	PLCB3	D45PI -> TPI + DAGLY	3.1.4.11
5333	PLCD1	D45PI -> TPI + DAGLY	3.1.4.11
5335	PLCG1, PLC1	D45PI -> TPI + DAGLY	3.1.4.11
5336	PLCG2	D45PI -> TPI + DAGLY	3.1.4.11
3612	IMPA1, IMPA	MI1P -> MYOI + PI	3.1.3.25
3613	IMPA2	MI1P -> MYOI + PI	3.1.3.25
3628	INPP1		3.1.3.57
3632	INPP5A		
3633	INPP5B		3.1.3.56
3636	INPPL1, SHIP2		3.1.3.56
4952	OCRL, LOCR, OCRL1, INPP5F		3.1.3.56
8867	SYNJ1, INPP5G		3.1.3.56
3706	ITPKA		2.7.1.127
51477	ISYNA1	G6P -> MI1P	5.5.1.4
3631	INPP4A, INPP4		3.1.3.66
8821	INPP4B		3.1.3.66
8.3	Sphingophospholipid biosynthesis PATH:hsa00570		
6609	SMPD1, NPD		3.1.4.12
8.4	Phospholipid degradation PATH:hsa00580		
1178	CLC		3.1.1.5
5321	PLA2G4A, CPLA2-ALPHA, PLA2G4		3.1.1.5
8.5	Sphingoglycolipid metabolism PATH:hsa00600		
10558	SPTLC1, LCB1, SPTI	PALCOA + SER -> COA + DHSPH + CO2	2.3.1.50
9517	SPTLC2, KIAA0526, LCB2	PALCOA + SER -> COA + DHSPH + CO2	2.3.1.50
427	ASAH, AC, PHP32		3.5.1.23
7357	UGCG, GCS		2.4.1.80
2629	GBA, GLUC		3.2.1.45
2583	GALGT, GALNACT		2.4.1.92
6489	SIAT8A, SIAT8, ST8SIA-I		2.4.99.8
6481	SIAT2		2.4.99.2
4668	NAGA, D22S674, GALB		3.2.1.49
9514	CST		2.8.2.11
410	ARSA, MLD		3.1.6.8
8.6	Blood group glycolipid biosynthesis - lact series PATH:hsa00601		
28	ABO		2.4.1.40
			2.4.1.37
2525	FUT3, LE		2.4.1.65
2527	FUT5, FUC-TV		2.4.1.65
2528	FUT6		2.4.1.65
2523	FUT1, H, HH		2.4.1.69
2524	FUT2, SE		2.4.1.69
8.7	Blood group glycolipid biosynthesis - neolact series PATH:hsa00602		
2651	GCNT2, IGNT, NACGT1, NAGCT1		2.4.1.150
8.8	Prostaglandin and leukotriene metabolism PATH:hsa00590		
239	ALOX12, LOG12		1.13.11.31
246	ALOX15		1.13.11.33
240	ALOX5		1.13.11.34
4056	LTC4S		2.5.1.37
4048	LTA4H		3.3.2.6
4051	CYP4F3, CYP4F, LTB4H		1.14.13.30
8529	CYP4F2		1.14.13.30
5742	PTGS1, PGHS-1		1.14.99.1
5743	PTGS2, COX-2, COX2		1.14.99.1
27306	PGDS		5.3.99.2
5730	PTGDS		5.3.99.2
5740	PTGIS, CYP8, PGIS		5.3.99.4
6916	TBXAS1, CYP5		5.3.99.5
873	CBR1, CBR		1.1.1.184

		1.1.1.189
		1.1.1.197
874 CBR3		1.1.1.184
9. Metabolism of Cofactors and Vitamins		
9.2 Riboflavin metabolism PATH:hsa00740		
52 ACP1		3.1.3.48
	FMN -> RIBOFLAV + PI	3.1.3.2
53 ACP2	FMN -> RIBOFLAV + PI	3.1.3.2
54 ACP5, TRAP	FMN -> RIBOFLAV + PI	3.1.3.2
55 ACPP, PAP	FMN -> RIBOFLAV + PI	3.1.3.2
9.3 Vitamin B6 metabolism PATH:hsa00750		
8566 PDXK, PKH, PNK	PYRDX + ATP -> P5P + ADP	2.7.1.35
	PDLA + ATP -> PDLA5P + ADP	
	PL + ATP -> PL5P + ADP	
9.4 Nicotinate and nicotinamide metabolism PATH:hsa00760		
23475 QPRT	QA + PRPP -> NAMN + CO2 + PPI	2.4.2.19
4837 NNMT		2.1.1.1
683 BST1, CD157	NAD -> NAM + ADPRIB	3.2.2.5
952 CD38	NAD -> NAM + ADPRIB	3.2.2.5
23530 NNT		1.6.1.2
9.5 Pantothenate and CoA biosynthesis PATH:hsa00770		
9.6 Biotin metabolism PATH:hsa00780		
3141 HLCS, HCS		6.3.4.-
		6.3.4.9
		6.3.4.10
		6.3.4.11
		6.3.4.15
686 BTD		3.5.1.12
9.7 Folate biosynthesis PATH:hsa00790		
2643 GCH1, DYT5, GCH, GTPCH1	GTP -> FOR + AHTD	3.5.4.16
1719 DHFR	DHF + NADPH -> NADP + THF	1.5.1.3
2356 FPGS	THF + ATP + GLU <-> ADP + PI + THFG	6.3.2.17
8836 GGH, GH		3.4.19.9
5805 PTS		4.6.1.10
6697 SPR		1.1.1.153
5860 QDPR, DHPR, PKU2	NADPH + DHBP -> NADP + THBP	1.6.99.7
9.8 One carbon pool by folate PATH:hsa00670		
10840 FTHFD		1.5.1.6
10588 MTHFS	ATP + FTHF -> ADP + PI + MTHF	6.3.3.2
9.10 Porphyrin and chlorophyll metabolism PATH:hsa00860		
210 ALAD	2 ALAV -> PBG	4.2.1.24
3145 HMBS, PBGD, UPS	4 PBG -> HMB + 4 NH3	4.3.1.8
7390 UROS	HMB -> UPRG	4.2.1.75
7389 UROD	UPRG -> 4 CO2 + CPP	4.1.1.37
1371 CPO, CPX	O2 + CPP -> 2 CO2 + PPHG	1.3.3.3
5498 PPOX, PPO	O2 + PPHGm -> PPIXm	1.3.3.4
2235 FECH, FCE	PPIXm -> PTHm	4.99.1.1
3162 HMOX1, HO-1		1.14.99.3
3163 HMOX2, HO-2		1.14.99.3
644 BLVRA, BLVR		1.3.1.24
645 BLVRB, FLR		1.3.1.24
		1.6.99.1
2232 FDXR, ADXR		1.18.1.2
3052 HCCS, CCHL		4.4.1.17
1356 CP		1.16.3.1
9.11 Ubiquinone biosynthesis PATH:hsa00130		
4938 OAS1, IFI-4, OIAS		2.7.7.-
4939 OAS2, P69		2.7.7.-
5557 PRIM1		2.7.7.-
5558 PRIM2A, PRIM2		2.7.7.-
5559 PRIM2B, PRIM2		2.7.7.-

7015 TERT, EST2, TCS1, TP2, TRT	2.7.7.-
8638 OASL, TRIP14	2.7.7.-
10. Metabolism of Other Substances	
10.1 Terpenoid biosynthesis PATH:hsa00900	
10.2 Flavonoids; stilbene and lignin biosynthesis PATH:hsa00940	
10.3 Alkaloid biosynthesis I PATH:hsa00950	
10.4 Alkaloid biosynthesis II PATH:hsa00960	
10.6 Streptomycin biosynthesis PATH:hsa00521	
10.7 Erythromycin biosynthesis PATH:hsa00522	
10.8 Tetracycline biosynthesis PATH:hsa00253	
10.14 gamma-Hexachlorocyclohexane degradation PATH:hsa00361	
5444 PON1, ESA, PON	3.1.8.1 3.1.1.2
5445 PON2	3.1.1.2 3.1.8.1
10.18 1,2-Dichloroethane degradation PATH:hsa00631	
10.20 Tetrachloroethene degradation PATH:hsa00625	
2052 EPHX1, EPHX, MEH	3.3.2.3
2053 EPHX2	3.3.2.3
10.21 Styrene degradation PATH:hsa00643	
11. Transcription (condensed)	
11.1 RNA polymerase PATH:hsa03020	
11.2 Transcription factors PATH:hsa03022	
12. Translation (condensed)	
12.1 Ribosome PATH:hsa03010	
12.2 Translation factors PATH:hsa03012	
1915 EEF1A1, EF1A, ALPHA, EEF-1, EEF1A	3.6.1.48
1917 EEF1A2, EF1A	3.6.1.48
1938 EEF2, EF2, EEF-2	3.6.1.48
12.3 Aminoacyl-tRNA biosynthesis PATH:hsa00970	
13. Sorting and Degradation (condensed)	
13.1 Protein export PATH:hsa03060	
23478 SPC18	3.4.21.89
13.4 Proteasome PATH:hsa03050	
5687 PSMA6, IOTA, PROS27	3.4.99.46
5683 PSMA2, HC3, MU, PMSA2, PSC2	3.4.99.46
5685 PSMA4, HC9	3.4.99.46
5688 PSMA7, XAPC7	3.4.99.46
5686 PSMA5, ZETA, PSC5	3.4.99.46
5682 PSMA1, HC2, NU, PROS30	3.4.99.46
5684 PSMA3, HC8	3.4.99.46
5698 PSMB9, LMP2, RING12	3.4.99.46
5695 PSMB7, Z	3.4.99.46
5691 PSMB3, HC10-II	3.4.99.46
5690 PSMB2, HC7-I	3.4.99.46
5693 PSMB5, LMPX, MB1	3.4.99.46
5689 PSMB1, HC5, PMSB1	3.4.99.46
5692 PSMB4, HN3, PROS26	3.4.99.46
14. Replication and Repair	
14.1 DNA polymerase PATH:hsa03030	
14.2 Replication Complex PATH:hsa03032	
23626 SPO11	5.99.1.3
7153 TOP2A, TOP2	5.99.1.3
7155 TOP2B	5.99.1.3
7156 TOP3A, TOP3	5.99.1.2
8940 TOP3B	5.99.1.2
22. Enzyme Complex	
22.1 Electron Transport System, Complex I PATH:hsa03100	
22.2 Electron Transport System, Complex II PATH:hsa03150	
22.3 Electron Transport System, Complex III PATH:hsa03140	

22.4 Electron Transport System, Complex IV PATH:hsa03130		
22.5 ATP Synthase PATH:hsa03110		
22.8 ATPases PATH:hsa03230		
23. Unassigned		
23.1 Enzymes		
5538 PPT1, CLN1, PPT, INCL	C160ACP + H2O -> C160 + ACP	3.1.2.22
23.2 Non-enzymes		
22934 RPIA, RPI	RL5P <-> R5P	5.3.1.6
5250 SLC25A3, PHC	PI + H <-> Hm + PIm	
6576	CIT + MALm <-> CITm + MAL	
51166 LOC51166	AADP + AKG -> GLU + KADP	2.6.1.39
5625 PRODH	PRO + FAD -> P5C + FADH2	1.5.3.-
6517 SLC2A4, GLUT4	GLCxt -> GLC	
6513 SLC2A1, GLUT1, GLUT	GLCxt -> GLC	
26275 HIBCH, HIBYL-COA-H	HIBCOAm + H2Om -> HIBm + COAm	3.1.2.4
23305 KIAA0837, ACS2, LACS5, LACS2	C160 + COA + ATP -> AMP + PPI + C160COA	
8611 PPAP2A, PAP-2A	PA + H2O -> DAGLY + PI	
8612 PPAP2C, PAP-2C	PA + H2O -> DAGLY + PI	
8613 PPAP2B, PAP-2B	PA + H2O -> DAGLY + PI	
56994 LOC56994	CDPCHO + DAGLY -> PC + CMP	
10400 PEMT, PEMT2	SAM + PE -> SAH + PMME	
5833 PCYT2, ET	PETHM + CTP -> CDPETN + PPI	
10390 CEPT1	CDPETN + DAGLY <-> CMP + PE	
8394 PIP5K1A	PINS4P + ATP -> D45PI + ADP	
8395 PIP5K1B, STM7, MSS4	PINS4P + ATP -> D45PI + ADP	
8396 PIP5K2B	PINS4P + ATP -> D45PI + ADP	
23396 PIP5K1C, KIAA0589, PIP5K-GAMMA	PINS4P + ATP -> D45PI + ADP	
24. Our own reactions which need to be found in KEGG		
	GL3P <-> GL3Pm	
	T3P2 <-> T3P2m	
	PYR <-> PYRm + Hm	
	ADP + ATPm + PI + H -> Hm + ADPm + ATP + PIm	
	AKG + MALm <-> AKGm + MAL	
	ASPm + GLU + H -> Hm + GLUm + ASP	
	GDP + GTPm + PI + H -> Hm + GDPm + GTP + PIm	
	C160Axt + FABP -> C160FP + ALBxt	
	C160FP -> C160 + FABP	
	C180Axt + FABP -> C180FP + ALBxt	
	C180FP -> C180 + FABP	
	C161Axt + FABP -> C161FP + ALBxt	
	C161FP -> C161 + FABP	
	C181Axt + FABP -> C181FP + ALBxt	
	C181FP -> C181 + FABP	
	C182Axt + FABP -> C182FP + ALBxt	
	C182FP -> C182 + FABP	
	C204Axt + FABP -> C204FP + ALBxt	
	C204FP -> C204 + FABP	
	O2xt -> O2	
	O2 <-> O2m	
	ACTACm + SUCCOAm -> SUCCm + AACCOAm	
	3HB -> 3HBm	
	MGCOAm + H2Om -> H3MCOAm	4.2.1.18
	OMVAL -> OMVALm	
	OIVAL -> OIVALm	
	OICAP -> OICAPm	
	C160CAR <-> C160CARm	
	CAR <-> CARm	
	DMMCOAm -> LMMCOAm	5.1.99.1
amino acid metabolism		
	THR -> NH3 + H2O + OBUT	4.2.1.16

	THR + NAD -> CO2 + NADH + AMA	1.1.1.103
	THR + NAD + COA -> NADH + ACCOA + GLY	
	AASA + NAD -> NADH + AADP	1.2.1.31
	FKYN + H2O -> FOR + KYN	3.5.1.9
	CMUSA -> CO2 + AM6SA	4.1.1.45
	AM6SA + NAD -> AMUCO + NADH	1.2.1.32
	AMUCO + NADPH -> KADP + NADP + NH4	1.5.1.-
	CYSS + AKG <-> GLU + SPYR	
	URO + H2O -> 4I5P	4.2.1.49
	4I5P + H2O -> FIGLU	3.5.2.7
	GLU <-> GLUm + Hm	
	ORN + Hm -> ORNm	
	ORN + Hm + CITRm <-> CITR + ORNm	
	GLU + ATP + NADPH -> NADP + ADP + PI + GLUGSAL	
	GLYAm + ATPm -> ADPm + 2PGm	
	AM6SA -> PIC	
	SPYR + H2O -> H2SO3 + PYR	
	P5C <-> GLUGSAL	
fatty acid synthesis	MALCOA + ACP <-> MALACP + COA	2.3.1.39
	ACCOA + ACP <-> ACACP + COA	
	ACACP + 4 MALACP + 8 NADPH -> 8 NADP + C100ACP + 4 CO2 + 4 ACP	
	ACACP + 5 MALACP + 10 NADPH -> 10 NADP + C120ACP + 5 CO2 + 5 ACP	
	ACACP + 6 MALACP + 12 NADPH -> 12 NADP + C140ACP + 6 CO2 + 6 ACP	
	ACACP + 6 MALACP + 11 NADPH -> 11 NADP + C141ACP + 6 CO2 + 6 ACP	
	ACACP + 7 MALACP + 14 NADPH -> 14 NADP + C160ACP + 7 CO2 + 7 ACP	
	ACACP + 7 MALACP + 13 NADPH -> 13 NADP + C161ACP + 7 CO2 + 7 ACP	
	ACACP + 8 MALACP + 16 NADPH -> 16 NADP + C180ACP + 8 CO2 + 8 ACP	
	ACACP + 8 MALACP + 15 NADPH -> 15 NADP + C181ACP + 8 CO2 + 8 ACP	
	ACACP + 8 MALACP + 14 NADPH -> 14 NADP + C182ACP + 8 CO2 + 8 ACP	
	C160COA + CAR -> C160CAR + COA	
	C160CARm + COAm -> C160COAm + CARm	
fatty acid degredation	GL3P + 0.017 C100ACP + 0.062 C120ACP + 0.1 C140ACP + 0.27 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> AGL3P + ACP	
	TAGLYm + 3 H2Om -> GLm + 3 C160m	
Phospholipid metabolism	SAM + PMME -> SAH + PDME	
	PDME + SAM -> PC + SAH	
	PE + SER <-> PS + ETHM	
Muscle contraction	MYOACT + ATP -> MYOATP + ACTIN	
	MYOATP + ACTIN -> MYOADPAC	
	MYOADPAC -> ADP + PI + MYOACT + CONTRACT	

Table 2

```
// Homo Sapiens Core Metabolic Network //

// Glycolysis //
-1 GLC -1 ATP +1 G6P +1 ADP  0 HK1
-1 G6P -1 H2O +1 GLC +1 PI  0 G6PC
-1 G6P +1 F6P  0 GPIR
-1 F6P -1 ATP +1 FDP +1 ADP  0 PFKL
-1 FDP -1 H2O +1 F6P +1 PI  0 FBP1
-1 FDP +1 T3P2 +1 T3P1  0 ALDOAR
-1 T3P2 +1 T3P1  0 TPI1R
-1 T3P1 -1 PI -1 NAD +1 NADH +1 13PDG  0 GAPDR
-1 13PDG -1 ADP +1 3PG +1 ATP  0 PGK1R
-1 13PDG +1 23PDG  0 PGAM1
-1 23PDG -1 H2O +1 3PG +1 PI  0 PGAM2
-1 3PG +1 2PG  0 PGAM3R
-1 2PG +1 PEP +1 H2O  0 ENO1R
-1 PEP -1 ADP +1 PYR +1 ATP  0 PKLR
-1 PYRm -1 COAm -1 NADm +1 NADHm +1 CO2m +1 ACCOAm  0 PDHA1
-1 NAD -1 LAC +1 PYR +1 NADH  0 LDHAR
-1 G1P +1 G6P  0 PGM1R

// TCA //
-1 ACCOAm -1 OAm -1 H2Om +1 COAm +1 CITm  0 CS
-1 CIT +1 ICIT  0 ACO1R
-1 CITm +1 ICITm  0 ACO2R
-1 ICIT -1 NADP +1 NADPH +1 CO2 +1 AKG  0 IDH1
-1 ICITm -1 NADPm +1 NADPHm +1 CO2m +1 AKGm  0 IDH2
-1 ICITm -1 NADm +1 CO2m +1 NADHm +1 AKGm  0 IDH3A
-1 AKGm -1 NADm -1 COAm +1 CO2m +1 NADHm +1 SUCCOAm  0 OGDH
-1 GTPm -1 SUCCm -1 COAm +1 GDPm +1 PIm +1 SUCCOAm  0 SUCLG1R
-1 ATPm -1 SUCCm -1 COAm +1 ADPm +1 PIm +1 SUCCOAm  0 SUCLA2R
-1 FUMm -1 H2Om +1 MALm  0 FHR
-1 MAL -1 NAD +1 NADH +1 OA  0 MDH1R
-1 MALm -1 NADm +1 NADHm +1 OAm  0 MDH2R
-1 PYRm -1 ATPm -1 CO2m +1 ADPm +1 OAm +1 PIm  0 PC
-1 OA -1 GTP +1 PEP +1 GDP +1 CO2  0 PCK1
-1 OAm -1 GTPm +1 PEPm +1 GDPm +1 CO2m  0 PCK2
-1 ATP -1 CIT -1 COA -1 H2O +1 ADP +1 PI +1 ACCOA +1 OA  0 ACLY
```

```
// PPP //
-1 G6P -1 NADP +1 D6PGL +1 NADPH  0 G6PDR
-1 D6PGL -1 H2O +1 D6PGC  0 PGLS
-1 D6PGC -1 NADP +1 NADPH +1 CO2 +1 RL5P  0 PGD
-1 RL5P +1 X5P  0 RPER
-1 R5P -1 X5P +1 T3P1 +1 S7P  0 TKT1R
-1 X5P -1 E4P +1 F6P +1 T3P1  0 TKT2R
-1 T3P1 -1 S7P +1 E4P +1 F6P  0 TALDO1R
-1 RL5P +1 R5P  0 RPIAR

// Glycogen //
-1 G1P -1 UTP +1 UDPG +1 PPI  0 UGP1
-1 UDPG +1 UDP +1 GLYCOGEN  0 GYS1
-1 GLYCOGEN -1 PI +1 G1P  0 GBE1

// ETS //
-1 MALm -1 NADPm +1 CO2m +1 NADPHm +1 PYRm  0 ME3
-1 MALm -1 NADm +1 CO2m +1 NADHm +1 PYRm  0 ME2
-1 MAL -1 NADP +1 CO2 +1 NADPH +1 PYR  0 ME1
-1 NADHm -1 Qm -4 Hm +1 QH2m +1 NADm +4 H 0 MTND1
-1 SUCCm -1 FADm +1 FUMm +1 FADH2m  0 SDHC1R
-1 FADH2m -1 Qm +1 FADm +1 QH2m 0 SDHC2R
-1 O2m -4 FEROm -4 Hm +4 FERIm +2 H2Om +4 H 0 UQCRFS1
-1 QH2m -2 FERIm -4 Hm +1 Qm +2 FEROm +4 H 0 COX5BL4
-1 ADPm -1 PIm -3 H +1 ATPm +3 Hm +1 H2Om 0 MTAT
-1 ADP -1 ATPm -1 PI -1 H +1 Hm +1 ADPm +1 ATP +1 PIm  0 ATPMC
-1 GDP -1 GTPm -1 PI -1 H +1 Hm +1 GDPm +1 GTP +1 PIm  0 GTPMC
-1 PPI +2 PI  0 PP

-1 ACCOA -1 ATP -1 CO2 +1 MALCOA +1 ADP +1 PI  0 ACACAR
-1 GDP -1 ATP +1 GTP +1 ADP  0 GOT3R


// Transporters //
-1 CIT -1 MALm +1 CITm +1 MAL  0 CITMCR
-1 PYR -1 H +1 PYRm +1 Hm  0 PYRMCR

// Glycerol Phosphate Shuttle //
-1 GL3Pm -1 FADm +1 T3P2m +1 FADH2m  0 GPD2
-1 T3P2 -1 NADH +1 GL3P +1 NAD  0 GPD1
-1 GL3P +1 GL3Pm  0 GL3PMCR
-1 T3P2 +1 T3P2m  0 T3P2MCR

// Malate/Aspartate Shuttle //
-1 OAm -1 GLUm +1 ASPm +1 AKGm  0 GOT1R
-1 ASP -1 AKG +1 OA +1 GLU  0 GOT2R
-1 AKG -1 MALm +1 AKGm +1 MAL  0 MALMCR
-1 ASPm -1 GLU -1 H +1 Hm +1 GLUm +1 ASP  0 ASPMC
```

```
// Exchange Fluxes //
+1 GLC 0 GLCexR
+1 PYR 0 PYRexR
+1 CO2 0 CO2exR
+1 O2  0 O2exR
+1 PI  0 PIexR
+1 H2O 0 H2OexR
+1 LAC 0 LACexR

+1 CO2m 0 CO2min
-1 CO2m 0 CO2mout
+1 O2m 0 O2min
-1 O2m  0 O2mout
+1 H2Om 0 H2Omin
-1 H2Om 0 H2Omout
+1 PIm  0 PImin
-1 PIm  0 PImout


// Output //
-1 ATP +1 ADP +1 PI 0 Output

0.0 end

end E 0

max
1 Output
0 end

0 GLCexR 1
-1000 PYRexR 0
-1000 LACexR 0

0 end 0
rev. rxn 33
nonrev. rxn 31
total rxn 64
matrix columns 97
unique enzymes 52
```

TABLE 3

Abbrev.	Reaction	Rxn Name
Glycolysis		
HK1	GLC + ATP -> G6P + ADP	HK1
G6PC, G6PT	G6P + H2O -> GLC + PI	G6PC
GPI	G6P <-> F6P	GPI
PFKL	F6P + ATP -> FDP + ADP	PFKL
FBP1, FBP	FDP + H2O -> F6P + PI	FBP1
ALDOA	FDP <-> T3P2 + T3P1	ALDOA
TPI1	T3P2 <-> T3P1	TPI1
GAPD, GAPDH	T3P1 + PI + NAD <-> NADH + 13PDG	GAPD
PGK1, PGKA	13PDG + ADP <-> 3PG + ATP	PGK1
PGAM1, PGAMA	13PDG <-> 23PDG	PGAM1
	23PDG + H2O -> 3PG + PI	PGAM2
	3PG <-> 2PG	PGAM3
ENO1, PPH, ENO1L1	2PG <-> PEP + H2O	ENO1
PKLR, PK1	PEP + ADP -> PYR + ATP	PKLR
PDHA1, PHE1A, PDHA	PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	PDHA1
LDHA, LDH1	NAD + LAC <-> PYR + NADH	LDHA
PGM1	G1P <-> G6P	PGM1
TCA		
CS	ACCOAm + OAm + H2Om -> COAm + CITm	CS
ACO1, IREB1, IRP1	CIT <-> ICIT	ACO1
ACO2	CITm <-> ICITm	ACO2
IDH1	ICIT + NADP -> NADPH + CO2 + AKG	IDH1
IDH2	ICITm + NADPm -> NADPHm + CO2m + AKGm	IDH2
IDH3A	ICITm + NADm -> CO2m + NADHm + AKGm	IDH3A
OGDH	AKGm + NADm + COAm -> CO2m + NADHm + SUCCOAm	OGDH
SUCLG1, SUCLA1	GTPm + SUCCm + COAm <-> GDPm + PIm + SUCCOAm	SUCLG1
SUCLA2	ATPm + SUCCm + COAm <-> ADPm + PIm + SUCCOAm	SUCLA2
FH	FUMm + H2Om <-> MALm	FH
MDH1	MAL + NAD <-> NADH + OA	MDH1
MDH2	MALm + NADm <-> NADHm + OAm	MDH2
PC, PCB	PYRm + ATPm + CO2m -> ADPm + OAm + PIm	PC
ACLY, ATPCL, CLATP	ATP + CIT + COA + H2O -> ADP + PI + ACCOA + OA	ACLY
PCK1	OA + GTP -> PEP + GDP + CO2	PCK1
PPP		
G6PD, G6PD1	G6P + NADP <-> D6PGL + NADPH	G6PD
PGLS, 6PGL	D6PGL + H2O -> D6PGC	PGLS
PGD	D6PGC + NADP -> NADPH + CO2 + RL5P	PGD
RPE	RL5P <-> X5P	RPE
TKT	R5P + X5P <-> T3P1 + S7P	TKT1
	X5P + E4P <-> F6P + T3P1	TKT2
TALDO1	T3P1 + S7P <-> E4P + F6P	TALDO1
UGP1	G1P + UTP -> UDPG + PPI	UGP1
ACACA, ACAC, ACC	ACCOA + ATP + CO2 <-> MALCOA + ADP + PI + H	ACACA
ETS		
ME3	MALm + NADPm -> CO2m + NADPHm + PYRm	ME3
MTND1	NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	MTND1
SDHC	SUCCm + FADm <-> FUMm + FADH2m	SDHC1
	FADH2m + Qm <-> FADm + QH2m	SDHC2
UQCRFS1, RIS1	O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	UQCRFS1
COX5BL4	QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	COX5BL4
MTATP6	ADPm + PIm + 3 H -> ATPm + 3 Hm + H2Om	MTAT
PP, SID6-8061	PPI -> 2 PI	PP
Malate Aspartate shunttle		
GOT1	OAm + GLUm <-> ASPm + AKGm	GOT1
GOT2	OA + GLU <-> ASP + AKG	GOT2
	GDP + ATP <-> GTP + ADP	GOT3

Glycogen		
GBE1	GLYCOGEN + PI -> G1P	GBE1
GYS1, GYS	UDPG -> UDP + GLYCOGEN	GYS1
Glycerol Phosphate Shunttle		
GPD2	GL3Pm + FADm -> T3P2m + FADH2m	GPD2
GPD1	T3P2 + NADH -> GL3P + NAD	GPD1
RPIA, RPI	RL5P <-> R5P	RPIA
Mitochondria Transport		
	CIT + MALm <-> CITm + MAL	CITMC
	GL3P <-> GL3Pm	GL3PMC
	T3P2 <-> T3P2m	T3P2MC
	PYR <-> PYRm + Hm	PYRMC
	ADP + ATPm + PI + H -> Hm + ADPm + ATP + PIm	ATPMC
	AKG + MALm <-> AKGm + MAL	MALMC
	ASPm + GLU + H -> Hm + GLUm + ASP	ASPMC
	GDP + GTPm + PI + H -> Hm + GDPm + GTP + PIm	GTPMC

TABLE 4

Metabolic Reaction for Muscle Cells

Reaction	*Rxt Name*
GLC + ATP -> G6P + ADP	0 HK1
G6P <-> F6P	0 GPI
F6P + ATP -> FDP + ADP	0 PFKL1
FDP + H2O -> F6P + PI	0 FBP1
FDP <-> T3P2 + T3P1	0 ALDOA
T3P2 <-> T3P1	0 TPI1
T3P1 + PI + NAD <-> NADH + 13PDG	0 GAPD
13PDG + ADP <-> 3PG + ATP	0 PGK1
3PG <-> 2PG	0 PGAM3
2PG <-> PEP + H2O	0 ENO1
PEP + ADP -> PYR + ATP	0 PK1
PYRm + COAm + NADm -> + NADHm + CO2m + ACCOAm	0 PDHA1
NAD + LAC <-> PYR + NADH	0 LDHA
G1P <-> G6P	0 PGM1
ACCOAm + OAm + H2Om -> COAm + CITm	0 CS
CIT <-> ICIT	0 ACO1
CITm <-> ICITm	0 ACO2
ICIT + NADP -> NADPH + CO2 + AKG	0 IDH1
ICITm + NADPm -> NADPHm + CO2m + AKGm	0 IDH2
ICITm + NADm -> CO2m + NADHm + AKGm	0 IDH3A
AKGm + NADm + COAm -> CO2m + NADHm + SUCCOAm	0 OGDH
GTPm + SUCCm + COAm <-> GDPm + Plm + SUCCOAm	0 SUCLG1
ATPm + SUCCm + COAm <-> ADPm + Plm + SUCCOAm	0 SUCLA2
FUMm + H2Om <-> MALm	0 FH
MAL + NAD <-> NADH + OA	0 MDH1
MALm + NADm <-> NADHm + OAm	0 MDH2
PYRm + ATPm + CO2m -> ADPm + OAm + Plm	0 PC
ATP + CIT + COA + H2O -> ADP + PI + ACCOA + OA	0 ACLY
OA + GTP -> PEP + GDP + CO2	0 PCK1
OAm + GTPm -> PEPm + GDPm + CO2m	0 PCK2
G6P + NADP <-> D6PGL + NADPH	0 G6PD
D6PGL + H2O -> D6PGC	0 H6PD
D6PGC + NADP -> NADPH + CO2 + RL5P	0 PGD
RL5P <-> X5P	0 RPE
R5P + X5P <-> T3P1 + S7P	0 TKT1
X5P + E4P <-> F6P + T3P1	0 TKT2
T3P1 + S7P <-> E4P + F6P	0 TALDO1
RL5P <-> R5P	0 RPIA
G1P + UTP -> UDPG + PPI	0 UGP1
GLYCOGEN + PI -> G1P	0 GBE1
UDPG -> UDP + GLYCOGEN	0 GYS1
MALm + NADm -> CO2m + NADHm + PYRm	0 ME2
MALm + NADPm -> CO2m + NADPHm + PYRm	0 ME3
MAL + NADP -> CO2 + NADPH + PYR	0 HUMNDME
NADHm + Qm + 4 Hm -> QH2m + NADm + 4 H	0 MTND1
SUCCm + FADm <-> FUMm + FADH2m	0 SDHC1
FADH2m + Qm <-> FADm + QH2m	0 SDHC2
O2m + 4 FEROm + 4 Hm -> 4 FERIm + 2 H2Om + 4 H	0 UQCRFS1
QH2m + 2 FERIm + 4 Hm -> Qm + 2 FEROm + 4 H	0 COX5BL4
ADPm + Plm + 3 H -> ATPm + 3 Hm + H2Om	0 MTAT1
ADP + ATPm + PI + H -> Hm + ADPm + ATP + Plm	0 ATPMC
GDP + GTPm + PI + H -> Hm + GDPm + GTP + Plm	0 GTPMC
PPI -> 2 PI	0 PP
GDP + ATP <-> GTP + ADP	0 NME1
ACCOA + ATP + CO2 <-> MALCOA + ADP + PI + H	0 ACACA
MALCOA + ACP <-> MALACP + COA	0 FAS1_1
ACCOA + ACP <-> ACACP + COA	0 FAS1_2
ACACP + 4 MALACP + 8 NADPH -> 8 NADP + C100ACP + 4 CO2 + 4 ACP	0 C100SY
ACACP + 5 MALACP + 10 NADPH -> 10 NADP + C120ACP + 5 CO2 + 5 ACP	0 C120SY
ACACP + 6 MALACP + 12 NADPH -> 12 NADP + C140ACP + 6 CO2 + 6 ACP	0 C140SY
ACACP + 6 MALACP + 11 NADPH -> 11 NADP + C141ACP + 6 CO2 + 6 ACP	0 C141SY
ACACP + 7 MALACP + 14 NADPH -> 14 NADP + C160ACP + 7 CO2 + 7 ACP	0 C160SY
ACACP + 7 MALACP + 13 NADPH -> 13 NADP + C161ACP + 7 CO2 + 7 ACP	0 C161SY

ACACP + 8 MALACP + 16 NADPH -> 16 NADP + C180ACP + 8 CO2 + 8 ACP	0 C180SY
ACACP + 8 MALACP + 15 NADPH -> 15 NADP + C181ACP + 8 CO2 + 8 ACP	0 C181SY
ACACP + 8 MALACP + 14 NADPH -> 14 NADP + C182ACP + 8 CO2 + 8 ACP	0 C182SY
C160ACP + H2O -> C160 + ACP	0 PPT1
C160 + COA + ATP -> AMP + PPI + C160COA	0 KIAA
C160COA + CAR -> C160CAR + COA	0 C160CA
C160CARm + COAm -> C160COAm + CARm	0 C160CB
C160CARm + COAm + FADm + NADm -> FADH2m + NADHm + C140COAm + ACCOAm	0 HADHA
C140COAm + 7 COAm + 7 FADm + 7 NADm -> 7 FADH2m + 7 NADHm + 7 ACCOAm	0 HADH2
TAGLYm + 3 H2Om -> GLm + 3 C160m	0 TAGRXN
GL3P + 0.017 C100ACP + 0.062 C120ACP + 0.1 C140ACP + 0.27 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> AGL3P + ACP	0 GAT1
AGL3P + 0.017 C100ACP + 0.062 C120ACP + 0.100 C140ACP + 0.270 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> PA + ACP	0 AGPAT1
ATP + CHO -> ADP + PCHO	0 CHKL1
PCHO + CTP -> CDPCHO + PPI	0 PCYT1A
CDPCHO + DAGLY -> PC + CMP	0 LOC
SAM + PE -> SAH + PMME	0 PEMT
SAM + PMME -> SAH + PDME	0 MFPS
PDME + SAM -> PC + SAH	0 PNMNM
G6P -> MI1P	0 ISYNA1
MI1P -> MYOI + PI	0 IMPA1
PA + CTP <-> CDPDG + PPI	0 CDS1
CDPDG + MYOI -> CMP + PINS	0 PIS
ATP + PINS -> ADP + PINSP	0 PIK3CA
ATP + PINS -> ADP + PINS4P	0 PIK4CA
PINS4P + ATP -> D45PI + ADP	0 PIP5K1
D45PI -> TPI + DAGLY	0 PLCB2
PA + H2O -> DAGLY + PI	0 PPAP2A
DAGLY + 0.017 C100ACP + 0.062 C120ACP + 0.100 C140ACP + 0.270 C160ACP + 0.169 C161ACP + 0.055 C180ACP + 0.235 C181ACP + 0.093 C182ACP -> TAGLY + ACP	0 DGAT
CDPDG + SER <-> CMP + PS	0 PTDS
CDPETN + DAGLY <-> CMP + PE	0 CEPT1
PE + SER <-> PS + ETHM	0 PESER
ATP + ETHM -> ADP + PETHM	0 EKI1
PETHM + CTP -> CDPETN + PPI	0 PCYT2
PS -> PE + CO2	0 PISD
3HBm + NADm -> NADHm + Hm + ACTACm	0 BDH
ACTACm + SUCCOAm -> SUCCm + AACOAm	0 3OCT
THF + SER <-> GLY + METTHF	0 SHMT1
THFm + SERm <-> GLYm + METTHFm	0 SHMT2
SERm + PYRm <-> ALAm + 3HPm	0 AGXT
3PG + NAD <-> NADH + PHP	0 PHGDH
PHP + GLU <-> AKG + 3PSER	0 PSA
3PSER + H2O -> PI + SER	0 PSPH
3HPm + NADHm -> NADm + GLYAm	0 GLYD
SER -> PYR + NH3 + H2O	0 SDS
GLYAm + ATPm -> ADPm + 2PGm	0 GLTK
PYR + GLU <-> AKG + ALA	0 GPT
GLUm + CO2m + 2 ATPm -> 2 ADPm + 2 Plm + CAPm	0 CPS1
AKGm + NADHm + NH3m <-> NADm + H2Om + GLUm	0 GLUD1
AKGm + NADPHm + NH3m <-> NADPm + H2Om + GLUm	0 GLUD2
GLUm + NH3m + ATPm -> GLNm + ADPm + Plm	0 GLUL
ASPm + ATPm + GLNm -> GLUm + ASNm + AMPm + PPIm	0 ASNS
ORN + AKG <-> GLUGSAL + GLU	0 OAT
GLU <-> GLUm + Hm	0 GLUMT
GLU + ATP + NADPH -> NADP + ADP + PI + GLUGSAL	0 P5CS
GLUP + NADH -> NAD + PI + GLUGSAL	0 PYCS
P5C <-> GLUGSAL	0 SPTC
HIS -> NH3 + URO	0 HAL
URO + H2O -> 4I5P	0 UROH
4I5P + H2O -> FIGLU	0 IMPR
FIGLU + THF -> NFTHF + GLU	0 FTCD
MET + ATP + H2O -> PPI + PI + SAM	0 MAT1A
SAM + DNA -> SAH + DNA5MC	0 DNMT1
SAH + H2O -> HCYS + ADN	0 AHCYL1

Table 5

Human Cell Types

Keratinizing epithelial cells

Epidermal keratinocyte (differentiating epidermal cell)
Epidermal basal cell (stem cell)
Keratinocyte of fingernails and toenails
Nail bed basal cell (stem cell)
Medullary hair shaft cell
Cortical hair shaft cell
Cuticular hair shaft cell
Cuticular hair root sheath cell
Hair root sheath cell of Huxley's layer
Hair root sheath cell of Henle's layer

External hair root sheath cell

Hair matrix cell (stem cell)

Wet stratified barrier epithelial cells

Surface epithelial cell of stratified squamous epithelium of cornea, tongue, oral cavity, esophagus, anal canal, distal urethra and vagina
basal cell (stem cell) of epithelia of cornea, tongue, oral cavity, esophagus, anal canal, distal urethra and vagina
Urinary epithelium cell (lining urinary bladder and urinary ducts)

Exocrine secretory epithelial cells

Salivary gland mucous cell (polysaccharide-rich secretion)
Salivary gland serous cell (glycoprotein enzyme-rich secretion)
Von Ebner's gland cell in tongue (washes taste buds)
Mammary gland cell (milk secretion)
Lacrimal gland cell (tear secretion)
Ceruminous gland cell in ear (wax secretion)
Eccrine sweat gland dark cell (glycoprotein secretion)
Eccrine sweat gland clear cell (small molecule secretion)
Apocrine sweat gland cell (odoriferous secretion, sex-hormone sensitive)
Gland of Moll cell in eyelid (specialized sweat gland)
Sebaceous gland cell (lipid-rich sebum secretion)
Bowman's gland cell in nose (washes olfactory epithelium)
Brunner's gland cell in duodenum (enzymes and alkaline mucus)
Seminal vesicle cell (secretes seminal fluid components, including fructose for swimming sperm)
Prostate gland cell (secretes seminal fluid components)
Bulbourethral gland cell (mucus secretion)
Bartholin's gland cell (vaginal lubricant secretion)
Gland of Littre cell (mucus secretion)
Uterus endometrium cell (carbohydrate secretion)
Isolated goblet cell of respiratory and digestive tracts (mucus secretion)
Stomach lining mucous cell (mucus secretion)
Gastric gland zymogenic cell (pepsinogen secretion)

HCYS + MTHF -> THF + MET	0 MTR
SER + HCYS -> LLCT + H2O	0 CBS
LLCT + H2O -> CYS + HSER	0 CTH1
OBUT + NH3 <-> HSER	0 CTH2
CYS + O2 <-> CYSS	0 CDO1
CYSS + AKG <-> GLU + SPYR	0 CYSAT
SPYR + H2O -> H2SO3 + PYR	0 SPTB
LYS + NADPH + AKG -> NADP + H2O + SAC	0 LKR1
SAC + H2O + NAD -> GLU + NADH + AASA	0 LKR2
AASA + NAD -> NADH + AADP	0 2ASD
AADP + AKG -> GLU + KADP	0 LOC5
TRP + O2 -> FKYN	0 TDO2
FKYN + H2O -> FOR + KYN	0 KYNF
KYN + NADPH + O2 -> HKYN + NADP + H2O	0 KMO
HKYN + H2O -> HAN + ALA	0 KYNU2
HAN + O2 -> CMUSA	0 HAAO
CMUSA -> CO2 + AM6SA	0 ACSD
AM6SA -> PIC	0 SPTA
AM6SA + NAD -> AMUCO + NADH	0 AMSD
AMUCQ + NADPH -> KADP + NADP + NH4	0 2AMR
ARG -> ORN + UREA	0 ARG2
ORN + Hm -> ORNm	0 ORNMT
ORN + Hm + CITRm <-> CITR + ORNm	0 ORNCITT
ORNm + CAPm -> CITRm + Pim + Hm	0 OTC
CITR + ASP + ATP <-> AMP + PPI + ARGSUCC	0 ASS
ARGSUCC -> FUM + ARG	0 ASL
PRO + FAD -> P5C + FADH2	0 PRODH
P5C + NADPH -> PRO + NADP	0 PYCR1
THR -> NH3 + H2O + OBUT	0 WTDH
THR + NAD -> CO2 + NADH + AMA	0 TDH
AMA + H2O + FAD -> NH3 + FADH2 + MTHGXL	0 MAOA
GLYm + THFm + NADm <-> METTHFm + NADHm + CO2m + NH3m	0 AMT
PHE + THBP + O2 -> TYR + DHBP + H2O	0 PAH
NADPH + DHBP -> NADP + THBP	0 QDPR
AKG + TYR -> HPHPYR + GLU	0 TAT
HPHPYR + O2 -> HGTS + CO2	0 HPD
HGTS + O2 -> MACA	0 HGD
MACA -> FACA	0 GSTZ1
FACA + H2O -> FUM + ACA	0 FAH
AKG + ILE -> OMVAL + GLU	0 BCAT1A
OMVALm + COAm + NADm -> MBCOAm + NADHm + CO2m	0 BCKDHAA
MBCOAm + FADm -> MCCOAm + FADH2m	0 ACADMA
MCCOAm + H2Om -> MHVCOAm	0 ECHS1B
MHVCOAm + NADm -> MAACOAm + NADHm	0 EHHADHA
MAACOAm -> ACCOAm + PROPCOAm	0 ACAA2
2 ACCOAm <-> COAm + AACCOAm	0 ACATm1
AKG + VAL -> OIVAL + GLU	0 BCAT1B
OIVALm + COAm + NADm -> IBCOAm + NADHm + CO2m	0 BCKDHAB
IBCOAm + FADm -> MACOAm + FADH2m	0 ACADSB
MACOAm + H2Om -> HIBCOAm	0 EHHADHC
HIBCOAm + H2Om -> HIBm + COAm	0 HIBCHA
HIBm + NADm -> MMAm + NADHm	0 EHHADHB
MMAm + COAm + NADm -> NADHm + CO2m + PROPCOAm	0 MMSDH
PROPCOAm + CO2m + ATPm -> ADPm + Pim + DMMCOAm	0 PCCA
DMMCOAm -> LMMCOAm	0 HIBCHF
LMMCOAm -> SUCCOAm	0 MUT
AKG + LEU -> OICAP + GLU	0 BCAT1C
OICAPm + COAm + NADm -> IVCOAm + NADHm + CO2m	0 BCKDHAC
OICAPm + COAm + NADH -> IVCOAm + NADHm + CO2m	0 BCKDHBC
OICAPm + COAm + NADHm -> IVCOAm + NADHm + CO2m	0 DBTC
IVCOAm + FADm -> MCRCOAm + FADH2m	0 IVD
MCRCOAm + ATPm + CO2m + H2Om -> MGCOAm + ADPm + Pim	0 MCCC1
MGCOAm + H2Om -> H3MCOAm	0 HIBCHB
H3MCOAm -> ACCOAm + ACTACm	0 HMGCL
MYOACT + ATP -> MYOATP + ACTIN	0 MYOSA
MYOATP + ACTIN -> MYOADPAC	0 MYOSB
MYOADPAC -> ADP + PI + MYOACT + CONTRACT	0 MYOSC
PCRE + ADP -> CRE + ATP	0 CREATA
AMP + H2O -> PI + ADN	0 CREATB
ATP + AMP <-> 2 ADP	0 CREATC
O2 <-> O2m	0 O2MT
3HB -> 3HBm	0 HBMT
CIT + MALm <-> CITm + MAL	0 CITMC
PYR <-> PYRm + Hm	0 PYRMC

C160CAR + COAm -> C160COAm + CAR	0 C160CM
OMVAL -> OMVALm	0 HIBCHC
OIVAL -> OIVALm	0 HIBCHD
OICAP -> OICAPm	0 HIBCHE
GL <-> GLm	0 GLMT
GL3Pm + FADm -> T3P2m + FADH2m	0 GPD2
T3P2 + NADH <-> GL3P + NAD	0 GPD1
GL3P <-> GL3Pm	0 GL3PMC
T3P2 <-> T3P2m	0 T3P2MC
OAm + GLUm <-> ASPm + AKGm	0 GOT1
OA + GLU <-> ASP + AKG	0 GOT2
AKG + MALm <-> AKGm + MAL	0 MALMC
ASPm + GLU + H -> Hm + GLUm + ASP	0 ASPMC
GLCxt -> GLC	0 GLUT4
O2xt -> O2	0 O2UP
C160Axt + FABP -> C160FP + ALBxt	0 FAT1
C160FP -> C160 + FABP	0 FAT2
C180Axt + FABP -> C180FP + ALBxt	0 FAT3
C180FP -> C180 + FABP	0 FAT4
C161Axt + FABP -> C161FP + ALBxt	0 FAT5
C161FP -> C161 + FABP	0 FAT6
C181Axt + FABP -> C181FP + ALBxt	0 FAT7
C181FP -> C181 + FABP	0 FAT8
C182Axt + FABP -> C182FP + ALBxt	0 FAT9
C182FP -> C182 + FABP	0 FAT10
C204Axt + FABP -> C204FP + ALBxt	0 FAT11
C204FP -> C204 + FABP	0 FAT12
PYRxt + HEXT <-> PYR + H	0 PYRUP
LACxt + HEXT <-> LAC + HEXT	0 LACUP
H <-> HEXT	0 HextUP
CO2 <-> CO2m	0 CO2MT
H2O <-> H2Om	0 H2OMT
ATP + AC + COA -> AMP + PPI + ACCOA	0 FLJ2
C160CAR <-> C160CARm	0 C160MT
CARm <-> CAR	0 CARMT
CO2xt <-> CO2	0 CO2UP
H2Oxt <-> H2O	0 H2OUP
PIxt + HEXT <-> HEXT + PI	0 PIUP
<-> GLCxt	0 GLCexR
<-> PYRxt	0 PYRexR
<-> CO2xt	0 CO2exR
<-> O2xt	0 O2exR
<-> PIxt	0 PIexR
<-> H2Oxt	0 H2OexR
<-> LACxt	0 LACexR
<-> C160Axt	0 C160AexR
<-> C161Axt	0 C161AexR
<-> C180Axt	0 C180AexR
<-> C181Axt	0 C181AexR
<-> C182Axt	0 C182AexR
<-> C204Axt	0 C204AexR
<-> ALBxt	0 ALBexR
<-> 3HB	0 HBexR
<-> GLYCOGEN	0 GLYex
<-> PCRE	0 PCREex
<-> TAGLYm	0 TAGmex
<-> ILE	0 ILEex
<-> VAL	0 VALex
<-> CRE	0 CREex
<-> ADN	0 ADNex
<-> PI	0 PIex

Gastric gland oxyntic cell (hydrogen chloride secretion)
Pancreatic acinar cell (bicarbonate and digestive enzyme secretion)
Paneth cell of small intestine (lysozyme secretion)
Type II pneumocyte of lung (surfactant secretion)
Clara cell of lung

Hormone secreting cells

Anterior pituitary cells
Somatotropes
Lactotropes
Thyrotropes
Gonadotropes
Corticotropes
Intermediate pituitary cell, secreting melanocyte-stimulating hormone
Magnocellular neurosecretory cells
secreting oxytocin
secreting vasopressin
Gut and respiratory tract cells secreting serotonin
secreting endorphin
secreting somatostatin
secreting gastrin
secreting secretin
secreting cholecystokinin
secreting insulin
secreting glucagon
secreting bombesin
Thyroid gland cells
thyroid epithelial cell
parafollicular cell
Parathyroid gland cells
Parathyroid chief cell
oxyphil cell
Adrenal gland cells
chromaffin cells
secreting steroid hormones (mineralcorticoids and gluco corticoids)
Leydig cell of testes secreting testosterone
Theca interna cell of ovarian follicle secreting estrogen
Corpus luteum cell of ruptured ovarian follicle secreting progesterone
Kidney juxtaglomerular apparatus cell (renin secretion)
Macula densa cell of kidney
Peripolar cell of kidney
Mesangial cell of kidney

Epithelial absorptive cells (Gut, Exocrine Glands and Urogenital Tract)

Intestinal brush border cell (with microvilli)
Exocrine gland striated duct cell
Gall bladder epithelial cell
Kidney proximal tubule brush border cell
Kidney distal tubule cell
Ductulus efferens nonciliated cell

Epididymal principal cell
Epididymal basal cell

Metabolism and storage cells

Hepatocyte (liver cell)
White fat cell
Brown fat cell
Liver lipocyte

Barrier function cells (Lung, Gut, Exocrine Glands and Urogenital Tract)

Type I pneumocyte (lining air space of lung)
Pancreatic duct cell (centroacinar cell)
Nonstriated duct cell (of sweat gland, salivary gland, mammary gland, etc.)
Kidney glomerulus parietal cell
Kidney glomerulus podocyte
Loop of Henle thin segment cell (in kidney)
Kidney collecting duct cell
Duct cell (of seminal vesicle, prostate gland, etc.)

Epithelial cells lining closed internal body cavities

Blood vessel and lymphatic vascular endothelial fenestrated cell
Blood vessel and lymphatic vascular endothelial continuous cell
Blood vessel and lymphatic vascular endothelial splenic cell
Synovial cell (lining joint cavities, hyaluronic acid secretion)
Serosal cell (lining peritoneal, pleural, and pericardial cavities)
Squamous cell (lining perilymphatic space of ear)
Squamous cell (lining endolymphatic space of ear)
Columnar cell of endolymphatic sac with microvilli (lining endolymphatic space of ear)

Columnar cell of endolymphatic sac without microvilli (lining endolymphatic space of ear)
Dark cell (lining endolymphatic space of ear)
Vestibular membrane cell (lining endolymphatic space of ear)
Stria vascularis basal cell (lining endolymphatic space of ear)
Stria vascularis marginal cell (lining endolymphatic space of ear)
Cell of Claudius (lining endolymphatic space of ear)
Cell of Boettcher (lining endolymphatic space of ear)
Choroid plexus cell (cerebrospinal fluid secretion)
Pia-arachnoid squamous cell
Pigmented ciliary epithelium cell of eye
Nonpigmented ciliary epithelium cell of eye
Corneal endothelial cell

Ciliated cells with propulsive function

Respiratory tract ciliated cell
Oviduct ciliated cell (in female)
Uterine endometrial ciliated cell (in female)
Rete testis cilated cell (in male)
Ductulus efferens ciliated cell (in male)
Ciliated ependymal cell of central nervous system (lining brain cavities)

Extracellular matrix secretion cells

Ameloblast epithelial cell (tooth enamel secretion)

Planum semilunatum epithelial cell of vestibular apparatus of ear (proteoglycan secretion)

Organ of Corti interdental epithelial cell (secreting tectorial membrane covering hair cells)
Loose connective tissue fibroblasts
Corneal fibroblasts
Tendon fibroblasts

Bone marrow reticular tissue fibroblasts

Other nonepithelial fibroblasts
Blood capillary pericyte
Nucleus pulposus cell of intervertebral disc
Cementoblast/cementocyte (tooth root bonelike cementum secretion)
Odontoblast/odontocyte (tooth dentin secretion)
Hyaline cartilage chondrocyte
Fibrocartilage chondrocyte
Elastic cartilage chondrocyte
Osteoblast/osteocyte
Osteoprogenitor cell (stem cell of osteoblasts)
Hyalocyte of vitreous body of eye
Stellate cell of perilymphatic space of ear

Contractile cells

Red skeletal muscle cell (slow)
White skeletal muscle cell (fast)
Intermediate skeletal muscle cell

nuclear bag cell of Muscle spindle
nuclear chain cell of Muscle spindle
Satellite cell (stem cell)
Ordinary heart muscle cell
Nodal heart muscle cell
Purkinje fiber cell
Smooth muscle cell (various types)
Myoepithelial cell of iris
Myoepithelial cell of exocrine glands

Red Blood Cell

Blood and immune system cells

Erythrocyte (red blood cell)
Megakaryocyte (platelet precursor)
Monocyte
Connective tissue macrophage (various types)
Epidermal Langerhans cell
Osteoclast (in bone)
Dendritic cell (in lymphoid tissues)
Microglial cell (in central nervous system)
Neutrophil granulocyte
Eosinophil granulocyte
Basophil granulocyte
Mast cell
Helper T cell
Suppressor T cell
Cytotoxic T cell
B cells
Natural killer cell
Reticulocyte
Stem cells and committed progenitors for the blood and immune system (various types)

Sensory transducer cells

Photoreceptor rod cell of eye
Photoreceptor blue-sensitive cone cell of eye
Photoreceptor green-sensitive cone cell of eye
Photoreceptor red-sensitive cone cell of eye
Auditory inner hair cell of organ of Corti
Auditory outer hair cell of organ of Corti
Type I hair cell of vestibular apparatus of ear (acceleration and gravity)
Type II hair cell of vestibular apparatus of ear (acceleration and gravity)
Type I taste bud cell
Olfactory receptor neuron
Basal cell of olfactory epithelium (stem cell for olfactory neurons)
Type I carotid body cell (blood pH sensor)
Type II carotid body cell (blood pH sensor)
Merkel cell of epidermis (touch sensor)
Touch-sensitive primary sensory neurons (various types)
Cold-sensitive primary sensory neurons
Heat-sensitive primary sensory neurons
Pain-sensitive primary sensory neurons (various types)
Proprioceptive primary sensory neurons (various types)

Autonomic neuron cells

Cholinergic neural cell (various types)
Adrenergic neural cell (various types)
Peptidergic neural cell (various types)

Sense organ and peripheral neuron supporting cells

Inner pillar cell of organ of Corti
Outer pillar cell of organ of Corti
Inner phalangeal cell of organ of Corti
Outer phalangeal cell of organ of Corti
Border cell of organ of Corti
Hensen cell of organ of Corti
Vestibular apparatus supporting cell
Type I taste bud supporting cell
Olfactory epithelium supporting cell
Schwann cell
Satellite cell (encapsulating peripheral nerve cell bodies)
Enteric glial cell

Central nervous system neurons and glial cells

Neuron cells (large variety of types, still poorly classified)
Astrocyte (various types)
Oligodendrocyte

Lens cells

Anterior lens epithelial cell
Crystallin-containing lens fiber cell

Pigment cells

Melanocyte
Retinal pigmented epithelial cell

Germ cells

Oogonium/Oocyte
Spermatid
Spermatocyte
Spermatogonium cell (stem cell for spermatocyte)
Spermatozoon

Nurse cells

Ovarian follicle cell
Sertoli cell (in testis)
Thymus epithelial cell

Table 6.

Human Tissues

Epithelial Tissue
- *Unilaminar (simple) epithelia*
  - Squamous
  - Cuboidal
  - Columnar
  - Sensory
  - Myoepitheliocyte
- *Multilaminar eipithelia*
  - Replacing or stratified squamous epithelia
  - Stratified cuboidal and columnar eipithelia
- *Urothelium (transitional epithelium)*
  - Seminiferous eipthelium
- *Glands*
  - Exocrine glands
    - Ducts and Tubules
  - Endocrine glands

Nervous Tissue
- *Neurons*
  - Multipolar Neurons in CNS
- *Nerves*
  - Nerves of the PNS
- *Receptors*
  - Miessner's and Pacinian Corpuscles

Connective Tissues
- *Fluid Connective Tissues*
  - Lymph
  - Blood
- *Connective Tissues Proper*
  - Loose Connective Tissues
    - Areolar
  - Loose Connective Tissues and Inflammation
    - Adipose
    - Reticular
  - Dense Connective Tissues
    - Regular(collagen)
    - Irregular(collagen)
    - Regular(elastic)
- *Supportive Connective Tissues*
  - Osseous Tissue
    - Compact
    - Cancellous
  - Cartilage
    - Hyaline
    - Elastic
    - Fibrocartilage

Muscle Tissue
- *Non-striated*
  - Smooth Muscle
- *Striated*
  - Skeletal Muscle
  - Cardiac Muscle

Systems	Major Structures
Skeletal	Bones, cartilage, tendons, ligaments, and joints
Muscular	Muscles (skeletal, cardiac, and smooth)
Integumentary	Skin, hair nails, breast
Circulatory	Heart, blood vessels, blood
Respiratory	Trachea, air passages, lungs
Immune	Lymph nodes and vessels, white blood cells
Digestive	Mouth, esophagus, stomach, liver, pancreas, duodenum, jejunum, ileum, caecum, rectum, gallbladder, pancreas, small and large intestines
Excretory and Urinary	Kidneys, ureters, bladder, urethra
Nervous	Brain, spinal cord, nerves, sense organs, receptors, dorsal root ganglion
Endocrine	Endocrine glands, pineal gland, pituitary gland, adrenal gland, thyroid gland, and hormones
Lymphatic	Lymph nodes, spleen, lymph vessels
Reproductive	Ovaries, uterus, fallopian tube, mammary glands (in females), vas deferens, prostate, testes (in males), umbilical cord, placenta

Functions
provides structure; supports and protects internal organs
provides structure; supports and moves trunk and limbs; moves substances through body
protects against pathogens; helps regulate body temperature
transports nutrients and wastes to and from all body tissues
carries air into and out of lungs, where gases (oxygen and carbon dioxide) are exchanged
provides protection against infection and disease
stores and digests food; absorbs nutrients; eliminates waste
eliminate waste; maintains water and chemical balance
controls and coordinates body movements and senses; controls consciousness and creativity; helps monitor and maintain other body systems
maintain homeostasis; regulates metabolism, water and mineral balance, growth and sexual development, and reproduction
cleans and returns tissue fluid to the blood and destroys pathogens that enter the body
produce gametes and offspring

Table 7

Cells of the Liver
Hepatocytes
Perisinusoidal (Ito) cells
Endotheliocytes
Macrophages (Kupffer cells)
Lymphocytes (pit cells)
Cells of the biliary tree
Cuboidal epitheliocytes
Columnar epitheliocytes
Connective tissue cells

Table 15. Adipocyte-myocyte reactions

Reaction Abbreviation	Reaction Name	Equation	Subsystem	Protein Classification
G6PASEer_ac	glucose-6-phosphatase	[f] : g6p + h2o --> glc-D + pi	Glycolysis/Gluconeogenesis	EC-3.1.3.9
G6PASEer_mc	glucose-6-phosphatase	[u] : g6p + h2o --> glc-D + pi	Glycolysis/Gluconeogenesis	EC-3.1.3.9
PFK26_ac	6-phosphofructo-2-kinase	[a] : atp + f6p --> adp + f26bp + h	Glycolysis/Gluconeogenesis	EC-2.7.1.105
PGI_ac	glucose-6-phosphate isomerase	[a] : g6p <==> f6p	Glycolysis/Gluconeogenesis	EC-5.3.1.9
PGK_ac	phosphoglycerate kinase	[a] : 13dpg + adp <==> 3pg + atp	Glycolysis/Gluconeogenesis	EC-2.7.2.3
PGM_ac	phosphoglycerate mutase	[a] : 3pg <==> 2pg	Glycolysis/Gluconeogenesis	EC-5.4.2.1
PYK_ac	pyruvate kinase	[a] : adp + h + pep --> atp + pyr	Glycolysis/Gluconeogenesis	EC-2.7.1.40
TPI_ac	triose-phosphate isomerase	[a] : dhap <==> g3p	Glycolysis/Gluconeogenesis	EC-5.3.1.1
ACONTm_ac	Aconitate hydratase	[b] : cit <==> icit	Central Metabolism	EC-4.2.1.3
ACONTm_mc	Aconitate hydratase	[z] : cit <==> icit	Central Metabolism	EC-4.2.1.3
AKGDm_ac	2-oxoglutarate dehydrogenase, mitochondrial	[b] : akg + coa + nad --> co2 + nadh + succoa	Central Metabolism	
AKGDm_mc	2-oxoglutarate dehydrogenase, mitochondrial	[z] : akg + coa + nad --> co2 + nadh + succoa	Central Metabolism	
CITL2_ac	Citrate lyase (ATP-requiring)	[a] : atp + cit + coa --> accoa + adp + oaa + pi	Central Metabolism	EC-4.1.3.8
CITL2_mc	Citrate lyase (ATP-requiring)	[y] : atp + cit + coa --> accoa + adp + oaa + pi	Central Metabolism	EC-4.1.3.8
CSm_ac	citrate synthase	[b] : accoa + h2o + oaa --> cit + coa + h	Central Metabolism	EC-4.1.3.7
CSm_mc	citrate synthase	[z] : accoa + h2o + oaa --> cit + coa + h	Central Metabolism	EC-4.1.3.7
ENO_ac	enolase	[a] : 2pg <==> h2o + pep	Central Metabolism	EC-4.2.1.11
ENO_mc	enolase	[y] : 2pg <==> h2o + pep	Central Metabolism	EC-4.2.1.11
FBA_ac	fructose-bisphosphate aldolase	[a] : fdp <==> dhap + g3p	Central Metabolism	EC-4.1.2.13
FBA_mc	fructose-bisphosphate aldolase	[y] : fdp <==> dhap + g3p	Central Metabolism	EC-4.1.2.13
FBP26_ac	Fructose-2,6-bisphosphate 2-phosphatase	[a] : f26bp + h2o --> f6p + pi	Central Metabolism	EC-3.1.3.46
FBP26_mc	Fructose-2,6-bisphosphate 2-phosphatase	[y] : f26bp + h2o --> f6p + pi	Central Metabolism	EC-3.1.3.46
FBP_ac	fructose-bisphosphatase	[a] : fdp + h2o --> f6p + pi	Central Metabolism	EC-3.1.3.11
FBP_mc	fructose-bisphosphatase	[y] : fdp + h2o --> f6p + pi	Central Metabolism	EC-3.1.3.11
FUMm_ac	fumarase, mitochondrial	[b] : fum + h2o <==> mal-L	Central Metabolism	EC-4.2.1.2

FUMm_mc	fumarase, mitochondrial	[z] : fum + h2o <==> mal-L	Central Metabolism	EC-4.2.1.2
G3PD1_ac	glycerol-3-phosphate dehydrogenase (NAD), adipocyte	[a] : glyc3p + nad <==> dhap + h + nadh	Central Metabolism	EC-1.1.1.94
G3PD_mc	Glycerol-3-phosphate dehydrogenase (NAD)	[y] : dhap + h + nadh --> glyc3p + nad	Central Metabolism	EC-1.1.1.8
G3PDm_ac	glycerol-3-phosphate dehydrogenase	[b] : fad + glyc3p --> dhap + fadh2	Central Metabolism	EC-1.1.99.5
G3PDm_mc	glycerol-3-phosphate dehydrogenase	[z] : fad + glyc3p --> dhap + fadh2	Central Metabolism	EC-1.1.99.5
G6PDH_ac	glucose 6-phosphate dehydrogenase	[a] : g6p + nadp --> 6pgl + h + nadph	Central Metabolism	EC-1.1.1.49
G6PDH_mc	glucose 6-phosphate dehydrogenase	[y] : g6p + nadp --> 6pgl + h + nadph	Central Metabolism	EC-1.1.1.49
GAPD_ac	glyceraldehyde-3-phosphate dehydrogenase (NAD)	[a] : g3p + nad + pi <==> 13dpg + h + nadh	Central Metabolism	EC-1.2.1.12
GAPD_mc	glyceraldehyde-3-phosphate dehydrogenase (NAD)	[y] : g3p + nad + pi <==> 13dpg + h + nadh	Central Metabolism	EC-1.2.1.12
GL3Ptm_ac	glycerol-3-phosphate transport, adipocyte mitochondrial	glyc3p[a] <==> glyc3p[b]	Central Metabolism	
GLCP_ac	glycogen phosphorylase	[a] : glycogen + pi --> g1p	Central Metabolism	EC-2.4.1.1
HCO3Em_ac	HCO3 equilibration reaction, mitochondrial	[b] : co2 + h2o <==> h + hco3	Central Metabolism	EC-4.2.1.1
HCO3Em_mc	HCO3 equilibration reaction, mitochondrial	[z] : co2 + h2o <==> h + hco3	Central Metabolism	EC-4.2.1.1
HEX1_ac	hexokinase (D-glucose:ATP)	[a] : atp + glc-D --> adp + g6p + h	Central Metabolism	EC-2.7.1.2
HEX1_mc	hexokinase (D-glucose:ATP)	[y] : atp + glc-D --> adp + g6p + h	Central Metabolism	EC-2.7.1.2
ICDHxm_ac	Isocitrate dehydrogenase (NAD+)	[b] : icit + nad --> akg + co2 + nadh	Central Metabolism	EC-1.1.1.41
ICDHxm_mc	Isocitrate dehydrogenase (NAD+)	[z] : icit + nad --> akg + co2 + nadh	Central Metabolism	EC-1.1.1.41
ICDHym_ac	Isocitrate dehydrogenase (NADP+)	[b] : icit + nadp --> akg + co2 + nadph	Central Metabolism	EC-1.1.1.42
ICDHym_mc	Isocitrate dehydrogenase (NADP+)	[z] : icit + nadp --> akg + co2 + nadph	Central Metabolism	EC-1.1.1.42
LDH_L_mc	L-lactate dehydrogenase	[y] : lac-L + nad <==> h + nadh + pyr	Central Metabolism	EC-1.1.1.27
MDH_ac	malate dehydrogenase	[a] : mal-L + nad <==> h + nadh + oaa	Central Metabolism	EC-1.1.1.37
MDH_mc	malate dehydrogenase	[y] : mal-L + nad <==> h + nadh + oaa	Central Metabolism	EC-1.1.1.37
MDHm_ac	malate dehydrogenase, mitochondrial	[b] : mal-L + nad <==> h + nadh + oaa	Central Metabolism	EC-1.1.1.37
MDHm_mc	malate dehydrogenase, mitochondrial	[z] : mal-L + nad <==> h + nadh + oaa	Central Metabolism	EC-1.1.1.37

ME1m_ac	malic enzyme (NAD), mitochondrial	[b] : mal-L + nad --> co2 + nadh + pyr	Central Metabolism	EC-1.1.1.38
ME1m_mc	malic enzyme (NAD), mitochondrial	[z] : mal-L + nad --> co2 + nadh + pyr	Central Metabolism	EC-1.1.1.38
ME2_ac	malic enzyme (NADP)	[a] : mal-L + nadp --> co2 + nadph + pyr	Central Metabolism	EC-1.1.1.40
ME2_mc	malic enzyme (NADP)	[y] : mal-L + nadp --> co2 + nadph + pyr	Central Metabolism	EC-1.1.1.40
ME2m_ac	malic enzyme (NADP), mitochondrial	[b] : mal-L + nadp --> co2 + nadph + pyr	Central Metabolism	EC-1.1.1.40
ME2m_mc	malic enzyme (NADP), mitochondrial	[z] : mal-L + nadp --> co2 + nadph + pyr	Central Metabolism	EC-1.1.1.40
PCm_mc	pyruvate carboxylase, mitochondrial	[z] : atp + hco3 + pyr --> adp + h + oaa + pi	Central Metabolism	EC-6.4.1.1
PDHm_mc	pyruvate dehydrogenase, mitochondrial	[z] : coa + nad + pyr --> accoa + co2 + nadh	Central Metabolism	EC-1.2.1.51
PFK26_mc	6-phosphofructo-2-kinase	[y] : atp + f6p --> adp + f26bp + h	Central Metabolism	EC-2.7.1.105
PFK_ac	phosphofructokinase	[a] : atp + f6p --> adp + fdp + h	Central Metabolism	EC-2.7.1.11
PFK_mc	phosphofructokinase	[y] : atp + f6p --> adp + fdp + h	Central Metabolism	EC-2.7.1.11
PGDH_mc	phosphogluconate dehydrogenase	[y] : 6pgc + nadp --> co2 + nadph + ru5p-D	Central Metabolism	EC-1.1.1.44
PGI_mc	glucose-6-phosphate isomerase	[y] : g6p <==> f6p	Central Metabolism	EC-5.3.1.9
PGK_mc	phosphoglycerate kinase	[y] : 13dpg + adp <==> 3pg + atp	Central Metabolism	EC-2.7.2.3
PGL_mc	6-phosphogluconolactonase	[y] : 6pgl + h2o --> 6pgc + h	Central Metabolism	EC-3.1.1.31
PGM_mc	phosphoglycerate mutase	[y] : 3pg <==> 2pg	Central Metabolism	EC-5.4.2.1
PPA_ac	inorganic diphosphatase	[a] : h2o + ppi --> h + (2) pi	Central Metabolism	EC-3.6.1.1
PPA_mc	inorganic diphosphatase	[y] : h2o + ppi --> h + (2) pi	Central Metabolism	EC-3.6.1.1
PPCKG_ac	phosphoenolpyruvate carboxykinase (GTP)	[a] : gtp + oaa --> co2 + gdp + pep	Central Metabolism	EC-4.1.1.32
PPCKG_mc	phosphoenolpyruvate carboxykinase (GTP)	[y] : gtp + oaa --> co2 + gdp + pep	Central Metabolism	EC-4.1.1.32
PYK_mc	pyruvate kinase	[y] : adp + h + pep --> atp + pyr	Central Metabolism	EC-2.7.1.40
RPE_mc	ribulose 5-phosphate 3-epimerase	[y] : ru5p-D <==> xu5p-D	Central Metabolism	EC-5.1.3.1
RPI_mc	ribose-5-phosphate isomerase	[y] : r5p <==> ru5p-D	Central Metabolism	EC-5.3.1.6
SUCD1m_mc	succinate dehydrogenase	[z] : succ + ubq <==> fum + qh2	Central Metabolism	EC-1.3.5.1
SUCD3m_mc	succinate dehydrogenase cytochrome b	[z] : fadh2 + ubq <==> fad + qh2	Central Metabolism	
SUCOASAm_mc	Succinate--CoA ligase (ADP-forming)	[z] : atp + coa + succ <==> adp + pi + succoa	Central Metabolism	EC-6.2.1.4
SUCOASGm_mc	Succinate--CoA ligase (GDP-forming)	[z] : coa + gtp + succ <==> gdp + pi + succoa	Central Metabolism	EC-6.2.1.4
TAL_mc	transaldolase	[y] : g3p + s7p <==> e4p + f6p	Central Metabolism	EC-2.2.1.2

TKT1_mc	transketolase	[y] : r5p + xu5p-D <==> g3p + s7p	Central Metabolism	EC-2.2.1.1
TKT2_mc	transketolase	[y] : e4p + xu5p-D <==> f6p + g3p	Central Metabolism	EC-2.2.1.1
TPI_mc	triose-phosphate isomerase	[y] : dhap <==> g3p	Central Metabolism	EC-5.3.1.1
SUCOASAm_ac	Succinate--CoA ligase (ADP-forming)	[b] : atp + coa + succ <==> adp + pi + succoa	Citrate Cycle (TCA)	EC-6.2.1.4
SUCOASGm_ac	Succinate--CoA ligase (GDP-forming)	[b] : coa + gtp + succ <==> gdp + pi + succoa	Citrate Cycle (TCA)	EC-6.2.1.4
PGDH_ac	phosphogluconate dehydrogenase	[a] : 6pgc + nadp --> co2 + nadph + ru5p-D	Pentose Phosphate Cycle	EC-1.1.1.44
PGL_ac	6-phosphogluconolactonase	[a] : 6pgl + h2o --> 6pgc + h	Pentose Phosphate Cycle	EC-3.1.1.31
RPE_ac	ribulose 5-phosphate 3-epimerase	[a] : ru5p-D <==> xu5p-D	Pentose Phosphate Cycle	EC-5.1.3.1
RPI_ac	ribose-5-phosphate isomerase	[a] : r5p <==> ru5p-D	Pentose Phosphate Cycle	EC-5.3.1.6
TAL_ac	transaldolase	[a] : g3p + s7p <==> e4p + f6p	Pentose Phosphate Cycle	EC-2.2.1.2
TKT1_ac	transketolase	[a] : r5p + xu5p-D <==> g3p + s7p	Pentose Phosphate Cycle	EC-2.2.1.1
TKT2_ac	transketolase	[a] : e4p + xu5p-D <==> f6p + g3p	Pentose Phosphate Cycle	EC-2.2.1.1
PCm_ac	pyruvate carboxylase, mitochondrial	[b] : atp + hco3 + pyr --> adp + h + oaa + pi	Pyruvate metabolism	EC-6.4.1.1
PDHm_ac	pyruvate dehydrogenase, mitochondrial	[b] : coa + nad + pyr --> accoa + co2 + nadh	Pyruvate metabolism	EC-1.2.1.51
ATPM_ac	ATP maintenance requirment	[a] : atp + h2o --> adp + h + pi	Energy Metabolism	
ATPM_mc	ATP maintenance requirment	[y] : atp + h2o --> adp + h + pi	Energy Metabolism	
ATPS4m_ac	ATP synthase, adipocyte mitochondrial	adp[b] + (4) h[a] + pi[b] --> atp[b] + (3) h[b] + h2o[b]	Energy Metabolism	EC-3.6.1.14,
ATPS4m_mc	ATP synthase, myocyte mitochondrial	adp[z] + (4) h[y] + pi[z] --> atp[z] + (3) h[z] + h2o[y]	Energy Metabolism	EC-3.6.1.14,
ATPSis_ac	ATPase, adipocyte cytosolic	atp[a] + h2o[a] --> adp[a] + h[i] + pi[a]	Energy Metabolism	EC-3.6.3.6,
ATPSis_mc	ATPase, myocyte cytosolic	atp[y] + h2o[y] --> adp[y] + h[c] + pi[y]	Energy Metabolism	EC-3.6.3.6,
CREATK_mc	creatine kinase, myocyte cytosol	[y] : atp + creat <==> adp + creatp	Energy Metabolism	EC-2.7.3.2
CREATPD_mc	creatine phosphate dephosphorylation, spontaneous	[y] : creatp --> crtn + h + pi	Energy Metabolism	
CYOO4m_ac	cytochrome c oxidase (adipocyte mitochondrial 4 protons)	(4) focytc[b] + (8) h[b] + o2[b] --> (4) ficytc[b] + (4) h[a] + (2) h2o[b]	Energy Metabolism	EC-1.9.3.1,
CYOO4m_mc	cytochrome c oxidase (myocyte mitochondrial 4 protons)	(4) focytc[z] + (8) h[z] + o2[z] --> (4) ficytc[z] + (4) h[y] + (2) h2o[z]	Energy Metabolism	EC-1.9.3.1,

CYOR4m_ac	ubiquinol cytochrome c reductase, adipocyte	(2) ficytc[b] + (2) h[b] + qh2[b] --> (2) focytc[b] + (4) h[a] + ubq[b]	Energy Metabolism	EC-1.10.2.2,
CYOR4m_mc	ubiquinol cytochrome c reductase, myocyte	(2) ficytc[z] + (2) h[z] + qh2[z] --> (2) focytc[z] + (4) h[y] + ubq[z]	Energy Metabolism	EC-1.10.2.2,
NADH4m_mc	NADH dehydrogenase, mitochondrial	(5) h[z] + nadh[z] + ubq[z] --> (4) h[y] + nad[z] + qh2[z]	Energy Metabolism	EC-1.6.99.3,
NADH4m_ac	NADH dehydrogenase, adipocyte mitochondrial	(5) h[b] + nadh[b] + ubq[b] --> (4) h[a] + nad[b] + qh2[b]	Oxidative phosphorylation	EC-1.6.99.3,
SUCD1m_ac	succinate dehydrogenase	[b] : succ + ubq <==> fum + qh2	Oxidative phosphorylation	EC-1.3.5.1
SUCD3m_ac	succinate dehydrogenase cytochrome b	[b] : fadh2 + ubq <==> fad + qh2	Oxidative phosphorylation	
GALUi_ac	UTP-glucose-1-phosphate uridylyltransferase (irreversible)	[a] : g1p + h + utp --> ppi + udpg	Galactose metabolism	EC-2.7.7.9
PGMT_ac	phosphoglucomutase	[a] : g1p <==> g6p	Galactose metabolism	EC-5.4.2.2
GALUi_mc	UTP-glucose-1-phosphate uridylyltransferase (irreversible)	[y] : g1p + h + utp --> ppi + udpg	Carbohydrate Metabolism	EC-2.7.7.9
GLCP_mc	glycogen phosphorylase	[y] : glycogen + pi --> g1p	Carbohydrate Metabolism	EC-2.4.1.1
GLYGS_ac	glycogen synthase (UDPGlc)	[a] : udpg --> glycogen + h + udp	Carbohydrate Metabolism	EC-2.4.1.11
GLYGS_mc	glycogen synthase (UDPGlc)	[y] : udpg --> glycogen + h + udp	Carbohydrate Metabolism	EC-2.4.1.11
PGMT_mc	phosphoglucomutase	[y] : g1p <==> g6p	Carbohydrate Metabolism	EC-5.4.2.2
ACACT10m_ac	acetyl-CoA C-acyltransferase, adipocyte mitochondrial	[b] : 2maacoa + coa --> accoa + ppcoa	Amino Acid Metabolism	EC-2.3.1.16
ACOAD3m_ac	acyl-CoA dehydrogenase, adipocyte mitochondrial	[b] : 2mbcoa + fad <==> 2mb2coa + fadh2	Amino Acid Metabolism	EC-1.3.99.3
ASPO_D_ac	D-aspartate oxidase	[a] : asp-D + h2o + o2 --> h + h2o2 + nh3 + oaa	Amino Acid Metabolism	EC-1.4.3.16
ASPR_ac	aspartase racemase, adipocyte cytosolic	[a] : asp-D <==> asp-L	Amino Acid Metabolism	EC-5.1.1.13
ASPTA1_ac	aspartate transaminase	[a] : akg + asp-L <==> glu-L + oaa	Amino Acid Metabolism	EC-2.6.1.1
ASPTA1_mc	aspartate transaminase	[y] : akg + asp-L <==> glu-L + oaa	Amino Acid Metabolism	EC-2.6.1.1
ASPTA1m_ac	aspartate transaminase, mitochondrial	[b] : akg + asp-L <==> glu-L + oaa	Amino Acid Metabolism	EC-2.6.1.1
ASPTA1m_mc	aspartate transaminase, mitochondrial	[z] : akg + asp-L <==> glu-L + oaa	Amino Acid Metabolism	EC-2.6.1.1
ECOAH3m_ac	enoyl-CoA hydratase, adipocyte mitochondrial	[b] : 2mb2coa + h2o <==> 3hmbcoa	Amino Acid Metabolism	EC-4.2.1.17

HACD8m_ac	3-hydroxyacyl-CoA dehydrogenase (2-Methylacetoacetyl-CoA), adipocyte mitochondrial	[b] : 3hmbcoa + nad <==> 2maacoa + h + nadh	Amino Acid Metabolism	EC-1.1.1.35
ILETA_ac	isoleucine transaminase, adipocyte cytosolic	[a] : akg + ile-L <==> 3mop + glu-L	Amino Acid Metabolism	EC-2.6.1.42
MOBD3m_ac	3-Methyl-2-oxobutanoate dehydrogenase, adipocyte mitochondrial	[b] : 3mop + coa + nad --> 2mbcoa + co2 + nadh	Amino Acid Metabolism	
CSNAT_mc	carnitine O-acetyltransferase, myocyte cytosol	[y] : accoa + crn --> acrn + coa	Carnitine Shuttle	EC-2.3.1.7
CSNATifm_mc	carnitine O-aceyltransferase, forward reaction, myocyte mitochondrial	[z] : acrn + coa --> accoa + crn	Carnitine Shuttle	EC-2.3.1.7
PPS_ac	propionyl-CoA synthetase, adipocyte cytosolic	[a] : atp + coa + ppa <==> amp + ppcoa + ppi	Propanoate Metabolism	EC-6.2.1.1
PPSm_ac	propionyl-CoA synthetase, adipocyte mitochondrial	[b] : atp + coa + ppa <==> amp + ppcoa + ppi	Propanoate Metabolism	EC-6.2.1.1
ACACT10m_mc	acetyl-CoA C-acyltransferase (octanoyl-CoA)	[z] : accoa + occoa <==> 3odcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT11m_mc	acetyl-CoA C-acyltransferase (nonanoyl-CoA)	[z] : accoa + nncoa <==> 3oedcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT12m_mc	acetyl-CoA C-acyltransferase (decanoyl-CoA)	[z] : accoa + dccoa <==> 3oddcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT13m_mc	acetyl-CoA C-acyltransferase (endecanoyl-CoA)	[z] : accoa + edcoa <==> 3otrdcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT145m_mc	acetyl-CoA C-acyltransferase (dodecenoyl-CoA C12:1CoA, n-3)	[z] : accoa + cis-dd2coa <==> 3otdecoa5 + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT14m_mc	acetyl-CoA C-acyltransferase (dodecanoyl-CoA)	[z] : accoa + ddcoa <==> 3otdcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT15m_mc	acetyl-CoA C-acyltransferase (tridecanoyl-CoA)	[z] : accoa + trdcoa <==> 3opdcoa + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT167m_mc	acetyl-CoA C-acyltransferase (tetradecenoyl-CoA C14:1CoA, n-5)	[z] : accoa + tdecoa5 <==> 3ohdecoa7 + coa	Fatty Acid Degradation	EC-2.3.1.16
ACACT16m_mc	acetyl-CoA C-acyltransferase (tetradecanoyl-CoA)	[z] : accoa + tdcoa <==> 3ohdcoa + coa	Fatty Acid Degradation	EC-2.3.1.16

ACACT189m_mc	acetyl-CoA C-acyltransferase (hexadecenoyl-CoA C16:1CoA, n-7)	[z] : accoa + hdcoa7 <==> 3oodcecoa9 + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT18m_mc	acetyl-CoA C-acyltransferase (palmitoyl-CoA C16:0CoA)	[z] : accoa + pmtcoa <==> 3oodcoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT20m_mc	acetyl-CoA C-acyltransferase (octadecanoyl-CoA C18:0CoA)	[z] : accoa + strcoa <==> 3oescoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT22p_mc	acetyl-CoA C-acyltransferase (eicosanoyl-CoA C20:0CoA)	[w] : accoa + ecsacoa <==> 3odscoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT4m_mc	acetyl-CoA C-acyltransferase (acetyl-CoA)	[z] : (2) accoa <==> aacoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT5m_mc	acetyl-CoA C-acyltransferase (propanoyl-CoA)	[z] : accoa + ppcoa <==> 3optcoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT6m_mc	acetyl-CoA C-acyltransferase (butanoyl-CoA)	[z] : accoa + btcoa <==> 3ohcoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT7m_mc	acetyl-CoA C-acyltransferase (pentanoyl-CoA)	[z] : accoa + ptcoa <==> 3ohpcoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT8m_mc	acetyl-CoA C-acyltransferase (hexanoyl-CoA)	[z] : accoa + hxcoa <==> 3oocoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACACT9m_mc	acetyl-CoA C-acyltransferase (heptanoyl-CoA)	[z] : accoa + hpcoa <==> 3onncoa + coa	Fatty Acid Degradation EC-2.3.1.16
ACOAD10m_mc	acyl-CoA dehydrogenase (decanoyl-CoA C10:0CoA)	[z] : dccoa + fad <==> dc2coa + fadh2	Fatty Acid Degradation EC-1.3.99.13
ACOAD11m_mc	acyl-CoA dehydrogenase (endecanoyl-CoA)	[z] : edcoa + fad <==> ed2coa + fadh2	Fatty Acid Degradation EC-1.3.99.13
ACOAD12m_mc	acyl-CoA dehydrogenase (dodecanoyl-CoA C12:0CoA)	[z] : ddcoa + fad <==> fadh2 + trans-dd2coa	Fatty Acid Degradation EC-1.3.99.13
ACOAD13m_mc	acyl-CoA dehydrogenase (tridecanoyl-CoA)	[z] : fad + trdcoa <==> fadh2 + trd2coa	Fatty Acid Degradation EC-1.3.99.13
ACOAD145m_mc	acyl-CoA dehydrogenase (tetradecenoyl-CoA, C14:1CoA, n-5)	[z] : fad + tdecoa5 <==> fadh2 + tde2coa5	Fatty Acid Degradation EC-1.3.99.13
ACOAD14m_mc	acyl-CoA dehydrogenase (tetradecanoyl-CoA)	[z] : fad + tdcoa <==> fadh2 + td2coa	Fatty Acid Degradation EC-1.3.99.13

ACOAD15m_mc	acyl-CoA dehydrogenase (pentadecanoyl-CoA)	[z] : fad + pdcoa <==> fadh2 + pd2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD167m_mc	acyl-CoA dehydrogenase (hexadecenoyl-CoA, C16:1CoA, n-7)	[z] : fad + hdcoa7 <==> fadh2 + hde2coa7	Fatty Acid Degradation	EC-1.3.99.13
ACOAD16m_mc	acyl-CoA dehydrogenase (hexadecanoyl-CoA C16:0CoA)	[z] : fad + pmtcoa <==> fadh2 + hdd2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD189m_mc	acyl-CoA dehydrogenase (octadecenoyl-CoA, C18:1CoA, n-9)	[z] : fad + odecoa9 <==> fadh2 + ode2coa9	Fatty Acid Degradation	EC-1.3.99.13
ACOAD18m_mc	acyl-CoA dehydrogenase (Stearyl-CoA, C18:0CoA)	[z] : fad + strcoa <==> fadh2 + od2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD20m_mc	acyl-CoA dehydrogenase (eicosanoyl-CoA, C20:0CoA)	[z] : ecsacoa + fad <==> es2coa + fadh2	Fatty Acid Degradation	EC-1.3.99.13
ACOAD22p_mc	acyl-CoA dehydrogenase (docosanoyl-CoA, C22:0CoA)	[w] : dcsacoa + fad <==> ds2coa + fadh2	Fatty Acid Degradation	EC-1.3.99.13
ACOAD4m_mc	acyl-CoA dehydrogenase (butanoyl-CoA C4:0CoA)	[z] : btcoa + fad <==> b2coa + fadh2	Fatty Acid Degradation	EC-1.3.99.13
ACOAD5m_mc	acyl-CoA dehydrogenase (pentanoyl-CoA)	[z] : fad + ptcoa <==> fadh2 + pt2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD6m_mc	acyl-CoA dehydrogenase (hexanoyl-CoA C8:0CoA)	[z] : fad + hxcoa <==> fadh2 + hx2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD7m_mc	acyl-CoA dehydrogenase (heptanoyl-CoA)	[z] : fad + hpcoa <==> fadh2 + hp2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD8m_mc	acyl-CoA dehydrogenase (octanoyl-CoA C8:0CoA)	[z] : fad + occoa <==> fadh2 + oc2coa	Fatty Acid Degradation	EC-1.3.99.13
ACOAD9m_mc	acyl-CoA dehydrogenase (nonanoyl-CoA)	[z] : fad + nncoa <==> fadh2 + nn2coa	Fatty Acid Degradation	EC-1.3.99.13
CRNDST_mc	carnitine docosanoyltransferase, myocyte	[y] : crn + dcsacoa --> coa + dcsacrn	Fatty Acid Degradation	EC-2.3.1.21
CRNDSTp_mc	carnitine docosanoyltransferase II, myocyte	coa[w] + dcsacrn[y] <==> crn[y] + dcsacoa[w]	Fatty Acid Degradation	
CRNDT_mc	carnitine dodecanoyltransferase, myocyte	[y] : crn + ddcoa <==> coa + ddcrn	Fatty Acid Degradation	EC-2.3.1.21

CRNDTm_mc	carnitine dodecanoyltransferase II, myocyte	coa[z] + ddcrn[y] <==> crn[y] + ddcoa[z]	Fatty Acid Degradation	
CRNET_mc	carnitine eicosanoyltransferase, myocyte	[y] : crn + ecsacoa <==> coa + ecsacrn	Fatty Acid Degradation	EC-2.3.1.21
CRNETm_mc	carnitine eicosanoyltransferase II, myocyte	coa[z] + ecsacrn[y] <==> crn[y] + ecsacoa[z]	Fatty Acid Degradation	
CRNETp_mc	carnitine eicosanoyltransferase II, myocyte	coa[w] + ecsacrn[y] <==> crn[y] + ecsacoa[w]	Fatty Acid Degradation	
CRNODET_mc	carnitine 9-cis-octadecenoyltransferase, myocyte	[y] : crn + odecoa9 <==> coa + odecrn9	Fatty Acid Degradation	EC-2.3.1.21
CRNOT_mc	carnitine octadecanoyltransferase, myocyte	[y] : crn + strcoa <==> coa + strcrn	Fatty Acid Degradation	EC-2.3.1.21
CRNOTm_mc	carnitine octadecanoyltransferase II, myocyte	coa[z] + strcrn[y] <==> crn[y] + strcoa[z]	Fatty Acid Degradation	
CRNPTDT_mc	carnitine pentadecanoyltransferase, myocyte	[y] : crn + pdcoa <==> coa + pdcrn	Fatty Acid Degradation	EC-2.3.1.21
CRNPT_mc	carnitine O-palmitoyltransferase, myocyte	[y] : crn + pmtcoa --> coa + pmtcrn	Fatty Acid Degradation	EC-2.3.1.21
CRNPTm_mc	carnitine O-palmitoyltransferase II, myocyte	coa[z] + pmtcrn[y] --> crn[y] + pmtcoa[z]	Fatty Acid Degradation	
CRNTT_mc	carnitine tetradecanoyltransferase, myocyte	[y] : crn + tdcoa <==> coa + tdcrn	Fatty Acid Degradation	EC-2.3.1.21
CRNTTm_mc	carnitine tetradecanoyltransferase II, myocyte	coa[z] + tdcrn[y] <==> crn[y] + tdcoa[z]	Fatty Acid Degradation	
DDCIm_mc	dodecenoyl-CoA D-isomerase, myocyte mitochondrial	[z] : cis-dd2coa <==> trans-dd2coa	Fatty Acid Degradation	EC-5.3.3.8
ECOAH10m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxydecanoyl-CoA)	[z] : 3hdcoa <==> dc2coa + h2o	Fatty Acid Degradation	EC-4.2.1.17
ECOAH11m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyendecanoyl-CoA)	[z] : 3hedcoa <==> ed2coa + h2o	Fatty Acid Degradation	EC-4.2.1.17
ECOAH12m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxydodecanoyl-CoA)	[z] : 3hddcoa <==> h2o + trans-dd2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH13m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxytridecanoyl-CoA)	[z] : 3htrdcoa <==> h2o + trd2coa	Fatty Acid Degradation	EC-4.2.1.17

ECOAH145m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxytetradecenoyl-CoA, C14:1CoA, n-5)	[z] : 3htdecoa5 <==> h2o + tde2coa5	Fatty Acid Degradation	EC-4.2.1.17
ECOAH14m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxytetradecanoyl-CoA)	[z] : 3htdcoa <==> h2o + td2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH15m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxypentadecanoyl-CoA)	[z] : 3hpdcoa <==> h2o + pd2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH167m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyhexadecenoyl-CoA, C16:1CoA, n-7)	[z] : 3hhdecoa7 <==> h2o + hde2coa7	Fatty Acid Degradation	EC-4.2.1.17
ECOAH16m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyhexadecanoyl-CoA)	[z] : 3hhdcoa <==> h2o + hdd2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH189m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyoctadecenoyl-CoA, C18:1CoA, n-9)	[z] : 3hodecoa9 <==> h2o + ode2coa9	Fatty Acid Degradation	EC-4.2.1.17
ECOAH18m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyoctadecanoyl-CoA, C18:0CoA)	[z] : 3hodcoa <==> h2o + od2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH20m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyeicosanoyl-CoA, C18:0CoA)	[z] : 3hescoa <==> es2coa + h2o	Fatty Acid Degradation	EC-4.2.1.17
ECOAH22p_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxydocosanoyl-CoA, C18:0CoA)	[w] : 3hdscoa <==> ds2coa + h2o	Fatty Acid Degradation	EC-4.2.1.17
ECOAH4m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxybutanoyl-CoA)	[z] : 3hbycoa <==> b2coa + h2o	Fatty Acid Degradation	EC-4.2.1.17
ECOAH5m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxypentanoyl-CoA)	[z] : 3hptcoa <==> h2o + pt2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH6m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyhexanoyl-CoA)	[z] : 3hhcoa <==> h2o + hx2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH7m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyheptanoyl-CoA)	[z] : 3hhpcoa <==> h2o + hp2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH8m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxyoctanoyl-CoA)	[z] : 3hocoa <==> h2o + oc2coa	Fatty Acid Degradation	EC-4.2.1.17
ECOAH9m_mc	3-hydroxyacyl-CoA dehydratase (3-hydroxynonanoyl-CoA)	[z] : 3hnncoa <==> h2o + nn2coa	Fatty Acid Degradation	EC-4.2.1.17

HACD10m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxodecanoyl-CoA)	[z] : 3odcoa + h + nadh <==> 3hdcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD11m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxoendecanoyl-CoA)	[z] : 3oedcoa + h + nadh <==> 3hedcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD12m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxododecanoyl-CoA)	[z] : 3oddcoa + h + nadh <==> 3hddcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD13m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxotridecanoyl-CoA)	[z] : 3otrdcoa + h + nadh <==> 3htrdcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD145m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxotetradecenoyl-CoA C14:1CoA, n-5)	[z] : 3otdecoa5 + h + nadh <==> 3htdecoa5 + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD14m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxotetradecanoyl-CoA)	[z] : 3otdcoa + h + nadh <==> 3htdcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD15m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxopentadecanoyl-CoA)	[z] : 3opdcoa + h + nadh <==> 3hpdcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD167m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxohexadecenoyl-CoA C16:1CoA, n-7)	[z] : 3ohdecoa7 + h + nadh <==> 3hhdecoa7 + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD16m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxohexadecanoyl-CoA)	[z] : 3ohdcoa + h + nadh <==> 3hhdcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD189m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxooctadecenoyl-CoA C18:1CoA, n-9)	[z] : 3oodcecoa9 + h + nadh <==> 3hodecoa9 + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD18m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxooctadecanoyl-CoA C18:0CoA)	[z] : 3oodcoa + h + nadh <==> 3hodcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD20m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxoeicosanoyl-CoA C18:0CoA)	[z] : 3oescoa + h + nadh <==> 3hescoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD22p_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxodocosanoyl-CoA C18:0CoA)	[w] : 3odscoa + h + nadh <==> 3hdscoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD4m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxobutanoyl-CoA)	[z] : aacoa + h + nadh <==> 3hbycoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD5m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxopentanoyl-CoA)	[z] : 3optcoa + h + nadh <==> 3hptcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD6m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxohexanoyl-CoA)	[z] : 3ohcoa + h + nadh <==> 3hhcoa + nad	Fatty Acid Degradation	EC-1.1.1.35

HACD7m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxoheptanoyl-CoA)	[z] : 3ohpcoa + h + nadh <==> 3hhpcoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD8m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxooctanoyl-CoA)	[z] : 3oocoa + h + nadh <==> 3hocoa + nad	Fatty Acid Degradation	EC-1.1.1.35
HACD9m_mc	3-hydroxyacyl-CoA dehydrogenase (3-oxononanoyl-CoA)	[z] : 3onncoa + h + nadh <==> 3hnncoa + nad	Fatty Acid Degradation	EC-1.1.1.35
MMEm_mc	methylmalonyl-CoA epimerase, myocyte mitochondrial	[z] : mmcoa-S <==> mmcoa-R	Fatty Acid Degradation	EC-5.1.99.1
MMMm_mc	R-methylmalonyl-CoA mutase, myocyte mitochondrial	[z] : mmcoa-R --> succoa	Fatty Acid Degradation	EC-5.4.99.2
PPCOACm_mc	Propionyl-CoA carboxylase, myocyte mitochondrial	[z] : atp + hco3 + ppcoa --> adp + h + mmcoa-S + pi	Fatty Acid Degradation	EC-6.4.1.3
FACOAL120_mc	fatty-acid--CoA ligase (dodecanoate, C12:0), myocyte	[y] : atp + coa + ddca <==> amp + ddcoa + ppi	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL140_mc	fatty-acid--CoA ligase (tetradecanoate, C14:0), myocyte	[y] : atp + coa + ttdca <==> amp + ppi + tdcoa	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL150_mc	fatty-acid--CoA ligase (pentadecanoate, C15:0), myocyte	[y] : atp + coa + ptdca <==> amp + pdcoa + ppi	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL160_mc	fatty-acid--CoA ligase (hexadecanoate, C16:0), myocyte	[y] : atp + coa + hdca <==> amp + pmtcoa + ppi	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL180_mc	fatty-acid--CoA ligase (octadecanoate, C28:0), myocyte	[y] : atp + coa + ocdca <==> amp + ppi + strcoa	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL181_9_mc	fatty-acid--CoA ligase (octadecenoate, C18:1 n-9), myocyte	[y] : atp + coa + ocdcea9 <==> amp + odecoa9 + ppi	Fatty Acid Metabolism	EC-6.2.1.3
FACOAL200_mc	fatty-acid--CoA ligase (eicosanoate, C20:0), myocyte	[y] : atp + coa + ecsa <==> amp + ecsacoa + ppi	Fatty Acid Metabolism	EC-6.2.1.3
ACCOAC_ac	acetyl-CoA carboxylase	[a] : accoa + atp + hco3 --> adp + h + malcoa + pi	Fatty Acid Synthesis	EC-6.4.1.2

GAT_ac_HS_u	unbalanced 1-Acyl-glycerol-3-phosphate acyltransferase, adipocyte cytosol, Homo sapiens specific	[a] : 1ag3p_HS + (0.00032) dcsacoa + (0.00698) ddcoa + (0.00024) dsecoa11 + (0.00056) dsecoa9 + (0.00172) dshcoa3 + (0.00163) dspcoa3 + (0.00016) dspcoa6 + (0.00182) ecsacoa + (0.00272) esdcoa6 + (0.00035) esdcoa9 + (0.00148) esecoa11 + (0.00026) esecoa7 + (0.00732) esecoa9 + (0.00036) espcoa3 + (0.00027) estcoa3 + (0.0023) estcoa6 + (0.00027) ettcoa3 + (0.00311) ettcoa6 + (0.02985) hdcoa7 + (0.00582) hdcoa9 + (0.00295) hpdcoa8 + (0.15761) ocdycacoa6 + (0.00499) odcoa3 + (0.00039) odcoa6 + (0.0026) odecoa5 + (0.01831) odecoa7 + (0.39309) odecoa9 + (0.00138) osttcoa6 + (0.00375) pdcoa + (0.24351) pmtcoa + (0.06379) strcoa + (0.03728) tdcoa + (0.00244) tdecoa5 + (0.00037) tdecoa7 --> coa + pa_HS	Fatty Acid Synthesis	
DESAT141_5_ac	Myristicoyl-CoA desaturase (n-C14:0CoA -> C14:1CoA, n-5), adipocyte	[a] : h + nadph + o2 + tdcoa --> (2) h2o + nadp + tdecoa5	Fatty Acid Synthesis	EC-1.14.19.1
DESAT141_7_ac	Myristicoyl-CoA desaturase (n-C14:0CoA -> C14:1CoA, n-7), adipocyte	[a] : h + nadph + o2 + tdcoa --> (2) h2o + nadp + tdecoa7	Fatty Acid Synthesis	EC-1.14.19.1
DESAT161_7_ac	Palmitoyl-CoA desaturase (n-C16:0CoA -> C16:1CoA, n-7), adipocyte	[a] : h + nadph + o2 + pmtcoa --> (2) h2o + hdcoa7 + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT161_9_ac	Palmitoyl-CoA desaturase (n-C16:0CoA -> C16:1CoA, n-9), adipocyte	[a] : h + nadph + o2 + pmtcoa --> (2) h2o + hdcoa9 + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT171_8_ac	Palmitoyl-CoA desaturase (n-C17:0CoA -> C17:1CoA, n-8), adipocyte	[a] : h + hpdcoa + nadph + o2 --> (2) h2o + hpdcoa8 + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT181_5_ac	stearoyl-CoA desaturase (n-C18:0CoA -> C18:1CoA, n-5), adipocyte	[a] : h + nadph + o2 + strcoa --> (2) h2o + nadp + odecoa5	Fatty Acid Synthesis	EC-1.14.19.1
DESAT181_7_ac	stearoyl-CoA desaturase (n-C18:0CoA -> C18:1CoA, n-7), adipocyte	[a] : h + nadph + o2 + strcoa --> (2) h2o + nadp + odecoa7	Fatty Acid Synthesis	EC-1.14.19.1

DESAT181_9_ac	stearoyl-CoA desaturase (n-C18:0CoA -> C18:1CoA, n-9), adipocyte	[a] : h + nadph + o2 + strcoa --> (2) h2o + nadp + odecoa9	Fatty Acid Synthesis	EC-1.14.19.1
DESAT201_11_ac	stearoyl-CoA desaturase (n-C20:0CoA -> C20:1CoA, n-11), adipocyte	[a] : ecsacoa + h + nadph + o2 --> esecoa11 + (2) h2o + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT201_7_ac	stearoyl-CoA desaturase (n-C20:0CoA -> C20:1CoA, n-7), adipocyte	[a] : ecsacoa + h + nadph + o2 --> esecoa7 + (2) h2o + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT201_9_ac	stearoyl-CoA desaturase (n-C20:0CoA -> C20:1CoA, n-9), adipocyte	[a] : ecsacoa + h + nadph + o2 --> esecoa9 + (2) h2o + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT202_9_ac	stearoyl-CoA desaturase (lumped: n-C20:0CoA -> C20:2CoA, n-9), adipocyte	[a] : ecsacoa + (2) h + (2) nadph + (2) o2 --> esdcoa9 + (4) h2o + (2) nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT221_11_ac	stearoyl-CoA desaturase (n-C22:0CoA -> C22:1CoA, n-11), adipocyte	[a] : dcsacoa + h + nadph + o2 --> dsecoa11 + (2) h2o + nadp	Fatty Acid Synthesis	EC-1.14.19.1
DESAT221_9_ac	stearoyl-CoA desaturase (n-C22:0CoA -> C22:1CoA, n-9), adipocyte	[a] : dcsacoa + h + nadph + o2 --> dsecoa9 + (2) h2o + nadp	Fatty Acid Synthesis	EC-1.14.19.1
FACOAL120_ac	fatty-acid--CoA ligase (dodecanoate, C12:0), adipocyte	[a] : atp + coa + ddca <==> amp + ddcoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL140_ac	fatty-acid--CoA ligase (tetradecanoate, C14:0), adipocyte	[a] : atp + coa + ttdca <==> amp + ppi + tdcoa	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL141_5_ac	fatty-acid--CoA ligase (tetradecenoate, C14:1 n-5), adipocyte	[a] : atp + coa + ttdcea5 <==> amp + ppi + tdecoa5	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL141_7_ac	fatty-acid--CoA ligase (tetradecenoate, C14:1 n-7), adipocyte	[a] : atp + coa + ttdcea7 <==> amp + ppi + tdecoa7	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL150_ac	fatty-acid--CoA ligase (heptadecanoate, C15:0), adipocyte	[a] : atp + coa + ptdca <==> amp + pdcoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL160_ac	fatty-acid--CoA ligase (hexadecanoate, C16:0), adipocyte	[a] : atp + coa + hdca <==> amp + pmtcoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL161_7_ac	fatty-acid--CoA ligase (hexadecenoate, C16:1 n-7), adipocyte	[a] : atp + coa + hdcea7 <==> amp + hdcoa7 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL161_9_ac	fatty-acid--CoA ligase (hexadecenoate, C16:1 n-9), adipocyte	[a] : atp + coa + hdcea9 <==> amp + hdcoa9 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL170_ac	fatty-acid--CoA ligase (heptadecanoate, C17:0), adipocyte	[a] : atp + coa + hpdca <==> amp + hpdcoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3

FACOAL171_8_ac	fatty-acid--CoA ligase (heptadecenoate, C17:1 n-8), adipocyte	[a] : atp + coa + hpdcea8 <==> amp + hpdcoa8 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL180_ac	fatty-acid--CoA ligase (octadecanoate, C18:0), adipocyte	[a] : atp + coa + ocdca <==> amp + ppi + strcoa	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL181_5_ac	fatty-acid--CoA ligase (octadecenoate, C18:1 n-5), adipocyte	[a] : atp + coa + ocdcea5 <==> amp + odecoa5 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL181_7_ac	fatty-acid--CoA ligase (octadecenoate, C18:1 n-7), adipocyte	[a] : atp + coa + ocdcea7 <==> amp + odecoa7 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL181_9_ac	fatty-acid--CoA ligase (octadecenoate, C18:1 n-9), adipocyte	[a] : atp + coa + ocdcea9 <==> amp + odecoa9 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL182_6_ac	fatty-acid--CoA ligase (octadecadienoate, C18:2 n-6), adipocyte	[a] : atp + coa + ocddea6 <==> amp + ocdycacoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL183_3_ac	fatty-acid--CoA ligase (octadecadienoate, C18:3 n-3), adipocyte	[a] : atp + coa + ocdctra3 <==> amp + odcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL183_6_ac	fatty-acid--CoA ligase (octadecadienoate, C18:3 n-6), adipocyte	[a] : atp + coa + ocdctra6 <==> amp + odcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL200_ac	fatty-acid--CoA ligase (eicosanoate, C20:0), adipocyte	[a] : atp + coa + ecsa <==> amp + ecsacoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL201_11_ac	fatty-acid--CoA ligase (eicosenoate, C20:1 n-11), adipocyte	[a] : atp + coa + ecsea11 <==> amp + esecoa11 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL201_7_ac	fatty-acid--CoA ligase (eicosenoate, C20:1 n-7), adipocyte	[a] : atp + coa + ecsea7 <==> amp + esecoa7 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL201_9_ac	fatty-acid--CoA ligase (eicosenoate, C20:1 n-9), adipocyte	[a] : atp + coa + ecsea9 <==> amp + esecoa9 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL202_6_ac	fatty-acid--CoA ligase (eicosadienoate, C20:2 n-6), adipocyte	[a] : atp + coa + ecsdea6 <==> amp + esdcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL202_9_ac	fatty-acid--CoA ligase (eicosadienoate, C20:2 n-9), adipocyte	[a] : atp + coa + ecsdea9 <==> amp + esdcoa9 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL203_3_ac	fatty-acid--CoA ligase (eicosatrienoate, C20:3 n-6), adipocyte	[a] : atp + coa + ecstea3 <==> amp + estcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL203_6_ac	fatty-acid--CoA ligase (eicosatrienoate, C20:3 n-6), adipocyte	[a] : atp + coa + ecstea6 <==> amp + estcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL204_3_ac	fatty-acid--CoA ligase (eicosatetraenoate, C20:4 n-3), adipocyte	[a] : atp + coa + ecsttea3 <==> amp + ettcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL204_6_ac	fatty-acid--CoA ligase (eicosatetraenoate, C20:4 n-6), adipocyte	[a] : atp + coa + ecsttea6 <==> amp + ettcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3

FACOAL205_3_ac	fatty-acid--CoA ligase (eicosapentaenoate, C20:5 n-3), adipocyte	[a] : atp + coa + ecspea3 <==> amp + espcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL220_ac	fatty-acid--CoA ligase (docosanoate, C22:0), adipocyte	[a] : atp + coa + dcsa <==> amp + dcsacoa + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL221_11_ac	fatty-acid--CoA ligase (docosenoate, C22:1 n-11), adipocyte	[a] : atp + coa + dcsea11 <==> amp + dsecoa11 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL221_9_ac	fatty-acid--CoA ligase (docosenoate, C22:1 n-9), adipocyte	[a] : atp + coa + dcsea9 <==> amp + dsecoa9 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL224_6_ac	fatty-acid--CoA ligase (ocosatetraenoate, C22:4 n-6), adipocyte	[a] : atp + coa + ocsttea6 <==> amp + osttcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL225_3_ac	fatty-acid--CoA ligase (docosapentaenoate, C22:5 n-3), adipocyte	[a] : atp + coa + dcspea3 <==> amp + dspcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL225_6_ac	fatty-acid--CoA ligase (docosapentaenoate, C22:5 n-6), adipocyte	[a] : atp + coa + dcspea6 <==> amp + dspcoa6 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FACOAL226_6_ac	fatty-acid--CoA ligase (docosahexaenoate, C22:6 n-6), adipocyte	[a] : atp + coa + dcshea3 <==> amp + dshcoa3 + ppi	Fatty Acid Synthesis	EC-6.2.1.3
FAS100_ac	fatty acid synthase (n-C10:0), adipocyte	[a] : (3) h + malcoa + (2) nadph + octa --> co2 + coa + dca + h2o + (2) nadp	Fatty Acid Synthesis	EC-2.3.1.85
FAS120_ac	fatty acid synthase (n-C12:0), adipocyte	[a] : dca + (3) h + malcoa + (2) nadph --> co2 + coa + ddca + h2o + (2) nadp	Fatty Acid Synthesis	EC-2.3.1.85
FAS140_ac	fatty acid synthase (n-C14:0), adipocyte	[a] : ddca + (3) h + malcoa + (2) nadph --> co2 + coa + h2o + (2) nadp + ttdca	Fatty Acid Synthesis	EC-2.3.1.85
FAS150_ac	fatty acid synthase (C15:0), adipocyte cytosol	[a] : (17) h + (6) malcoa + (12) nadph + ppcoa --> (6) co2 + (7) coa + (5) h2o + (12) nadp + ptdca	Fatty Acid Synthesis	
FAS160_ac	fatty acid synthase (n-C16:0), adipocyte	[a] : (3) h + malcoa + (2) nadph + ttdca --> co2 + coa + h2o + hdca + (2) nadp	Fatty Acid Synthesis	EC-2.3.1.85
FAS170_ac	fatty acid synthase (C17:0), adipocyte cytosol	[a] : (3) h + malcoa + (2) nadph + ptdca --> co2 + coa + h2o + hpdca + (2) nadp	Fatty Acid Synthesis	
FAS180_ac	fatty acid synthase (n-C18:0), adipocyte	[a] : (3) h + hdca + malcoa + (2) nadph --> co2 + coa + h2o + (2) nadp + ocdca	Fatty Acid Synthesis	EC-2.3.1.85
FAS200_ac	fatty acid synthase (n-C20:0), adipocyte	[a] : (3) h + malcoa + (2) nadph + ocdca --> co2 + coa + ecsa + h2o + (2) nadp	Fatty Acid Synthesis	EC-2.3.1.85
FAS220_ac	fatty acid synthase (n-C22:0), adipocyte	[a] : ecsa + (3) h + malcoa + (2) nadph --> co2 + coa + dcsa + h2o + (2) nadp	Fatty Acid Synthesis	EC-2.3.1.85
FAS80_L_ac	fatty acid synthase (n-C8:0), lumped reaction, adipocyte	[a] : accoa + (8) h + (3) malcoa + (6) nadph --> (3) co2 + (4) coa + (2) h2o + (6) nadp + octa	Fatty Acid Synthesis	EC-2.3.1.85

GAT1_ac_HS_ub	unbalanced glycerol 3-phosphate acyltransferase (glycerol 3-phosphate), adipocyte cytosol, Homo sapiens specific	[a] : (0.00032) dcsacoa + (0.00698) ddcoa + (0.00024) dsecoa11 + (0.00056) dsecoa9 + (0.00172) dshcoa3 + (0.00163) dspcoa3 + (0.00016) dspcoa6 + (0.00182) ecsacoa + (0.00272) esdcoa6 + (0.00035) esdcoa9 + (0.00148) esecoa11 + (0.00026) esecoa7 + (0.00732) esecoa9 + (0.00036) espcoa3 + (0.00027) estcoa3 + (0.0023) estcoa6 + (0.00027) ettcoa3 + (0.00311) ettcoa6 + glyc3p + (0.02985) hdcoa7 + (0.00582) hdcoa9 + (0.00295) hpdcoa8 + (0.15761) ocdycacoa6 + (0.00499) odcoa3 + (0.00039) odcoa6 + (0.0026) odecoa5 + (0.01831) odecoa7 + (0.39309) odecoa9 + (0.00138) osttcoa6 + (0.00375) pdcoa + (0.24351) pmtcoa + (0.06379) strcoa + (0.03728) tdcoa + (0.00244) tdecoa5 + (0.00037) tdecoa7 --> 1ag3p_HS + coa	Fatty Acid Synthesis
12DGRH_ac_HS_ub	unbalanced diacylglycerol hydrolase, adipocyte cytosol, Homo sapiens specific	[a] : 12dgr_HS + h2o --> (0.00032) dcsa + (0.00024) dcsea11 + (0.00056) dcsea9 + (0.00172) dcshea3 + (0.00163) dcspea3 + (0.00016) dcspea6 + (0.00698) ddca + (0.00182) ecsa + (0.00272) ecsdea6 + (0.00035) ecsdea9 + (0.00148) ecsea11 + (0.00026) ecsea7 + (0.00732) ecsea9 + (0.00036) ecspea3 + (0.00027) ecstea3 + (0.0023) ecstea6 + (0.00027) ecsttea3 + (0.00311) ecsttea6 + h + (0.24351) hdca + (0.02985) hdcea7 + (0.00582) hdcea9 + (0.00295) hpdcea8 + mglyc_HS + (0.06379) ocdca + (0.0026) ocdcea5 + (0.01831) ocdcea7 + (0.39309) ocdcea9 + (0.00499) ocdctra3 + (0.00039) ocdctra6 + (0.15761) ocddea6 + (0.00138) ocsttea6 + (0.00375) ptdca + (0.03728) ttdca + (0.00244) ttdcea5 + (0.00037) ttdcea7	Triglycerol Degradation EC-3.1.1.3

MGLYCH_ac_HS_ub	unbalanced monoglycerol hydrolase, adipocyte cytosol, Homo sapiens specific	[a] : h2o + mglyc_HS --> (0.00032) dcsa + (0.00024) dcsea11 + (0.00056) dcsea9 + (0.00172) dcshea3 + (0.00163) dcspea3 + (0.00016) dcspea6 + (0.00698) ddca + (0.00182) ecsa + (0.00272) ecsdea6 + (0.00035) ecsdea9 + (0.00148) ecsea11 + (0.00026) ecsea7 + (0.00732) ecsea9 + (0.00036) ecspea3 + (0.00027) ecstea3 + (0.0023) ecstea6 + (0.00027) ecsttea3 + (0.00311) ecsttea6 + glyc + h + (0.24351) hdca + (0.02985) hdcea7 + (0.00582) hdcea9 + (0.00295) hpdcea8 + (0.06379) ocdca + (0.0026) ocdcea5 + (0.01831) ocdcea7 + (0.39309) ocdcea9 + (0.00499) ocdctra3 + (0.00039) ocdctra6 + (0.15761) ocddea6 + (0.00138) ocsttea6 + (0.00375) ptdca + (0.03728) ttdca + (0.00244) ttdcea5 + (0.00037) ttdcea7	Triglycerol Degradation	EC-3.1.1.3
TRIGH_ac_HS_ub	unbalanced triacylglycerol hydrolase, adipocyte cytosol, Homo sapiens specific	[a] : h2o + triglyc_HS --> 12dgr_HS + (0.00032) dcsa + (0.00024) dcsea11 + (0.00056) dcsea9 + (0.00172) dcshea3 + (0.00163) dcspea3 + (0.00016) dcspea6 + (0.00698) ddca + (0.00182) ecsa + (0.00272) ecsdea6 + (0.00035) ecsdea9 + (0.00148) ecsea11 + (0.00026) ecsea7 + (0.00732) ecsea9 + (0.00036) ecspea3 + (0.00027) ecstea3 + (0.0023) ecstea6 + (0.00027) ecsttea3 + (0.00311) ecsttea6 + h + (0.24351) hdca + (0.02985) hdcea7 + (0.00582) hdcea9 + (0.00295) hpdcea8 + (0.06379) ocdca + (0.0026) ocdcea5 + (0.01831) ocdcea7 + (0.39309) ocdcea9 + (0.00499) ocdctra3 + (0.00039) ocdctra6 + (0.15761) ocddea6 + (0.00138) ocsttea6 + (0.00375) ptdca + (0.03728) ttdca + (0.00244) ttdcea5 + (0.00037) ttdcea7	Triglycerol Degradation	EC-3.1.1.3
DAGPYP_ac_HS_ub	unbalanced diacylglycerol pyrophosphate phosphatase, adipocyte cytosol, Homo sapiens specific	[a] : h2o + pa_HS --> 12dgr_HS + pi	Triglycerol Synthesis	EC-3.1.3.4

RIGS_ac_HS_u	unbalanced triglycerol synthesis, adipocyte cytosol, Homo sapiens specific	[a] : 12dgr_HS + (0.00032) dcsacoa + (0.00698) ddcoa + (0.00024) dsecoa11 + (0.00056) dsecoa9 + (0.00172) dshcoa3 + (0.00163) dspcoa3 + (0.00016) dspcoa6 + (0.00182) ecsacoa + (0.00272) esdcoa6 + (0.00035) esdcoa9 + (0.00148) esecoa11 + (0.00026) esecoa7 + (0.00732) esecoa9 + (0.00036) espcoa3 + (0.00027) estcoa3 + (0.0023) estcoa6 + (0.00027) ettcoa3 + (0.00311) ettcoa6 + (0.02985) hdcoa7 + (0.00582) hdcoa9 + (0.00295) hpdcoa8 + (0.15761) ocdycacoa6 + (0.00499) odcoa3 + (0.00039) odcoa6 + (0.0026) odecoa5 + (0.01831) odecoa7 + (0.39309) odecoa9 + (0.00138) osttcoa6 + (0.00375) pdcoa + (0.24351) pmtcoa + (0.06379) strcoa + (0.03728) tdcoa + (0.00244) tdecoa5 + (0.00037) tdecoa7 --> coa + triglyc_HS	Triglycerol Synthesis	

NDPK1_ac	nucleoside-diphosphate kinase (ATP:GDP)	[a] : atp + gdp <==> adp + gtp	Nucleotide Metabolism	EC-2.7.4.6
NDPK1_mc	nucleoside-diphosphate kinase (ATP:GDP)	[y] : atp + gdp <==> adp + gtp	Nucleotide Metabolism	EC-2.7.4.6
ADK1_mc	adenylate kinase, myocyte cytosolic	[y] : amp + atp <==> (2) adp	Nucleotide Salvage Pathways	EC-2.7.4.3
NTPP6m_ac	Nucleoside triphosphate pyrophosphorylase (atp), adipocyte mitochondrial	[b] : atp + h2o --> amp + h + ppi	Nucleotide Salvage Pathways	
ADK1_ac	adenylate kinase, adipocyte cytosolic	[a] : amp + atp <==> (2) adp	Nucleotide Savage Pathway	EC-2.7.4.3
CAT_ac	catalase, adipocyte cytosolic	[a] : (2) h2o2 --> (2) h2o + o2	Other	EC-1.11.1.6
HCO3E_ac	carbonate dehydratase (HCO3 equilibration reaction), adipocyte cytosolic	[a] : co2 + h2o <==> h + hco3	Other	EC-4.2.1.1
HCO3E_mc	carbonate dehydratase (HCO3 equilibration reaction), myocyte cytosolic	[y] : co2 + h2o <==> h + hco3	Other	EC-4.2.1.1
HCO3Ei	carbonate dehydratase (HCO3 equilibration reaction), intra-organism	[i] : co2 + h2o <==> h + hco3	Other	EC-4.2.1.1

NH4DIS_ac	nh4 Dissociation	[a] : nh4 <==> h + nh3	Other
CONTRACTION_mc	muscle contraction, myocyte cytosol	[y] : myoactinADPPi --> adp + myoactin + pi	Contraction
MYOADPPIA_mc	myosin-ADP-Pi attachment, myocyte cytosol	[y] : actin + myosinADPPi --> myoactinADPPi	Contraction
MYOSINATPB_mc	mysosin ATP binding, myocyte cytosol	[y] : atp + myoactin --> actin + myosinATP	Contraction
MYOSINATPH_mc	myosin-ATP hydrolysis, myocyte cytosol	[y] : h2o + myosinATP --> h + myosinADPPi	Contraction
CREATt2is_mc	Creatine Na+ symporter, myocyte cytosol	creat[i] + na1[c] <==> creat[y] + na1[y]	Transport
CRTNtis_mc	creatinine transport, myocyte cytosol	crtn[i] <==> crtn[y]	Transport
Clt_xo	chlorideion transport out via diffusion	cl[e] --> cl[i]	Transport
DCSAtis_ac	docosanoate (C22:0) adipocyte transport	dcsa[a] --> dcsa[i]	Transport
DCSEA11tis_ac	docosenoate (C22:1, n-11) adipocyte transport	dcsea11[a] --> dcsea11[i]	Transport
DCSEA9tis_ac	docosenoate (C22:1, n-9) adipocyte transport	dcsea9[a] --> dcsea9[i]	Transport
DCSHEA3t	docosahexaenoate (C22:6, n-3) transport	dcshea3[e] <==> dcshea3[i]	Transport
DCSHEA3tis_ac	docosahexaenoate (C22:6, n-3) adipocyte transport	dcshea3[i] <==> dcshea3[a]	Transport
DCSPEA3t	Docosapentaenoate (C22:5, n-3) transport	dcspea3[e] <==> dcspea3[i]	Transport
DCSPEA3tis_ac	Docosapentaenoate (C22:5, n-3) adipocyte transport	dcspea3[i] <==> dcspea3[a]	Transport
DCSPEA6t	Docosapentaenoate (C22:5, n-6) transport	dcspea6[e] <==> dcspea6[i]	Transport
DCSPEA6tis_ac	Docosapentaenoate (C22:5, n-6) adipocyte transport	dcspea6[i] <==> dcspea6[a]	Transport
DDCAtis_ac	dodecanoate (C12:0) adipocyte transport	ddca[a] --> ddca[i]	Transport
DDCAtis_mc	dodecanoate (C12:0) myocyte transport	ddca[i] --> ddca[y]	Transport
ECSAtis_ac	eicosanoate (C20:0) adipocyte transport	ecsa[a] --> ecsa[i]	Transport
ECSDEA6t	Eicosadienoate (C20:2, n-6) transport	ecsdea6[e] <==> ecsdea6[i]	Transport
ECSDEA6tis_ac	Eicosadienoate (C20:2, n-6) adipocyte transport	ecsdea6[i] <==> ecsdea6[a]	Transport
ECSDEA9tis_ac	eicosadienoate (C20:2, n-9) adipocyte transport	ecsdea9[a] --> ecsdea9[i]	Transport
ECSEA11tis_ac	eicosenoate (C20:1, n-11) adipocyte transport	ecsea11[a] --> ecsea11[i]	Transport
ECSEA7tis_ac	eicosenoate (C20:1, n-7) adipocyte transport	ecsea7[a] --> ecsea7[i]	Transport

ECSEA9tis_ac	eicosenoate (C20:1, n-9) adipocyte transport	ecsea9[a] --> ecsea9[i]	Transport	
ECSFAtis_mc	eicosanoate transport (n-C20:0)	ecsa[i] <==> ecsa[y]	Transport	
ECSPEA3t	Eicosapentaenoate (C20:5, n-3) transport	ecspea3[e] <==> ecspea3[i]	Transport	
ECSPEA3tis_ac	Eicosapentaenoate (C20:5, n-3) adipocyte transport	ecspea3[i] <==> ecspea3[a]	Transport	
ECSTEA3t	Eicosatrienoate (C20:3, n-3) transport	ecstea3[e] <==> ecstea3[i]	Transport	
ECSTEA3tis_ac	Eicosatrienoate (C20:3, n-3) adipocyte transport	ecstea3[i] <==> ecstea3[a]	Transport	
ECSTEA6t	Eicosatrienoate (C20:3, n-6) transport	ecstea6[e] <==> ecstea6[i]	Transport	
ECSTEA6tis_ac	Eicosatrienoate (C20:3, n-6) adipocyte transport	ecstea6[i] <==> ecstea6[a]	Transport	
ECSTTEA3t	Eicosatetraenoate (C20:4, n-3) transport	ecsttea3[e] <==> ecsttea3[i]	Transport	
ECSTTEA3tis_ac	Eicosatetraenoate (C20:4, n-3) adipocyte transport	ecsttea3[i] <==> ecsttea3[a]	Transport	
ECSTTEA6t	Eicosatetraenoate (C20:4, n-6) transport	ecsttea6[e] <==> ecsttea6[i]	Transport	
ECSTTEA6tis_ac	Eicosatetraenoate (C20:4, n-6) adipocyte transport	ecsttea6[i] <==> ecsttea6[a]	Transport	
GLYCt6is_ac	glycerol transport in/out via symporter, adipocyte	glyc[a] + h[a] <==> glyc[i] + h[i]	Transport	
HCO3t2	HCO3 transport out via diffusion	hco3[e] <==> hco3[i]	Transport	
HDCAtis_ac	hexadecanoate (C16:0) adipocyte transport	hdca[a] --> hdca[i]	Transport	
HDCAtis_mc	hexadecanoate (C16:0) myocyte transport	hdca[i] --> hdca[y]	Transport	
HDCEA7tis_ac	hexadecenoate (C16:1, n-7) adipocyte transport	hdcea7[a] --> hdcea7[i]	Transport	
HDCEA9tis_ac	hexadecenoate (C16:1, n-9) adipocyte transport	hdcea9[a] --> hdcea9[i]	Transport	
HPDCEA8tis_ac	heptadecenoate (C17:1, n-8) adipocyte transport	hpdcea8[a] --> hpdcea8[i]	Transport	
ILEtis_ac	L-isoeucine transport in/out via proton symport, adipocyte	h[i] + ile-L[i] <==> h[a] + ile-L[a]	Transport	TC-2.A.26
NAt	sodium transport in/out via proton antiport (one H+)	h[i] + na1[e] <==> h[e] + na1[i]	Transport	TC-2.A.36
NAtis_mc	sodium transport in/out via the non-selective cation channel	na1[i] <==> na1[y]	Transport	TC-1.A.15
NH4CLt_xo	ammonium chloride transport	cl[i] + nh4[i] <==> cl[e] + nh4[e]	Transport	
NH4tis_ac	ammonia transport via diffusion, adipocyte cytosolic	nh4[i] <==> nh4[a]	Transport	

OCDCAtis_ac	octadecanoate (C18:0) adipocyte transport	ocdca[a] --> ocdca[i]	Transport
OCDCAtis_mc	octadecanoate (C18:0) myocyte transport	ocdca[i] --> ocdca[y]	Transport
OCDCEA5tis_ac	octadecenoate (C18:1, n-5) adipocyte transport	ocdcea5[a] --> ocdcea5[i]	Transport
OCDCEA7tis_ac	octadecenoate (C18:1, n-7) adipocyte transport	ocdcea7[a] --> ocdcea7[i]	Transport
OCDCEA9tis_ac	octadecenoate (C18:1, n-9) adipocyte transport	ocdcea9[a] --> ocdcea9[i]	Transport
OCDCEA9tis_mc	octadecenoate (C18:1, n-9) myocyte transport	ocdcea9[i] --> ocdcea9[y]	Transport
OCDCTRA3t	Octadecatrienoate (C18:3, n-3) transport	ocdctra3[e] <==> ocdctra3[i]	Transport
OCDCTRA3tis_ac	Octadecatrienoate (C18:3, n-3) adipocyte transport	ocdctra3[i] <==> ocdctra3[a]	Transport
OCDCTRA6t	Octadecatrienoate (C18:3, n-6) transport	ocdctra6[e] <==> ocdctra6[i]	Transport
OCDCTRA6tis_ac	Octadecatrienoate (C18:3, n-6) adipocyte transport	ocdctra6[i] <==> ocdctra6[a]	Transport
OCDDEA6t	Octadecadienoate (C18:2, n-6) transport	ocddea6[e] <==> ocddea6[i]	Transport
OCDDEA6tis_ac	Octadecadienoate (C18:2, n-6) adipocyte transport	ocddea6[i] <==> ocddea6[a]	Transport
OCSTTEA6t	Ocosatetraenoate (C22:4, n-6) transport	ocsttea6[e] <==> ocsttea6[i]	Transport
OCSTTEA6tis_ac	Ocosatetraenoate (C22:4, n-6) adipocyte transport	ocsttea6[i] <==> ocsttea6[a]	Transport
Plt2_xo	phosphate transport in via proton symport	h[e] + pi[e] <==> h[i] + pi[i]	Transport
PTDCAtis_ac	pentadecanoate (C15:0) adipocyte transport	ptdca[a] --> ptdca[i]	Transport
PTDCAtis_mc	pentadecanoate (C15:0) myocyte transport	ptdca[i] --> ptdca[y]	Transport
TTDCAtis_ac	tetradecanoate (C14:0) adipocyte transport	ttdca[a] --> ttdca[i]	Transport
TTDCAtis_mc	tetradecanoate (C14:0) myocyte transport	ttdca[i] --> ttdca[y]	Transport
TTDCEA5tis_ac	tetradecenoate (C14:1, n-5) adipocyte transport	ttdcea5[a] --> ttdcea5[i]	Transport
TTDCEA7tis_ac	tetradecenoate (C14:1, n-7) adipocyte transport	ttdcea7[a] --> ttdcea7[i]	Transport
G6Pter_ac	glucose 6-phosphate adipocyte endoplasmic reticular transport via diffusion	g6p[a] <==> g6p[f]	Transport, Endoplasmic Reticular

G6Pter_mc	glucose 6-phosphate myocyte endoplasmic reticular transport via diffusion	g6p[y] <==> g6p[u]	Transport, Endoplasmic Reticular
GLCter_ac	glucose transport, endoplasmic reticulum	glc-D[a] <==> glc-D[f]	Transport, Endoplasmic Reticular.
GLCter_mc	glucose transport, endoplasmic reticulum	glc-D[y] <==> glc-D[u]	Transport, Endoplasmic Reticular
CO2t_xo	CO2 transport via diffusion	co2[e] <==> co2[i]	Transport, Extracellular
CO2tis_ac	CO2 adipocyte transport out via diffusion	co2[i] <==> co2[a]	Transport, Extracellular
CO2tis_mc	CO2 myocyte transport out via diffusion	co2[i] <==> co2[y]	Transport, Extracellular
CRTNt	creatinine transport	crtn[i] <==> crtn[e]	Transport, Extracellular
GLCt1_xo	glucose transport (uniport: facilitated diffusion), intra-organism	glc-D[e] <==> glc-D[i]	Transport, Extracellular
GLCt1is_ac	glucose transport into adipocyte (uniport: facilitated diffusion)	glc-D[i] <==> glc-D[a]	Transport, Extracellular
GLCt1is_mc	glucose transport into myocyte (uniport: facilitated diffusion)	glc-D[i] <==> glc-D[y]	Transport, Extracellular
H2Ot5_xo	H2O transport via diffusion	h2o[e] <==> h2o[i]	Transport, Extracellular
H2Ot5is_ac	H2O transport into adipocyte via diffusion	h2o[i] <==> h2o[a]	Transport, Extracellular
H2Ot5is_mc	H2O transport into myocyte via diffusion	h2o[i] <==> h2o[y]	Transport, Extracellular
ILEt	L-isoeucine transport in/out via proton symport	h[e] + ile-L[e] <==> h[i] + ile-L[i]	Transport, Extracellular TC-2.A.26
L-LACt2_xo	L-lactate transport via proton symport	h[e] + lac-L[e] <==> h[i] + lac-L[i]	Transport, Extracellular
L-LACt2is_mc	L-lactate reversible transport into myocyte via proton symport	h[i] + lac-L[i] <==> h[y] + lac-L[y]	Transport, Extracellular
O2t_xo	O2 transport via diffusion	o2[e] <==> o2[i]	Transport, Extracellular
O2tis_ac	O2 transport into adipocyte via diffusion	o2[i] <==> o2[a]	Transport, Extracellular
O2tis_mc	O2 transport into myocyte via diffusion	o2[i] <==> o2[y]	Transport, Extracellular
Plt2_xo [deleted 08/26/2004 01:34:57 PM]	phosphate transport in via proton symport	h[e] + pi[e] --> h[i] + pi[i]	Transport, Extracellular
Plt6is_ac	phosphate transport in/out of adipocyte via proton symporter	h[i] + pi[i] <==> h[a] + pi[a]	Transport, Extracellular TC-2.A.20

Pit6is_mc	phosphate transport in/out of myocyte via proton symporter	h[i] + pi[i] <==> h[y] + pi[y]	Transport, Extracellular TC-2.A.20
3MOPtm_ac	3-Methyl-2-oxopentanoate transport, diffusion, adipocyte mitochondrial	3mop[a] <==> 3mop[b]	Transport, Mitochondrial
ATP/ADPtm_ac	ATP/ADP transport, adipocyte mitochondrial	adp[a] + atp[b] <==> adp[b] + atp[a]	Transport, Mitochondrial
ATP/ADPtm_mc	ATP/ADP transport, myocyte mitochondrial	adp[y] + atp[z] <==> adp[z] + atp[y]	Transport, Mitochondrial
CITtam_ac	citrate transport, adipocyte mitochondrial	cit[a] + mal-L[b] <==> cit[b] + mal-L[a]	Transport, Mitochondrial
CITtam_mc	citrate transport, myocyte mitochondrial	cit[y] + mal-L[z] <==> cit[z] + mal-L[y]	Transport, Mitochondrial
CO2tm_ac	CO2 transport (diffusion), adipocyte mitochondrial	co2[a] <==> co2[b]	Transport, Mitochondrial
CO2tm_mc	CO2 transport (diffusion), myocyte mitochondrial	co2[y] <==> co2[z]	Transport, Mitochondrial
CRNCARtm_mc	carnithine-acetylcarnithine carrier, myocyte mitochondrial	acrn[y] + crn[z] --> acrn[z] + crn[y]	Transport, Mitochondrial
CRNODETm_mc	carnitine 9-cis-octadecenoyltransferase II, myocyte	coa[z] + odecrn9[y] <==> crn[y] + odecoa9[z]	Transport, Mitochondrial
CRNPTDTm_mc	carnitine pentadecanoyltransferase II, myocyte	coa[z] + pdcrn[y] <==> crn[y] + pdcoa[z]	Transport, Mitochondrial
DHAP1tm_ac	dihydroxyacetone phosphate transport, adipocyte mitochondrial	dhap[a] <==> dhap[b]	Transport, Mitochondrial
DHAP1tm_mc	dihydroxyacetone phosphate transport, myocyte mitochondrial	dhap[y] <==> dhap[z]	Transport, Mitochondrial
GACm_ac	glutamate aspartate carrier, adipocyte cytosolic/mitochondrial	asp-L[b] + glu-L[a] + h[a] --> asp-L[a] + glu-L[b] + h[b]	Transport, Mitochondrial
GACm_mc	glutamate aspartate carrier, myocyte cytosolic/mitochondrial	asp-L[z] + glu-L[y] + h[y] --> asp-L[y] + glu-L[z] + h[z]	Transport, Mitochondrial
GL3Ptm_mc	glycerol-3-phosphate transport, myocyte mitochondrial	glyc3p[y] <==> glyc3p[z]	Transport, Mitochondrial
GTPt3m_ac	GTP/GDP transporter, adipocyte mitochondrial	gdp[b] + gtp[a] + h[a] --> gdp[a] + gtp[b] + h[b]	Transport, Mitochondrial
GTPt3m_mc	GTP/GDP transporter, myocyte mitochondrial	gdp[z] + gtp[y] + h[y] --> gdp[y] + gtp[z] + h[z]	Transport, Mitochondrial
H2Otm_ac	H2O transport, adipocyte mitochondrial	h2o[a] <==> h2o[b]	Transport, Mitochondrial
H2Otm_mc	H2O transport, myocyte mitochondrial	h2o[y] <==> h2o[z]	Transport, Mitochondrial

MALAKGtm_ac	malate-alphaketoglutarate transporter, adipocyte mitochondria	akg[b] + mal-L[a] --> akg[a] + mal-L[b]	Transport, Mitochondrial	
MALAKGtm_mc	malate-alphaketoglutarate transporter, myocyte mitochondria	akg[z] + mal-L[y] --> akg[y] + mal-L[z]	Transport, Mitochondrial	
O2trm_ac	O2 transport into adipocyte mitochondria (diffusion)	o2[a] <==> o2[b]	Transport, Mitochondrial	
O2trm_mc	O2 transport into myocyte mitochondria (diffusion)	o2[y] <==> o2[z]	Transport, Mitochondrial	
PItm_ac	phosphate transporter, adipocyte mitochondrial	h[a] + pi[a] <==> h[b] + pi[b]	Transport, Mitochondrial	
PItm_mc	phosphate transporter, myocyte mitochondrial	h[y] + pi[y] <==> h[z] + pi[z]	Transport, Mitochondrial	
PPAtm_ac	propionate transport in/out via proton symport, adipocyte	h[a] + ppa[a] <==> h[b] + ppa[b]	Transport, Mitochondrial	TC-2.A.20
PYRtm_ac	pyruvate transport, adipocyte mitochondrial	h[a] + pyr[a] <==> h[b] + pyr[b]	Transport, Mitochondrial	
PYRtm_mc	pyruvate transport, myocyte mitochondrial	h[y] + pyr[y] <==> h[z] + pyr[z]	Transport, Mitochondrial	
CRNCARtp_mc	carnithine-acetylcarnithine carrier, myocyte peroxixome	acrn[y] + crn[w] <==> acrn[w] + crn[y]	Transport, Peroxisomal	

What is claimed is:

1. A computer readable medium or media, comprising:

(a) a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(b) a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(c) a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(d) a constraint set for said plurality of reactions for said first, second and third data structures, and

(e) commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

2. The computer readable medium or media of claim 1, wherein said first data structure comprises a first reaction network.

3. The computer readable medium or media of claim 1, wherein said second data structure comprises a second reaction network.

4. The computer readable medium or media of claim 1, wherein said first or second data structures comprise a plurality of reaction networks.

5. The computer readable medium or media of claim 1, further comprising one or more fourth data structures and one or more fourth constraint sets, each fourth data structure relating a plurality of reactants to a plurality of reactions from a one or more

third cells within a multicellular organism, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product.

6. The computer readable medium or media of claim 5, wherein said one or more fourth data structures comprises a plurality of data structures.

7. The computer readable medium or media of claim 6, wherein said plurality of data structures comprise a data structure for a plurality of different cells.

8. The computer readable medium or media of claim6, wherein said plurality of data structures comprise a data structure for a plurality of different cell types.

9. The computer readable medium or media of claim 7 or 8, wherein said one or more third cells comprise at least 4 cells, 5 cells, 6 cells, 7 cells, 8 cells, 9 cells, 10 cells, 100 cells, 1000 cells, 5000 cells, 10,000 cells or more.

10. The computer readable medium or media of claim 1, wherein said first and second cells comprise eukaryotic cells.

11. The computer readable medium or media of claim 1, wherein said first and second cells comprise prokaryotic cells.

12. The computer readable medium or media of claim 10, wherein said first and second eukaryotic cells comprise cells of the same tissue or organ.

13. The computer readable medium or media of claim 10, wherein said first and second eukaryotic cells comprise cells of different tissues or organs.

14. The computer readable medium or media of claim 1, wherein at least one of said reactions is annotated to indicate an associated gene.

15. The computer readable medium or media of 14, further comprising a gene database having information characterizing said associated gene.

16. The computer readable medium or media of claim 1, wherein at least one of said reactions is a regulated reaction.

17. The computer readable medium or media of claim 16, wherein said constraint set includes a variable constraint for said regulated reaction.

18. The computer readable medium or media of claim 1, wherein said at least one intra-system reaction comprises one or more reactions performed in the hematopoietic system, urine, connective tissue, contractile system, lymphatic system, respiratory system or renal system..

19. The computer readable medium or media of claim 18, wherein said intra-system reactions comprise a reactant or reactions selected from the group consisting of a bicarbonate buffer system, an ammonia buffer system, a hormone, a signaling molecule, a vitamin, a mineral or a combination thereof.

20. The computer readable medium or media of claim 1, wherein said first or second cell is selected from a mammary gland cell, hepatocyte, white fat cell, brown fat cell, liver lipocyte, red skeletal muscle cell, white skeletal muscle cell, intermediate skeletal muscle cell, smooth muscle cell, red blood cell, adipocyte, monocyte, reticulocyte, fibroblast, neuronal cell epithelial cell or a cell set forth in Table 5.

21. The computer readable medium or media of claim 1, wherein said physiological function is selected from metabolite yield, ATP yield, biomass demand, growth, triacylglycerol storage, muscle contraction, milk secretion and oxygen transport capacity.

22. The computer readable medium or media of claim 1, wherein said data structure comprises a set of linear algebraic equations.

23. The computer readable medium or media of claim 1, wherein said commands comprise an optimization problem.

24. The computer readable medium or media of claim 1, wherein at least one reactant in said plurality of reactants or at least one reaction in said plurality of reactions is annotated with an assignment to a subsystem or compartment.

25. The computer readable medium or media of claim 24, wherein a first substrate or product in said plurality of reactions is assigned to a first compartment and a

second substrate or product in said plurality of reactions is assigned to a second compartment.

26. The computer readable medium or media of claim 15, wherein a plurality of reactions is annotated to indicate a plurality of associated genes and wherein said gene database comprises information characterizing said plurality of associated genes.

27. A computer readable medium or media, comprising:

(a) a plurality of first data structures each relating a plurality of reactants to a plurality of reactions from a plurality of first cells within a multicellular organism, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;;

(b) a plurality of second data structures each relating a plurality of reactants to a plurality of reactions from a plurality of second cells within said multicellular organism, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(c) a plurality of third data structures each relating a plurality of intra-system reactants to a plurality of intra-system reactions within said multicellular organism, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(d) a constraint set for said plurality of reactions for said first, second and third data structures, and

(e) commands for determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said multicellular organism.

28. The computer readable medium or media of claim 27, wherein said first data structure comprises a first reaction network.

29. The computer readable medium or media of claim 27, wherein said second data structure comprises a second reaction network.

30. The computer readable medium or media of claim 27, wherein said first or second data structures comprise a plurality of reaction networks.

31. The computer readable medium or media of claim 27, further comprising plurality of fourth data structures and one or more fourth constraint sets, each of said plurality of fourth data structures relating a plurality of reactants to a plurality of reactions from a plurality of third cells within a multicellular organism, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product.

32. The computer readable medium or media of claim 31, wherein said plurality of first through fourth data structures comprise data structures for a plurality of different cells.

33. The computer readable medium or media of claim 31, wherein said plurality of first through fourth data structures comprise data structures for a plurality of different cell types.

34. The computer readable medium or media of claim 32 or 33, wherein said one or more third cells comprise at least 4 cells, 5 cells, 6 cells, 7 cells, 8 cells, 9 cells, 10 cells, 100 cells, 1000 cells, 5000 cells, 10,000 cells or more.

35. A method for predicting a physiological function of a multicellular organism, comprising:

(a) providing a first data structure relating a plurality of reactants to a plurality of reactions from a first cell, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(b) providing a second data structure relating a plurality of reactants to a plurality of reactions from a second cell, each of said reactions comprising a reactant

identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(c) providing a third data structure relating a plurality of intra-system reactants to a plurality of intra-system reactions between said first and second cells, each of said intra-system reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product;

(d) providing a constraint set for said plurality of reactions for said first, second and third data structures;

(e) providing an objective function, and

(f) determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said first and second data structures, wherein said at least one flux distribution is predictive of a physiological function of said first and second cells.

36. The computer readable medium or media of claim 35, wherein said first data structure comprises a first reaction network.

37. The computer readable medium or media of claim 35, wherein said second data structure comprises a second reaction network.

38. The computer readable medium or media of claim 35, wherein said first or second data structures comprise a plurality of reaction networks.

39. The computer readable medium or media of claim 35, further comprising one or more fourth data structures and one or more fourth constraint sets, each fourth data structure relating a plurality of reactants to a plurality of reactions from a one or more third cells within a multicellular organism, each of said reactions comprising a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product.

40. The computer readable medium or media of claim 39, wherein said one or more fourth data structures comprises a plurality of data structures.

41. The computer readable medium or media of claim 40, wherein said plurality of data structures comprise a data structure for a plurality of different cells.

42. The computer readable medium or media of claim 40, wherein said plurality of data structures comprise a data structure for a plurality of different cell types.

43. The computer readable medium or media of claim 41 or 42, wherein said one or more third cells comprise at least 4 cells, 5 cells, 6 cells, 7 cells, 8 cells, 9 cells, 10 cells, 100 cells, 1000 cells, 5000 cells, 10,000 cells or more.

44. The computer readable medium or media of claim 35, wherein said first and second cells comprise eukaryotic cells.

45. The computer readable medium or media of claim 35, wherein said first and second cells comprise prokaryotic cells.

46. The computer readable medium or media of claim 44, wherein said first and second eukaryotic cells comprise cells of the same tissue or organ.

47. The computer readable medium or media of claim 44, wherein said first and second eukaryotic cells comprise cells of different tissues or organs.

48. The computer readable medium or media of claim 35, wherein at least one of said reactions is annotated to indicate an associated gene.

49. The computer readable medium or media of 48, further comprising a gene database having information characterizing said associated gene.

50. The computer readable medium or media of claim 35, wherein at least one of said reactions is a regulated reaction.

51. The computer readable medium or media of claim 50, wherein said constraint set includes a variable constraint for said regulated reaction.

52. The computer readable medium or media of claim 35, wherein said at least one intra-system reaction comprises one or more reactions performed in the

hematopoietic system, urine, connective tissue, contractile system, lymphatic system, respiratory system or renal system..

53. The computer readable medium or media of claim 52, wherein said intra-system reactions comprise a reactant or reactions selected from the group consisting of a bicarbonate buffer system, an ammonia buffer system, a hormone, a signaling molecule, a vitamin, a mineral or a combination thereof.

54. The computer readable medium or media of claim 35, wherein said first or second cell is selected from a mammary gland cell, hepatocyte, white fat cell, brown fat cell, liver lipocyte, red skeletal muscle cell, white skeletal muscle cell, intermediate skeletal muscle cell, smooth muscle cell, red blood cell, adipocyte, monocyte, reticulocyte, fibroblast, neuronal cell epithelial cell or a cell set forth in Table 5.

55. The computer readable medium or media of claim 35, wherein said physiological function is selected from metabolite yield, ATP yield, biomass demand, growth, triacylglycerol storage, muscle contraction, milk secretion and oxygen transport capacity.

56. The computer readable medium or media of claim 35, wherein said data structure comprises a set of linear algebraic equations.

57. The computer readable medium or media of claim 35, wherein said commands comprise an optimization problem.

58. The computer readable medium or media of claim 35, wherein at least one reactant in said plurality of reactants or at least one reaction in said plurality of reactions is annotated with an assignment to a subsystem or compartment.

59. The computer readable medium or media of claim 58, wherein a first substrate or product in said plurality of reactions is assigned to a first compartment and a second substrate or product in said plurality of reactions is assigned to a second compartment.

60. The computer readable medium or media of claim 49, wherein a plurality of reactions is annotated to indicate a plurality of associated genes and wherein said gene database comprises information characterizing said plurality of associated genes.

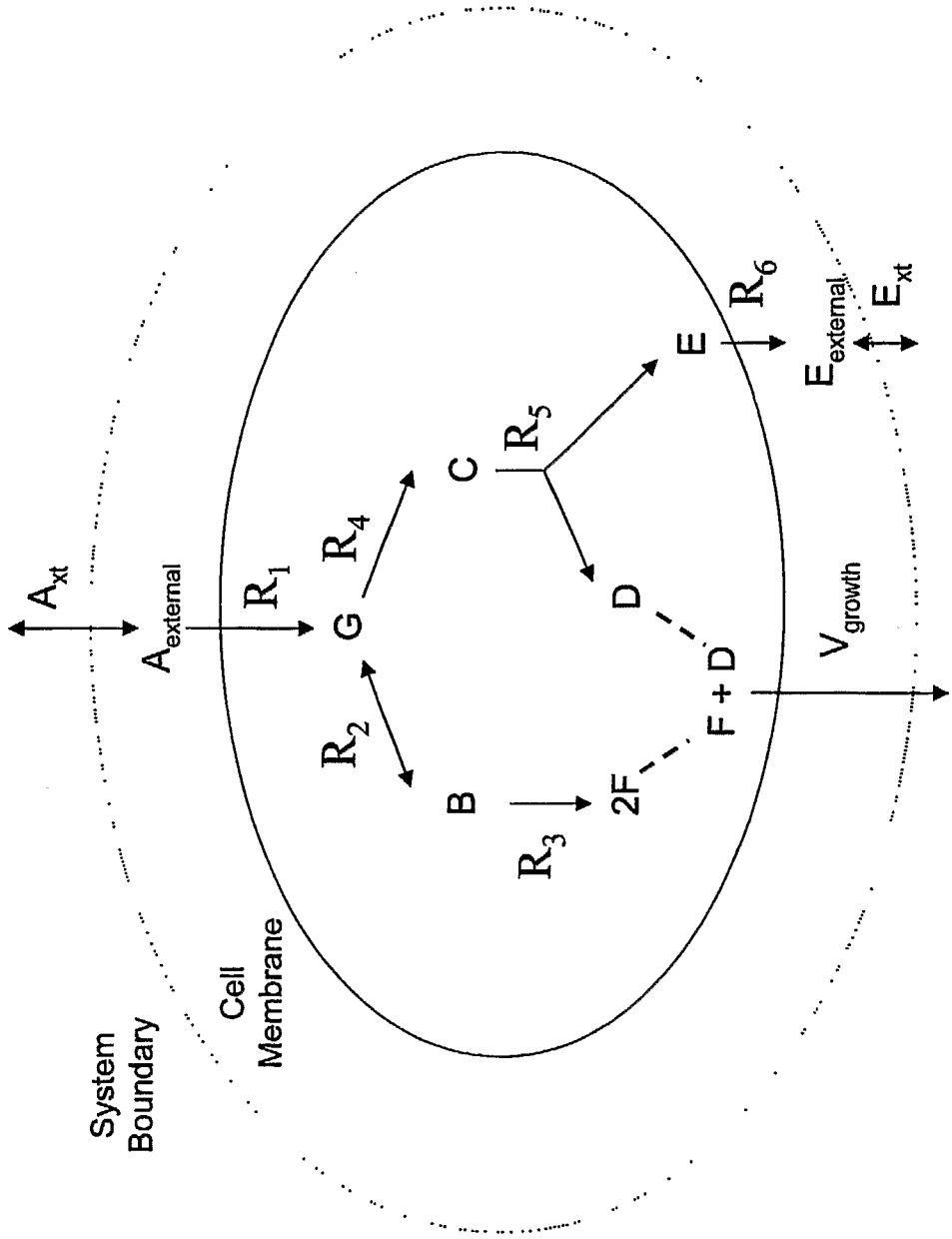

System Boundary
Cell Membrane
A_{xt}
$A_{external}$
R_1
G
R_4
C
R_5
E
R_6
$E_{external}$
E_{xt}
R_2
D
F + D
V_{growth}
B
2F
R_3

FIGURE 1

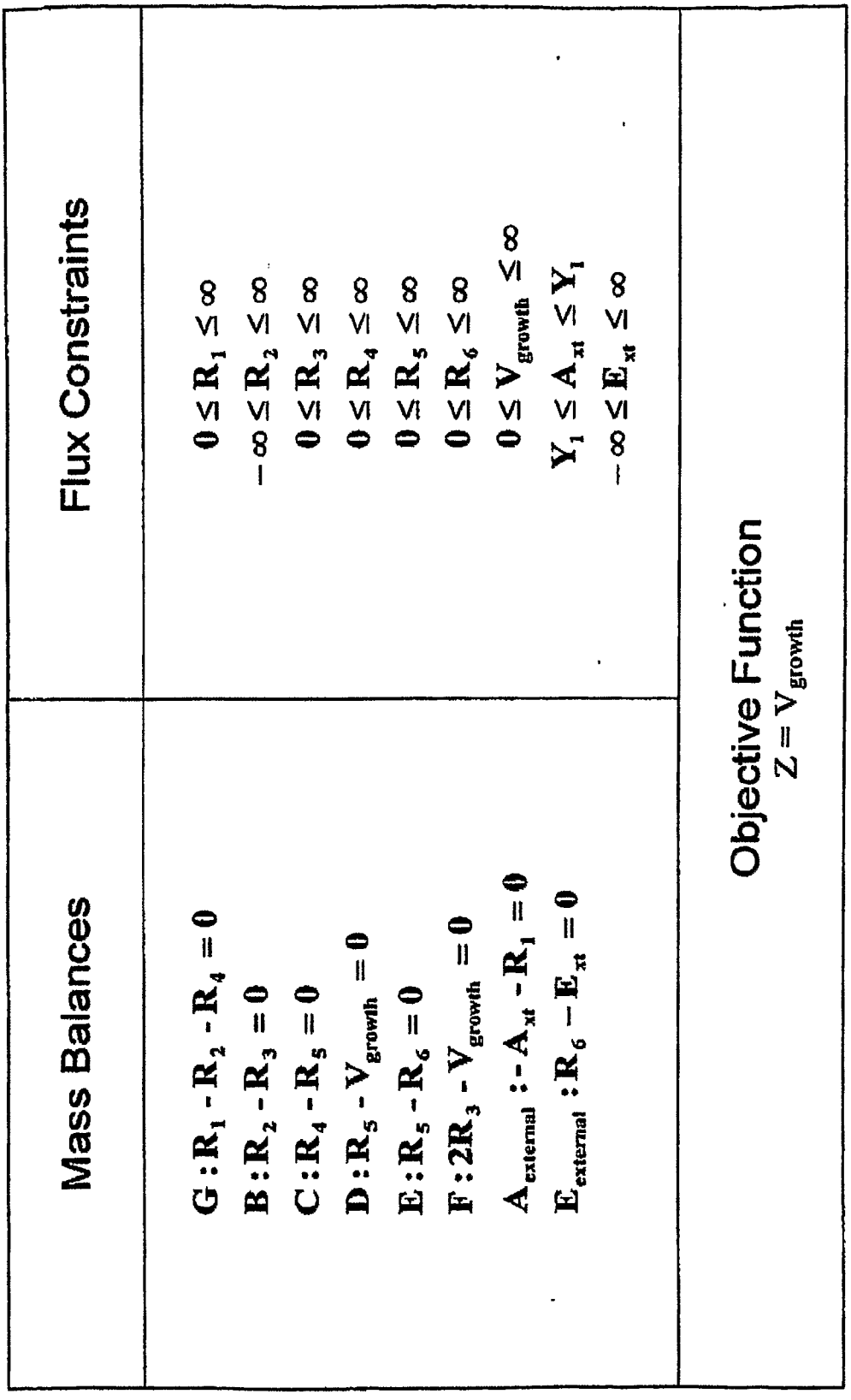

Mass Balances
Flux Constraints
$G: R_1 - R_2 - R_4 = 0$
$B: R_2 - R_3 = 0$
$C: R_4 - R_5 = 0$
$D: R_5 - V_{growth} = 0$
$E: R_5 - R_6 = 0$
$F: 2R_3 - V_{growth} = 0$
$A_{external}: -A_{xt} - R_1 = 0$
$E_{external}: R_6 - E_{xt} = 0$
$0 \le R_1 \le \infty$
$-\infty \le R_2 \le \infty$
$0 \le R_3 \le \infty$
$0 \le R_4 \le \infty$
$0 \le R_5 \le \infty$
$0 \le R_6 \le \infty$
$0 \le V_{growth} \le \infty$
$Y_1 \le A_{xt} \le Y_1$
$-\infty \le E_{xt} \le \infty$
Objective Function
$Z = V_{growth}$

Figure 2

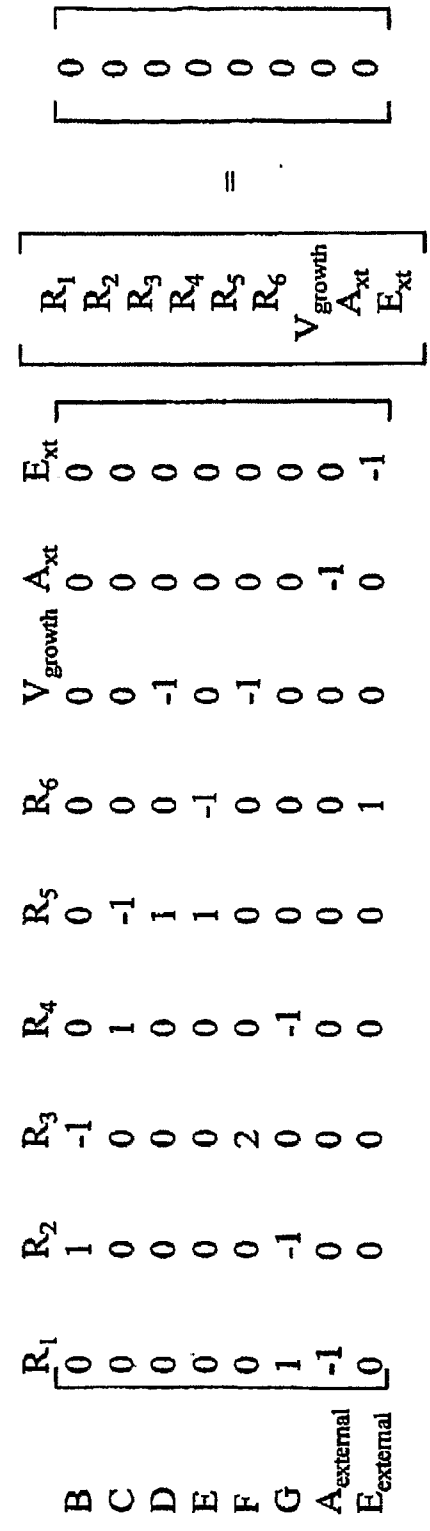

R1 R2 R3 R4 R5 R6 Vgrowth Axt Ext
B 0 1 -1 0 0 0 0 0
C 0 0 0 1 -1 0 0 0
D 0 0 0 0 1 -1 0 0
E 0 0 0 0 0 1 -1 0
F 0 0 2 0 0 0 0 0
G 1 -1 0 -1 0 0 0 0
Aexternal -1 0 0 0 0 0 -1 0
Eexternal 0 0 0 0 0 0 0 -1
=
0 0 0 0 0 0 0 0

Figure 3

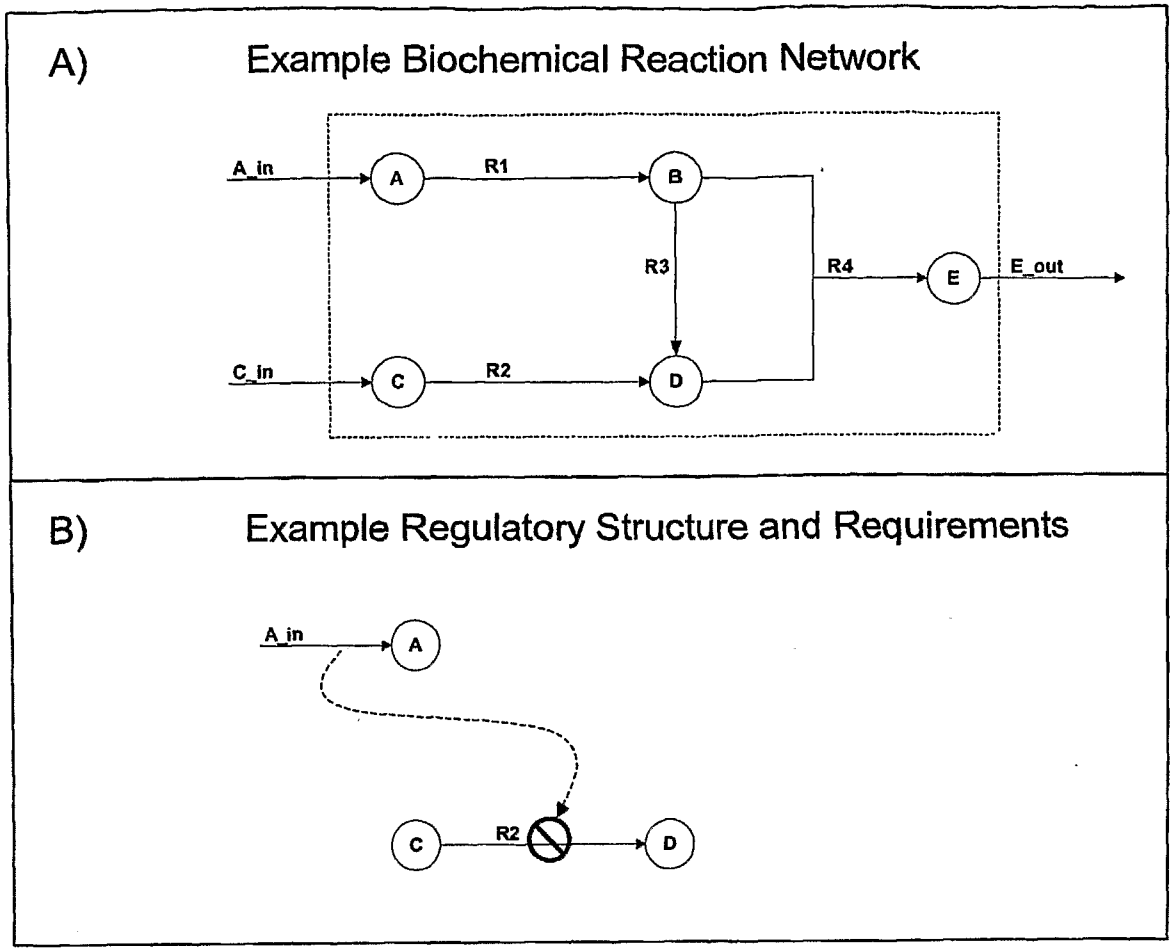

A)
Example Biochemical Reaction Network
A_in
A
R1
B
R3
R4
E
E_out
C_in
C
R2
D
B)
Example Regulatory Structure and Requirements
A_in
A
C
R2
D

FIGURE 4

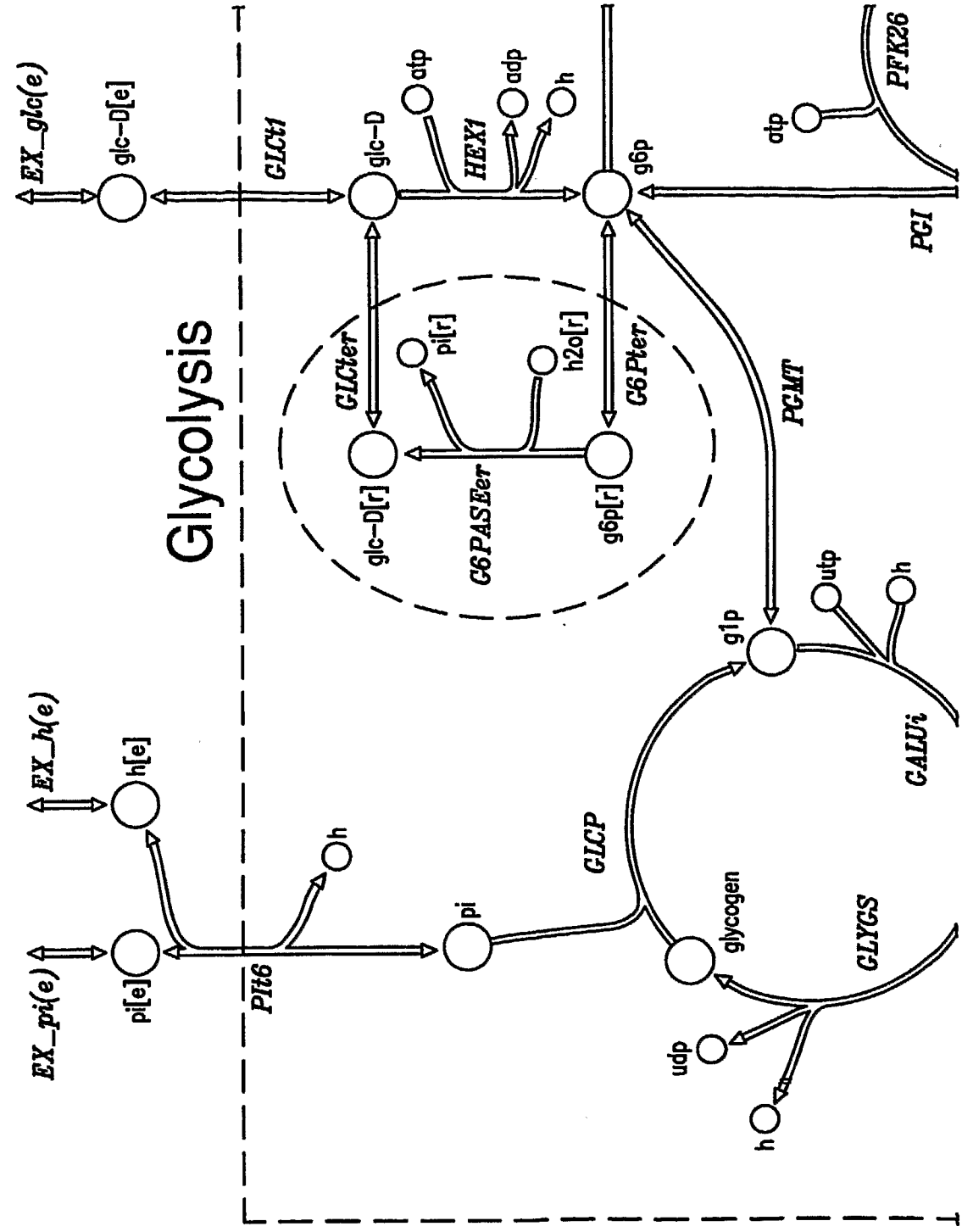
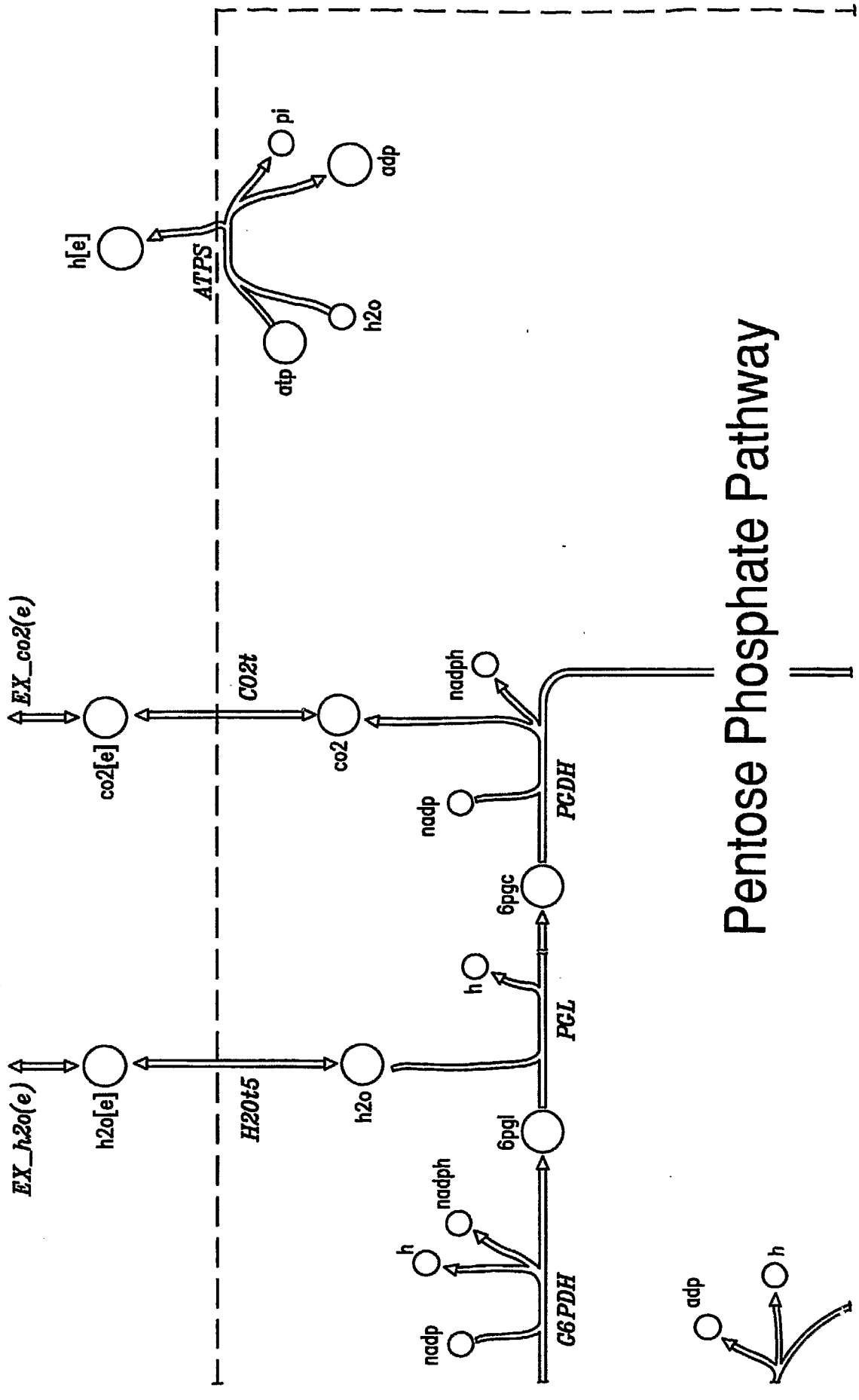

Glycolysis
EX_glc(e)
glc-D[e]
GLCt1
glc-D
atp
HEX1
adp
h
g6p
atp
PFK26
PGI
GLCter
pi[r]
h2o[r]
G6Pter
glc-D[r]
G6PASEer
g6p[r]
PGMT
g1p
utp
h
GALUi
EX_h(e)
h[e]
h
GLCP
pi
glycogen
GLYGS
EX_pi(e)
pi[e]
Pit6
udp
h

FIG. 5-1

FIG. 5-2


Pentose Phosphate Pathway
h[e]
ATPS
pi
adp
atp
h2o
EX_co2(e)
co2[e]
CO2t
co2
nadph
nadp
PGDH
6pgc
h
PGL
EX_h2o(e)
h2o[e]
H2Ot5
h2o
6pgl
nadph
h
nadp
G6PDH
adp
h

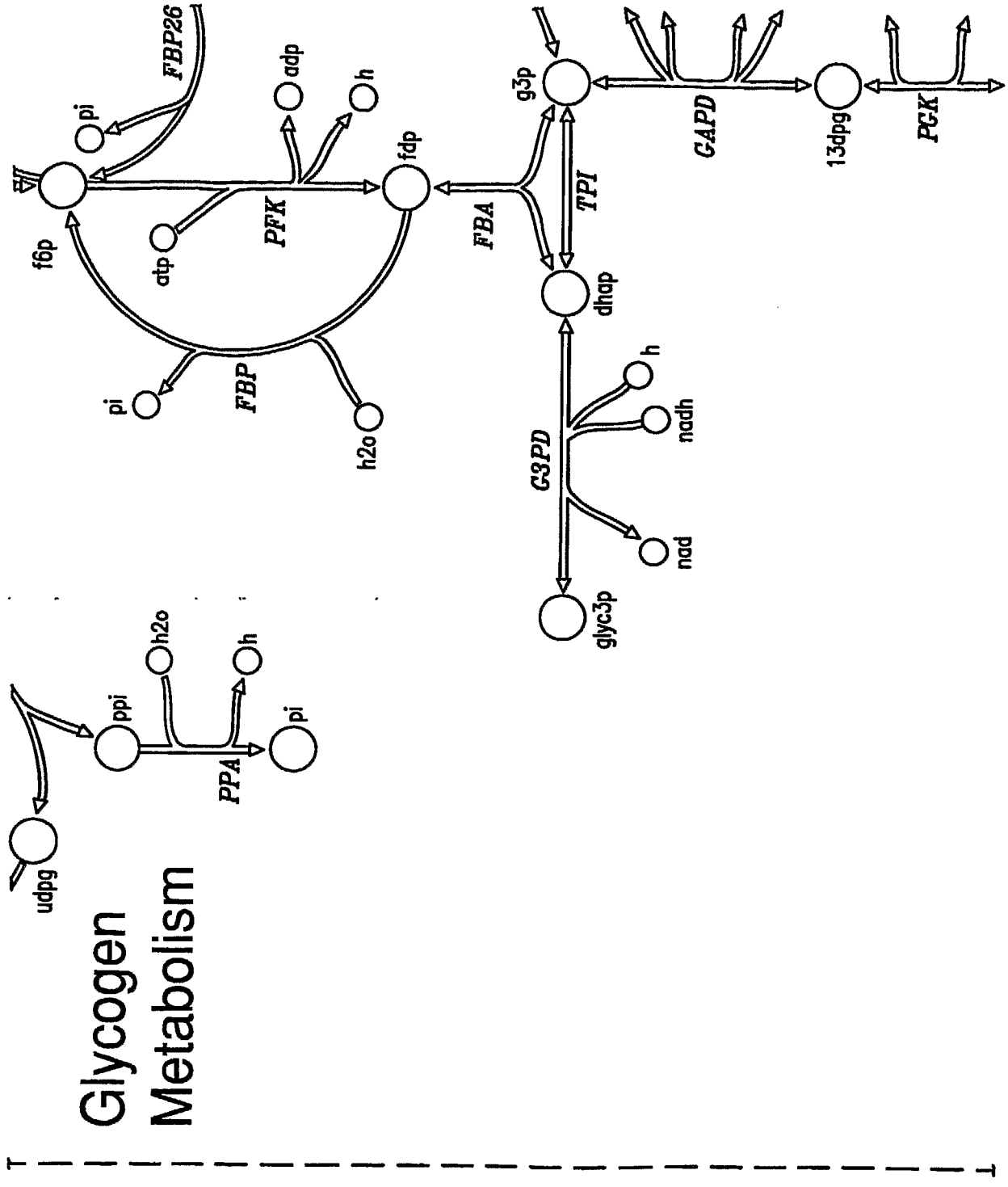
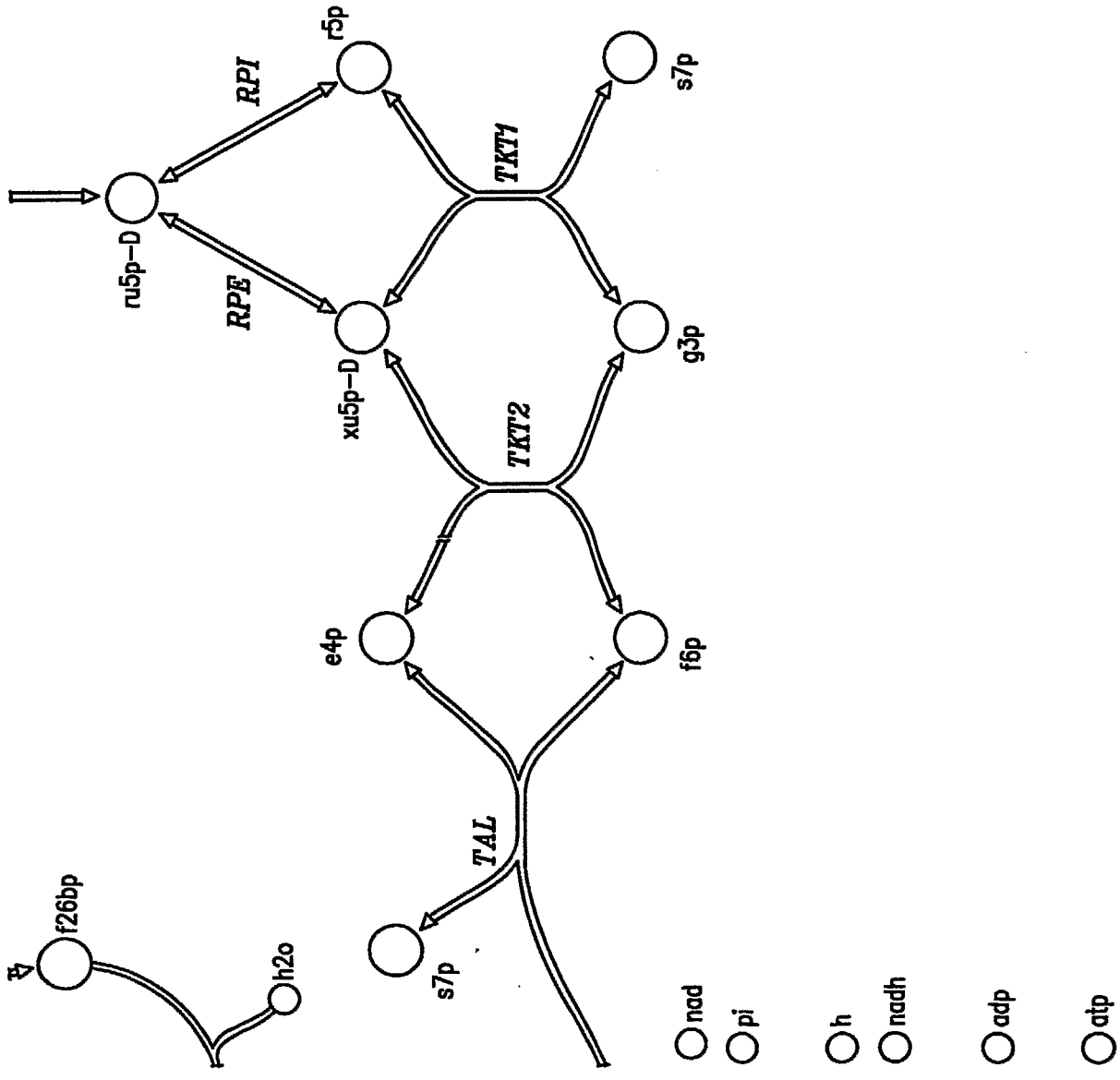

Glycogen Metabolism
udpg
ppi
h2o
h
pi
PPA
f6p
pi
FBP26
adp
h
atp
PFK
fdp
pi
FBP
h2o
g3p
FBA
TPI
dhap
GAPD
13dpg
PGK
h
nadh
G3PD
nad
glyc3p

FIG. 5-3

FIG. 5-4


ru5p-D
RPI
RPE
r5p
xu5p-D
TKT1
TKT2
s7p
g3p
e4p
f6p
TAL
s7p
f26bp
h2o
nad
pi
h
nadh
adp
atp

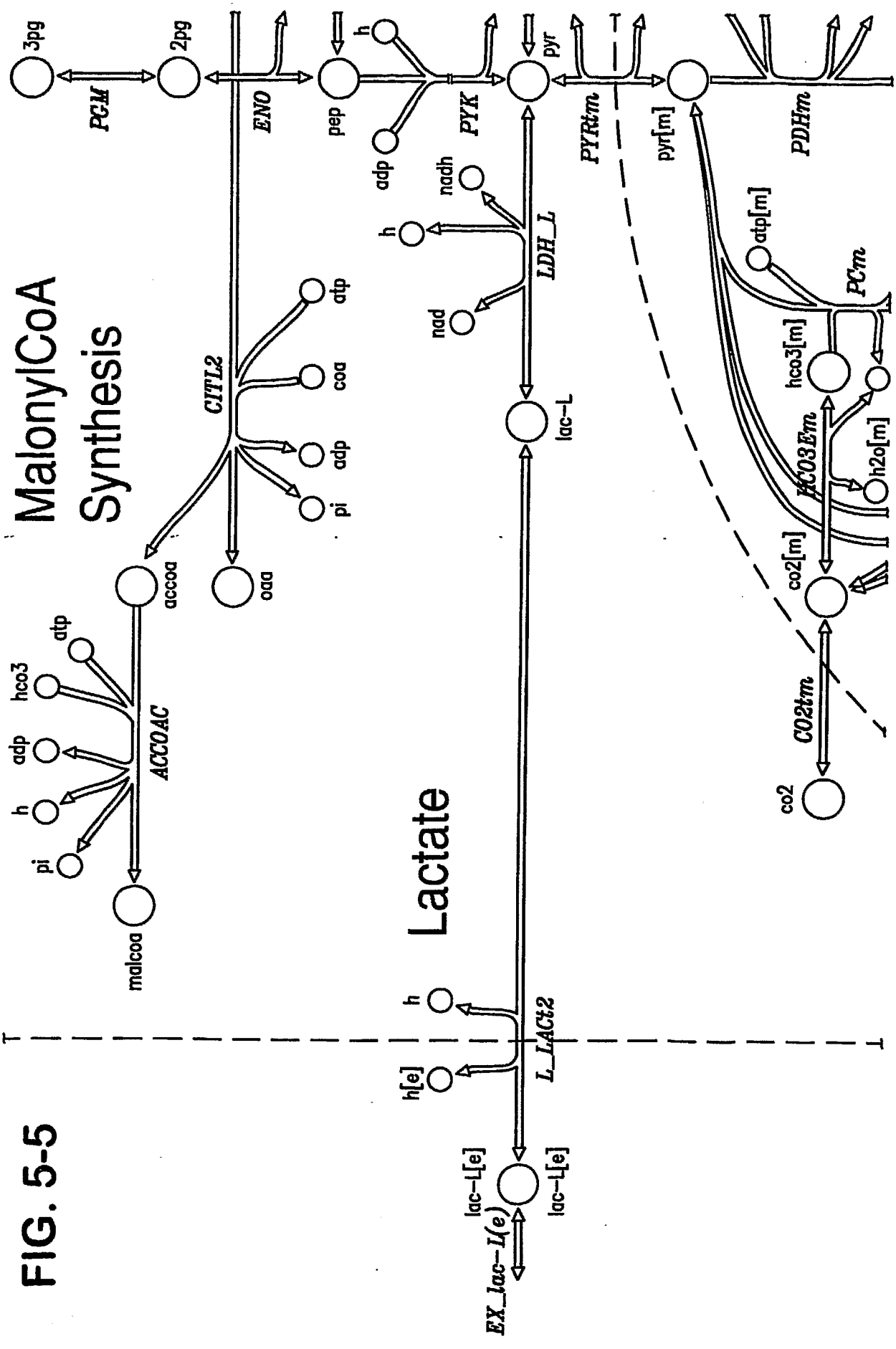

MalonylCoA Synthesis
Lactate
3pg
2pg
PGM
ENO
pep
h
adp
PYK
pyr
PYRtm
pyr[m]
PDHm
nadh
h
nad
LDH_L
lac-L
atp
coa
adp
pi
CITL2
accoa
oaa
atp
hco3
adp
h
pi
ACCOAC
malcoa
atp[m]
PCm
hco3[m]
HCO3Em
h2o[m]
co2[m]
CO2tm
co2
h
h[e]
L_LACt2
lac-L[e]
lac-L[e]
EX_lac-L(e)

FIG. 5-5

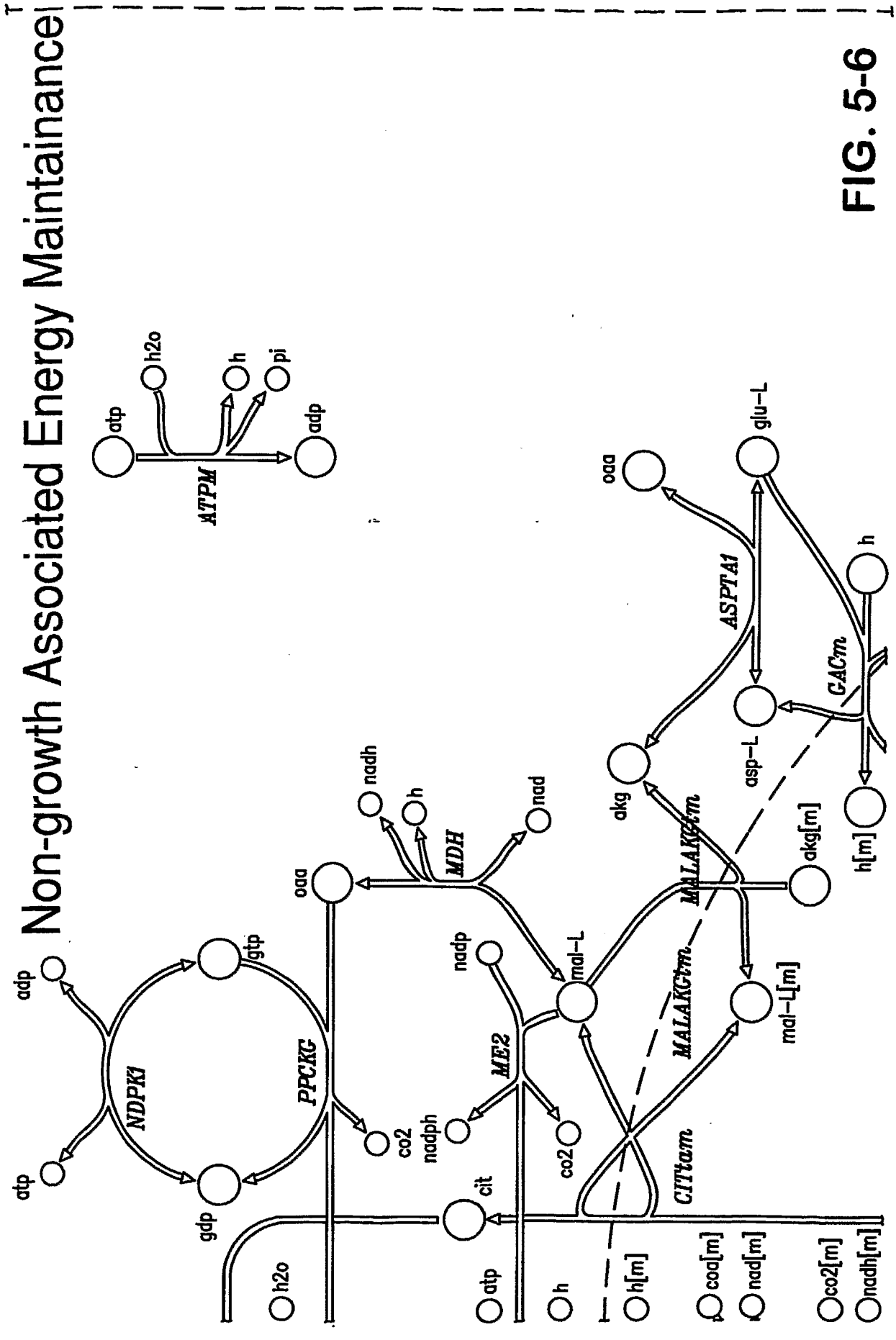

Non-growth Associated Energy Maintainance
atp
h2o
h
pi
adp
ATPM
adp
gtp
NDPK1
atp
gdp
PPCKG
co2
oaa
nadh
h
MDH
nad
nadp
nadph
ME2
co2
mal-L
cit
CITtam
h2o
atp
h
h[m]
coa[m]
nad[m]
co2[m]
nadh[m]
MALAKGtm
MALAKGtm
akg
akg[m]
mal-L[m]
oaa
ASPTA1
glu-L
asp-L
GACm
h
h[m]

FIG. 5-6

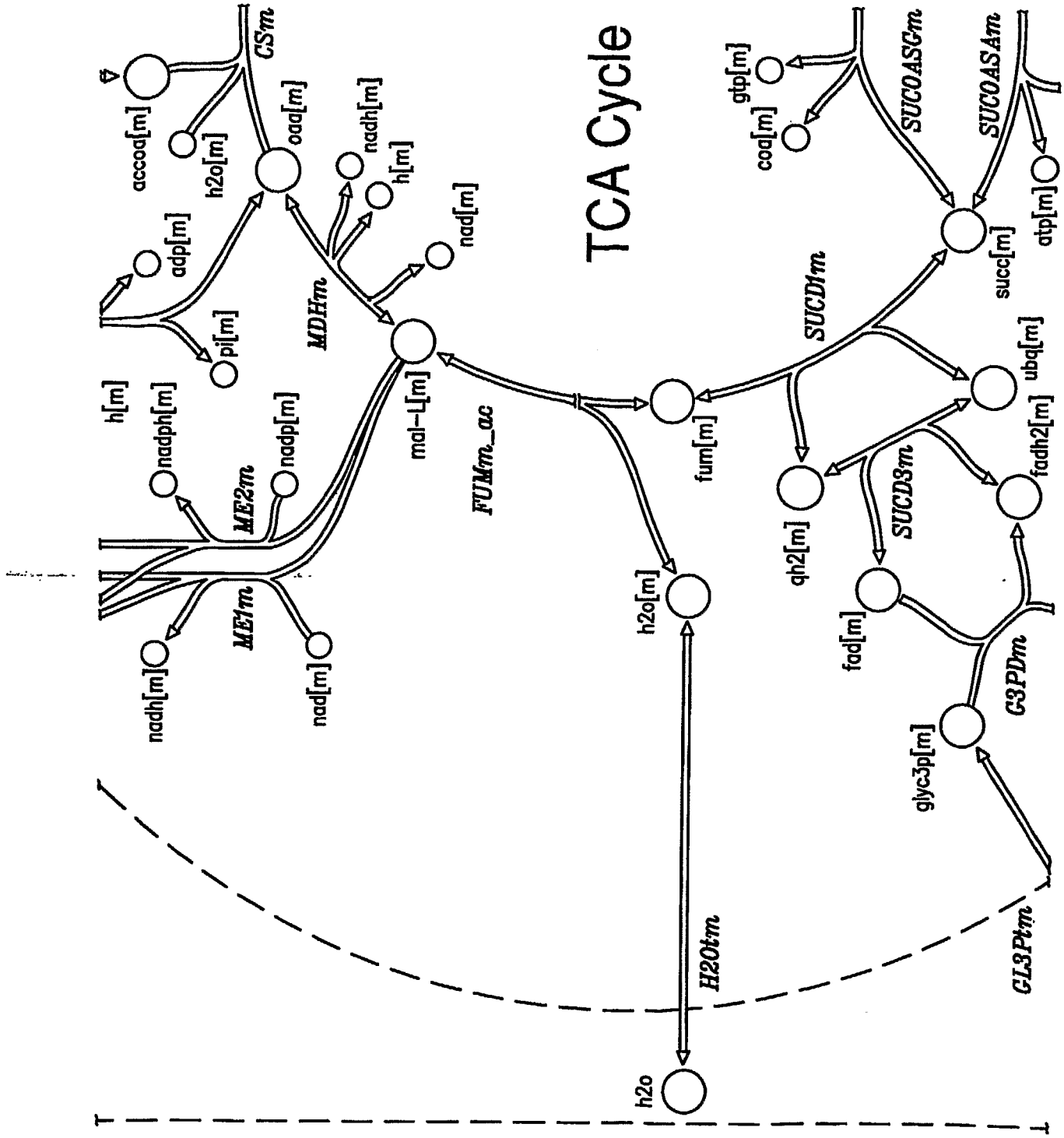

TCA Cycle
accoa[m]
h2o[m]
CSm
oaa[m]
nadh[m]
h[m]
nad[m]
MDHm
adp[m]
pi[m]
h[m]
nadph[m]
nadp[m]
ME2m
ME1m
nadh[m]
nad[m]
mal-L[m]
FUMm_ac
fum[m]
h2o[m]
h2o
H2Otm
gtp[m]
coa[m]
SUCOASGm
SUCOASAm
atp[m]
succ[m]
SUCDtm
ubq[m]
fadh2[m]
qh2[m]
SUCD3m
fad[m]
glyc3p[m]
G3PDm
GL3Ptm

FIG. 5-7

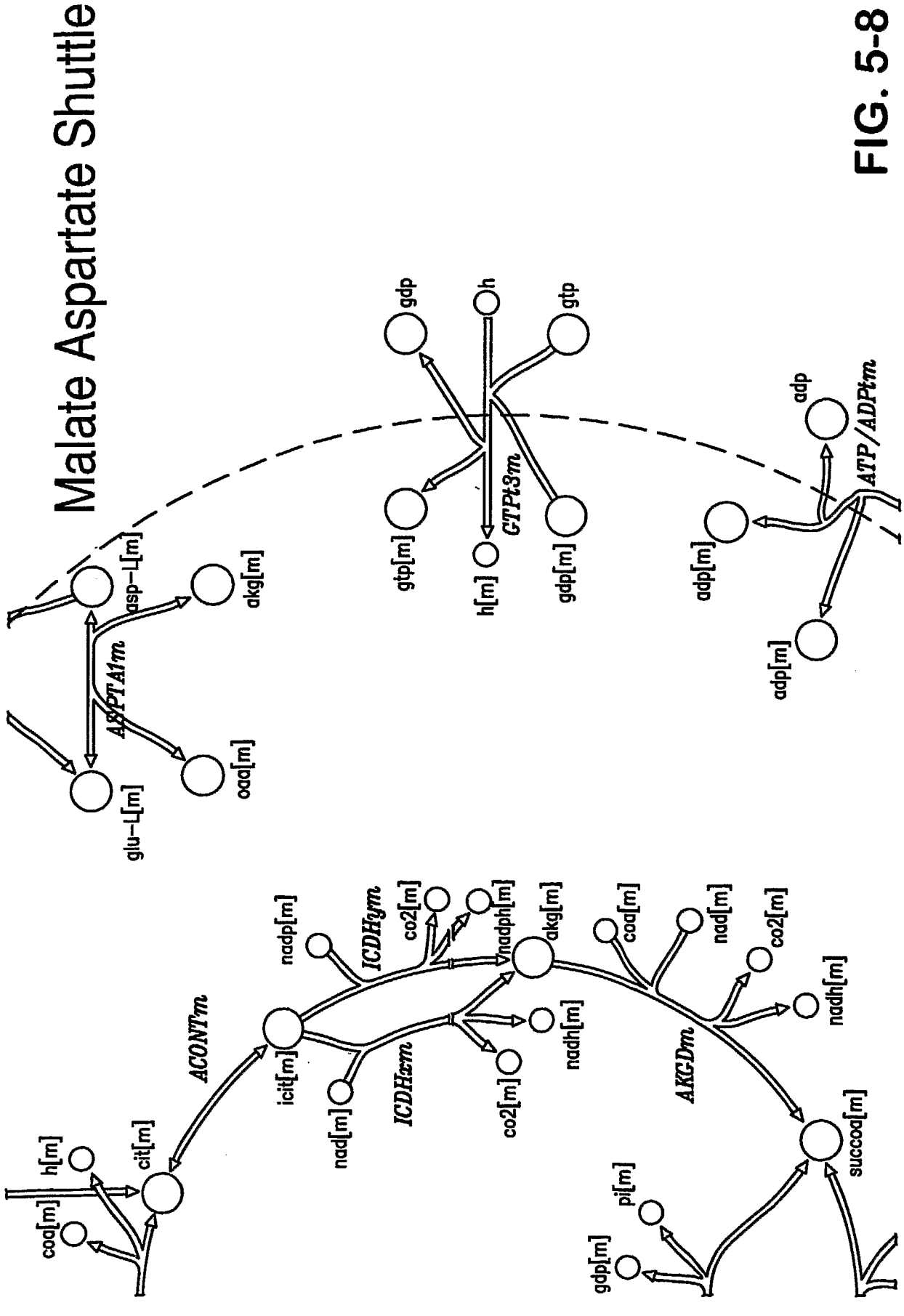

Malate Aspartate Shuttle
asp-L[m]
akg[m]
ASPTA1m
glu-L[m]
oaa[m]
gdp
h
gtp
gtp[m]
h[m]
GTPt3m
gdp[m]
adp
ATP/ADPtm
adp[m]
adp[m]
nadp[m]
ICDHym
co2[m]
nadph[m]
akg[m]
coa[m]
nad[m]
co2[m]
nadh[m]
ACONTm
icit[m]
nad[m]
ICDHxm
co2[m]
nadh[m]
AKGDm
succoa[m]
h[m]
cit[m]
coa[m]
pi[m]
gdp[m]

FIG. 5-8

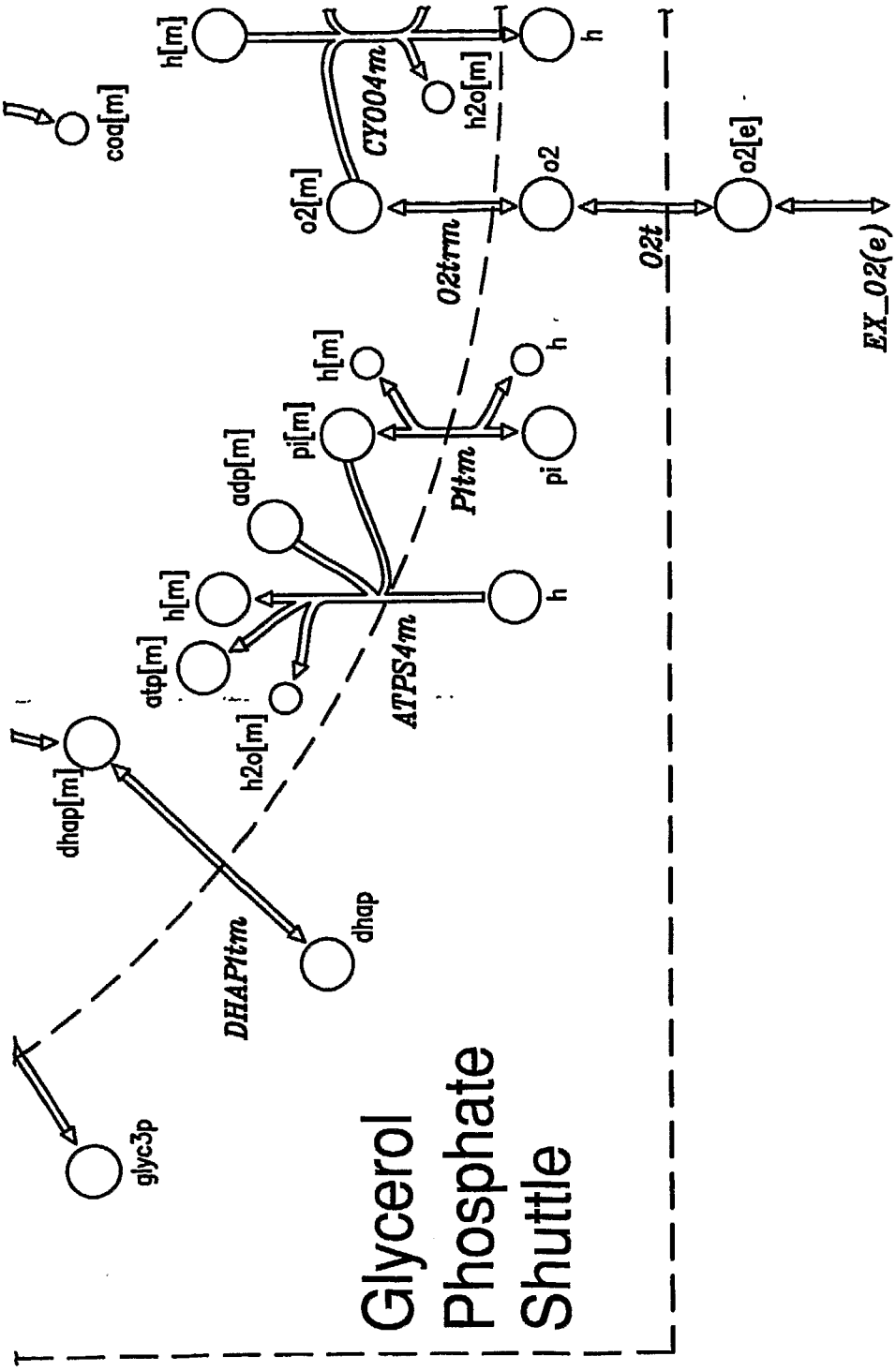

Glycerol
Phosphate
Shuttle
glyc3p
dhap[m]
DHAPtm
dhap
h2o[m]
atp[m]
h[m]
ATPS4m
adp[m]
pi[m]
h[m]
Ptm
h
pi
h[m]
02trm
o2[m]
CY004m
h2o[m]
h
coa[m]
o2
02t
o2[e]
EX_02(e)

FIG. 5-9

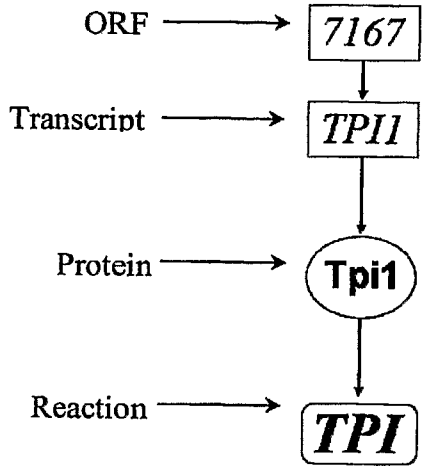


FIGURE 6

FIG. 7-1

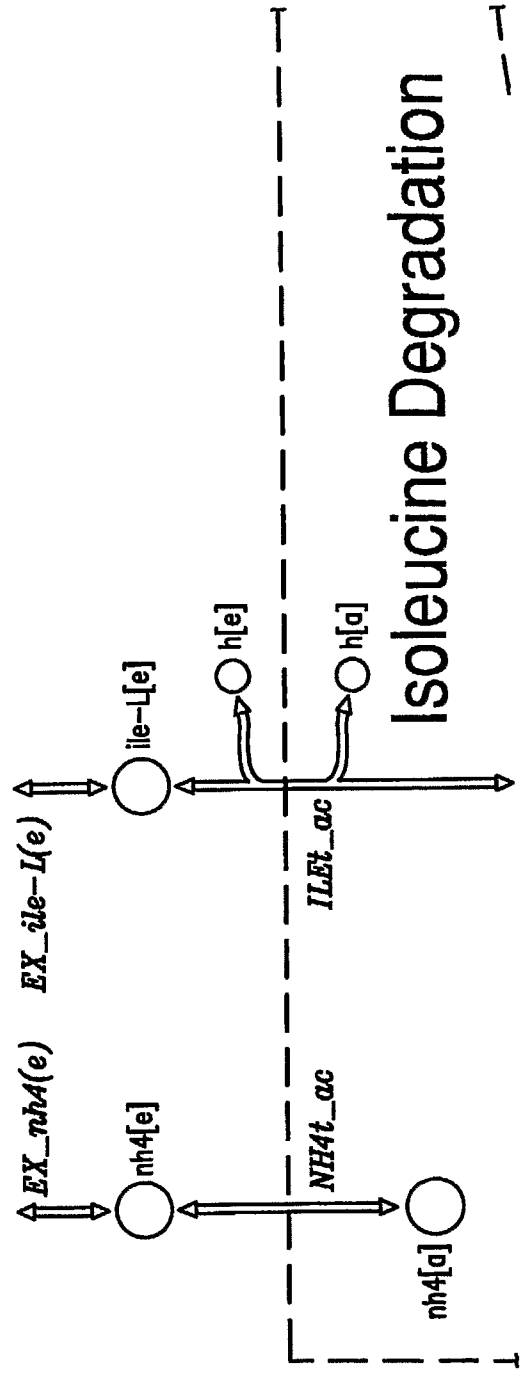

Isoleucine Degradation
ile-L[e]
h[e]
h[c]
EX_ile-L(e)
ILEt_ac
EX_nh4(e)
nh4[e]
NH4t_ac
nh4[c]

FIG. 7-2

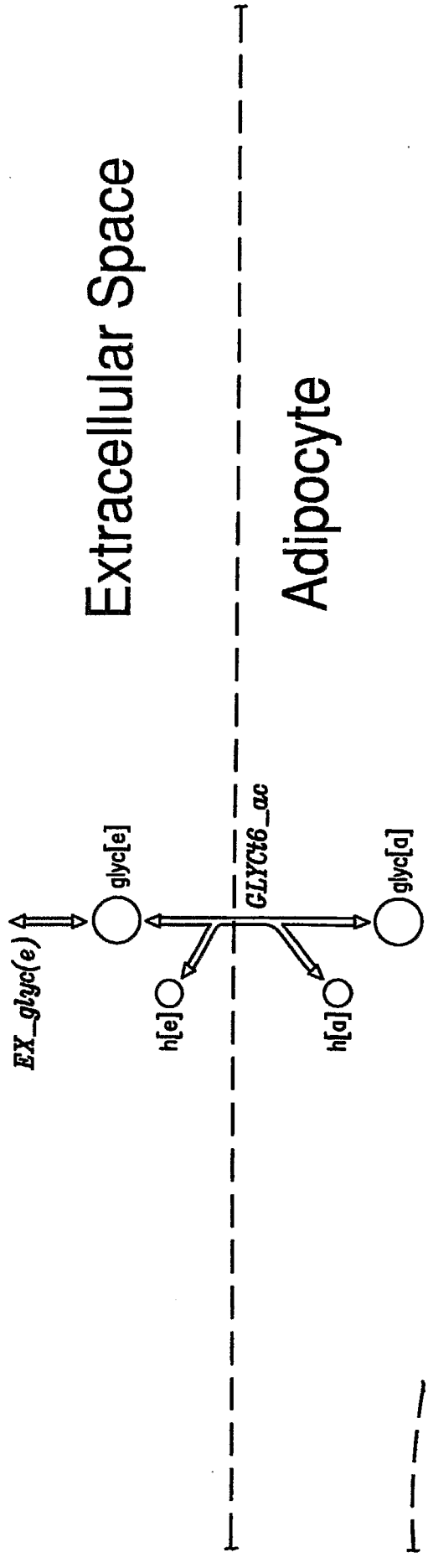

Extracellular Space
Adipocyte
glyc[e]
GLYCt6_ac
glyc[a]
EX_glyc(e)
h[e]
h[a]

FIG. 7-3

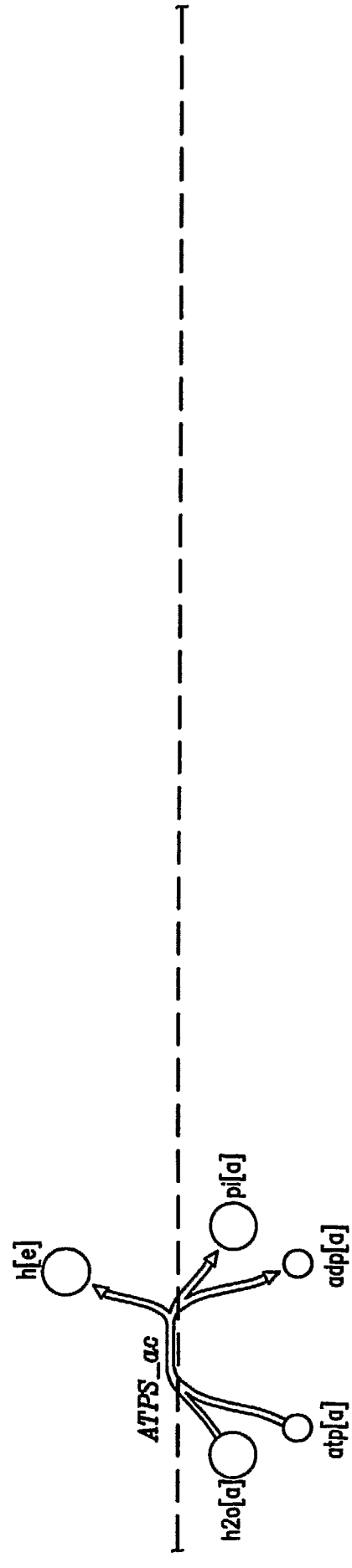


FIG. 7-4

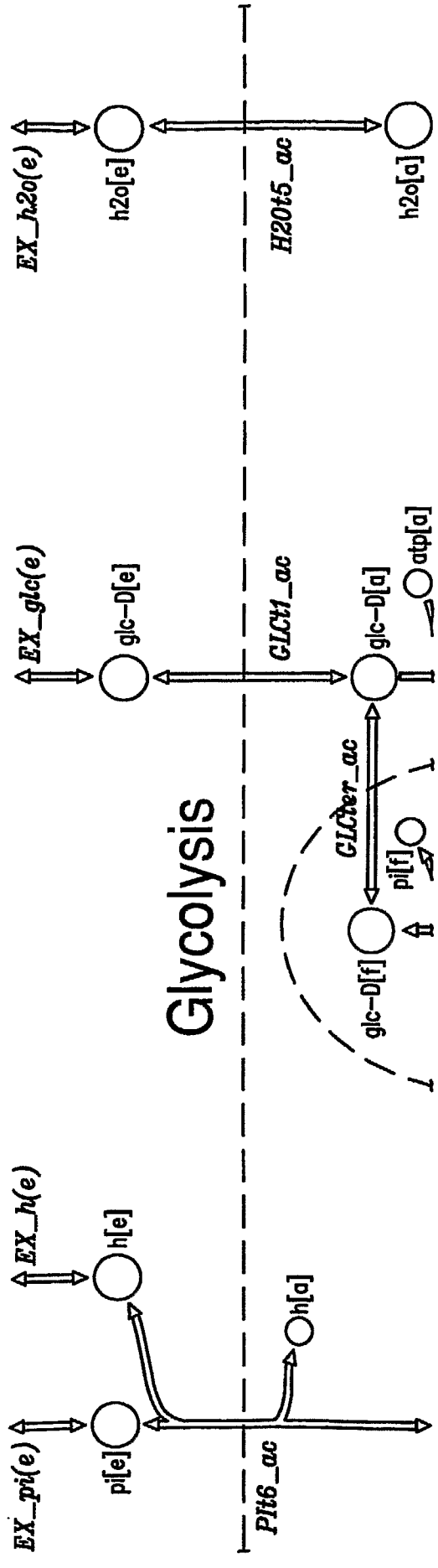
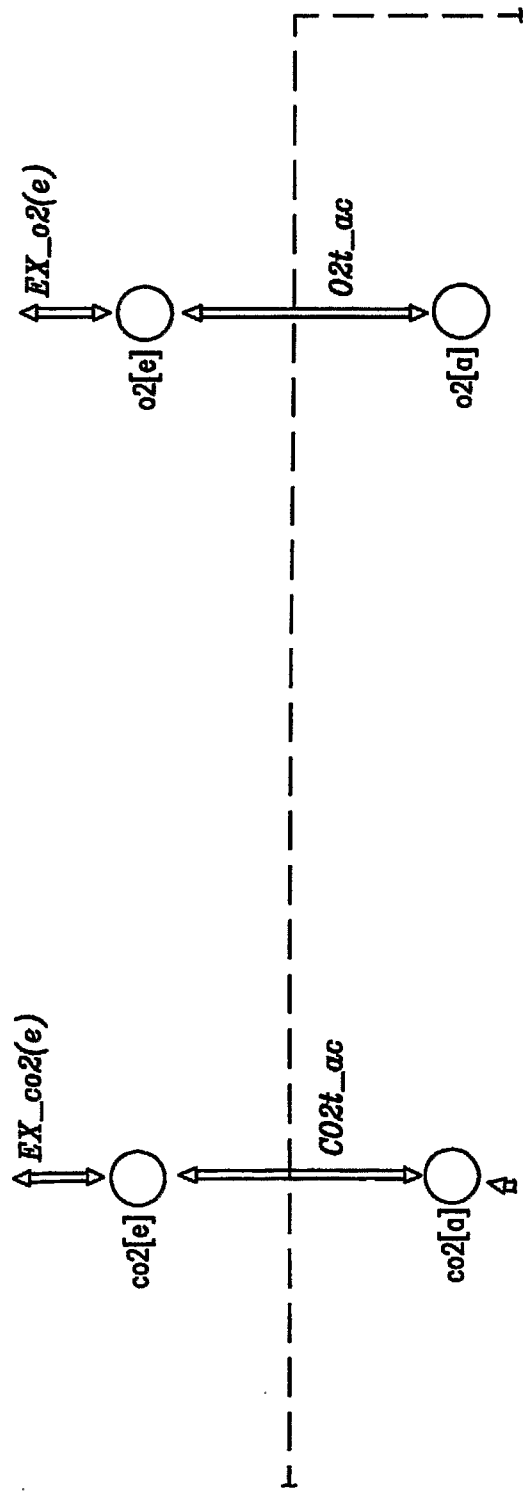

EX_h2o(e)
h2o[e]
H2Ot5_ac
h2o[a]
EX_glc(e)
glc-D[e]
GLCt1_ac
glc-D[a]
atp[a]
GLCter_ac
pi[f]
glc-D[f]
Glycolysis
EX_h(e)
h[e]
h[a]
EX_pi(e)
pi[e]
Pit6_ac

FIG. 7-5



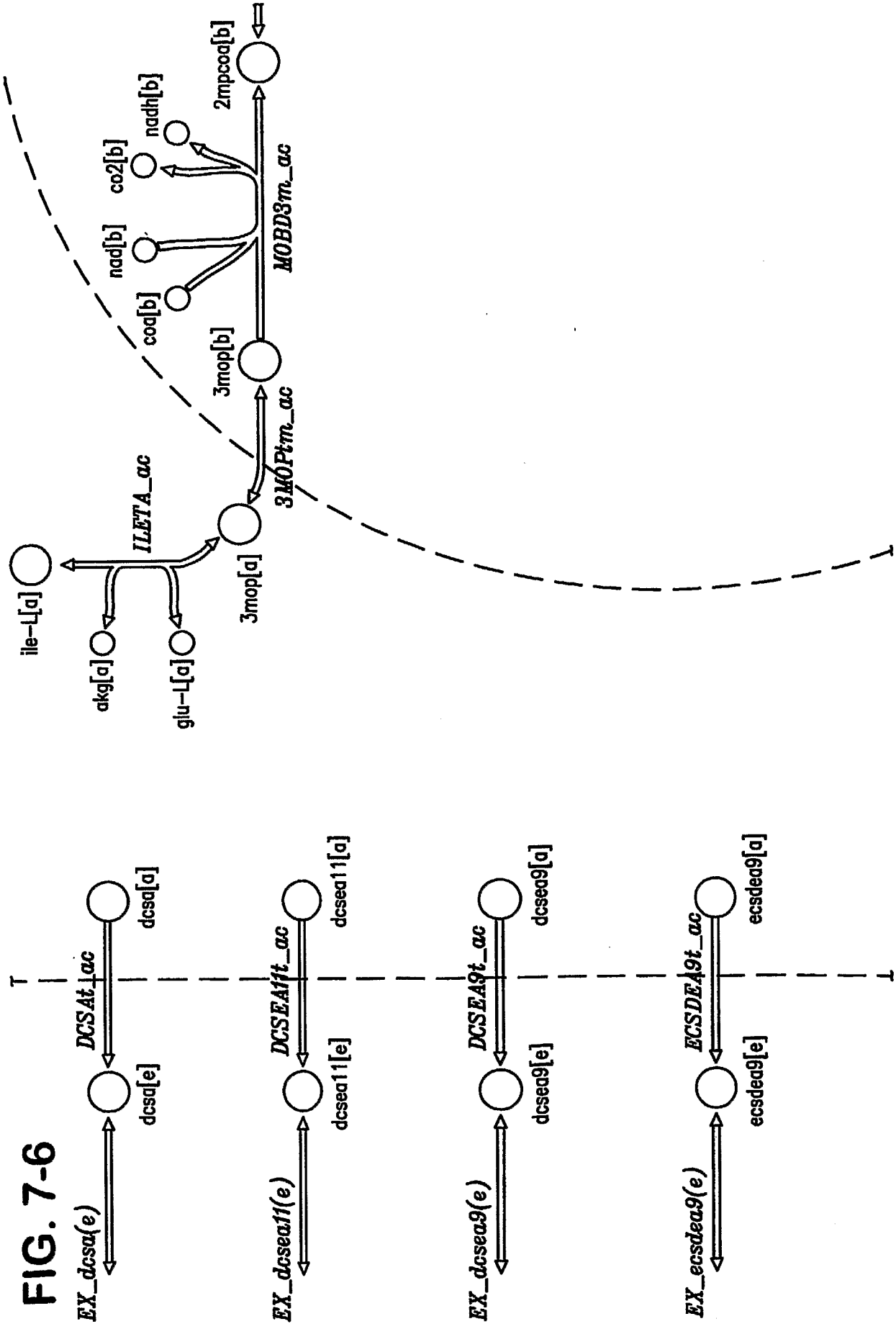

ile-L[a]
akg[a]
glu-L[a]
ILETA_ac
3mop[a]
3MOPtm_ac
3mop[b]
MOBD3m_ac
coa[b]
nad[b]
co2[b]
nadh[b]
2mpcoa[b]
dcsa[a]
DCSAt_ac
dcsa[e]
EX_dcsa(e)
dcsea11[a]
DCSEA11t_ac
dcsea11[e]
EX_dcsea11(e)
dcsea9[a]
DCSEA9t_ac
dcsea9[e]
EX_dcsea9(e)
ecsdea9[a]
ECSDEA9t_ac
ecsdea9[e]
EX_ecsdea9(e)

FIG. 7-6

FIG. 7-7

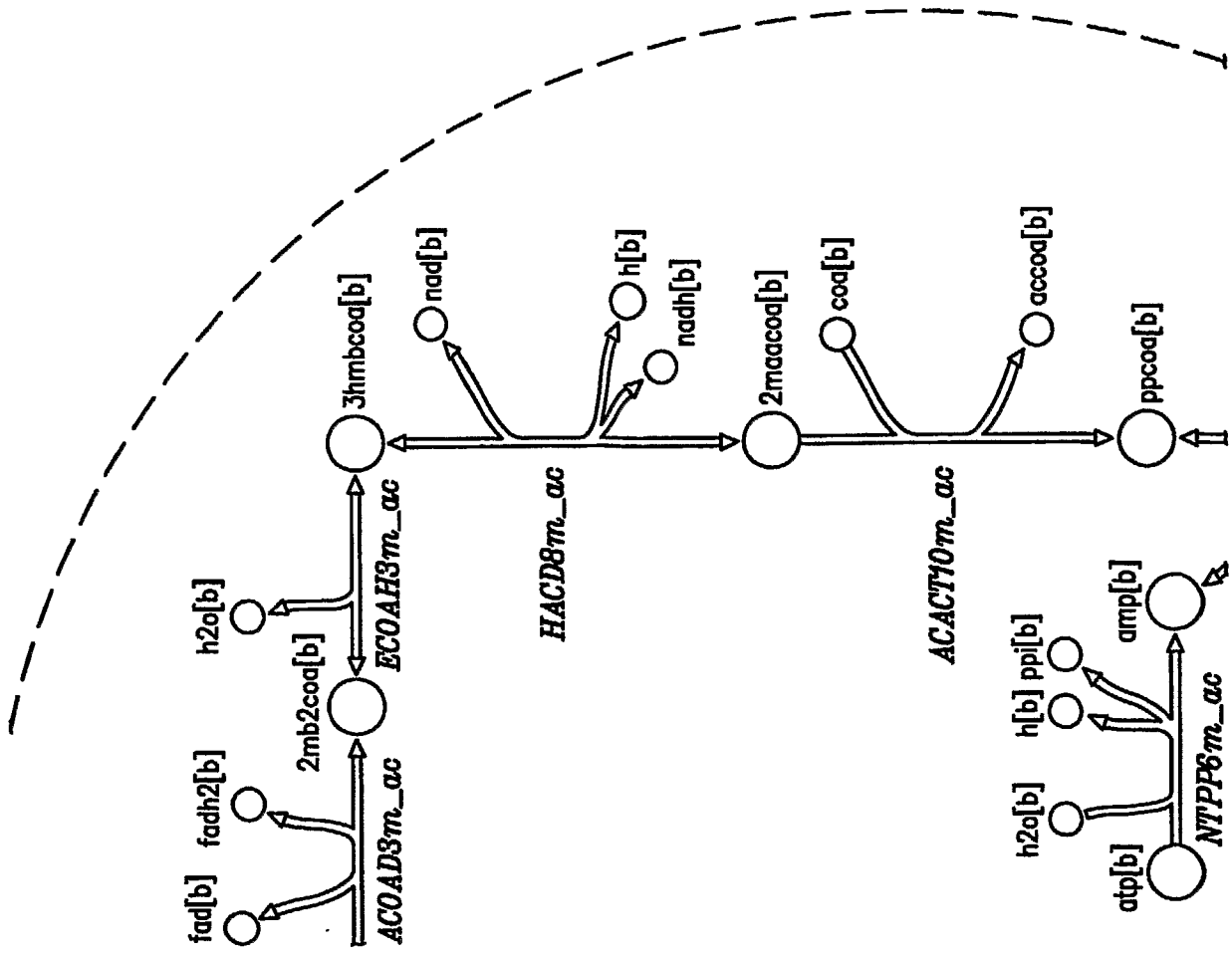
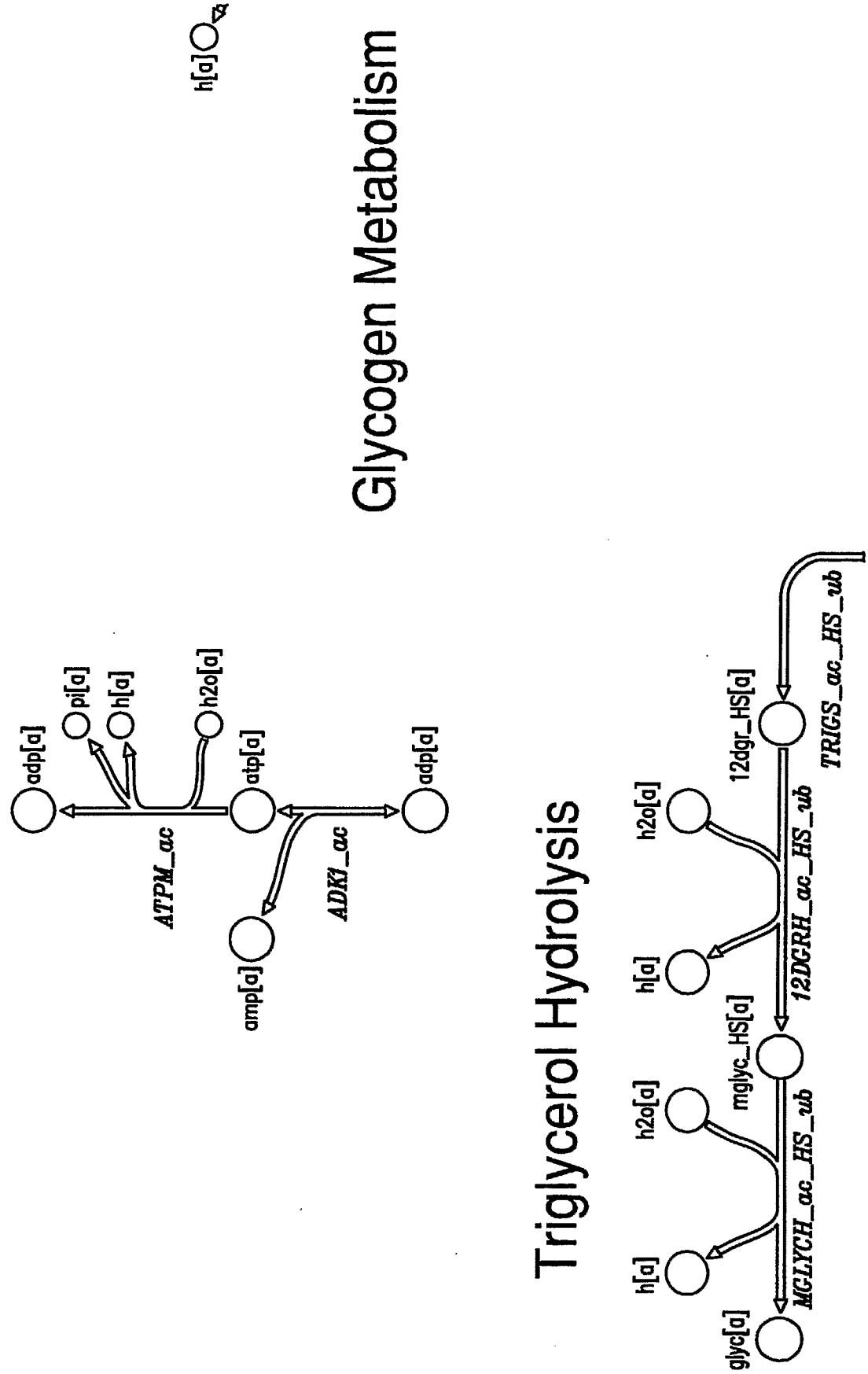

fad[b]
fadh2[b]
h2o[b]
2mb2coa[b]
ACOAD3m_ac
ECOAH3m_ac
3hmbcoa[b]
nad[b]
h[b]
nadh[b]
HACD8m_ac
2maacoa[b]
coa[b]
accoa[b]
ACACT10m_ac
ppcoa[b]
h2o[b]
h[b] ppi[b]
amp[b]
atp[b]
NTPP6m_ac

FIG. 7-8 Non-growth Associated Energy Maintainance



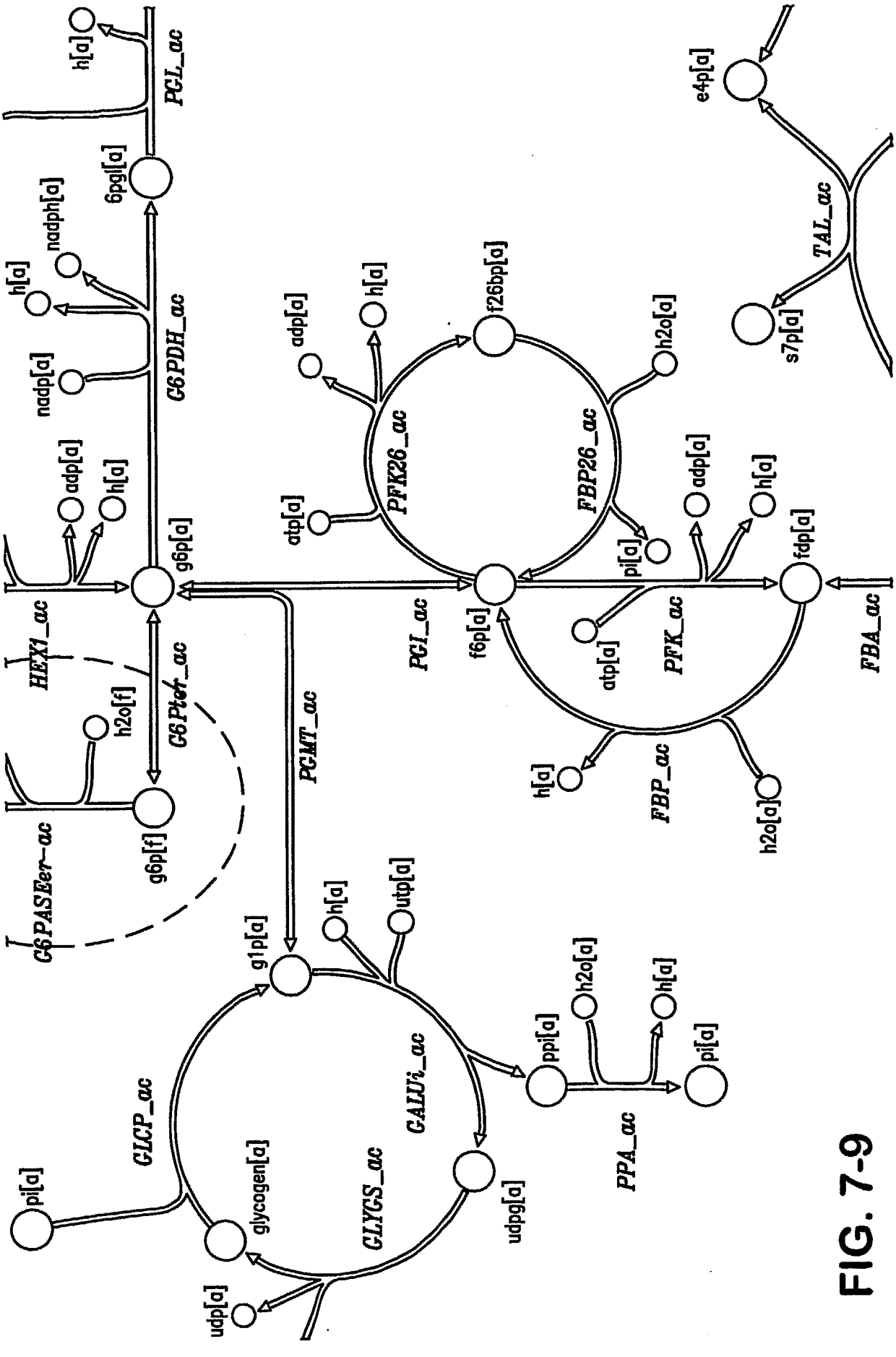
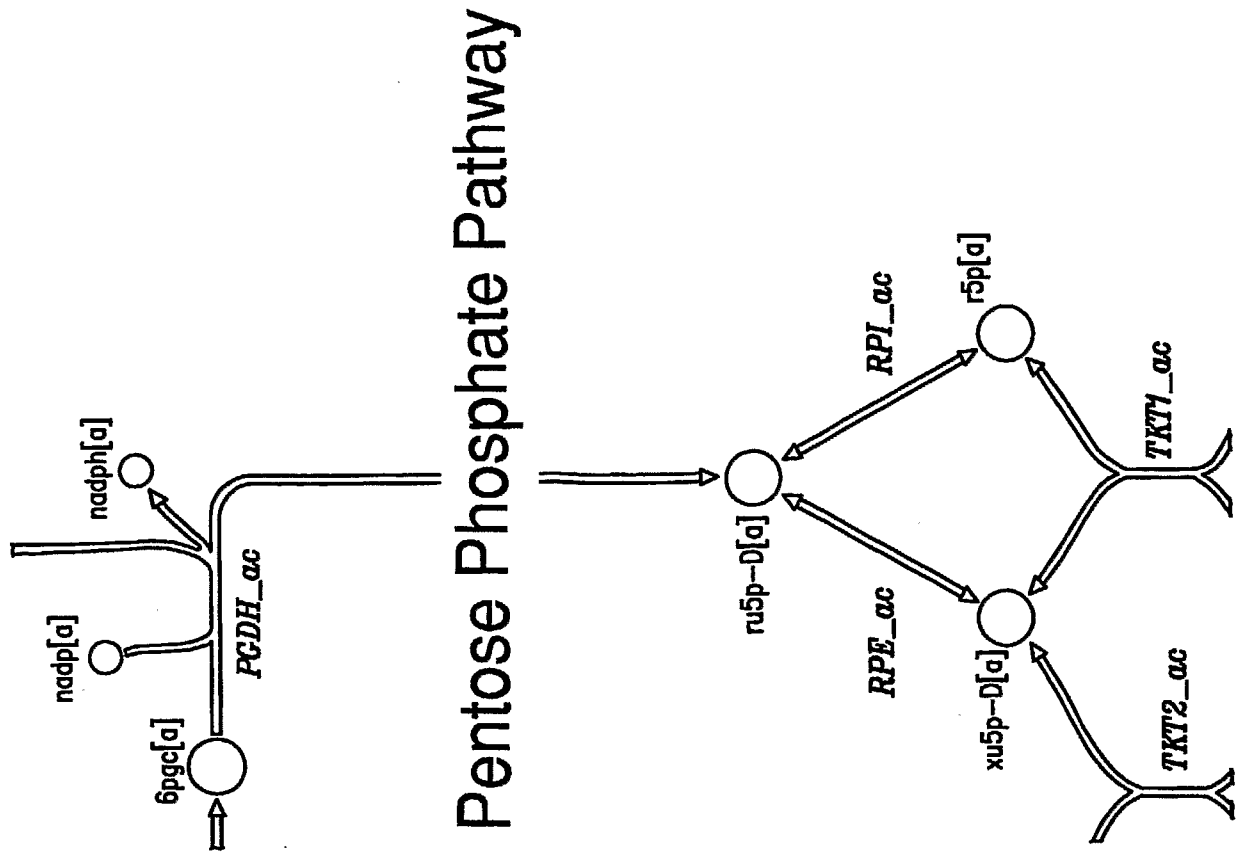

h[a]
PGL_ac
6pgl[a]
nadph[a]
h[a]
nadp[a]
G6PDH_ac
adp[a]
h[a]
g6p[a]
HEX1_ac
h2o[f]
G6Pter_ac
G6PASEer_ac
g6p[f]
PGMT_ac
g1p[a]
h[a]
utp[a]
GLCP_ac
pi[a]
glycogen[a]
GLYCS_ac
GALUi_ac
udpg[a]
udp[a]
ppi[a]
h2o[a]
h[a]
pi[a]
PPA_ac
adp[a]
h[a]
atp[a]
PFK26_ac
f26bp[a]
FBP26_ac
h2o[a]
pi[a]
PGI_ac
f6p[a]
atp[a]
PFK_ac
adp[a]
h[a]
fdp[a]
FBA_ac
h[a]
FBP_ac
h2o[a]
e4p[a]
TAL_ac
s7p[a]

FIG. 7-9

FIG. 7-10


Pentose Phosphate Pathway
6pgc[c]
nadp[c]
nadph[c]
PGDH_ac
ru5p-D[c]
RPI_ac
r5p[c]
TKT1_ac
RPE_ac
xu5p-D[c]
TKT2_ac

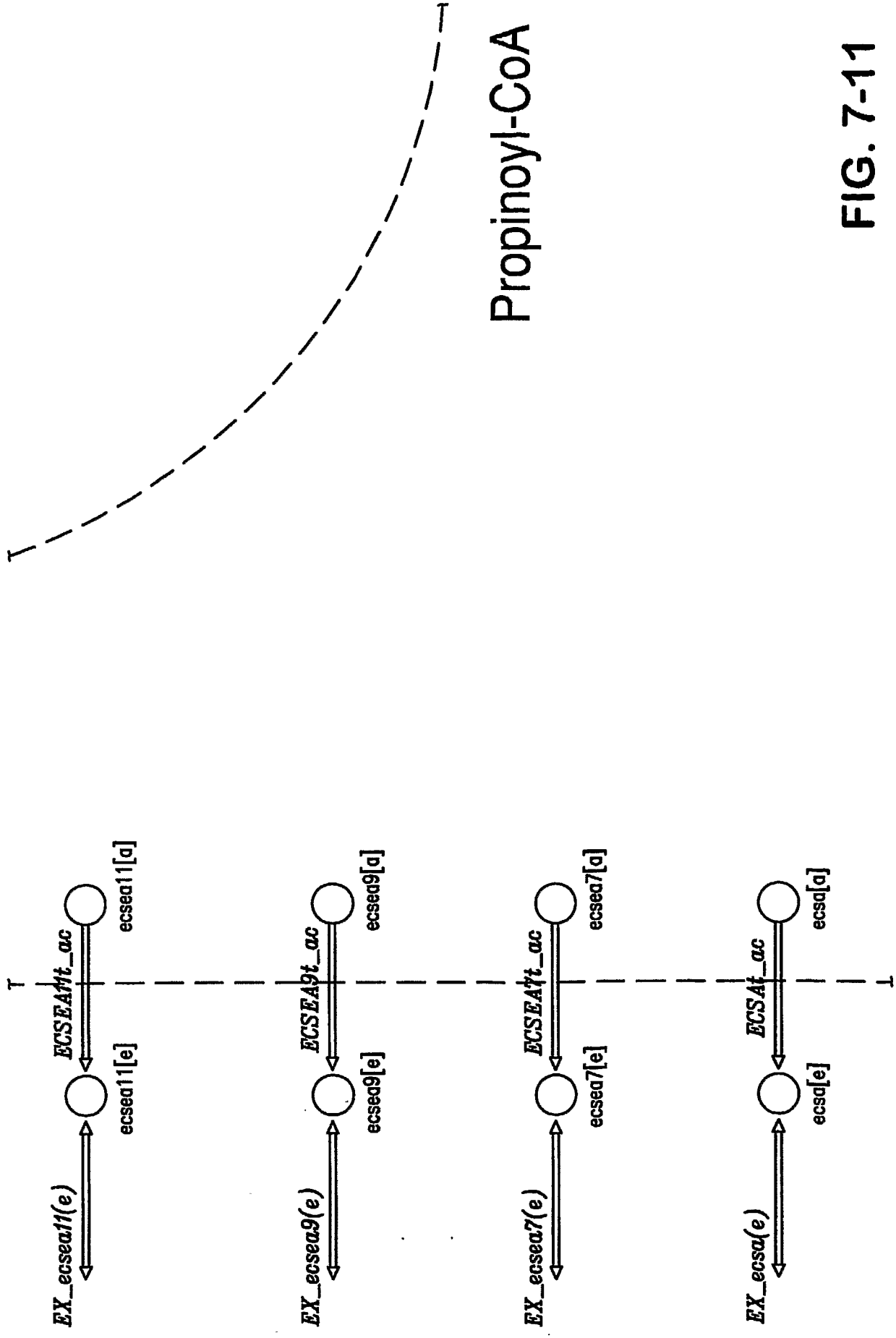

Propinoyl-CoA
T
T
ecsea11[a]
ECSEA11t_ac
ecsea11[e]
EX_ecsea11(e)
ecsea9[a]
ECSEA9t_ac
ecsea9[e]
EX_ecsea9(e)
ecsea7[a]
ECSEA7t_ac
ecsea7[e]
EX_ecsea7(e)
ecsa[a]
ECSAt_ac
ecsa[e]
EX_ecsa(e)

FIG. 7-11

FIG. 7-12

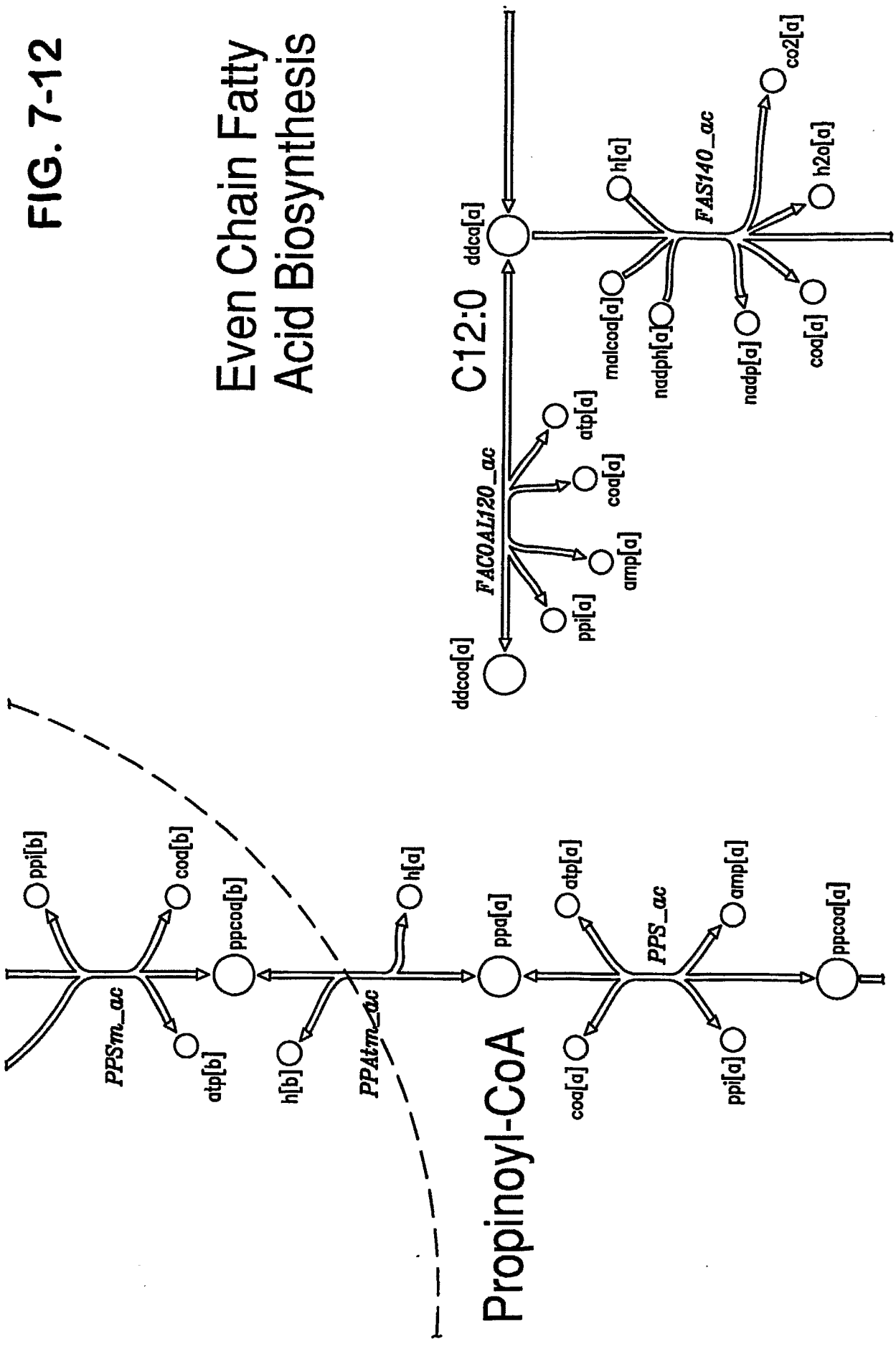
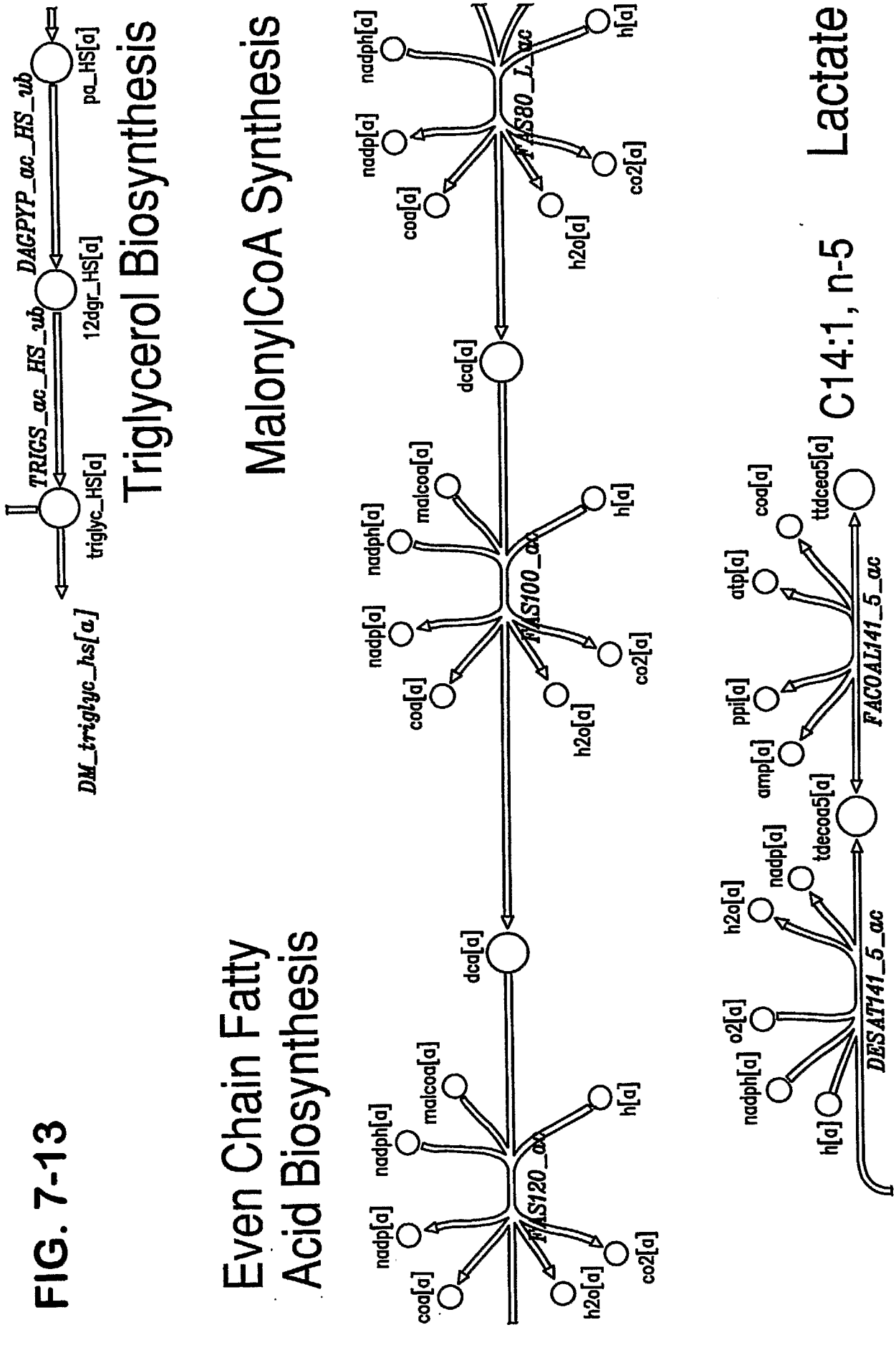

Even Chain Fatty Acid Biosynthesis
C12:0
ddcoa[a]
FACOAL120_ac
atp[a]
coa[a]
amp[a]
ppi[a]
ddcoa[a]
FAS140_ac
h[a]
co2[a]
h2o[a]
malcoa[a]
nadph[a]
nadp[a]
coa[a]
Propinoyl-CoA
ppi[b]
coa[b]
PPSm_ac
ppcoa[b]
atp[b]
h[b]
PPAtm_ac
h[a]
ppa[a]
atp[a]
PPS_ac
amp[a]
ppcoa[a]
coa[a]
ppi[a]

FIG. 7-13


Triglycerol Biosynthesis
DAGPYP_ac_HS_ub
TRIGS_ac_HS_ub
DM_triglyc_hs[a]
triglyc_HS[a]
12dgr_HS[a]
pa_HS[a]
MalonylCoA Synthesis
Even Chain Fatty Acid Biosynthesis
FAS80_L_ac
FAS100_ac
FAS120_ac
nadph[a]
nadp[a]
coa[a]
co2[a]
h2o[a]
h[a]
malcoa[a]
dca[a]
C14:1, n-5 Lactate
FACOAL141_5_ac
DESAT141_5_ac
ttdcea5[a]
atp[a]
ppi[a]
amp[a]
tdecoa5[a]
o2[a]

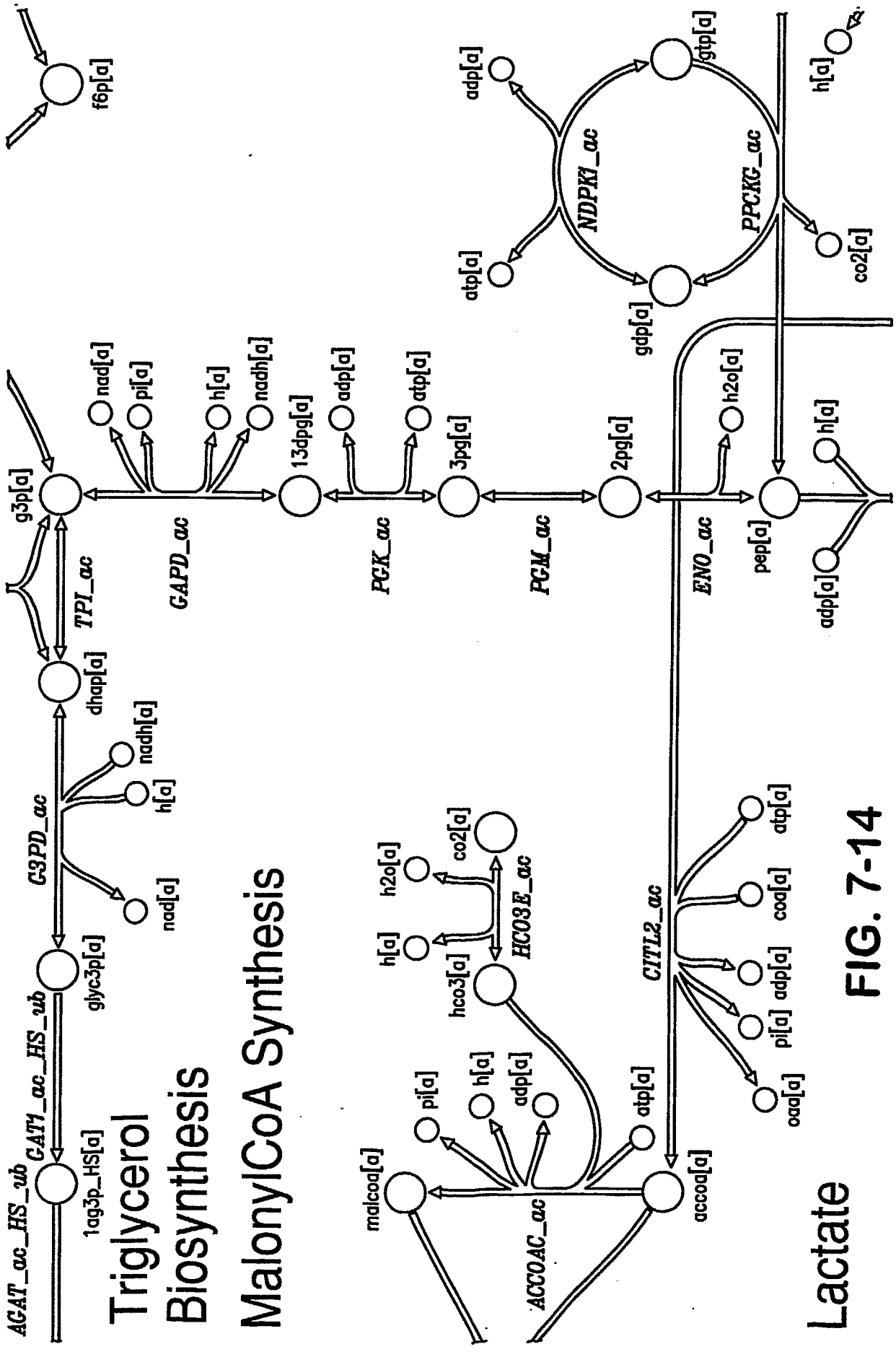

Triglycerol Biosynthesis
MalonylCoA Synthesis
Lactate
f6p[a]
g3p[a]
dhap[a]
glyc3p[a]
1ag3p_HS[a]
nad[a]
pi[a]
h[a]
nadh[a]
13dpg[a]
adp[a]
atp[a]
3pg[a]
2pg[a]
h2o[a]
pep[a]
gtp[a]
gdp[a]
co2[a]
hco3[a]
malcoa[a]
accoa[a]
coa[a]
oaa[a]
TPI_ac
GAPD_ac
PGK_ac
PGM_ac
ENO_ac
NDPK1_ac
PPCKG_ac
G3PD_ac
GAT1_ac_HS_ub
AGAT_ac_HS_ub
HCO3E_ac
ACCOAC_ac
CITL2_ac

FIG. 7-14

FIG. 7-15

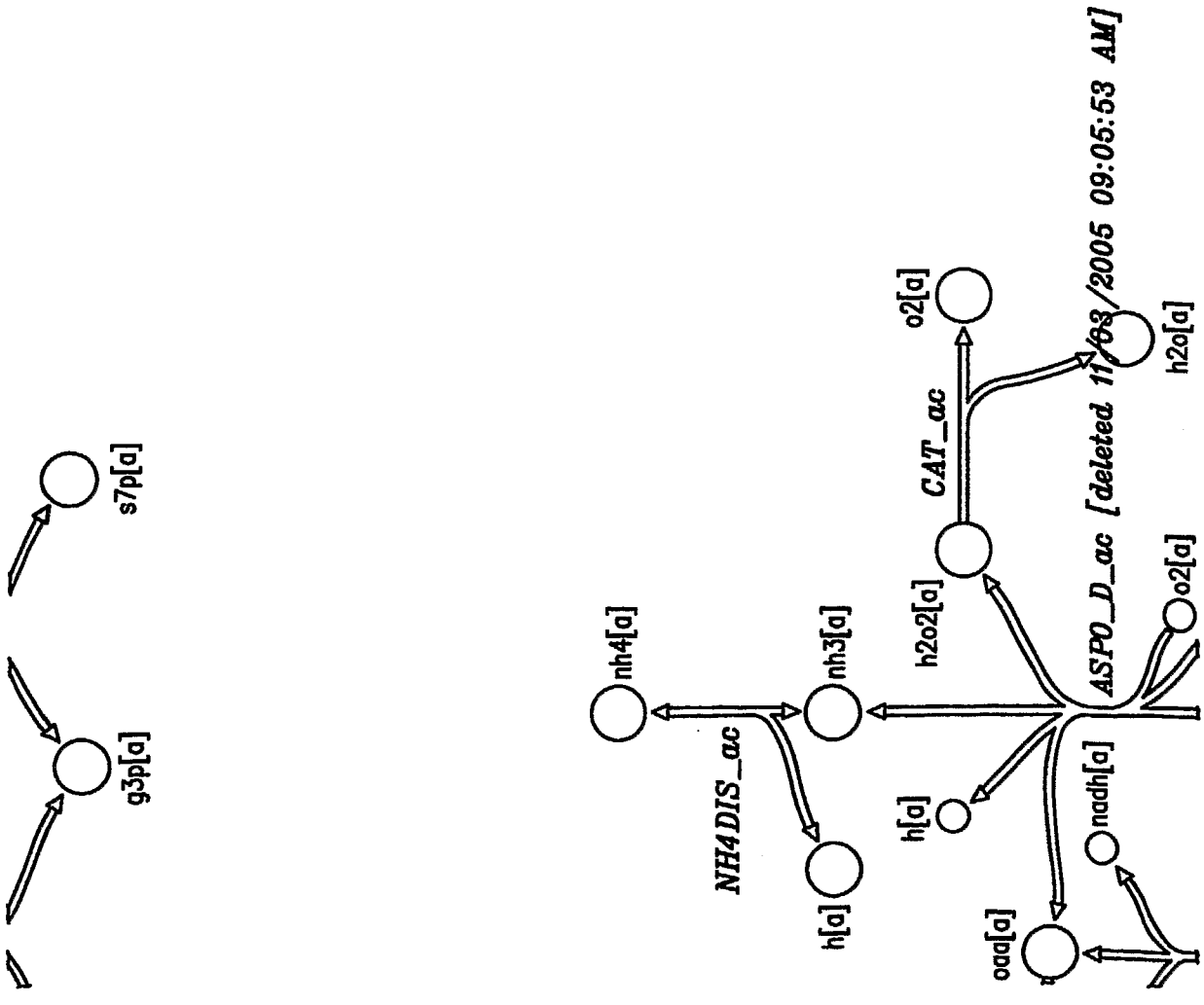
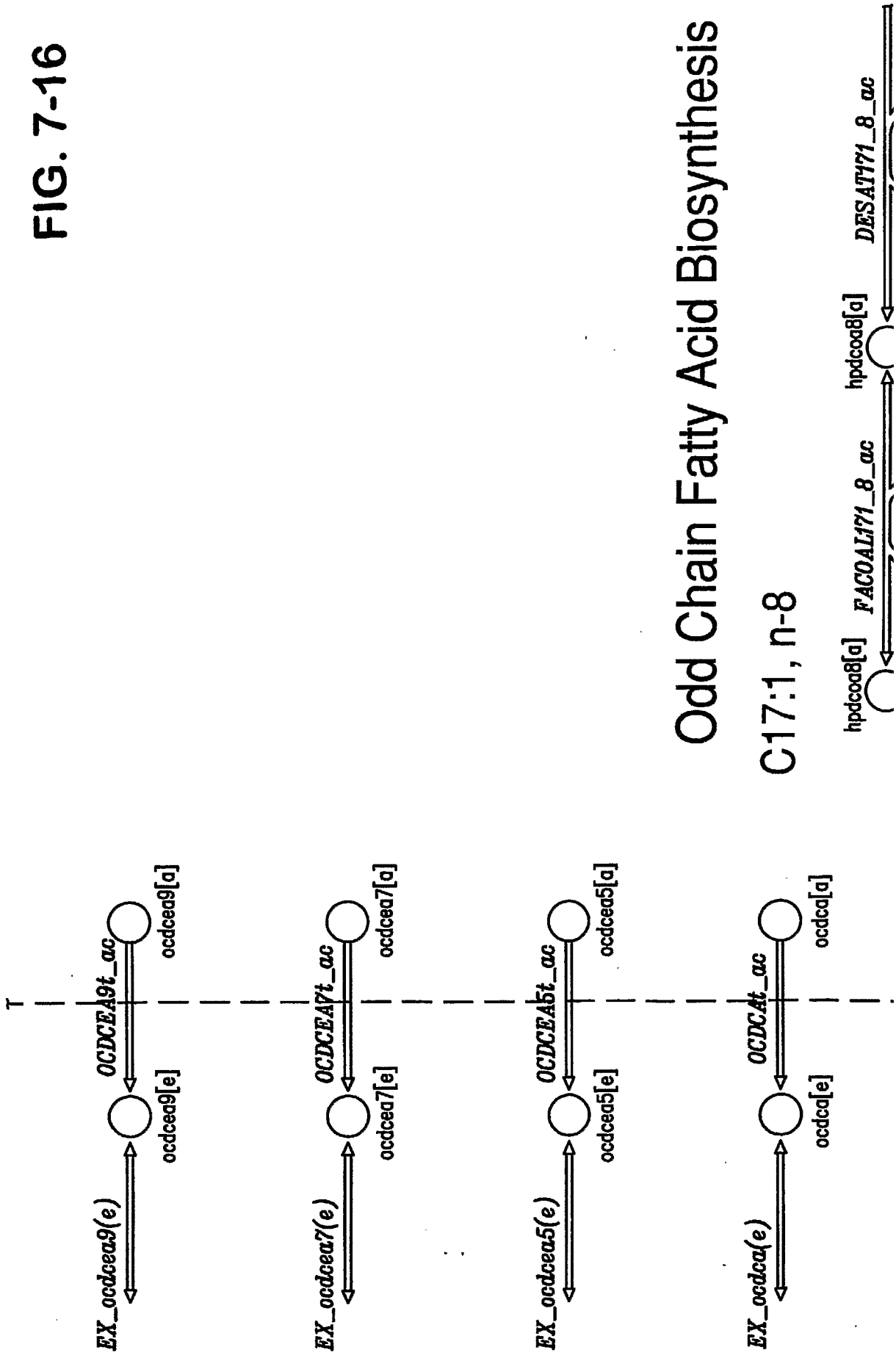

s7p[a]
g3p[a]
nh4[a]
nh3[a]
NH4DIS_ac
h[a]
h2o2[a]
CAT_ac
o2[a]
h2o[a]
ASPO_D_ac [deleted 11/03/2005 09:05:53 AM]
o2[a]
h[a]
nadh[a]
oaa[a]

FIG. 7-16


Odd Chain Fatty Acid Biosynthesis
C17:1, n-8
hpdcoa8[a]
FACOAL171_8_ac
hpdcoa8[a]
DESAT171_8_ac
T
EX_ocdcea9(e)
ocdcea9[e]
OCDCEA9t_ac
ocdcea9[a]
EX_ocdcea7(e)
ocdcea7[e]
OCDCEA7t_ac
ocdcea7[a]
EX_ocdcea5(e)
ocdcea5[e]
OCDCEA5t_ac
ocdcea5[a]
EX_ocdca(e)
ocdca[e]
OCDCAt_ac
ocdca[a]

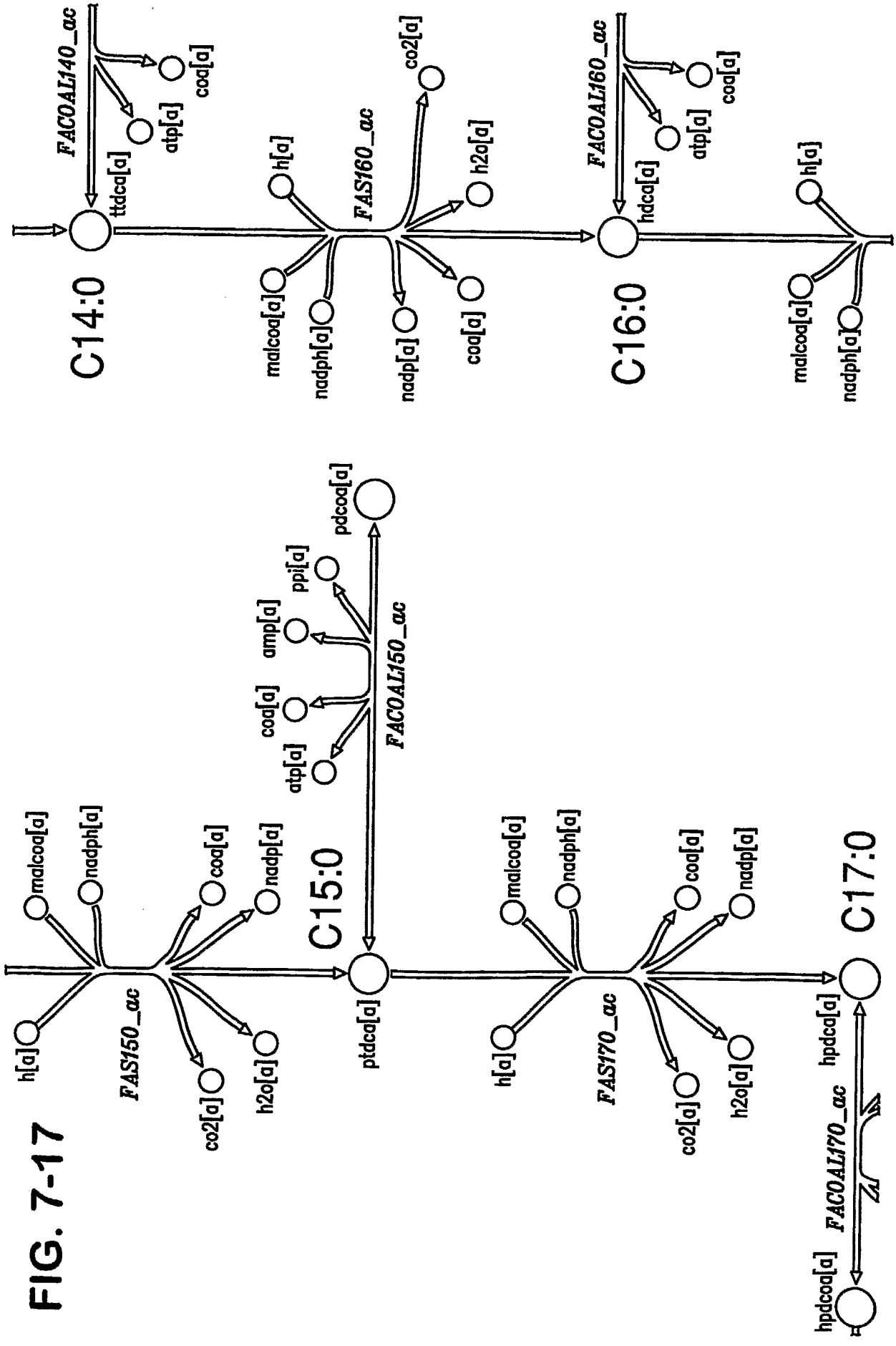
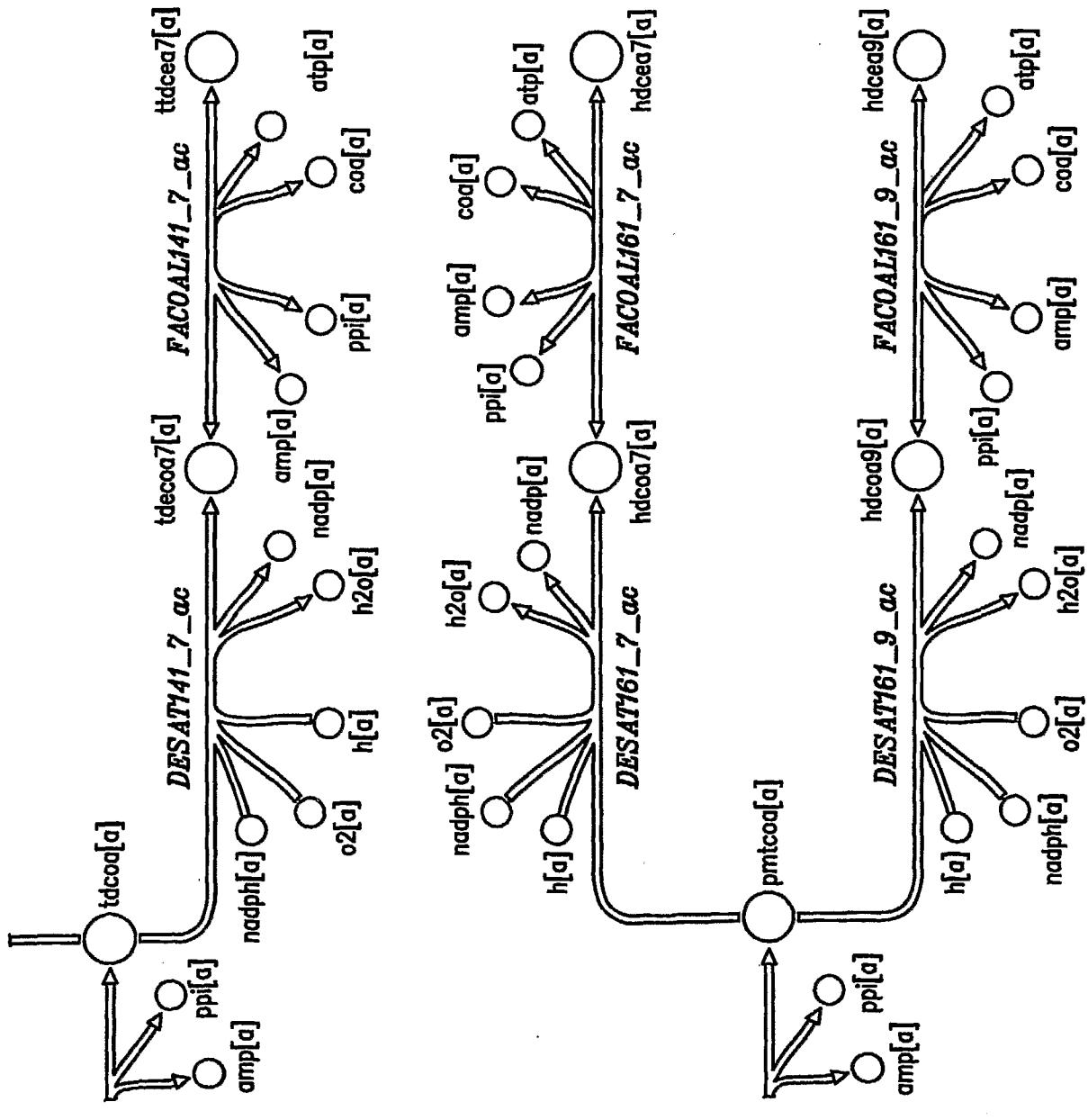

FACOAL140_ac
ttdca[a]
atp[a]
coa[a]
C14:0
h[a]
FAS160_ac
malcoa[a]
nadph[a]
co2[a]
h2o[a]
nadp[a]
coa[a]
FACOAL160_ac
hdca[a]
atp[a]
coa[a]
C16:0
h[a]
malcoa[a]
nadph[a]
pdcoa[a]
ppi[a]
amp[a]
coa[a]
atp[a]
FACOAL150_ac
C15:0
h[a]
FAS150_ac
malcoa[a]
nadph[a]
coa[a]
nadp[a]
co2[a]
h2o[a]
ptdca[a]
h[a]
FAS170_ac
malcoa[a]
nadph[a]
coa[a]
nadp[a]
co2[a]
h2o[a]
C17:0
hpdca[a]
FACOAL170_ac
hpdcoa[a]

FIG. 7-17

FIG. 7-18


C14:1, n-7
C16:1, n-7
C16:1, n-9
tdcoa[a]
ppi[a]
amp[a]
DESAT141_7_ac
nadph[a]
o2[a]
h[a]
tdecoa7[a]
nadp[a]
h2o[a]
FACOAL141_7_ac
amp[a]
ppi[a]
coa[a]
atp[a]
ttdcea7[a]
pmtcoa[a]
DESAT161_7_ac
hdcoa7[a]
FACOAL161_7_ac
hdcea7[a]
DESAT161_9_ac
hdcoa9[a]
FACOAL161_9_ac
hdcea9[a]

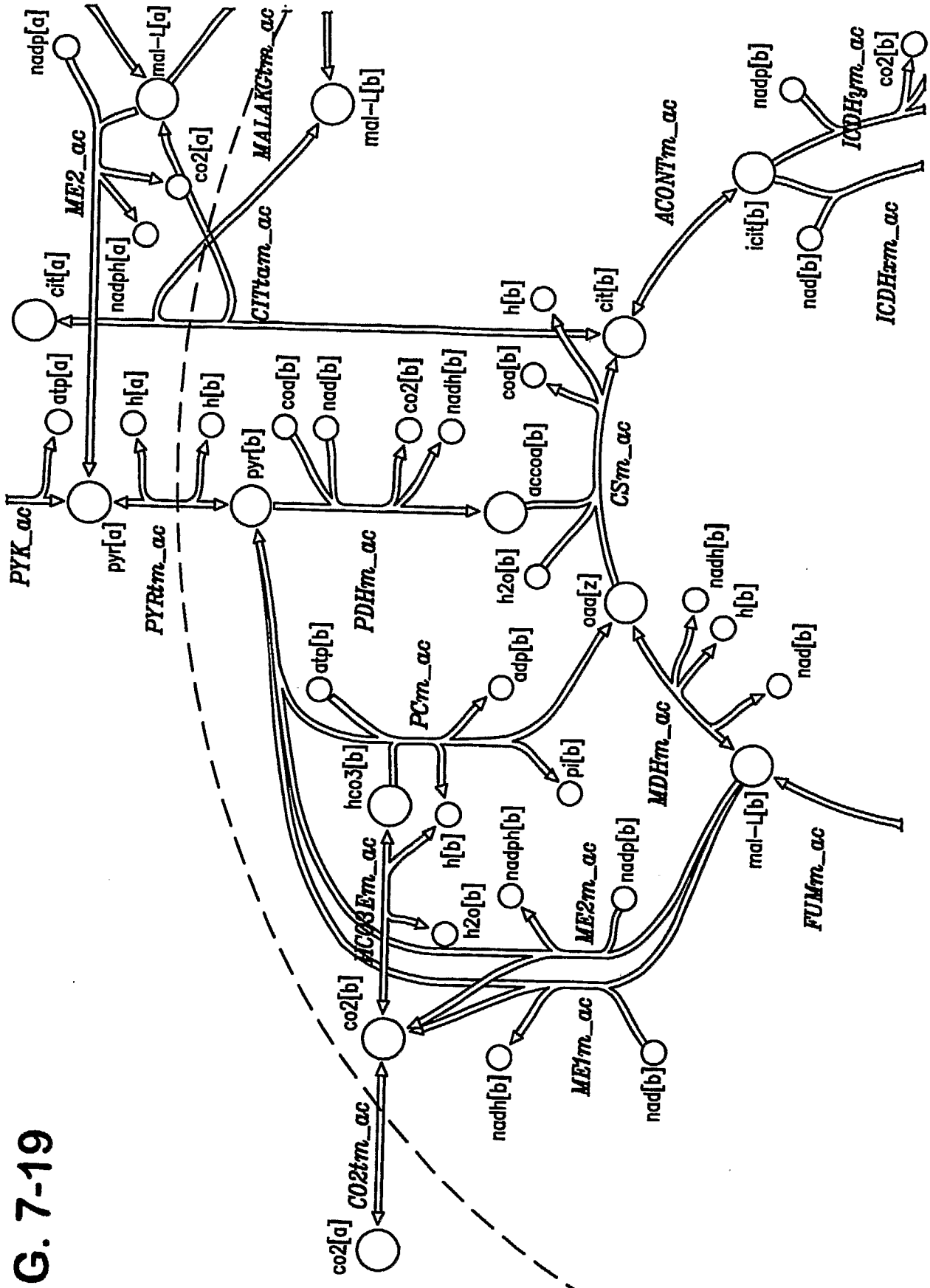
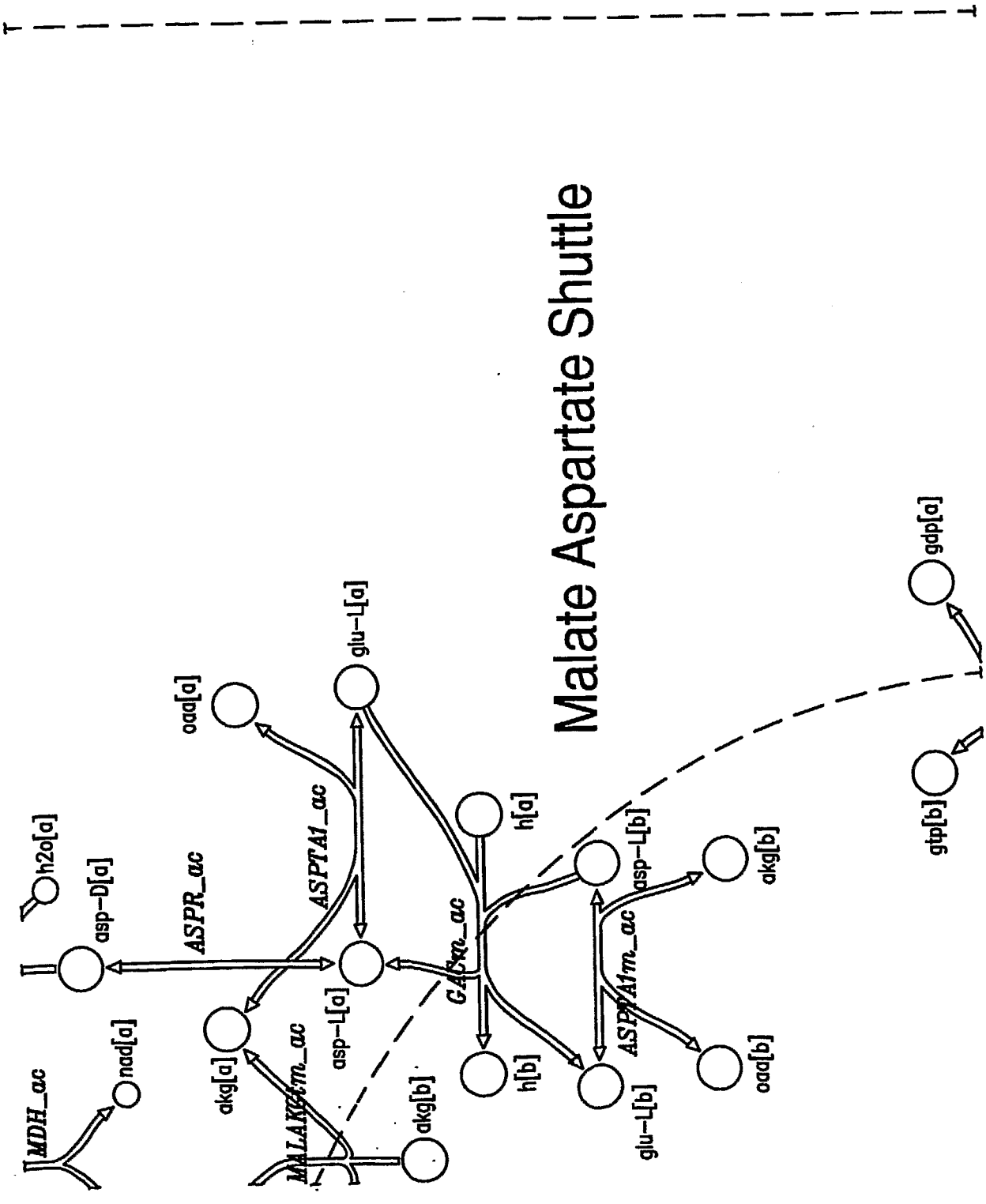

nadp[a]
mal-L[a]
ME2_ac
co2[a]
MALAKGtm_ac
mal-L[b]
nadph[a]
cit[a]
CITtam_ac
h[b]
cit[b]
ACONTm_ac
nadp[b]
ICDHygm_ac
co2[b]
icit[b]
nad[b]
ICDHxm_ac
atp[a]
h[a]
h[b]
coa[b]
nad[b]
co2[b]
nadh[b]
coa[b]
pyr[b]
accoa[b]
CSm_ac
PYK_ac
pyr[a]
PYRtm_ac
PDHm_ac
h2o[b]
oaa[z]
nadh[b]
h[b]
nad[b]
atp[b]
PCm_ac
adp[b]
MDHm_ac
hco3[b]
pi[b]
h[b]
nadph[b]
nadp[b]
mal-L[b]
FUMm_ac
h2o[b]
HCO3Em_ac
ME2m_ac
co2[b]
ME1m_ac
nadh[b]
nad[b]
CO2tm_ac
co2[a]

FIG. 7-19

FIG. 7-20


Malate Aspartate Shuttle
h2o[a]
asp-D[a]
ASPR_ac
oaa[a]
ASPTA1_ac
glu-L[a]
h[a]
GABtm_ac
asp-L[a]
akg[a]
MDH_ac
nad[a]
MALAKGtm_ac
akg[b]
h[b]
asp-L[b]
ASPTA1m_ac
glu-L[b]
akg[b]
oaa[b]
gdp[a]
gtp[b]

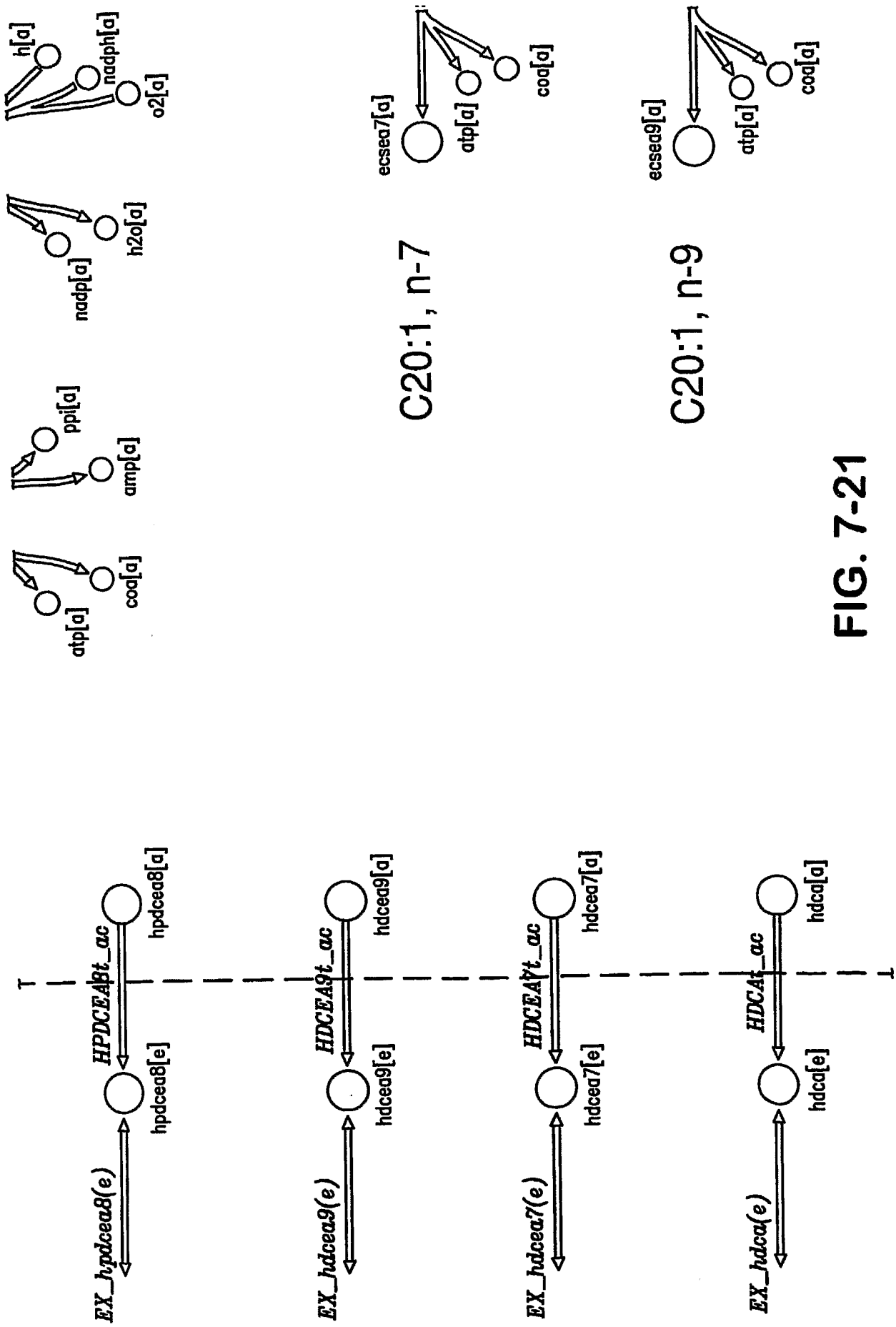

h[a]
nadph[a]
o2[a]
nadp[a]
h2o[a]
ppi[a]
amp[a]
atp[a]
coa[a]
ecsea7[a]
atp[a]
coa[a]
C20:1, n-7
ecsea9[a]
atp[a]
coa[a]
C20:1, n-9
HPDCEAPt_ac
hpdcea8[a]
hpdcea8[e]
EX_hpdcea8(e)
HDCEA9t_ac
hdcea9[a]
hdcea9[e]
EX_hdcea9(e)
HDCEA7t_ac
hdcea7[a]
hdcea7[e]
EX_hdcea7(e)
HDCAt_ac
hdca[a]
hdca[e]
EX_hdca(e)

FIG. 7-21

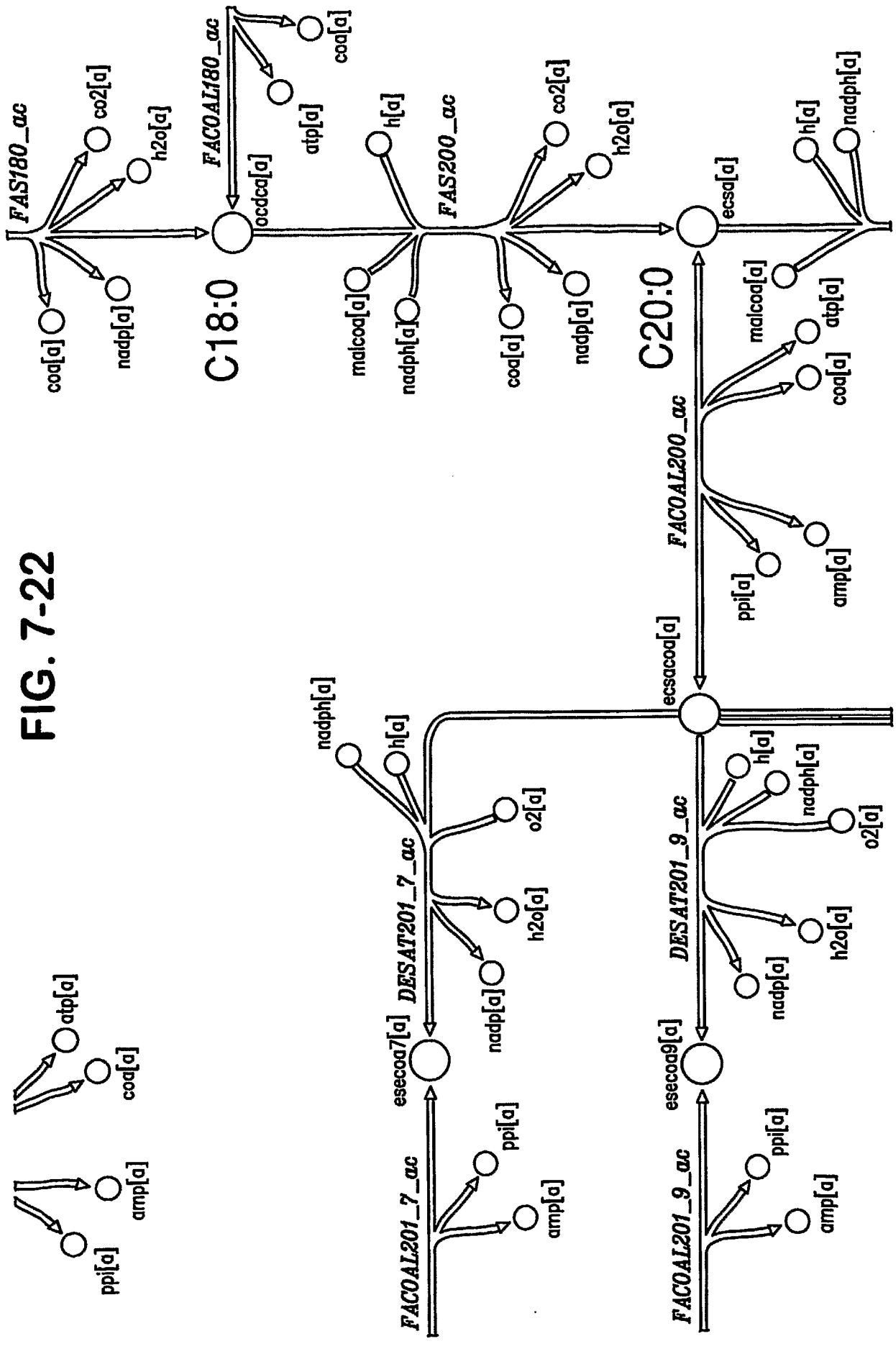
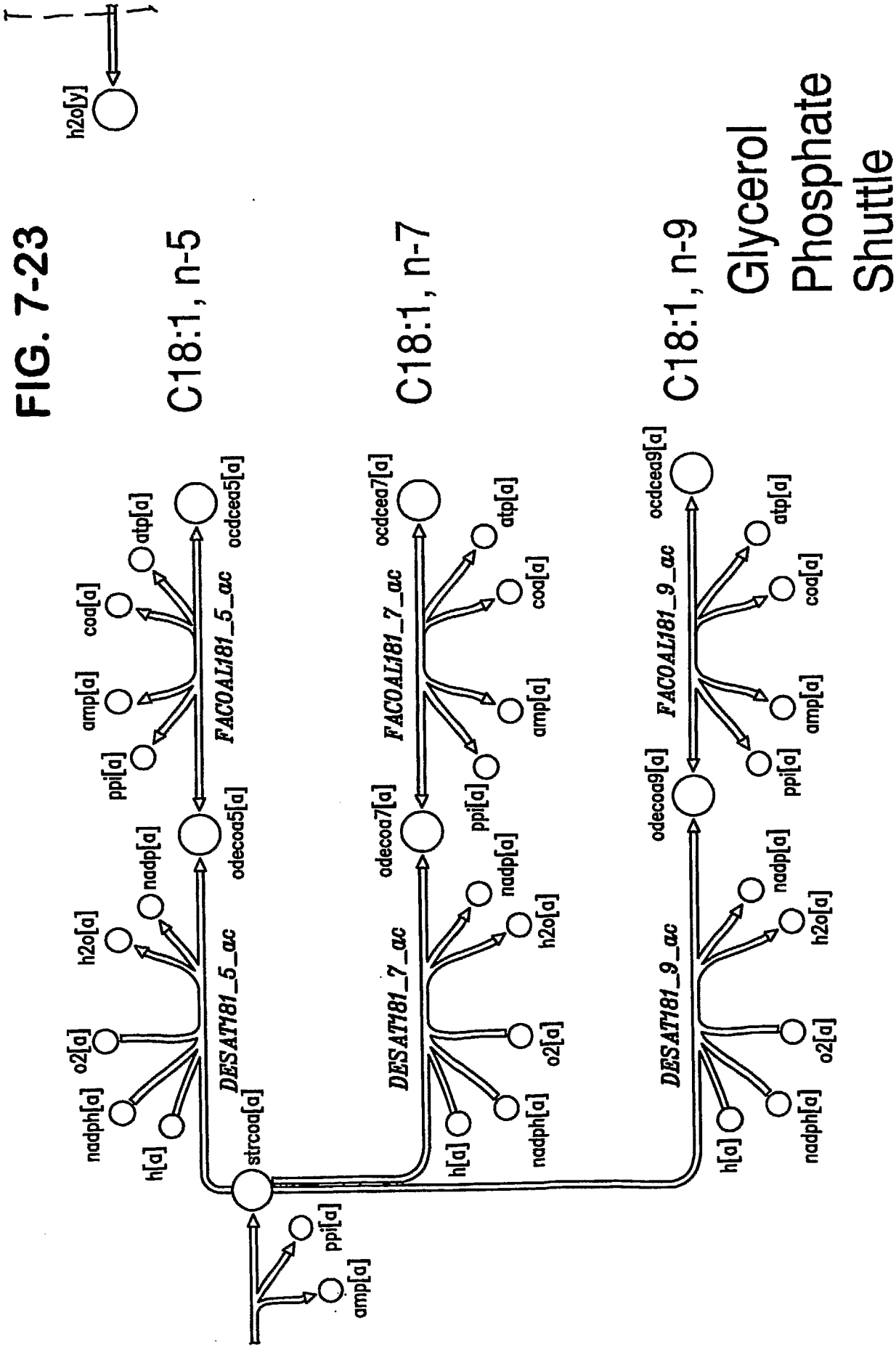

FAS180_ac
co2[a]
h2o[a]
coa[a]
nadp[a]
FACOAL180_ac
ocdca[a]
coa[a]
atp[a]
C18:0
FAS200_ac
h[a]
malcoa[a]
nadph[a]
co2[a]
h2o[a]
coa[a]
nadp[a]
ecsa[a]
C20:0
h[a]
nadph[a]
malcoa[a]
atp[a]
coa[a]
FACOAL200_ac
ppi[a]
amp[a]
ecsacoa[a]
nadph[a]
h[a]
o2[a]
h2o[a]
nadp[a]
DESAT201_7_ac
esecoa7[a]
ppi[a]
amp[a]
FACOAL201_7_ac
h[a]
nadph[a]
o2[a]
h2o[a]
nadp[a]
DESAT201_9_ac
esecoa9[a]
ppi[a]
amp[a]
FACOAL201_9_ac
atp[a]
coa[a]
amp[a]
ppi[a]

FIG. 7-22

FIG. 7-23


h2o[y]
C18:1, n-5
C18:1, n-7
C18:1, n-9
Glycerol Phosphate Shuttle
FACOAL181_5_ac
FACOAL181_7_ac
FACOAL181_9_ac
DESAT181_5_ac
DESAT181_7_ac
DESAT181_9_ac
ocdcea5[a]
ocdcea7[a]
ocdcea9[a]
odecoa5[a]
odecoa7[a]
odecoa9[a]
strcoa[a]
atp[a]
coa[a]
amp[a]
ppi[a]
nadp[a]
h2o[a]
o2[a]
nadph[a]
h[a]

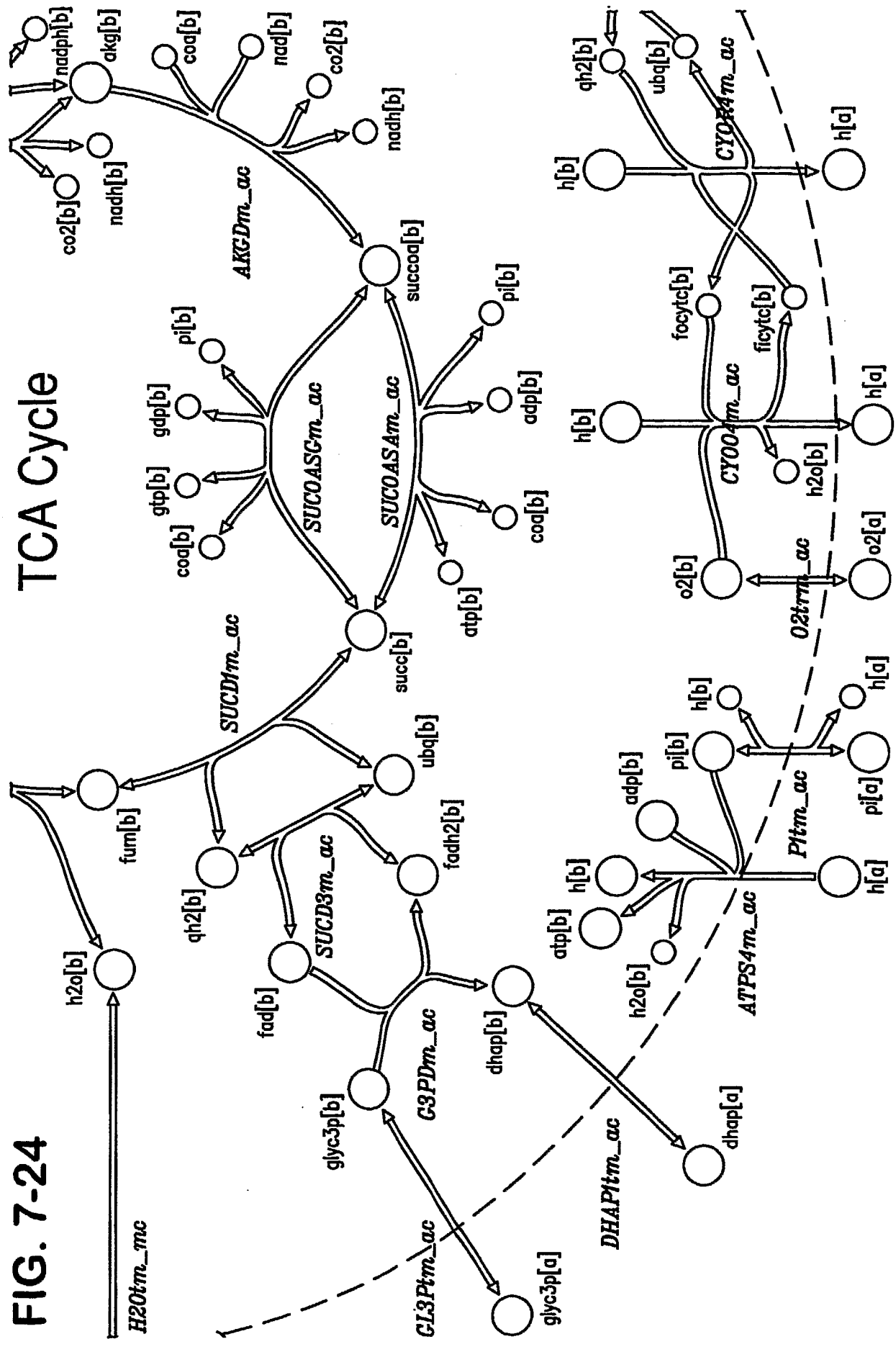

TCA Cycle
nadph[b]
akg[b]
coa[b]
nad[b]
co2[b]
co2[b]
nadh[b]
nadh[b]
AKGDm_ac
succoa[b]
pi[b]
gdp[b]
gtp[b]
coa[b]
SUCOASGm_ac
SUCOASAm_ac
pi[b]
adp[b]
coa[b]
atp[b]
succ[b]
SUCDm_ac
fum[b]
ubq[b]
qh2[b]
SUCD3m_ac
fadh2[b]
fad[b]
h2o[b]
H2Otm_mc
glyc3p[b]
C3PDm_ac
dhap[b]
GL3Ptm_ac
glyc3p[a]
DHAPtm_ac
dhap[a]
qh2[b]
ubq[b]
CYOR4m_ac
h[b]
h[a]
focytc[b]
ficytc[b]
CYOO4m_ac
h[b]
h[a]
h2o[b]
o2[b]
O2tm_ac
o2[a]
h[b]
h[a]
pi[b]
adp[b]
Pitm_ac
pi[a]
h[b]
h[a]
atp[b]
h2o[b]
ATPS4m_ac

FIG. 7-24

FIG. 7-25

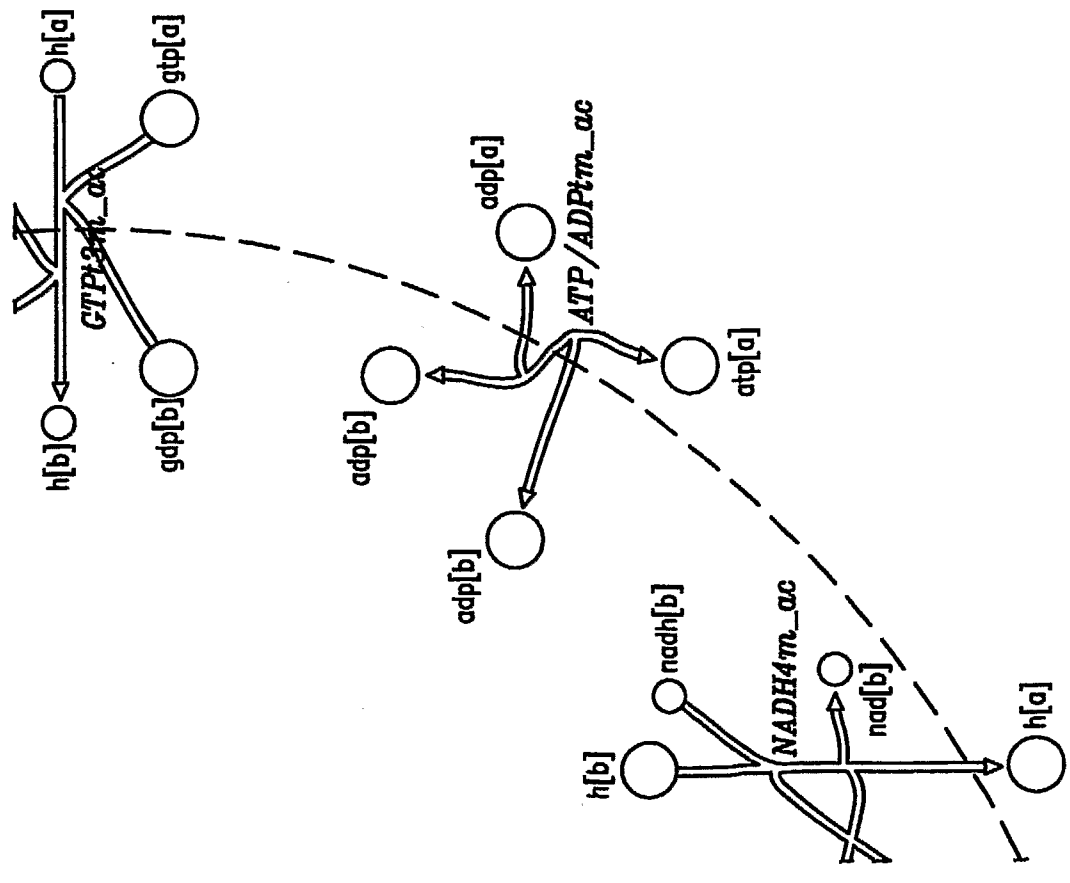
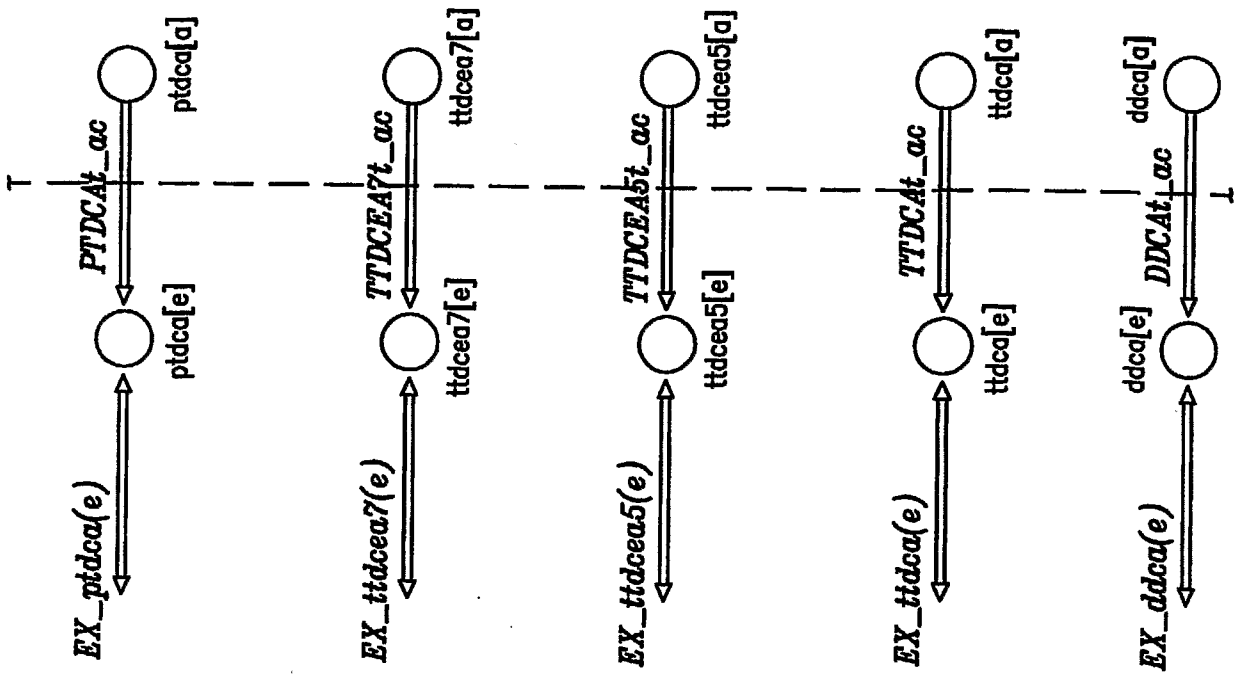

h[a]
gtp[a]
GTPt3m_ac
h[b]
gdp[b]
adp[a]
ATP/ADPtm_ac
adp[b]
atp[a]
adp[b]
nadh[b]
NADH4m_ac
nad[b]
h[b]
h[a]
Electron Transport Chain

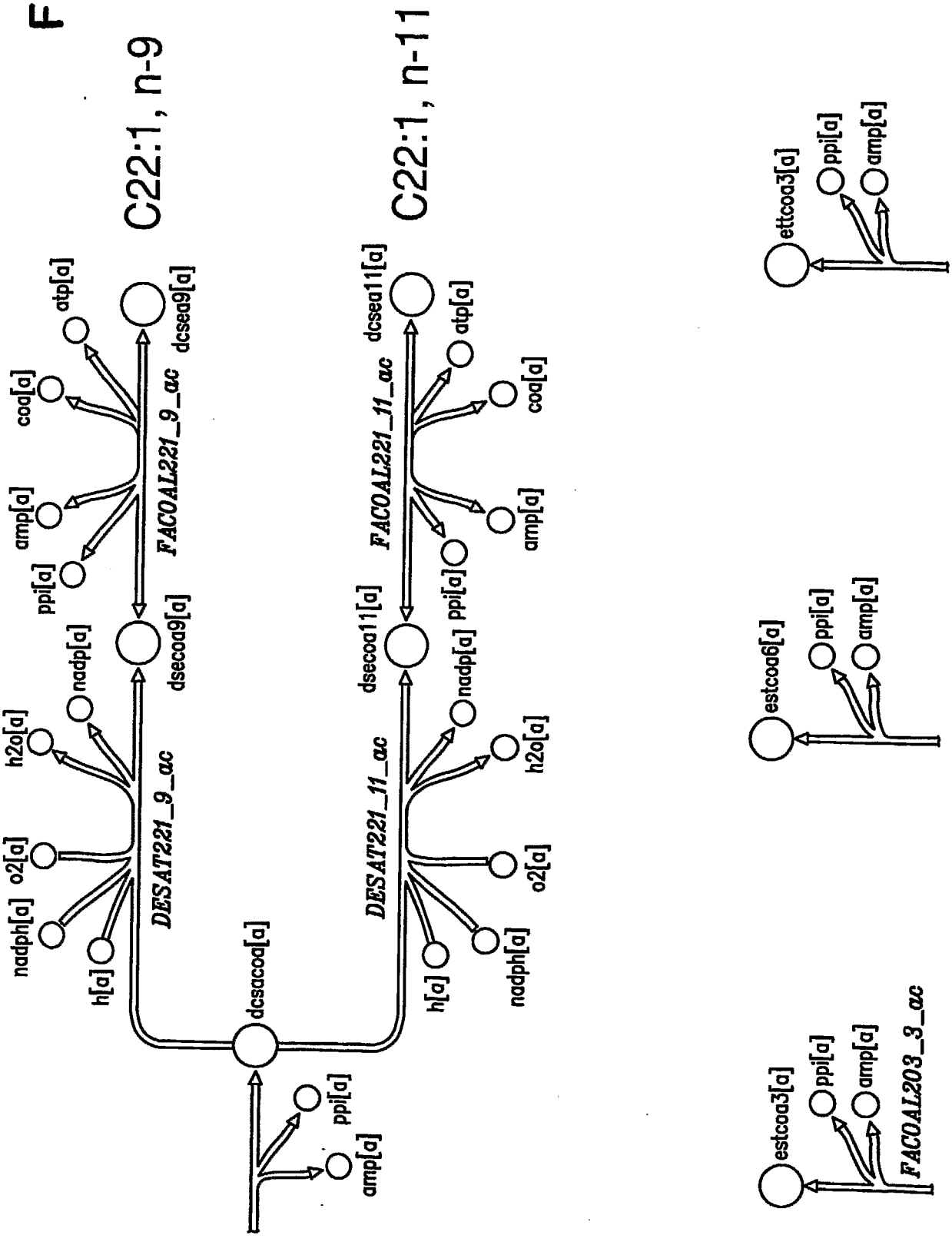
FIG. 7-26


C20:1, n-11
ecsea11[a]
atp[a]
coa[a]
C20:2, n-9
ecsdea9[a]
atp[a]
coa[a]
ocdycacoa6[a]
ppi[a]
amp[a]
T
PTDCAt_ac
ptdca[a]
ptdca[e]
EX_ptdca(e)
TTDCEA7t_ac
ttdcea7[a]
ttdcea7[e]
EX_ttdcea7(e)
TTDCEA5t_ac
ttdcea5[a]
ttdcea5[e]
EX_ttdcea5(e)
TTDCAt_ac
ttdca[a]
ttdca[e]
EX_ttdca(e)
DDCAt_ac
ddca[a]
ddca[e]
EX_ddca(e)
T

FAS220_ac
co2[a]
h2o[a]
coa[a]
nadp[a]
C22:0
FACOAL220_ac
dcsa[a]
atp[a]
coa[a]
esdcoa6[a]
ppi[a]
amp[a]
odcoa6[a]
ppi[a]
amp[a]
odcoa3[a]
ppi[a]
amp[a]
FACOAL201_11_ac
ppi[a]
amp[a]
esecoa11[a]
DESAT201_11_ac
h[a]
nadph[a]
o2[a]
nadp[a]
h2o[a]
FACOAL202_9_ac
ppi[a]
amp[a]
esdcoa9[a]
DESAT202_9_ac
h[a]
nadph[a]
o2[a]
nadp[a]
h2o[a]

FIG. 7-27

FIG. 7-28


C22:1, n-9
C22:1, n-11
dcsacoa[a]
DESAT221_9_ac
DESAT221_11_ac
dsecoa9[a]
dsecoa11[a]
FACOAL221_9_ac
FACOAL221_11_ac
dcsea9[a]
dcsea11[a]
nadph[a]
o2[a]
h2o[a]
nadp[a]
h[a]
ppi[a]
amp[a]
atp[a]
coa[a]
ettcoa3[a]
estcoa6[a]
estcoa3[a]
FACOAL203_3_ac

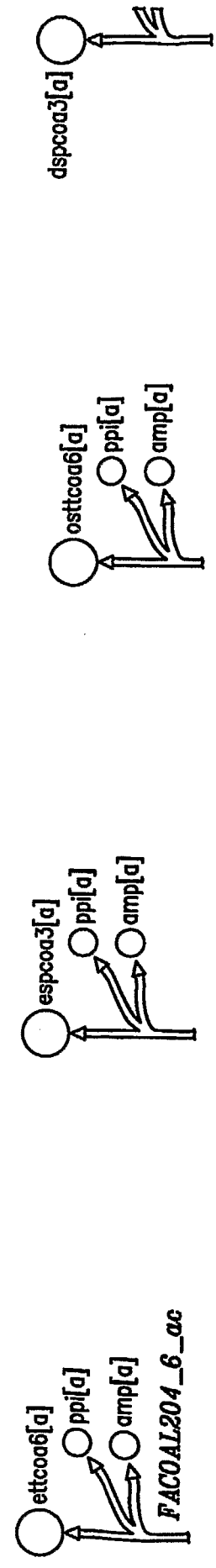
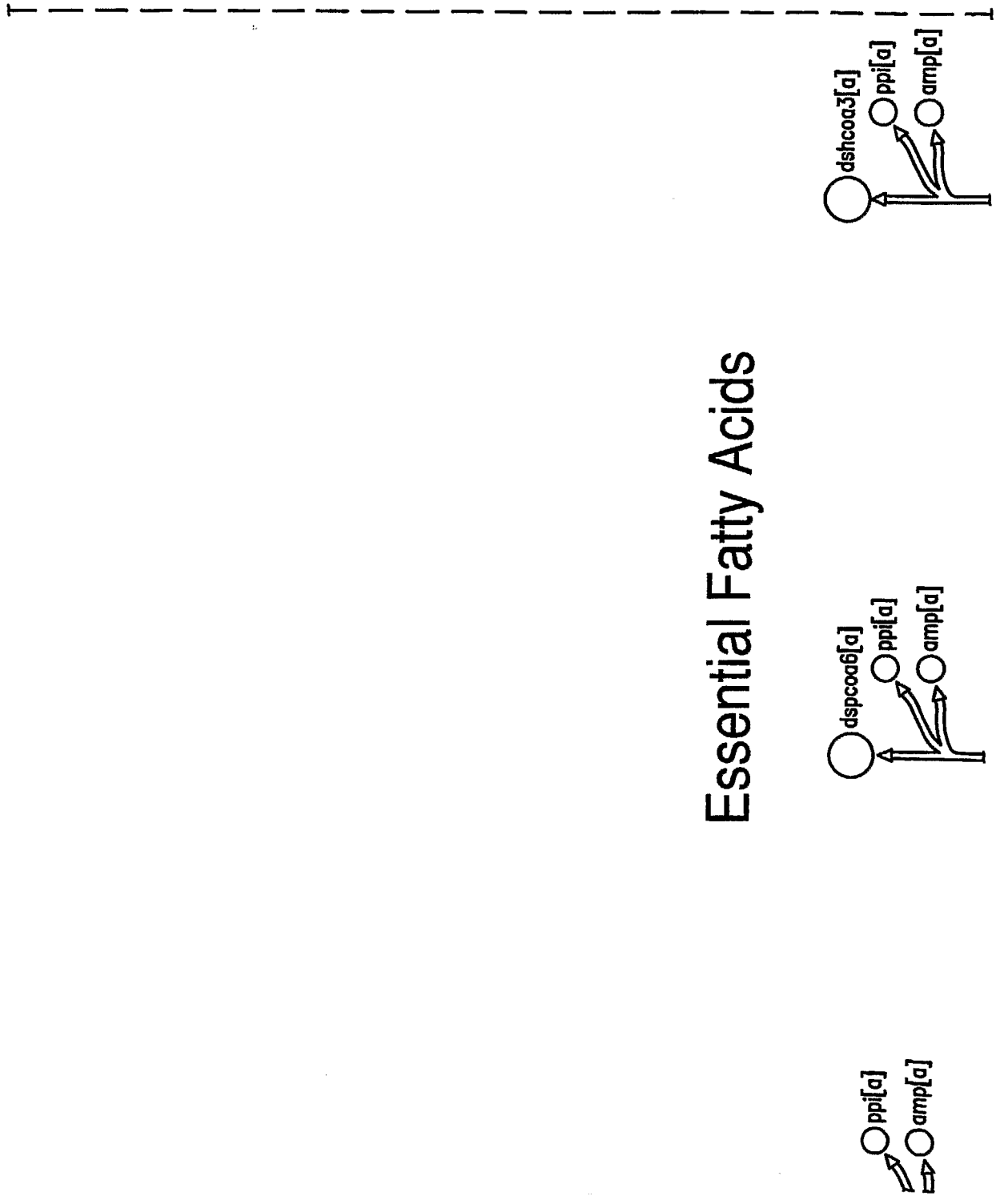

dspcoa3[a]
osttcoa6[a]
ppi[a]
amp[a]
espcoa3[a]
ppi[a]
amp[a]
ettcoa6[a]
ppi[a]
amp[a]
FACOAL204_6_ac

FIG. 7-29

FIG. 7-30


Essential Fatty Acids
dshcoa3[a]
ppi[a]
amp[a]
dspcoa6[a]
ppi[a]
amp[a]
ppi[a]
amp[a]

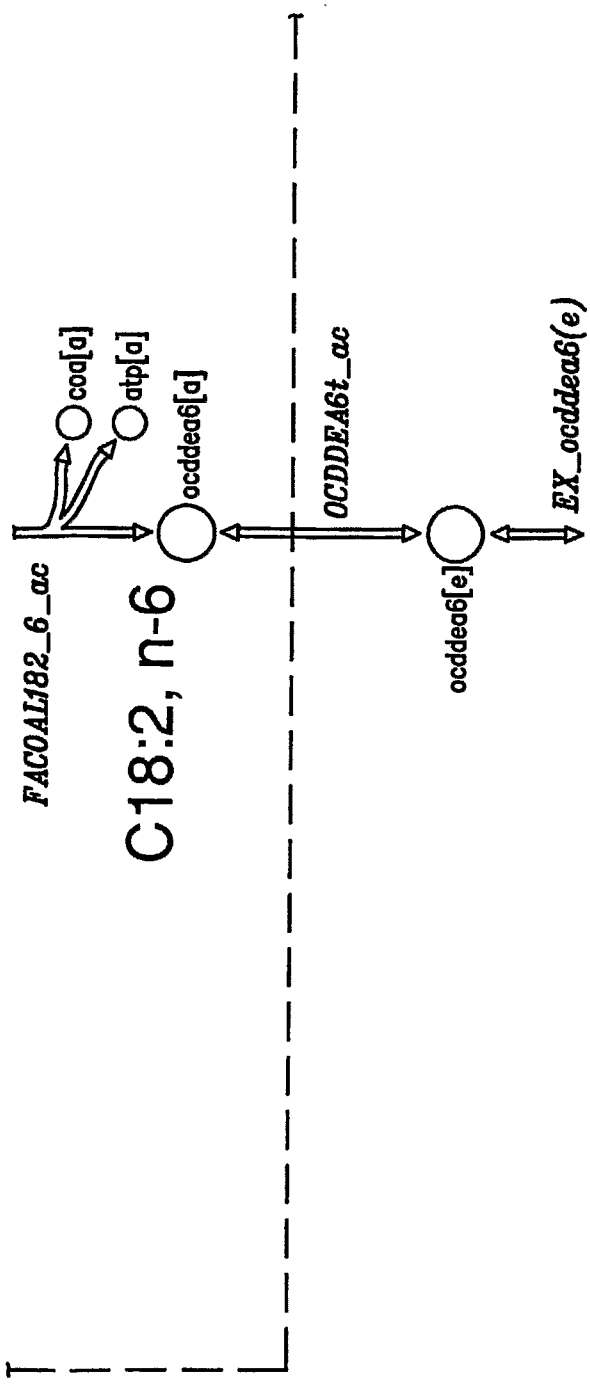

FACOAL182_6_ac
coa[a]
atp[a]
C18:2, n-6
ocddea6[a]
OCDDEA6t_ac
ocddea6[e]
EX_ocddea6(e)

FIG. 7-31

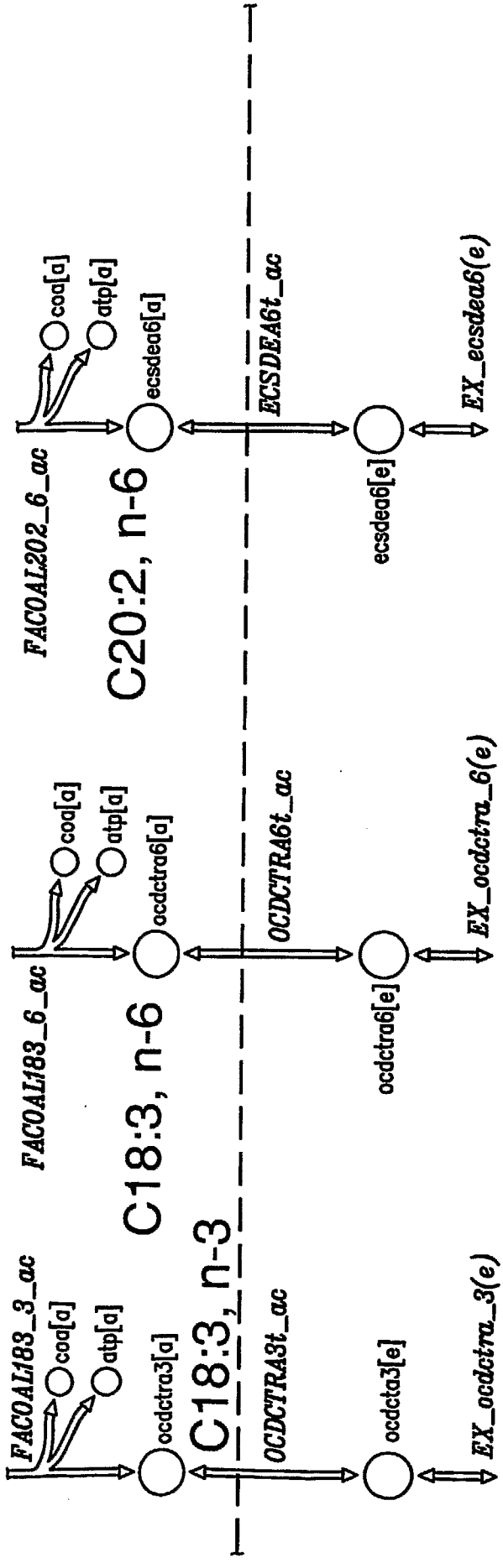

C18:3, n-3
FACOAL183_3_ac
coa[a]
atp[a]
ocdctra3[a]
OCDCTRA3t_ac
ocdcta3[e]
EX_ocdctra_3(e)
C18:3, n-6
FACOAL183_6_ac
coa[a]
atp[a]
ocdctra6[a]
OCDCTRA6t_ac
ocdctra6[e]
EX_ocdctra_6(e)
C20:2, n-6
FACOAL202_6_ac
coa[a]
atp[a]
ecsdea6[a]
ECSDEA6t_ac
ecsdea6[e]
EX_ecsdea6(e)

FIG. 7-32

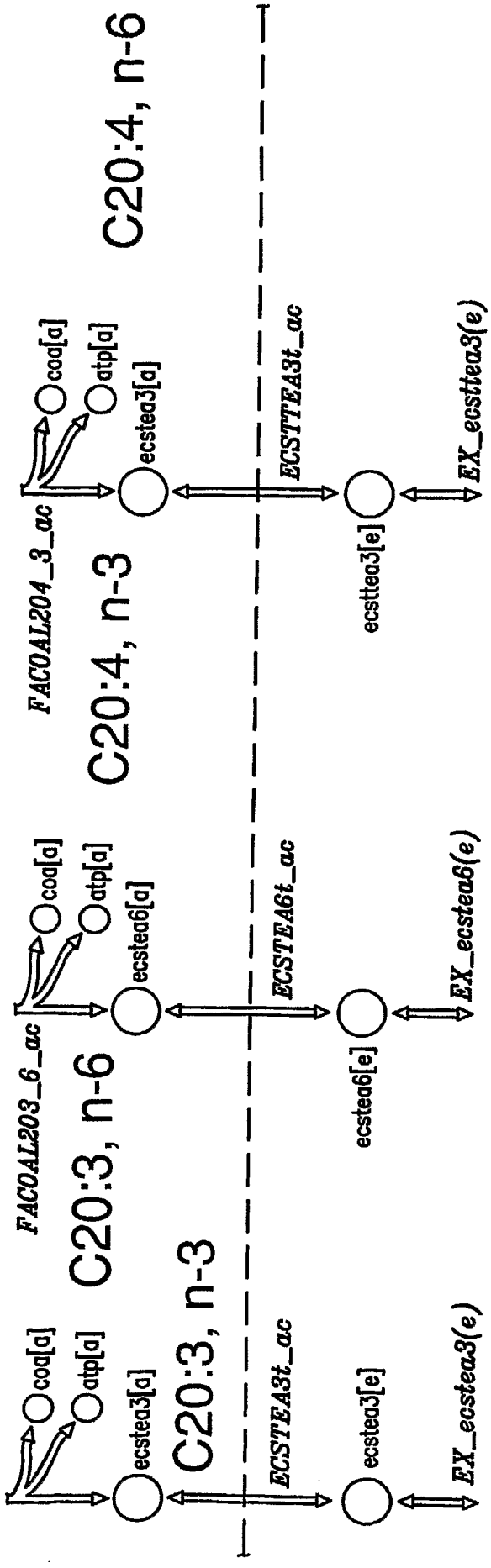

C20:3, n-3
C20:3, n-6
C20:4, n-3
C20:4, n-6
coa[a]
atp[a]
ecstea3[a]
ECSTEA3t_ac
ecstea3[e]
EX_ecstea3(e)
FACOAL203_6_ac
ecstea6[a]
ECSTEA6t_ac
ecstea6[e]
EX_ecstea6(e)
FACOAL204_3_ac
ecsttea3[a]
ECSTTEA3t_ac
ecsttea3[e]
EX_ecsttea3(e)

FIG. 7-33

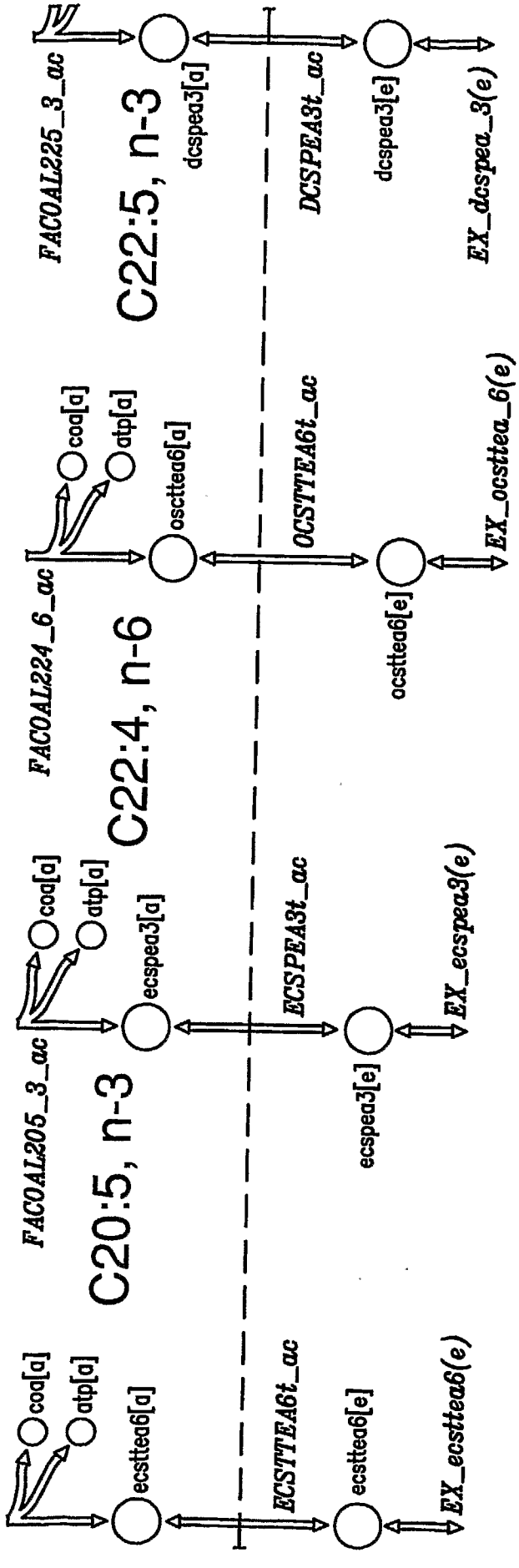

C20:5, n-3
C22:4, n-6
C22:5, n-3
FACOAL205_3_ac
FACOAL224_6_ac
FACOAL225_3_ac
coa[a]
atp[a]
ecsttea6[a]
ECSTTEA6t_ac
ecsttea6[e]
EX_ecsttea6(e)
ecspea3[a]
ECSPEA3t_ac
ecspea3[e]
EX_ecspea3(e)
oscttea6[a]
OCSTTEA6t_ac
ocsttea6[e]
EX_ocsttea_6(e)
dcspea3[a]
DCSPEA3t_ac
dcspea3[e]
EX_dcspea_3(e)

FIG. 7-34

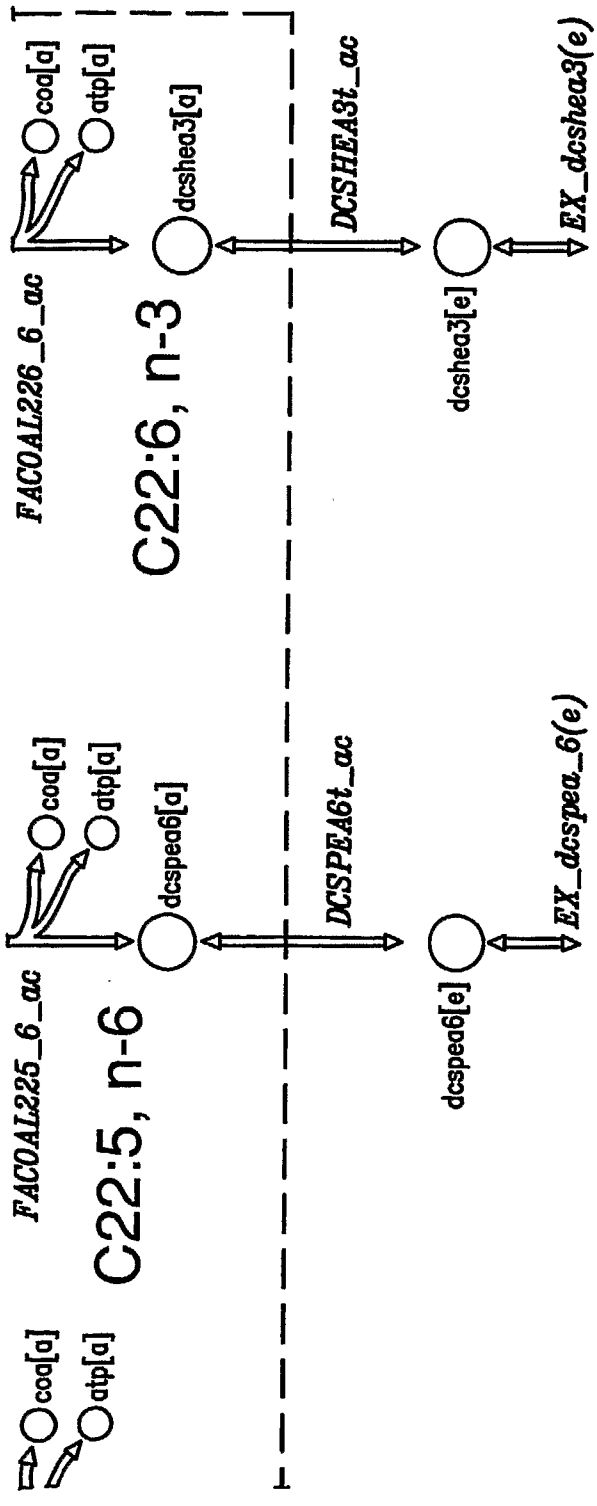
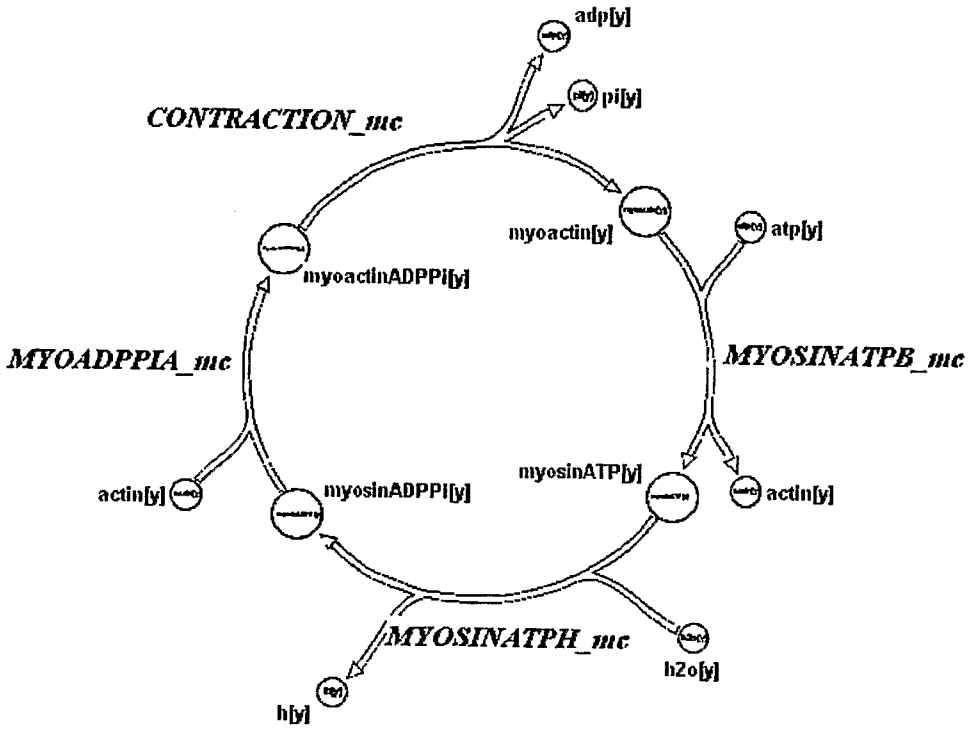

coa[a]
atp[a]
FACOAL225_6_ac
C22:5, n-6
dcspea6[a]
DCSPEA6t_ac
dcspea6[e]
EX_dcspea_6(e)
coa[a]
atp[a]
FACOAL226_6_ac
C22:6, n-3
dcshea3[a]
DCSHEA3t_ac
dcshea3[e]
EX_dcshea3(e)

FIG. 7-35



Net Reaction: ATP + H2O → ADP + Pi + H

FIGURE 8

FIG. 9-1

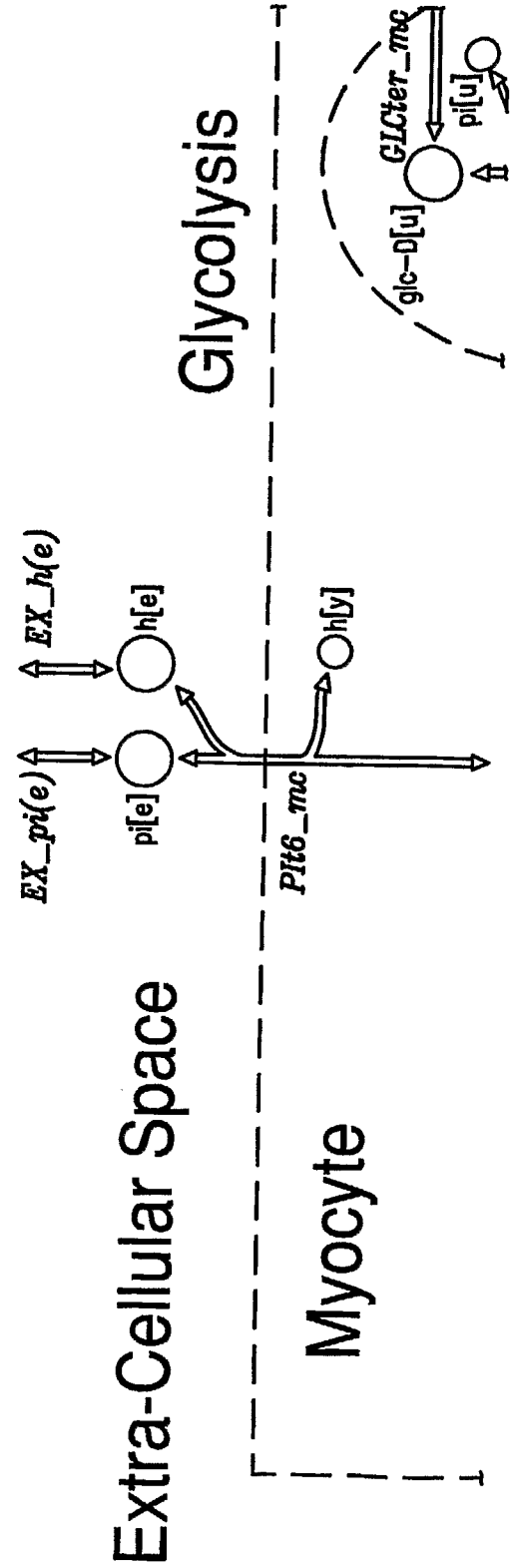

Glycolysis
Extra-Cellular Space
Myocyte
EX_h(e)
h[e]
h[y]
EX_pi(e)
pi[e]
Pit6_mc
GLCter_mc
pi[u]
glc-D[u]

FIG. 9-2

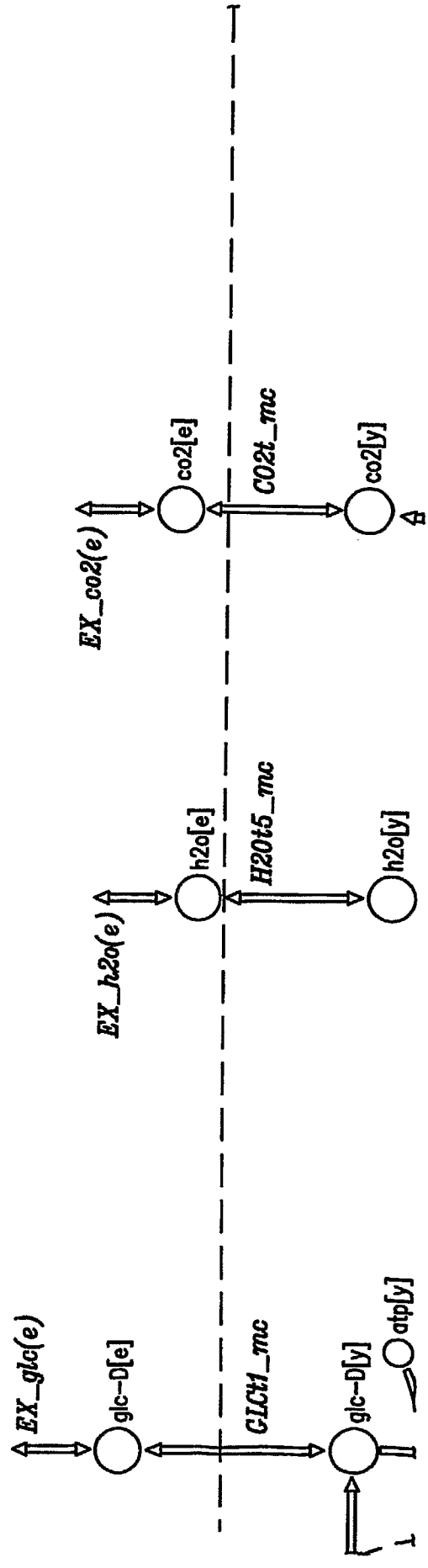

EX_co2(e)
co2[e]
CO2t_mc
co2[y]
EX_h2o(e)
h2o[e]
H2Ot5_mc
h2o[y]
EX_glc(e)
glc-D[e]
GLCt1_mc
glc-D[y]
atp[y]

FIG. 9-3

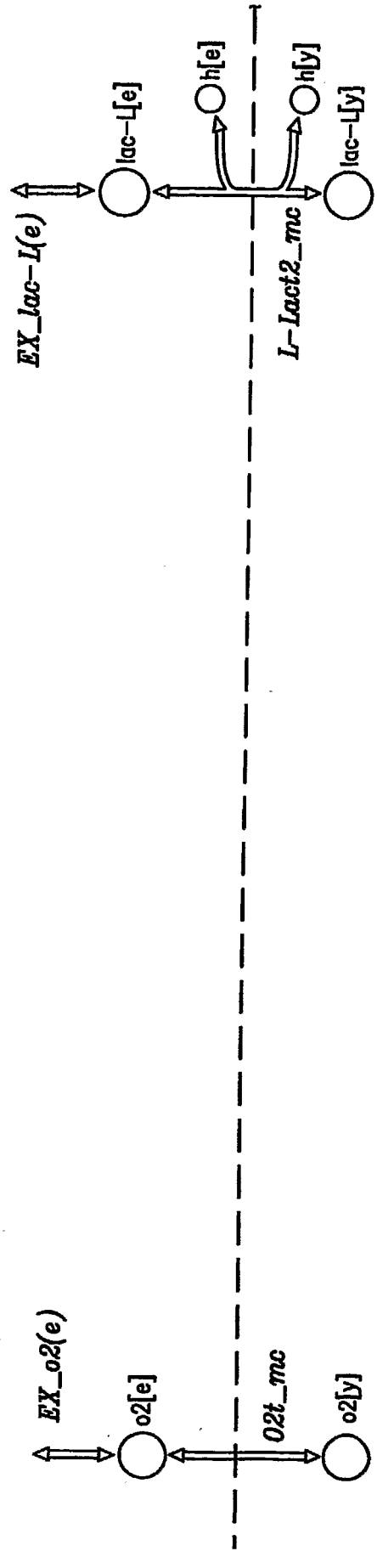


FIG. 9-4

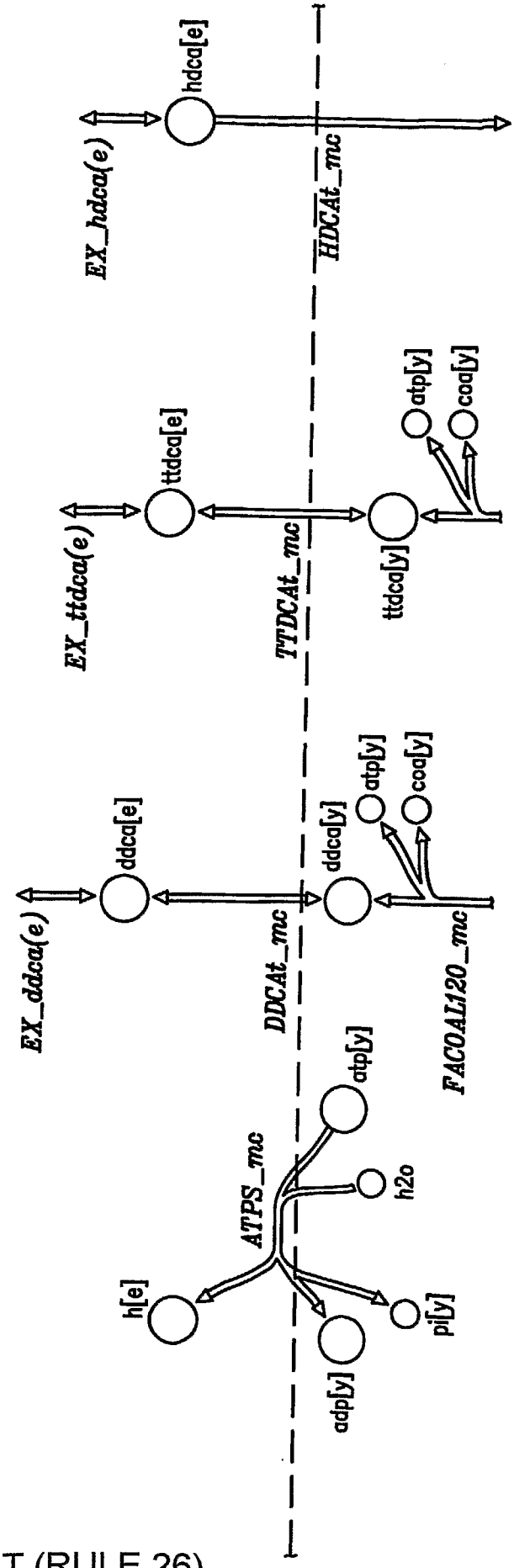
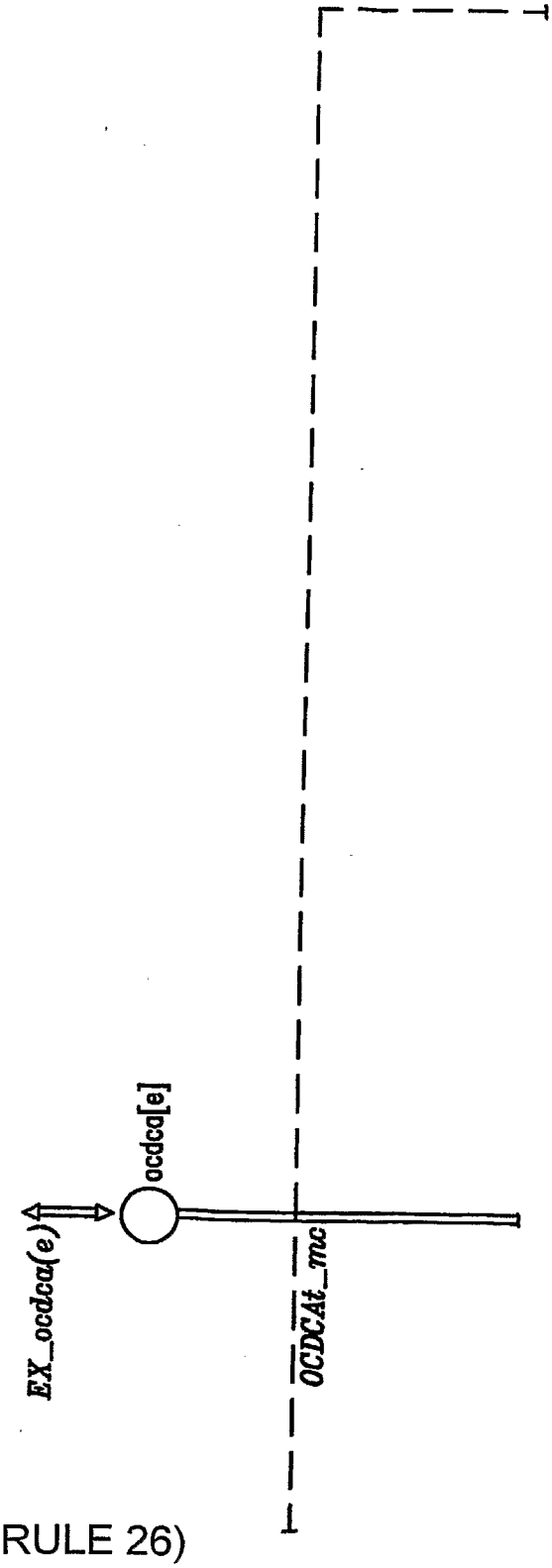

hdca[e]
EX_hdca(e)
HDCAt_mc
atp[y]
coa[y]
ttdca[e]
EX_ttdca(e)
TTDCAt_mc
ttdca[y]
atp[y]
coa[y]
ddca[e]
EX_ddca(e)
DDCAt_mc
ddca[y]
atp[y]
coa[y]
FACOAL120_mc
atp[y]
ATPS_mc
h2o
h[e]
pi[y]
adp[y]

FIG. 9-5



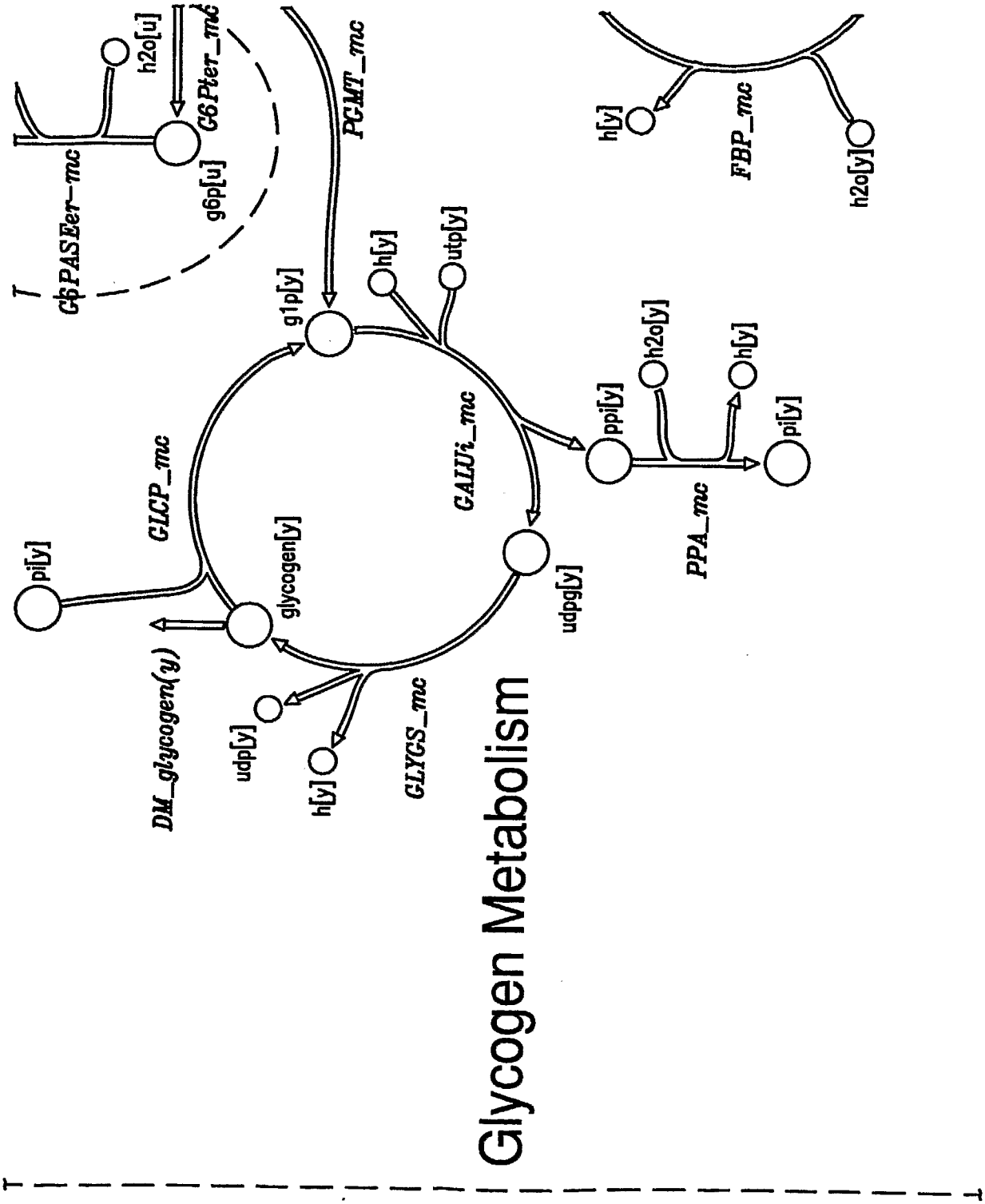

Glycogen Metabolism
GLCP_mc
GLYGS_mc
GALUi_mc
PGMT_mc
G6PTer_mc
G6PASEer_mc
PPA_mc
FBP_mc
DM_glycogen(y)
glycogen[y]
g1p[y]
udpg[y]
udp[y]
utp[y]
ppi[y]
pi[y]
h[y]
h2o[y]
h2o[u]
g6p[u]

FIG. 9-6

FIG. 9-7

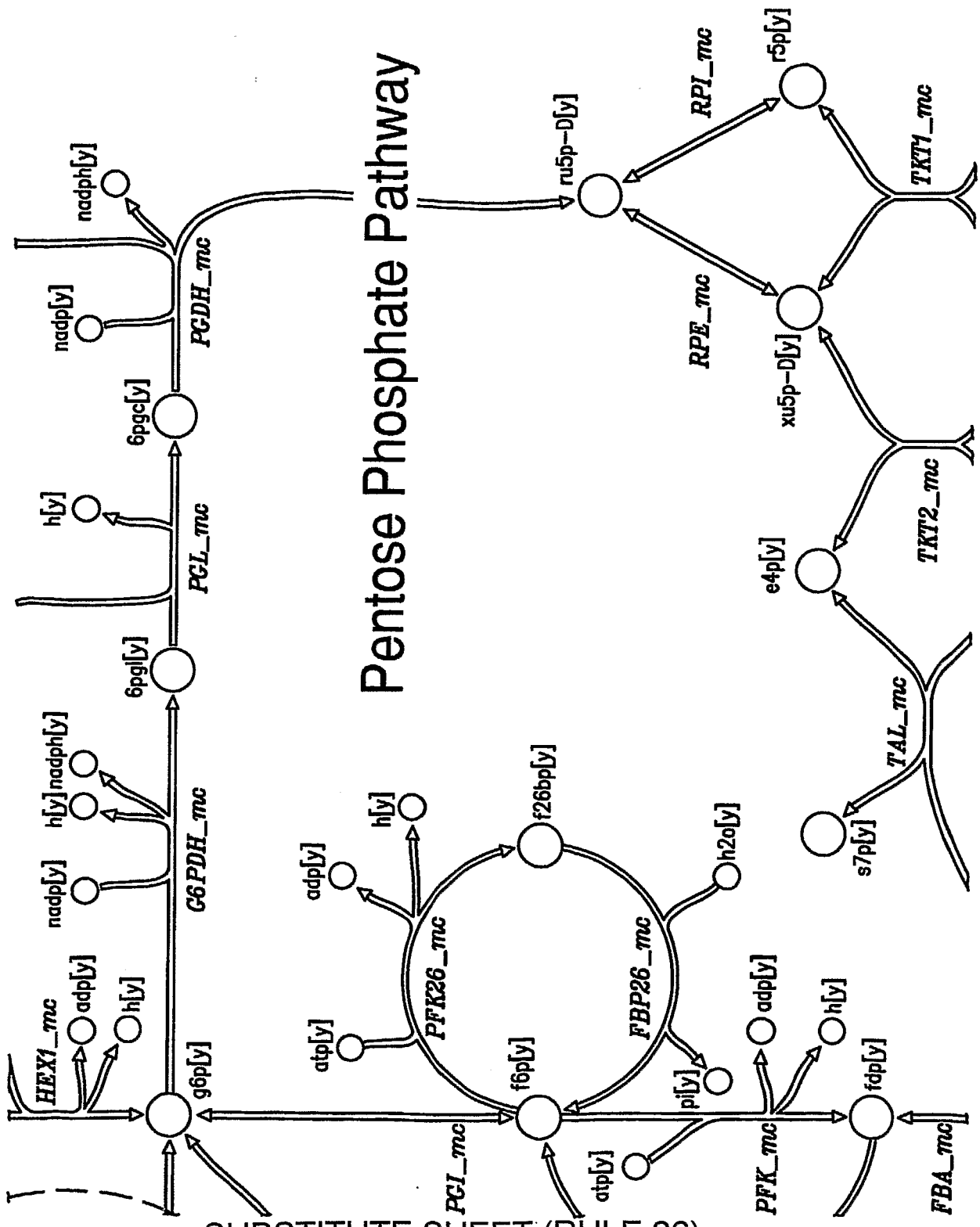
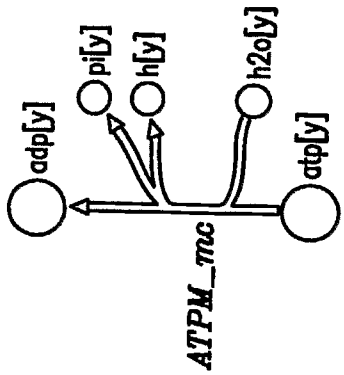

Pentose Phosphate Pathway
HEX1_mc
adp[y]
h[y]
g6p[y]
nadp[y]
h[y]
nadph[y]
G6PDH_mc
6pgl[y]
h[y]
PGL_mc
6pgc[y]
nadp[y]
nadph[y]
PGDH_mc
ru5p-D[y]
RPI_mc
r5p[y]
TKT1_mc
RPE_mc
xu5p-D[y]
TKT2_mc
e4p[y]
TAL_mc
s7p[y]
adp[y]
h[y]
PFK26_mc
atp[y]
f26bp[y]
h2o[y]
FBP26_mc
f6p[y]
pi[y]
PGI_mc
atp[y]
adp[y]
h[y]
PFK_mc
fdp[y]
FBA_mc

FIG. 9-8 Non-growth Associated Energy Maintainance



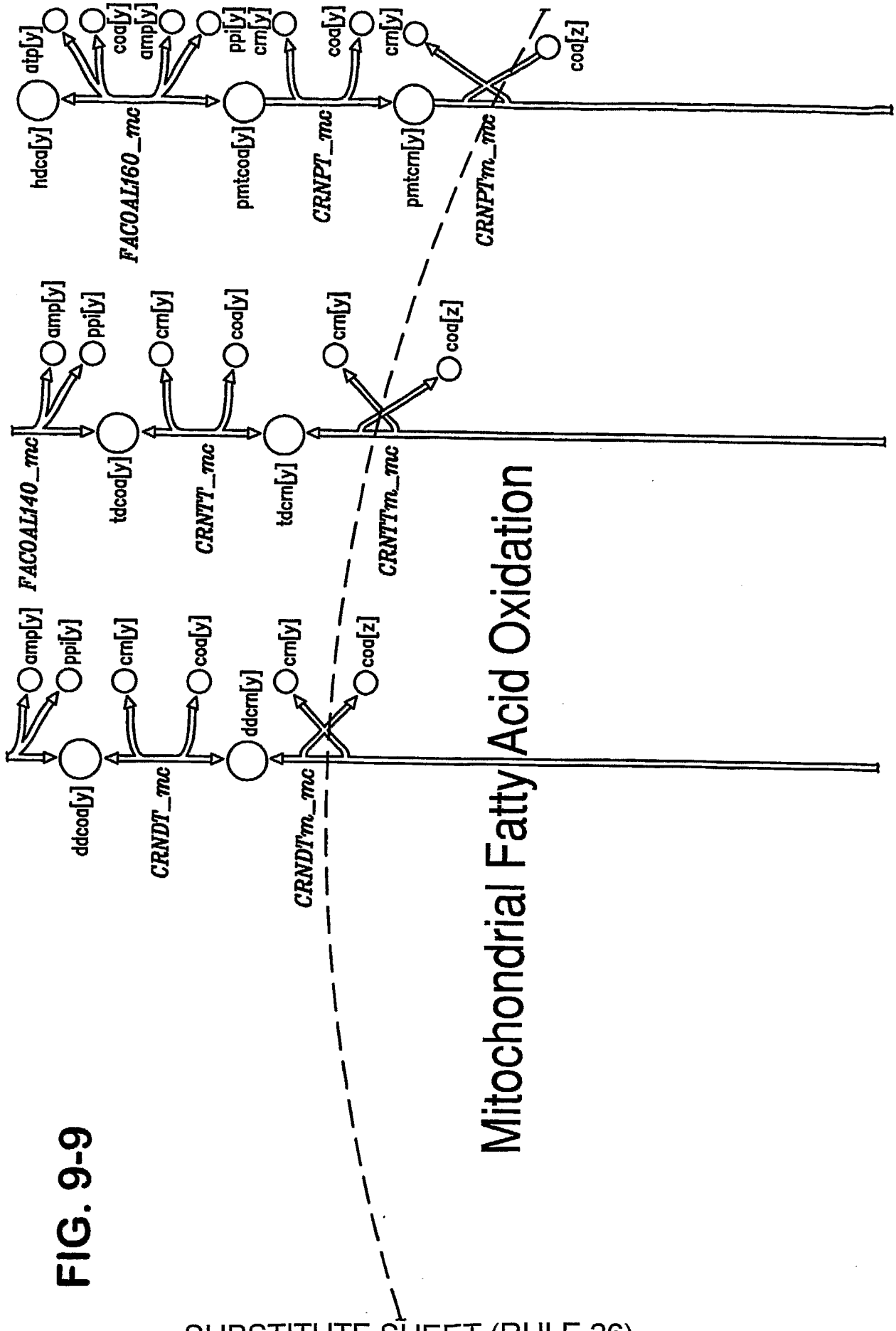
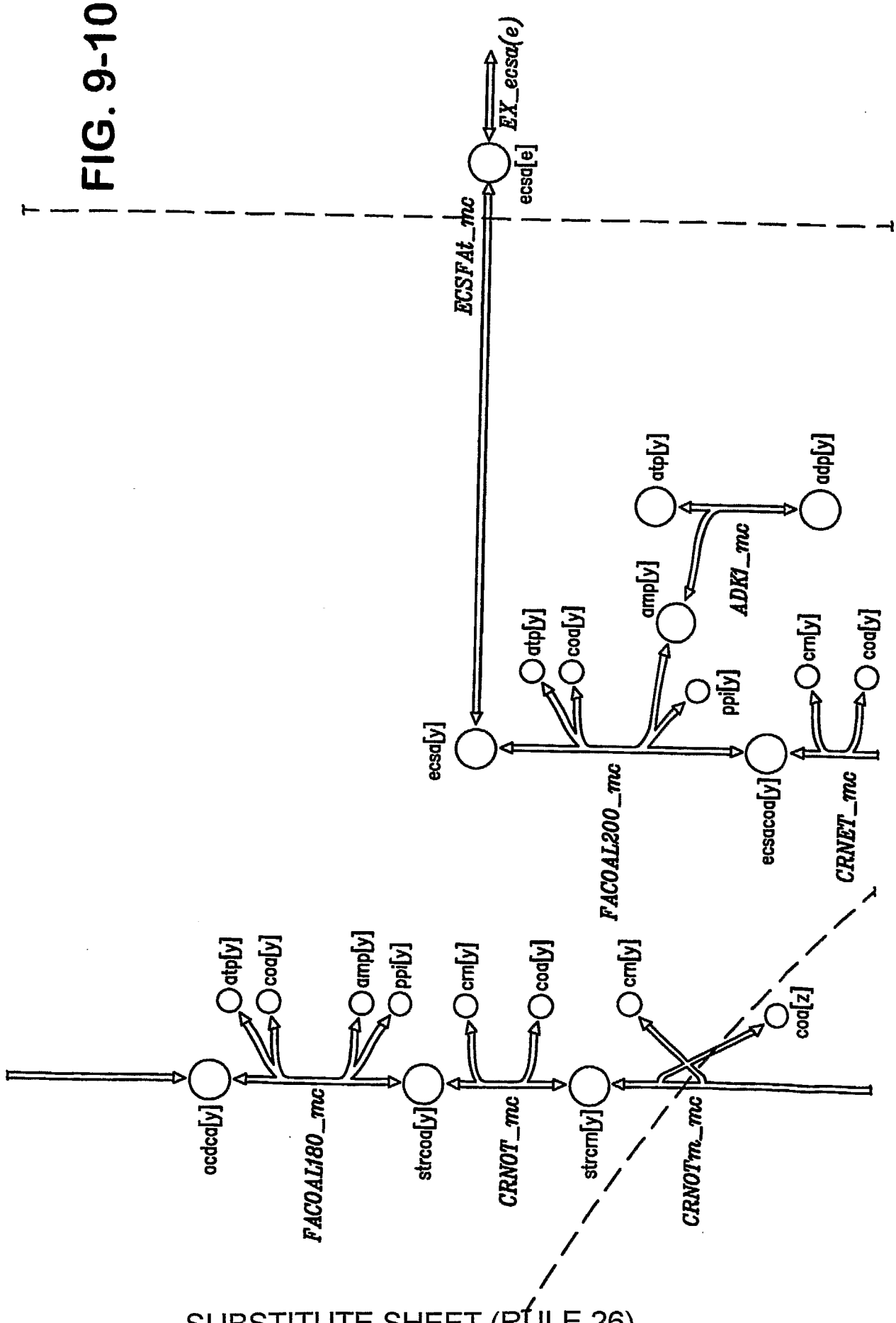

Mitochondrial Fatty Acid Oxidation
hdcoa[y]
atp[y]
coa[y]
amp[y]
FACOAL160_mc
pmtcoa[y]
ppi[y]
crn[y]
CRNPT_mc
coa[y]
pmtcrn[y]
crn[y]
coa[z]
CRNPTm_mc
tdcoa[y]
FACOAL140_mc
amp[y]
ppi[y]
CRNTT_mc
crn[y]
coa[y]
tdcrn[y]
crn[y]
coa[z]
CRNTTm_mc
ddcoa[y]
FACOAL140_mc
amp[y]
ppi[y]
CRNDT_mc
crn[y]
coa[y]
ddcrn[y]
crn[y]
coa[z]
CRNDTm_mc

FIG. 9-9

FIG. 9-10


EX_ecsa(e)
ecsa[e]
ECSFAt_mc
atp[y]
adp[y]
ADK1_mc
amp[y]
atp[y]
coa[y]
ppi[y]
ecsa[y]
FACOAL200_mc
cm[y]
coa[y]
ecsacoa[y]
CRNET_mc
ocdca[y]
FACOAL180_mc
strcoa[y]
CRNOT_mc
strcm[y]
CRNOTm_mc
coa[z]

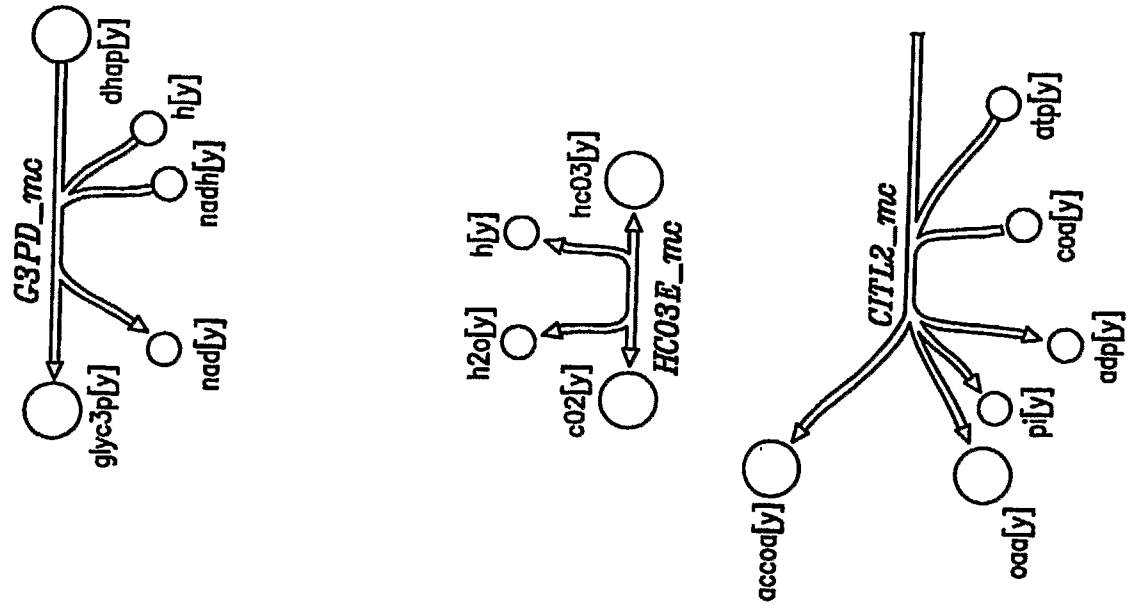

G3PD_mc
dhap[y]
h[y]
nadh[y]
nad[y]
glyc3p[y]
HCO3E_mc
h[y]
hco3[y]
h2o[y]
co2[y]
CITL2_mc
atp[y]
coa[y]
adp[y]
pi[y]
accoa[y]
oaa[y]

FIG. 9-11

FIG. 9-12

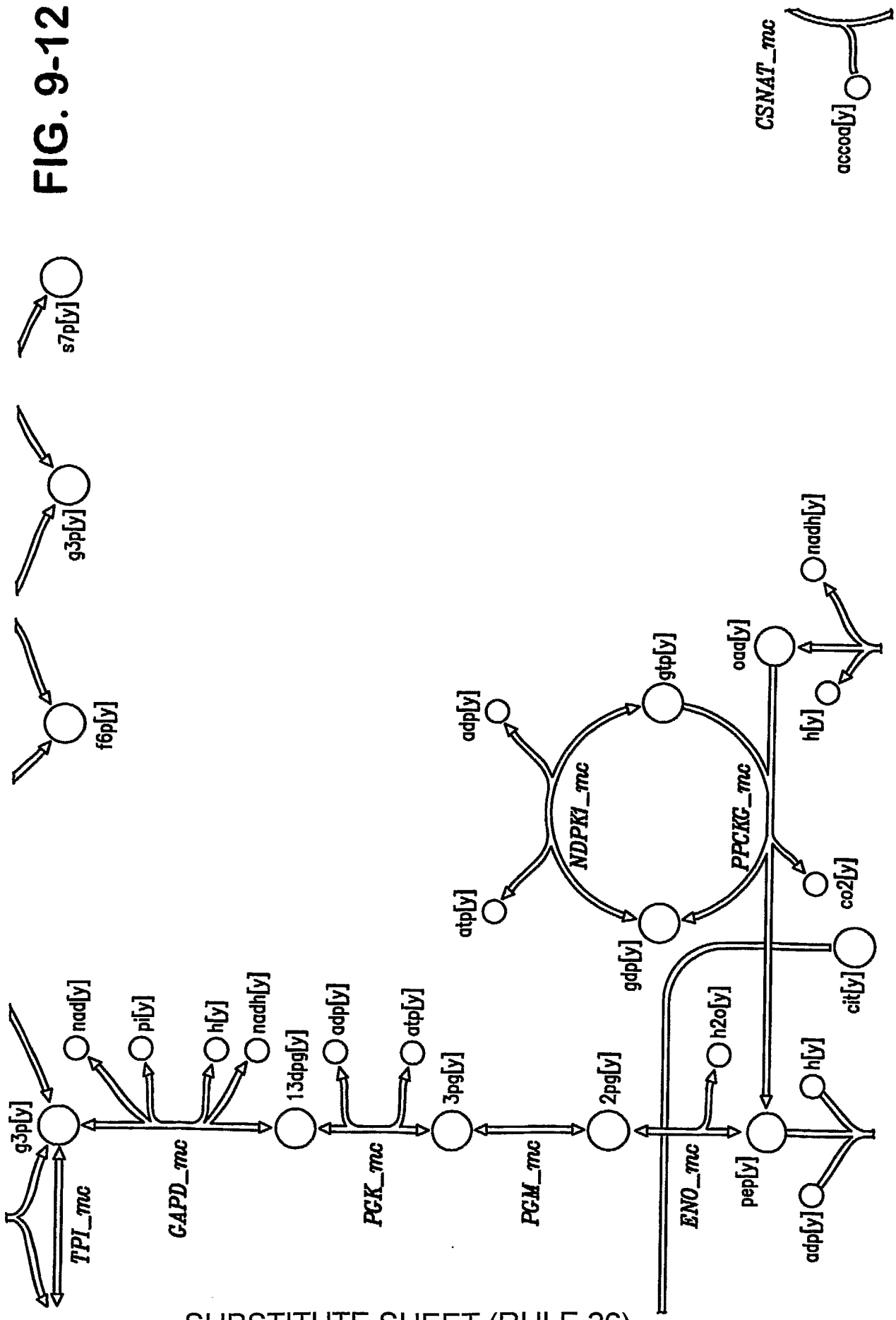
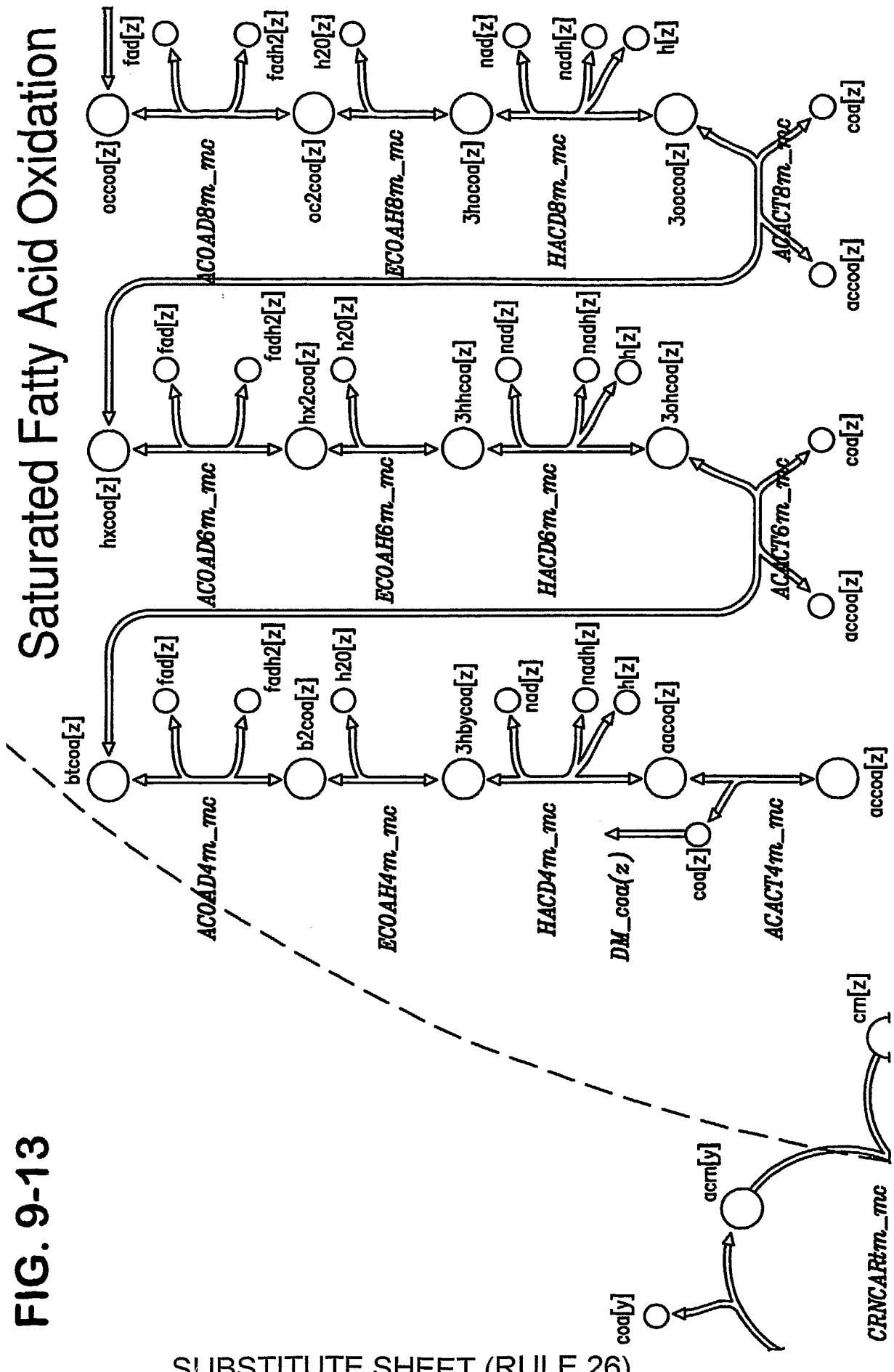

s7p[y]
g3p[y]
f6p[y]
CSNAT_mc
accoa[y]
nadh[y]
h[y]
oaa[y]
gtp[y]
adp[y]
NDPK1_mc
PPCKG_mc
atp[y]
co2[y]
gdp[y]
cit[y]
h2o[y]
h[y]
g3p[y]
nad[y]
pi[y]
h[y]
nadh[y]
13dpg[y]
adp[y]
atp[y]
3pg[y]
2pg[y]
pep[y]
adp[y]
TPI_mc
GAPD_mc
PGK_mc
PGM_mc
ENO_mc

FIG. 9-13


Saturated Fatty Acid Oxidation
btcoa[z]
fad[z]
fadh2[z]
h20[z]
ACOAD4m_mc
b2coa[z]
ECOAH4m_mc
3hbycoa[z]
nad[z]
nadh[z]
h[z]
HACD4m_mc
aacoa[z]
DM_coa(z)
coa[z]
ACACT4m_mc
accoa[z]
hxcoa[z]
ACOAD6m_mc
hx2coa[z]
ECOAH6m_mc
3hhcoa[z]
HACD6m_mc
3ohcoa[z]
ACACT6m_mc
occoa[z]
ACOAD8m_mc
oc2coa[z]
ECOAH8m_mc
3hocoa[z]
HACD8m_mc
3oocoa[z]
ACACT8m_mc
cm[z]
acm[y]
coa[y]
CRNCARtm_mc

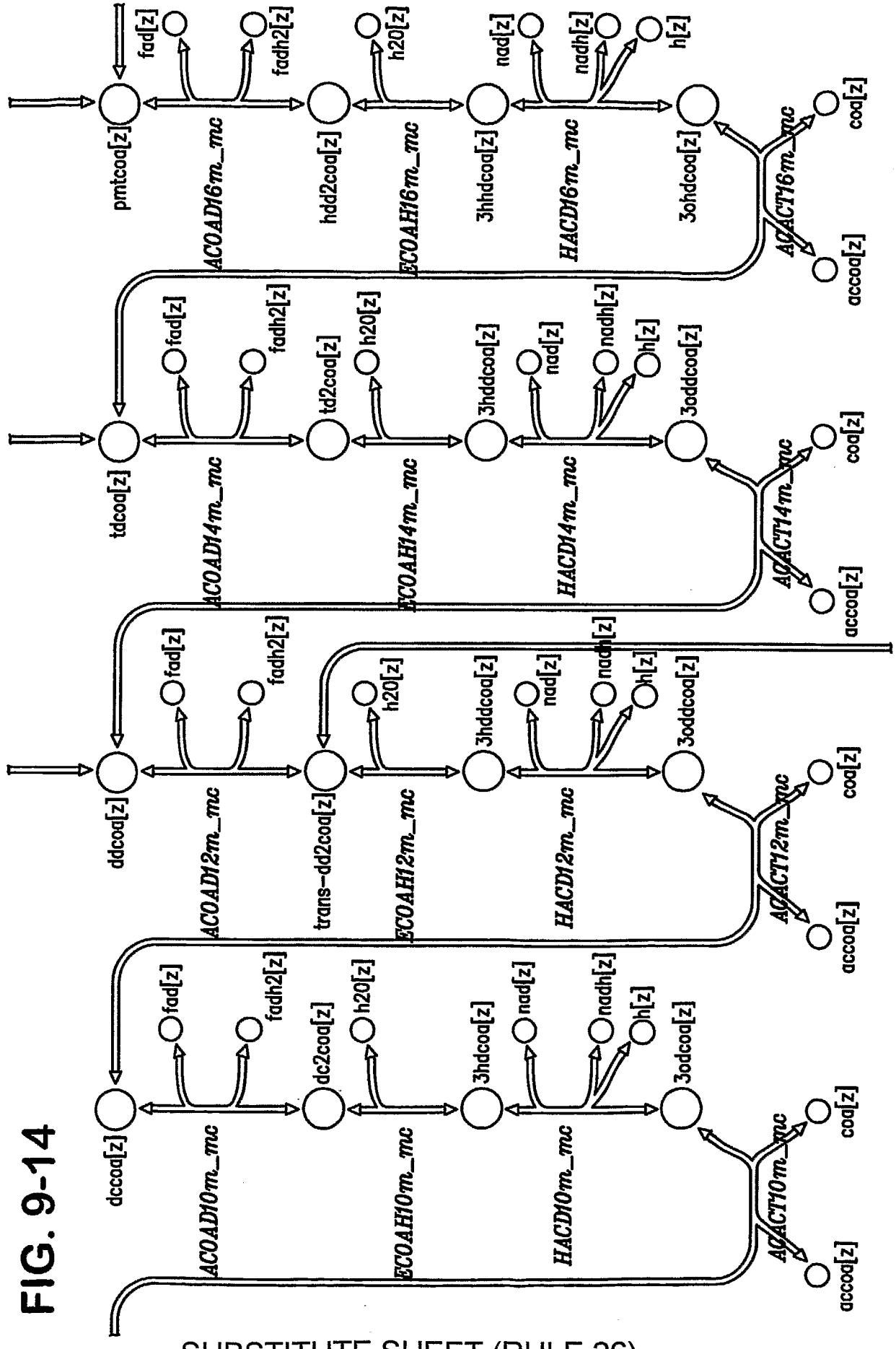
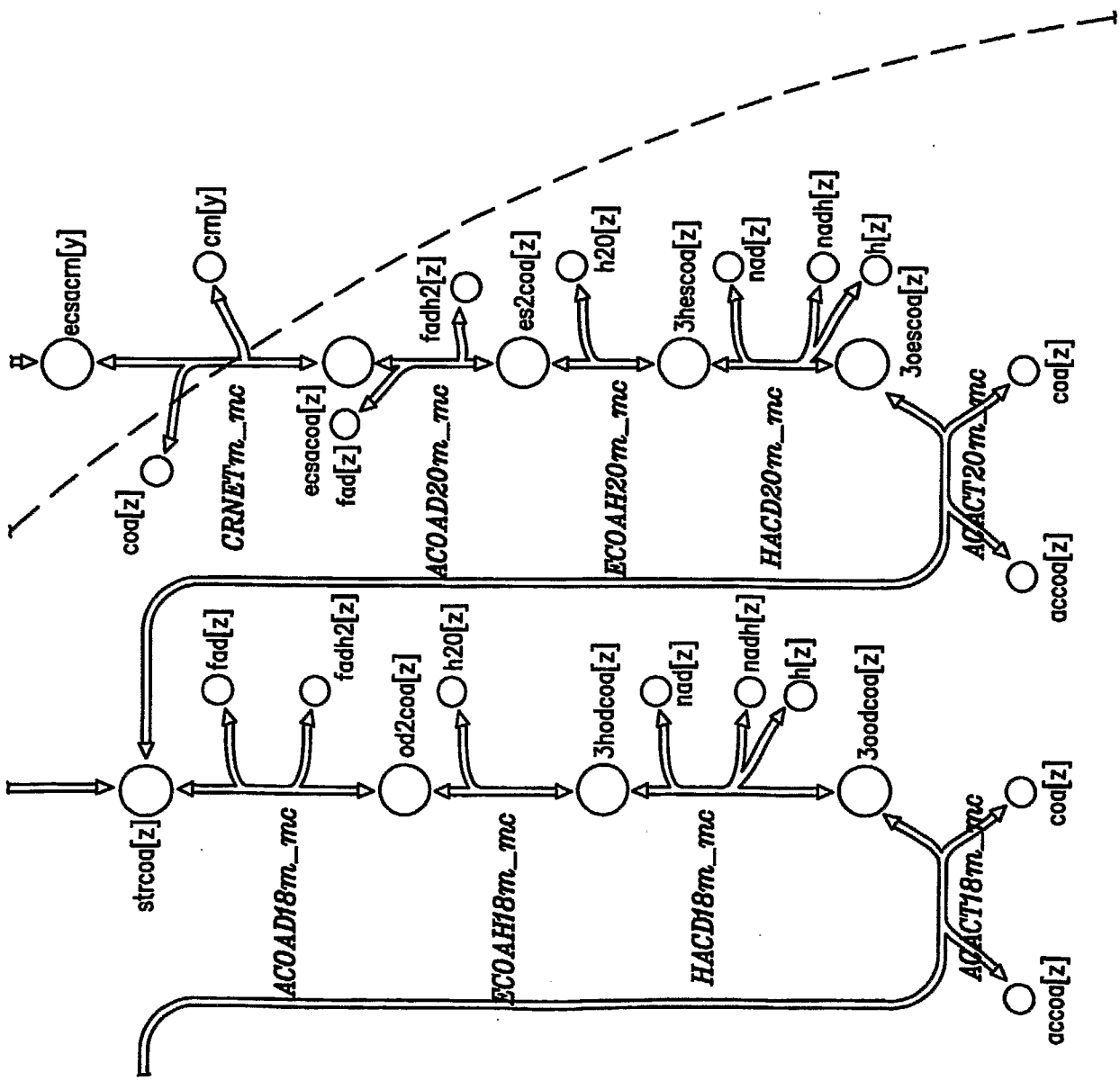

pmtcoa[z]
fad[z]
fadh2[z]
ACOAD16m_mc
hdd2coa[z]
h20[z]
ECOAH16m_mc
3hhdcoa[z]
nad[z]
nadh[z]
h[z]
HACD16m_mc
3ohdcoa[z]
AOACT16m_mc
coa[z]
accoa[z]
tdcoa[z]
fad[z]
fadh2[z]
ACOAD14m_mc
td2coa[z]
h20[z]
ECOAH14m_mc
3hddcoa[z]
nad[z]
nadh[z]
h[z]
HACD14m_mc
3oddcoa[z]
AOACT14m_mc
coa[z]
accoa[z]
ddcoa[z]
fad[z]
fadh2[z]
ACOAD12m_mc
trans-dd2coa[z]
h20[z]
ECOAH12m_mc
3hddcoa[z]
nad[z]
nadh[z]
h[z]
HACD12m_mc
3oddcoa[z]
AOACT12m_mc
coa[z]
accoa[z]
dccoa[z]
fad[z]
fadh2[z]
ACOAD10m_mc
dc2coa[z]
h20[z]
ECOAH10m_mc
3hdcoa[z]
nad[z]
nadh[z]
h[z]
HACD10m_mc
3odcoa[z]
AOACT10m_mc
coa[z]
accoa[z]

FIG. 9-14

FIG. 9-15


ecsacm[y]
cm[y]
coa[z]
CRNETm_mc
essacoa[z]
fad[z]
fadh2[z]
ACOAD20m_mc
es2coa[z]
h20[z]
ECOAH20m_mc
3hescoa[z]
nad[z]
nadh[z]
h[z]
HACD20m_mc
3oescoa[z]
ACACT20m_mc
coa[z]
accoa[z]
strcoa[z]
fad[z]
fadh2[z]
ACOAD18m_mc
od2coa[z]
h20[z]
ECOAH18m_mc
3hodcoa[z]
nad[z]
nadh[z]
h[z]
HACD18m_mc
3oodcoa[z]
ACACT18m_mc
coa[z]
accoa[z]

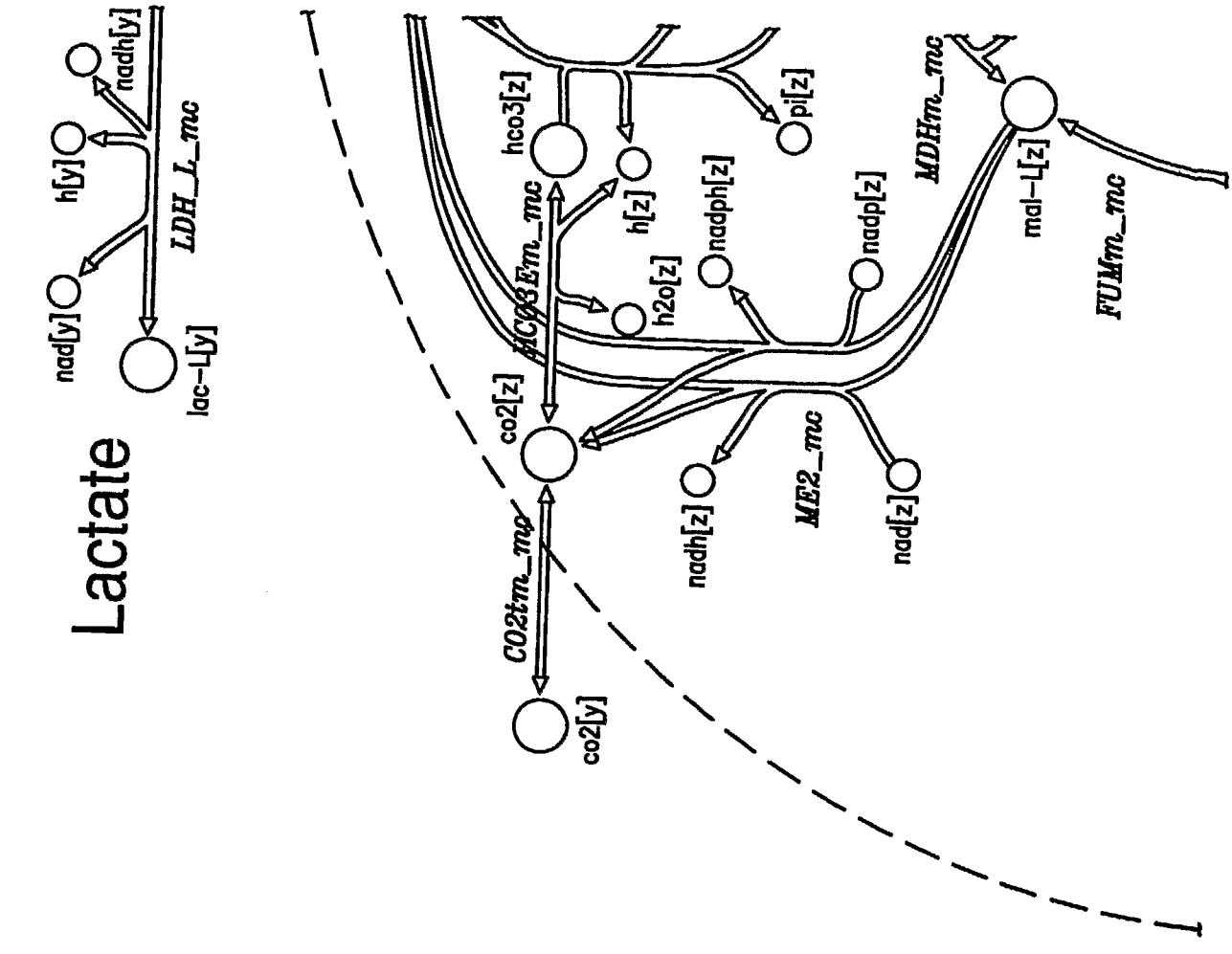

Lactate
nad[y]
h[y]
nadh[y]
LDH_L_mc
lac-L[y]
hco3[z]
h[z]
pi[z]
nadph[z]
nadp[z]
MDHm_mc
mal-L[z]
FUMm_mc
h2o[z]
co2[z]
nadh[z]
ME2_mc
nad[z]
co2[y]

FIG. 9-16

FIG. 9-17

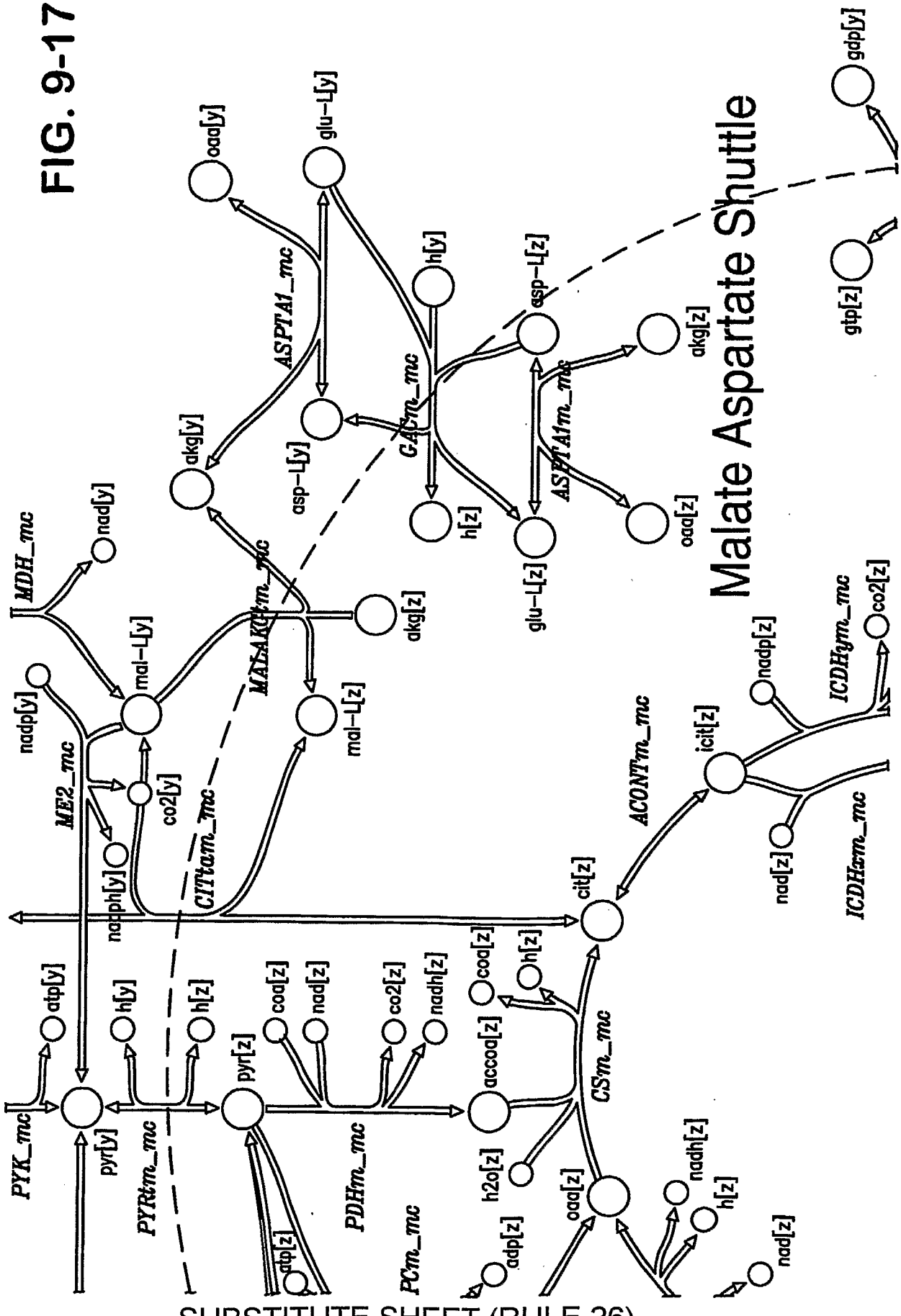
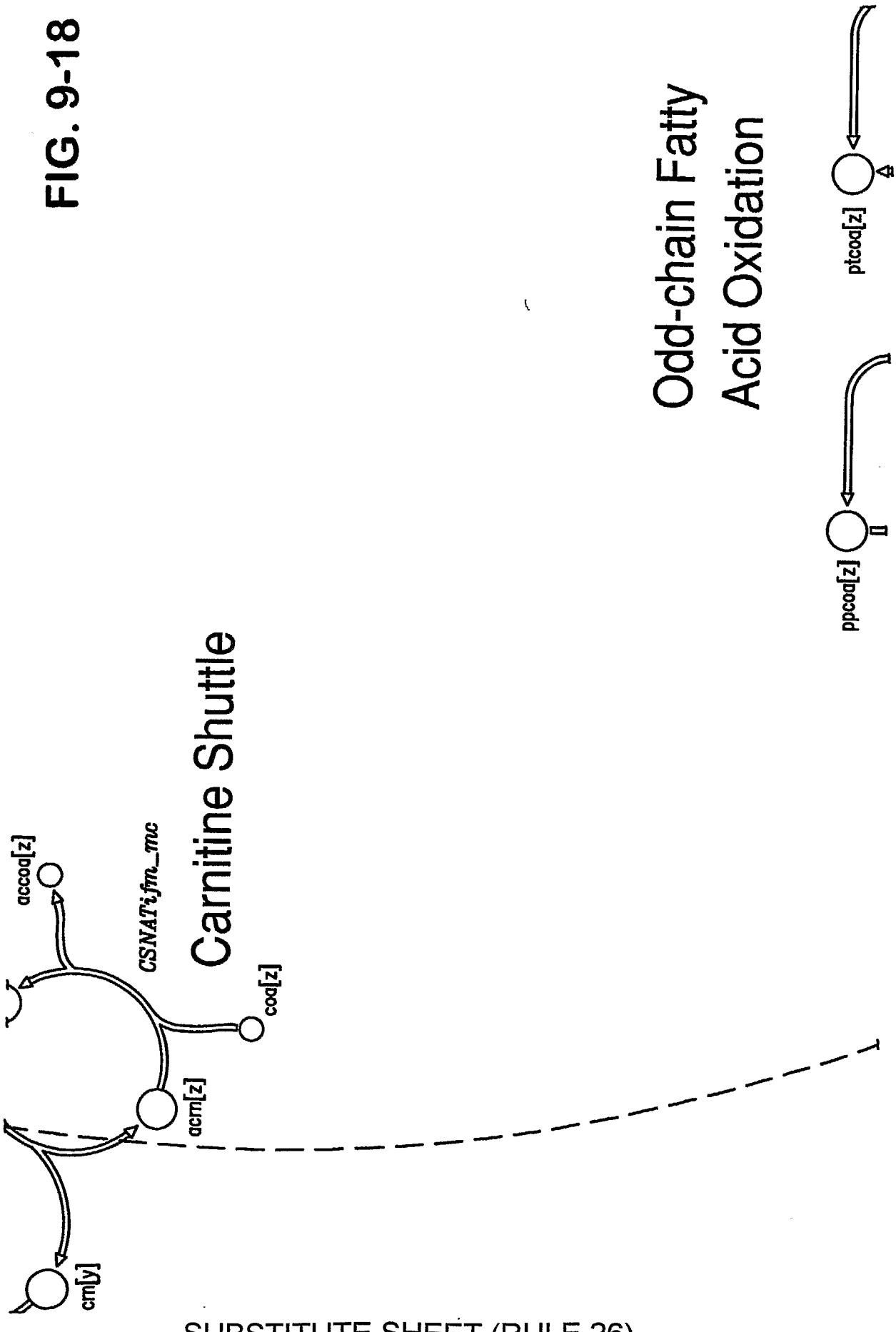

Malate Aspartate Shuttle
PYK_mc
PYRtm_mc
PDHm_mc
PCm_mc
CSm_mc
ACONTm_mc
ICDHxm_mc
ICDHym_mc
ME2_mc
CITtam_mc
MDH_mc
MALtam_mc
ASPTA1_mc
GAStm_mc
ASPTA1m_mc
pyr[y]
atp[y]
h[y]
h[z]
pyr[z]
coa[z]
nad[z]
co2[z]
nadh[z]
accoa[z]
h2o[z]
adp[z]
oaa[z]
cit[z]
h[z]
nadh[z]
h[z]
nad[z]
icit[z]
nadp[z]
nad[z]
co2[z]
nadp[y]
nadph[y]
co2[y]
mal-L[y]
nad[y]
akg[y]
asp-L[y]
oaa[y]
glu-L[y]
mal-L[z]
akg[z]
h[y]
h[z]
glu-L[z]
asp-L[z]
akg[z]
oaa[z]
gtp[z]
gdp[y]

FIG. 9-18


Odd-chain Fatty Acid Oxidation
ptcoa[z]
ppcoa[z]
Carnitine Shuttle
accoa[z]
CSNATi,fm_mc
coa[z]
acm[z]
cm[y]

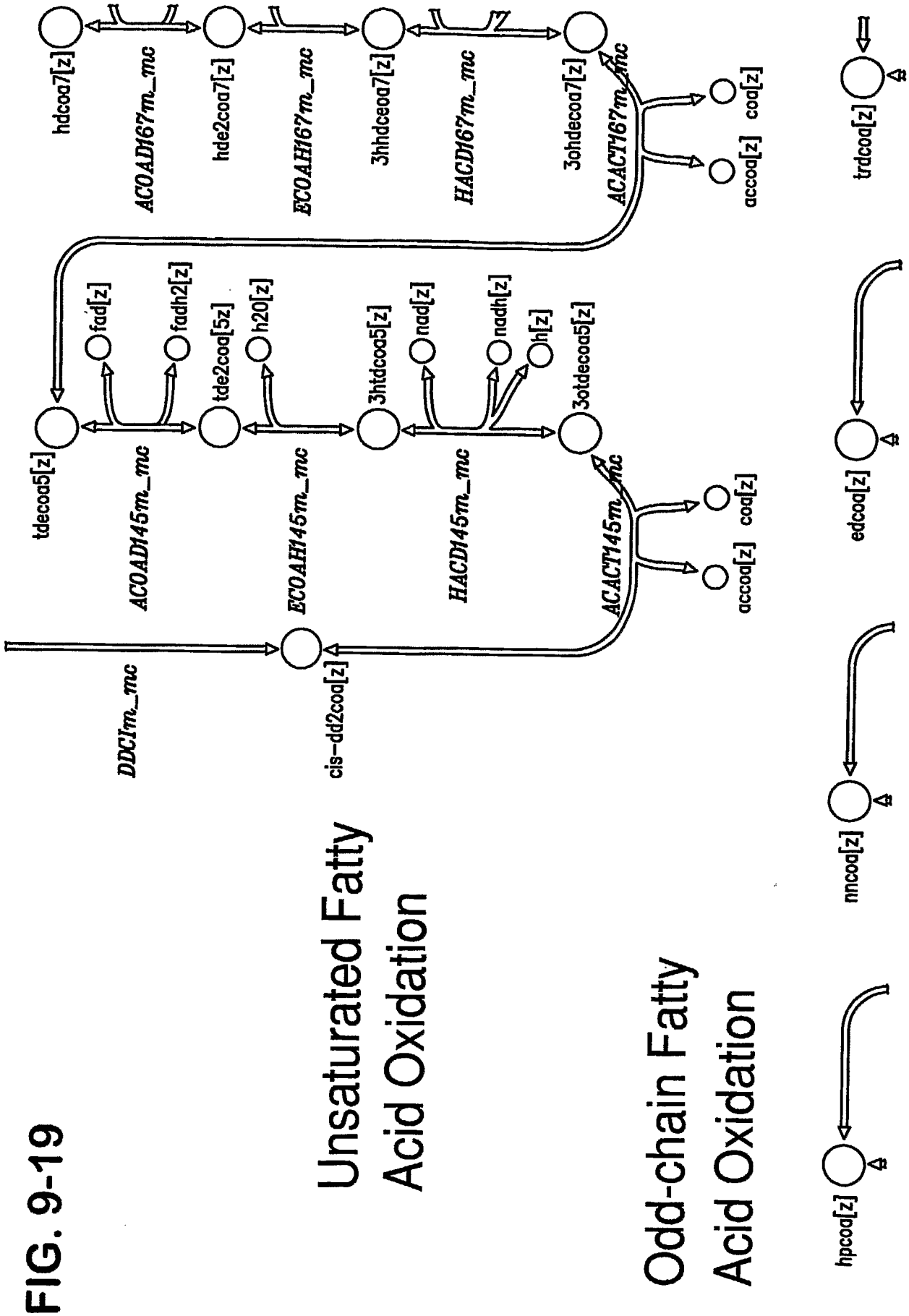

hdcoa7[z]
ACOAD167m_mc
hde2coa7[z]
ECOAH167m_mc
3hhdceoa7[z]
HACD167m_mc
3ohdecoa7[z]
ACACT167m_mc
accoa[z]
coa[z]
trdcoa[z]
tdecoa5[z]
fad[z]
ACOAD145m_mc
fadh2[z]
tde2coa[5z]
h20[z]
ECOAH145m_mc
3htdcoa5[z]
nad[z]
HACD145m_mc
nadh[z]
h[z]
3otdecoa5[z]
ACACT145m_mc
accoa[z]
coa[z]
edcoa[z]
DDCIm_mc
cis-dd2coa[z]
nncoa[z]
hpcoa[z]
Unsaturated Fatty Acid Oxidation
Odd-chain Fatty Acid Oxidation

FIG. 9-19

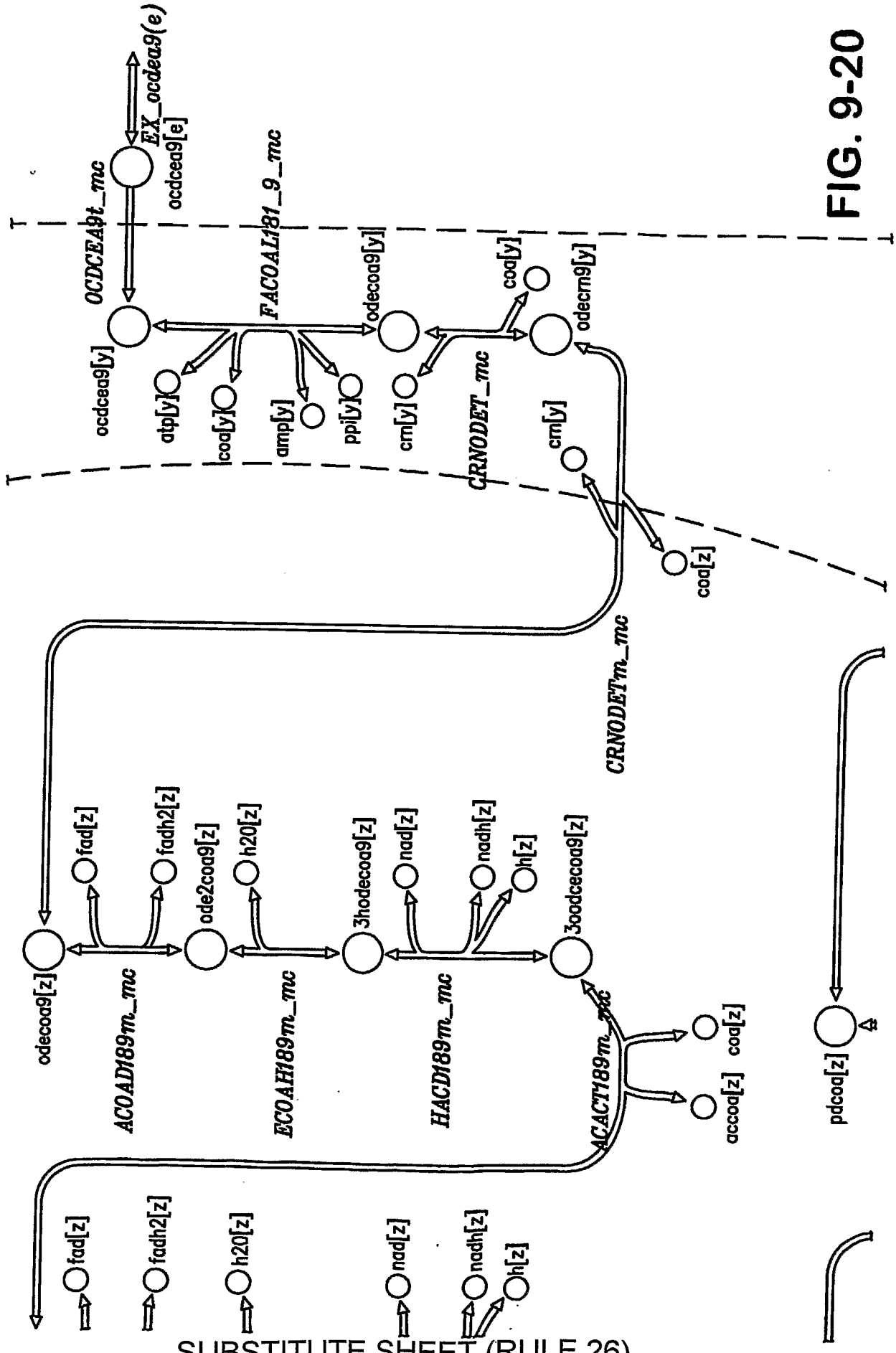

EX_ocdcea9(e)
ocdcea9[e]
OCDCEA9t_mc
ocdcea9[y]
FACOAL181_9_mc
atp[y]
coa[y]
amp[y]
ppi[y]
odecoa9[y]
cm[y]
CRNODET_mc
coa[y]
odecm9[y]
cm[y]
coa[z]
CRNODETm_mc
odecoa9[z]
ACOAD189m_mc
fad[z]
fadh2[z]
ode2coa9[z]
ECOAH189m_mc
h2O[z]
3hodecoa9[z]
HACD189m_mc
nad[z]
nadh[z]
h[z]
3oodcoa9[z]
ACACT189m_mc
accoa[z]
coa[z]
pdcoa[z]
fad[z]
fadh2[z]
h2O[z]
nad[z]
nadh[z]
h[z]

FIG. 9-20

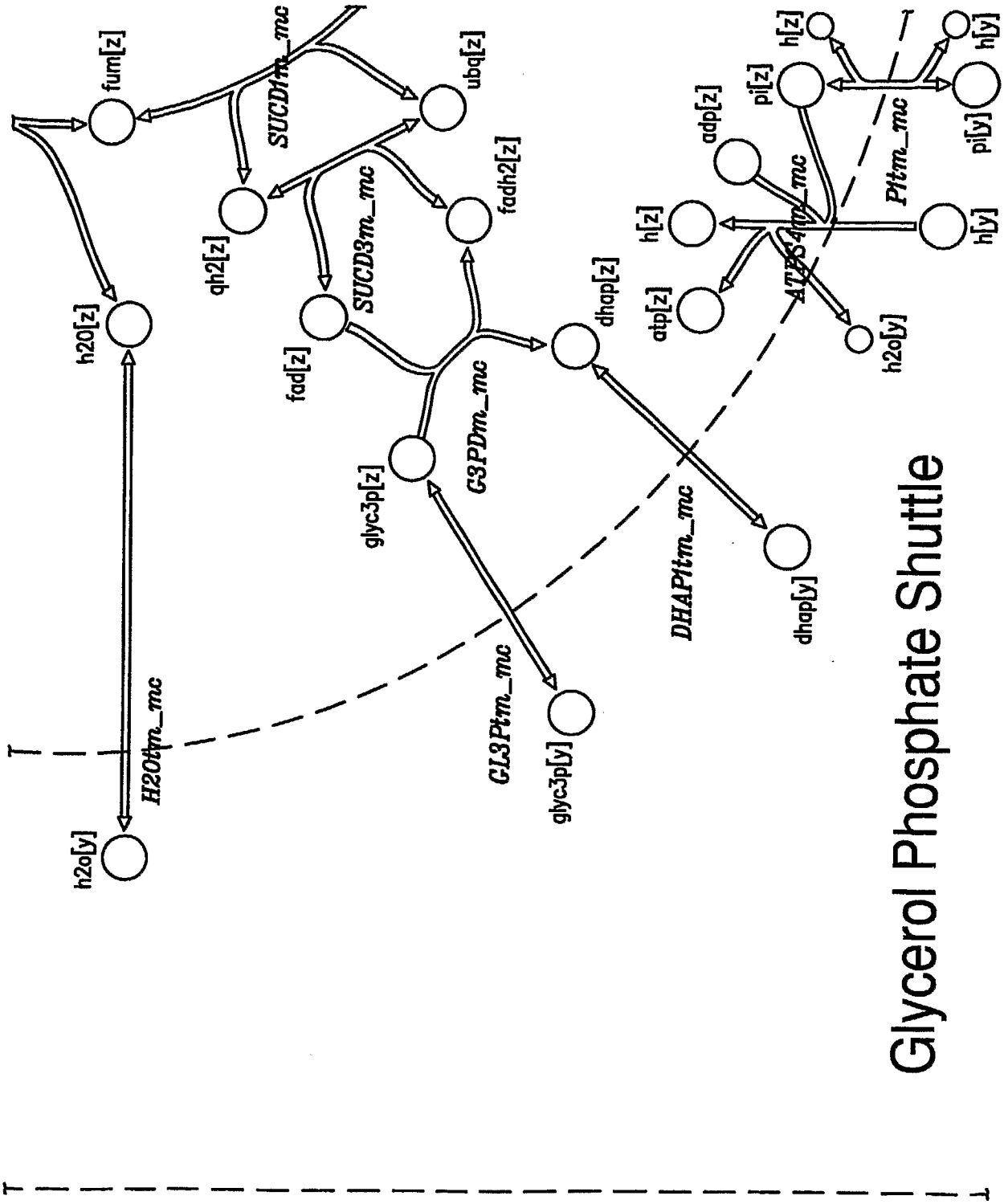

Glycerol Phosphate Shuttle
fum[z]
SUCDtm_mc
ubq[z]
qh2[z]
SUCD3m_mc
fadh2[z]
fad[z]
h2o[z]
dhap[z]
G3PDm_mc
glyc3p[z]
H2Otm_mc
h2o[y]
GL3Ptm_mc
glyc3p[y]
DHAPtm_mc
dhap[y]
adp[z]
pi[z]
h[z]
pi[y]
h[y]
Ptm_mc
ATPS4tm_mc
atp[z]
h2o[y]

FIG. 9-21

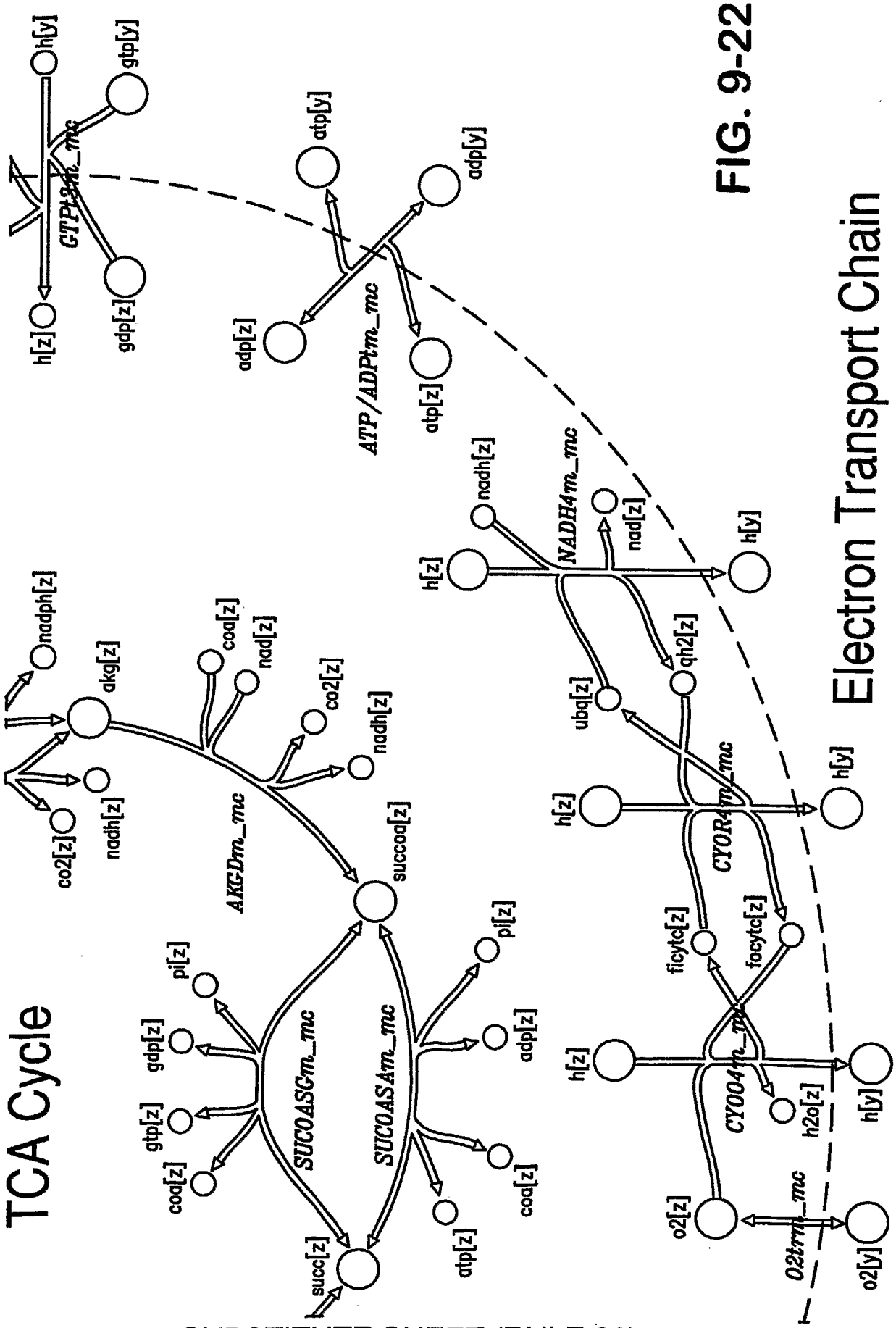

TCA Cycle
Electron Transport Chain
AKGDm_mc
SUCOASGm_mc
SUCOASAm_mc
CYOR4m_mc
CYOO4m_mc
ATP/ADPtm_mc
NADH4m_mc
02trm_mc
nadph[z]
akg[z]
co2[z]
nadh[z]
coa[z]
nad[z]
co2[z]
nadh[z]
succoa[z]
pi[z]
gdp[z]
gtp[z]
coa[z]
succ[z]
pi[z]
adp[z]
coa[z]
atp[z]
h[z]
gtp[y]
gdp[z]
h[y]
adp[z]
atp[y]
atp[z]
adp[y]
h[z]
nadh[z]
nad[z]
h[y]
ubq[z]
qh2[z]
h[z]
h[y]
ficytc[z]
focytc[z]
h[z]
h[y]
o2[z]
h2o[z]
o2[y]

FIG. 9-22

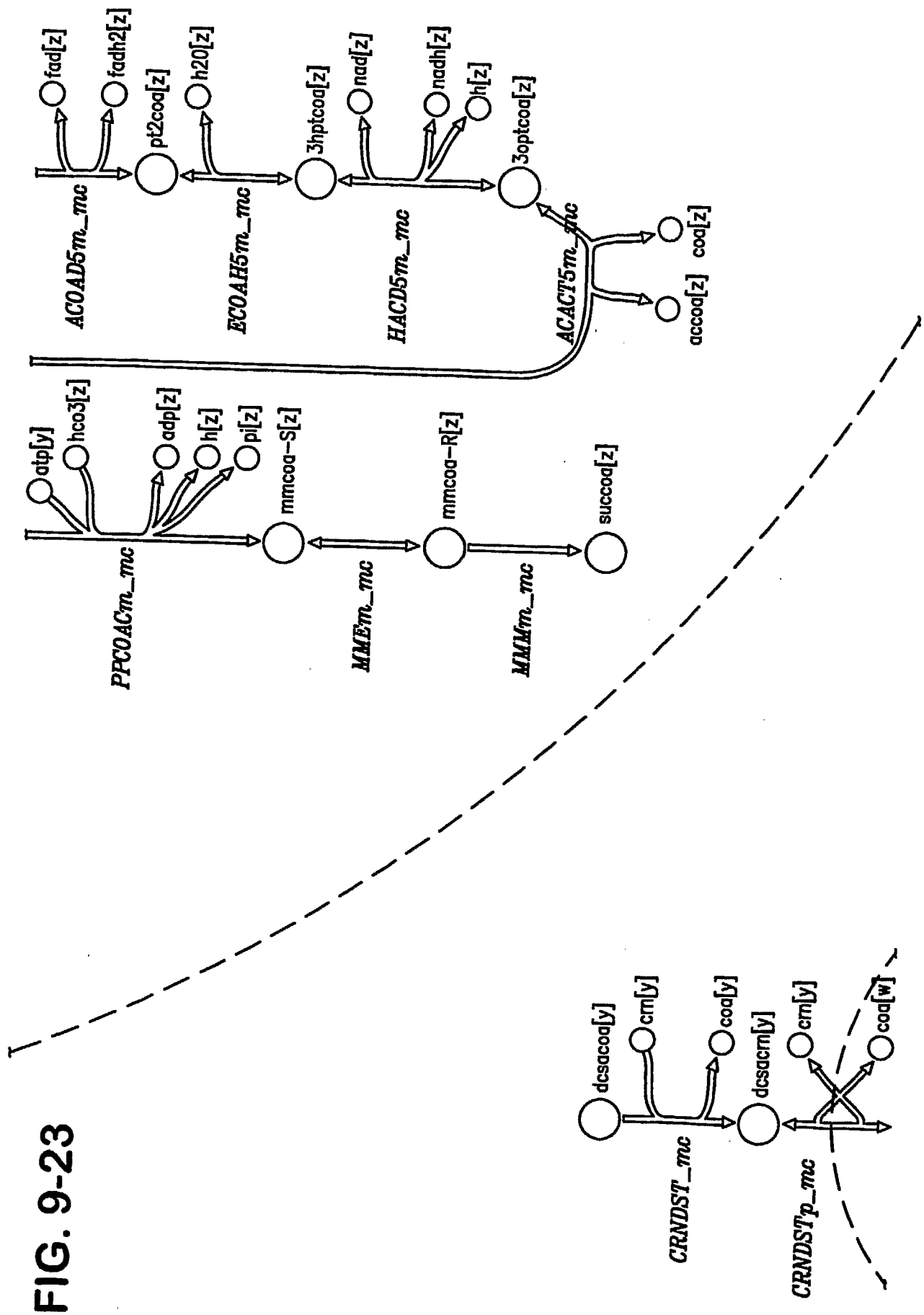

fad[z]
fadh2[z]
ACOAD5m_mc
pt2coa[z]
h2O[z]
ECOAH5m_mc
3hptcoa[z]
nad[z]
nadh[z]
HACD5m_mc
h[z]
3optcoa[z]
ACACT5m_mc
coa[z]
accoa[z]
atp[y]
hco3[z]
adp[z]
h[z]
pi[z]
PPCOACm_mc
mmcoa-S[z]
MMEm_mc
mmcoa-R[z]
MMMm_mc
succoa[z]
dcsacoa[y]
cm[y]
coa[y]
CRNDST_mc
dcsacm[y]
cm[y]
coa[w]
CRNDSTp_mc

FIG. 9-23

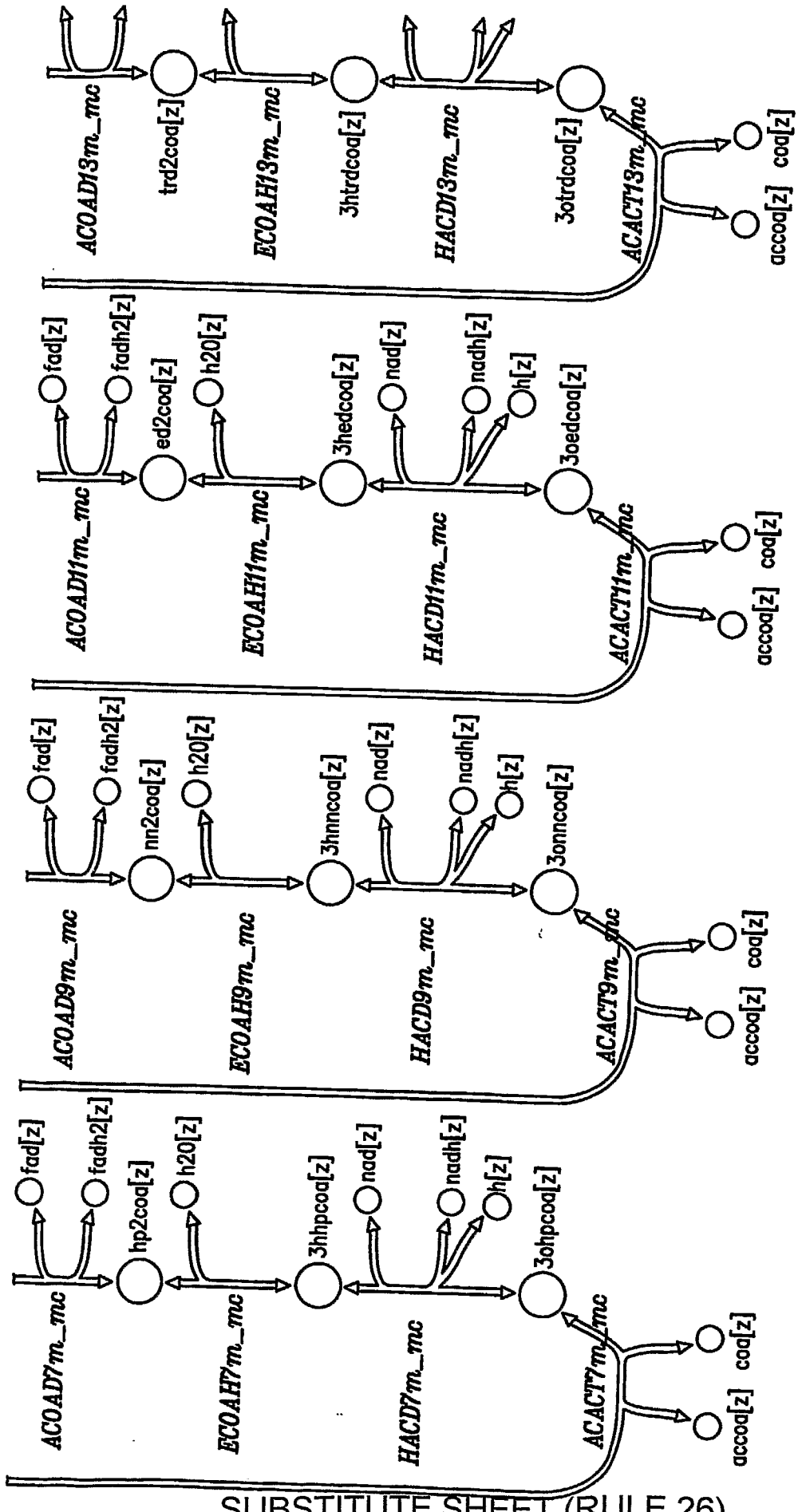
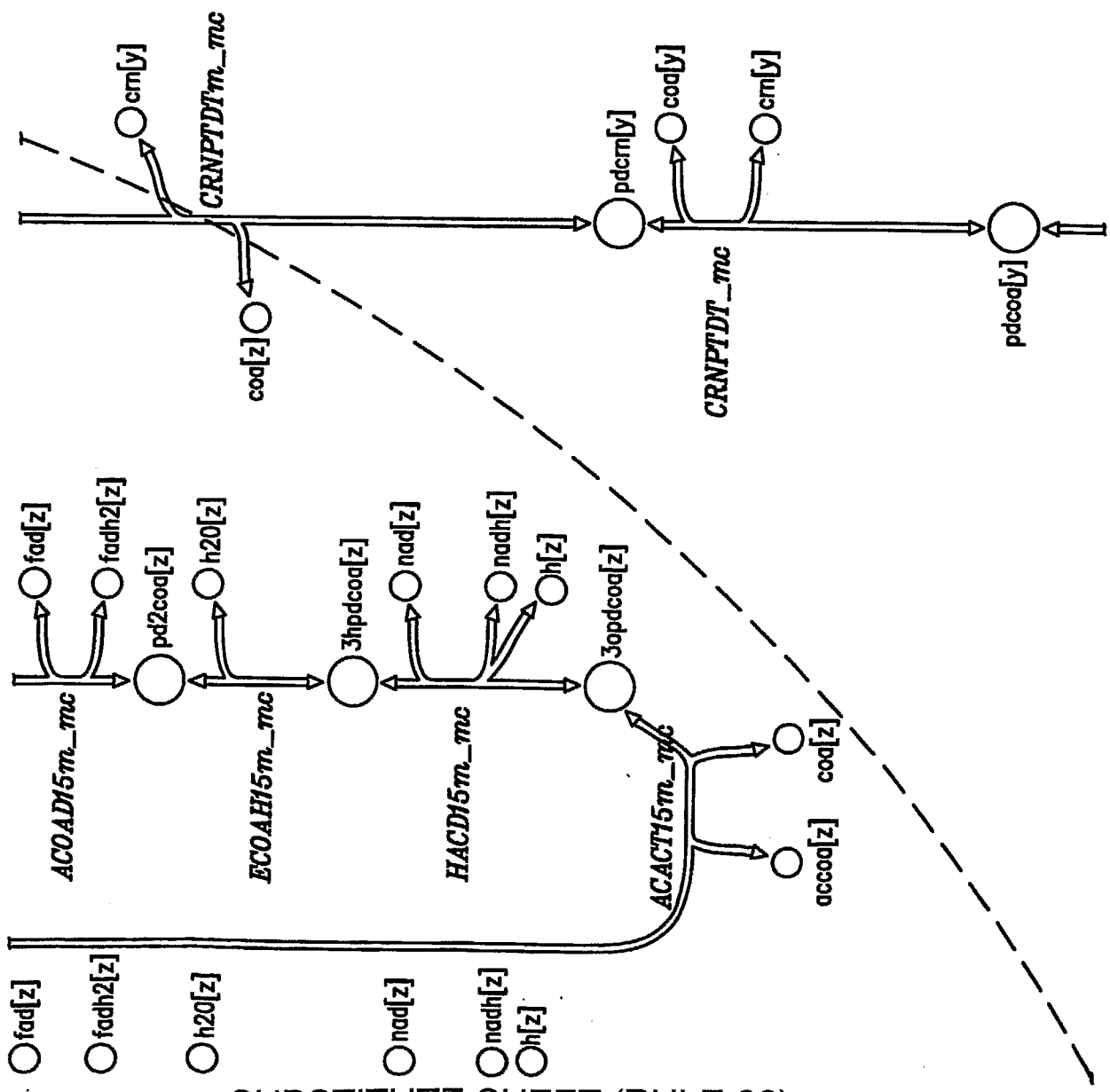

ACOAD7m_mc
fad[z]
fadh2[z]
hp2coa[z]
h20[z]
ECOAH7m_mc
3hhpcoa[z]
nad[z]
nadh[z]
h[z]
HACD7m_mc
3ohpcoa[z]
ACACT7m_mc
accoa[z]
coa[z]
ACOAD9m_mc
fad[z]
fadh2[z]
nn2coa[z]
h20[z]
ECOAH9m_mc
3hnncoa[z]
nad[z]
nadh[z]
h[z]
HACD9m_mc
3onncoa[z]
ACACT9m_mc
accoa[z]
coa[z]
ACOAD11m_mc
fad[z]
fadh2[z]
ed2coa[z]
h20[z]
ECOAH11m_mc
3hedcoa[z]
nad[z]
nadh[z]
h[z]
HACD11m_mc
3oedcoa[z]
ACACT11m_mc
accoa[z]
coa[z]
ACOAD13m_mc
trd2coa[z]
ECOAH13m_mc
3htrdcoa[z]
HACD13m_mc
3otrdcoa[z]
ACACT13m_mc
accoa[z]
coa[z]

FIG. 9-24

FIG. 9-25


crn[y]
CRNPTDT_mc
coa[z]
pdcrn[y]
coa[y]
crn[y]
CRNPTDT_mc
pdcoa[y]
fad[z]
fadh2[z]
pd2coa[z]
h2O[z]
ACOAD15m_mc
ECOAH15m_mc
3hpdcoa[z]
nad[z]
nadh[z]
h[z]
HACD15m_mc
3opdcoa[z]
ACACT15m_mc
coa[z]
accoa[z]
fad[z]
fadh2[z]
h2O[z]
nad[z]
nadh[z]
h[z]

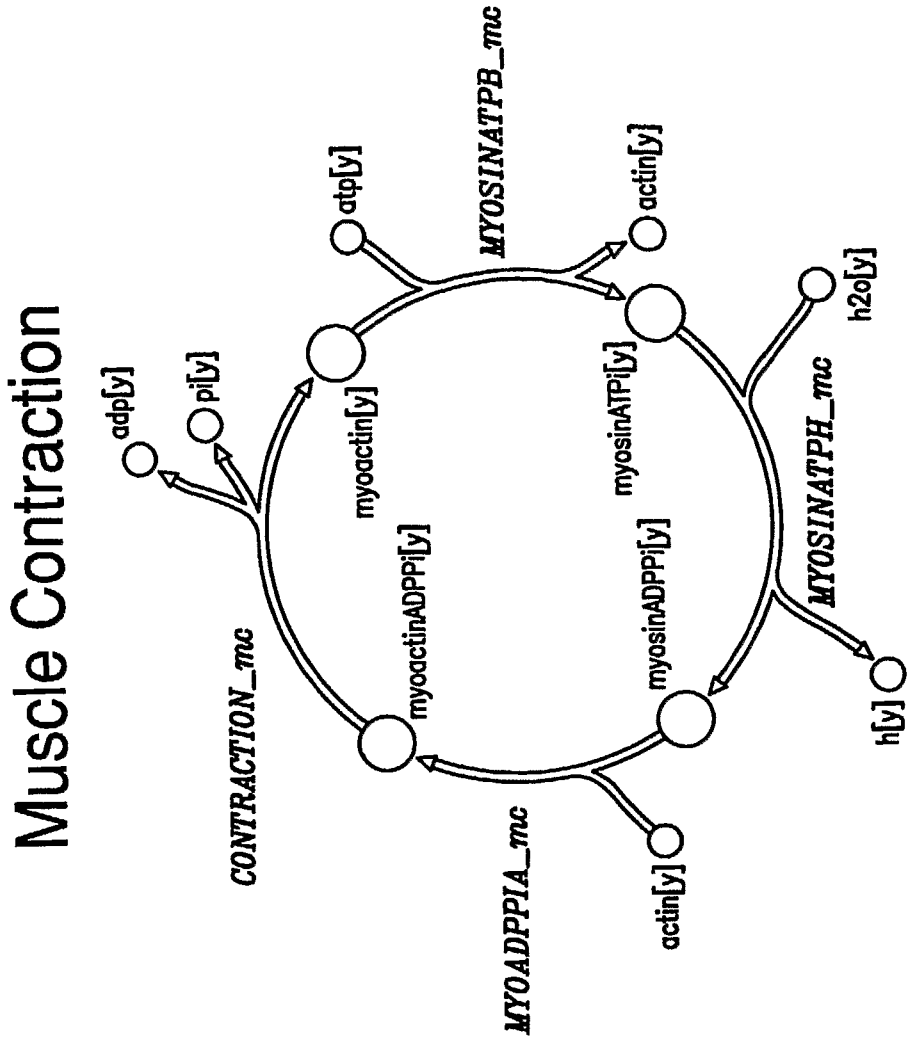
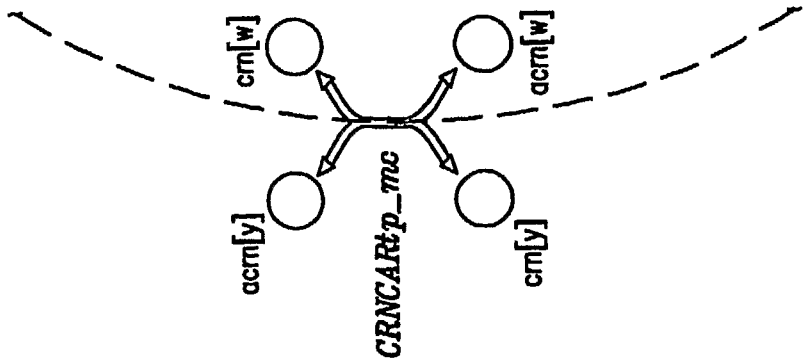

Muscle Contraction
adp[y]
pi[y]
CONTRACTION_mc
myoactin[y]
myoactinADPPi[y]
MYOADPPIA_mc
atp[y]
MYOSINATPB_mc
actin[y]
myosinATPi[y]
myosinADPPi[y]
actin[y]
h2o[y]
MYOSINATPH_mc
h[y]

FIG. 9-26


cm[w]
acm[w]
acm[y]
CRNCARtp_mc
cm[y]


Phosphocreatine
DM_creatp(u)
adp[y]
atp[y]

FIG. 9-27

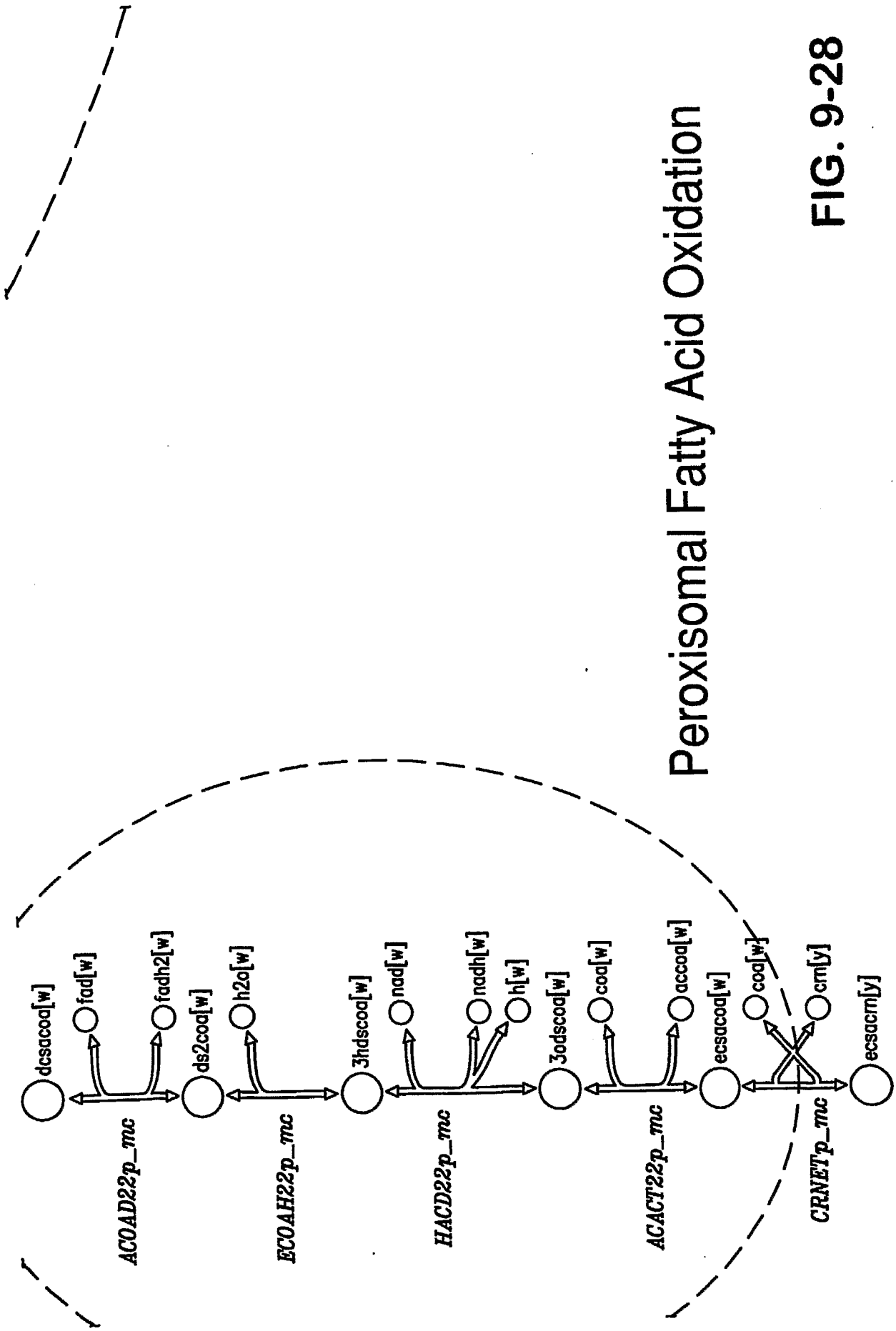

Peroxisomal Fatty Acid Oxidation
dcsacoa[w]
fad[w]
fadh2[w]
ds2coa[w]
h2o[w]
3hdscoa[w]
nad[w]
nadh[w]
h[w]
3odscoa[w]
coa[w]
accoa[w]
ecsacoa[w]
coa[w]
cm[y]
ecsacm[y]
ACOAD22p_mc
ECOAH22p_mc
HACD22p_mc
ACACT22p_mc
CRNETp_mc

FIG. 9-28

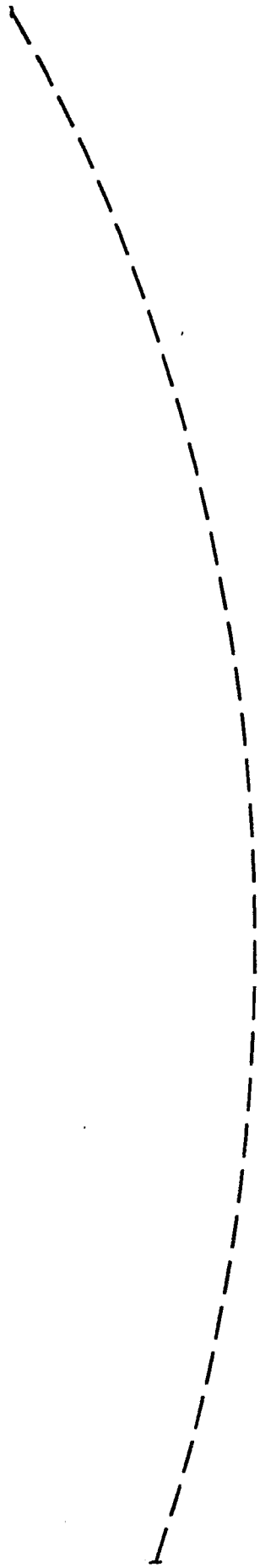


FIG. 9-29

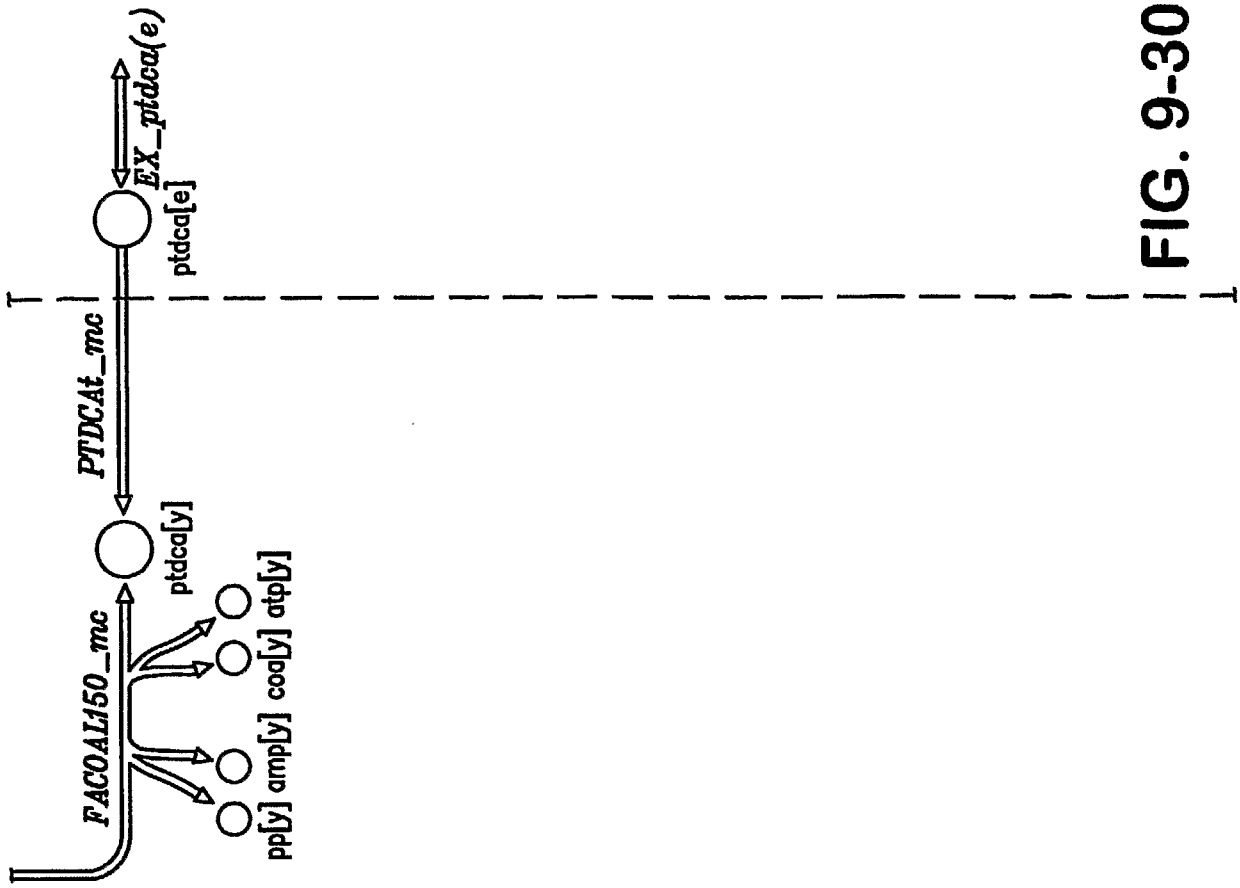

EX_ptdca(e)
ptdca[e]
PTDCAt_mc
ptdca[y]
FACOAL150_mc
pp[y] amp[y] coa[y] atp[y]

FIG. 9-30

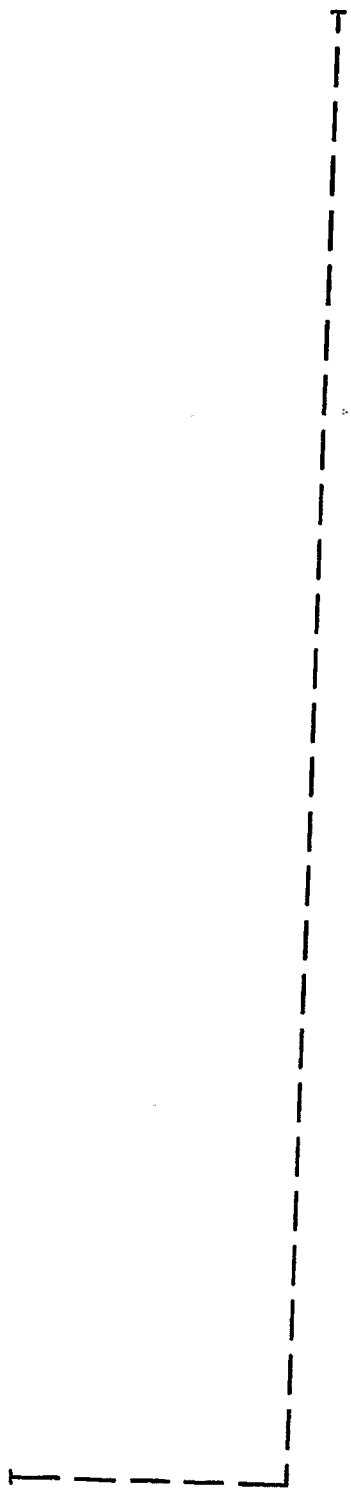


FIG. 9-31

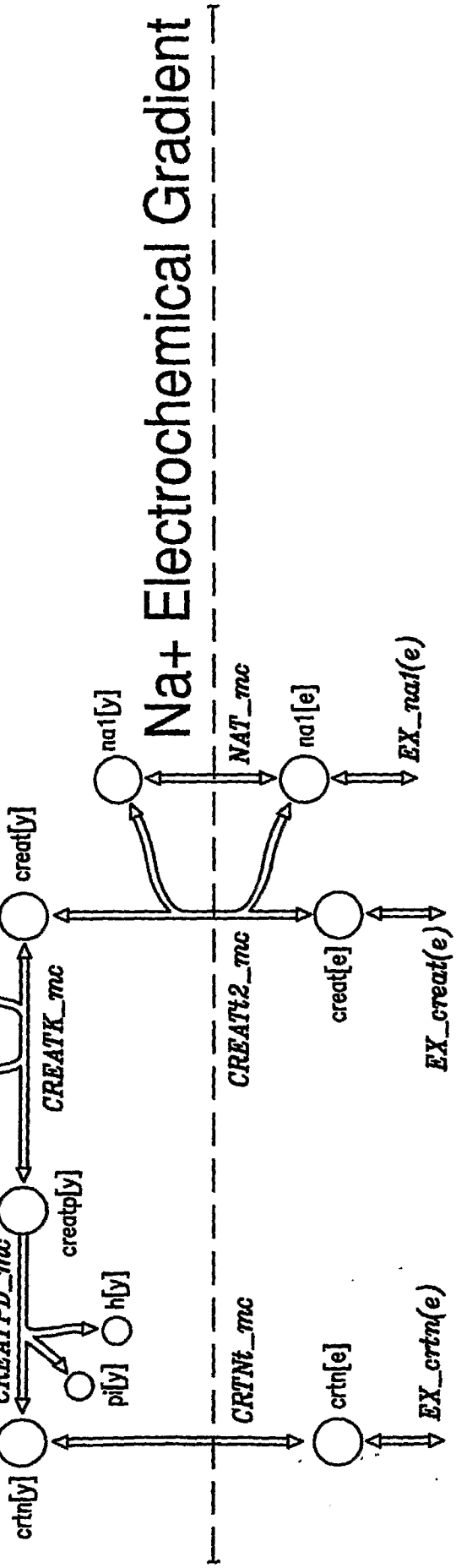

Na+ Electrochemical Gradient
crtn[y]
creatp[y]
creat[y]
na1[y]
h[y]
pi[y]
CREATPD_mc
CREATK_mc
CRTNt_mc
CREATt2_mc
NAT_mc
crtn[e]
creat[e]
na1[e]
EX_crtn(e)
EX_creat(e)
EX_na1(e)

FIG. 9-32

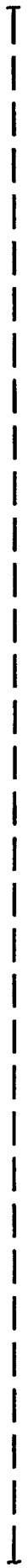


FIG. 9-33

FIG. 9-34

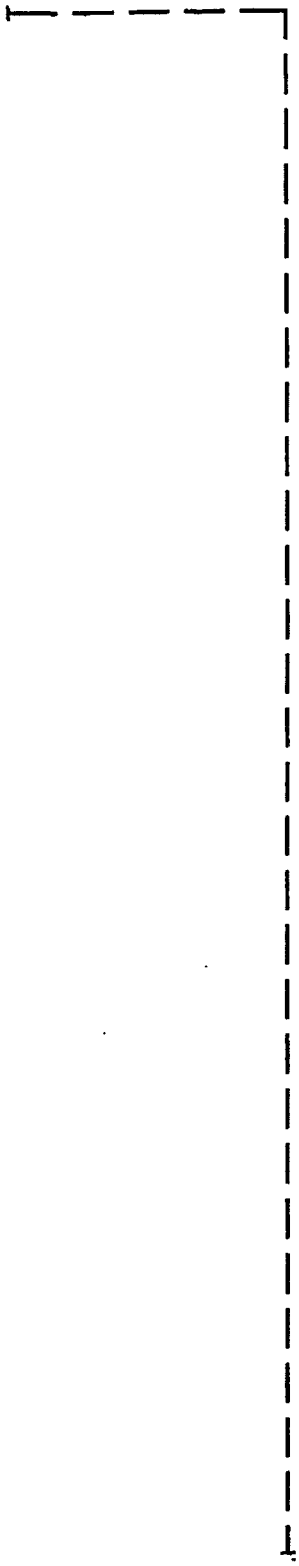


FIG. 9-35

FIG. 10-1

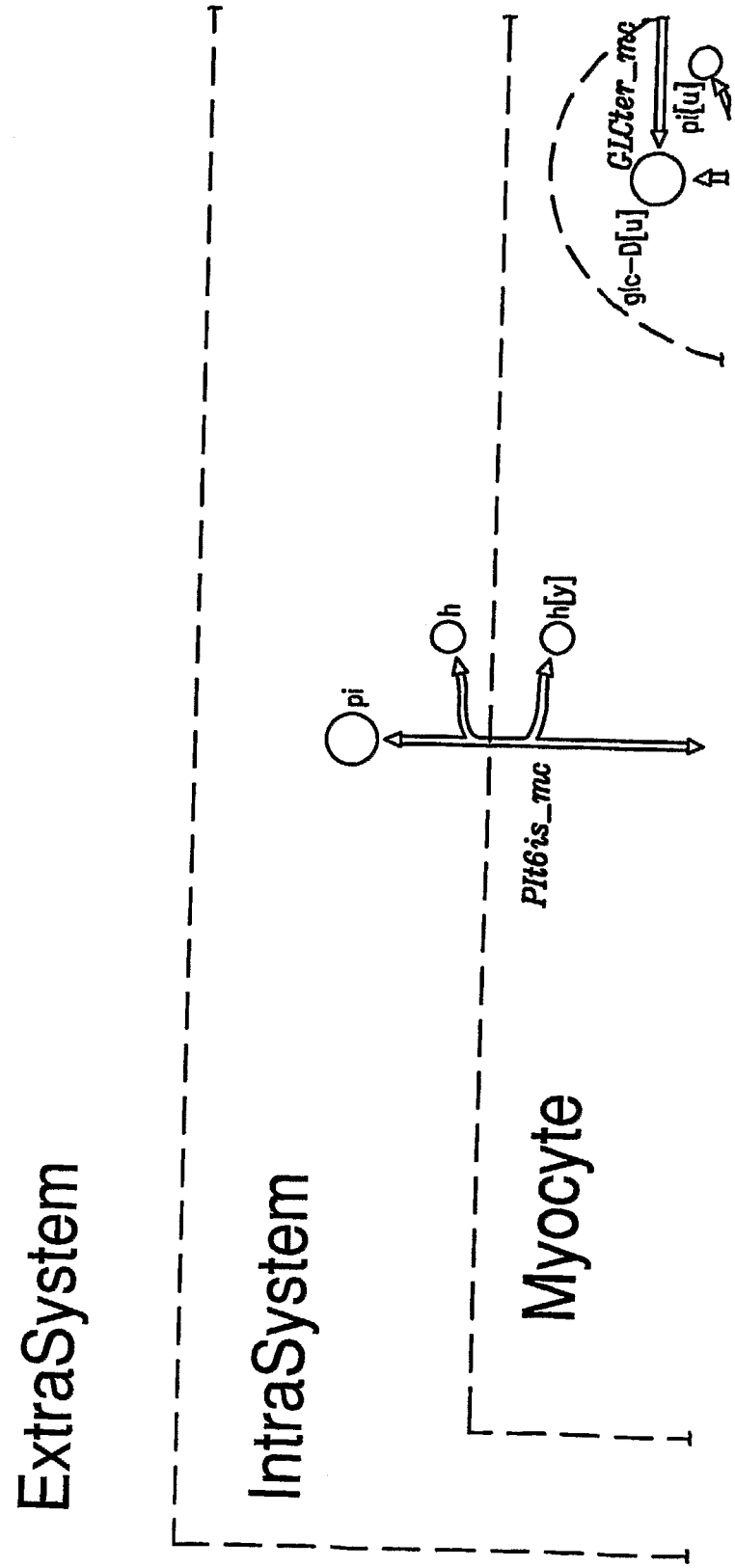

ExtraSystem
IntraSystem
Myocyte
pi
h
h[y]
Pit6is_mc
glc-D[u]
GLCter_mc
pi[u]

FIG. 10-2

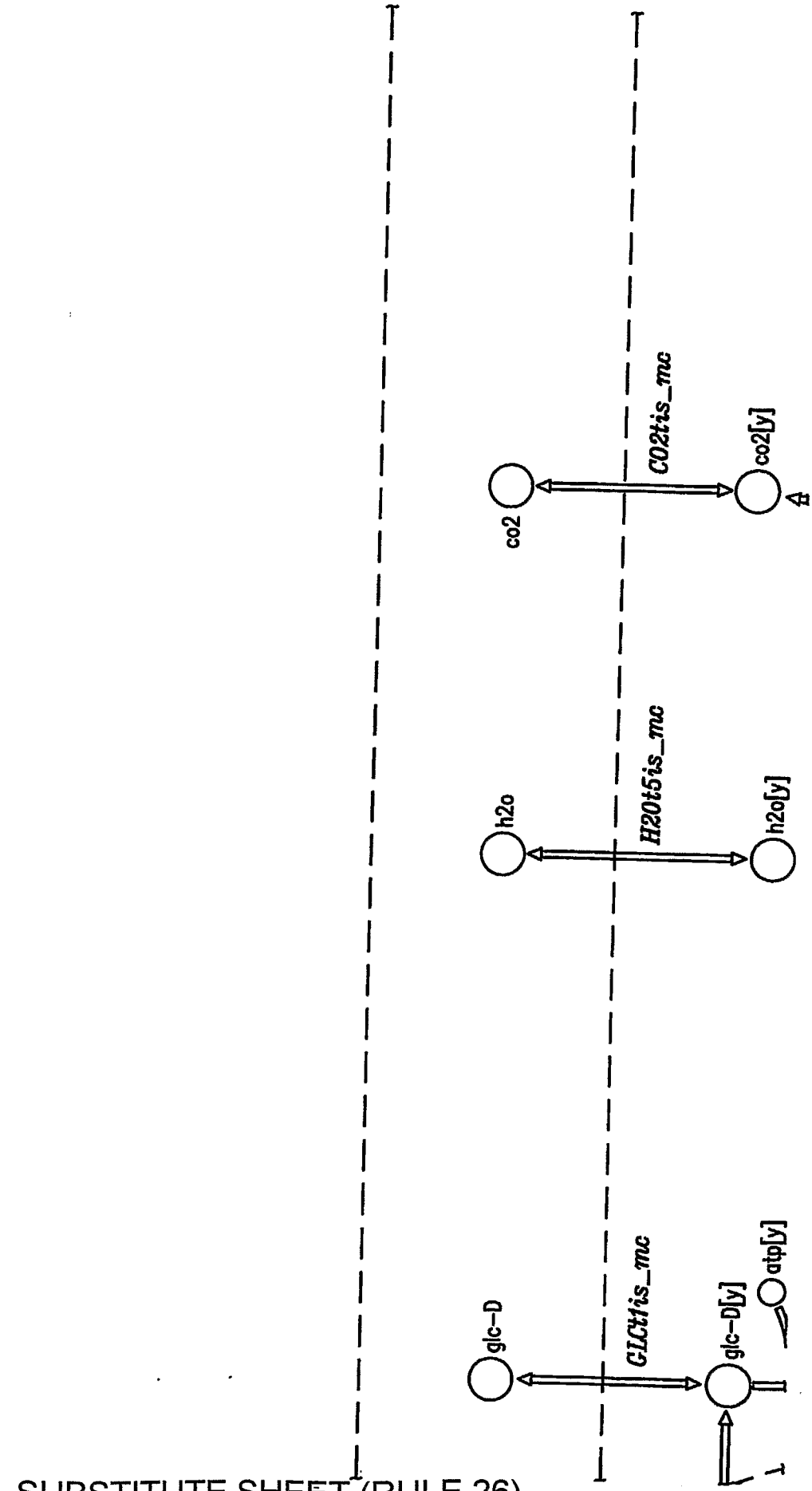

co2
CO2tis_mc
co2[y]
h2o
H2Otis_mc
h2o[y]
glc-D
GLCtis_mc
glc-D[y]
atp[y]

FIG. 10-3

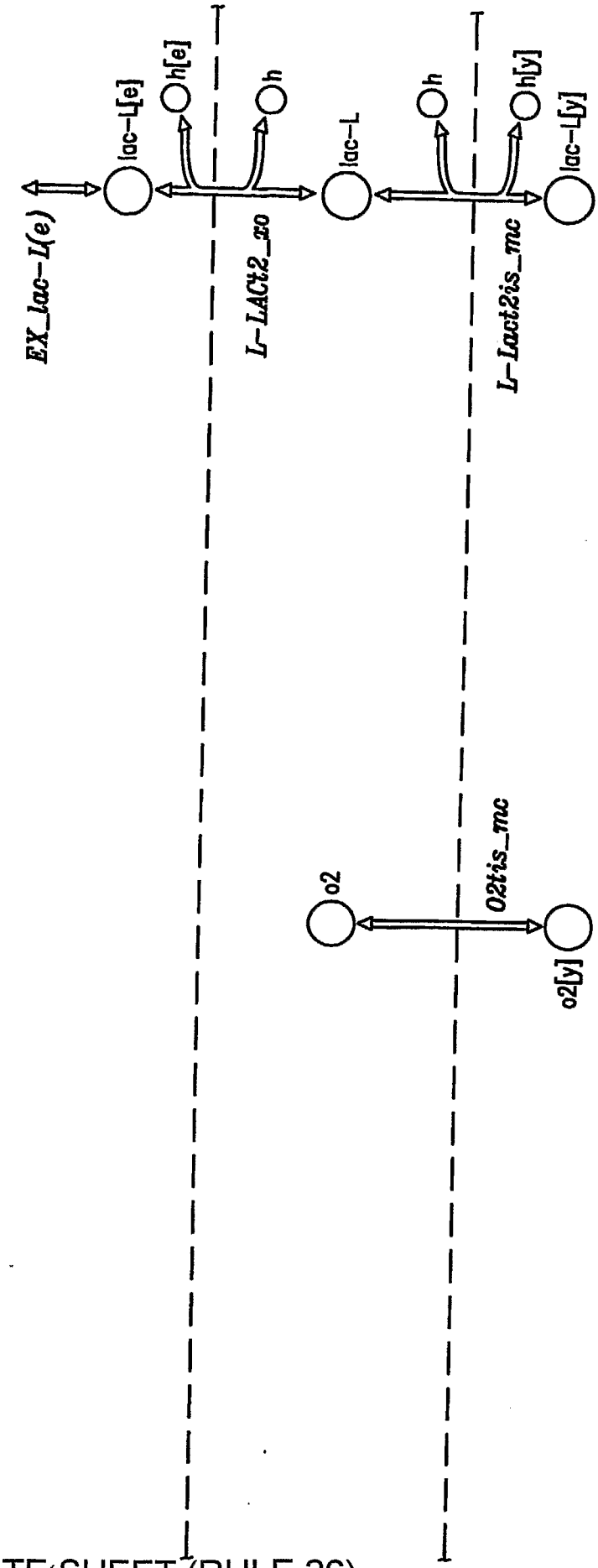
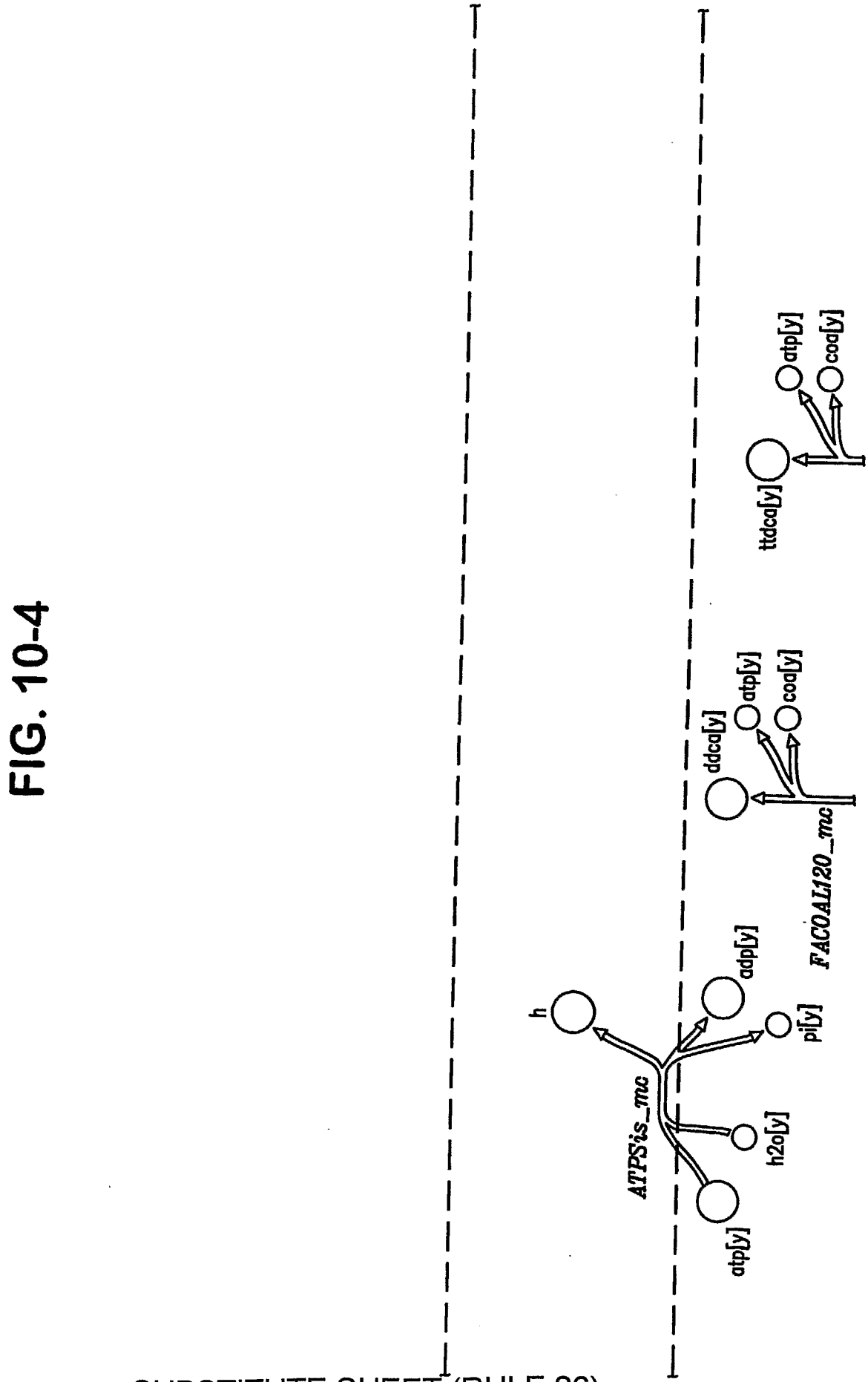

lac-L[e]
h[e]
h
lac-L
h
h[y]
lac-L[y]
EX_lac-L(e)
L-LACt2_zo
L-Lact2is_mc
o2
o2tis_mc
o2[y]

FIG. 10-4


atp[y]
coa[y]
ttdca[y]
atp[y]
coa[y]
ddca[y]
FACOAL120_mc
adp[y]
h
pi[y]
ATPSis_mc
h2o[y]
atp[y]

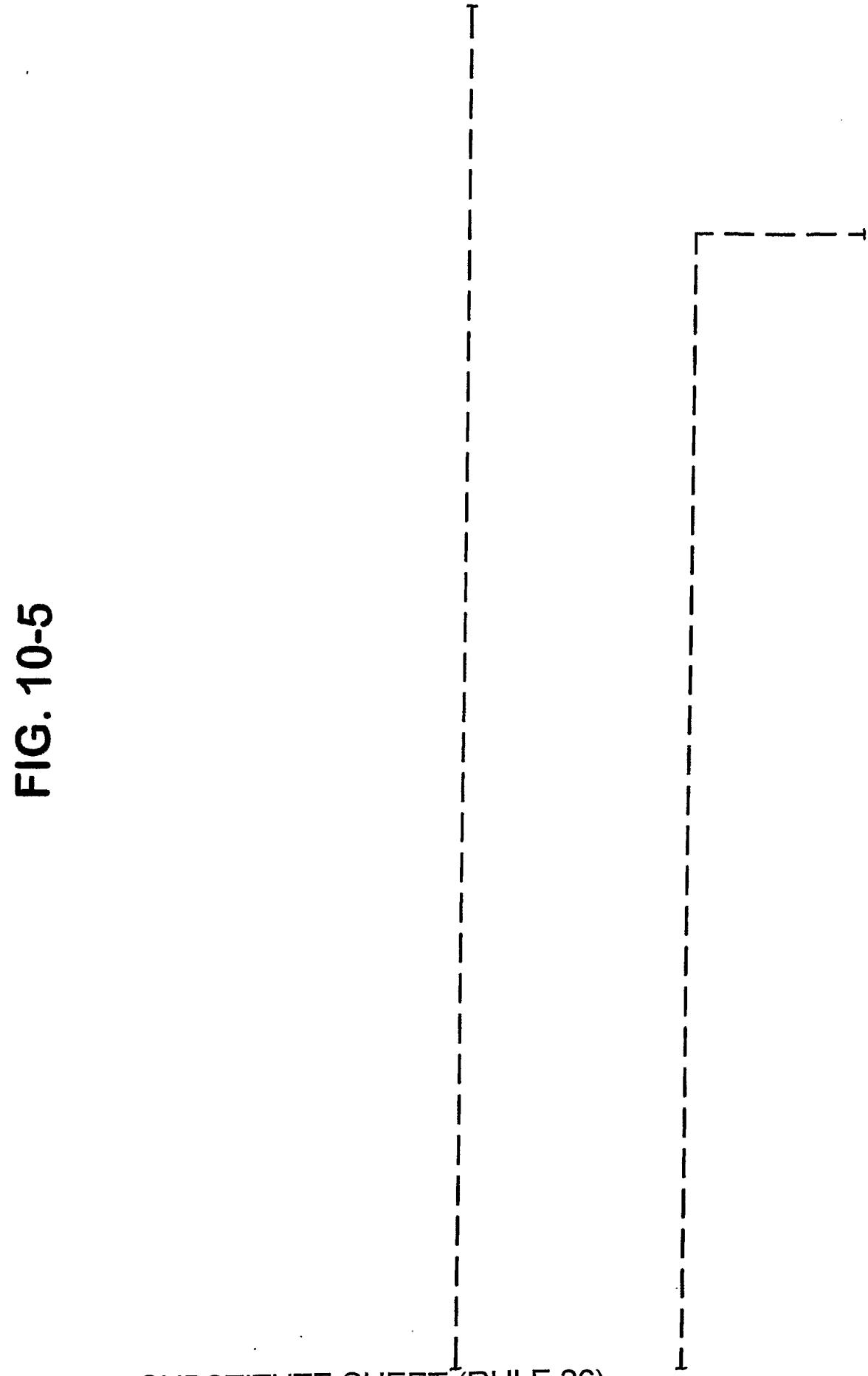


FIG. 10-5

FIG. 10-6

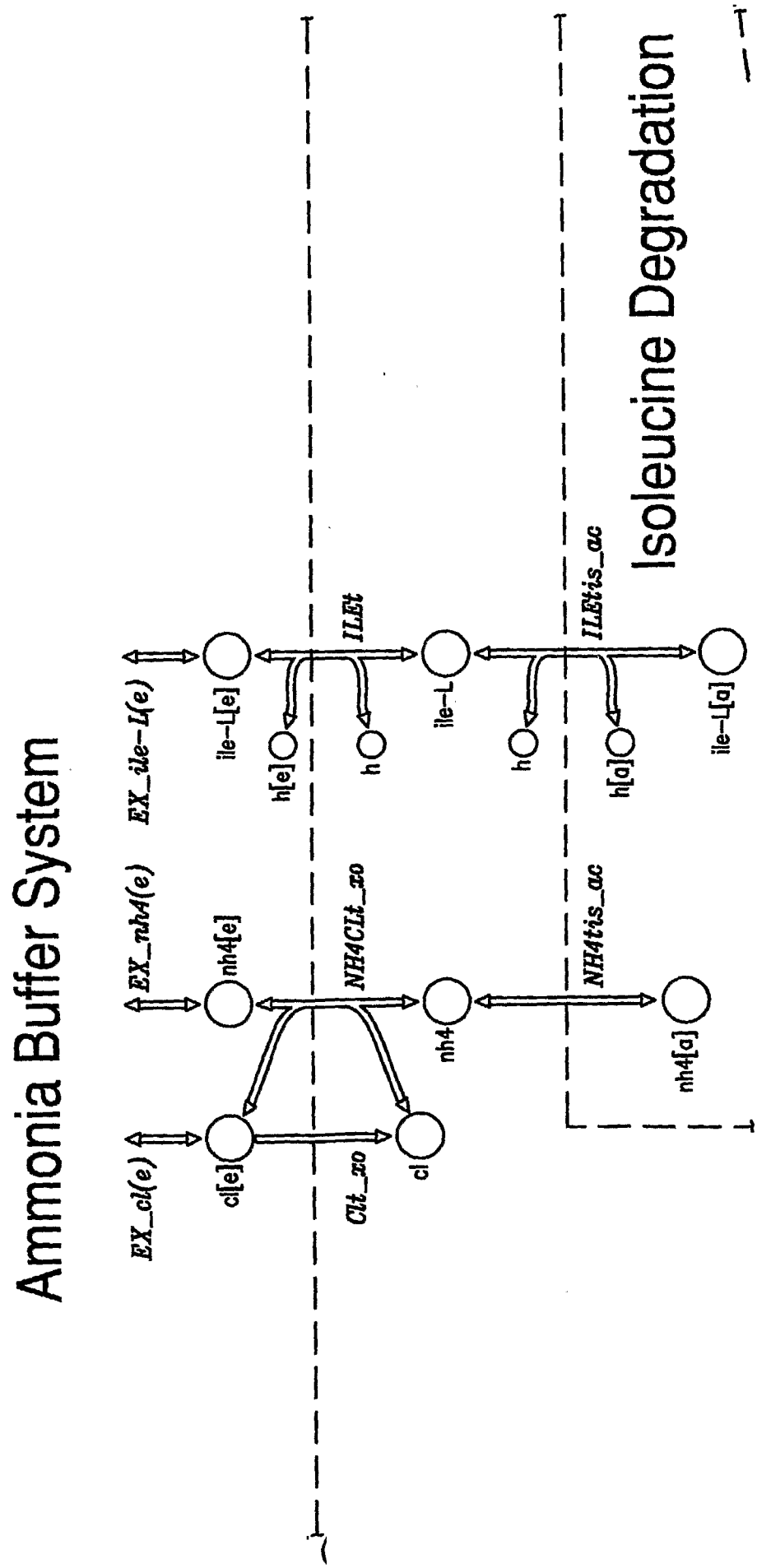

Ammonia Buffer System
Isoleucine Degradation
EX_ile-L(e)
ile-L[e]
ILEt
h[e]
h
ile-L
ILEtis_ac
h
h[a]
ile-L[a]
EX_nh4(e)
nh4[e]
NH4Clt_ac
nh4
NH4tis_ac
nh4[a]
EX_cl(e)
cl[e]
Clt_ac
cl

FIG. 10-7

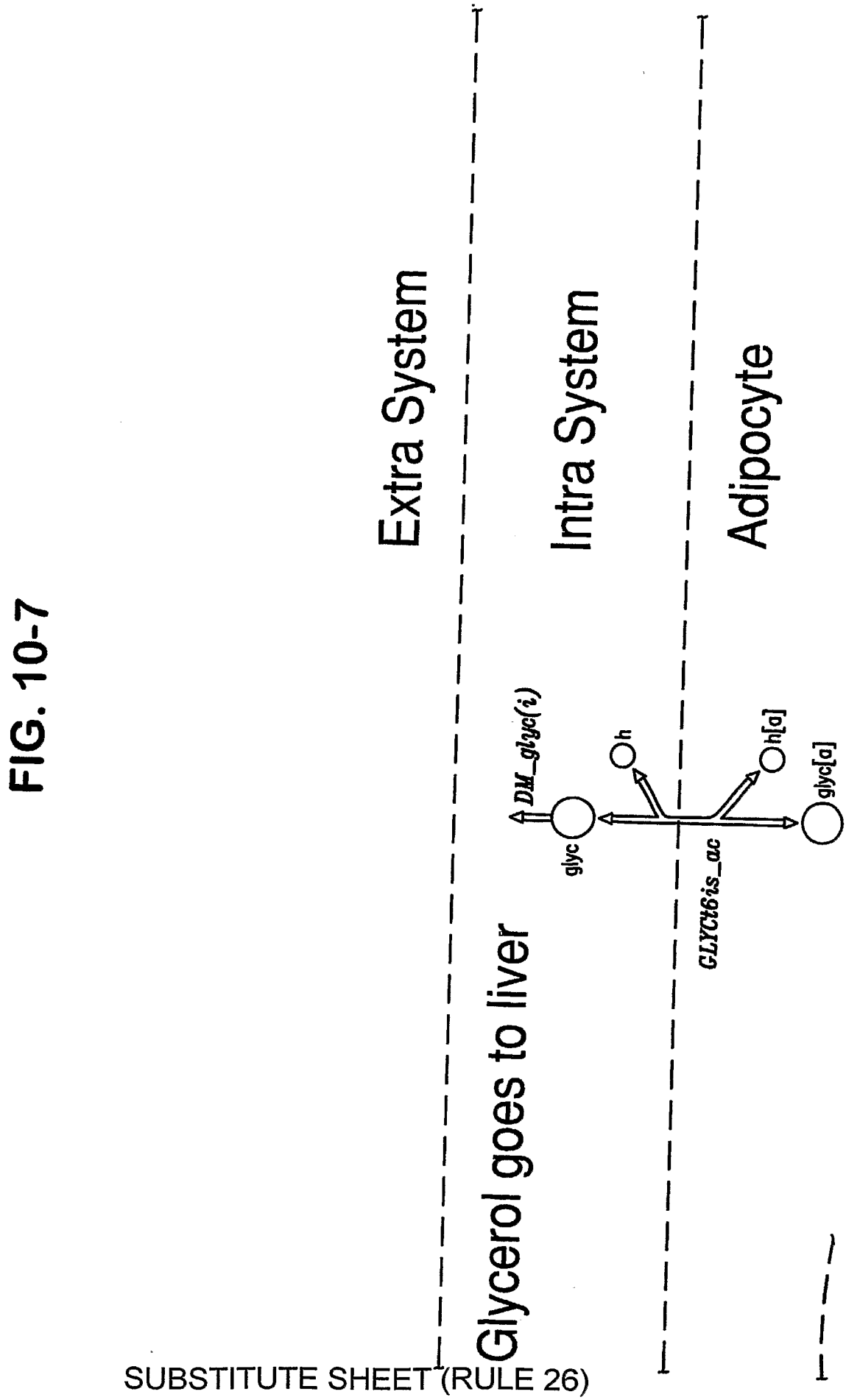

Extra System
Intra System
Adipocyte
Glycerol goes to liver
DM_glyc(i)
glyc
h
GLYCtbis_ac
h[a]
glyc[a]

FIG. 10-8

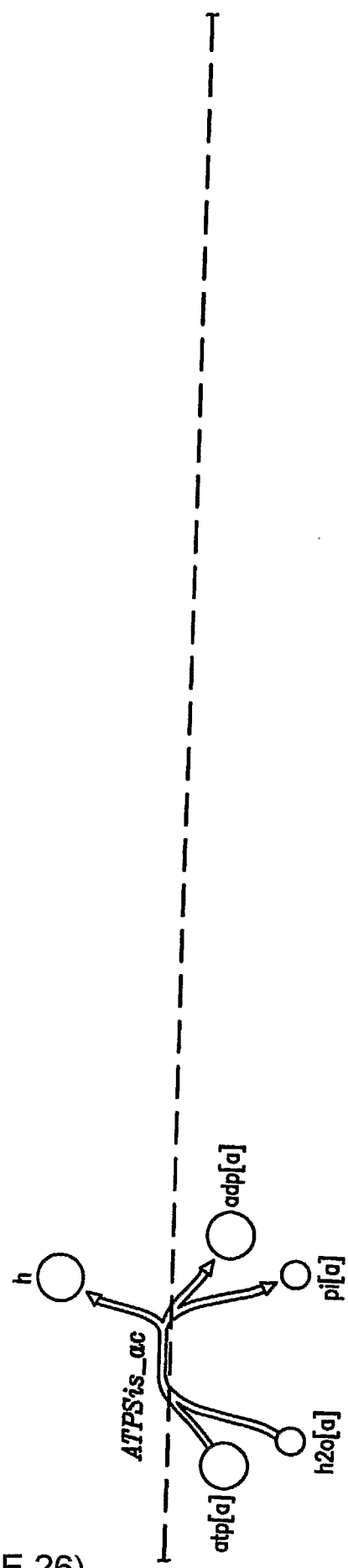


FIG. 10-9

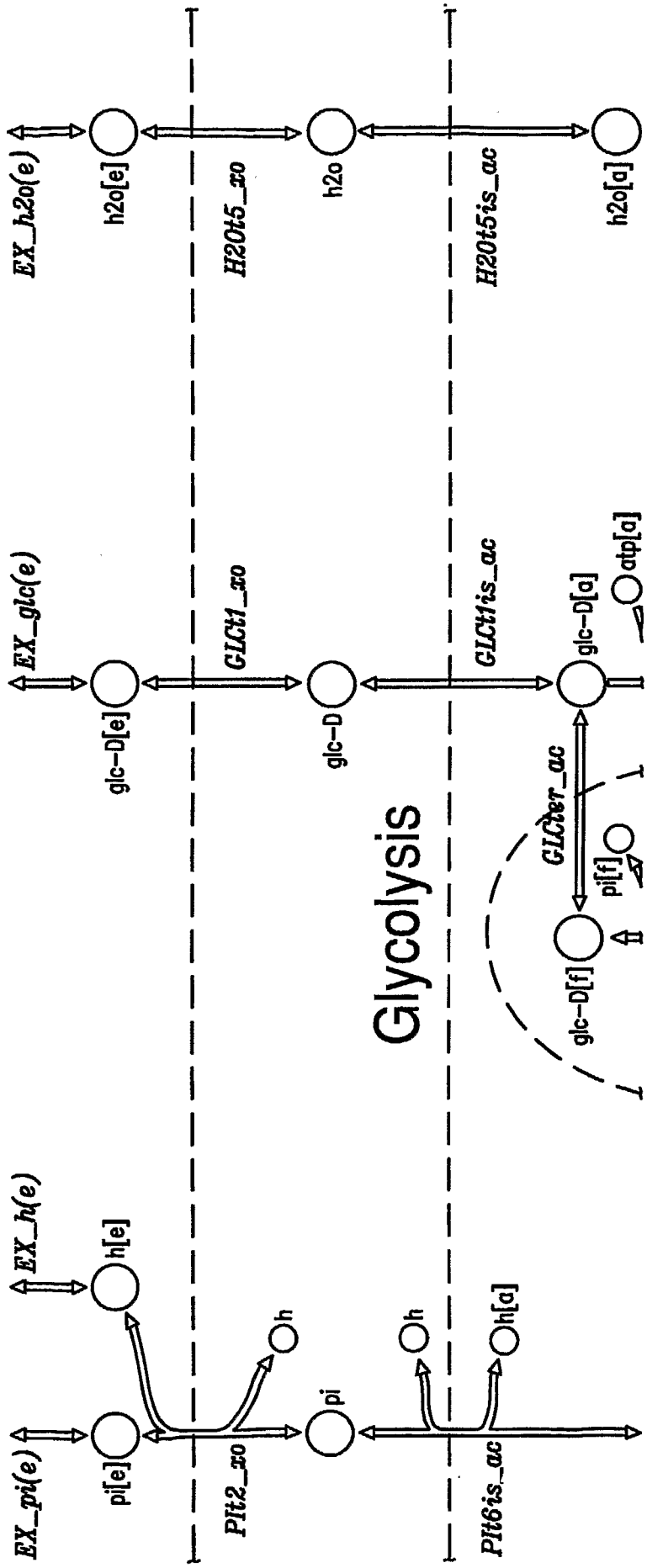
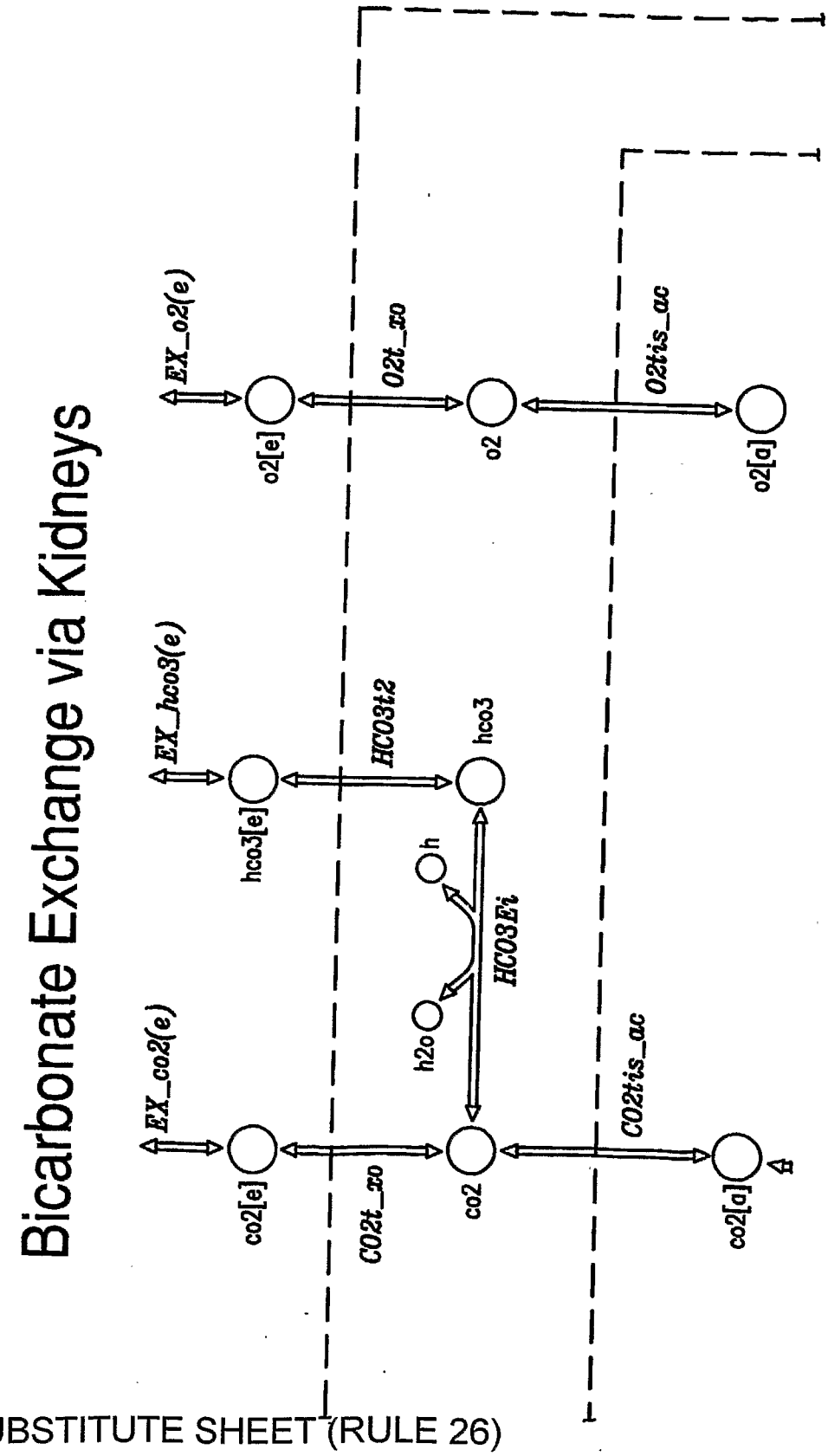

Glycolysis
EX_h2o(e)
h2o[e]
H2Ot5_xo
h2o
H2Ot5is_ac
h2o[a]
EX_glc(e)
glc-D[e]
GLCt1_xo
glc-D
GLCt1is_ac
glc-D[a]
atp[a]
GLCter_ac
pi[f]
glc-D[f]
EX_h(e)
h[e]
h
pi
h
h[a]
EX_pi(e)
pi[e]
Pit2_xo
Pit6is_ac

FIG. 10-10


Bicarbonate Exchange via Kidneys
EX_o2(e)
o2[e]
O2t_no
o2
O2tis_ac
o2[a]
EX_hco3(e)
hco3[e]
HCO3t2
hco3
h
HCO3Ei
h2o
EX_co2(e)
co2[e]
CO2t_no
co2
CO2tis_ac
co2[a]

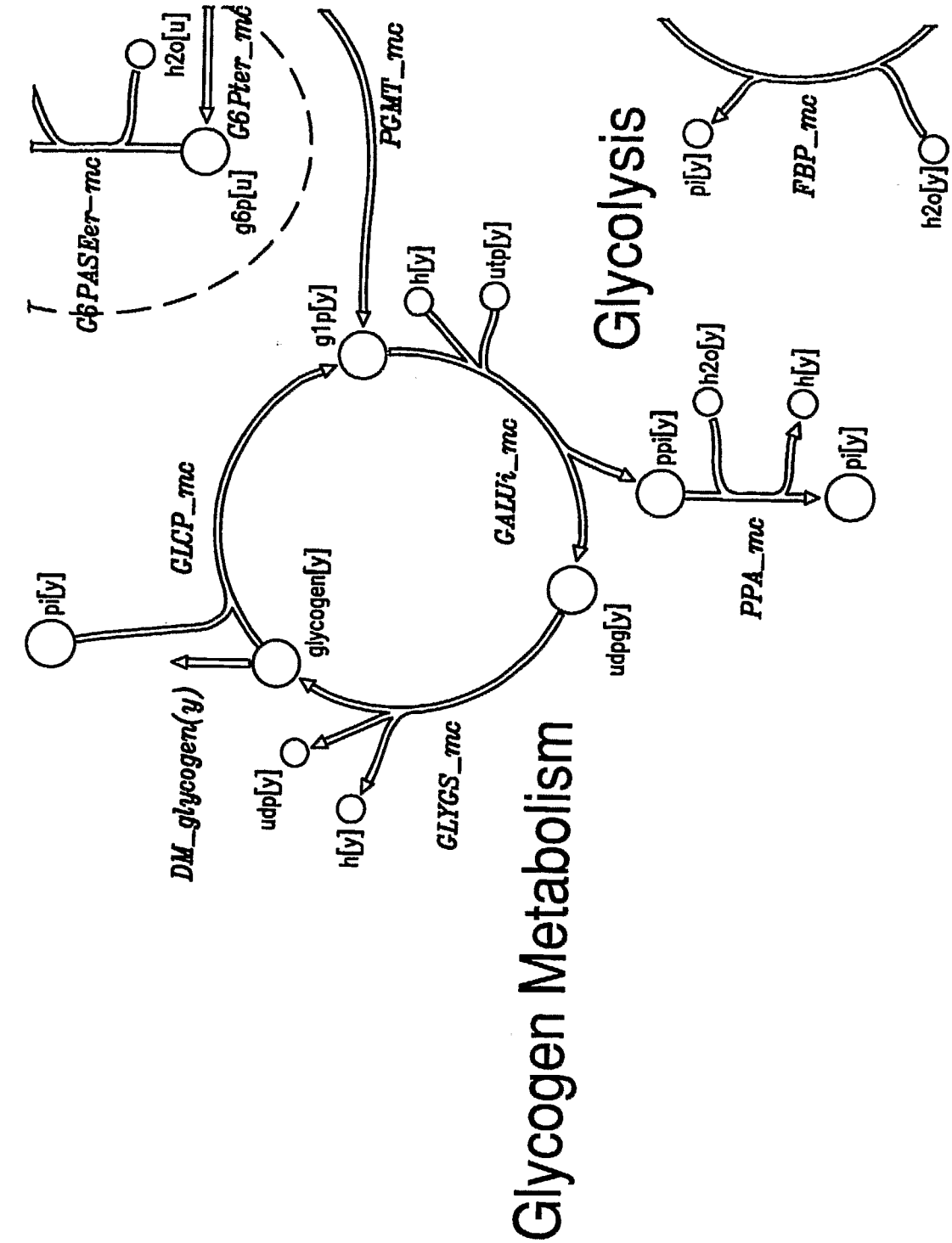
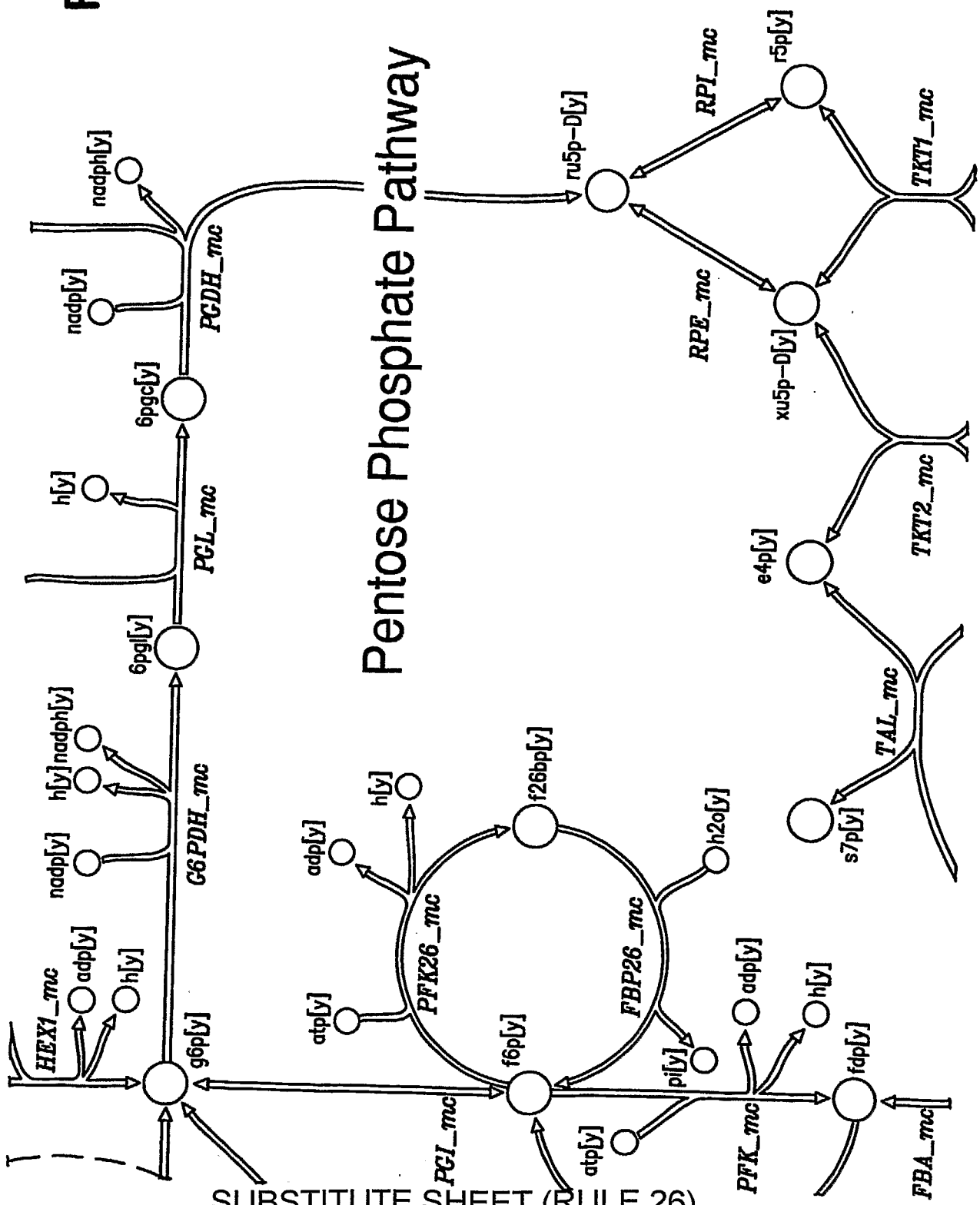

Glycogen Metabolism
Glycolysis
pi[y]
GLCP_mc
glycogen[y]
DM_glycogen(y)
udp[y]
h[y]
GLYGS_mc
g1p[y]
GALUi_mc
udpg[y]
h[y]
utp[y]
PGMT_mc
ppi[y]
h2o[y]
h[y]
pi[y]
PPA_mc
pi[y]
FBP_mc
h2o[y]
G6PTer_mc
h2o[u]
g6p[u]
G6PASEer_mc

FIG. 10-11

FIG. 10-12


Pentose Phosphate Pathway
HEX1_mc
adp[y]
h[y]
g6p[y]
G6PDH_mc
nadp[y]
h[y]
nadph[y]
6pgl[y]
PGL_mc
h[y]
6pgc[y]
PGDH_mc
nadp[y]
nadph[y]
PGI_mc
f6p[y]
atp[y]
PFK26_mc
adp[y]
h[y]
f26bp[y]
FBP26_mc
h2o[y]
pi[y]
PFK_mc
atp[y]
adp[y]
h[y]
fdp[y]
FBA_mc
ru5p-D[y]
RPI_mc
r5p[y]
TKT1_mc
RPE_mc
xu5p-D[y]
TKT2_mc
e4p[y]
TAL_mc
s7p[y]

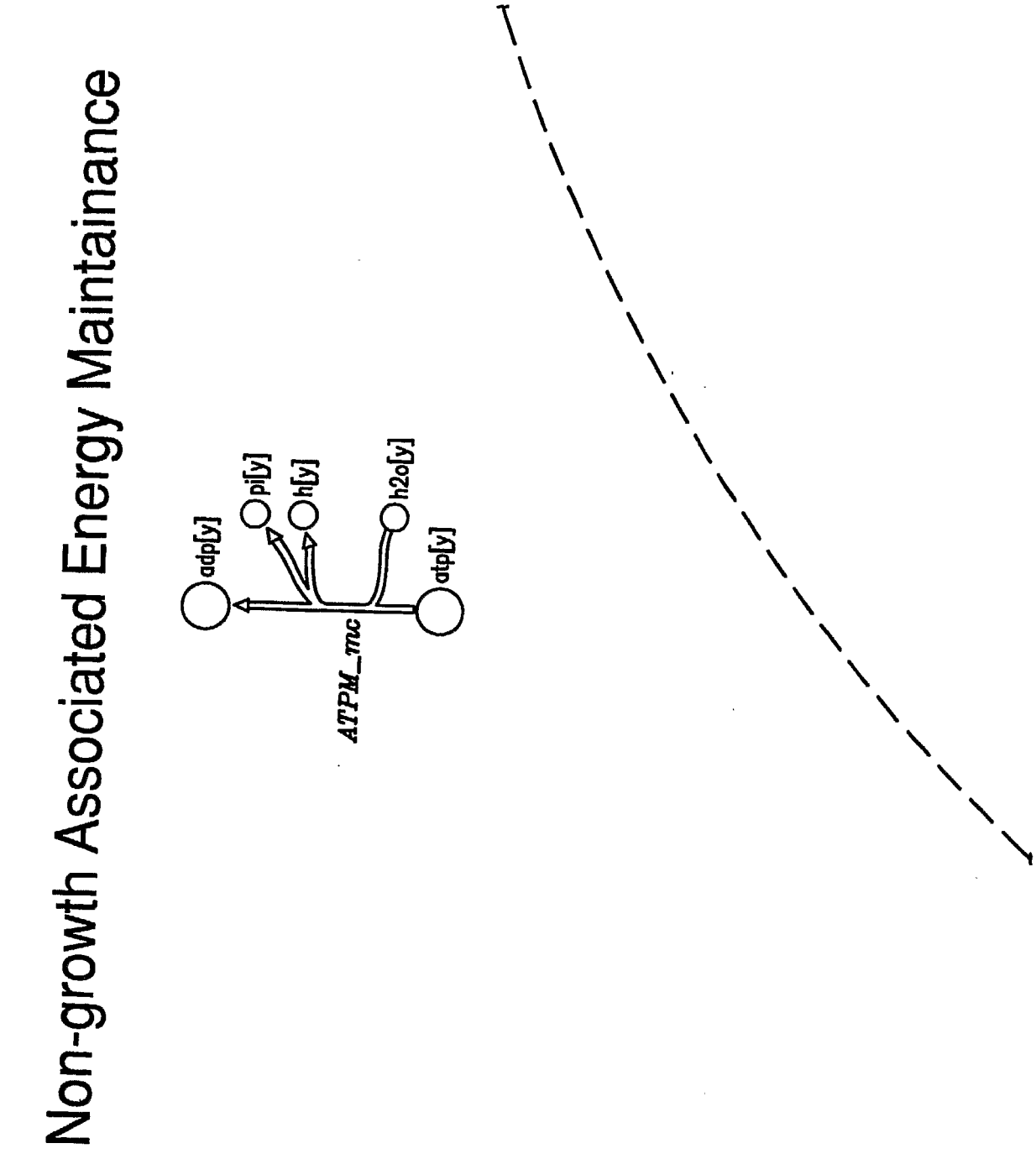

Non-growth Associated Energy Maintainance
adp[y]
pi[y]
h[y]
h2o[y]
atp[y]
ATPM_mc

FIG. 10-13

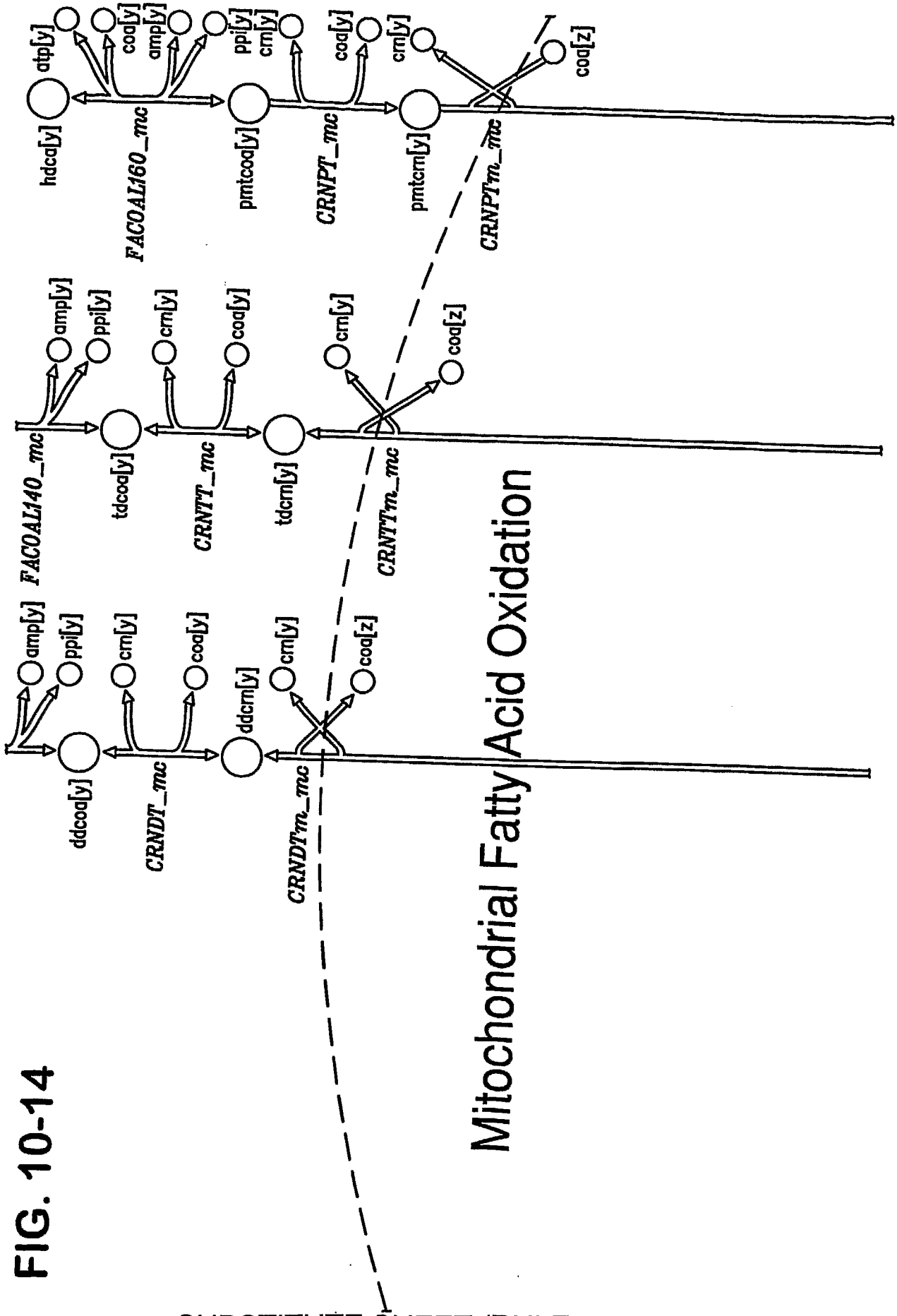
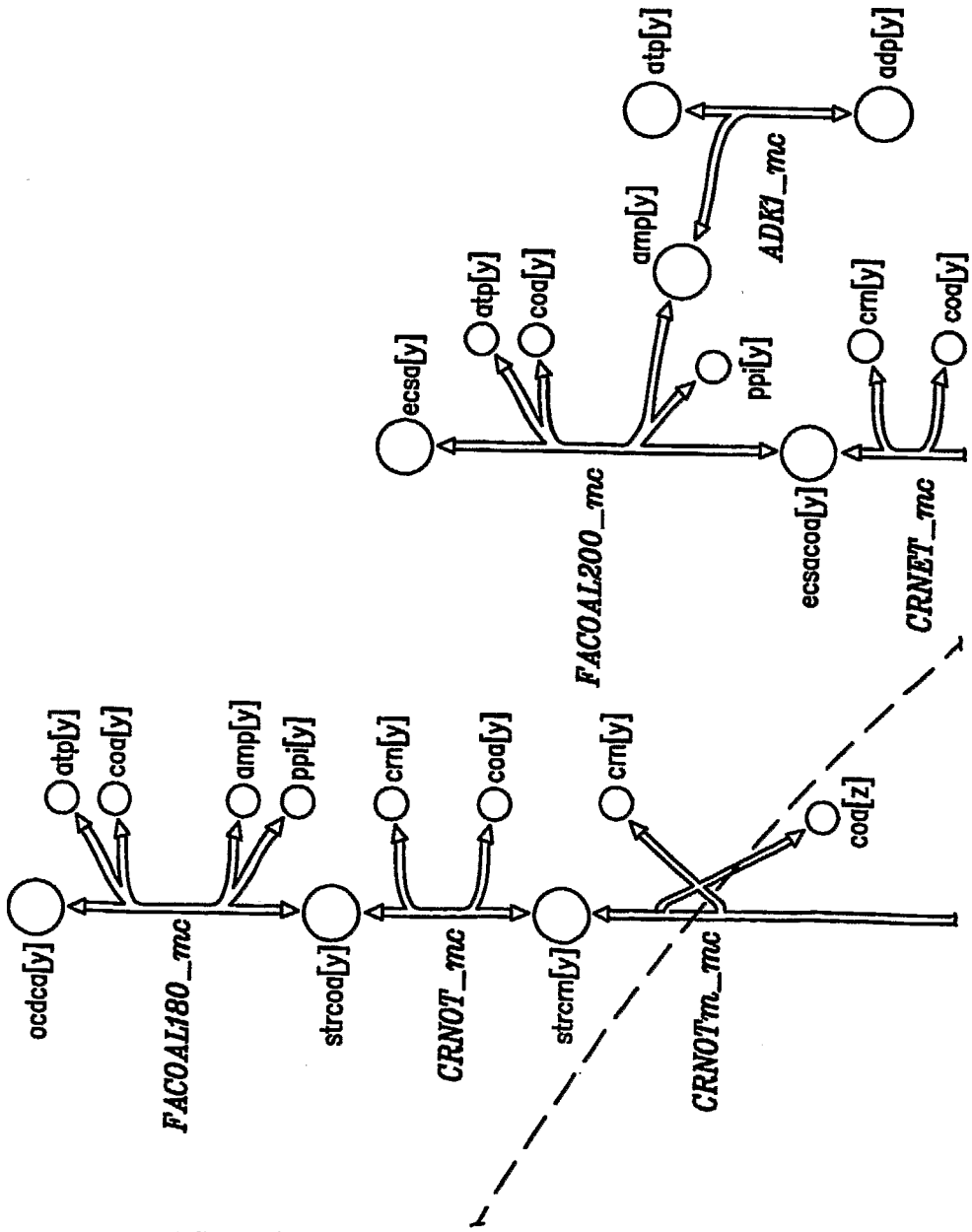

Mitochondrial Fatty Acid Oxidation
hdca[y]
atp[y]
coa[y]
amp[y]
ppi[y]
cm[y]
FACOAL160_mc
pmtcoa[y]
CRNPT_mc
pmtcrn[y]
CRNPTm_mc
coa[z]
FACOAL140_mc
tdcoa[y]
CRNTT_mc
tdcrn[y]
CRNTTm_mc
ddcoa[y]
CRNDT_mc
ddcrn[y]
CRNDTm_mc

FIG. 10-14

FIG. 10-15


atp[y]
adp[y]
ADK1_mc
amp[y]
atp[y]
coa[y]
ecsa[y]
ppi[y]
FACOAL200_mc
ecsacoa[y]
crn[y]
coa[y]
CRNET_mc
atp[y]
coa[y]
amp[y]
ppi[y]
ocdca[y]
FACOAL180_mc
strcoa[y]
crn[y]
coa[y]
CRNOT_mc
strcrn[y]
crn[y]
coa[z]
CRNOTm_mc

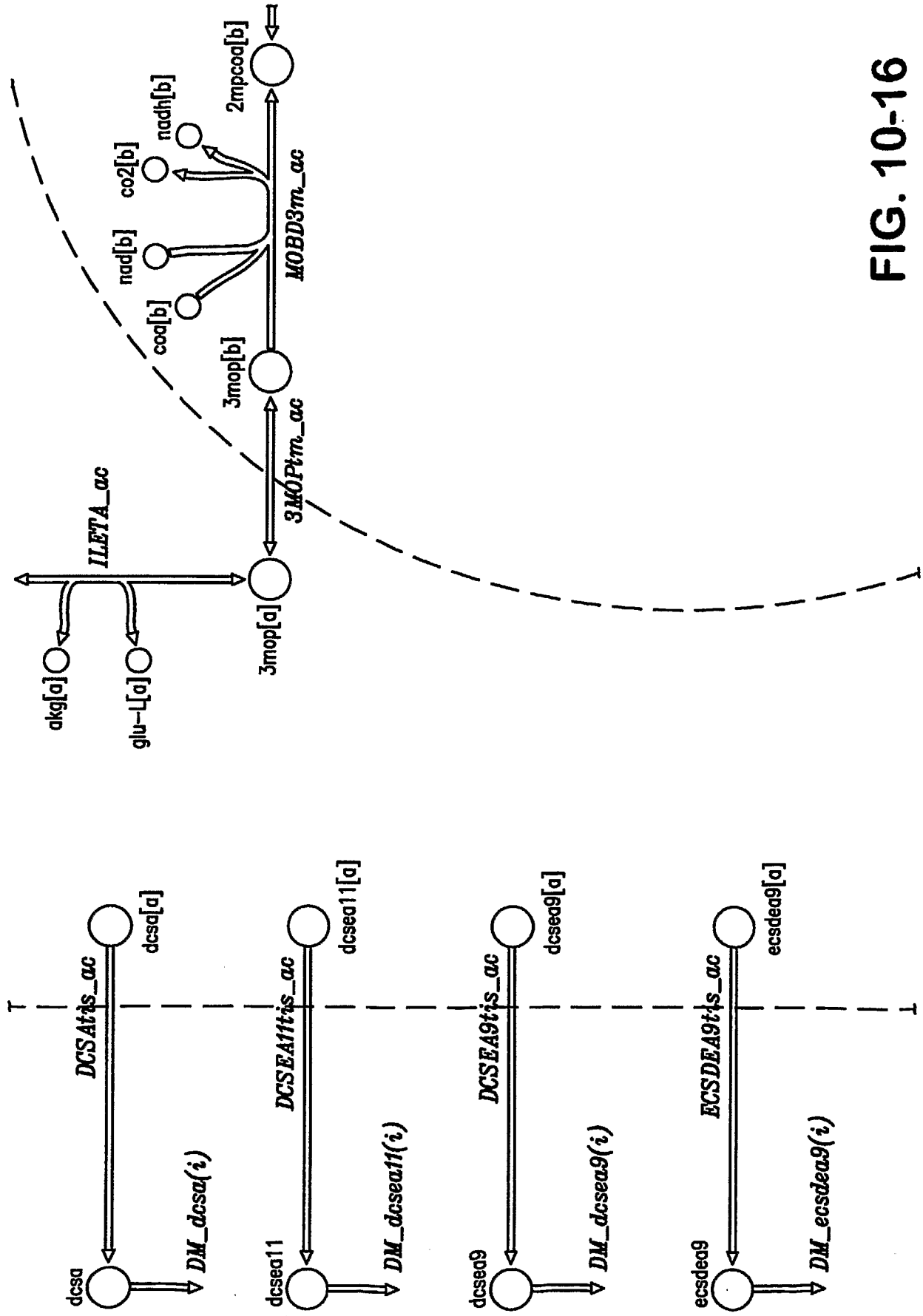
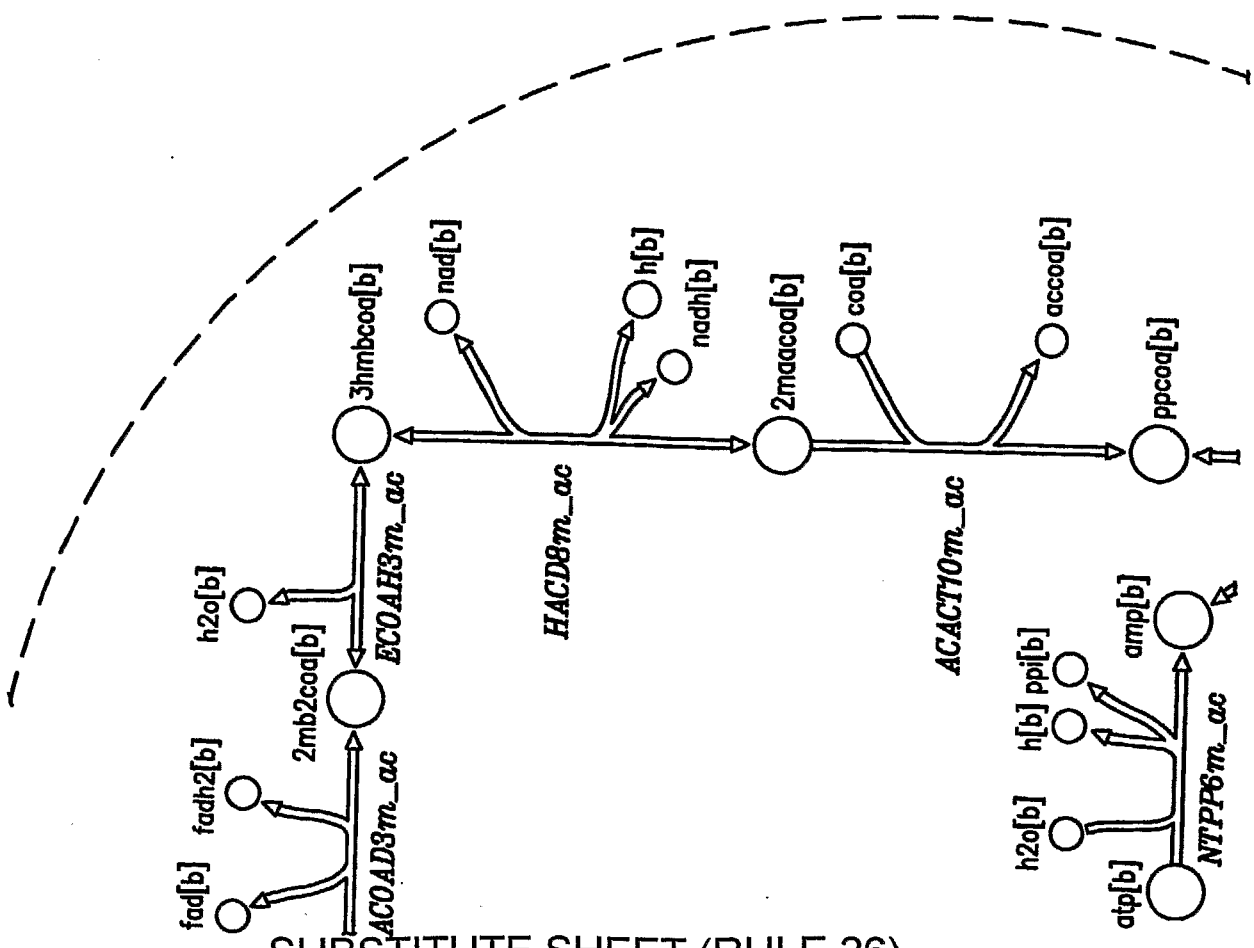

2mpcoa[b]
nadh[b]
co2[b]
nad[b]
coa[b]
MOBD3m_ac
3mop[b]
3MOPtm_ac
ILETA_ac
3mop[a]
akg[a]
glu-L[a]
DCSAtis_ac
dcsa[a]
DM_dcsa(i)
dcsa
DCSEA11tis_ac
dcsea11[a]
DM_dcsea11(i)
dcsea11
DCSEA9tis_ac
dcsea9[a]
DM_dcsea9(i)
dcsea9
ECSDEA9tis_ac
ecsdea9[a]
DM_ecsdea9(i)
ecsdea9

FIG. 10-16

FIG. 10-17


3hmbcoa[b]
nad[b]
h[b]
nadh[b]
2maacoa[b]
coa[b]
accoa[b]
ppcoa[b]
h2o[b]
ECOAH3m_ac
HACD8m_ac
ACACT10m_ac
2mb2coa[b]
fadh2[b]
fad[b]
ACOAD3m_ac
amp[b]
h[b]
ppi[b]
h2o[b]
atp[b]
NTPP6m_ac


Non-growth Associated Energy Maintainance
h[a]
Glycogen Metabolism
adp[a]
pi[a]
h[a]
h2o[a]
atp[a]
adp[a]
ATPM_ac
ADK1_ac
amp[a]
Triglycerol Biosynthesis
12dgr_HS[a]
TRIGH_ac_HS_ub
12DGRH_ac_HS_ub
MGLYCH_ac_HS_ub
mglyc_HS[a]
glyc[a]

FIG. 10-18

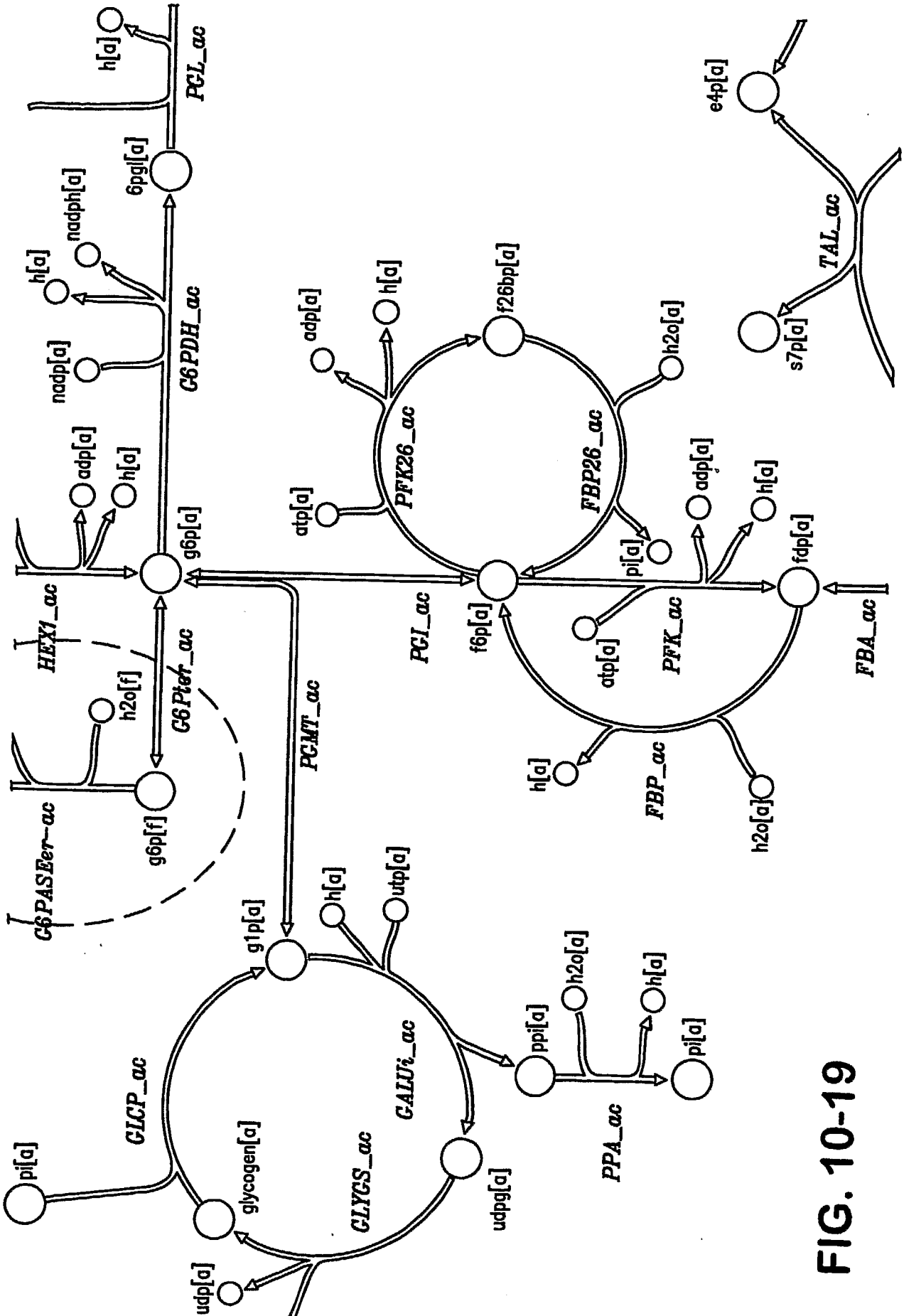
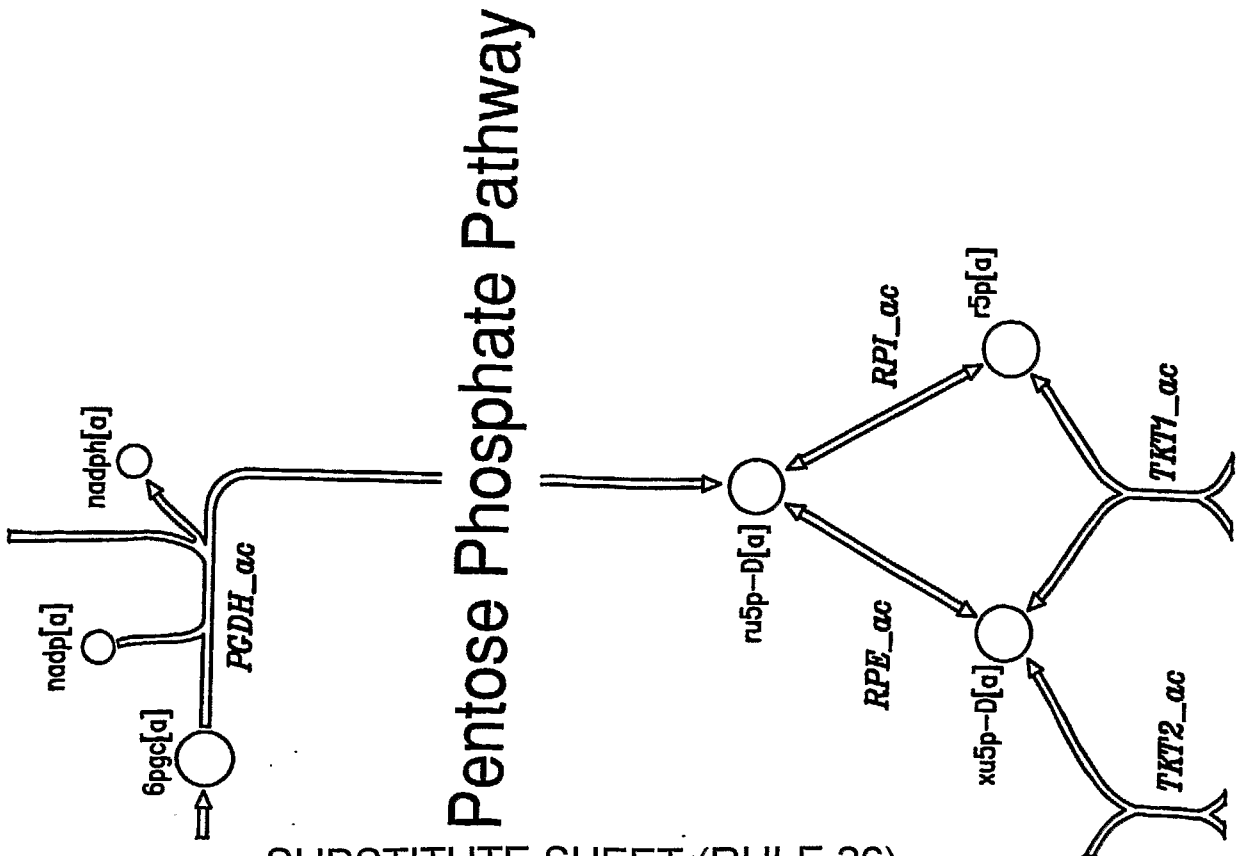

h[a]
PGL_ac
6pgl[a]
nadph[a]
h[a]
nadp[a]
G6PDH_ac
adp[a]
h[a]
g6p[a]
HEX1_ac
h2o[f]
G6Pter_ac
g6p[f]
G6PASEer_ac
PGMT_ac
g1p[a]
h[a]
utp[a]
GLCP_ac
pi[a]
glycogen[a]
GLYCS_ac
GALUi_ac
udpg[a]
udp[a]
ppi[a]
h2o[a]
h[a]
pi[a]
PPA_ac
atp[a]
PFK26_ac
adp[a]
h[a]
f26bp[a]
FBP26_ac
h2o[a]
PGI_ac
f6p[a]
atp[a]
PFK_ac
pi[a]
adp[a]
h[a]
fdp[a]
FBA_ac
h[a]
FBP_ac
h2o[a]
e4p[a]
TAL_ac
s7p[a]

FIG. 10-19

FIG. 10-20


Pentose Phosphate Pathway
nadph[a]
nadp[a]
6pgc[a]
PGDH_ac
ru5p-D[a]
RPI_ac
r5p[a]
TKT1_ac
RPE_ac
xu5p-D[a]
TKT2_ac

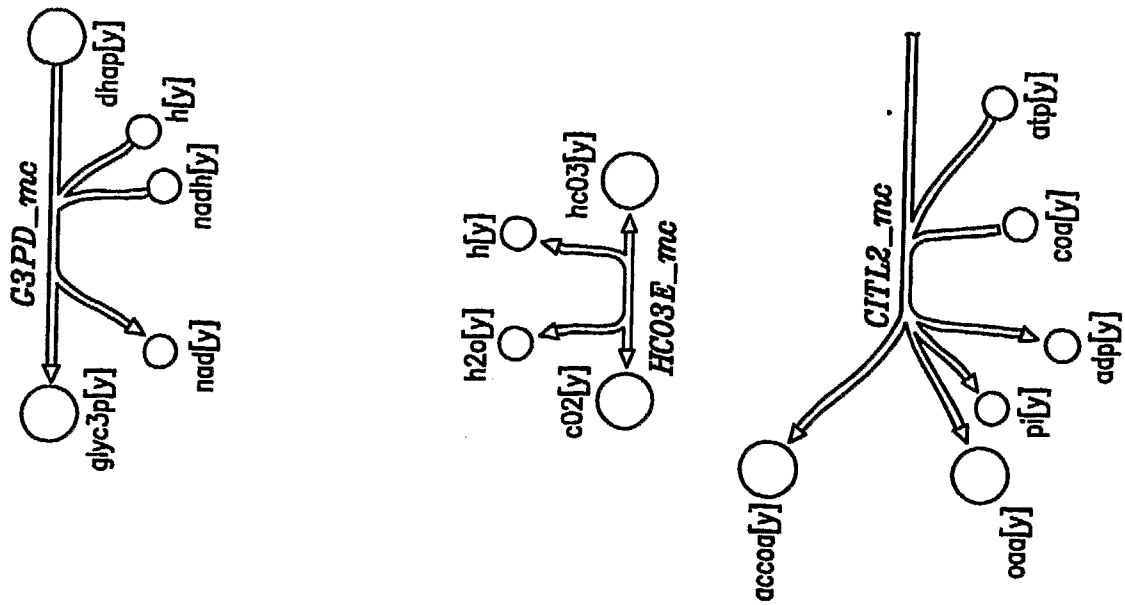
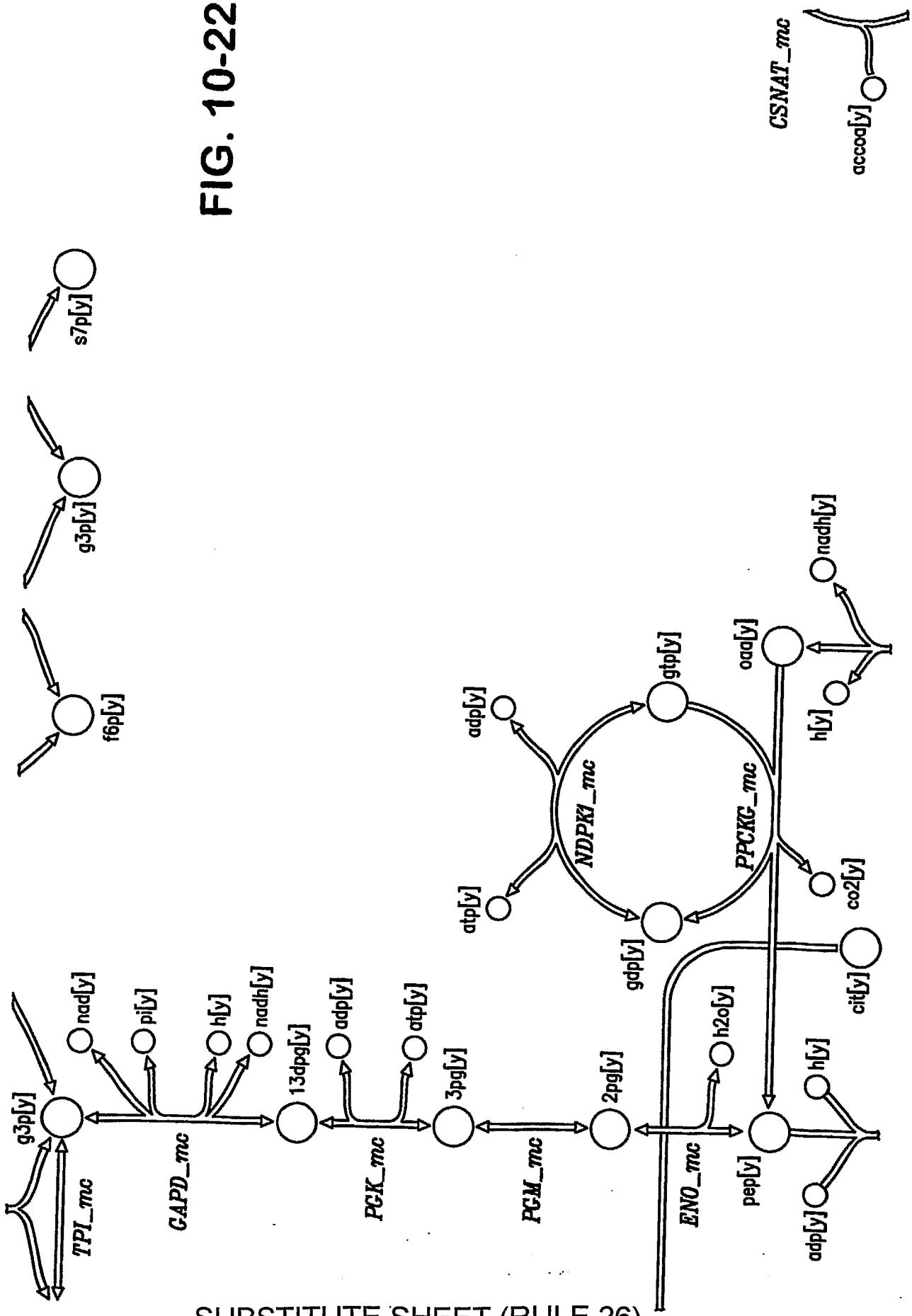

C3PD_mc
dhap[y]
h[y]
nadh[y]
nad[y]
glyc3p[y]
HCO3E_mc
hco3[y]
h[y]
h2o[y]
co2[y]
CITL2_mc
atp[y]
coa[y]
adp[y]
pi[y]
accoa[y]
oaa[y]

FIG. 10-21

FIG. 10-22


s7p[y]
g3p[y]
f6p[y]
CSNAT_mc
accoa[y]
nadh[y]
h[y]
oaa[y]
gtp[y]
adp[y]
NDPK1_mc
PPCKG_mc
atp[y]
co2[y]
gdp[y]
cit[y]
h2o[y]
h[y]
g3p[y]
nad[y]
pi[y]
h[y]
nadh[y]
13dpg[y]
adp[y]
atp[y]
3pg[y]
2pg[y]
pep[y]
adp[y]
TPI_mc
GAPD_mc
PGK_mc
PGM_mc
ENO_mc

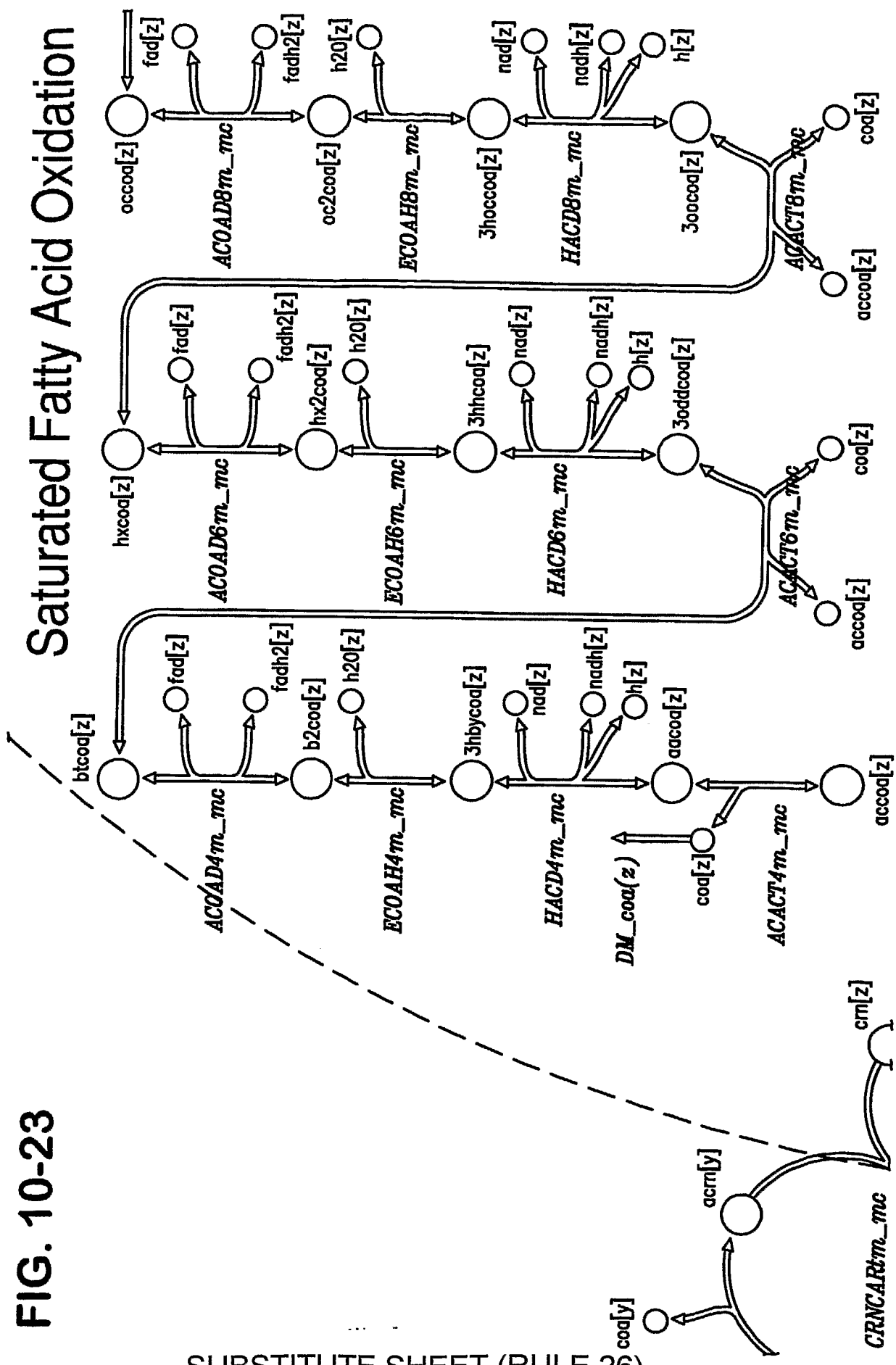

Saturated Fatty Acid Oxidation
accoa[z]
fad[z]
fadh2[z]
ACOAD8m_mc
oc2coa[z]
h2o[z]
ECOAH8m_mc
3hoccoa[z]
nad[z]
nadh[z]
h[z]
HACD8m_mc
3oacoa[z]
coa[z]
ACACT8m_mc
accoa[z]
hxcoa[z]
fad[z]
fadh2[z]
ACOAD6m_mc
hx2coa[z]
h2o[z]
ECOAH6m_mc
3hhcoa[z]
nad[z]
nadh[z]
h[z]
HACD6m_mc
3oddcoa[z]
coa[z]
ACACT6m_mc
accoa[z]
btcoa[z]
fad[z]
fadh2[z]
ACOAD4m_mc
b2coa[z]
h2o[z]
ECOAH4m_mc
3hbycoa[z]
nad[z]
nadh[z]
h[z]
HACD4m_mc
aacoa[z]
DM_coa(z)
coa[z]
ACACT4m_mc
accoa[z]
cm[z]
acm[y]
CRNCARtm_mc
coa[y]

FIG. 10-23

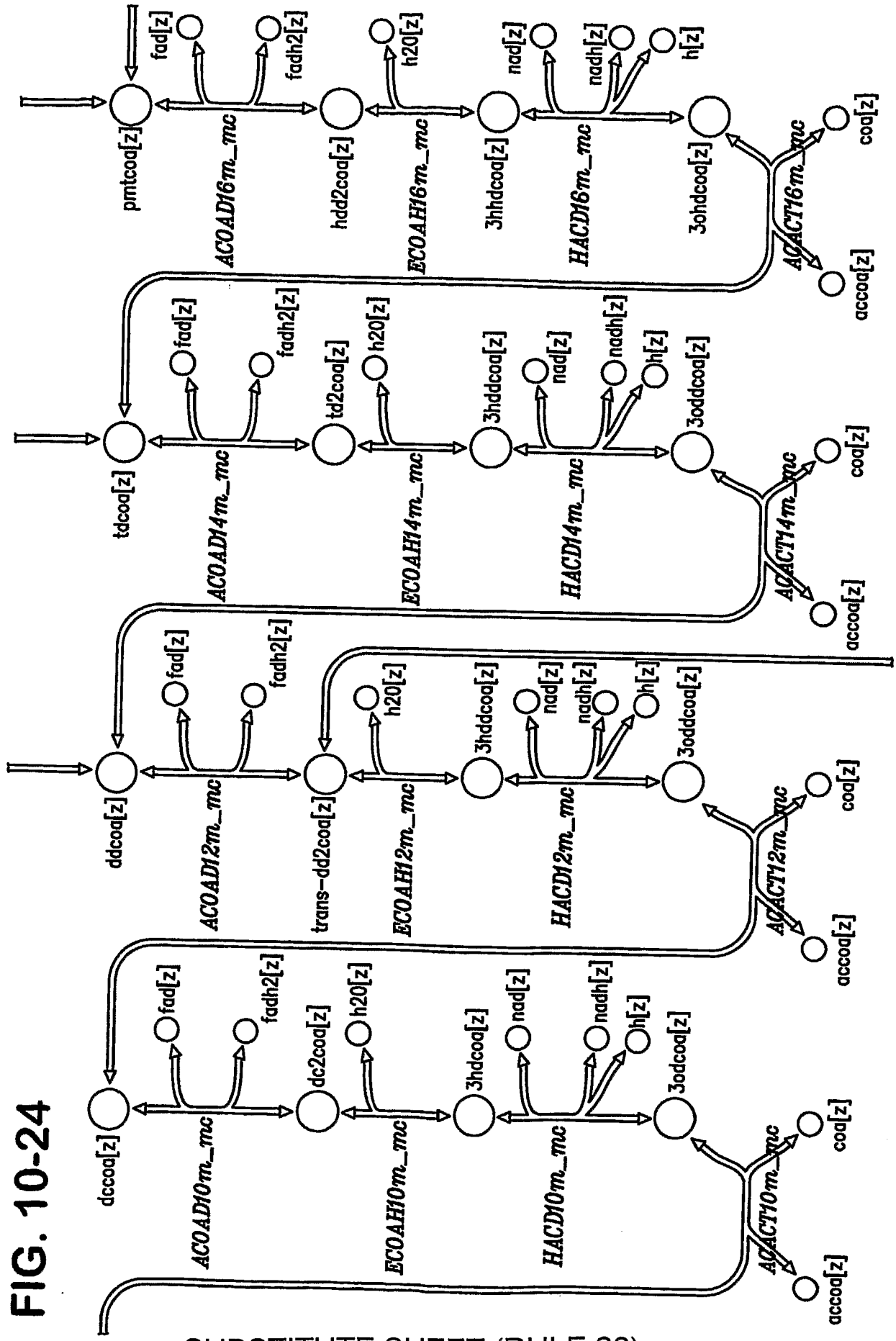

pmtcoa[z]
fad[z]
fadh2[z]
ACOAD16m_mc
hdd2coa[z]
h2o[z]
ECOAH16m_mc
3hhdcoa[z]
nad[z]
nadh[z]
h[z]
HACD16m_mc
3ohdcoa[z]
AOACT16m_mc
coa[z]
accoa[z]
tdcoa[z]
fad[z]
fadh2[z]
ACOAD14m_mc
td2coa[z]
h2o[z]
ECOAH14m_mc
3hddcoa[z]
nad[z]
nadh[z]
h[z]
HACD14m_mc
3oddcoa[z]
AOACT14m_mc
coa[z]
accoa[z]
ddcoa[z]
fad[z]
fadh2[z]
ACOAD12m_mc
trans-dd2coa[z]
h2o[z]
ECOAH12m_mc
3hddcoa[z]
nad[z]
nadh[z]
h[z]
HACD12m_mc
3oddcoa[z]
AOACT12m_mc
coa[z]
accoa[z]
dccoa[z]
fad[z]
fadh2[z]
ACOAD10m_mc
dc2coa[z]
h2o[z]
ECOAH10m_mc
3hdcoa[z]
nad[z]
nadh[z]
h[z]
HACD10m_mc
3odcoa[z]
AOACT10m_mc
coa[z]
accoa[z]

FIG. 10-24

FIG. 10-25

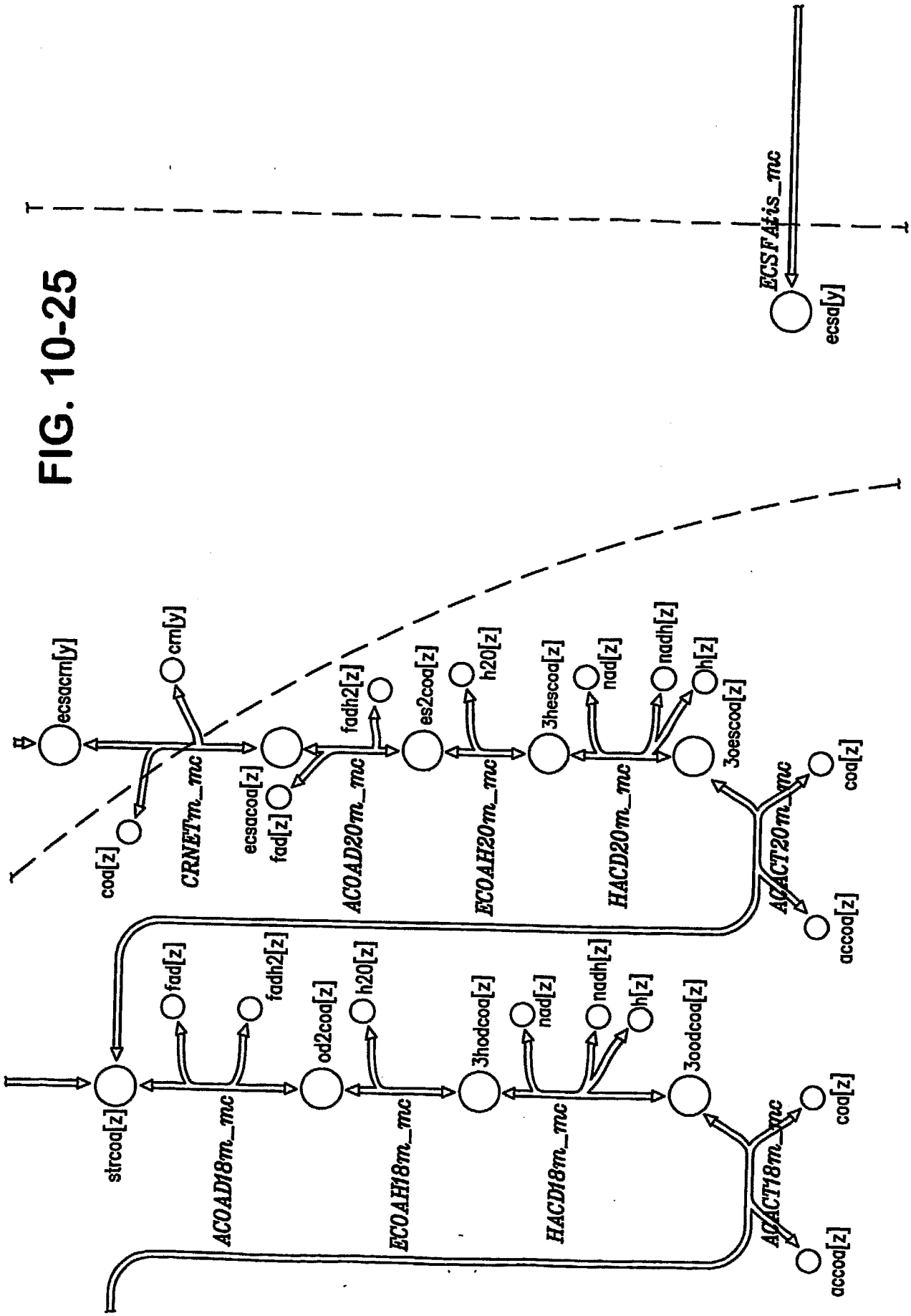

ecsacm[y]
cm[y]
coa[z]
CRNETm_mc
ecsacoa[z]
fad[z]
fadh2[z]
ACOAD20m_mc
es2coa[z]
h20[z]
ECOAH20m_mc
3hescoa[z]
nad[z]
nadh[z]
h[z]
HACD20m_mc
3oescoa[z]
ACACT20m_mc
coa[z]
accoa[z]
ECSFAtis_mc
ecsa[y]
strcoa[z]
fad[z]
fadh2[z]
ACOAD18m_mc
od2coa[z]
h20[z]
ECOAH18m_mc
3hodcoa[z]
nad[z]
nadh[z]
h[z]
HACD18m_mc
3oodcoa[z]
ACACT18m_mc
coa[z]
accoa[z]

FIG. 10-26

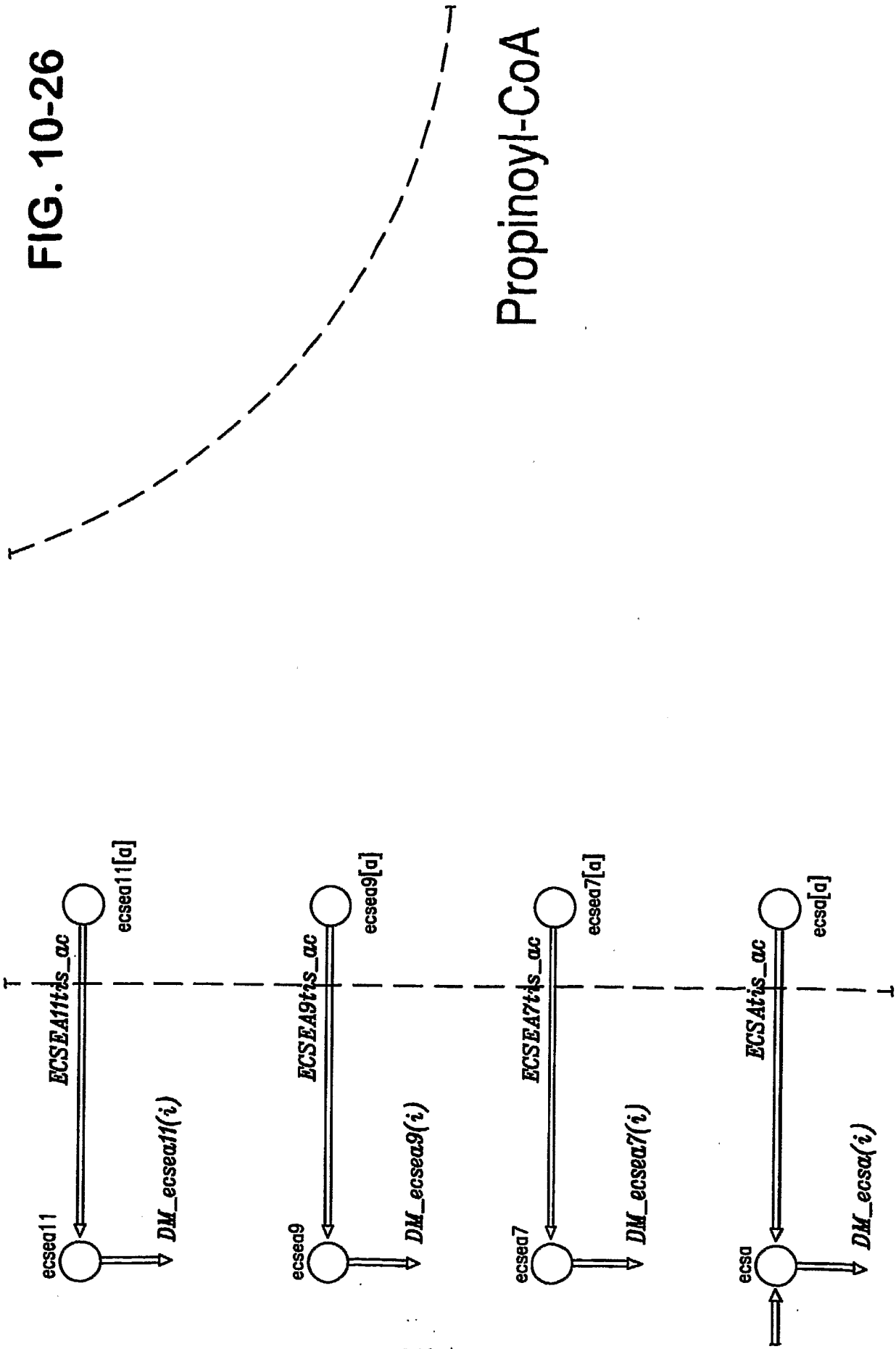

Propinoyl-CoA
ecsea11[a]
ECSEA11tis_ac
DM_ecsea11(i)
ecsea11
ecsea9[a]
ECSEA9tis_ac
DM_ecsea9(i)
ecsea9
ecsea7[a]
ECSEA7tis_ac
DM_ecsea7(i)
ecsea7
ecsa[a]
ECSAtis_ac
DM_ecsa(i)
ecsa

FIG. 10-27

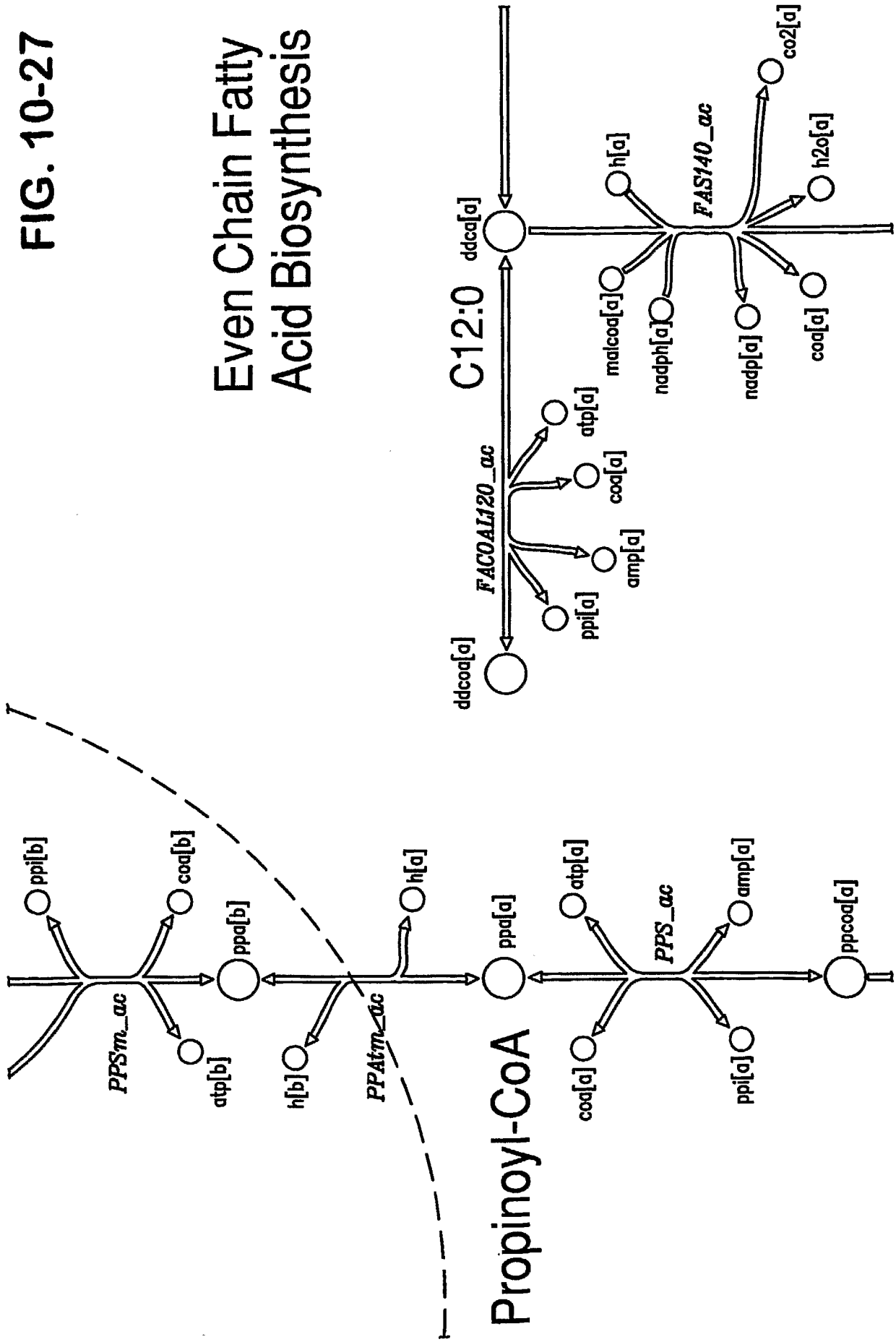
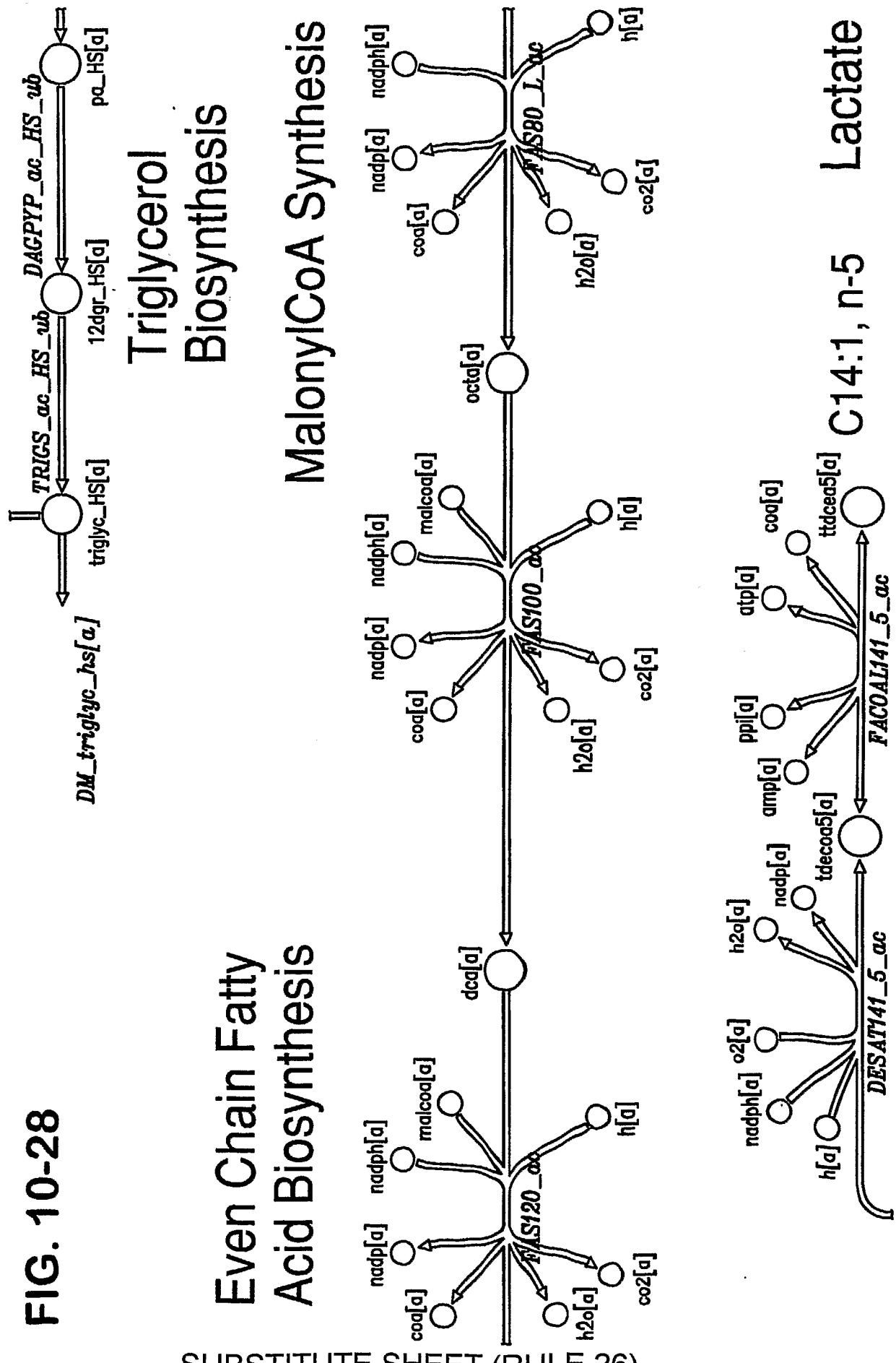

Even Chain Fatty Acid Biosynthesis
C12:0
ddca[a]
FACOAL120_ac
ddcoa[a]
atp[a]
coa[a]
amp[a]
ppi[a]
FAS140_ac
h[a]
malcoa[a]
nadph[a]
nadp[a]
co2[a]
h2o[a]
coa[a]
Propinoyl-CoA
PPSm_ac
ppi[b]
coa[b]
ppa[b]
atp[b]
PPAtm_ac
h[b]
h[a]
ppa[a]
PPS_ac
atp[a]
amp[a]
ppcoa[a]
coa[a]
ppi[a]

FIG. 10-28


Triglycerol Biosynthesis
DAGPYP_ac_HS_ub
pa_HS[a]
TRIGS_ac_HS_ub
12dgr_HS[a]
triglyc_HS[a]
DM_triglyc_hs[a]
MalonylCoA Synthesis
FAS80_L_ac
nadph[a]
nadp[a]
coa[a]
co2[a]
h2o[a]
h[a]
octa[a]
FAS100_ac
malcoa[a]
dca[a]
FAS120_ac
Even Chain Fatty Acid Biosynthesis
C14:1, n-5 Lactate
ttdcea5[a]
atp[a]
ppi[a]
amp[a]
FACOAL141_5_ac
tdecoa5[a]
DESAT141_5_ac
o2[a]

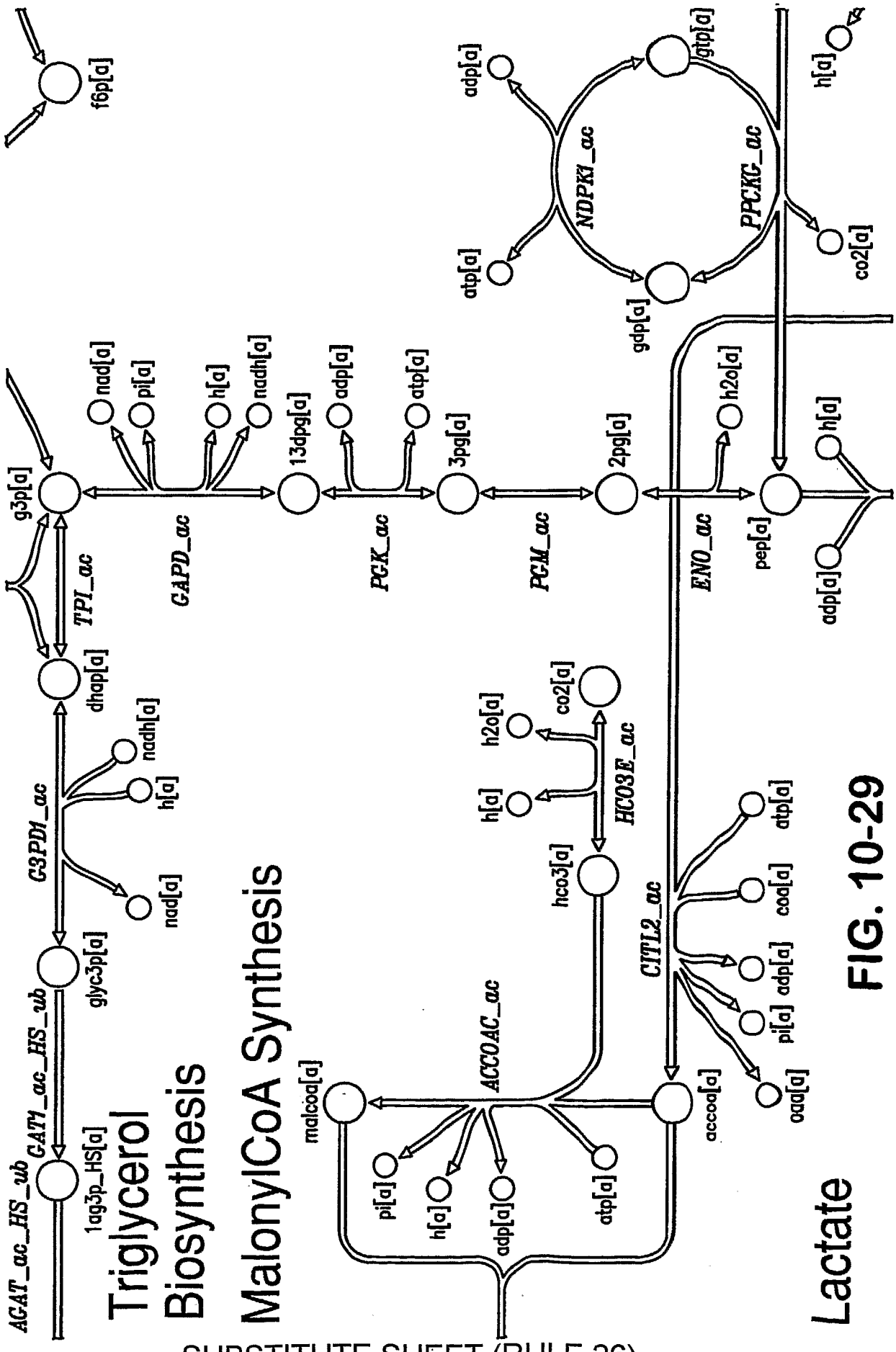
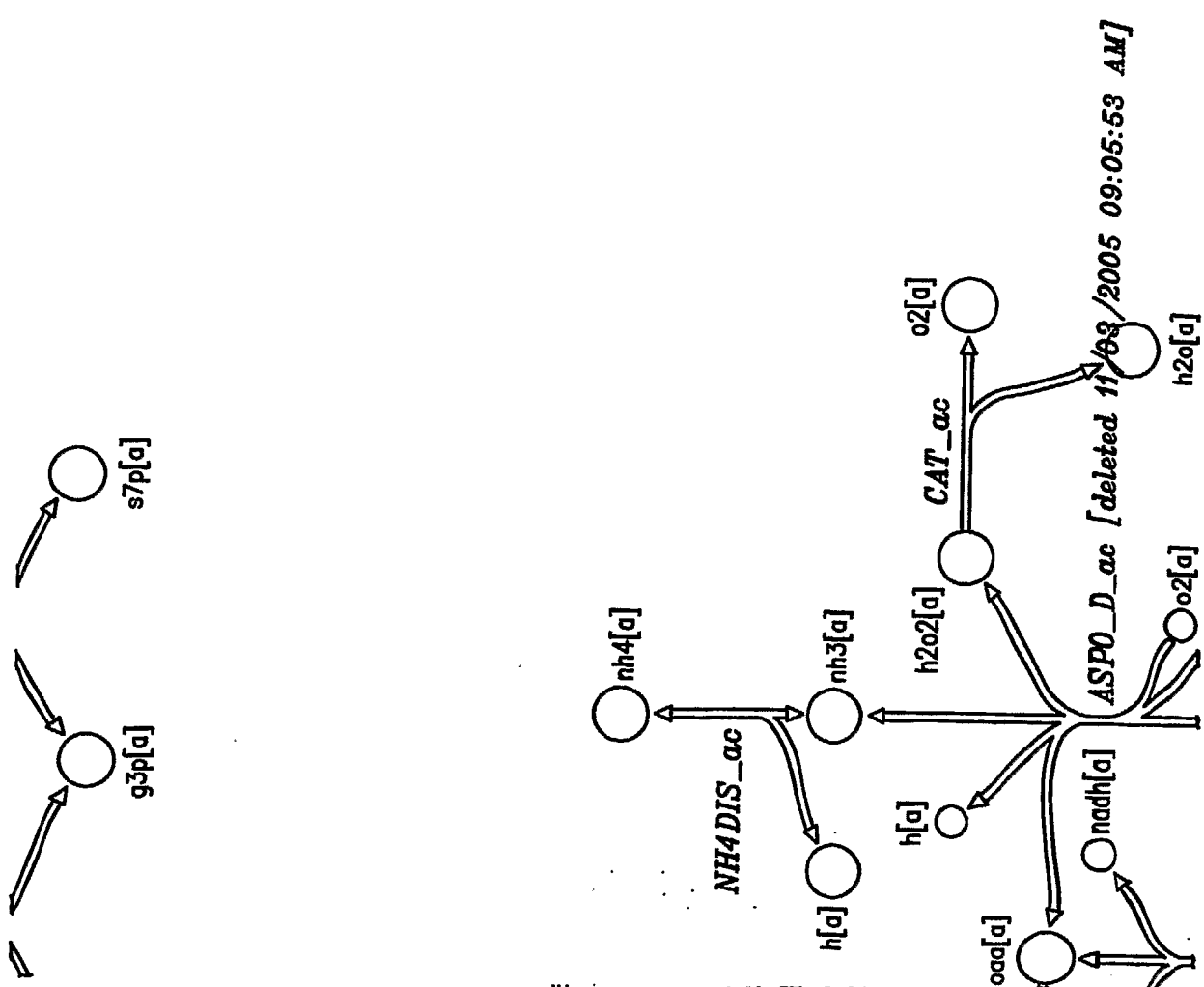

f6p[a]
g3p[a]
nad[a]
pi[a]
h[a]
nadh[a]
13dpg[a]
adp[a]
atp[a]
3pg[a]
2pg[a]
h2o[a]
pep[a]
h[a]
adp[a]
adp[a]
atp[a]
gtp[a]
gdp[a]
h[a]
co2[a]
TPI_ac
GAPD_ac
PGK_ac
PGM_ac
ENO_ac
NDPK1_ac
PPCKC_ac
dhap[a]
nadh[a]
h[a]
nad[a]
G3PD1_ac
glyc3p[a]
GAT1_ac_HS_ub
1ag3p_HS[a]
AGAT_ac_HS_ub
h2o[a]
co2[a]
h[a]
hco3[a]
HCO3E_ac
malcoa[a]
pi[a]
h[a]
adp[a]
atp[a]
ACCOAC_ac
accoa[a]
CITL2_ac
atp[a]
coa[a]
pi[a]
adp[a]
oaa[a]
Triglyceride Biosynthesis
Malonyl CoA Synthesis
Lactate

FIG. 10-29

FIG. 10-30


s7p[a]
g3p[a]
nh4[a]
nh3[a]
NH4DIS_ac
h[a]
h2o2[a]
CAT_ac
o2[a]
h2o[a]
ASPO_D_ac [deleted 11/03/2005 09:05:53 AM]
o2[a]
h[a]
nadh[a]
oaa[a]

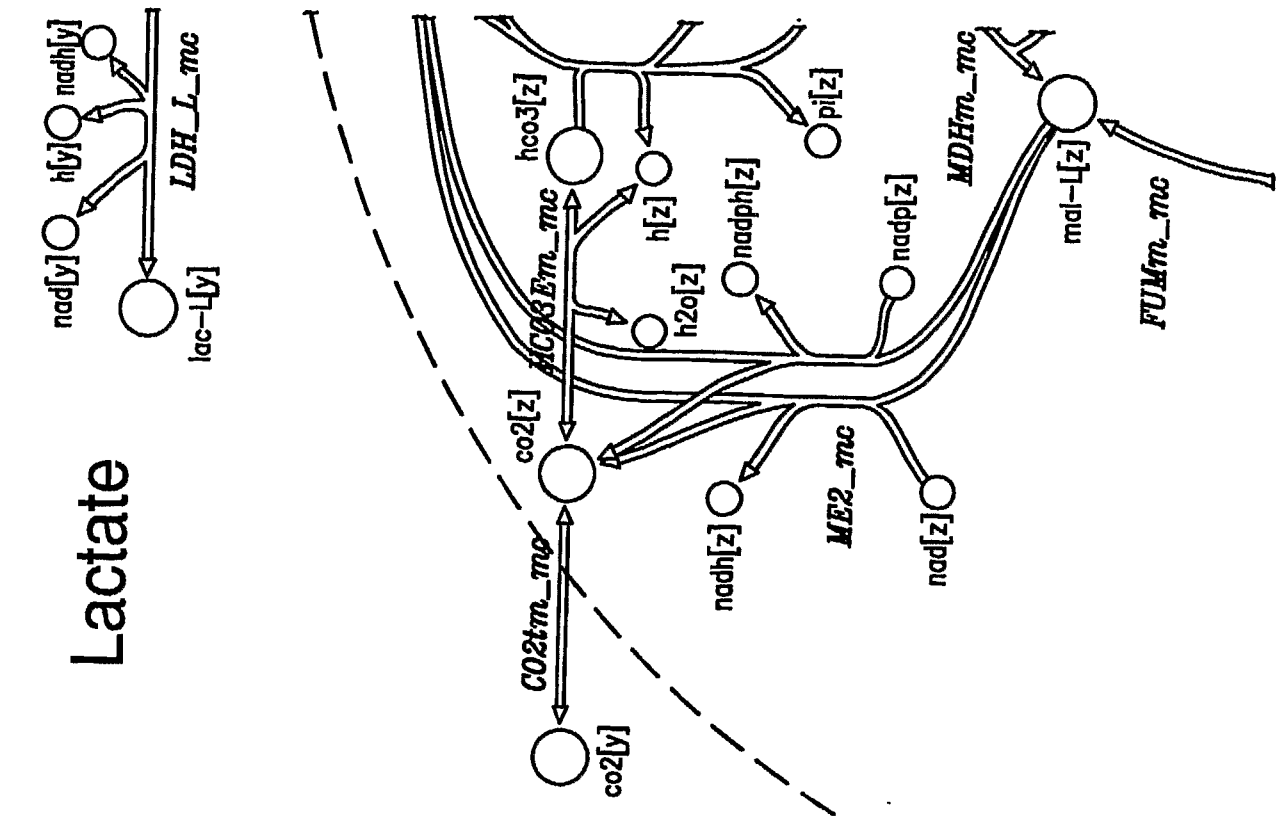

Lactate
nad[y]
h[y]
nadh[y]
LDH_L_mc
lac-L[y]
hco3[z]
h[z]
pi[z]
nadph[z]
nadp[z]
MDHm_mc
mal-L[z]
FUMm_mc
h2o[z]
co2[z]
nadh[z]
ME2_mc
nad[z]
CO2tm_mc
co2[y]

FIG. 10-31

FIG. 10-32

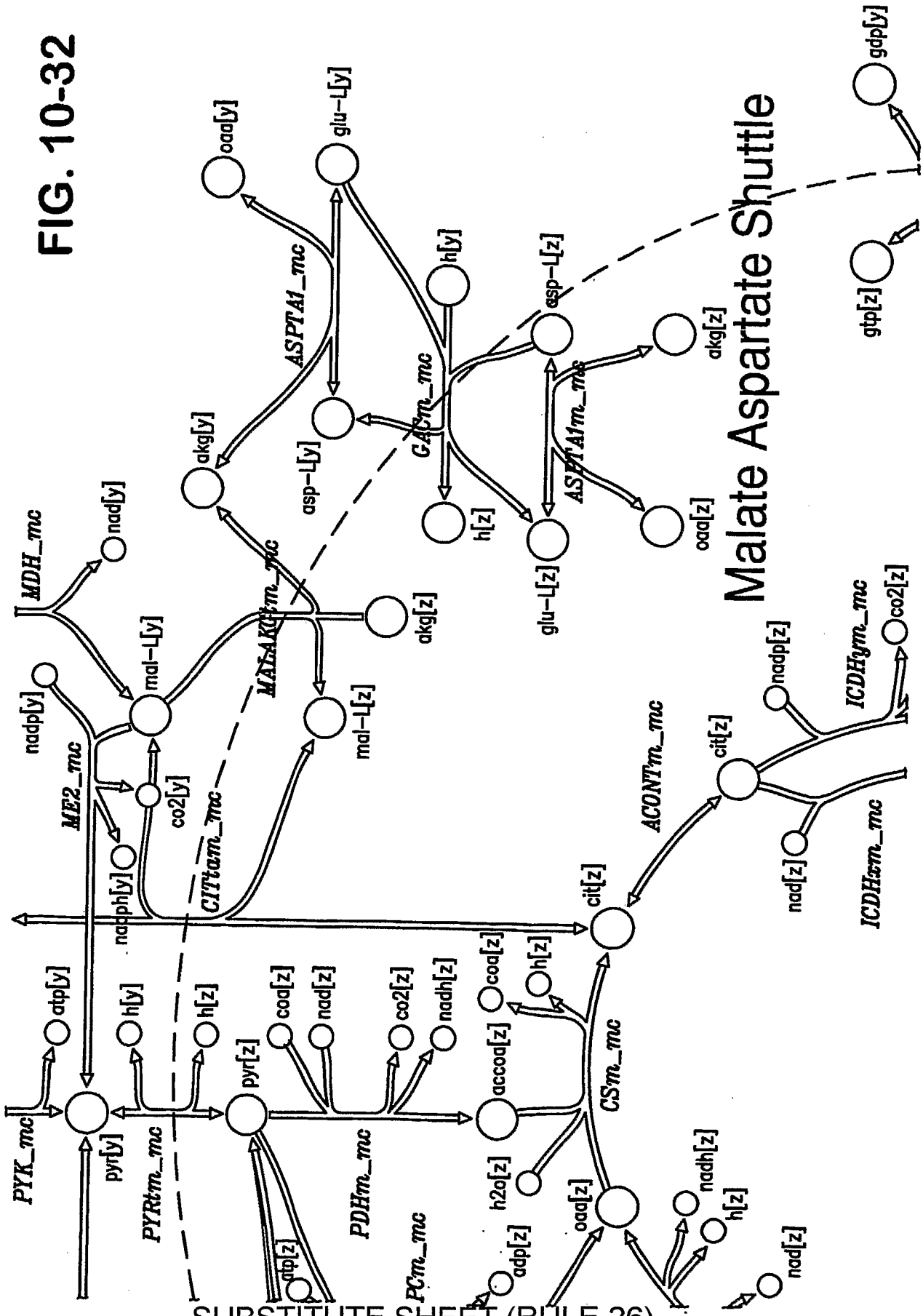
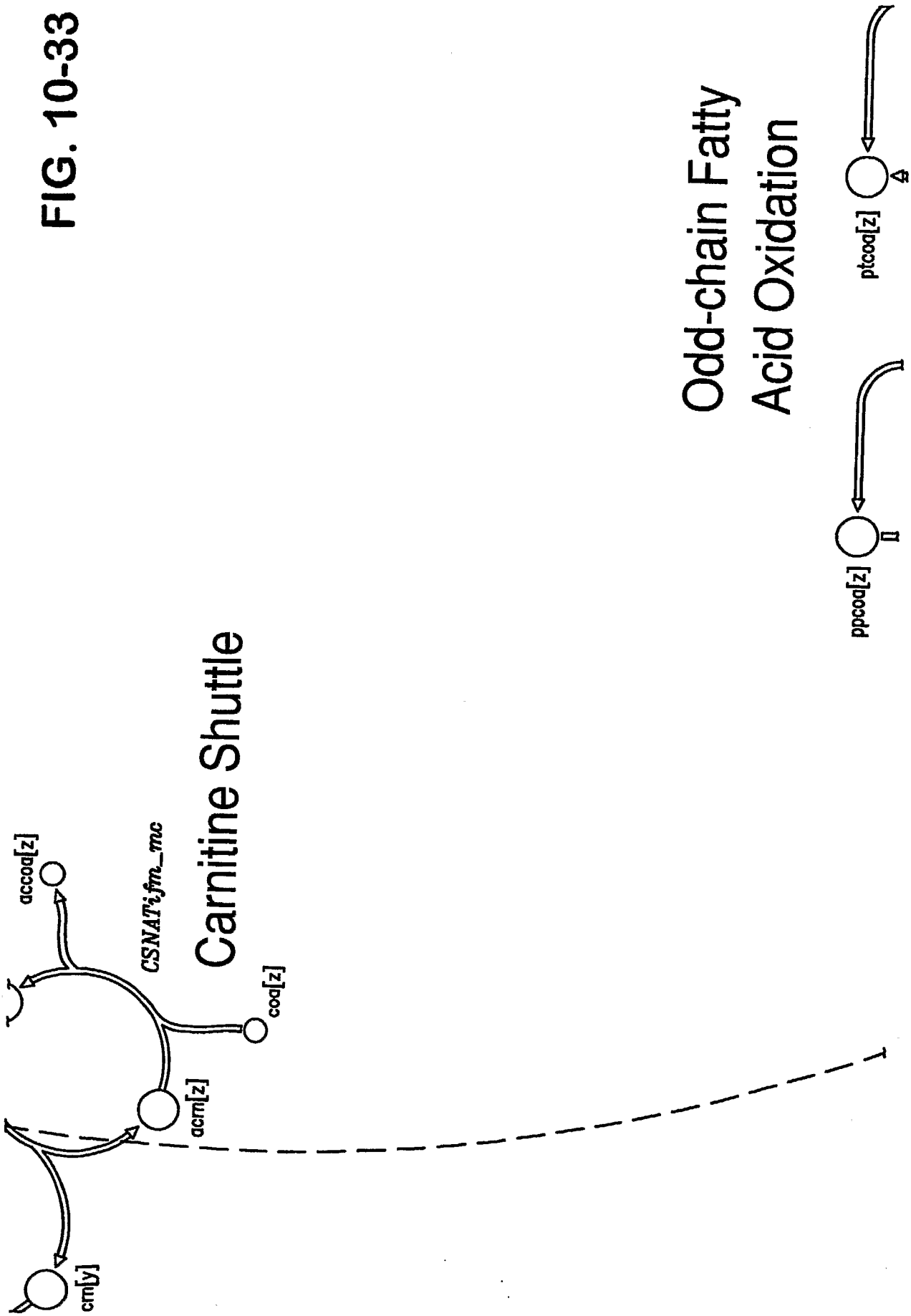

Malate Aspartate Shuttle
MDH_mc
nad[y]
mal-L[y]
ME2_mc
nadp[y]
co2[y]
nadph[y]
PYK_mc
atp[y]
pyr[y]
PYRtm_mc
h[y]
h[z]
pyr[z]
coa[z]
nad[z]
co2[z]
nadh[z]
PDHm_mc
accoa[z]
coa[z]
h[z]
CSm_mc
cit[z]
ACONTm_mc
cit[z]
nadp[z]
ICDHym_mc
co2[z]
nad[z]
ICDHxm_mc
gdp[y]
gtp[z]
akg[z]
glu-L[z]
ASPTA1m_mc
oaa[z]
h[z]
GAGSm_mc
asp-L[z]
h[y]
ASPTA1_mc
glu-L[y]
oaa[y]
asp-L[y]
akg[y]
MAKGTm_mc
akg[z]
mal-L[z]
CITtam_mc
PCm_mc
adp[z]
atp[z]
h2o[z]
oaa[z]
nadh[z]
h[z]
nad[z]

FIG. 10-33


Odd-chain Fatty Acid Oxidation
ptcoa[z]
ppcoa[z]
Carnitine Shuttle
accoa[z]
CSNATi,fm_mc
coa[z]
acm[z]
cm[y]

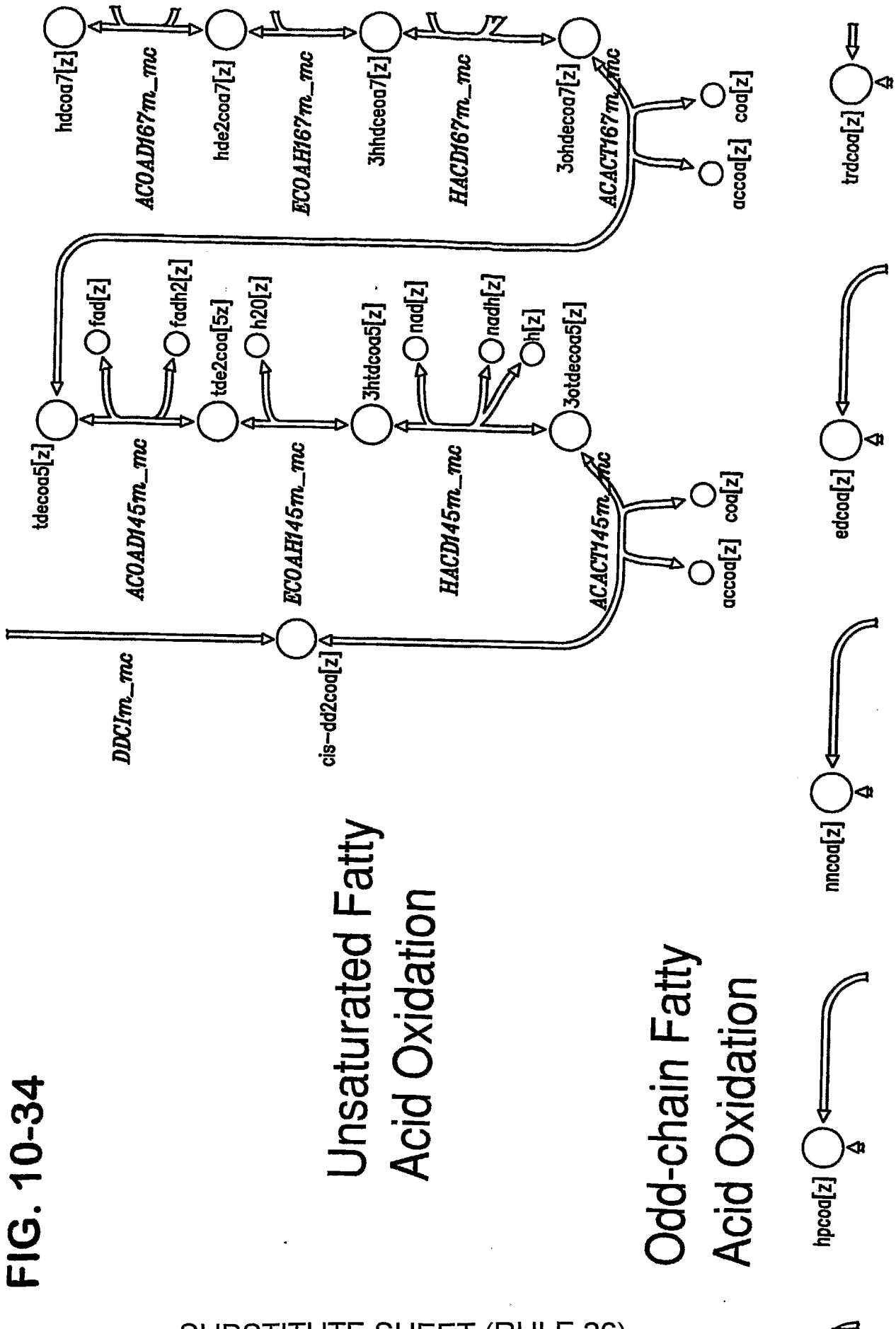

hdcoa7[z]
ACOAD167m_mc
hde2coa7[z]
ECOAH167m_mc
3hhdceoa7[z]
HACD167m_mc
3ohdecoa7[z]
ACACT167m_mc
accoa[z]
coa[z]
trdcoa[z]
tdecoa5[z]
fad[z]
ACOAD145m_mc
fadh2[z]
tde2coa[5z]
h2O[z]
ECOAH145m_mc
3htdcoa5[z]
nad[z]
HACD145m_mc
nadh[z]
h[z]
3otdecoa5[z]
ACACT145m_mc
accoa[z]
coa[z]
edcoa[z]
DDCIm_mc
cis-dd2coa[z]
nncoa[z]
hpcoa[z]
Unsaturated Fatty Acid Oxidation
Odd-chain Fatty Acid Oxidation

FIG. 10-34

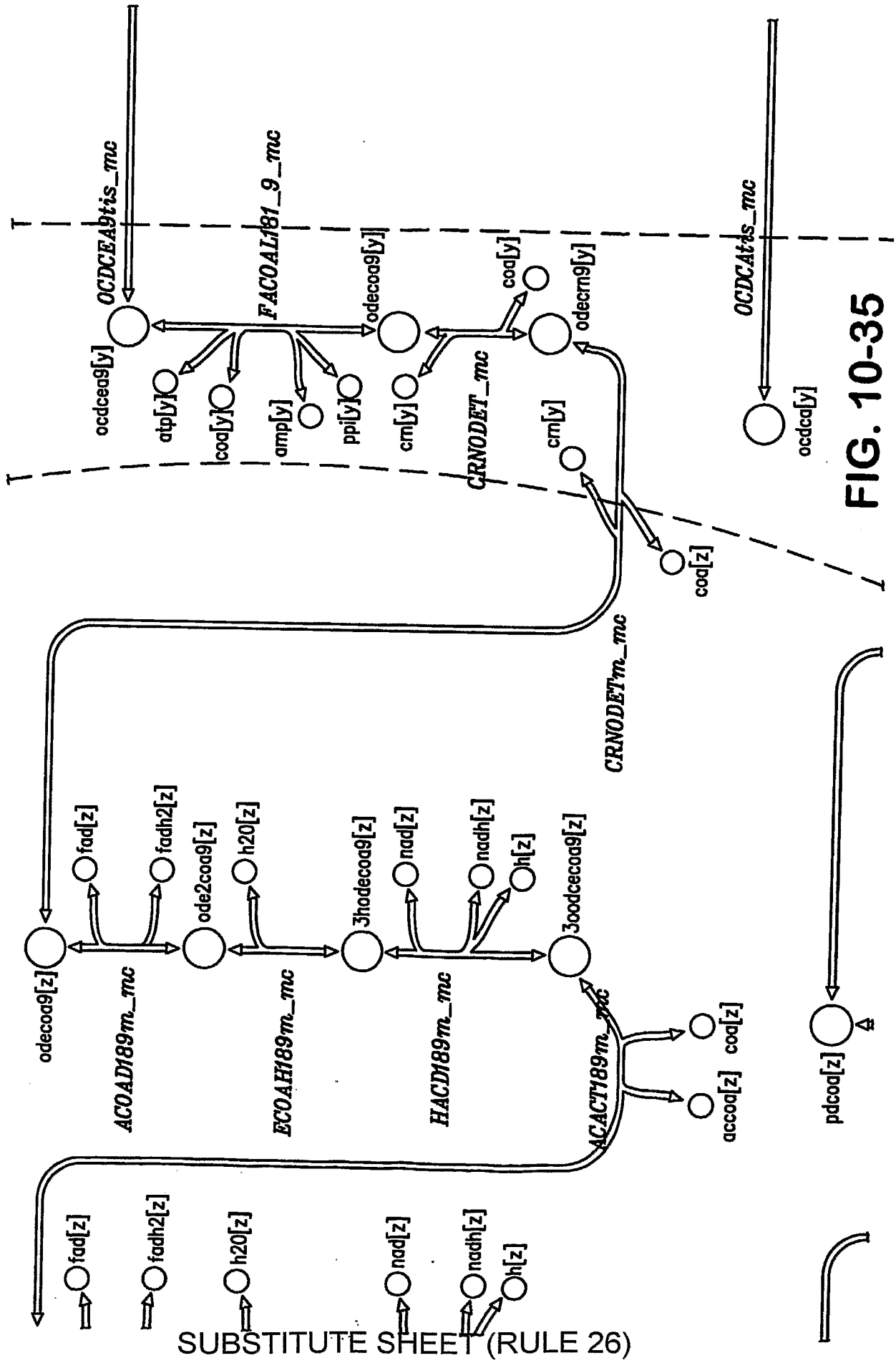
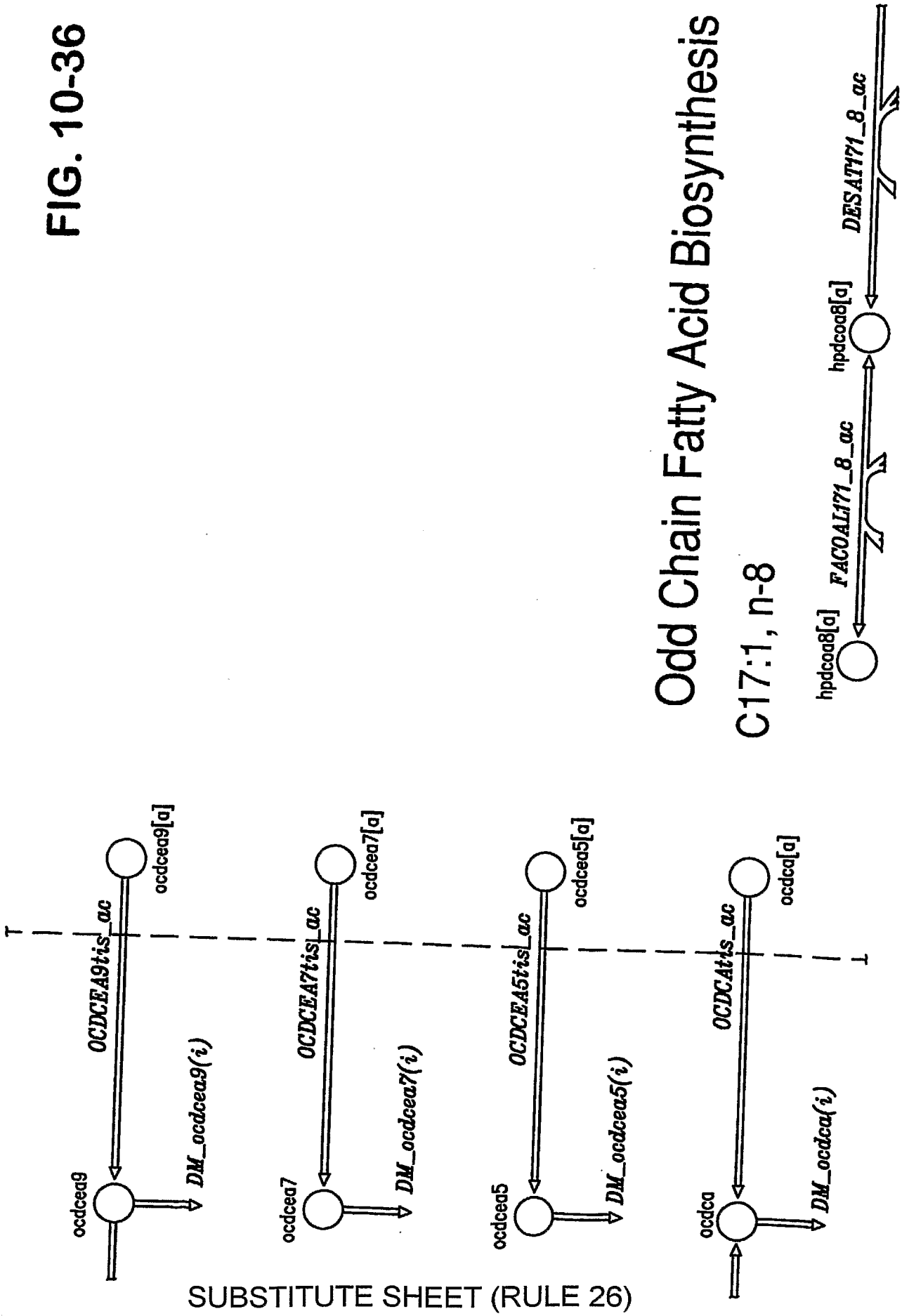

OCDCEA9tis_mc
FACOAL181_9_mc
OCDCAtis_mc
ocdcea9[y]
atp[y]
coa[y]
amp[y]
ppi[y]
odecoa9[y]
cm[y]
coa[y]
odecm9[y]
ocdca[y]
CRNODET_mc
cm[y]
coa[z]
CRNODETm_mc
odecoa9[z]
fad[z]
fadh2[z]
ode2coa9[z]
h20[z]
3hodecoa9[z]
nad[z]
nadh[z]
h[z]
3oodcecoa9[z]
ACOAD189m_mc
ECOAH189m_mc
HACD189m_mc
ACACT189m_mc
coa[z]
accoa[z]
pdcoa[z]
fad[z]
fadh2[z]
h20[z]
nad[z]
nadh[z]
h[z]

FIG. 10-35

FIG. 10-36


Odd Chain Fatty Acid Biosynthesis
C17:1, n-8
hpdcoa8[a]
FACOAL171_8_ac
hpdcoa8[a]
DESAT171_8_ac
T
ocdcea9[a]
OCDCEA9tis_ac
DM_ocdcea9(i)
ocdcea9
ocdcea7[a]
OCDCEA7tis_ac
DM_ocdcea7(i)
ocdcea7
ocdcea5[a]
OCDCEA5tis_ac
DM_ocdcea5(i)
ocdcea5
ocdca[a]
OCDCAtis_ac
DM_ocdca(i)
ocdca
T

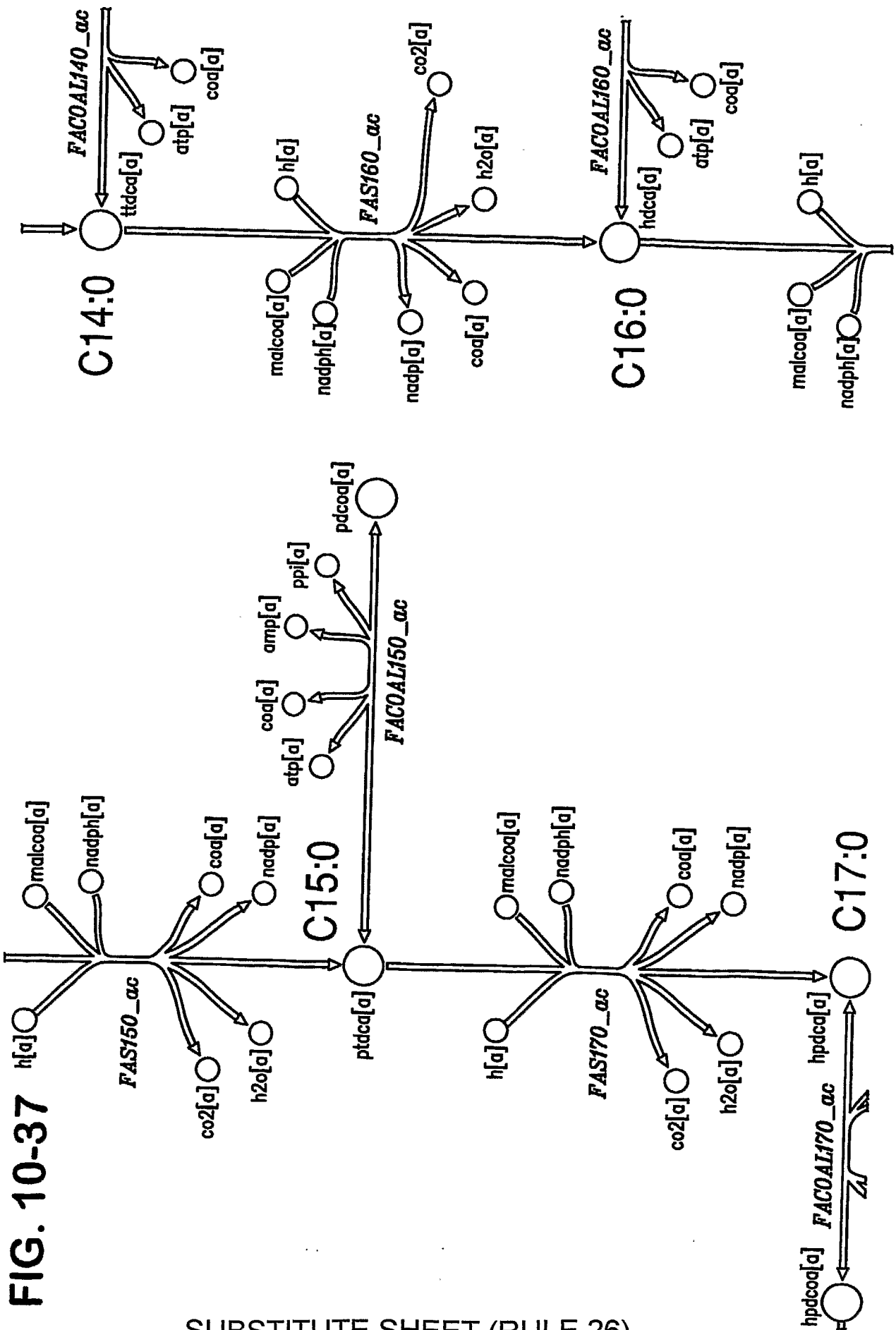
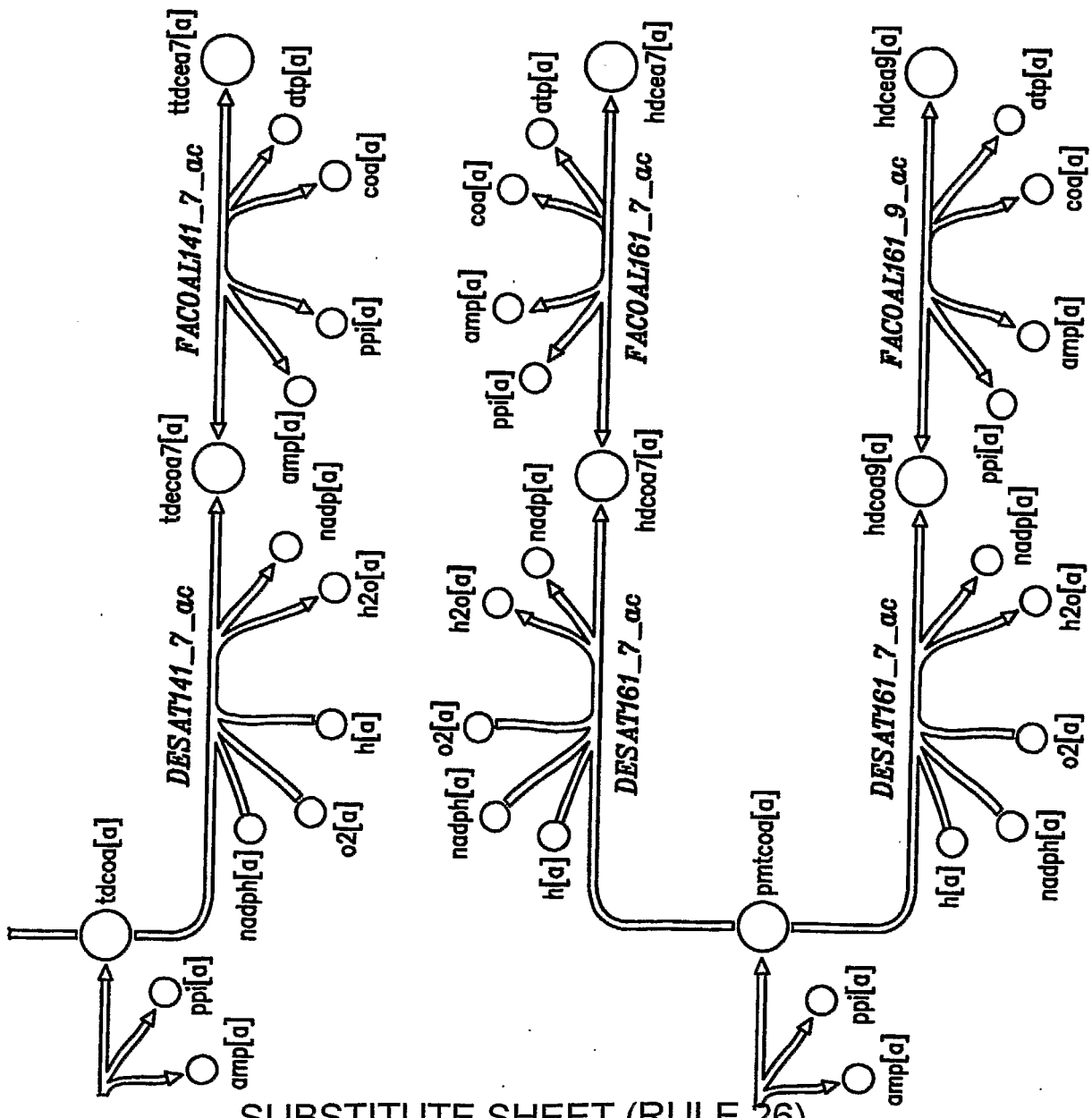

C14:0
FACOAL140_ac
ttdca[a]
atp[a]
coa[a]
FAS160_ac
h[a]
malcoa[a]
nadph[a]
co2[a]
h2o[a]
nadp[a]
coa[a]
C16:0
FACOAL160_ac
hdca[a]
atp[a]
coa[a]
h[a]
malcoa[a]
nadph[a]
C15:0
FACOAL150_ac
pdcoa[a]
ppi[a]
amp[a]
coa[a]
atp[a]
FAS150_ac
h[a]
malcoa[a]
nadph[a]
coa[a]
nadp[a]
co2[a]
h2o[a]
ptdca[a]
C17:0
FAS170_ac
h[a]
malcoa[a]
nadph[a]
coa[a]
nadp[a]
co2[a]
h2o[a]
hpdca[a]
FACOAL170_ac
hpdcoa[a]

FIG. 10-37

FIG. 10-38


C14:1, n-7
C16:1, n-7
C16:1, n-9
tdcoa[a]
ppi[a]
amp[a]
nadph[a]
DESAT141_7_ac
tdecoa7[a]
FACOAL141_7_ac
ttdcea7[a]
atp[a]
coa[a]
ppi[a]
amp[a]
nadp[a]
h2o[a]
h[a]
o2[a]
pmtcoa[a]
DESAT161_7_ac
hdcoa7[a]
FACOAL161_7_ac
hdcea7[a]
DESAT161_7_ac
hdcoa9[a]
FACOAL161_9_ac
hdcea9[a]

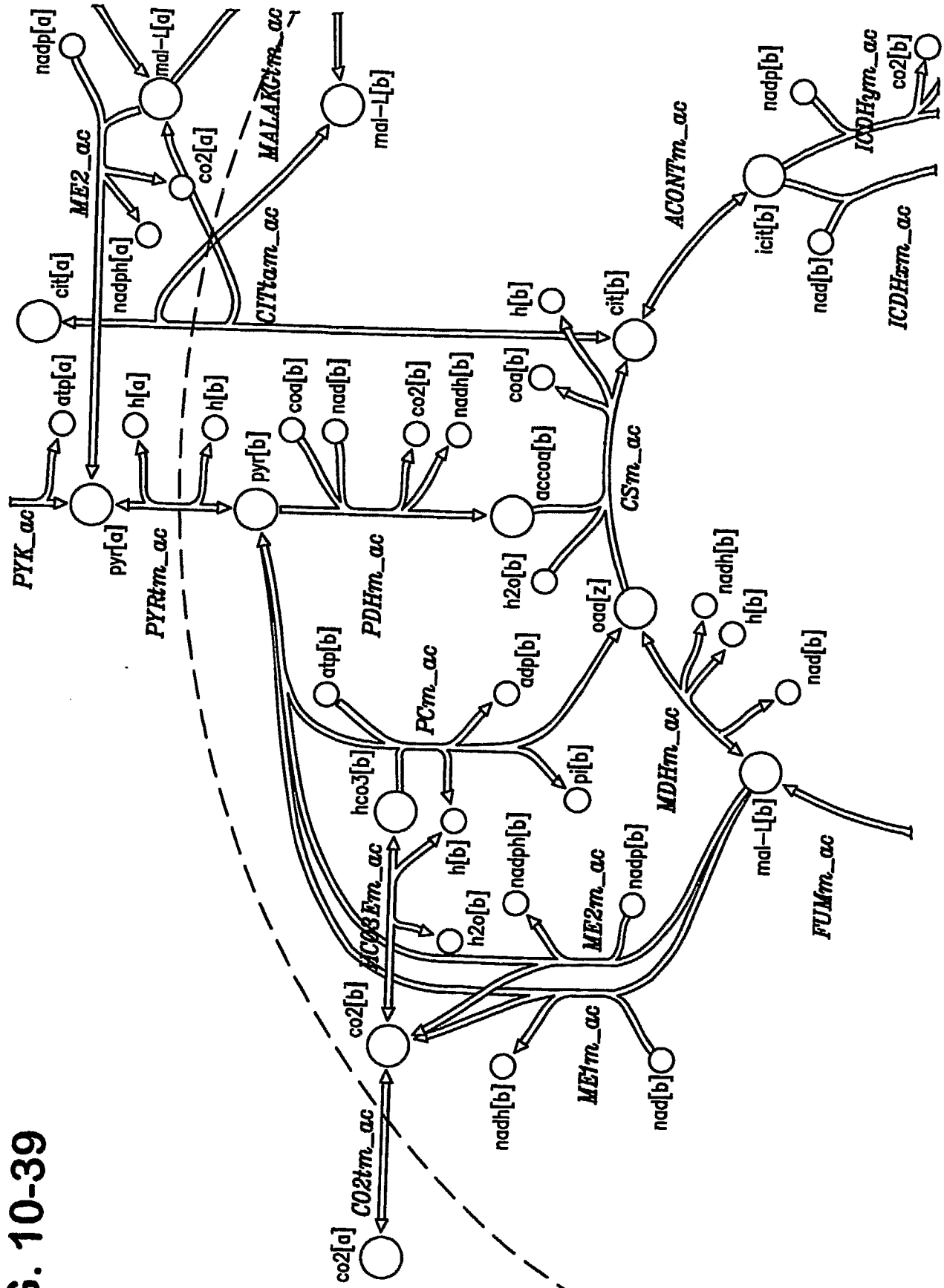
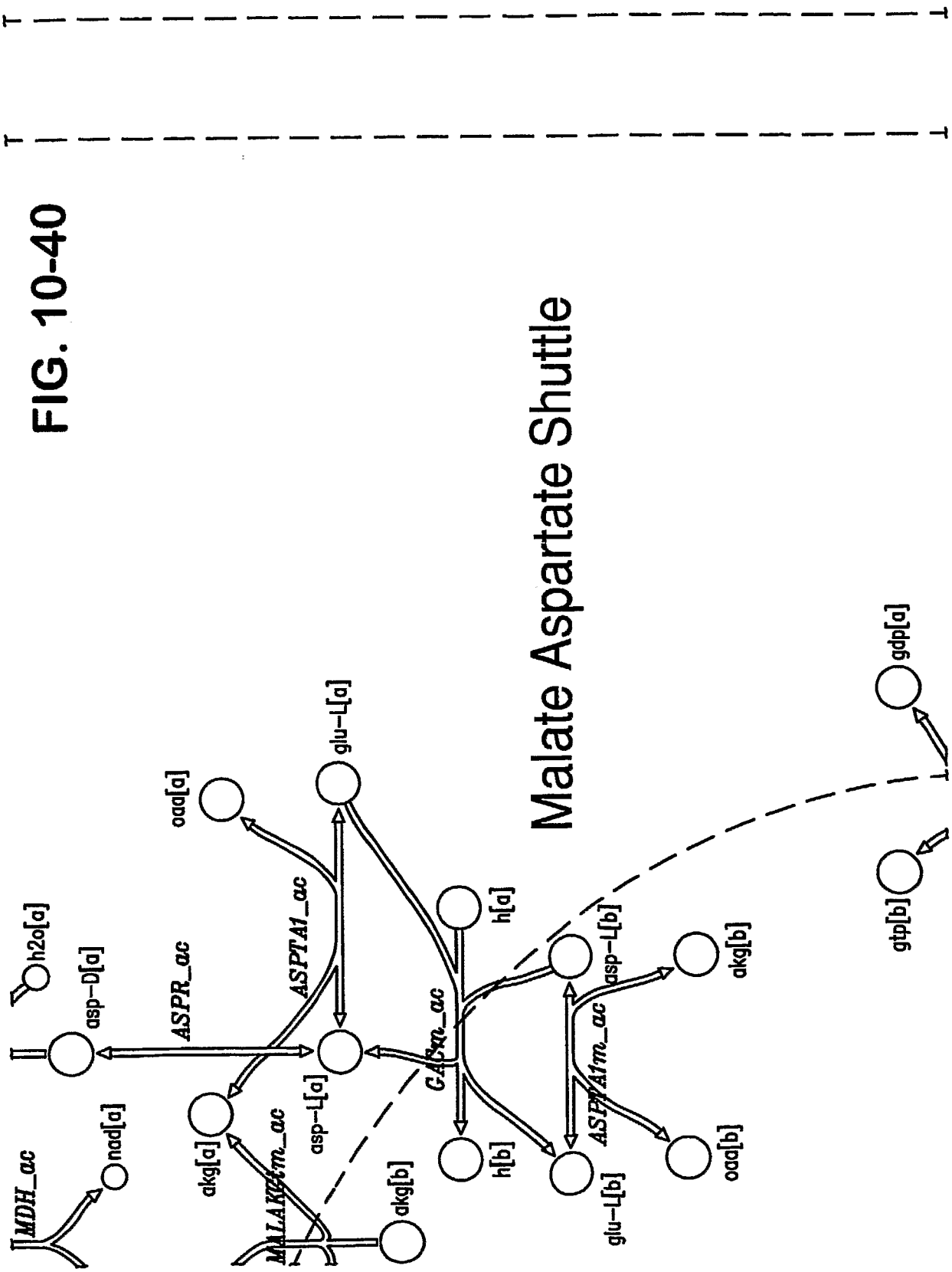

nadp[a]
mal-L[a]
MALARGtm_ac
mal-L[b]
ME2_ac
co2[a]
nadph[a]
cit[a]
CITtam_ac
h[b]
cit[b]
ACONTm_ac
nadp[b]
ICDHym_ac
co2[b]
icit[b]
nad[b]
ICDHxm_ac
atp[a]
h[a]
h[b]
coa[b]
nad[b]
co2[b]
nadh[b]
coa[b]
pyr[b]
accoa[b]
CSm_ac
PYK_ac
pyr[a]
PYRtm_ac
PDHm_ac
h2o[b]
oaa[z]
nadh[b]
h[b]
nad[b]
atp[b]
PCm_ac
adp[b]
MDHm_ac
hco3[b]
pi[b]
h[b]
nadph[b]
nadp[b]
mal-L[b]
FUMm_ac
HCO3Em_ac
h2o[b]
ME2m_ac
co2[b]
ME1m_ac
nadh[b]
nad[b]
CO2tm_ac
co2[a]

FIG. 10-39

FIG. 10-40


Malate Aspartate Shuttle
h2o[a]
asp-D[a]
ASPR_ac
oaa[a]
ASPTA1_ac
glu-L[a]
h[a]
GABTm_ac
asp-L[b]
akg[b]
gdp[a]
gtp[b]
MDH_ac
nad[a]
akg[a]
MALAKGLm_ac
asp-L[a]
akg[b]
h[b]
ASPTA1m_ac
glu-L[b]
oaa[b]

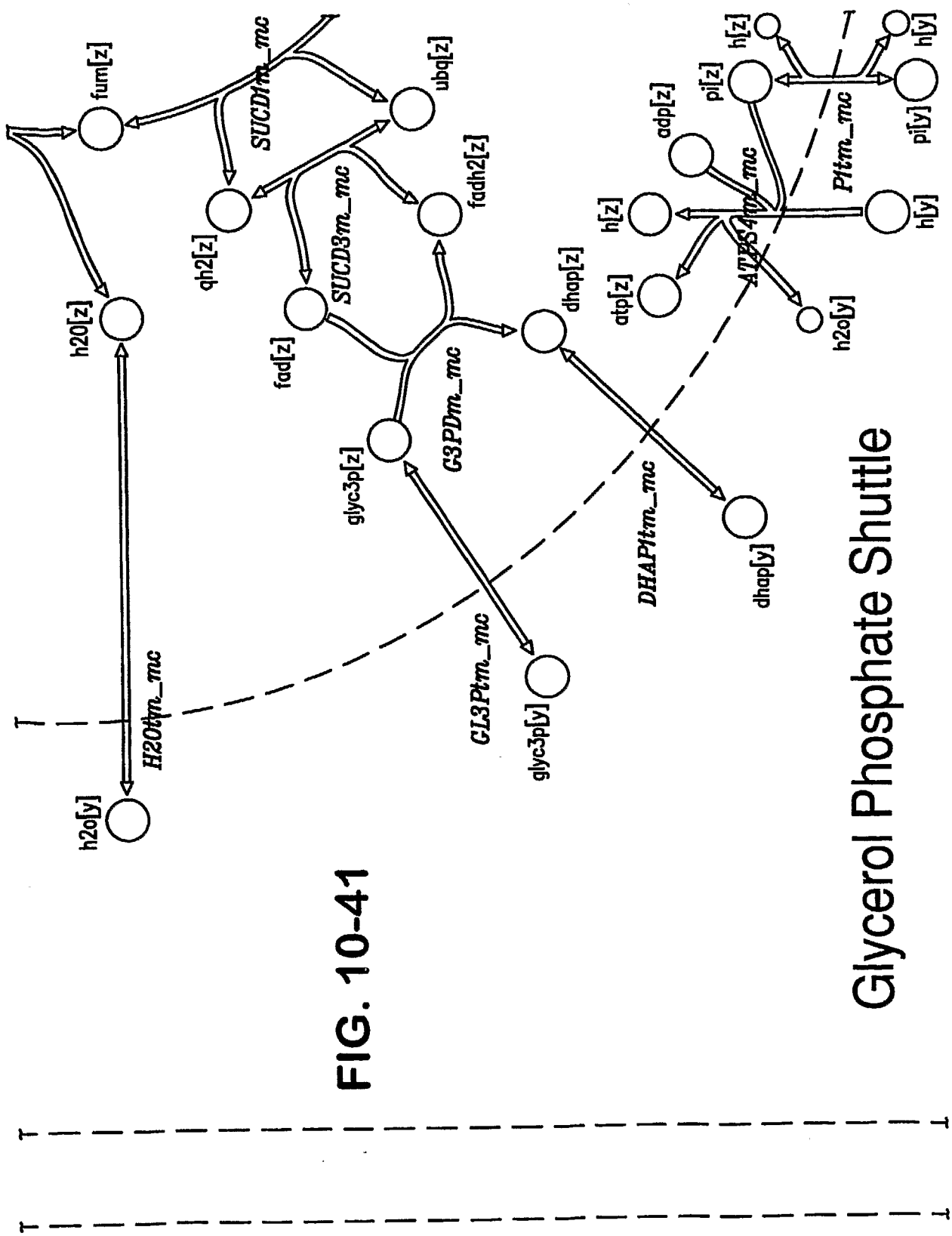

fum[z]
SUCD1m_mc
ubq[z]
qh2[z]
SUCD3m_mc
fadh2[z]
h2o[z]
fad[z]
dhap[z]
G3PDm_mc
glyc3p[z]
H2Otm_mc
GL3Ptm_mc
glyc3p[y]
DHAPtm_mc
dhap[y]
h2o[y]
adp[z]
pi[z]
h[z]
Ptm_mc
pi[y]
h[y]
atp[z]
h2o[y]
Glycerol Phosphate Shuttle

FIG. 10-41

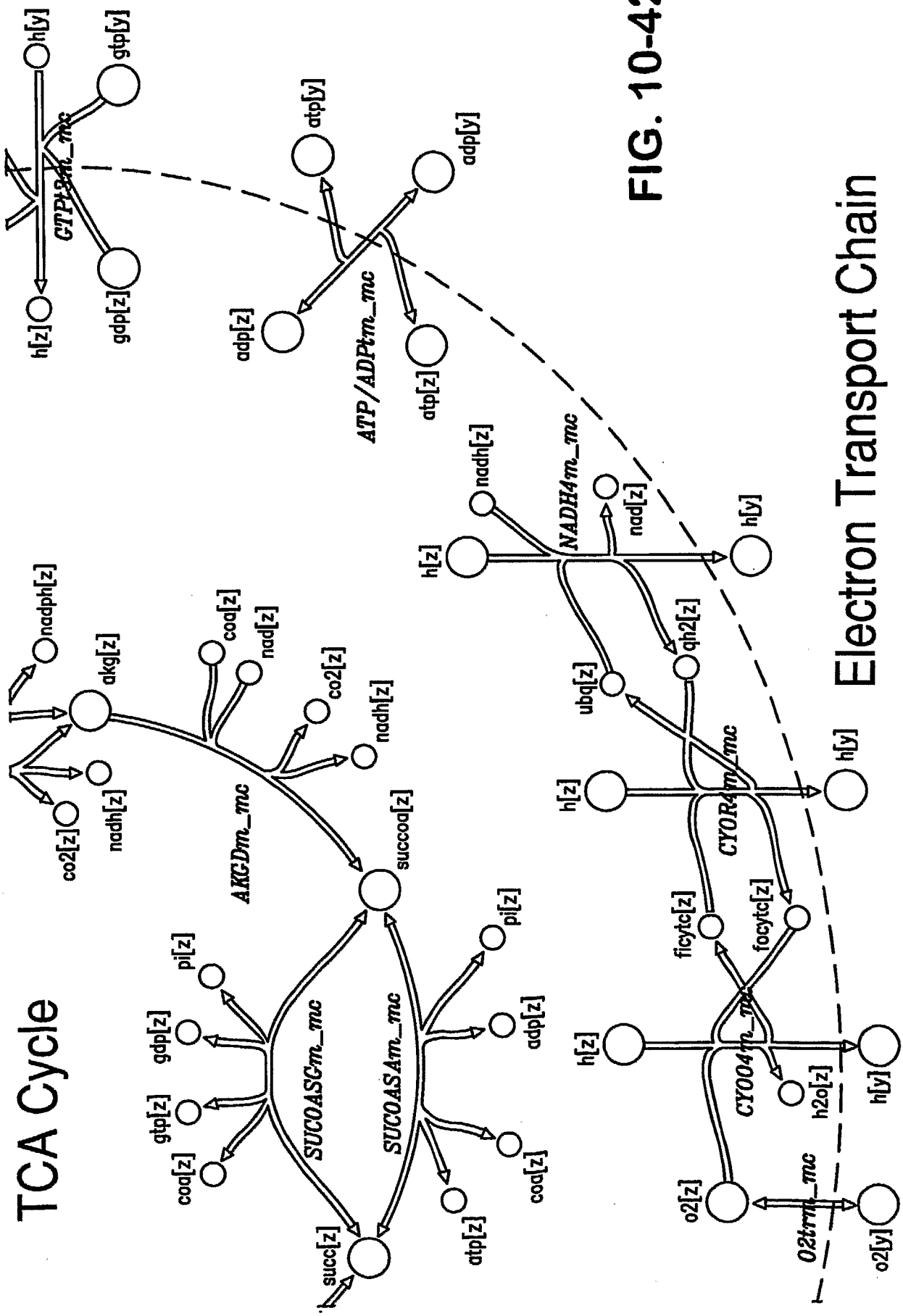

TCA Cycle
Electron Transport Chain
AKGDm_mc
SUCOASGm_mc
SUCOASAm_mc
ATP/ADPtm_mc
NADH4m_mc
CYOR4m_mc
CYOO4m_mc
O2trm_mc
akg[z]
nadph[z]
co2[z]
nadh[z]
coa[z]
nad[z]
co2[z]
nadh[z]
succoa[z]
pi[z]
gdp[z]
gtp[z]
coa[z]
succ[z]
pi[z]
adp[z]
coa[z]
atp[z]
h[y]
gtp[y]
h[z]
gdp[z]
atp[y]
adp[z]
adp[y]
atp[z]
nadh[z]
h[z]
nad[z]
h[y]
ubq[z]
qh2[z]
h[z]
h[y]
ficytc[z]
focytc[z]
h[z]
h[y]
o2[z]
h2o[z]
o2[y]

FIG. 10-42

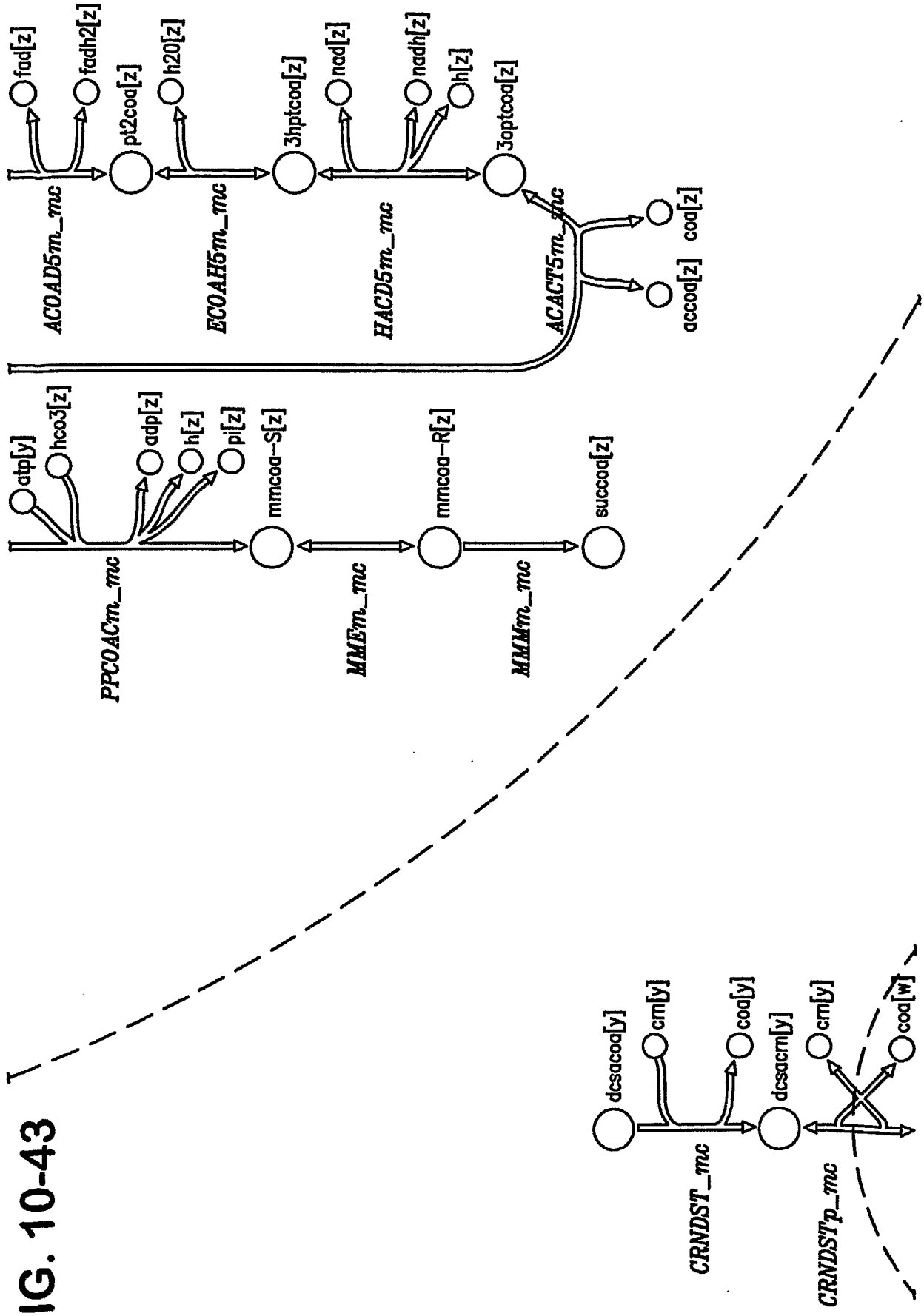

fad[z]
fadh2[z]
ACOAD5m_mc
pt2coa[z]
h2o[z]
ECOAH5m_mc
3hptcoa[z]
nad[z]
nadh[z]
h[z]
HACD5m_mc
3optcoa[z]
ACACT5m_mc
accoa[z]
coa[z]
atp[y]
hco3[z]
adp[z]
h[z]
pi[z]
PPCOACm_mc
mmcoa-S[z]
MMEm_mc
mmcoa-R[z]
MMMm_mc
succoa[z]
dcsacoa[y]
cm[y]
coa[y]
CRNDST_mc
dcsacm[y]
cm[y]
coa[w]
CRNDSTp_mc

FIG. 10-43

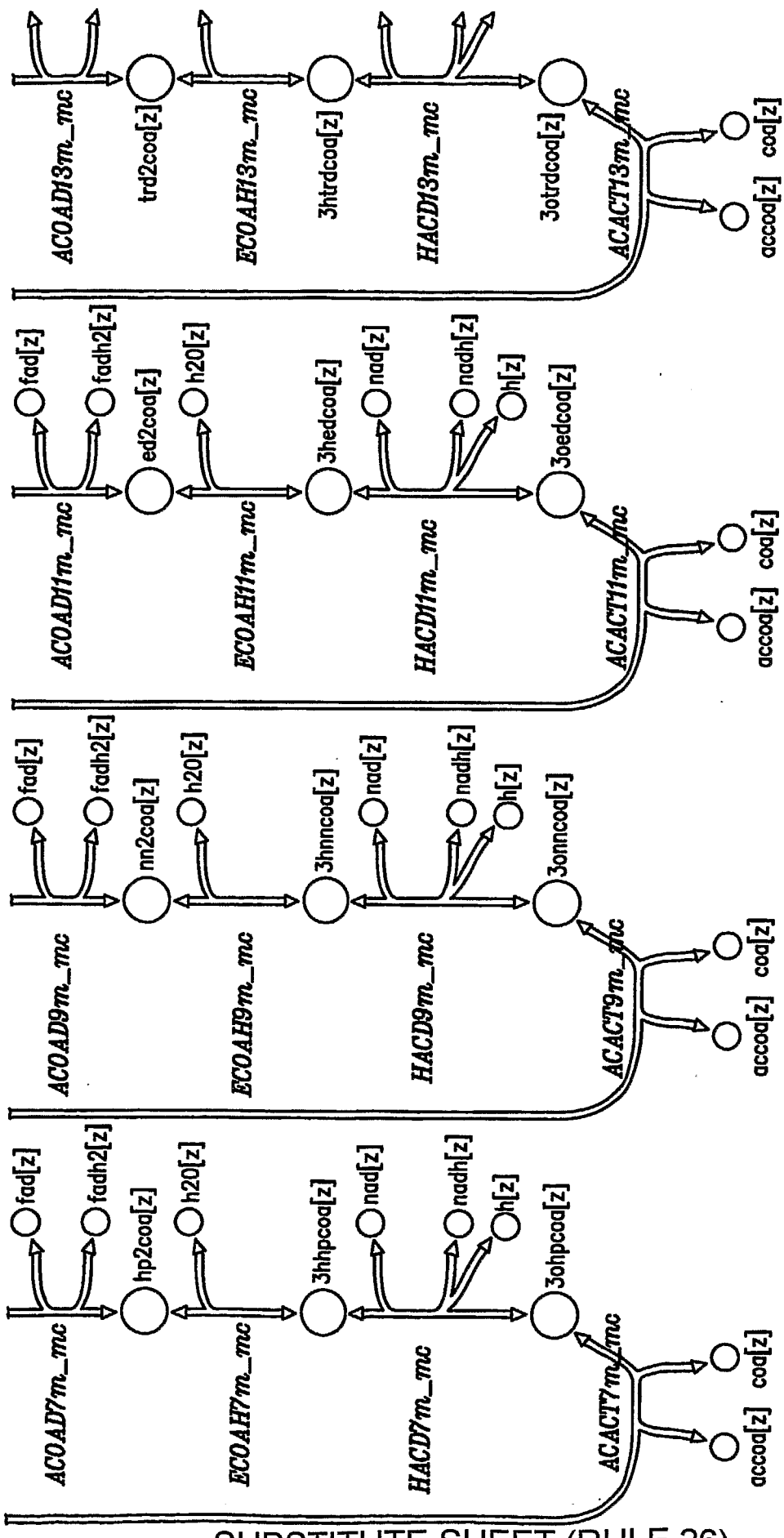

ACOAD7m_mc
fad[z]
fadh2[z]
hp2coa[z]
h20[z]
ECOAH7m_mc
3hhpcoa[z]
nad[z]
nadh[z]
h[z]
HACD7m_mc
3ohpcoa[z]
ACACT7m_mc
accoa[z]
coa[z]
ACOAD9m_mc
fad[z]
fadh2[z]
nn2coa[z]
h20[z]
ECOAH9m_mc
3hnncoa[z]
nad[z]
nadh[z]
h[z]
HACD9m_mc
3onncoa[z]
ACACT9m_mc
accoa[z]
coa[z]
ACOAD11m_mc
fad[z]
fadh2[z]
ed2coa[z]
h20[z]
ECOAH11m_mc
3hedcoa[z]
nad[z]
nadh[z]
h[z]
HACD11m_mc
3oedcoa[z]
ACACT11m_mc
accoa[z]
coa[z]
ACOAD13m_mc
trd2coa[z]
ECOAH13m_mc
3htrdcoa[z]
HACD13m_mc
3otrdcoa[z]
ACACT13m_mc
accoa[z]
coa[z]

FIG. 10-44

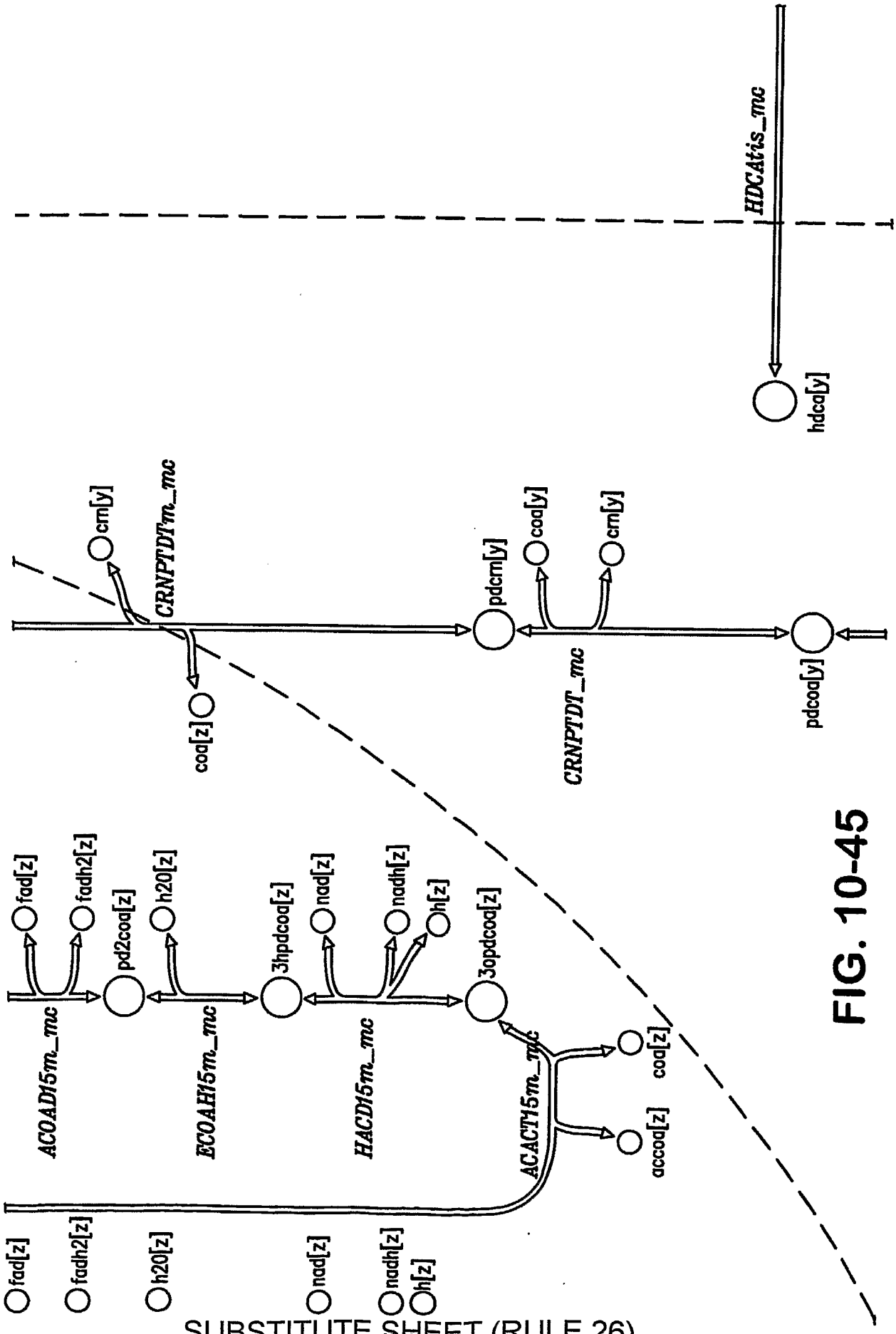

HDCAtis_mc
hdca[y]
cm[y]
CRNPTDTm_mc
coa[z]
pdcm[y]
coa[y]
cm[y]
CRNPTDT_mc
pdcoa[y]
fad[z]
fadh2[z]
pd2coa[z]
h20[z]
3hpdcoa[z]
nad[z]
nadh[z]
h[z]
3opdcoa[z]
ACOADH5m_mc
ECOAH5m_mc
HACDH5m_mc
ACACT5m_mc
coa[z]
accoa[z]
fad[z]
fadh2[z]
h20[z]
nad[z]
nadh[z]
h[z]

FIG. 10-45

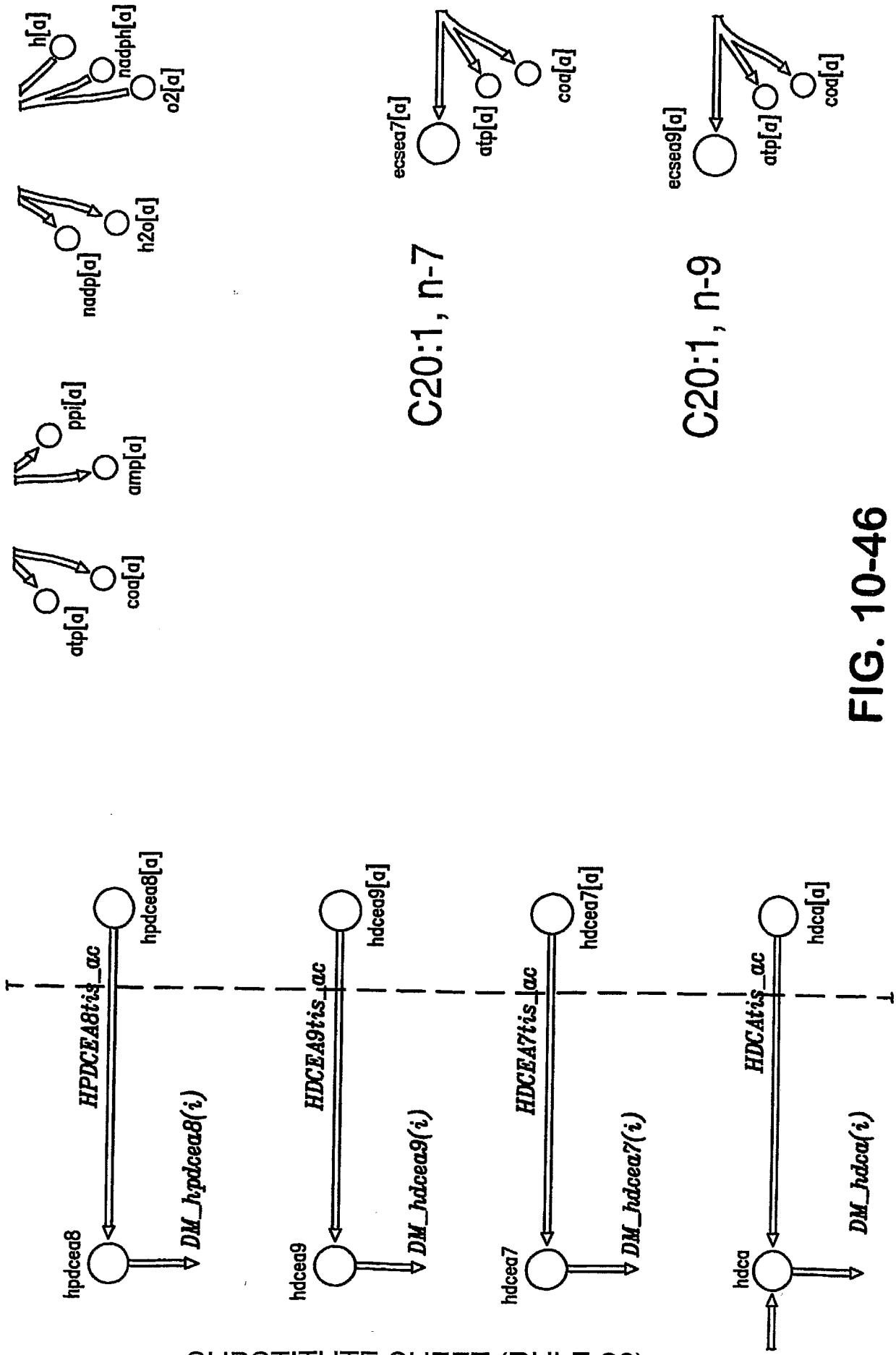

h[a]
nadph[a]
o2[a]
nadp[a]
h2o[a]
ppi[a]
amp[a]
atp[a]
coa[a]
ecsea7[a]
atp[a]
coa[a]
C20:1, n-7
ecsea9[a]
atp[a]
coa[a]
C20:1, n-9
T
HPDCEA8tis_ac
hpdcea8[a]
DM_hpdcea8(i)
hpdcea8
HDCEA9tis_ac
hdcea9[a]
DM_hdcea9(i)
hdcea9
HDCEA7tis_ac
hdcea7[a]
DM_hdcea7(i)
hdcea7
HDCAtis_ac
hdca[a]
DM_hdca(i)
hdca
T

FIG. 10-46

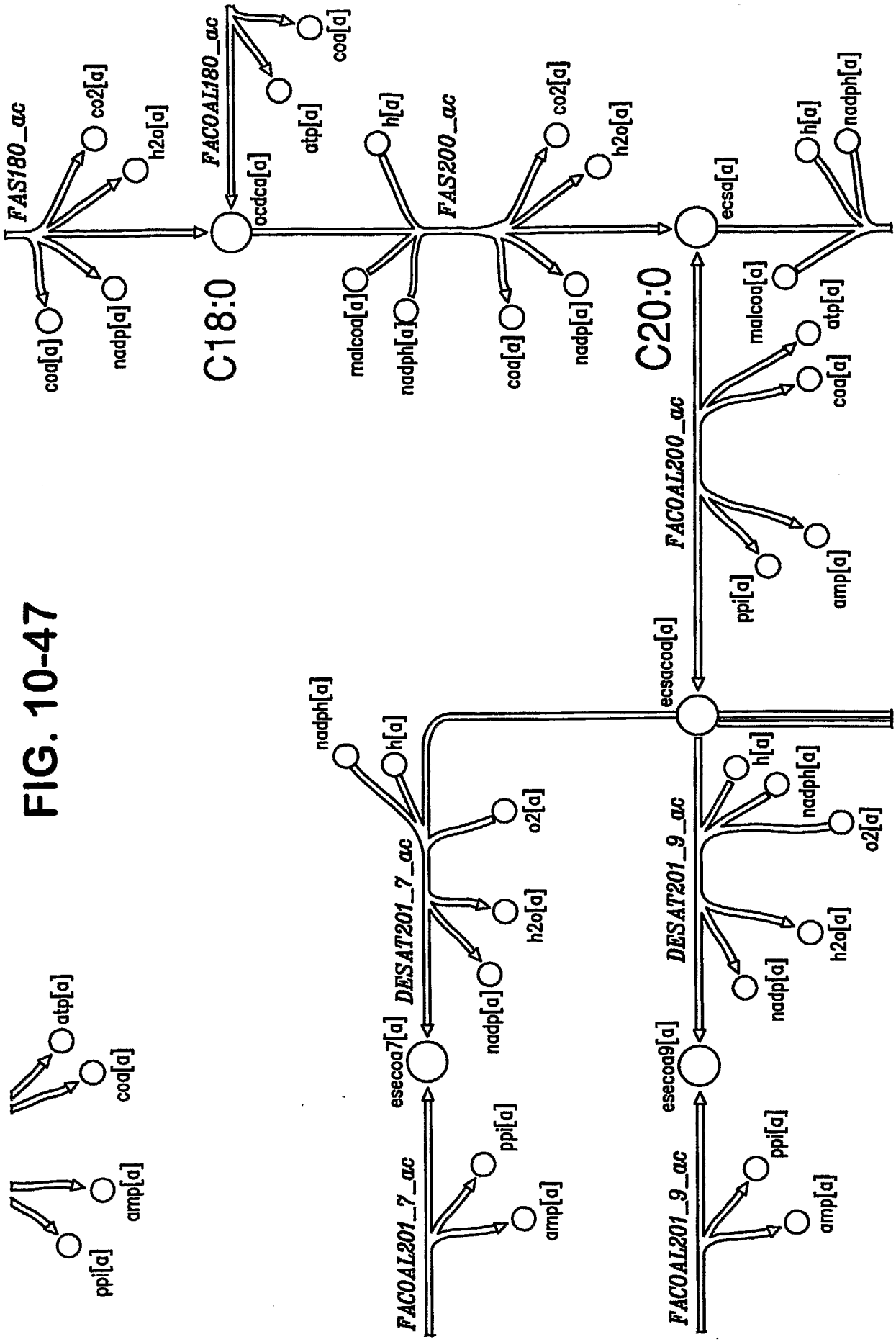

FAS180_ac
co2[a]
h2o[a]
coa[a]
nadp[a]
FACOAL180_ac
ocdca[a]
atp[a]
coa[a]
C18:0
FAS200_ac
h[a]
malcoa[a]
nadph[a]
co2[a]
h2o[a]
coa[a]
nadp[a]
C20:0
ecsa[a]
h[a]
nadph[a]
malcoa[a]
atp[a]
coa[a]
FACOAL200_ac
ppi[a]
amp[a]
ecsacoa[a]
nadph[a]
h[a]
o2[a]
DESAT201_7_ac
h2o[a]
nadp[a]
esecoa7[a]
ppi[a]
amp[a]
FACOAL201_7_ac
h[a]
nadph[a]
o2[a]
DESAT201_9_ac
h2o[a]
nadp[a]
esecoa9[a]
ppi[a]
amp[a]
FACOAL201_9_ac
atp[a]
coa[a]
ppi[a]
amp[a]

FIG. 10-47

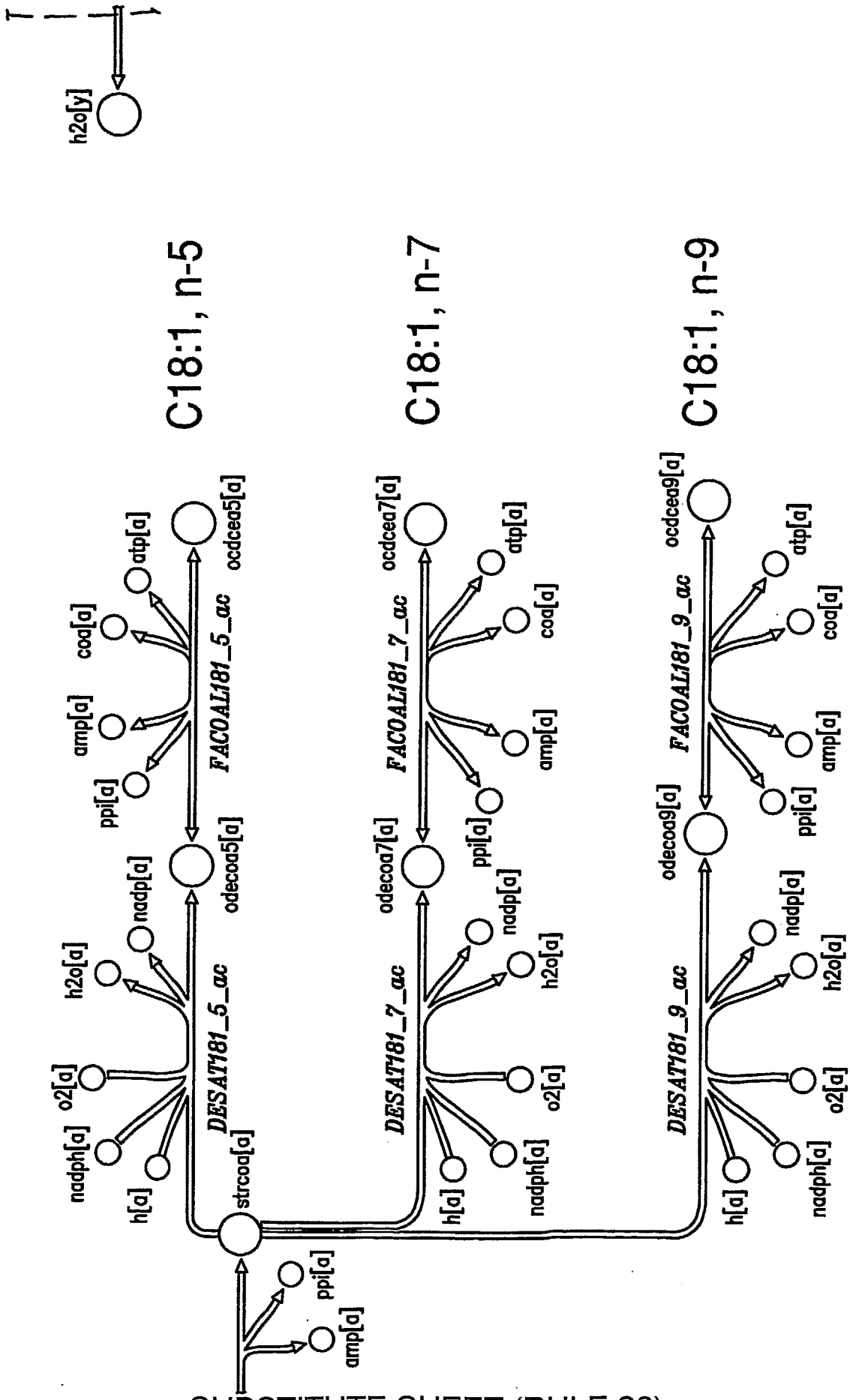

h2o[y]
C18:1, n-5
C18:1, n-7
C18:1, n-9
ocdcea5[a]
ocdcea7[a]
ocdcea9[a]
atp[a]
coa[a]
amp[a]
ppi[a]
FACOAL181_5_ac
FACOAL181_7_ac
FACOAL181_9_ac
odecoa5[a]
odecoa7[a]
odecoa9[a]
nadp[a]
h2o[a]
o2[a]
nadph[a]
h[a]
DESAT181_5_ac
DESAT181_7_ac
DESAT181_9_ac
strcoa[a]
ppi[a]
amp[a]

FIG. 10-48

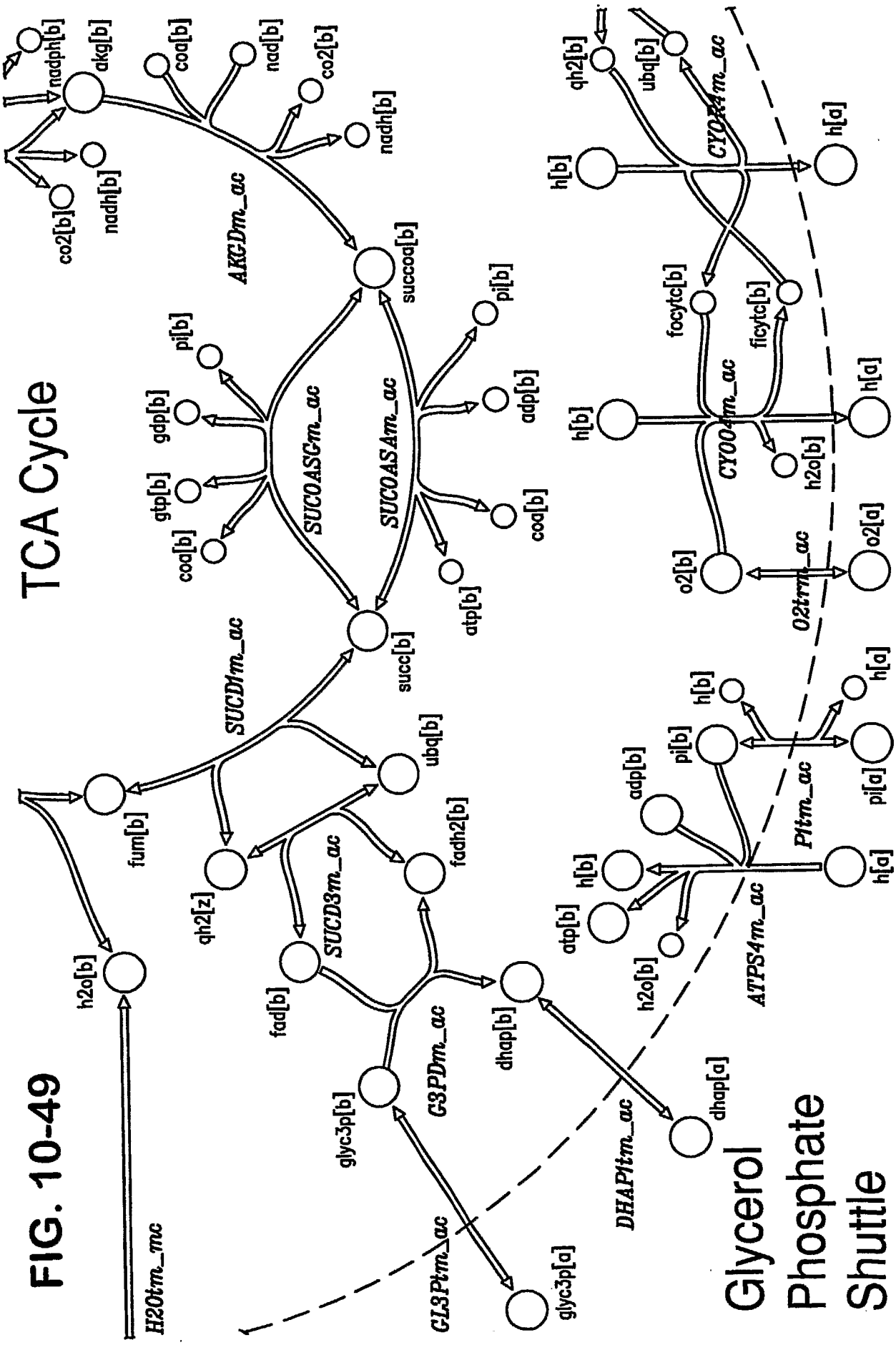
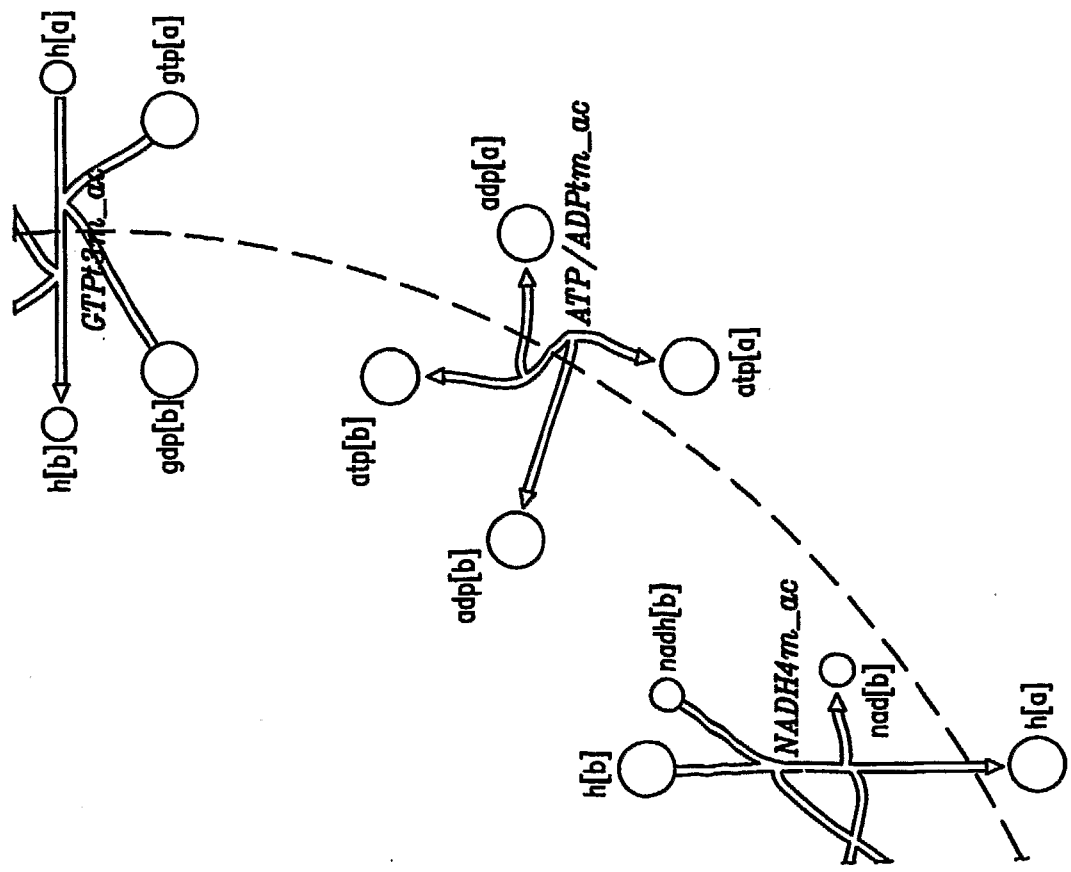

TCA Cycle
Glycerol Phosphate Shuttle
akg[b]
coa[b]
nad[b]
co2[b]
nadh[b]
AKGDm_ac
succoa[b]
SUCOASGm_ac
SUCOASAm_ac
gtp[b]
gdp[b]
pi[b]
adp[b]
atp[b]
succ[b]
SUCDfm_ac
fum[b]
qh2[z]
SUCD3m_ac
fad[b]
fadh2[b]
ubq[b]
h2o[b]
H2Otm_mc
glyc3p[b]
G3PDm_ac
dhap[b]
GL3Ptm_ac
glyc3p[a]
DHAPtm_ac
dhap[a]
qh2[b]
CYO24m_ac
h[b]
h[a]
focytc[b]
ficytc[b]
CYOOm_ac
o2[b]
o2[a]
02tm_ac
h2o[b]
adp[b]
pi[b]
Ptm_ac
pi[a]
atp[b]
ATPS4m_ac

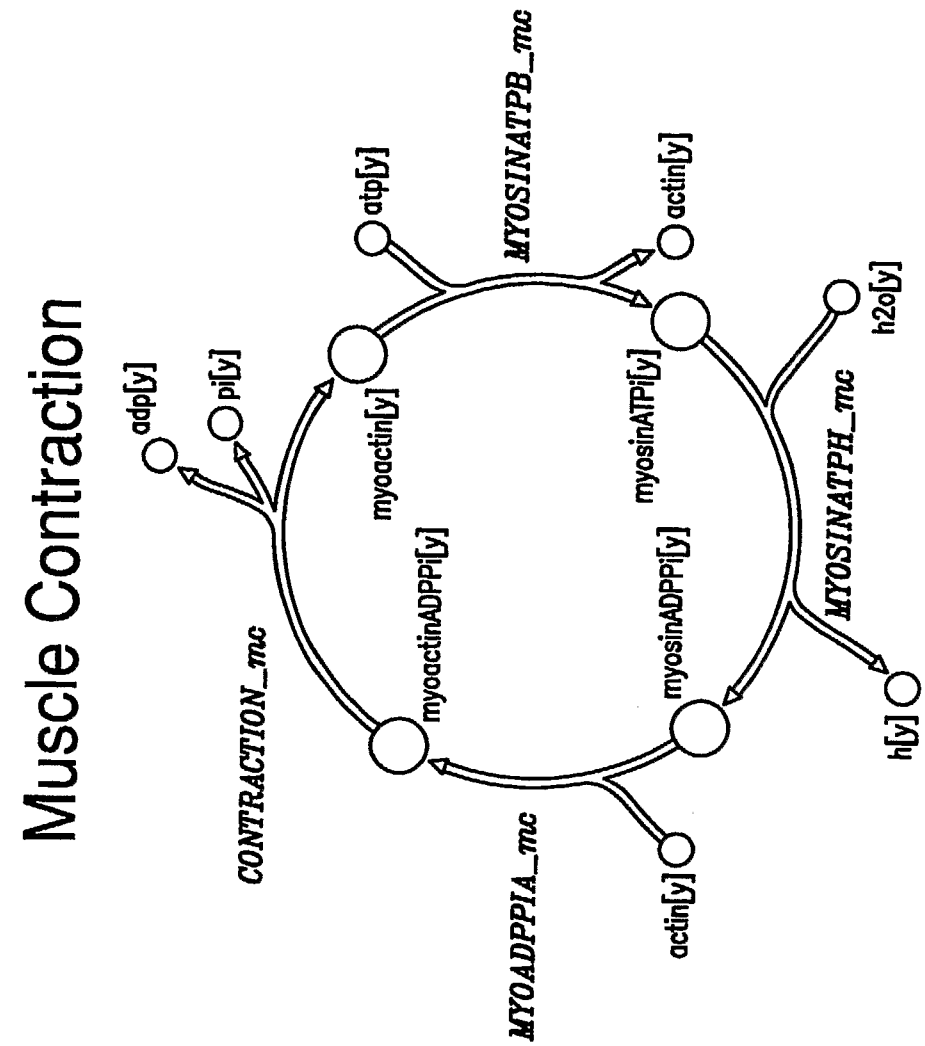
FIG. 10-49

FIG. 10-50



Electron Transport Chain

FIG. 10-51


Muscle Contraction
adp[y]
pi[y]
atp[y]
MYOSINATPB_mc
actin[y]
h2o[y]
myoactin[y]
myosinATPi[y]
MYOSINATPH_mc
CONTRACTION_mc
myoactinADPPi[y]
myosinADPPi[y]
h[y]
MYOADPPIA_mc
actin[y]

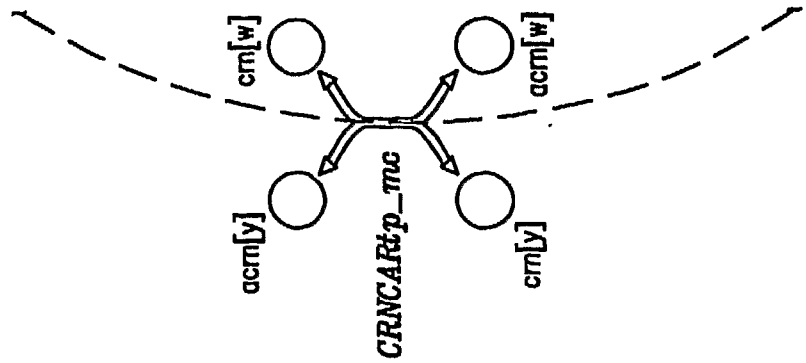
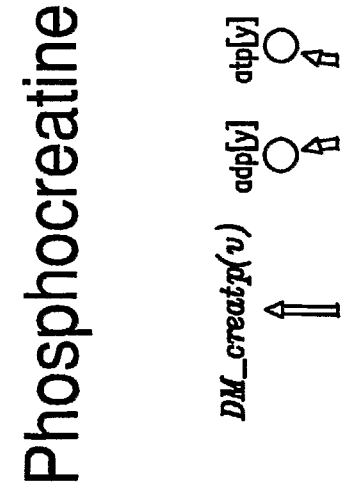

cm[w]
acm[w]
acm[y]
CRNCARtp_mc
cm[y]

FIG. 10-52


Phosphocreatine
DM_creatp(v)
adp[y]
atp[y]

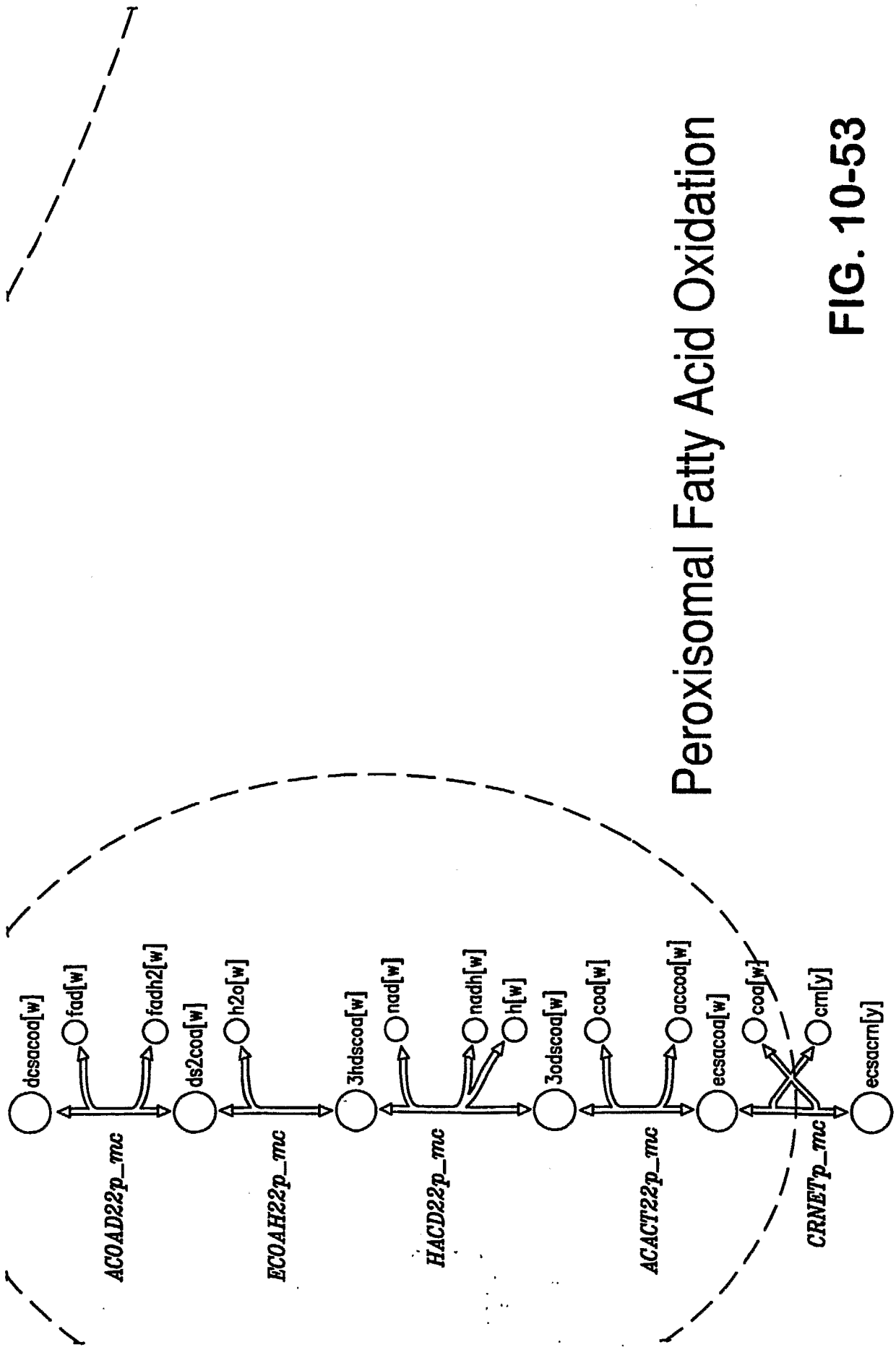

Peroxisomal Fatty Acid Oxidation
dcsacoa[w]
fad[w]
fadh2[w]
ds2coa[w]
h2o[w]
3hdscoa[w]
nad[w]
nadh[w]
h[w]
3odscoa[w]
coa[w]
accoa[w]
ecsacoa[w]
coa[w]
cm[y]
ecsacm[y]
ACOAD22p_mc
ECOAH22p_mc
HACD22p_mc
ACACT22p_mc
CRNETp_mc

FIG. 10-53

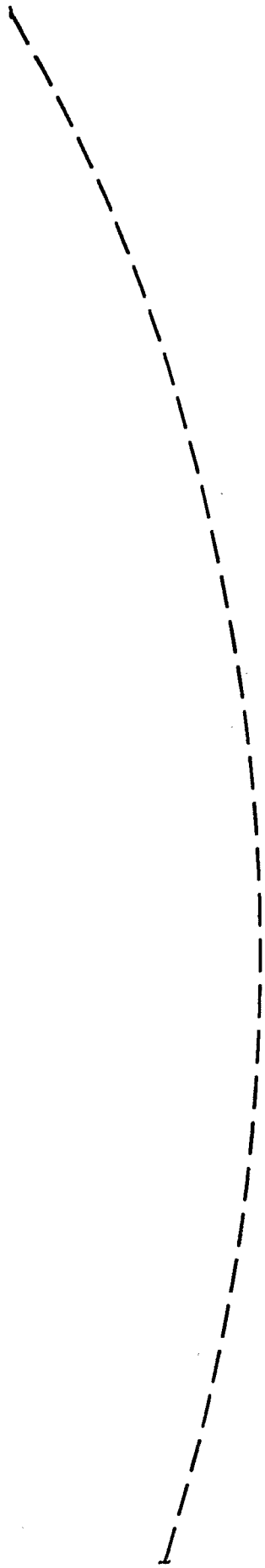


FIG. 10-54

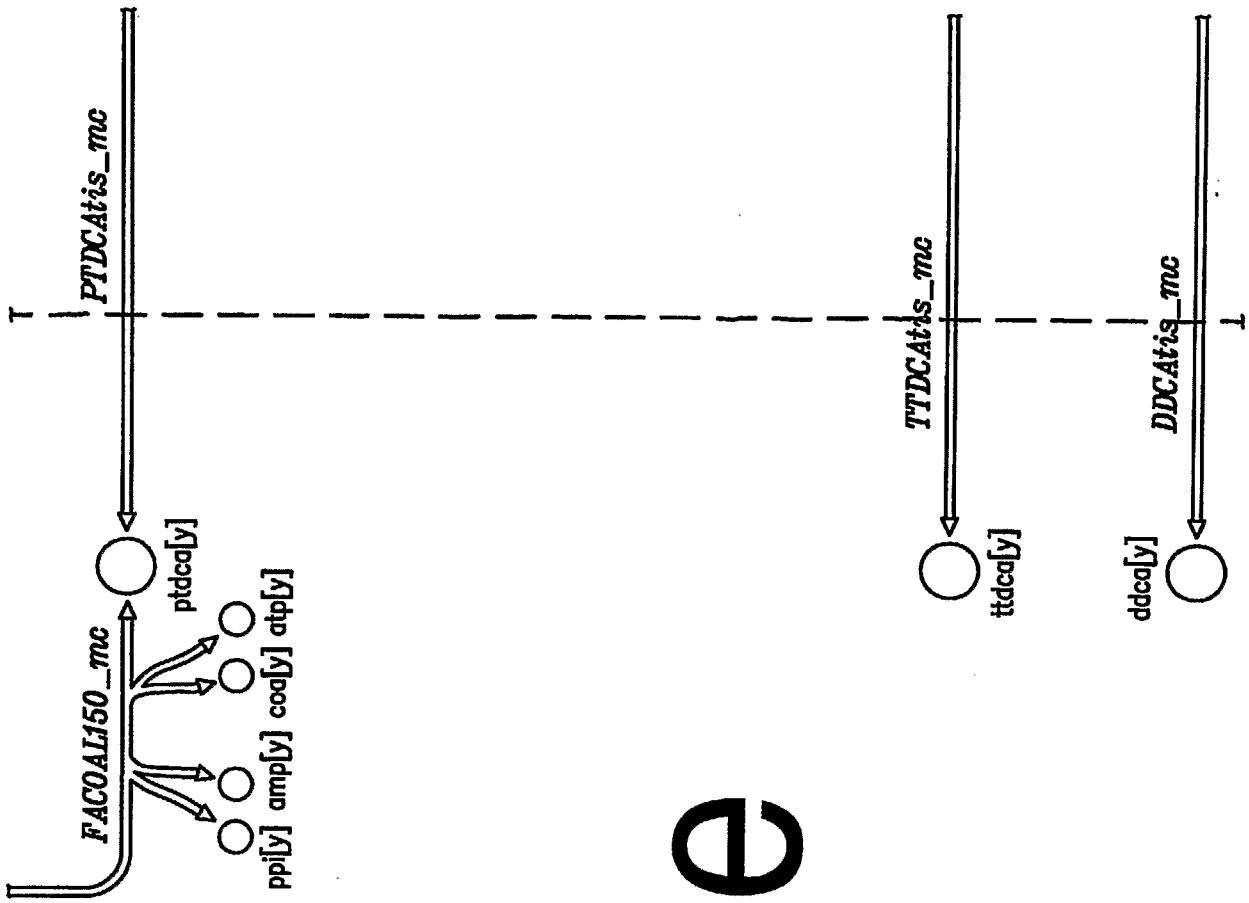

PTDCAtis_mc
TTDCAtis_mc
DDCAtis_mc
FACOAL150_mc
ptdca[y]
ttdca[y]
ddca[y]
ppi[y]
amp[y]
coa[y]
atp[y]
Myocyte

FIG. 10-55

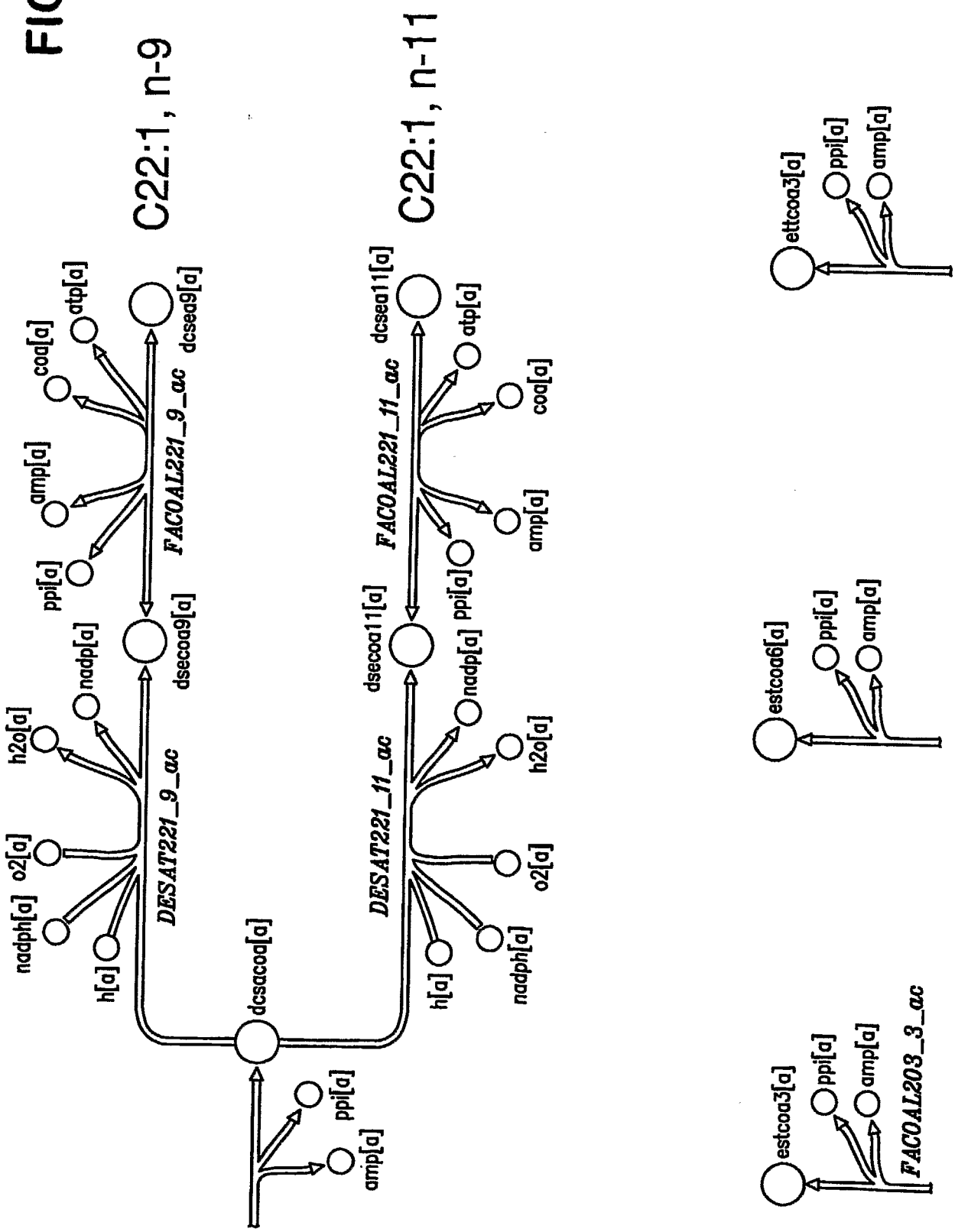
FIG. 10-56

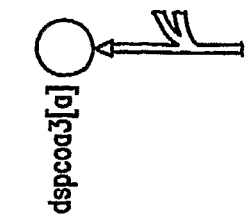

Adipocyte
C20:1, n-11
ecsea11[a]
atp[a]
coa[a]
C20:2, n-9
ecsdea9[a]
atp[a]
coa[a]
ocdycacoa6[a]
ppi[a]
amp[a]
PTDCAtis_ac
ptdca[a]
DM_ptdca(i)
ptdca
TTDCEA7tis_ac
ttdcea7[a]
DM_ttdcea7(i)
ttdcea7
TTDCEA5tis_ac
ttdcea5[a]
DM_ttdcea5(i)
ttdcea5
TTDCAtis_ac
ttdca[a]
DM_ttdca(i)
ttdca
DDCAtis_ac
ddca[a]
ddca

FAS220_ac
co2[a]
h2o[a]
nadp[a]
coa[a]
C22:0
FACOAL220_ac
dcsa[a]
atp[a]
coa[a]
esdcoa6[a]
ppi[a]
amp[a]
odcoa6[a]
ppi[a]
amp[a]
odcoa3[a]
ppi[a]
amp[a]
DESAT201_11_ac
h[a]
nadph[a]
o2[a]
h2o[a]
nadp[a]
esecoa11[a]
FACOAL201_11_ac
ppi[a]
amp[a]
DESAT202_9_ac
h[a]
nadph[a]
o2[a]
h2o[a]
nadp[a]
esdcoa9[a]
FACOAL202_9_ac
ppi[a]
amp[a]

FIG. 10-57

FIG. 10-58


C22:1, n-9
C22:1, n-11
dcsacoa[a]
DESAT221_9_ac
dsecoa9[a]
FACOAL221_9_ac
dcsea9[a]
DESAT221_11_ac
dsecoa11[a]
FACOAL221_11_ac
dcsea11[a]
nadph[a]
o2[a]
h2o[a]
nadp[a]
h[a]
ppi[a]
amp[a]
coa[a]
atp[a]
ettcoa3[a]
estcoa6[a]
estcoa3[a]
FACOAL203_3_ac


dspcoa3[a]

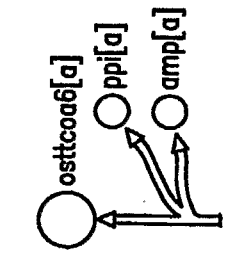
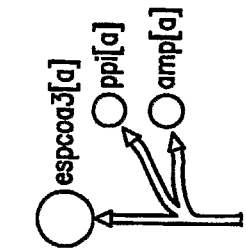
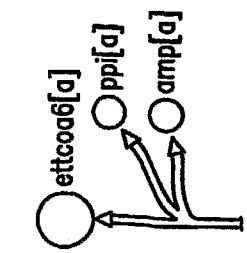

osttcoa6[a]
ppi[a]
amp[a]

FIG. 10-59


espcoa3[a]
ppi[a]
amp[a]


ettcoa6[a]
ppi[a]
amp[a]

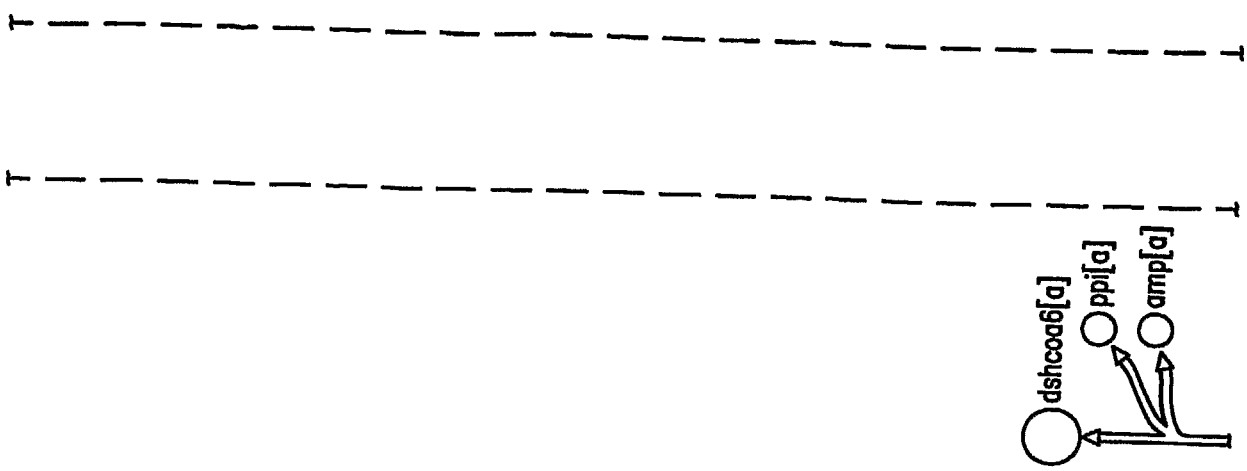
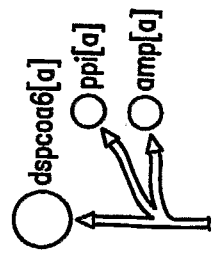
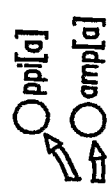


FIG. 10-60

Essential Fatty Acids





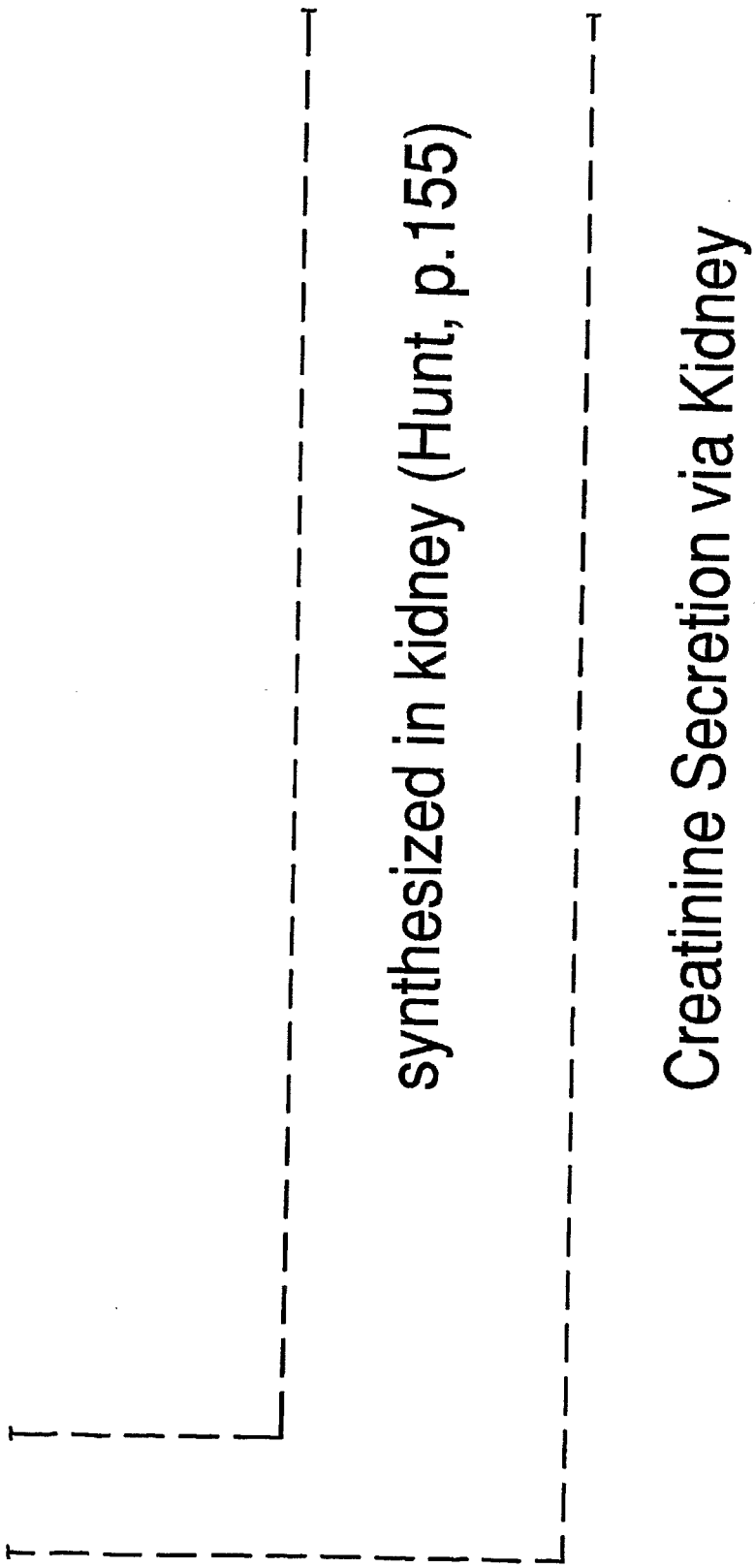

synthesized in kidney (Hunt, p.155)
Creatinine Secretion via Kidney

FIG. 10-61

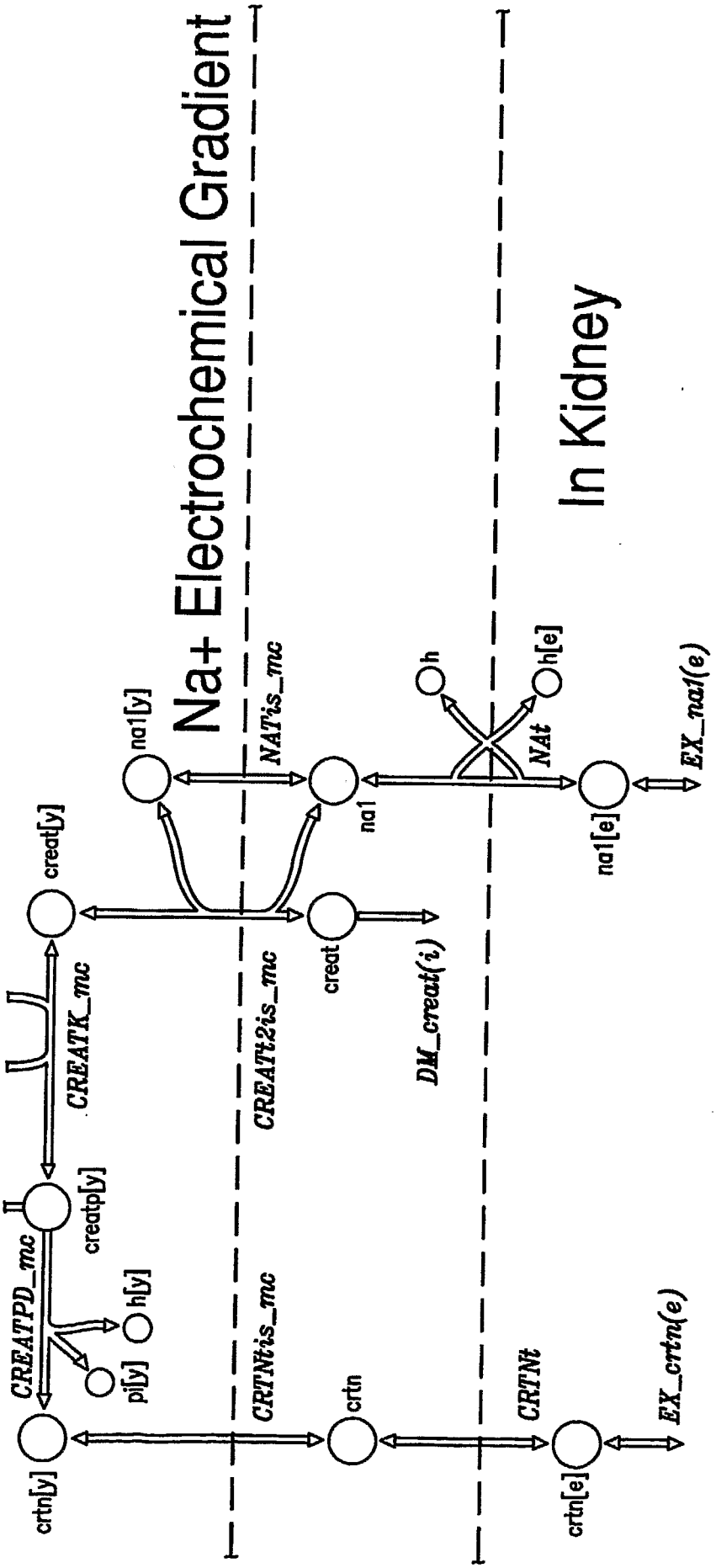

Na+ Electrochemical Gradient
In Kidney
na1[y]
NATis_mc
h
h[e]
NAt
EX_na1(e)
na1
na1[e]
creat[y]
creat
DM_creat(i)
CREATK_mc
CREATt2is_mc
creatp[y]
CREATPD_mc
h[y]
pi[y]
CRTNtis_mc
crtn
CRTNt
EX_crtn(e)
crtn[y]
crtn[e]

FIG. 10-62

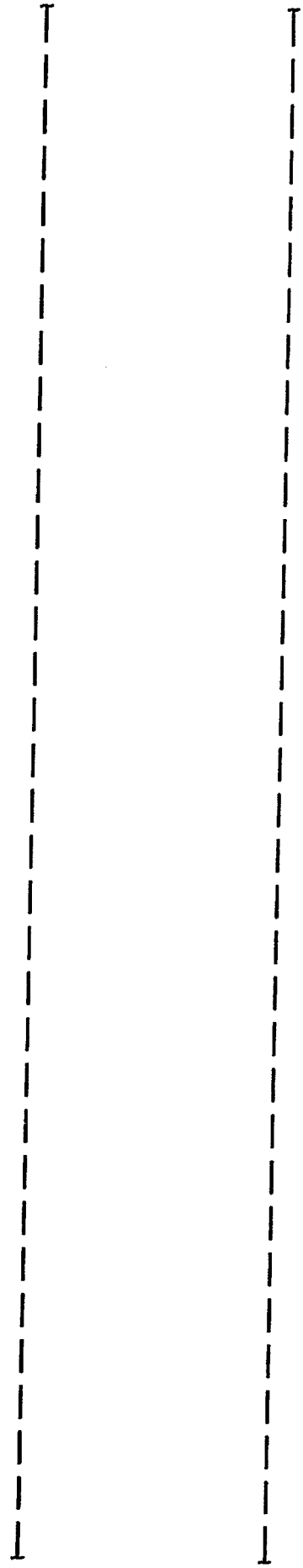


FIG. 10-63

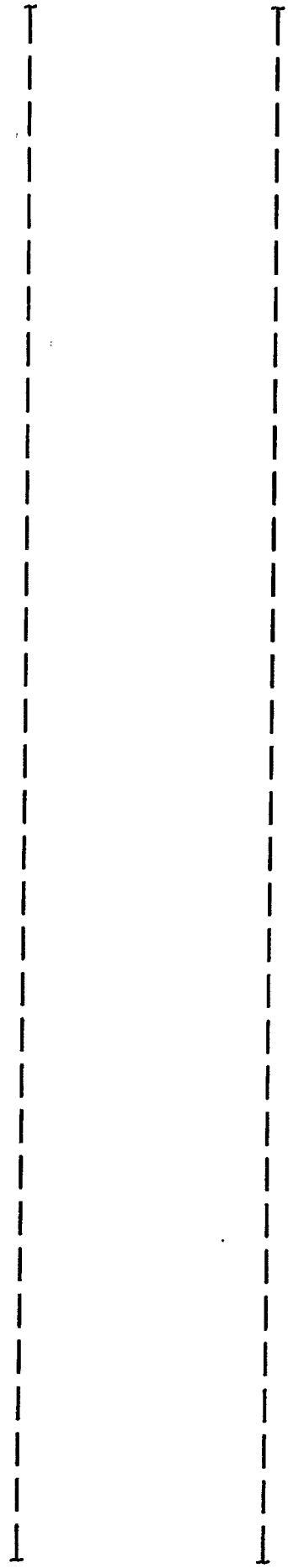


FIG. 10-64

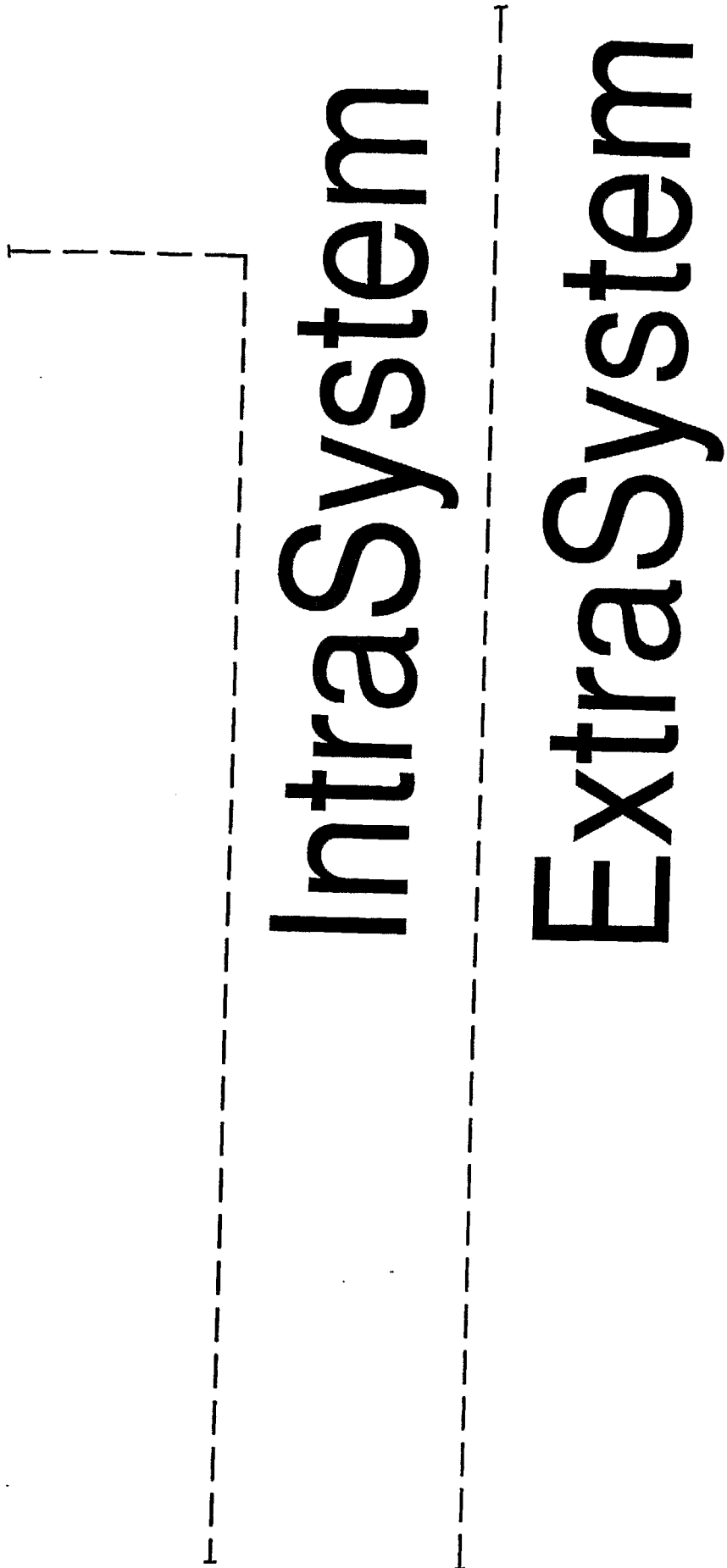


FIG. 10-65

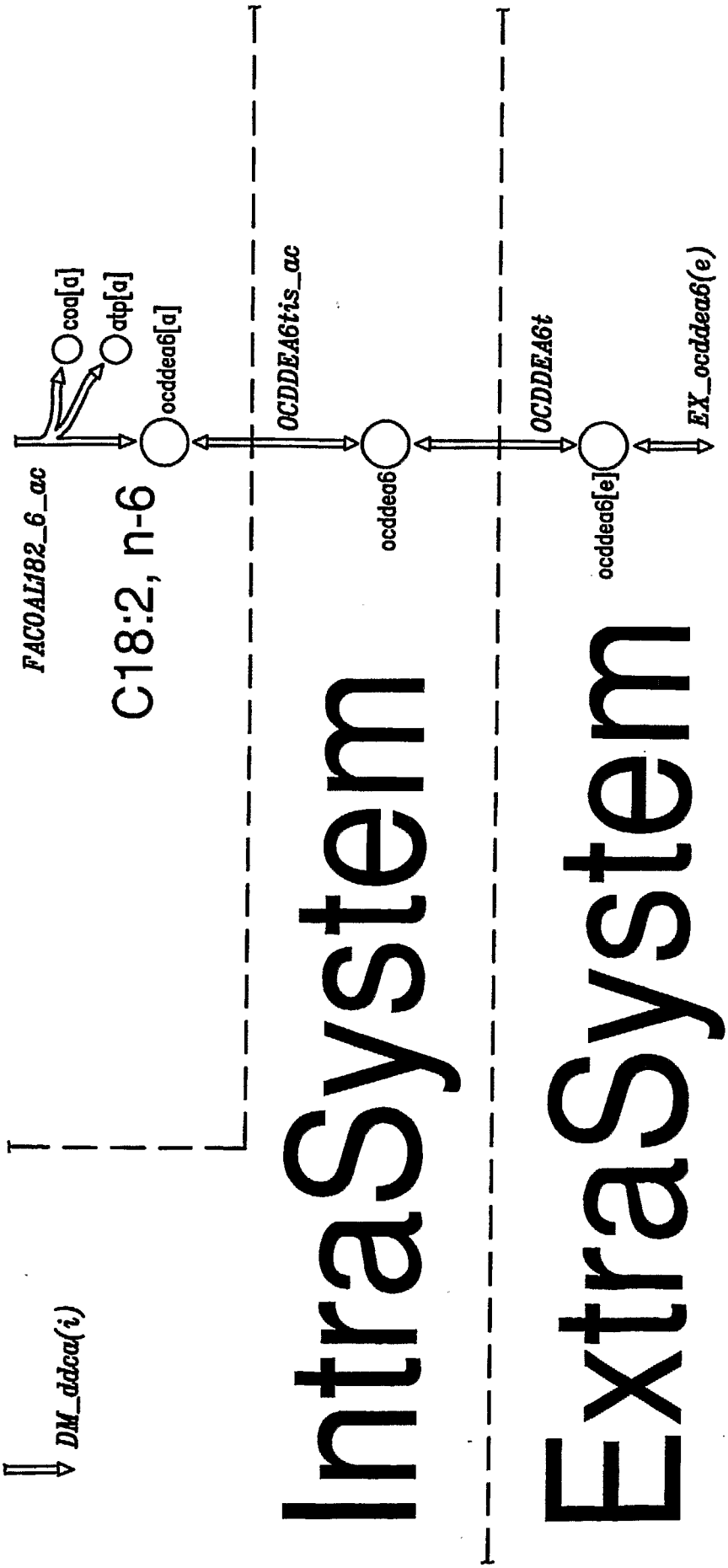

IntraSystem
ExtraSystem
DM_ddca(i)
FACOAL182_6_ac
C18:2, n-6
coa[a]
atp[a]
ocddea6[a]
OCDDEA6tis_ac
ocddea6
OCDDEA6t
ocddea6[e]
EX_ocddea6(e)

FIG. 10-66

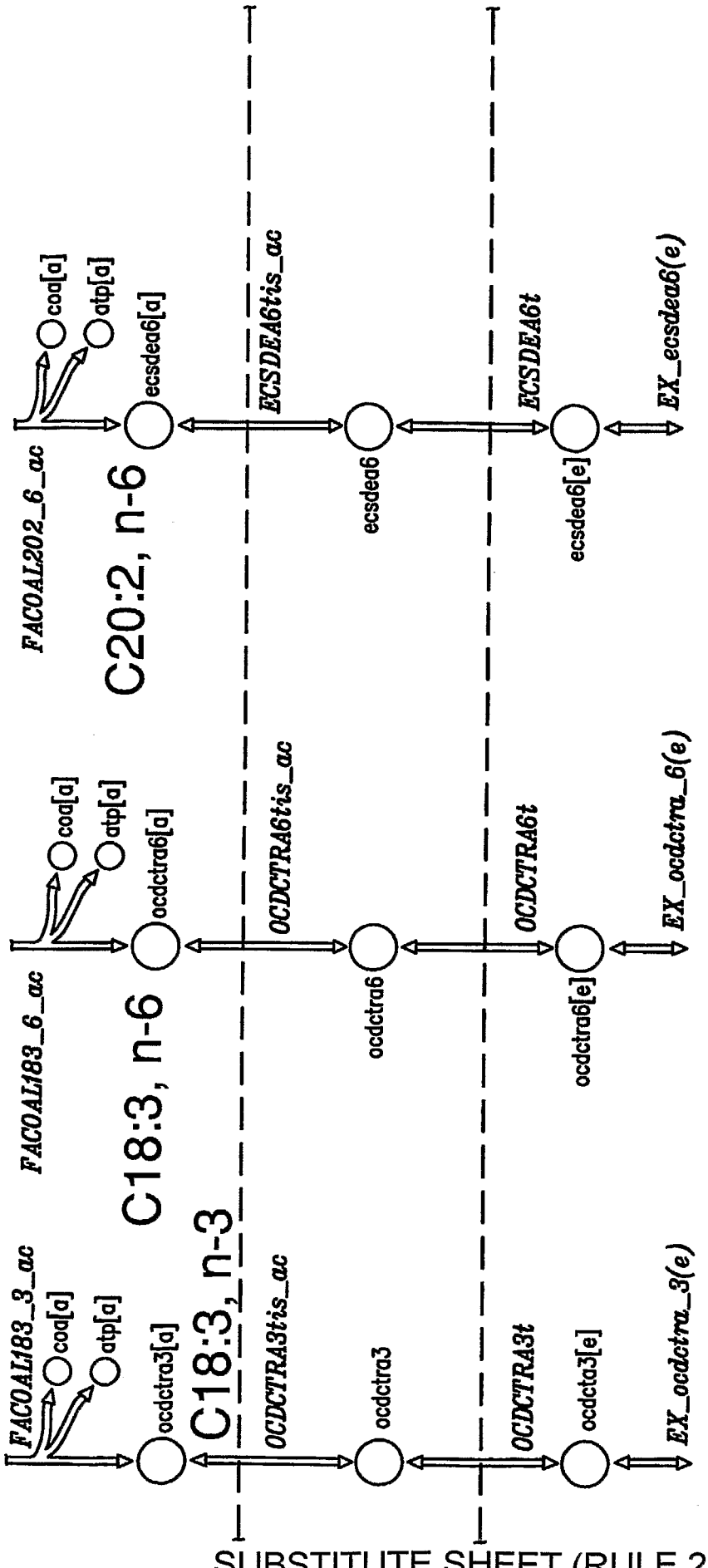

C18:3, n-3
C18:3, n-6
C20:2, n-6
FACOAL183_3_ac
FACOAL183_6_ac
FACOAL202_6_ac
coa[a]
atp[a]
ocdctra3[a]
ocdctra6[a]
ecsdea6[a]
OCDCTRA3tis_ac
OCDCTRA6tis_ac
ECSDEA6tis_ac
ocdctra3
ocdctra6
ecsdea6
OCDCTRA3t
OCDCTRA6t
ECSDEA6t
ocdcta3[e]
ocdctra6[e]
ecsdea6[e]
EX_ocdctra_3(e)
EX_ocdctra_6(e)
EX_ecsdea6(e)

FIG. 10-67

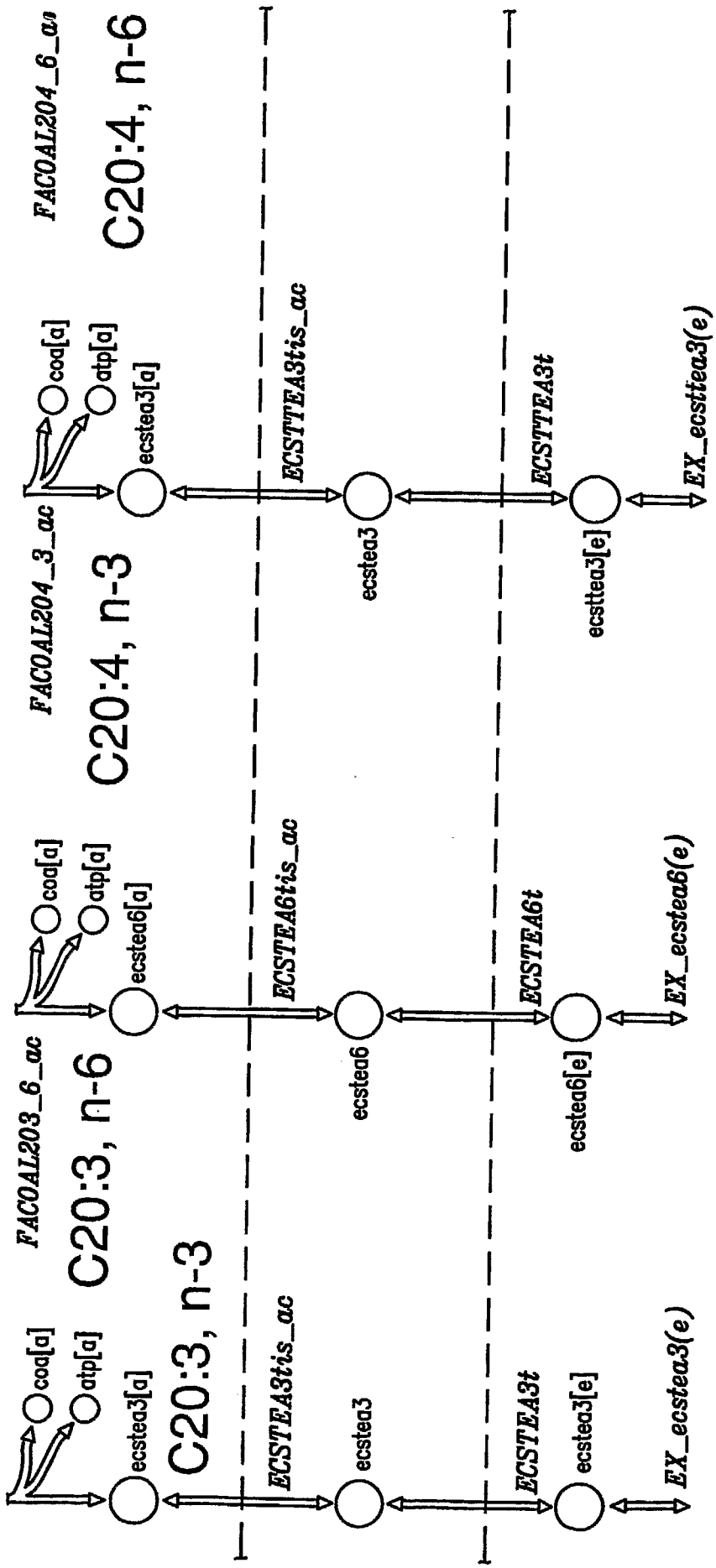

C20:3, n-3
C20:3, n-6
C20:4, n-3
C20:4, n-6
FACOAL203_6_ac
FACOAL204_3_ac
FACOAL204_6_as
coa[a]
atp[a]
ecstea3[a]
ecstea6[a]
ECSTEA3tis_ac
ECSTEA6tis_ac
ecstea3
ecstea6
ECSTEA3t
ECSTEA6t
ecstea3[e]
ecstea6[e]
EX_ecstea3(e)
EX_ecstea6(e)

FIG. 10-68

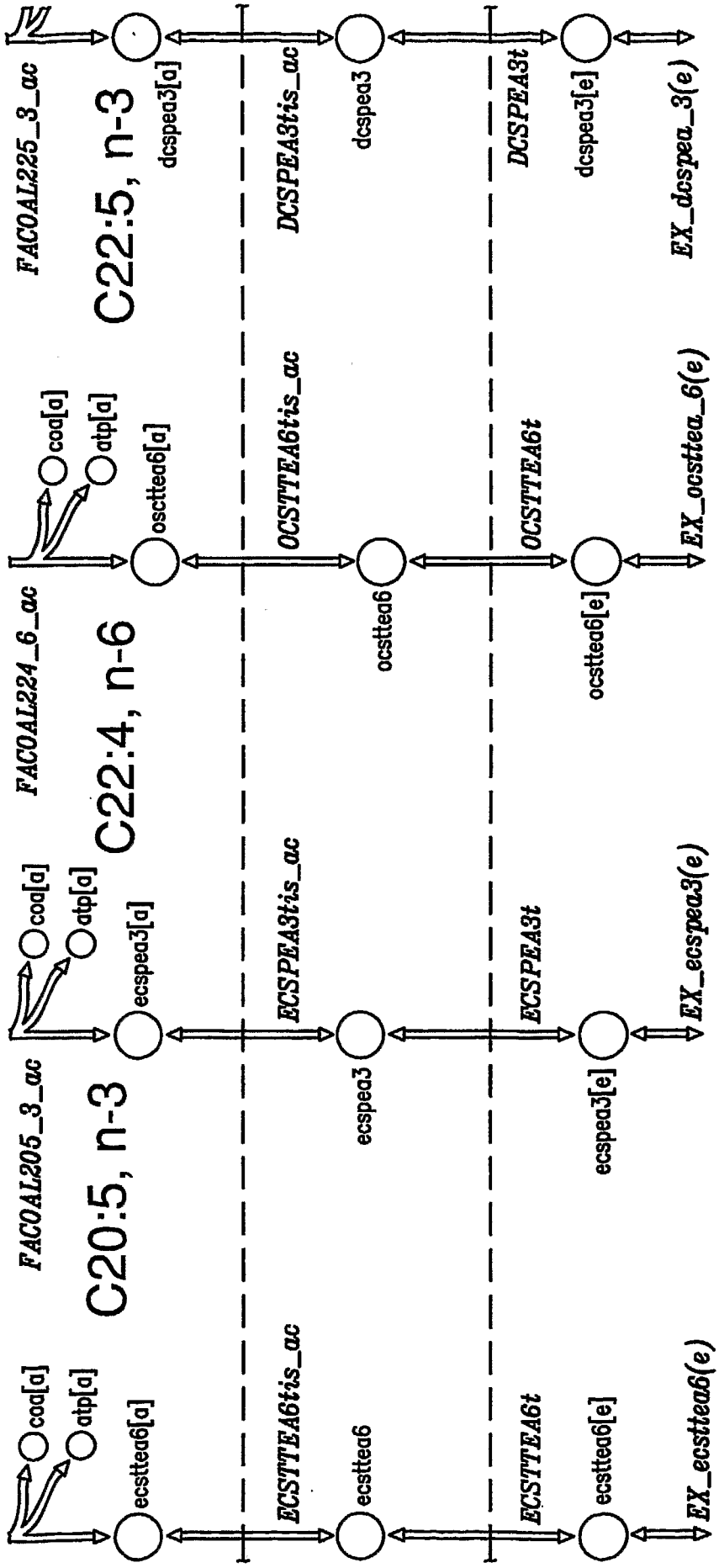

C20:5, n-3
C22:4, n-6
C22:5, n-3
FACOAL205_3_ac
FACOAL224_6_ac
FACOAL225_3_ac
coa[a]
atp[a]
ecsttea6[a]
ecspea3[a]
oscttea6[a]
dcspea3[a]
ECSTTEA6tis_ac
ECSPEA3tis_ac
OCSTTEA6tis_ac
DCSPEA3tis_ac
ecsttea6
ecspea3
oscttea6
dcspea3
ECSTTEA6t
ECSPEA3t
OCSTTEA6t
DCSPEA3t
ecsttea6[e]
ecspea3[e]
oscttea6[e]
dcspea3[e]
EX_ecsttea6(e)
EX_ecspea3(e)
EX_ocsttea_6(e)
EX_dcspea_3(e)

FIG. 10-69

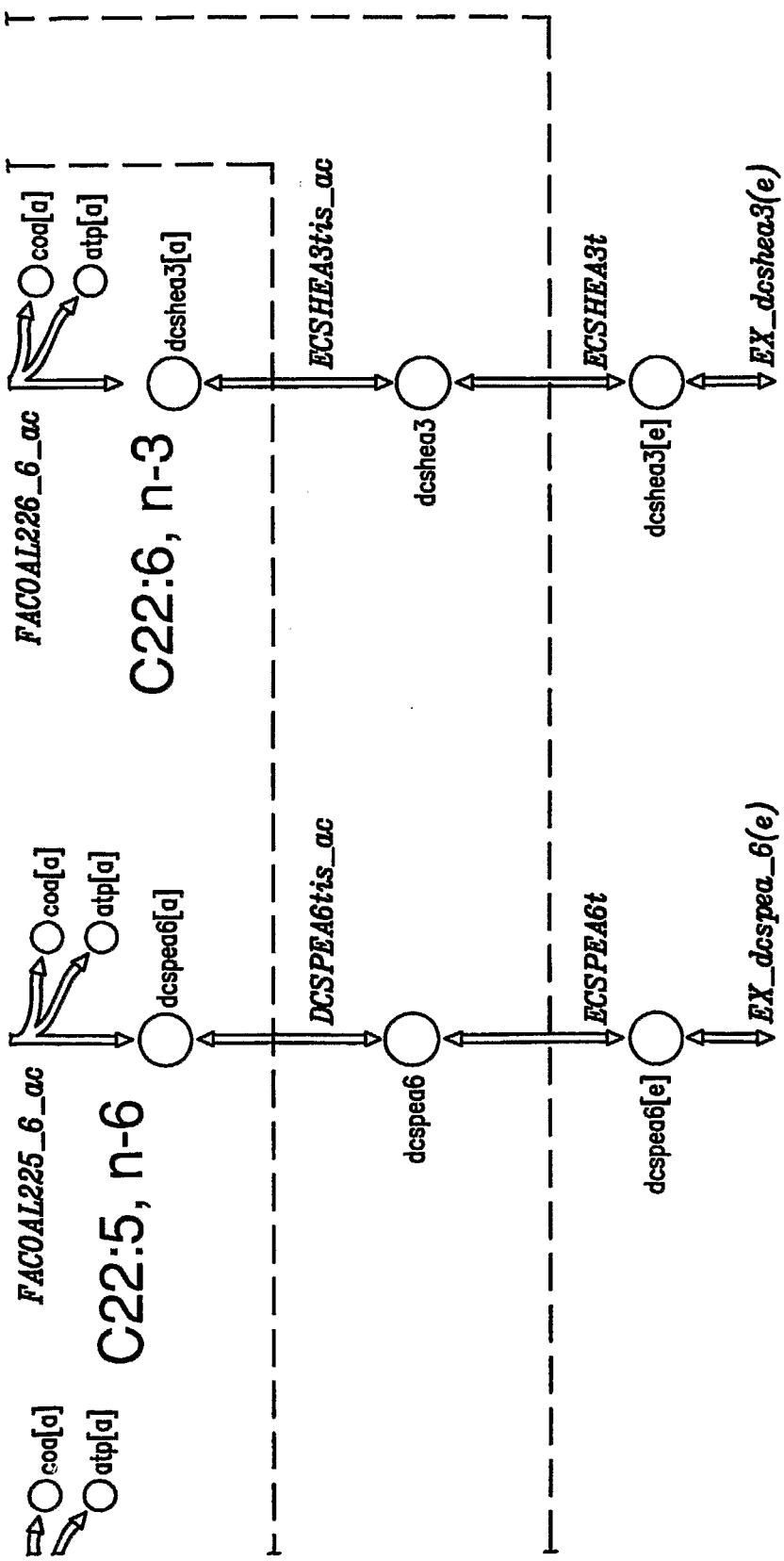

coa[a]
atp[a]
FACOAL226_6_ac
dcshea3[a]
C22:6, n-3
ECSHEA3tis_ac
dcshea3
ECSHEA3t
dcshea3[e]
EX_dcshea3(e)
coa[a]
atp[a]
FACOAL225_6_ac
dcspea6[a]
C22:5, n-6
DCSPEA6tis_ac
dcspea6
ECSPEA6t
dcspea6[e]
EX_dcspea_6(e)
coa[a]
atp[a]

FIG. 10-70

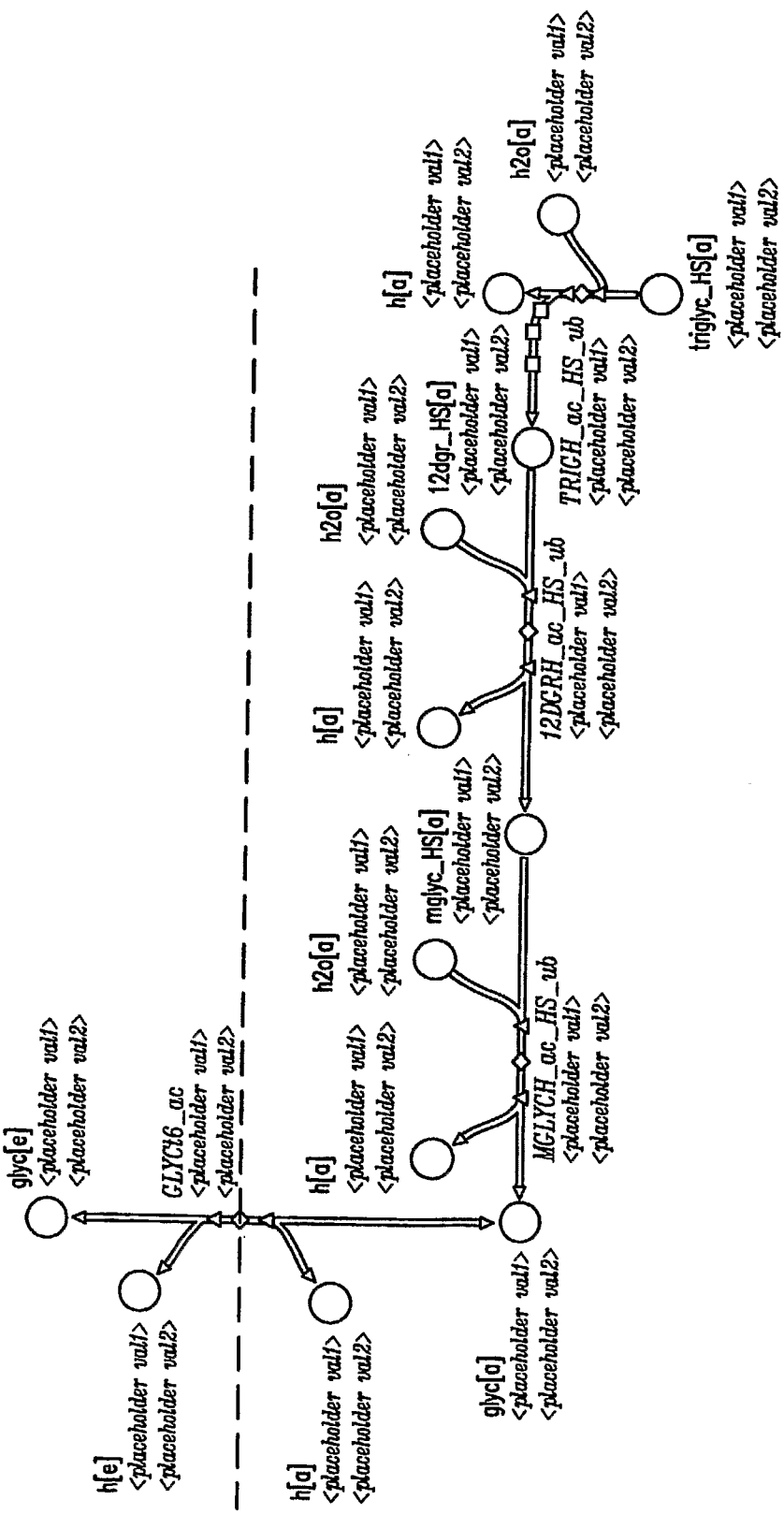

glyc[e]
<placeholder val1>
<placeholder val2>
GLYC16_ac
<placeholder val1>
<placeholder val2>
h[e]
<placeholder val1>
<placeholder val2>
h[a]
<placeholder val1>
<placeholder val2>
h2o[a]
<placeholder val1>
<placeholder val2>
h[a]
<placeholder val1>
<placeholder val2>
mglyc_HS[a]
<placeholder val1>
<placeholder val2>
MGLYCH_ac_HS_ub
<placeholder val1>
<placeholder val2>
glyc[a]
<placeholder val1>
<placeholder val2>
h2o[a]
<placeholder val1>
<placeholder val2>
h[a]
<placeholder val1>
<placeholder val2>
12dgr_HS[a]
<placeholder val1>
<placeholder val2>
12DGRH_ac_HS_ub
<placeholder val1>
<placeholder val2>
h[a]
<placeholder val1>
<placeholder val2>
TRIGH_ac_HS_ub
<placeholder val1>
<placeholder val2>
h2o[a]
<placeholder val1>
<placeholder val2>
triglyc_HS[a]
<placeholder val1>
<placeholder val2>

FIG. 11

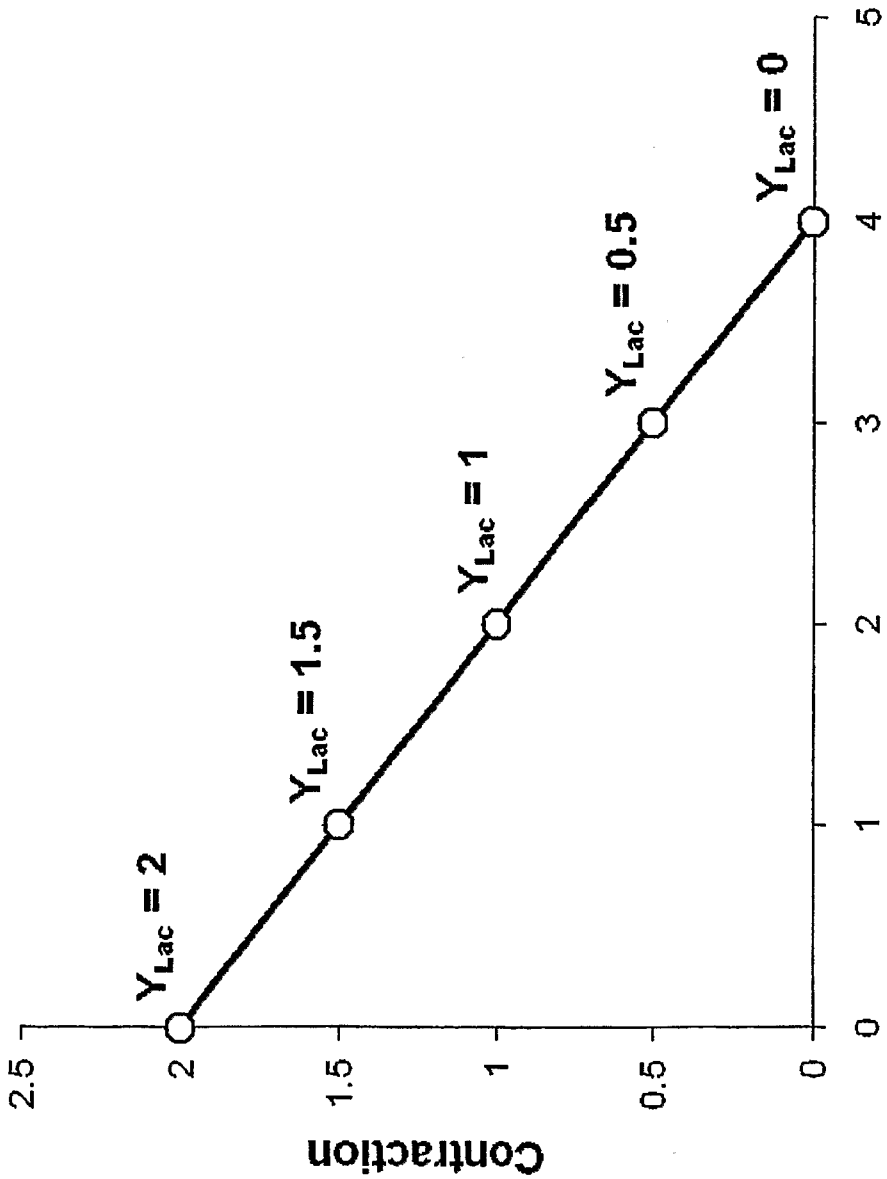

Contraction
2.5
2
1.5
1
0.5
0
Time Point
0
1
2
3
4
5
Y_{Lac} = 2
Y_{Lac} = 1.5
Y_{Lac} = 1
Y_{Lac} = 0.5
Y_{Lac} = 0

Figure 12

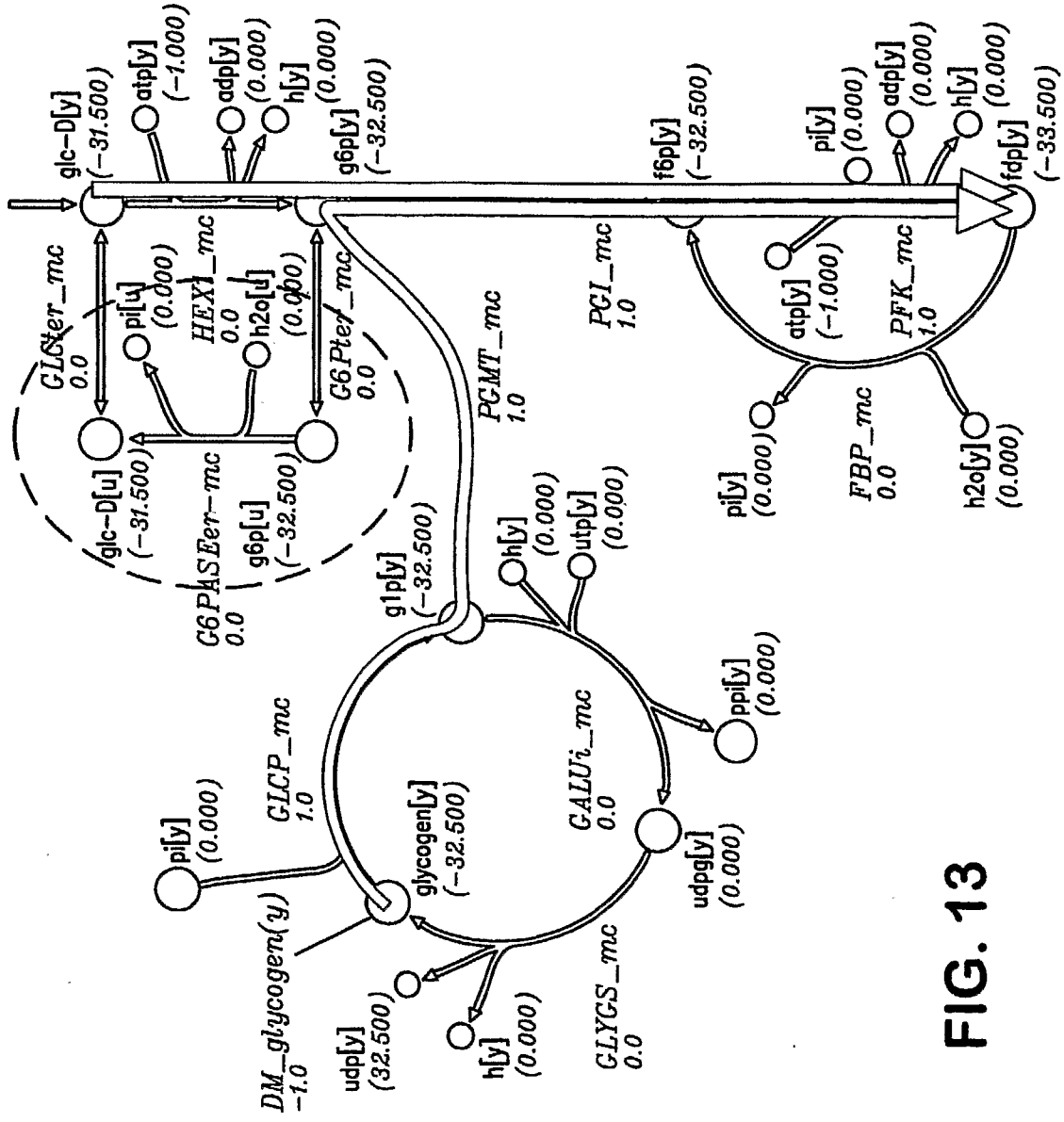

glc-D[y]
(-31.500)
atp[y]
(-1.000)
adp[y]
(0.000)
h[y]
(0.000)
g6p[y]
(-32.500)
f6p[y]
(-32.500)
pi[y]
(0.000)
adp[y]
(0.000)
h[y]
(0.000)
fdp[y]
(-33.500)
GLCter_mc
0.0
pi[u]
(0.000)
HEX1_mc
0.0
h2o[u]
(0.000)
G6Pter_mc
0.0
PGMT_mc
1.0
PGI_mc
1.0
atp[y]
(-1.000)
PFK_mc
1.0
glc-D[u]
(-31.500)
G6PASEer_mc
0.0
g6p[u]
(-32.500)
g1p[y]
(-32.500)
h[y]
(0.000)
utp[y]
(0.000)
pi[y]
(0.000)
FBP_mc
0.0
h2o[y]
(0.000)
ppi[y]
(0.000)
pi[y]
(0.000)
GLCP_mc
1.0
glycogen[y]
(-32.500)
GALUi_mc
0.0
udpg[y]
(0.000)
DM_glycogen(y)
-1.0
udp[y]
(32.500)
h[y]
(0.000)
GLYGS_mc
0.0

FIG. 13