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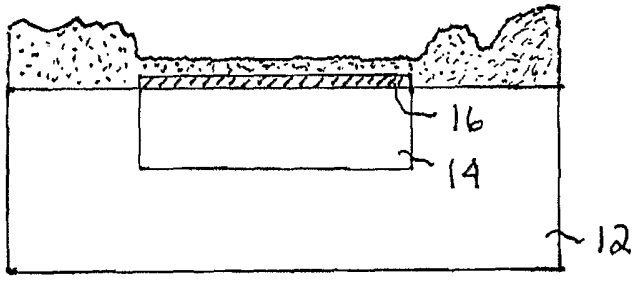
(54) Title: IMPLANTABLE SENSOR WITH BIOCOMPATIBLE COATING FOR CONTROLLING TISSUE GROWTH



(57) Abstract: [0001] All or a portion of a surface of an implantable sensor is covered with a biocompatible coating formed at least partially of a biomaterial matrix having properties that promote a substantially even growth of tissue cells over the surface of the coating. Additional materials, such as growth factors, agents that recruit endogenous stem cells, and cell adhesion motif arginine, glycine, aspartic acid may be included in the coating. Autologous cells may be added to the coating prior to implantation. The sensor surface may also be textured, by etching or abrading, in order to promote even tissue growth. Alternatively, the sensor surface may be covered with a coating having properties that inhibit the growth of tissue. These coatings may include a biomaterial, a biomaterial matrix having a drug, such as a sirolimus or a steroid, an active component, or a self assembled monolayer.

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IMPLANTABLE SENSOR WITH BIOCOMPATIBLE COATING FOR CONTROLLING TISSUE GROWTH

CLAIM OF PRIORITY

[0001] Benefit of priority is hereby claimed to U.S. Patent Application Serial Number 10/888,340, filed on July 9, 2004, which application is herein incorporated by reference.

BACKGROUND OF THE INVENTION

Field of the Invention:

[0002] The invention relates generally to implantable medical devices and, more particularly, to implantable sensors having a biocompatible coating that controls the growth of tissue, or inhibits the growth of tissue, over and around the sensor.

Description of Related Art:

[0003] Human implantable sensors may be used to gather important information about the body's internal environment on a regular basis. Pressure inside an artery, fluid flow inside an artery, body temperature, posture sensing and monitoring of chemical changes are among the different types of information that could be gathered by an implantable sensor.

[0004] A problem exists in that any sensor that is implanted into living tissue is subject to tissue growth over and around it. Some tissue growth may be desired in order to embed the sensor and make it a more integral part of the body. However, the sensor's calibration and sensitivity can be adversely effected by different factors of this tissue growth including, but not limited to, the type of tissue that grows over the sensor, the thickness, and the evenness of the tissue growth. For example, in the case of a pressure sensor, the sensitivity of the sensor is affected by the thickness of the tissue while sensor drift is affected by the tension exerted on the sensor by the tissue. This tension, in turn, leads to additional pressure bias that affects the accuracy of the pressure measurements provided by the sensor.

[0005] Those skilled in the art have recognized a need for providing a more consistent and predictable growth process in relation to implanted sensors to thereby mitigate the problem of unpredictable tissue growth and its impact on the sensitivity and calibration of sensors. The need for inhibiting tissue growth to further mitigate the foregoing problems has also been recognized. The invention fulfills these needs and others.

SUMMARY OF THE INVENTION

[0006] Briefly, and in general terms, the invention is directed to implantable sensors having a biocompatible coating that either controls the growth of tissue, or inhibits the growth of tissue, over and around the sensor. As used herein, "inhibit" means to substantially prevent the growth or formation of tissue. "Control" means to promote the growth or formation of a substantially even layer of tissue.

[0007] In one aspect, all or a portion of a sensor surface is covered with a biocompatible coating formed at least partially of a biomaterial matrix having properties that promote a substantially even growth of tissue cells over the surface of the coating. Additional materials, such as growth factors, agents that recruit endogenous stem cells and cell adhesion motif arginine, glycine, aspartic acid may be included in the coating. Also, autologous cells may be added to the coating prior to implantation.

[0008] In another aspect, all or a portion of a sensor surface is textured in order to promote even tissue growth over the surface. The texture may be provided by etching or abrading the surface of the interface.

[0009] In other aspects, all or a portion of a sensor surface is covered with a coating having properties that inhibit the growth of tissue. These coatings may include a biomaterial, such as polytetraflouroethylene (PTFE) and polyethylene glycol (PEG) or a biomaterial matrix having an active component that imparts growth-inhibiting properties to the coating.

[0010] These and other aspects and advantages of the invention will become apparent from the following detailed description and the accompanying drawings which illustrate by way of example the features of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] Figure 1 is a cross section of a sensor including a sensor body and a sensor interface;

[0012] FIG. 2a is a cross section of the sensor of FIG. 1 including a biocompatible coating over a surface of the sensor interface;

[0013] FIG. 2b is a cross section of the coated sensor of FIG. 2a depicting substantially even tissue growth over the coated surface of the sensor interface and uneven tissue growth over the uncoated surface of the sensor body;

[0014] FIG. 2c is a cross section of the coated sensor of FIG. 2a depicting substantially no tissue growth over the coated surface of the sensor interface and uneven tissue growth over the uncoated surface of the sensor body;

[0015] FIG. 3a is a cross section of the sensor of FIG. 1 including a biocompatible coating over a surface of the sensor interface and a surface of the sensor body;

[0016] FIG. 3b is a cross section of the coated sensor of FIG. 3a depicting substantially even tissue growth over the coated surface of the sensor interface and the coated surface of the sensor body; and

[0017] FIG. 3c is a cross section of the coated sensor of FIG. 3a depicting substantially no tissue growth over the coated surface of the sensor interface and the coated surface of the sensor body.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0018] The invention is directed to implantable sensors which are coated with a biocompatible coating that either controls or inhibits the growth of tissue over and around the sensor. The sensor may be, for example, anyone of a pressure sensor, posture sensor, chemical sensor, temperature sensor or flow sensor that is introduced temporarily or permanently into a mammal for the prophylaxis or therapy of a medical condition and that is designed to monitor physiological activity within the body. These sensors may be introduced subcutaneously, percutaneously or surgically to rest within an organ, tissue or lumen of an organ, such as arteries, veins, ventricles or atrium of the heart.

[0019] With reference to FIG. 1, an exemplary sensor 10 includes a sensor body 12 and a sensor interface 14. The sensor interface 14 is that portion of the sensor 10 that provides the interface between the actual sensing elements (not shown) within the sensor and that portion or element, *e.g.*, blood, vascular tissue, atrial wall, *etc.*, of the body from which the activity being monitored propagates. For example, with respect to a pressure sensor, the sensor interface may include a pressure diaphragm. The sensor interface 14 shown in FIG. 1 is flush with a surface of the sensor body 12. In other sensor configurations, the sensor interface 14 may protrude or project from the surface of the sensor body 12 or may be recessed within the sensor body. The sensor body 12 and/or sensor interface 14 may be made of a biocompatible metal, such as stainless steel, Nitinol, gold, tantalum, titanium, platinum or platinum irdium, or other biocompatible metals and/or alloys such as carbon or carbon fiber. Alternatively, the sensor body 12 and/or sensor interface 14 may be made of a biocompatible plastic or polymer.

[0020] The sensor 10 may be included as part of an implanted device, such as the lead of a cardiac rhythm management device, in which case the data gathered by the sensor is transferred to the device through a hardwire electrical connection. The sensor 10 may be configured as a wireless device, in which case the sensor interface 14 may include a transmission device for transmitting the data gathered by the sensor to a receiver remote from the sensor. For example, the sensor interface 14 may be formed of an optically compatible material that allows for certain wavelength of intra-red light to pass efficiently. In this configuration, the biocompatible coating not only serves to maintain sensor calibration and sensitivity, it also protects against interference that uneven tissue growth may impart on data transmission between transmitter and receiver. A wireless sensor may, for example, be mounted to a stent to facilitate implantation.

[0021] While the sensor 10 shown in FIG. 1 includes only one sensor interface 14, a sensor may have more than one such interface. For example, a wireless sensor may have one sensor interface 14 for its sensing functions and a second, separate sensor interface for its data transmission functions. The

biocompatible coating 16 covers at least one of these interfaces 14 and preferably, both of the interfaces.

[0022] With reference to FIG. 2a, the sensor 10 may be configured such that a layer 16 of the biocompatible coating covers only a surface of the sensor interface 14 portion of the sensor 10. Alternatively, as shown in FIG. 3a, the layer 16 may cover the entire surface of the sensor 10 including the sensor interface 14. In other configurations (not shown), the entire surface of the sensor body or only select portions may be covered with the coating. As explained further below, in all configurations, the composition of the coating is such that it either promotes an even layer of cell growth over the coated surfaces of the sensor (as shown in FIGS. 2b and 3b) or it inhibits cell growth over the coated surfaces of the sensor (as shown in FIGS. 2c and 3c). Thus, after implantation of the sensor, the sensitivity and calibration of the sensor will, in the case of even tissue growth, change in a way that is more predictable or, in the case of substantially no tissue growth, not experience a significant change. The inhibition of tissue growth and/or the promotion of a more even tissue growth of a particular type helps to ensure that the sensor's sensitivity and calibration changes remain within a desired range and facilitates sensor recalibration after tissue growth.

[0023] In one embodiment, the biocompatible coating consists of a biomaterial matrix favorable to tissue growth allowing for formation of a substantially even neointimal layer of tissue over the sensor. The biomaterial matrix comprises a polymer, oligomer or co-polymer for coating the sensor from various types and sources, including, natural or synthetic polymers, which are at least biocompatible. The polymers may also be biodegradable and/or bioabsorbable. For example, a natural polymer such as an extracellular matrix (ECM) material may be used, including, for example, intestine submucosa (SIS) and urinary bladder matrix (UBM) substances. Such ECMs are composed of three major classes of biomolecules including structured proteins, *e.g.*, collagen and elastin, specialized proteins, *e.g.*, fibrillin, fibronectin and laminin and proteoglycans. Proteoglycans are composed of a protein core to which is attached long chains of repeating disaccharide units termed of glycosaminoglycans (GAGs) forming extremely complex high molecular weight

components of the ECM. Independent of their inclusion in the ECMs, both proteoglycans and proteins, including collagen, fibrin, elastin, fibrillin, fibronectin, and laminin, may themselves be used as the polymer. Another example of a natural polymer which may be used as a coating is phosphytidyl choline.

[0024] Synthetic polymers may be selected from polyhydroxyvalerate, poly(L)lactic acid, polycaprolactone, polylactide-co-glycolide, polyhydroxybutyrate, polyhydroxybutyrate-co-valerate, polydioxanone, polyorthoesters, polyanhydrides, polyacetic or polyglycolic acid and derivatives thereof, poly(D,L)lactic acid, polyglycolic acid-co-trimethylene carbonate, polysebacic acid, polylactic-co-sebacic acid, polyglycolic-co-sebacid acid, polyphosphoesters, polyphosphoester urethanes, polyamino acids, such as polylysine, lactic/glycolic acid copolymers, and ion exchange resins such as sulfonated polytetrafluorethylene, or combinations thereof; cyanoacrylates, polytrimethylene carbonate, polyiminocarbonate, copolyether-esters (*e.g.*, PEO/PLA), polyalkylene oxalates and polyphosphazenes. Polymers with a relatively low chronic tissue response such as polyurethanes, silicones, and polyesters could be used.

[0025] Other polymers could also be used if they can be dissolved and cured or polymerized on the sensor such as polyolefin, polyisobutylene and ethylene-alphaolefin copolymers; acrylic polymers and copolymers, vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride and polyvinylidene chloride; polyacrylonitrile; polyvinyl ketones; polyvinyl aromatics, such as polystyrene; polyvinyl esters, such as polyvinyl acetate; copolymers of vinyl monomers with each other and olefins, such as ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins, and ethylene-vinyl acetate copolymers; polyamides, such as Nylon 66 and polycaprolactam; alkyd resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins; rayon and rayon-triacetate.

[0026] The polymer coating may be applied to the sensor is any one of several ways known in the art including those disclosed in the following U.S. Patents, the disclosures of which are hereby incorporated by reference:

6,713,119, titled "Biocompatible Coating for a Prosthesis and a Method of Forming the Same," 6,673,385, titled "Methods for Polymeric Coating Stents," 6,616,765, titled "Apparatus and Method for Depositing a Coating onto a Surface of a Prosthesis," 6,555,157, titled "Method for Coating an Implantable Device and System for Performing the Method," 6,544,582, titled "Method and Apparatus for Coating an Implantable Device" and 6,506,437, titled "Methods of Coating an Implantable Device Having Depots Formed in a Surface Thereof."

[0027] In another embodiment, the biocompatible coating includes a biomaterial matrix having an added growth factor, agent, cytokine or the like, which stimulates local cell growth to promote a substantially even tissue growth. The coating is preferably formed to provide a sustained release of the agent. The biomaterial matrix may be either a natural or synthetic polymer like those previously listed. The added growth factor may include one or more of vascular endothelial cell growth factor (VEGF) and isoforms, basic fibroblast growth factor (bFGF), platelet-induced growth factor (PDGF), transforming growth factor beta (TGF.b), acidic fibroblast growth factor (aFGF), osteonectin, angiopoietin 1, angiopoietin 2, insulin-like growth factor (IGF), platelet-derived growth factor AA (PDGF-AA), platelet-derived growth factor BB (PDGF-BB), platelet-derived growth factor AB (PDGF-AB), granulocyte-macrophage colony-stimulating factor (GM-CSF), and the like, or functional fragments thereof.

[0028] In another embodiment, the biocompatible coating includes a biomaterial matrix having an added agent, cytokine or the like, which recruits endogenous stem cells to promote a substantially even tissue growth. The coating is preferably formed to provide a sustained release of the agent. The biomaterial matrix may be either a natural or synthetic polymer like those previously listed. The added agent may include one or more of granulocyte colony-stimulating factor (G-CSF), stem cell factor (SCF-l), stromal-derived factor (SDF-l), insulin-like growth factor (IGH) or hepatocyte growth factor (HGF).

[0029] In another embodiment, the biocompatible coating includes a biomaterial matrix having attached thereto a cell adhesion motif arginine, glycine, aspartic acid (RGD), which is a ligand for integrin cell adhesion receptors. RGD recruits the adhesion of cells and thus forms a type of

neointimal layer of endothelia cells to thereby promote a substantially even tissue growth. The biomaterial matrix may be either a natural or synthetic polymer like those previously listed.

[0030] In each of the preceding three embodiments, the biocompatible coating, *i.e.*, biomaterial matrix plus added growth factor, agent and/or RGD, may be formed and applied to the sensor is anyone of several ways known in the art including those disclosed in the previously cited U.S. Patents and the following U.S. Patents, the disclosures of which are also hereby incorporated by reference: 6,743,462, titled "Apparatus and Method for Coating Implantable Devices," 6,716,444, titled "Barriers for Polymer-Coated Implantable Medical Devices and Method for Making the Same" and 6,712,845, titled "Coating for a Stent and a Method of Forming the Same."

[0031] In another embodiment, the biocompatible coating is formed to provide a sustained release of an active component that inhibits tissue growth. The coating is formed of a biomaterial matrix, like those previously listed, and an active component. The active component may include, for example, a sirolimus or a steroid. The coating may be formed and applied to the sensor in any one of the ways described in the previously cited U.S. Patents.

[0032] Alternatively, the active component may include an anti-thrombotic substance and an anti-inflammatory substance. Possible anti-thrombotic substances include heparin, sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogs, D-phe-pro-arg-chloromethylketone, dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antibody, and recombinant hirudin. Possible anti-inflamatory substance includes aspirin, diclofenac, etodolac, ibuprofen, ketoprofen, ketorolac, nabumetone, naproxen, oxaprozin, clobetasol, diflucortolone, flucinolone, halcinolonide, halobetasol, dexamethasone, betamethasone, corticol, cortisone, prednisone, and prednisolone.

[0033] In another configuration, instead of the anti-thrombotic substance of the active component being released, the sensor is coated with an anti-thrombogenic material which is not substantially released from the surface. Such anti-thrombogenic coatings can be made from either an active thrombin inhibitor, typically heparin, a heparin derivative, or a heparin analog, or can be

made from a passively thromboresistant material, such as a hydro-gel, or any combination of active and passive thromboresistant material. Examples of useful hydro-gels include polyethylene oxide, albumin, hydrophilic poly-(meth)acrylates, and hydrophilic poly-urethanes. In another embodiment, an anti-thrombotic substance may also be releasably contained with the anti-inflammatory substance in the anti-thrombogenic coating. Details of these active components are disclosed in U.S. Patent Application Publication No. 20010007082, titled "Device and Active Component for Inhibiting Formation of Thrombus-Inflammatory Cell Matrix," which is hereby incorporated by reference.

[0034] In another embodiment, the biocompatible coating is a biomaterial having properties that substantially inhibit growth of tissue cells over its surface. The biomaterial may be polytetraflouroethylene (PTFE) or polyethylene glycol (PEG). In another configuration, the biomaterial is formed of an anti-thrombogenic material, such as those described above. The material may be applied to the sensor in anyone of several ways known in the art.

[0035] In another embodiment, substantially even tissue cell growth is promoted by texturing portions of the sensor. As used herein, a "textured" surface includes a surface that is roughened, unsmooth or uneven. For example, metallic portions of the sensor may be textured by etching or abrading the surface of the metal. Such texturing is intended to promote cell adhesion to the surface of the metal which will lead to the formation of a neointimal layer of endothelial cells and ECM which then inhibits the formation of thrombosis or other potential fibrotic responses.

[0036] In another embodiment, the biocompatible coating includes a biomaterial matrix that is applied during the manufacturing of the sensor (using known methods or those method described in the U.S. Patents previously incorporated by reference) and an additive including autologous cells that are added to the matrix after the manufacturing process and at a pre-defined time prior to actual implantation of the sensor in the body. The autologous cells may be added to the biomaterial matrix by any standard method.

[0037] In one such embodiment, the additive includes disassociated autologous cells which may be harvested from the patient's mesenchymal stem

cells (MSC), endothelial progenitor cells (EPC), smooth muscle cells (SMC), endothelial cells, hematopoietic stem cells, for instance, cells from cord blood and isolated $CD34^+$ cells, multipotent adult progenitor cells, side population stem cells, adult stem cells and embryonic stem cells or differentiated cells derived from any of, but not limited to, the stem cells listed above. The biomaterial matrix with autologous cells is preferably cultured in vitro prior to implantation in the patient. The particular autologous cells added to the matrix may be selected based on the implantation cite. For example, EPC cells would most likely be used for intra artery implants while SMC cells would be used for intra muscle implants.

[0038] Possible biomaterial matrixes for use in this embodiment include the polymers previously listed. Other useful polymers include polymers or copolymers of caprolactones, carbonates, amides, amino acids, orthoesters, acetals, cyanoacrylates and degradable urethanes, as well as copolymers of these with straight chain or branched, substituted or unsubstituted, alkanyl, haloalkyl, thioalkyl, aminoalkyl, alkenyl, or aromatic hydroxy- or di-carboxylic acids. In addition, the biologically important amino acids with reactive side chain groups, such as lysine, arginine, aspartic acid, glutamic acid, serine, threonine, tyrosine and cysteine, or their enantiomers, may be included in copolymers with any of the aforementioned materials.

[0039] In another embodiment, the biocompatible coating includes a self-assembled monolayer (SAM) coating, such as pre-formed carboxylic acid alkanethiolate. This coating prevents cell growth and thus the growth of tissue on the sensor surface. In this embodiment, the sensor surface includes gold which allows for the attachment of the SAM coating. The gold may be an integral part of the sensor surface or, alternatively, the gold may be included in a layer of metallic material that is applied to the sensor surface prior to the application of the SAM coating.

[0040] While the sensors shown in the figures and described have only one type of biocompatible coating, *i.e.*, either growth inhibiting or even-growth promoting, a sensor may be coated with both types of coatings. For example, it may be beneficial to apply the growth inhibiting coating only to the sensor interface and the even-growth promoting coating to the remainder of the sensor.

[0041] It will be apparent from the foregoing that while particular forms of the invention have been illustrated and described, various modifications can be made without departing from the spirit and scope of the invention. Accordingly, it is not intended that the invention be limited, except as by the appended claims.

WHAT IS CLAIMED IS:

1. A sensor comprising:

a sensor surface; and

a biocompatible coating comprising a biomaterial matrix, the coating covering at least a portion of the sensor surface and having properties that promote a substantially even growth of tissue cells over the surface of the coating.

2. The sensor of claim 1 wherein the biomaterial matrix comprises a natural polymer.

3. The sensor of claim 2 wherein the natural polymer comprises extracellular matrix material.

4. The sensor of claim 3 wherein the extracellular matrix material is selected from the group consisting of intestine submucosa and urinary bladder matrix.

5. The sensor of claim 2 wherein the natural polymer comprises a protein.

6. The sensor of claim 5 wherein the protein is selected from the group consisting of collagen, fibrin, elastin, fibrillin, fibronectin, and laminin.

7. The sensor of claim 2 wherein the natural polymer comprises proteoglycans.

8. The sensor of claim 2 wherein the natural polymer comprises phosphytidyl choline.

9. The sensor of claim 1 wherein the biomaterial matrix comprises a synthetic polymer.

10. The sensor of claim 9 wherein the synthetic polymer is selected from the group consisting of polyhydroxyvalerate, poly(L)lactic acid, polycaprolactone, polylactide-co-glycolide, polyhydroxybutyrate, polyhydroxybutyrate-co-valerate, polydioxanone, polyorthoesters, polyanhydrides, polyacetic, polyglycolic acid, poly(D,L)lactic acid, polyglycolic acid-co-trimethylene carbonate, polysebacic acid, polylactic-co-sebacic acid, polyglycolic-co-sebacid acid, polyphosphoesters, polyphosphoester urethanes, polyamino acids, ion exchange resins, cyanoacrylates, polytrimethylene carbonate, polyiminocarbonate, copolyether-esters, polyalkylene oxalates and polyphosphazenes.

11. The sensor of claim 9 wherein the synthetic polymer is selected from the group consisting of polyurethanes, silicones and polyesters.

12. The sensor of claim 9 wherein the synthetic polymer is selected from the group consisting of polyolefin, polyisobutylene, ethylene-alphaolefin copolymers, acrylic polymers and copolymers, vinyl halide polymers and copolymers, polyvinyl ethers, polyvinylidene halides, polyacrylonitrile, polyvinyl ketones, polyvinyl aromatics, polyvinyl esters, copolymers of vinyl monomers with each other and olefins, polyamides, alkyd resins, polycarbonates, polyoxymethylenes, polyimides, polyethers, epoxy resins, rayon and rayon-triacetate.

13. The sensor of any one of claims 1 to 12 wherein the coating further comprises a growth factor.

14. The sensor of claim 13 wherein the growth factor is selected from the group consisting of vascular endothelial cell growth factor (VEGF) and isoforms, basic fibroblast growth factor (bFGF), platelet-induced growth factor (PDGF), transforming growth factor beta (TGF.b), acidic fibroblast growth factor (aFGF), osteonectin, angiopoietin 1, angiopoietin 2, insulin-like growth factor (IGF), platelet-derived growth factor AA (PDGF -AA), platelet-derived growth factor BB (PDGF-BB), platelet-derived growth factor AB (PDGF-AB), granulocyte-

macrophage colony-stimulating factor (GM-CSF), and the like, or functional fragments thereof.

15. The sensor of any one of claims 1 to 14 wherein the coating further comprises an agent that recruits endogenous stem cells.

16. The sensor of claim 15 wherein the agent is selected from the group consisting of granulocyte colony-stimulating factor (G-CSF), stem cell factor (SCF-1), stromal-derived factor (SDF-l), insulin-like growth factor (IGH) and hepatocyte growth factor (HGF).

17. The sensor of any one of claims 1 to 16 wherein the coating further comprises cell adhesion motif arginine, glycine, aspartic acid (RGD).

18. A sensor comprising:

a sensor surface formed of a metallic material;

wherein at least a portion of the sensor surface is textured to promote a substantially even growth of tissue cells over the portion.

19. A sensor comprising:

a sensor surface; and

a biocompatible coating comprising a biomaterial matrix and autologous cells, the coating covering at least a portion of the surface and having properties that promote a substantially even growth of tissue cells over the surface of the coating.

20. The sensor of claim 19 wherein the biomaterial matrix comprises a natural polymer.

21. The sensor of claim 20 wherein the natural polymer comprises extracellular matrix material.

22. The sensor of claim 21 wherein the extracellular matrix material is selected from the group consisting of intestine submucosa and urinary bladder matrix.

23. The sensor of claim 20 wherein the natural polymer comprises a protein.

24. The sensor of claim 23 wherein the protein is selected from the group consisting of collagen, fibrin, elastin, fibrillin, fibronectin, and laminin.

25. The sensor of claim 20 wherein the natural polymer comprises proteoglycans.

26. The sensor of claim 20 wherein the natural polymer comprises phosphytidyl choline.

27. The sensor of claim 19 wherein the biomaterial matrix comprises a synthetic polymer.

28. The sensor of claim 27 wherein the synthetic polymer is selected from the group consisting of polyhydroxyvalerate, poly(L)lactic acid, polycaprolactone, polylactide-co-glycolide, polyhydroxybutyrate, polyhydroxybutyrate-co-valerate, polydioxanone, polyorthoesters, polyanhydrides, polyacetic, polyglycolic acid, poly(D,L)lactic acid, polyglycolic acid-co-trimethylene carbonate, polysebacic acid, polylactic-co-sebacic acid, polyglycolic-co-sebacid acid, polyphosphoesters, polyphosphoester urethanes, polyamino acids, ion exchange resins, cyanoacrylates, polytrimethylene carbonate, polyiminocarbonate, copolyether-esters, polyalkylene oxalates and polyphosphazenes.

29. The sensor of claim 27 wherein the synthetic polymer is selected from the group consisting of polyurethanes, silicones and polyesters.

30. The sensor of claim 27 wherein the synthetic polymer is selected from the group consisting of polyolefin, polyisobutylene, ethylene-alphaolefin copolymers, acrylic polymers and copolymers, vinyl halide polymers and copolymers, polyvinyl ethers, polyvinylidene halides, polyacrylonitrile, polyvinyl ketones, polyvinyl aromatics, polyvinyl esters, copolymers of vinyl monomers with each other and olefins, polyamides, alkyd resins, polycarbonates, polyoxymethylenes, polyimides, polyethers, epoxy resins, rayon and rayon-triacetate.

31. The sensor of claim 27 wherein the synthetic polymer is selected from the group consisting of polymers or copolymers of caprolactones, carbonates, amides, amino acids with reactive side chains including lysine, arginine, aspartic acid, glutamic acid, serine, threonine, tyrosine and cysteine, or their enantiomers, orthoesters, acetals, cyanoacrylates and degradable urethanes, as well as copolymers of these with straight chain or branched, substituted or unsubstituted, alkanyl, haloalkyl, thioalkyl, aminoalkyl, alkenyl, or aromatic hydroxy- or di-carboxylic acids.

32. The sensor of claim 19 wherein the autologous cells comprise stem cells.

33. The sensor of claim 32 wherein the stem cells are selected from the group consisting of mesenchymal stem cell (MSC), endothelial progenitor cell (EPC), smooth muscle cell (SMC), endothelial cell, hematopoietic stem cells, multipotent adult progenitor cells, adult stem cells and embryonic stem cells.

34. The sensor of claim 19 wherein the autologous cells comprise differentiated cells derived from stem cells.

35. A sensor comprising:

a sensor surface; and

a biocompatible coating comprising a biomaterial covering at least a portion of the surface, the coating having properties that inhibit the growth of tissue over the surface of the coating.

36. The sensor of claim 35 wherein the biomaterial is selected from the group consisting of polytetraflouroethylene and polyethylene glycol.

37. The sensor of claim 35 wherein the biomaterial comprises an anti-thrombogenic material.

38. The sensor of claim 37 wherein the anti-thrombogenic material comprises a hydro-gel.

39. The sensor of claim 38 wherein the hydro-gel is selected from a group of polyethylene oxide, albumin, hydrophilic poly-methacrylates and hydrophilic poly urethanes.

40. A sensor comprising:

a sensor surface; and

a biocompatible coating covering at least a portion of the surface, the coating comprising a biomaterial matrix and an active component, wherein the active component imparts properties to the coating that inhibits the growth of tissue over the surface of the coating.

41. The sensor of claim 40 wherein the biomaterial matrix comprises a natural polymer.

42. The sensor of claim 41 wherein the natural polymer comprises extracellular matrix material.

43. The sensor of claim 42 wherein the extracellular matrix material is a material selected from the group consisting of intestine submucosa and urinary bladder matrix.

44. The sensor of claim 41 wherein the natural polymer comprises a protein.

45. The sensor of claim 44 wherein the protein is selected from the group consisting of collagen, fibrin, elastin, fibrillin, fibronectin, and laminin.

46. The sensor of claim 44 wherein the natural polymer comprises proteoglycans.

47. The sensor of claim 44 wherein the natural polymer comprises phosphytidyl choline.

48. The sensor of claim 40 wherein the biomaterial matrix comprises a synthetic polymer.

49. The sensor of claim 48 wherein the synthetic polymer is selected from the group consisting of polyhydroxyvalerate, poly(L)lactic acid, polycaprolactone, polylactide-co-glycolide, polyhydroxybutyrate, polyhydroxybutyrate-co-valerate, polydioxanone, polyorthoesters, polyanhydrides, polyacetic, polyglycolic acid, poly(D,L)lactic acid, polyglycolic acid-co-trimethylene carbonate, polysebacic acid, polylactic-co-sebacic acid, polyglycolic-co-sebacid acid, polyphosphoesters, polyphosphoester urethanes, polyamino acids, ion exchange resins, cyanoacrylates, polytrimethylene carbonate, polyiminocarbonate, copolyether-esters, polyalkylene oxalates and polyphosphazenes.

50. The sensor of claim 48 wherein the synthetic polymer is selected from the group consisting of polyurethanes, silicones and polyesters.

51. The sensor of claim 48 wherein the synthetic polymer is selected from the group consisting of polyolefin, polyisobutylene, ethylene-alphaolefin copolymers, acrylic polymers and copolymers, vinyl halide polymers and copolymers, polyvinyl ethers, polyvinylidene halides, polyacrylonitrile, polyvinyl ketones, polyvinyl aromatics, polyvinyl esters, copolymers of vinyl monomers with each other and olefins, polyamides, alkyd resins, polycarbonates, polyoxymethylenes, polyimides, polyethers, epoxy resins, rayon and rayon-triacetate.

52. The sensor of claim 40 wherein the active component comprises a sirolimus.

53. The sensor of claim 40 wherein the active component comprises a steroid.

54. The sensor of claim 40 wherein the active component comprises at least one anti-thrombotic substance and at least one anti-inflammatory substance.

55. The sensor of claim 54 wherein the anti-thrombotic substance is selected from a group of heparin, sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogs, D-phe-pro-arg-chloromethylketone, dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antibody, and recombinant hirudin; and the anti-inflamatory substance is selected from a group of aspirin, diclofenac, etodolac, ibuprofen, ketoprofen, ketorolac, nabumetone, naproxen, oxaprozin, clobetasol, diflucortolone, flucinolone, halcinolonide, halobetasol, dexamethasone, betamethasone, corticol, cortisone, prednisone, and prednisolone.

56. A sensor comprising:

a sensor surface comprising gold; and

a biocompatible coating comprising self-assembled monolayer covering at least a portion of the sensor surface.

57. The sensor of claim 56 wherein the self assembled monolayer comprises preformed carboxylic acid alkanethiolate.

58. A sensor comprising:

a sensor surface;

a layer of a metallic material comprising gold covering a portion of the sensor surface; and

a biocompatible coating comprising a self assembled monolayer covering at least a portion of the metallic material layer.

59. The sensor of claim 58 wherein the self assembled monolayer comprises preformed carboxylic acid alkanethiolate.

60. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface and a biocompatible coating comprising a biomaterial matrix, the coating covering at least a portion of the sensor surface and having properties that promote a substantially even growth of tissue cells over the surface of the coating.

61. The method of claim 60 wherein the biomaterial matrix comprises a polymer.

62. The method of any one of claims 60 to 61 wherein the coating further comprises a growth factor.

63. The method of any one of claims 60 to 62 wherein the coating further comprises an agent that recruits endogenous stem cells.

64. The method of any one of claims 60 to 63 wherein the coating further comprises cell adhesion motif argine, glycine, aspartic acid.

65. The method of any one of claims 60 to 64 wherein the coating further comprises autologous cells.

66. The method of claim 65 wherein the biomaterial matrix is coated onto the surface during sensor manufacturing and the autologous cells are added to the biomaterial matrix independent of the manufacturing process and prior to implantation.

67. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface formed of a metallic material and at least a portion of the sensor surface is textured to promote a substantially even growth of tissue cells over the portion.

68. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface and a biocompatible coating comprising a biomaterial covering at least a portion of the surface, the coating having properties that inhibit the growth of tissue over the surface of the coating.

69. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface and a biocompatible coating covering at least a portion of the surface, the coating comprising a biomaterial matrix and an active component, wherein the active component imparts properties to the coating that inhibit the growth of tissue over the surface of the coating.

70. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface comprising gold and a biocompatible coating

comprising a self-assembled monolayer covering at least a portion of the sensor surface.

71. The method of claim 70 wherein the self assembled monolayer comprises pre-formed carboxylic acid alkanethiolate.

72. A method of monitoring biological activity within a body, said method comprising introducing a sensor in the body in the region to be monitored, wherein the sensor comprises a sensor surface, a layer of a metallic material comprising gold covering a portion of the sensor surface, and a biocompatible coating comprising a self assembled monolayer covering at least a portion of the metallic material layer.

73. The method of claim 72 wherein the self assembled monolayer comprises pre-formed carboxylic acid alkanethiolate.

74. A process of manufacturing a sensor for implantation into a body, said process comprising coating at least a portion of a surface of a sensor with a biocompatible coating comprising a biomaterial matrix, the coating having properties that promote a substantially even growth of tissue cells over the surface of the coating.

75. The process of claim 74 further comprising adding a growth factor to the biomaterial matrix prior to coating.

76. The process of any one of claims 74 to 75 further comprising adding an agent that recruits endogenous stem cells to the biomaterial matrix prior to coating.

77. The process of any one of claims 74 to 76 further comprising adding cell adhesion motif argine, glycine, aspartic acid to the biomaterial matrix prior to coating.

78. The process of claim 74 wherein the biomaterial matrix allows for the addition of autologous cells independent of the manufacturing process and prior to implantation.

79. A process of manufacturing a sensor for implantation into a body, said process comprising texturing at least a portion of a surface of a sensor to promote a substantially even growth of tissue cells over the portion.

80. A process of manufacturing a sensor for implantation into a body, said process comprising coating at least a portion of a surface of a sensor with a biomaterial covering having properties that inhibit the growth of tissue cells over the surface of the coating.

81. A process of manufacturing a sensor for implantation into a body, said process comprising coating at least a portion of a surface of a sensor with a biocompatible coating comprising a biomaterial matrix and an active component, wherein the active component imparts properties to the coating that inhibit the growth of tissue cells over the surface of the coating.

82. A process of manufacturing a sensor for implantation into a body, said process comprising coating at least a portion of a sensor surface comprising gold with a biocompatible coating comprising a self-assembled monolayer.

83. A process of manufacturing a sensor for implantation into a body, said process comprising:

coating at least a portion of a sensor surface with a layer of a metallic material comprising gold; and

coating at least a portion of the layer of metallic material with a biocompatible coating comprising a self assembled monolayer.

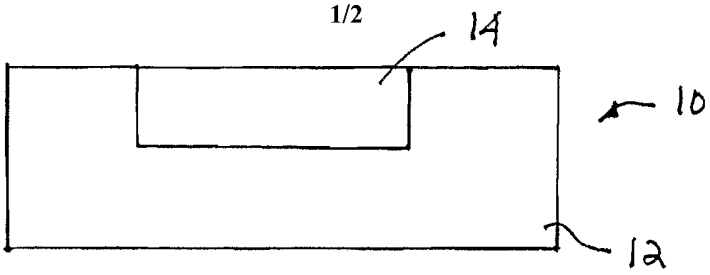

FIG. 1

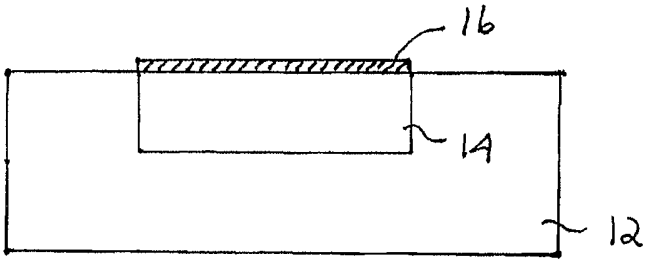

FIG. 2a

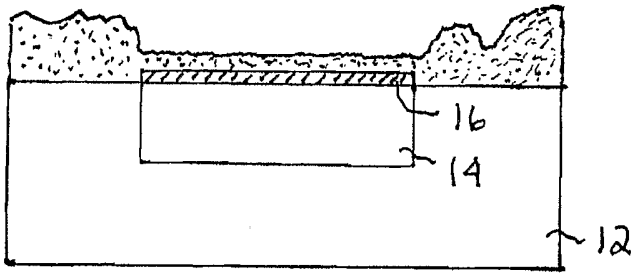

FIG. 2b

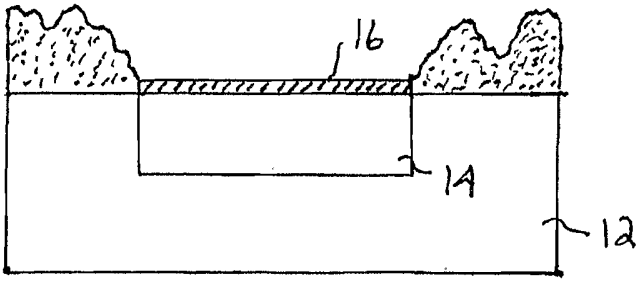

FIG. 2c

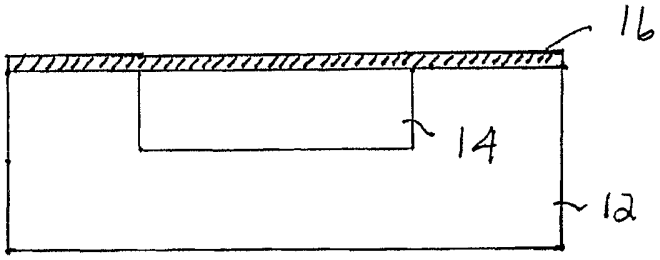

FIG. 3a

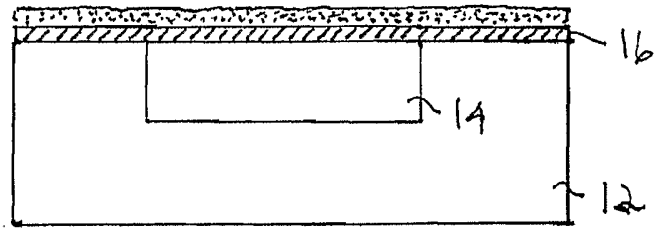

FIG. 3b

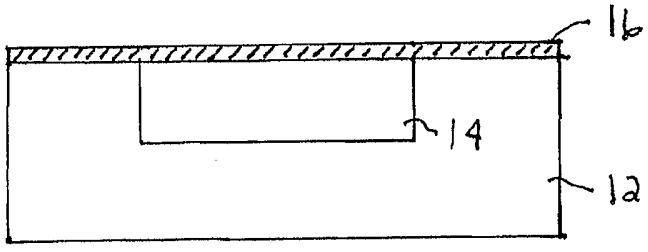

FIG. 3c