FMRI Time Series Activation

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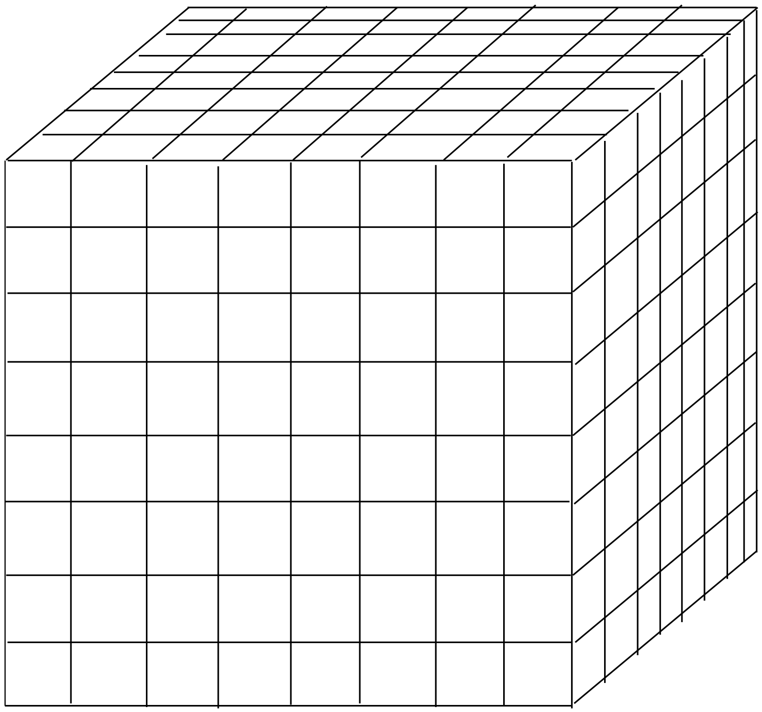
Outline

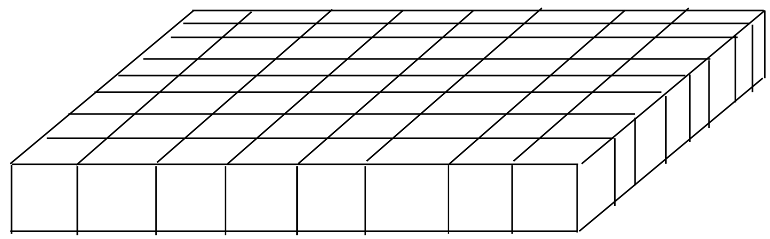
- ➢ Complex Image Reconstruction Review
  - Complex voxels from complex k-space measurements
- ➢ Phase Information
  - Vascular, Neural firing, Respiration
- ➢ Complex Statistical Activation Methods
  - Complex-Valued: Magnitude & Phase
  - Real-Valued: Magnitude-Only, Phase-Only
- ➢ Complex Magnitude with Constant Phase
  - Simulations, Real data
- ➢ Complex Magnitude with GLM Phase
  - Simulations, Real data
- ➢ Discussion

Complex Image Reconstruction Review

In MRI we image a real-valued 3D object, $R(x, y, z)$.
Lattice of volume elements, voxels.



$->$

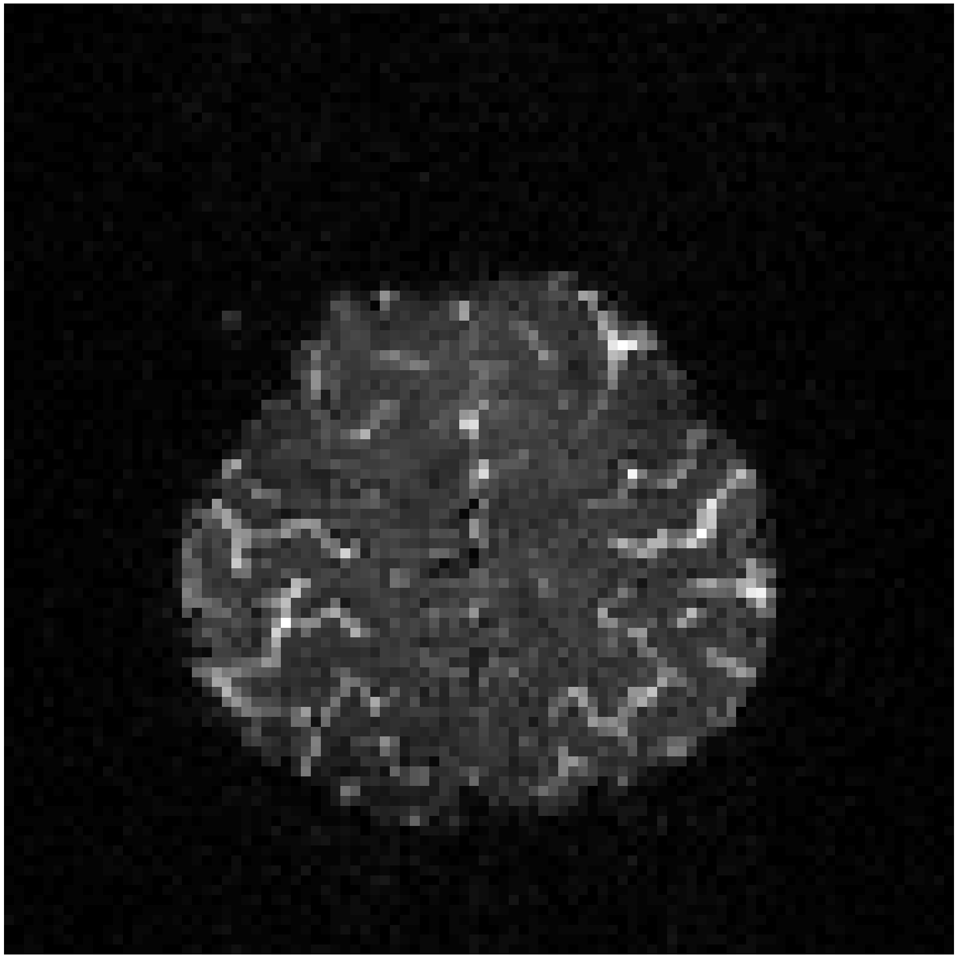


Volume Slice

Generally echo planar imaging and not echo volume imaging.
Consider a single slice $R(x, y)$.

Complex Image Reconstruction Review

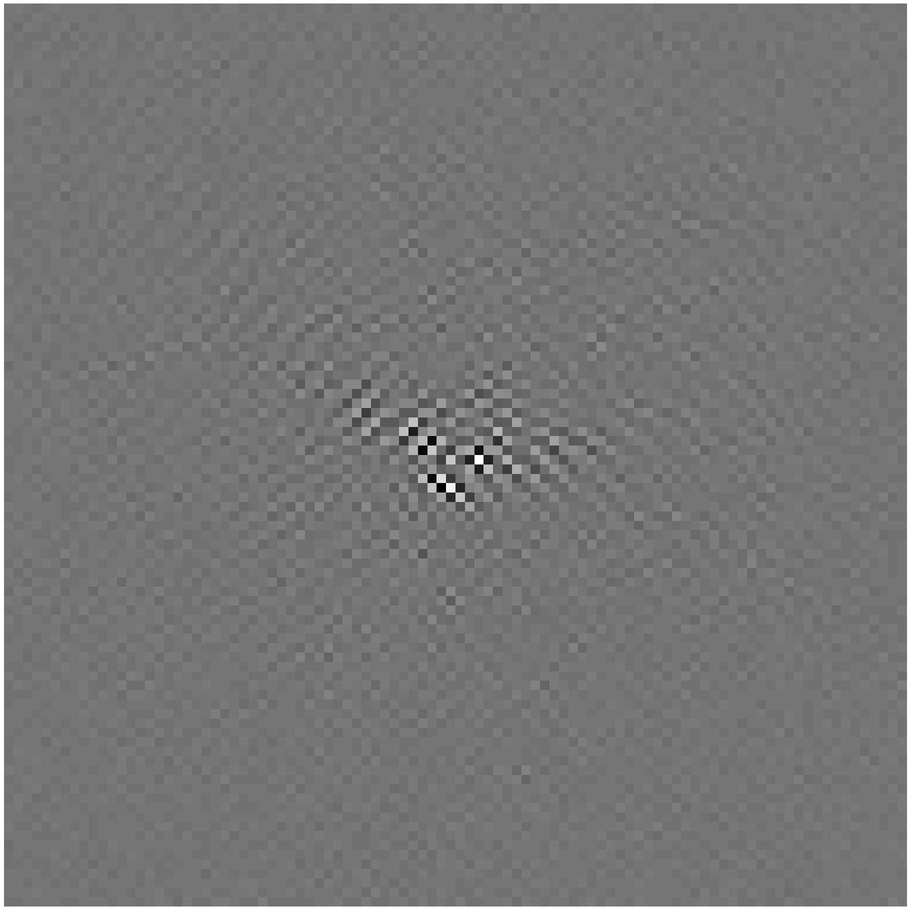
In MRI we aim to image a real-valued object, $R(x, y)$.
Different tissues have different magnetic properties yielding contrast.



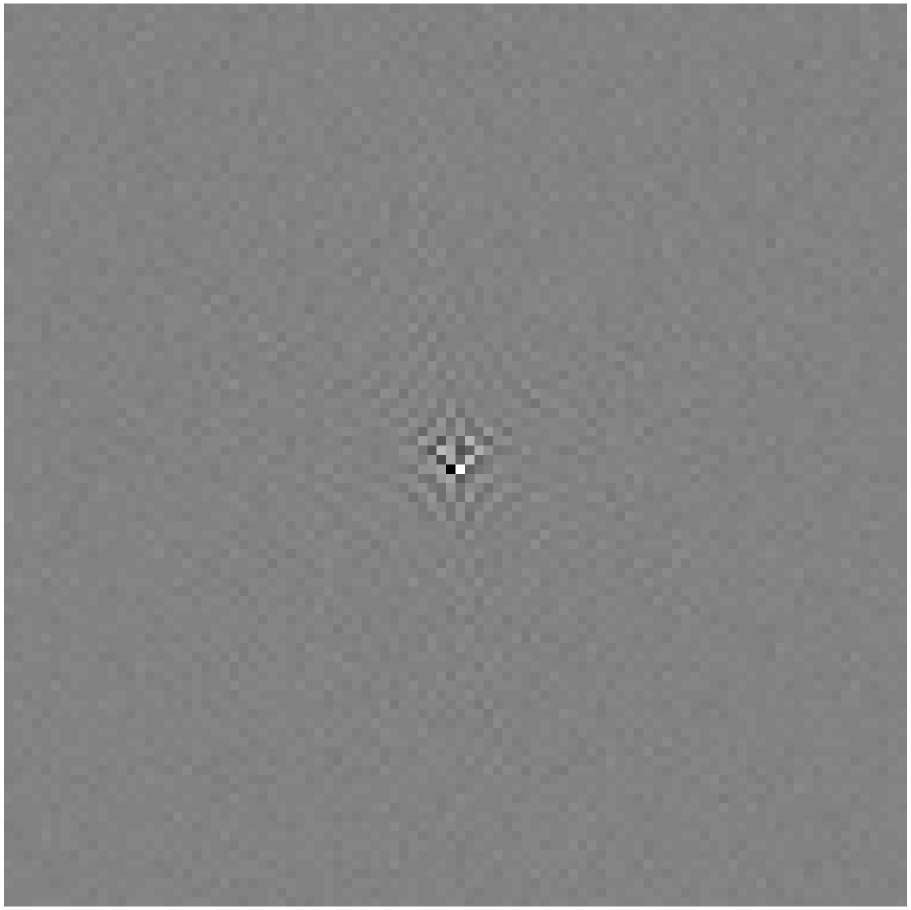
T_2^* weighted image

Complex Image Reconstruction Review: 2D

$F(k_x, k_y) = F_R(k_x, k_y) + iF_I(k_x, k_y)$, the complex-valued DFT of object



(a) real: 96×96



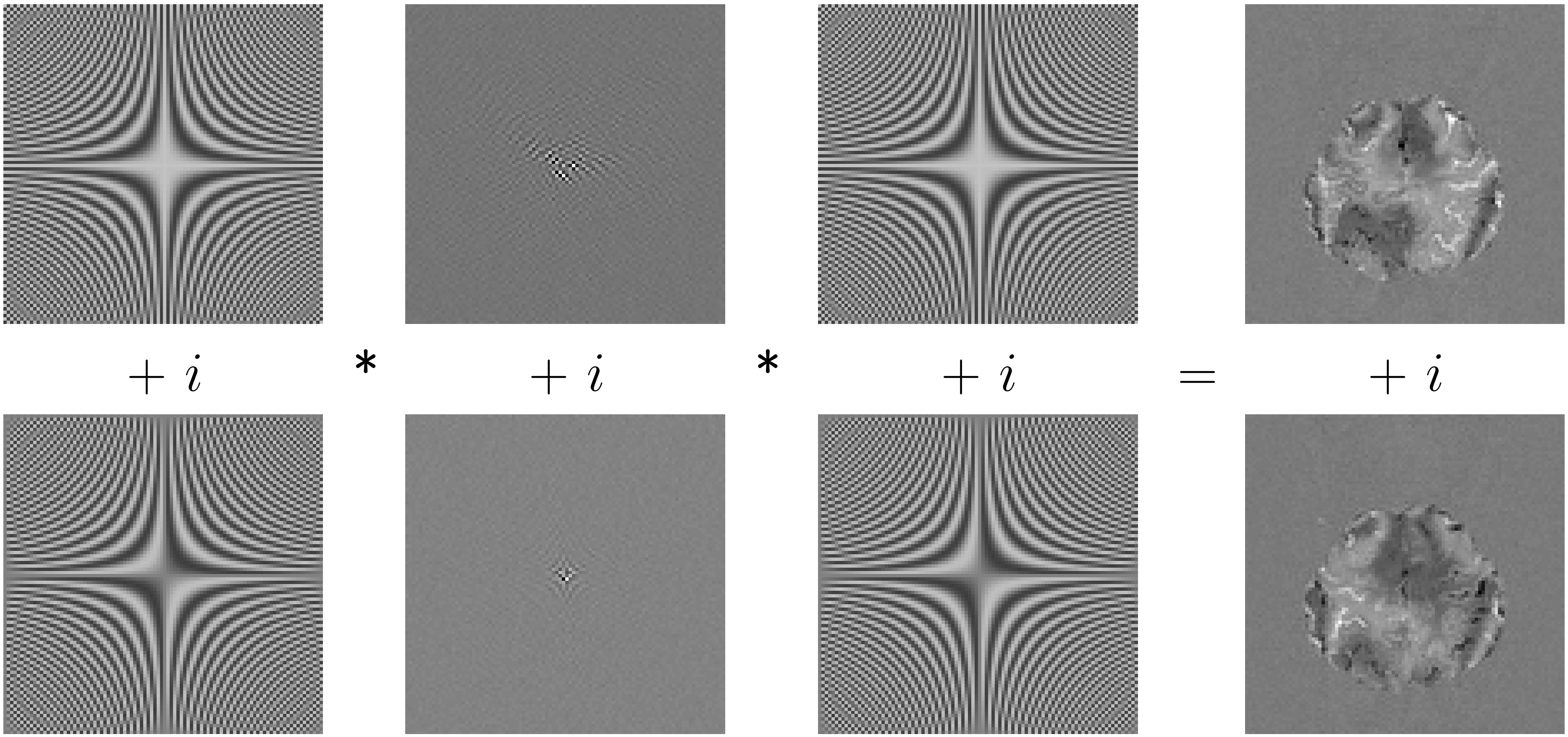
(b) imaginary: 96×96

FOV=192 mm, mat=96×96, vox=2 mm^3

Complex Image Reconstruction Review: 2D

complex-valued 2D IFT

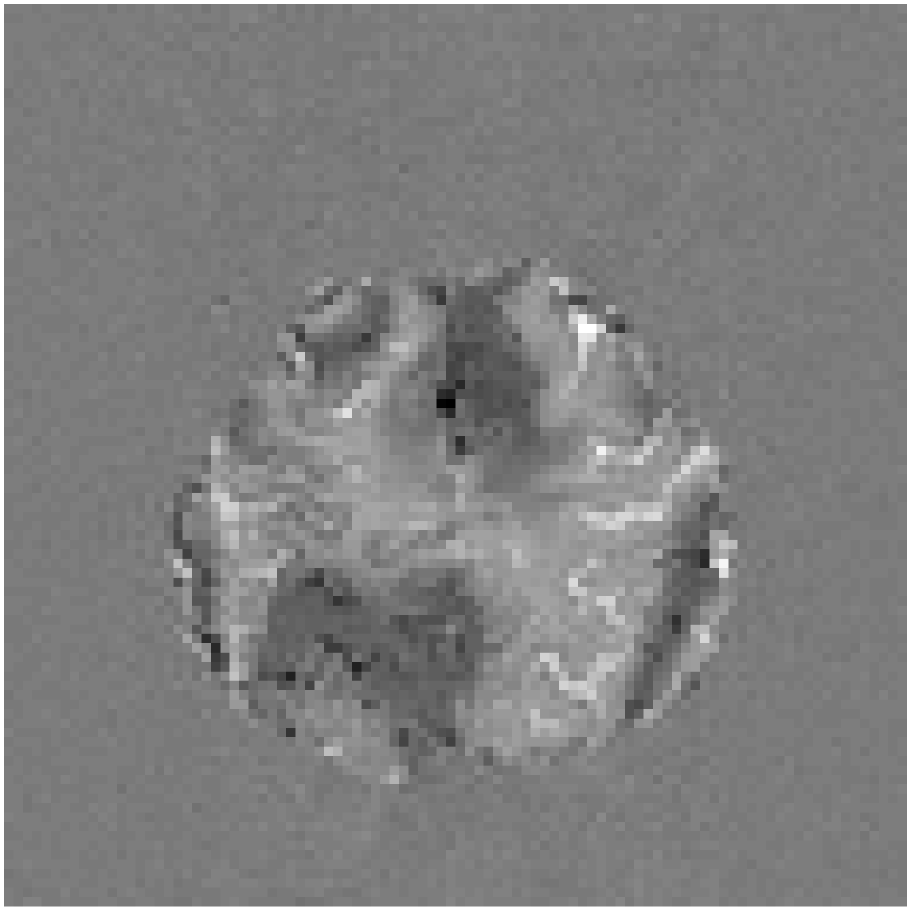
$$(\Omega_{yR} + i\Omega_{yI}) \quad * \quad (F_R + iF_I) \quad * \quad (\Omega_{xR} + i\Omega_{xI})^T \quad = \quad (Y_R + iY_I)$$



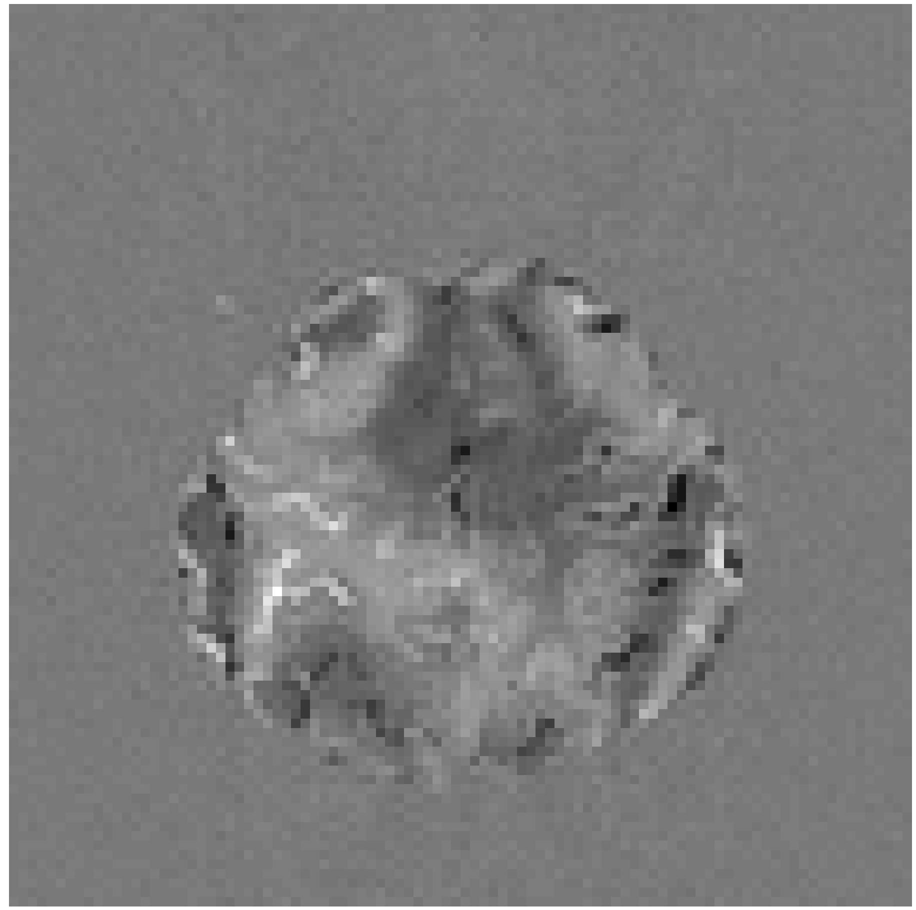
FOV=192 mm, mat=96×96, vox=2 mm^3

Complex Image Reconstruction Review: 2D

Due to the imperfect Fourier encoding, the IFT reconstructed object is complex-valued, $Y(x, y) = Y_R(x, y) + iY_I(x, y)$.



(a) Real image, y_R

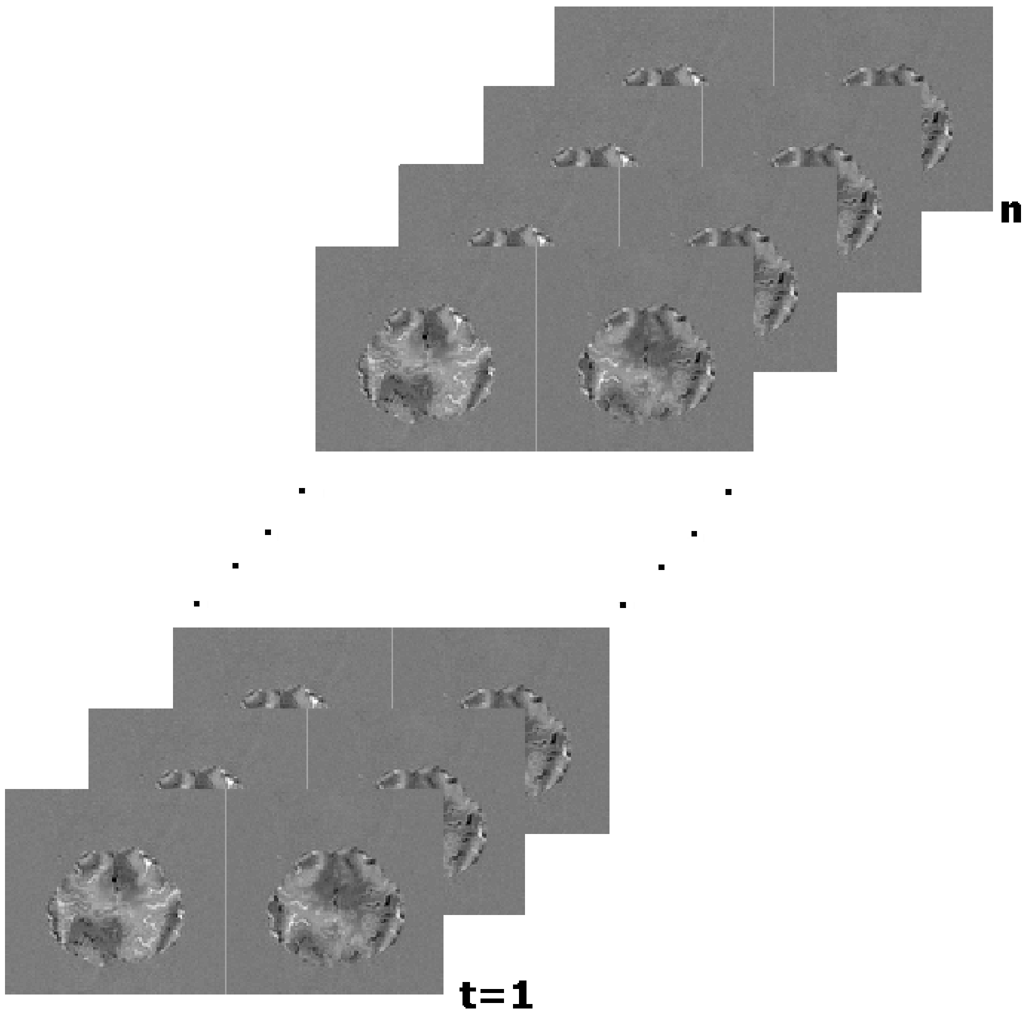


(b) Imaginary image, y_I

FOV=192 mm, mat=96×96, vox=2 mm^3

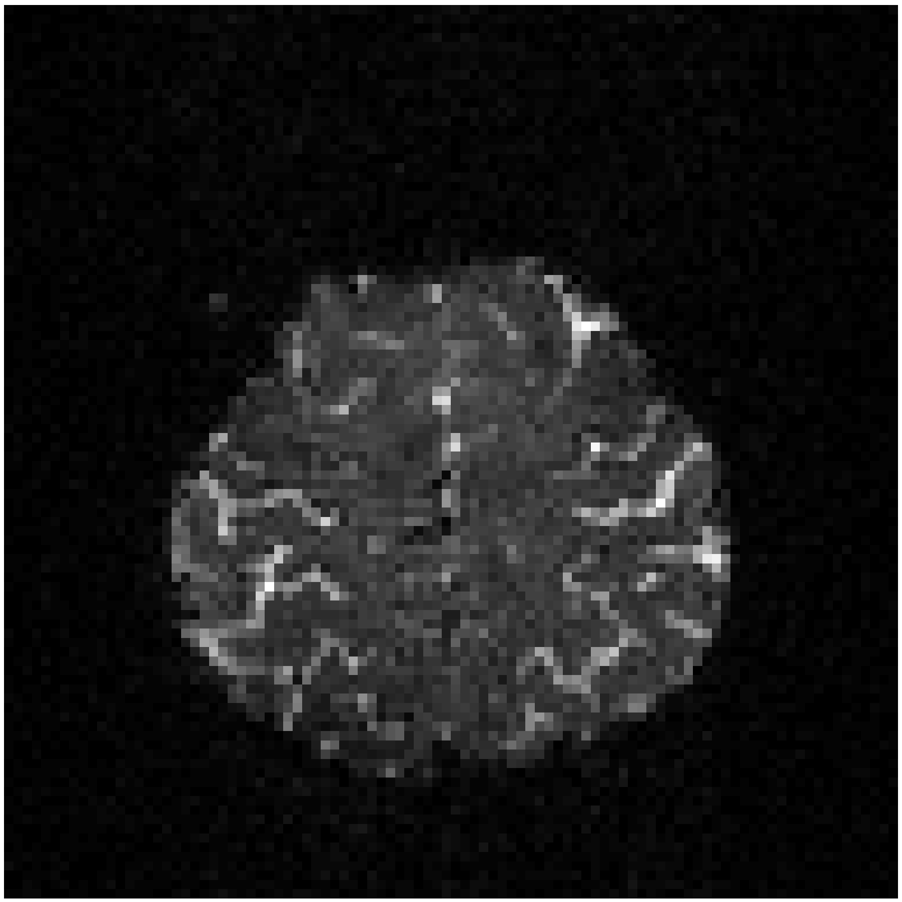
Complex Image Reconstruction Review: 2D

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

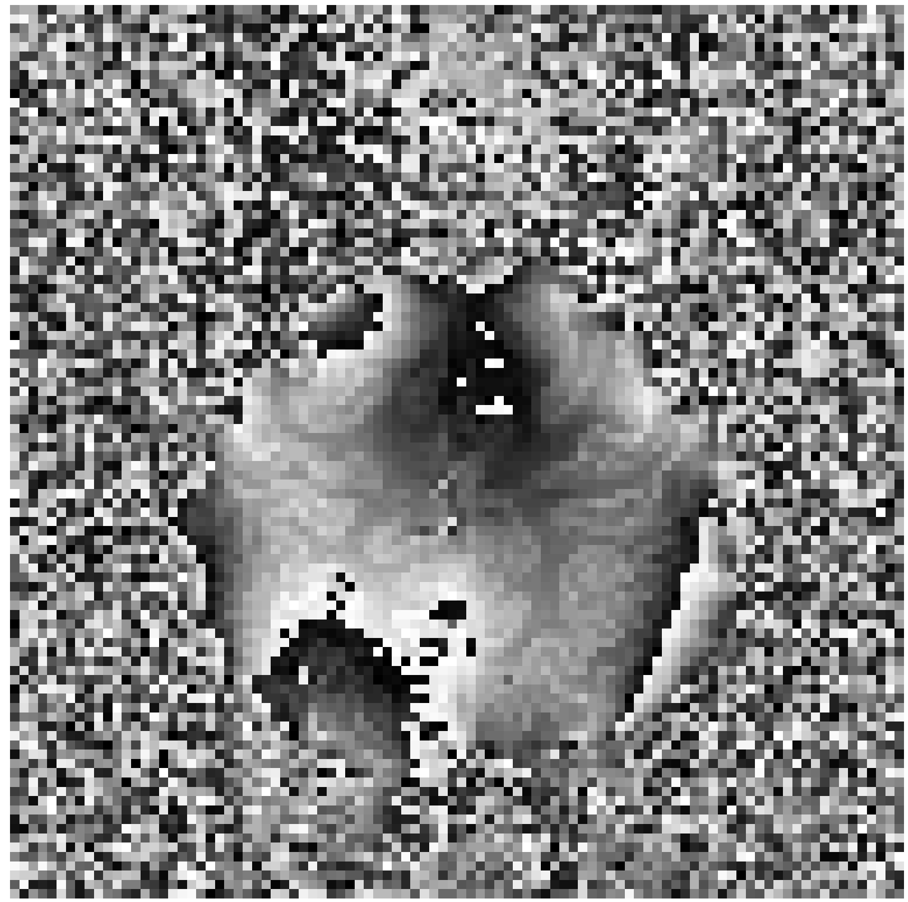


Complex Image Reconstruction Review: 2D

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



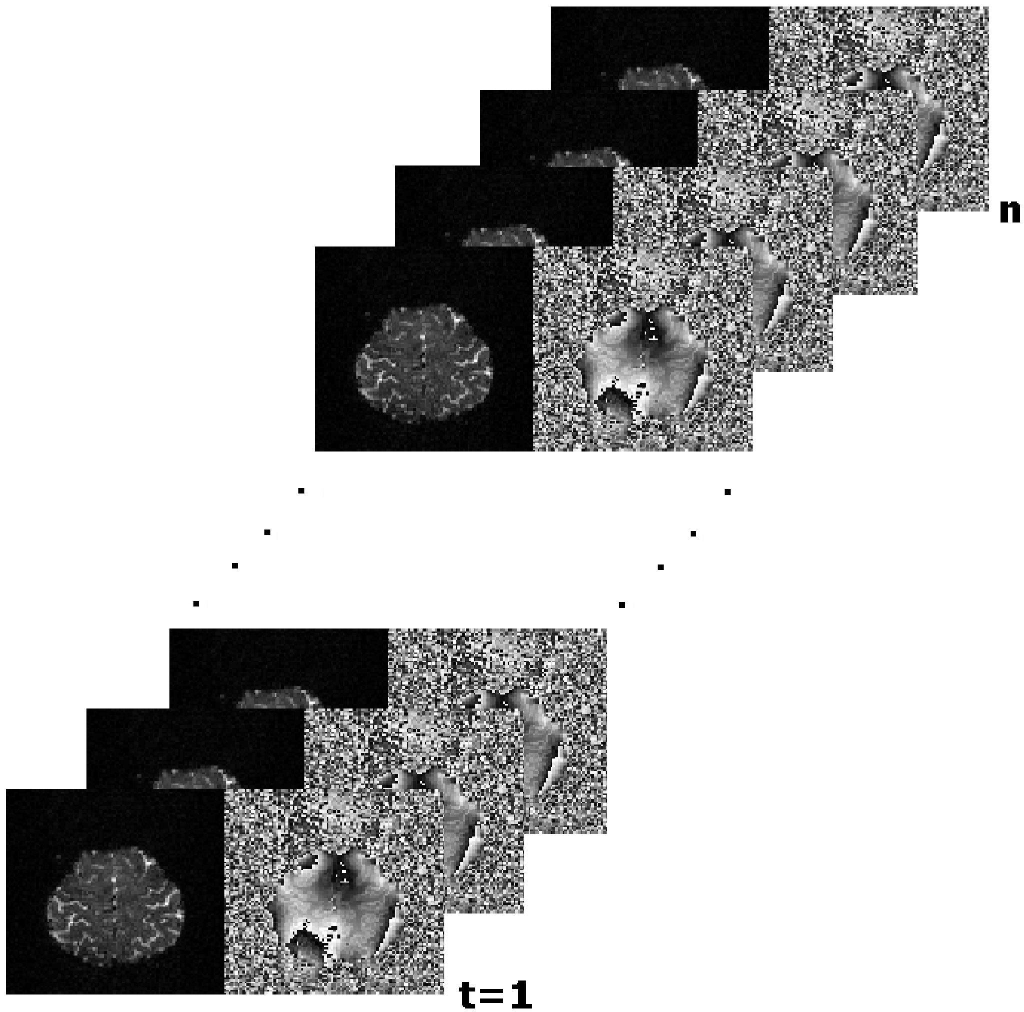
(a) Magnitude, $r_t = \sqrt{y_{Rt}^2 + y_{It}^2}$



(b) Phase, $\phi_t = \text{atan}_4(y_{It}/y_{Rt})$

Complex Image Reconstruction Review: 2D

Collect a sequence of these reconstructed images over time.
Form voxel time courses, $y_t = r_t e^{i\phi_t}$.



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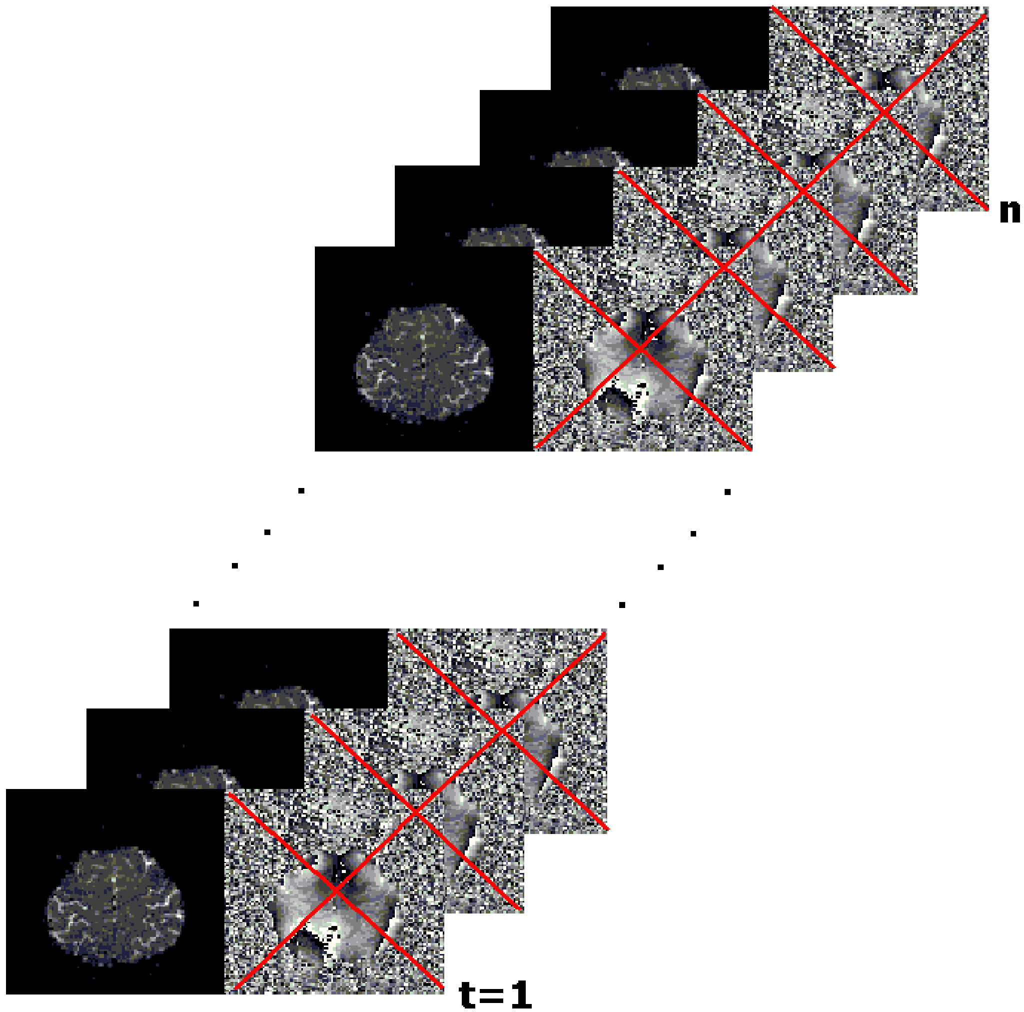
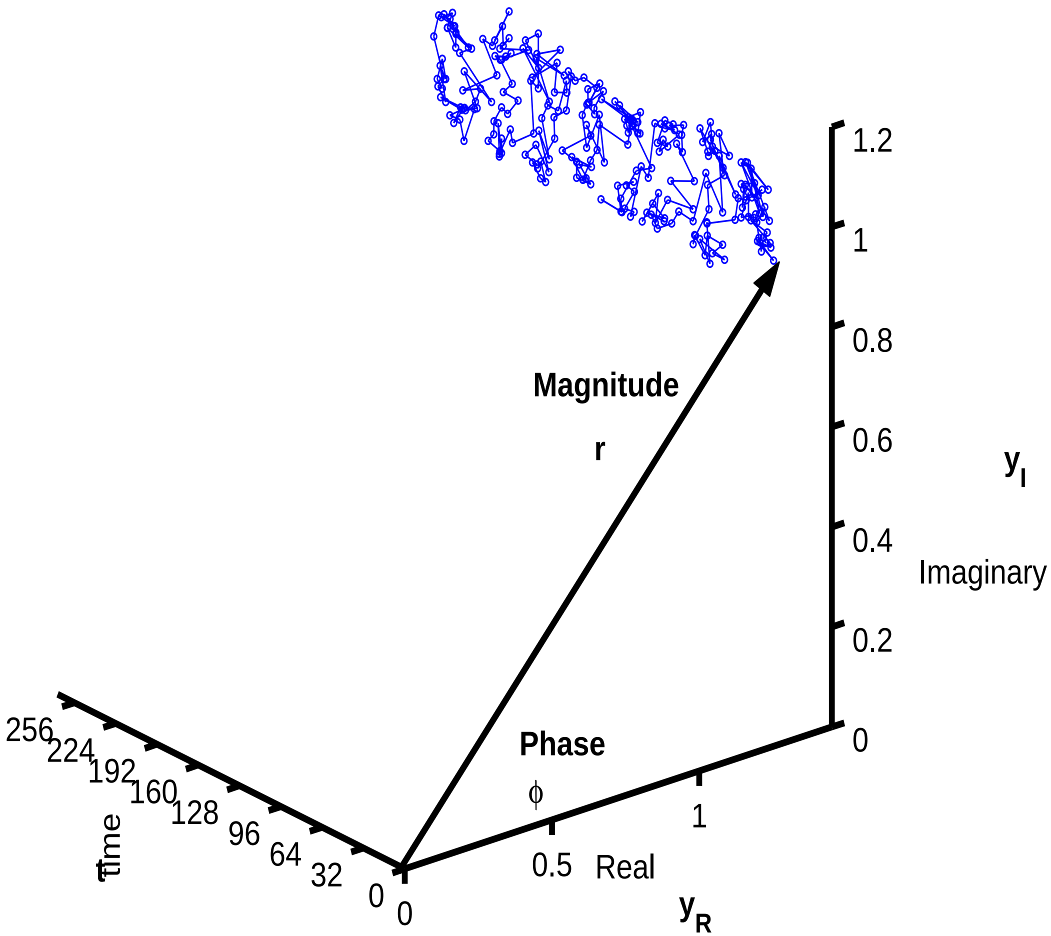
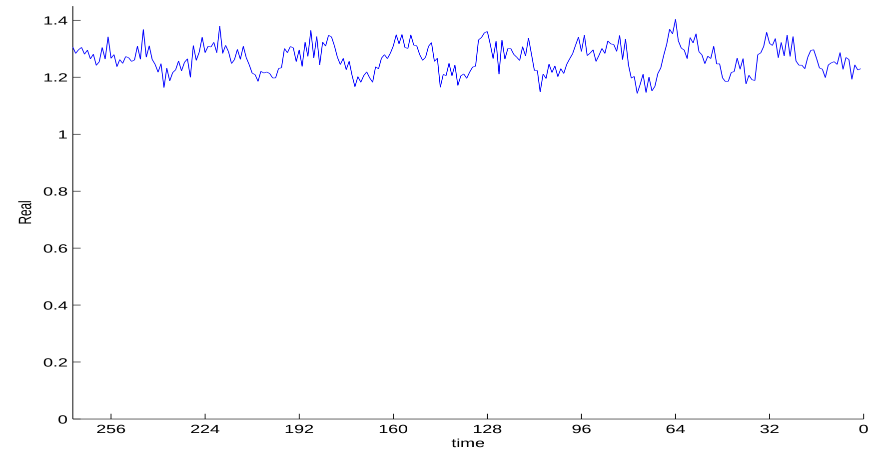


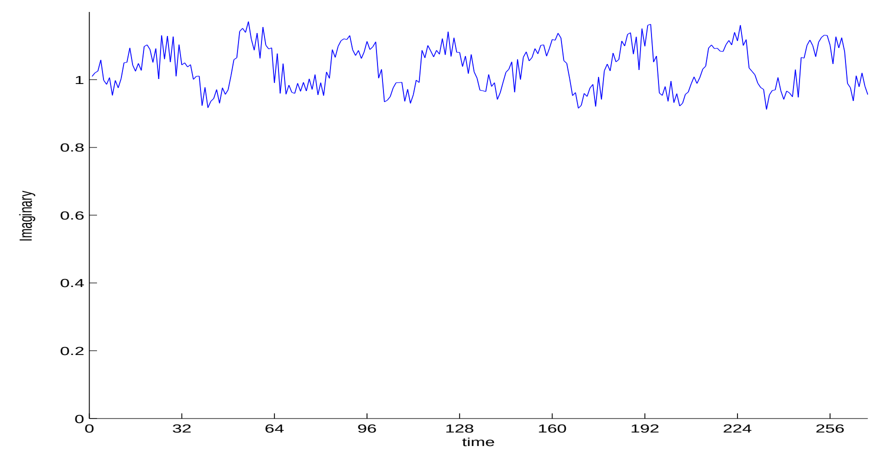
Phase Information

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





Real: Task related changes!



Imaginary: Task related changes!

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

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

Phase Information

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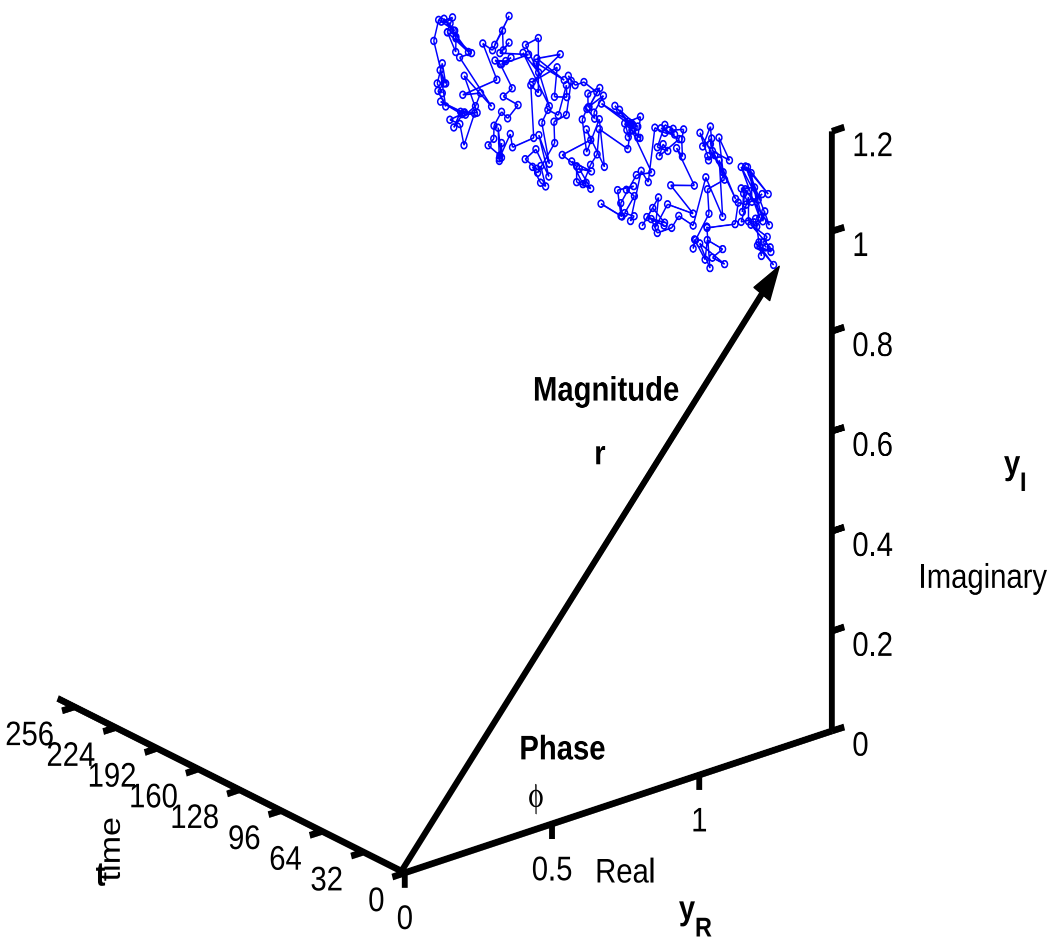
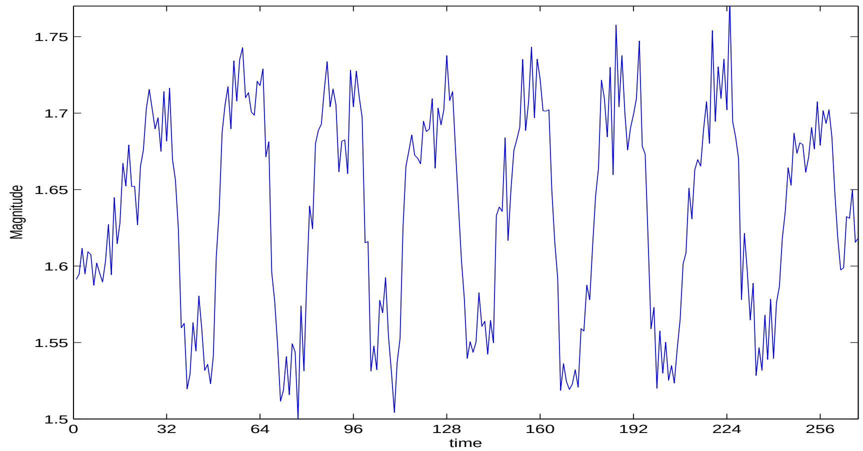
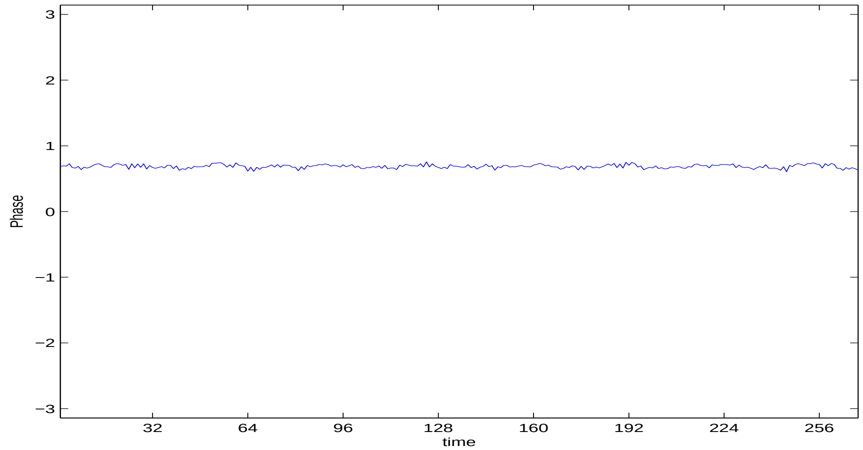




Magnitude: Task related magnitude changes!



Phase: Often relatively constant temporally.

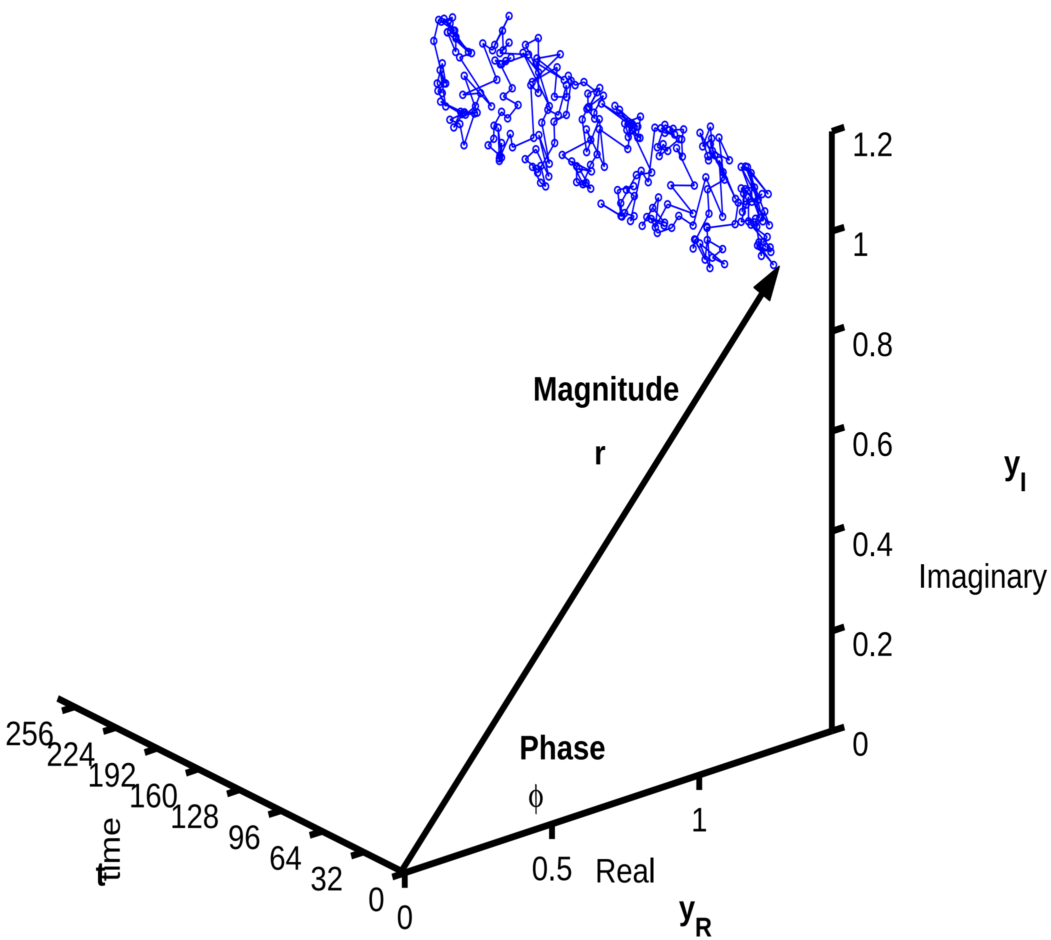
MO time courses only have vector length info!

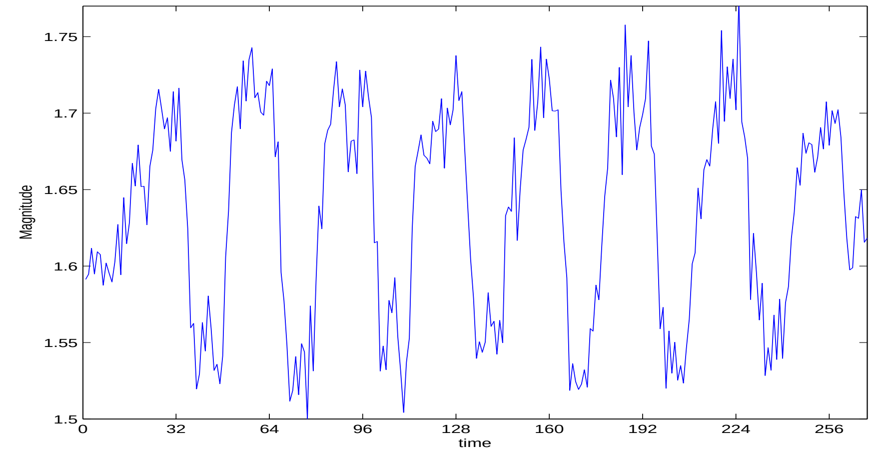
PO time courses only has vector angle info!

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

Phase Information

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





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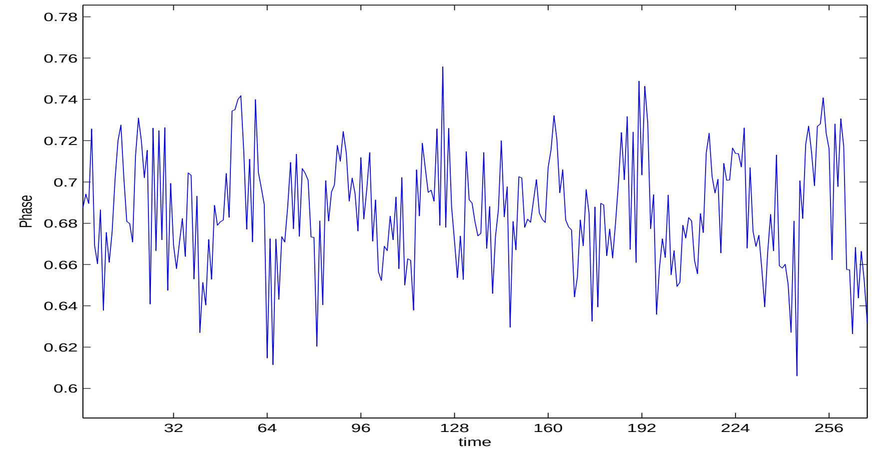


Phase: Task related phase changes!

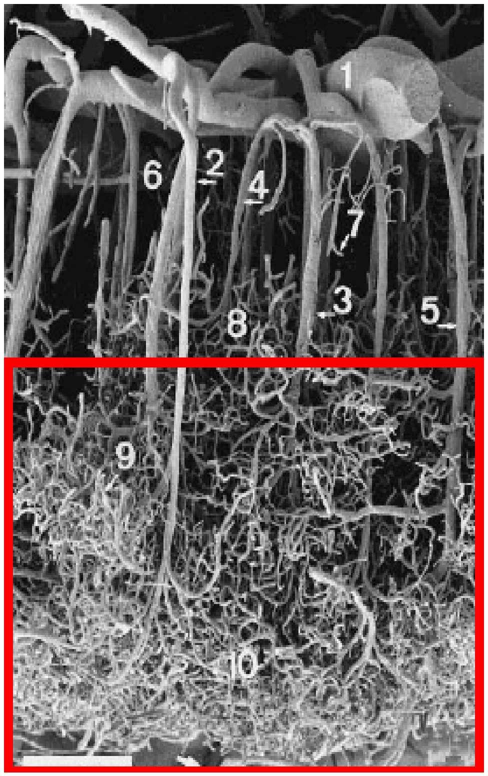
Real-Imaginary or Magnitude-Phase time courses have all info!

Recent work indicates that phase time courses may exhibit TRPCs

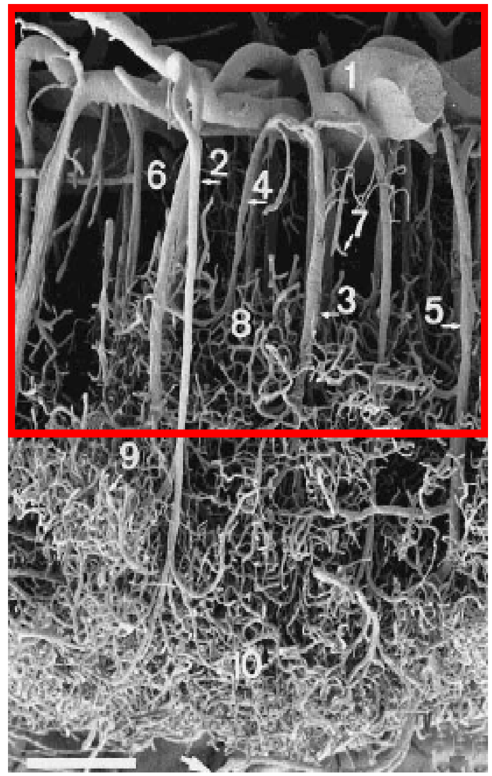
Menon, 2002; Hoogenrad et al., 1998; Borduka et al., 1999; Chow et al., 2006;

Phase Information: Vascular Structure and BOLD

- ➢ 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.

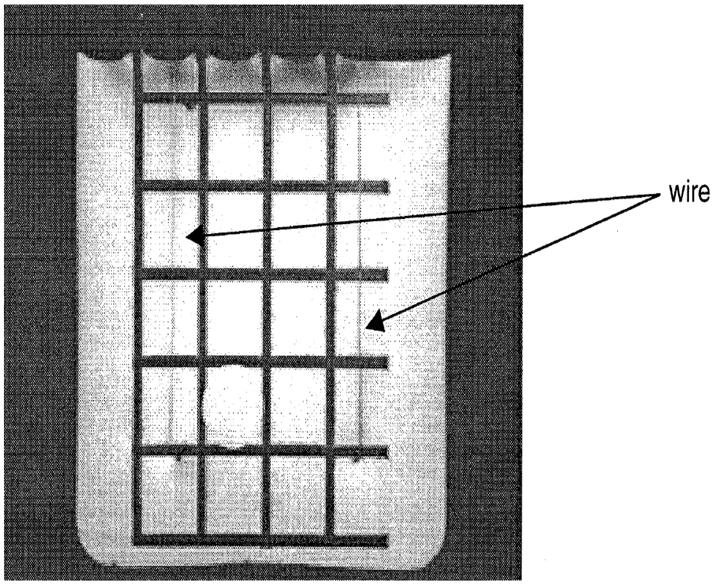
[2]Hoogenraad: MRM, 45:233-246, 2001.

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

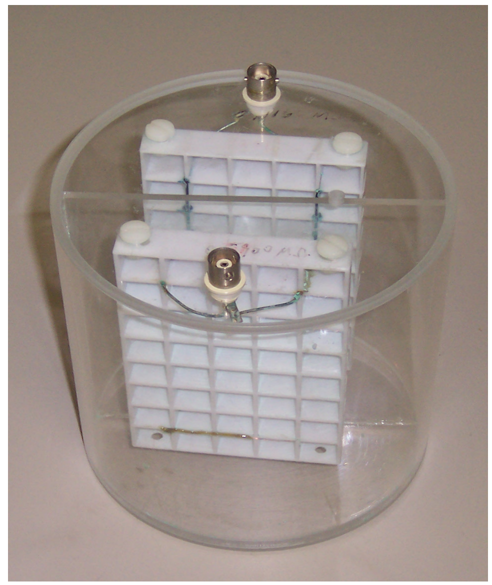
Phase Information: Direct Neuronal Current

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

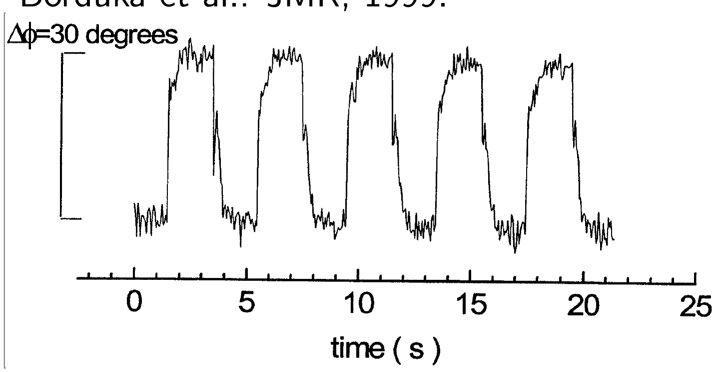
➢ Voxels w/ optic nerve, task related magnitude & phase change



[1]Borduka et al.: JMR, 1999.

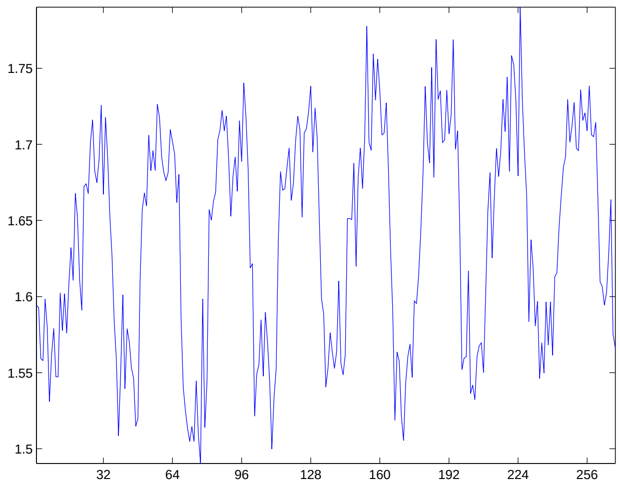


[2]Chow et al.: NeuroImage, 2006.

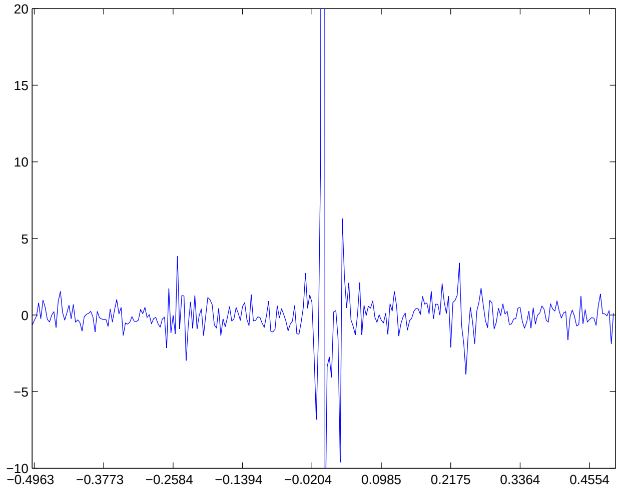


Phase Information: Other Magnetic Field Changes

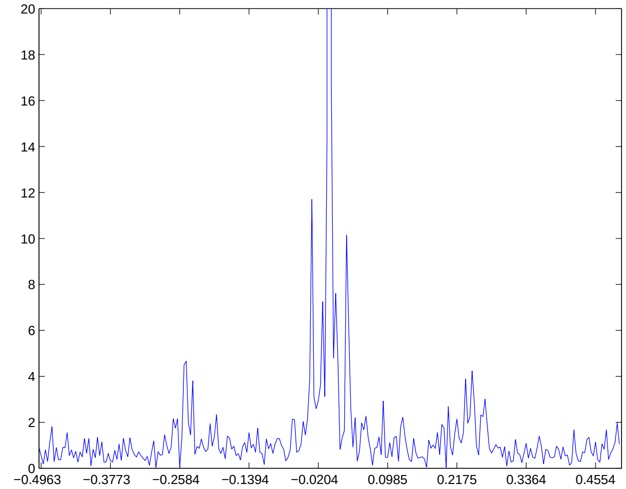
Some voxels phase contain other info: respiration, cardiac, motion



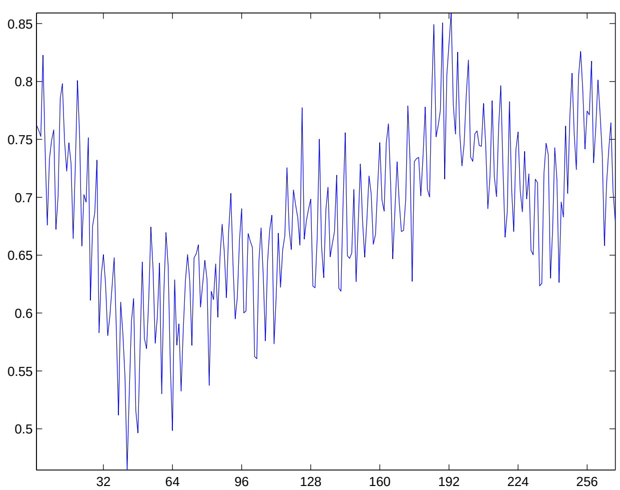
TS Mag.



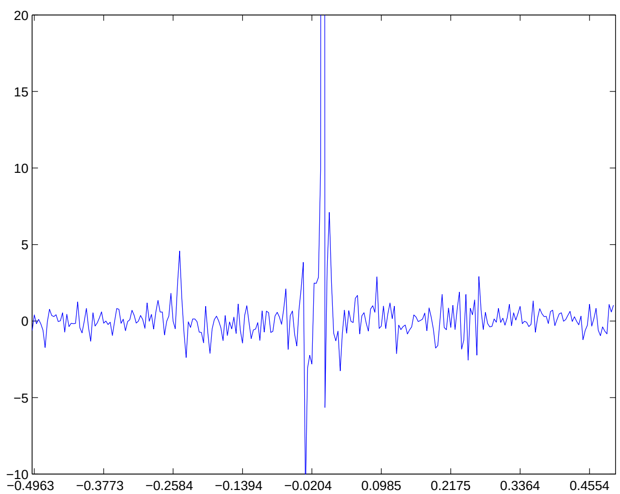
TS FT real



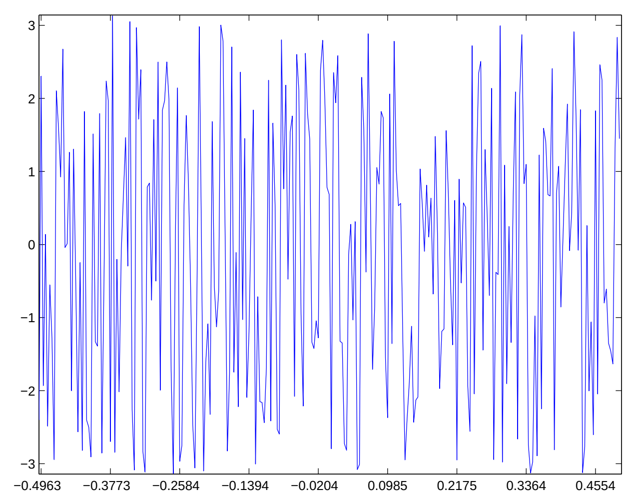
TS FT Mag.



TS Phase



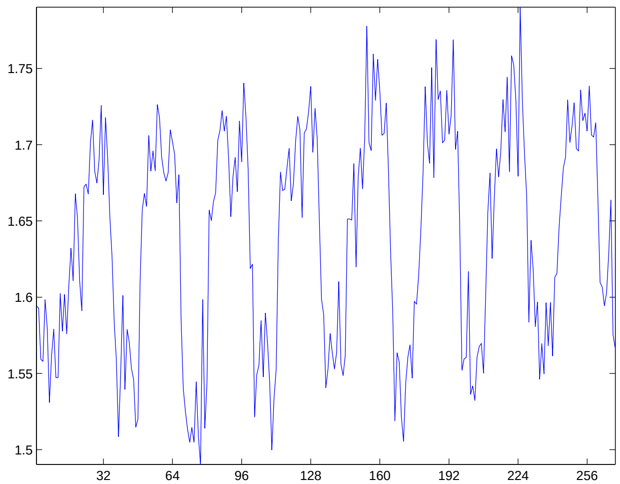
TS FT Imag



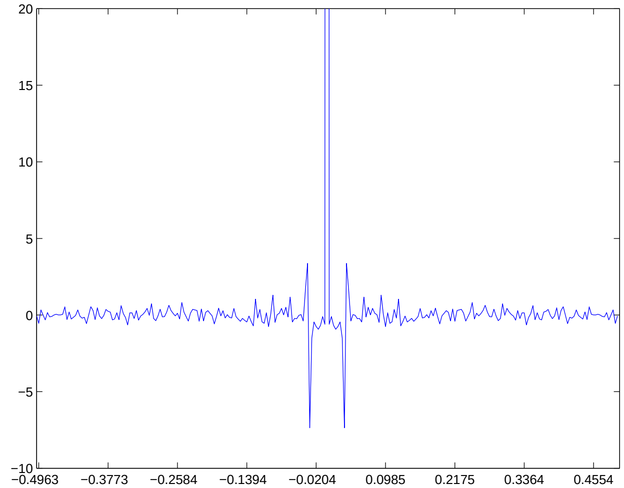
TS FT Phase

Phase Information: Other Magnetic Field Changes

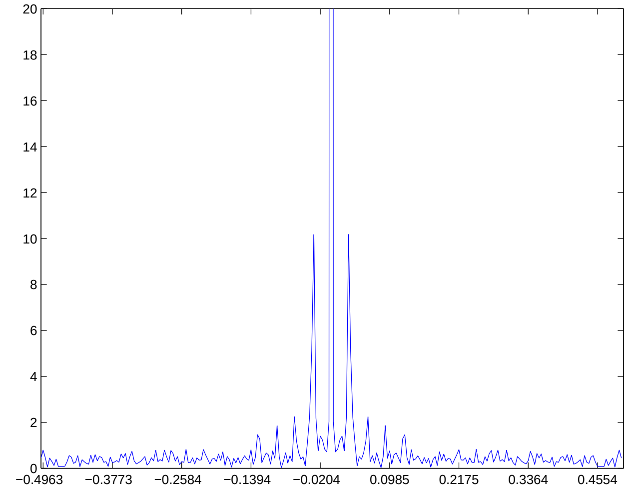
Let's consider only the magnitude of the time series and its FT.



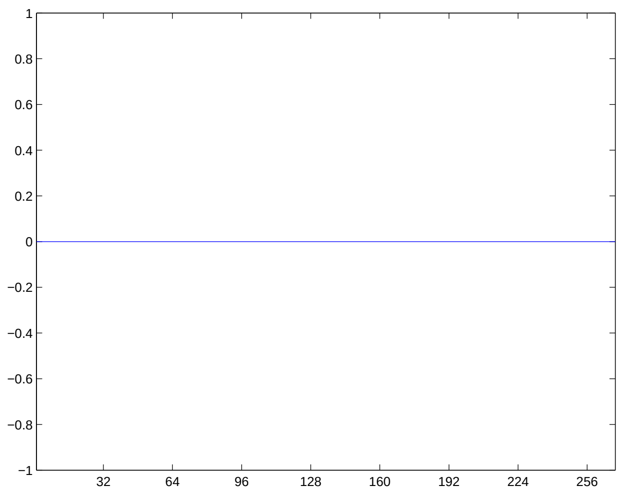
TS Mag.



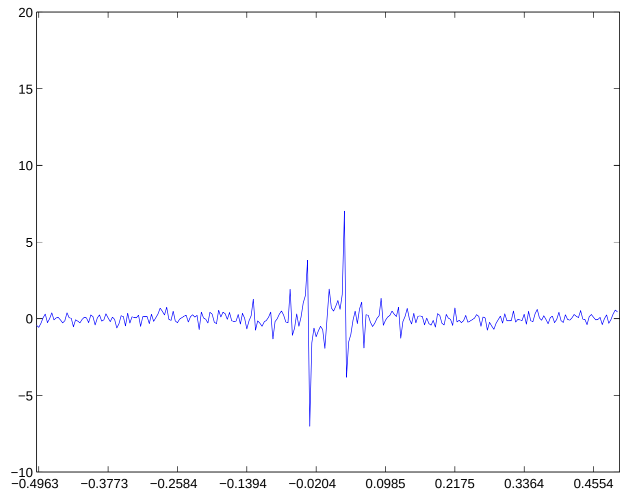
TS FT real



TS FT Mag.



TS Phase



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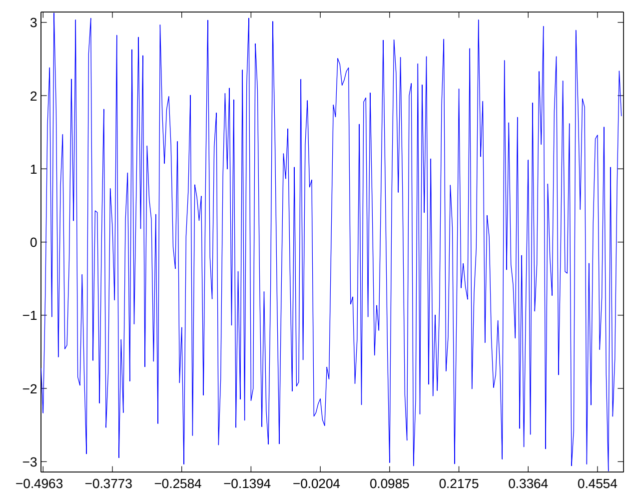
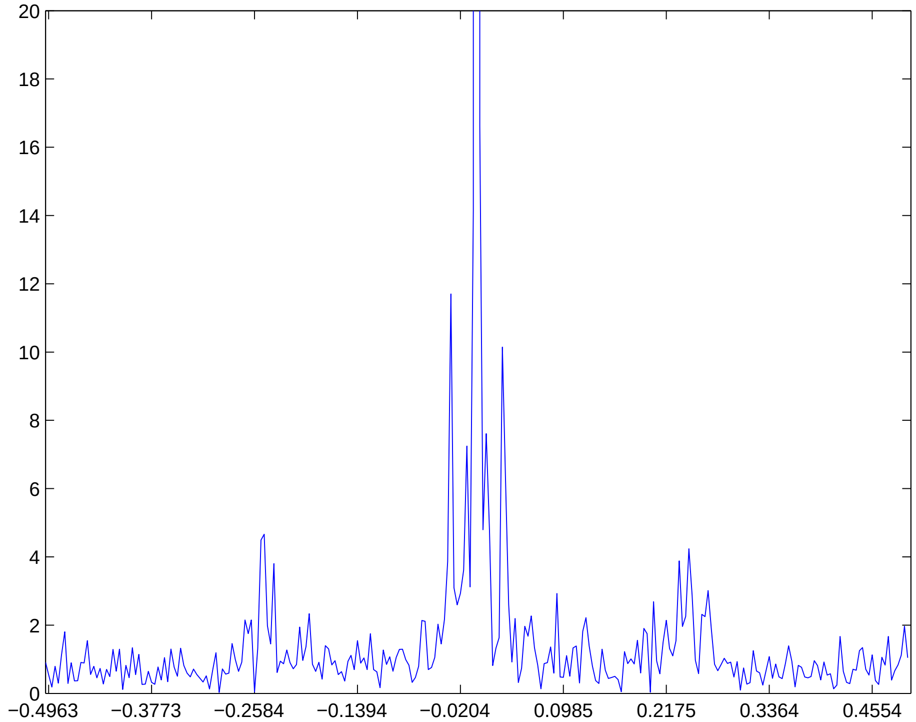
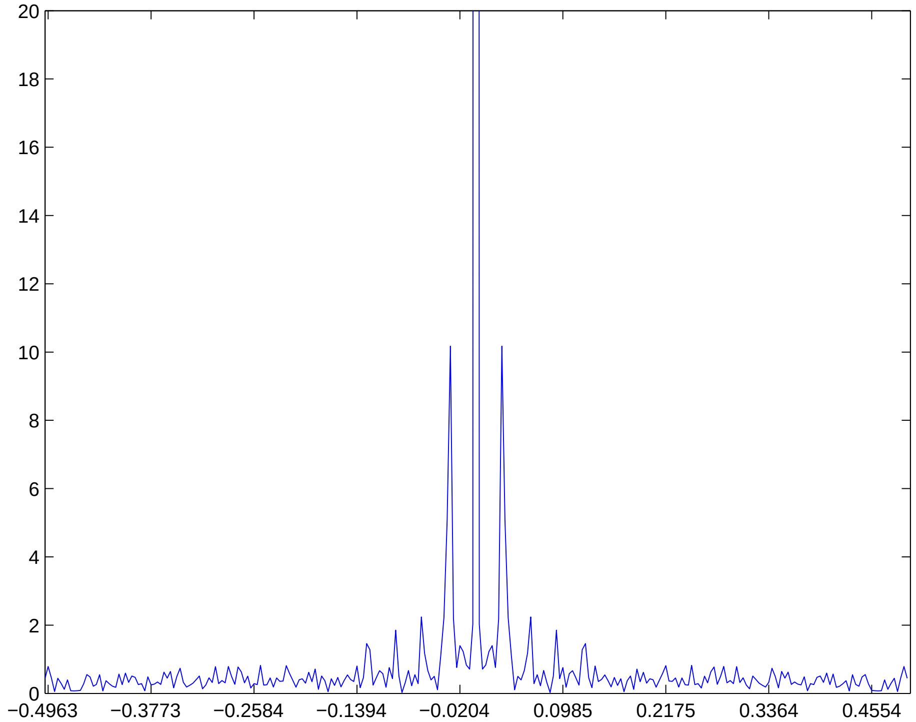


TS FT Phase

Phase Information: Other Magnetic Field Changes



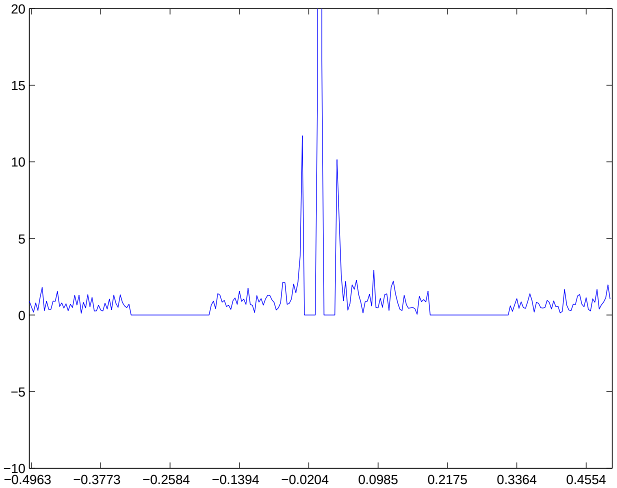
Original Time Series FT Mag.



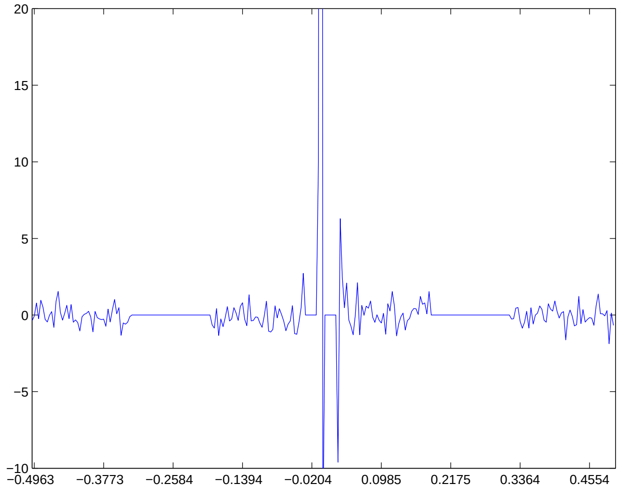
Magnitude Time Series FT Mag.

Phase Information: Other Magnetic Field Changes

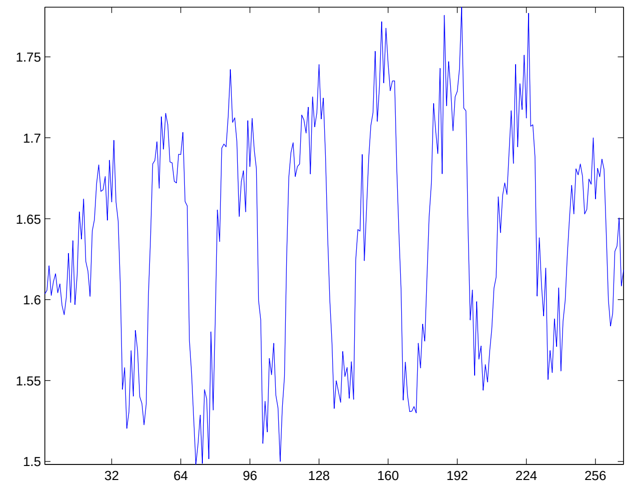
Some voxels phase contain other info: respiration, cardiac, motion



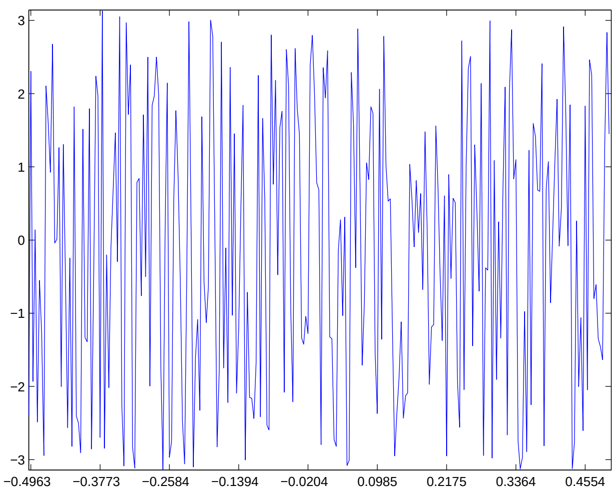
TS FT Mag.



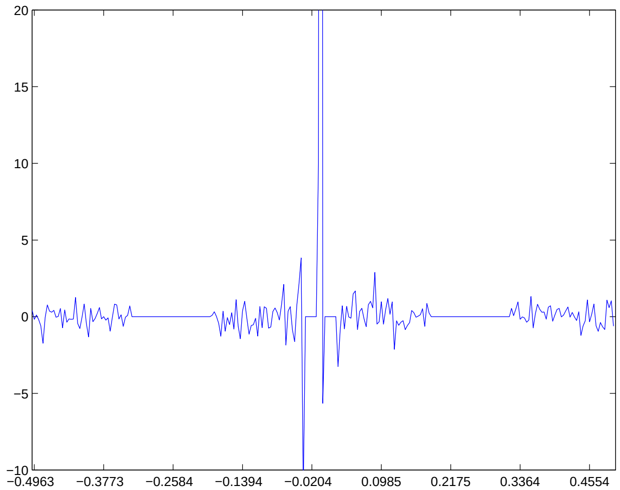
TS FT real



TS Mag.



TS FT Phase



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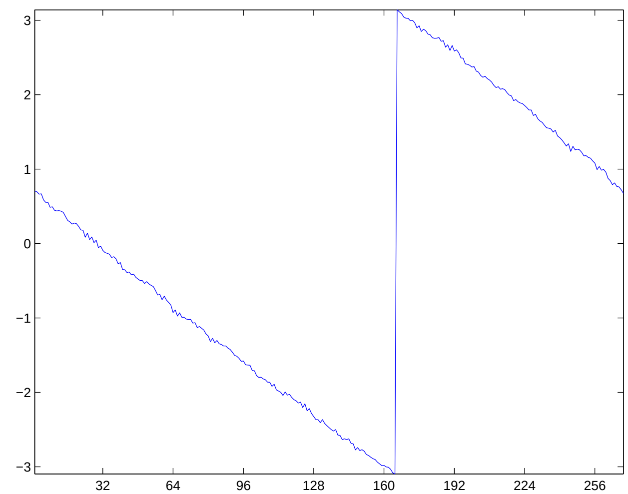
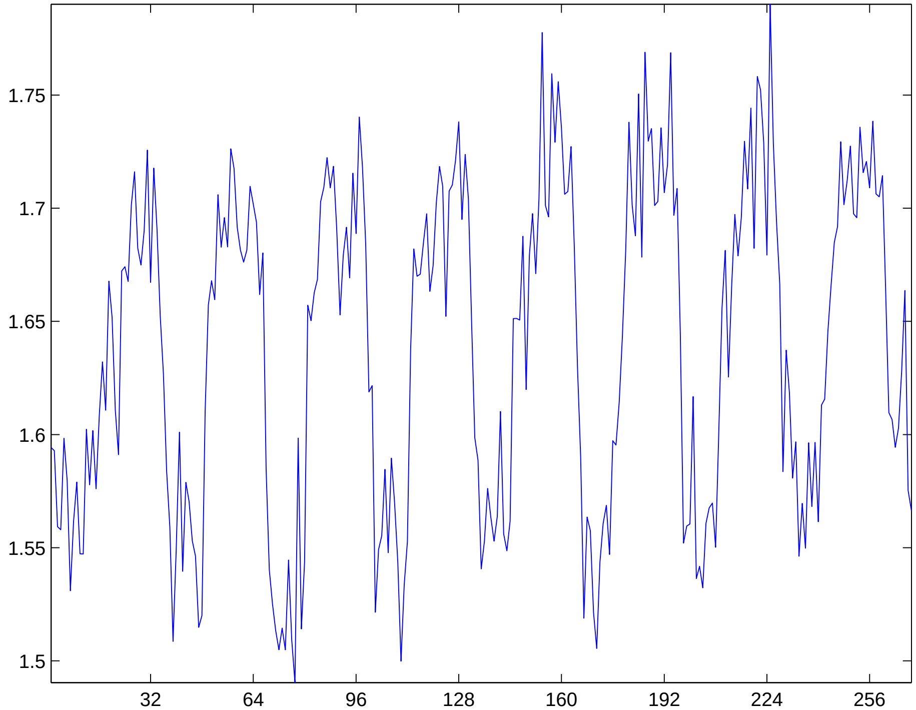
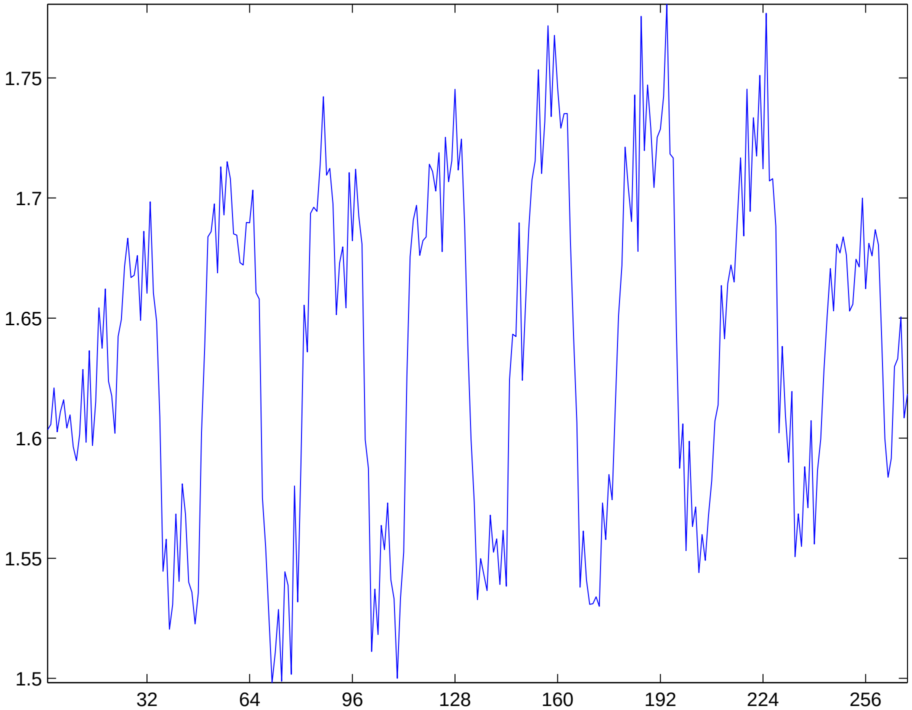


TS Phase

Phase Information: Other Magnetic Field Changes



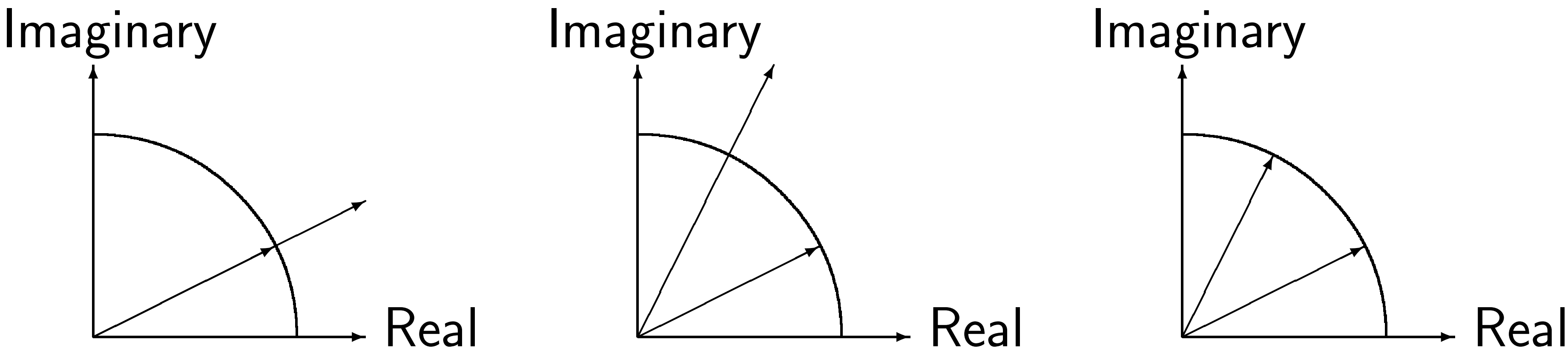
Original Time Series Mag.



Filtered Time Series Mag.

Complex Statistical Activation Methods

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



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

[1] Rowe and Logan: NeuroImage, 23:1078-1092, 2004.
[2] Rowe: NeuroImage 25:1124-1132, 2005a.
[3] Rowe: NeuroImage, 25:1310-1324, 2005b.
[4] Bandettini et al.: Magn Reson Med, 30:161-173, 1993.
[5] Friston et al.: Hum Brain Mapp, 2:189-210, 1995.
[6] Rowe, Meller, Hoffmann: J Neurosci Meth, 161:331-341, 2007.

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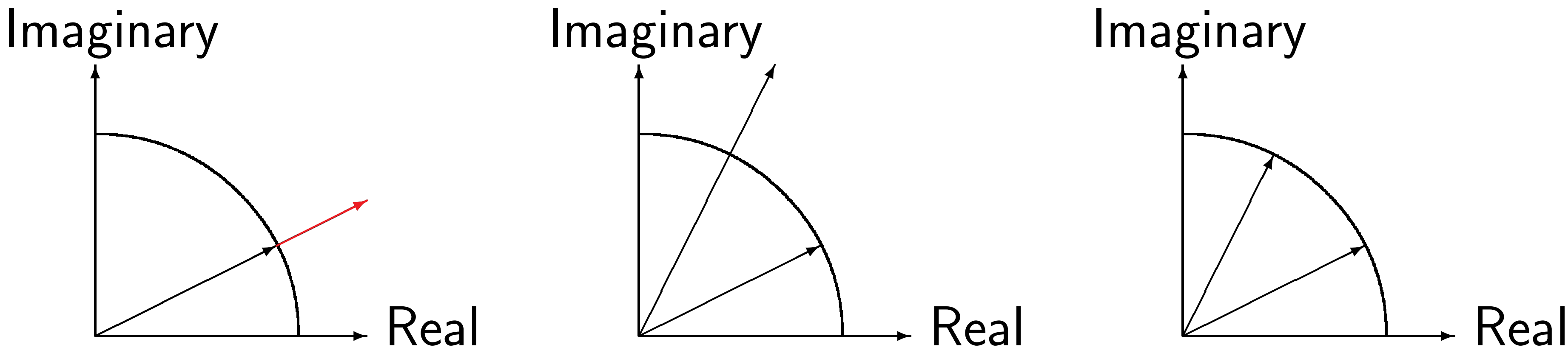

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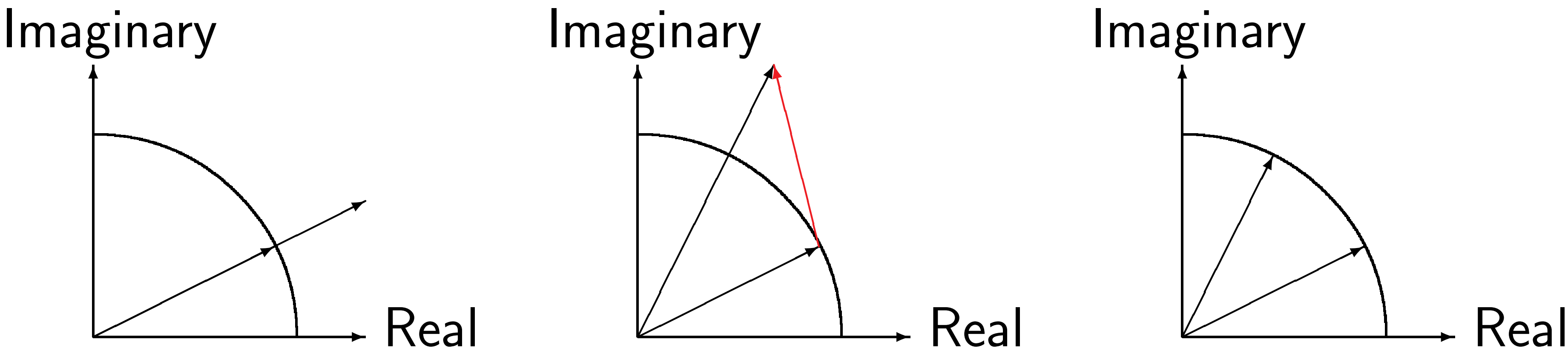

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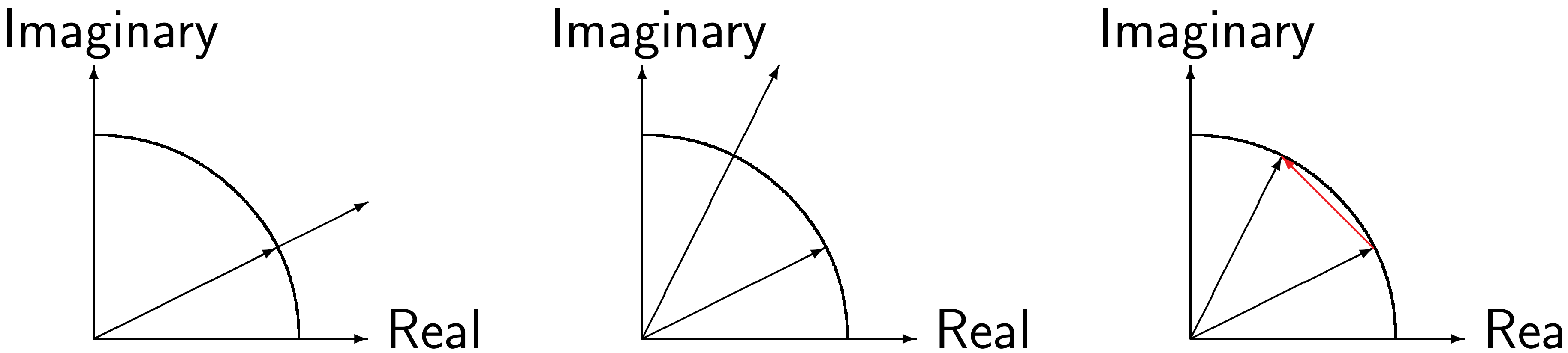

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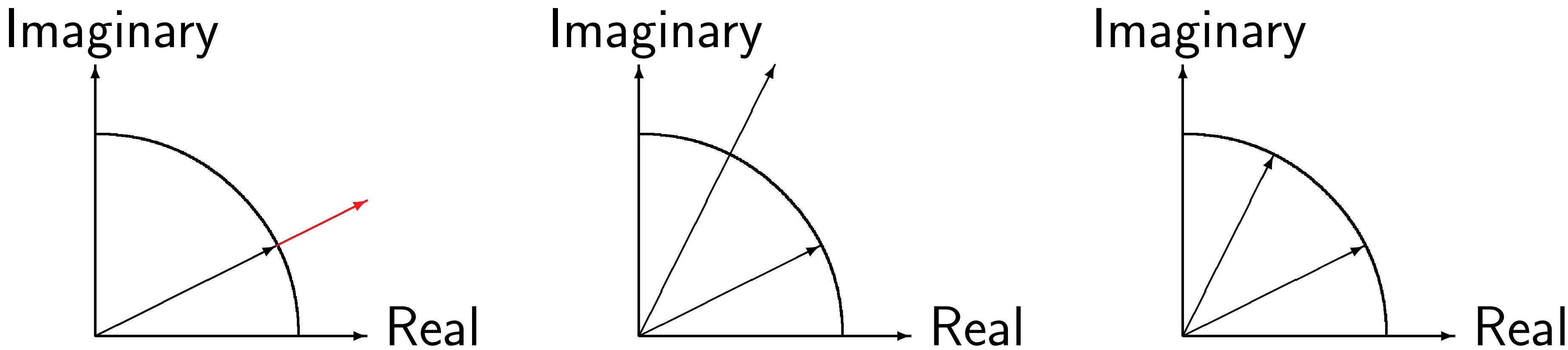
Complex Statistical Activation Methods

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



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

[1] Rowe and Logan: NeuroImage, 23:1078-1092, 2004.
[2] Rowe: NeuroImage 25:1124-1132, 2005a.
[3] Rowe: NeuroImage, 25:1310-1324, 2005b.
[4] Bandettini et al.: Magn Reson Med, 30:161-173, 1993.
[5] Friston et al.: Hum Brain Mapp, 2:189-210, 1995.
[6] Rowe, Meller, Hoffmann: J Neurosci Meth, 161:331-341, 2007.

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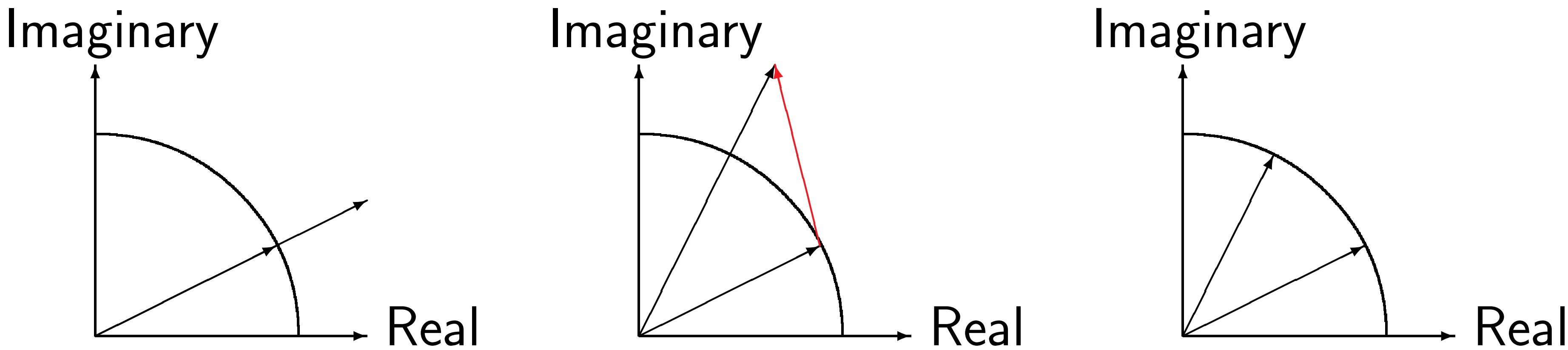

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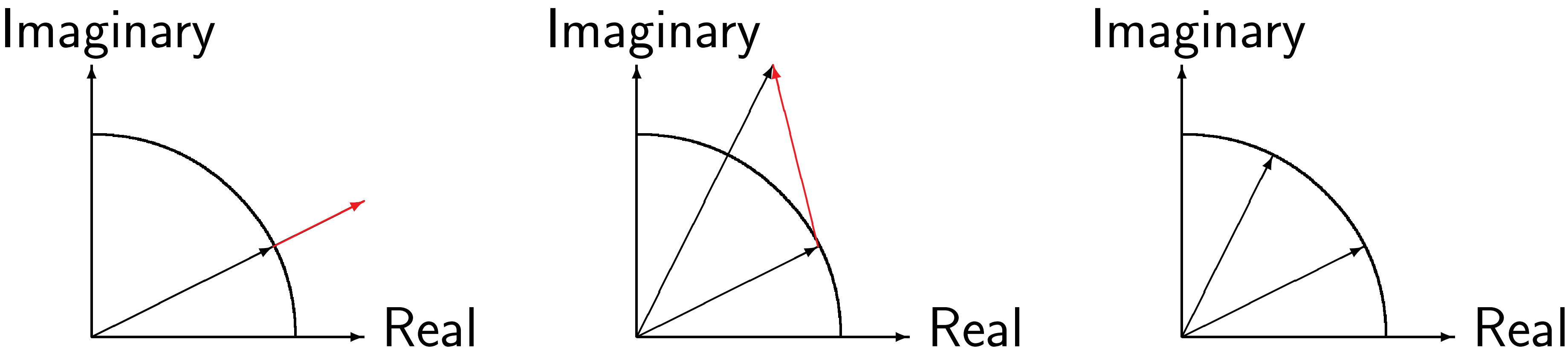

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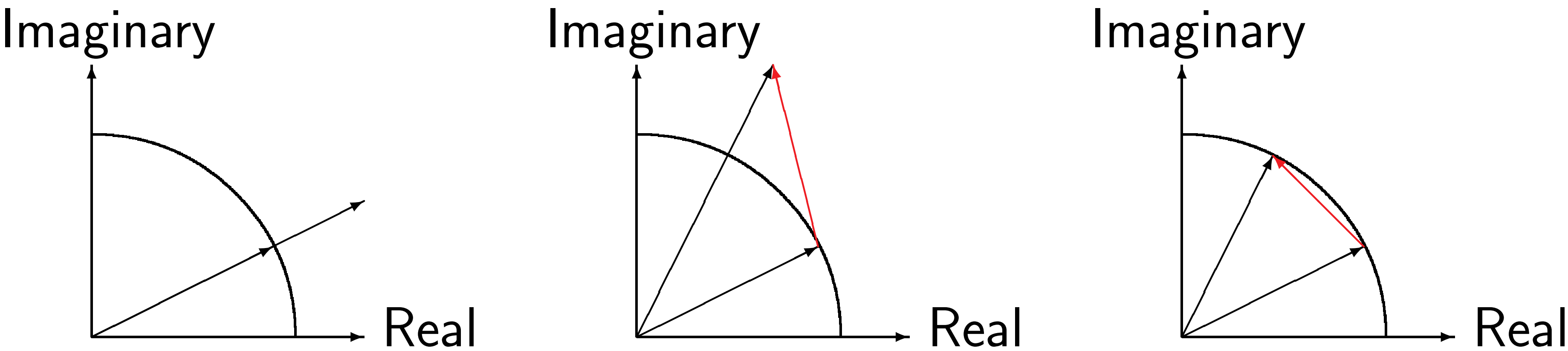

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Complex Statistical Activation Methods

In a voxel, the complex valued quantity measured over time is

$$y_t = (y_{Rt} + \eta_{Rt}) + i(y_{It} + \eta_{It}), \quad t = 1, ..., n$$

$y_t =$ complex voxel measurement at time t
$y_{Rt} =$ true real part of voxel measurement at time t
$y_{It} =$ imaginary part voxel measurement at time t
$\eta_{Rt} =$ noise real part voxel measurement at time t
$\eta_{It} =$ noise imaginary part voxel measurement at time t

$(\eta_{Rt}, \eta_{It})' \sim \mathcal{N}(0, \Sigma)$, $\Sigma = \sigma^2 I_2$.

The distributional specification is on the real and imaginary parts of the image and not on the magnitude.

Complex Statistical Activation Methods

In a voxel, the complex valued quantity measured over time is

$$y_t = (\rho_t \cos\theta_t + \eta_{Rt}) + i(\rho_t \sin\theta_t + \eta_{It}), \quad t = 1, ..., n$$

$y_t =$ complex voxel measurement at time t
$\rho_t =$ true magnitude of voxel measurement at time t
$\theta_t =$ true phase of voxel measurement at time t
$\eta_{Rt} =$ noise real part voxel measurement at time t
$\eta_{It} =$ noise imaginary part voxel measurement at time t

$(\eta_{Rt}, \eta_{It})' \sim \mathcal{N}(0, \Sigma)$, $\Sigma = \sigma^2 I_2$.

The distributional specification is on the real and imaginary parts of the image and not on the magnitude.

Complex Statistical Activation Methods

In a voxel, the complex valued quantity measured over time is

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

y_t = complex voxel measurement at time t

ρ_t = true magnitude of voxel measurement at time t

θ_t = true phase of voxel measurement at time t

η_{Rt} = noise real part voxel measurement at time t

η_{It} = noise imaginary part voxel measurement at time t

$(\eta_{Rt}, \eta_{It})' \sim \mathcal{N}(0, \Sigma)$, $\Sigma = \sigma^2 I_2$.

The distributional specification is on the real and imaginary parts of the image and not on the magnitude.

Complex Statistical Activation Methods

In a voxel, the complex valued quantity measured over time is

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

Want to describe the temporal changes in ρ_t and θ_t
in terms of a smaller number of parameters,
$\rho_t = \rho_t(\beta_0, \beta_1, ...)$ and $\theta_t = \theta_t(\gamma_0, \gamma_1, ...)$.

Can use a Taylor series expansion agrument and write

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

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.

Complex Statistical Activation Methods

Complex Magnitude with Constant Phase Activation

➢ Magnitude activation in complex data[1]

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

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

➢ y_R and y_I are the n reals and n imaginaries

➢ X & $\beta = (\beta_0, \beta_1, \beta_2)'$ same as MO, $C\beta = 0$ vs $C\beta \neq 0$, $C = (0,0,1)$

➢ A LRT[1] activation, χ^2, F, or z and threshold[2,3]

$$\chi^2_{CP} = -2\log(\lambda_{CP}) => \quad z_{CP} = \text{sign}(C\hat{\beta})\sqrt{-2\log(\lambda_{MO})}$$

➢ Large sample χ^2 & z checked by complex permutation resampling[1,3]

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

Complex Statistical Activation Methods

Complex Magnitude and/or Phase Activation

➢ 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.

Complex Statistical Activation Methods

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[1]

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

➢ Use GLM on the magnitudes[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 z and threshold[4]

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

[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.

Complex Statistical Activation Methods

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

➢ Assume nothing about the phase in voxels?

➢ 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 Statistical Activation Methods

Real Phase-Only Activation OLS & FL

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

$$\phi_t = \mathrm{atan}_4\left(y_{It}/y_{Rt}\right)$$

➢ Assume a high SNR for complicated phase dist. to be normal[1]

$$\frac{e^{-\frac{\rho^2}{2\sigma^2}}}{2\pi}\left[1 + \frac{\rho\ \cos(\phi_t-\theta_t)}{2\pi\sigma} e^{\frac{\rho^2\ \cos^2(\phi_t-\theta_t)}{2\sigma^2}} \Phi\left(\frac{\rho\ \cos(\phi_t-\theta_t)}{\sigma}\right)\right]$$

$$\approx \left[2\pi\left(\sigma/\rho\right)^2\right]^{-1/2} e^{-\frac{(\phi_t-\theta_t)^2}{2(\sigma/\rho)^2}}$$

➢ Use GLM on the phases[1], $D\gamma = 0$ vs $D\gamma \neq 0$, $D = (0, 0, 1)$

$$\phi = U\gamma + \delta, \qquad \delta \sim N(0, \tau^2 I_n), \quad \gamma = (\gamma_0, \gamma_1, \gamma_2)'$$

➢ No high SNR assumption made, von Mises angular distribution[1,2]

$$p(\phi_t) \ = \ e^{\kappa \cos(\phi_t-\theta_t)}/[2\pi I_0(\kappa)]$$

➢ Estimation in Fisher & Lee with $z = \hat{\gamma}_2/\sqrt{var(\hat{\gamma}_2)}$ activation statistic

[1] Rowe, Meller, Hoffmann: J Neurosci Meth, 161:331-341, 2007. [2] Fisher and Lee: Biometrics, 48:665-677, 1992.

Complex Statistical Activation Methods

Magnitude-only GLM individually for each voxel

$\rho_t = x_t'\beta = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_q x_{qt}.$

$$y_t = x_t'\beta + \epsilon_t, \quad t = 1, ..., n$$

Also written as

$$\underset{n \times 1}{y} = \underset{n \times (q+1)}{X} \; \underset{(q+1) \times 1}{\beta} + \underset{n \times 1}{\epsilon}$$

and $\epsilon \sim \mathcal{N}(0, \sigma^2\Phi)$, Φ is the temporal correlation matrix usually $\Phi = I_n$.

Complex Statistical Activation Methods

The magnitude-only GLM activation likelihood is given by

$$p(y|\beta, \sigma^2, X) = (2\pi)^{-\frac{n}{2}}(\sigma^2)^{-\frac{n}{2}}e^{-\frac{(y-X\beta)'(y-X\beta)}{2\sigma^2}}.$$

We want to see if the observed time course has a component related to the reference function.

$H_0: \; C\beta = \delta$ vs $H_1: \; C\beta \neq \delta$
i.e. Is the coefficient for the reference function zero.

$C = (0, ..., 0, 1)$, $\beta' = (\beta_0, \beta_1, \cdots, \beta_q)$, $\delta = 0$

Complex Statistical Activation Methods

By maximizing the MO likelihood under the unconstrained alternative

$$\hat{\beta} = (X'X)^{-1}X'y,$$
$$\hat{\sigma}^2 = \frac{1}{n}\left(y - X\hat{\beta}\right)'\left(y - X\hat{\beta}\right) \; .$$

By maximizing the MO likelihood under the constrained null hypotheses

$$\tilde{\beta} = \Psi\hat{\beta} \qquad\qquad + (X'X)^{-1}C'[C(X'X)^{-1}C']^{-1}\delta,$$
$$\tilde{\sigma}^2 = \frac{1}{n}\left(y - X\tilde{\beta}\right)'\left(y - X\tilde{\beta}\right)$$

$$\Psi = I_{q+1} - (X'X)^{-1}C'[C(X'X)^{-1}C']^{-1}C \; .$$

Complex Statistical Activation Methods

A non-linear complex-valued GLM can be introduced in which

$$\rho_t = x_t'\beta = \beta_0 + \beta_1 x_{1t} + \cdots + \beta_q x_{qt}$$

as in the magnitude model, with

$$\theta_t = \theta$$

then written in terms of matrices as

$$\underset{2n \times 1}{y} = \underset{2n \times 2(q+1)}{\begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}} \underset{2(q+1) \times 1}{\begin{pmatrix} \beta\cos\theta \\ \beta\sin\theta \end{pmatrix}} + \underset{2n \times 1}{\eta}$$

where $y = (y_R', y_I')'$ and $\eta = (\eta_{Rt}', \eta_{It}')' \sim \mathcal{N}(0, \Sigma \otimes \Phi)$

$\Sigma = \sigma^2 I_2$, $\Phi = I_n$.

Complex Statistical Activation Methods

The non-linear complex-valued GLM

$$\underset{2n \times 1}{y} = \underset{2n \times 2(q+1)}{\begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}} \underset{2(q+1) \times 1}{\begin{pmatrix} \beta\cos\theta \\ \beta\sin\theta \end{pmatrix}} + \underset{2n \times 1}{\eta}$$

$y = (y_R', y_I')'$, $\eta = (\eta_{Rt}', \eta_{It}')' \sim \mathcal{N}(0, \Sigma \otimes \Phi)$, $\Sigma = \sigma^2 I_2$ and $\Phi = I_n$.

The complex-valued GLM likelihood is

$$p(y|\beta, \theta, \sigma^2, X) = (2\pi)^{-\frac{2n}{2}} (\sigma^2)^{-\frac{2n}{2}} e^{-\frac{h}{2\sigma^2}}$$

where

$$h = \left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix} \begin{pmatrix} \beta\cos\theta \\ \beta\sin\theta \end{pmatrix}\right]' \left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix} \begin{pmatrix} \beta\cos\theta \\ \beta\sin\theta \end{pmatrix}\right] .$$

Complex Statistical Activation Methods

Just as in the magnitude model, we want to see if the observed time course has a component related to the reference function.

$H_0: \ C\beta = \delta$ vs $H_1: \ C\beta \neq \delta$

i.e. Is the coefficient for the reference function zero.

$C = (0, ..., 0, 1)$, $\beta' = (\beta_0, \beta_1, \cdots, \beta_q)$, $\delta = 0$

Complex Statistical Activation Methods

By maximizing CP GLM the likelihood under the unconstrained alternative

$$\hat{\theta} = \frac{1}{2}\tan_4^{-1}\left[\frac{\hat{\beta}_R'(X'X)\hat{\beta}_I}{(\hat{\beta}_R'(X'X)\hat{\beta}_R - \hat{\beta}_I'(X'X)\hat{\beta}_I)/2}\right]$$

$$\hat{\beta} = \hat{\beta}_R \cos\hat{\theta} + \hat{\beta}_I \sin\hat{\theta},$$

$$\hat{\sigma}^2 = \frac{1}{2n}\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \hat{\beta}\cos\hat{\theta} \\ \hat{\beta}\sin\hat{\theta} \end{pmatrix}\right]'\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \hat{\beta}\cos\hat{\theta} \\ \hat{\beta}\sin\hat{\theta} \end{pmatrix}\right]$$

$$\hat{\beta}_R = (X'X)^{-1}X'y_R,$$
$$\hat{\beta}_I = (X'X)^{-1}X'y_I \ .$$

Complex Statistical Activation Methods

By maximizing the CP GLM likelihood under the constrained null hypotheses

$$\tilde{\theta} = \frac{1}{2}\tan_4^{-1}\left[\frac{\hat{\beta}_R'\Psi(X'X)\hat{\beta}_I}{(\hat{\beta}_R'\Psi(X'X)\hat{\beta}_R - \hat{\beta}_I'\Psi(X'X)\hat{\beta}_I)/2}\right]$$

$$\tilde{\beta} = \Psi[\hat{\beta}_R\cos\tilde{\theta} + \hat{\beta}_I\sin\tilde{\theta}] \qquad + (X'X)^{-1}C'[C(X'X)^{-1}C']^{-1}\delta,$$

$$\tilde{\sigma}^2 = \frac{1}{2n}\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \tilde{\beta}\cos\tilde{\theta} \\ \tilde{\beta}\sin\tilde{\theta} \end{pmatrix}\right]'\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \tilde{\beta}\cos\tilde{\theta} \\ \tilde{\beta}\sin\tilde{\theta} \end{pmatrix}\right]$$

$$\Psi = I_{q+1} - (X'X)^{-1}C'[C(X'X)^{-1}C']^{-1}C\ .$$

Complex Magnitude with Constant Phase

In each voxel, simulate complex valued time courses like real data.

$$\begin{aligned} y_t = & [(\beta_0 + \beta_1 x_{1t} + \beta_2 x_{2t}) \cos(\hat{\theta}) + n_{Rt}] \\ & + i[(\beta_0 + \beta_1 x_{1t} + \beta_2 x_{2t}) \sin(\hat{\theta}) + n_{It}] \end{aligned}$$

From a real dataset, fitted complex model, took $\hat{\beta}_C$ and $\hat{\sigma}_C^2$ from a "highly activated" voxel. $\hat{\theta}$'s from whole image.

Created complex data where the coefficients in each voxel were the first two elements of $\hat{\beta}_C$. $CNR = \beta_2/\hat{\sigma}_C$.

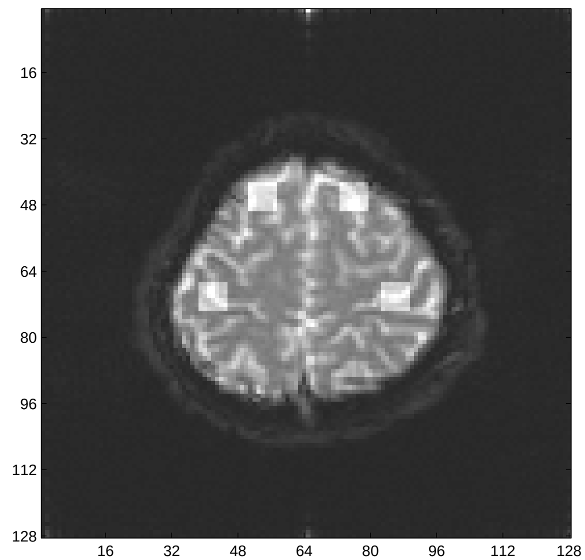
Created four 7×7 square ROI's, $CNR = 1, 1/2, 1/4, 1/8$, $\beta_2 = 0$ outside ROI's.

Added normal noise $\mathcal{N}(0, \hat{\sigma}_C^2)$. Varied $SNR = \beta_0/\sigma$.

Complex Magnitude with Constant Phase: Simulation

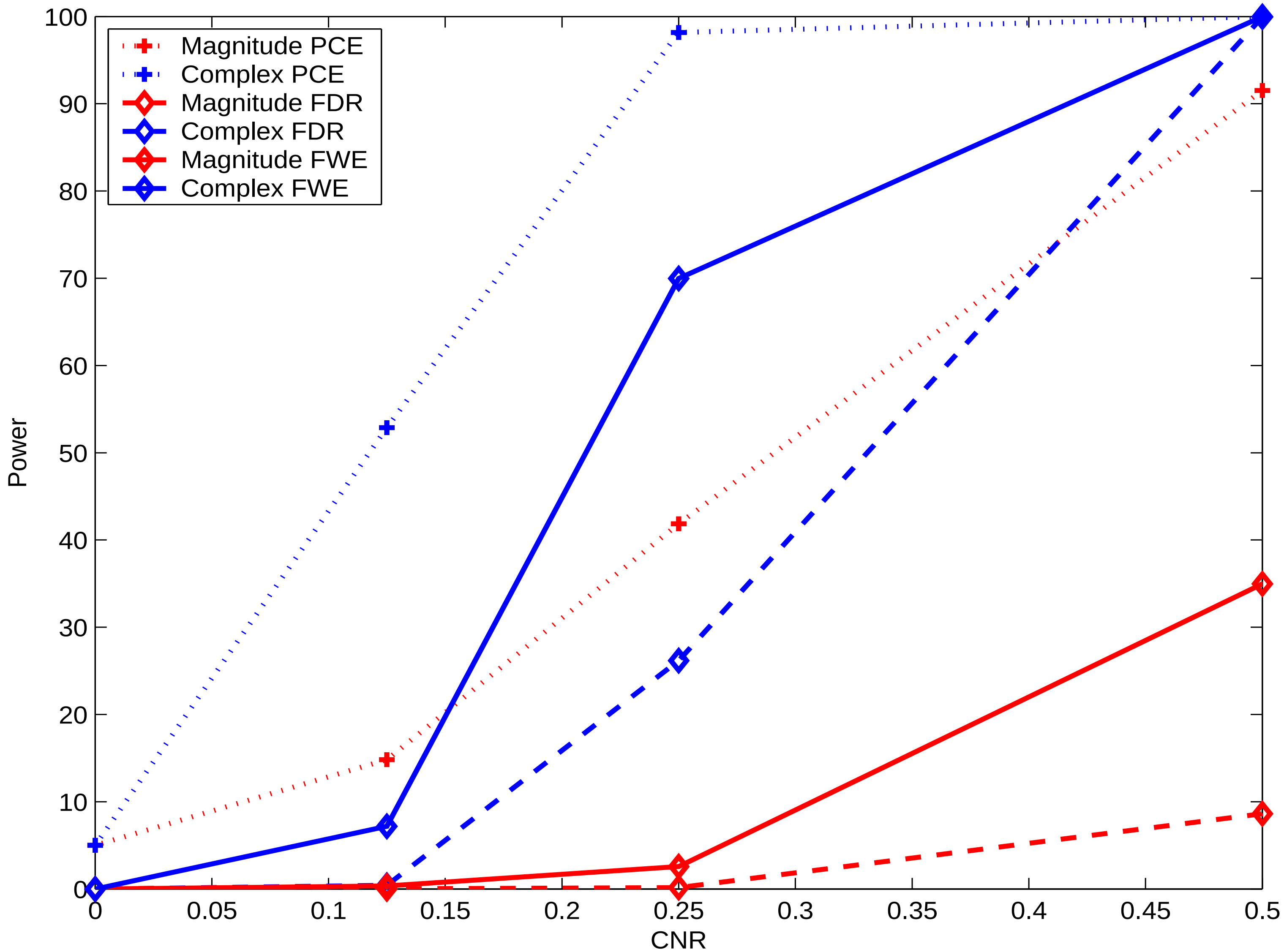
Repeated simulation 1000 times.

For each thresholding method, the power in, or relative frequency over the 1000 simulated images with which each voxel was detected as active, was recorded.



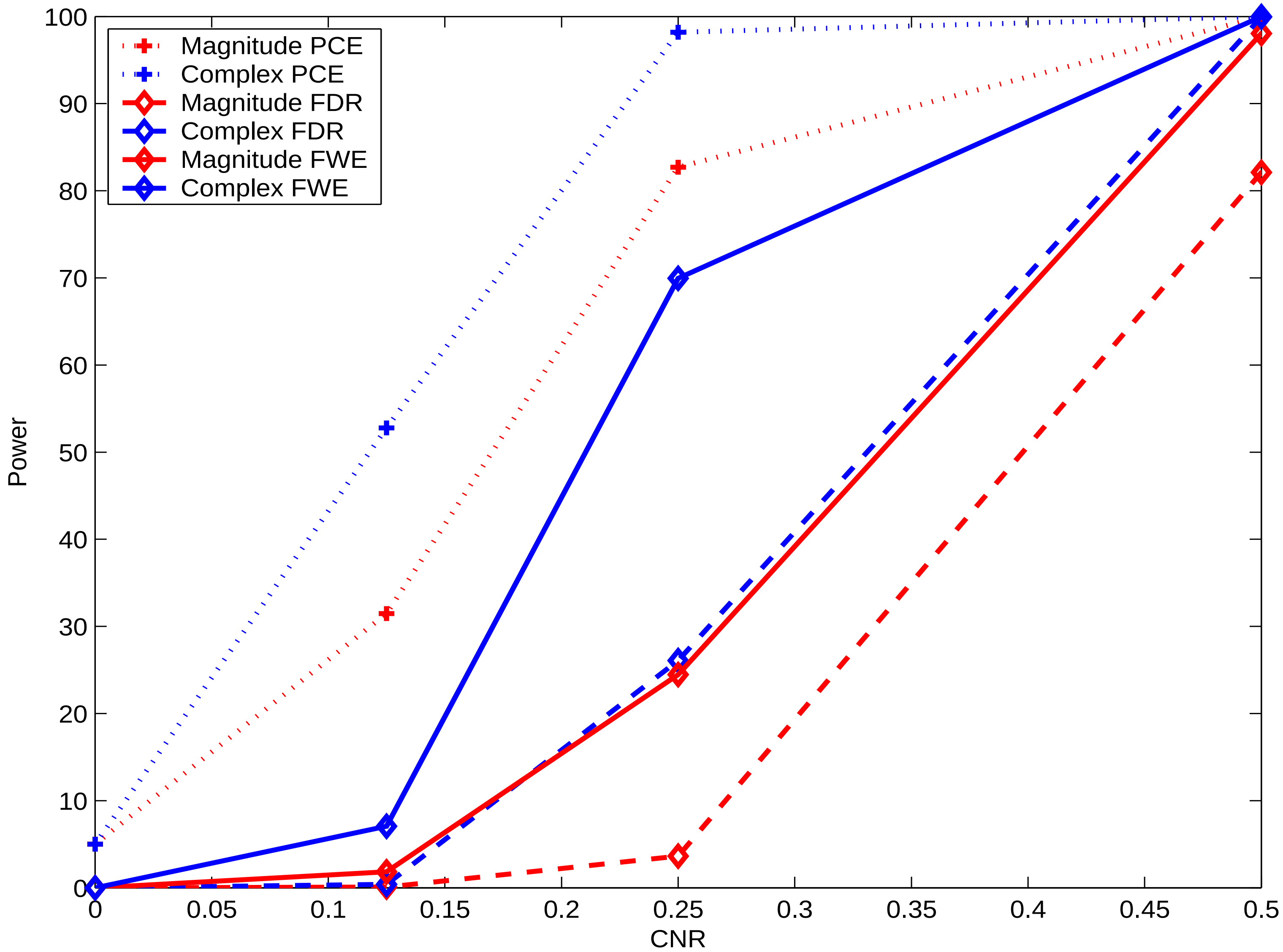
5% Unadjusted, 5% FDR, and 5% Bonferroni thresholds.

Power versus CNR: Complex (blue) and magnitude (red)



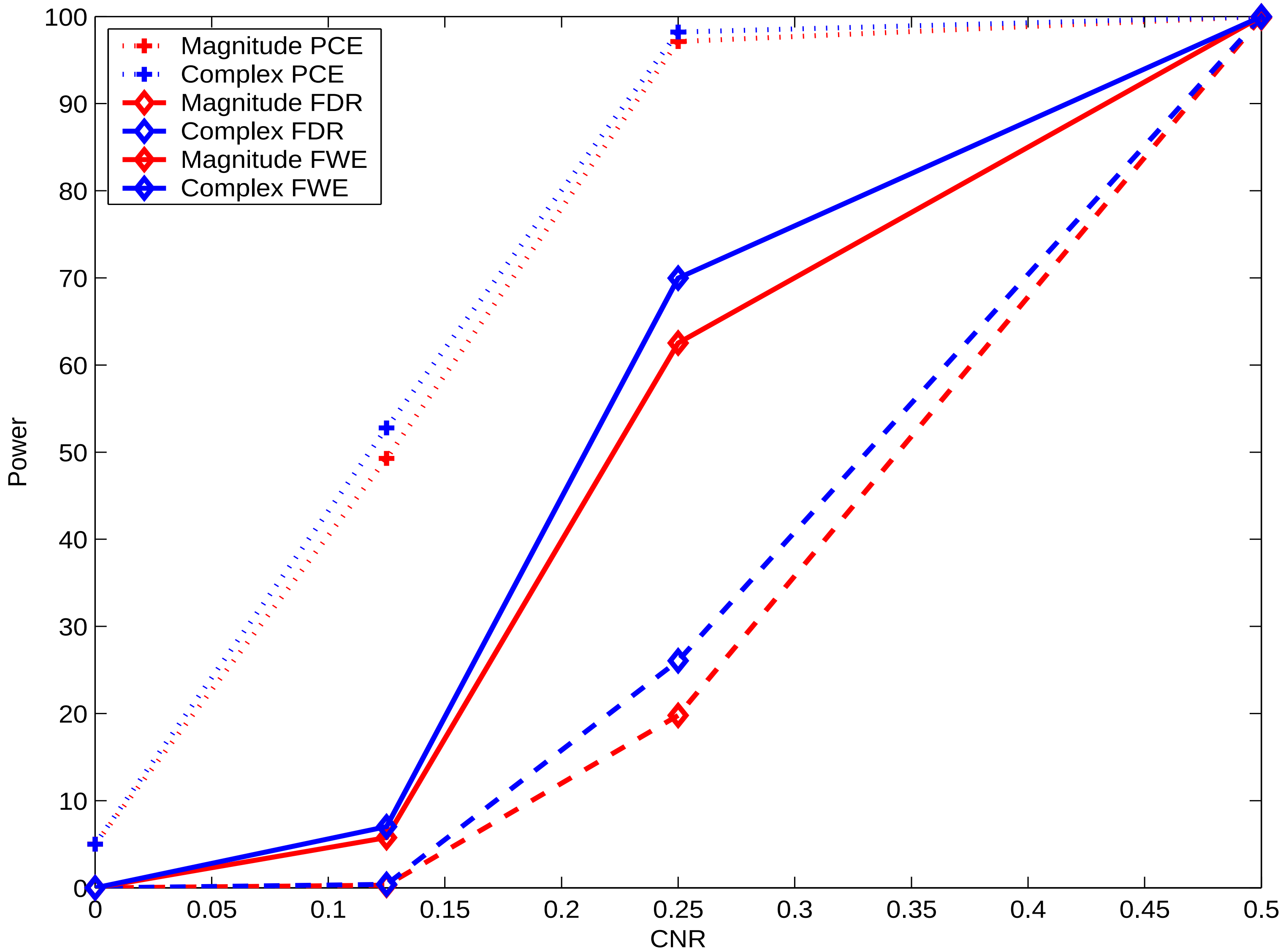
SNR $= 1$

Power versus CNR: Complex (blue) and magnitude (red)



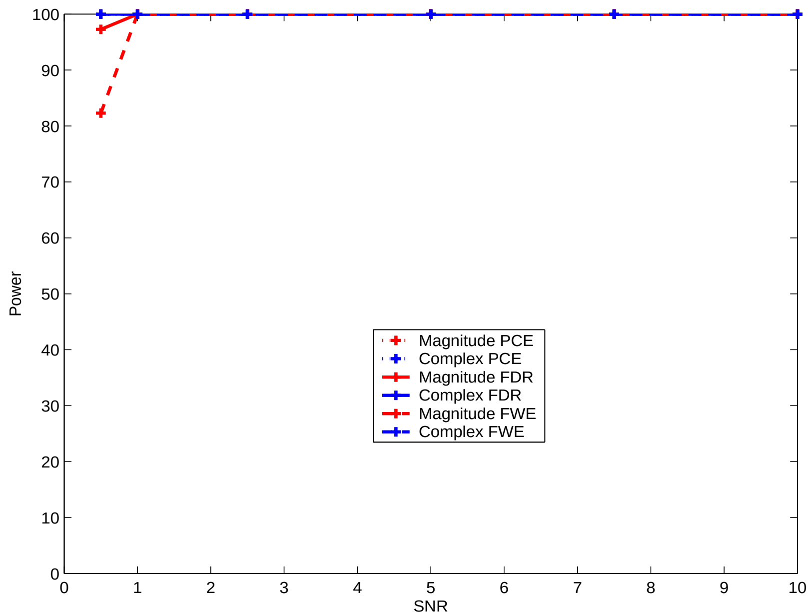
SNR $= 2.5$

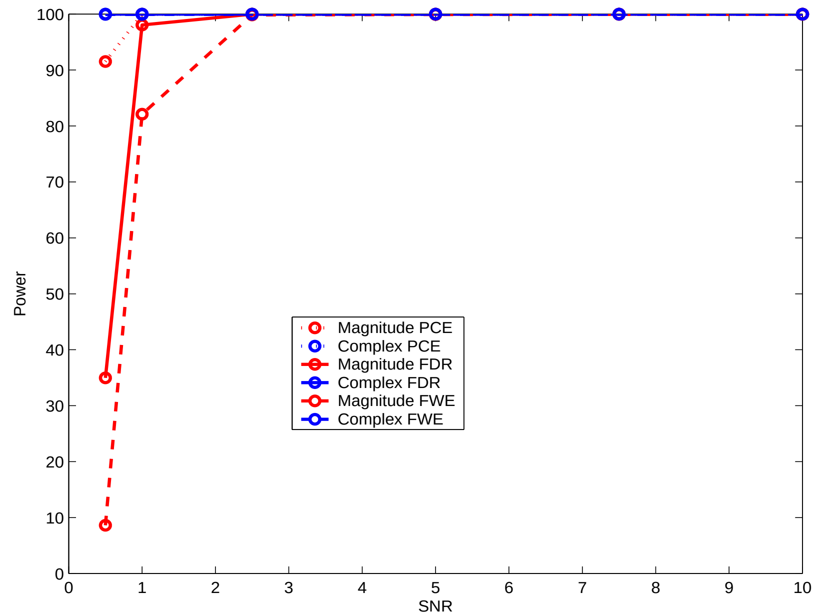
Power versus CNR: Complex (blue) and magnitude (red)



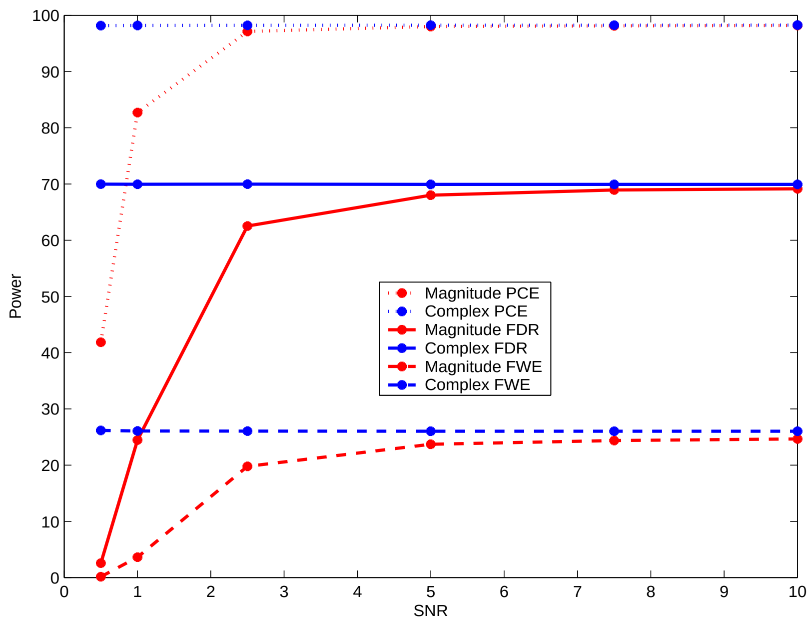
SNR $= 5$

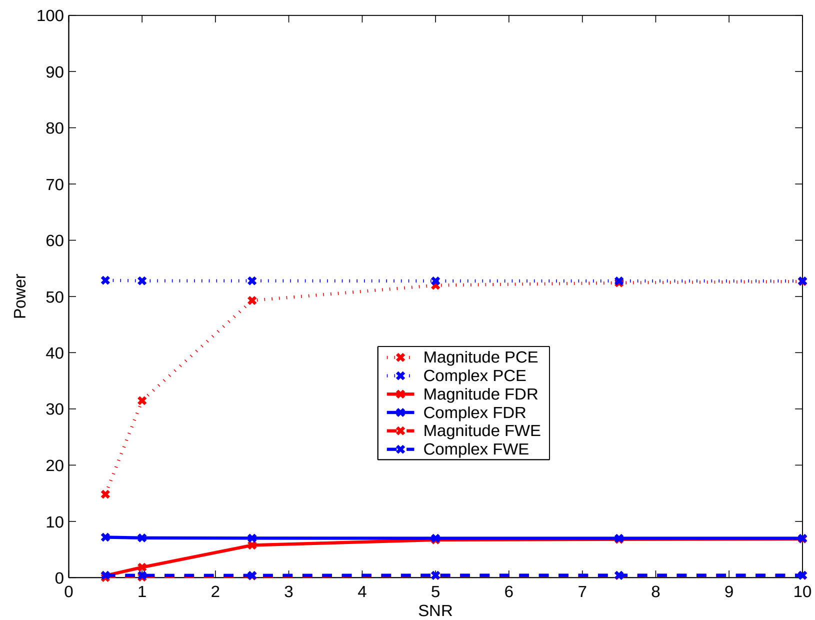
Power versus SNR: Complex (blue) and magnitude (red)





CNR= 1,1/2



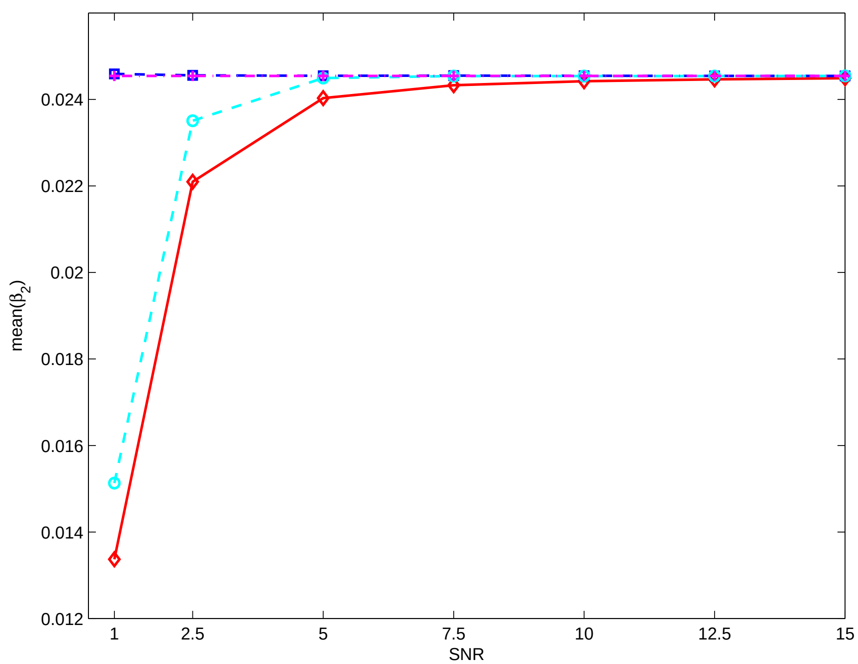


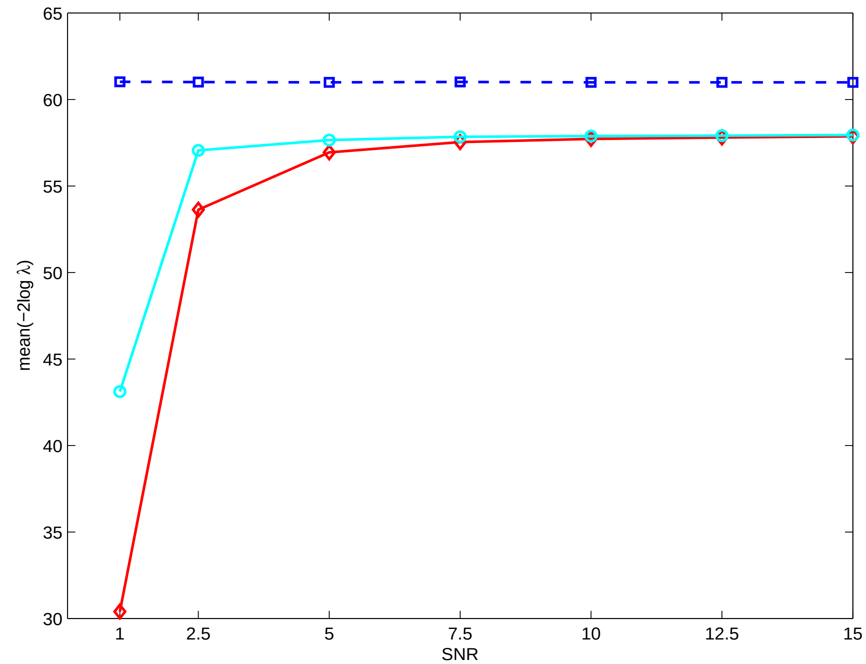
CNR= 1/4,1/8

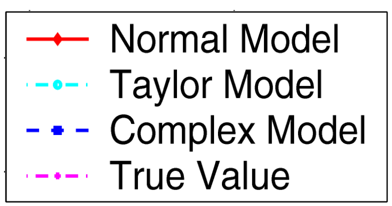
Complex Magnitude with Constant Phase Activation

When voxel phase is relatively constant get[1]: (CNR$=1/2$)

- unbiased parameter estimators
- increased activation statistic







- SNR decreases as voxel volume decreases
- SNR decreases in voxels of susceptibility dropout

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

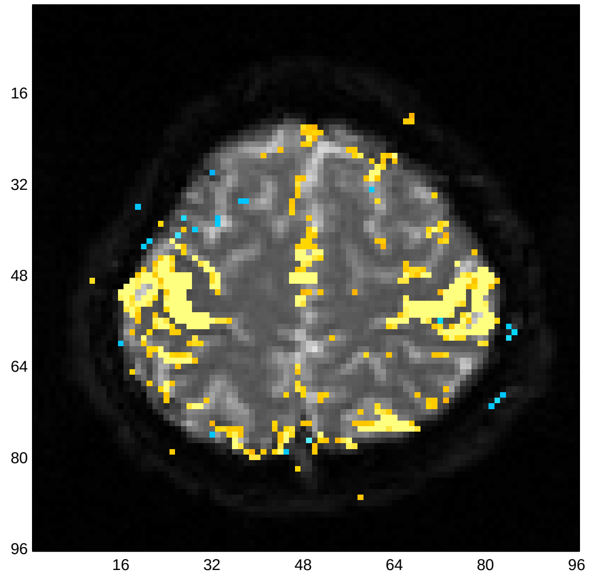
Complex Magnitude with Constant Phase: Real Data

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°

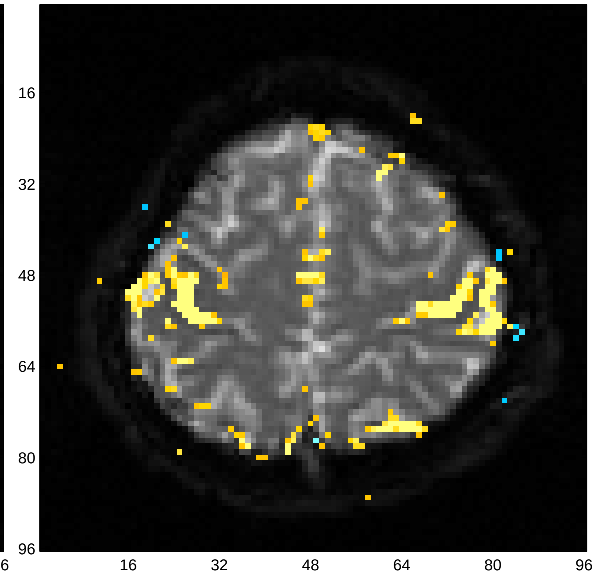
Task:
RH male Bilateral sequential finger tapping light triggered
Block design
16 off $+$ 8$\times$(16on$+$16off);

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

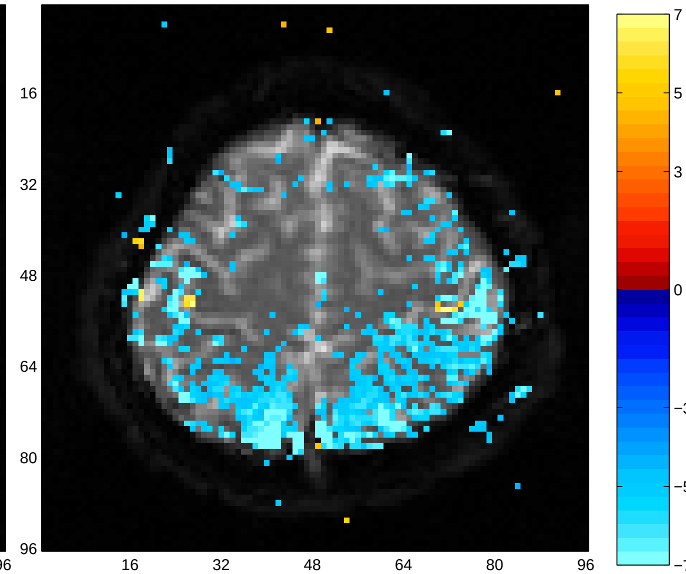
z Maps: 5% Bonferroni Threshold



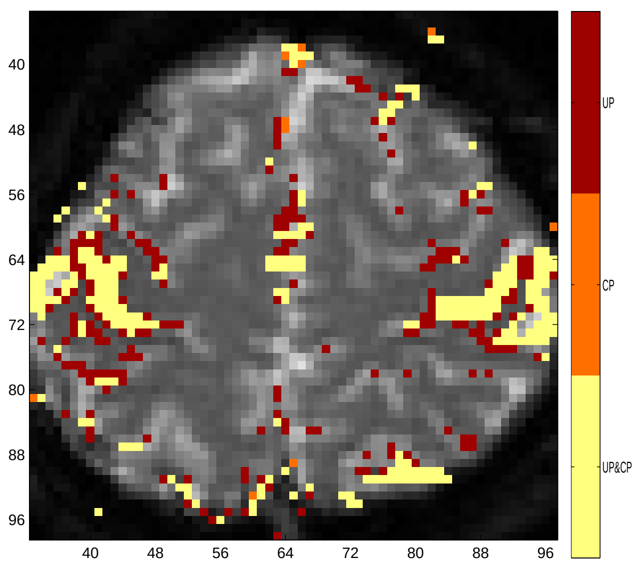
(a) UP/MO



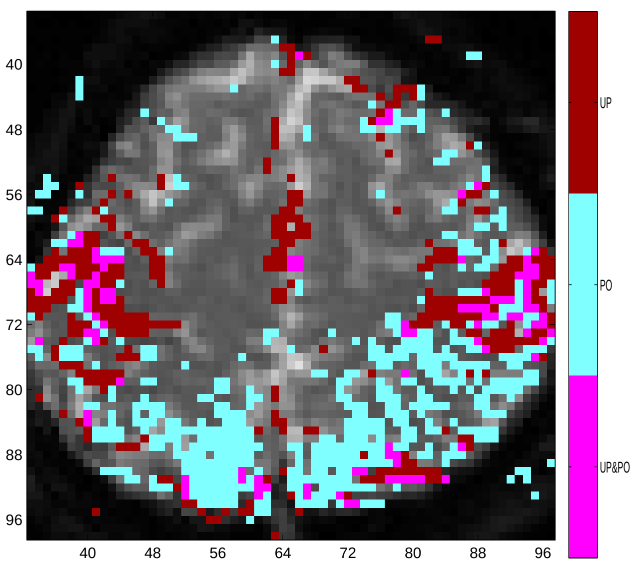
(b) CP



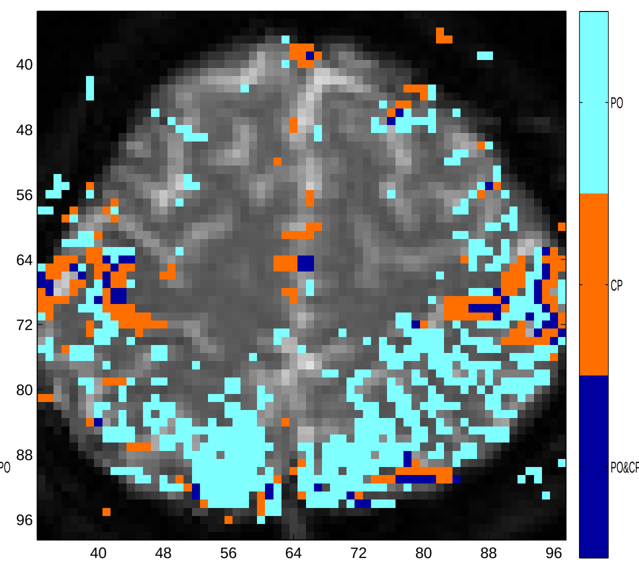
(c) PO



(d) UP/MO & CP



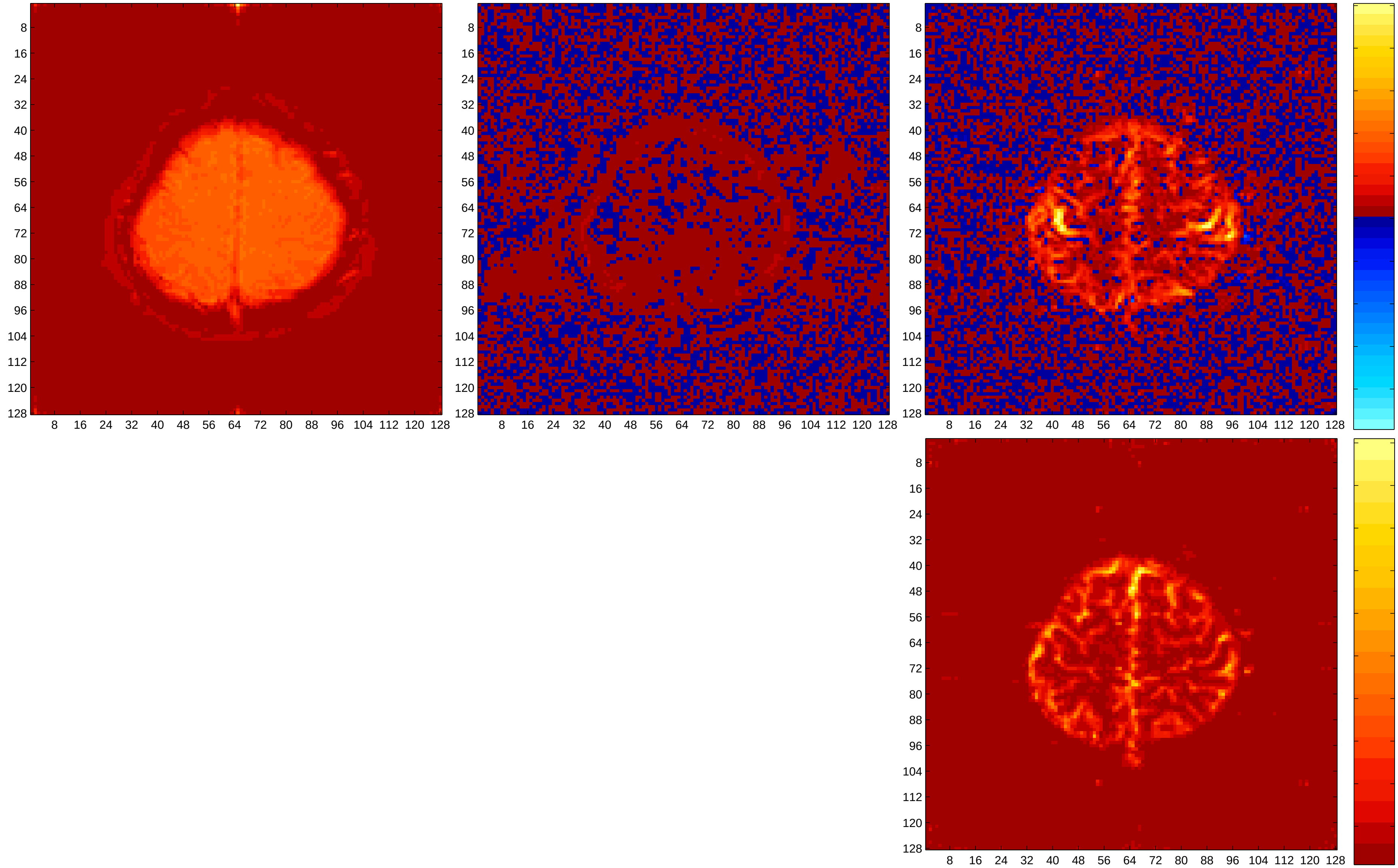
(e) UP/MO &PO



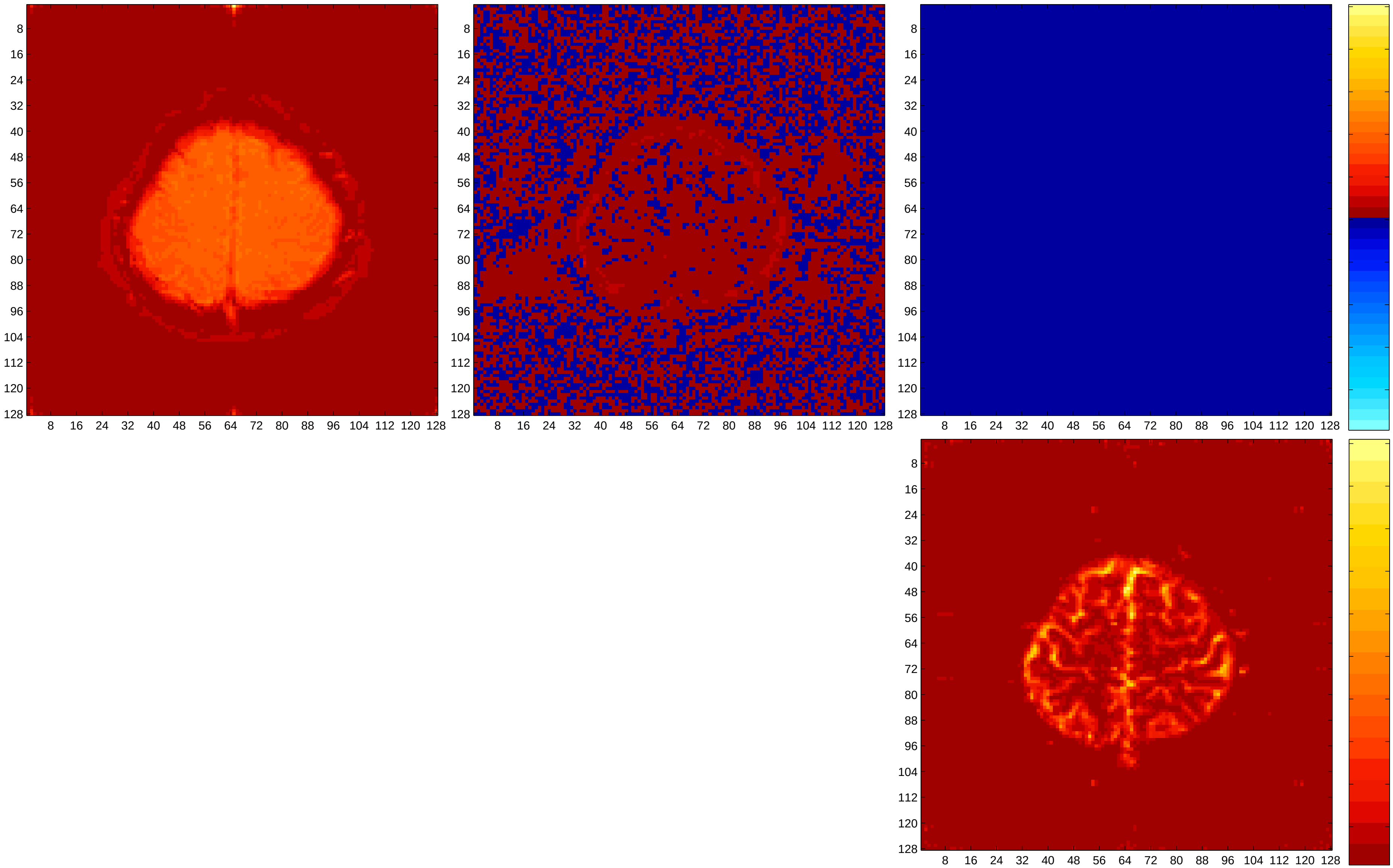
(f) CP & PO

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

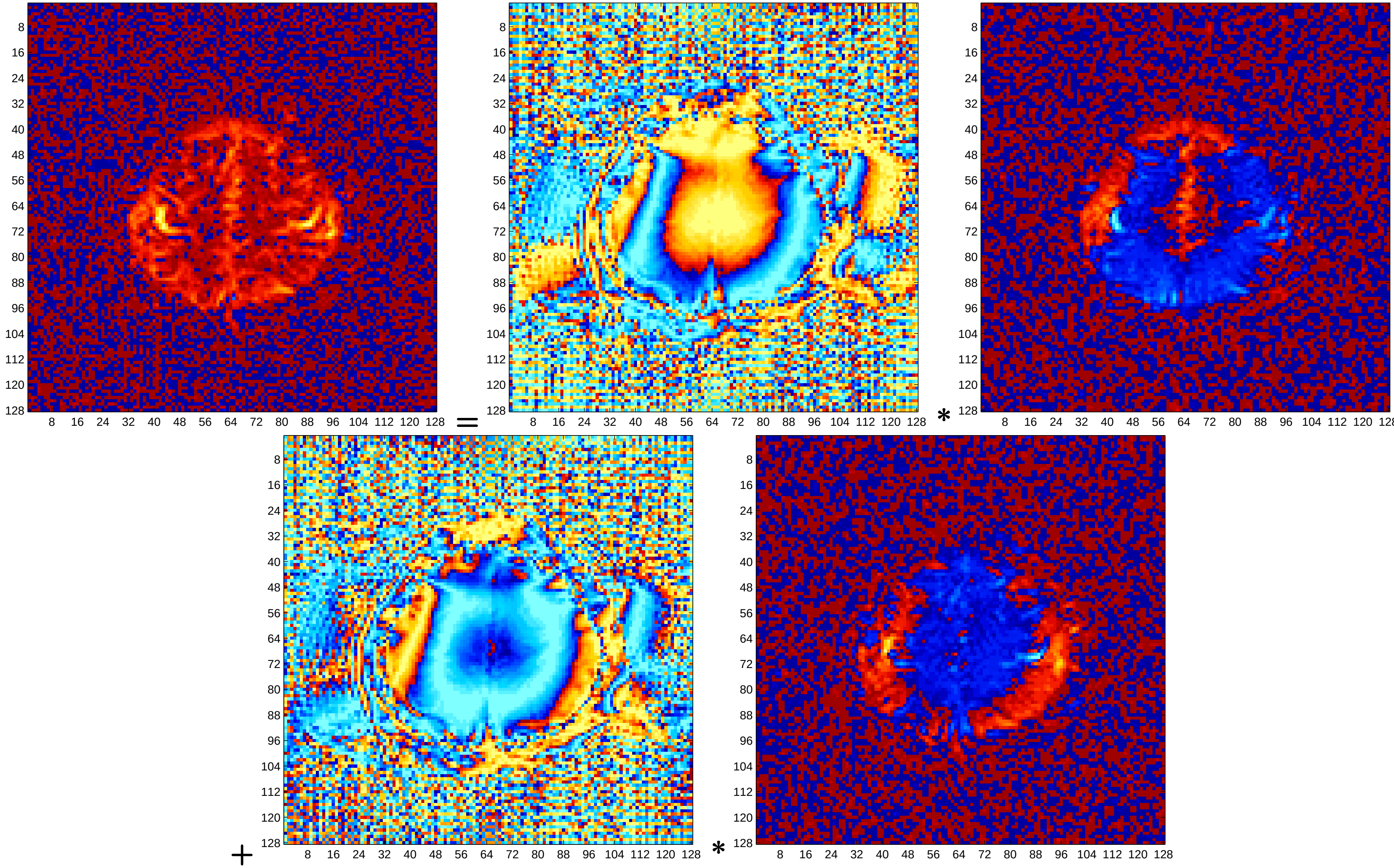
Real fMRI-Magnitude H1 Estimated: $\hat{\beta}_0, \hat{\beta}_1, \hat{\beta}_2, \hat{\sigma}^2$



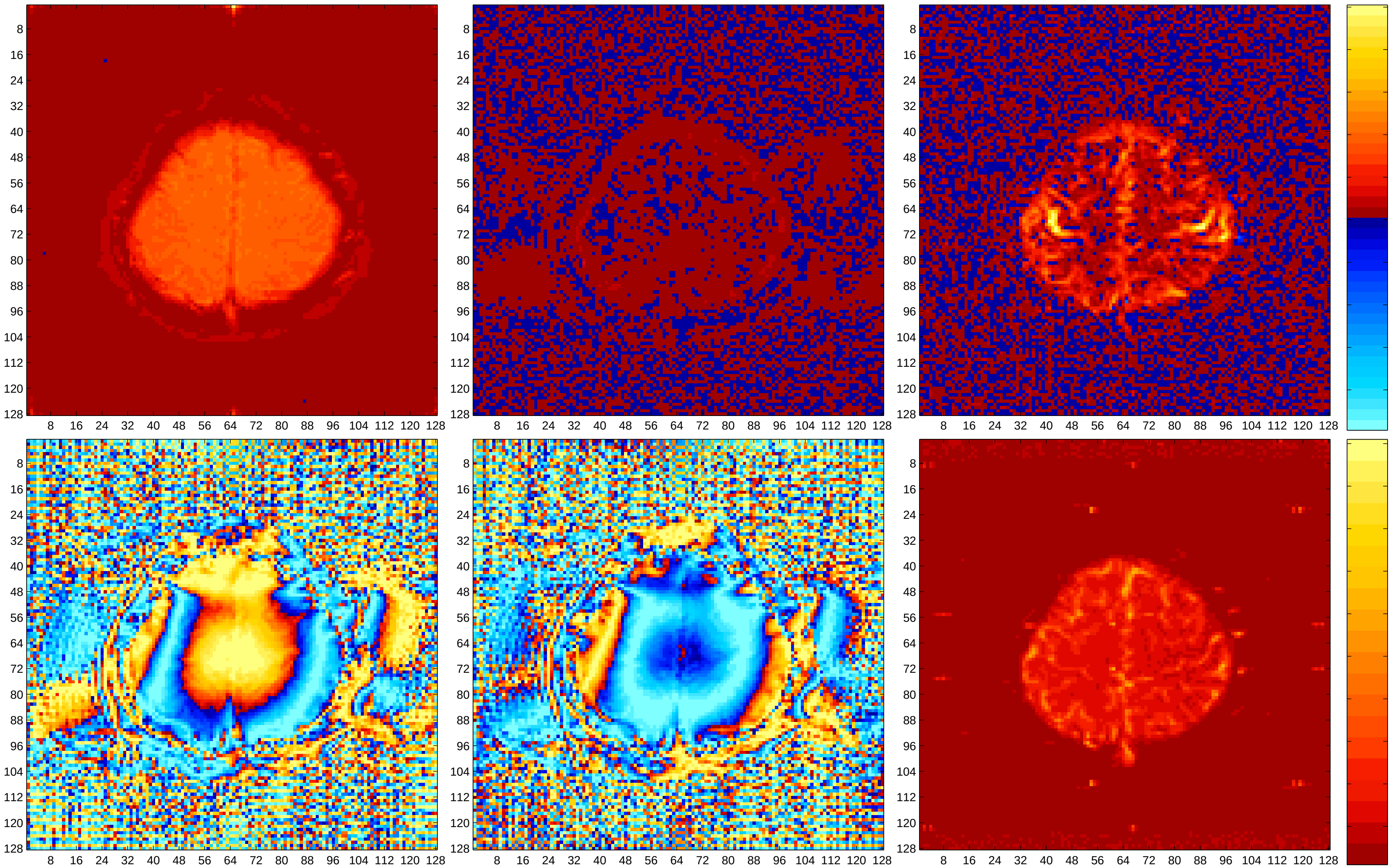
Real fMRI-Magnitude H0 Estimated: $\tilde{\beta}_0, \tilde{\beta}_1, \tilde{\beta}_2, \tilde{\sigma}^2$



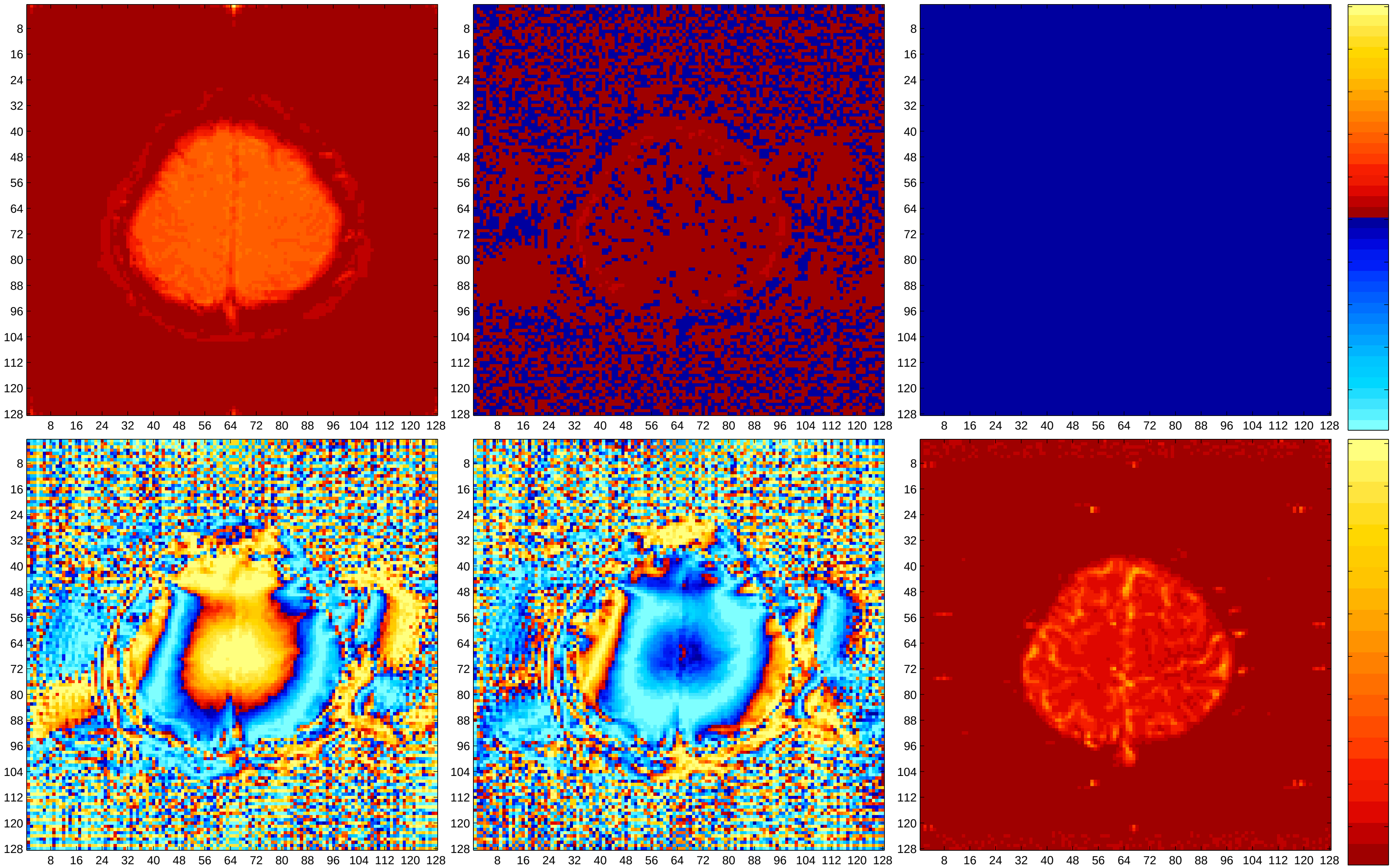
Real fMRI-Complex H1 Estimated: $\hat{\beta} = \hat{\beta}_R \cos\hat{\theta} + \hat{\beta}_I \sin\hat{\theta}$



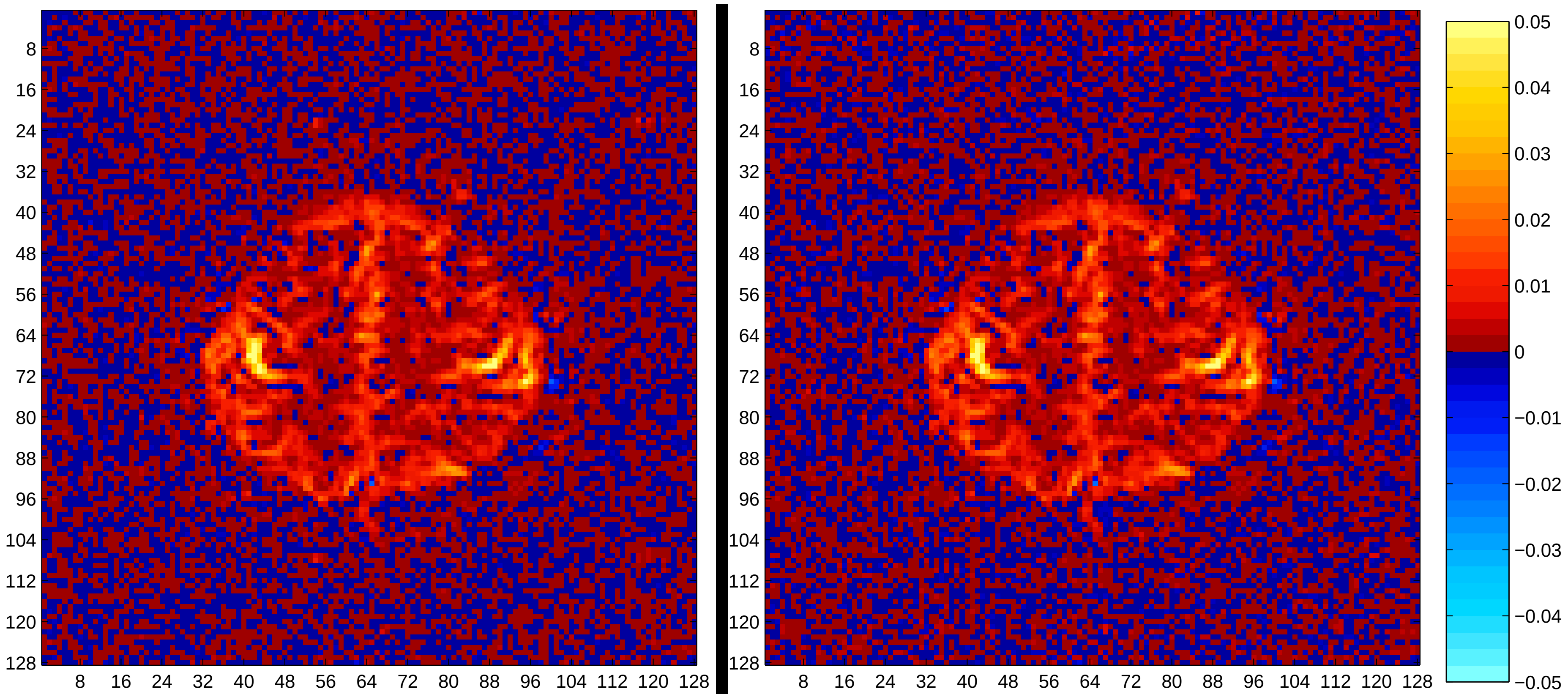
Real fMRI-Complex H1 Estimated: $\hat{\beta}_0, \hat{\beta}_1, \hat{\beta}_2, \cos\hat{\theta}, \sin\hat{\theta}, \hat{\sigma}^2$



Real fMRI-Complex H0 Estimated: $\tilde{\beta}_0, \tilde{\beta}_1, \tilde{\beta}_2, \cos\tilde{\theta}, \sin\tilde{\theta}, \tilde{\sigma}^2$



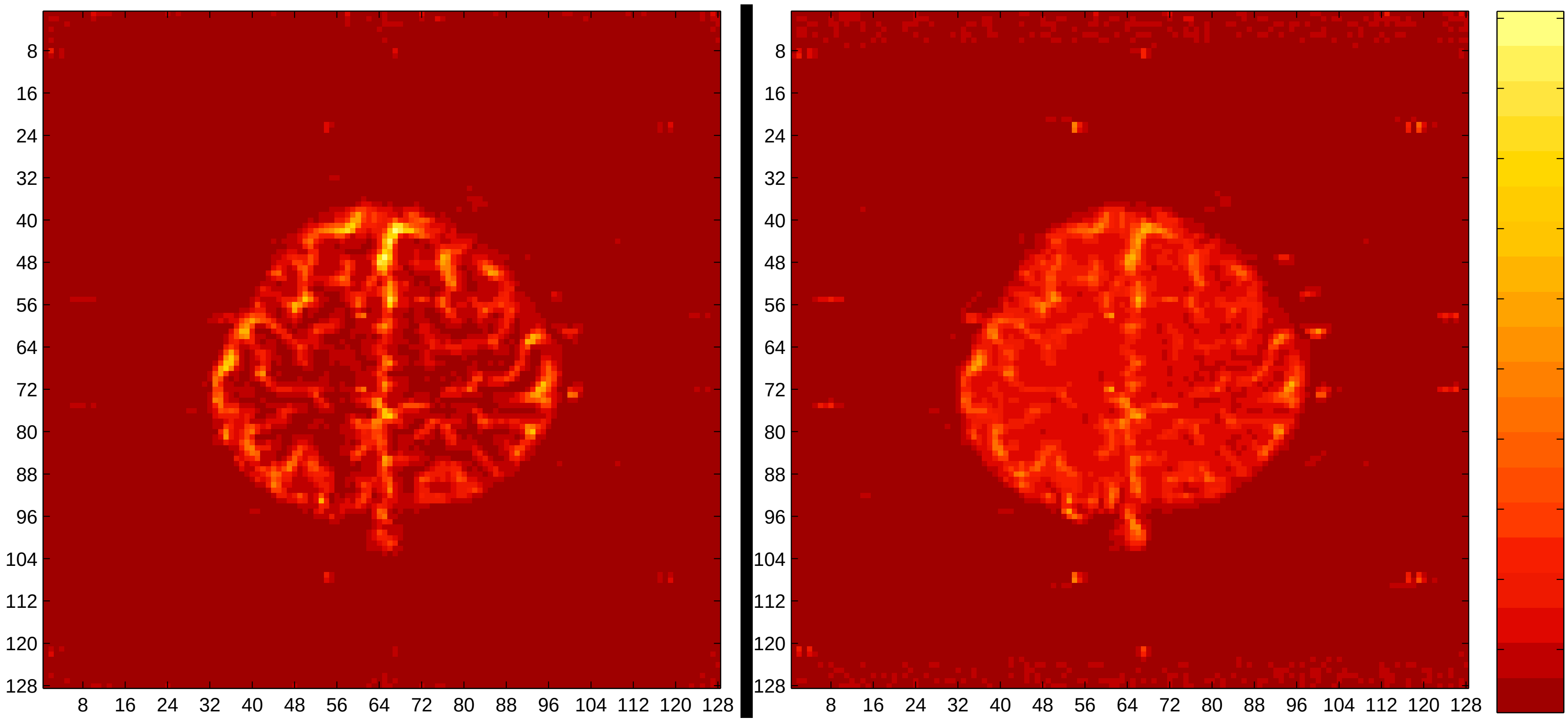
Real fMRI-Magnitude/Complex H1 Estimated $\hat{\beta}_2$



MO Act. Coefs. CP Act. Coefs.

Coefficients are not visually that different but slightly numerically different.

Real fMRI-Magnitude/Complex H1 Estimated $\hat{\sigma}^2$

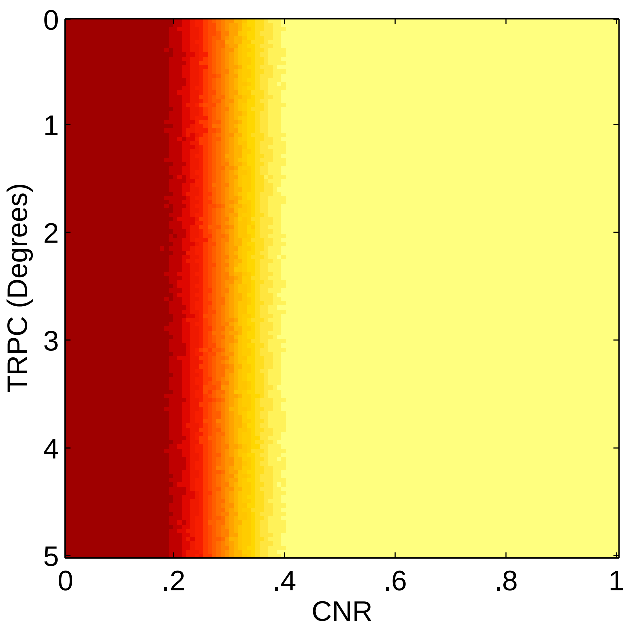


MO Act. Variances CP Act. Variances

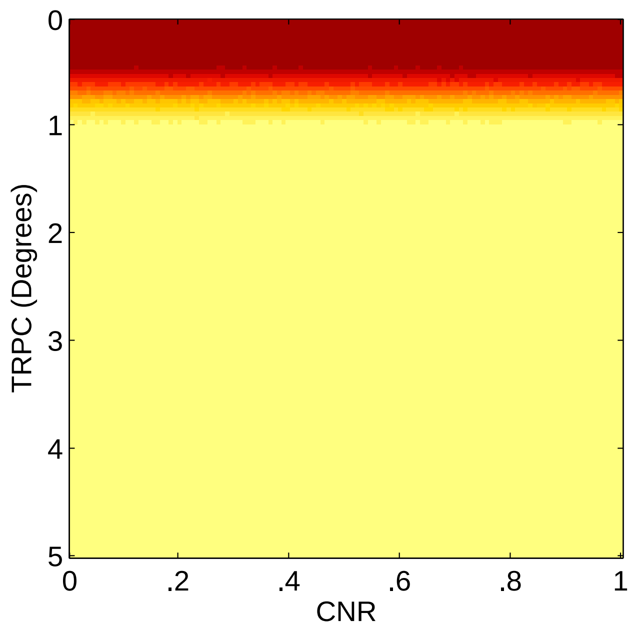
Variances are visually different and numerically different.

Complex Time Course Model

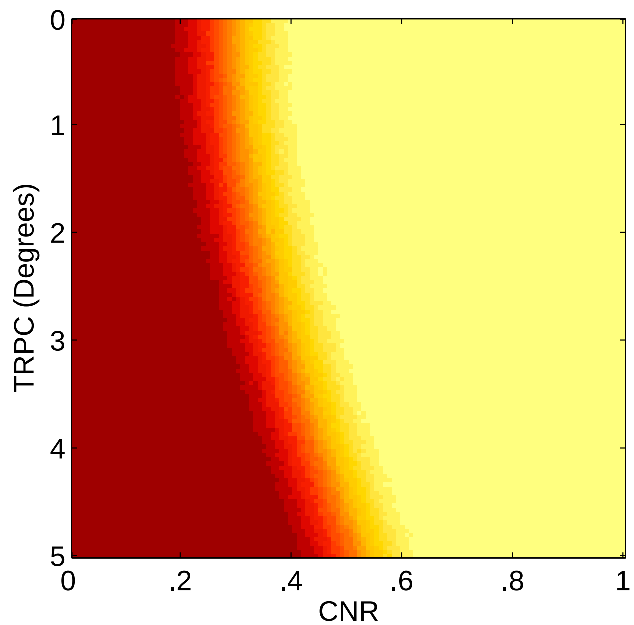
Using phase to eliminate venous BOLD. Nencka & Rowe, NIMG, Accepted 2007.



MO Act. Power



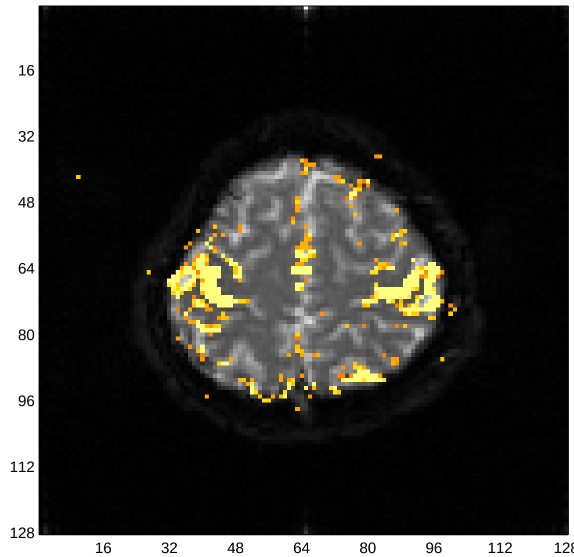
PO Act. Power



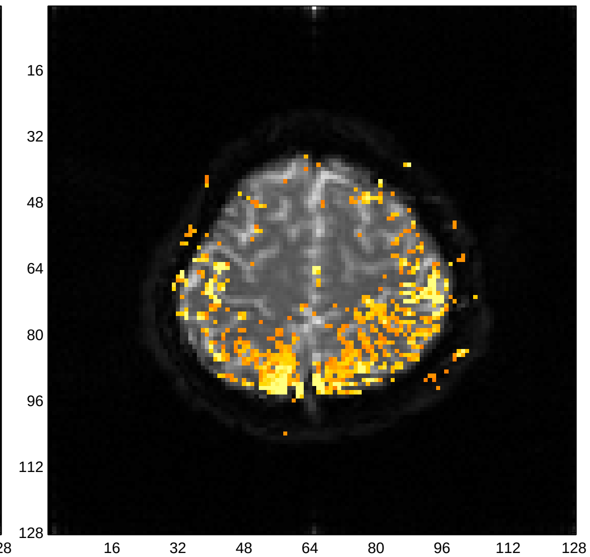
CP Act. Power

$SNR = 20$

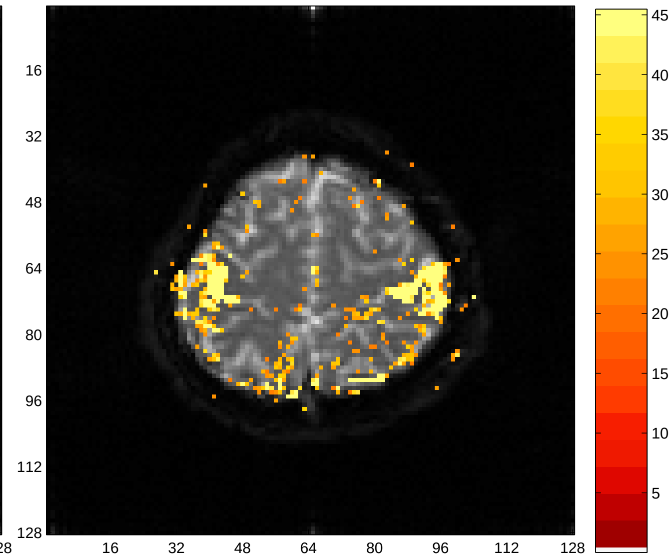
Activation Maps 5% Bonferroni Combination Threshold



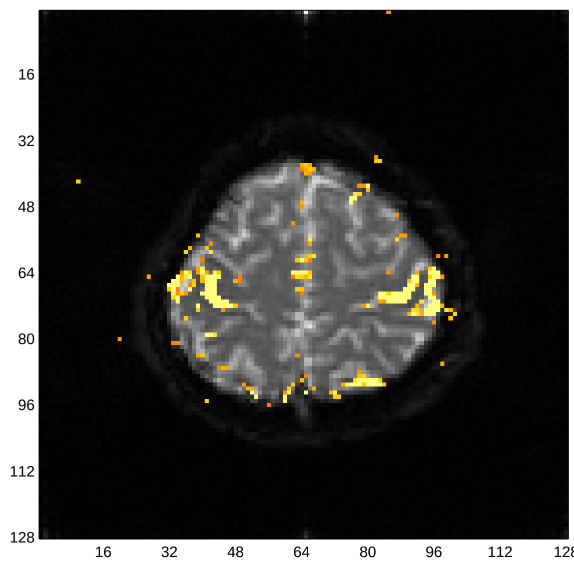
(a) UP/MO



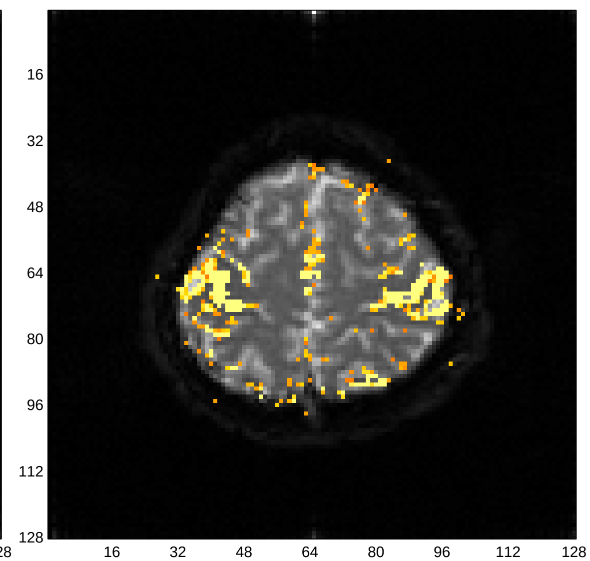
(b) PO



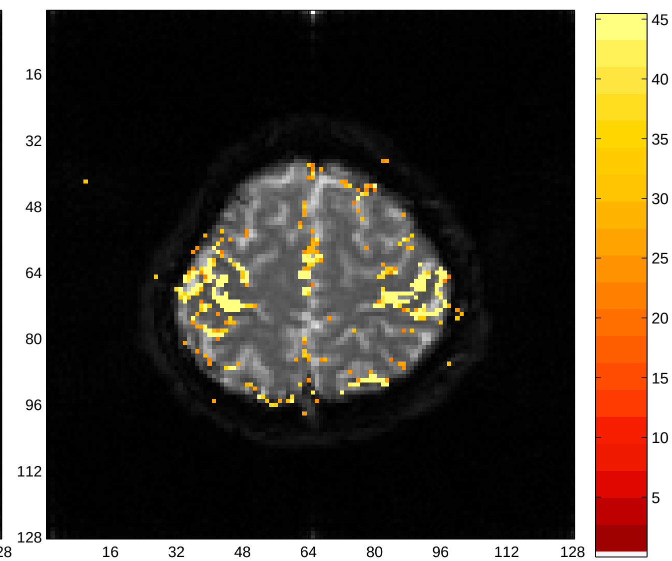
(c) PR



(d) CP

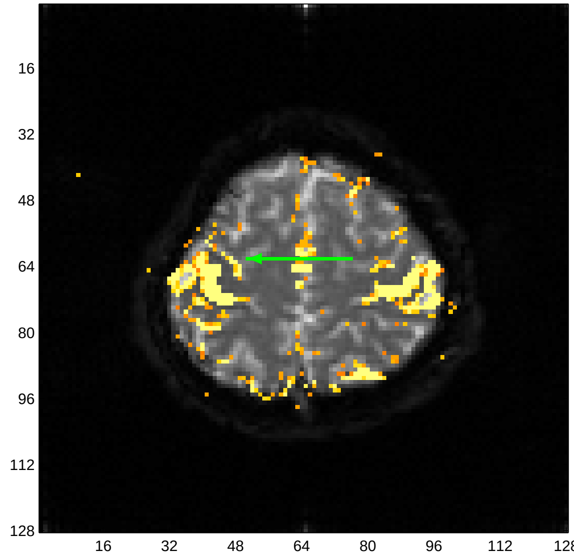


(e) $|TRPC| < 1°$

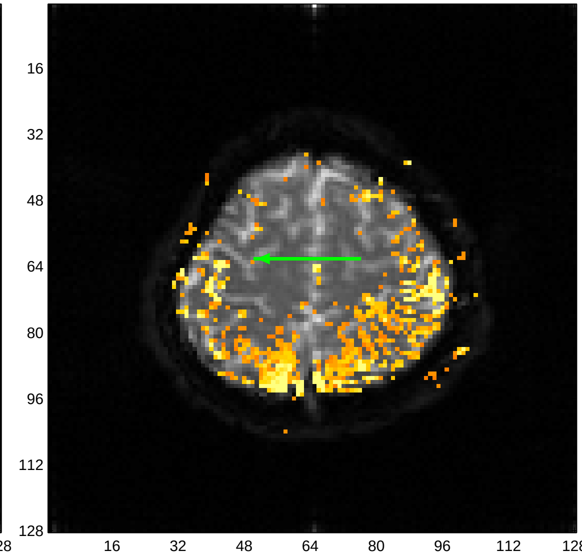


(f) MO & PO 5% Bonf.

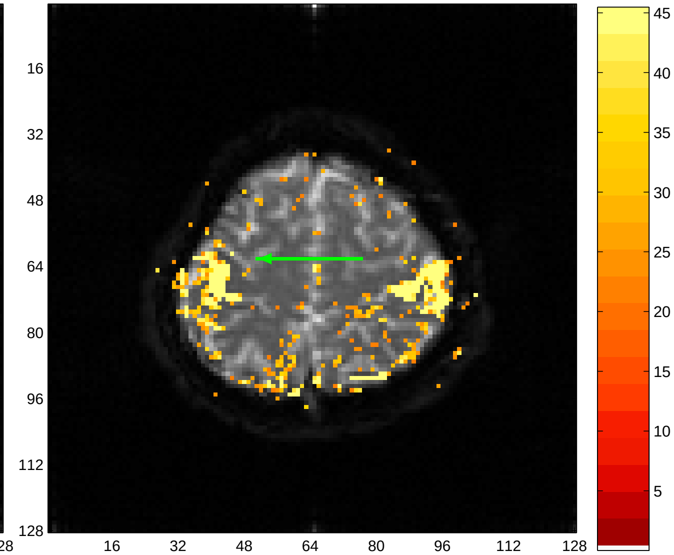
Activation Maps 5% Bonferroni Combination Threshold



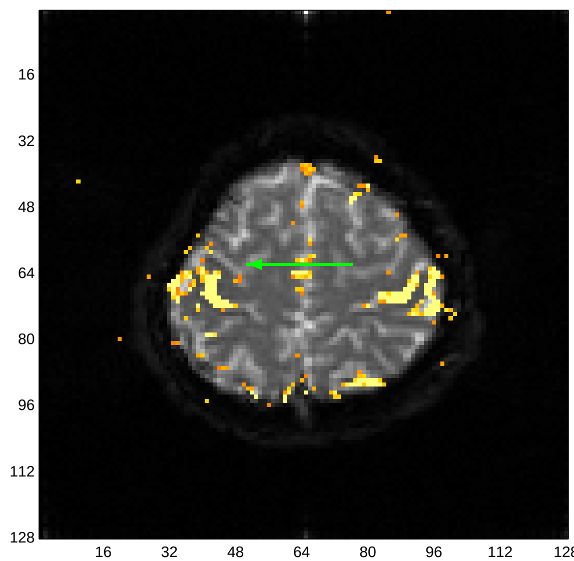
(a) UP/MO



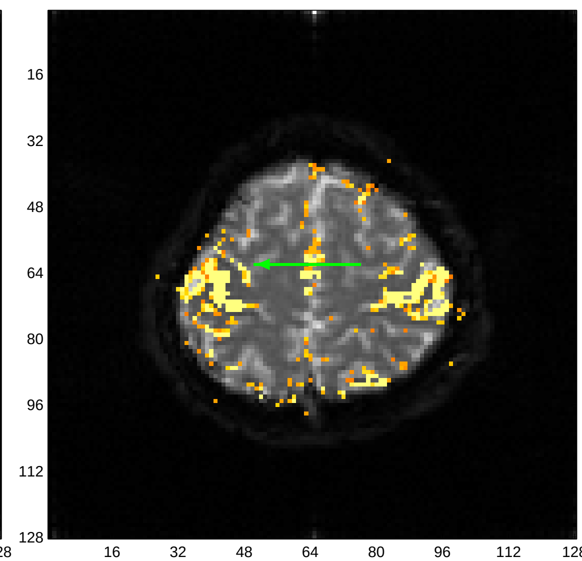
(b) PO



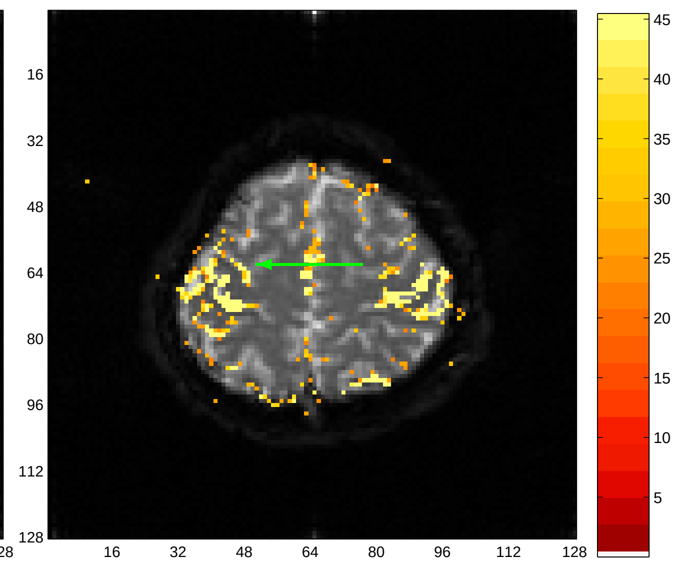
(c) PR



(d) CP

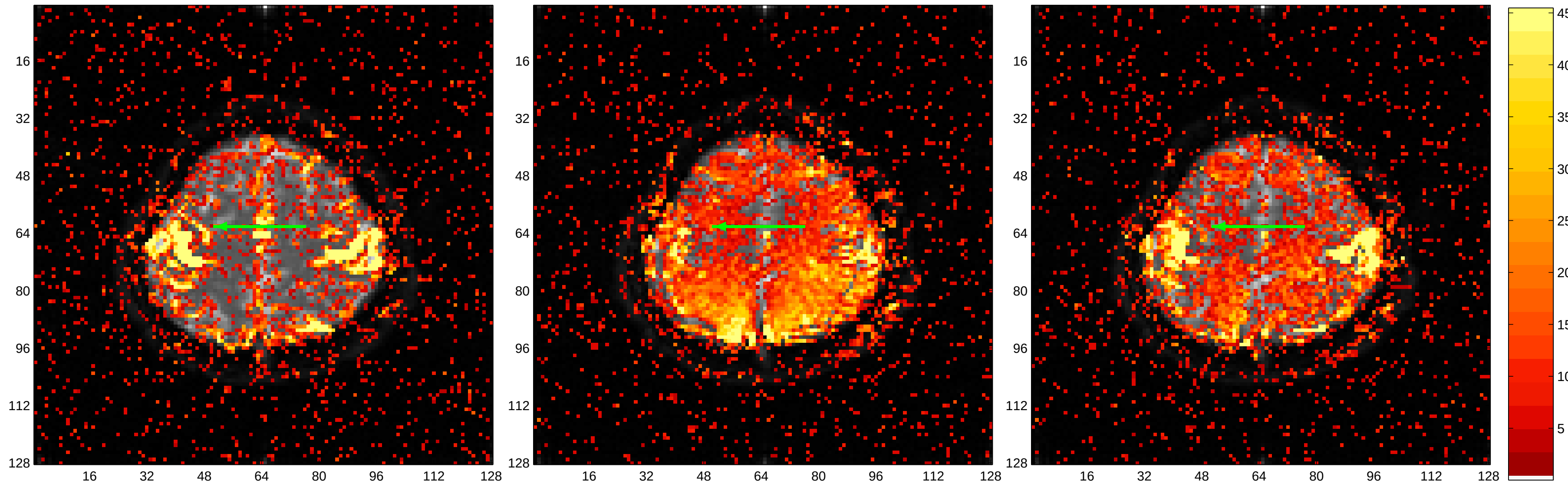


(e) $|TRPC| < 1°$

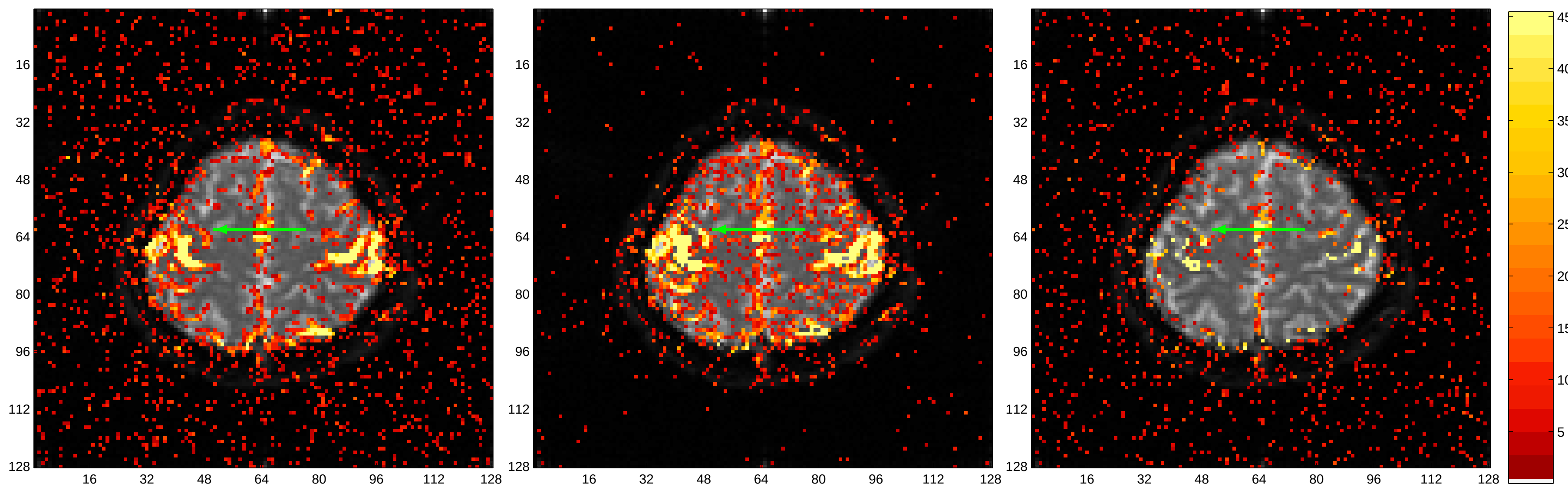


(f) MO & PO 5% Bonf.

Activation Maps 5% Unadjusted Combination Threshold

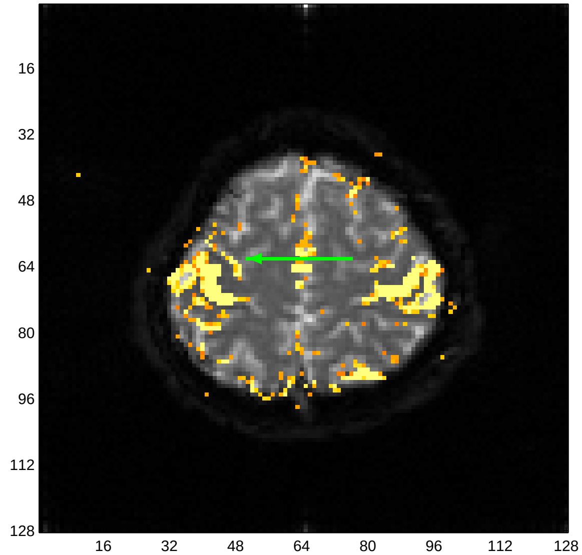


(a) UP/MO (b) PO (c) PR

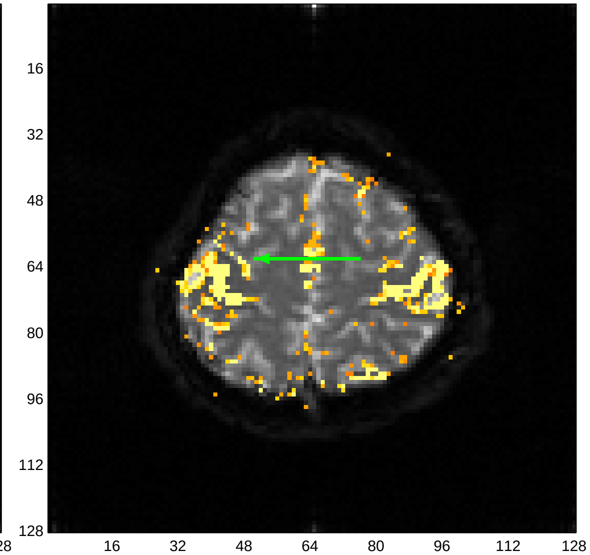


(d) CP (e) $|TRPC| < 1^\circ$ (f) MO & PO 5% Unadj.

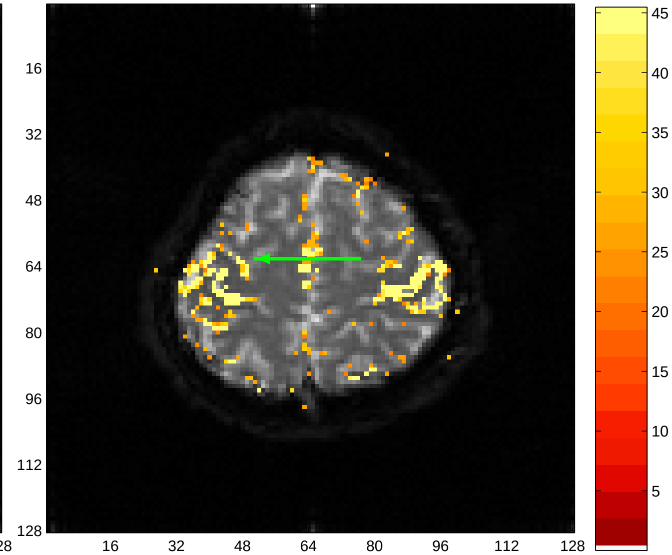
Activation Maps 5% Bonferroni Combination Threshold



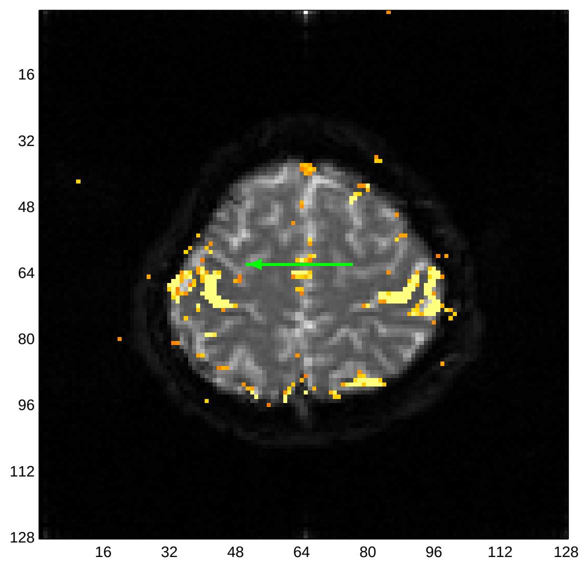
(a) UP/MO



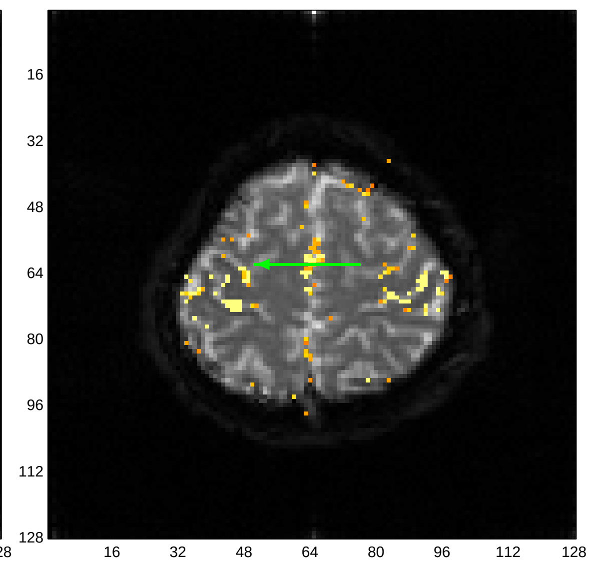
(b) $|TRPC| < 1°$



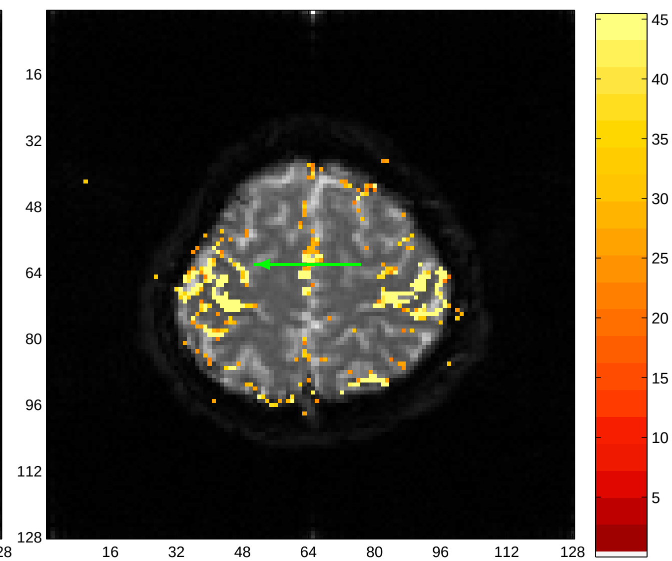
(c) $|TRPC| < 1/2°$



(d) CP

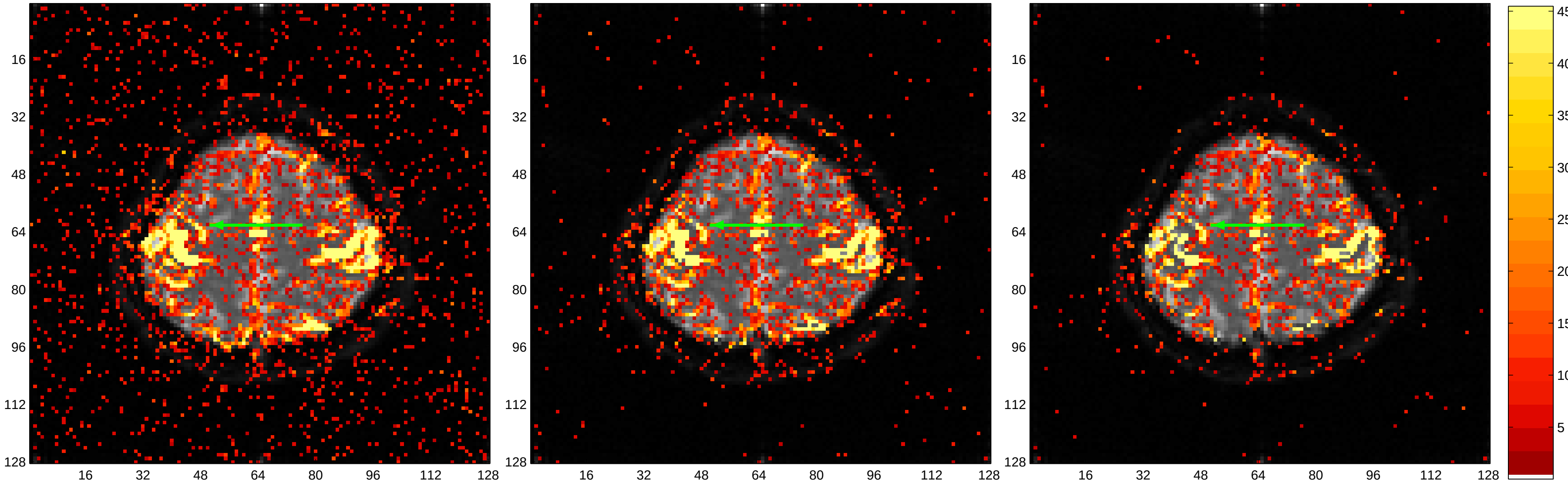


(e) $|TRPC| < 1/4°$

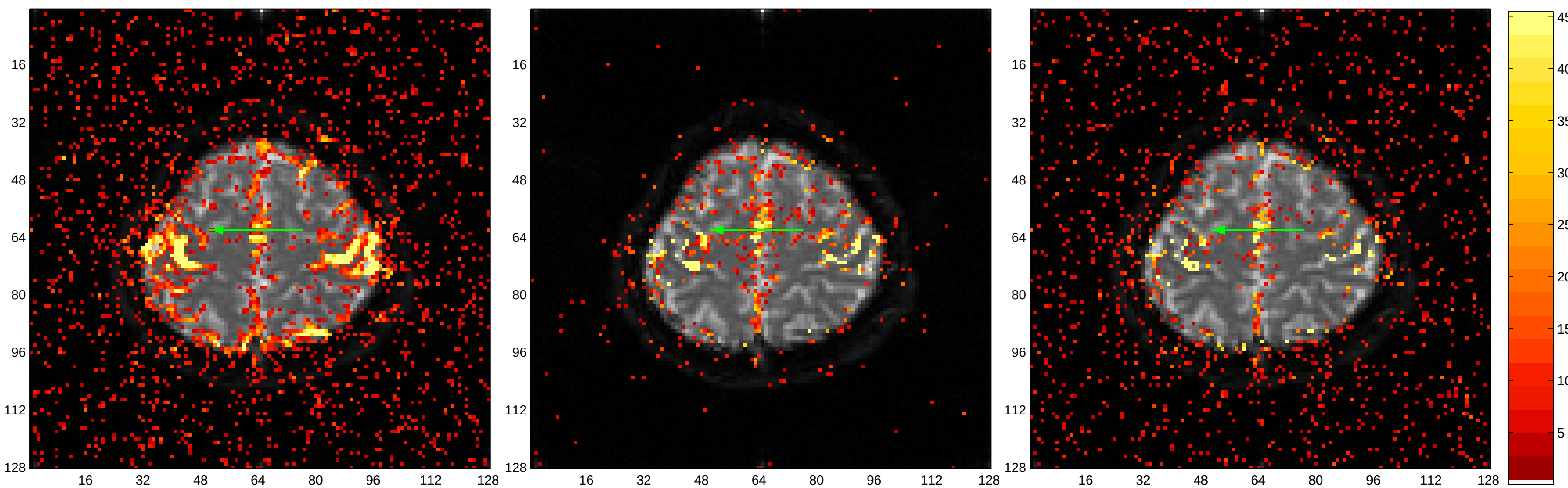


(f) MO & PO 5% Bonf.

Activation Maps 5% Unadjusted Combination Threshold

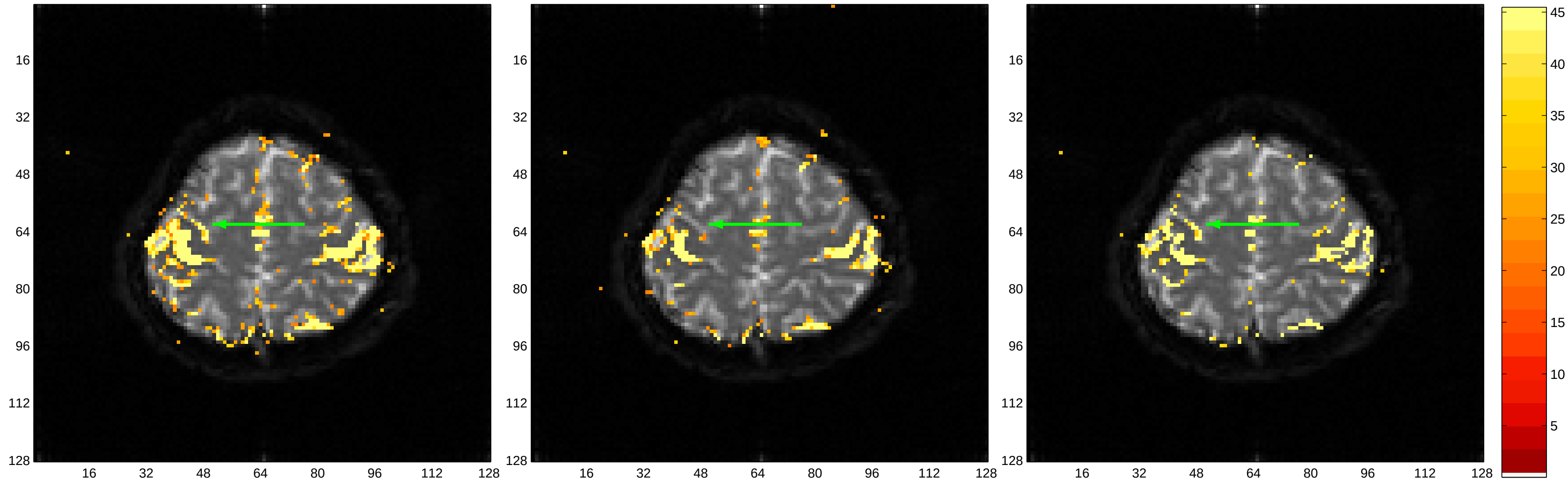


(a) UP/MO (b) $|TRPC| < 1°$ (c) $|TRPC| < 1/2°$



(d) CP (e) $|TRPC| < 1/4°$ (f) MO & PO 5% Unadj.

Activation Maps Combination Threshold



(a) UP/MO 5% Bonf (b) CP 5% Bonf (c) MO & PO Combo Thresh

$\alpha = 5\%$, $p = 16384$ voxels

TRMC$> \chi^2(\alpha/100/p) = 30.67433022214556$

TRPC$< \chi^2(\alpha/p) = 21.78373828128818$

But $p(r_t, \phi_t) \neq p(r_t)p(\phi_t)$!

They should be considered jointly as the complex model does and not independently as the ad hoc thresholds I applied do!

Activations in Human Experimental Data

3T GE Signa LX

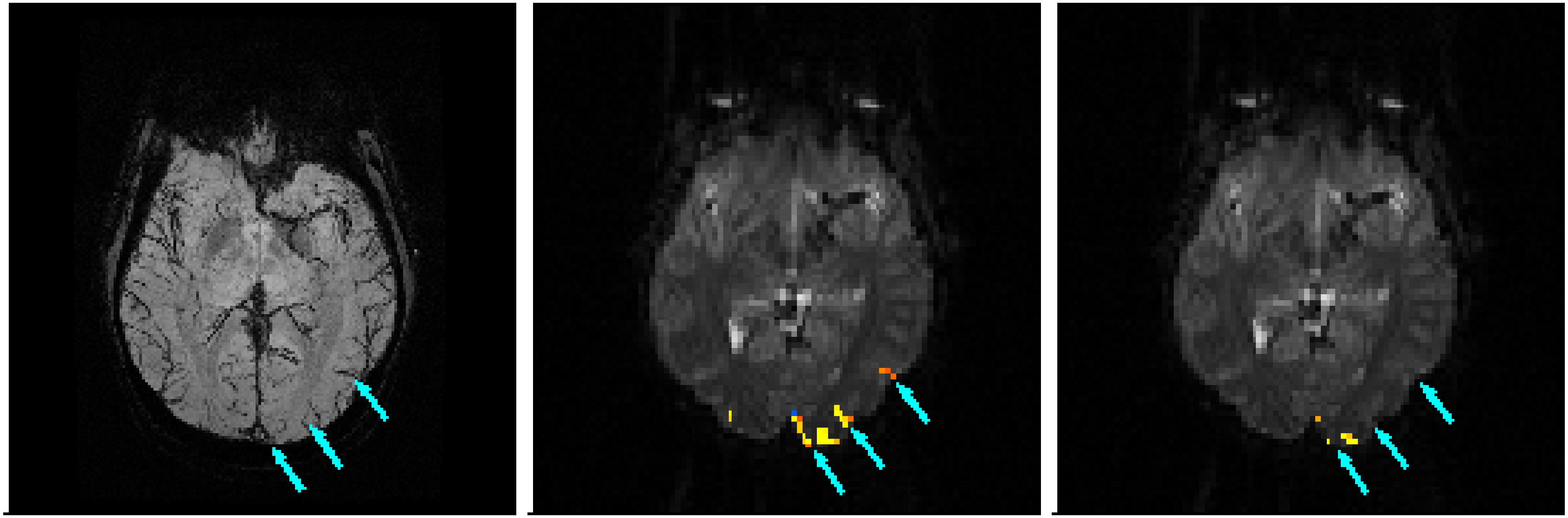
Imaging Parameters: Venogram
FOV $=24\times18\times6$ cm^3
$512\times256\times60$
TR$=$46 ms
TE$=$28 ms
FA$=20^\circ$
minimum intensity projection

Imaging Parameters: EPI
FOV $=24$ cm^2
$96\times96\times19$ (2.5 mm^3)
TR$=$2000 ms
TE$=$45.3 ms
FA$=77^\circ$

Task: RH male, fixation vs. flashing checkerboard at 4 Hz
Design: Block 20s off $+\ 8\times$(16s on$+$16s off);

$*$Nencka Data 2006

Activations in Human Experimental Data



Venogram Anatomical Magnitude-only Complex CP

(a) Minimum intensity projection venogram with veins (arrows)
(b) Magnitude-only activations with correspondence to draining veins
(c) Complex constant phase activations exclude draining vein activations preserving a cluster where no large draining veins are observed.

∗Nencka Data 2006

Complex Magnitude with GLM Phase

We want to see if there is anything in either the magnitude or phase of the observed complex valued time course has a component related to the reference function.

i.e.
$C = (0, ..., 0, 1)$, $\beta = (\beta_0, \beta_1, \cdots, \beta_{q_1})'$
$D = (0, ..., 0, 1)$, $\gamma = (\gamma_0, \gamma_1, \cdots, \gamma_{q_2})'$

MLE's from both under null and alternative hypotheses.

Form GLR test statistic, λ.

Complex Magnitude with GLM Phase

Four readily visible hypotheses for testing.

$$H_a : C\beta \neq 0,\; D\gamma \neq 0$$
$$H_b : C\beta = 0,\; D\gamma \neq 0$$
$$H_c : C\beta \neq 0,\; D\gamma = 0$$
$$H_d : C\beta = 0,\; D\gamma = 0$$

We can combine these four hypotheses in different ways to form specific hypothesis pairs to detect different Mag/Phase changes.

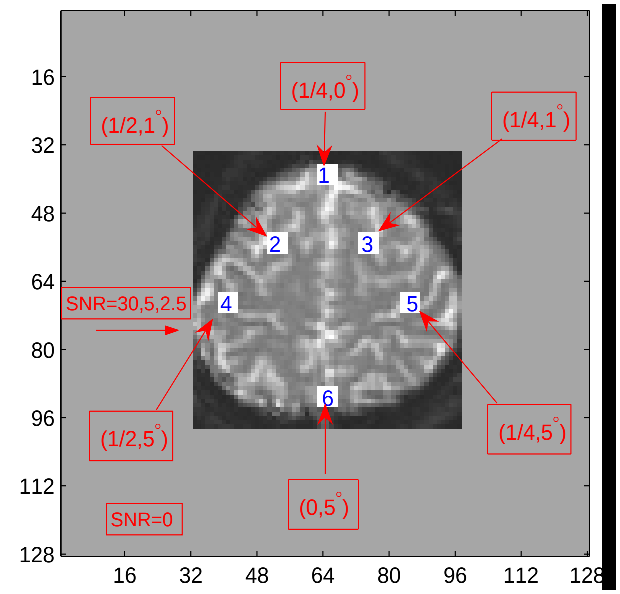
Can write down the likelihood and Log likelihood.

Can maximize the log likelihood under each hypothesis using various Lagrange constraints.

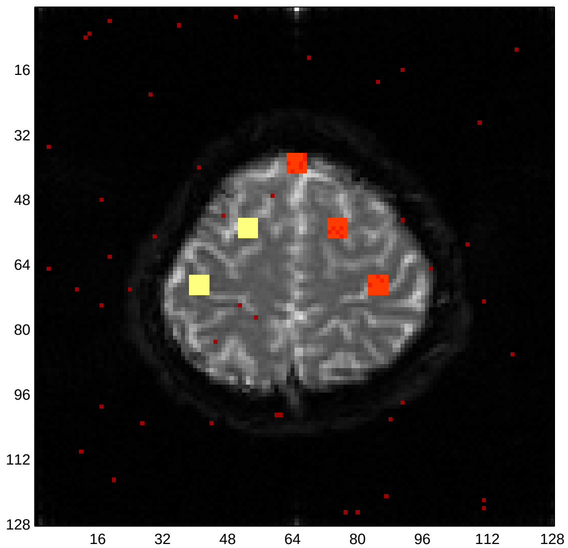
Complex Magnitude with GLM Phase: Simulation

➢ Simulation

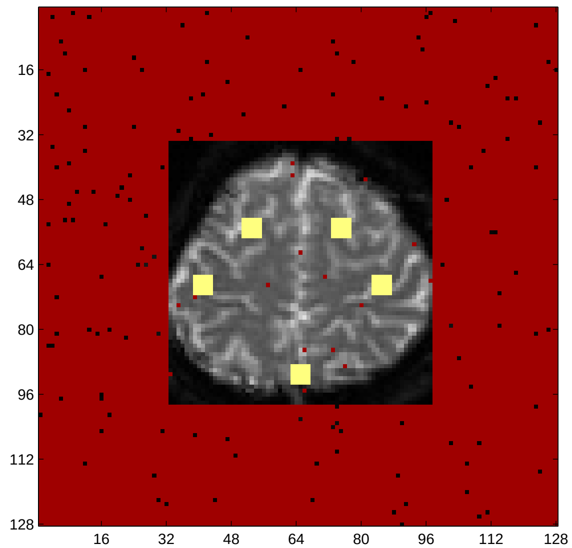
- ○ A 128×128 image was created, central 64×64 represent the brain
- ○ SNR outside brain equal zero, and inside set to 30, 5 or 2.5 in different trials.
- ○ Complex-valued time series were generated for all voxels in the array
- ○ Six ROIs were created in which the time series were made "active" with different CNR-TRPC combinations:
  - 1: $(\frac{1}{4}, 0°)$, 2: $(\frac{1}{2}, 1°)$, 3: $(\frac{1}{4}, 1°)$, 4: $(\frac{1}{2}, 5°)$, 5: $(\frac{1}{4}, 5°)$, 6: $(0, 5°)$



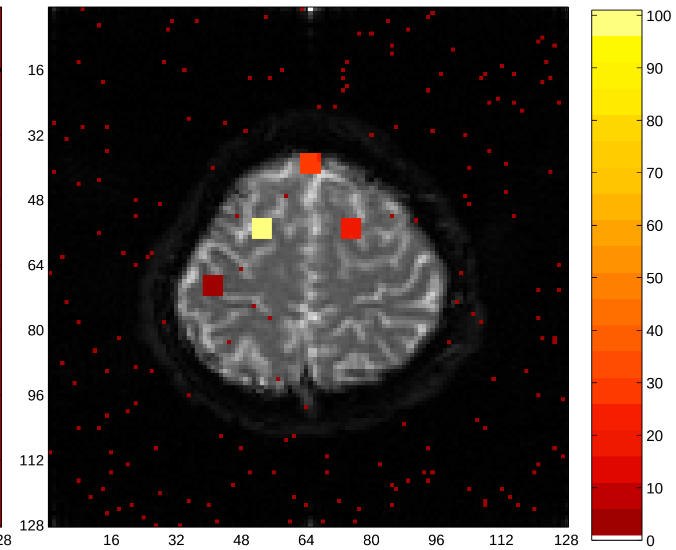
Simulated Data Power Maps: SNR=30



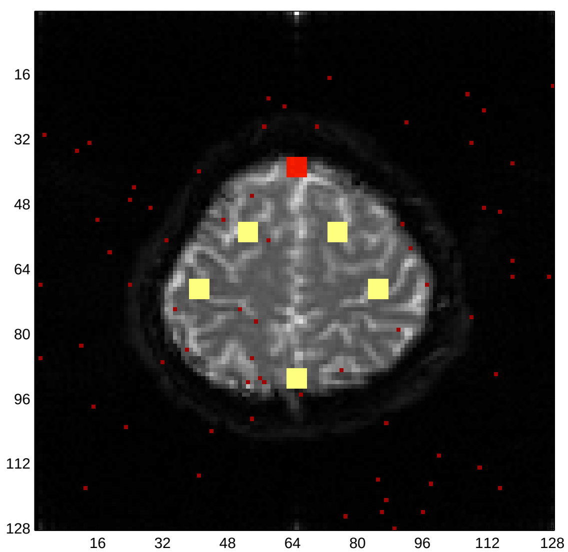
(a) Unrestricted Phase



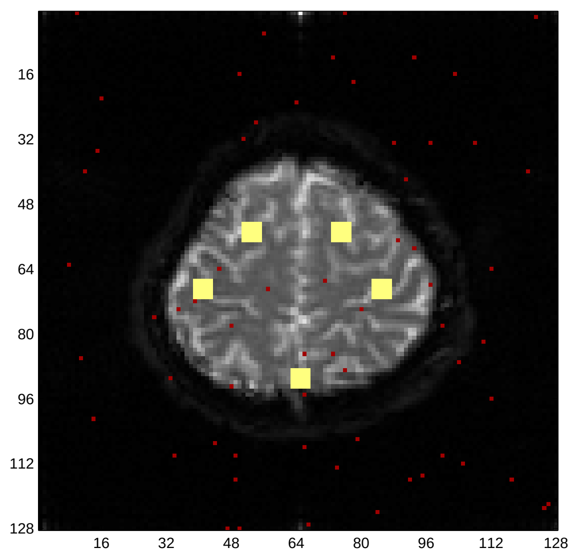
(b) Phase-Only Data



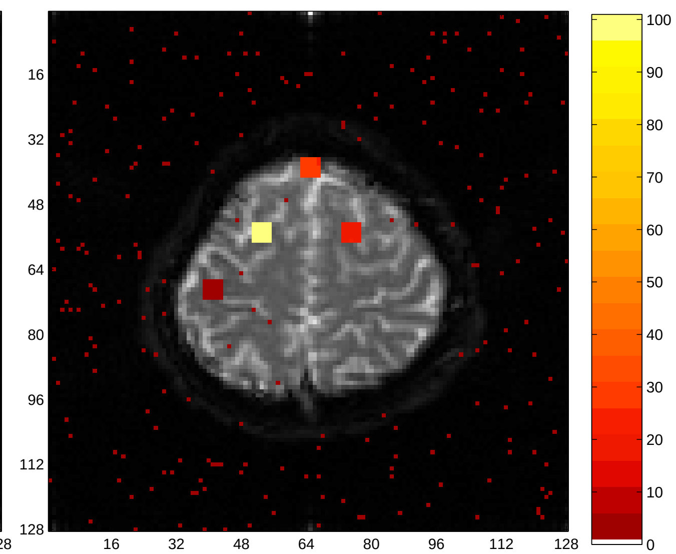
(c) Constant Phase



(d) $C\beta{=}0, D\gamma{=}0; C\beta{\neq}0, D\gamma{\neq}0$

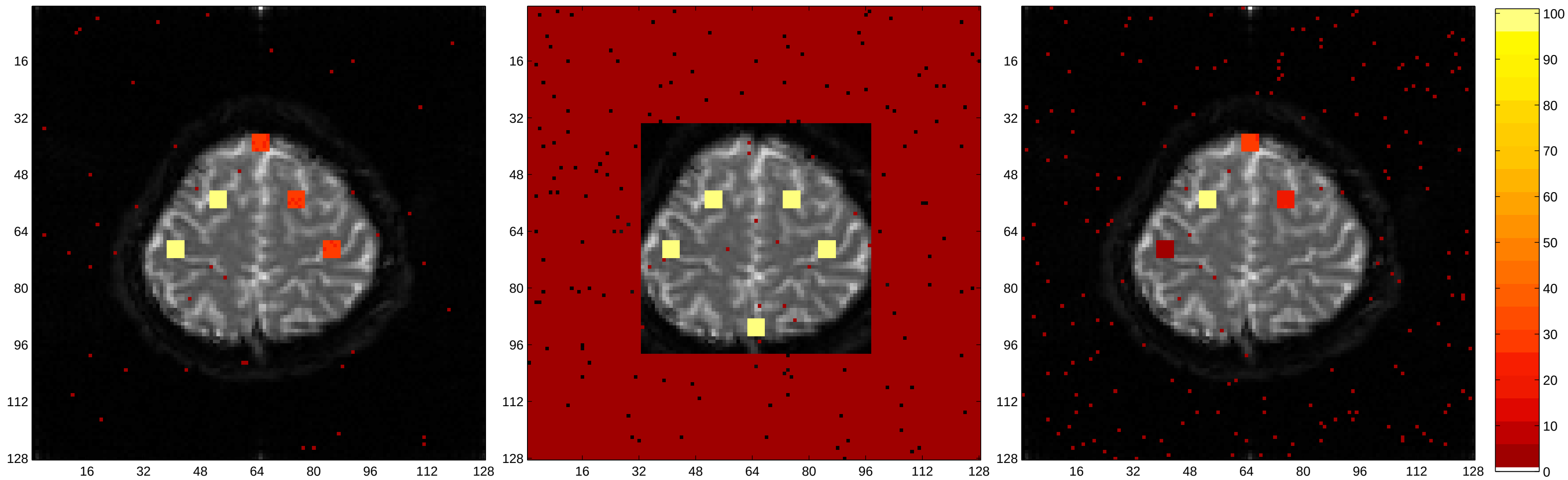


(e) $C\beta{=}0, D\gamma{=}0; C\beta{=}0, D\gamma{\neq}0$

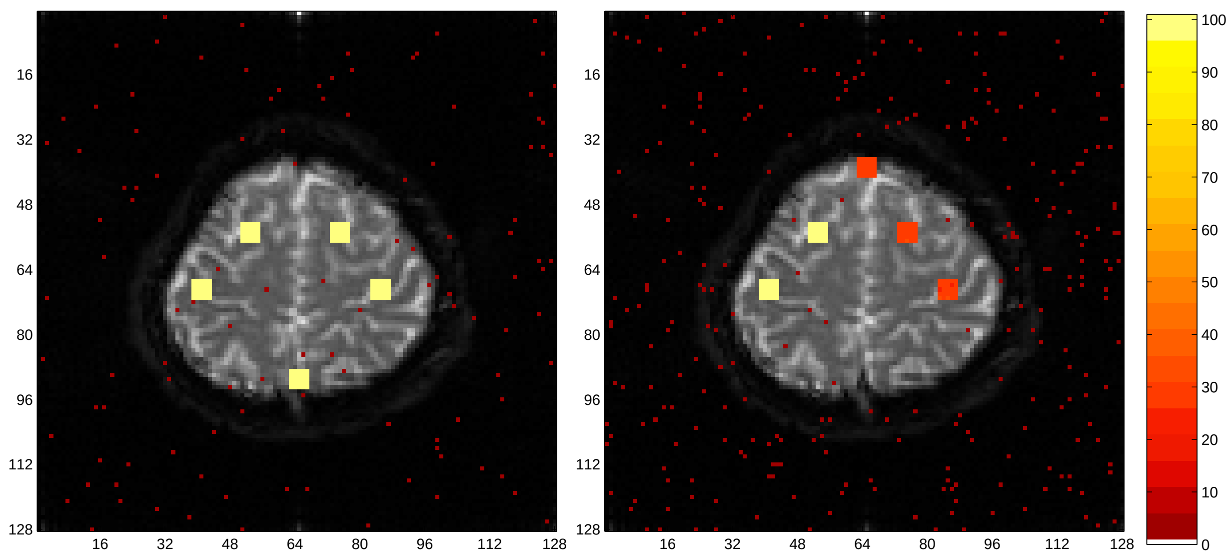


(f) $C\beta{=}0, D\gamma{=}0; C\beta{\neq}0, D\gamma{=}0$

Simulated Data Power Maps: SNR=30

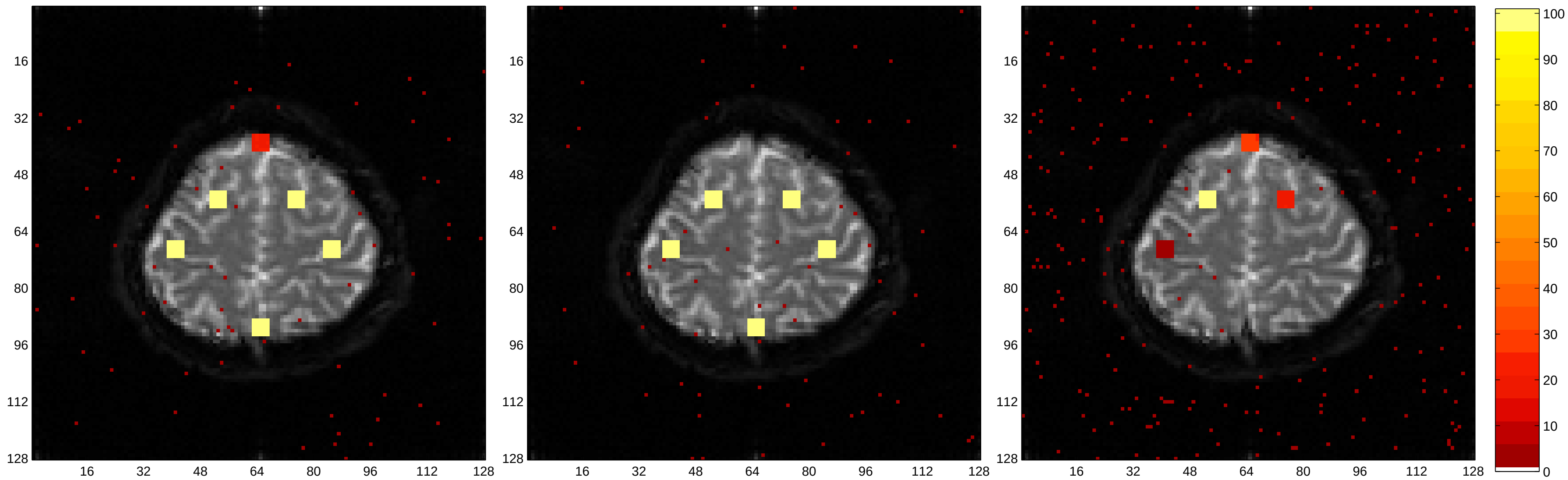


(a) Unrestricted Phase (b) Phase-Only Data (c) Constant Phase

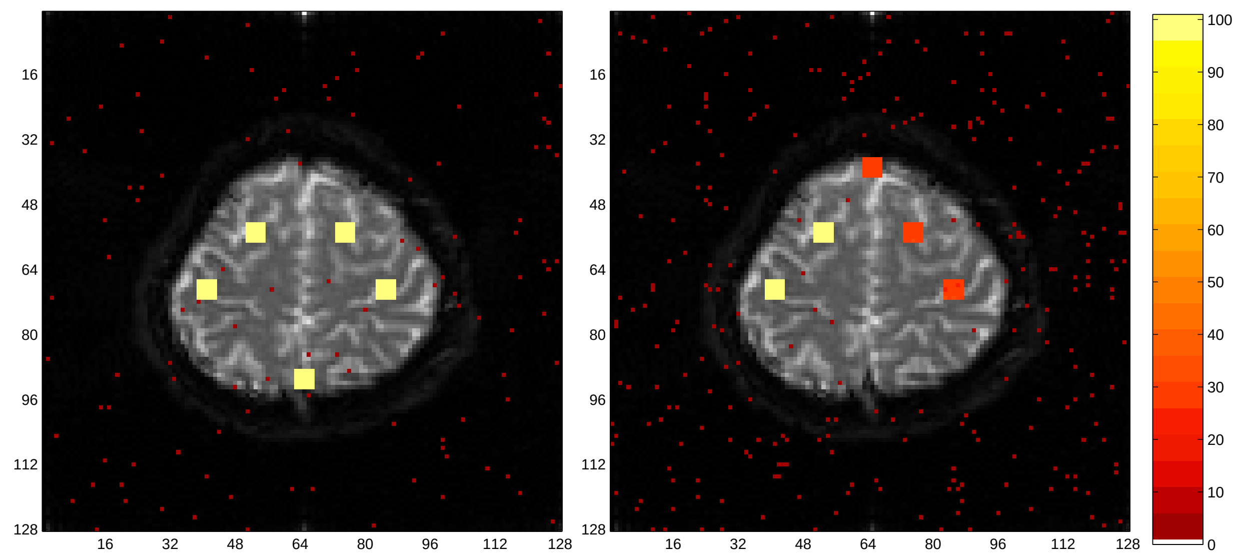


(d) $C\beta\neq0,D\gamma=0;C\beta\neq0,D\gamma\neq0$ (e) $C\beta=0,D\gamma\neq0;C\beta\neq0,D\gamma\neq0$

Simulated Data Power Maps: SNR=30

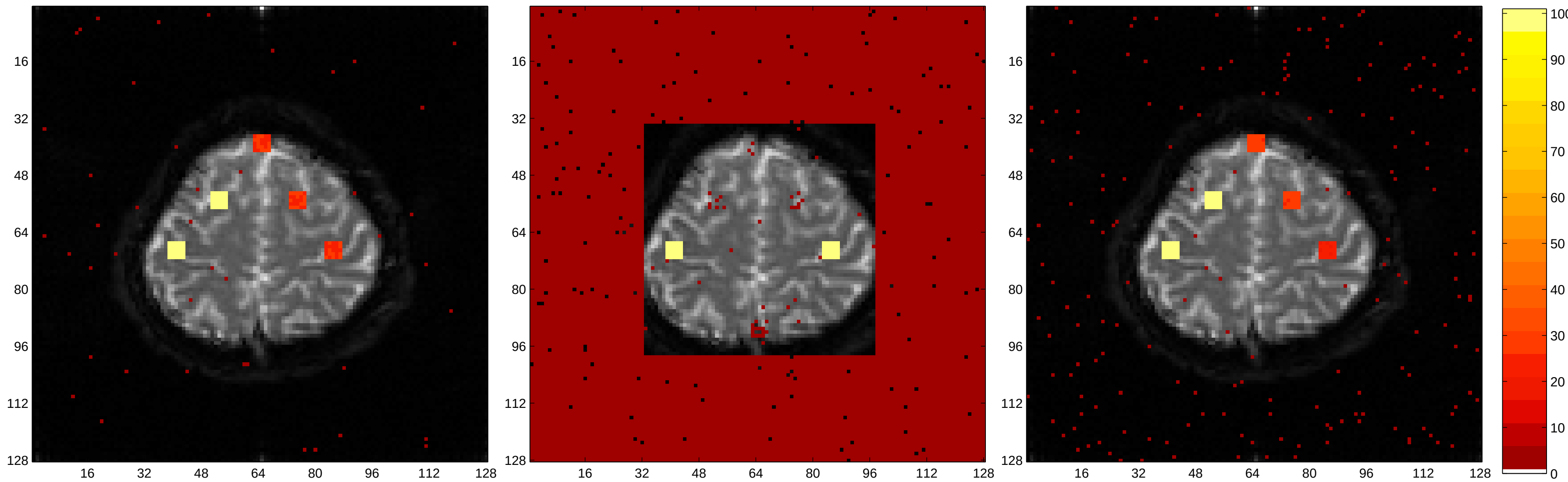


(a) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma\neq$ 0 (b) $C\beta$=0,$D\gamma$=0;$C\beta$=0,$D\gamma\neq$0 (c) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma$=0

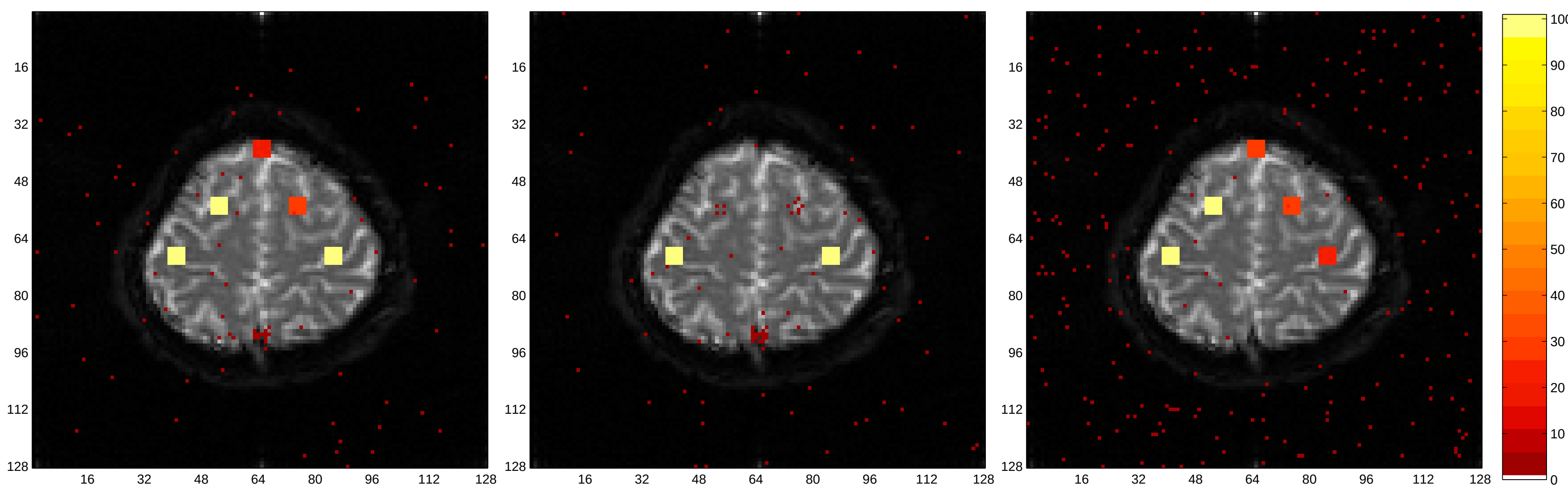


(d) $C\beta\neq$0,$D\gamma$=0;$C\beta\neq$0,$D\gamma\neq$0 (e) $C\beta$=0,$D\gamma\neq$0;$C\beta\neq$0,$D\gamma\neq$0

Simulated Data Power Maps: SNR=5

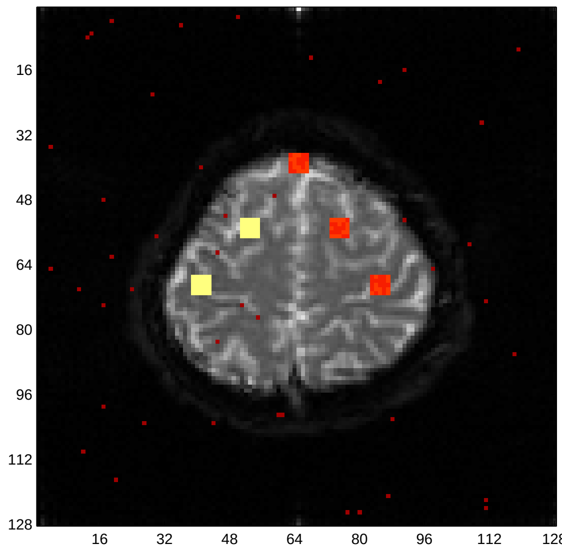


(a) Unrestricted Phase (b) Phase-Only Data (c) Constant Phase

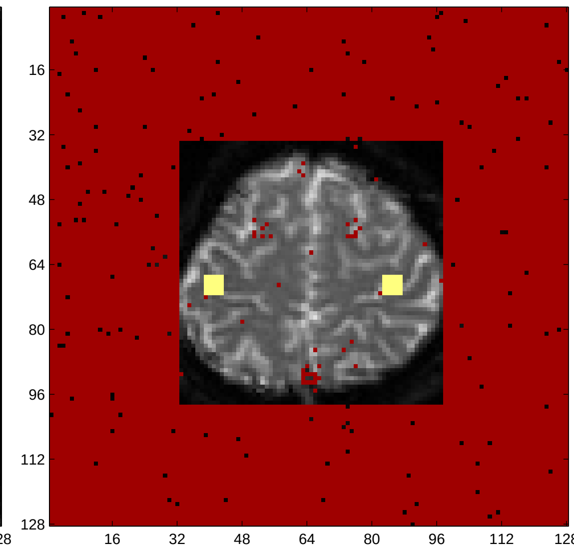


(d) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma\neq$0 (e) $C\beta$=0,$D\gamma$=0;$C\beta$=0,$D\gamma\neq$ 0 (f) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma$= 0

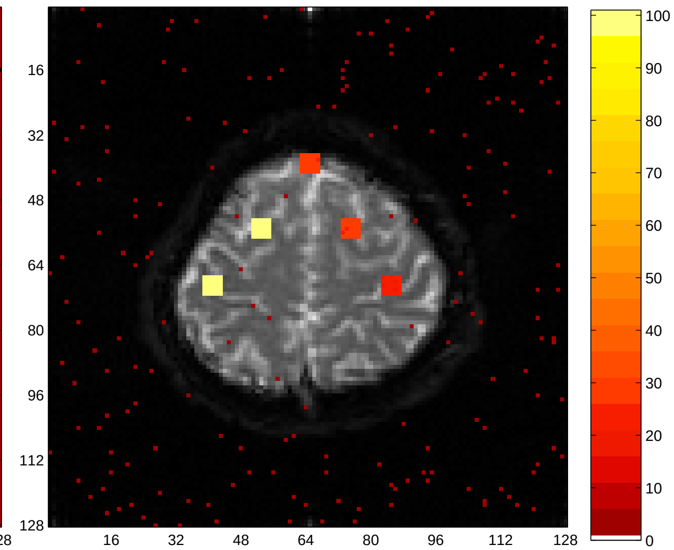
Simulated Data Power Maps: SNR=5



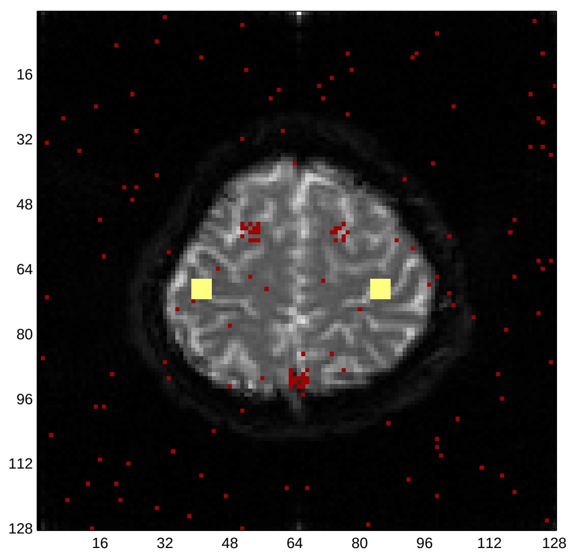
(a) Unrestricted Phase



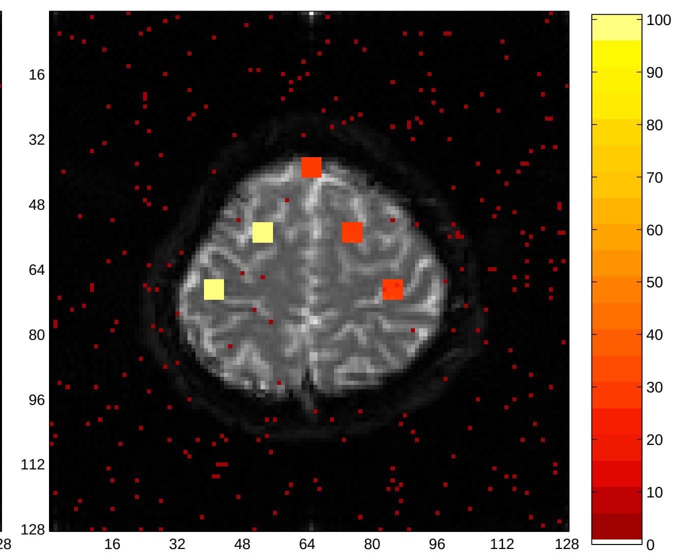
(b) Phase-Only Data



(c) Constant Phase

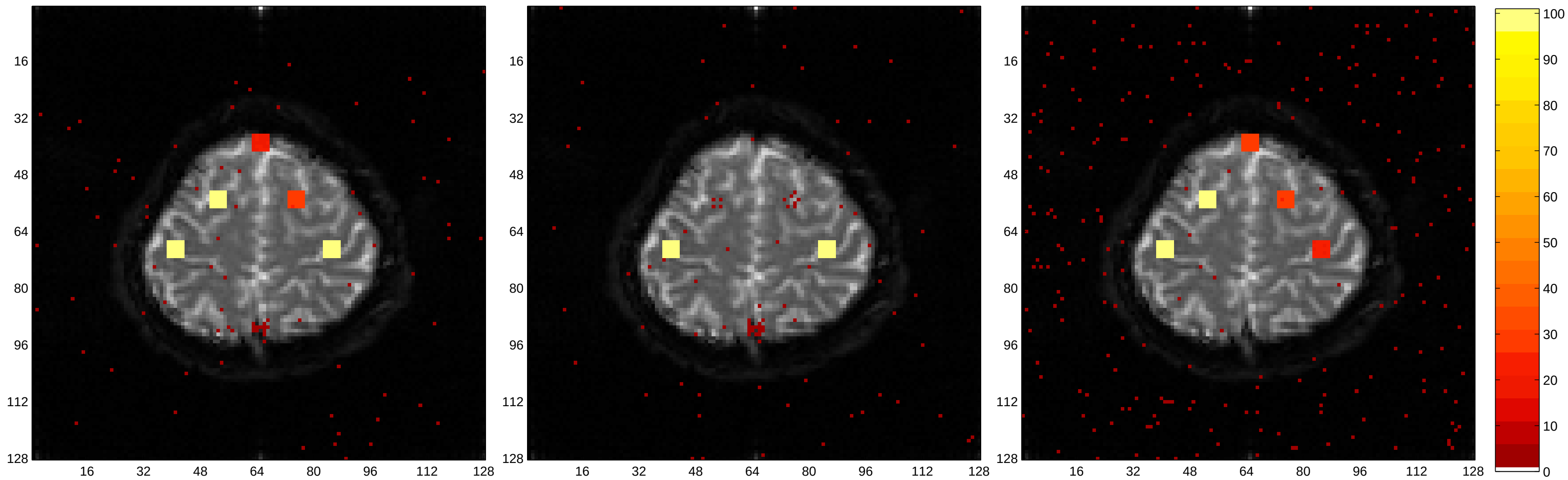


(d) $C\beta\neq 0, D\gamma=0; C\beta\neq 0, D\gamma\neq 0$

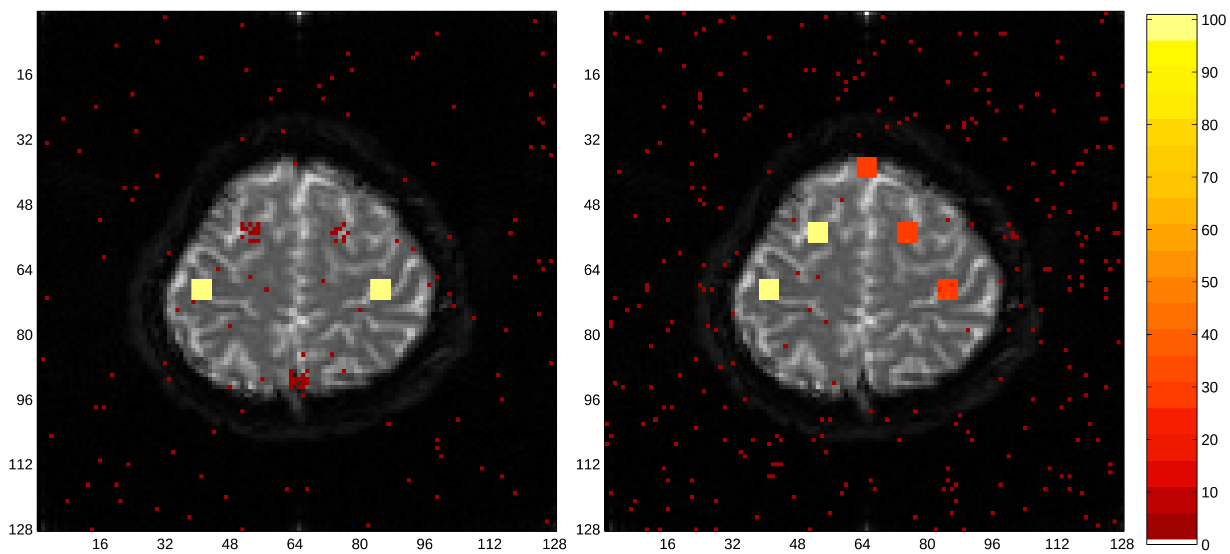


(e) $C\beta=0, D\gamma\neq 0; C\beta\neq 0, D\gamma\neq 0$

Simulated Data Power Maps: SNR=5

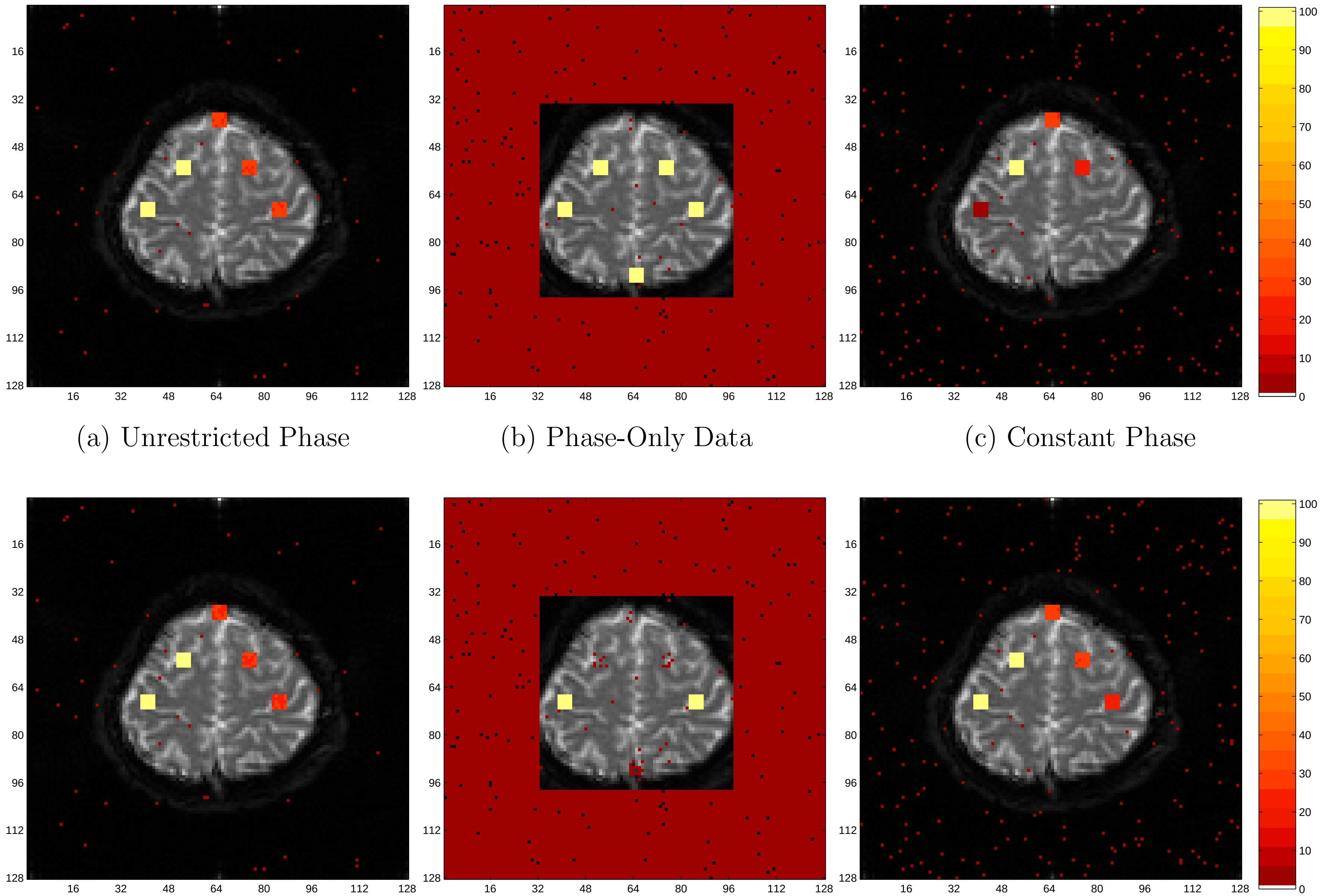


(a) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma\neq$0 (b) $C\beta$=0,$D\gamma$=0;$C\beta$=0,$D\gamma\neq$0 (c) $C\beta$=0,$D\gamma$=0;$C\beta\neq$0,$D\gamma$=0



(d) $C\beta\neq$0,$D\gamma$=0;$C\beta\neq$0,$D\gamma\neq$0 (e) $C\beta$=0,$D\gamma\neq$0;$C\beta\neq$0,$D\gamma\neq$0

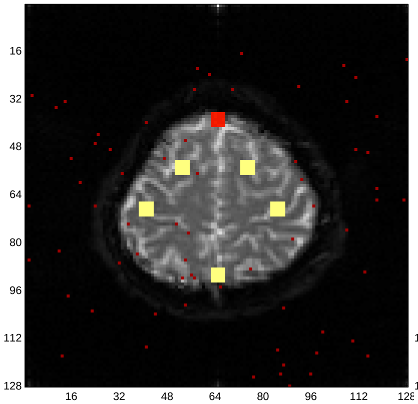
Simulated Data Power Maps: SNR=30 vs SNR=5



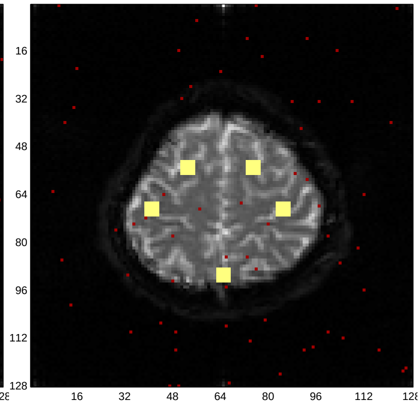
(a) Unrestricted Phase (b) Phase-Only Data (c) Constant Phase

(d) Unrestricted Phase (e) Phase-Only Data (f) Constant Phase

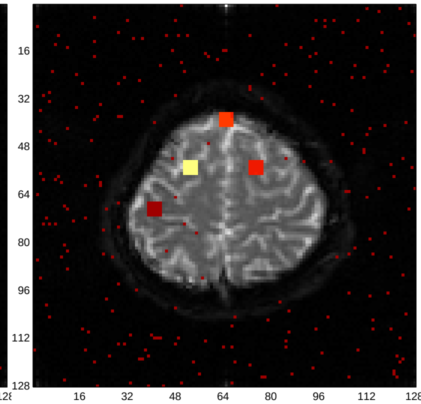
Simulated Data Power Maps: SNR=30 vs SNR=5



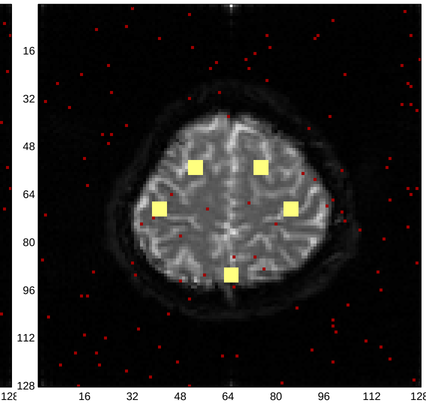
(a) =,=;≠,≠



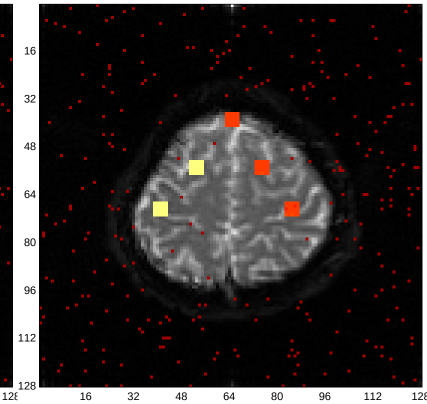
(b) =,=;=,≠



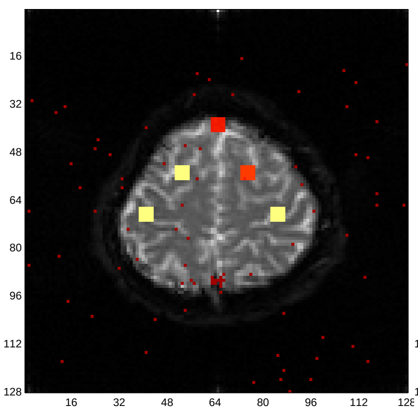
(c) =,=;≠,=



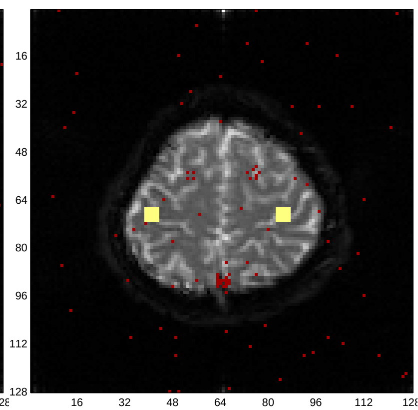
(d) ≠,=;≠,≠



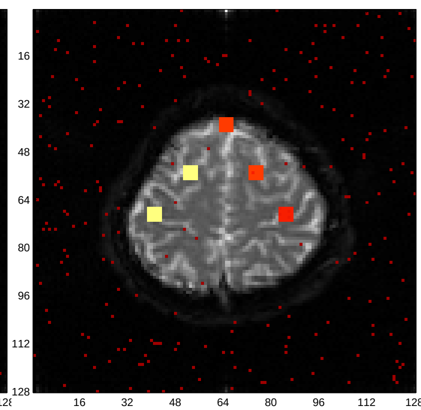
(e) =,≠;≠,≠



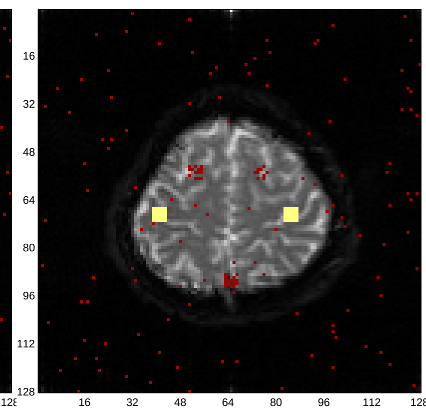
(f) =,=;≠,≠



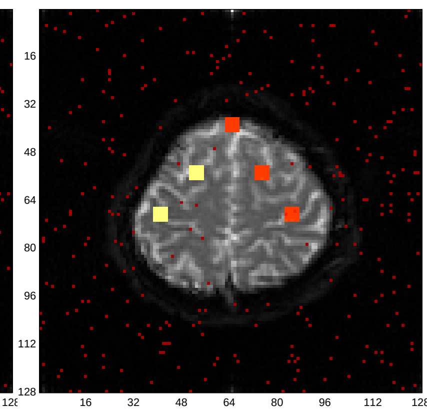
(g) =,=;=,≠



(h) =,=;≠,=



(i) ≠,=;≠,≠



(j) =,≠;≠,≠

Discussion

Complex Image Reconstruction Review.

Phase Information.

Complex Statistical Activation Methods.

Complex Magnitude with Constant Phase.

Complex Magnitude with GLM Phase.

Further research is needed.

Thank You.

Should complex activation be part of the future of fMRI analysis?

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