Statistical Analysis of Functional ASL Images

Daniel B. Rowe, Ph.D.

Department of Mathematics, Statistics, and Computer Science

Department of Biophysics

Department of EE and CS

Outline:

1. Control/Label Images
2. GLM Statistical Modeling - Magnitude
3. GLM Statistical Modeling - Complex
4. ASL Activation Results
5. Discussion

1. Control/Label Images

ASL images come in Control/Label pairs with task.

Control	Label	Control	Label	…	Control	Label	
1	2	3	4	…	n-1	n	TR
y_1	y_2	y_3	y_4	…	$y_{n\text{-}1}$	y_n	

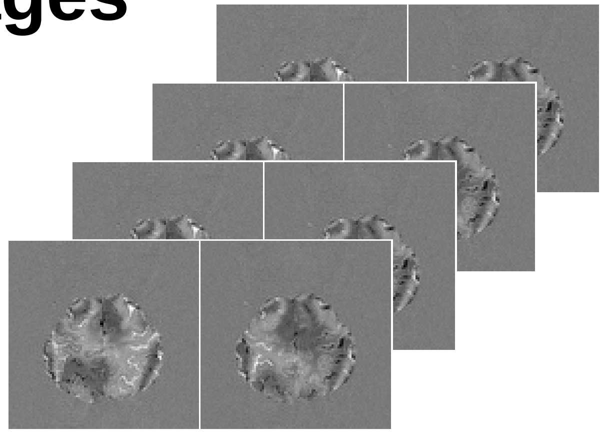
These pairs are often subtracted with the task effect modeled and significance determined.

1. Control/Label Images

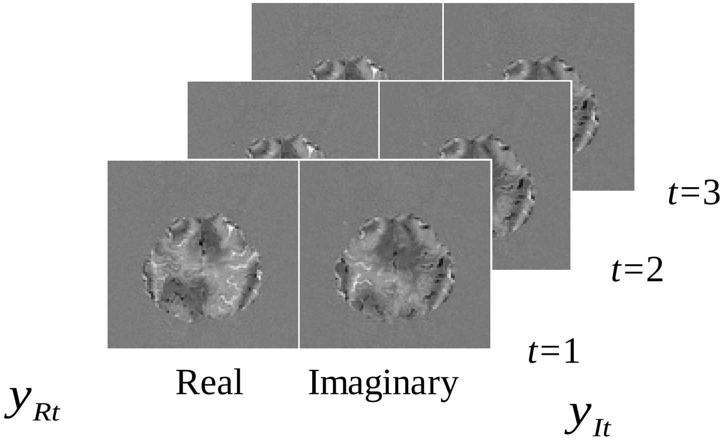
Magnetic Resonance Images are generally complex-valued when reconstructed, but converted to magnitude and phase images with the phase generally discarded.

1. Control/Label Images

GRE-EPI nonASL

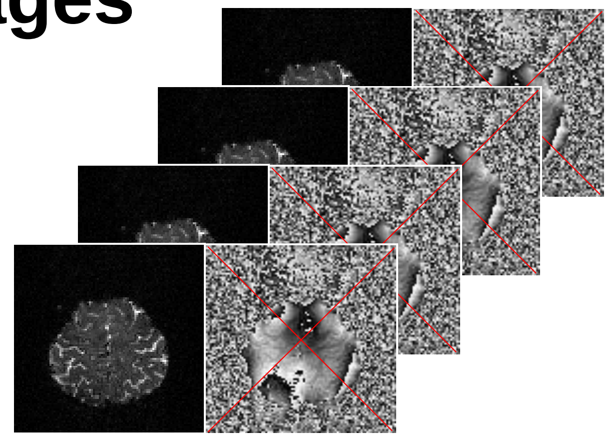


Complex-valued k-space
Complex-valued IFT
Complex-valued Images

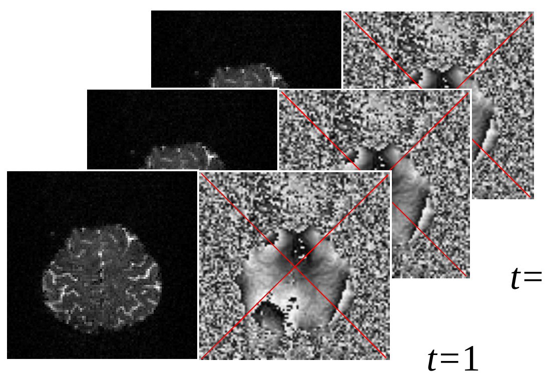


1. Control/Label Images

GRE-EPI nonASL



Phase discarded!
(in nearly all fMRI)



½ of numbers
are discarded
(and processed)

Biological information
in phase through space!
And also through time!

2. GLM Statistical Modeling - Magnitude

The unsubtracted magnitude data at time t

can be described as $y_t = \beta_0 + \beta_1 x_{1t} + \ldots + \beta_q x_{qt} + \varepsilon_t$

where the y_t's are the observed data, the β's are

the regression coefficients, the x_j's are the regressors,

and ε_t is assumed to be normally distributed with

mean zero and variance σ^2.

2. GLM Statistical Modeling - Magnitude

The unsubtracted magnitude data can be described as

$y = X\beta + \varepsilon$ where

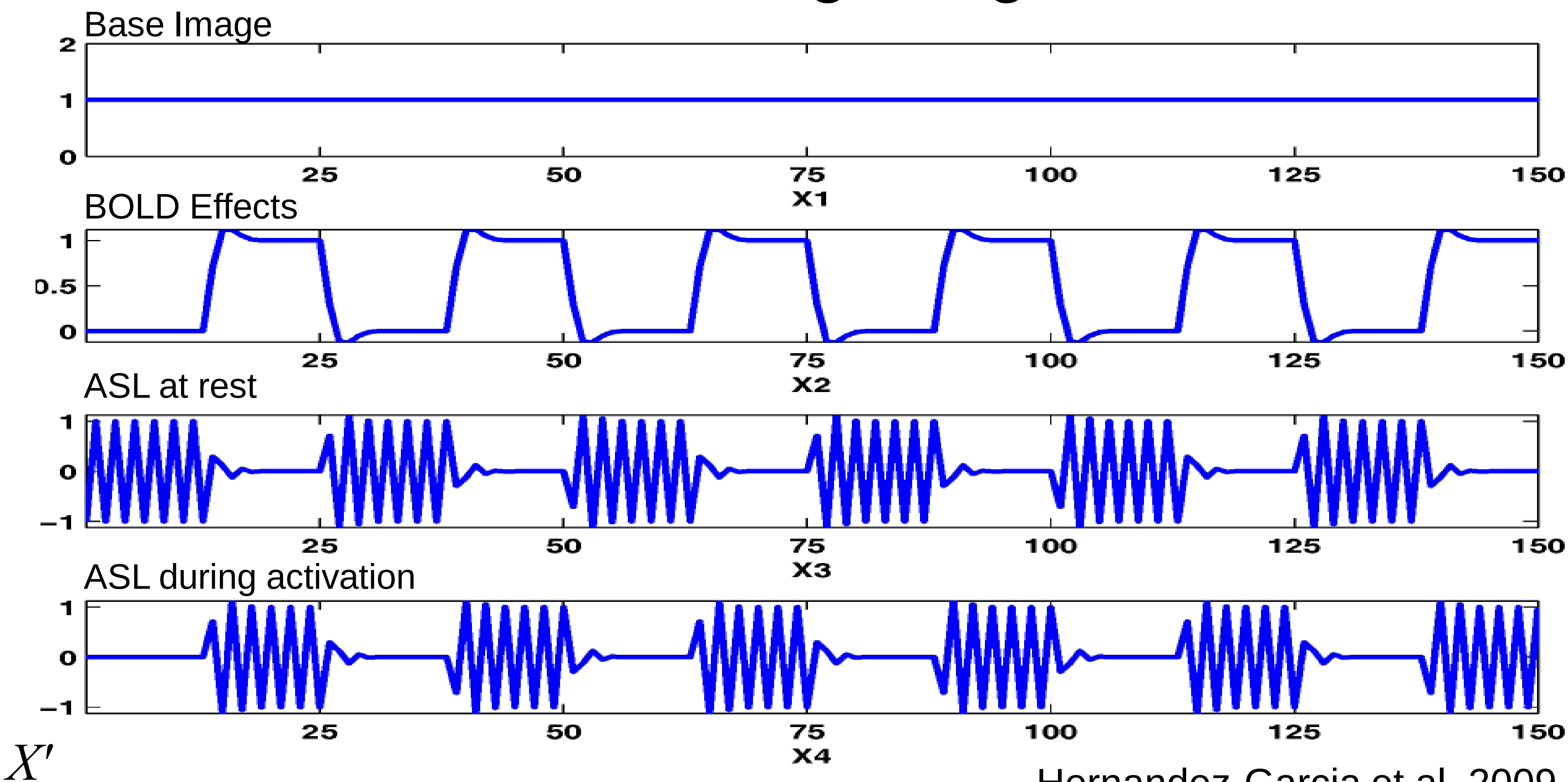
y is a $n\times 1$ vector of the data

X is an $n\times q$ matrix of regressors,

β is a $q\times 1$ vector of regression coefficients and

ε is an $n\times 1$ vector of error.

2. GLM Statistical Modeling - Magnitude



Hernandez-Garcia et al. 2009.

2. GLM Statistical Modeling - Magnitude

With the specification of Gaussian errors, and that the data have been prewhitened or low frequency drift sufficiently modeled using additional regressors, the regression coefficients are estimated as $\hat{\beta} = (X'X)^{-1}X'y$.

Mumford et al, 2006.

2. GLM Statistical Modeling - Magnitude

Statistically speaking, the mean and standard error of the

regression coefficients are $E(\hat{\beta}) = \beta$ and $\mathrm{cov}(\hat{\beta}) = \sigma^2 W$

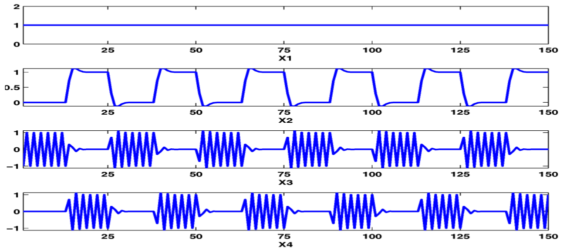
where $W = (X'X)^{-1}$.

$$\hat{\beta} = (X'X)^{-1}X'y$$

Statistical significance of the j^{th} regressor is determined with

$$t_j = \frac{\hat{\beta}_j}{s\sqrt{W_{jj}}}$$

where W_{jj} is the j^{th} diagonal element of W.

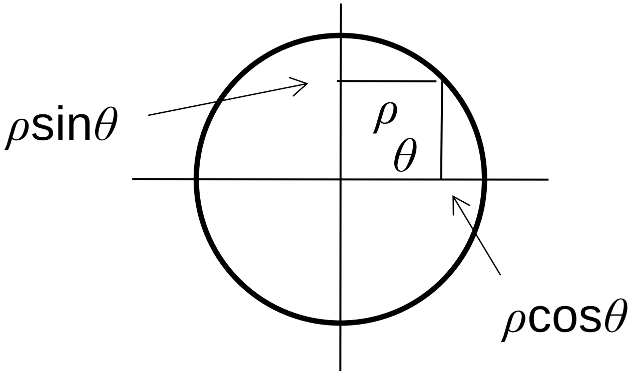


j=2 for activation

2. GLM Statistical Modeling - Complex

The unsubtracted complex data at time t can be described as

$$y_R = \rho\cos\theta + \varepsilon_R$$
$$y_I = \rho\sin\theta + \varepsilon_I$$



y_R and y_I are measurements for the real and imaginary parts

ε_R and ε_I are error terms for the real and imaginary parts

ρ and θ are the population magnitude and phase.

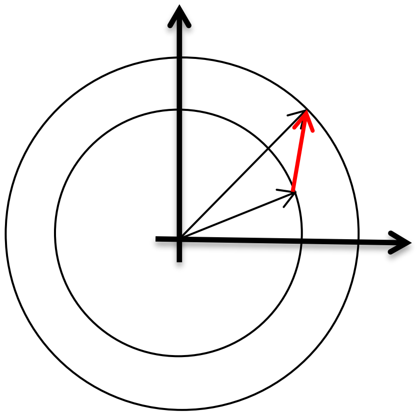
2. GLM Statistical Modeling - Complex

The unsubtracted complex data at time t can be described as

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

$$\rho_t = \beta_0 + \beta_1 x_1 + \cdots + \beta_q x_{qt}$$

$$\theta_t = \gamma_0 + \gamma_1 x_{1t} + \cdots + \gamma_q x_{qt}$$



and thus task related magnitude and/or phase changes in complex data can be determined from β_j and γ_j.

3. GLM Statistical Modeling - Complex

The unsubtracted complex data can be described as

$$\begin{pmatrix} y_R \\ y_I \end{pmatrix} = \begin{pmatrix} CX\beta \\ SX\beta \end{pmatrix} + \begin{pmatrix} \varepsilon_R \\ \varepsilon_I \end{pmatrix}$$ where $$C_t = (\cos\theta_t) \quad S_t = (\sin\theta_t)$$

y_R and y_I are n×1 vectors of the real and imaginary data

X is an n×q matrix of regressors (same as magnitude),

β is a q×1 vector of regression coefficients and

ε_R and ε_I are n×1 vectors of real/imaginary errors.

Rowe, 2005.

3. GLM Statistical Modeling

Statistical significance for task related magnitude

and/or phase activation can be determined via a likelihood

ratio statistic of null (tilde) and alternative (hat) variances

$$-2\log(\lambda) = 2n\log\left(\frac{\tilde{\sigma}^2}{\hat{\sigma}^2}\right)$$

which has a large sample chi-square distribution.

Rowe, 2005.

4. ASL Activation Results

Parameters:
3.0 T Signa LX Excite scanner
PCASL SE-Spiral Sequence
TR=4 s, TE=15 ms, SLTH=7 mm, FOV=24 cm, 64×64

Task:
8 Hz flashing checkerboard: 6×(50 s rest,50 s active)

Processing:
complex data quadratic detrended and ideal filtering of first four frequencies

Hernandez-Garcia et al. 2009.

4. ASL Activation Results

Three Data sets Acquired:

Whole: without arterial suppression or postinversion delays

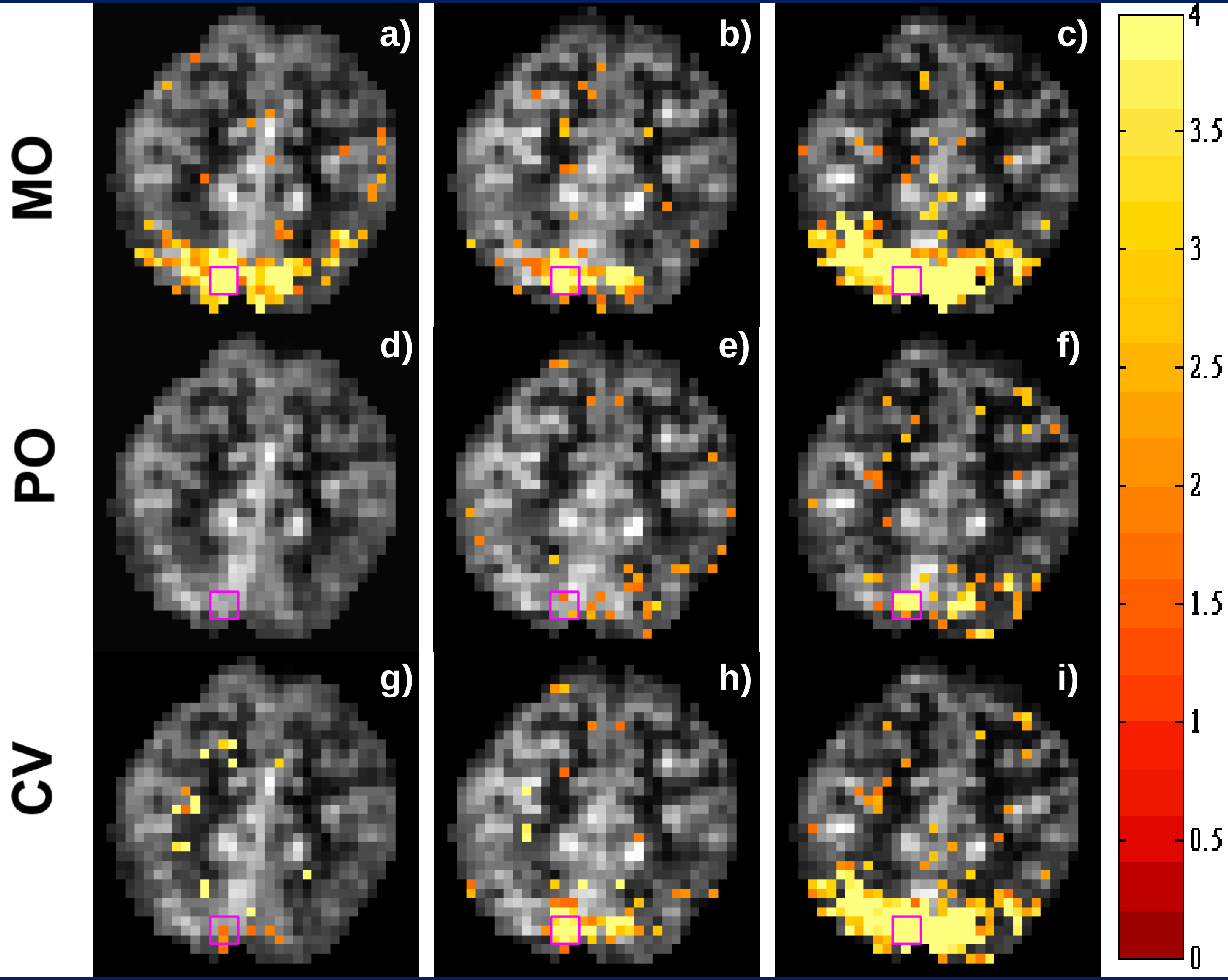
Crush: With flow crushers

PID: Postinversion delay of 1200 ms

Activation was also computed from phase-only (PO) data in addition to magnitude-only (MO) data and complex-valued (CV) data.

Hernandez-Garcia et al. 2009.

4. ASL Activation Results



Crush PID Whole

Hernandez-Garcia et al. 2009.

4. ASL Activation Results

MO activation in all three sets of data a)-c).

PO activation was detected in whole data d)
but not in the crush and PID cases d) and e).
Indicative that activation-induced perfusion changes are accompanied by changes in the phase difference between tagged and control images.

CV activation is clear in the whole and PID data i) and h)
but much reduced in the crush data g).

Hernandez-Garcia et al. 2009.

5. Discussion

ASL fMRI data can be successfully modeled using a GLM with data that is not first differenced.

Magnitude-only and complex-valued models can be applied to ASL fMRI data and CV model can potentially yield additional physiological insights.

Hernandez-Garcia et al. 2009.

Thank You!

References

- Rowe, Logan: A complex way to compute fMRI activation. NIMG, 23:1078-1092, 2004.
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- Mumford, Hernandez-Garcia, Lee, Nichols: Estimation efficiency and statistical power in arterial spin labeling fMRI. NIMG 33:103-114, 2006.
- Hernandez-Garcia, Vazquez, Rowe: Complex-valued analysis of arterial spin labeling based fMRI signals. MRM 62:1597-1608, 2009.