Estimation, Detection and Filtering of Medical Images

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Outline

- Part I : Basics of Medical image Filtering and Convolution
- Part II : Estimation Theory and examples
- Part III: Detection Theory and examples

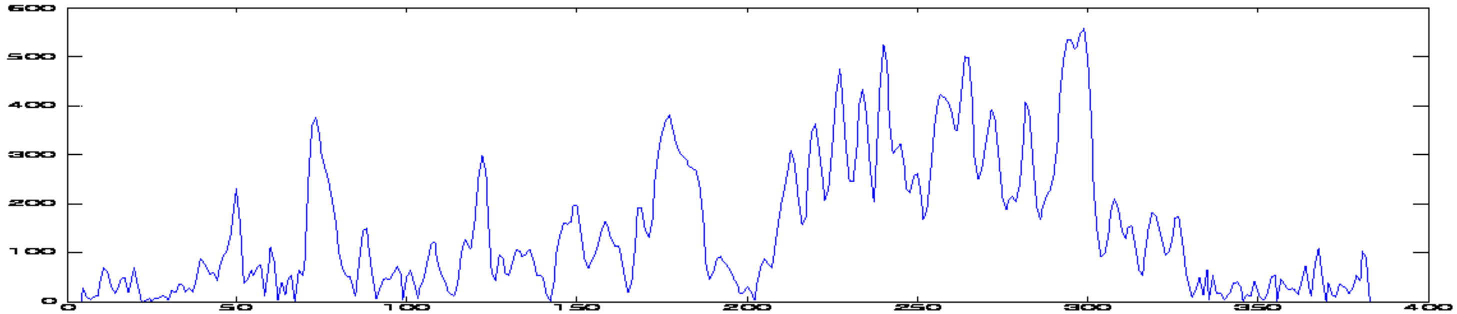
Convolution Basics

- Convolution is defined as

$$y(t) = x(t) * h(t) = \int_{-\infty}^{\infty} y(\tau)h(t-\tau)d\tau$$

- Practically achieved as follows:
  - Flip h(t)
  - Slide it into x(t) by amount tau
  - At each position tau, calculate the area of overlap between x and h

Example


600
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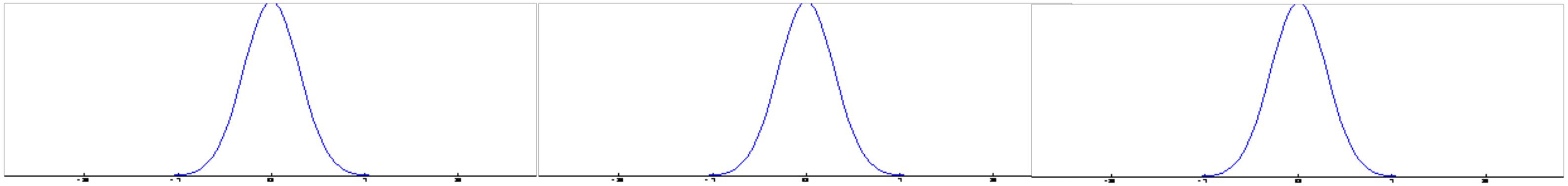

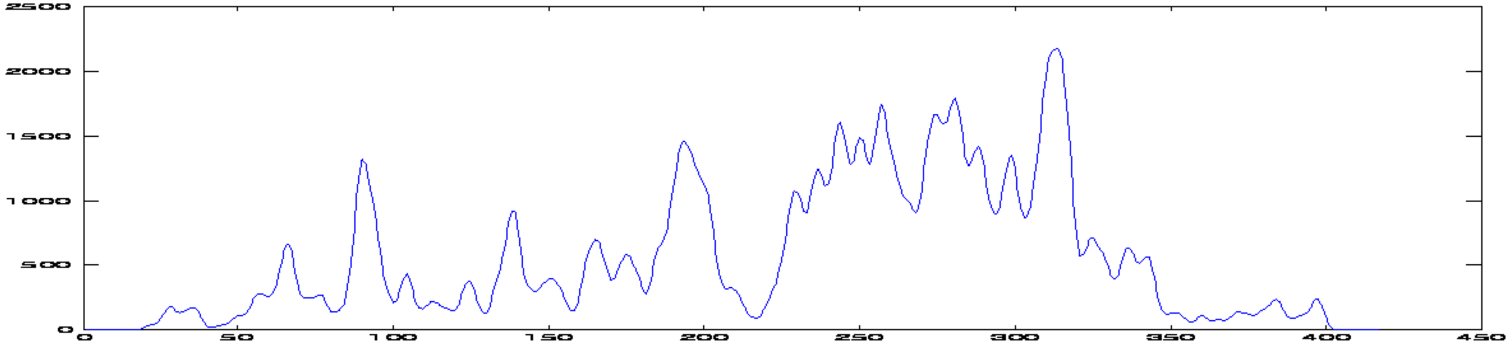
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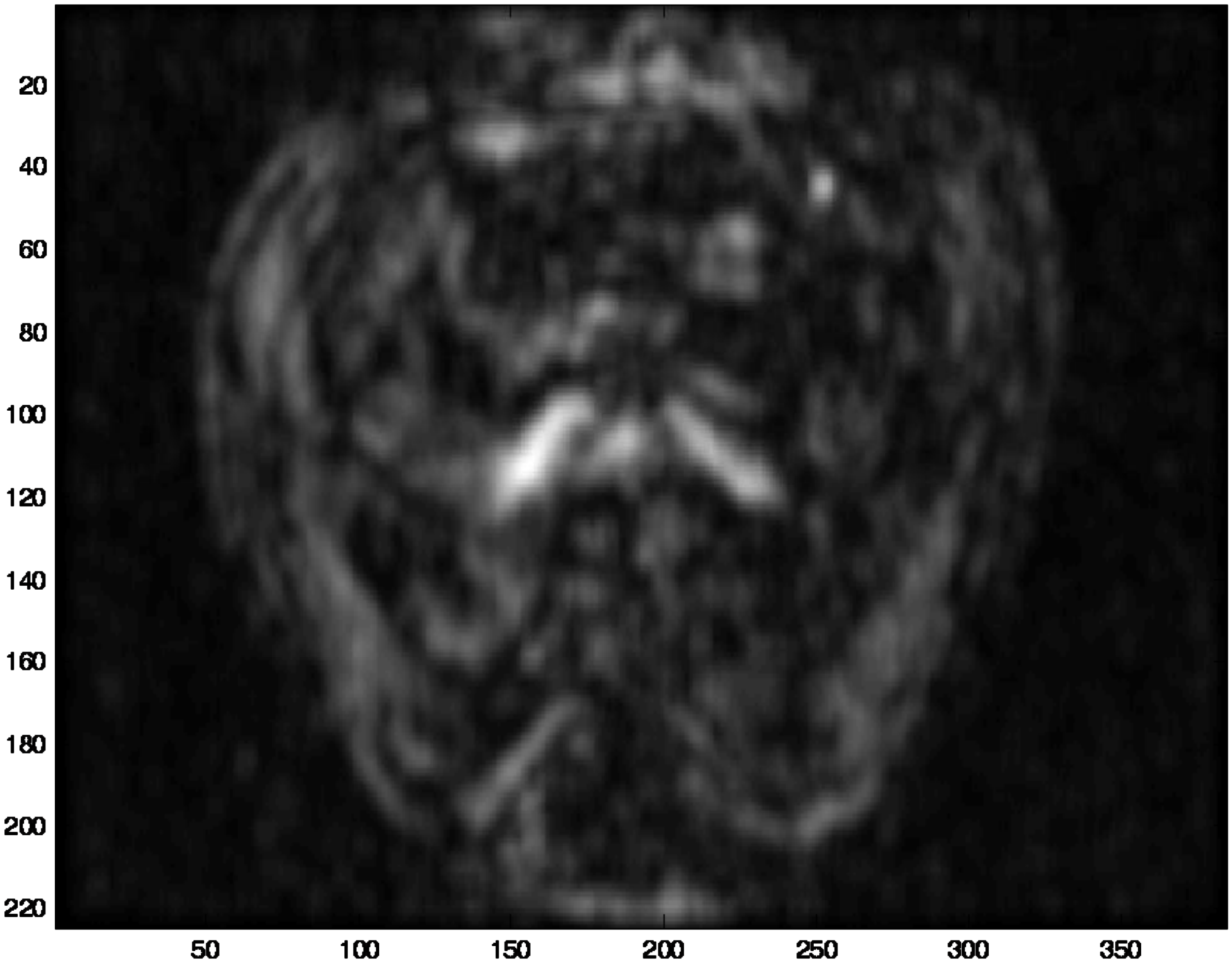
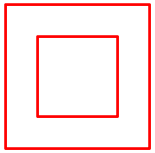
Filtering and Convolution

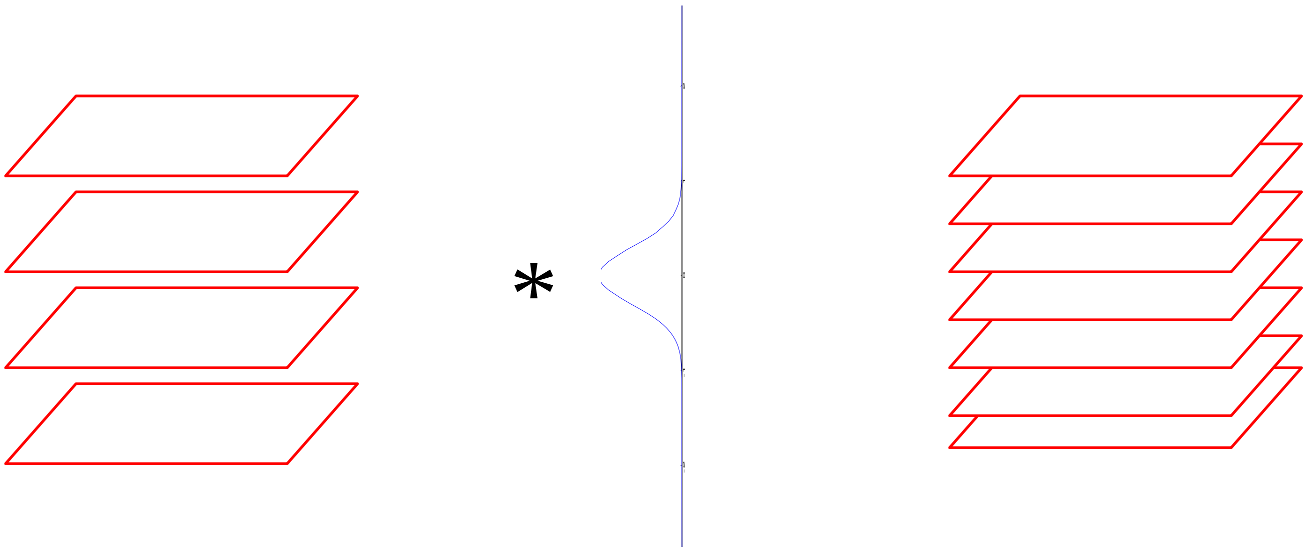




Convolution For Interpolation and Resampling

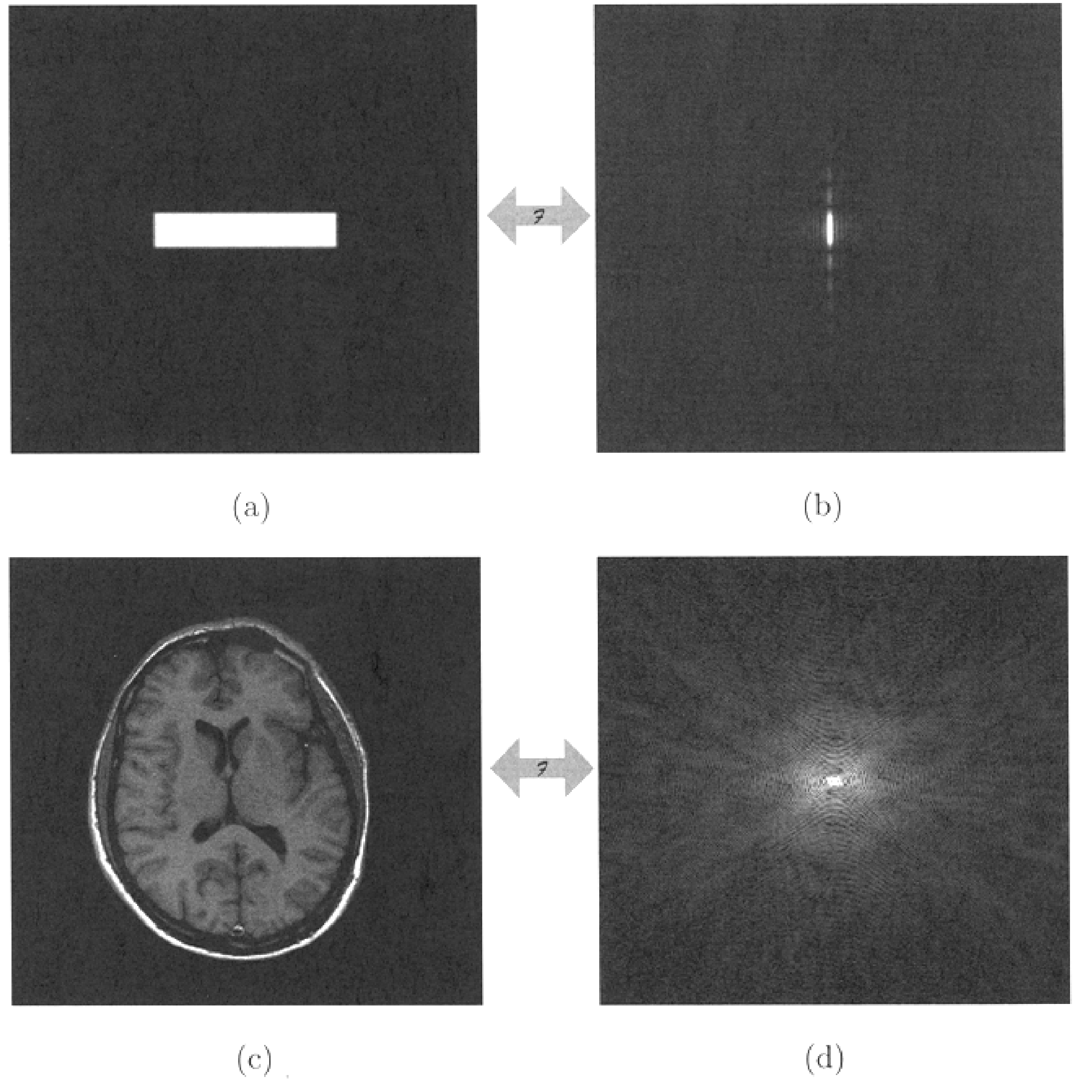
- Sometimes need to “fill in” missing data
- Interpolation – to resample image on finer grid
- Resampling is used to change the “nonminal” resolution of images
- Example: if multi-slice images with non-isotropic resolution, resampling can make it isotropic
- IMPORTANT: resampling, filtering or interpolation does NOT increase “actual” resolution

Resampling example



k-space and image-space

k-space & image-space are related by the 2D FT



How many points do we need to sample?

- $\Delta k = 1/FOV$
- Why? Due to the Sampling Theorem

> "Suppose a signal $I(x)$ is non-zero only within $[-W/2, W/2]$. Then its Fourier transform $F(I)(k_x)$ must be sampled at least as densely as $\Delta k_x = 1/W$."

- Note this works regardless of direction of transform (Duality property)
- What happens if this is violated? ALIASING

Aliasing Example

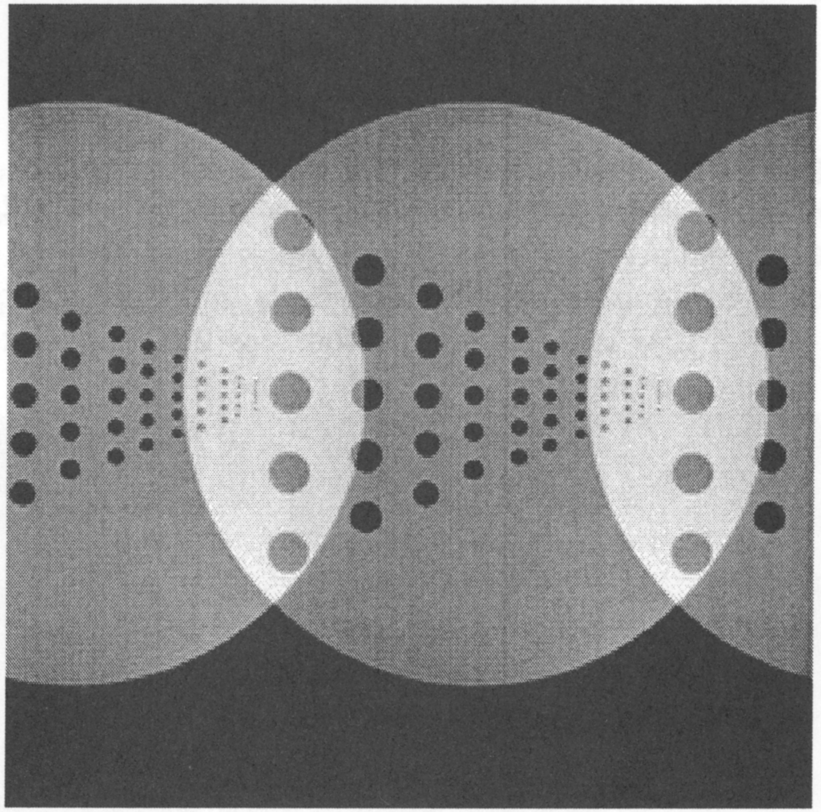
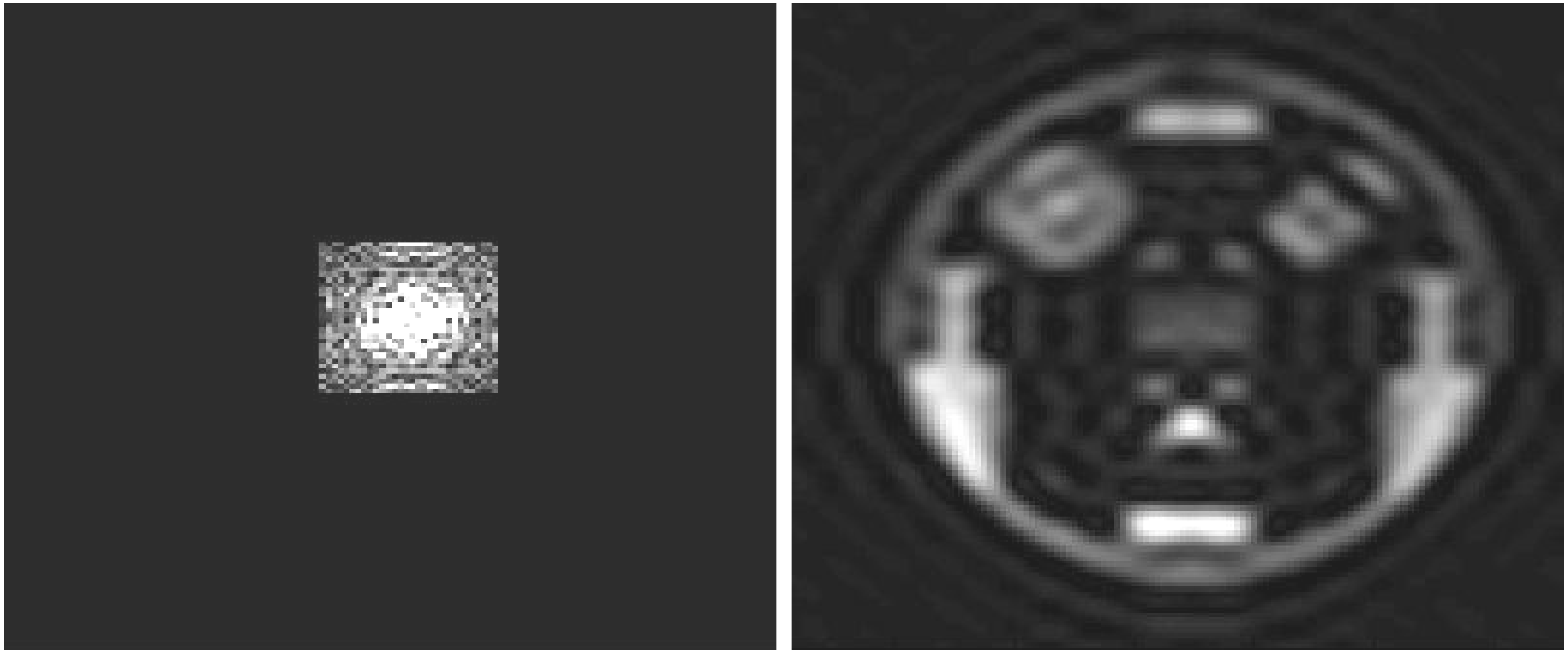


Figure 8.9 Aliasing artifacts due to undersampling along the horizontal direction by a factor of two.

Truncation

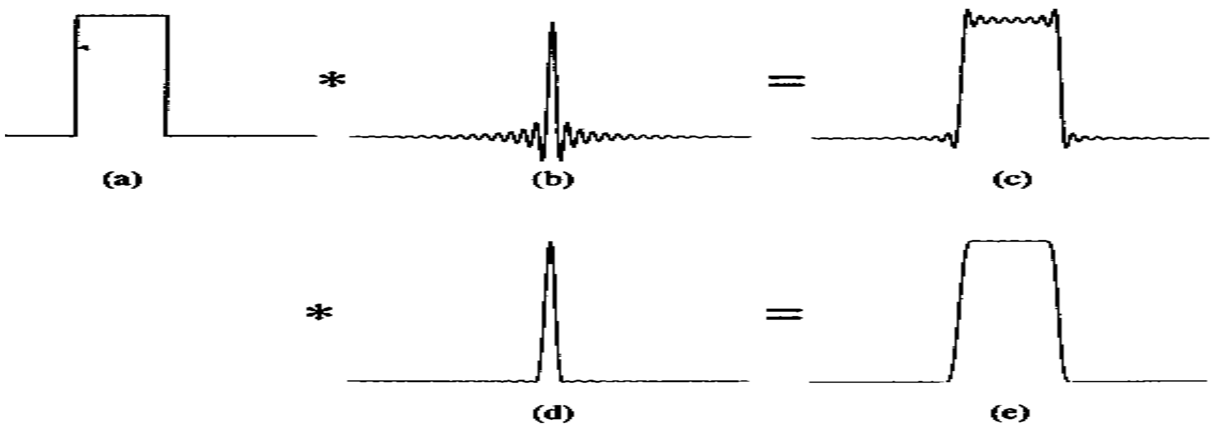
- Truncation = sampling central part of k-space



Truncation

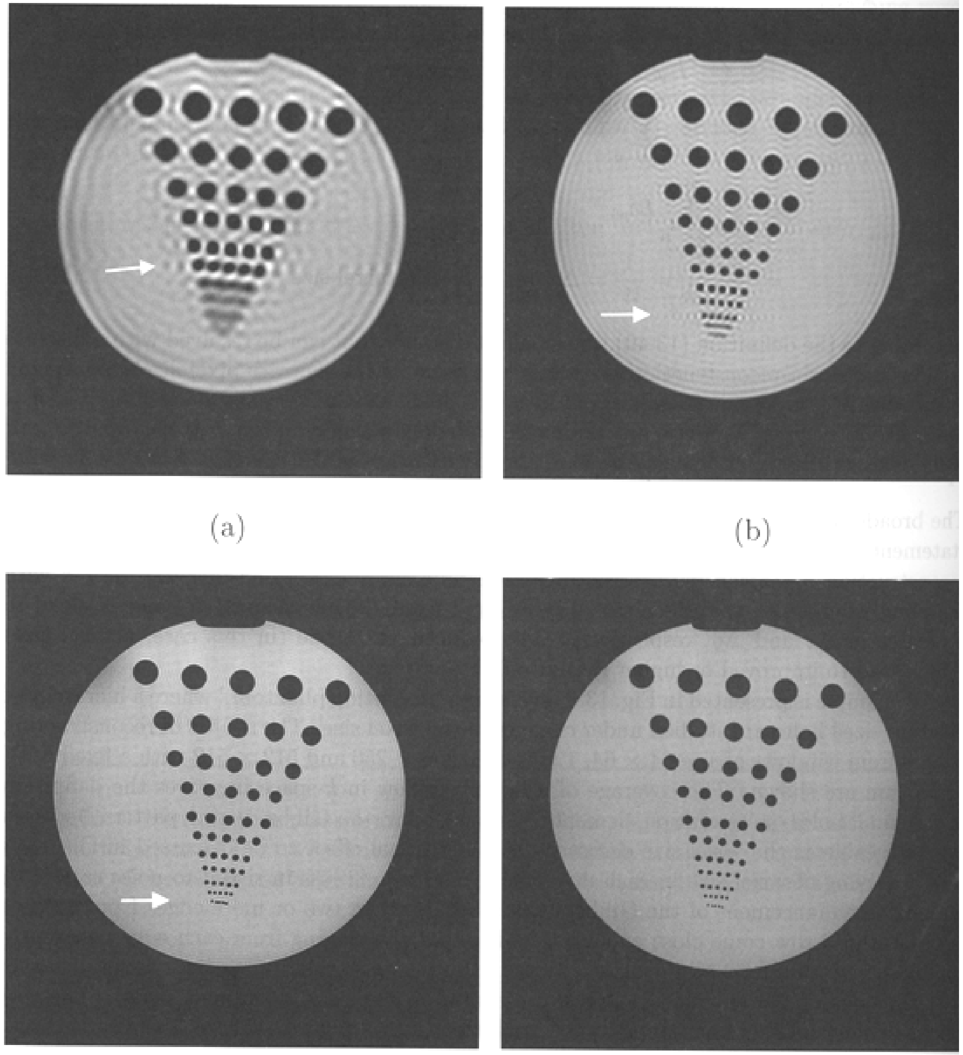
- Both blurring and ringing are a result of truncation
- Intrinsic resolution = size of the blur
- To reduce blur (hence increase resolution) we need to sample up to a larger k-space radius
- Can characterise resolution by the point spread function (PSF) which is simply the blurring kernel
- Note: zero-padding can increase matrix size but can not increase resolution!

Ringing



- ringing can be reduced by multiplying the signal by a smooth window - called windowing
- Popular window choices:
  - Kaiser-Bessel
  - Hanning
  - Raised cosine

Ringing Example



(a) (b) (c) (d)

Part II : Estimation Theory and Examples

- Introduction to optimal estimates
- Different types of optimal estimates
- Estimation examples from MR

Estimation Theory

- Consider a linear process

  $$y = H\,\theta + n$$

  y = observed data

  θ = set of model parameters

  n = additive noise
- Then Estimation is the problem of finding the statistically optimal θ, given y, H and knowledge of noise properties
- MR is full of estimation problems

Different approaches to estimation

- Minimum variance unbiased estimators
- Least Squares
- Maximum-likelihood
- Maximum entropy
- Maximum a posteriori

has no statistical basis

uses knowledge of noise PDF

uses prior information about θ

Least Squares Estimator

- Least Squares:

  $$\theta_{LS} = \text{argmin } ||y - H\theta||^2$$

- Natural estimator– want solution to match observation
- Does not use any information about n
- There is a simple solution (a.k.a. pseudo-inverse):

  $$\theta_{LS} = (H^T H)^{-1} H^T y$$

  What if we know something about the noise?

  Say we know Pr(n)…

Maximum Likelihood Estimator

- Simple idea: want to maximize $\Pr(y|\theta)$
- Can write $\Pr(n) = e^{-L(n)}$, $n = y - H\theta$, and

  $\Pr(n) = \Pr(y|\theta) = e^{-L(y,\, \theta)}$
- if white Gaussian n, $\Pr(n) = e^{-||n||^2/2\,\sigma^2}$ and

  $L(y, \theta) = ||y - H\theta||^2/2\sigma^2$

  $\theta_{ML} = \text{argmax} \Pr(y|\theta) = \text{argmin}\, L(y, \theta)$
  - called the likelihood function

  $\theta_{ML} = \text{argmin}\, ||y - H\theta||^2/2\sigma^2$
- This is the same as Least Squares!

Maximum Likelihood Estimator

- But if noise is jointly Gaussian with cov. matrix C
- Recall C , E(nn^T). Then

$$Pr(n) = e^{-\frac{1}{2} n^T C^{-1} n}$$

$$L(y|\theta) = \frac{1}{2} (y-H\theta)^T C^{-1} (y-H\theta)$$

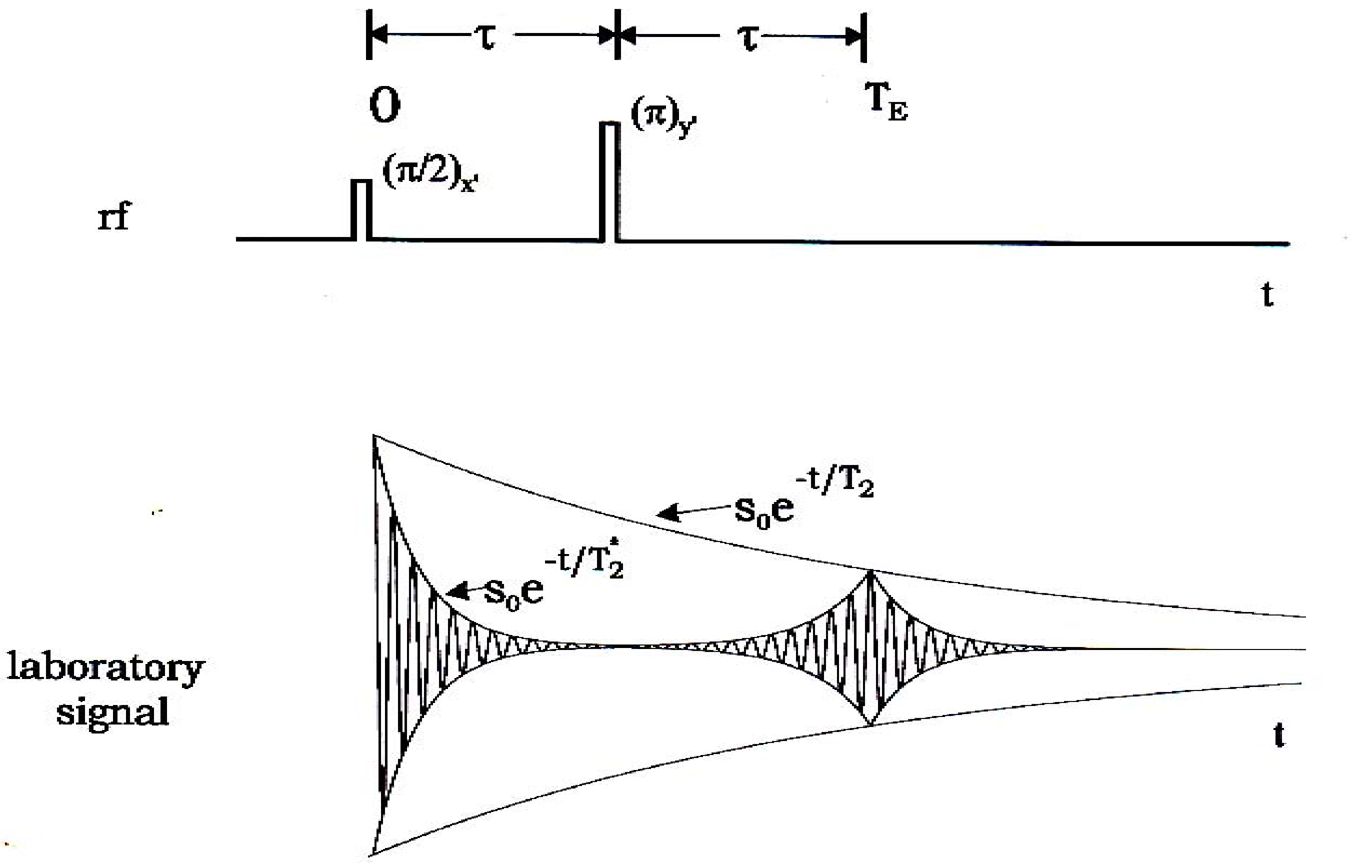
$$\theta_{ML} = \text{argmin } \frac{1}{2} (y-H\theta)^T C^{-1} (y-H\theta)$$

- This also has a closed form solution

$$\theta_{ML} = (H^T C^{-1} H)^{-1} H^T C^{-1} y$$

- If n is not Gaussian at all, ML estimators become complicated and non-linear
- Fortunately, in MR noise is usually Gaussian

Example - estimating T_2 in repeated spin echo data



Example – estimating T_2 in repeated spin echo data

$$s(t) = e^{-t/T_2} \int dr\, \rho(r)$$

- Need only 2 data points to estimate T_2:

$$T_{2est} = [T_{E2} - T_{E1}] / \ln[s(T_{E1})/s(T_{E2})\ ]$$

- However, not good due to noise, timing issues
- In practice we have many data samples from various echoes

Example – estimating T_2

$$\underbrace{\begin{pmatrix} \ln(s(t_1)) \\ \ln(s(t_2)) \\ \vdots \\ \ln(s(t_n)) \end{pmatrix}}_{y} = \underbrace{\begin{pmatrix} 1 & -t_1 \\ 1 & -t_2 \\ & \vdots \\ 1 & -t_n \end{pmatrix}}_{H} \underbrace{\begin{bmatrix} a \\ r \end{bmatrix}}_{\theta}$$

Least Squares estimate:

$$\theta_{LS} = (H^T H)^{-1} H^T y$$

$$T_2 = 1/r_{LS}$$

Can we do better by ML estimate?

- if noise is correlated across time
- if noise variance changes over time

Estimation example - Denoising

- Suppose we have a noisy MR image y, and wish to obtain the noiseless image x, where

  $$y = x + n$$

- Can we use Estimation theory to find x?
- Try: $H = I$, $\theta = x$ in the linear model
- Both LS and ML estimators simply give $x = y$!
- ➔ we need a more powerful model
- Suppose the image x can be approximated by a polynomial, i.e. a mixture of 1st p powers of r:

  $$x = \Sigma_{i=0}^{p} a_i r^i$$

Example – denoising

$$\underbrace{\begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{pmatrix}}_{y} = \underbrace{\begin{pmatrix} 1 & r_1^1 & \cdots & r_1^p \\ 1 & r_2^1 & \cdots & r_2^p \\ & \vdots & & \\ 1 & r_n^1 & \cdots & r_n^p \end{pmatrix}}_{H} \underbrace{\begin{pmatrix} a_0 \\ a_1 \\ \vdots \\ a_p \end{pmatrix}}_{\theta} + \begin{pmatrix} n_1 \\ n_2 \\ \vdots \\ n_n \end{pmatrix}$$

Least Squares estimate:

$$\theta_{LS} = (H^T H)^{-1} H^T y$$

$$x = \Sigma_{i=0}^{p} a_i r^i$$

Can we do better by ML estimate? YES

Noise in MR can be spatially correlated

- ML with covariance matrix C is better

Multi-variate FLASH

- Acquire 6-10 accelerated FLASH data sets at different flip angles or TR's
- Generate T_1 maps by fitting to:

$$S = \exp\left(-TE/T_2^*\right)\sin\alpha \frac{1-\exp\left(-TR/T_1\right)}{1-\cos\alpha\exp\left(-TR/T_1\right)}$$

• Not enough info in a single voxel

• Noise causes incorrect estimates

• Error in flip angle varies spatially!

Spatially Coherent T_1, ρ estimation

- First, stack parameters from all voxels in one big vector **x**
- Stack all observed flip angle images in **y**
- Then we can write **y** = **M** (**x**) + **n**
- Recall **M** is the (nonlinear) functional obtained from

$$S = \exp\left(-TE/T_2^*\right)\sin\alpha \frac{1-\exp\left(-TR/T_1\right)}{1-\cos\alpha\exp\left(-TR/T_1\right)}$$

- Solve for **x** by non-linear least square fitting, PLUS spatial prior:

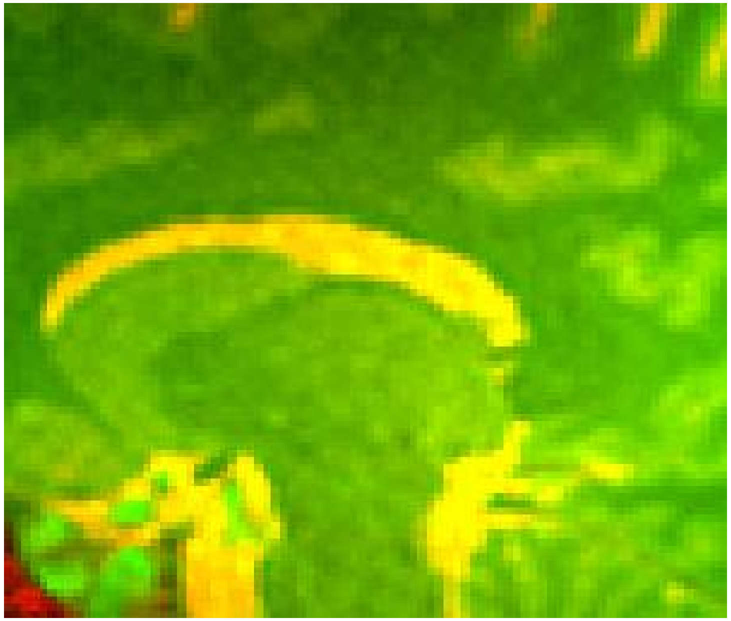
$$\mathbf{x}_{est} = \arg\min_{\mathbf{x}} \|\mathbf{y} - \mathbf{M}(\mathbf{x})\|^2 + \mu^2\|D\mathbf{x}\|^2 \quad \leftarrow E(\mathbf{x})$$

Makes M(x) close to y

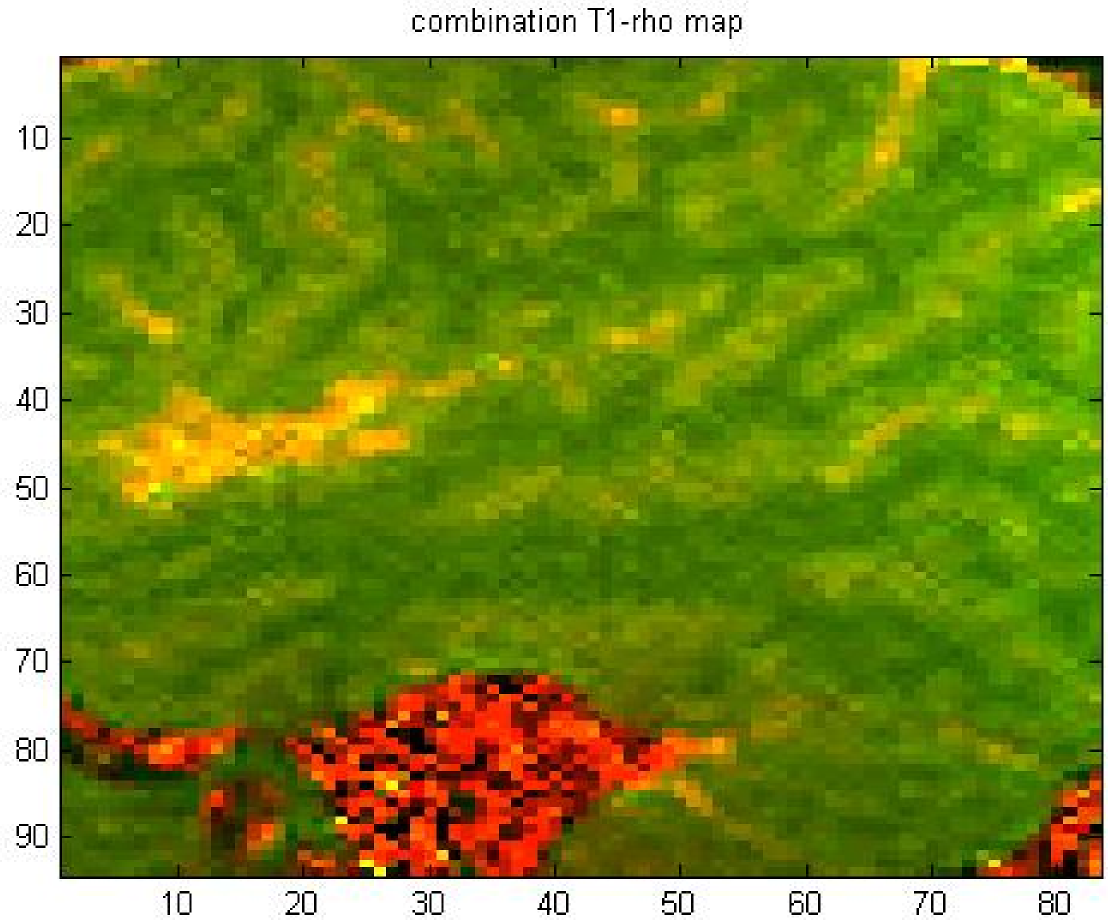
Makes x smooth

- Minimize via MATLAB's *lsqnonlin* function
- How? Construct $\delta = [\mathbf{y} - \mathbf{M}(\mathbf{x}); \mu D\mathbf{x}]$. Then $E(\mathbf{x}) = \|\delta\|^2$

Multi-Flip Results – combined ρ, T_1 in pseudocolour



Multi-Flip Results – combined ρ, T_1 in pseudocolour



Maximum a Posteriori Estimate

- This is an example of using an image prior
- Priors are generally expressed in the form of a PDF Pr(x)
- Once the likelihood L(x) and prior are known, we have complete statistical knowledge
- LS/ML are suboptimal in presence of prior
- MAP (aka Bayesian) estimates are optimal

posterior

Bayes Theorem:

$$\Pr(x|y) = \frac{\Pr(y|x) \,.\, \Pr(x)}{\Pr(y)}$$

likelihood

prior

Other example of Estimation in MR

- Image denoising: H = I
- Image deblurring: H = convolution mtx in img-space
- Super-resolution: H = diagonal mtx in k-space
- Metabolite quantification in MRSI

What Is the Right Imaging Model?

$$y = H x + n, \quad n \text{ is Gaussian} \qquad (1)$$

$$y = H x + n, \quad n, x \text{ are Gaussian} \qquad (2)$$

MAP Sense

- *MAP Sense = Bayesian (MAP) estimate of (2)*

Intro to Bayesian Estimation

- Bayesian methods maximize the posterior probability:

$$Pr(x|y) \propto Pr(y|x) \,.\, Pr(x)$$

- $Pr(y|x)$ (likelihood function) = $\exp(-\,||y-Hx||^2)$
- $Pr(x)$ (prior PDF) = $\exp(-G(x))$
- Gaussian prior:

$$\mathrm{Pr(x)} = \exp\{-\tfrac{1}{2}\; \mathrm{x}^T \mathrm{R_x}^{-1}\, \mathrm{x}\}$$

- MAP estimate:

$$x_{est} = \arg\min ||y-Hx||^2 + G(x)$$

- MAP estimate for Gaussian everything is known as Wiener estimate

Regularization = Bayesian Estimation!

- For any regularization scheme, its almost always possible to formulate the corresponding MAP problem
- MAP = superset of regularization

Prior model → *MAP* → *Regularization scheme*

So why deal with regularization??

Lets talk about Prior Models

- Temporal priors: smooth time-trajectory
- Sparse priors: L0, L1, L2 (=Tikhonov)
- Spatial Priors: most powerful for images
- I recommend robust spatial priors using Markov Fields
- Want priors to be general, not too specific
- Ie, weak rather than strong priors

How to do regularization

- First model physical property of image,
- then create a prior which captures it,
- then formulate MAP estimator,
- Then find a good algorithm to solve it!

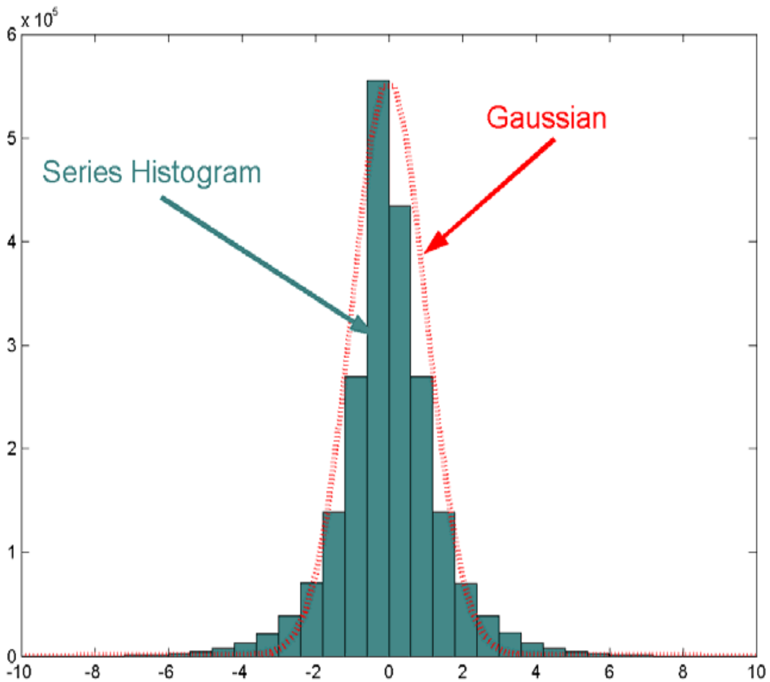
How NOT to do regularization

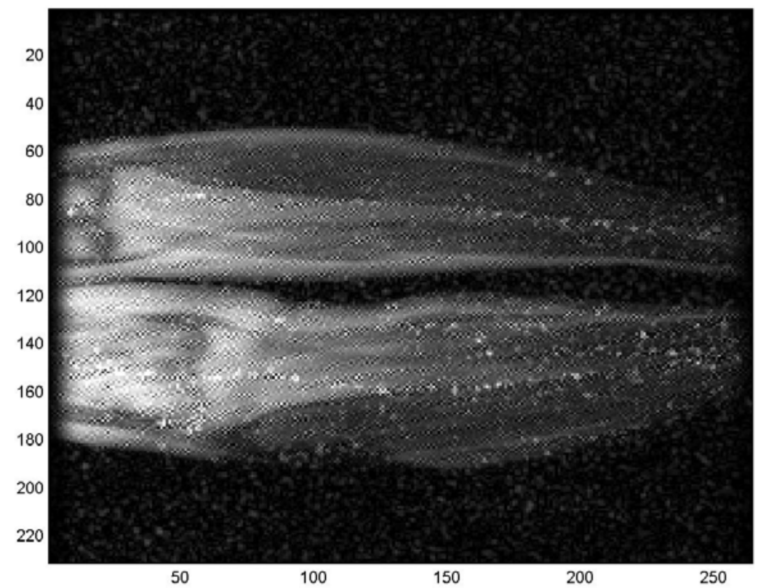
- DON'T use regularization scheme without bearing on physical property of image!
- Example: L1 or L0 prior in k-space!
- Specifically: deblurring in k-space (handy b/c convolution becomes multiply)
- BUT: hard to impose smoothness priors in k-space → no meaning

Spatial Priors For Images - Example

Frames are tightly distributed around mean

After subtracting mean, images are close to Gaussian





envelope *a(i,j)*

Prior: -mean is μ_x

-local std.dev. varies as *a(i,j)*

Spatial Priors for MR images

stationary process

- Stochastic MR image model:

$$x(i,j) = \boldsymbol{\mu}_{\boldsymbol{x}}(i,j) + a(i,j) \,.\, (h ** p)(i,j) \qquad (1)$$

$r(\tau_1, \tau_2) = (h ** h)(\tau_1, \tau_2)$

  ** denotes 2D convolution

  $\boldsymbol{\mu}_{\boldsymbol{x}}(i,j)$ is mean image for class

  $p(i,j)$ is a unit variance i.i.d. stochastic process

  $a(i,j)$ is an envelope function

  $h(i,j)$ simulates correlation properties of image x

$$x = ACp + \boldsymbol{\mu} \qquad (2)$$

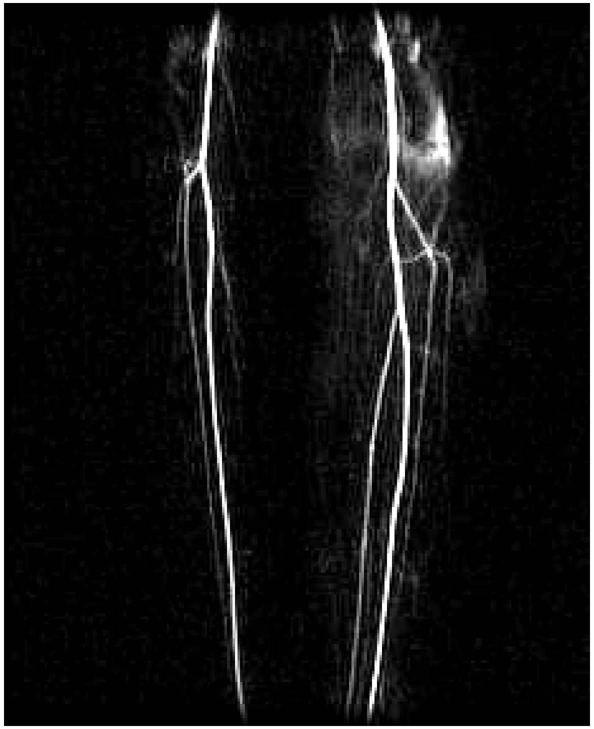
where $A = diag(a)$, and C is the Toeplitz matrix generated by h

- Can model many important stationary and non-stationary cases

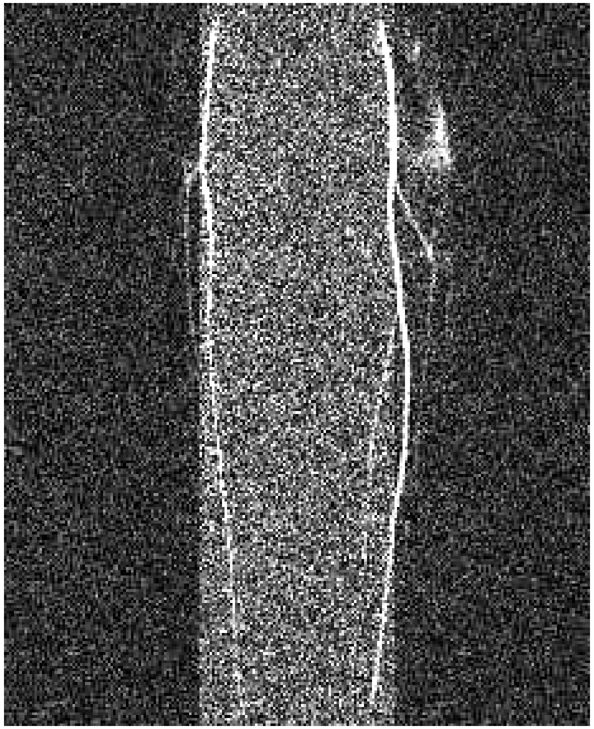
MAP-SENSE Preliminary Results

- Scans acceleraty 5x
- The angiogram was computed by:

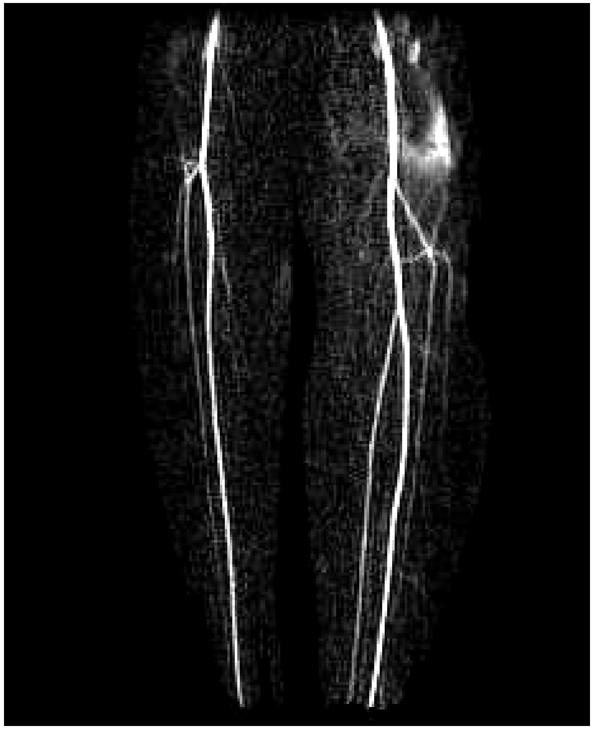
  avg(post-contrast) – avg(pre-contrast)



Unaccelerated

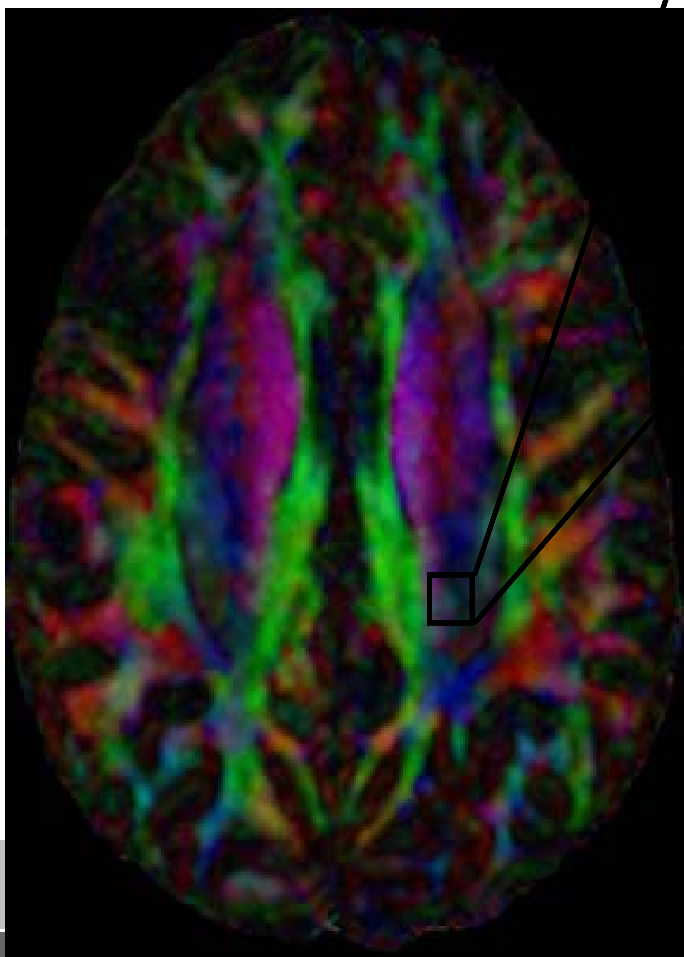


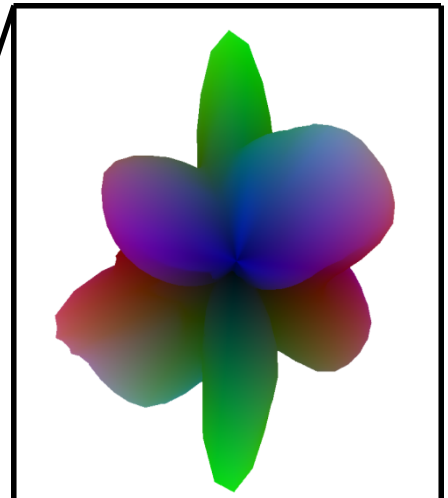
5x faster: SENSE



5x faster: MAP-SENSE

Spatially Constrained High Angular Resolution Diffusion Imaging





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Joint work with:
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Sri Nagarajan, PhD

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MR Diffusion Imaging

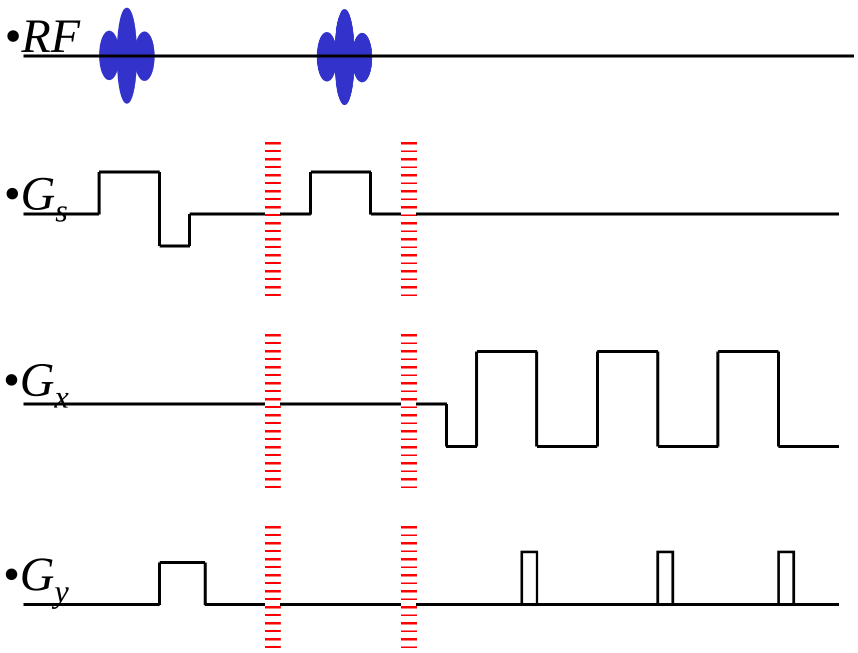
- Diffusion MRI has revolutionized in vivo imaging of brain
- A new contrast mechanism in addition to T1 or T2
- Measures the directionally varying diffusion properties of water in tissue
- Anisotropy of diffusion is an important marker of extant fiber organization
- Enables non-invasive characterization of white matter integrity
- Enables probing of fiber connectivity in the brain, through tractography

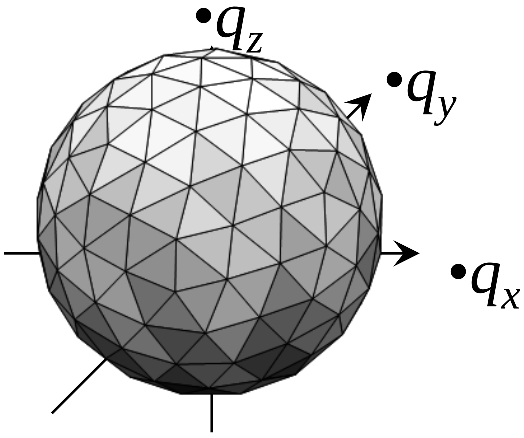
Diffusion Tensor Imaging (DTI)

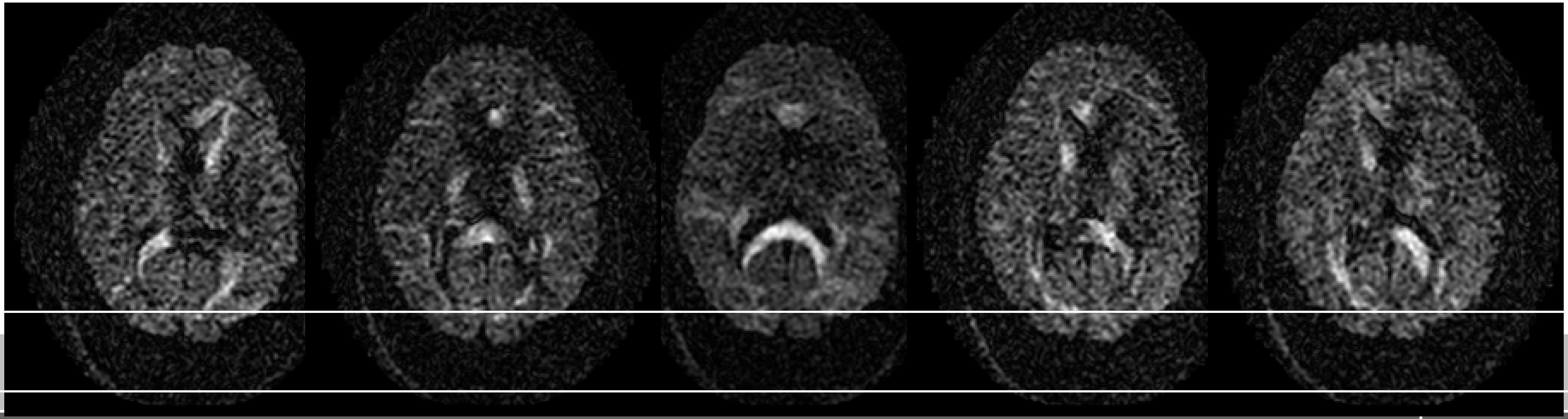
- DTI involves taking 6 directional diffusion imaging measurements
- Then it fits a 3D ellipsoid to these measurements
- Anisotropy of the ellipsoid is correlated with white matter fiber integrity

- Cannot resolve crossing fibers
- Fitting an ellipsoid to crossings gives isotropic spheres
  - Erroneously low FA at crossing fibers
  - Messes up tractography, as well as voxel-wise comparisons
- Need much more than 6 directional measurements to resolve crossing fibers

•Data Acquisition Strategy



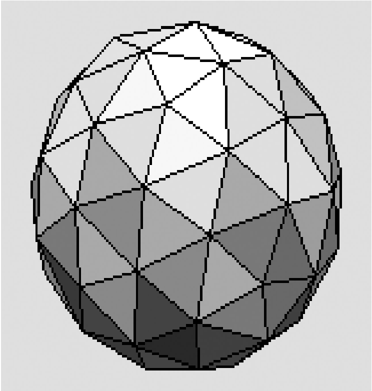




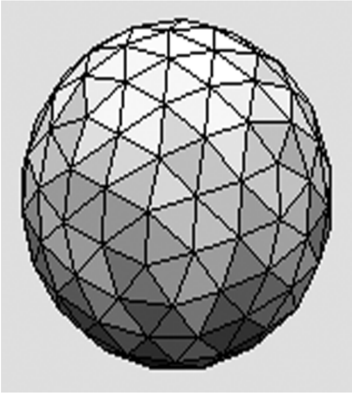
· High Angular Resolution Diffusion Imaging

· Diffusion-encoding Geometries

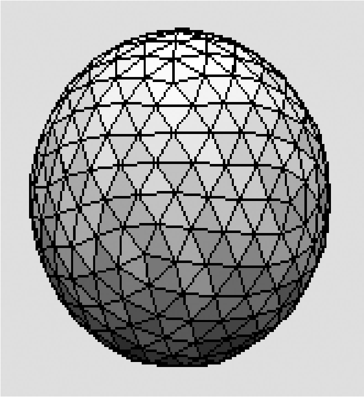
· 55 directions



· 131 directions



· 282 directions



•Gradient directions are determined using an "electrostatic repulsion" model,

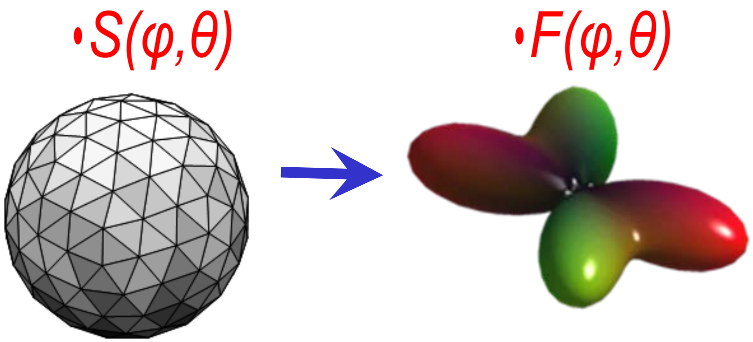
•for the most uniform sampling of 3D space:

•http://www.research.att.com/~njas/electrons/

Reconstruction Problem

•*Goal:*

•*Construct a spherical function that characterizes the angular structure of diffusion anisotropy in each voxel.*



•*Solutions:*

• *Multi-tensor fitting*	*Tuch et al, MRM 2002*
• *Generalized DTI*	*Özarslan et al, MRM 2003*
• *Persistent angular structure*	*Jansons et al, Inv. Prob. 2003*
• *Spherical encoding*	*Lin et al, ISMRM 2003*
• *Spherical harmonic "ADC profile"*	*Frank, MRM 2002; Alexander DC et al, MRM 2002*
• *Circular spectrum mapping*	*Zhan et al, Neuroimage 2004*
• *Spherical deconvolution*	*Tournier et al, Neuroimage 2004*
• *q-ball imaging*	*Tuch et al, Neuron 2003; Tuch MRM 2004*
• *Harmonic q-Ball*	*Hess et al, ISMRM 2005; MRM 2006*

· High Angular Resolution Diffusion Imaging:

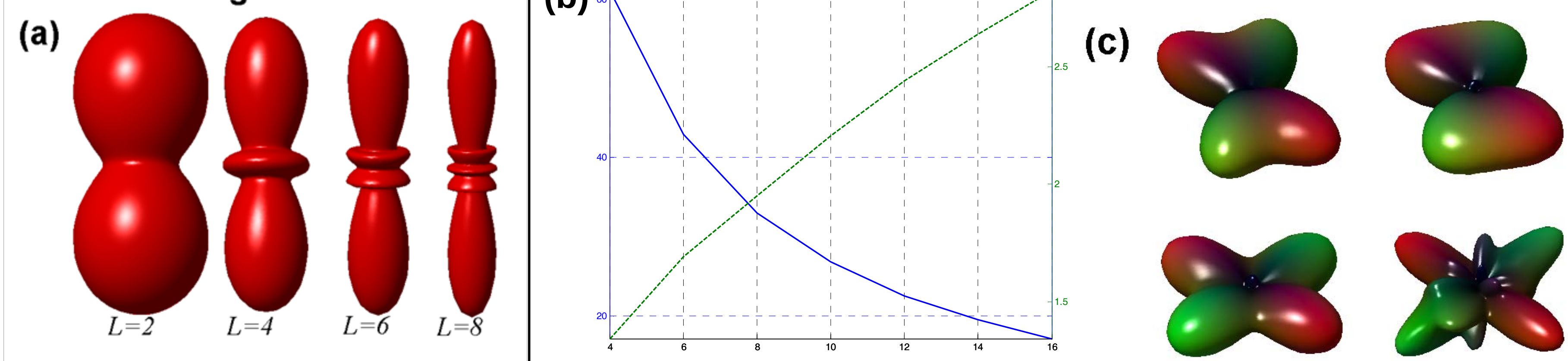
Spherical Harmonic Q-ball

•Point Spread Functions

•Model Order vs
•Angular Resolution

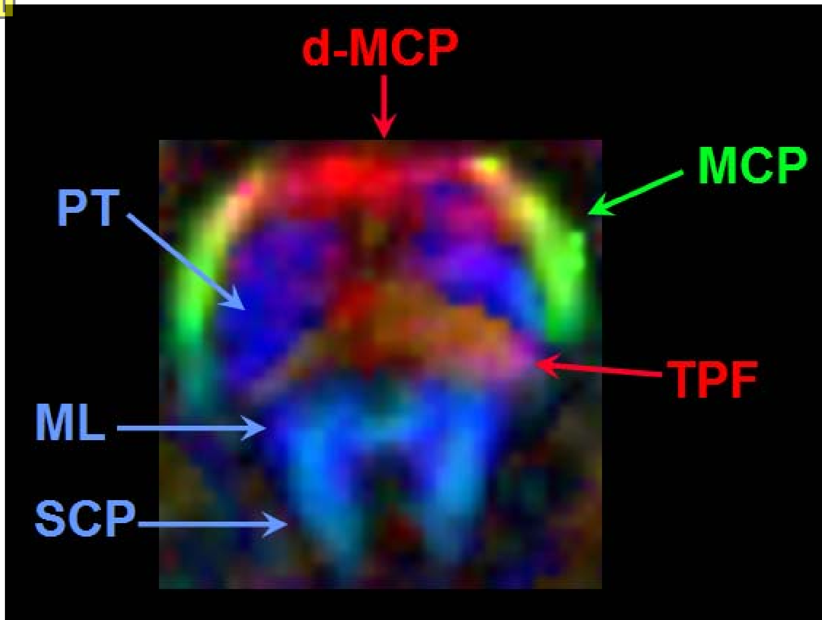
•Simulated
•ODFs

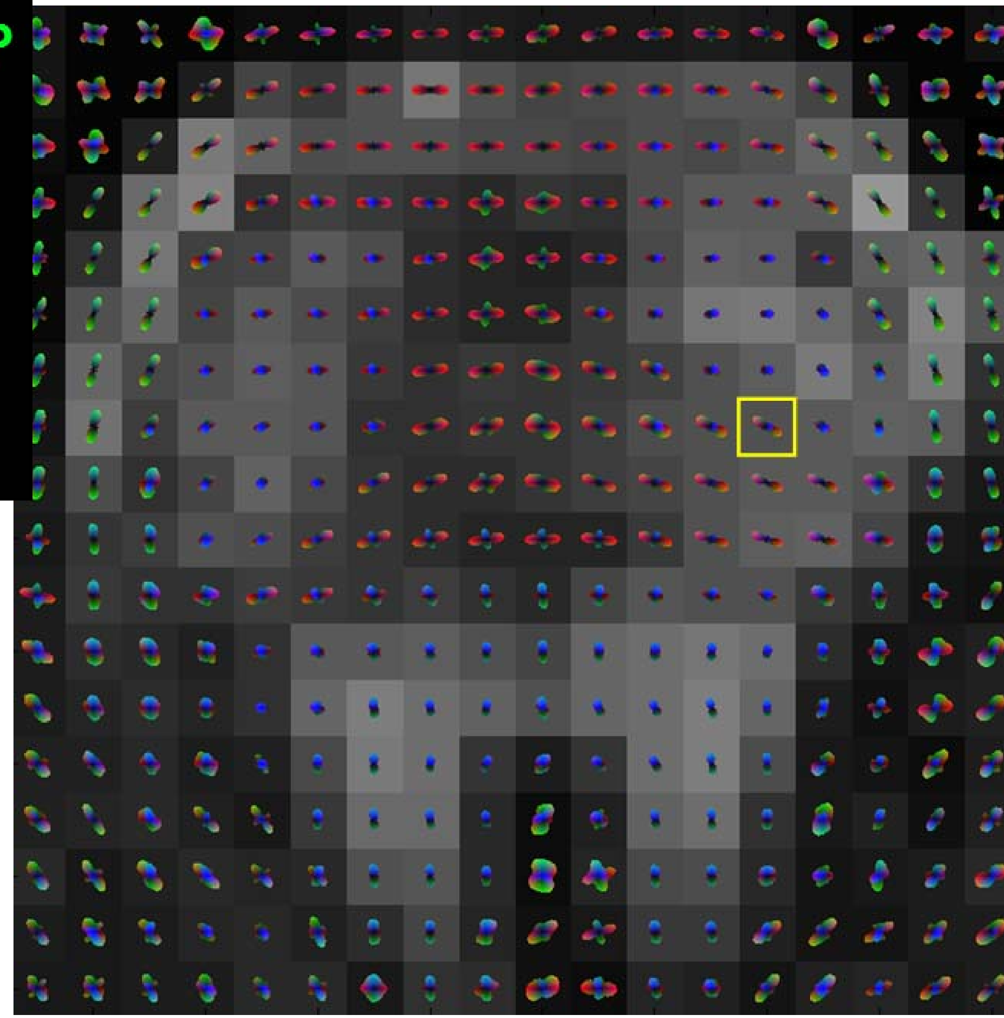
Figure 1



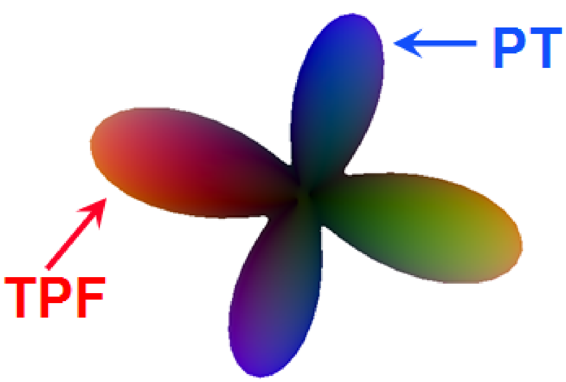
• more computationally efficient
• more numerically stable
• more analytically tractable

•Hess CP, Mukherjee P, Han ET, Xu D, Vigneron DB
•Magn Reson Med 2006;56:104-117



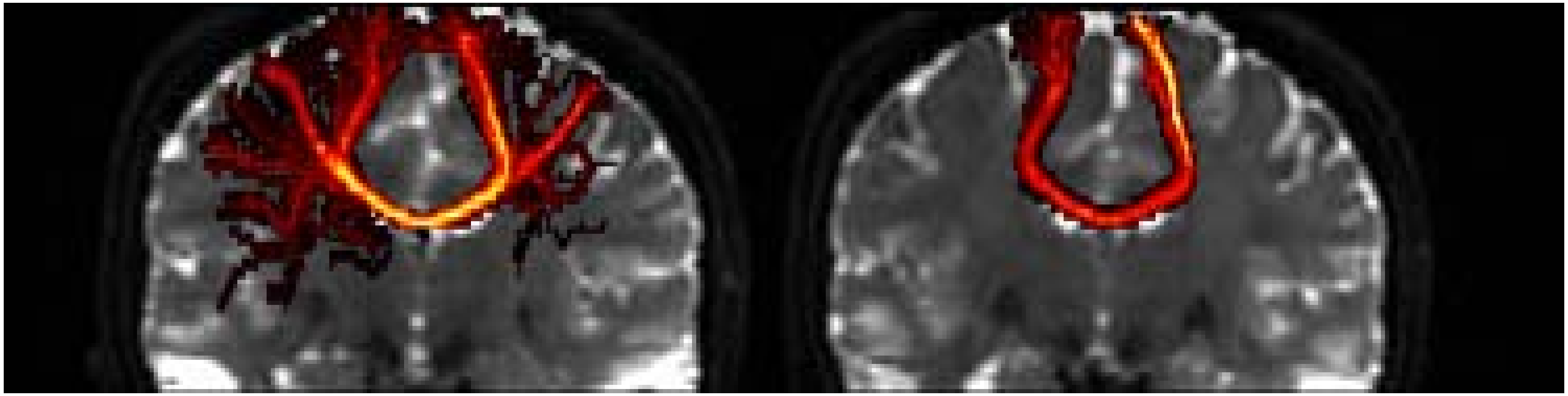


- Middle cerebellar peduncle (MCP)
- Superior cerebellar peduncle (SCP)
- Pyramidal tract (PT)
- Trans pontocerebellar fibers (TPF)



Hess CP, Mukherjee P, Han ET, Xu D, Vigneron DB
Magn Reson Med 2006; 56:104-117

Clinically Feasible HARDI Tractography



Harmonic *q*-ball

DTI

- Bootstrapping to generate probability distribution function for orientations
- Probabilistic streamline tracking
- 55 direction HARDI protocol, 1x1x2 mm resolution at b=3000 s/mm^2

Berman JI, Chung S, Mukherjee P, Hess CP, Han ET, Henry RG. Neuroimage (2007)

Problems

- ODF reconstruction suffers from noise
- Matrix is ill-conditioned
  - i.e. its inverse “magnifies” small noise values into large ones
- There are not enough diffusion directions
- HARDI with high b ➔ very low SNR (<20)

Current Solutions

- Use efficient representation of ODFs
  - Spherical harmonic basis
  - Radial basis
- Limit the order of the basis to use as few basis functions as possible
  - Currently we use spherical harmonics only up to order 4 or 6.
  - Higher order harmonics contain mostly noise
- (but this limits the angular resolution achievable, thus negating the motivation for HARDI)

Linear System

- Capture the model (whether RBF, SH, ...) into the linear model (matrix) H

  $$y = Hx + n$$

Then solve for x by inverting H

Usually inversion of H is ill-posed, so add a regularization term

This process is the same for ALL linear estimation problems!

Regularization

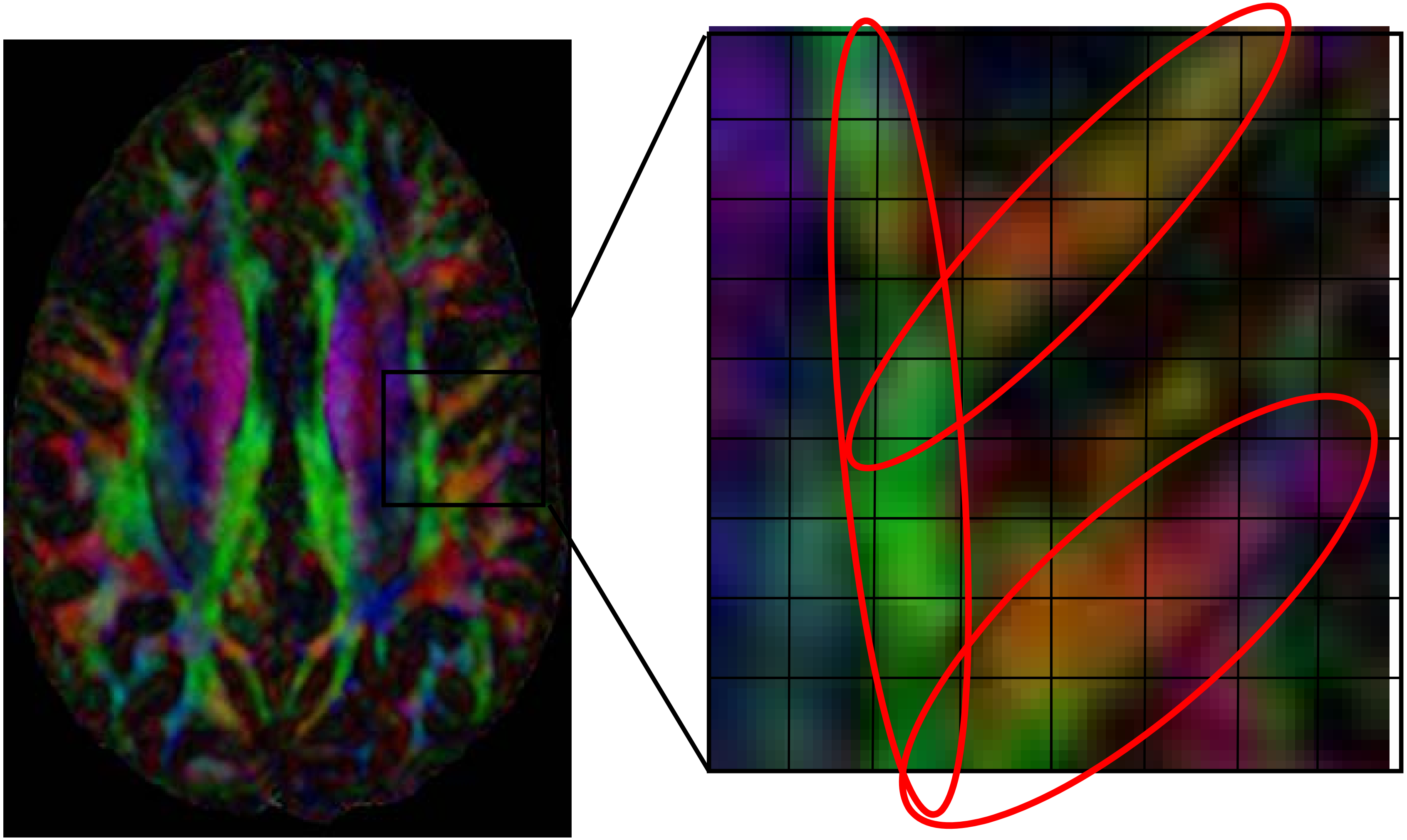
- Regularization of matrix inverse
  - Tikhonov
  - Laplace-Beltrami
- Tikhonov Regularization penalizes all harmonic coefficients
- Laplace-Beltrami penbalizes higher harmonic coefficients more
- Both methods serve to limit the effective angular resolution of reconstructed ODFs

A New Approach: add spatial constraints

- Fibers are not arbitrarily arranged in space
- Organized structure – follow coherent fiber tracts
- ODFs also have this organized structure
- ODF at one voxel is therefore related to ODF at its neighbours

1. How to characterize this neighbourhood relationship?
2. How to exploit these spatial constraints to improve ODF reconstruction?

Adding Spatial Constraints



- Neighbours are “like” each other, likely to have similar ODFs
- But need to allow for discontinuous boundaries

Iterative Algorithm

$$\textit{Begin with } \boldsymbol{\eta} = \boldsymbol{\eta}_0 .\ \textit{Then for } k = 1 \textit{ to } K, \textit{repeat:}$$

$$\hat{\boldsymbol{\eta}}^k = \arg\min_{\boldsymbol{\eta}} \left\{ \| \mathbf{e} - \overline{\mathbf{P}}\overline{\mathbf{Z}}_Q \boldsymbol{\eta} \|^2 + \lambda^2 \| \boldsymbol{\eta} \|^2 + \mu^2 \| \mathbf{D}\mathbf{W}(\boldsymbol{\eta}^{k-1}) \boldsymbol{\eta} \|^2 \right\}$$

$$\textit{where } \mathbf{W}(\boldsymbol{\eta}) = [w_{p,q}],\ w_{p,q} = 1 - \frac{\| \boldsymbol{\eta}_p - \boldsymbol{\eta}_q \|}{\| \boldsymbol{\eta}_p \| \| \boldsymbol{\eta}_q \|}$$

Iterative Algorithm

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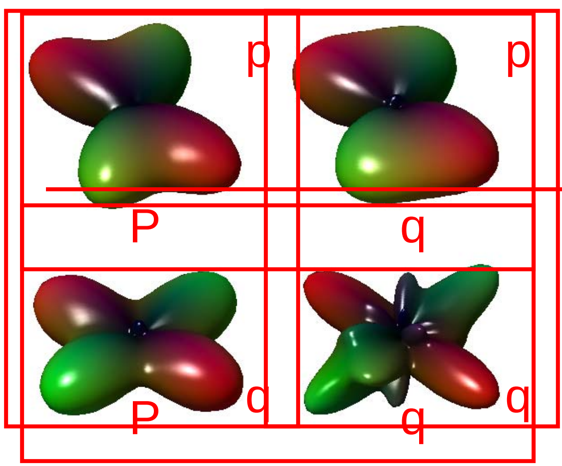
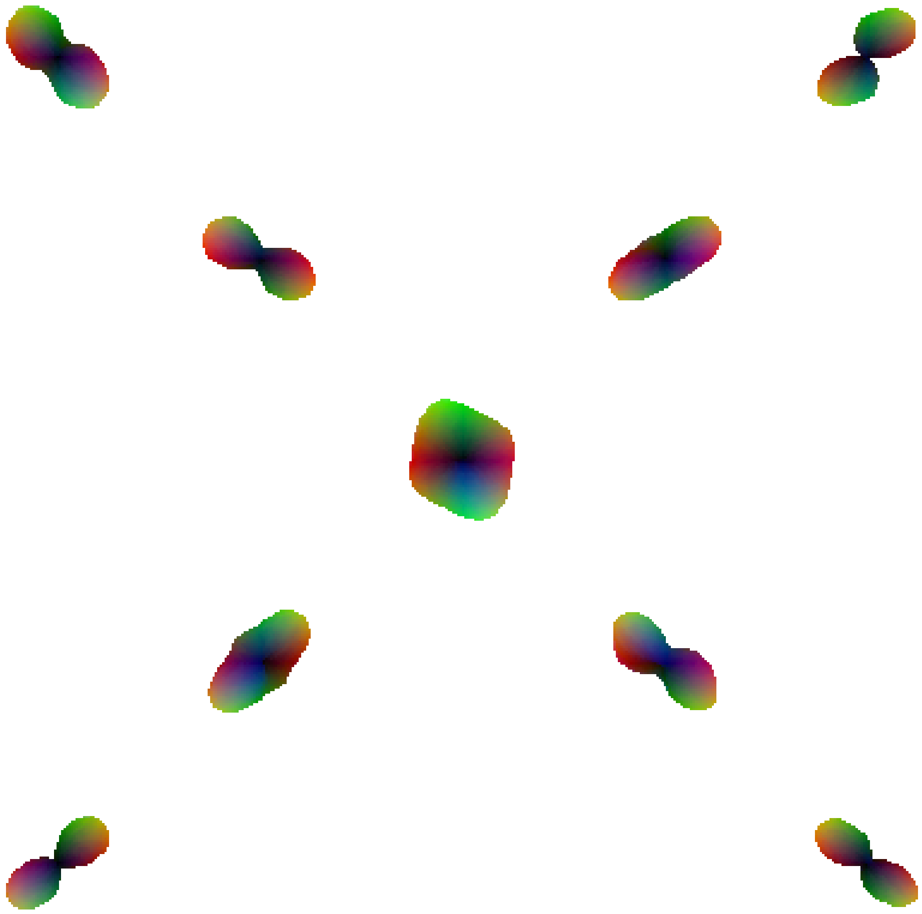
$$\textit{where } \mathbf{W}(\boldsymbol{\eta}) = [w_{p,q}], w_{p,q} = 1 - \frac{\| \boldsymbol{\eta}_p - \boldsymbol{\eta}_q \|}{\| \boldsymbol{\eta}_p \| \| \boldsymbol{\eta}_q \|}$$

small $w_{p,q}$

large $w_{p,q}$

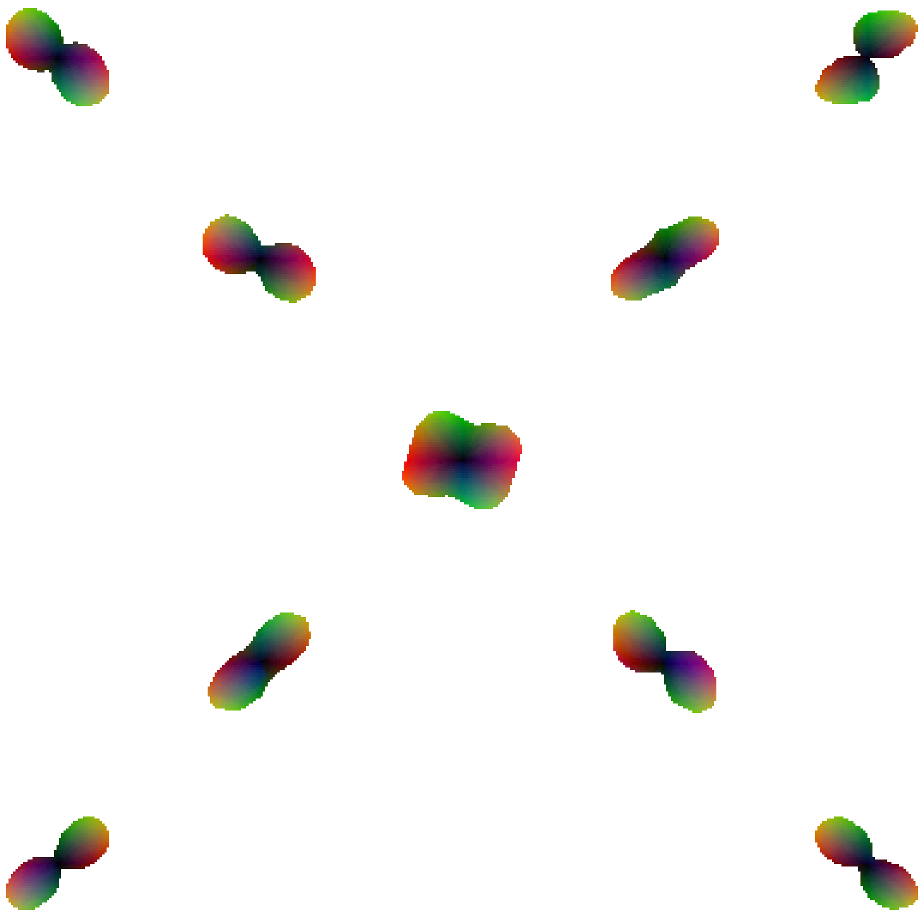


Results – simulation



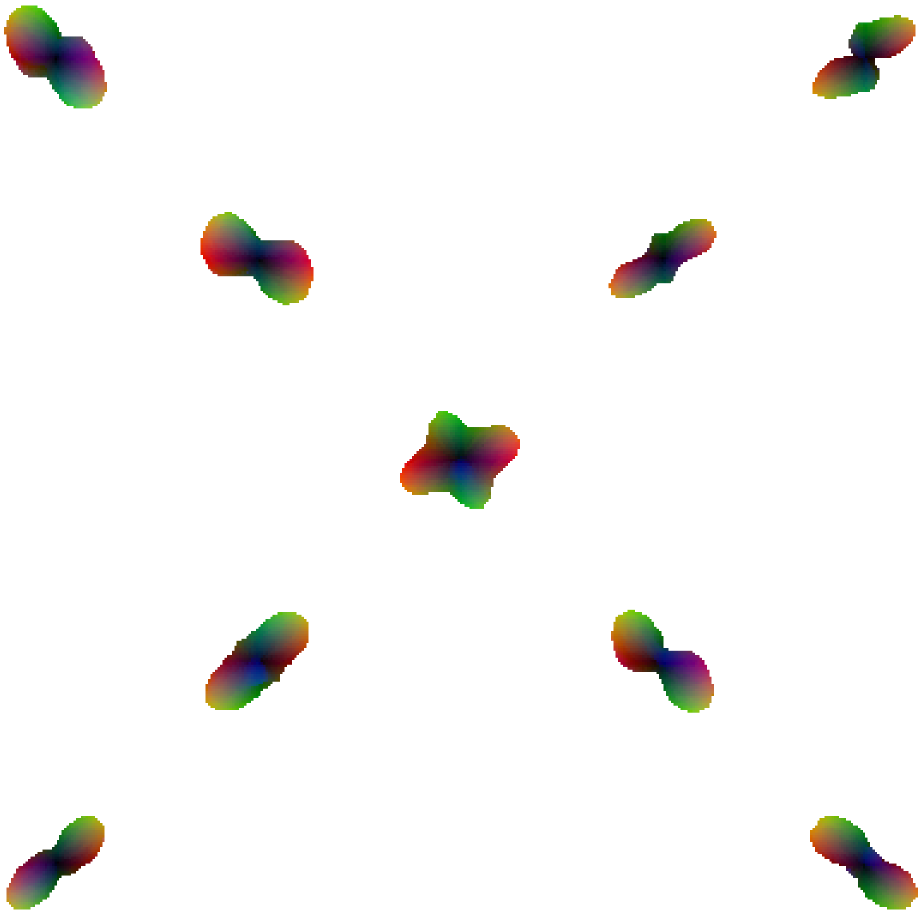
sh-QBI reconstruction

Results – simulation



sh-QBI + smoothing

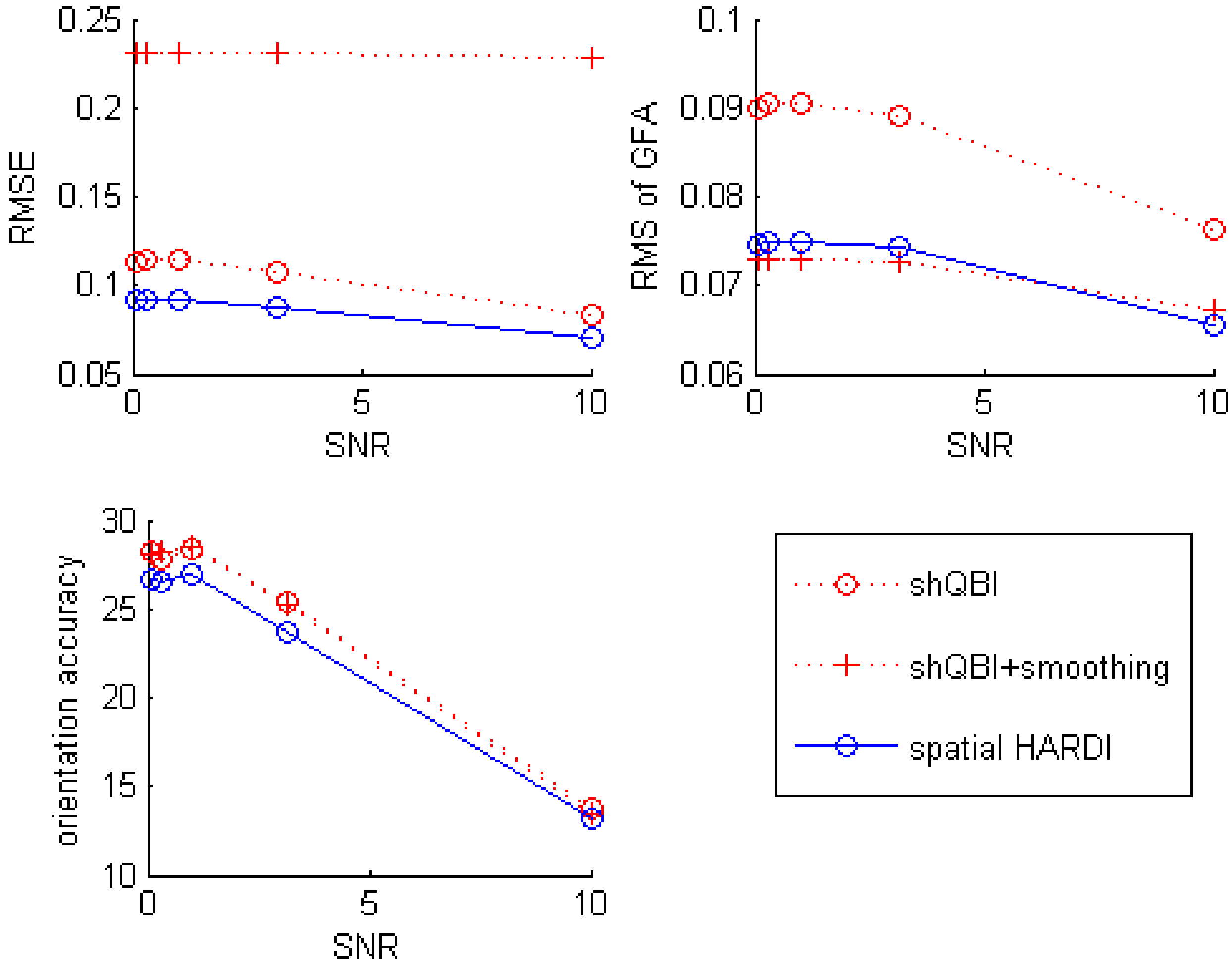
Results – simulation



Monte Carlo simulations

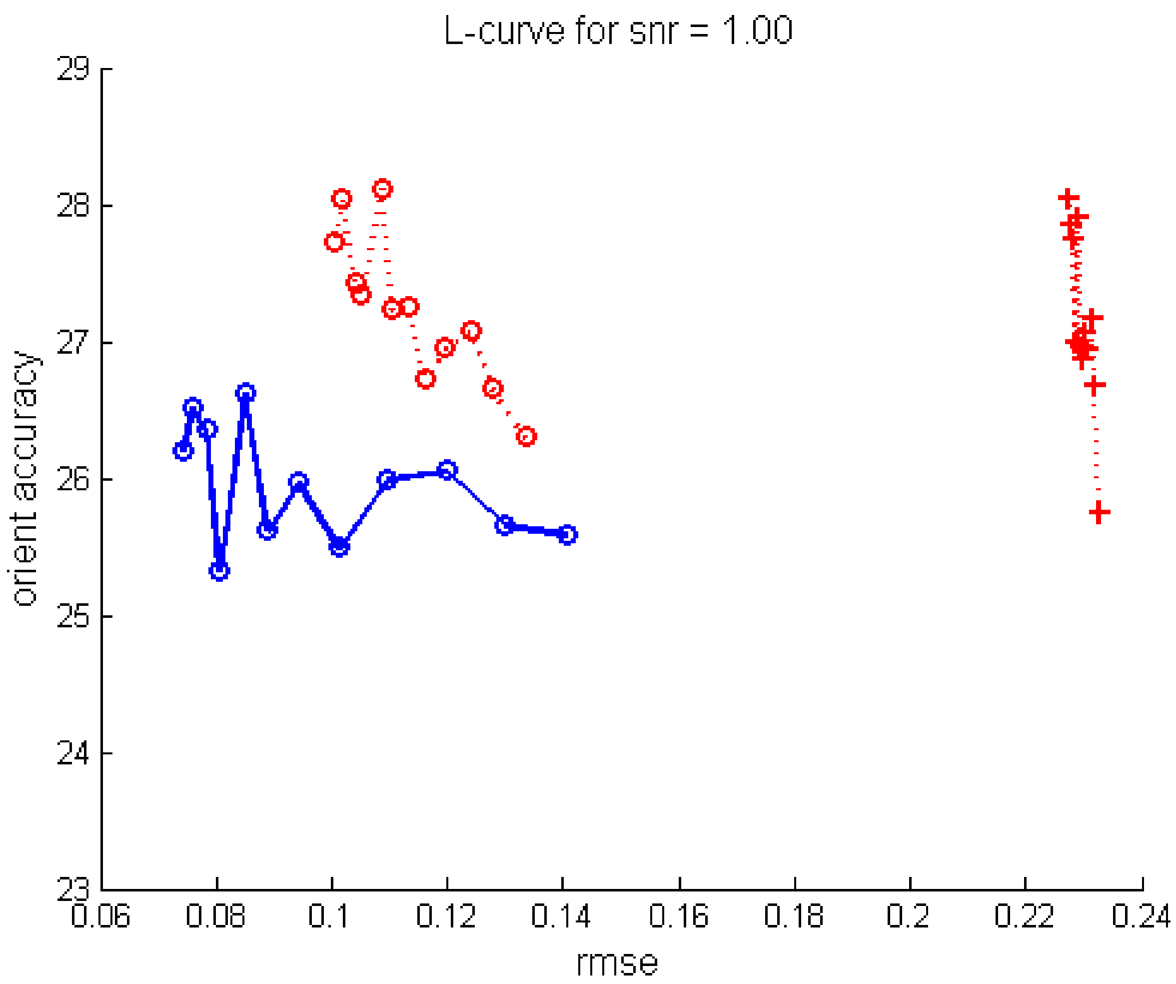
- Repeated multiple times for multiple, random 3D tracts within a 15 x 15 x 15 voxel volume
- Repeated for varying :
  - SNR
  - Algorithm parameters (lambda, mu)
- Evaluation criteria:
  - RMSE
  - Generalized FA
  - Orientation accuracy

Monte Carlo simulations

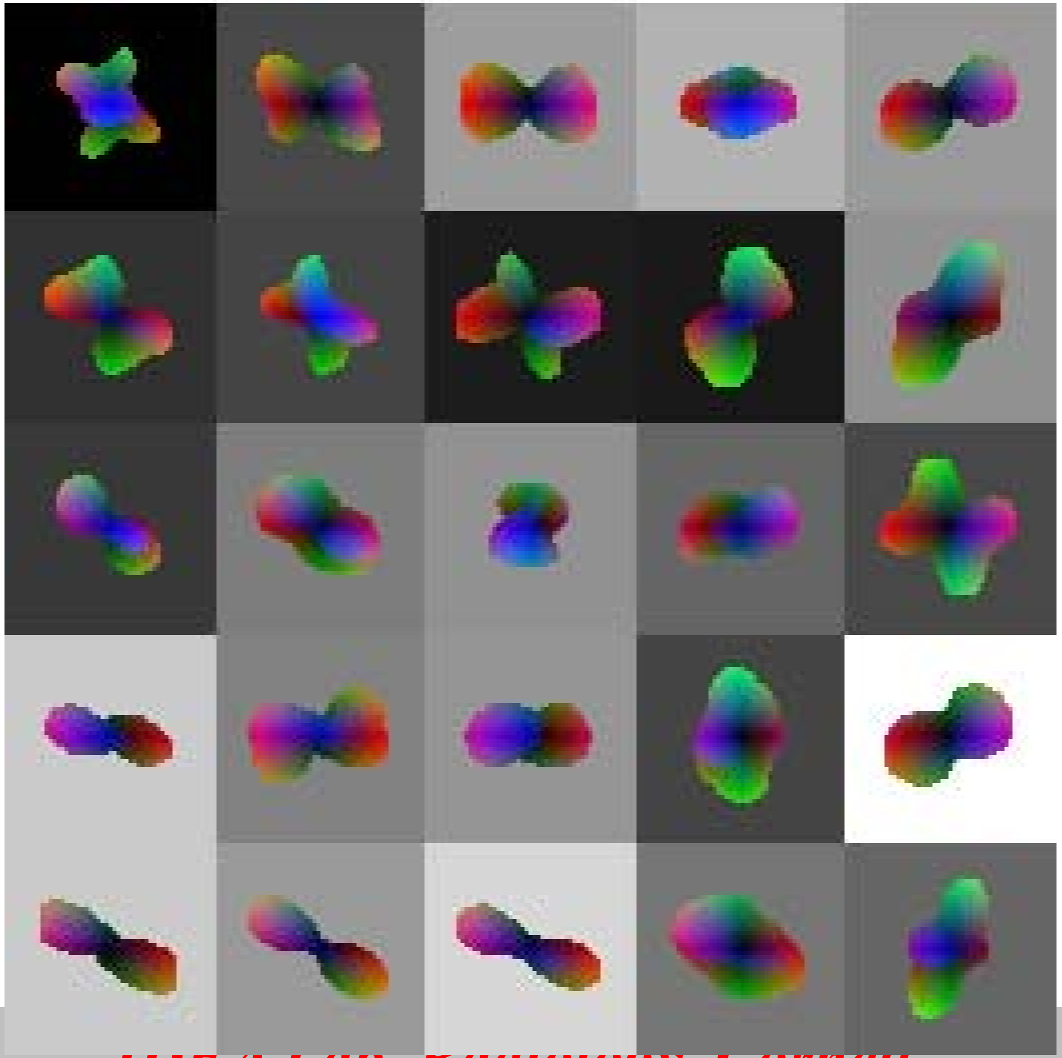


Performance against input SNR

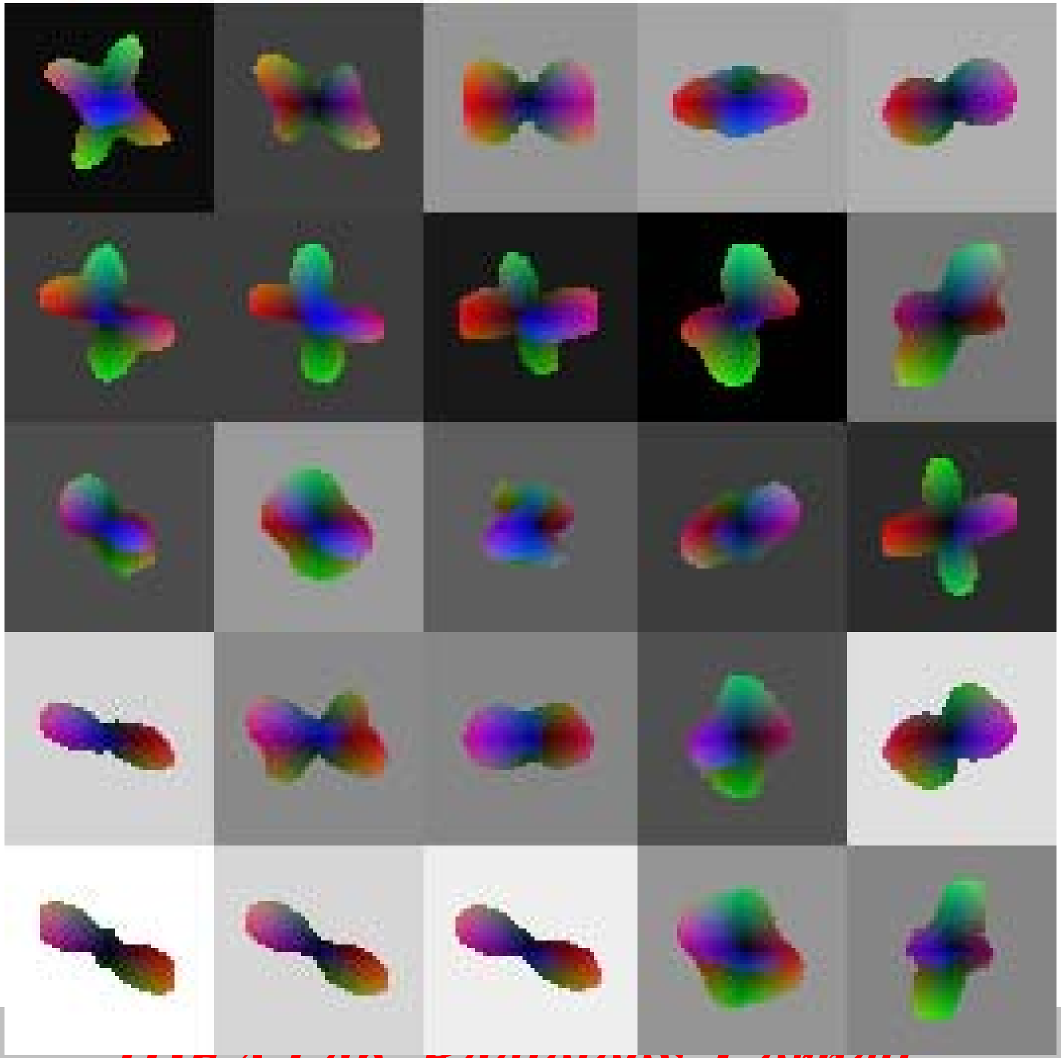
Monte Carlo simulations



In vivo results



In vivo results



Part IV : Detection Theory and Examples

- Introduction to optimal detection
- Matched filter detectors
- Detection examples from MR

What is Detection

- Deciding whether, and when, an event occurs
- a.k.a. Decision Theory, Hypothesis testing
- Presence/absence of
  - signal
  - activation (fMRI)
  - foreground/background
  - tissue – WM/GM/CSF (segmentation)
- Measures whether statistically significant change has occurred or not

Detection

- "Spot the Money"

Hypothesis Testing with Matched Filter

- Let the signal be $y(t)$, model be $h(t)$

  Hypothesis testing:

  H_0: $y(t) = n(t)$ (no signal)

  H_1: $y(t) = h(t) + n(t)$ (signal)

- The optimal decision is given by the Likelihood ratio test (Nieman-Pearson Theorem)

  Select H_1 if $L(y) = Pr(y|H_1)/Pr(y|H_0) > \gamma$

- It can be shown (Kay 01) to be equivalent to

  $y(t) * h(t) > \gamma'$

  Matched Filter

Matched Filters

- If the profile of a certain signal is known, it can be detected using the Matched Filter
- If the question is not IF but WHERE...
- Maximum of MF output denotes the most likely location of the object h(t)

Matched Filters

- Example 1: activation in fMRI
  – Need profile model: hemodynamic response function
- Example 2: Detecting malignant tumours in mammograms
  – need profile model: temporal response to contrast agent
- Example 3: Edge detection
- Example 4: detecting contrast arrival in CE-MRA
- In each case need a model to “match” the signal

Edge Detection

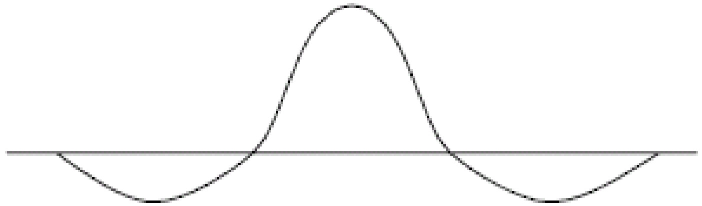
- Edge information can be used for segmentation
- Detect edges by finding areas of max intensity change
- DoG (Derivative of Gaussian):

  $\nabla^2 (I(x,y) * G(x,y,\sigma))$
- $G(x,y,\sigma)$ = Gaussian
- ∇^2 = Laplacian operator
- Marr-Hildreth, Canny, Roberts, etc
- Problems: very sensitive to noise, choice of σ

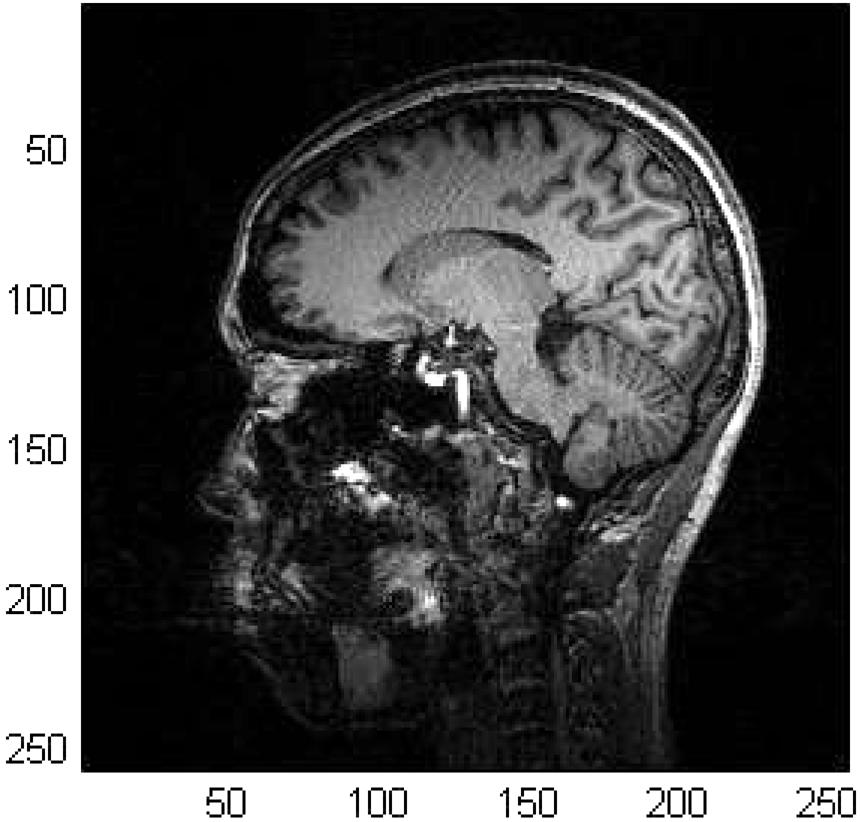
Edge Detection

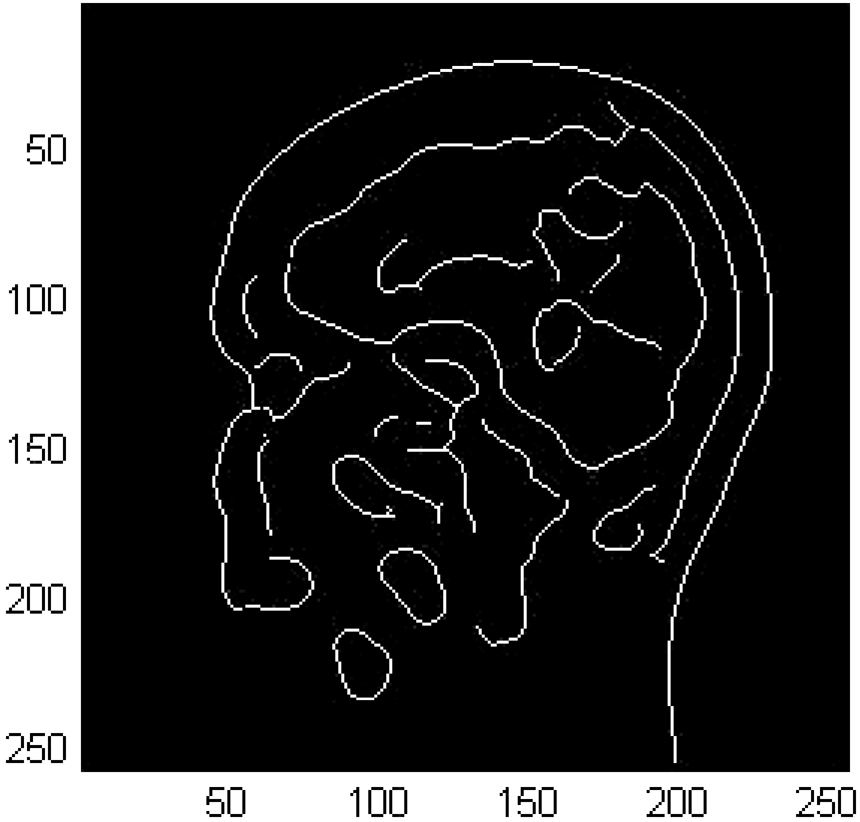
	1	
1	-4	1
	1	

$$\nabla^2 (G_\sigma \star I) \ .$$



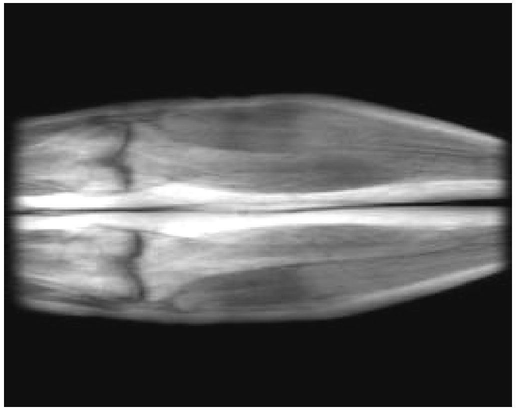
Edge Detection example using MATLAB





bw = edge(I, ‘canny’, sigma);

Example: Contrast Arrival in CE-MRA



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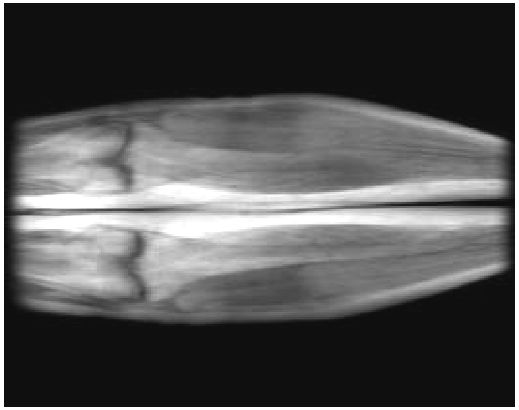

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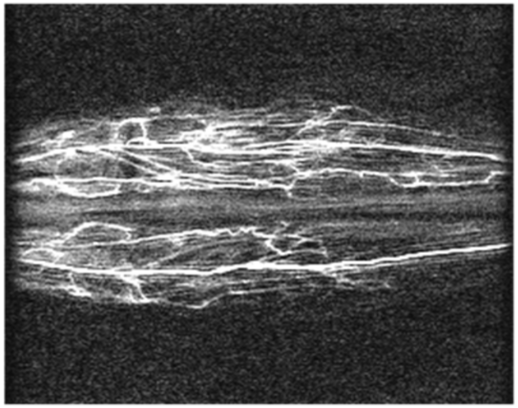
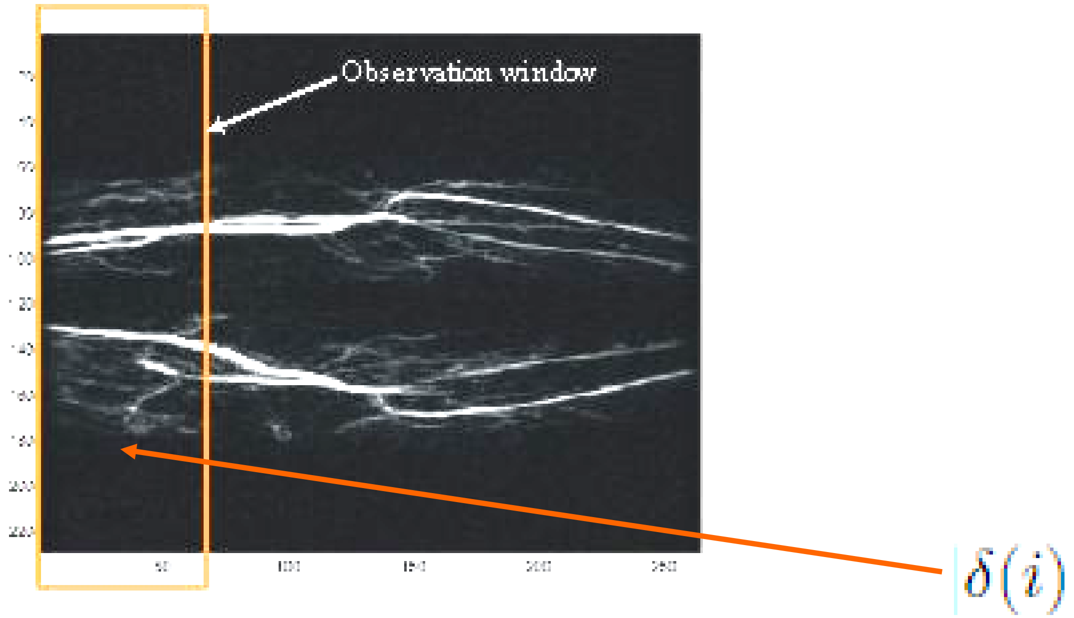


Mask subtraction in MRA gives vasculature

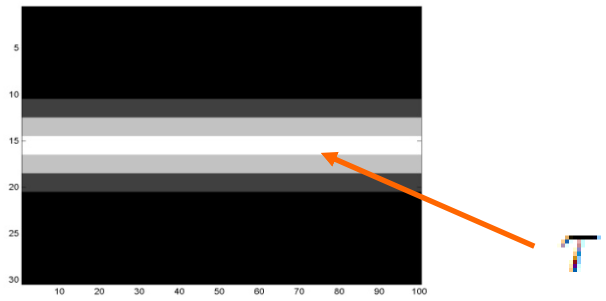
Automatic Detection of Contrast Arrival

- MRDSA relies on good estimate of contrast arrival
- Completely unsupervised, reliable automatic method
- >90% accuracy, c.f. earlier reported method (~60% accuracy)
  - matched filter - spatial metric
  - keyhole - frequency metric

Vasculature strongly oriented horizontally

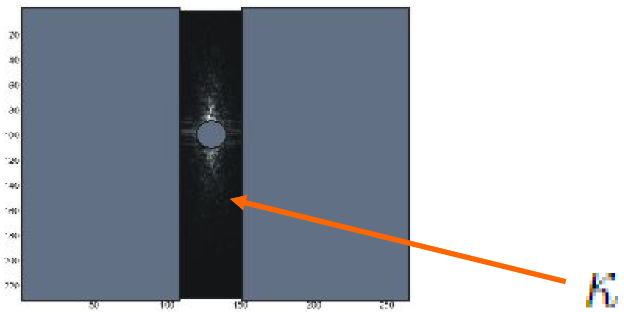


Matched Filter



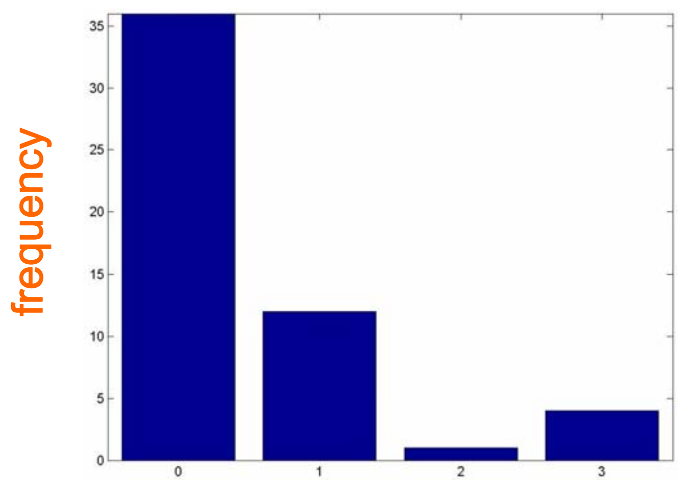
$$\lambda_{MF}(i) = \frac{||\delta(i) ** \tau||}{||\tau|| \cdot ||\delta(i)||},$$

Keyhole



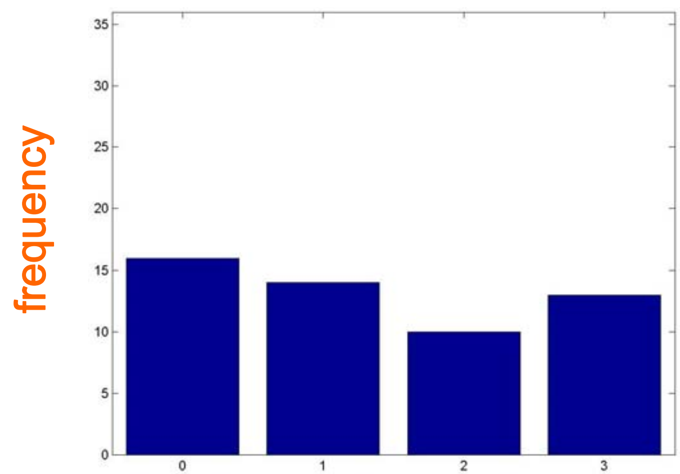
$$\lambda_{KH}(i) = \frac{||\delta_K(i) \cdot \kappa||}{||\delta_K(i)||}.$$

Results : Our method



accurate -----> inaccurate

Earlier method



accurate -----> inaccurate

Estimation and Detection of MR Signals

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Visit:
http://www.cs.cornell.edu/~rdz/SENSE.htm

This concludes today’s lecture.

Next week: Classification, Image segmentation, Registration

References

- Simon Kay. Statistical Signal Processing. Part I: Estimation Theory. Prentice Hall 2002
- Simon Kay. Statistical Signal Processing. Part II: Detection Theory. Prentice Hall 2002
- Haacke et al. Fundamentals of MRI.
- Zhi-Pei Liang and Paul Lauterbur. Principles of MRI – A Signal Processing Perspective.

Info on part IV:

- Ashish Raj. Improvements in MRI Using Information Redundancy. PhD thesis, Cornell University, May 2005.

- Website: http://www.cs.cornell.edu/~rdz/SENSE.htm