Pharmacokinetics course

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Contents

- Introduction to PET & SPECT (09.00-09.45)
  - Tomographic methods
  - PET / SPECT acquisition
  - Image reconstruction
  - Resolution / Partial Volume Effects
- Receptor kinetics (10.00-12.00)
  - In vitro concepts
  - Quantification
  - Kinetic modeling
  - Assumptions

Introduction to PET & SPECT

March 2, 2022

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Copenhagen University Hospital

What is tomogaraphy?

MRI
Magnetic Resonance …

CT
Computed …

SPECT
Single Photon Emission Computed …

TOMOGRAPHY

PET
Positron Emission …

ET
Electron …

MT
Muon …

Tomos:
Slice / Section

Graphein:
To write

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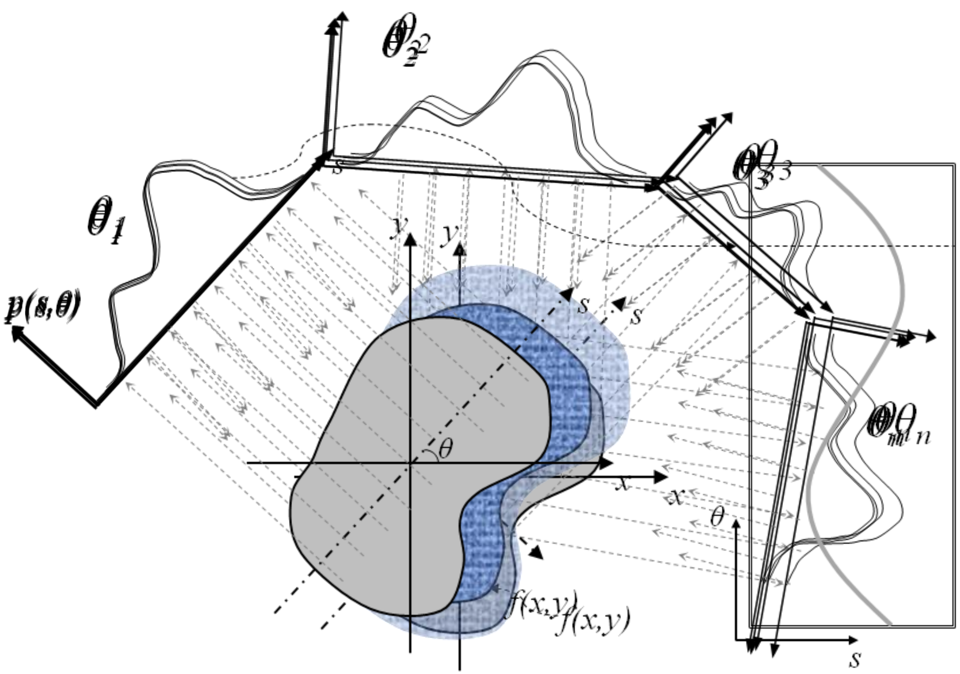
What is tomogaraphy?

1. Measure ”Projections” for each angle
2. The object (3D) giving rise to the measured projections is reconstructed



Johann Radon, 1887-1956

Dr J. Radon

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NRU, Copenhagen University Hospital, Rigshospitalet

What is tomogaraphy?

MRI

Radio waves

CT

X-rays

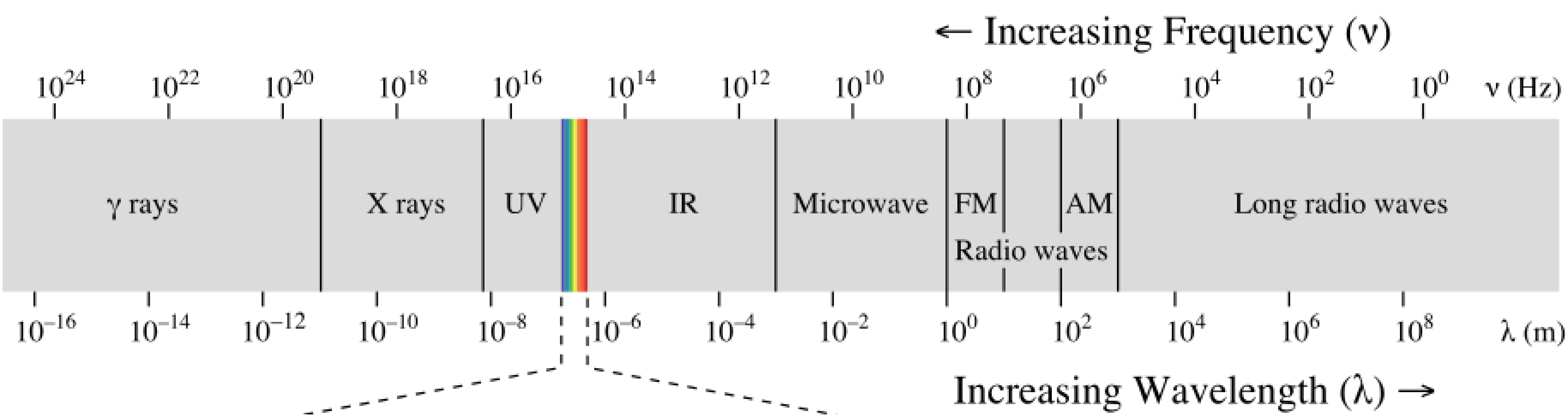
SPECT

γ-rays

TOMOGRAPHY

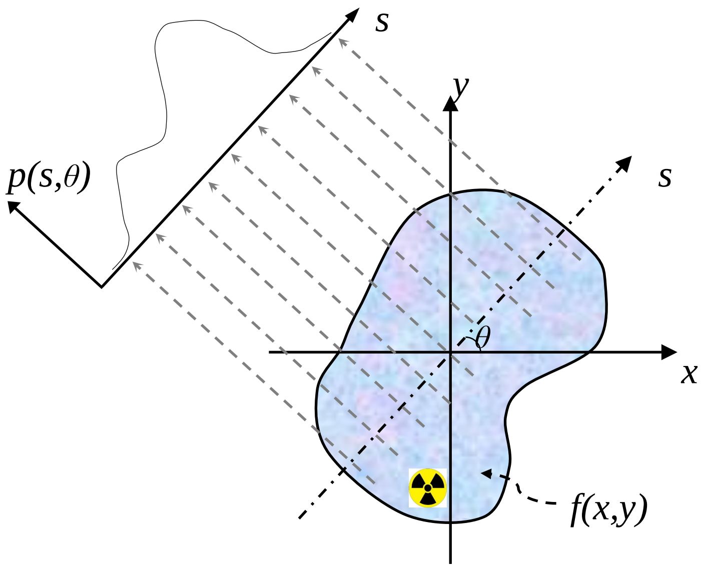
PET

γ-rays



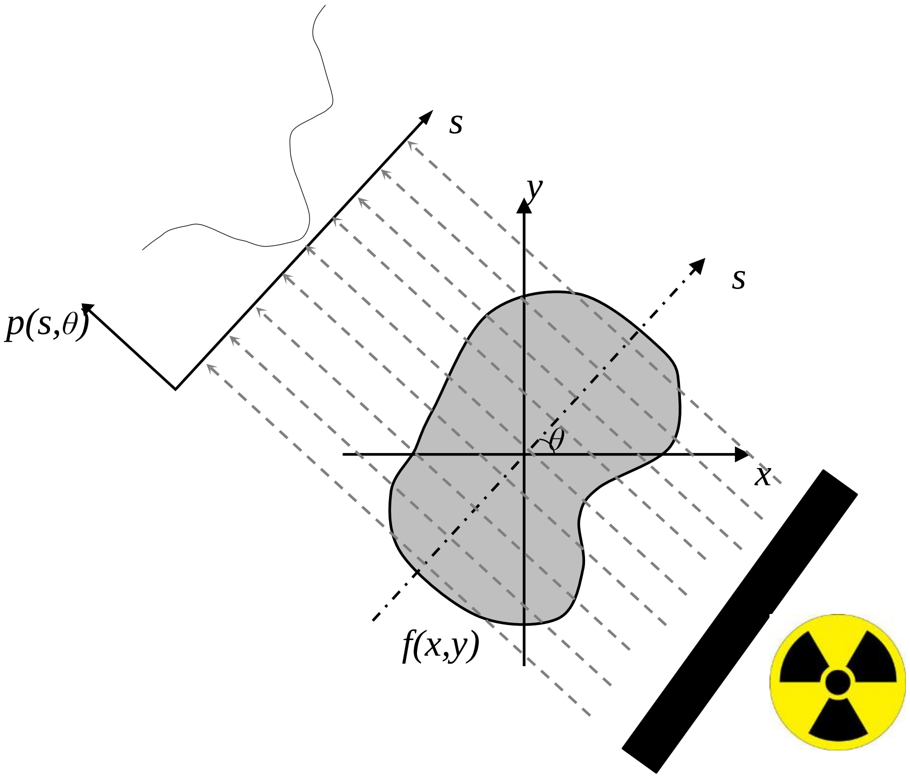
What is tomogaraphy?

Emission Tomography



PET, SPECT, MRI

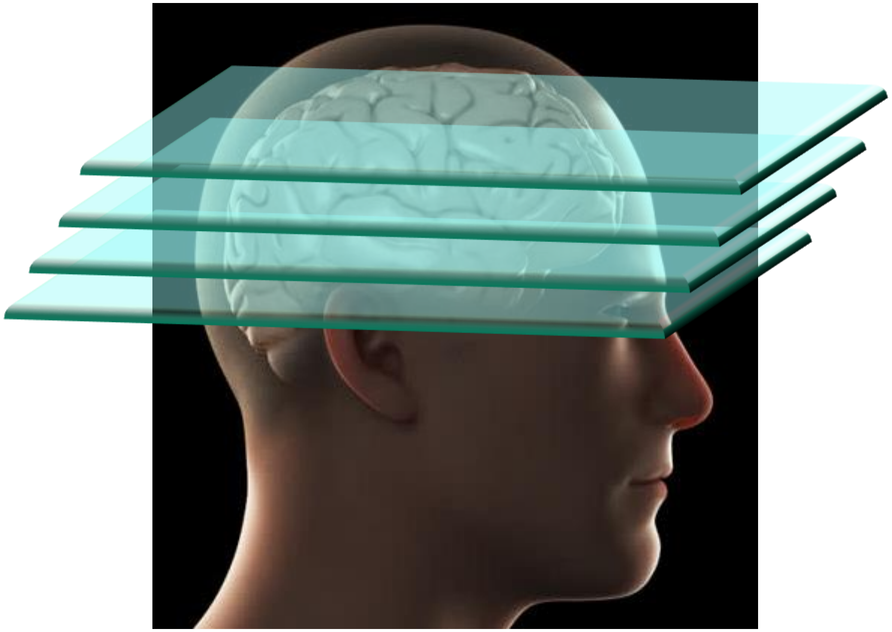
Transmission Tomography



CT, ET, MT

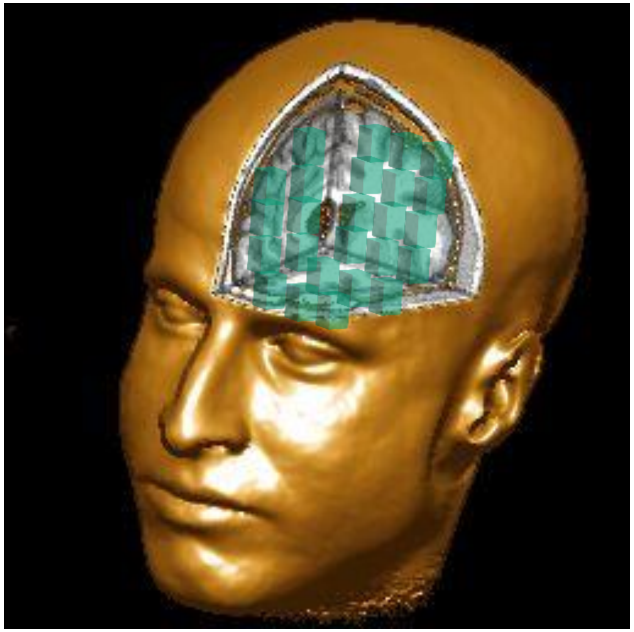
What is tomogaraphy?

Image several 2D slices (2D images)



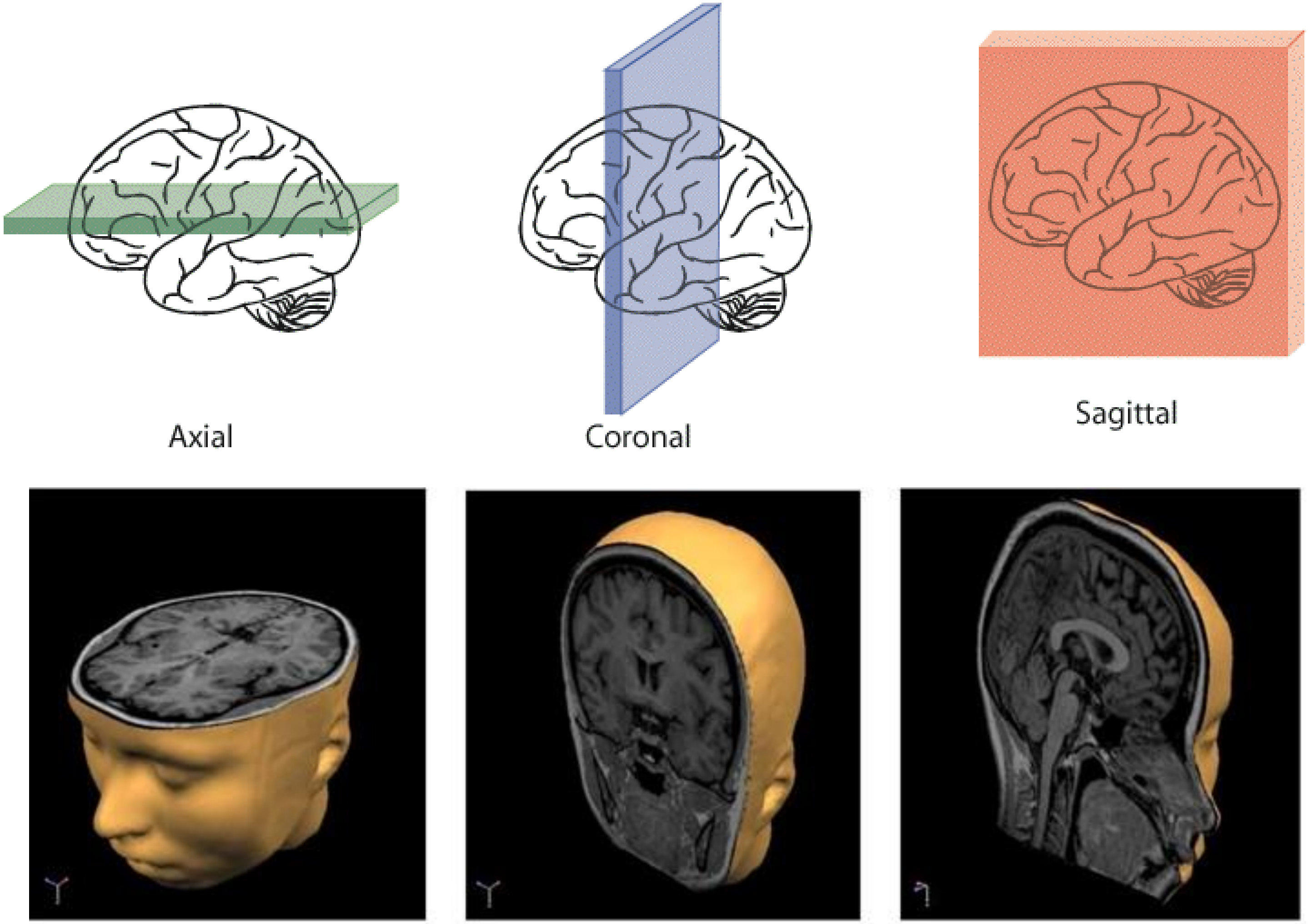
2D image element: Pixel

Stacking 2D slices creates an image volume



3D image element: Voxel

What is tomogaraphy?



Positron Emission Tomography (PET)

We are all children of broken symmetry

- Nobel prize in physics, 2008 (Nambu, Konayashi and Masakawa)

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- Big bang

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$\boxed{\text{antimatter}}$

Positron Emission Tomography

We are all children of broken symmetry

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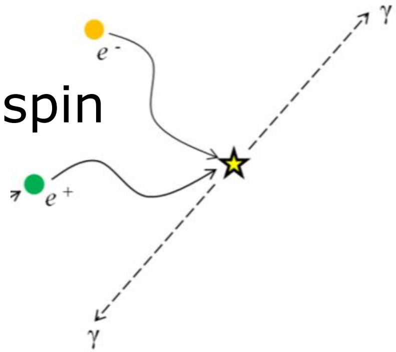
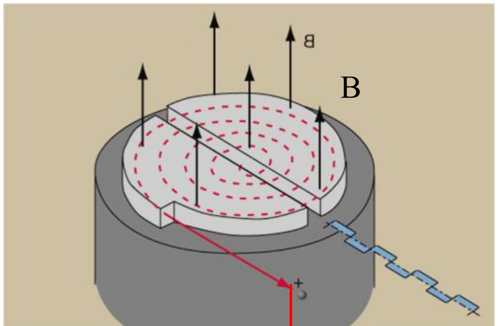
<u>Antimatter</u>

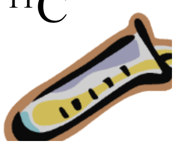
- Matter composed by antiparticles
- Same mass, opposite charge, opposite quantum spin
- Annihilates in presence of matter counterparticle
- Matter AND antimatter was created in Big Bang!
- Positron: antiparticle of the electron



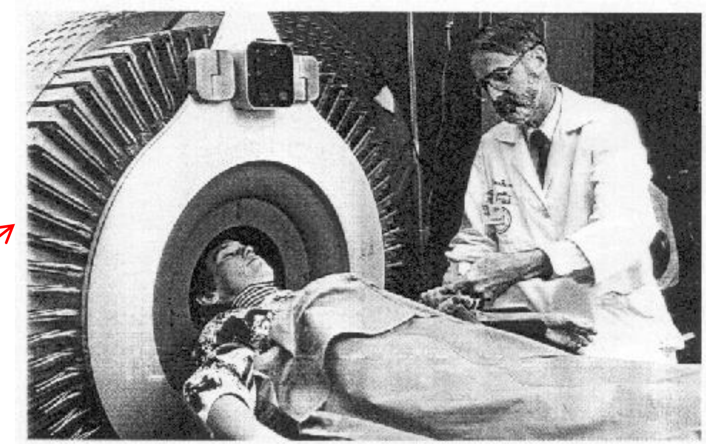
PET -- Physics

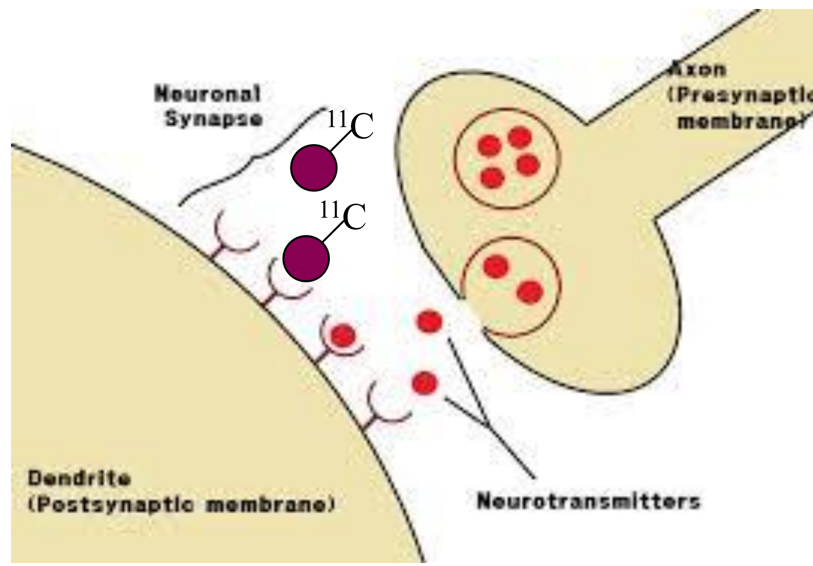


$^{12}C \rightarrow {}^{11}C$

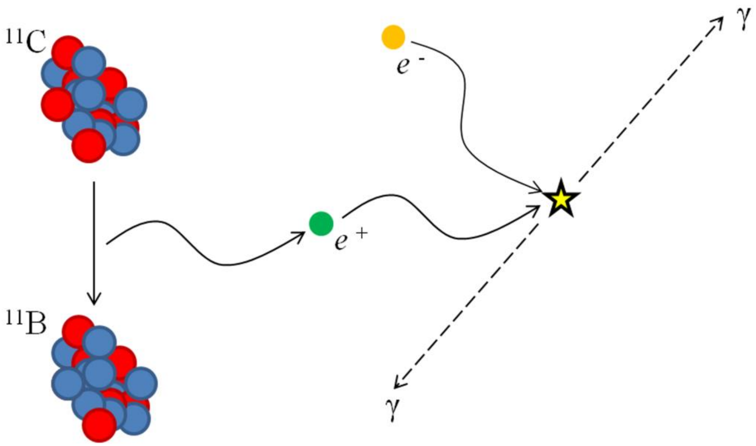


[^{11}C]Raclopride

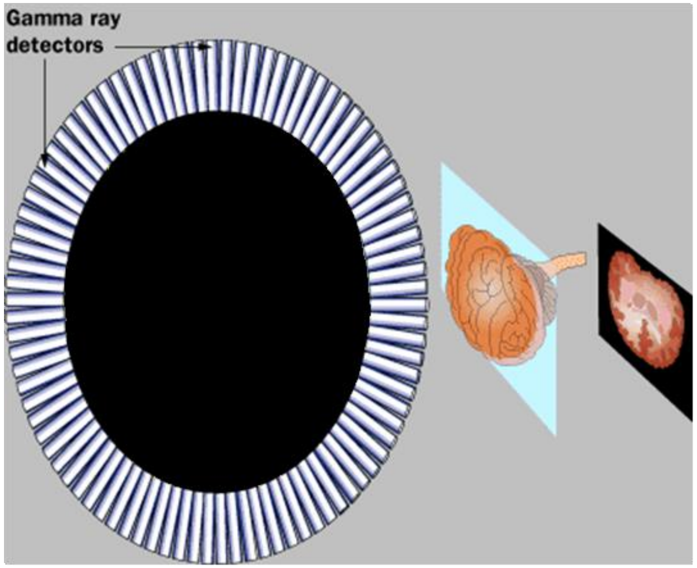




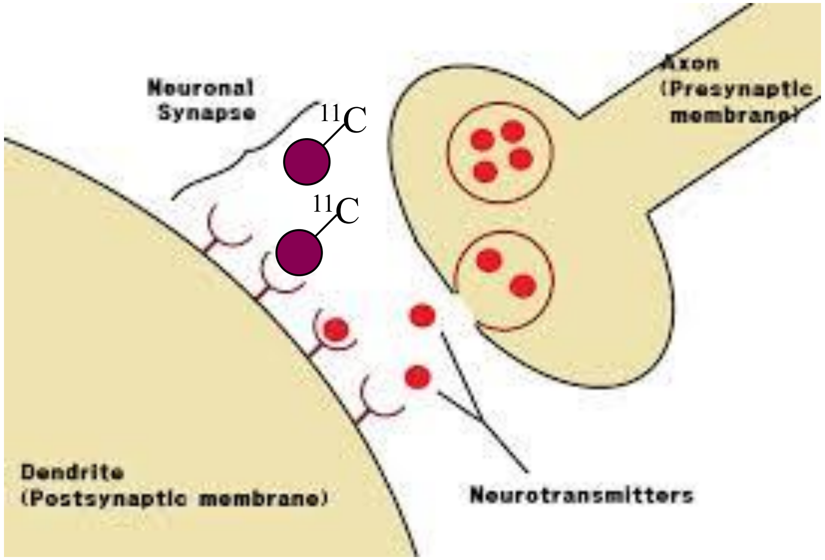
PET -- Physics



11C
11B
e -
e +
γ
γ

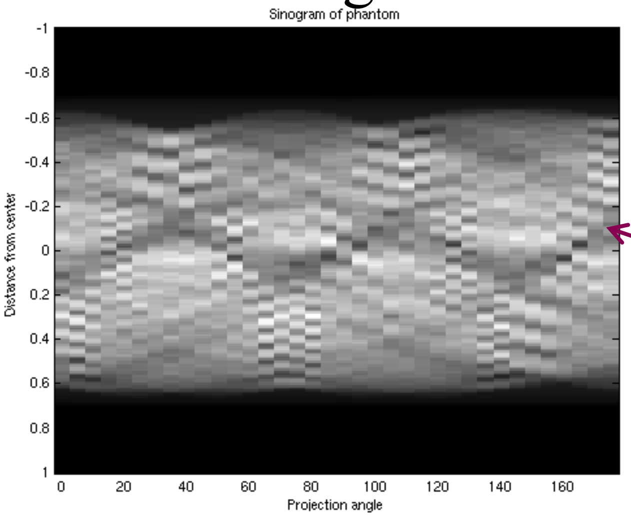


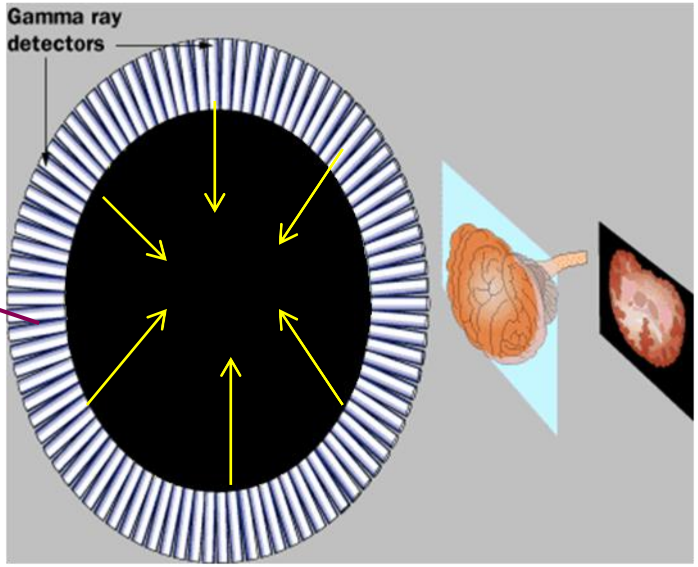
Gamma ray
detectors

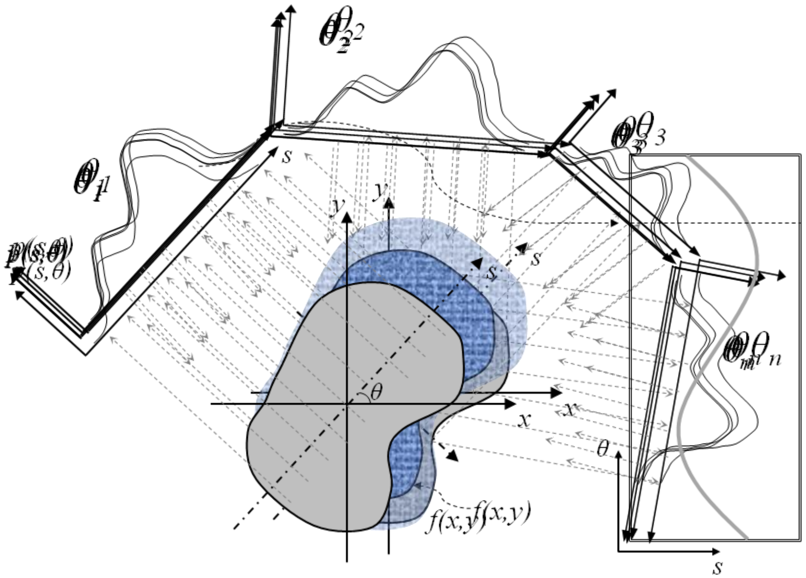


Neuronal
Synapse
11C
11C
Axon
(Presynaptic
membrane)
Dendrite
(Postsynaptic membrane)
Neurotransmitters

Sinogram





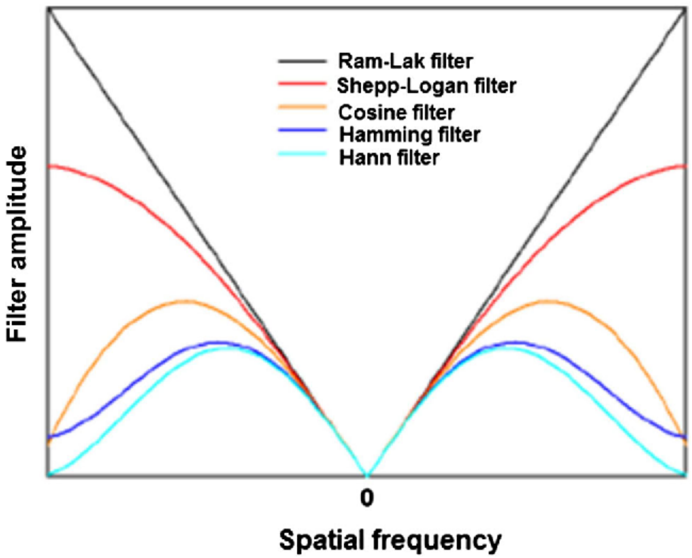


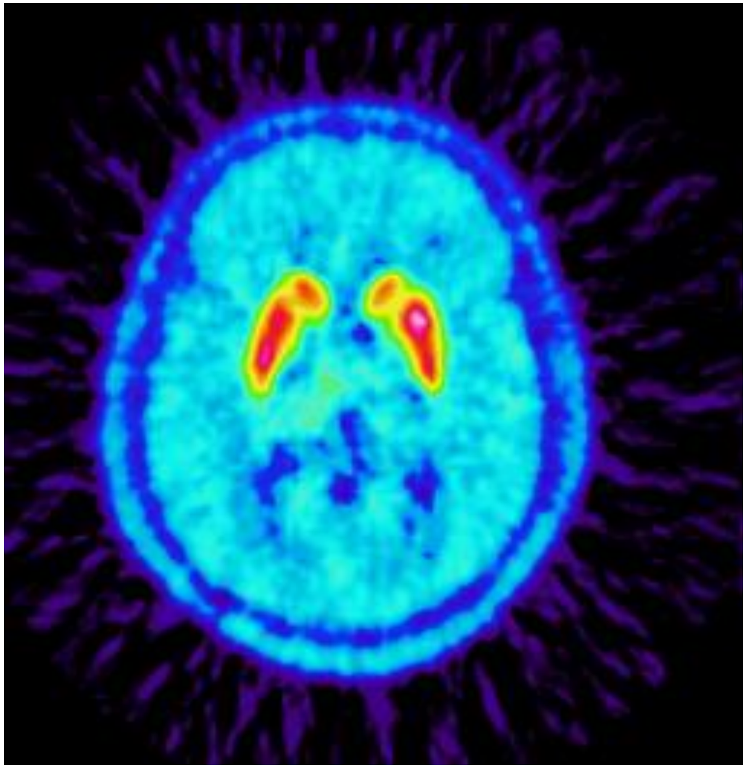
Radon Transform
Object -> Projections

Inverse Radon Tranform
Projections -> Object
(Back projection)

PET – Reconstruction (Filtered back projection)

Filter:
Amplify high frequencies
Supress low frequencies



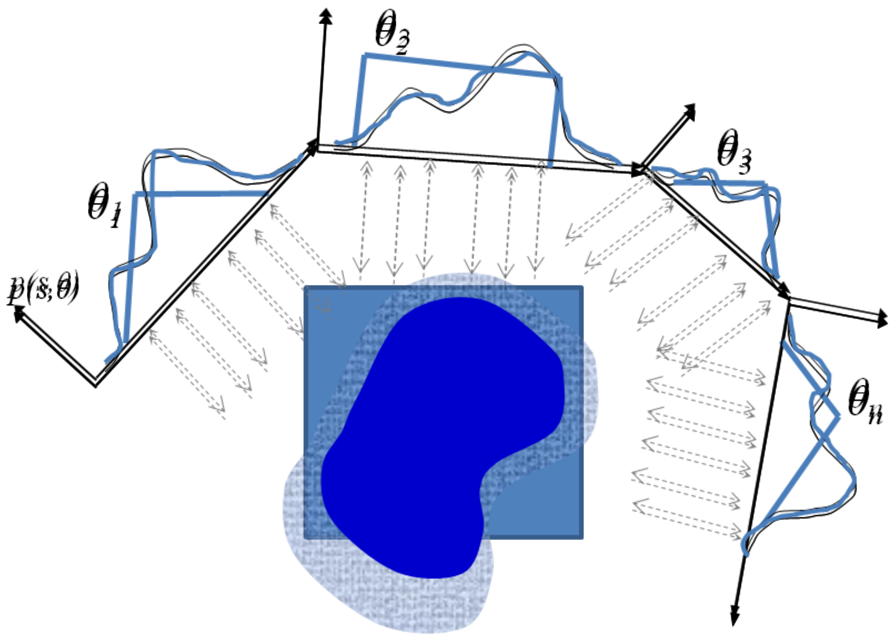


PET image of [11C]raclopride – reconstructed with filtered back projection

Main problem:
Inverse function is hard (ill-posed)

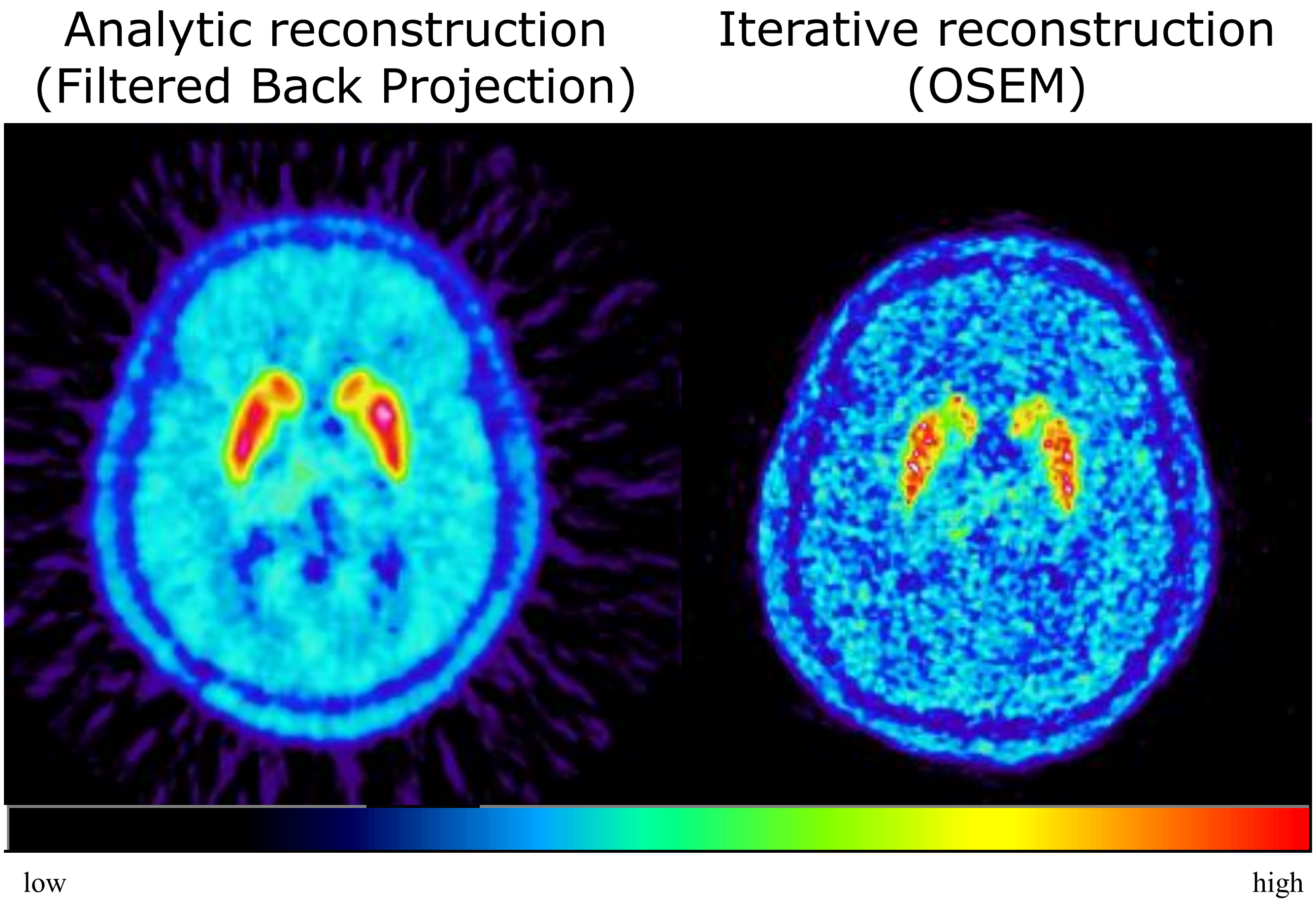
Iterative Reconstruction

(Ordered Subset Expectation Maximization)

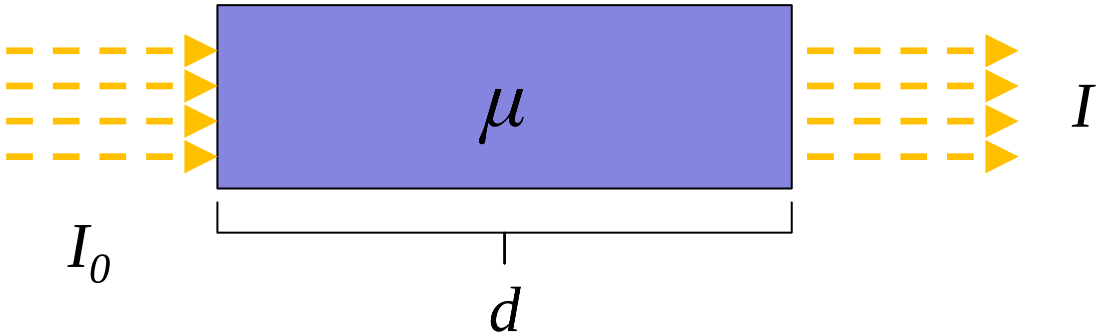


1. Guess an object (maybe a blue square?)
2. Forward project – i.e., obtain the projections for this guessed object
3. Compare the projections to those obtained from the measurement
4. Update object
5. Repeat!

Same subject – scanned with [11C]raclopride

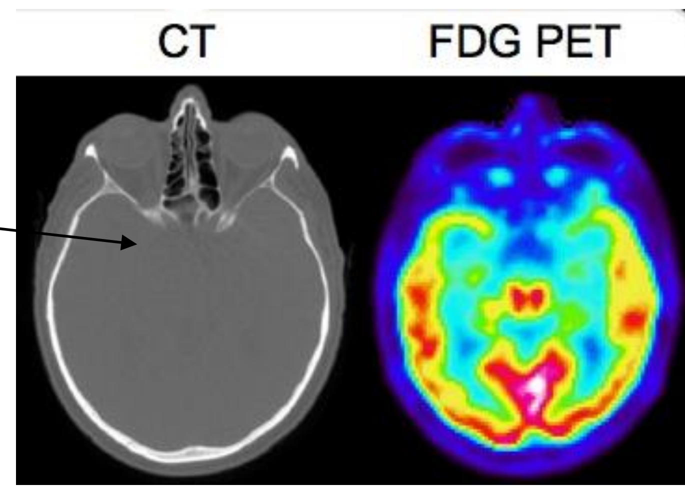


Attenuation correction



Beer Lambert law: $I = I_0 e^{-d \cdot \mu}$

μ-map,
$\mu(x)$



$$I = I_0 e^{-\int_0^d \mu(x)dx}$$

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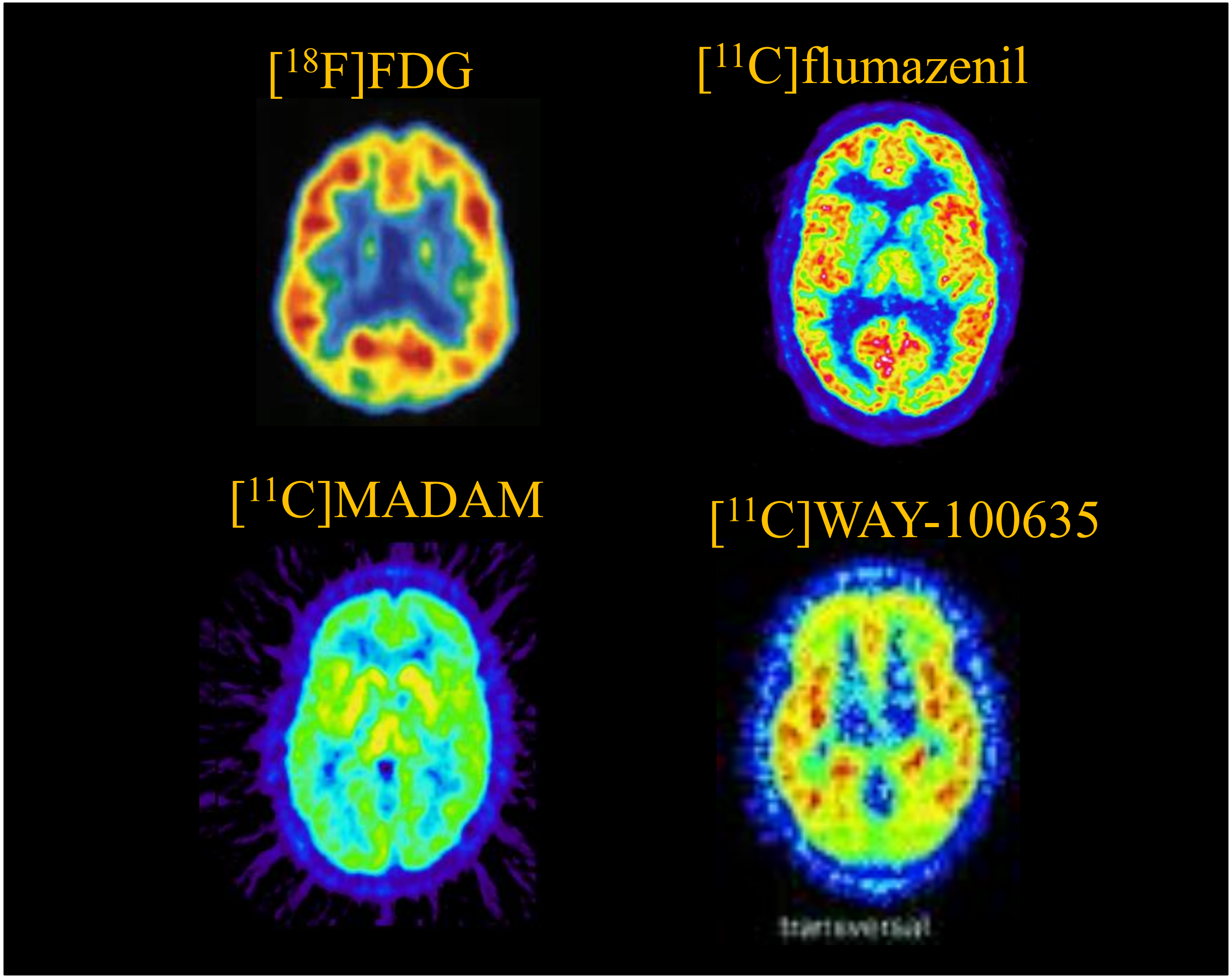
PET – Radioligands



What can possibly go wrong?

Non-correctable physical properties

- Non-colinearity
- Positron travel

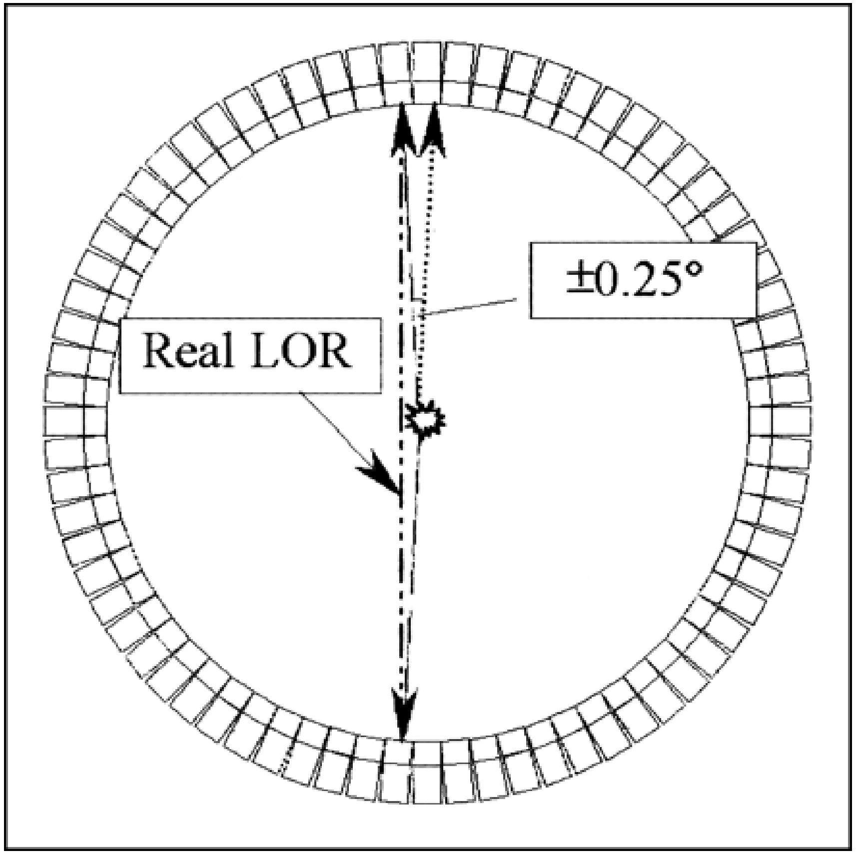
Correctable physical properties

- Scatter
- Randoms

What can possibly go wrong?

Non-correctable physical properties

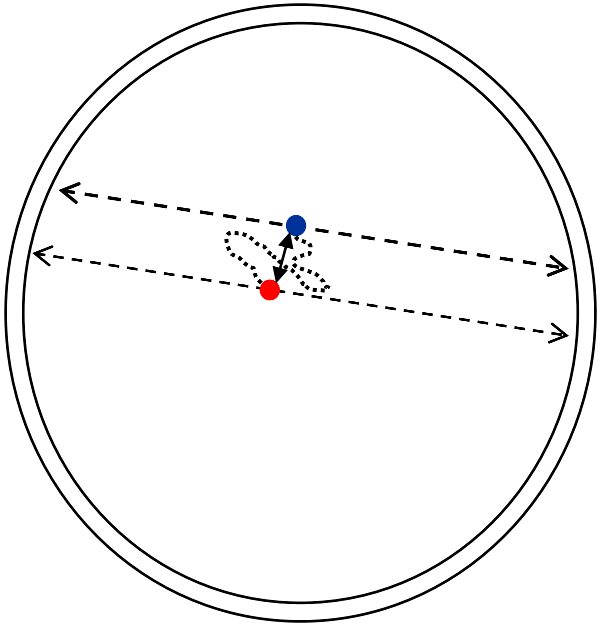
- **Non-colinearity**
- Positron travel



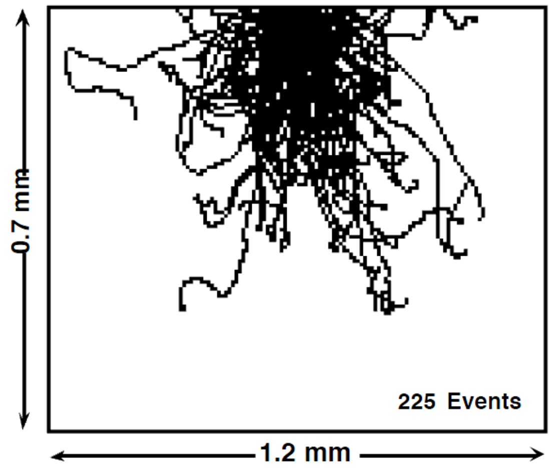
What can possibly go wrong?

Non-correctable physical properties

- Non-colinearity
- **Positron travel**



Simulated ^{18}F positron tracks in a scintillation detector



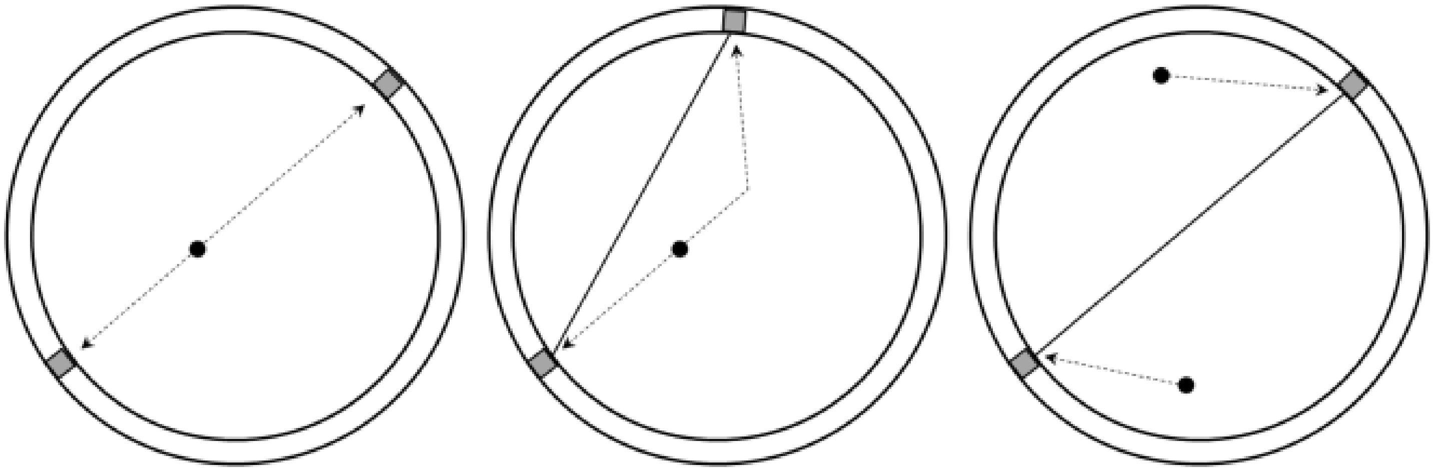
Isotope	Endpoint energy (MeV)	fwhm (mm)
^{18}F	0.64	0.54
^{11}C	0.96	0.92
^{13}N	1.22	1.49
^{15}O	1.72	2.48
^{68}Ga	1.90	2.83
^{82}Rb	3.35	6.14

W.W. Moses / Nuclear Instruments and Methods in Physics Research, (2011)

What can possibly go wrong?

Correctable physical properties

Ideal	Scatter	Randoms



~50%

de Jong et al., Phys Med Biol, 2007

~10-50%

Badawi et al., Phys Med Biol, 1999

What is the main effect of these errors?

Non-correctable physical properties

- Non-colinearity
- Positron travel

Correctable physical properties

- Scatter
- Randoms

Camera Properties

- Detector size
- Penetration
- Gantry radius
- Non-uniform Sampling

Resolution ↓

Single Photon Emission Computed Tomography (SPECT)

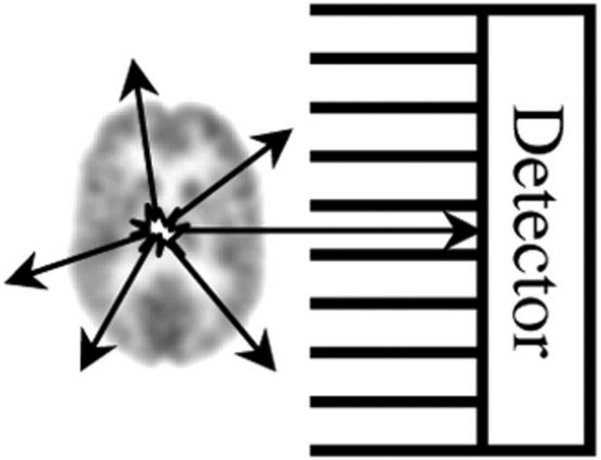
”Like PET but cheaper”

Single (or a few) circulating detector head (i.e., no ring of detectors)

Decay of isotope directly produce gamma particle (i.e., no detour via positrons)

Each decay produce at most 1 detection

Only particles perpendicular to the head is assured via collimators



Single Photon Emission Computed Tomography (SPECT)

PET		SPECT	
Material	Halflife	Material	Halflife
^{11}C	20.3 min	^{99m}Tc	6.0 hours
^{18}F	110 min	^{123}I	13.1 hours
^{15}O	122 sec	^{111}In	2.8 days

Availability of different isotopes provide somewhat complementary information

Longer half life removes the need of on-site cyclotron

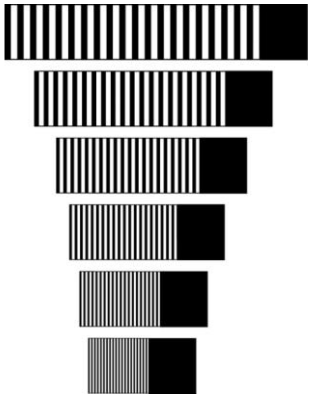
SPECT camera significantly cheaper (order of magnitude)

Emission tomography: What do we mean with ”resolution”?

Resolution: 16 megapixels

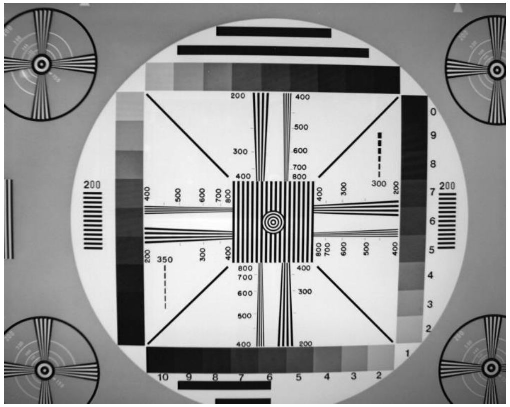
Emission tomography: What do we mean with ”resolution”?

The resolution of a sensor is the smallest change it can detect in the quantity that it is measuring (wikipedia)



http://gene.bio.jhu.edu/resolution/resolution.html

Resolution
=
Amount of information / unit area (volume)



http://en.wikipedia.org/wiki/Optical_resolution

Nbr of pixels
=
Upper Limit

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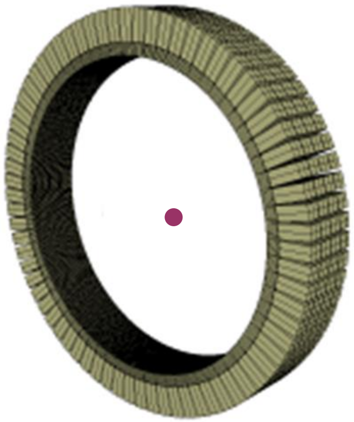
How do we measure the resolution of a PET / SPECT system?

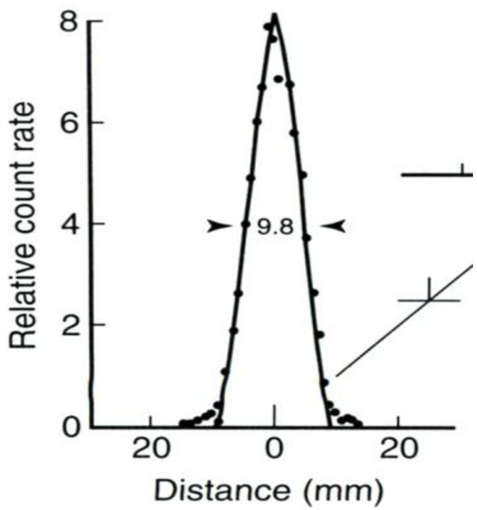


Acquisition + Reconstruction

"Point Spread Function" (PSF)

Measure intensity line profile through PSF

Point source in air



System resolution
=
FWHM of the PSF!

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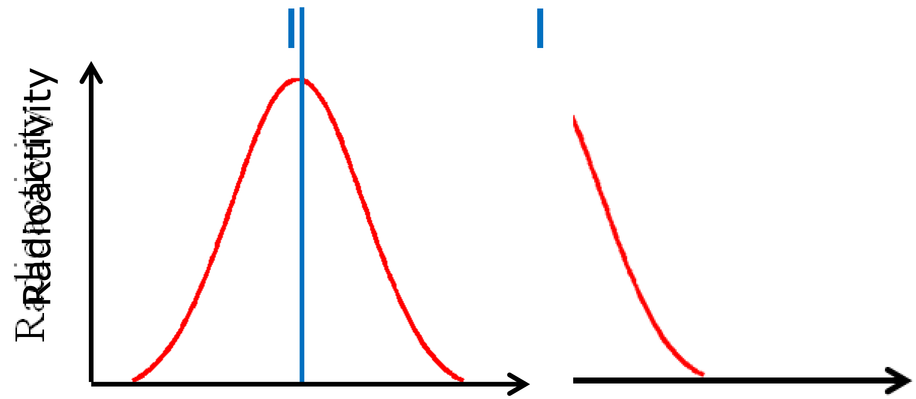
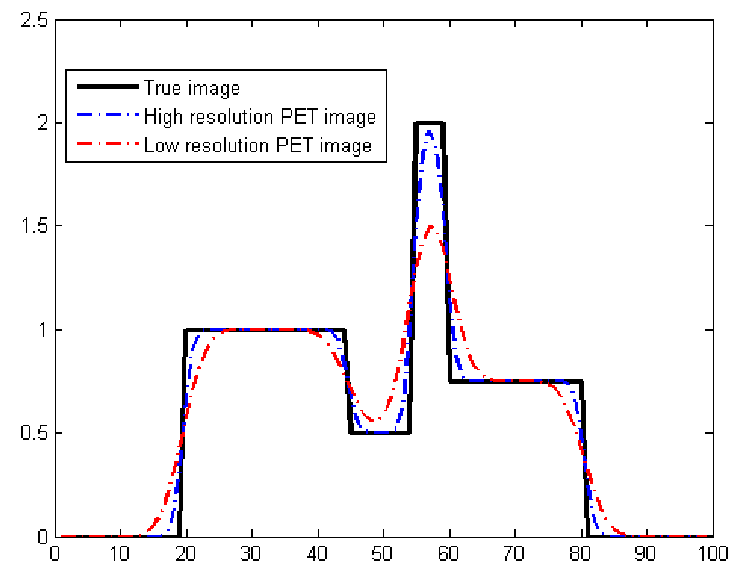
What are the consequences of low spatial resolution?

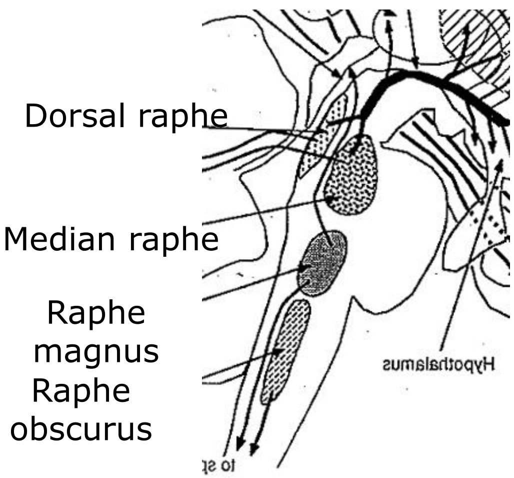
Partial Volume Effect (PVE)

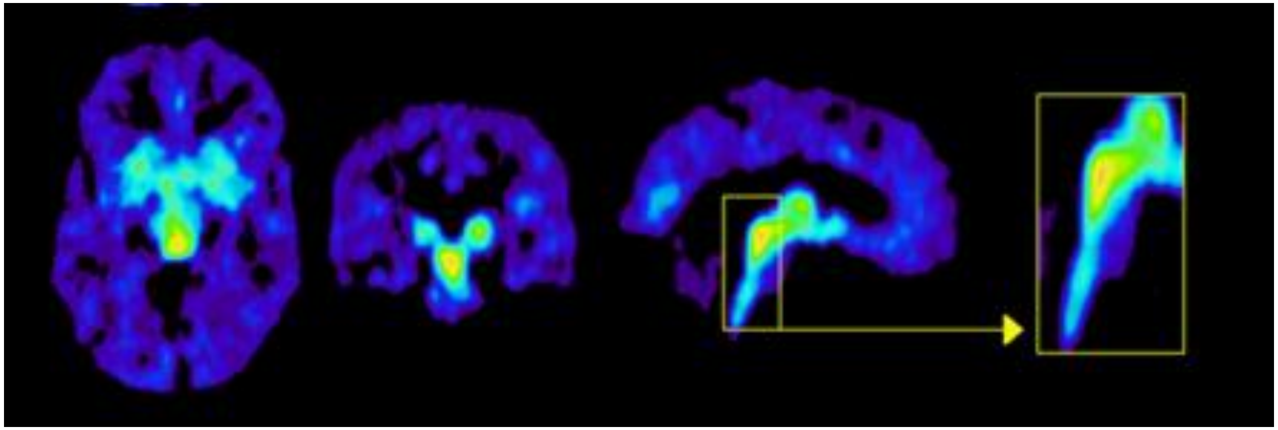
- ”Spill-out” of activity from regions with high signal.
- All nearby structures contaminate each other.
- The effect is most pronounced in small regions – radioligand binding cannot be reliably quantified!





What are the consequences of low spatial resolution - Example





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Summary

- PET and SPECT provides information on brain function (densities of various proteins)
- Tomographic methods: measure projections and recreate the object
- PET and SPECT: Emission tomography
  - PET: Decay → Positron → 2 photons detected
  - SPECT: Decay → 1 photon detected
- Reconstruction can be analytical or iterative
- Resolution is poor → hard to measure small brain structures