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(54) Title: GLUCOSE ANALYZING BLOOD EXAMINER

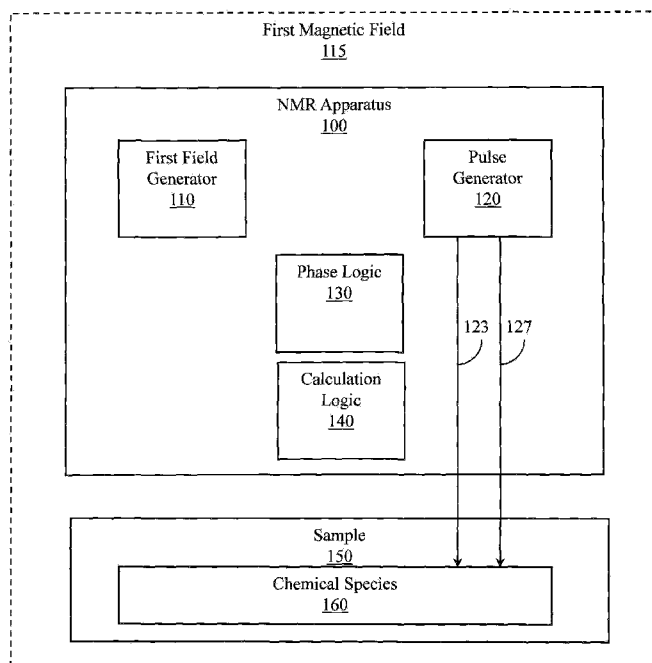


Figure 1

(57) Abstract: In one embodiment, a nuclear magnetic resonance (NMR) apparatus is described. The example NMR apparatus includes a first field generator configured to apply a first magnetic field to a sample (e.g., blood, interstitial fluid). A pulse generator is configured to provide a radio frequency (RF) pulse sequence. The pulse sequence may include a first RF pulse and a second RF pulse. The frequency of the RF pulses is chosen to produce an NMR signal associated with a specific chemical species (e.g., glucose) in the sample. A phase logic is configured to measure the decay of the NMR signal by measuring the phase differences that have accumulated between the spins of the nuclei of the chemical species in the sample. A calculation logic is configured to measure the amount of the chemical species in the sample.



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GLUCOSE ANALYZING BLOOD EXAMINER

PRIORITY CLAIM

[0001] This Application claims the benefit of United States Utility Patent Application 13/017,126, filed January 31, 2011.

BACKGROUND

[0002] According to NIH Publication No. 99-4398, in 1999, diabetes affected an estimated 16 million Americans. As of 1999, about 800,000 new cases were diagnosed annually. In 1999, diabetes was the sixth leading cause of death due to disease in the United States. Since 1980, the age-adjusted death rate due to diabetes has increased by 30 percent. Over the same time period the death rate has decreased for other common multifactorial diseases (e.g., cardiovascular disease, stroke). In 1999, the cost of diabetes to the United States was over \$105 billion. More than one out of every ten U.S. health care dollars was spent for diabetes. About one out of every four Medicare dollars was spent on health care for people with diabetes.

[0003] Diabetes Mellitus, which is commonly referred to more concisely as diabetes, is a chronic disease that affects the ability of the body to maintain desired blood sugar levels. Type 1 diabetes occurs when the pancreas is unable to produce insulin in amounts sufficient to properly control blood sugar levels. Type 1 diabetes may occur when the body actually attacks and destroys cells that are supposed to produce insulin. Thus, type 1 diabetes is considered to be an autoimmune disease in which unknown environmental factors combine with genetic susceptibility to destroy pancreatic beta cells that produce insulin in healthy humans.

[0004] The pancreas is supposed to produce two hormones that together act to maintain desired blood sugar levels. Insulin is supposed to be produced when blood glucose levels get too high. Insulin instructs the body's cells to take in glucose from the blood. Glucagon is supposed to be released when blood glucose levels start to fall too low. Glucagon instructs the liver to convert stored glycogen into glucose and release it into the bloodstream. The action of glucagon is thus opposite to that of insulin. Glucagon also stimulates the release of insulin, so that newly-available glucose in the bloodstream can be taken up and used by insulin-dependent tissues. A diabetic pancreas does not produce appropriate hormones in appropriate amounts at appropriate times, and thus, blood glucose levels can reach undesired levels. Thus, the key characteristic of type 1 diabetes is the inability to manufacture desired amounts of insulin.

[0005] Even though the causes are different, a similar set of dysfunctions occur with Type II diabetes. In Type II diabetes, the cells of the body are unable to receive or transport the sugars from the blood stream into the cells, again leading to a lack of control of blood glucose concentration.

[0006] Undesired blood glucose levels can include too much sugar in the blood (hyperglycemia) and too little sugar in the blood (hypoglycemia). Eating can increase blood sugar levels. Insulin can lower blood sugar levels. Therefore, all people with type 1 diabetes and some with type II take insulin.

[0007] Historically, insulin has been injected under the skin. To achieve the goal of maintaining blood sugar levels in a desired range, diabetics will frequently test their blood sugar levels. Based on the measured blood sugar level, diabetics will ideally inject an appropriate amount and type of insulin at an appropriate time.

[0008] Recently, insulin pumps have been used to deliver insulin continuously and/or periodically. Insulin pumps may be programmed to deliver insulin in set amounts at set times. Some insulin pumps may even be programmed to deliver different amounts on demand based on blood sugar level measurements.

[0009] Determining insulin dosage and delivery time depends on accurately measuring blood sugar levels. Conventionally, measuring blood sugar levels has been

performed by chemically analyzing blood or interstitial fluids. Chemically analyzing blood has conventionally required access to blood and then sacrificing the accessed blood during the chemical test. To acquire the blood a diabetic may prick their finger to get a blood drop. The diabetic will then put the drop of blood in a glucose meter and read the measurement. Alternatively, a probe (e.g., catheter) may be inserted into the body to maintain substantially constant access to a blood or interstitial fluid source.

[0010] Both the finger prick technique and the inserted probe technique are invasive, can be painful, and can provide entry points for bacteria, virus, and infection. Furthermore, since both techniques involve a chemical reaction, the measurements may not always be as accurate as desired. Also, when the diabetic has to read the measurement from the device, there is an opportunity for the measurement to be misread. These inaccuracies can lead to inappropriate amounts of insulin being delivered at inappropriate times.

[0011] Issues associated with inaccurate blood sugar level measurements are exacerbated by the fact that different insulin preparations have different characteristics. For example, different insulin preparations may begin working at different times, may work at different rates, and may work for different periods of time. Making things even worse, different insulin preparations may act differently under different conditions (e.g., age of preparation, exposure to heat, exposure to other chemicals). Conventionally it may have been difficult for the diabetic, especially under certain conditions (e.g., stress, shock) to compute proper dosages and/or mixtures. Thus, it becomes even more likely that inappropriate amounts of insulin can be delivered at inappropriate times. Even if accurate measurements were taken and accurate dosages computed, the actual effect of the injected insulin can only be analyzed by a subsequent measurement.

[0012] A diabetic may experience different insulin demands from day to day, and even from moment to moment as a function of activity, stress, environmental factors, and so on. Therefore, the diabetic may need to be provided with different amounts of insulin when exercising, when sick, when eating more or less than normal, when travelling, when under stress, and under other conditions. However, the conditions that produce the varying needs may also make it difficult, if even possible at all, to make an

accurate blood sugar level measurement. Particularly difficult conditions for monitoring blood sugar levels and delivering appropriate amounts of insulin include during surgery, during high intensity exercise, while asleep, while in a coma, during childbirth, while suffering from dementia, while suffering from Alzheimer's, and so on.

[0013] Therefore, attempts are constantly being made to improve blood sugar level measurement techniques and accuracy and to identify feedback mechanisms to facilitate delivering appropriate amounts of insulin at appropriate times.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate various example systems, methods, and other example embodiments of various aspects of the invention. It will be appreciated that the illustrated element boundaries (e.g., boxes, groups of boxes, or other shapes) in the figures represent one example of the boundaries. One of ordinary skill in the art will appreciate that in some examples one element may be designed as multiple elements or that multiple elements may be designed as one element. In some examples, an element shown as an internal component of another element may be implemented as an external component and vice versa. Furthermore, elements may not be drawn to scale.

[0015] Figure 1 illustrates an embodiment of an NMR apparatus to measure an amount of the chemical species in a sample.

[0016] Figure 2 illustrates an embodiment of an NMR apparatus configured with therapeutic elements.

[0017] Figure 3 illustrates an embodiment of an NMR apparatus configured with drug delivery elements.

[0018] Figure 4 illustrates an embodiment of an NMR apparatus configured with a second field generating apparatus.

[0019] Figure 5 illustrates a method associated with measuring an amount of chemical species in a sample associated with an NMR apparatus.

[0020] Figure 6 illustrates a method associated with measuring an amount of chemical species in a sample associated with an NMR apparatus.

DETAILED DESCRIPTION

[0021] Example systems and methods non-invasively and accurately measure blood sugar glucose levels substantially constantly and substantially in real-time. Example systems and methods employ diffusion nuclear magnetic resonance (NMR) to non-invasively determine blood glucose levels. Blood cells, other cells, and fluid in intercellular spaces will produce different NMR signals as a function of different blood glucose levels. Diffusion speed in the interstitial fluid is affected by the amount of glucose in the fluid. Therefore, the described NMR methods can be used to measure blood glucose levels.

[0022] Envision a twelve ounce glass filled with six ounces of pure water. Now envision adding one tablespoon of sugar to the water. Adding the tablespoon of sugar to the water changes the water. Now envision adding ten or a hundred tablespoons of sugar to the water. Understandable properties of the water will change as the amount of sugar in the water changes. For example, the viscosity of the water will change. Similarly, the transparency of the water may change. In particular, the amount of glucose in a fluid affects diffusion. The higher the glucose level, the lower the diffusion of the water through the solution. This effect is observable using NMR techniques.

[0023] Example systems and methods facilitate acquiring NMR signals from the water and monitoring their decay rates under defined situations. The NMR signals accurately measure the amount of sugar in the water and/or the change in the amount of sugar in the water. The NMR signals are acquired without touching the water. Thus, example systems and methods do not require a finger stick or an embedded sensor that is in contact with blood to be able to measure blood sugar levels.

[0024] Example systems measure the decay of the NMR signal in the presence of either a switched or constant inhomogeneous applied magnetic field. Example systems may employ a constant inhomogeneous main magnetic field, or a gradient field. One example system measures the apparent NMR signal decay rate using an inhomogeneous permanent magnet as the polarizing field for the NMR experiment. Another example system performs conventional diffusion weighted NMR using pulsed or constant field gradients.

[0025] Conventionally, NMR systems have been room-sized. Therefore, conventionally it has been impractical to measure blood sugar levels for diabetics using an NMR system. It is impractical to live inside an MRI apparatus. Therefore, example systems provide miniaturized apparatus that produce very local conditions sufficient to perform very local NMR. Example methods employ the miniaturized apparatus to acquire NMR signals. The NMR signals are then analyzed to determine blood sugar levels. In one embodiment, the blood sugar levels determined from the NMR signals are then used to control an insulin pump.

[0026] NMR spectroscopy provides a non-destructive, quantitative analytical method. Many organic molecules have NMR-active nuclei. Diffusion constants for molecular sized objects in solution can be measured using NMR. The diffusion constants can be measured with an accuracy approaching 1%. Example systems and methods employ diffusion NMR to measure blood glucose levels. Diffusion NMR separates mixture components spectrally based on differing translational diffusion coefficients of chemical species in solution. Therefore, example systems and methods acquire NMR diffusion measurements of complex samples including glucose and other chemicals found in the human body.

[0027] Example systems and methods may probe diffusion using pulsed field gradient NMR. Pulsed field gradient NMR applies magnetic gradient pulses to a sample located in a static magnetic field produced by the apparatus. The magnetic field generated by the gradient pulse varies across the sample. Therefore, molecules in one sample area are subjected to a different magnetic field than molecules in a different sample area. Therefore, the Larmor frequency of the molecules is different meaning that the gradient pulse phase encodes spins according to molecular position. After the gradient pulse, molecules may diffuse from one sample location to another sample location. After a period of time, a dephasing gradient is applied to reverse the phase change produced by the encoding gradient. If an encoded molecule has moved from one location to another, then it will not have its phase encoding reversed and will not be decoded.

[0028] A nearly identical effect occurs when the field gradient or inhomogeneity is constant or nearly constant in time. RF pulses are applied and the decay rate of the signal represents both the intrinsic relaxation of the molecule under investigation as well as additional relaxation due to diffusion. Thus, either system configuration can result in an accurate measurement of molecular motion or diffusion.

[0029] In one example, a sample is subjected to a radio frequency (RF) pulse. The sample includes fluid in which glucose may be present. The RF pulse turns the equilibrium magnetization M_0 in the sample into the transverse plane, which is perpendicular to the main static magnetic field B_0 . The magnetization vector rotates around B_0 at an angular frequency $\omega = d\phi/dt$ given by the Larmor equation:

$$\omega = \gamma B_0$$

where γ is the gyromagnetic ratio ($\gamma = 2\pi \times 42.576 \text{ rad s}^{-1} \text{ T}^{-1}$ for a hydrogen proton).

[0030] After the initial excitation by the RF pulse, some additional magnetic field is present. This could take the form of an inhomogeneous main field or a gradient field $G(x,y,z)$. For example, applying $G(x)$ changes B_0 to a spatially variable field $B(x,y,z) = B_0 + G(x,y,z)$ where $G(x,y,z)$ is substantially non-zero over some fraction of the sensitive volume of the system. A similar formulation can be made in the case of an inhomogeneous main field. Because the field is now spatially varying, Larmor frequencies become different at different places in the sample. Thus, after some period of time, some phase differences may have accumulated between the spins at different positions.

[0031] After waiting for a diffusion time $t = n\Delta t$, an additional RF pulse is applied that flips the spins in the transverse plane. This causes the spins to start to rephase according to their spatial position in the field inhomogeneity. For spins that did not change positions during the diffusion time, the phase differences will be completely reversed. For spins that did change position during the diffusion time, they will not see exactly the same inhomogeneity, and thus, the spins will not exactly reverse phase difference from the first period. This incomplete reversal yields a phase dispersion in the measured sample. Faster diffusion means that the spins have more opportunity to

travel farther and therefore experience larger magnetic field changes. Slower diffusion means that spins have less opportunity to travel and therefore experience smaller magnetic field changes. Diffusion speed in the interstitial fluid is affected by the amount of glucose in the fluid. Therefore, the described NMR methods can be used to measure blood glucose levels.

[0032] Figure 1 illustrates an embodiment of a NMR apparatus 100 for determining the amount of a chemical species in a sample. The NMR apparatus includes a first field generator 110 that is configured to provide a first magnetic field 115 suitable for NMR. The first magnetic field 115 may be a static inhomogeneous applied magnetic field configured not to change in time. The first magnetic field 115 is sufficiently large to encompass a sample 150 or a region of interest of the sample 150.

[0033] A pulse generator 120 provides a first RF pulse sequence. The pulse generator 120 uses frequencies associated with NMR. The RF pulse sequence may include a first RF pulse 123 to excite nuclei associated with a chemical species 160 in the sample 150. The pulse sequence may also include a second RF pulse 127 to cause the nuclei of the chemical species 160 to rephase according to their spatial position in the first magnetic field 115. The frequency of the RF pulse sequence is chosen to produce an NMR signal associated with a specific chemical species 160 (e.g., glucose) in the sample 150 (e.g., blood, tissue, organ). The amount of the chemical species 160 in the sample 150 can be measured as a function of the decay of the NMR signal. A phase logic 130 is configured to measure the NMR signal decay.

[0034] The phase logic 130 measures NMR signal decay by measuring the phase differences that have accumulated between the spins of the nuclei of the chemical species 160 in the sample 150. The NMR signal may be used to discern information about the chemical species 150 in the sample 160. In one embodiment, the NMR signal decay represents, at least in part, the intrinsic relaxation of the chemical species 160. In another embodiment, the NMR signal decay may represent decay due to diffusion.

[0035] The sample 150 may be an interstitial fluid and the chemical species 160 may be glucose. Interstitial fluid is capable of diffusion in the body. Therefore, the phase logic 130 may be configured to measure NMR diffusion. In one embodiment, the pulse

generator is configured to initially excite the nuclei of the chemical species 160 with a first RF pulse 123. The pulse generator is configured to apply a second RF pulse 127 to the sample 150. The second RF pulse 127 causes the spins of the nuclei of the chemical species 160 in the sample 150 to rephase based on their position in the first magnetic field 115.

[0036] A calculation logic 140 is configured to measure the amount of the chemical species 160 (e.g., glucose) in the sample 150 (e.g., interstitial fluid) as a function of the NMR signal decay. If the nuclei of the glucose were able to travel through interstitial fluid, the glucose would experience larger magnetic field changes. Therefore, if the glucose experiences larger magnetic field changes, the interstitial fluid was able to diffuse more quickly indicating less glucose in the interstitial fluid. Conversely, if the glucose experiences fewer magnetic field changes, the glucose was not able to diffuse as quickly, indicating more of the glucose in the interstitial fluid.

[0037] Recall that conventional NMR systems have issues associated with size. The example apparatuses and methods do not require the use of conventional NMR systems. Instead, NMR 100 apparatus may be a miniaturized apparatus that produces very local conditions sufficient to perform very local NMR. For example, the first field generator 110 may be a small neodymium magnet used to generate a first magnetic field 115 that will not change in time. The pulse generator 120 provides an RF pulse sequence with an oscillation rate in a range of approximately 30 kHz to 300 GHz. A pulse generator 120 capable of this oscillation rate may be very small and stamped on a small circuit board using surface mount technology (SMT) or through hole technology (THT) mounts. In one embodiment, the phase logic 130 and a calculation logic 140 are implemented on a microprocessor. Accordingly, the NMR apparatus may be sufficiently small to be mobile.

[0038] In one embodiment, NMR apparatus 100 is mobile to be more practical for patients that may require constant measurements of a chemical species 160 in their bodies. For example, a diabetic patient may require substantially constant monitoring of glucose levels in the blood. A mobile NMR apparatus 100 may be wearable or implantable. Rather than incessant finger pricks or invasive probing (e.g. catheter), a

mobile NMR device that could be worn (e.g. in manner of a watch, pendant) or implanted allows a patient a greater degree of freedom and convenience. Furthermore, a wearable or implantable NMR apparatus 100 does not introduce the risk of infection of its transdermal counterparts (e.g. finger prick, probe, catheter).

[0039] Figure 2 illustrates an embodiment of NMR apparatus 100 that is configured with a therapeutic logic 170. In this embodiment, the therapeutic logic 170 is configured to determine an amount of insulin to be administered to a patient as a function of the measure of the amount of the chemical species 160 (e.g., glucose) in the sample 150 (e.g., interstitial fluid, blood).

[0040] In one embodiment, the calculation logic 140 may measure the amount of chemical species 160 in the sample 150 based on a diffusion rate that is determined to be low. If the measurement of the chemical species 160 in the sample 150 is outside of a predetermined range, the therapeutic logic 170 may determine an amount of insulin to be administered to the patient corresponding to the measured amount of chemical species 160 in the sample 150.

[0041] Recall that there are several opportunities for error when a patient attempts to determine the correct amount of insulin to give self-administer. Therefore, the therapeutic logic 170 determining the correct amount of insulin for the patient, rather than having a patient calculate the amount of insulin, eliminates an opportunity for error. To further reduce the opportunity for error, the NMR apparatus 100 may include an insulin pump to administer the amount of insulin to the patient.

[0042] Figure 3 illustrates an embodiment of an NMR apparatus 100 that is configured with an insulin pump 180 and a feedback logic 190. The insulin pump 180 is configured to administer to the patient the amount of insulin determined by the therapeutic logic 170. The feedback logic 190 is configured to adjust the amount of insulin administered to the patient as a function of a change in the measurement of the amount of the chemical 160 species in the sample 150.

[0043] In one embodiment, the calculation logic 140 determines an amount of chemical species 160 (e.g., glucose) in a sample 150 (e.g., interstitial fluid, blood). A therapeutic logic 170 determines the amount of insulin to be administered to the patient

based, at least in part, on the amount of chemical species 160 in the sample 150. In response to the therapeutic logic 170 determining the amount of insulin to be administered to the patient, the insulin pump 180 administers the amount of insulin to the patient. The feedback logic 190 will adjust the amount of insulin administered to the patient as the amount of chemical species 160 in the sample 150 changes.

[0044] Recall that the blood glucose levels of a diabetic patient vary throughout the day as a function of many variables (e.g., types of food consumed, when food is consumed, how much food is consumed, exercise habits). Therefore, patients must consistently monitor their glucose levels throughout the day and may need varying amounts of insulin based on their insulin level at any given time. The feedback logic 190 allows the insulin pump 180 to administer varying amounts of insulin as a function of a change in the measured amount of glucose in a blood sample.

[0045] Figure 4 illustrates an embodiment of an NMR apparatus 100 that is configured with a second field generator 210. The second field generator 210 is configured to apply a second magnetic field 215. The second magnetic field 215 may be spatially inhomogeneous, a pulsed field gradient, or a constant field. The first magnetic field 115 and the second magnetic field 215 are applied so that the first magnetic field 115 and the second magnetic field 215 can be applied to the sample 150.

[0046] In one embodiment, the second magnetic field 215 affects the pulse sequence applied by the pulse generator 120. In one embodiment, the NMR apparatus 100 may be used to measure the diffusion of the chemical species 160 in a sample 150. Accordingly, the pulse generator 120 may apply derivatives of the stimulated echo pulse sequence (PFG-STE). The pulse generator 120 may apply pulses in pairs. Specifically, the pairs may be bipolar pairs of gradient pulses to reduce artifacts in diffusion spectra.

[0047] In one embodiment, the pulse generator 120 provides the RF sequence a plurality of times. The NMR signal decay is measured by comparing a plurality of NMR signals acquired after the pulse generator 120 has provided the RF sequence a plurality of times.

[0048] Figure 5 illustrates a method associated with of an NMR apparatus for determining the amount of a chemical species in a sample. For example, the method 500 may be employed to determine the amount of glucose in a blood sample.

[0049] Method 500 includes, at 510, controlling an NMR apparatus to apply a first magnetic field to a sample in a patient and to apply a RF pulse sequence to produce an NMR signal in nuclei associated with a chemical species in the sample.

[0050] Method 500 also includes, at 520, acquiring NMR signal decay data associated with a decay of the NMR signal produced in response to applying the first magnetic field and the RF signal.

[0051] Method 500 also includes, at 530, producing a characterization of a chemical species in the sample as a function of the NMR signal decay data. One of ordinary skill in the art will appreciate that the characterization includes information about the chemical species in the sample including, but not limited to, the amount of the chemical species in the sample, and the diffusion rate of the chemical species in the sample.

[0052] Figure 6 illustrates a method 600 associated with of an NMR apparatus for determining the amount of a chemical species in a sample. Method 600 includes, at 610, controlling a NMR apparatus to apply a first magnetic field to a sample in a patient. The first magnetic field may be a static inhomogeneous applied magnetic field configured not to change in time.

[0053] Method 600 also includes, at 620, controlling the NMR apparatus to apply a second magnetic field to the sample. The second magnetic field may be a pulsed field gradient or a constant field gradient. In one embodiment, applying the first magnetic field at 610, and applying the second magnetic field at 620, is done in a manner that produces a spatially inhomogeneous field.

[0054] Method 600 also includes, at 630, applying an RF signal. The RF signal may be configured as a pulse sequence including a first RF pulse and a second RF pulse. The RF signal is configured to produce an NMR signal in nuclei associated with a chemical species in the sample located in the first magnetic field.

[0055] Method 600 also includes, at 640, acquiring NMR signal decay data associated with a decay of the NMR signal produced in response to applying the first magnetic field and the RF signal. The signal decay data may be used to discern information about the chemical species in the sample. For example, the NMR signal data may represent decay due to diffusion.

[0056] Method 600 also includes, at 650, producing a characterization of a chemical species in the sample as a function of the NMR signal decay data. The characterization of a chemical species in the sample may be a measurement at a specific point in time or continually track the chemical species in the sample to measure changes in the chemical species in the sample (e.g., amount of chemical species in the sample).

[0057] Method 600 includes, at 660, controlling an insulin providing apparatus to provide a first dosage of insulin to the patient based, at least in part, on the amount of the chemical species in the sample.

[0058] Method 600 includes, at 670, controlling an insulin providing apparatus to provide a second different dosage of insulin to the patient, based at least in part, on a change in the characterization of the chemical species in the sample.

[0059] To the extent that the term “includes” or “including” is employed in the detailed description or the claims, it is intended to be inclusive in a manner similar to the term “comprising” as that term is interpreted when employed as a transitional word in a claim.

[0060] While example systems, methods, and so on have been illustrated by describing examples, and while the examples have been described in considerable detail, it is not the intention of the applicants to restrict or in any way limit the scope of the appended claims to such detail. It is, of course, not possible to describe every conceivable combination of components or methodologies for purposes of describing the systems, methods, and so on described herein. Therefore, the invention is not limited to the specific details, the representative apparatus, and illustrative examples shown and described. Thus, this application is intended to embrace alterations, modifications, and variations that fall within the scope of the appended claims

Listing of the Claims:

1. A nuclear magnetic resonance (NMR) apparatus, comprising:
 - a first field generator configured to provide a first magnetic field suitable for NMR;
 - a pulse generator configured to provide a radio frequency (RF) sequence at a frequency configured to produce an NMR signal in nuclei associated with a chemical species in a sample located in the first magnetic field;
 - a phase logic configured to measure NMR signal decay; and
 - a calculation logic configured to measure an amount of the chemical species in the sample as a function of the NMR signal decay.
2. The NMR apparatus of claim 1, where the chemical species is glucose, and where the sample is a sample of interstitial fluid.
3. The NMR apparatus of claim 1, where the NMR apparatus is one of, mobile, wearable, and implantable.
4. The NMR apparatus of claim 1, comprising a therapeutic logic configured to determine an amount of insulin to be administered to a patient as a function of the measure of the amount of the chemical species in the sample.
5. The NMR apparatus of claim 4, comprising an insulin pump configured to administer the amount of insulin to the patient.
6. The NMR apparatus of claim 5, where the insulin pump comprises a feedback logic configured to adjust the amount of insulin administered to the patient as a function of a change in the measure of the amount of the chemical species in the sample.
7. The NMR apparatus of claim 1, where the first magnetic field is a static inhomogeneous applied magnetic field configured not to change in time.

8. The NMR apparatus of claim 1, where the pulse sequence comprises a first RF pulse to excite nuclei associated with a chemical species in a sample and a second RF pulse to cause the nuclei of the chemical species to rephase according to their spatial position in the first magnetic field.
9. The NMR apparatus of claim 1, comprising a second field generating apparatus configured to provide a second magnetic field, where the superposition of the first magnetic field and the second magnetic field is spatially inhomogeneous.
10. The NMR apparatus of claim 9, where the second magnetic field is one of, a pulsed field gradient, and a constant field gradient.
11. The NMR apparatus of claim 1, where the NMR signal decay represents decay due to diffusion.
12. The NMR apparatus of claim 1, where the NMR signal decay represents the intrinsic relaxation of the chemical species.
13. The NMR apparatus of claim 1, where the NMR signal decay is measured by comparing a plurality of NMR signals acquired after the pulse generator has provided the RF sequence a plurality of times.
14. A method, comprising:
 - controlling a NMR apparatus to apply a first magnetic field to a sample in a patient and to apply a RF signal to produce an NMR signal in nuclei associated with a chemical species in the sample;
 - acquiring NMR signal decay data associated with a decay of the NMR signal produced in response to applying the first magnetic field and the RF signal; and
 - producing a characterization of a chemical species in the sample as a function of the NMR signal decay data.

15. The method of claim 14, where producing the characterization comprises identifying an amount of the chemical species in the sample.
16. The method of claim 14, comprising:
 - controlling an insulin providing apparatus to provide a first dosage of insulin to the patient based, at least in part, on the amount of the chemical species in the sample.
17. The method of claim 16, comprising:
 - controlling the insulin providing apparatus to provide a second, different dosage of insulin to the patient based at least in part, on a change in the characterization of the chemical species in the sample.
18. The method of claim 14, comprising:
 - controlling the NMR apparatus to apply a second magnetic field to the sample.
19. The method of claim 18, where the NMR apparatus is controlled to apply the first magnetic field and the second magnetic field in a manner that produces a spatially inhomogeneous field.
20. The method of claim 19, where the NMR apparatus is controlled to apply the second magnetic field as one of a pulsed field gradient and a constant field gradient.
21. The method of claim 14, where the NMR apparatus is at least one of mobile, and wearable.
22. A system for determining an amount of a chemical species in a solvent in a patient, comprising:
 - means for applying a static inhomogeneous magnetic field to the solvent;
 - means for applying a spatially inhomogeneous magnetic field to the solvent;

means for applying a RF signal to produce a NMR signal in nuclei associated with the chemical species in the solvent, where the solvent is in the static inhomogeneous magnetic field and the spatially inhomogeneous magnetic field;

means for characterizing a decay of the NMR signal;

means for characterizing the amount of the chemical species in the solvent based, at least in part, on the decay;

means for administering a dosage of insulin to a patient, where the dosage amount is a function of the characterization of the chemical species in the solvent; and

means for adjusting the dosage of insulin to the patient based, at least in part, on a change in the characterization of the chemical species in the solvent.

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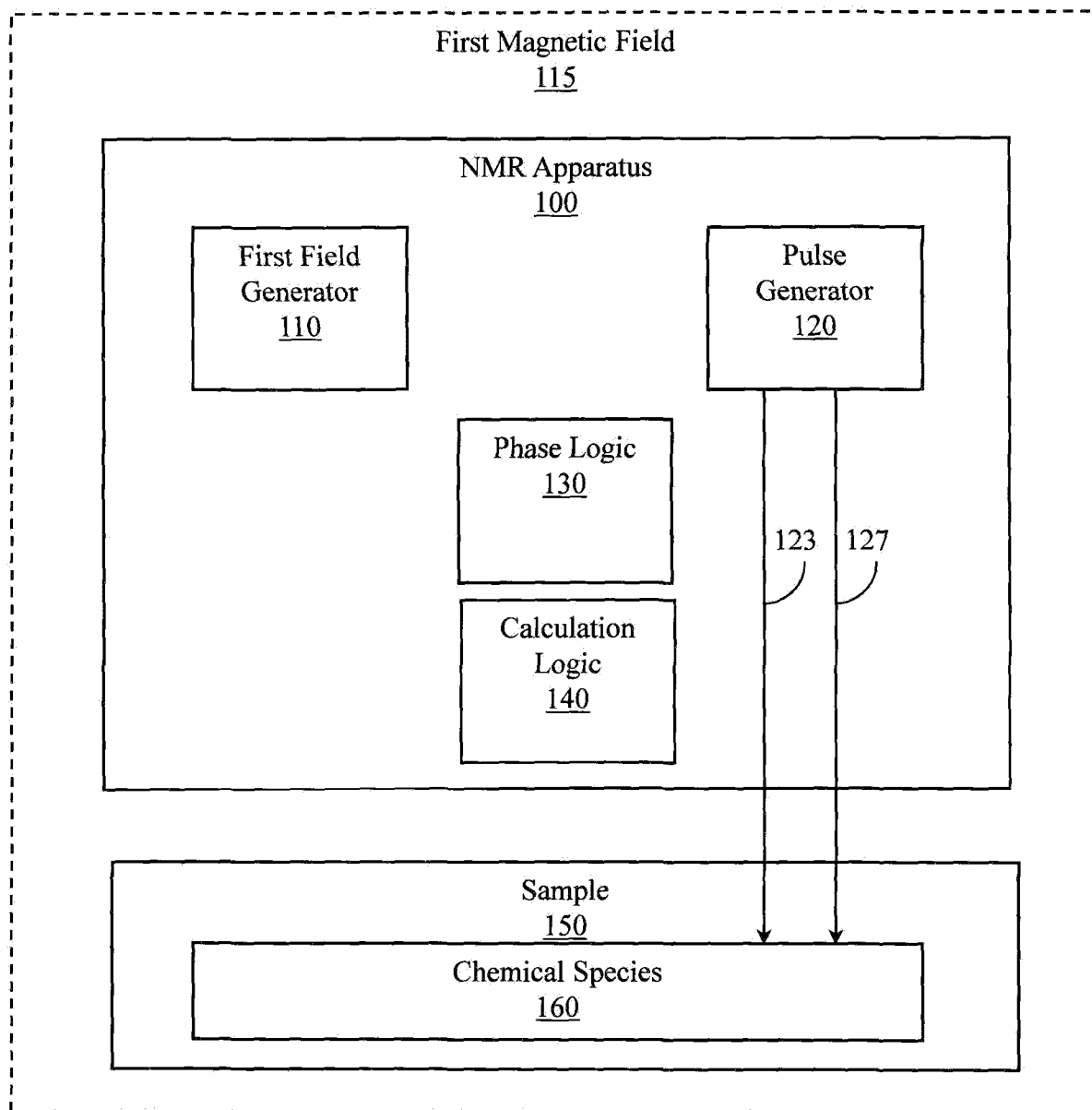


Figure 1

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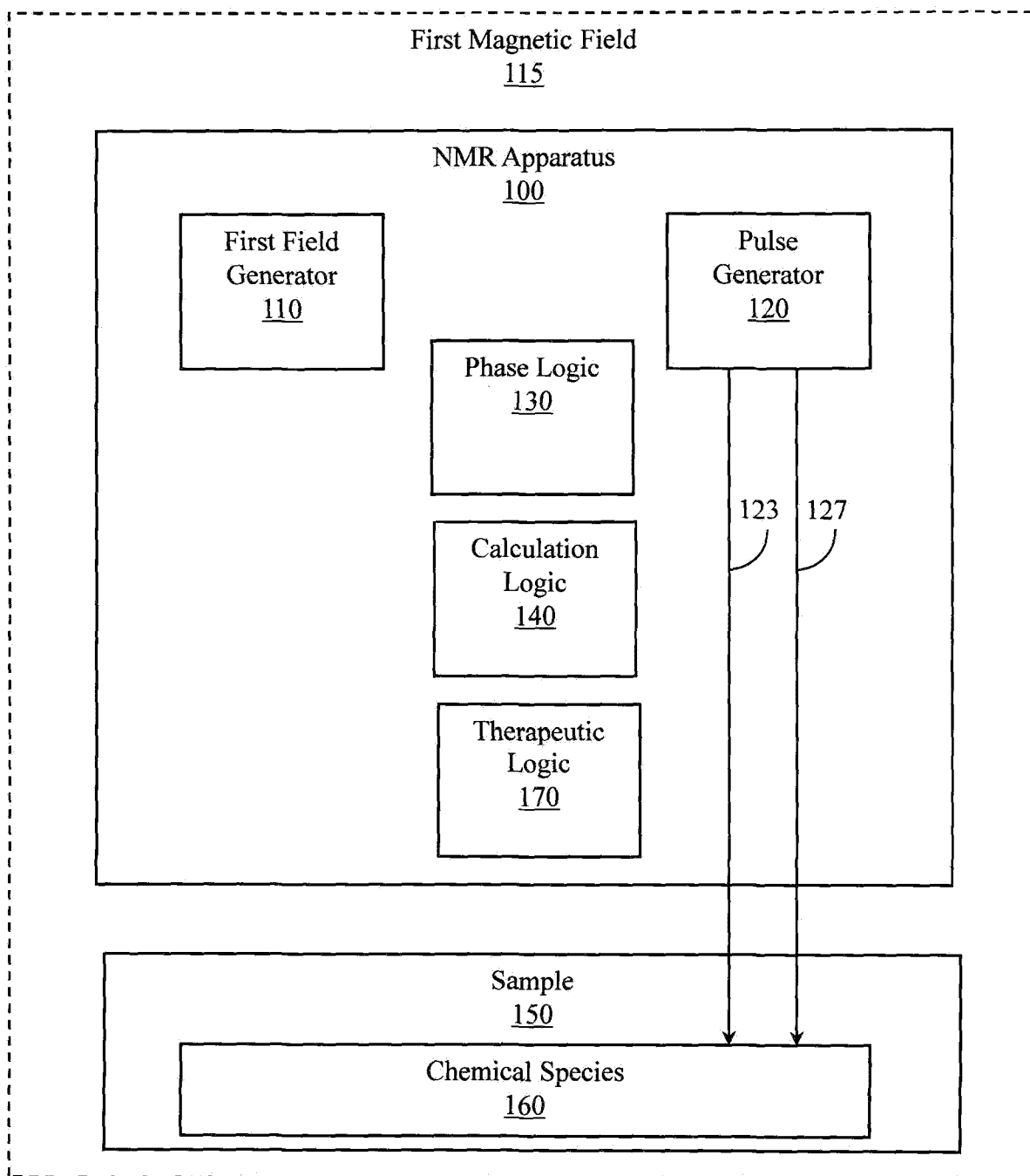


Figure 2

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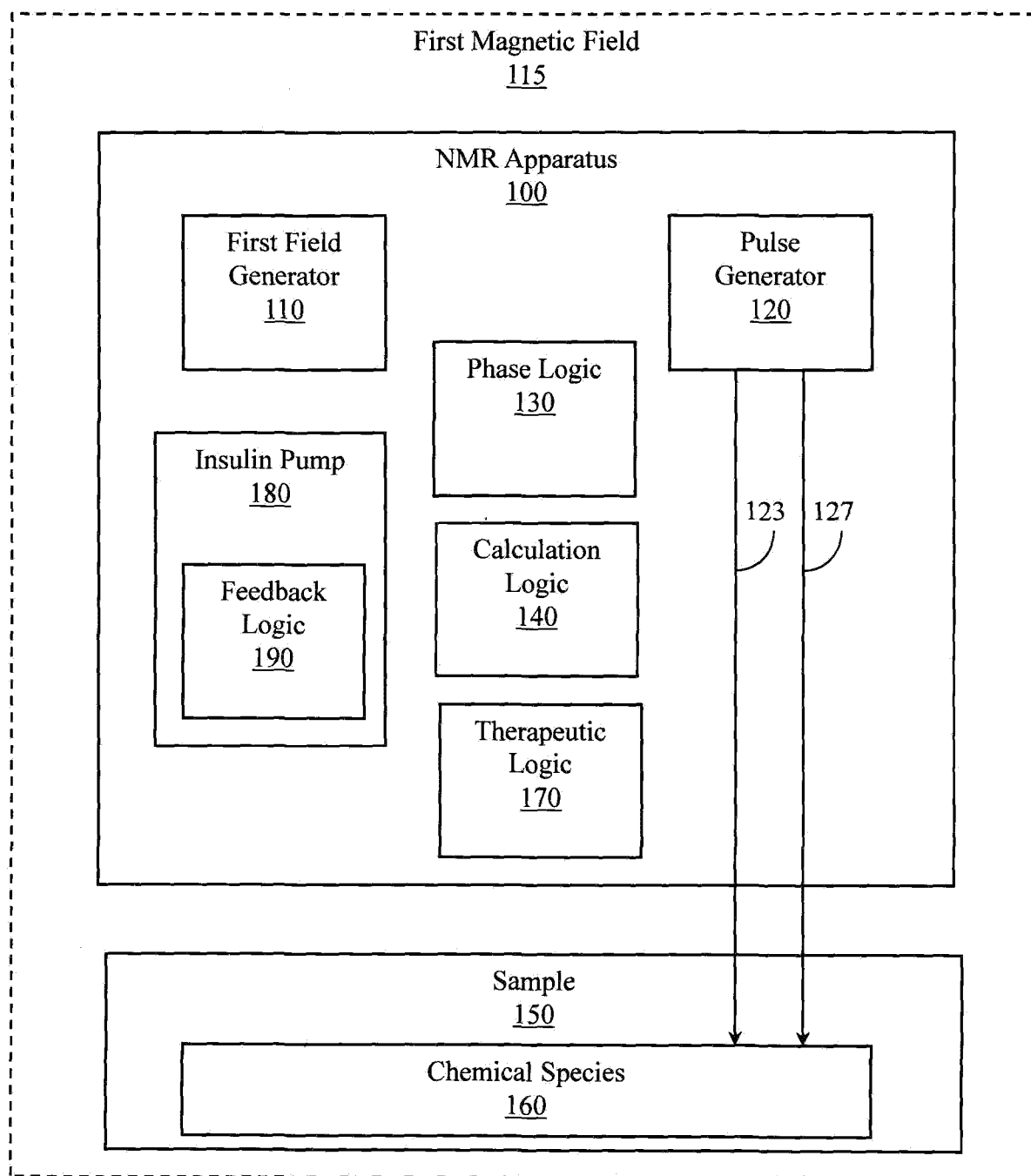


Figure 3

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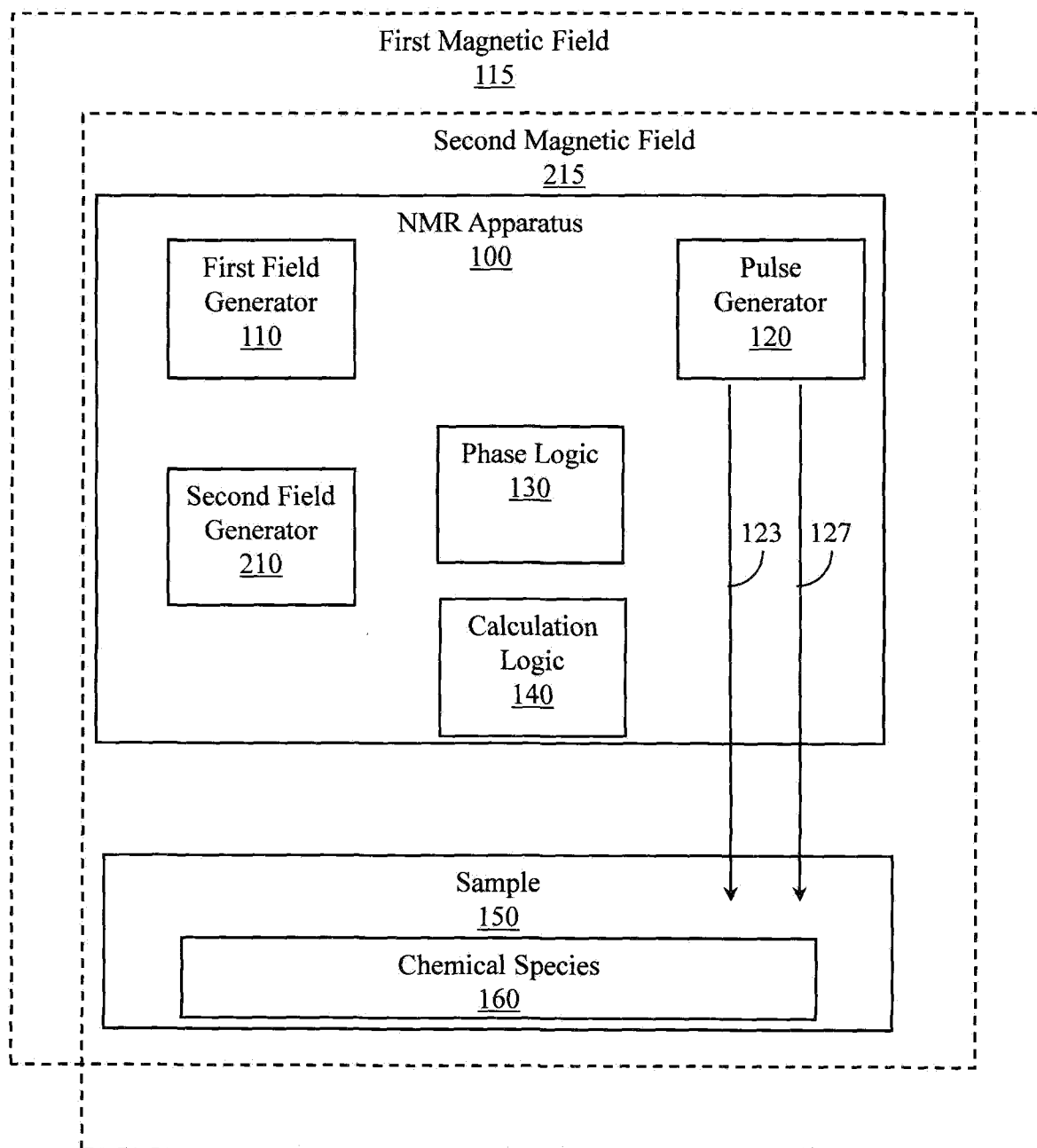


Figure 4

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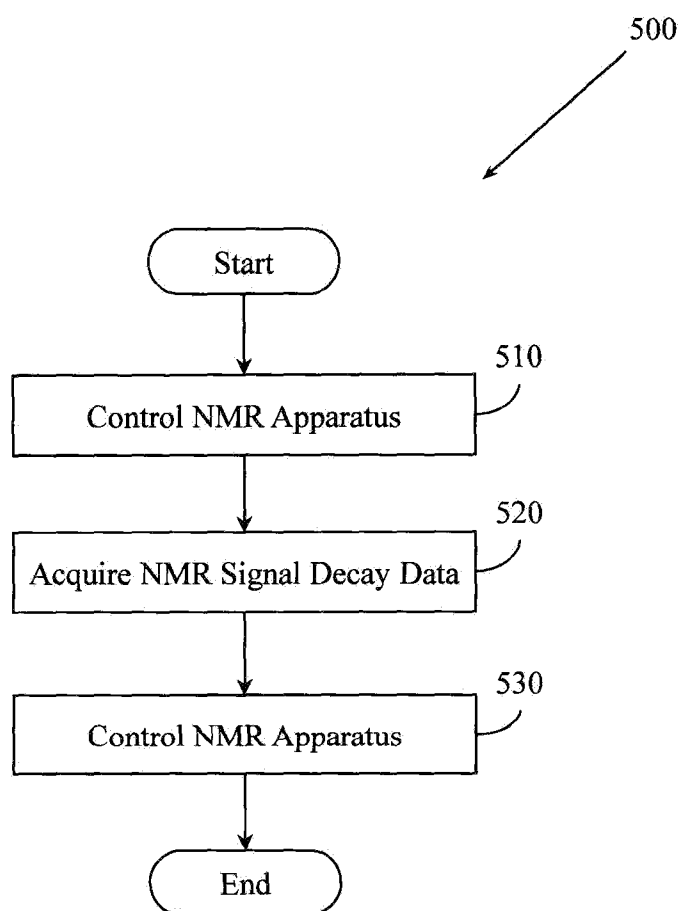


Figure 5

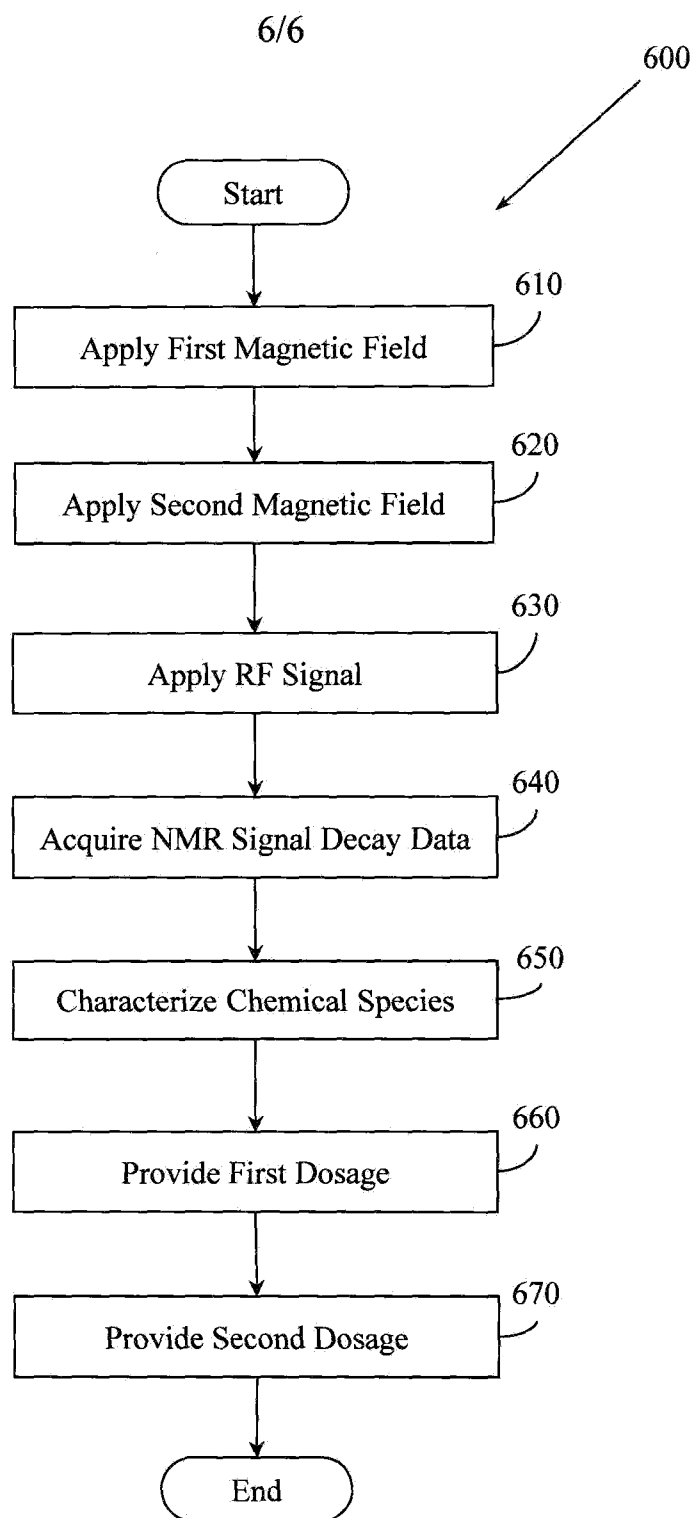


Figure 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/22427

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01V 3/00 (2012.01)

USPC - 324/309; 324/300; 324/307

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC -- 324/309; 324/300; 324/307

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC -- 324/309; 324/300; 324/307 (keyword delimited)

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

PubWEST (USPT, PGPB, JPAB, EPAB); Google

Search Terms Used: Glucose, diabetes, insulin, analyte, assay, NMR, magnetic field, pulse generator, signal decay, implant, mobile, frequency, insulin pump

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US 2009/0134869 A1 (Lee) 28 May 2009 (28.05.2009), entire document especially Abstract, para [0011]-[0012], [0022], [0017]-[0018], [0176], [0035], [0049], [0067] and [0189]	1-3, 7-15, 18-21 ----- 4-6, 16, 17, 22
Y	US 2010/0228111 A1 (Friman et al.) 09 September 2010 (09.09.2010), entire document especially Abstract, para [0044] and [0046]-[0047]	4-6, 16, 17, 22
A	US 5,685,300 A (Kuenstner) 11 November 1997 (11.11.1997), entire document	1-22

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

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

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30 April 2012 (30.04.2012)

Date of mailing of the international search report

08 MAY 2012

Name and mailing address of the ISA/US

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