Positron Emission Tomography: Basics of Data Acquisition and Image Reconstruction

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Overview of Seminar

- Overview of Positron Emission Tomography (PET)
- PET data acquisition types
- The system matrix
- Image reconstruction
Overview of PET

- Choose a molecule of interest
- Radioactively label the molecule
- Inject a trace amount of this radioactive compound (the PET radiotracer)
- Place the radioactive subject into the PET scanner
- Detect the radiation
- Reconstruct the Image
- Measure functional information from the reconstruction of the space-time distribution of the PET radiotracer

Wikipedia inspired!

1. Injection of radiotracer
2. a) Positron (e⁺) emission, b) Annihilation with electron (e⁻) and c) 511 keV photon (γ) pair emission
3. Detection of photon pair
4. Acquisition of 100s of millions of such pairs
5. Reconstruction of data
### PET at the Montreal Neurological Institute

#### PET scanners

<table>
<thead>
<tr>
<th></th>
<th>HR+</th>
<th>HRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystals used</td>
<td>BGO (4x72x8x8=18432)</td>
<td>LSO/LYSO (8x117x8x8x2=59904x2)</td>
</tr>
<tr>
<td>Crystal size</td>
<td>4 mm x 4 mm x 30 mm</td>
<td>2.1 mm x 2.1 mm x 20 mm</td>
</tr>
<tr>
<td>Number of LORs</td>
<td>~20 million</td>
<td>&gt;4.5 billion</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td>4 – 8.3 mm FWHM</td>
<td>2 - 3.5 mm FWHM</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>21.9 kcps/kBq/mL</td>
<td>39.8 kcps/kBq/mL</td>
</tr>
<tr>
<td>Field of view</td>
<td>155 mm axial (56 cm port)</td>
<td>250 mm axial (31 cm port)</td>
</tr>
</tbody>
</table>
PET at the Montreal Neurological Institute

<table>
<thead>
<tr>
<th>Measured quantity &amp; radiotracer</th>
<th>Stress, schizophrenia</th>
<th>Addiction</th>
<th>Depression</th>
<th>Alzheimer’s disease</th>
<th>Stroke recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine release [15C] Raclopride</td>
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<tr>
<td>Dopamine release [18F] Fallypride</td>
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<tr>
<td>Serotonin receptor density [18F] MPPF</td>
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<tr>
<td>Glutamate receptor density [11C] ABP688</td>
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<tr>
<td>Glucose metabolic rate [18F] FDG</td>
<td></td>
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<tr>
<td>Cortical thickness [18F] Flumazenil</td>
<td></td>
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</tr>
</tbody>
</table>

**Example studies**

**Measured quantity & radiotracer**
- Dopamine release [15C] Raclopride
- Dopamine release [18F] Fallypride
- Serotonin receptor density [18F] MPPF
- Glutamate receptor density [11C] ABP688
- Glucose metabolic rate [18F] FDG
- Cortical thickness [18F] Flumazenil

**Functional parameters of interest**
- BP
- BP
- BP
- BP and $K_i$
- BP

**Example coronal section**

**Positron Emission (β+ decay)**

Atoms with too few neutrons can be unstable

Stability can be achieved by:
- proton $\rightarrow$ neutron + positron + neutrino

$$E = mc^2$$

$2.998 \times 10^8$ ms$^{-1}$

9.109 x 10$^{-31}$ kg

511 keV

E.g. Carbon 11

Positron $+ \rightarrow$ Electron + Neutrino

γ Photon

9.109 x 10$^{-31}$ kg

511 keV

γ Photon

γ Photon
The raw data: events detected along lines of response (LORs)
e.g. 500 million events
[position, time, energy]

PET scanner detector ring

What is the object which gave rise to the data?

? OBJECT ?

(256 x 256 x 250 x 20)
>300 million parameters
**How then do we make images?**

The following is a list of “ingredients” for image reconstruction:

- The PET scanner collects **measured data** (counts detected outside the patient).
- But we seek to estimate **parameters** which are not directly measured by the PET scanner.
- A **model** of the imaging process is needed to provide an estimate of the mean of the measured data (given a current estimate of the parameters).
- These parameters and their expected data should agree in some way with the measured data (e.g. least squares, maximum likelihood) – the **objective**.
- An **algorithm** is needed to estimate the parameters, so that the objective is achieved.
- So we need: **data**, **parameters**, **model**, **objective** and an **algorithm**!

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**THE DATA**

Understanding the acquired PET data

- PET data can be acquired / represented in 2 main ways
- **SINOGRAMS** (projections)
- **LIST-MODE DATA**
- ...also, **BACKPROJECTED IMAGES**
THE DATA

PET Measured Data 1

Point Source

$n(x, y)$

3 data formats

List-mode data

$D1, D2, E_1, E_2, t, ...$

Backprojected image

Sinogram

PET Measured Data 2

Point Source

List-mode data

$D1, D2, E_1, E_2, t, ...$

$D3, D4, E_1, E_2, t, ...$

Backprojected image

Sinogram
### PET Measured Data 3

**Point Source**
- $3^{rd}$ positron emission, and annihilation photons

**List-mode data**
- $D_1, D_2, E_1, E_2, t, ...$
- $D_3, D_4, E_1, E_2, t, ...$
- $D_5, D_6, E_1, E_2, t, ...$

**Backprojected image**

**Sinogram**

### PET Measured Data (AFTER 6 EMISSIONS)

**Point Source**
- Site of $6^{th}$ emission, and annihilation photons

**List-mode data**
- $D_1, D_2, E_1, E_2, t, ...$
- $D_3, D_4, E_1, E_2, t, ...$
- $D_5, D_6, E_1, E_2, t, ...$
- $D_7, D_8, E_1, E_2, t, ...$
- $D_9, D_{10}, E_1, E_2, t, ...$
- $D_{11}, D_{12}, E_1, E_2, t, ...$
**THE DATA**

**PET Measured Data (after ~1000 emissions)**

**Point Source**

Many events will occur along any given line through the point source.

The number of events detected along this line (LOR) ≥ sum of activity along a line through the FOV.

**List-mode data**

- $D_1, D_2, E_p, E_2, t, ...$
- $D_3, D_4, E_p, E_2, t, ...$
- $D_5, D_6, E_p, E_2, t, ...$
- $D_7, D_8, E_p, E_2, t, ...$
- $D_9, D_{10}, E_p, E_2, t, ...$
- $D_{11}, D_{12}, E_p, E_2, t, ...$
- $D_{13}, D_{14}, E_p, E_2, t, ...$
- $D_{15}, D_{16}, E_p, E_2, t, ...$
- $D_{17}, D_{18}, E_p, E_2, t, ...$

**Backprojected image**

**Sinogram**

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**THE DATA**

**PET Measured Data: Multiple Points (5k events)**

**Multiple Point Sources**

Sites of positron emission, and annihilation photons.

Note that the simple model of CONVOLUTION can be used: each point source is replaced by a point spread function (valid for 2D PET).

**List-mode data**

- $D_1, D_2, E_p, E_2, t, ...$
- $D_3, D_4, E_p, E_2, t, ...$
- $D_5, D_6, E_p, E_2, t, ...$
- $D_7, D_8, E_p, E_2, t, ...$
- $D_9, D_{10}, E_p, E_2, t, ...$
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- $D_{13}, D_{14}, E_p, E_2, t, ...$
- $D_{15}, D_{16}, E_p, E_2, t, ...$
- $D_{17}, D_{18}, E_p, E_2, t, ...$

**Backprojected image**

**Sinogram**
The backproject then filter (BPF) method (e.g. [1] Chu & Tam 1977) (same mathematical principles as filtered backprojection (FBP))

\[ g(\mathbf{r}) = \int n(\mathbf{r'})h(\mathbf{r} - \mathbf{r'})d\mathbf{r'} \]

\[ G(\mathbf{k}) = N(\mathbf{k})H(\mathbf{k}) \]

\[ N(\mathbf{k}) = \frac{G(\mathbf{k})}{H(\mathbf{k})} \]

PROBLEM: Only works for shift-invariant PSF \( H \)

THE DATA

PET Measured Data: test phantom (60k events)

TRUE Sites of positron emission, and annihilation photons

List-mode data

\[ D1, D2, E_p, E_\gamma, t, \ldots \]
\[ D3, D4, E_p, E_\gamma, t, \ldots \]
\[ D5, D6, E_p, E_\gamma, t, \ldots \]
\[ D7, D8, E_p, E_\gamma, t, \ldots \]
\[ D9, D10, E_p, E_\gamma, t, \ldots \]
\[ D11, D12, E_p, E_\gamma, t, \ldots \]
\[ D13, D14, E_p, E_\gamma, t, \ldots \]
\[ D15, D16, E_p, E_\gamma, t, \ldots \]
\[ D17, D18, E_p, E_\gamma, t, \ldots \]

Backprojected image

Sinogram
PET Measured Data: a brain (100k events)

TRUE Sites of positron emission, and annihilation photons

List-mode data
- $D_1, D_2, E_p, E_2, t, ...$
- $D_3, D_4, E_p, E_2, t, ...$
- $D_5, D_6, E_p, E_2, t, ...$
- $D_7, D_8, E_p, E_2, t, ...$
- $D_9, D_{10}, E_p, E_2, t, ...$
- $D_{11}, D_{12}, E_p, E_2, t, ...$
- $D_{13}, D_{14}, E_p, E_2, t, ...$
- $D_{15}, D_{16}, E_p, E_2, t, ...$
- $D_{17}, D_{18}, E_p, E_2, t, ...$

Backprojected image
Sinogram

Images (objects) and sinograms are VECTORS

Any object (e.g. point source)
Call this a vector $n$
what we want to find

Regard as a list of numbers:
- $(0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0)$
This is a VECTORS

Sinogram
Call this a vector $m$
what we have

Regard as a list of numbers:
- $(1,0,0,0,0,1,0,0,0,0,0,0,0,0,1,0,0,0,0,0,1,0,0,0,0,1,0)$
This is a VECTORS
Object representation

Reminder: the 5 ingredients of image reconstruction

- The vector of parameters $n$ representing the object to be found, and a noisy measured data vector $m$
- A model which maps the vector of parameters to an expected measured data vector (system matrix $A$)
- An objective function: the expected data should agree with the measured data in some way
  - E.g. Least squares, Maximum Likelihood, Maximum a posteriori
- An algorithm which estimates the parameters of the object representation, to achieve the objective
  - E.g. EM (expectation maximization), FBP, PCG
- 5 ingredients: model, parameters, data, objective and the algorithm
From object to sinogram: the system matrix

We need to model the measurement process to do a reconstruction

\[ A \]

How do we create this matrix?

Creating the system matrix:

populate columns with sinograms from point source data

\[ A = \]

Hence the system matrix contains columns which are the responses to point sources at different positions in the FOV

...via an analytic model, or Monte Carlo simulation, or just measuring a point source!
Creating the system matrix:
Alternative method: fill the rows with images

\[
A = \begin{bmatrix}
0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\end{bmatrix}
\]

etc

For Time of Flight:
*use a Gaussian PDF along the line*

Often, these elements are calculated “on the fly” using ray-tracing (e.g. Siddon method [6]), or symmetry is exploited in the case of sinogram data.

Hence the system matrix contains rows which indicate which pixels / voxels contribute to each measurement (list-mode event or sinogram bin).

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**Model Summary**

Each row of \( A \) corresponds to a sensitivity image for each sinogram bin.

\[
\{ a_{ij} \} = A = \ldots.
\]

Each column of \( A \) corresponds to a sinogram response for each pixel in the object.
THE MODEL

What the system matrix can contain

- Model the entire measurement process!
- Convenient to factorize (e.g. [6] Mumcuoglu et al 1994)
- Include object motion \( M \) (e.g. [8] Carson et al 2003)
- Include positron range \( P \) (e.g. convolution resolution model, [9] Reader et al 2003)
- Include the main mapping (e.g. the Radon, or x-ray, transform) \( X \)
  - Could include scatter here (e.g. [5] Markiewicz)
- Include time-of-flight (TOF) information (e.g. [10] Vandenbergh et al 2006)
- Include attenuation \( L \) (e.g. [11] Hebert & Leahy 1990, “attenuation weighting” AW)
- Include detector non-uniformities (normalization) \( N \) (e.g. [12] Michel et 1999)
- Can include detector resolution / response models as well (e.g. [13] Panin et al 2006)

\[
A = DNLX_{\text{for PM}}
\]

- In general, the system matrix is a mapping from the parameters to the expected data (the mean of the data) – we are free to choose our parameters, but this choice will of course affect the model

THE MODEL

Applying the system matrix (when \( A = X \) only)

case 1: central point source
Applying the system matrix (when $A=X$ only)
case 2: off centre point source

Applying the system matrix (when $A=X$ only)
case 3: multiple point sources
Applying the system matrix (when $A=X$ only)

case 4: general distribution

THE OBJECTIVE FUNCTION

Criteria for finding the object ($n$) from the data ($m$)

i.e. "Image Reconstruction"!

- If we do a PET (or SPECT) scan, we obtain the measured data vector $m$
- We can study (analytically, empirically, by simulation) our system, and create a matrix $A$
- We then need to find the underlying object $n$, which gave rise to the measured data $m$
- We seek
  - An estimate of $n$, which produces expected (mean) data $<m> = q = An$
  - We need to minimise the discrepancy between $q$ and $m$
  - Many ways of defining the difference. E.g.
    - Least squares
      \[ O_{LS}(m|n^k) = \sum_{i=1}^{I} (m_i - q_i^k)^2 \]
    - Maximum likelihood
      \[ O_{ML}(m|n^k) = \prod_{i=1}^{I} \frac{(q_i^k)^{m_i} \exp[-q_i^k]}{m_i!} \]
Example

ML-EM algorithm

\[ n^{k+1} = \frac{n^k}{A^T1} A^T \left( \frac{m}{A n^k + b} \right) \]

Current estimate of 3D image
Forward project (e.g. integrate along lines through the image)
Add scatter and randoms background (‘Ordinary Poisson’)
Compare to measured data: obtain a ratio (=correction factors)
Backproject these correction factors
Multiply (and normalise)
Obtain new estimate of 3D image

[9] Shepp & Vardi 1982
[10] Lange & Carson 1984

Example (4 iterations)
**OSEM** (Ordered Subsets Expectation Maximization)  
(Hudson & Larkin)

- Uses a subset of the sinograms (usually just a few angles)
- Since only part (a subset) of the measured data are used for each update, the processing required per update is reduced!
- However, convergence is lost: limit cycle encountered

**EXAMPLE ALGORITHM**

EM and its variants

| OS-EM (not ML) |

\[
\sum_{i \in S_l} a_{ij} m_i \frac{\sum_{j} a_{ib} n_{b}^{k,l}}{\sum_{i \in S_l} a_{ij} n_{j}^{k,l+1}}
\]
Example (8 iterations, 4 subsets)

**Analytic ALGORITHM**

**Fourier Reconstruction (PET, SPECT, CT)**

\[ N(\omega_x, \omega_y) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} n(l,s) \exp[-i\omega_x l - i\omega_y s] \, dl \, ds \]

\[ M(\omega_x) = \int_{-\infty}^{\infty} n(l,s) \exp[-i\omega_x s] \, ds \]

- Normalize for varying contributions
  
  \( \frac{1}{r} \) density corrected by the ramp filter \( |r| \)
- Take inverse 2D Fourier Transform to find \( n \)
- Mathematically equivalent to: filter sinogram, then backproject (FBP)

2D FT of Image

sinogram
The central section theorem

Example ML-EM and FBP reconstructions

TRUE

Example FBP reconstruction

Iteration 100

At convergence, both points are equally visible
Example ML-EM and FBP reconstructions (2D, \(\sim 10^5\) events)

TRUE

Example FBP reconstruction

Iteration 75

Post-reconstruction smoothing

3D FBP
3D OSEM
3D OSEM+PSF

(3D, \(\sim 10^9\) events)

Raw data courtesy A. Thiel, MNI
Thank you