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(12) United States Patent
Ishikawa et al.**(10) Patent No.: US 9,211,332 B2****(45) Date of Patent: *Dec. 15, 2015****(54) SELECTIVE RESONANCE OF BODILY AGENTS****(75) Inventors:** **Muriel Y. Ishikawa**, Livermore, CA (US); **Edward K. Y. Jung**, Bellevue, WA (US); **Eric C. Leuthardt**, St. Louis, MO (US); **Nathan P. Myhrvold**, Medina, WA (US); **Lowell L. Wood, Jr.**, Livermore, CA (US)**(73) Assignee:** **The Invention Science Fund I, LLC**, Bellevue, WA (US)**(*) Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 225 days.

This patent is subject to a terminal disclaimer.

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Related U.S. Application Data**(60)** Continuation-in-part of application No. 11/186,633, filed on Jul. 21, 2005, now Pat. No. 7,979,213, and a division of application No. 11/441,786, filed on May 26, 2006, now Pat. No. 8,195,403, and a continuation-in-part of application No. 11/186,635, filed on Jul. 21, 2005, now Pat. No. 8,112,233, and a continuation-in-part of application No. 12/313,418, filed on Nov. 19, 2008, now Pat. No. 8,364,412, and a continuation-in-part of application No. 11/186,632, filed on Jul. 21, 2005, now Pat. No. 8,364,407, and a continuation-in-part of application No. 12/313,411, filed on Nov. 19, 2008, now Pat. No. 8,346,484, and a continuation-in-part of application No. 11/186,394, filed on Jul. 21, 2005, now abandoned, and a continuation-in-part of application No. 13/134,267, filed on Jun. 3, 2011, now Pat. No. 8,364,423, and a continuation-in-part of application No. 11/186,634, filed on Jul. 21, 2005, and a continuation-in-part of application No. 12/313,419, filed on Nov. 19, 2008, now Pat. No. 8,386,186, and a continuation-in-part of application No. 11/186,631, filed on Jul. 21, 2005, now abandoned, and a continuation-in-part of application No. 12/313,417, filed on Nov. 19, 2008, and a continuation-in-part of application No. 11/260,467, filed on Oct. 26, 2005, and a continuation-in-part of application No. 11/904,044, filed on Sep. 24, 2007, now Pat. No. 8,386,183.**(51) Int. Cl.****G01N 33/48** (2006.01)
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G01N 31/00 (2006.01)
A61K 41/00 (2006.01)
G06F 19/24 (2011.01)
G06F 19/16 (2011.01)**G06F 19/12** (2011.01)**A61N 5/00** (2006.01)**A61M 37/00** (2006.01)**A61B 5/00** (2006.01)**A61B 18/00** (2006.01)**A61N 5/06** (2006.01)**(52) U.S. Cl.**CPC **A61K 41/0004** (2013.01); **A61M 37/0092** (2013.01); **A61N 5/00** (2013.01); **G06F 19/12** (2013.01); **G06F 19/16** (2013.01); **G06F 19/24** (2013.01); **A61B 5/0059** (2013.01); **A61B 2018/00577** (2013.01); **A61N 5/062** (2013.01)**(58) Field of Classification Search**

None

See application file for complete search history.

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Primary Examiner — Russell S Negin**(57) ABSTRACT**

Chemical compositions may be selectively or preferentially excited by the application of scores comprising a series of energy inputs.

26 Claims, 11 Drawing Sheets

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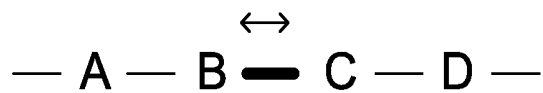
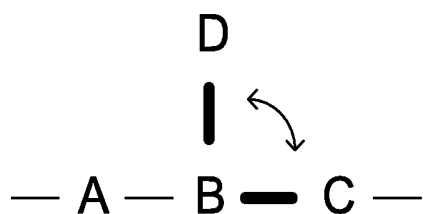
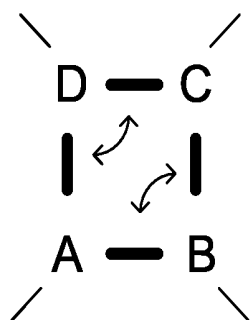
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**FIG. 1A****FIG. 1B****FIG. 1C**

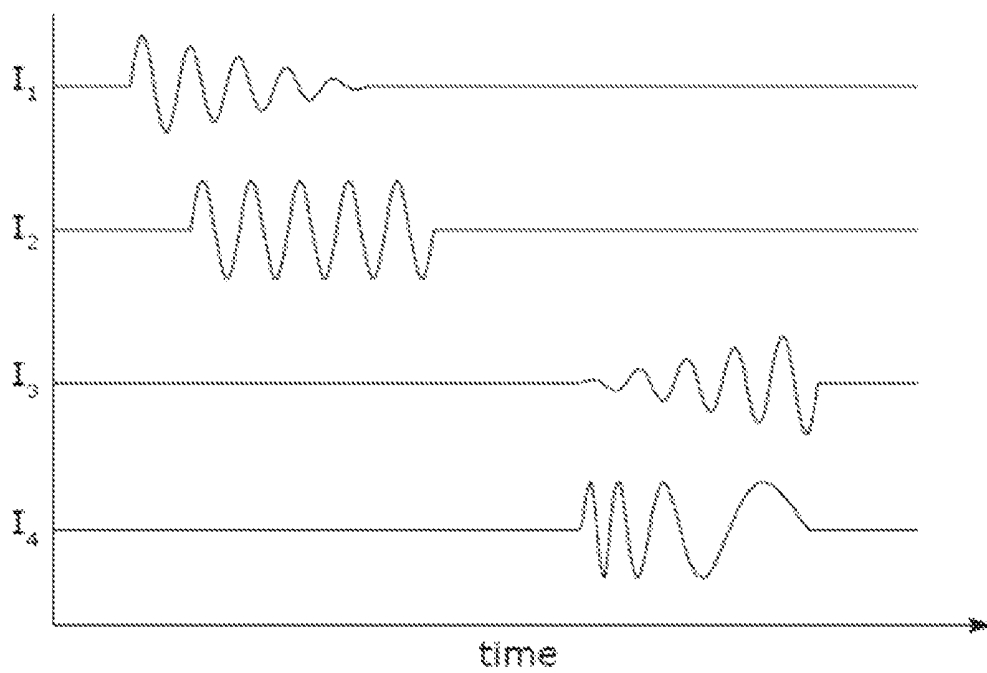


FIG. 2

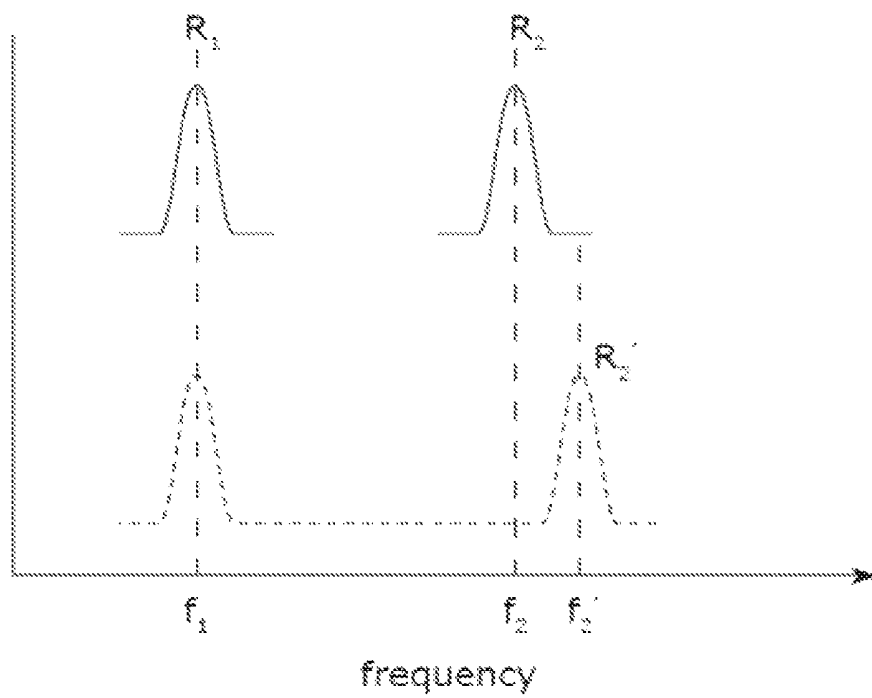
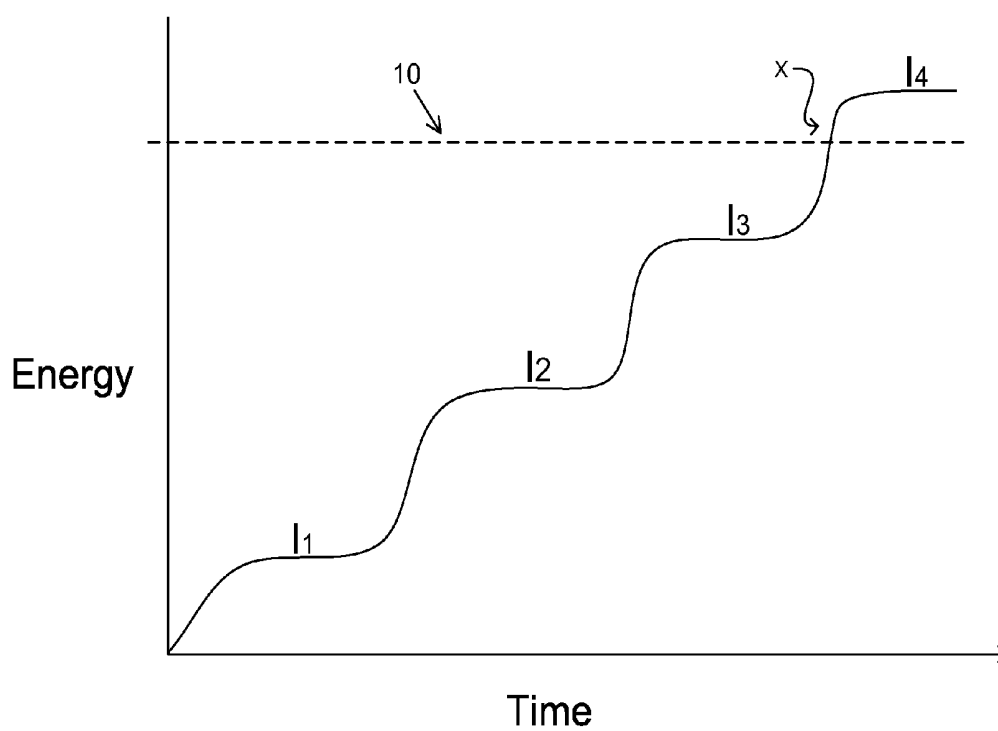


FIG. 3

**FIG. 4**

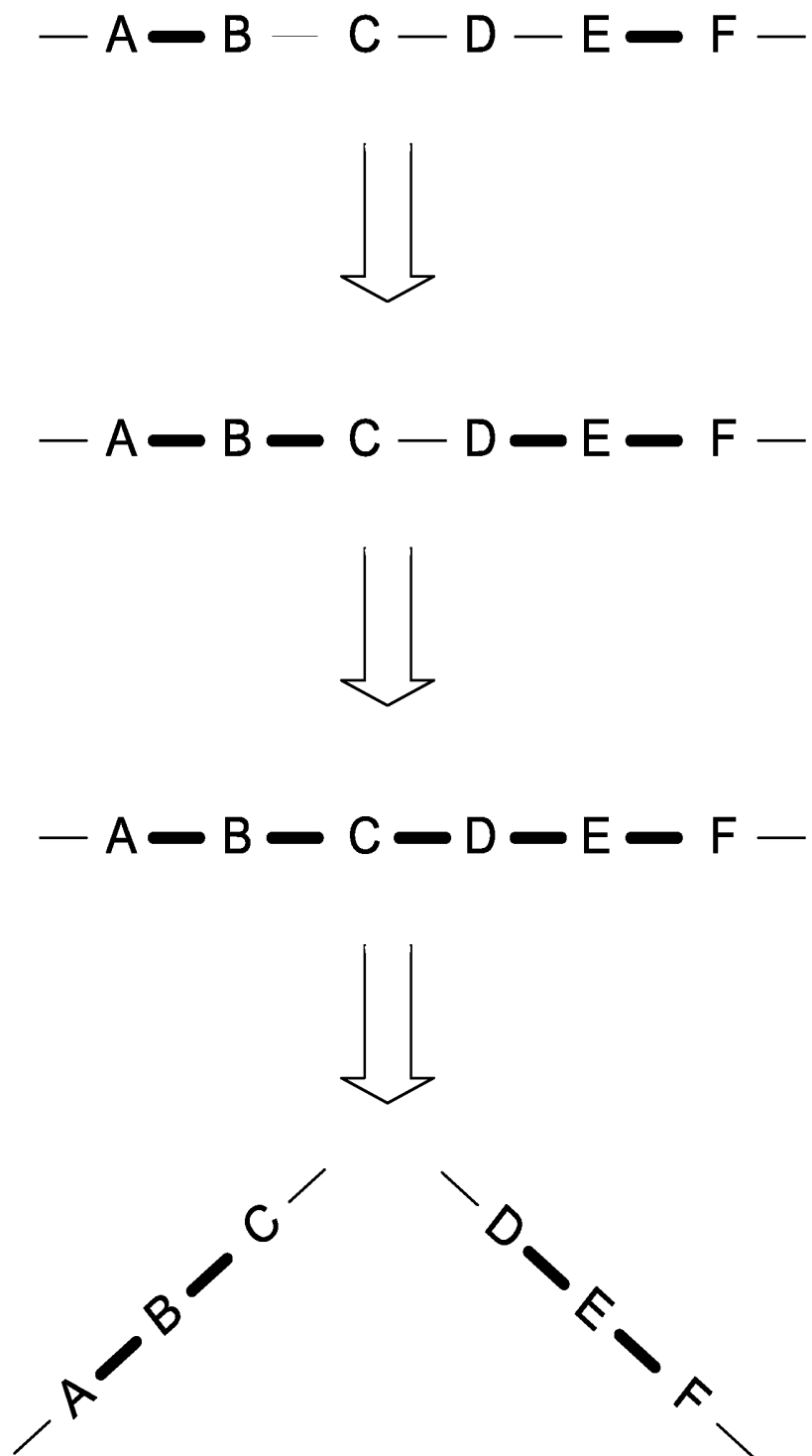


FIG. 5

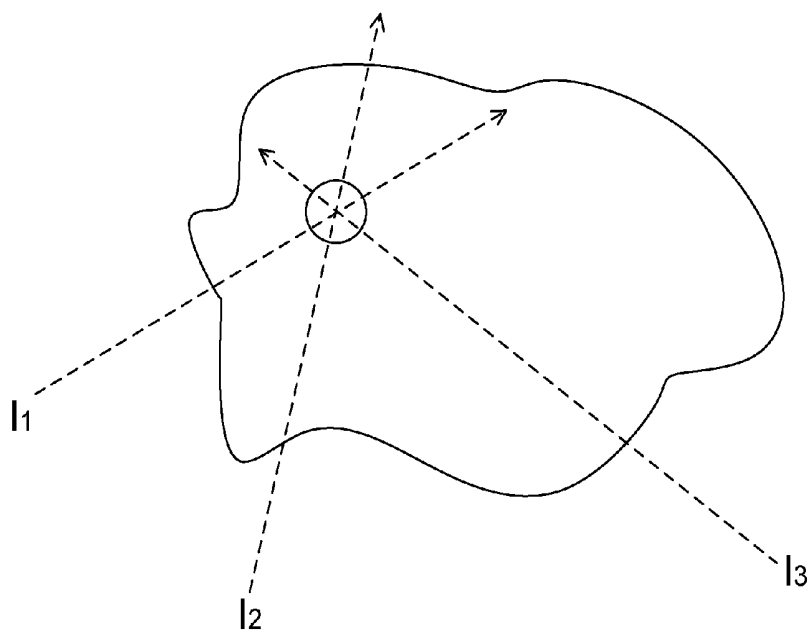


FIG. 6

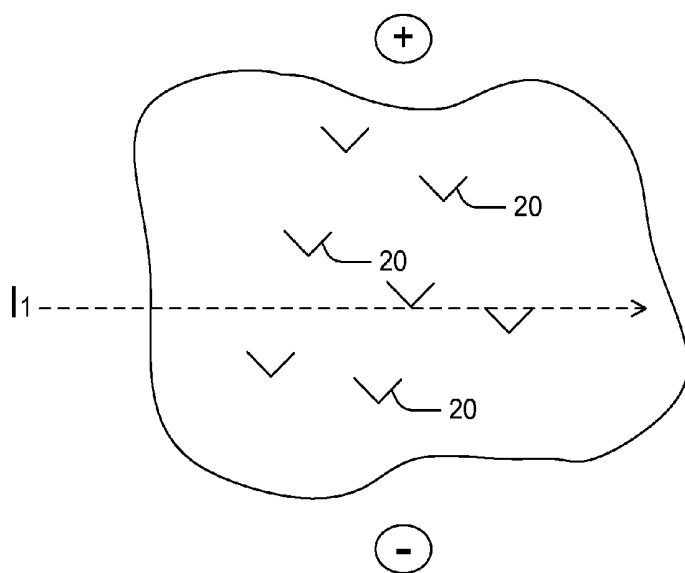
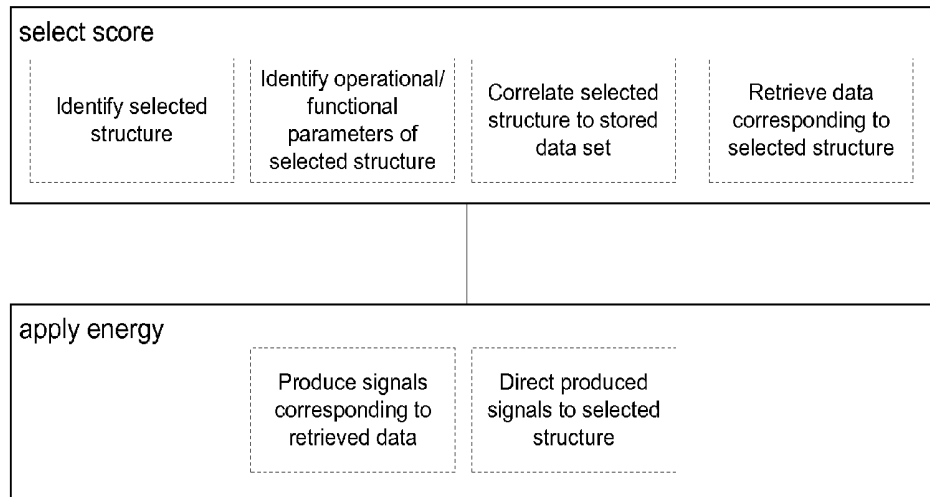
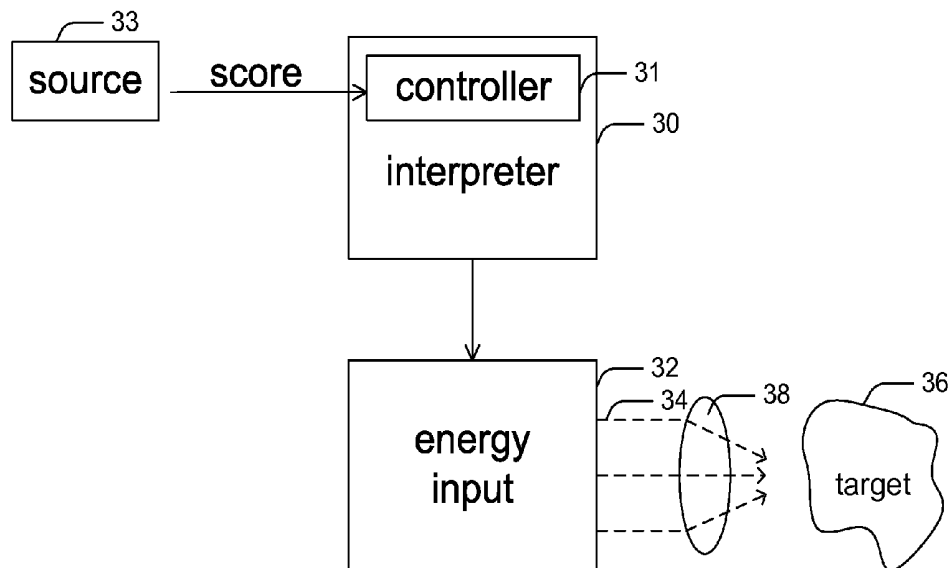
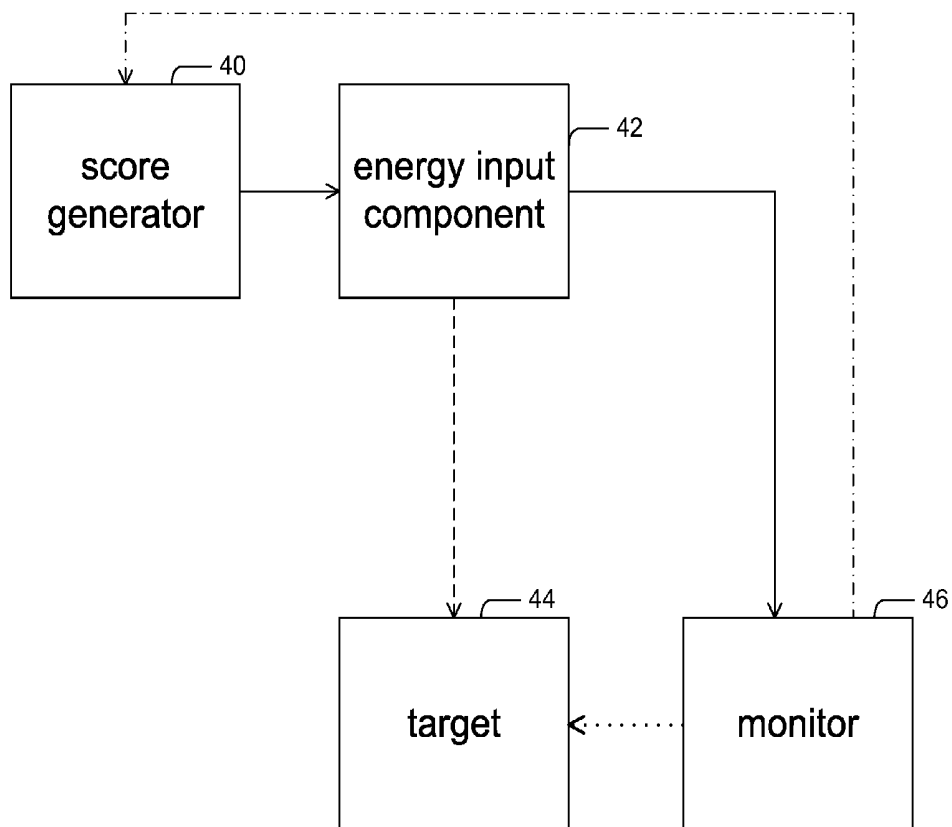
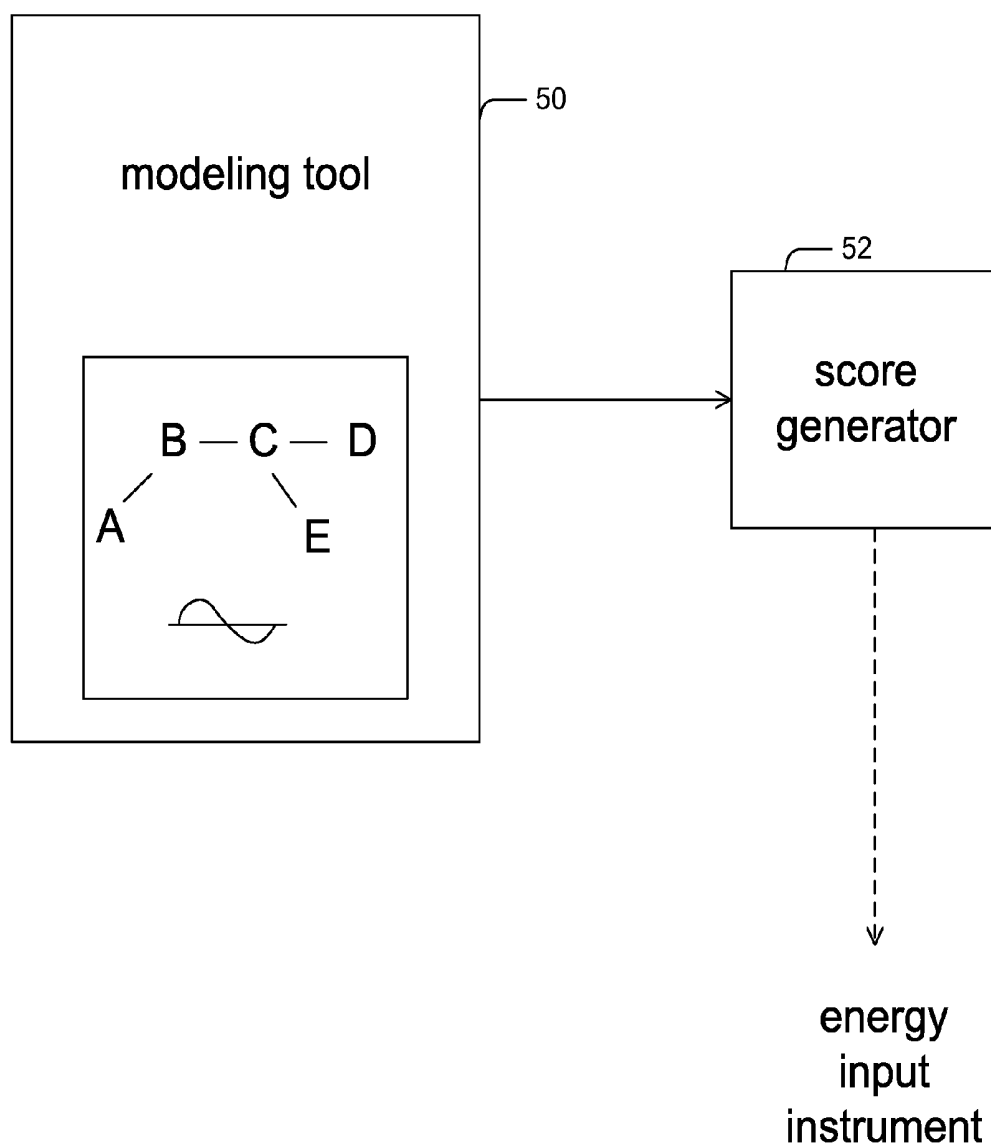


FIG. 7

**FIG. 8****FIG. 9**

**FIG. 10**

**FIG. 11**

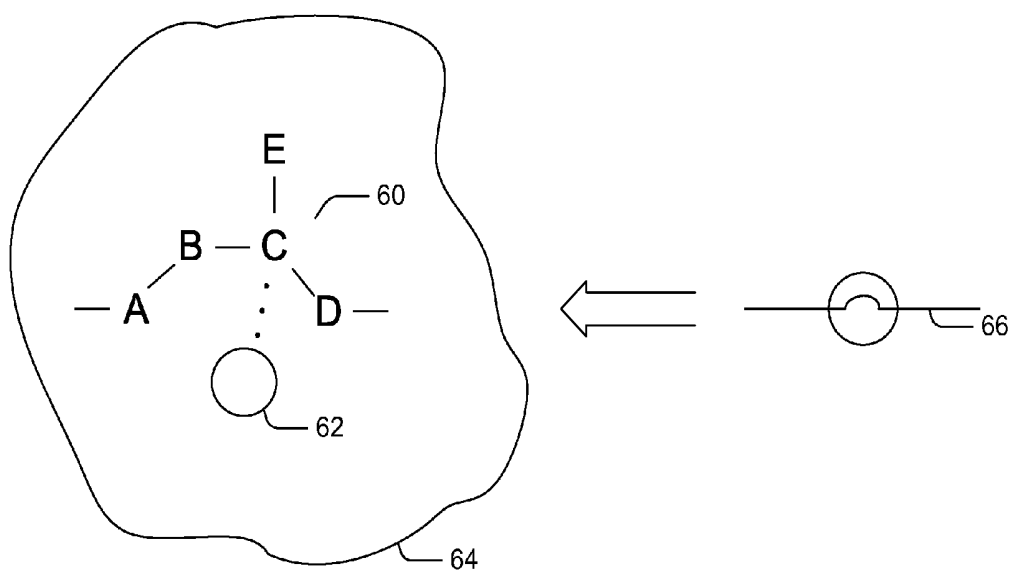
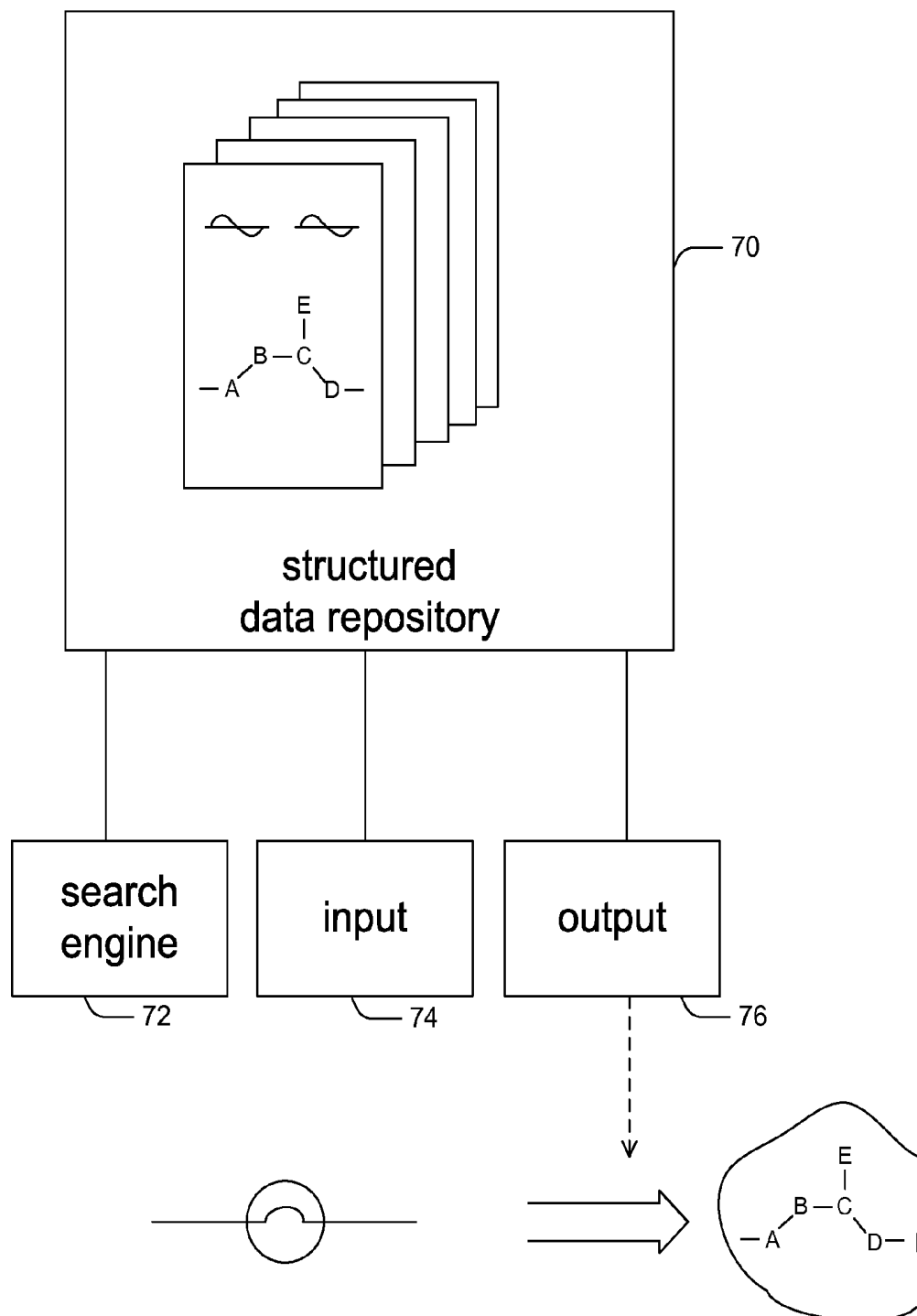
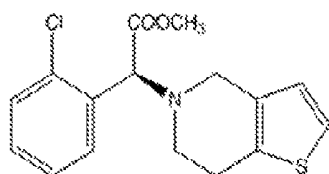
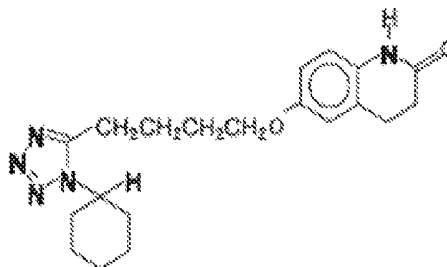


FIG. 12

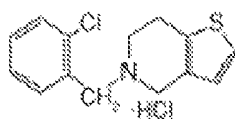
**FIG. 13**



Clopidogrel



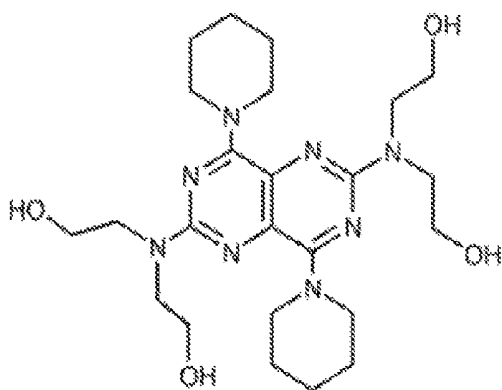
Cilostazol



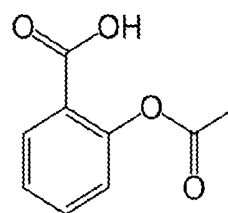
Ticlopidine



Tirofiban



Dipyramidol



Aspirin

FIG. 14

SELECTIVE RESONANCE OF BODILY AGENTS

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is related to and claims the benefit of the earliest available effective filing date(s) from the following listed application(s) (the "Related Applications") (e.g., claims earliest available priority dates for other than provisional patent applications or claims benefits under 35 USC §119(e) for provisional patent applications, for any and all parent, grandparent, great-grandparent, etc. applications of the Related Application(s)).

RELATED APPLICATIONS

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/186,633, now issued as U.S. Pat. No. 7,979,213, entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jul. 21, 2005.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a divisional of U.S. patent application Ser. No. 11/441,786 entitled SELECTIVE RESONANCE OF BODILY AGENTS, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Eric C. Leuthardt, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed May 26, 2006 now U.S. Pat. No. 8,195,403.

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For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 12/313,418 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Nov. 19, 2008 now U.S. Pat. No. 8,364,412.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/186,632 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jul. 21, 2005 now U.S. Pat. No. 8,364,407.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 12/313,411 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Nov. 19, 2008 now U.S. Pat. No. 8,346,483.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/186,394 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jul. 21, 2005 now abandoned.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 13/134,267 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jun. 3, 2011 now U.S. Pat. No. 8,364,423.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/186,634 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jul. 21, 2005.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 12/313,419 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Nov. 19, 2008 now U.S. Pat. No. 8,386,186.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/186,631 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Jul. 21, 2005 now abandoned.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 12/313,417 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Nov. 19, 2008.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/260,467 entitled SELECTIVE RESONANCE OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, and Lowell L. Wood, Jr. as inventors, filed Oct. 26, 2005.

For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/904,044 entitled SELECTIVE RESONANT RECONFIGURATION OF CHEMICAL STRUCTURES, naming Muriel Y. Ishikawa, Edward K. Y. Jung, Nathan P. Myhrvold, Eric C. Leuthardt, and Lowell L. Wood, Jr. as inventors, filed Sep. 24, 2007 now U.S. Pat. No. 8,386,183.

The United States Patent Office (USPTO) has published a notice to the effect that the USPTO's computer programs require that patent applicants reference both a serial number and indicate whether an application is a continuation or continuation-in-part. Stephen G. Kunin, Benefit of Prior-Filed Application, USPTO Official Gazette Mar. 18, 2003, available at <http://www.uspto.gov/web/offices/com/sol/og/2003/week11/pathbene.htm>. The present applicant entity has provided above a specific reference to the application(s) front which priority is being claimed as recited by statute. Applicant entity understands that the statute is unambiguous in its specific reference language and does not require either a serial number or any characterization, such as "continuation" or "continuation-in-part," for claiming priority to U.S. patent applications. Notwithstanding the foregoing, applicant entity understands that the USPTO's computer programs have certain data entry requirements, and hence applicant entity is

designating the present application as a continuation-in-part of its parent applications as set forth above, but expressly points out that such designations are not to be construed in any way as any type of commentary and/or admission as to whether or not the present application contains any new matter in addition to the matter of its parent application(s).

All subject matter of the Related Applications and of any and all parent, grandparent, great-grandparent, etc. applications of the Related Applications is incorporated herein by reference to the extent such subject matter is not inconsistent herewith.

SUMMARY

In one aspect, a method includes introducing an agent into a body, and directing a set of differing energy inputs towards the agent, where the set of differing energy inputs selectively resonates a plurality of resonant structures in the agent. The agent may have a therapeutic effect in the body, which may be modulated by the set of differing energy inputs (e.g., by initiating, terminating, or changing the character of the therapeutic effect in the body). Directing the set of differing energy inputs towards the agent may destroy it. The agent may be selected from the group consisting of analgesics, antacids, antianxiety drugs, antiarrhythmics, anticoagulants, anticonvulsants, antidepressants, antidiarrheals, antiemetics, antifungals, antihistamines, antihypertensives, anti-inflammatories, antiplatelet drugs, antipsychotics, antipyretics, antivirals, barbiturates, beta-blockers, bronchodilators, chemotherapy drugs, corticosteroids, cough suppressants, cytotoxics, decongestants, diuretics, expectorants, hormones, hypoglycemics, immunosuppressives, laxatives, muscle relaxants, sedatives, sex hormones, sleeping drugs, tranquilizers, and vitamins. The agent may be an antiplatelet drug such as clopidogrel, which may be destroyed by the set of differing energy inputs, and the method may further include performing an incision on the body. The body may be alive and/or human. Introducing the agent to the body may include introducing the agent into the blood, in which case the set of differing energy inputs may be directed into the body, or may be directed into blood external to the body that is then returned to the body. The method may include monitoring the body for the activity and/or quantity of the agent. The agent may include a functional group selected to be responsive to the set of differing energy inputs, and/or it may be modified to add a functional group selected to be responsive to the set of differing energy inputs (e.g., before it is introduced into the body).

In another aspect, a method includes identifying an agent in the body, selecting a set of differing energy inputs specific to the agent, and directing the set of differing energy inputs towards the agent. The set of differing energy inputs selectively resonates a plurality of resonant structures in the agent. The agent may have a therapeutic effect in the body, which may be modulated by the set of differing energy inputs (e.g., by initiating, terminating, or changing the character of the therapeutic effect in the body). Directing the set of differing energy inputs towards the agent may destroy it. The agent may be selected from the group consisting of analgesics, antacids, antianxiety drugs, antiarrhythmics, anticoagulants, anticonvulsants, antidepressants, antidiarrheals, antiemetics, antifungals, antihistamines, antihypertensives, anti-inflammatories, antiplatelet drugs, antipsychotics, antipyretics, antivirals, barbiturates, beta-blockers, bronchodilators, chemotherapy drugs, corticosteroids, cough suppressants, cytotoxics, decongestants, diuretics, expectorants, hormones, hypoglycemics, immunosuppressives, laxatives, muscle

relaxants, sedatives, sex hormones, sleeping drugs, tranquilizers, and vitamins. The agent may be an antiplatelet drug such as clopidogrel, which may be destroyed by the set of differing energy inputs, and the method may further include performing an incision on the body. The body may be alive and/or human. The agent may be present in blood, in which case the set of differing energy inputs may be directed into the body, or may be directed into blood external to the body that is then returned to the body. The method may include monitoring the body for the activity and/or quantity of the agent. The agent may include a functional group selected to be responsive to the set of differing energy inputs, and/or it may be modified to add a functional group selected to be responsive to the set of differing energy inputs (e.g., before it is introduced into the body). The agent may be selected from the group consisting of blood clotting factors (e.g., prekallikrein, high molecular weight kininogen, any of clotting factors I-XIII, von Willebrand factor, protein C, protein S, thrombomodulin, and/or antithrombin III), sugars (e.g., glucose, fructose, sucrose, galactose, mannose, glycerol, and/or glucuronate), lipids and lipoproteins (e.g., cholesterol, triglycerides, triacylglycerols, chylomicrons, very low density lipoproteins, low density lipoproteins, intermediate density lipoproteins, and/or high density lipoproteins), vitamins, minerals, hormones (e.g., adrenalin, adrenocorticotrophic hormone, aldosterone, calcitonin, cortisol, insulin, gastrin, glucagon, glucocorticoids, thyroid hormone, gastrin, secretin, cholecystokinin, somatostatin, neuropeptide Y, other hormones of the gut, thyrotropin-releasing hormone, gonadotropin-releasing hormone, growth hormone-releasing hormone, ghrelin, corticotrophin-releasing hormone, somatostatin, dopamine, antidiuretic hormone, oxytocin, other hormones of the hypothalamus, renin, erythropoietin, calcitriol, other hormones of the kidney, insulin-like growth factor-1, angiotensinogen, thrombopoietin, other hormones of the liver, thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, prolactin, growth hormone, adrenocorticotrophic hormone, antidiuretic hormone, other hormones of the pituitary, estrogen, testosterone, progesterone, anabolic steroids, other reproductive hormones, melanocyte-stimulating hormone, parathyroid hormone, melatonin, prolactin, and/or thyroid hormones), enzymes (e.g., creatine kinase, lactate dehydrogenase, troponin, other cardiac enzymes, aspartate transaminase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyltranspeptidase, and/or other liver enzymes), antibodies (e.g., antibodies to autoimmune disorders such as acute transverse myelitis, allergic (Henoch-Schönlein) purpura, alopecia areata, aplastic anemia, brachial neuritis, bulbous pemphigoid, dermatitis herpetiformis, polymyositis, dermatomyositis, Eaton-Lambert syndrome, eosinophilic fasciitis, Goodpasture's syndrome, Guillain-Barré syndrome, hemolytic anemia, hepatitis, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, pemphigus, peripheral ulcerative keratitis, polyglandular deficiency syndrome, relapsing polychondritis, rheumatoid arthritis, scleroderma, Sjögren's syndrome, and/or system lupus erythematosus, or normal antibodies to transplanted materials such as organs, stem cells, and/or device implants), proteins (e.g., albumins, globulins, fibrinogens, and/or hemoglobins).

The foregoing summary is illustrative only and is not intended to be in any way limiting. In addition to the illustrative aspects, embodiments, and features described above, further aspects, embodiments, and features will become apparent by reference to the drawings and the following detailed description.

BRIEF DESCRIPTION OF THE FIGURES

FIGS. 1A, 1B, and 1C illustrate longitudinal, bending, and squashing modes, respectively, of resonant structures.

FIG. 2 is a schematic representation of a four-note score.

FIG. 3 illustrates how a frequency of one resonant structure may shift as another resonant structure is excited.

FIG. 4 is a schematic representation of the response of a molecule to a series of energy inputs.

FIG. 5 illustrates diagrammatically excitation to breakage of a bond in a linear molecule.

FIG. 6 illustrates diagrammatically the application of multiple intersecting energy inputs to a target voxel.

FIG. 7 is a schematic showing the application of an electric field to align resonant structures in a medium.

FIG. 8 is a schematic representation of an energy application method.

FIG. 9 is a schematic representation of a device for applying energy according to a score.

FIG. 10 is a schematic representation of a device with optional monitoring and feedback control for score application.

FIG. 11 is a schematic representation of an apparatus for generating score.

FIG. 12 illustrates a system for introducing a chemical agent into a medium.

FIG. 13 is a schematic representation of a library of excitation energy specifications.

FIG. 14 is the chemical structure of several antiplatelet agents.

DETAILED DESCRIPTION

In the following detailed description, reference is made to the accompanying drawings, which form a part hereof. In the drawings, similar symbols typically identify similar components, unless context dictates otherwise. The illustrative embodiments described in the detailed description, drawings, and claims are not meant to be limiting. Other embodiments may be utilized, and other changes may be made, without departing from the spirit or scope of the subject matter presented here.

The term “biomolecule,” as used herein, includes without limitation proteins, peptides, amino acids, nucleotides, nucleic acids, carbohydrates, sugars, glycoproteins, lipids, viruses, prions, antibodies, and enzymes, and fragments, derivatives, and modified forms of any of these, and any other naturally-occurring or synthetic molecule or complex of molecules that has a biological activity or that is effective in modulating a biological activity.

The term “bond,” as used herein, includes without limitation covalent, ionic, metallic, van der Waals, hydrogen, coulombic, and magnetic attractions, as well as any other attractive force between atoms or other particles.

Resonant structures of molecules, crystals, and other compositions have one or more characteristic resonant frequencies, at which they relatively efficiently absorb or otherwise interact with energy applied at matching frequencies. Spectroscopic techniques exploit these characteristic resonances to extract information about chemical structure and properties. For example, covalent bonds typically have a characteristic frequency of longitudinal vibration which depends in significant part upon the masses of the atoms forming the bond and the strength of the bond (e.g., single, double, triple, etc).

FIG. 1A shows a single covalent bond between atoms B and C, which may vibrate in such a longitudinal mode. Vibra-

tion of ionic bonds is similarly affected by the mass, atomic radius, and charge of the atoms involved. Resonant structures may also be formed by groups of bonds, e.g., in bending or squashing modes (shown in FIGS. 1B and 1C, respectively), each with its own characteristic resonant frequency or frequencies. Crystals may exhibit resonances based on their periodic structures or other properties. Molecule complexes may have resonances that include hydrogen bonds or other attractions between molecules of the complex. The characteristic frequencies of any of these structures may be shifted by a wide variety of factors, including without limitation the properties of adjacent bonds, the excitation state of the molecule or crystal, the presence of defects in a crystal (e.g., free surfaces that cause the resonant properties of “quantum dot” crystallites to depend on their size), stresses in the structure, electric or magnetic fields, or other factors that may influence the properties of the structure. Spectroscopy involves directing energy at a target, and examining the absorbed, transmitted, reflected, and/or emitted frequency spectrum to characterize the physical properties of the target.

Methods are provided herein for directing energy inputs into a target to manipulate or otherwise interact selectively with its structures. In particular, a set of energy inputs analogous to a musical score may be identified, where different “notes” of the score transfer energy with spatio-temporal selectivity to a target composition, for example by resonating different resonant structures. For scores having a sufficient number of notes, high specificity may be obtained, for example wherein compositions having all or most of the corresponding resonant structures are preferentially excited by “playing the score” to the target composition. Even for “short” scores, energy may be efficiently transmitted to a target composition that matches most or all of the resonances identified by the score. Notes as used in this description are not limited to representations of frequency. Notes may also represent, without limitation, amplitudes, polarizations, phase components, gradients, or other characteristics of input energies. While resonance is an exemplary method of transferring energy that can provide spatio-temporal control or other selectivity as discussed below, scores may also include energy inputs that transfer energy to molecules in a nonresonant fashion. For example one or more optical beams, coherent optical pulses, or other controllable inputs can transfer energy selectively to particular portions of a molecule and/or at particular times.

In one aspect, the scores may be used to characterize or identify compositions, as an alternative nomenclature to conventional chemical composition and structure notation. Digital or analog processing, visually presenting, or otherwise processing or treating the scores may indicate or reveal into similarities between compositions that are less readily identified using conventional nomenclature.

Scores having desired effects on particular compositions may be determined by a variety of methods. One starting point for determining a score may be to examine a spectrogram of a composition of interest, since the spectrogram reflects certain resonant responses of the composition. Alternatively, resonances may be calculated by computational methods. Scores may also be determined and/or refined on an empirical basis, using “trial and error” approaches, inferential approaches, observations of trends or other empirical approaches. Typically, such approaches would include applying a candidate score, a portion of a candidate score, or a selected set of notes to a composition and observing the corresponding effects, such as energy absorption, polarization changes, chemical reactions, optical characteristics, vibrations, stresses, changes in electrical or magnetic prop-

erties, or other effects. The score, portion of a score, or notes may be applied at an amplitude level that may differ from the level to be used in applying the determined score at a later time. For example, a sample note may be applied at a significantly higher amplitude as part of the characterization than may be appropriate for later applications.

Scores may have a diverse set of potential effects on various compositions. A score may resonate a particular bond in a molecule to breakage, for example, or it may change a kinetic parameter of an affected composition or cause local heating in the vicinity of the composition. In some embodiments, the scores can act as a form of energy catalyst, preferentially shifting the kinetics of selected chemical reactions. For example, a score could alter the kinetics of a chromatography column, causing a reactant to bind or to unbind in response to an applied score. Similarly, a score may alter the migration rate of composition during an electrophoresis process. In this approach, the score may be used to separate stereoisomers during electrophoresis.

Other embodiments include selectively destroying a contaminant or other unwanted composition, such as removing an undesirable metabolic product (e.g., beta-amyloid plaques in Alzheimer's disease patients, gallstones, or kidney stones), a contaminant (e.g., accumulations of tobacco residue in the lungs), a therapeutic agent not desirable for long-term use (e.g., heparin from the blood of dialysis patients downstream of the dialysis unit), or cell type (e.g., cancerous cells) from living tissue, breaking down pollutants in a smokestack, or selectively destroying viruses, either in vivo or in vitro. Still other embodiments include selective repair of biomolecules, e.g., repair of thymine dimers or breaks in the DNA molecule. Unbound base pairs could be specifically excited, or DNA could even be intentionally further damaged in a way selected to trigger the body's own DNA repair mechanism.

An arrangement of inputs that form a score may be analogized to a musical score to aid in understanding some of the aspects. For example, in one approach a score specifies a set of differing energy inputs that may be in sequential, parallel, or other arrangements. These inputs may be specified in terms of frequency, modulation frequency, phase, amplitude, temporal profile, polarization, direction, and/or coherence. The set of energy inputs may be played in the form of a "melody" (in which each energy input ends before or as the next begins), in the form of a "chord" (in which all the energy inputs begin and end together), or in a more complex structure, which may include one or more overlapping energy inputs. In addition, the specifications for frequency, modulation frequency, phase, amplitude, polarization, direction, and/or coherence may change over the duration of an energy input. In some embodiments, the energy inputs are electromagnetic beams, such as infrared, visible or ultraviolet beams. The electromagnetic beams may be frequency, phase, amplitude, polarization, pulse width, or otherwise modulated. Such modulation may be applied to the base frequency of the electromagnetic beam or may be applied to a beam envelope. In another approach that may be applied independently or in conjunction with the previously described approaches, two or more beams may provide more flexibility in supplying energy to a selected location, locations, or structures, at frequencies, spatial selectivities, or other parameters, than single source approaches. In one exemplary approach pairs (or larger sets) of inputs can produce beat frequencies, harmonics, interference patterns, or other configurations. In some such configurations and/or combinations, the energy inputs may have frequencies differing from the resonant frequencies of the resonant structures, and yet interact appropriately with the molecules.

While the previously described approaches have been exemplified in terms of additive combinations of energy inputs, in some embodiments, a portion of the series of energy inputs may interact with structures to negate, e.g., by damping or cancellation, rather than enhance, vibrations or other interactions with certain resonant structures. Alternatively or in addition, a structure to which it is desired not to transfer energy may be "deactivated" before, or together with, applying an energy input. For example, the response of the structure may be "deactivated" or otherwise reduced by temporarily bonding it to another structure that changes its resonant frequency or absorbs vibrational energy. In other approaches, locally heating the structure, applying a magnetic or electric field, or applying a local or vector stress or pressure, or otherwise interacting with the structure can change its resonance, or otherwise reduce its response.

When an application of a score involves affecting compositions in a medium (such as but not limited to living tissue), the score may include electromagnetic energy inputs in frequency ranges that penetrate the medium. For example, where a material is contained within a container, the frequencies may be selected to correspond to ranges or single frequencies where the container is transmissive, yet, the material is responsive. If desired, suitable modulation or beat frequencies may then be used to resonate the resonant structures of the composition.

A schematic of a four-note score illustrating induced changes is shown in FIG. 2. Energy inputs I_1 and I_2 overlap in time, with input I_1 beginning before input I_2 begins and ending before input I_2 ends. Input I_1 has a decreasing amplitude with time, while the amplitude of I_2 is substantially constant. Inputs I_3 and I_4 begin at substantially the same time, but input I_3 terminates before input I_4 . The amplitude of input I_3 increases with time while maintaining a constant frequency, while the amplitude of input I_4 stays constant with time while the frequency decreases. Phase, polarization, direction, and coherence are not specified in FIG. 2, but each of these properties may similarly change with time within a single energy input, or differ from one energy input to another. In particular, phase control between multiple beams may provide spatial, temporal, or other specificity that can provide selectivity in resonating only certain structures within a molecule or in targeting molecules having a certain orientation or position. Moreover, polarization of the energy inputs may be useful in distinguishing molecules on the basis of chirality, for example to excite only molecules having a desired chirality. One skilled in the art will recognize that other combinations, including a larger number of energy inputs or more complex energy inputs may be implemented. For example, frequency and amplitude of an energy input may both be varied. As another example, the frequency and/or amplitude of an energy input may be increased during one time interval and decreased during another. As still another example, an energy input may be "chopped" to provide a sequence of energy input components, which may be periodic or aperiodic. Several other approaches to varying amplitude, frequency, duration or other characteristics of the energy inputs may also be implemented according to design and response characteristics of a given application.

In the specific exemplary case where the score is targeted to a specific molecule (such as a biomolecule or macromolecule) or a set of molecules, the energy inputs of the score will generally correspond to enough resonant structures in the target molecule to distinguish the target molecule from other molecules in its environment (as discussed above, the energy inputs may, but need not, have the same frequencies as the resonant structures to which they correspond). Since most or

all of the energy inputs will resonate the target molecule, while only a subset of the energy inputs will resonate other molecules sharing some but not all of the resonant structures of the target, the target will absorb enough energy from the score to distinguish it. This effect may cause, for example, local heating in the area of the target molecule, breaking one or more bonds in or to the target molecule, or changing a kinetic parameter of a reaction involving the molecule.

In many cases, characteristics of systems including one or more atoms and corresponding bonds may be considered independently. In other applications, it may be appropriate to analyze, compensate for, adjust for, or otherwise consider shifts or changes in characteristics of a first system including one or more atoms responsive to interaction with a second system having one or more atoms or of energy input to the first system of one or more atoms.

For example, one can identify shifts in the resonant longitudinal vibrational frequency of one or more atomic bonds as a result of optical power input, as described in for example, in Andrews and Crisp, "Laser-Induced Vibrational Frequency Shift," bearing a date of 25 Feb. 2005 and available at <http://xxx.lanl.gov/ftp/physics/papers/0502/0502136.pdf>, which is incorporated by reference herein and is appended hereto. This effect may be used to tailor the transfer of energy to a molecule, by adjusting the excitation frequency to match the shift as the vibration increases.

FIG. 3 illustrates how the frequency of one resonant structure may shift as a nearby resonant structure is excited. When inputs R_1 and R_2 are separately applied (solid lines), they resonate structures at frequencies f_1 and f_2 . However, when the structures are coupled in a particular composition, the application of input R_1 may shift the resonant frequency f_2 to f_2' . Thus, that particular composition may be more efficiently excited by resonating with input R_1 and an input R_2' that is frequency shifted relative to input R_2 . In a similar approach, the resonant frequency of one resonant structure may shift as the resonant structure is subjected to other influences, such as temperature changes or electric or magnetic fields. The energy inputs may be varied to accommodate such variations in a similar fashion.

FIG. 4 illustrates schematically how a score may be used to selectively excite a particular molecule sufficiently to break a bond, which can destroy the molecule. As shown, energy inputs I_1 , I_2 , I_3 , and I_4 are applied to the composition in a sequence which may include temporal overlap. Input I_1 excites a first resonant structure, adding energy to the molecule. As each additional input excites its own respective resonant structure in the molecule, the energy added increases as shown, until input I_4 drives the vibration past the breaking strength for a bond (shown schematically as dashed line 10). Each of the individual inputs I_1 , I_2 , I_3 , I_4 may be insufficient alone to destroy the molecule, but acting in concert, they do. Where the energy to break the bond is higher than that which would be provided by a combination of less than all four inputs (assuming no increase in the amplitudes of the individual inputs), only molecules having the four resonant structures in sufficient proximity will experience the breaking of the bond (it will of course be understood that this technique is not limited to scores specifying exactly four inputs, but that it may be applied with as few as two inputs or as many as appropriate to achieve the final effect).

This selectivity can be further enhanced by exploiting frequency shifts as discussed above, to more selectively interact with molecules whose resonant structures are responsive to the shifted frequencies. Note that the effect of combining respective inputs to provide cumulative energy input is not limited to breaking bonds as presented in this illustrative

embodiment. For example, the approaches described herein may also be used to alter kinetic parameters or to achieve any other appropriate chemical, physical or other effect.

FIG. 5 illustrates another scenario in which a bond in a molecule having a substantially linear portion can be excited to breakage. As shown, the molecule includes a chain of atoms A, B, C, D, E, and F. Initially, respective inputs excite the bonds linking atoms A-B and E-F (indicated with heavy lines in the uppermost portion of FIG. 5), causing secondary excitation and/or frequency shifting of adjacent bonds linking atoms B-C and D-E. Subsequent inputs excite the adjacent bonds B-C and D-E (indicated with heavy lines in the second tier of FIG. 5).

The excitations of the bonds linking atoms B-C and D-E causes a further excitation and/or frequency shift of center bond linking atoms C-D. The cumulative effect of the inputs to bonds linking atoms A-B, B-C, D-E, E-F excites the bond linking atoms C-D. In some applications, the cumulative excitation of the bond linking atoms C-D from the adjacent bonds is sufficient to break the bond linking atoms C-D. In some cases, additional excitation directed at the bond linking atoms C-D is combined with the cumulative excitation of the bond linking atoms C-D from the adjacent bond to produce the intended result, such as severing the bond linking atoms C-D. Of course, the technique is not limited to molecules having the simple linear structure shown in FIG. 5, but can be applied to any composition in which two sequences of resonant structures can be identified that lead to a common center. In addition, it may not be necessary to actively excite all of the bonds or other structures along the path to the common center. For example, the excitation of the A-B and E-F bonds shown in FIG. 5 may be sufficient to cause secondary excitation of the B-C and/or D-E bonds without additional energy inputs. In this way, energy inputs targeted to remote structures A-B and E-F may propagate along the molecule, meeting to cause a desired effect at targeted center structure C-D. In such embodiments, the targeted bond need not be exactly at the midpoint between the remote structures as shown in FIG. 5; the timing of the excitation of the remote structures may be adjusted to determine a desired "meeting point" for the propagated excitations.

Moreover, depending upon the amount of energy and the particular characteristics of the bonds and atoms, the inputs to excite the various bonds may be applied substantially simultaneously, may be applied at times that only overlap partially, or that are non-overlapping. Further, certain resonant structures may be "rung up" and "rung down" in a multi-step process by applying excitation and anti-excitation (e.g., damping or canceling) energy inputs as discussed above. Controlling the relative timing, intensities, orientations, or other characteristics of the plurality of energy inputs according to the ring up response, or other transient response characteristics of the resonant structures can increase the selectivity, efficiency, or other parameters of energy transfers to or from the resonant structures. Such techniques may also be useful to create intermediate structures or effects, analogous to the creation of intermediate structures in a multi-step chemical synthesis or reaction.

For certain compositions, transfer of energy to the resonant structures will be a function of the orientation of the resonant structure relative to the direction of the energy input. FIGS. 6 and 7 illustrate two embodiments that allow this relative orientation effect to be exploited.

In FIG. 6, three energy inputs I_1 , I_2 , and I_3 that may be beams of optical or non-optical energy from different directions converge at a target location (voxel) within a medium containing direction-dependent resonant structures. Since the

energy inputs come from different directions, each affects resonant structures in a different orientation. By selecting an appropriate number of energy inputs in different directions, an arbitrarily high percentage of the target resonant structures can be affected by the beams. These energy inputs need not be simultaneously applied from separate sources, as shown in FIG. 6; they may also be applied by a single source, where either the source or the target material is rotated in order to change the effective direction of the energy input, or where the single source is redirected by means of reflectors, beam splitters, optical fibers, applied fields, or other known energy directing elements. In addition, the energy input(s) may be scanned relative to the material to affect a plurality of voxels within the material. Further, multiple energy inputs need not always intersect as shown in FIG. 6, but may be independently directed according to the needs of a particular application. The plurality of energy inputs shown may have either the same or differing frequency, phase, amplitude, temporal profile, polarization, and/or coherence, depending on the needs of the particular application. Multiple energy inputs may also be used even with non-direction-dependent structures, for example in order to overcome scattering within the medium. Where a plurality of inputs excite a given voxel, from differing locations or orientations, the excitation in the voxel may exceed that of locations outside of the voxel, thereby allowing selective excitation of the voxel at a selected level.

In another aspect, shown in FIG. 7, an additional influence can activate, orient, or otherwise influence resonant structures 20 to interact appropriately with resonant inputs. In the exemplary approach of FIG. 7, an electric field applied to the target material aligns resonant structures 20 prior to application of an energy input. While the exemplary embodiment employs an electric field to influence the resonant structures, any applied field that tends to affect the interaction of the resonant structures with the energy input may be applied, including without limitation a magnetic field, an applied mechanical stress, a lowered or elevated temperature or pressure, a phase change, introduction of an adsorbing surface or catalyst, or the application of another energy input. Rotating a number of resonant structures into a known orientation may allow more efficient excitation, a simpler configuration, or a reduced number of energy inputs. (e.g., only input I_1 as shown in FIG. 7) to resonate the resonant structures appropriately. As previously described in reference to FIG. 6, the applied energy input(s) may be scanned, rotated, or otherwise adjusted relative to the material. In addition, the applied field itself may be scanned, rotated, or otherwise adjusted relative to the target, for example by movement or rotation of the field or by movement or rotation of the target.

FIG. 8 shows schematically a method of applying energy. A suitable score is selected by any of a variety of methods, some of which are detailed herein, and then energy is applied to a target in conformance with the score. For example, in some embodiments, selecting the score may include one or more of the following steps: identify a selected structure, identify operational and/or functional parameters of the selected structure, correlate the selected structure to a stored data set, and retrieve data corresponding to the selected structure. The score specifies a plurality of energy inputs that are applied. The energy may, for example, be applied in the form of one or more electromagnetic beam(s), in which case the score may specify frequency, modulation frequency, phase, amplitude, temporal profile, polarization, and/or coherence for the beam(s). In some embodiments, applying energy may include one or more of the following steps: producing signals

corresponding to retrieved data, and directing the produced signals towards a selected structure.

FIG. 9 shows schematically a device for applying energy in accordance with a score. Interpreter 30 accepts a score which specifies a plurality of energy inputs. The interpreter may include an electronic controller 31 that can receive the score from a source 33, such as a database or library (e.g., the library described below with reference to FIG. 13), a feedback system (e.g., the feedback system described below with reference to FIG. 10), a score generator (e.g., the modeling tool described below with reference to FIG. 11) or other source of a score. The source 33 may be within or integral to the interpreter 30, or external to or remote from the interpreter 30.

Additionally, the source 33 may be located proximate to the interpreter, may be separate from the interpreter, or may be distributed. In one example, the source may be implemented logic or circuitry that also includes logic or circuitry that forms a part of the interpreter. In one example of a distributed source, a remotely located component, such as a central database, provides information relative to the score that is converted by a local component, such as a computer, to data appropriate for use by the interpreter 30. Alternatively, the information relative to the score may be converted by the electronic controller 31 within the interpreter, or may be provided to the interpreter in a format not requiring conversion.

An energy application device may also include a score location component (not shown), which may select a score for conversion by the interpreter, for example from a library of scores, or a score input component (not shown) that accepts a score from a user. In other embodiments, an input component may accept an input composition or structure (e.g., from a user), and return a score that has an effect on the accepted composition or structure or on a portion of the accepted composition or structure, to the interpreter. In some embodiments, the input component may then present the returned score to the user for approval before passing it to the interpreter.

The presented returned score may be represented to the user visually in a variety of manners. For example, the score may be presented graphically as a spectrographic representation, a dynamic model, a spreadsheet, or other user perceivable representation. The representation may also include additional information, such as a visual representation of a different score. Such presentation may provide a visually perceivable contrast to the user, for example by highlighting energy inputs that are added, subtracted, or modified in one score relative to another.

In another approach, audio corresponding to the score may be presented audibly to the user. In such a case, each note of the score may be converted to a corresponding audible note that the user can detect. In some cases, it may be appropriate for the correspondence between the notes of the score and the presented audible notes to be established according to a standardized protocol. This can aid a user in detecting patterns and deviations from such patterns by identifying "off-key" audible notes. In one such protocol, a range of frequencies of the input energies can map to a range of audible frequencies, in a linear, logarithmic, or other mapping, such that increases in the input energy frequency can be represented as increases in the audible frequency. Moreover, intensities or amplitudes may also be mapped to provide audible indications of the amplitudes of the notes in the score. One skilled in the art will recognize that other types of mapping or correlations may also be applied. For example, the frequency mapping may be inverted, the various input frequencies may be mapped into

subsets of frequencies (e.g., ranges of input frequencies mapped to selected octaves of the audible frequencies), or other types of audible presentations may be developed. Further, in addition to, or in lieu of, a signal audible to a user, the score may be mapped to an acoustic signal detectible by an acoustic receiver that can act as a monitor of the score components.

In another aspect, the information representing the score may be compressed or encrypted according to known techniques. The interpreter may accept an authorization (e.g., a decryption key or authorization code) or may decompress the information to produce a more complete representation of the score before continuing the process, as described below.

The interpreter converts the score into appropriate control instructions for an energy input device 32 (e.g., one or more lasers, which may be wavelength tunable). The energy input device applies the energy inputs 34 to a target 36. The energy input device may apply energy using either a single or a plurality of beams (e.g., an array of lasers). The energy input device may further comprise optional elements 38 that direct and/or modify the beam (e.g., reflectors, polarizers, optical fibers, lenses, and/or other optical coupling elements).

FIG. 10 shows schematically a device with optional monitoring and feedback control for score application. A score generator 40 (which may include, for example and without limitation, a database of scores, a molecular modeling device that determines resonant frequencies, a database of spectrographs, or another source of scores as described herein) provides a score to an energy input component 42. The energy input component applies energy inputs to a target 44 as specified by the score. In addition, a monitor 46 may observe the effect on the target of the applied energy inputs. In embodiments in which a monitor is present, it may optionally provide feedback to the score generator, which may then provide a new or adjusted score to the energy input component in response to the observations of the monitor. The monitor may be of a type that identifies energy levels, kinetic effects, structural variations, chemical variations or any other appropriate variation in the target 44. For example, thermal imaging can provide an indication of thermal buildup in the target. In another example, an optical beam may pass through or be reflected from the target. As is known, in some materials, the optical transmission or reflection properties (e.g., index or refraction, diffraction phenomena, or absorption) can be a function of stresses, thermal effects, or other effects that may be induced by the input component 42; the monitor uses the optical beam to detect these changed properties, revealing the effects induced by the input component.

In biological applications, scores may be used for diagnostic and/or therapeutic purposes. For example, in embodiments involving the treatment of blood, a monitoring device may be placed over a blood vessel (e.g., in the wrist or on the earlobe), continually monitoring and/or altering blood chemistry as blood flows close to the skin. Alternatively, a fiber optic cable or other physical device for energy transmission may deliver energy impulses deeper into the body. In either case, a substantial portion, or even all, of the entire volume of blood of a patient can be treated in a relatively short amount of time as the blood circulates through a targeted vessel. The monitoring device may, for example, observe and/or chemically modify proteins in the blood. In another embodiment, the monitoring device may continuously monitor blood components such as sugars, triglycerides, or cholesterol, and optionally moderate their levels if they pass a threshold.

FIG. 11 shows schematically an apparatus for generating scores based on computational modeling of resonant structures. A modeling tool 50 generates a model of a structure

(e.g., a molecular model of a chemical composition, or a quantum mechanical model of the energy levels of a quantum dot) in order to determine its predicted resonances. A score generator 52 then incorporates the predicted resonances into a score. The generated score may be passed to an energy input instrument, such as energy input device 32 described with reference to FIG. 9.

FIG. 12 shows schematically a system for introducing a chemical agent into a medium, which may in some embodiments be used for therapeutic purposes. As shown, the chemical agent comprises a composition 60 bound to an optional carrier 62, which is located within a medium 64. Energy input device 66 applies energy inputs corresponding to a score to the medium. In some embodiments, this score is selected to sever the bond between the composition and the carrier, thereby releasing the composition into the medium. In other embodiments, the applied score activates the composition directly, for example by breaking one or more bonds of the composition, ablating material surrounding the composition, heating material surrounding the composition, or reacting with material surrounding the composition. In some embodiments, these techniques may be used to deliver a catalyst or other chemical agent to difficult-to-reach areas. For example, a cleaning or recharging agent could be dispersed throughout a water treatment system in an inert form, and then rendered active by application of a score to the whole system. Such an embodiment may in some cases allow more uniform application of the cleaning or recharging agent, particularly in high-surface-area systems where a reactive agent may be difficult to disperse throughout the system.

For use in vivo, the optional carrier or the composition may have an affinity to a selected substance or tissue, which forms the medium of FIG. 12. The optional carrier or the composition may be placed directly in a particular tissue (e.g., by injection into the tissue), or may be introduced into the body and allowed to accumulate at the selected tissue. For example, an iodine-containing composition may be introduced into the body orally or by injection into the bloodstream, and, allowed to accumulate in the thyroid gland. A score comprising infrared energy inputs (to which the body is substantially transparent) may then be used to heat the iodine-containing composition, thereby ablating a tumor and/or a portion of the thyroid gland itself. Other compositions or carriers may similarly be chosen to accumulate in other tissues (e.g., calcium in the bones or teeth or organic compounds in the liver), and then activated by application of a score (e.g., to release a stimulant to cell division and/or growth). Inhaled compositions, optionally bound to fine carriers, may be distributed to the alveoli for treatment of the lungs.

FIG. 13 shows schematically a library of excitation energy specifications, comprising a structured data repository 70 comprising a plurality of score records. Each score record includes descriptors for a plurality of energy inputs, a descriptor for associated composition(s) affected by the plurality of energy inputs, and optionally a descriptor describing the effect of the plurality of energy inputs on the composition. The energy input descriptors describe at least one of frequency, modulation frequency, phase, amplitude, temporal profile, polarization and direction for each energy input. The library may also include additional features such as a search engine 72, an input component 74, and/or an output component 76. If provided, the output component may provide a user with a score record for download, for example so that it may be used to direct an energy input device to play the score in order to affect the associated composition. The library may be used to screen for a composition, by accessing the library to locate a score record for the composition, applying the

energy inputs described by the energy input descriptors of the score record to a medium, and observing the medium for reaction of the composition to the applied inputs. The library may also be used to excite the composition, by accessing the library to locate a score record for the composition and applying the energy inputs described by the score record to the composition (e.g., to destroy the composition). Alternatively, the selected score record may comprise a descriptor of a composition sharing a functional group with the composition to be excited.

In some embodiments, the compositions to be excited may be agents that have been or will be administered in vivo, such as but not limited to therapeutic agents (e.g., analgesics, antacids, antianxiety drugs, antiarrhythmics, anticoagulants, anticonvulsants, antidepressants, antidiarrheals, antiemetics, antifungals, antihistamines, antihypertensives, anti-inflammatories, antiplatelet drugs, antipsychotics, antipyretics, antivirals, barbiturates, beta-blockers, bronchodilators, chemotherapy drugs, corticosteroids, cough suppressants, cytotoxics, decongestants, diuretics, expectorants, hormones, hypoglycemics, immunosuppressives, laxatives, muscle relaxants, sedatives, sex hormones, sleeping drugs, tranquilizers, and vitamins). In many cases, these agents have a well-defined chemical structure including functional groups whose resonances can be accurately measured and/or computationally modeled. The selective resonance of these agents may serve to catalyze, release, activate, inactivate, or destroy the agent, depending on the agent and the score applied. Dual-function agents are also envisioned, in which an agent has one therapeutic effect before application of the score, and is switched to another therapeutic effect after application of the score.

Certain therapeutic agents may have undesirable side effects, may trigger allergic reactions, or may have positive effects in some areas of the body and negative effects in others. In some situations, the negative effects cannot be accurately predicted prior to administration of the agent. In these cases, the application of a score that inactivates or destroys the agent may mitigate these negative effects. For example, if a patient experiences an allergic action to an antibiotic, it may be possible to destroy it throughout the patient's system by application of an appropriate score to the body. In particular, tetracycline and fluoroquinolone class antibiotics (e.g., ciprofloxacin and levofloxacin) have specific absorption spectra not characteristic of naturally occurring biomolecules, and thus should be susceptible to selective excitation without substantial damage to surrounding tissue (see, e.g., Lacher, et al., "The Infrared Absorption Spectra of Some Antibiotics in Antimony Trichloride Solution," *J. Phys. Chem.* 59:610, July 1955, and Albini, et al., "Photophysics and photochemistry of fluoroquinolones," *Chem. Soc. Rev.*, 32:238-250, May 2003, both of which are incorporated herein by reference). Allergic reactions to fluoroquinolones are infrequent but range from a skin rash that may be itchy, red, or swollen to life-threatening reactions such as severe difficulty breathing and shock. Allergic reactions to tetracycline are also uncommon, but may result in various types of skin rash, and rarely, liver disease. This method of destruction has the advantage of being substantially noninvasive, and of potentially being able to reach substantially all of the affected tissue. Therapeutic agents may similarly be partially or fully destroyed in the case of an overdose.

In another example, a patient receiving a stent may routinely be administered antiplatelet agents (e.g., clopidogrel, sold under the trademark PLAVIX, ticlopidine, sold under the trademark TICLID, cilostazol, sold under the trademark PLETAL, abciximab, sold under the trademark REOPRO,

eptifibatide, sold under the trademark INTEGRILIN, tirofiban, sold under the trademark AGGRASTAT, dipyridamole, sold under the trademark PERSANTINE, or aspirin). While these agents are beneficial in preventing blood from clotting at the site of the stent, they become a liability if it becomes necessary to operate on the patient, since clotting at the incision site will be inhibited. Clopidogrel, in particular, may require waiting times of as long as two weeks before surgery may be performed, which may substantially endanger a patient in need of emergency treatment. Application of the appropriate score to a patient having clopidogrel in his system may destroy the agent and allow surgery to be performed substantially sooner. FIG. 14 shows the chemical structure of several antiplatelet agents. The thiophene ring present in clopidogrel and in ticlopidine, in particular, is not typical of biological structures, and should be susceptible to selective excitation without substantial damage to surrounding tissue. Thus, clopidogrel and ticlopidine may be broken down and removed from the system in order that normal clotting function may be rapidly restored.

For humoral agents, a score may be applied to blood as it passes through a dialysis unit, or is otherwise removed from and then returned to the body. Such embodiments may be useful in situations where the known score for an agent includes radiation that may be detrimental to living tissue, or when preferred inputs are at frequencies to which intervening tissue is substantially opaque.

Some agents (for example, those that have similar structure to naturally occurring biomolecules) may require relatively long or complex scores to resonate without substantially affecting ordinary tissue in vivo. For such agents, or for other therapeutic agents for which a score is not known, is not practical to apply, or is otherwise undesirable, it may be appropriate to append a functional group that can be readily resonated. This group may be used to catalyze, release, activate, inactivate, or destroy the agent as described above.

In some embodiments, inactive forms of anticlotting agents may be introduced into the body. These agents may then be activated by application of an activating score. The activating score may be applied only at selected locations of the body (e.g., in the vicinity of a stent) as discussed above, allowing normal clotting action elsewhere in the body.

In other embodiments, the body may be monitored to determine the quantity or activity of an agent, which may be modulated in response to the monitor. For example, some pharmaceuticals (e.g., certain immunosuppressants or chemotherapy agents) have noticeably different activities in different patients. These agents may be administered beginning in very low doses, and gradually titrated up while monitoring blood levels to reach an optimal concentration without risking an overdose. However, a patient may have inadequate protection during the titration process. If the pharmaceutical can be destroyed by application of a score to the body, the dose may be more rapidly increased, and any detected superabundance destroyed, allowing more rapid stabilization at the desired blood level. In other embodiments, monitoring may be used to modulate application of a score that activates an agent (e.g., lithium, whose therapeutic blood levels are relatively close to its threshold of toxicity) from a reservoir of an inactive form of the agent placed in the body. In either type of system, feedback from the monitor may be used either manually or automatically to establish optimal blood levels for the agent.

In some embodiments, it may be desirable to catalyze, release, activate, inactivate, or destroy endogenous agents in the blood or in other tissue. These may include, for example, blood clotting factors (e.g., prekallikrein, high molecular weight kininogen, any of clotting factors I-XIII, von Will-

ebrand factor, protein C, thrombomodulin, or anti-thrombin III), sugars (e.g., glucose, fructose, sucrose, galactose, mannose, glycerol, or glucuronate), lipids and lipoproteins (e.g., cholesterol, triglycerides, triacylglycerols, chylomicrons, very low density lipoproteins, low density lipoproteins, intermediate density lipoproteins, or high density lipoproteins), vitamins, minerals, hormones (e.g., adrenalin, adrenocorticotrophic hormone, aldosteron, calcitonin, cortisol, insulin, gastrin, glucagon, glucocorticoids, thyroid hormone, gastrin, secretin, cholecystokinin, somatostatin, neuropeptide Y, other hormones of the gut, thyrotropin-releasing hormone, gonadotropin-releasing hormone, growth hormone-releasing hormone, ghrelin, corticotrophin-releasing hormone, somatostatin, dopamine, antidiuretic hormone, oxytocin, other hormones of the hypothalamus, renin, erythropoietin, calcitriol, other hormones of the kidney, insulin-like growth factor-I, angiotensinogen, thrombopoietin, other hormones of the liver, thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, prolactin, growth hormone, adrenocorticotrophic hormone, antidiuretic hormone, other hormones of the pituitary, estrogen, testosterone, progesterone, anabolic steroids, other reproductive hormones, melanocyte-stimulating hormone, parathyroid hormone, melatonin, prolactin, or thyroid hormones), enzymes (e.g., creatine kinase, lactate dehydrogenase, troponin, other cardiac enzymes, aspartate transaminase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl-transpeptidase, or other liver enzymes), antibodies (e.g., antibodies to autoimmune disorders such as acute transverse myelitis, allergic (Henoch-Schönlein) purpura, alopecia areata, aplastic anemia, brachial neuritis, bullous pemphigoid, dermatitis herpetiformis, polymyositis, dermatomyositis, Eaton-Lambert syndrome, eosinophilic fasciitis, Goodpasture's syndrome, Guillain-Barré syndrome, hemolytic anemia, hepatitis, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, pemphigus, peripheral ulcerative keratitis, polyglandular deficiency syndrome, relapsing polychondritis, rheumatoid arthritis, scleroderma, Sjögren's syndrome, or system lupus erythematosus, or normal antibodies to transplanted materials such as organs, stem cells, or device implants), proteins (e.g., albumins, globulins, fibrinogens, or hemoglobins), including modified, functionalized, and/or synthetic forms of any of these.

In some embodiments, the techniques described herein may be applied to living tissue. In other embodiments, it may be desirable to apply energy according to a score to nonliving tissue. It has been reported that irradiation at wavelengths of 1210 nm or 1720 nm preferentially heated fat below the surface of skin in pig skin-and-fat tissue samples (see "Free-Electron Laser Targets Fat," *Jefferson Lab News*, bearing a date of Apr. 10, 2006, available at <http://www.jlab.org/news/releases/2006/fel.html>, which is incorporated herein by reference). The application of a set of differing energy inputs as described herein may achieve higher specificity for particular compositions within tissue, whether living or nonliving. Such specificity may be used, for example, to catalyze, release, activate, inactivate, or destroy extrinsic agents (e.g., drugs) or endogenous agents (e.g., viruses) from tissue before it is transplanted into a patient.

Those having skill in the art will recognize that the state of the art of circuit design has progressed to the point where there is typically little distinction left between hardware and software implementations of aspects of systems. The use of hardware or software is generally a design choice representing tradeoffs between cost, efficiency, flexibility, and other implementation considerations. Those having skill in the art will appreciate that there are various vehicles by which pro-

cesses, systems and/or other technologies involving the use of logic and/or circuits can be effected (e.g., hardware, software, and/or firmware), and that the preferred vehicle will vary with the context in which the processes, systems and/or other technologies are deployed. For example, if an implementer determines that speed is paramount, the implementer may opt for a mainly hardware and/or firmware vehicle. Alternatively, if flexibility is paramount, the implementer may opt for a mainly software implementation. In these or other situations, the implementer may also opt for some combination of hardware, software, and/or firmware. Hence, there are several possible vehicles by which the processes, devices and/or other technologies involving logic and/or circuits described herein may be effected, none of which is inherently superior to the other. Those skilled in the art will recognize that optical aspects of implementations may require optically-oriented hardware, software, and/or firmware.

The foregoing detailed description has set forth various embodiments, some of which incorporate logic and/or circuits, via the use of block diagrams, flow diagrams, operation diagrams, flowcharts, illustrations, and/or examples. Insofar as such block diagrams, operation diagrams, flowcharts, illustrations, and/or examples contain one or more functions, operations, or data structures to be performed, manipulated, or stored by logic and/or circuits, it will be understood by those within the art that each such logic and/or circuit can be embodied, individually and/or collectively, by a wide range of hardware, software, firmware, or virtually any combination thereof. For example, some embodiments of the subject matter described herein may be implemented via Application Specific Integrated Circuits (ASICs), Field Programmable Gate Arrays (FPGAs), digital signal processors (DSPs), or other integrated formats. However, those skilled in the art will recognize that other embodiments disclosed herein can be equivalently implemented in whole or in part in standard integrated circuits, as one or more computer programs running on one or more computers (e.g., as one or more programs running on one or more computer systems), as one or more programs running on one or more processors (e.g., as one or more programs running on one or more microprocessors), as firmware, as analog circuitry, or as virtually any combination thereof, and that designing the circuitry and/or writing the code for the software and/or firmware would be well within the skill of one of skill in the art in light of this disclosure. In addition, those skilled in the art will appreciate that the operations, functions, and data (e.g., scores) described herein are capable of being distributed or stored in a variety of signal bearing media. Examples of a signal bearing media include, but are not limited to, recordable type media such as floppy disks, hard disk drives, CD ROMs, digital tape, and computer memory, and transmission type media such as digital and analog communication links using TDM or IP based communication links (e.g., packet links). The choice of signal bearing media will generally be a design choice representing tradeoffs between cost, efficiency, flexibility, and other implementation considerations in a particular context, and none of these signal bearing media is inherently superior to the other.

While various aspects and embodiments have been disclosed herein, other aspects and embodiments will be apparent to those skilled in the art. The various aspects and embodiments disclosed herein are for purposes of illustration and are not intended to be limiting, with the true scope and spirit being indicated by the following claims.

What is claimed is:

1. A method, comprising
identifying an agent in a body that modulates a biological
activity in the body;
selecting a set of noncontinuous differing energy inputs
specific to the agent, wherein the set of differing energy
inputs selectively resonates a plurality of resonant struc-
tures in the agent, including resonating at least one bond;
and
directing the set of differing energy inputs towards the
agent while it is in the body,
wherein directing the set of differing energy inputs towards
the agent changes its modulation of the biological activ-
ity in the body.
2. The method of claim 1, wherein directing the set of
differing energy inputs towards the agent initiates a therapeu-
tic effect in the body.
3. The method of claim 1, wherein directing the set of
differing energy inputs towards the agent terminates a thera-
peutic effect in the body.
4. The method of claim 1, wherein directing the set of
differing energy inputs towards the agent destroys the agent.
5. The method of claim 1, wherein the agent is selected
from the group consisting of analgesics, antacids, antianxiety
drugs, antiarrhythmics, anticoagulants, anticonvulsants, anti-
depressants, antidiarrheals, antiemetics, antifungals, antihis-
tamines, antihypertensives, anti-inflammatories, antiplatelet
drugs, antipsychotics, antipyretics, antivirals, barbiturates,
beta-blockers, bronchodilators, chemotherapy drugs, corti-
costeroids, cough suppressants, cytotoxics, decongestants,
diuretics, expectorants, hormones, hypoglycemics, immuno-
suppressives, laxatives, muscle relaxants, sedatives, sex hor-
mones, sleeping drugs, tranquilizers, and vitamins.
6. The method of claim 5, wherein the agent is an antiplate-
let drug.
7. The method of claim 6, wherein directing the set of
differing energy inputs towards the agent destroys the agent.
8. The method of claim 7, wherein the agent is clopidogrel.
9. The method of claim 7, further comprising performing
an incision on the body.
10. The method of claim 1, wherein the body is alive.
11. The method of claim 1, wherein the body is human.
12. The method of claim 1, wherein the agent is present in
blood.
13. The method of claim 1, further comprising monitoring
the body for activity of the agent.
14. The method of claim 1, further comprising monitoring
the body for quantity of the agent.
15. The method of claim 1, wherein the agent comprises a
functional group selected to be responsive to the set of differ-
ing energy inputs.
16. The method of claim 1, further comprising modifying
the agent to add a functional group selected to be responsive
to the set of differing energy inputs.
17. The method of claim 1, wherein the agent is selected
from the group consisting of blood clotting factors, sugars,
lipids, lipoproteins, vitamins, minerals, hormones, enzymes,
antibodies, and proteins.
18. The method of claim 17, wherein the agent is a blood
clotting factor selected from the group consisting of prekall-

likein, high molecular weight kininogen, clotting factors
I-XIII, von Willebrand factor, protein C, protein S, thrombo-
modulin, and antithrombin III.

19. The method of claim 17, wherein the agent is a sugar
selected from the group consisting of glucose, fructose,
sucrose, galactose, mannose, glycerol, and glucuronate.

20. The method of claim 17, wherein the agent is a lipid or
lipoprotein selected from the group consisting of cholesterol,
triglycerides, triacylglycerols, chylomicrons, very low den-
sity lipoproteins, low density lipoproteins, intermediate den-
sity lipoproteins, and high density lipoproteins.

21. The method of claim 17, wherein the agent is a hor-
mone selected from the group consisting of adrenalin,
adrenocorticotrophic hormone, aldosterone, calcitonin, corti-
sol, insulin, gastrin, glucagon, glucocorticoids, thyroid hor-
mone, gastrin, secretin, cholecystokinin, somatostatin, neu-
ropeptide Y, other hormones of the gut, thyrotropin-releasing
hormone, gonadotropin-releasing hormone, growth hor-
mone-releasing hormone, ghrelin, corticotrophin-releasing
hormone, somatostatin, dopamine, antidiuretic hormone,
oxytocin, other hormones of the hypothalamus, renin, eryth-
ropoietin, calcitriol, other hormones of the kidney, insulin-like
growth factor-1, angiotensinogen, thrombopoietin, other hor-
mones of the liver, thyroid-stimulating hormone, follicle-
stimulating hormone, luteinizing hormone, prolactin, growth
hormone, adrenocorticotrophic hormone, antidiuretic hor-
mone, other hormones of the pituitary, estrogen, testosterone,
progesterone, anabolic steroids, other reproductive hor-
mones, melanocyte-stimulating hormone, parathyroid hor-
mone, melatonin, prolactin, and thyroid hormones.

22. The method of claim 17, wherein the agent is an
enzyme selected from the group consisting of creatine kinase,
lactate dehydrogenase, troponin, other cardiac enzymes,
aspartate transaminase, alanine aminotransferase, alkaline
phosphatase, gamma-glutamyltranspeptidase, and other liver
enzymes.

23. The method of claim 17, wherein the agent is an anti-
body to an autoimmune disorders selected from the group
consisting of acute transverse myelitis, allergic (Henoch-
Schönlein) purpura, alopecia areata, aplastic anemia, brachial
neuritis, bullous pemphigoid, dermatitis herpetiformis, poly-
myositis, dermatomyositis, Eaton-Lambert syndrome, eosi-
nophilic fasciitis, Goodpasture's syndrome, Guillain-Barré
syndrome, hemolytic anemia, hepatitis, mixed connective tis-
sue disease, multiple sclerosis, myasthenia gravis, pemphi-
gus, peripheral ulcerative keratitis, polyglandular deficiency
syndrome, relapsing polychondritis, rheumatoid arthritis,
scleroderma, Sjögren's syndrome, and system lupus erythe-
matosus.

24. The method of claim 17, wherein the agent is an anti-
body to a transplanted material.

25. The method of claim 24, wherein the transplanted
material is selected from the group consisting of organs, stem
cells, and device implants.

26. The method of claim 17, wherein the agent is a protein
selected from the group consisting of albumins, globulins,
fibrinogens, and hemoglobins.

* * * * *

专利名称(译)	身体药物的选择性共振		
公开(公告)号	US9211332	公开(公告)日	2015-12-15
申请号	US13/457993	申请日	2012-04-27
[标]申请(专利权)人(译)	希尔莱特有限责任公司		
申请(专利权)人(译)	SEARETE LLC		
当前申请(专利权)人(译)	发明科学基金I, LLC		
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其他公开文献	US20120215156A1		
外部链接	Espacenet USPTO		

摘要(译)

通过应用包括一系列能量输入的分数的，可以选择性地或优先地激发化学组合物。

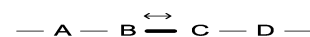


FIG. 1A

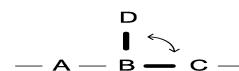


FIG. 1B

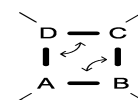


FIG. 1C