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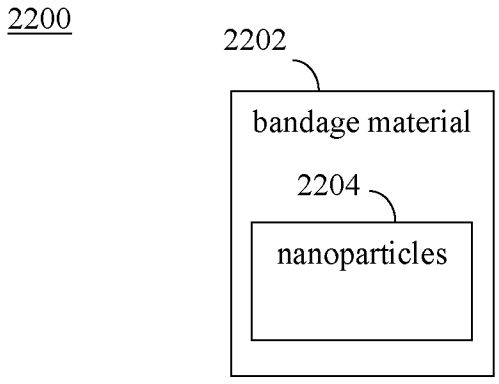

FIG. 22

(57) Abstract: Methods, systems, and apparatuses for nanomaterial-enhanced hemostatic medical devices are provided. Hemostatic materials and structures are provided that induce coagulation of blood at a wound/opening caused by trauma, a surgical procedure, ulceration, or other cause. The hemostatic materials and structures may incorporate nanostructures and/or further hemostatic elements such as polymers and/or glass beads. The hemostatic materials and structures may be resorbable. Example embodiments include hemostatic bandages, hemostatic plugs, and hemostatic formulations.

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RESORBABLE NANOENHANCED HEMOSTATIC STRUCTURES AND BANDAGE MATERIALS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present invention relates to hemostatic materials incorporating various structures, such as nanostructures.

Background of the Invention

[0002] Coagulation is a process by which blood forms solid clots. Coagulation is an important part of hemostasis (the process of halting blood flow). During natural hemostasis, a damaged blood vessel wall is covered by a platelet- and fibrin-containing clot to stop bleeding and begin repair of the damaged vessel. Various materials, referred to as "hemostats" or "hemostatic materials," have been developed to help stop wounds from bleeding excessively and to increase a rate of clotting. Such materials may be used in surgical procedures and/or by first responders to traumatic events, for example.

[0003] Some hemostatic materials that have been developed are bandage based, including oxidized resorbable cellulose materials, or cotton gauze sponges used to pack wounds prior to the application of pressure. Such bandage based materials are typically not inherently hemostatic, functioning more as absorbers of blood and leading to a plugging of a wound. Products are available that increase the hemostatic activity of a bandage material by incorporating biological agents of the natural physiological clotting cascade, such as thrombin. Such products suffer from cost and stability issues that limit their use. Thus, a need exists to increase the rate of hemostasis on bandage materials, while eliminating the conventional problems of high cost and instability.

[0004] Some bulk hemostatic materials exist that are poured into a wound to clot blood, such as QuikClot®, distributed by Z-Medica Corporation, Wallingford, CT. Such bulk hemostats have disadvantages. For example, such existing bulk hemostats do not function as quickly as desired, may be difficult to apply, and not all existing bulk hemostats can be absorbed by the human body. Furthermore, existing bulk hemostats

have an exothermic reaction with blood. Thus, a need exists for bulk hemostatic materials that overcome at least some of these disadvantages.

[0005] Biocompatible polymers have also been used as hemostats. For example, resorbable expandable polymers have been used for wound closure to prevent blood loss after endoscopic surgery where the entry/exit point of the endoscopic device is through a blood vessel. An example such device is the Angioseal™ vascular closure device sold by St. Jude Medical, St. Paul, MN. Absorbent materials, such as cotton gauze or tampon structures, have also been used for wound closure. In a device using an expandable material, blood and/or other fluids are absorbed by the material, and the material swells to cause a physical barrier. Static blood may be entrapped within pores of the material, and the entrapped blood subsequently clots due to stasis. It would be advantageous if the blood within the expanded material could be made to clot more rapidly. One possibility for increasing a rate of clotting is a biological technique using clotting enzymes. However, such a technique would be expensive. A need exists for expandable and/or absorbent material-based devices that have improved rates of clotting, while keeping down device costs.

SUMMARY OF THE INVENTION

[0006] Methods, systems, and apparatuses for nanomaterial-enhanced hemostatic medical dressings are provided. Hemostatic materials and structures are provided that induce coagulation of blood at a wound/opening caused by trauma, a surgical procedure, ulcerations, or other cause. The hemostatic materials and structures may incorporate nanostructures and/or further hemostatic elements such as polymers and/or glass beads. The hemostatic materials and structures may be durable or resorbable. Example nanomaterial-enhanced hemostatic medical device embodiments include hemostatic bandages, hemostatic plugs, moist dressings, biological dressings, and hemostatic formulations.

[0007] In a first aspect of the present invention, a hemostatic structure is provided. The hemostatic structure includes a base structure. The base structure may have a variety of formes, including that of a woven material (e.g., weave of fibers) or nonwoven material,

The hemostatic structure further includes nanostructures incorporated with the base structure (e.g., a coating of nanostructures on the base structure, a mixing of nanostructures with the material of the base structure, etc.). The nanostructures are configured to induce hemostasis when the hemostatic structure is contacted with blood.

[0008] In an example, the base structure may be a bandage. The material may be cotton (e.g., gauze) or other non-resorbable material. In an alternative aspect, the material may be a resorbable material such as oxidized regenerated cellulose, collagen, gelatin, or glass microfibers.

[0009] In another aspect of the present invention, a method for forming a hemostatic structure is provided. Nanostructures are incorporated with a material, such as a woven or nonwoven substrate material, to form the hemostatic structure. For instance, the material may be coated with nanostructures to form the hemostatic structure. The coating of nanostructures is configured to induce hemostasis when the hemostatic structure is contacted with blood.

[0010] In an example, the coating of nanostructures may be performed as follows: A nanostructure suspension is formed. The substrate is mounted in a frame. The mounted substrate is soaked in the nanostructure suspension. The soaked substrate is dried.

[0011] In an alternative example, charge-based attraction may be used to coat the substrate material with the nanostructures. For example, the substrate material may be positively or negatively charged, to attract nanostructures having an opposite charge to the substrate material. In an example aspect, the substrate material may be soaked in a solution containing a positively charged polymer to impart a positive charge to the substrate material. The substrate material may be washed and dried. A solution containing the nanostructures may be applied to the substrate material. The nanostructures are attracted from the solution to the substrate material due to the imparted positive charge to coat the substrate material. The coated substrate material may be incubated and dried.

[0012] Further techniques may be used alternatively to soaking and/or charge-based attraction to incorporate nanostructures with a substrate material, including nano-spinning, weaving, and/or further techniques described herein.

[0013] In another aspect of the present invention, a hemostat includes an expandable hemostatic material and a plurality of nanostructures combined in a mixture. The mixture is configured to be inserted into a wound to plug the wound. The nanostructures are configured to induce coagulation of blood in the wound.

[0014] In another aspect of the present invention, a hemostat includes a plurality of glass beads and a plurality of nanostructures. The glass beads and nanostructures are combined to form a mixture. The mixture is configured to induce hemostasis when the hemostat is contacted with blood.

[0015] In still another example aspect, a hemostat includes a substrate formed of a plurality of hemostatic particles. Each hemostatic particle is a core material coated with a shell layer. The shell layer is configured to induce coagulation of blood. A rate of resorption of the core material is greater than a rate of resorption of the shell layer, to increase an overall rate of resorption of the hemostatic particles. The hemostat may further include nanostructures, glass beads, and/or other materials mixed with the hemostatic particles.

[0016] In still another aspect, a hemostatic bandage includes a bandage material and a nanopowder formed of nanoparticles having an outer thin oxide layer. A coating of nanowires may optionally be formed on a surface of the bandage material. The nanopowder is dispersed in and/or on the bandage material. The thin oxide layer of the nanoparticles may be a naturally-occurring oxide layer.

[0017] In still another aspect, a hemostatic bandage includes a bandage material, a first plurality of nanowires formed to each have a first length, and a second plurality of nanowires formed to each have a second length. The second length is greater than the first length. The first plurality of nanowires is dispersed in a first region of the bandage material, and the second plurality of nanowires is dispersed in a second region of the bandage material.

[0018] In still another aspect, a surgical staple is provided. The surgical staple has a body having a base portion, a first leg, and a second leg. The first leg extends at a first angle from a first end of a first surface of the base portion, and the second leg extends at a second angle from a second end of the first surface of the base portion. A layer of nanostructures coats at least a portion of the body.

[0019] In still another aspect, a surgical suture is provided. The surgical suture includes a thread and a layer of nanostructures that coats at least a portion of the thread.

[0020] Further embodiments, features, and advantages of the invention, as well as the structure and operation of the various embodiments of the invention are described in detail below with reference to accompanying drawings.

BRIEF DESCRIPTION OF THE FIGURES

[0021] The invention is described with reference to the accompanying drawings. In the drawings, like reference numbers indicate identical or functionally similar elements. The drawing in which an element first appears is indicated by the left-most digit in the corresponding reference number.

[0022] FIG. 1A is a diagram of a nanowire.

[0023] FIG. 1B is a diagram of a nanowire having a core-shell (CS) structure.

[0024] FIG. 1C is a diagram of a nanowire having a core-shell-shell (CSS) structure.

[0025] FIG. 2 shows a process for forming a hemostatic structure, according to example embodiments of the present invention.

[0026] FIG. 3 shows a base structure that is a weave of fibers, according to an example embodiment of the present invention.

[0027] FIG. 4 shows a portion of the base structure shown in FIG. 3 coated with nanostructures according to the process of FIG. 2, according to an embodiment of the present invention.

[0028] FIGS. 5 and 6 show processes for performing the process of FIG. 2, according to embodiments of the present invention.

[0029] FIG. 7 shows a flowchart providing steps for coating a framed base material with nanofibers, according to an example embodiment of the present invention.

[0030] FIG. 8 shows the base structure of FIG. 3 mounted in a frame, according to an example embodiment of the present invention.

[0031] FIGS. 9 and 10 show images of a base structure that was coated with nanofibers in the manner of the flowchart of FIG. 7, according to an example embodiment of the present invention.

[0032] FIG. 11 shows a flowchart providing steps for coating a base material with nanofibers using charge-based attraction, according to an example embodiment of the present invention.

[0033] FIGS. 12 and 13 show images of a base structure that was coated with nanofibers in the manner of the flowchart of FIG. 11, according to an example embodiment of the present invention.

[0034] FIG. 14 shows a graph illustrating average times to hemostasis for a conventional cotton gauze bandage and nanofiber coated cotton gauze bandages, according to example embodiments of the present invention.

[0035] FIG. 15 shows a process for forming a hemostat, according to an example embodiment of the present invention.

[0036] FIG. 16 shows a block diagram of a mixing system, according to an example embodiment of the present invention.

[0037] FIG. 17 shows a cross-sectional view of a hemostat inserted in an opening through tissue, according to an example embodiment of the present invention.

[0038] FIG. 18 shows a process for forming a hemostat, according to an example embodiment of the present invention.

[0039] FIG. 19 shows a block diagram of a mixing system, according to an example embodiment of the present invention.

[0040] FIG. 20 shows a cross-sectional view of a core-shell particle, according to an example embodiment of the present invention.

[0041] FIG. 21 shows a process for forming a core-shell hemostat, according to an example embodiment of the present invention.

[0042] FIGS. 22 and 23 show block diagrams of hemostatic bandages, according to example embodiments of the present invention.

[0043] FIG. 24 shows a graph of clot time in the presence of a silicon nanopowder, according to an example embodiment of the present invention.

[0044] FIG. 25 shows a flowchart for forming a hemostatic bandage, according to an example embodiment of the present invention.

[0045] FIG. 26 shows a block diagram of a hemostatic bandage fabrication system, according to an embodiment of the present invention.

[0046] FIG. 27 shows a block diagram cross-sectional view of a nanowire-coated hemostatic bandage, according to an example embodiment of the present invention.

[0047] FIG. 28 shows a block diagram of a hemostatic bandage that includes multiple lengths of nanowires, according to an example embodiment of the present invention.

[0048] FIG. 29 shows a flowchart for forming a hemostatic bandage having multiple lengths of nanowires, according to an example embodiment of the present invention.

[0049] FIG. 30 shows a block diagram of a hemostatic bandage fabrication system, according to an embodiment of the present invention.

[0050] FIG. 31 shows a block diagram cross-sectional view of a hemostatic bandage, according to an embodiment of the present invention.

[0051] FIG. 32 shows a view of a surface of a hemostatic bandage, according to an embodiment of the present invention.

[0052] FIG. 33 shows a perspective view of an example surgical staple.

[0053] FIG. 34 shows a process for functionalizing a surgical staple with hemostatic nanostructures, according to an example embodiment of the present invention.

[0054] FIG. 35 shows a staple coating system, according to an example embodiment of the present invention.

[0055] FIG. 36 shows a perspective view of a surgical staple, which is a modified form of the surgical staple of FIG. 33, according to an example embodiment of the present invention.

[0056] FIG. 37 show a perspective view of the surgical staple of FIG. 36 partially coated with nanostructures, according to an example embodiment of the present invention.

[0057] FIG. 38 shows a portion of a suture coated with a layer of nanostructures, according to an example embodiment of the present invention.

[0058] FIG. 39 shows an example of a nanofiber functionalized with a material, according to an embodiment of the present invention.

[0059] The present invention will now be described with reference to the accompanying drawings. In the drawings, like reference numbers indicate identical or functionally similar elements. Additionally, the left-most digit(s) of a reference number identifies the drawing in which the reference number first appears.

DETAILED DESCRIPTION OF THE INVENTION

[0060] It should be appreciated that the particular implementations shown and described herein are examples of the invention and are not intended to otherwise limit the scope of the present invention in any way. Indeed, for the sake of brevity, conventional manufacturing and nanowire (NW), nanorod, nanotube, and nanoribbon technologies and other functional aspects of the systems (and components of the individual operating components of the systems) may not be described in detail herein. Furthermore, for purposes of brevity, the invention is frequently described herein as pertaining to nanowires/nanofibers.

[0061] It should be appreciated that although nanowires/nanofibers are frequently referred to, the techniques described herein are also applicable to other nanostructures, such as nanorods, nanotubes, nanotetrapods, nanoribbons and/or combinations thereof. It should further be appreciated that the manufacturing techniques described herein could be used to create any type of bandage or other nanostructure receiving structure, and other medical device types.

[0062] As used herein, an "aspect ratio" is the length of a first axis of a nanostructure divided by the average of the lengths of the second and third axes of the nanostructure, where the second and third axes are the two axes whose lengths are most nearly equal to each other. For example, the aspect ratio for a perfect rod would be the length of its long axis divided by the diameter of a cross-section perpendicular to (normal to) the long axis.

[0063] The term "heterostructure" when used with reference to nanostructures refers to nanostructures characterized by at least two different and/or distinguishable material types. Typically, one region of the nanostructure comprises a first material type, while a second region of the nanostructure comprises a second material type. In certain embodiments, the nanostructure comprises a core of a first material and at least one shell of a second (or third etc.) material, where the different material types are distributed radially about the long axis of a nanowire, a long axis of an arm of a branched nanocrystal, or the center of a nanocrystal, for example. A shell need not completely cover the adjacent materials to be considered a shell or for the nanostructure to be considered a heterostructure. For example, a nanocrystal characterized by a core of one

material covered with small islands of a second material is a heterostructure. In other embodiments, the different material types are distributed at different locations within the nanostructure. For example, material types can be distributed along the major (long) axis of a nanowire or along a long axis of arm of a branched nanocrystal. Different regions within a heterostructure can comprise entirely different materials, or the different regions can comprise a base material.

[0064] As used herein, a "nanostructure" is a structure having at least one region or characteristic dimension with a dimension of less than about 500 nm, e.g., less than about 200 nm, less than about 100 nm, less than about 50 nm, or even less than about 20 nm. Typically, the region or characteristic dimension will be along the smallest axis of the structure. Examples of such structures include nanowires, nanorods, nanotubes, branched nanocrystals, nanotetrapods, tripods, bipods, nanocrystals, nanodots, quantum dots, nanoparticles, branched tetrapods (e.g., inorganic dendrimers), and the like. Nanostructures can be substantially homogeneous in material properties, or in certain embodiments can be heterogeneous (e.g., heterostructures). Nanostructures can be, for example, substantially crystalline, substantially monocrystalline, polycrystalline, amorphous, or a combination thereof. In one aspect, each of the three dimensions of the nanostructure has a dimension of less than about 500 nm, for example, less than about 200 nm, less than about 100 nm, less than about 50 nm, or even less than about 20 nm.

[0065] The terms “nanofiber” and “nanowire” are used interchangeably herein. As used herein, the terms “nanofiber” and "nanowire" generally refer to any elongated conductive or semiconductive material (or other material described herein) that includes at least one cross-sectional dimension that is less than 500nm, and preferably, equal to or less than less than about 100 nm, and has an aspect ratio (length : width) of greater than 10, preferably greater than 50, and more preferably, greater than 100. Exemplary nanofibers/nanowires for use in the practice of the methods and systems of the present invention are on the order of 10's of microns long (e.g., about 10, 20, 30, 40, 50 microns, etc.) and about 30-100 nm in diameter.

[0066] The nanowires of this invention can be substantially homogeneous in material properties, or in certain embodiments can be heterogeneous (*e.g.,* nanowire heterostructures). The nanowires can be fabricated from essentially any convenient

material or materials, and can be, e.g., substantially crystalline, substantially monocrystalline, polycrystalline, or amorphous. Nanowires can have a variable diameter or can have a substantially uniform diameter, that is, a diameter that shows a variance less than about 20% (e.g., less than about 10%, less than about 5%, or less than about 1%) over the region of greatest variability and over a linear dimension of at least 5 nm (e.g., at least 10 nm, at least 20 nm, or at least 50 nm). Typically the diameter is evaluated away from the ends of the nanowire (e.g., over the central 20%, 40%, 50%, or 80% of the nanowire). A nanowire can be straight or can be e.g., curved or bent, over the entire length of its long axis or a portion thereof.

[0067] Examples of such nanowires include semiconductor nanowires as described in Published International Patent Application Nos. WO 02/17362, WO 02/48701, and WO 01/03208, carbon nanotubes, and other elongated conductive or semiconductive structures of like dimensions, which are incorporated herein by reference.

[0068] As used herein, the term "nanorod" generally refers to any elongated semiconductive material (or other material described herein) similar to a nanowire, but having an aspect ratio (length : width) less than that of a nanowire.

[0069] A wide range of types of materials for nanowires, nanorods, nanotubes and nanoribbons can be used, including semiconductor material selected from, e.g., Si, Ge, Sn, Se, Te, B, C (including diamond), P, B-C, B-P(BP_6), B-Si, Si-C, Si-Ge, Si-Sn and Ge-Sn, SiC, BN, BP, BAs, AlN, AlP, AlAs, AlSb, GaN, GaP, GaAs, GaSb, InN, InP, InAs, InSb, ZnO, ZnS, ZnSe, ZnTe, CdS, CdSe, CdTe, HgS, HgSe, HgTe, BeS, BeSe, BeTe, MgS, MgSe, GeS, GeSe, GeTe, SnS, SnSe, SnTe, PbO, PbS, PbSe, PbTe, CuF, CuCl, CuBr, CuI, AgF, AgCl, AgBr, AgI, $BeSiN_2$, $CaCN_2$, $ZnGeP_2$, $CdSnAs_2$, $ZnSnSb_2$, $CuGeP_3$, $CuSi_2P_3$, (Cu, Ag)(Al, Ga, In, Tl, Fe)(S, Se, $Te)_2$, Si_3N_4, Ge_3N_4, Al_2O_3, (Al, Ga, $In)_2$ (S, Se, $Te)_3$, Al_2CO, and an appropriate combination of two or more such semiconductors. Other now known or later developed semiconductor materials can be employed. Other types of materials can be used for nanostructures, including metals such as titanium, zirconium, and tantalum, combinations of metals/alloys such as cobalt-chromium or steel, oxides of these metals, and further material types.

[0070] Additionally, the nanowires or nanoribbons can include nanotubes formed of semiconductive organic polymer materials, (e.g., pentacene), or transition metal oxides.

[0071] Hence, although the term "nanowire" is referred to throughout the description herein for illustrative purposes, it is intended that the description herein also encompass the use of nanotubes (e.g., nanowire-like structures having a hollow tube formed axially therethrough).

[0072] It should be understood that the spatial descriptions (e.g., "above", "below", "up", "down", "top", "bottom," "vertical," "horizontal," etc.) made herein are for purposes of illustration only, and that devices of the present invention can be spatially arranged in any orientation or manner.

[0073] Embodiments of the present invention relate to any type of nanowire. FIG. 1A illustrates a nanowire core (hereafter "nanowire") 100. Nanowire 100 is a single crystal semiconductor or other material, uniform or otherwise. FIG. 1B shows a nanowire 110 having a core-shell structure, with a shell 112 around the nanowire core. An insulating layer, such as an oxide coating, can be formed on a nanowire as the shell layer. Other more complex NW core-shell structures may also be used to include a core of a first material, an inner-shell of a second material, and an outer-shell of a third material, such as shown in FIG. 1C. FIG. 1C shows a nanowire 114 having a core-shell-shell structure, with an inner shell 112 and outer shell 116 around the nanowire core. This can be realized by depositing a layer of TaAlN, WN, or amorphous silicon around the Si/SiO_x core-shell structure (described above) as the outer-gate shell, for example. Note that although a length of the nanowire core (at an end of the nanowire core) is shown exposed (not covered) in FIGS. 1B and 1C, in embodiments, the nanowire core may be completely covered by one or both of shells 112 and 116.

[0074] Generally, the core nanostructure can be made from any metallic or semiconductor material, and the one or more shell layers deposited on the core can be made from the same or a different material. For example, the first core material can comprise a first semiconductor selected from the group consisting of: a Group II-VI semiconductor, a Group III-V semiconductor, a Group IV semiconductor, and an alloy thereof. Similarly, the second material of the one or more shell layers can comprise an oxide layer, a second semiconductor, the same as or different from the first semiconductor, e.g., selected from the group consisting of: a Group II-VI semiconductor, a Group III-V semiconductor, a Group IV semiconductor, and an alloy thereof. Example

semiconductors include, but are not limited to, CdSe, CdTe, InP, InAs, CdS, ZnS, ZnSe, ZnTe, HgTe, GaN, GaP, GaAs, GaSb, InSb, Si, Ge, AlAs, AlSb, PbSe, PbS, and PbTe.

[0075] Nanostructures can be fabricated and their size can be controlled by any of a number of convenient methods that can be adapted to different materials. For example, synthesis of nanocrystals of various composition is described in, e.g., Peng et al. (2000) "Shape Control of CdSe Nanocrystals" Nature 404, 59-61; Puntes et al. (2001) "Colloidal nanocrystal shape and size control: The case of cobalt" Science 291, 2115-2117; U.S. Patent No. 6,306,736 to Alivisatos et al. (October 23, 2001) entitled "Process for forming shaped group III-V semiconductor nanocrystals, and product formed using process"; U.S. Patent No. 6,225,198 to Alivisatos et al. (May 1, 2001) entitled "Process for forming shaped group II-VI semiconductor nanocrystals, and product formed using process"; U.S. Patent No. 5,505,928 to Alivisatos et al. (April 9, 1996) entitled "Preparation of III-V semiconductor nanocrystals"; U.S. Patent No. 5,751,018 to Alivisatos et al. (May 12, 1998) entitled "Semiconductor nanocrystals covalently bound to solid inorganic surfaces using self-assembled monolayers"; U.S. Patent No. 6,048,616 to Gallagher et al. (April 11, 2000) entitled "Encapsulated quantum sized doped semiconductor particles and method of manufacturing same"; and U.S. Patent No. 5,990,479 to Weiss et al. (November 23, 1999) entitled "Organo luminescent semiconductor nanocrystal probes for biological applications and process for making and using such probes."

[0076] Growth of nanowires having various aspect ratios, including nanowires with controlled diameters, is described in, e.g., Gudiksen et al (2000) "Diameter-selective synthesis of semiconductor nanowires" J. Am. Chem. Soc. 122, 8801-8802; Cui et al. (2001) "Diameter-controlled synthesis of single-crystal silicon nanowires" Appl. Phys. Lett. 78, 2214-2216; Gudiksen et al. (2001) "Synthetic control of the diameter and length of single crystal semiconductor nanowires" J. Phys. Chem. B 105,4062-4064; Morales et al. (1998) "A laser ablation method for the synthesis of crystalline semiconductor nanowires" Science 279, 208-211; Duan et al. (2000) "General synthesis of compound semiconductor nanowires" Adv. Mater. 12, 298-302; Cui et al. (2000) "Doping and electrical transport in silicon nanowires" J. Phys. Chem. B 104, 5213-5216; Peng et al. (2000) "Shape control of CdSe nanocrystals" Nature 404, 59-61; Puntes et al. (2001) "Colloidal nanocrystal shape and size control: The case of cobalt" Science 291, 2115-

2117; U.S. Patent No. 6,306,736 to Alivisatos et al. (October 23, 2001) entitled "Process for forming shaped group III-V semiconductor nanocrystals, and product formed using process"; U.S. Patent No. 6,225,198 to Alivisatos et al. (May 1, 2001) entitled "Process for forming shaped group II-VI semiconductor nanocrystals, and product formed using process"; U.S. Patent No. 6,036,774 to Lieber et al. (March 14, 2000) entitled "Method of producing metal oxide nanorods"; U.S. Patent No. 5,897,945 to Lieber et al. (April 27, 1999) entitled "Metal oxide nanorods"; U.S. Patent No. 5,997,832 to Lieber et al. (December 7, 1999) "Preparation of carbide nanorods"; Urbau et al. (2002) "Synthesis of single-crystalline perovskite nanowires composed of barium titanate and strontium titanate" J. Am. Chem. Soc., 124, 1186; and Yun et al. (2002) "Ferroelectric Properties of Individual Barium Titanate Nanowires Investigated by Scanned Probe Microscopy" Nanoletters 2, 447.

[0077] Growth of branched nanowires (e.g., nanotetrapods, tripods, bipods, and branched tetrapods) is described in, e.g., Jun et al. (2001) "Controlled synthesis of multi-armed CdS nanorod architectures using monosurfactant system" J. Am. Chem. Soc. 123, 5150-5151; and Manna et al. (2000) "Synthesis of Soluble and Processable Rod-,Arrow-, Teardrop-, and Tetrapod-Shaped CdSe Nanocrystals" J. Am. Chem. Soc. 122, 12700-12706.

[0078] Synthesis of nanoparticles is described in, e.g., U.S. Patent No. 5,690,807 to Clark Jr. et al. (November 25, 1997) entitled "Method for producing semiconductor particles"; U.S. Patent No. 6,136,156 to El-Shall, et al. (October 24, 2000) entitled "Nanoparticles of silicon oxide alloys"; U.S. Patent No. 6,413,489 to Ying et al. (July 2, 2002) entitled "Synthesis of nanometer-sized particles by reverse micelle mediated techniques"; and Liu et al. (2001) "Sol-Gel Synthesis of Free-Standing Ferroelectric Lead Zirconate Titanate Nanoparticles" J. Am. Chem. Soc. 123, 4344. Synthesis of nanoparticles is also described in the above citations for growth of nanocrystals, nanowires, and branched nanowires, where the resulting nanostructures have an aspect ratio less than about 1.5.

[0079] Synthesis of core-shell nanostructure heterostructures, namely nanocrystal and nanowire (e.g., nanorod) core-shell heterostructures, are described in, e.g., Peng et al. (1997) "Epitaxial growth of highly luminescent CdSe/CdS core/shell nanocrystals with photostability and electronic accessibility" J. Am. Chem. Soc. 119, 7019-7029; Dabbousi et al. (1997) "(CdSe)ZnS core-shell quantum dots: Synthesis and characterization of a

size series of highly luminescent nanocrysallites" J. Phys. Chem. B 101, 9463-9475; Manna et al. (2002) "Epitaxial growth and photochemical annealing of graded CdS/ZnS shells on colloidal CdSe nanorods" J. Am. Chem. Soc. 124, 7136-7145; and Cao et al. (2000) "Growth and properties of semiconductor core/shell nanocrystals with InAs cores" J. Am. Chem. Soc. 122, 9692-9702. Similar approaches can be applied to growth of other core-shell nanostructures.

[0080] Growth of nanowire heterostructures in which the different materials are distributed at different locations along the long axis of the nanowire is described in, e.g., Gudiksen et al. (2002) "Growth of nanowire superlattice structures for nanoscale photonics and electronics" Nature 415, 617-620; Bjork et al. (2002) "One-dimensional steeplechase for electrons realized" Nano Letters 2, 86-90; Wu et al. (2002) "Block-by-block growth of single-crystalline Si/SiGe superlattice nanowires" Nano Letters 2, 83-86; and U.S. patent application No. 60/370,095 (April 2, 2002) to Empedocles entitled "Nanowire heterostructures for encoding information." Similar approaches can be applied to growth of other heterostructures.

Example Hemostatic Material/Structure Embodiments

[0081] Embodiments of the present invention relate to medical devices, and in particular relate to materials and structures ("hemostatic materials" and "hemostatic structures") used to reduce/prevent blood loss from trauma, a surgical procedure, ulcerations or other application requiring blood clotting. In embodiments, the materials and structures may incorporate nanostructures and/or further hemostatic materials such as glass beads, core-shell particles, etc. Such nanostructures and/or further hemostatic materials further enhance hemostatic characteristics and/or provide hemostatic properties to the base materials and structures. Example embodiments include hemostatic wound dressings, hemostatic plugs, and other hemostatic formulations such as liquids, powders, foams and gels. The base materials/structures (e.g., a matrix, a substrate, etc.) can be in a bandage format (e.g., gauze, etc.), a gel format that can be squeezed onto a wound (e.g., a bleeding site), a liquid format that can be sprayed or squirted onto a wound, a dry powder that can be sprayed or squirted onto a wound, or a foam that can be extruded/squirted/injected

into/onto a wound. A hemostat formed by the combination of base materials/structures and nanostructures (e.g., a nanostructure-enhanced material/structure) may have a solid, liquid, powder, foam, or gel form. A hemostat having a non-solid form may remain in non-solid format upon contact with a wound, may solidify on contact, or may harden shortly after being dispensed, depending on the particular embodiment.

[0082] In embodiments, the nanostructure-enhanced materials/structures have a profound effect on inducing hemostasis, reducing blood clotting time as compared to conventional clotting materials, such as QuikClot®, distributed by Z-Medica Corporation, Wallingford, CT. In some embodiments, the nanostructure-enhanced materials/structures are resorbable (dissolved and assimilated or excreted by a mammalian body). The use of resorbable materials (e.g., silicon nanowires) to induce hemostasis has an advantage of leaving little or no residue after use of the materials. Furthermore, the nanostructure-enhanced materials/structures do not cause a significant increase in temperature during use, as opposed to QuikClot®, which can cause an increase in temperature of about 20 degrees C or more when used in/on the human body.

[0083] Example embodiments are described below, including hemostatic bandage embodiments, expandable hemostatic structures, and hemostatic materials. These example embodiments described herein are provided for illustrative purposes, and are not limiting. Furthermore, additional structural and operational embodiments, including modifications/alterations, will become apparent to persons skilled in the relevant art(s) from the teachings herein. Features of the embodiments described herein may be combined in any manner. Example embodiments of the present invention are described in detail in the following subsections.

Example Hemostatic Bandage Embodiments

[0084] In an embodiment, nanostructures, such as inorganic silica nanofibers, are applied onto the surface of bandages/bandage fibers. Such nanostructures (e.g., nanofibers, nanoparticles, etc.) assist in activating the intrinsic (contact) clotting cascade, leading to the slowdown or stoppage of bleeding. The dimensions of the nanostructures are such that they provide an excellent surface for activation of the contact pathway, and thus

provide a non-biological way of enhancing clotting on bandage surfaces. Such nanostructures may be nanowires, nanofibers, nanoparticles, and/or any other nanostructure type described herein. Such nanostructures may be made of silicon, silicon having a thin oxide layer, silica, potassium (including potassium nanofibers, nanowires, or nanoparticles), silicon nanostructures functionalized with potassium (e.g., silicon nanofibers functionalized with potassium), etc.

[0085] In example embodiments, bandage materials that may be coated and/or otherwise enhanced with nanostructures include resorbable and/or non-resorbable substrate materials such as organic materials, inorganic materials, woven materials/fabrics, nonwoven materials/fabrics (e.g., nonwoven fiber materials such as a cotton ball), synthetic materials (e.g., rayon, nylon/lycra, Gore-Tex®, a film such as a plastic film, etc.), natural materials (e.g., cotton), biologics/biological derived materials (e.g., chitosan, including chitosan microparticles, collagen, gelatin, cellulose, etc.), porous materials, non-porous materials, and/or particles (e.g., glass or polymer beads). For instance, in embodiments, nanofibers may be applied to a resorbable bandage material, such as an oxidized regenerated cellulose (ORC) material (e.g., Surgicel®, which is manufactured by Ethicon, Inc.), a resorbable biopolymer, a gelatin bandage material (e.g., Gelfoam®, which is manufactured by Pfizer Inc.), or a glass microfiber material. The bandage materials may be hemostatic or non-hemostatic. In embodiments, a resorbable, nanostructure-enhanced bandage material may be applied to a wound as a hemostatic bandage/plug to reduce/prevent blood loss, without a subsequent need for removal of the entire bandage material. In another embodiment, nanofibers may be applied to alternate bandage materials that are non-resorbable, to create hemostatic bandage/plugs for the prevention of blood loss. An example of such non-resorbable bandage material is "supergauze" that combines nanofibers with conventional absorbent cotton gauze materials.

[0086] FIG. 2 shows a step 200 for forming a hemostatic structure, according to example embodiments of the present invention. Step 200 may be used to form hemostatic structures such as hemostatic bandages or plugs. Further structural and operational embodiments will be apparent to persons skilled in the relevant art(s) based on the discussion regarding step 200.

[0087] As shown in FIG. 2, in step 200, nanostructures are incorporated with a weave of fibers of a first material to form the hemostatic structure. For example, FIG. 3 shows a base structure 300 that is a weave of fibers 302, according to an example embodiment of the present invention. Base structure 300 may be gauze, ORC, a biocompatible polymer such as PGA (polyglycolide), PLA (polylactic acid), PCLA (poly (caprolactone-lactide) random copolymer), or other polymer, a glass microfiber weave, or other type of weave. Fibers 302 may be cotton fibers, cellulose fibers, glass fibers, collagen, or fibers of other material. Note that in an alternative embodiment, base structure 300 may be a solid material, including a plurality of layers of a solid material (e.g., layered ORC) rather than a weave of fibers, may be a nonwoven fiber material such as a cotton ball, or may be another material (woven or nonwoven, hemostatic or non-hemostatic, etc.) mentioned above or elsewhere herein. Nanostructures may be incorporated with (e.g., in and/or on) base structure 300 in any manner, including being coated on base structure 300, being mixed with weave of fibers 302, etc.

[0088] As used herein "coating", "coatings", "coated" and "coat" are forms of the same term defining material and process for making a material where a first substance is at least partially covered or associated with a second substance. Both the first and second substance do not have to be different. Further, when a nanostructure is "coated" as used herein, the coating may be may be effectuated by any chemical or mechanical bond or force, including linking agents. Thus a nanowire comprising a first substance may be "coated" with a second substance via a linking agent that is a third substance. As used herein, the "coating" need not be complete or cover the entire surface of the first substance to be "coated." The "coating" may be complete as well, i.e. completely covering the first substance. There may be multiple coatings and multiple substances within each coating.

[0089] FIG. 4 shows a magnified view of a portion 400 of base structure 300 of FIG. 3 coated with nanostructures 402 according to step 200 of FIG. 2. As shown in FIG. 4, portion 400 includes fibers 302a-302f. Fibers 302a-302c are woven with fibers 302d-302f. Fibers 302a-302c are aligned along a first axis that is perpendicular to a second axis along which fibers 302d-302f are aligned. Nanostructures 402 coat fibers 302a-302f. Nanostructures 402 are shown as nanofibers in FIG. 4 for illustrative purposes, but in

alternative embodiments may include one or more other types of nanostructures described elsewhere herein or otherwise known.

[0090] Note that although step 200 recites a weave of fibers, any suitable base structure described herein or otherwise known, woven or un-woven, may have nanostructures incorporated therein. Step 200 of FIG. 2 may be performed in any manner to incorporate nanostructures with a base structure. For example, FIGS. 5 and 6 show example processes for performing step 200, according to embodiments of the present invention. In the embodiment of FIG. 5, in step 500, the weave of fibers may be mounted (e.g., in a frame) and soaked in a nanostructure suspension to coat the weave of fibers with nanostructures. In the embodiment of FIG. 6, in step 600, charge-based attraction is used to coat the weave of fibers with the nanostructures. The embodiments of FIGS. 5 and 6 are described in detail as follows.

[0091] Step 500 of FIG. 5 may be performed in any manner. For example, step 500 may be performed according to flowchart 700 of FIG. 7. Flowchart 700 is described as follows. Note that the steps of flowchart 700 do not necessarily need to be performed in the order shown, and that not all of the steps shown in FIG. 7 may need to be performed in all situations. Steps 702-706 illustrate a process of forming a nanostructure suspension. Other techniques for forming a nanostructure suspension may alternatively be used, as would be known to persons skilled in the relevant art(s).

[0092] Flowchart 700 begins with step 702. In step 702, a wafer coated with nanostructures is sonicated in a liquid. Any size wafer and suitable liquid may be used. For example, a double sized 4 inch wafer coated with 60 nanometer silicon nanowires may be soaked in ethanol (e.g., soaked in 80 milliliters of ethanol for four minutes).

[0093] In step 704, the sonicated nanostructures are filtered. Any suitable filtering technique may be used. For instance, in the current example, the sonicated nanowires may be filtered using a vacuum filter having a 0.45 micrometer filter membrane.

[0094] In step 706, the filtered nanostructures are suspended in a liquid to form a nanostructure suspension. Any suitable liquid may be used in step 702. For instance, in the current example, the nanowires may be scraped from the filter membrane, and suspended in ethanol (e.g., 6 milliliters).

[0095] In step 708, the weave of fibers is mounted in a frame. For example, FIG. 8 shows base structure 300 of FIG. 3 mounted in a frame 802, according to an example embodiment of the present invention. Base structure 300 may be clamped between first and second portions of frame 802, attached to frame 802 by an adhesive material such as an adhesive tape or epoxy, or may be otherwise mounted to frame 802. Frame 802 may be made from plastic, metal, or other material. In the current example, base structure 300 is gauze. The gauze may be folded as needed to fit frame 802. For example, gauze may be folded into a 2 inch by 2.5 inch rectangle, or other size and/or shape, as needed.

[0096] In step 710, the mounted weave of fibers is soaked in the nanostructure suspension. For instance, in the current example, frame 802 and the mounted gauze may be soaked in the nanostructure suspension formed at step 706 for any suitable length of time, such as 4 minutes in the current example. In an embodiment, frame 802 and the mounted gauze may be sonicated while soaking in the nanostructure suspension. The weave of fibers may soak up a portion of all of the nanostructure suspension during step 710, in embodiments.

[0097] In step 712, the soaked weave of fibers is dried. The soaked weave of fibers may be dried for any length of time by air drying or by application of heat (e.g., flash drying). For instance, in the current example, frame 802 and the mounted gauze may be placed in an oven (e.g., at 121° C, for 15 minutes) to dry.

[0098] FIGS. 9 and 10 show magnified images 900 and 1000 of a base structure 902 that was coated with nanofibers in a manner similar to flowchart 700 of FIG. 7, according to an example embodiment of the present invention. Images 900 and 1000 were captured by a scanning electron microscope (SEM), where image 900 is a lower magnification relative to image 1000. In FIGS. 9 and 10, base structure 902 is a gauze bandage formed of cotton fiber bundles 904. As shown in FIG. 9, a coating 906 of silica nanofibers on fiber bundles 904 of base structure 902 is somewhat patchy, with nanofibers clumped in various locations. At higher magnification, FIG. 10 shows individual nanofibers 1002 coating fiber bundles 904 in a substantially uniform manner.

[0099] The use of charge-based attraction (e.g., electrostatic attraction) to coat a bandage structure or other substrate material with nanostructures according step 600 of FIG. 6 may be accomplished in any manner. In embodiments, the weave of fibers may be positively

or negatively charged, to attract nanostructures having an opposite charge to the weave of fibers. For example, step 600 may be performed according to flowchart 1100 of FIG. 11. Flowchart 1100 is described as follows. Note that the steps of flowchart 1100 do not necessarily need to be performed in the order shown, and that not all of the steps shown in FIG. 11 may need to be performed in all situations.

[0100] Flowchart 1100 begins with step 1102. In step 1102, the weave of fibers is soaked in a solution containing a positively charged polymer. Any polymer may used in step 1102, including polymers mentioned elsewhere herein or otherwise known. For instance, base structure 300 shown in FIG. 3 may be soaked (e.g., for 30 minutes) in a solution of a positively charged polymer, such as Poly-l-lysine. The positively charged polymer imparts a positive charge to the weave of fibers.

[0101] In step 1104, the weave of fibers is washed. The weave of fibers may be washed in any suitable manner and any number of one or more times. Any suitable material may be used to wash base structure 300, including water, isopropanol alcohol, another solution, or other material. In the current example, base structure 300 is removed from the polymer solution, and is washed twice in water and once in isopropanol.

[0102] In step 1106, the weave of fibers is dried. The washed base structure 300 may be dried for any length of time, and in any manner, such as by air drying or by application of heat (e.g., flash drying).

[0103] In step 1108, a solution containing the nanostructures is applied to the weave of fibers to coat the weave of fibers. The nanostructures in the solution may have a negative charge, and thus are attracted to the weave of fibers due to the imparted positive charge (of step 1102) to coat the weave of fibers. Any suitable solution of nanostructures may be used, including any nanostructure solution described elsewhere herein or otherwise known. For instance, in the current example, an ethanol solution (e.g., 10 milliliters) containing nanofibers is used. The nanostructure solution may be applied to base structure 300 in any manner, including pouring the solution on base structure 300, dipping or depositing base structure 300 in the solution, or in other manner. In the current example, the nanofibers are attracted to base structure 300, coating base structure 300 due to the positive charge of base structure 300.

[0104] In step 1110, the coated weave of fibers is incubated. The coated weave of fibers may be incubated in any manner and at any temperature. For instance, in the current example, coated base structure 300 may be incubated at room temperature for 20 minutes.

[0105] In step 1112, the coated weave of fibers is dried. The coated weave of fibers may be dried for any length of time, and in any manner, such as by air drying or by application of heat (e.g., flash drying). For instance, in the current example, coated base structure 300 may be dried at 100° C (e.g., for 10 minutes).

[0106] FIGS. 12 and 13 show magnified images 1200 and 1300 of a base structure 1202 that was coated with nanofibers using charge-based attraction in a manner similar to flowchart 1100 of FIG. 11, according to an example embodiment of the present invention. Images 1200 and 1300 were captured by a SEM, and image 1200 is a lower magnification relative to image 1300. In FIGS. 12 and 13, coated base structure 1202 is a gauze bandage formed of cotton fiber bundles 1204. As shown in FIG. 12, fiber bundles 1204 are more evenly coated with nanofibers as compared to fiber bundles 904 in images 900 and 1000 (FIGS. 9 and 10) described above. At higher magnification, FIG. 13 shows individual nanofibers 1302 coating individual fibers 1304 of fiber bundles 1204 in a substantially uniform layer. In addition to achieving a substantially even coating of nanofibers 1302, the resulting coated base structure 1202 has handling properties very similar to untreated cotton gauze. Coated base structure 1202 is very flexible, and extraneous shedding of nanofibers 1302 is not apparent upon handling of coated base structure 1202.

[0107] The hemostatic capability of a base structure coated with nanostructures according to embodiments of the present invention may be compared to that of non-nanostructure enhanced bandages. In a first example comparison, a time to initiation of clotting ("R-time") for nanofiber coated base structure 902 (when cotton gauze) was reduced when compared to cotton gauze without a nanofiber coating. Coated base structure 902 initiated clotting in approximately 9 minutes, while the uncoated gauze initiated clotting in approximately 12 minutes. In another example, clotting was initiated for a conventional cotton gauze bandage at an average of approximately 455 seconds, while clotting was initiated for nanofiber coated base structure 902 at an average of approximately 380 seconds, and clotting was initiated for nanofiber coated base structure

1202 in less than 5 minutes (approximately 275 seconds). FIG. 14 shows a graph 1400, illustrating average times to hemostasis for a conventional cotton gauze bandage (plot 1402), for nanofiber coated base structure 902 (cotton gauze bandage in the current example) (plot 1404), and for nanofiber coated base structure 1202 (cotton gauze bandage in the current example) (plot 1406), as determined using a thromboelastograph (TEG). As shown in FIG. 14, according to plot 1402, hemostasis for conventional cotton gauze bandage was measured to occur during a range of approximately 450 to 570 seconds. According to plot 1404, hemostasis for nanofiber coated base structure 902 was measured to occur during a range of approximately 380-390 seconds. According to plot 1406, hemostasis for nanofiber coated base structure 1202 was measured to occur during a range of approximately 275-300 seconds.

[0108] These results indicate that nanofiber coated base structures, such as nanofiber coated gauze, activate the contact coagulation pathway. It is likely that blood components vital for initiating the contact cascade (i.e., high molecular weight kininogens), bind to the nanofiber surfaces leading to an activation of the early factors in the coagulation cascade (i.e., prekallikrein and factor 12). Once these early factors/elements are activated, the cascade can be propagated into the bulk of the blood. Hence, a reduction in clotting time with blood extracted from the nanofiber coated gauze is achieved.

[0109] Note that further techniques may be used alternatively to soaking (FIG. 5) and/or charge-based attraction (FIG. 6) to incorporate nanostructures with a substrate material according to step 200 in FIG. 2, including nano-spinning, weaving, and/or further techniques described herein.

[0110] In an embodiment, nanostructures may be incorporated with a weave of fibers or other bandage material described elsewhere herein or otherwise known throughout the entire bandage material. In another embodiment, nanostructures may be incorporated with a weave of fibers or other bandage material described elsewhere herein or otherwise known at just a portion of the bandage material. For example, the nanostructures may be incorporated with a bandage material in a pattern (e.g., a surface pattern, a pattern internal to the bandage material). For instance, nanostructures may be incorporated in a portion of a bandage material that is configured to come into contact with a wound when the

bandage is applied to a subject, and may not be incorporated in other portions of the bandage material. In another example, nanostructures may be applied to a portion of a closure device that is not within the lumen of a blood vessel. Any suitable pattern of nanostructures may be incorporated with a bandage material or other medical device, including patterns described elsewhere herein.

Example Expandable and Absorbent Hemostatic Material Embodiments

[0111] Expandable polymers have been used for wound closure to prevent blood loss after endoscopic surgery where the entry/exit point of the endoscopic device is through a blood vessel. An example of such device is the Angioseal™ vascular closure device sold by St. Jude Medical of St. Paul, MN. Absorbent materials, such as cotton gauze or tampon structures, have also been used for wound closure. In a device using an expandable material, blood and/or other fluids are absorbed by the material, and the material swells to cause a physical barrier. Static blood may be entrapped within pores of the material, which clots due to stasis. It would be advantageous if the blood within the expanded material could be made to clot more rapidly. Embodiments of the present invention enable an increased rate of clotting for devices based on expandable materials and non-expandable materials (e.g., cotton-based, such as gauze, tampon, and other such non-expanding materials).

[0112] In an embodiment, nanostructures, such as nanofibers, are co-formulated with one or more polymers such that the surface of the polymer remains hemostatic – the polymer is not coated so tightly by the nanofibers such that blood cannot access it. Silicon nanowires having an outer core of silicon dioxide are hemostatic due to the procoagulative nature of a negatively charged silicon dioxide surface. By dispersing these nanowires within a material in such a way as to be entrapped by the polymer, but not tightly coating the polymer, an additional surface at which accelerated hemostasis can occur is provided by the nanowires.

[0113] FIG. 15 shows a step 1500 for forming a hemostat, according to an example embodiment of the present invention. Step 1500 may be used to form hemostatic structures such as hemostatic bandages or plugs. Further structural and operational

embodiments will be apparent to persons skilled in the relevant art(s) based on the discussion regarding step 1500.

[0114] As shown in FIG. 15, in step 1500, an expandable hemostatic material is mixed with a plurality of nanostructures. For example, FIG. 16 shows a block diagram illustrating a mixing system 1600, according to an example embodiment of the present invention. As shown in FIG. 16, a mixer 1602 receives an expandable hemostatic material 1604 and a plurality of nanostructures 1606. Mixer 1602 mixes expandable hemostatic material 1604 and nanostructures 1606 to generate hemostat 1608, which includes an expandable hemostatic material and nanostructure mixture 1610. Mixer 1602 may be any type of mixer, including a vortex mixer, mixing by human/manual effort, or other type of mixer.

[0115] Expandable hemostatic material 1604 may be any type of expandable hemostatic material, including gauze (e.g., cotton or other material), a tampon (e.g., cotton or other material), a polymer such as polyethylene glycol (PEG), or other material that expands due to fluid absorption and/or other cause. Nanostructures 1606 may be any type of nanostructure mentioned elsewhere herein or otherwise known. For example, in an embodiment, nanostructures 1606 may include nanowires. The nanowires included in nanostructures 1606 may be similar to nanowire 100 shown in FIG. 1A (a core nanowire structure), or may be core-shell nanowires similar to nanowire 110 of FIG. 1B, having a shell 112 around a nanowire core. When present, shell 112 may be a hemostatic material, such as silicon dioxide.

[0116] By mixing nanowires having a hemostatic material shell layer with expandable hemostatic material 1604 using mixer 1602 to form hemostat 1608, an improved hemostatic material is formed over conventional hemostatic materials. Mixer 1602 may be configured to mix nanostructures 1606 and expandable hemostatic material 1604 in a manner (e.g., in a particular ratio) such that nanostructures 1606 are entrapped by expandable hemostatic material 1604, but do not tightly coat expandable hemostatic material 1604. In this manner, an additional surface at which accelerated hemostasis can occur is provided by nanostructures 1606 without blocking the surface of expandable hemostatic material 1604.

[0117] Hemostat 1608 can be used to induce clotting by being applied to, or inserted in (e.g., plugging) wounds. For example, FIG. 17 shows a cross-sectional view of hemostat 1608 inserted in an opening 1702 (on a catheter 1704) through tissue 1710, according to an example embodiment of the present invention. For instance, opening 1702 may be formed to enter catheter 1704 in an artery 1708 through an artery wall 1706 during an arteriotomy. Hemostat 1608 may be released from a sheath (not shown in FIG. 17) of catheter 1704 prior to withdrawing catheter 1704 from opening 1702. In an embodiment where expandable hemostatic material 1604 is freeze dried PEG, after being exposed in opening 1702, the porous PEG material of hemostat 1608 rapidly swells by an amount of around 3 to 4 times its original size, such that hemostat 1608 becomes approximately 5% PEG/nanostructures 1606 and 95% blood and other absorbed fluids. When expanded, hemostat 1608 conforms to opening 1702 to provide a seal, and provides hemostasis. Blood collects in hemostat 1608, and clots, providing a platform for natural vessel healing.

[0118] In an embodiment, expandable hemostatic material 1604 and nanostructures 1606 are resorbable materials, so that hemostat 1608 is resorbable. Example resorbable materials for expandable hemostatic material 1604 include polymers such as PEG and other resorbable materials mentioned elsewhere herein or otherwise known, and example resorbable nanostructures for nanostructure 1606 include silicon nanowires, including nanowires having a silicon dioxide shell.

Example Hemostatic Material Embodiments

[0119] Various materials have been developed to help stop wounds from bleeding excessively and to increase a rate of clotting. Such materials may be used in surgical procedures and/or by first responders to traumatic events, for example. Existing bulk hemostats have disadvantages, however. For example, it would advantageous if existing bulk hemostats functioned more quickly, were resorbable, and/or did not have an exothermic reaction with blood. Embodiments of the present invention overcome these limitations of conventional bulk hemostats.

[0120] In an embodiment, nanostructures, such as nanofibers, are co-formulated with glass microspheres (either solid or porous). This co-formulated material has an enhanced

hemostatic activity that is not purely additive – i.e., the combination of the nanostructures and glass microspheres has a faster hemostatic activity (e.g., when measured in a TEG) than the nanostructures or glass microspheres alone, which is not necessarily explained purely by a resulting increase in surface area of the hemostat.

[0121] FIG. 18 shows a step 1800 for forming a hemostat, according to an example embodiment of the present invention. Step 1800 may be used to form hemostatic materials, such as bulk hemostats, which may be in granular, powder, or other form. Further structural and operational embodiments will be apparent to persons skilled in the relevant art(s) based on the discussion regarding step 1800.

[0122] As shown in FIG. 18, in step 1800, a plurality of glass beads is mixed with a plurality of nanostructures. For example, FIG. 19 shows a block diagram illustrating a mixing system 1900, according to an example embodiment of the present invention. As shown in FIG. 19, a mixer 1902 receives glass beads 1904 and a plurality of nanostructures 1906. Mixer 1902 mixes glass beads 1904 and nanostructures 1906 to generate hemostat 1908, which includes a glass bead and nanostructure mixture 1910. Mixer 1902 may be any type of mixer, including a vortex mixer, mixing by manual/human effort, or other type of mixer.

[0123] Glass beads 1904 may be solid or porous, and may have any size, including being microspheres. For instance, in an embodiment, glass beads 1904 have diameters in the range of 3-10 micrometers. Nanostructures 1906 may be any type of nanostructure mentioned elsewhere herein or otherwise known. For example, in an embodiment, nanostructures 1906 may include nanowires such as silicon nanowires. The nanowires included in nanostructures 1906 may be similar to nanowire 100 shown in FIG. 1A (a core nanowire structure), or may be core-shell nanowires similar to nanowire 110 of FIG. 1B, having a shell 112 around a nanowire core. When present, shell 112 may be a hemostatic material, such as silicon dioxide.

[0124] Hemostat 1908 can be used to induce clotting by being applied to wounds, such as by pouring hemostat 1908 onto/into a wound. By mixing nanowires having a hemostatic material shell layer with glass beads 1904 to form hemostat 1908, an improved hemostatic material is formed over conventional hemostatic materials.

[0125] As described above, in embodiments, glass beads 1904 may be solid or porous. In further embodiments, glass beads 1904 may be formed from a uniform glass material, or may be core-shell structures, having a core of a first material and a shell layer of a second material. For example, FIG. 20 shows a cross-sectional view of a hemostatic core-shell particle 2000, according to an example embodiment of the present invention. Core-shell particle 2000 has a core portion 2002 surrounded by a shell 2004. Core portion 2002 may have any shape, including being spherical, elongated, irregular, or other shape. Shell 2004 has a thickness 2006. Core portion 2002 and shell 2004 may be made of hemostatic materials to induce coagulation of blood, as described herein. For example, core portion 2002 may be a resorbable polymer, including a copolymer, blend, or other polymer such as lactic acid (e.g., polylactic acid (PLA)), glycolic acid (e.g., polyglycolic acid (PGA)), an amide, an anhydride, an ester, a dioxanone, or other polymer mentioned elsewhere herein or otherwise known. Shell 2004 may be a layer of a hemostatic material, including a glass such as silicon dioxide, a spin-on glass, or other hemostatic material. Alternatively, core portion 2002 may be a glass material, and shell may be a non-glass (e.g., a polymer) material.

[0126] In an embodiment, core-shell particle 2000 may be formed according to step 2100 shown in FIG. 21. In step 2100, particles of a resorbable core material are coated with a hemostatic material, wherein a rate of resorption of the core material is greater than a rate of resorption of the hemostatic material. In such an embodiment, shell 2004 may be selected as a material having greater hemostatic properties than core portion 2002, while core portion 2002 may be selected as a material that has a greater rate of resorption than shell 2004. In this manner, core-shell particle 2000 may be useful at clotting blood (due to shell 2004), while being resorbed by the body faster than conventional hemostatic materials (due to core portion 2002).

[0127] For example, shell 2004 may be a glass such as silicon dioxide, a spin-on glass, or other glass or other hemostatic material, which induces clotting upon contact with blood. Core portion 2002 may be a polymer that has a rate of resorption that is greater than a rate of resorption of silicon dioxide, so that an overall rate of resorption of core-shell particle 2000 is increased relative to a solid glass bead (e.g., formed of silicon dioxide). Thickness 2006 of shell 2004 may be tailored to balance the clotting functionality of core-

shell particle 2000 (primarily due to shell 2004) with an overall resorption time of core-shell particle 2000 (due to shell 2002 and core portion 2002).

[0128] In embodiments, core-shell particle 2000 may be incorporated in (e.g., mixed into) a hemostatic material, such as hemostat 1908 and/or other hemostatic materials/structures described elsewhere herein, along with or in place of nanostructures, glass beads, and/or other particles described herein.

Further Example Hemostatic Bandage Embodiments

[0129] As described above, nanostructures may be applied to bandages to assist in activating the intrinsic (contact) clotting cascade, leading to the slowdown or stoppage of bleeding. In embodiments, the nanostructures may be nanoparticles, such as silicon nanoparticles. The nanoparticles may be dispersed in a bandage material to provide enhanced clotting to the bandage material.

[0130] For example, FIG. 22 shows a block diagram of a hemostatic bandage 2200, according to an example embodiment of the present invention. As shown in FIG. 22, hemostatic bandage 2200 includes a bandage material 2202 and a plurality of nanoparticles 2204 (which may collectively be referred to as a "nanopowder"). Bandage material 2202 may be any bandage material described elsewhere herein, including resorbable and/or non-resorbable substrate materials such as organic materials, inorganic materials, woven materials/fabrics, nonwoven materials/fabrics (e.g., nonwoven fiber materials such as a cotton ball), synthetic materials (e.g., rayon, nylon/lycra, Gore-Tex®, polymers, etc.), natural materials (e.g., cotton), biologics/biological derived materials (e.g., chitosan, including chitosan microparticles, collagen, gelatin, cellulose, etc.), and/or particles (e.g., glass or polymer beads).

[0131] Nanoparticles 2204 may be any type of nanoparticles, such as silicon nanoparticles, for example. Such nanoparticles may have an outer thin oxide layer, which may be naturally occurring. For example, FIG. 23 shows a block diagram of hemostatic bandage 2200 of FIG. 22, where nanoparticles 2204 are naturally-oxidized silicon nanoparticles 2302. Naturally-oxidized silicon nanoparticles 2302 have an outer thin oxide layer that is formed by the natural oxidation of silicon nanoparticles (e.g., due to the

exposure to air or other oxygen-containing environment). Naturally-oxidized silicon nanoparticles 2302 may perform better as a hemostatic material (e.g., may be more glass-like) as compared to fumed silica (which is completely oxidized silicon particles), because the thin oxide layer is absorbed by the human body to which bandage material 2202 is applied, exposing the underlying silicon material of naturally-oxidized silicon nanoparticles 2302 to the human body, which may be important in inducing the clotting effect.

[0132] For instance, FIG. 24 shows a graph 2400 of clot time for a bandage containing a silicon nanopowder, according to an example embodiment of the present invention. The data of graph 2400 was obtained using a thromboelastograph (TEG), for a bandage that included commercial silicon nanopowder (manufactured by laser decomposition) that included nanoparticles having an average particle size of approximately 50 nm. As shown in FIG. 24, R-time (in seconds) is plotted on the Y-axis versus an amount of blood (in milligram/milliliter or mg/mL). A plot line 2402 in graph 2400 indicates that at approximately 1.8 mg/mL, the R-time is approximately 310 seconds, at approximately 3.8 mg/ML, the R-time is approximately 280 seconds, and at approximately 10 mg/mL, and the R-time is approximately 210 seconds (plot line 2402 is a continuous line connected between these points in graph 2400). While the indicated clot time in the presence of silicon nanopowder is in the range of approximately 210 seconds to 310 seconds, when silicon nanopowder is not present, a bandage has an R-time of approximately 800 seconds. Thus, the addition of a silicon nanopowder to a bandage forms a hemostat with substantially faster clotting time than bandages without a hemostat.

[0133] Silicon nanoparticles (e.g., silicon particles of less than about 100 nm in diameter) may have a same hemostatic efficacy as silicon nanowires based on preliminary testing results. Based on TEG testing results, fumed silica is determined to not perform as well as silicon nanowires in initiating the clotting cascade in vitro. Thus, silicon nanoparticles and silicon nanowires, which both have a thin oxide layer, are preferable to fumed silica.

[0134] Hemostatic bandage 2200 may be formed in any manner. For instance, FIG. 25 shows a flowchart 2500 for forming a hemostatic bandage, according to an example embodiment of the present invention. Various systems may be configured to perform flowchart 2500 to form a hemostatic bandage 2200. For example, FIG. 26 shows a block

diagram of a hemostatic bandage fabrication system 2600, according to an embodiment of the present invention. As shown in FIG. 26, system 2600 includes a wafer grinder 2602, a bandage processor 2604, and a bandage coater 2606. Flowchart 2500 is described with respect to system 2600 for purposes of illustration. Note that not all of the steps shown in FIG. 25 need to be performed in all embodiments. Flowchart 2500 is described as follows.

[0135] Flowchart 2500 begins with step 2502. In step 2502, a silicon wafer is milled to generate a nanopowder. For instance, wafer grinder 2602 shown in FIG. 26 may be configured to perform step 2502. As shown in FIG. 26, wafer grinder 2602 receives wafer 2608, which may be a silicon wafer. Wafer grinder 2602 is configured to grind wafer 2608 according to any suitable grinding process, including milling wafer 2608 (e.g., using a physical milling mechanism, jet milling, etc.), applying laser decomposition to wafer 2608, or any other suitable technique. In the current example, wafer grinder 2602 generates a silicon nanopowder 2610.

[0136] In an embodiment, silicon nanopowder 2610 is naturally oxidized by exposure to the air or other oxygen containing environment. The natural oxidation of silicon nanopowder 2610 creates a thin oxide layer on the silicon nanoparticles of silicon nanopowder 2610 (e.g., creating naturally-oxidized silicon nanoparticles 2302 shown in FIG. 23). Alternatively, silicon nanopowder 2610 may be thermally oxidized to create a thin oxide layer on the nanoparticles of silicon nanopowder 2610, or may be oxidized (naturally or thermally) such that the nanoparticles are fully oxidized into fumed silica nanoparticles.

[0137] In step 2504, a nanopowder formed of nanoparticles having an outer thin oxide layer is dispersed in a bandage material. For example, bandage processor 2604 shown in FIG. 26 may be configured to perform step 2504. As shown in FIG. 26, bandage processor 2604 receives silicon nanopowder 2610 and a bandage material 2612. Bandage material 2612 may include completed bandages or may include materials used to create bandages, include any of the bandage materials described elsewhere herein or otherwise known. Bandage processor 2604 may be configured to disperse silicon nanopowder 2610 into the completed bandages of bandage material 2612, or may be configured to fabricate bandages that include silicon nanopowder 2610 dispersed therein.

[0138] For example, in an embodiment where bandage processor 2604 receives completed bandages, silicon nanopowder 2610 may be poured or injected onto the completed bandages in a solid form or in the form of a liquid having silicon nanopowder 2610 dissolved therein (e.g., flowed through the bandages, leaving silicon nanopowder 2610 embedded in the bandages). In an embodiment where bandage processor 2604 receives bandage materials, silicon nanopowder 2610 may be applied to the bandage materials (e.g., coated onto, flowed through, mixed into, etc.), and the bandage materials may be subsequently fabricated into completed bandages by bandage processor 2604. Persons skilled in the relevant art(s) will know how to configure bandage processor 2604 to fabricate bandages from bandage materials (e.g., by weaving fibers into bandages, etc.). As shown in FIG. 26, bandage processor 2604 generates hemostatic bandages 2614.

[0139] As described above, silicon nanopowder 2610 in hemostatic bandages 2614 increases a rate of blood clotting for hemostatic bandages 2614 relative to bandages that do not include a hemostatic element. Furthermore, silicon nanopowder 2610 is resorbable, and thus does not have to be subsequently manually removed from a human subject. When silicon nanopowder 2610 includes silicon nanoparticles having a thin-oxide layer, silicon nanopowder 2610 may perform better as a hemostatic material as compared to fumed silica. This may be because the thin oxide layer is absorbed by the human body to which hemostatic bandages 2614 are applied, exposing the underlying silicon material of silicon nanopowder 2610 to the human body, which may induce the clotting effect.

[0140] In step 2506, a surface of the bandage material is coated with nanowires. Step 2506 is optional. In an embodiment, bandage coater 2606 shown in FIG. 26, bandage coater 2606 receives hemostatic bandages 2614 and nanowires 2616. For example, nanowires 2616 may include silicon nanowires, potassium nanowires, silicon nanowires functionalized with potassium, silicon nanowires having an outer layer of silicon dioxide, and/or other type of nanowire described elsewhere herein or otherwise known. Bandage coater 2606 is configured to coat hemostatic bandages 2614 with nanowires 2616 to generate nanowire-coated hemostatic bandages 2618. For instance, FIG. 27 shows a block diagram of a cross-sectional view of a nanowire-coated hemostatic bandage 2700, which is an example bandage of nanowire-coated hemostatic bandages 2618, according to

an embodiment. As shown in FIG. 27, nanowire-coated hemostatic bandage 2700 includes a nanowire coating 2702, a bandage material 2704, and nanoparticles 2706. Bandage material 2704 contains nanoparticles 2706 of nanopowder 2610. Nanowire coating 2702 is a coating of nanowires 2616 over a surface of bandage material 2704.

[0141] Bandage coater 2606 may be configured to coat a portion of all of a surface of hemostatic bandages 2614 with nanowires 2616 in any suitable manner, including as described above with respect to step 200 in FIG. 2, step 500 in FIG. 5, step 600 in FIG. 6, flowchart 700 in FIG. 7, or flowchart 1100 in FIG. 11, where weaves of fibers are coated with nanostructures. For example, bandage coater 2606 may spray nanowires 2616 onto hemostatic bandages 2614 in solid or liquid form, may pour spray nanowires 2616 onto hemostatic bandages 2614 in liquid form, may soak hemostatic bandages 2614 in a solution that contains nanowires 2616, etc. In an embodiment, hemostatic bandages 2614 may have a charge (either positive or negative) imparted thereon, while nanowires 2616 may be imparted with an opposite charge, which causes nanowires 2616 to be attracted to hemostatic bandages 2614, in a similar manner as described elsewhere herein.

[0142] Nanowires 2616 coating nanowire-coated hemostatic bandages 2618 increase a rate of blood clotting relative to bandages that do not include a hemostatic element. Furthermore, nanowires 2616 may have a higher tissue adhesion ability relative to nanopowder 2610, thus enhancing tissue adhesion by nanowire-coated hemostatic bandages 2618. Furthermore, silicon nanowires 2616 are resorbable, and thus do not have to be subsequently manually removed from a human subject. Still further, the combination of nanowires 2616 and silicon nanopowder 2610 in nanowire-coated hemostatic bandages 2618, as described above, may reduce a cost of bandages relative to bandages that include nanowires 2616 throughout, because nanowires 2616 are more expensive than silicon nanopowder 2610.

[0143] One possible mechanism for a hemostatic action that may be provided/enhanced by nanowire-coated hemostatic bandages 2618 is described as follows: A nanowire-coated hemostatic bandage 2618 is applied to a wound. Nanowires 2616 coating nanowire-coated hemostatic bandage 2618 increase adhesion to the wound. Blood from the wound comes into contact with nanowires 2616, and is drawn into nanowire-coated hemostatic bandage 2618, which may be porous. An intrinsic coagulation pathway is

triggered by the binding of HMwt kininogen to the surface of nanowires 2616 (which may be negatively charged). The intrinsic coagulation cascade proceeds, and is amplified by the presence of nanowires 2616. Thrombin is activated, and a fibrin clot is formed that integrates within a mesh of nanowires 2616. A binding and aggregation of platelets occurs, which completes formation of the clot. An overall rate of the coagulation and a strength of the clot is aided by nanowires 2616. In this manner, hemostasis is achieved.

[0144] Note that this example possible mechanism for hemostatic action that may be provided/enhanced by nanowire-coated hemostatic bandages 2618 is provided for purposes of illustration, and is not intended to be limiting. Further mechanisms and/or variations of this illustrated mechanism may alternatively be performed by nanowire-coated hemostatic bandages 2618.

Example Hemostatic Material Embodiments with Multiple Lengths of Nanowires

[0145] As described above, nanowires may be applied to bandages to assist in activating the intrinsic (contact) clotting cascade, leading to the slowdown or stoppage of bleeding. In embodiments, nanowires of different lengths may be applied to bandages to tailor the clotting and tissue adhesion characteristics of the bandages. Any number of different lengths of nanowires may be applied to bandages to tailor the clotting and tissue adhesion characteristics.

[0146] Shorter nanowires penetrate more deeply and provide extra surface area for enhanced clotting. Longer nanowires tend to remain at the bandage surface, where they assist in adhesion to tissue. Relatively longer nanowires demonstrate better adhesion properties than do shorter nanowires. Shorter nanowires, however, are more easily incorporated at high concentrations into bandage materials, because longer nanowires tend to be filtered by the bandage material and remained largely on the surface of the bandage material. The presence of longer nanowires at the bandage surface is beneficial for imparting adhesive properties to the bandage, but such filtering makes it difficult to achieve nanowire concentrations in the bandage that are optimal for accelerating clotting using longer nanowires alone.

[0147] In an embodiment, both short and long nanowires may be dispersed in a bandage to optimize separately both adhesion and clotting acceleration. For example, an

optimized ratio of concentrations of short and long nanowires may be added homogeneously to a bandage, or the short and long nanowires may be spatially separated in the bandage to optimize a hemostatic efficacy. For example, it may be beneficial to position a high concentration of shorter nanowires in a center of the bandage, and to position longer nanowires around a periphery of the bandage. This arrangement can be used to form a seal with tissue at the perimeter edges of the bandage where the longer nanowires are concentrated, and may enable a clotting rate to be optimized directly over the wound (adjacent to a central region of the bandage where shorter nanowires are concentrated). Any arrangement of nanowires may be formed, including forming concentric rings of short and long nanowires radiating from the center of the bandage, for example.

[0148] For example, FIG. 28 shows a block diagram of a hemostatic bandage 2800 that includes multiple lengths of nanowires, according to an example embodiment of the present invention. As shown in FIG. 28, hemostatic bandage 2800 includes a bandage material 2802, a plurality of first length nanowires 2804, and a plurality of second length nanowires 2806. Bandage material 2802 may be any bandage material described elsewhere herein, including resorbable and/or non-resorbable substrate materials such as organic materials, inorganic materials, woven materials/fabrics, nonwoven materials/fabrics (e.g., nonwoven fiber materials such as a cotton ball), synthetic materials (e.g., rayon, nylon/lycra, Gore-Tex®, polymers, etc.), natural materials (e.g., cotton), biologics/biological derived materials (e.g., chitosan, including chitosan microparticles, collagen, gelatin, etc.), and/or particles (e.g., glass or polymer beads).

[0149] First length nanowires 2804 includes nanowires formed to each have a first length. Second length nanowires 2806 includes nanowires formed to each have a second length. The second length of second length nanowires 2806 is greater than the first length of first length nanowires 2804.

[0150] Hemostatic bandage 2800 may be formed in any manner. For instance, FIG. 29 shows a flowchart 2900 for forming a hemostatic bandage having multiple lengths of nanowires, according to an example embodiment of the present invention. Various systems may be configured to perform flowchart 2900 to form hemostatic bandage 2800. For example, FIG. 30 shows a block diagram of a hemostatic bandage fabrication system

3000, according to an embodiment of the present invention. As shown in FIG. 30, system 3000 includes a nanowire fabricator 3002 and a bandage processor 3004. Flowchart 2900 is described with respect to system 3000 for purposes of illustration. Note that not all of the steps shown in FIG. 29 need to be performed in all embodiments, and the steps of flowchart 2900 do not necessarily need occur in the order shown. Flowchart 2900 is described as follows.

[0151] Flowchart 2900 begins with step 2902. In step 2902, a first plurality of nanowires is formed that includes nanowires having a first length. For example, nanowire fabricator 3002 shown in FIG. 30 may be configured to perform step 2902. As shown in FIG. 30, nanowire fabricator 3002 generates first length nanowires 2804. Nanowire fabricator 3002 may be configured to generate first length nanowires 2804 according to any suitable nanowire fabrication technique described or referenced herein, or otherwise known. Nanowire fabricator 3002 generates first length nanowires 2804 to have a relatively short length, such as having lengths in the range of 0 to 500 nm.

[0152] In step 2904, a second plurality of nanowires is formed that includes nanowires having a second length. For example, nanowire fabricator 3002 shown in FIG. 30 may also be configured to perform step 2904. As shown in FIG. 30, nanowire fabricator 3002 generates second length nanowires 2806. Nanowire fabricator 3002 may be configured to generate second length nanowires 2806 according to any suitable nanowire fabrication technique described or referenced herein, or otherwise known. Nanowire fabricator 3002 generates second length nanowires 2806 to have a relatively longer length, such as having lengths in the range of 20 to 30 microns. For example, longer nanowires may be generated by nanowire fabricator 3002 by allowing a longer nanowire growth time relative to a growth time for shorter nanowires (in step 2902), or by other suitable technique.

[0153] In step 2906, the first plurality of nanowires is dispersed in a first region of a bandage material. For example, bandage processor 3004 may be configured to perform step 2906. As shown in FIG. 30, bandage processor 3004 receives first length nanowires 2804, second length nanowires 2806, and a bandage material 3006. Bandage material 3006 may include completed bandages or may include materials used to create bandages, include any of the bandage materials described elsewhere herein or otherwise known.

Bandage processor 3004 may be configured to disperse first length nanowires 2804 into a first region of the completed bandages of bandage material 3006, or may be configured to fabricate bandages that include first length nanowires 2804 dispersed in the first region.

[0154] For example, in an embodiment where bandage processor 3004 receives completed bandages, first length nanowires 2804 may be poured or injected onto the completed bandages in a solid or liquid form (e.g., a liquid including first length nanowires 2804 may be flowed through the bandages, leaving first length nanowires 2804 embedded in the first region of the bandages). In an embodiment where bandage processor 3004 receives bandage materials, first length nanowires 2804 may be applied to the first region of the bandage materials (e.g., coated onto, flowed through, etc.), and the bandage materials may be subsequently fabricated into completed bandages by bandage processor 3004. Persons skilled in the relevant art(s) will know how to configure bandage processor 3004 to fabricate bandages from bandage materials (e.g., by weaving fibers into bandages, etc.).

[0155] In step 2908, the second plurality of nanowires is dispersed in a second region of the bandage material. For example, bandage processor 3004 may be configured to perform step 2908. Similarly to step 2906, bandage processor 3004 may be configured to disperse second length nanowires 2806 into a second region of the completed bandages of bandage material 3006, or may be configured to fabricate bandages that include second length nanowires 2806 dispersed in the second region.

[0156] In a similar fashion as described above, second length nanowires 2806 may be poured or injected onto completed bandages in a solid or liquid form. In an embodiment where bandage processor 3004 receives bandage materials, second length nanowires 2806 may be applied to the second region of the bandage materials (e.g., coated onto, flowed through, etc.), and the bandage materials may be subsequently fabricated into completed bandages by bandage processor 3004. As shown in FIG. 26, bandage processor 3004 generates a hemostatic bandage 2800.

[0157] In embodiments, the first and second regions into which first and second length nanowires 2804 and 2806 are dispersed may be spatially arranged in any manner. For example, in one embodiment, the first region may be an interior region of hemostatic bandage 2800 and the second region may be an exterior region of bandage 2800. For

instance, FIG. 31 shows a block diagram cross-sectional view of a hemostatic bandage 3100, which is an example of hemostatic bandage 2800, according to an embodiment. As shown in FIG. 31, hemostatic bandage 3100 includes first length nanowires 2804, a bandage material 3102, and second length nanowires 2806. Bandage material 3102 contains first length nanowires 2804 in an interior region 3104 of bandage material 3102. Second length nanowires 2806 are contained in a coating 3106 formed over a surface of bandage material 3102.

[0158] Hemostatic bandage 3100 increases a rate of blood clotting relative to bandages that do not include a hemostatic element. Longer nanowires, such as second length nanowires 2806, have a higher tissue adhesion ability relative to shorter nanowires, such as first length nanowires 2804, and by being located in coating 3106, enhance tissue adhesion by hemostatic bandage 3100. Furthermore, shorter length nanowires, such as first length nanowires 2804, are more easily incorporated at high concentrations into bandage materials by soaking, filtration, or other procedures, and thus enable a larger total amount of nanowires (and total surface area of nanowires) to be contained by hemostatic bandage 3100 relative to second length nanowires 2806 alone.

[0159] Note that steps 2906 and 2908 may be performed separately or simultaneously to form hemostatic bandage 3100. For example, step 2906 may be first performed to disperse first length nanowires 2804 in interior region 3104 of bandage material 3102, and then step 2908 may be formed to form coating 3106 containing second length nanowires 2806 on the surface of bandage material 3102. In a simultaneous dispersing embodiment, referring to FIG. 30, first and second length nanowires 2804 and 2806 may be mixed together by bandage processor 3004, and the mixture may be applied to bandage material 3006. Because first length nanowires 2804 are smaller than second length nanowires 2806, first length nanowires 2804 may penetrate into bandage material 3102 into interior region 3104, while bandage material 3006 (e.g., a fibrous material, etc.) may prevent second length nanowires 2806 from penetrating into bandage material 3102 because of their larger size, and thus second length nanowires 2806 remain at the surface of bandage material 3102.

[0160] In another embodiment, the first region may be a central region of a surface of hemostatic bandage 2800 and the second region may be a perimeter region of the surface

of bandage 2800. For instance, FIG. 32 shows a view of a surface of a hemostatic bandage 3200, which is an example of hemostatic bandage 2800, according to an embodiment. As shown in FIG. 32, hemostatic bandage 3200 includes first length nanowires 2804, a bandage material 3202, and second length nanowires 2806. Bandage material 3102 contains first length nanowires 2804 in a central region 3204 of the surface of bandage material 3202. Second length nanowires 2806 are contained in a perimeter region 3206 of the surface of bandage material 3202.

[0161] Because longer nanowires, such as second length nanowires 2806, have a higher tissue adhesion ability relative to shorter nanowires, perimeter region 3206 may adhere better to a subject than central region 3204, forming a seal with tissue of the subject around central region 3204, which may be positioned adjacent to a wound of the subject.

[0162] First and second length nanowires 2804 and 2806, and optionally further lengths of nanowires, may be used in any combination and relative positioning in hemostatic bandages. The different length nanowires may be spatially distributed in the bandage in a controlled manner to impart various degrees of clotting acceleration and tissue adhesion to different portions of the bandage. Furthermore, in embodiments, laminated materials may be used.

Example Hemostatic Surgical Staple and Suture Embodiments

[0163] In embodiments, surgical staples and sutures used for suturing wounds may be functionalized with hemostatic nanomaterials to improve clotting. For example, FIG. 33 shows a perspective view of an example surgical staple 3300. As shown in FIG. 33, surgical staple 3300 includes a body 3302 having a base portion 3304, a first leg 3306, and a second leg 3308. Base portion 3304 has opposing first and second surfaces 3310 and 3312. First leg 3306 extends at a first angle (e.g., 90 degrees in FIG. 33) from a first end 3314 of first surface 3310, and second leg 3306 extends at a second angle (e.g., 90 degrees in FIG. 33) from a second end 3316 of first surface 3308. First and second legs 3306 and 3308 each have a respective pointed end portion 3318 and 3320 at a respective end extending away from base portion 3304. Although surgical staple 3300 is shown in FIG. 33 as being a flat piece that is bent, molded, or otherwise formed into a rectangular shape, surgical staple 3300 may have other shapes, including being curved and/or

rounded. Surgical staple 3300 may be made from a non resorbable material, such as a metal or a polymer, or may be made from a resorbable material.

[0164] When surgical staple 3300 is applied to a subject, pointed end portions 3318 and 3320 of surgical staple 3300 penetrate tissue of the subject, such that legs 3306 and 3308 at least partially penetrate the subject. Legs 3306 and 3308 (and/or base portion 3304) are subsequently bent such that pointed end portions 3318 and 3320 approach each other, overlap each other, are bent past each other, and/or make contact with each other, so that surgical staple 3300 is bonded to the subject, to hold closed a portion of a wound bridged by base portion 3304.

[0165] In embodiments, surgical staple 3300 may be functionalized with hemostatic nanostructures to enable faster clotting to occur when staple 3300 is used, relative to non-hemostatic staples. For example, in an embodiment, step 3400 shown in FIG. 34 may be performed. In step 3400, at least a portion of a surgical staple is coated with a layer of nanostructures. Any portion of surgical staple 3300 may be coated with a layer of nanostructures, including surface 3310 (which is in contact with tissue when staple 3300 is in use), legs 3306 and 3308 (which penetrate tissue when staple 3300 is in use), other portion of surgical staple 3300, the entirety of surgical staple 3300, etc.

[0166] Step 3400 may be performed in any manner. For instance, FIG. 35 shows a staple coating system 3500, according to an example embodiment of the present invention. Staple coating system 3500 may perform step 3400 in an embodiment. As shown in FIG. 34, system 3500 includes a coater 3502. Coater 3502 receives nanostructures 3504 and staples 3506. Coater 3502 is configured to coat staples 3506 with nanostructures 3504 to generate coated staples 3508. Coater 3502 may be configured to coat a portion or the entirety of each staple of staples 3506, in embodiments. Coater 3502 may coat staples 3506 with nanostructures 3504 in any manner, including by spray coating or soaking staples 3506 in a liquid that includes nanostructures 3504, followed by a drying process, or according to any other suitable technique. In an embodiment, staples 3506 may be imparted with a first charge (either positive or negative), and nanostructures 3504 may be imparted with an opposite second charge, to attract nanostructures 3504 to staples 3506.

[0167] In another embodiment, staple coating system 3500 may be configured to perform step 3400 by growing nanostructures directly on staples 3506. Any suitable nanostructure

growth technique may be used by staple coating system 3500, including those techniques described elsewhere herein (including those growth techniques disclosed in documents referenced elsewhere herein).

[0168] In an embodiment, a shape of surgical staple 3300 may be modified to enable additional nanostructures to coat surgical staple 3300 and to thereby come into contact with the subject. For example, FIG. 36 shows a perspective view of a surgical staple 3600, which is a modified form of surgical staple 3300, according to an example embodiment of the present invention. Surgical staple 3600 is similar to surgical staple 3300, with differences described as follows. As shown in FIG. 33, base portion 3304 of surgical staple 3300 has a width (perpendicular to an axis along base portion 3304 through first and second ends 3314 and 3316) that is substantially equal to a width of legs 3306 and 3308. As shown in FIG. 36, base portion 3304 of surgical staple 3600 is wider than base portion 3304 of surgical staple 3300. Base portion 3304 of surgical staple 3600 has a first width 3602 (perpendicular to the first axis through first and second ends 3314 and 3316), and first and second legs 3306 and 3308 each have a second width 3604 (parallel to first width 3602) located between base portion 3304 and pointed end portions 3318 and 3320. First width 3602 of base portion 3304 is greater than second width 3604 of first and second legs 3306 and 3308. In this manner, surfaces 3310 and 3312 of base portion 3304 in FIG. 36 have greater surface area than surfaces 3310 and 3312 of base portion 3304 in FIG. 34, and can thus be coated with a greater amount of nanostructures.

[0169] For example, FIG. 37 shows surgical staple 3600 of FIG. 36, where first surface 3310 of base portion 3304 is coated with a layer 3702 of nanostructures. First surface 3310 of base portion 3310 typically comes into contact with tissue of a subject when surgical staple 3600 is applied to the subject. In such case, layer 3702 of nanostructures comes into contact with the tissue, enabling the nanostructures to provide enhanced clotting, as described herein. The nanostructures may be any type of nanostructures described herein, including silicon nanowires, silicon nanofibers, silicon nanoparticles, potassium nanofibers, nanowires/nanofibers/nanoparticles having a thin oxide layer, etc.

[0170] In a similar manner as described above, threads/sutures used to hold together wounds in tissue may be functionalized with hemostatic nanomaterials to improve clotting. For example, FIG. 38 shows a portion of a suture 3800 coated with a layer 3802

of nanostructures, according to an example embodiment of the present invention. Suture 3800 may be made of any suitable resorbable materials described elsewhere herein or otherwise known, including natural or synthetic resorbable materials such as polyglycolic acid, polylactic acid, or caprolactone. Suture 3800 may alternatively be made of any suitable non-resorbable materials described elsewhere herein or otherwise known, including artificial fibers such as polypropylene, polyester, nylon, stainless steel, etc. Suture 3800 may be coated with a layer of nanostructures according to a coating system similar to staple coating system 3500 shown in FIG. 35.

Functionalized Nanostructures Embodiments

[0171] In embodiments, the nanostructures incorporated with structures/materials to form hemostats, as described herein, may be functionalized with additional materials. Such additional materials may improve and/or modify characteristics of the nanostructures. FIG. 39 shows a surface 3902 of a portion of a nanofiber 3900 that is functionalized with a material 3904, according to an embodiment of the present invention.

[0172] Nanostructures (such as nanofiber 3900) offer an external surface that can easily be modified using any number of coating or functionalization chemistries (e.g., growth of nitride or carbide layers for improved strength and durability, growth of titanium oxide, Ag, Zn etc. layers for improved biocompatibility with existing implant materials (e.g., titanium), and/or growth of specific organosilanes to facilitate linkage chemistries such as hydrophobic and/or hydrophilic coatings, etc.) developed for attaching biomolecules. For example, a nanofiber surface can be functionalized with a coating material to render it hydrophobic, lipophobic, or amphiphobic. The coating material can comprise, for example, ceramics, polymers, inorganic materials, organic materials, or organic/inorganic hybrid materials including, for example, Teflon®, Tri-sil, tridecafluoro 1,1,2,2, tetrahydrooctyl-l-tricholorosilane, a fluoride containing compound, a silane containing compound, PTFE, hexamethyldisilazane, an aliphatic hydrocarbon containing molecule, an aromatic hydrocarbon containing molecule, a halogen containing molecule and paralyene.

[0173] Nanostructures (such as nanofiber 3900) incorporated with structures/materials to form hemostats, as described herein, may be further or alternatively functionalized with one or more hemostatic agents to improve and/or modify their hemostatic characterstics. For example, nanostructures may be functionalized with potassium, fibrin, fibrinogen, thrombin, microfibrillar collagen, polysaccharides, chitosan, zeolite, anhydrous aluminum sulfate, titanium dioxide, antifibrinolytics, and/or further hemostatic agents mentioned elsewhere herein or otherwise known.

[0174] Nanostructures in accordance with embodiments of the present invention may be functionalized to target a particular cell, tissue or organ, to enable greater bandage adhesion and/or for further reasons. For instance, techniques and chemistries are known for the precise drug delivery to a particular cell or organ. See, for example, Cotten et al., Methods Enzym. 217:618, 1993, the contents of which are hereby incorporated by reference in its entirety. Nanostructures allow for different functionalization and targeted delivery of different molecules, by "designing" the segments along the length of each nanowire. For example, different segments of the nanowires may be made of different materials, and the different materials may be chosen such that they have different affinities for different functional linking agents or functional moieties.

[0175] Examples of materials that may used to functionalize nanostructures, and example techniques for functionalizing nanostructures, are described in U.S. Pub. Appl. No. 2007/0282247, titled "Medical Device Applications of Nanostructured Surfaces," which is incorporated by reference herein in its entirety.

Conclusion

[0176] Exemplary embodiments of the present invention have been presented. The invention is not limited to these examples. These examples are presented herein for purposes of illustration, and not limitation. Alternatives (including equivalents, extensions, variations, deviations, etc., of those described herein) will be apparent to persons skilled in the relevant art(s) based on the teachings contained herein. Such alternatives fall within the scope and spirit of the invention.

[0177] All publications, patents and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication,

patent or patent application was specifically and individually indicated to be incorporated by reference.

WHAT IS CLAIMED IS:

1. A hemostatic structure, comprising:

a base structure that includes a first material; and

a plurality of nanostructures incorporated with the base structure;

wherein the nanostructures are configured to induce hemostasis when the hemostatic structure is contacted with blood.

2. The hemostatic structure of claim 1, wherein the base structure includes a woven or nonwoven fiber of the first material.

3. The hemostatic structure of claim 1, wherein the nanostructures coat the base structure.

4. The hemostatic structure of claim 1, wherein the first material is resorbable.

5. The hemostatic structure of claim 1, wherein the first material includes cotton.

6. The hemostatic structure of claim 2, wherein the first material is a natural fiber.

7. The hemostatic structure of claim 2, wherein the first material is a synthetic fiber.

8. The hemostatic structure of claim 1, wherein the first material includes oxidized cellulose.

9. The hemostatic structure of claim 1, wherein the first material includes collagen.

10. The hemostatic structure of claim 1, wherein the first material includes a biologically-derived material.

11. The hemostatic structure of claim 1, wherein the first material is an organic or inorganic polymer.

12. The hemostatic structure of claim 2, wherein the fiber is a glass microfiber.

13. The hemostatic structure of claim 1, wherein the hemostatic structure is a bandage.

14. The hemostatic structure of claim 1, wherein the base structure is a bandage.

15. A method for forming a hemostatic structure, comprising:

incorporating nanostructures with a first material to form the hemostatic structure.

16. The method of claim 15, wherein said incorporating comprises:

incorporating the nanostructures with a weave of fibers of the first material to form the hemostatic structure.

17. The method of claim 16, wherein said incorporating comprises:

coating the weave of fibers with the nanostructures to form the hemostatic structure.

18. The method of claim 17, wherein said coating comprises:

sonicating a wafer coated with nanostructures in a liquid;

filtering the sonicated nanostructures;

suspending the filtered nanostructures in a liquid to form a nanostructure suspension;

soaking the weave of fibers in the nanostructure suspension; and

drying the soaked weave of fibers.

19. The method of claim 18, wherein said coating further comprises:

mounting the weave of fibers in a frame;

wherein said soaking comprises:

soaking the weave of fibers mounted in the frame.

20. The method of claim 17, wherein said coating comprises:

using charge-based attraction to coat the weave of fibers with the nanostructures.

21. The method of claim 20, wherein said coating comprises:

soaking the weave of fibers in a solution containing a positively charged polymer to impart a positive charge to the weave of fibers;

washing the weave of fibers;

drying the weave of fibers;

applying a solution containing the nanostructures to the weave of fibers, wherein the nanostructures are attracted to the weave of fibers due to the imparted positive charge to coat the weave of fibers;

incubating the coated weave of fibers; and

drying the coated weave of fibers.

22. A hemostat, comprising:

a material; and

a plurality of nanostructures;

wherein the material and the nanostructures form a mixture.

23. The hemostat of claim 22, wherein the material is hemostatic.

24. The hemostat of claim 23, wherein the hemostatic material is expandable.

25. The hemostat of claim 24, wherein the expandable hemostatic material is a polymer.

26. The hemostat of claim 23, wherein the hemostatic material is a non-expandable material.

27. The hemostat of claim 22, wherein the material is resorbable in a mammalian body.

28. The hemostat of claim 22, wherein the material comprises chitosan.

29. The hemostat of claim 28, wherein the material comprises chitosan microparticles.

30. The hemostat of claim 22, wherein the material comprises biocompatible polymers.

31. The hemostat of claim 22, wherein the nanostructures include nanofibers.

32. The hemostat of claim 31, wherein the nanofibers are coated with silicon dioxide.

33. The hemostat of claim 31, wherein the nanofibers are potassium nanofibers.

34. The hemostat of claim 31, wherein the nanofibers are silicon nanofibers functionalized with potassium.

35. The hemostat of claim 23, wherein the mixture is configured to be inserted into a wound to plug the wound.

36. The hemostat of claim 22, wherein the material is a powder.

37. The hemostat of claim 22, wherein the material is a gel.

38. The hemostat of claim 22, wherein the material is a foam.

39. The hemostat of claim 22, wherein the material is a liquid.

40. The hemostat of claim 22, wherein the nanostructures are functionalized with a second material.

41. The hemostat of claim 40, wherein the second material is a hemostatic material.

42. A method for forming a hemostat, comprising:
mixing an expandable hemostatic material with a plurality of nanostructures.

43. A hemostat, comprising:
a plurality of glass beads; and
a plurality of nanostructures;
wherein the glass beads and the nanostructures are combined to form a mixture.

44. The hemostat of claim 43, wherein at least some of the glass beads have a diameter in the range of 3-10 micrometers.

45. The hemostat of claim 43, wherein the nanostructures include nanowires.

46. The hemostat of claim 45, wherein the nanowires are inorganic.

47. The hemostat of claim 43, wherein the nanowires include silicon.

48. The hemostat of claim 47, wherein the nanowires comprise a core of silicon and at least one shell layer disposed about the core comprising silicon dioxide.

49. A method for forming a hemostat, comprising:
mixing a plurality of glass beads with a plurality of nanostructures.

50. A hemostat, comprising:
a plurality of hemostatic particles;

wherein each hemostatic particle comprises a core material coated with a hemostatic material; and

wherein a rate of resorption of the core material is greater than a rate of resorption of the hemostatic material.

51. The hemostat of claim 50, wherein the core material is a polymer.

52. The hemostat of claim 50, wherein the hemostatic material comprises silicon dioxide.

53. The hemostat of claim 50, wherein the hemostatic material comprises spin-on glass.

54. The hemostat of claim 50, further comprising:

a plurality of nanostructures that are mixed with the plurality of particles.

55. The hemostat of claim 54, wherein the nanostructures include nanofibers.

56. The hemostat of claim 55, wherein the nanofibers are coated with silicon dioxide.

57. A method for forming a hemostat, comprising:

forming a plurality of hemostatic particles by coating particles of a resorbable core material with a hemostatic material;

wherein a rate of resorption of the core material is greater than a rate of resorption of the hemostatic material.

58. The method of claim 57, wherein the hemostatic material comprises silicon dioxide, wherein said forming comprises:

forming the plurality of hemostatic particles by coating particles of a resorbable core material with silicon dioxide.

59. The method of claim 57, wherein the hemostatic material comprises spin-on glass, wherein said forming comprises:

forming the plurality of hemostatic particles by coating particles of a resorbable core material with spin-on glass.

60. A hemostatic bandage, comprising:

a bandage material; and

a nanopowder formed of nanoparticles having an outer thin oxide layer;

wherein the nanopowder is dispersed in the bandage material.

61. The hemostatic bandage of claim 60, wherein the thin oxide layer of the nanoparticles is a naturally-occurring oxide layer.

62. The hemostatic bandage of claim 60, further comprising:

a coating of nanowires on a surface of the bandage material.

63. The hemostatic bandage of claim 62, wherein the nanowires have an outer layer of silicon dioxide.

64. A method of forming a hemostatic bandage, comprising:

dispersing in a bandage material a nanopowder formed of nanoparticles having an outer thin oxide layer.

65. The method of claim 64, wherein the thin oxide layer of the nanoparticles is a naturally-occurring oxide layer, said dispersing comprising:

dispersing in the bandage material the nanoparticles having the naturally-occurring oxide layer.

66. The method of claim 64, further comprising:

coating a surface of the bandage material with nanowires.

67. The method of claim 65, wherein the nanowires have an outer layer of silicon dioxide, said coating comprising:

coating the surface of the bandage material with the nanowires having the outer layer of silicon dioxide.

68. The method of claim 64, further comprising:

milling a silicon wafer to generate the nanopowder.

69. A hemostatic bandage, comprising:

a bandage material; and

a first plurality of nanowires formed to each have a first length; and

a second plurality of nanowires formed to each have a second length, wherein the second length is greater than the first length;

wherein the first plurality of nanowires is dispersed in a first region of the bandage material, and the second plurality of nanowires is dispersed in a second region of the bandage material.

70. The hemostatic bandage of claim 69, wherein the first region is an interior region and the second region is a coating layer on a surface of the bandage material.

71. The hemostatic bandage of claim 69, wherein the bandage material has opposing first and second surfaces, wherein the first region is a central region of the first surface and the second region is a perimeter region of the first surface.

72. The hemostatic bandage of claim 69, wherein the bandage material is a gelatin bandage material or a collagen bandage material.

73. A method for forming a hemostatic bandage, comprising:

dispersing a first plurality of nanowires formed to each have a first length in a first region of a bandage material; and

dispersing a second plurality of nanowires formed to each have a second length in a second region of the bandage material.

74. The method of claim 73, wherein said dispersing a first plurality of nanowires formed to each have a first length in a first region of a bandage material comprises:

dispersing the first plurality of nanowires in an interior region of the bandage material; and

wherein said dispersing a second plurality of nanowires formed to each have a second length in a second region of the bandage material comprises:

applying the second plurality of nanowires to the bandage material to form a coating layer on a surface of the bandage material.

75. The method of claim 73, wherein the bandage material has opposing first and second surfaces, wherein said dispersing a first plurality of nanowires formed to each have a first length in a first region of a bandage material comprises:

applying the first plurality of nanowires to the bandage material in a central region of the first surface; and

wherein said dispersing a second plurality of nanowires formed to each have a second length in a second region of the bandage material comprises:

applying the second plurality of nanowires to the bandage material in a perimeter region of the first surface.

76. The method of claim 73, wherein the bandage material is a gelatin bandage material.

77. A surgical staple, comprising:

a body having a base portion, a first leg, and a second leg, the first leg extending at a first angle from a first end of a first surface of the base portion, and the second leg extending at a second angle from a second end of the first surface of the base portion; and

a layer of nanostructures that coats at least a portion of the body.

78. The surgical staple of claim 77, wherein the layer of nanostructures coats the first surface of the base portion.

79. The surgical staple of claim 78, wherein the base portion has a first axis through the first end and the second end, the first surface of the base portion has a first width perpendicular to the first axis, the first and second legs each have a second width parallel to the first width that is located between the base portion and a respective pointed end portion, and the first width is greater than the second width.

80. The surgical staple of claim 77, wherein the nanostructures include nanofibers.

81. The surgical staple of claim 80, wherein the nanofibers have an outer layer of silicon dioxide.

82. A method for forming a hemostatic surgical staple, comprising:

receiving a surgical staple having a base portion, a first leg, and a second leg, the first leg extending at a first angle from a first end of a first surface of the base portion, and the second leg extending at a second angle from a second end of the first surface of the base portion; and

coating at least a portion of the surgical staple with a layer of nanostructures.

83. The method of claim 82, wherein said coating comprises:

coating the first surface of the base portion with the layer of nanostructures.

84. The method of claim 83, wherein the base portion has a first axis through the first end and the second end, the first surface of the base portion has a first width perpendicular to the first axis, the first and second legs each have a second width parallel to the first width that is located between the base portion and a respective pointed end portion, the method further comprising:

forming the surgical staple so that the first width is greater than the second width.

85. The method of claim 82, wherein the nanostructures include nanofibers, wherein said coating comprises:

coating the at least a portion of the surgical staple with the nanofibers.

86. The method of claim 85, wherein the nanofibers have an outer layer of silicon dioxide, wherein said coating comprises:

coating the at least a portion of the surgical staple with the silicon dioxide-coated nanofibers.

87. A surgical suture, comprising:

a thread; and

a layer of nanostructures that coats at least a portion of the thread.

88. A method for forming a hemostatic surgical suture, comprising:

coating at least a portion of a thread with a layer of nanostructures.

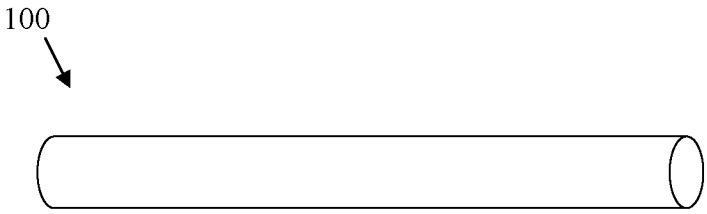

FIG. 1A

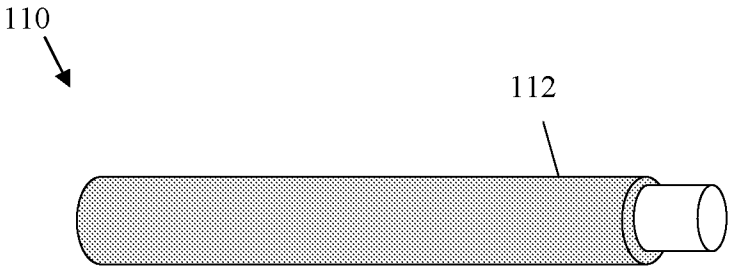

FIG. 1B

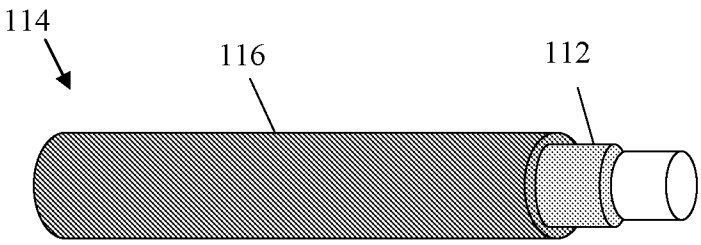

FIG. 1C

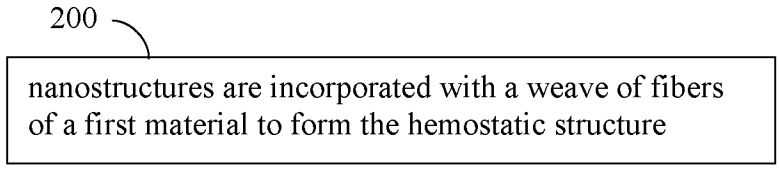

FIG. 2

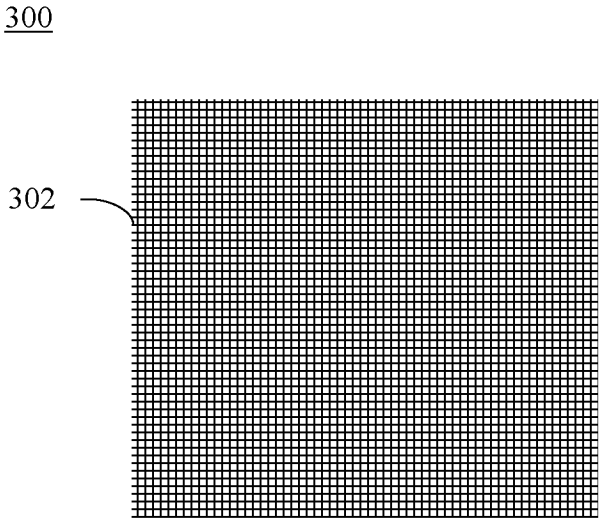

FIG. 3

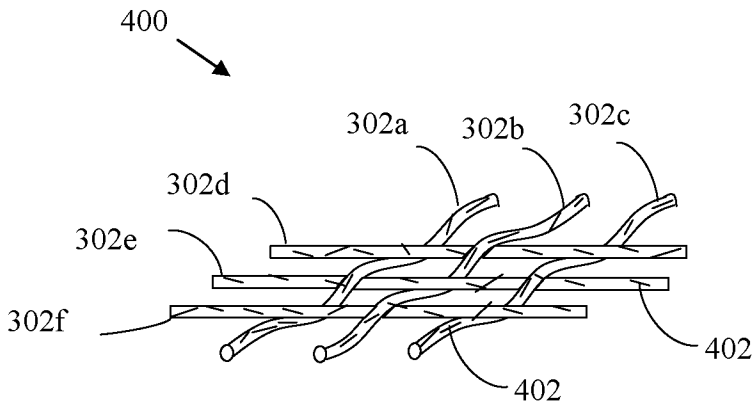

FIG. 4

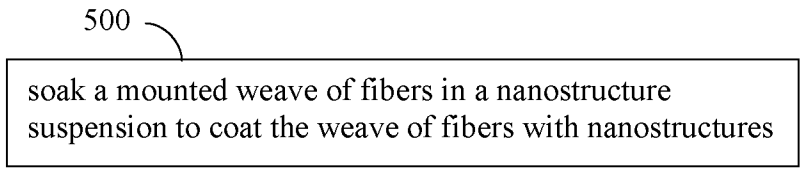

FIG. 5

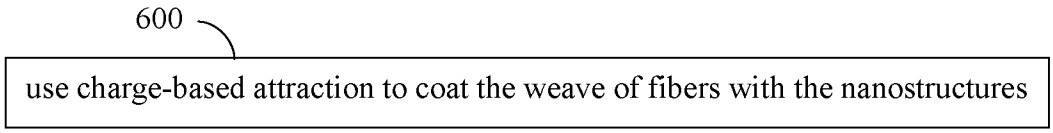

FIG. 6

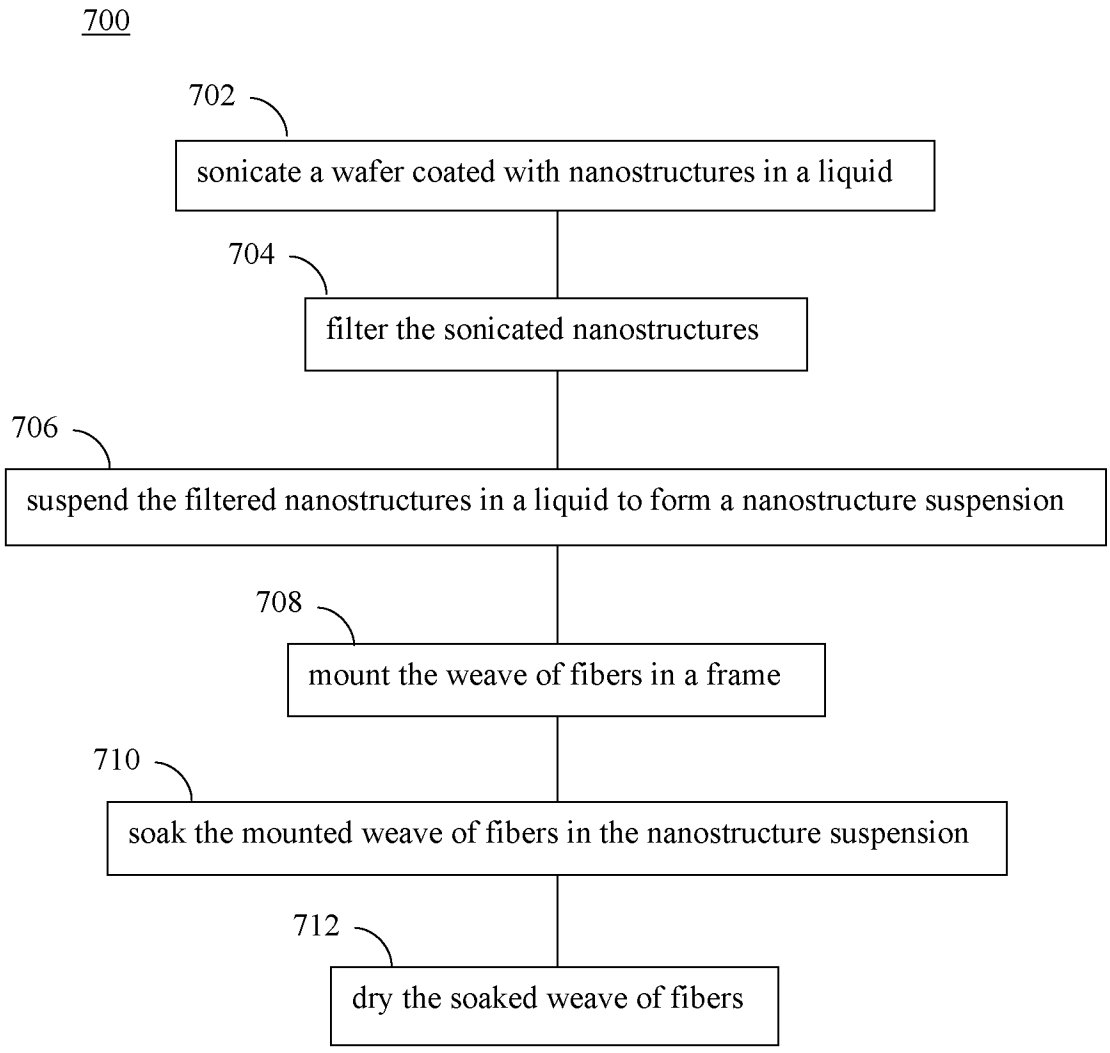

FIG. 7

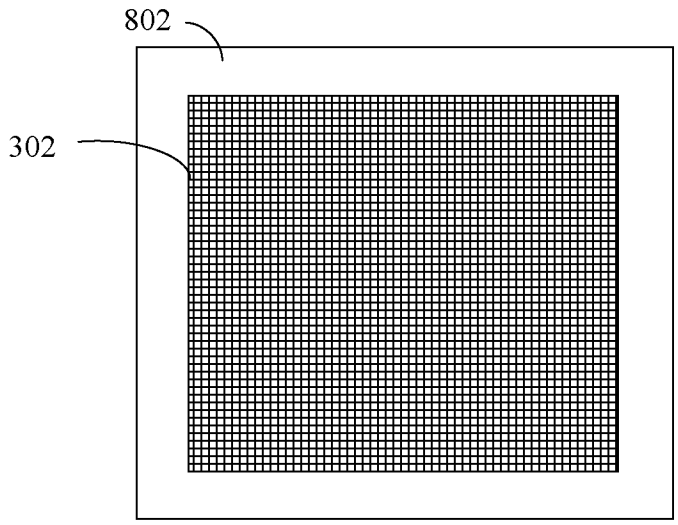

FIG. 8

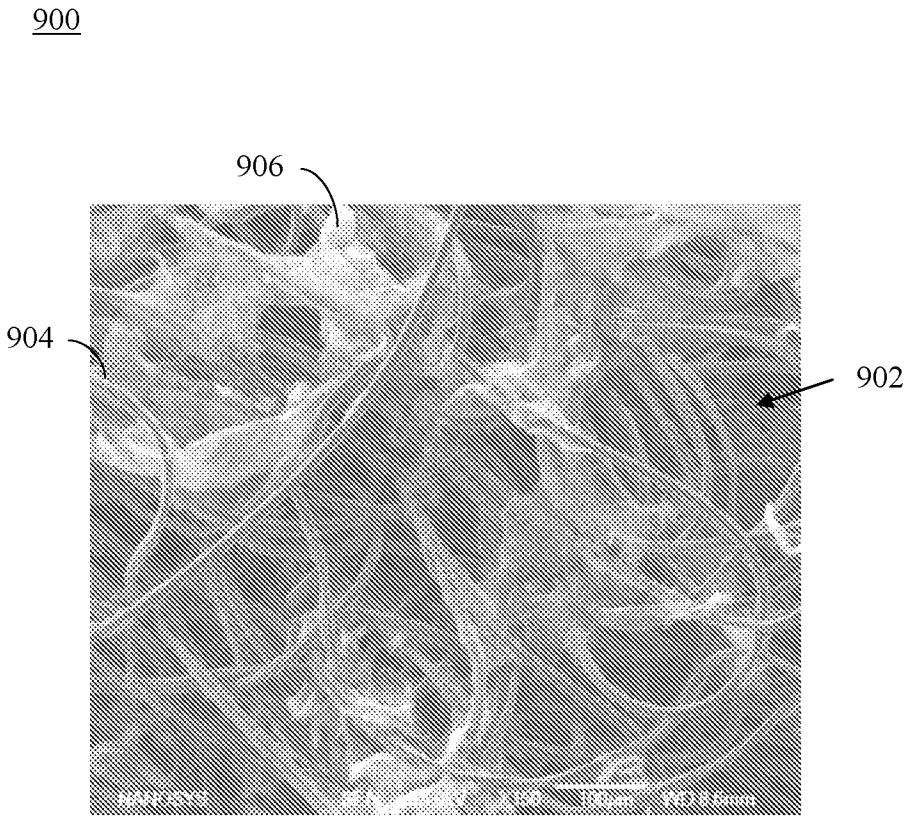

FIG. 9

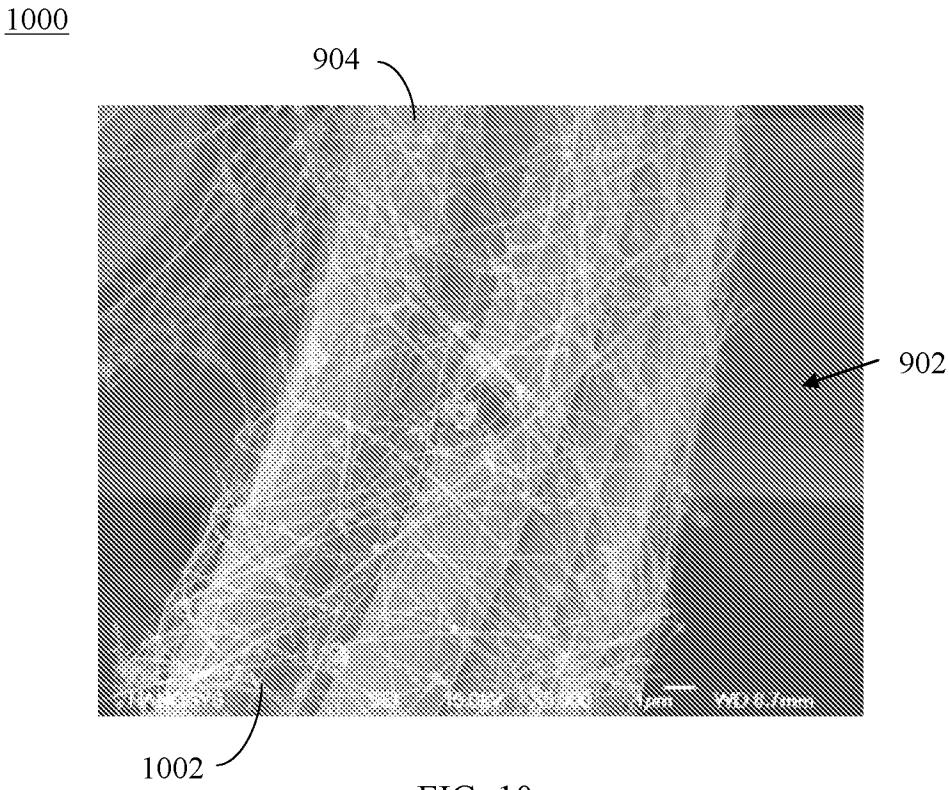
1000
904
902
1002

FIG. 10

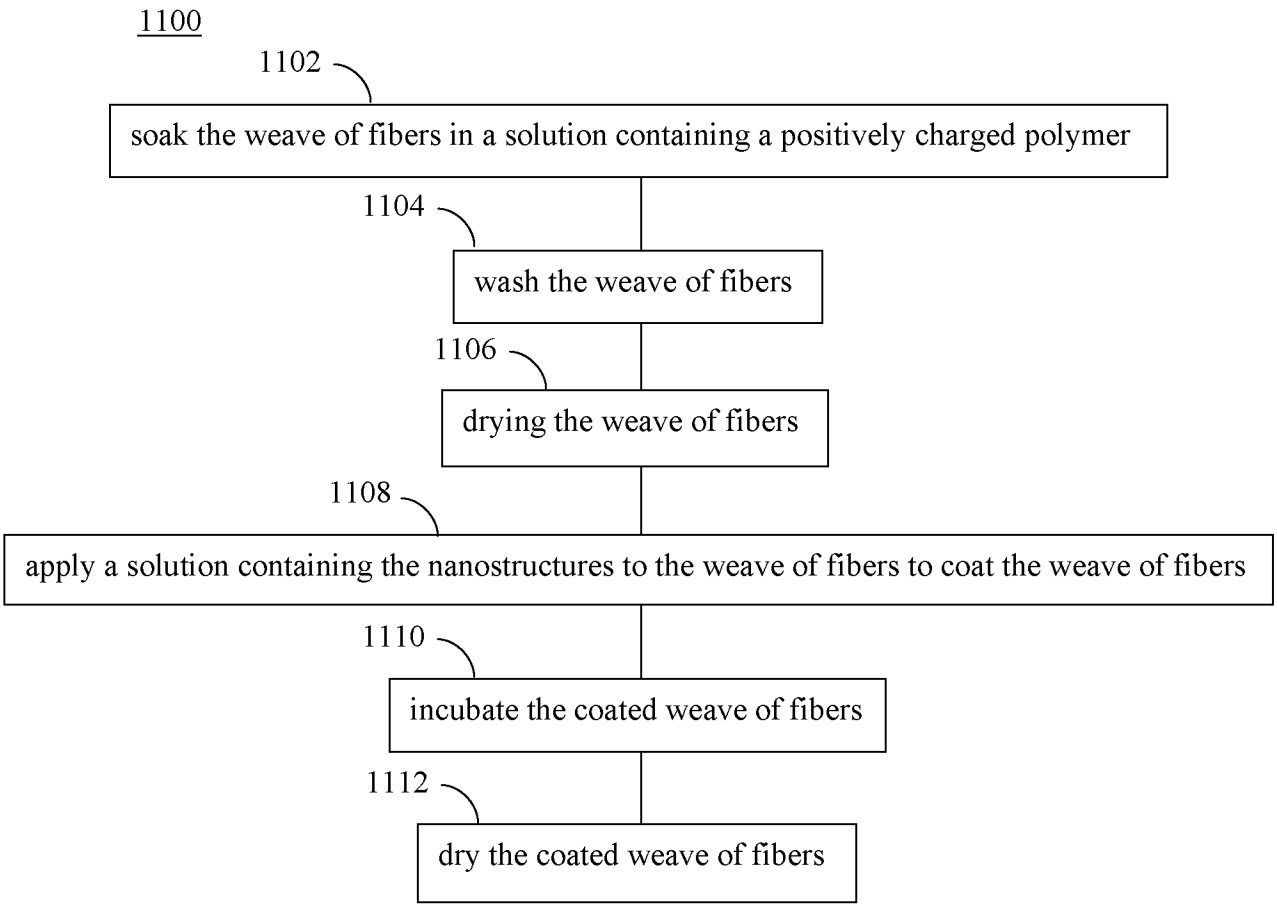
1100
1102
soak the weave of fibers in a solution containing a positively charged polymer
1104
wash the weave of fibers
1106
drying the weave of fibers
1108
apply a solution containing the nanostructures to the weave of fibers to coat the weave of fibers
1110
incubate the coated weave of fibers
1112
dry the coated weave of fibers

FIG. 11

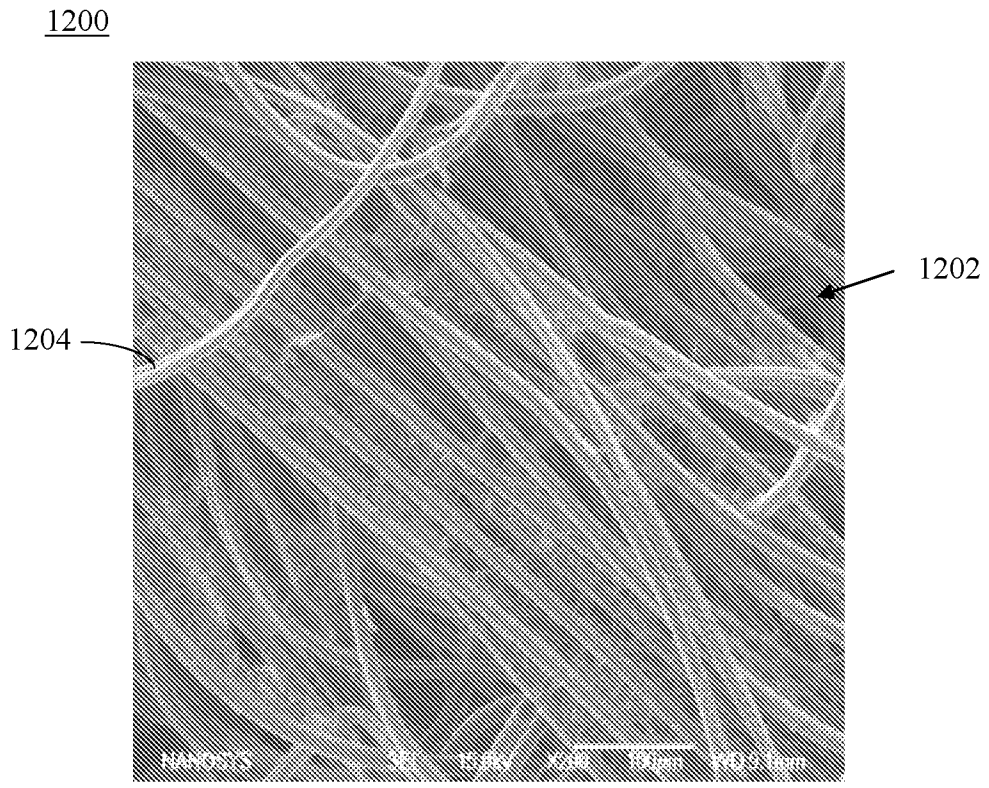

FIG. 12

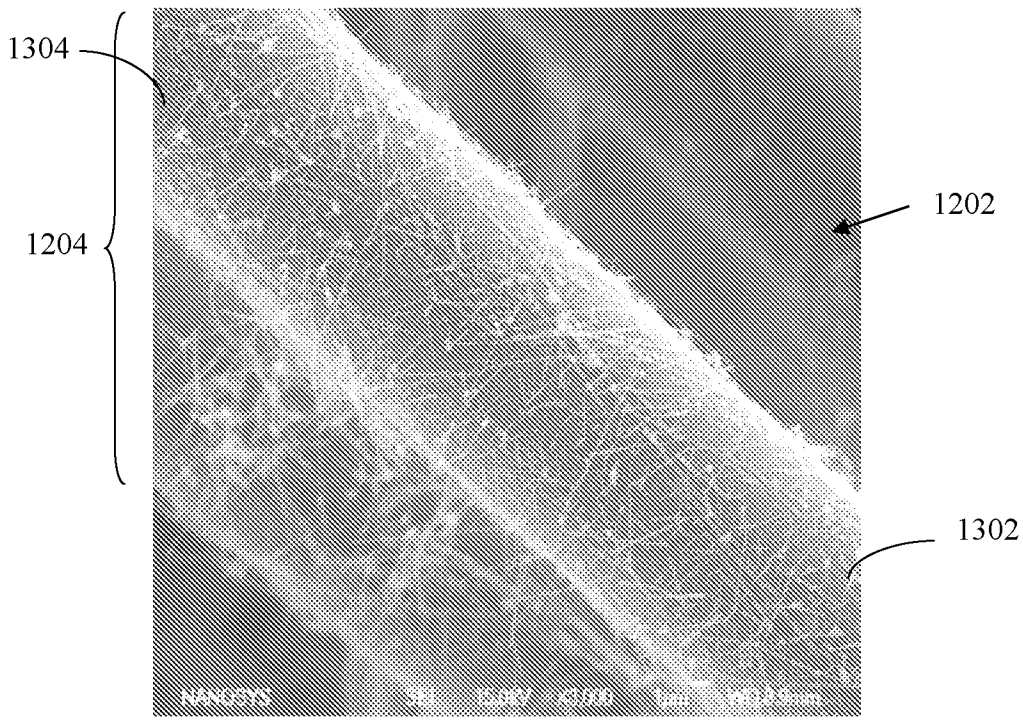

FIG. 13

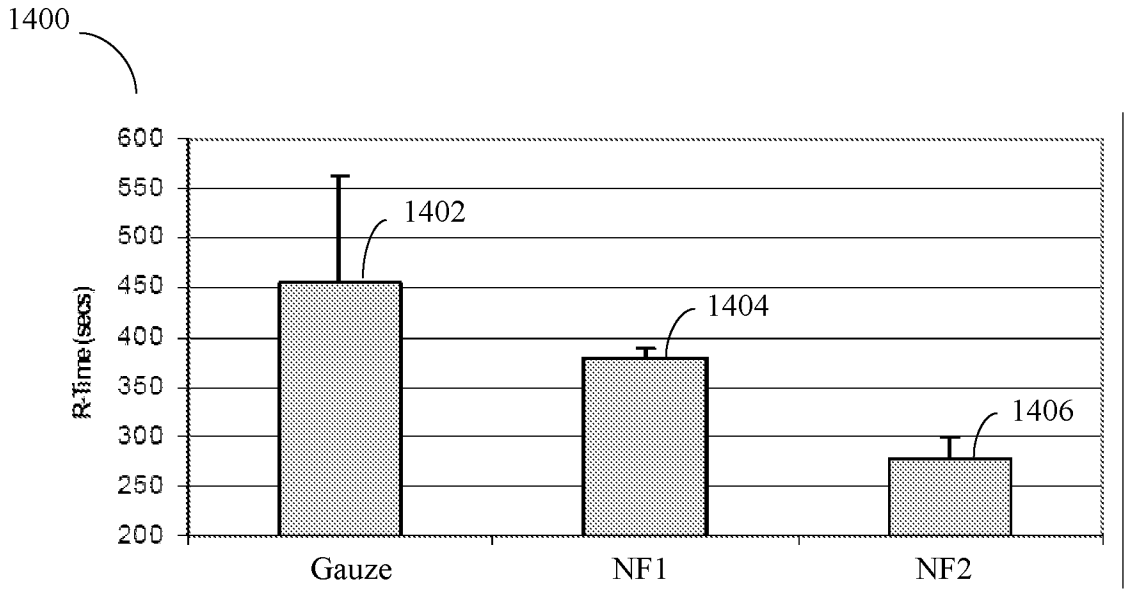
1400
600
550
500
450
400
350
300
250
200
R-time (secs)
1402
1404
1406
Gauze
NF1
NF2

FIG. 14

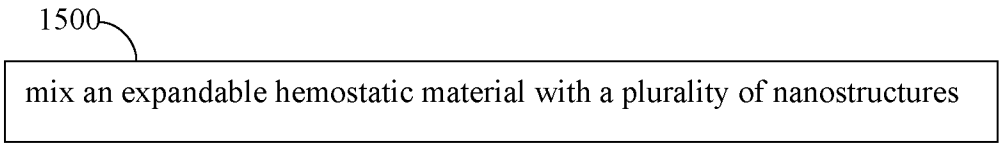
1500
mix an expandable hemostatic material with a plurality of nanostructures

FIG. 15

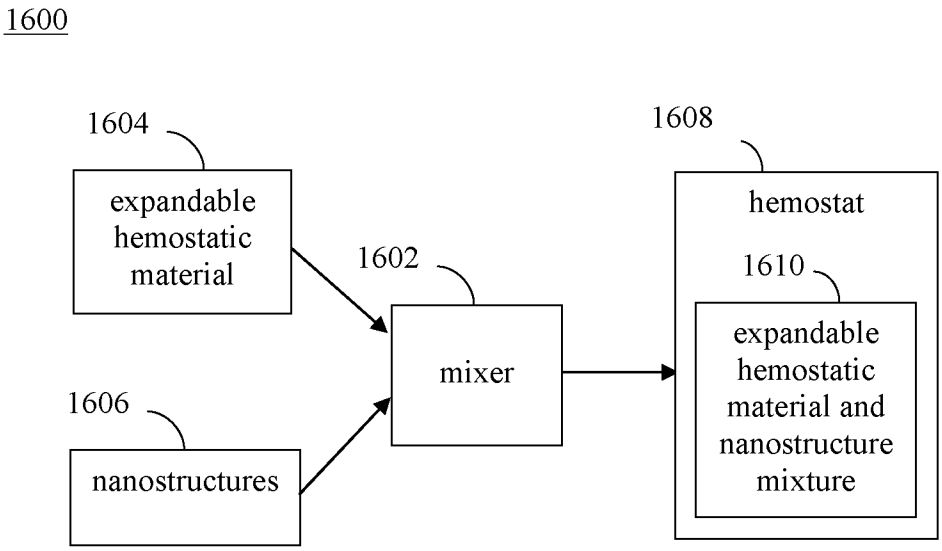
1600
1604
expandable hemostatic material
1606
nanostructures
1602
mixer
1608
hemostat
1610
expandable hemostatic material and nanostructure mixture

FIG. 16

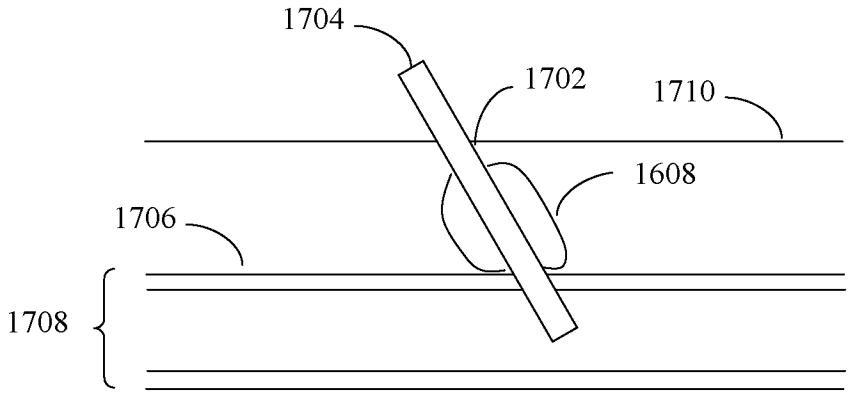

FIG. 17

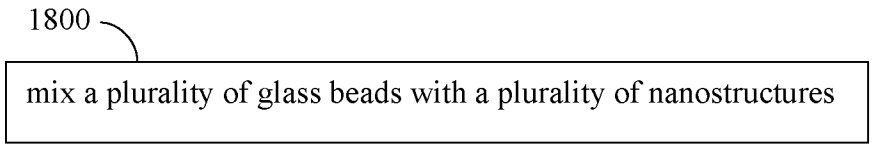
1800
mix a plurality of glass beads with a plurality of nanostructures

FIG. 18

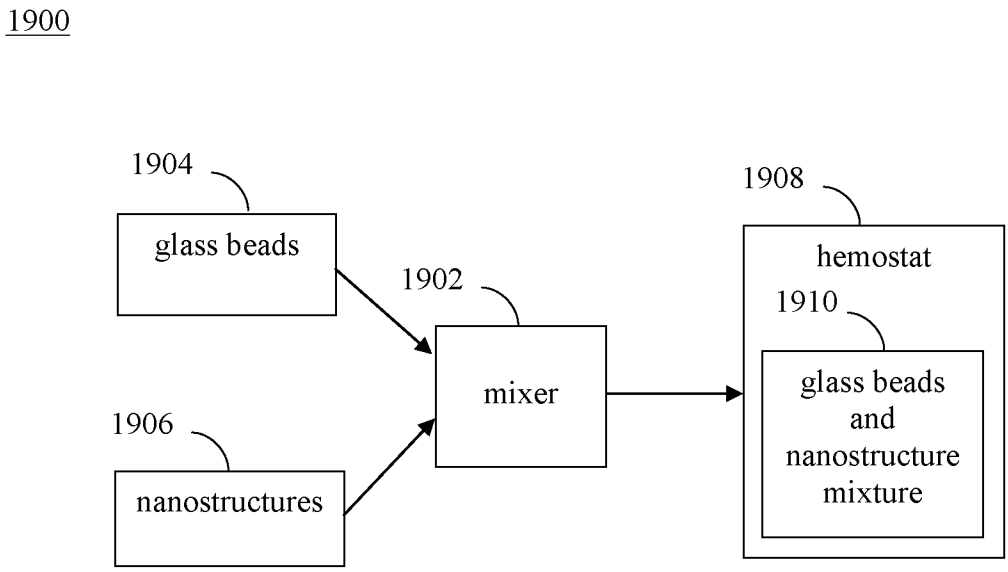
1900
1904
glass beads
1902
1906
nanostructures
mixer
1908
hemostat
1910
glass beads and nanostructure mixture

FIG. 19

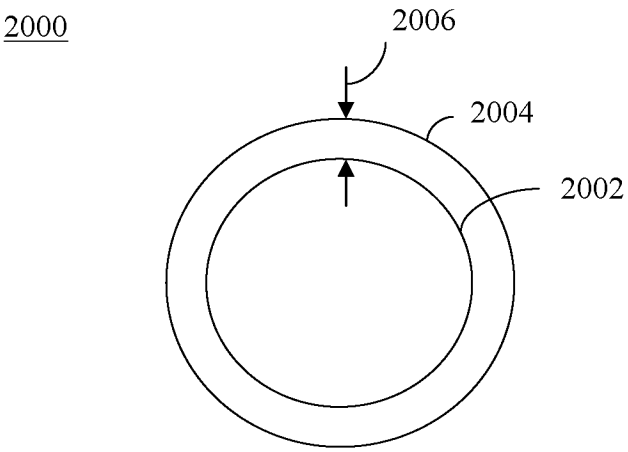
2000
2006
2004
2002

FIG. 20

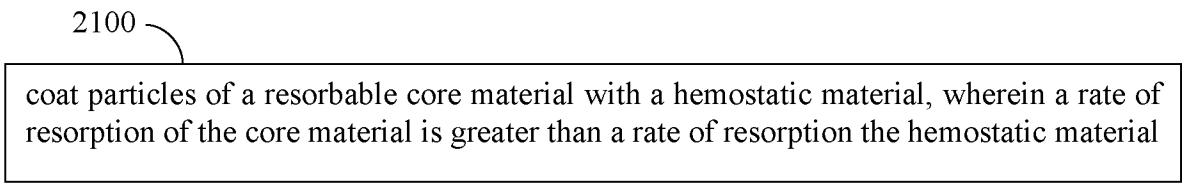
2100
coat particles of a resorbable core material with a hemostatic material, wherein a rate of resorption of the core material is greater than a rate of resorption the hemostatic material

FIG. 21

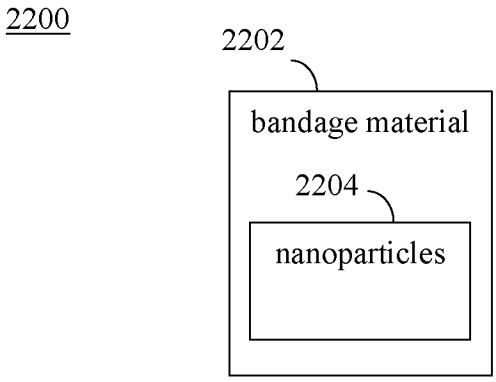

FIG. 22

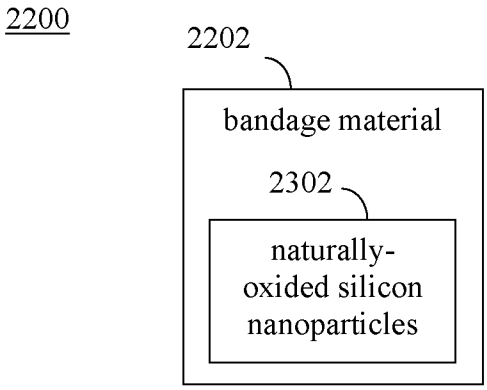

FIG. 23

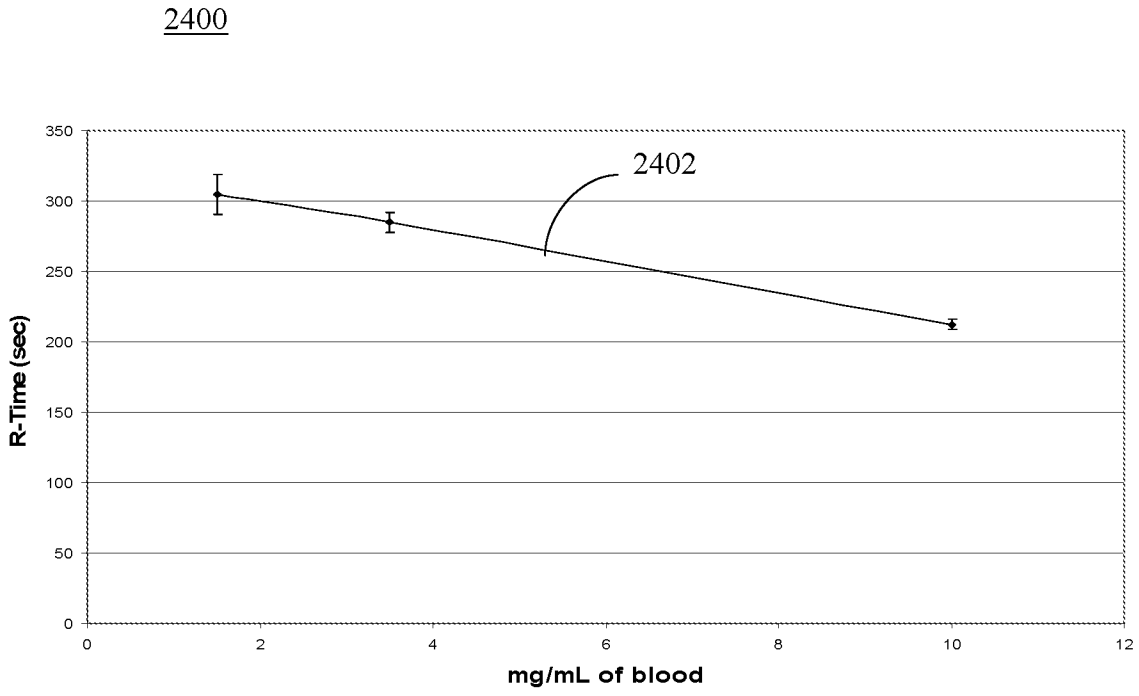

FIG. 24

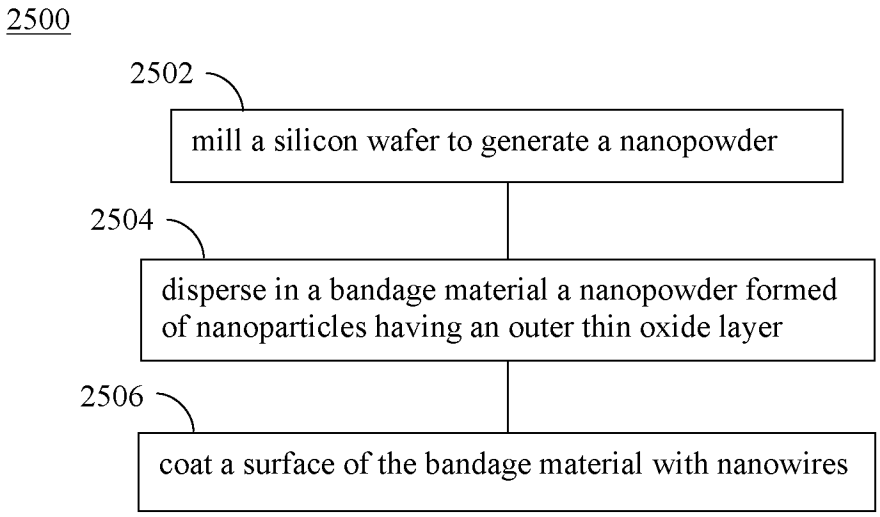

FIG. 25

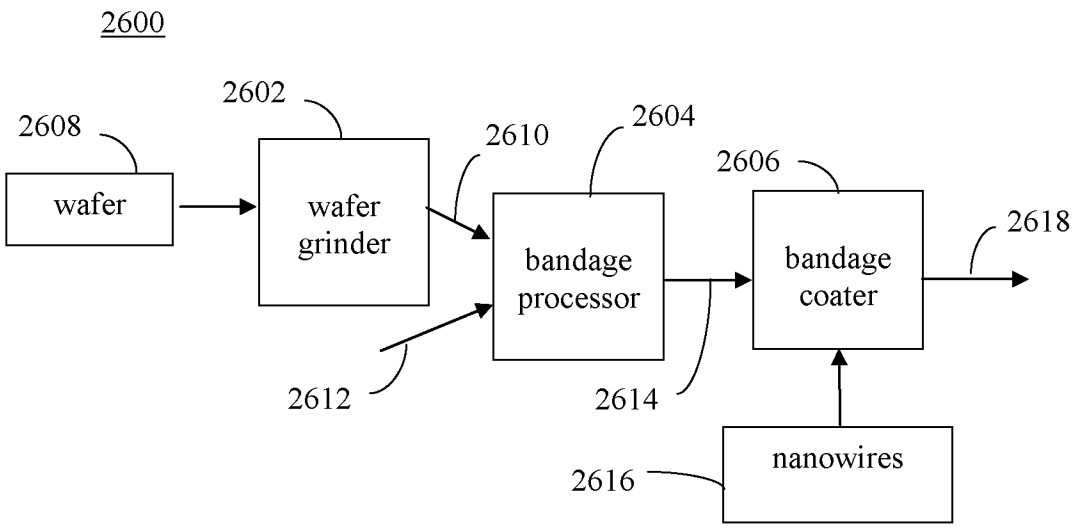

FIG. 26

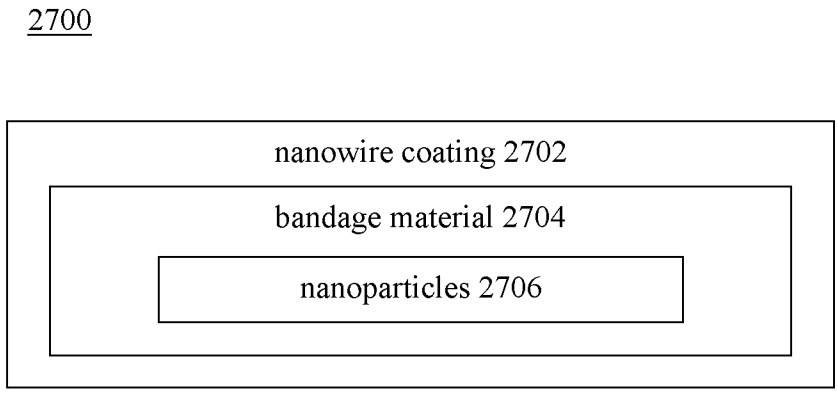

FIG. 27

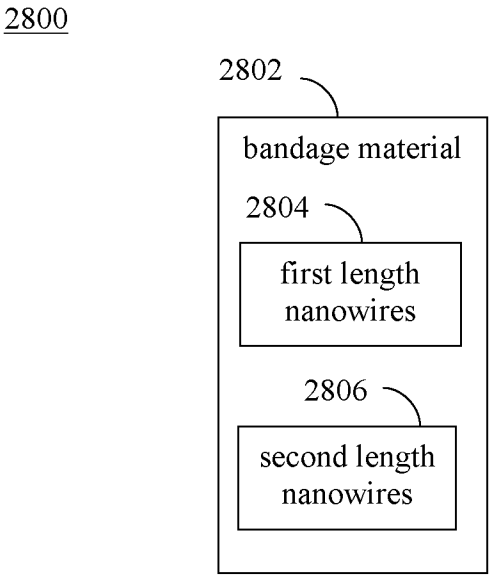
2800
2802
bandage material
2804
first length nanowires
2806
second length nanowires

FIG. 28

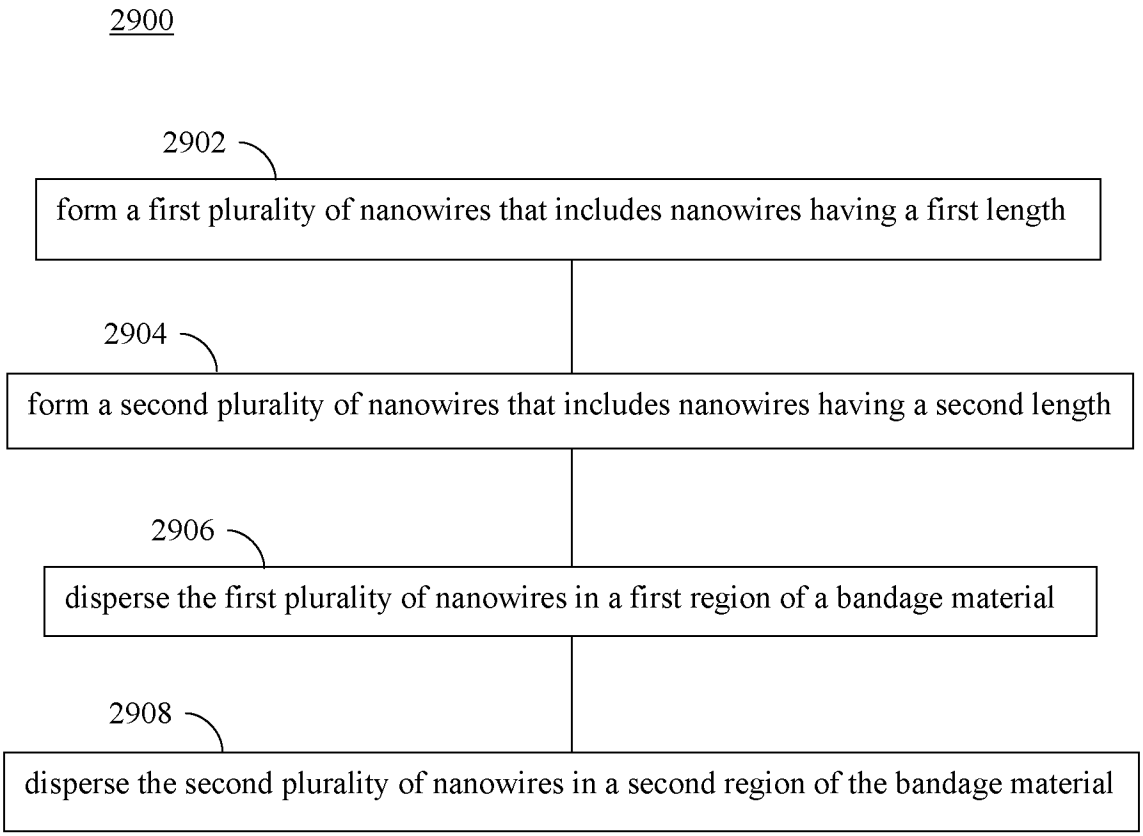
2900
2902
form a first plurality of nanowires that includes nanowires having a first length
2904
form a second plurality of nanowires that includes nanowires having a second length
2906
disperse the first plurality of nanowires in a first region of a bandage material
2908
disperse the second plurality of nanowires in a second region of the bandage material

FIG. 29

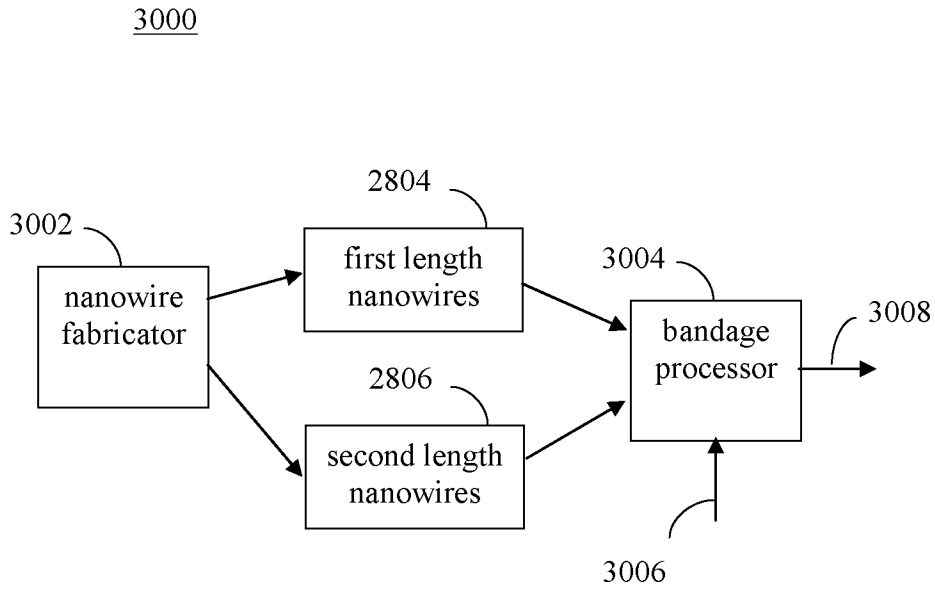
3000
2804
3002
first length nanowires
3004
nanowire fabricator
bandage processor
3008
2806
second length nanowires
3006

FIG. 30

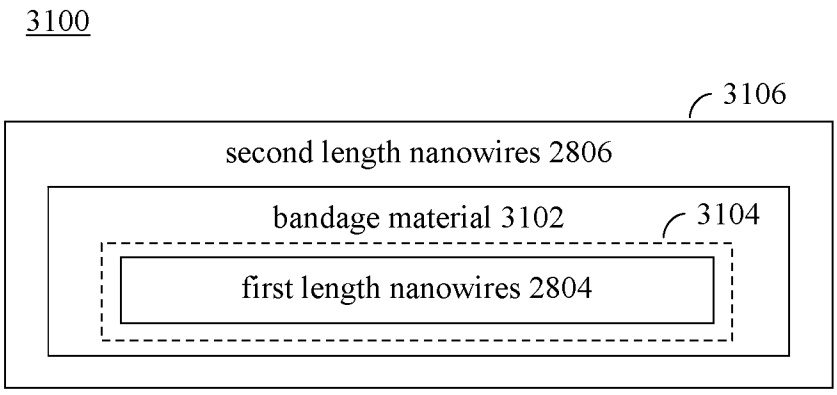
3100
3106
second length nanowires 2806
bandage material 3102
3104
first length nanowires 2804

FIG. 31

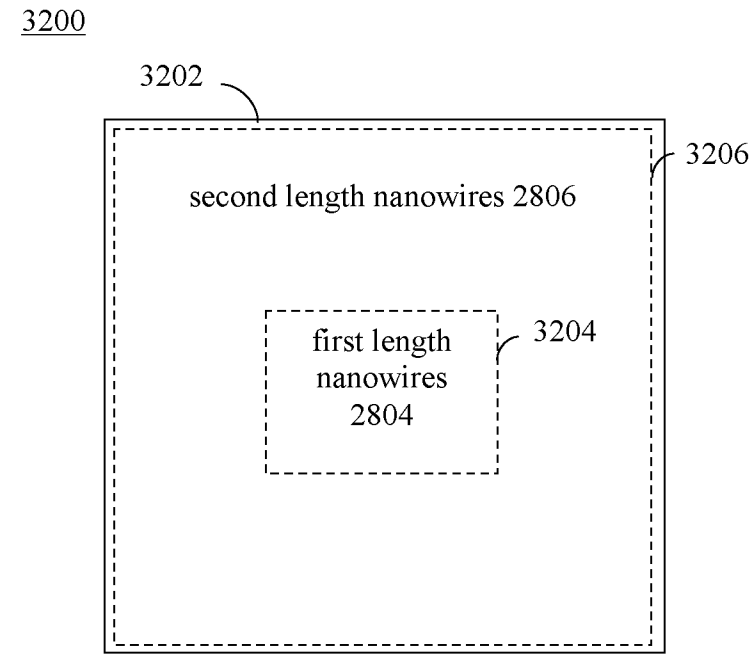
3200
3202
3206
second length nanowires 2806
first length nanowires 2804
3204

FIG. 32

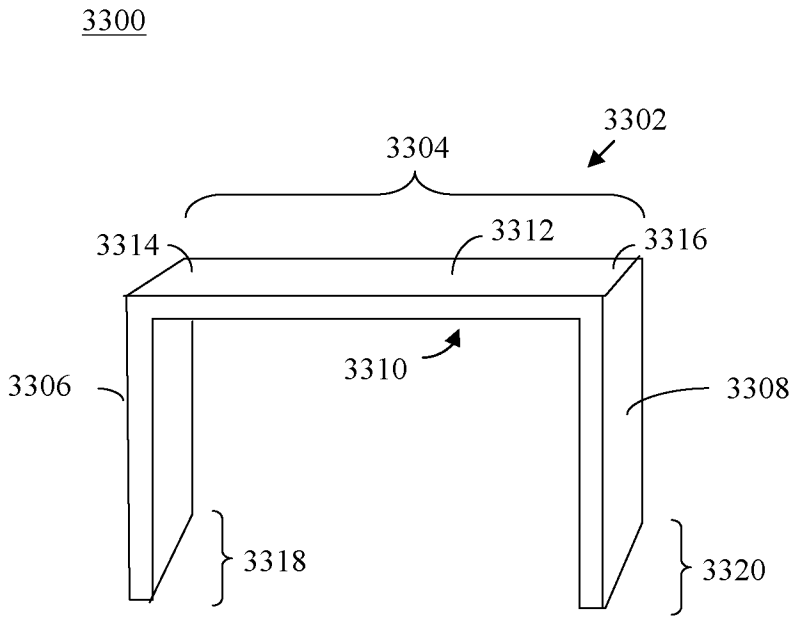
3300
3302
3304
3314
3312
3316
3310
3306
3308
3318
3320

FIG. 33

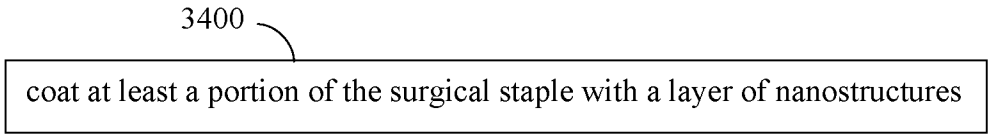
3400
coat at least a portion of the surgical staple with a layer of nanostructures

FIG. 34

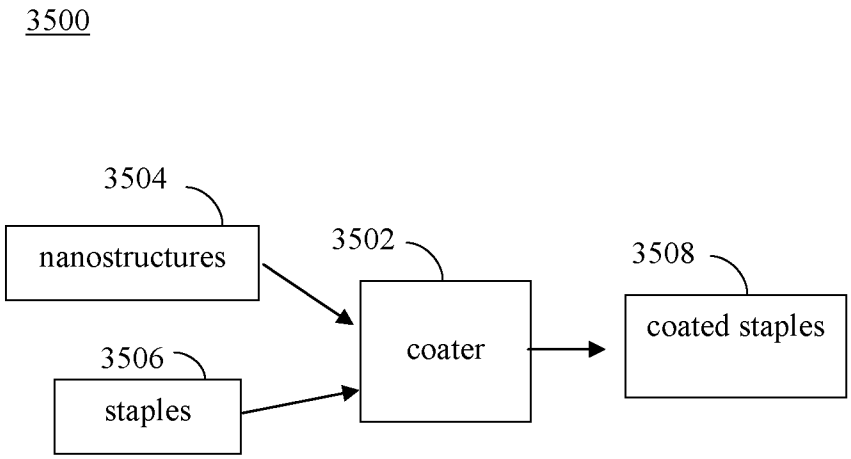
3500
3504
nanostructures
3502
3508
coater
coated staples
3506
staples

FIG. 35

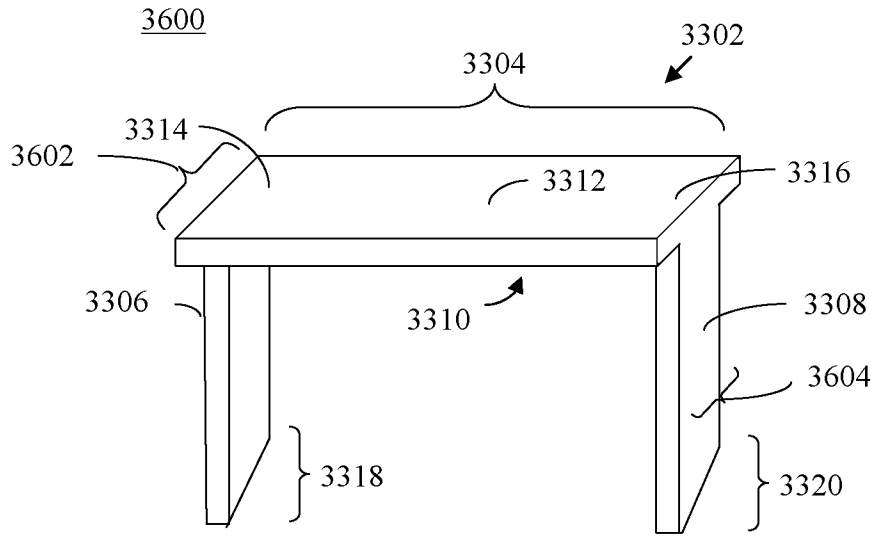
3600
3302
3304
3314
3602
3312
3316
3306
3310
3308
3604
3318
3320

FIG. 36

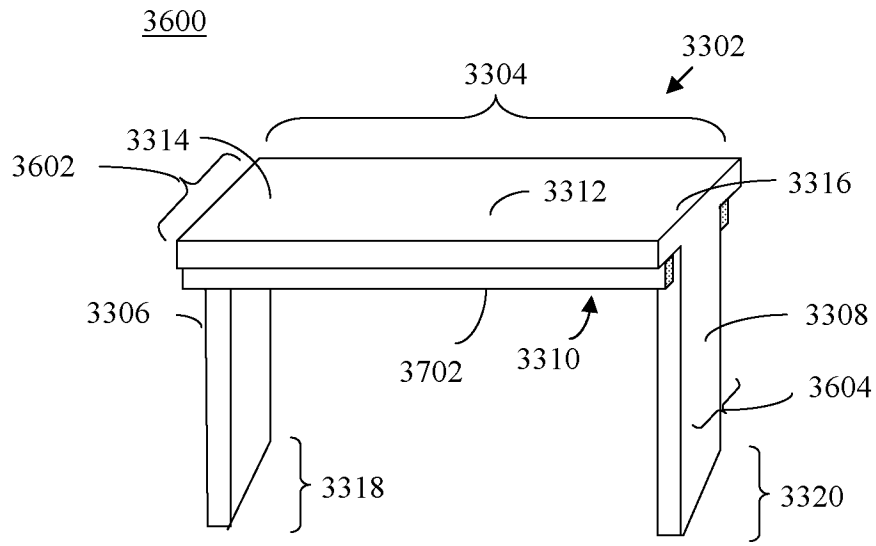
3600
3302
3304
3314
3602
3312
3316
3306
3702
3310
3308
3604
3318
3320

FIG. 37

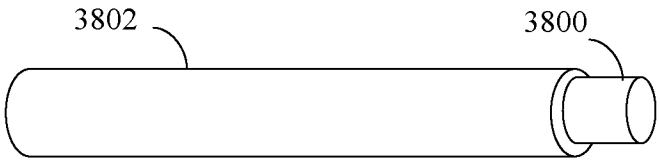

FIG. 38

FIG. 39

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/85719

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 13/00 (2009.01)
USPC - 424/443
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)
IPC8 : A61F 13/00 (2009.01)
USPC : 424/443

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC8 : A61F 13/15, A61L 15/00, A61L 15/16 (2009.01)
USPC : 602/1, 602/41, 602/48, 424/444, 424/445, 424/447

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB,USPT,EPAB,JPAB), Google Scholar
bandage, hemostasis$, hemostatic$, base, substrate, matrix, nano$, coated, resorb$, resorp$, decompos$, degenerat$, degrad$, depolymeriz$, biodegrad$, rate, glass, particle, powder, bead, charge, solution, suspension, emulsion, soak$, dip, dipped, dipping,SiO2

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2007/0225631 A1 (BOWLIN et al) 27 September 2007 (27.09.2007) see especially para [0042], [0044], [0078], [0086], [0090], [0102], [0119], [0122], [0125], [0164], [0165], [0168], [0177], [0178], [0180], [0193]	1-4, 13-17, 20-23, 27, 31, 35-41, 87, 88 --- 5-12, 18, 19, 24-26, 28-30, 32-34, 42-86
Y	US 2007/0160653 A1 (FISCHER et al) 12 July 2007 (12.07.2007) see especially para [0044], [0049]	5-12
Y	US 2007/0190100 A1 (SHASTRI et al) 16 August 2007 (16.08.2007) see especially para [0055], [0107]	18, 19
Y	US 2006/0292125 A1 (KELLAR et al) 28 December 2006 (28.12.2006) see especially para [0027], [0033]	24-26, 28-30, 42
Y	US 2007/0154510 A1 (WILCHER et al) 5 July 2007 (05.07.2007) see especially para [0017]	43-49
Y	US 2007/0141130 A1 (VILLANUEVA et al) 21 June 2007 (21.06.2007) see especially para [0039]	69-76
Y	US 2007/0212388 A1 (PATRAVALE et al) 13 September 2007 (13.09.2007) see especially para [0164]	77-86
Y	US 2006/0204738 A1 (DUBROW et al) 14 September 2006 (14.09.2006) see especially para [0012]-[0015], [0260], [0280]	32-34, 47, 48, 50-68, 81, 86

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* Special categories of cited documents:
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"E" earlier application or patent 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
21 January 2009 (21.01.2009)	09 FEB 2009

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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