December 28, 2020

Nuclear diagnostics and Magnetic Resonance Imaging

Week 1; Lecture 1; Introduction, nuclear medicine o/v, nuclear decay theory

K. Long (k.long@imperial.ac.uk)
Department of Physics, Imperial College London/STFC
R. McLauchlan (ruth.mclauchlan@nhs.net)
Radiation Physics & Radiobiology Department, Imperial College Healthcare NHS Trust

Contents

Section 1

Introduction

Aims

With the course we aim to:

- Provide students with a general overview of the physical principles that underlie nuclear diagnostics (ND) and magnetic resonance imaging (MRI);
- Allow students to appreciate the factors that influence the development of contrast in ND and MRI; and
- Give students the means to estimate the resolution, speed, and sensitivity of ND and MRI imaging modalities.

Objectives 1: radionuclides and gamma camera

At the end of the course students will be able to:

- Explain the principal methods used for the production of radionuclides;
- Explain and apply the definitions of activity, half-life and decay constant;
- Calculate the energies of the particles involved in radioactive decay in a given situation;
- Explain the principal radioactive decay pathways and the application of the radiation produced to medical imaging;
- Explain how a gamma camera operates and discuss the main parameters that affect its performance;
- Calculate the resolution and efficiency of a gamma camera in a particular situation; and
- Explain the different types of event that can be recorded by using a gamma camera and discuss how these affect the image.

Objectives 2: SPECT and PET

At the end of the course students will be able to:

- Explain how Single Photon Emission Computed Tomography (SPECT) is performed;
- Explain the methods typically used in the reconstruction of a SPECT images;
- Explain how a Positron Emission Tomography (PET) image is produced and discuss the principal limitations of PET;
- Discuss the different types of detection events recorded by a PET system and how they affect the image;
- Calculate the resolution, detection efficiency, detection rate, and coincidence rate for a particular PET scanner;
- Explain how to compensate for attenuation and unwanted random and scatter events in PET; and
- Describe and discuss the main differences between 2D and 3D PET image acquisition

Objectives 3: Magnetic resonance imaging

At the end of the course students will be able to:

- Describe the principles of nuclear magnetic resonance (NMR);
- Discuss how relaxation mechanisms contribute to the generation of contrast in magnetic resonance imaging (MRI);
- Describe techniques for spatial localisation of the NMR signals in MRI;
- Distinguish between phase and frequency encoding is used in MRI to enable the spatial localisation of the NMR signal;
- Use the Fourier-transform technique to exploit ‘k-space’ to describe MRI images in this space;
- Connect the receiver bandwidth, acquisition time, and sampling frequency to the field of view and resolution;
- Identify the causes of the most common image artefacts;
- Show how the signal-to-noise ratio (SNR) is affected by the choice of data acquisition parameters;
- Recall the major hardware components necessary for MRI;
- Recall, devise, and interpret typical MRI pulse sequences and discuss the changes in image contrast induced by changes in the pulse sequences; and
- Calculate the optimal ‘TR’ and ‘TE’ to maximise image contrast for ‘proton density’, ‘T1’, and ‘T2’ weighted imaging.

Recommended books

Nuclear Medicine

- **Physics in Nuclear Medicine**
  S. Cherry, J.A. Sorenson, M.E. Phelps
  Central Library: 616.075 CHE also available as an e-book
- **The Essential Physics of Medical Imaging**
  J. Bushberg, J. Seibert, E. Leidholdt, J. Boone
  Central Library: 616.075 BUS and as an e-book
- **Practical Nuclear Medicine**
  P.F. Sharp, H.G. Gemmell, A.D Murray (Eds.)
  Central Library: 615.849 BUS and as an e-book
- **Essentials of Nuclear Medicine Physics and Instrumentation**
  R.A. Powsner, M.R. Palmer, E,R. Powsner
  Available at Hammersmith Library Main floor (WN440 POW) and as an e-book

Recommended books

Magnetic resonance imaging

- **MRI: the basics**
  R. Hasgemi, W. Bradley, C. Lisanti
  Central Library: 616.075 HAS
- **MRI: from picture to proton**
  D.W. McRobbie, M.J. Graves, E.A. Moore, M.R. Prince
  Central Library: 616.075 HAS and available online at:
  https://doi.org/10.1017/9781107706958
- **Electromagnetics in Magnetic Resonance Imaging**
  C.M. Collins
  Available as an e-book and online at:
  https://iopscience-iop-org.iclibezp1.cc.ic.ac.uk/book/978-1-6817-4083-6

Taught sections

The course material is broken down into:

- "Weeks"; each week will contain roughly 2 "lectures"
- "Lectures"; each lecture is broken down into a number of "sections"
- "Sections" will usually contain the material related to a particular (sub-)topic
    - Each section will be presented as a set of slides and a Panopto presentation
- "Active-learning" exercises will be interspersed with the sections

In a non-Covid year:

- The material presented in a "lecture" would correspond to that contained in a single 50-minute lecture

Discussion sessions

The course is intended as an introduction to the clinical application of NM and MRI techniques:

- Both the physical principles; and
- Aspects of the practical clinical application

So, after the presentation of a particular technique there will be:

- "Questions and applications" (Q&A) sessions led by a medical physicist
  - . . . your opportunity to ask questions!

Q&A sessions have dual purpose:

- Presentation of practical aspects of the technique
- Student-led question-and-answer session (≈ "office hour")

Problem sheets

There will be two problem sheets:

1. Towards the end of the presentation of the nuclear diagnostics
2. Towards the end of the presentation of MRI

The problem sheets are not assessed

Communication: Blackboard and Piazza

Blackboard will be used for the distibution of course materials

Piazza will be used as a discussion forum:

- You should have received an invitation to the Piazza discussion group;
- Please do use it to raise issues, discuss course materials etc.

Overview of schedule in weeks, lectures, and sections

Week	**Lecture**	**Section**
1. 15Feb21	1. Introduction, nuclear medicine o/v, nuclear decay theory	1. Introduction
		2. Nuclear medicine
		3. Nuclear decay, revision
	2. Radionuclides, production methods, gamma-camera intro	1. Radionuclides for nuclear medicine
		2. Methods for production of radionuclides
	3. The gamma camera	1. Introduction
		2. Gamma camera
		3. Collimator
		4. Scintillator
		5. Examples
2. 22Feb21	4. Single photon emission computed tomography	1. Introduction
		2. Reconstruction
		3. Attenuation correction
		4. Scattering correction
		5. Examples
	5. Positron emission tomography I	1. Principles of positron emission tomography
		2. System resolution
		3. Sensitivity
3. 01Mar21	6. Positron emission tomography II	1. Types of coincidence event
		2. System resolution
		3. Data acquisition
		4. Comparison of sensitivity and corrections
		5. Examples

Week	**Lecture**	**Section**
3. 01Mar21	7. Introduction to MRI and quantum-mechanical foundations	1. Introduction to MRI
		2. Quantum mechanical foundations
4. 08Mar21	8. Classical development of principles of MRI	1. Classical derivation of Larmor equation
		2. Rotating the magnetisation
		3. Free induction decay
	9. Determination of T1 and T2	1. Determination of the spin-lattice relaxation time, T1
		2. Determination of the spin-spin relaxation time, T2
6. 15Mar21	10. Magnetic Resonance Imaging: spatial localisation	1. Slice selective excitation
		2. Encoding spatial information in k-space
		3. Encoding spatial information into net magnetisation
	11. Magnetic Resonance Imaging: contrast	1. Spin-echo sequence for proton-density weighted image
		2. Spin-echo sequence for T1-weighted image
		3. Spin-echo sequence for T2-weighted image
		4. Comparison of T1, T2, and proton-weighted images
		5. Inversion recovery
7. 22Mar21	12. Magnetic Resonance Imaging: artefacts	1. Aliasing (wraparound) and the Nyquist theorem
		2. Truncation artefact; Gibbs phenomenon
		3. Random motion artefacts
	13. More MRI artefacts	1. MRI artefacts: periodic motion
		2. MRI artefacts: chemical shift

The Physics Undergraduate office will release the week's material by the end of the morning on Monday each week

Assessment: 100% by examination

1 hour remote timed assessment

- Four questions
- **All** questions compulsory

Section 2

Nuclear medicine

What is “nuclear diagnostics” (aka nuclear medicine)?

Imaging using radio-isotopes:

- Introduce radionuclide into the body:
  - A ‘radiotracer’ is usually introduced into the body on a ‘radiophamaceutical’;
  - Detectors external to body used to ‘image’ distribution of radiotracer within body;
  - Spatial distribution depends on ‘take-up’ of radiopharmaceutical in tissue.
- ND (NM) usually ‘emission imaging’ . . .
  to be contrasted with conventional x-ray imaging which is ‘transmission imaging’.

Sensitivity!

- Goal is to use such a small amount of radiotracer that biological system under investigation is not perturbed.

Radiopharmaceuticals

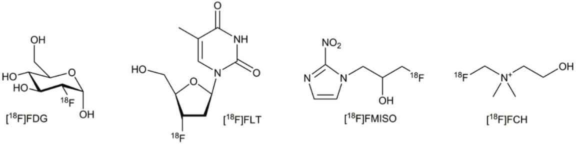
Enormous field! Beyond the scope of this course; some examples later.

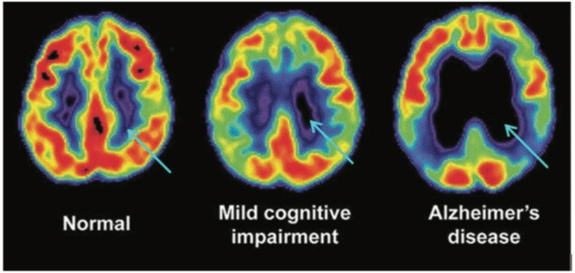
Consider the radiopharmaceutical as a means of delivering an isotope to a particular location:

- Compound tagged with a radionuclide;
- Accumulation, rate of uptake and clearance related to physiological, biochemical and/or molecular processes;
- Carrier molecule designed to target organ or function;
- Radionuclide required to produce emissions that can be detected outside the body;:
    - Require penetrating radiation: primary gammas, photons produced in positron annihilation;
- Radionuclides delivered in tiny amounts: nanograms:
    - Require sensitive detectors.
- Administration:
    - Intravenous, inhalation, subcutaneous, oral

Radiopharmaceuticals: an example

Delivering ^{18}F, and exploitation in diagnosis of Alzheimer's disease using PET.



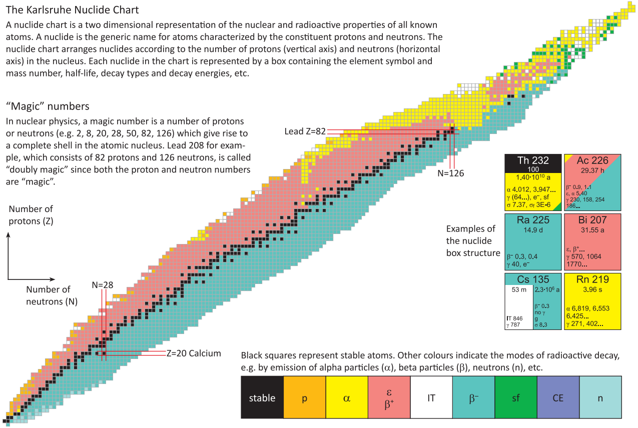


http://real.mtak.hu/41305/1/225_247_BRC_2015_Vol_2.pdf

Radioactivity '101'

- Radioactivity is an intrinsic property of unstable nuclei;
- Quantum-mechanical process: uniform probability of decay;
- Radioactive decays:
  - Electromagnetic: de-excitation yielding photons . . . gammas;
  - Weak:
    - $N \rightarrow N' + e^- + \bar{\nu}_e$
    - $N \rightarrow N' + e^+ + \nu_e$ ← the basis of PET.
  - Strong: e.g. α-decay; not of use for ND (NM).
- Isotopes have the same number of protons;
- Isotones have the same number of neutrons;
- Isobars have the same number of nucleons.

Nuclei and decay modes



The Karlsruhe Nuclide Chart

A nuclide chart is a two dimensional representation of the nuclear and radioactive properties of all known atoms. A nuclide is the generic name for atoms characterized by the constituent protons and neutrons. The nuclide chart arranges nuclides according to the number of protons (vertical axis) and neutrons (horizontal axis) in the nucleus. Each nuclide in the chart is represented by a box containing the element symbol and mass number, half-life, decay types and decay energies, etc.

"Magic" numbers

In nuclear physics, a magic number is a number of protons or neutrons (e.g. 2, 8, 20, 28, 50, 82, 126) which give rise to a complete shell in the atomic nucleus. Lead 208 for example, which consists of 82 protons and 126 neutrons, is called "doubly magic" since both the proton and neutron numbers are "magic".

Black squares represent stable atoms. Other colours indicate the modes of radioactive decay, e.g. by emission of alpha particles (α), beta particles (β), neutrons (n), etc.

`https://www.epj-n.org/articles/epjn/full_html/2019/01/epjn180014/epjn180014.html`

β decay

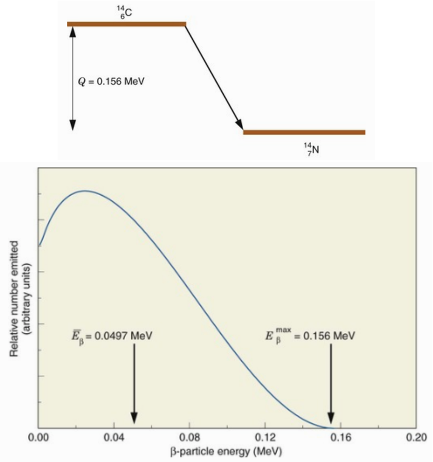
Underlying process: $n \rightarrow p + e^- + \bar{\nu}_e$

$$ {}^A_Z X \xrightarrow{e^-(\beta^-)} {}_{Z+1}^{\;\;A} Y $$

$$ {}^A_Z X + e^- \rightarrow {}_{Z+1}^{\;\;A} Y + e^- + \bar{\nu}_e $$

Kinematics requires neutral atoms, hence e^- on LHS.

Continuous electron-energy spectrum due to 3-body decay.



(β, γ) decay

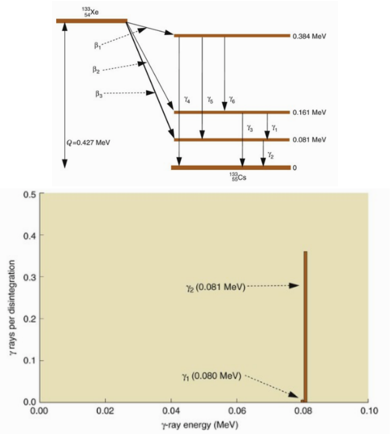
β absorbed in short distance; no use for ND (NM).
Exploit de-excitation γs.

$$ {}^{A}_{Z}X \xrightarrow{\beta^-} {}^{\;\;\;A}_{Z+1}Y^* \xrightarrow{\gamma} {}^{\;\;\;A}_{Z+1}Y $$

β-decay leaves Y in excited state—indicated by ‘$*$’.

Discrete photon energy or energies.

Electron from β decay absorbed in tissue.



Isomeric transition (IT)

Daughter nuclide produced in long-lived, 'metastable' state.
Again, exploit de-excitation γs.

$$ {}^{A}_{Z}X \xrightarrow{\beta^-} {}^{Am}_{Z+1}Y \xrightarrow{\gamma} {}^{A}_{Z+1}Y $$

β-decay leaves Y in metastable excited state—indicated by 'm'.

Discrete photon energy or energies.

IT identical to decay by γ production, except that lifetime is much longer.

Important example:

$$ {}^{99}Mo \xrightarrow{\beta^-} {}^{99m}Tc \xrightarrow{\gamma} {}^{99}Tc $$

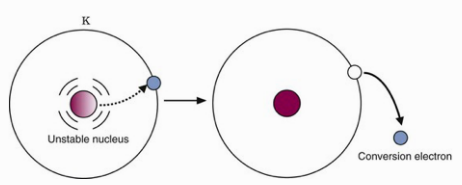
$\tau_{1/2}$ = 66 hrs $\tau_{1/2}$ = 6 hrs

Halflife of ^{99}Tc is 211 millennia:

- Decay rate of ^{99}Tc is low; but
- Clearly important to ensure 'waste' radionuclide is excreted.

Internal conversion (IC)

$$^{A}_{Z}X^{*} \xrightarrow{\text{IC}} {}^{A}_{Z}X + e$$



Nucleus in an excited state or a meta-stable excited state may decay such that:

- Energy from nuclear is transition transferred to orbital electron which is emitted;
- Electron emitted has an energy typical of a nuclear transition;
- Orbital vacancy is filled creating characteristic X-rays or Auger electrons.

In a sense, the γ that might have been emitted is ‘internally converted’ into an electron.

Positron emission

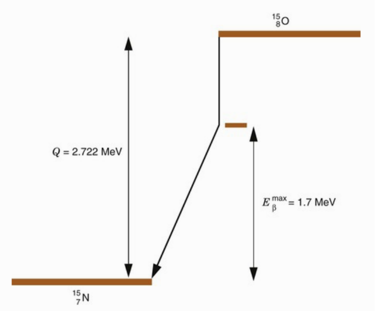
Underlying process: $p \rightarrow n + e^+ + \nu_e$

$$^A_Z X \xrightarrow{e^+(\beta^+)} {}_{Z-1}^{\;\;A}Y$$

$$^A_Z X \rightarrow {}_{Z-1}^{\;\;A}Y + e^- + e^+ + \nu_e$$

Kinematics requires neutral atoms,
hence e^- on RHS.
[Orbital electron ‘lost’ from atom after decay]

Continuous electron-energy spectrum due to 3-body decay.



$$\begin{aligned} Q &= 2.72\,\mathrm{MeV} \\ &= 2m_e c^2 + E_\beta^{\mathrm{max}} \\ &= 1.022\,\mathrm{MeV} + 1.7\,\mathrm{MeV} \end{aligned}$$

Summary of section 2

Radiopharmaceuticals are designed to deliver radio-isotopes to particular locations in the body

Emission imaging requires that the radionuclide produces penetrating radiation (γ-rays)

Decay modes exploited in ND (NM):

- Beta decay – especially β^+ decay
- (β, γ) decay
- Isomeric transition (IT)
- Internal conversion (IC)

Section 3

Revision of theory of nuclear decay

Radioactive decay

Observation:

"Activity", $A =$ number of disintegrations per second, decays exponentialy with time

So, if there are N nuclei at time t:

$$N(t) = N(0)\exp(-\lambda t) \qquad \ldots \text{ and so } \ldots \qquad \frac{dN}{dt} = -\lambda N$$

λ is the decay constant. The "lifetime", τ, and "halflife", $t_{\frac{1}{2}}$, are related to λ by:

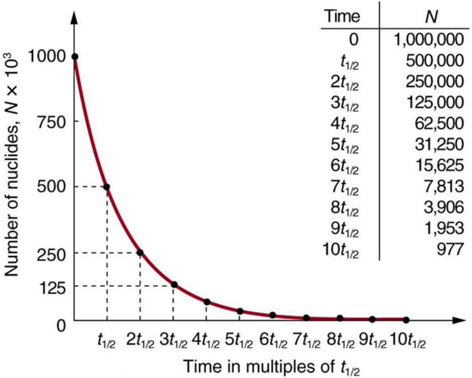
$$\tau = \frac{1}{\lambda} \qquad \ldots \text{ and } \ldots \qquad t_{\frac{1}{2}} = \frac{\ln(2)}{2}\tau = \frac{\ln(2)}{2}\frac{1}{\lambda}$$

The observation implies that the chance that a nucleus will decay per unit time is constant and is given by λ

Activity

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

- SI unity of activity: Becquerel (Bq):
  - $1\,\mathrm{Bq} = 1$ decay per second
- Curie (Ci):
  - $1\,\mathrm{Ci} = 3.7 \times 10^{10}\,\mathrm{Bq}$



Time	N
0	1,000,000
$t_{1/2}$	500,000
$2t_{1/2}$	250,000
$3t_{1/2}$	125,000
$4t_{1/2}$	62,500
$5t_{1/2}$	31,250
$6t_{1/2}$	15,625
$7t_{1/2}$	7,813
$8t_{1/2}$	3,906
$9t_{1/2}$	1,953
$10t_{1/2}$	977

`https://courses.lumenlearning.com/physics/chapter/31-5-half-life-and-activity/`

Branching ratio

Decay constant, λ, determines the decay rate. The 'lifetime', τ is defined to be:

$$\tau = \frac{1}{\lambda} \qquad \ldots \text{ and so } \ldots \qquad \lambda = \frac{1}{\tau}$$

The decay rate for the transition of X into Y may be calculated using "Fermi's Golden Rule":

$$\lambda_{X \to Y} = \eta \left| M_{X \to Y} \right|^2 \rho_f$$

Where η is a constant and ρ_f is the density of final states. $M_{X \to Y}$ is the quantum-mechanical 'matrix element' for the transition $X \to Y$. Some radionuclides may decay via more than one route. For such nuclei:

$$\lambda_T = \lambda_{X \to Y} + \lambda_{X \to Z} + \cdots = \sum_i \lambda_i$$

λ_T is the 'total decay rate' (sometimes referred to as 'total width'). The λ_i are the 'partial' decay rates, or 'partial widths'.

Branching ratios; an additional constraint

'Branching ratio' (BR): fraction of all decays that result in a particular final state:

$$BR = \frac{\lambda_{X \to Y}}{\lambda_T}$$

Decay chain may include beneficial radiation, suitable for imaging, and harmful radiation.

Example: ^{131}I decay — $^{131}\mathrm{I}(e^-, \gamma)^{131}\mathrm{Xe}$

- Some γs in useful range for imaging, but
- e^- and low-energy γs simply deposit dose.

Has application in therapy, e.g., thyroid tumours.

Not widely used today for imaging.

So, consider ^{123}I, which decays via EC.

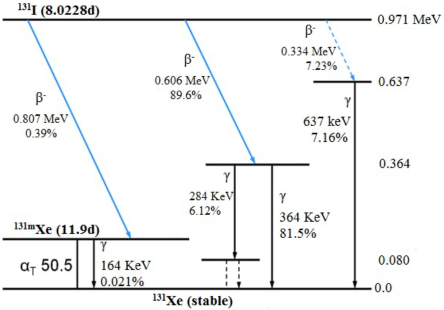


Figure from https://www.researchgate.net/publication/295919808_Radioiodine_I-131_for_Diagnosing_and_Treatment_of_Thyroid_Diseases

Parent-daughter decay chain

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

Rate of ‘decay’of daughter nuclei:

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

I.e.:

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

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:

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

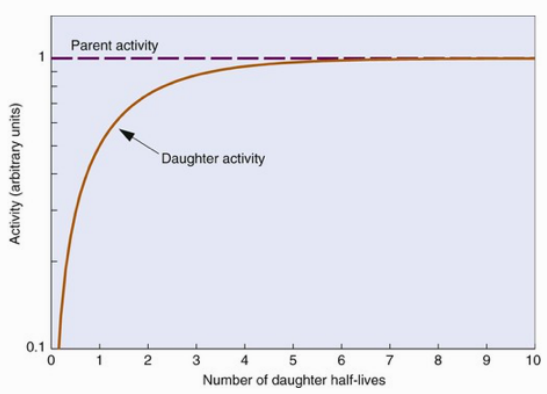
$T_P >> T_D$; secular equilibrium

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

So, equation 1 becomes:

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

If $A_{D0} = 0$ and $\beta = 1$, then the build up of N_D reaches ‘secular equilibrium after 5–6 T_D.



$T_P > T_D$; transient equilibrium

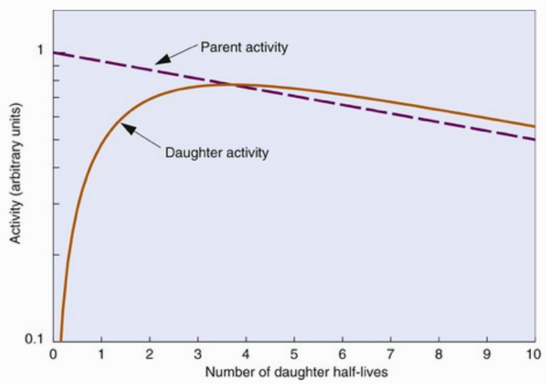
Transient equilibrium occurs at $t_{\rm eq}$ given by:

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

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

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

If $A_{D0} = 0$, $\beta = 1$, and $T_D = 0.1\,T_P$, then build up and decay of N_D reaches 'transient equilibrium' after $\sim 2.6\,T_D$.



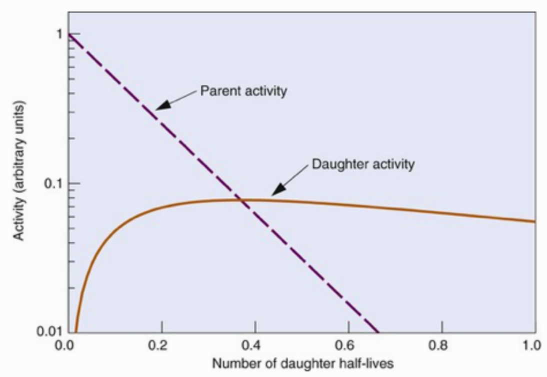
$T_P < T_D$; no equilibrium

Maximum activity of daughter is still given by:

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

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

If $A_{D0} = 0$, $\beta = 1$, and $T_D = 10\,T_P$, then build up of N_D reaches maximum activity at $\sim 0.26\,T_D$.



Summary of section 3

Radioactive decay law:

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

implies that chance that a nucleus will decay per unit time is λ

Branching ratio for decay $X \rightarrow Y$: $\mathrm{BR} = \frac{\lambda_{X\rightarrow Y}}{\lambda_T}$

Can solve for evolution of samples of parent, daughter, grand-daughter, etc. in decay chain and distinguish between:

- Secular equilibrium for $T_P >> T_D$
- Transient equilibrium for $T_P > T_D$
- No equilibrium for $T_P < T_D$