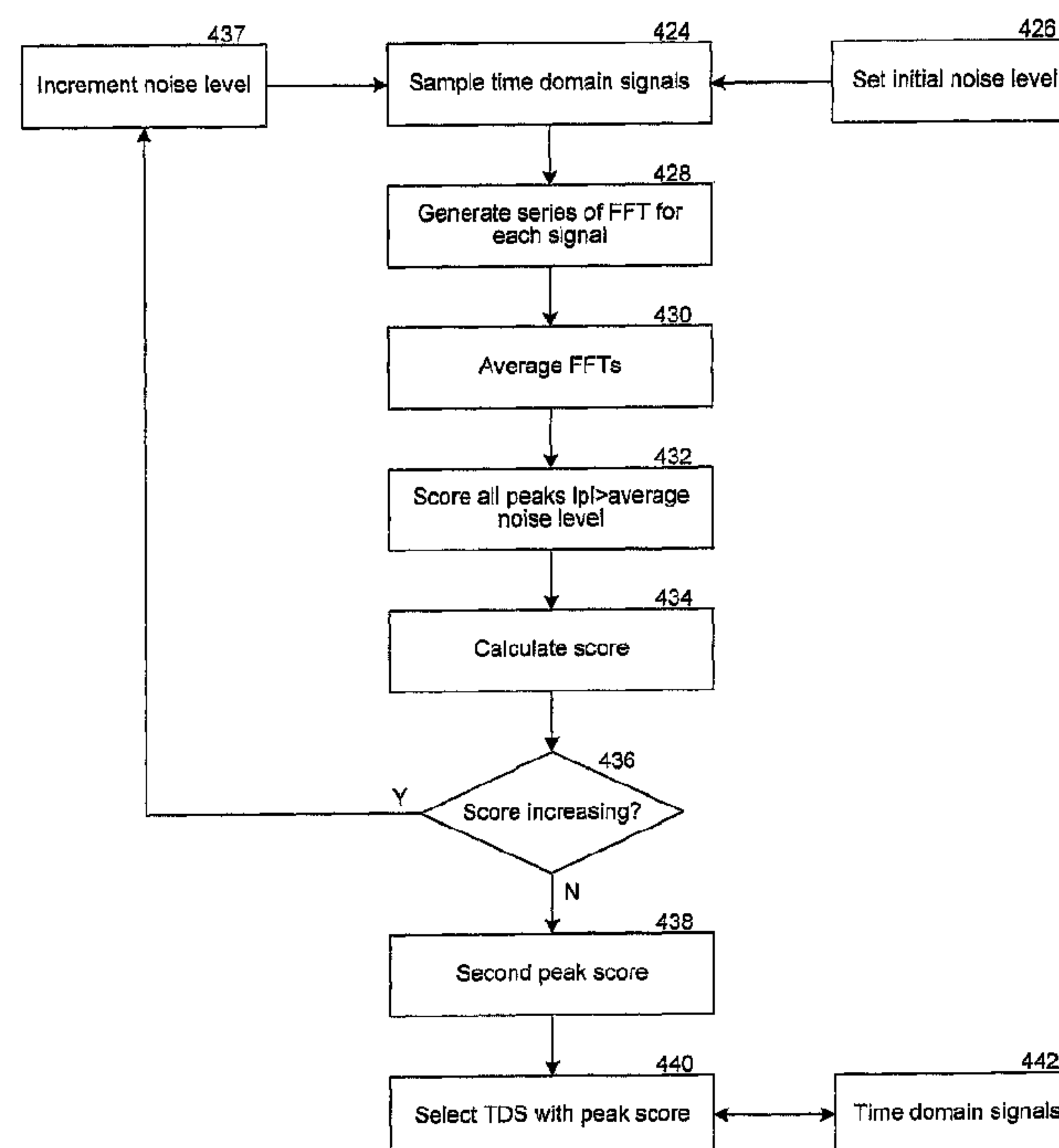




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PRESENTING VERY LOW AMPLITUDE SIGNALS



(57) Abrégé/Abstract:

An electromagnetic signal effective to produce selected chemical or biological effects associated with a selected chemical or biological agent is generated. The method for generating the electromagnetic signal includes inserting a sample containing the agent into a magnetically shielded detection apparatus to provide molecular signals; injecting noise into the sample at a selected noise amplitude; and recording a time-domain signal produced by the sample upon injecting the noise and composed of sample source radiation superimposed on the injected noise. The injection of noise and the recording of the time-domain signal may be repeated at each of a plurality of different noise amplitudes within a selected range, and spectral- feature scores for the recorded signals may be calculated. A recorded signal may then be selected based on its calculated score.



**SYSTEM AND METHOD FOR COLLECTING, STORING, PROCESSING,
TRANSMITTING AND PRESENTING VERY LOW AMPLITUDE SIGNALS**

ABSTRACT OF THE DISCLOSURE

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10 The injection of noise and the recording of the time-domain signal may be repeated at each of a plurality of different noise amplitudes within a selected range, and spectral-feature scores for the recorded signals may be calculated. A recorded signal may then be selected based on its calculated score.

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SYSTEM AND METHOD FOR COLLECTING, STORING, PROCESSING,
TRANSMITTING AND PRESENTING VERY LOW AMPLITUDE SIGNALS

TECHNICAL FIELD

[0002] Embodiments of the present invention relate to signals readable by a system for converting or transducing the signal into electromagnetic waves, and to methods of producing and applying such signals.

BACKGROUND

[0003] One of the accepted paradigms in the fields of chemistry and biochemistry is that chemical or biochemical effector agents, e.g., molecules, interact with target systems through various physicochemical forces, such as ionic, charge, or dispersion forces or through the cleavage or formation of covalent or charge-induced bonds. These forces may involve vibrational or rotational energy modes in either the effector agent or target system.

[0004] A corollary of this paradigm is the requirement, in effector-target systems, of the effector agent in the target environment. However, what is not

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known or understood is whether this requirement is related to the actual presence of the effector, or whether it may be due, at least as to certain effector functions, to the presence of energetic modes that are characteristic of the effector. If effector function can be simulated, at least in part, by certain characteristic energetic modes, it may be possible to "simulate" the effect of the effector agent in a target system by exposing the system to certain energetic modes that are characteristic of the effector. If so, the questions that naturally arise are: what effector-molecule energy modes are effective, how can they be converted or transduced into the form of measurable signals, and how can these signals be used to effect a target system, that is, mimic at least some of the effector functions of the molecule in a target system?

[0005]

Experiments conducted in support of the invention described in the application demonstrate that certain effector functions on a target system (in this case, one of a number of biological systems), can be duplicated by exposing the target system to electromagnetic waves produced by "transducing" a time-domain signal of the effector compound. According to the earlier-described invention, the time-domain signal is produced by recording a signal produced by the compound in a shielded environment, while injecting noise into the recording apparatus at a level that enhances the ability to observe low-frequency stochastic events produced by the compound. In the earlier-described application, the transducing signal was the actual compound time-domain signal of the effector compound.

[0006] The possibility of achieving effector-molecule functions by exposing a target system to characteristic effector-molecule signals, without the need for the actual presence of the effector agent, has a number of important and intriguing applications. Instead of treating an organism by the application of a drug, the same effect may be achieved by exposing the organism to drug-specific signals. In the field of nanofabrication, it might now be possible to catalyze or encourage self-assembly patterns by introducing in the assembly system, signals characteristic of a multivalent effector molecules capable of promoting the desired pattern of self-assembly.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] Figure 1 is an isometric view of one embodiment of a molecular electromagnetic signaling detection apparatus formed in accordance with one embodiment of the present invention;

[0008] Figure 2 is an enlarged, detail view of the faraday cage and its contents shown in Figure 1; and

[0009] Figure 3 is an enlarged, cross sectional view of one of the attenuation tubes shown in Figures 1 and 2.

[0010] Figure 4 is a cross-section view of the faraday cage and its contents shown in Figure 2.

[0011] Figure 5 is a diagram of an alternative electromagnetic emission detection system.

[0012] Figure 6 diagram of the processing unit included in the detection system of the above Figures.

[0013] Figure 7 is a diagram of an alternative processing unit to that of Figure 6.

[0014] Figure 8 is a flow diagram of the signal detection and processing performed by the present system.

[0015] Figure 9 shows a high-level flow diagram of data flow for the histogram spectral plot method of the invention;

[0016] Figure 10 is a flow diagram of the algorithm for generating a spectral plot histogram, in accordance with the invention, and

[0017] Figure 11 is a flow diagram of steps in identify optimal time-domain signals in accordance with a second embodiment of the method of the invention;

[0018] Figure 12 is a flow diagram of steps to identify optimal time-domain signals in accordance with a third embodiment of the method of the invention;

[0019] Figure 13 shows the transduction equipment layout in a typical transduction experiment.

[0020] Figure 14 shows a transduction coil and container used in a typical transduction experiment.

[0021] Figures 15A-15E show a portion of a time-domain signal for a sample containing 40% of an herbicide compound (15A), an FFT of autocorrelated time-domain signals from the sample in 15A, recorded at a noise levels of 70.9 -dbm (15B), 74.8-dbm (15C and 15D), and 78.3 dbm (15E);

[0022] Figure 15F is a plot of autocorrelation scores vs noise setting for the sample in Figure 15;

[0023] Figure 16 is a block diagram illustrating a process flow for creating a signal from a sample that may be applied to a biological system.

[0024] Figure 17 is a block diagram illustrating a suitable system for applying to a patient electromagnetic waves that are generated from signals created from a sample under the inventive system.

[0025] Figure 18 is a flow diagram illustrating one example of a signal processing routine for modifying one or more starting waveforms.

[0026] Figures 19A-19D show modification of a spectral plot using a graphical user interface.

[0027] Figure 20 is a block diagram illustrating alternatives for distributing a signal generated and processed by the detection system and processing unit.

[0028] Figure 21 is a block diagram illustrating a transducer-receiver/transceiver for the distribution system of Figure 20.

[0029] Figure 22 is a Helmholtz-type induction coil for use with the present system.

[0030] Figure 23 is an implantable coil for transducing a sample under embodiments of the invention.

[0031] The headings provided herein are for convenience only and do not necessarily affect the scope or meaning of the claimed invention.

DETAILED DESCRIPTION

I. Definitions

[0032] The terms below have the following definitions unless indicated otherwise.

[0033] "Sample that exhibits molecular rotation" refers to a sample material, which may be in gaseous, liquid or solid form (other than a solid metal) in which one or more of the molecular compounds or atomic ions making up or present in the sample exhibit rotation.

[0034] "Magnetic shielding" refers to shielding that decreases, inhibits or prevents passage of magnetic flux as a result of the magnetic permeability of the shielding material.

[0035] "Electromagnetic shielding" refers to, e.g., standard Faraday electromagnetic shielding, or other methods to reduce passage of electromagnetic radiation.

[0036] "Time-domain signal" or "time-series signal" refers to a signal with transient signal properties that change over time.

[0037] "Sample-source radiation" refers to magnetic flux or electromagnetic flux emissions resulting from molecular motion of a sample, such as the rotation of a molecular dipole in a magnetic field.

[0038] "Gaussian noise" means random noise having a Gaussian power distribution. "Stationary white Gaussian noise" means random Gaussian noise that has no predictable future components. "Structured noise" may contain a logarithmic characteristic which shifts energy from one region of the spectrum to another, or it may be designed to provide a random time element while the amplitude remains constant. These two represent pink and uniform noise, as compared to truly random noise which has no predictable future component. "Uniform noise" means noise having a constant amplitude.

[0039] "Frequency-domain spectrum" refers to a Fourier frequency plot of a time-domain signal.

[0040] "Spectral components" refer to singular or repeating qualities within a time-domain signal that can be measured in the frequency, amplitude, and/or phase domains. Spectral components will typically refer to signals present in the frequency domain.

[0041] "Similar sample," with reference to a first sample, refers to the same sample or a sample having substantially the same sample components as the first sample.

[0042] "Faraday cage" refers to an electromagnetic shielding configuration that provides an electrical path to ground for unwanted electromagnetic radiation, thereby quieting an electromagnetic environment.

[0043] A "spectral-features score" refers to a score based on the number and/or amplitude of agent-specific spectral peaks observed over a selected low-frequency range, e.g., DC to 1 kHz or DC to 8 kHz, in a time-domain signal recorded for an agent or sample that has been processed by a suitable method, such as one of the three methods described herein, to reveal identifiable spectral features that are specific to the agent or sample.

[0044] An "optimized agent-specific time-domain signal" refers to a time-domain signal having a maximum or near-maximum spectral-features score.

II. Suitable apparatus for producing and processing time-domain signals

[0045] Described in detail below is a system and method for detecting, processing, and presenting low frequency electromagnetic emissions or signals of a sample of interest. In one embodiment, a known white or Gaussian noise signal is introduced to the sample. The Gaussian noise is configured to permit the electromagnetic emissions from the sample to be sufficiently detected by a signal detection system. Sets of detected signals are processed together to ensure repeatability and statistical relevance. The resulting emission pattern or spectrum can be displayed, stored, and/or identified as a particular substance.

[0046] Some embodiments of the present invention describe signals for use with a transducing system for producing compound-specific electromagnetic waves that can act on target systems placed in the field of the waves, and methods of producing such signals. Other embodiments, relate to generating and distributing such signals.

[0047] The following description provides specific details for a thorough understanding of, and enabling description for, embodiments of the invention. However, one skilled in the art will understand that the invention may be practiced

without these details. In other instances, well-known structures and functions have not been shown or described in detail to avoid unnecessarily obscuring the description of embodiments of the invention.

[0048] As explained in detail below, embodiments of the present invention are directed to providing an apparatus and method for the repeatable detection and recording of low-threshold molecular electromagnetic signals for later, remote use. A magnetically shielded faraday cage shields the sample material and detection apparatus from extraneous electromagnetic signals. Within the magnetically shielded faraday cage, a coil injects white or Gaussian noise, a nonferrous tray holds the sample, and a gradiometer detects low-threshold molecular electromagnetic signals. The apparatus further includes a superconducting quantum interference device ("SQUID") and a preamplifier.

[0049] The apparatus is used by placing a sample within the magnetically shielded faraday cage in close proximity to the noise coil and gradiometer. White noise is injected through the noise coil and modulated until the molecular electromagnetic signal is enhanced through stochastic resonance. The enhanced molecular electromagnetic signal, shielded from external interference by the faraday cage and the field generated by the noise coil, is then detected and measured by the gradiometer and SQUID. The signal is then amplified and transmitted to any appropriate recording or measuring equipment.

[0050] Referring to Figure 1, there is shown a shielding structure 10 which includes, in an outer to inner direction, a conductive wire cage 16 which is a magnetic shield and inner conductive wire cages 18 and 20 which provide electromagnetic shielding. In another embodiment, the outer magnetic shield is formed of a solid aluminum plate material having an aluminum-nickel alloy coating, and the electromagnetic shielding is provided by two inner wall structures, each formed of solid aluminum.

[0051] Referring to Figure 2, the faraday cage 10 is open at the top, and includes side openings 12 and 14. The faraday cage 10 is further comprised of three copper mesh cages 16, 18 and 20, nestled in one another. Each of the copper mesh cages 16, 18 and 20 is electrically isolated from the other cages by dielectric barriers (not shown) between each cage.

[0052] Side openings 12 and 14 further comprise attenuation tubes 22 and 24 to provide access to the interior of the faraday cage 10 while isolating the interior of the cage from external sources of interference. Referring to Figure 3, attenuation tube 24 is comprised of three copper mesh tubes 26, 28 and 30, nestled in one another. The exterior copper mesh cages 16, 18 and 20 are each electrically connected to one of the copper mesh tubes 26, 28 and 30, respectively. Attenuation tube 24 is further capped with cap 32, with the cap having hole 34. Attenuation tube 22 is similarly comprised of copper mesh tubes 26, 28 and 30, but does not include cap 32.

[0053] Referring again to Figure 2, a low-density nonferrous sample tray 50 is mounted in the interior of the faraday cage 10. The sample tray 50 is mounted so that it may be removed from the faraday cage 10 through the attenuation tube 22 and side opening 12. Three rods 52, each of which is greater in length than the distance from the center vertical axis of the faraday cage 10 to the outermost edge of the attenuation tube 22, are attached to the sample tray 50. The three rods 52 are adapted to conform to the interior curve of the attenuation tube 22, so that the sample tray 50 may be positioned in the center of the faraday cage 10 by resting the rods in the attenuation tube. In the illustrated embodiment, the sample tray 50 and rods 52 are made of glass fiber epoxy. It will be readily apparent to those skilled in the art that the sample tray 50 and rods 52 may be made of other nonferrous materials, and the tray may be mounted in the faraday cage 10 by other means, such as by a single rod.

[0054] Referring again to Figure 2, mounted within the faraday cage 10 and above the sample tray 50 is a cryogenic dewar 100. In the disclosed embodiment, the dewar 100 is adapted to fit within the opening at the top of faraday cage 10 and is a Model BMD-6 Liquid Helium Dewar manufactured by Tristan Technologies, Inc. The dewar 100 is constructed of a glass-fiber epoxy composite. A gradiometer 110 with a very narrow field of view is mounted within the dewar 100 in position so that its field of view encompasses the sample tray 50. In the illustrated embodiment, the gradiometer 110 is a first order axial detection coil, nominally 1 centimeter in diameter, with a 2 % balance, and is formed from a superconductor. The gradiometer can be any form of gradiometer excluding a planar gradiometer. The gradiometer 110 is connected to the input coil of one low temperature direct current

superconducting quantum interference device ("SQUID") 120. In the disclosed embodiment, the SQUID is a Model LSQ/20 LTS dc SQUID manufactured by Tristan Technologies, Inc. It will be recognized by those skilled in the art that high temperature or alternating current SQUIDs can be used without departing from the spirit and scope of the invention. In an alternative embodiment, the SQUID 120 includes a noise suppression coil 124.

[0055] The disclosed combination of gradiometer 110 and SQUID 120 have a sensitivity of 5 microTesla/ $\sqrt{\text{Hz}}$ when measuring magnetic fields.

[0056] The output of SQUID 120 is connected to a Model SP Cryogenic Cable 130 manufactured by Tristan Technologies, Inc. The Cryogenic Cable 130 is capable of withstanding the temperatures within and without the dewar 100 and transfers the signal from the SQUID 120 to Flux-Locked Loop 140, which is mounted externally to the faraday cage 10 and dewar 100. The Flux-Locked Loop 140 in the disclosed embodiment is an iFL-301-L Flux-Locked Loop manufactured by Tristan Technologies, Inc.

[0057] Referring to Figure 1, the Flux Locked Loop 140 further amplifies and outputs the signal received from the SQUID 120 via high-level output circuit 142 to an iMC-303 iMAG® SQUID controller 150. The Flux-Locked Loop 140 is also connected via a model CC-60 six-meter fiber-optic composite connecting cable 144 to the SQUID controller 150. The fiber-optic connecting cable 144 and SQUID controller 150 are manufactured by Tristan Technologies, Inc. The controller 150 is mounted externally to the magnetic shielding cage 40. The fiber-optic connecting cable 144 carries control signals from the SQUID controller 150 to the Flux Locked Loop 140, further reducing the possibility of electromagnetic interference with the signal to be measured. It will be apparent to those skilled in the art that other Flux-Locked Loops, connecting cables, and Squid controllers can be used without departing from the spirit and scope of the invention.

[0058] The SQUID controller 150 further comprises high resolution analog to digital converters 152, a standard GP-IB bus 154 to output digitalized signals, and BNC connectors 156 to output analog signals. In the illustrated embodiment, the BNC connectors are connected to a dual trace oscilloscope 160 through patch cord 162.

[0059] Referring to Figure 2, a two-element Helmholtz transformer 60 is installed to either side of the sample tray 50 when the sample tray is fully inserted within the faraday cage 10. In the illustrated embodiment, the coil windings 62 and 64 of the Helmholtz transformer 60 are designed to operate in the direct current to 50 kilohertz range, with a center frequency of 25 kilohertz and self-resonant frequency of 8.8 megahertz. In the illustrated embodiment, the coil windings 62 and 64 are generally rectangular in shape and are approximately 8 inches tall by 4 inches wide. Other Helmholtz coil shapes may be used but should be shaped and sized so that the gradiometer 110 and sample tray 50 are positioned within the field produced by the Helmholtz coil. Each of coil windings 62 and 64 is mounted on one of two low-density nonferrous frames 66 and 68. The frames 66 and 68 are hingedly connected to one another and are supported by legs 70. Frames 66 and 68 are slidably attached to legs 70 to permit vertical movement of the frames in relation to the lower portion of dewar 100. Movement of the frames permits adjustment of the coil windings 62 and 64 of the Helmholtz transformer 60 to vary the amplitude of white noise received at gradiometer 110. The legs 70 rest on or are epoxied onto the bottom of the faraday cage 10. In the illustrated embodiment, the frames 66 and 68 and legs 70 are made of glass fiber epoxy. Other arrangements of transformers or coils may be used around the sample tray 50 without departing from the spirit and scope of the invention.

[0060] Referring to Figure 4, there is shown a cross-sectional view of the faraday cage and its contents, showing windings 62 of Helmholtz transformer 60 in relation to dewar 100 and faraday cage 10. Note also in Figure 4 the positioning of sample tray 50 and sample 200.

[0061] Referring again to Figure 1, an amplitude adjustable white noise generator 80 is external to magnetic shielding cage 40, and is electrically connected to the Helmholtz transformer 60 through filter 90 by electrical cable 82. Referring to Figure 3, cable 82 is run through side opening 12, attenuation tube 24, and through cap 32 via hole 34. Cable 82 is a co-axial cable further comprising a twisted pair of copper conductors 84 surrounded by interior and exterior magnetic shielding 86 and 88, respectively. In other embodiments, the conductors can be any nonmagnetic electrically conductive material, such as silver or gold. The interior and exterior magnetic shielding 86 and 88 terminates at cap 32, leaving the twisted pair 84 to

span the remaining distance from the end cap to the Helmholtz transformer 60 shown in Figure 1. The interior magnetic shielding 86 is electrically connected to Faraday cage 16 through cap 32, while the exterior magnetic shielding is electrically connected to the magnetically shielded cage 40 shown in Figure 1.

[0062] Referring to Figure 1, the white noise generator 80 can generate nearly uniform noise across a frequency spectrum from zero to 100 kilohertz. In the illustrated embodiment, the filter 90 filters out noise above 50 kilohertz, but other frequency ranges may be used without departing from the spirit and scope of the invention.

[0063] White noise generator 80 is also electrically connected to the other input of dual trace oscilloscope 160 through patch cord 164.

[0064] Referring to Figures 1, 2 and 3, a sample of the substance 200 to be measured is placed on the sample tray 50 and the sample tray is placed within the faraday cage 10. In the first embodiment, the white noise generator 80 is used to inject white noise through the Helmholtz transformer 60. The noise signal creates an induced voltage in the gradiometer 110. The induced voltage in the gradiometer 110 is then detected and amplified by the SQUID 120, the output from the SQUID is further amplified by the flux locked loop 140 and sent to the SQUID controller 150, and then sent to the dual trace oscilloscope 160. The dual trace oscilloscope 160 is also used to display the signal generated by white noise generator 80.

[0065] The white noise signal is adjusted by altering the output of the white noise generator 80 and by rotating the Helmholtz transformer 60 around the sample 200, shown in Figure 2. Rotation of the Helmholtz transformer 60 about the axis of the hinged connection of frames 66 and 68 alters its phasing with respect to the gradiometer 110. Depending upon the desired phase alteration, the hinged connection of frames 66 and 68 permits windings 62 and 64 to remain parallel to one another while rotating approximately 30 to 40 degrees around sample tray 50. The hinged connection also permits windings 62 and 64 to rotate as much as approximately 60 degrees out of parallel, in order to alter signal phasing of the field generated by Helmholtz transformer 60 with respect to gradiometer 110. The typical adjustment of phase will include this out-of-parallel orientation, although the other orientation may be preferred in certain circumstances, to accommodate an irregularly

shaped sample 200, for example. Noise is applied and adjusted until the noise is 30 to 35 decibels above the molecular electromagnetic emissions sought to be detected. At this noise level, the noise takes on the characteristics of the molecular electromagnetic signal through the well-known phenomenon of stochastic resonance. The stochastic product sought is observed when the oscilloscope trace reflecting the signal detected by gradiometer 110 varies from the trace reflecting the signal directly from white noise generator 80. In alternative embodiments, the signal can be recorded and or processed by any commercially available equipment.

[0066] In an alternative embodiment, the method of detecting the molecular electromagnetic signals further comprises injecting noise 180° out of phase with the original noise signal applied at the Helmholtz transformer 60 through the noise suppression coil 124 of the SQUID 120. The stochastic product sought can then be observed when the oscilloscope trace reflecting the signal detected by gradiometer 110 becomes non-random.

[0067] Regardless of how the noise is injected and adjusted, the stochastic product can also be determined by observing when an increase in spectral peaks occurs. The spectral peaks can be observed as either a line plot on oscilloscope 160 or as numerical values, or by other well known measuring devices.

[0068] Embodiments of the present invention provide a method and apparatus for detecting extremely low-threshold molecular electromagnetic signals without external interference. They further provide for the output of those signals in a format readily usable by a wide variety of signal recording and processing equipment.

[0069] Referring now to Figure 5, an alternative embodiment to the molecular electromagnetic emission detection and processing system of the above Figures is shown. A system 700 includes a detection unit 702 coupled to a processing unit 704. Although the processing unit 704 is shown external to the detection unit 702, at least a part of the processing unit can be located within the detection unit.

[0070] The detection unit 702, which is shown in a cross-sectional view in Figure 5, includes multiple components nested or concentric with each other. A sample chamber or faraday cage 706 is nested within a metal cage 708. Each of the sample chamber 706 and the metal cage 708 can be comprised of aluminum material. The sample chamber 706 can be maintained in a vacuum and may be

temperature controlled to a preset temperature. The metal cage 708 is configured to function as a low pass filter.

[0071] Between the sample chamber 706 and the metal cage 708 and encircling the sample chamber 706 are a set of parallel heating coils or elements 710. One or more temperature sensor 711 is also located proximate to the heating elements 710 and the sample chamber 706. For example, four temperature sensors may be positioned at different locations around the exterior of the sample chamber 706. The heating elements 710 and the temperature sensor(s) 711 may be configured to maintain a certain temperature inside the sample chamber 706.

[0072] A shield 712 encircles the metal cage 708. The shield 712 is configured to provide additional magnetic field shielding or isolation for the sample chamber 706. The shield 712 can be comprised of lead or other magnetic shielding materials. The shield 712 is optional when sufficient shielding is provided by the sample chamber 706 and/or the metal cage 708.

[0073] Surrounding the shield 712 is a cryogen layer 716 with G10 insulation. The cryogen may be liquid helium. The cryogen layer 716 (also referred to as a cryogenic Dewar) is at an operating temperature of 4 degrees Kelvin. Surrounding the cryogen layer 716 is an outer shield 718. The outer shield 718 is comprised of nickel alloy and is configured to be a magnetic shield. The total amount of magnetic shielding provided by the detection unit 702 is approximately -100 dB, -100 dB, and -120 dB along the three orthogonal planes of a Cartesian coordinate system.

[0074] The various elements described above are electrically isolated from each other by air gaps or dielectric barriers (not shown). It should also be understood that the elements are not shown to scale relative to each other for ease of description.

[0075] A sample holder 720 can be manually or mechanically positioned within the sample chamber 706. The sample holder 720 may be lowered, raised, or removed from the top of the sample chamber 706. The sample holder 720 is comprised of a material that will not introduce Eddy currents and exhibits little or no inherent molecular rotation. As an example, the sample holder 720 can be comprised of high quality glass or Pyrex.

[0076] The detection unit 702 is configured to handle solid, liquid, or gas samples. Various sample holders may be utilized in the detection unit 702. For

example, depending on the size of the sample, a larger sample holder may be utilized. As another example, when the sample is reactive to air, the sample holder can be configured to encapsulate or form an airtight seal around the sample. In still another example, when the sample is in a gaseous state, the sample can be introduced inside the sample chamber 706 without the sample holder 720. For such samples, the sample chamber 706 is held at a vacuum. A vacuum seal 721 at the top of the sample chamber 706 aids in maintaining a vacuum and/or accommodating the sample holder 720.

[0077] A sense coil 722 and a sense coil 724, also referred to as detection coils, are provided above and below the sample holder 720, respectively. The coil windings of the sense coils 722, 724 are configured to operate in the direct current (DC) to approximately 50 kilohertz (kHz) range, with a center frequency of 25 kHz and a self-resonant frequency of 8.8 MHz. The sense coils 722, 724 are in the second derivative form and are configured to achieve approximately 100% coupling. In one embodiment, the coils 722, 724 are generally rectangular in shape and are held in place by G10 fasteners. The coils 722, 724 function as a second derivative gradiometer.

[0078] Helmholtz coils 726 and 728 may be vertically positioned between the shield 712 and the metal cage 708, as explained herein. Each of the coils 726 and 728 may be raised or lowered independently of each other. The coils 726 and 728, also referred to as a white or Gaussian noise generation coils, are at room or ambient temperature. The noise generated by the coils 726, 728 is approximately 0.10 Gauss.

[0079] The degree of coupling between the emissions from the sample and the coils 722, 724 may be changed by repositioning the sample holder 720 relative to the coils 722, 724, or by repositioning one or both of the coils 726, 728 relative to the sample holder 720.

[0080] The processing unit 704 is electrically coupled to the coils 722, 724, 726, and 728. The processing unit 704 specifies the white or Gaussian noise to be injected by the coils 726, 728 to the sample. The processing unit 104 also receives the induced voltage at the coils 722, 724 from the sample's electromagnetic emissions mixed with the injected Gaussian noise.

[0081] Referring to Figure 6, a processing unit employing aspects of the invention includes a sample tray 840 that permits a sample 842 to be inserted into, and removed from, a Faraday cage 844 and Helmholtz coil 746. A SQUID/gradiometer detector assembly 848 is positioned within a cryogenic dewar 850. A flux-locked loop 852 is coupled between the SQUID/gradiometer detector assembly 848 and a SQUID controller 854. The SQUID controller 854 may be a model iMC-303 iMAG multichannel controller provided by Tristan.

[0082] An analog noise generator 856 provides a noise signal (as noted above) to a phase lock loop 858. The x-axis output of the phase lock loop is provided to the Helmholtz coil 846, and may be attenuated, such as by 20 dB. The y-axis output of the phase lock loop is split by a signal splitter 860. One portion of the y-axis output is input the noise cancellation coil at the SQUID, which has a separate input for the gradiometer. The other portion of the y-axis signal is input oscilloscope 862, such as an analog/digital oscilloscope having Fourier functions like the Tektronix TDS 3000b (e.g., model 3032b). That is, the x-axis output of the phase lock loop drives the Helmholtz coil, and the y-axis output, which is in inverted form, is split to input the SQUID and the oscilloscope. Thus, the phase lock loop functions as a signal inverter. The oscilloscope trace is used to monitor the analog noise signal, for example, for determining when a sufficient level of noise for producing non-stationary spectral components is achieved. An analog tape recorder or recording device 864, coupled to the controller 854, records signals output from the device, and is preferably a wideband (e.g. 50 kHz) recorder. A PC controller 866 may be an MS Windows based PC interfacing with the controller 854 via, for example, an RS 232 port.

[0083] In Figure 7, a block diagram of another embodiment of the processing unit is shown. A dual phase lock-in amplifier 202 is configured to provide a first signal (e.g., "x" or noise signal) to the coils 726, 728 and a second signal (e.g., "y" or noise cancellation signal) to a noise cancellation coil of a superconducting quantum interference device (SQUID) 206. The amplifier 202 is configured to lock without an external reference and may be a Perkins Elmer model 7265 DSP lock-in amplifier. This amplifier works in a "virtual mode," where it locks to an initial reference frequency, and then removes the reference frequency to allow it to run freely and lock to "noise."

[0084] An analog noise generator 200 is electrically coupled to the amplifier 202. The generator 200 is configured to generate or induce an analog white Gaussian noise at the coils 726, 728 via the amplifier 202. As an example, the generator 200 may be a model 1380 manufactured by General Radio.

[0085] An impedance transformer 204 is electrically coupled between the SQUID 206 and the amplifier 202. The impedance transformer 204 is configured to provide impedance matching between the SQUID 206 and amplifier 202.

[0086] The noise cancellation feature of the SQUID 206 can be turned on or off. When the noise cancellation feature is turned on, the SQUID 206 is capable of canceling or nullifying the injected noise component from the detected emissions. To provide the noise cancellation, the first signal to the coils 726, 728 is a noise signal at 20 dB or 35 dB above the molecular electromagnetic emissions sought to be detected. At this level, the injected noise takes on the characteristics of the molecular electromagnetic signal through stochastic resonance. The second signal to the SQUID 206 is a noise cancellation signal and is inverted from the first signal at an amplitude sufficient to null the noise at the SQUID output (e.g., 180 degrees out of phase with respect to the first signal).

[0087] The SQUID 206 is a low temperature direct element SQUID. As an example, the SQUID 206 may be a model LSQ/20 LTS dC SQUID manufactured by Tristan Technologies, Inc. Alternatively, a high temperature or alternating current SQUID can be used. The coils 722, 724 (e.g., gradiometer) and the SQUID 206 (collectively referred to as the SQUID/gradiometer detector assembly) combined has a magnetic field measuring sensitivity of approximately 5 microTesla/ $\sqrt{\text{Hz}}$. The induced voltage in the coils 722, 724 is detected and amplified by the SQUID 206. The output of the SQUID 206 is a voltage approximately in the range of 0.2-0.8 microVolts.

[0088] The output of the SQUID 206 is the input to a SQUID controller 208. The SQUID controller 208 is configured to control the operational state of the SQUID 206 and further condition the detected signal. As an example, the SQUID controller 208 may be an iMC-303 iMAG multi-channel SQUID controller manufactured by Tristan Technologies, Inc.

[0089] The output of the SQUID controller 208 is inputted to an amplifier 210. The amplifier 210 is configured to provide a gain in the range of 0-100 dB. A gain of approximately 20 dB is provided when noise cancellation node is turned on at the SQUID 206. A gain of approximately 50 dB is provided when the SQUID 206 is providing no noise cancellation.

[0090] The amplified signal is inputted to a recorder or storage device 212. The recorder 212 is configured to convert the analog amplified signal to a digital signal and store the digital signal. In one embodiment, the recorder 212 stores 8600 data points per Hz and can handle 2.46 Mbits/sec. As an example, the recorder 212 may be a Sony digital audiotape (DAT) recorder. Using a DAT recorder, the raw signals or data sets can be sent to a third party for display or specific processing as desired.

[0091] A lowpass filter 214 filters the digitized data set from the recorder 212. The lowpass filter 214 is an analog filter and may be a Butterworth filter. The cutoff frequency is at approximately 50 kHz.

[0092] A bandpass filter 216 next filters the filtered data sets. The bandpass filter 216 is configured to be a digital filter with a bandwidth between DC to 50 kHz. The bandpass filter 216 can be adjusted for different bandwidths.

[0093] The output of the bandpass filter 216 is the input to a Fourier transform processor 218. The Fourier transform processor 218 is configured to convert the data set, which is in the time domain, to a data set in the frequency domain. The Fourier transform processor 218 performs a Fast Fourier Transform (FFT) type of transform.

[0094] The Fourier transformed data sets are the input to a correlation and comparison processor 220. The output of the recorder 212 is also an input to the processor 220. The processor 220 is configured to correlate the data set with previously recorded data sets, determine thresholds, and perform noise cancellation (when no noise cancellation is provided by the SQUID 206). The output of the processor 220 is a final data set representative of the spectrum of the sample's molecular low frequency electromagnetic emissions.

[0095] A user interface (UI) 222, such as a graphical user interface (GUI), may also be connected to at least the filter 216 and the processor 220 to specify signal processing parameters. The filter 216, processor 218, and the processor 220 can be

implemented as hardware, software, or firmware. For example, the filter 216 and the processor 218 may be implemented in one or more semiconductor chips. The processor 220 may be software implemented in a computing device.

[0096] This amplifier works in a "virtual mode," where it locks to an initial reference frequency, and then removes the reference frequency to allow it to run freely and lock to "noise." The analog noise generator (which is produced by General Radio, a truly analog noise generator) requires 20 dB and 45-dB attenuation for the Helmholtz and noise cancellation coil, respectively.

[0097] The Helmholtz coil may have a sweet spot of about one cubic inch with a balance of $1/100^{\text{th}}$ of a percent. In an alternative embodiments, the Helmholtz coil may move both vertically, rotationally (about the vertical axis), and from a parallel to spread apart in a pie shape. In one embodiment, the SQUID, gradiometer, and driving transformer (controller) have values of 1.8, 1.5 and 0.3 micro-Henrys, respectively. The Helmholtz coil may have a sensitivity of 0.5 Gauss per amp at the sweet spot.

[0098] Approximately 10 to 15 microvolts may be needed for a stochastic response. By injecting noise, the system has raised the sensitivity of the SQUID device. The SQUID device had a sensitivity of about 5 femtotesla without the noise. This system has been able to improve the sensitivity by 25 to 35 dB by injecting noise and using this stochastic resonance response, which amounts to nearly a 1,500% increase.

[0099] After receiving and recording signals from the system, a computer, such as a mainframe computer, supercomputer or high-performance computer does both pre and post processing, such by employing the Autosignal software product by Systat Software of Richmond CA, for the pre-processing, while Flexpro software product does the post-processing. Flexpro is a data (statistical) analysis software supplied by Dewetron, Inc. The following equations or options may be used in the Autosignal and Flexpro products.

[00100] "A flow diagram of the signal detection and processing performed by the system 100 is shown in Figure 8. When a sample is of interest, at least four signal detections or data runs are performed: a first data run at a time t_1 without the sample, a second data run at a time t_2 with the sample, a third data run at a time t_3

with the sample, and a fourth data run at a time t_4 without the sample. Performing and collecting data sets from more than one data run increases accuracy of the final (e.g., correlated) data set. In the four data runs, the parameters and conditions of the system 100 are held constant (e.g., temperature, amount of amplification, position of the coils, the noise signal, etc.).

[00101] At a block 300, the appropriate sample (or if it's a first or fourth data run, no sample), is placed in the system 100. A given sample, without injected noise, emits electromagnetic emissions in the DC-50 kHz range at an amplitude equal to or less than approximately 0.001 microTesla. To capture such low emissions, a white Gaussian noise is injected at a block 301.

[00102] At a block 302, the coils 722, 724 detect the induced voltage representative of the sample's emission and the injected noise. The induced voltage comprises a continuous stream of voltage values (amplitude and phase) as a function of time for the duration of a data run. A data run can be 2-20 minutes in length and hence, the data set corresponding to the data run comprises 2-20 minutes of voltage values as a function of time.

[00103] At a block 304, the injected noise is cancelled as the induced voltage is being detected. This block is omitted when the noise cancellation feature of the SQUID 206 is turned off.

[00104] At a block 306, the voltage values of the data set are amplified by 20-50 dB, depending on whether noise cancellation occurred at the block 304. And at a block 308, the amplified data set undergoes analog to digital (A/D) conversion and is stored in the recorder 212. A digitized data set can comprise millions of rows of data.

[00105] After the acquired data set is stored, at a block 310 a check is performed to see whether at least four data runs for the sample have occurred (e.g., have acquired at least four data sets). If four data sets for a given sample have been obtained, then lowpass filtering occurs at a block 312. Otherwise, the next data run is initiated (return to the block 300).

[00106] After lowpass filtering (block 312) and bandpass filtering (at a block 314) the digitized data sets, the data sets are converted to the frequency domain at a Fourier transform block 316.

[00107] Next, at a block 318, like data sets are correlated with each other at each data point. For example, the first data set corresponding to the first data run (e.g., a baseline or ambient noise data run) and the fourth data set corresponding to the fourth data run (e.g., another noise data run) are correlated to each other. If the amplitude value of the first data set at a given frequency is the same as the amplitude value of the fourth data set at that given frequency, then the correlation value or number for that given frequency would be 1.0. Alternatively, the range of correlation values may be set at between 0-100. Such correlation or comparison also occurs for the second and third data runs (e.g., the sample data runs). Because the acquired data sets are stored, they can be accessed at a later time as the remaining data runs are completed.

[00108] When the SQUID 206 provides no noise cancellation, then predetermined threshold levels are applied to each correlated data set to eliminate statistically irrelevant correlation values. A variety of threshold values may be used, depending on the length of the data runs (the longer the data runs, greater the accuracy of the acquired data) and the likely similarity of the sample's actual emission spectrum to other types of samples. In addition to the threshold levels, the correlations are averaged. Use of thresholds and averaging correlation results in the injected noise component becoming very small in the resulting correlated data set.

[00109] If noise cancellation is provided at the SQUID 206, then the use of thresholds and averaging correlations are not necessary.

[00110] Once the two sample data sets have been refined to a correlated sample data set and the two noise data sets have been refined to a correlated noise data set, the correlated noise data set is subtracted from the correlated sample data set. The resulting data set is the final data set (e.g., a data set representative of the emission spectrum of the sample) (block 320).

[00111] Since there can be 8600 data points per Hz and the final data set can have data points for a frequency range of DC-50 kHz, the final data set can comprise several hundred million rows of data. Each row of data can include the frequency, amplitude, phase, and a correlation value.

III. Method of producing an optimized time-domain signal

[00112] According to one aspect of the invention, it has been discovered that sample-dependent spectral features in a low-frequency time-domain signal obtained for a given sample can be optimized by recording time-domain signals for sample over a range of noise levels, that is power gain on the noise injected into the sample during signal recording. The recorded signals are then processed to reveal spectral signal features, and the time domain signal having an optimal spectral-features score, as detailed below, is selected. The selection of optimized or near-optimized time-domain signals is useful because it has been found, also in accordance with the invention, that transducing a chemical or biological system with an optimized time-domain signal gives a stronger and more predictable response than with a non-optimized time-domain signal. Viewed another way, selecting an optimized (or near-optimized) time-domain signal is useful in achieving reliable, detectable sample effects when a target system is transduced by the sample signal.

[00113] In general, the range of injected noise levels over which time-domain signals are typically recorded between about 0 to 1 volt, typically, or alternatively, the noise injected is preferably between about 30 to 35 decibels above the molecular electromagnetic emissions sought to be detected, e.g., in the range 70-80 -dbm. The number of samples that are recorded, that is, the number of noise-level intervals over which time-domain signals are recorded may vary from 10-100 or more, typically, and in any case, at sufficiently small intervals so that a good optimum signal can be identified. For example, the power gain of the noise generator level can be varied over 50 20 mV intervals. As will be seen below, when the spectral-feature scores for the signals are plotted against level of injected noise, the plot shows a peak extending over several different noise levels when the noise-level increments are suitable small.

[00114] The present invention contemplates three different methods for calculating spectral-feature scores for the recorded time-domain signals. These are (1) a histogram bin method, (2) generating an FFT of autocorrelated signals, and (3) averaging of FFTs, and each of these is detailed below.

[00115] Although not specifically described, it will be appreciated that each method may be carried out in a manual mode, where the user evaluates the spectra

on which a spectral-feature score is based, makes the noise-level adjustment for the next recording, and determines when a peak score is reached, or it may be carried out in an automated or semi-automated mode, in which the continuous incrementing of noise level and/or the evaluation of spectral-feature score, is performed by a computer-driven program.

A. Histogram Method of Generating Spectral Information

[00116] Figure 9 is a high level data flow diagram in the histogram method for generating spectral information. Data acquired from the SQUID (box 2002) or stored data (box 2004) is saved as 16 bit WAV data (box 2006), and converted into double-precision floating point data (box 2008). The converted data may be saved (box 2010) or displayed as a raw waveform (box 2012). The converted data is then passed to the algorithm described below with respect to Figure 10, and indicated by the box 2014 labeled Fourier Analysis. The histogram can be displayed at 2016. Alternatively, and as will be described below, the converted data may be passed to one of two additional al

[00117] With reference to Figure 10, the general flow of the histogram algorithm is to take a discrete sampled time-domain signal and use Fourier analysis to convert it to a frequency domain spectrum for further analysis. The time-domain signals are acquired from an ADC (analog/digital converter) and stored in the buffer indicated at 2102. This sample is *SampleDuration* seconds long, and is sampled at *SampleRate* samples per second, thus providing *SampleCount* ($SampleDuration * SampleRate$) samples. The *FrequencyRange* that can be recovered from the signal is defined as half the *SampleRate*, as defined by Nyquist. Thus, if a time-series signal is sampled at 10,000 samples per second, the *FrequencyRange* will be 0 Hz to 5 kHz. One Fourier algorithm that may be used is a Radix 2 Real Fast Fourier Transform (RFFT), which has a selectable frequency domain resolution (*FFTSize*) of powers of two up to 2^{16} . An *FFTSize* of 8192 is selected, to provide provides enough resolution to have at least one spectrum bin per Hertz as long as the *FrequencyRange* stays at or below 8 kHz. The *SampleDuration* should be long enough such that $SampleCount > (2 * FFTSize * 10)$ to ensure reliable results.

[00118] Since this FFT can only act on *FFTSize* samples at a time, the program must perform the FFT on the samples sequentially and average the results together

to get the final spectrum. If one chooses to skip *FFTSize* samples for each FFT, a statistical error of $1 / \text{FFTSize}^{0.5}$ is introduced. If, however, one chooses to overlap the FFT input by half the *FFTSize*, this error is reduced to $1 / (0.81 * 2 * \text{FFTSize})^{0.5}$. This reduces the error from 0.0110485435 to 0.0086805556. Additional information about errors and correlation analyses in general, consult Bendat & Piersol, "Engineering Applications of Correlation and Spectral Analysis", 1993.

[00119] Prior to performing the FFT on a given window, a data tapering filter may be applied to avoid spectral leakage due to sampling aliasing. This filter can be chosen from among Rectangular (no filter), Hamming, Hanning, Bartlett, Blackman and Blackman/Harris, as examples.

[00120] In an exemplary method, and as shown in box 2104, we have chosen 8192 for the variable *FFTSize*, which will be the number of time-domain samples we operate on at a time, as well as the number of discrete frequencies output by the FFT. Note that *FFTSize* = 8192 is the resolution, or number of bins in the range which is dictated by the sampling rate. The variable *n*, which dictates how many discrete RFFT's (Real FFT's) performed, is set by dividing the *SampleCount* by *FFTSize* * 2, the number of FFT bins. In order for the algorithm to generate sensible results, this number *n* should be at least 10 to 20 (although other values are possible), where more may be preferred to pick up weaker signals. This implies that for a given *SampleRate* and *FFTSize*, the *SampleDuration* must be long enough. A counter *m*, which counts from 0 to *n*, is initialized to zero, also as shown in box 2104.

[00121] The program first establishes three buffers: buffer 2108 for *FFTSize* histogram bins, that will accumulate counts at each bin frequency; buffer 2110 for average power at each bin frequency, and a buffer 2112 containing the *FFTSize* copied samples for each *m*.

[00122] The program initializes the histograms and arrays (box 2113) and copies *FFTSize* samples of the wave data into buffer 2112, at 2114, and performs an RFFT on the wave data (box 2115). The FFT is normalized so that the highest amplitude is 1 (box 2116) and the average power for all *FFTSize* bins is determined from the normalized signal (box 2117). For each bin frequency, the normalized value from the FFT at that frequency is added to each bin in buffer 2108 (box 2118).

[00123] In box 2119 the program then looks at the power at each bin frequency, relative to the average power calculated from above. If the power is within a certain factor epsilon (between 0 and 1) of the average power, then it is counted and the corresponding bin is incremented in the histogram buffer at 16. Otherwise it is discarded.

[00124] Note that the average power it is comparing to is for this FFT instance only. An enhanced, albeit slower algorithm might take two passes through the data and compute the average over all time before setting histogram levels. The comparison to epsilon helps to represent a power value that is significant enough for a frequency bin. Or in broader terms, the equation employing epsilon helps answer the question, "is there a signal at this frequency at this time?" If the answer is yes, it could due be one of two things: (1) stationary noise which is landing in this bin just this one time, or (2) a real low level periodic signal which will occur nearly every time. Thus, the histogram counts will weed out the noise hits, and enhance the low level signal hits. So, the averaging and epsilon factor allow one to select the smallest power level considered significant.

[00125] Counter m is incremented at box 2120, and the above process is repeated for each n set of WAV data until m is equal to n (box 2121). At each cycle, the average power for each bin is added to the associated bin at 2118, and each histogram bin is incremented by one when the power amplitude condition at 2114 is met.

[00126] When all n cycles of data have been considered, the average power in each bin is determined by dividing the total accumulated average power in each bin by n, the total number of cycles (box 2122) and the results displayed (box 2123). Except where structured noise exists, e.g., DC = 0 or at multiples of 60 Hz, the average power in each bin will be some relatively low number.

[00127] The relevant settings in this method are noise gain and the value of epsilon. This value determines a power value that will be used to distinguish an event over average value. At a value of 1, no events will be detected, since power will never be greater than average power. As epsilon approaches zero, virtually every value will be placed in a bin. Between 0 and 1, and typically at a value that gives a number of bin counts between about 20-50% of total bin counts for

structured noise, epsilon will have a maximum "spectral character," meaning the stochastic resonance events will be most highly favored over pure noise.

[00128] Therefore, one can systematically increase the power gain on the noise input, e.g., in 50 mV increments between 0 and 1 V, and at each power setting, adjust epsilon until a histogram having well defined peaks is observed. Where, for example, the sample being processed represents a 20 second time interval, total processing time for each different power and epsilon will be about 25 seconds. When a well-defined signal is observed, either the power setting or epsilon or both can be refined until an optimal histogram, meaning one with the largest number of identifiable peaks, is produced.

[00129] Under this algorithm, numerous bins may be filled and associated histogram rendered for low frequencies due to the general occurrence of noise (such as environmental noise) at the low frequencies. Thus, the system may simply ignore bins below a given frequency (e.g., below 1 kHz), but still render sufficient bin values at higher frequencies to determine unique signal signatures between samples.

[00130] Alternatively, since a purpose of the epsilon variable is to accommodate different average power levels determined in each cycle, the program could itself automatically adjust epsilon using a predefined function relating average power level to an optimal value of epsilon.

[00131] Similarly, the program could compare peak heights at each power setting, and automatically adjust the noise power setting until optimal peak heights or character is observed in the histograms.

[00132] Although the value of epsilon may be a fixed value for all frequencies, it is also contemplated to employ a frequency-dependent value for epsilon, to adjust for the higher value average energies that may be observed at low frequencies, e.g., DC to 1,000. A frequency-dependent epsilon factor could be determined, for example, by averaging a large number of low-frequency FFT regions, and determining a value of epsilon that "adjusts" average values to values comparable to those observed at higher frequencies.

B. FFT of autocorrelated signals

[00133] In a second general method for determining spectral-feature scores, time-domain signals recorded at a selected noise are autocorrelated, and a fast Fourier transform (FFT) of the autocorrelated signal is used to generate a spectral-features plot, that is, a plot of the signal in the frequency domain. The FFTs are then used to score the number of spectral signals above an average noise level over a selected frequency range, e.g., DC to 1 kHz or DC to 8 kHz.

[00134] Figure 11 is a flow diagram of steps carried out in scoring recorded time-domain signals according to this second embodiment. Time-domain signals are sampled, digitized, and filtered as above (box 402), with the gain on the noise level set to an initial level, as at 404. A typical time domain signal for a sample compound 402 is autocorrelated, at 408, using a standard autocorrelation algorithm, and the FFT of the autocorrelated function is generated, at 410, using a standard FFT algorithm.

[00135] An FFT plot is scored, at 412, by counting the number of spectral peaks that are statistically greater than the average noise observed in the autocorrelated FFT and the score is calculated at 414. This process is repeated, through steps 416 and 406, until a peak score is recorded, that is, until the score for a given signal begins to decline with increasing noise gain. The peak score is recorded, at 418, and the program or user selects, from the file of time-domain signals at 422, the signal corresponding to the peak score (box 420).

[00136] As above, this embodiment may be carried out in a manual mode, where the user manually adjusts the noise setting in increments, analyzes (counts peaks) from the FFT spectral plots by hand, and uses the peak score to identify one or more optimal time-domain signals. Alternatively, one or more aspects of the steps can be automated.

C. Averaged FFTs

[00137] In another embodiment for determining spectral-peak scores, an FFT of many, e.g., 10-20 time domain signals at each noise gain are averaged to produce a spectral-peaks plot, and scores are calculated as above.

[00138] Figure 12 is a flow diagram of steps carried out in scoring recorded time-domain signals according to this third embodiment. Time-domain signals are sampled, digitized, and filtered as above (box 424), with the gain on the noise level set to an initial level, as at 426. The program then generates a series of FFTs for the time domain signal(s) at each noise gain, at 428, and these plots are averaged at 430. Using the averaged FFT plot, scoring is done by counting the number of spectral peaks that are statistically greater than the average noise observed in the averaged FFT, as at 432, 434. This process is repeated, through the logic of 436 and 437, until a peak score is recorded, that is, until the score for a given signal begins to decline with increasing noise gain. The peak score is recorded, at 438, and the program or user selects, from the file of time-domain signals at 442, the signal corresponding to the peak score (box 440).

[00139] As above, this method may be carried out in a manual, semi-automated, or fully automated mode.

IV. Forming transducing signals

[00140] Signals for various therapeutic uses, or for uses to otherwise effect biological systems, may be generated directly from processed time-domain signals. Signals may also be formed by constructing a signal having specific identified peak frequencies. For example, the system can take advantage of "signal-activity relationship" in which molecular signal features, e.g., characteristic peak frequencies of a compound, are related to actual chemical activity for the compound, analogous to structure-activity relationships used in traditional drug design. In one general application, signal-activity relationships are used for drug screening, following, in one example, the following method.

[00141] First, one or more compounds having desired activity are identified, e.g., compounds capable of producing a desired response in a biological system. The system records a time-series signal for one of these compounds, and the wave form is processed or otherwise optimized to identify low-frequency peaks for that compound. ("Low-frequency" in this case refers to peaks at or below 10 kHz.) The steps are repeated for each of a group of structurally related compounds. The structurally related compounds include those that are active (produce a desired response), and some that are inactive for the tested biological response. The

spectral components of the two groups of compounds are compared to identify those spectral components that are uniquely associated with compound activity. For example, by analyzing forms from three active and two inactive compounds, one may identify those peaks in the signal found in the active compounds, and not in the inactive compounds, some of which are presumed to provide the desired biological response.

[00142] In like manner, the system may record and optimize any unknown compound. One may then analyze the resulting wave form with signals associated with known compounds to see if the unknown compound displays structural features associated the desired activity, and lack components associated with inactive components to help identify an active compound. Rules derivable from signal-structure relationships are more accessible and more predictive than rules derived from structure-activity relationships, since activity can be correlated with a relatively small number of peak frequencies, rather than a large number of structural variables. Thus, for use in drug design, one can use the presence or absence of certain peak frequencies to guide synthesis of drugs with improved pharmacokinetic or target activity. For example, if poor pharmacokinetic properties, or an undesired side effect, can be correlated with certain peak frequencies, novel compounds that lack or have reduced amplitudes in these frequencies would be suggested. As a result, the inventive system greatly simplifies the task of formulating useful drug-design rules, since the rules can be based on the relatively small number of peak frequencies.

[00143] A large database of spectral peak frequencies representing numerous compounds would allow one to combine signal features to "synthesize" virtually any drug or drug-combination property desired. By combining this database with a chemical compound database, one may generate chemical structures that display a desired peak-frequency set. This approach would be similar to current computer-assisted chemical-synthesis programs used to generate compound syntheses for novel compounds of interest.

[00144] The system can employ numerous signal processing techniques, as described herein. For example, signals from two or more structurally-related compounds can be compared with one or more signals from a structurally-related, but inactive or undesirable compound to identify only the desired frequency components between the signals. A resulting signal may thus be constructed that

includes only the desired peaks. By then generating a time-domain signal, that time-domain signal may be used for therapeutic purposes.

[00145] Of course, a time-domain signal may be generated from the processed frequency-domain signal of a single compound. For example, one may obtain the frequency-domain signal for a desired sample, and produce a processed, desired signal. From the processed signal, a time-domain signal may be generated using known techniques, which can then be employed for therapeutic or other uses as an analog to the compound itself.

[00146] Figure 15A shows a typical time domain signal for a sample compound, in this case the herbicide glyphosphate (RoundupR). The segment shown here is taken over the time interval 14.08 to 14.16 seconds. The time-domain signal is then autocorrelated using a standard autocorrelation algorithm, and the FFT of the autocorrelated function is generated using a standard FFT algorithm.

[00147] Using the FFT plot, such as shown in Figures 15B-15E, the plot is scored by counting the number of spectral peaks that are statistically greater than the average noise observed in the autocorrelated FFT. This process is repeated until a peak score is recorded, that is, until the score for a given signal begins to decline with increasing noise gain. The peak score is recorded and the program or user selects, from the file of time-domain signals, the signal corresponding to the peak score.

[00148] The series of autocorrelated FFT plots in Figures 15B-15E illustrate the signal analysis involved in this method. At a noise level of 70.9 -dbm (Figure 15B), very few peaks above background noise are observed (the highest spike represents 60 cycle noise). At the optimum noise level of 74.8 -dbm (Figures 15C and 15D), which represent different recordings at the same noise level), numerous peaks statistically greater than average noise are observed throughout the frequency range of DC-8 kHz. Several of these peaks are less prominent or have disappeared at the higher noise gain of 78.3 -dbm (Figure 15E).

[00149] When the spectral-features scores for these signals are plotted as a function of noise setting, as shown in Figure 15F, the peak score in the noise setting of about 75 -dbm is observed. From this plot, the time-domain signals corresponding to one or the peak score is selected.

V. Transduction apparatus and protocols

[00150] This section describes equipment and methodology for transducing a sample with signals formed in accordance with aspects of the present invention, and summarizes experiments that demonstrate the response of various biological systems to time-domain signals of the present invention. The signals employed in these experiments, which are optimized time-domain signals formed in accordance with the method described above demonstrate the ability of signals in accordance with the invention to produce a compound-specific response in various biological systems.

[00151] Figure 13 shows the layout of equipment for transducing a sample with an agent-specific signal, in accordance with the invention. The particular layout accommodates five different samples, including three samples 444, 446, and 448 which are held within transductions coils, and exposed to electromagnetic signals, a sample 450 that serves as a control, and a sample 452 that serves as a chemical-induction control. The system of Figure 13 may be used for experimentation; if used for treating a patient, then some elements may be omitted, such as 448, 450, 452, etc.

[00152] Transduction by an agent-specific signal is carried out by "playing" the optimized agent-specific signal to the sample, using, where the signal is recorded on a CD, and is played on a CD recorded 454 through a preamplifier 456 and an audio amplifier 458. This signal is supplied to the electromagnetic coils 444 and 446 through separate channels, as shown. In one embodiment, a Sony Model CDP CE375 CD Player is used. Channel 1 of the Player is connected to CD input 1 of Adcom Pre Amplifier Model GFP 750. Channel 2 is connected to CD input 2 of Adcom Pre Amplifier Model GFP 750. CD's are recorded to play identical signals from each channel. Alternatively, CD's may be recorded to play different signals from each channel. The coil in sample 448 is used primarily to produce a white noise field as a control for experiments. For example, a GR analog noise generator provides a white Gaussian noise source for this coil. Alternatively, this coil can be used to play any pre recorded transduction signal via a second Crown amplifier.

[00153] Figure 14 shows sample transduction equipment 466 such as represented by any of samples 444, 446, and 448 in Figure 13. The equipment

includes a chamber 468 housing an electromagnet 470, and various probes for monitoring conditions within the chamber, e.g., temperature. The electromagnet sits on a base 474, and includes, conventionally a toroidal ferromagnetic core and wire windings.

[00154] In one embodiment, the coils are engineered and manufactured by American Magnetics to provide uniform performance between coils. Each coil consists of 416 turns of #8 gauge (awg) square copper magnet wire, enamel coated, about a 2" air core. Each coil can produce approximately 1500 Gauss in the center at 10 Volts RMS at 10 Amps RMS at 11 Hertz without exceeding a 15 degree Celsius rise in temperature.

[00155] In operation, the sample, e.g., a human patient or a portion of the patient's body is placed between the centrally between the coils. Thus, for example, the coils may be at opposite ends of a support bed, or on opposite sides of the bed, and on opposite sides of the patient's head. The coil is then activated, using signal-generation equipment like that shown in Figure 13, for a predetermined therapeutic period, e.g., 1 to several hours.

[00156] Figure 16 shows an example of a process for creating and applying signals under the inventive system. Under block 3102, the system receives and records a time domain signal from one or more samples, in a manner described above. Under block 3104, the system generates a frequency domain signal, and then processes that signal to isolate the desired frequency components from undesired components. Under block 3106, the processed frequency domain signal is converted back into a time domain signal. The time domain signal may then be applied to a biological system to generate a desired result, under block 3108.

[00157] Referring to Figure 18, a method 3300 for modifying waveforms begins in block 3302 where the user obtains a starting waveform. For example, the user, using standard user interface techniques, selects and retrieves from data storage a desired waveform. Alternatively, the user may obtain a signal during "live" interrogation of a sample.

[00158] In block 3304, the user can combine the starting waveform with another waveform and if so desired, the user retrieves another waveform under block 3306. Of course, the user can simply modify the starting waveform, if desired.

[00159] Under block 3308, the user modifies the starting waveform using any of a variety of techniques. Figure 19C shows an example where the user may simply employ standard user interface techniques, such as a mouse, to manipulate a pointer 3404 and attenuate (or amplify) one or more frequency peaks in the starting waveform as displayed on a display device. For example, the user can simply click on a peak 3402 of a displayed portion of a waveform and, using the mouse, drag the peak down to attenuate its magnitude, as shown in Figure 19D.

[00160] Many other techniques may be employed. The user may simply select a portion of a waveform, cut or copy it, and then paste it into the starting waveform. For example, referring to Figure 19A, the user may move the cursor about a portion of a waveform to select that portion of the waveform (shown as a dashed line box 3406). Once selected, the user can select from one of several menu choices, such as to cut that portion from the waveform. Alternatively, once selected, the user may modify that portion of the waveform, such as by replacing it with a flat line, attenuate it, amplify it, or perform various other signal processing techniques.

[00161] The system may employ a library of waveforms that can be inserted or employed as desired by the user. The user can select a portion of the signal and cause it to filter out all peaks, thereby eliminating noise or undesired frequency components in the waveform. For example, Figure 19B shows an example of a waveform or filter signal 3408 that may be stored in a library. By applying the signal 3408 to the waveform of Figure 19A, the system provides the resulting, processed waveform shown in Figure 19C.

[00162] The system may employ various mathematical techniques under block 3308 to modify the starting waveform. For example, the starting waveform may be combined using a variety of mathematical techniques with one or more waveforms retrieved under block 3306. Examples of such mathematical operations include: addition, subtraction, multiplication, convolution, cross-correlation, scaling of starting waveform (SW) as a linear or non-linear function of other waveforms, etc.

[00163] Under block 3310, the routine 3300 queries the user regarding whether more modifications to the starting waveform are desired. If so, the routine loops back to again perform under blocks 3304 through 3308. If not, then in block 3312, the user may store the resulting waveform. The stored waveform can then be used

for future modifications to other starting waveforms, used for therapeutic effect, or a variety of other reasons, described herein.

[00164] The following are some examples of additional techniques to shape a waveform or set of waveforms in time series.

[00165] Passive Filters: simple electronic filters are based on combinations of resistors, inductors and capacitors (or logical or programmed representations of same). These filters can be used to shape the waveform prior to recording, prior to processing, or prior to transduction. Various existing software packages or routines permit a user to model the responsive electronic filters. Such software routines may be readily employed under the inventive system to filter frequency domain waveforms using software modeled versions of such electronic filters.

[00166] Active Filters: hardware or software filters can also be implemented using a combination of passive components and amplifiers to create active filters. These can have high Q, and achieve resonance without the use of inductors. As with passive filters, software applications or routines exist for modeling the response of active filters, and such routines may be employed herein to modify waveforms using one or more active filter models. The inventive system may employ similar existing software routines to implement with the filters, processing and shaping described below.

[00167] Digital Filters: a digital filter is an electronic filter (usually linear), in discrete time, that is normally implemented through digital electronic computation. Digital filters are typically either finite impulse response (FIR) or infinite impulse response (IIR), though there are others, such as a hybrid class of filters known as truncated infinite impulse response (TIIR) filters, which show finite impulse responses despite being made from IIR components.

[00168] Digital Signal Processing: digital signal processing (e.g., executed as a computer program) may simulate, e.g., comb filter having a tapped delay line. The program selects numbers from a string of digital values representing the signal, at a spacing that simulates a comb of a tapped delay line. These numbers are multiplied by constants, and added together to make the output of the filter. DSP allows for multiple pass bands or multiple band gaps, essentially allowing only a select set of frequencies to make it to an output stage.

[00169] Wave Shaping: many well known methods exist for shaping a waveform by altering its rise time, sustain time, and decay time, or otherwise altering a signal from, or to a sine wave using full wave rectifiers or pulse width modulation (as examples).

[00170] All of the equipment described herein may be scaled to produce systems of greater or lesser size or intensity for various applications. For example, if the system to be used to treat the human patient, then a system having a coil for generating electromagnetic waves to be directed at a patient may be constructed. In one example, a bed having embedded therein round or square Helmholtz coils would receive the time-domain signal created from the processed frequency-domain signal. The patient would then receive the resulting electromagnetic wave to induce the desired biological effect that would otherwise be provided by, for example, ingesting the compound from which the signals was generated.

~~**[00171]**~~ A system for more targeted application of electromagnetic waves to a patient is of course possible. For example, one or more coils may be provided within a small device (such as a helmet, or handheld wand). This output device receives the time-domain signal produced from a desired frequency-domain signal, as noted above. Resulting electromagnetic waves can be directed to specific parts of a patient's body via the output device to produce a desired effect at a localized portion of the patient.

[00172] Figure 17 shows an example of such a signal output device. A database 3202 stores signals from one or more compounds or samples. Alternatively, the signals may be unprocessed frequency- or time-domain signals generated as noted above. A computer 3204 retrieves the signal (or signals) and provides it to a signal generator 3206. For example, the computer retrieves a desired time-domain signal generated from a processed frequency domain signal that was created from a specific compound. The computer then provides the time domain signal to the signal generator 3206 to simply amplify the signal. Alternatively, the computer may retrieve processed frequency-domain signals that the signal generator converts into time-domain signals. The signals output from the signal generator 3206 may be modified by a signal modifier 3208. The signal modifier may perform additional amplification, filtering, and so forth. In an alternative embodiment, the computer 3204 performs the necessary signal generation modification, and thus separate circuitry for the signal

generator 3206 and signal modifier 3208 may be omitted. Alternatively, the signal generator 3206 or signal modifier 3208 may be eliminated.

[00173] The signal output device 3210 receives the signal and applies to a patient 3212. As noted above, the signal output device may be a patient bed having embedded therein one or more coils to output electromagnetic waves. Alternatively, the signal output device 3210 can be a small, handheld device, a wearable device (such as an article of clothing containing a coil), and so forth.

[00174] The detector 702 obtains a signal from the sample 200, and that signal is processed by the processing unit 704 to produce a digital file 1501, such as a .wav file. That file may then be stored on a storage media 1502 and distributed or transported to a remote computer or other device. Any of the storage media noted above may be employed for transporting signals or data files.

[00175] Aspects of the invention may be implemented in computer-executable instructions, such as routines executed by a general-purpose computer, e.g., a server computer, wireless device or personal computer. Those skilled in the relevant art will appreciate that the invention can be practiced with other communications, data processing, or computer system configurations, including: Internet appliances, hand-held devices (including personal digital assistants (PDAs)), wearable computers, all manner of cellular or mobile phones, multi-processor systems, microprocessor-based or programmable consumer electronics, set-top boxes, network PCs, mini-computers, mainframe computers, and the like. Indeed, the terms "computer," "computing device," and similar terms are generally used interchangeably herein, and refer to any of the above devices and systems, as well as any data processor.

[00176] Aspects of the invention can be embodied in a special purpose computer or data processor that is specifically programmed, configured, or constructed to perform one or more of the computer-executable instructions explained in detail herein. Aspects of the invention can also be practiced in distributed computing environments where tasks or modules are performed by remote processing devices, which are linked through a communications network, such as a Local Area Network (LAN), Wide Area Network (WAN), or the Internet. In a distributed computing

environment, program modules may be located in both local and remote memory storage devices.

[00177] Aspects of the invention, such as data files, may be stored or distributed on computer-readable media, including magnetically or optically readable computer discs, hard-wired or preprogrammed chips (e.g., EEPROM semiconductor chips), nanotechnology memory, biological memory, or other data storage media. Indeed, computer implemented instructions, data structures, screen displays, wave/signal files, and other data under aspects of the invention may be distributed over the Internet or over other networks (including wireless networks), on a propagated signal on a propagation medium (e.g., an electromagnetic wave(s), a sound wave, etc.) over a period of time, or they may be provided on any analog or digital network (packet switched, circuit switched, or other scheme).

[00178] Alternatively, a transmitter 1504 within a signal collection, processing and transmission system 1500 transmits the file to a network 1506 (e.g., the Internet), either via an appropriate cable or wire, or wirelessly. The file then may be transmitted to a computer 1512 (again, wired or wirelessly).

[00179] The file may be transmitted via the network to a remote location, such as to a transducer-receiver 1508. For example, a satellite network 1510 could be used to transmit the file to the transducer-receiver 1508.

[00180] The transducer-receiver 1508 could be a standard receiver for receiving the file, and include a transducer for transducing the file as an electromagnetic signal to be applied. In one embodiment, an implanted transducer-receiver is implanted into a patient, body or structure. Where the receiver component of the transducer-receiver 1508 is a wireless receiver, then the transducer/receiver may receive the file wirelessly via the network (or satellite). In an alternative embodiment, a cell phone or mobile device 1514 receives the file from the network and relays it to the transducer-receiver via any known wireless protocol, including short range wireless protocols such as Bluetooth, any of the IEEE802.11 protocols, etc.

[00181] A transducer-transceiver 1516, similar to the transducer-receiver 1508, has a sensor 1518. Thus, the transducer-transceiver 1516 can not only similarly receive the transmitted file 1501 and transduce or apply it to a biological system, but

also obtain data from the sensor 1518 and transmit that data back to the system 1500 (e.g., via the network).

[00182] According to Figure 21, an example of the transducer-receiver 1508 and transducer-transceiver 1516 is provided which includes a power source 1530 for providing power to the device. A receiver-transceiver 1532 wired or wirelessly receives the file 1501, which may then be transduced or applied to a subject or sample via a transducer 1534. The file may be amplified by an amplifier 1536 and/or processed by a processor 1538. Memory 1540 may store the file, or store data obtained from one or more optional sensors 1518.

[00183] Figures 22 and 23 show transduction coils suitable for use in aspects of the invention. A transducer 494 in Figure 22 is a long solenoid, e.g., up to several feet in length. The field inside the solenoid is parallel to the axis of the solenoid and constant within the solenoid, going to zero outside the solenoid (in an approximation of an infinitely long solenoid). This finite length coil will have a substantially uniform field only near its center. Thus, by placing the sample or subject at the center of the coil, a substantially uniform magnetic field is created at the sample when the coil is energized with the data file 1501 or MIDS signal.

[00184] By adding additional turns to the solenoid, such as additional turns 500 in solenoid 496 in Figure 23, additional field strength can be added at the ends of the coil to compensate for the fall off of the coil's magnetic fields at its ends.

[00185] With either or additional embodiments, the transduction coil may be a small implantable ferromagnetic coil, such as a vascular stent coil capable of receiving transducing signals either by electrodes attached to opposite ends of the coil, by an implantable system (like systems 1508, 1516) or by a remote, inductive system in which an electromagnet is placed near the body surface, against the patient's chest, and signals are transmitted inductively to the implanted coil.

[00186] As noted above, the system utilizes, as input, soundfiles obtained in stochastic resonance experiments and outputs frequencies, amplitudes, and phases of the content sinusoids. The system may employ a software routine, dubbed "peakfinder," which in turn employ other software packages, such as Octave, and Pd, both of which are open-source and currently supported software platforms.

[00187] In addition, two environment variables may be used: PF_TMP which specifies a temporary directory and PF_BASE which specifies the location of a peakfinder folder. If PF_BASE is not supplied, a peakfinder.sh script attempts to infer it from its own invocation (assuming it is invoked as an absolute pathname). The input file is a stereo soundfile, assumed to be at a standard sample rate of 44100. The file format may be "wav," "au," or "aiff," in 16, 24, or 32 bit sample frames. The output file is an ASCII file specifying one sinusoid. For instance:

595	100.095749	0.095624	-0.091218	-0.028693
1487	250.155258	0.100177	0.040727	0.091524

[00188] Here the first field is the frequency in units of the fundamental analysis frequency, explained below, the second is the frequency in Hertz, the third is the peak magnitude of the sinusoid, in the input soundfile native units, and the fourth and fifth are the amplitudes of the cosine and sine components of the sinusoid, the real and imaginary parts of the complex amplitude. The magnitude could, of course, be inferred from the real and imaginary components. The first field has no physical meaning and is intended for debugging purposes.

[00189] A technique for determining the amplitude and frequency of a single sinusoid in white noise is the Maximum Likelihood (ML) method, which has been extended to multiple sinusoids. This methods assume that the number of sinusoids is known in advance. The problem of finding an un-predetermined number of sinusoids is harder to treat mathematically but can be dealt with assuming that the sinusoids in question are adequately separated in frequency. Furthermore, a method is needed to discriminate between the presence and absence of a sinusoid.

[00190] The following analysis starts by considering a single sinusoid in white noise and progresses to the problems of multiple sinusoids and non-white (e.g., pink) noise. Given a measured signal:

$$x[n], n = 0, \dots, N,$$

the (discrete-time) unnormalized Fourier transform is defined as:

$$FT\{x[n]\}(k) = \sum_{n=0}^{N-1} e^{-2\pi i n k / N} x[n],$$

where k is the frequency in units of the fundamental frequency of the analysis; $2\pi/N$ radians per sample. k need not be an integer; in practice extra values of k can be filled in as needed by zero-padding the signal. With the assumption that a single sinusoid is present, its most likely frequency is given by:

$$k = \arg \max |FT\{x[n]\}(k)|.$$

In other words, the best estimate is simply the value of k at which the Fourier transform's magnitude is the largest.

[00191] Next, the system determines if the estimated value of k corresponds to a true sinusoid or simply to random fluctuations. For this, the null hypothesis is analyzed to determine whether $x[n]$ only contains white noise, with mean 0 and RMS amplitude σ , for instance. The Fourier transform at each point k is a sum of N independent random variables, each equal to a sample $x[n]$ times a complex number of unit magnitude, so the mean of each point of the Fourier transform is still zero, and the standard deviation is $\sigma\sqrt{N}$. If the tail behavior of the individual noise samples is well behaved (which it is for Gaussian or Uniform noise, for instance) the resulting random variable $FT\{x[n]\}(k)$ will be very nearly Gaussian for the values of N used (on the order of 10^6). So the probability of exceeding more than about $5\sigma\sqrt{N}$ is very small.

[00192] On the other hand, a real-valued sinusoid with peak amplitude a and frequency k (in the usual units of $2\pi/N$) has a Fourier transform magnitude of $aN/2$. To get a magnitude of $5\sigma\sqrt{N}$, we only need a to be at least

$$a \approx \frac{10\sigma}{\sqrt{N}} \sim \frac{\sigma}{100}$$

[00193] The method zero-pads the recorded soundfile (between a factor of two and four, depending on the next power of two), and then reports peaks that exceed this amplitude threshold. A peak is defined as having greater magnitude for the given value of k than for its neighbors, and also having at least half again the magnitude of the twenty neighboring values of k (a band of roughly $20\pi/N$ Hz, or 1/3 Hz. for a one-minute sample.)

[00194] If several sinusoids are present, provided their frequencies are mutually spaced more than about $20\pi/N$, the above method should resolve them separately; each sinusoid's influence on the calculated Fourier transform drops off as $2/3\pi k$ in amplitude at k frequency units away from the peak.

[00195] To compensate for the non-white nature of noise signals, the spectral envelope of the measured signal is estimated. The noise can be assumed to be locally white in each narrow range of frequency ($20\pi/N$ as above), with the value of σ varying gently according to the frequency range chosen. Another issue is to determine whether the injected noise sample can be subtracted from the measured output of the experiment. In such a situation, with an easily measurable transfer function relating the two, even if it is nonlinear, an estimate of the transfer function is used to remove the bulk of the noise from the measured signal. This also increases the sensitivity of the method.

[00196] As can be seen from the description provided above, the system allows a user to create waveforms that may be used for therapeutic affect or otherwise induce a reaction in a biological system. Waveforms or spectral series generated from two or more compounds may be obtained. These two signals may then be combined to create a single, combined signal having the properties of the two individual signals. If, for example, the two original signals related to two different compounds having two different therapeutic properties, then the resulting, combined signal would have the combined therapeutic properties of the two compounds. The combined signal may then be manipulated to remove unwanted frequency component that have been found to be associated with side effects or negative reactions in a biological system.

[00197] Alternatively, if the two compounds produce similar responses in a biological system, then the two signals generated from those compounds can be compared to identify common frequency components associated with generating the biological effect. A third signal may then be generated that includes only those frequency components associated with the biological effect. Thus, for example, signals from certain pain reliever drugs may be compared to identify common frequency components, and then generate a resulting signal for use in transmission, storage, or application to a biological system. Indeed, the system permits a new signal to be constructed that is not based directly on signals generated from one or more compounds. Instead, the system permits a signal to be generated having only

peaks at desired frequencies, where such peaks have a desired result in a biological system. Thus, such a synthesized signal is independent of existing compounds.

CONCLUSION

[00198] Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise," "comprising," and the like are to be construed in an inclusive sense, as opposed to an exclusive or exhaustive sense; that is to say, in the sense of "including, but not limited to." The word "coupled", as generally used herein, refers to two or more elements that may be either directly connected, or connected by way of one or more intermediate elements. Additionally, the words "herein," "above," "below," and words of similar import, when used in this application, shall refer to this application as a whole and not to any particular portions of this application. Where the context permits, words in the above Detailed Description using the singular or plural number may also include the plural or singular number respectively. The word "or" in reference to a list of two or more items, that word covers all of the following interpretations of the word: any of the items in the list, all of the items in the list, and any combination of the items in the list.

[00199] The above detailed description of embodiments of the invention is not intended to be exhaustive or to limit the invention to the precise form disclosed above. While specific embodiments of, and examples for, the invention are described above for illustrative purposes, various equivalent modifications are possible within the scope of the invention, as those skilled in the relevant art will recognize. For example, while processes or blocks are presented in a given order, alternative embodiments may perform routines having steps, or employ systems having blocks, in a different order, and some processes or blocks may be deleted, moved, added, subdivided, combined, and/or modified. Each of these processes or blocks may be implemented in a variety of different ways. Also, while processes or blocks are at times shown as being performed in series, these processes or blocks may instead be performed in parallel, or may be performed at different times.

[00200] The teachings of the invention provided herein can be applied to other systems, not necessarily the system described above. The elements and acts of the

various embodiments described above can be combined to provide further embodiments.

[00201]

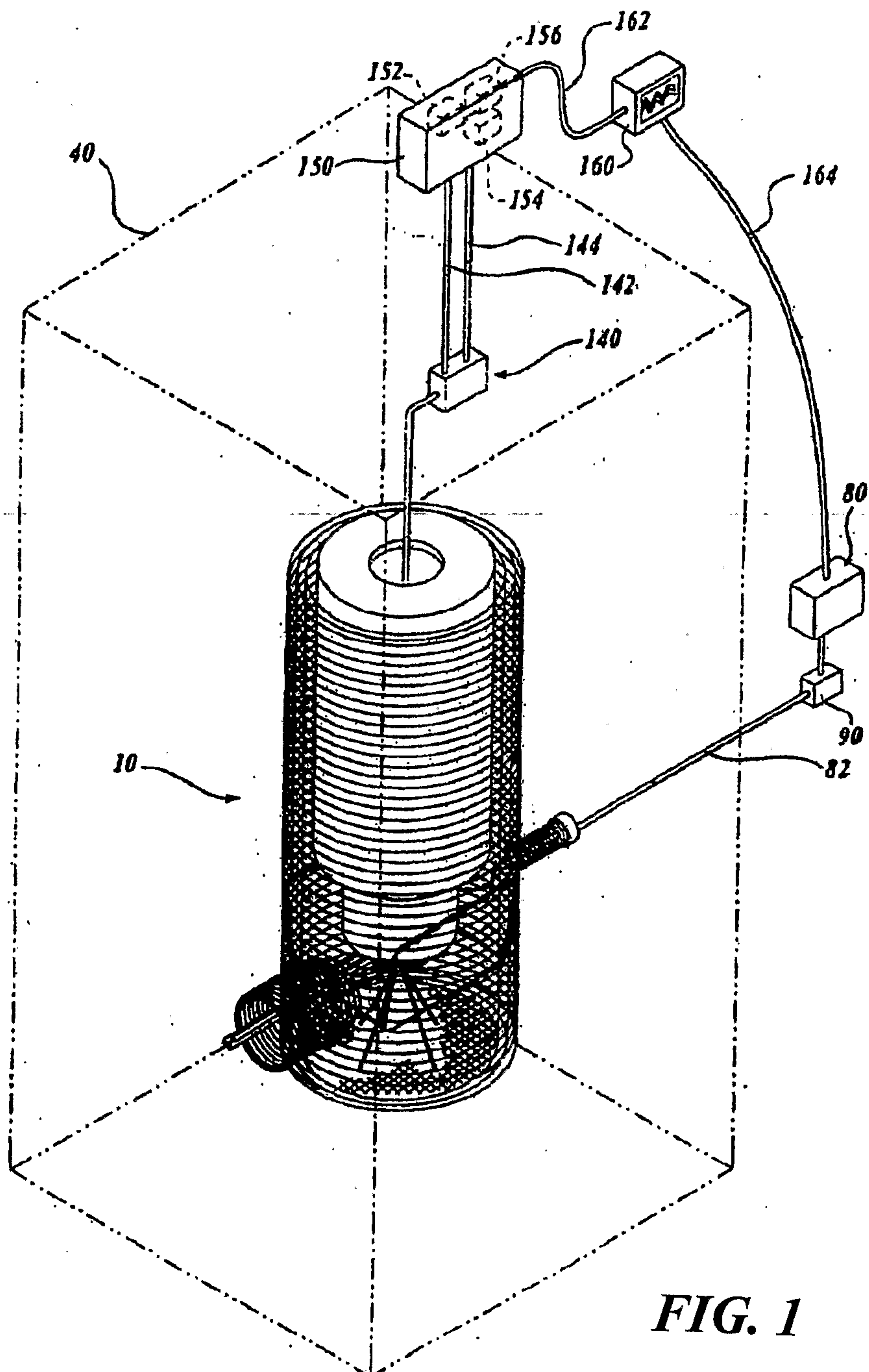
Aspects of the invention can be modified, if necessary, to employ the systems, functions, and concepts of the various references described above to provide yet further embodiments of the invention.

[00202] These and other changes can be made to the invention in light of the above Detailed Description. While the above description details certain embodiments of the invention and describes the best mode contemplated, no matter how detailed the above appears in text, the invention can be practiced in many ways. Details of the signal processing system may vary considerably in its implementation details, while still being encompassed by the invention disclosed herein. As noted above, particular terminology used when describing certain features or aspects of the invention should not be taken to imply that the terminology is being redefined herein to be restricted to any specific characteristics, features, or aspects of the invention with which that terminology is associated. In general, the terms used in the following claims should not be construed to limit the invention to the specific embodiments disclosed in the specification, unless the above Detailed Description section explicitly defines such terms. Accordingly, the actual scope of the invention encompasses not only the disclosed embodiments, but also all equivalent ways of practicing or implementing the invention under the claims.

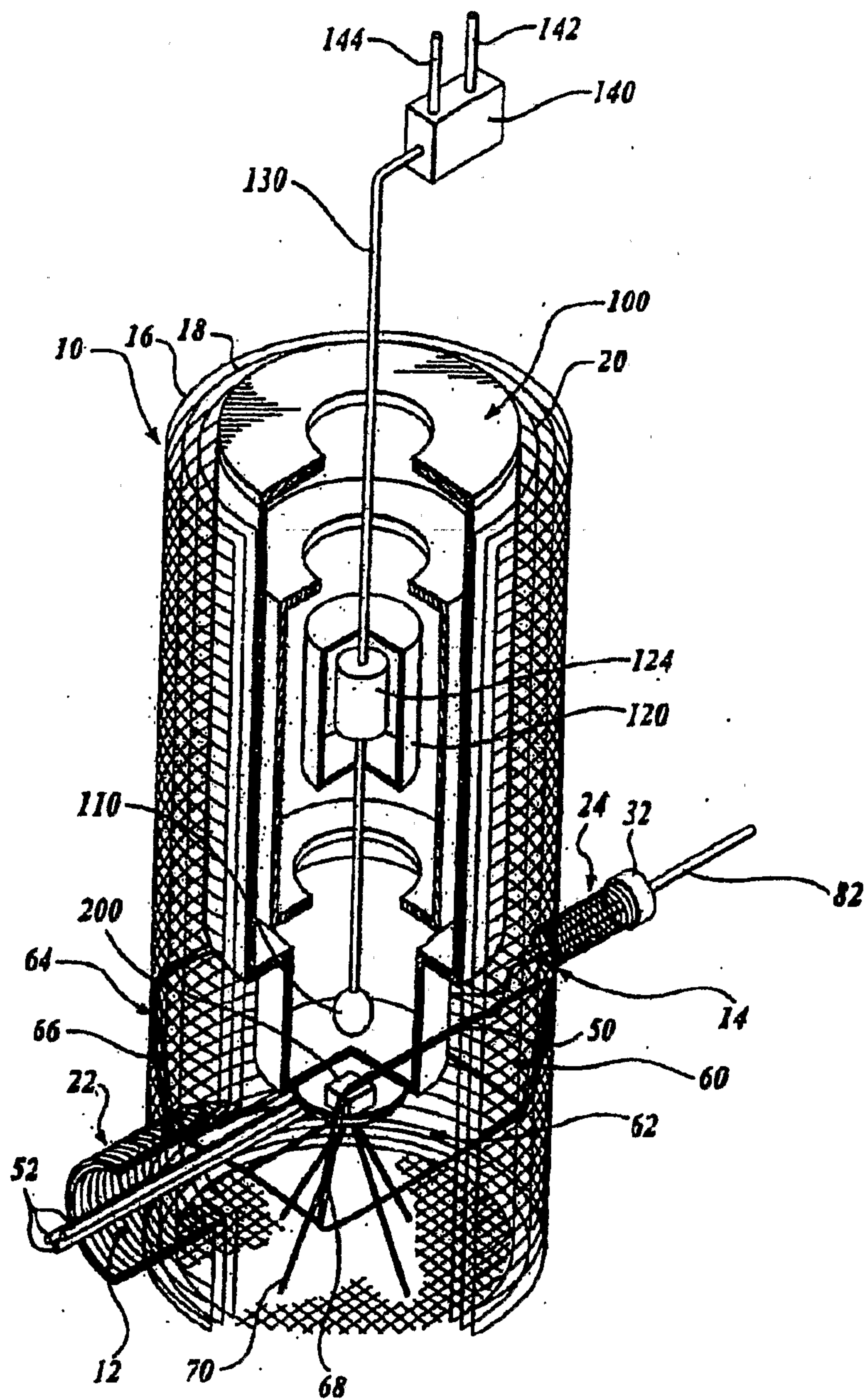
WHAT IS CLAIMED IS:

1. A method for generating an electromagnetic signal effective to produce selected chemical or biological effects associated with a selected chemical or biological agent, the method comprising:
 - 5 (a) inserting a sample containing the agent into a magnetically shielded detection apparatus to provide molecular signals;
 - (b) injecting noise into the sample in the magnetically shielded detection apparatus at a selected noise amplitude;
 - 10 (c) recording a time-domain signal produced by the sample during step (b) and composed of sample source radiation superimposed on the injected noise;
 - (d) repeating steps (b)-(c) at each of a plurality of different noise amplitudes within a selected range;
 - 15 (e) calculating spectral-feature scores for the recorded signals from step (d); and
 - (f) selecting a recorded signal based on its score calculated in step (e).

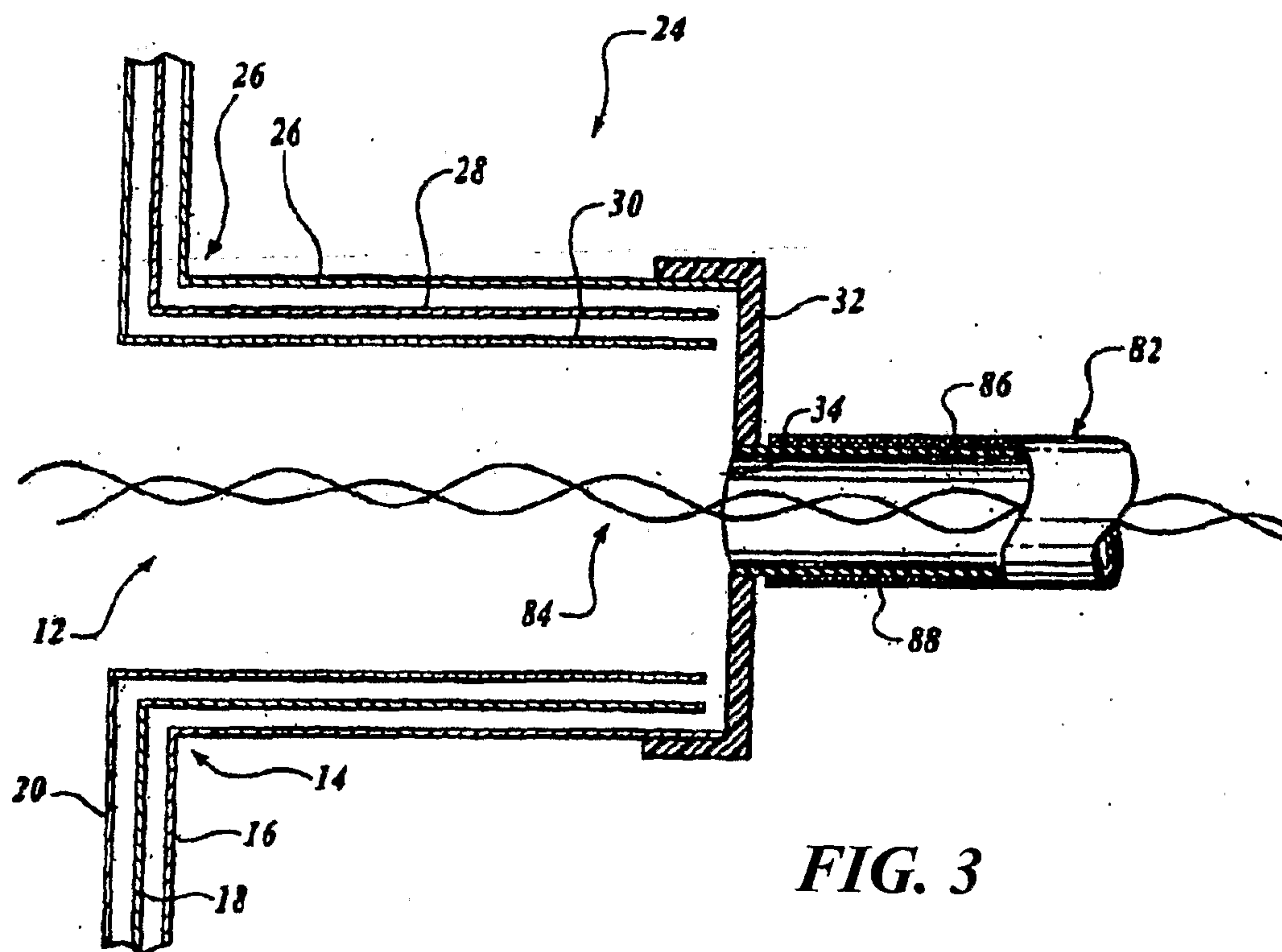
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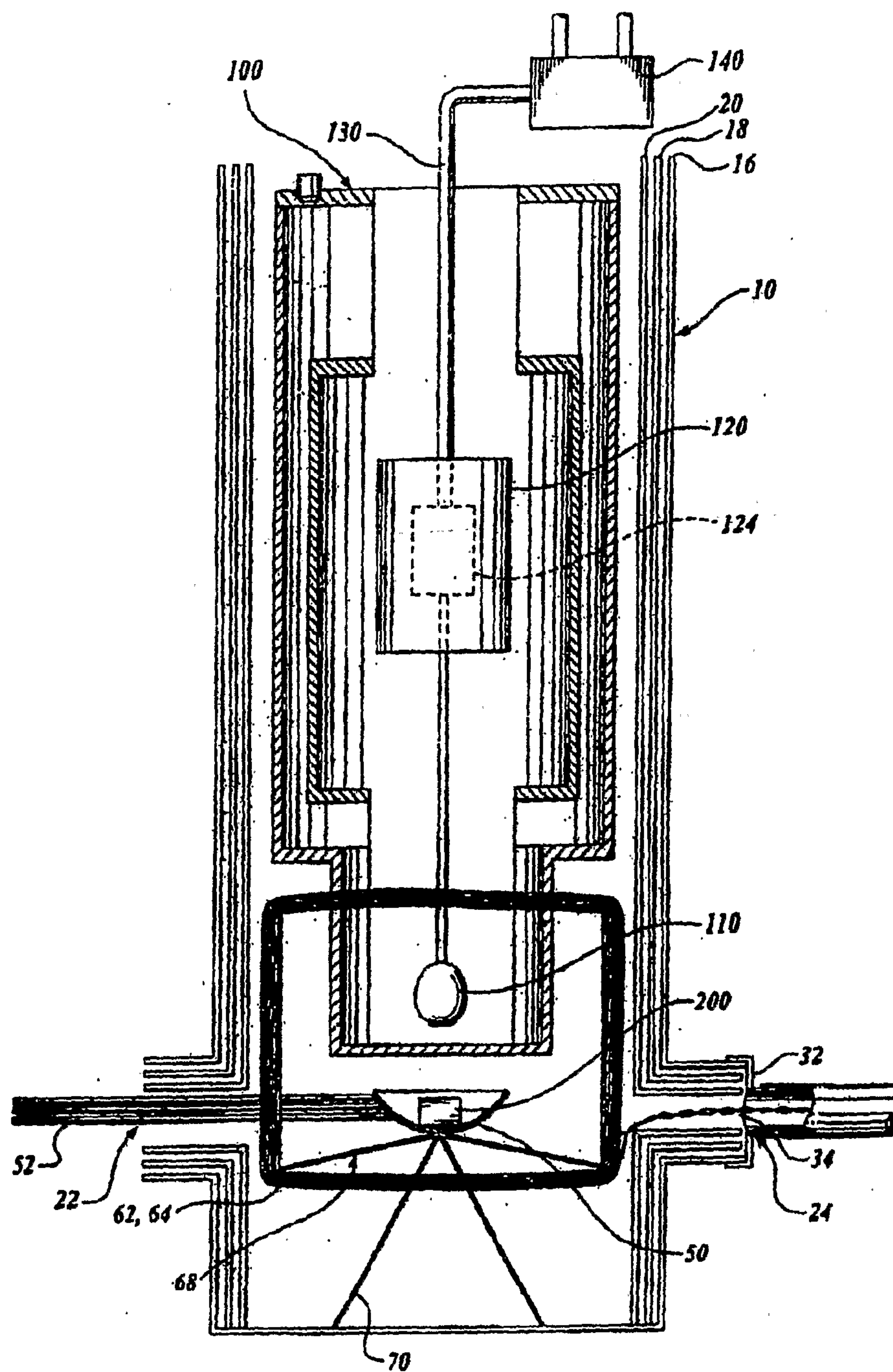
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**FIG. 2**

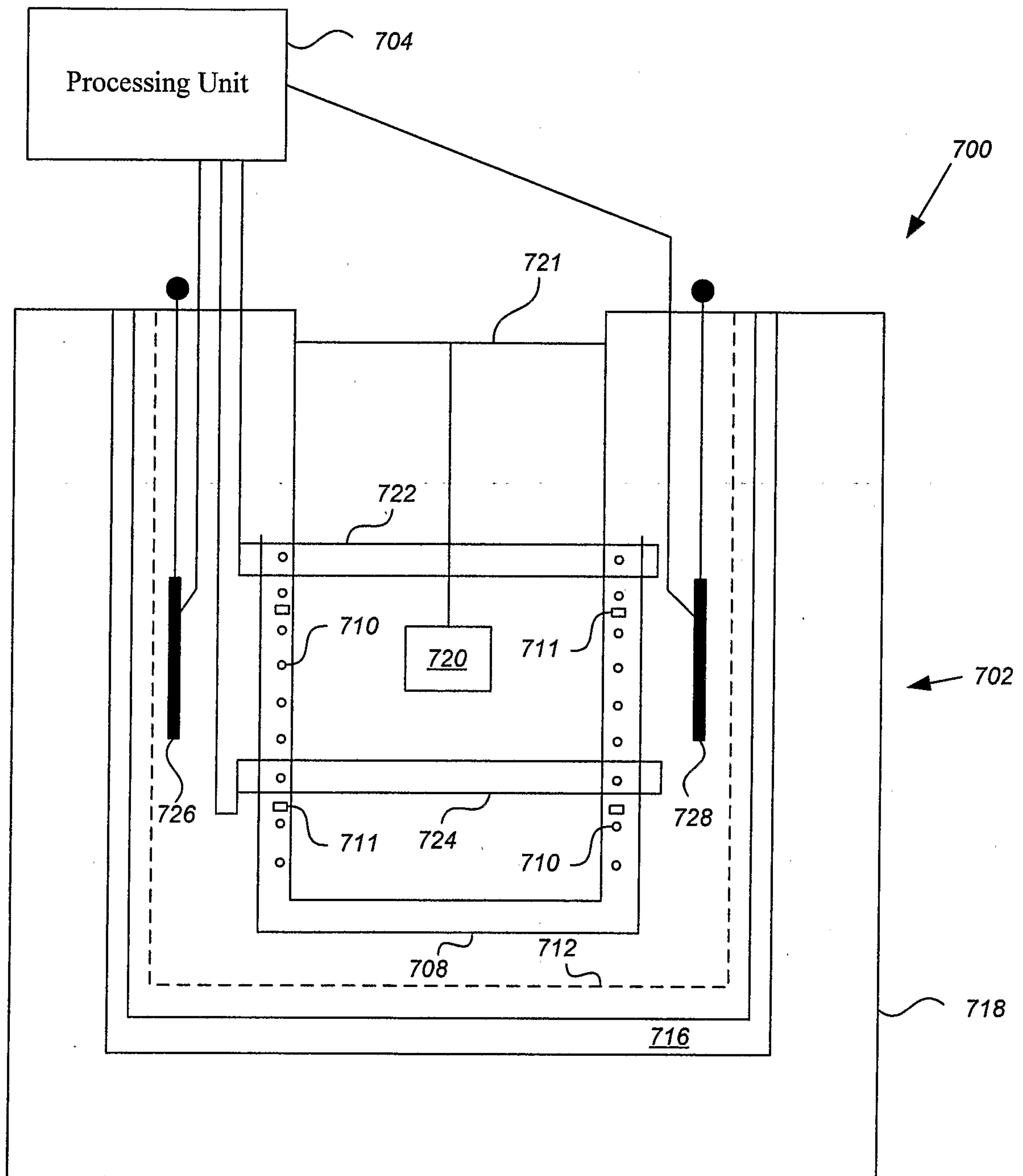
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**FIG. 4**

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**FIG. 5**

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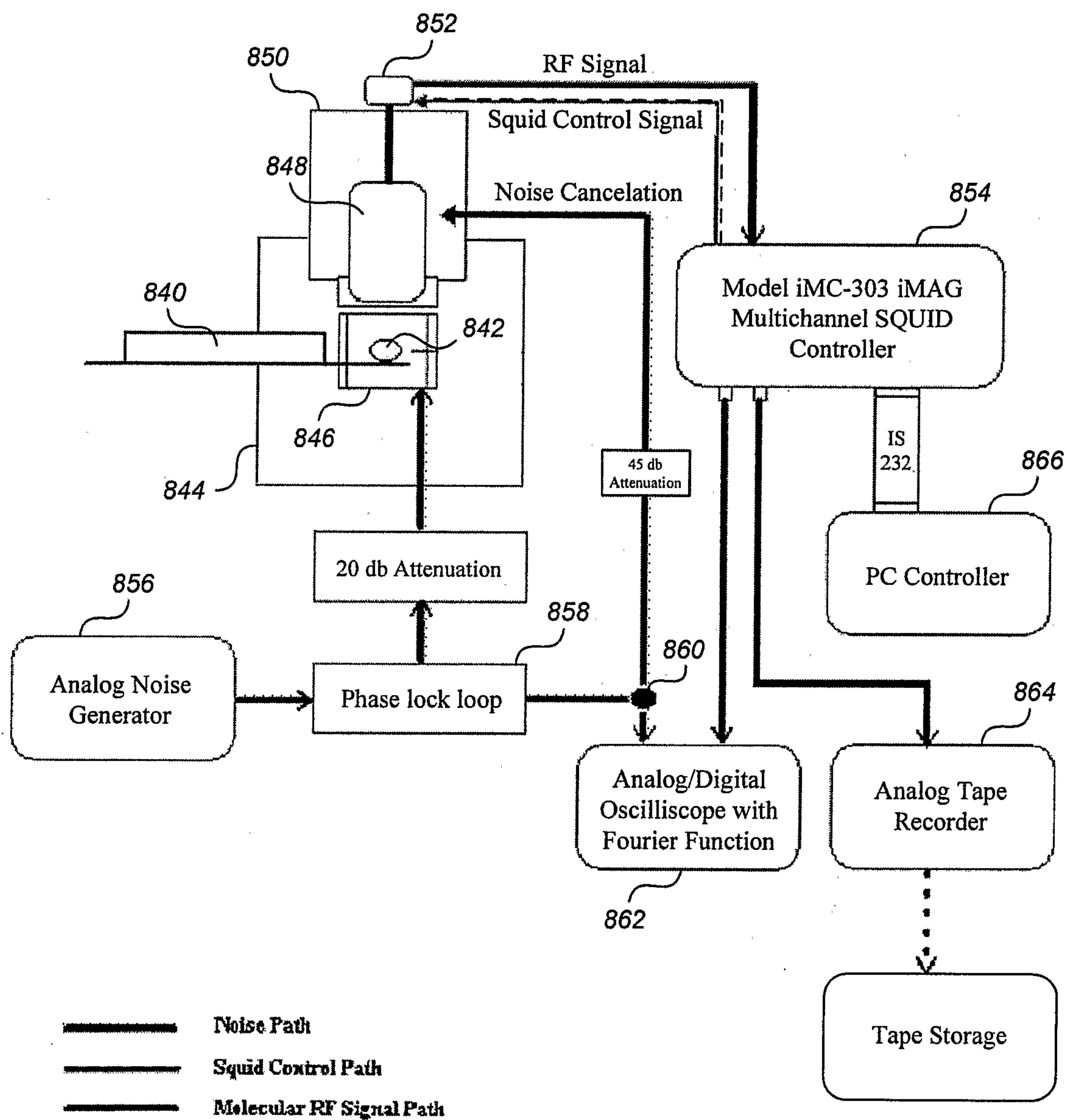


FIG. 6

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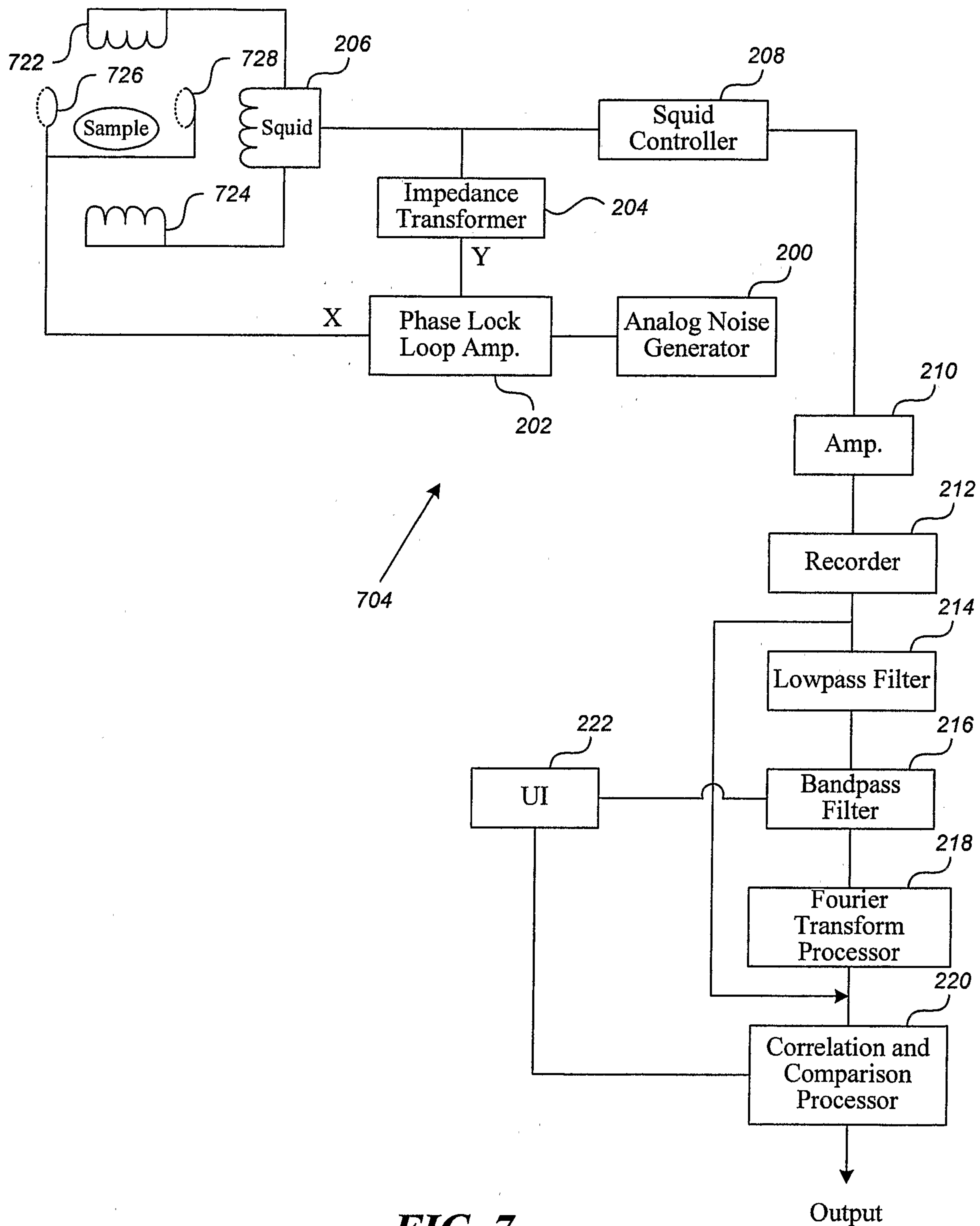
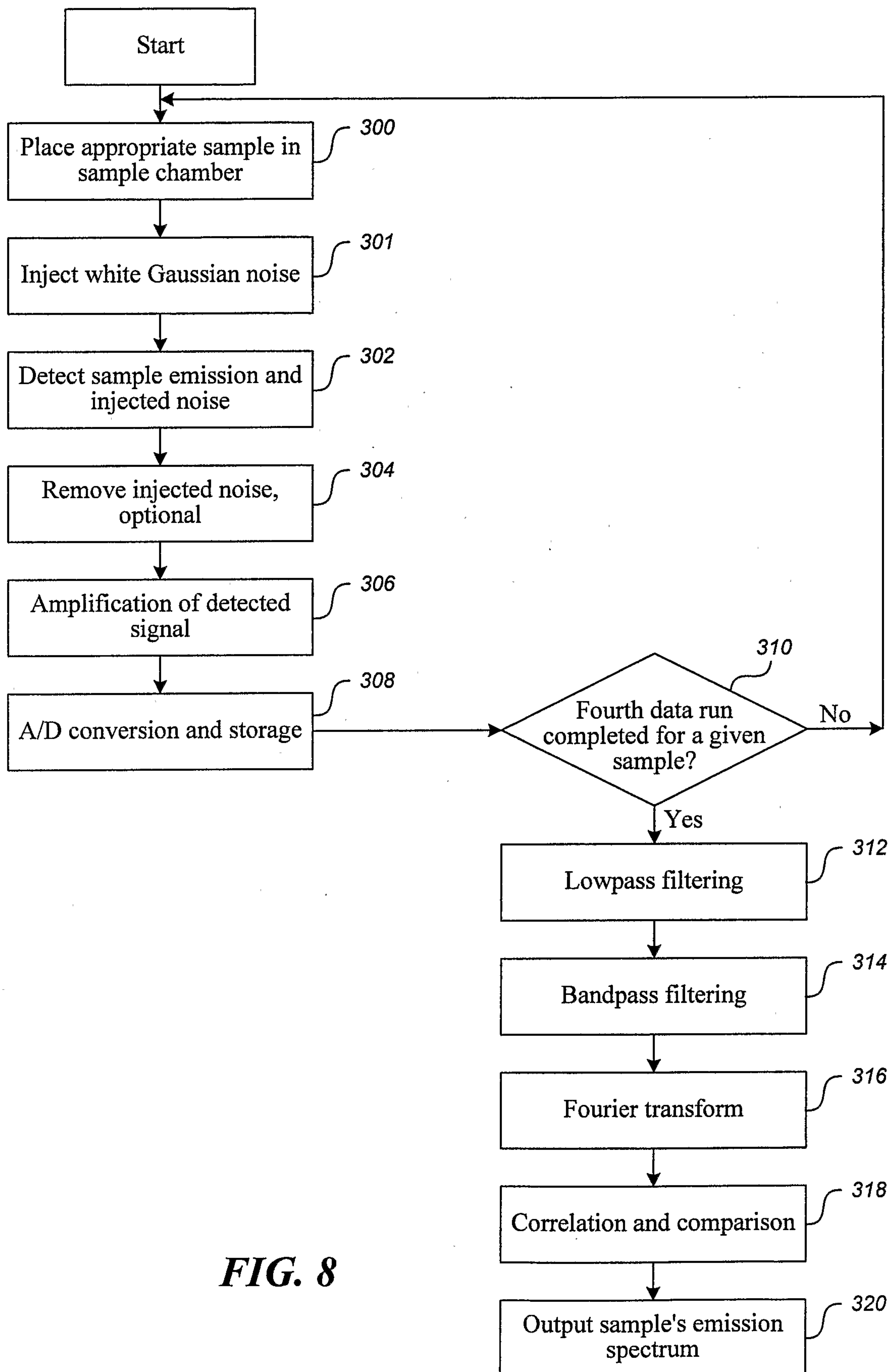
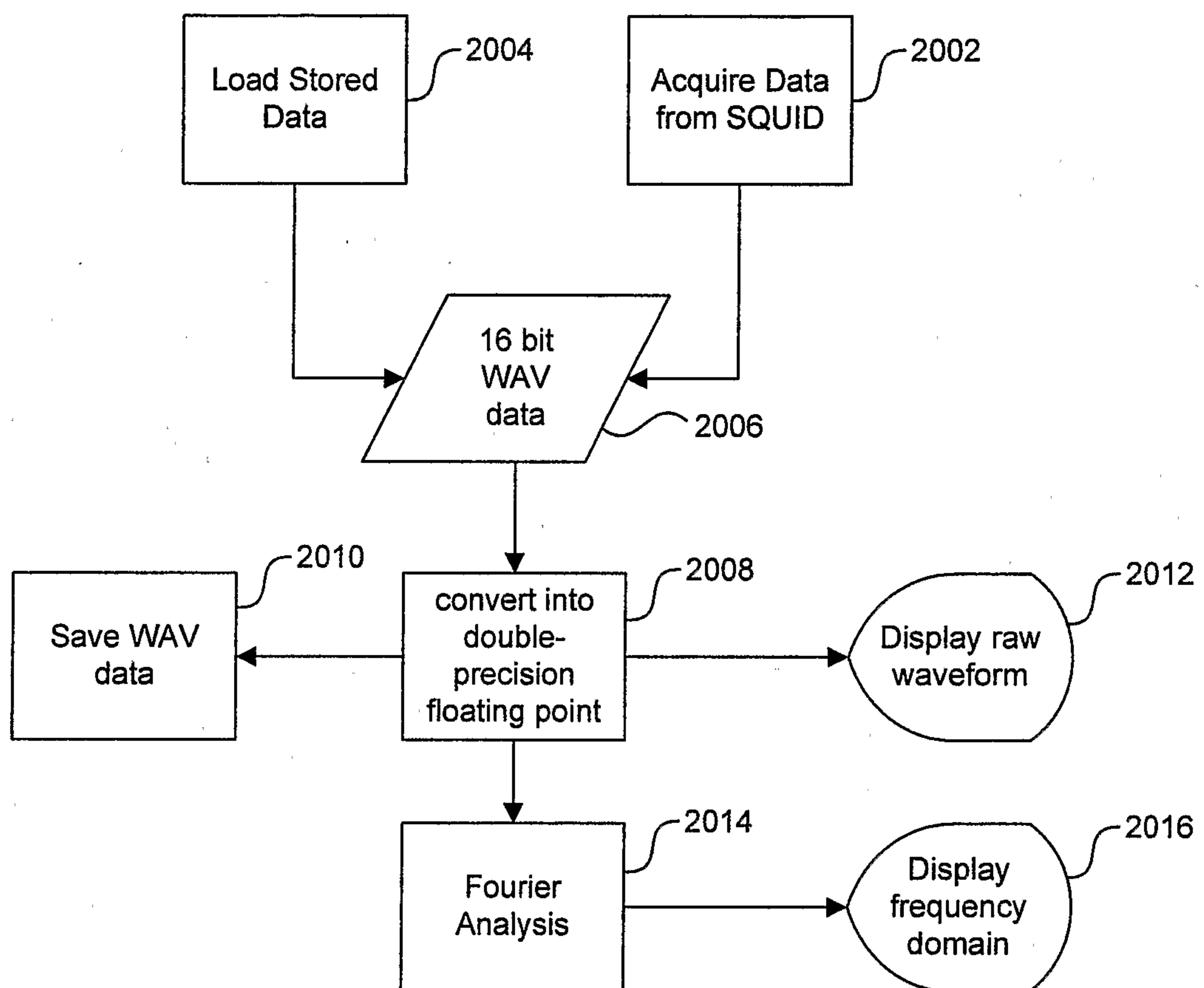


FIG. 7

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**FIG. 8**

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**FIG. 9**

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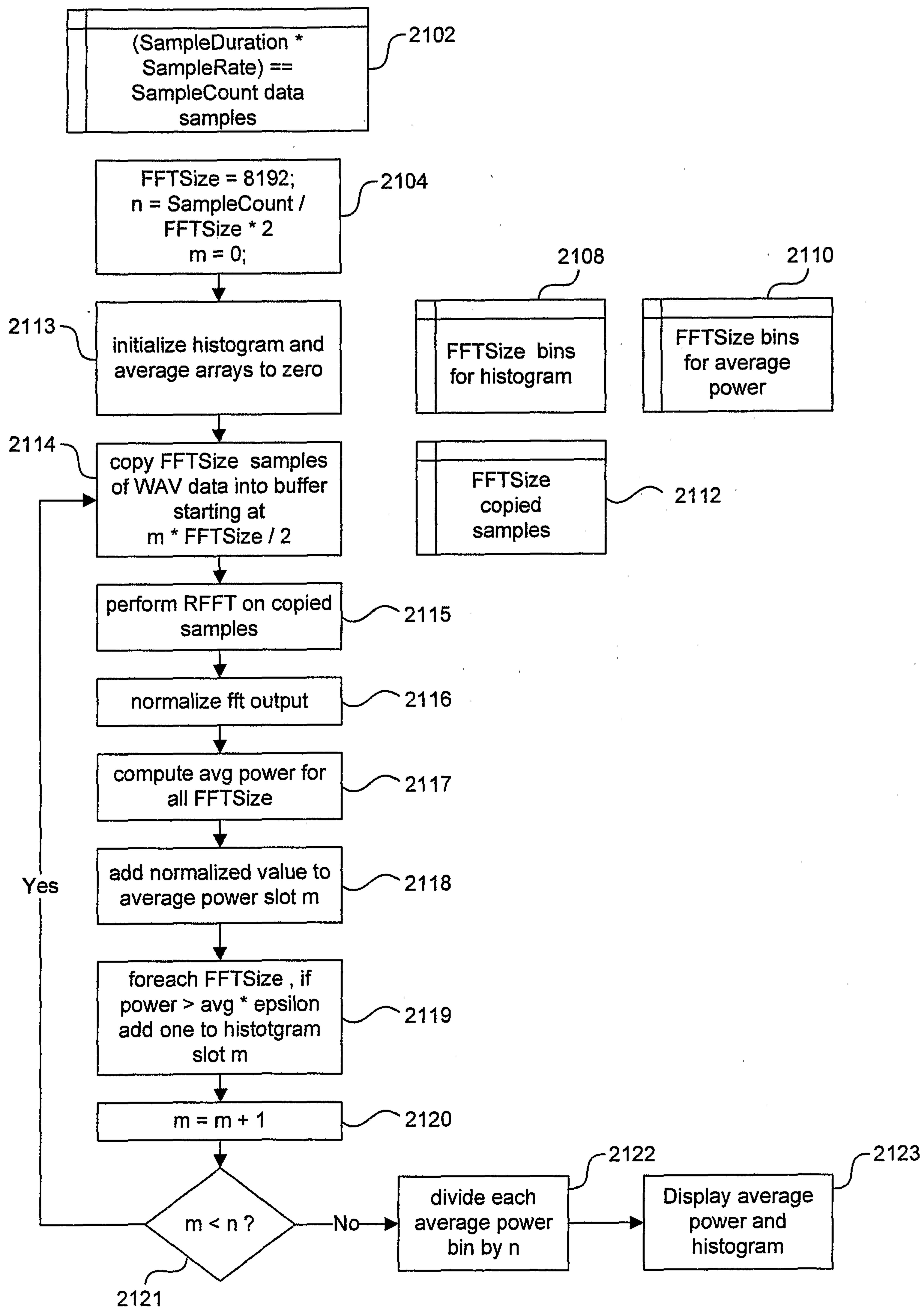
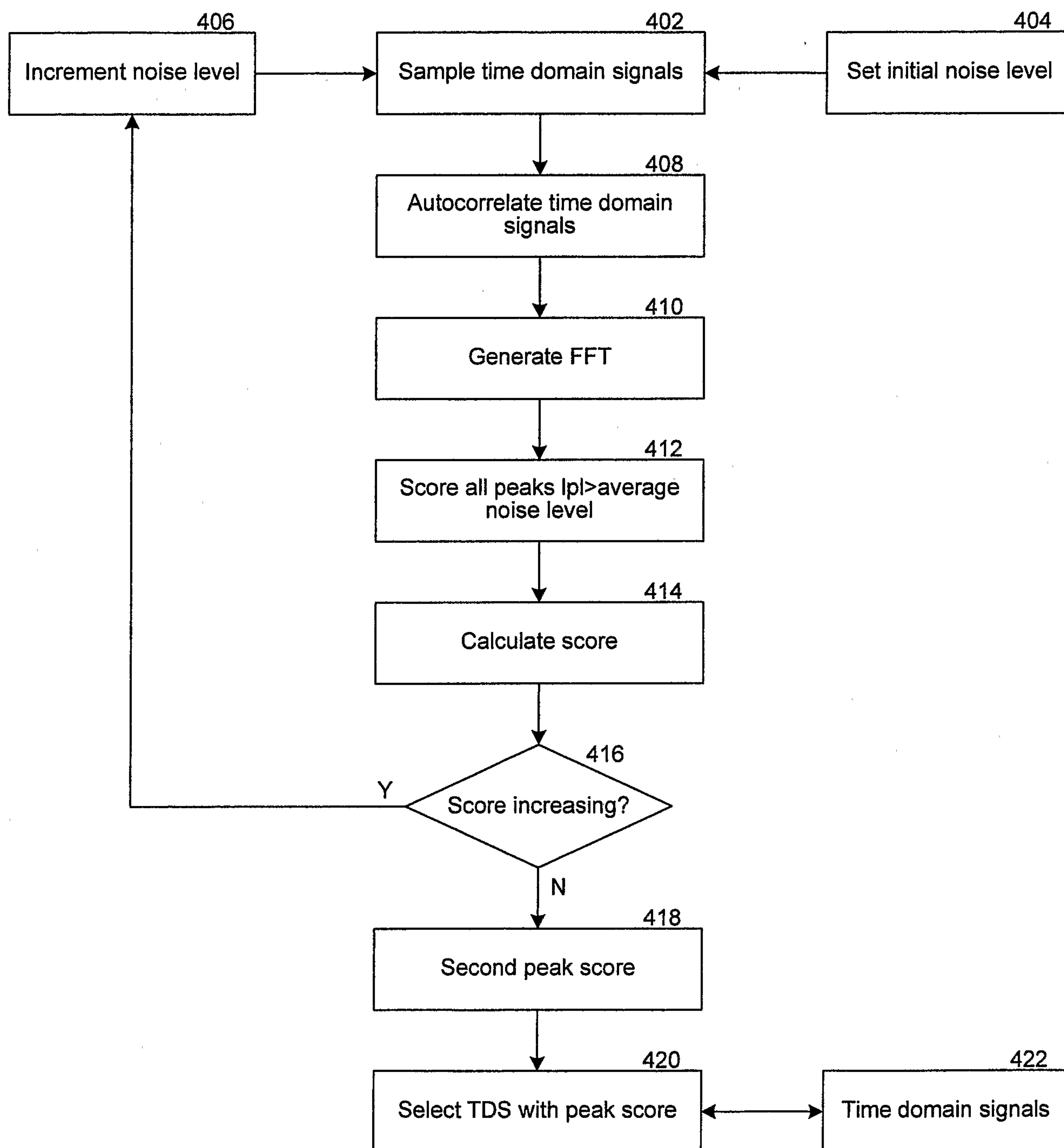
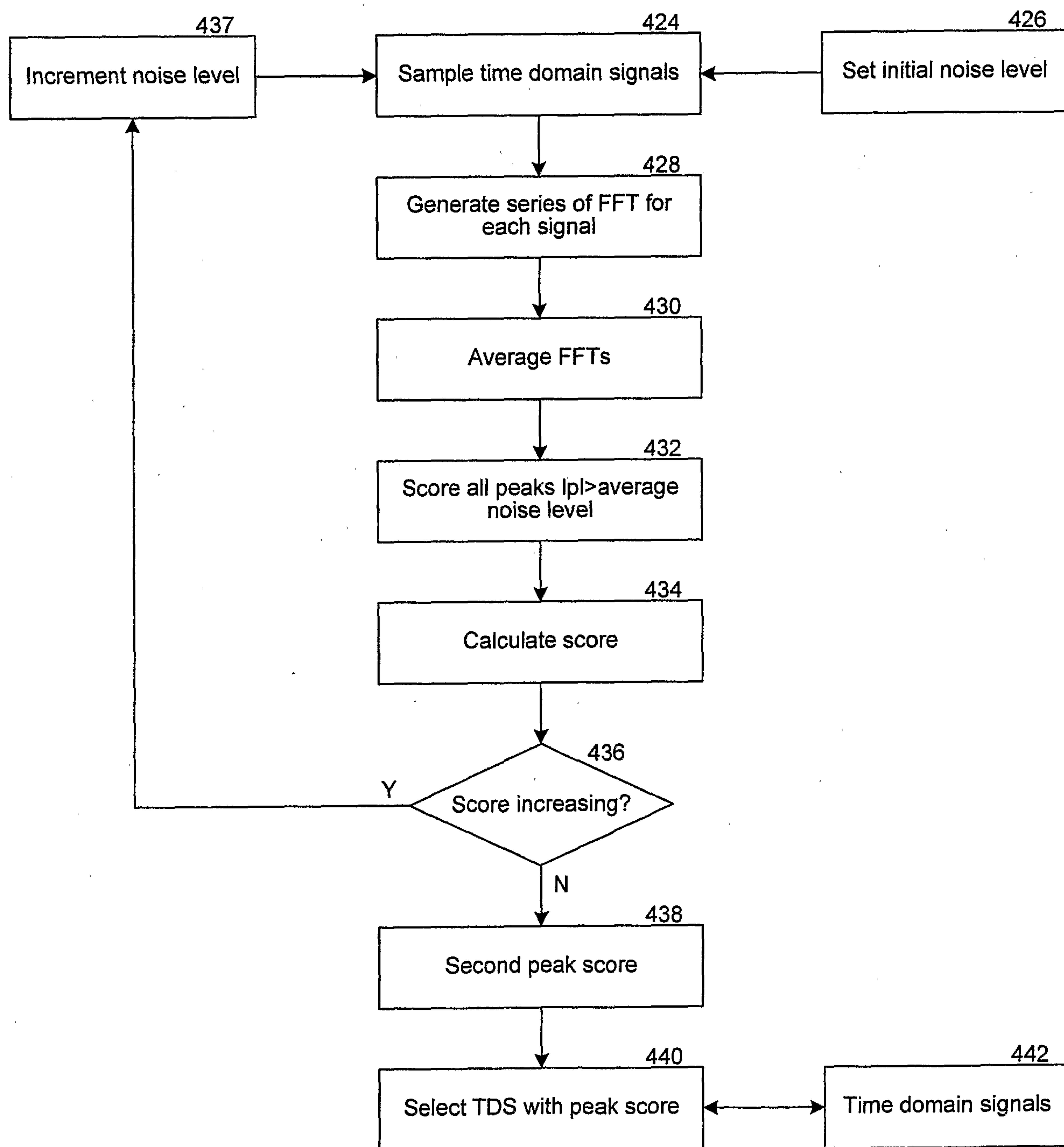


FIG. 10

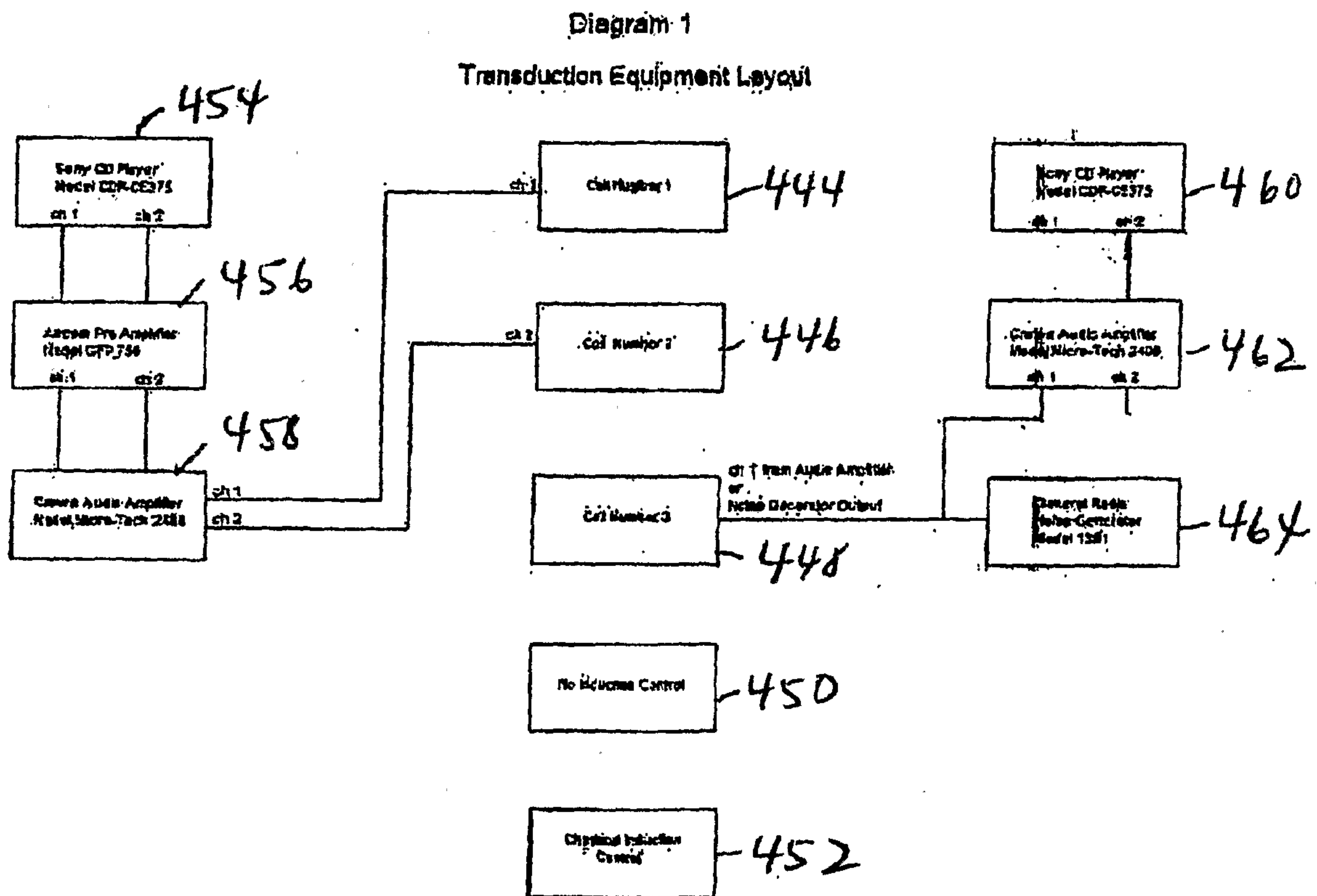
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**FIG. 11**

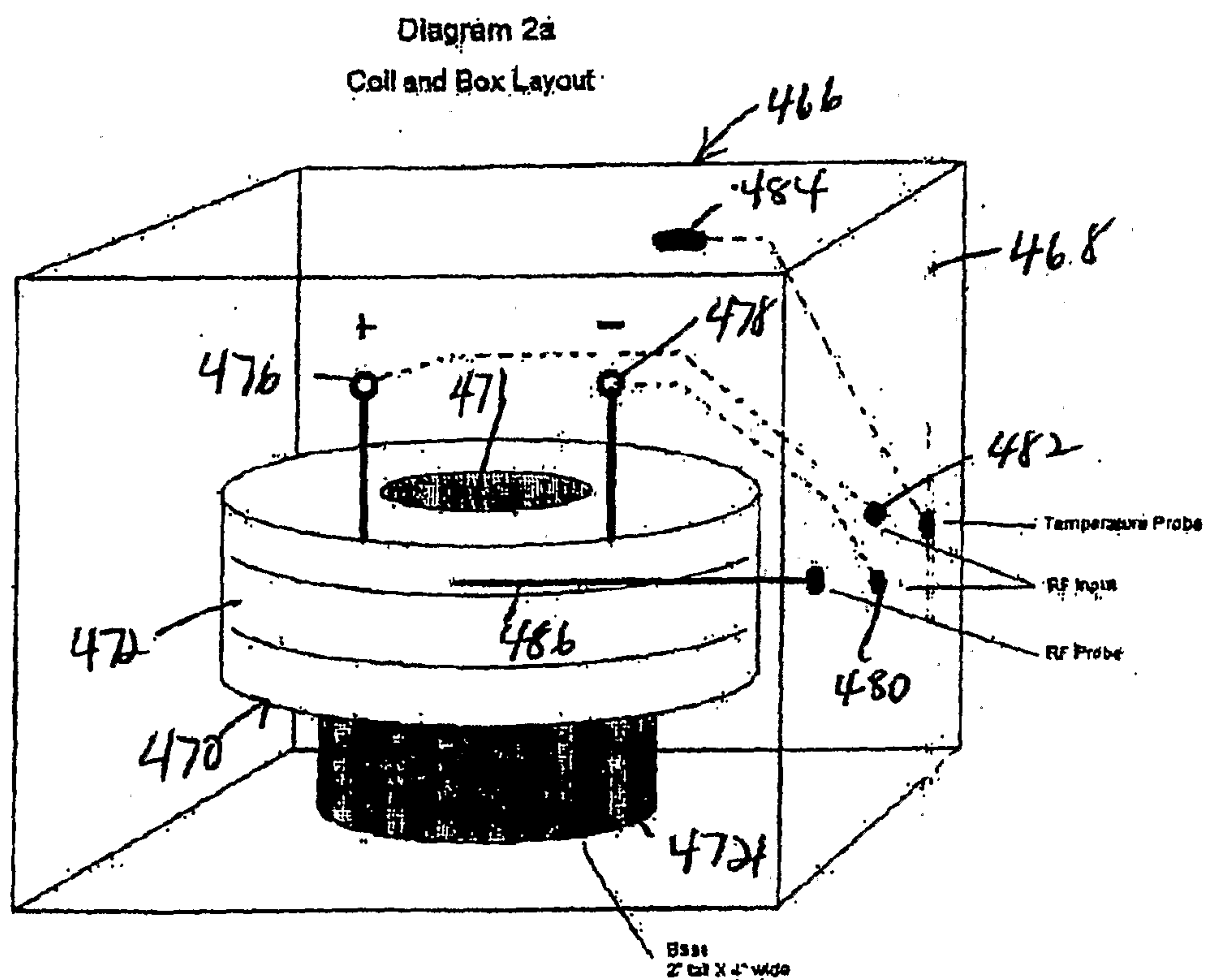
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**FIG. 12**

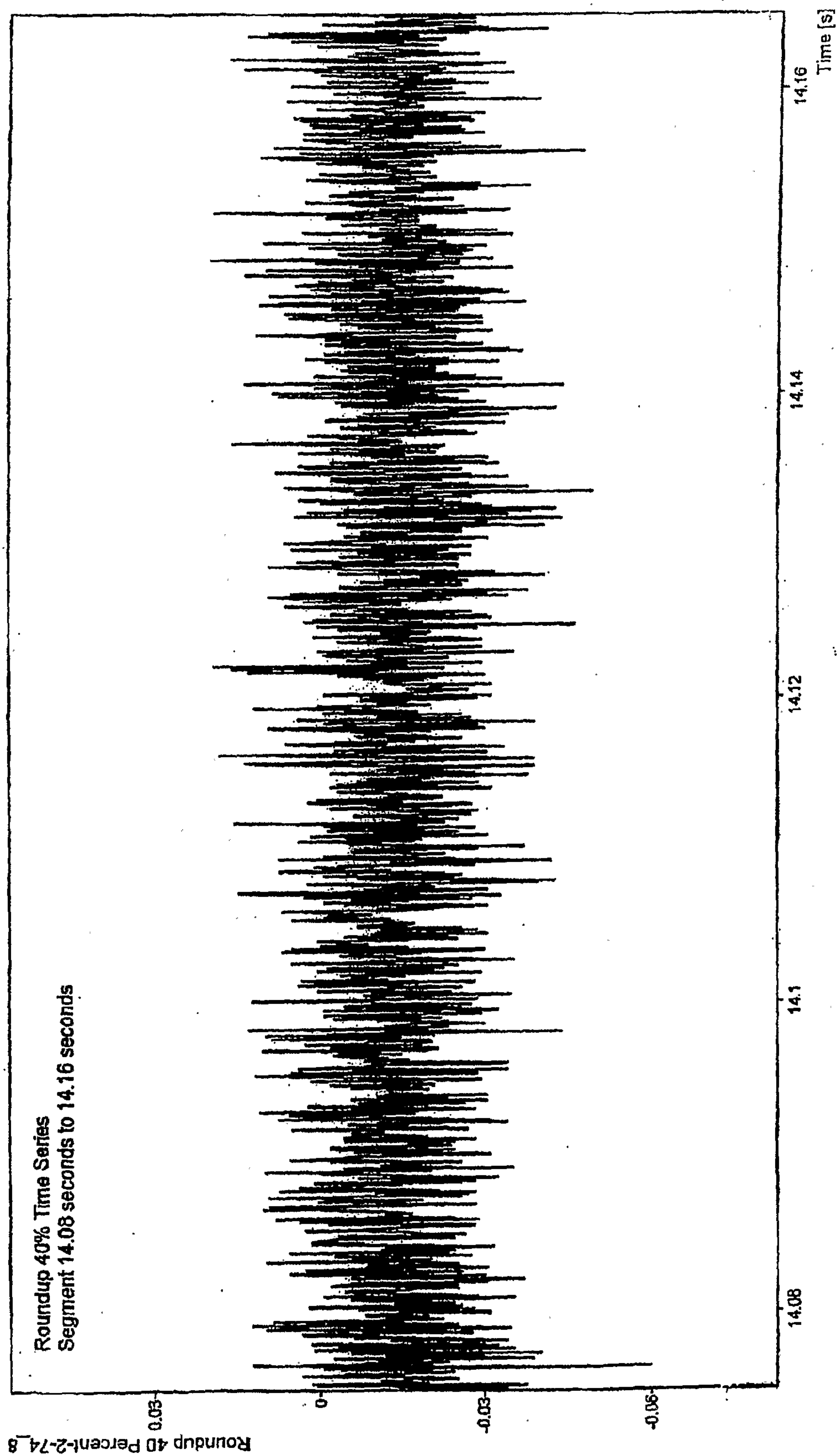
13/26

**FIG. 13**

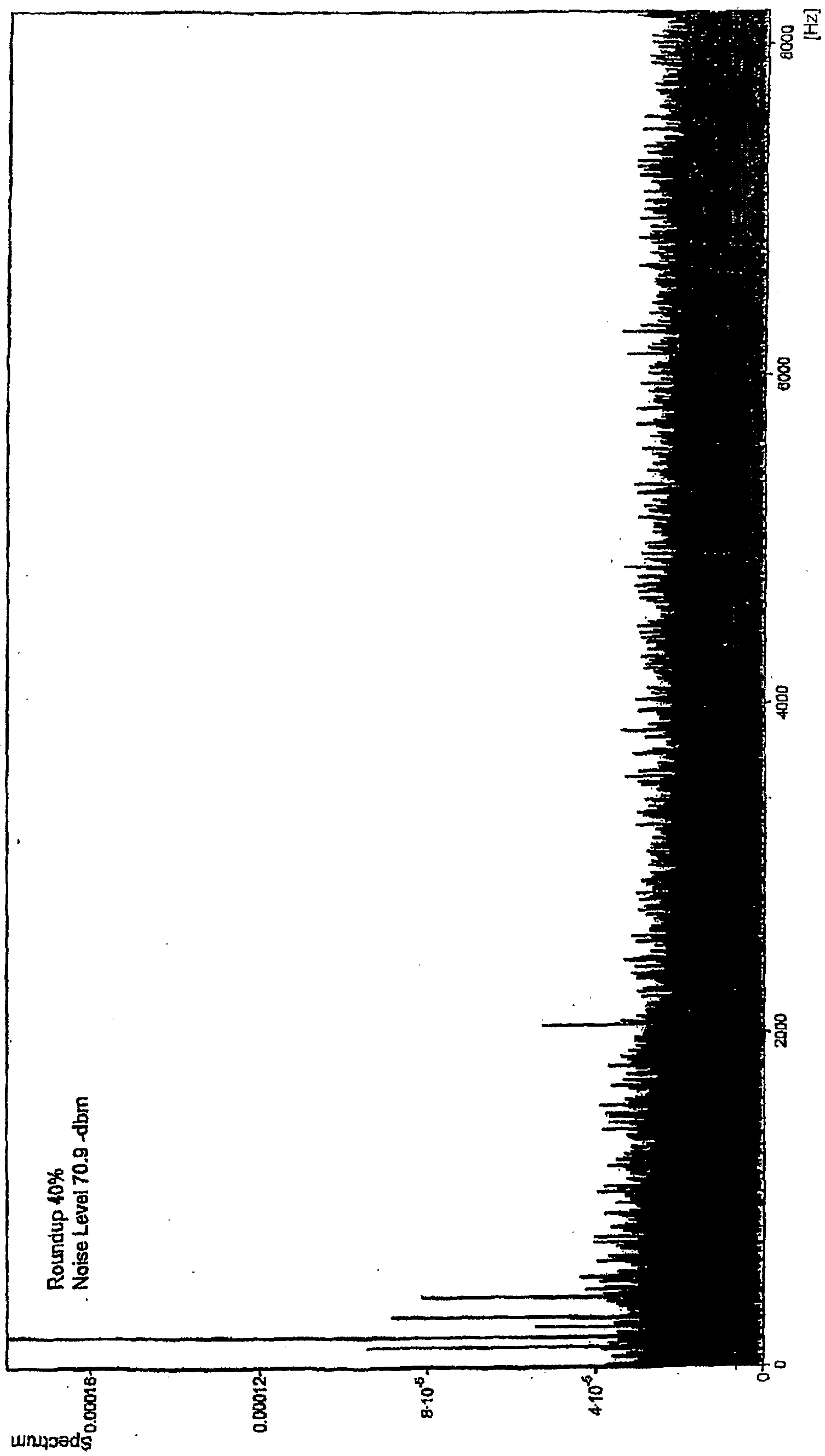
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**FIG. 14**

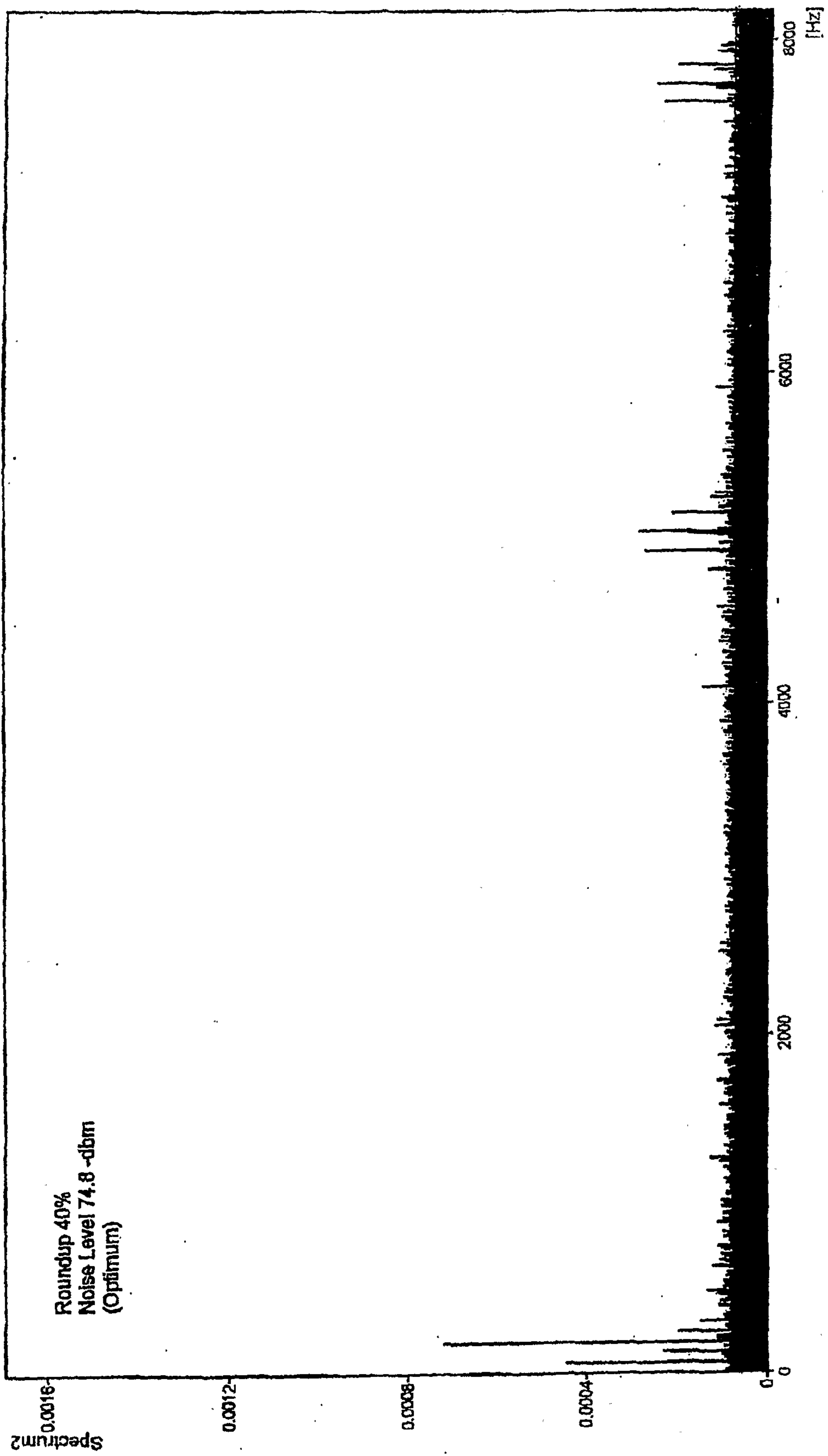
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*FIG. 15A*

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*FIG. 15B*

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*FIG. 15C*

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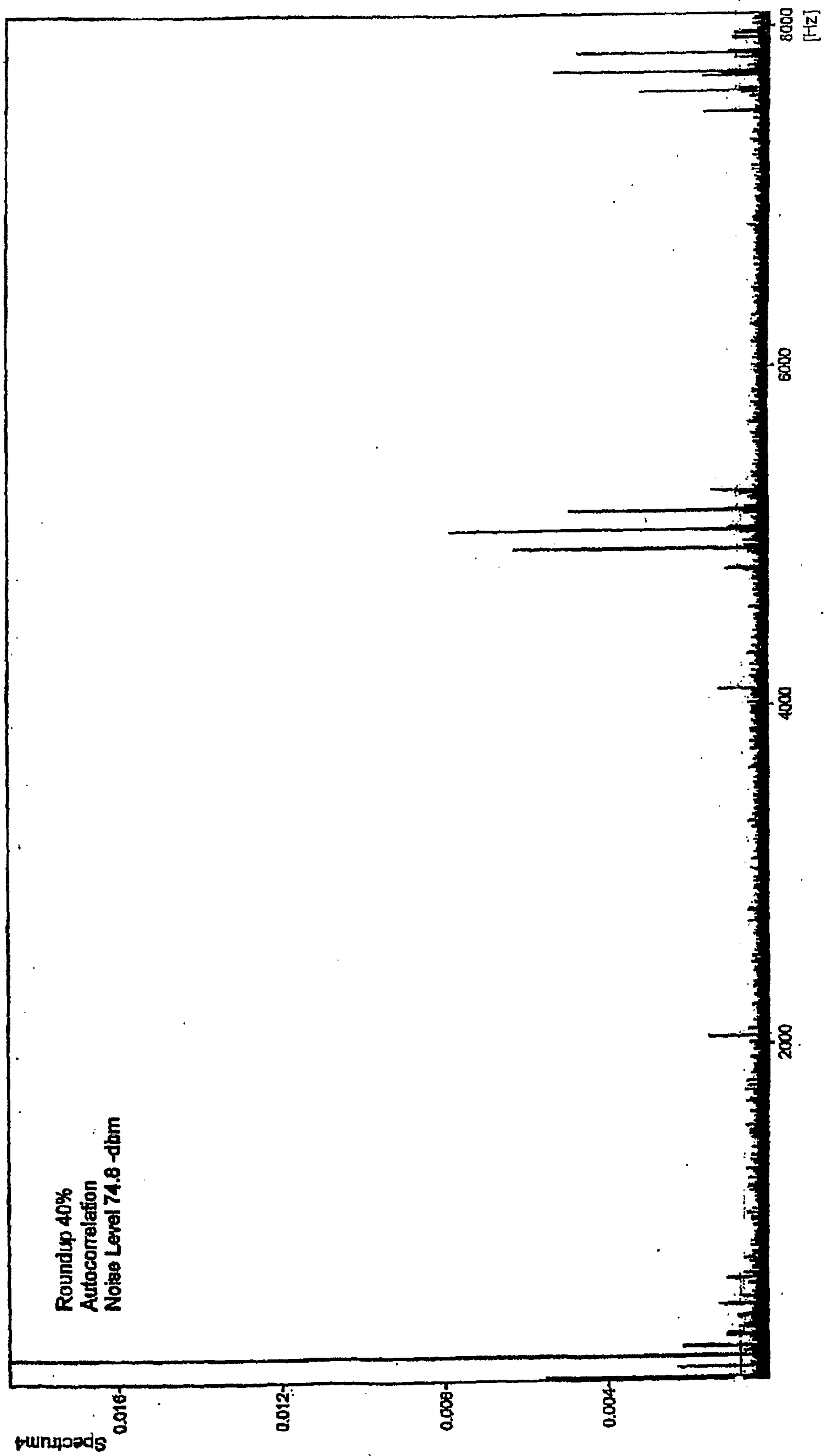


FIG. 15D

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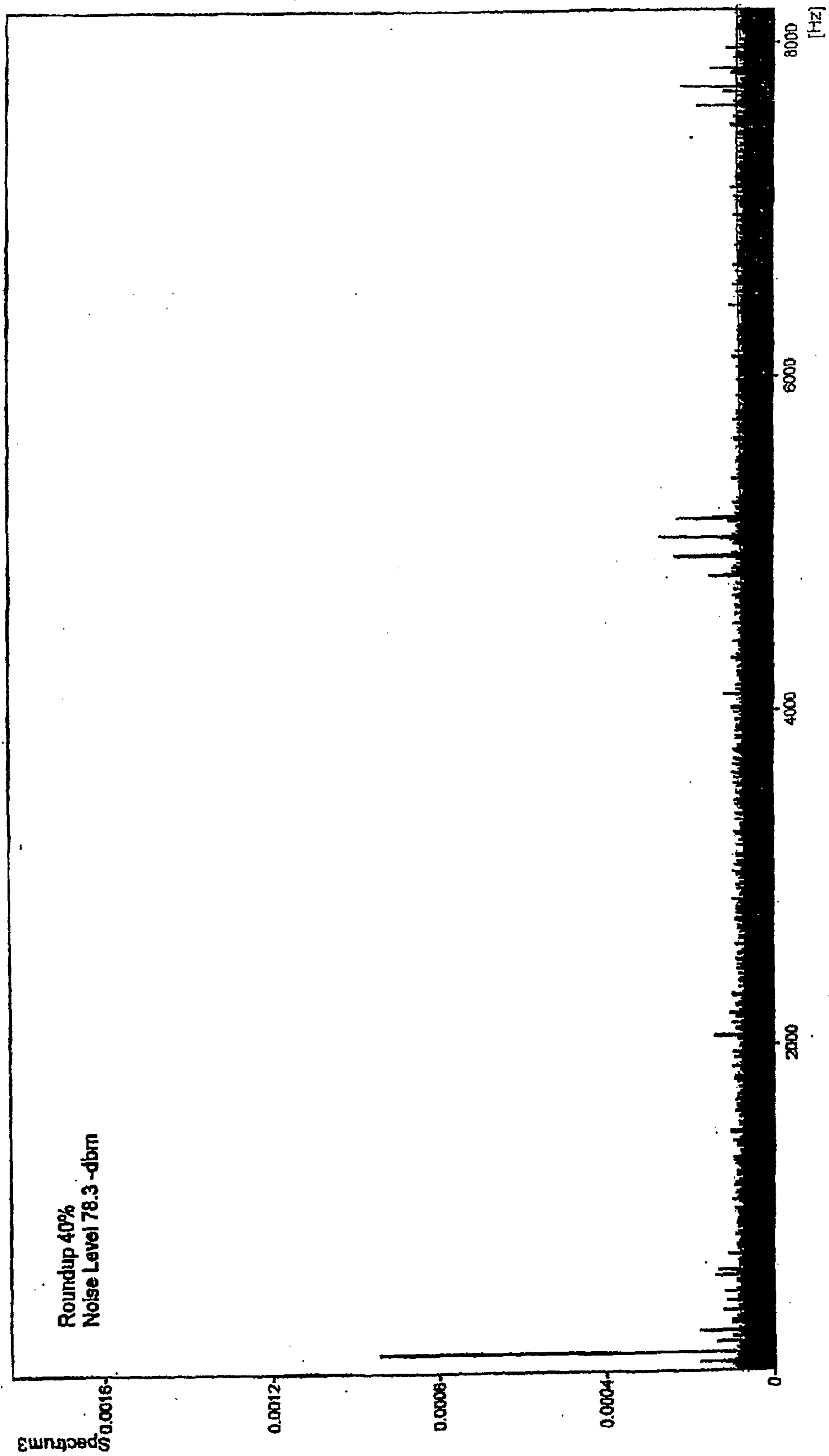


FIG. 15E

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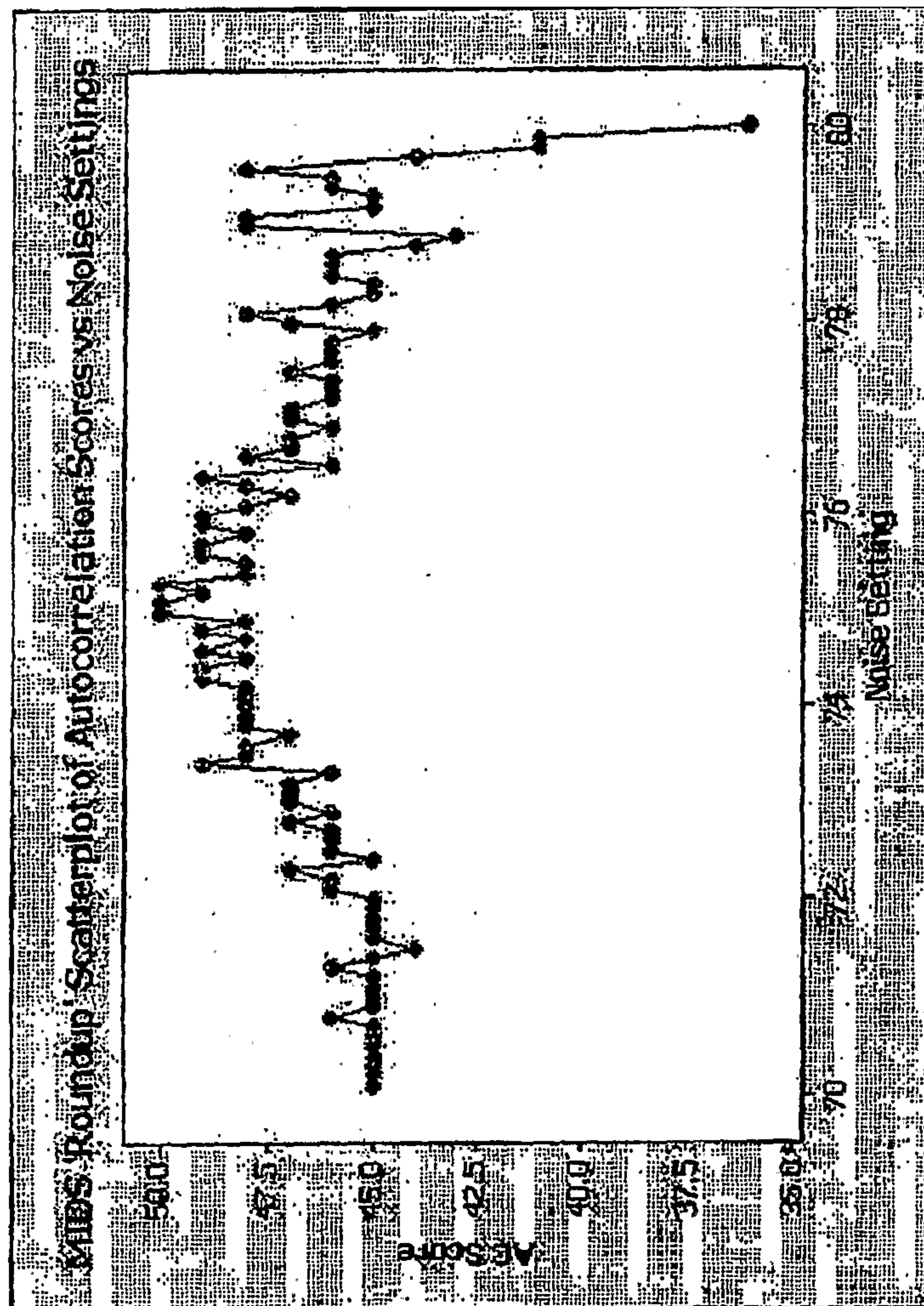
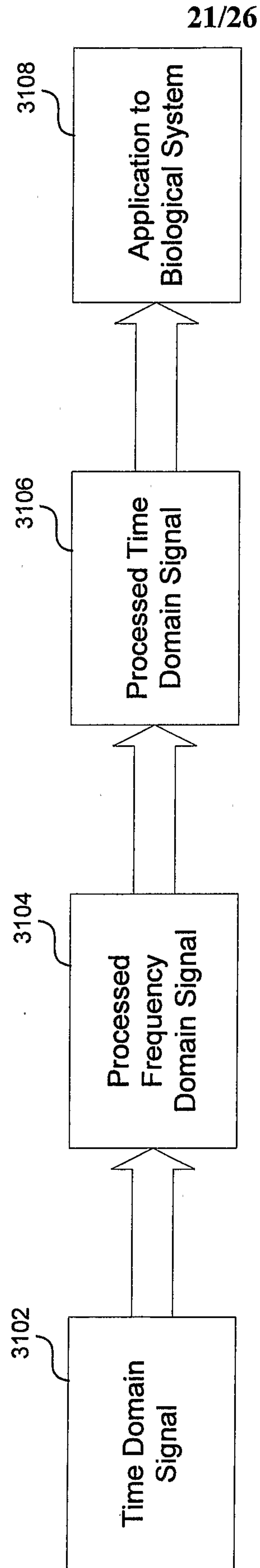
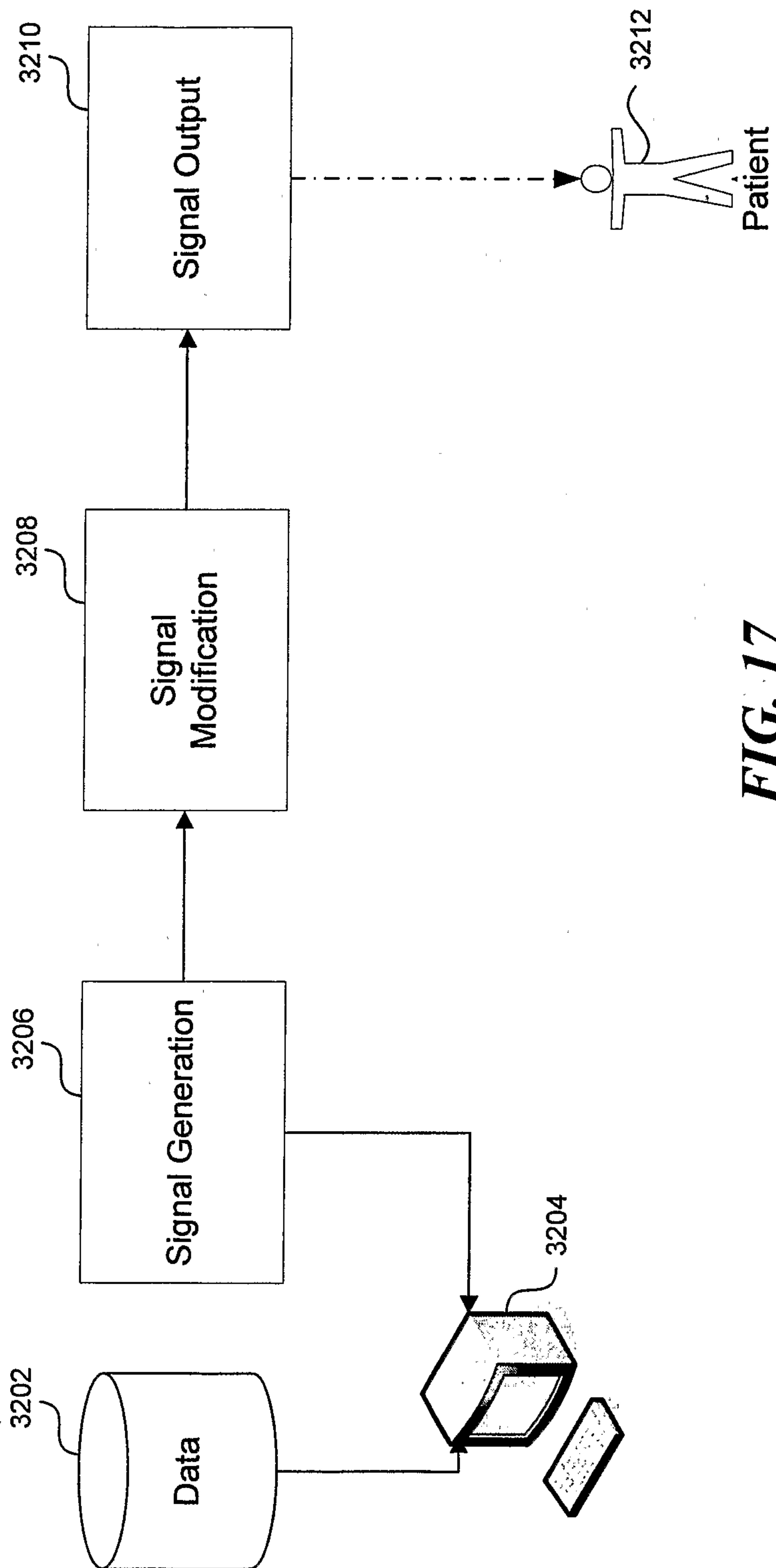


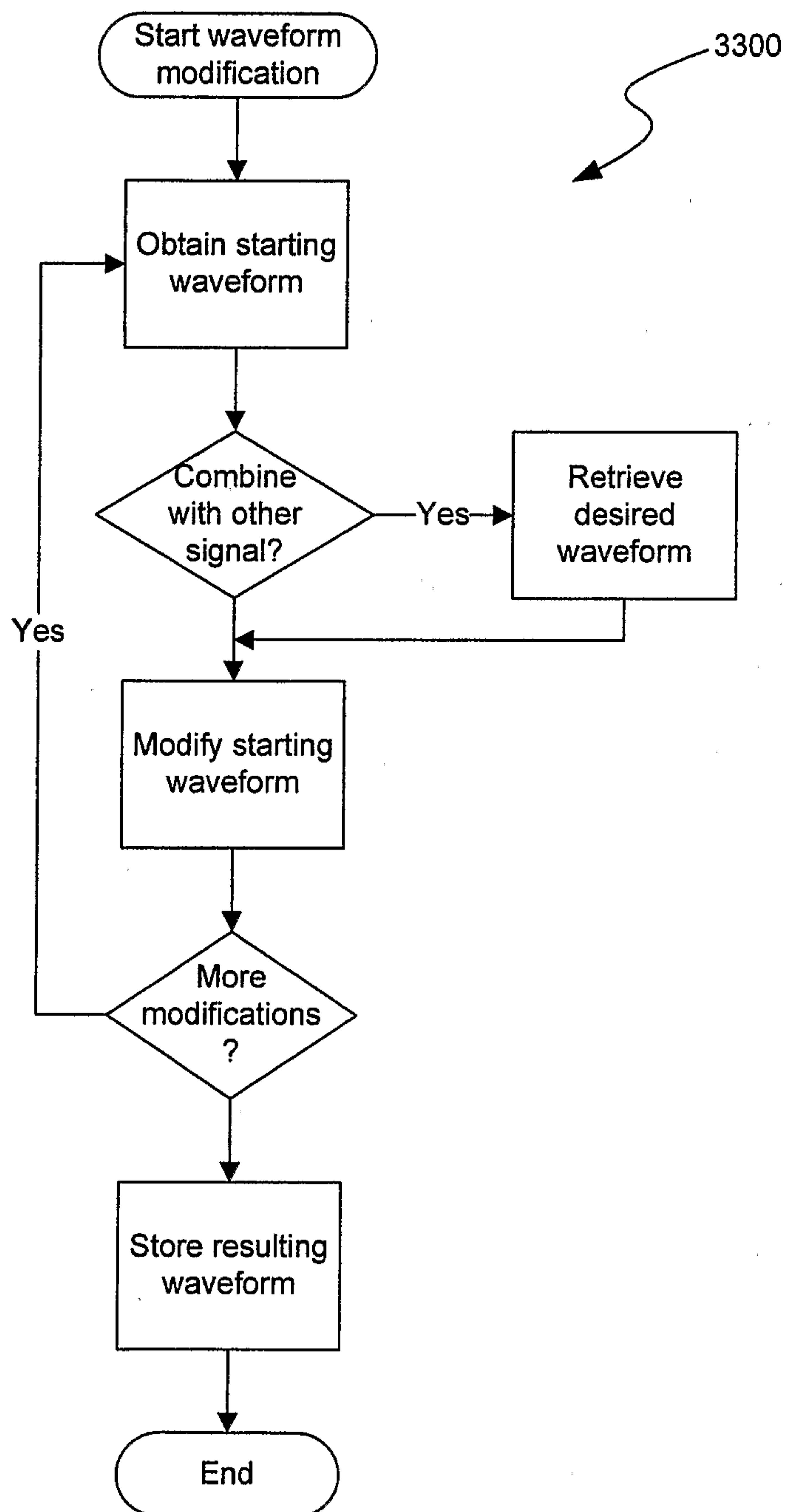
FIG. 15F

**FIG. 16**

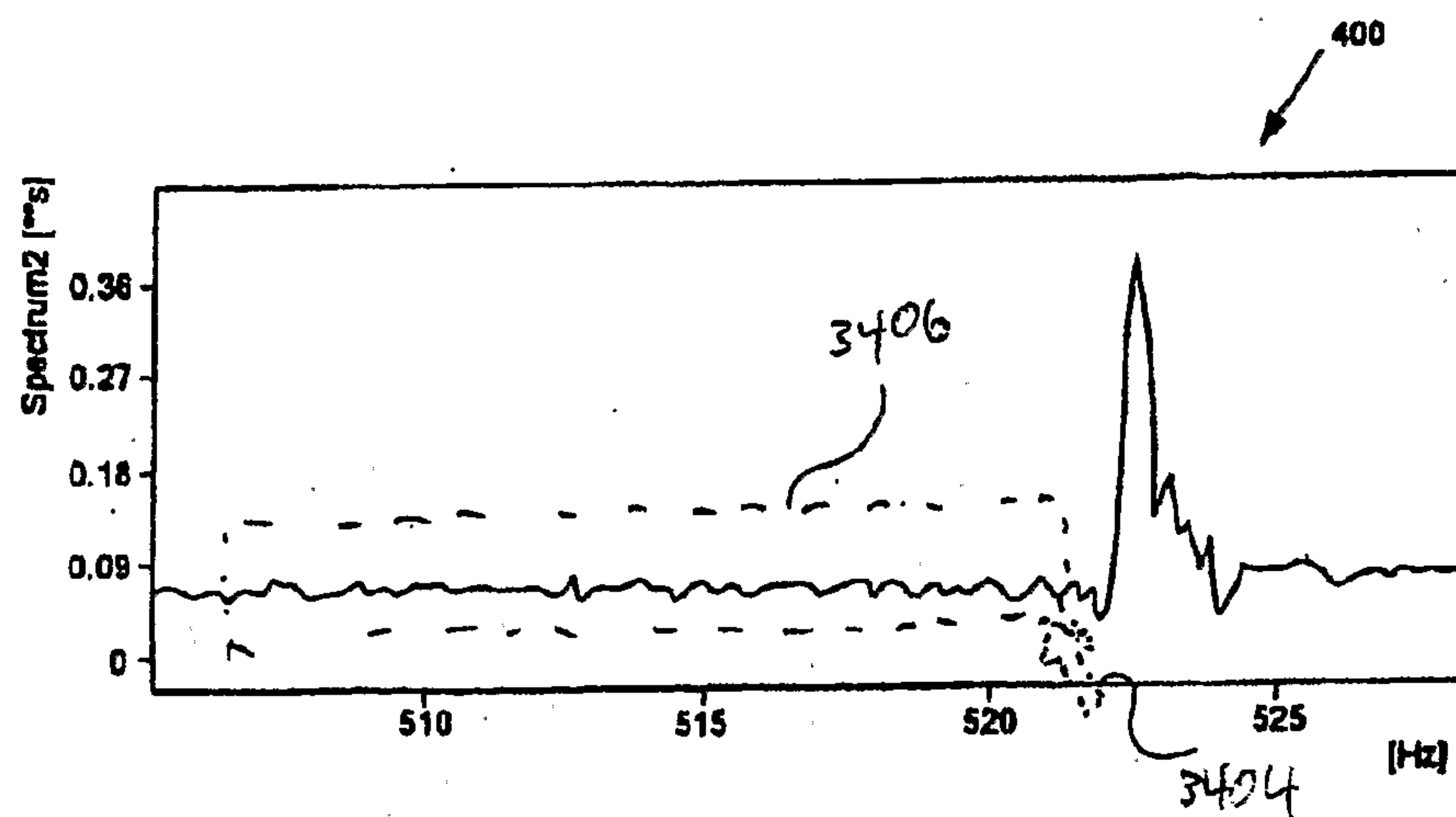
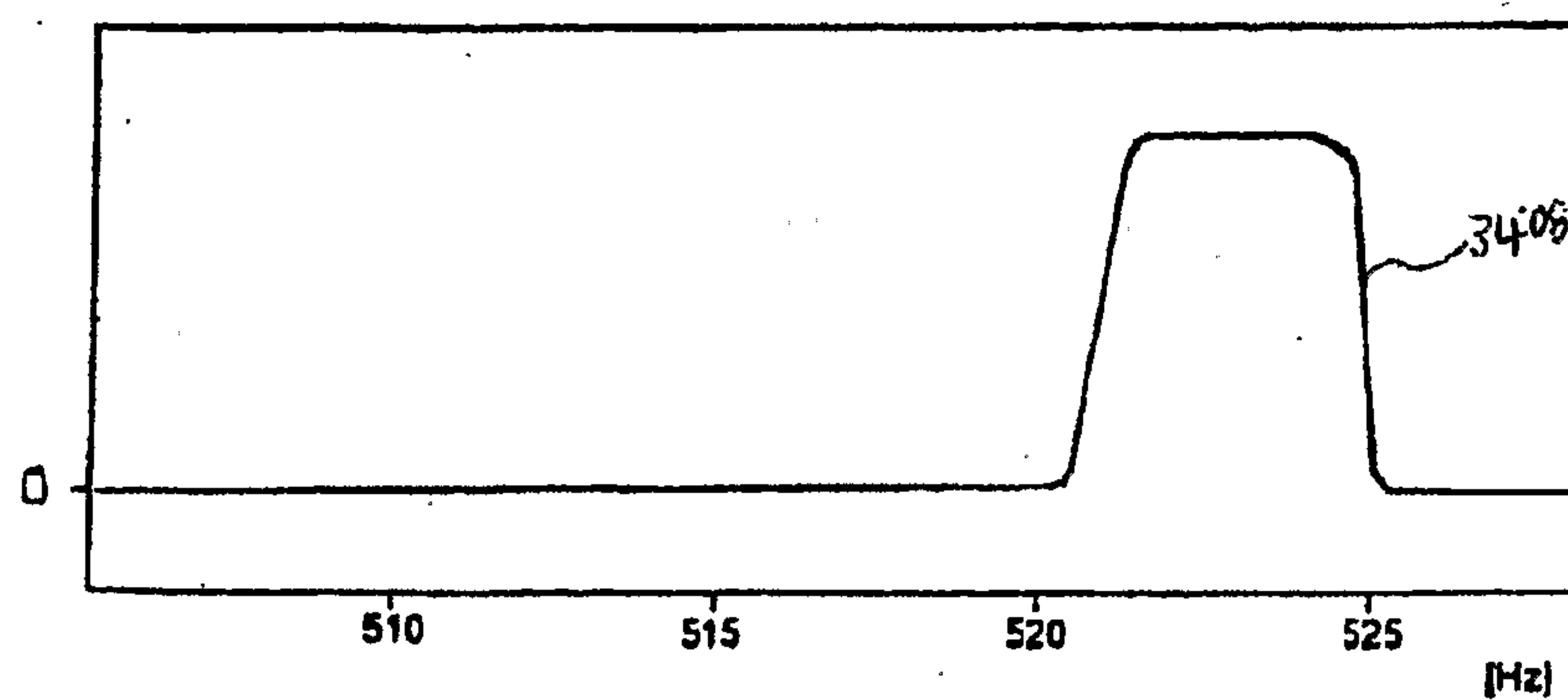
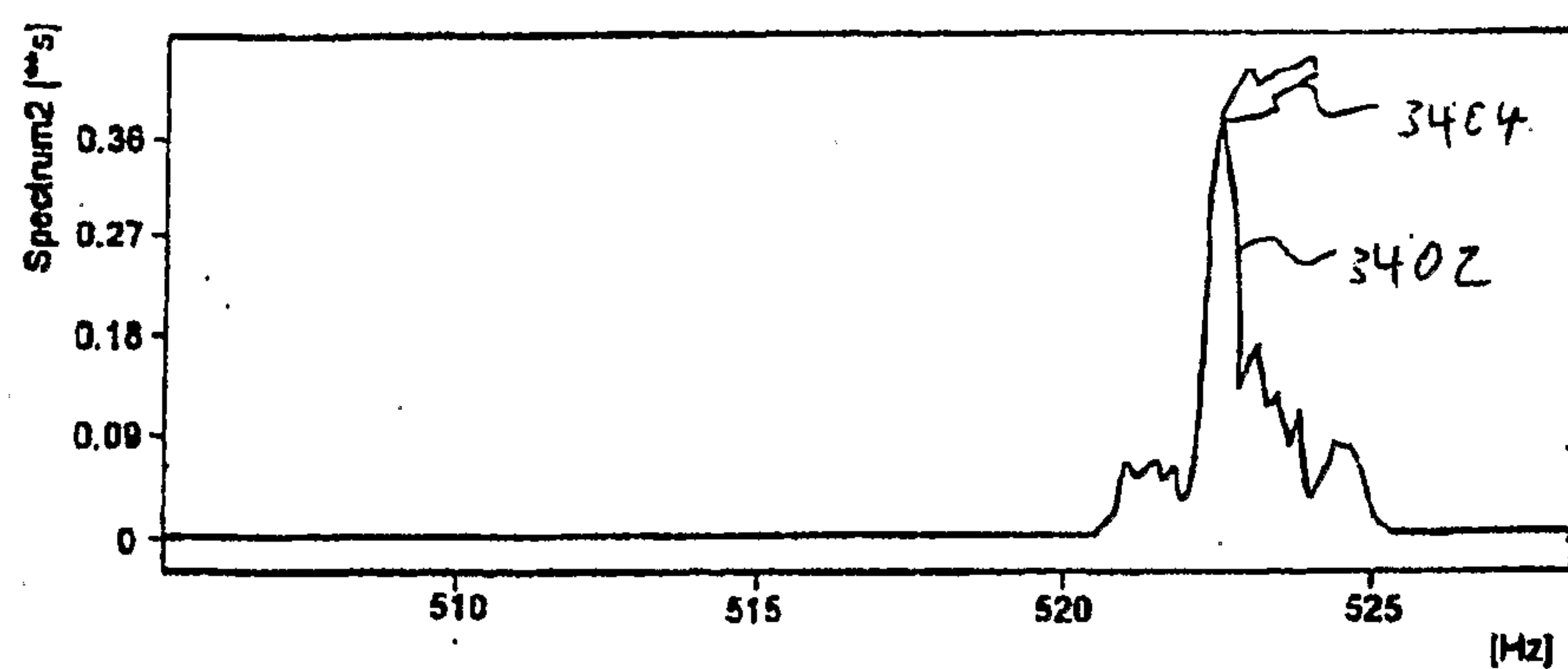
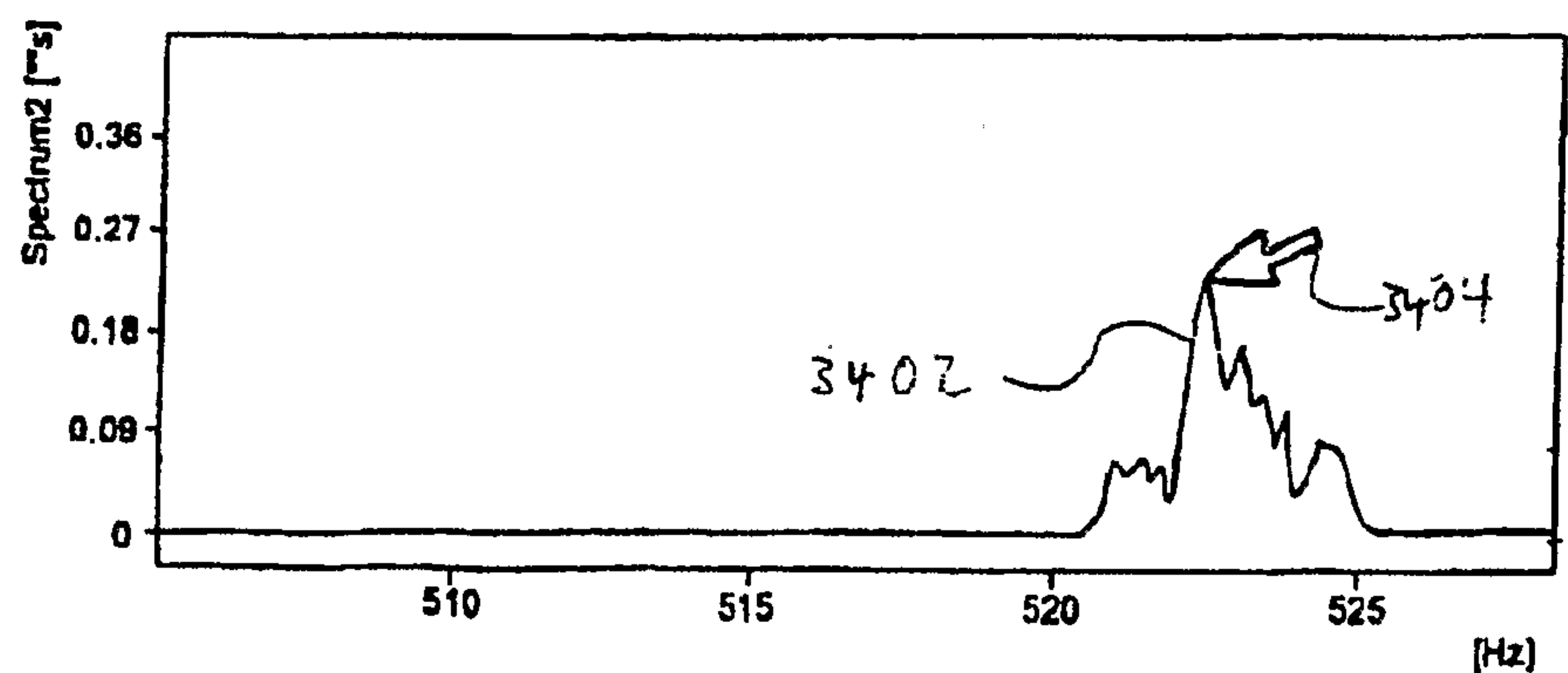
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**FIG. 17**

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**FIG. 18**

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**FIG. 19A****FIG. 19B****FIG. 19C****FIG. 19D**

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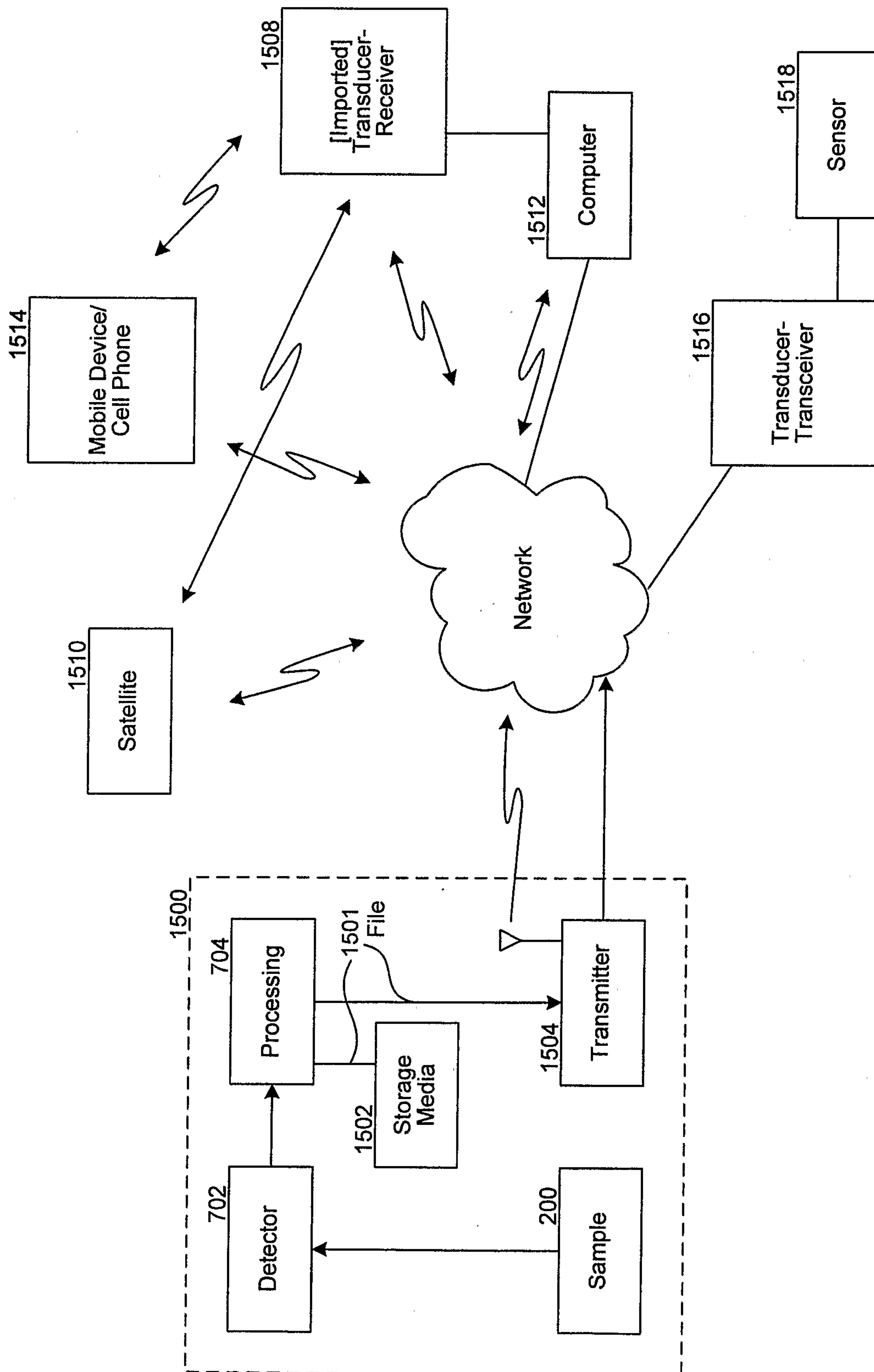
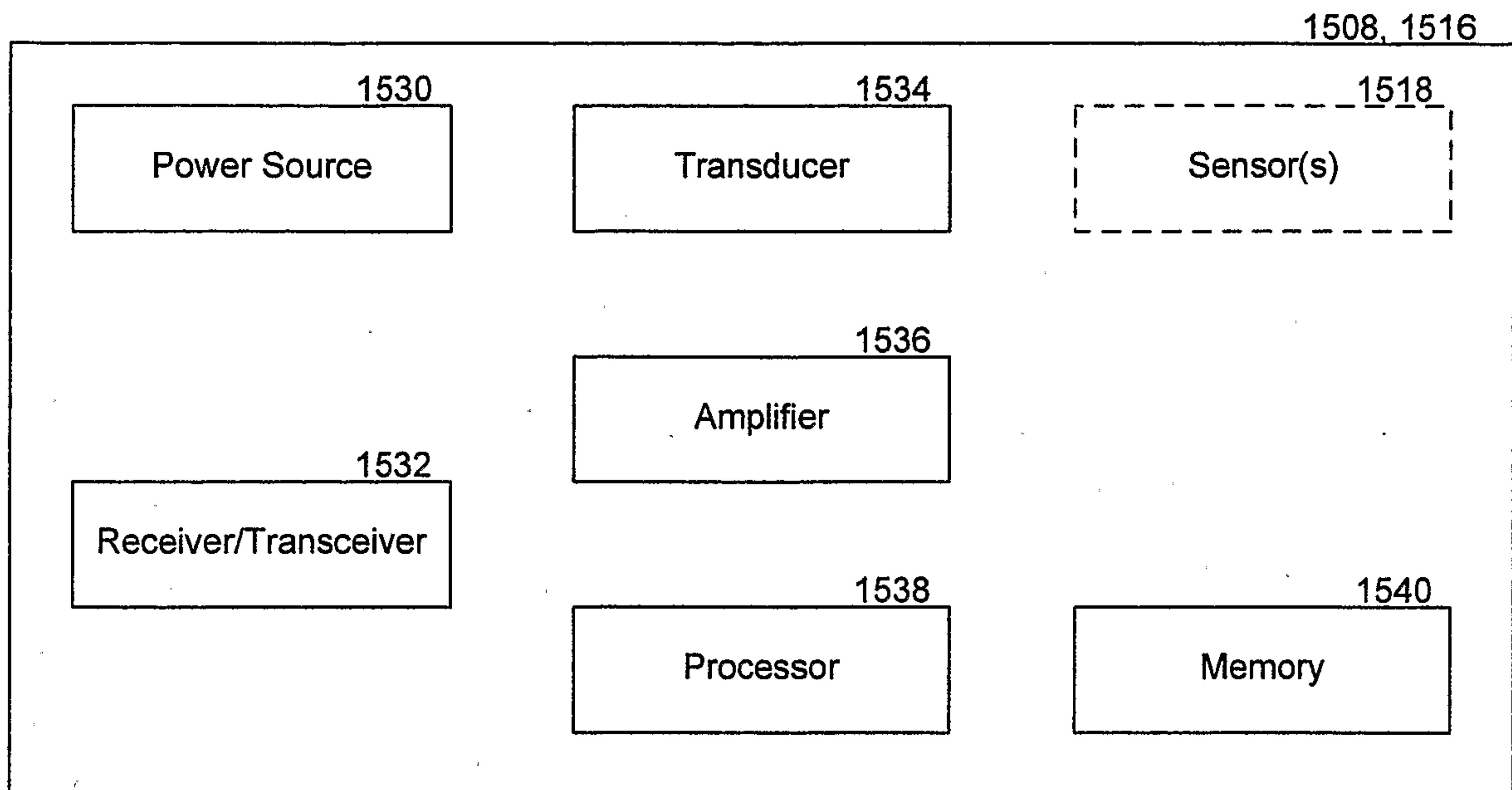
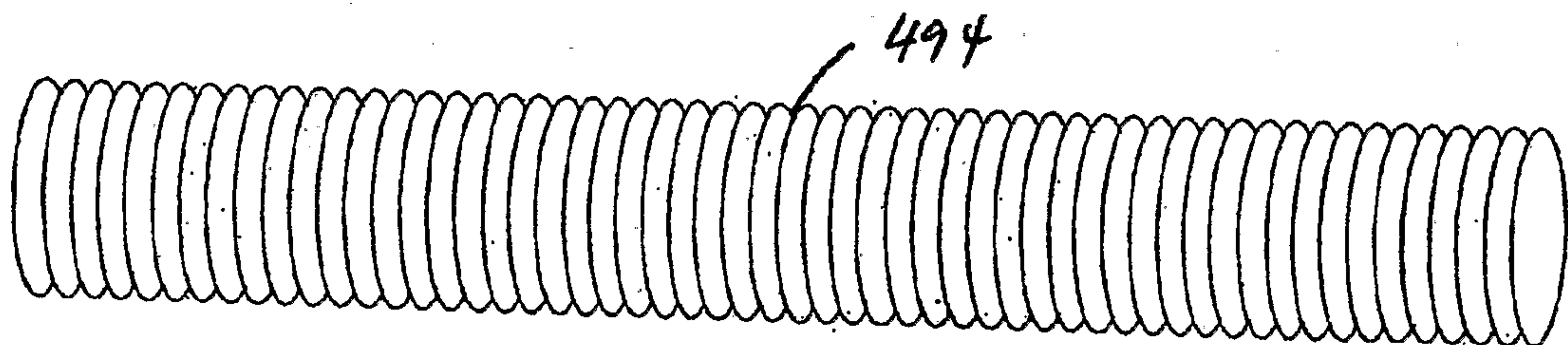
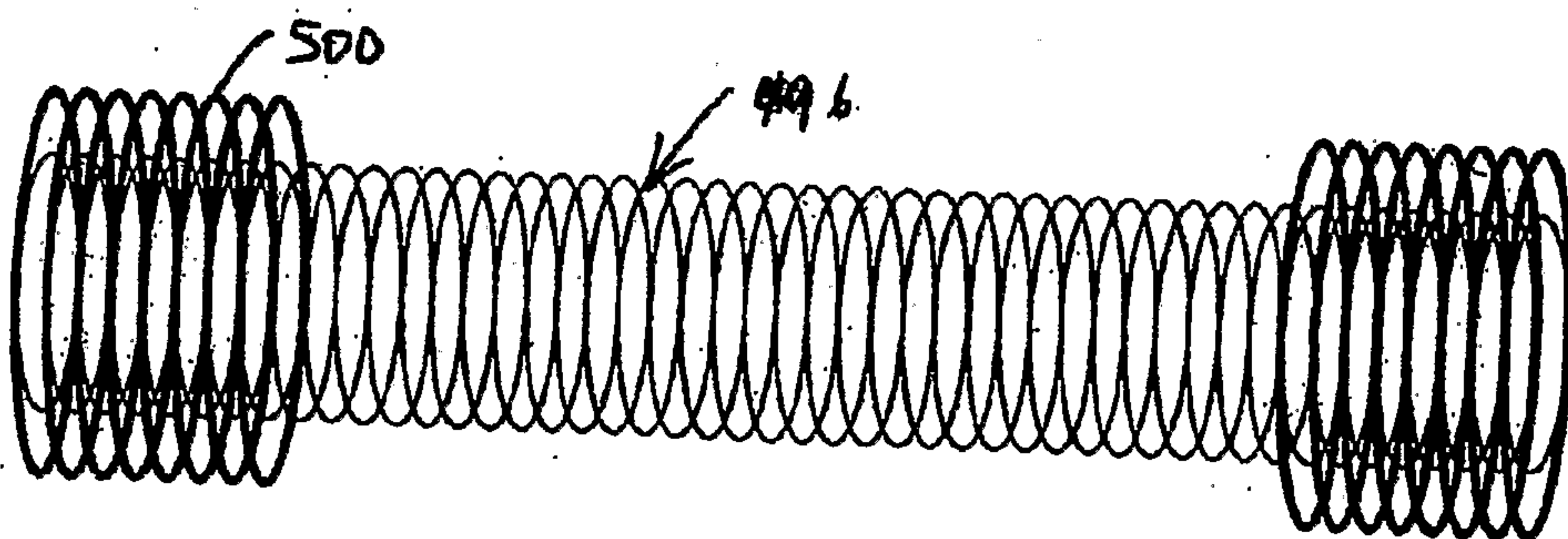


FIG. 20

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**FIG. 21****FIG. 22****FIG. 23**

