Inverse problems and machine learning in medical physics

Numerical image reconstruction

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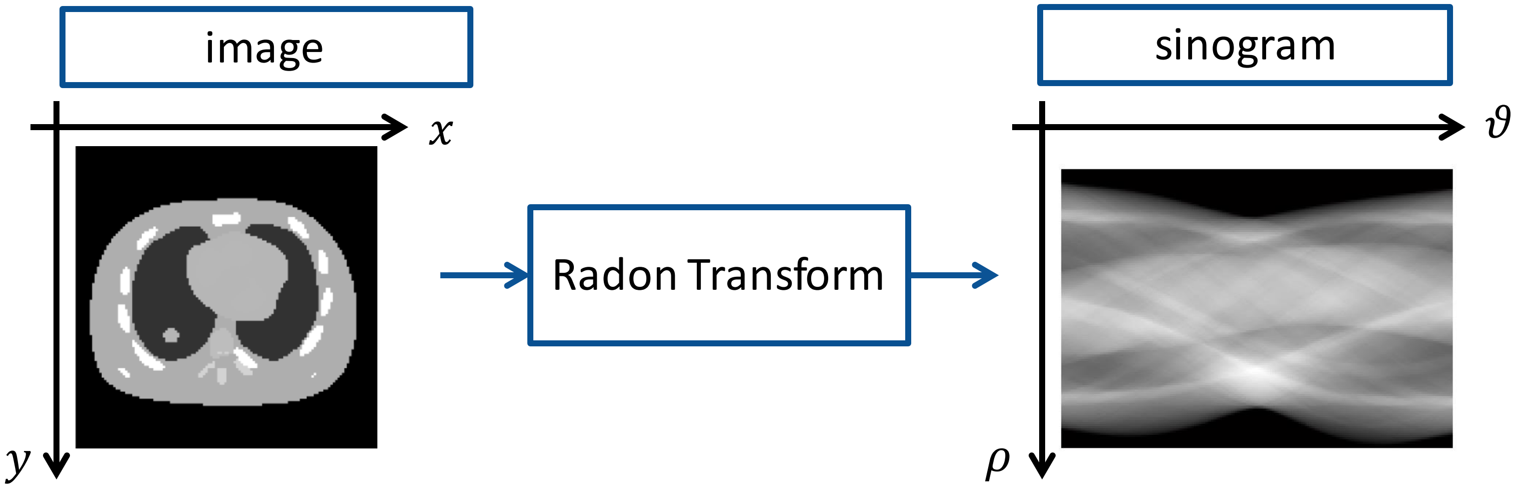
Outlook from the previous lecture

- Analytical image reconstruction is based on the continuous form of the Radon Transform



$$\Delta\vartheta = arctan\left(\frac{1}{\frac{\sqrt{N}}{2}}\right)$$

N pixels of the image

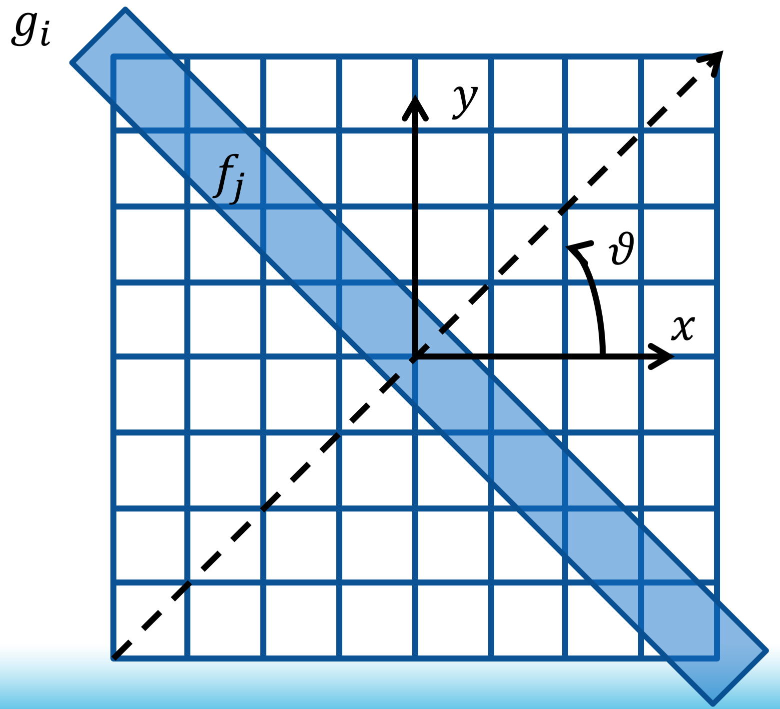
- The Fourier Slice Theorem, provided with the Nyquist theorem of sampling, enables the implementation and application of analytical reconstruction algorithms (i.e., the filtered back-projection)

$$\hat{f}_{\rho}(w_x, w_y) = \int_{-\infty}^{+\infty} R(f)e^{-2\pi i(\rho w_{\rho})}d\rho = \hat{R}(w_{\rho})$$

Numerical image reconstruction

- Numerical image reconstruction does not rely on the Fourier Slice Theorem and the Nyquist theorem of sampling
  - The image and the sinogram have not necessarily to be continuous, thus enabling the reconstruction in presence of geometrical constraints
- Numerical image reconstruction can be described as the solution of a linear system of equations
  - I equations, one for each projection
  - J unknowns, one for each pixel

$$\begin{cases} a_{11}f_1 + a_{12}f_2 + \cdots a_{1J}f_J = g_1 \\ \quad\quad\quad\quad\quad\quad \ldots \\ a_{I1}f_1 + a_{I2}f_2 + \cdots a_{IJ}f_J = g_I \end{cases}$$



Numerical image reconstruction

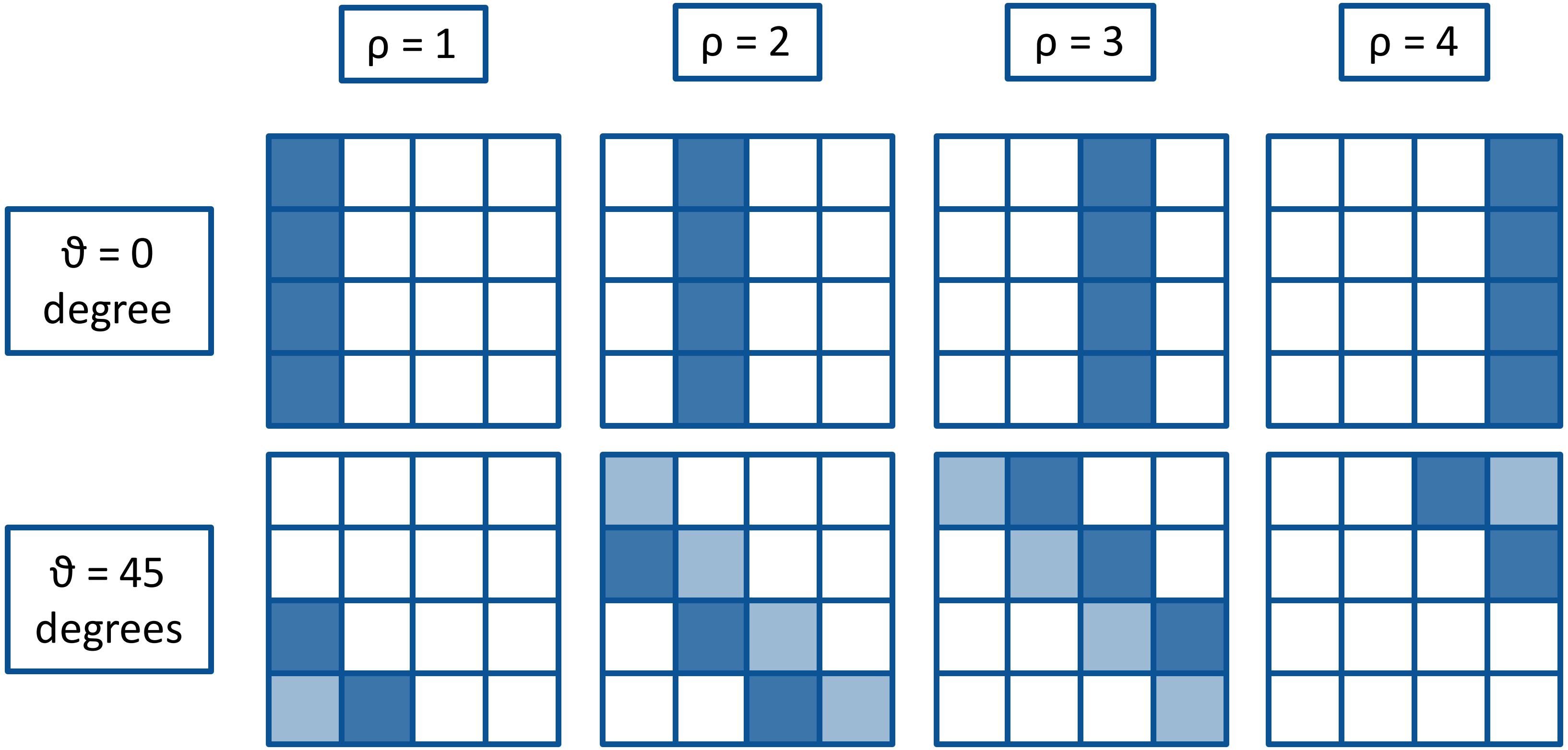
- Numerical image reconstruction requires the description of the imaging system model in terms of geometry of the integration lines

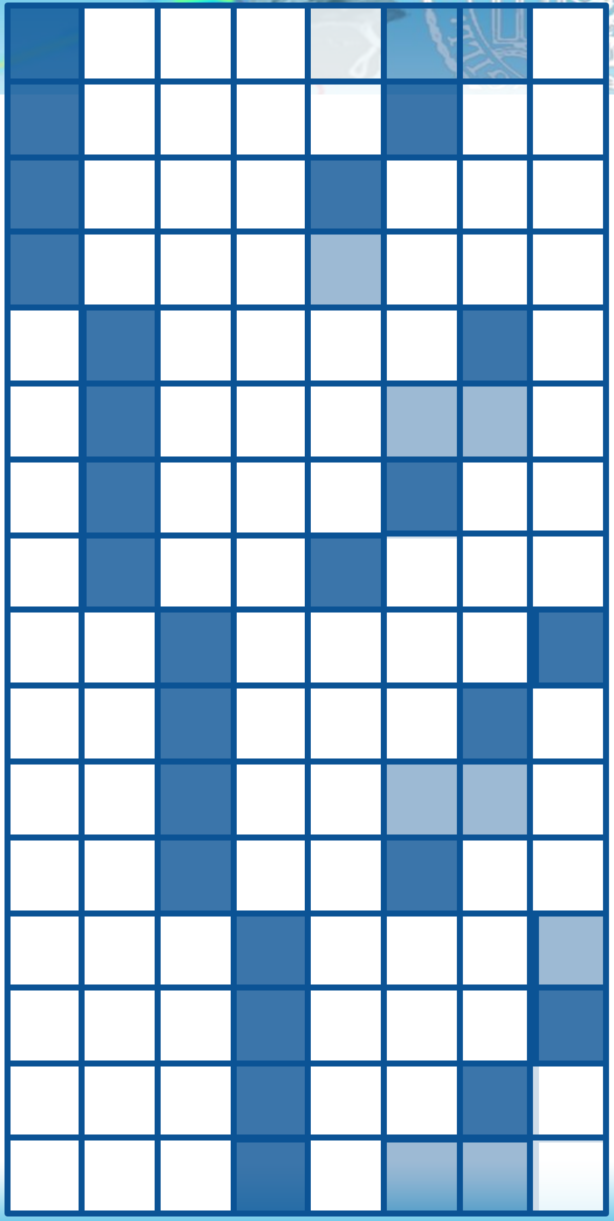
$$\bar{g}_i = \sum_{j=1}^{J} a_{ij} f_j \qquad\qquad g_i = \bar{g}_i + noise$$

Model of the projections	Measurement (projections)

- The imaging system model is described in the system matrix of the numerical reconstruction $A = \{a_{ij}\}$, whose size is $I \times J$
  - The integration line is traced as intersection length/area/volume with the image pixels/voxels

The system matrix





- Matrix construction for each integration line and for each projection angle
- Vectorization or linearization of this matrix
- Assembly in the system matrix
- System matrix transposition

The system matrix

- The forward-projection of the image is calculated as a matrix-vector product of the system matrix and the "vectorized" image

One column for each projection

A^T — One row for each pixel

a_{11}	a_{21}			…			a_{I1}
a_{1J}	a_{2J}						a_{IJ}

$$g = Af$$

$$\begin{cases} a_{11}f_1 + a_{12}f_2 + \cdots\ a_{1J}f_J = g_1 \\ \cdots \\ a_{I1}f_1 + a_{I2}f_2 + \cdots\ a_{IJ}f_J = g_I \end{cases}$$

The system matrix

- The back-projection of the sinogram is calculated as a matrix-vector product of the transposed system matrix and the "vectorized" sinogram

One column for each projection

A^T — One row for each pixel

a_{11}	a_{21}			…			a_{I1}
a_{1J}	a_{2J}						a_{IJ}

$$f = A^T g$$

$$\begin{cases} a_{11} g_1 + a_{21} g_2 + \cdots \ a_{I1} g_I = f_1 \\ \quad \ldots \\ a_{1J} g_1 + a_{2J} g_2 + \cdots \ a_{IJ} g_I = f_J \end{cases}$$

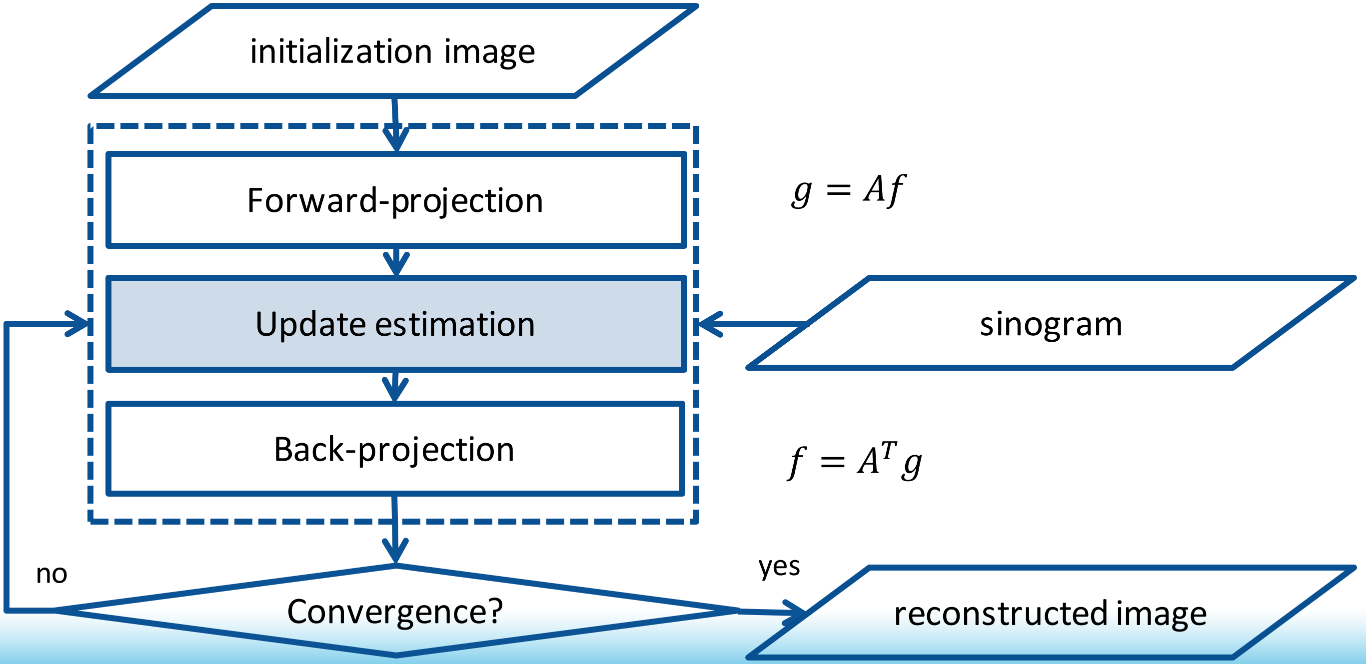
Numerical image reconstruction

- Several computational methods aim at solving linear systems of equations
  - Least square optimization for overdetermined system of equations (more equations than unknowns)

$$f_{min} = argmin \left\| g_i - \sum_{j=1}^{J} a_{ij} f_j \right\|^2 \qquad f_{min} = (A^T A)^{-1} A^T g_i$$

  - Numerical (iterative) optimization

$$f_{\min} = \text{argmin}_{f_j} F(\bar{g}_i, g_i)$$



Principle of X-ray transmission tomography

- The physical properties of the object of interest cause the attenuation of X-ray beams, described through attenuation coefficients μ, assumed to be constant for different energies (and assuming a mono-energetic X-ray beam)
  - The projection expresses the intensity reduction due to photon attenuation in the object of interest
  - The attenuation is described by Lambert Beer's law:

$$I(x+\Delta x) = I(x) - \mu(x) I(x) \Delta x \qquad \frac{dI}{dx} = -\mu(x) I(x)$$

differential equations

- The tomographic image reconstruction of the attenuation coefficients μ is enabled by the Lambert Beer's law that models the projection as a line integral of the physical variables

$$-\ln \frac{I(x=X)}{I(x=0)} = \int_0^X \mu(x) d\,x$$

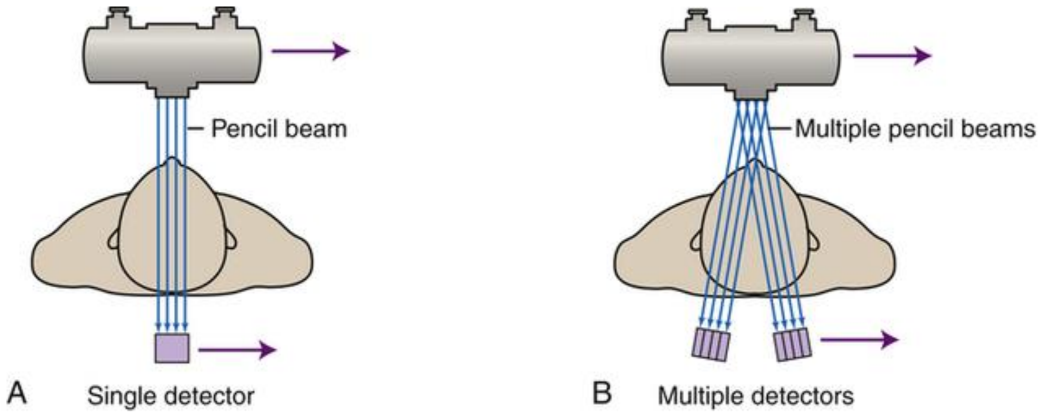
integral equation

$$\int \frac{1}{x} dx = \ln(x)$$

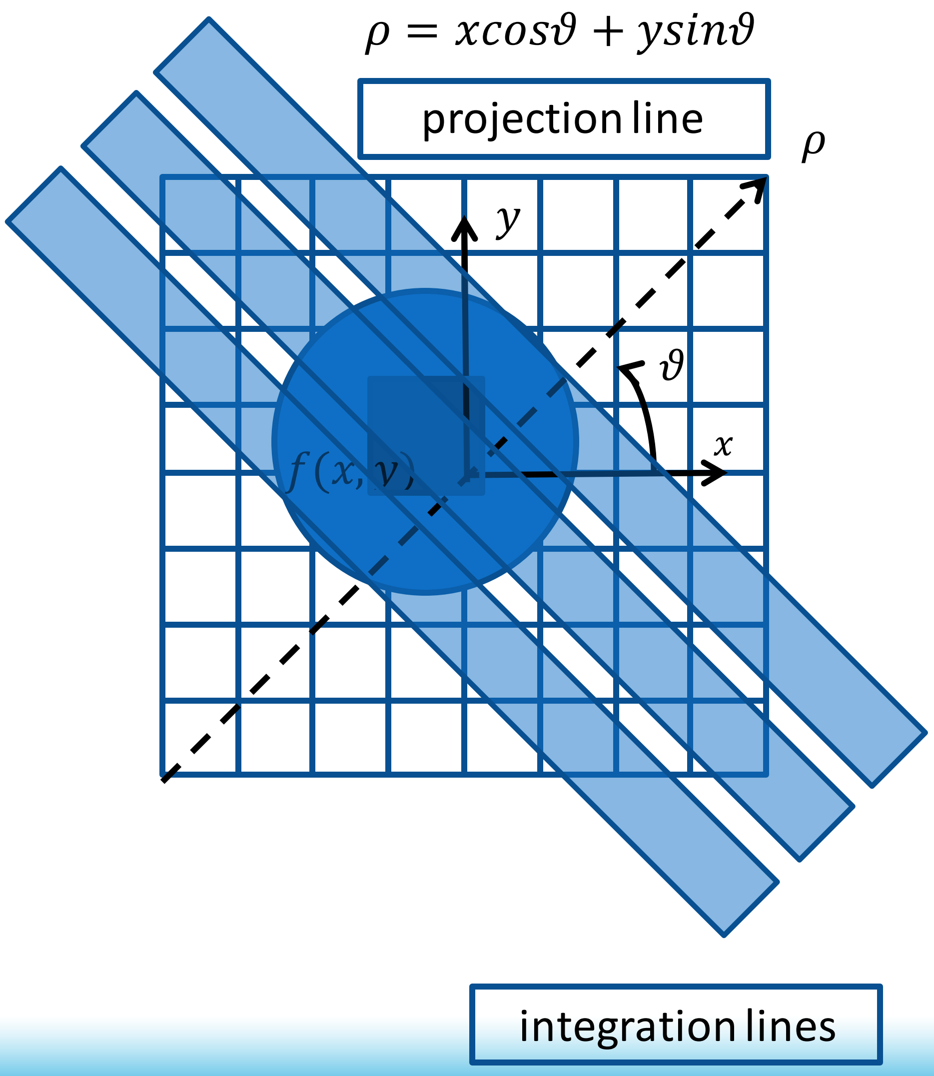
Imaging system geometry in X-ray CT

Parallel geometry

- Infinite center of projection
- Fixed projection angle for the projection line, parallel integration lines



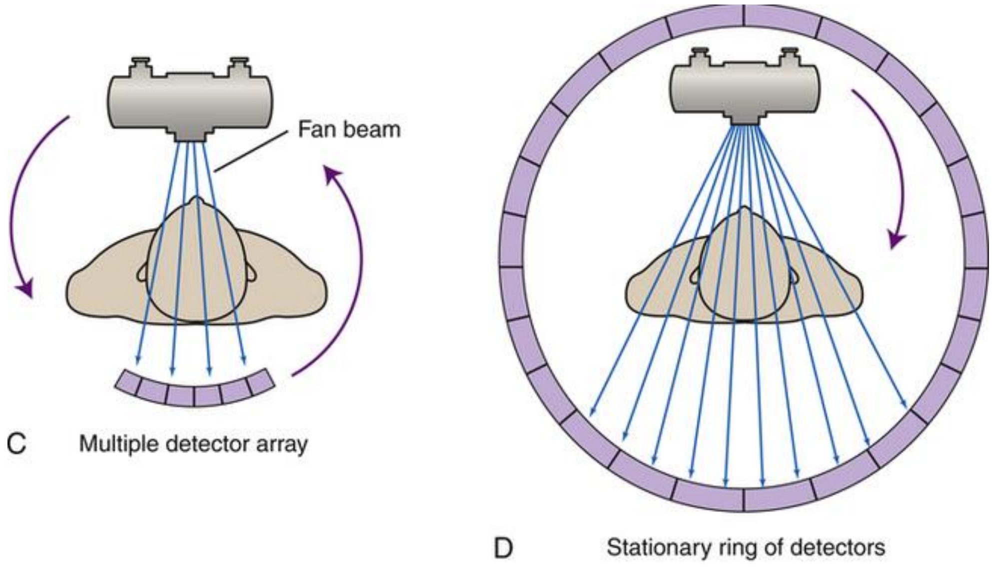
https://radiologykey.com/computed-tomography-3/



Imaging system geometry in X-ray CT

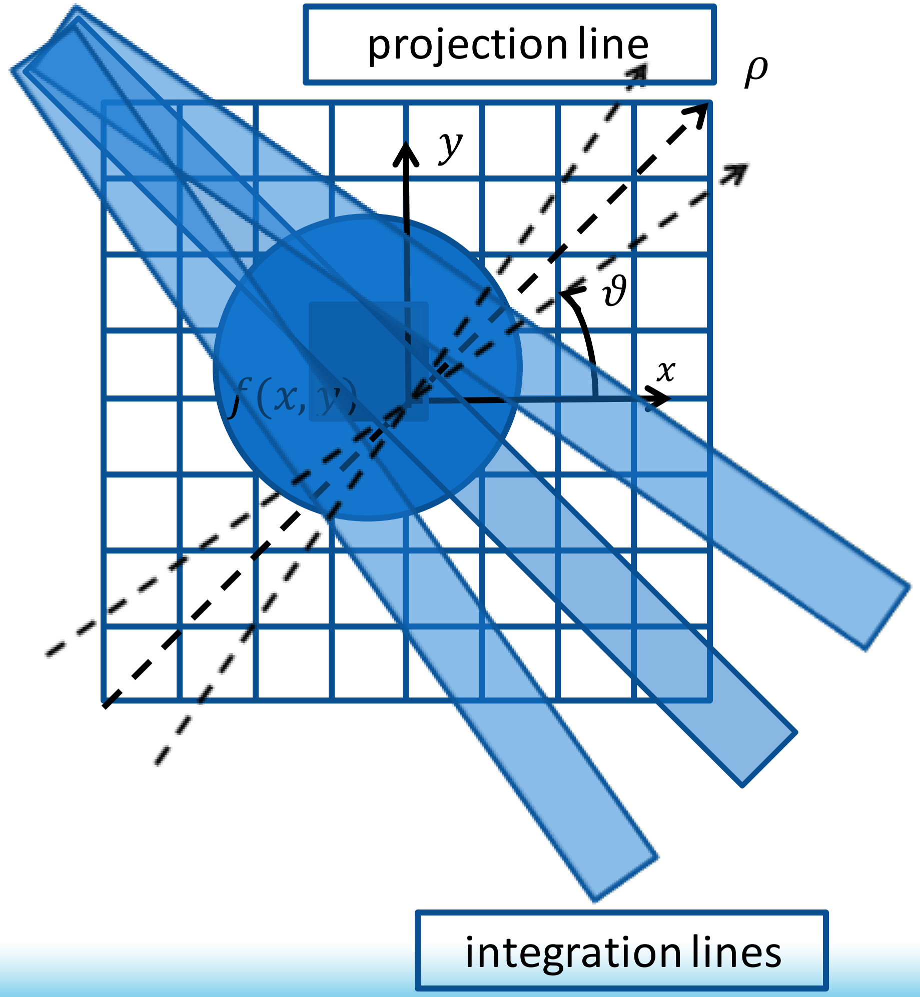
Fan geometry

- Finite center of projection
- Variable projection angle for the projection line, diverging integration lines



https://radiologykey.com/computed-tomography-3/

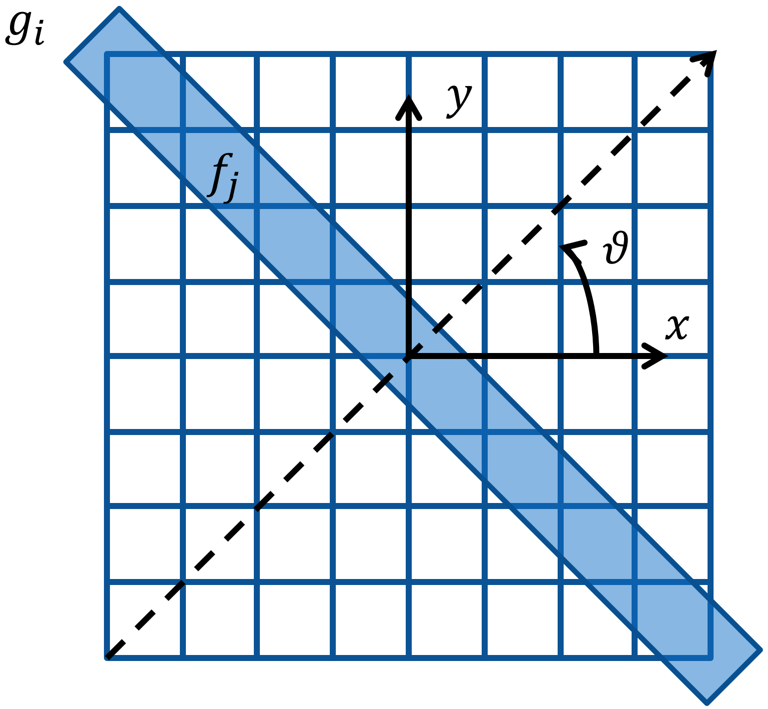
$\rho = x cos\vartheta + y sin\vartheta$



Algebraic Reconstruction Technique

- The reconstruction consists in solving a system of I equations, where I is the number of boundaries (the number of projections), relying on the constants a_{ij} describing the imaging system model (the system matrix)

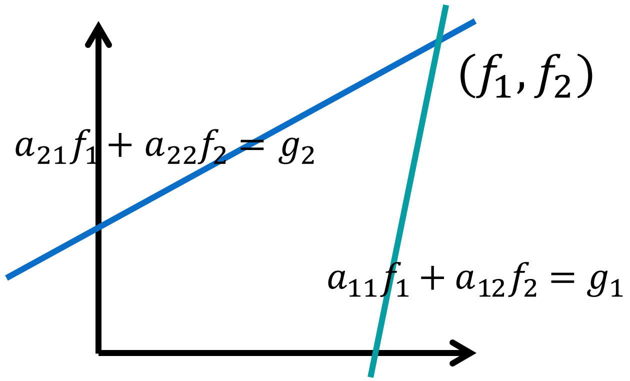
- Each projection is interpreted as an hyperplane in a J-dimensional space, where J is the degrees of freedom (the number of pixels/voxels of the image and thus, the number of the unknowns)
  - If existing, the intersection of the I hyperplanes represents the solution of the system of equations
  - The dimension of the hyperplane is J-1

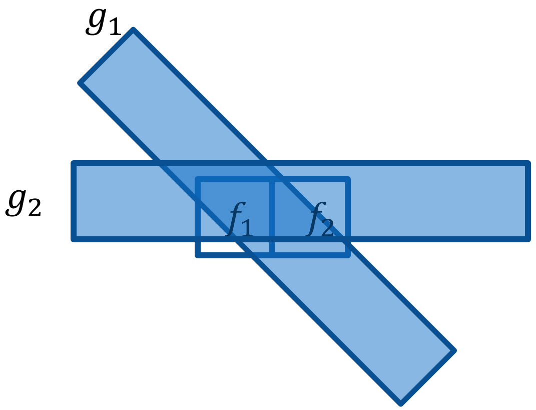


$$\begin{cases} a_{11}f_1 + a_{12}f_2 + \cdots a_{1J}f_J = g_1 \\ \quad\quad\quad\quad \dots \\ a_{I1}f_1 + a_{I2}f_2 + \cdots a_{IJ}f_J = g_I \end{cases}$$

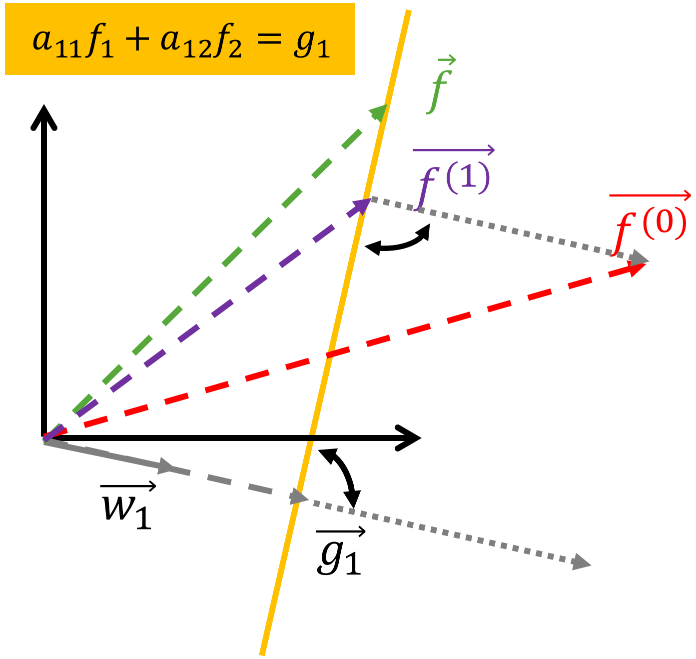
Algebraic Reconstruction Technique

- Simplified imaging system geometry: 2 unknowns and 2 parameters
  - The lines, or 1-dimensional hyperplanes, represent the boundaries (i.e. the projections)
  - The intersection point represents the solution (i.e. the image)





Algebraic Reconstruction Technique



- Describe the projection g_1 as a line (i.e., the yellow line)
- Define the vector $\overrightarrow{a_1}$ as the 2 coefficients of the system matrix relevant to the projection

$$\overrightarrow{a_1} = (a_{11}, a_{12})$$

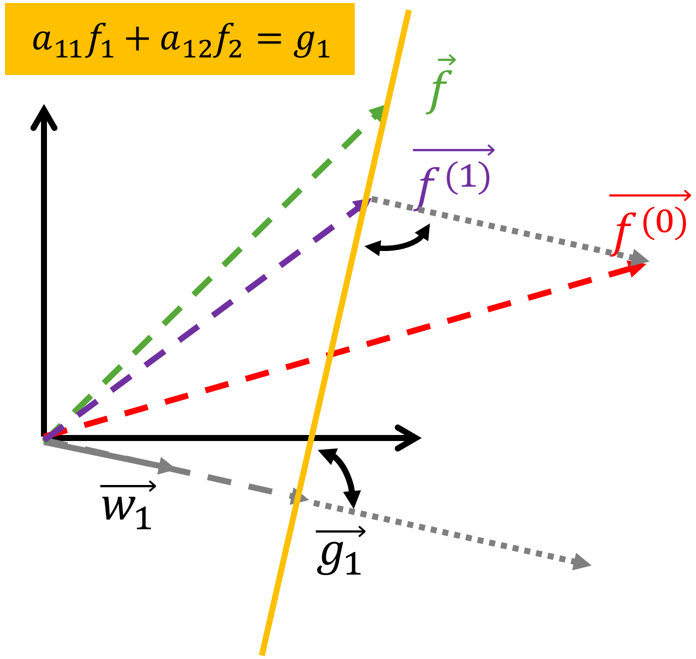
- Express the unit vector $\overrightarrow{w_1}$ as the vector $\overrightarrow{a_1}$ (perpendicular to the line by construction) divided by its modulus

$$\overrightarrow{w_1} = \frac{\overrightarrow{a_1}}{\sqrt{\overrightarrow{a_1} \cdot \overrightarrow{a_1}}}$$

- Define $g_1 = |\overrightarrow{g_1}|$ as the scalar product (dot product) of an arbitrary vector $\vec{f}$ laying on the line by the unit vector $\overrightarrow{w_1}$ (or project an arbitrary vector $\vec{f}$ laying on the line along $\overrightarrow{w_1}$)

$$g_1 = |\overrightarrow{g_1}| = \vec{f} \cdot \overrightarrow{w_1} = \frac{\overrightarrow{a_1} \cdot \vec{f}}{\sqrt{\overrightarrow{a_1} \cdot \overrightarrow{a_1}}}$$

Algebraic Reconstruction Technique



- Define $\overrightarrow{f^{(0)}}$ as a vector not laying on the line
- Define $\overrightarrow{f^{(1)}}$ as a vector laying on the line, as the solution lays on the line
- Express the update vector as difference between $\overrightarrow{f^{(1)}}$ and $\overrightarrow{f^{(0)}}$

$$\overrightarrow{f^{(0)}} - \overrightarrow{f^{(1)}} = (\overrightarrow{f^{(0)}} \cdot \overrightarrow{w_1} - g_1) \cdot \overrightarrow{w_1}$$

$$\overrightarrow{f^{(1)}} = \overrightarrow{f^{(0)}} - (\overrightarrow{f^{(0)}} \cdot \overrightarrow{w_1} - g_1) \cdot \overrightarrow{w_1}$$

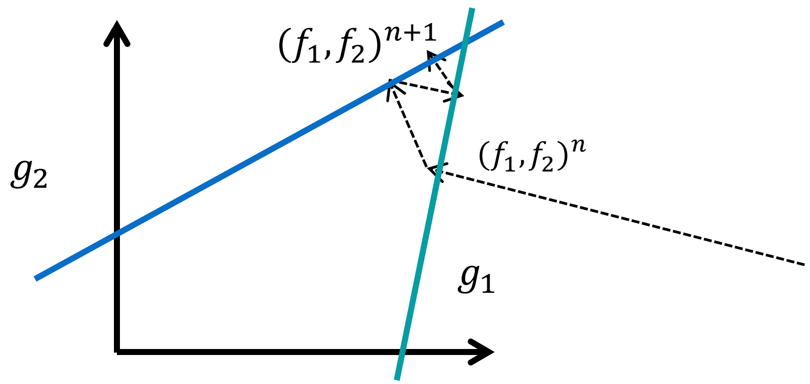
- Substitute $\overrightarrow{w_1}$

$$\overrightarrow{f^{(1)}} = \overrightarrow{f^{(0)}} - (\overrightarrow{f^{(0)}} \cdot \frac{\overrightarrow{a_1}}{\sqrt{\overrightarrow{a_1} \cdot \overrightarrow{a_1}}} - g_1) \cdot \frac{\overrightarrow{a_1}}{\sqrt{\overrightarrow{a_1} \cdot \overrightarrow{a_1}}}$$

$$\overrightarrow{f^{(1)}} = \overrightarrow{f^{(0)}} - \frac{\left(\overrightarrow{f^{0}} \cdot \overrightarrow{a_1} - g_1\right)}{\overrightarrow{a_1} \cdot \overrightarrow{a_1}} \cdot \overrightarrow{a_1}$$

Algebraic Reconstruction Technique

- The update vector moves perpendicularly within boundaries (the Kaczmarz method)
- Additive update of the image, after the projection has been considered (projection line per projection line)
- One iteration of ART is completed when all the projections have been considered



Algebraic Reconstruction Technique (ART)

- The update vector is calculated for each projection i, defined by $\vec{a_i}$

$$a_i = (a_{i1}, a_{i2}, \dots, a_{iN})$$

$$\overrightarrow{f^{(n+1)}} = \overrightarrow{f^{(n)}} - \frac{\left(\overrightarrow{f^{(n)}} \cdot \vec{a_i} - g_i\right)}{\vec{a_i} \cdot \vec{a_i}} \cdot \vec{a_i}$$

Forward projection (scalar)

Back projection (vector of length J)

Initialization $\overrightarrow{f^{(0)}}$

```
for it = 1: nIterations
    for i = 1: I
        update estimation
    end
end
```

Simultaneous Algebraic Reconstruction Technique (SART)

- Additive update of the image, contemporaneous for all the projection lines
- Under ideal conditions, one iteration of SART coincides with I updates of the ART

$$\overrightarrow{f^{(n+1)}} = \overrightarrow{f^{(n)}} - \frac{\sum_i \left(a_{ij} \cdot \left(\frac{\overrightarrow{f^{(n)}} \cdot \overrightarrow{a_{ij}}^T - \vec{g}}{\sum_j a_{ij}} \right) \right)}{\sum_i a_{ij}}$$

Forward projection (vector of length I)

Back projection (vector of length J)

Initialization $\overrightarrow{f^{(0)}}$

for it = 1: nIterations

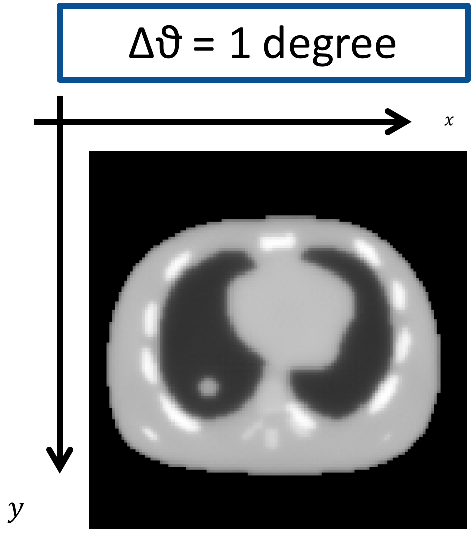
update estimation

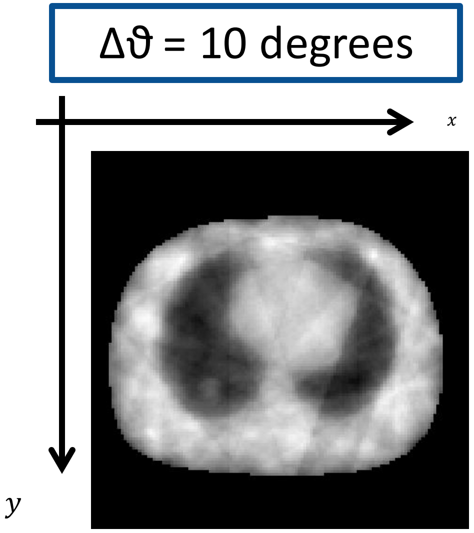
end

Andersen, A. H., & Kak, A. C. (1984). Simultaneous algebraic reconstruction technique (SART): a superior implementation of the ART algorithm. Ultrasonic imaging, 6(1), 81-94.

Simultaneous Algebraic Reconstruction Technique

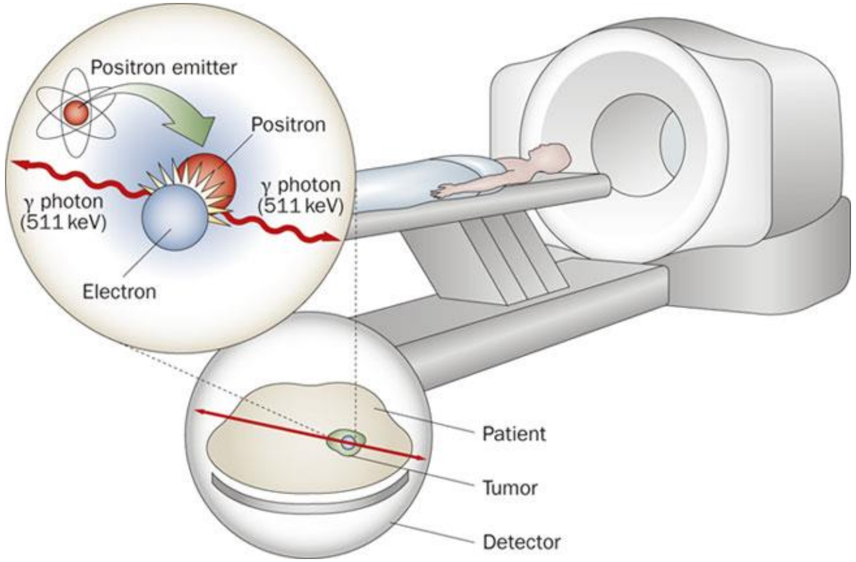
- Image reconstructed according to Simultaneous Algebraic Reconstruction Technique (SART) by setting the number of projection angles $n\vartheta = 180$ with spacing $\Delta\vartheta = 1$ degree and 10 degrees, the number of projection lines $n\rho = 128$ and the number of iterations equal to 40

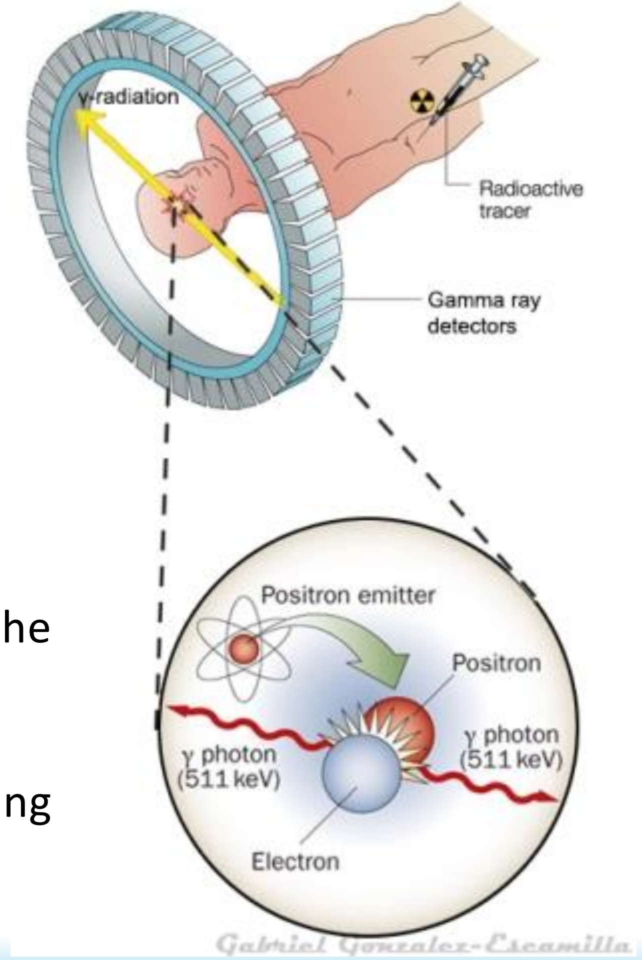




Principle of positron emission tomography

- The energy source is the β⁺ emitter and concentrates in the object of interest due to biological properties of the radiotracer
- The physical effect relevant to PET imaging is the β⁺ emission inside the object of interest
- Two synchronized crystals detect the two annihilation photons in time coincidence (“the count”)



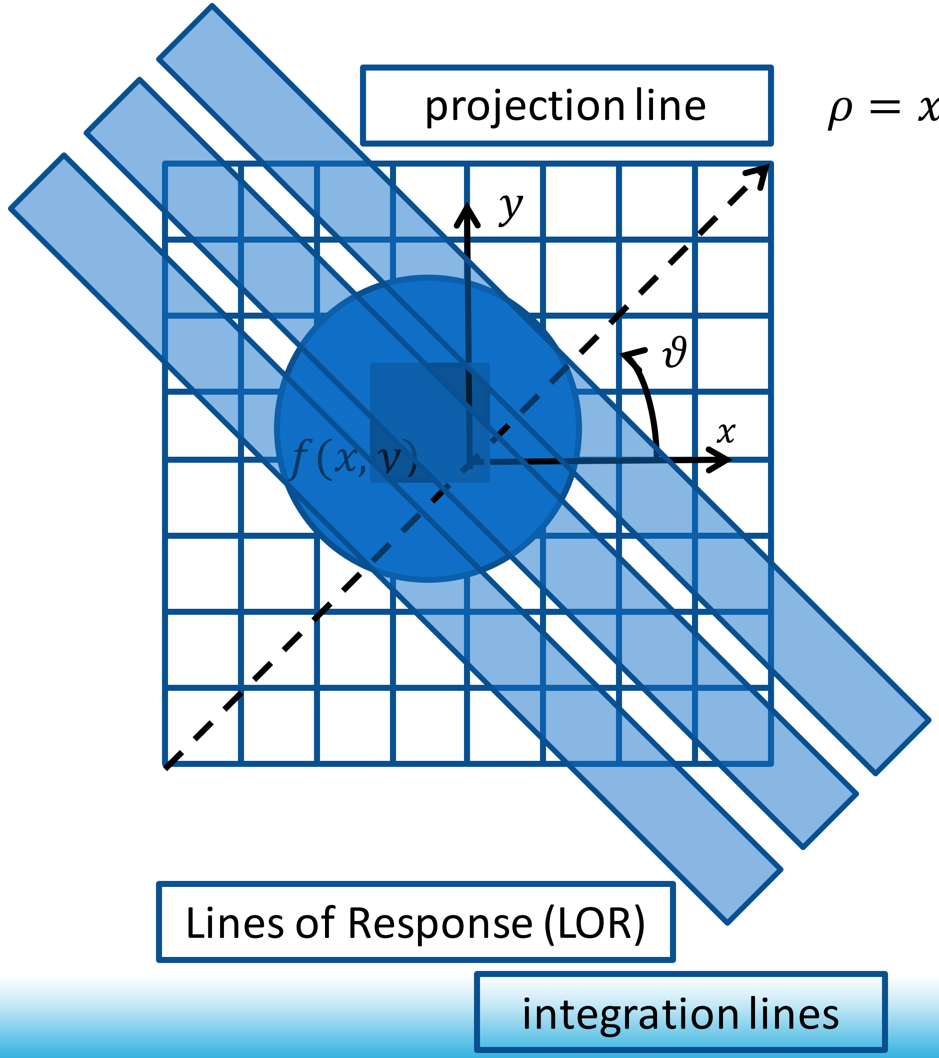


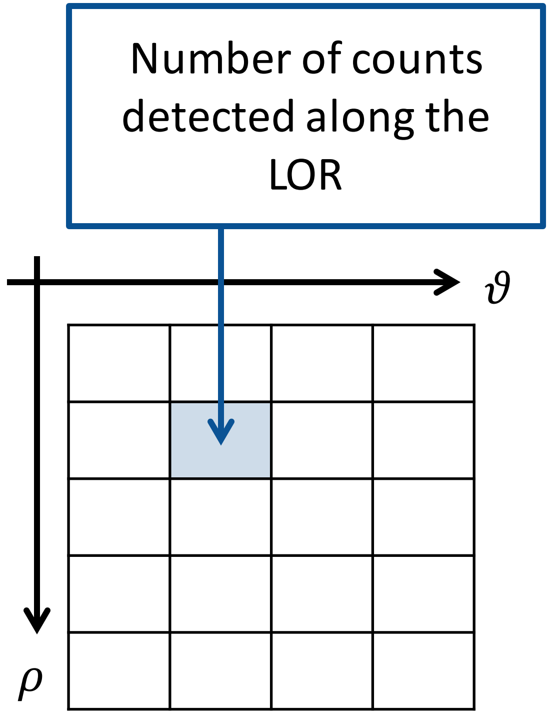
- The integration line is defined along the Line of Response (LOR) as the line along which the count is detected
- The projection line is defined by parallel (co-planar or not) integration lines connecting different crystals

https://multimodalneuroimaging.wordpress.com

The imaging system geometry

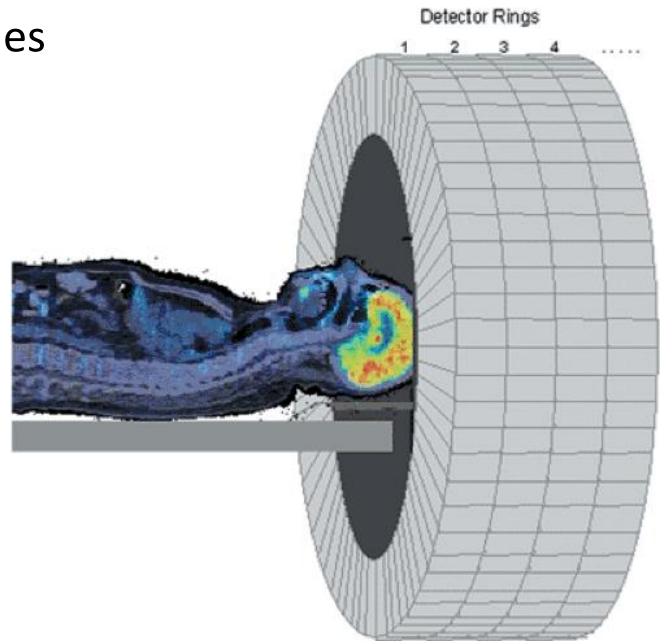
- The counts are organized in the sinogram, as a function of projection lines and projection angles





The imaging system geometry

- The PET scanner is composed by several rings of crystals that can be synchronized or not
  - The synchronization of crystals belonging to the same ring defines the direct sinogram
    - The projection line is defined by parallel and co-planar integration lines
    - The sinogram is defined by co-planar projection lines
  - The synchronization of crystals belonging to different rings defines an oblique sinogram
    - The projection line is defined by parallel but not co-planar integration lines



https://radiologykey.com

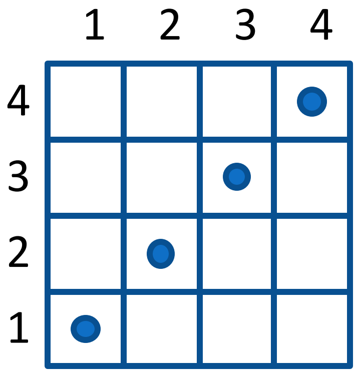
1 2 3 4

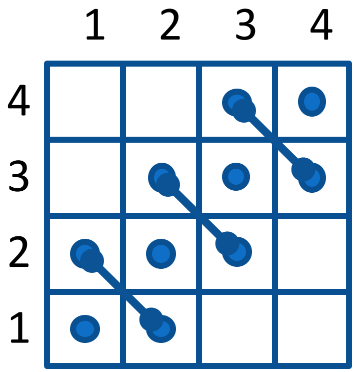
The imaging system geometry

- The "michelogram" displays the crystal synchronization and thus, the acquisition/reconstruction modality

  - The "2D-mode" is defined for direct sinograms and averaged oblique sinograms (= average)

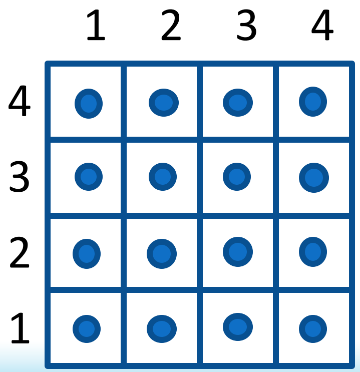
    - 2D tomographic image reconstruction





  - The "3D-mode" is defined for direct and oblique sinograms

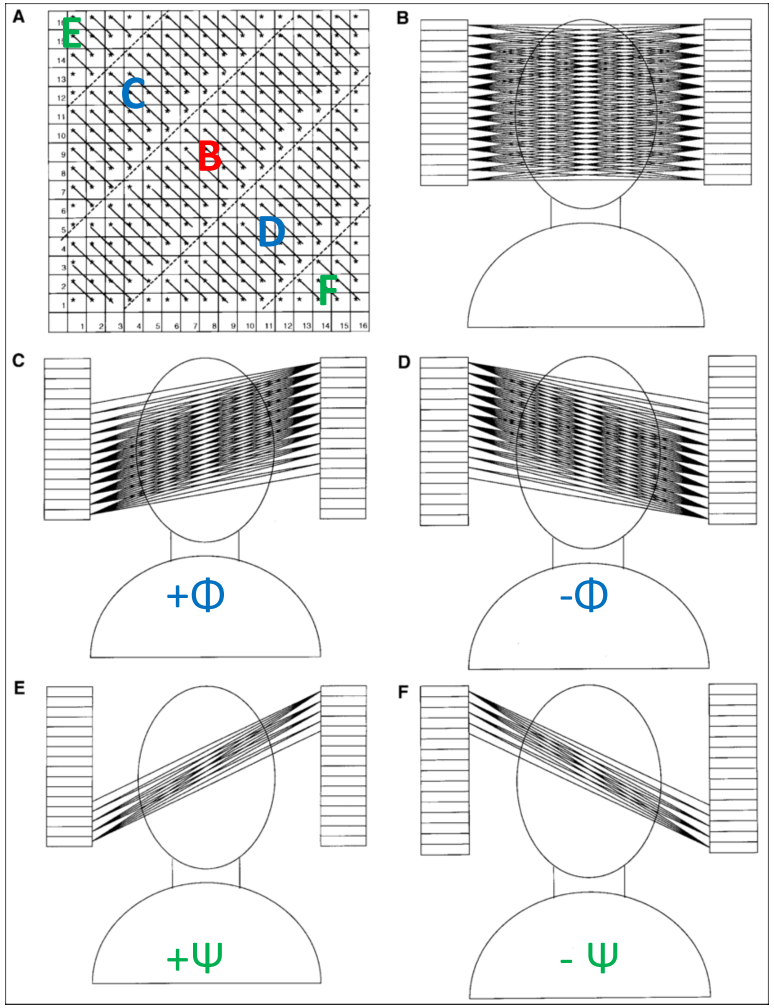
    - 3D tomographic image reconstruction



Defrise, M., Kinahan, P. E., & Michel, C. J. (2005). Image reconstruction algorithms in PET. In Positron Emission Tomography (pp. 63-91). Springer, London.

The imaging system geometry

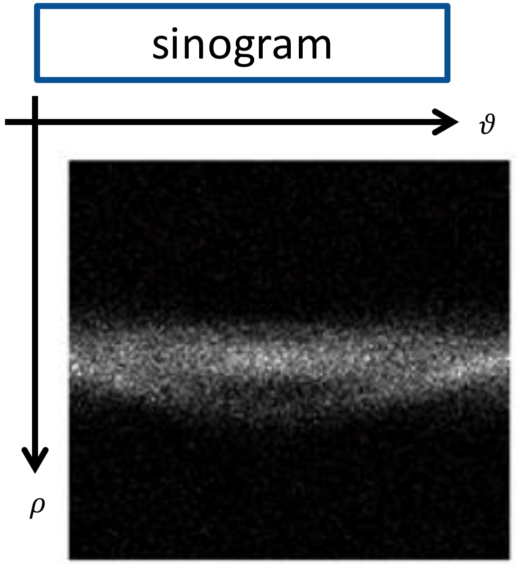
- A → example of 3D-mode michelogram
- B → direct sinograms and averaged oblique sinograms (Φ=0)
- C, D → oblique sinograms, +Φ and – Φ
- E, F → oblique sinograms, +Ψ and – Ψ

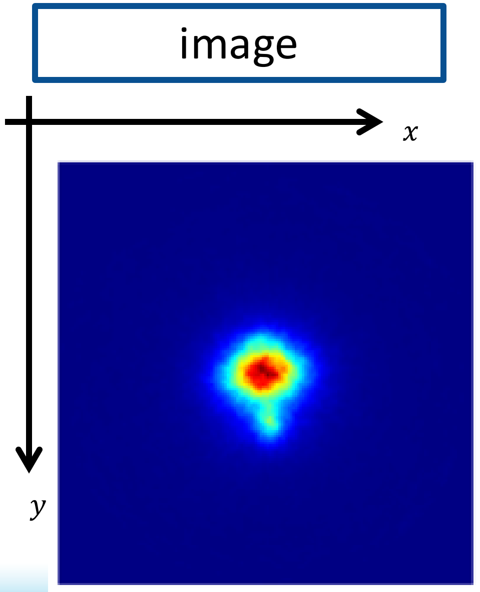


Fahey, F. H. (2002). Data acquisition in PET imaging. *Journal of nuclear medicine technology*, *30*(2), 39-49.

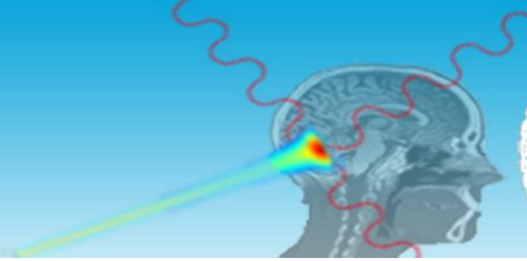
Poisson noise in PET imaging

- The observations in PET imaging are the measurements of the annihilation photons in coincidence, subsequent to radioactive decay
  - “Indirect” observation of the cause
- Poisson statistics describe random, independent events that occur at a fixed mean rate λ, as radioactive decay
  - Each projection is a Poisson variable
  - The sinogram is intrinsically affected by Poisson noise





Poisson noise in PET imaging



- Numerical image reconstruction aims at finding the image that satisfies: $f_{\min} = \mathrm{argmin}_{f_j} F(\bar{g}_i, g_i)$

$$\bar{g}_i = \sum_{j=1}^{J} a_{ij} f_j \qquad\qquad g_i = \bar{g}_i + noise$$

Model | Measurement

- Numerical image reconstruction is based on the Poisson probability model for radioactive decay

$$g_i \approx P(\bar{g}_i)$$

$$p(\bar{g}_i = g_i) = \frac{e^{-\bar{g}_i} \cdot \bar{g}_i^{\,g_i}}{g_i!}$$

The probability of observing *k* counts in a certain interval of time is defined by λ, or mean rate of counts, according to:

$$p(\lambda = k) = \frac{e^{-\lambda} \cdot \lambda^k}{k!}$$

Maximum Likelihood Expectation Maximization (MLEM) algorithm

- The update estimation defines the tomographic reconstruction algorithm

  - The Maximum Likelihood (ML) approach is a method of estimating the parameters of a statistical model (i.e., the Poisson probability model for radioactive decay) given the observations (i.e., the number of counts detected along the LOR)

$$L(g,f) = p(\overline{g_1} = g_1) \cdot p(\overline{g_2} = g_2) \cdot \ \ldots \cdot p(\overline{g_I} = g_I)$$

  - The update estimation is based on the Expectation Maximization (EM) of the likelihood function, which express the probability to observe the measured projections g if the reconstructed image is f

$$\frac{\partial L(g,f)}{\partial f} = 0$$

Maximum Likelihood Expectation Maximization (MLEM) algorithm

- To simplify the maximization of L, the natural logarithm of the function is taken (the log-likelihood)
  - For *x>0* (the probability), both *y=x* and *y=ln(x)* are minimized for *x→0*

$$\ln(L(g,f)) = ln\left(p(\overline{g_1} = g_1)\cdot p(\overline{g_2} = g_2)\cdot \ \dots \ \cdot p(\bar{g}_I = g_I)\right)$$

$$ln\left(\prod_i \frac{e^{-\overline{g}_i}\cdot \overline{g}_i^{\,g_i}}{g_i!}\right) = ln\left(\prod_i \frac{e^{-\sum_j a_{ij} f_j}\cdot \left(\sum_j a_{ij} f_j\right)^{g_i}}{g_i!}\right) = ln\frac{e^{-\sum_i \sum_j a_{ij} f_j}\cdot \prod_i \left(\sum_j a_{ij} f_j\right)^{g_i}}{\prod_i g_i!} =$$

$$= -\sum_i \sum_j a_{ij} f_j + \sum_i g_i \left(ln \sum_j a_{ij} f_j\right) - \sum_i ln(g_i!)$$

$e^a e^b = e^{a+b}$	$ln(a^b)=b\cdot ln(a)$	$ln(a\cdot b)=ln(a)+ln(b)$	$ln(a/b)=ln(a)-ln(b)$

Maximum Likelihood Expectation Maximization (MLEM) algorithm

- To simplify the maximization of L, the not observable variable x_{ij} (expectation or expected projection) is introduced

$$x_{ij} = \frac{a_{ij} f_j}{\sum_j a_{ij} f_j} g_i \qquad \text{so that} \qquad g_i = \sum_j a_{ij} f_j = \sum_j x_{ij}$$

  - x_{ij} expresses the number of counts detected along the LOR *i* and emitted from the pixel *j*

    - The projection is expressed in function of x_{ij}

$$ln(L(g,f)) = -\sum_i \sum_j a_{ij} f_j + \sum_i g_i \left(ln \sum_j a_{ij} f_j \right) - \sum_i \ln(g_i!) =$$

$$= \sum_i \sum_j \left(-a_{ij} f_j + x_{ij} ln(a_{ij} f_j) - \ln(x_{ij}!) \right) =$$

$$= \sum_i \sum_j \left(-a_{ij} f_j + x_{ij} ln(a_{ij} f_j) \right)$$

    - The term independent by f_j is deleted from the maximization

Maximum Likelihood Expectation Maximization (MLEM) algorithm

Step by step

$$ln\big(L(g,f)\big) = -\sum_i \sum_j a_{ij} f_j + \sum_i g_i \left(ln \sum_j a_{ij} f_j \right) - \sum_i \ln(g_i!) =$$

$$ln\big(L(g,f)\big) = -\sum_i \sum_j a_{ij} f_j + \sum_i \sum_j x_{ij} \left(ln \sum_j a_{ij} f_j \right) - \sum_i \ln(g_i!) =$$

$$ln\big(L(g,f)\big) = -\sum_i \sum_j a_{ij} f_j + \sum_i \sum_j \left(x_{ij} \ln\big(a_{ij} f_j\big) \right) - \sum_i \ln\left(\sum_j x_{ij}\,! \right) =$$

$$= \sum_i \sum_j \left(-a_{ij} f_j + x_{ij} ln\big(a_{ij} f_j\big) - \ln\big(x_{ij}!\big) \right) =$$

Maximum Likelihood Expectation Maximization (MLEM) algorithm

- The maximization of L is based on the annulling of the first derivative

$$\frac{\partial L(g,f)}{\partial f} = \frac{\partial L(x,f)}{\partial f} = \sum_i \sum_j \left(-a_{ij} + \frac{x_{ij}}{f_j}\right) = 0$$

$$\frac{\partial L(g,f_j)}{\partial f_j} = \frac{\partial L(x,f_j)}{\partial f_j} = \sum_i \left(-a_{ij} + \frac{x_{ij}}{f_j}\right) \rightarrow \sum_i \left(-a_{ij} + \frac{x_{ij}}{f_j^{n+1}}\right) = 0$$

$$x_{ij} = \frac{a_{ij} f_j}{\sum_j a_{ij} f_j} g_i \rightarrow \frac{a_{ij} f_j^n}{\sum_j a_{ij} f_j^n} g_i$$

- The updating formula of the ML-EM algorithm is derived accordingly

$$f_j^{n+1} = f_j^n \frac{1}{\sum_i a_{ij}} \sum_i \frac{a_{ij} g_i}{\sum_j a_{ij} f_j^n}$$

Maximum Likelihood Expectation Maximization (MLEM) algorithm

- Interpretation of the multiplicative updating formula of the ML-EM algorithm

Estimated number of counts along the LOR *i* as forward-projection of the image at current iteration

$$f_j^{n+1} = f_j^n \frac{1}{\sum_i a_{ij}} \sum_i a_{ij} \cdot \frac{g_i}{\sum_j a_{ij} \cdot f_j^n}$$

Image at next iteration

Image at current iteration

Weighted average of the back projected error

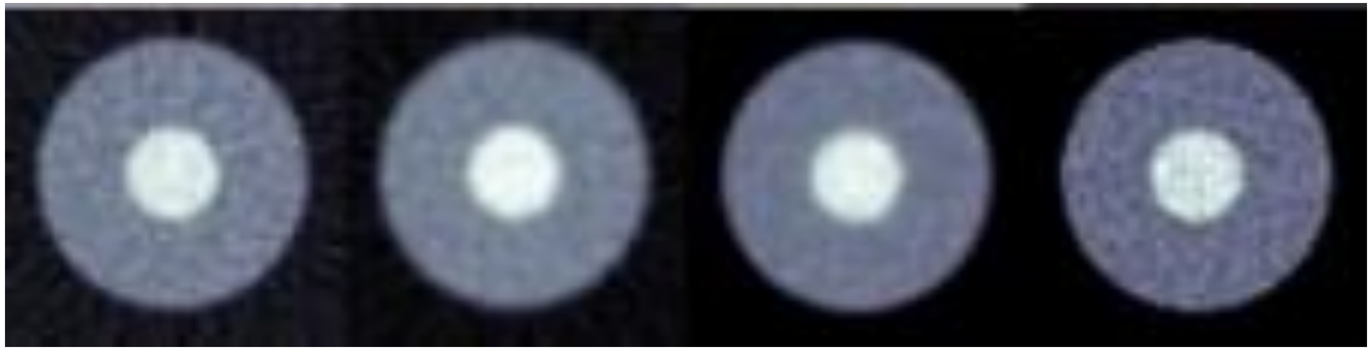
Error along the LOR *i*

Outlook

- The noise on the projections makes the tomographic image reconstruction in PET imaging an ill-posed inverse problem

- The iterations of the ML-EM algorithm must be stopped before image convergence due to noise break-up

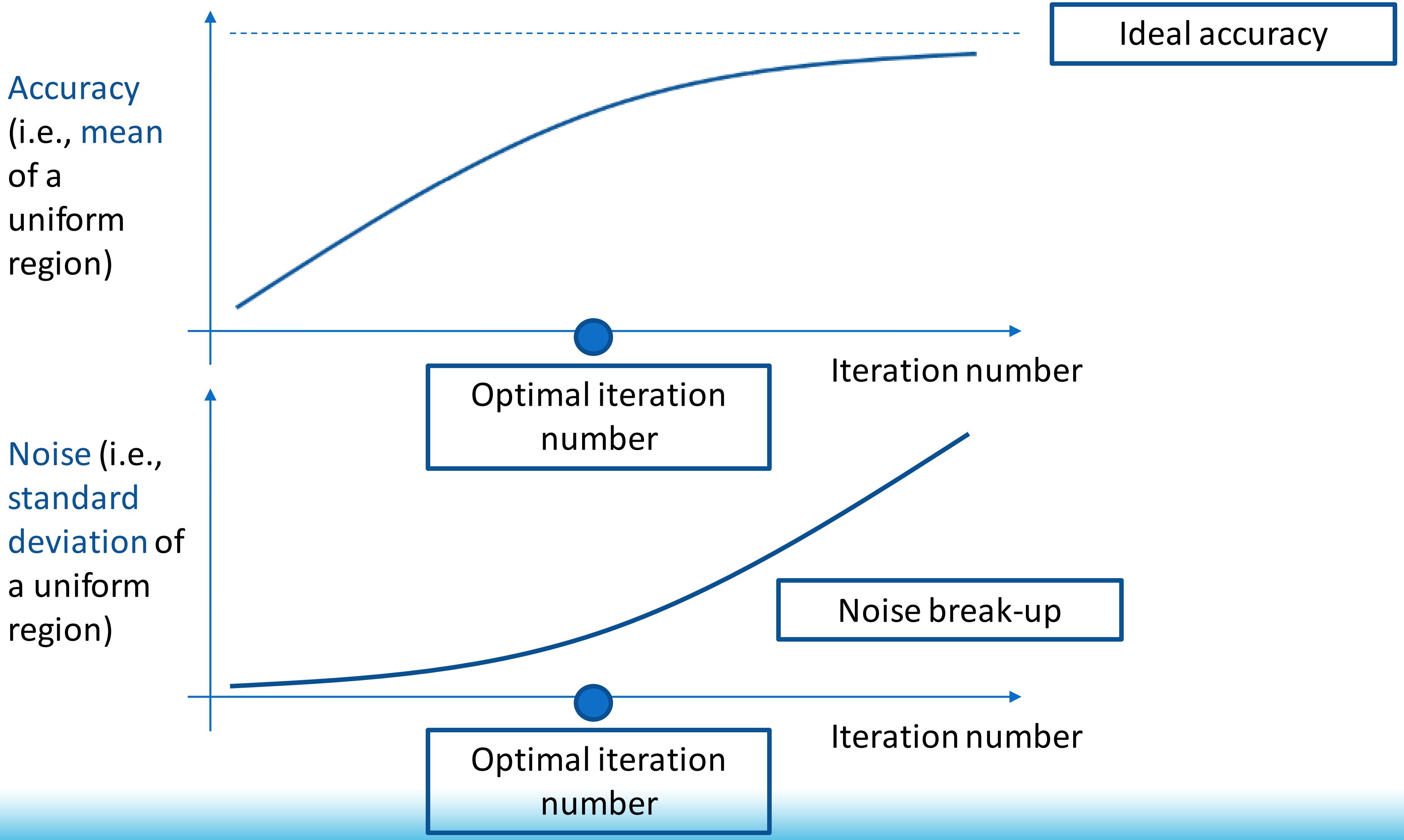
FBP, different windowing of the Ramp filter | ML-EM, different number of iterations



Adapted from Wieczorek, Herfried. "The image quality of FBP and MLEM reconstruction". Physics in Medicine and Biology, 55.11 (2010).

- This translates into a trade-off between noise and accuracy (spatial resolution) which affects clinical applications

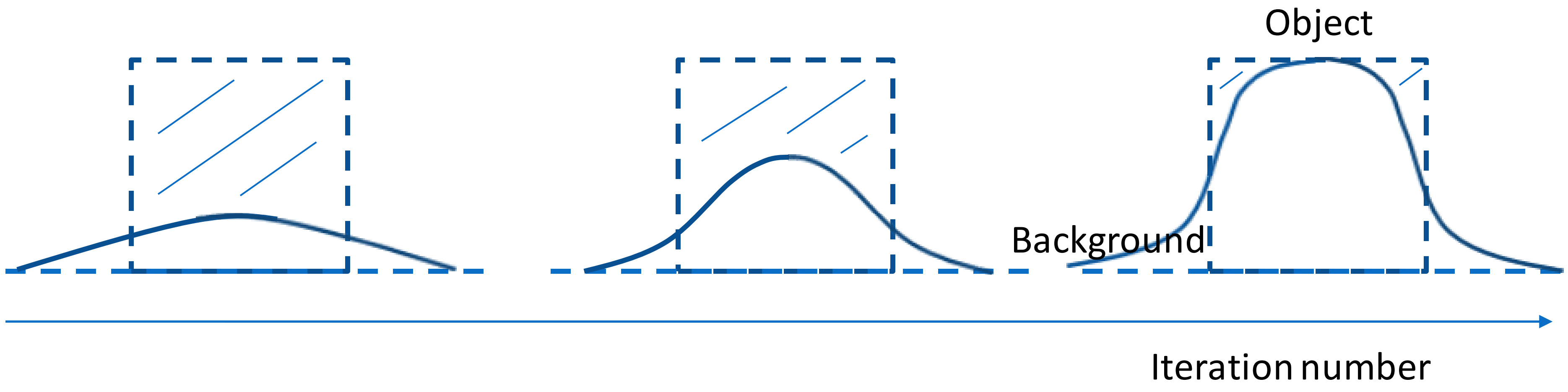
Outlook



Ideal accuracy
Accuracy (i.e., mean of a uniform region)
Iteration number
Optimal iteration number
Noise (i.e., standard deviation of a uniform region)
Noise break-up
Iteration number
Optimal iteration number

Outlook

- The accuracy embeds information about spatial resolution



- An increase in accuracy (i.e., mean of a uniform region) corresponds to an increase of spatial resolution (i.e., full width at half maximum)

- The missing area/volume ( ) of the object is known as “partial volume” and it is one of the most important limitations in quantitative PET imaging (i.e., quantification of tumor uptake)

Outlook

- Numerical image reconstruction makes use of the discrete form of the Radon Transform (the sinogram)

- Numerical image reconstruction algorithms are simply enabled by the modeling of the imaging system geometry in a system matrix

- The choice of analytical or numerical reconstruction algorithms depends on the specific application in terms of geometry of the projection lines, angular coverage and angular sampling (i.e. geometrical constraints), noise level on the projections (i.e. dosimetric constraints)

  - If the continuity hypothesis of the image and the sinogram is matched and the noise level is low, analytical image reconstruction algorithms can be considered

  - Otherwise, more flexible (but more expensive under a computational point of view) numerical image reconstruction algorithms are preferred