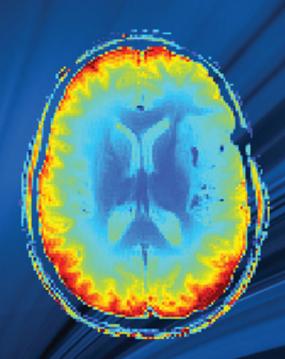
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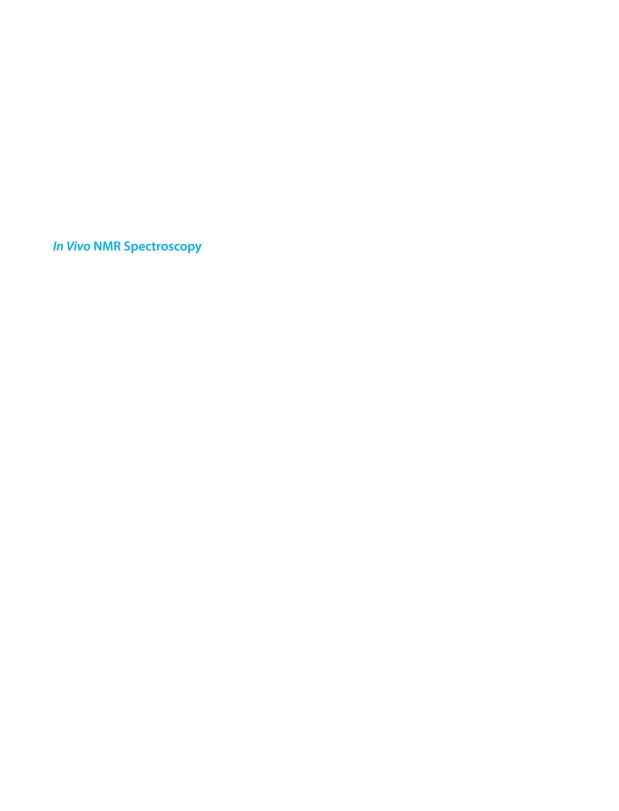


in vivo NMR Spectroscopy

Principles and Techniques

Robin A. de Graaf

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In Vivo NMR Spectroscopy

Principles and Techniques

Third Edition

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Preface

The main driving force to write a third edition was the inadequate description of several basic NMR phenomena in the earlier editions, as well as in the majority of NMR textbooks. The quantum picture of NMR provides the most general description that is applicable to all NMR experiments. As a result, the quantum description of NMR often takes center stage, but comes at the expense of forfeiting a physically intuitive picture. Inappropriate descriptions of NMR result when the quantum mechanics are incorrectly simplified to a classical picture. However, ever since the very first report on NMR in bulk matter by Felix Bloch, it is known that the NMR phenomenon for many compounds, like water, can be quantitatively described based on classical arguments without the need to invoke quantum mechanics. The current edition adopts this classical description for a very intuitive and straightforward description of NMR. While many aspects of *in vivo* NMR, including MR imaging, magnetization transfer, and diffusion can be successfully described, the classical description does prove inadequate in the presence of scalar coupling. At this point the classical description is replaced with a semiclassical correlated vector model that naturally leads to the quantum-mechanical product operator formalism.

The third edition also takes the opportunity to correct misconceptions about the nature of radiofrequency (RF) pulses and coils, and provides an updated review of novel methods, including hyperpolarized MR, deuterium metabolic imaging (DMI), MR fingerprinting, advanced magnetic field shimming, and chemical exchange saturation transfer (CEST) methods. However, it should be stressed that this book does not set out to present complete, detailed, and in-depth reviews of *in vivo* MRS methods.

The main objective of the book has always been to provide an educational explanation and overview of *in vivo* NMR, without losing the practical aspects appreciated by experimental NMR spectroscopists. This objective has been enhanced in this edition by relegating a significant number of mathematical equations to the exercises in favor of more intuitive, descriptive explanations and graphical depictions of NMR phenomena. The exercises are designed to review, but often also to extend the presented NMR principles and techniques, including a more in-depth exploration of quantitative MR equations. The textual description of RF pulses has been reduced and supplemented with PulseWizard, a Matlab-based RF pulse generation and simulation graphical user interface available for download at the accompanying website (http://booksupport.wiley.com).

Many of the ideas and changes that formed the basis for this third edition came from numerous discussions with colleagues. I would like to thank Henk De Feyter, Chathura Kumaragamage, Terry Nixon, Graeme Mason, Kevin Behar, and Douglas Rothman for many fruitful discussions.

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Abbreviations

1D one-dimensional 2D two-dimensional 2HG 2-hydoxyglutarate 3D three-dimensional 5-FU 5-fluoruracil AC alternating current

Ace acetate

ADC analog-to-digital converter ADC apparent diffusion coefficient

ADP adenosine diphosphate AFP adiabatic full passage AHP adiabatic half passage

Ala alanine Asc ascorbic acid Asp aspartate

ATP adenosine triphosphate BHB β -hydroxy-butyrate BIR B_1 -insensitive rotation

 $\begin{array}{ll} {\rm BISEP} & B_1\text{-insensitive spectral editing pulse} \\ {\rm BOLD} & {\rm blood\ oxygen\ level-dependent} \\ {\rm BPP} & {\rm Bloembergen,\ Purcell,\ Pound} \end{array}$

BS Bloch–Siegert
CBF cerebral blood flow
CBV cerebral blood volume

CEST chemical exchange saturation transfer

CHESS chemical shift selective

Cho choline-containing compounds

CK creatine kinase

 ${\rm CMR_{Glc}}$ cerebral metabolic rate of glucose consumption ${\rm CMR_{O_2}}$ cerebral metabolic rate of oxygen consumption

COSY correlation spectroscopy CPMG Carr–Purcell–Meiboom–Gill

Cr creatine

CRLB Cramer-Rao lower bound

Crn carnitine

CSDA chemical shift displacement artifact CSDE chemical shift displacement error

xviii Abbreviations

CSF cerebrospinal fluid CW continuous wave

DANTE delays alternating with nutation for tailored excitation

dB decibel
DC direct current

DEFT driven equilibrium Fourier transform

DEPT distortionless enhancement by polarization transfer

DMb deoxymyoblobin

DMI deuterium metabolic imaging

DNA deoxyribonucleic acid

DNP dynamic nuclear polarization DQC double quantum coherence

DSS 2,2-dimethyl-2-silapentane-5-sulfonate

DSV diameter spherical volume DTI diffusion tensor imaging

EA ethanolamine

EMCL extramyocellular lipids EMF electromotive force EPI echo planar imaging

EPSI echo planar spectroscopic imaging

FDG 2-fluoro-2-deoxy-glucose

FDG-6P 2-fluoro-2-deoxy-glucose-6-phosphate

FFT fast Fourier transformation FID free induction decay FLASH fast low-angle shot

fMRI functional magnetic resonance imaging FOCI frequency offset corrected inversion

FOV field of view

FSW Fourier series windows FT Fourier transformation

FWHM Frequency width at half maximum

GABA γ-aminobutyric acid GE gradient echo

Glc glucose
Gln glutamine
Glu glutamate

Glx glutamine and glutamate

Gly glycine

GOIA gradient-offset-independent adiabaticity

GPC glycerophosphorylcholine GPE glycerophosphorylethanolamine

GRAPPA generalized autocalibrating partially parallel acquisitions

GSH glutathione (reduced form)

HLSVD Hankel Lanczos singular value decomposition

HMPT hexamethylphosphorustriamide

HMQC heteronuclear multiple quantum correlation HSQC heteronuclear single quantum correlation

Ile isoleucine

IMCL intramyocellular lipids

INEPT insensitive nuclei enhanced by polarization transfer

IR inversion recovery

ISIS image-selected in vivo spectroscopy

IT inversion transfer **IVS** inner volume selection

JR jump-return

IRES J-resolved spectroscopy

Lac lactate

LASER localization by adiabatic selective refocusing

Leu leucine myoglobin Mb MC multi-coil

MEGA Mescher-Garwood

mΙ *myo*-inositol Malcolm Levitt **MLEV** MM macromolecules

MOC multiple quantum coherence MRF magnetic resonance fingerprinting MRI magnetic resonance imaging MRS magnetic resonance spectroscopy

magnetic resonance spectroscopic imaging **MRSI**

MT magnetization transfer

MTC magnetization transfer contrast

N-acetyl aspartate NAA

N-acetyl aspartyl glutamate NAAG

nicotinamide adenine dinucleotide oxidized (reduced) NAD(H)

NADP(H) nicotinamide adenine dinucleotide phosphate oxidized (reduced)

NDP nucleoside diphosphate nuclear magnetic resonance **NMR**

nuclear Overhauser effect (or enhancement) nOe **NOESY** nuclear Overhauser effect spectroscopy

NTP nucleoside triphosphate

OSIRIS outer volume suppressed image-related in vivo spectroscopy

OVS outer volume suppression

PCA perchloric acid **PCr** phosphocreatine **PDE** phosphodiesters

PE phosphorylethanolamine positron emission tomography PET

PFC perfluorocarbons

PHIP para-hydrogen-induced polarization

 P_i inorganic phosphate **PME** phosphomonoesters

POCE proton-observed carbon-edited

PPM parts per million

PRESS point resolved spectroscopy **PSF** point spread function

QSM quantitative susceptibility mapping

QUALITY quantification by converting line shapes to the Lorentzian type

time-reversed adiabatic half passage **RAHP RARE** rapid acquisition, relaxation enhanced

RF radiofrequency **RMS** root mean squared **RNA** ribonucleic acid ROI region of interest

SABRE signal amplification by reversible exchange

SAR specific absorption rate

SE spin-echo

SENSE sensitivity encoding

SEOP spin-exchange optical pumping

SH spherical harmonics scyllo-inositol sΙ

SI spectroscopic imaging

SLIM spectral localization by imaging

SLR Shinnar-Le Roux S/Nsignal-to-noise ratio **SNR** signal-to-noise ratio

SPECIAL spin-echo, full intensity acquired localized

SQC single quantum coherence

SSAP solvent suppression adiabatic pulse

SSFP steady-state free precession

ST saturation transfer STE stimulated echo

STEAM stimulated echo acquisition mode

SV single voxel (or volume) **SVD** singular value decomposition

SWAMP selective water suppression with adiabatic-modulated pulses

Tau taurine

TCA tricarboxylic acid tCho total choline tCr total creatine

TEM transverse electromagnetic mode

Thr threonine

trimethylammonium **TMA TMS** tetramethylsilane

TOCSY total correlation spectroscopy

TPPI time proportional phase incrementation

Trp tryptophan

TSP 3-(trimethylsilyl)-propionate

Tyr tyrosine UV ultraviolet Val valine

VAPOR variable pulse powers and optimized relaxation delays

VARPRO variable projection

VERSE variable rate selective excitation **VNA** variable nutation angle VOI volume of interest

VSE volume selective excitation

WALTZ wideband alternating phase low-power technique for zero residue splitting

WEFT water eliminated Fourier transform

WET water suppression enhanced through T_1 effects

ZQC zero quantum coherence

Symbols

Α absorption frequency domain signal

Fourier coefficients A_n, B_n *b*-value (in s/m^2) b-value matrix b

 B_0 external magnetic field (in T)

 B_1 magnetic radiofrequency field of the transmitter (in T) $B_{1\text{max}}$ maximum amplitude of the irradiating B_1 field (in T) B_{1rms} root mean square B_1 amplitude of a RF pulse (in T)

real and imaginary components of the irradiating B_1 field (in T) B_{1x} , B_{1y}

 B_2 magnetic, radiofrequency field of the decoupler (in T)

 $B_{\rm e}$ effective magnetic field in the laboratory and frequency frames (in T)

 $B_{
m e}^{'}$ effective magnetic field in the second rotating frame (in T)

 B_{loc} local magnetic field (in T)

Ccapacitance (in F)

Ccorrection factor for calculating absolute concentrations

(apparent) diffusion coefficient (in m² s⁻¹) D

D(apparent) diffusion tensor

Ddispersion frequency domain signal

Е energy (in J)

F Nyquist frequency (in 1 s⁻¹)

F noise figure (in dB)

normalized RF amplitude modulation function $f_B(t)$ normalized RF frequency modulation function $f_{\nu}(t)$ magnetic field gradient strength (in T m⁻¹) G

G(t)correlation function

Planck's constant $(6.626208 \times 10^{-34} \text{Js})$ h

H Hadamard matrix

Ι imaginary time- or frequency-domain signal

spin quantum number

Boltzmann equilibrium magnetization for spin I I_0 I_{nm} shim current for shim coil of order n and degree m spin-spin or scalar coupling constant (in Hz)

zero-order Bessel function J_0 $J(\nu)$ spectral density function

Boltzmann equilibrium constant $(1.38066 \times 10^{-23} \text{ J K}^{-1})$

k-space variable (in m⁻¹) k

k-space variable in frequency-encoding direction (in m⁻¹) $k_{\rm f}$ k-space variable in phase-encoding direction (in m⁻¹) $k_{\rm p}$

unidirectional rate constants (in s⁻¹) k_{AB} , k_{BA} forward, unidirectional rate constant (in s⁻¹) $k_{\rm for}$ reversed, unidirectional rate constant (in s⁻¹) $k_{\rm rev}$

inductance (in H) L

magnetic quantum number m

mass (in kg) m

Μ macroscopic magnetization

M magnitude-mode frequency domain signal

M mutual inductance (in H)

 M_0 macroscopic equilibrium magnetization

 M_x , M_y , M_z orthogonal components of the macroscopic magnetization

N number of phase-encoding increments

N total number of nuclei or spins in a macroscopic sample

order of coherence Q quality factor distance (in m)

R composite pulse (sequence)

product of bandwidth and pulse length R R real time- or frequency-domain signal

R resistance (in Ω) R rotation matrix

 R_{1A} , R_{1B} longitudinal relaxation rate constants for spins A and B in the absence of

chemical exchange or cross-relaxation (in s⁻¹)

transverse relaxation rate (in s⁻¹) R_2

 R_A , R_B longitudinal relaxation rate constants for spins A and B in the presence of

chemical exchange (in s⁻¹)

 $R_{\rm H}$ hydrodynamic radius (in m) S measured NMR signal

S(k)spatial frequency sampling function

time (in s) t

 t_1 incremented time in 2D NMR experiments (in s)

maximum t_1 period in constant time 2D NMR experiments (in s) $t_{1\max}$

detection period in 2D NMR experiments (in s) t_2

diffusion time (in s) $t_{
m diff}$

time of zero-crossing (nulling) during an inversion recovery experiment (in s) $t_{\rm null}$

absolute temperature (in K)

Tpulse length (in s)

 T_1 longitudinal relaxation time constant (in s)

 $T_{1,obs}$ observed, longitudinal relaxation time constant (in s)

 T_2 transverse relaxation time constant (in s)

 $T_2^{\bar{*}}$ apparent transverse relaxation time constant (in s) $T_{2,\mathrm{obs}}$ observed, transverse relaxation time constant (in s)

 $T_{\rm acq}$ acquisition time (in s) TE echo time (in s)

echo time in a CPMG experiment (in s) TE_{CPMG}

ΤI inversion time (in s) TI1 first inversion time (in s) TI2 second inversion time (in s)

TM delay time between the second and third 90° pulses in STEAM (in s) TR repetition time (in s) velocity (in m s⁻¹) ν W transition probability (in 1 s⁻¹) angular function of spherical polar coordinates W_{nm} W(k)spatial frequency weighting function molar fraction x X_C capacitive reactance (in Ω) inductive reactance (in Ω) X_L Zimpedance (in Ω) nutation angle (in rad) α β precession angle of magnetization perpendicular to the effective magnetic field B_e gyromagnetic ratio (in rad T⁻¹ s⁻¹) γ δ chemical shift (in ppm) δ gradient duration (in s) separation between a pair of gradients (in s) Δ ΔB_0 magnetic field shift (in T) frequency offset (in Hz) $\Delta \nu$ full width at half maximum of an absorption line (in Hz) $\Delta \nu_{1/2}$ maximum frequency modulation of an adiabatic RF pulse (in Hz) $\Delta \nu_{
m max}$ gradient rise time for a trapezoidal magnetic field gradient (in s) ε nuclear Overhauser enhancement η viscosity (in Ns m⁻²) η nutation angle (in rad) θ magnetic moment (in A·m²) μ permeability constant in vacuum $(4\pi \cdot 10^{-7} \text{ kg} \cdot \text{m} \cdot \text{s}^{-2} \cdot \text{A}^{-2})$ μ_0 electronic magnetic moment (in A·m2) $\mu_{\rm e}$ Larmor frequency (in Hz) ν_0 frequency of a non-protonated compound A (in Hz) $\nu_{\rm A}$ frequency of a protonated compound HA (in Hz) $\nu_{\rm HA}$ reference frequency (in Hz) ν_{ref} electromotive force (in V) density matrix σ rotation correlation time (in s) $\tau_{\rm c}$ mixing time in 2D NMR experiments (in s) $\tau_{
m m}$ phase (in rad) φ ϕ_0 zero-order (constant) phase (in rad) first-order (linear) phase (in rad) ϕ_1 phase correction (in rad) $\phi_{\rm c}$ magnetic susceptibility χ Larmor frequency (in rad s⁻¹) ω_0 \prod concentration (in M)

Supplementary Material

To access supplementary materials for this book please use the download links shown below. There you will find valuable material designed to enhance your learning, including:



- Solutions to the exercises in the book
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1

Basic Principles

1.1 Introduction

Spectroscopy is the study of the interaction between matter and electromagnetic radiation. Atoms and molecules have a range of discrete energy levels corresponding to different, quantized electronic, vibrational, or rotational states. The interaction between atoms and electromagnetic radiation is characterized by the absorption and emission of photons with an energy that exactly matches the energy level difference between two states. Since the energy of a photon is proportional to the frequency, the different forms of spectroscopy are often distinguished on the basis of the frequencies involved. For instance, absorption and emission between the electronic states of the outer electrons typically require frequencies in the ultraviolet (UV) range, hence giving rise to UV spectroscopy. Molecular vibrational modes are characterized by frequencies just below visible red light and are thus studied with infrared (IR) spectroscopy. Nuclear magnetic resonance (NMR) spectroscopy uses radiofrequencies, which are typically in the range of $10-1000\,\mathrm{MHz}$.

NMR is the study of the magnetic properties and related energies of nuclei. The absorption of radiofrequency energy can be observed when the nuclei are placed in a (strong) external magnetic field. Purcell et al. [1] at MIT, Cambridge and Bloch et al. [2–4] at Stanford simultaneously, but independently discovered NMR in 1945. In 1952, Bloch and Purcell shared the Nobel Prize in Physics in recognition of their pioneering achievements [5, 6]. At this stage, NMR was purely an experiment for physicists to determine the nuclear magnetic moments of nuclei. NMR could only develop into one of the most versatile forms of spectroscopy after the discovery that nuclei within the same molecule absorb energy at different resonance frequencies. These so-called chemical shift effects, which are directly related to the chemical environment of the nuclei, were first observed in 1949 by Proctor and Yu [7], and independently by Dickinson [8]. The ability of NMR to provide detailed chemical information on compounds was firmly established when Arnold et al. [9] in 1951 published a high-resolution ¹H NMR spectrum of ethanol in which separate signals from methyl, methylene, and hydroxyl protons could be clearly recognized.

In the first two decades, NMR spectra were recorded in a continuous wave mode in which the magnetic field strength or the radio frequency was swept through the spectral area of interest, while keeping the other fixed. In 1966, NMR was revolutionized by Ernst and Anderson [10] who introduced pulsed NMR in combination with Fourier transformation. Pulsed or Fourier transform NMR is at the heart of all modern NMR experiments.

The induced energy level difference of nuclei in an external magnetic field is very small when compared to the thermal energy at room temperature, making it that the energy levels

are almost equally populated. As a result the absorption of photons is very low, making NMR a very insensitive technique when compared to the other forms of spectroscopy. However, the low-energy absorption makes NMR also a noninvasive and nondestructive technique, ideally suited for in vivo measurements. It is believed that, by observing the water signal from his own finger, Bloch was the first to perform an *in vivo* NMR experiment. Over the following decades, NMR studies were carried out on various biological samples like vegetables and mammalian tissue preparations. Continued interest in defining and explaining the properties of water in biological tissues led to the promising report of Damadian in 1971 [11] that NMR properties (relaxation times) of malignant tumorous tissues significantly differs from normal tissue, suggesting that proton NMR may have diagnostic value. In the early 1970s, the first experiments of NMR spectroscopy on intact living tissues were reported. Moon and Richards [12] used ³¹P NMR on intact red blood cells and showed how the intracellular pH can be determined from chemical shift differences. In 1974, Hoult et al. [13] reported the first study of ³¹P NMR to study intact, excised rat hind leg. Acquisition of the first ¹H NMR spectra was delayed by almost a decade due to technical difficulties related to spatial localization, and water and lipid suppression. Behar et al. [14] and Bottomley et al. [15] reported the first ¹H NMR spectra from rat and human brain, respectively. Since the humble beginnings, in vivo MR spectroscopy (MRS) has grown as an important technique to study static and dynamic aspects of metabolism in disease and in health.

In parallel with the onset of *in vivo* MRS, the world of high-resolution, liquid-state NMR was revolutionized by the introduction of 2D NMR by Ernst and coworkers [16] based on the concept proposed by Jeener in 1971 [17]. The development of hundreds of 2D methods in the following decades firmly established NMR as a leading analytical tool in the identification and structure determination of low-molecular weight chemicals. Richard Ernst was awarded the 1991 Nobel Prize in Chemistry for his contributions to the methodological development of NMR [18]. The application of multidimensional NMR to the study of biological macromolecules allowed determination of the 3D structure of proteins in an aqueous environment, providing an alternative to X-ray crystallography. Kurt Wuthrich was awarded the 2002 Nobel Prize in Chemistry for his contributions to the development of protein NMR and 3D protein structure determination [19].

Around the same time reports on *in vivo* MRS appeared, Lauterbur [20] and Mansfield and Grannell [21] described the first reports on a major constituent of modern NMR, namely *in vivo* NMR imaging or magnetic resonance imaging (MRI). By applying position-dependent magnetic fields in addition to the static magnetic field, they were able to reconstruct the spatial distribution of nuclear spins in the form of an image. Lauterbur and Mansfield shared the 2003 Nobel Prize in Medicine [22, 23]. Since its inception, MRI has flourished to become the leading method for structural and functional imaging with methods like diffusion tensor imaging (DTI) and blood oxygenation level-dependent (BOLD) functional MRI.

As a leading clinical and research imaging modality, the theoretical and practical aspects of MRI are covered in a wide range of excellent textbooks [24–26]. While MRS is based on the same fundamental principles as MRI, the practical considerations for high-quality MRS are very different. This book is dedicated to providing a robust description of current *in vivo* MRS methods, with an emphasis on practical challenges and considerations. This chapter covers the principles of NMR that are common to both MRI and MRS. Starting with classical arguments, the concepts of precession, coherence, resonance, excitation, induction, and relaxation are explained. The quantum mechanical view of NMR is briefly reviewed after which the phenomena of chemical shift and scalar coupling will be described, as well as some elementary processing of the NMR signal.

1.2 **Classical Magnetic Moments**

The discovery of NMR by Bloch and Purcell in 1945 was not a serendipitous event, but was based on the work by Rabi [27, 28] in the previous decade on magnetic resonance of individual particles in a molecular beam for which he received the 1944 Nobel Prize in Physics. While both groups reported the detection of signal associated with proton magnetic moments, the experimental setups as well as the conceptualization of the NMR phenomenon were very different.

Bloch approached NMR from a classical point of view in which the orientation of magnetic moments is gradually changed by an oscillating magnetic field. This would ultimately lead to the detection of NMR signal from water protons through electromagnetic induction in a nearby receiver coil. Purcell viewed the NMR phenomenon based on quantum mechanics, in close analogy to other spectroscopic methods in which transitions are induced between energy levels by quanta of energy provided by radiofrequency (RF) waves. Purcell described the absorption of energy provided by an oscillating RF field by the protons in solid paraffin. A wonderful overview of the two discoveries of NMR is given by Rigden [29] and Becker et al. [30] as well as by the Nobel lectures of Bloch [5] and Purcell [6].

The spectroscopic or quantum mechanical view often takes center stage in the introduction of many text books, including the previous editions of this book. The main reason for this approach is that a full quantum mechanical description of NMR can account for all observed phenomena, including those that have no classical analog, like scalar or J-coupling. However, as the quantum description of NMR does not deal directly with observable magnetization, but rather with the energetic state of the system, it does not provide an intuitive, physical picture. In the classical view of NMR, the magnetic moments of the individual nuclear spins are summed up to form a macroscopic magnetization vector that can be followed over time using classical electromagnetism concepts. This provides a familiar picture that can be used to follow the fate of magnetization under a wide range of experimental conditions. The classical picture is advocated here, starting with a magnetized needle as found in a compass.

As with all magnets, the compass needle is characterized by a magnetic north and south pole from which the magnetic field lines exit and enter the needle, respectively (Figure 1.1A). The magnetic field lines shown in Figure 1.1A can be summarized by a magnetic moment, μ_1 describing both the amplitude and direction. In the absence of an external magnetic field the compass needle has no preference in spatial orientation and can therefore point in any direction.

When placed in an external magnetic field, such as the Earth's magnetic field, the compass needle experiences a torque (or rotational force) that rotates the magnetic moment towards a parallel orientation with the external field (Figure 1.1B). As the magnetic moment "overshoots" the parallel orientation, the torque is reversed and the needle will settle into an oscillation or frequency that depends on the strengths of the external magnetic field and the magnetic moment. Due to friction between the needle and the mounting point, the amplitude of the oscillation is dampened and will ultimately result in the stabile, parallel orientation of the needle with respect to the external field (Figure 1.1C) representing the lowest magnetic energy state (the antiparallel orientation represents the highest magnetic energy state).

The equilibrium situation (Figure 1.1C) can, besides mechanical means, be perturbed by additional magnetic fields as shown in Figure 1.1D. When a bar magnet is moved towards the compass, the needle experiences a torque and is pushed away from the parallel orientation. When the bar magnet is removed, the needle oscillates as shown in Figure 1.1B before returning to the equilibrium situation (Figure 1.1C). However, if the bar magnet is moved back and

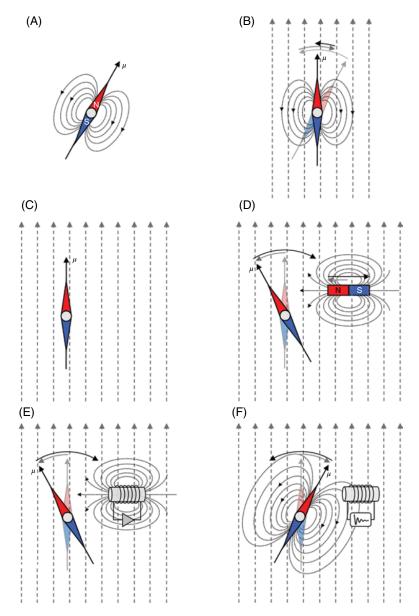


Figure 1.1 Oscillations of a classical compass needle. (A) A compass needle with a magnetic north and south pole creates a dipolar magnetic field distribution of which the amplitude and direction are characterized by the magnetic moment μ . (B) When placed in an external magnetic field the magnetic moment oscillates a number of times before (C) settling in a parallel orientation with the external magnetic field. Note that in Earth's magnetic field the compass needle points to the magnetic south, which happens to be close to geographical north. (D) The needle can be perturbed with a bar magnet, whereby the perturbation reaches maximum effect when the bar movement matches the natural frequency of the needle. (E) The bar magnet can be replaced by an alternating current in a coil. (F) The same coil can also be used to detect the oscillating magnetic moment of the needle through electromagnetic induction.

forth relative to the compass, the needle can be made to oscillate continuously. When the movement frequency of the bar magnet is very different from the natural frequency of the needle (Figure 1.1B), the effect of the bar magnet is not constructive and the needle never deviates far from the parallel orientation. However, when the frequency of the bar magnet