Pharmacokinetics course

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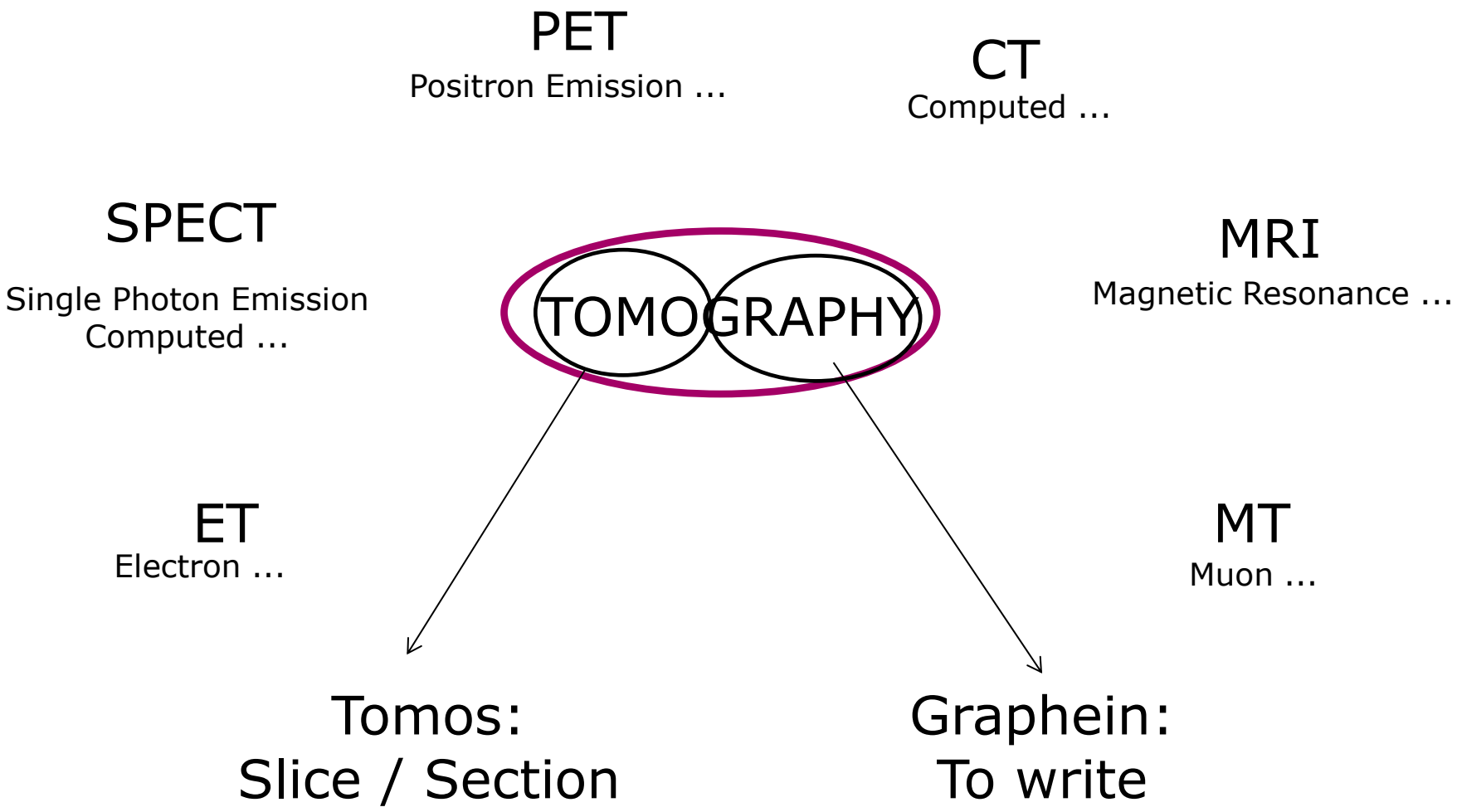
Antaros Medical

Contents

- Introduction to PET & SPECT (09.00-09.45)
  - Tomographic methods
  - PET / SPECT acquisition
  - Image reconstruction
  - Resolution / Partial Volume Effects

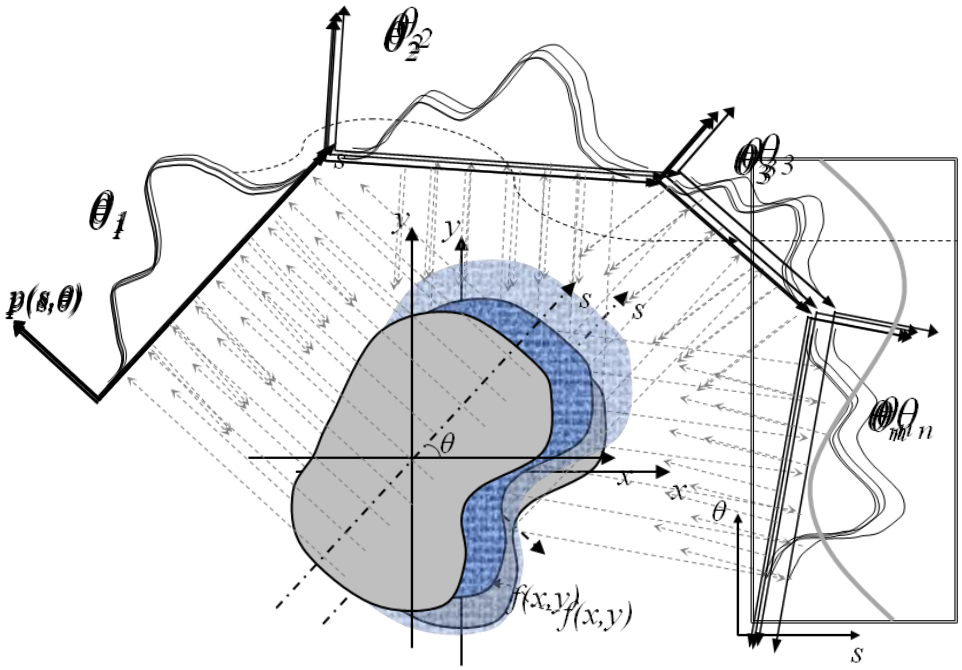
- Receptor kinetics (10.00-12.00)
  - In vitro concepts
  - Quantification
  - Kinetic modeling
  - Assumptions

What is tomogaraphy?

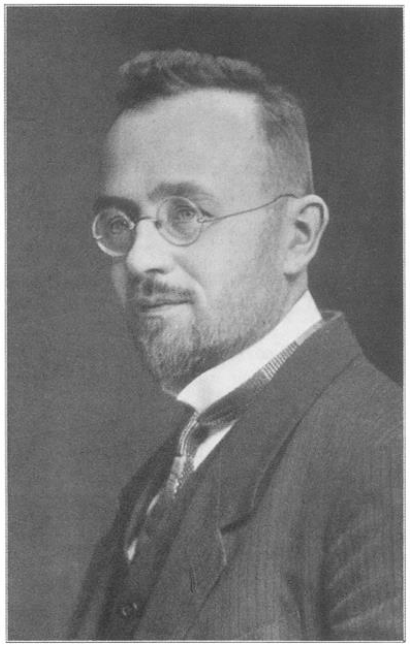


What is tomogaraphy?

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



Johann Radon, 1887-1956



What is tomogaraphy?

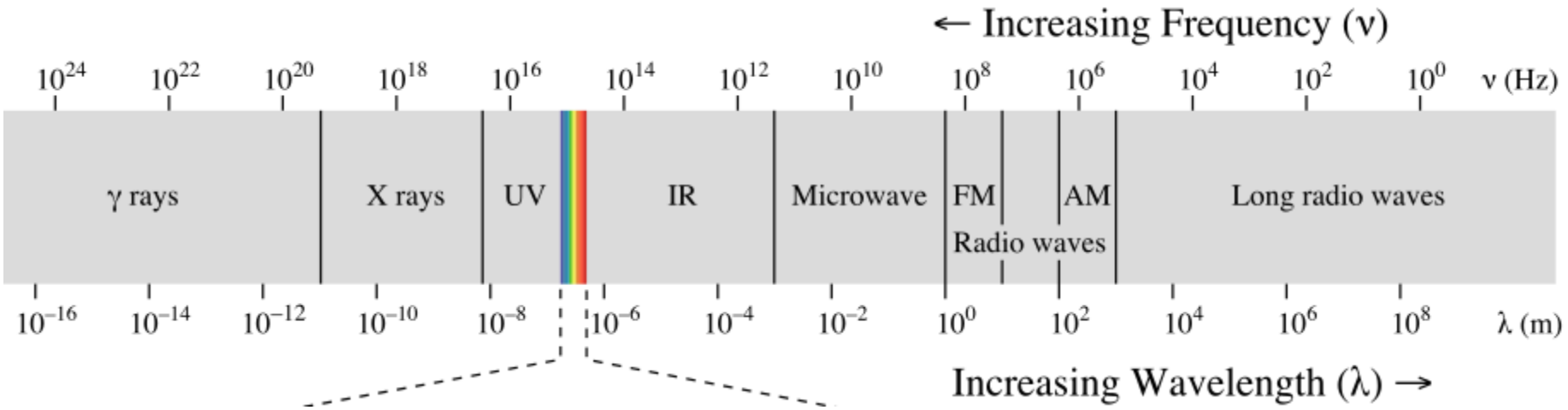
MRI
Radio waves

CT
X-rays

SPECT
γ-rays

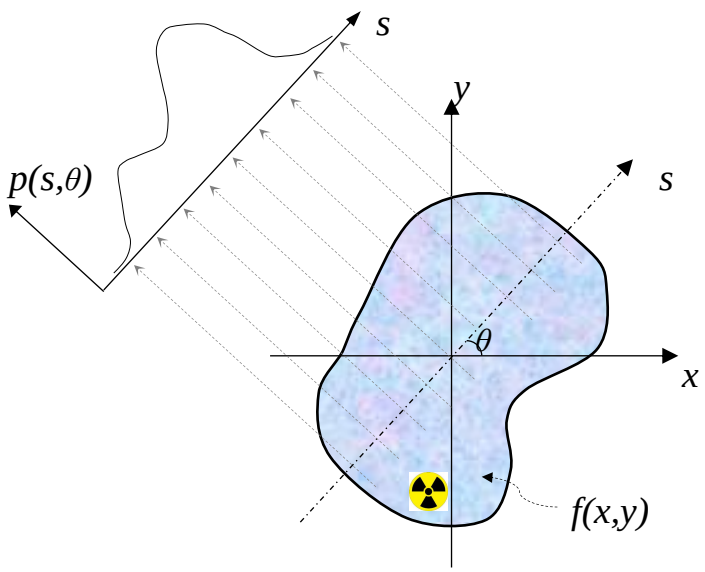
TOMOGRAPHY

PET
γ-rays



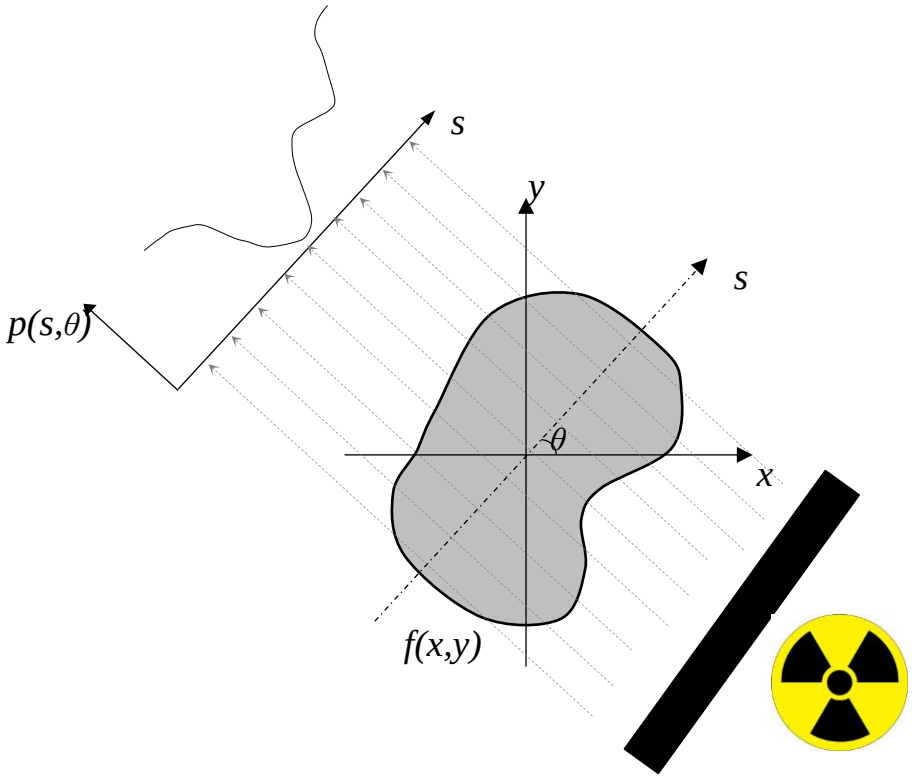
What is tomogaraphy?

Emission Tomography



PET, SPECT, MRI

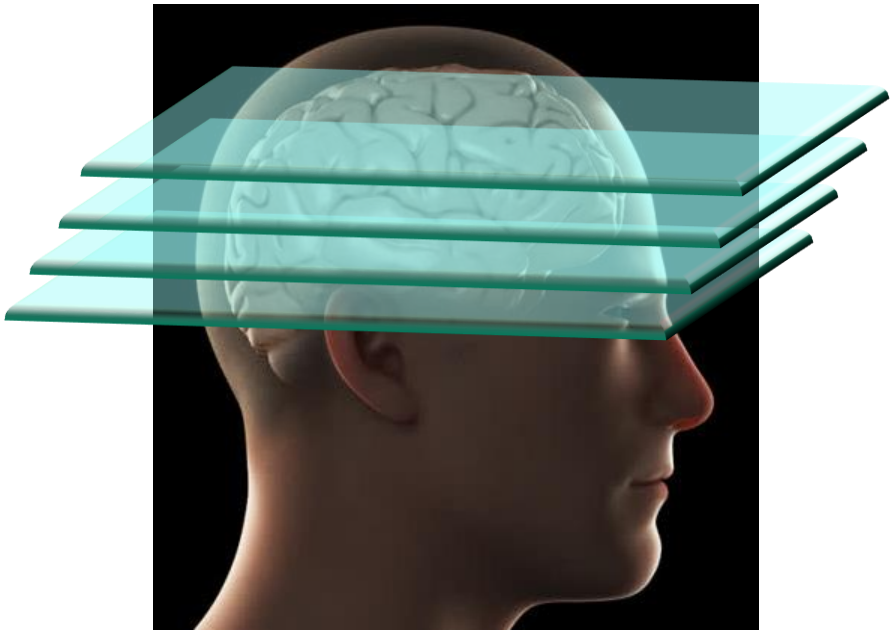
Transmission Tomography



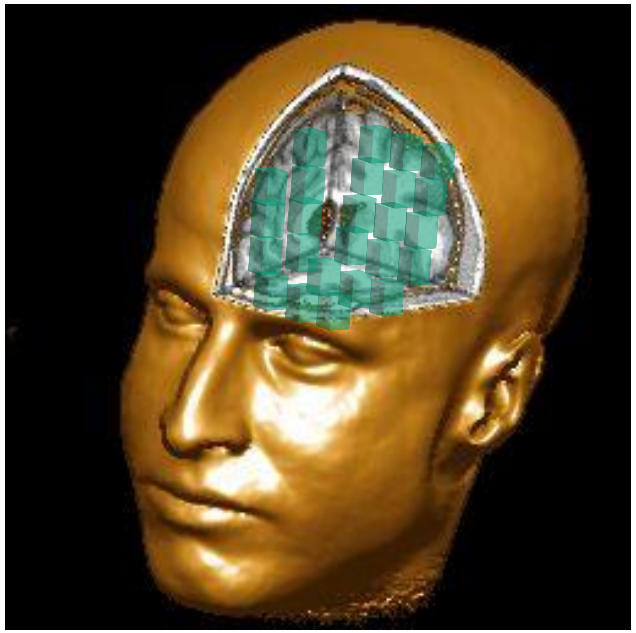
CT, ET, MT

What is tomogaraphy?

Image several 2D slices (2D images)



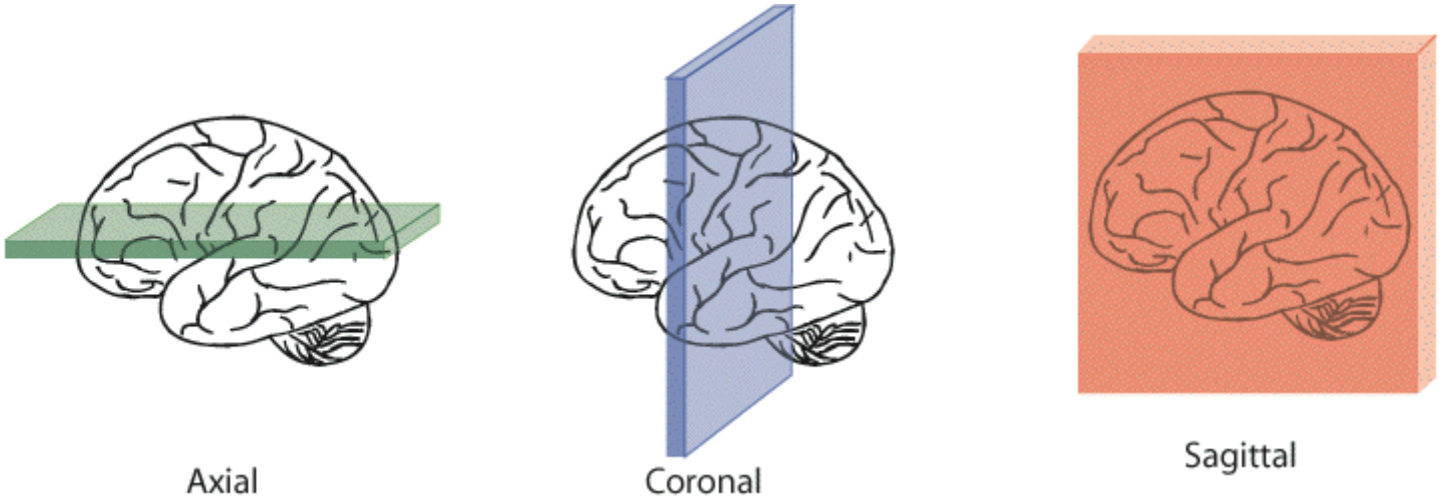
Stacking 2D slices creates an image volume



2D image element: Pixel

3D image element: Voxel

What is tomogaraphy?



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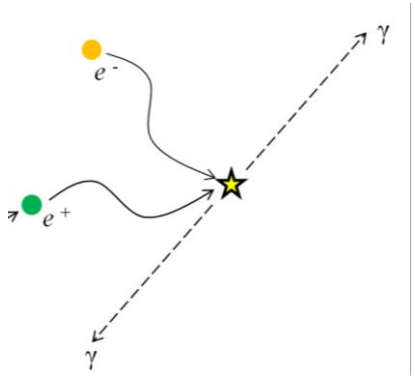
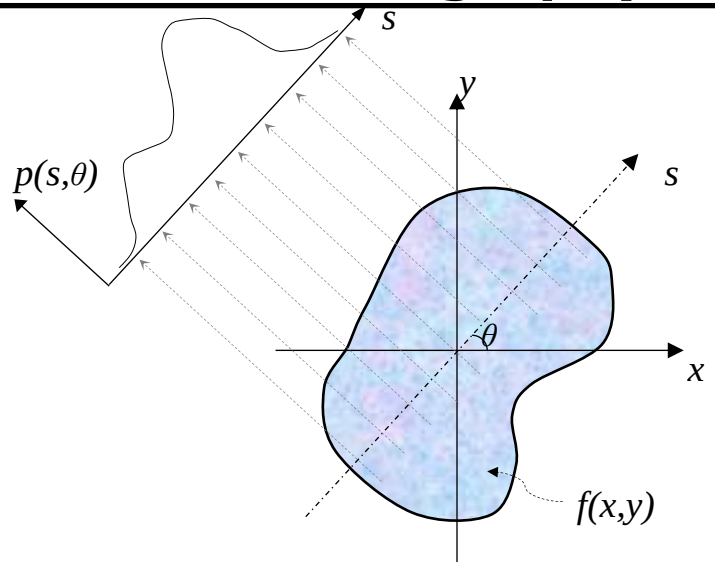
Positron Emission Tomography (PET)

Positron

- Antiparticle of the electron
- Same mass, opposite charge,
- Annihilates in presence of counterparticle

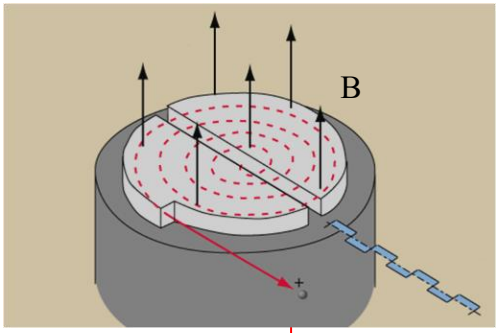


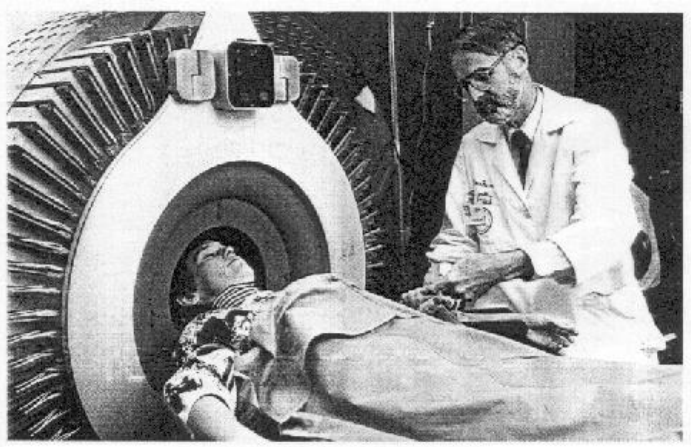
Emission Tomography



- We are all children of broken symmetry
  - Nobel prize in physics, 2008 (Nambu, Konayashi and Masakawa)
- How entanglement has become a powerful tool
  - Nobel prize in physics, 2022 (Aspect, Clauser and Zeilinger)

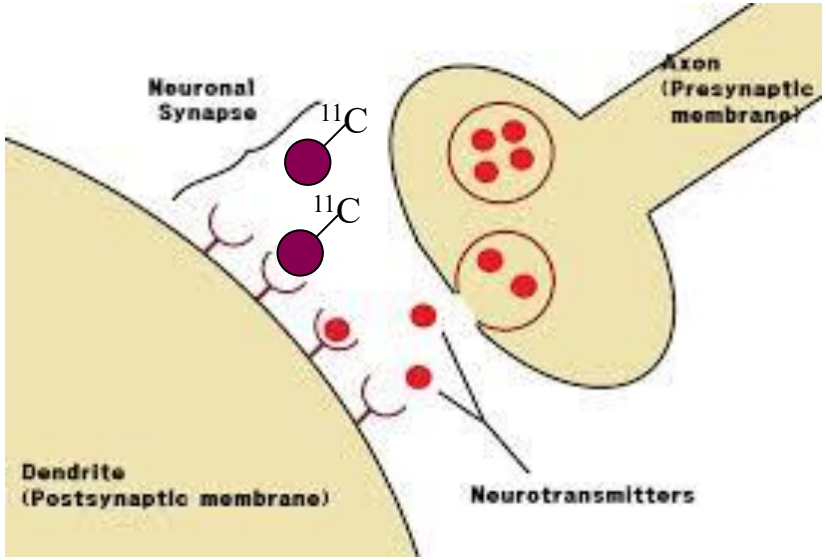
PET -- Physics



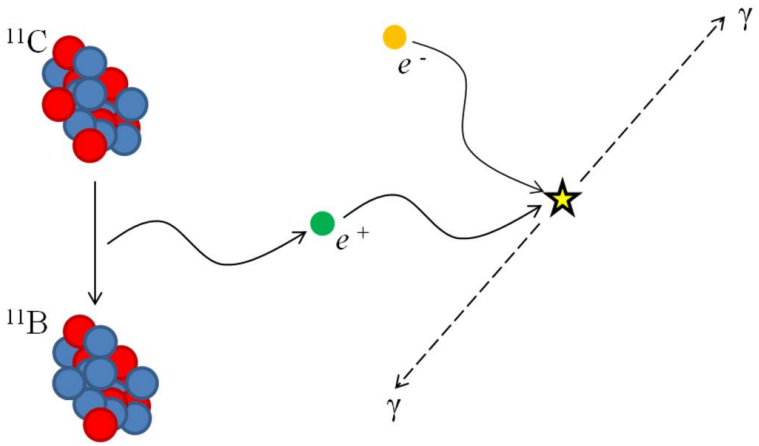


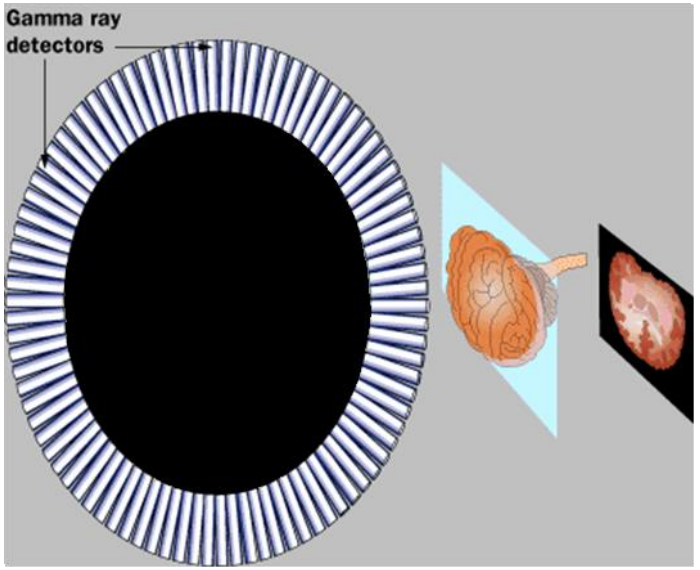
[^{11}C]raclopride

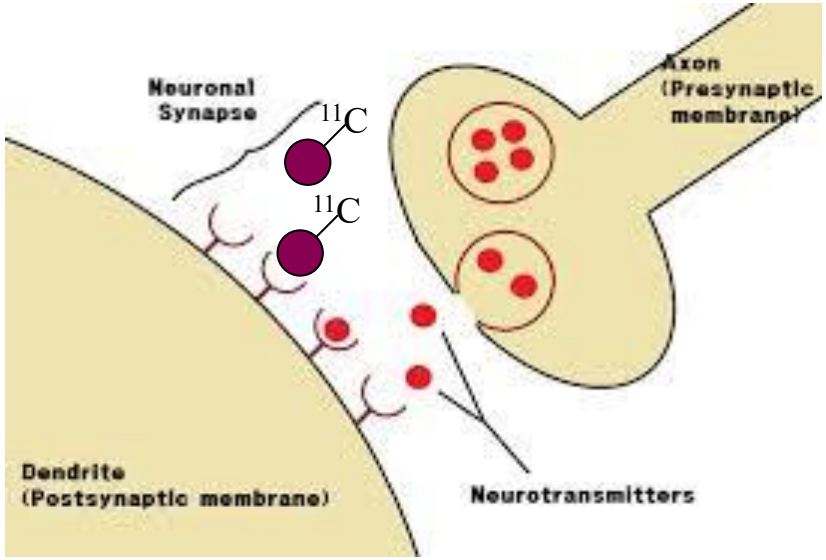
$^{12}C \rightarrow {}^{11}C$



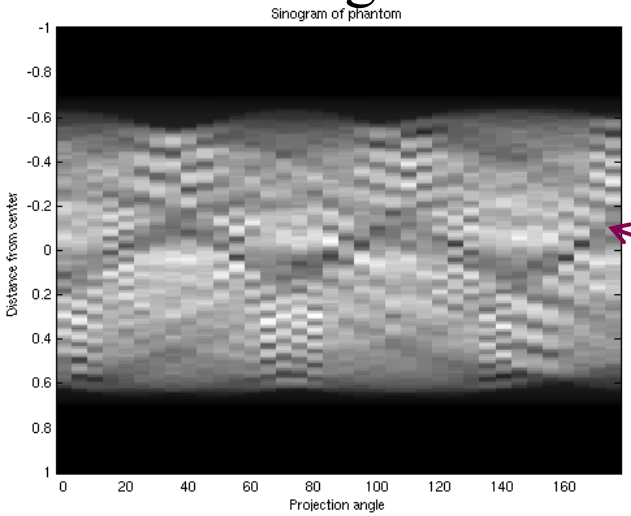
PET -- Physics

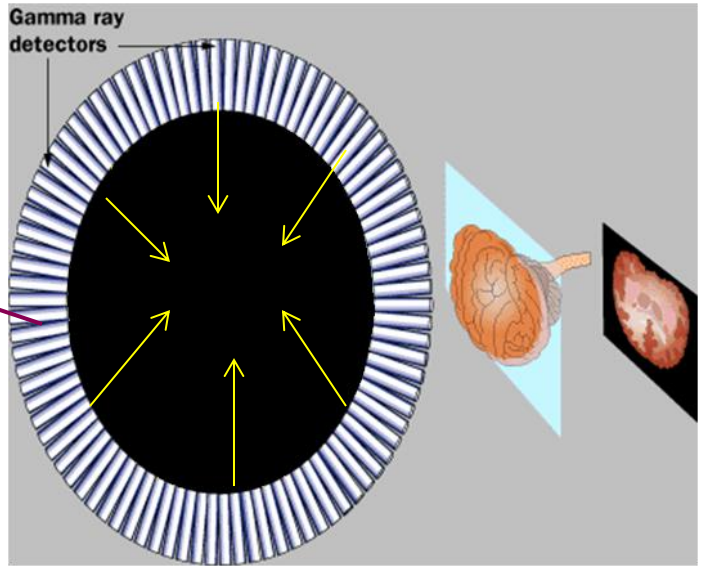

^{11}C
e^-
γ
e^+
^{11}B
γ

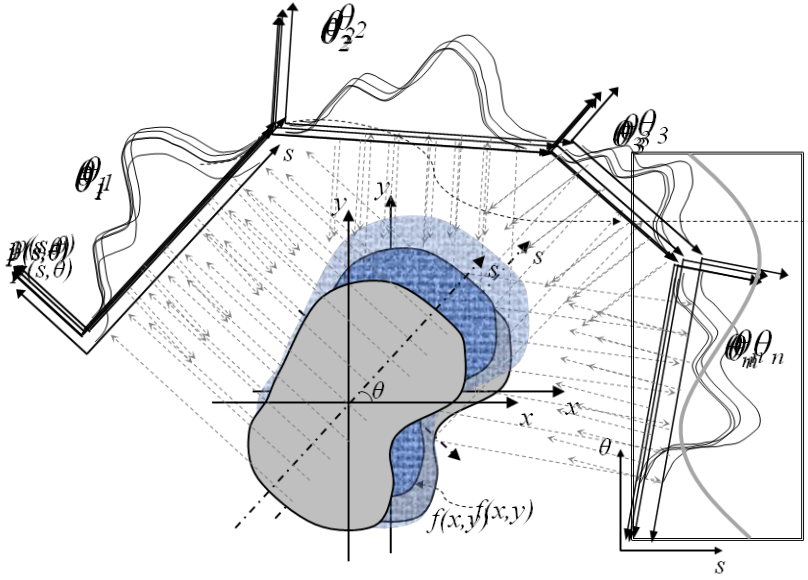

Gamma ray
detectors


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

Sinogram







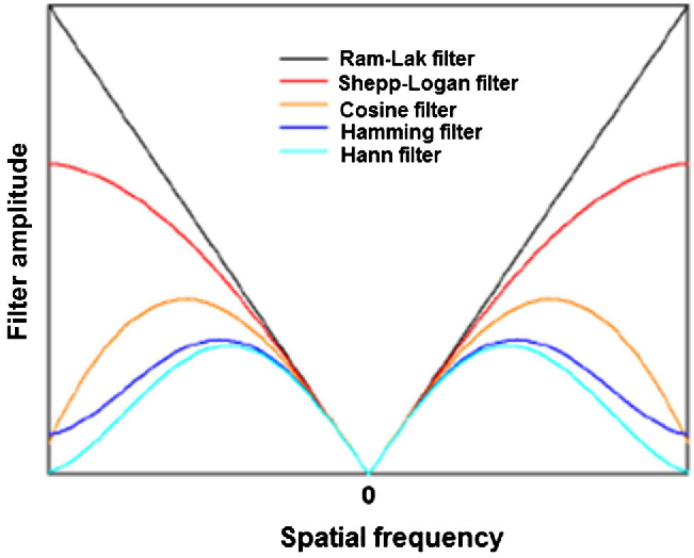
Radon Transform
Object -> Projections

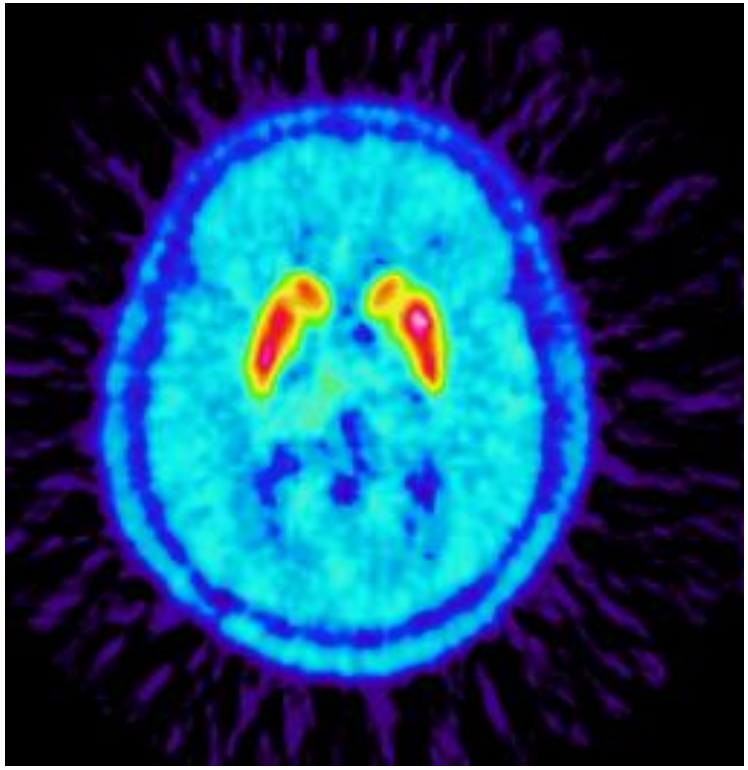
Inverse Radon Tranform
Projections -> Object
(Back projection)

PET – Reconstruction (Filtered back projection)

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

Filter:
Amplify high frequencies
Supress low frequencies

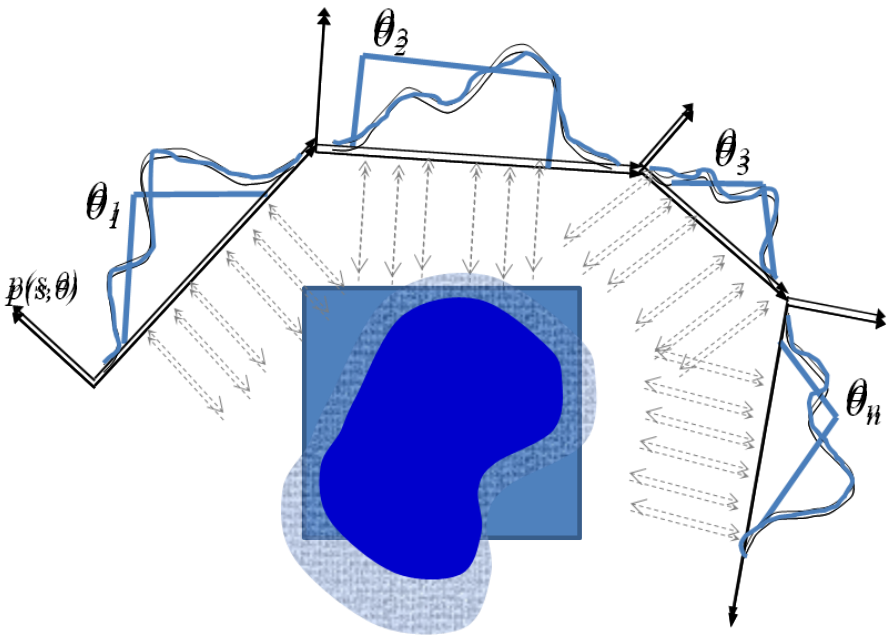




PET image of [11C]raclopride – reconstructed with filtered back projection

Iterative Reconstruction

(Ordered Subset Expectation Maximization)

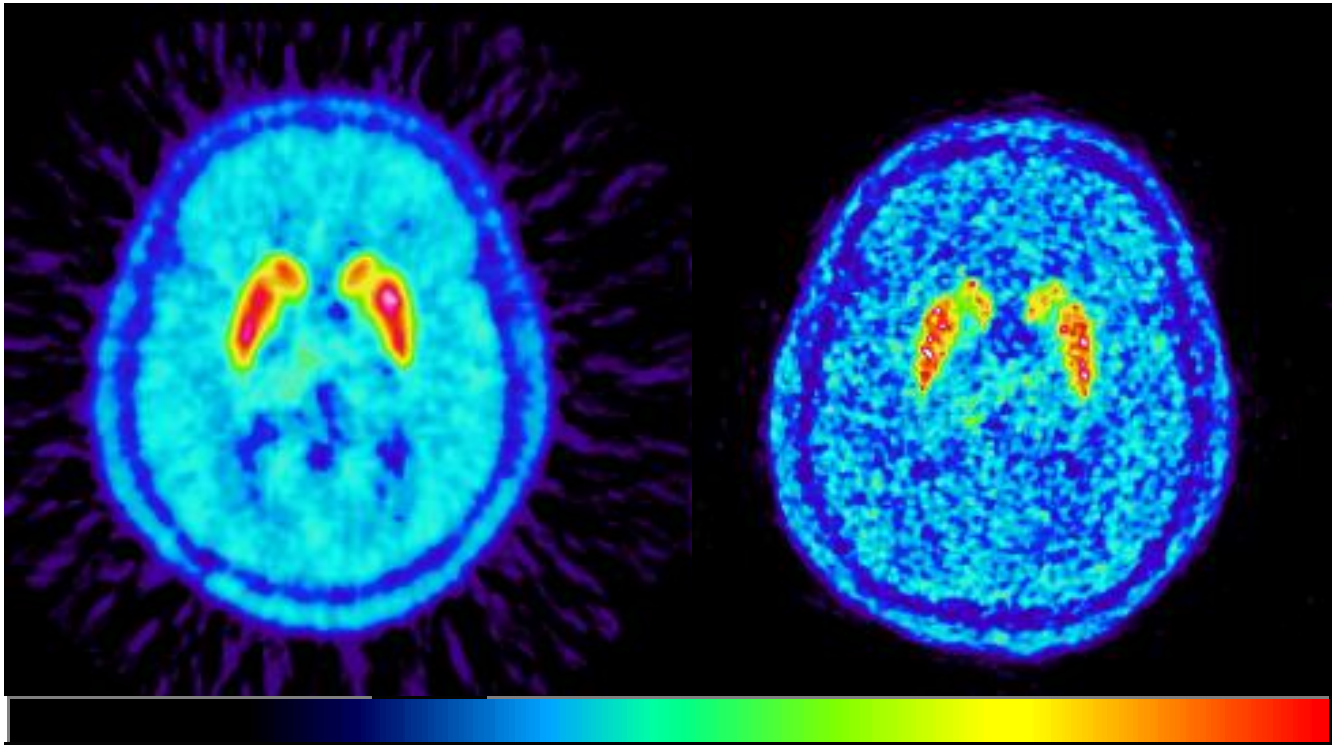


1. Guess an object (maybe a blue square?)
2. Forward project – i.e., obtain the projections for this guessed object
3. Compare the projections to those obtained from the measurement
4. Update object
5. Repeat!

Same subject – scanned with [11C]raclopride

Analytic reconstruction (Filtered Back Projection)

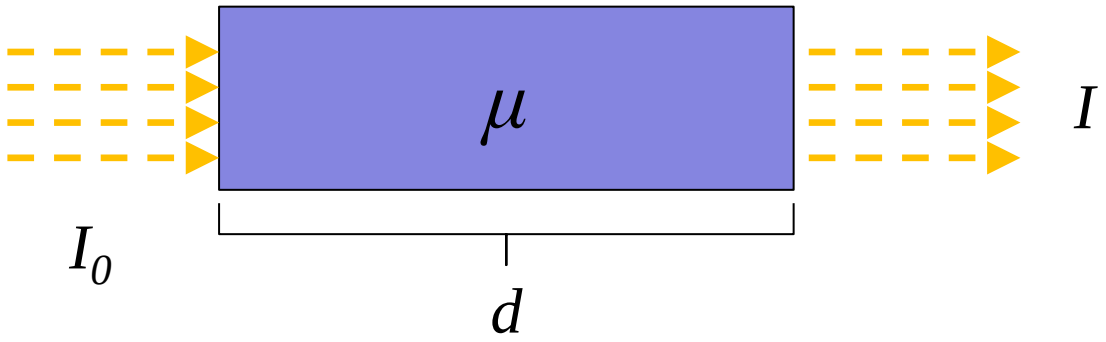
Iterative reconstruction (OSEM)



low

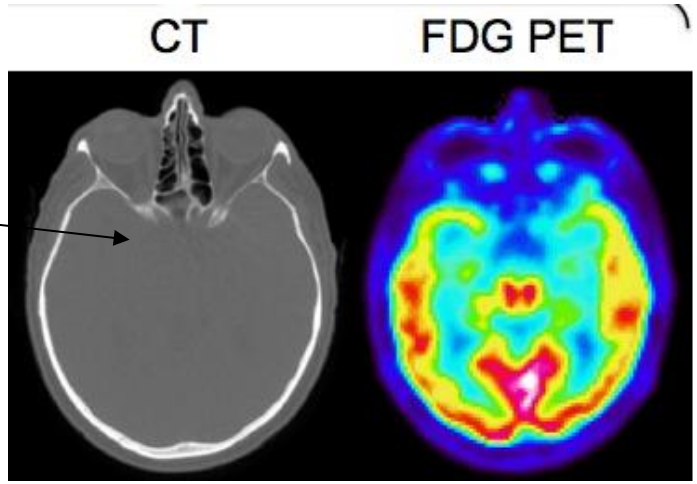
high

Attenuation correction



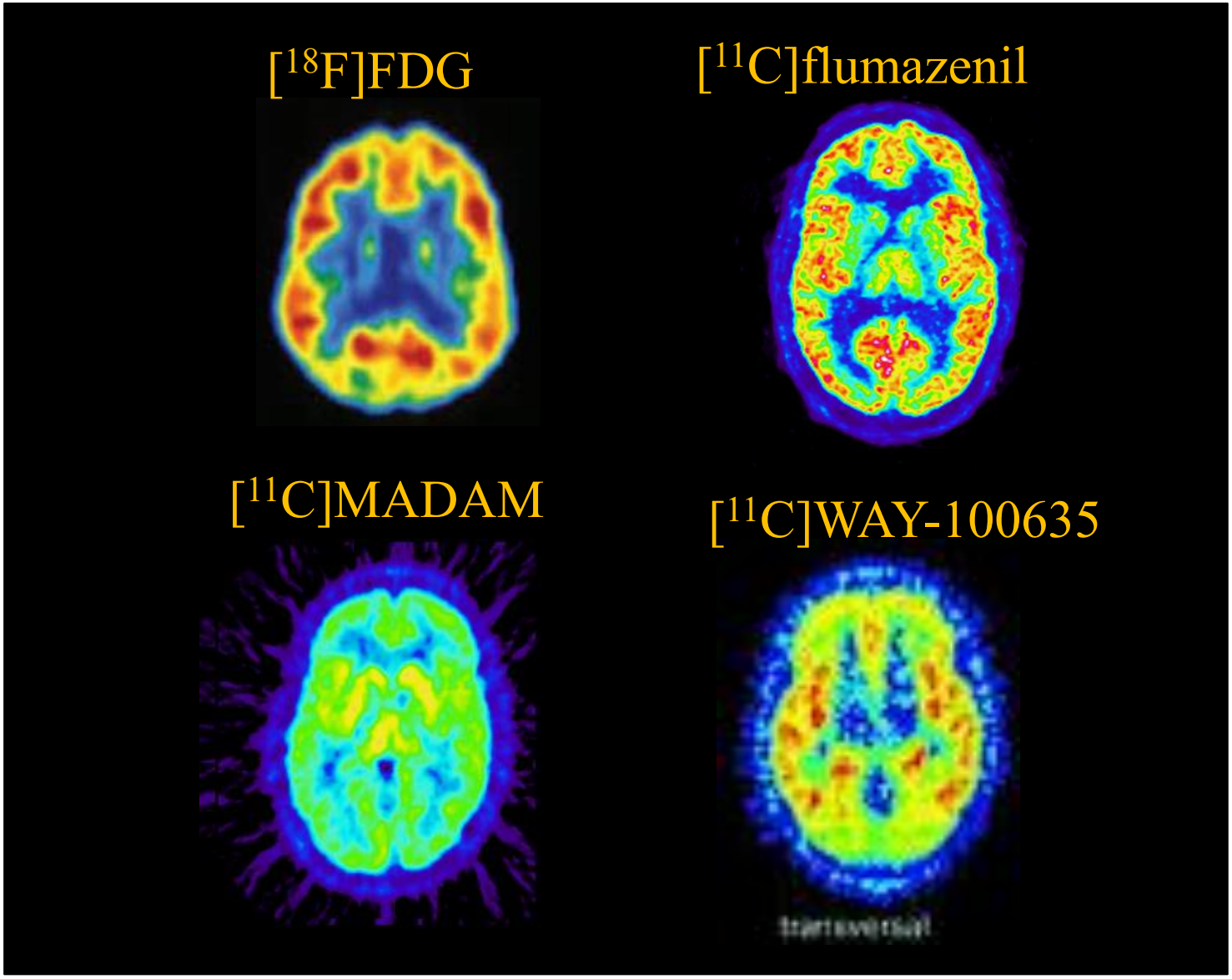
Beer Lambert law: $I = I_0 e^{-d \cdot \mu}$

μ-map,
$\mu(x)$



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

PET – Radioligands



What can possibly go wrong?

Non-correctable physical properties

- Non-colinearity
- Positron travel

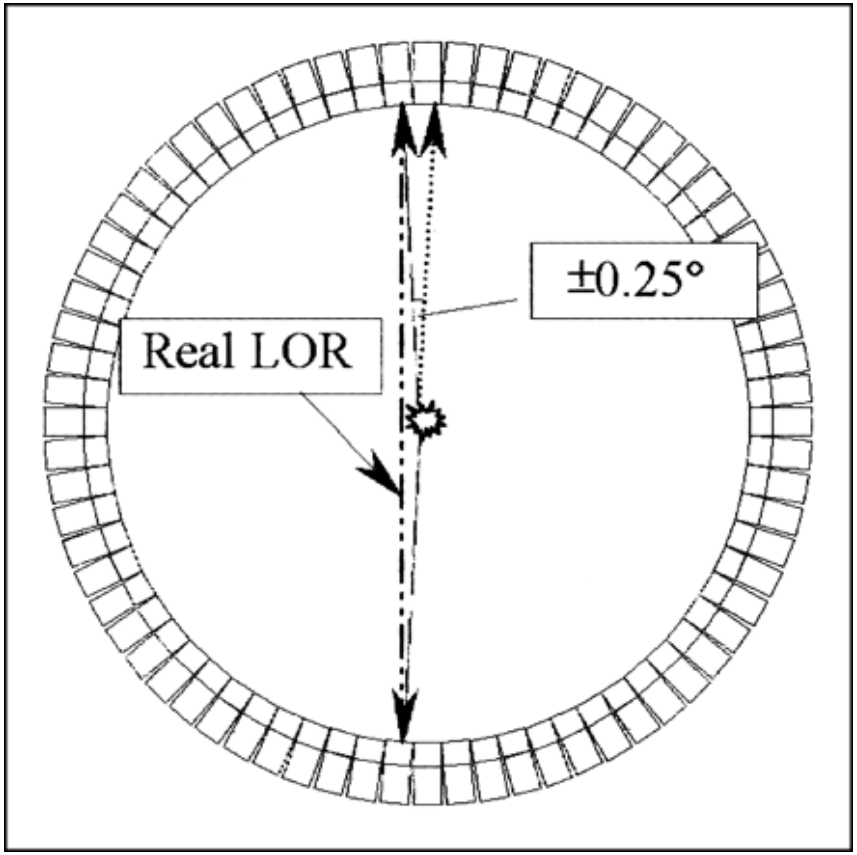
Correctable physical properties

- Scatter
- Randoms

What can possibly go wrong?

Non-correctable physical properties

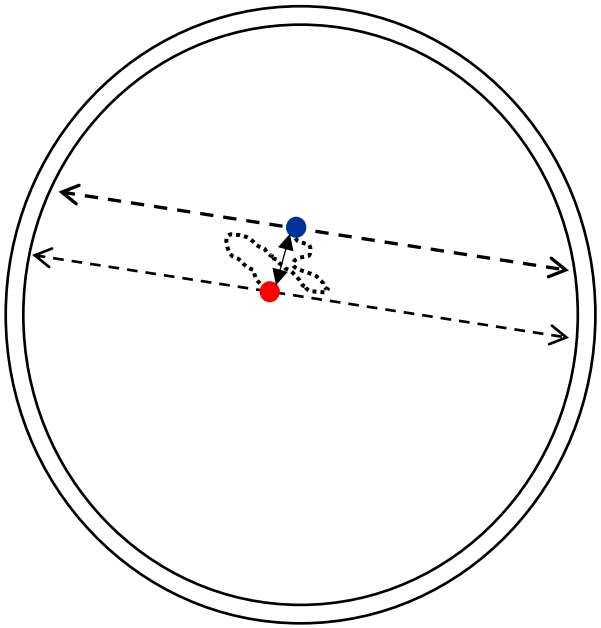
- **Non-colinearity**
- Positron travel

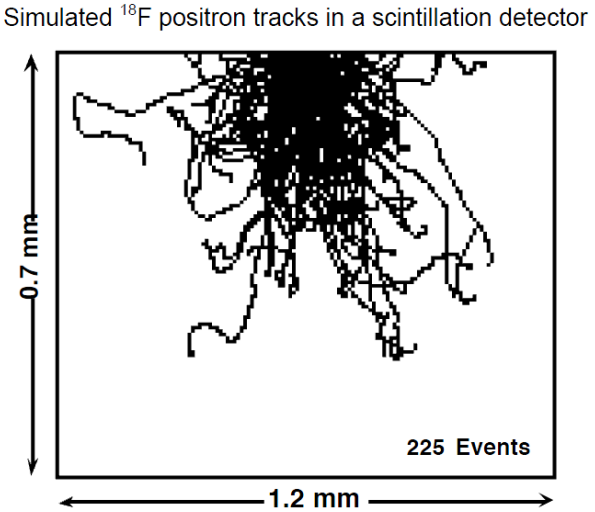


What can possibly go wrong?

Non-correctable physical properties

- Non-colinearity
- **Positron travel**





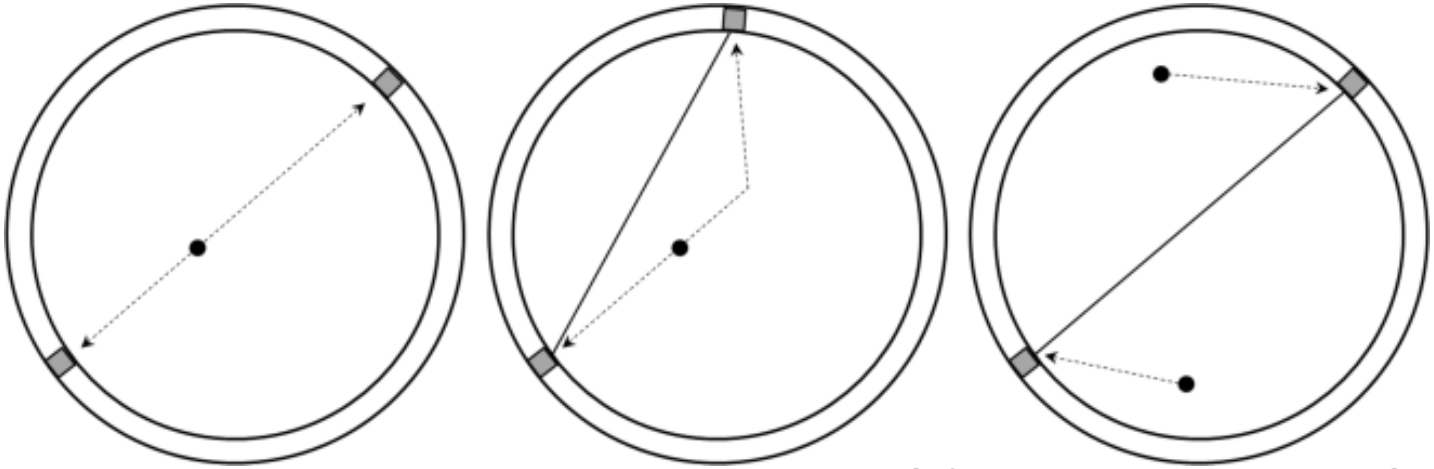
Isotope	Endpoint energy (MeV)	fwhm (mm)
^{18}F	0.64	0.54
^{11}C	0.96	0.92
^{13}N	1.22	1.49
^{15}O	1.72	2.48
^{68}Ga	1.90	2.83
^{82}Rb	3.35	6.14

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	Correctable physical properties	Camera Properties
• Non-colinearity • Positron travel	• Scatter • Randoms	• Detector size • Penetration • Gantry radius • Non-uniform Sampling

Resolution ↓

Single Photon Emission Computed Tomography (SPECT)

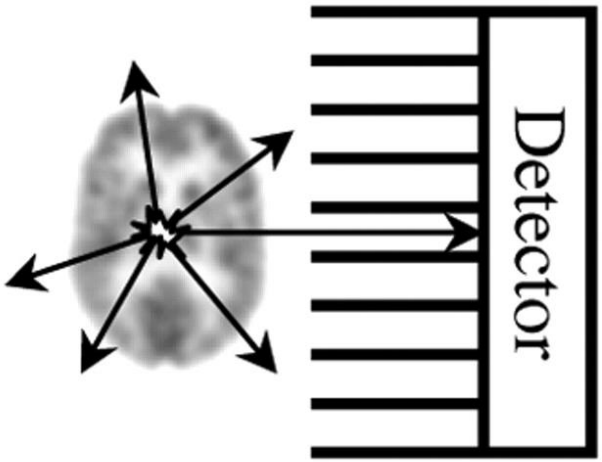
”Like PET but cheaper”

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)

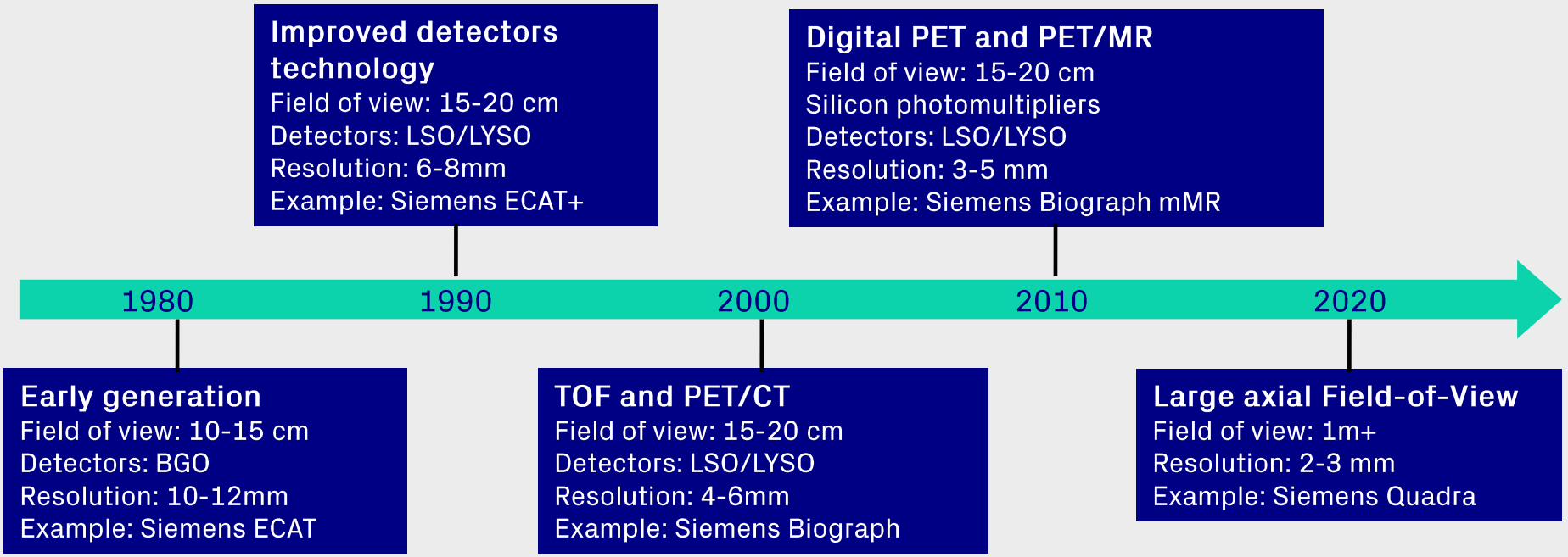
PET		SPECT	
Material	Halflife	Material	Halflife
^{11}C	20.3 min	^{99m}Tc	6.0 hours
^{18}F	110 min	^{123}I	13.1 hours
^{15}O	122 sec	^{111}In	2.8 days

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)

Evolution of PET instrumentation



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

Resolution: 16 megapixels

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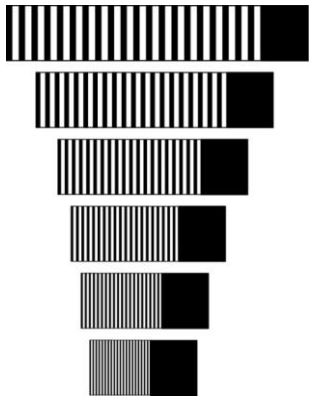
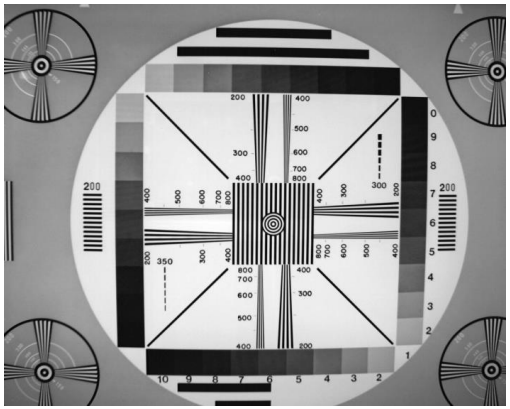
Emission tomography: What do we mean with ”resolution”?

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

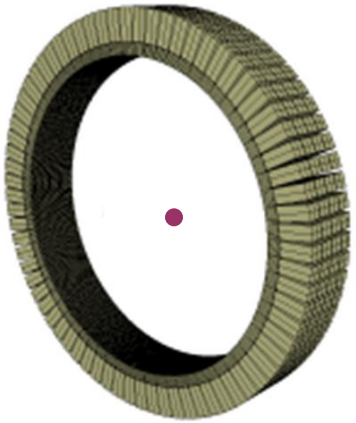
Resolution
=
Amount of information / unit area (volume)



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

Nbr of pixels
=
Upper Limit

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

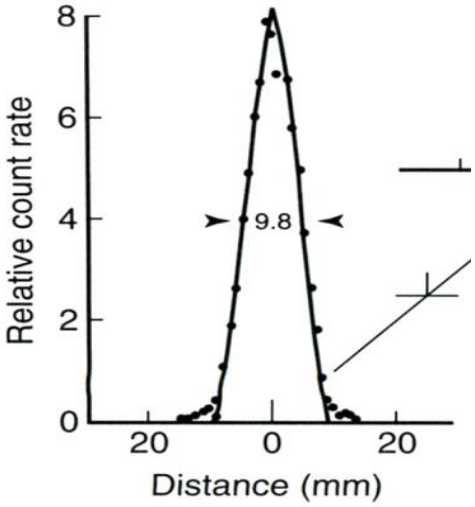


Point source in air

Acquisition + Reconstruction

”Point Spread Function” (PSF)

Measure intensity line profile through PSF

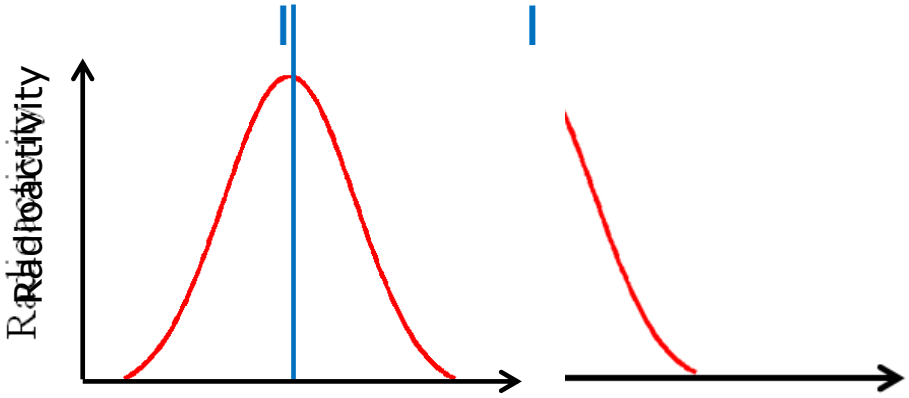


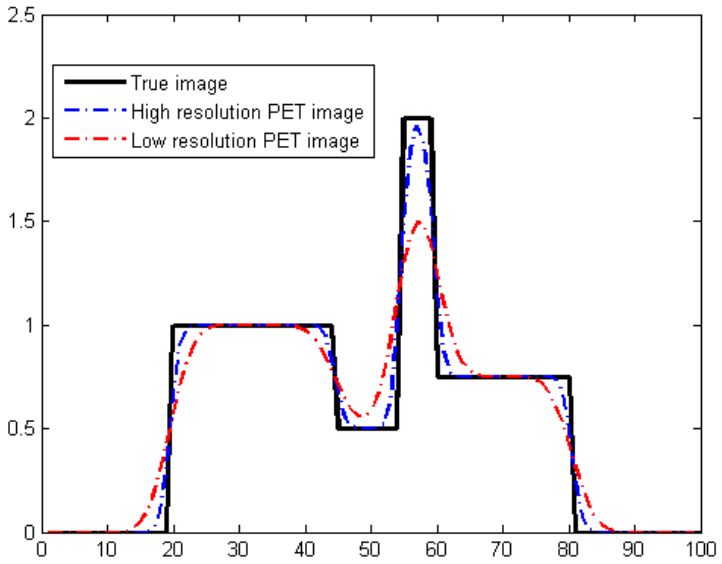
System resolution
=
FWHM of the PSF!

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!





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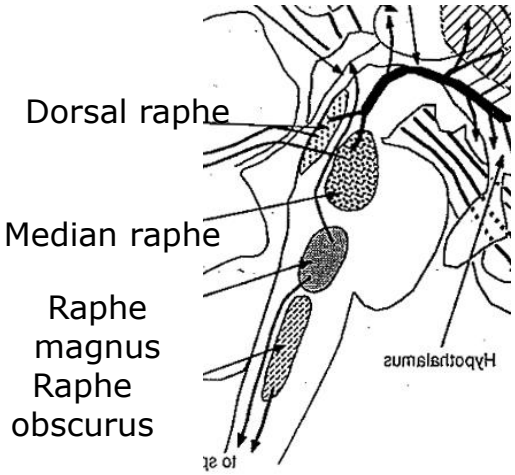
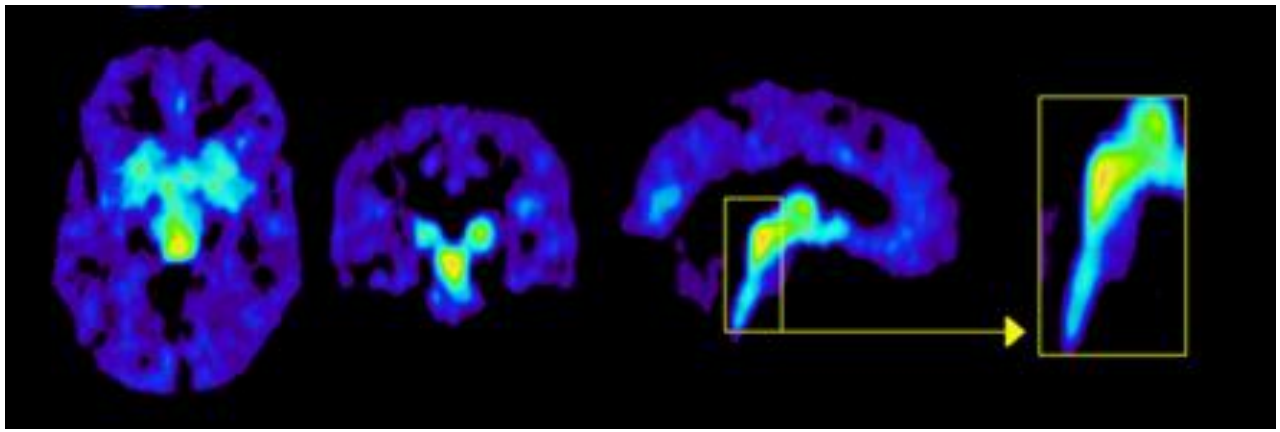
What are the consequences of low spatial resolution - Example





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

Positron Emission Tomography (PET)

We are all children of broken symmetry

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

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- $E = mc^2$
- Big bang

Positron Emission Tomography (PET)

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?

Positron Emission Tomography (PET)

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} antimatter

Positron Emission Tomography

We are all children of broken symmetry

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Antimatter

- 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