(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 March 2006 (16.03.2006)

PCT

(10) International Publication Number
WO 2006/028588 A2

(51) International Patent Classification:
G01R 19/18 (2006.01)

(21) International Application Number:
PCT/US2005/026229

(22) International Filing Date: 21 July 2005 (21.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/590,581 22 July 2004 (22.07.2004) US
60/609,032 9 September 2004 (09.09.2004) US

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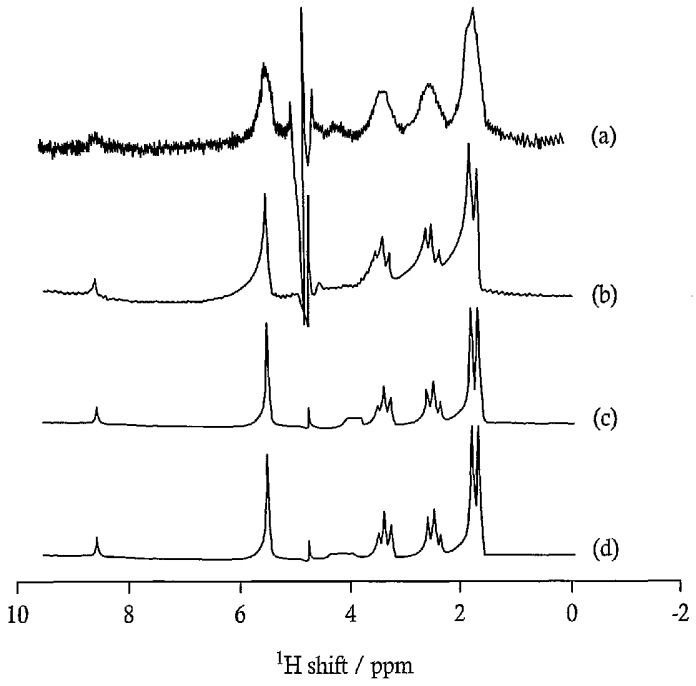
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,

[Continued on next page]

(54) Title: NUCLEAR MAGNETIC RESONANCE DETECTION IN INHOMOGENEOUS MAGNETIC FIELDS



(57) Abstract: Methods and systems for compensating for static magnetic field inhomogeneities during nuclear magnetic resonance detection are disclosed. Application of radio frequency pulses and/or magnetic field gradients may be used to correct for spin dephasing caused by the inhomogeneities. The methods and system may be used to improve signal-to-noise ratios in NMR and MRI systems where magnetic field inhomogeneity may have an effect.

WO 2006/028588 A2

RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

NUCLEAR MAGNETIC RESONANCE DETECTION IN INHOMOGENEOUS MAGNETIC FIELDS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] This invention pertains generally to nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI), and more particularly to a method and apparatus for NMR and MRI in inhomogeneous magnetic fields.

Description of the Related Art

[0002] Modern NMR spectroscopy and MRI require highly homogeneous strong magnetic fields over a region of interest, such as limiting inhomogeneities to as little as 1 part per billion (1 ppb). This leads to physically large and expensive super-conducting magnets due to shimming magnets used to achieve extreme field homogeniety. In NMR, highly homogeneous magnets (superconducting, permanent magnets or electromagnets) are used in order to detect the Free Induction Decay (FID) of the nuclear magnetization. The frequency and the intensity of this signal is proportional to the applied magnetic field. In an inhomogeneous magnetic field the magnetization dephases because of different precession frequencies in different parts of the sample. Field inhomogeneities lead to line broadening, poor signal-to-noise ratio, and loss of spectral information. For this reason special effort is made in the construction of electromagnetic coils (shims) which are used in order to render the original magnetic field as homogeneous as possible over the detected sample volume. The excitation and detection of the FID is made using a radio-frequency (RF) coil also having very good homogeneity. RF inhomogeneities have been traditionally seen as sources of imperfection in excitation, inversion and decoupling, leading to spectral artifacts and poor signal-to-noise ratios.

[0003] The following publications provide additional background information and are incorporated herein by reference in their entirety:

[0004] High-resolution NMR of anisotropic samples with spinning away from the magic angle, 377, 333-339 (2003), *Chem. Phys. Lett* (D. Sakellariou, C.A. Meriles, R.W. Martin and A. Pines).

[0005] Broadband Phase Modulation by Adiabatic Pulses, *Journal of Magnetic Resonance,* 164, 177181 (2003), (C.A. Meriles, D. Sakellariou and A. Pines).

[0006] Variable Rotation Composite Pulses for High Resolution Nuclear Magnetic Resonance Using Inhomogeneous Magnetic and Radiofrequency Fields *Chem. Phys. Lett.,* 363, 25-33 (2002) (Dimitris Sakellariou, Carlos Andres Meriles, Adam Moule and Alexander Pines).

Gradients, *J. Magn. Reson.* 156 (1), 146-151 (2002) (Henrike Heise, Dimitris Sakellanou, Carlos Meriles, Adam Moule and Alexander Pines).

[0008] Resolved magic-angle spinning of anisotropic samples in Inhomogeneous Fields, *Chem. Phys. Lett.* 358 (5,6), 391-395 (2002) (Carlos Andres Meriles, Dimitris Sakellariou and Alexander Pines).

[0009] Nuclear Magnetic Resonance in inhomogeneous magnetic fields, *J. Magn Reson.,* 145, 246-258, (2000), (F. Balibanu, K. Hailu, D.E. Demco, and B. Blumich).

[0010] Approach to High-Resolution *Ex-Situ* NMR Spectroscopy, *Science,* 293, No. 5527, 82-85 2001 (Carlos Meriles, Dimitris Sakellariou, Henrike Heise, Adam Moule, Alexander Pines).

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[0013] Measurement of High-Resolution NMR spectra in a inhomogeneous magnetic field, J. *Am. Chem. Society, 109,7579-7581,* (1987) (L.D. Hall, T.J. Norwood).

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[0015] Total Spin Coherence Transfer Echo Spectroscopy, J. Chem. Phys. 79, 5301-5310 (1983) (J.R. Garbow, D.P. Weitekamp, and A. Pines).

[0016] High Resolution NMR in Inhomogeneous Magnetic Fields: Application of Total Spin Coherence Transfer Echoes, J. *Am. Chem. Soc., 103,* 3578-3579 (1981) (D.P. Weitekamp, J.R. Garbow, J.B. Murdoch, and A. Pines).

SUMMARY OF THE INVENTION

[0017] One embodiment disclosed herein includes a method for detecting nuclear magnetic resonance of a sample in magnetic fields having at least about 0.5 ppm (or alternatively, 500 ppb) inhomogeneity in static magnetic field strength, including applying a radio frequency pulse comprising a time-varying frequency to the sample and simultaneously applying a time varying magnetic field gradient to the sample, wherein the time varying magnetic field gradient is superimposed over the inhomogeneous magnetic field.

[0019] Another embodiment disclosed herein includes a method for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field within a volume substantially enclosed by a magnet, including applying a first radio

magnetic field, and applying a second radio frequency inversion pulse.

[0020] Another embodiment disclosed herein includes a system for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field, including a radio frequency coil, one or more magnetic field generating coils, a first current generating module coupled to the radio frequency coil, and at least one second current generating module coupled to at least one of the magnetic field generating coils, wherein the first and second current generating modules are adapted to apply currents through the coils so that a radio frequency pulse and magnetic field gradient are applied in such a manner that effects of inhomogeneity in the static magnetic field are substantially counteracted.

[0021] Another embodiment disclosed herein includes a system for detecting a magnetic resonance signal, including means for applying a static magnetic field to a sample, means for counteracting effects of inhomogeneity in the static magnetic field, and means for detecting a magnetic resonance signal from the sample.

[0022] Another embodiment disclosed herein includes a system for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field as substantially shown and described.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] FIGURES 1A through 1D depict four examples where static magnetic field inhomogeneity may need to be corrected in NMR and MRI applications.

[0024] FIGURE 2 depicts application of spatially matched inhomogeneous z-rotation pulses for compensation of magnetic field inhomogeneity in NMR and MRI systems.

[0025] FIGURE 3 depicts application of magnetic field gradient pulses for compensation of magnetic field inhomogeneity in NMR and MRI systems.

[0026] FIGURE 4 depicts a system comprising radio frequency coils and magnetic field gradient coils for applying "shim pulses" to compensate for magnetic field inhomogeneity in NMR and MRI systems.

[0027] FIGURE 5 depicts a simulated 2D saddle-shaped quadratic magnetic field inhomogeneity.

[0028] FIGURE 6A depicts a time-modulated rf pulse frequency sweep useful for compensating for the inhomogeneity depicted in Figure 5.

[0029] FIGURE 6B depicts a time-modulated magnetic field gradient useful for compensating for the inhomogeneity depicted in Figure 5.

[0030] FIGURE 6C depicts the effect on NMR spectra by applying the pulses depicted in Figures 6A and 6B.

with radial symmetry.

[0032] FIGURE 8A depicts a time-modulated rf pulse frequency sweep useful for compensating for the inhomogeneity depicted in Figure 7.

[0033] FIGURE 8B depicts a time-modulated magnetic field gradient useful for compensating for the inhomogeneity depicted in Figure 7.

[0034] FIGURE 8C depicts the effect on NMR spectra by applying the pulses depicted in Figures 8A and 8B.

[0035] FIGURE 9A depicts time-modulated radio frequency amplitude pulses useful for compensating for quadratic magnetic field inhomogeneity.

[0036] FIGURE 9B depicts an adiabatic frequency sweep in time-modulated radio frequency pulses useful for compensating for quadratic magnetic field inhomogeneity.

[0037] FIGURE 9C depicts a time-modulated magnetic field gradient useful for compensating for quadratic magnetic field inhomogeneity.

[0038] FIGURE 10A depicts an NMR spectrum of thiamine hydrochloride in the presence of an inhomogeneous static magnetic field.

[0039] FIGURE 10B depicts an NMR spectrum of thiamine hydrochloride in the presence of an inhomogeneous static magnetic field utilizing compensating shim pulses with a constant magnetic field gradient to correct only linear inhomogeneities.

[0040] FIGURE 10C depicts an NMR spectrum of thiamine hydrochloride in the presence of an inhomogeneous static magnetic field utilizing compensating shim pulses with a time-modulated magnetic field gradient to correct linear and quadratic inhomogeneities.

[0041] FIGURE 10D depicts an NMR spectrum of thiamine hydrochloride in the presence of a homogeneous static magnetic field.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0042] In various embodiments, methods and systems are provided for detecting nuclear magnetic resonance signals in inhomogeneous static magnetic fields. In some embodiments, the methods and systems may be used to improve the signal-to-noise ratio in currently available NMR and MRI. For example, higher resolution NMR spectra can be obtained. Additionally, the useful sample volume for NMR can be increased. Furthermore the time needed to render a magnet more homogeneous can be minimized. The methods and systems may also offer significant advantages in cases where a signal needs to be acquired very rapidly (e.g., no time for classical shimming of the magnet). Another possible application is with very high field magnets (proton Larmor frequency higher than 1 Ghz), which are not able to provide enough homogeneity in order to perform high-resolution NMR. In other embodiments, the methods and systems may be

magnetic fields. In some embodiments, NMR and MRI systems may be used that contain little or no shim magnets or shim magnets consisting of permanent non-adjustable magnets. In some embodiments, the methods and systems disclosed herein may be used in conjunction with magnets where the sample being analyzed is not within a volume substantially enclosed by the magnet. Thus, more flexible magnet geometry is possible.

[0043] The methods and systems disclosed herein can be used for analytical purposes for higher resolution NMR spectroscopy of various molecules. Higher resolution can be used to obtain enhanced structural and dynamic information, identification and product control. The methods may be particularly useful for detecting insensitive nuclei, such as C^{13}, N^{15}, and others present in bio-organic and inorganic materials. The same rationale allows for the acquisition of many samples inside the same magnet at the same time, leading to high-throughput NMR. A significant gain in acquisition time and thus in signal-to-noise ratio can be obtained. Also the time and procedure necessary to render a magnet homogeneous (shimming) could be greatly enhanced by the methods disclosed herein.

[0044] Figures 1A-1D depict four embodiments where the methods and systems disclosed herein may be used to counteract the effects caused by inhomogeneities in static magnetic field. In Figure 1A, a system is used where the static magnetic field is not homogeneous at the sample location 100 within the magnet bore because a cheaper magnet 102 or little or no shim coils are used. By using the methods disclosed herein, the effects of the inhomogeneity can be compensated for to obtain a high quality signal. In Figure 1B, a system is used where the sample 104 is too large to fit within the homogeneous region of the static magnetic field generated by a high quality magnet 106. The methods disclosed herein may be used to extend the capability of such systems (e.g., an existing NMR or MRI machine) in order to detect signals from larger sample sizes. In Figure 1C, a system is used where the static magnetic field generated is homogeneous enough to measure a single sample 108 that is small enough to fit within a region of homogeneous magnetic field. However, the methods disclosed herein may be used to allow simultaneous measurement of multiple such samples within the bore of the magnet 106, even though the magnetic field homogeneity does not extend throughout the entire region. In Figure 1D, a system is used where the sample 110 is placed in a location other than within a volume substantially enclosed by the magnet 112. Although the static magnetic field at such a location may not be homogeneous, the methods disclosed herein may be used to compensate for the effects of the inhomogeneity, allowing high quality detection. Those of skill in the art will recognize many other configurations and systems where the methods disclosed herein can be used to improve nuclear magnetic resonance detection in the presence of inhomogeneous magnetic fields.

magnetic field generated within a volume substantially enclosed by a magnet may be counteracted by applying radio frequency pulses from inhomogeneous radio frequency coils that are spatially matched to the static magnetic field. In another embodiment, the dephasing effects caused by an inhomogeneous static magnetic field generated within a volume substantially enclosed by a magnet may be counteracted by applying a magnetic field gradient from inhomogeneous gradient coils that are spatially matched to the static magnetic field. In still another embodiment, the dephasing effects caused by an inhomogeneous static magnetic field generated by a magnet, either within a volume substantially enclosed by a magnet or outside of the geometry of the magnet, may be counteracted by applying radio frequency pulses in combination with magnetic field gradients. In various embodiments, the amount of inhomogeneity compensated for by the methods and systems disclosed herein are at least about 0.3 ppm, at least about 0.5 ppm, at least about 0.8 ppm, or at least about 1 ppm.

Correcting of B_0 Inhomogeneity Using Spatially Matched Inhomogeneous RF Coils and RF Pulse Sequences

[0046] In one embodiment, spatially matched inhomogeneous rf coils are used to counteract static magnetic field inhomogeneity. The spatial matching between the static field and the set of rf coils guarantees a correlation of the fields and the possibility of mutual canceling of their effects. The effects of an inhomogeneous static or rf field are similar and lead to dephasing in their respective frames of reference. Z-rotation composite or adiabatic pulses may be used to compensate for these dephasings and can produce inhomogeneity free NMR spectra in the presence of inhomogeneous field. Relevant information is preserved because, contrary to what happens during free evolution periods, the dephasing due to chemical shift differences is negligible during the irradiation period: the rf pulses only eliminate the dephasing induced by the static field gradient. Separate coils can be used for detection, or alternatively other detection methods could be implemented without loss of information. Related ex-situ techniques are described in US Patent 6,674,282 to Pines, et al., which is hereby incorporated by reference in its entirety.

[0047] Figure 2 depicts one such embodiment. A spatially matched inhomogeneous rf excitation coil may be provided to apply z-rotation pulses 150 to the sample. The excitation pulse scheme can be broadband or selective over a region of special interest. Such a region could be for example a region of good correlation between the static and rf fields. The z-rotation pulses may comprise a windowed or windowless pulse train to cancel periodically the effects of inhomogeneities, giving rise to nutation echoes maxima. An rf detection coil may then be used to acquire inhomogeneity free FIDs 152 at the nutation echoes maxima times 154. Fourier transformation of the FIDs will yield an inhomogeneity free NMR spectrum. In some

order to compensate for higher order inhomogeneity effects.

Correcting of B_0 Inhomogeneity Using Spatially Matched Gradient Coils And RF Pulse Sequences

[0048] In another embodiment, spatially matched inhomogeneous gradient coils may used to apply a magnetic field gradient to a sample in an inhomogeneous static magnetic field in order to compensate for the inhomogeneity of the static field. The coil may serve to temporally increment the field inhomogeneity of the static field in the detection region. However, it should preserve the general functional dependence of the static field in the area. In other words, the magnetic field created by the gradient coil should match the static field inhomogeneity profile. Ideally, the average contribution of this "refocusing field" in the zone is zero.

[0049] Figure 3 depicts one such embodiment. An interval in which the gradient field is on 170 follows an interval of free evolution 172. Before and after switching the gradient coil on and off, respectively, inversion pulses (e.g., π pulses 174) may be applied to generate nutation echoes. Because, by construction, this coil increases the total field inhomogeneity, the duration of the interval with the coil on (e.g., t_1) is advantageously shorter than the interval of free-evolution (e.g., t_2). As a result, the amplitude of the echoes becomes modulated by a residual dephasing due to the chemical shift. Detection of FIDs 176 at the echo centers 178 leads to the reconstruction of the high-resolution spectrum.

[0050] In principle, temporal evolution is slower when using spatially matched inhomogeneous magnetic field coils as compared to spatially matched inhomogeneous rf coils because the chemical-shift induced dephasing is partially inverted during the refocusing period when applying the spatially matched magnetic field. As depicted in Figures 2 and 3, the scaling factors (S_1) for each method may be calculated as a function of the ratio between the gradient of the refocusing field (G_G) and the gradient of the static field (G_S). For a fixed value of this ratio, using spatially matched inhomogeneous rf coils provides a higher scaling factor. However, because the gradient coil does not need to be part of a tuned circuit, its geometry and number of turns can substantially differ from those used in an rf excitation coil. Thus, the produced gradient amplitude could be considerably higher than amplitudes generated by rf coils.

"Shim Pulses" - Correction of B_0 Inhomogeneity Using Time-Dependent B_0 Gradient Pulses and RF Pulse Sequences

[0051] In one embodiment, rf pulses are applied simultaneously with magnetic field gradients to compensate for static magnetic field inhomogeneity. No need to match the static field inhomogeniety is necessary, and in some embodiments, the rf pulses are substantially spatially uniform, where "substantially spatially uniform" means that no intentional field strength variation

gradient coils do not need to be spatially matched to the static magnetic field. The frequency and amplitude of the rf signal during application of the pulse may be made to vary with time. Similarly, the amplitude of the magnetic field gradient may vary with time during application of the pulse. Static field gradients produced by gradient coils impose a spatial dependence of the spin precession frequency. Frequency selective rf pulses applied in the presence of B_0 gradients thus affect spins in a spatially selective way. An adiabatic full passage of an rf pulse induces a B_0-dependent phase shift, which is canceled by a second passage if B_0 remains the same. Adiabatic pulses are described in Garwood, et. al, Journal of Magnetic Resonance 153 (2000), pages 155-177, which is hereby incorporated by reference in its entirety. By changing the B_0 gradients during the two passages the phase of the spins are affected with a magnitude that depends on position in space. Conditions can be achieved where the imposed phase shift exactly cancels the phase shift originating from the B_0 field imperfections. The applied B_0 give the spatial selectivity, the change of the B_0 gradients with time determines the amount and shape of the correction, and the adiabatic double passage is the "engine" with which the correction is driven. A constant magnetic field gradient provides linear corrections to the magnetic field inhomogeneity. Time dependence of the applied gradients make higher order corrections possible. 3D inhomogeneity can be corrected by simultaneously applying B_0 gradients in three directions. In one embodiment, linear gradients are applied in three orthogonal directions and a homogeneous rf sweep is applied.

[0052] An NMR spectrum free from the broadening caused by imperfect B_0 can be obtained by the application of an rf-pulse with B_0 gradients between each detected point in the time-domain NMR signal. One or more "shim pulses" as described above may be applied in a pulse train with FID acquisition between each series of pulses. In another embodiment, the "shim pulses" may be applied between acquisitions during magnetic resonance imaging.

[0053] In one embodiment, coils may be used to detect and map the inhomogeneity in the static magnetic field. Using the mapped inhomogeneity, the appropriate application of rf pulses and magnetic field gradients may be numerically determined to compensate for the inhomogeneity. In one embodiment, the same coils as used to apply the magnetic field gradients may be used to detect and map the inhomogeneity.

Shim Pulse Systems

[0054] In one embodiment, a system for applying compensating rf pulses and magnetic field gradients is provided. Figure 4 depicts one such embodiment. A radio frequency coil 200 is provided to apply homogeneous rf signals to sample 202. A current generating module 204 is coupled to the radio frequency coil 200 for driving current through the coil 200. The current generating module 204 may be adapted to apply rf pulses that sweep across a desired time-

field passing through the sample 202 may be compensated for. Multiple magnetic field gradient coils 206 and 208 are provided. In one embodiment, the coils 206 and 208 are positioned orthogonal to each other. The magnetic field gradient coils 206 and 208 are coupled to current generating modules 210 and 212 for driving current through the coils 206 and 208. The current generating modules 210 and 212 may be adapted to apply time-modulated magnetic field gradients through the sample 202 such that when combined with the rf pulses from the rf coil 200, the effects of inhomogeneity in a static magnetic field passing through the sample 202 may be compensated for. In one embodiment, a computation module 214, such as a general purpose computer, may be coupled to the current generating modules 204, 210, and 212 for computing the current waveforms that need to be applied by the modules 204, 210, and 212 so that inhomogeneity compensating pulses and gradients are applied.

[0055] In one embodiment, current measurement modules 216 and 218 may be coupled to the magnetic field gradient coils 206 and 208 so that the static magnetic field may be measured by the coils 206 and 208. The computation module 214 may receive the current measured by the modules 216 and 218 as input so that it can map the inhomogeneity of the static magnetic field through the sample 202. The computation module 214 may then numerically calculate the current needed to be applied by current generating modules 204, 210, and 212 in order to compensate for the inhomogeneity.

[0056] In one embodiment, the sample 202 and coils 200, 206, and 208 may be placed within a volume substantially enclosed by a magnet that generates a static magnetic field. The inhomogeneities in the field generated by the magnet may be compensated for using the coils 200, 206, and 208. In another embodiment, the sample 202 and coils 200, 206, and 208 may be placed outside of a volume substantially enclosed by a magnet. In one embodiment, a sample holder is supplied to hold the sample in a desired position relative to the coils 200, 206, and 208. In one embodiment, an rf probe coil is proved for detecting nuclear magnetic resonance signals from the sample. Those of skill in the art will recognize many probe coil designs suitable for this purpose.

EXAMPLES

Example 1 – 2D Simulated Quadratic Inhomogeneity (Saddle Shaped)

[0057] Figure 5 depicts a simulated saddle shaped 2D B_0 inhomogeneity in the y,z-plane. Extension to 3D is straightforward. A 1×1 cm sample is located in a B_0 field with a saddle-shaped quadratic inhomogeneity with 1 ppm difference between the extremes. This inhomogeneity is sufficient to degrade the chemical shift resolution. Static linear B_0 gradients are not capable of correcting the quadratic inhomogeneity. Similarly, two adiabatic radio frequency pulses of the hyperbolic secant type applied in the presence of static B_0 gradients will have no net effect if the rf

compensating shim pulses. An rf frequency sweep having hyperbolic secant shape and indicated amplitude is swept twice through the sample (Figure 6A). The y and z magnetic field gradients are modulated as depicted in Figure 6B during application of the rf sweeps. The phase spread originating from the quadratic inhomogeneity is canceled yielding an NMR spectrum of a quality comparable to the one that would be obtained in a homogeneous B_0 field (Figure 6C). Subtle changes of the gradient strengths during the two frequency sweeps are sufficient to correct this particular B_0 imperfection.

Example 2 – 2D Simulated Quadratic Inhomogeneity (Radial Symmetry)

[0058] Figure 7 depicts a simulated quadratic 2D B_0 inhomogeneity with radial symmetry in the y,z-plane. Extension to 3D is straightforward. In contrast to the previous example, this inhomogeneity cannot be considered as a superposition of 1D inhomogeneities. However, two orthogonal linear B_0 gradients are capable of correcting this non-linear inhomogeneity. In this case a continuous modulation of the gradients is necessary in order to guide the RF frequency sweep through the sample. Again, a hyperbolic secant frequency sweep is applied (Figure 8A). However, the y and z magnetic field gradients are continuously modulated (Figure 8B). The result is that the inhomogeneity is compensated for, yielding a quality NMR spectrum (Figure 8C).

Example 3 – Inhomogeneity Compensation in Vitamin B_1 Spectrum

[0059] A Bruker Avance-700 NMR spectrometer with a triple resonance probe was used to measure the NMR spectrum of 5 mg/ml thiamine hydrochloride (vitamin B_1) in D_2O in a standard 5 mm sample tube. The probe contained x, y, and z gradient coils for multiple quantum coherence selection. The signal from the residual ^1H in the D_2O was suppressed by accumulating 64 transients with a recycle delay which was short in comparison to the relaxation time of water. The main magnetic field was made inhomogeneous by misadjusting the z^1 and z^2 shim coils. A z-gradient modulation was numerically optimized to give rise to a quadratic phase shift across the z-axis of the sample volume. This modulation was added to a constant gradient to provide simultaneous linear and quadratic corrections. A homogeneous rf pulse was simultaneously applied consisting of four identical sech/tanh adiabatic passages sweeping a frequency range of 40 kHz with a peak rf amplitude of 33 kHz. Figures 9A-9C depict the resulting shim pulse with time-modulated rf amplitude (Figure 9A), time-modulated rf frequency (Figure 9B), and time-modulated magnetic field gradient (Figure 9C).

[0060] The time domain NMR signal was recorded during a train of 1024 interleaved shim pulses and free precession delays. For each 2 ms shim pulse, 150 μs of chemical shift

compensation (Figure 10A), with linear corrections by applying a constant magnetic field gradient (Figure 10B), with both linear and quadratic corrections by applying the time-modulated magnetic field of Figure 9C (Figure 10C), and with a properly shimmed homogeneous magnetic field (Figure 10D). The spectrum obtained with inhomogeneous B_0 without correction has poor signal-to-noise ratio and lacks the fine details (Figure 10A). A constant gradient corrects only for the z^1 term of the inhomogeneity yielding a spectrum with highly asymmetric peaks, which are typical for a z^2 inhomogeneity (Figure 10B). With full gradient modulation, the homogeneous spectrum is recovered (Figure 10C).

[0061] Although the invention has been described with reference to embodiments and examples, it should be understood that numerous and various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

1. A method for detecting nuclear magnetic resonance of a sample in magnetic fields having at least about 500 ppb inhomogeneity in static magnetic field strength, the method comprising:

applying a radio frequency pulse comprising a time-varying phase or frequency to the sample; and

simultaneously applying a time varying magnetic field gradient to the sample,

wherein said time varying magnetic field gradient is superimposed over said inhomogeneous static magnetic field.

2. The method of claim 1, wherein said static magnetic field has greater than 500 ppb inhomogeneity.

3. The method of claim 1, wherein said static magnetic field has greater than 200 ppb inhomogeneity.

4. The method of claim 1, wherein said static magnetic field has greater than 100 ppb inhomogeneity.

5. The method of claim 1, wherein said static magnetic field has greater than 50 ppb inhomogeneity.

6. The method of claim 1, wherein said static magnetic field has greater than 20 ppb inhomogeneity.

7. The method of claim 1, wherein said static magnetic field has greater than 10 ppb inhomogeneity.

8. The method of claim 1, wherein said static magnetic field has greater than 5 ppb inhomogeneity.

9. The method of claim 1, further comprising determining a spatial map of the inhomogeneity in the static magnetic field prior to applying the radio frequency pulse and magnetic field gradient.

10. The method of claim 9, wherein determining the spatial map of the inhomogeneity comprises detecting the static magnetic field with one or more magnetic field coils that are also used to apply the magnetic field gradient.

11. The method of claim 1, wherein the applied magnetic field gradient is adapted to provide a linear correction to the static magnetic field inhomogeneity.

12. The method of claim 4, wherein the applied magnetic field gradient is adapted to provide a non-linear correction to the static magnetic field inhomogeneity.

13. The method of claim 1, wherein the sample is not located within a volume substantially enclosed by a magnet.

enclosed by a magnet of a nuclear magnetic spectrometer or magnetic resonance imager.

15. The method of claim 7, wherein the nuclear magnetic spectrometer or magnetic resonance imager does not comprise any shim magnets.

16. The method of claim 7, wherein at least some shim magnets in the nuclear magnetic spectrometer or magnetic resonance imager are permanent magnets.

17. The method of claim 1, further comprising detecting a nuclear magnetic resonance spectrum of the sample.

18. The method of claim 1, further comprising detecting a magnetic resonance image of the sample.

19. The method of claim 1, wherein the radio frequency pulse comprises a time-varying amplitude and either a time-varying frequency or phase.

20. The method of claim 1, further comprising detecting nuclear magnetic resonance of the sample after application of the radio frequency pulse and magnetic field gradient.

21. The method of claim 1, wherein the radio frequency pulse is substantially spatially uniform.

22. A method for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field, the method comprising:

applying a first radio frequency inversion pulse;

applying a magnetic field gradient spatially matched to a static magnetic field inhomogeneity;

applying a second radio frequency inversion pulse; and

detecting a spin echo after said second radio frequency inversion pulse.

23. The method of claim 15, further comprising detecting a nuclear magnetic resonance spectrum.

24. The method of claim 15, further comprising detecting a magnetic resonance image.

25. The method of claim 15, wherein said sample is placed in a volume substantially enclosed by a magnet in a nuclear magnetic resonance spectrometer or a magnetic resonance imager.

26. A system for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field, the system comprising:

a radio frequency coil;

one or more magnetic field generating coils;

a first current generating module coupled to the radio frequency coil; and

at least one second current generating module coupled to at least one of the magnetic field generating coils,

coils so that a radio frequency pulse and magnetic field gradient are generated in such a manner that effects of inhomogeneities in the static magnetic field are substantially eliminated.

27. The system of claim 19, wherein the radio frequency coil is adapted to generate spatially uniform radio frequency signals.

28. The system of claim 19, wherein the magnetic field generating coils are adapted to generate magnetic field gradients in one or more orthogonal directions.

29. The system of claim 19, further comprising at least one current measurement module coupled to the magnetic field generating coils, the current measurement modules adapted to detect inhomogeneities in the static magnetic field.

30. The system of claim 19, further comprising a magnet adapted to generate the static magnetic field.

31. The system of claim 19, further comprising a sample holder adapted to hold a sample within a volume substantially enclosed by the magnet.

32. The system of claim 19, further comprising a sample holder adapted to hold a sample outside of a volume substantially enclosed by the magnet.

33. The system of claim 19, further comprising a probe adapted to detect a nuclear magnetic resonance of a sample.

34. The system of claim 26, wherein the probe is adapted to detect a nuclear magnetic resonance spectrum of the sample.

35. The system of claim 26, wherein the probe is adapted to detect a magnetic resonance image of the sample.

36. The system of claim 19, wherein the first current generating module is adapted to apply current through the radio frequency coil such that a radio frequency pulse comprising a time-varying frequency is generated.

37. The system of claim 19, wherein the second current generating module is adapted to apply current through at least one magnetic field generating coil such that a magnetic field gradient is generated.

38. The system of claim 20, wherein the second current generating module is adapted to apply current through at least one magnetic field generating coil such that a time-varying magnetic field gradient is generated.

39. A method of detecting a magnetic resonance signal comprising:

simultaneously applying radio frequency pulses and a time varying gradient field to a sample volume in a static magnetic field having an inhomogeniety of at least about 0.5 ppm over the sample volume, wherein said radio frequency pulses adiabadically rotate a

field; and

detecting magnetic resonance signals from said sample.

40. The method of Claim 32, wherein said time varying gradient field comprises a constant gradient component selected to correct for linear inhomogenieties in said static magnetic field.

41. The method of Claim 33, wherein the time dependence of the gradient field is selected to correct for quadratic inhomogenieties in said static magnetic field.

42. A system for detecting a magnetic resonance signal, comprising:

means for applying a static magnetic field to a sample;

means for counteracting effects of inhomogeneity in the static magnetic field with radio frequency pulses that adiabatically rotate a bulk magnetization vector by 360 degrees during the application of a time varying gradient field; and

means for detecting a magnetic resonance signal from the sample.

43. A system for improving detection of a nuclear magnetic resonance signal from a sample in an inhomogeneous static magnetic field as substantially shown and described.

FIG. 1A

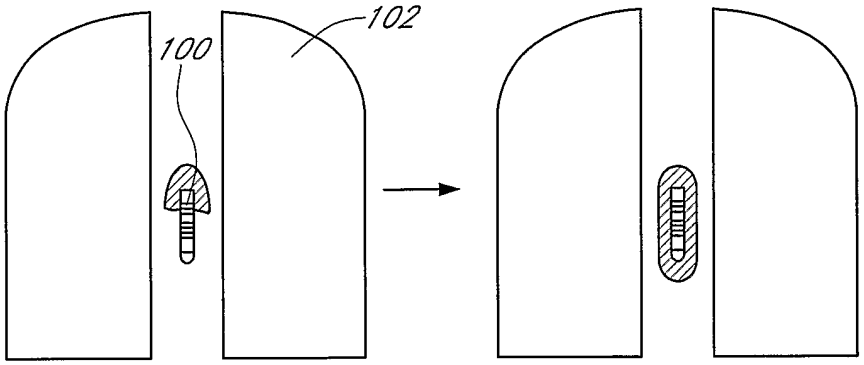


FIG. 1B

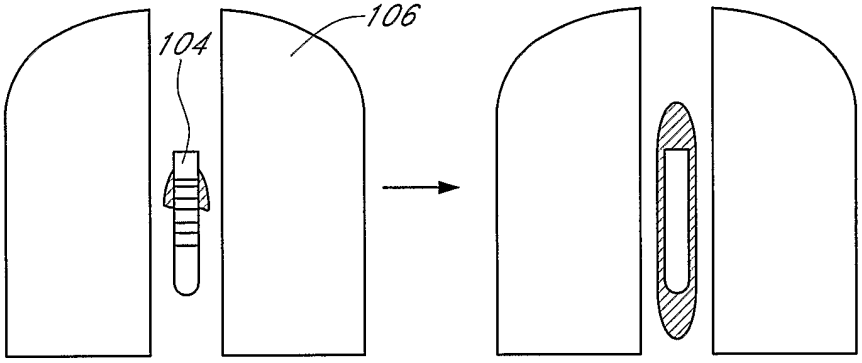


FIG. 1C

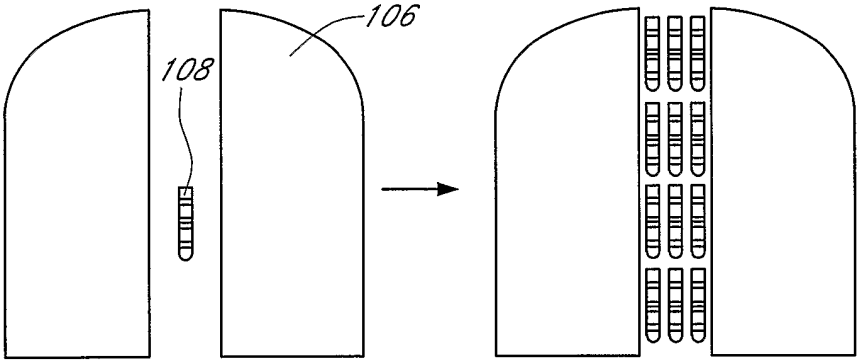
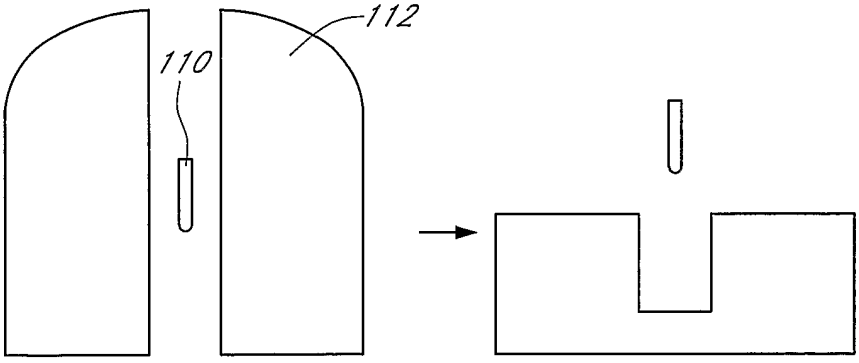


FIG. 1D



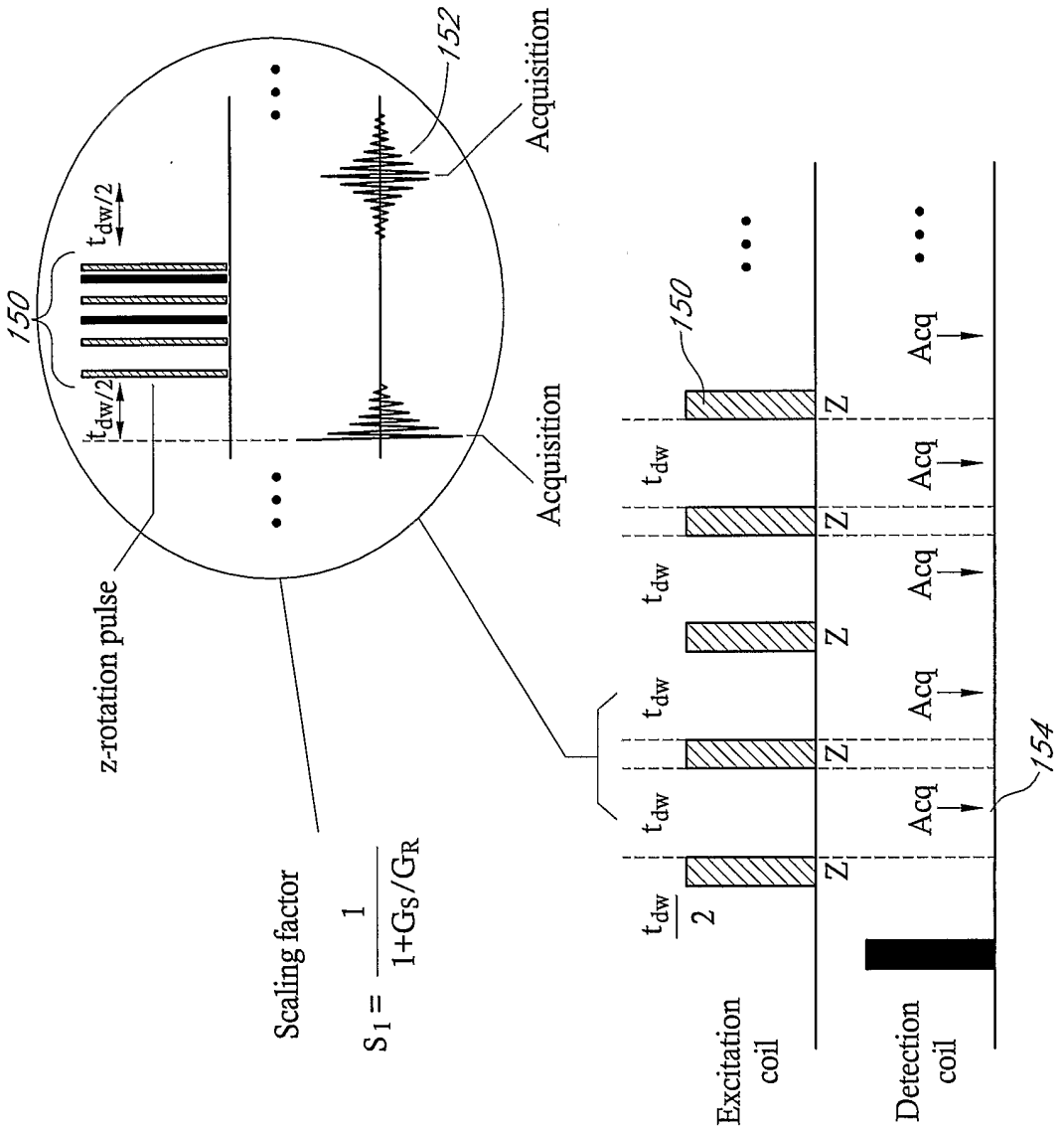

150
$t_{dw}/2$
$t_{dw}/2$
z-rotation pulse
152
Acquisition
Acquisition
Scaling factor
$S_1 = \frac{1}{1+G_S/G_R}$
150
t_{dw}
$\frac{t_{dw}}{2}$
Z
Acq
154
Excitation coil
Detection coil

FIG. 2

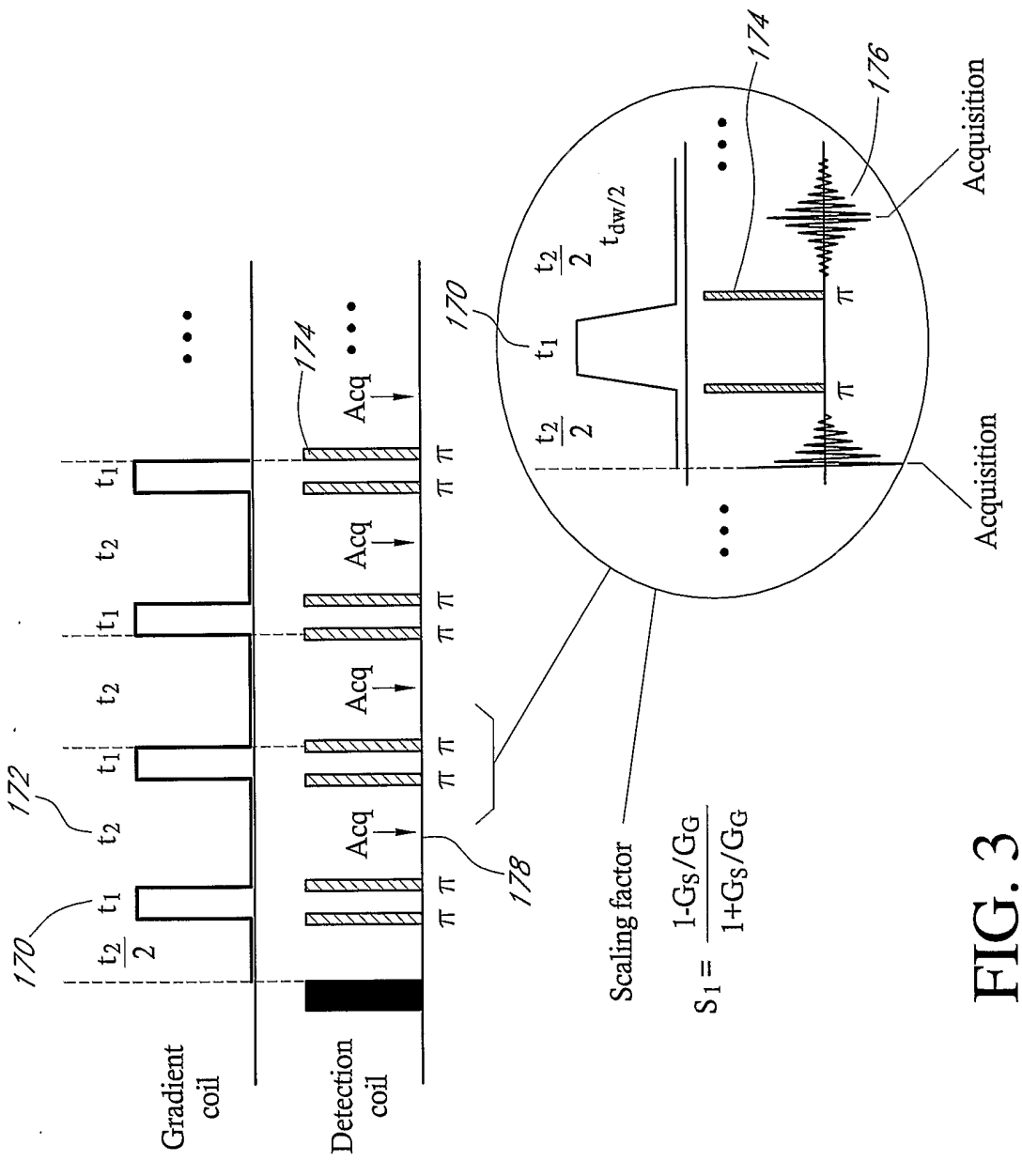

Gradient coil
Detection coil
170
172
174
176
178
Acq
π
Acquisition
Scaling factor
$S_1 = \frac{1-G_S/G_G}{1+G_S/G_G}$

FIG. 3

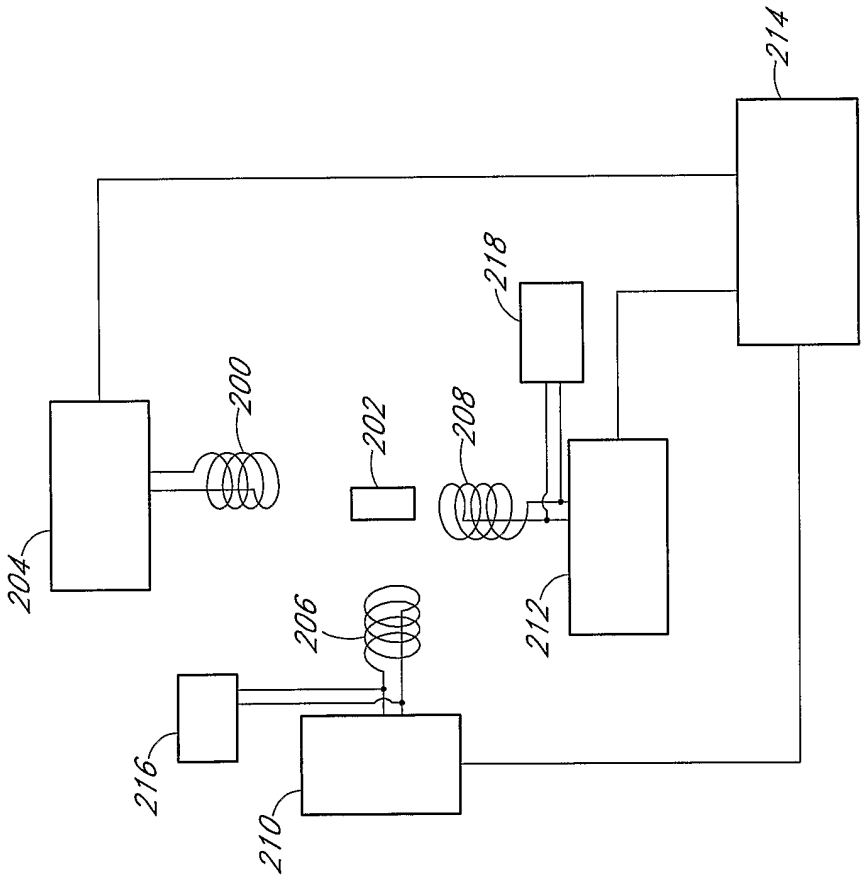


FIG. 4

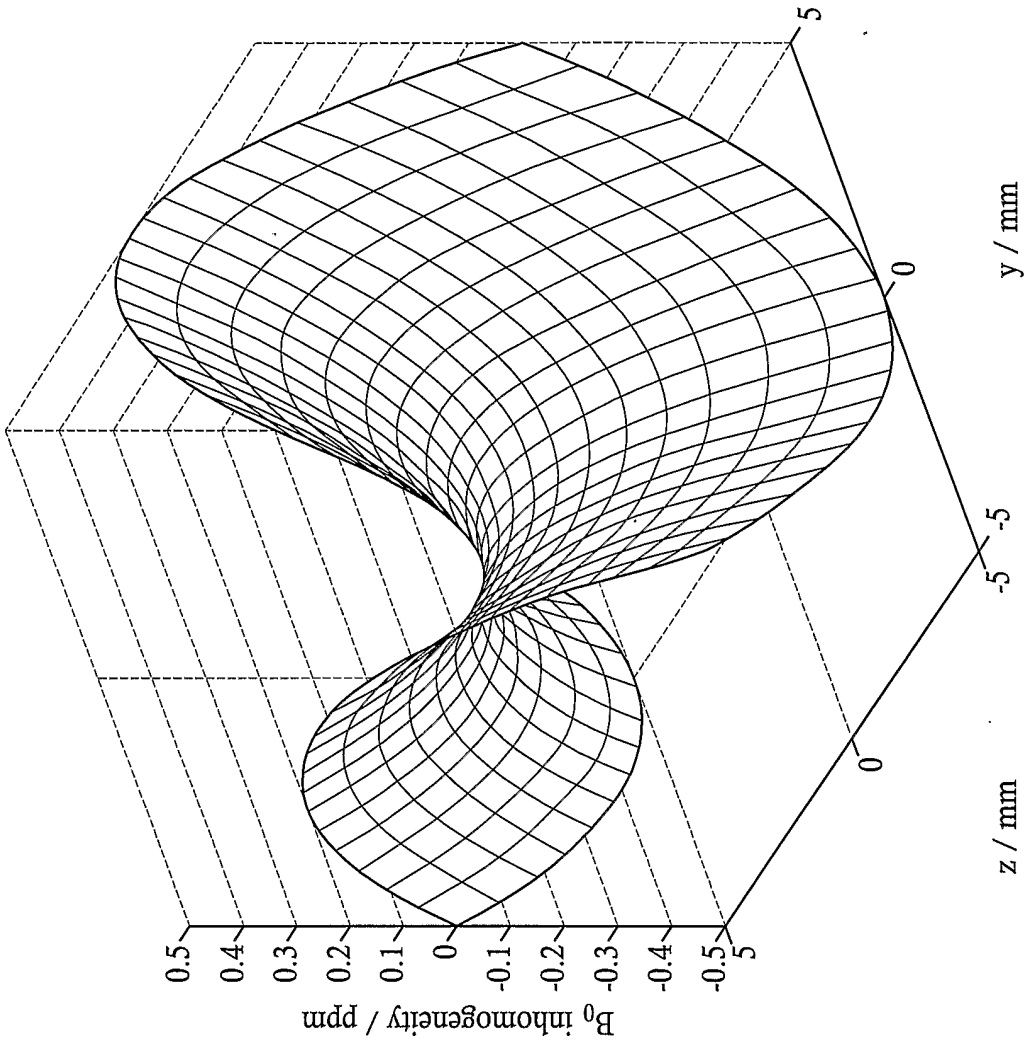

B0 inhomogeneity / ppm
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
5
0
-5
z / mm
5
0
-5
y / mm

FIG. 5

FIG. 6A

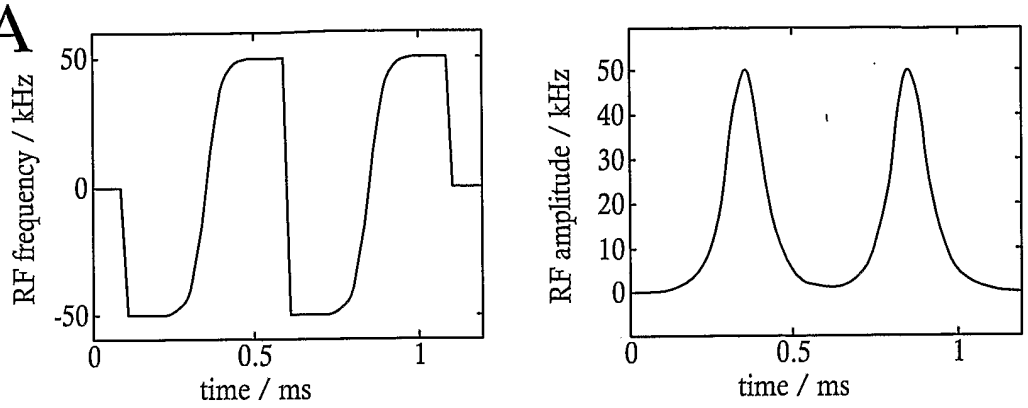


FIG. 6B

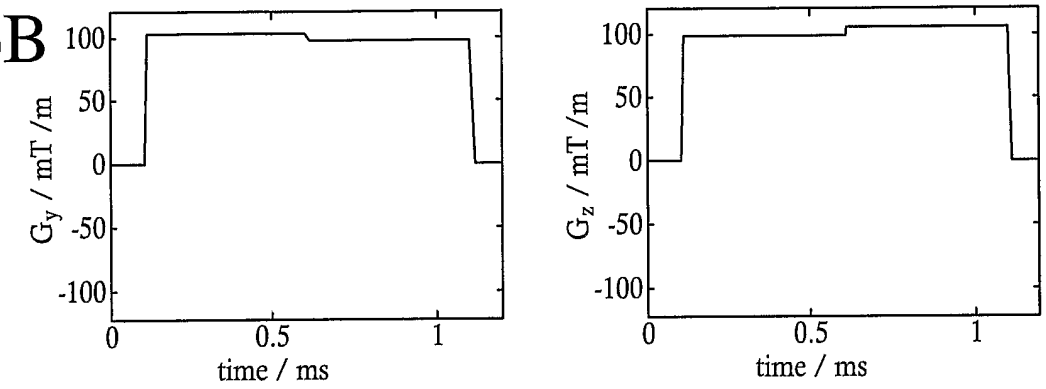
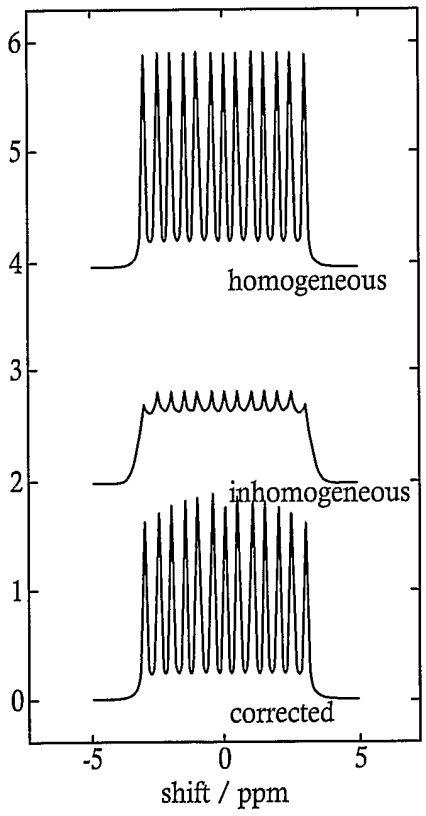


FIG. 6C



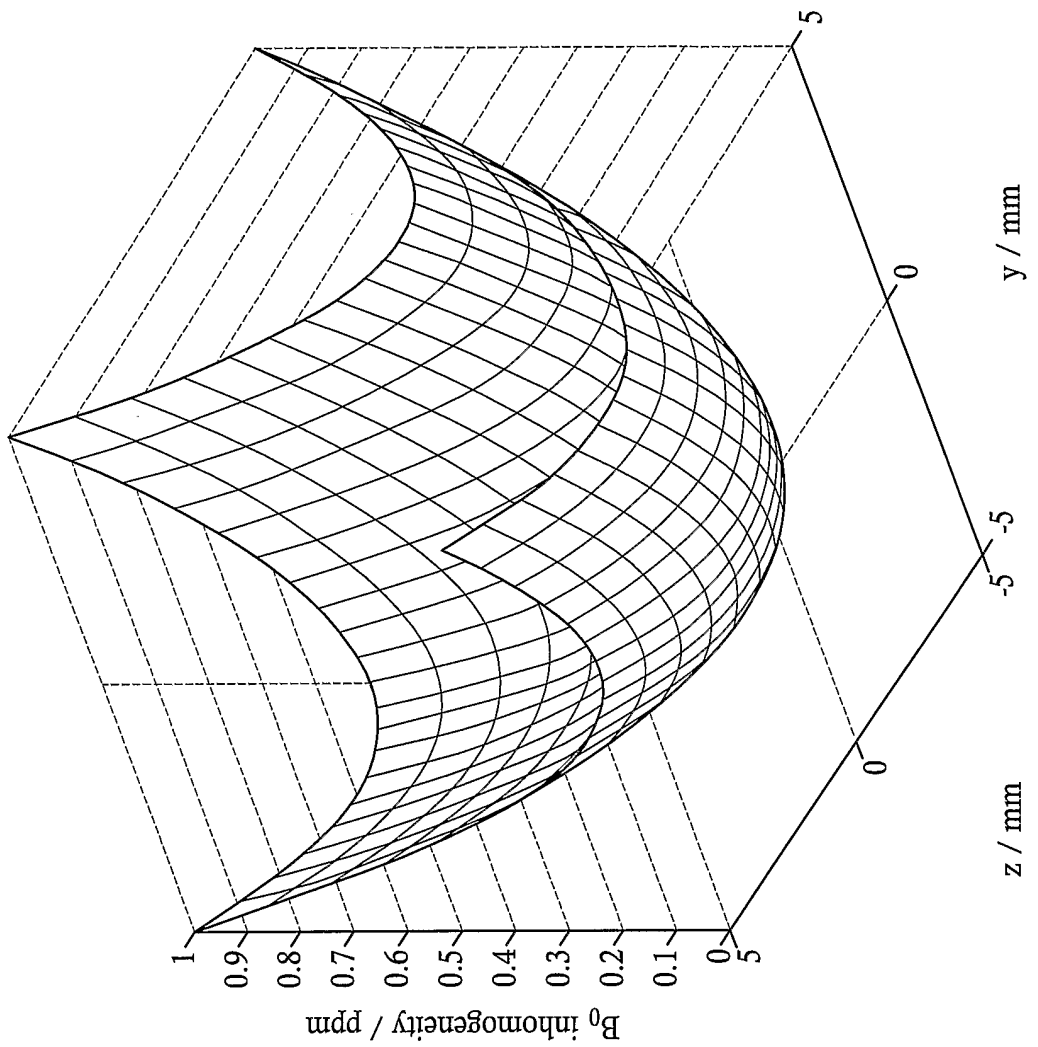

B0 inhomogeneity / ppm
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
5
0
-5
z / mm
-5
0
5
y / mm

FIG. 7

FIG. 8A

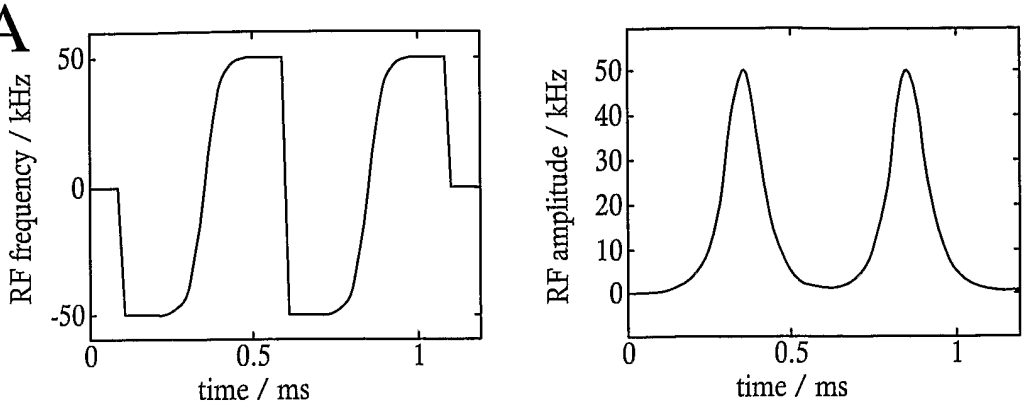


FIG. 8B

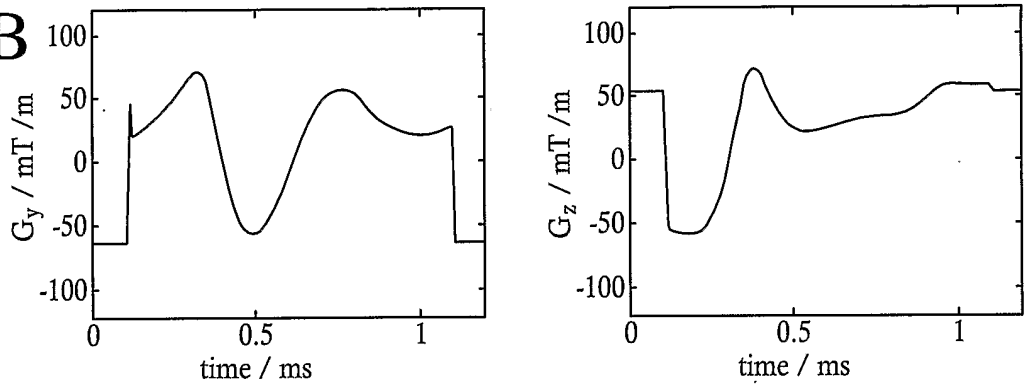


FIG. 8C

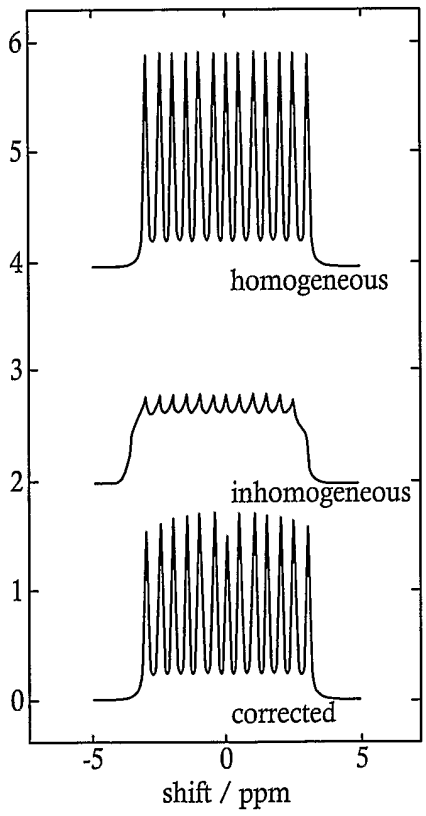


FIG. 9A

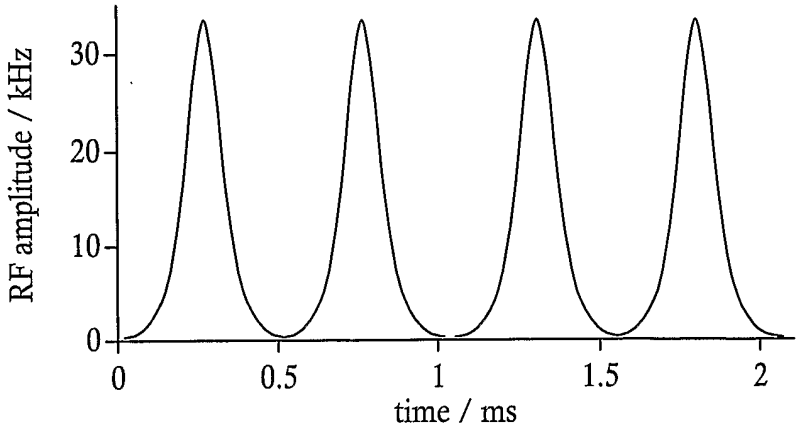


FIG. 9B

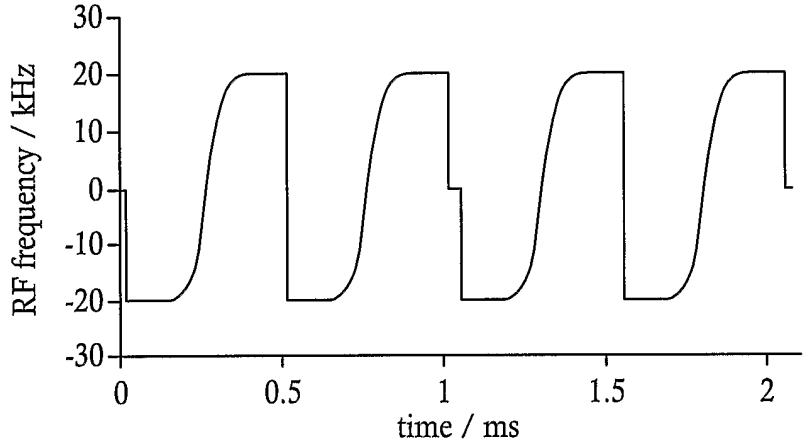
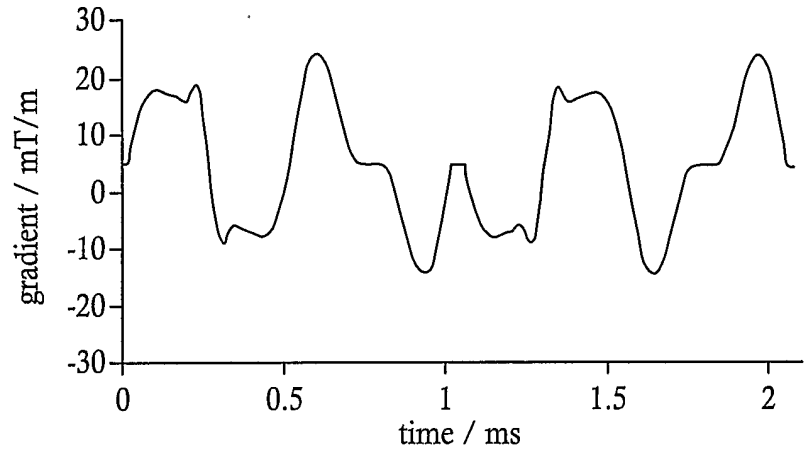


FIG. 9C



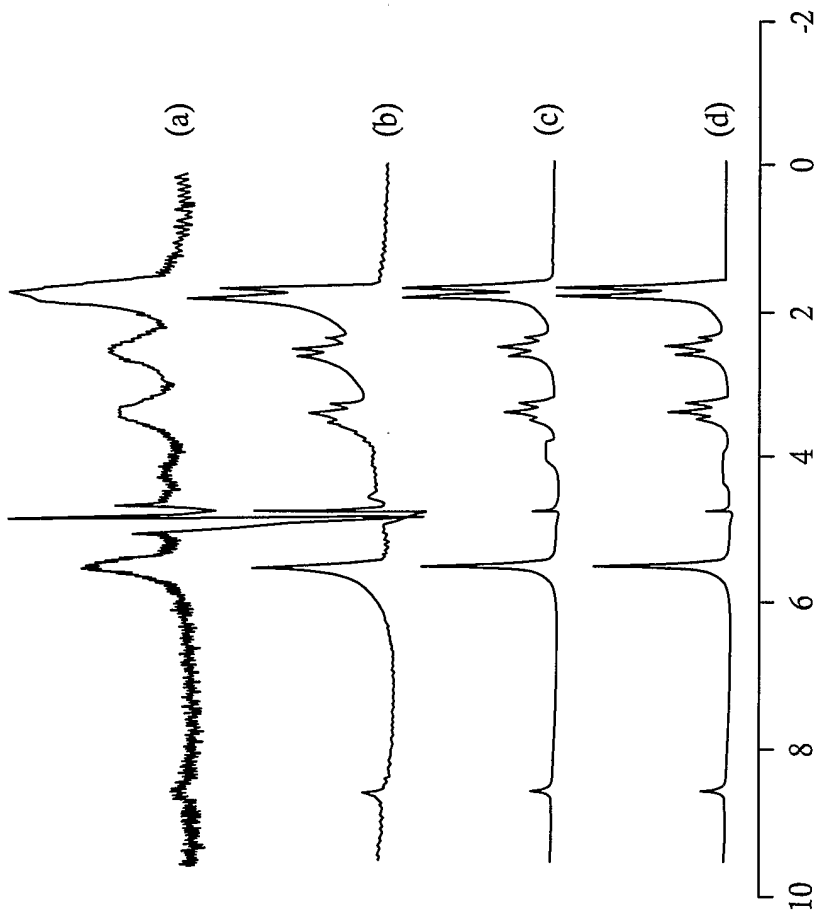


FIG. 10