Nuclear Medicine: Physics and Imaging Methods (SPECT and PET)

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Based on Prince and Links, Medical Imaging Signals and Systems and Lecture Notes by Prince. Figures are from the book.
Lecture Outline

• Nuclide Imaging Overview
• Physics of Radioactive Decay
• Single Photon Emission Computed Tomography (SPECT)
• Positron Emission Tomography (PET)
• Image Quality consideration
  – Resolution, noise, SNR, blurring
• Image Reconstruction Problems as Solving Linear Equations
  – Least squares
  – POCS
  – Maximum likelihood
  – Sparse reconstruction
What is Nuclear Medicine

- Also known as nuclide imaging
- Introduce radioactive substance into body
- Detect regional variations of radioactivity as indication of presence or absence of specific physiologic function
  - Tumors may disrupt the normal decay process
  - Blockage in a blood vessel may affect the distribution
- Detection by “gamma camera” or detector array

From H. Graber, Lecture Note for BMI1, F05
Examples: PET vs. CT

- **X-ray projection and tomography:**
  - X-ray transmitted through a body from a outside source to a detector (transmission imaging)
  - Measuring anatomic structure

- **Nuclear medicine:**
  - Gamma rays emitted from within a body (emission imaging)
  - Imaging of functional or metabolic contrasts (not anatomic)
    - Brain perfusion
    - Myocardial perfusion
    - Tumor detection (metastases)

From H. Graber, Lecture Note, F05
Atomic Structure

- An atom={a nucleus, electrons}
- nucleons = {protons; neutrons}
- Nuclide: unique combination of protons and neutrons in a nucleus
- mass number $A = \# \text{ nucleons}$
- atomic number $Z = \# \text{ protons} = \# \text{ electrons}$
- An element is denoted by its $A$ and $Z$
  - Ex: $^{12}_6 C$ or C-12
Stable vs. Unstable Nuclides

• Stable nuclides:
  – $\# \text{ neutrons} \sim \# \text{ protons} \ (A \sim 2Z)$ when $Z$ is small
  – $\# \text{ neutrons} > \# \text{ protons}$ when $Z$ is large

• Unstable nuclides (radionuclides, radioactive atoms)
  – Likely to undergo radioactive decay, which gives off energy and results in a more stable nucleus
Line of Stability

- Nuclides divide into two groups:
  - Non-radioactive — i.e., stable atoms
  - Radioactive — i.e., unstable atoms

- “Line” of stability:

Stability depends on ratio $Z/N$
Isotopes, etc

- **Isotopes**: atoms with the same Z but different A
  - E.g. C-12 and C-11
  - Chemically identical
- **Isobars**: atoms with the same A but different Z
  - Different elements
  - E.g. Carbon-11 and boron-11
- **Isotones**: atoms with the same number of neutrons but different A
- **Isomers**: atoms with the same Z and A but with different energy levels (produced after gamma decay)
What is Radioactivity?

- Radioactive decay: rearrangement of nuclei to lower energy states = greater mass defect
- Parent atom decays to daughter atom
- Daughter has higher binding energy/nucleon than parent
- A radioatom is said to decay when its nucleus is rearranged
- A disintegration is a radioatom undergoing radioactive decay.
- Energy is released with disintegration.
Decay Modes

- Four main modes of decay:
  - alpha particles (2 protons, 2 neutrons)
  - beta particles (electrons)
  - positrons (anti-matter electrons)
  - isomeric transition (gamma rays produced)
- Medical imaging is only concerned with:
  - positrons (PET), and
  - gamma rays (scintigraphy, SPECT)
Alpha Decay

- Alpha decay: the nucleus emits a Helium-4 particle (alpha particle)
  - Alpha decay occurs most often in massive nuclei that have a proton to neutron ratio too large. Alpha radiation reduces the ratio of protons to neutrons in the parent nucleus, bringing it to a more stable configuration.
  - mostly occurring for parent with $Z > 82$

From: http://www.lbl.gov/abc/wallchart/chapters/03/1.html
Beta Decay

- Beta decay occurs when, in a nucleus with too many protons or too many neutrons, one of the protons or neutrons is transformed into the other.
- Mass number $A$ does not change after decay, proton number $Z$ increases or decreases.
- Beta minus decay (or simply Beta decay): A neutron changes into a proton, an electron (beta particle) and an antineutrino.

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html
Positron Decay

- Also known as Beta Plus decay
  - A proton changes to a neutron, a positron (positive electron), and a neutrino

\[ p \ (\text{proton}) \rightarrow n \ (\text{neutron}) + \beta^+ \ (\text{positron}) + \nu \ (\text{neutrino}) \]

- Mass number \( A \) does not change, proton number \( Z \) is reduced

From: http://www.lbl.gov/abc/wallchart/chapters/03/2.html
Mutual Annihilation after Positron Decay

- The positron later annihilate a free electron, generate two gamma photons in opposite directions
  - The two photons each have energy 511 KeV, which is the energy equivalent to the rest mass of an electron or positron
  - These gamma rays are used for medical imaging (Positron Emission Tomography), detected using a coincidence detection circuit
Gamma Decay (Isometric Transition)

- A nucleus (which is unstable) changes from a higher energy state to a lower energy state through the emission of electromagnetic radiation (photons) (called gamma rays). The daughter and parent atoms are isomers.
  - The gamma photon is used in Single photon emission computed tomography (SPECT)
- Gamma rays have same properties as X-rays, but are generated differently:
  - X-ray through energetic electron interactions
  - Gamma-ray through isometric transition in nucleus

From: http://www.lbl.gov/abc/wallchart/chapters/03/3.html
Measurement of Radioactivity

- **Radioactivity, \( A \), \# disintegrations per second**

\[
1 \text{ Bq} = 1 \text{ dps} \\
1 \text{ Ci} = 3.7 \times 10^{10} \text{ Bq}
\]

(Orig.: activity of 1 g of 226 Radium)

Naturally occurring radioisotopes discovered 1896 by Becquerel
First artificial radioisotopes produced by Curie 1934 (32P)

Inverse square law: The intensity of radiation incident on a detector at range \( r \) from a radioactive source is

\[
I = \frac{AE}{4\pi r^2}
\]

A: radioactivity of the material; E: energy of each photon

Bq = Becquerel (1 decay/sec)
Ci = Curie:
Radioactive Decay Law

- $N(t)$: the number of radioactive atoms at a given time
- $A(t)$: is proportional to $N(t)$

\[
A = -\frac{dN}{dt} = \lambda N
\]

$\lambda$: decay constant

- From above, we can derive

\[
N(t) = N_0 e^{-\lambda t} \\
A(t) = A_0 e^{-\lambda t} = \lambda N_0 e^{-\lambda t}
\]

- The number of photons generated (=number of disintegrations) during time $T$ is

\[
\Delta N = \int_{0}^{T} A(t) dt = \int_{0}^{T} \lambda N_0 e^{-\lambda t} dt = N_0 (1 - e^{-\lambda T})
\]
Half-Life

- Half-life is the time it takes for the radioactivity to decrease by \( \frac{1}{2} \).

\[
\frac{A_{t_{1/2}}}{A_0} = \frac{1}{2} = e^{-\lambda t_{1/2}}
\]

- It follows that

\[
t_{1/2} = \frac{0.693}{\lambda}
\]
Statistics of Decay

- The exponential decay law only gives the expected number (mean value) of atoms at a certain time $t$.
- The number of disintegrated atoms over a short time $\Delta t \ll T_{1/2}$ after time $t=0$ with $N_0$ atoms follows Poisson distribution

$$
\text{Pr}\{ \Delta N = k \} = \frac{a^k e^{-a}}{k!}; \quad a = \lambda N_0 \Delta t;
$$

$\lambda N_0$ is called the Poisson rate.

Strictly speaking

$$a = N_0 (1 - e^{-\lambda \Delta t})$$

When $\lambda \Delta t$ is small, $e^{-\lambda \Delta t} \approx 1 - \lambda \Delta t$, $a = N_0 \lambda \Delta t$
Radiotracers: Desired Property

- **Decay mode:**
  - Clean gamma decay: do not emit alpha or beta articles
  - Positron decay: positron will annihilate with electrons to produce gamma rays
- **Energy of photon:**
  - Should be high so that photons can leave the body w/ little attenuation
  - Hard to detect if the energy is too high
  - Desired energy range: 70-511 KeV
- **Half-life**
  - Should not be too short (before detector can capture) or too long (longer patient scan time)
  - Minutes to hours desired
- **Half-value-layer (HVL)**
  - Thickness of tissue that absorbs half of the radioactivity produced
  - Should be around the dimension of the organ to be imaged
- **Monoenergetic**
  - Energy sensitive detectors can discriminate the primary photons from scattered ones.
Decay Process Examples

$\alpha$ decay

$^{238}_{92}\text{U} \rightarrow ^{234}_{90}\text{Th} + ^4_2\text{He}, \quad T_{1/2} \approx 4.5 \times 10^9 \text{y}$

$\beta^-$ decay

$^{234}_{90}\text{Th} \rightarrow ^{234}_{91}\text{Pa} + e^- + \bar{\nu}_e, \quad T_{1/2} = 24.1 \text{d}$

$^0_1\text{n} \rightarrow ^1_1\text{H} + e^- + \bar{\nu}_e, \quad T_{1/2} = 10.6 \text{m}$

$\beta^+$ decay

$^{11}_6\text{C} \rightarrow ^{11}_5\text{B} + e^+ + \nu_e, \quad T_{1/2} = 20.38 \text{ m}$

$^{10}_6\text{C} \rightarrow ^{10}_5\text{B} + e^+ + \nu_e, \quad T_{1/2} = 19.2 \text{ s}$

$^{15}_8\text{O} \rightarrow ^{15}_7\text{N} + e^+ + \nu_e, \quad T_{1/2} = 122 \text{ s}$

$e^-$ capture

$^{41}_{20}\text{Ca} + e^- \rightarrow ^{41}_{19}\text{K} + \nu_e, \quad T_{1/2} \approx 1 \times 10^5 \text{y}$

Most of these naturally occurring processes are not useful for medical imaging applications, with too long half-time, too short HVL, too high energy.

They can be used as radiotherapeutic agents, if they can be targeted to tumors, to destroy diseased tissue and stops the cancer from proliferating.
Radionuclides in Clinical Use

- Most naturally occurring radioactive isotopes not clinically useful (long $T_{1/2}$, charged particle emission, alpha or beta decay)
- Artificial radioactive isotopes produced by bombarding stable isotopes with high-energy photons or charged particles

$\nu = -\rightarrow + +$

From H. Graber, Lecture Note, F05

- Nuclear reactors ($n$), charged particle accelerators (Linacs, Cyclotrons)

\[
^{99}\text{Mo} \quad ^{T_{1/2}=2.5\text{d}} \rightarrow ^{99m}\text{Tc} + e^- + \bar{\nu}
\]

Molybdenum \quad \text{Technetium}

From H. Graber, Lecture Note, F05
The Technetium Generator

- Can be produced from an on-site generator
  - $^{99}\text{Mo}$ (Molybdenum) $\rightarrow$ $^{99m}\text{Tc}$ (Technetium) $\rightarrow$ $^{99}\text{Tc}$,

- Decay characteristics of $^{99m}\text{Tc}$:
  - half life = 6.02h, $E=140$ keV, HVL=4.6 cm

$$^{99m}\text{Tc} \quad T_{1/2}=6\text{ h} \quad \rightarrow \quad ^{99}\text{Tc} \quad + \quad \gamma (140 \text{ keV})$$

- Used in more than 90% of nuclear imaging
- More detail: see [Webb, sec. 2.5]
Radiopharmaceuticals

- Radionuclide is bound to pharmaceuticals specific to metabolic activities (cancer, myocardial perfusion, brain perfusion)
- Gamma emitters
  - $^{99m}$Tc-Sestamibi (myocardial perfusion, cancer)
  - $^{99m}$Tc-labeled hexamethyl-propyleneamine (brain perfusion)
- Positron emitters
  - $^{11}$C, $T_{1/2} = 20$ min $[^{12}$C $(p, pn)$ $^{11}$C; $^{14}$N $(p, \alpha)$ $^{11}$C]:
    - many organic compounds (binding to nerve receptors, metabolic activity)
  - $^{13}$N, $T_{1/2} = 10$ min $[^{16}$O $(p, \alpha)$ $^{13}$N; $^{13}$C $(p, n)$ $^{13}$N]:
    - NH$_3$ (blood flow, regional myocardial perf.)
  - $^{15}$O, $T_{1/2} = 2.1$ min $[^{15}$N $(p, n)$ $^{15}$O; $^{14}$N $(d, n)$ $^{15}$O]:
    - CO$_2$ (cerebral blood flow), O$_2$ (myoc. O$_2$ consumption), H$_2$O (myoc. O$_2$ consumption & blood perfusion)
  - $^{18}$F, $T_{1/2} = 110$ min $[^{18}$O $(p, n)$ $^{18}$F; $^{20}$Ne $(d, \alpha)$ $^{18}$F]:
    - 2-deoxy-2-[$^{18}$F]-fluorogluucose (FDG, neurology, cardiology, oncology, metabolic activity)

From H. Graber, Lecture Note, F05
Common Radiotracers

- Gamma Ray Emitters:
  - Iodine-123 (13.3 h, 159 keV)
  - Iodine-131 (8.04 d, 364 keV)
  - Iodine-125 (60 d, 35 keV) (Bad. Why?)
  - Thallium-201 (73 h, 135 keV)
  - Technetium-99m (6 h, 140 keV)

- Positron Emitters:
  - Fluorine-18 (110 min, 202 keV)
  - Oxygen-15 (2 min, 696 keV)
Summary of Physics

• Radioactive decay is the process when a unstable nuclide is changed to a more stable one
  – Four modes of decay, generating alpha particles, beta particles, positrons and gamma rays respectively
  – Medical imaging exploits positron decay and gamma rays
• Radioactivity follows an exponential decay law in time, characterized by the decay constant or the half-life
• Desired properties for radio tracers
• Common radiotracers in nuclear medicine
Overview of Nuclear Imaging Modalities

- **Planar Scintigraphy**
  - Use radiotracers that generate gamma decay, which generates one photon in random direction at a time
  - Capture photons in one direction only, similar to X-ray, but uses emitted gamma rays from patient
  - Use an Anger scintillation camera

- **SPECT (single photon emission computed tomography)**
  - Use radiotracers that generate gamma decay
  - Capture photons in multiple directions, similar to X-ray CT
  - Uses a rotating Anger camera to obtain projection data from multiple angles

- **PET (Positron emission tomography)**
  - Uses radiotracers that generate positron decay
  - Positron decay produces two photons in two opposite directions at a time
  - Use special coincidence detection circuitry to detect two photons in opposite directions simultaneously
  - Capture projections on multiple directions

- **Will focus on SPECT and PET only**
SPECT Instrumentation

- Similar to CT, uses a rotating Anger camera to detect photons traversing paths with different directions.
- Must use collimators so that each detector only detects photons in a straight line parallel with the collimator wall.
- Recent advances uses multiple Anger cameras (multiple heads), reducing scanning time (below 30 minutes).
- Anger cameras in SPECT must have significantly better performances than for planar scintigraphy to avoid reconstruction artifacts.
A typical SPECT system

Fig. 9.1 A dual head system
Anger Scintillation Camera

- Absorb scattered photons
- Convert detected photons to lights
- Convert light to electrical currents
- Compute the location with highest activity
- Compare the detected signal to a threshold
- Absorb scattered photons
Collimators

(a) Parallel hole
(b) Converging hole (magnifies)
(c) Diverging hole (minifies)
(d) Pin-hole (2–5 mm)
Imaging Equation when $\theta = 0$

$$\phi(z, \ell) = \int_{-\infty}^{R} \frac{A(x, y, z)}{4\pi(y - R)^2} \exp \left\{ - \int_y^R \mu(x, y', z; E) \, dy' \right\} \, dy$$

Replace $x$ by $l$.
Examples

• Example 1: Imaging of a slab
• Example 2: Imaging of a two-layer slab

• Go through on the board
General Case: Imaging Geometry

Note: correction to Fig. 9.8

\[ x(s) = \ell \cos \theta - s \sin \theta \]
\[ y(s) = \ell \sin \theta + s \cos \theta \]
General Case: Imaging Equation

\[ \phi(\ell, \theta) = \int_{-\infty}^{R} \frac{A(x(s), y(s))}{4\pi(s - R)^2} \exp \left\{ -\int_{s}^{R} \mu(x(s'), y(s'); E) ds' \right\} ds \]

Note: There should be some constant in front of the integral. See textbook
Example 1

- Imaging of a rectangular region, with the following structure. Derive detector readings in 4 positions (A, B, C, D)

Do you expect the reading at B and D be the same? What about at A and C?
How to Reconstruct $A(x,y)$?

Two unknowns: $A(x,y)$, $\mu(x,y)$

Inverse square law effect: $A(x,y)$ is weighted differently in different detector readings ($s$ depends on $l, \theta$)

$$
\phi(l, \theta) = \int_{-\infty}^{R} \frac{A(x(s), y(s))}{4\pi(s - R)^2} \exp \left\{ -\int_{s}^{R} \mu(x(s'), y(s'); E) \, ds' \right\} \, ds
$$
Approximation for Reconstruction

- Bold approximations: ignore attenuation, inverse square law, and scale factors:
  \[
  \phi(\ell, \theta) = \int_{-\infty}^{\infty} A(x(s), y(s)) ds
  \]

- Under this assumption, the measurements \(\phi(\ell, \theta)\) are the Radon transform of \(A(x,y)\)!
- \(A(x,y)\) can be reconstructed using the reconstruction methods for CT (e.g. convolution backprojection or filtered backprojection)
- The filter cut-off frequency needs to be chosen properly to balance between removing noise and blurring
- Commonly used filter in frequency domain

\[
C(\rho) = |\rho| W(\rho), W(\rho) = \sqrt{\frac{1}{1 + \left(\frac{\rho}{\rho_c}\right)^{2n}}}
\]

F16
Yao Wang @ NYU
Correction for Attenuation Factor

• Use CT imaging to generate an estimate of the tissue \( \mu \) at each location, before radiotracer is introduced or before significant radioactive decay starts

• Based on the estimate of \( \mu(x,y) \), derive the correction factor \( a(x,y) \)
  
  – Assuming \( A(x,y)=1 \) everywhere. Numerically compute the expected measurement \( \varphi(l,\theta) \) based on the estimated \( \mu(x,y) \) using the forward model, which can be thought of as the Randon transform of \( a(x,y) \). Solve \( a(x,y) \) by performing inverse Randon transform on \( \varphi(l,\theta) \)

  – Recover \( A_0(x,y) \) from the real detector readings assuming the readings are sum of \( A_0(x,y) \) along all projection lines \( (l,\theta) \). Call

  – Then correct by \( A(x,y)=A_0(x,y)/a(x,y) \)

  – See textbook for more detail (only in the 2\textsuperscript{nd} edition, pp 307-309)
CT/SPECT Imaging

• Obtaining CT and SPECT measurement successively while the patient is inside the imaging apparatus
  – CT before radionuclide injection
  – SPECT after
  – Reconstruct \( \mu(x,y) \) from CT measurement
  – Reconstruct \( A(x,y) \) with correction based on \( \mu(x,y) \)
  – Patient must stay as stationary as possible to avoid misregistration

• Simultaneous display of \( \mu(x,y) \) and \( A(x,y) \) images can provide more useful information!
  – CT: provides high resolution anatomical information
  – SPECT: Low resolution functional imaging
Figure 3.17

(Left) A SPECT/CT system using a shared bed for the patient. (Right) A commercial system. There are two gamma cameras, one above and one below the patient, and a circular entry for the multi-detector CT.

From [Smith&Webb]
Table 3.1: Properties of common radiotracers used in planar scintigraphy and SPECT

<table>
<thead>
<tr>
<th>Radiotracer</th>
<th>Half-life (hours)</th>
<th>γ-ray energy (keV)</th>
<th>Clinical application</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>6.0</td>
<td>140</td>
<td>various</td>
</tr>
<tr>
<td>$^{67}$Ga</td>
<td>76.8</td>
<td>93, 185, 300, 394</td>
<td>tumour detection</td>
</tr>
<tr>
<td>$^{201}$Tl</td>
<td>72</td>
<td>167, 68–82 (X-rays)</td>
<td>myocardial viability</td>
</tr>
<tr>
<td>$^{133}$Xe</td>
<td>127.2</td>
<td>81</td>
<td>lung ventilation</td>
</tr>
<tr>
<td>$^{111}$In</td>
<td>67.2</td>
<td>171, 245</td>
<td>inflammation</td>
</tr>
</tbody>
</table>

From [Smith&Webb]
SPECT applications

- Heart (most used):
  - Coronary artery disease
  - Myocardial infarcts
- Brain:
  - Perfusion (stroke, epilepsy, schizophrenia, dementia [Alzheimer])
  - Tumors
- Respiratory
- Liver
- Kidney

• From Graber, Lecture Slides for BMI1,F05
• See Webb Sec. 2.10
PET Principle

- Positron emitters
- Positron annihilation:
  - short distance from emission
  - produces two 511 keV gamma rays
  - gamma rays 180° opposite directions
- Principle: detect coincident gamma rays
Annihilation Coincidence Detection

- Detect two events in opposite directions occurring “simultaneously”
- Time window is 2-20 ns, typically 12 ns
- No detector collimation is required
  - Higher sensitivity
The principle of annihilation coincidence detection. (left) The two $\gamma$-rays reach detectors 2 and 10, triggering respective logic pulses of length $\tau$. (right) If both logic pulses are sent to the coincidence detector within the system coincidence resolving time $2\tau$, then the summed signal lies above the threshold value (dashed line) and a coincidence is recorded.
Detected PET Events

- True
- Scattered
- Random
Coincidence Timing

- Three classes of events
  - true coincidence
  - scattered coincidence
  - random coincidence
- Sensitivity in PET
  - measures capability of system to detect “trues” and reject “randoms”
A Typical PET Scanner
3D Scanner has higher SNR because it does not reject photons through septal collimators. But must have more sophisticated mechanism to deal with false coincidences. Majority of commercial systems are 3D.
Imaging Equation

See derivation in the textbook (2\textsuperscript{nd} ed, pp 309-312)!

\[
\phi(l, \theta) = K \int_{-R}^{R} A(x(s), y(s)) \exp\left\{- \int_{-R}^{R} \mu(x(s'), y(s')) ds'\right\} ds
\]

\[
= K \int_{-R}^{R} A(x(s), y(s)) ds \cdot \exp\left\{- \int_{-R}^{R} \mu(x(s'), y(s')) ds'\right\}
\]

\(A(x, y)\) and \(\mu(x, y)\) can be separated!
Example 2

- Imaging of a rectangular region, with the following structure. Derive detector readings in 2 paired positions (A-C, B-D)
**Attenuation Correction**

- Corrected sinogram
  \[
  \phi_c(\ell, \theta) = \frac{\phi(\ell, \theta)}{K \exp \left\{ - \int_R^R \mu(x(s), y(s); E) \, ds \right\}}
  \]

- \(\mu(x, y)\) found from CT (transmission PET)

  - One can apply filtered backprojection algorithm to reconstruct \(A(x,y)\) from the corrected sinogram \(\phi_c(l,\theta)\)
  - Difference from SPECT:
    - Attenuation correction much easier!
  - Can we directly use the CT measurement or reconstructed \(\mu(x,y)\) by CT for correction?
Attenuation Correction (2)

- CT uses X-rays at different energy (e.g. E1 roughly 80-140 KeV) than PET scan (e.g. E2=511KeV)
- One cannot use the CT measurement or reconstructed $\mu(x,y)$ for correction, because $\mu(x,y)$ is energy dependent!
- The reconstructed $\mu(x,y; E1)$ image is segmented into a number of tissue types (muscle, lipid, bone), to which standard values of $\mu$ at $E2=511KeV$ are assigned.
- Based on the segmented image with assigned $\mu$ values, $\mu(x,y; E2)$, correction factors can be numerically generated.
- The CT-based attenuation map is smoothed to match PET resolution before calculating the correction factor.
- PET scan takes quite long during which the patient may have natural cardiac or breathing motion. The two reconstructed images need to be registered before using CT-based attenuation map for correction of PET measurement.
Reconstruction from Corrected Sinogram

- Convolution backprojection yields $A(x, y)$

$$A_c(x, y) = \int_0^\pi \int_{-\infty}^{\infty} \phi_c(\ell, \theta) \tilde{c}(x \cos \theta + y \sin \theta - \ell) \, d\ell \, d\theta$$
All commercial PET systems sold are now combined CT/SPECT scanners!

Overlaying the two reconstructed images can provide more info than each alone!
PET applications

• Brain:
  – Tumor detection
  – Neurological function (pathologic, neuroscience app.)
  – Perfusion

• Cardiac
  – Blood flow
  – Metabolism

• Tumor detection (metastatic cancer)

• From H. Graber, lecture slides for BMI1,F05
• See Webb Sec. 2.11.7
Radiotracers for PET (Except $^{82}$Rb) must be synthesized on site using a cyclotron
FDG is used in 80% of PET studies

Bio-chemical research: Design of radio tracers to reveal different types of medical problems

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life (minutes)</th>
<th>Radiotracer</th>
<th>Clinical applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F</td>
<td>109.7</td>
<td>$^{18}$FDG</td>
<td>oncology, inflammation, cardiac viability</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>20.4</td>
<td>$^{11}$C-palmitate</td>
<td>cardiac metabolism</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>2.07</td>
<td>$^{15}$O</td>
<td>cerebral blood flow</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.96</td>
<td>$^{13}$NH$_3$</td>
<td>cardiac blood flow</td>
</tr>
<tr>
<td>$^{82}$Rb</td>
<td>1.27</td>
<td>$^{82}$RbCl$_2$</td>
<td>cardiac perfusion</td>
</tr>
</tbody>
</table>
PET Application: See and Hear

The PET scan on the left shows two areas of the brain (red and yellow) that become particularly active when volunteers read words on a video screen: the primary visual cortex and an additional part of the visual system, both in the back of the left hemisphere. Other brain regions become especially active when subjects hear words through ear-phones, as seen in the PET scan on the right.

Marcus E. Raichle, M.D., Washington University School of Medicine in St. Louis
PET evolution

From H. Graber, lecture slides for BMI1,F05
Image Quality Consideration

- We will consider the following for scintigraphy, SPECT, and PET together
  - Resolution: collimator, detector intrinsic
  - Noise
  - SNR
- Read: Sec. 8.4 in Textbook
Limit of PET Resolution

- The positron will travel a random distance before it is annihilated by an electron.
- The reconstructed image shows the radioactivity at the annihilation site, but the site where positron is produced.
- Inherent limit of PET resolution: cannot be less than the mean traveling range!
- Long range (hence low resolution) with high energy positron and less dense tissue.

$^{18}$F (640 keV, 0.2 mm), $^{11}$C (960 keV, 0.4 mm), $^{13}$N (1.2 MeV, 0.6 mm), $^{15}$O (1.7 MeV, 1 mm), and $^{82}$Rb (3.15 MeV, 2.6 mm),
Relation between True Image and Reconstructed Image in SPECT/PET

● Approximation:

\[ \hat{f}(x, y) = f(x, y) \ast h(r) \]

● In SPECT, \( h(r) \) includes:
  – collimator and intrinsic resolutions
  – ramp filter window effect

● In PET, \( h(r) \) includes:
  – the positron range function
  – detector width effects
  – ramp filter window effect
PET vs. SPECT

• PET has much higher SNR and resolution because
  – Not using collimator (hence higher signal strength)
  – Reduced attenuation of higher energy photons (511 vs. 140 KeV) by tissue
  – Use of complete ring of detector
  – PET reconstruction is not affected by larger attenuation deep inside the body as is with SPECT =>PET reconstruction has same resolution/accuracy throughout the body, but SPECT has low resolution/accuracy deeper inside the body
  – PET has higher spatial resolution (8mm vs 15 mm)

• Faster imaging with PET

• PET is more expensive and bulky (need an on site cyclotron to produce positron emitting radiotracers)
Formulation of Reconstruction Problem as Solving a Linear Equation

- Reconstruction algorithms discussed so far assume the measured data are Radon transform (line integral) of the unknown image or some weighted versions of the unknown image pixels.
- Measurements in practical systems may not follow the assumed relations exactly, especially the assumed weighting factors.
- More general modeling

\[ g_k = \sum_i a_{ik} f_i; \]

- Matrix representation

\[ Af = g; \text{ or } A_k^T f = g_k, k = 1, 2, \ldots, K \]

\( f_i \): Unknown image pixel value at pixel i, \( g_k \): measurement by detector k, \( a_{ik} \) depends on the imaging modalities
Pop Quiz

• What are $f_i$ and $a_{ik}$ for different imaging systems (CT, SPECT, PET)?
Least squares solution

- When the number of measurements $\geq$ Number of pixels, we want to solve $f$ so that it satisfies all the equations with minimal sum of squared errors 

$$E(f) = \sum_k \left( A_k^T f - g_k \right)^2 = \left\| Af - g \right\|^2 = (Af - g)^T(Af - g)$$

- Closed form solution for minimizing the above error (obtained by setting the derivative with respect to $f$ to zero):

$$f = (A^T A)^{-1} A^T g$$

- Direct inverse is not feasible if the number of image pixels and the number measurements are very large.

- Iterative algorithms: Solving the matrix equation iteratively based on a given criterion (not necessarily least squares)
Gradient Descent Algorithms for Least Squares Solution

- Least squares problem is an optimization problem:
  \[ E(f) = \| Af - g \|^2 = (Af - g)^T (Af - g) \]

- Gradient descent
  \[ f = \arg \min E(f); \]
  \[ f^{t+1} = f^t - \alpha \frac{\partial E}{\partial f} \bigg|_{f^t} \]
  \[ \frac{\partial E}{\partial f} = A^T (Af - g) \]

Starting with an initial solution \( f^0 \), iteratively update

At iterative \( t \), compare the error before the update \( E^t \) and after update \( E^t \).

IF error reduction ratio is sufficiently small, e.g. \( \frac{E^t - E^{t+1}}{E^t} < T \), stop.

- Guaranteed to converge to global minimum because the energy function is a convex function of \( f \)
POCS (Projection onto convex set)

• General idea: If f is known to lie in some convex sets, one can iteratively project the current f to each convex set successively. The iteration will converge to the intersection of all convex sets! And if the intersection is non-empty, it will go to the point on the intersection that is closest to the initial solution.

• Common convex constraints: positivity, norm, linear constraint, etc.

POCS for Linear Equations

Treat each measurement as setting a convex set constraint:
$$A_k^T f = g_k \quad (A_k^T \text{ is k-th row of matrix } A)$$

Projection of $f^t$ to the k-th set: $$f^{t+1} = f^t - \frac{A_k^T f^t - g_k}{A_k^T A_k} A_k$$

Proof:
$$A_k^T f^{t+1} = A_k^T f^t - \frac{A_k^T f^t - g_k}{A_k^T A_k} A_k^T A_k = g_k$$

This particular solution is known as the Kaczmarz method. But POCS is more general and can handle many other convex constraints!

For example, if it is known that each component in $f$ lies in a certain range, one can simply clip $f$ to that range after the update above.
Maximum Likelihood Estimate

• Why minimize the sum of square errors?

Assume the detector readings are noisy. Correct readings should be $A_k^T f$. Actual readings are $g_k$.

Errors are $e_k = A_k^T f - g_k$.

If the error at each detector follows a Gaussian distribution with mean=0, variances=$\sigma_k^2$, and detector errors at different detectors are independent. The probability density function for the errors are: $p(e_k, k=1,\ldots,K) = \Lambda \exp\left\{ -\sum_k e_k^2 / \sigma_k^2 \right\}$.

Maximum likelihood estimator determines $f$ by maximizing the above probability, which is equivalent to minimizing its negative logarithm, which is

$$J(f) = -\log p(e_k, k=1,\ldots,K) = \sum_k e_k^2 / \sigma_k^2 = \sum_k (A_k^T f - g_k)^2 / \sigma_k^2$$

If all detectors are equally reliable, i.e. $\sigma_k^2$ are constant, then the above objective function is exactly the same as the sum of squared error!

When we know about the noise variance of each detector, we should minimize the above weighted error!

In CT, PET, SPET, the detector measures the number of incoming photons, which actually follows a Poisson distribution. The log likelihood function is not the sum of weighted squared errors. See the textbook for the solution for this case.
Using Prior Information

- Sometimes we have prior knowledge about certain properties of \( f \). We can incorporate such knowledge in the energy function to be minimized, or simply add the knowledge as explicit constraint to solve a constrained optimization problem. Such prior constraints are particularly important if the equation is under determined (i.e. number of unknowns or pixels < number of measurements).

- Popular approach: Assume the image to be reconstructed is sparse in the wavelet transform domain, and minimize the following energy function

\[
\min \| Af - g \|_2^2 + \lambda \| Tf \|_0
\]

\( \| Tf \|_0 \) is the L0 norm of \( Tf \), which is the number of non-zero transform coefficients. Directly minimizing the above non-convex energy function is hard. Instead of using the L0 norm, we can relax it to the L1 norm, and solve the following convex optimization problem:

\[
\min \| Af - g \|_2^2 + \lambda \| Tf \|_1
\]

Many iterative algorithms have been developed to solve the above problem, or similar problems. Generally, when the number of measurement is less than the number of unknowns and we use the prior information together with the measure information to solve \( f \) is known as "Compressive Sensing".
Summary of Nuclear Imaging Principles

- Three major imaging modalities:
  - Planar scintigraphy
  - SPECT
  - PET
- Principle of Anger camera: collimator, scintillation crystal, photomultiplier
- Imaging principles of planar scintigraphy and SPECT
  - Both based on gamma decay
  - Very similar to X-ray projection and CT, except for the attenuation factor
  - Combined SPECT/CT systems
- Imaging principle of PET:
  - Coincidence detection: detect two photons reaching two opposite detectors simultaneously (within a short time window)
  - Detected signal is the product of two terms, depending on the radioactivity $A(x,y)$ and attenuation $\mu(x,y)$ separately
  - The measurement can be corrected based on known $\mu(x,y)$
  - $A(x,y)$ can be reconstructed using convolution or filtered backprojection on the corrected measurement
  - Combined PET/CT systems
Reference

- Prince and Links, Medical Imaging Signals and Systems, Chap 7,8,9.
  - Section on attenuation correction for SPECT and PET reconstruction are revised in 2nd ed.
  - New section added on Iterative Image Reconstruction
- A. Webb, Introduction to Biomedical Imaging, Chap. 2
  - Sec. 2.5 for Technetium generation; Sec. 2.10, Sec. 2.11.7 for Clinical applications of nuclear medicine.

- Other recommended readings:
  - M. Reivich and A. Alavi (Eds.), *Positron Emission Tomography* (A. R. Liss, NY, 1985).
Homework

• Reading:
  – Prince and Links, Medical Imaging Signals and Systems, Ch. 7, 8,9.
• Note down all the corrections for Ch. 7,8,9 on your copy of the textbook based on the provided errata.
• Problems from Chap 7,8,9 of the text book
  – P.7.4
  – P7.6
  – P7.7 (assume the energy of the photons is E)
  – P7.9
  – P9.9 (P9.4 in 1st edition)
  – P9.3 (not present in 1st edition)
  – P9.4 (not present in 1st edition)
  – P.9.10 (not present in 1st edition)
• Homework will not be collected, solutions will be available Monday October 15.