Modeling and Analysis of Inherently Complex-Valued FMRI Data

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Outline

Introduction
MRI, fMRI and fcMRI data are truly complex-valued.

Modeling
Use complex-valued time series! Greater sensitivity/specificity.

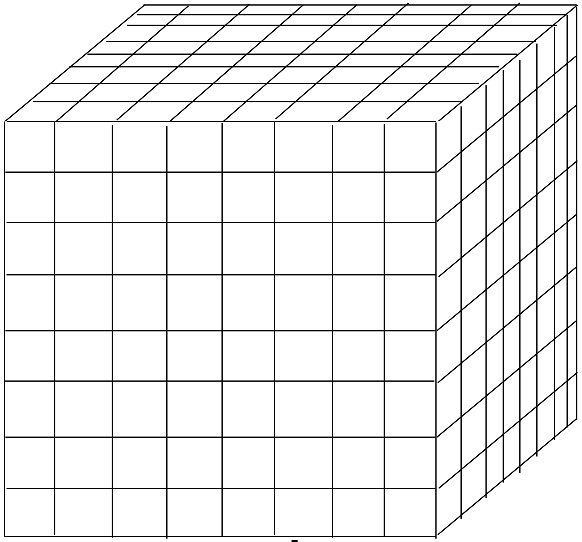
Phase Information
Studies have demonstrated biological information in the phase.

Results
Gains from not throwing away phase half of data.

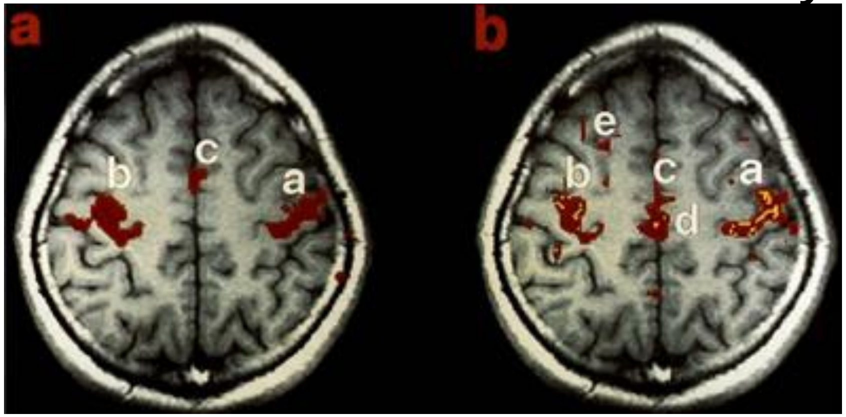
Discussion
We need utilize as much of the rawest data as possible.

Introduction

Voxels

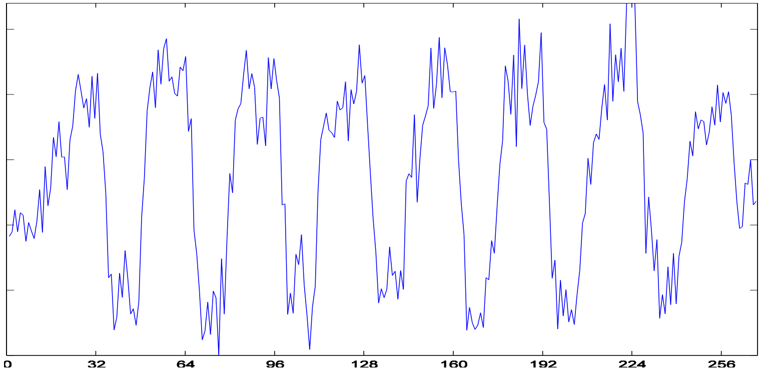


Activation or Connectivity

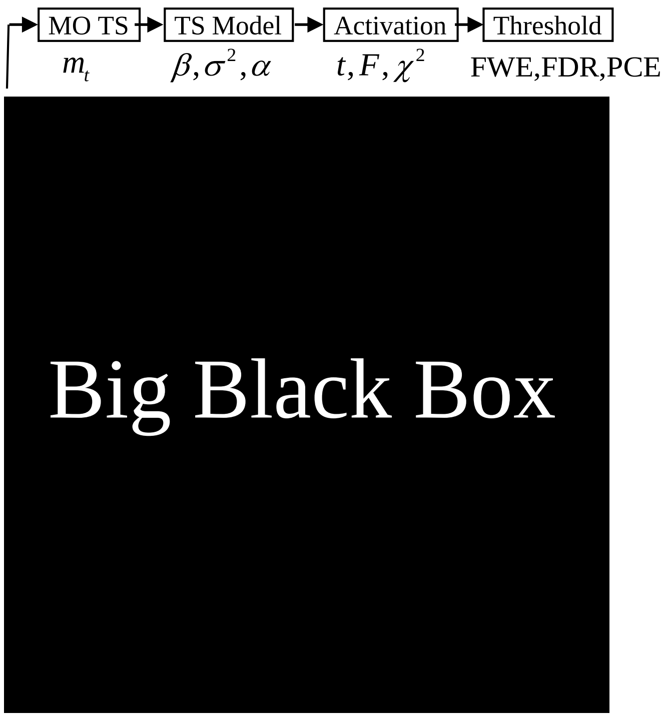


Biswal, MRM 1995.

Time Course



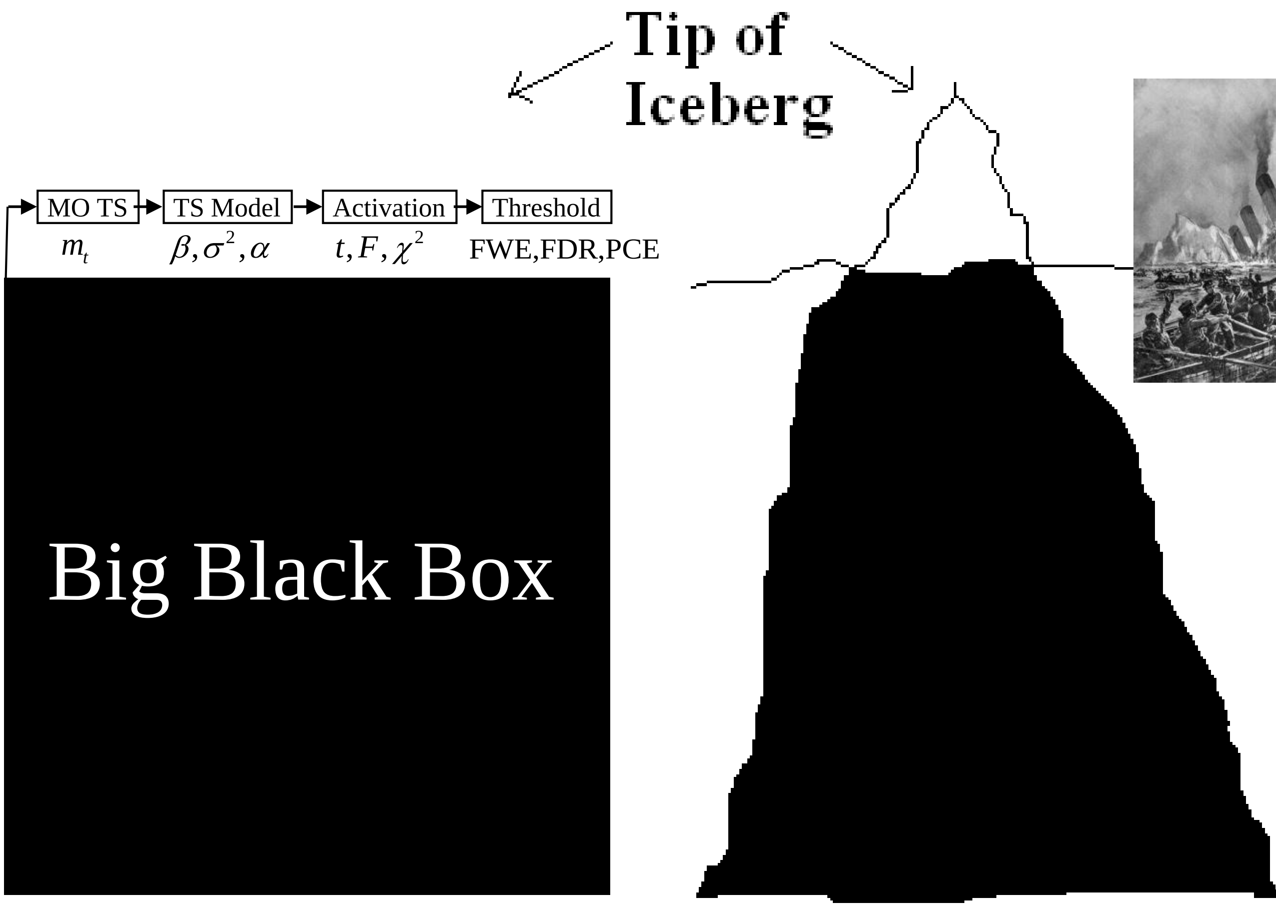
Introduction



In fMRI the statistical analysis (almost) always begins with magnitude-only time series.

There is a **Big Black Box** that is ignored between MO TS model and the physical quantities.

Introduction



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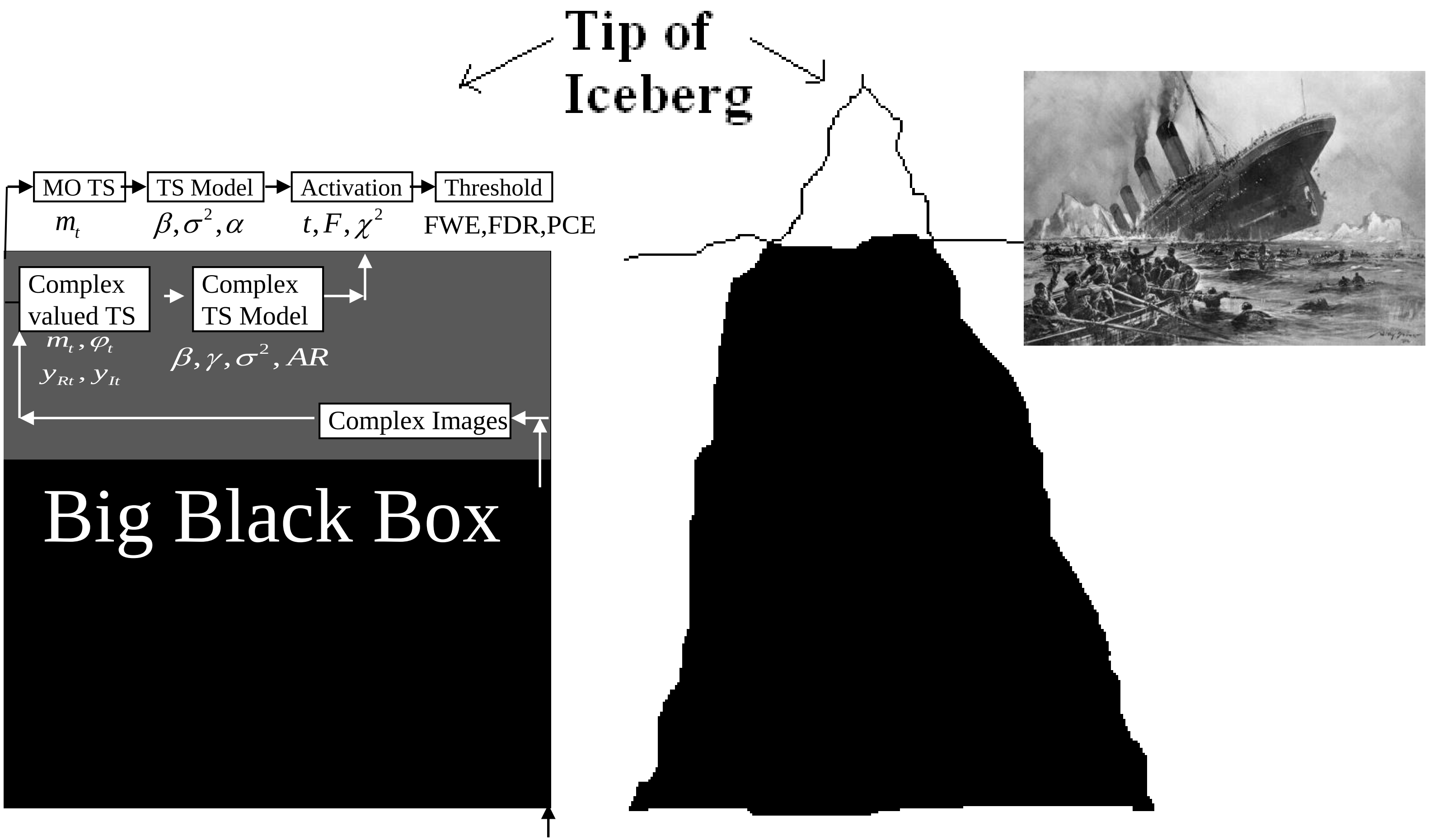


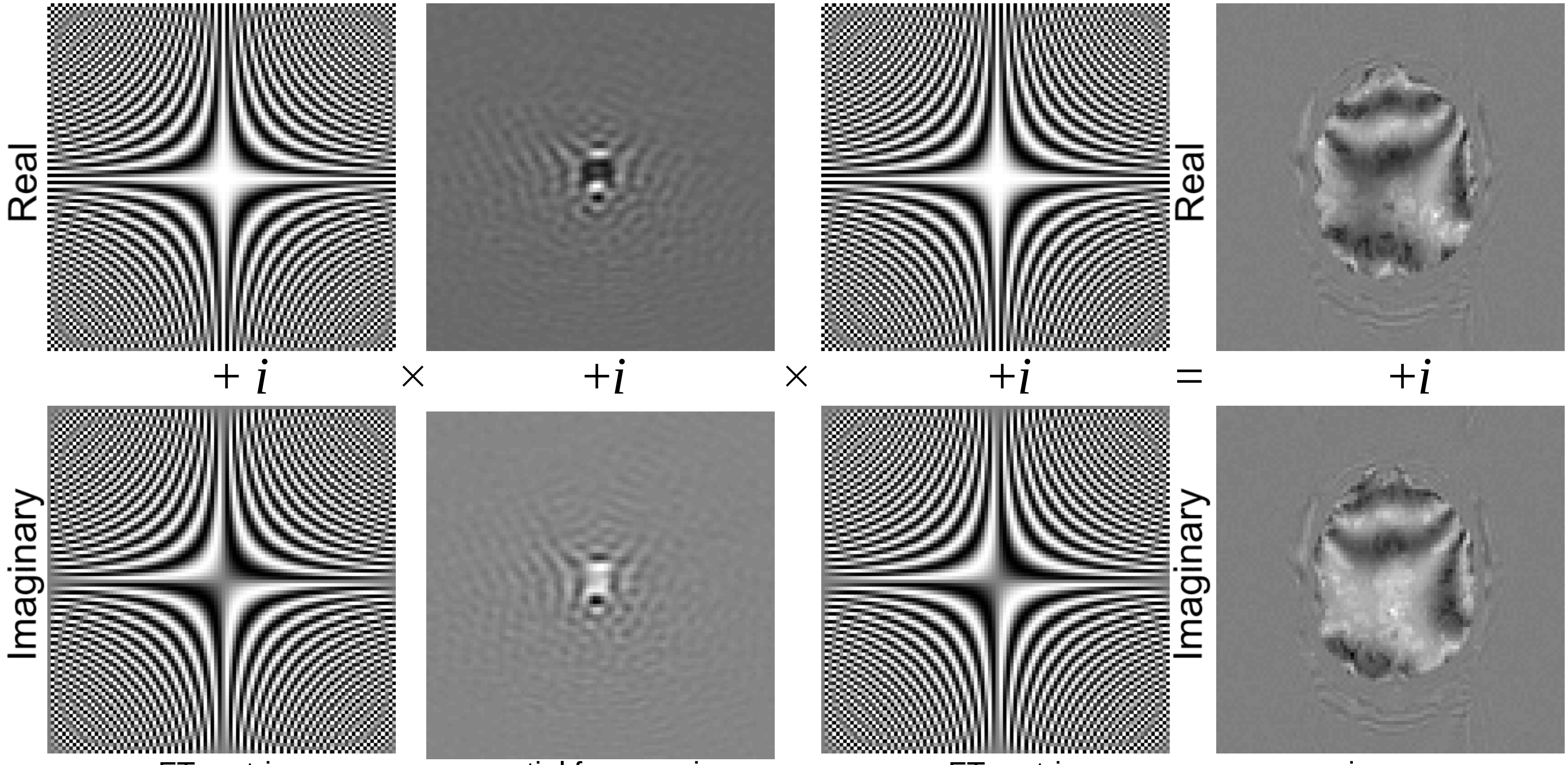
Shed light on part of the **black box**!

(FOV=240 mm)

(n_x=n_y=96, Δx=Δy=2.5 mm)

Introduction

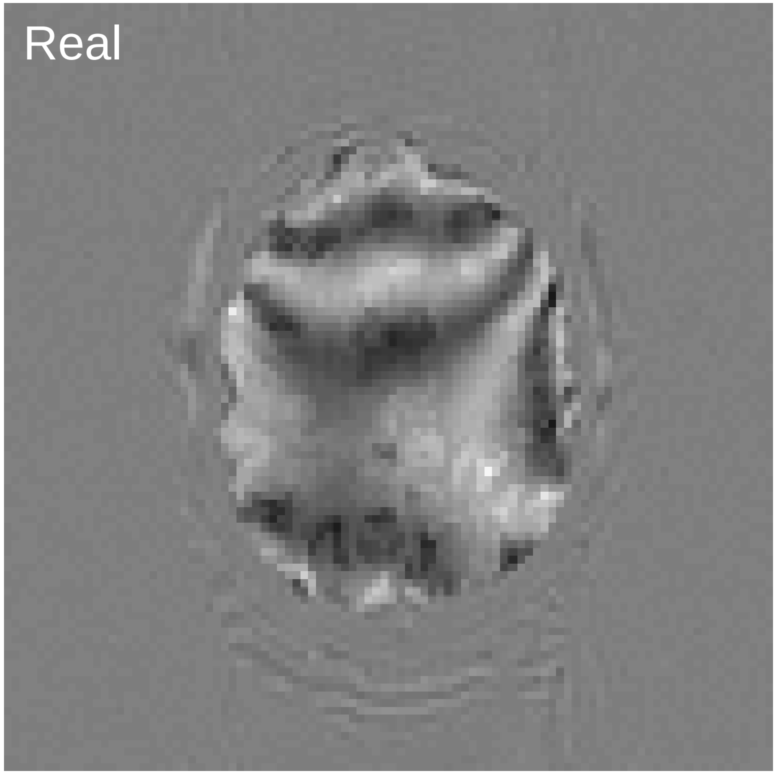
We inverse Fourier transform spatial freqs to generate image.

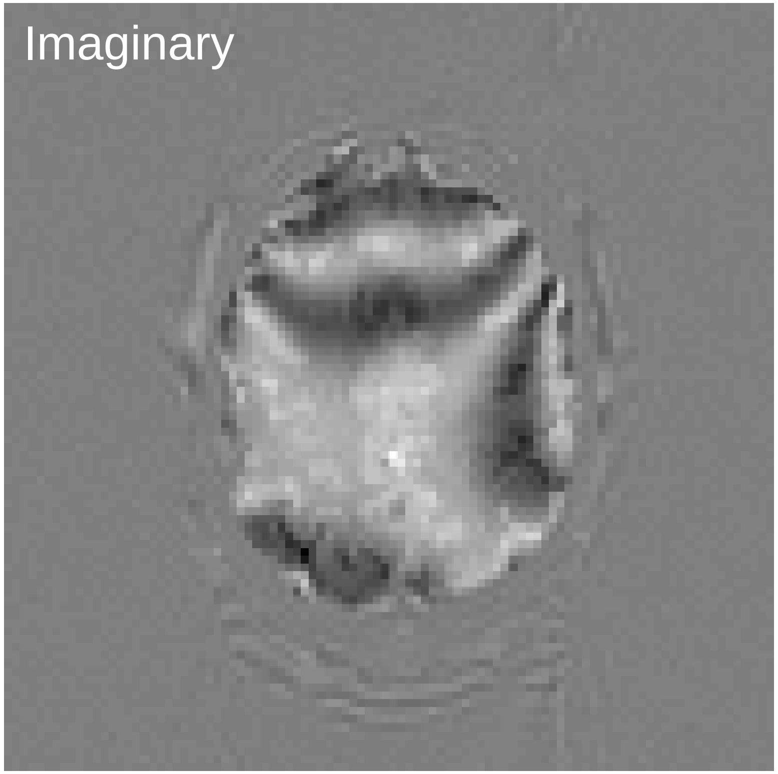


FT matrix | spatial frequencies | FT matrix | image

Introduction

Due to imperfect reconstruction (noise, T_2*, ΔB, …), image is complex-valued, $Y(x,y)=Y_R(x,y)+iY_I(x,y)$.





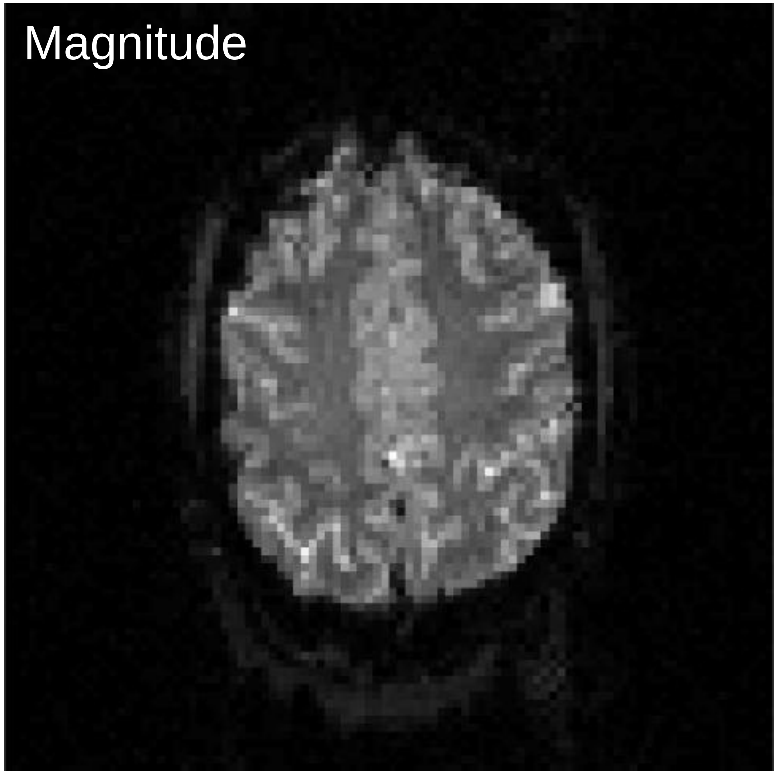
96×96
240mm FOV
2.5 mm^2
In-Plane

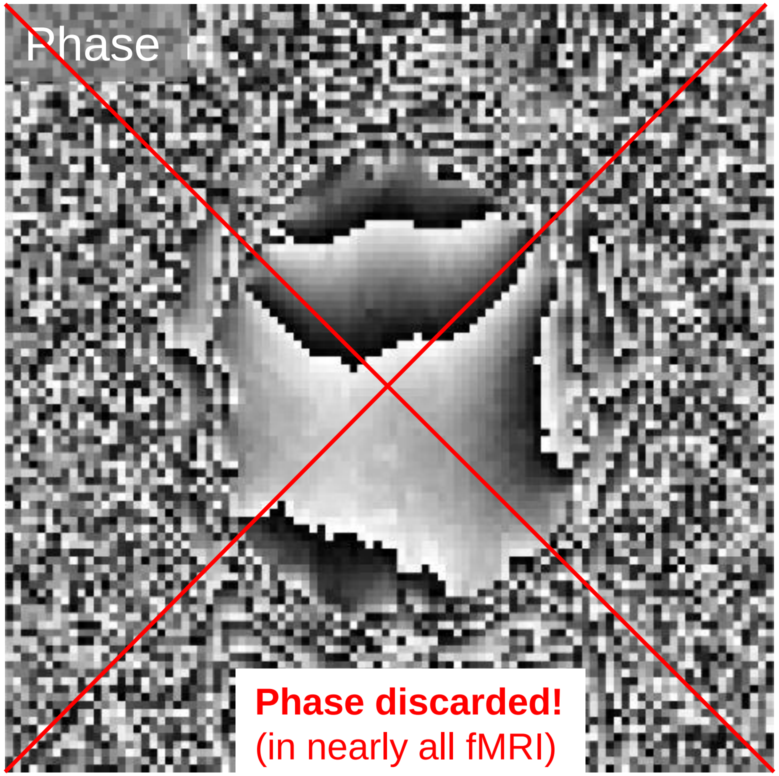
Real Image, y_{Rt} Imaginary Image, y_{It}

given voxel at time *t*

Introduction

Due to imperfect reconstruction (noise, T_2*, ΔB, …), image is complex-valued, $Y(x,y)=M(x,y)\exp[i\Phi(x,y)]$





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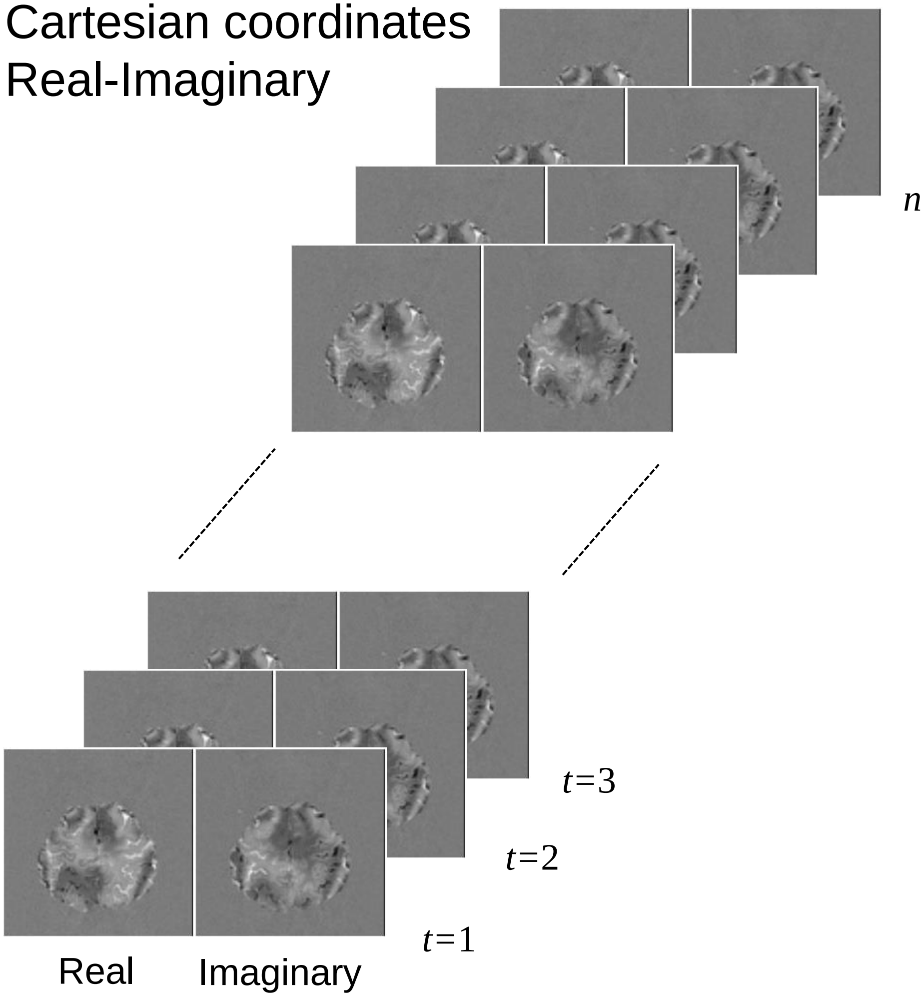
240mm FOV
2.5 mm^2
In-Plane

Magnitude Image, $m_t=\sqrt{y_{Rt}^2+y_{It}^2}$ Phase Image, $\varphi_t=\tan^{-1}(y_{It}/y_{Rt})$

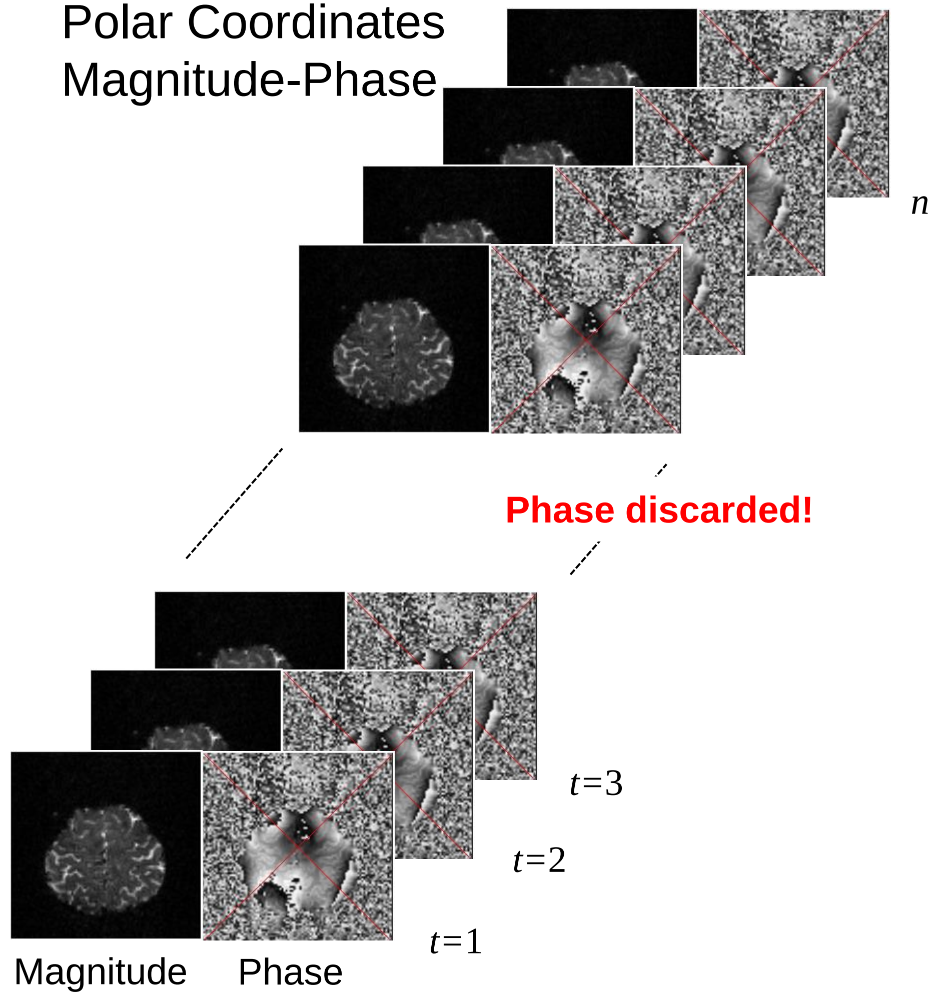
given voxel at time t

Introduction

Cartesian coordinates
Real-Imaginary



Polar Coordinates
Magnitude-Phase

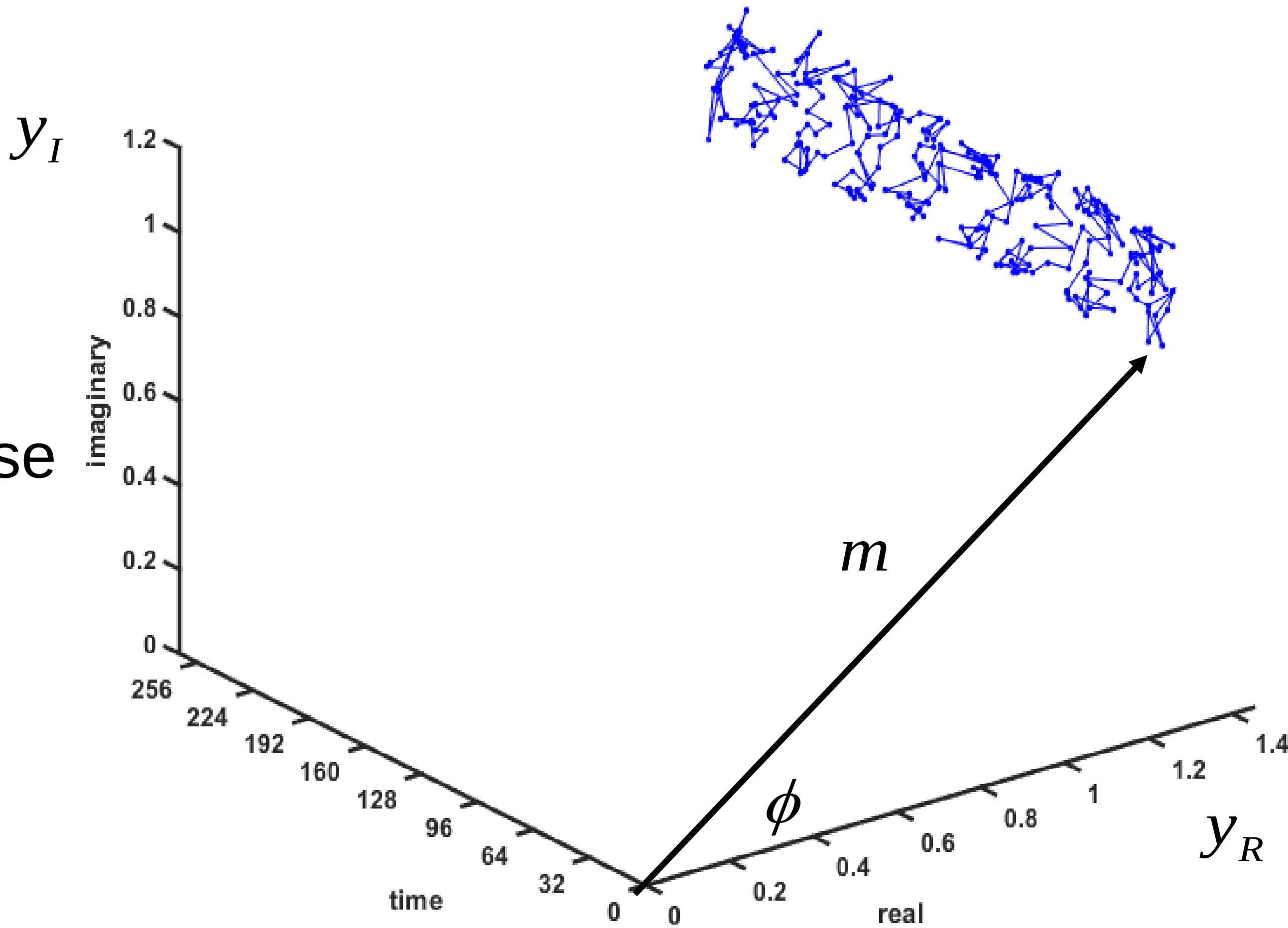


Modeling

This opens up the opportunity for complex-valued analysis!

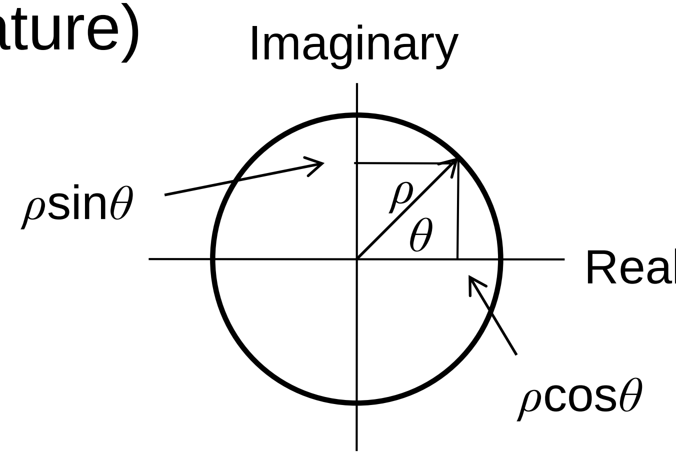
Complex-valued activation and/or Complex-valued correlation?

Magnitude and Phase or equivalently Real and Imaginary



Modeling

Voxel measurements are described as (absorption/dispersion, in-phase/quadrature)

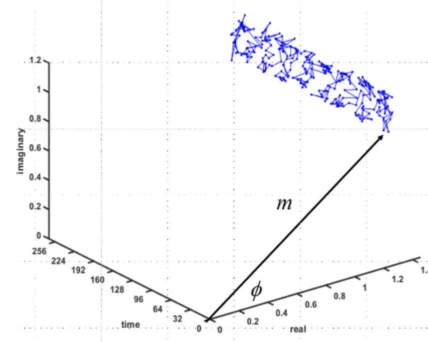


$$y_R = \rho\cos\theta + \eta_R$$
$$y_I = \rho\sin\theta + \eta_I$$

y_R and y_I are measurements for the real and imaginary parts

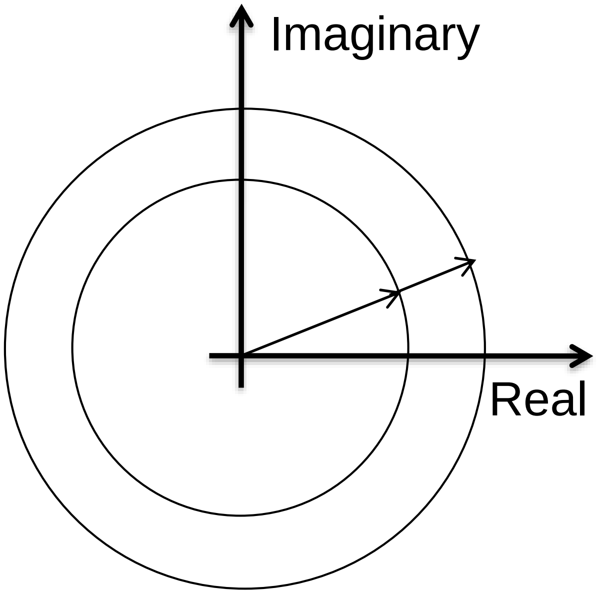
η_R and η_I are error terms for the real and imaginary parts

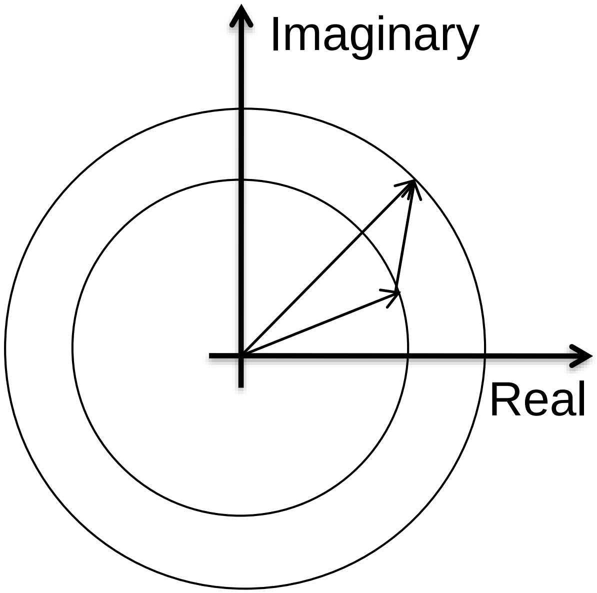
ρ and θ are the population magnitude and phase.

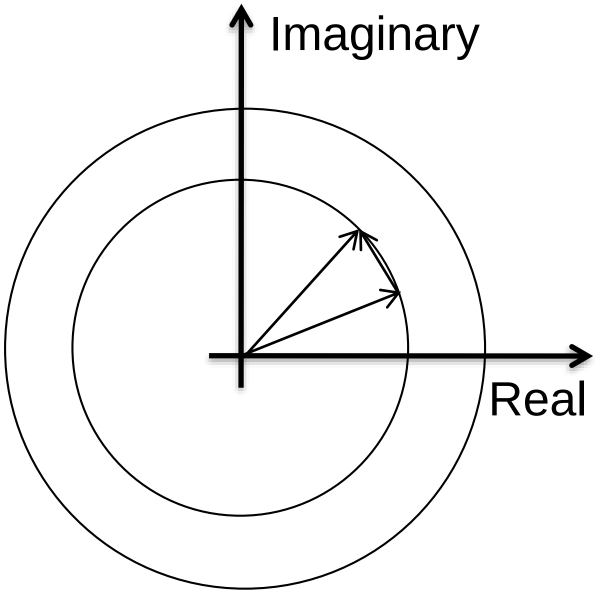


Modeling

Three non-zero changes possible.







- Complex Magnitude w/ Constant Phase (CP) Activation[1,2]
- Complex Magnitude and/or Phase (MP) Activation[3,7]
- Real Magnitude-Only (MO/UP) Activation (Discard Phase)[4,5]
- Real Phase-Only (PO) Activation (Discard Magnitude)[6]

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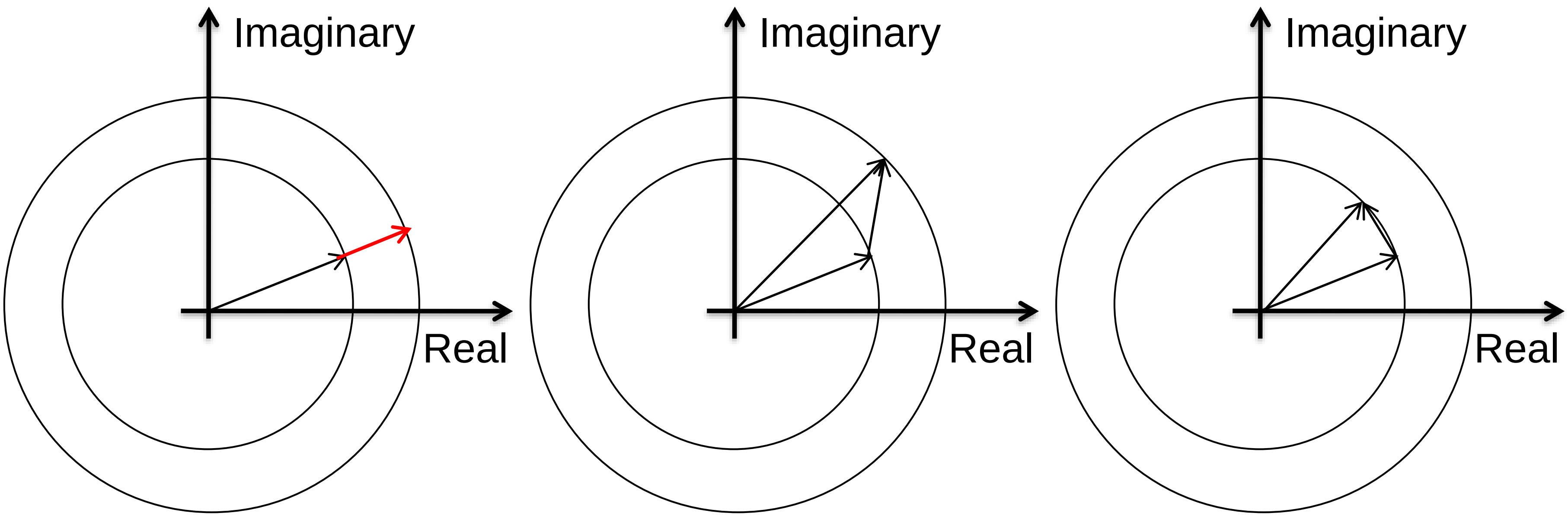

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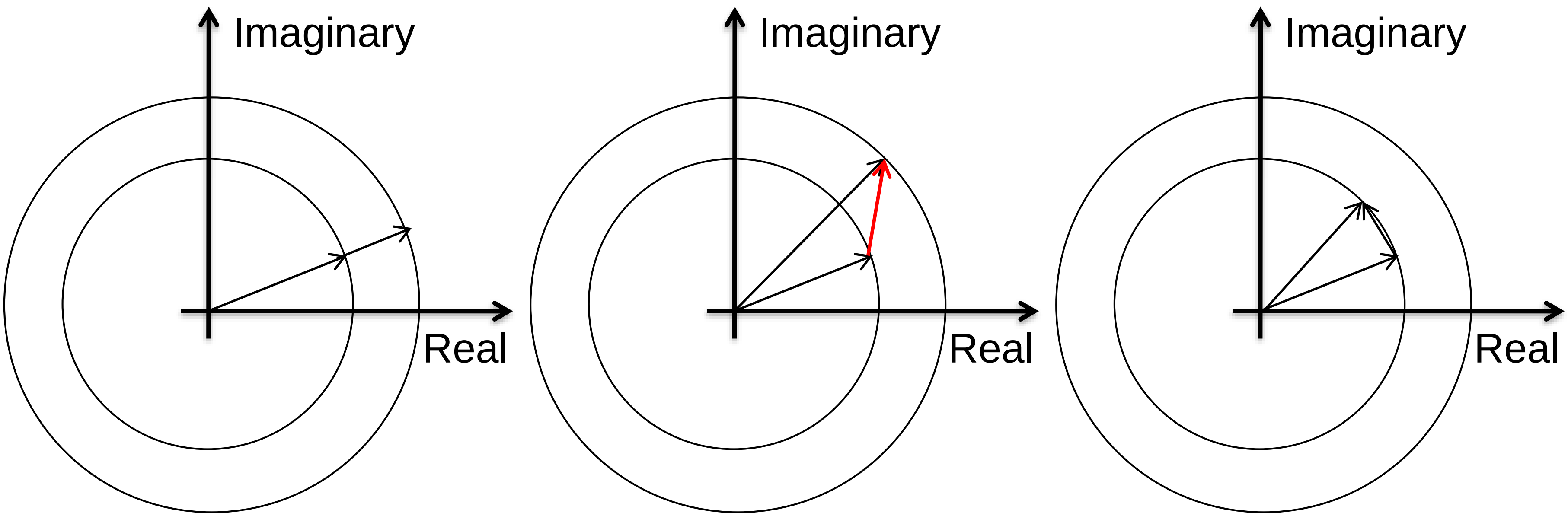

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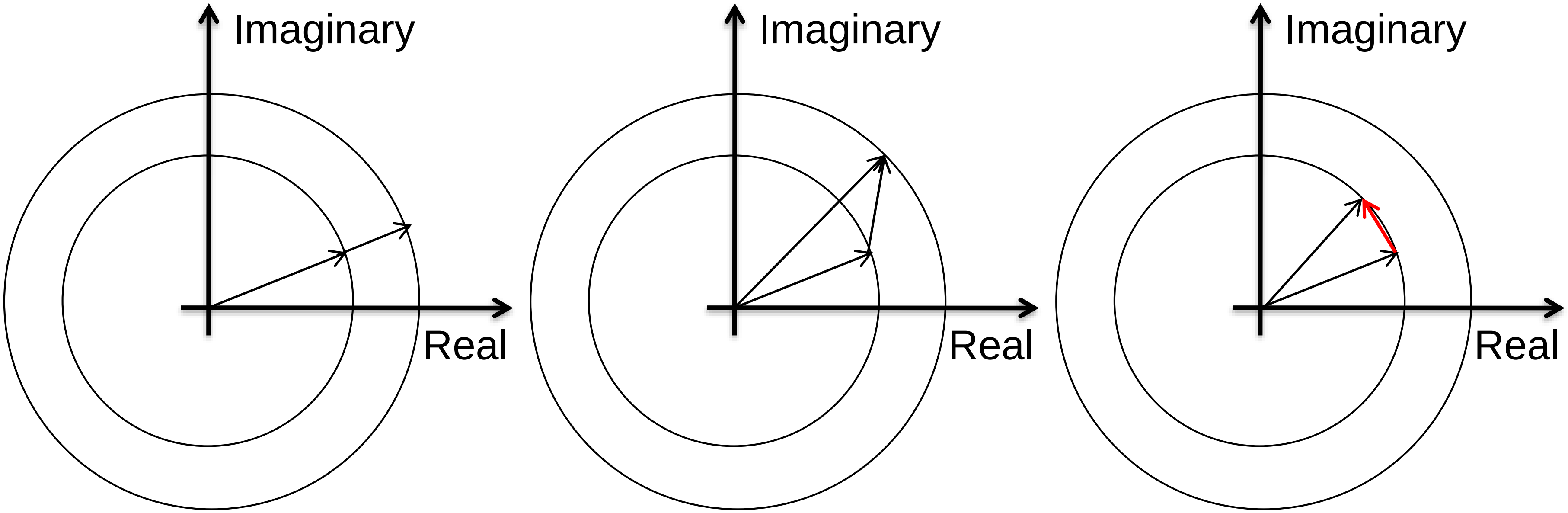

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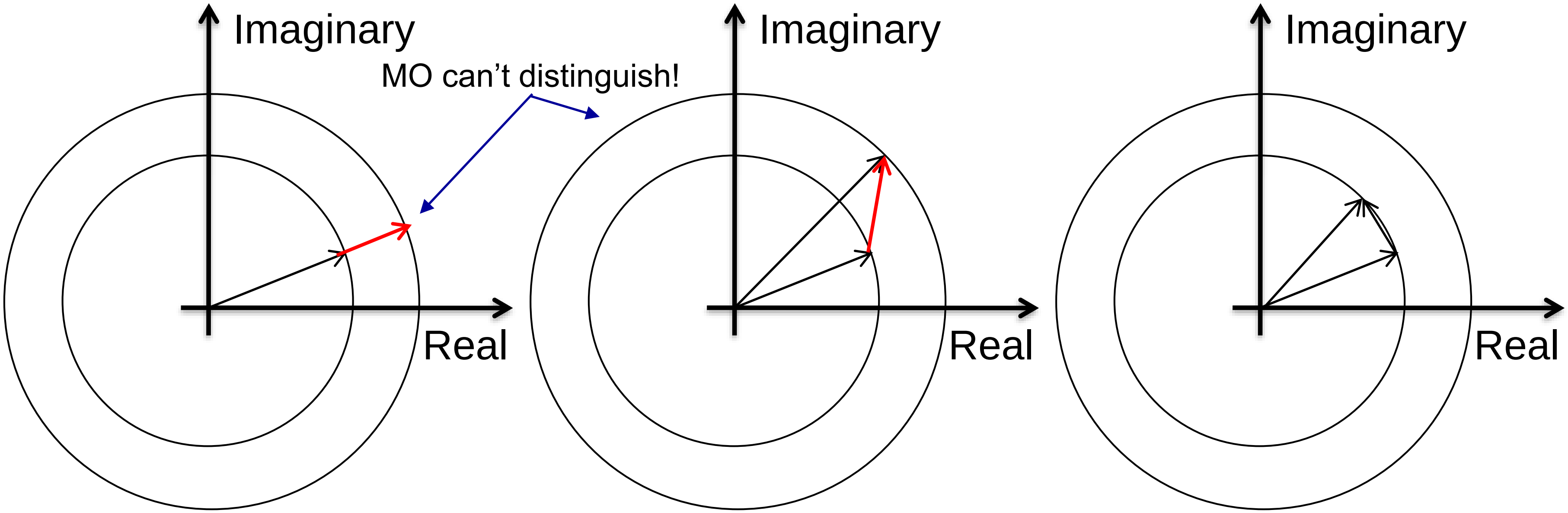

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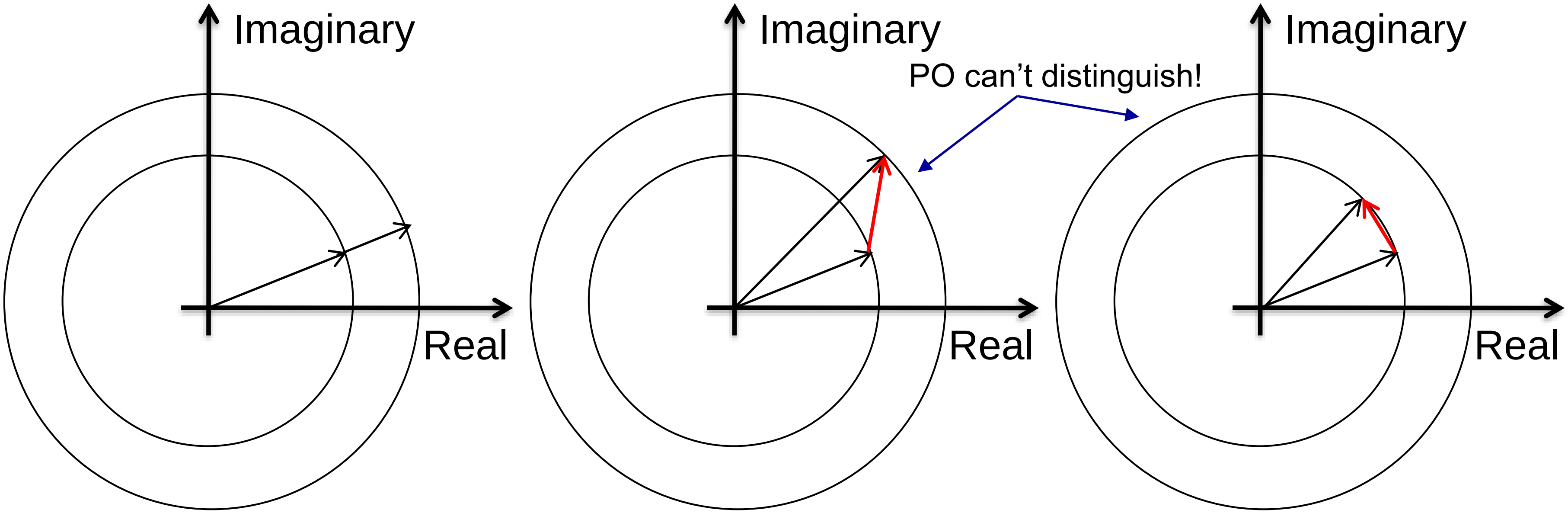

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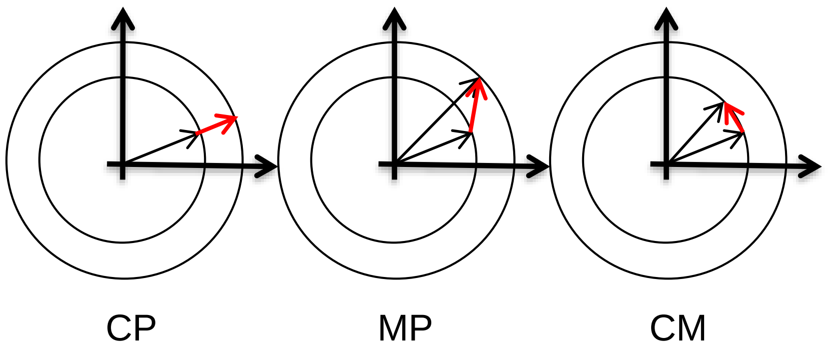
Modeling

Three non-zero changes possible.

In each voxel at time t:

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix}$$



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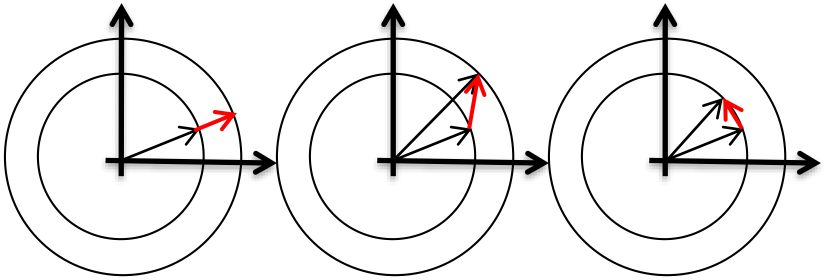

CP[1,2]:

$$\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$$
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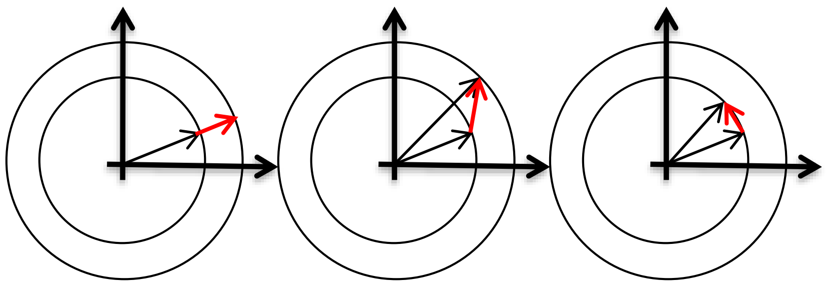

CP[1,2]: $\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$

$\theta_t = \theta$

MO/UP[4,5]: $\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$

$\theta_t \neq \theta_{t'}$

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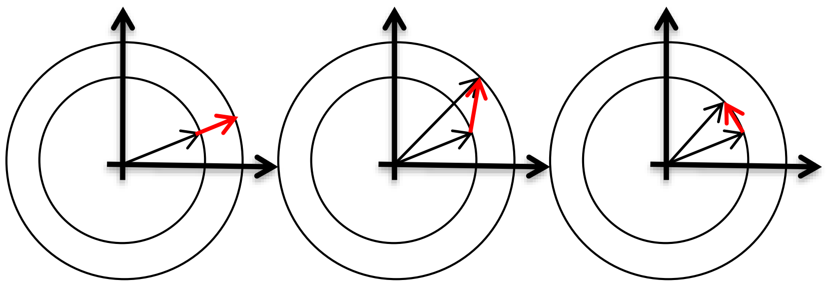

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MP[3,7]:
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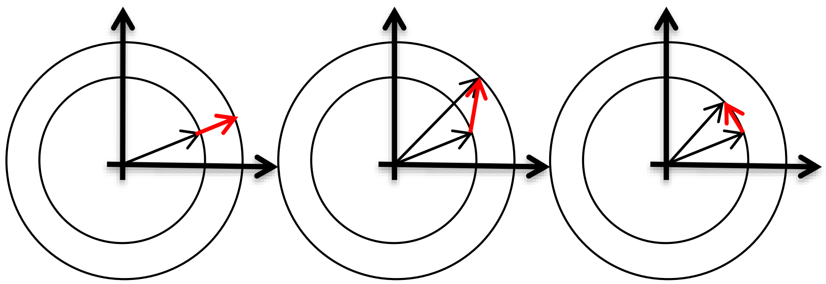

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PO/UM[6]: $\beta_t \neq \beta_{t'}$
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Modeling

Statistical properties of magnitude-only data

and of various complex-valued data.

$$y_{Rt} = \rho_t \cos\theta_t + \eta_{Rt}$$
$$y_{It} = \rho_t \sin\theta_t + \eta_{It}$$

Real and Imaginary

$$m_t = \sqrt{y_{Rt}^2 + y_{It}^2}$$

Magnitude

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix}$$

Bivariate Observations

Modeling

The complex-valued voxel measurement is $y_{Ct}=y_{Rt}+iy_{It}$

with $y_{Rt}\sim N(\mu_{Rt},\sigma^2)$ and $y_{It}\sim N(\mu_{It},\sigma^2)$

where $\mu_{Rt}=\rho_t\cos(\theta_t)$ and $\mu_{It}=\rho_t\cos(\theta_t)$.

So the joint distribution of (y_{Rt},y_{It}) is

$$p(y_{Rt},y_{It})=\frac{1}{2\pi\sigma^2}\exp\left\{-\frac{1}{2\sigma^2}\left[(y_{Rt}-\mu_{Rt})^2+(y_{It}-\mu_{It})^2\right]\right\}.$$

Bivariate normal with phase coupled means.

Modeling

$$\mu_{Rt} = \rho_t \sin\theta_t$$
$$\mu_{It} = \rho_t \cos\theta_t$$

Get $p(m_t)$ from $p(y_{Rt}, y_{It})$.

Convert from (y_{Rt}, y_{It}) to (m_t, φ_t).

$$p(y_{Rt}, y_{It}) = \frac{1}{2\pi\sigma^2}\exp\left\{-\frac{1}{2\sigma^2}\left[(y_{Rt}-\rho_t\cos\theta_t)^2+(y_{It}-\rho_t\sin\theta_t)^2\right]\right\}$$

$$p(m_t, \varphi_t) = \frac{m_t}{2\pi\sigma^2}\exp\left\{-\frac{1}{2\sigma^2}\left[m_t^2+\rho_t^2-2m_t\rho_t\cos(\varphi_t-\theta_t)\right]\right\}$$

$$p(m_t) = \frac{m_t}{\sigma^2}\exp\left\{-\frac{m_t^2+\rho_t^2}{2\sigma^2}\right\}\underbrace{I_0\left(\frac{\rho_t m_t}{\sigma^2}\right)}$$

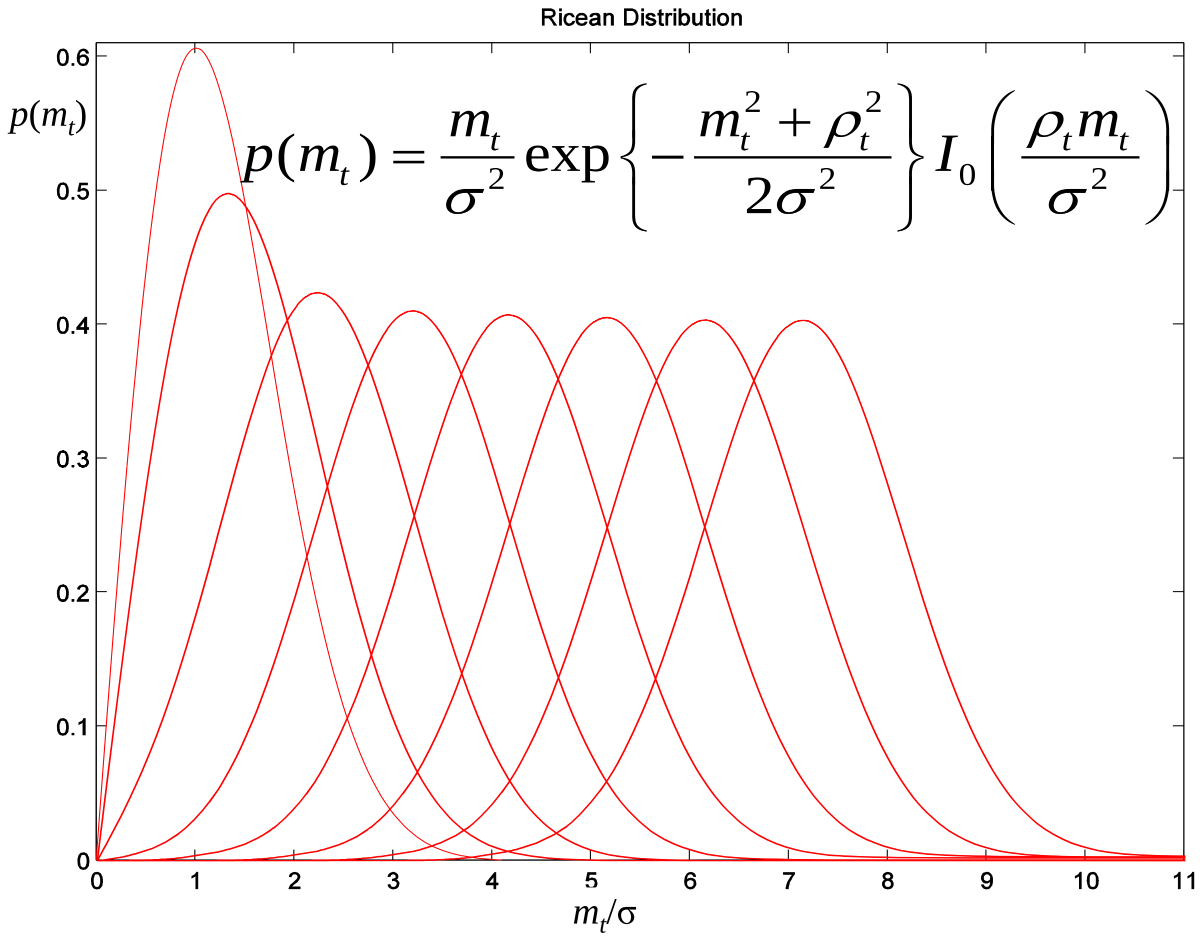
zeroth order modified Bessel function of first kind

$$\frac{1}{2\pi}\int_{\varphi_t=-\pi}^{\pi} e^{\frac{\rho_t m_t}{\sigma^2}\cos(\varphi_t-\theta_t)}\,d\varphi_t$$

Rice,S.O., Bell Syst. Tech. 23:282, 1944.
Gudbjartsson, Patz. MRM 34:910–914, 1995.
Rowe and Logan: NIMG, 23:1078-1092, 2004.

Modeling

The Rice distribution for varying $SNR=\rho_t/\sigma^2$.

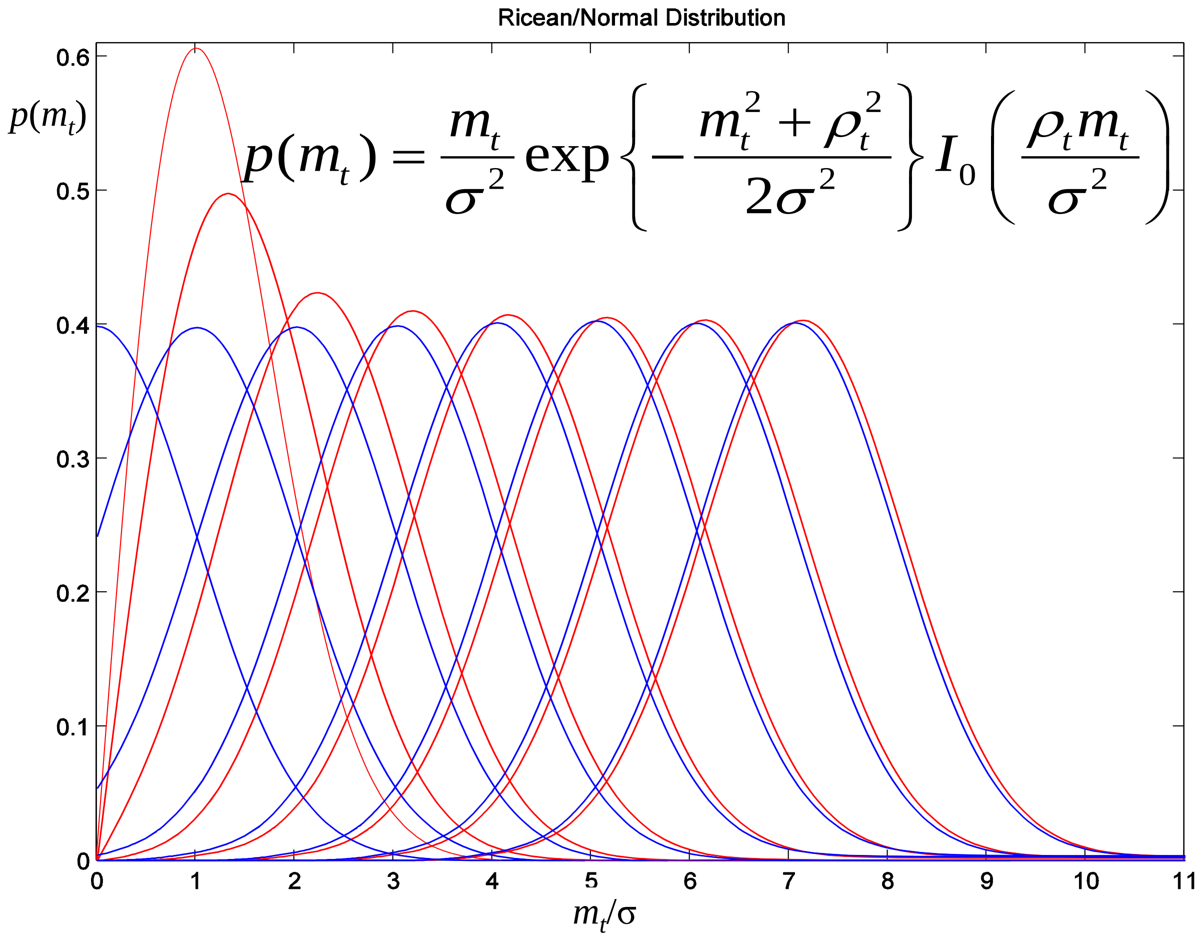


The magnitude, does not have a normal distribution!

Ricean Distribution!

Modeling

The Rice & Normal distributions for varying $SNR=\rho_t/\sigma^2$.



The magnitude, does not have a normal distribution!

Ricean Distribution!

Ricean $\rightarrow$ Normal as the SNR $\uparrow$

Modeling

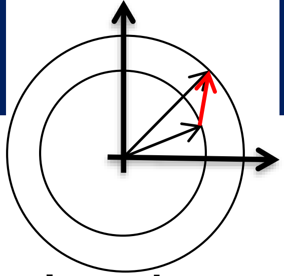
The high SNR normality of m_t can be seen as

$$
\begin{aligned}
m_t &= \left[(y_{Rt})^2 + (y_{It})^2\right]^{1/2} \\
&= \left[(\rho_t \cos\theta_t + \eta_{Rt})^2 + (\rho_t \sin\theta_t + \eta_{It})^2\right]^{1/2} \\
&= \left[\rho_t^2 + (\eta_{Rt}^2 + \eta_{It}^2) + 2\rho_t(\eta_{Rt}\cos\theta_t + \eta_{It}\sin\theta_t)\right]^{1/2} \\
&= \rho_t\left[1 + 2\frac{(\eta_{Rt}\cos\theta_t + \eta_{It}\sin\theta_t)}{\rho_t} + \underbrace{\cancel{\frac{(\eta_{Rt}^2 + \eta_{It}^2)}{\rho_t^2}}}_{0}\right] \\
&\approx \rho_t + \varepsilon_t
\end{aligned}
$$

where $\varepsilon_t = 2\eta_{Rt}\cos\theta_t + 2\eta_{It}\sin\theta_t$

$$\varepsilon_t \sim N(0, 2\sigma^2)$$

$$\sqrt{1+u^2} \approx 1 + u/2, \quad |u| \ll 1$$



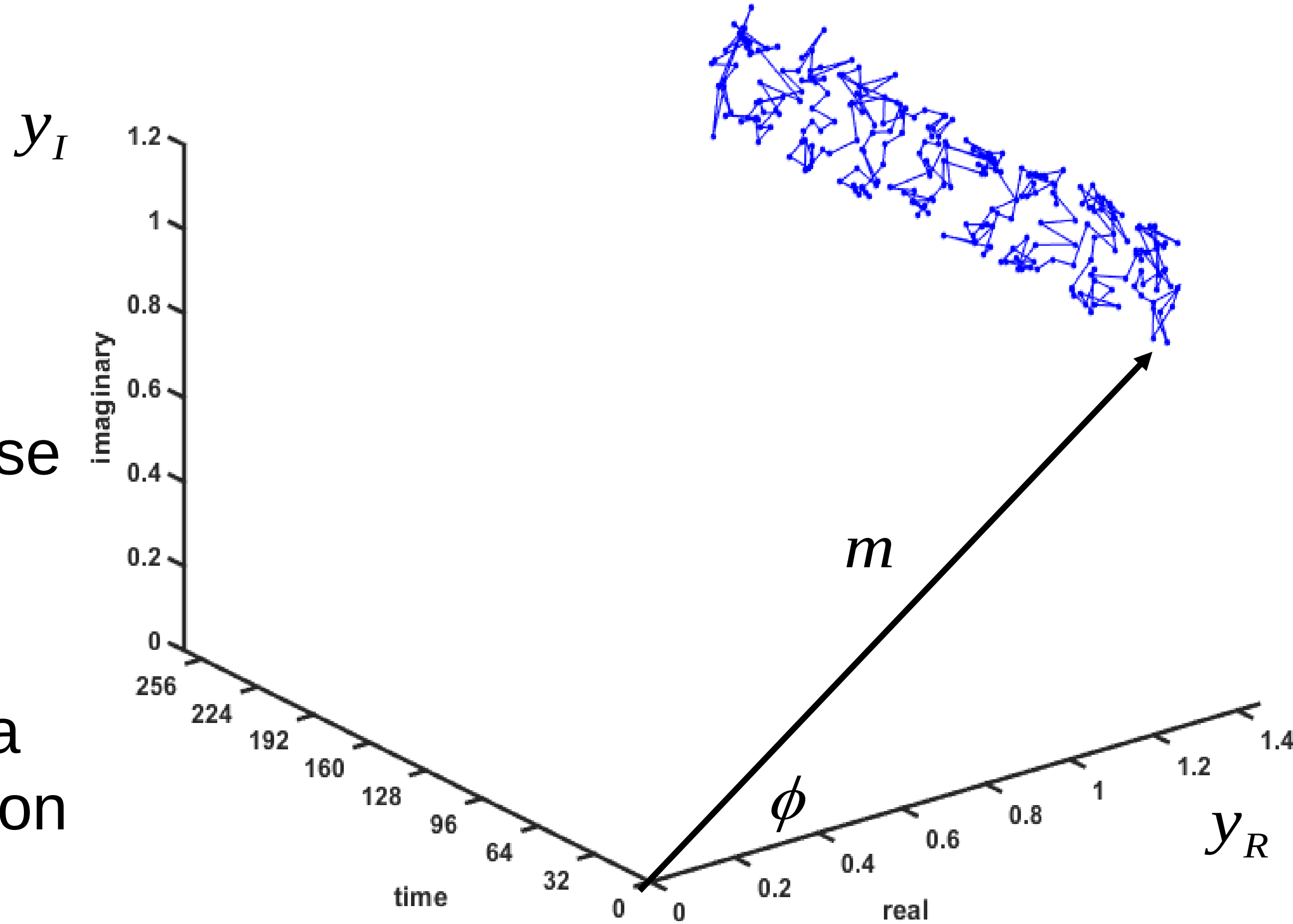
Phase Information

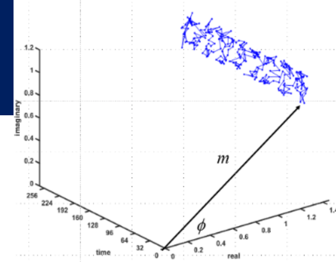
This opens up the opportunity for complex-valued analysis!

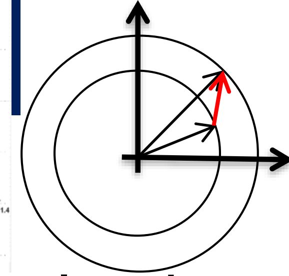
Complex-valued activation and/or Complex-valued correlation?

Magnitude and Phase or equivalently Real and Imaginary

Some voxels have a lengthening & rotation with task!







Phase Information

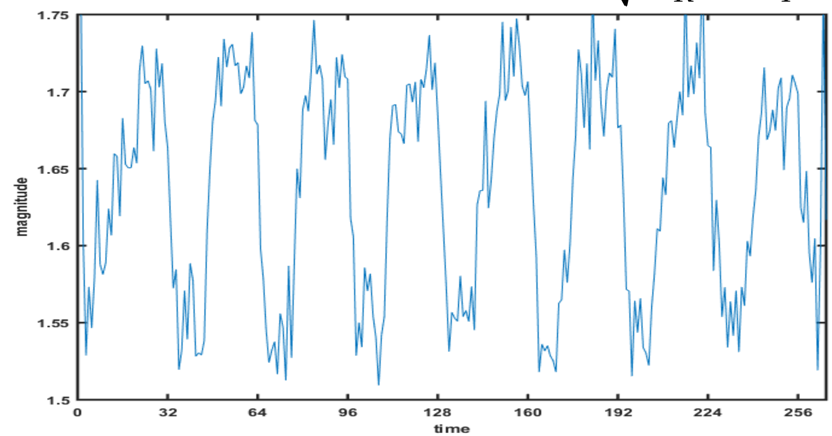
This opens up the opportunity for complex-valued analysis!

Complex-valued activation
and/or
Complex-valued correlation?

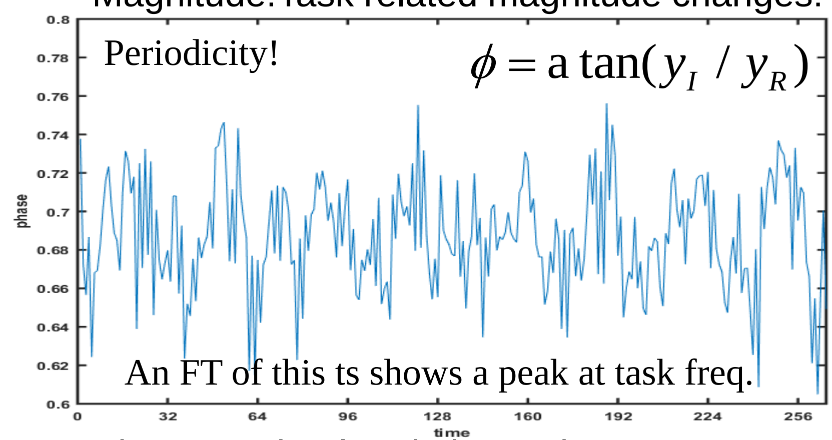
Magnitude and Phase
or equivalently
Real and Imaginary

Lengthening &
Rotation with task!

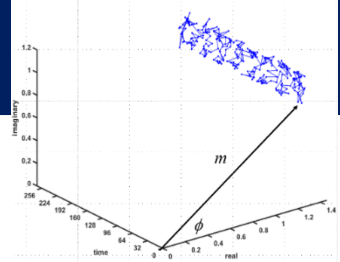
$$m = \sqrt{y_R^2 + y_I^2}$$

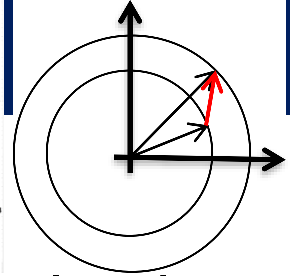


Magnitude:Task related magnitude changes!



Phase: Task related phase changes!





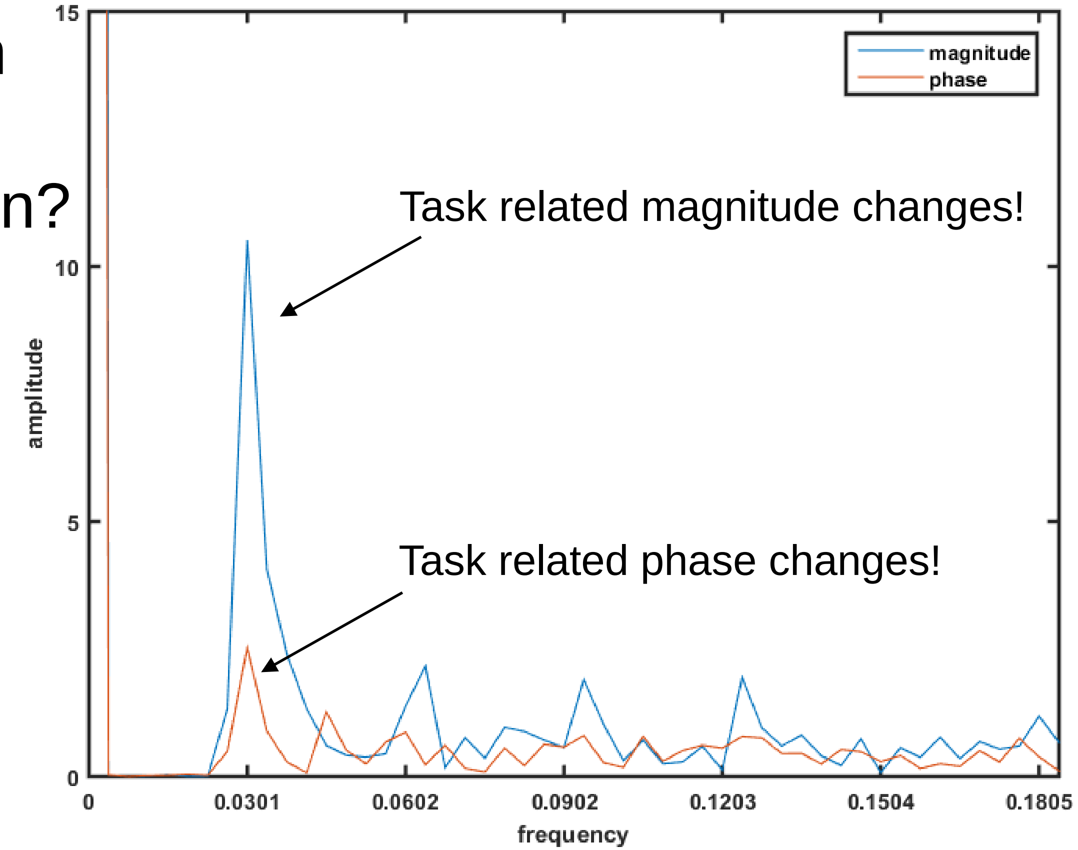
Phase Information

This opens up the opportunity for complex-valued analysis!

Complex-valued activation
and/or
Complex-valued correlation?

Magnitude and Phase
or equivalently
Real and Imaginary

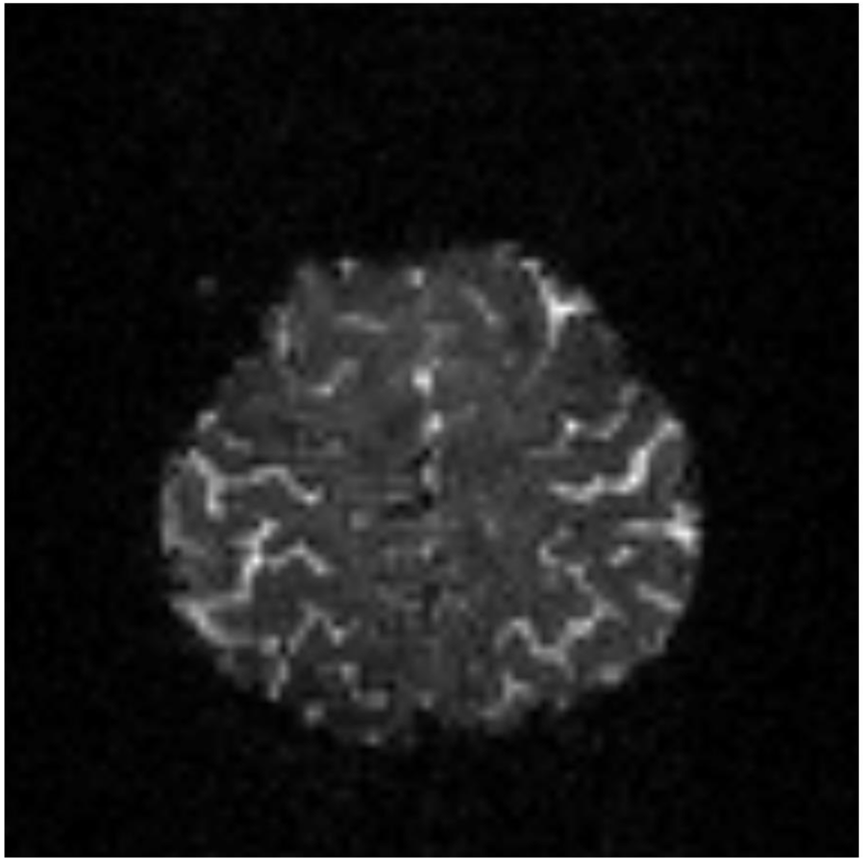
Lengthening &
Rotation with task!



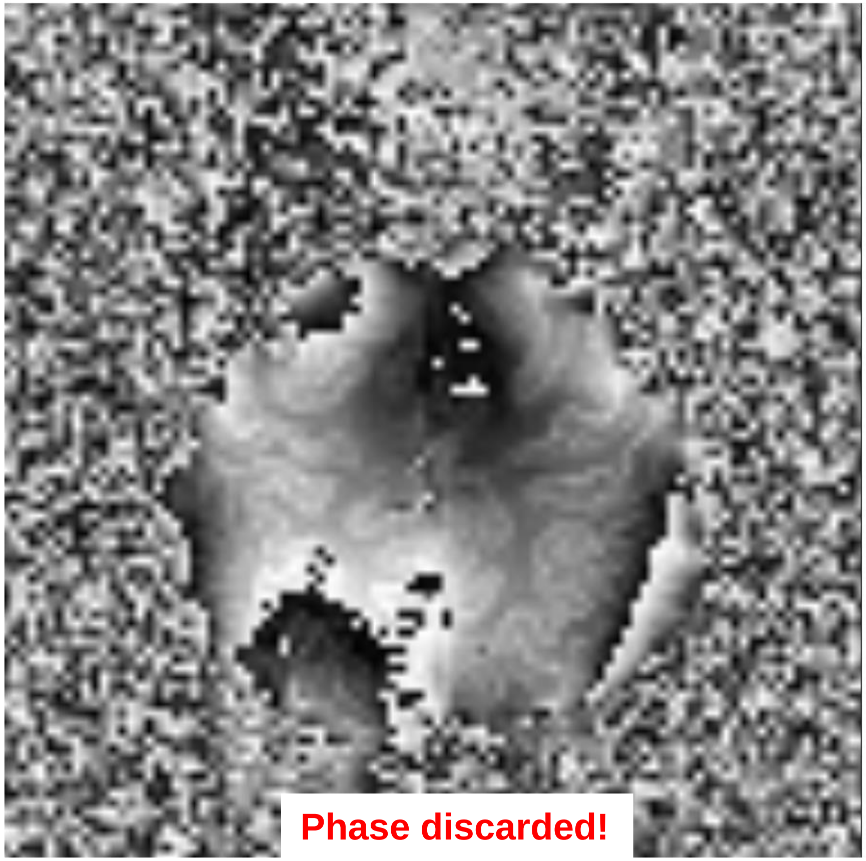
Phase Information

There is biological information in the phase!

GRE EPI Image



Magnitude Image

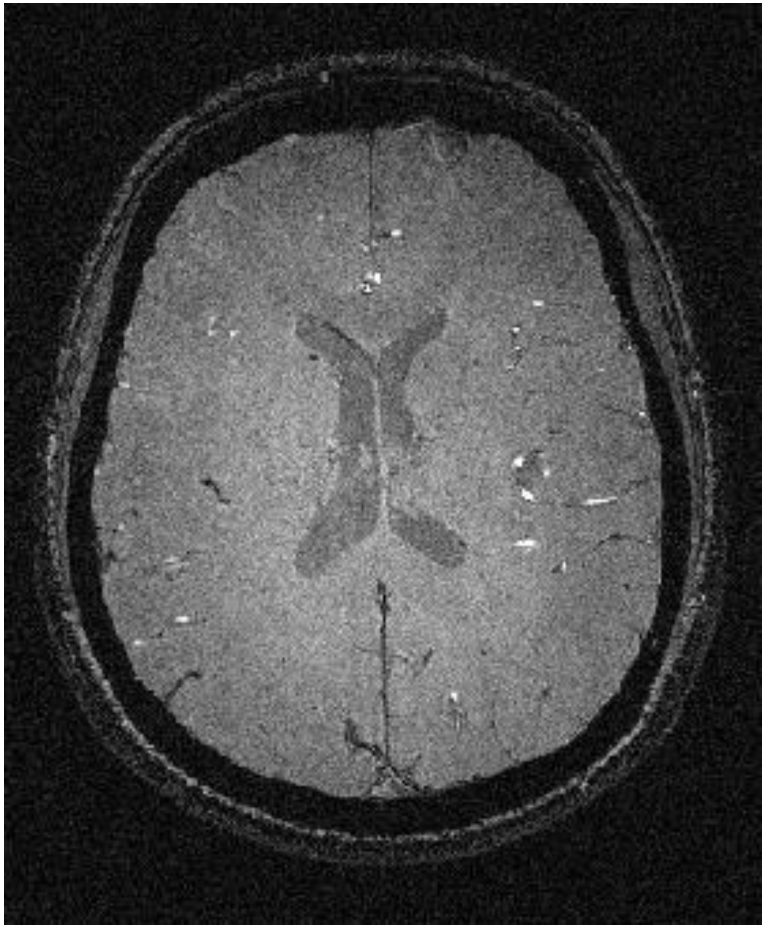


Phase Image

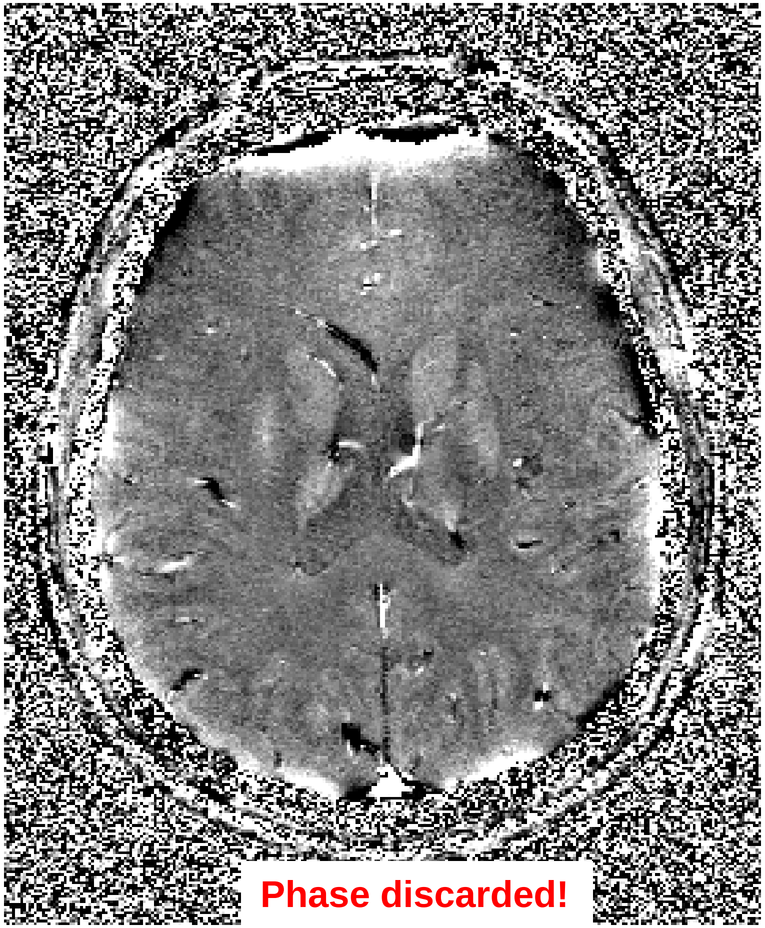
Phase Information

There is biological information in the phase!

"SWI" Anatomical Image



Magnitude Image

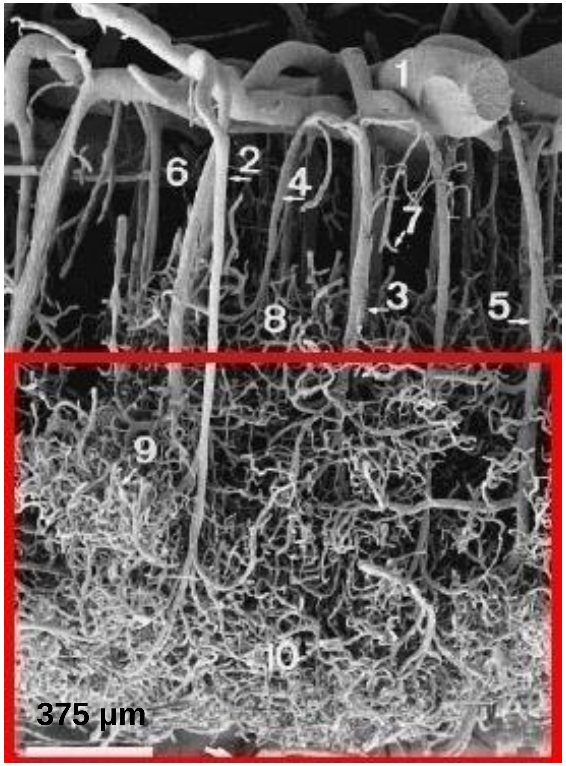


Phase discarded!

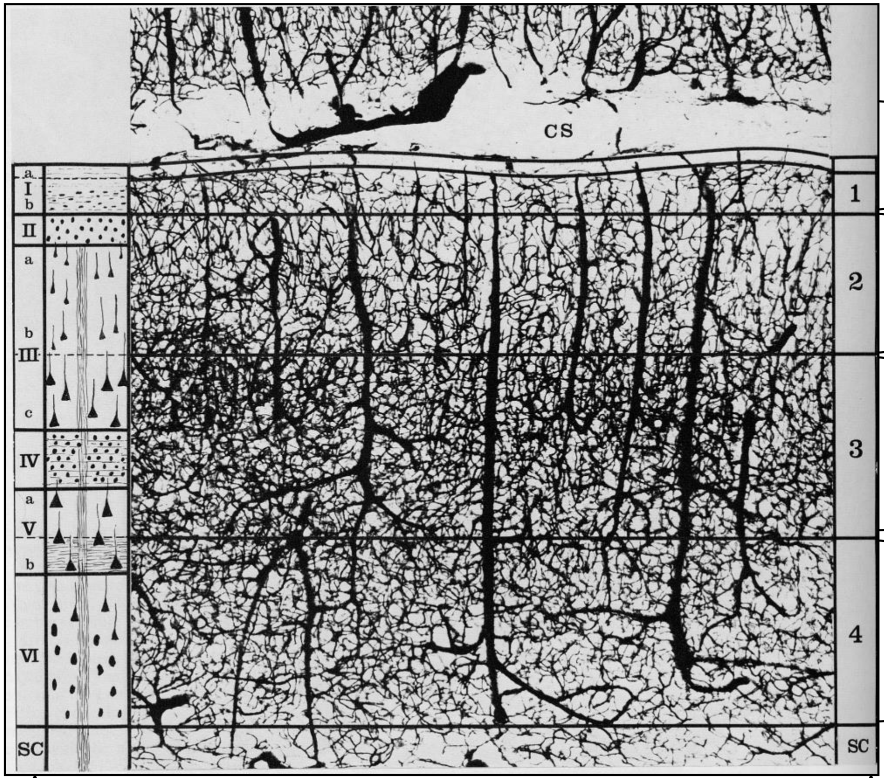
Phase Image

Phase Information

There is biological information in the phase!



1. pial artery
2. long cortical artery
3. middle cortical artery
4. short cortical artery
5. cortical vein
6. subpial zone
7. precapillary vessels
8. superficial capillary zone
9. middle capillary zone
10. deep capillary zone



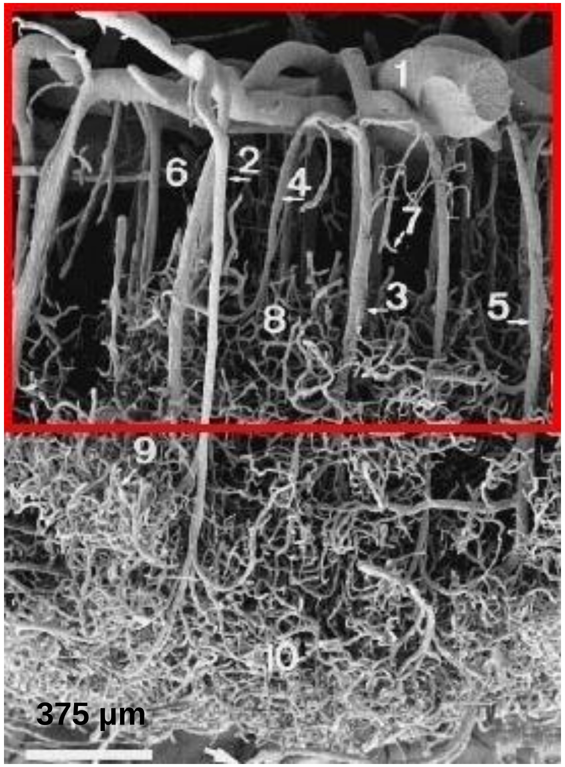
cortical layers (I-VI) vascular layers (1-4)

Figure (left) Reina-de la Torre et al.: The Anatomical Record, 1998.
Figure (right) Duvernoy et al. Brain Res Bull 7:519-579, 1981.
Data (right) Yamaguchi et al. Int J Microcirc Clin Exp 1992.

 [1]Menon: MRM, 47:1-9, 2002., [2]Nencka, Rowe: NIMG, 177-88, 2007.

Phase Information

There is biological information in the phase!



1. pial artery
2. long cortical artery
3. middle cortical artery
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5. cortical vein
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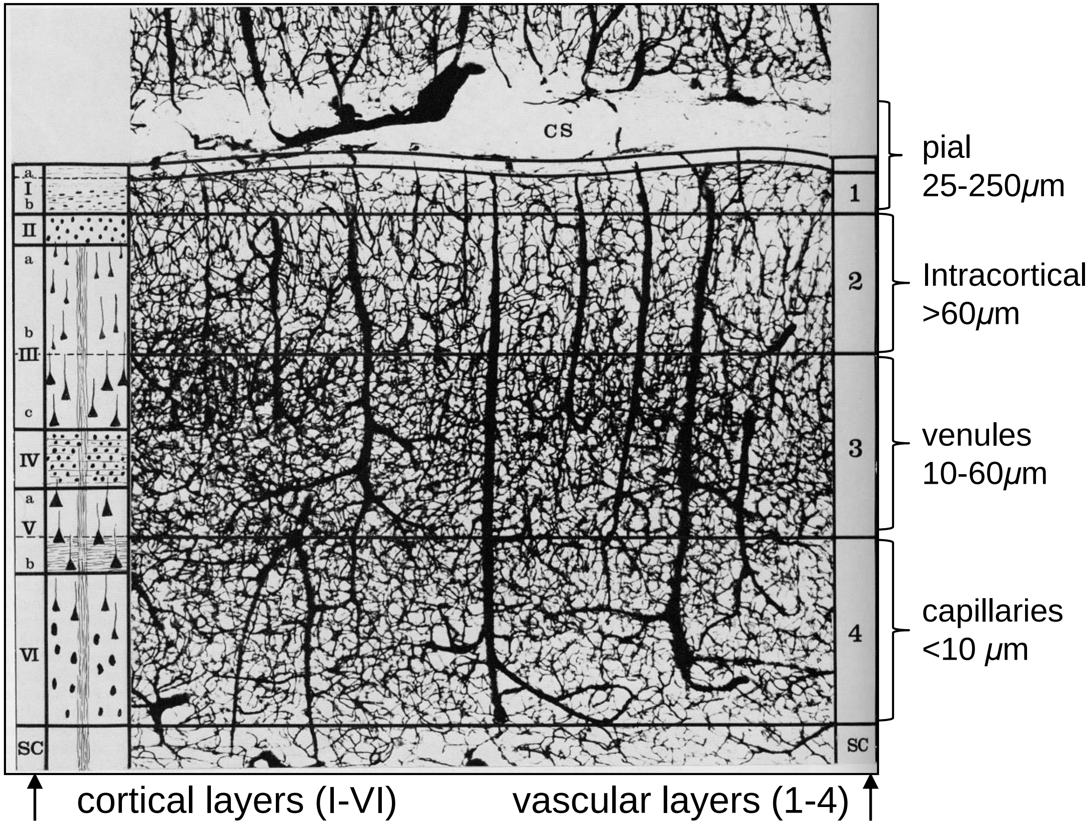
7. precapillary vessels
8. superficial capillary zone
9. middle capillary zone
10. deep capillary zone



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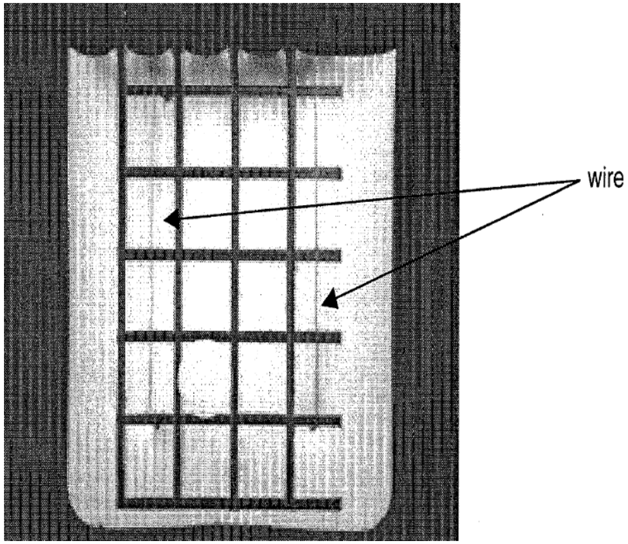
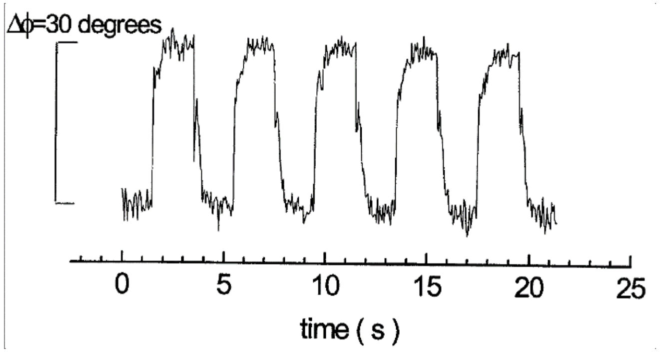
Phase Information

There is biological information in the phase!



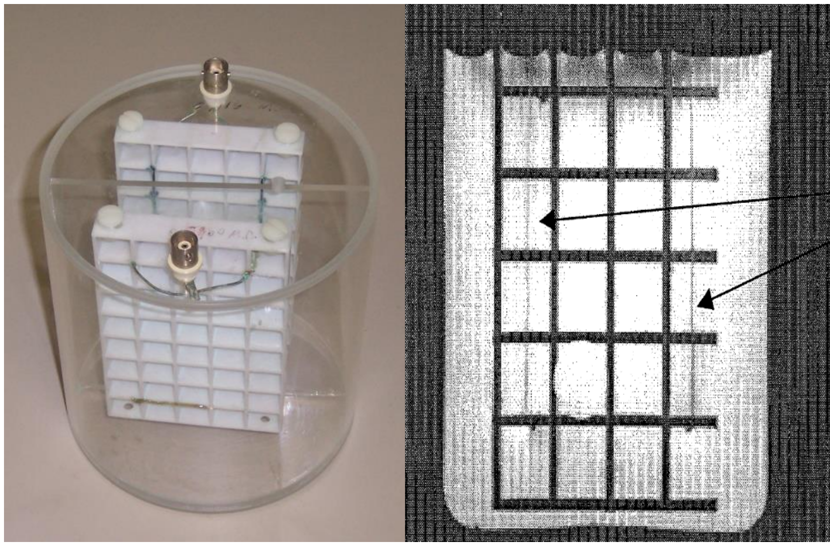
Bodurka et al.: JMR, 1999.



phase time series

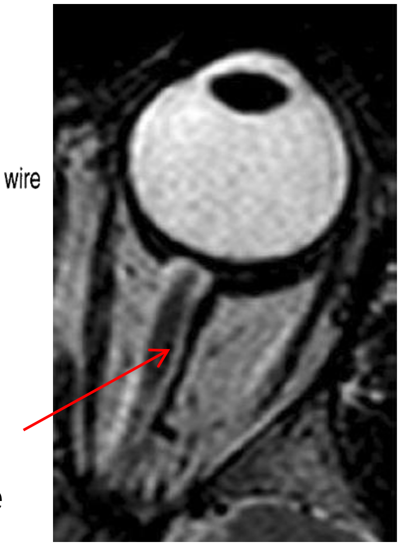
Phase Information

There is biological information in the phase!



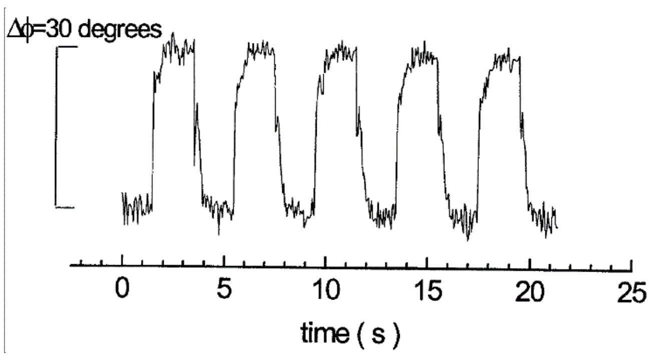
wire

optic
nerve



Bodurka et al.: JMR, 1999.

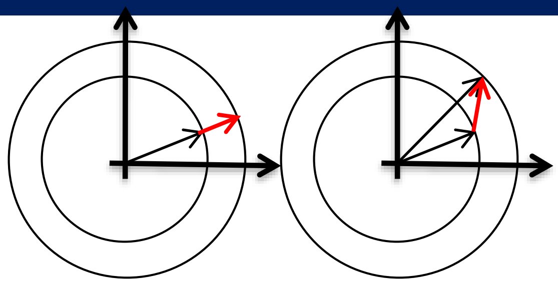
Chow et al.: NIMG, 2006.



phase time series

Phase contains other magnetic field change info: respiration, motion!

Results



Magnitude-only (MO) model (large SNR normal approximation)

$$p(m_t) = \frac{1}{2\pi\sigma^2} \exp\left\{ -\frac{1}{2\sigma^2} \left[(m_t - \rho_t)^2 \right] \right\}$$

vs.

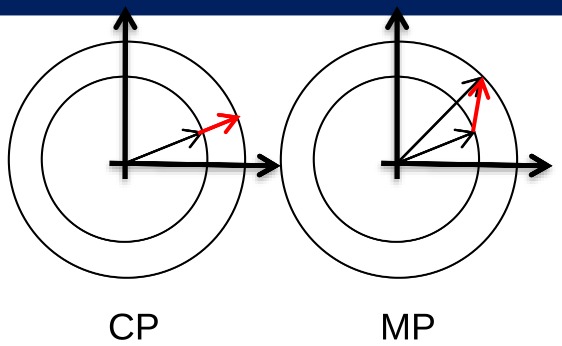
$$p(m_t) = \frac{m_t}{\sigma^2} \exp\left\{ -\frac{m_t^2 + \rho_t^2}{2\sigma^2} \right\} I_0\left(\frac{\rho_t m_t}{\sigma^2} \right)$$

Complex-valued with a constant phase (CP).

$$p(y_{Rt}, y_{It}) = \frac{1}{2\pi\sigma^2} \exp\left\{ -\frac{1}{2\sigma^2} \left[(y_{Rt} - \rho_t \cos\theta)^2 + (y_{It} - \rho_t \sin\theta)^2 \right] \right\}$$

$$\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$$

Results



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$$p(m_t) = \frac{1}{2\pi\sigma^2} \exp\left\{-\frac{1}{2\sigma^2}\left[(m_t - \rho_t)^2\right]\right\}$$

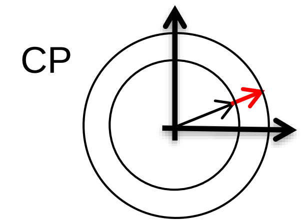
vs.

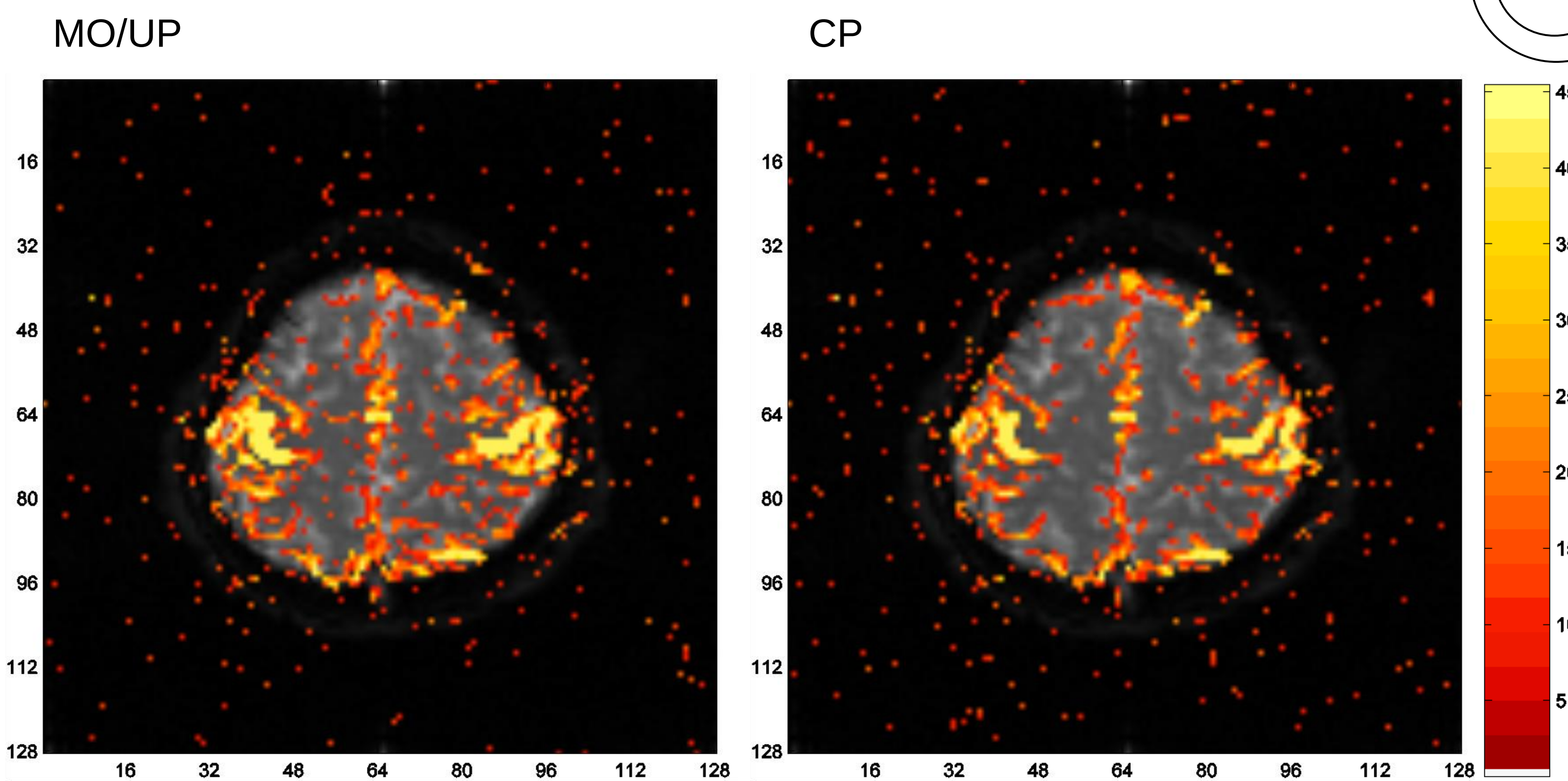
Complex-valued with a constant phase (CP).

$$p(y_{Rt}, y_{It}) = \frac{1}{2\pi\sigma^2} \exp\left\{-\frac{1}{2\sigma^2}\left[(y_{Rt} - \rho_t \cos\theta)^2 + (y_{It} - \rho_t \sin\theta)^2\right]\right\}$$

$$\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$$

Results Activations in Human Data





Bilateral finger Tapping

5% FDR Threshold

CP activation has greater specificity than MO activation.

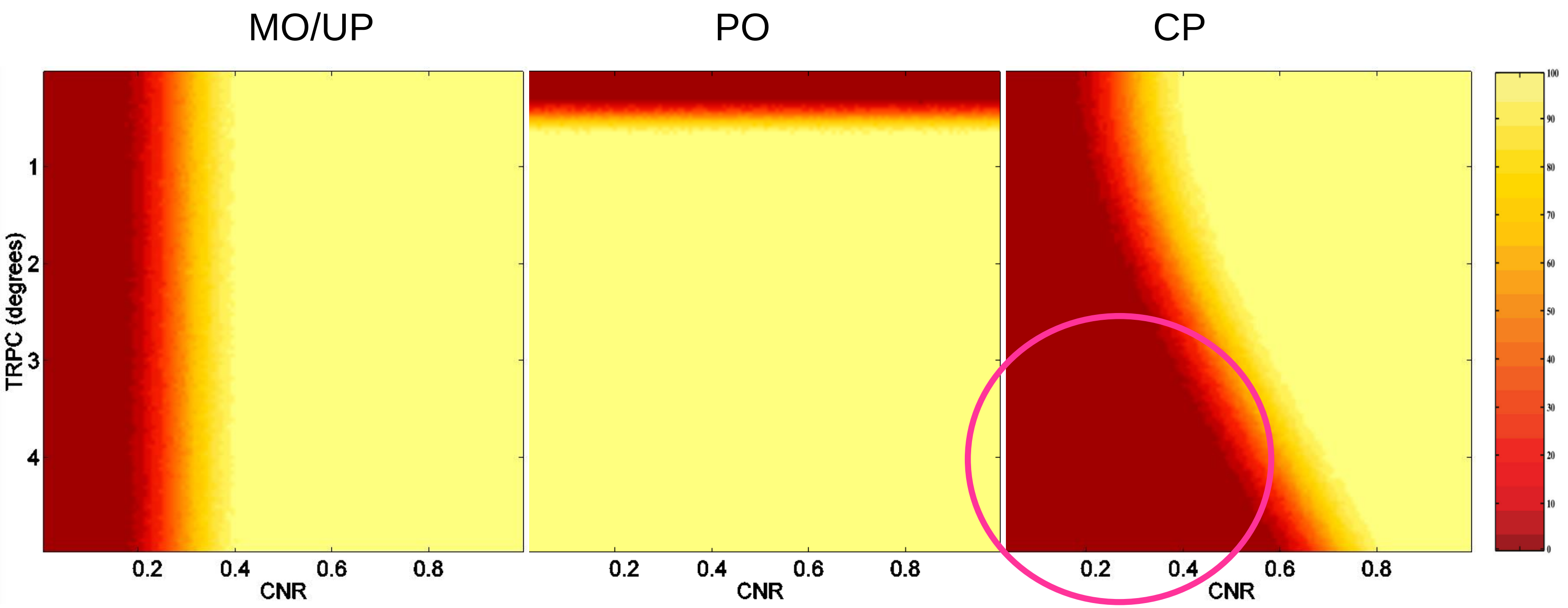
Rowe and Logan: NIMG, 23:1078-1092, 2004.

Rowe: NIMG, 25:1310-1324, 2005b.

Results

$CNR=\beta_{ref}/\sigma$
$TRPC=\gamma_{ref}$

Power Analysis



detects only magnitude changes

detects only phase changes

detection bias against phase changes

5% Bonferroni FWE

Biases against downstream voxels!

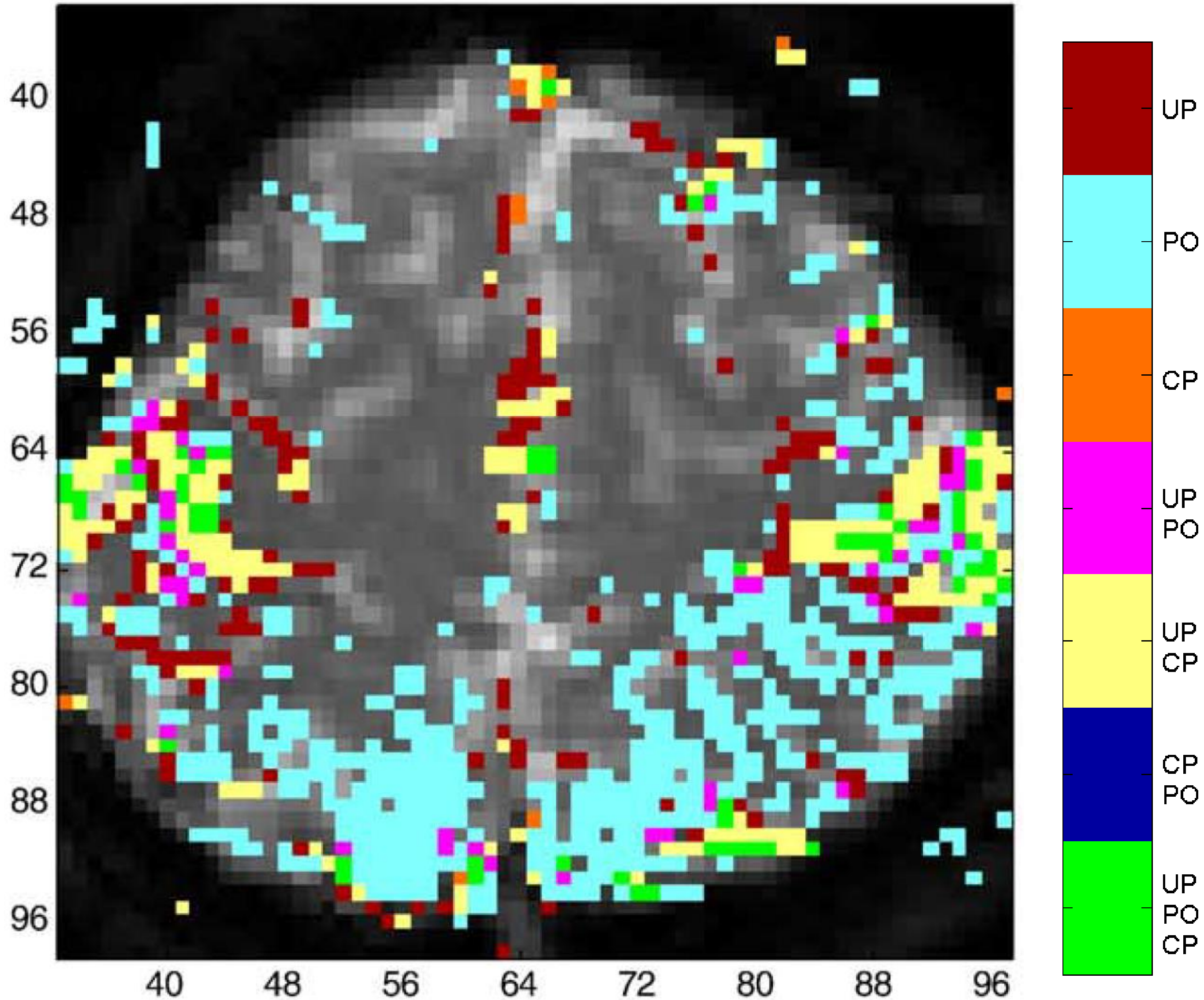
Nencka and Rowe, NIMG, 37, 177-188, 2007.

Results

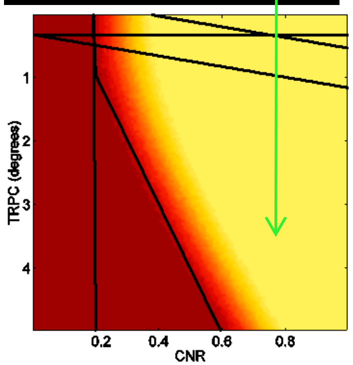
MO

PO

CP



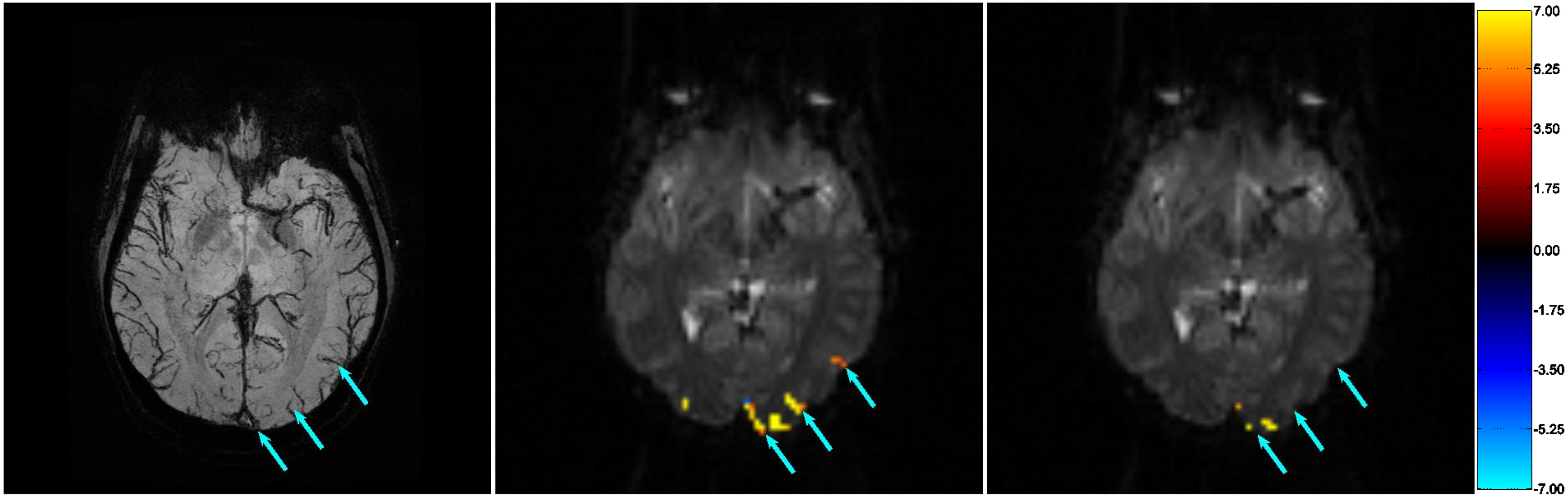
Magnitude CNR is high enough to overcome phase change bias



Rowe and Logan: NIMG, 23:1078-1092, 2004.

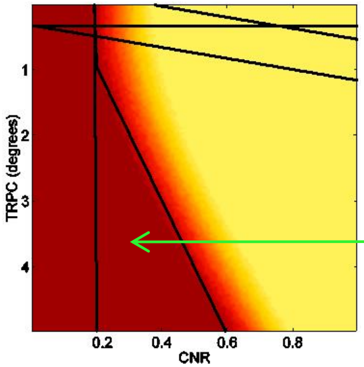
Rowe: NIMG, 25:1310-1324, 2005b.

Results Activations in Human Data



Venogram MO/UP CP

More localized activation.



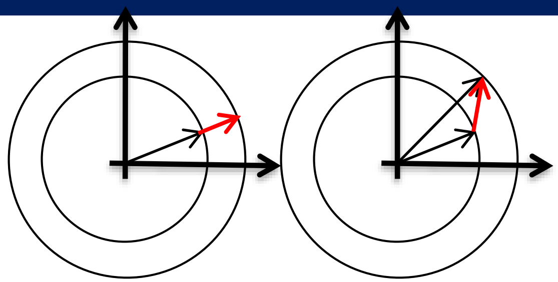
Magnitude CNR
Not high enough to
overcome phase
change bias

3T GE Signa LX
5 axial slices
96x96
FOV =24 cm
TR=2000 ms
TE=45.3 ms
FA=77°

RH male
Flashing checkerboard 4Hz
Block design
20s off + 8x(16s on+16s off)

Nencka, Paulson, Rowe: ISMRM, 16:2338, 2008.

Results



Magnitude-only (MO) model (large SNR normal approximation)

$$p(m_t) = \frac{1}{2\pi\sigma^2} \exp\left\{ -\frac{1}{2\sigma^2} \left[(m_t - \rho_t)^2 \right] \right\}$$

$$\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$$

vs.

Complex-valued magnitude and/or phase (MP).

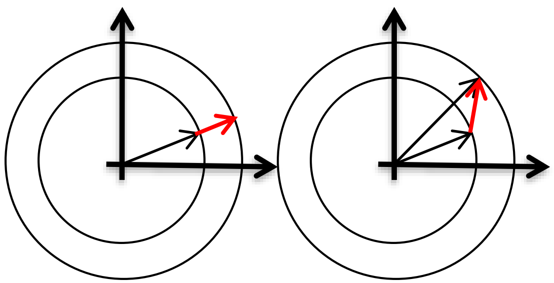
$$p(y_{Rt}, y_{It}) = \frac{1}{2\pi\sigma^2} \exp\left\{ -\frac{1}{2\sigma^2} \left[(y_{Rt} - \rho_t \cos\theta_t)^2 + (y_{It} - \rho_t \sin\theta_t)^2 \right] \right\}$$

$$\rho_t = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$$

$$\theta_t = \gamma_0 + \gamma_1 u_{1t} + \cdots + \gamma_{q_2} u_{q_2 t}$$

Results

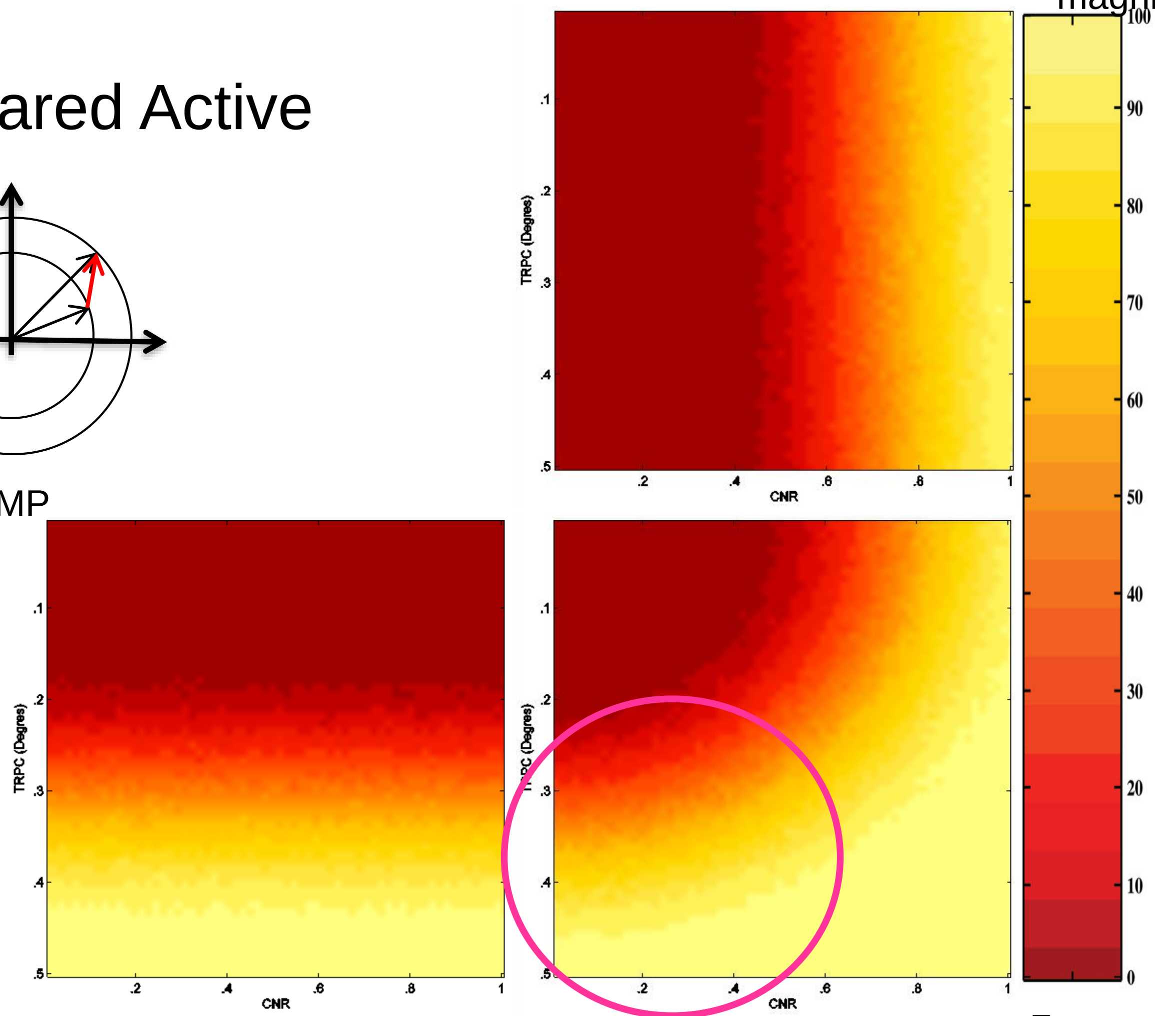
Percent Declared Active



CP MP

MO/UP

detects only
magnitude changes



detects only
phase changes

PO MP

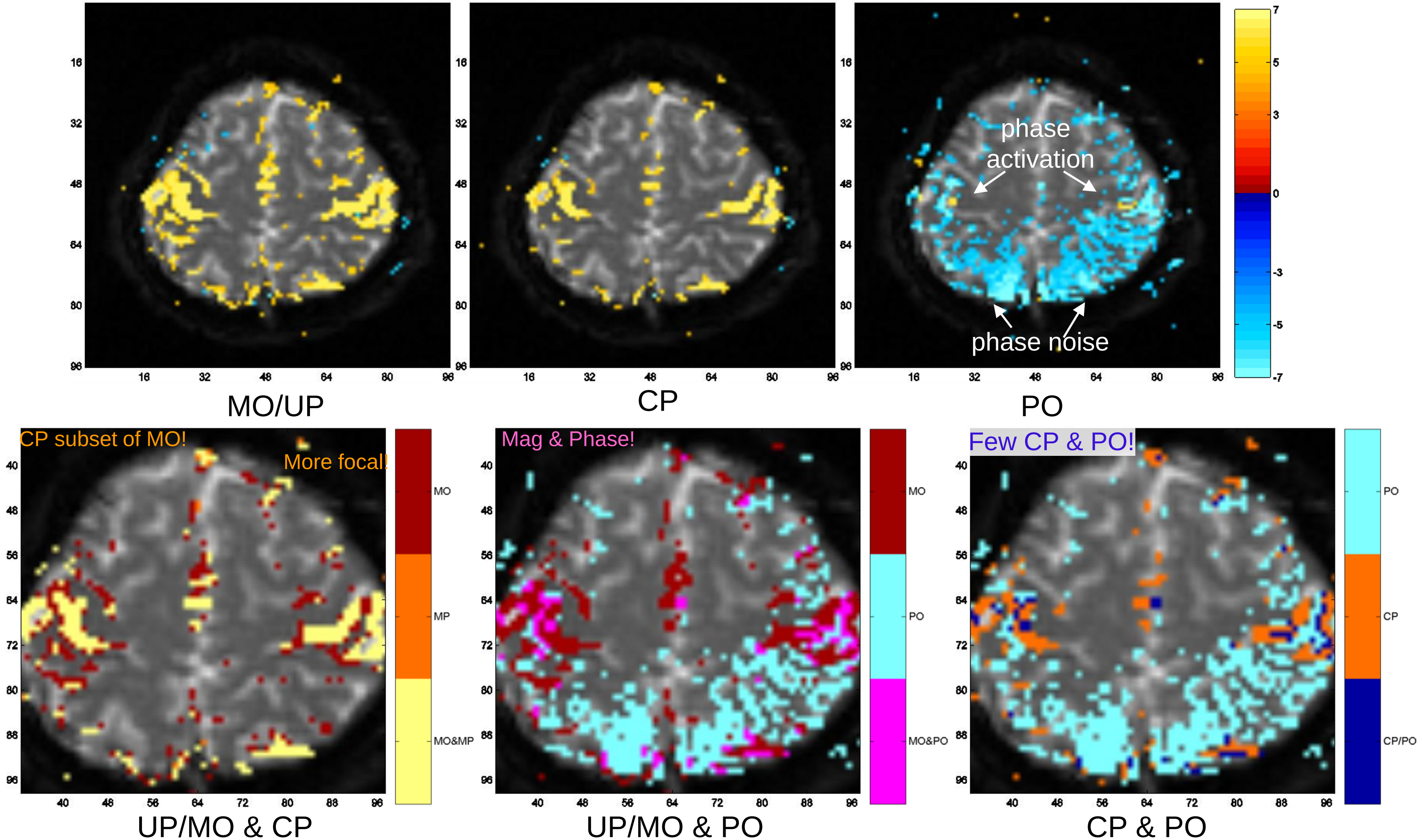
detects magnitude
and phase changes

5% PCE

Hernandez-Garcia, Vazquez, Rowe, MRM 62:1597-1608, 2009.

Results

Presented at 2005 JSM



Rowe and Logan: NIMG, 23:1078-1092, 2004.

Rowe: NIMG, 25:1310-1324, 2005b.

Results

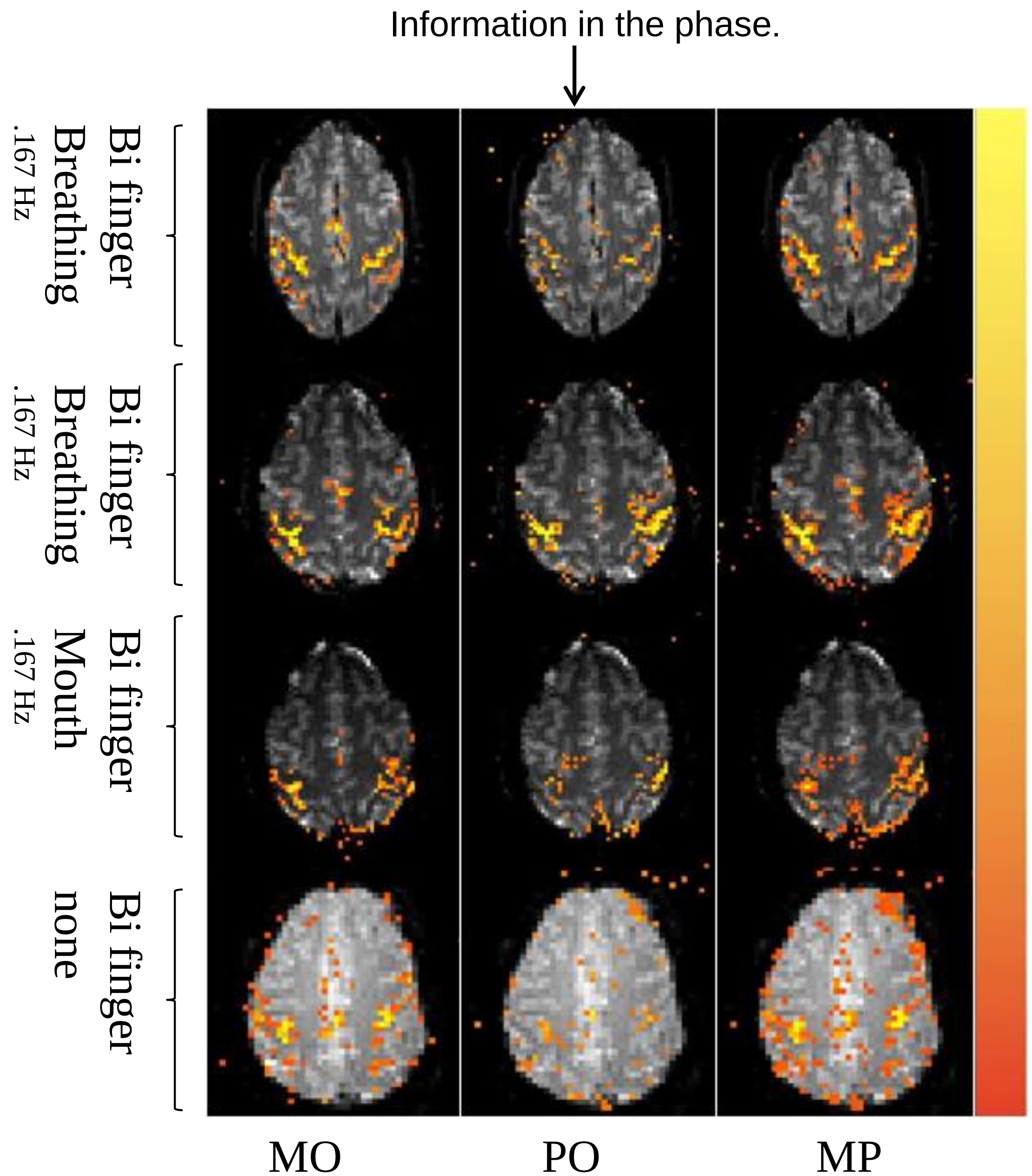
3.0T GE LX

20s off+16×(8 s on 8 s off), 276 TRs
12 axial slices, 96 × 96, FOV = 24 cm
TH = 2.5 mm, TR = 1 s, TE = 34.6 ms
FA = 45◦, BW = 125 kHz, ES = .708 ms

20s off+16×(8 s on 8 s off), 276 TRs
10 axial slices, 96 × 96, FOV = 24 cm
TH = 2.5 mm, TR = 1 s, TE = 42.8 ms
FA = 45◦, BW = 125 kHz, ES = .768 ms

20s off+16×(8 s on 8 s off), 276 TRs
10 axial slices, 96 × 96, FOV = 24 cm,
TH = 2.5 mm, TR = 1 s, TE = 42.8 ms
FA = 45◦, BW = 125 kHz, ES = . 768 ms

20s off+10×(8 s on 8 s off), 180 TRs
9 axial slices, 64 × 64, FOV = 24 cm
TH = 3.8 mm, TR = 1 s, TE = 26.0 ms
FA = 45◦, BW = 125 kHz, ES = .680 ms



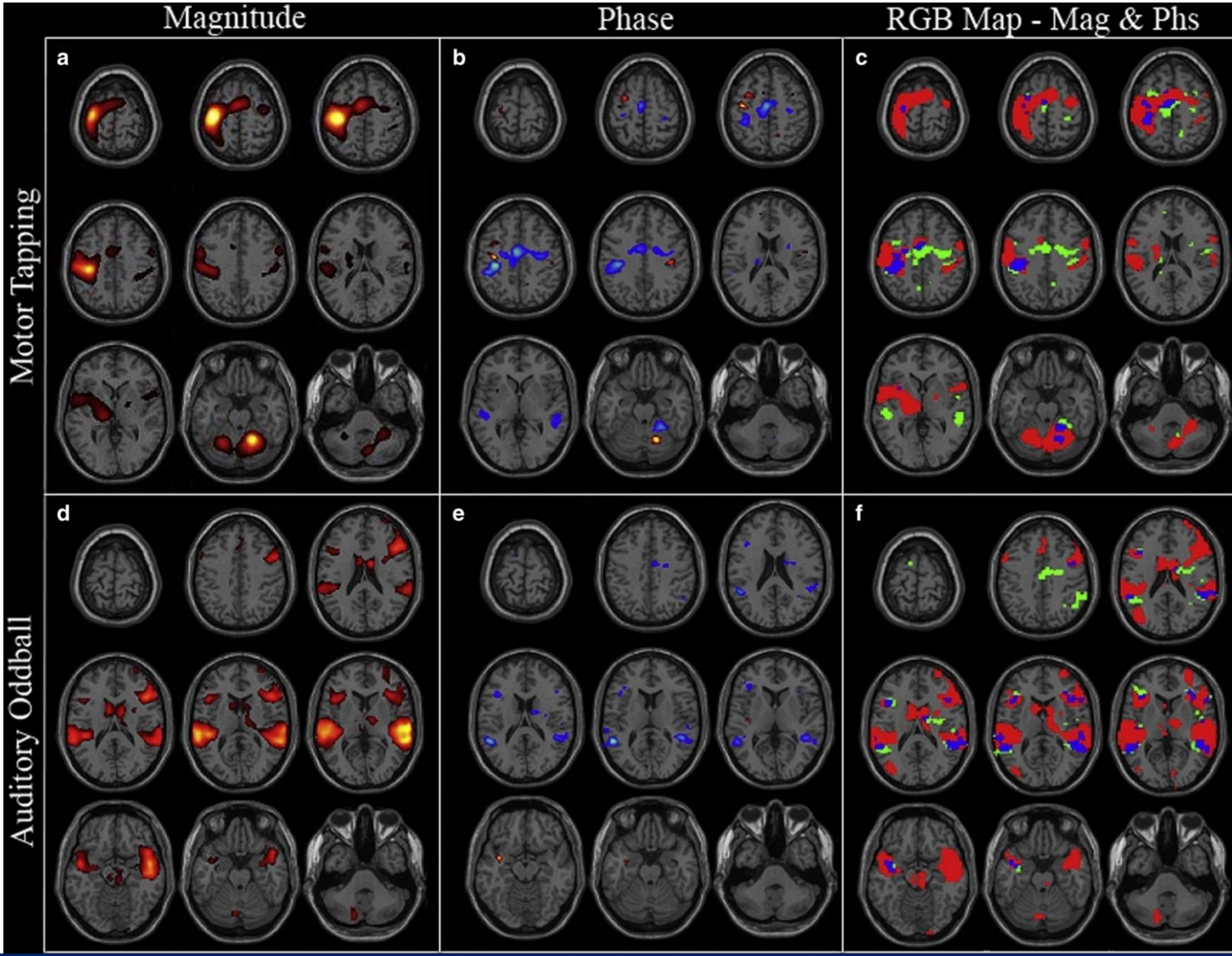
Results

Group analysis.
Not just single
subject effect!

n=20

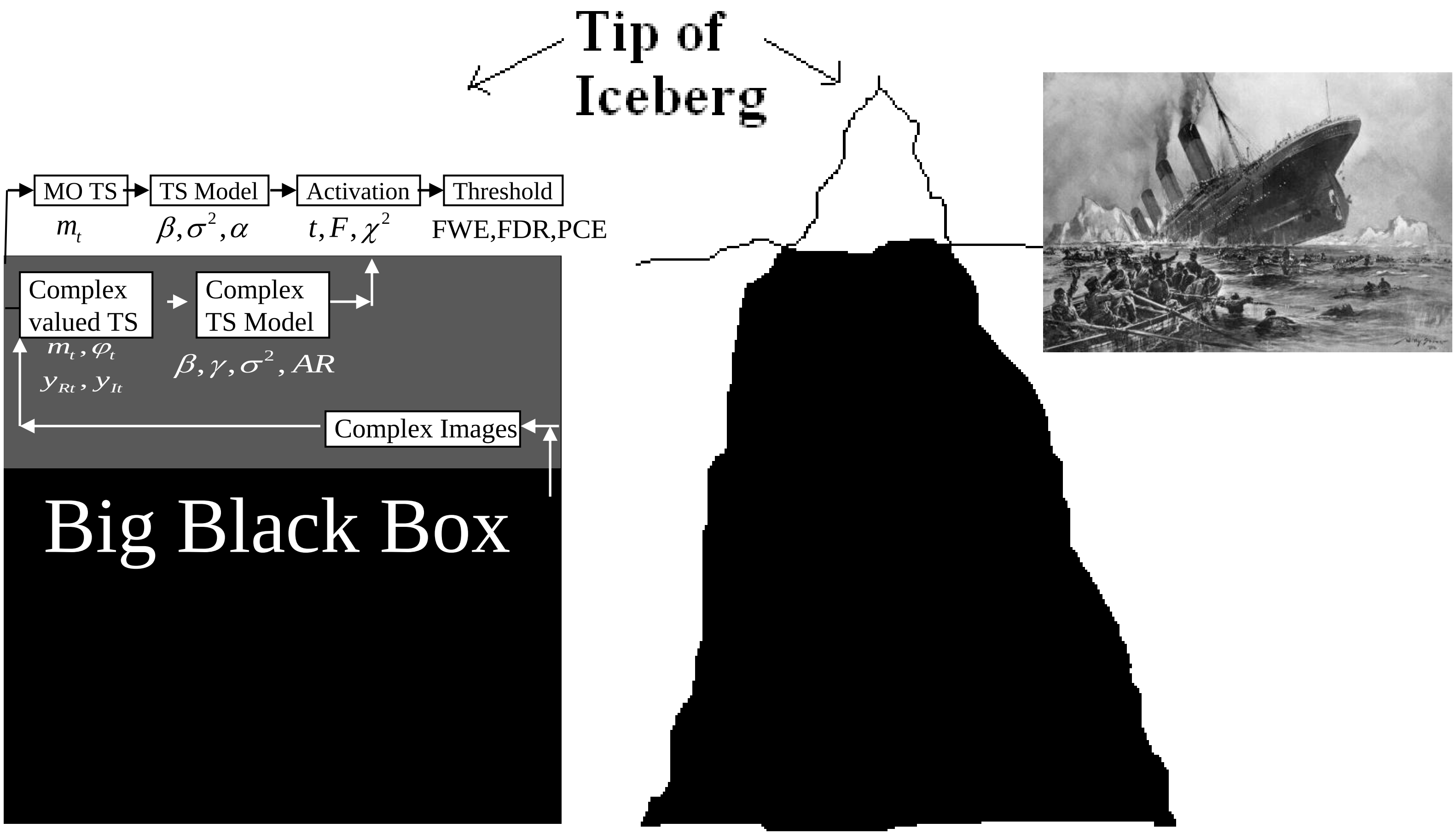
n=34

No MP analysis!



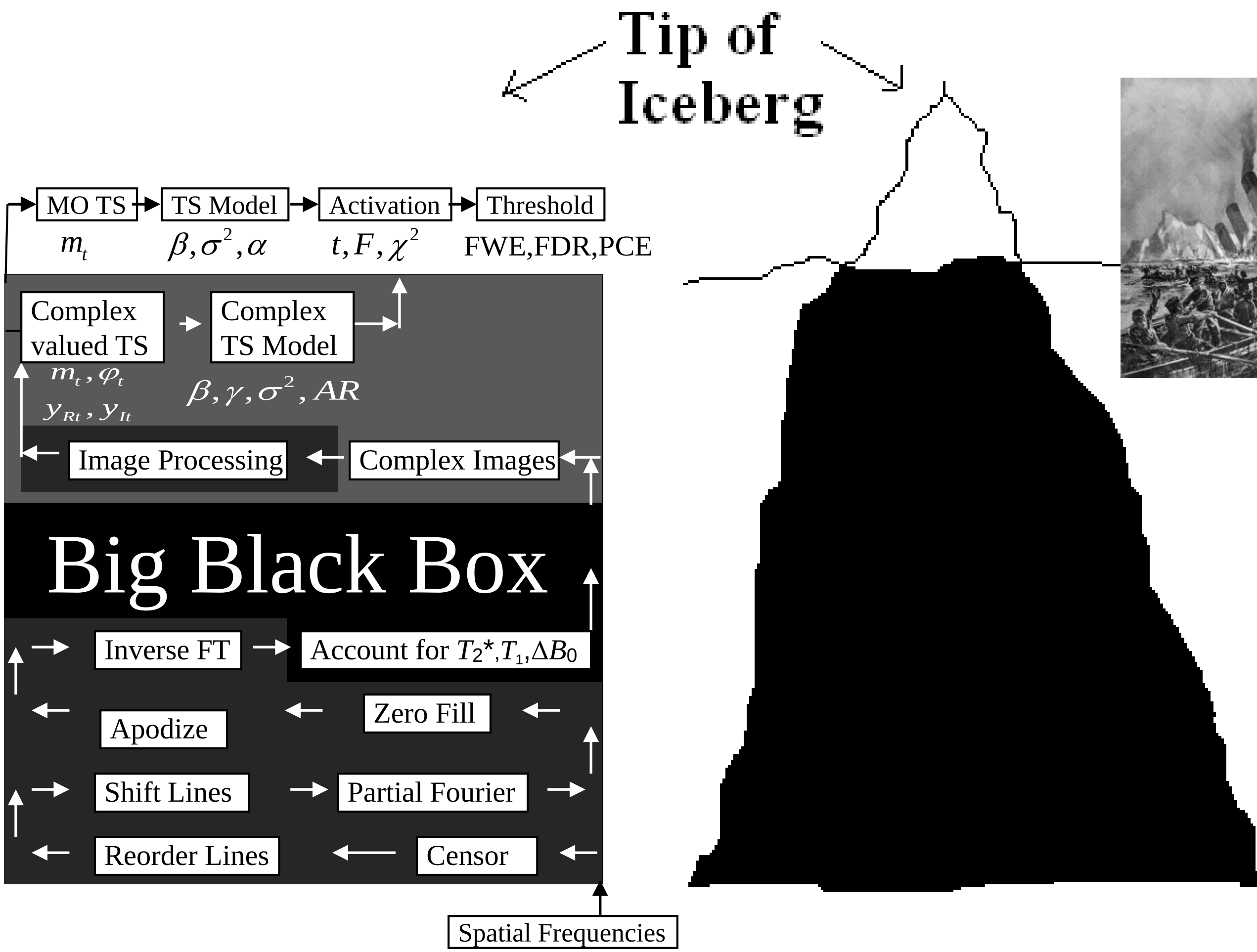
Arja, et al.: Changes in fMRI magnitude data and phase data observed in block-design and event-related tasks. NIMG 3149-3160, 2010.

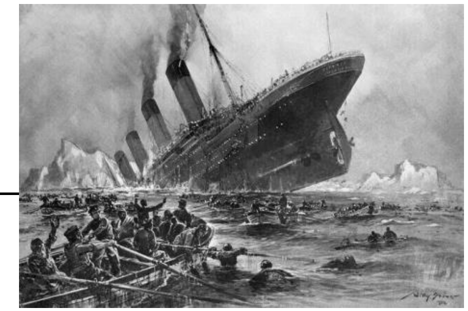
Discussion



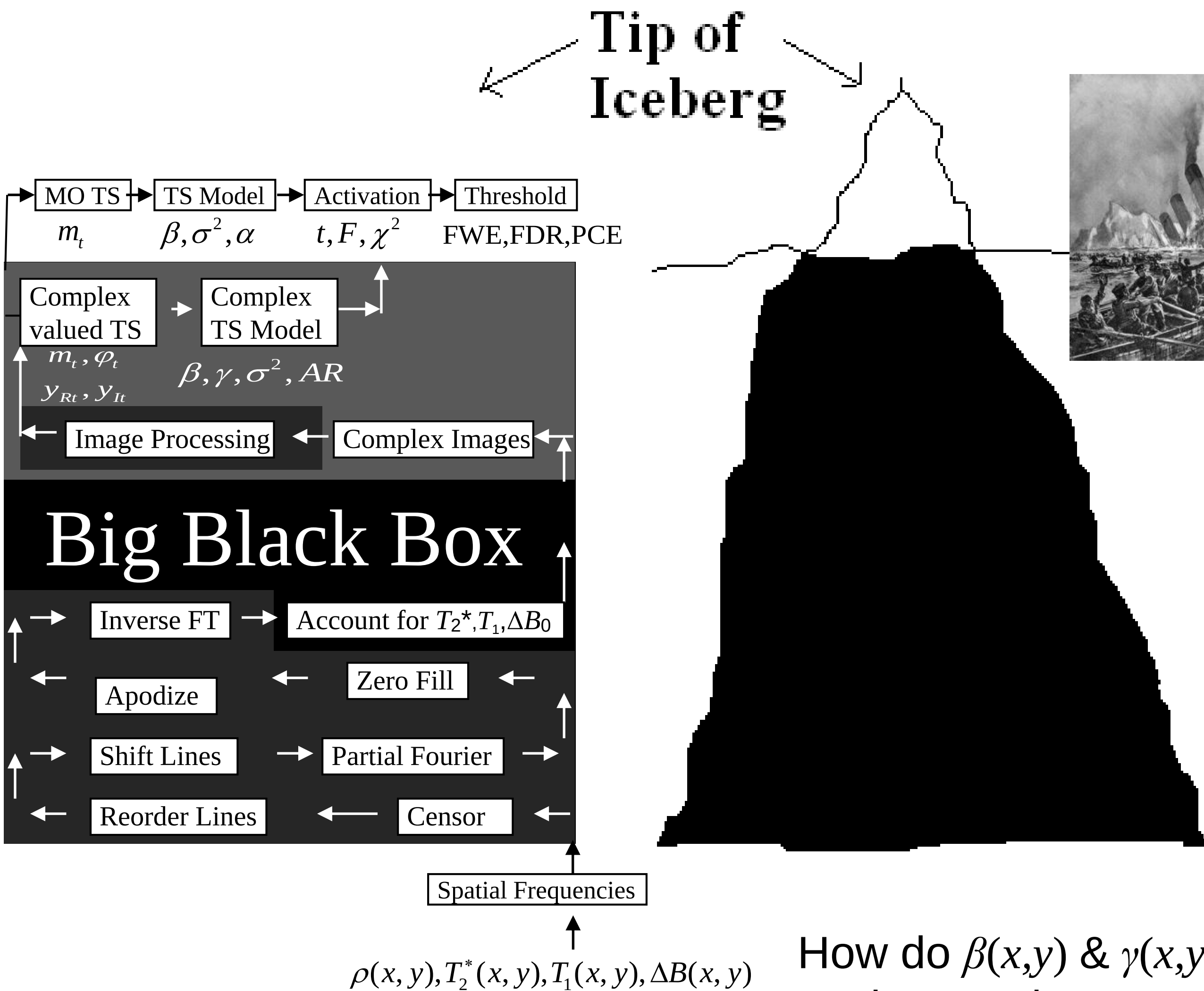
Shed light on part of the **black box**!

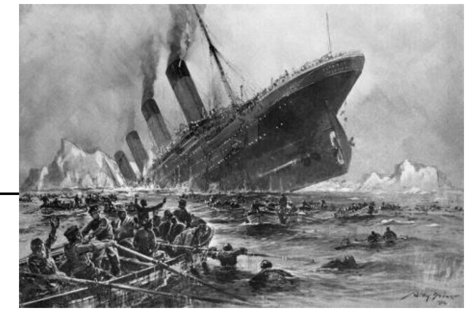
Discussion


Tip of Iceberg
MO TS
TS Model
Activation
Threshold
m_t
β,σ^2,α
t,F,χ^2
FWE,FDR,PCE
Complex valued TS
Complex TS Model
m_t,φ_t
y_{Rt},y_{It}
β,γ,σ^2,AR
Image Processing
Complex Images
Big Black Box
Inverse FT
Account for T_2*,T_1,ΔB_0
Apodize
Zero Fill
Shift Lines
Partial Fourier
Reorder Lines
Censor
Spatial Frequencies



Discussion

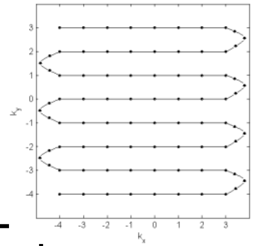


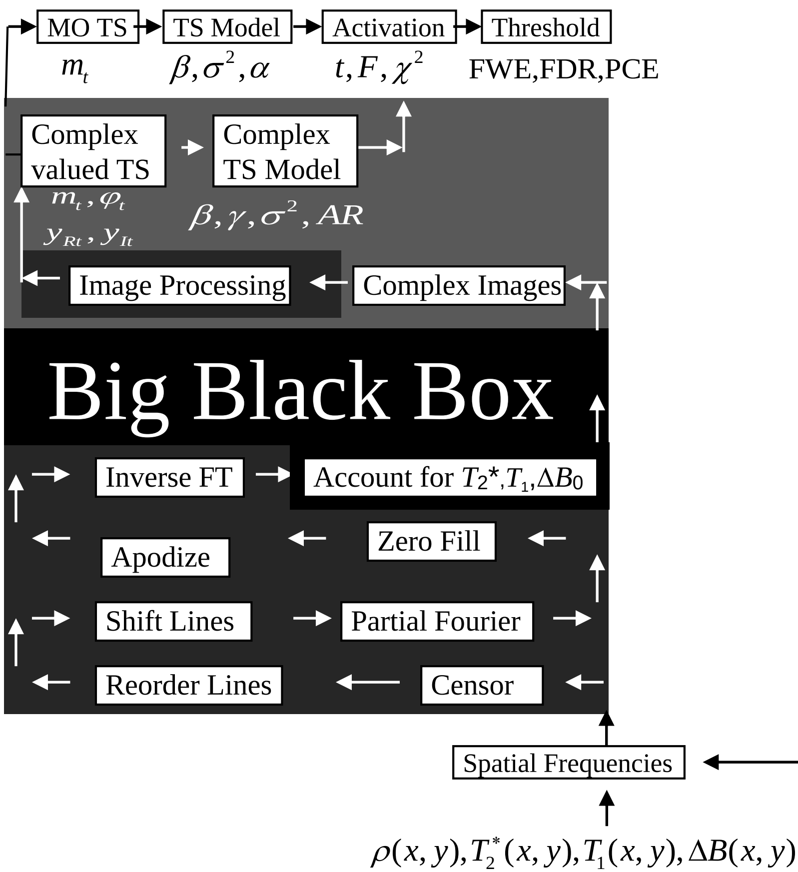


How do $\beta(x,y)$ & $\gamma(x,y)$ changes relate to changes in $\rho(x,y)$, $T_2{}^*(x,y)$, & $\Delta B(x,y)$?

Discussion

$$\mathcal{S}(t)=\int_{-\infty}^{+\infty}\int_{-\infty}^{+\infty}\rho(x,y)\left(1-e^{-TR/T_1(x,y)}\right)e^{-t/T_2^*(x,y)}e^{-i\gamma\Delta B(x,y)t}e^{-i2\pi(k_x x+k_y y)}dxdy$$





Sampling every Δt.

$\mathcal{S}(j\Delta t),\quad j=1,\ldots,p$

k_x and k_y
changing but known

$\rho(x,y),T_2^*(x,y),\Delta B(x,y)$
unknown

How do $\beta(x,y)$ & $\gamma(x,y)$ changes relate to changes in $\rho(x,y)$, $T_2{}^*(x,y)$, & $\Delta B(x,y)$?

Results

DeTeCT Model

$$y_{t_{DT}} = M_t\left(\cos\theta + i\sin\theta\right) + (\eta_{R_t} + i\eta_{I_t}).$$

$$M_t = \left[M_{t-1}\exp\left(-\frac{TR}{T_1}\right)\cos(\phi) + M_0\left(1-\exp\left(-\frac{TR}{T_1}\right)\right)\right]\sin(\phi)\exp\left(-\frac{TE_t}{T_2 * + \delta z_t}\right) + x_{1_t}'\beta_1$$

$$p(y_{Rt}, y_{It}) = \frac{1}{2\pi\sigma^2}\exp\left\{-\frac{1}{2\sigma^2}\left[(y_{Rt} - \rho_t\cos\theta_t)^2 + (y_{It} - \rho_t\sin\theta_t)^2\right]\right\}$$

δ: differential signal change

β_1: coefficient for a time trend

TE: temporally varying echo time

z_t: reference function

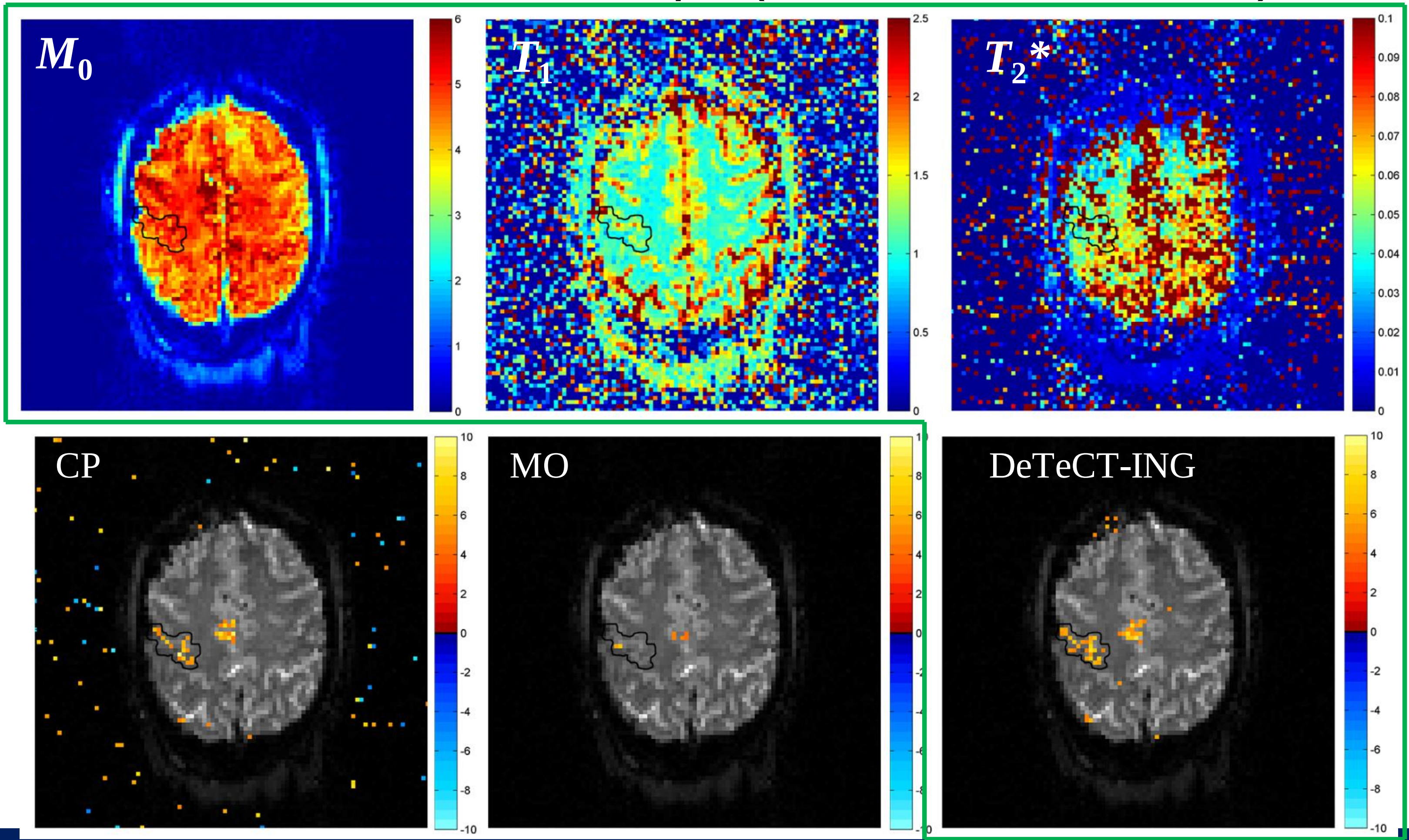
$$\sigma^2\left(M_0, T_1, T_2^*, \delta, \beta, \theta \middle| y_{R_t}, y_{I_t}, TR, \phi, TE_t, z_t\right) = \frac{1}{2n}\sum_{t=1}^{n}\left[\left(y_{R_t} - M_t\cos\theta\right)^2 + \left(y_{I_t} - M_t\sin\theta\right)^2\right].$$

$$Z_C = sign(\hat{\delta})\sqrt{2n\log(\tilde{\sigma}^2 / \hat{\sigma}^2)}.$$

Karaman, Bruce, Rowe: Magn. Reson. Imaging, 32:9-27, 2014.

Results

Estimated M_0, T_1, and T_2^* using the nonlinear least squares estimation and activation maps (5% Bonferroni FWE):



Discussion

Care needs to be taken when we obtain data.

We should get data in its originally measured form.

We should do any required processing ourselves.

Our models should incorporate processing.

We should use all of the data (magnitude and phase).

Discussion

It's been 13 years since I started this.

STATISTICS-BIOSTATISTICS  SEMINAR

TITLE: **A COMPLEX WAY TO COMPUTE fMRI ACTIVATION**

SPEAKER: Daniel B. Rowe
Department of Biophysics
Medical College of Wisconsin

TIME: 4:00 P.M.

DATE: Wednesday, November 19, 2003

ROOM: 1221 CSSC

ABSTRACT:

In functional magnetic resonance imaging, Fourier "image reconstruction" results in complex valued proton spin densities that make up our voxel time course observations. The complex part of the proton spin density is a result of phase errors due to magnetic field inhomogeneities. Nearly all fMRI studies obtain a statistical measure of functional "activation" based on magnitude image time courses. However, it is the real and imaginary parts of the original signal that are measured with (normally distributed) error, and not the magnitude. The two error specifications are equivalent for "large" signal to noise ratios. The image information is contained in both the real and imaginary parts or in the magnitude and phase. A more accurate model should use the correct distributional specification and all the information contained in the data. A model is presented that uses the original complex form of the data and not the magnitude. By doing this, there are approximately twice as many quantities used to estimate the model parameters which results in improved power.

Coffee and Cookies at 3:30 p.m. in Room 4331 CSSC

Discussion

The GE scanner produces a P-file.

Name	Type	Date modified	Size
P02048.7	7 File	6/24/2005 8:43 AM	52,328 KB
P52224.7	7 File	6/24/2005 7:13 AM	52,328 KB
⋮			
P28160.7	7 File	1/3/2013 1:25 PM	272,847 KB
P26112.7	7 File	1/3/2013 1:24 PM	272,847 KB
⋮			
P07680.7	7 File	11/3/2015 2:40 PM	1,875,118 KB
P08704.7	7 File	11/3/2015 2:35 PM	1,250,130 KB
P09216.7	7 File	11/3/2015 2:40 PM	240,534 KB
P10240.7	7 File	11/3/2015 2:39 PM	14,999,866 KB
P11264.7	7 File	11/3/2015 2:40 PM	290,626 KB
P12800.7	7 File	11/3/2015 2:39 PM	266,794 KB
P07168.7	7 File	11/3/2015 2:40 PM	1,730,890 KB

Thank You!

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Mr. Kevin K. Liu, Marquette University