

Statistical Methods for Image Reconstruction

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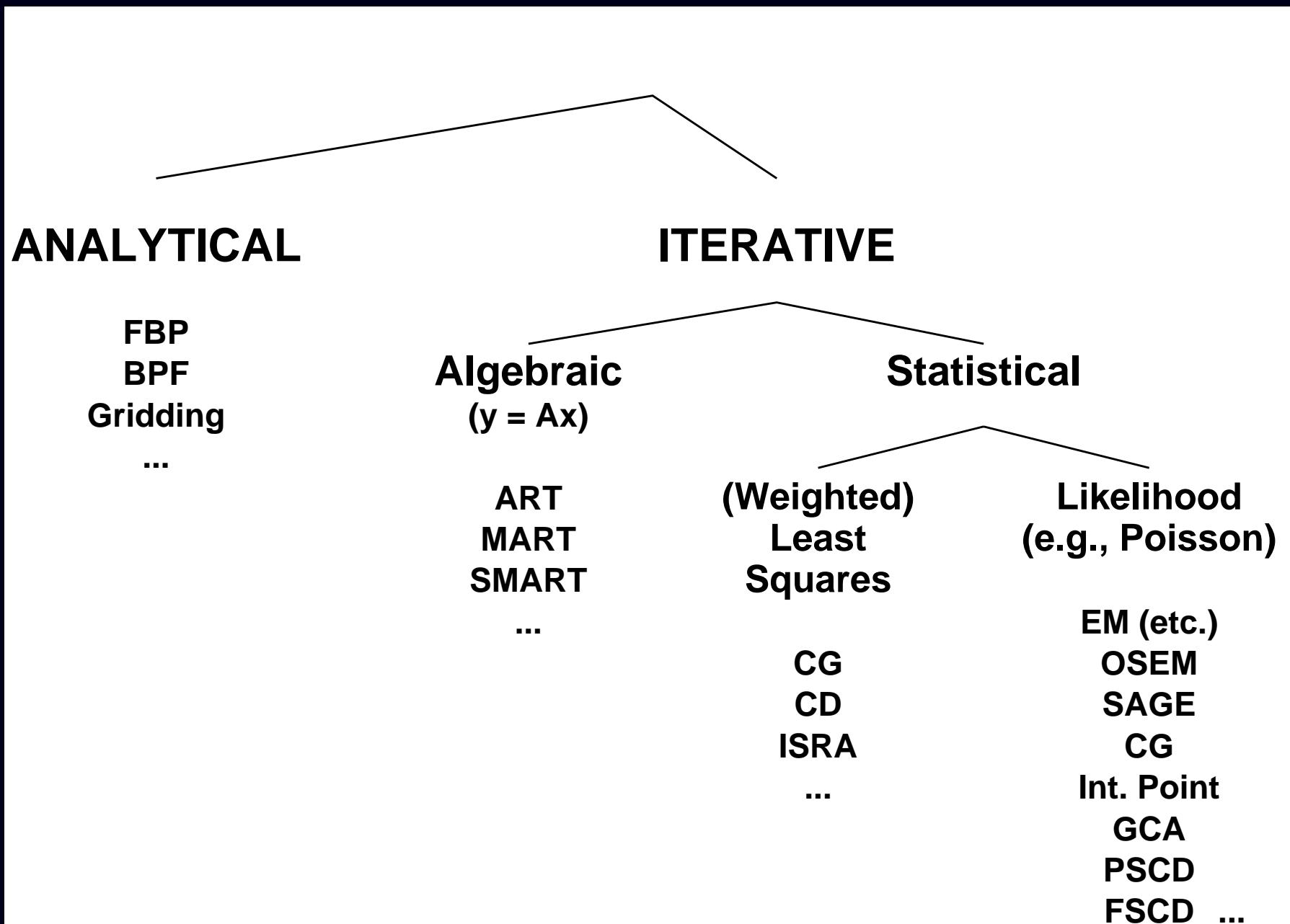
Image Reconstruction Methods

(Simplified View)

Analytical
(FBP)

Iterative
(OSEM?)

Image Reconstruction Methods / Algorithms



Outline

Part 0: Introduction / Overview / Examples

Part 1: From Physics to Statistics (Emission tomography)

- Assumptions underlying Poisson statistical model
- Emission reconstruction problem statement

Part 2: Four of Five Choices for Statistical Image Reconstruction

- Object parameterization
- System physical modeling
- Statistical modeling of measurements
- Cost functions and regularization

Part 3: Fifth Choice: Iterative algorithms

- Classical optimization methods
- Considerations: nonnegativity, convergence rate, ...
- Optimization transfer: EM etc.
- Ordered subsets / block iterative / incremental gradient methods

Part 4: Performance Analysis

- Spatial resolution properties
- Noise properties
- Detection performance

Part 5: Miscellaneous topics (?)

- ...

History

- Iterative method for X-ray CT (Hounsfield, 1968)
- ART for tomography (Gordon, Bender, Herman, JTB, 1970)
- Richardson/Lucy iteration for image restoration (1972, 1974)
- Weighted least squares for 3D SPECT (Goitein, NIM, 1972)
- Proposals to use Poisson likelihood for emission and transmission tomography
 - Emission: (Rockmore and Macovski, TNS, 1976)
 - Transmission: (Rockmore and Macovski, TNS, 1977)
- First expectation-maximization (EM) algorithms for Poisson model
 - Emission: (Shepp and Vardi, TMI, 1982)
 - Transmission: (Lange and Carson, JCAT, 1984)
- First regularized (aka Bayesian) Poisson emission reconstruction Geman and McClure, ASA, 1985
- Ordered-subsets EM algorithm Hudson and Larkin, TMI, 1994
- Commercial introduction of OSEM for PET scanners circa 1997

Why Statistical Methods?

- Object constraints (e.g., nonnegativity, object support)
- Accurate physical models (less bias \Rightarrow improved quantitative accuracy)
improved spatial resolution?
(e.g., nonuniform attenuation in SPECT)
- Appropriate statistical models (less variance \Rightarrow lower image noise)
(FBP treats all rays equally)
- Side information (e.g., MRI or CT boundaries)
- Nonstandard geometries (“missing” data)

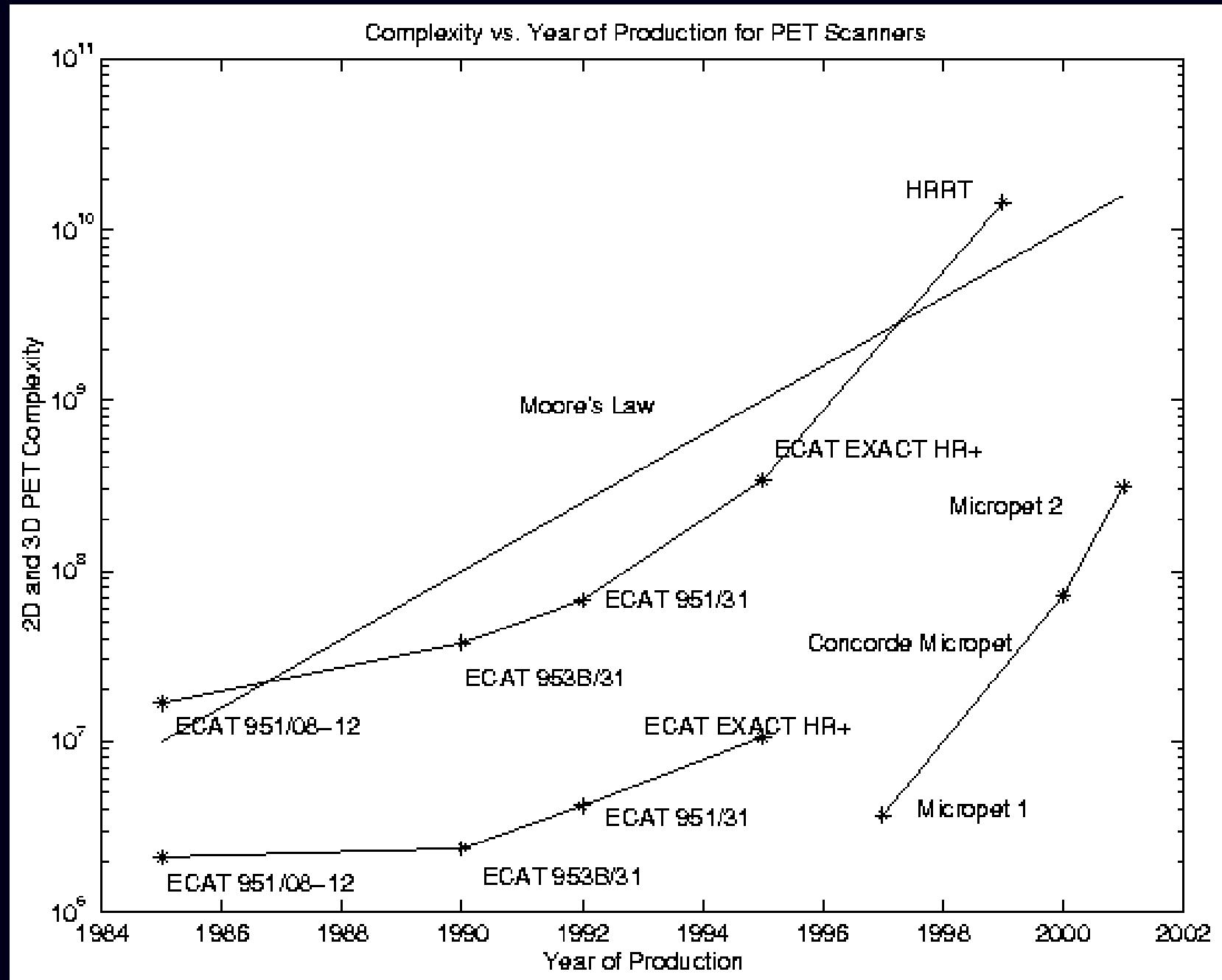
Disadvantages?

- Computation time
- Model complexity
- Software complexity

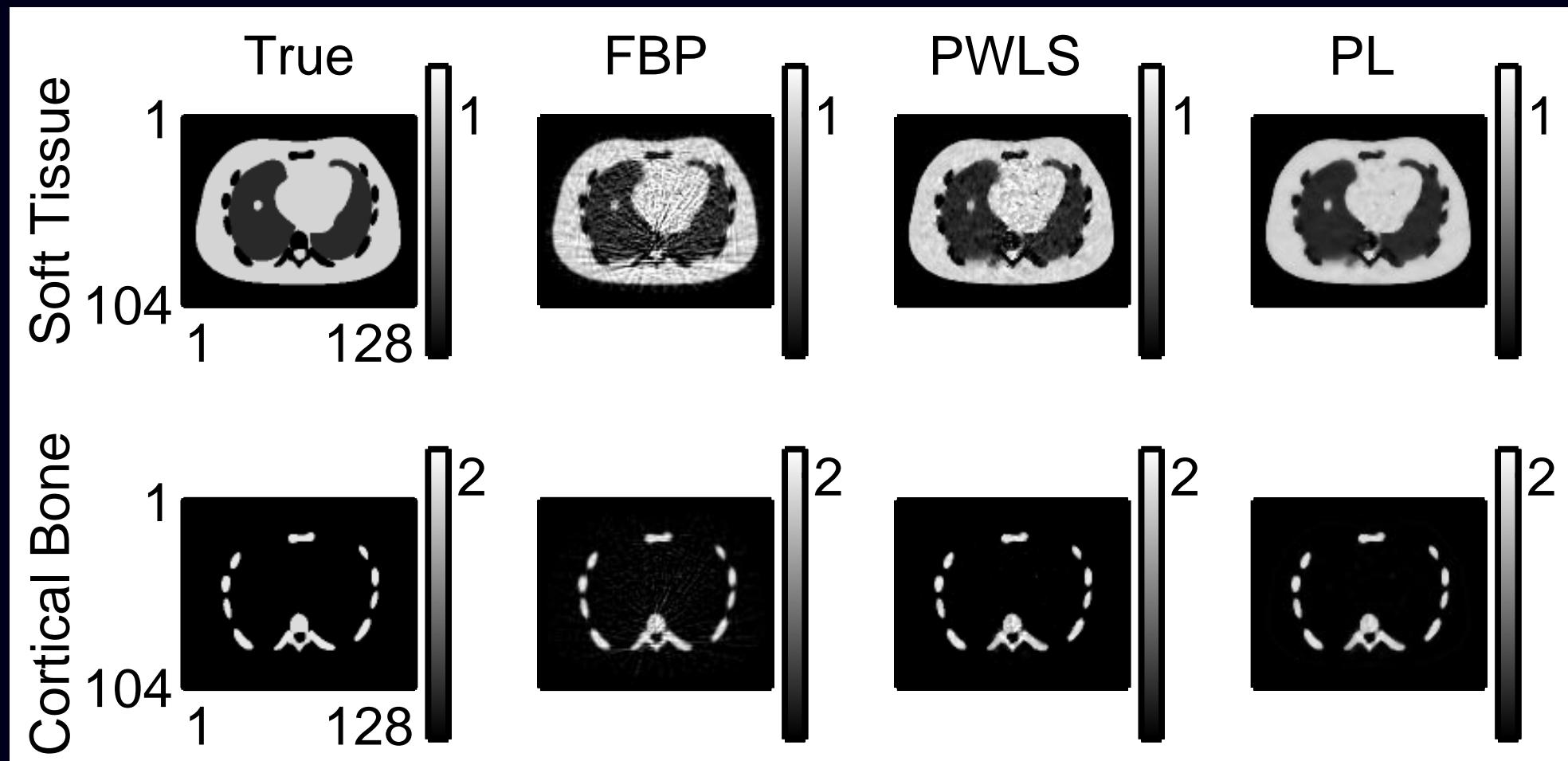
Analytical methods (a different short course!)

- Idealized mathematical model
 - Usually geometry only, greatly over-simplified physics
 - Continuum measurements
- No statistical model
- Easier analysis of properties (due to linearity)
e.g., Huesman (1984) FBP ROI variance for kinetic fitting

What about Moore's Law?



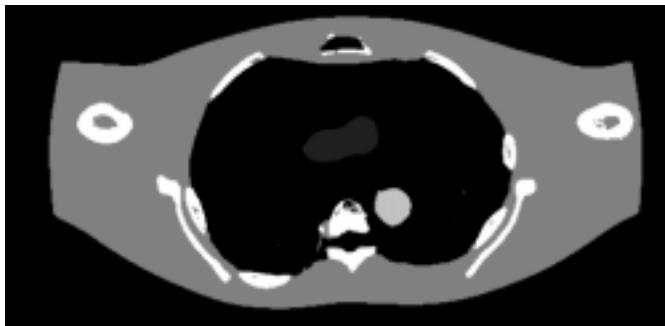
Benefit Example: Statistical Models



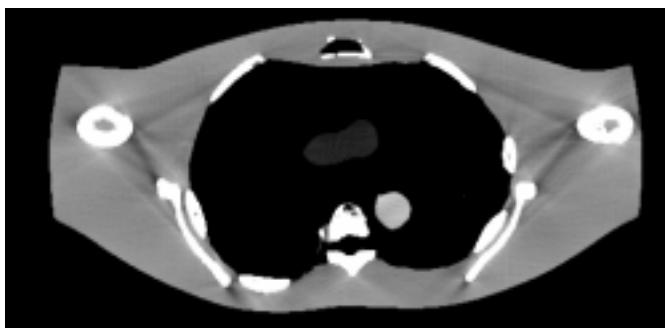
Method	NRMS Error	
	Soft Tissue	Cortical Bone
FBP	22.7%	29.6%
PWLS	13.6%	16.2%
PL	11.8%	15.8%

Benefit Example: Physical Models

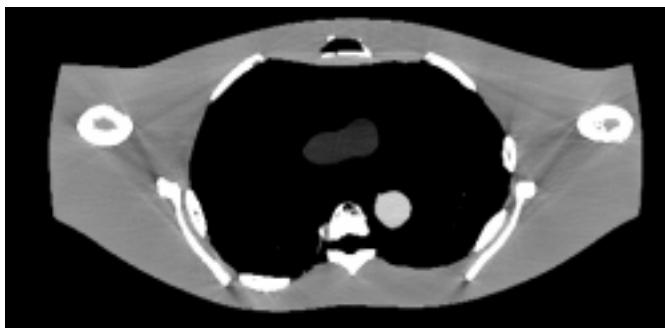
a. True object



b. Unorrected FBP

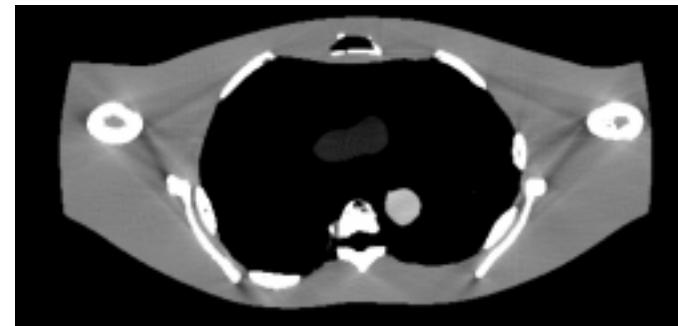


c. Monoenergetic statistical reconstruction

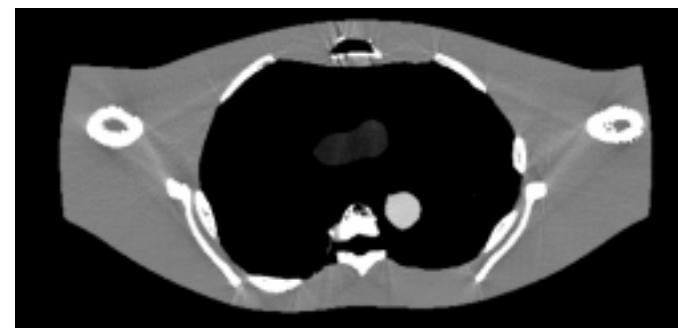


0.8 1 1.2

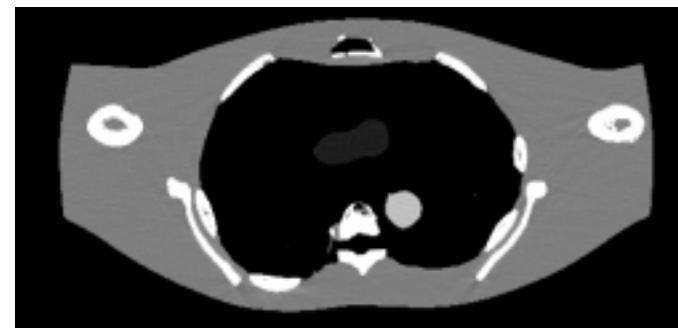
a. Soft-tissue corrected FBP



b. JS corrected FBP



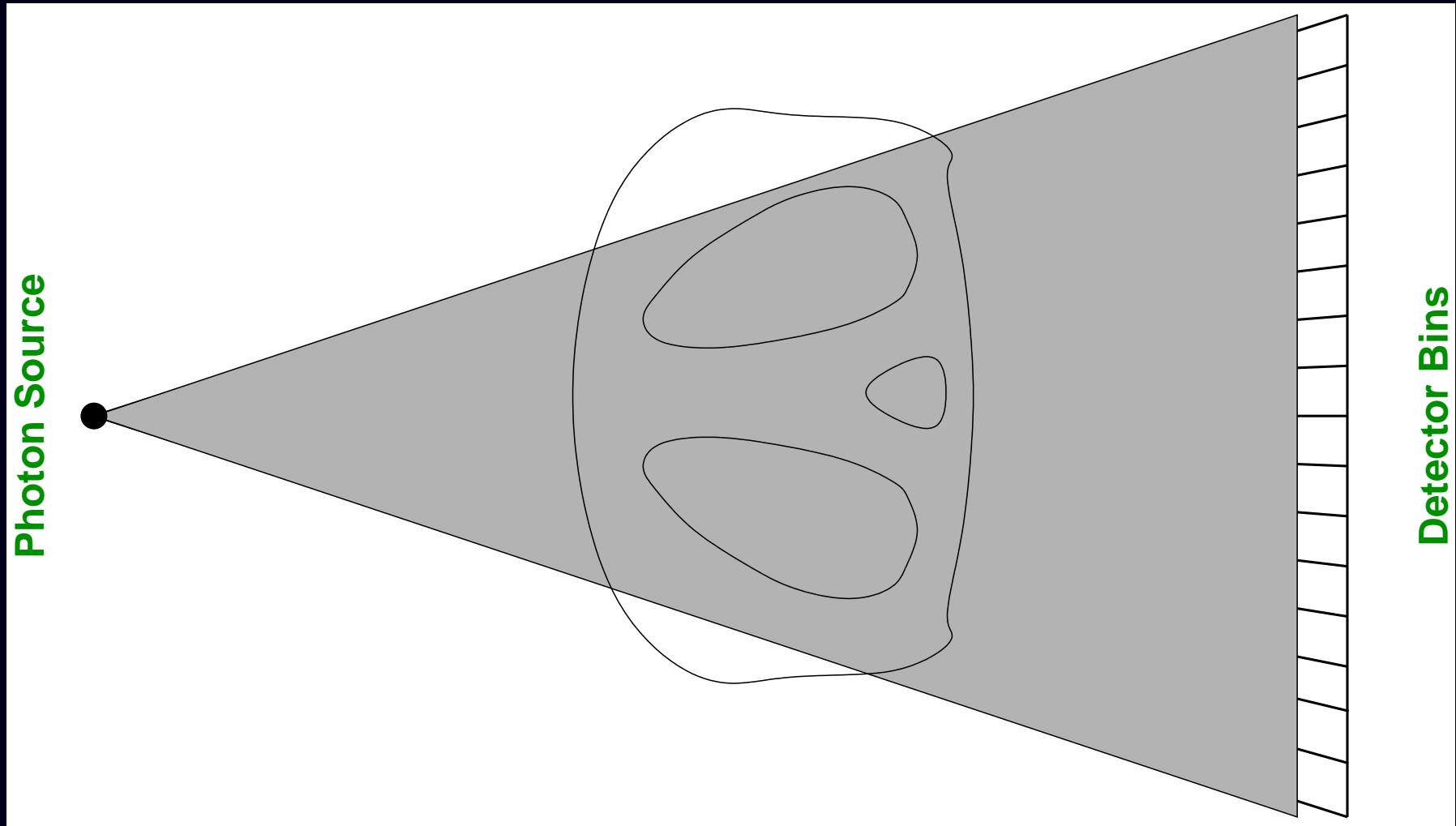
c. Polyenergetic Statistical Reconstruction



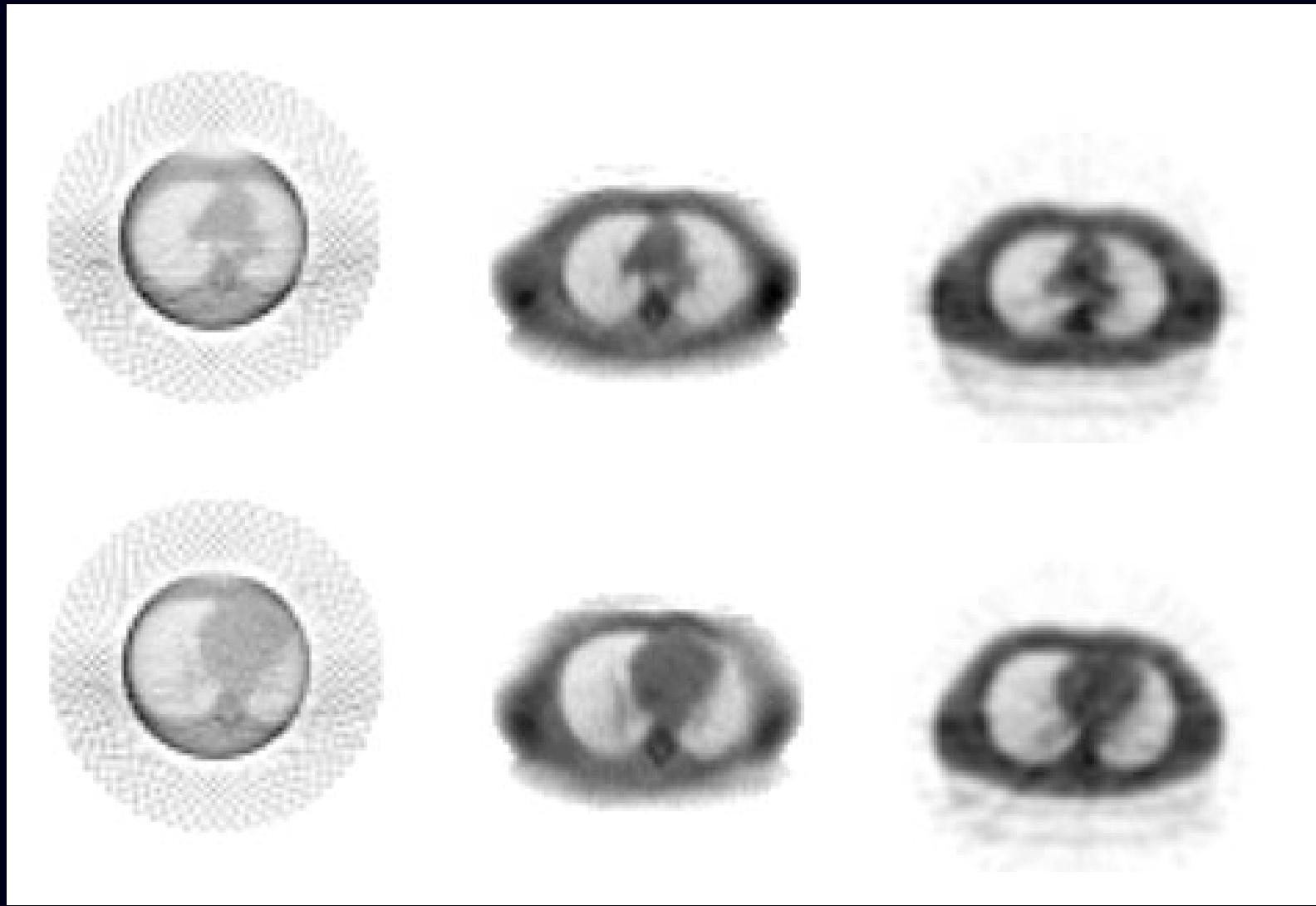
0.8 1 1.2

0.8

Benefit Example: Nonstandard Geometries



Truncated Fan-Beam SPECT Transmission Scan

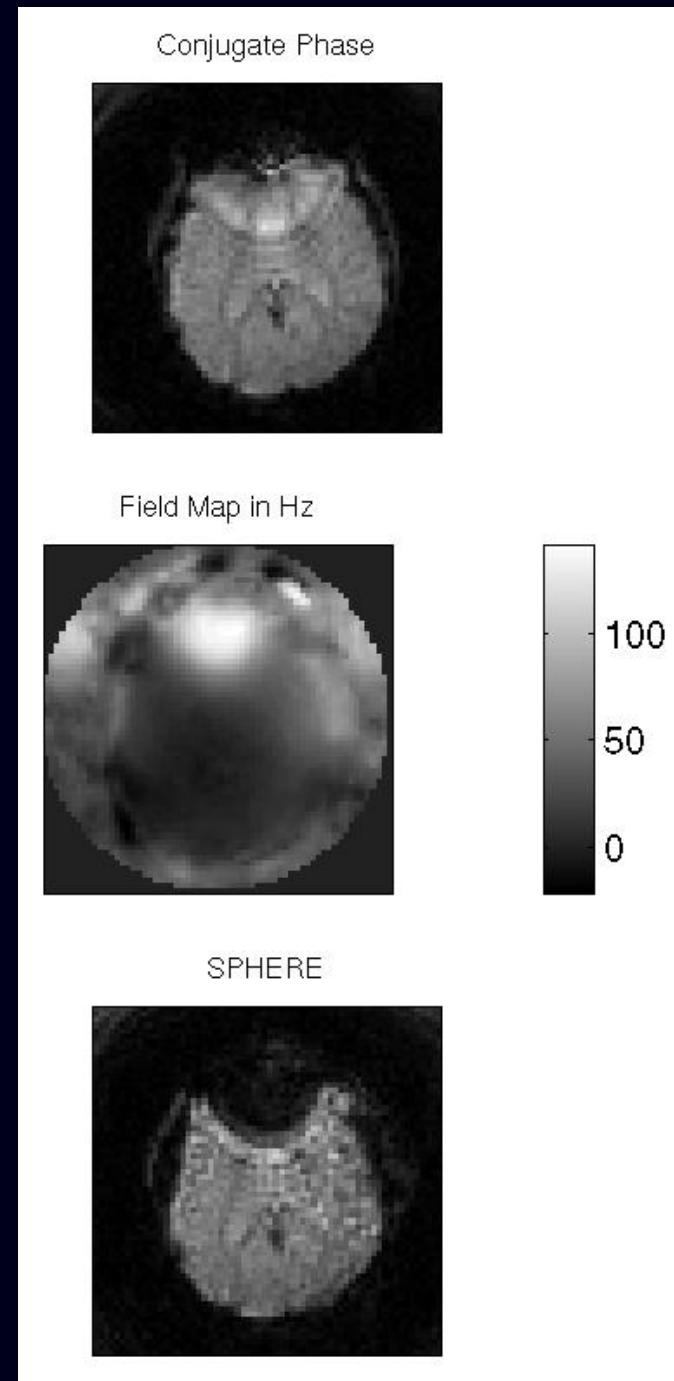
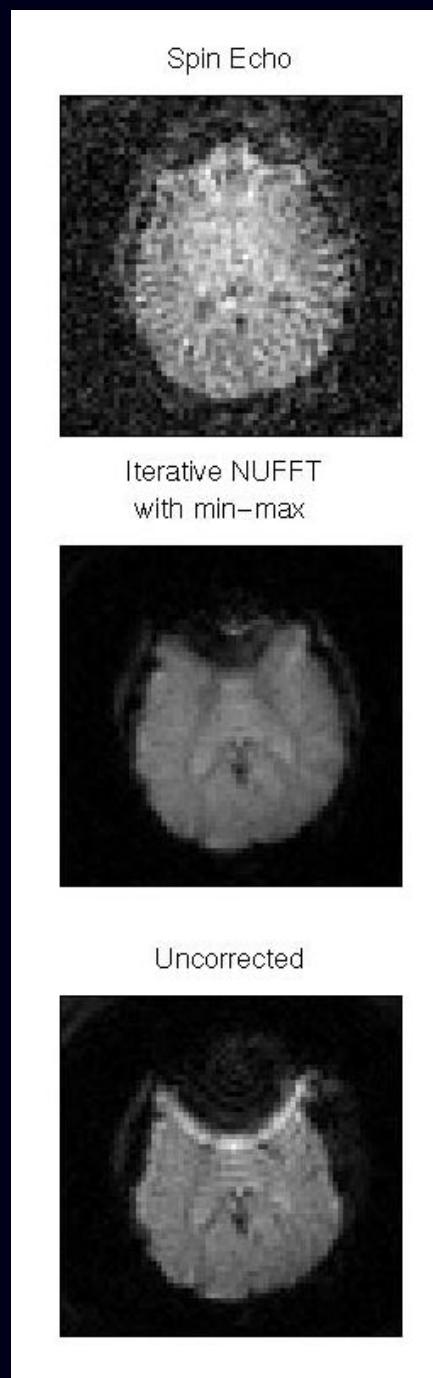


Truncated
FBP

Truncated
PWLS

Untruncated
FBP

One Final Advertisement: Iterative MR Reconstruction



Part 1: From Physics to Statistics

or

“What quantity is reconstructed?”
(in emission tomography)

Outline

- Decay phenomena and fundamental assumptions
- Idealized detectors
- Random phenomena
- Poisson measurement statistics
- State emission tomography reconstruction problem

What Object is Reconstructed?

In *emission imaging*, our aim is to image the *radiotracer distribution*.

The what?

At time $t = 0$ we inject the patient with some *radiotracer*, containing a “large” number N of metastable atoms of some radionuclide.

Let $\vec{X}_k(t) \in \mathbb{R}^3$ denote the position of the k th *tracer atom* at time t .

These positions are influenced by blood flow, patient physiology, and other unpredictable phenomena such as Brownian motion.

The ultimate imaging device would provide an exact list of the spatial locations $\vec{X}_1(t), \dots, \vec{X}_N(t)$ of all tracer atoms for the entire scan.

Would this be enough?

Atom Positions or Statistical Distribution?

Repeating a scan would yield different tracer atom sample paths $\left\{\vec{X}_k(t)\right\}_{k=1}^N$.

.: statistical formulation

Assumption 1. The spatial locations of individual tracer atoms at any time $t \geq 0$ are *independent* random variables that are all *identically distributed* according to a common probability density function (pdf) $f_{\vec{X}(t)}(\vec{x})$.

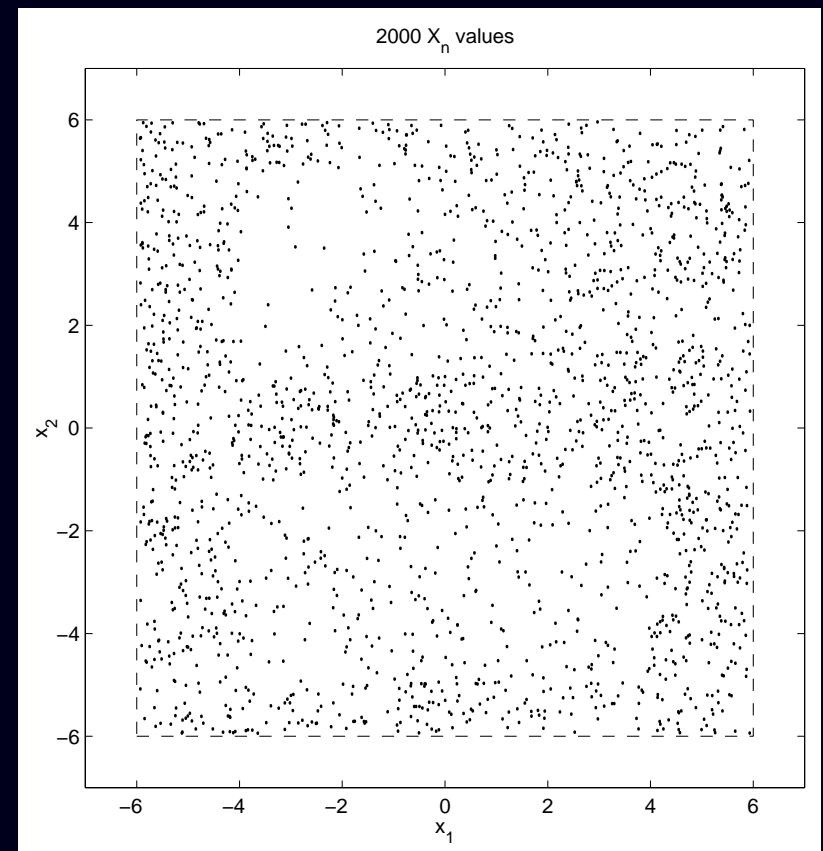
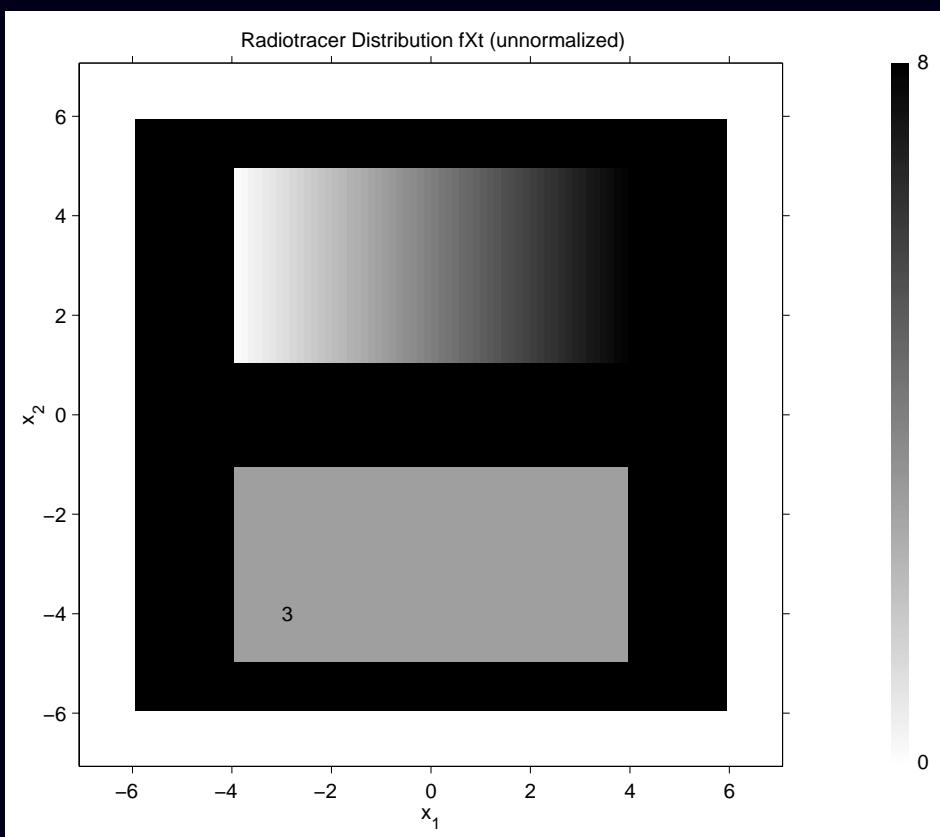
This pdf is determined by patient physiology and tracer properties.

Larger values of $f_{\vec{X}(t)}(\vec{x})$ correspond to “hot spots” where the tracer atoms tend to be located at time t . Units: inverse volume, e.g., atoms per cubic centimeter.

The *radiotracer distribution* $f_{\vec{X}(t)}(\vec{x})$ is the quantity of interest.

(Not $\left\{\vec{X}_k(t)\right\}_{k=1}^N$!)

Example: Perfect Detector

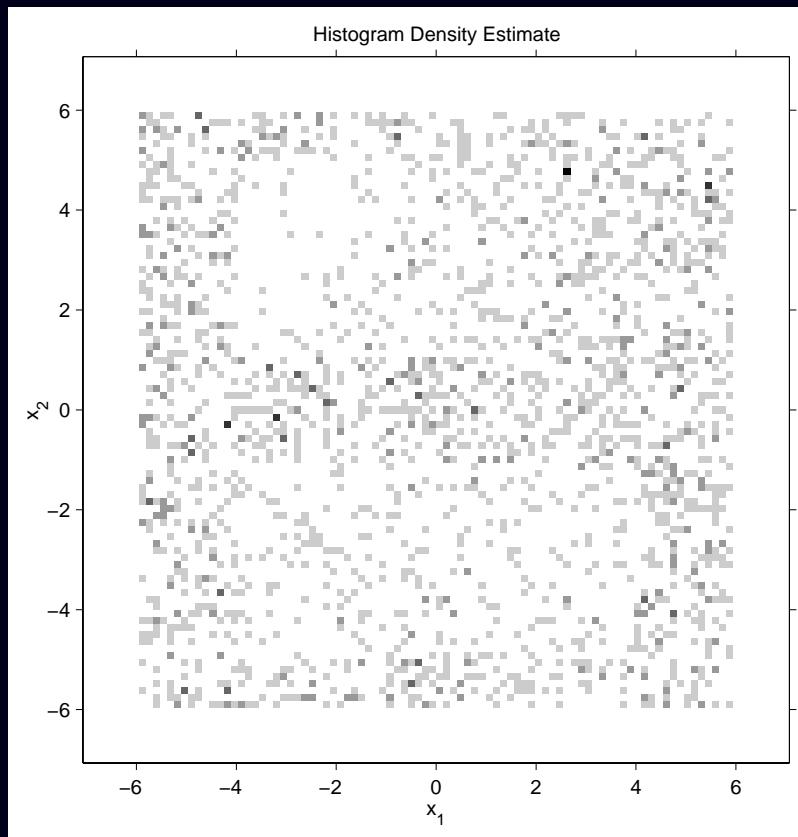


True radiotracer distribution $f_{\vec{X}(t)}(\vec{x})$ at some time t .

A realization of $N = 2000$ i.i.d. atom positions (dots) recorded “exactly.”

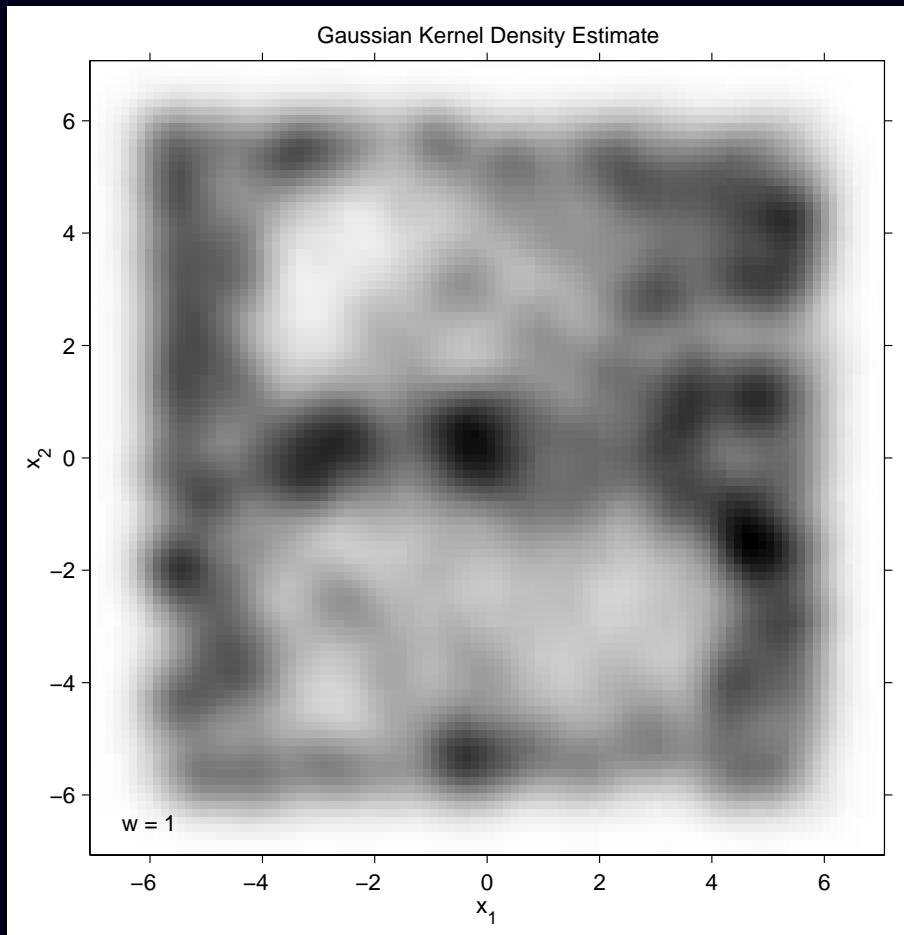
Little similarity!

Binning/Histogram Density Estimator

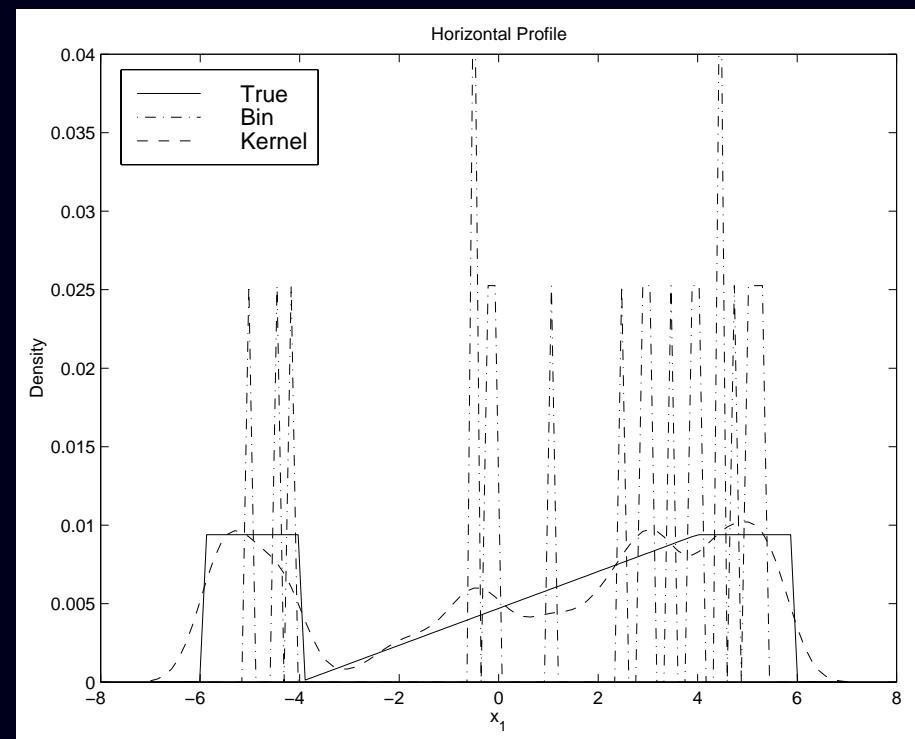


Estimate of $f_{\vec{X}(t)}(\vec{x})$ formed by histogram binning of $N = 2000$ points.
Ramp remains difficult to visualize.

Kernel Density Estimator



Gaussian kernel density estimator
for $f_{\vec{X}(t)}(\vec{x})$ from $N = 2000$ points.



Horizontal profiles at $x_2 = 3$ through
density estimates.

Poisson Spatial Point Process

Assumption 2. The number of injected tracer atoms N has a Poisson distribution with some mean

$$\mu_N \triangleq E[N] = \sum_{n=0}^{\infty} n P[N = n].$$

Let $N(B)$ denote the number of tracer atoms that have spatial locations in any set $B \subset \mathbb{R}^3$ (VOI) at time t_0 after injection.

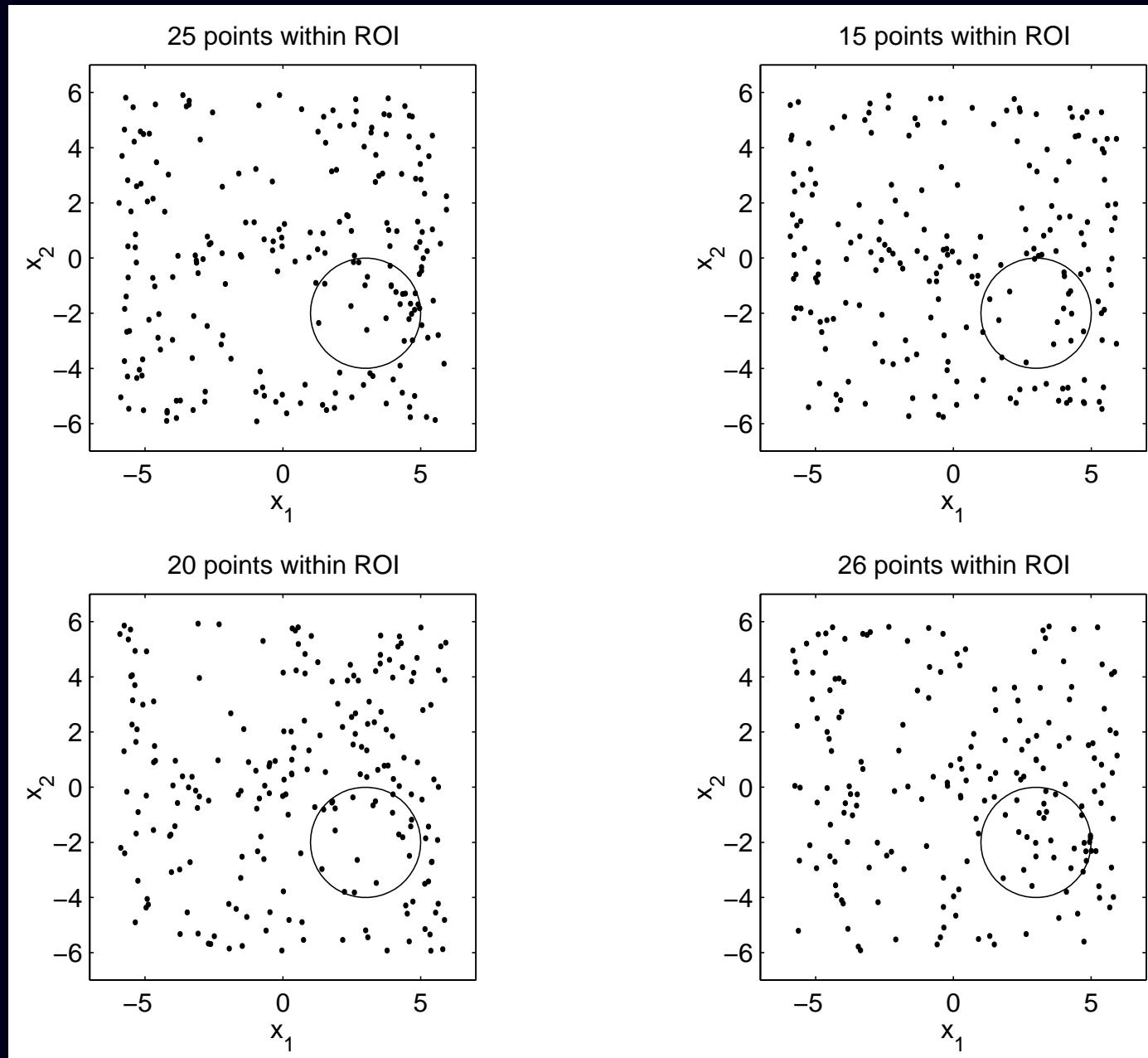
$N(\cdot)$ is called a *Poisson spatial point process*.

Fact. For any set B , $N(B)$ is Poisson distributed with mean:

$$E[N(B)] = E[N]P[\vec{X} \in B] = \mu_N \int_B f_{\vec{X}(t_0)}(\vec{x}) d\vec{x}.$$

Poisson N injected atoms + i.i.d. locations \Rightarrow Poisson point process

Illustration of Point Process ($\mu_N = 200$)



Radionuclide Decay

Preceding quantities are all unobservable.

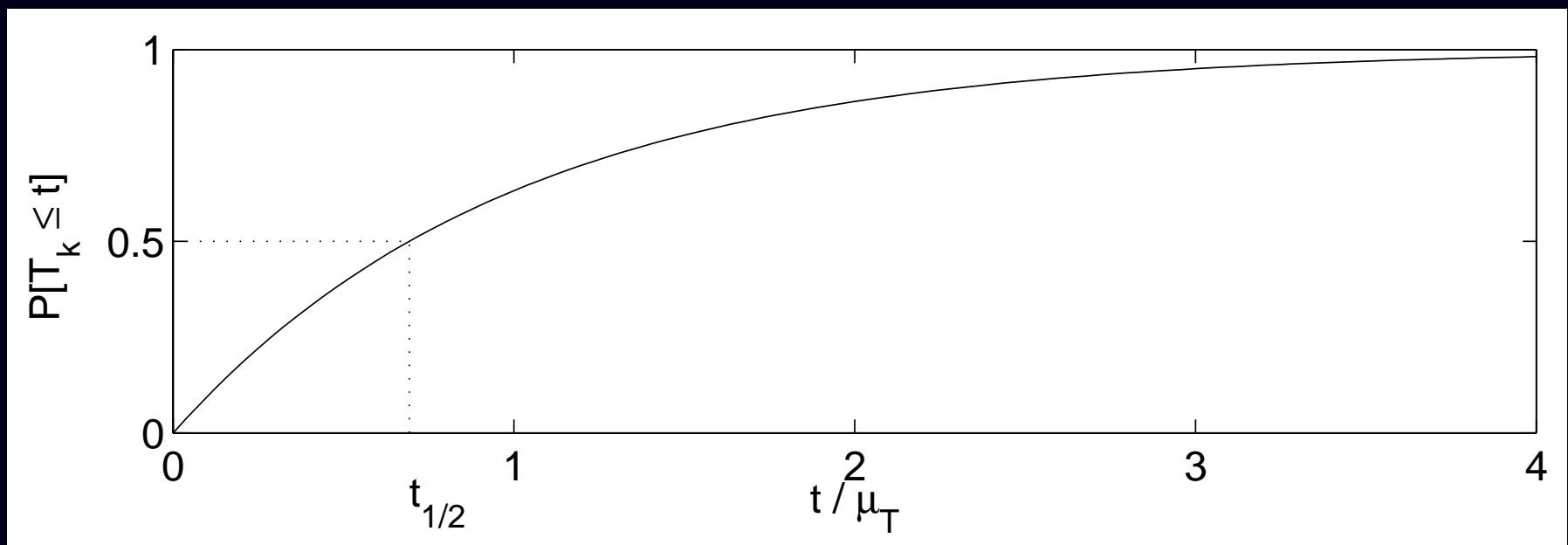
We “observe” a tracer atom only when it decays and emits photon(s).

The time that the k th tracer atom decays is a random variable T_k .

Assumption 3. The T_k 's are statistically *independent* random variables, and are independent of the (random) spatial location.

Assumption 4. Each T_k has an exponential distribution with mean $\mu_T = t_{1/2}/\ln 2$.

Cumulative distribution function: $P[T_k \leq t] = 1 - \exp(-t/\mu_T)$



Statistics of an Ideal Decay Counter

Let $K(t, B)$ denote the number of tracer atoms that decay by time t , and that were located in the VOI $B \subset \mathbb{R}^3$ at the time of decay.

Fact. $K(t, B)$ is a *Poisson counting process* with mean

$$E[K(t, B)] = \int_0^t \int_B \lambda(\vec{x}, \tau) d\vec{x} d\tau,$$

where the (nonuniform) *emission rate density* is given by

$$\lambda(\vec{x}, t) \triangleq \mu_N \frac{e^{-t/\mu_T}}{\mu_T} \cdot f_{\vec{X}(t)}(\vec{x}).$$

Ingredients: “dose,” “decay,” “distribution”

Units: “counts” per unit time per unit volume, e.g., $\mu\text{Ci}/\text{cc}$.

“Photon emission is a Poisson process”

What about the actual measurement statistics?

Idealized Detector Units

A nuclear imaging system consists of n_d conceptual *detector units*.

Assumption 5. Each decay of a tracer atom produces a recorded count in at most one detector unit.

Let $S_k \in \{0, 1, \dots, n_d\}$ denote the index of the incremented detector unit for decay of k th tracer atom. ($S_k = 0$ if decay is undetected.)

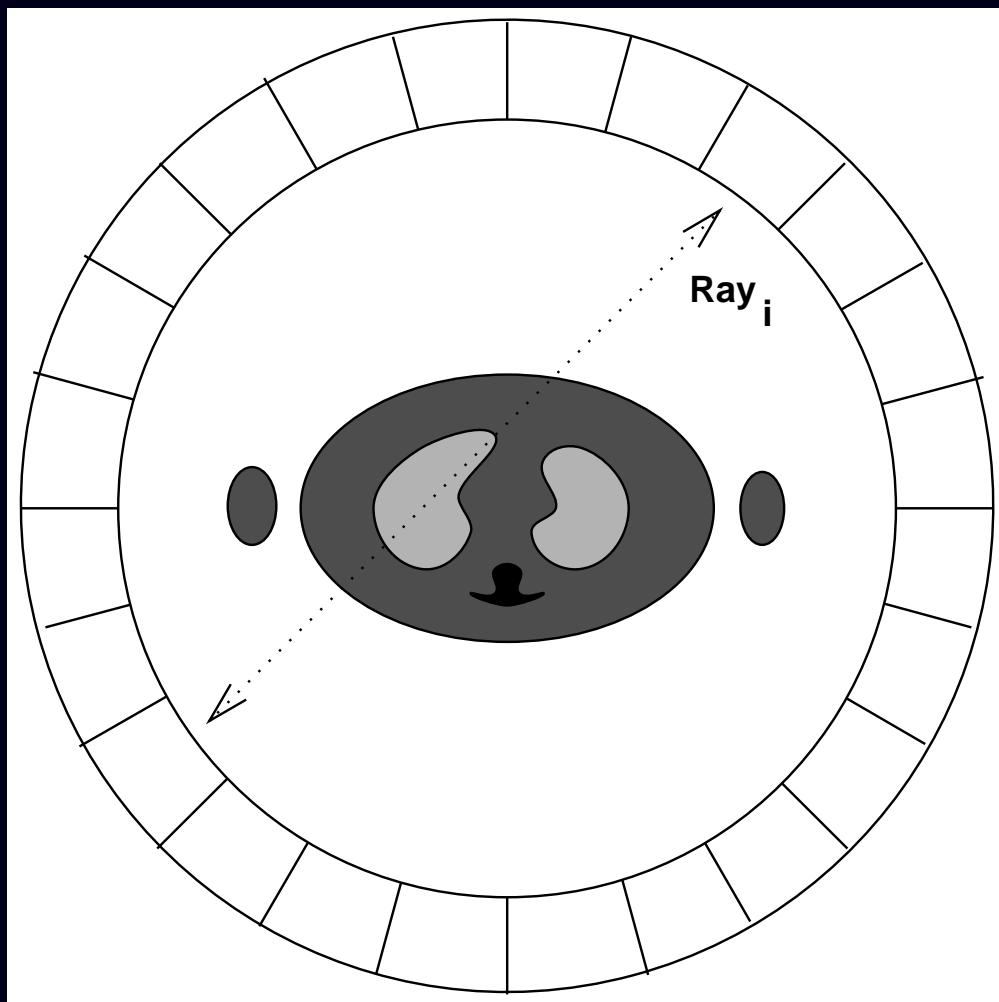
Assumption 6. The S_k 's satisfy the following conditional independence:

$$P(S_1, \dots, S_N | N, T_1, \dots, T_N, \vec{X}_1(\cdot), \dots, \vec{X}_N(\cdot)) = \prod_{k=1}^N P(S_k | \vec{X}_k(T_k)).$$

The recorded bin for the k th tracer atom's decay depends only on its position when it decays, and is independent of all other tracer atoms.

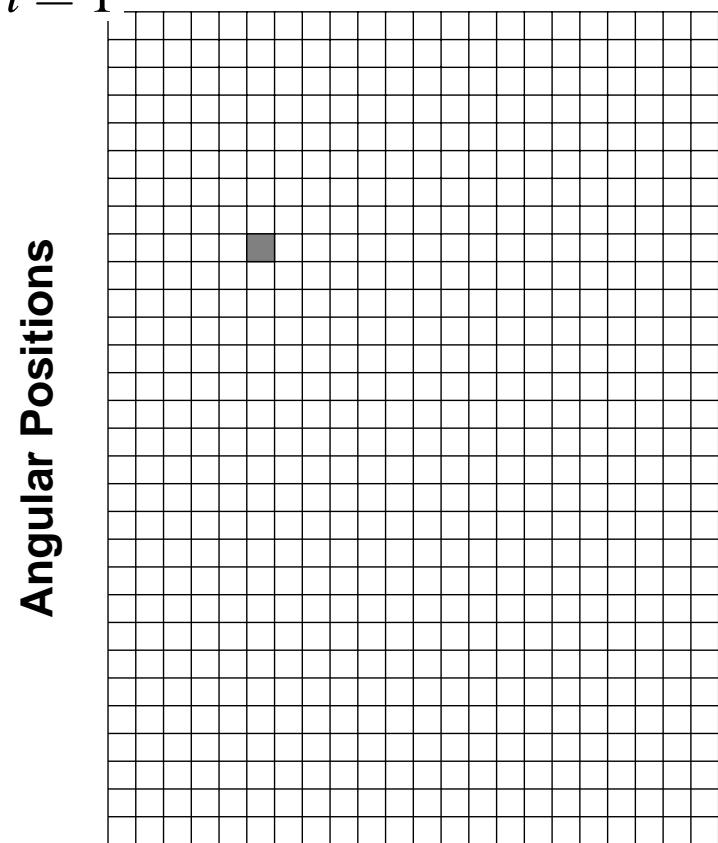
(No event pileup; no deadtime losses.)

PET Example



Sinogram

$i = 1$



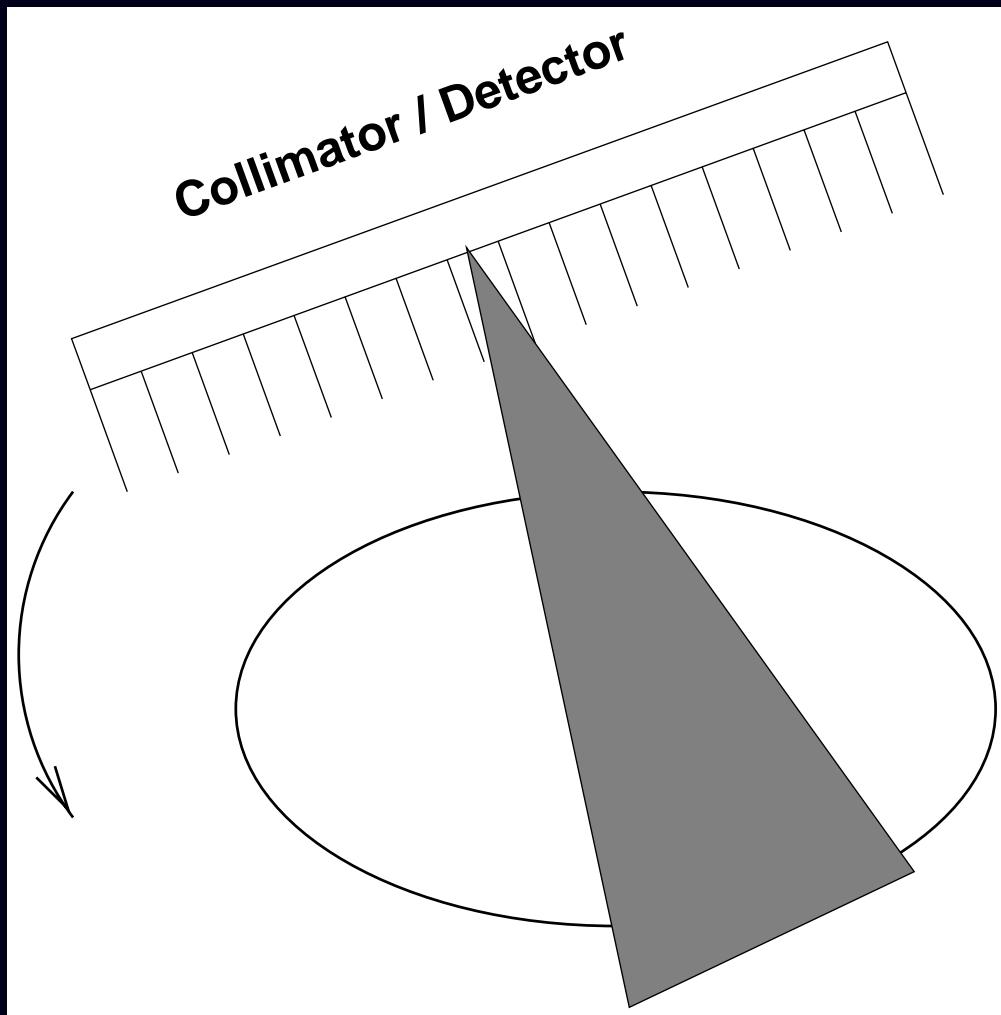
Angular Positions

Radial Positions

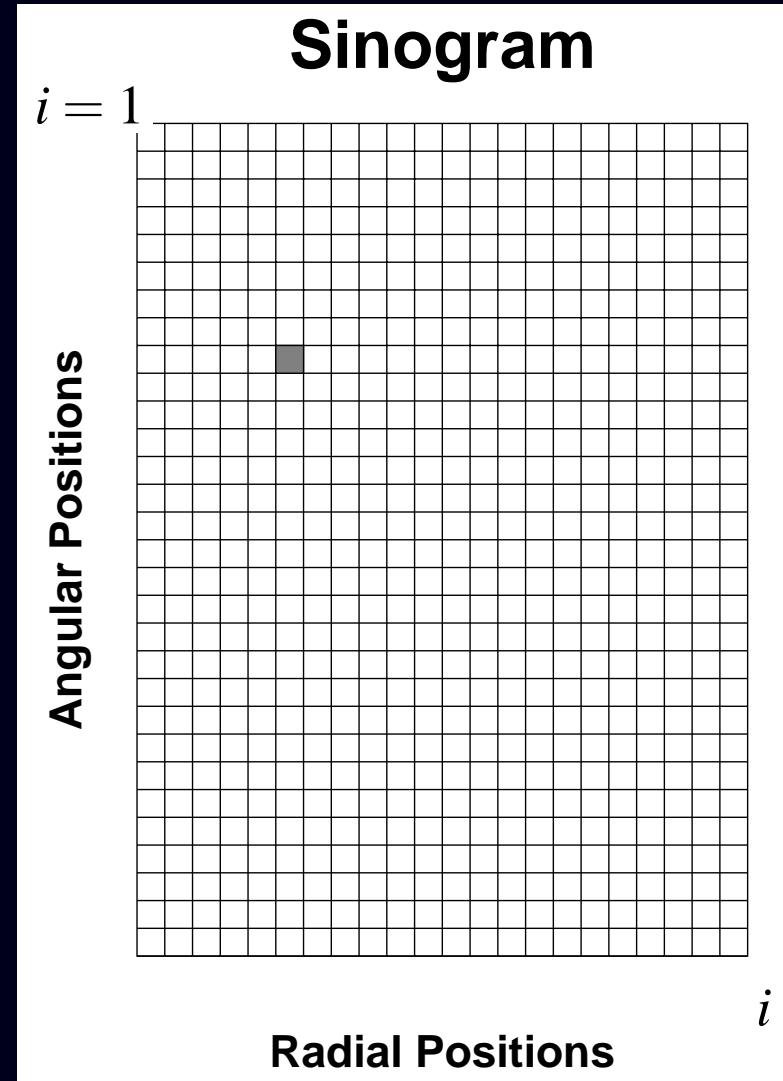
$i = n_d$

$$n_d \leq (n_{\text{crystals}} - 1) \cdot n_{\text{crystals}} / 2$$

SPECT Example



$$n_d = n_{\text{radial_bins}} \cdot n_{\text{angular_steps}}$$



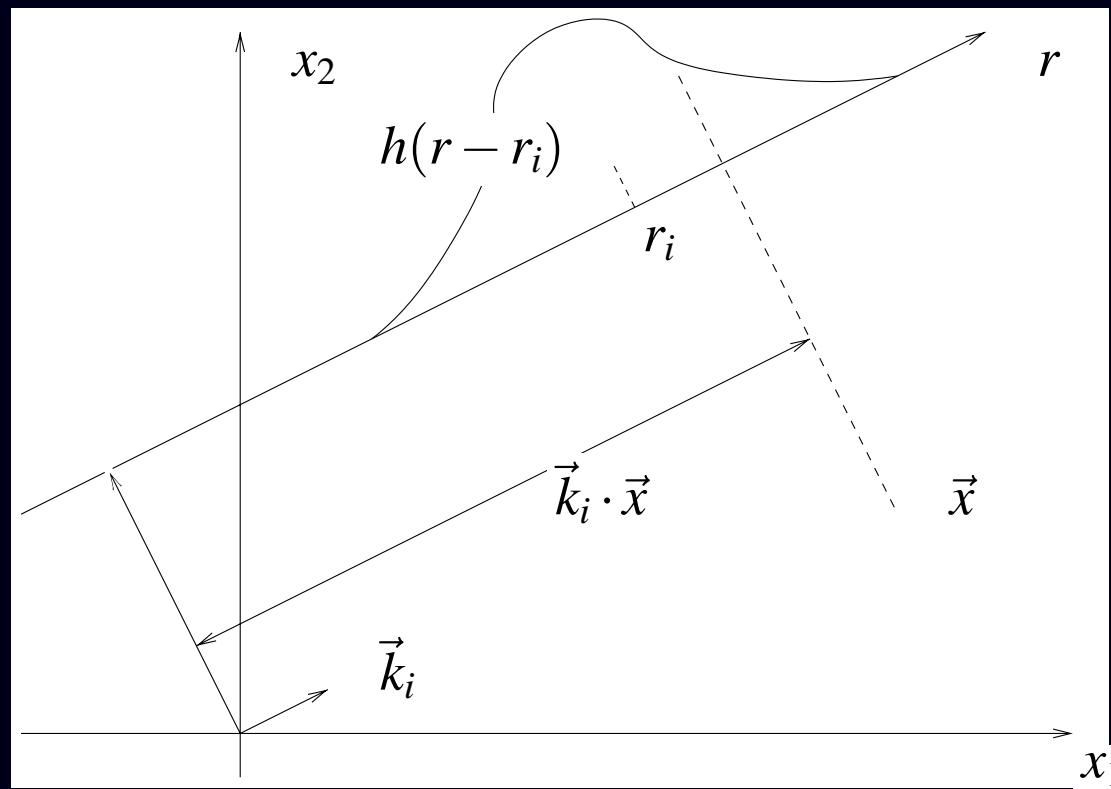
Detector Unit Sensitivity Patterns

Spatial localization:

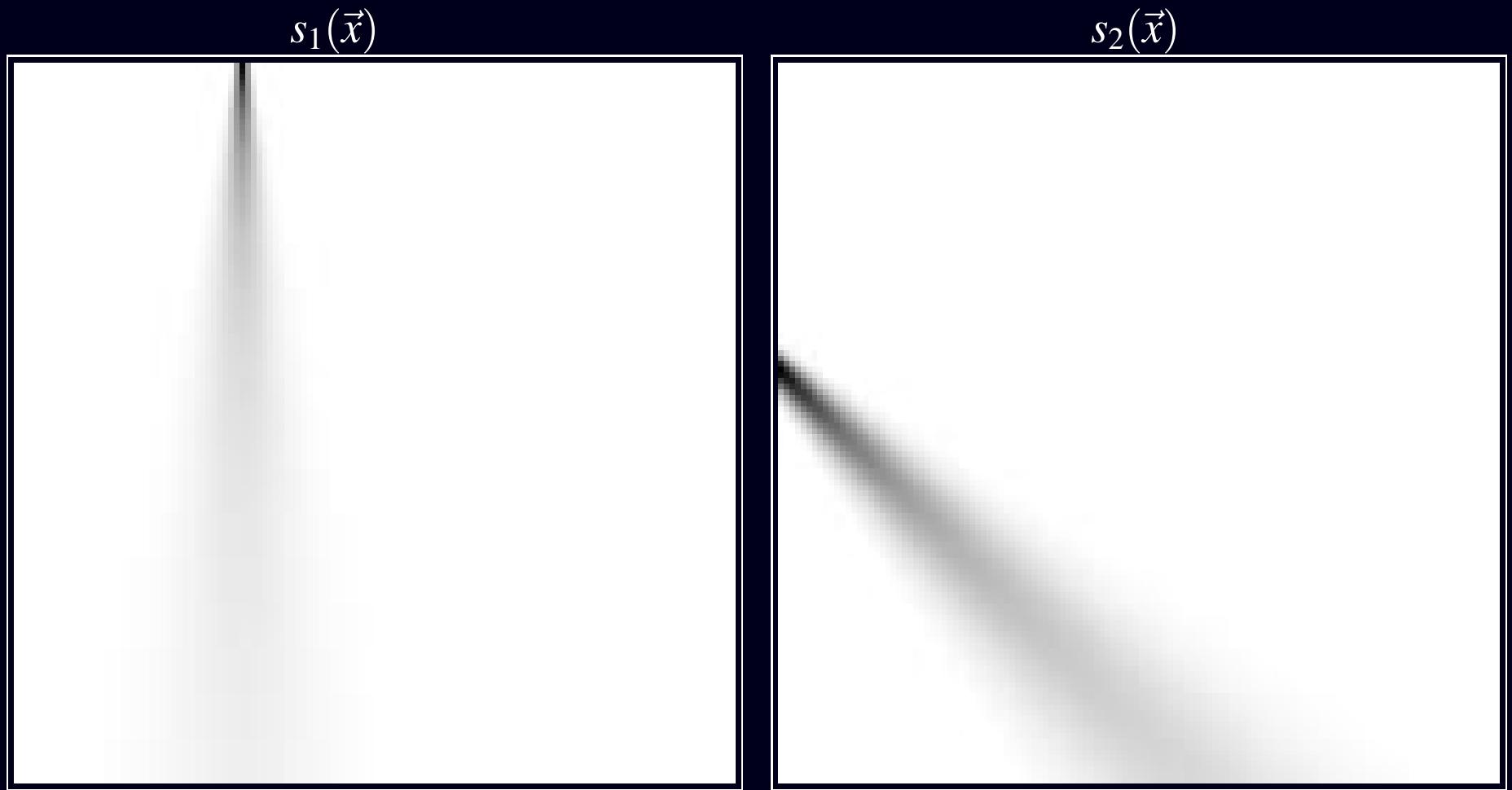
$s_i(\vec{x}) \triangleq$ probability that decay at \vec{x} is recorded by i th detector unit.

Idealized Example. Shift-invariant PSF: $s_i(\vec{x}) = h(\vec{k}_i \cdot \vec{x} - r_i)$

- r_i is the radial position of i th ray
- \vec{k}_i is the unit vector orthogonal to i th parallel ray
- $h(\cdot)$ is the shift-invariant radial PSF (e.g., Gaussian bell or rectangular function)

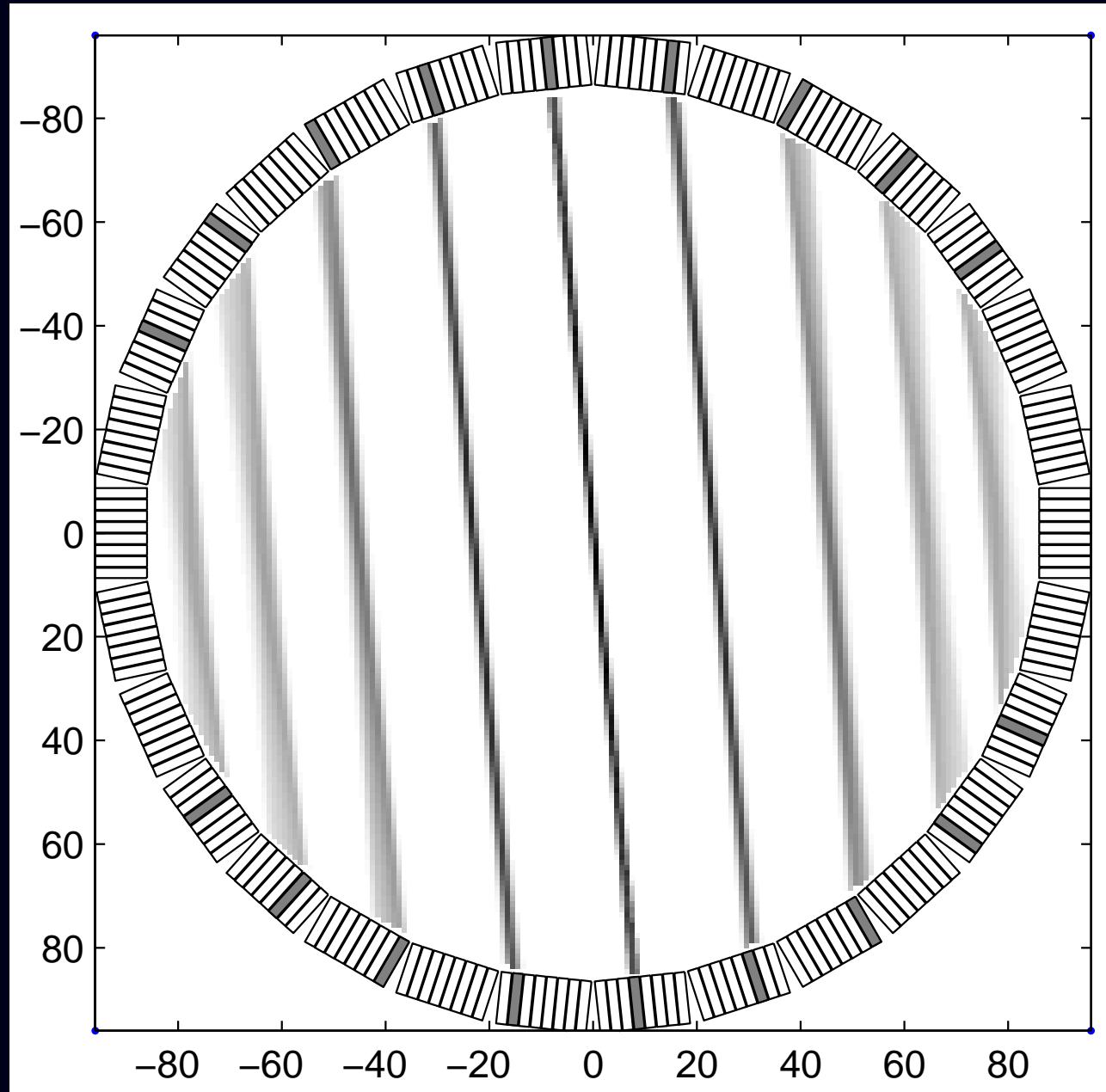


Example: SPECT Detector-Unit Sensitivity Patterns



Two representative $s_i(\vec{x})$ functions for a collimated Anger camera.

Example: PET Detector-Unit Sensitivity Patterns



Detector Unit Sensitivity Patterns

$s_i(\vec{x})$ can include the effects of

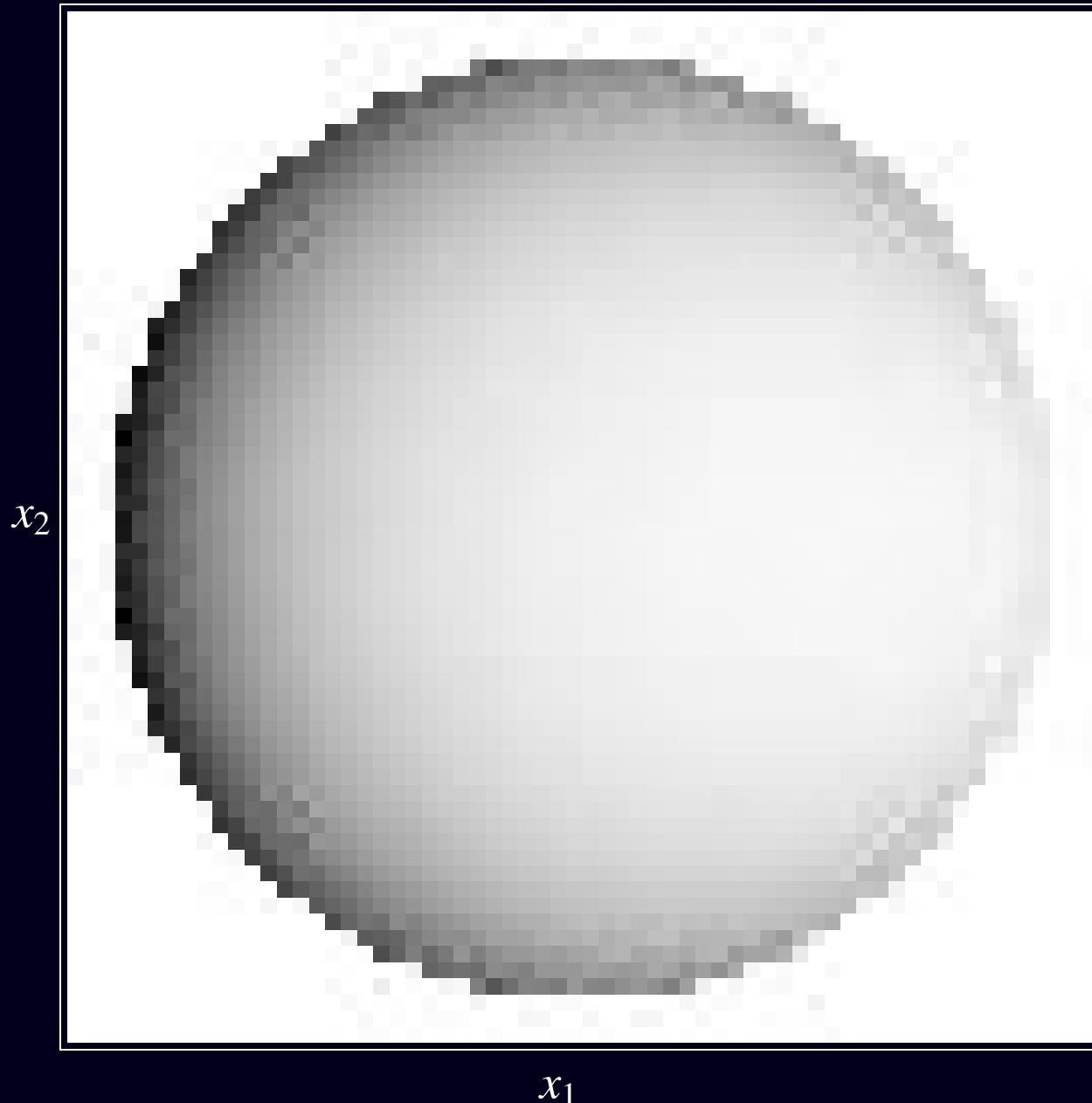
- geometry / solid angle
- collimation
- scatter
- attenuation
- detector response / scan geometry
- duty cycle (dwell time at each angle)
- detector efficiency
- positron range, noncollinearity
- ...

System sensitivity pattern:

$$s(\vec{x}) \triangleq \sum_{i=1}^{n_d} s_i(\vec{x}) = 1 - s_0(\vec{x}) \leq 1$$

(probability that decay at location \vec{x} will be detected *at all* by system)

(Overall) System Sensitivity Pattern: $s(\vec{x}) = \sum_{i=1}^{n_d} s_i(\vec{x})$



Example: collimated 180° SPECT system with uniform attenuation.

Detection Probabilities $s_i(\vec{x}_0)$ (vs det. unit index i)

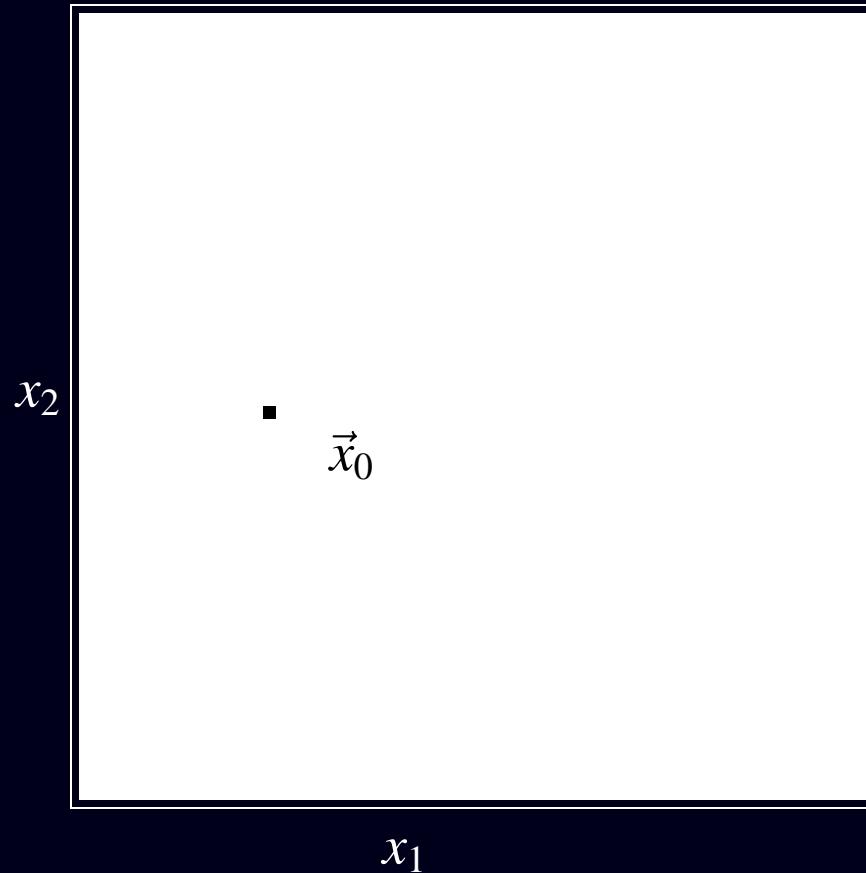
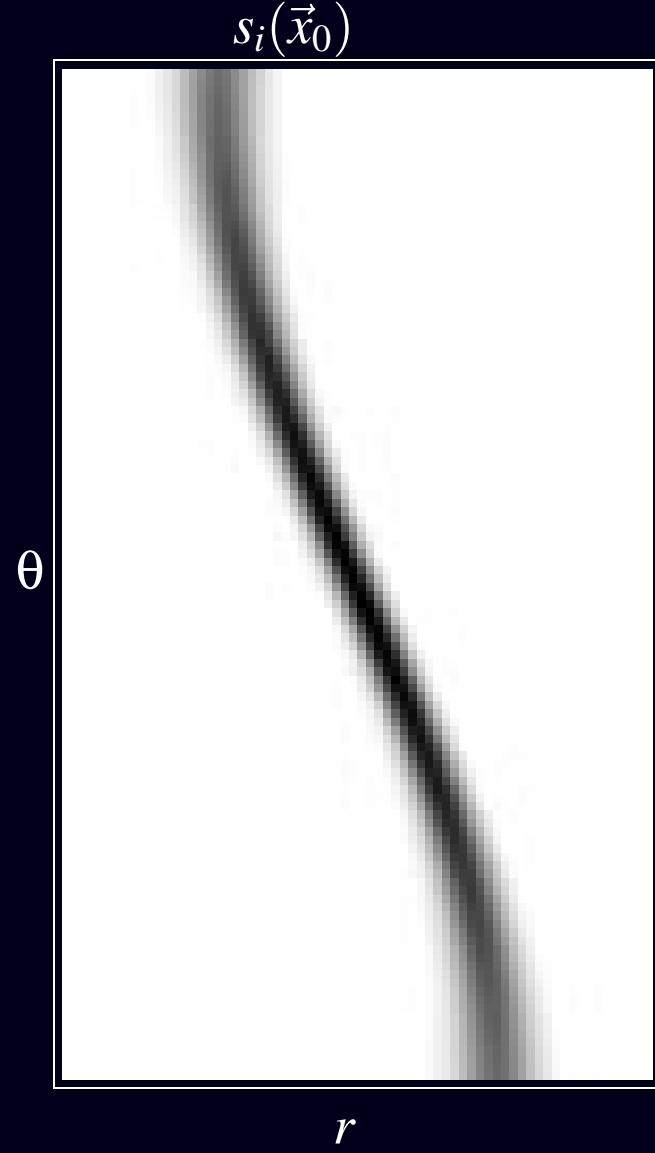


Image domain



Sinogram domain

Summary of Random Phenomena

- Number of tracer atoms injected N
- Spatial locations of tracer atoms $\{\vec{X}_k\}_{k=1}^N$
- Time of decay of tracer atoms $\{T_k\}_{k=1}^N$
- Detection of photon $[S_k \neq 0]$
- Recording detector unit $\{S_k\}_{i=1}^{n_d}$

Emission Scan

Record events in each detector unit for $t_1 \leq t \leq t_2$.

$Y_i \triangleq$ number of events recorded by i th detector unit during scan, for $i = 1, \dots, n_d$.

$$Y_i \triangleq \sum_{k=1}^N \mathbf{1}_{\{S_k=i, T_k \in [t_1, t_2]\}}.$$

The collection $\{Y_i : i = 1, \dots, n_d\}$ is our *sinogram*.

Note $0 \leq Y_i \leq N$.

Fact. Under Assumptions 1-6 above,

$$Y_i \sim \text{Poisson} \left\{ \int s_i(\vec{x}) \lambda(\vec{x}) d\vec{x} \right\} \quad (\text{cf "line integral"})$$

and Y_i 's are statistically independent random variables,
where the *emission density* is given by

$$\lambda(\vec{x}) = \mu_N \int_{t_1}^{t_2} \frac{1}{\mu_T} e^{-t/\mu_T} f_{\vec{X}(t)}(\vec{x}) dt.$$

(Local number of decays per unit volume during scan.)

Ingredients:

- dose (injected)
- duration of scan
- decay of radionuclide
- distribution of radiotracer

Poisson Statistical Model (Emission)

Actual measured counts = “foreground” counts + “background” counts.

Sources of background counts:

- cosmic radiation / room background
- random coincidences (PET)
- scatter not account for in $s_i(\vec{x})$
- “crosstalk” from transmission sources in simultaneous T/E scans
- anything else not accounted for by $\int s_i(\vec{x})\lambda(\vec{x}) d\vec{x}$

Assumption 7.

The background counts also have independent Poisson distributions.

Statistical model (continuous to discrete)

$$Y_i \sim \text{Poisson} \left\{ \int s_i(\vec{x})\lambda(\vec{x}) d\vec{x} + r_i \right\}, \quad i = 1, \dots, n_d$$

r_i : mean number of “background” counts recorded by i th detector unit.

Emission Reconstruction Problem

Estimate the emission density $\lambda(\cdot)$ using (something like) this model:

$$Y_i \sim \text{Poisson} \left\{ \int s_i(\vec{x}) \lambda(\vec{x}) d\vec{x} + r_i \right\}, \quad i = 1, \dots, n_d.$$

Knowns:

- $\{Y_i = y_i\}_{i=1}^{n_d}$: observed counts from each detector unit
- $s_i(\vec{x})$ sensitivity patterns (determined by system models)
- r_i 's : background contributions (determined separately)

Unknown: $\lambda(\vec{x})$

List-mode acquisitions

Recall that conventional sinogram is temporally binned:

$$Y_i \stackrel{\triangle}{=} \sum_{k=1}^N \mathbf{1}_{\{S_k=i, T_k \in [t_1, t_2]\}}.$$

This binning discards temporal information.

List-mode measurements: record all (detector,time) pairs in a list, *i.e.*,

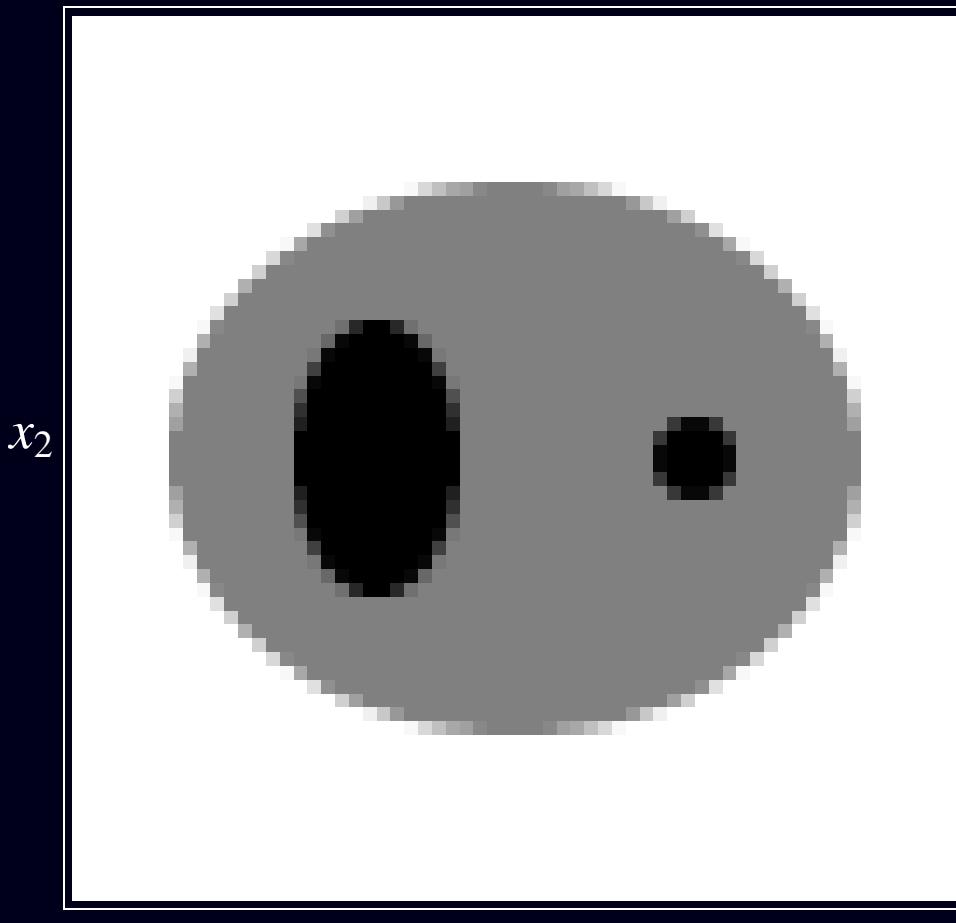
$$\{(S_k, T_k) : k = 1, \dots, N\}.$$

List-mode dynamic reconstruction problem:

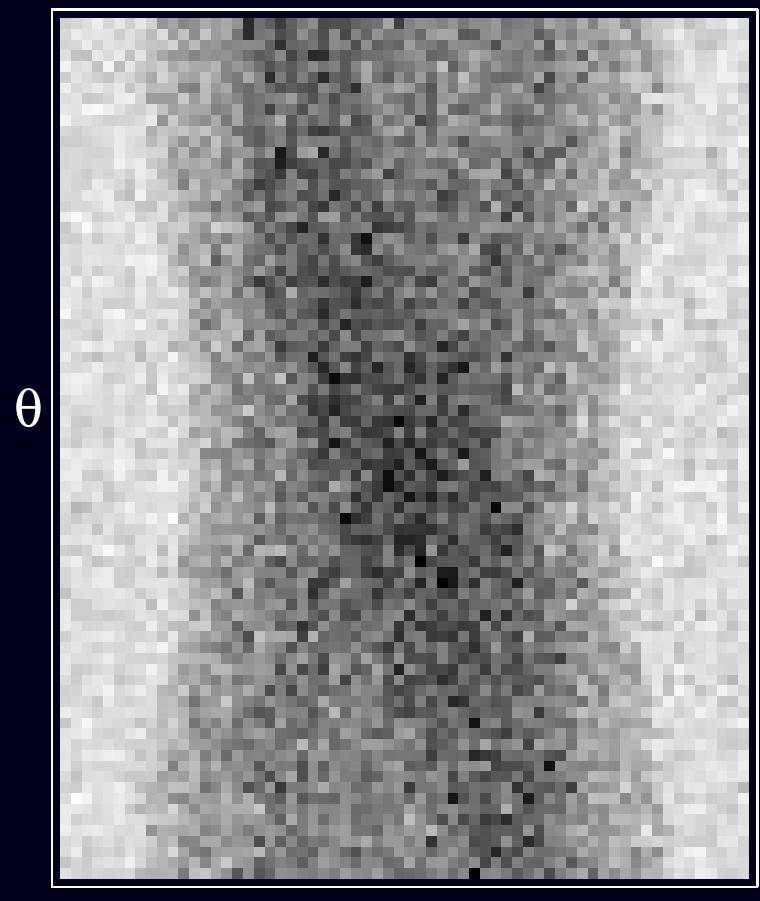
Estimate $\lambda(\vec{x}, t)$ given $\{(S_k, T_k)\}$.

Emission Reconstruction Problem - Illustration

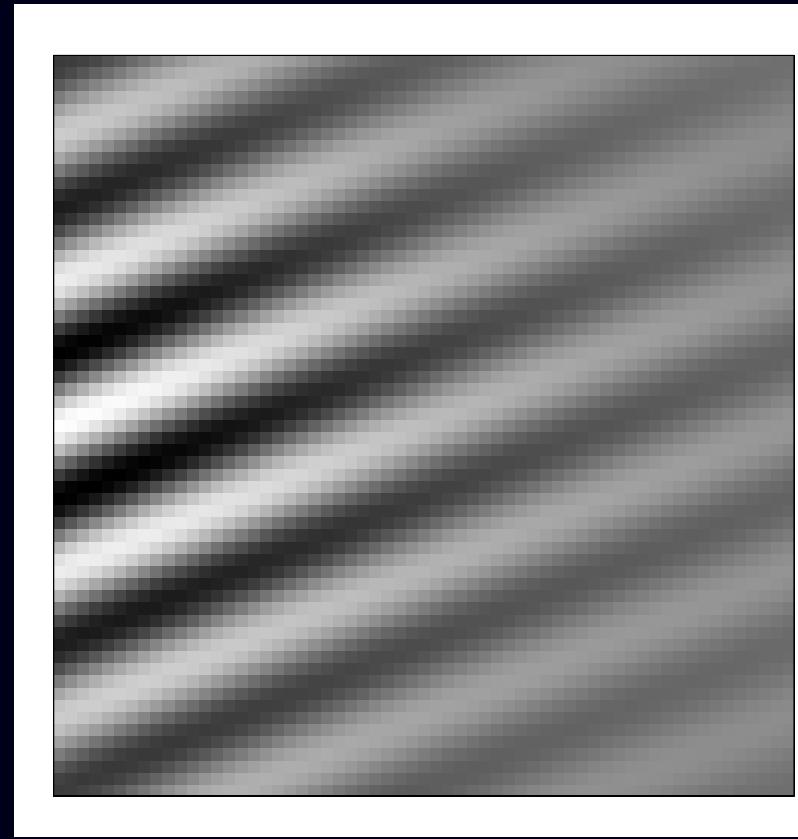
$\lambda(\vec{x})$



$\{Y_i\}$



Example: MRI “Sensitivity Pattern”



Each “k-space sample” corresponds to a sinusoidal pattern weighted by:

- RF receive coil sensitivity pattern
- phase effects of field inhomogeneity
- spin relaxation effects.

$$y_i = \int f(\vec{x}) c_{\text{RF}}(\vec{x}) \exp(-\imath \omega(\vec{x}) t_i) \exp(-t_i/T_2(\vec{x})) \exp\left(-\imath 2\pi \vec{k}(t_i) \cdot \vec{x}\right) d\vec{x} + \varepsilon_i$$

Part 2: Five Categories of Choices

- Object parameterization: function $f(\vec{r})$ vs finite coefficient vector x
- System physical model: $\{s_i(\vec{r})\}$
- Measurement statistical model $y_i \sim [?]$
- Cost function: data-mismatch and regularization
- Algorithm / initialization

No perfect choices - one can critique all approaches!

Choice 1. Object Parameterization

Finite measurements: $\{y_i\}_{i=1}^{n_d}$. Continuous object: $f(\vec{r})$. Hopeless?

All models are wrong but some models are useful.

Linear *series expansion* approach. Replace $f(\vec{r})$ by $\mathbf{x} = (x_1, \dots, x_{n_p})$ where

$$f(\vec{r}) \approx \tilde{f}(\vec{r}) = \sum_{j=1}^{n_p} x_j b_j(\vec{r}) \leftarrow \text{"basis functions"}$$

Forward projection:

$$\begin{aligned} \int s_i(\vec{r}) f(\vec{r}) \, d\vec{r} &= \int s_i(\vec{r}) \left[\sum_{j=1}^{n_p} x_j b_j(\vec{r}) \right] \, d\vec{r} = \sum_{j=1}^{n_p} \left[\int s_i(\vec{r}) b_j(\vec{r}) \, d\vec{r} \right] x_j \\ &= \sum_{j=1}^{n_p} a_{ij} x_j = [\mathbf{A}\mathbf{x}]_i, \quad \text{where } a_{ij} \triangleq \int s_i(\vec{r}) b_j(\vec{r}) \, d\vec{r} \end{aligned}$$

- Projection integrals become finite summations.
- a_{ij} is contribution of j th basis function (e.g., voxel) to i th detector unit.
- The units of a_{ij} and x_j depend on the user-selected units of $b_j(\vec{r})$.
- The $n_d \times n_p$ matrix $\mathbf{A} = \{a_{ij}\}$ is called the *system matrix*.

(Linear) Basis Function Choices

- Fourier series (complex / not sparse)
- Circular harmonics (complex / not sparse)
- Wavelets (negative values / not sparse)
- Kaiser-Bessel window functions (blobs)
- Overlapping circles (disks) or spheres (balls)
- Polar grids, logarithmic polar grids
- “Natural pixels” $\{s_i(\vec{r})\}$
- B-splines (pyramids)
- Rectangular pixels / voxels (rect functions)
- Point masses / bed-of-nails / lattice of points / “comb” function
- Organ-based voxels (e.g., from CT), ...

Considerations

- Represent $f(\vec{r})$ “well” with moderate n_p
- Orthogonality? (not essential)
- “Easy” to compute a_{ij} ’s and/or Ax
- Rotational symmetry
- If stored, the system matrix A should be sparse (mostly zeros).
- Easy to represent nonnegative functions e.g., if $x_j \geq 0$, then $f(\vec{r}) \geq 0$.
A sufficient condition is $b_j(\vec{r}) \geq 0$.

Nonlinear Object Parameterizations

Estimation of intensity *and* shape (*e.g.*, location, radius, etc.)

Surface-based (homogeneous) models

- Circles / spheres
- Ellipses / ellipsoids
- Superquadrics
- Polygons
- Bi-quadratic triangular Bezier patches, ...

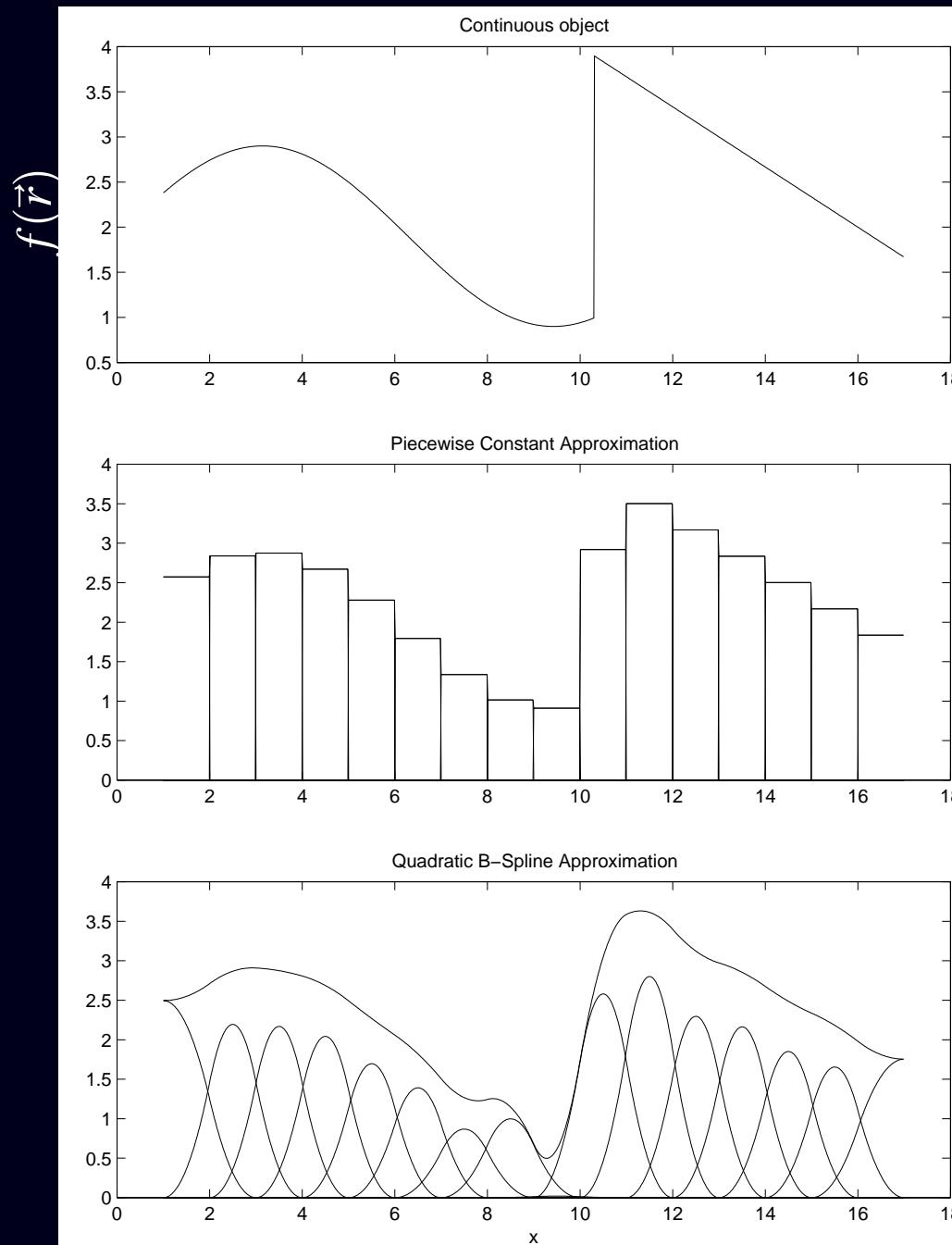
Other models

- Generalized series $f(\vec{r}) = \sum_j x_j b_j(\vec{r}, \theta)$
- Deformable templates $f(\vec{r}) = b(T_\theta(\vec{r}))$
- ...

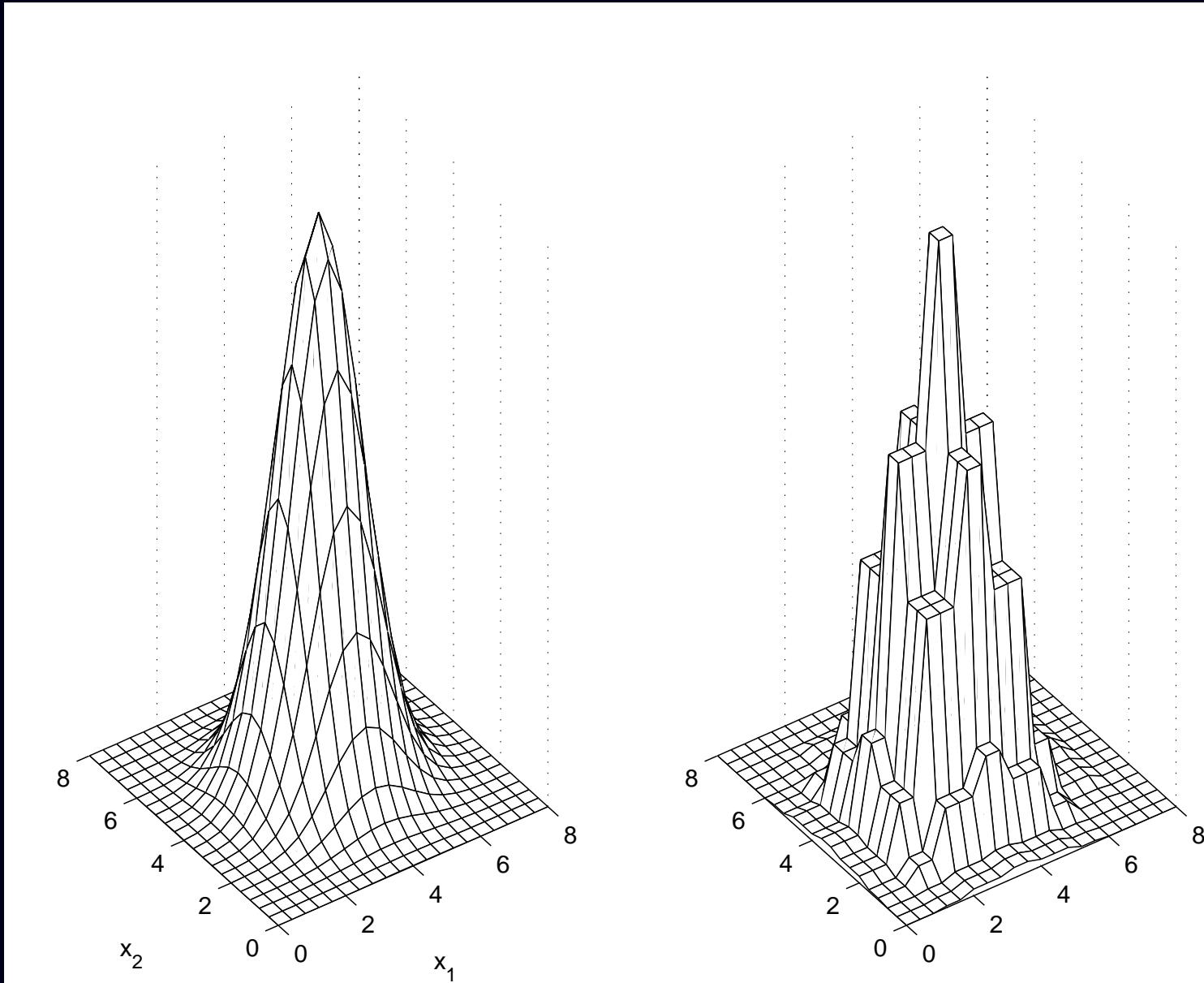
Considerations

- Can be considerably more parsimonious
- If correct, yield greatly reduced estimation error
- Particularly compelling in limited-data problems
- Often oversimplified (all models are wrong but...)
- Nonlinear dependence on location induces non-convex *cost functions*, complicating optimization

Example Basis Functions - 1D



Pixel Basis Functions - 2D



Continuous image $f(\vec{r})$

Pixel basis approximation
 $\sum_{j=1}^{n_p} x_j b_j(\vec{r})$

Discrete-Discrete Emission Reconstruction Problem

Having chosen a basis and *linearly* parameterized the emission density...

Estimate the emission density coefficient vector $\mathbf{x} = (x_1, \dots, x_{n_p})$ (aka “image”) using (something like) this statistical model:

$$y_i \sim \text{Poisson} \left\{ \sum_{j=1}^{n_p} a_{ij} x_j + r_i \right\}, \quad i = 1, \dots, n_d.$$

- $\{y_i\}_{i=1}^{n_d}$: observed counts from each detector unit
- $\mathbf{A} = \{a_{ij}\}$: system matrix (determined by system models)
- r_i 's : background contributions (determined separately)

Many image reconstruction problems are “find \mathbf{x} given \mathbf{y} ” where

$$y_i = g_i([\mathbf{Ax}]_i) + \varepsilon_i, \quad i = 1, \dots, n_d.$$

Choice 2. System Model

$$\text{System matrix elements: } a_{ij} = \int s_i(\vec{r}) b_j(\vec{r}) d\vec{r}$$

- scan geometry
- collimator/detector response
- attenuation
- scatter (object, collimator, scintillator)
- duty cycle (dwell time at each angle)
- detector efficiency / dead-time losses
- positron range, noncollinearity, crystal penetration, ...
- ...

Considerations

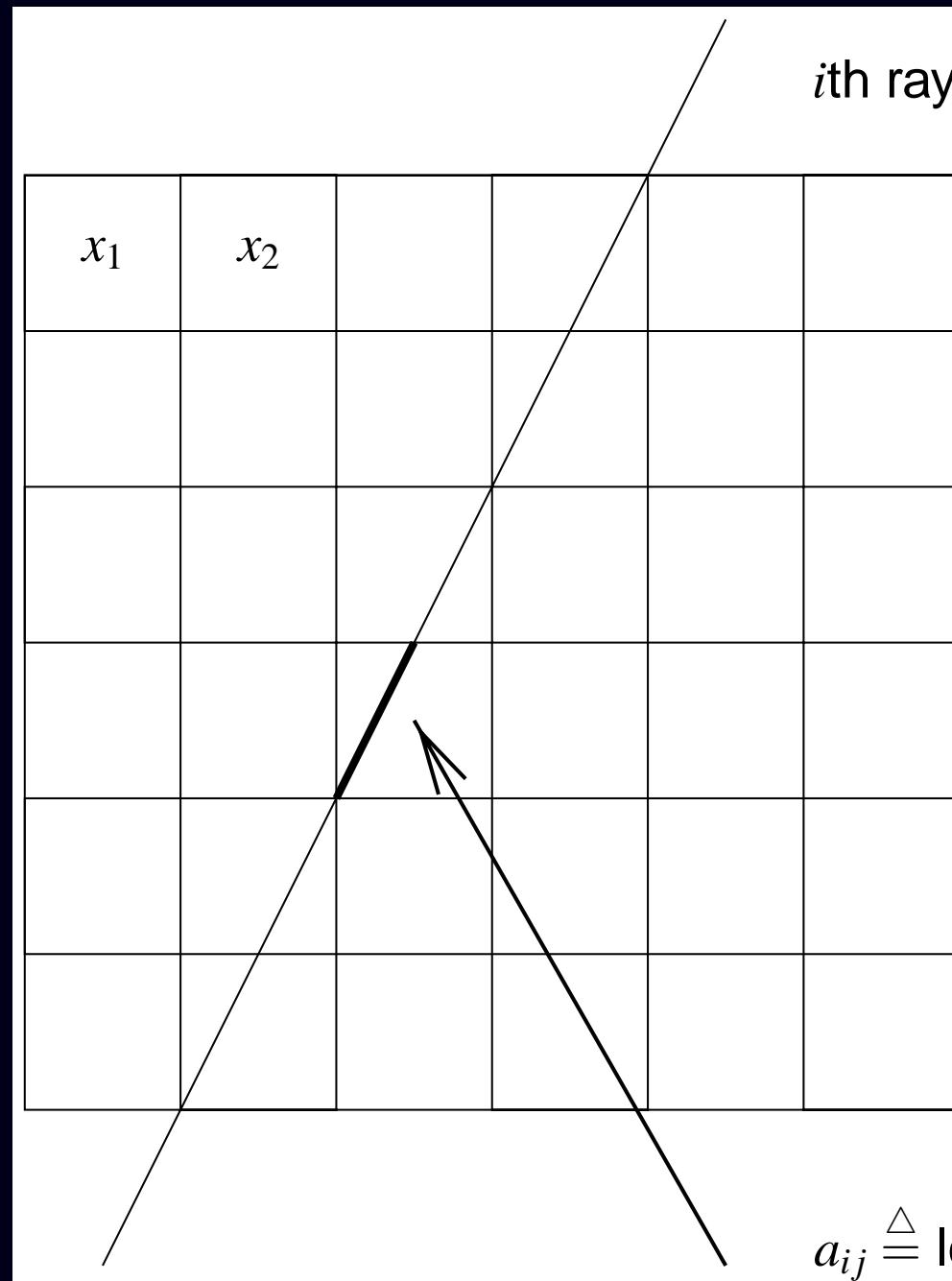
- Improving system model can improve
 - Quantitative accuracy
 - Spatial resolution
 - Contrast, SNR, detectability
- Computation time (and storage vs compute-on-fly)
- Model uncertainties
 - (e.g., calculated scatter probabilities based on noisy attenuation map)
- Artifacts due to over-simplifications

Measured System Model?

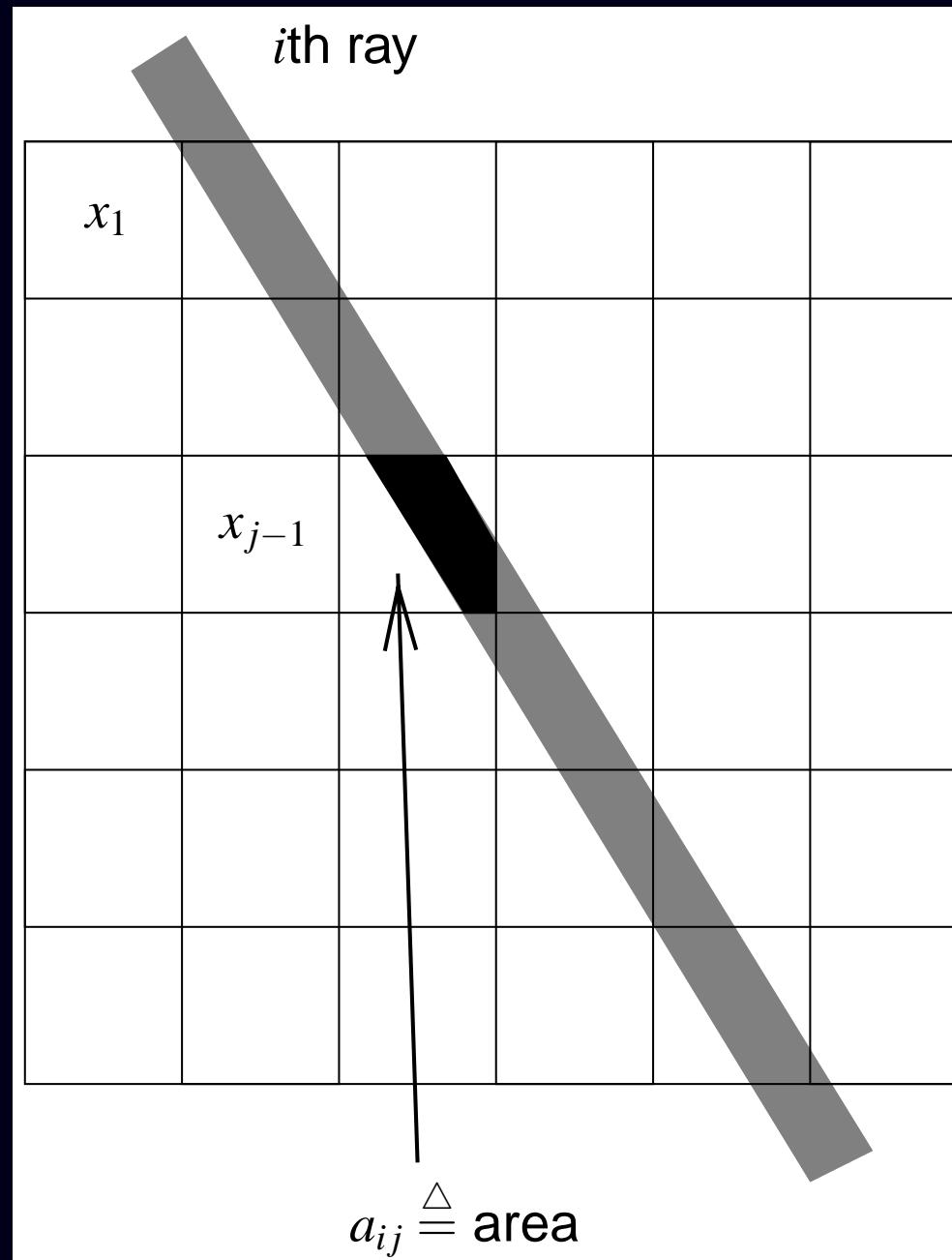
Determine a_{ij} 's by scanning a voxel-sized cube source over the imaging volume and recording counts in all detector units (separately for each voxel).

- Avoids mathematical model approximations
- Scatter / attenuation added later (object dependent), approximately
- Small probabilities \Rightarrow long scan times
- Storage
- Repeat for every voxel size of interest
- Repeat if detectors change

“Line Length” System Model

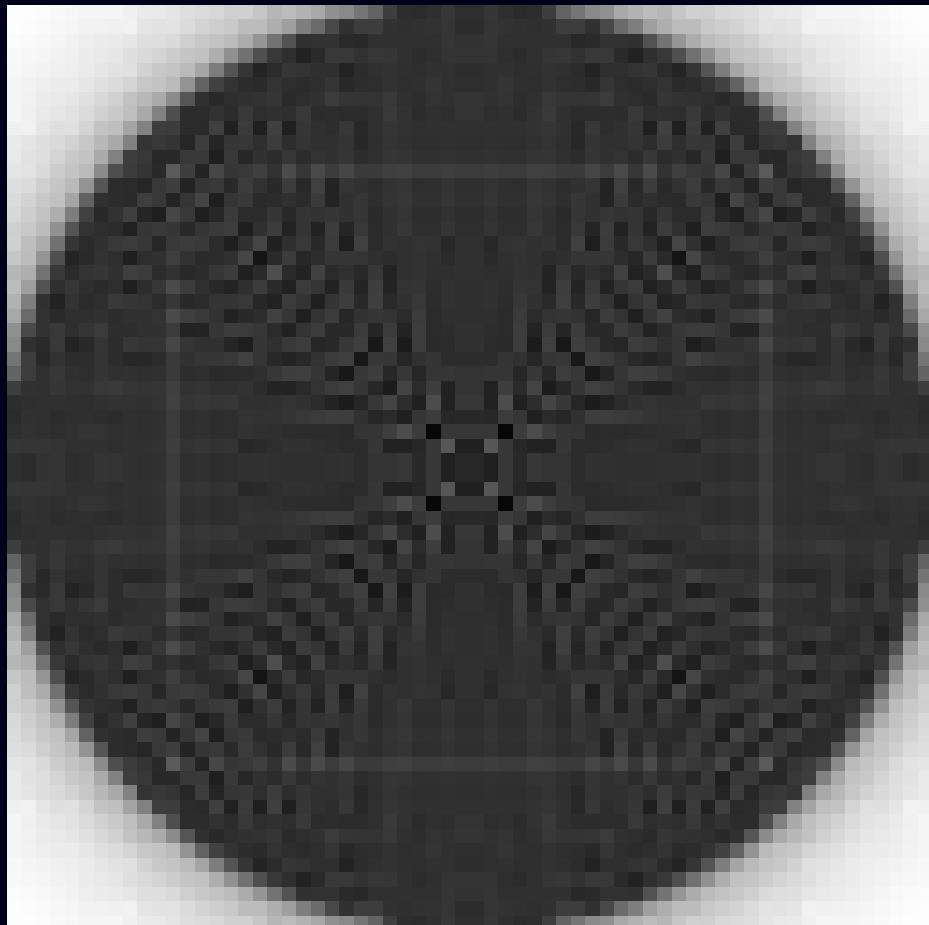


“Strip Area” System Model

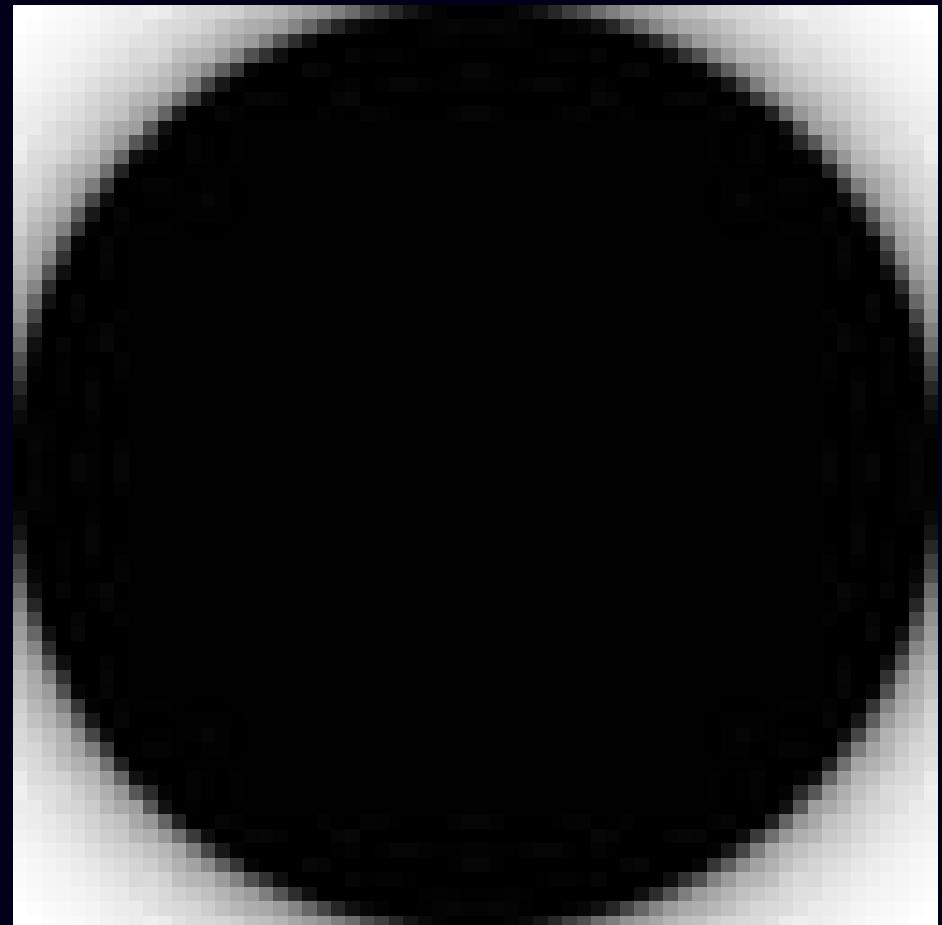


(Implicit) System Sensitivity Patterns

$$\sum_{i=1}^{n_d} a_{ij} \approx s(\vec{r}_j) = \sum_{i=1}^{n_d} s_i(\vec{r}_j)$$

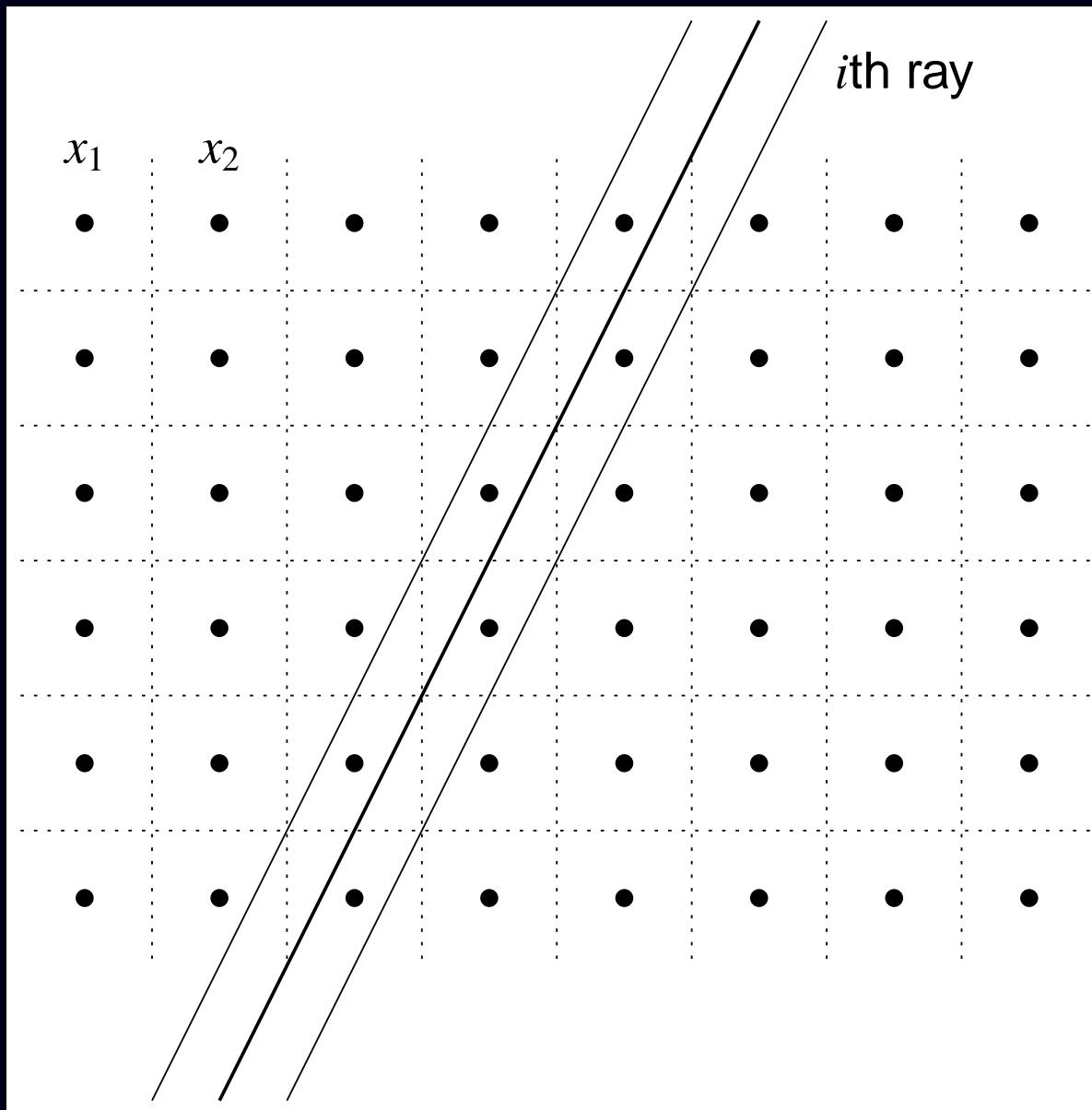


Line Length



Strip Area

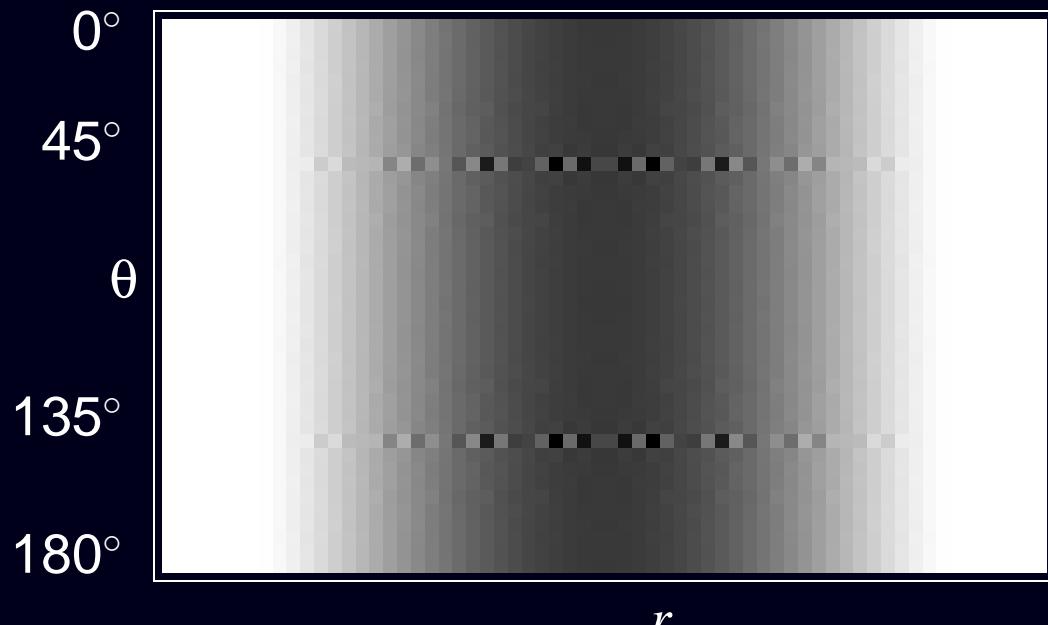
Point-Lattice Projector/Backprojector



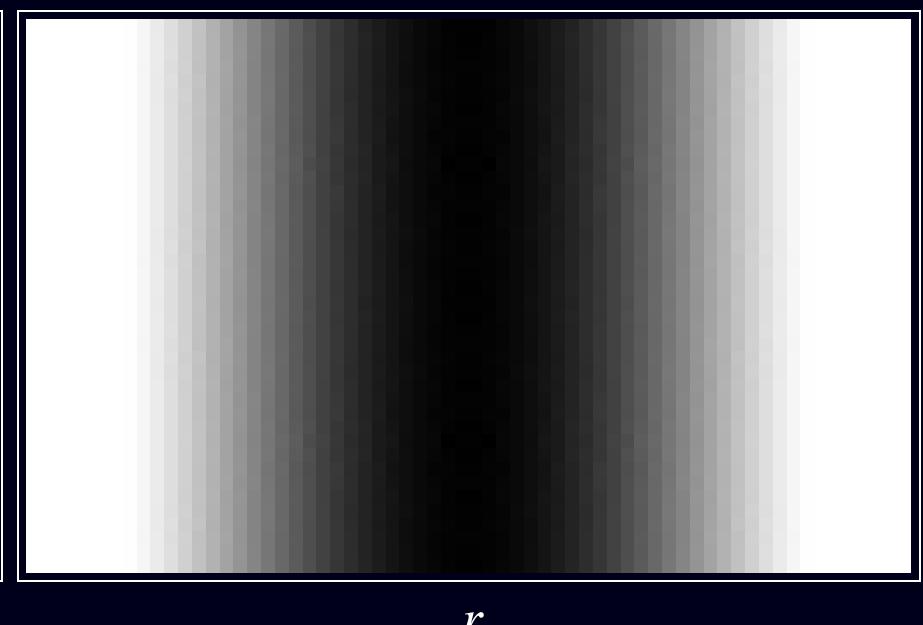
a_{ij} 's determined by linear interpolation

Point-Lattice Artifacts

Projections (sinograms) of uniform disk object:



Point Lattice



Strip Area

Forward- / Back-projector “Pairs”

Forward projection (image domain to projection domain):

$$\bar{y}_i = \int s_i(\vec{r}) f(\vec{r}) \, d\vec{r} = \sum_{j=1}^{n_p} a_{ij} x_j = [\mathbf{A}\mathbf{x}]_i, \text{ or } \bar{\mathbf{y}} = \mathbf{A}\mathbf{x}$$

Backprojection (projection domain to image domain):

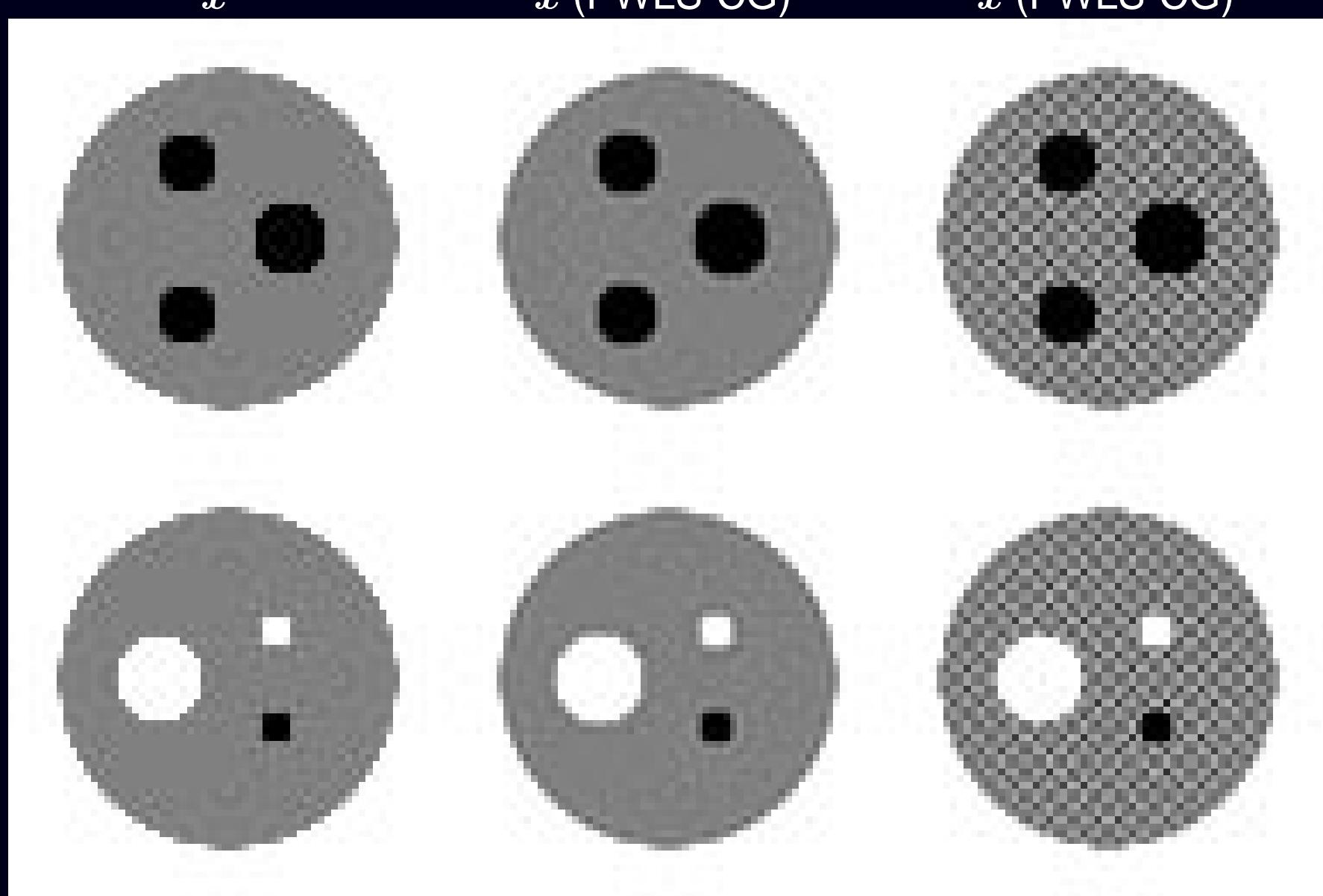
$$\mathbf{A}'\mathbf{y} = \left\{ \sum_{i=1}^{n_d} a_{ij} y_i \right\}_{j=1}^{n_p}$$

Often $\mathbf{A}'\mathbf{y}$ is implemented as $\mathbf{B}\mathbf{y}$ for some “backprojector” $\mathbf{B} \neq \mathbf{A}'$

Least-squares solutions (for example):

$$\hat{\mathbf{x}} = [\mathbf{A}'\mathbf{A}]^{-1} \mathbf{A}'\mathbf{y} \neq [\mathbf{B}\mathbf{A}]^{-1} \mathbf{B}\mathbf{y}$$

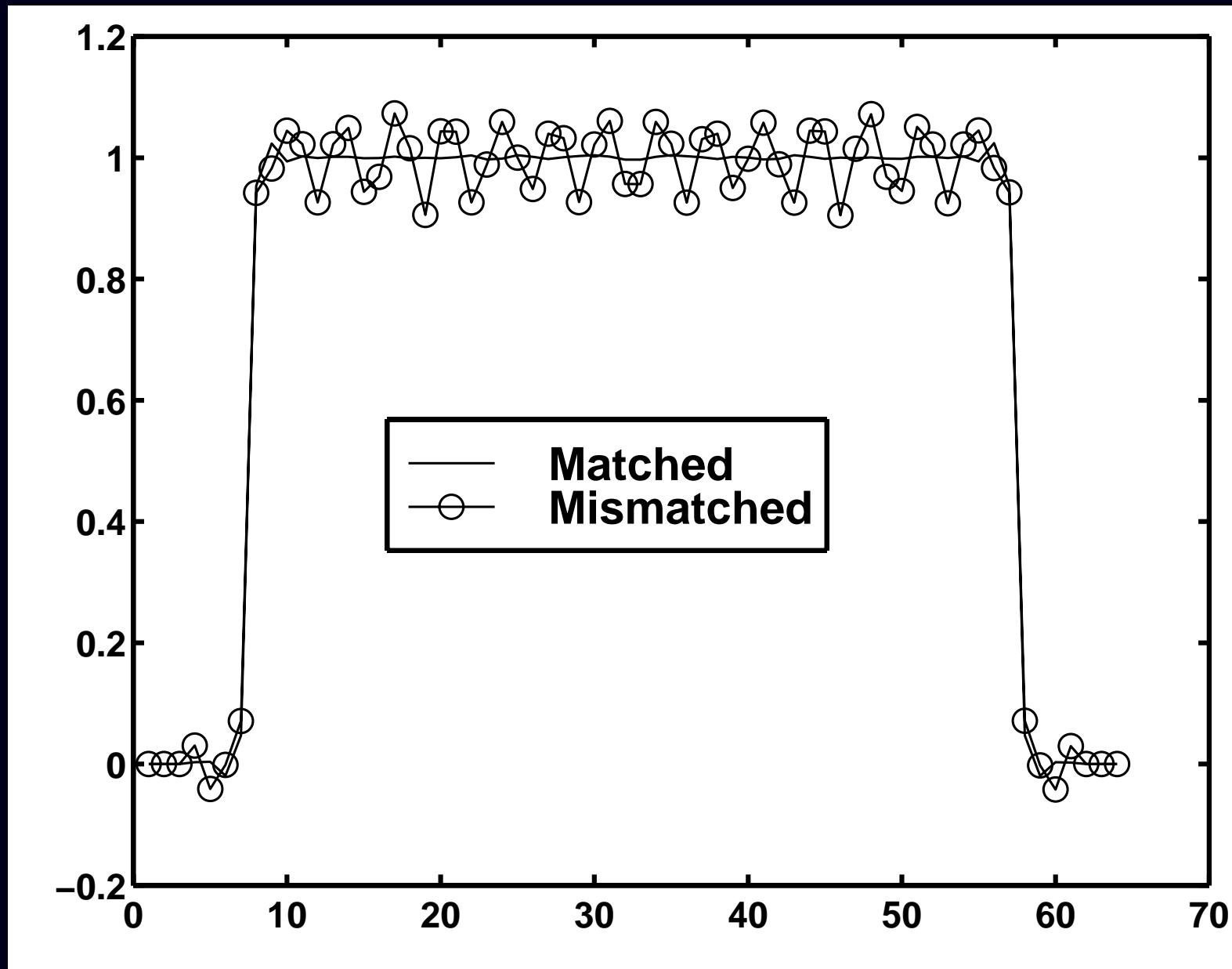
Mismatched Backprojector $B \neq A'$



Matched

Mismatched

Horizontal Profiles



System Model Tricks

- Factorize (e.g., PET Gaussian detector response)

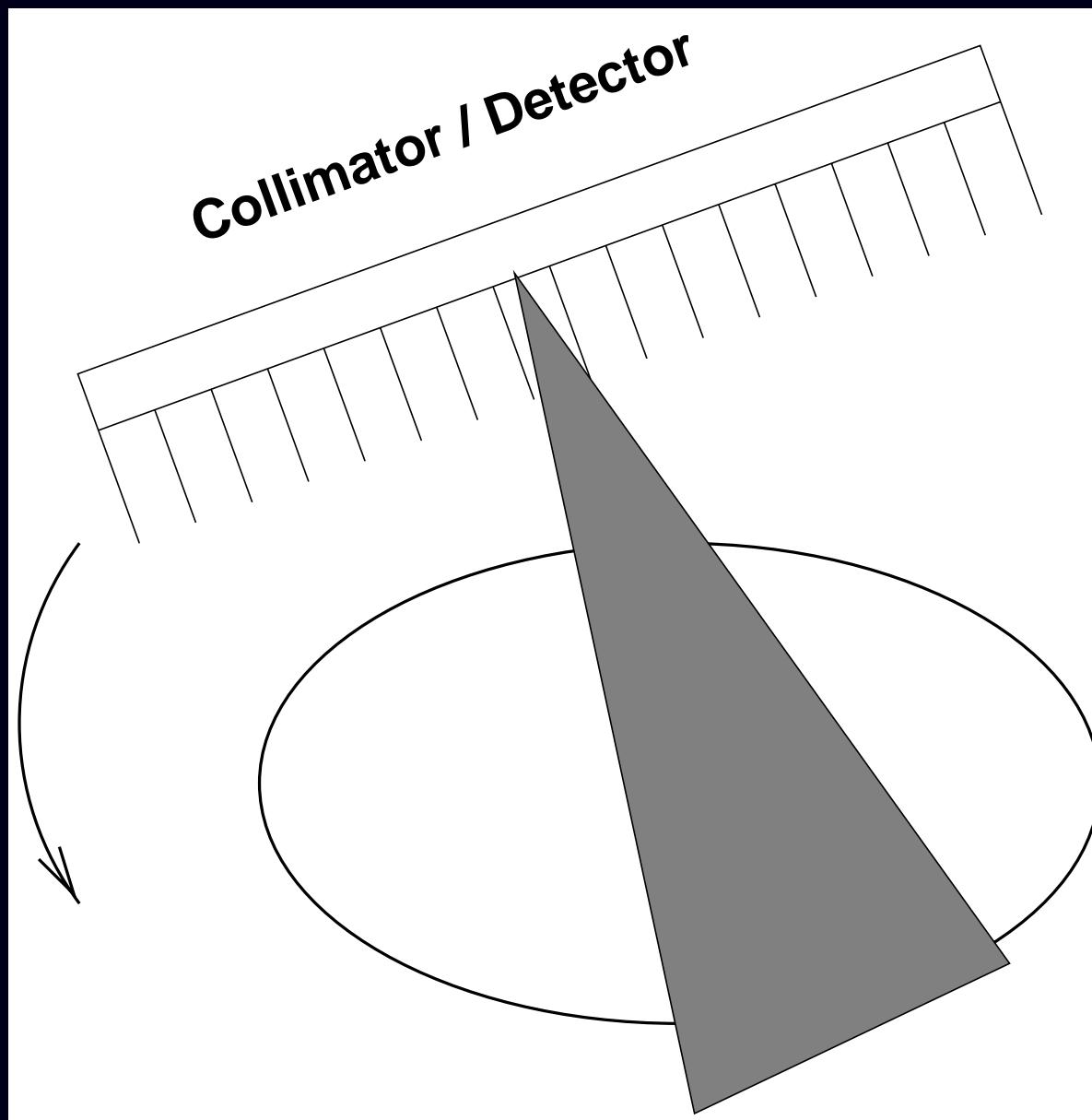
$$A \approx SG$$

(geometric projection followed by Gaussian smoothing)

- Symmetry
- Rotate and Sum
- Gaussian diffusion
for SPECT Gaussian detector response
- Correlated Monte Carlo (Beekman *et al.*)

In all cases, consistency of backprojector with A' requires care.

SPECT System Model



Complications: nonuniform attenuation, depth-dependent PSF, Compton scatter

Choice 3. Statistical Models

After modeling the system physics, we have a deterministic “model:”

$$y_i \approx g_i([\mathbf{A}\mathbf{x}]_i)$$

for some functions g_i , e.g., $g_i(l) = l + r_i$ for emission tomography.

Statistical modeling is concerned with the “ \approx ” aspect.

Considerations

- More accurate models:
 - can lead to lower variance images,
 - may incur additional computation,
 - may involve additional algorithm complexity
(e.g., proper transmission Poisson model has nonconcave log-likelihood)
- Statistical model errors (e.g., deadtime)
- Incorrect models (e.g., log-processed transmission data)

Statistical Model Choices for Emission Tomography

- “None.” Assume $\mathbf{y} - \mathbf{r} = \mathbf{Ax}$. “Solve algebraically” to find \mathbf{x} .
- White Gaussian noise. Ordinary least squares: minimize $\|\mathbf{y} - \mathbf{Ax}\|^2$
- Non-white Gaussian noise. Weighted least squares: minimize

$$\|\mathbf{y} - \mathbf{Ax}\|_W^2 = \sum_{i=1}^{n_d} w_i (y_i - [\mathbf{Ax}]_i)^2, \text{ where } [\mathbf{Ax}]_i \triangleq \sum_{j=1}^{n_p} a_{ij} x_j$$

(e.g., for Fourier rebinned (FORE) PET data)

- Ordinary Poisson model (ignoring or precorrecting for background)

$$y_i \sim \text{Poisson}\{[\mathbf{Ax}]_i\}$$

- Poisson model

$$y_i \sim \text{Poisson}\{[\mathbf{Ax}]_i + r_i\}$$

- Shifted Poisson model (for randoms precorrected PET)

$$y_i = y_i^{\text{prompt}} - y_i^{\text{delay}} \sim \text{Poisson}\{[\mathbf{Ax}]_i + 2r_i\} - 2r_i$$

Shifted Poisson model for PET

Precorrected random coincidences: $y_i = y_i^{\text{prompt}} - y_i^{\text{delay}}$

$$y_i^{\text{prompt}} \sim \text{Poisson}\{[\mathbf{Ax}]_i + r_i\}$$

$$y_i^{\text{delay}} \sim \text{Poisson}\{r_i\}$$

$$E[y_i] = [\mathbf{Ax}]_i$$

$$\text{Var}\{y_i\} = [\mathbf{Ax}]_i + 2r_i \quad \text{Mean} \neq \text{Variance} \Rightarrow \text{not Poisson!}$$

Statistical model choices

- Ordinary Poisson model: ignore randoms

$$[y_i]_+ \sim \text{Poisson}\{[\mathbf{Ax}]_i\}$$

Causes bias due to truncated negatives

- Data-weighted least-squares (Gaussian model):

$$y_i \sim N([\mathbf{Ax}]_i, \hat{\sigma}_i^2), \quad \hat{\sigma}_i^2 = \max(y_i + 2\hat{r}_i, \sigma_{\min}^2)$$

Causes bias due to data-weighting

- Shifted Poisson model (matches 2 moments):

$$[y_i + 2\hat{r}_i]_+ \sim \text{Poisson}\{[\mathbf{Ax}]_i + 2\hat{r}_i\}$$

Insensitive to inaccuracies in \hat{r}_i .

Shifted-Poisson Model for X-ray CT

Model with both photon variability and readout noise:

$$y_i \sim \text{Poisson}\{\bar{y}_i(\boldsymbol{\mu})\} + N(0, \sigma^2)$$

Shifted Poisson approximation

$$y_i + \sigma^2 \sim \text{Poisson}\{\bar{y}_i(\boldsymbol{\mu}) + \sigma^2\}$$

or just use WLS...

Complications:

- Intractability of likelihood for Poisson+Gaussian
- Compound Poisson distribution due to photon-energy-dependent detector signal.

X-ray statistical models is a current research area in several groups!

Choice 4. Cost Functions

Components:

- *Data-mismatch* term
- *Regularization* term (and regularization parameter β)
- Constraints (e.g., nonnegativity)

$$\Psi(\mathbf{x}) = \text{DataMismatch}(\mathbf{y}, \mathbf{A}\mathbf{x}) + \beta \cdot \text{Roughness}(\mathbf{x})$$

$$\hat{\mathbf{x}} \stackrel{\triangle}{=} \arg \min_{\mathbf{x} \geq 0} \Psi(\mathbf{x})$$

Actually *several* sub-choices to make for Choice 4 ...

Distinguishes “statistical methods” from “algebraic methods” for “ $\mathbf{y} = \mathbf{A}\mathbf{x}$.”

Why Cost Functions?

(vs “procedure” e.g., adaptive neural net with wavelet denoising)

Theoretical reasons

ML is based on minimizing a *cost function*: the negative log-likelihood

- ML is asymptotically consistent
- ML is asymptotically unbiased
- ML is asymptotically efficient (under true statistical model...)
- **Estimation**: Penalized-likelihood achieves uniform CR bound asymptotically
- **Detection**: Qi and Huesman showed analytically that MAP reconstruction outperforms FBP for SKE/BKE lesion detection (T-MI, Aug. 2001)

Practical reasons

- Stability of estimates (if Ψ and algorithm chosen properly)
- Predictability of properties (despite nonlinearities)
- Empirical evidence (?)

Bayesian Framework

Given a prior distribution $p(\mathbf{x})$ for image vectors \mathbf{x} , by Bayes' rule:

$$\text{posterior: } p(\mathbf{x}|\mathbf{y}) = p(\mathbf{y}|\mathbf{x})p(\mathbf{x})/p(\mathbf{y})$$

so

$$\log p(\mathbf{x}|\mathbf{y}) = \log p(\mathbf{y}|\mathbf{x}) + \log p(\mathbf{x}) - \log p(\mathbf{y})$$

- $-\log p(\mathbf{y}|\mathbf{x})$ corresponds to data mismatch term
- $-\log p(\mathbf{x})$ corresponds to regularizing penalty function

Maximum a posteriori (MAP) estimator:

$$\hat{\mathbf{x}} = \arg \max_{\mathbf{x}} \log p(\mathbf{x}|\mathbf{y})$$

- Has certain optimality properties (provided $p(\mathbf{y}|\mathbf{x})$ and $p(\mathbf{x})$ are correct).
- Same form as Ψ

Choice 4.1: Data-Mismatch Term

Options (for emission tomography):

- Negative log-likelihood of statistical model. Poisson *emission* case:

$$-L(\mathbf{x}; \mathbf{y}) = -\log p(\mathbf{y}|\mathbf{x}) = \sum_{i=1}^{n_d} ([\mathbf{Ax}]_i + r_i) - y_i \log([\mathbf{Ax}]_i + r_i) + \log y_i!$$

- Ordinary (unweighted) least squares: $\sum_{i=1}^{n_d} \frac{1}{2}(y_i - \hat{r}_i - [\mathbf{Ax}]_i)^2$
- Data-weighted least squares: $\sum_{i=1}^{n_d} \frac{1}{2}(y_i - \hat{r}_i - [\mathbf{Ax}]_i)^2 / \hat{\sigma}_i^2$, $\hat{\sigma}_i^2 = \max(y_i + \hat{r}_i, \sigma_{\min}^2)$, (causes bias due to data-weighting).
- Reweighted least-squares: $\hat{\sigma}_i^2 = [\mathbf{A}\hat{\mathbf{x}}]_i + \hat{r}_i$
- Model-weighted least-squares (nonquadratic, but convex!)

$$\sum_{i=1}^{n_d} \frac{1}{2}(y_i - \hat{r}_i - [\mathbf{Ax}]_i)^2 / ([\mathbf{Ax}]_i + \hat{r}_i)$$

- Nonquadratic cost-functions that are robust to outliers
- ...

Considerations

- Faithfulness to statistical model vs computation
- Ease of optimization (convex?, quadratic?)
- Effect of statistical modeling errors

Choice 4.2: Regularization

Forcing too much “data fit” gives noisy images

Ill-conditioned problems: small data noise causes large image noise

Solutions:

- Noise-reduction methods
- True regularization methods

Noise-reduction methods

- Modify the *data*
 - Prefilter or “denoise” the sinogram measurements
 - Extrapolate missing (e.g., truncated) data
- Modify an *algorithm* derived for an ill-conditioned problem
 - Stop algorithm before convergence
 - Run to convergence, post-filter
 - Toss in a filtering step every iteration or couple iterations
 - Modify update to “dampen” high-spatial frequencies [115]

Noise-Reduction vs True Regularization

Advantages of noise-reduction methods

- Simplicity (?)
- Familiarity
- Appear less subjective than using penalty functions or priors
- Only fiddle factors are # of iterations, amount of smoothing
- Resolution/noise tradeoff usually varies with iteration
(stop when image looks good - in principle)
- Changing post-smoothing does not require re-iterating

Advantages of true regularization methods

- Stability
- Faster convergence
- Predictability
- Resolution can be made object independent
- Controlled resolution (e.g., spatially uniform, edge preserving)
- Start with decent image (e.g., FBP) \Rightarrow reach solution faster.

True Regularization Methods

Redefine the *problem* to eliminate ill-conditioning,
rather than patching the data or algorithm!

- Use bigger pixels (fewer basis functions)
 - Visually unappealing
 - Can only preserve edges coincident with pixel edges
 - Results become even less invariant to translations
- Method of sieves (constrain image roughness)
 - Condition number for “pre-emission space” can be even worse
 - Lots of iterations
 - Commutability condition rarely holds exactly in practice
 - Degenerates to post-filtering in some cases
- Change *cost function* by adding a roughness penalty / prior
 - Disadvantage: apparently subjective choice of penalty
 - Apparent difficulty in choosing penalty parameters
(cf apodizing filter / cutoff frequency in FBP)

Penalty Function Considerations

- Computation
- Algorithm complexity
- Uniqueness of minimizer of $\Psi(x)$
- Resolution properties (edge preserving?)
- # of adjustable parameters
- Predictability of properties (resolution and noise)

Choices

- separable vs nonseparable
- quadratic vs nonquadratic
- convex vs nonconvex

Penalty Functions: Separable vs Nonseparable

Separable

- Identity norm: $R(\mathbf{x}) = \frac{1}{2}\mathbf{x}'\mathbf{I}\mathbf{x} = \sum_{j=1}^{n_p} x_j^2/2$
penalizes large values of \mathbf{x} , but causes “squashing bias”
- Entropy: $R(\mathbf{x}) = \sum_{j=1}^{n_p} x_j \log x_j$
- Gaussian prior with mean μ_j , variance σ_j^2 : $R(\mathbf{x}) = \sum_{j=1}^{n_p} \frac{(x_j - \mu_j)^2}{2\sigma_j^2}$
- Gamma prior $R(\mathbf{x}) = \sum_{j=1}^{n_p} p(x_j, \mu_j, \sigma_j)$ where $p(x, \mu, \sigma)$ is Gamma pdf

The first two basically keep pixel values from “blowing up.”

The last two encourage pixels values to be close to prior means μ_j .

$$\text{General separable form: } R(\mathbf{x}) = \sum_{j=1}^{n_p} f_j(x_j)$$

Simple, but these do not explicitly enforce smoothness.

Penalty Functions: Separable vs Nonseparable

Nonseparable (partially couple pixel values) to penalize *roughness*

x_1	x_2	x_3
x_4	x_5	

Example

$$R(\mathbf{x}) = (x_2 - x_1)^2 + (x_3 - x_2)^2 + (x_5 - x_4)^2 + (x_4 - x_1)^2 + (x_5 - x_2)^2$$

2	2	2
2	1	

$$R(\mathbf{x}) = 1$$

3	3	1
2	2	

$$R(\mathbf{x}) = 6$$

1	3	1
2	2	

$$R(\mathbf{x}) = 10$$

Rougher images \Rightarrow greater $R(\mathbf{x})$

Roughness Penalty Functions

First-order neighborhood and pairwise pixel differences:

$$R(\mathbf{x}) = \sum_{j=1}^{n_p} \frac{1}{2} \sum_{k \in N_j} \psi(x_j - x_k)$$

$N_j \triangleq$ neighborhood of j th pixel (e.g., left, right, up, down)

ψ called the *potential function*

Finite-difference approximation to continuous roughness measure:

$$R(f(\cdot)) = \int \|\nabla f(\vec{r})\|^2 d\vec{r} = \int \left| \frac{\partial}{\partial x} f(\vec{r}) \right|^2 + \left| \frac{\partial}{\partial y} f(\vec{r}) \right|^2 + \left| \frac{\partial}{\partial z} f(\vec{r}) \right|^2 d\vec{r}.$$

Second derivatives also useful:
(More choices!)

$$\left. \frac{\partial^2}{\partial x^2} f(\vec{r}) \right|_{\vec{r}=\vec{r}_j} \approx f(\vec{r}_{j+1}) - 2f(\vec{r}_j) + f(\vec{r}_{j-1})$$

$$R(\mathbf{x}) = \sum_{j=1}^{n_p} \psi(x_{j+1} - 2x_j + x_{j-1}) + \dots$$

Penalty Functions: General Form

$$R(\mathbf{x}) = \sum_k \psi_k([C\mathbf{x}]_k) \quad \text{where} \quad [C\mathbf{x}]_k = \sum_{j=1}^{n_p} c_{kj} x_j$$

Example:

x_1	x_2	x_3
x_4	x_5	

$$C\mathbf{x} = \begin{bmatrix} -1 & 1 & 0 & 0 & 0 \\ 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 \\ -1 & 0 & 0 & 1 & 0 \\ 0 & -1 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \end{bmatrix} = \begin{bmatrix} x_2 - x_1 \\ x_3 - x_2 \\ x_5 - x_4 \\ x_4 - x_1 \\ x_5 - x_2 \end{bmatrix}$$

$$R(\mathbf{x}) = \sum_{k=1}^5 \psi_k([C\mathbf{x}]_k) = \psi_1(x_2 - x_1) + \psi_2(x_3 - x_2) + \psi_3(x_5 - x_4) + \psi_4(x_4 - x_1) + \psi_5(x_5 - x_2)$$

Penalty Functions: Quadratic vs Nonquadratic

$$R(\mathbf{x}) = \sum_k \psi_k([\mathbf{C}\mathbf{x}]_k)$$

Quadratic ψ_k

If $\psi_k(t) = t^2/2$, then $R(\mathbf{x}) = \frac{1}{2}\mathbf{x}'\mathbf{C}'\mathbf{C}\mathbf{x}$, a quadratic form.

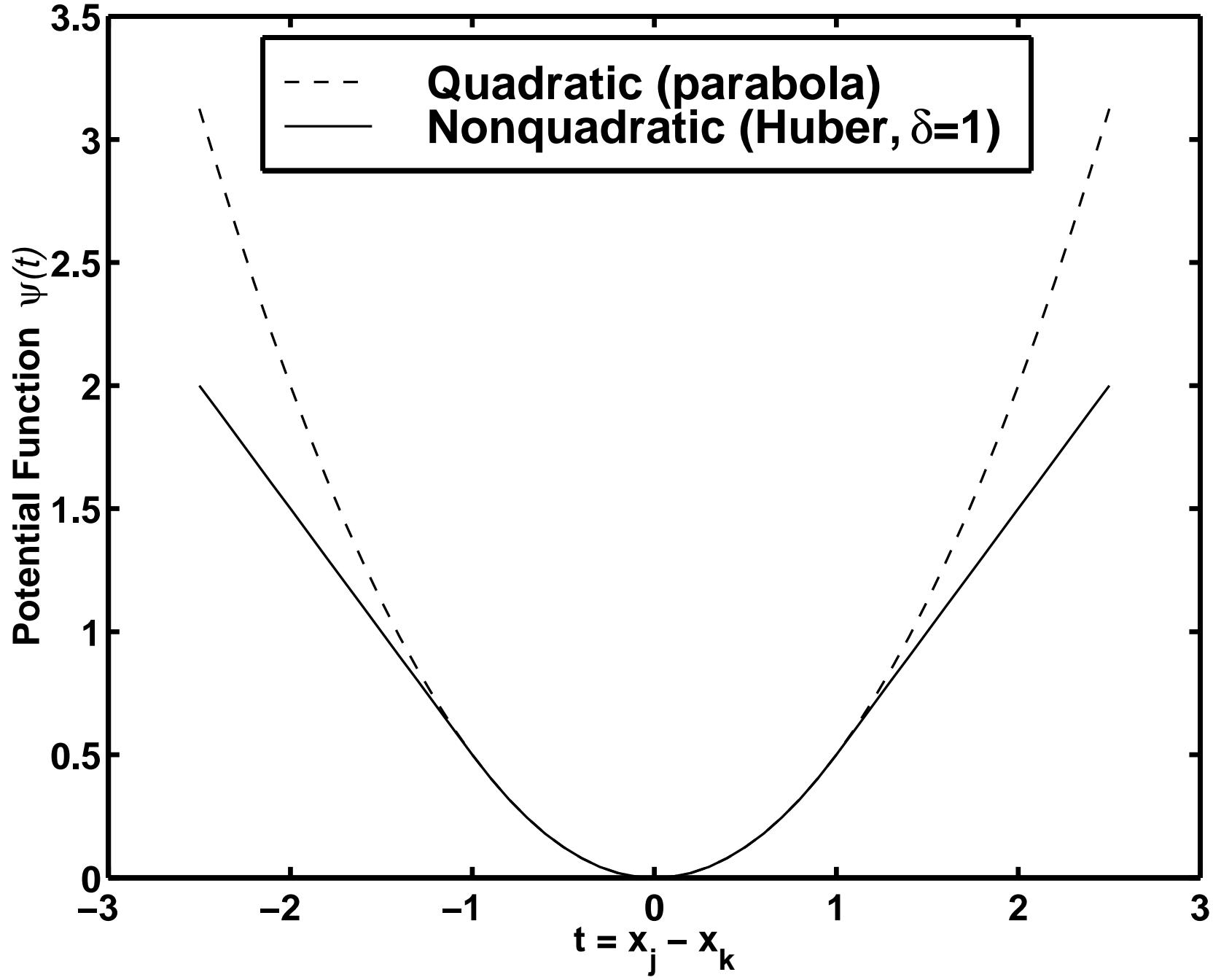
- Simpler optimization
- Global smoothing

Nonquadratic ψ_k

- Edge preserving
- More complicated optimization. (This is essentially solved in convex case.)
- Unusual noise properties
- Analysis/prediction of resolution and noise properties is difficult
- More adjustable parameters (e.g., δ)

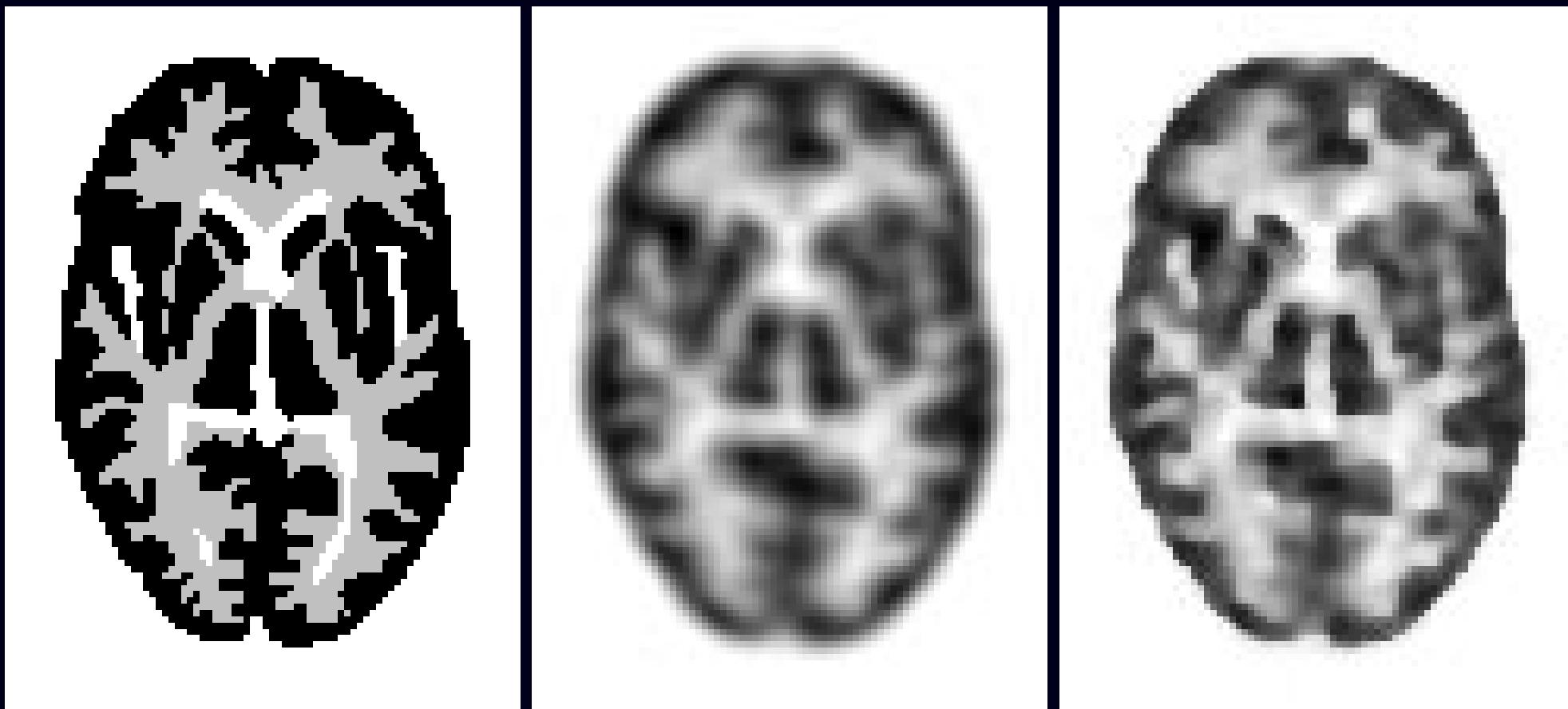
Example: Huber function. $\psi(t) \triangleq \begin{cases} t^2/2, & |t| \leq \delta \\ \delta|t| - \delta^2/2, & |t| > \delta \end{cases}$

Quadratic vs Nonquadratic Potential Functions



Lower cost for large differences \Rightarrow edge preservation

Edge-Preserving Reconstruction Example



Phantom

Quadratic Penalty

Huber Penalty

A transmission example would be preferable...

Penalty Functions: Convex vs Nonconvex

Convex

- Easier to optimize
- Guaranteed unique minimizer of Ψ (for convex negative log-likelihood)

Nonconvex

- Greater degree of edge preservation
- Nice images for piecewise-constant phantoms!
- Even more unusual noise properties
- Multiple extrema
- More complicated optimization (simulated / deterministic annealing)
- Estimator \hat{x} becomes a discontinuous function of data \mathbf{Y}

Nonconvex examples

- “broken parabola”

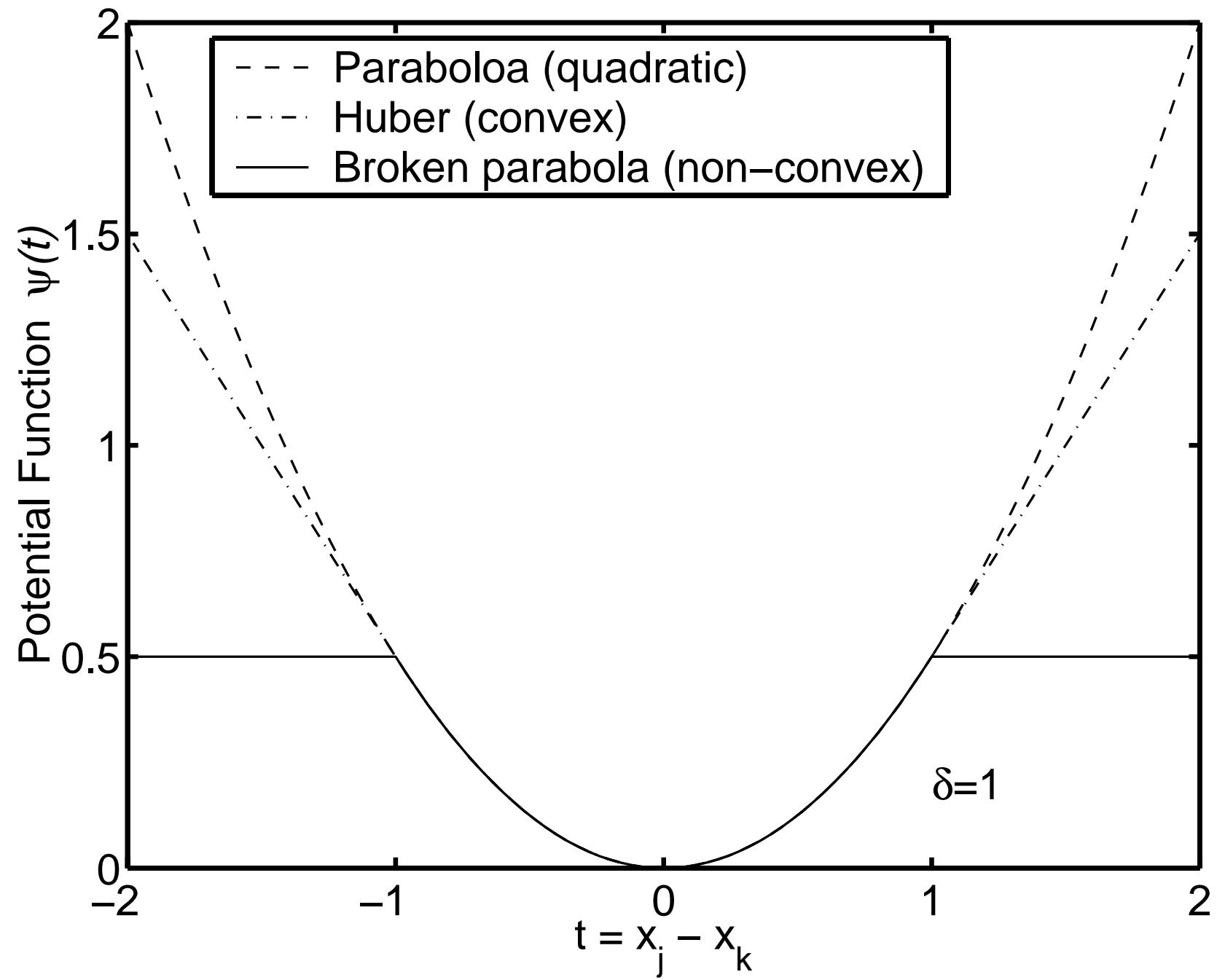
$$\psi(t) = \min(t^2, t_{\max}^2)$$

- true median root prior:

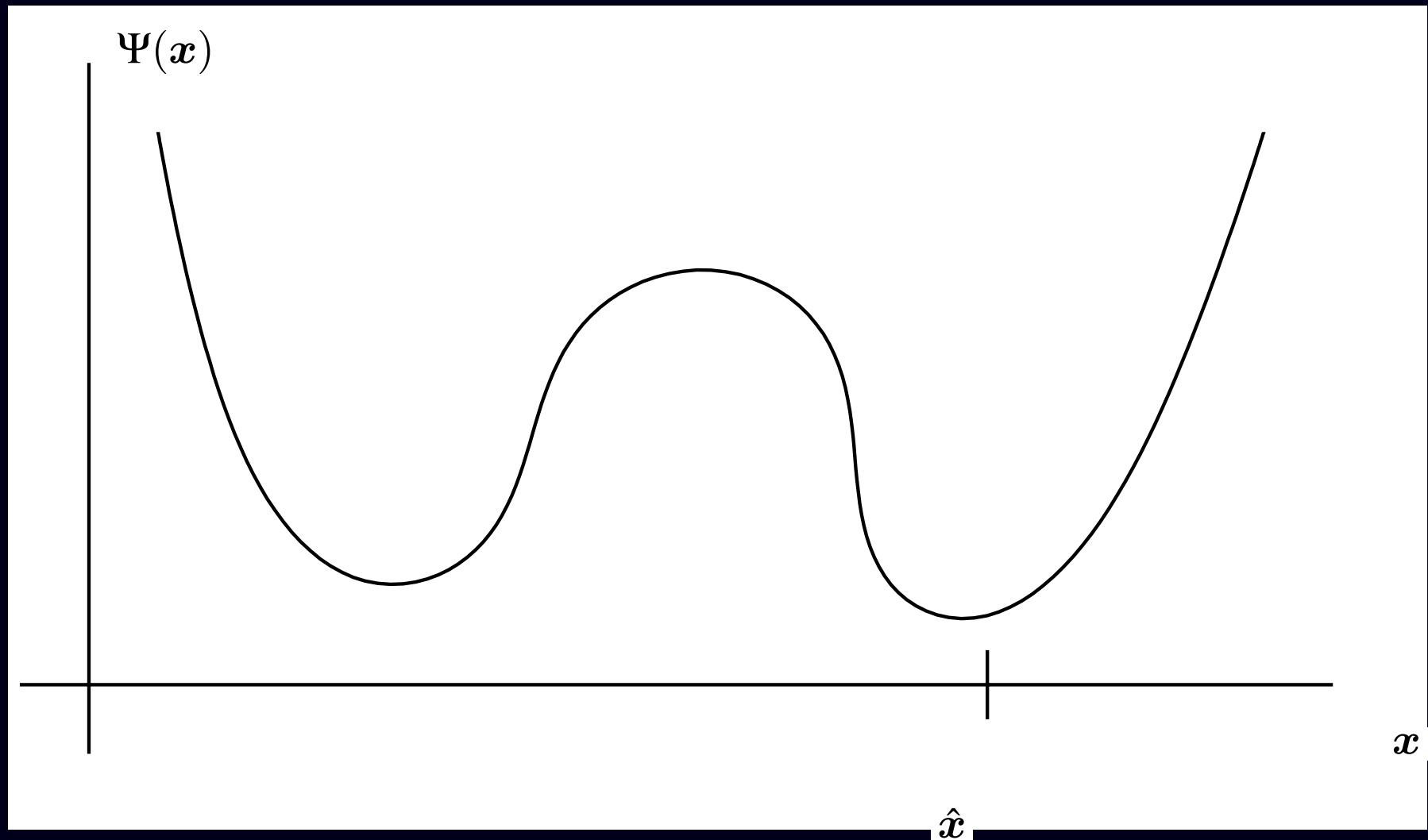
$$R(\mathbf{x}) = \sum_{j=1}^{n_p} \frac{(x_j - \text{median}_j(\mathbf{x}))^2}{\text{median}_j(\mathbf{x})} \quad \text{where } \text{median}_j(\mathbf{x}) \text{ is local median}$$

Exception: orthonormal wavelet threshold *denoising* via nonconvex potentials!

Potential Functions



Local Extrema and Discontinuous Estimators



Small change in data \Rightarrow large change in minimizer \hat{x} .
Using convex penalty functions obviates this problem.

Augmented Regularization Functions

Replace roughness penalty $R(\mathbf{x})$ with $R(\mathbf{x}|\mathbf{b}) + \alpha R(\mathbf{b})$,
where the elements of \mathbf{b} (often binary) indicate boundary locations.

- Line-site methods
- Level-set methods

Joint estimation problem:

$$(\hat{\mathbf{x}}, \hat{\mathbf{b}}) = \arg \min_{\mathbf{x}, \mathbf{b}} \Psi(\mathbf{x}, \mathbf{b}), \quad \Psi(\mathbf{x}, \mathbf{b}) = -L(\mathbf{x}; \mathbf{y}) + \beta R(\mathbf{x}|\mathbf{b}) + \alpha R(\mathbf{b}).$$

Example: b_{jk} indicates the presence of edge between pixels j and k :

$$R(\mathbf{x}|\mathbf{b}) = \sum_{j=1}^{n_p} \sum_{k \in N_j} (1 - b_{jk}) \frac{1}{2} (x_j - x_k)^2$$

Penalty to discourage too many edges (e.g.):

$$R(\mathbf{b}) = \sum_{jk} b_{jk}.$$

- Can encourage local edge continuity
- Require annealing methods for minimization

Modified Penalty Functions

$$R(\mathbf{x}) = \sum_{j=1}^{n_p} \frac{1}{2} \sum_{k \in N_j} w_{jk} \psi(x_j - x_k)$$

Adjust weights $\{w_{jk}\}$ to

- Control resolution properties
- Incorporate anatomical side information (MR/CT)
(avoid smoothing across anatomical boundaries)

Recommendations

- Emission tomography:
 - begin with quadratic (nonseparable) penalty functions
 - Consider modified penalty for resolution control and choice of β
 - Use modest regularization and post-filter more if desired
- Transmission tomography (attenuation maps), X-ray CT
 - consider convex nonquadratic (*e.g.*, Huber) penalty functions
 - choose δ based on attenuation map **units** (water, bone, etc.)
 - choice of regularization parameter β remains nontrivial,
learn appropriate values by experience for given study type

Choice 4.3: Constraints

- Nonnegativity
- Known support
- Count preserving
- Upper bounds on values
 - e.g., maximum μ of attenuation map in transmission case

Considerations

- Algorithm complexity
- Computation
- Convergence rate
- Bias (in low-count regions)
- ...

Open Problems

Modeling

- Noise in a_{ij} 's (system model errors)
- Noise in \hat{r}_i 's (estimates of scatter / randoms)
- Statistics of corrected measurements
- Statistics of measurements with deadtime losses

Cost functions

- Performance prediction for nonquadratic penalties
- Effect of nonquadratic penalties on detection tasks
- Choice of regularization parameters for nonquadratic regularization

Summary

- 1. Object parameterization: function $f(\vec{r})$ vs vector x
- 2. System physical model: $s_i(x)$
- 3. Measurement statistical model $Y_i \sim [?]$
- 4. Cost function: data-mismatch / regularization / constraints

Reconstruction Method = Cost Function + Algorithm

Naming convention:

- ML-EM, MAP-OSL, PL-SAGE, PWLS+SOR, PWLS-CG, ...

Part 3. Algorithms

Method = Cost Function + Algorithm

Outline

- Ideal algorithm
- Classical general-purpose algorithms
- Considerations:
 - nonnegativity
 - parallelization
 - convergence rate
 - monotonicity
- Algorithms tailored to *cost functions* for imaging
 - Optimization transfer
 - EM-type methods
 - Poisson emission problem
 - Poisson transmission problem
- Ordered-subsets / block-iterative algorithms

Why iterative algorithms?

- For nonquadratic Ψ , no closed-form solution for minimizer.
- For quadratic Ψ with nonnegativity constraints, no closed-form solution.
- For quadratic Ψ without constraints, closed-form solutions:

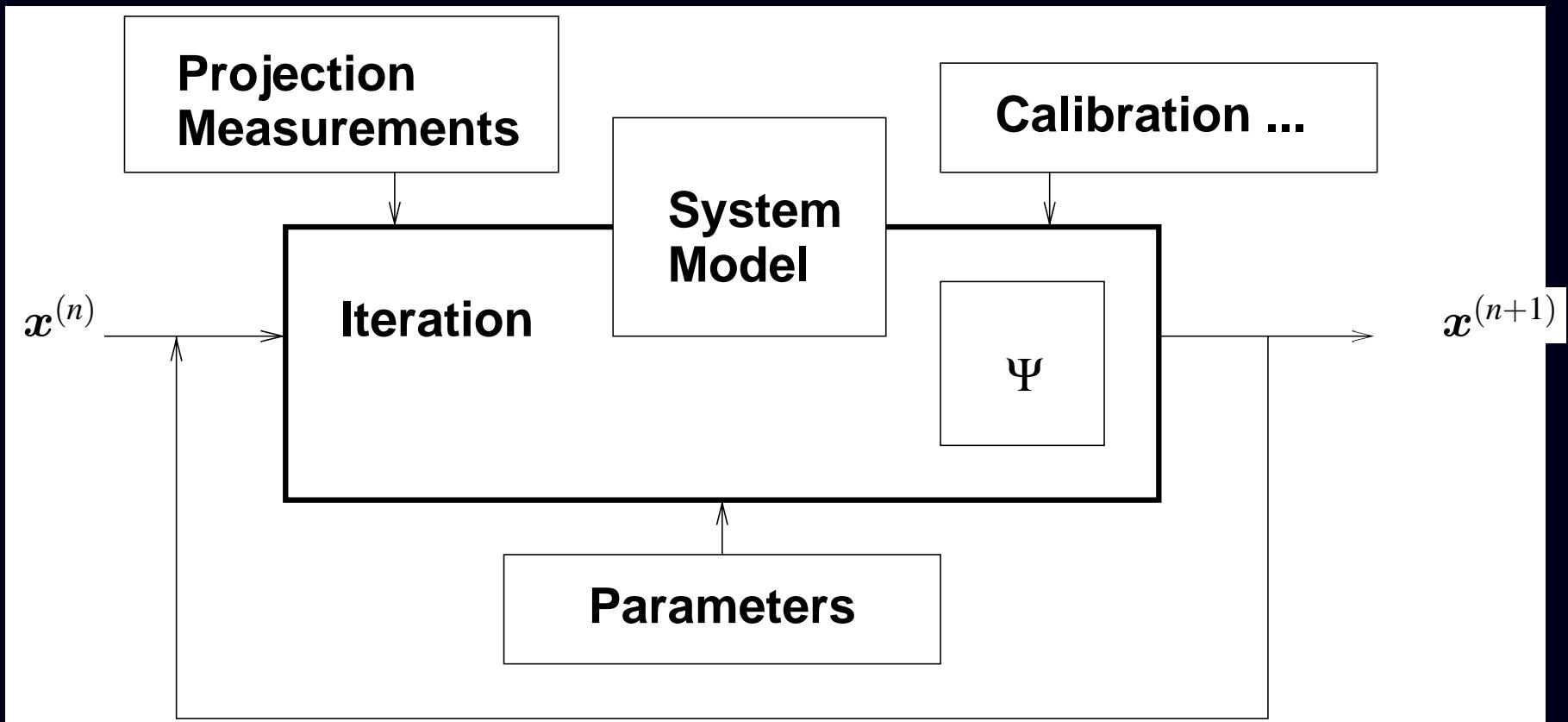
$$\text{PWLS: } \hat{\mathbf{x}} = [\mathbf{A}'\mathbf{W}\mathbf{A} + \mathbf{R}]^{-1}\mathbf{A}'\mathbf{W}\mathbf{y}$$

$$\text{OLS: } \hat{\mathbf{x}} = [\mathbf{A}'\mathbf{A}]^{-1}\mathbf{A}'\mathbf{y}$$

Impractical (memory and computation) for realistic problem sizes.
 \mathbf{A} is sparse, but $\mathbf{A}'\mathbf{A}$ is not.

All algorithms are imperfect. No single best solution.

General Iteration



Deterministic iterative mapping: $x^{(n+1)} = M(x^{(n)})$

Ideal Algorithm

$$\boldsymbol{x}^* \triangleq \arg \min_{\boldsymbol{x} \geq 0} \Psi(\boldsymbol{x}) \quad (\text{global minimizer})$$

Properties

stable and convergent
converges quickly
globally convergent
fast
robust
user friendly

parallelizable
simple
flexible
(matrix stored by row or column or projector/backprojector)
(when necessary)
easy to program and debug
accommodates any type of system model

Choices: forgo one or more of the above

Classic Algorithms

Non-gradient based

- Exhaustive search
- Nelder-Mead simplex (amoeba)

Converge very slowly, but work with nondifferentiable *cost functions*.

Gradient based

- Gradient descent

$$\boldsymbol{x}^{(n+1)} \triangleq \boldsymbol{x}^{(n)} - \alpha \nabla \Psi(\boldsymbol{x}^{(n)})$$

Choosing α to ensure convergence is nontrivial.

- Steepest descent

$$\boldsymbol{x}^{(n+1)} \triangleq \boldsymbol{x}^{(n)} - \alpha_n \nabla \Psi(\boldsymbol{x}^{(n)}) \text{ where } \alpha_n \triangleq \arg \min_{\alpha} \Psi\left(\boldsymbol{x}^{(n)} - \alpha \nabla \Psi(\boldsymbol{x}^{(n)})\right)$$

Computing α_n can be expensive.

Limitations

- Converge slowly.
- Do not easily accommodate nonnegativity constraint.

Gradients & Nonnegativity - A Mixed Blessing

Unconstrained optimization of differentiable *cost functions*:

$$\nabla \Psi(\mathbf{x}) = \mathbf{0} \text{ when } \mathbf{x} = \mathbf{x}^*$$

- A necessary condition always.
- A sufficient condition for strictly convex *cost functions*.
- Iterations search for zero of gradient.

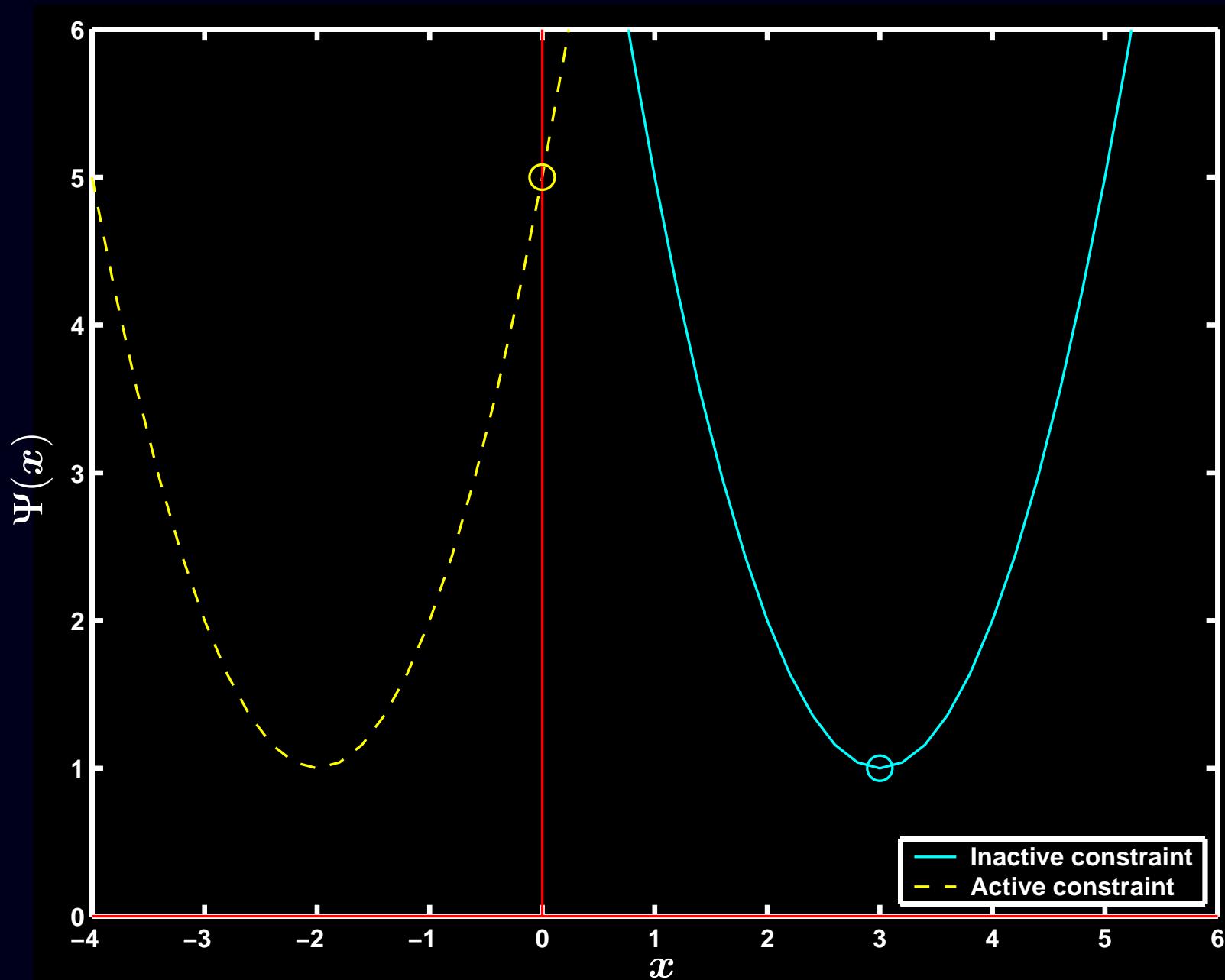
Nonnegativity-constrained minimization:

Karush-Kuhn-Tucker conditions

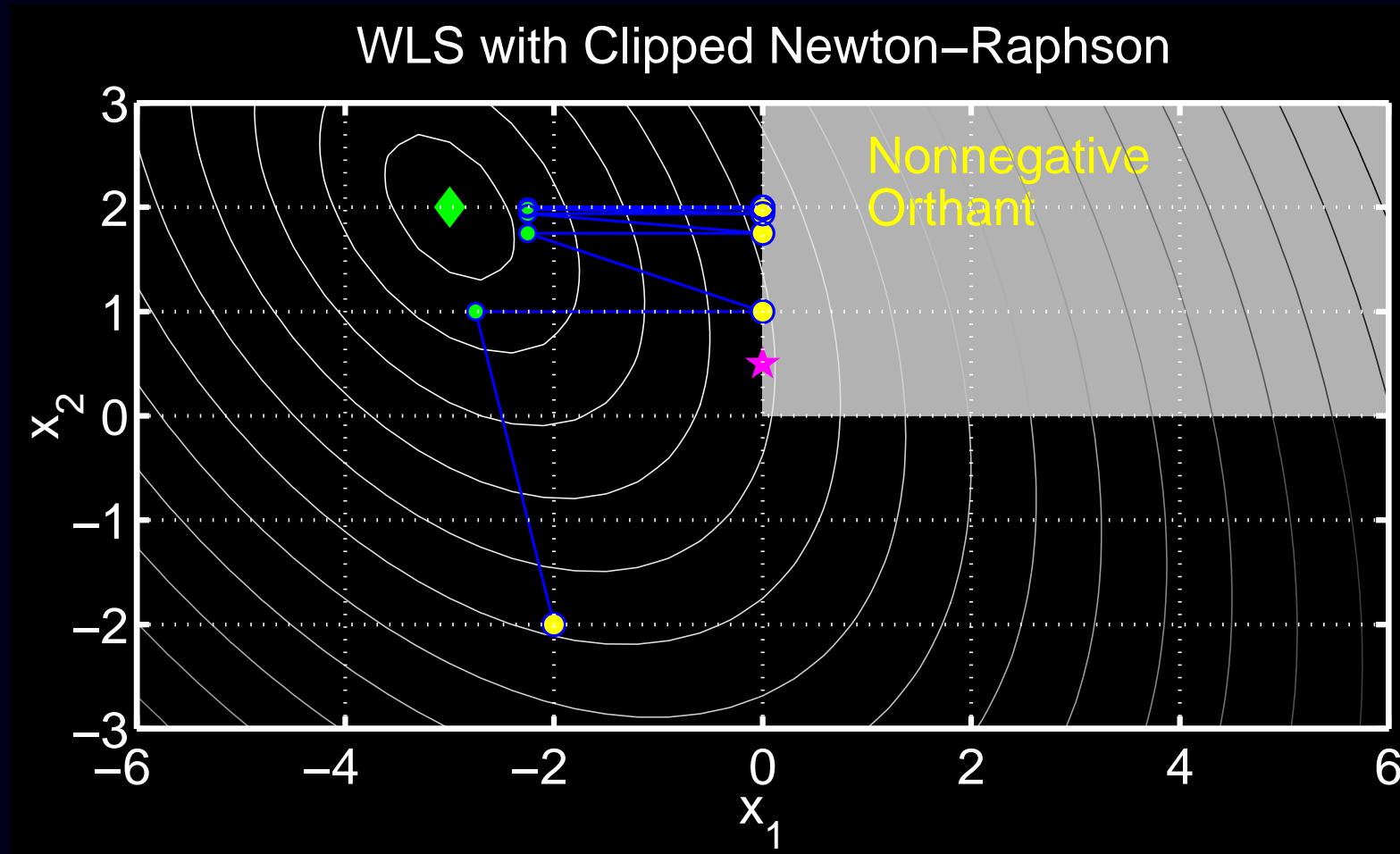
$$\left. \frac{\partial}{\partial x_j} \Psi(\mathbf{x}) \right|_{\mathbf{x}=\mathbf{x}^*} \text{ is } \begin{cases} = 0, & x_j^* > 0 \\ \geq 0, & x_j^* = 0 \end{cases}$$

- A necessary condition always.
- A sufficient condition for strictly convex *cost functions*.
- Iterations search for ???
- $0 = x_j^* \frac{\partial}{\partial x_j} \Psi(\mathbf{x}^*)$ is a necessary condition, but never sufficient condition.

Karush-Kuhn-Tucker Illustrated



Why Not Clip Negatives?



Newton-Raphson with negatives set to zero each iteration.
Fixed-point of iteration is not the constrained minimizer!

Newton-Raphson Algorithm

$$\boxed{\boldsymbol{x}^{(n+1)} = \boldsymbol{x}^{(n)} - [\nabla^2 \Psi(\boldsymbol{x}^{(n)})]^{-1} \nabla \Psi(\boldsymbol{x}^{(n)})}$$

Advantage:

- Super-linear convergence rate (if convergent)

Disadvantages:

- Requires twice-differentiable Ψ
- Not guaranteed to converge
- Not guaranteed to monotonically decrease Ψ
- Does not enforce nonnegativity constraint
- Impractical for image recovery due to matrix inverse

General purpose remedy: bound-constrained Quasi-Newton algorithms

Newton's Quadratic Approximation

2nd-order Taylor series:

$$\Psi(\mathbf{x}) \approx \phi(\mathbf{x}; \mathbf{x}^{(n)}) \triangleq \Psi(\mathbf{x}^{(n)}) + \nabla \Psi(\mathbf{x}^{(n)})(\mathbf{x} - \mathbf{x}^{(n)}) + \frac{1}{2}(\mathbf{x} - \mathbf{x}^{(n)})^T \nabla^2 \Psi(\mathbf{x}^{(n)}) (\mathbf{x} - \mathbf{x}^{(n)})$$

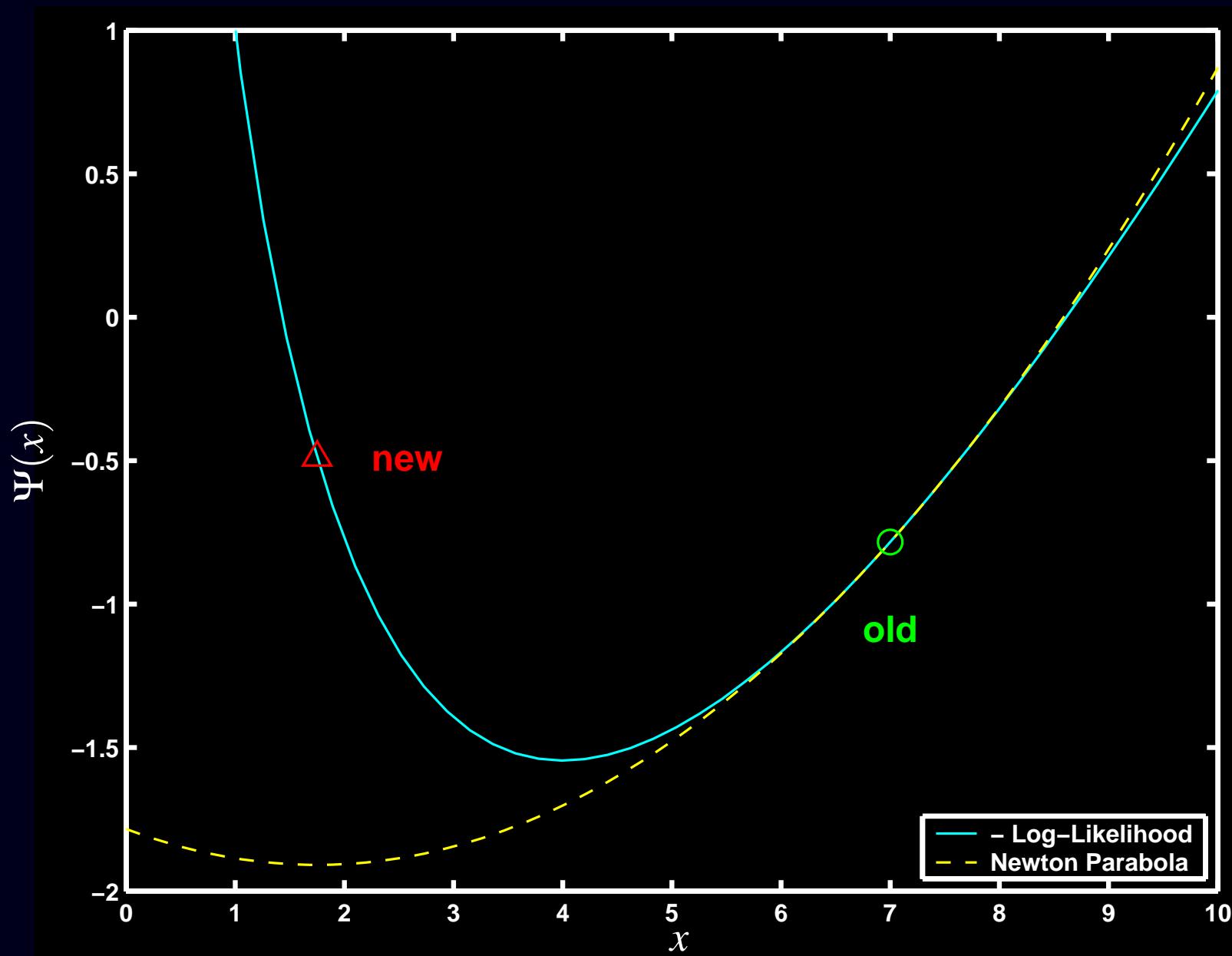
Set $\mathbf{x}^{(n+1)}$ to the ("easily" found) minimizer of this quadratic approximation:

$$\begin{aligned}\mathbf{x}^{(n+1)} &\triangleq \arg \min_{\mathbf{x}} \phi(\mathbf{x}; \mathbf{x}^{(n)}) \\ &= \mathbf{x}^{(n)} - [\nabla^2 \Psi(\mathbf{x}^{(n)})]^{-1} \nabla \Psi(\mathbf{x}^{(n)})\end{aligned}$$

Can be nonmonotone for Poisson emission tomography log-likelihood, even for a single pixel and single ray:

$$\Psi(x) = (x + r) - y \log(x + r)$$

Nonmonotonicity of Newton-Raphson



Consideration: Monotonicity

An algorithm is monotonic if

$$\Psi(\mathbf{x}^{(n+1)}) \leq \Psi(\mathbf{x}^{(n)}), \quad \forall \mathbf{x}^{(n)}.$$

Three categories of algorithms:

- Nonmonotonic (or unknown)
- Forced monotonic (e.g., by line search)
- **Intrinsically monotonic** (by design, simplest to implement)

Forced monotonicity

Most nonmonotonic algorithms can be converted to forced monotonic algorithms by adding a line-search step:

$$\mathbf{x}^{\text{temp}} \triangleq M(\mathbf{x}^{(n)}), \quad \mathbf{d} = \mathbf{x}^{\text{temp}} - \mathbf{x}^{(n)}$$

$$\mathbf{x}^{(n+1)} \triangleq \mathbf{x}^{(n)} - \alpha_n \mathbf{d}^{(n)} \quad \text{where} \quad \alpha_n \triangleq \arg \min_{\alpha} \Psi\left(\mathbf{x}^{(n)} - \alpha \mathbf{d}^{(n)}\right)$$

Inconvenient, sometimes expensive, nonnegativity problematic.

Conjugate Gradient Algorithm

Advantages:

- Fast converging (if suitably preconditioned) (in unconstrained case)
- Monotonic (forced by line search in nonquadratic case)
- Global convergence (unconstrained case)
- Flexible use of system matrix A and tricks
- Easy to implement in unconstrained quadratic case
- Highly parallelizable

Disadvantages:

- Nonnegativity constraint awkward (slows convergence?)
- Line-search awkward in nonquadratic cases

Highly recommended for unconstrained quadratic problems (e.g., PWLS without nonnegativity). Useful (but perhaps not ideal) for Poisson case too.

Consideration: Parallelization

Simultaneous (fully parallelizable)

update all pixels simultaneously using all data

EM, Conjugate gradient, ISRA, OSL, SIRT, MART, ...

Block iterative (ordered subsets)

update (nearly) all pixels using one subset of the data at a time

OSEM, RBBI, ...

Row action

update many pixels using a single ray at a time

ART, RAMLA

Pixel grouped (multiple column action)

update some (but not all) pixels simultaneously a time, using all data

Grouped coordinate descent, multi-pixel SAGE

(Perhaps the most nontrivial to implement)

Sequential (column action)

update one pixel at a time, using all (relevant) data

Coordinate descent, SAGE

Coordinate Descent Algorithm

aka Gauss-Siedel, successive over-relaxation (SOR), iterated conditional modes (ICM)

Update one pixel at a time, holding others fixed to their most recent values:

$$x_j^{\text{new}} = \arg \min_{x_j \geq 0} \Psi(x_1^{\text{new}}, \dots, x_{j-1}^{\text{new}}, x_j, x_{j+1}^{\text{old}}, \dots, x_{n_p}^{\text{old}}), \quad j = 1, \dots, n_p$$

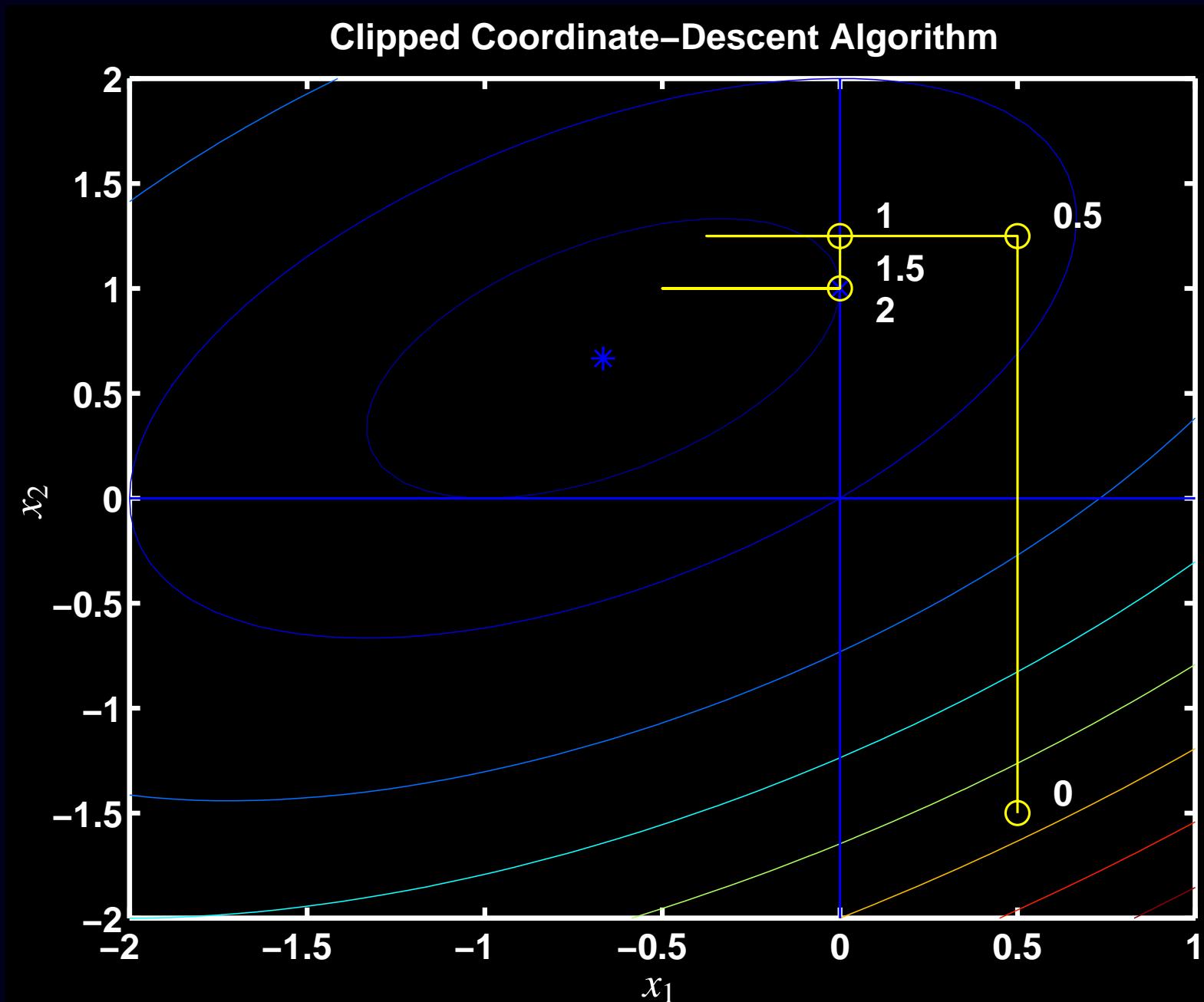
Advantages:

- Intrinsically monotonic
- Fast converging (from good initial image)
- Global convergence
- Nonnegativity constraint trivial

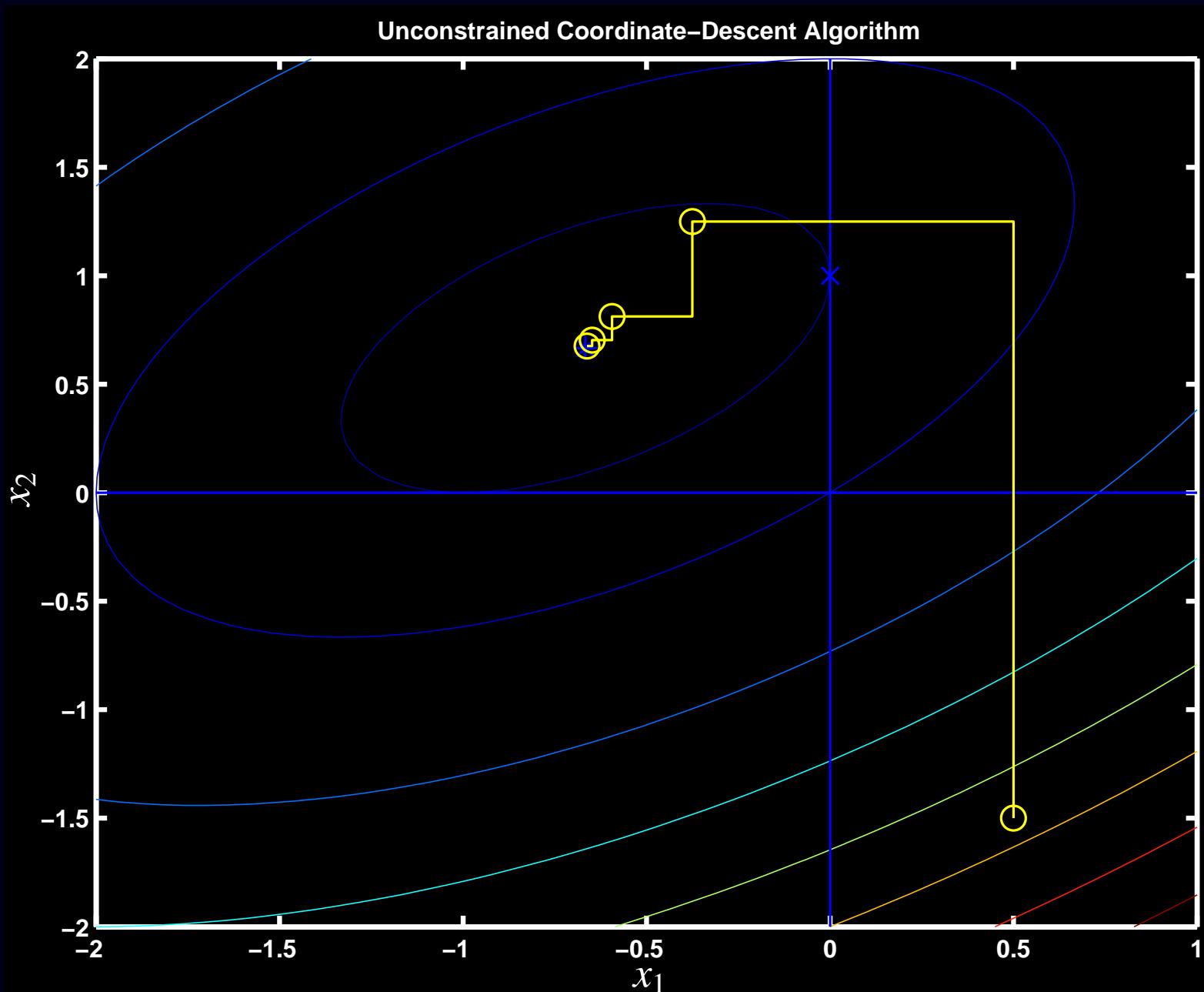
Disadvantages:

- Requires column access of system matrix A
- Cannot exploit some “tricks” for A
- Expensive “arg min” for nonquadratic problems
- Poorly parallelizable

Constrained Coordinate Descent Illustrated



Coordinate Descent - Unconstrained



Coordinate-Descent Algorithm Summary

Recommended when all of the following apply:

- quadratic or nearly-quadratic convex *cost function*
- nonnegativity constraint desired
- precomputed and stored system matrix A with column access
- parallelization not needed (standard workstation)

Cautions:

- Good initialization (e.g., properly scaled FBP) essential.
(Uniform image or zero image cause slow initial convergence.)
- Must be programmed carefully to be efficient.
(Standard Gauss-Siedel implementation is suboptimal.)
- Updates high-frequencies fastest \Rightarrow poorly suited to unregularized case

Used daily in UM clinic for 2D SPECT / PWLS / nonuniform attenuation

Summary of General-Purpose Algorithms

Gradient-based

- Fully parallelizable
- Inconvenient line-searches for nonquadratic *cost functions*
- Fast converging in unconstrained case
- Nonnegativity constraint inconvenient

Coordinate-descent

- Very fast converging
- Nonnegativity constraint trivial
- Poorly parallelizable
- Requires precomputed/stored system matrix

CD is well-suited to moderate-sized 2D problem (e.g., 2D PET),
but poorly suited to large 2D problems (X-ray CT) and fully 3D problems

Neither is ideal.

.: need *special-purpose algorithms* for image reconstruction!

Data-Mismatch Functions Revisited

For fast converging, intrinsically monotone algorithms, consider the form of Ψ .

WLS:

$$-L(\mathbf{x}) = \sum_{i=1}^{n_d} \frac{1}{2} w_i (y_i - [\mathbf{Ax}]_i)^2 = \sum_{i=1}^{n_d} h_i([\mathbf{Ax}]_i), \quad \text{where } h_i(l) \triangleq \frac{1}{2} w_i (y_i - l)^2.$$

Emission Poisson log-likelihood:

$$-L(\mathbf{x}) = \sum_{i=1}^{n_d} ([\mathbf{Ax}]_i + r_i) - y_i \log([\mathbf{Ax}]_i + r_i) = \sum_{i=1}^{n_d} h_i([\mathbf{Ax}]_i)$$

where $h_i(l) \triangleq (l + r_i) - y_i \log(l + r_i)$.

Transmission Poisson log-likelihood:

$$-L(\mathbf{x}) = \sum_{i=1}^{n_d} \left(b_i e^{-[\mathbf{Ax}]_i} + r_i \right) - y_i \log \left(b_i e^{-[\mathbf{Ax}]_i} + r_i \right) = \sum_{i=1}^{n_d} h_i([\mathbf{Ax}]_i)$$

where $h_i(l) \triangleq (b_i e^{-l} + r_i) - y_i \log(b_i e^{-l} + r_i)$.

MRI, polyenergetic X-ray CT, confocal microscopy, image restoration, ...
All have same *partially separable* form.

General Imaging Cost Function

General form for data-mismatch function:

$$-L(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{A}\mathbf{x}]_i)$$

General form for regularizing penalty function:

$$R(\mathbf{x}) = \sum_k \psi_k([\mathbf{C}\mathbf{x}]_k)$$

General form for *cost function*:

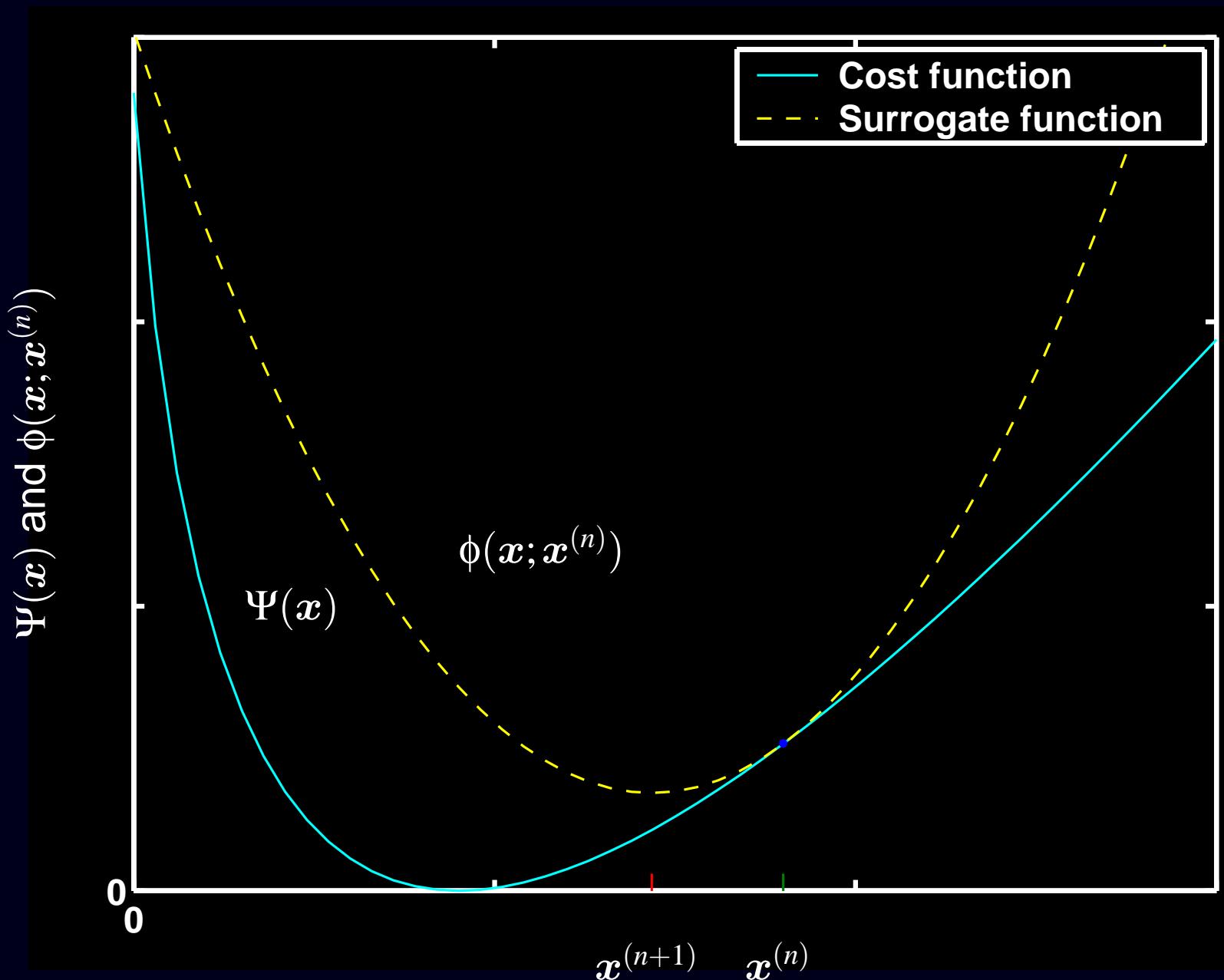
$$\boxed{\Psi(\mathbf{x}) = -L(\mathbf{x}) + \beta R(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{A}\mathbf{x}]_i) + \beta \sum_k \psi_k([\mathbf{C}\mathbf{x}]_k)}$$

Properties of Ψ we can exploit:

- summation form (due to independence of measurements)
- convexity of h_i functions (usually)
- summation argument (inner product of \mathbf{x} with i th row of \mathbf{A})

Most methods that use these properties are forms of *optimization transfer*.

Optimization Transfer Illustrated



Optimization Transfer

General iteration:

$$\boxed{\boldsymbol{x}^{(n+1)} = \arg \min_{\boldsymbol{x} \geq 0} \phi(\boldsymbol{x}; \boldsymbol{x}^{(n)})}$$

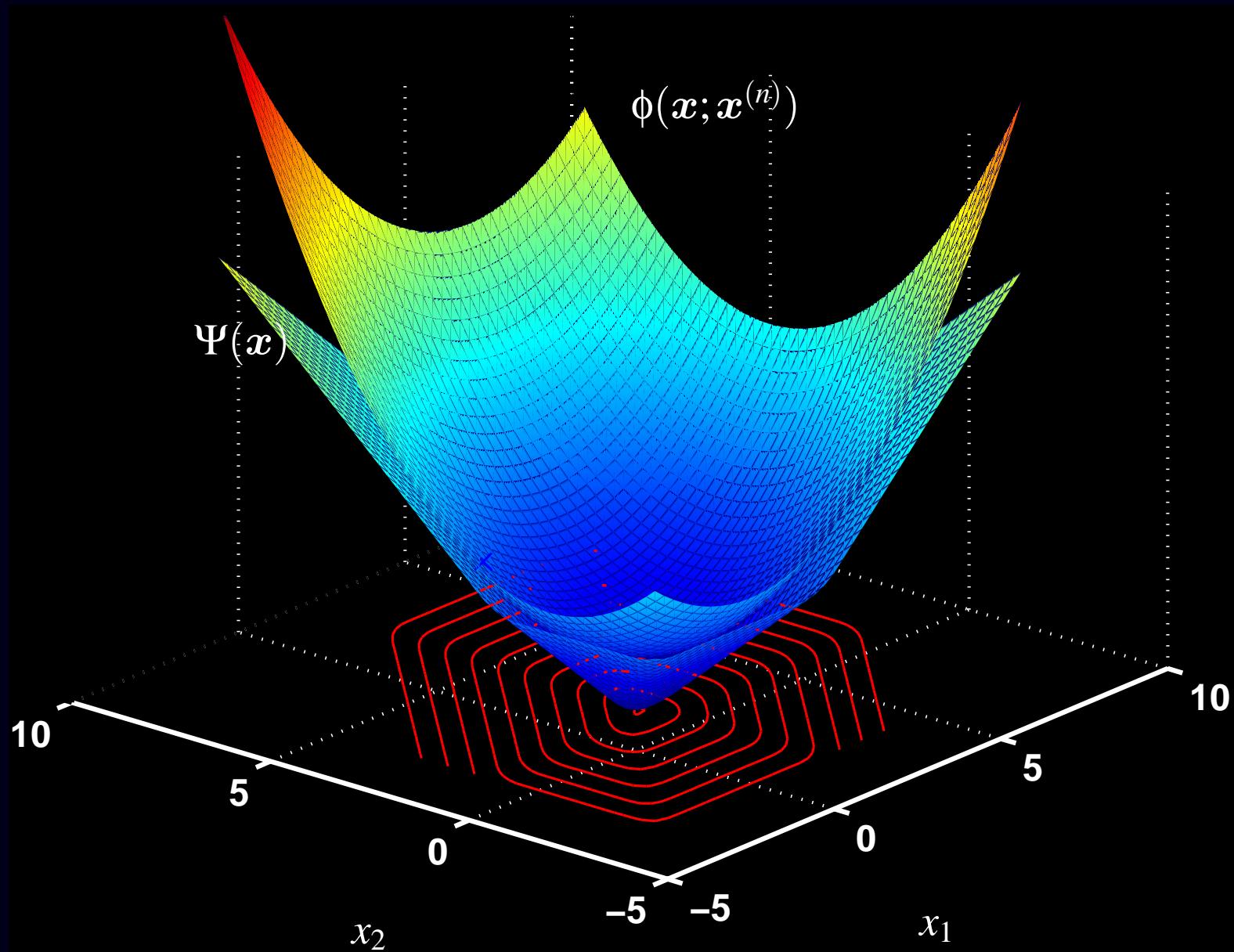
Monotonicity conditions (Ψ decreases provided these hold):

- $\phi(\boldsymbol{x}^{(n)}; \boldsymbol{x}^{(n)}) = \Psi(\boldsymbol{x}^{(n)})$ (matched current value)
- $\nabla_{\boldsymbol{x}} \phi(\boldsymbol{x}; \boldsymbol{x}^{(n)}) \Big|_{\boldsymbol{x}=\boldsymbol{x}^{(n)}} = \nabla \Psi(\boldsymbol{x}) \Big|_{\boldsymbol{x}=\boldsymbol{x}^{(n)}}$ (matched gradient)
- $\phi(\boldsymbol{x}; \boldsymbol{x}^{(n)}) \geq \Psi(\boldsymbol{x}) \quad \forall \boldsymbol{x} \geq \mathbf{0}$ (lies above)

These 3 (sufficient) conditions are satisfied by the Q function of the EM algorithm (and SAGE).

The 3rd condition is *not* satisfied by the Newton-Raphson quadratic approximation, which leads to its nonmonotonicity.

Optimization Transfer in 2d



Optimization Transfer cf EM Algorithm

E-step: choose surrogate function $\phi(\mathbf{x}; \mathbf{x}^{(n)})$

M-step: minimize surrogate function

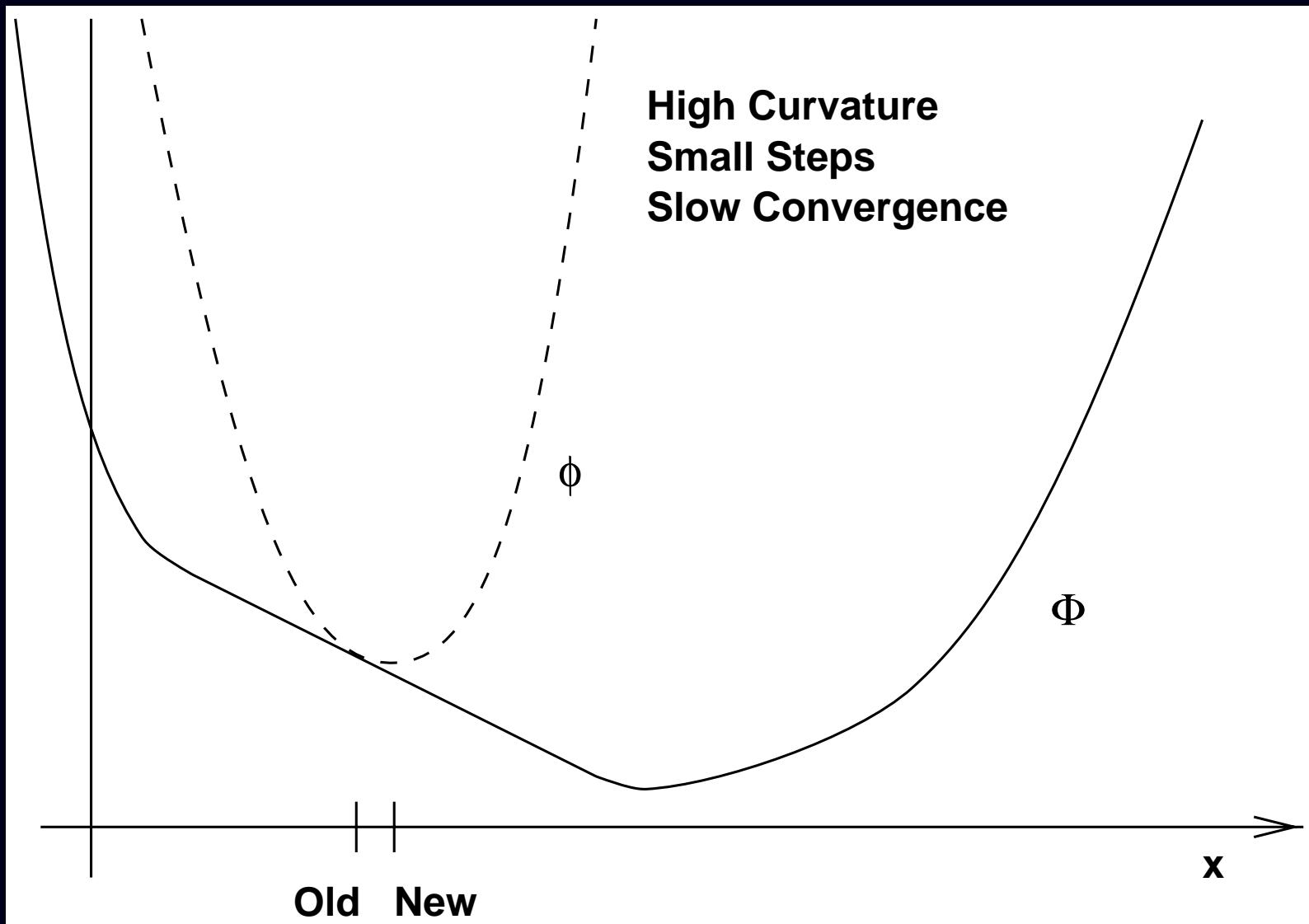
$$\mathbf{x}^{(n+1)} = \arg \min_{\mathbf{x} \geq 0} \phi(\mathbf{x}; \mathbf{x}^{(n)})$$

Designing surrogate functions

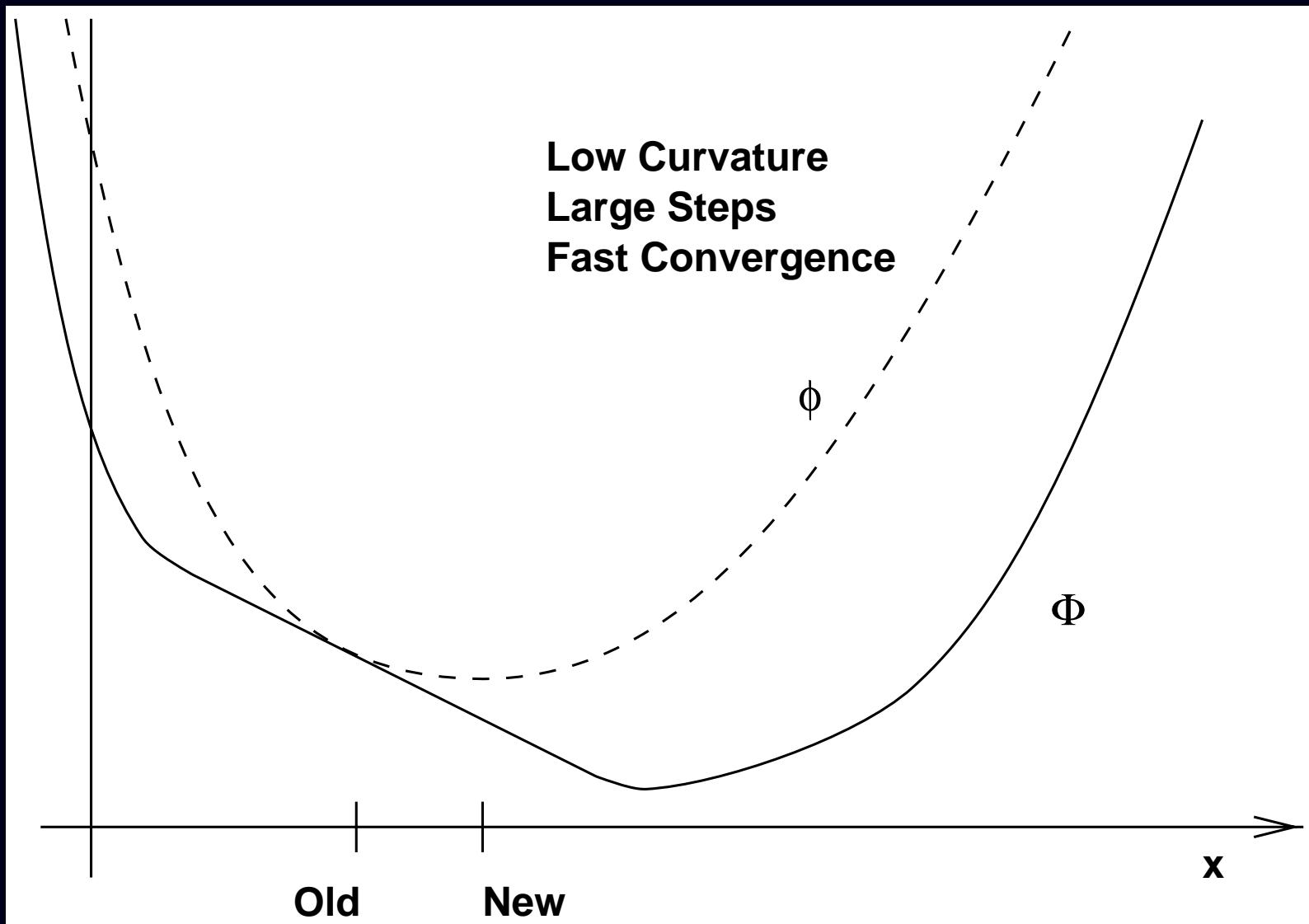
- Easy to “compute”
- Easy to minimize
- Fast convergence rate

Often mutually incompatible goals ∴ compromises

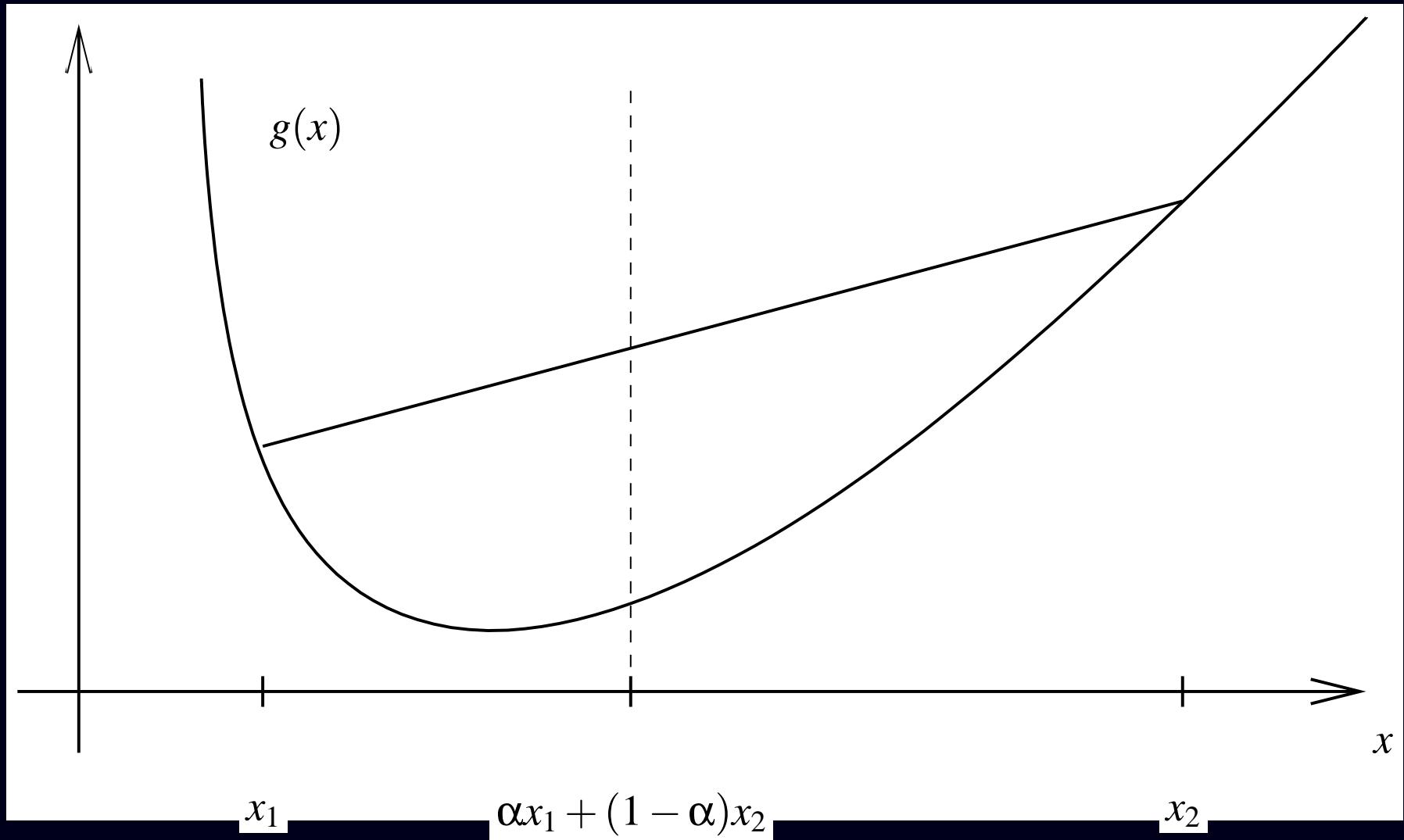
Convergence Rate: Slow



Convergence Rate: Fast



Tool: Convexity Inequality



g convex $\Rightarrow g(\alpha x_1 + (1 - \alpha)x_2) \leq \alpha g(x_1) + (1 - \alpha)g(x_2)$ for $\alpha \in [0, 1]$

More generally: $\alpha_k \geq 0$ and $\sum_k \alpha_k = 1 \Rightarrow g(\sum_k \alpha_k x_k) \leq \sum_k \alpha_k g(x_k)$. Sum outside!

Example 1: Classical ML-EM Algorithm

Negative Poisson log-likelihood *cost function* (unregularized):

$$\Psi(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{Ax}]_i), \quad h_i(l) = (l + r_i) - y_i \log(l + r_i).$$

Intractable to minimize directly due to summation within logarithm.

Clever trick due to De Pierro (let $\bar{y}_i^{(n)} = [\mathbf{Ax}^{(n)}]_i + r_i$):

$$[\mathbf{Ax}]_i = \sum_{j=1}^{n_p} a_{ij} x_j = \sum_{j=1}^{n_p} \left[\frac{a_{ij} x_j^{(n)}}{\bar{y}_i^{(n)}} \right] \left(\frac{x_j}{x_j^{(n)}} \bar{y}_i^{(n)} \right).$$

Since the h_i 's are **convex** in Poisson emission model:

$$h_i([\mathbf{Ax}]_i) = h_i \left(\sum_{j=1}^{n_p} \left[\frac{a_{ij} x_j^{(n)}}{\bar{y}_i^{(n)}} \right] \left(\frac{x_j}{x_j^{(n)}} \bar{y}_i^{(n)} \right) \right) \leq \sum_{j=1}^{n_p} \left[\frac{a_{ij} x_j^{(n)}}{\bar{y}_i^{(n)}} \right] h_i \left(\frac{x_j}{x_j^{(n)}} \bar{y}_i^{(n)} \right)$$

$$\Psi(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{Ax}]_i) \leq \phi(\mathbf{x}; \mathbf{x}^{(n)}) \triangleq \sum_{i=1}^{n_d} \sum_{j=1}^{n_p} \left[\frac{a_{ij} x_j^{(n)}}{\bar{y}_i^{(n)}} \right] h_i \left(\frac{x_j}{x_j^{(n)}} \bar{y}_i^{(n)} \right)$$

Replace convex *cost function* $\Psi(\mathbf{x})$ with **separable** surrogate function $\phi(\mathbf{x}; \mathbf{x}^{(n)})$.

“ML-EM Algorithm” M-step

E-step gave separable surrogate function:

$$\phi(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)}), \quad \text{where } \phi_j(x_j; \mathbf{x}^{(n)}) \triangleq \sum_{i=1}^{n_d} \left[\frac{a_{ij}x_j^{(n)}}{\bar{y}_i^{(n)}} \right] h_i\left(\frac{x_j}{\bar{y}_i^{(n)}}\right).$$

M-step separates:

$$\mathbf{x}^{(n+1)} = \arg \min_{\mathbf{x} \geq 0} \phi(\mathbf{x}; \mathbf{x}^{(n)}) \Rightarrow x_j^{(n+1)} = \arg \min_{x_j \geq 0} \phi_j(x_j; \mathbf{x}^{(n)}), \quad j = 1, \dots, n_p$$

Minimizing:

$$\frac{\partial}{\partial x_j} \phi_j(x_j; \mathbf{x}^{(n)}) = \sum_{i=1}^{n_d} a_{ij} h_i'\left(\frac{\bar{y}_i^{(n)} x_j}{x_j^{(n)}}\right) = \sum_{i=1}^{n_d} a_{ij} \left[1 - \frac{y_i}{\bar{y}_i^{(n)} x_j / x_j^{(n)}} \right] \Big|_{x_j=x_j^{(n+1)}} = 0.$$

Solving (in case $r_i = 0$):

$$x_j^{(n+1)} = x_j^{(n)} \left[\sum_{i=1}^{n_d} a_{ij} \frac{y_i}{[\mathbf{A}\mathbf{x}^{(n)}]_i} \right] / \left(\sum_{i=1}^{n_d} a_{ij} \right), \quad j = 1, \dots, n_p$$

- Derived without any statistical considerations, unlike classical EM formulation.
- Uses only convexity and algebra.
- Guaranteed monotonic: surrogate function ϕ satisfies the 3 required properties.
- M-step trivial due to ***separable surrogate***.

ML-EM is Scaled Gradient Descent

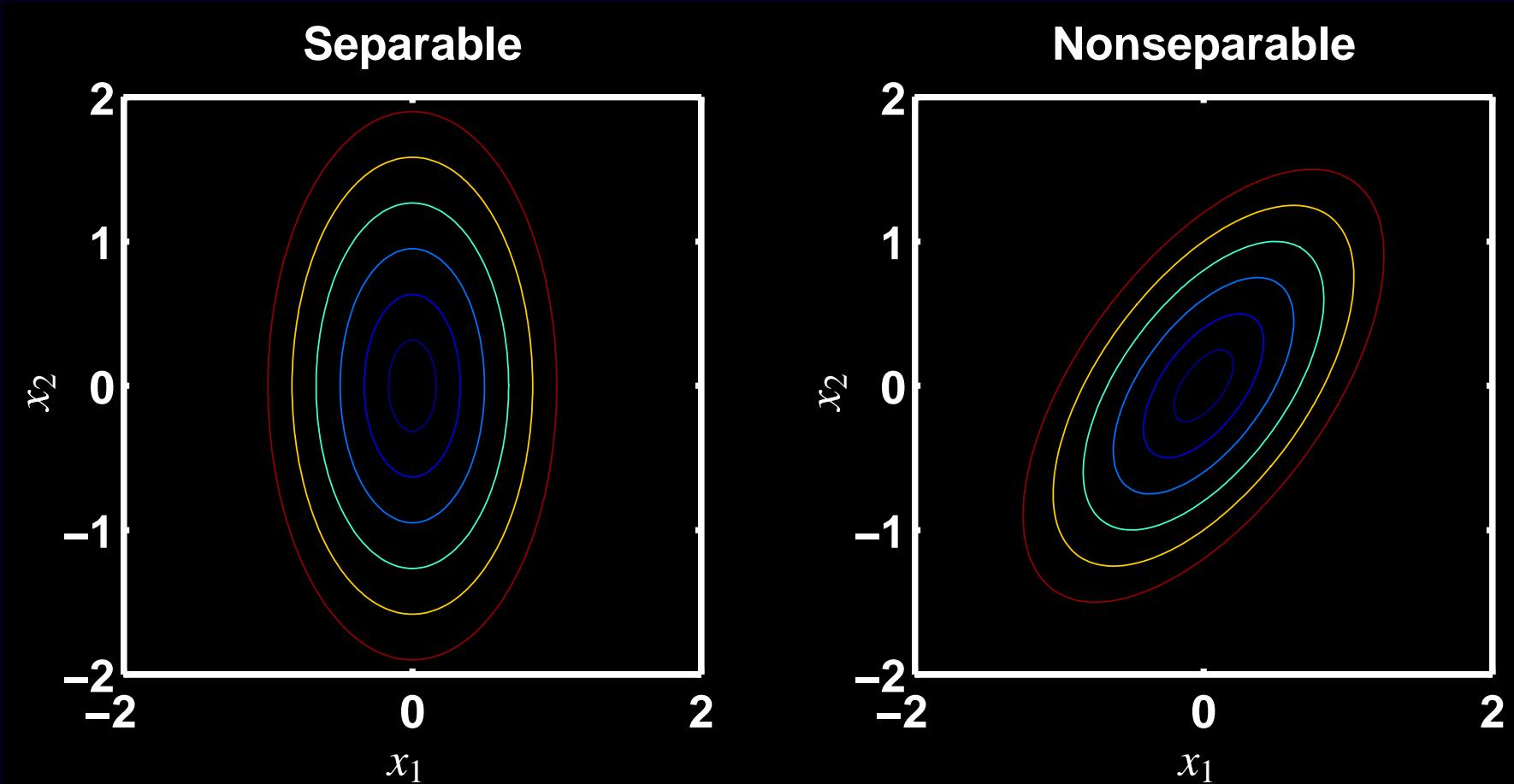
$$\begin{aligned}x_j^{(n+1)} &= x_j^{(n)} \left[\sum_{i=1}^{n_d} a_{ij} \frac{y_i}{\bar{y}_i^{(n)}} \right] / \left(\sum_{i=1}^{n_d} a_{ij} \right) \\&= x_j^{(n)} + x_j^{(n)} \left[\sum_{i=1}^{n_d} a_{ij} \left(\frac{y_i}{\bar{y}_i^{(n)}} - 1 \right) \right] / \left(\sum_{i=1}^{n_d} a_{ij} \right) \\&= \boxed{x_j^{(n)} - \left(\frac{x_j^{(n)}}{\sum_{i=1}^{n_d} a_{ij}} \right) \frac{\partial}{\partial x_j} \Psi(\mathbf{x}^{(n)})}, \quad j = 1, \dots, n_p\end{aligned}$$

$$\mathbf{x}^{(n+1)} = \mathbf{x}^{(n)} + \mathbf{D}(\mathbf{x}^{(n)}) \nabla \Psi(\mathbf{x}^{(n)})$$

This particular diagonal scaling matrix remarkably

- ensures monotonicity,
- ensures nonnegativity.

Consideration: Separable vs Nonseparable



Contour plots: loci of equal function values.

Uncoupled vs coupled minimization.

Separable Surrogate Functions (Easy M-step)

The preceding EM derivation structure applies to *any cost function* of the form

$$\Psi(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{A}\mathbf{x}]_i).$$

cf ISRA (for nonnegative LS), “convex algorithm” for transmission reconstruction

Derivation yields a separable surrogate function

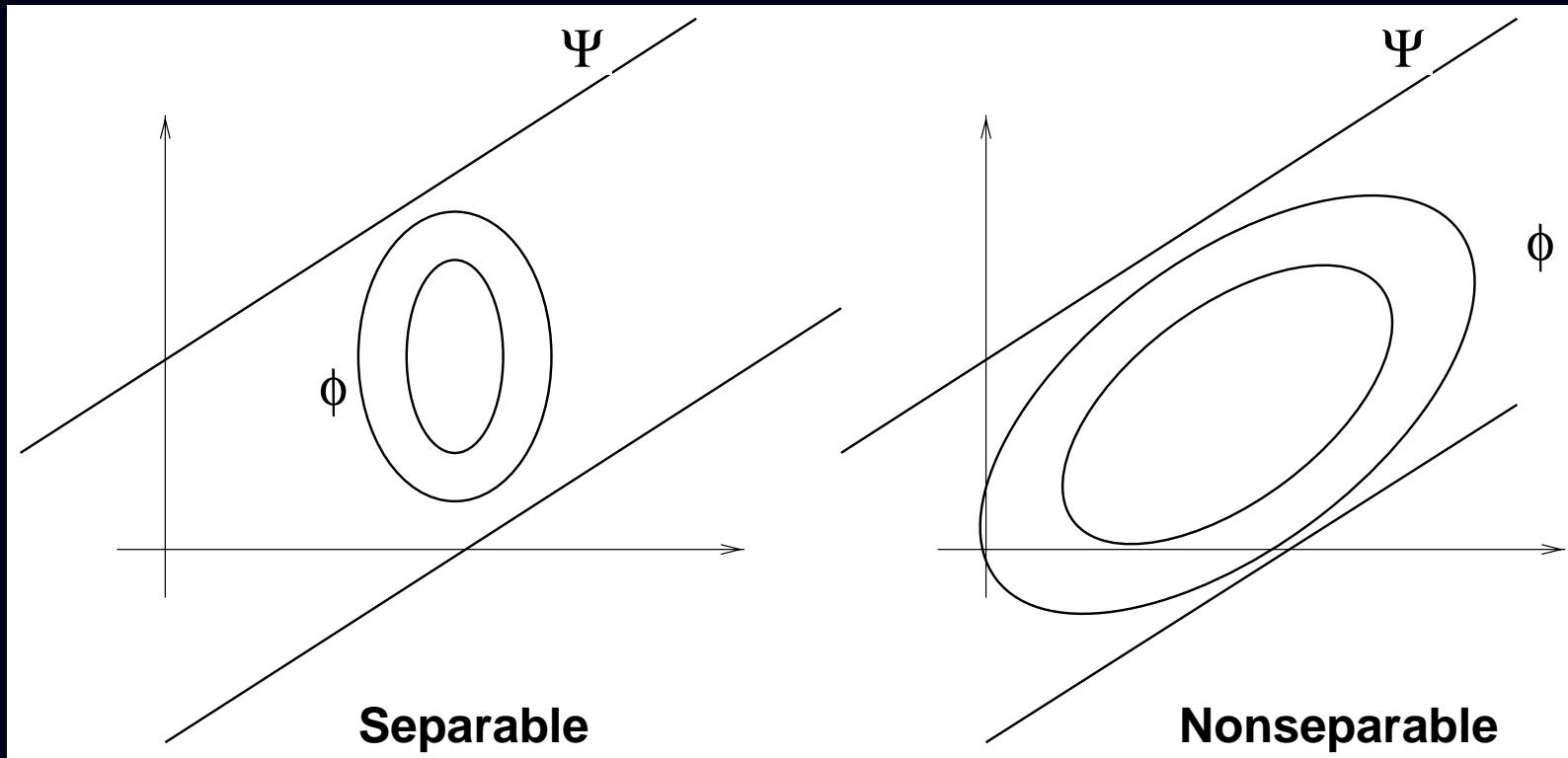
$$\Psi(\mathbf{x}) \leq \phi(\mathbf{x}; \mathbf{x}^{(n)}), \text{ where } \phi(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)})$$

M-step separates into 1D minimization problems (fully parallelizable):

$$\mathbf{x}^{(n+1)} = \arg \min_{\mathbf{x} \geq 0} \phi(\mathbf{x}; \mathbf{x}^{(n)}) \Rightarrow x_j^{(n+1)} = \arg \min_{x_j \geq 0} \phi_j(x_j; \mathbf{x}^{(n)}), \quad j = 1, \dots, n_p$$

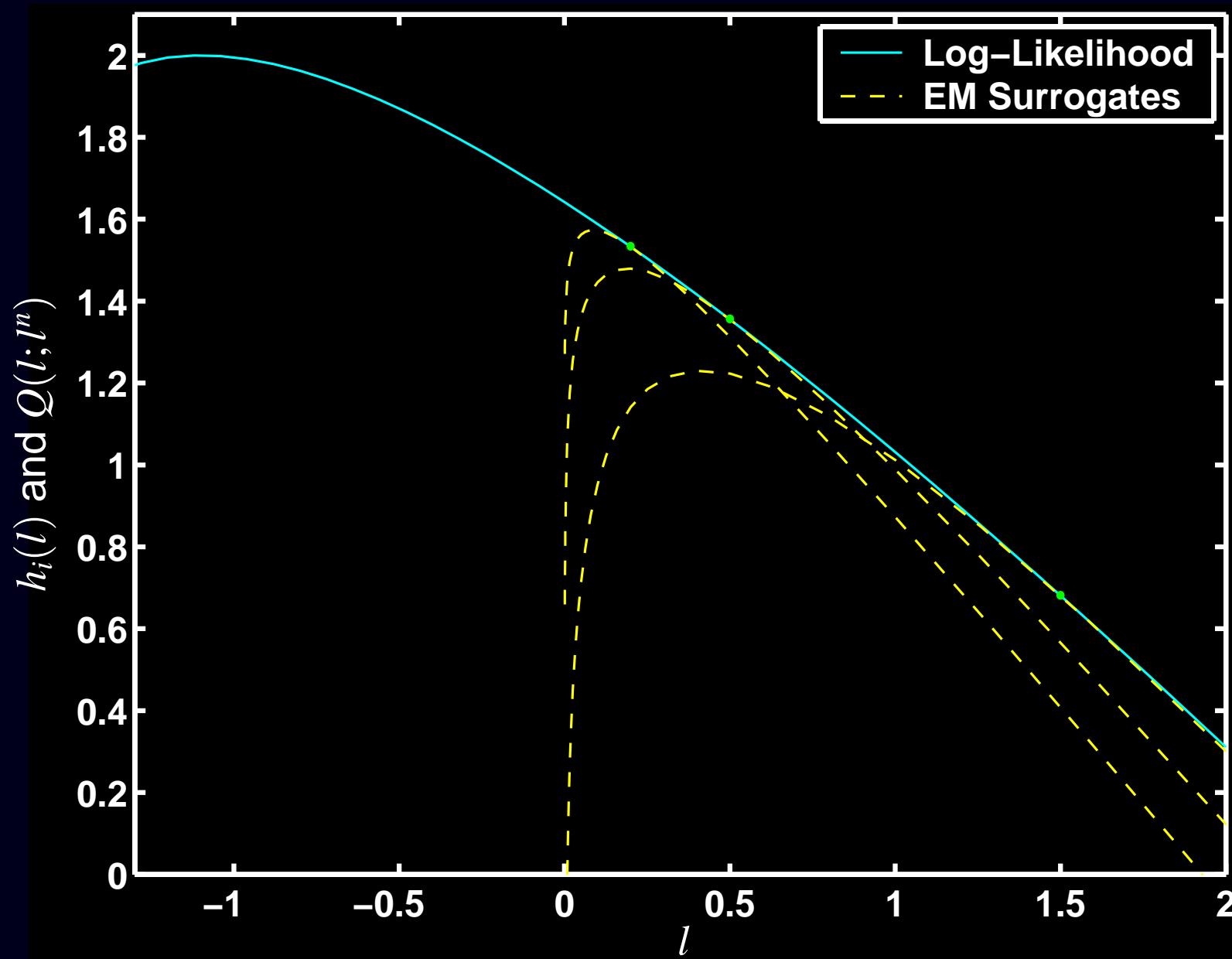
Why do EM / ISRA / convex-algorithm / etc. converge so slowly?

Separable vs Nonseparable



Separable surrogates (e.g., EM) have high curvature \therefore slow convergence.
Nonseparable surrogates can have lower curvature \therefore faster convergence.
Harder to minimize? Use paraboloids (quadratic surrogates).

High Curvature of EM Surrogate



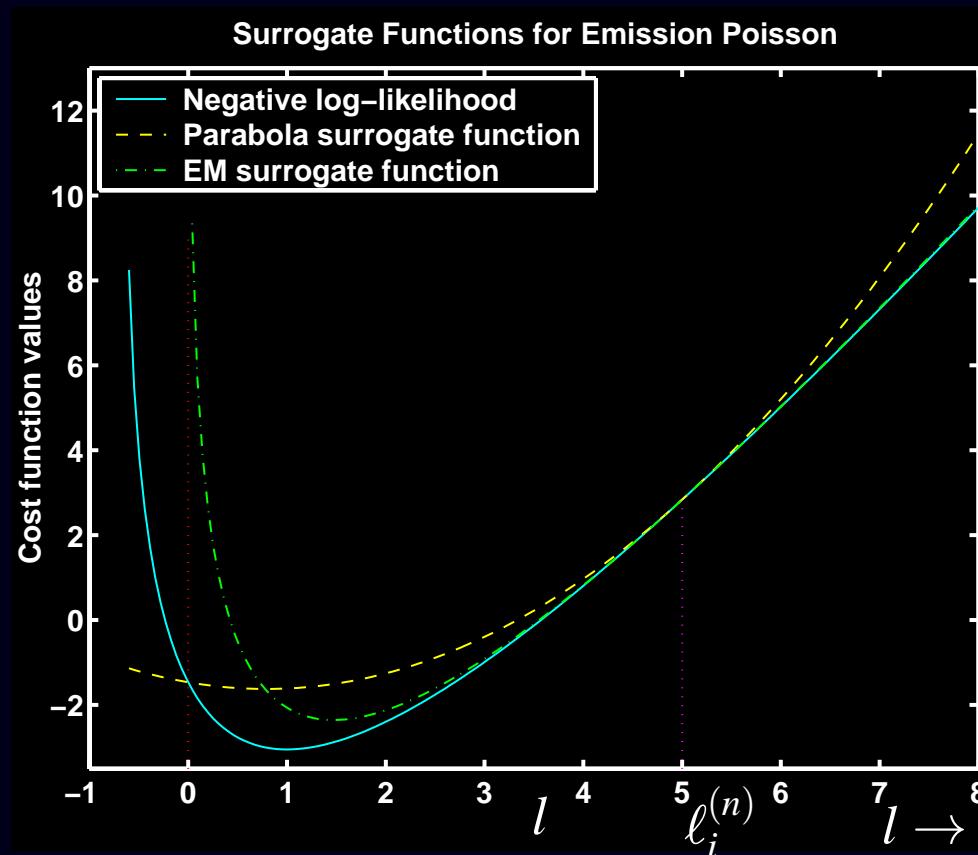
1D Parabola Surrogate Function

Find parabola $q_i^{(n)}(l)$ of the form:

$$q_i^{(n)}(l) = h_i(\ell_i^{(n)}) + \dot{h}_i(\ell_i^{(n)})(l - \ell_i^{(n)}) + c_i^{(n)} \frac{1}{2}(l - \ell_i^{(n)})^2, \text{ where } \ell_i^{(n)} \triangleq [Ax^{(n)}]_i$$

Satisfies tangent condition. Choose curvature to ensure “lies above” condition:

$$c_i^{(n)} \triangleq \min \left\{ c \geq 0 : q_i^{(n)}(l) \geq h_i(l), \quad \forall l \geq 0 \right\}.$$



Lower curvature!

Paraboloidal Surrogate

Combining 1D parabola surrogates yields *paraboloidal surrogate*:

$$\Psi(\mathbf{x}) = \sum_{i=1}^{n_d} h_i([\mathbf{A}\mathbf{x}]_i) \leq \phi(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{i=1}^{n_d} q_i^{(n)}([\mathbf{A}\mathbf{x}]_i)$$

$$\text{Rewriting: } \phi(\boldsymbol{\delta} + \mathbf{x}^{(n)}; \mathbf{x}^{(n)}) = \Psi(\mathbf{x}^{(n)}) + \nabla \Psi(\mathbf{x}^{(n)}) \boldsymbol{\delta} + \frac{1}{2} \boldsymbol{\delta}' \mathbf{A}' \text{diag} \left\{ c_i^{(n)} \right\} \mathbf{A} \boldsymbol{\delta}$$

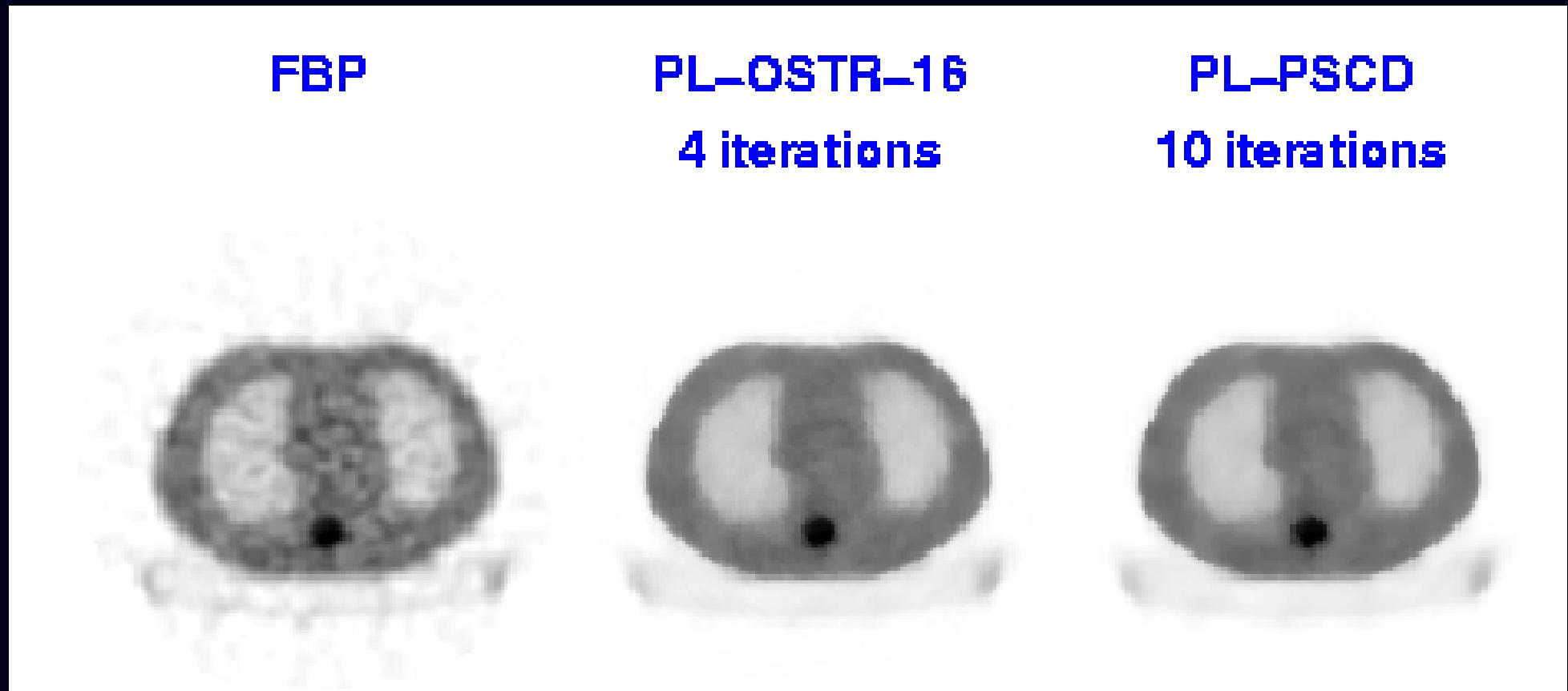
Advantages

- Surrogate $\phi(\mathbf{x}; \mathbf{x}^{(n)})$ is *quadratic*, unlike Poisson log-likelihood
⇒ easier to minimize
- Not separable (unlike EM surrogate)
- Not self-similar (unlike EM surrogate)
- Small curvatures ⇒ fast convergence
- Intrinsicly monotone global convergence
- Fairly simple to derive / implement

Quadratic minimization

- Coordinate descent
 - + fast converging
 - + Nonnegativity easy
 - precomputed column-stored system matrix
- Gradient-based quadratic minimization methods
 - Nonnegativity inconvenient

Example: PSCD for PET Transmission Scans



- square-pixel basis
- strip-integral system model
- shifted-Poisson statistical model
- edge-preserving convex regularization (Huber)
- nonnegativity constraint
- inscribed circle support constraint
- paraboloidal surrogate coordinate descent (PSCD) algorithm

Separable Paraboloidal Surrogate

To derive a parallelizable algorithm apply another De Pierro trick:

$$[\mathbf{A}\mathbf{x}]_i = \sum_{j=1}^{n_p} \pi_{ij} \left[\frac{a_{ij}}{\pi_{ij}} (x_j - x_j^{(n)}) + \ell_i^{(n)} \right], \quad \ell_i^{(n)} = [\mathbf{A}\mathbf{x}^{(n)}]_i.$$

Provided $\pi_{ij} \geq 0$ and $\sum_{j=1}^{n_p} \pi_{ij} = 1$, since parabola q_i is convex:

$$\begin{aligned} q_i^{(n)}([\mathbf{A}\mathbf{x}]_i) &= q_i^{(n)} \left(\sum_{j=1}^{n_p} \pi_{ij} \left[\frac{a_{ij}}{\pi_{ij}} (x_j - x_j^{(n)}) + \ell_i^{(n)} \right] \right) \leq \sum_{j=1}^{n_p} \pi_{ij} q_i^{(n)} \left(\frac{a_{ij}}{\pi_{ij}} (x_j - x_j^{(n)}) + \ell_i^{(n)} \right) \\ \therefore \phi(\mathbf{x}; \mathbf{x}^{(n)}) &= \sum_{i=1}^{n_d} q_i^{(n)}([\mathbf{A}\mathbf{x}]_i) \leq \tilde{\phi}(\mathbf{x}; \mathbf{x}^{(n)}) \triangleq \sum_{i=1}^{n_d} \sum_{j=1}^{n_p} \pi_{ij} q_i^{(n)} \left(\frac{a_{ij}}{\pi_{ij}} (x_j - x_j^{(n)}) + \ell_i^{(n)} \right) \end{aligned}$$

Separable Paraboloidal Surrogate:

$$\tilde{\phi}(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)}), \quad \phi_j(x_j; \mathbf{x}^{(n)}) \triangleq \sum_{i=1}^{n_d} \pi_{ij} q_i^{(n)} \left(\frac{a_{ij}}{\pi_{ij}} (x_j - x_j^{(n)}) + \ell_i^{(n)} \right)$$

Parallelizable M-step (cf gradient descent!):

$$x_j^{(n+1)} = \arg \min_{x_j \geq 0} \phi_j(x_j; \mathbf{x}^{(n)}) = \left[x_j^{(n)} - \frac{1}{d_j^{(n)}} \frac{\partial}{\partial x_j} \Psi(\mathbf{x}^{(n)}) \right]_+, \quad d_j^{(n)} = \sum_{i=1}^{n_d} \frac{a_{ij}^2}{\pi_{ij}} c_i^{(n)}$$

Natural choice is $\pi_{ij} = |a_{ij}| / \|a\|_i$, $\|a\|_i = \sum_{j=1}^{n_p} |a_{ij}|$

Example: Poisson ML Transmission Problem

Transmission negative log-likelihood (for i th ray):

$$h_i(l) = (b_i e^{-l} + r_i) - y_i \log(b_i e^{-l} + r_i).$$

Optimal (smallest) parabola surrogate curvature (Erdoğan, T-MI, Sep. 1999):

$$c_i^{(n)} = c(\ell_i^{(n)}, h_i), \quad c(l, h) = \begin{cases} \left[\frac{h(0) - h(l) + \dot{h}(l)l}{l^2} \right]_+, & l > 0 \\ [\ddot{h}(l)]_+, & l = 0. \end{cases}$$

Separable Paraboloidal Surrogate Algorithm:

Precompute $|a|_i = \sum_{j=1}^{n_p} a_{ij}$, $i = 1, \dots, n_d$

$$\begin{aligned} \ell_i^{(n)} &= [\mathbf{A}\mathbf{x}^{(n)}]_i, && \text{(forward projection)} \\ \bar{y}_i^{(n)} &= b_i e^{-\ell_i^{(n)}} + r_i && \text{(predicted means)} \\ \dot{h}_i^{(n)} &= 1 - y_i / \bar{y}_i^{(n)} && \text{(slopes)} \\ c_i^{(n)} &= c(\ell_i^{(n)}, h_i) && \text{(curvatures)} \end{aligned}$$

$$x_j^{(n+1)} = \left[x_j^{(n)} - \frac{1}{d_j^{(n)}} \frac{\partial}{\partial x_j} \Psi(\mathbf{x}^{(n)}) \right]_+ = \left[x_j^{(n)} - \frac{\sum_{i=1}^{n_d} \mathbf{a}_{ij} \dot{h}_i^{(n)}}{\sum_{i=1}^{n_d} \mathbf{a}_{ij} |a|_i c_i^{(n)}} \right]_+, \quad j = 1, \dots, n_p$$

Monotonically decreases *cost function* each iteration.

No logarithm!

The MAP-EM M-step “Problem”

Add a penalty function to our surrogate for the negative log-likelihood:

$$\Psi(\mathbf{x}) = -L(\mathbf{x}) + \beta R(\mathbf{x})$$

$$\phi(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)}) + \beta R(\mathbf{x})$$

$$\text{M-step: } \mathbf{x}^{(n+1)} = \arg \min_{\mathbf{x} \geq 0} \phi(\mathbf{x}; \mathbf{x}^{(n)}) = \arg \min_{\mathbf{x} \geq 0} \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)}) + \beta R(\mathbf{x}) = ?$$

For nonseparable penalty functions, the M-step is coupled ∴ difficult.

Suboptimal solutions

- Generalized EM (GEM) algorithm (coordinate descent on ϕ)
Monotonic, but inherits slow convergence of EM.
- One-step late (OSL) algorithm (use outdated gradients) (Green, T-MI, 1990)

$$\frac{\partial}{\partial x_j} \phi(\mathbf{x}; \mathbf{x}^{(n)}) = \frac{\partial}{\partial x_j} \phi_j(x_j; \mathbf{x}^{(n)}) + \beta \frac{\partial}{\partial x_j} R(\mathbf{x}) \stackrel{?}{\approx} \frac{\partial}{\partial x_j} \phi_j(x_j; \mathbf{x}^{(n)}) + \beta \frac{\partial}{\partial x_j} R(\mathbf{x}^{(n)})$$

Nonmonotonic. Known to diverge, depending on β .

Temptingly simple, but *avoid!*

Contemporary solution

- Use separable surrogate for penalty function too (De Pierro, T-MI, Dec. 1995)
Ensures monotonicity. Obviates all reasons for using OSL!

De Pierro's MAP-EM Algorithm

Apply separable paraboloidal surrogates to penalty function:

$$R(\mathbf{x}) \leq R_{\text{SPS}}(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} R_j(x_j; \mathbf{x}^{(n)})$$

Overall separable surrogate: $\phi(\mathbf{x}; \mathbf{x}^{(n)}) = \sum_{j=1}^{n_p} \phi_j(x_j; \mathbf{x}^{(n)}) + \beta \sum_{j=1}^{n_p} R_j(x_j; \mathbf{x}^{(n)})$

The M-step becomes fully parallelizable:

$$x_j^{(n+1)} = \arg \min_{x_j \geq 0} \phi_j(x_j; \mathbf{x}^{(n)}) - \beta R_j(x_j; \mathbf{x}^{(n)}), \quad j = 1, \dots, n_p.$$

Consider quadratic penalty $R(\mathbf{x}) = \sum_k \psi([\mathbf{C}\mathbf{x}]_k)$, where $\psi(t) = t^2/2$.

If $\gamma_{kj} \geq 0$ and $\sum_{j=1}^{n_p} \gamma_{kj} = 1$ then

$$[\mathbf{C}\mathbf{x}]_k = \sum_{j=1}^{n_p} \gamma_{kj} \left[\frac{c_{kj}}{\gamma_{kj}} (x_j - x_j^{(n)}) + [\mathbf{C}\mathbf{x}^{(n)}]_k \right].$$

Since ψ is convex:

$$\begin{aligned} \psi([\mathbf{C}\mathbf{x}]_k) &= \psi \left(\sum_{j=1}^{n_p} \gamma_{kj} \left[\frac{c_{kj}}{\gamma_{kj}} (x_j - x_j^{(n)}) + [\mathbf{C}\mathbf{x}^{(n)}]_k \right] \right) \\ &\leq \sum_{j=1}^{n_p} \gamma_{kj} \psi \left(\frac{c_{kj}}{\gamma_{kj}} (x_j - x_j^{(n)}) + [\mathbf{C}\mathbf{x}^{(n)}]_k \right) \end{aligned}$$

De Pierro's Algorithm Continued

So $R(\mathbf{x}) \leq R(\mathbf{x}; \mathbf{x}^{(n)}) \stackrel{\triangle}{=} \sum_{j=1}^{n_p} R_j(x_j; \mathbf{x}^{(n)})$ where

$$R_j(x_j; \mathbf{x}^{(n)}) \stackrel{\triangle}{=} \sum_k \gamma_{kj} \Psi\left(\frac{c_{kj}}{\gamma_{kj}}(x_j - x_j^{(n)}) + [\mathbf{C}\mathbf{x}^{(n)}]_k\right)$$

M-step: Minimizing $\phi_j(x_j; \mathbf{x}^{(n)}) + \beta R_j(x_j; \mathbf{x}^{(n)})$ yields the iteration:

$$x_j^{(n+1)} = \frac{x_j^{(n)} \sum_{i=1}^{n_d} a_{ij} y_i / \bar{y}_i^{(n)}}{B_j + \sqrt{B_j^2 + \left(x_j^{(n)} \sum_{i=1}^{n_d} a_{ij} y_i / \bar{y}_i^{(n)}\right) \left(\beta \sum_k c_{kj}^2 / \gamma_{kj}\right)}}$$

$$\text{where } B_j \stackrel{\triangle}{=} \frac{1}{2} \left[\sum_{i=1}^{n_d} a_{ij} + \beta \sum_k \left(c_{kj} [\mathbf{C}\mathbf{x}^{(n)}]_k - \frac{c_{kj}^2}{\gamma_{kj}} x_j^{(n)} \right) \right], \quad j = 1, \dots, n_p$$

and $\bar{y}_i^{(n)} = [\mathbf{A}\mathbf{x}^{(n)}]_i + r_i$.

Advantages: Intrinsically monotone, nonnegativity, fully parallelizable.
Requires only a couple % more computation per iteration than ML-EM

Disadvantages: Slow convergence (like EM) due to separable surrogate

Ordered Subsets Algorithms

aka *block iterative* or *incremental gradient* algorithms

The gradient appears in essentially every algorithm:

$$\frac{\partial}{\partial x_j} \Psi(\mathbf{x}) = \sum_{i=1}^{n_d} a_{ij} \dot{h}_i([\mathbf{A}\mathbf{x}]_i).$$

This is a *backprojection* of a sinogram of the derivatives $\{\dot{h}_i([\mathbf{A}\mathbf{x}]_i)\}$.

Intuition: with half the angular sampling, this backprojection would be fairly similar

$$\frac{1}{n_d} \sum_{i=1}^{n_d} a_{ij} \dot{h}_i(\cdot) \approx \frac{1}{|S|} \sum_{i \in S} a_{ij} \dot{h}_i(\cdot),$$

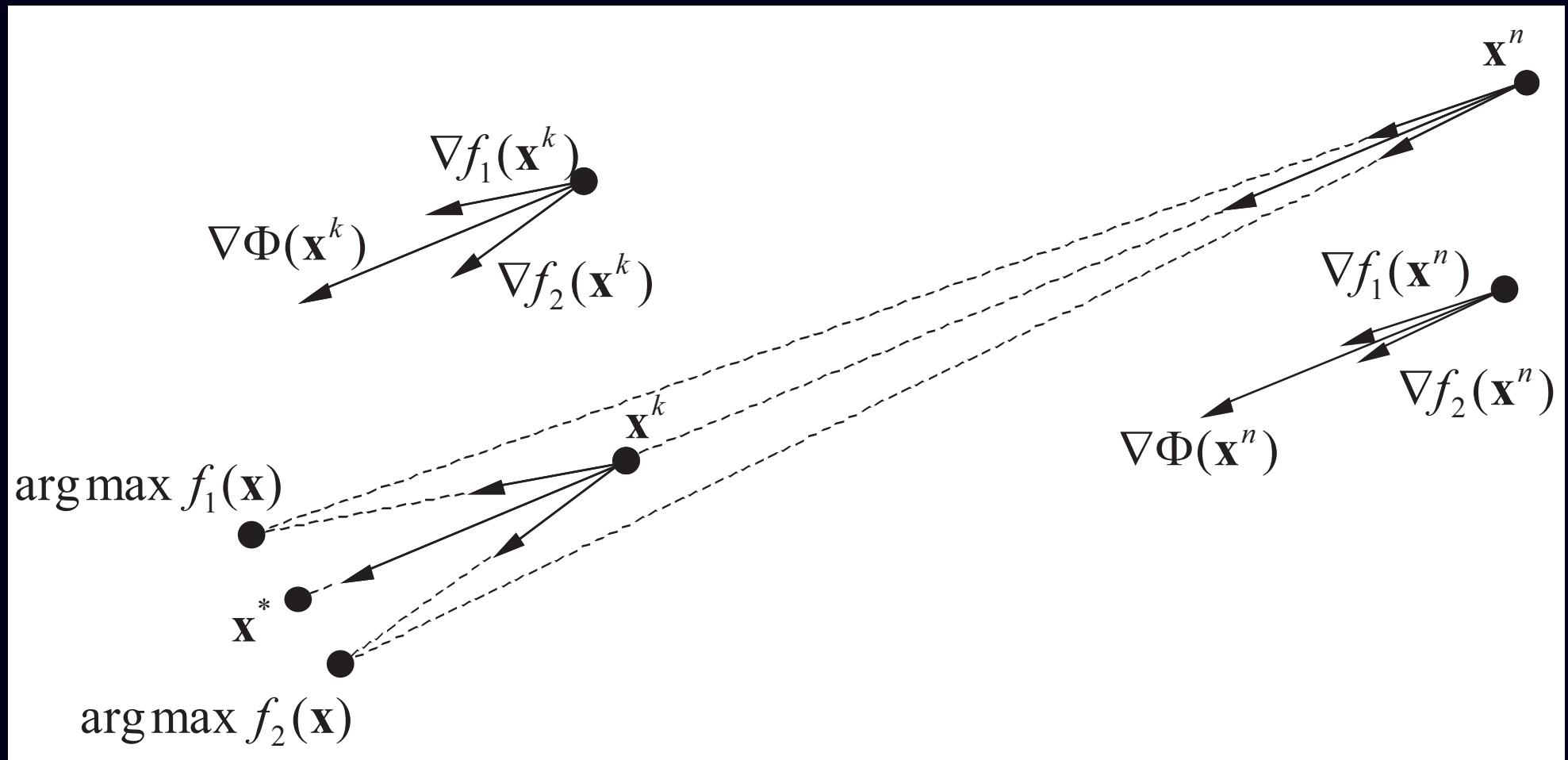
where S is a subset of the rays.

To “OS-ize” an algorithm, replace all backprojections with partial sums.

Recall typical iteration:

$$\mathbf{x}^{(n+1)} = \mathbf{x}^{(n)} - \mathbf{D}(\mathbf{x}^{(n)}) \nabla \Psi(\mathbf{x}^{(n)}).$$

Geometric View of Ordered Subsets



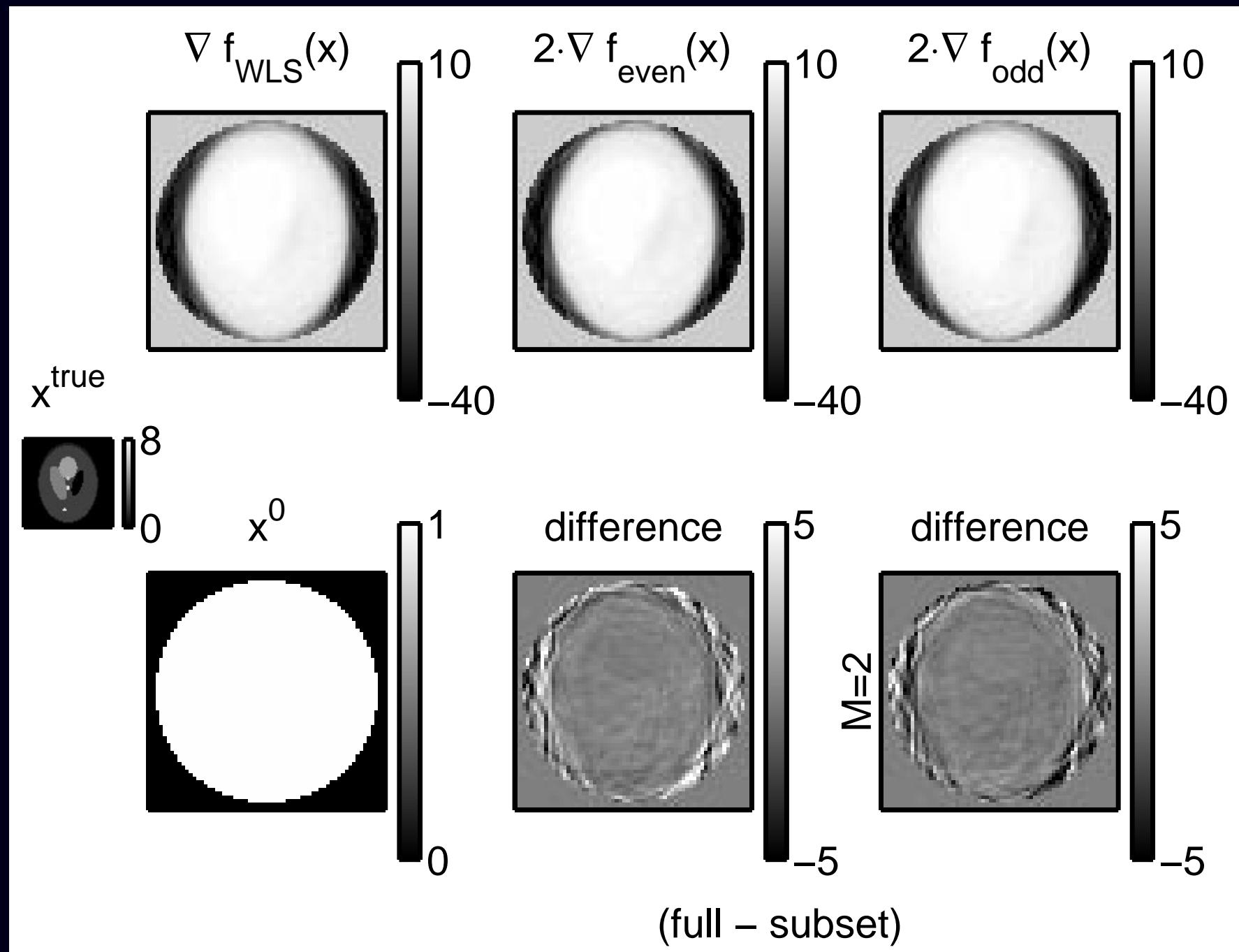
Two subset case: $\Psi(\mathbf{x}) = f_1(\mathbf{x}) + f_2(\mathbf{x})$ (e.g., odd and even projection views).

For $\mathbf{x}^{(n)}$ far from \mathbf{x}^* , even partial gradients should point roughly towards \mathbf{x}^* .

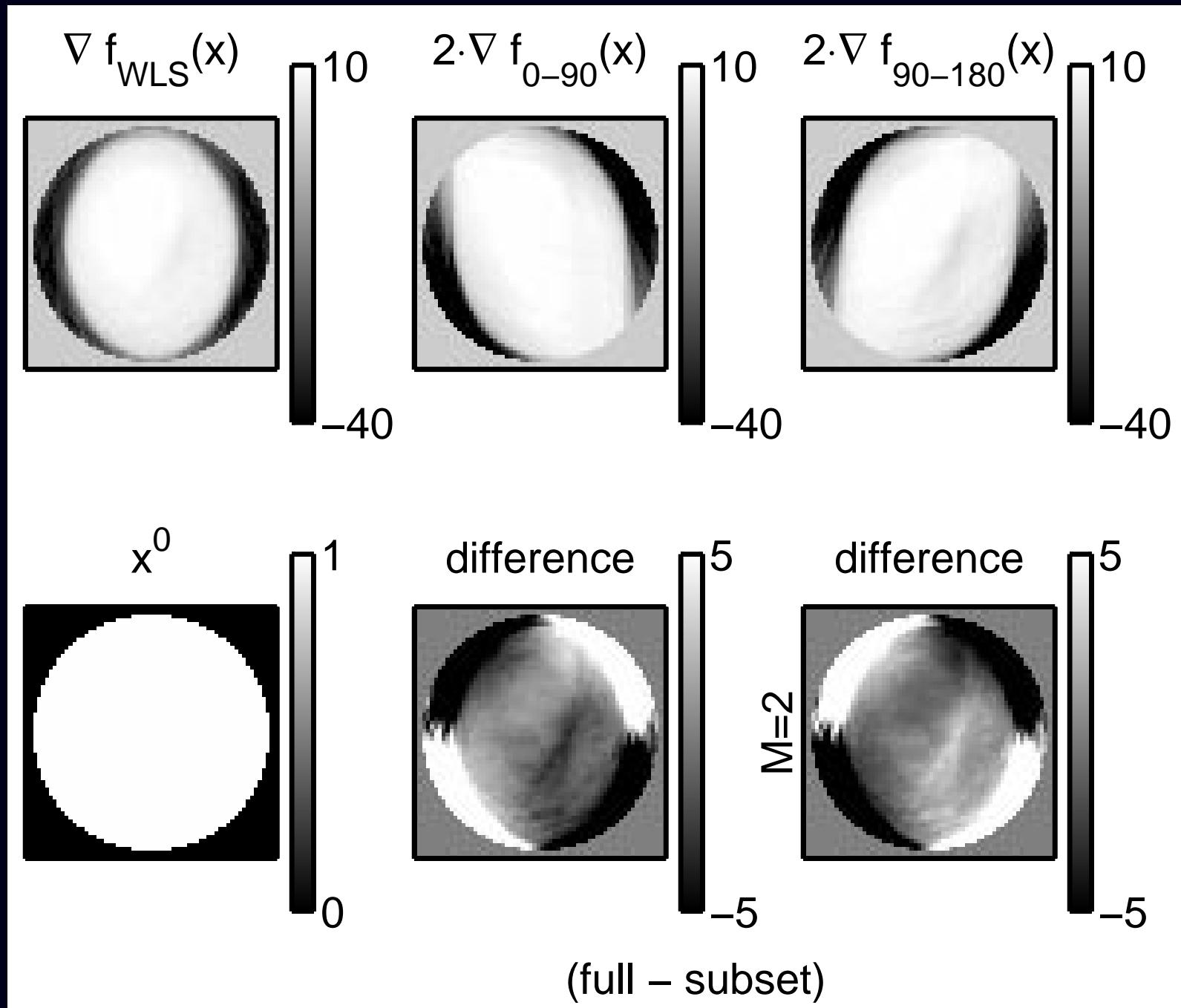
For $\mathbf{x}^{(n)}$ near \mathbf{x}^* , however, $\nabla \Psi(\mathbf{x}) \approx 0$, so $\nabla f_1(\mathbf{x}) \approx -\nabla f_2(\mathbf{x}) \Rightarrow$ cycles!

Issues. “Subset gradient balance”: $\nabla \Psi(\mathbf{x}) \approx M \nabla f_k(\mathbf{x})$. Choice of ordering.

Incremental Gradients (WLS, 2 Subsets)



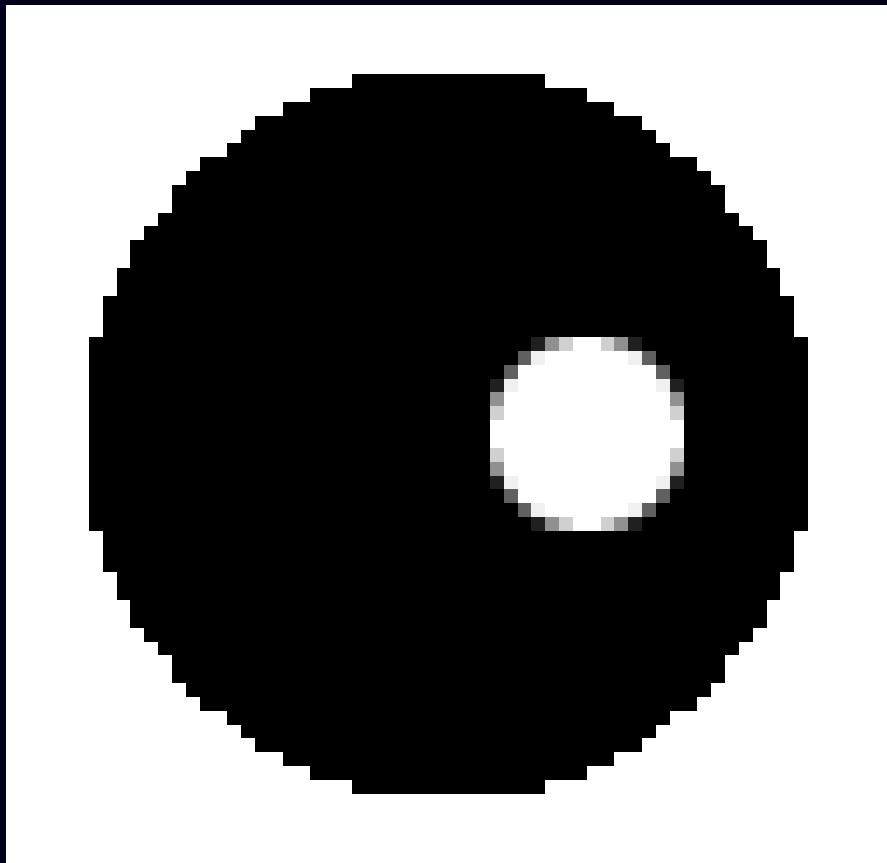
Subset Gradient Imbalance



Problems with OS-EM

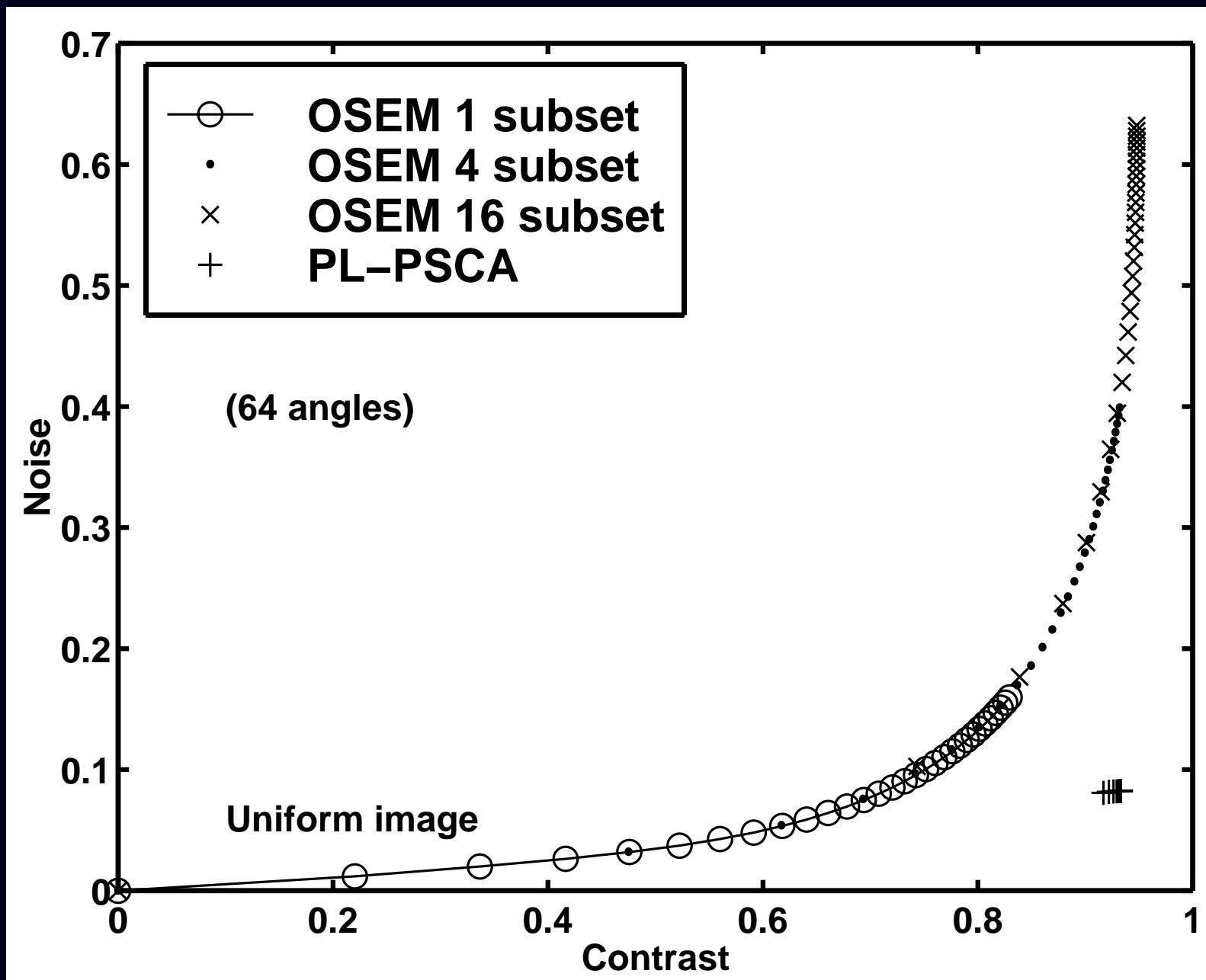
- Non-monotone
- Does not converge (may cycle)
- Byrne's RBBI approach only converges for consistent (noiseless) data
- ∴ unpredictable
 - What resolution after n iterations?
Object-dependent, spatially nonuniform
 - What variance after n iterations?
 - ROI variance? (e.g., for Huesman's WLS kinetics)

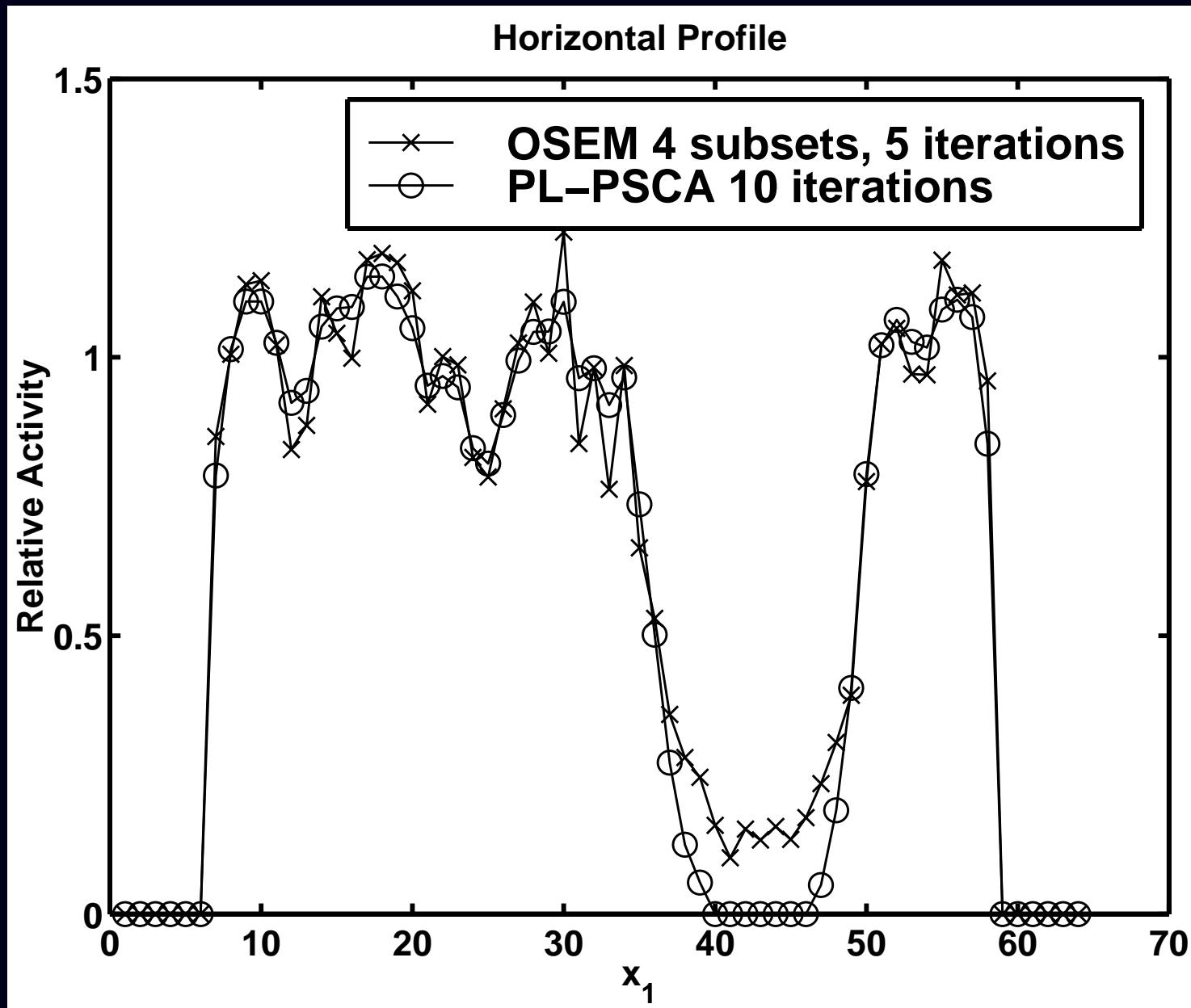
OSEM vs Penalized Likelihood



- 64×62 image
- 66×60 sinogram
- 10^6 counts
- 15% randoms/scatter
- uniform attenuation
- contrast in cold region
- within-region σ opposite side

Contrast-Noise Results





An Open Problem

Still no algorithm with all of the following properties:

- Nonnegativity easy
- Fast converging
- Intrinsically monotone global convergence
- Accepts any type of system matrix
- Parallelizable

Relaxed block-iterative methods

$$\Psi(\mathbf{x}) = \sum_{k=1}^K \Psi_k(\mathbf{x})$$

$$\mathbf{x}^{(n+(k+1)/K)} = \mathbf{x}^{(n+k/K)} - \alpha_n D(\mathbf{x}^{(n+k/K)}) \nabla \Psi_k(\mathbf{x}^{(n+k/K)}), \quad k = 0, \dots, K-1$$

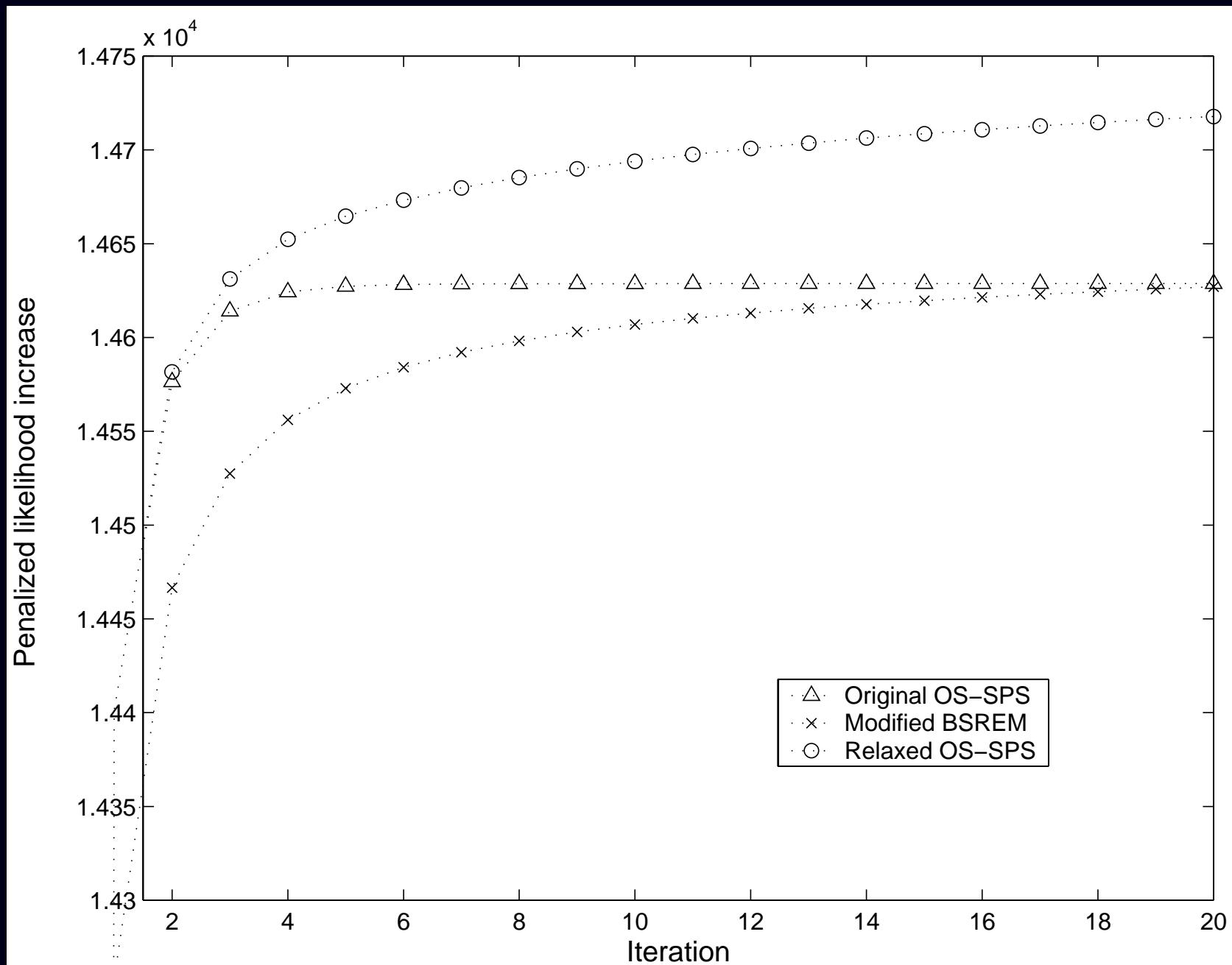
Relaxation of step sizes:

$$\alpha_n \rightarrow 0 \text{ as } n \rightarrow \infty, \quad \sum_n \alpha_n = \infty, \quad \sum_n \alpha_n^2 < \infty$$

- ART
- RAMLA, BSREM (De Pierro, T-MI, 1997, 2001)
- Ahn and Fessler, NSS/MIC 2001, T-MI (to appear)

Proper relaxation can induce convergence, *but* still lacks monotonicity.
Choice of relaxation schedule requires experimentation.

Relaxed OS-SPS



OSTR aka Transmission OS-SPS

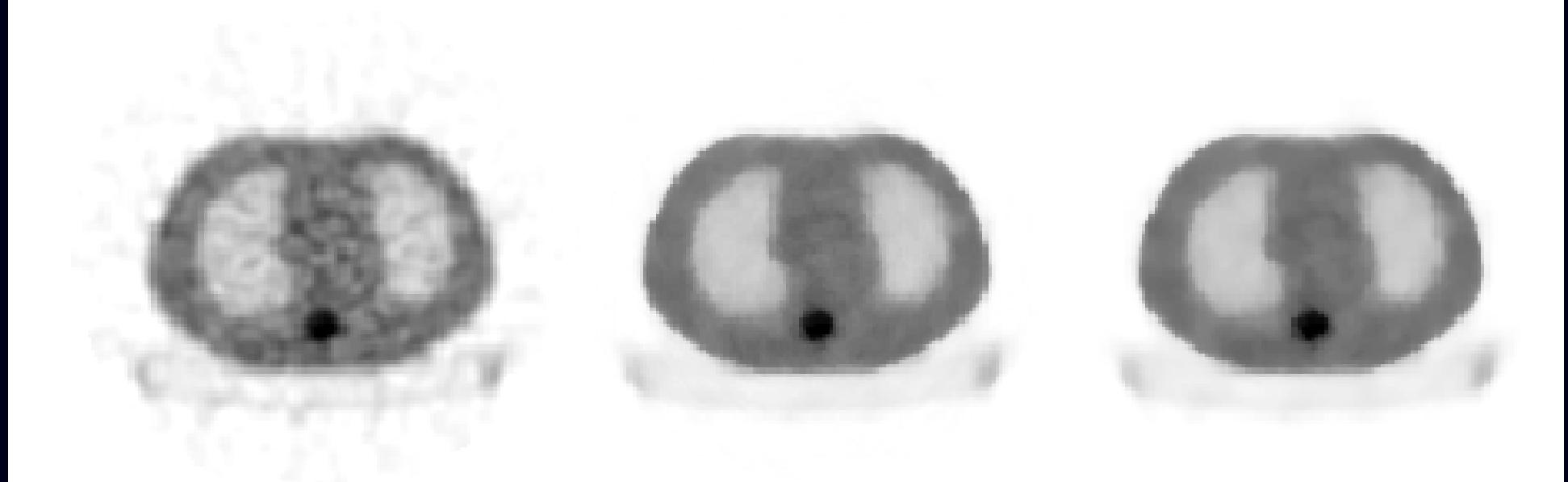
FBP

PL-OSTR-16

4 iterations

PL-PSCD

10 iterations



Ordered subsets version of separable paraboloidal surrogates
for PET transmission problem with nonquadratic convex *regularization*

Matlab m-file [http://www.eecs.umich.edu/~fessler
/code/transmission/tpl_osp.m](http://www.eecs.umich.edu/~fessler/code/transmission/tpl_osp.m)

Precomputed curvatures for OS-SPS

Separable Paraboloidal Surrogate (SPS) Algorithm:

$$x_j^{(n+1)} = \left[x_j^{(n)} - \frac{\sum_{i=1}^{n_d} \mathbf{a}_{ij} \dot{h}_i([\mathbf{A}\mathbf{x}^{(n)}]_i)}{\sum_{i=1}^{n_d} \mathbf{a}_{ij} |a|_i c_i^{(n)}} \right]_+, \quad j = 1, \dots, n_p$$

Ordered-subsets abandons monotonicity, so why use optimal curvatures $c_i^{(n)}$?

Precomputed curvature:

$$c_i = \ddot{h}_i(\hat{l}_i), \quad \hat{l}_i = \arg \min_l h_i(l)$$

Precomputed denominator (saves one backprojection each iteration!):

$$d_j = \sum_{i=1}^{n_d} a_{ij} |a|_i c_i, \quad j = 1, \dots, n_p.$$

OS-SPS algorithm with M subsets:

$$x_j^{(n+1)} = \left[x_j^{(n)} - \frac{\sum_{i \in S^{(n)}} \mathbf{a}_{ij} \dot{h}_i([\mathbf{A}\mathbf{x}^{(n)}]_i)}{d_j/M} \right]_+, \quad j = 1, \dots, n_p$$

Summary of Algorithms

- General-purpose optimization algorithms
- Optimization transfer for image reconstruction algorithms
- Separable surrogates \Rightarrow high curvatures \Rightarrow slow convergence
- Ordered subsets accelerate *initial* convergence
require relaxation for true convergence
- Principles apply to emission and transmission reconstruction
- Still work to be done...

Part 4. Performance Characteristics

- Spatial resolution properties
- Noise properties
- Detection properties

Spatial Resolution Properties

Choosing β can be painful, so ...

For true minimization methods:

$$\hat{\mathbf{x}} = \arg \min_{\mathbf{x}} \Psi(\mathbf{x})$$

the *local impulse response* is approximately (Fessler and Rogers, T-MI, Sep. 1996):

$$l_j(\mathbf{x}) = \lim_{\delta \rightarrow 0} \frac{E[\hat{\mathbf{x}}|\mathbf{x} + \delta e_j] - E[\hat{\mathbf{x}}|\mathbf{x}]}{\delta} \approx [-\nabla^{20}\Psi]^{-1} \nabla^{11}\Psi \frac{\partial}{\partial x_j} \bar{\mathbf{y}}(\mathbf{x}).$$

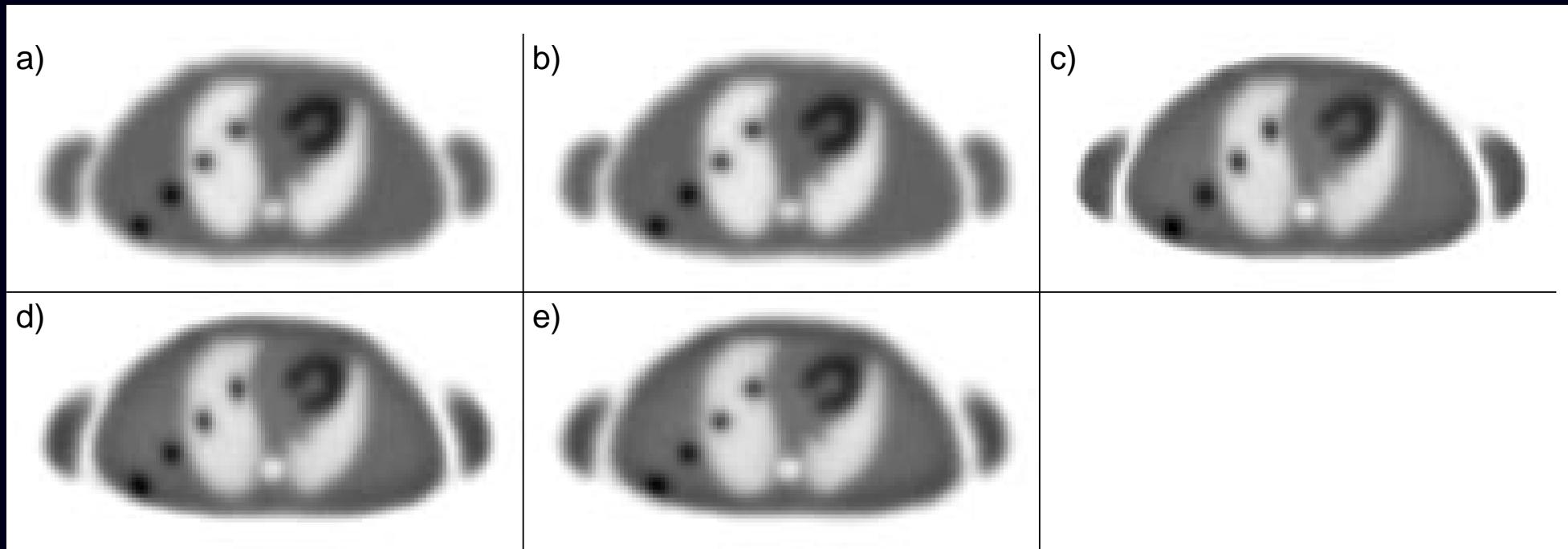
Depends only on chosen *cost function* and statistical model.
Independent of optimization algorithm.

- Enables prediction of resolution properties
(provided Ψ is minimized)
- Useful for designing regularization penalty functions
with desired resolution properties

$$l_j(\mathbf{x}) \approx [\mathbf{A}' \mathbf{W} \mathbf{A} + \beta \mathbf{R}]^{-1} \mathbf{A}' \mathbf{W} \mathbf{A} \mathbf{x}^{\text{true}}.$$

- Helps choose β for desired spatial resolution

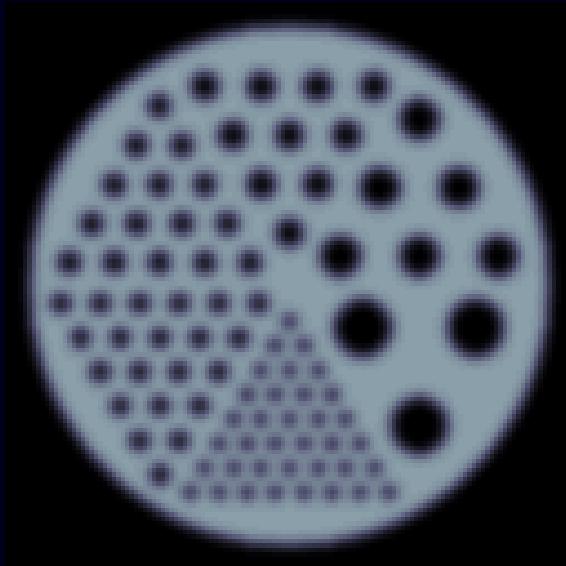
Modified Penalty Example, PET



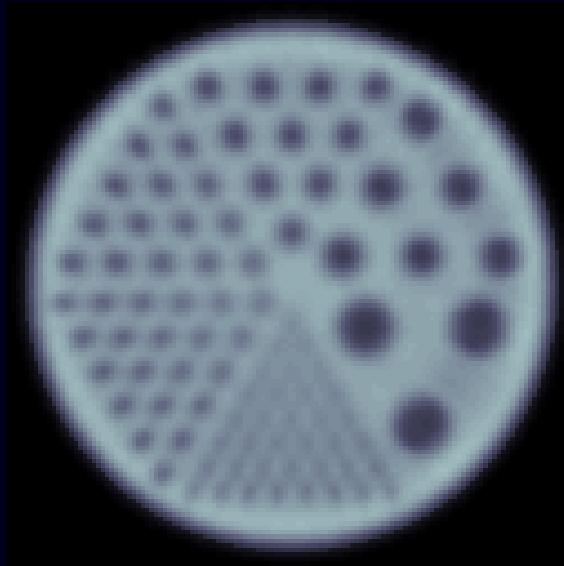
- a) filtered backprojection
- b) Penalized unweighted least-squares
- c) PWLS with conventional regularization
- d) PWLS with certainty-based penalty [25]
- e) PWLS with modified penalty [147]

Modified Penalty Example, SPECT - Noiseless

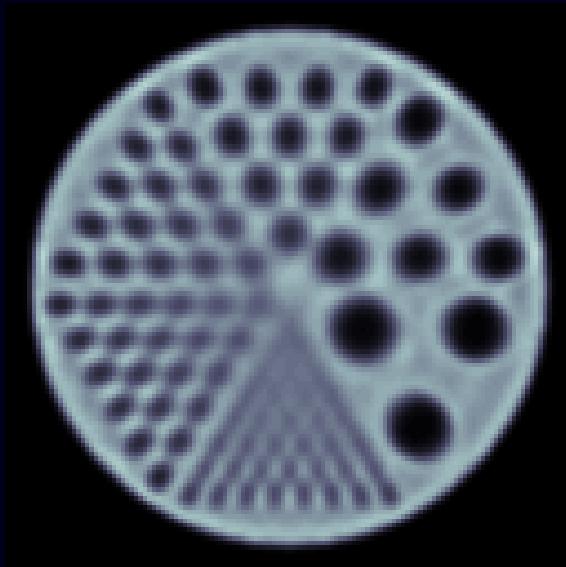
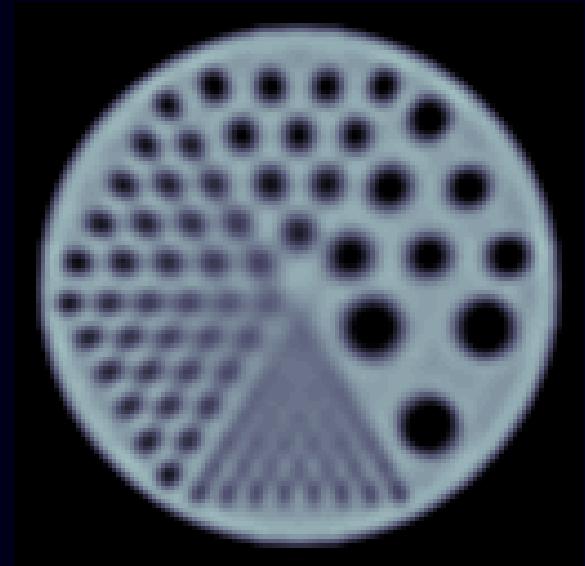
Target filtered object



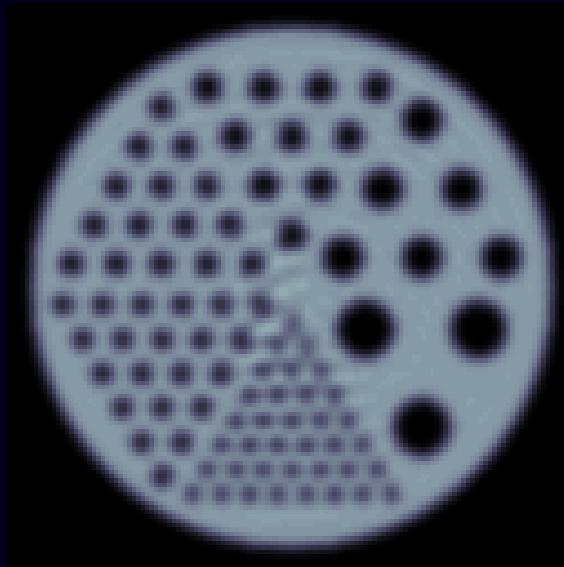
FBP



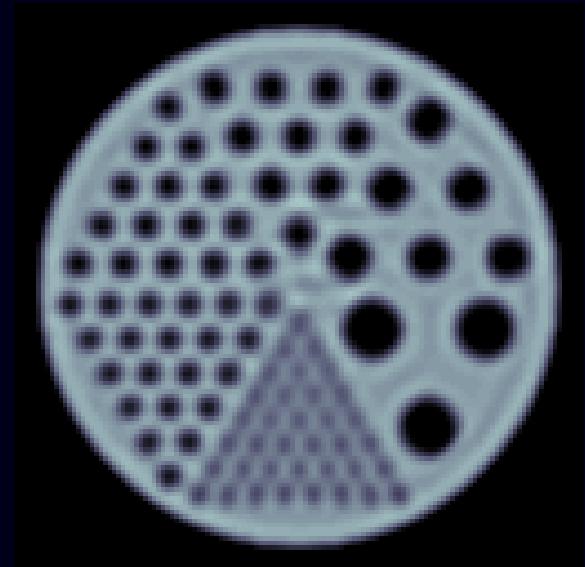
Conventional PWLS



Truncated EM



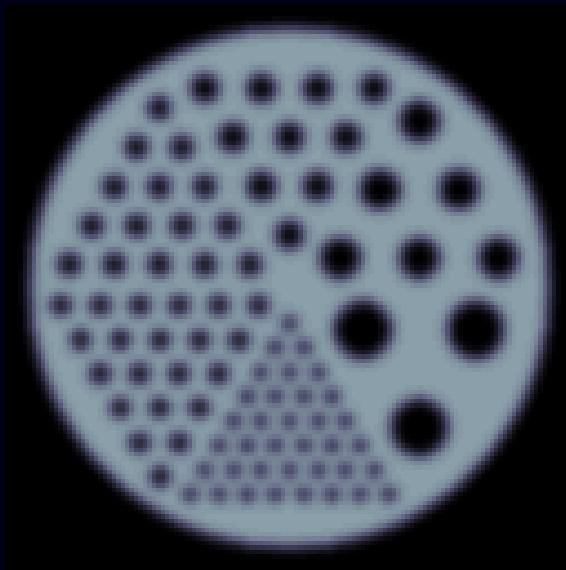
Post-filtered EM



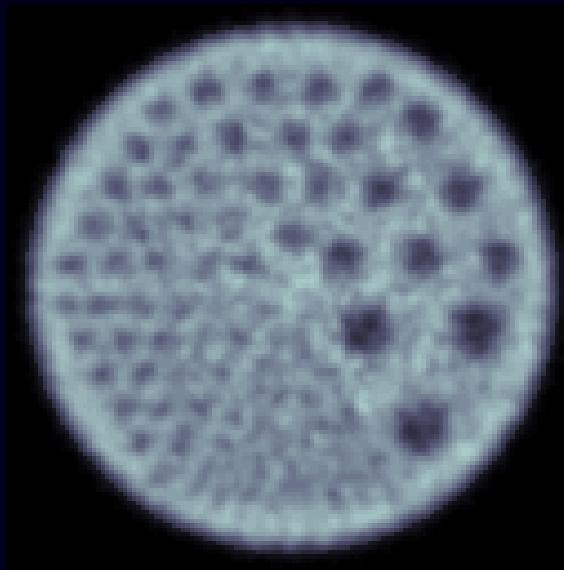
Modified Regularization

Modified Penalty Example, SPECT - Noisy

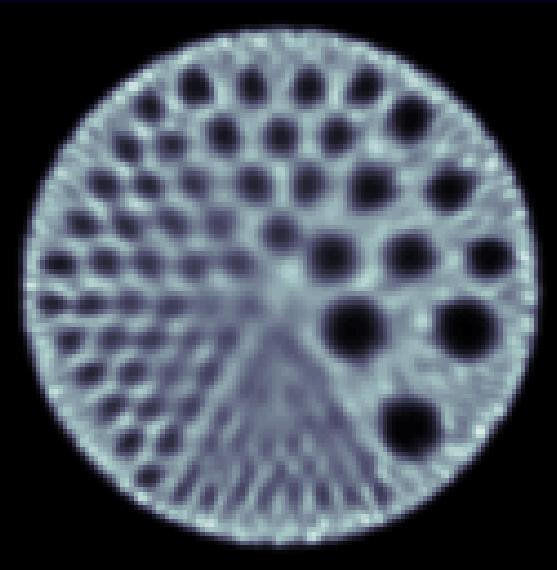
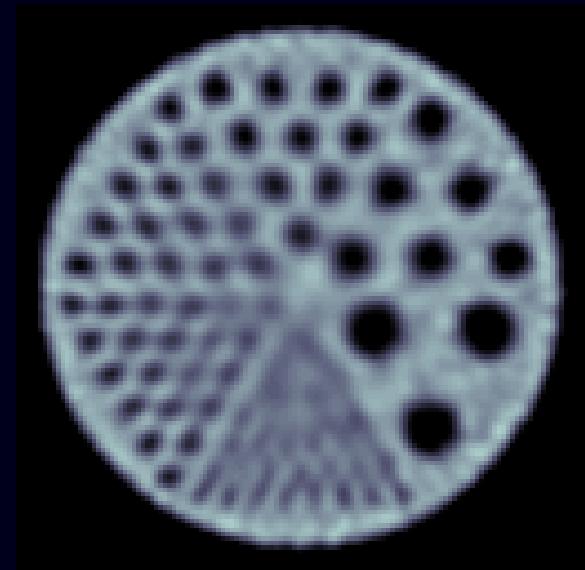
Target filtered object



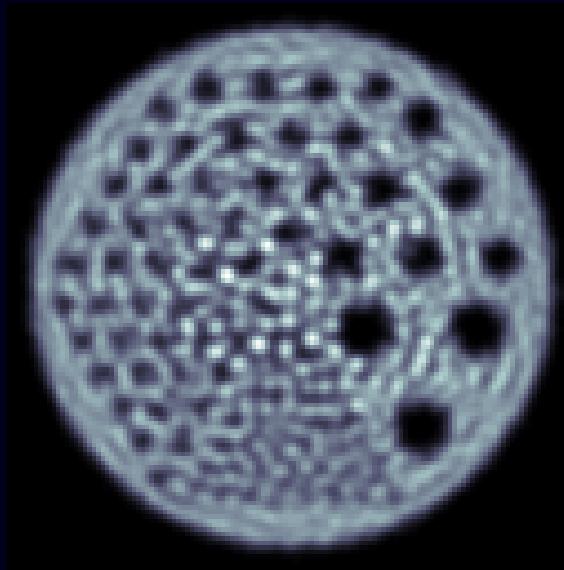
FBP



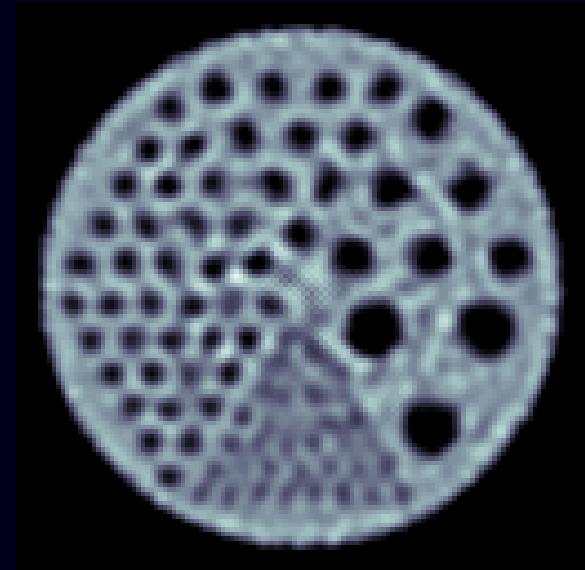
Conventional PWLS



Truncated EM

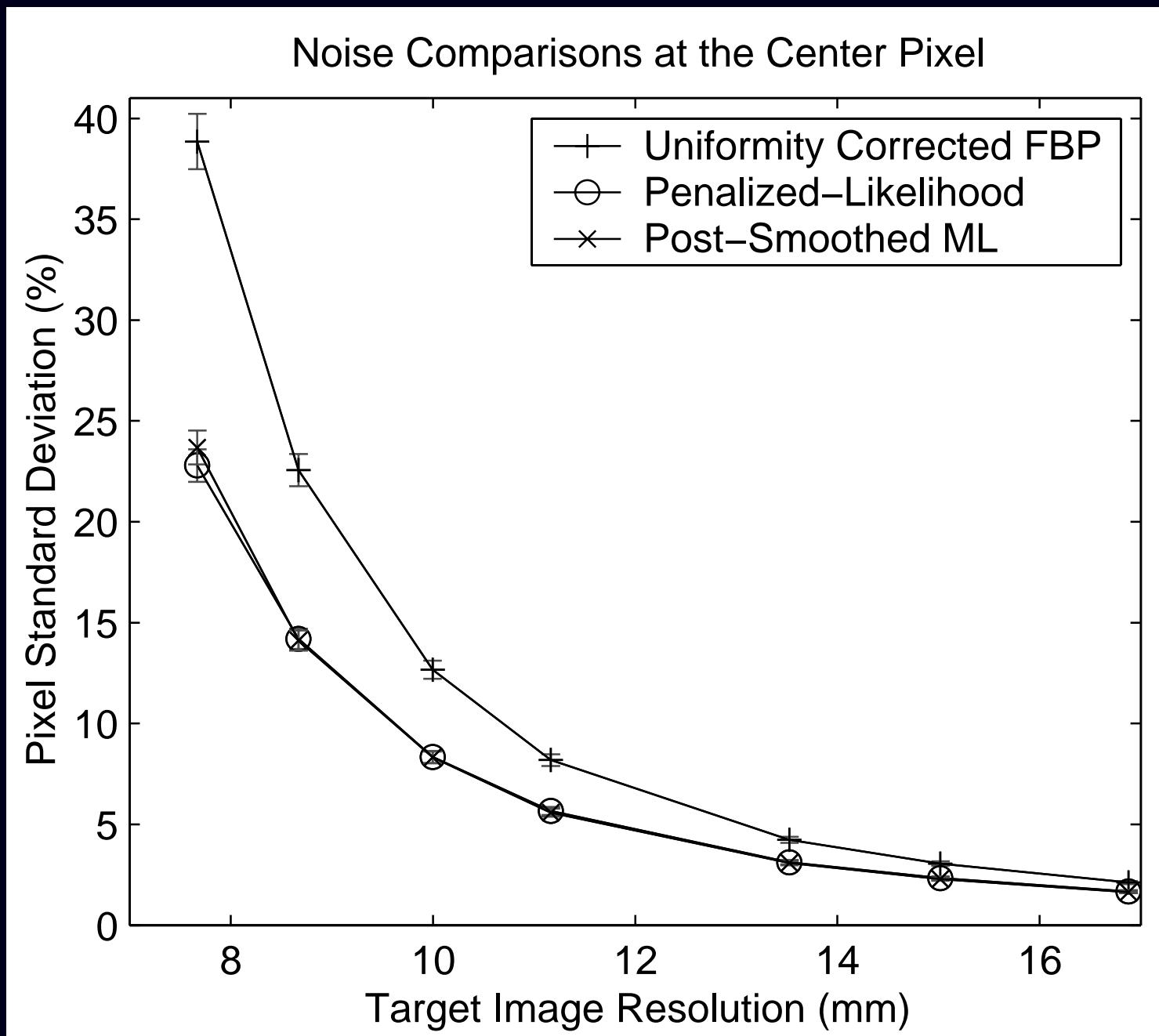


Post-filtered EM



Modified Regularization

Regularized vs Post-filtered, with Matched PSF



Reconstruction Noise Properties

For unconstrained (converged) minimization methods, the estimator is *implicit*:

$$\hat{\mathbf{x}} = \hat{\mathbf{x}}(\mathbf{y}) = \arg \min_{\mathbf{x}} \Psi(\mathbf{x}, \mathbf{y}).$$

What is $\text{Cov}\{\hat{\mathbf{x}}\}$?

New simpler derivation.

Denote the column gradient by $g(\mathbf{x}, \mathbf{y}) \triangleq \nabla_{\mathbf{x}} \Psi(\mathbf{x}, \mathbf{y})$.

Ignoring constraints, the gradient is zero at the minimizer: $g(\hat{\mathbf{x}}(\mathbf{y}), \mathbf{y}) = 0$.

First-order Taylor series expansion:

$$\begin{aligned} g(\hat{\mathbf{x}}, \mathbf{y}) &\approx g(\mathbf{x}^{\text{true}}, \mathbf{y}) + \nabla_{\mathbf{x}} g(\mathbf{x}^{\text{true}}, \mathbf{y})(\hat{\mathbf{x}} - \mathbf{x}^{\text{true}}) \\ &= g(\mathbf{x}^{\text{true}}, \mathbf{y}) + \nabla_{\mathbf{x}}^2 \Psi(\mathbf{x}^{\text{true}}, \mathbf{y})(\hat{\mathbf{x}} - \mathbf{x}^{\text{true}}). \end{aligned}$$

Equating to zero:

$$\hat{\mathbf{x}} \approx \mathbf{x}^{\text{true}} - [\nabla_{\mathbf{x}}^2 \Psi(\mathbf{x}^{\text{true}}, \mathbf{y})]^{-1} \nabla_{\mathbf{x}} \Psi(\mathbf{x}^{\text{true}}, \mathbf{y}).$$

If the Hessian $\nabla_{\mathbf{x}}^2 \Psi$ is weakly dependent on \mathbf{y} , then

$$\text{Cov}\{\hat{\mathbf{x}}\} \approx [\nabla_{\mathbf{x}}^2 \Psi(\mathbf{x}^{\text{true}}, \bar{\mathbf{y}})]^{-1} \text{Cov}\{\nabla_{\mathbf{x}} \Psi(\mathbf{x}^{\text{true}}, \mathbf{y})\} [\nabla_{\mathbf{x}}^2 \Psi(\mathbf{x}^{\text{true}}, \bar{\mathbf{y}})]^{-1}.$$

If we further linearize w.r.t. the data: $g(\mathbf{x}, \mathbf{y}) \approx g(\mathbf{x}, \bar{\mathbf{y}}) + \nabla_{\mathbf{y}} g(\mathbf{x}, \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})$, then

$$\text{Cov}\{\hat{\mathbf{x}}\} \approx [\nabla_{\mathbf{x}}^2 \Psi]^{-1} (\nabla_{\mathbf{x}} \nabla_{\mathbf{y}} \Psi) \text{Cov}\{\mathbf{y}\} (\nabla_{\mathbf{x}} \nabla_{\mathbf{y}} \Psi)' [\nabla_{\mathbf{x}}^2 \Psi]^{-1}.$$

Covariance Continued

Covariance approximation:

$$\text{Cov}\{\hat{x}\} \approx [\nabla_x^2 \Psi(\mathbf{x}^{\text{true}}, \bar{\mathbf{y}})]^{-1} \text{Cov}\{\nabla_{\mathbf{x}} \Psi(\mathbf{x}^{\text{true}}, \mathbf{y})\} [\nabla_x^2 \Psi(\mathbf{x}^{\text{true}}, \bar{\mathbf{y}})]^{-1}$$

Depends only on chosen **cost function** and **statistical model**.
Independent of optimization algorithm.

- Enables prediction of noise properties
- Can make variance images
- Useful for computing ROI variance (e.g., for weighted kinetic fitting)
- Good variance prediction for quadratic regularization in nonzero regions
- Inaccurate for nonquadratic penalties, or in nearly-zero regions

Qi and Huesman's Detection Analysis

SNR of MAP reconstruction > SNR of FBP reconstruction (T-MI, Aug. 2001)

quadratic regularization

SKE/BKE task

prewhitened observer

non-prewhitened observer

Open issues

Choice of regularizer to optimize detectability?
(2002 MIC poster by Fessler & Yendiki.)

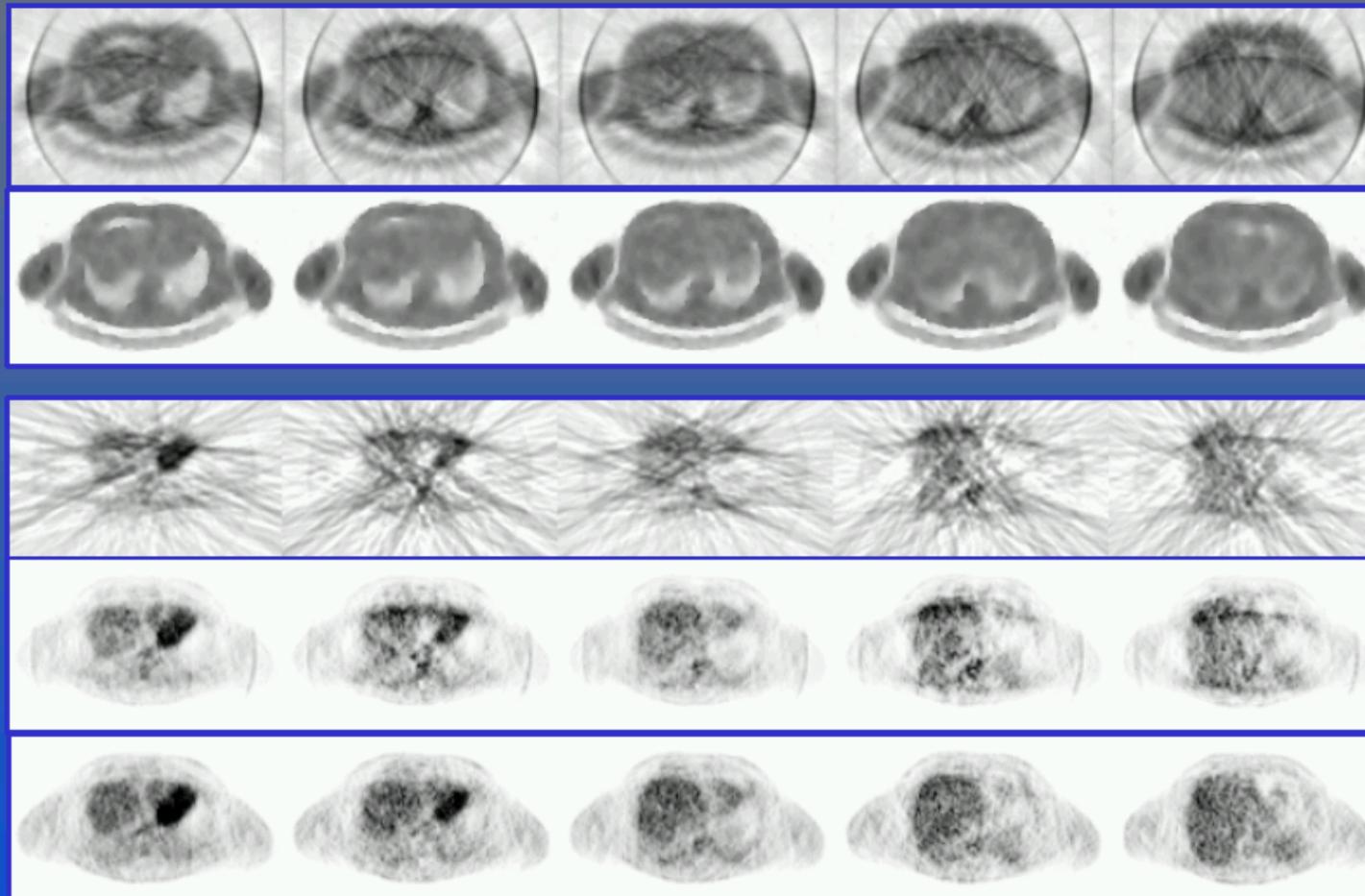
Part 5. Miscellaneous Topics

(Pet peeves and more-or-less recent favorites)

- Short transmission scans
- 3D PET options
- OSEM of transmission data (ugh!)
- Precorrected PET data
- Transmission scan problems
- List-mode EM
- List of other topics I wish I had time to cover...

PET Attenuation Correction (J. Nuyts)

Short transmission scan



Classic
Transm.

M.A.P.
Reconstr.

•Classic
Atten cor
•FBP

•Classic
Atten cor
•MLEM

•M.A.P.
Atten cor
•MLEM

Iterative reconstruction for 3D PET

- Fully 3D iterative reconstruction
- Rebinning / 2.5D iterative reconstruction
- Rebinning / 2D iterative reconstruction
 - PWLS
 - OSEM with attenuation weighting
- 3D FBP
- Rebinning / FBP

OSEM of Transmission Data?

Bai and Kinahan *et al.* “Post-injection single photon transmission tomography with ordered-subset algorithms for whole-body PET imaging”

- 3D penalty better than 2D penalty
- OSTR with 3D penalty better than FBP and OSEM
- standard deviation from a single realization to estimate noise can be misleading

Using OSEM for transmission data requires taking logarithm, whereas OSTR does not.

Precorrected PET data

C. Michel examined shifted-Poisson model, “weighted OSEM” of various flavors.
concluded attenuation weighting matters especially

Transmission Scan Challenges

- Overlapping-beam transmission scans
- Polyenergetic X-ray CT scans
- Sourceless attenuation correction

All can be tackled with optimization transfer methods.

List-mode EM

$$\begin{aligned}x_j^{(n+1)} &= x_j^{(n)} \left[\sum_{i=1}^{n_d} a_{ij} \frac{y_i}{\bar{y}_i^{(n)}} \right] / \left(\sum_{i=1}^{n_d} a_{ij} \right) \\&= \frac{x_j^{(n)}}{\sum_{i=1}^{n_d} a_{ij}} \sum_{i:y_i \neq 0} a_{ij} \frac{y_i}{\bar{y}_i^{(n)}}\end{aligned}$$

- Useful when $\sum_{i=1}^{n_d} y_i \leq \sum_{i=1}^{n_d} 1$
- Attenuation and scatter non-trivial
- Computing a_{ij} on-the-fly
- Computing sensitivity $\sum_{i=1}^{n_d} a_{ij}$ still painful
- List-mode ordered-subsets is naturally balanced

Misc

- 4D regularization (reconstruction of dynamic image sequences)
- “Sourceless” attenuation-map estimation
- Post-injection transmission/emission reconstruction
- μ -value priors for transmission reconstruction
- Local errors in $\hat{\mu}$ propagate into emission image (PET and SPECT)

Summary

- Predictability of resolution / noise and controlling spatial resolution argues for regularized *cost function*
- todo: Still work to be done...



References

- [1] S. Webb. *From the watching of shadows: the origins of radiological tomography*. A. Hilger, Bristol, 1990.
- [2] G. Hounsfield. A method of apparatus for examination of a body by radiation such as x-ray or gamma radiation, 1972. US Patent 1283915. British patent 1283915, London. Issued to EMI Ltd. Filed Aug. 1968. See [1, Ch. 5].
- [3] R. Gordon, R. Bender, and G. T. Herman. Algebraic reconstruction techniques (ART) for the three-dimensional electron microscopy and X-ray photography. *J. Theor. Biol.*, 29:471–81, 1970.
- [4] R. Gordon and G. T. Herman. Reconstruction of pictures from their projections. *Comm. ACM*, 14:759–68, 1971.
- [5] G. T. Herman, A. Lent, and S. W. Rowland. ART: mathematics and applications (a report on the mathematical foundations and on the applicability to real data of the algebraic reconstruction techniques). *J. Theor. Biol.*, 42:1–32, 1973.
- [6] R. Gordon. A tutorial on ART (algebraic reconstruction techniques). *IEEE Tr. Nuc. Sci.*, 21:78–93, 1974.
- [7] R. Richardson. Bayesian-based iterative method of image restoration. *J. Opt. Soc. Am.*, 62(1):55–9, January 1972.
- [8] L. Lucy. An iterative technique for the rectification of observed distributions. *The Astronomical J.*, 79(6):745–54, June 1974.
- [9] A. J. Rockmore and A. Macovski. A maximum likelihood approach to emission image reconstruction from projections. *IEEE Tr. Nuc. Sci.*, 23:1428–32, 1976.
- [10] A. J. Rockmore and A. Macovski. A maximum likelihood approach to transmission image reconstruction from projections. *IEEE Tr. Nuc. Sci.*, 24(3):1929–35, June 1977.
- [11] A. P. Dempster, N. M. Laird, and D. B. Rubin. Maximum likelihood from incomplete data via the EM algorithm. *J. Royal Stat. Soc. Ser. B*, 39(1):1–38, 1977.
- [12] L. A. Shepp and Y. Vardi. Maximum likelihood reconstruction for emission tomography. *IEEE Tr. Med. Im.*, 1(2):113–22, October 1982.
- [13] K. Lange and R. Carson. EM reconstruction algorithms for emission and transmission tomography. *J. Comp. Assisted Tomo.*, 8(2):306–16, April 1984.
- [14] S. Geman and D. E. McClure. Bayesian image analysis: an application to single photon emission tomography. In *Proc. of Stat. Comp. Sect. of Amer. Stat. Assoc.*, pages 12–8, 1985.
- [15] H. M. Hudson and R. S. Larkin. Accelerated image reconstruction using ordered subsets of projection data. *IEEE Tr. Med. Im.*, 13(4):601–9, December 1994.
- [16] M. Goitein. Three-dimensional density reconstruction from a series of two-dimensional projections. *Nucl. Instr. Meth.*, 101(15):509–18, June 1972.
- [17] T. F. Budinger and G. T. Gullberg. Three dimensional reconstruction in nuclear medicine emission imaging. *IEEE Tr. Nuc. Sci.*, 21(3):2–20, 1974.
- [18] R. H. Huesman, G. T. Gullberg, W. L. Greenberg, and T. F. Budinger. *RECLBL library users manual*. Lawrence Berkeley Laboratory, Berkeley, CA, 1977.

- [19] R. H. Huesman. A new fast algorithm for the evaluation of regions of interest and statistical uncertainty in computed tomography. *Phys. Med. Biol.*, 29(5):543–52, 1984.
- [20] D. W. Wilson and B. M. W. Tsui. Noise properties of filtered-backprojection and ML-EM reconstructed emission tomographic images. *IEEE Tr. Nuc. Sci.*, 40(4):1198–1203, August 1993.
- [21] D. W. Wilson and B. M. W. Tsui. Spatial resolution properties of FB and ML-EM reconstruction methods. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 1189–1193, 1993.
- [22] H. H. Barrett, D. W. Wilson, and B. M. W. Tsui. Noise properties of the EM algorithm: I. Theory. *Phys. Med. Biol.*, 39(5):833–46, May 1994.
- [23] D. W. Wilson, B. M. W. Tsui, and H. H. Barrett. Noise properties of the EM algorithm: II. Monte Carlo simulations. *Phys. Med. Biol.*, 39(5):847–72, May 1994.
- [24] J. A. Fessler. Mean and variance of implicitly defined biased estimators (such as penalized maximum likelihood): Applications to tomography. *IEEE Tr. Im. Proc.*, 5(3):493–506, March 1996.
- [25] J. A. Fessler and W. L. Rogers. Spatial resolution properties of penalized-likelihood image reconstruction methods: Space-invariant tomographs. *IEEE Tr. Im. Proc.*, 5(9):1346–58, September 1996.
- [26] W. Wang and G. Gindi. Noise analysis of regularized EM SPECT reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1933–7, 1996.
- [27] C. K. Abbey, E. Clarkson, H. H. Barrett, S. P. Mueller, and F. J. Rybicki. Approximate distributions for maximum likelihood and maximum a posteriori estimates under a Gaussian noise model. In J. Duncan and G. Gindi, editors, *Information Processing in Medical Im.*, pages 167–75. Springer-Verlag, Berlin, 1997.
- [28] W. Wang and G. Gindi. Noise analysis of MAP-EM algorithms for emission tomography. *Phys. Med. Biol.*, 42(11):2215–32, November 1997.
- [29] S. J. Glick and E. J. Soares. Noise characteristics of SPECT iterative reconstruction with a mis-matched projector-backprojector pair. *IEEE Tr. Nuc. Sci.*, 45(4):2183–8, August 1998.
- [30] E. J. Soares, C. L. Byrne, T-S. Pan, S. J. Glick, and M. A. King. Modeling the population covariance matrices of block-iterative expectation-maximization reconstructed images. In *Proc. SPIE 3034, Med. Im. 1997: Im. Proc.*, volume 1, pages 415–25, 1997.
- [31] J. Qi and R. H. Huesman. Theoretical study of lesion detectability of MAP reconstruction using computer observers. *IEEE Tr. Med. Im.*, 20(8):815–22, August 2001.
- [32] J. A. Fessler, I. Elbakri, P. Sukovic, and N. H. Clinthorne. Maximum-likelihood dual-energy tomographic image reconstruction. In *Proc. SPIE 4684, Medical Imaging 2002: Image Proc.*, pages 38–49, 2002.
- [33] Bruno De Man, J. Nuyts, P. Dupont, G. Marchal, and P. Suetens. An iterative maximum-likelihood polychromatic algorithm for CT. *IEEE Tr. Med. Im.*, 20(10):999–1008, October 2001.
- [34] I. A. Elbakri and J. A. Fessler. Statistical image reconstruction for polyenergetic X-ray computed tomography. *IEEE Tr. Med. Im.*, 21(2):89–99, February 2002.

- [35] I. A. Elbakri and J. A. Fessler. Segmentation-free statistical image reconstruction for polyenergetic X-ray computed tomography. In *Proc. IEEE Intl. Symp. Biomedical Imaging*, pages 828–31, 2002.
- [36] P. E. Kinahan, J. A. Fessler, and J. S. Karp. Statistical image reconstruction in PET with compensation for missing data. *IEEE Tr. Nuc. Sci.*, 44(4):1552–7, August 1997.
- [37] J. A. Fessler and B. P. Sutton. Tomographic image reconstruction using the nonuniform FFT. In *SIAM Conf. Imaging Sci., Abstract Book*, page 21, 2002. Invited presentation.
- [38] B. P. Sutton, J. A. Fessler, and D. Noll. A min-max approach to the nonuniform N-D FFT for rapid iterative reconstruction of MR images. In *Proc. Intl. Soc. Mag. Res. Med.*, page 763, 2001.
- [39] B. P. Sutton, D. C. Noll, and J. A. Fessler. Fast, iterative, field-corrected image reconstruction for MRI. In *Proc. IEEE Intl. Symp. Biomedical Imaging*, pages 489–92, 2002.
- [40] J. A. Fessler. Spatial resolution and noise tradeoffs in pinhole imaging system design: A density estimation approach. *Optics Express*, 2(6):237–53, March 1998.
- [41] B. W. Silverman. *Density estimation for statistics and data analysis*. Chapman and Hall, New York, 1986.
- [42] J. A. Sorenson and M. E. Phelps. *Physics in nuclear medicine*. Saunders, Philadelphia, 2 edition, 1987.
- [43] R. D. Evans. *The atomic nucleus*. McGraw-Hill, New York, 1955.
- [44] U. Engeland, T. Striker, and H. Luig. Count-rate statistics of the gamma camera. *Phys. Med. Biol.*, 43(10):2939–47, October 1998.
- [45] D. F. Yu and J. A. Fessler. Mean and variance of singles photon counting with deadtime. *Phys. Med. Biol.*, 45(7):2043–56, July 2000.
- [46] D. F. Yu and J. A. Fessler. Mean and variance of coincidence photon counting with deadtime. *Nucl. Instr. Meth. Phys. Res. A.*, 488(1-2):362–74, August 2002.
- [47] M. A. Limber, M. N. Limber, A. Celler, J. S. Barney, and J. M. Borwein. Direct reconstruction of functional parameters for dynamic SPECT. *IEEE Tr. Nuc. Sci.*, 42(4):1249–56, August 1995.
- [48] G. L. Zeng, G. T. Gullberg, and R. H. Huesman. Using linear time-invariant system theory to estimate kinetic parameters directly from projection measurements. *IEEE Tr. Nuc. Sci.*, 42(6-2):2339–46, December 1995.
- [49] E. Hebbel, D. Oldenburg, T. Farncombe, and A. Celler. Direct estimation of dynamic parameters in SPECT tomography. *IEEE Tr. Nuc. Sci.*, 44(6-2):2425–30, December 1997.
- [50] R. H. Huesman, B. W. Reutter, G. L. Zeng, and G. T. Gullberg. Kinetic parameter estimation from SPECT cone-beam projection measurements. *Phys. Med. Biol.*, 43(4):973–82, April 1998.
- [51] B. W. Reutter, G. T. Gullberg, and R. H. Huesman. Kinetic parameter estimation from attenuated SPECT projection measurements. *IEEE Tr. Nuc. Sci.*, 45(6):3007–13, December 1998.
- [52] H. H. Bauschke, D. Noll, A. Celler, and J. M. Borwein. An EM algorithm for dynamic SPECT. *IEEE Tr. Med. Im.*, 18(3):252–61, March 1999.

- [53] T. Farncombe, A. Celler, D. Noll, J. Maeght, and R. Harrop. Dynamic SPECT imaging using a single camera rotation (dSPECT). *IEEE Tr. Nuc. Sci.*, 46(4-2):1055–61, August 1999.
- [54] J. S. Maltz. Direct recovery of regional tracer kinetics from temporally inconsistent dynamic ECT projections using dimension-reduced time-activity basis. *Phys. Med. Biol.*, 45(11):3413–29, November 2000.
- [55] B. W. Reutter, G. T. Gullberg, and R. H. Huesman. Direct least squares estimation of spatiotemporal distributions from dynamic SPECT projections using a spatial segmentation and temporal B-splines. *IEEE Tr. Med. Im.*, 19(5):434–50, May 2000.
- [56] J. S. Maltz. Optimal time-activity basis selection for exponential spectral analysis: application to the solution of large dynamic emission tomographic reconstruction problems. *IEEE Tr. Nuc. Sci.*, 48(4-2):1452–64, August 2001.
- [57] T. E. Nichols, J. Qi, E. Asma, and R. M. Leahy. Spatiotemporal reconstruction of list mode PET data. *IEEE Tr. Med. Im.*, 21(4):396–404, April 2002.
- [58] B. W. Silverman. Some aspects of the spline smoothing approach to non-parametric regression curve fitting. *J. Royal Stat. Soc. Ser. B*, 47(1):1–52, 1985.
- [59] R Van de Walle, H. H. Barrett, K. J. Myers, M. I. Altbach, B. Desplanques, A. F. Gmitro, J. Cornelis, and I. Lemahieu. Reconstruction of MR images from data acquired on a general non-regular grid by pseudoinverse calculation. *IEEE Tr. Med. Im.*, 19(12):1160–7, December 2000.
- [60] M. Bertero, C De Mol, and E. R. Pike. Linear inverse problems with discrete data, i: General formulation and singular system analysis. *Inverse Prob.*, 1(4):301–30, November 1985.
- [61] E. J. Mazur and R. Gordon. Interpolative algebraic reconstruction techniques without beam partitioning for computed tomography. *Med. Biol. Eng. Comput.*, 33(1):82–6, January 1995.
- [62] Y. Censor. Finite series expansion reconstruction methods. *Proc. IEEE*, 71(3):409–419, March 1983.
- [63] D. L. Snyder. Utilizing side information in emission tomography. *IEEE Tr. Nuc. Sci.*, 31(1):533–7, February 1984.
- [64] R. E. Carson, M. V. Green, and S. M. Larson. A maximum likelihood method for calculation of tomographic region-of-interest (ROI) values. *J. Nuc. Med.*, 26:P20, 1985.
- [65] R. E. Carson and K. Lange. The EM parametric image reconstruction algorithm. *J. Am. Stat. Ass.*, 80(389):20–2, March 1985.
- [66] R. E. Carson. A maximum likelihood method for region-of-interest evaluation in emission tomography. *J. Comp. Assisted Tomo.*, 10(4):654–63, July 1986.
- [67] A. R. Formiconi. Least squares algorithm for region-of-interest evaluation in emission tomography. *IEEE Tr. Med. Im.*, 12:90–100, 1993.
- [68] D. J. Rossi and A. S. Willsky. Reconstruction from projections based on detection and estimation of objects—Parts i & II: Performance analysis and robustness analysis. *IEEE Tr. Acoust. Sp. Sig. Proc.*, 32(4):886–906, August 1984.
- [69] S P Müller, M. F. Kijewski, S. C. Moore, and B. L. Holman. Maximum-likelihood estimation: a mathematical model for quantitation in nuclear medicine. *J. Nuc. Med.*, 31(10):1693–701, October 1990.

- [70] P. C. Chiao, W. L. Rogers, N. H. Clinthorne, J. A. Fessler, and A. O. Hero. Model-based estimation for dynamic cardiac studies using ECT. *IEEE Tr. Med. Im.*, 13(2):217–26, June 1994.
- [71] Z. P. Liang, F. E. Boada, R. T. Constable, E. M. Haacke, P. C. Lauterbur, and M. R. Smith. Constrained reconstruction methods in MR imaging. *Reviews of Magnetic Resonance in Medicine*, 4:67–185, 1992.
- [72] G. S. Cunningham and A. Lehovich. 4D reconstructions from low-count SPECT data using deformable models with smooth interior intensity variations. In *Proc. SPIE 3979: Medical Imaging 2000: Image Proc.*, 2000.
- [73] J. Qi, R. M. Leahy, E. U. Mumcuoglu, S. R. Cherry, A. Chatzioannou, and T. H. Farquhar. High resolution 3D Bayesian image reconstruction for microPET. In *Conf. Record, 1997 Int'l Meeting on Fully 3D Image Recon. in Rad. and Nuc. Med*, 1997.
- [74] T. Hebert, R. Leahy, and M. Singh. Fast MLE for SPECT using intermediate polar representation and a stopping criterion. *IEEE Tr. Nuc. Sci.*, 35(1):615–9, 1988.
- [75] T. J. Hebert and R. Leahy. Fast methods for including attenuation in the EM algorithm. *IEEE Tr. Nuc. Sci.*, 37(2):754–758, April 1990.
- [76] C. A. Johnson, Y. Yan, R. E. Carson, R. L. Martino, and M. E. Daube-Witherspoon. A system for the 3D reconstruction of retracted-septa PET data using the EM algorithm. *IEEE Tr. Nuc. Sci.*, 42(4):1223–7, August 1995.
- [77] J. M. Ollinger and A. Goggin. Maximum likelihood reconstruction in fully 3D PET via the SAGE algorithm. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1594–8, 1996.
- [78] E V R Di Bella, A. B. Barclay, R. L. Eisner, and R. W. Schafer. Comparison of rotation-based methods for iterative reconstruction algorithms. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 1146–50, 1995.
- [79] M. I. Miller and B. Roysam. Bayesian image reconstruction for emission tomography incorporating Good's roughness prior on massively parallel processors. *Proc. Natl. Acad. Sci.*, 88:3223–3227, April 1991.
- [80] A. W. McCarthy and M. I. Miller. Maximum likelihood SPECT in clinical computation times using mesh-connected parallel processors. *IEEE Tr. Med. Im.*, 10(3):426–436, September 1991.
- [81] T. R. Miller and J. W. Wallis. Fast maximum-likelihood reconstruction. *J. Nuc. Med.*, 33(9):1710–11, September 1992.
- [82] B. E. Oppenheim. More accurate algorithms for iterative 3-dimensional reconstruction. *IEEE Tr. Nuc. Sci.*, 21:72–77, June 1974.
- [83] T. M. Peters. Algorithm for fast back- and reprojection in computed tomography. *IEEE Tr. Nuc. Sci.*, 28(4):3641–3647, August 1981.
- [84] P. M. Joseph. An improved algorithm for reprojecting rays through pixel images. *IEEE Tr. Med. Im.*, 1(3):192–6, November 1982.
- [85] R. L. Siddon. Fast calculation of the exact radiological path for a three-dimensional CT array. *Med. Phys.*, 12(2):252–255, March 1985.
- [86] R. Schwinger, S. Cool, and M. King. Area weighted convolutional interpolation for data reprojection in single photon emission computed tomography. *Med. Phys.*, 13(3):350–355, May 1986.
- [87] S. C. B. Lo. Strip and line path integrals with a square pixel matrix: A unified theory for computational CT projections. *IEEE Tr. Med. Im.*, 7(4):355–363, December 1988.

- [88] Z. H. Cho, C. M. Chen, and S. Y. Lee. Incremental algorithm—a new fast backprojection scheme for parallel geometries. *IEEE Tr. Med. Im.*, 9(2):207–17, June 1990.
- [89] K. Ziernons, H. Herzog, P. Bosetti, and L. E. Feinendegen. Iterative image reconstruction with weighted pixel contributions to projection elements. *Eur. J. Nuc. Med.*, 19:587, 1992.
- [90] Y. J. He, A. Cai, and J. A. Sun. Incremental backprojection algorithm: modification of the searching flow scheme and utilization of the relationship among projection views. *IEEE Tr. Med. Im.*, 12(3):555–559, September 1993.
- [91] B. Sahiner and A. E. Yagle. A fast algorithm for backprojection with linear interpolation. *IEEE Tr. Im. Proc.*, 2(4):547–549, October 1993.
- [92] D. C. Yu and S. C. Huang. Study of reprojection methods in terms of their resolution loss and sampling errors. *IEEE Tr. Nuc. Sci.*, 40(4):1174–1178, August 1993.
- [93] P. Schmidlin. Improved iterative image reconstruction using variable projection binning and abbreviated convolution. *Eur. J. Nuc. Med.*, 21(9):930–6, September 1994.
- [94] W. Zhuang, S. S. Gopal, and T. J. Hebert. Numerical evaluation of methods for computing tomographic projections. *IEEE Tr. Nuc. Sci.*, 41(4):1660–1665, August 1994.
- [95] E. L. Johnson, H. Wang, J. W. McCormick, K. L. Greer, R. E. Coleman, and R. J. Jaszcak. Pixel driven implementation of filtered backprojection for reconstruction of fan beam SPECT data using a position dependent effective projection bin length. *Phys. Med. Biol.*, 41(8):1439–52, August 1996.
- [96] H W A M de Jong, E. T. P. Slijpen, and F. J. Beekman. Acceleration of Monte Carlo SPECT simulation using convolution-based forced detection. *IEEE Tr. Nuc. Sci.*, 48(1):58–64, February 2001.
- [97] C. W. Stearns and J. A. Fessler. 3D PET Reconstruction with FORE and WLS-OS-EM. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, 2002. To appear.
- [98] M. Yavuz and J. A. Fessler. Objective functions for tomographic reconstruction from randoms-precorrected PET scans. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 1067–71, 1996.
- [99] M. Yavuz and J. A. Fessler. New statistical models for randoms-precorrected PET scans. In J. Duncan and G. Gindi, editors, *Information Processing in Medical Im.*, volume 1230 of *Lecture Notes in Computer Science*, pages 190–203. Springer Verlag, Berlin, 1997.
- [100] M. Yavuz and J. A. Fessler. Statistical image reconstruction methods for randoms-precorrected PET scans. *Med. Im. Anal.*, 2(4):369–78, December 1998.
- [101] M. Yavuz and J. A. Fessler. Penalized-likelihood estimators and noise analysis for randoms-precorrected PET transmission scans. *IEEE Tr. Med. Im.*, 18(8):665–74, August 1999.
- [102] D. L. Snyder, A. M. Hammoud, and R. L. White. Image recovery from data acquired with a charge-couple-device camera. *J. Opt. Soc. Am. A*, 10(5):1014–23, May 1993.
- [103] D. L. Snyder, C. W. Helstrom, A. D. Lanterman, M. Faisal, and R. L. White. Compensation for readout noise in CCD images. *J. Opt. Soc. Am. A*, 12(2):272–83, February 1995.

- [104] J. A. Fessler. Penalized weighted least-squares image reconstruction for positron emission tomography. *IEEE Tr. Med. Im.*, 13(2):290–300, June 1994.
- [105] C. Comtat, P. E. Kinahan, M. Defrise, C. Michel, and D. W. Townsend. Fast reconstruction of 3D PET data with accurate statistical modeling. *IEEE Tr. Nuc. Sci.*, 45(3):1083–9, June 1998.
- [106] B. R. W. Signal statistics in x-ray computed tomography. In *Proc. SPIE 4682, Medical Imaging 2002: Med. Phys.*, 2002.
- [107] B. R. Whiting, L. J. Montagnino, and D. G. Politte. Modeling X-ray computed tomography sinograms, 2001. submitted to mp.
- [108] A. O. Hero, J. A. Fessler, and M. Usman. Exploring estimator bias-variance tradeoffs using the uniform CR bound. *IEEE Tr. Sig. Proc.*, 44(8):2026–41, August 1996.
- [109] E. Mumcuoglu, R. Leahy, S. Cherry, and E. Hoffman. Accurate geometric and physical response modeling for statistical image reconstruction in high resolution PET scanners. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1569–73, 1996.
- [110] P. J. Green. Iteratively reweighted least squares for maximum likelihood estimation, and some robust and resistant alternatives. *J. Royal Stat. Soc. Ser. B*, 46(2):149–92, 1984.
- [111] J. M. M. Anderson, B. A. Mair, M. Rao, and C. H. Wu. A weighted least-squares method for PET. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 1292–6, 1995.
- [112] J. M. M. Anderson, B. A. Mair, M. Rao, and C-H. Wu. Weighted least-squares reconstruction methods for positron emission tomography. *IEEE Tr. Med. Im.*, 16(2):159–65, April 1997.
- [113] P. J. Huber. *Robust statistics*. Wiley, New York, 1981.
- [114] C. Bouman and K. Sauer. A generalized Gaussian image model for edge-preserving MAP estimation. *IEEE Tr. Im. Proc.*, 2(3):296–310, July 1993.
- [115] E. Tanaka. Improved iterative image reconstruction with automatic noise artifact suppression. *IEEE Tr. Med. Im.*, 11(1):21–7, March 1992.
- [116] B. W. Silverman, M. C. Jones, J. D. Wilson, and D. W. Nychka. A smoothed EM approach to indirect estimation problems, with particular reference to stereology and emission tomography. *J. Royal Stat. Soc. Ser. B*, 52(2):271–324, 1990.
- [117] T. R. Miller, J. W. Wallis, C. S. Butler, M. I. Miller, and D. L. Snyder. Improved brain SPECT by maximum-likelihood reconstruction. *J. Nuc. Med. (Abs. Book)*, 33(5):964, May 1992.
- [118] F. J. Beekman, E. T. P. Slijpen, and W. J. Niessen. Selection of task-dependent diffusion filters for the post-processing of SPECT images. *Phys. Med. Biol.*, 43(6):1713–30, June 1998.
- [119] D. S. Lalush and B. M. Tsui. Performance of ordered-subset reconstruction algorithms under conditions of extreme attenuation and truncation in myocardial SPECT. *J. Nuc. Med.*, 41(4):737–44, April 2000.
- [120] E. T. P. Slijpen and F. J. Beekman. Comparison of post-filtering and filtering between iterations for SPECT reconstruction. *IEEE Tr. Nuc. Sci.*, 46(6):2233–8, December 1999.

- [121] R. H. Huesman. The effects of a finite number of projection angles and finite lateral sampling of projections on the propagation of statistical errors in transverse section reconstruction. *Phys. Med. Biol.*, 22(3):511–521, 1977.
- [122] D. L. Snyder and M. I. Miller. The use of sieves to stabilize images produced with the EM algorithm for emission tomography. *IEEE Tr. Nuc. Sci.*, 32(5):3864–71, October 1985.
- [123] D. L. Snyder, M. I. Miller, L. J. Thomas, and D. G. Politte. Noise and edge artifacts in maximum-likelihood reconstructions for emission tomography. *IEEE Tr. Med. Im.*, 6(3):228–38, September 1987.
- [124] T. R. Miller and J. W. Wallis. Clinically important characteristics of maximum-likelihood reconstruction. *J. Nuc. Med.*, 33(9):1678–84, September 1992.
- [125] A. Tikhonov and V. Arsenin. *Solution of ill-posed problems*. Wiley, New York, 1977.
- [126] I Csiszár. Why least squares and maximum entropy? An axiomatic approach to inference for linear inverse problems. *Ann. Stat.*, 19(4):2032–66, 1991.
- [127] D. L. Donoho, I. M. Johnstone, A. S. Stern, and JC. Hoch. Does the maximum entropy method improve sensitivity. *Proc. Natl. Acad. Sci.*, 87(13):5066–8, July 1990.
- [128] D. L. Donoho, I. M. Johnstone, J. C. Hoch, and A. S. Stern. Maximum entropy and the nearly black object. *J. Royal Stat. Soc. Ser. B*, 54(1):41–81, 1992.
- [129] R. T. Constable and R. M. Henkelman. Why MEM does not work in MR image reconstruction. *Magnetic Resonance in Medicine*, 14(1):12–25, April 1990.
- [130] A. H. Delaney and Y. Bresler. A fast and accurate Fourier algorithm for iterative parallel-beam tomography. *IEEE Tr. Im. Proc.*, 5(5):740–53, May 1996.
- [131] S. J. Lee, A. Rangarajan, and G. Gindi. A comparative study of the effects of using higher order mechanical priors in SPECT reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 4, pages 1696–1700, 1994.
- [132] S-J. Lee, A. Rangarajan, and G. Gindi. Bayesian image reconstruction in SPECT using higher order mechanical models as priors. *IEEE Tr. Med. Im.*, 14(4):669–80, December 1995.
- [133] S. Geman and D. Geman. Stochastic relaxation, Gibbs distributions, and Bayesian restoration of images. *IEEE Tr. Patt. Anal. Mach. Int.*, 6(6):721–41, November 1984.
- [134] B. W. Silverman, C. Jennison, J. Stander, and T. C. Brown. The specification of edge penalties for regular and irregular pixel images. *IEEE Tr. Patt. Anal. Mach. Int.*, 12(10):1017–24, October 1990.
- [135] V. E. Johnson, W. H. Wong, X. Hu, and C. T. Chen. Image restoration using Gibbs priors: Boundary modeling, treatment of blurring, and selection of hyperparameter. *IEEE Tr. Patt. Anal. Mach. Int.*, 13(5):413–25, May 1991.
- [136] V. E. Johnson. A model for segmentation and analysis of noisy images. *J. Am. Stat. Ass.*, 89(425):230–41, March 1994.

- [137] S. Alenius and U. Ruotsalainen. Bayesian image reconstruction for emission tomography based on median root prior. *Eur. J. Nuc. Med.*, 24(3):258–65, 1997.
- [138] S. Alenius, U. Ruotsalainen, and J. Astola. Using local median as the location of the prior distribution in iterative emission tomography image reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, page 1726, 1997.
- [139] S. Alenius, U. Ruotsalainen, and J. Astola. Using local median as the location of the prior distribution in iterative emission tomography image reconstruction. *IEEE Tr. Nuc. Sci.*, 45(6):3097–104, December 1998.
- [140] I-T. Hsiao, A. Ragharajan, and G. Gindi. A new convex edge-preserving median prior with applications to tomography, 2002.
- [141] M. Nikolova. Thresholding implied by truncated quadratic regularization. *IEEE Tr. Sig. Proc.*, 48(12):3437–50, December 2000.
- [142] A. Antoniadis and J. Fan. Regularization and wavelet approximations. *J. Am. Stat. Ass.*, 96(455):939–55, September 2001.
- [143] D. F. Yu and J. A. Fessler. Edge-preserving tomographic reconstruction with nonlocal regularization. In *Proc. IEEE Intl. Conf. on Image Processing*, volume 1, pages 29–33, 1998.
- [144] D. F. Yu and J. A. Fessler. Edge-preserving tomographic reconstruction with nonlocal regularization. *IEEE Tr. Med. Im.*, 21(2):159–73, February 2002.
- [145] J. Ye, Y. Bresler, and P. Moulin. A self-referencing level-set method for image reconstruction from sparse fourier samples. In *Proc. IEEE Intl. Conf. on Image Processing*, volume 2, pages 33–6, 2001.
- [146] M. J. Black and A. Rangarajan. On the unification of line processes, outlier rejection, and robust statistics with applications in early vision. *Intl. J. Comp. Vision*, 19(1):57–91, July 1996.
- [147] J. W. Stayman and J. A. Fessler. Regularization for uniform spatial resolution properties in penalized-likelihood image reconstruction. *IEEE Tr. Med. Im.*, 19(6):601–15, June 2000.
- [148] J. W. Stayman and J. A. Fessler. Nonnegative definite quadratic penalty design for penalized-likelihood reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, pages M1–1, 2001.
- [149] C. T. Chen, X. Ouyang, W. H. Wong, and X. Hu. Improvement of PET image reconstruction using high-resolution anatomic images. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, page 2062, 1991. (Abstract.).
- [150] R. Leahy and X. H. Yan. Statistical models and methods for PET image reconstruction. In *Proc. of Stat. Comp. Sect. of Amer. Stat. Assoc.*, pages 1–10, 1991.
- [151] J. A. Fessler, N. H. Clinthorne, and W. L. Rogers. Regularized emission image reconstruction using imperfect side information. *IEEE Tr. Nuc. Sci.*, 39(5):1464–71, October 1992.
- [152] I. G. Zubal, M. Lee, A. Rangarajan, C. R. Harrell, and G. Gindi. Bayesian reconstruction of SPECT images using registered anatomical images as priors. *J. Nuc. Med. (Abs. Book)*, 33(5):963, May 1992.
- [153] G. Gindi, M. Lee, A. Rangarajan, and I. G. Zubal. Bayesian reconstruction of functional images using anatomical information as priors. *IEEE Tr. Med. Im.*, 12(4):670–680, December 1993.

- [154] X. Ouyang, W. H. Wong, V. E. Johnson, X. Hu, and C-T. Chen. Incorporation of correlated structural images in PET image reconstruction. *IEEE Tr. Med. Im.*, 13(4):627, December 1994.
- [155] S. J. Lee, G. R. Gindi, I. G. Zubal, and A. Rangarajan. Using ground-truth data to design priors in Bayesian SPECT reconstruction. In Y. Bizais, C. Barillot, and R. D. Paola, editors, *Information Processing in Medical Im.* Kluwer, ?, 1995.
- [156] J. E. Bowsher, V. E. Johnson, T. G. Turkington, R. J. Jaszczak, C. E. Floyd, and R. E. Coleman. Bayesian reconstruction and use of anatomical a priori information for emission tomography. *IEEE Tr. Med. Im.*, 15(5):673–86, October 1996.
- [157] S. Sastry and R. E. Carson. Multimodality Bayesian algorithm for image reconstruction in positron emission tomography: a tissue composition model. *IEEE Tr. Med. Im.*, 16(6):750–61, December 1997.
- [158] R. Piramuthu and A. O. Hero. Side information averaging method for PML emission tomography. In *Proc. IEEE Intl. Conf. on Image Processing*, 1998.
- [159] C. Comtat, P. E. Kinahan, J. A. Fessler, T. Beyer, D. W. Townsend, M. Defrise, and C. Michel. Reconstruction of 3d whole-body PET data using blurred anatomical labels. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1651–5, 1998.
- [160] A. O. Hero, R. Piramuthu, S. R. Titus, and J. A. Fessler. Minimax emission computed tomography using high resolution anatomical side information and B-spline models. *IEEE Tr. Info. Theory*, 45(3):920–38, April 1999.
- [161] Y. S. Shim and Z. H. Cho. SVD pseudoinversion image reconstruction. *IEEE Tr. Acoust. Sp. Sig. Proc.*, 29(4):904–909, August 1981.
- [162] U. Raff, D. N. Stroud, and W. R. Hendee. Improvement of lesion detection in scintigraphic images by SVD techniques for resolution recovery. *IEEE Tr. Med. Im.*, 5(1):35–44, March 1986.
- [163] D. A. Fish, J. Grochmalicki, and E. R. Pike. Scanning SVD method for restoration of images with space-variant blur. *J. Opt. Soc. Am. A*, 13(3):464–9, March 1996.
- [164] A. Caponnetto and M. Bertero. Tomography with a finite set of projections: singular value decomposition and resolution. *Inverse Prob.*, 13(5):1191–1205, October 1997.
- [165] A. K. Louis. Incomplete data problems in x-ray computerized tomography. I. Singular value decomposition of the limited angle transform. *Numerische Mathematik*, 48(3):251–62, 1986.
- [166] F. Natterer. Numerical treatment of ill-posed problems. In G. Talenti, editor, *Inverse Prob.*, volume 1225, pages 142–67. Berlin, Springer, 1986. Lecture Notes in Math.
- [167] R. C. Liu and L. D. Brown. Nonexistence of informative unbiased estimators in singular problems. *Ann. Stat.*, 21(1):1–13, March 1993.
- [168] J. Ory and R. G. Pratt. Are our parameter estimators biased? The significance of finite-different regularization operators. *Inverse Prob.*, 11(2):397–424, April 1995.
- [169] I. M. Johnstone. On singular value decompositions for the Radon Transform and smoothness classes of functions. Technical Report 310, Dept. of Statistics, Stanford, January 1989.

- [170] M. F. Smith, C. E. Floyd, R. J. Jaszczak, and R. E. Coleman. Reconstruction of SPECT images using generalized matrix inverses. *IEEE Tr. Med. Im.*, 11(2), June 1992.
- [171] M. Lavielle. A stochastic algorithm for parametric and non-parametric estimation in the case of incomplete data. *Signal Processing*, 42(1):3–17, 1995.
- [172] W. H. Press, B. P. Flannery, S. A. Teukolsky, and W. T. Vetterling. *Numerical recipes in C*. Cambridge Univ. Press, New York, 1988.
- [173] K. Sauer and C. Bouman. Bayesian estimation of transmission tomograms using local optimization operations. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 2089–93, 1991.
- [174] K. Sauer and C. Bouman. Bayesian estimation of transmission tomograms using segmentation based optimization. *IEEE Tr. Nuc. Sci.*, 39(4):1144–52, August 1992.
- [175] D. P. Bertsekas and S. K. Mitter. A descent numerical method for optimization problems with nondifferentiable cost functionals. *SIAM J. Control*, 1:637–52, 1973.
- [176] W. C. Davidon. Variable metric methods for minimization. Technical Report ANL-5990, AEC Research and Development Report, Argonne National Laboratory, USA, 1959.
- [177] H. F. Khalfan, R. H. Byrd, and R. B. Schnabel. A theoretical and experimental study of the symmetric rank-one update. *SIAM J. Optim.*, 3(1):1–24, 1993.
- [178] C. Zhu, R. H. Byrd, P. Lu, and J. Nocedal. Algorithm 778: L-BFGS-B: Fortran subroutines for large-scale bound-constrained optimization. *ACM Tr. Math. Software*, 23(4):550–60, December 1997.
- [179] T. G. Kolda, D. P. O’Leary, and L. Nazareth. BFGS with update skipping and varying memory. *SIAM J. Optim.*, 8(4):1060–83, 1998.
- [180] K. Lange. *Numerical analysis for statisticians*. Springer-Verlag, New York, 1999.
- [181] B. T. Polyak. *Introduction to optimization*. Optimization Software Inc, New York, 1987.
- [182] D. P. Bertsekas. *Constrained optimization and Lagrange multiplier methods*. Academic-Press, New York, 1982.
- [183] R. H. Byrd, P. Lu, J. Nocedal, and C. Zhu. A limited memory algorithm for bound constrained optimization. *SIAM J. Sci. Comp.*, 16:1190–1208, 1995.
- [184] L. Kaufman. Reduced storage, Quasi-Newton trust region approaches to function optimization. *SIAM J. Optim.*, 10(1):56–69, 1999.
- [185] M. Hanke, J. G. Nagy, and C. Vogel. Quasi-Newton approach to nonnegative image restorations. *Linear Algebra and its Applications*, 316(1):223–36, September 2000.
- [186] J. L. Morales and J. Nocedal. Automatic preconditioning by limited memory Quasi-Newton updating. *SIAM J. Optim.*, 10(4):1079–96, 2000.
- [187] R. R. Meyer. Sufficient conditions for the convergence of monotonic mathematical programming algorithms. *J. Comput. System. Sci.*, 12(1):108–21, 1976.

- [188] L. Kaufman. Implementing and accelerating the EM algorithm for positron emission tomography. *IEEE Tr. Med. Im.*, 6(1):37–51, March 1987.
- [189] N. H. Clinthorne, T. S. Pan, P. C. Chiao, W. L. Rogers, and J. A. Stamos. Preconditioning methods for improved convergence rates in iterative reconstructions. *IEEE Tr. Med. Im.*, 12(1):78–83, March 1993.
- [190] J. A. Fessler and S. D. Booth. Conjugate-gradient preconditioning methods for shift-variant PET image reconstruction. *IEEE Tr. Im. Proc.*, 8(5):688–99, May 1999.
- [191] E. U. Mumcuoglu, R. Leahy, S. R. Cherry, and Z. Zhou. Fast gradient-based methods for Bayesian reconstruction of transmission and emission PET images. *IEEE Tr. Med. Im.*, 13(3):687–701, December 1994.
- [192] E Ü Mumcuoglu, R. M. Leahy, and S. R. Cherry. Bayesian reconstruction of PET images: methodology and performance analysis. *Phys. Med. Biol.*, 41(9):1777–1807, September 1996.
- [193] J. A. Fessler and A. O. Hero. Space-alternating generalized expectation-maximization algorithm. *IEEE Tr. Sig. Proc.*, 42(10):2664–77, October 1994.
- [194] J. A. Fessler and A. O. Hero. Penalized maximum-likelihood image reconstruction using space-alternating generalized EM algorithms. *IEEE Tr. Im. Proc.*, 4(10):1417–29, October 1995.
- [195] J. A. Fessler, E. P. Ficaro, N. H. Clinthorne, and K. Lange. Grouped-coordinate ascent algorithms for penalized-likelihood transmission image reconstruction. *IEEE Tr. Med. Im.*, 16(2):166–75, April 1997.
- [196] J. A. Fessler and A. O. Hero. Space-alternating generalized EM algorithms for penalized maximum-likelihood image reconstruction. Technical Report 286, Comm. and Sign. Proc. Lab., Dept. of EECS, Univ. of Michigan, Ann Arbor, MI, 48109-2122, February 1994.
- [197] J. A. Browne and A. R. D. Pierro. A row-action alternative to the EM algorithm for maximizing likelihoods in emission tomography. *IEEE Tr. Med. Im.*, 15(5):687–99, October 1996.
- [198] C. L. Byrne. Block-iterative methods for image reconstruction from projections. *IEEE Tr. Im. Proc.*, 5(5):792–3, May 1996.
- [199] C. L. Byrne. Convergent block-iterative algorithms for image reconstruction from inconsistent data. *IEEE Tr. Im. Proc.*, 6(9):1296–304, September 1997.
- [200] C. L. Byrne. Accelerating the EMML algorithm and related iterative algorithms by rescaled block-iterative methods. *IEEE Tr. Im. Proc.*, 7(1):100–9, January 1998.
- [201] M. E. Daube-Witherspoon and G. Muehllehner. An iterative image space reconstruction algorithm suitable for volume ECT. *IEEE Tr. Med. Im.*, 5(2):61–66, June 1986.
- [202] J. M. Ollinger. Iterative reconstruction-reprojection and the expectation-maximization algorithm. *IEEE Tr. Med. Im.*, 9(1):94–8, March 1990.
- [203] A R De Pierro. On the relation between the ISRA and the EM algorithm for positron emission tomography. *IEEE Tr. Med. Im.*, 12(2):328–33, June 1993.
- [204] P. J. Green. Bayesian reconstructions from emission tomography data using a modified EM algorithm. *IEEE Tr. Med. Im.*, 9(1):84–93, March 1990.

- [205] P. J. Green. On use of the EM algorithm for penalized likelihood estimation. *J. Royal Stat. Soc. Ser. B*, 52(3):443–452, 1990.
- [206] K. Sauer and C. Bouman. A local update strategy for iterative reconstruction from projections. *IEEE Tr. Sig. Proc.*, 41(2):534–48, February 1993.
- [207] K. G. Murty. *Linear complementarity, linear and nonlinear programming*. Helderman Verlag, Berlin, 1988.
- [208] C. A. Bouman, K. Sauer, and S. S. Saquib. Tractable models and efficient algorithms for Bayesian tomography. In *Proc. IEEE Conf. Acoust. Speech Sig. Proc.*, volume 5, pages 2907–10, 1995.
- [209] C. A. Bouman and K. Sauer. A unified approach to statistical tomography using coordinate descent optimization. *IEEE Tr. Im. Proc.*, 5(3):480–92, March 1996.
- [210] J. A. Fessler. Hybrid Poisson/polynomial objective functions for tomographic image reconstruction from transmission scans. *IEEE Tr. Im. Proc.*, 4(10):1439–50, October 1995.
- [211] H Erdogan and J. A. Fessler. Monotonic algorithms for transmission tomography. *IEEE Tr. Med. Im.*, 18(9):801–14, September 1999.
- [212] C. A. Johnson, J. Seidel, and A. Sofer. Interior point methodology for 3-D PET reconstruction. *IEEE Tr. Med. Im.*, 19(4):271–85, April 2000.
- [213] K. Lange and J. A. Fessler. Globally convergent algorithms for maximum a posteriori transmission tomography. *IEEE Tr. Im. Proc.*, 4(10):1430–8, October 1995.
- [214] J. A. Fessler, N. H. Clinthorne, and W. L. Rogers. On complete data spaces for PET reconstruction algorithms. *IEEE Tr. Nuc. Sci.*, 40(4):1055–61, August 1993.
- [215] A R De Pierro. A modified expectation maximization algorithm for penalized likelihood estimation in emission tomography. *IEEE Tr. Med. Im.*, 14(1):132–137, March 1995.
- [216] J. A. Fessler and H Erdogan. A paraboloidal surrogates algorithm for convergent penalized-likelihood emission image reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 1132–5, 1998.
- [217] T. Hebert and R. Leahy. A Bayesian reconstruction algorithm for emission tomography using a Markov random field prior. In *Proc. SPIE 1092, Med. Im. III: Im. Proc.*, pages 458–4662, 1989.
- [218] T. Hebert and R. Leahy. A generalized EM algorithm for 3-D Bayesian reconstruction from Poisson data using Gibbs priors. *IEEE Tr. Med. Im.*, 8(2):194–202, June 1989.
- [219] T. J. Hebert and R. Leahy. Statistic-based MAP image reconstruction from Poisson data using Gibbs priors. *IEEE Tr. Sig. Proc.*, 40(9):2290–303, September 1992.
- [220] E. Tanaka. Utilization of non-negativity constraints in reconstruction of emission tomograms. In S L Bacharach, editor, *Information Processing in Medical Im.*, pages 379–93. Martinus-Nijhoff, Boston, 1985.
- [221] R. M. Lewitt and G. Muehllehner. Accelerated iterative reconstruction for positron emission tomography based on the EM algorithm for maximum likelihood estimation. *IEEE Tr. Med. Im.*, 5(1):16–22, March 1986.

- [222] T. Hebert, R. Leahy, and M. Singh. Three-dimensional maximum-likelihood reconstruction for an electronically collimated single-photon-emission imaging system. *J. Opt. Soc. Am. A*, 7(7):1305–13, July 1990.
- [223] S. Holte, P. Schmidlin, A. Lindén, G. Rosenqvist, and L. Eriksson. Iterative image reconstruction for emission tomography: A study of convergence and quantitation problems. *IEEE Tr. Nuc. Sci.*, 37(2):629–635, April 1990.
- [224] D. P. Bertsekas. A new class of incremental gradient methods for least squares problems. *SIAM J. Optim.*, 7(4):913–26, November 1997.
- [225] R. Neal and G. E. Hinton. A view of the EM algorithm that justifies incremental, sparse and other variants. In M. I. Jordan, editor, *Learning in Graphical Models*, pages 255–68. Kluwer, Dordrecht, 1998.
- [226] A. Nedic and D. Bertsekas. Convergence rate of incremental subgradient algorithms. In S. Uryasev and P. M. Pardalos, editors, *Stochastic Optimization: Algorithms and Applications*, pages 263–304. Kluwer, New York, 2000.
- [227] A. Nedic, D. Bertsekas, and V. Borkar. Distributed asynchronous incremental subgradient methods. In D. Butnariu Y. Censor S. Reich, editor, *Inherently Parallel Algorithms in Feasibility and Optimization and Their Applications*. Elsevier, Amsterdam, 2000.
- [228] A. Nedic and D. P. Bertsekas. Incremental subgradient methods for nondifferentiable optimization. *SIAM J. Optim.*, 12(1):109–38, 2001.
- [229] V. M. Kibardin. Decomposition into functions in the minimization problem. *Avtomatika i Telemekhanika*, 9:66–79, September 1979. Translation: p. 1311-23 in Plenum Publishing Co. "Adaptive Systems".
- [230] H. Kudo, H. Nakazawa, and T. Saito. Convergent block-iterative method for general convex cost functions. In *Proc. of the 1999 Intl. Mtg. on Fully 3D Im. Recon. in Rad. Nuc. Med.*, pages 247–250, 1999.
- [231] A R De Pierro and M. E. B. Yamagishi. Fast EM-like methods for maximum ‘a posteriori’ estimates in emission tomography. *IEEE Tr. Med. Im.*, 20(4):280–8, April 2001.
- [232] S. Ahn and J. A. Fessler. Globally convergent image reconstruction for emission tomography using relaxed ordered subsets algorithms. *IEEE Tr. Med. Im.*, ?, 2002. Submitted.
- [233] S. Ahn and J. A. Fessler. Globally convergent ordered subsets algorithms: Application to tomography. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, pages M1–2, 2001.
- [234] H Erdogan and J. A. Fessler. Ordered subsets algorithms for transmission tomography. *Phys. Med. Biol.*, 44(11):2835–51, November 1999.
- [235] J. W. Stayman and J. A. Fessler. Spatially-variant roughness penalty design for uniform resolution in penalized-likelihood image reconstruction. In *Proc. IEEE Intl. Conf. on Image Processing*, volume 2, pages 685–9, 1998.
- [236] J. W. Stayman and J. A. Fessler. Compensation for nonuniform resolution using penalized-likelihood reconstruction in space-variant imaging systems. *IEEE Tr. Med. Im.*, ?, 2002. Submitted.
- [237] J. Qi and R. M. Leahy. Resolution and noise properties of MAP reconstruction for fully 3D PET. In *Proc. of the 1999 Intl. Mtg. on Fully 3D Im. Recon. in Rad. Nuc. Med.*, pages 35–9, 1999.
- [238] X. Liu, C. Comtat, C. Michel, P. Kinahan, M. Defrise, and D. Townsend. Comparison of 3D reconstruction with OSEM and FORE+OSEM for PET. In *Proc. of the 1999 Intl. Mtg. on Fully 3D Im. Recon. in Rad. Nuc. Med.*, pages 39–42, 1999.

- [239] X. Liu, C. Comtat, C. Michel, P. Kinahan, M. Defrise, and D. Townsend. Comparison of 3D reconstruction with OSEM and FORE+OSEM for PET. *IEEE Tr. Med. Im.*, 20(8):804–13, August 2001.
- [240] C. Bai, P. E. Kinahan, D. Brasse, C. Comtat, and D. Townsend. Post-injection single photon transmission tomography with ordered-subset algorithms for wholebody PET imaging. *IEEE Tr. Nuc. Sci.*, ?, 2001.
- [241] C. Michel, M. Sibomana, A. Bol, X. Bernard, M. Lonneux, M. Defrise, C. Comtat, P. E. Kinahan, and D. W. Townsend. Preserving Poisson characteristics of PET data with weighted OSEM reconstruction. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, pages 1323–9, 1998.
- [242] C. Michel, X. Liu, S. Sanabria, M. Lonneux, M. Sibomana, A. Bol, C. Comtat, P. E. Kinahan, D. W. Townsend, and M. Defrise. Weighted schemes applied to 3D-OSEM reconstruction in PET. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1152–7, 1999.
- [243] D. F. Yu, J. A. Fessler, and E. P. Ficaro. Maximum likelihood transmission image reconstruction for overlapping transmission beams. *IEEE Tr. Med. Im.*, 19(11):1094–1105, November 2000.
- [244] I. Elbakri and J. A. Fessler. Ordered subsets transmission reconstruction with beam hardening correction for x-ray CT. In *Proc. SPIE 4322, Medical Imaging 2001: Image Proc.*, volume 1, pages 1–12, 2001.
- [245] D. L. Snyder. Parameter estimation for dynamic studies in emission-tomography systems having list-mode data. *IEEE Tr. Nuc. Sci.*, 31(2):925–31, April 1984.
- [246] J. M. Ollinger and D. L. Snyder. A preliminary evaluation of the use of the EM algorithm for estimating parameters in dynamic tracer-studies. *IEEE Tr. Nuc. Sci.*, 32(1):848–54, February 1985.
- [247] J. M. Ollinger and D. L. Snyder. An evaluation of an improved method for computing histograms in dynamic tracer studies using positron-emission tomography. *IEEE Tr. Nuc. Sci.*, 33(1):435–8, February 1986.
- [248] J. M. Ollinger. Estimation algorithms for dynamic tracer studies using positron-emission tomography. *IEEE Tr. Med. Im.*, 6(2):115–25, June 1987.
- [249] J. M. Ollinger. An evaluation of a practical algorithm for estimating histograms in dynamic tracer studies using positron-emission tomography. *IEEE Tr. Nuc. Sci.*, 34(1):349–53, February 1987.
- [250] F. O’Sullivan. Imaging radiotracer model parameters in PET: a mixture analysis approach. *IEEE Tr. Med. Im.*, 12(3):399–412, September 1993.
- [251] P. C. Chiao, W. L. Rogers, J. A. Fessler, N. H. Clinthorne, and A. O. Hero. Model-based estimation with boundary side information or boundary regularization. *IEEE Tr. Med. Im.*, 13(2):227–34, June 1994.
- [252] J. M. Borwein and W. Sun. The stability analysis of dynamic SPECT systems. *Numerische Mathematik*, 77(3):283–98, 1997.
- [253] J. S. Maltz, E. Polak, and T. F. Budinger. Multistart optimization algorithm for joint spatial and kinetic parameter estimation from dynamic ECT projection data. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 3, pages 1567–73, 1998.
- [254] D. S. Lalush and B. M. W. Tsui. Block-iterative techniques for fast 4D reconstruction using a priori motion models in gated cardiac SPECT. *Phys. Med. Biol.*, 43(4):875–86, April 1998.
- [255] T. E. Nichols, J. Qi, and R. M. Leahy. Continuous time dynamic PET imaging using list mode data. In A. Todd-Pokropek A. Kuba, M. Smal, editor, *Information Processing in Medical Im.*, pages 98–111. Springer, Berlin, 1999.

- [256] E. Asma, T. E. Nichols, J. Qi, and R. M. Leahy. 4D PET image reconstruction from list mode data. In *Proc. IEEE Nuc. Sci. Symp. Med. Im. Conf.*, volume 2, pages 15/57–65, 2000.
- [257] U. Schmitt and A. K. Louis. Efficient algorithms for the regularization of dynamic inverse problems: I. Theory. *Inverse Prob.*, 18(3):645–58, June 2002.
- [258] U. Schmitt, A. K. Louis, C. Wolters, and M. Vauhkonen. Efficient algorithms for the regularization of dynamic inverse problems: II. Applications. *Inverse Prob.*, 18(3):659–76, June 2002.
- [259] C-M. Kao, J. T. Yap, J. Mukherjee, and M. N. Wernick. Image reconstruction for dynamic PET based on low-order approximation and restoration of the sinogram. *IEEE Tr. Med. Im.*, 16(6):727–37, December 1997.
- [260] J. Matthews, D. Bailey, P. Price, and V. Cunningham. The direct calculation of parametric images from dynamic PET data using maximum-likelihood iterative reconstruction. *Phys. Med. Biol.*, 42(6):1155–73, June 1997.
- [261] S. R. Meikle, J. C. Matthews, V. J. Cunningham, D. L. Bailey, L. Livieratos, T. Jones, and P. Price. Parametric image reconstruction using spectral analysis of PET projection data. *Phys. Med. Biol.*, 43(3):651–66, March 1998.
- [262] M. V. Narayanan, M. A. King, E. J. Soares, C. L. Byrne, P. H. Pretorius, and M. N. Wernick. Application of the Karhunen-Loeve transform to 4D reconstruction of cardiac gated SPECT images. *IEEE Tr. Nuc. Sci.*, 46(4-2):1001–8, August 1999.
- [263] M. N. Wernick, E. J. Infusino, and M. Milosevic. Fast spatio-temporal image reconstruction for dynamic PET. *IEEE Tr. Med. Im.*, 18(3):185–95, March 1999.
- [264] M. V. Narayanan, M. A. King, M. N. Wernick, C. L. Byrne, E. J. Soares, and P. H. Pretorius. Improved image quality and computation reduction in 4-D reconstruction of cardiac-gated SPECT images. *IEEE Tr. Med. Im.*, 19(5):423–33, May 2000.
- [265] J. E. Koss, D. L. Kirch, E. P. Little, T. K. Johnson, and P. P. Steele. Advantages of list-mode acquisition of dynamic cardiac data. *IEEE Tr. Nuc. Sci.*, 44(6-2):2431–8, December 1997.
- [266] Y. Censor, D. E. Gustafson, A. Lent, and H. Tuy. A new approach to the emission computerized tomography problem: simultaneous calculation of attenuation and activity coefficients. *IEEE Tr. Nuc. Sci.*, 26(2), January 1979.
- [267] P. R. R. Nunes. *Estimation algorithms for medical imaging including joint attenuation and emission reconstruction*. PhD thesis, Stanford Univ., Stanford, CA., June 1980.
- [268] M. S. Kaplan, D. R. Haynor, and H. Vija. A differential attenuation method for simultaneous estimation of SPECT activity and attenuation distributions. *IEEE Tr. Nuc. Sci.*, 46(3):535–41, June 1999.
- [269] C. M. Laymon and T. G. Turkington. Calculation of attenuation factors from combined singles and coincidence emission projections. *IEEE Tr. Med. Im.*, 18(12):1194–200, December 1999.
- [270] R. Ramlau, R. Clackdoyle, F. Noo, and G. Bal. Accurate attenuation correction in SPECT imaging using optimization of bilinear functions and assuming an unknown spatially-varying attenuation distribution. *Zeitschrift fur Angewandte Mathematik und Mechanik*, 80(9):613–21, 2000.
- [271] A. Krol, J. E. Bowsher, S. H. Manglos, D. H. Feiglin, M. P. Tornai, and F. D. Thomas. An EM algorithm for estimating SPECT emission and transmission parameters from emission data only. *IEEE Tr. Med. Im.*, 20(3):218–32, March 2001.

- [272] J. Nuyts, P. Dupont, S. Stroobants, R. Benninck, L. Mortelmans, and P. Suetens. Simultaneous maximum a-posteriori reconstruction of attenuation and activity distributions from emission sinograms. *IEEE Tr. Med. Im.*, 18(5):393–403, May 1999.

The literature on image reconstruction is enormous and growing. Many valuable publications are not included in this list, which is not intended to be comprehensive.

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Glossary of Symbols

\mathbb{R}^3	3-dimensional Euclidian space
\vec{r}	position in 3-dimensional Euclidian space
B	subset of \mathbb{R}^3
$\lambda(\vec{r})$	emission density
λ	vector of emission density expansion coefficients
$\hat{\lambda}$	estimate of λ
$\vec{X}_k(t)$	position of k th tracer atom vs time t
$f_{\vec{X}(t)}(\vec{r})$	radiotracer distribution function (pdf of $\vec{X}_k(t)$)
T_k	decay time of k th tracer atom
$t_{1/2}$	halflife of radionuclide
S_k	detector unit that records k th decay
μ_N	mean number of injected tracer atoms
μ_T	mean of T_k
$1_{\{\cdot\}}$	indicator function
n_p	number of pixels
n_d	number of detector units
s_i	sensitivity pattern of i th detector unit
$s(\vec{r})$	system sensitivity pattern
A'	matrix transpose
Ψ	<i>cost function</i> : $\Psi : \mathbb{R}^{n_p} \rightarrow \mathbb{R}$
\dot{h}_i	derivative of h_i
Y_i	counts recorded by i th detector unit during scan
y_i	particular realization of Y_i
\bar{y}_i	mean of Y_i
r_i	mean number of background counts for i th detector unit
a_{ij}	system matrix element
λ_j	j th element of λ
$[Ax]_i$	shorthand for $\sum_{j=1}^{n_p} a_{ij}x_j$
$R(\mathbf{x})$	penalty function
ψ	potential function
N_j	neighborhood of j th pixel
c_{kj}	element of C
\mathbf{x}	generic parameter vector to be estimated
$\mathbf{x}^{(n)}$	value of \mathbf{x} at n th iteration