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(71) Applicant: **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 5th Floor, Oakland, CA 94607-5200 (US).

(72) Inventors: **GUMA, Monica**; 1111 Franklin Street, 5th Floor, Oakland, CA 94607-5200 (US). **FRIEND, James**; 1111 Franklin Street, 5th Floor, Oakland, CA 94607-5200 (US). **MENA, Oscar, Vazquez**; 1111 Franklin Street, 5th Floor, Oakland, CA 94607-5200 (US).

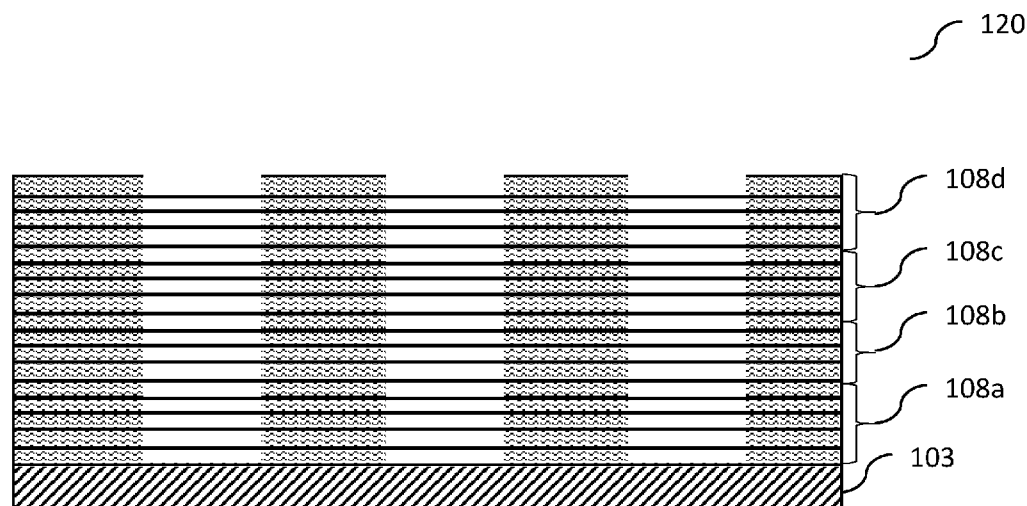
(74) Agent: **MATVENKO, Boris, A.**; Mintz Levin Cohn Ferris Glovsky And Popeo P.C., 666 Third Avenue, New York, NY 10017 (US).

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(54) Title: SYSTEM AND METHOD FOR RENDERING OBJECTS TRANSPARENT TO ULTRASOUND

FIG. 1e.



(57) Abstract: Non-resonant acoustic meta-material, method of fabrication, and uses thereof are disclosed herein. A layer of a first material is formed on a first substrate. A layer of a second material is formed on the layer of the first material to produce a stacked layer of first and second materials. At least a portion of the stacked layer of first and second materials is exposed to a radiation. The exposed portion of the second material is removed from the stacked layer of first and second materials. A cavity is formed using the removed exposed portion of the second material. The cavity includes a membrane formed from at least a portion of the first material. Additionally, an ultrasound system includes an ultrasound transducer and the non-resonant acoustic metamaterial coupled to the ultrasound transducer.

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SYSTEM AND METHOD FOR RENDERING OBJECTS TRANSPARENT TO ULTRASOUND

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Patent Appl. No. 62/747,641 to Guma et al., filed October 18, 2018, and entitled “Method for Rendering Cortical Bone Transparent to Ultrasound”, and incorporates its disclosure herein by reference in its entirety.

GOVERNMENT LICENSE RIGHTS

[0002] This invention was made with government support under D18AP00062 awarded by Defense Advanced Research Projects Agency. The government has certain rights in the invention.

BACKGROUND

[0003] Ultrasound is an effective imaging technique that is used by medical professionals for non-invasively imaging various tissues inside a body of the patient. However, in some cases, ultrasound cannot be effectively used. For example, ultrasound cannot be used to effectively penetrate a cortical bone. The transition to cortical bone from soft tissue outside when using an ultrasound transducer aberrates ultrasound waves, rendering it impossible to refocus for the purposes of detection and/or imaging. As such, many potential medical diagnostic and/or treatment methods cannot be used, leaving medical professionals to rely on other tools for diagnosis, imaging, treatment, etc., e.g., a magnetic resonance imaging (MRI) which is costly.

[0004] One such challenging diagnostic problem that cannot be currently diagnosed using ultrasound is rheumatoid arthritis (RA). RA is a debilitating, chronic systemic

autoimmune disease of the synovial joints that leads to joint destruction and loss of function for ~1% of the worldwide population. Early bone damage due to RA is correlated with poor long-term patient outcomes, and bone marrow lesions – especially, bone marrow edema (BME) – are a useful prognostic indicator of disabling RA. Because ultrasound cannot cross cortical bone to image the bone marrow within, MRI has been used to detect BME (at a significant cost). However, MRI cannot be used in every case. For example, MRI cannot be used on patients with joint replacement and other types of metal implants. Further, some patients also encounter adverse side effects from the gadolinium contrast agent administered prior to MRI procedures. Hence, there is a need for an improved approach for using ultrasound to diagnose, image, treat, etc. various medical conditions.

SUMMARY

[0005] In some implementations, the current subject matter relates to a method for fabricating a non-resonant acoustic metamaterial (NRAM). The method may include forming a layer of a first material on a first substrate, forming a layer of a second material on the layer of the first material to produce a stacked layer of first and second materials, exposing at least a portion of the stacked layer of first and second materials to a radiation, removing the exposed portion of the second material from the stacked layer of first and second materials, and forming a cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material.

[0006] In some implementations, the current subject matter may include one or more of the features disclosed herein including following optional features. The method may include removing at least a portion of the first substrate subsequent to the forming of the layer of a second material on the layer of the first material. The method may also include transferring the stacked layer of the first and second materials onto a second substrate.

[0007] In some implementations, the stacked layer of the first and second materials may include a plurality of alternating layers of the first material and the second material. In some implementations, the removing may further include removing a plurality of layers of the second materials from the stacked layer of the first and second materials while retaining a plurality of first materials. The cavity may include a plurality of portions of layers of the first material forming a plurality of membranes. Further, the plurality of membranes may be configured to resonate at a predetermined operating frequency and configured to shift phase and/or amplitude of one or more ultrasound waves passing through the cavity. The predetermined operating frequency may be in a range of approximately 100 KHz to approximately 250 MHz.

[0008] In some implementations, the first material may be a hard material and the second material is a soft material. The first material may include at least one of the following: a silicon oxide, a silicon nitride, a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and any combinations thereof. Any other metal may also be used. The second material may include at least one of the following: a polymethyl methacrylate (PMMA) material, SU-8 material, silicon, polymer, and any combinations thereof.

[0009] In some implementations, the cavity may be filled with at least one of the following: a fluid, a gas, and any combinations thereof.

[0010] In some implementations, the cavity may be configured to be connected to at least another cavity formed in at least another second layer and further configured to be separated from at least another cavity by at least one of: the membrane and at least another

membrane.

[0011] In some implementations, the current subject matter relates to a non-resonant acoustic metamaterial apparatus that may be formed in accordance with the method above. The apparatus may include a layer of a first material on a first substrate, a layer of a second material formed on the layer of the first material to produce a stacked layer of first and second materials and a cavity. The cavity may be formed by exposing at least a portion of the stacked layer of first and second materials to a radiation, removing the exposed portion of the second material from the stacked layer of first and second materials, and forming the cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material. The apparatus may include some of the optional features discussed above.

[0012] In some implementations, the current subject matter relates to an ultrasound system that may include an ultrasound transducer and the non-resonant acoustic metamaterial coupled to the ultrasound transducer having features discussed above.

[0013] In some implementations, there is provided a method for rendering cortical bone that is transparent to conventional ultrasound. The method may include introducing an acoustic metamaterial layer between a standard ultrasound clinical imaging probe and the soft tissues adjacent to the target bone marrow imaging region, thereby compensating for the subsequent aberration of the cortical bone as the ultrasound makes its way to and from the marrow and trabecular structure within. The acoustic metamaterial layer may be formed from a non-resonant acoustic metamaterial (NRAM) that is suitable for the transmission of ultrasound at clinically relevant frequencies through a cortical bone analog.

[0014] Implementations of the current subject matter can include, but are not limited to, systems and methods consistent including one or more features are described as well as articles that comprise a tangibly embodied machine-readable medium operable to cause one or

more machines (e.g., computers, etc.) to result in operations described herein. Similarly, computer systems are also described that may include one or more processors and one or more memories coupled to the one or more processors. A memory, which can include a computer-readable storage medium, may include, encode, store, or the like one or more programs that cause one or more processors to perform one or more of the operations described herein. Computer implemented methods consistent with one or more implementations of the current subject matter can be implemented by one or more data processors residing in a single computing system or multiple computing systems. Such multiple computing systems can be connected and can exchange data and/or commands or other instructions or the like via one or more connections, including a connection over a network (e.g. the Internet, a wireless wide area network, a local area network, a wide area network, a wired network, or the like), via a direct connection between one or more of the multiple computing systems, etc.

[0015] The details of one or more variations of the subject matter described herein are set forth in the accompanying drawings and the description below. Other features and advantages of the subject matter described herein will be apparent from the description and drawings, and from the claims. While certain features of the currently disclosed subject matter are described for illustrative purposes in relation to the rendering of objects using ultrasound, it should be readily understood that such features are not intended to be limiting. The claims that follow this disclosure are intended to define the scope of the protected subject matter.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] The accompanying drawings, which are incorporated in and constitute a part of this specification, show certain aspects of the subject matter disclosed herein and, together with the description, help explain some of the principles associated with the disclosed

implementations. In the drawings,

[0017] FIGS. 1a-1e illustrate an exemplary process for forming a non-resonant acoustic metamaterial (NRAM), according to some implementations of the current subject matter;

[0018] FIG. 2a and 2b illustrate an exemplary top view and perspective top view, respectively, of the NRAM material formed by the process shown in FIGS. 1a-1e, according to some implementations of the current subject matter;

[0019] FIG. 2c exemplary cuboid cavity, according to some implementations of the current subject matter;

[0020] FIG. 3 illustrates an exemplary process for forming the non-resonant acoustic metamaterial, according to some implementations of the current subject matter;

[0021] FIG. 4 illustrates an exemplary process for imaging a tissue using an non-resonant acoustic metamaterial, according to some implementations of the current subject matter;

[0022] FIG. 5 illustrates exemplary images generated by an ultrasound equipment with and without use of the NRAM material formed using process shown in FIGS. 1a-e;

[0023] FIG. 6 illustrates an exemplary process for executing a quantitative ultrasound procedure using an ultrasound transducer together with the NRAM material, according to some implementations of the current subject matter;

[0024] FIGS. 7a-b illustrate exemplary parametric maps of diffraction coefficients, according to some implementations of the current subject matter;

[0025] FIG. FIG. 8 illustrates an exemplary architecture of the NRAM material having membranes (SiN) and open channels along with the equivalent circuit and a low frequency behavior circuit, according to some implementations of the current subject matter;

[0026] FIGS. 9a-9b illustrate exemplary methods for fabricating the NRAM material, according to some implementations of the current subject matter;

[0027] FIG. 10 illustrates an exemplary ultrasound system that implements the NRAM material described above in connection with FIGS. 1a-9a, according to some implementations of the current subject matter; and

[0028] FIG. 11 illustrates an exemplary method, according to some implementations of the current subject matter.

DETAILED DESCRIPTION

[0029] In some implementations, the current subject matter provides an ability to make it possible to effectively transmit ultrasound waves across different types of tissues (e.g., cortical bone, and/or other tissues) for the purposes of imaging, detection, diagnosis, treatment, etc. using ultrasound. The current subject matter relates to a non-resonant acoustic metamaterial (NRAM) layer that may be positioned between a standard ultrasound clinical imaging probe and soft and/or any other tissues of the patient (e.g., adjacent to the target bone marrow imaging region). Such non-resonant acoustic metamaterial may be configured to compensate for any subsequent aberration (e.g., as the ultrasound waves traverse cortical bone on its way to and from the marrow and trabecular structure within). The NRAM materials may be used with a variety of ultrasound frequencies for traversal of various tissues (e.g., soft tissue, cortical bone, etc.), objects, etc. The current subject matter's system, method, material, etc. may also be used for a variety of purposes, including medical as well as non-medical purposes and/or uses.

[0030] For ease of illustration only, the following description will be presented in connection with using the NRAM material together with an ultrasound probe for transmission of ultrasound waves at various frequencies through a cortical bone. However, as can be understood and as stated above, the current subject matter may be used for any other purposes (e.g., neurointervention to osteoarthritis, myeloma, peripheral musculoskeletal injuries,

imaging of any human/animal/organic/inorganic/etc. tissues, any objects, etc.).

[0031] In some implementations, the NRAM material may be fabricated via a combination of nanofabrication methods and/or guidance of non-contact acoustic measurements. The NRAM material may be a layer that may possess a negative density and stiffness along the ultrasound wave propagation direction. The NRAM materials may be a composite with regularly-spaced, fluid-filled internal cavities having a size smaller than the wavelength of the ultrasound. When ultrasound waves pass through the NRAM material from an ultrasound source to the target tissue and back to the source (i.e., each way via other soft tissue and hard tissue (e.g., the cortical bone)), the NRAM material may be configured to compensate for the aberration (or incoherency) that may induced by the interfering tissues and/or objects (e.g., cortical bone and/or other tissues). Thus, various implementations of the current subject matter may enable use of ultrasound to characterize, image, treat, etc. tissues beyond interfering tissues and/or objects (e.g., cortical bone, other soft tissues, etc.). Through the design and construction of NRAM attached to an ultrasound transducer, in some exemplary, non-limiting implementations, the cortical bone may be rendered transparent to the ultrasound, thereby facilitating characterization, imaging, treatment, etc. of the bone marrow.

[0032] In some implementations, the NRAM material may be fabricated using 3-dimensional nanofabrication methods. The methods may be based on stacking and/or on multilayer nanostructuring techniques, which in some exemplary, non-limiting, implementations, may have a resolution of less than 1 μm , which is less than ultrasound-relevant wavelengths. The NRAM material may be configured to be used with ultrasound frequencies from approximately 100 kHz to at least 250 MHz.

[0033] In some exemplary, non-limiting implementations, the NRAM material, when used together with an ultrasound transducer, may be used to characterize and/or diagnose presence of bone marrow lesions via quantitative ultrasound (QUS). Further, NRAM material

together with an ultrasound transducer may be used to detect, diagnose, etc. BME in the small joints of RA patients with and/or without BME. As can be understood, the NRAM material when used together with any ultrasound system may be used for the purposes of scanning, imaging, detection, diagnosis, treatment, etc. of objects, tissues, materials, etc. (whether animate and/or inanimate).

[0034] In some implementations, the current subject matter's NRAM material may be used for efficiently passing acoustic waves through high acoustic impedance materials (such as bone and/or metal objects), surrounded by relatively low acoustic impedance materials (e.g., tissue, water, etc.). The NRAM material may have a substantially crystalline structure (e.g., millimeter to micrometer-scale structure) that may include high and/or low density elastic media at dimensions that may be smaller than the wavelength of the acoustic waves. The current subject matter's NRAM material may produce negative density and/or stiffness values in a desired direction by having one or more cavities disposed therein.

[0035] In some exemplary, non-limiting implementations, the current subject matter's NRAM material may have one or more layers approximately 50 nm thick and lateral features approximately 250 nm. The NRAM material may be configured to enable passing of up to 250 MHz ultrasound through 400 μm of cortical bone to generate coherent ultrasound waves, facilitate bone marrow characterization, etc. Upon reflection, the ultrasound waves may reform in a coherent fashion to generate imagery. Thus, the current subject matter's NRAM material may be configured to operate in both directions (from source to target and from target to source).

[0036] FIGS. 1a-1e illustrate an exemplary step-by-step process for forming a non-resonant acoustic metamaterial 100, according to some implementations of the current subject matter. FIG. 2a and 2b illustrate an exemplary top view and perspective top view, respectively, of the NRAM material formed by the process shown in FIGS. 1a-1e.

[0037] Referring to FIG. 1a, the process for forming a non-resonant acoustic

metamaterials 100 may be initiated by providing a pre-fabrication substrate 102. A patterned polymer layer 104 may then be deposited on the substrate 102. The patterned polymer layer 104 may include a polymethyl methacrylate (PMMA) material, SU-8 material (a Bisphenol A Novolac epoxy dissolved in an organic solvent (e.g., gamma-butyrolactone GBL, cyclopentanone) and up to 10 wt% of mixed triarylsulfonium/hexafluoroantimonate salt (a photoacid generator)), silicon, polymer, and/or any other material. A layer 106 of thin, stiff material may then be deposited on the patterned polymer layer 104. For example, the layer 106 may be a silicon oxide (SiO_2), silicon nitride (SiN), graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and/or any other material. Any other metals and/or materials may also be used. One or more combinations of layers 104 and 106 may be stacked on top of each other to form a stacked layer 108, as shown in FIG. 1a.

[0038] To form cavities, the stacked layer 108 may be exposed to an electron beam 110, as shown in FIG. 1b, to remove portions of the soft photoresist material 106, as shown in FIG. 1c. In some implementations, one or more portions of and/or the entire stiff material 104 might not be removed. Removal of the portions of material 106 may be configured to form cavities 112 (a, b, c), as shown in FIG. 1c. The cavities 112 may have any desired shape, e.g., round, square, rectangular, oval, and/or any other desired shape. Any number of cavities may be formed. In some implementations, the number of cavities may be formed in accordance with a particular ultrasound application, ultrasound probe, and/or any other factors. The cavities 112 may be formed using electron beam photolithography and/or any other methods.

[0039] In some implementations, the stacked layer 108 may include any number of

layers of the soft material 106 and stiff material 104. The number of layers of materials 104, 106 may be selected in accordance with a particular ultrasound application, ultrasound probe, and/or any other factors. Referring to FIGS. 1d-1e, the layers 108 may be stacked on top of one another to form stacked structures 115 (having two layers 108a, 108b, as shown in FIG. 1d) or 120 (having four layers 108 (a, b, c, d), as shown in FIG. 1e). The stacking of layers 108 may be configured to position one or more cavities under one another, where the stiff materials 104 may be configured to separate one cavity from another below it in a vertical plane. Soft materials 106 may be configured to separate neighboring cavities in a horizontal plane.

[0040] In some implementations, the layers 108 may be deposited and/or structured on a prefabrication substrate 102 and then transferred onto a final stacking substrate 103 (as shown in FIG. 1e). The stacking of layers 108 may be configured to form the metamaterial up to a desired thickness that may be needed for the ultrasound to penetrate the desired objects, tissues, etc. (e.g., cortical bone, and/or any other tissues, depending on a particular application). The thickness of the final metamaterial may be determined in accordance with a particular ultrasound application, ultrasound probe, and/or any other factors.

[0041] FIG. 2a is a top view of the stacked metamaterial 120 having one or more cavities 121. FIGS. 2b-c show a perspective view of the metamaterial 120 and a cavity 121, respectively. As shown in FIGS. 2a-c, material 104 may form the “bottom” of the cavity 121 and the material 106 may form the “sidewalls” of the cavity 121. While FIGS. 2b-c illustrate circular cavities 121, other shapes of cavities 121 are possible.

[0042] FIG. 3 illustrates an exemplary process 300 for forming the non-resonant acoustic metamaterial, according to some implementations of the current subject matter. At 302, alternating layers of materials (e.g., soft material 104 and stiff material 106) may be formed on a substrate (e.g., a prefabrication substrate 102). Any number of alternating layers may be formed to form a stacked structure or layer 108. The stacked structure 108 may be exposed to an

electron beam, at 304 (e.g., as shown in FIG. 1b). At 306, exposed portions (e.g., the soft material 106) of the stacked structure 108 may be selectively removed from the stacked layer 108. Then, the modified structure 108 may be stacked with one or more other modified structures 108 on a substrate (e.g., final substrate 103 as shown in FIG. 1e), while aligning the structures 108 to ensure that the removed portions or cavities are positioned under each other, to form the metamaterial, at 308.

[0043] In some exemplary, non-limiting, implementations, the NRAM material may controllably scatter ultrasound waves prior to passage through skin, muscle, bone, and/or any other tissues and/or objects to compensate for the presence of the cortical bone along the ultrasound wave propagation path, thereby producing a coherent, focused ultrasound beam after passage through the cortical bone for characterization, imaging, etc. of tissue beyond it. The NRAM material may be configured to scatter the ultrasound waves to generate a plurality of foci of ultrasound at the inner surface of the cortical bone, each of which may constructively interfere with each other to generate coherent ultrasound wave to propagate through the bone to the marrow tissue within. Similarly, the NRAM material may be configured to focus the reflected ultrasound waves. In particular, a point or planar ultrasound transducer may generate a pulse that propagates through the NRAM material, skin, muscle, bone, etc. and to the tissue beyond, and then may detect the returning ultrasound signal from that tissue through these interceding layers as if the bone is transparent to it. The current subject matter system may be further configured to quantify the tissue's acoustic properties beyond the cortical bone, and particularly, the relative attenuation and backscatter coefficients, to generate one or more planar images.

[0044] FIG. 4 illustrates an exemplary process 400 for imaging a tissue using an non-resonant acoustic metamaterial, according to some implementations of the current subject matter. At 402, the NRAM material may be positioned on an ultrasound probe or transducer.

The NRAM material may be positioned anywhere in the path of the ultrasound wave. Moreover, one or more NRAM materials (formed in accordance with the process described above) having any desired thickness, width, shape, shape of cavities, number of cavities, etc. may be used together with the ultrasound probe/transducer. The NRAM materials may be positioned at any location along the path of the ultrasound wave. The NRAM materials may be permanently positioned and/or temporarily positioned along the path of the ultrasound wave (transmitting and/or receiving).

[0045] At 404, an ultrasound wave is generated by the ultrasound probe/transducer and transmitted toward a target tissue (e.g., marrow tissue beyond cortical bone). The ultrasound wave may be initially transmitted through the NRAM material, which may be configured to generate a coherent ultrasound wave for penetration through the skin, soft tissue, and cortical bone to reach the target tissue, at 406.

[0046] At 408, the ultrasound wave may be reflected and transmitted toward the receiver in the ultrasound probe/transducer. The reflected wave may be again passed through the NRAM material, at 410, which may shift at least of one of a phase and an amplitude of the wave to generate a coherent beam.

[0047] At 412, an image may be generated by the ultrasound probe/transducer, upon receiving the reflected coherent beam. In some implementations, the NRAM material's sensitivity to variations in bone, tissue, etc. may be weak, thereby allowing a combination of the NRAM material and the ultrasound probe to be independent of the various factors that are routinely associated with conventional ultrasound probes.

[0048] In some exemplary implementations, referring back to FIGS. 1a-e and 2a-c, the NRAM material may include a periodic arrangement of thin rectangular (or any other shape) fluid cavities, e.g., cuboids. Each cuboid may be defined above and below by 50 nm of the stiff material 106 (e.g., SiN, SiO₂, and/or multilayer graphene), with spacers formed from 250

nm wide walls of soft photosensitive polymer such as acrylic (PMMA), epoxy (SU-8), silicon, polymer, and/or any other materials that may be patterned below 1 μm resolution. The individual cuboids may have lateral vents 122 (as, for example, shown in FIG. 2c). The size, shape, anisotropy, etc. of the cavities may create anisotropic effective mass density and/or compressibility, sufficiently anisotropic such that these values may become negative along the ultrasound wave propagation direction through the thickness of the material. These effective negative acoustic properties of the metamaterial may compensate for the stiffness of the cortical bone, thereby allowing efficient transmission of ultrasound waves. An effective stiffness, the compressibility b_e , of the NRAM material may be determined using

$$b_e = b_o[1 - S(2Ad\rho L_e f)]$$

where b_o and ρ are the compressibility and density of the gas, the cross-sectional area for the vent is S , and the lateral area of the cuboid is A , d is the side length of the cuboid, L_e is the total height of the metamaterial, and f is the frequency of the ultrasound.

[0049] The effective density of the material may be made strongly anisotropic by the relative width of the walls to cavities, to the extent that a negative density may be obtained along the ultrasound propagation direction.

[0050] In some implementations, the configuration of the NRAM material shown in FIGS. 1a-2c may have a negative stiffness and density for ultrasound waves up having frequencies in a range of up at least 20 MHz. In some exemplary implementations, an operating frequency in a range of up to 250 MHz may be used to compensate for the stiff cortical bone that may be present along the ultrasound propagation path

[0051] FIG. 5 illustrates images 502a-d generated by an ultrasound equipment with and without use of the NRAM material. In particular, image 502a illustrates an ultrasound wave (US) being transmitted by an ultrasound transducer (“Transducer” shown by a black solid line in all images) into the tissue without presence of an abberator (e.g., a cortical bone). The

ultrasound wave transmission is unobstructed, i.e., strong, and a generated image is clear. However, once an abberator (e.g., a cortical bone) is introduced into the image path, the ultrasound wave is blocked and hence, fails to generate an image, as shown by the image 502b.

[0052] Image 502c illustrates use of current subject matter's NRAM material ("Metamaterial") with no abberator (i.e., cortical bone) present in the path of the ultrasound wave. Similar to image 502a, the generated image is clear. Hence, presence of the NRAM material does not affect image generation when there is no abberator. Image 502d illustrates use of the NRAM material when abberator (i.e., cortical bone) is present in the path of the transmitted ultrasound wave. Contrary to the image 502b, the NRAM material may allow the ultrasound wave to pass through the abberator to generate a clear ultrasound image. The NRAM material may operate without resonance, unlike traditional forms of acoustic metamaterials, to reduce their sensitivity to small changes in frequency, long range ordering, adjacent material properties, and/or morphology, which is important for various clinical uses.

[0053] In some implementations, the NRAM material may incorporate suspended silicon nitride (or any other materials, e.g., a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, etc.; any other metals and/or materials may be used) membranes supported on microstructure pillars using multi-stack processing and thin film transfer to create cavities (or cuboids) having a size in a range of approximately 200 nm to approximately 20 μm that may be used for anisotropic sound propagation. High-resolution electron beam lithography and/or any other methods may be used to create cavity having the above dimensions. As stated above, the cavities may be created using tough, stiff, and atomically thin graphene. The nanoscale NRAM material may be

configured to operate with ultrasound waves having higher operating frequencies (as compared to the conventional materials).

[0054] In some implementations, to fabricate a device having the NRAM material for use with an ultrasound transducer/probe, one or more individual cuboid cells may be created. A finite element analysis (FEA, ANSYS) of individual cuboid unit cells may be conducted to determine a net density and stiffness of the NRAM material using an extensive symmetry in the structure. The individual unit cell model of the NRAM material structure may be used to determine an effect of geometry and/or material choices on the NRAM material and acoustic wave propagation through it.

[0055] The NRAM's characteristics determined from one unit cell model may then be applied to the following, two-dimensional solid media *in-silico* representation of the entire multicellular material, together with a viscoelastic layer of tissue, an elastic layer of cortical bone, and a viscoelastic layer of bone marrow. This model may be used to identify an ability of the material to transmit coherent ultrasound in time-domain FEA analyses, applied as a displacement boundary condition at the NRAM's outer surface, to the opposite side of the model, the surface of the bone marrow. By applying either a perfectly reflecting and/or perfectly absorbing boundary condition at the bone marrow surface, it may be possible to determine an ability of the material to aid in transmission and/or detection of ultrasound through the system. The current subject matter system may be configured to compute both A-scan (amplitude versus time) and/or C-scan (spatial imagery) representations that may be used to assess the NRAM material for the purposes of increasing a return signal intensity and/or coherence from the bone marrow and reducing them from the tissue-cortical bone interface. This model may also be used for determination of the sensitivity of the NRAM to the thicknesses and material properties of the tissue, bone, and marrow, and/or the misalignment of the layers with respect to each other.

[0056] As discussed above, the NRAM material may be fabricated in a stacked form that may be, in some exemplary implementations, be approximately 1 mm thick, which may be used for ultrasound wave to penetrate into the bone marrow. The exemplary fabrication process may be performed by nanostructuring 1–10 μm thick multilayer films and thin film transferring and stacking of these multilayer films to form the final 0.1 to 1 mm thick NRAM material. A stack of alternating thin films of silicon nitride (SiN) and of acrylic (e.g., PMMA) may be initially created, as discussed above. SiN is a hard, transparent and a stable material with a Young's modulus (E) of 350 GPa, while PMMA is relatively soft ($E \sim 2$ GPa) but patternable via electron-beam radiation and thus, may be used for nanostructuring to form the NRAM cuboids within the 1–10 μm thick multilayer structure. The e-beam radiation may expose selected regions of the PMMA within the intercalated SiN-PMMA stack. The exposed PMMA may be then removed via one or more vent ports positioned in the same plane as the cuboid structures. These same vent ports may be used to provide negative density for ultrasound passing across the NRAM material, and the cuboid structure may provide a desired negative stiffness. Since layers 0.1 to 1 mm in thickness may be needed to compensate for the cortical bone layer, 100–1000 (or any other number) of these multilayer films may be stacked using a combinatorial process and a final bond of the layers may be performed to form the NRAM material. Next, an alignment may be performed to transfer and stack the modules. In some exemplary implementations, if necessary, the layers may be further aligned and/or sealed, however, because the one or more NRAM material size features are smaller than the wavelength of the ultrasound, the NRAM material and its corresponding functionalities may be able to perform its intended functionalities even if layers are misaligned.

[0057] In some implementations, the NRAM material may be used to make up to approximately 0.4 mm (or any other thickness) of cortical bone transparent to ultrasound at frequencies of approximately 250 MHz (or any other frequency discussed above), including

the interceding soft tissue, enabling assessment of the state of bone marrow within, with useful experimental and analysis data describing the material characteristics and expected behavior in ultrasound phantoms.

[0058] In some implementations, to allow venting of each nanoscale cell, the NRAM material's cells may include a gradient in the vent size laterally across each layer of the NRAM material. Further, through-thickness venting and/or lateral isolation of groups of unit cuboid cells with gaps between them may be used for venting purposes.

[0059] In some implementations, a quantitative ultrasound (QUS) methods for both NRAM performance and bone marrow characterization may be used to provide frequency-dependent attenuation (AC) and backscatter coefficients (BSC) for the useful bandwidth of ultrasound transducers for *ex vivo* and/or *in vivo* application. AC and BSC are frequency-dependent fundamental properties of tissue, reflecting tissue's composition and structure. QUS may acquire a raw beam-formed radio frequency ultrasound (RF) echo data, correct for machine-and/or transducer-dependent factors, and/or correct for overall attenuation (it may be used for a variety of *ex-* and *in vivo* pre-clinical and/or clinical applications).

[0060] FIG. 6 illustrates an exemplary process 600 for executing a quantitative ultrasound procedure using an ultrasound transducer together with the NRAM material, according to some implementations of the current subject matter. The process 600 may be applied to single-element transducers, arrays and/or plane-wave imaging methods to generate BSC and/or AC spectra using a reference phantom technique with standard clinical arrays to estimate a fat fraction. At 602, radio frequency ultrasound (RF) echo data may be acquired using the ultrasound transducer with the NRAM material/device coupled to it. At 604, a windowing gate function may be used to perform analysis of gate signals of the acquired data. This analysis may be performed by the processing circuitry of the ultrasound machine (that may include transducer, processors, memory, etc.). At 606, power spectrum may be determined

and averaged. The average power spectrum may be divided by a calibration spectrum value(s), at 608. At 610, attenuation correction may be executed, which may be followed by diffraction correction, at 612. Thereafter, diffraction coefficients (AC and/or BSC) may be determined, at 614. The process 600 may be used to generate one or more parametric maps of BSC coefficient 702 (as shown in FIG. 7a) and AC coefficient 704 (as shown in FIG. 7b) that may be overlaid on the B-mode images, where the maps illustrate variations in coefficients for patients having differing proton density fat fraction (PDFF) (e.g., participant A may have a PDFF of 27.9%, AC=0.93 dB/cm/MHz, BSC=0.045/cm-sr; participant B may have a PDFF of 1.4%, AC=0.53 dB/cm/MHz, BSC=0.00047/cm-sr). Using an ultrasound transducer and the NRAM materials, ultrasound waves may be transmitted through cortical bone to the trabecular bone and marrow within, to identify presence of BML using B-mode and QUS (whereby MRI may be used to provide location and/or extent for comparison).

[0061] In some implementations, the current subject matter's NRAM material may be configured to avoid narrow band operation and/or high losses that may be typically associated with resonant metamaterials. NRAM material may be configured to have a frequency window $\Delta f/f_0$ of approximately 5-10% to tune modulus and density, which may be advantageous in view of skull variations in thickness and/or composition. As described above, the NRAM material may include one or more acoustic wave-guiding cavities having the following components: membranes 808 producing negative density and open channels 806 giving negative modulus. FIG. 8 illustrates an exemplary architecture 800 of the NRAM material having membranes (SiN) 808 and open channels 806 along with the equivalent circuit 802 and a low frequency behavior circuit 804. At low frequency, below resonance, the dominant elements may be an acoustic compliance of the membranes 808 C_a (series capacitors in the circuit), and the acoustic mass of the open channels 806 m_a (shunt inductors). The equations relating acoustic compliance and masses with effective density and modulus may be expressed as follows:

$$\rho_{eq} = \frac{Z_{as}}{i\omega} \frac{S}{d} = \frac{1}{i\omega} \frac{S}{d} \left(i\omega m_{as} + \frac{1}{i\omega C_{as}} \right); K_{eq}^{-1} = \frac{Y_{ap}}{i\omega} \frac{1}{Sd} = \frac{1}{i\omega} \frac{1}{Sd} \left(i\omega C_{ap} + \frac{1}{i\omega m_{ap}} \right)$$

[0062] From the above equations, NRAM operating frequencies and sizes of unit cells may be determined (e.g., operating frequencies of 1-250 MHz may require 100-10 μm unit cells. By way of a non-limiting example, the NRAM material may be configured to have an operating frequency of 5.5 MHz, having density $\rho^{[M]}$ approximately -4000kg/m^3 , $K^{[M]}$ approximately -10 GPa , channel diameter of approximately $20\text{ }\mu\text{m}$, cavity length of approximately $20\text{ }\mu\text{m}$, SiN_x membrane being approximately 750 nm thick, and an open channel (channel 122 as shown in FIG. 2c) being approximately $5\text{ }\mu\text{m}$ wide. As can be understood, other values may be used.

[0063] FIGS. 9a-9b illustrate exemplary methods 900 and 920 for fabricating the NRAM material, according to some implementations of the current subject matter. The processes are similar to those described above in connection with FIGS. 1a-2c. In particular, FIG. 9a illustrates a process 900 for fabricating NRAM material by stacking of SiN_x and SU-8 layers, whereby the fabricated NRAM material may be capable of having an operating frequency of 1-250 MHz. FIG. 9b illustrates a process 920 for fabricating NRAM material by stacking of SiN_x and Si layers, whereby the fabricated NRAM material may be capable of having an operating frequency of 1-5 MHz. The processes 900, 920 may be configured to produce NRAM materials having cavity sizes of less than $100\text{ }\mu\text{m}$. A silicon clean room technology (UV approximately $1\text{ }\mu\text{m}$) may be used to fabricate SiN_x membranes. In some exemplary implementations, SiN_x may be configured to have a modulus $E > 170\text{ GPa}$, a tunable tensile stress and high fracture toughness (KIC), as well as high chemical stability. By way of a non-limiting example, a $10\text{ }\mu\text{m}$ wide SiN_x membrane may be capable of resonating at an operating frequency of $>250\text{ MHz}$.

[0064] Referring to FIG. 9a, the process 900 may be initiated by growing SiN_x layer

on a substrate (e.g., Cu foil substrate having a thickness of 25 μm (or any other material/thickness)), at 902. SU-8 material (or any other material, e.g., silicon, polymer, etc.) may be spin-coated on the SiNx layer-substrate combination, at 904. A portion of the substrate or an entire substrate may be removed, such as by performing a wet etching and/or any other methods, at 906. Then, one or more stacks of SiNx-SU-8 layers may be fabricated and wet-transferred on a substrate (e.g., LiNb substrate and/or any other substrate), at 908. After such repeated transfers, multiple stacked layers of SiNx-SU-8 layers may be produced. During a lithographic stage, at 910, SU-8 material may be exposed to UV radiation for the purposes of removing it at the next stage. At a development/membrane release stage, at 912, the SU-8 material may be removed to form cavities/membranes and open channels.

[0065] An alternative process 920, as shown in FIG. 9b, illustrates use of the Si materials together with the SiNx materials to form an NRAM material. As part of the process 920, individual chips with etched channels and SiNx membranes may be fabricated. Then, the layers may be stacked and clamped using one or more micro-precision screws, as shown in FIG. 9b. In an exemplary, non-limiting implementations, 50 μm thick chips may be capable of having an operating frequency of 1-5 MHz.

[0066] FIG. 10 illustrates an exemplary ultrasound system 1000 that implements the NRAM material described above in connection with FIGS. 1a-9a, according to some implementations of the current subject matter. The system 1000 may include an ultrasound processing system 1002, an ultrasound probe and/or transducer 1004, and the NRAM material or device 1006. In some implementations, the processing system 1002 and the probe/transducer 1004 may be a single unit. The NRAM material or device 1006 may be configured to be coupled to the probe/transducer 1004. The coupling may be optical, mechanical, electro-mechanical, optico-mechanical, optico-electro-mechanical, and/or any other type of coupling.

[0067] In some implementations, the NRAM material 1006 may be configured to be

placed directly on the skin of the object 1008 (e.g., via an ultrasound gel). The probe/transducer 1004 may be configured to generate one or more ultrasound waves 1014 that may be configured to pass through the NRAM material 1006 and toward a target tissue 1012, where the target tissue (e.g., marrow) 1012 may be located “behind” an abberator tissue 1010 (e.g., cortical bone). The NRAM material 1006 may be configured to shift phase and/or amplitude of the ultrasound waves 1014 passing through it to penetrate the abberator tissue 1010 to reach the target tissue 1012 and be reflected back to through the abberator tissue 1012, where the NRAM material may also focus and/or shift phase and/or amplitude of the reflected waves toward the receiver in the probe/transducer for processing by the system 1002.

[0068] FIG. 11 illustrates an exemplary method for fabricating a non-resonant acoustic metamaterial (e.g., similar to the one shown in FIGS. 1a-10), according to some implementations of the current subject matter. At 1102, a layer of a first material may be formed on a first substrate. At 1104, a layer of a second material may be formed on the layer of the first material to produce a stacked layer of first and second materials. At 1106, at least a portion of the stacked layer of first and second materials may be exposed to a radiation. At 1108, the exposed portion of the second material may be removed from the stacked layer of first and second materials. At 1110, a cavity may be formed using the removed exposed portion of the second material. The cavity may include a membrane formed from at least a portion of the first material.

[0069] In some implementations, the current subject matter may include one or more of the following optional features. The method may include removing at least a portion of the first substrate subsequent to the forming of the layer of a second material on the layer of the first material. The method may also include transferring the stacked layer of the first and second materials onto a second substrate.

[0070] In some implementations, the stacked layer of the first and second materials

may include a plurality of alternating layers of the first material and the second material. In some implementations, the removing may further include removing a plurality of layers of the second materials from the stacked layer of the first and second materials while retaining a plurality of first materials. The cavity may include a plurality of portions of layers of the first material forming a plurality of membranes. Further, the plurality of membranes may be configured to resonate at a predetermined operating frequency and configured to shift phase and/or amplitude of one or more ultrasound waves passing through the cavity. The predetermined operating frequency may be in a range of approximately 100 KHz to approximately 250 MHz.

[0071] In some implementations, the first material may be a hard material and the second material is a soft material. The first material may include at least one of the following: a silicon oxide, a silicon nitride, a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and any combinations thereof. Any other metals and/or materials may be used. The second material may include at least one of the following: a polymethyl methacrylate (PMMA) material, SU-8 material, silicon, polymer, and any combinations thereof.

[0072] In some implementations, the cavity may be filled with at least one of the following: a fluid, a gas, and any combinations thereof.

[0073] In some implementations, the cavity may be configured to be connected to at least another cavity formed in at least another second layer and further configured to be separated from at least another cavity by at least one of: the membrane and at least another membrane.

[0074] In some implementations, the current subject matter relates to a non-resonant acoustic metamaterial apparatus that may be formed in accordance with the discussion above (e.g., method 1100 shown in FIG. 11). The apparatus may include a layer of a first material on a first substrate, a layer of a second material formed on the layer of the first material to produce a stacked layer of first and second materials and a cavity. The cavity may be formed by exposing at least a portion of the stacked layer of first and second materials to a radiation, removing the exposed portion of the second material from the stacked layer of first and second materials, and forming the cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material. The apparatus may include some of the optional features discussed above.

[0075] In some implementations, the current subject matter relates to an ultrasound system that may include an ultrasound transducer and the non-resonant acoustic metamaterial coupled to the ultrasound transducer having features discussed above.

[0076] Without in any way limiting the scope, interpretation, or application of the claims appearing below, a technical effect of one or more of the example embodiments disclosed herein may provide an ability to allow imaging of objects, tissues, materials, etc. using ultrasound waves, where the objects may be located behind an interfering body (e.g., in case of a bone marrow, a cortical bone, etc.). This advantage may be achieved through controllable scattering of ultrasound waves prior to passage through interfering objects to compensate for the presence of the such objects along the ultrasound wave propagation path, thereby producing a coherent, focused ultrasound beam after passage through the objects for characterization, imaging, etc. of objects beyond it.

[0077] One or more aspects or features of the subject matter described herein can be realized in digital electronic circuitry, integrated circuitry, specially designed application specific integrated circuits (ASICs), field programmable gate arrays (FPGAs) computer

hardware, firmware, software, and/or combinations thereof. These various aspects or features can include implementation in one or more computer programs that are executable and/or interpretable on a programmable system including at least one programmable processor, which can be special or general purpose, coupled to receive data and instructions from, and to transmit data and instructions to, a storage system, at least one input device, and at least one output device. The programmable system or computing system may include clients and servers. A client and server are generally remote from each other and typically interact through a communication network. The relationship of client and server arises by virtue of computer programs running on the respective computers and having a client-server relationship to each other.

[0078] These computer programs, which can also be referred to as programs, software, software applications, applications, components, or code, include machine instructions for a programmable processor, and can be implemented in a high-level procedural and/or object-oriented programming language, and/or in assembly/machine language. As used herein, the term “machine-readable medium” refers to any computer program product, apparatus and/or device, such as for example magnetic discs, optical disks, memory, and Programmable Logic Devices (PLDs), used to provide machine instructions and/or data to a programmable processor, including a machine-readable medium that receives machine instructions as a machine-readable signal. The term “machine-readable signal” refers to any signal used to provide machine instructions and/or data to a programmable processor. The machine-readable medium can store such machine instructions non-transitorily, such as for example as would a non-transient solid-state memory or a magnetic hard drive or any equivalent storage medium. The machine-readable medium can alternatively, or additionally, store such machine instructions in a transient manner, such as for example, as would a processor cache or other random access memory associated with one or more physical processor cores.

[0079] The subject matter described herein can be embodied in systems, apparatus, methods, and/or articles depending on the desired configuration. The implementations set forth in the foregoing description do not represent all implementations consistent with the subject matter described herein. Instead, they are merely some examples consistent with aspects related to the described subject matter. Although a few variations have been described in detail above, other modifications or additions are possible. In particular, further features and/or variations can be provided in addition to those set forth herein. For example, the implementations described above can be directed to various combinations and subcombinations of the disclosed features and/or combinations and subcombinations of several further features disclosed above. In addition, the logic flows depicted in the accompanying figures and/or described herein do not necessarily require the particular order shown, or sequential order, to achieve desirable results. Other implementations may be within the scope of the following claims.

What is claimed:

1. A method, comprising:
forming a layer of a first material on a first substrate;
forming a layer of a second material on the layer of the first material to produce a stacked layer of first and second materials;
exposing at least a portion of the stacked layer of first and second materials to a radiation;
removing the exposed portion of the second material from the stacked layer of first and second materials; and
forming a cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material.
2. The method according to claim 1, further comprising removing at least a portion of the first substrate subsequent to the forming of the layer of a second material on the layer of the first material.
3. The method according to any of the preceding claims, further comprising transferring the stacked layer of the first and second materials onto a second substrate.
4. The method according to any of the preceding claims, wherein the stacked layer of the first and second materials includes a plurality of alternating layers of the first material and the second material.
5. The method according to any of the preceding claims, wherein the removing

further comprises removing a plurality of layers of the second materials from the stacked layer of the first and second materials while retaining a plurality of first materials.

6. The method according to any of the preceding claims, wherein the cavity includes a plurality of portions of layers of the first material forming a plurality of membranes.

7. The method according to any of the preceding claims, wherein the plurality of membranes is configured to resonate at a predetermined operating frequency and configured to shift at least one of a phase and an amplitude of one or more ultrasound waves passing through the cavity.

8. The method according to any of the preceding claims, wherein the predetermined operating frequency is in a range of approximately 100 KHz to approximately 250 MHz.

9. The method according to any of the preceding claims, wherein the first material is a hard material and the second material is a soft material.

10. The method according to any of the preceding claims, wherein the first material includes at least one of the following: a silicon oxide, a silicon nitride, a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and any combinations thereof.

11. The method according to any of the preceding claims, wherein the second material includes at least one of the following: a polymethyl methacrylate (PMMA) material, SU-8 material, silicon, polymer, and any combinations thereof.

12. The method according to any of the preceding claims, wherein the cavity is filled with at least one of the following: a fluid, a gas, and any combinations thereof.

13. The method according to any of the preceding claims, wherein the cavity is configured to be connected to at least another cavity formed in at least another second layer and further configured to be separated from the at least another cavity by at least one of: the membrane and at least another membrane.

14. A non-resonant acoustic metamaterial apparatus, comprising;
a layer of a first material formed on a first substrate;
a layer of a second material formed on the layer of the first material to produce a stacked layer of first and second materials; and
a cavity formed by at least:
exposing at least a portion of the stacked layer of first and second materials to a radiation;
removing the exposed portion of the second material from the stacked layer of first and second materials; and
forming the cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material.

15. The apparatus according to claim 14, wherein at least a portion of the first substrate is removed subsequent to the forming of the layer of a second material on the layer of the first material.

16. The apparatus according to any of the preceding claims 14-15, wherein the stacked layer of the first and second materials is transferred onto a second substrate.

17. The apparatus according to any of the preceding claims 14-16, wherein the stacked layer of the first and second materials includes a plurality of alternating layers of the first material and the second material.

18. The apparatus according to any of the preceding claims 14-17, wherein the removal further comprises removing a plurality of layers of the second materials from the stacked layer of the first and second materials while retaining a plurality of first materials.

19. The apparatus according to any of the preceding claims 14-18, wherein the cavity includes a plurality of portions of layers of the first material forming a plurality of membranes.

20. The apparatus according to any of the preceding claims 14-19, wherein the plurality of membranes is configured to resonate at a predetermined operating frequency and configured to shift at least one of a phase and an amplitude of one or more ultrasound waves passing through the cavity.

21. The apparatus according to any of the preceding claims 14-20, wherein the predetermined operating frequency is in a range of approximately 100 KHz to approximately 250 MHz.

22. The apparatus according to any of the preceding claims 14-21, wherein the first material is a hard material and the second material is a soft material.

23. The apparatus according to any of the preceding claims 14-22, wherein the first material includes at least one of the following: a silicon oxide, a silicon nitride, a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and any combinations thereof.

24. The apparatus according to any of the preceding claims 14-23, wherein the second material includes at least one of the following: a polymethyl methacrylate (PMMA) material, SU-8 material, silicon, polymer, and any combinations thereof.

25. The apparatus according to any of the preceding claims 14-24, wherein the cavity is filled with at least one of the following: a fluid, a gas, and any combinations thereof.

26. The apparatus according to any of the preceding claims 14-25, wherein the cavity is configured to be connected to at least another cavity formed in at least another second layer and further configured to be separated from the at least another cavity by at least one of:

the membrane and at least another membrane.

27. An ultrasound system, comprising:

an ultrasound transducer;

a non-resonant acoustic metamaterial coupled to the ultrasound transducer;

wherein the non-resonant acoustic metamaterial includes

a layer of a first material formed on a first substrate;

a layer of a second material formed on the layer of the first material to produce

a stacked layer of first and second materials; and

a cavity formed by:

exposing at least a portion of the stacked layer of first and second materials to a radiation;

removing the exposed portion of the second material from the stacked layer of first and second materials; and

forming the cavity using the removed exposed portion of the second material, wherein the cavity includes a membrane formed from at least a portion of the first material.

28. The system according to claim 27, wherein the cavity includes a plurality of portions of layers of the first material forming a plurality of membranes.

29. The system according to any of the preceding claims 27-28, wherein the plurality of membranes is configured to resonate at a predetermined operating frequency and configured to shift at least one of a phase and an amplitude of one or more ultrasound waves generated by the ultrasound transducer and passing through the cavity.

30. The system according to any of the preceding claims 27-29, wherein the predetermined operating frequency is in a range of approximately 100 KHz to approximately 250 MHz.

31. The system according to any of the preceding claims 27-30, wherein the first material is a hard material and the second material is a soft material.

32. The system according to any of the preceding claims 27-31, wherein the first material includes at least one of the following: a silicon oxide, a silicon nitride, a graphene, a diamond, a metal nitride, a metal carbide, a silicon carbide, a metal oxide, a metal oxide bilayer, a silicon oxide bilayer, metal nitride bilayer, silicon nitride bilayer, aluminum nitride, aluminum carbide, aluminum oxide, aluminum oxide bilayer, aluminum nitride bilayer, chromium nitride, chromium carbide, chromium oxide, chromium oxide bilayer, chromium nitride bilayer, and any combinations thereof.

33. The system according to any of the preceding claims 27-32, wherein the second material includes at least one of the following: a polymethyl methacrylate (PMMA) material, SU-8 material, silicon, polymer, and any combinations thereof.

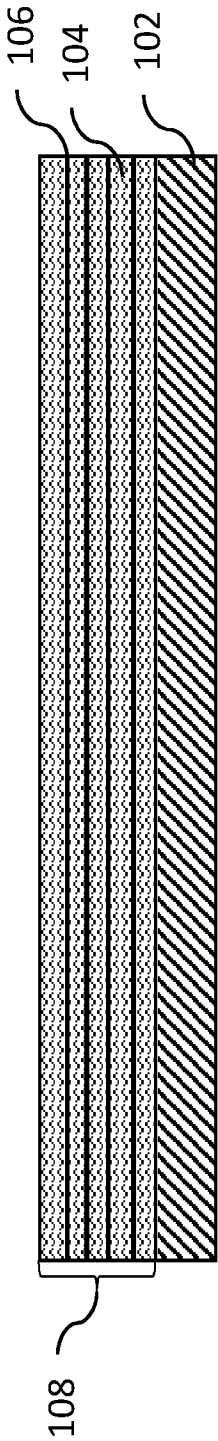
34. The system according to any of the preceding claims 27-33, wherein the cavity is filled with at least one of the following: a fluid, a gas, and any combinations thereof.

35. The system according to any of the preceding claims 27-33, wherein the

cavity is configured to be connected to at least another cavity formed in at least another second layer and further configured to be separated from the at least another cavity by at least one of: the membrane and at least another membrane.

100

FIG. 1a.



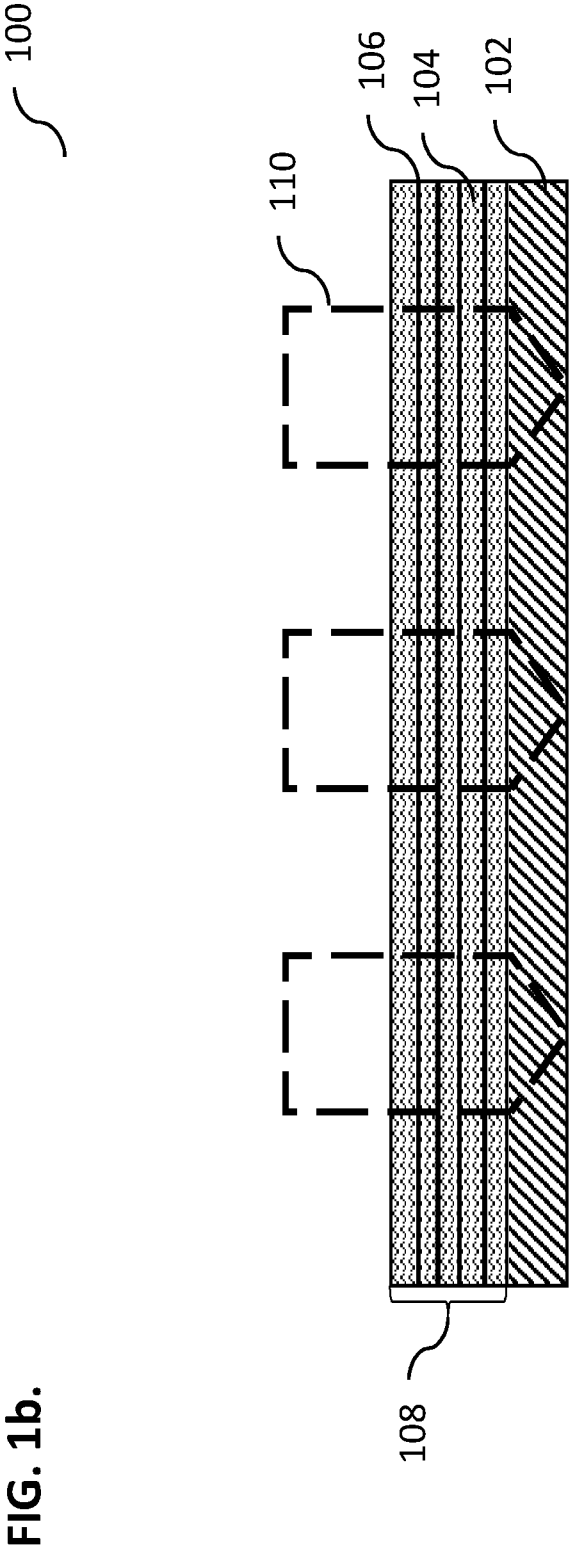


FIG. 1c.

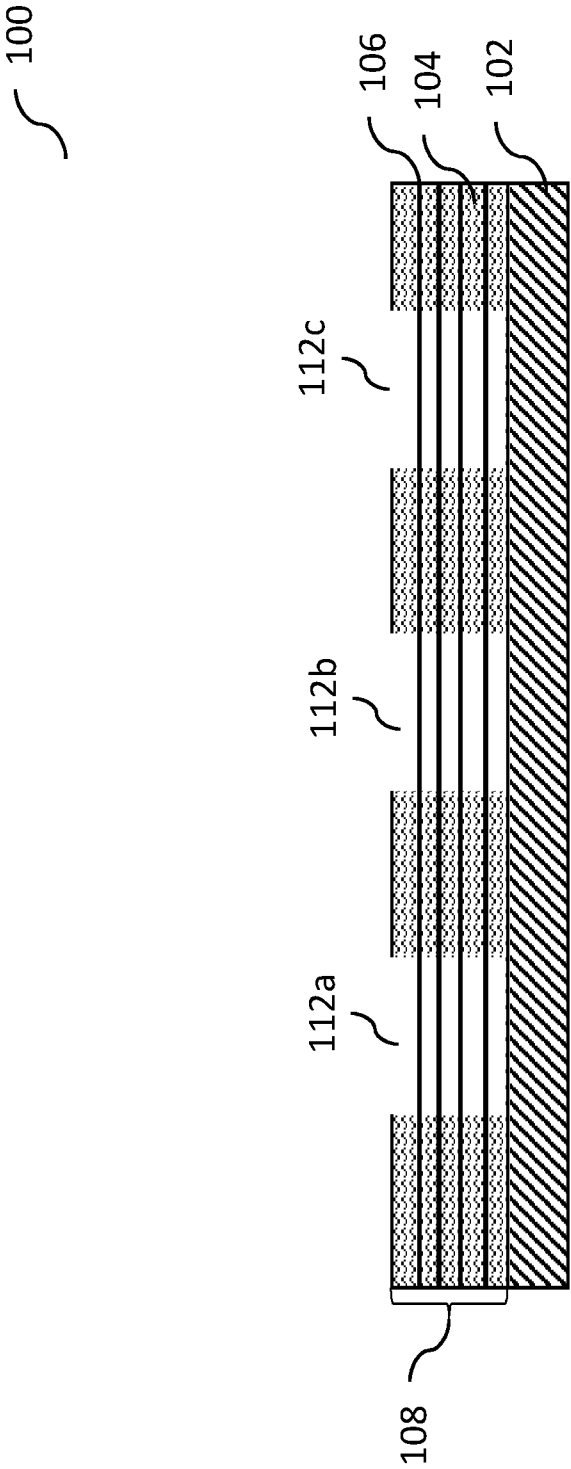
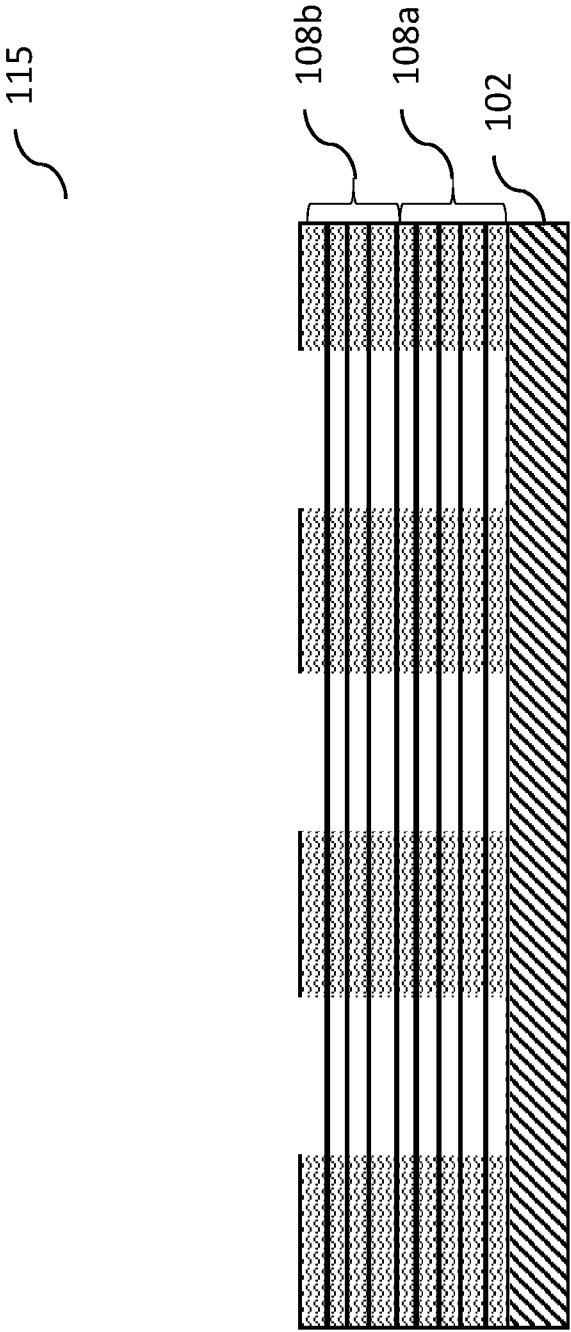


FIG. 1d.



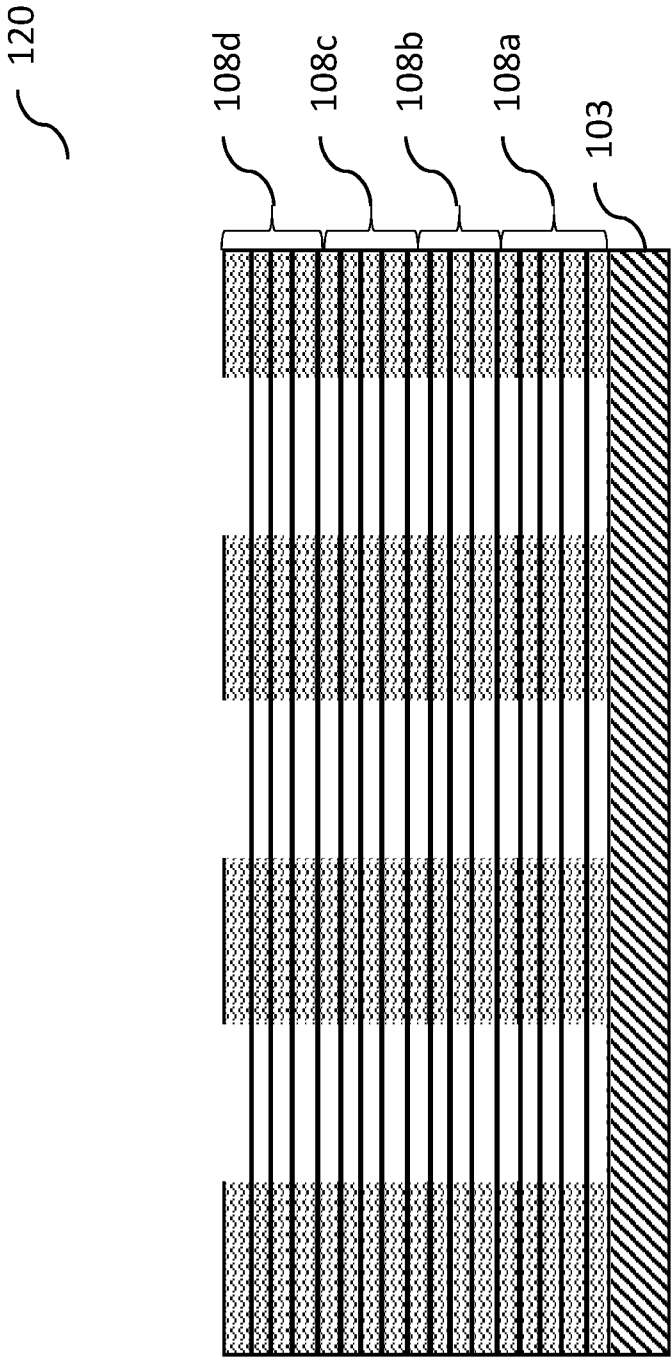
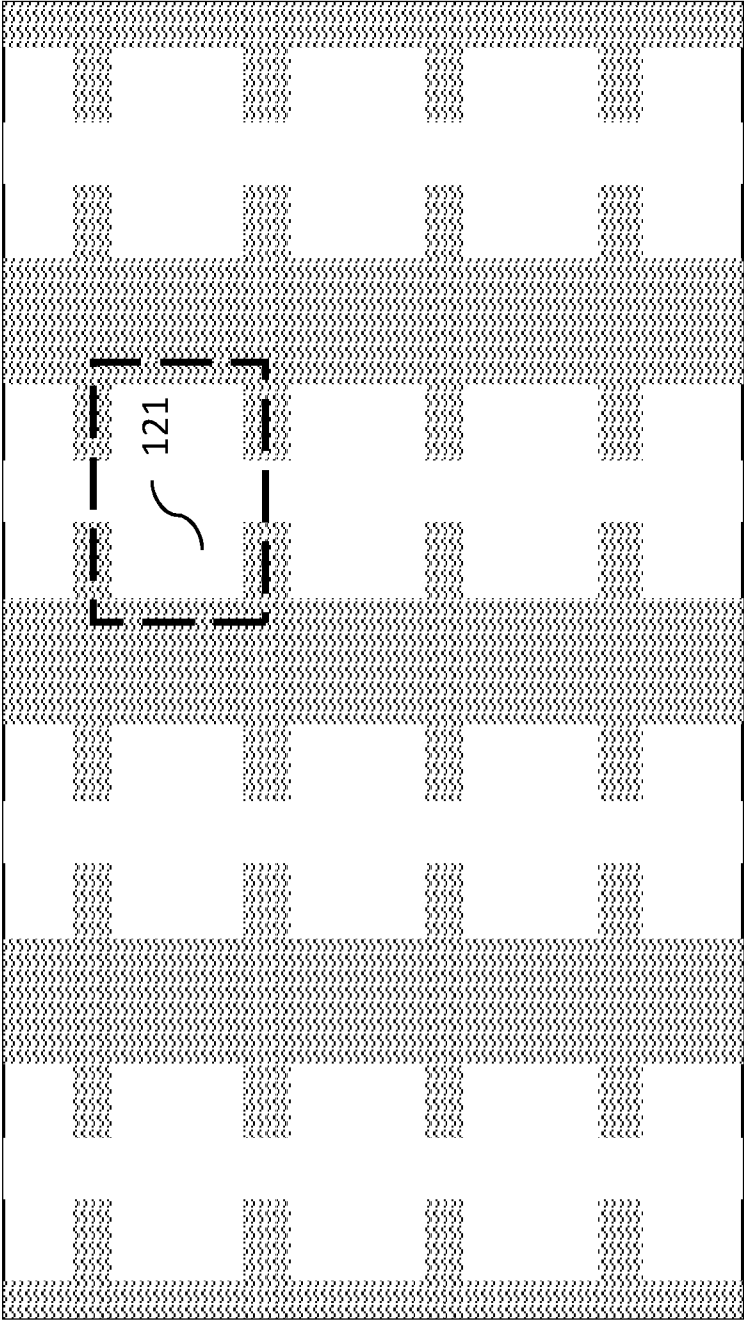


FIG. 2a.

120



120

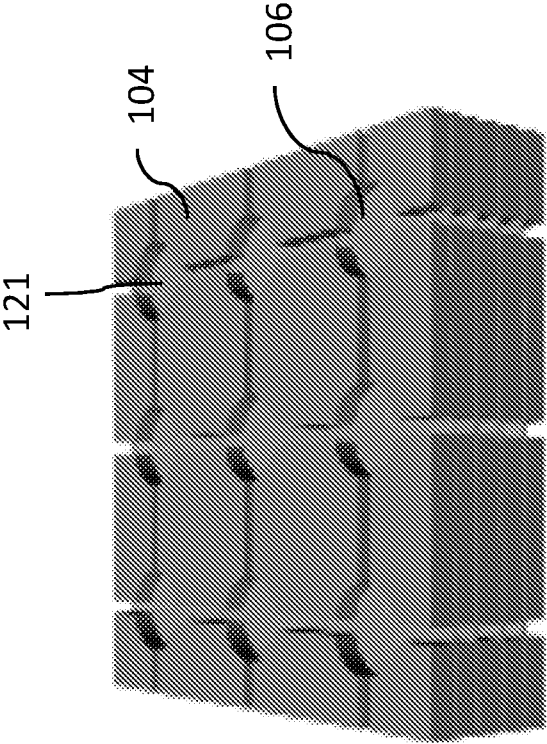


FIG. 2b.

121

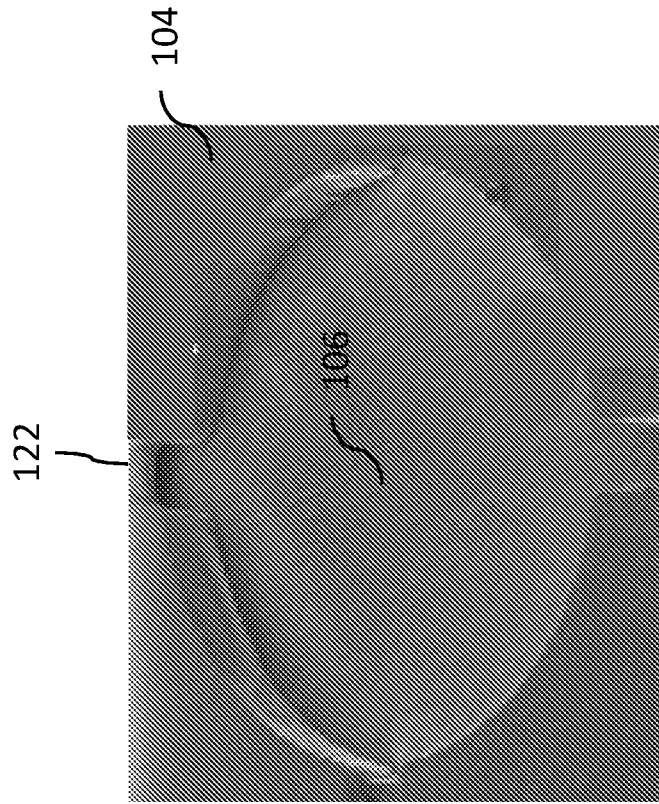
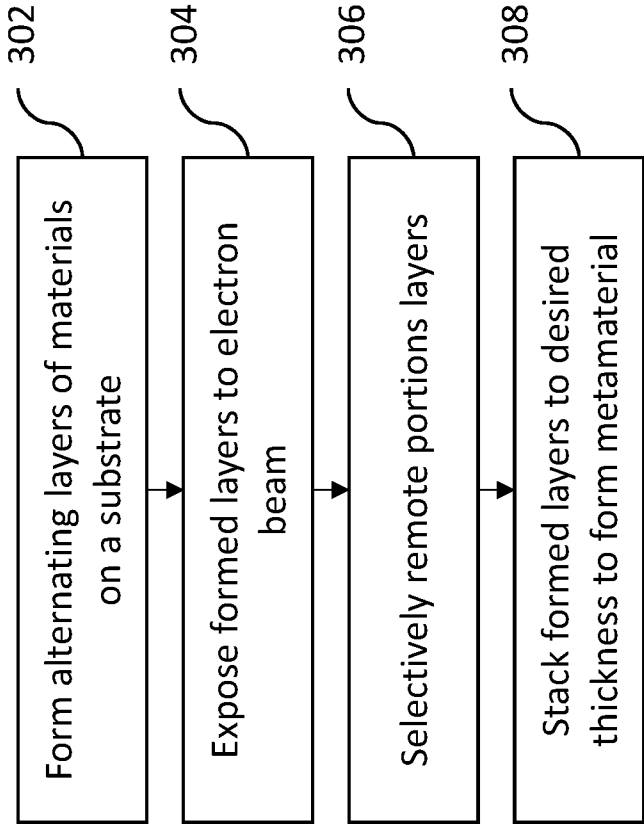


FIG. 2c.

300

FIG. 3.



400

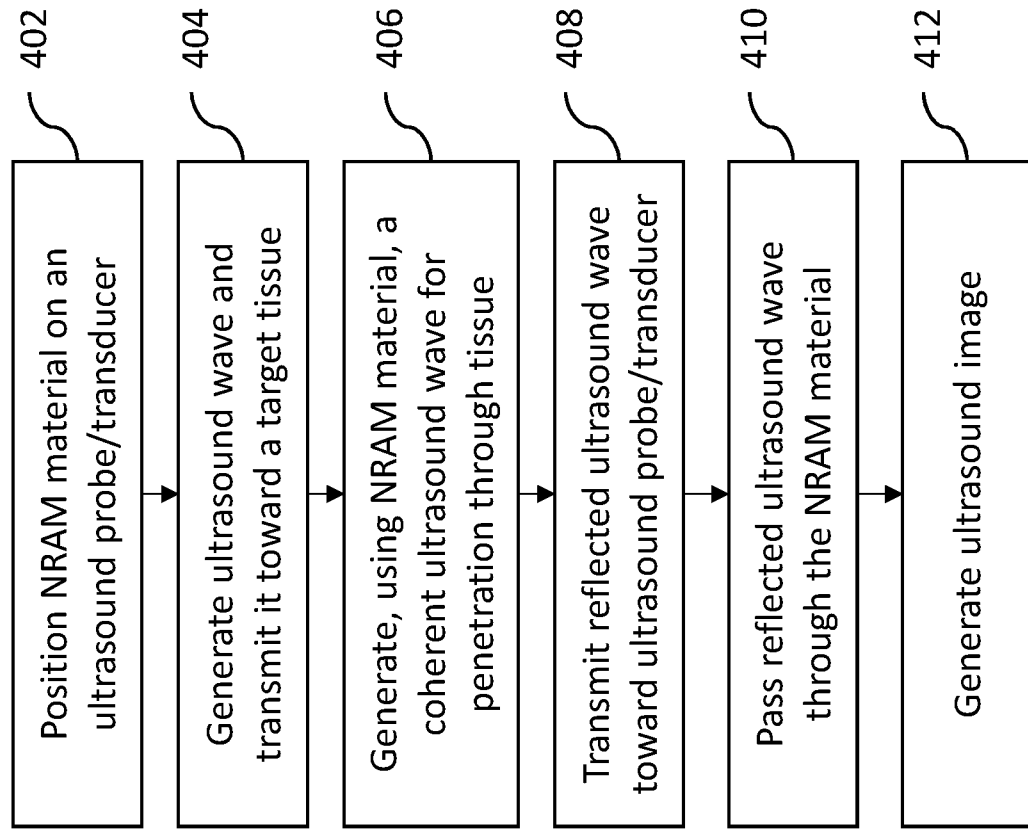
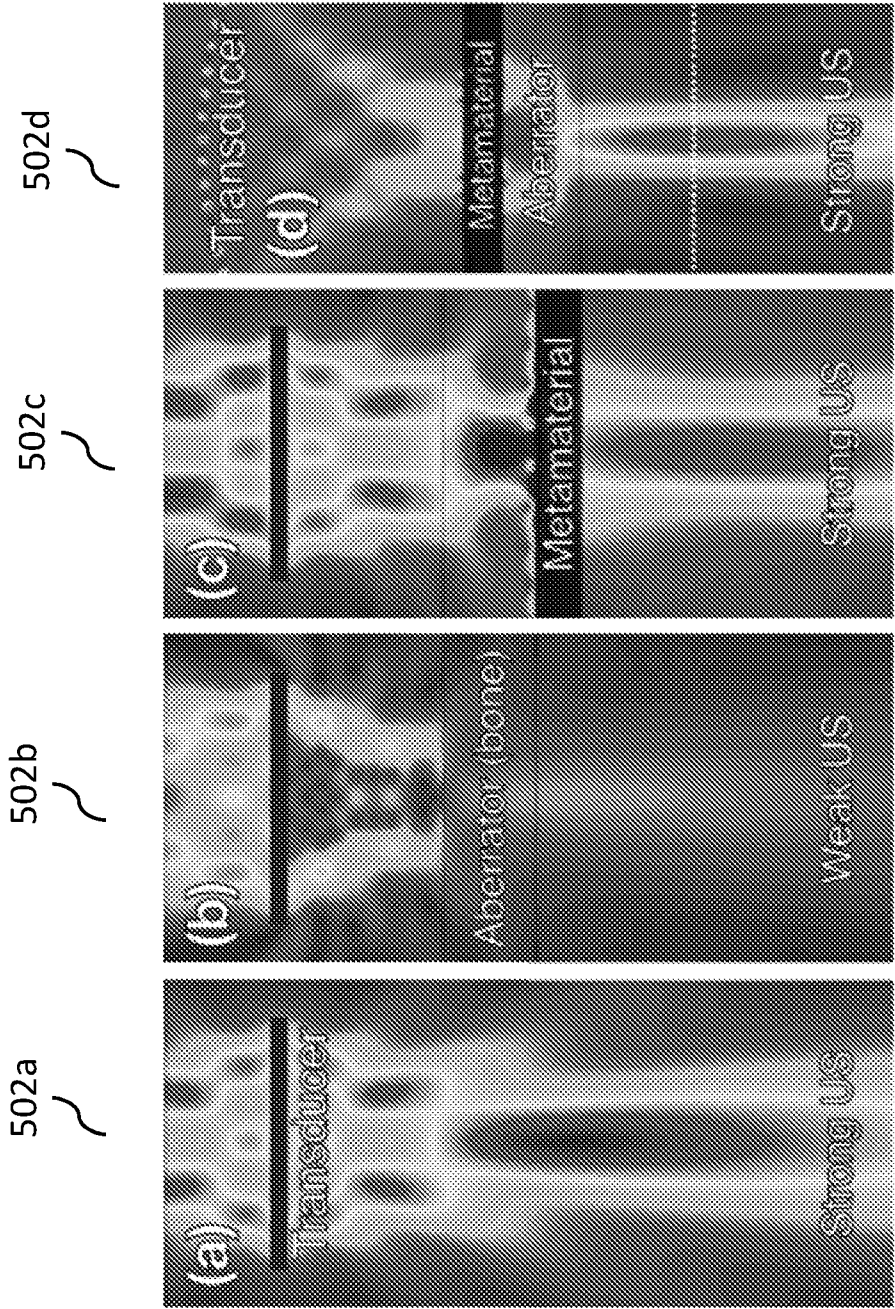


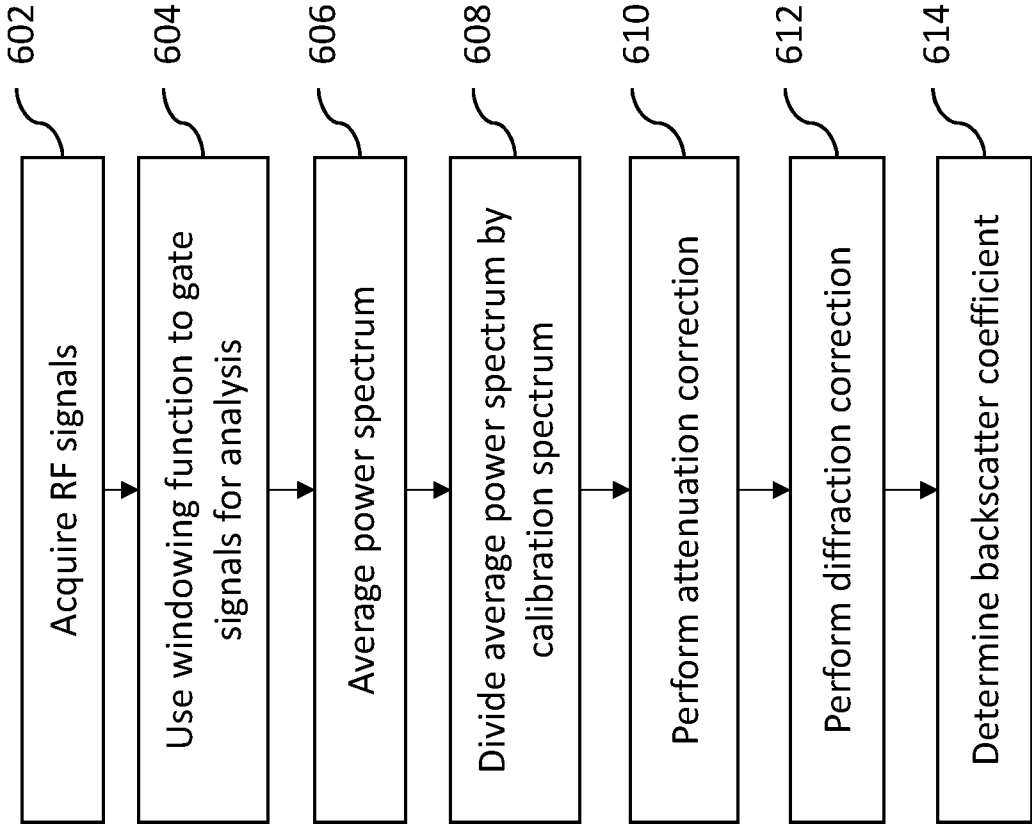
FIG. 4.

FIG. 5.



600

FIG. 6.



702

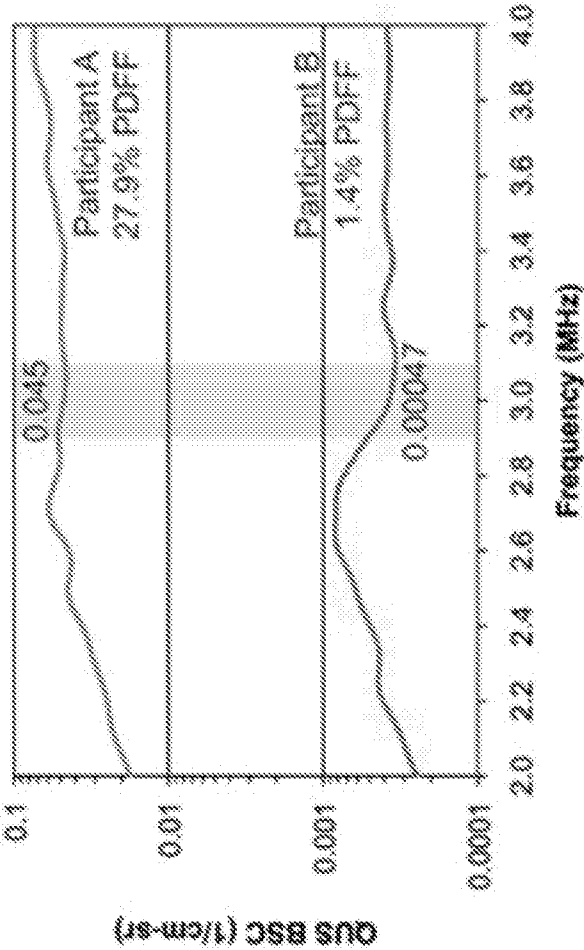


FIG. 7a.

704

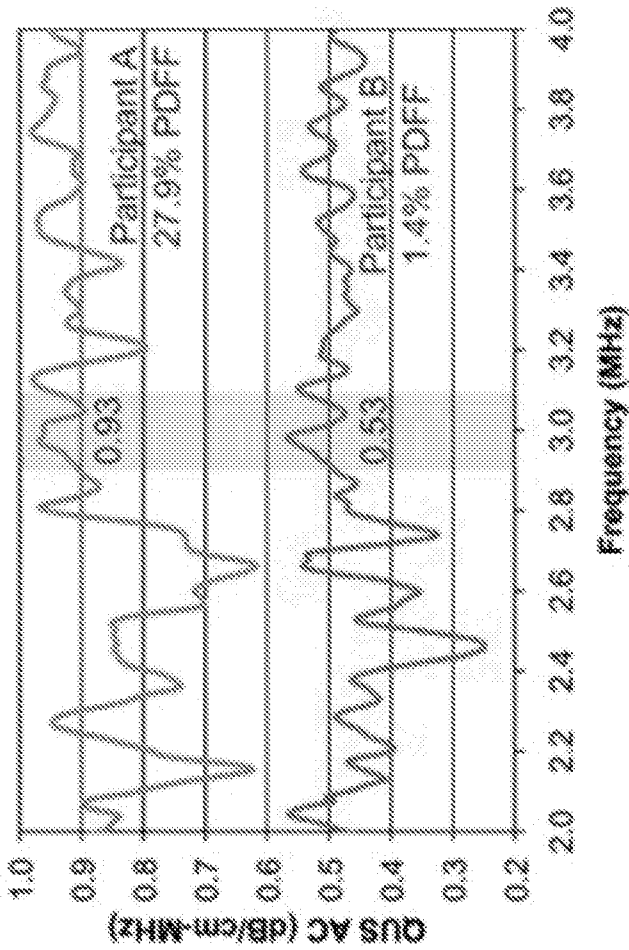


FIG. 7b.

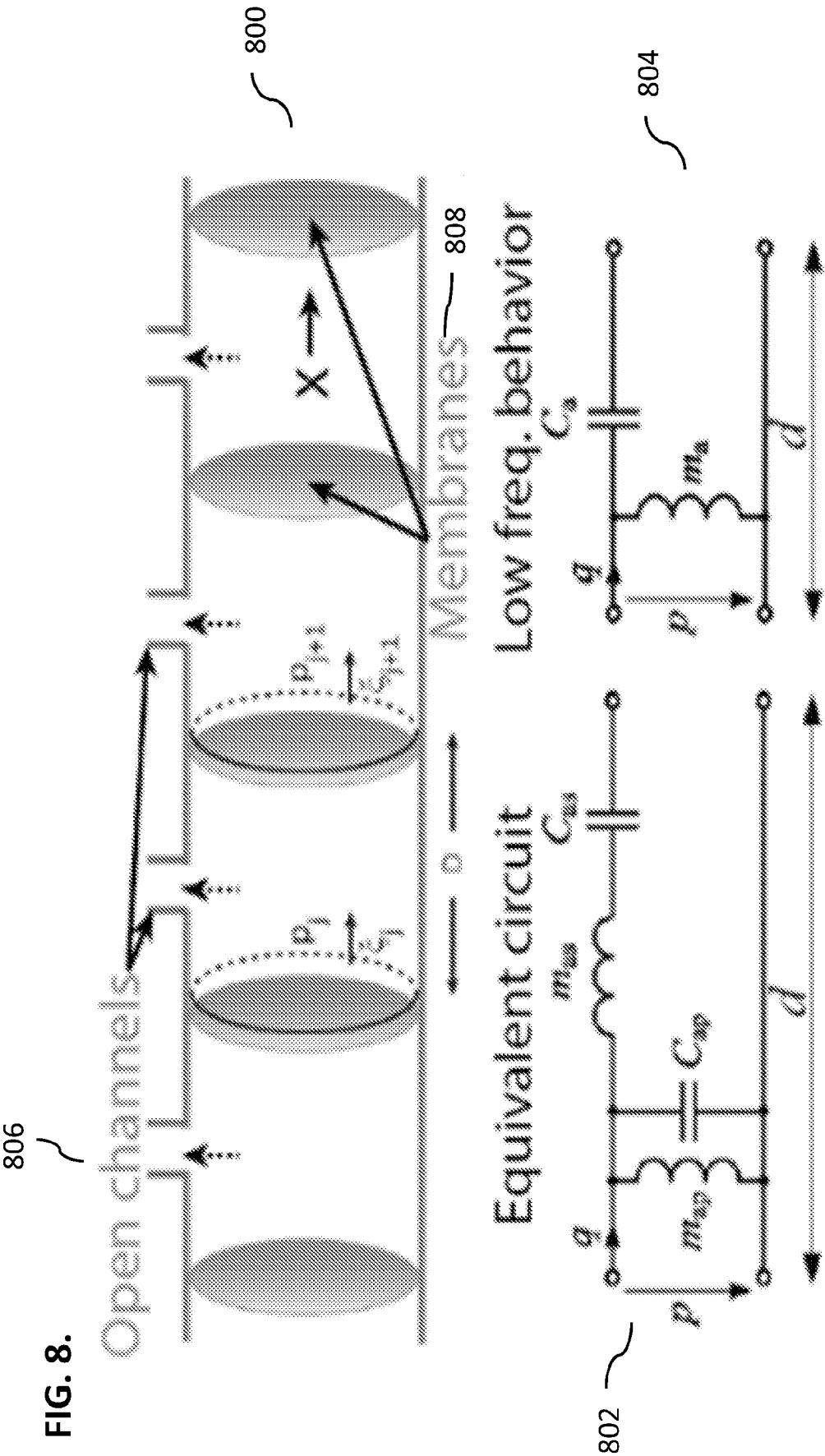


FIG. 9a.

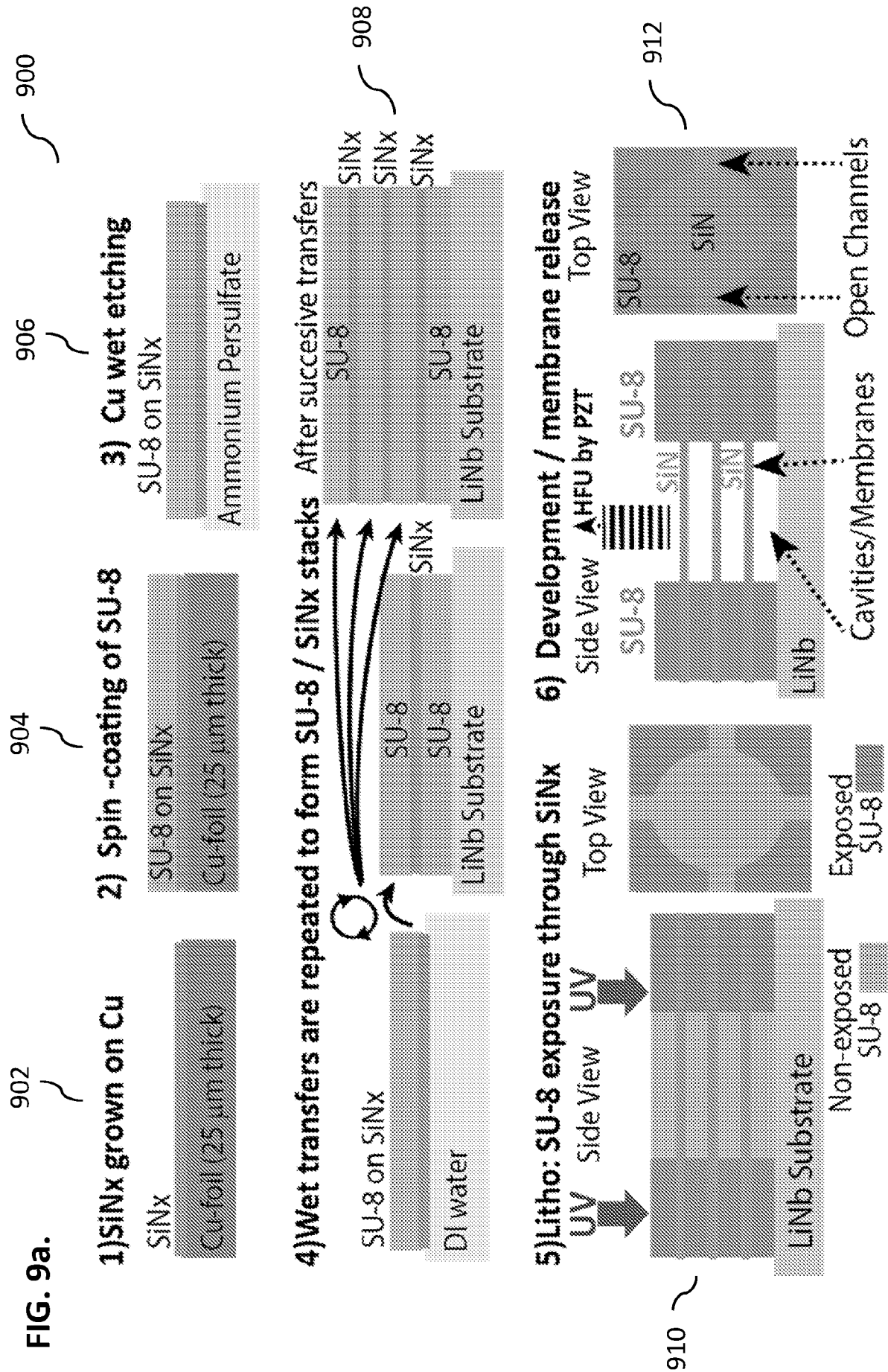
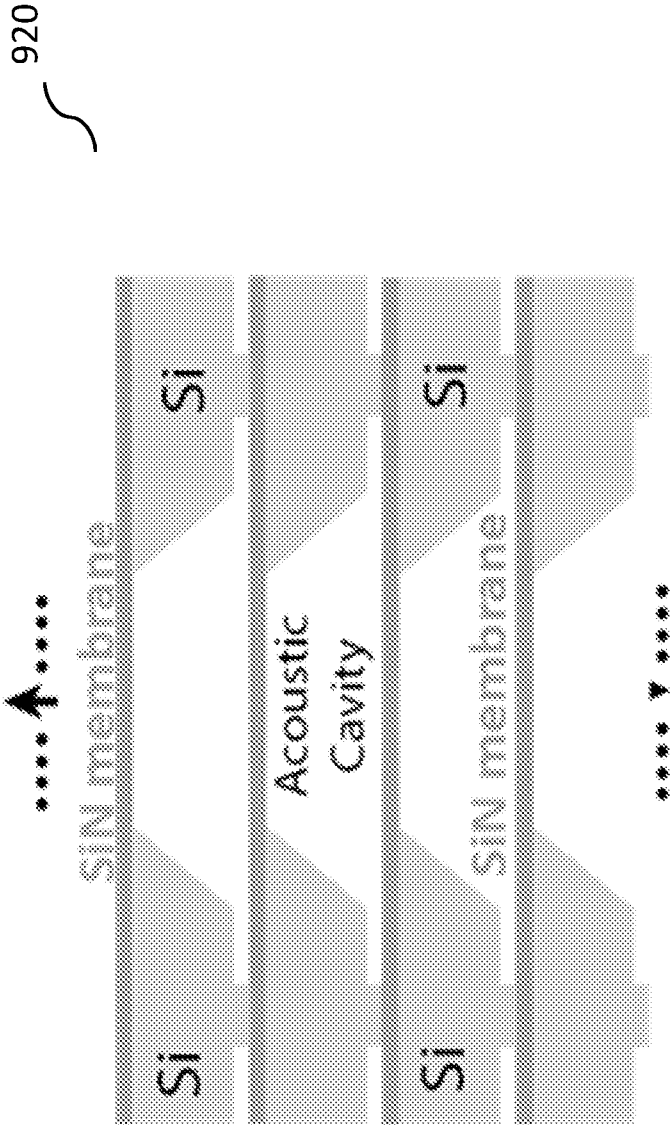


FIG. 9b.



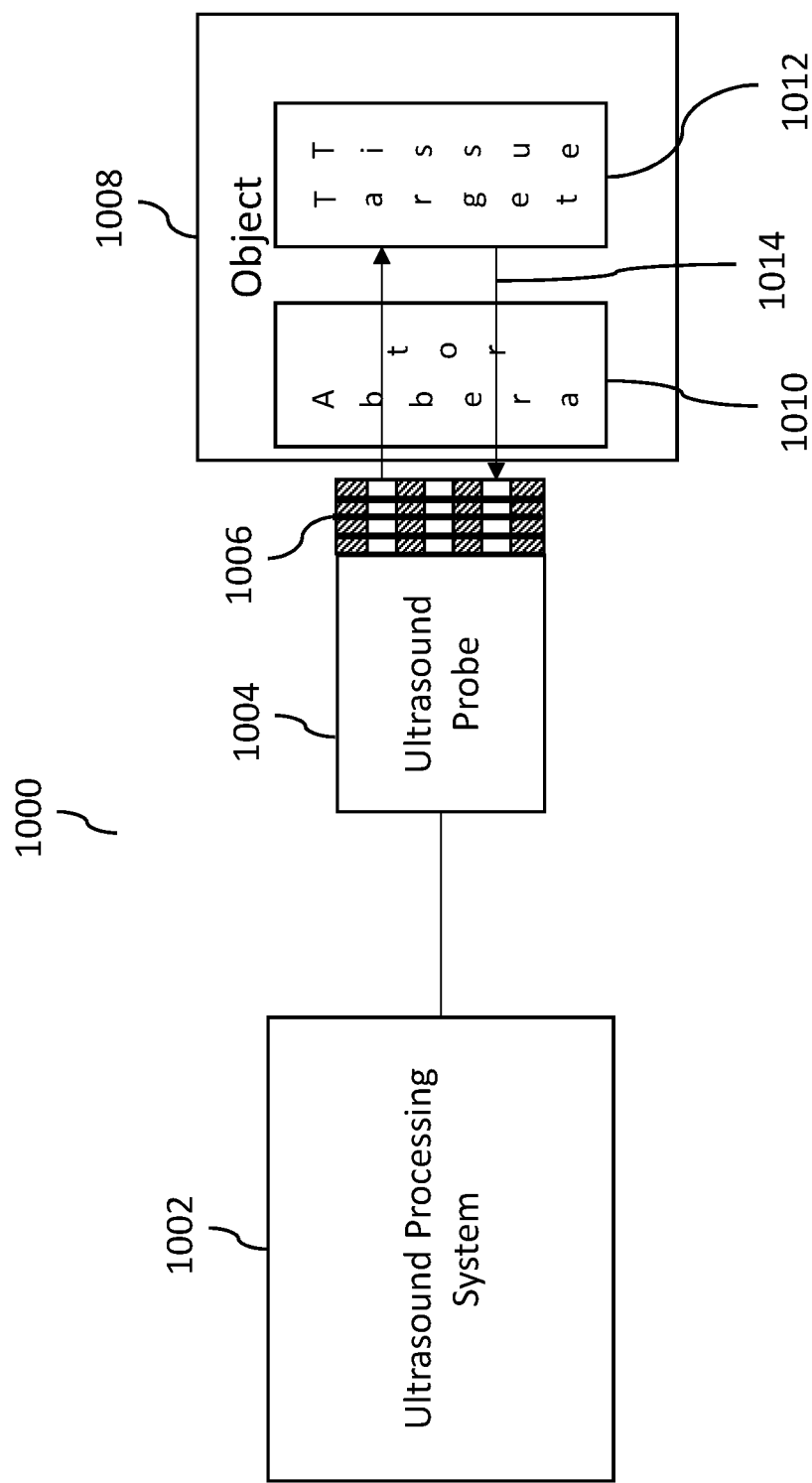
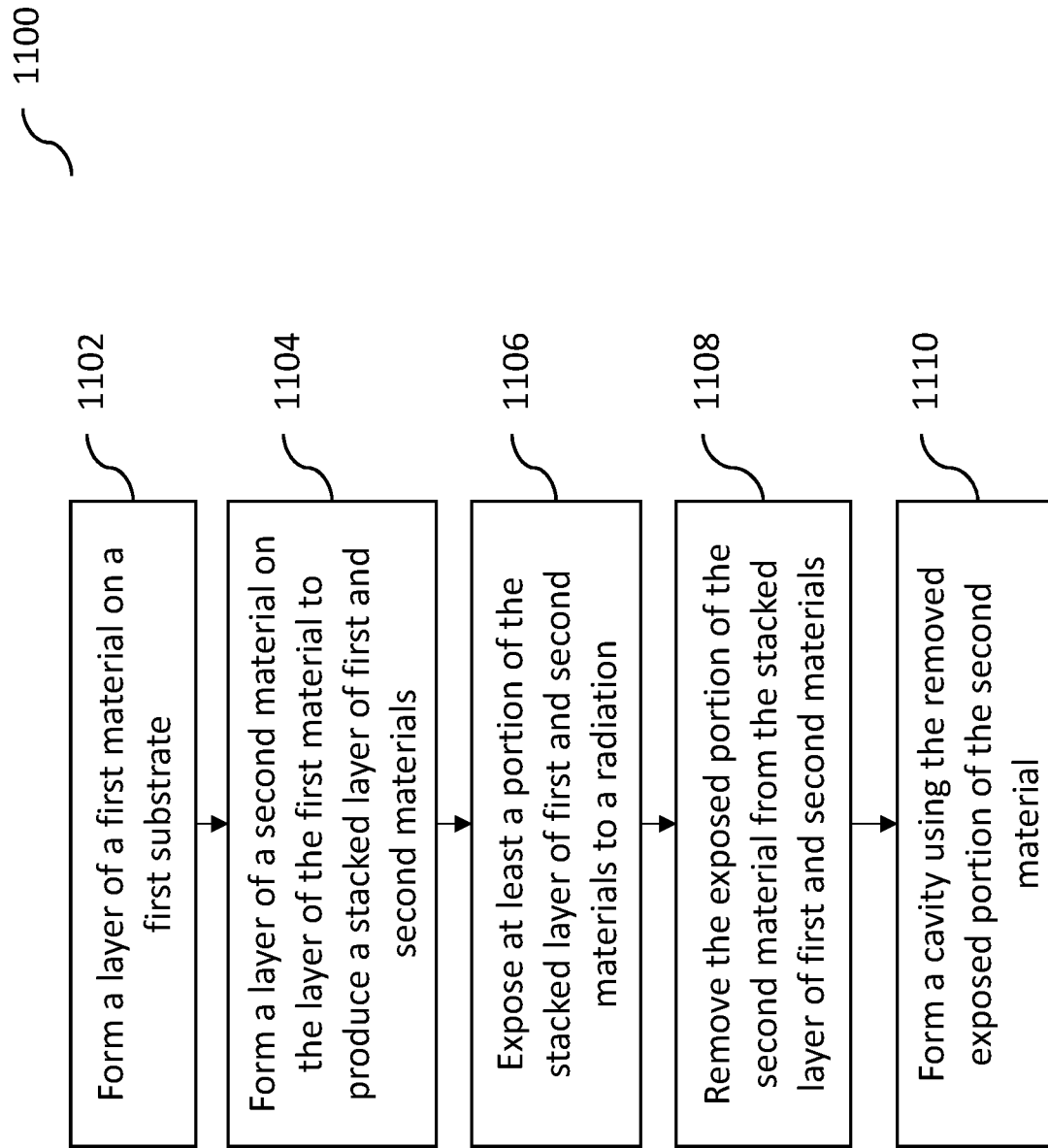


FIG. 10.

FIG. 11.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/057047

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - H01Q 15/00; H01P 1/00; H01P 1/32; H01Q 9/04 (2019.01)

CPC - H01Q 15/00; H01P 1/00; H01P 1/32; H01Q 9/04 (2019.08)

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)

See Search History document

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

USPC - 181/175; 181/180; 977/700; 977/840; 977/888 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016/0043253 A1 (Q1 NANOSYSTEMS CORPORATION) 11 February 2016 (11.02.2016)	1-3
---	entire document	---
Y		14-16, 27, 28
Y	US 9,390,702 B2 (MATHUR) 12 July 2016 (12.07.2016) entire document	14-16, 27, 28
Y	US 9,761,324 B2 (CORNELL UNIVERSITY) 12 September 2017 (12.09.2017) entire document	27, 28
A	WO 2009/116956 A1 (NATIONAL UNIVERSITY OF SINGAPORE et al) 24 September 2009 (24.09.2009) entire document	1-3, 14-16, 27-29

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

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

"E" earlier 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

15 December 2019

Date of mailing of the international search report

06 JAN 2020

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Blaine R. Copenheaver

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/057047

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-13, 17-26, 30-35
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

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

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.