Karlsruhe Institute of Technology

At the intersection of microengineering and magnetic resonance: challenges and opportunities

Dr. Neil MacKinnon: neil.mackinnon@kit.edu
Dr. Mazin Jouda, Dr. Vlad Badilita, Dr. Sören Lehmkuhl, Prof. Jürgen Brandner

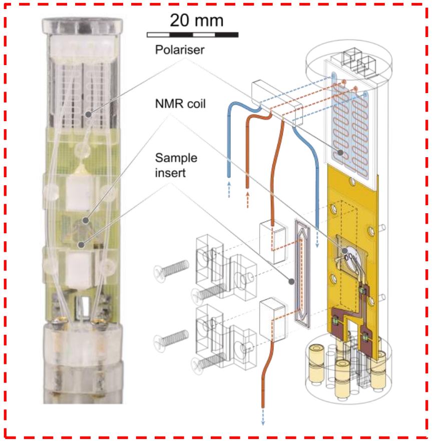
INSTITUTE OF MICROSTRUCTURE TECHNOLOGY

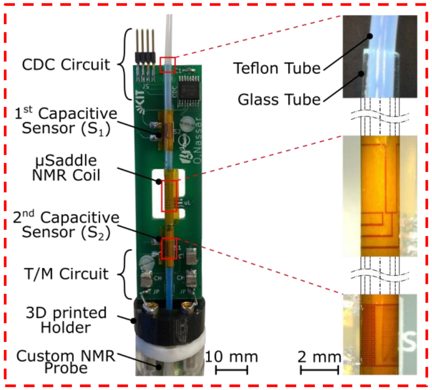
Welcome!

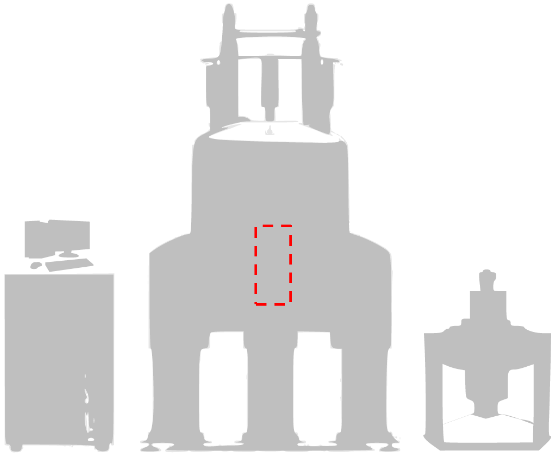
What are your first thoughts when you think about magnetic resonance?

Organization of this week's lecture series

- General NMR & MRI Introduction
- Electronics, spectrometer, and µNMR hardware
- Hyperpolarization
- Applications

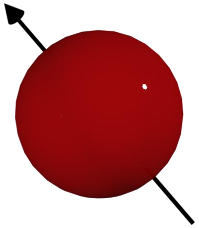


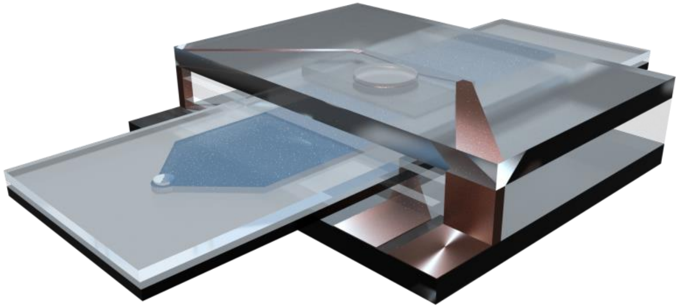




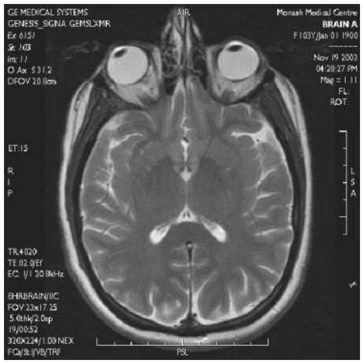
Welcome! Today's Outline

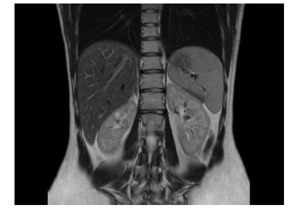
- **General introduction to Nuclear Magnetic Resonance**
- General introduction to Magnetic Resonance Imaging

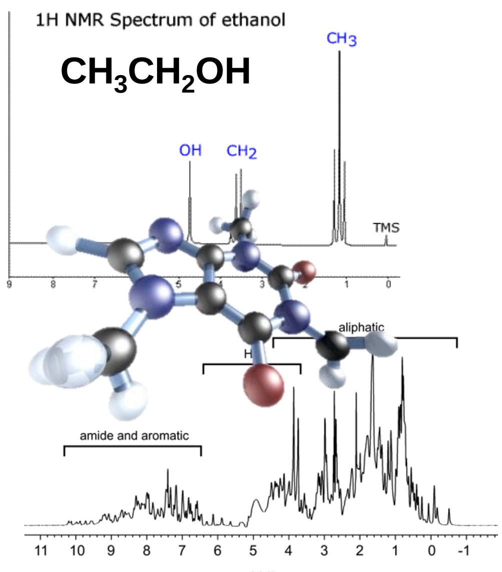


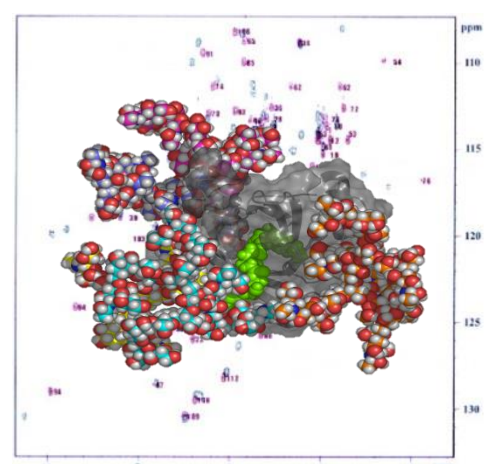


Non-invasive imaging and spectroscopy









NMR as recognized by Nobel

Otto Stern
Nobel Prize in Physics
1943

"for his contribution to the development of the molecular ray method and his discovery of the magnetic moment of the proton"

Isidor Isaac Rabi
Nobel Prize in Physics
1944

"for his resonance method for recording the magnetic properties of atomic nuclei"

Felix Bloch & Edward Mills Purcell
Nobel Prize in Physics
1952

"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"

Richard R. Ernst
Nobel Prize in Chemistry
1991

"for his contributions to the development of the methodology of high resolution nuclear magnetic resonance (NMR) spectroscopy"

Kurt Wüthrich
Nobel Prize in Chemistry
2002

"for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution"

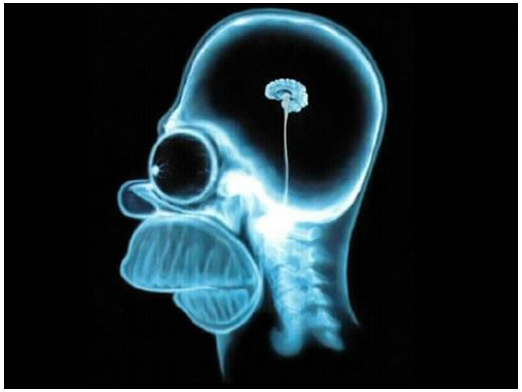
Paul C. Lauterbur & Sir Peter Mansfield
Nobel Prize in Physiology or Medicine
2003

"for their discoveries concerning magnetic resonance imaging"

What is Nuclear Magnetic Resonance?

Nuclear

- Signal originates from the nucleus of an atom!

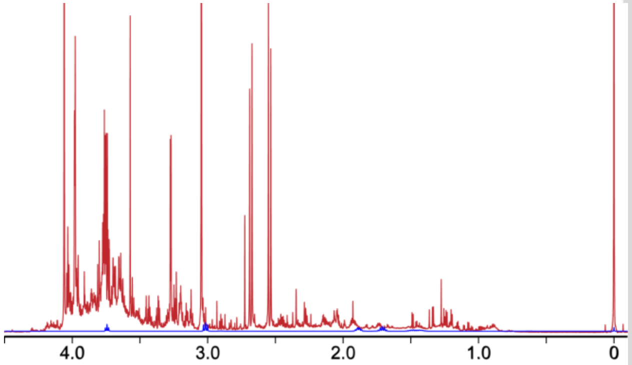


Magnetic

- Strong magnetic fields create new nuclear quantum states

Resonance

- Induce transitions between energy levels



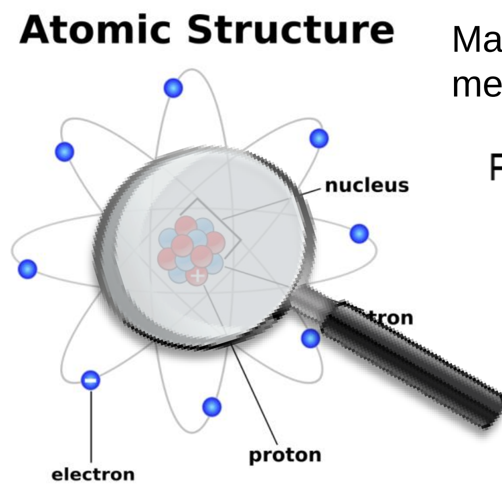
What is Nuclear Magnetic Resonance?

Nuclear

- Signal originates from the nucleus of an atom!

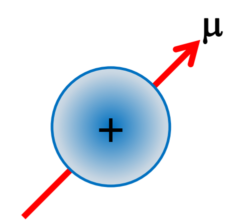
Magnetic

- Strong magnetic fields create new nuclear quantum states



Many nuclei posses quantum mechanical property of spin, I

Particles with spin also have spin angular momentum, $\hat{\mathbf{I}}$

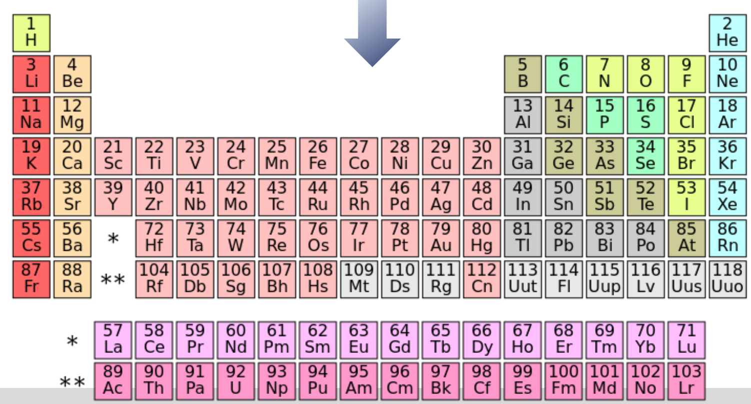


$$\vec{\mu} = \gamma \vec{\mathbf{J}}$$

Nuclear spin results in a nuclear magnetic moment, μ

γ is dependent on the atom

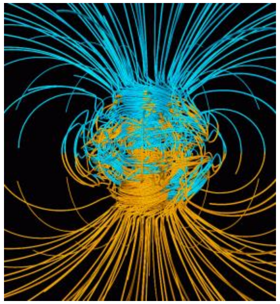
Σ (protons + neutrons)	# protons	I
Odd	-	1/2, 3/2, …
Even	Odd	1, 2, …
Even	Even	0



What is Nuclear Magnetic Resonance?

Nuclear

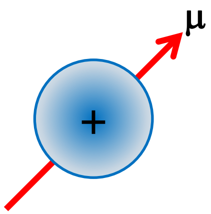
- Signal originates from the nucleus of an atom!



Earth's magnetic field ≅ 50 μT

Magnetic

- Strong magnetic fields create new nuclear quantum states



NMR magnet ≅ 1 – 23 T

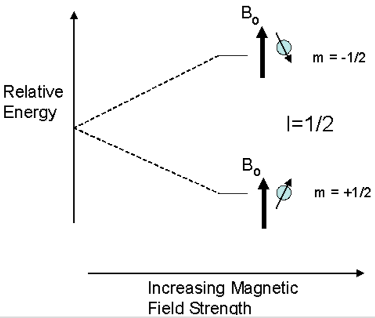
Resonance

- Induce transitions between energy levels

Zeeman Splitting

Quantum mechanics allows for two orientations of μ in **B**

$$E = -\mu \cdot \mathbf{B}$$



What is Nuclear Magnetic Resonance?

Nuclear

- Signal originates from the nucleus of an atom!

Magnetic

- Strong magnetic fields create new nuclear quantum states

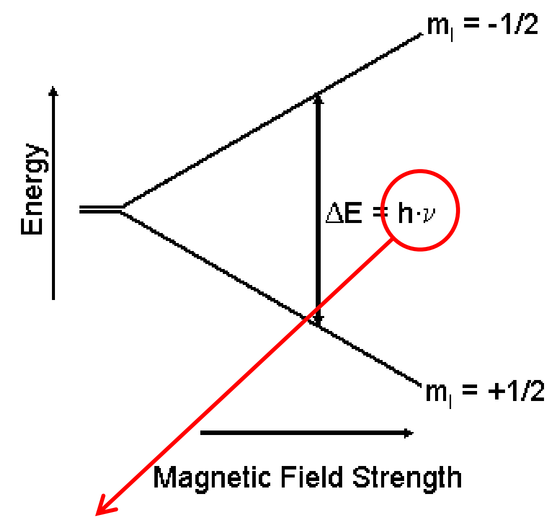
Resonance

- Induce transitions between energy levels

Large magnetic field usually directed along z-axis, B_z

$$\mathbf{B} = B_z \qquad \hat{\mathbf{I}} = \hat{I}_z = m\hbar$$

$$E = -\gamma m \hbar B_z$$



$$I = \frac{1}{2} \qquad m = \pm\frac{1}{2}$$

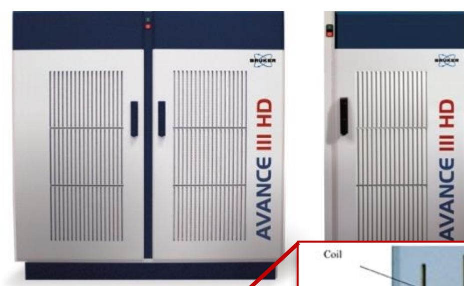
Assume:

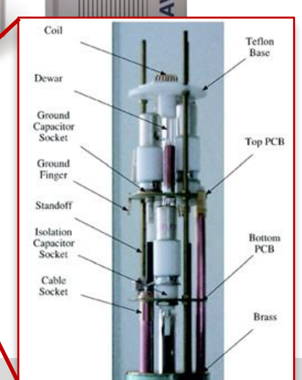
- nucleus is [1]H (hydrogen), γ = 42.576 MHz / T
- then $\nu \cong$ **40 – 1000 MHz** for **B** = 1 – 23 T

NMR is a technique reliant on radio frequencies

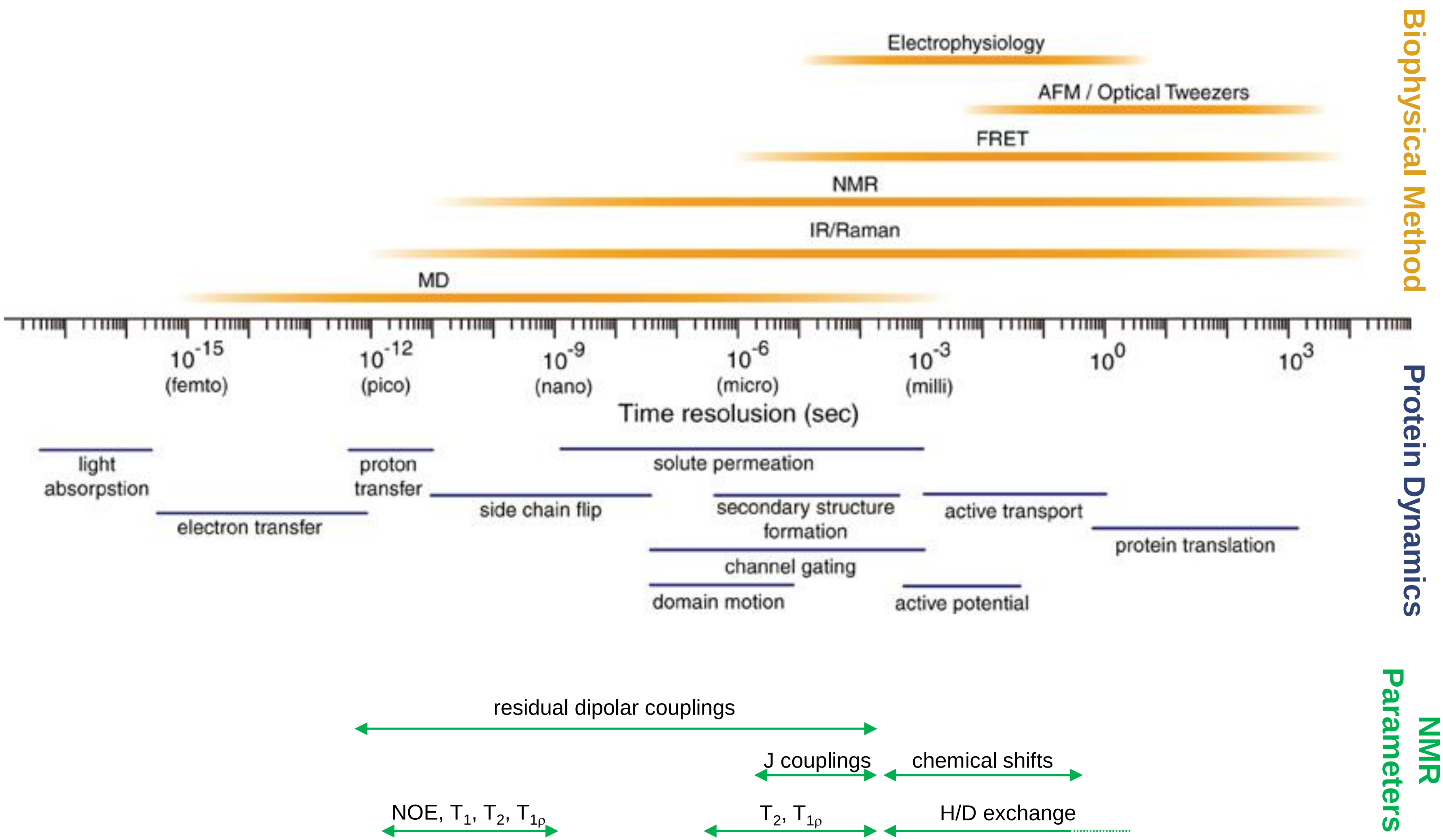
Spectrometer components

- Magnetic field – Earth field (50 µT) to pulsed fields (90+ T)
- Console –transmit excitation signals (1 KW), receive sample signals (~ 10’s µW) in frequencies from KHz to GHz
- Probe – delivers excitation signals to sample, first step in receiving signal from sample
- Disciplines involved:
  - Mathematics
  - Physics
  - Chemistry
  - Biology
  - Engineering
  - Informatics
  - Medicine



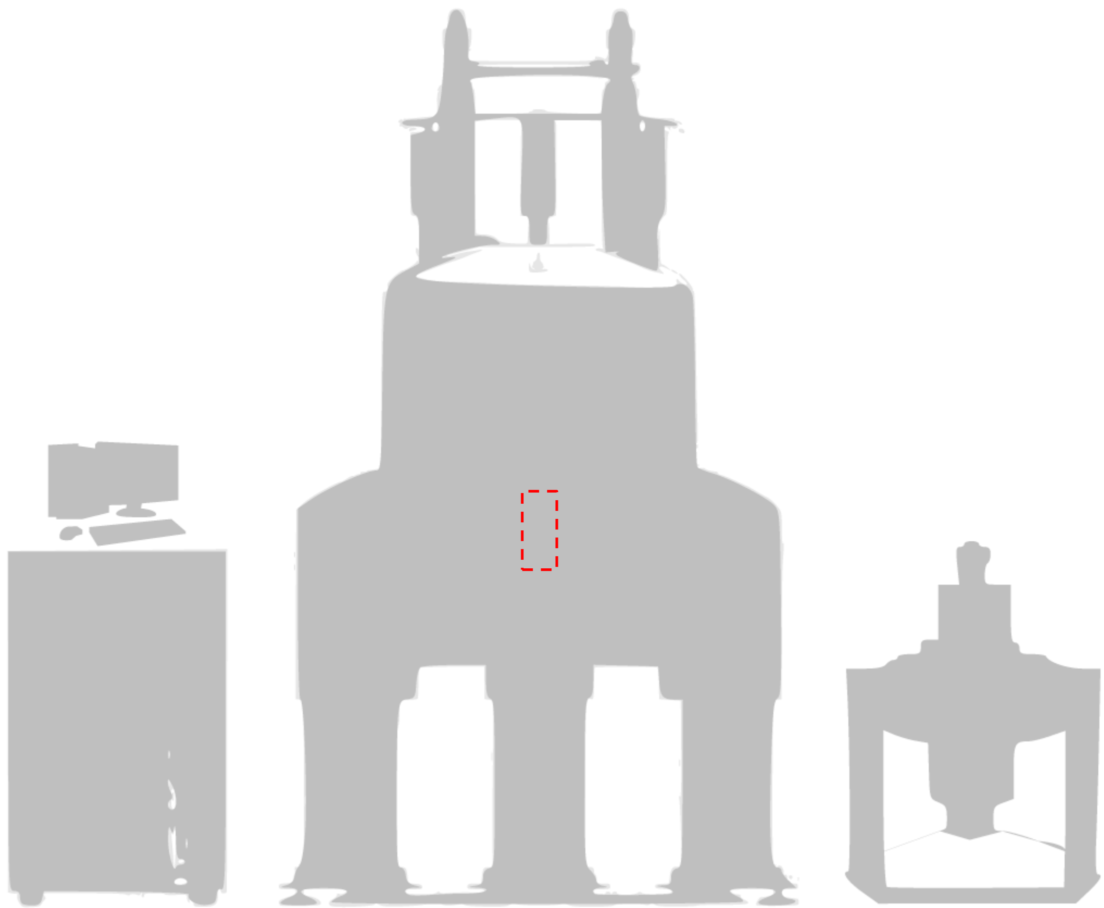


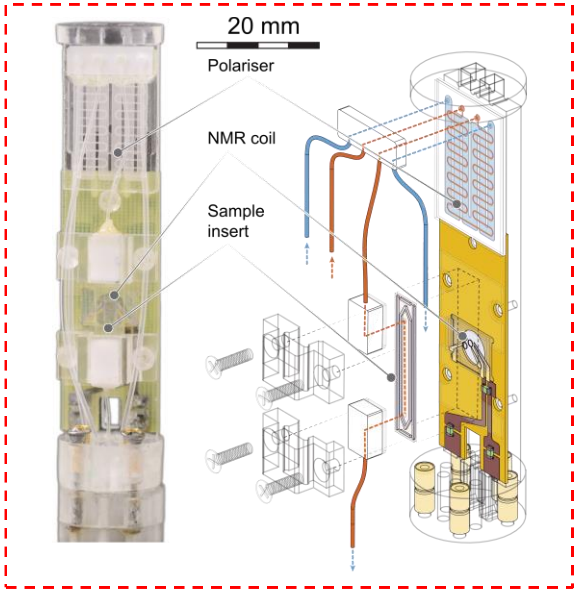
NMR is sensitive to Dynamics

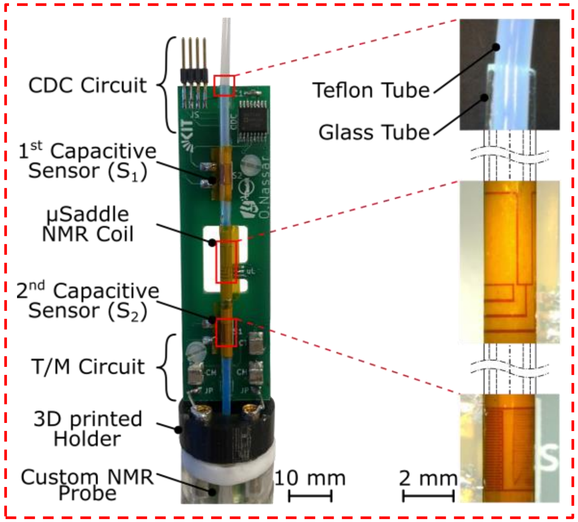


Ode, H. et. al., *Front. Microbiol.* 3 (2012) 258.
Prof. David Case: casegroup.rutgers.edu

Why Micro-MR?

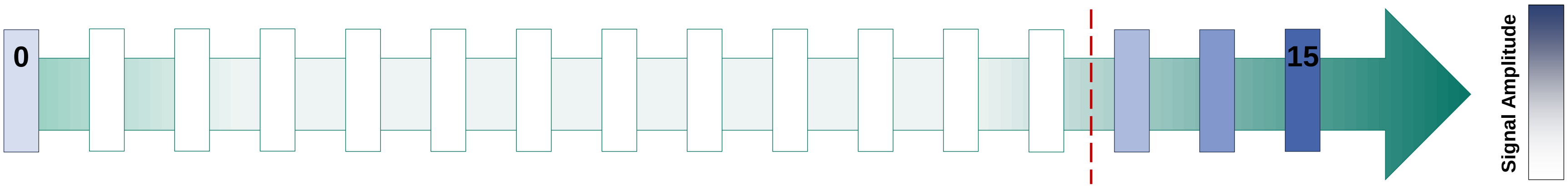



20 mm
Polariser
NMR coil
Sample insert


CDC Circuit
1st Capacitive Sensor (S1)
μSaddle NMR Coil
2nd Capacitive Sensor (S2)
T/M Circuit
3D printed Holder
Custom NMR Probe
Teflon Tube
Glass Tube
10 mm
2 mm

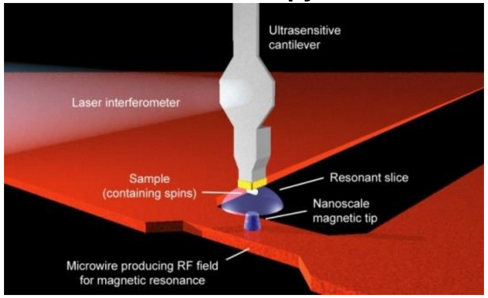
Why Micro-MR?

— Number of Spins (10^x) →

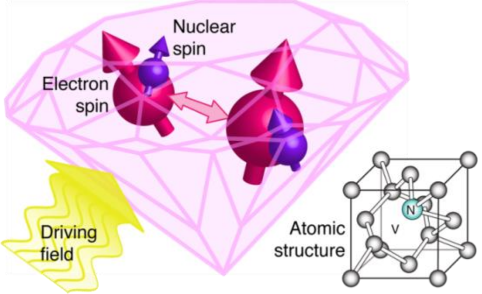


LOD (Faraday detection)

Magnetic Resonance Force Microscopy



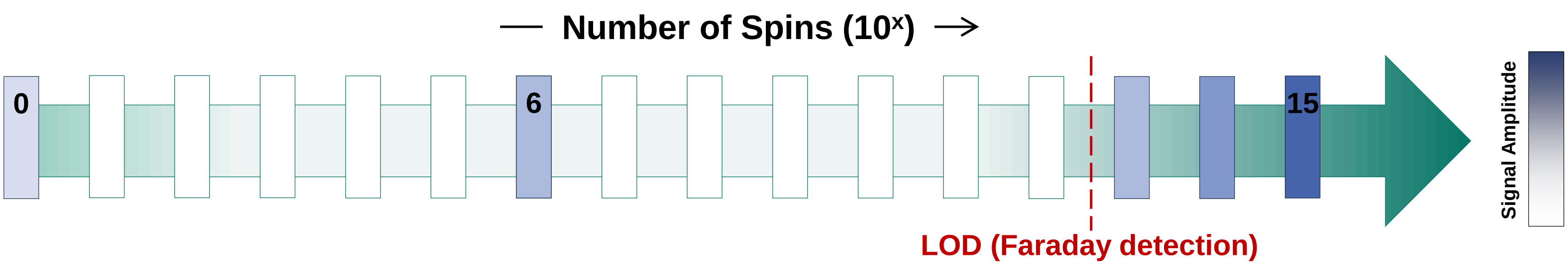
Nitrogen-vacancy centers in diamond



Standard MR sample

µNMR detectors

Why Micro-MR?



How can we bridge this gap?

$$\mathrm{SNR} = \frac{k_o \left(\frac{B_1}{i}\right) V_s N \gamma \hbar^2 I(I+1) \frac{\omega_o^2}{k_B T 3\sqrt{2}}}{F\sqrt{4 k_B T R \Delta f}}$$

High fill factor

High induction efficiency

High homogeneity

High field

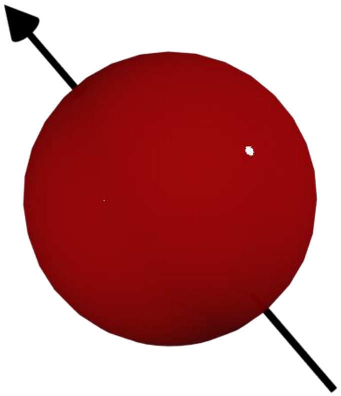
Larmor frequency $\omega_o = \gamma B_o$

Cool sensor

Low resistance

Introduction to NMR theory

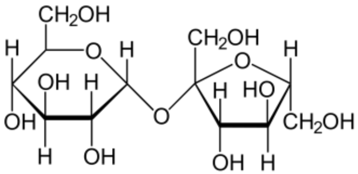
- **Classical Description**
- Quantum Description
- Nuclear Interactions
- Relaxation
- MR Pulse sequences
- ➢ Magnetic Resonance Imaging (MRI)

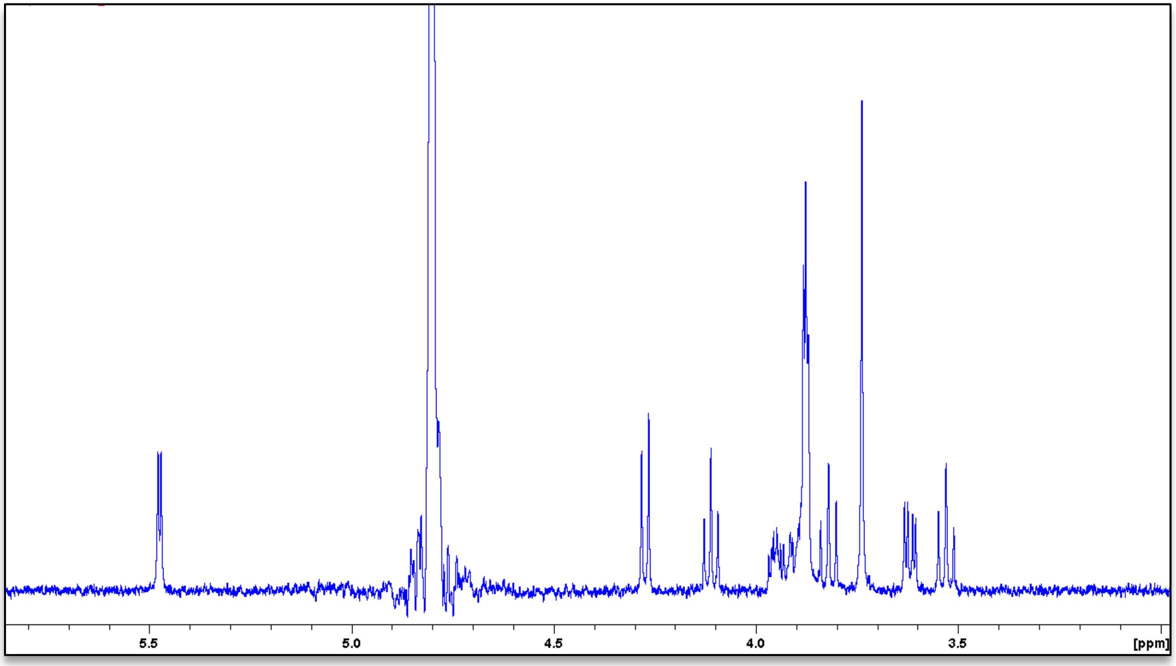


Learning Objectives

- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

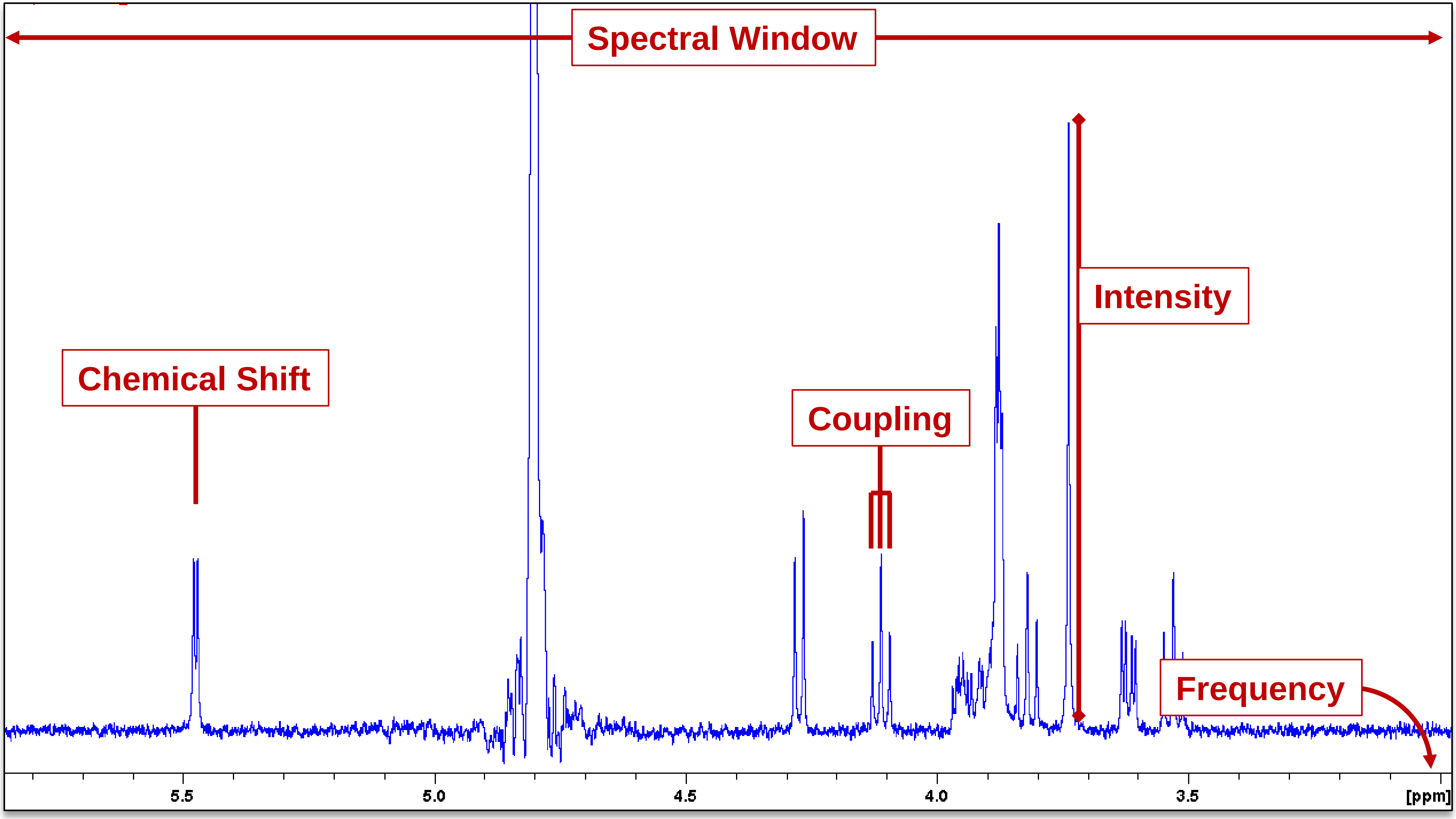
An NMR experiment





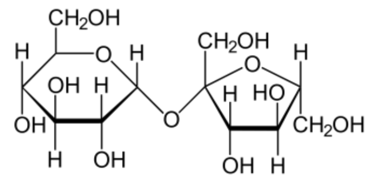
https://www.acs.org/content/acs/en/education/resources/highschool/chemmatters/past-issues/archive-2014-2015/candymaking.html

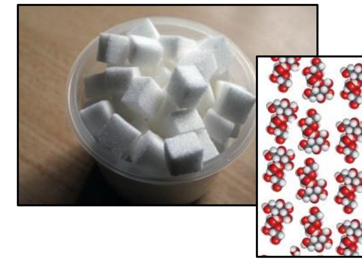
An NMR experiment

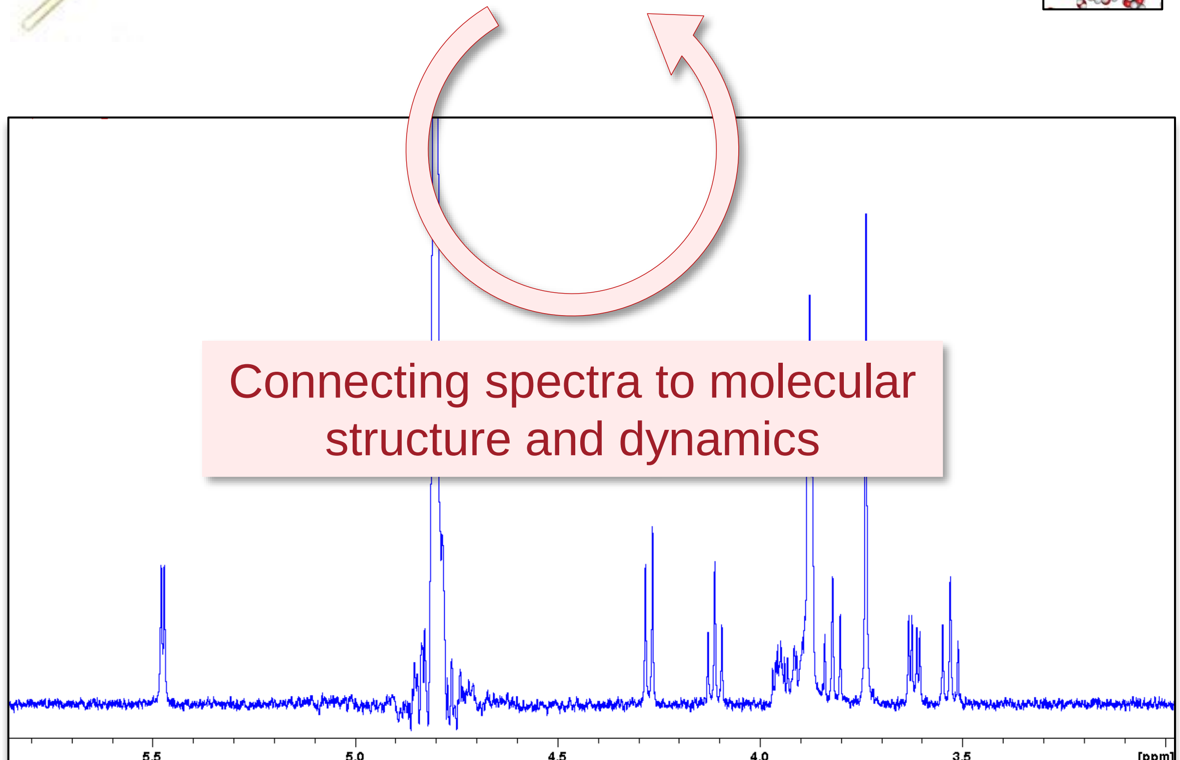


https://www.acs.org/content/acs/en/education/resources/highschool/chemmatters/past-issues/archive-2014-2015/candymaking.html

An NMR experiment





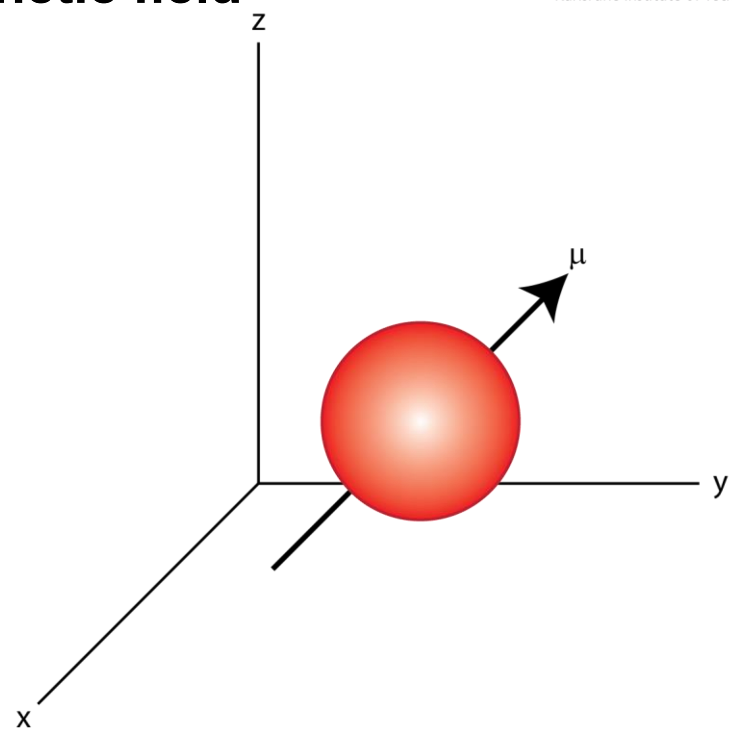


Connecting spectra to molecular structure and dynamics

https://www.acs.org/content/acs/en/education/resources/highschool/chemmatters/past-issues/archive-2014-2015/candymaking.html

Magnetic moments in an external magnetic field

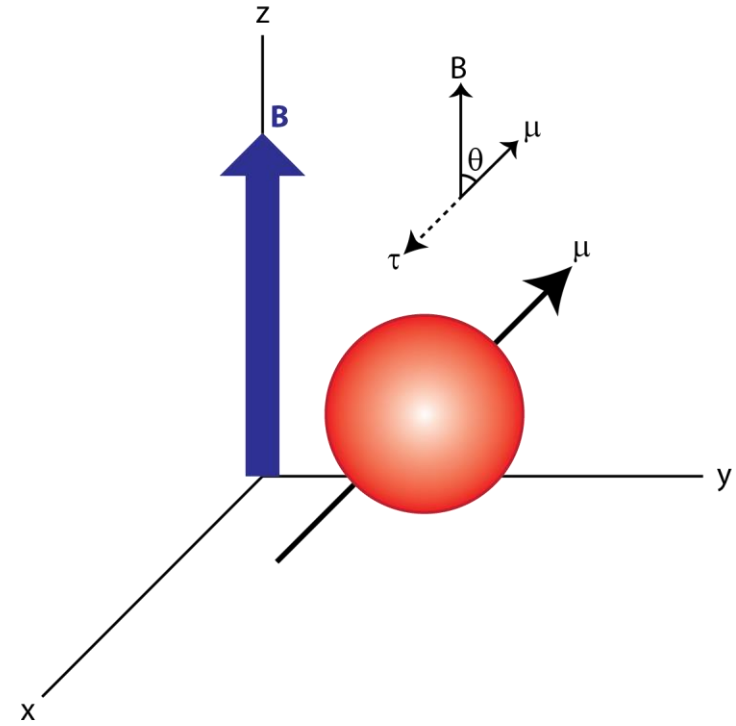
$$\vec{\mu} = \gamma\vec{J}$$



Magnetic moments in an external magnetic field

$$\vec{\mu} = \gamma \vec{J}$$

$$\tau = \frac{dJ}{dt} = \mu \times B$$



Magnetic moments in an external magnetic field

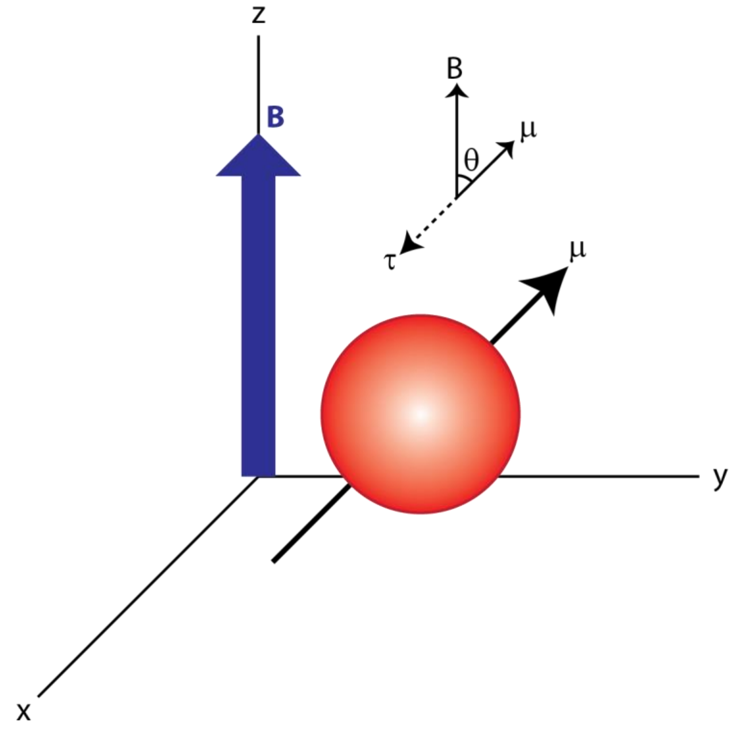
$$\vec{\mu} = \gamma \vec{J}$$

$$\tau = \frac{dJ}{dt} = \mu \times B$$

$$\frac{d\vec{\mu}}{dt} = \frac{\gamma d\vec{J}}{dt}$$

$$\frac{d\vec{\mu}}{\gamma dt} = \frac{d\vec{J}}{dt}$$

$$\frac{d\mu}{dt} = \gamma(\mu \times B)$$



Magnetic moments in an external magnetic field

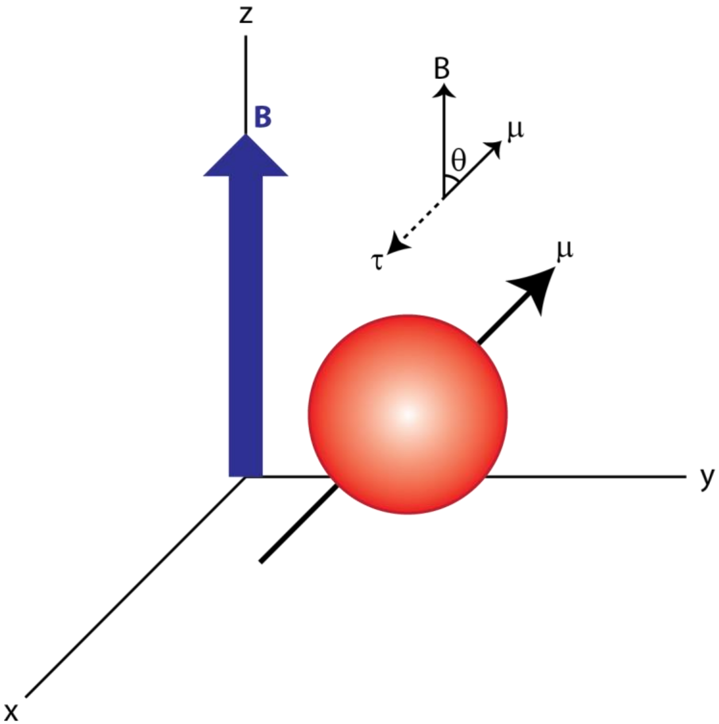
$$\vec{\mu} = \gamma\vec{J}$$

$$\tau = \frac{dJ}{dt} = \mu \times B$$

$$\frac{d\vec{\mu}}{dt} = \frac{\gamma d\vec{J}}{dt}$$

$$\frac{d\vec{\mu}}{\gamma dt} = \frac{d\vec{J}}{dt}$$

$$\frac{d\mu}{dt} = \gamma(\mu \times B)$$



$$\frac{d\mu}{dt} = \gamma \begin{vmatrix} i & j & k \\ \mu_x & \mu_y & \mu_z \\ B_x & B_y & B_z \end{vmatrix}$$

$$\frac{\delta\mu_x}{\delta t} = \gamma(\mu_y B_z - \mu_z B_y)$$

$$\frac{\delta\mu_y}{\delta t} = -\gamma(\mu_x B_z - \mu_z B_x)$$

$$\frac{\delta\mu_z}{\delta t} = \gamma(\mu_x B_y - \mu_y B_x)$$

Magnetic moments in an external magnetic field

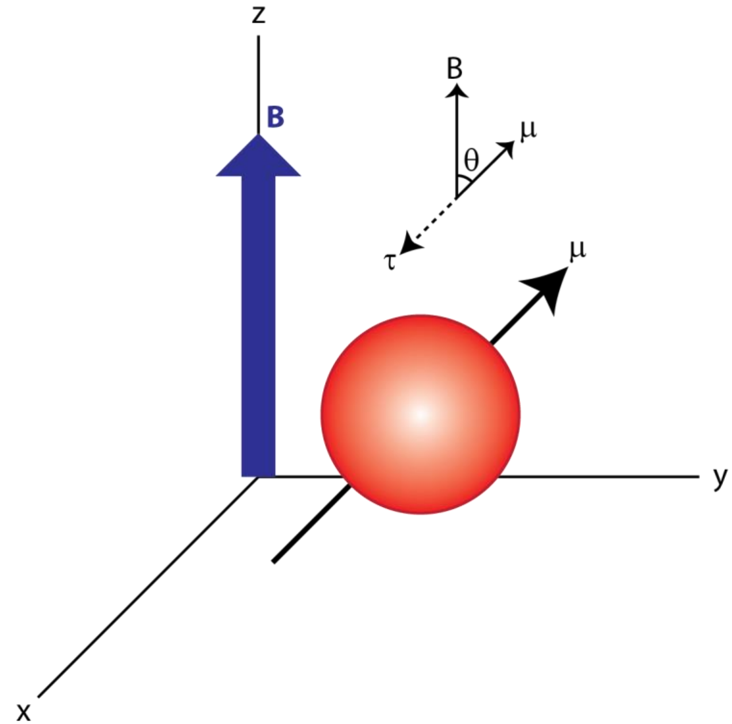
$$\vec{\mu} = \gamma \vec{J}$$

$$\tau = \frac{dJ}{dt} = \mu \times B$$

$$\frac{d\vec{\mu}}{dt} = \frac{\gamma d\vec{J}}{dt}$$

$$\frac{d\vec{\mu}}{\gamma dt} = \frac{d\vec{J}}{dt}$$

$$\frac{d\mu}{dt} = \gamma(\mu \times B)$$



$$\frac{d\mu}{dt} = \gamma \begin{vmatrix} i & j & k \\ \mu_x & \mu_y & \mu_z \\ B_x & B_y & B_z \end{vmatrix}$$

$$\frac{\delta\mu_x}{\delta t} = \gamma(\mu_y B_z - \mu_z B_y) \qquad \frac{\delta\mu_x}{\delta t} = \gamma\mu_y B_z$$

$$\frac{\delta\mu_y}{\delta t} = -\gamma(\mu_x B_z - \mu_z B_x) \qquad \frac{\delta\mu_y}{\delta t} = -\gamma\mu_x B_z$$

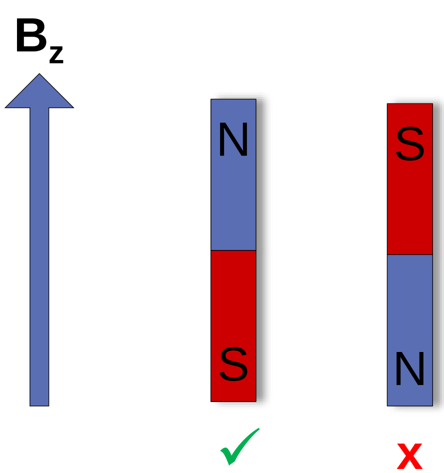
$$\frac{\delta\mu_z}{\delta t} = \gamma(\mu_x B_y - \mu_y B_x) \qquad \frac{\delta\mu_z}{\delta t} = 0$$

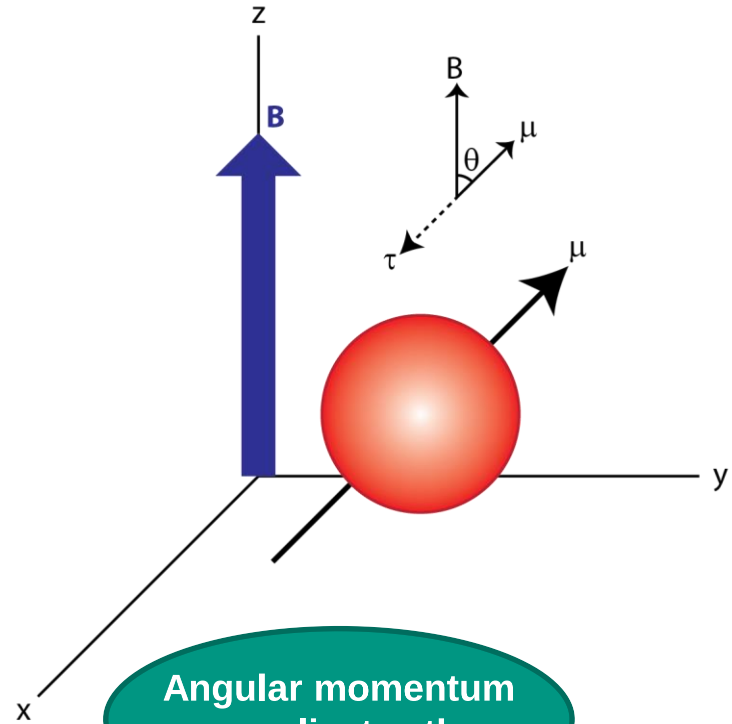
Energy associated with magnetic moments in an external magnetic field

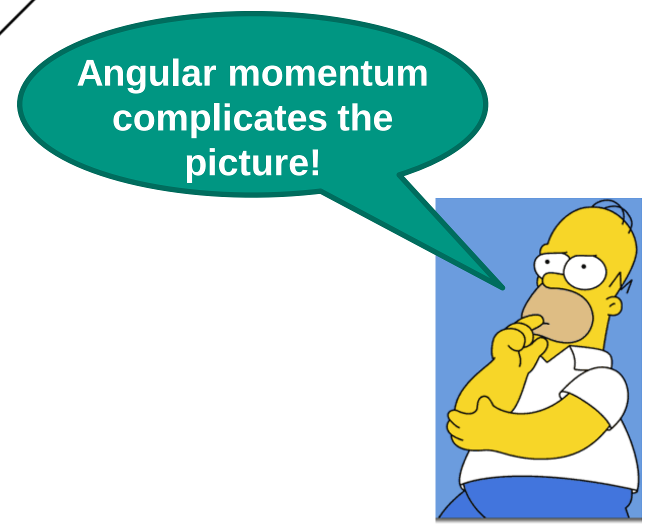
$$\frac{d\mu}{dt} = \gamma(\mu \times B)$$

$$E = -\mu \cdot B = -\mu_z \cdot B_z$$

$$E = -\mu \cdot B = -|\mu_z||B_z|\cos\theta$$





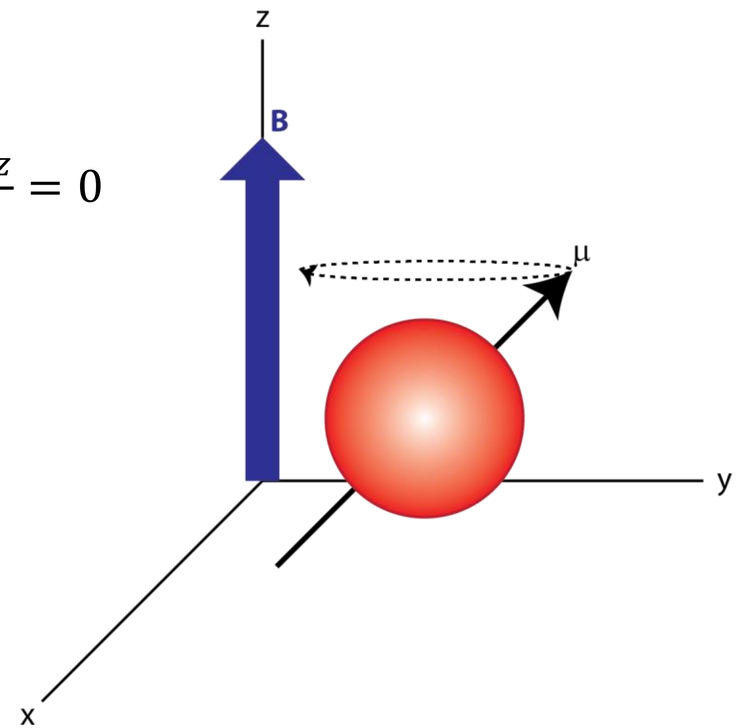


Solution to precession

$$\frac{\delta\mu_x}{\delta t} = \gamma\mu_y B_z \qquad \frac{\delta\mu_y}{\delta t} = -\gamma\mu_x B_z \qquad \frac{\delta\mu_z}{\delta t} = 0$$

$$\boldsymbol{\mu_x(t) = \mu_x(0)cos(\gamma B_z t) - \mu_y(0)sin(\gamma B_z t)}$$

$$\boldsymbol{\mu_y(t) = \mu_y(0)cos(\gamma B_z t) + \mu_x(0)sin(\gamma B_z t)}$$



Nucleus	**γ (MHz / T)**	**ω_o (MHz)**	
		11.74 T	28.2 T
^{1}H	42.576	500	1200
^{13}C	10.705	126	302
^{15}N	-4.316	-51	-122
^{19}F	40.052	470	1130

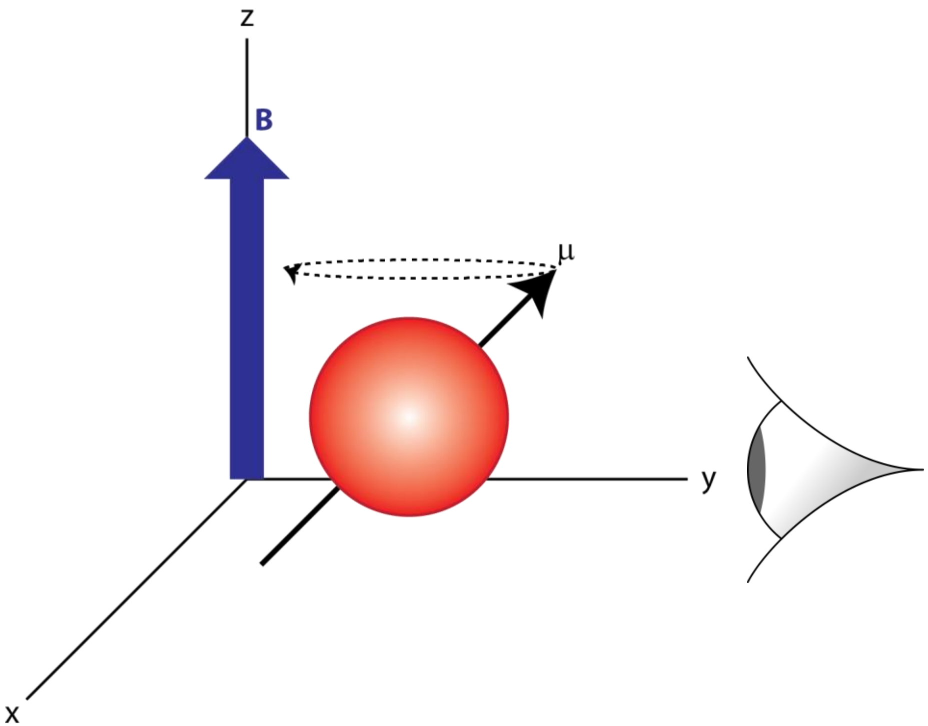
Important notes:

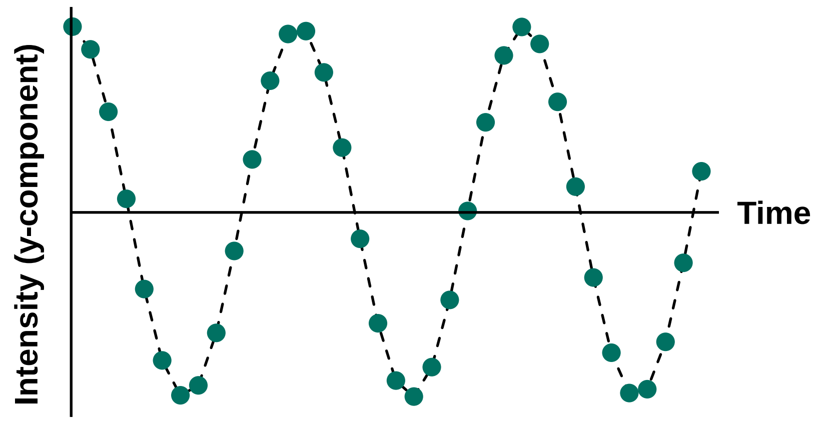
1. γ**B_z** is a frequency, defined as ω_o.

   Larmor Frequency: $\omega_o = -\gamma B_z$

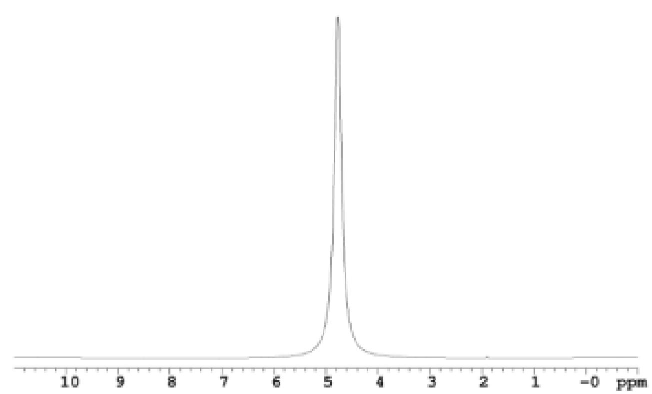
2. NMR is sensitive to radio frequencies (RF)

Precession generates the MR signal





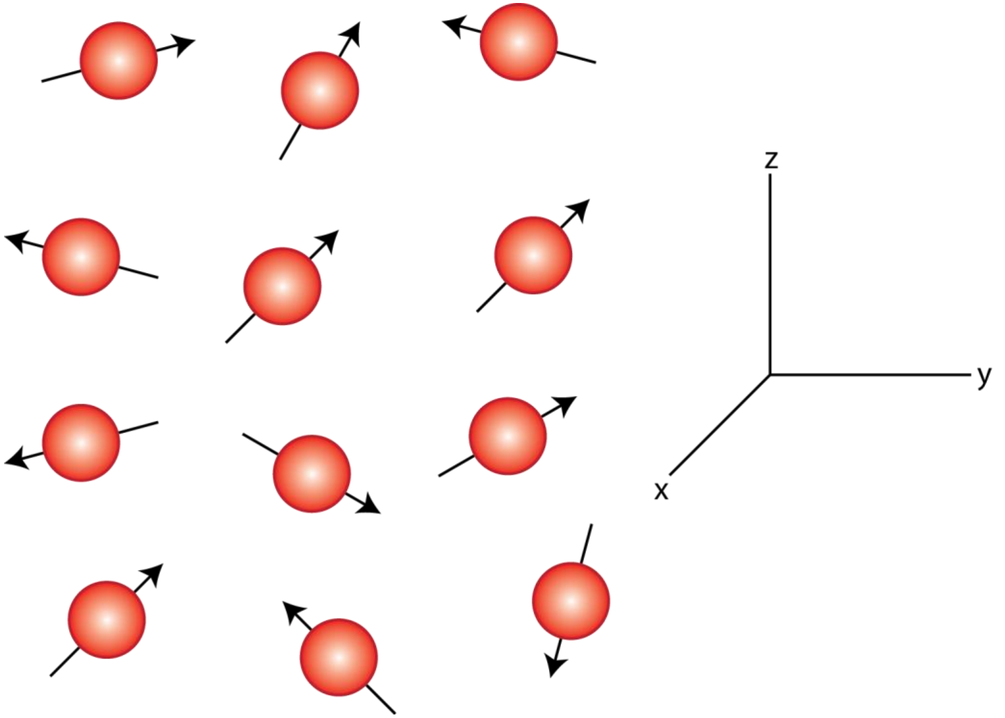
Fourier Transform

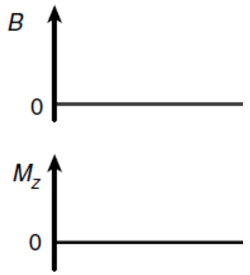


$$\mu_y(t) = \mu_y(0)cos(\gamma B_z t) + \mu_x(0)sin(\gamma B_z t)$$

Bulk magnetization

- A collection of nuclear spins with randomly oriented magnetic moments



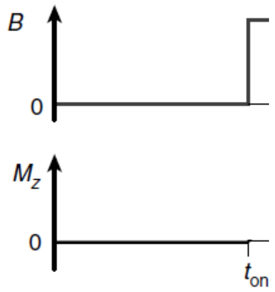


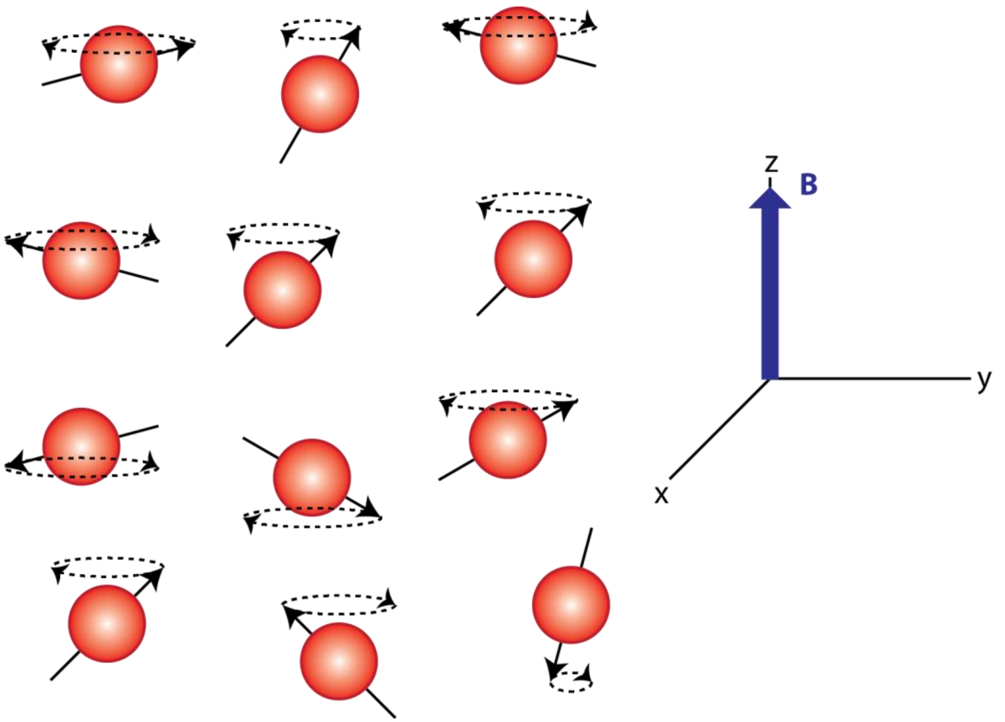
Levitt, M., *Spin Dynamics 2nd Ed.*, John Wiley & Sons Ltd, 2008

Bulk magnetization

- A collection of nuclear spins with randomly oriented magnetic moments

- In presence of magnetic field, precession at Larmor frequency begins



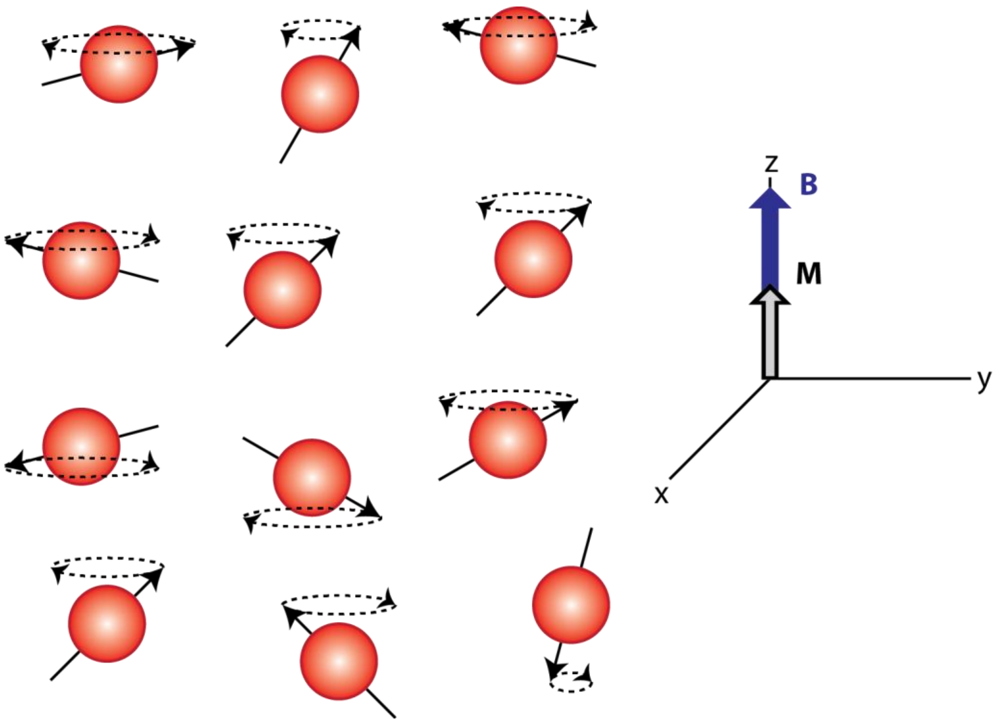


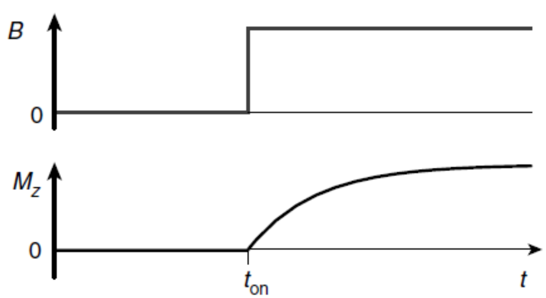
Levitt, M., *Spin Dynamics 2nd Ed.*, John Wiley & Sons Ltd, 2008

Bulk magnetization

- A collection of nuclear spins with randomly oriented magnetic moments
- In presence of magnetic field, precession at Larmor frequency begins
- Bulk magnetization **M** will build up with time constant $\mathbf{T_1}$

$$\mathbf{E = -\mu_z B_z}$$





$$\mathbf{M_x(t) = M_x(0)\cos(\gamma B_z t) - M_y(0)\sin(\gamma B_z t)}$$

$$\mathbf{M_y(t) = M_y(0)\cos(\gamma B_z t) + M_x(0)\sin(\gamma B_z t)}$$

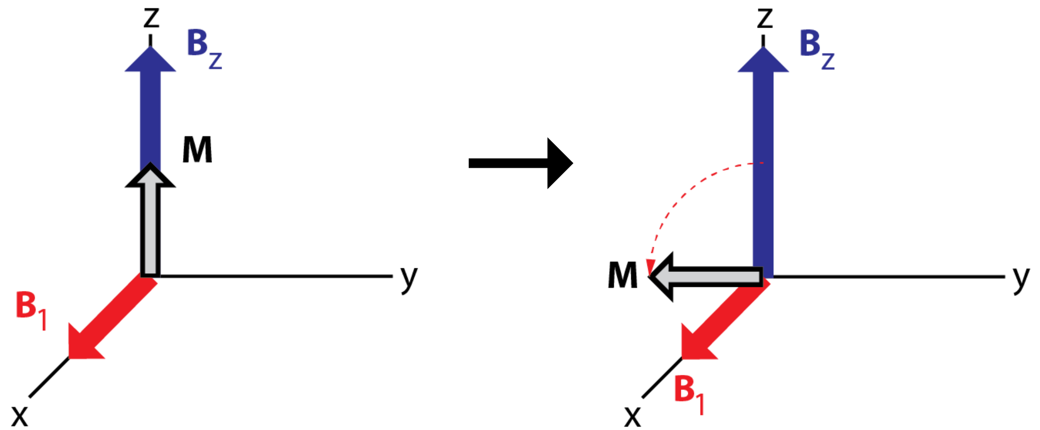
Levitt, M., *Spin Dynamics 2nd Ed.*, John Wiley & Sons Ltd, 2008

Application of RF energy

$$\mathbf{B_1(t) = B_1(0)\cos(\omega_1 t)}$$

$$B_1{}^{+} = \frac{1}{2}B_1[x * \cos(\omega_1 t) + y * \sin(\omega_1 t)]$$

$$B_1{}^{-} = \frac{1}{2}B_1[x * \cos(\omega_1 t) - y * \sin(\omega_1 t)]$$



$$\mathbf{\frac{dM}{dt} = \gamma(M \times B)}$$

$$B = B_z + B_1$$

$$\mathbf{\frac{dM}{dt} = \gamma \begin{vmatrix} i & j & k \\ M_x & M_y & M_z \\ B_1\cos(\omega_1 t) & -B_1\sin(\omega_1 t) & B_z \end{vmatrix}}$$

$$\frac{\delta M_x}{\delta t} = \gamma(M_y B_z + M_z B_1 \sin(\omega_1 t))$$

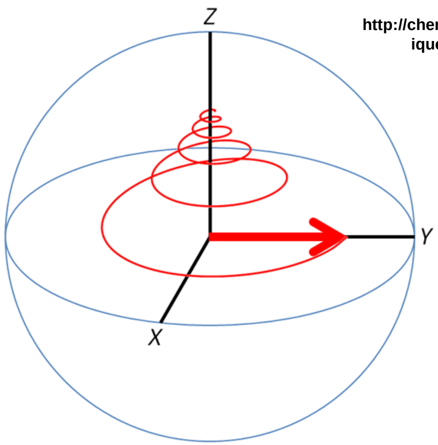
$$\frac{\delta M_y}{\delta t} = \gamma(M_x B_z - M_z B_1 \cos(\omega_1 t))$$

$$\frac{\delta M_z}{\delta t} = \gamma(-M_x B_1 \sin(\omega_1 t) - M_y B_1 \cos(\omega_1 t))$$

Bloch Equations

Felix Bloch
Nobel Prize in Physics
(shared), 1952

"for their development of new methods for nuclear magnetic precision measurements and discoveries in connection therewith"



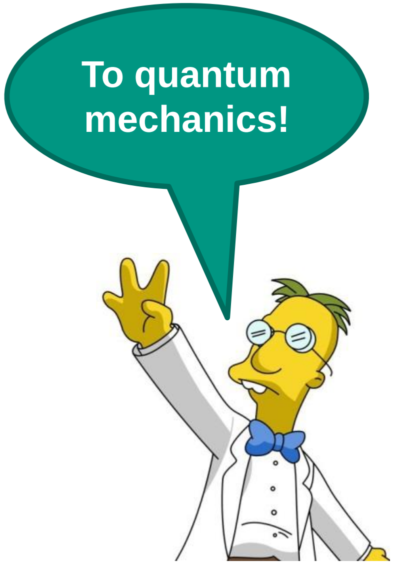
http://chem.ch.huji.ac.il/nmr/techniques/1d/pulseq_files/fid.gif

- Bulk magnetization precesses
  - about B_z
  - about B_1 if $\omega_1 \cong \omega_o$ (resonance!)
- Equilibrium (re)established according to:
  - Longitudinal relaxation time, T_1
  - Transverse relaxation time, T_2
- Bloch equations successfully describe simple cases, but start to break down in complex situations

$$\frac{\delta M_x}{\delta t} = \gamma\left(M_y B_z + M_z B_1 \sin(\omega_1 t)\right) - \frac{M_x}{T_2}$$

$$\frac{\delta M_y}{\delta t} = \gamma(M_x B_z - M_z B_1 \cos(\omega_1 t)) - \frac{M_y}{T_2}$$

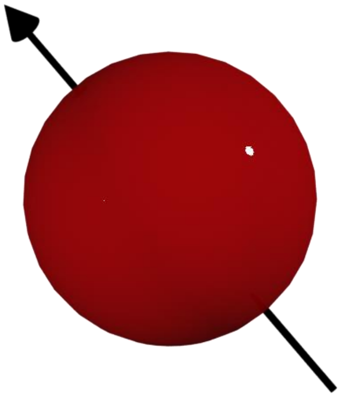
$$\frac{\delta M_z}{\delta t} = \gamma\left(-M_x B_1 \sin(\omega_1 t) - M_y B_1 \cos(\omega_1 t)\right) - \frac{M_z - M_o}{T_1}$$



Today's Outline

- Classical Description
- **Quantum Description**
- Nuclear Interactions
- Relaxation
- MR Pulse sequences

➢ Magnetic Resonance Imaging (MRI)



Learning Objectives

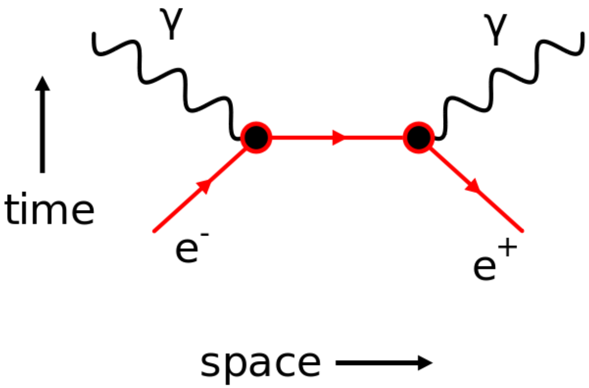
- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

Quantum mechanics - definitions

First thoughts of quantum mechanics …

$$\frac{-\hbar^2}{2m}\frac{\partial^2\Psi}{\partial x^2} + U\Psi = E\Psi$$

http://teecraze.com/wp-content/uploads/schrodingerscat2.jpg



Erwin Schrödinger
Nobel Prize in Physics
(shared), 1933

"for the discovery of new productive forms of atomic theory"

Richard Feynman
Nobel Prize in Physics
(shared), 1965

"for their fundamental work in quantum electrodynamics, with deep-ploughing consequences for the physics of elementary particles"

Quantum mechanics - definitions

What we already know

$\vec{\mu} = \gamma \vec{J}$	Magnetic moment
$J = \hbar\sqrt{I(I+1)}$	Angular momentum
$E = -\mu_z B_z$	Energy

Extending our definintions

$J_z = \hbar m_I$	z-component of angular momentum
$\mu_z = \gamma \hbar m_I$	z-component of magnetic moment
$E = -\gamma \hbar m_I B_z$	Energy
$m_I = I, I-1, \dots, -I$	Allowed values of the spin quantum number

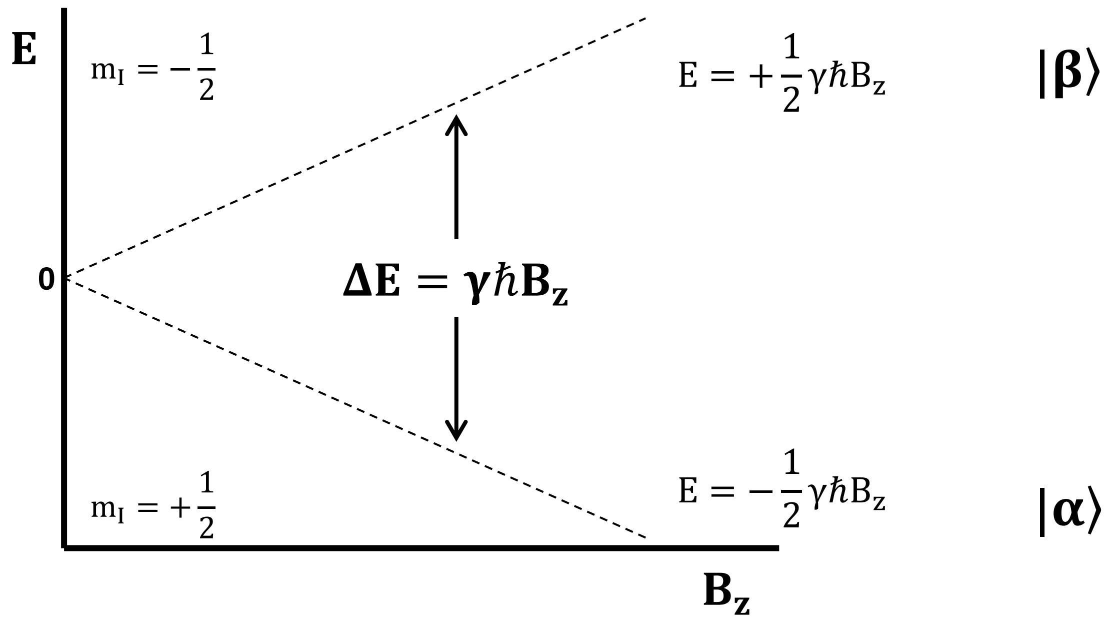
$$\mathbf{I = \frac{1}{2}}, \boldsymbol{m_I} = \mathbf{\frac{1}{2}, -\frac{1}{2}}$$

^1H, ^{13}C, ^{19}F, ^{15}N, ^{31}P, …

$$\mathbf{E = \pm\frac{1}{2}\gamma\hbar B_z}$$

Quantized Energy!

Energy level diagram, I = ½



Bra-ket notation:

$$I = \frac{1}{2}, m_I = \frac{1}{2}, -\frac{1}{2} \rightarrow |I, m_I\rangle \rightarrow \left|\frac{1}{2}, \frac{1}{2}\right\rangle = |\alpha\rangle \quad \left|\frac{1}{2}, -\frac{1}{2}\right\rangle = |\beta\rangle$$

What are the populations of the states?

$$n_i = \frac{\exp(-\frac{E_i}{k_B T})}{\sum \exp(-\frac{E_j}{k_B T})}$$

Energy of state i

Sum over all states j = 1 to 2I+1

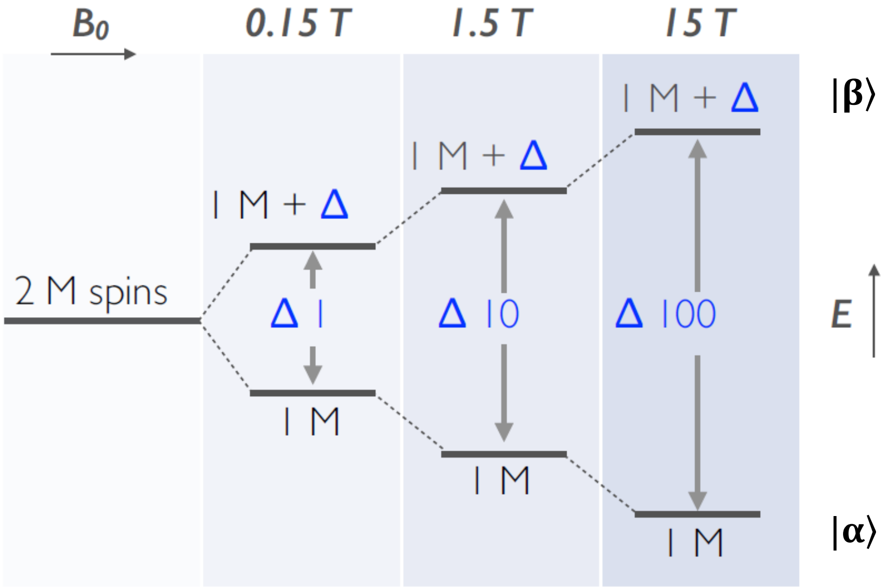
$$\frac{n_\beta}{n_\alpha} = \exp\left(-\frac{\Delta E}{k_B T}\right) \cong 1 - \frac{\Delta E}{k_B T}$$

Ludwig Boltzmann

Thermal energy at 293 K: $k_b T \cong 4.1 \times 10^{-21}$ J

Spectroscopic energy at 11.74 T: $\Delta E \cong 3.3 \times 10^{-25}$ J

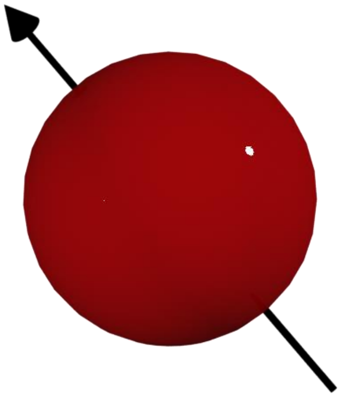
Boltzmann distribution at 11.74 T: $n_\beta = 0.9999195\, n_\alpha$



Increasing field strength increases population *difference* → increased signal!

Introduction to NMR theory

- Classical Description
- Quantum Description
- **Nuclear Interactions**
- Relaxation
- MR Pulse sequences
- ➢ Magnetic Resonance Imaging (MRI)

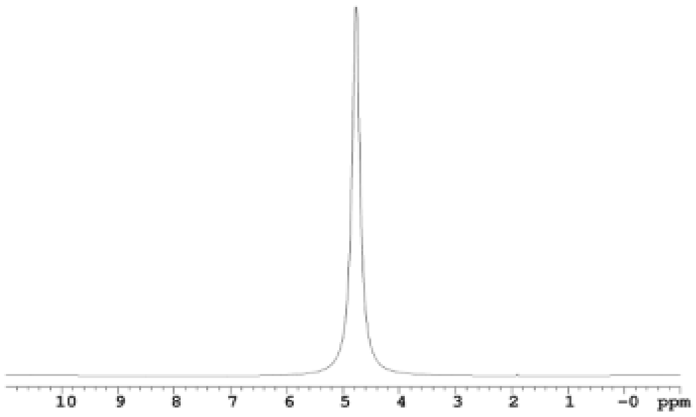


Learning Objectives

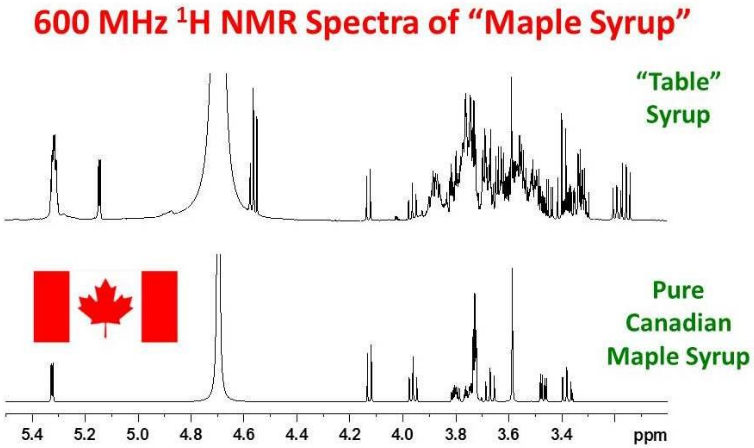
- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

Communication permits relative position determination

- An ensemble of non-interacting spins would give a single resonance – not very informative!
- Spin-spin interactions result in the rich detail obtained by NMR spectroscopy



http://nmr.chem.indiana.edu/images/bionmr/water_sup1.png



http://u-of-o-nmr-facility.blogspot.de/

Mechanisms of spin-spin communication

- All mechanisms cause local magnetic field perturbations
  - Small field perturbations translate to small frequency changes

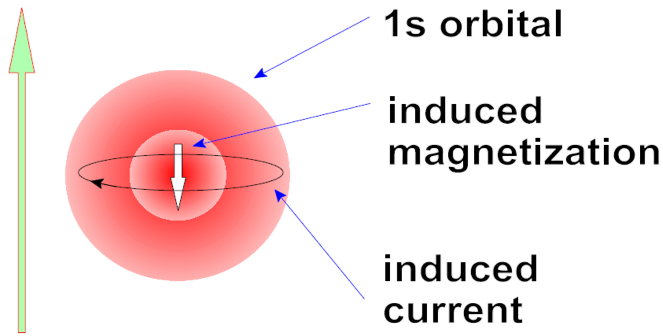
- Hamiltonian based description:

$$\hat{H}_{TOTAL} = \hat{H}_Z + \hat{H}_{RF} + \hat{H}_{CS} + \hat{H}_D^{II} + \hat{H}_D^{IS} + \hat{H}_J + \hat{H}_Q$$

$\hat{H}_Z = -\gamma B_O \cdot I$	external	Zeeman
$\hat{H}_{RF} = -\gamma B_1 \cos(\omega t) I_x$	external	Applied RF
$\hat{H}_{CS} = -\gamma B_O \cdot \hat{\sigma} \cdot I$	internal	Chemical shift
$\hat{H}_D^{II} = \sum_{i \neq j} (\gamma_i \gamma_j \hbar) I_i \cdot D \cdot I_j$	internal	Dipolar coupling (homonuclear)
$\hat{H}_D^{IS} = \sum_{i \neq j} (\gamma_I \gamma_S \hbar) I \cdot D \cdot S$	internal	Dipolar coupling (heteronuclear)
$\hat{H}_J = \sum_{i \neq j} I_i \cdot J \cdot I_j$	internal	*J*-coupling
$\hat{H}_Q = \frac{eQ}{2I(2I-1)\hbar} I \cdot V \cdot I$	internal	Quadrupole coupling

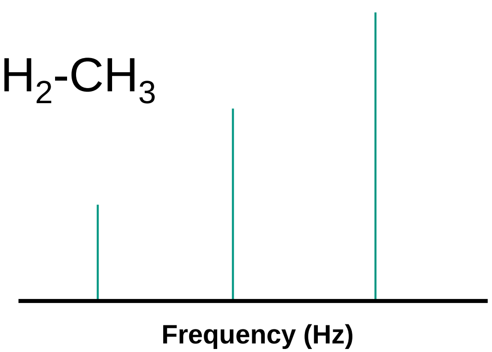
Through bond interactions

- Chemical shift
  - Electron density shields the nuclear spin from the applied magnetic field

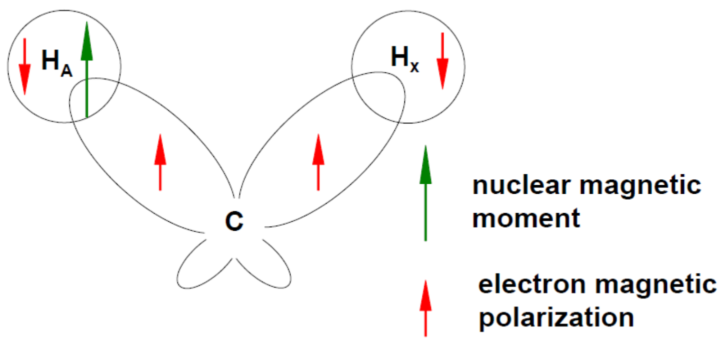


$$\omega = \omega_L + \frac{1}{2}\delta\left[3\cos^2\theta - 1 - \eta\sin^2\theta\cos2\phi\right]$$

$HO\text{-}CH_2\text{-}CH_3$

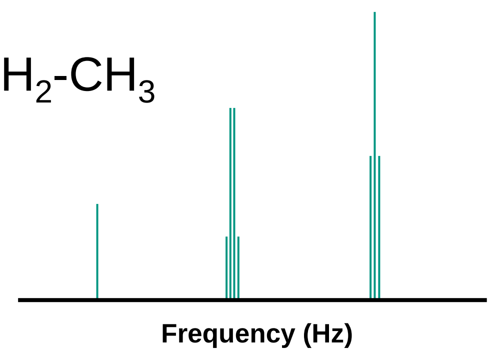


- *J*-coupling
  - Orientation of nuclear spin A is transmitted via electrons of chemical bonds to influence nuclear spin B



$$\hat{H}_J = \sum_{i \neq j} I_i \cdot J \cdot I_j$$

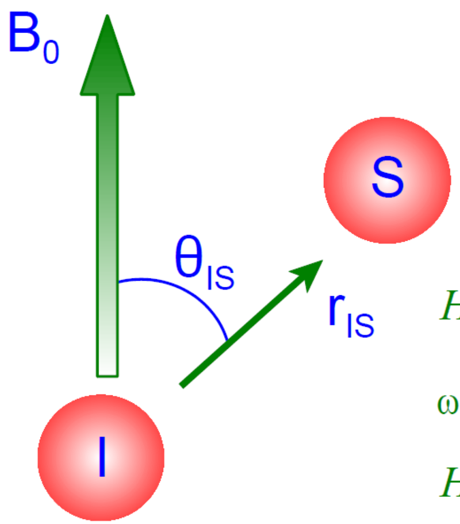
$HO\text{-}CH_2\text{-}CH_3$



Through space interactions

- Dipolar coupling
  - Spin I senses position of spin S through dipole interaction
  - Strongly dependent on distance and orientation wrt Bo

- Quadrupole coupling
  - If I > ½, nuclear charge distribution not spherical (quadrupole moment)
  - Quadrupole moment interacts with electric field gradients at the nucleus



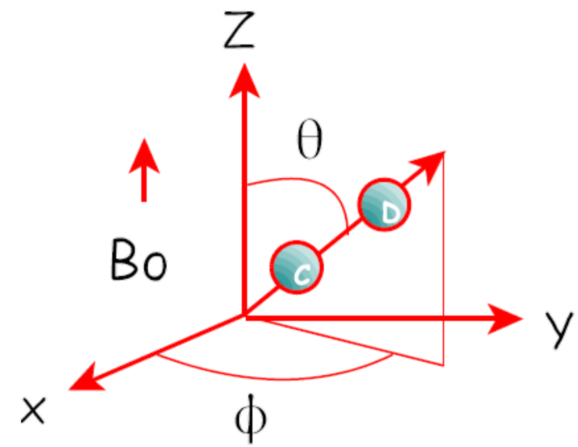
Hetero

$$\omega = \omega_0 \pm \frac{1}{2} R(3\cos^2\theta - 1)$$

Homo

$$\omega = \omega_0 \pm \frac{3}{2} R(3\cos^2\theta - 1)$$

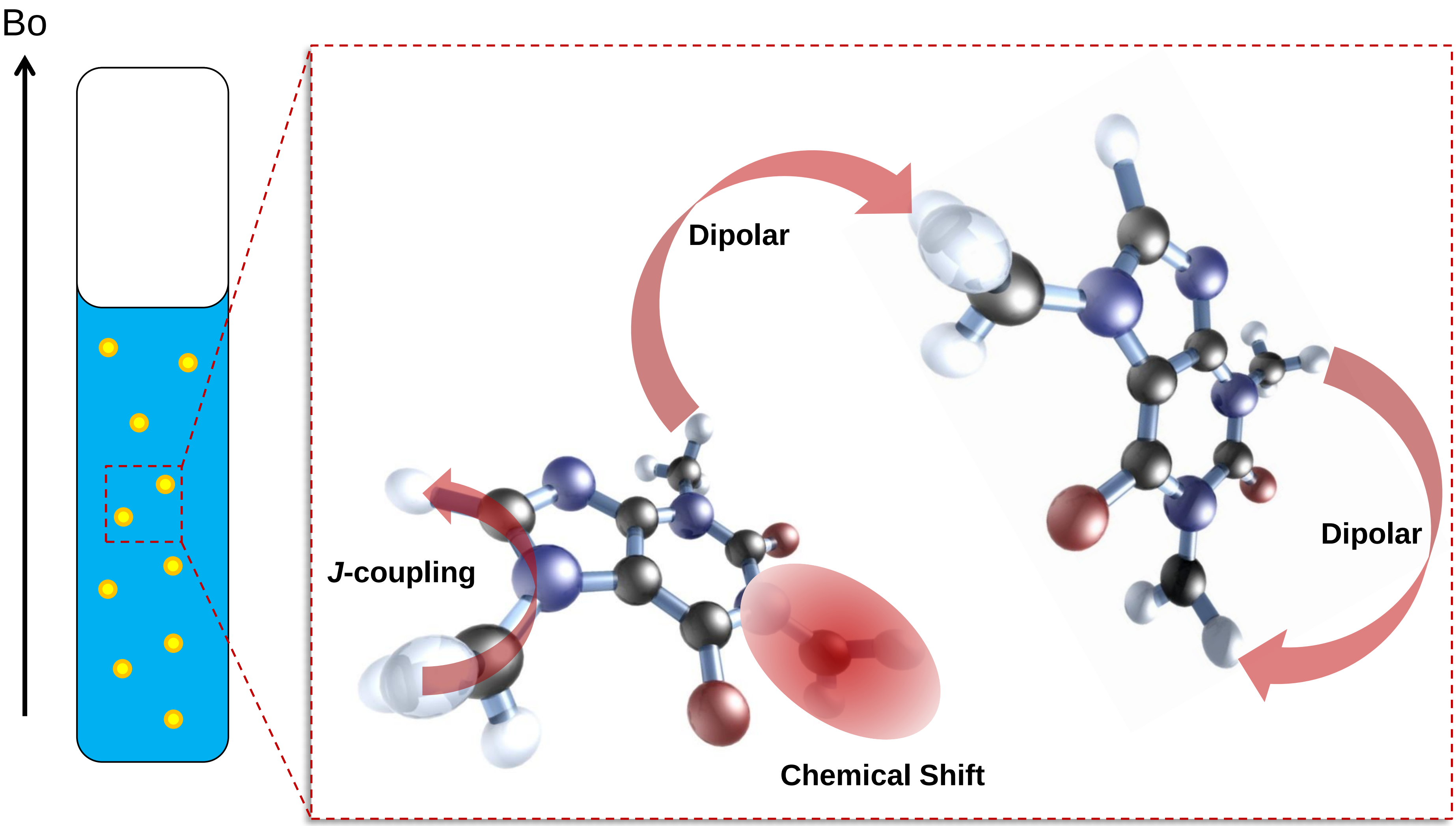
$$R = \gamma_I \gamma_S \left(\frac{\mu_0 \hbar}{4\pi}\right) \langle r_{IS}^{-3} \rangle$$



$$\omega = \omega_0 \pm \frac{1}{2} \omega_Q (3\cos^2\theta - 1 + \eta \sin^2\theta \cos 2\phi)$$

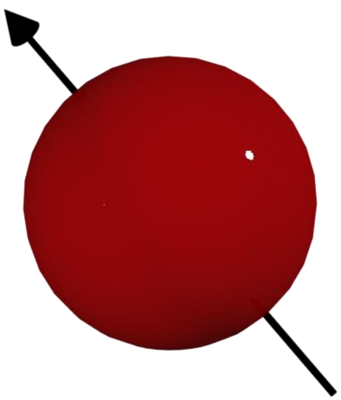
$$\omega_Q = 3e^2 qQ / 4\hbar$$

Interaction summary (I = ½)



Introduction to NMR theory

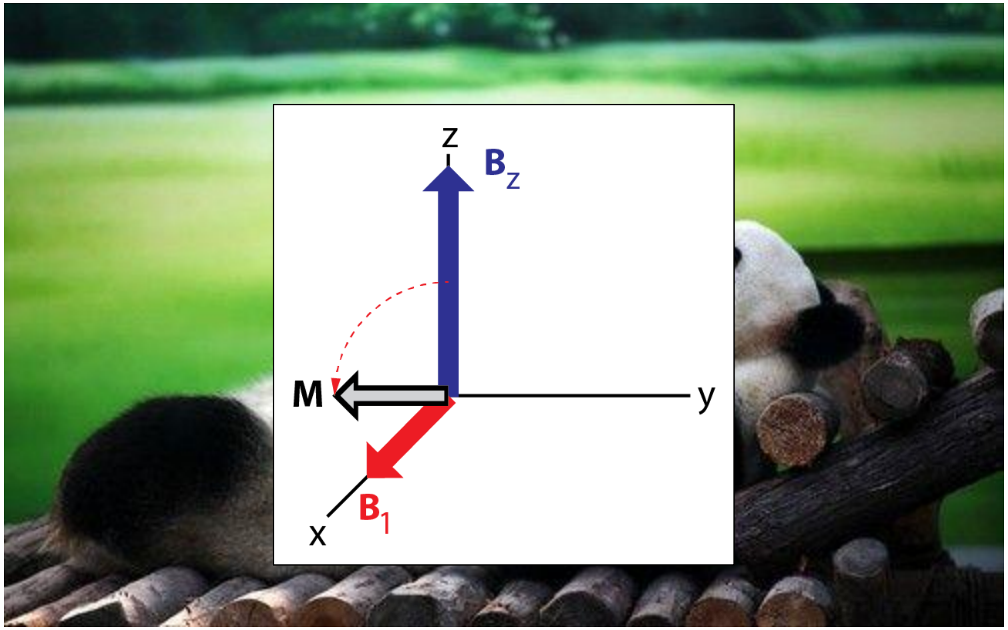
- Classical Description
- Quantum Description
- Nuclear Interactions
- **Relaxation**
- MR Pulse sequences
- ➢ Magnetic Resonance Imaging (MRI)



Learning Objectives

- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

What do we mean by ‘Relaxation’?



http://cdn.attackofthecute.com/October-30-2012-02-41-43-ttttt.jpg

How does **M** return to equilibrium?

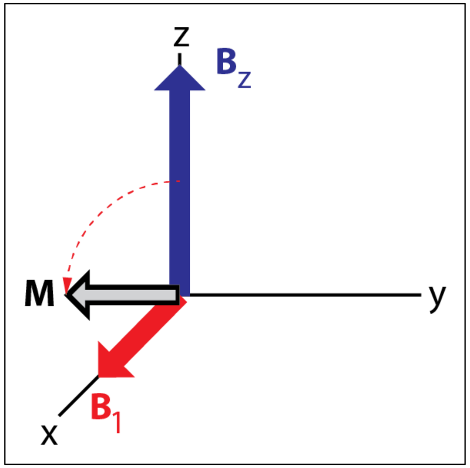
Relaxation is defined by two time constants

Bloch Equations

$$\frac{\delta M_x}{\delta t} = \gamma\left(M_y B_z + M_z B_1 \sin(\omega_1 t)\right) - \frac{M_x}{T_2}$$

$$\frac{\delta M_y}{\delta t} = \gamma(M_x B_z - M_z B_1 \cos(\omega_1 t)) - \frac{M_y}{T_2}$$

$$\frac{\delta M_z}{\delta t} = \gamma\left(-M_x B_1 \sin(\omega_1 t) - M_y B_1 \cos(\omega_1 t)\right) - \frac{M_z - M_o}{T_1}$$

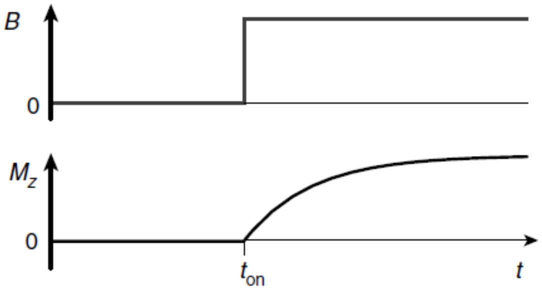


T_1: Longitudinal relaxation time (spin-lattice)

- characteristic time constant for M_z to approach **M**

T_2: Transverse relaxation time (spin-spin)

- characteristic time constant for $M_{x,y}$ to approach **0**



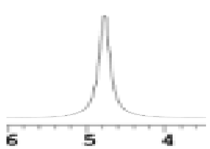
Levitt, M., *Spin Dynamics 2nd Ed.*, John Wiley & Sons Ltd, 2008

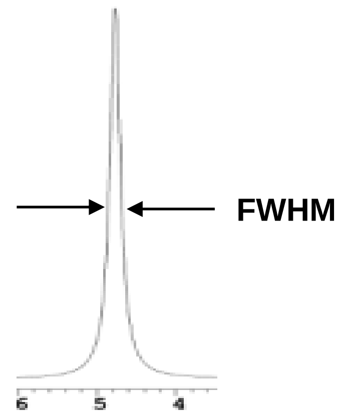
Importance of relaxation time

- Spin-lattice T_1
  - Reflected in signal intensity
  - Determines maximum repetition rate of equilibrium magnetization
- Spin-spin T_2
  - Reflected in signal line width
  - A significant factor determining maximum spectral resolution

Optimal recovery delay
Full signal recovered

Sub-optimal recovery delay
Partial signal recovered



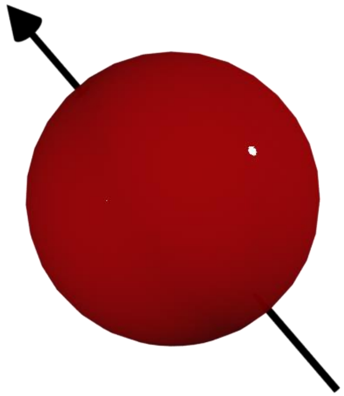


$$\text{Line width (Hz)} \approx \frac{1}{\pi T_2}$$

Introduction to NMR theory

- Classical Description
- Quantum Description
- Nuclear Interactions
- Relaxation
- **MR Pulse sequences**

➢ Magnetic Resonance Imaging (MRI)

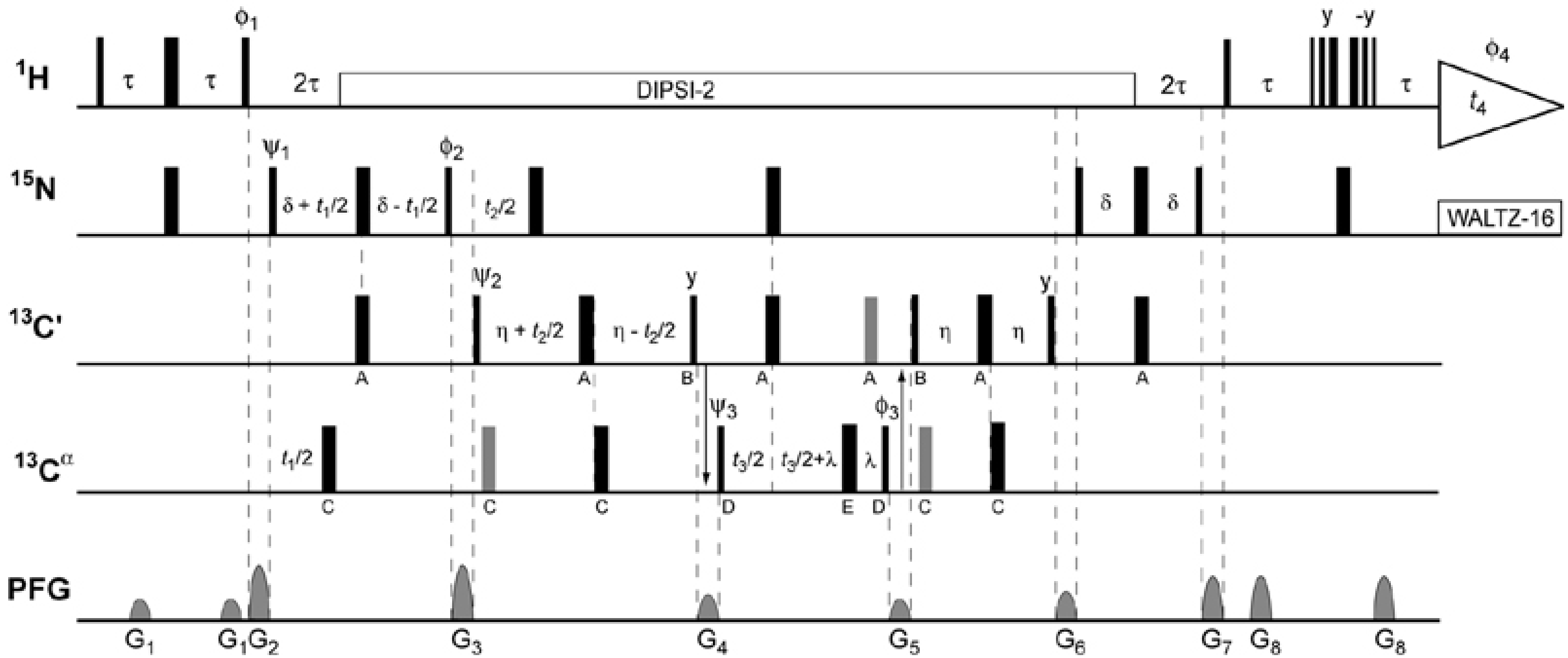


Learning Objectives

- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

Reading NMR pulse sequences

- How does one measure an MR signal?

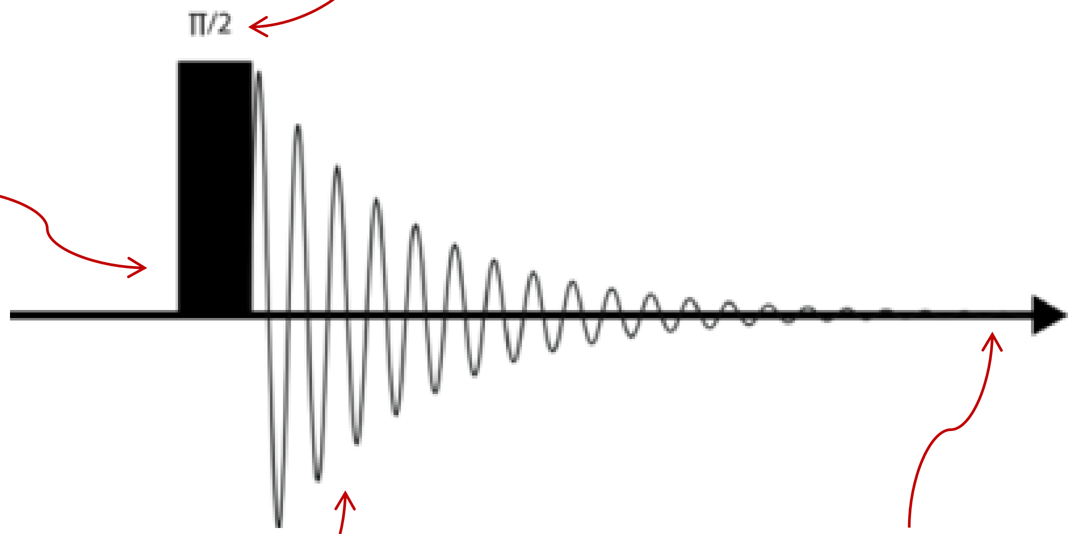


Hiller, S. et al., Automated projection spectroscopy, PNAS 102 (2005) 10876.

Timing diagrams = pulse sequences

Desired flip angle
(sometimes with an associated phase)

Rectangles
Height – RF amplitude
Width – RF pulse time

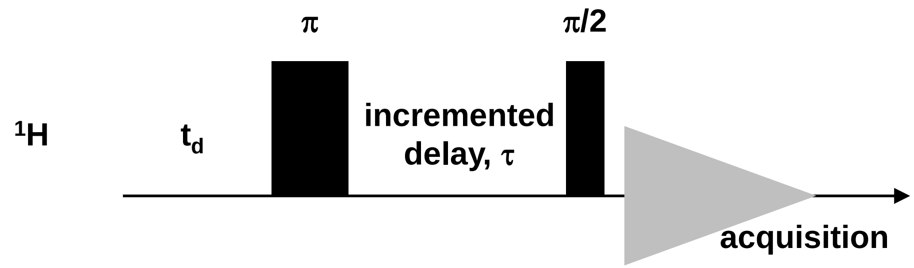


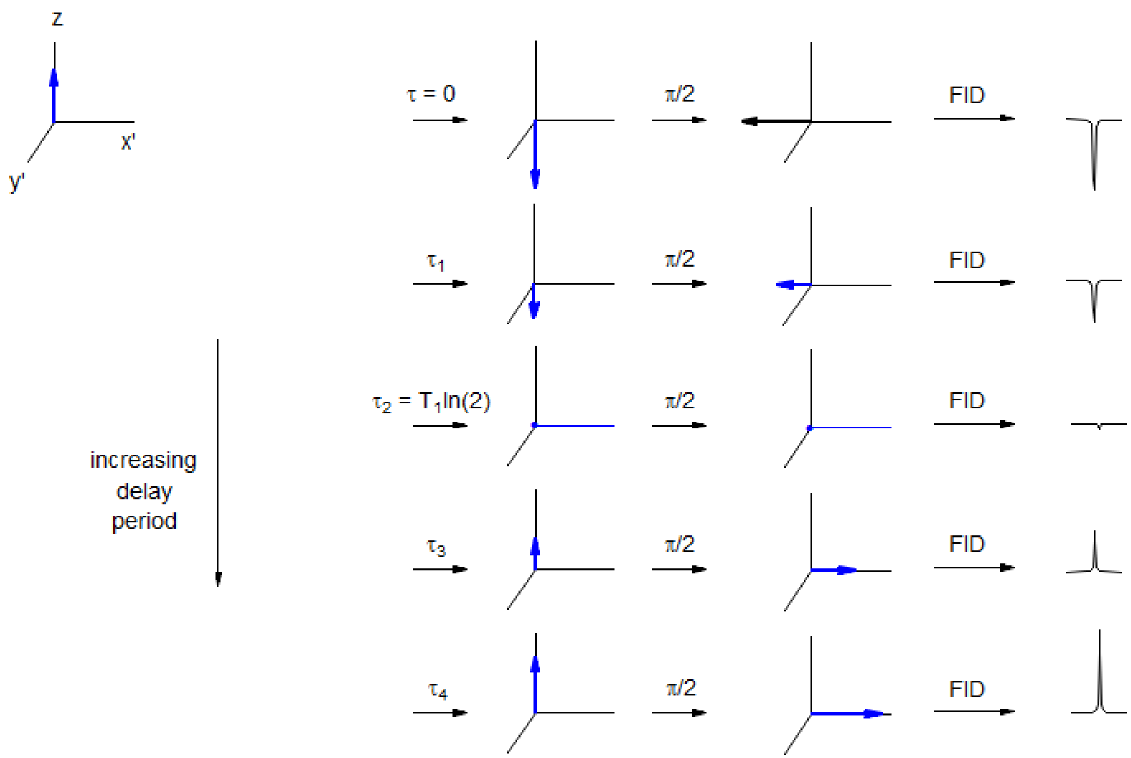
Time axis
(one time axis per channel)

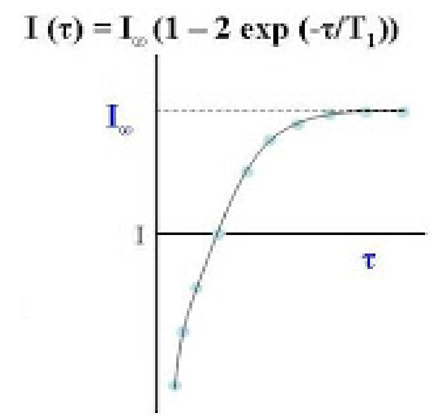
FID
Free Induction Decay

Example – measuring T_1

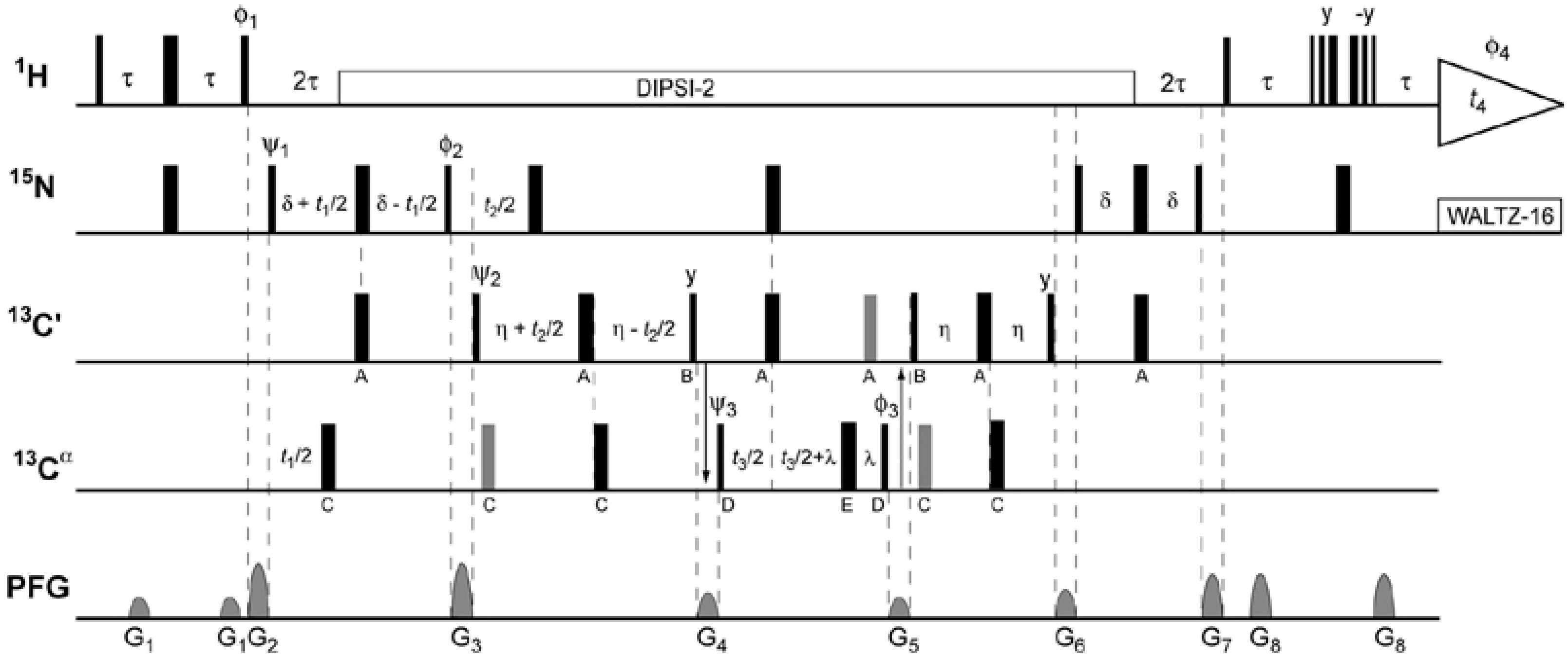
Inversion Recovery







Now we can interpret this sequence …



Hiller, S. et al., Automated projection spectroscopy, PNAS 102 (2005) 10876.

Summary

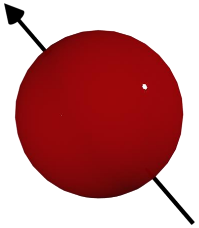
- Magnetic resonance is dependent on nuclear spin
- Classical description is useful for simple experiments
- Quantum description is necessary for complicated spin systems
  - Hamiltonian formalism is common
- Relaxation of magnetization should be considered
- Pulse sequences are how NMR signals are encoded

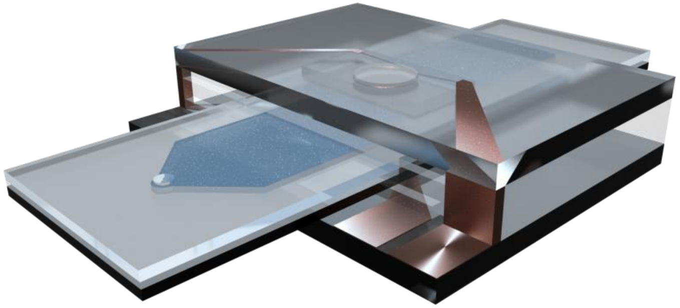
Learning Objectives

- Differentiate between Classical and Quantum description of NMR
- List the interactions that influence the NMR spectrum
- Describe the relaxation mechanisms that drive the sample to equilibrium
- Identify the main components of an NMR pulse sequence

Welcome! Today’s Outline

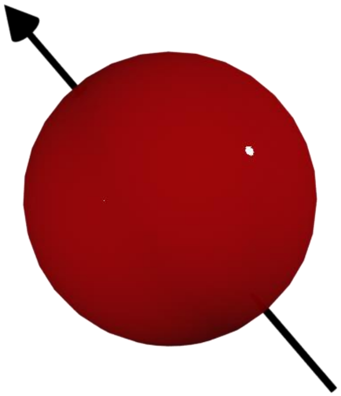
- General introduction to Nuclear Magnetic Resonance
- **General introduction to Magnetic Resonance Imaging**





Magnetic Resonance Imaging

- **General Introduction**
- Origin of MR signal
- Pulse sequences
- Magnetic Resonance Imaging
- MR image contrast



Learning Objectives

- Students will be able to identify the source of the MRI signal
- Students will be able to describe the process of producing an image
- Students will be able to identify the types of contrast available in MRI

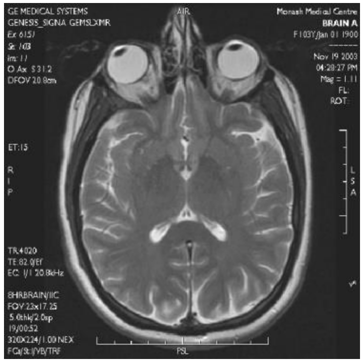
Magnetic resonance imaging - MRI

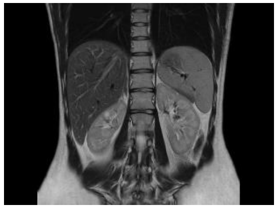
- Relies on nuclear magnetic resonance
  - Large magnet
  - Magnetic field gradients
  - Coils as inductive detectors
  - Radio frequency electronics

- Non-invasive!

- Non-destructive!

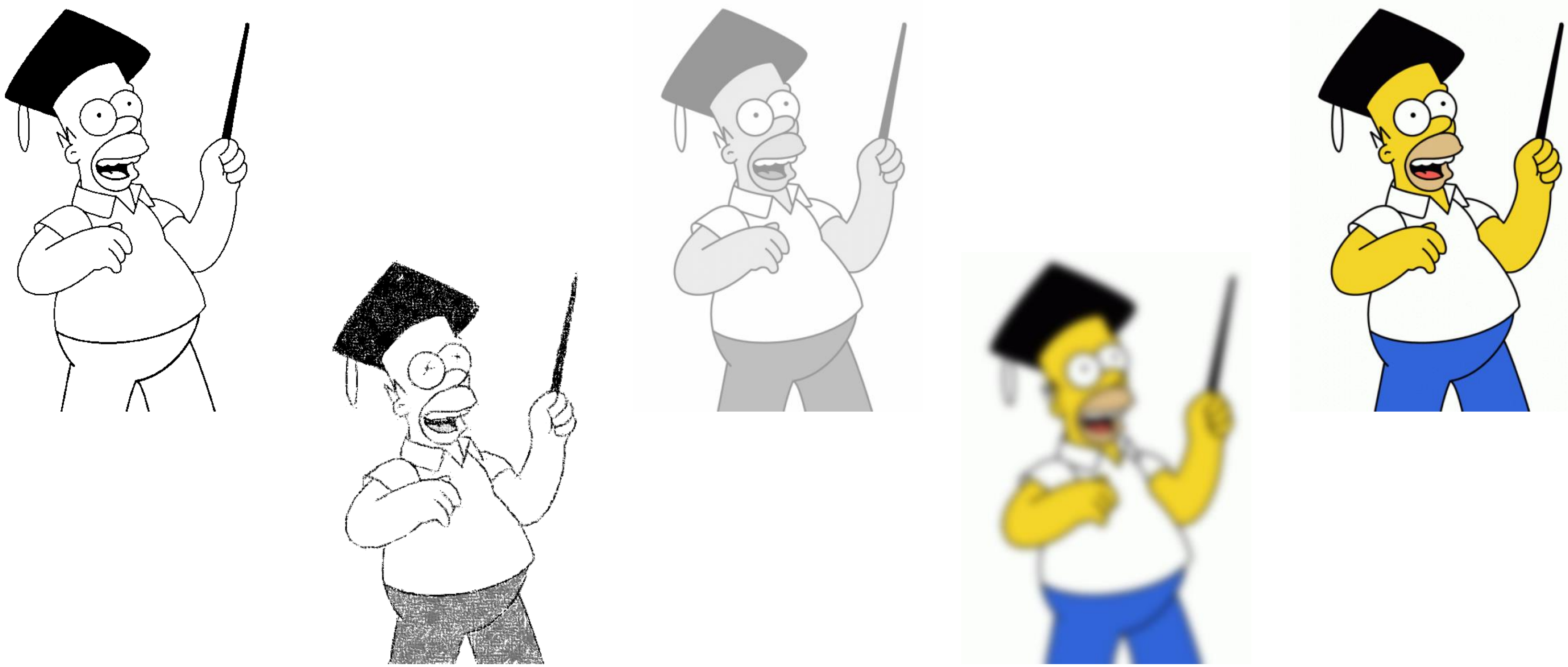
- Can reveal dynamics
  - Functional MRI (fMRI)
  - Diffusion/flow imaging





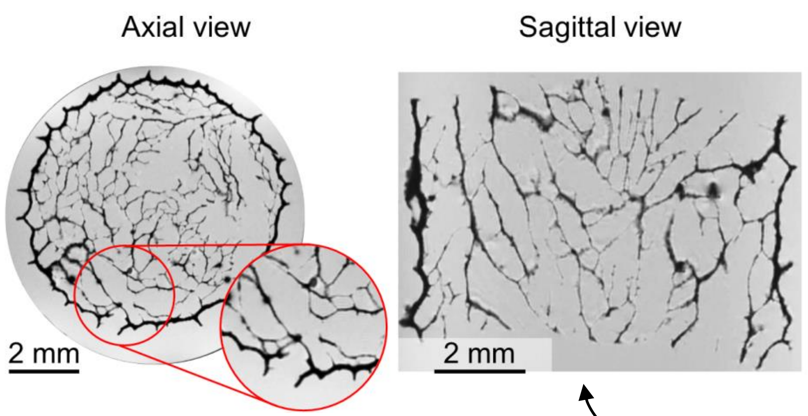
General image quality

- Features of good image quality
  - Color
  - Contrast
  - Resolution

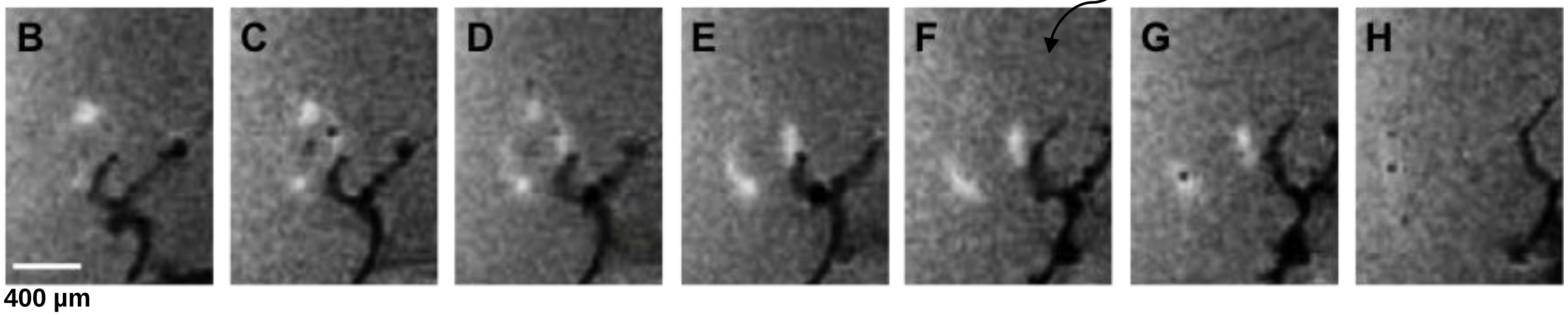


Features of an MRI image

- Resolution
  - Size of each pixel in image
- Contrast
  - What distinguishes bright from dark spots?

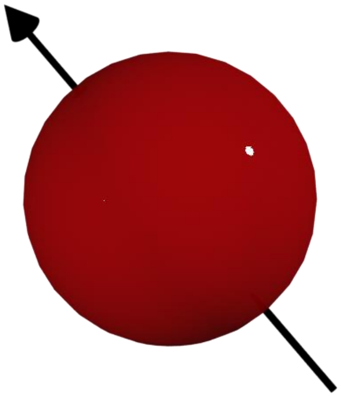


30 µm³ isotropic resolution



Magnetic Resonance Imaging

- General Introduction
- **Origin of MR signal**
- Magnetic Resonance Imaging
- MR image contrast



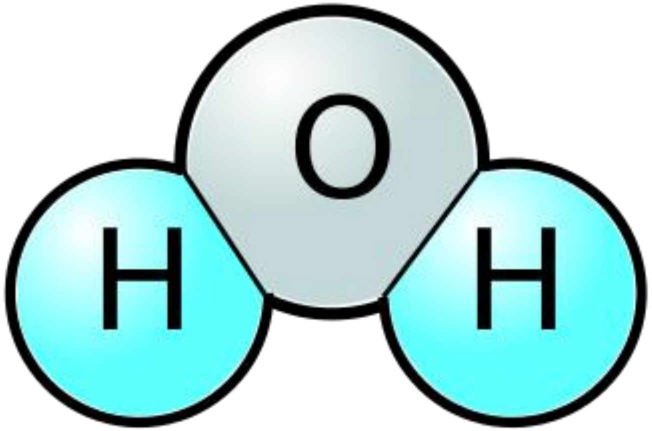
Learning Objectives

- Students will be able to identify the source of the MRI signal
- Students will be able to describe the process of producing an image
- Students will be able to identify the types of contrast available in MRI

Water is the key

- Medical MR images are produced by measuring the hydrogen of water*

- Water chemical composition:
  - Hydrogen (2 atoms)
  - Oxygen

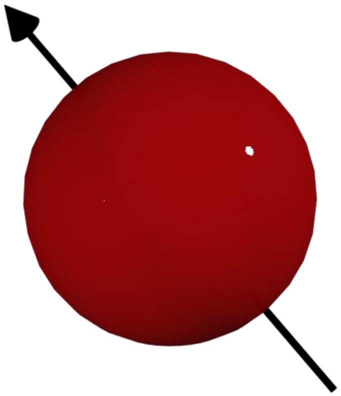


- Hydrogen nucleus
  - 1 proton
  - 3 isotopes: ^{1}H, ^{2}H, ^{3}H
  - Abundancies: 99.98, 0.02, trace
- Oxygen nucleus
  - 8 protons
  - 3 isotopes: ^{16}O, ^{17}O, ^{18}O
  - Abundancies: 99.76, 0.04, 0.20

***of course, other molecules can be imaged as well, but these are specialized examples.**

Magnetic Resonance Imaging

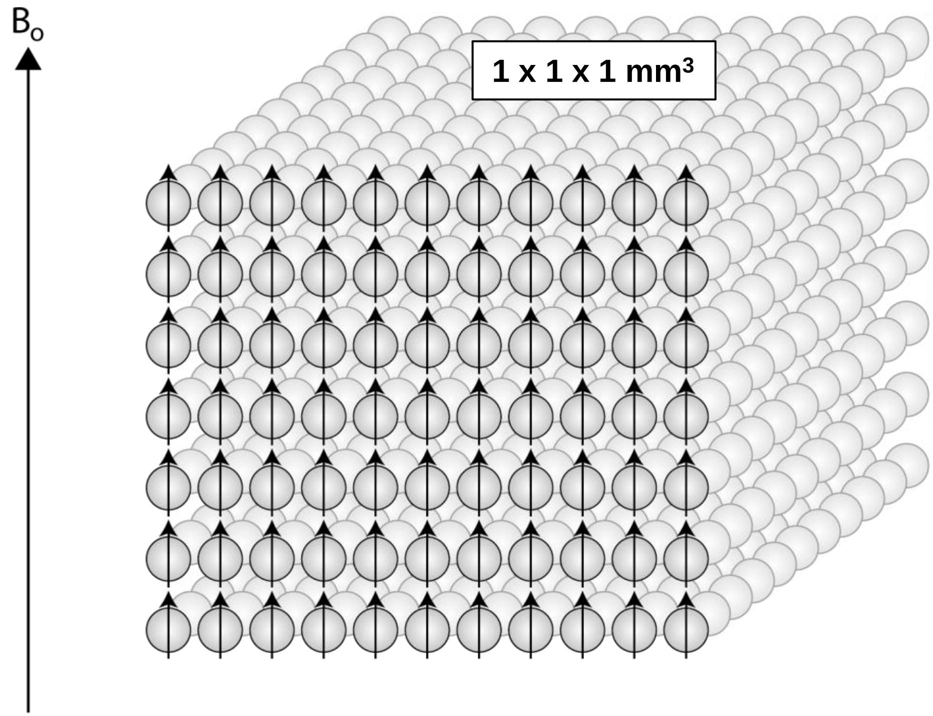
- General Introduction
- Origin of MR signal
- **Magnetic Resonance Imaging**
- MR image contrast



Learning Objectives

- Students will be able to identify the source of the MRI signal
- Students will be able to describe the process of producing an image
- Students will be able to identify the types of contrast available in MRI

Basics of MRI



Extremely simplified MRI pulse sequence

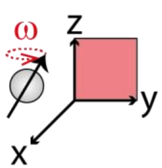
RF

G_{slice}

G_{phase}

$G_{frequency}$

Signal

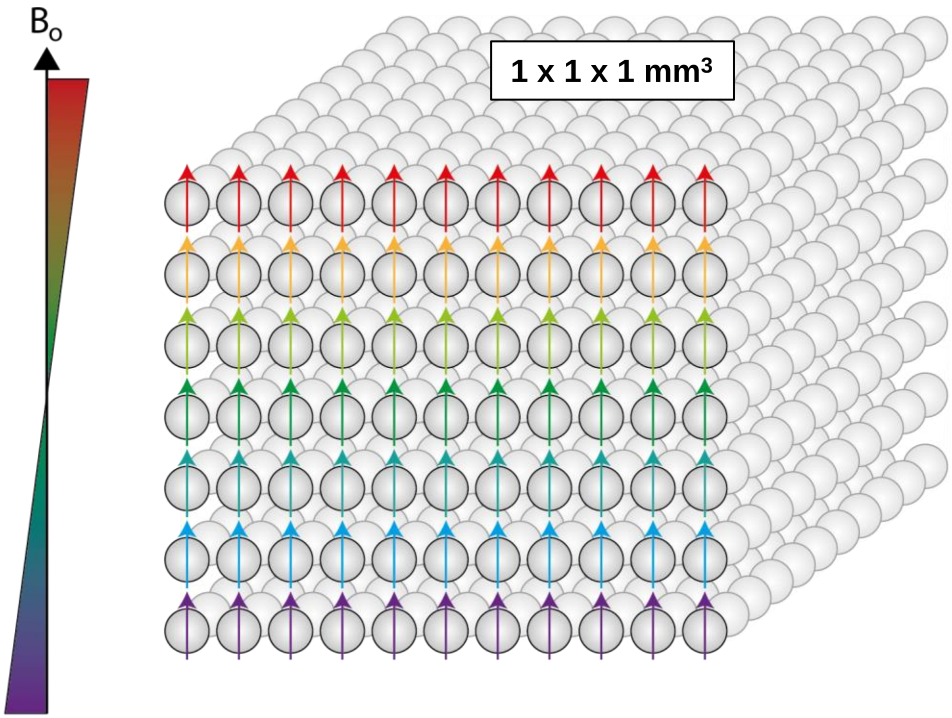


$$\omega = \gamma B_o$$

Key concept
Spatial labeling of the spins is accomplished by creating well defined magnetic field gradients in 3 dimensions.

For an excellent description, see:
https://www.cis.rit.edu/htbooks/mri/inside.htm

Slice selection



Extremely simplified MRI pulse sequence

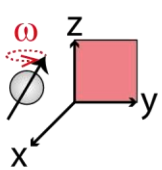
RF

G_{slice}

G_{phase}

$G_{frequency}$

Signal

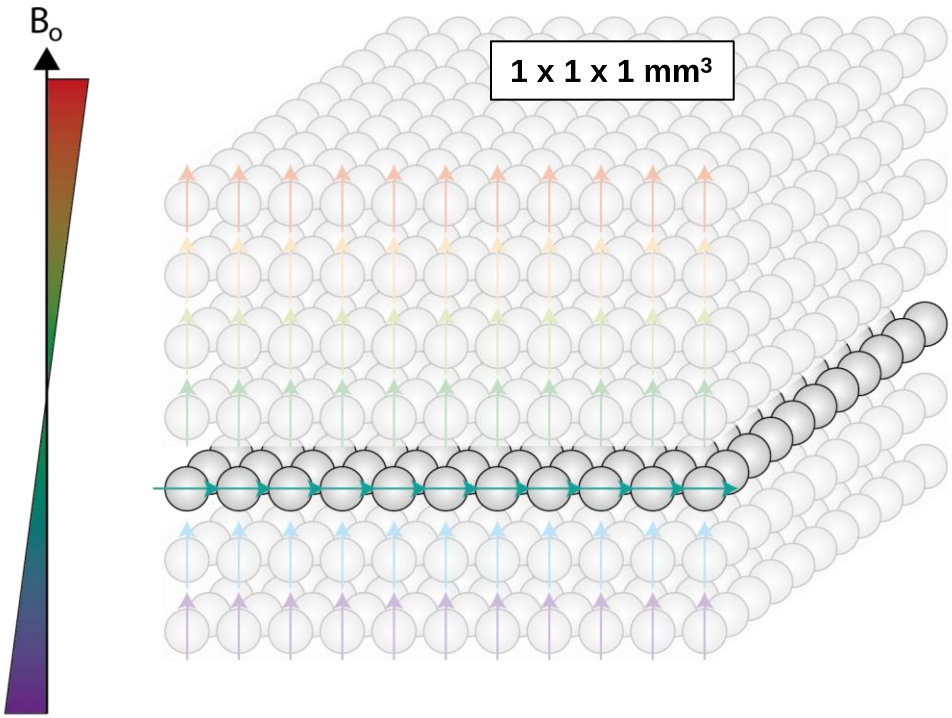


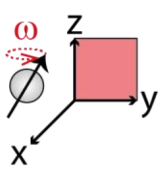
$$\omega = \gamma(Bo + zG_z)$$

<u>Apply 5 T/m gradient:</u>

What is the frequency difference between ^{1}H spins at the bottom and top of the sample?

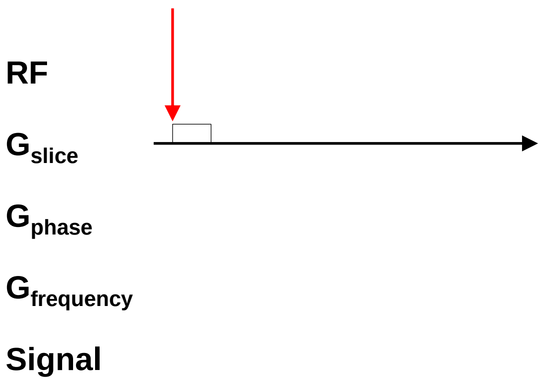
Slice selection



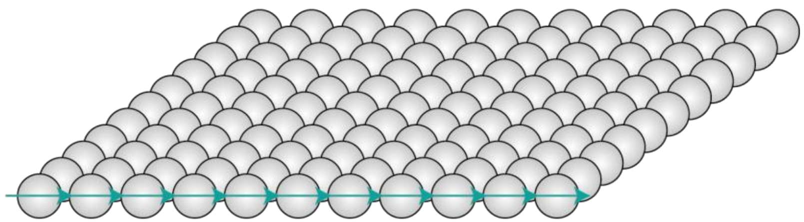


$$\omega = \gamma(Bo + zG_z)$$

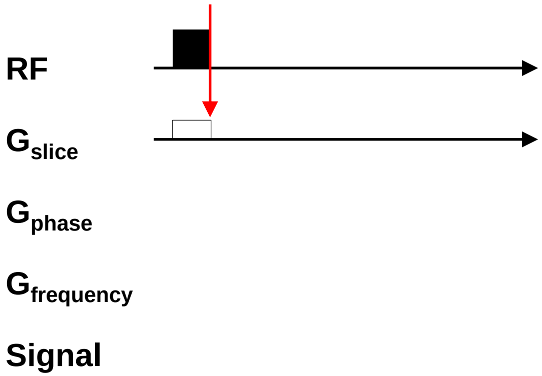
Extremely simplified MRI pulse sequence

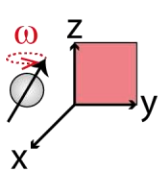


Slice selection



Extremely simplified MRI pulse sequence

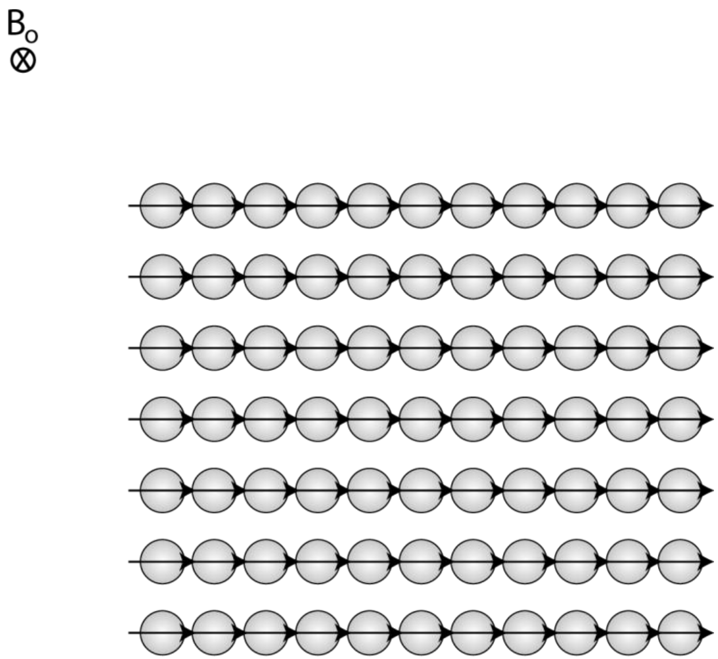




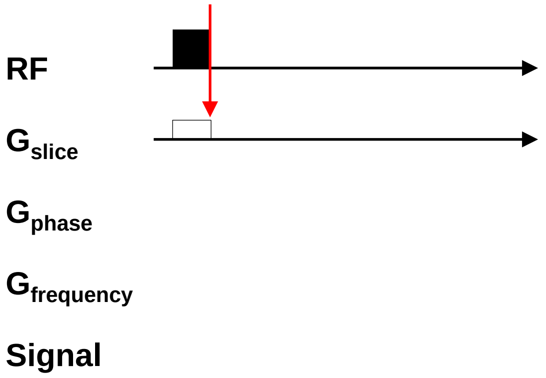
$$\omega = \gamma(Bo + zG_z)$$

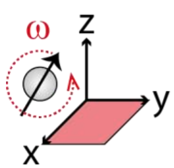
<u>Apply RF with 10 kHz bandwidth:</u>
What is the thickness of the slice excited when 5 T/m gradient is simultaneously applied?

Phase encoding



Extremely simplified MRI pulse sequence

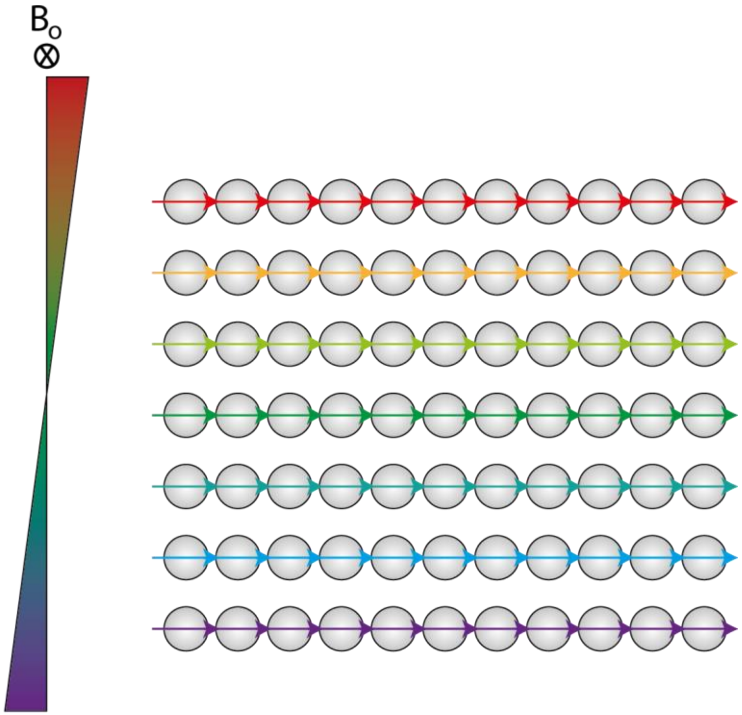


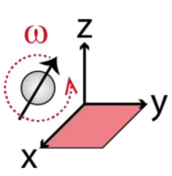


$$\omega = \gamma B_o$$

*** Note change in perspective!**

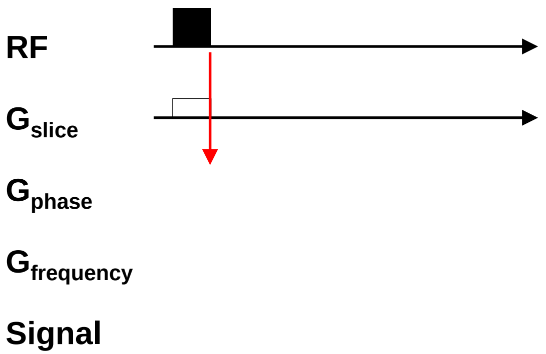
Phase encoding



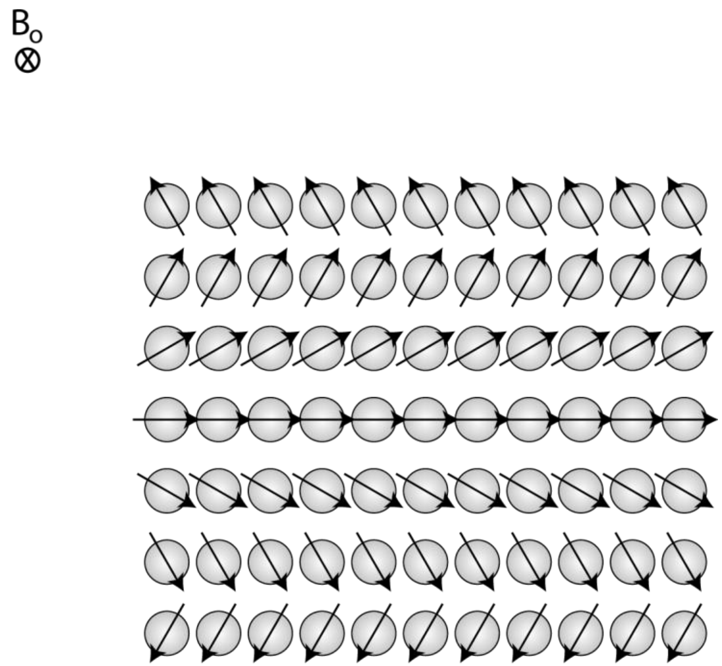


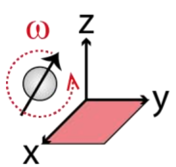
$$\omega = \gamma(Bo + xG_x)$$

Extremely simplified MRI pulse sequence



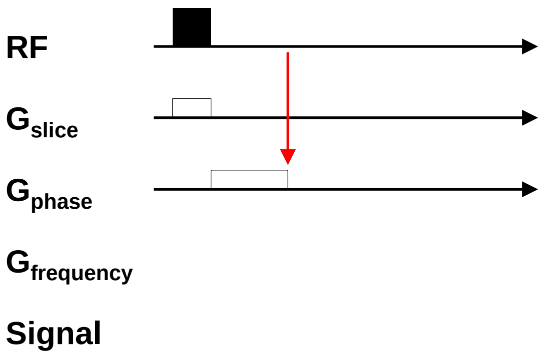
Phase encoding



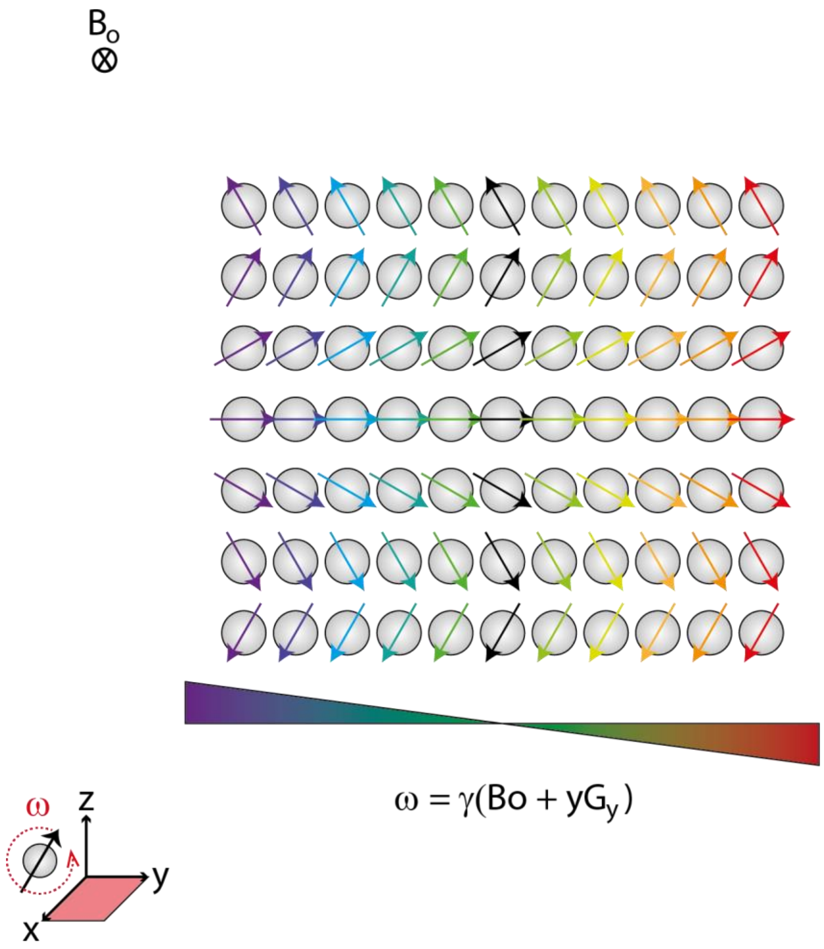


$$\omega = \gamma B_o$$

Extremely simplified MRI pulse sequence

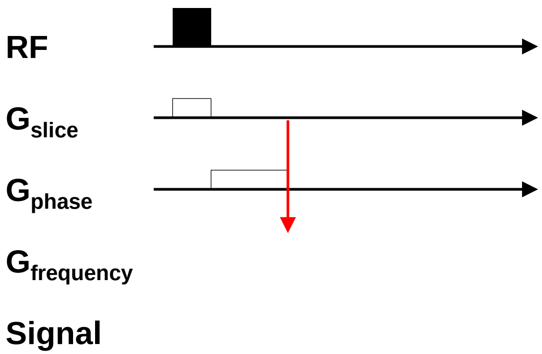


Frequency encoding



$$\omega = \gamma(Bo + yG_y)$$

Extremely simplified MRI pulse sequence

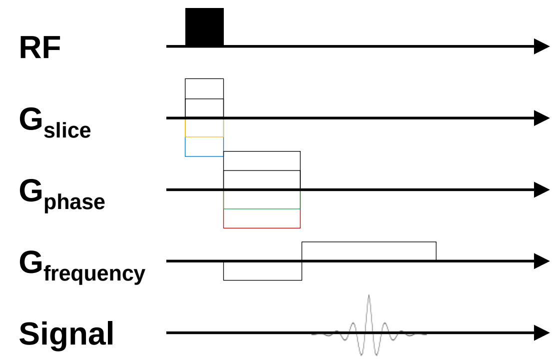


Decoding the signal to produce an image

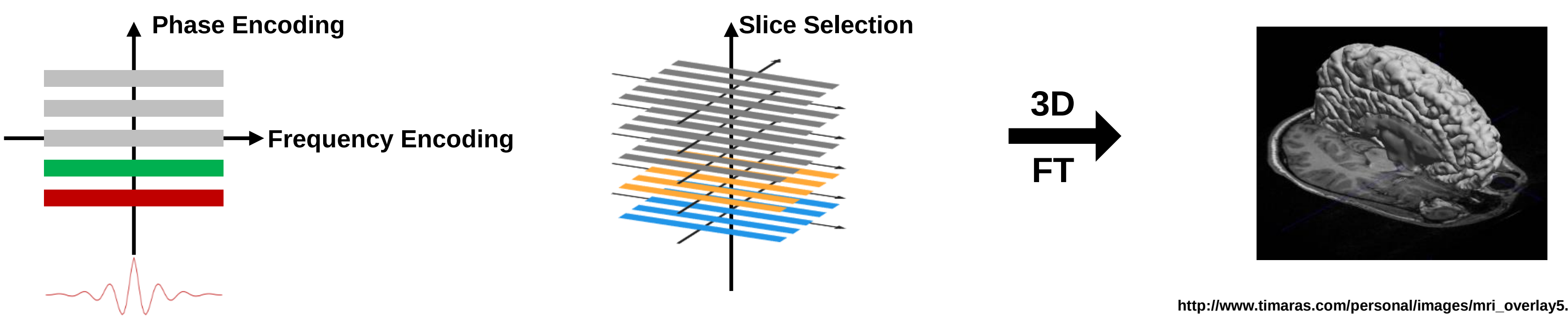
- Running the sequence once will produce 1 FID
  - 3D image reconstruction not possible (not even 2D)!

- Incrementing $\mathbf{G_{phase}}$ can generate a 2D image
  - # of increments = # of lines in image

- Incrementing $\mathbf{G_{slice}}$ can generate a 3D image
  - # of increments = # of slices in image

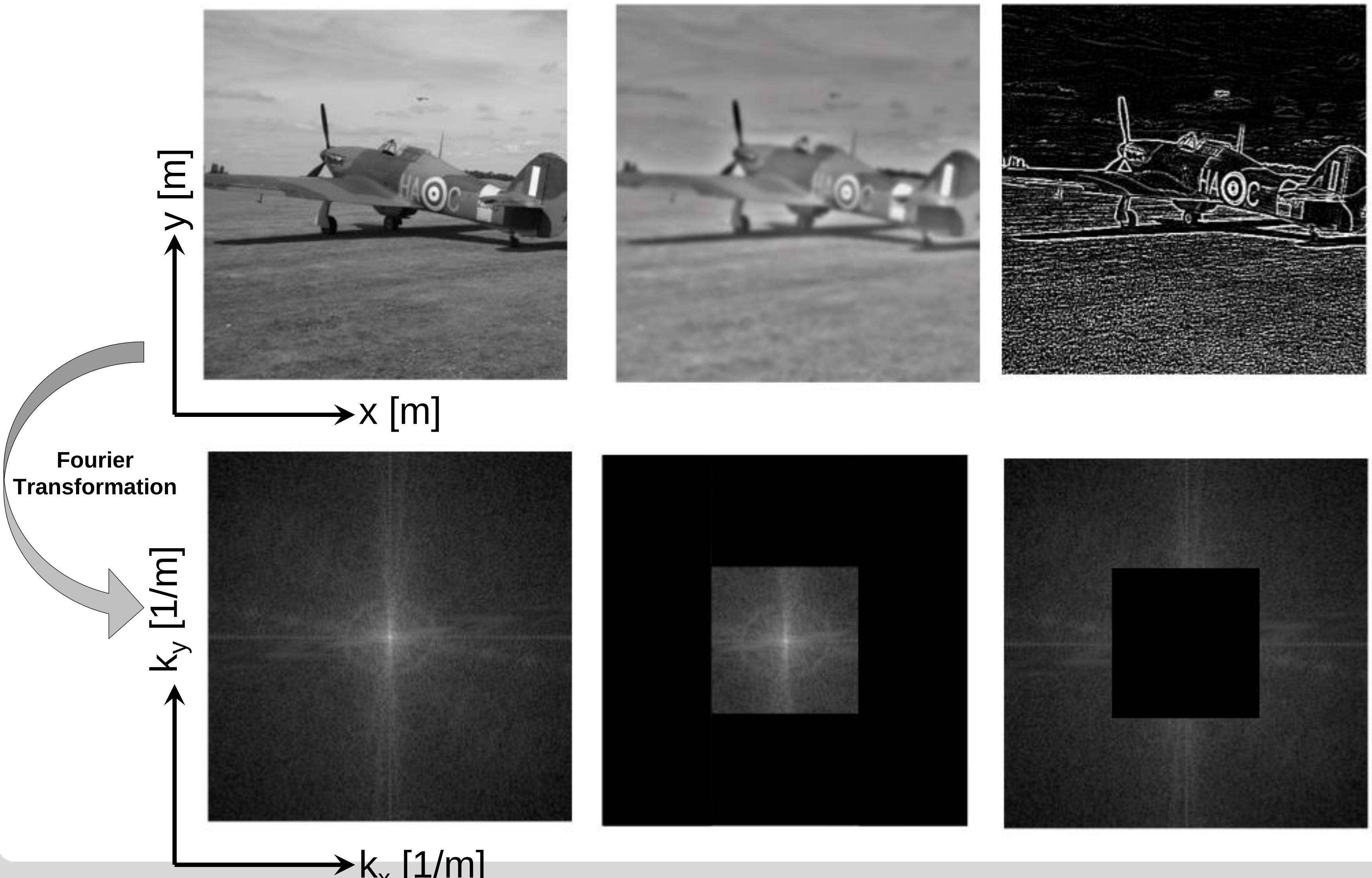


- *k*-space data representation:



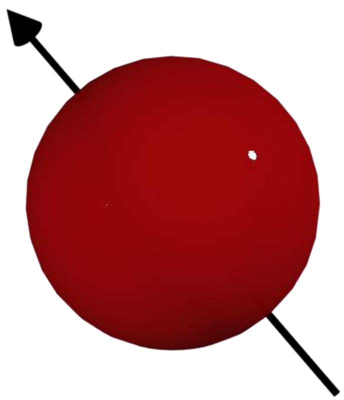
http://www.timaras.com/personal/images/mri_overlay5.jpg

K-Space – a spatial frequency domain



Magnetic Resonance Imaging

- General Introduction
- Origin of MR signal
- Magnetic Resonance Imaging
- **MR image contrast**



Learning Objectives

- Students will be able to identify the source of the MRI signal
- Students will be able to describe the process of producing an image
- Students will be able to identify the types of contrast available in MRI

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- T1
- T2
- Diffusion
- Flow
- Chemical contrast agent

Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

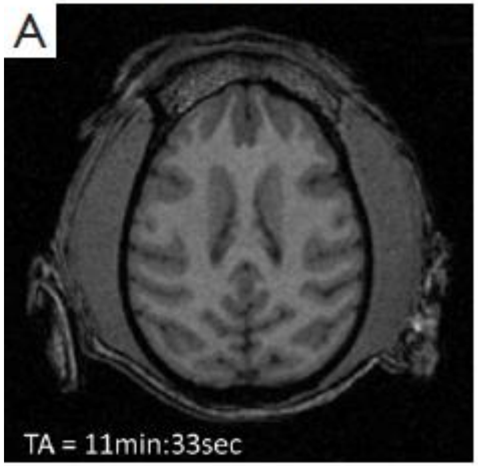
https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- **T1**
- T2
- Diffusion
- Flow
- Chemical contrast agent

T1-weighted



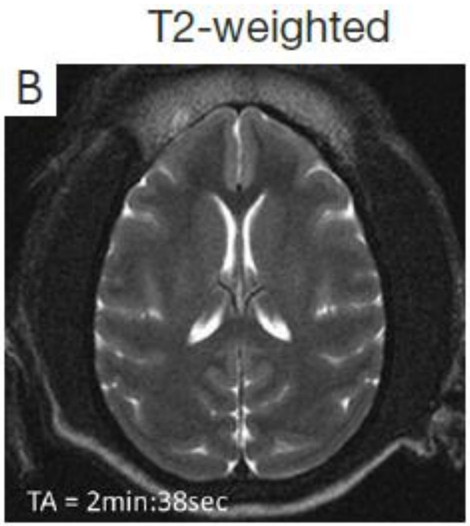
Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- T1
- **T2**
- Diffusion
- Flow
- Chemical contrast agent



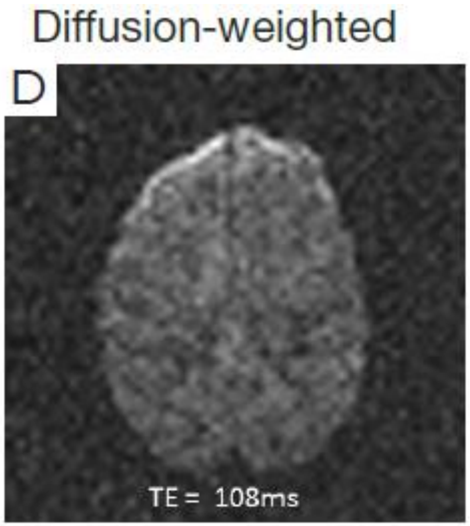
Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- T1
- T2
- **Diffusion**
- Flow
- Chemical contrast agent



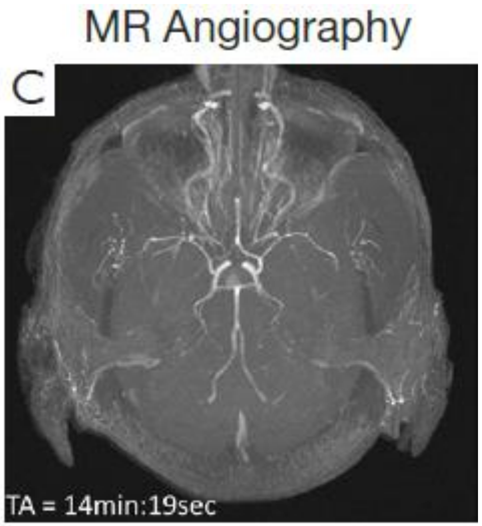
Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- T1
- T2
- Diffusion
- **Flow**
- Chemical contrast agent



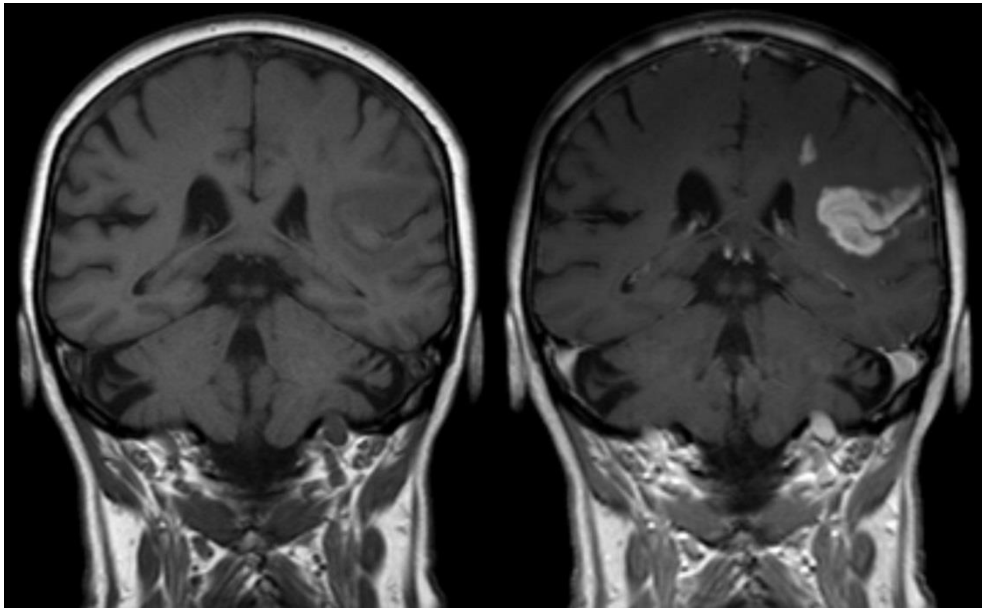
Xiaodong Zhang, et al., ***Quantitative Imaging in Medicine and Surgery 4 (2014) 112.***

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!

- Proton density
- T1
- T2
- Diffusion
- Flow
- **Chemical contrast agent**

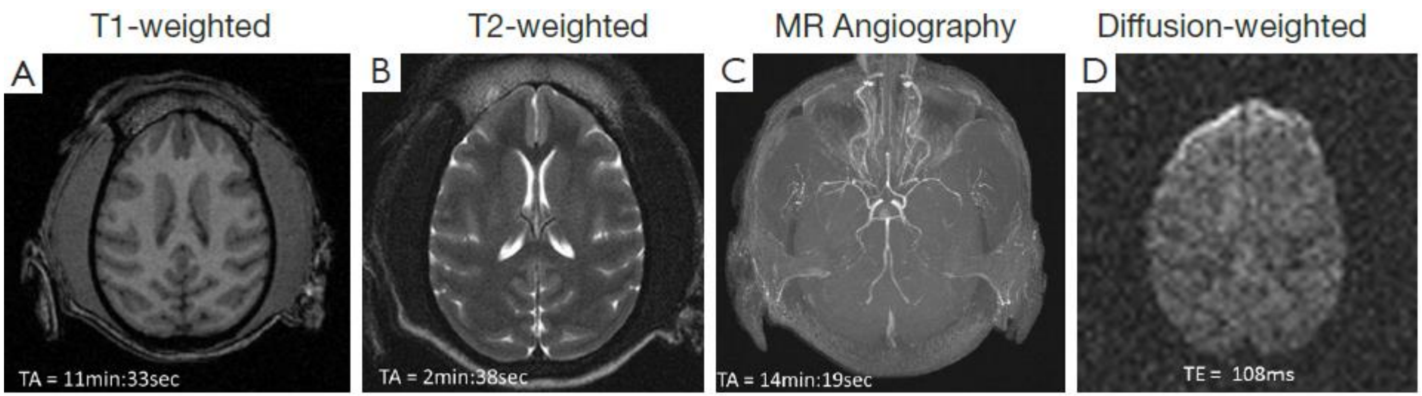


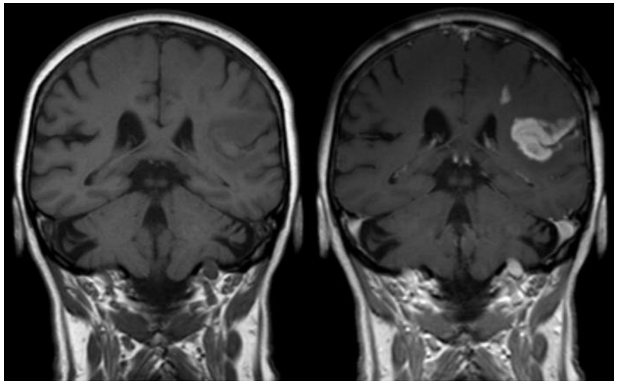
Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

MR image contrast

- Many parameters contribute to image contrast
  - The beauty of MRI!





Xiaodong Zhang, et al., *Quantitative Imaging in Medicine and Surgery 4 (2014) 112.*

https://upload.wikimedia.org/wikipedia/commons/8/85/Bluthirnschranke_nach_Infarkt_nativ_und_KM.png

Summary

- Magnetic resonance is dependent on nuclear spin
- MRI is a powerful technique to observe internal structures non-invasively
- Several forms of contrast are possible, extending the utility of MRI even further