CCAP
Centre for the Clinical Application of Particles

Nuclear diagnostics and Magnetic Resonance Imaging

Revision lecture

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Drawing heavily on material prepared in 2018/19 by J. Pozimski

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Section 2

Nuclear diagnostics

Radio-active decay

Modes:

- β decay
- $\beta - \gamma$ decay
- **Isomeric transition**
  Used in γ-camera, SPECT
- Internal conversion
- **Positron emission**
  Basis of PET
- **Electron capture**
  Used in γ-camera, SPECT

Nuclear decay; N nuclei at time t:

$$\frac{dN}{dt} = -\lambda N \quad \Rightarrow \quad N(t) = N(0)\exp(-\lambda t)$$

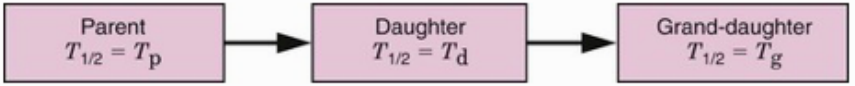
λ is the decay constant. The 'halflife' and 'lifetime':

$$t_{\frac{1}{2}} = \frac{\ln(2)}{2}\tau = \frac{\ln(2)}{2}\frac{1}{\lambda}$$

Activity: $A = \left|\frac{dN}{dt}\right| = \gamma N$

- Curie (Ci):
  - $1\,\text{Ci} = 3.7 \times 10^{10}\,\text{Bq}$

Parent-daughter decay chain



Branching ratio [Parent $\rightarrow$ Daughter] $= \beta$

Rate of 'decay'of daughter nuclei:

$$\begin{aligned} \frac{dN_D}{dt} &= \lambda_P N_P \beta - \lambda_D N_D \\ &= \lambda_P N_{P0} \beta \exp(-\lambda_P t) - \lambda_D N_D \end{aligned}$$

I.e.:

$$\frac{dN_D}{dt} + \lambda_D N_D - \lambda_P \beta N_{P0} \exp(-\lambda_P t) = 0\,.$$

Solution:

$$N_D = \frac{\lambda_P}{\lambda_D - \lambda_P} \beta N_{P0} \left[\exp(-\lambda_P t) - \exp(-\lambda_D t)\right] + N_{D0} \exp(-\lambda_D t)$$

Or in terms of activation:

$$A_D = \frac{\lambda_D}{\lambda_D - \lambda_P} \beta A_{P0} \left[\exp(-\lambda_P t) - \exp(-\lambda_D t)\right] + A_{D0} \exp(-\lambda_D t) \quad (1)$$

Parent-daughter decay chains: equilibrium ... or no equilibrium?

Secular equilibrium:

- $T_P >> T_D \Rightarrow \frac{\lambda_P}{\lambda_D} << 1$ and $\exp(-\lambda_P t) \sim 1$.
- Activity evolves according to:

$$A_D = \beta A_{P0}\left[1 - \exp(-\lambda_D t)\right] + A_{D0}\exp(-\lambda_D t)$$

Transient equilibrium:

- $T_P > T_D$
- Activity (also) evolves according to:

$$A_D = \beta A_{P0}\left[1 - \exp(-\lambda_D t)\right] + A_{D0}\exp(-\lambda_D t)$$

No equilibrium:

- $T_D > T_P$
- The daughter activity grows until $t_{\max}$ and then decreases. The parent activity 'falls away' and therefore fails to replenish the daughter.

$T_P > T_D$; transient equilibrium

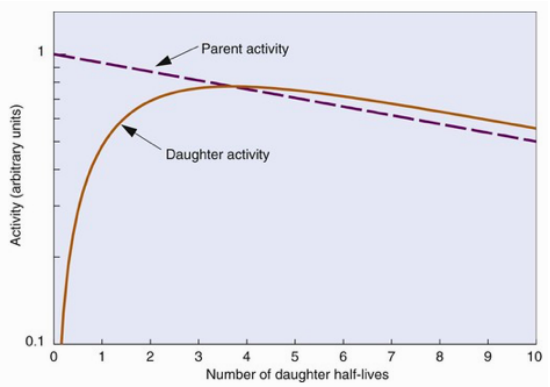
Transient equilibrium occurs at t_{eq} given by:

$$t_{\mathrm{eq}} = \frac{\ln\left[\frac{\lambda_P}{\lambda_D}\right]}{\lambda_P - \lambda_D}$$

At this time the activity of the daughter is a maximum, so one may write:

$$t_{\mathrm{max}} = t_{\mathrm{eq}} = \frac{1.44\,T_P\,T_D}{T_P - T_D}\ln\left[\frac{T_P}{T_D}\right]$$

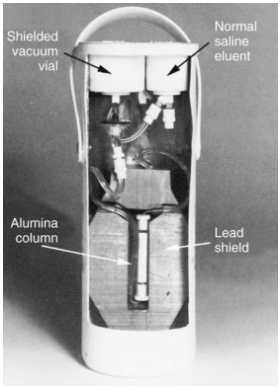
If $A_{D0} = 0$, $\beta = 1$, and $T_P = 10\,T_D$, then build up and decay of N_D reaches 'transient equilibrium' after $\sim 3.5\,T_D$.



Radionuclide generator: ^{99m}Tc for imaging

$$^{99}\text{Mo} \xrightarrow{\beta^-;\ T_{\frac{1}{2}}=66\ hr} {}^{99m}\text{Tc} \xrightarrow{\gamma;\ T_{\frac{1}{2}}=6\ hr} {}^{99}\text{Tc}$$

- ^{99}Mo bound to an alumina column in form of molybdate ion (MoO_4^-)
- ^{99m}Tc, the decay product, is not bound to column; it is chemically different
- ^{99m}Tc is eluted from column with 5–25 ml saline
- 75–85% of available ^{99m}Tc can be extracted
- Typically used for one week
- Often refereed as a 'Molly' or a 'Cow'



Methods for the production of radionuclides; overview

Nuclear reactor:

- Neutron capture
- Fission fragments

Radionuclide generators:

- Portable devices widely used in hospitals
- Require materials produced in nuclear reactors or accelerators

Accelerator:

- Cyclotron
- Active area of research; may return to this if there is time

Imaging techniques

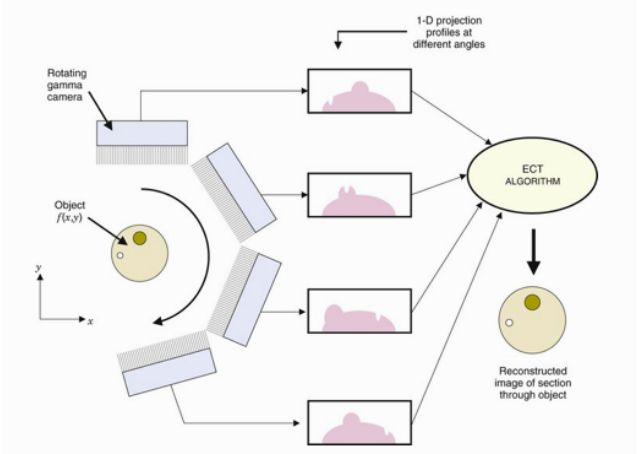
Related techniques:

- Gamma camera;
- Single Photon Emission Tomography (SPECT)

Common issues:

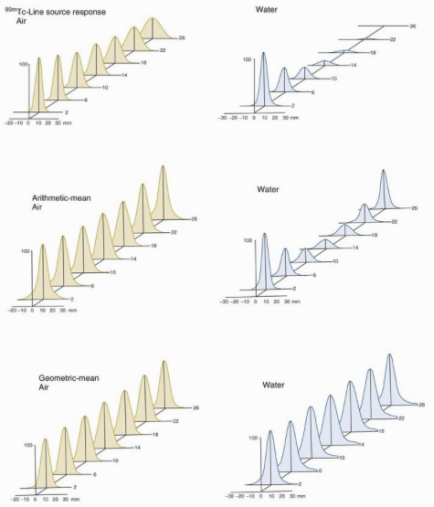
- Resolution:
  Detector thickness (geometrical) effect, scattering correction,
  statistical fluctation of photon counts, intrinsic resolution a function of energy;
- Selection of γs . . . energy window;
- Types of event:
  Good (wanted) event, scatter in detector, scatter in patient, septal penetration
- Image formation:
  Role of collimator, collimator types, contribution of collimator to resolution and geometrical efficiency
- Spatial resolution:
  Contributions from collimator, intrinisic resolution and Compton scattering

Back projection



ECT: Emission computed tomography

Attenuation

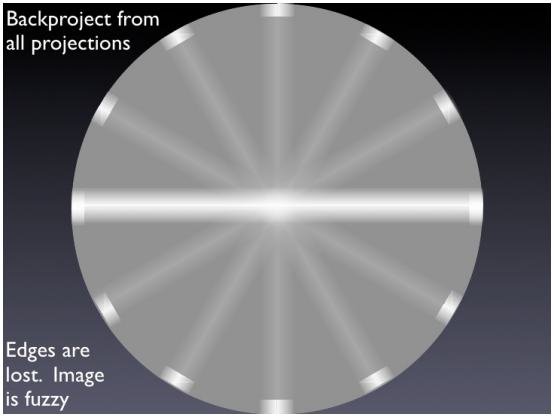


Example:

- High-resolution pin-hole collimator
- Resolution for line source diameter 2.5 mm:
  - As a function of distance source→detector
  - In air (left) and in water (right)
- Corrections applied:
  - Top: no correction
  - Middle: arithmetic mean:
    $$I_A = \frac{1}{2}(I_1 + I_2)$$
  - Bottom: geometric mean:
    $$I_G = (I_1 \times I_2)^{\frac{1}{2}}$$

Arithmetic mean gives most uniform response

Attenuation correction



Define, attenuation correction factor, ACF:

$$\mathrm{ACF} = \exp\left(\mu \frac{D}{2}\right)$$

The corrected intensity I_{corr} is then calculated by evaluating:

$$I_{\mathrm{corr}} = \mathrm{ACF} \times I_G$$

Attenuation correction strategies

1. Exploit ACF in "Chang's multiplicative method"
2. Generate a transmission map using "attenuation scans"
3. Use mean patient shape
   - Disadvantage "there is no mean (or average) patient"
4. Exploit CT image:
   - X-ray image processed to give transmission map that can be used to calculate ACF as a function of position

Considered 1 and 2

Positron Emission Tomography; the process

PET exploits photons generated in annihilation: $e^+ + e^- \rightarrow \gamma_1 + \gamma_2$

β^+ from decay scatters elastically off atomic electrons, loosing energy, until it annihilates

Annihilation assumed to be at rest. To conserve energy and momentum:

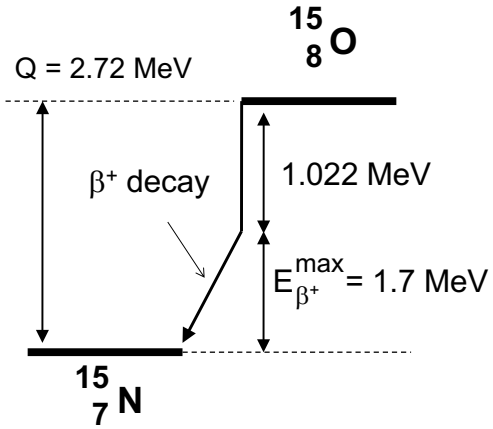
- Photons produced back-to-back
- Photon energies equal: $E_{\gamma_1} = E_{\gamma_2} = E_\gamma = mc^2 = 511\,\mathrm{keV}$

Back-to-back topology localises annihilation signal to a line in 3D space

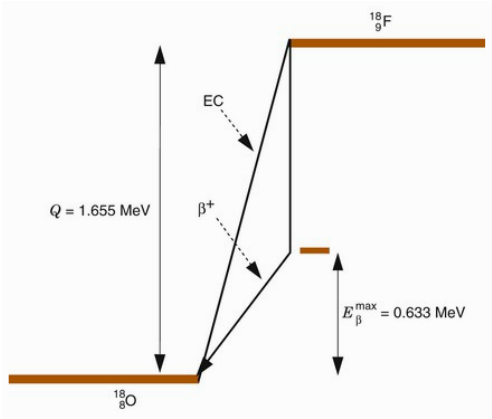
PET detectors use inorganic scintillators with large Z:

- E_γ large compared to photons used in SPECT
- So require dense scintillator with greater "stopping power" than NaI

Beta($^+$) decay



$$^{15}_{8}\mathrm{O} \rightarrow ^{15}_{7}\mathrm{N} + e^- + e^+ + \nu_e$$



$$^{18}_{9}\mathrm{F} \rightarrow ^{18}_{8}\mathrm{O} + e^- + e^+ + \nu_e$$

System resolution

System resolution, taken to be the resolution of the hardware, may now be evaluated:

- In terms of FWHM:

$$R_{\mathrm{sys}} = \sqrt{R_{\mathrm{int}}^2 + R_{\mathrm{range}}^2 + R_{180}^2}$$

- In terms of resolution:

$$\sigma_{\mathrm{sys}} = \sqrt{\sigma_{\mathrm{int}}^2 + \sigma_{\mathrm{range}}^2 + \sigma_{180}^2}$$

Example: clinical PET scanner:

- 5 mm scintillator: $R_{\mathrm{int}} = 2.5\,\mathrm{mm}$
- ^{18}F-labelled tracer: $R_{\mathrm{range}} = 0.6\,\mathrm{mm}$
- 800 mm diameter scanner: $R_{180} = 1.8\,\mathrm{mm}$

Yields:

- $R_{\mathrm{sys}} = 3.1\,\mathrm{mm}$

Sensitivity

Sensitivity is determined primarily by detector efficiency and solid angle coverage

True coincidence count rate $\mathcal{R}_{\mathrm{True}}$ for a positron-emitting source in air near midpoint between a pair of detectors is:

$$\mathcal{R}_{\mathrm{True}} = (\mathcal{R}_{\mathrm{e}^+})\,\epsilon^2 G \exp(-\mu T)$$

where:

- $\mathcal{R}_{\mathrm{e}^+}$ is the rate of positron emission (positrons/sec)
- ϵ is the intrinsic detector efficiency
  (no of γ-rays recorded by detector)/(no of γ-rays 'hitting' detector)
- G is the geometric efficiency of an individual detector
  $G = \frac{A_{\mathrm{det}}}{\pi D^2}$
- μ is the linear attenuation coefficient, T the total thickness

To get the best out of PET systems requires corrections

During reconsruction of PET images, corrections are applied for:

- Normalisation: to cross calibrate signals from each channel
- Random coincidences
- Scatter coincidences
- Attenuation
- Dead time

Section 3

Magnetic resonance imaging

Interaction of nuclear magnetic dipole with uniform magnetic field

The contribution, $\delta\mathcal{U}$, to the potential energy of a proton immersed in a magnetic field, $\mathbf{B}$, is given by:

$$\delta\mathcal{U} = -\mathbf{B} \cdot \boldsymbol{\mu}$$

Lets consider a proton which, in the absence of a magnetic field has energy E. Applying the magnetic field introduces $\delta\mathcal{U}$ into the Schrödinger equation resulting in a splitting of the proton energy level such that $E \rightarrow E'$ given by:

$$E' = E \pm E_{m_s}$$

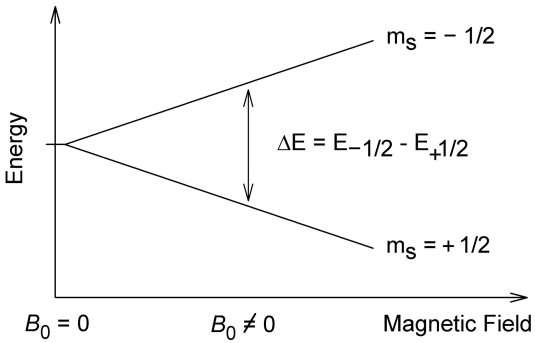
where

$$E_{m_s} = -m\gamma\hbar B_0$$

where m is the quantum number associated with the component of the proton spin parallel to $\mathbf{B}$, $\hbar$ is Planck's constant divided by 2π, and B_0 is the magnitude of $\mathbf{B}$
For the proton:

$$m_s = \pm\frac{1}{2}$$

Larmor equation



ΔE, splitting between two levels with $m_s = \pm\frac{1}{2}$:

$$\Delta E = \gamma \hbar B_0$$

Planck's law relates energy splitting to the angular frequency, ω, of the radiation required to excite the transition, therefore:

$$\Delta E = \hbar \omega$$

Writing ω in terms of γ and B_0 yields the Larmor equation:

$$\omega = \gamma B_0$$

The Larmor equation and bulk magnetisation

The quantum mechanical treatment presented in lecture 7 led to the **Larmor equation**:

$$\omega = \gamma B_0$$

ω is the Larmor frequency, B_0 the magnitude of the magnetic field, γ the gyromagnetic ratio

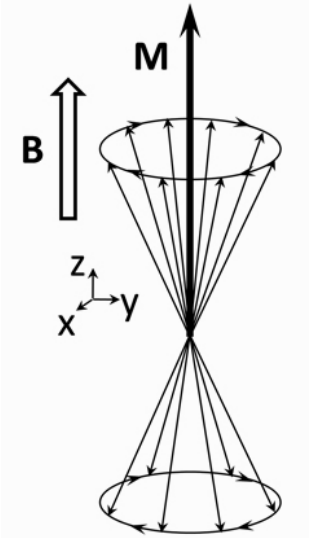
ω is the resonant frequency in an external magnetic field

The **bulk magnetisation** was obtained by considering the partition between the two energy states of the ^{1}H nuclei in the magnetic field:

$$N_- - N_+ \approx N_S \frac{\Delta E}{2k_B T} = N_S \frac{\gamma \hbar B_0}{2k_B T}$$

where the notation is that defined in lecture 7

Larmor precession



Ensemble of ^{1}H nuclei, the majority (by $\approx 3\,\mathrm{ppm\,T^{-1}}$) orientated parallel to **B** precess at equilibrium around **B** at the Larmor angular frequency ω

Net magnetisation, **M**, produced is parallel to **B**.

There is no net magnetisation in the transverse (x, y) plane; sum of all contributions cancel

Result is that there is no change in the magnitude or direction of the magnetisation vector so no RF signal is produced

Key feature of MRI: manipulate **M** so as to produce a measurable RF signal

Rotating the magnetisation vector in MRI

One of the two counter rotating fields will rotate in the same direction as the nuclear precession

In the frame that is co-rotating with the precession of the net magnetisation vector the magnetic field will appear stationary in the transverse (x, y) plane. Call the co-rotating field B_1^+

B_1^+ is equal to either $B_{1_{ac}}$ or B_{1_c} depending on the direction of $\mathbf{B}_0$

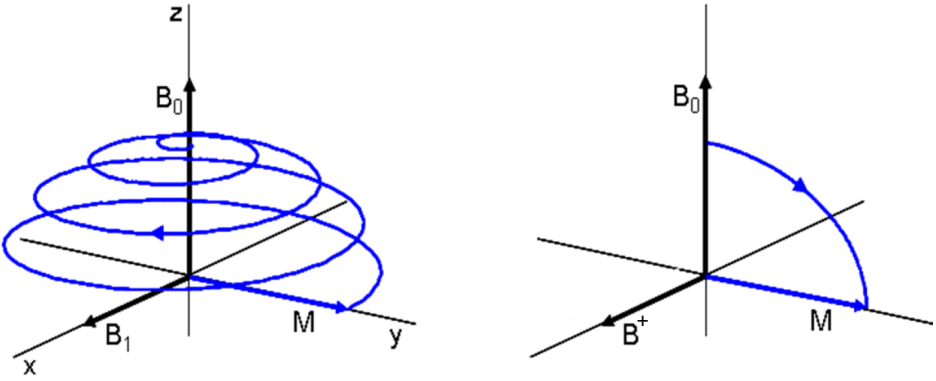
The stationary field will therefore cause $\mathbf{M}$ to precess about a rotating axis in the (x, y) plane

The net result is that $\mathbf{M}$ can be rotated into the x, y plane where it will continue to precess

The precession of $\mathbf{M}$ in the x, y plane gives a detectable RF signal

Rotating the magnetisation vector in MRI

M is initially parallel to $\mathbf{B}_0$



(a) Laboratory Frame of Reference *(b) Rotating Frame of Reference*

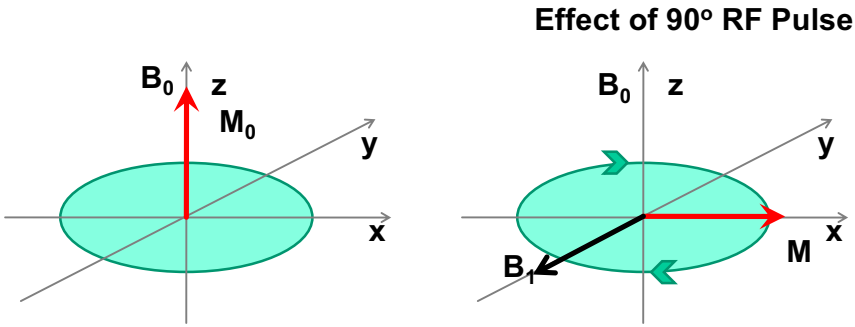
The flip angle

The flip angle, α (in radians), is proportional to the magnitude and duration of the RF pulse:

$$\alpha = \gamma B_1 t_P$$

where t_P is the duration of the RF pulse

90° pulse rotates magnetisation into transverse plane where it continues to precess



The Bloch equation and free inductiond decay (FID)

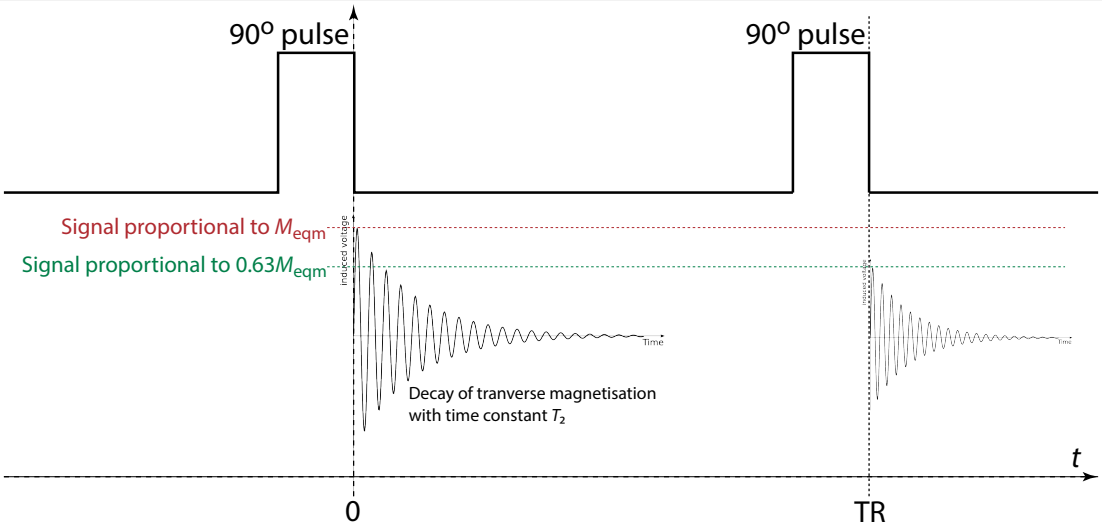
Block equation may now be updated to include FID:

$$\frac{d\mathbf{M}}{dt} = \gamma(\mathbf{M} \times \mathbf{B}_0) - \frac{\mathbf{M}_{xy}}{T_2} + \frac{M_0 - M_z}{T_1}\hat{\mathbf{k}}$$

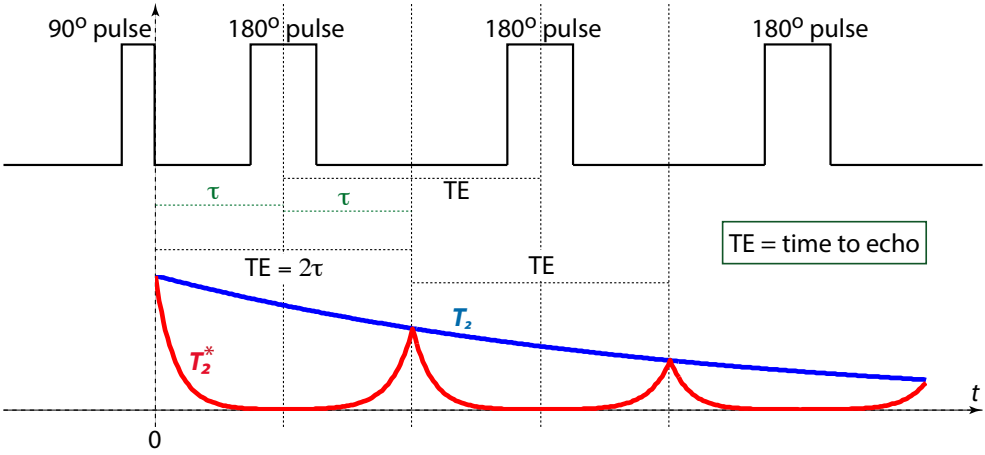
where:

- The first term describes the torque produced by the main (solenoid) field $\mathbf{B}_0$
- The second term describes the evolution of the transverse magnetisation vector $\mathbf{M}_{xy}$ due to the spin-spin interaction; time constant T_2
- The third term describes the evolution of the longitudinal magnetisation M_z due to the spin-lattice interaction; time constant T_1
- M_0 is the net magnetisation at equilibrium aligned with and proportional to $\mathbf{B}_0$

The spin-lattice relaxation time constant, T_1



Spin-spin relaxation time, T_2



$$M_{xy}(\mathrm{TE}) = M_{\mathrm{eqm}} \exp\left(-\frac{\mathrm{TE}}{T_2}\right)$$

Complication: additional factors affecting the decay of the transverse magnetisation

T_2, the intrinsic spin-spin relaxation time is determined by non-reversible thermodynamic processes at the nuclear level.

The spin-spin time constant is reduced by a number of factors. A significant contribution comes from inhomogeneities in the main field $\mathbf{B}_0$

Inhomogeneities give rise to reversible thermodynamic processes. The associated relaxation of the transverse magnetisation is characterised by a time constant T_2'

The effective spin-spin time constant, T_2^* is given by:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_2'}$$

$T_2' < T_2$ and so $T_2^* < T_2$. Need to develop techniques to recover T_2 as this carries the clinically-relevant information

Comparison of T_2 and T_2'

T_2

- The individual dipoles that sum up to produce the transverse magnetization are not precessing at precisely the same rate
- As a water molecule tumbles due to thermal motions, each H nucleus feels a small, randomly varying magnetic field in addition to B_0
- When the random field adds to B_0, the dipole precesses a little faster, and when it subtracts from B_0, it precesses a little slower
- For each nucleus the pattern of random fields is different, so as time goes on the dipoles get progressively more out of phase with one another, and as a result no longer add coherently

T_2'

- The source of this T_2' effect is magnetic field inhomogeneity
- Because the precession frequency of the local transverse magnetization is proportional to the local magnetic field, any field inhomogeneity will lead to a range of precession rates
- Over time the precessing magnetization vectors will get out of phase with one another so that they no longer add coherently to form the net magnetization
- As a result, the net signal is reduced because of this destructive interference
- Static field offsets rather than fluctuating fields

What does it take to make an MRI image

NMR can be used to generate signals that depend on the concentration of ^{1}H in tissue; the basis of an imaging technique

The spin-lattice and spin-spin relaxation times, T_1 and T_2 respectively, depend on tissue type—so can be used to distinguish neighbouring tissues

To generate an image need to:

- Extract T_1 and T_2; and
- Spatially localise the signal

Contrast introduced by isolation of T_1 and T_2 using RF pulse sequences

Spatial localisation achieved using magnetic gradients

Proton-density weighted image

Tissue	Proton density	1.5 T		3 T	
		T_1 ms	T_2 ms	T_1 ms	T_2 ms
Cartilage	0.94	1024	42	1168	37
Skeletal muscle	0.95	1084	37	1416	41
Blood	0.97	1441	308	1932	275
Fat	0.94	343	160	380	130
CSF	1.00	4550	60	4550	30
Brain matter (white)	0.99	688	81	833	68
Brain matter (grey)	1.00	1195	97	1436	93

Proton-density weighted image:

- TR long: long enough that M_{eqm} is restored between repetitions
- TE short: such that effects of different $T2$ are not allowed to evolve

Such images have strong signal from all tissues, but relatively low contrast between them

T_1 weighted image

Tissue	Proton density	1.5 T		3 T	
		T_1 ms	T_2 ms	T_1 ms	T_2 ms
Cartilage	0.94	1024	42	1168	37
Skeletal muscle	0.95	1084	37	1416	41
Blood	0.97	1441	308	1932	275
Fat	0.94	343	160	380	130
CSF	1.00	4550	60	4550	30
Brain matter (white)	0.99	688	81	833	68
Brain matter (grey)	1.00	1195	97	1436	93

T_1 weighted image enhancing signal from e.g. fat, white mater:

- TR short: such that M_{eqm} can only recover fully between repetitions in tissues with low T_1
- TE short: enough that the effects of different $T2$ are not allowed to evolve

Tissues such as fat appear bright in such images

T_2-weighted image

Tissue	Proton density	1.5 T		3 T	
		T_1 ms	T_2 ms	T_1 ms	T_2 ms
Cartilage	0.94	1024	42	1168	37
Skeletal muscle	0.95	1084	37	1416	41
Blood	0.97	1441	308	1932	275
Fat	0.94	343	160	380	130
CSF	1.00	4550	60	4550	30
Brain matter (white)	0.99	688	81	833	68
Brain matter (grey)	1.00	1195	97	1436	93

T_2 weighted image enhancing signal from e.g. blood and CSF:

- TR long: long enough that M_{eqm} is restored between repetitions
- TE long: enough that the decay rates determined by $T2$ **are** allowed to evolve

"Tissues" such as blood & CSF appear bright in such images

Bloch equation and pulse-sequence summary

Block equation taking into account effective spin-spin relaxation time, T_2^*:

$$\frac{d\mathbf{M}}{dt} = \gamma\left(\mathbf{M} \times \mathbf{B}_0\right) - \frac{\mathbf{M}_{xy}}{T_2^*} + \frac{M_0 - M_z}{T_1}\hat{\mathbf{k}}$$

Partial saturation pulse sequence: series of 90° pulses separated by TR:

$$M_z(\mathrm{TR}) = M_{\mathrm{eqm}}\left[1 - \exp\left(-\frac{\mathrm{TR}}{T_1}\right)\right]$$

Inversion recovery pulse sequence: 180° pulse followed at $t = \mathrm{TI}$ by a 90° pulse. Sequence repeats after $t > 5T_1$:

$$M_z(\mathrm{TI}) = M_{\mathrm{eqm}}\left[1 - 2\exp\left(-\frac{\mathrm{TI}}{T_1}\right)\right]$$

Spin-echo pulse sequence: 90° pulse followed by series of 180° pulses separated by TE:

$$M_{xy}(\mathrm{TE}) = M_{\mathrm{eqm}}\exp\left(-\frac{\mathrm{TE}}{T_2}\right)$$

Reconstruction of the MR image

Gradient pulses G_i are used to allow slice-selective excitation and to allow spatial information to be encoded into the net magnetisation:

$$B_z(x, y, z, t) = B_0 + xG_x(t) + yG_y(t) + zG_z(t)$$

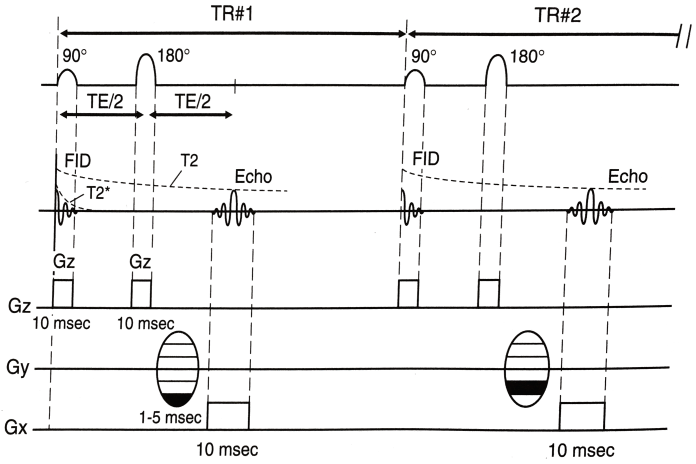
Spatial information is encoded into net magnetisation in k-space, often:

- Frequency encoding is used to encode features in the x direction
- Phase encoding is used to encode features in the y direction

2D Fourier transform used to transform image in k space to image in coordinate space

Pulse sequence is repeated to collect data for all $N_x \times N_y$ pixels of image

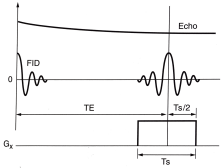
Spin-echo sequence



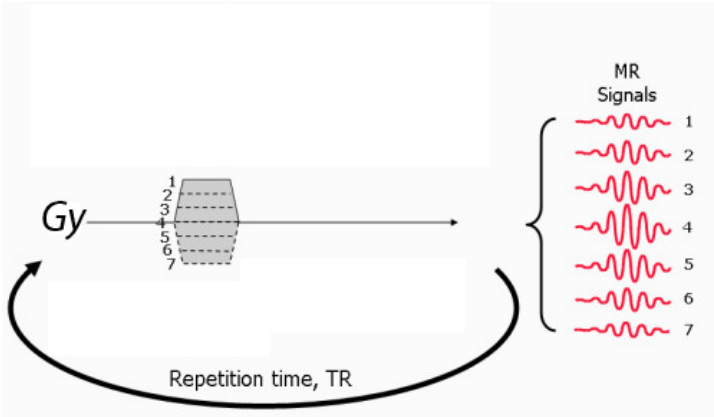
Readout occurs when frequency-encoding pulse (G_x) is on (T_S, the sampling time)

Each repetition corresponds to a new G_y, i.e. a new encoding of phase

Take N_y repetitions to fill N_y rows in the image



Phase encoding

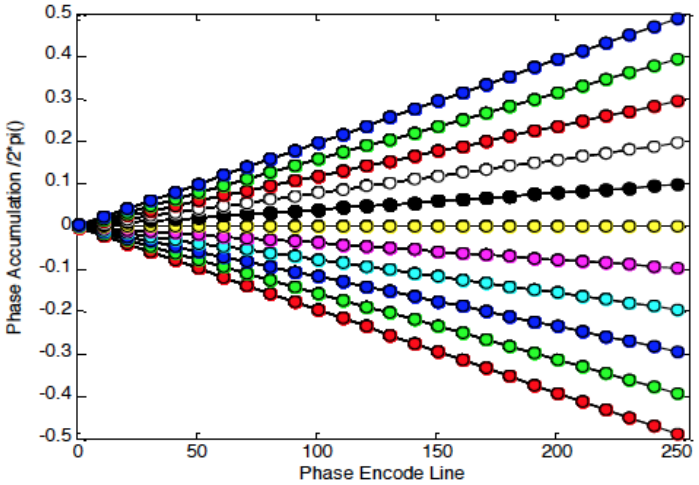


Central line in k-space will contain phase-encoding step with weakest gradient and strongest signal

Periphery of k-space sill contain phase-encoding steps with the strongest gradients and weakest signal

Each slice "has its own k-space because excitation is tuned to G_z

Phase encoding



Phase wrt $y = 0$ accumulates with time, t, while phase-encoding gradient, G_y, is on:

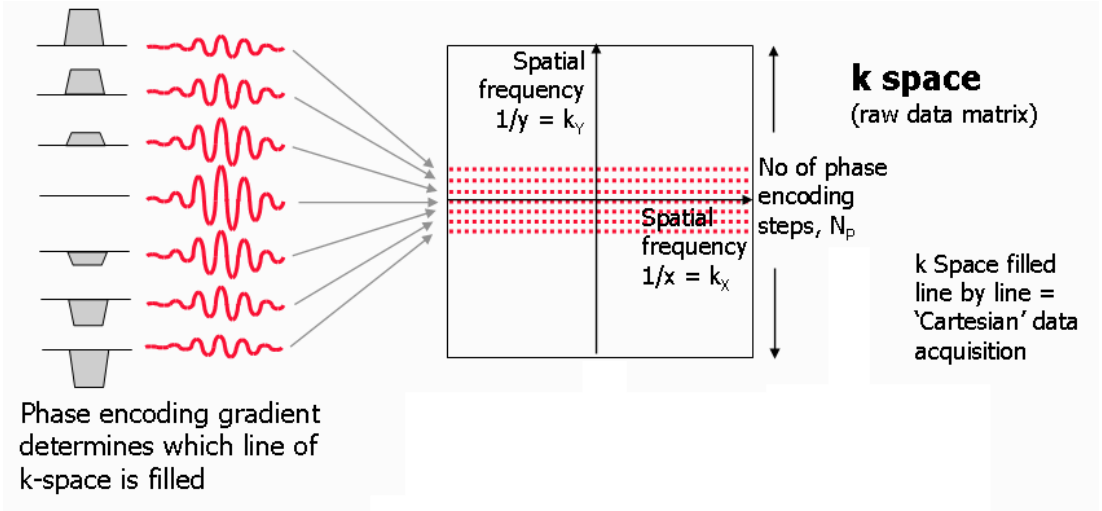
$$\Phi(G_y, y, t) = (\gamma G_y)\, yt \qquad (2)$$

The slope of the line in the figure is determined by y

I.e. the rate of change of phase (frequency) is given by:

$$\frac{\Delta\Phi}{\Delta t} = (\gamma G_y)\, y$$

Phase encoding



Overview of encoding

The slice is selected by tuning the RF frequency and G_z

The k_x coordinate is obtained from frequency encoding **at readout**

The k_y coordinate is obtained from phase encoding **"passively" by manipulating phase during free induction decay (FID)**

A selection of sources of artefact that arise in the reconstruction of MRI images was discussed in the lectures

Section 4

. . . and finally . . .

The exam

Imperial College London

BSc/MSci EXAMINATION May 2020

This paper is also taken for the relevant Examination for the Associateship

MEDICAL IMAGING : ND & MRI

For Third and Fourth-Year Physics Students

13 May 2020: 10:00 to 11:15

The paper consists of two sections A & B.
Section A contains two questions [20 marks each]
Section B contains four questions [5 marks each]

*Candidates are required to answer **ALL** parts of Section A and **TWO** questions from Section B.*

Marks shown on this paper are indicative of those the Examiners anticipate assigning.

General Instructions

At the top of each page of your answers, write your CID number, module code, question number and page number. Scan and upload your answers to the Turnitin dropboxes as described in the guidance documents in the Blackboard module for this exam. Upload each answer to the dropbox provided for that specific question.

Your uploaded file name should be of the form CID_ModuleCode_QuestionNumber(s).pdf

For each answer you should prepare a coversheet which should be the first page of your scanned answer. The coversheet should contain the following:

- your CID
- module name and code
- the question number
- the number of pages in your answer

You should not write your name anywhere on your answers.

You are reminded that Examiners attach great importance to legibility, accuracy and clarity of expression.

[Examination instructions continue on next page. . .]

2020 ND&MRI exam—rubric same as in previous years

Section A — compulsory

- 1 question on nuclear diagnostics – from lectures 1 to 6
- 1 question on MRI – from lectures 7 to 13

Section B — also compulsory

- 2 questions on nuclear diagnostics – from lectures 1 to 6
- 2 questions on MRI – from lectures 7 to 13