Seminar: Methods of Physics in Biology and Medicine

The Physics of Nuclear Spin Systems

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Motivation

- 1920s: unexplained splitting of atomic spectral lines

→ proposed solution: concept of spin[1]

- led to huge advancements in the medical field
- one specific real-world application of spin physics: NMR imaging

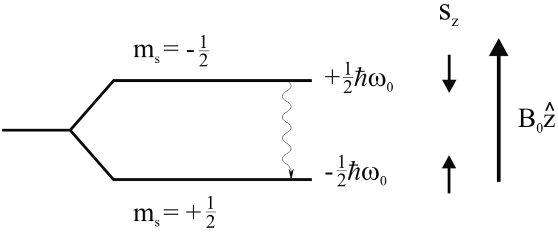

Figure: Zeeman splitting for spin-$\frac{1}{2}$ system.[2]

[1] G. E. Uhlenbeck *et al.*, Ersetzung der Hypothese vom unmechanischen Zwang durch eine Forderung bezüglich des inneren Verhaltens jedes einzelnen Elektrons, 1925.

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

Spin - Fundamentals

- fundamental quantum property of subatomic particles
- independent of particle's motion
- can be visualised as intrinsic angular momentum (no classical analogue)
- follows angular momentum rules of computation

→ particles behave as though they were spinning

→ associated with a magnetic moment

→ interacts with magnetic fields (precession)

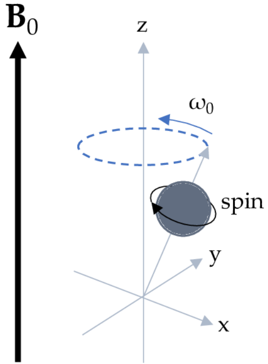

Figure: Nuclear spin of hydrogen in an applied field.[3]

[3] J. Denck, Machine learning-based workflow enhancements in magnetic resonance imaging, 2022.

Spin - Fundamentals

- difference in spin statistics between particles:

→ integer-spin particles follow Bose-Einstein statistics (bosons)

→ half-integer-spin particles follow Fermi-Dirac statistics (fermions)

- spin must be ascribed, whether a particle is elementary or composite

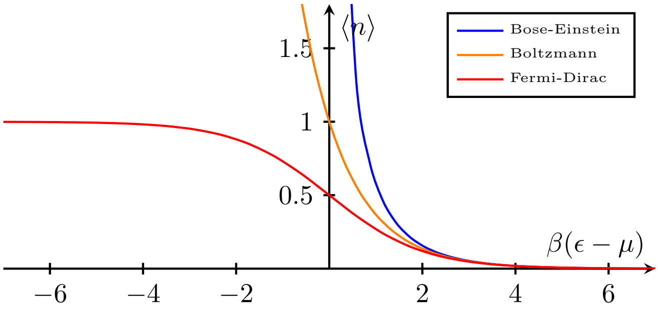

Figure: Energy distribution functions.

Understanding Spin

semi-classical approach:

- spin behavior under an applied magnetic field
- assumptions: quantised angular momenta and energies
- spins are treated as magnetic dipoles with nuclear magnetic moment $\underline{\mu}$
- the angle $\angle(\underline{\mu}, \underline{\mathbf{B}})$ determines the energy of the state

$$E = -\underline{\mu} \cdot \underline{\mathbf{B}} = -\mu_z B_0 = -\hbar m \cdot \gamma B_0$$

- for nucleus $I = \frac{1}{2}$, possible spin states $m = \pm\frac{1}{2}$:

$$E_{|\downarrow\rangle}\left(m = -\frac{1}{2}\right) = +\frac{1}{2}\hbar \cdot \gamma B_0$$

$$E_{|\uparrow\rangle}\left(m = +\frac{1}{2}\right) = -\frac{1}{2}\hbar \cdot \gamma B_0$$

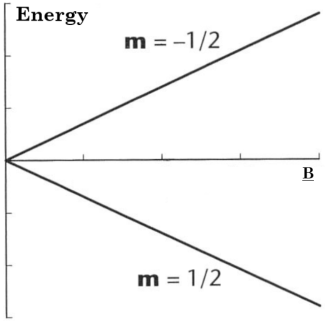

Figure: Energy splitting of nuclear spin levels.[4]

[4] Adapted from: T. C. Pochapsky *et al.*, NMR for physical and biological scientists, Garland Science, 2019.

Understanding Spin

- classically: B field exerts a torque $\underline{\tau} = \underline{\mu} \wedge \underline{\mathbf{B}}$ on a magnetic dipole $\underline{\mu}$
- result of the applied torque: top-like rotation of the magnetic moment around the applied field

→ precession at Larmor frequency $\omega_0 = \gamma B_0$

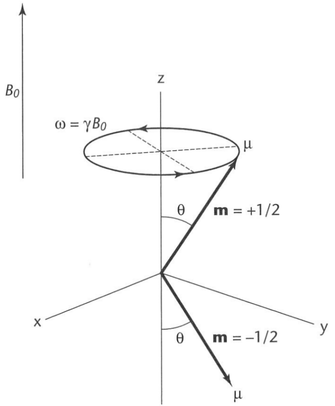

Figure: Classical picture.[4]

[4] T. C. Pochapsky *et al.*, NMR for physical and biological scientists, Garland Science, 2019.

Nuclear Magnetism and Nuclear Spin

- magnetism is a QM effect (operators)
- nuclear magnetism is a pure spin magnetism
- magnetic moment $\hat{\mu} = \gamma \hat{\mathbf{I}}$
- spin operator eigenstates follow those of the angular momentum operator

$$\hat{\mathbf{I}}^2 |\psi\rangle = \hbar^2 I(I+1)|\psi\rangle$$

$$\hat{I}_z |\psi\rangle = \hbar m |\psi\rangle$$

- $2I+1$ possible spin states: $m = -I, -(I-1), \ldots, (I-1), I$
- any nucleus $I \neq 0$ will exhibit a splitting of spin energy levels in a $\underline{\mathbf{B}}$-field

→ Zeeman splitting

$I > \frac{1}{2}$ Nuclei

- Nuclei $I > \frac{1}{2}$ have quadrupole moments
- experience Zeeman splitting (splitting of spin energy levels in B field)
- also experience splitting of spin energy levels in the presence of an electric field gradient

→ causing frequency shifts and relaxation effects

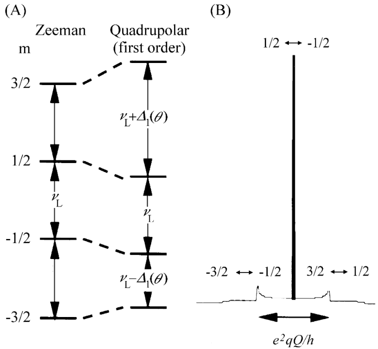

Figure: First order frequency shift by perturbing electric field gradient.[5]

[5] A. Medek *et al.*, Multiple-quantum magic-angle spinning NMR, J. Braz. Chem. Soc., 1999.

Magnetic Moment in B-Field

- consider a ^1H nucleus with $I = \frac{1}{2}$, *i.e.* 2 possible spin states
- an energy (frequency) is associated with each spin state

I $\underline{\mathbf{B}} = 0$

- spin states are degenerate and energetically equivalent

→ possible states are equally probable

- no absorption or emission of energy possible

II $\underline{\mathbf{B}} = B_0 \hat{\mathbf{e}}_z$

- spins precess around $\underline{\mathbf{B}}$ with Larmor frequency $\omega_0 \equiv \gamma B_0$ after perturbation from equilibrium position
- spin states are non-degenerate and energetically non-equivalent
- Zeeman splitting

$$\hat{H}_z = -\underline{\hat{\mu}}\underline{\mathbf{B}} = -\gamma \hat{\mathbf{I}} B_0 \hat{\mathbf{e}}_z = -\hat{I}_z \gamma B_0$$

$$\hat{H}_z |\psi\rangle = E_m |\psi\rangle = -\hbar m \cdot \gamma B_0 |\psi\rangle$$

$$\Rightarrow E_m = -\hbar m \cdot \gamma B_0 = -\hbar m \cdot \omega_0$$

Magnetic Moment in B-Field

- 2 spin states: **up** $|\uparrow\rangle$ ($m = +\frac{1}{2}$) and **down** $|\downarrow\rangle$ ($m = -\frac{1}{2}$), with energies

$$\Rightarrow E_m = -\hbar m \cdot \omega_0$$

$$E_{|\downarrow\rangle}\left(m = -\frac{1}{2}\right) = +\frac{1}{2}\hbar \cdot \omega_0$$

$$E_{|\uparrow\rangle}\left(m = +\frac{1}{2}\right) = -\frac{1}{2}\hbar \cdot \omega_0$$

- transitions between the quantised spin states require absorption or emission of energy

$$\Delta E = E_{|\downarrow\rangle} - E_{|\uparrow\rangle} = \hbar\omega_0$$

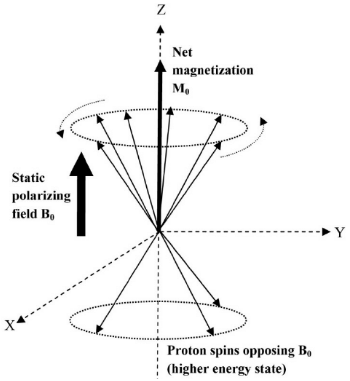

Figure: Precession of ^1H nuclei around an applied field.[6]

[6] L. Bond *et al.*, Evaluation of non-nuclear techniques for well logging: Final report, U.S. Department of Energy, 2011.

Spin Systems

- collection of interacting spins in a spin ensemble
- energy state populations are determined at thermal equilibrium

→ lower energy states are more populated

- applied field B_0 and temperature T determine how the states are populated:

$$\frac{N_{|\downarrow\rangle}}{N_{|\uparrow\rangle}} = e^{-\beta \Delta E} = e^{-\beta \hbar \omega_0} \leq 1, \qquad \beta \equiv \frac{1}{k_B T}$$

- population difference is described by the Boltzmann distribution
- net absorption or emission of energy is only possible as long as there is a population difference: $\Delta N = N_{|\uparrow\rangle} - N_{|\downarrow\rangle} \neq 0$
- ΔN very small $\frac{\Delta N}{N} \sim 10^{-6}$, but immensely important
- system perturbations, like RF pulses, can lead to $\Delta N \to 0$

→ ΔN must be reestablished by relaxation

Magnetisation $\underline{\mathbf{M}}$

- macroscopic observable that makes it possible to measure microscopic spin behavior
- net magnetisation represents the bulk magnetic properties of the spin system

$$\underline{\mathbf{M}} = \frac{1}{V} \sum_i \underline{\mu}_i$$

- in thermal equilibrium: $\underline{\mathbf{M}}$ aligned with applied field $\underline{\mathbf{B}}_0 \parallel \underline{\mathbf{M}} = M_0 \hat{\mathbf{e}}_z$

$\rightarrow$ $\underline{\mathbf{M}}$ must be tipped away from $\underline{\mathbf{B}}_0$ to initiate precession around the applied field

- magnetisation can be separated into a longitudinal $\underline{\mathbf{M}}_z = M_z \hat{\mathbf{e}}_z$ and a transverse $\underline{\mathbf{M}}_\perp = M_x \hat{\mathbf{e}}_x + M_y \hat{\mathbf{e}}_y$ component
- simplify the system by transitioning into a rotating frame S'

$\rightarrow$ trivialise precessional motion

Rotating Reference Frame

- transformation into rotating frame of reference $S \rightarrow S'$

→ simplifies calculations and formulas

→ magnetic moment μ, and magnetisation $\underline{\mathbf{M}}$ in S' behave as in a resting frame experiencing $\underline{\mathbf{B}}_{eff}$ instead of $\underline{\mathbf{B}}$

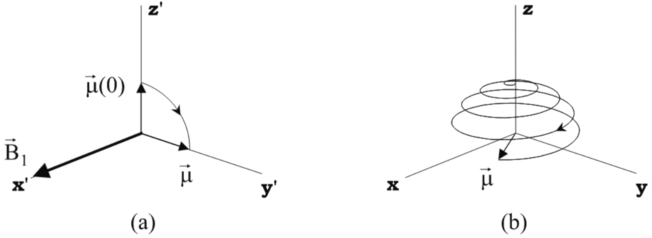

Figure: Effect of rf pulse on magnetic moment in (**a**) rotating and (**b**) lab frame.[2]

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

T_1 Longitudinal Relaxation

- spin-lattice interaction
- transfer of energy from the spin system to the lattice
- excited nuclei from the high energy state return to the ground state
- return of M_z to equilibrium state M_0

$$\frac{\mathrm{d}}{\mathrm{dt}} M_z = \frac{1}{T_1}(M_0 - M_z)$$

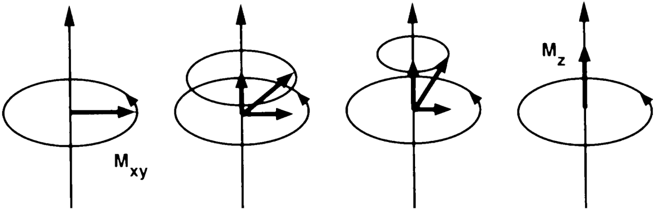

Figure: T_1 relaxation.[7]

[7] D. Weishaupt, How does MRI work?, Springer-Verlag, 2008.

T_2 Transverse Relaxation

- spin-spin interaction
- spins experience local fields (combinations of the applied field and the fields of their neighbors)

→ variations in the local fields lead to different precessional frequencies

→ individual spins dephase over time

- net transverse magnetisation decreases during the precession

$$\frac{\mathrm{d}}{\mathrm{dt}}\underline{\mathbf{M}}_{\perp} = -\frac{1}{T_2}\underline{\mathbf{M}}_{\perp}$$

- $T_2^* < T_2 < T_1$

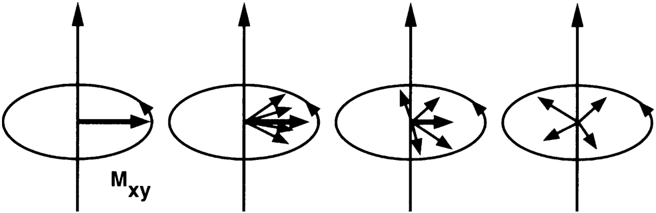

Figure: T_2 relaxation.[7]

[7] D. Weishaupt, How does MRI work?, Springer-Verlag, 2008.

Dynamics of Spin Systems

- net magnetisation of a spin ensemble

$$\underline{\mathbf{M}} = \frac{1}{V}\sum_i \underline{\mu}_i$$

- Equation of Motion: Bloch Equation

$$\frac{\mathrm{d}}{\mathrm{dt}}\underline{\mathbf{M}} = \underbrace{\underline{\mathbf{M}} \wedge \gamma \underline{\mathbf{B}}_{eff}}_{\text{classical EoM}} + \underbrace{\frac{1}{T_1}(M_0 - M_z)\hat{\mathbf{e}}_z}_{\text{longitudinal recovery}} \underbrace{- \frac{1}{T_2}\underline{\mathbf{M}}_\perp}_{\text{spin dephasing}}$$

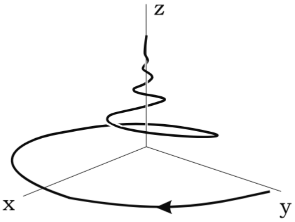

Figure: Time evolution of the magnetisation in the lab frame.[2]

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

Dynamics of Spin Systems

- the solutions of the EoM yield the time evolutions of the long. and transverse magnetisations

$$M_z(t) = M_z(0)e^{-t/T_1} + M_0(1 - e^{-t/T_1})$$

$$\boxed{\underline{\mathbf{M}}_\perp(t) = \underline{\mathbf{M}}_\perp(0)e^{-t/T_2}} \quad \text{(FID)}$$

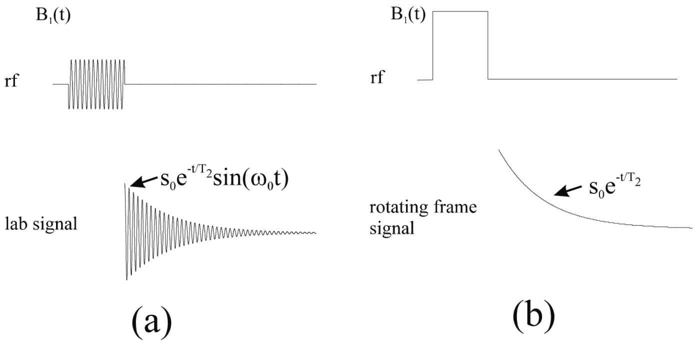

Figure: FID signal of the transverse magnetisation in the (**a**) lab and (**b**) rotating frame.[2]

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

Dynamics of Spin Systems

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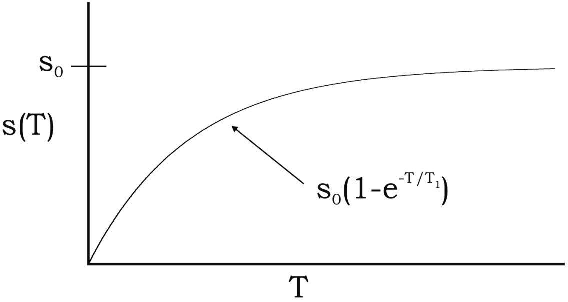

Figure: Signal of the longitudinal magnetisation.[2]

[2] Adapted from R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

Example: NMR Imaging

- used for creating detailed images of soft tissue
- based on the interactions of nuclear spins with an external magnetic field
- dominated by the proton in hydrogen

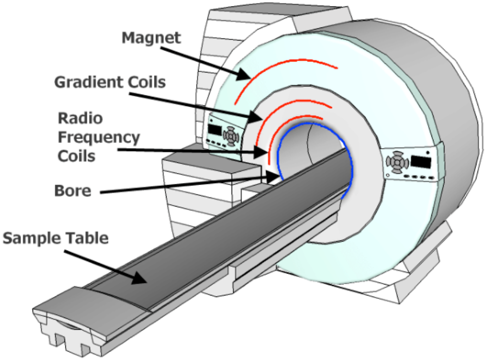

Figure: Schematic diagram of an MRI machine.[8]

[8] H. Haynes *et al.*, 'The emergence of magnetic resonance imaging (MRI) for 3d analysis of sediment beds,' in 2013.

How MRI Works

- strong $\underline{\mathbf{B}}_0$ field aligns the spins
- rf pulses are then used to perturb the spins

→ the relaxation process of the spins back to equilibrium is what emits detectable signal

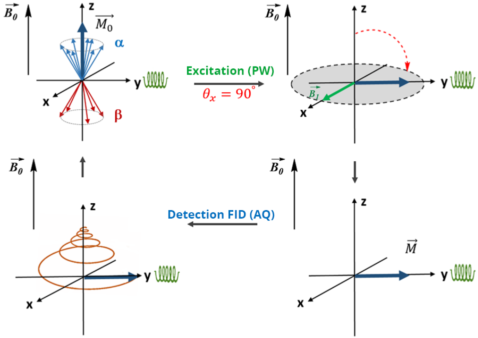

Figure: MRI process signal acquisition.[9]

[9] *NMR principles*, https://chimactiv.agroparistech.fr/en/bases/rmn/theorie/3, accessed: 12/01/2024.

Spatial Encoding through Gradient Coils

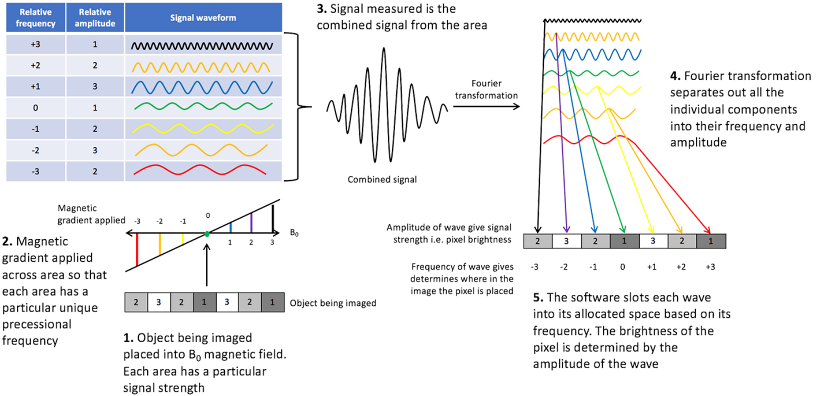

Figure: Spatial encoding steps illustration.[10]

[10] S. Abdulla, *FRCR physics notes: MRI*, https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/spatial-encoding/, accessed: 12/01/2024.

Spin Echo Sequence

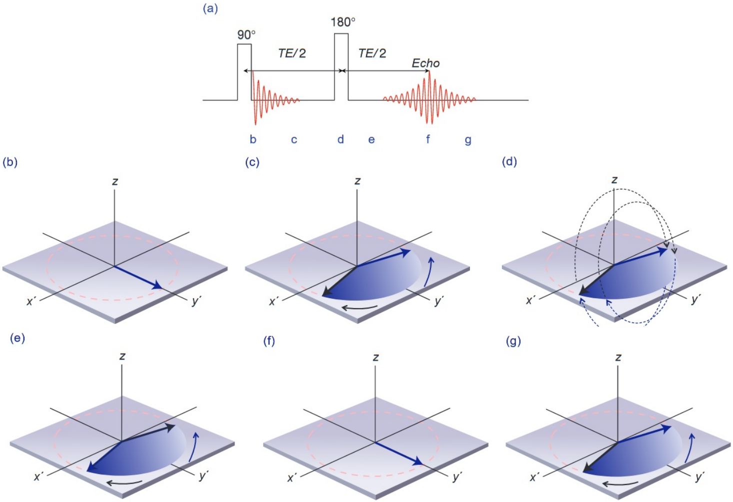

Figure: Spin echo sequence.[11]

[11] Adapted from D. W. McRobbie *et al.*, MRI from picture to proton, Cambridge University Press, 2017.

Different Imaging Techniques

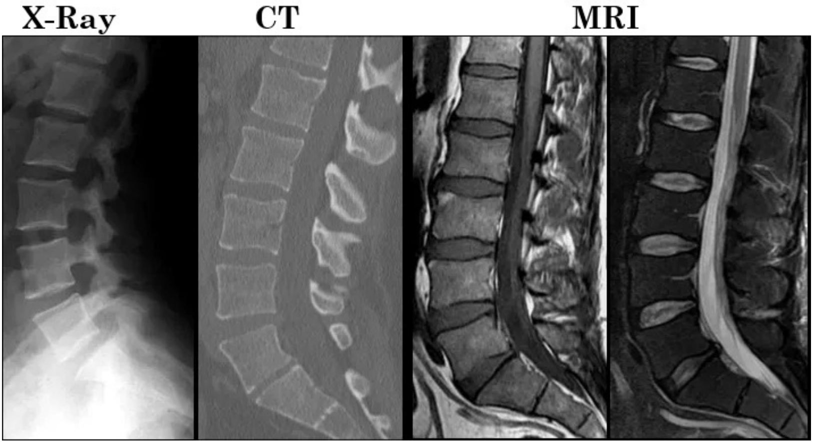

Figure: Comparing different imaging techniques.[12]

[12] *No longer available*, https://www.greenriverspine.org/, accessed: 12/01/2024.

Conclusion

- spin physics underpins MRI technology

$\rightarrow$ allowing non-invasive soft tissue imaging with high spatial resolution

- several different techniques to improve on regular MRI (*e.g.* hyperpolarisation)
- allows studying biological systems without altering or intervening in them

$\rightarrow$ innovations and continued advancements hold a lot of potential

References I

[1] G. E. Uhlenbeck *et al.*, Ersetzung der Hypothese vom unmechanischen Zwang durch eine Forderung bezüglich des inneren Verhaltens jedes einzelnen Elektrons, 1925.

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

[3] J. Denck, Machine learning-based workflow enhancements in magnetic resonance imaging, 2022.

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[6] L. Bond *et al.*, Evaluation of non-nuclear techniques for well logging: Final report, U.S. Department of Energy, 2011.

[7] D. Weishaupt, How does MRI work?, Springer-Verlag, 2008.

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References II

[9] *NMR principles*, https://chimactiv.agroparistech.fr/en/bases/rmn/theorie/3, accessed: 12/01/2024.

[10] S. Abdulla, *FRCR physics notes: MRI*, https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/spatial-encoding/, accessed: 12/01/2024.

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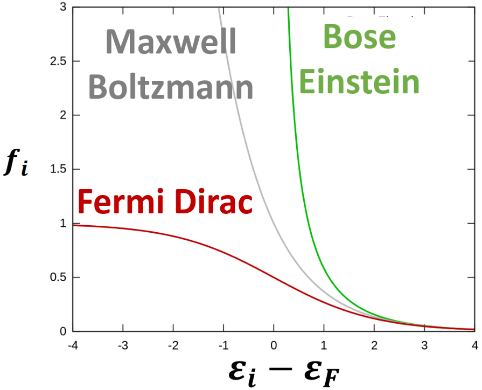
[12] *No longer available*, https://www.greenriverspine.org/, accessed: 12/01/2024.

[13] D. Weishaupt *et al.*, Wie funktioniert MRI?, Springer-Verlag, 2014.

BACKUP

Statistics

Statistical distribution laws



$$f_i = \exp\left(-\frac{\varepsilon_i - \varepsilon_F}{k_B T}\right)$$

$$f_i = \frac{1}{\exp\left(\frac{\varepsilon_i - \varepsilon_F}{k_B T}\right) - 1}$$

$$f_i = \frac{1}{\exp\left(\frac{\varepsilon_i - \varepsilon_F}{k_B T}\right) + 1}$$

Nuclear Magnetism and Nuclear Spin

- magnetism is a QM effect
- nuclear magnetism is a pure spin magnetism
- magnetic moment $\underline{\mu} = \gamma \underline{\mathbf{I}}$
- composite particles carry spin, respecting spin statistics
- composition of angular momenta from nucleons:

  even #p and even #n in nucleus: $I = 0$

  odd #(p + n) in nucleus: $I =$ half-integer

  odd #p and odd #n in nucleus: $I =$ integer

Nuclear Magnetism and Nuclear Spin

- composite particles carry spin, respecting spin statistics
- composition of angular momenta from nucleons is complex

→ depending on how many p and n are present and how they pair

- any nucleus $I \neq 0$ will exhibit a splitting of spin energy levels in a $\underline{\mathbf{B}}$-field

→ Zeeman splitting

- an energy (frequency) is associated with each spin state
- transitions between the quantised spin states require absorption or emission of energy (Larmor frequency ω_0)

Zeeman Splitting

- Zeeman operator: $\hat{H}_z = -\underline{\hat{\mu}}\underline{\mathbf{B}} = -\gamma\underline{\hat{\mathbf{I}}}B_0\hat{e}_z$
- $\hat{I}_z|I,m\rangle = E_m|I,m\rangle = -\gamma\hbar m B_0$
- 2 spin states: up $|\uparrow\rangle$ $(m = +\frac{1}{2})$ and down $|\downarrow\rangle$ $(m = -\frac{1}{2})$
- $\Delta E = \hbar\gamma B_0 = \hbar\omega_0$

Magnetisation Population

- system of ^1H nuclei
- in thermal eq.: population $\sim e^{-\beta E}$ with $\beta = \frac{1}{k_B T}$
- $N_{|\uparrow\rangle,|\downarrow\rangle} = \dfrac{N}{e^{\beta\mu B_0} + e^{-\beta\mu B_0}} e^{\pm\beta\mu B_0}$
- $M = (N_{|\uparrow\rangle} - N_{|\downarrow\rangle})\mu = N_\mu \tanh(\beta\mu B_0)$
- high T approximation: Curie Law: $M \simeq \frac{1}{4}\beta\gamma^2\hbar^2 N B_0$

Rotating Reference Frame

- transformation into rotating frame of reference $S \rightarrow S'$

→ simplifies calculations and formulas

- rotation is defined by a rotational angular velocity vector $\underline{\mathbf{\Omega}}$
- the effective magnetic field is the superposition of the applied field and a fictitious field with the same direction as the rotational axis

$$\underline{\mathbf{B}}_{eff} = \underline{\mathbf{B}} + \frac{1}{\gamma}\underline{\mathbf{\Omega}}$$

→ magnetic moment $\underline{\mu}$, and magnetisation $\underline{\mathbf{M}}$ in S' behave as in a resting frame experiencing $\underline{\mathbf{B}}_{eff}$ instead of $\underline{\mathbf{B}}$

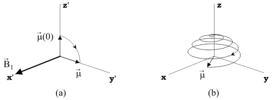


Figure: Effect of rf pulse on magnetic moment in (**a**) rotating and (**b**) lab frame[2].

[2] R. W. Brown *et al.*, Magnetic resonance imaging: Physical principles and sequence design, Wiley Blackwell, 2014.

Spatial Encoding through Gradient Coils

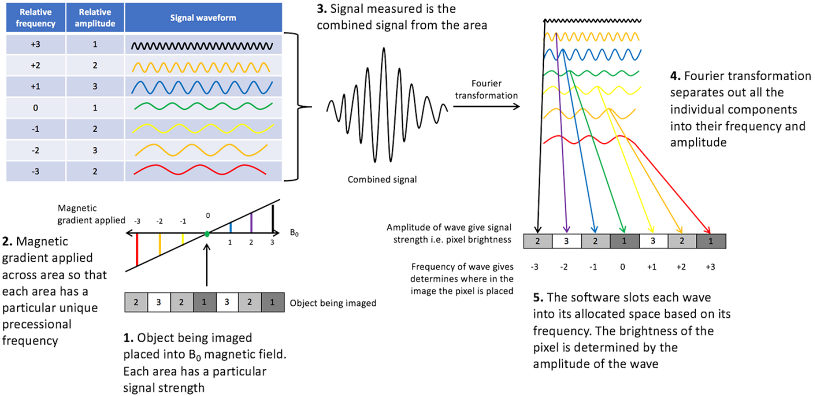


Figure: Spatial encoding steps illustration[10].

1. slice selection (gradient during rf pulse)
2. spatial encoding (phase and frequency encoding)

[10] Adapted from FRCR Physics Notes: MRI, https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/spatial-encoding/, accessed on 21/01/24.

Spatial Localisation

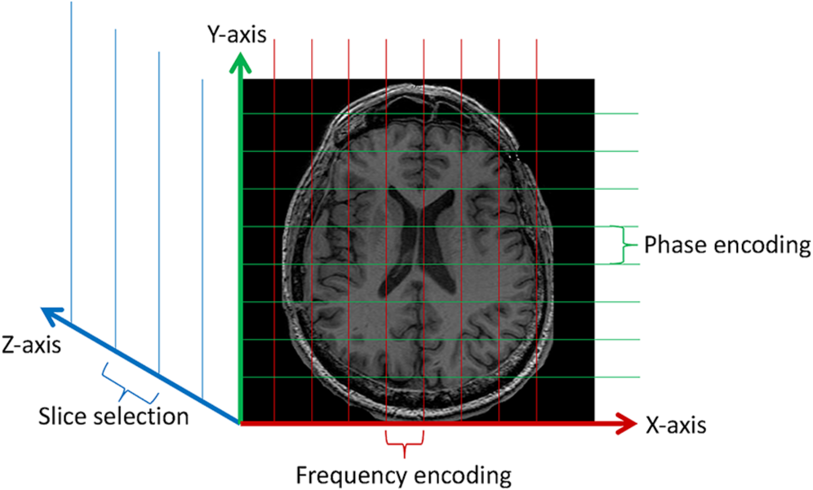
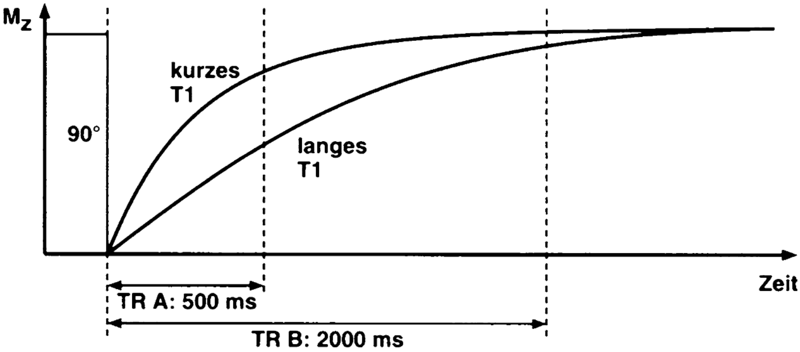


Figure: Spatial localisation illustration[10].

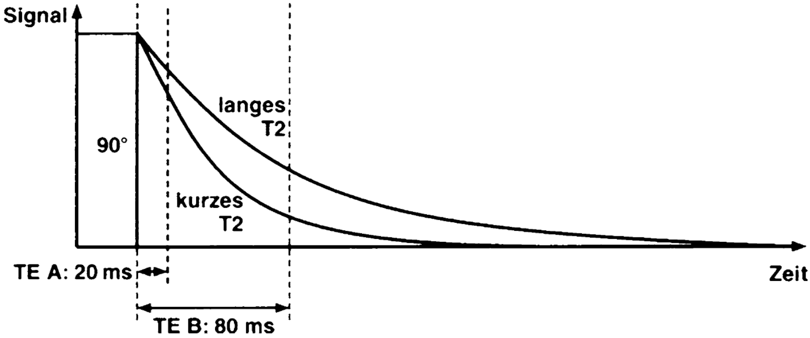
[10] Adapted from FRCR Physics Notes: MRI, https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/spatial-encoding/, accessed on 21/01/24.

T1 Relaxation



D. Weishaupt *et al.*, Wie funktioniert MRI?, Springer-Verlag, 2014

T2 Relaxation



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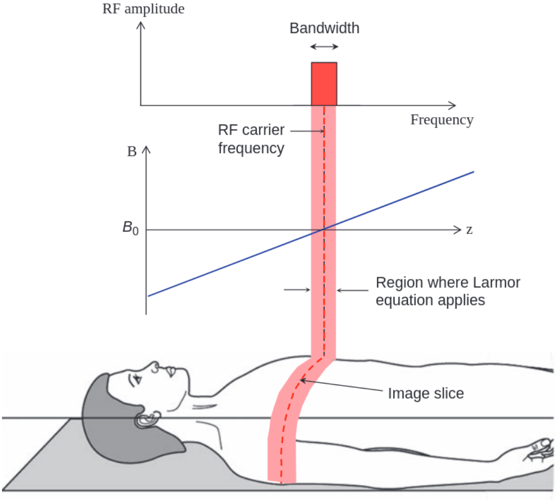
Slice Selection



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