True Complex-Valued fMRI Time Series and Activation

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Outline

- ➢ fMRI BOLD Response
- ➢ Complex Image Reconstruction
- ➢ Statistical Activation Methods
  - Real-Valued: Magnitude-Only, Phase-Only
  - Complex-Valued: Magnitude & Phase
- ➢ Biological Phase Information
  - Unwanted Vascular
  - Neuronal Firing
- ➢ Activations in Computer Simulated Data
- ➢ Activations in Human Experimental Data
- ➢ Discussion

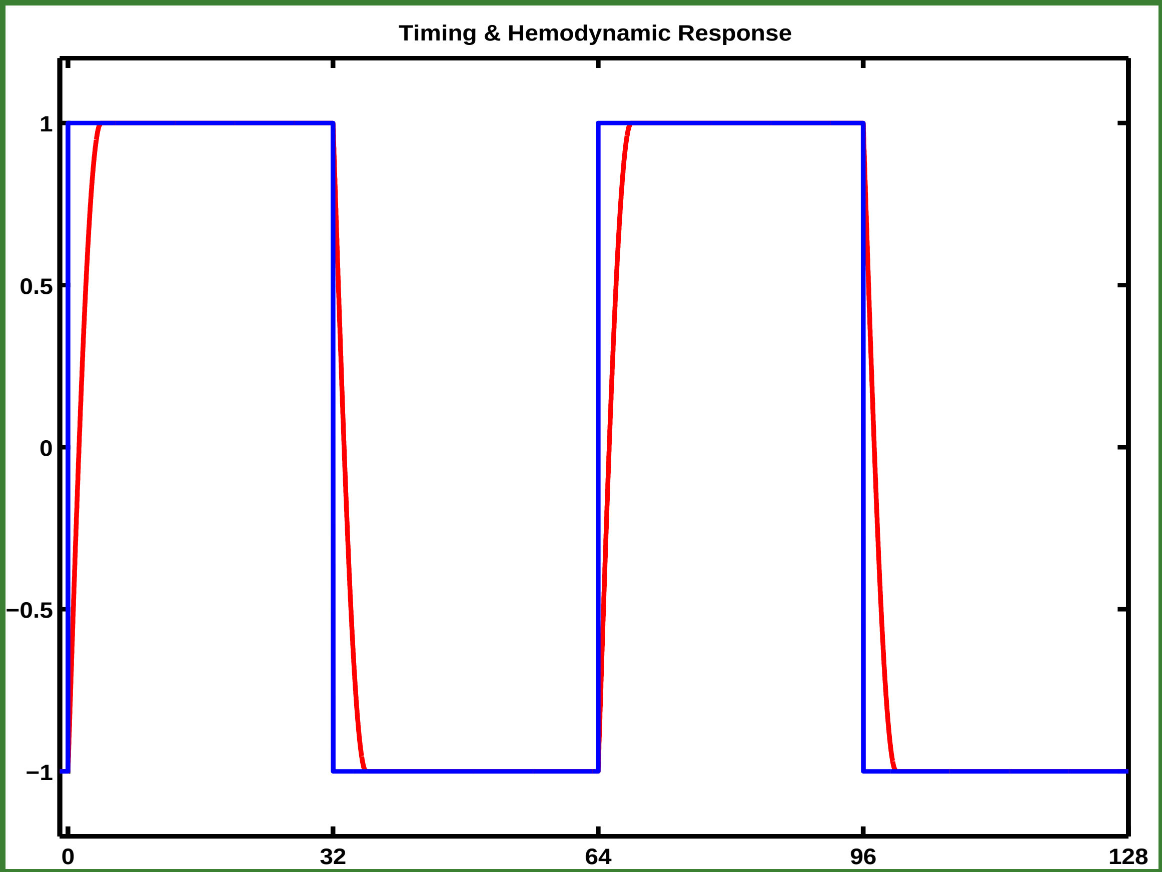
fMRI BOLD Response

Place volunteer into MRI scanner.

GE 3T Long Bore

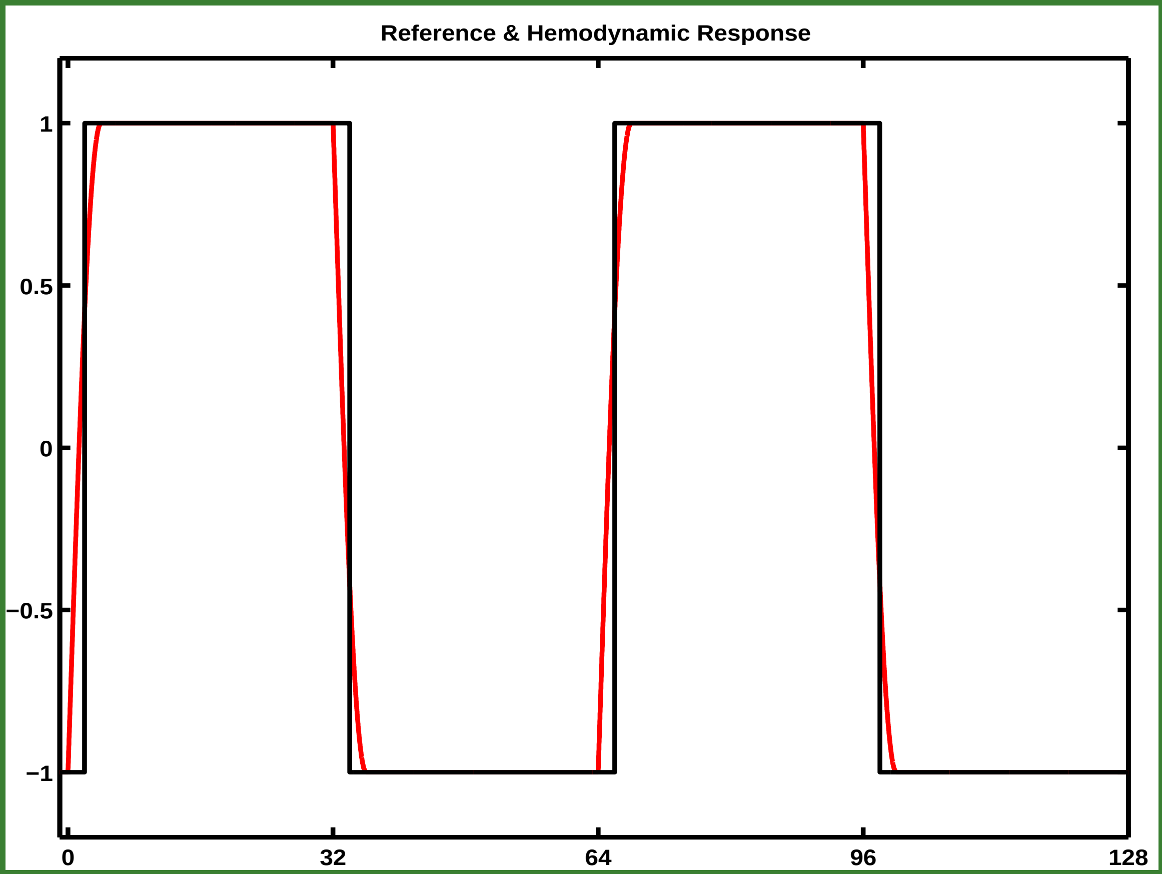
fMRI BOLD Response

We have the volunteer do something often in a block design.
Motor movement; sound, visual, or smell presentation; etc.
And measure what happens, BOLD response in voxels.



fMRI BOLD Response

Compute a measure of association between BOLD response in voxels and a pre determined "reference function" such as a shifted version of experimental paradigm.



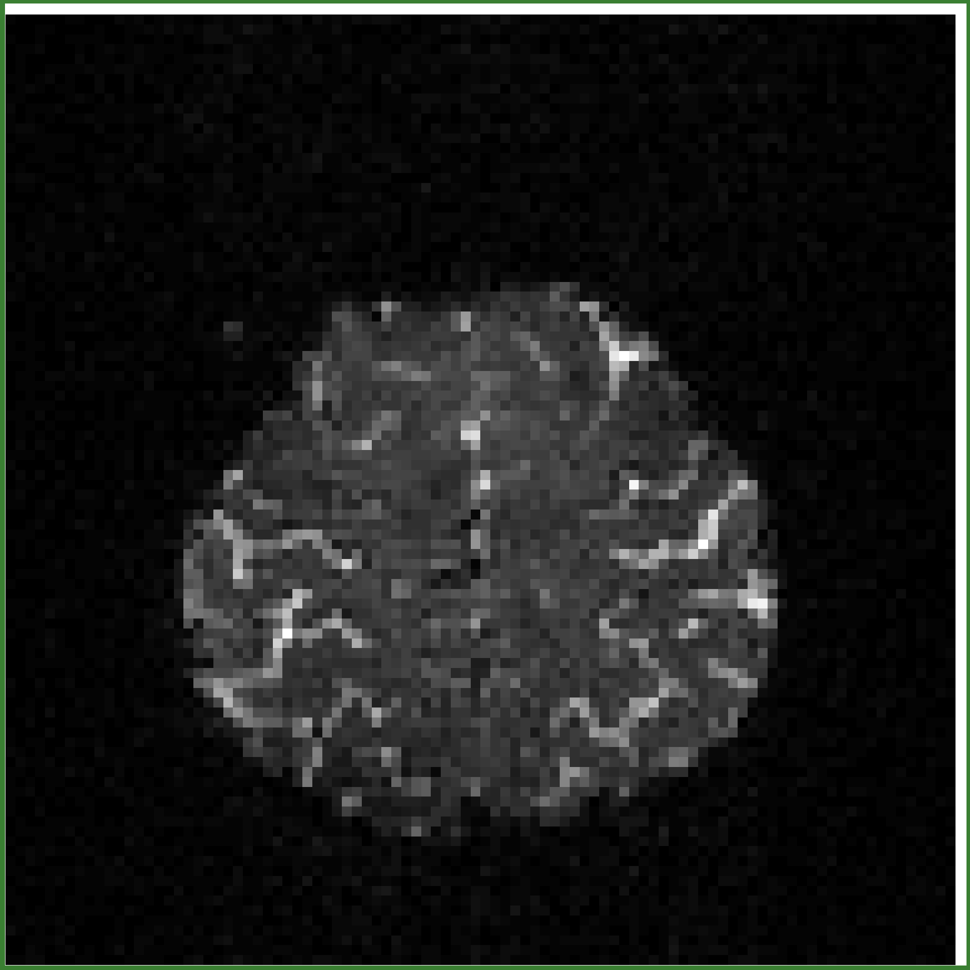
fMRI BOLD Response

In vivo measurement of local temporal magnetic field changes from the neural correlate BOLD response can be performed via an MRI machine.

GE 3T Long Bore

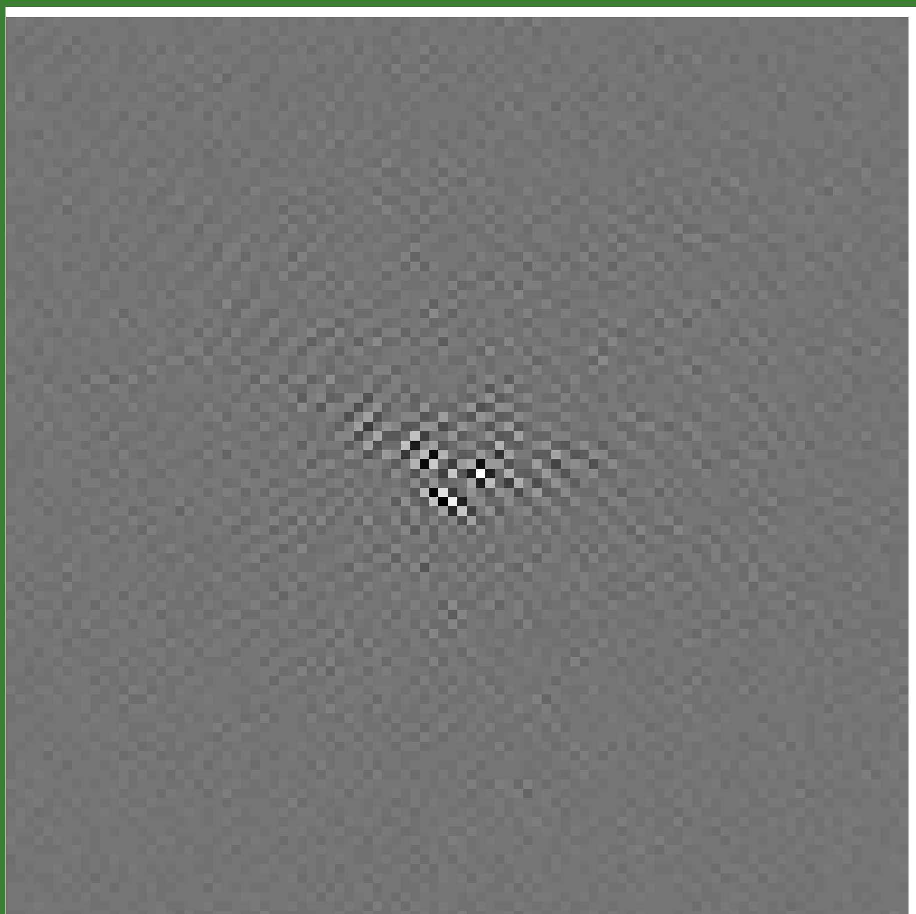
Complex Image Reconstruction

In MRI we aim to image a real-valued object, $\rho(x, y)$.
Different tissues have different magnetic properties yielding contrast.

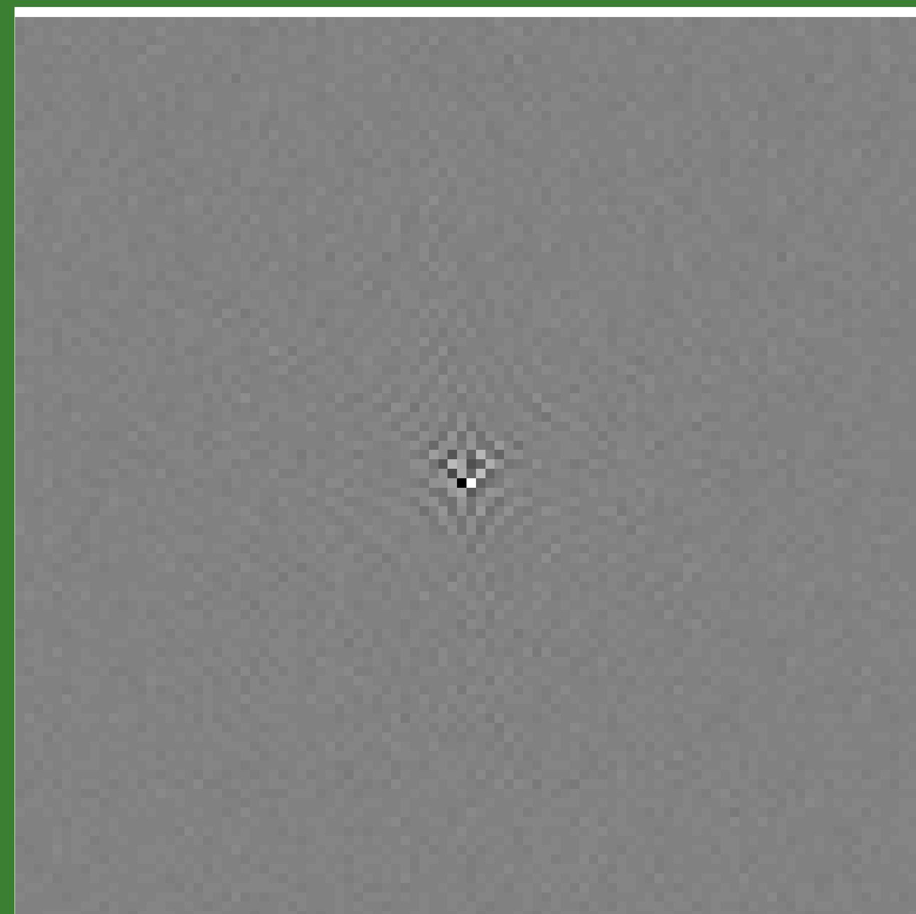


Complex Image Reconstruction

$s(k_x, k_y) = s_R(k_x, k_y) + is_I(k_x, k_y)$, the complex-valued FT of the object.



(a) real



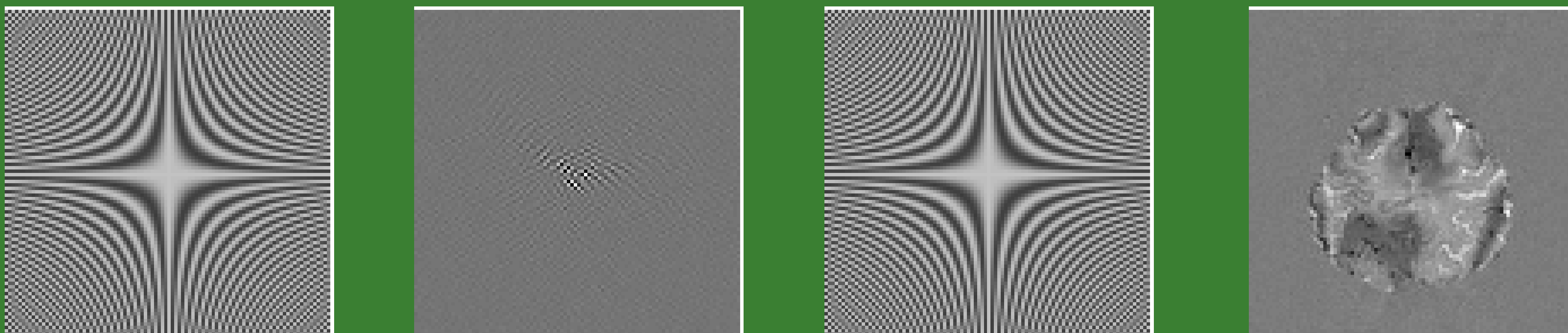
(b) imaginary

Haacke et al.: *Magnetic Resonance Imaging: Physical Principles and Sequence Design*, 1999.

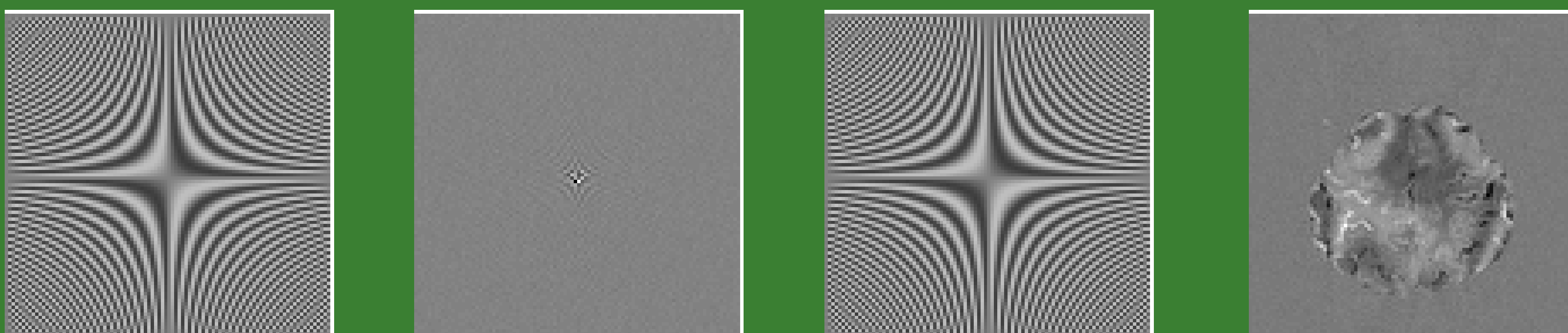
Complex Image Reconstruction

complex-valued 2D IFT

$$(\Omega_R + i\Omega_I) \quad * \quad (s_R + is_I) \quad * \quad (\Omega_R + i\Omega_I)^T \quad = \quad (\rho_R + i\rho_I)$$

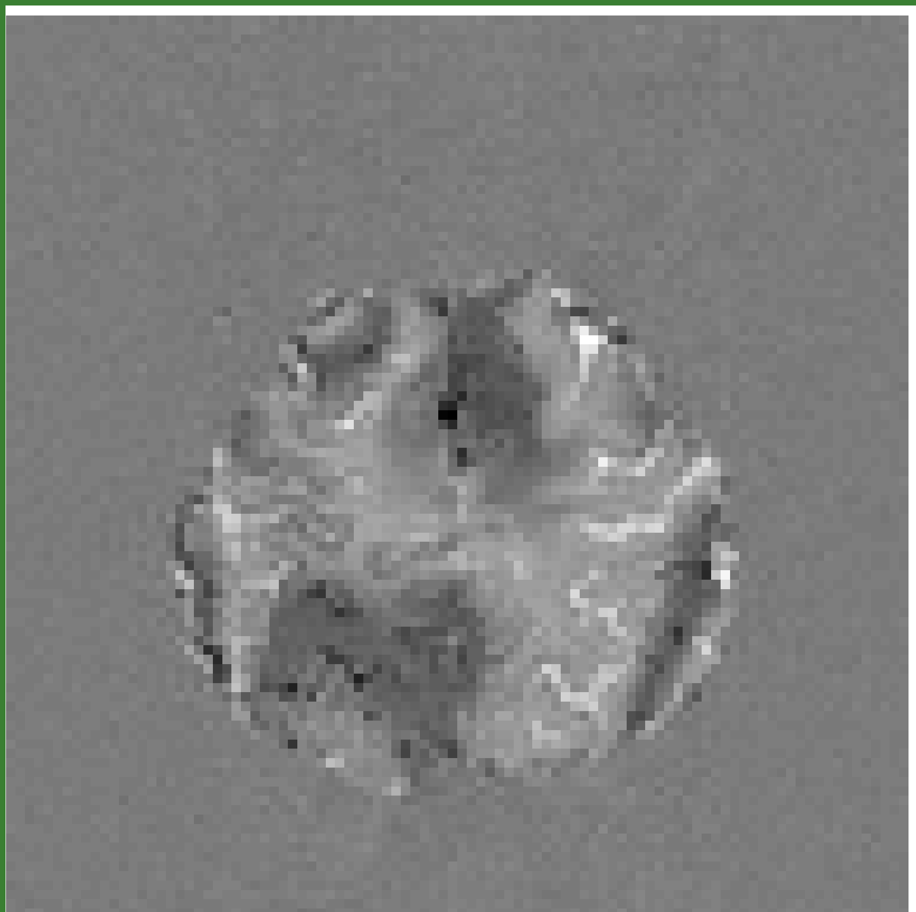


$$+\, i \quad * \quad +\, i \quad * \quad +\, i \quad = \quad +\, i$$

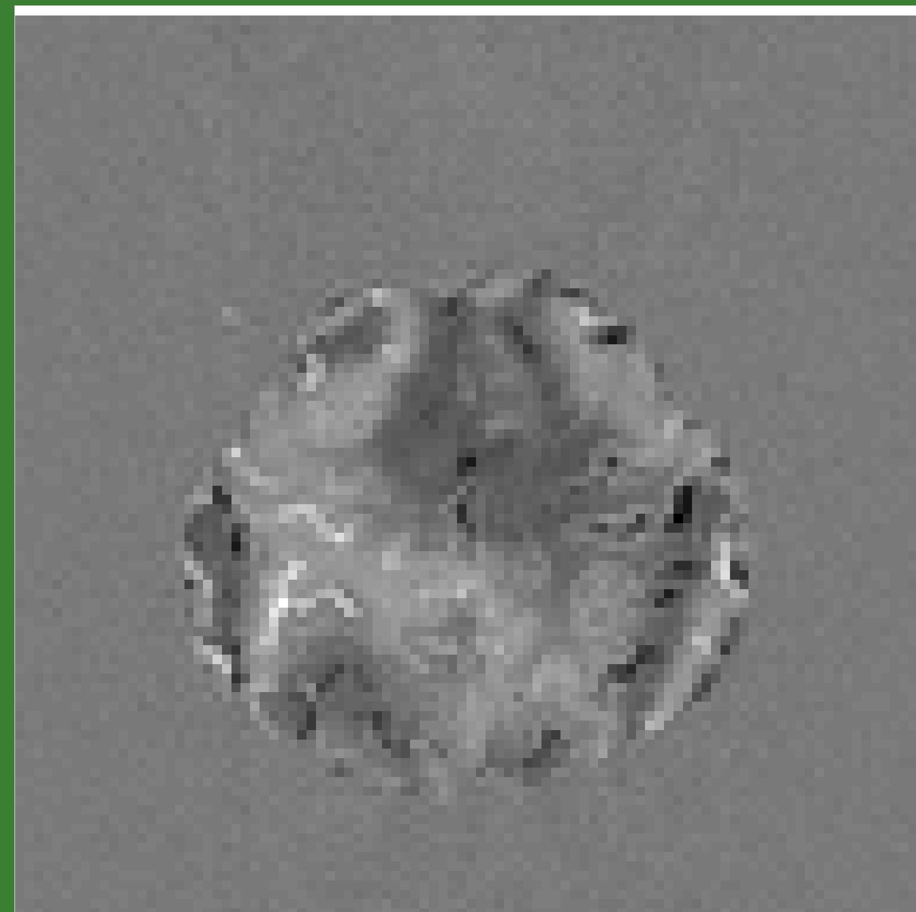


Complex Image Reconstruction

Due to the imperfect Fourier encoding, the IFT reconstructed object is complex-valued, $\rho(x,y) = \rho_R(x,y) + i\rho_I(x,y)$.



(a) Real image, y_{Rt}

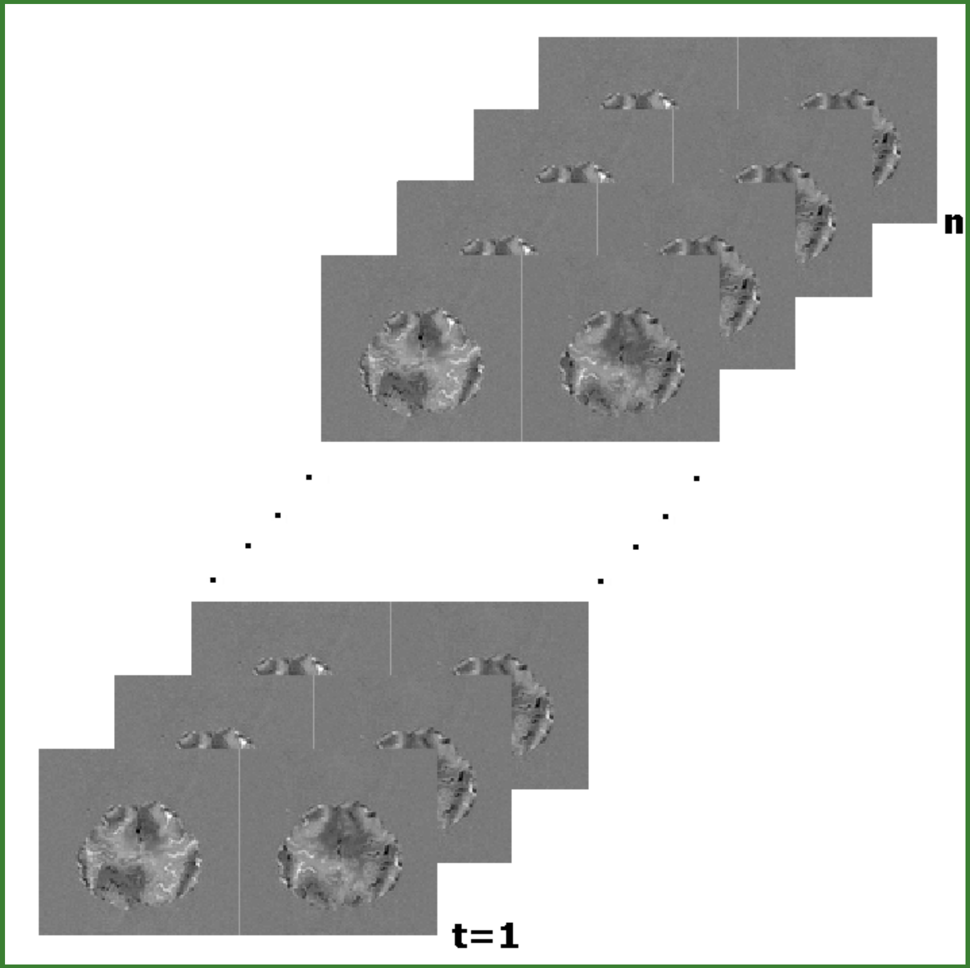


(b) Imaginary image, y_{It}

Haacke et al.: *Magnetic Resonance Imaging: Physical Principles and Sequence Design*, 1999.

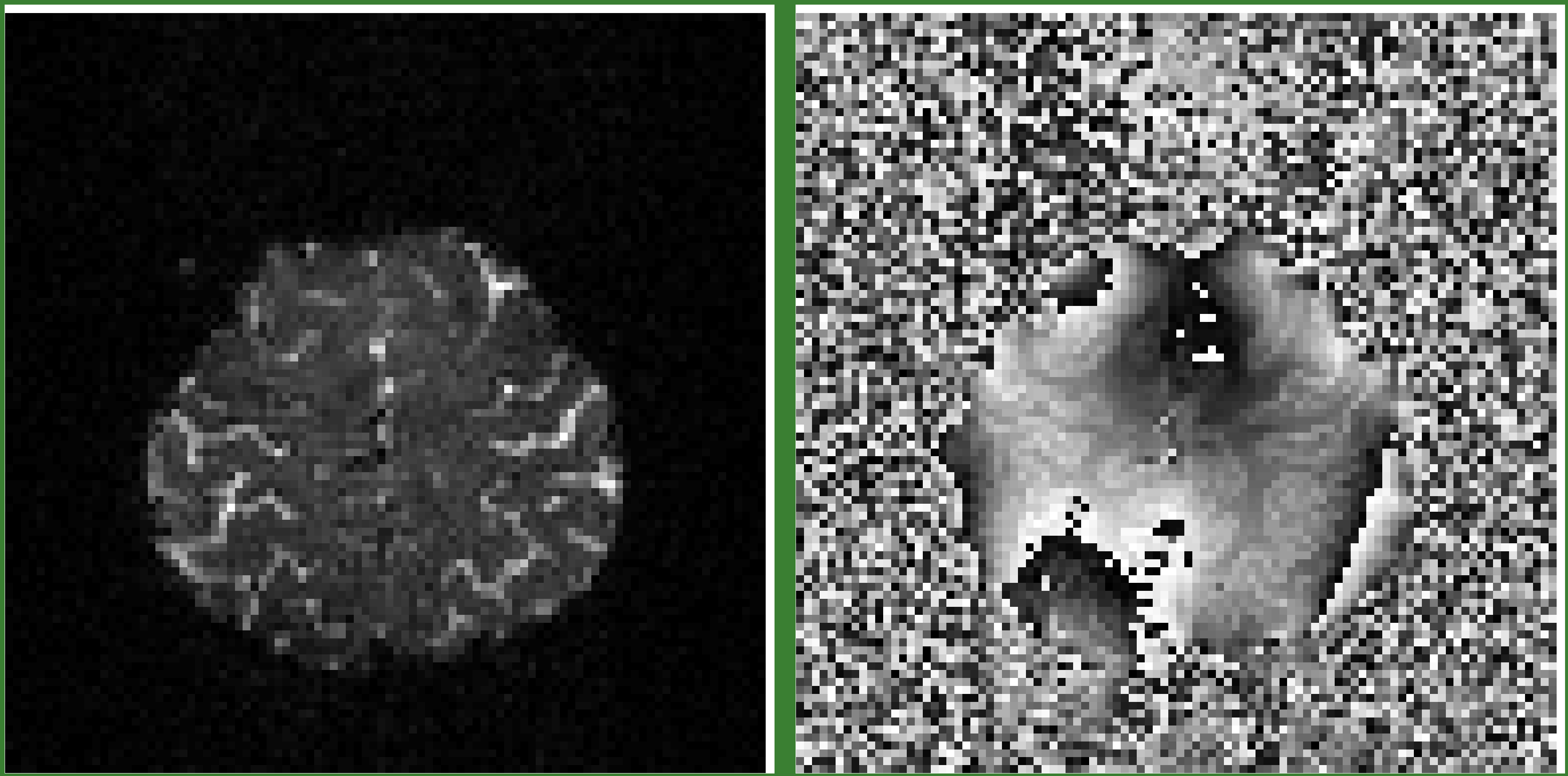
Complex Image Reconstruction

This occurs over time in fMRI and results in complex-valued images and voxel time course observations, $y_t = y_{Rt} + iy_{It}$.



Complex Image Reconstruction

Most fMRI studies transform from real-imaginary rectangular coordinates to magnitude-phase polar coordinates, $\rho(x,y) = r(x,y)e^{i\phi(x,y)}$.



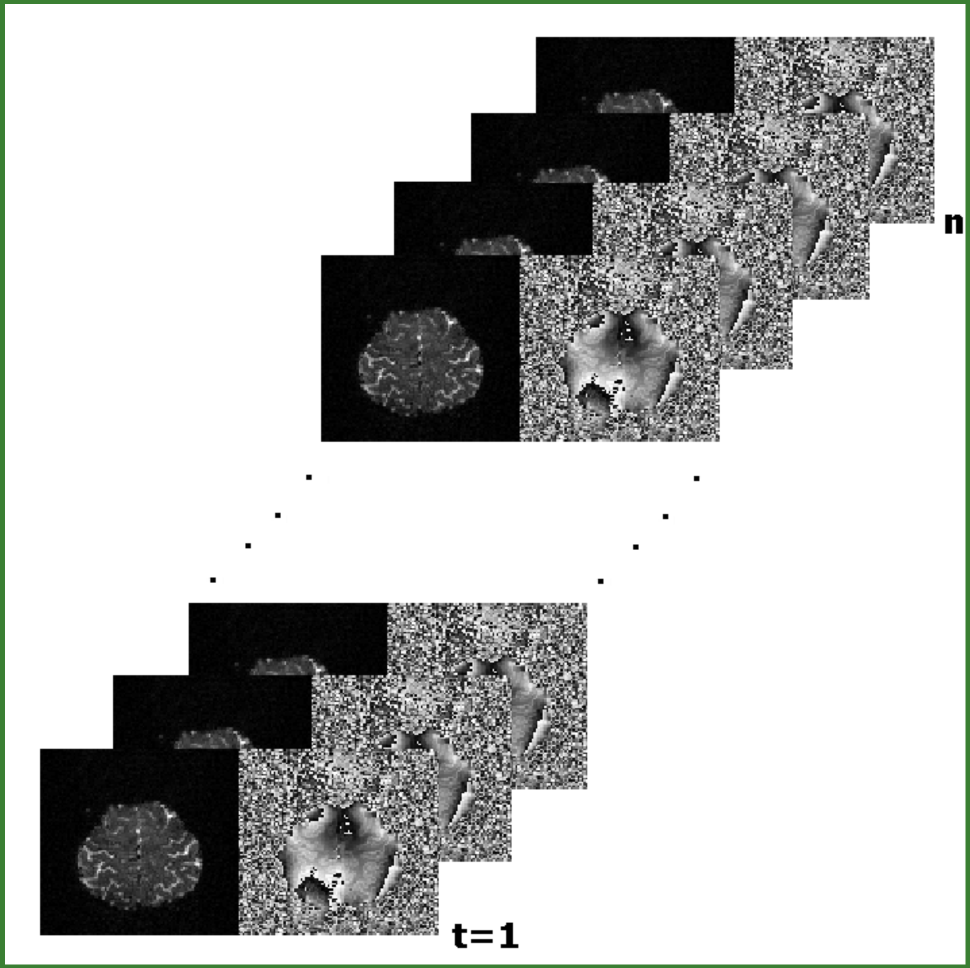
(a) Magnitude, $r_t = \sqrt{y_{Rt}^2 + y_{It}^2}$ (b) Phase, $\phi_t = \text{atan}_4(y_{It}/y_{Rt})$

Haacke et al.: *Magnetic Resonance Imaging: Physical Principles and Sequence Design*, 1999.

Complex Image Reconstruction

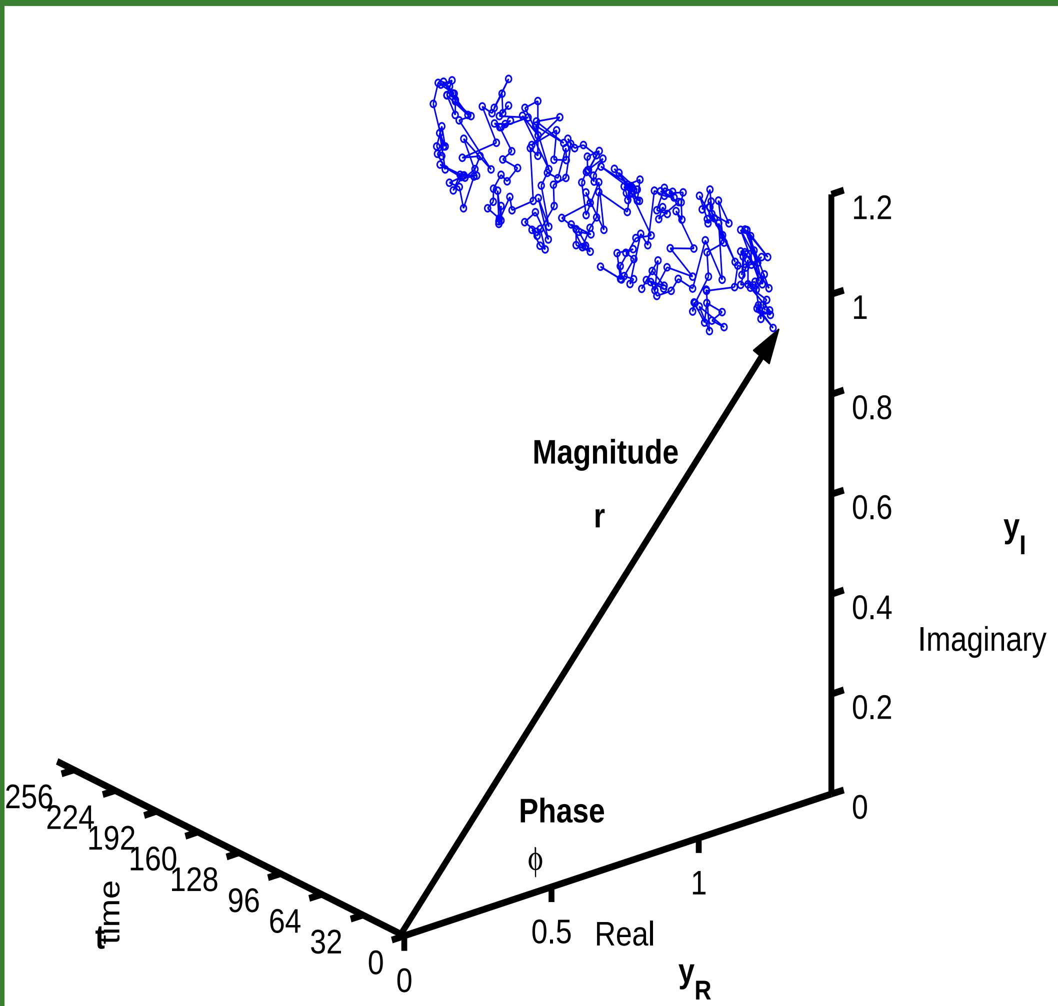
Collect a sequence of these reconstructed images over time.

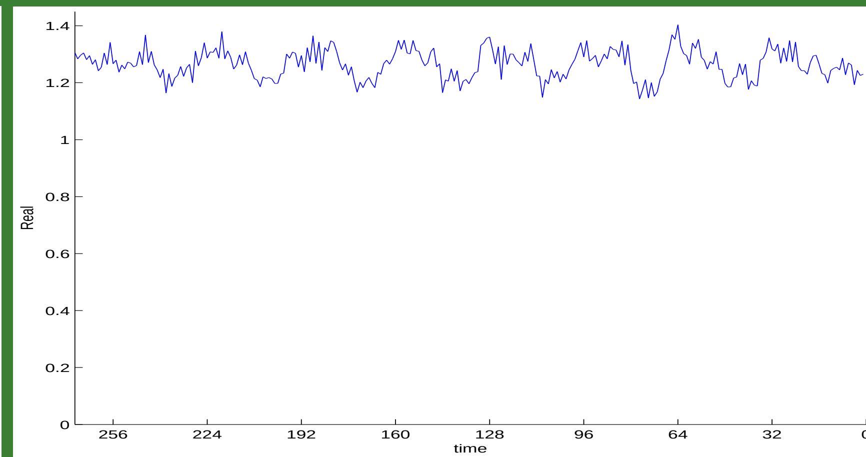
Form voxel time courses, $y_t = r_t e^{i\phi_t}$.



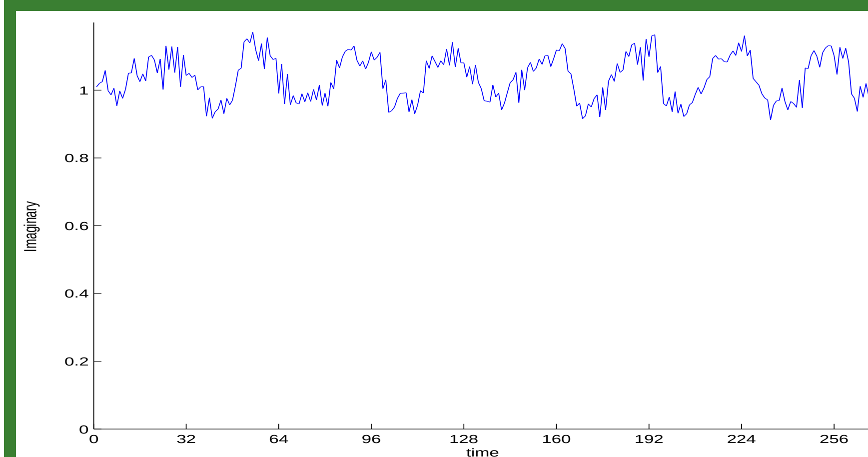
Activation Methods

Time series are complex-valued or bivariate with phase coupled means.





Real



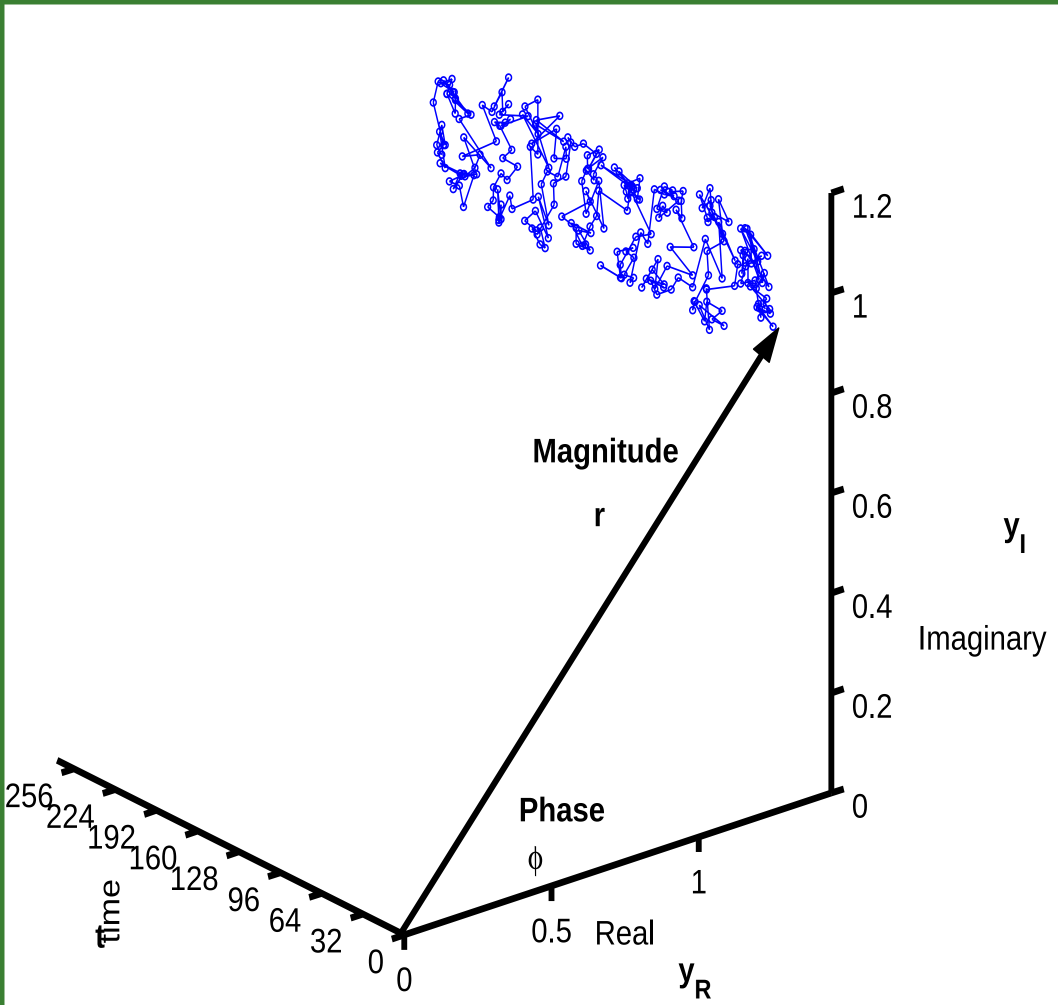
Imaginary

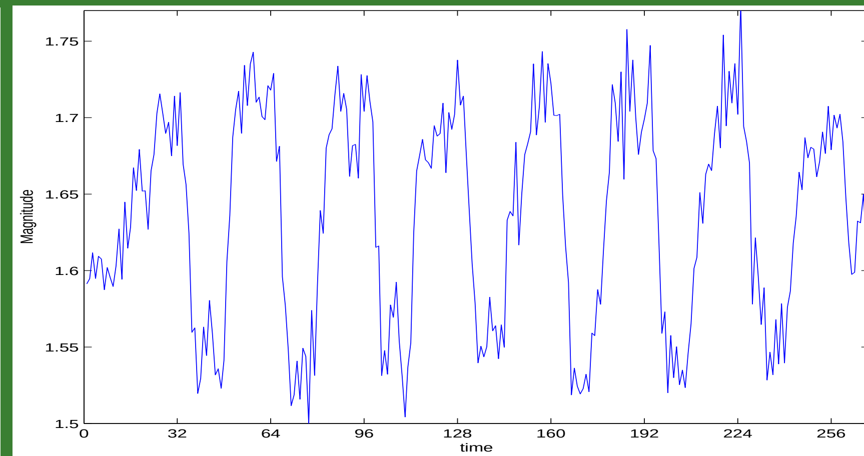
The y_R and y_I time courses have related vector length info!

This is a time series from a actual human experimental data!

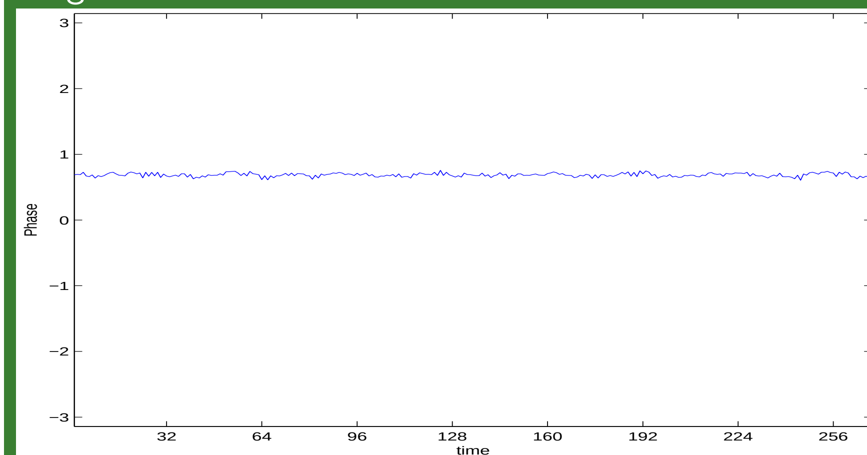
Activation Methods

Time series are complex-valued or bivariate with phase coupled means.





Magnitude



Phase

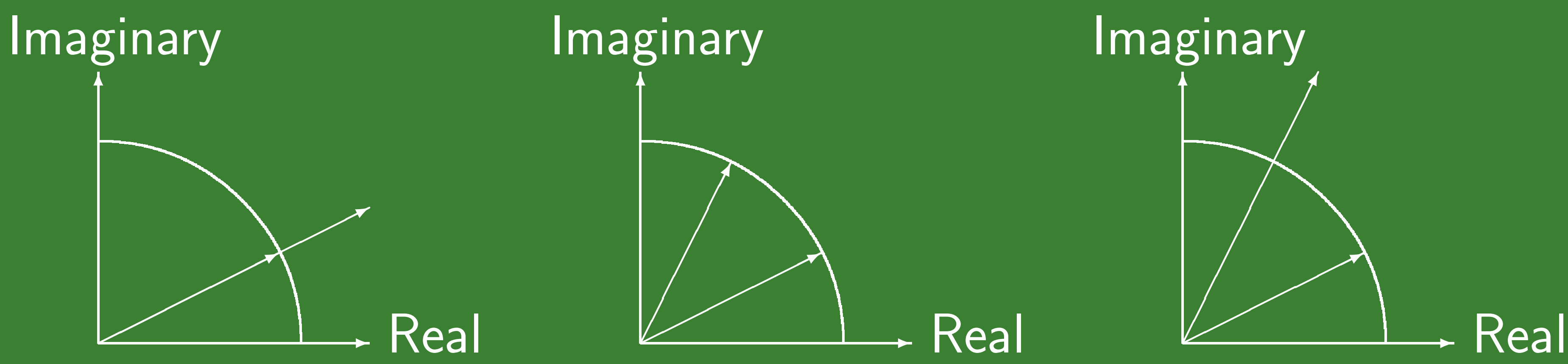
MO time courses only have vector length info!

PO time courses only has vector angle info!

Real-Imaginary or Magnitude-Phase time courses have all info!

Activation Methods

Block-designed experiment: Off-On-Off-...-On-Off task



- ➢ Real Magnitude-Only (MO/UP) Activation[1,2,3]
- ➢ Real Phase-Only (PO) Activation[4]
- ➢ Complex Magnitude w/ Constant Phase (CP) Activation[5]
- ➢ Complex Magnitude &/or Phase (CM) Activation[6]
- ➢ Complex Magnitude w/ Phase Regressor Activation[7,8]

[1]Bandettini et al.: MRM, 30:161-173, 1993.
[2]Friston et al.: HBM, 2:189-210, 1995.
[3]Rowe and Logan: NeuroImage, 24:603-606, 2005.
[4]Rowe, Meller, and Hoffmann: Submitted, 2006
[5]Rowe and Logan: NeuroImage, 23:1078-1092, 2004.
[6]Rowe: NeuroImage, 25:1310-1324, 2005b.
[7]Menon, MRM, 47:1-9, 2002.
[8]Nencka and Rowe: Submitted, 2006.

Activation Methods

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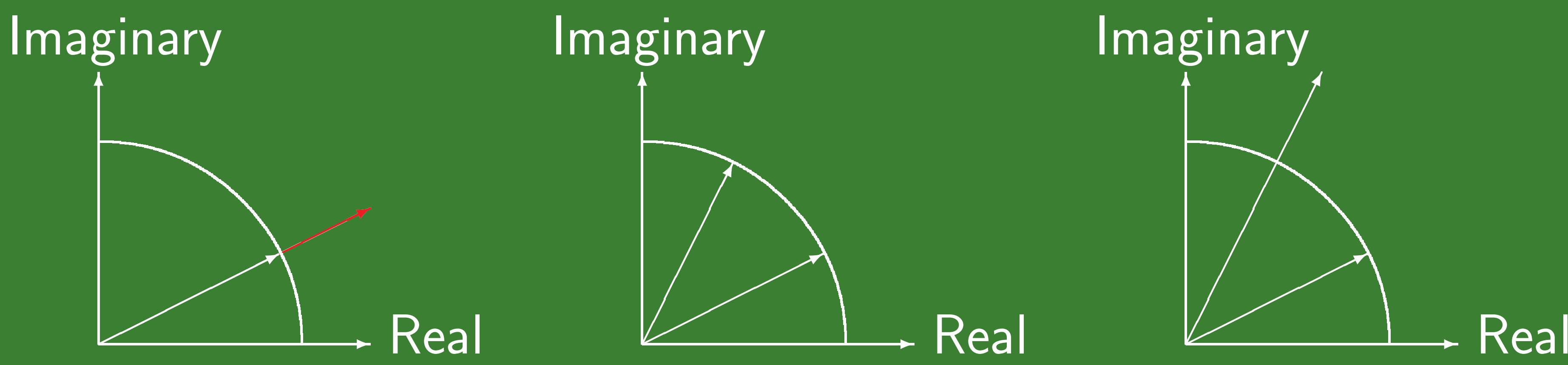

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Activation Methods

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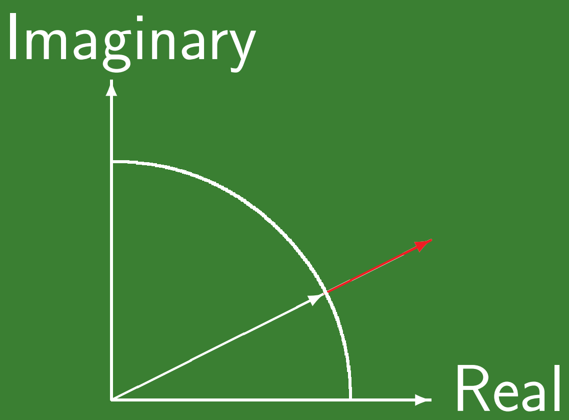

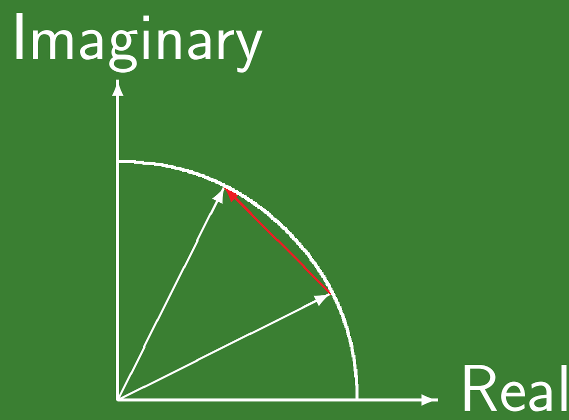

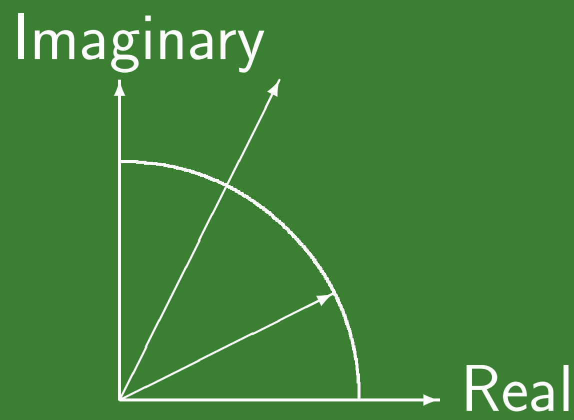

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Activation Methods

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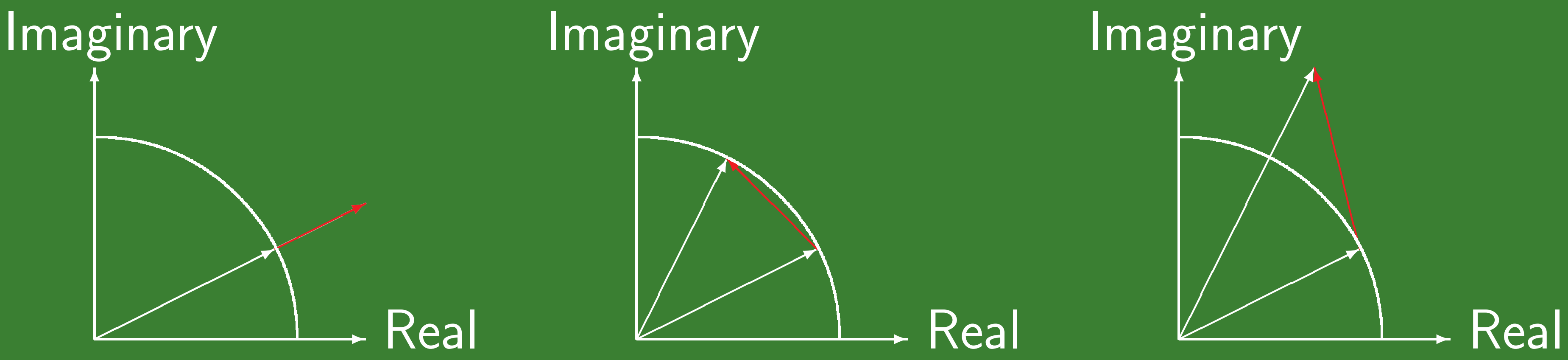

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[6]Rowe: NeuroImage, 25:1310-1324, 2005b.
[7]Menon, MRM, 47:1-9, 2002.
[8]Nencka and Rowe: Submitted, 2006.

Real Usual Magnitude-Only Activation

➢ Convert to magnitude series discarding phase info, $p(r) = \int p(r,\phi)\, d\phi$

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

➢ Assume a high SNR to approximate Ricean noise by normal noise

$$\frac{r_t}{\sigma^2} e^{-\frac{(r_t^2+\rho_t^2)}{2\sigma^2}} \int_{-\pi}^{\pi} \frac{1}{2\pi} e^{\frac{r_t \rho_t}{\sigma^2}\cos(\phi_t - \theta_t)} d\phi_t \approx \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(r_t-\rho_t)^2}{2\sigma^2}}$$

➢ Use GLM on the magnitudes[1,2], $C\beta = 0$ vs $C\beta \neq 0$, $C = (0,0,1)$

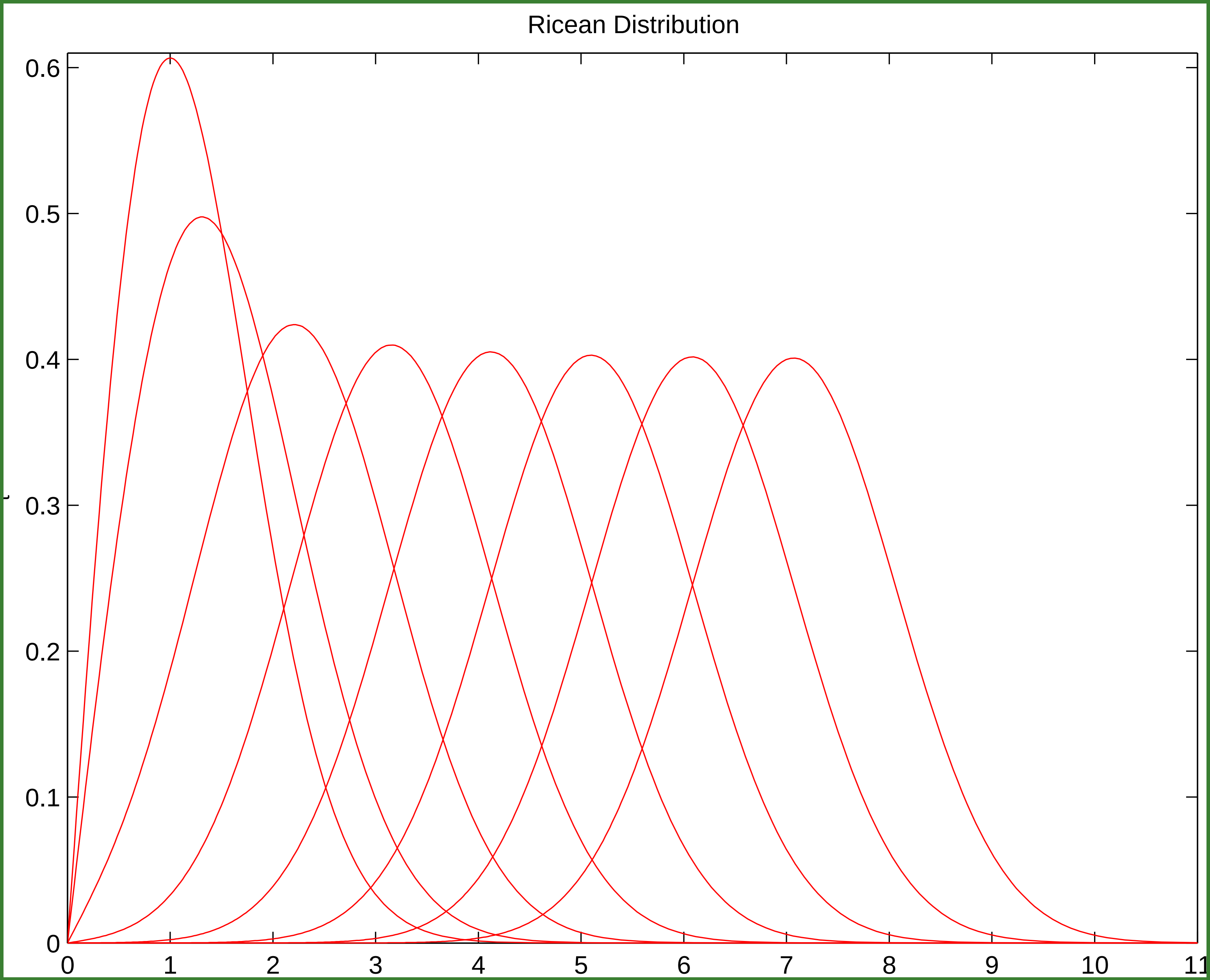
$$r = X\beta + \epsilon, \qquad \epsilon \sim N(0, \sigma^2 I_n), \quad \beta = (\beta_0, \beta_1, \beta_2)'$$

➢ A LRT[3] activation, χ^2, F, or t (z) and threshold[4]

$$-2\log(\lambda_{MO}) = n \log(\frac{\tilde{\sigma}^2}{\hat{\sigma}^2}) \quad => \quad z_{MO} = \text{sign}(C\hat{\beta})\sqrt{-2\log(\lambda_{MO})}$$

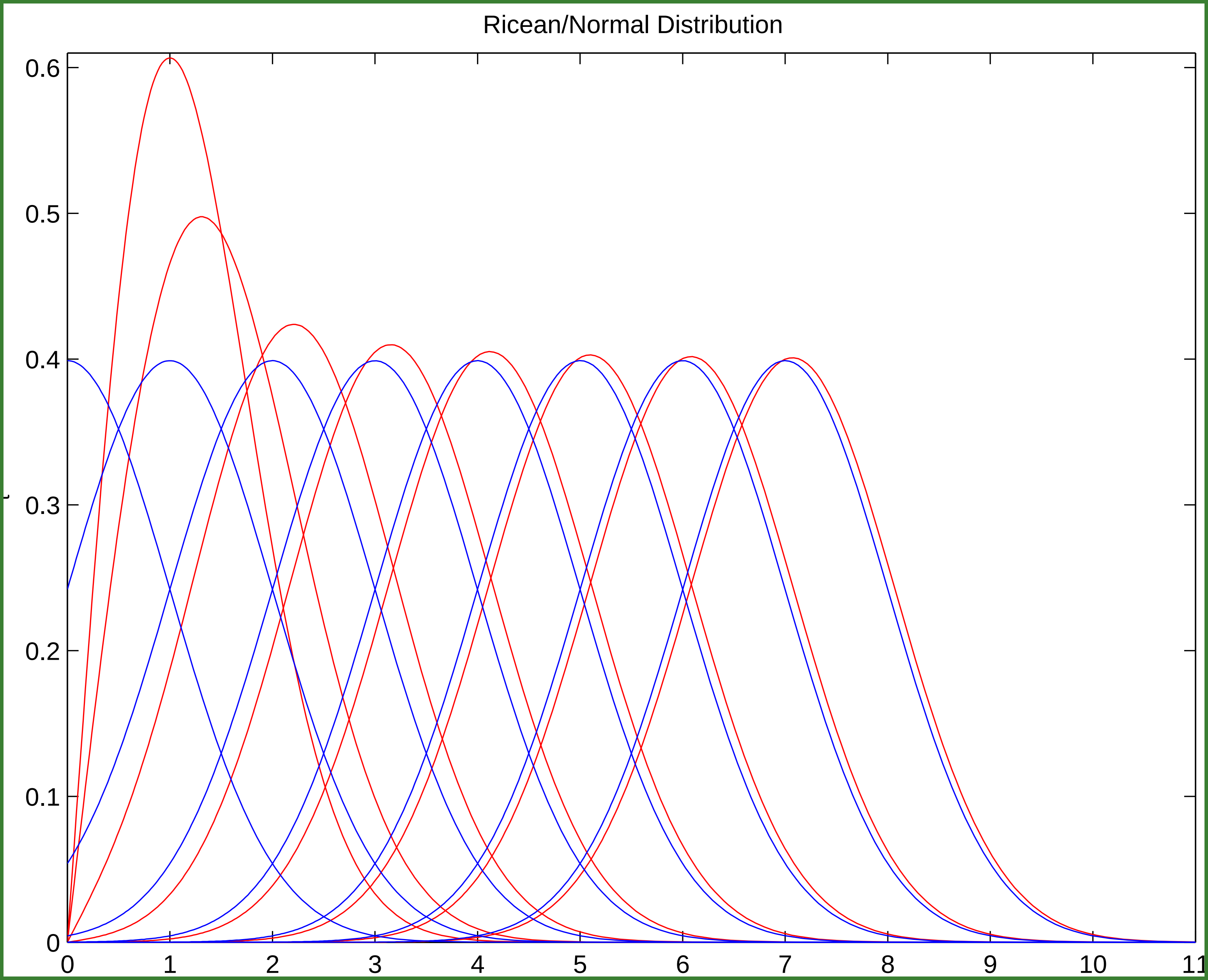
[1] Gudbjartsson and Patz: MRM, 34:910-914, 1995. [2] Rowe: NeuroImage, 25:1124-1132, 2005a.
[3] Rowe and Logan: NeuroImage, 23:603-606, 2005a. [4] Logan and Rowe: NeuroImage, 22:95-108, 2004.

Magnitude-Only Ricean Distribution



SNR=ρ/σ. Looks normal for decent SNR.

Magnitude-Only Ricean Distribution



Does it still look normal? Tails?

Complex Model

A very general bivariate or complex model can be written as[1]

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix}, \qquad \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix} \sim N\left(0, \sigma^2 I_2\right) .$$

with PDF

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

or in polar coordinates

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

where $r_t^2 = y_{Rt}^2 + y_{It}^2$, $\phi_t = \mathrm{atan}_4(y_{It}/y_{Rt})$, and $J = r_t$.

Note: $p(r_t, \phi_t) \neq p(r_t)p(\phi_t)$!

[1]Rowe: NeuroImage, 25:1310-1324, 2005b.

Complex Unrestricted Phase (UP) Model, $\theta_t \neq \theta_{t'}$

What if we don't specify anything about the phase in voxels?

So consider $\theta_t \neq \theta_{t'} \; \forall t, t'$
Unique phase at each time point.

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix}, \qquad \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix} \sim N\left(0, \sigma^2 I_2\right) .$$

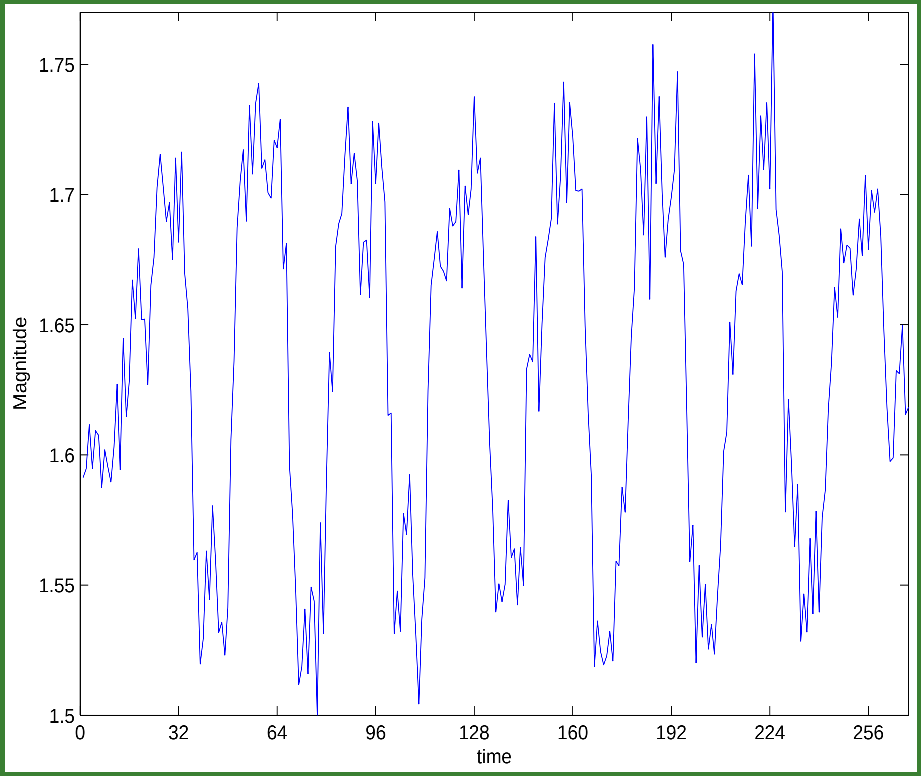
$\rho_t = x_t'\beta = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$
$\theta_t \neq \theta_{t'}$

Same regression coefficients and activation statistics as MO model[1].
In essence deriving the MO model from complex data!
MO=UP

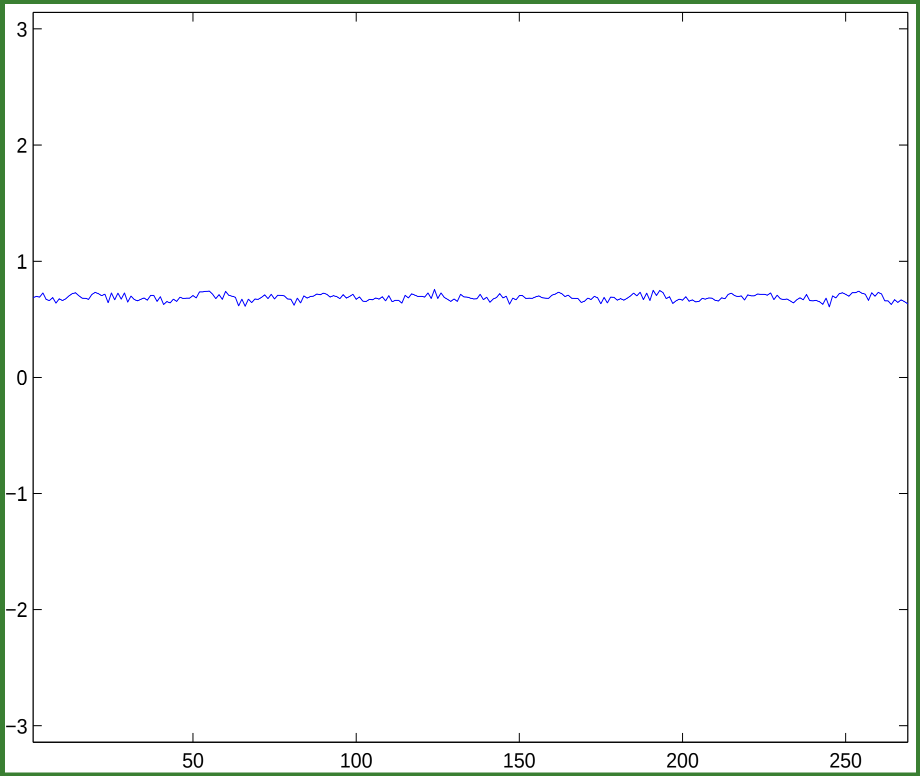
[1]Rowe and Logan: NeuroImage, 24:603-606, 2005.

Complex Voxel Time Course

Traditional beliefs were that the phase in a voxel is relatively constant.



(a) Magnitude over time plot.



(b) Phase over time plot.

Complex Magnitude with Constant Phase Activation

- Magnitude activation in complex data[1]

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix} , \qquad \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix} \sim N\left(0, \sigma^2 I_2\right) .$$

$\rho_t = x_t'\beta = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t}$
$\theta_t = \theta$, is a temporally constant voxel-wise phase angle.

- y_R and y_I are the n reals and n imaginaries
- X and β same as the MO model, θ is constant in grey matter.
- A LRT[1] activation, χ^2, F, or z and threshold[3]

$$-2\log(\lambda_{MO}) = n\log(\frac{\tilde{\sigma}^2}{\hat{\sigma}^2}) \quad => \quad z_{MO} = \text{sign}(C\hat{\beta})\sqrt{-2\log(\lambda_{MO})}$$

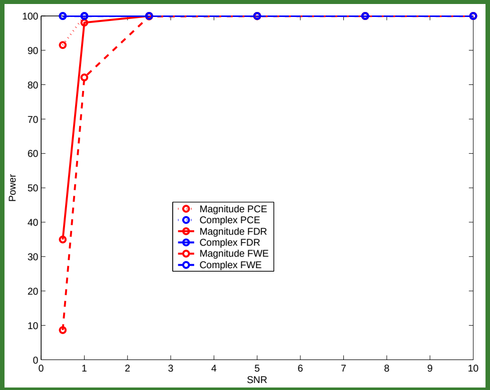
- Large sample χ^2 dist. checked by complex permutation resampling[2,3]

[1]Rowe and Logan: NeuroImage, 23:1078-1092, 2004. [2]Logan and Rowe: NeuroImage, 22:95-108, 2004.
[3]Nichols and Holmes: HBM, 15:125, 2002.

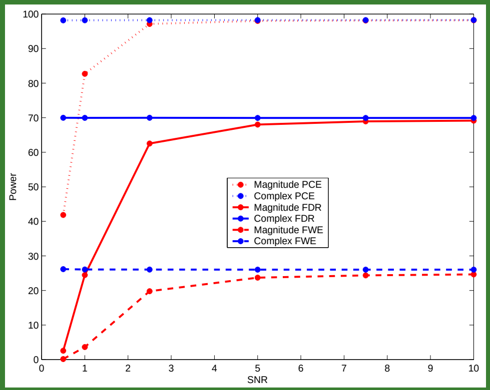
Complex Magnitude with Constant Phase Activation

Relatively constant voxel phase get[1,2,3]:

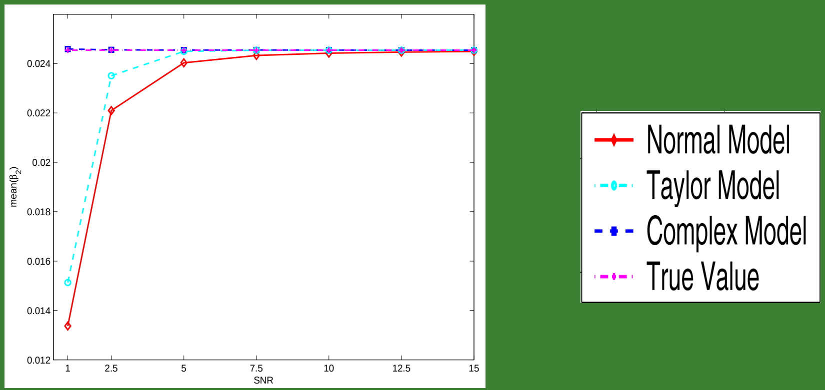
•higher power (CNR=1/2)



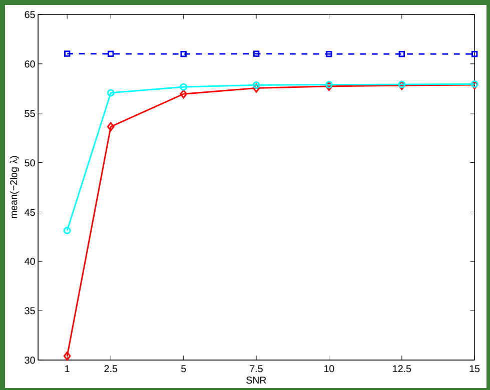
•higher power (CNR=1/4)



•unbiased estimators (CNR=1/2)



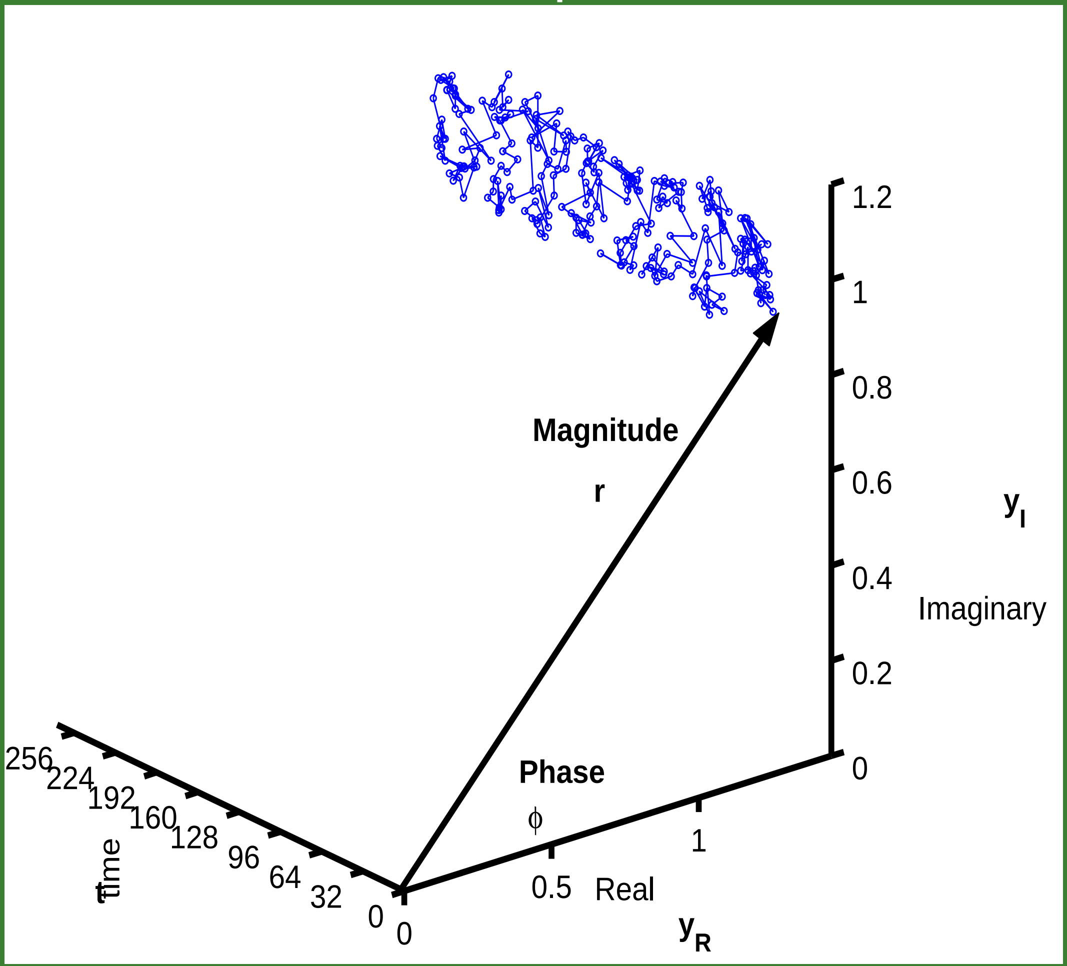
•higher activation (CNR=1/2)

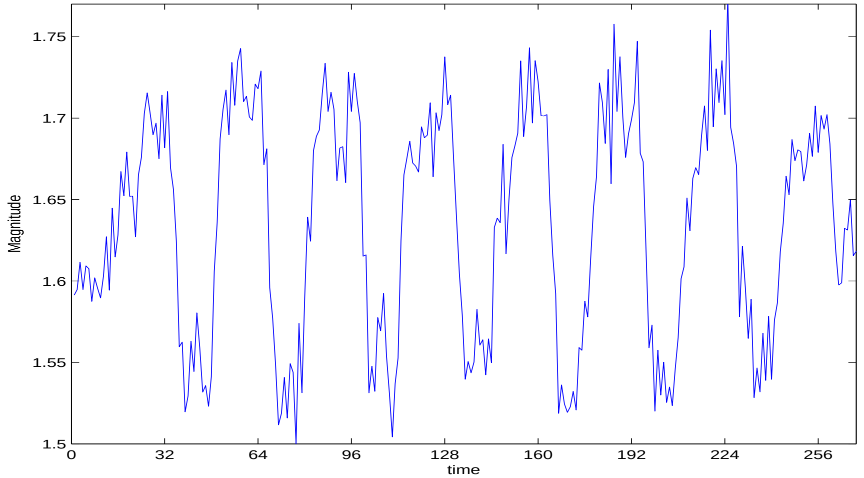


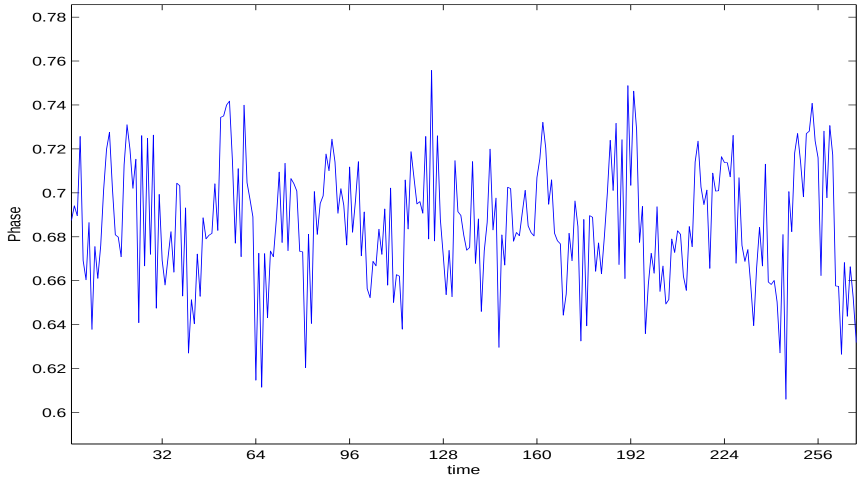
[1]Rowe and Logan: NeuroImage, 25:1310-1324, 2004. [2]Logan and Rowe: NeuroImage, 22:95-108, 2004.
[3]Rowe: NeuroImage, 25:1124-1132, 2005a.

Activation Methods

Time series are complex-valued or bivariate with phase coupled means.







Task related Magnitude and Phase changes!

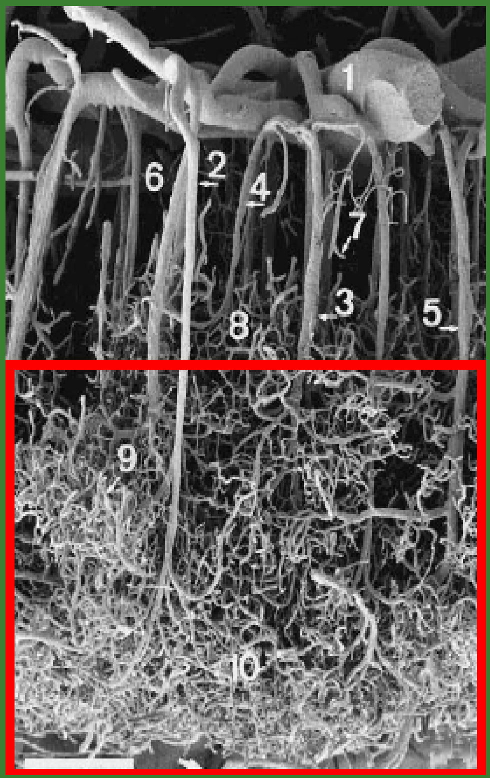
This is a time series from a actual human experimental data!

Real-Imaginary or Magnitude-Phase time courses have all info!

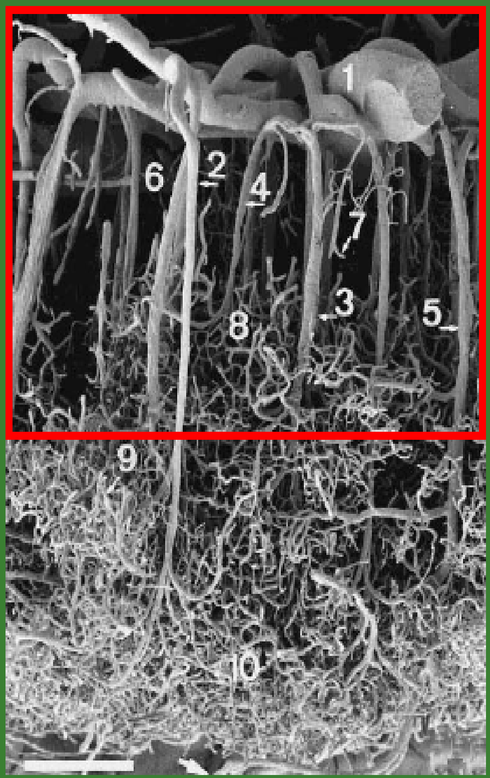
Phase Information: Vascular Structure and BOLD

Recent work indicates that phase time courses may exhibit TRPCs

- ➢ Voxels w/ small random veins, task related magnitude w/o phase change
- ➢ Voxels w/ large draining veins, task related magnitude w/ phase change



375μm



375μm

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

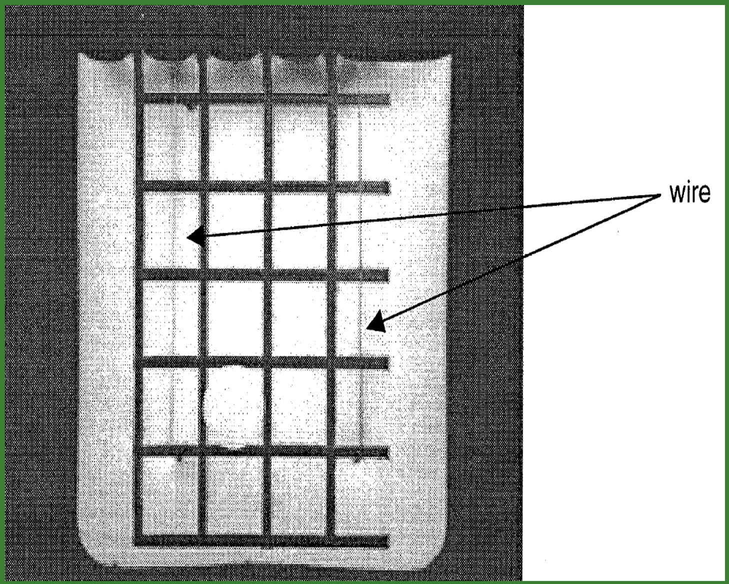
10) deep capillary zone.

[1]Menon: MRM, 47:1-9, 2002. [2]Hoogenraad: MRM, 45:233-246, 2001.

Figure from Reina-de la Torre et al.: The Anatomical Record, 251:87-96, 1998.

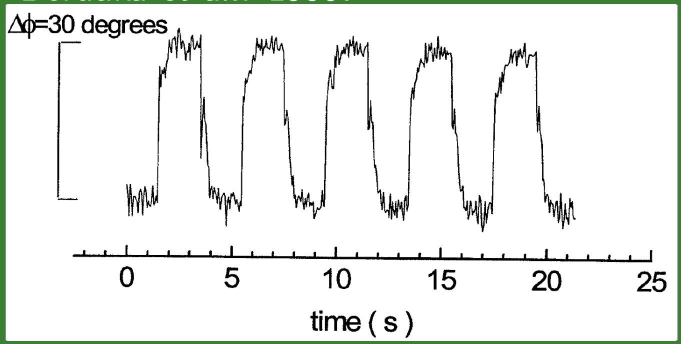
Phase Information: Direct Neuronal Current

- ➢ Voxels w/ wire, task related magnitude & phase change
- ➢ Voxels w/ optic nerve, task related magnitude & phase change



[1]Borduka et al.: 1999.

[2]Chow et al.: 2006.



[1]Borduka et al., JMR, 1999; [2]Chow et al., NeuroImage, 2006;

Complex Magnitude and/or Phase Activation

Considered magnitude linearly changing w/ constant & unrestricted phase.

Now both magnitude and phase change linearly over time.

$$\begin{pmatrix} y_{Rt} \\ y_{It} \end{pmatrix} = \begin{pmatrix} \rho_t \cos\theta_t \\ \rho_t \sin\theta_t \end{pmatrix} + \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix}, \qquad \begin{pmatrix} \eta_{Rt} \\ \eta_{It} \end{pmatrix} \sim N\left(0, \sigma^2 I_2\right) .$$

$$\begin{aligned} \rho_t &= x_t'\beta = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_{q_1} x_{q_1 t} \\ \theta_t &= u_t'\gamma = \gamma_0 + \gamma_1 u_{1t} + \cdots + \gamma_{q_2} u_{q_2 t}, \qquad t = 1, \ldots, n \end{aligned}$$

x_t' is the t^{th} row of a design matrix X for the magnitude and
u_t' is the t^{th} row of a design matrix U for the phase.

Form GLR test statistic, λ, $-2\log\lambda$, and $\text{sign}(C\hat{\beta})\sqrt{-2\log(\lambda)}$.

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

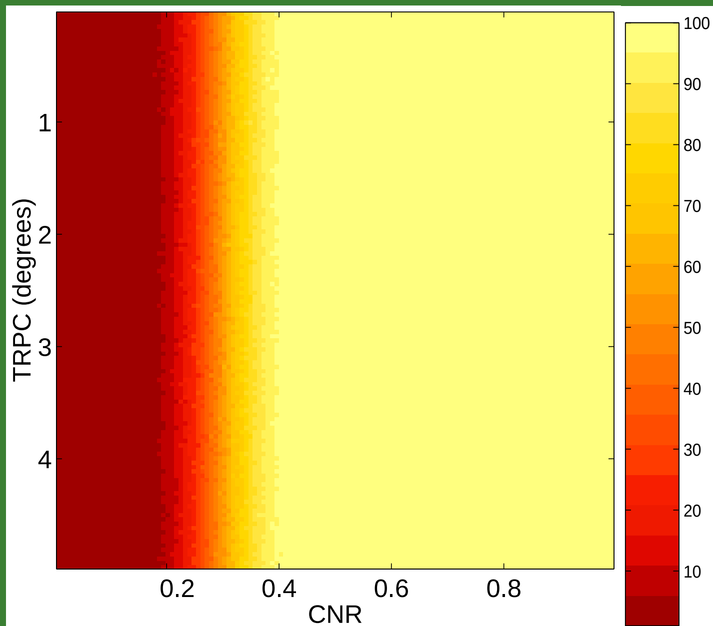
Simulation:

➢ Simulation Parameters

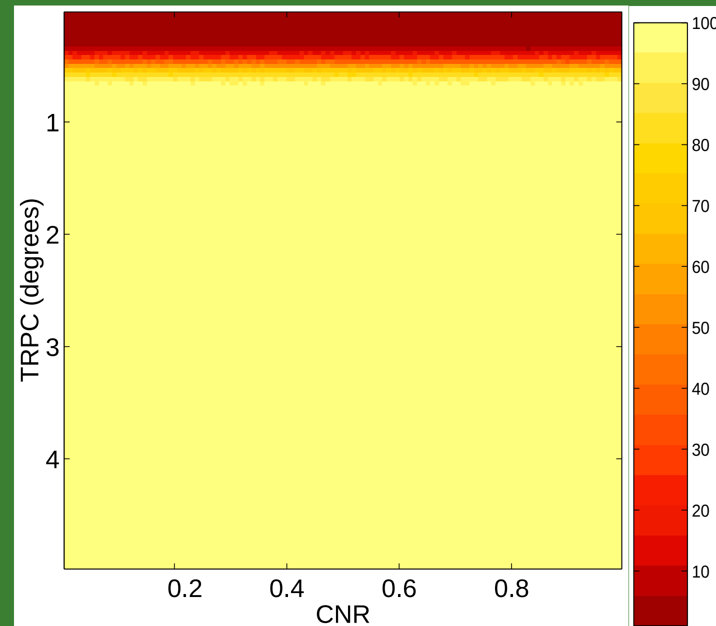
- An array of 128×128 voxels was created
- Complex-valued time series were generated for all voxels
  - Time series represented "active" voxels, different (CNR,TRPC)
  - CNR varies in 128 equal steps from 0 to 1 from L to R
  - TRPC varies in 128 equal steps from 0° to 5° from T to B
- Normally distributed noise added to the real and imaginary signals
- The SNR of the voxels was set to 30
- Activations were computed on simulated data with four methods
- 1000 iterations were performed to create power maps

Computer Simulated Data: Detection Power, SNR=30[1,2]

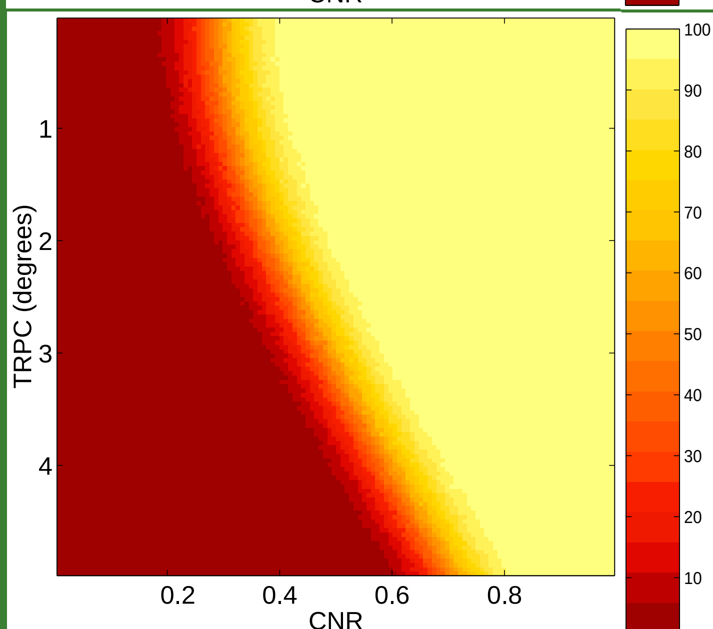
MO:



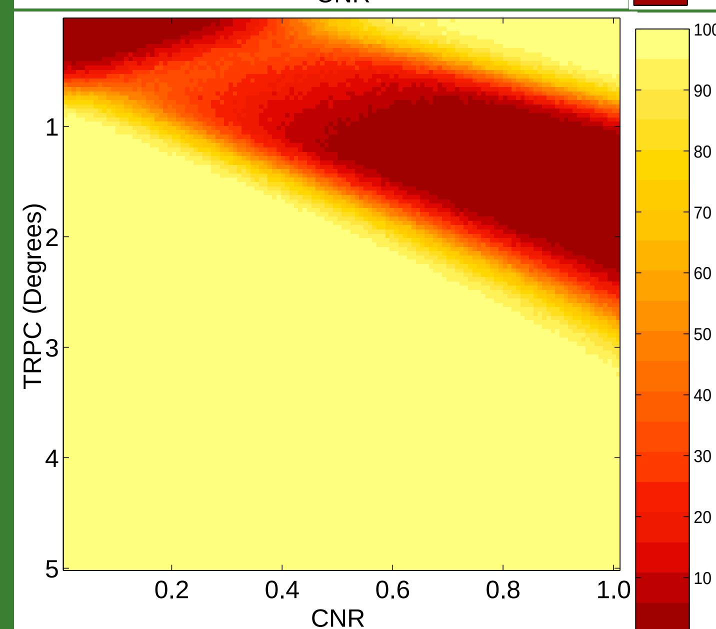
PO:



CP:



PR:



[1]Nencka and Rowe, Submitted, 2006. [2]Rowe and Logan: NeuroImage, 25:1310-1324, 2004.

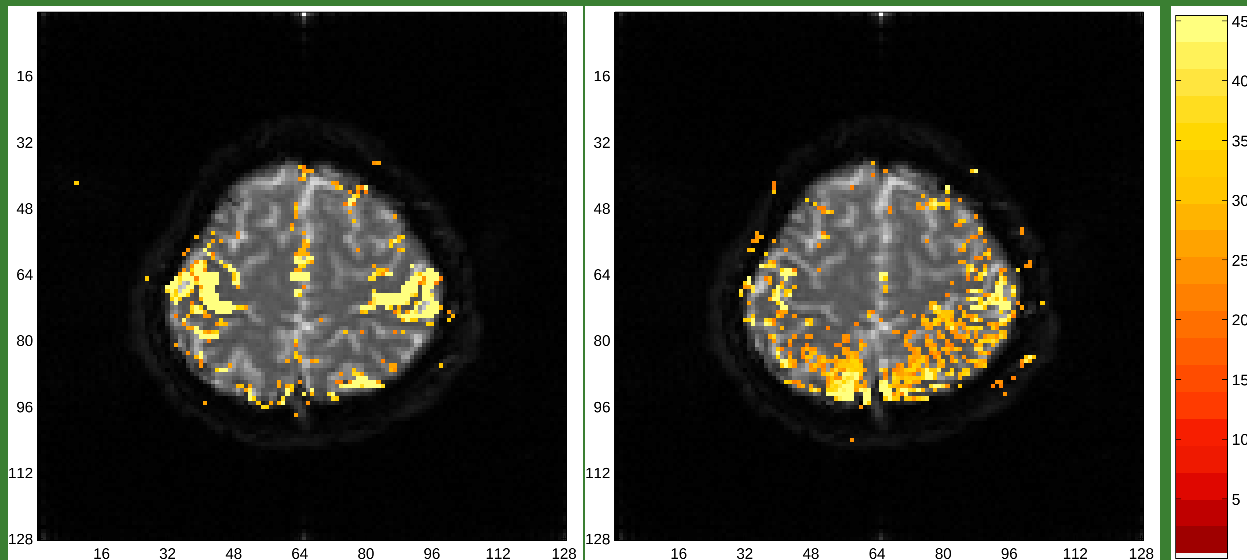
Activations in Human Experimental Data I

Imaging Parameters:
1.5T GE Signa
5 axial slices of 128x128
96 acq.-2.0833mm^2
128 recon.-1.5625mm^2
FOV =20cm
TR=1000ms
TE=47ms
FA=90°

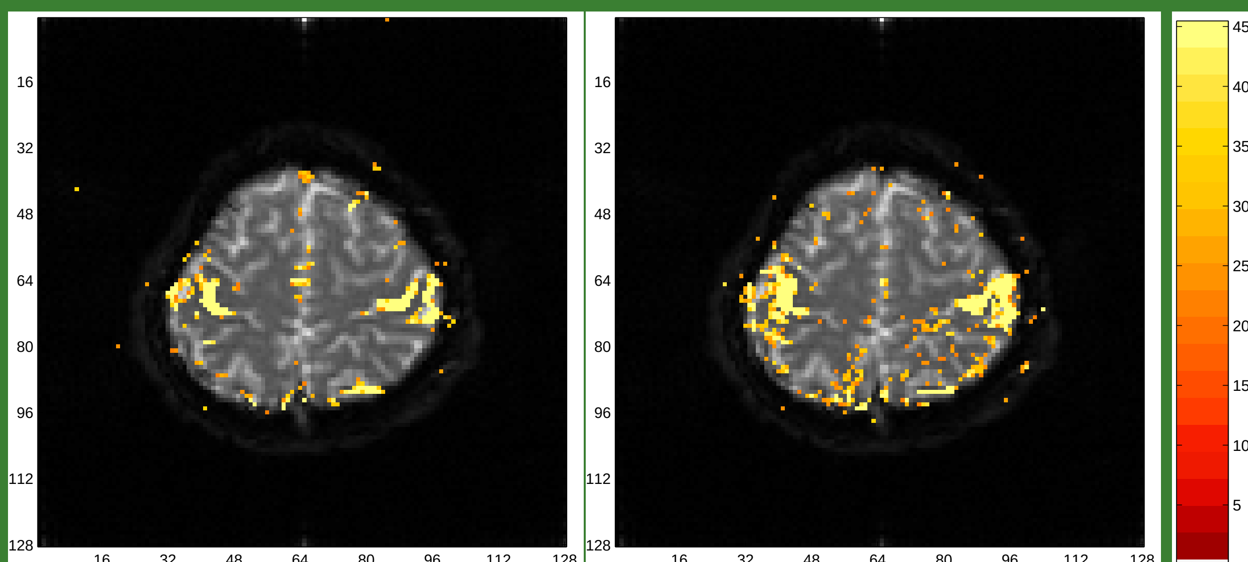
Task:
RH male Bilateral sequential finger tapping light triggered
Block design
16 off + 8$\times$(16on+16off);

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

χ^2 Maps: 5% Bonferroni Threshold



(a) UP/MO (b) PO



(c) CP (d) PR

[1] Rowe and Logan: NeuroImage, 23:1078-1092, 2004. [2] Logan and Rowe: NeuroImage, 22:95-108, 2004.

Thank You.

Could complex-valued activation be the future of fMRI analysis?

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