Small Animal PET & Monte Carlo Simulations in Nuclear Medicine

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I.Small Animal PET

- What is PET?
- Instrumentation
- Image reconstruction
- Why is necessary to have a small animal PET?
- Challenges of small animal PET

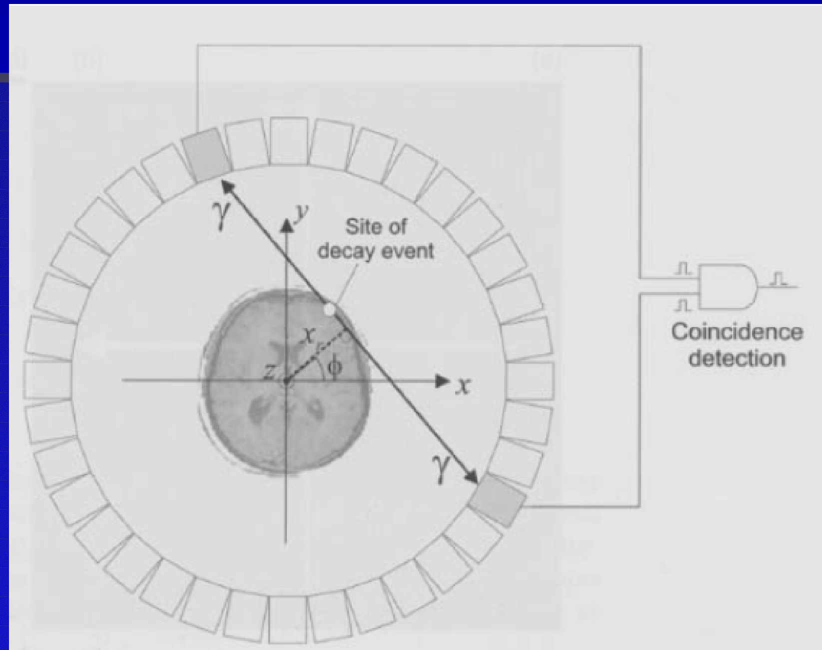
The basis of PET

Small Animal PET

The basis of PET

- Positron Emission Tomography (PET) is a non invasive technique that provides three-dimensional (3D) tomographic images of radiotracer distribution within a living subject
- Positron emitting nuclides: ^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{64}Cu
- PET physics

ß+ decay



$$ {}^{A}_{Z}X_{N} \longrightarrow {}^{A}_{Z-1}Y_{N+1} + e^{+} + \nu $$

Positron annihilation

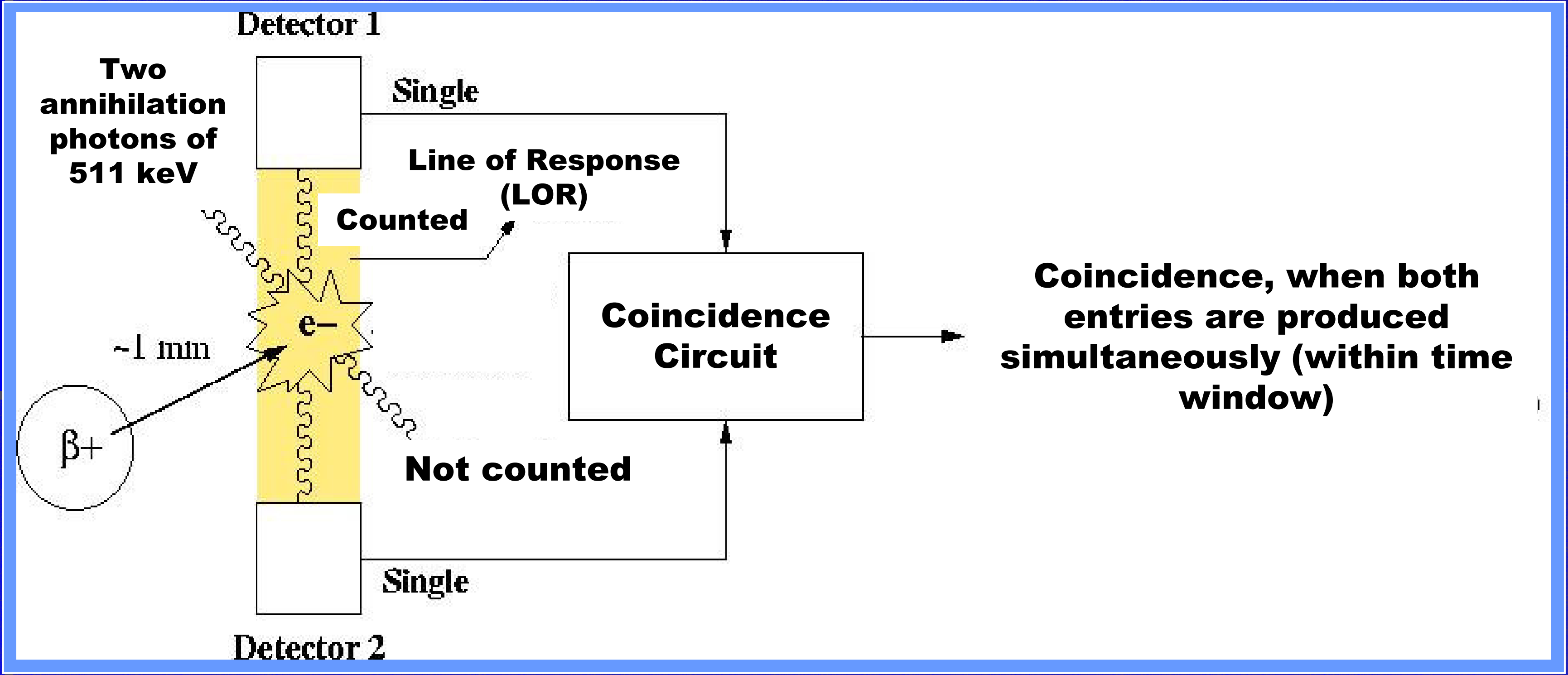
$$ e^{+} + e^{-} \longrightarrow \gamma + \gamma $$

γ

γ

The basis of PET

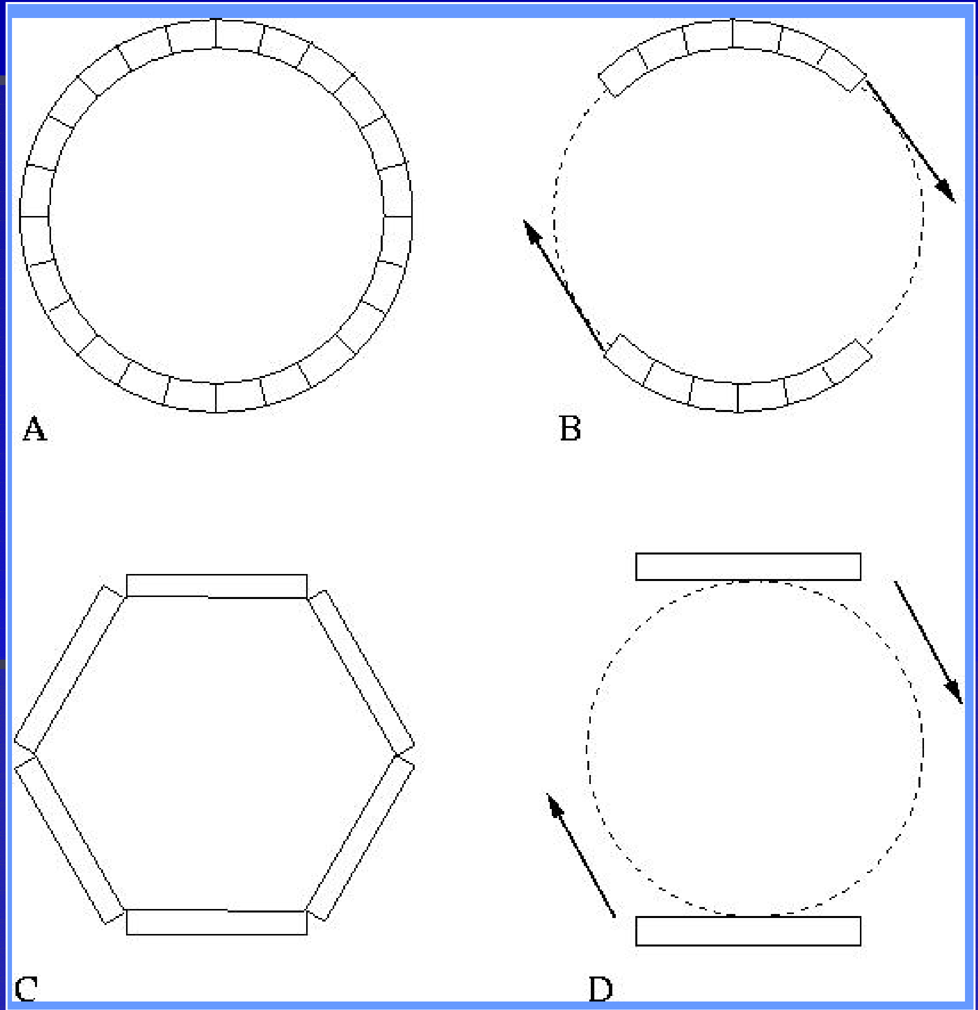
- Coincidence Detection



The basis of PET

- Instrumentation
  - Material sensitive to radiation: scintillators (γ → visible light)
  - Photomultiplier tube (visible light → electrons)
  - System electronics (signal processing)
- Scintillators used in PET:

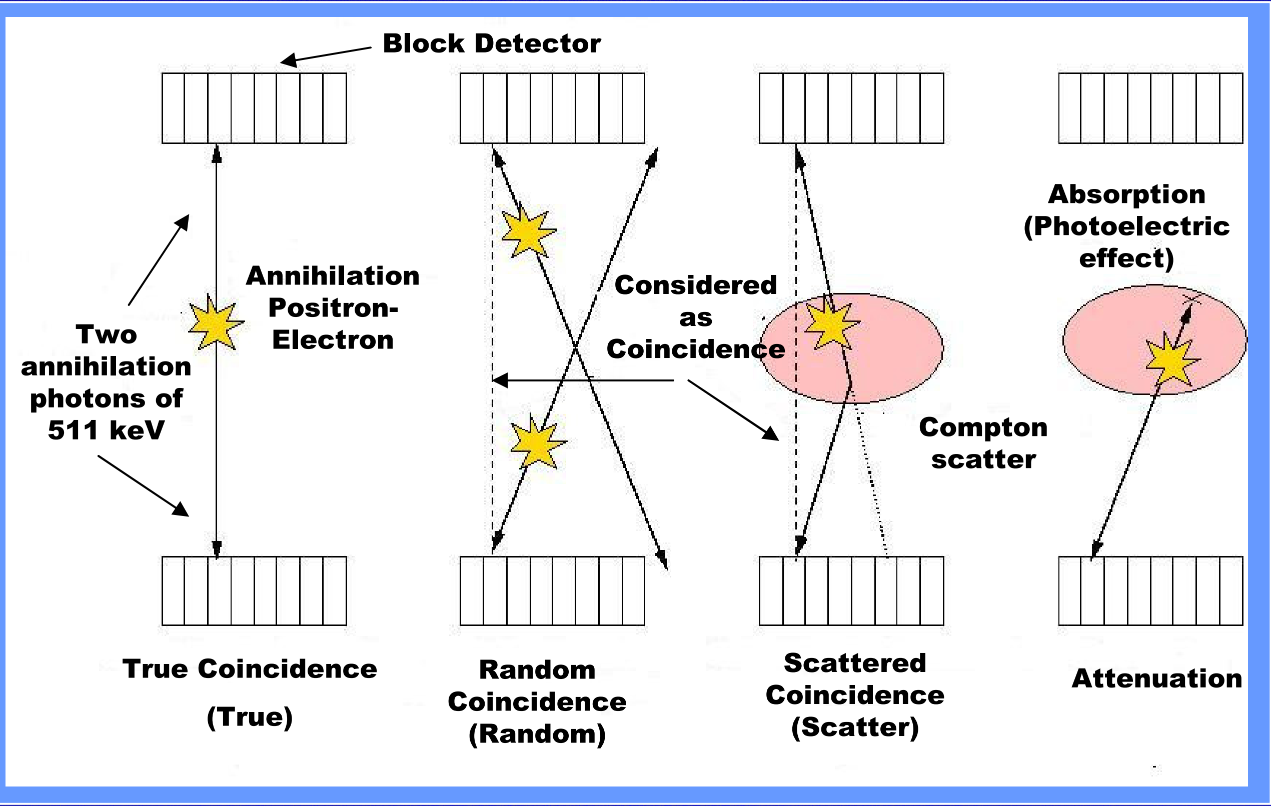
NaI, BGO, LSO, GSO



Basic tomographic system geometries

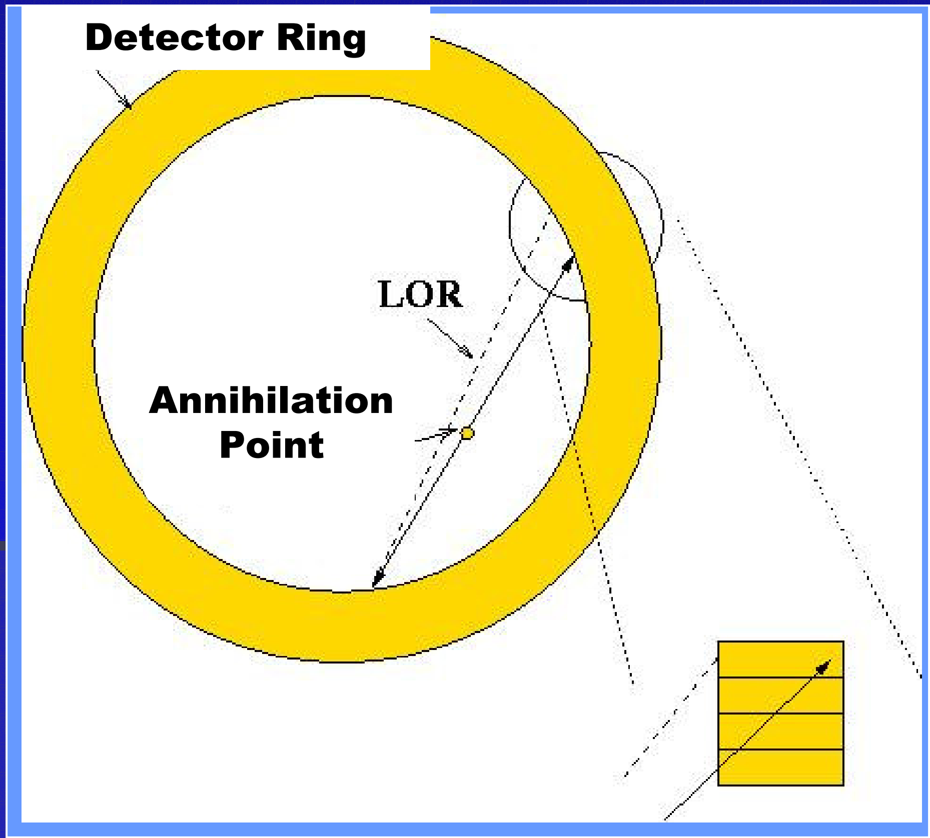
The basis of PET

- Image blurring (I)
  - Randoms
  - Scatter
  - Attenuation
  - Dead time
  - Noise



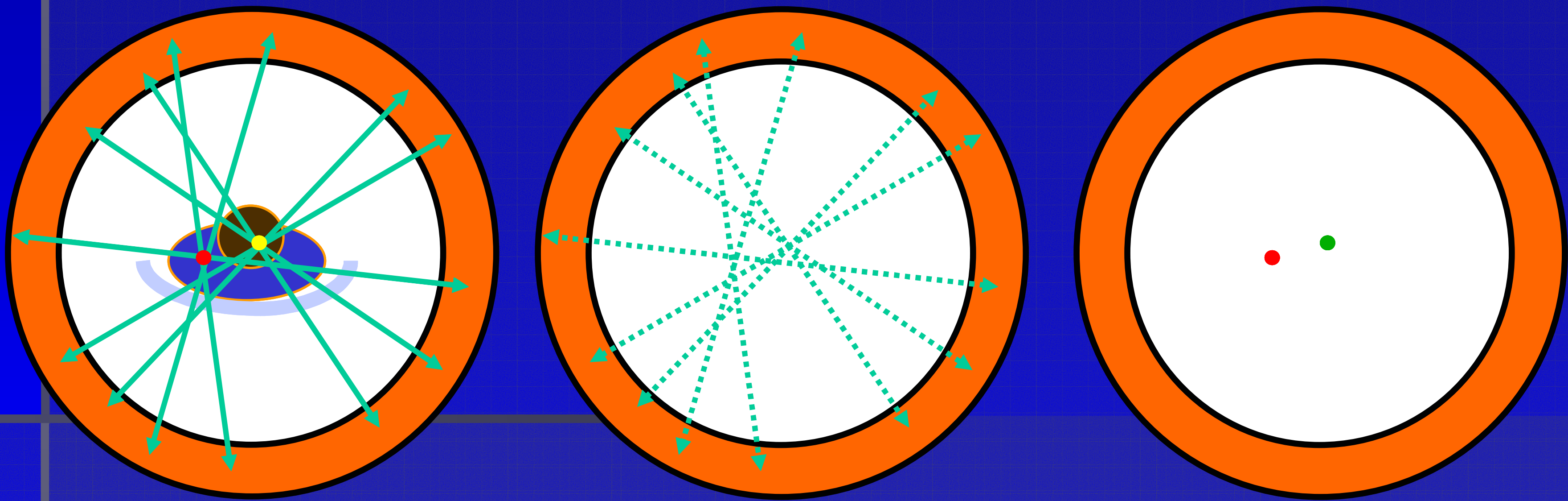
The basis of PET

- Image blurring (II)
  - Spatial resolution
    - Positron range
    - Noncolinearity
    - Detector intrinsic resolution
    - Parallax error: DOI, depth of interaction



The basis of PET

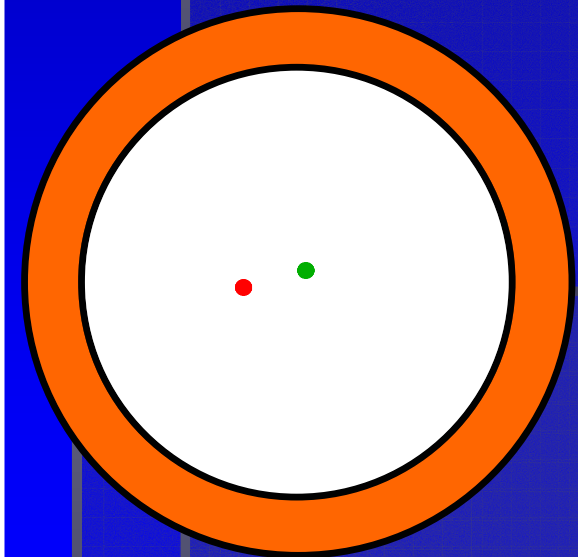
This is...



what happened what we measure what we are looking for!

The basis of PET

- The reconstruction problem



Emission + Detection

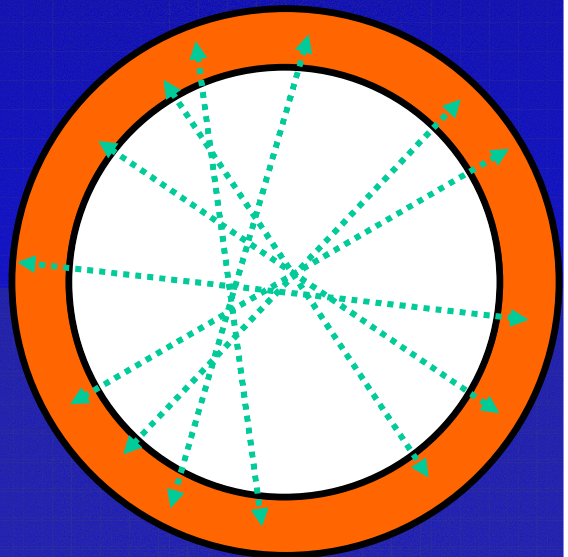
Direct problem

→

←

Inverse problem

RECONSTRUCTION



The basis of PET

- Image reconstruction algorithms
  - Analytical
    - FBP
  - Iterative
    - Algebraic
      - ART
    - Statistical
      - Least Squares
        - LS, PWLS
      - Max. Likelihood
        - MLEM, OSEM
      - Bayesians
        - MAP

The basis of PET

- Problem formulation

Continuous-discrete problem

- Unknown, $f(x,y,z)$: Spatial distribution of radioisotope (continuous function)

- Measured data, $\mathbf{g}$:

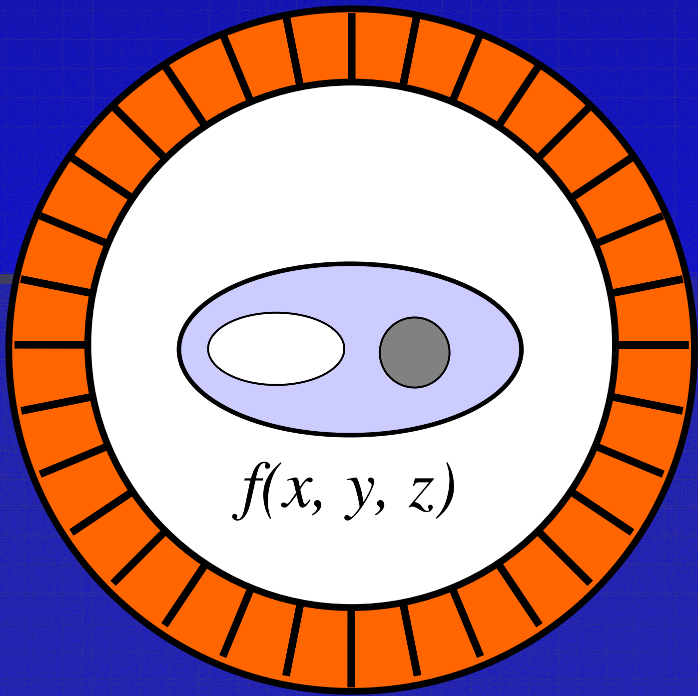
  g_i: Number of coincidences registered by detector pair *i* (discrete)

- System response, $h_i(x,y,z)$: Contribution of radioactivity located at (x,y,z) to measured counts by detector pair *i*

The basis of PET

- Problem formulation

$$g_i = \iiint_V f(x, y, z)\, h_i(x, y, z)\, dx\, dy\, dz$$



The basis of PET

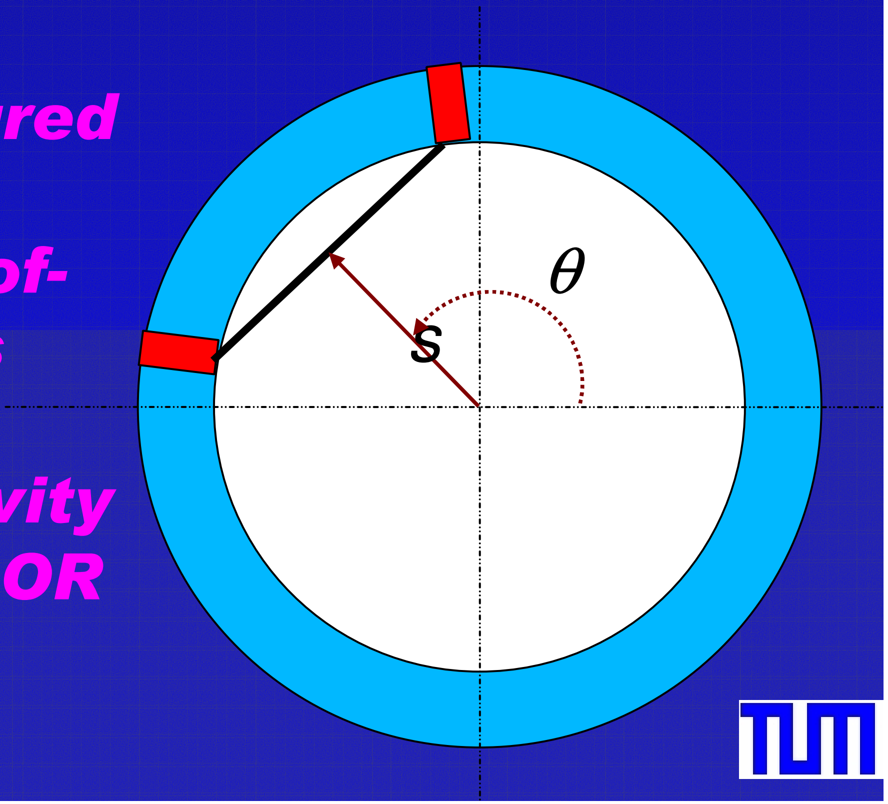
- Analytical Methods

Simplified modeling of detection process:

$$p(\theta, s) = \iint dxdy\, f(x, y)$$

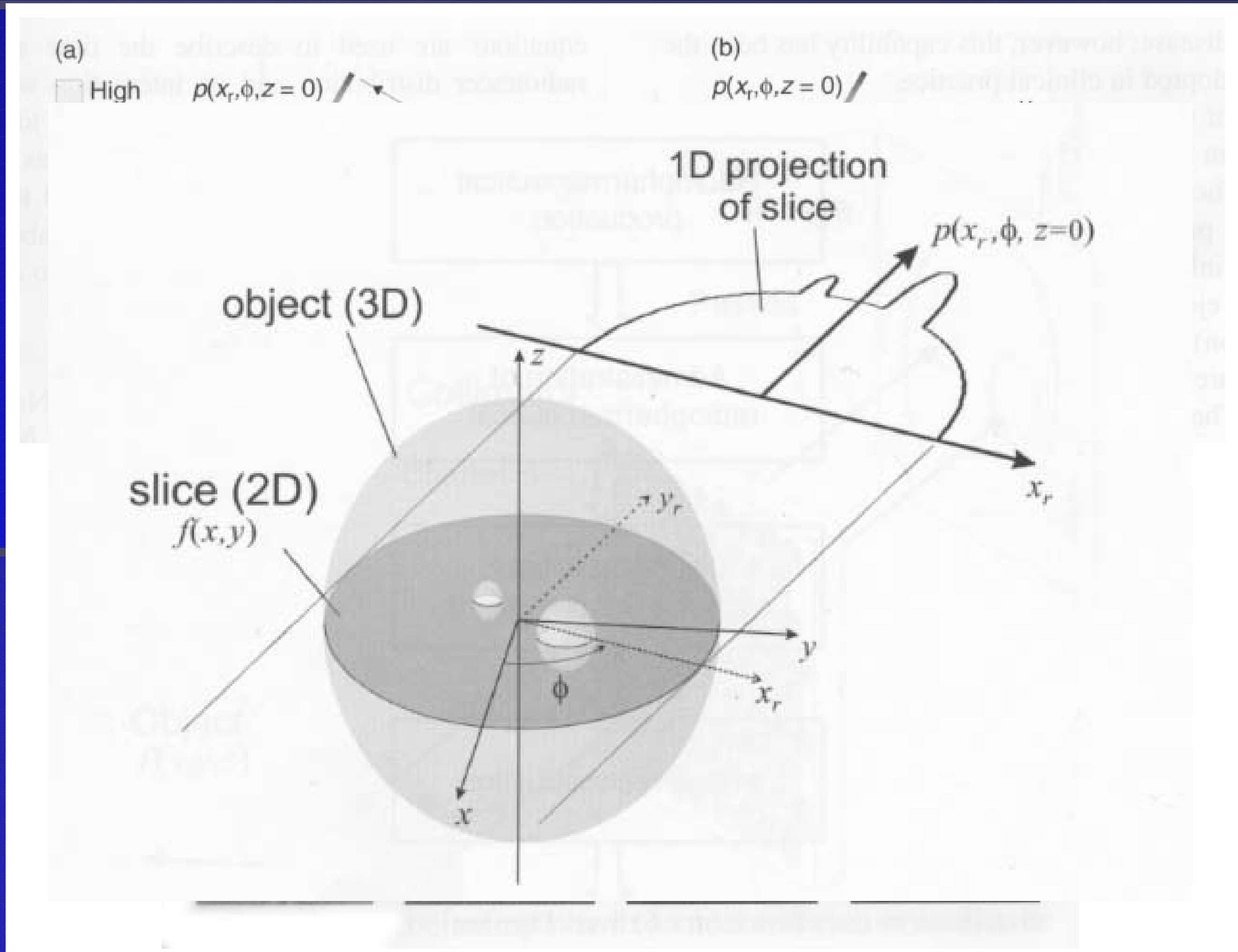
← **Radon transform**

The radioactivity measured by the detector pairs characterized by a line-of-response (LOR) L(θ, s) is assumed to be the line integral of the radioactivity distribution along that LOR



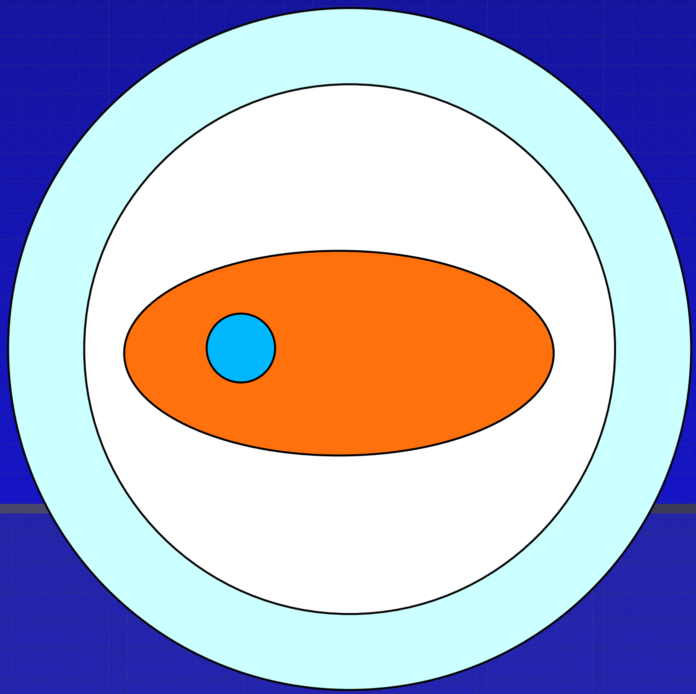
The basis of PET

- Analytical Methods: FBP, Filtered Back Projection

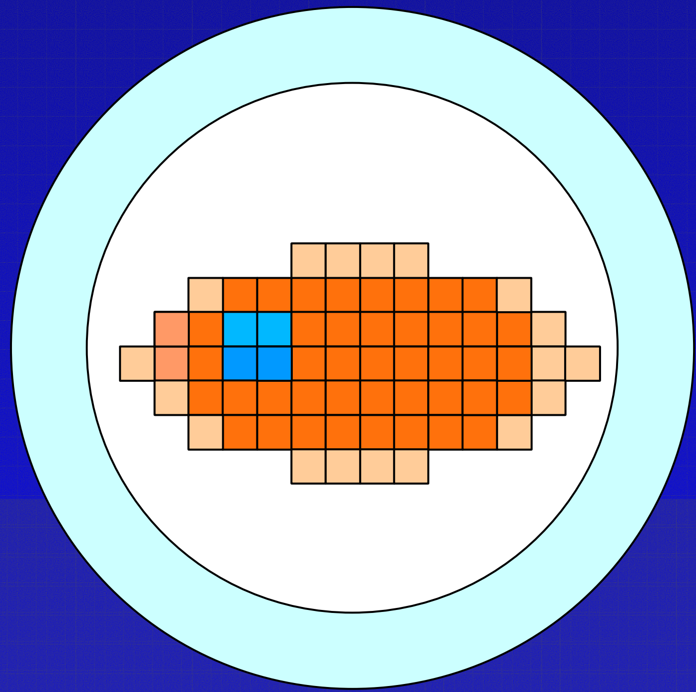


The basis of PET

- Iterative Methods:



The real object



The unknown

The basis of PET

- Iterative Methods:

Discrete-Discrete Problem

$$g = A\, f$$

g Measurement vector → **known**

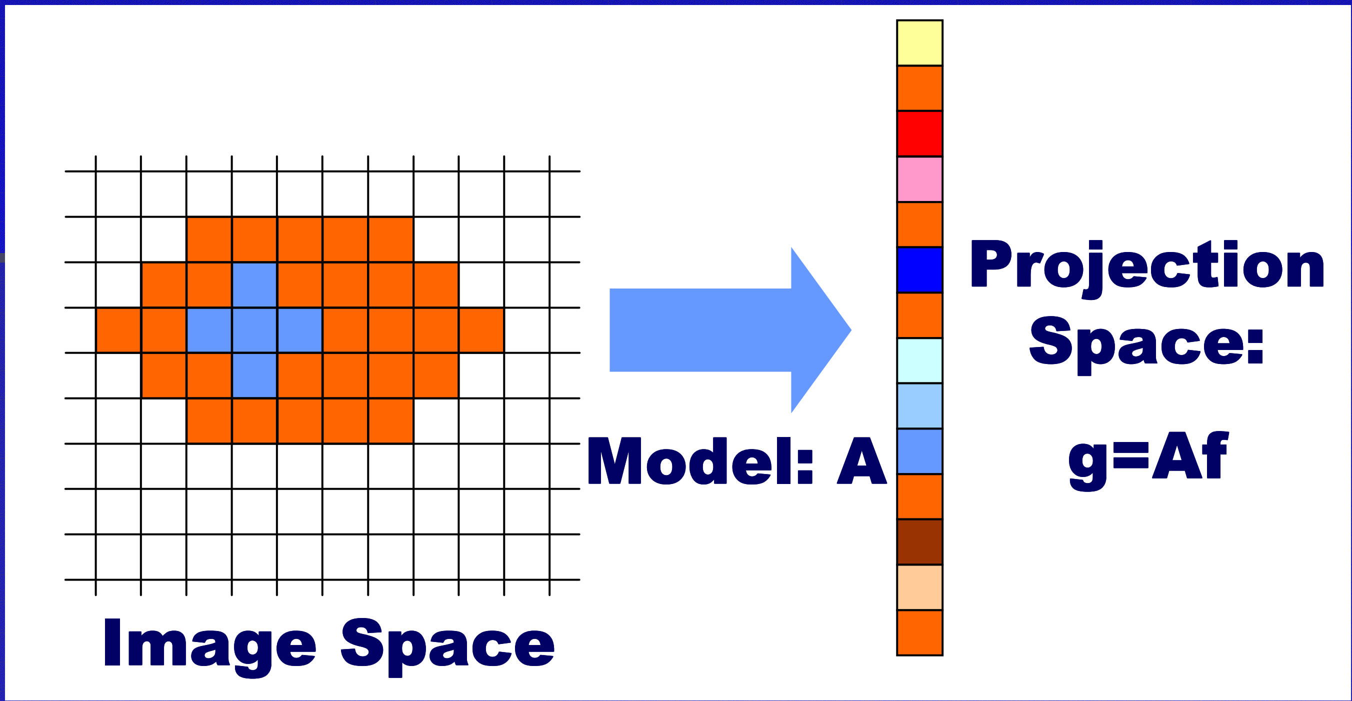
f Image vector → **unknown**

A System matrix (modelling of system response)

→ **To be determined!!!**

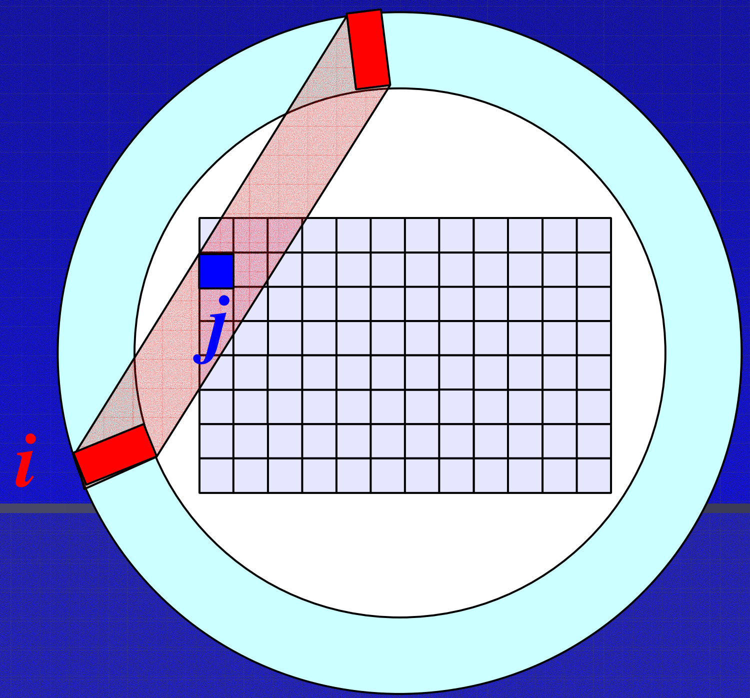
The basis of PET

- Iterative Methods
  - System matrix (describes image process)
    - It can represent attenuation or any linear blurring mechanism
    - It can be estimated from knowledge of the system design, measurement of the patient attenuation distribution, …



The basis of PET

- Iterative Methods:



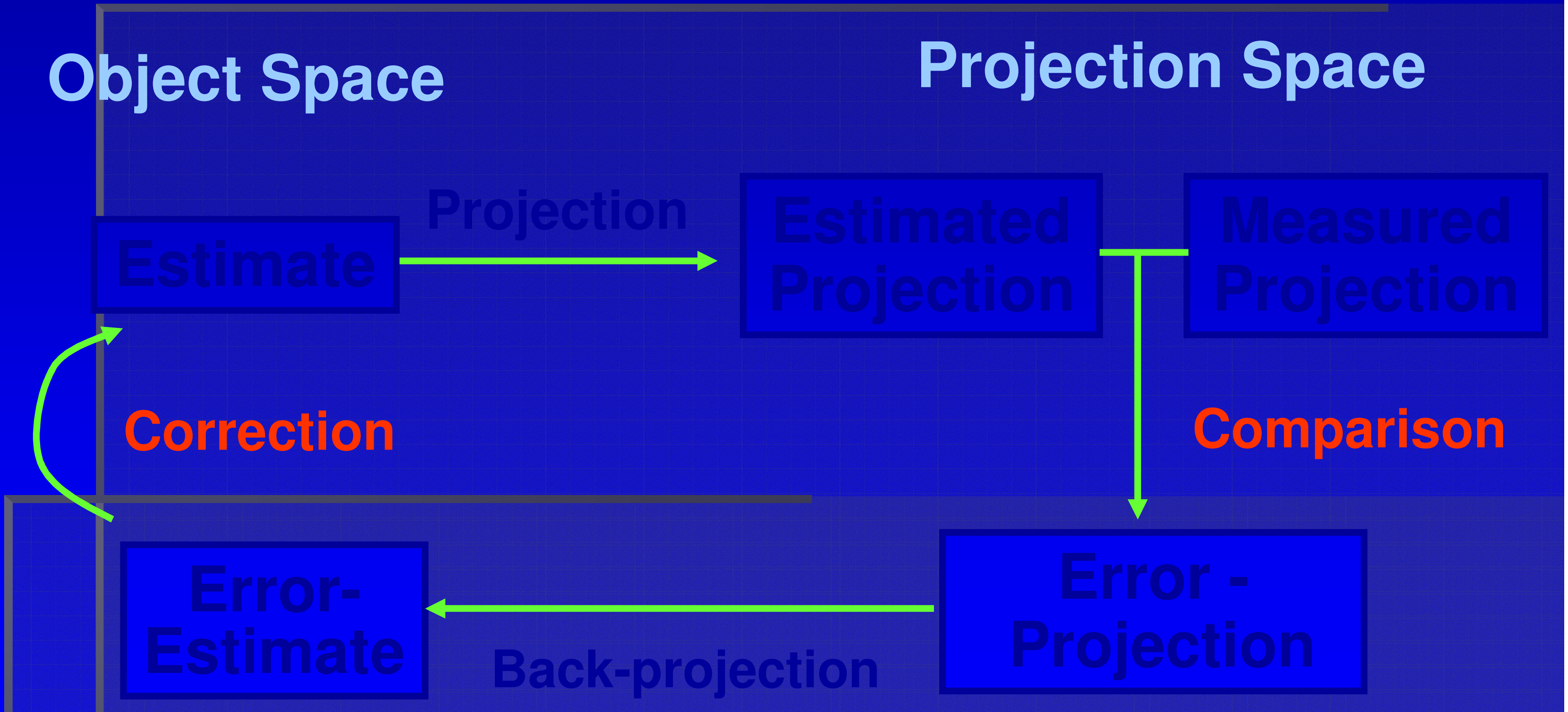
The system matrix

$$A_{ij}$$

Probability for any pair of photons emitted from voxel *j* of being registered by pair of detectors *i*

The basis of PET

- Iterative Methods:



Small Animal PET

- Why is necessary to have a small animal PET?

- PET provides spatial and temporal measurements of the distribution of biomolecules within a living subject

Small Animal PET

- **Challenges of small animal PET?**
  - Spatial resolution

    < 1 mm

  - Sensitivity

    2D: 0.3-0.6%, 3D: 2-4%

    At least as good, and preferably better

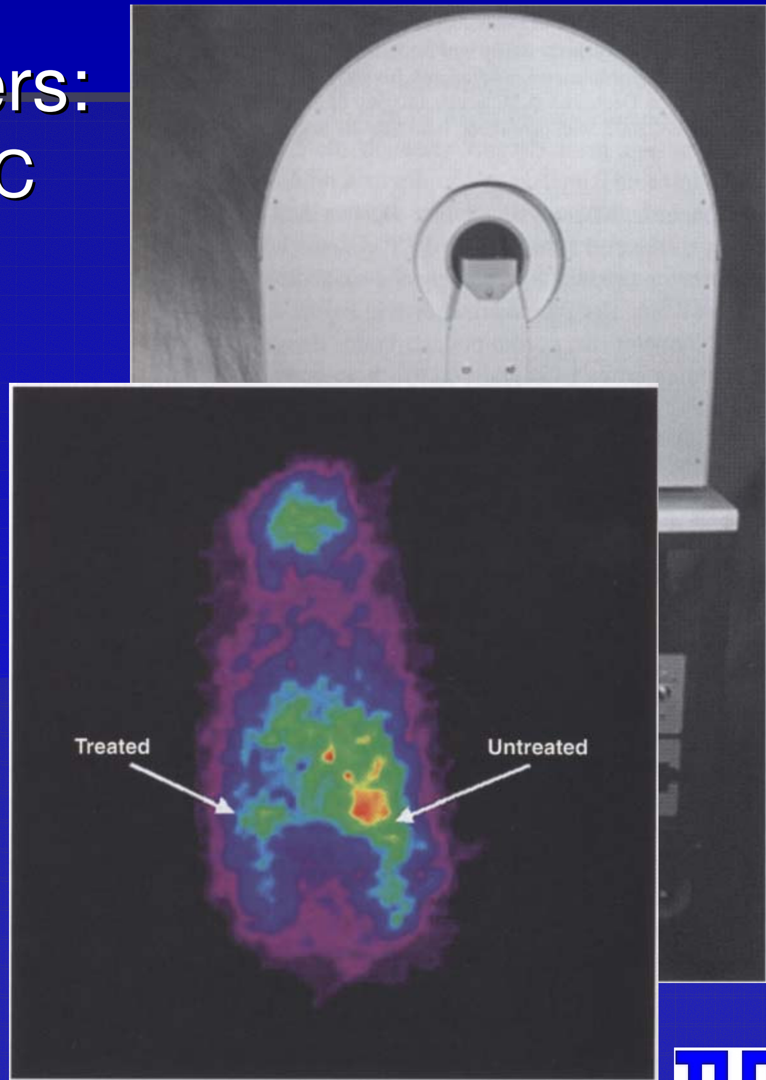
  - Dose and Mass Injected

    Tracer Principle: limit mass, limit dose

Factor 1000

Small Animal PET

- Commercialized scanners:
  microPET, MOSAIC, HIDAC

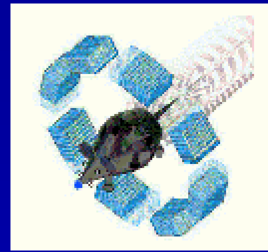


- Field:
  - Neurology
  - Cardiology
  - Oncology

Small Animal PET

- Current developments of Animal PET
  - Detector Technology:
    - Scintilliator detectors
    - Light detectors:
      - PMT→PSPMT
      - APD, Avalanche Photodiodes
      - SiPM, silicon photomultiplier
    - Semicondutor detectors
  - Detector Design: high resolution detectors with DOI capability
    - Distribution of scintillation light
    - Multiple layers of detector material

Small Animal PET



- Image Reconstruction:
  - Iterative statistical reconstruction algorithms that
    - r e, n
    - g ndent e
    - S

Str orithm ca spatial resc o-noise ic

II.Monte Carlo Simulations

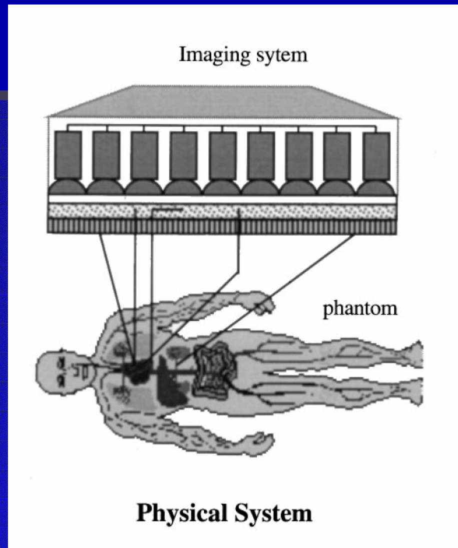
- Introduction
- Monte Carlo method: theory and computational issues
- Application of the Monte Carlo method in Nuclear Medical Imaging techniques
- Monte Carlo Computer Codes

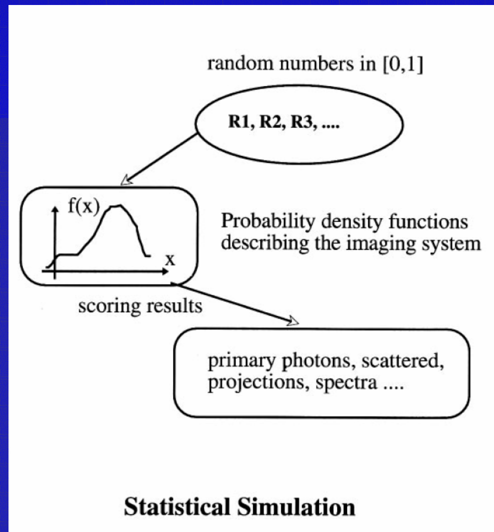
Monte Carlo Simulations

- Introduction:
  - Nuclear Medicine imaging modalities as single-photon emission computed tomography (SPET)and positron emission tomography (PET) are ideal for Monte Carlo modelling techniques because of the stochastic nature of radiation emission, transport and detection processes.
  - The use of Monte Carlo techniques has increased because of the improved models of radiation transport processes, the practicability of application with the development of acceleration schemes and the improved speed of computers.
  - Applications areas of Monte Carlo technique in nuclear imaging: detector modeling and systems design, image reconstruction and scatter correction techniques, internal dosimetry and phamacokinetic modeling

Monte Carlo Simulations

- Monte Carlo Method (I)
  - Ingredients
    1. Probability density functions (pdf)
    2. Random number generator
    3. Sampling rule
    4. Scoring
    5. Error estimation
    6. Variance reduction techniques
    7. Parallelization and vectorization algorithms





Monte Carlo Simulations

- Monte Carlo method (II):
  - Randoms numbers generation
    - All random number generators (RNG) are based upon specific mathematical algorithms, which are repeatable (pseudo-random)
    - The RNG is one of the crucial subroutines in any Monte Carlo simulation code
  - Photon transport (photoelectric, incoherent scattering, coherent scattering)
  - Electron transport (not considered, deposition of their energy at the point of interaction)

Monte Carlo Simulations

- Monte Carlo method (III):
  - Analog sampling
    - Simulate the full statistic development of the electromagnetic cascade
      - Direct method
      - Rejection method
      - Mixed methods
  - Nonanalog sampling “variance reduction techniques”
    - To bias the sampling by introducing different types of importance sampling and other variance reduction techniques to improve the computational efficiency to improve the computational efficiency of the Monte Carlo method

Monte Carlo Simulations

- Applications of the MC method in nuclear imaging(I)
  - Detector modeling
    - Detection efficiency with the aim to design an optimized detector for nuclear medicien studies
    - Comparative study of several crystals used in time-of-flight PET
    - Compensation for crystal penetration → modules that measure DOI
  - Imaging systems and collimators design
    - Analyze the performance of new collimator design for planar gamma camera, SPECT and PET
    - Study potential designs of dedicated small animal positron tomograph

Monte Carlo Simulations

- Applications of the MC method in nuclear imaging(II)
  - Image reconstruction algorithms
    - Comparing different algorithms for performing image reconstruction
    - Convergence propierties of the MLEM algorithm
    - Validate new algorithms
    - Build a system matrix
    - Study the noise propierties of the MLEM, MAPEM and OSL algorithms and to test the prediction of the theory

Monte Carlo Simulations

- Applications of the MC method in nuclear imaging(III)
  - Attenuation and scatter correction techniques
    - Information of the different processes occurring within the phantom and the detectors (scatter fraction).
    - Factors mostly responsible for spectral contamination (overlapping of unscattered and scattered events throughout the energy spectrum)
    - Scatter compensation required for quantitative SPECT
    - Scatter components in PET divided into primaries, object scatter, gantry scatter and mixed scatter and their effects on the degradation of reconstructed images
    - Comparisons between the approaches for scatter correction and the simulations
  - Dosimetry and treatment planning
    - Derive specific absorbed fractions and delivered doses for electron and photon sources uniformly distributed in organs of mathematical phantoms
  - Pharmacokinetic modeling

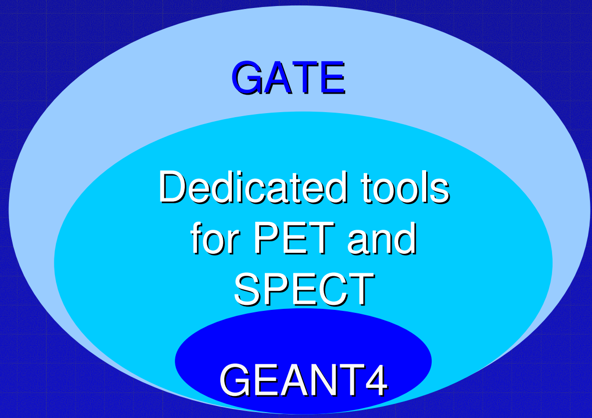
Monte Carlo Simulations

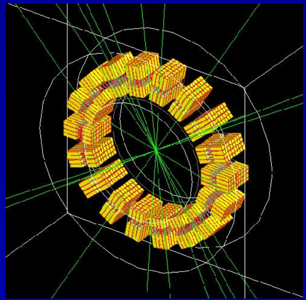
- Monte Carlo computer codes (I)

MC code	General Description	MC code	General Description
EGS4	Generic Code FORTRAN	**MCNP**	Generic Code FORTRAN
ITS	Generic Code FORTRAN	**SIMSPECT**	Dedicated SPECT FORTRAN/C
GEANT	Generic Code FORTRAN and C	**MCMATV**	Dedicated SPECT FORTRAN
SIMSET	Dedicated SPECT & PET C	**PETSIM**	Dedicated PET FORTRAN
SIMIND	Dedicated SPECT FORTRAN	**EIDOLON**	Dedicated PET C

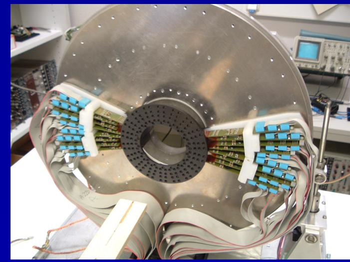
Monte Carlo Simulations

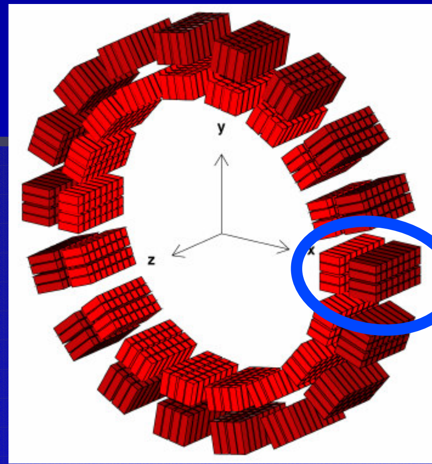
- Monte Carlo computer codes (II): **GATE**
  - Encapsulates GEANT4 libraries in order to achieve a modular, versatile, scripted simulation toolkit adapted to the field of the Nuclear Medicine.
  - User friendly
  - Provides the capability for modelling time dependent phenomena such as detector movements or source decay kinetics

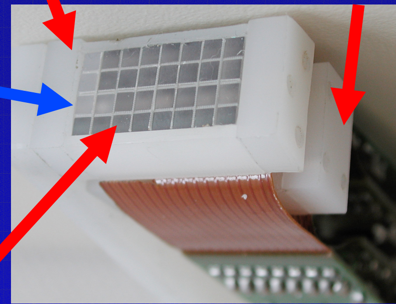


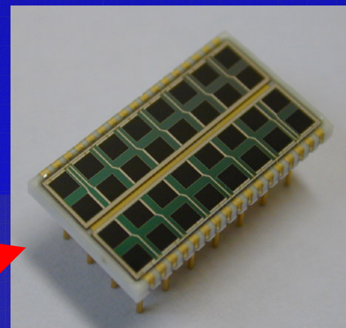


GATE & MADPET II

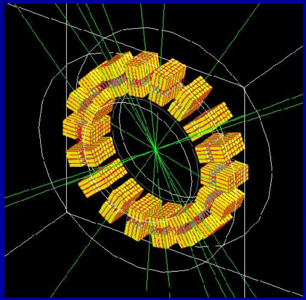




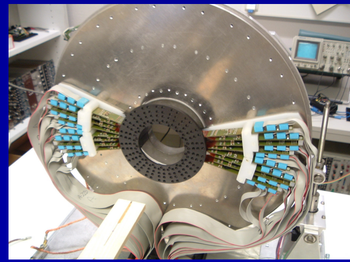




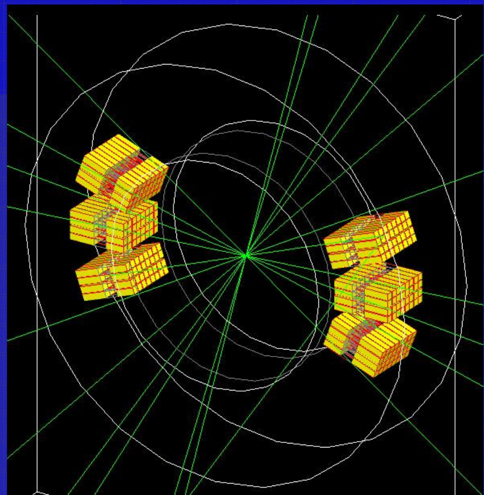
- MADPET-II
  - **2 independent radial layers**
  - **18 dual-layer modules**
    - One module: 2 detector blocks
    - Each block: **4 x 8 array of LSO** crystals
    - Crystal size: **2 x 2 x 6 mm³** (front layer)
      2 x 2 x 8 mm³ (back layer)
    - Individual Read-out:
      - **One-to-one** coupling to a **4 x 8 APD array**
      - Each crystal read out by an independent electronic channel
    - Coincidences sorted post-acquisition in software from singles list-mode data
    - Total number of crystals and electronic channels: **1152**

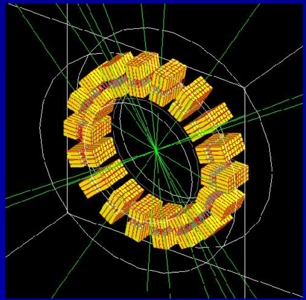


GATE & MADPET II

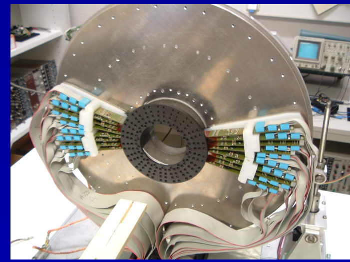


- With GATE it is possible to simulate MADPET II:
  - Study randoms (primary source of background noise and image distortion in a PET scanner)
  - Build system matrix (iterative reconstruction methods)
  - Normalization (correct for the different detector efficiencies)





GATE & MADPET II



- Example of photon transport using GATE to simulate MADPET II