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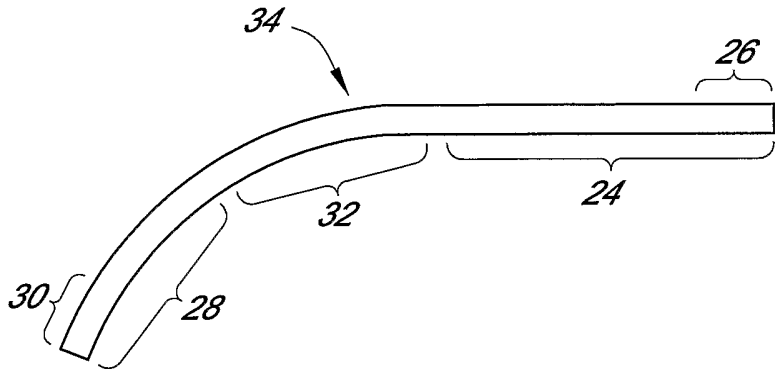
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(54) **Title:** TRANSCUTANEOUS ANALYTE SENSOR WITH VARIABLE STIFFNESS



(57) **Abstract:** The present invention relates generally to variable stiffness transcutaneous medical devices (34) including a distal tip (30) on a distal portion (28) designed to be more flexible than a proximal portion (24) having a proximal tip (26), wherein the distal portion (28) and the proximal portion (24) are separated by an intermediate portion (32). The variable stiffness can be provided by a variable pitch in one or more wires of the device, a variable cross-section in one or more wires of the device, and/or a variable hardening and/or softening in one or more wires of the device.

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TRANSCUTANEOUS ANALYTE SENSOR WITH VARIABLE STIFFNESS

Field of the Invention

[0001] The present invention relates generally to systems and methods for use with partially implantable medical devices. More particularly, the present invention relates to systems and methods for use with transcutaneous analyte sensors.

Background of the Invention

[0002] Transcutaneous medical devices are useful in medicine for providing the enhanced functionality of a wholly implantable medical device while avoiding many of the complications associated with a wholly implantable device. For example, transcutaneous analyte sensors are generally minimally invasive compared to wholly implantable sensor, and are capable of measuring an analyte concentration for a short period of time (e.g., three days) with similar accuracy as in a wholly implantable sensor.

Summary of the Invention

[0003] In a first aspect, a transcutaneous analyte sensor is provided, the sensor comprising an elongated flexible portion, wherein the elongated flexible portion has a variable stiffness along at least a portion of its length.

[0004] In an embodiment of the first aspect, the sensor comprises at least one wire in a helical configuration, and wherein the variable stiffness is provided by a variable pitch of the helical configuration.

[0005] In an embodiment of the first aspect, the sensor comprises at least one wire in a helical configuration, and wherein the variable stiffness is provided by a variable cross-section of the wire.

[0006] In an embodiment of the first aspect, the sensor comprises at least one wire, and wherein the variable stiffness is provided by a variable hardness of the wire.

[0007] In an embodiment of the first aspect, the variable stiffness of the elongated flexible portion is produced by subjecting the wire to an annealing process.

[0008] In an embodiment of the first aspect, the sensor comprises at least one wire, the wire having a variable diameter.

[0009] In an embodiment of the first aspect, a distal portion of the sensor is more flexible than a proximal portion of the sensor.

[0010] In an embodiment of the first aspect, an intermediate portion of the sensor is more flexible than at least one of a distal portion of the sensor and a proximal portion of the sensor.

[0011] In an embodiment of the first aspect, a distal tip of the sensor is stiffer than at least one of an intermediate portion of the sensor and a proximal portion of the sensor.

[0012] In a second aspect, a transcutaneous analyte sensor is provided, the sensor comprising a distal portion, an intermediate portion, and a proximal portion, wherein the distal portion is adapted to be inserted through a skin of a host, wherein the proximal portion is adapted to remain substantially external to the host when the distal portion is inserted in the host, and wherein a stiffness of the sensor is variable along a length of the sensor.

[0013] In an embodiment of the second aspect, the proximal portion is stiffer than the distal portion.

[0014] In an embodiment of the second aspect, the sensor comprises at least one wire in a helical configuration, and wherein a difference in stiffness of the distal portion and the proximal portion is provided by varying a pitch of the helical configuration.

[0015] In an embodiment of the second aspect, the sensor comprises at least one wire in a helical configuration, and wherein a difference in flexibility of the distal portion and the proximal portion is provided by a varying a cross-section of the wire.

[0016] In an embodiment of the second aspect, the sensor comprises at least one wire, and wherein a difference in flexibility of the distal portion and the proximal portion is provided by a varying a hardness of the wire.

[0017] In an embodiment of the second aspect, a variation in stiffness of the elongated flexible portion is produced by subjecting the wire to an annealing process.

[0018] In an embodiment of the second aspect, the intermediate portion is more flexible than at least one of the distal portion and the proximal portion.

[0019] In an embodiment of the second aspect, the distal portion comprises a distal tip on an end of the sensor that is stiffer a substantial portion of the sensor.

[0020] In an embodiment of the second aspect, the intermediate portion is more flexible than at least one of the distal portion and the proximal portion.

[0021] In an embodiment of the second aspect, the distal portion comprises a distal tip on an end of the sensor that is stiffer a substantial portion of the sensor.

[0022] In a third aspect, a transcutaneous analyte sensor is provided, the sensor comprising an *in vivo* portion adapted for insertion into a host and an *ex vivo* portion adapted for operable connection to a device that remains external to the host, wherein the sensor is configured to absorb a relative movement between the *ex vivo* portion of the sensor and the *in vivo* portion of the sensor.

[0023] In an embodiment of the third aspect, the sensor is configured to absorb a relative movement by a flexibility of at least an intermediate portion located between the *in vivo* portion and the *ex vivo* portion.

[0024] In an embodiment of the third aspect, the device comprises a housing adapted for mounting on a skin of a host, wherein the housing comprises electrical contacts operably connected to the sensor.

[0025] In an embodiment of the third aspect, the *ex vivo* portion of the sensor is has a preselected stiffness to maintain a stable connection between the sensor and the electrical contacts.

[0026] In an embodiment of the third aspect, the *in vivo* portion of the sensor has a preselected flexibility to minimize mechanical stresses caused by motion of the host.

[0027] In an embodiment of the third aspect, a stiffness of the *ex vivo* portion of the sensor is greater than a stiffness of the *in vivo* portion of the sensor.

Brief Description of the Drawings

[0028] Fig. 1A is a perspective view of a transcutaneous sensor assembly.

[0029] Fig. 1B is a side cross-sectional view of the transcutaneous sensor assembly of Fig. 1A.

[0030] Fig. 2 is a schematic side view of a transcutaneous medical device.

[0031] Fig. 3A is a schematic side view of a first transcutaneous medical device having a variable stiffness.

[0032] Fig. 3B is a schematic side view of a second transcutaneous medical device having a variable stiffness.

[0033] Fig. 3C is a schematic side view of a third transcutaneous medical device having a variable stiffness.

[0034] Figs. 4A to 4D are perspective and side views of a first variable stiffness wire for use with a transcutaneous analyte sensor.

[0035] Figs. 5A and 5B are perspective and cross-sectional views of a second variable stiffness wire for use with a transcutaneous analyte sensor.

[0036] Figs. 6A and 6B are perspective and cross-sectional views of a third variable stiffness wire suitable for use with a transcutaneous analyte sensor.

[0037] Fig. 7 is an expanded view of distal and proximal portions of a transcutaneous sensor in one example.

Detailed Description of the Preferred Embodiment

[0038] The following description and examples illustrate some exemplary embodiments of the disclosed invention in detail. Those of skill in the art will recognize that there are numerous variations and modifications of this invention that are encompassed by its scope. Accordingly, the description of a certain exemplary embodiment should not be deemed to limit the scope of the present invention.

Definitions

[0039] In order to facilitate an understanding of the preferred embodiments, a number of terms are defined below.

[0040] The term "analyte" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to a substance or chemical constituent in a biological fluid (for example, blood, interstitial fluid, cerebral spinal fluid, lymph fluid or urine) that can be analyzed. Analytes can include naturally occurring substances, artificial substances, metabolites, and/or reaction products. In some embodiments, the analyte for measurement by the sensing regions, devices, and methods is glucose. However, other analytes are contemplated as well, including but not limited to acarboxyprothrombin; acylcarnitine; adenine phosphoribosyl transferase; adenosine deaminase; albumin; alpha-fetoprotein; amino acid profiles (arginine (Krebs cycle), histidine/urocanic acid, homocysteine, phenylalanine/tyrosine, tryptophan); andrenostenedione; antipyrine; arabinitol enantiomers; arginase; benzoylecgonine (cocaine); biotinidase; biopterin; c-reactive protein; carnitine; carnosinase; CD4; ceruloplasmin; chenodeoxycholic acid; chloroquine; cholesterol; cholinesterase; conjugated 1-ß hydroxy-cholic acid; cortisol; creatine kinase; creatine kinase MM isoenzyme; cyclosporin A; d-penicillamine; de-ethylchloroquine; dehydroepiandrosterone sulfate; DNA (acetylator polymorphism, alcohol dehydrogenase, alpha 1-antitrypsin, cystic fibrosis, Duchenne/Becker muscular dystrophy, glucose-6-phosphate dehydrogenase, hemoglobin A, hemoglobin S, hemoglobin C, hemoglobin D, hemoglobin E, hemoglobin F, D-Punjab, beta-thalassemia, hepatitis B virus, HCMV, HIV-1, HTLV-1, Leber hereditary optic neuropathy, MCAD, RNA, PKU, Plasmodium vivax, sexual differentiation, 21-deoxycortisol); desbutylhalofantrine; dihydropteridine reductase; diptheria/tetanus antitoxin; erythrocyte arginase; erythrocyte protoporphyrin; esterase D; fatty acids/acylglycines; free ß-human chorionic gonadotropin; free erythrocyte porphyrin; free thyroxine (FT4); free tri-iodothyronine (FT3); fumarylacetoacetase; galactose/gal-1-phosphate; galactose-1-phosphate uridyltransferase; gentamicin; glucose-6-phosphate dehydrogenase; glutathione; glutathione perioxidase; glycocholic acid; glycosylated hemoglobin; halofantrine; hemoglobin variants; hexosaminidase A; human erythrocyte carbonic anhydrase I; 17-alpha-hydroxyprogesterone; hypoxanthine phosphoribosyl transferase; immunoreactive trypsin; lactate; lead; lipoproteins ((a), B/A-1, ß); lysozyme; mefloquine; netilmicin; phenobarbitone; phenytoin; phytanic/pristanic acid; progesterone; prolactin; prolidase; purine nucleoside phosphorylase; quinine; reverse tri-iodothyronine (rT3); selenium; serum pancreatic lipase; sissomicin; somatomedin C; specific antibodies (adenovirus, anti-nuclear antibody, anti-zeta antibody, arbovirus, Aujeszky's disease virus, dengue virus, Dracunculus medinensis, Echinococcus granulosus, Entamoeba histolytica, enterovirus, Giardia duodenalisa, Helicobacter pylori, hepatitis B virus, herpes virus, HIV-1, IgE (atopic disease), influenza virus, Leishmania donovani, leptospira, measles/mumps/rubella, Mycobacterium leprae, Mycoplasma pneumoniae,

Myoglobin, Onchocerca volvulus, parainfluenza virus, Plasmodium falciparum, poliovirus, Pseudomonas aeruginosa, respiratory syncytial virus, rickettsia (scrub typhus), Schistosoma mansoni, Toxoplasma gondii, Trepenoma pallidium, Trypanosoma cruzi/rangeli, vesicular stomatis virus, Wuchereria bancrofti, yellow fever virus); specific antigens (hepatitis B virus, HIV-1); succinylacetone; sulfadoxine; theophylline; thyrotropin (TSH); thyroxine (T4); thyroxine-binding globulin; trace elements; transferrin; UDP-galactose-4-epimerase; urea; uroporphyrinogen I synthase; vitamin A; white blood cells; and zinc protoporphyrin. Salts, sugar, protein, fat, vitamins and hormones naturally occurring in blood or interstitial fluids can also constitute analytes in certain embodiments. The analyte can be naturally present in the biological fluid, for example, a metabolic product, a hormone, an antigen, an antibody, and the like. Alternatively, the analyte can be introduced into the body, for example, a contrast agent for imaging, a radioisotope, a chemical agent, a fluorocarbon-based synthetic blood, or a drug or pharmaceutical composition, including but not limited to insulin; ethanol; cannabis (marijuana, tetrahydrocannabinol, hashish); inhalants (nitrous oxide, amyl nitrite, butyl nitrite, chlorohydrocarbons, hydrocarbons); cocaine (crack cocaine); stimulants (amphetamines, methamphetamines, Ritalin, Cylert, Preludin, Didrex, PreState, Voranil, Sandrex, Plegine); depressants (barbituates, methaqualone, tranquilizers such as Valium, Librium, Miltown, Serax, Equanil, Tranxene); hallucinogens (phencyclidine, lysergic acid, mescaline, peyote, psilocybin); narcotics (heroin, codeine, morphine, opium, meperidine, Percocet, Percodan, Tussionex, Fentanyl, Darvon, Talwin, Lomotil); designer drugs (analogs of fentanyl, meperidine, amphetamines, methamphetamines, and phencyclidine, for example, Ecstasy); anabolic steroids; and nicotine. The metabolic products of drugs and pharmaceutical compositions are also contemplated analytes. Analytes such as neurochemicals and other chemicals generated within the body can also be analyzed, such as, for example, ascorbic acid, uric acid, dopamine, noradrenaline, 3-methoxytyramine (3MT), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 5-hydroxytryptamine (5HT), and 5-hydroxyindoleacetic acid (FHIAA).

[0041] The terms "operably connected" and "operably linked" as used herein are broad terms and are used in their ordinary sense, including, without limitation, to refer to one or more components linked to one or more other components. The terms can refer to a mechanical connection, an electrical connection, or a connection that allows transmission of signals between the components. For example, one or more electrodes can be used to detect the amount of analyte in a sample and to convert that information into a signal; the signal can then be transmitted to a circuit. In such an example, the electrode is "operably linked" to the electronic circuitry.

[0042] The term "host" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to mammals, particularly humans.

[0043] The term "exit-site" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the area where a medical device (for example, a sensor and/or needle) exits from the host's body.

[0044] The phrase "continuous (or continual) analyte sensing" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the period in which monitoring of analyte concentration is continuously, continually, and or intermittently (regularly or irregularly) performed, for example, about every 5 to 10 minutes.

[0045] The term "electrochemically reactive surface" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the surface of an electrode where an electrochemical reaction takes place. For example, a working electrode measures hydrogen peroxide produced by the enzyme-catalyzed reaction of the analyte detected, which reacts to create an electric current. Glucose analyte can be detected utilizing glucose oxidase, which produces H_2O_2 as a byproduct. H_2O_2 reacts with the surface of the working electrode, producing two protons ($2H^+$), two electrons ($2e^-$) and one molecule of oxygen (O_2), which produces the electronic current being detected. In the case of the counter electrode, a reducible species, for example, O_2 is reduced at the electrode surface in order to balance the current being generated by the working electrode.

[0046] The term "sensing region" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the region of a monitoring device responsible for the detection of a particular analyte. The sensing region generally comprises a non-conductive body, a working electrode (anode), a reference electrode (optional), and/or a counter electrode (cathode) passing through and secured within the body forming electrochemically reactive surfaces on the body and an electronic connective means at another location on the body, and a multi-domain membrane affixed to the body and covering the electrochemically reactive surface.

[0047] The terms "electronic connection" and "electrical connection" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to any electronic connection known to those in the art that can be utilized to interface the sensing region electrodes with the electronic circuitry of a device, such as mechanical (for example, pin and socket) or soldered electronic connections.

[0048] The term "domain" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to a region of the membrane system that can be a layer, a uniform or non-uniform gradient (for example, an anisotropic region of a membrane), or a portion of a membrane.

[0049] The term "distal to" as used herein is a broad term and is used in its ordinary sense, including, without limitation, the spatial relationship between various elements in comparison to a particular point of reference.

[0050] The term "proximal to" as used herein is a broad term and is used in its ordinary sense, including, without limitation, the spatial relationship between various elements in comparison to a particular point of reference.

[0051] The terms "*in vivo* portion" and "distal portion" as used herein are broad terms and are used in their ordinary sense, including, without limitation, to refer to the portion of the device (for example, a sensor) adapted for insertion into and/or existence within a living body of a host.

[0052] The terms "ex *vivo* portion" and "proximal portion" as used herein are broad terms and are used in their ordinary sense, including, without limitation, to refer to the portion of the device (for example, a sensor) adapted to remain and/or exist outside of a living body of a host.

[0053] The term "intermediate portion" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to a portion of the device between a distal portion and a proximal portion.

[0054] The terms "transdermal" and "transcutaneous" as used herein are broad terms and is used in their ordinary sense, including, without limitation, to refer to extending through the skin of a host. For example, a transdermal analyte sensor is one that extends through the skin of a host.

[0055] The term "hardening" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to an increase in hardness of a metal induced by a process such as hammering, rolling, drawing, or the like.

[0056] The term "softening" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to an increase in softness of a metal induced by processes such as annealing, tempering, or the like.

[0057] The term "tempering" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the heat-treating of metal alloys, particularly steel, to reduce brittleness and restore ductility.

[0058] The term "annealing" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to the treatment of a metal or alloy by heating to a predetermined temperature, holding for a certain time, and then cooling to room temperature to improve ductility and reduce brittleness.

[0059] The term "stiff" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to a material not easily bent, lacking in suppleness or

responsiveness. In the preferred embodiments, the degree of stiffness can be relative to other portions of the device.

[0060] The term "flexible" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to a material that is bendable, pliable, or yielding to influence. In the preferred embodiments, the degree of flexibility can be relative to other portions of the device.

[0061] The devices of the preferred embodiments include transdermal medical devices, such as transcutaneous sensor assemblies, with variable stiffness configured along at least a portion of the device. In one aspect of the preferred embodiments, a transcutaneous sensor assembly is provided, including a sensor for sensing an analyte linked to a housing for mounting on the skin of the host. The housing houses an electronics unit associated with the sensor and is adapted for secure adhesion to the host's skin.

Transcutaneous Sensors

[0062] Figs. 1A and 1B are perspective and side cross-sectional views of a transcutaneous sensor assembly **10** of a preferred embodiment. The sensor system includes a housing 12 and preferably includes an adhesive material **14** on its backside **16** for adhesion to a host's skin. A sensor **18** extends from the housing and is adapted for transdermal insertion through the skin of the host. The sensor portion can be configured for insertion into a variety of *in vivo* locations, including subcutaneous, venous, or arterial locations, for example. One or more contacts **22** are configured to provide secure electrical contact between sensor **18** and an electronics unit **20**. The housing **12** is designed to maintain the integrity of the sensor in the host so as to reduce or eliminate translation of motion between the housing **12**, the host, and/or the sensor **18**.

[0063] In general, the sensor includes at least one electrode configured for measuring an analyte. In one embodiment, the sensor **18** includes at least two electrodes: a working electrode and at least one additional electrode, which can function as a counter and/or reference electrode. Preferably, the working electrode comprises a wire formed from a conductive material, such as platinum, palladium, graphite, gold, carbon, conductive polymer, or the like. In some embodiments, the wire is formed from a bulk material, or alternatively, a composite of two or more metals and/or insulators (*e.g.*, platinum plated steel). The working electrode is configured to measure the concentration of an analyte. The reference electrode, which can function as a reference electrode alone, or as a dual reference and counter electrode, is preferably formed from silver, silver/silver chloride, or the like. In preferred embodiments, the reference electrode is twisted with or around the working electrode; however other configurations for the working electrode and the reference electrode are also possible, for example juxtapositioned, adjacent, coaxial, concentric, interdigitated, spiral-wound, or the like.

[0064] In some alternative embodiments, additional electrodes can be included within the assembly. For example, a three-electrode system (working, reference, and counter electrodes) and/or a system including an additional working electrode (which can be used to generate oxygen or can be configured as a baseline subtracting electrode, for example) can be employed. Other sensor/wire/electrode configurations (for example one, two, three, four, or more wires and/or electrode configurations) are also within the scope of the preferred embodiments. For example, U.S. Patent No. 6,613,379 to Ward et al. describes a bundle of wires around which a counter electrode is deposed and configured for measuring an analyte, and U.S. Patent No. 6,329,161 to Heller et al. describes a single wire electrode configured for measuring an analyte. Any such configuration adapted for transcutaneous analyte measurement can be configured with a variable stiffness in accordance with the preferred embodiments.

[0065] In some embodiments (for example, enzymatic-based sensors), a membrane system is disposed over some or all of the electroactive surfaces of the sensor **18** (working and/or reference electrodes) and provides one or more of the following functions: 1) protection of the exposed electrode surface from the biological environment; 2) diffusion resistance (limitation) of the analyte; 3) a catalyst for enabling an enzymatic reaction; 4) hindering or blocking passage of interfering species; and 5) hydrophilicity at the electrochemically reactive surfaces of the sensor interface, such as is described in co-pending U.S. Patent Application No. 11/077,715, filed on March 10, 2005 and entitled "TRANSCUTANEOUS ANALYTE SENSOR".

[0066] The electronics unit **20** can be integral with or removably attached to the housing **12**, and includes hardware, firmware and/or software that enable measurement of levels of the analyte via the sensor **18**. For example, the electronics unit **20** comprises a potentiostat, a power source for providing power to the sensor, other components useful for signal processing, and preferably an RF module for transmitting data from the electronics unit **20** to a receiver. Electronics can be affixed to a printed circuit board (PCB), or the like, and can take a variety of forms. For example, the electronics can take the form of an integrated circuit (IC), such as an application-specific integrated circuit (ASIC), a microcontroller, or a processor. Preferably, the electronics unit **20** houses the sensor electronics, which comprise systems and methods for processing sensor analyte data. Examples of systems and methods for processing sensor analyte data are described in more detail below and in co-pending U.S. Application No. 10/633,367 filed August 1, 2003 entitled, "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA."

[0067] Co-pending U.S. Patent Application 11/077,715 filed on March 10, 2005, and entitled, "TRANSCUTANEOUS ANALYTE SENSOR," describes an embodiment of a transcutaneous analyte sensor that benefits from variable stiffness. Variable stiffness configurations along at least a portion of the device can be employed with devices such as are

described in U.S. Patent No. 6,613,379 to Ward et al., U.S. Patent No. 6,122,536 to Sun et al., U.S. Patent No. 6,329,161 to Heller et al., U.S. Patent No. 6,477,395 to Schulman, and U.S. Patent No. 4,671,288 to Gough.

Variable Stiffness

[0068] Conventional transcutaneous devices can be subject to motion artifact associated with host movement when the host is using the device. For example, in the example of a transcutaneous analyte sensor such as described above, various movements on the sensor (for example, relative movement within and between the subcutaneous space, dermis, skin, and external portions of the sensor) create stresses on the device, which are known to produce artifacts on the sensor signal.

[0069] Accordingly, the design considerations (for example, stress considerations) vary for different sections of a transcutaneous medical device. For example, certain portions of the device can benefit in general from greater flexibility as the portion of the device encounters greater mechanical stresses caused by movement of the tissue within the patient and relative movement between the *in vivo* and *ex vivo* portions of the sensor. Additionally or alternatively, certain portions of the device can benefit in general from a stiffer, more robust design to ensure structural integrity and/or reliable electrical connections. Additionally, in some embodiments wherein an insertion device (for example, needle that aids in insertion) is retracted over the device, a stiffer design can enable minimized crimping and/or easy retraction. Thus, by designing greater flexibility into the some portions of the device, the flexibility can compensate for movement and noise associated therewith; and by designing greater stiffness into other portions, column strength (for retraction of the needle over the sensor), electrical connections, and structural integrity can be enhanced.

[0070] Fig. 2 is a side schematic view of a transcutaneous medical device **34**, such as illustrated as the transcutaneous analyte sensor **18** of Fig. 1. In general, a transcutaneous medical device **34**, can be divided into three zones, a proximal portion **24** with a proximal tip **26**, a distal portion **28** with a distal tip **30**, and an intermediate portion **32**. The preferred embodiments can employ a variety of configurations that provide variable stiffness along at least a portion of the device in order to overcome disadvantages of conventional transcutaneous devices. Although the following description is focused on an embodiment of a transcutaneous analyte sensor, one skilled in the art can appreciate that the variable stiffness of the preferred embodiments can be implemented with a variety of transcutaneous medical devices.

[0071] Generally, the proximal portion **24** is adapted to remain above the host's skin after device insertion and operably connects to a housing *ex vivo,* for example. The proximal portion **24** typically provides the mechanical and/or electrical connections of the device to housings, electronics, or the like. The proximal portion includes a proximal tip **26** on an end

thereof. It is noted that the terms "proximal portion," "*ex vivo* portion," and "proximal tip" do not necessarily imply an exact length or section, rather is generally a section that is more proximal than distal relative to the housing. In some embodiments, the proximal portion (or proximal tip) is stiffer than at least one of the intermediate and distal portions.

[0072] Generally, the distal portion **28** of the sensor is adapted for insertion under the host's skin, and is also referred to as the *in vivo* portion. The distal portion **28** typically provides the device function *in vivo*, and therefore encounters stresses caused by insertion of the device into the host's tissue and subsequent movement of the tissue of the patient. The distal portion includes a distal tip **30** on an end thereof. It is noted that the terms "distal portion," "*in vivo* portion," and "distal tip" do not necessarily imply an exact length or section, rather is generally a section that is more distal than proximal relative to the housing. In some embodiments, the distal portion is more flexible than at least one of the intermediate and proximal portions. In some embodiments, the distal tip is less flexible than at least one of the remaining (non-tip) distal portion, the intermediate portion, and the proximal portion.

[0073] Generally, the intermediate portion **32** is located between the proximal portion **24** and the distal portion and may include portions adapted for insertion or adapted to remain above the skin. The intermediate portion **32** typically provides a transition between the *in vivo* and *ex vivo* portions, and can incur stresses caused by relative movement between the *in vivo* and *ex vivo* portions of the sensor, for example. It is noted that the term "intermediate portion" does not necessarily imply an exact length or section, rather is generally a section that in-between the proximal and distal portions. In some embodiments, the intermediate portion is more flexible than one or both of the distal and proximal portions.

[0074] Fig. 3A is a side schematic view of a transcutaneous medical device **34a** in one embodiment adapted for insertion through the skin of a host. In this embodiment, the device **34a** is designed with greater flexibility generally in a distal portion **28** (relative to intermediate and/or proximal portions), which is illustrated by light cross-hatching in the distal portion of the device. Stated in another way, the device is designed with a greater stiffness generally in the proximal portion **24** than the intermediate and/or the distal portions, which is illustrated by heavy cross-hatching in the proximal portion **24** of the device. In some embodiments, the intermediate portion includes a flexibility substantially similar to that of the distal portion; in other embodiments, the intermediate portion gradually transitions between the flexibility of the distal portion and the stiffness of the proximal portion. For example, in situations wherein movement of the tissue within the patient and relative movement between the *in vivo* and *ex vivo* portions of the device create stresses on the device, greater flexibility in a distal portion (relative to intermediate and/or proximal portions) can provide relief from these mechanical stresses, protecting both the integrity of the sensor and the host tissue. Additionally or alternatively, in

situations wherein mechanical and/or electrical connections are required for accurate device function, greater stiffness in the proximal portion **24** (and/or the proximal tip) of the device can increase the stability and reliability of these connections. Thus, the *ex-vivo* or proximal portion **24** of the sensor is configured for stable connection to the electronics and can additionally be configured to receive an insertion device (such as a needle that aids in sensor insertion) upon retraction from the skin of the host (see co-pending U.S. Patent Application 11/077715 filed on March 10, 2005 and entitled "TRANSCUTANEOUS ANALYTE SENSOR").

[0075] Fig. 3B is a side schematic view of a transcutaneous medical device **34b** of a preferred embodiment adapted to be inserted through the skin of a host. In this embodiment, the device is designed with an increased stiffness at a distal tip **30** (or a distal portion **28**) of the device (relative to intermediate and/or proximal portions) in order to provide increased strength and/or structural integrity to the tip, which is illustrated by heavy cross-hatching. In some situations, the device is inserted into the host such that a tunnel is formed therein. When the device abuts the tunnel end, increased stress to the distal tip can occur. This increased stress can cause the device to bend, resulting in malfunctioning of the device.

[0076] In some embodiments, this increased stiffness is designed into the device by creating a greater hardness of the distal tip of the device, for example, by annealing or coating the device. In one embodiment of a transcutaneous analyte sensor as described above with reference to Fig. 1, a higher pitch of the helically wound reference electrode for at least a few windings at a distal end of the reference electrode creates a relative stiffness of the distal portion or tip of the device. It is believed that a stiffer distal portion or tip advantageously provides increased stability, column strength, and proper placement of the device in the host.

[0077] Fig. 3C is a side schematic view of a transcutaneous medical device **34c** in yet another embodiment adapted to be inserted through the skin of a host. In this embodiment, the device **34c** is designed with an increased flexibility at an intermediate portion **32** thereof. Namely, the intermediate portion of the device is designed to absorb shock between the proximal and distal portions, for example, such that movement of the *ex vivo* portion of the device does not substantially translate to the *in vivo* portion of the device (and vice versa). In some aspects of this embodiment, the distal portion is designed with a flexibility similar to that of the intermediate portion. In some aspects of this embodiment, the flexibility gradually changes from the distal portion to the proximal portion, including a relatively flexible intermediate portion **32**.

[0078] In some embodiments, any combination of the above described relatively stiff or flexible portions can be designed into a transcutaneous medical device. In fact, a variety of additional stiff and/or flexible portions can be incorporated into the distal and/or proximal portions of the device without departing from the scope of the preferred embodiments. The flexibility and/or stiffness can be stepped, gradual, or any combination thereof.

[0079] The variable stiffness (flexibility) of the preferred embodiments can be provided by a variable pitch of any one or more wires of the device, a variable cross-section of any one or more wires of the device, and/or a variable hardening and/or softening of any one or more wires of the device, for example, as is described in more detail below.

[0080] Figs. 4A to 4D are perspective and side views of a variable stiffness wire used in a transcutaneous medical device, such as an analyte sensor. In Fig. 4A, a wire **36** is shown, which can represent the working electrode or reference electrode of the embodiment described with reference to Fig. 1, for example. Alternatively, the wire **36** can represent one or more wires of a multiple wire sensor (examples of each are described above). The variable stiffness wire described herein can be employed in a transcutaneous medical device to provide variable stiffness along a portion of the length of the device, such as in an analyte sensor.

[0081] Fig. 4B is a side view of a variable stiffness wire **36b** wherein physical processing of the distal, intermediate, and/or proximal portions of the wire provide for variability of the stiffness of the wire. In some embodiments, some portion (for example, the distal portion) of the wire is softened using a process such as annealing or tempering. In some embodiments, some portion (for example, the proximal portion) of the wire is hardened using a process such as drawing or rolling. In some embodiments, some combination of softening and hardening as described herein are employed to provide variable stiffness of the wire. In the embodiment described with reference to Fig. 1, including a working electrode and a reference electrode, the working electrode can be hardened and/or softened to provide for the variable stiffness of one or more portions of the device, such as is described in more detail elsewhere herein. Another alternative embodiment provides a varying modulus of elasticity of the material to provide the variable stiffness of the preferred embodiments.

[0082] Fig. 4C is a side view of an alternative variable stiffness wire **36c**, wherein the wire has a gradually increasing or decreasing diameter along its length. The variability in diameter can be produced by physical or chemical processes, for example, by grinding, machining, rolling, pulling, etching, drawing, swaging, or the like. In this way, a transcutaneous analyte sensor, or other transcutaneous medical device, can be produced having a variable stiffness. In the embodiment described with reference to Fig. 1, for example, including a working electrode and a reference electrode, the working electrode can be formed with a variable diameter to provide for the variable stiffness of one or more portions of the device, such as described in more detail elsewhere herein.

[0083] Fig. 4D is a side view of another alternative variable stiffness wire **36d**, wherein the wire is step increased or decreased to provide two (or more) different flexibilities of the wire. The wire can be stepped by physical or chemical processes known in the art, such as described with reference to Fig. 4C. In this way, a transcutaneous analyte sensor, or other

transcutaneous medical device, can be produced with a variable stiffness. A noted advantage of the smaller diameter configurations of Figs. 4C and 4D include reduced sizing of the *in vivo* portion of the device, which is believed to be more comfortable for the patient and to induce less invasive trauma around the device, thereby providing an optimized device design.

[0084] Figs. 5A and 5B are perspective and cross-sectional views of a variable stiffness wire **38** in an alternative embodiment representing any one or more wires associated with a transcutaneous medical device, such as an analyte sensor. For example, the wire **38** can represent the reference electrode of the embodiment described with reference to Fig. 1. Alternatively, the wire **38** can represent the wire of a single or multiple wire sensor (examples of each are described above).

[0085] In this embodiment, two distinct portions **40, 42** are shown with first and second pitches; however, the illustration is not meant to be limiting and the variable pitch can include any number of gradual portions, stepped portions, or the like. Additionally, the variable pitch and/or helical configuration can be provided on only a portion of the wire or on the entire length of the wire, and can include any number of pitch changes. In this embodiment, a first portion **40** is wound to have relatively closely spaced coils, namely, a high helix pitch, whereas a second **42** portion is not subjected to high stress levels and can include coils wound with a lower helix pitch. The helix pitch is defined as the number of coils of the wire core per unit length of the device, or the distance between the coils.

[0086] Fig. 5B is a cross-sectional view along line B-B of the device of Fig. 5A, illustrating a first distance d_1 between the coils in the first portion **40** and a second distance d_2 between the coils in the second portion **42**, wherein d_2 is greater than d_1. Thus, the wire has a variable stiffness attributable to the varying helix pitch over the length of the sensor. In this way, portions of a device having wire with a low helix pitch are designed with greater flexibility and are more able to handle the stresses associated with motion of the sensor while portions of the sensor having wire with a high helix pitch are designed with more stiffness and provide more stability for the sensor in the housing. Any portions (proximal, intermediate, and/or distal portions (or tips)) can be designed with a variable pitch to impart variable stiffness.

[0087] Figs. 6A and 6B are perspective and longitudinal views of a variable stiffness wire **44** in yet another alternative embodiment representing any one or more wires associated with a transcutaneous medical device, such as an analyte sensor. For example, the wire **44** can be the reference electrode of the embodiment described with reference to Fig. 1. Alternatively, the wire **44** can be a working electrode, and/or one or more wires of a multiple wire sensor (examples of each are described above).

[0088] In this embodiment, two distinct portions **46, 48** are shown with first and second wire diameters that provide a variable cross-section; however, the illustration is not meant

to be limiting and the variable cross-section can be gradual, stepped, or the like. Additionally, the variable cross-section and/or helical configuration can be provided on only a portion of the wire or on the entire length of the wire, and can include any number of cross-section changes. In this embodiment, the helically wound wire is designed with a variable cross-sectional area over the length of the sensor from a small cross-sectional area in the first portion **46** to a larger cross-sectional area in the second portion **48**.

[0089] Fig. 6B is a cross-sectional view along line B-B of the device of Fig. 6A, revealing cross-sectional information about one or more wires that make up the coil, including a first cross-section x_1 of the wire in the first portion **20** and a second cross-section x_2 of the wire in the second portion **48**, wherein x_2 is greater than x_1. Thus, the device of this embodiment has a variable stiffness attributable to the varying cross-section over the length of the sensor. In this way, first portion **46** has a smaller cross-sectional area and is therefore more flexible and capable of withstanding the stresses associated with patient movement, for example; while the second portion **48** has a larger cross-sectional area and is stiffer and provides more stability and column strength desirable for mechanical and electrical connections, for example.

[0090] The transcutaneous analyte sensor of Fig. 1 includes a helical configuration. The helical surface topography of the reference electrode surrounding the working electrode not only provides electrochemical functionality, but can also provide anchoring within the host tissue. The device preferably remains substantially stationary within the tissue of the host, such that migration or motion of the sensor with respect to the surrounding tissue is minimized. Migration or motion can cause inflammation at the sensor implant site due to irritation and can also cause noise on the sensor signal due to motion-related artifact, for example. Therefore, it can be advantageous to provide an anchoring mechanism that provides support for the sensor *in vivo* portion to avoid or minimize the above-mentioned problems. Combining advantageous sensor geometry with advantageous anchoring minimizes additional parts in the device, and allows for an optimally small or low profile design of the sensor. Additionally or alternatively, anchoring can be provided by prongs, spines, barbs, wings, hooks, rough surface topography, gradually changing diameter, or the like, which can be used alone or in combination with the helical surface topography to stabilize the sensor within the subcutaneous tissue.

Example

[0091] Fig. 7 is an expanded view of distal and proximal portions of a transcutaneous sensor **50** in one example. Fig. 7 illustrates a sensor **50** broken away between its distal portion **52** and proximal portion **54**, representing any length or configuration there between. In the illustrated embodiment, the sensor **50** includes two electrodes: a working electrode **56** and one additional electrode, which can function as a counter and/or reference

electrode, hereinafter referred to as the reference electrode **58**. Each electrode is formed from a fine wire with a diameter of approximately 0.0045 inches.

[0092] The working electrode **56** comprises a platinum wire and is configured and arranged to measure the concentration of an analyte. In this example of an enzymatic electrochemical sensor, the working electrode measures the hydrogen peroxide produced by an enzyme catalyzed reaction of the analyte being detected and creates a measurable electronic current (for example, detection of glucose utilizing glucose oxidase produces H_2O_2 peroxide as a by product, H_2O_2 reacts with the surface of the working electrode producing two protons ($2H^+$), two electrons ($2e^-$) and one molecule of oxygen (O_2) which produces the electronic current being detected).

[0093] The working electrode **56** is covered with an insulator **57**, *e.g.,* Parylene, which is vapor-deposited on the working electrode. Parylene is an advantageous conformal coating because of its strength, lubricity, and electrical insulation properties; however, a variety of other insulating materials can also be used, for example, fluorinated polymers, polyethyleneterephthalate, polyurethane, polyimide, or the like. The reference electrode **58**, which can function as a counter electrode alone, or as a dual reference and counter electrode, is preferably silver or a silver-containing material. In this example, the reference electrode **58** is helically twisted around the working electrode **56**. A window **55** is formed on the insulating material to expose an electroactive surface of the working electrode **56**. Other methods and configurations for exposing electroactive surfaces can also be employed.

[0094] In this example, the reference electrode **58** is wound with a variable pitch that creates a variable stiffness along the length of the sensor **50**. Namely, the sensor **50** is designed with a greater stiffness generally in the proximal portion **54** than the intermediate and/or the distal portions **52**. However, an increased stiffness of a section of the distal portion **52,** shown adjacent to the window **55** wherein the reference electrode **58** includes a higher helix pitch for a few windings, provides increased strength in a high stress location, without inhibiting the overall flexibility of the distal portion **52.** It is believed that in situations wherein movement of the tissue within the patient and relative movement between the *in vivo* and *ex vivo* portions of the device create stresses on the device, greater flexibility in a distal portion (and optionally in the intermediate portion relative to the proximal portion) can provide relief from these mechanical stresses, protecting both the integrity of the sensor and the host tissue. Additionally or alternatively, in situations wherein mechanical and/or electrical connections are employed for accurate function, greater stiffness in the proximal portion (and/or the proximal tip) of the device can increase the stability and reliability of these connections. Additionally, this exemplary configuration is advantageous for the reasons described above, and further provides an enhanced mechanical stability by the distribution of forces of the helical wire along the straight wire.

[0095] Methods and devices that are suitable for use in conjunction with aspects of the preferred embodiments are disclosed in U.S. Patent No. 4,994,167 issued February 19, 1991 and entitled "BIOLOGICAL FLUID MEASURING DEVICE"; U.S. Patent No. 4,757,022 issued February July 12, 1988 and entitled "BIOLOGICAL FLUID MEASURING DEVICE"; U.S. Patent No. 6,001,067 issued February December 14, 1999 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Patent No. 6,741,877 issued February May 25, 2004 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Patent No. 6,702,857 issued February March 9, 2004 and entitled "MEMBRANE FOR USE WITH IMPLANTABLE DEVICES"; and U.S. Patent No. 6,558,321 issued February May 6, 2003 and entitled "SYSTEMS AND METHODS FOR REMOTE MONITORING AND MODULATION OF MEDICAL DEVICES." Methods and devices that are suitable for use in conjunction with aspects of the preferred embodiments are disclosed in co-pending U.S. Application No. 10/991,353 filed November 16, 2004 and entitled "AFFINITY DOMAIN FOR ANALYTE SENSOR"; U.S. Application No. 11/055,779 filed February 9, 2005 and entitled "BIOINTERFACE WITH MACRO-AND-MICRO-ARCHITECTURE"; U.S. Application No. 11/004,561 filed December 3, 2004 and entitled "CALIBRATION TECHNIQUES FOR A CONTINUOUS ANALYTE SENSOR"; U.S. Application No. 11/034,343 filed January 11, 2005 and entitled "COMPOSITE MATERIAL FOR IMPLANTABLE DEVICE"; U.S. Application No. 09/447,227 filed November 22, 1999 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 11/021,046 filed December 22, 2004 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 09/916,858 filed July 27, 2001 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 11/039,269 filed January 19, 2005 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 10/897,377 filed July 21, 2004 and entitled "ELECTROCHEMICAL SENSORS INCLUDING ELECTRODE SYSTEMS WITH INCREASED OXYGEN GENERATION"; U.S. Application No. 10/897,312 filed July 21, 2004 and entitled "ELECTRODE SYSTEMS FOR ELECTROCHEMICAL SENSORS"; U.S. Application No. 10/838,912 filed May 3, 2004 and entitled "IMPLANTABLE ANALYTE SENSOR"; U.S. Application No. 10/838,909 filed May 3, 2004 and entitled "IMPLANTABLE ANALYTE SENSOR"; U.S. Application No. 10/838,658 filed May 3, 2004 and entitled "IMPLANTABLE ANALYTE SENSOR"; U.S. Application No. 11/034,344 filed January 11, 2005 and entitled "IMPLANTABLE DEVICE WITH IMPROVED RADIO FREQUENCY CAPABILITIES"; U.S. Application No. 10/896,772 filed July 21, 2004 and entitled "INCREASING BIAS FOR OXYGEN PRODUCTION IN AN ELECTRODE SYSTEM"; U.S. Application No. 10/789,359 filed February 26, 2004 and entitled "INTEGRATED DELIVERY

DEVICE FOR CONTINUOUS GLUCOSE SENSOR"; U.S. Application No. 10/991,966 filed November 17, 2004 and entitled "INTEGRATED RECEIVER FOR CONTINUOUS ANALYTE SENSOR"; U.S. Application No. 10/646,333 filed August 22, 2003 and entitled "OPTIMIZED SENSOR GEOMETRY FOR AN IMPLANTABLE GLUCOSE SENSOR"; U.S. Application No. 10/896,639 filed July 21, 2004 and entitled "OXYGEN ENHANCING MEMBRANE SYSTEMS FOR IMPLANTABLE DEVICES"; U.S. Application No. 10/647,065 filed August 22, 2003 and entitled "POROUS MEMBRANES FOR USE WITH IMPLANTABLE DEVICES"; U.S. Application No. 10/896,637 filed July 21, 2004 and entitled "ROLLED ELECTRODE ARRAY AND ITS METHOD FOR MANUFACTURE"; U.S. Application No. 09/916,711 filed July 27, 2001 and entitled "SENSOR HEAD FOR USE WITH IMPLANTABLE DEVICE"; U.S. Application No. 11/021,162 filed December 22, 2004 and entitled "SENSOR HEAD FOR USE WITH IMPLANTABLE DEVICES"; U.S. Application No. 11/007,920 filed December 8, 2004 and entitled "SIGNAL PROCESSING FOR CONTINUOUS ANALYTE SENSOR"; U.S. Application No. 10/695,636 filed October 28, 2003 and entitled "SILICONE COMPOSITION FOR BIOCOMPATIBLE MEMBRANE"; U.S. Application No. 11/038,340 filed January 18, 2005 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA"; U.S. Application No. 11/007,635 filed December 7, 2004 and entitled "SYSTEMS AND METHODS FOR IMPROVING ELECTROCHEMICAL ANALYTE SENSORS"; U.S. Application No. 10/885,476 filed July 6, 2004 and entitled "SYSTEMS AND METHODS FOR MANUFACTURE OF AN ANALYTE-MEASURING DEVICE INCLUDING A MEMBRANE SYSTEM"; U.S. Application No. 10/648,849 filed August 22, 2003 and entitled "SYSTEMS AND METHODS FOR REPLACING SIGNAL ARTIFACTS IN A GLUCOSE SENSOR DATA STREAM"; U.S. Application No. 10/153,356 filed May 22, 2002 and entitled "TECHNIQUES TO IMPROVE POLYURETHANE MEMBRANES FOR IMPLANTABLE GLUCOSE SENSORS"; U.S. Application No. 10/846,150 filed May 14, 2004 and entitled "ANALYTE MEASURING DEVICE"; U.S. Application No. 10/842,716 filed May 10, 2004 and entitled "BIOINTERFACE MEMBRANES INCORPORATING BIOACTIVE AGENTS"; U.S. Application No. 10/657,843 filed September 9, 2003 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 10/768,889 filed January 29, 2004 and entitled "MEMBRANE FOR USE WITH IMPLANTABLE DEVICES"; U.S. Application No. 10/633,367 filed August 1, 2003 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA"; U.S. Application No. 10/632,537 filed August 1, 2003 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA"; U.S. Application No. 10/633,404 filed August 1, 2003 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA"; and U.S. Application No.

10/633,329 filed August 1, 2003 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA."

[0096] All references cited herein, including but not limited to published and unpublished applications, patents, and literature references, are incorporated herein by reference in their entirety and are hereby made a part of this specification. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

[0097] The term "comprising" as used herein is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

[0098] All numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth herein are approximations that may vary depending upon the desired properties sought to be obtained. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of any claims in any application claiming priority to the present application, each numerical parameter should be construed in light of the number of significant digits and ordinary rounding approaches.

[0099] The above description discloses several methods and materials of the present invention. This invention is susceptible to modifications in the methods and materials, as well as alterations in the fabrication methods and equipment. Such modifications will become apparent to those skilled in the art from a consideration of this disclosure or practice of the invention disclosed herein. Consequently, it is not intended that this invention be limited to the specific embodiments disclosed herein, but that it cover all modifications and alternatives coming within the true scope and spirit of the invention.

WHAT IS CLAIMED IS:

1. A transcutaneous analyte sensor, the sensor comprising an elongated flexible portion, wherein the elongated flexible portion has a variable stiffness along at least a portion of its length.

2. The sensor of claim 1, wherein the sensor comprises at least one wire in a helical configuration, and wherein the variable stiffness is provided by a variable pitch of the helical configuration.

3. The sensor of claim 1, wherein the sensor comprises at least one wire in a helical configuration, and wherein the variable stiffness is provided by a variable cross-section of the wire.

4. The sensor of claim 1, wherein the sensor comprises at least one wire, and wherein the variable stiffness is provided by a variable hardness of the wire.

5. The sensor of claim 4, wherein the variable stiffness of the elongated flexible portion is produced by subjecting the wire to an annealing process.

6. The sensor of claim 1, wherein the sensor comprises at least one wire, the wire having a variable diameter.

7. The sensor of claim 1, wherein a distal portion of the sensor is more flexible than a proximal portion of the sensor.

8. The sensor of claim 1, wherein an intermediate portion of the sensor is more flexible than at least one of a distal portion of the sensor and a proximal portion of the sensor.

9. The sensor of claim 1, wherein a distal tip of the sensor is stiffer than at least one of an intermediate portion of the sensor and a proximal portion of the sensor.

10. A transcutaneous analyte sensor, the sensor comprising a distal portion, an intermediate portion, and a proximal portion, wherein the distal portion is adapted to be inserted through a skin of a host, wherein the proximal portion is adapted to remain substantially external to the host when the distal portion is inserted in the host, and wherein a stiffness of the sensor is variable along a length of the sensor.

11. The sensor of claim 10, wherein the proximal portion is stiffer than the distal portion.

12. The sensor of claim 11, wherein the sensor comprises at least one wire in a helical configuration, and wherein a difference in stiffness of the distal portion and the proximal portion is provided by varying a pitch of the helical configuration.

13. The sensor of claim 11, wherein the sensor comprises at least one wire in a helical configuration, and wherein a difference in flexibility of the distal portion and the proximal portion is provided by a varying a cross-section of the wire.

14. The sensor of claim 11, wherein the sensor comprises at least one wire, and wherein a difference in flexibility of the distal portion and the proximal portion is provided by a varying a hardness of the wire.

15. The sensor of 14, wherein a variation in stiffness of the elongated flexible portion is produced by subjecting the wire to an annealing process.

16. The sensor of claim 11, wherein the intermediate portion is more flexible than at least one of the distal portion and the proximal portion.

17. The sensor of claim 16, wherein the distal portion comprises a distal tip on an end of the sensor that is stiffer a substantial portion of the sensor.

18. The sensor of claim 10, wherein the intermediate portion is more flexible than at least one of the distal portion and the proximal portion.

19. The sensor of claim 18, wherein the distal portion comprises a distal tip on an end of the sensor that is stiffer a substantial portion of the sensor.

20. A transcutaneous analyte sensor, the sensor comprising an *in vivo* portion adapted for insertion into a host and an *ex vivo* portion adapted for operable connection to a device that remains external to the host, wherein the sensor is configured to absorb a relative movement between the *ex vivo* portion of the sensor and the *in vivo* portion of the sensor.

21. The sensor of claim 20, wherein the sensor is configured to absorb a relative movement by a flexibility of at least an intermediate portion located between the *in vivo* portion and the *ex vivo* portion.

22. The sensor of claim 20, wherein the device comprises a housing adapted for mounting on a skin of a host, wherein the housing comprises electrical contacts operably connected to the sensor.

23. The sensor of claim 21, wherein the *ex vivo* portion of the sensor is has a preselected stiffness to maintain a stable connection between the sensor and the electrical contacts.

24. The sensor of claim 20, wherein the *in vivo* portion of the sensor has a preselected flexibility to minimize mechanical stresses caused by motion of the host.

25. The sensor of claim 20, wherein a stiffness of the *ex vivo* portion of the sensor is greater than a stiffness of the *in vivo* portion of the sensor.

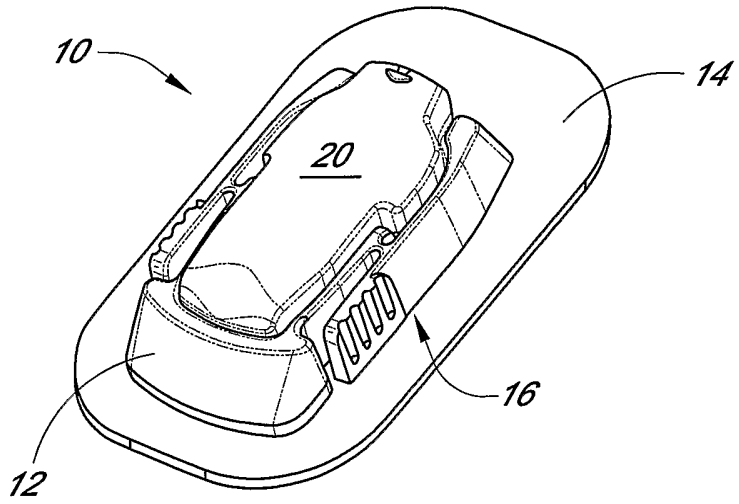


FIG. 1A

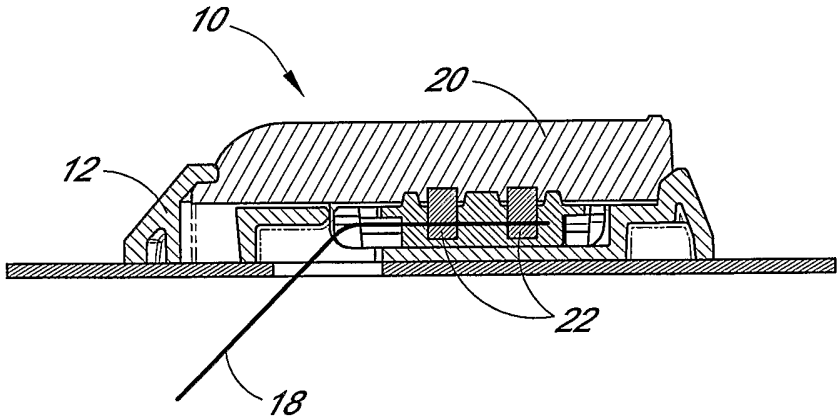


FIG. 1B

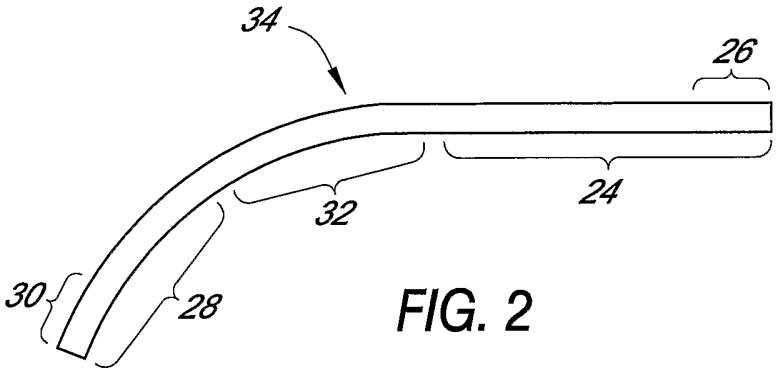


FIG. 2

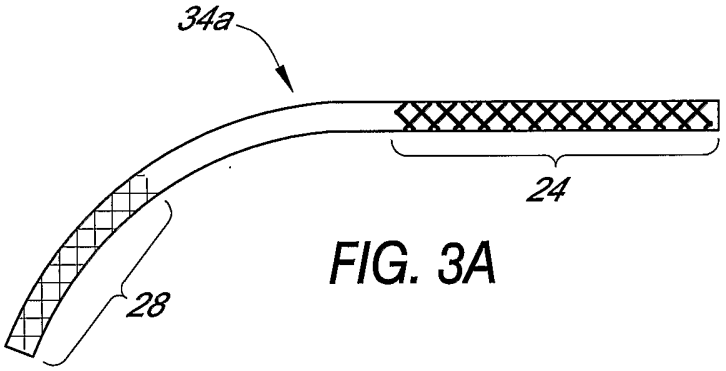


FIG. 3A

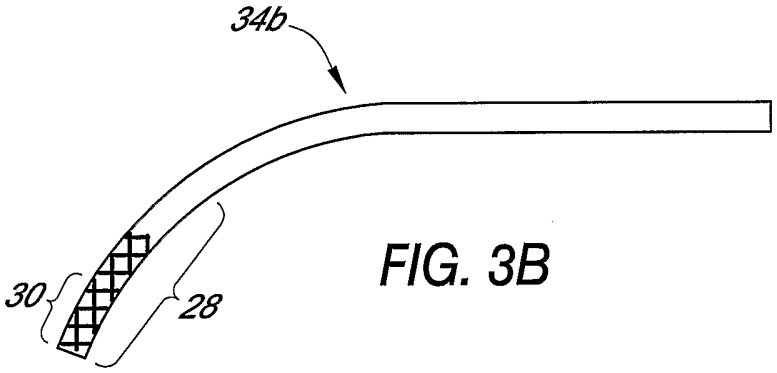


FIG. 3B

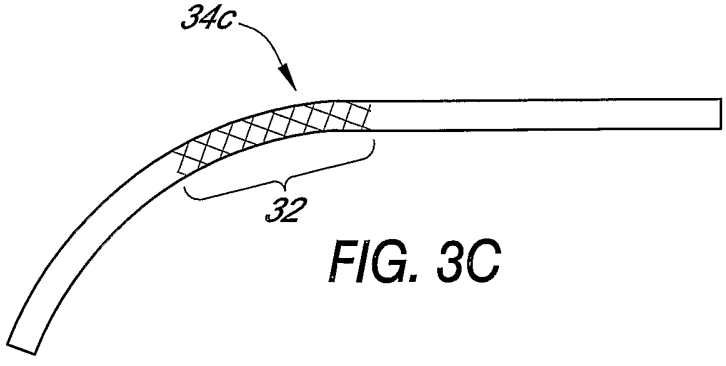


FIG. 3C

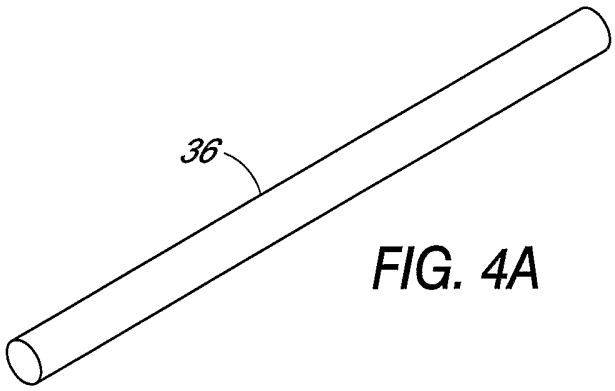


FIG. 4A

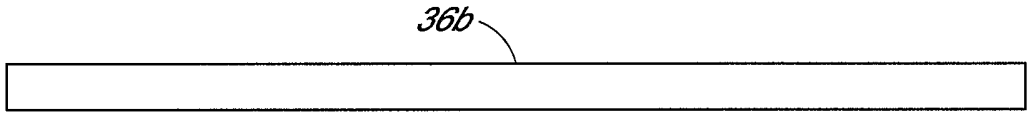


FIG. 4B

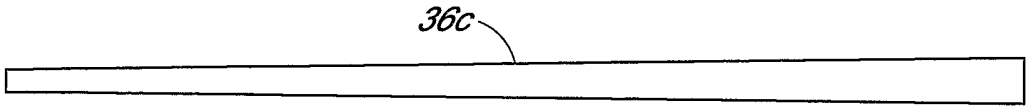


FIG. 4C

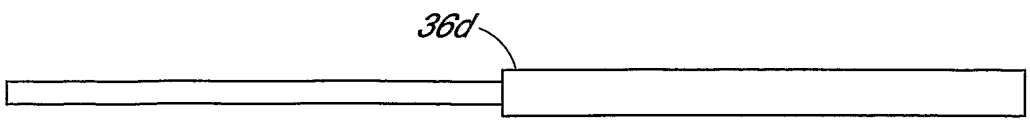


FIG. 4D

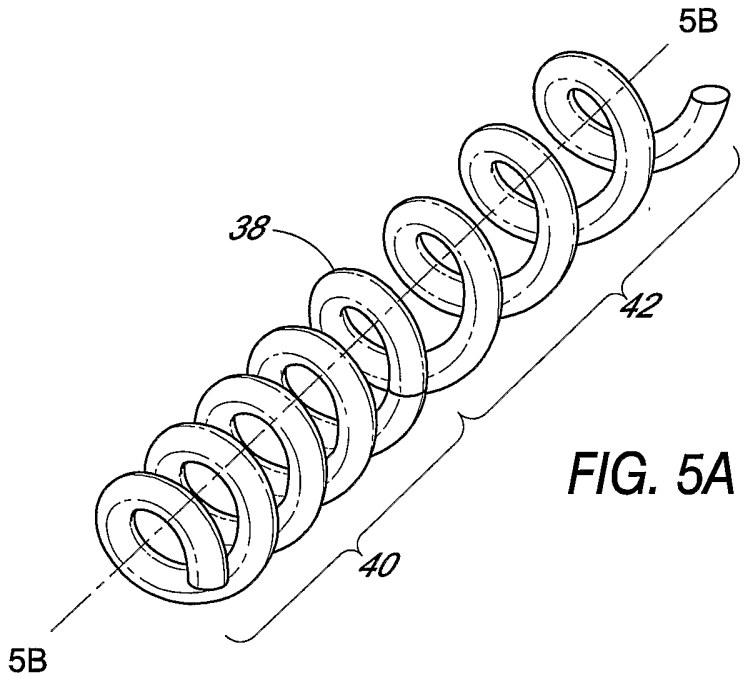


FIG. 5A

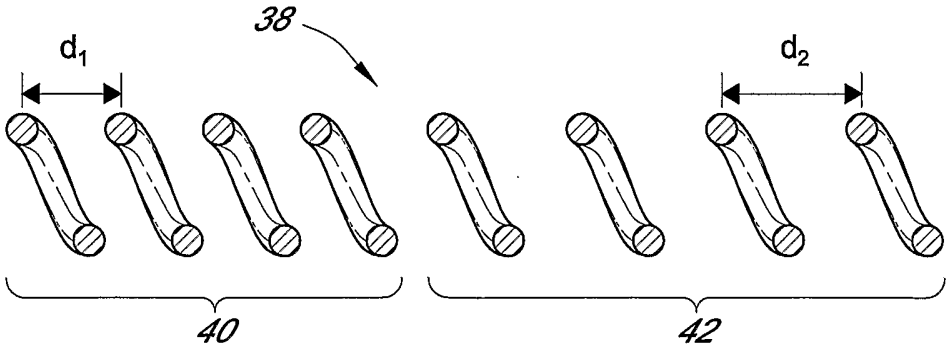


FIG. 5B

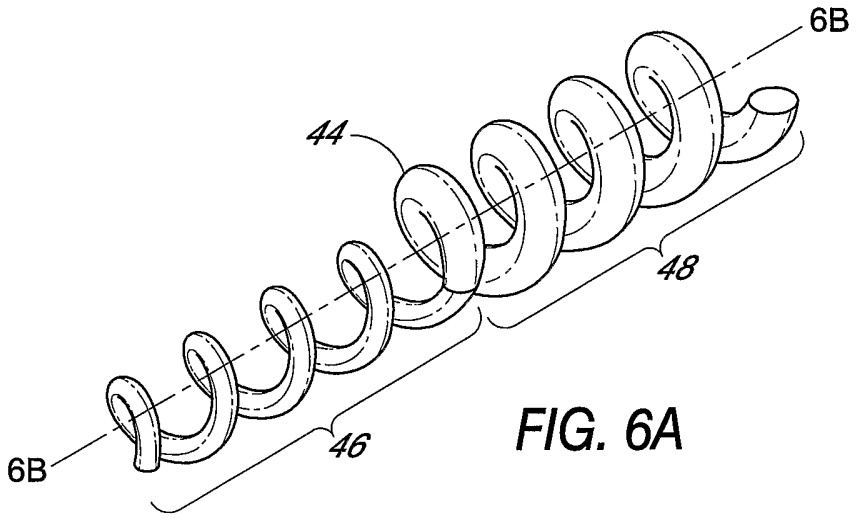


FIG. 6A

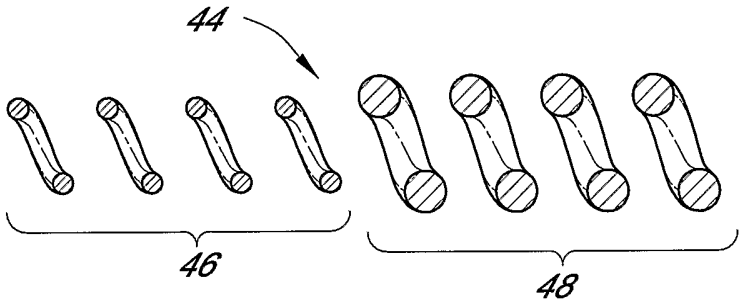


FIG. 6B

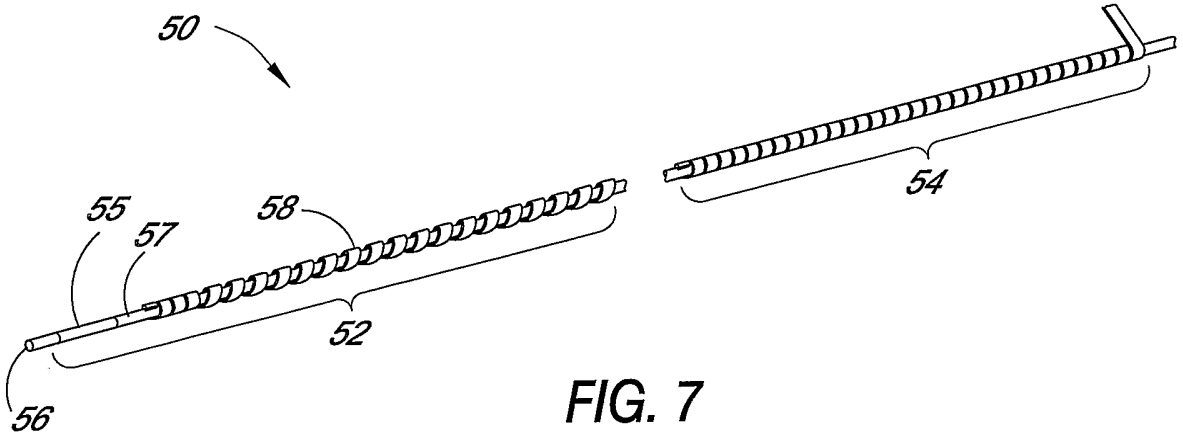


FIG. 7

INTERNATIONAL SEARCH REPORT

national Application No
T/US2005/024994

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/097082 A1 (PURDY PHILLIP D ET AL) 22 May 2003 (2003-05-22) paragraphs '0077!, '0080!, '0136!	1,2,10
A	US 2002/119711 A1 (VANANTWERP NANNETTE M ET AL) 29 August 2002 (2002-08-29) abstract	1,10
A	EP 0 838 230 A (TERUMO KABUSHIKI KAISHA) 29 April 1998 (1998-04-29) page 1, lines 17-20 page 7, lines 19-25	1,10

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 November 2005	15/11/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Martelli, L

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 20-25

These claims do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem of absorbing a relative movement between the ex vivo portion and the in vivo portion of the sensor, without providing the technical features (variable stiffness) necessary for achieving this result as explained, e.g., on paragraph 74 of the description.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/024994

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 20-25
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

ational Application No
/US2005/024994

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 1408844 A2	21-04-2004
		JP 2004534590 T	18-11-2004
		WO 03005908 A2	23-01-2003
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		US 2003093105 A1	15-05-2003
		US 2003014016 A1	16-01-2003
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EP 0838230 A	29-04-1998	DE 69724903 D1	23-10-2003
		DE 69724903 T2	15-07-2004
		US 6001068 A	14-12-1999