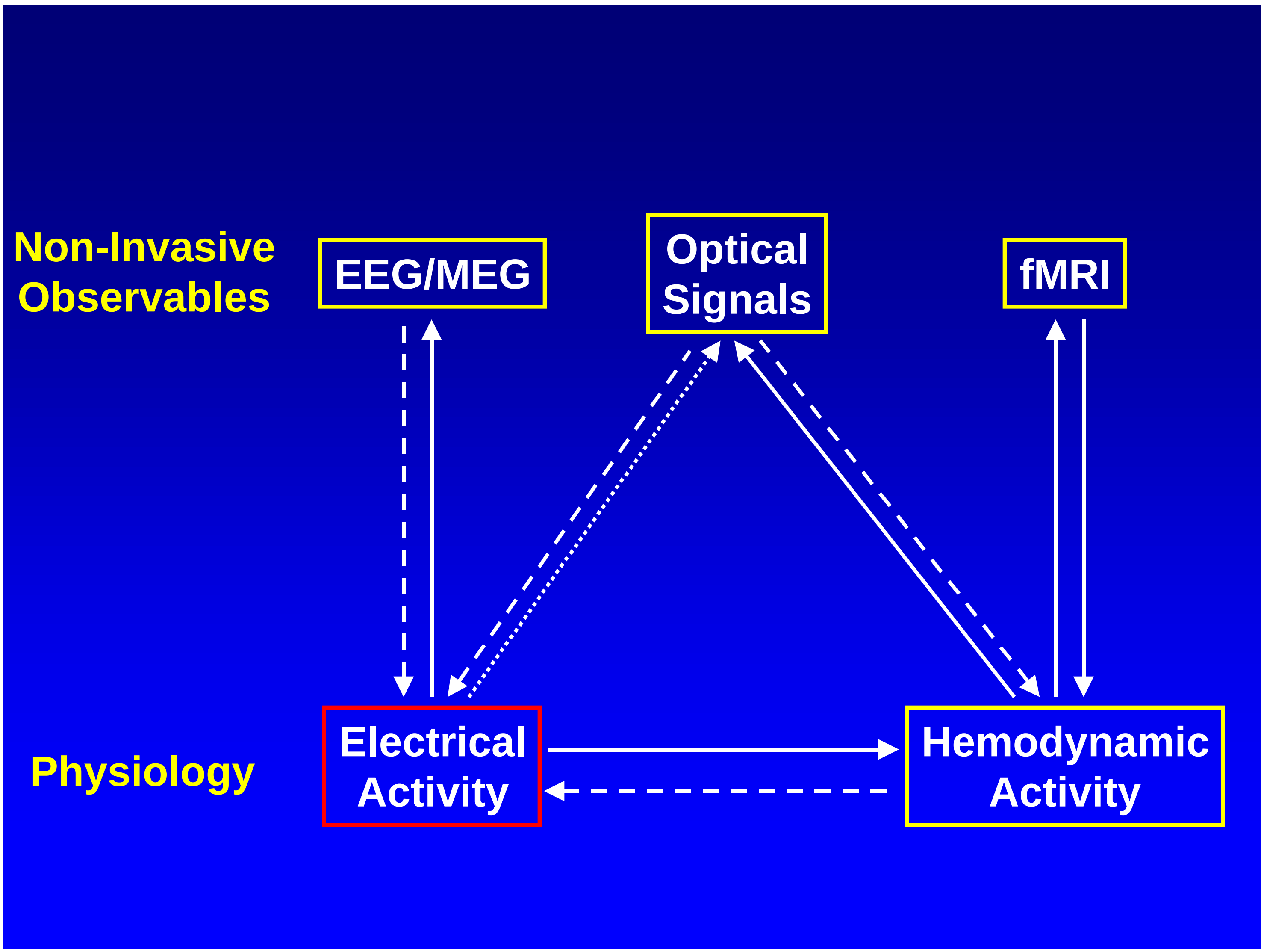

Non-Invasive Observables
EEG/MEG
Optical Signals
fMRI
Physiology
Electrical Activity
Hemodynamic Activity

A General Framework for Multi-Modality Integration

Objective: to determine solution which is maximally consistent with all observables

Maximize:

MAP: $P(\beta_E \mid \mathbf{Y}_{EM}, \mathbf{Y}_{OPT}, \mathbf{Y}_{MRI}) \quad [\, P(\mathbf{Y}_{EM} \mid \beta_E) \_ P(\mathbf{Y}_{OPT} \mid \beta_E) \_ P(\mathbf{Y}_{MRI} \mid \beta_E) \,] \_ P(\beta_E)$

$P(\mathbf{Y}_{EM} \mid \beta_E)$ — EEG/MEG forward solution (Quasistatic Maxwel's eqs, Laplace eq., Biot-Savart's law)

$P(\mathbf{Y}_{OPT} \mid \beta_E) \quad P(\mathbf{Y}_{OPT} \mid \beta_H) \_ P(\beta_H \mid \beta_E)$ — Coupling between electrical activity and optical signals

$P(\mathbf{Y}_{OPT} \mid \beta_H)$ — Optical forward solution (Photon migration thry, Beer-Lambert law, Rad Trans eqs.)

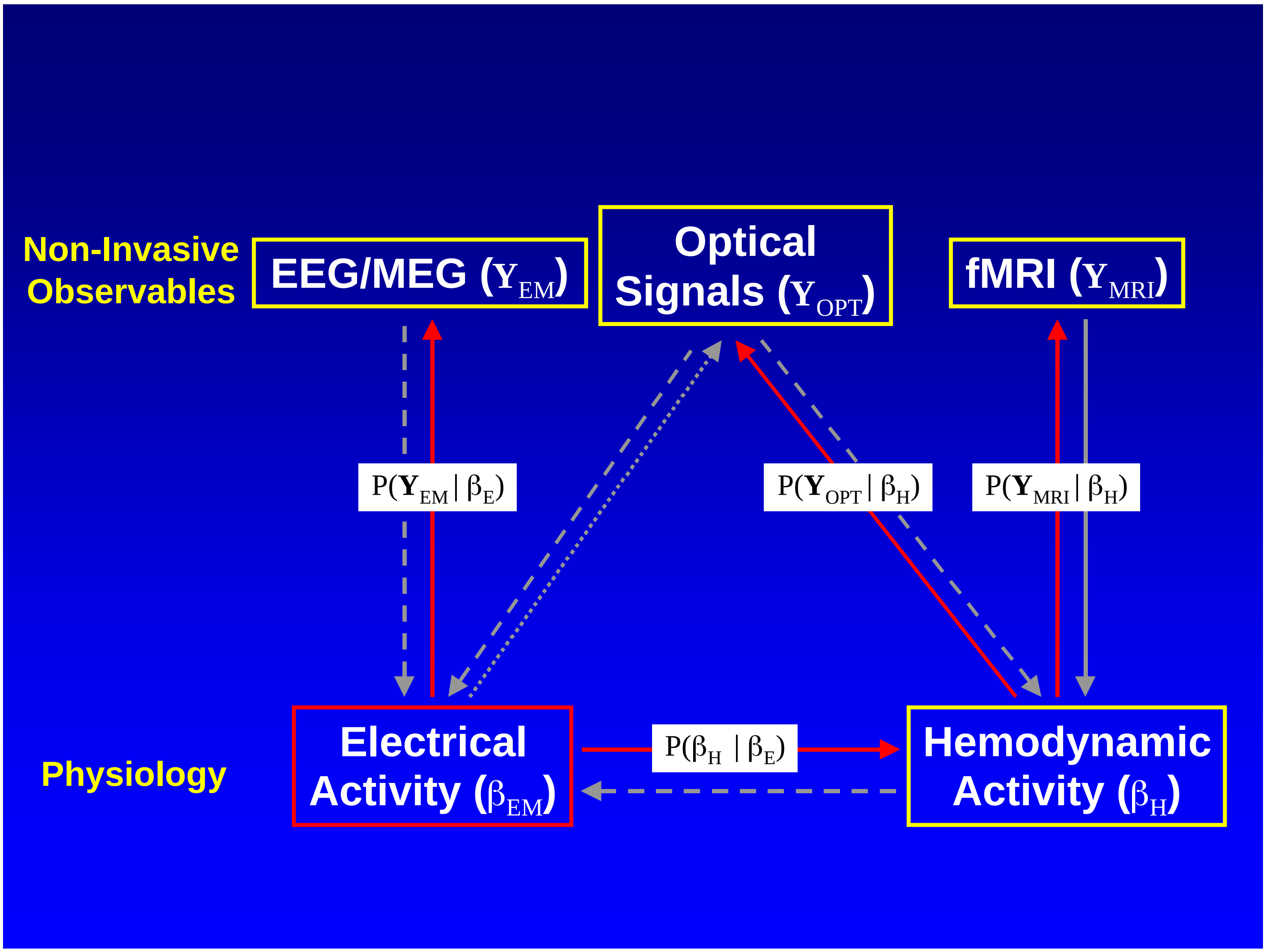
$P(\beta_H \mid \beta_E)$ — Coupling between electrical activity and hemodynamics

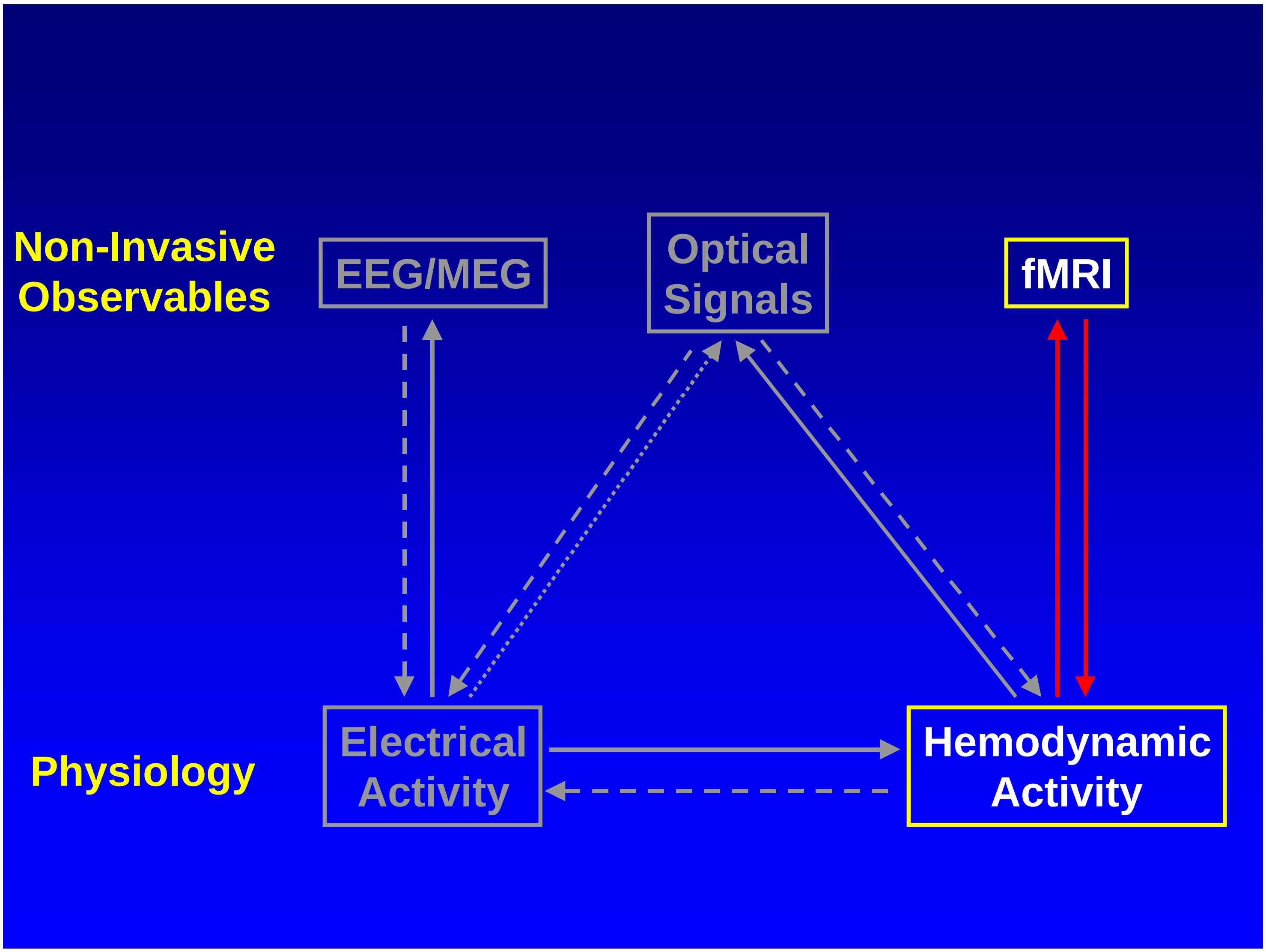
$P(\mathbf{Y}_{MRI} \mid \beta_E) \quad P(\mathbf{Y}_{MRI} \mid \beta_H) \_ P(\beta_H \mid \beta_E)$ — Coupling between electrical activity and fMRI signals

$P(\mathbf{Y}_{MRI} \mid \beta_H)$ — MRI forward solution (Maxwell's eqs., Bloch eqs.)

$P(\beta_H \mid \beta_E)$ — Coupling between electrical activity and hemodynamics

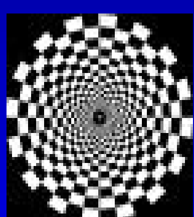
$P(\beta_E)$ — Priors on spatiotemporal patterns of neuronal electrical activity


Non-Invasive Observables
EEG/MEG (Y_{EM})
Optical Signals (Y_{OPT})
fMRI (Y_{MRI})
P($\mathbf{Y}_{EM}$ | β_E)
P($\mathbf{Y}_{OPT}$ | β_H)
P($\mathbf{Y}_{MRI}$ | β_H)
Physiology
Electrical Activity (β_{EM})
P(β_H | β_E)
Hemodynamic Activity (β_H)


Non-Invasive
Observables
EEG/MEG
Optical
Signals
fMRI
Physiology
Electrical
Activity
Hemodynamic
Activity

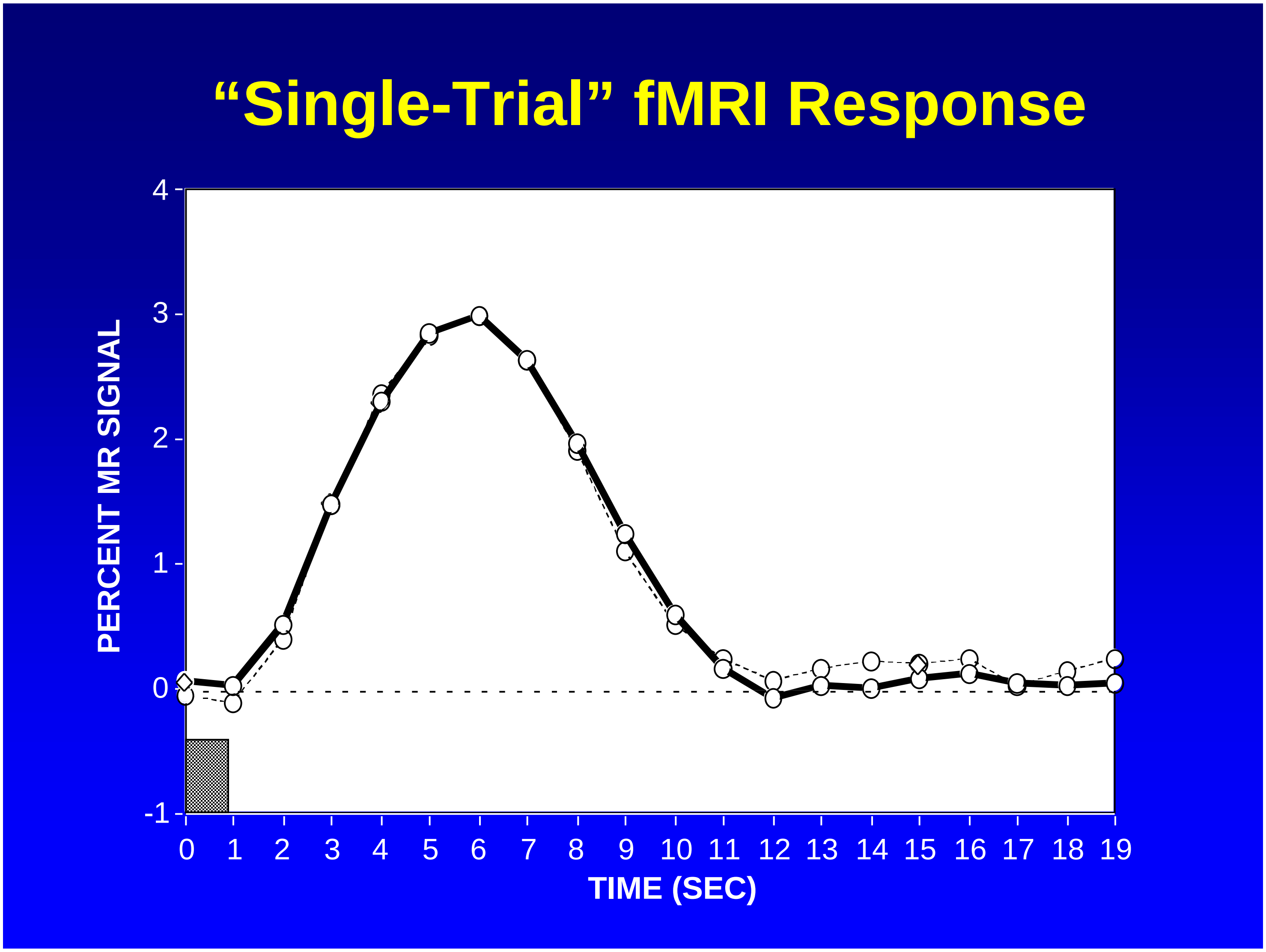
Measurement of fMRI "Impulse Response"

1 sec
on

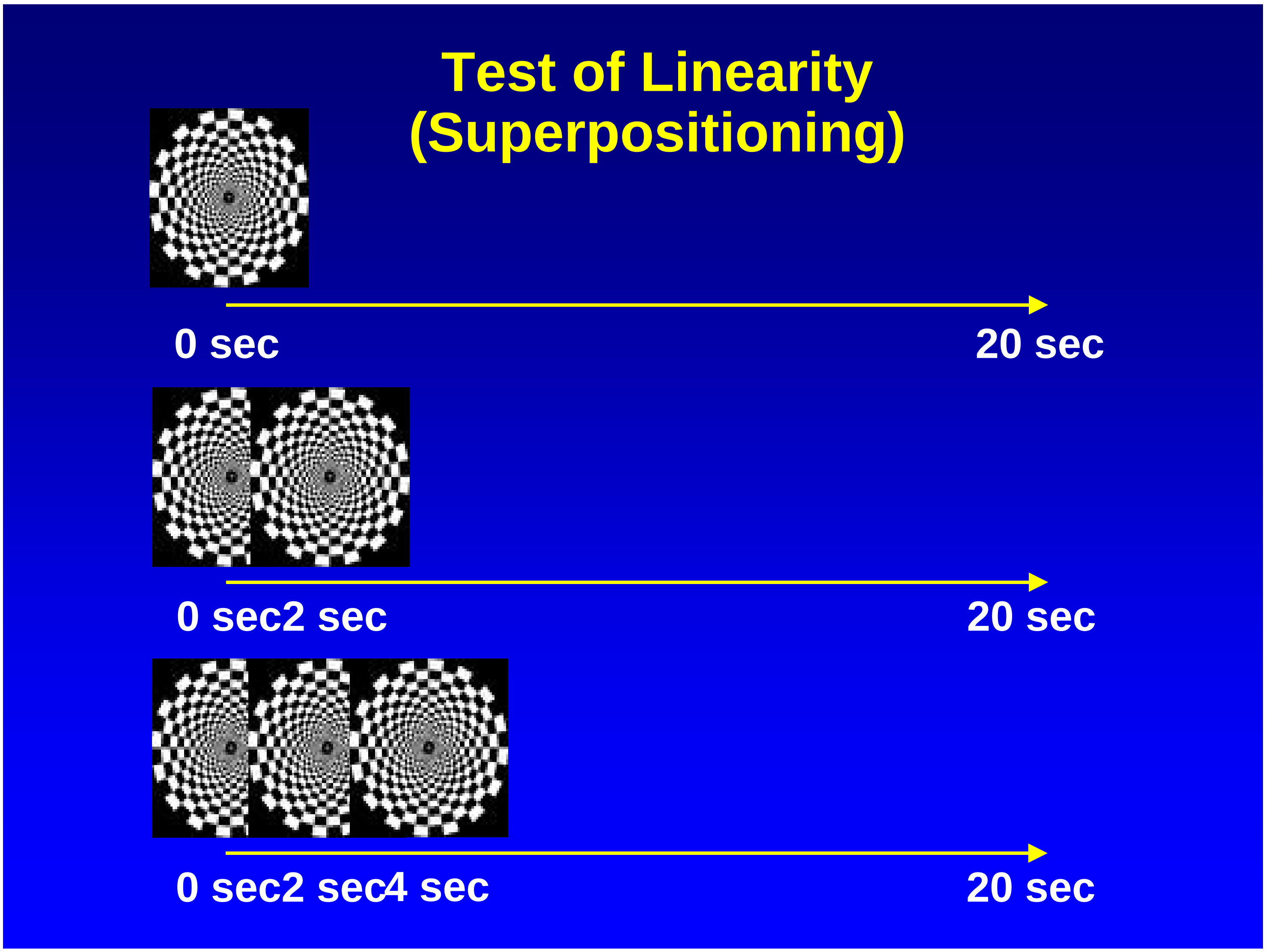


0 sec

20 sec

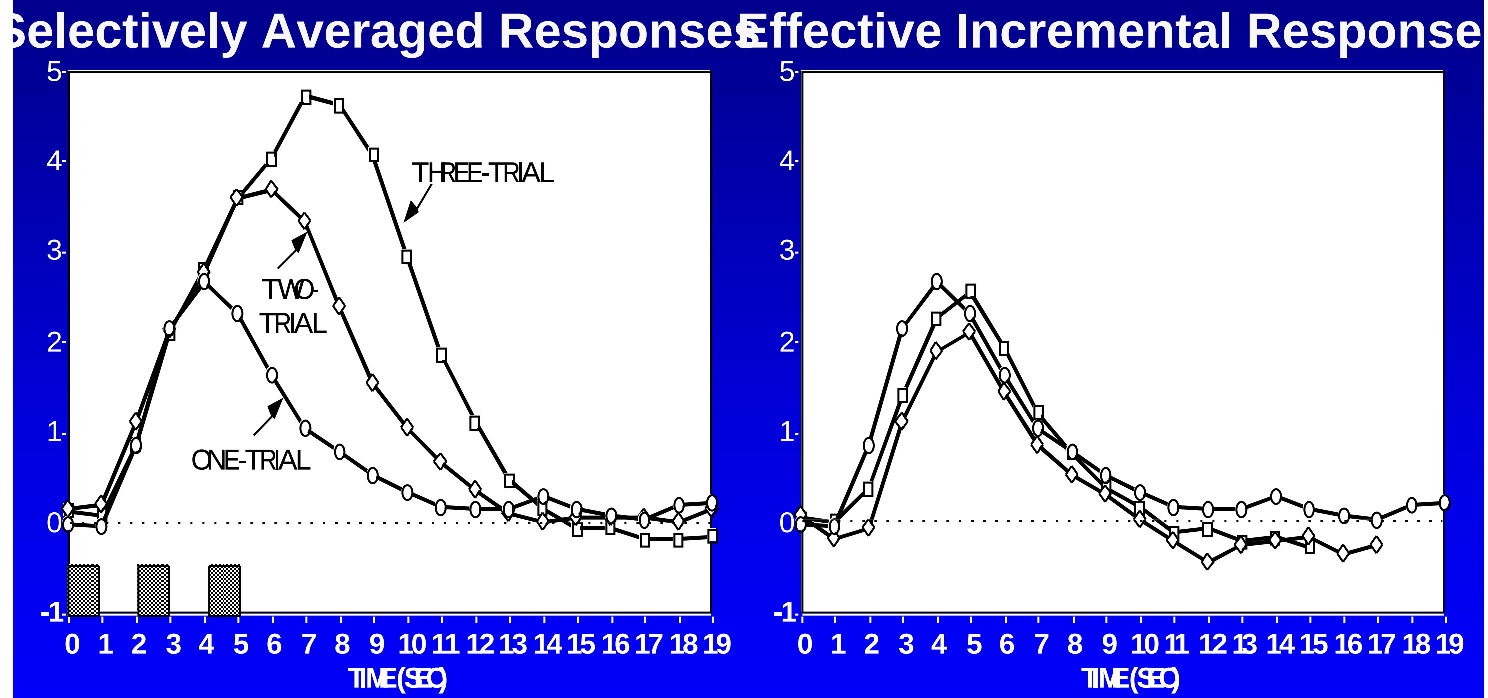


“Single-Trial” fMRI Response
PERCENT MR SIGNAL
4
3
2
1
0
-1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
TIME (SEC)



Test of Linearity
(Superpositioning)
0 sec
20 sec
0 sec
2 sec
20 sec
0 sec
2 sec
4 sec
20 sec

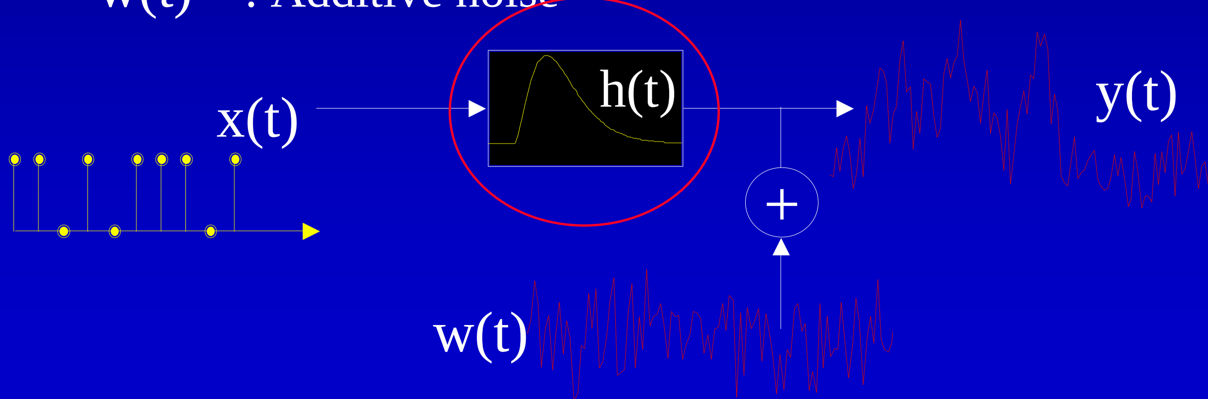
Test of Linearity (Superpositioning)



Linear Hemodynamic Response Model

$$y(t) = \sum_{i}^{N} x_i(t)\ h_i(t) + w(t)$$

y(t) : Measured bold timecourse
$x_i(t)$: Binary event paradigm for trial type *i*
$h_i(t)$: Hemodynamic impulse response for trial type *i*
w(t) : Additive noise



Estimation of Event-Related Responses with Uncorrelated Noise

$$y[n] = x_1[n] \quad h_1[n] + x_2[n] \quad h_2[n] + \ldots + x_i[n] \quad h_i[n] + w[n]$$

Matrix Form: $\mathbf{y} = \mathbf{X}\mathbf{h} + \mathbf{w}$

$$\hat{\mathbf{h}}_{OLS} = \left(\mathbf{X}^T \mathbf{X}\right)^{-1} \mathbf{X}^T \mathbf{y}$$

$$\hat{\mathbf{h}}_{ML} = \hat{\mathbf{h}}_{OLS} \text{ if } \mathbf{w} \sim N\left(\mathbf{0}, \sigma^2 \mathbf{I}\right)$$

Estimation of Event-Related Responses with Temporally Correlated Noise

$$\hat{\mathbf{h}}_{ML} = \left(\mathbf{X}^T \Lambda_{\mathbf{w}}^{-1} \mathbf{X}\right)^{-1} \mathbf{X}^T \Lambda_{\mathbf{w}}^{-1} \mathbf{y} \text{ if } \mathbf{w} \sim N\left(\mathbf{0}, \Lambda_{\mathbf{w}}\right)$$

$$\hat{\mathbf{h}}_{FGLS} = \left(\mathbf{X}^T \hat{\Lambda}_{\mathbf{w}}^{-1} \mathbf{X}\right)^{-1} \mathbf{X}^T \hat{\Lambda}_{\mathbf{w}}^{-1} \mathbf{y}, \quad \hat{\Lambda}_{\mathbf{w}} = \Lambda_{\mathbf{w}}\left(\hat{\Theta}\right)$$

Noise parameter fitting: $\hat{\Theta} = \left(\hat{\alpha}, \hat{\rho}\right)$

$$K_{\mathbf{ww}}[n] = \sigma^2 \left(\alpha \delta[n] + (1-\alpha)\rho^{|n|}\right) \quad 1 ? \alpha, \rho ? 0$$

Summary of Computational Procedure

1) Compute $\hat{\mathbf{h}}_{OLS}$ **(unbiased, but inefficient)**

2) From residual error $\mathbf{e} = \mathbf{y} - \mathbf{X}\hat{\mathbf{h}}_{OLS}$ **, estimate** $\hat{\Lambda}_{\mathbf{w}} = \Lambda_{\mathbf{w}}(\hat{\alpha}, \hat{\rho})$

3) Compute $\hat{\mathbf{h}}_{FGLS}$

4) Compute statistical maps

Statistical Inference

Null hypothesis $H_0 : \mathbf{Rh} = \mathbf{0}$

$$F[J, n-K] = \frac{(\mathbf{R}\hat{\mathbf{h}}_{FGLS})^T [\hat{\sigma}^2 \mathbf{R}(\mathbf{X}^T \hat{\Lambda}_{\mathbf{w}}^{-1} \mathbf{X})^{-1} \mathbf{R}^T]^{-1} (\mathbf{R}\hat{\mathbf{h}}_{FGLS})}{J}$$

Test 1 $\mathbf{R} = \mathbf{I}$

Test 2 $\mathbf{R} = \begin{bmatrix} 0 & \cdots & 1 & \cdots & 0 & 0 & 0 \\ 0 & 0 & \cdots & 1 & \cdots & 0 & 0 \\ 0 & 0 & 0 & \cdots & 1 & \cdots & 0 \end{bmatrix}$

Test 3 $\mathbf{R} = \mathbf{h}_{IDEAL}^T$

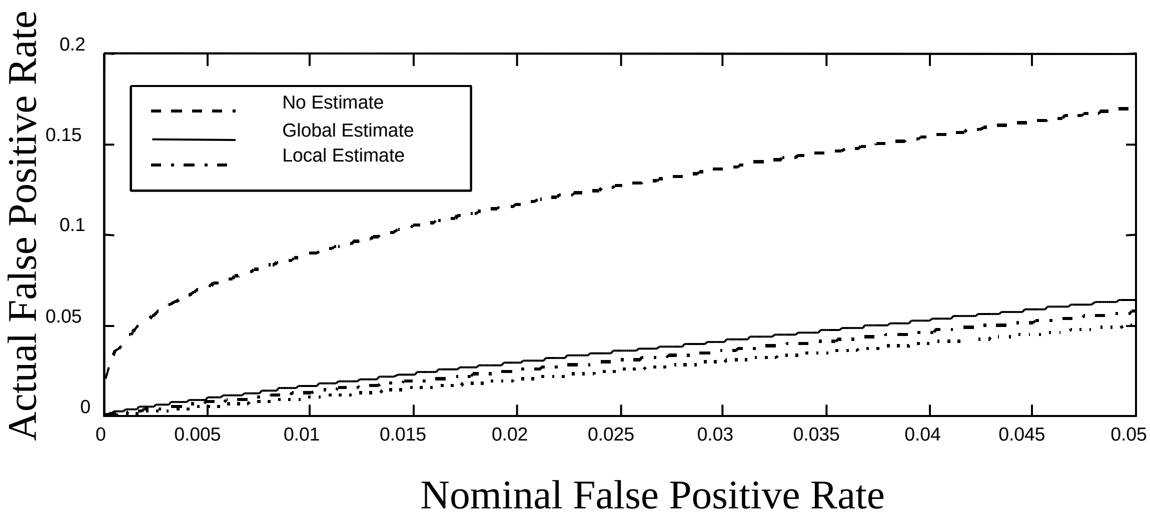
Statistical Inference
Special Case: t-test

Null hypothesis $H_0 : \mathbf{Rh} = \mathbf{0}$

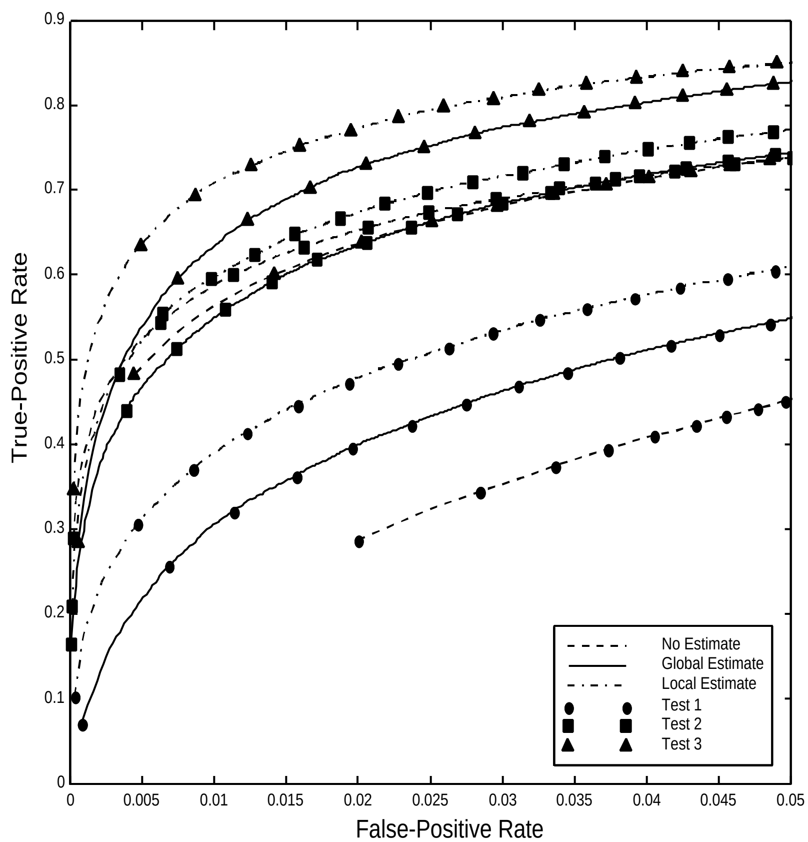
Test 3 $\mathbf{R} = \mathbf{h}_{IDEAL}^{T}$

$$t[n-K] = \frac{\tilde{\mathbf{h}}_{IDEAL}{}^{T}\hat{\mathbf{h}}_{FGLS}}{\hat{\sigma}^{2}\tilde{\mathbf{h}}^{T}(\mathbf{X}^{T}\hat{\Lambda}_{\mathbf{w}}^{-1}\mathbf{X})^{-1}\tilde{\mathbf{h}}}$$

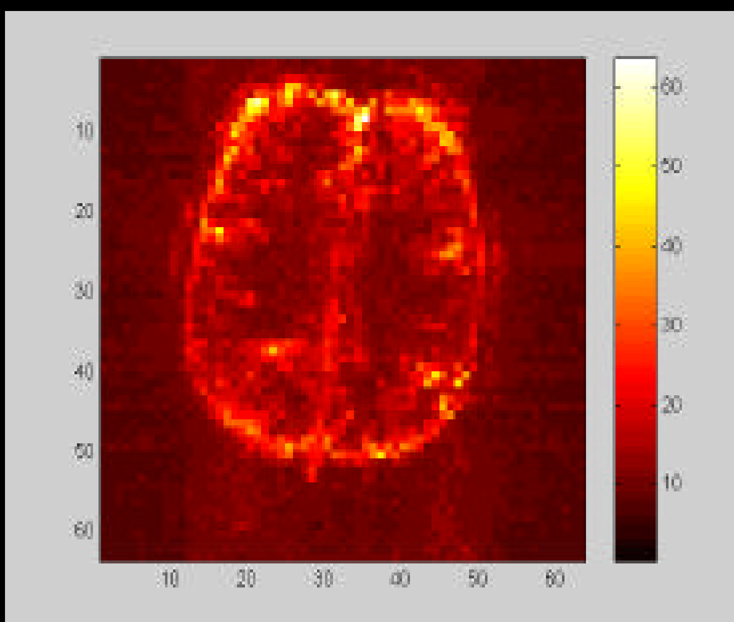
Validation of Statistical Procedure with Actual fMRI Noise



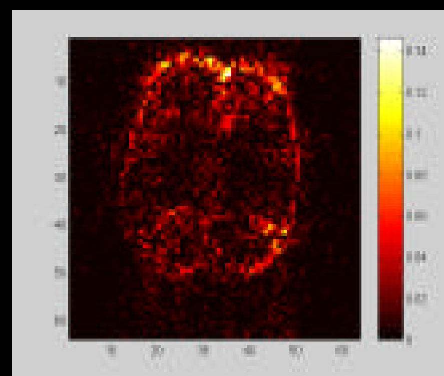
Statistical Power (ROC)



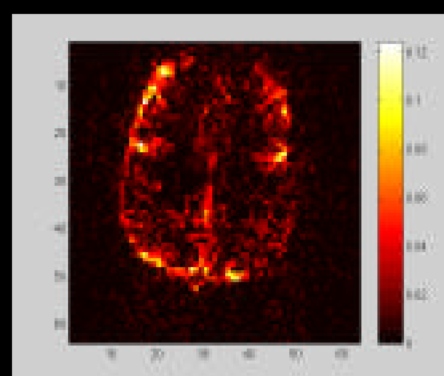
fMRI Noise Correlation



Total Variance Image

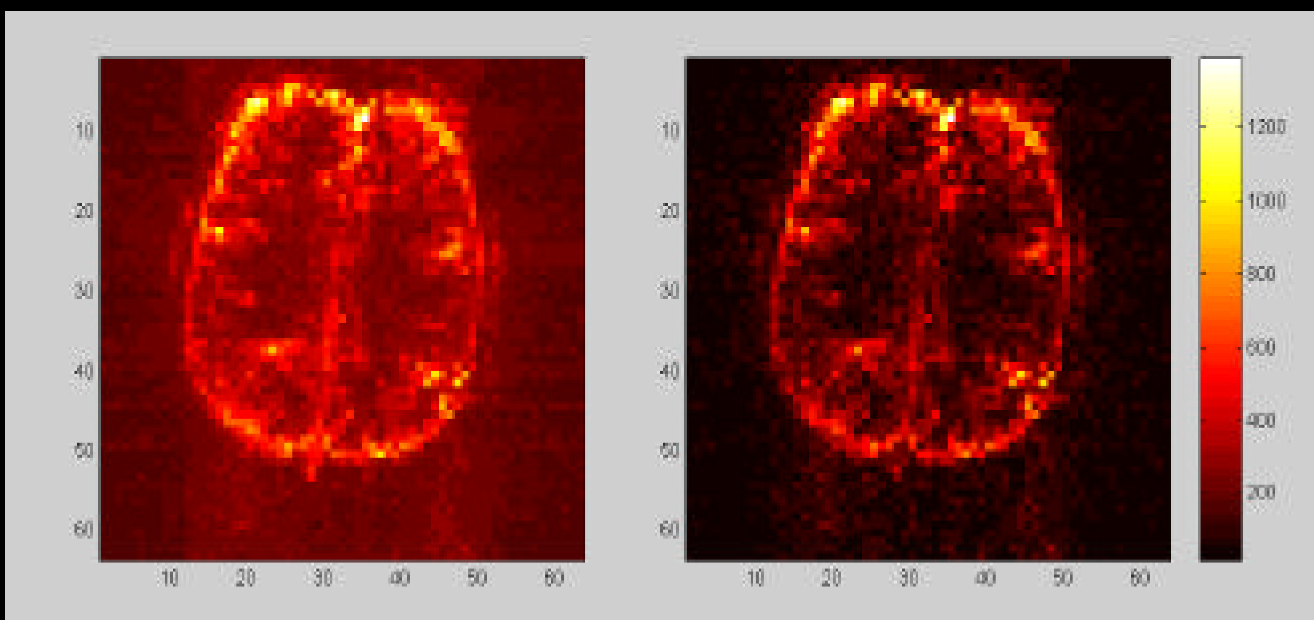


1st Spatial Component



2nd Spatial Component

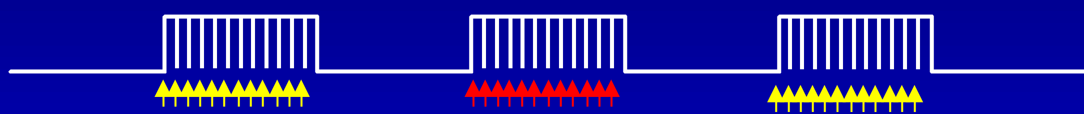
Spatial Correlation in fMRI Noise



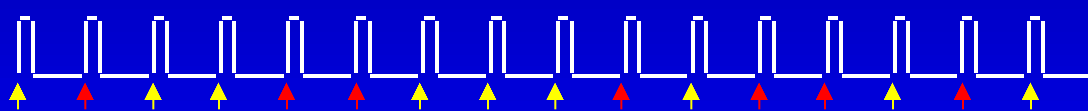
Total Variance Image **Components 1 through 6**

Blocked versus Event-Related Designs

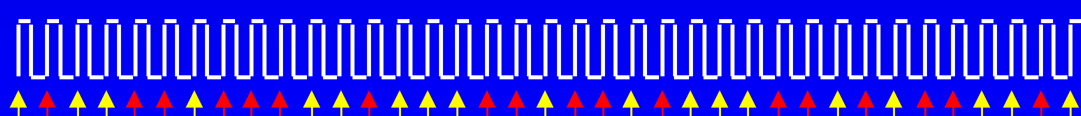
Blocked:



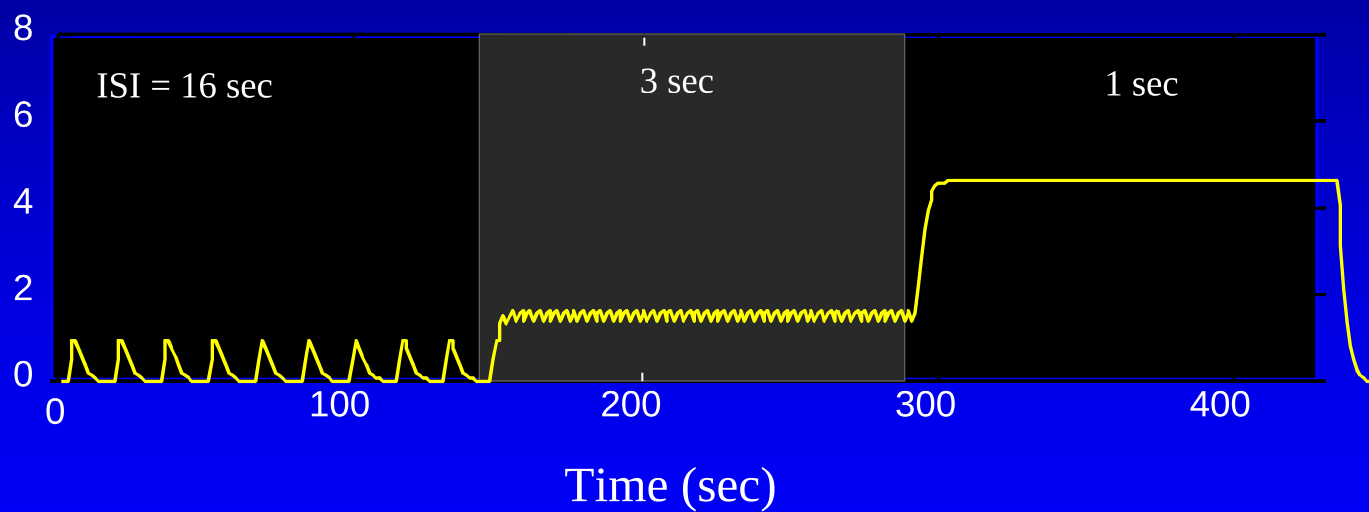
Event-Related:



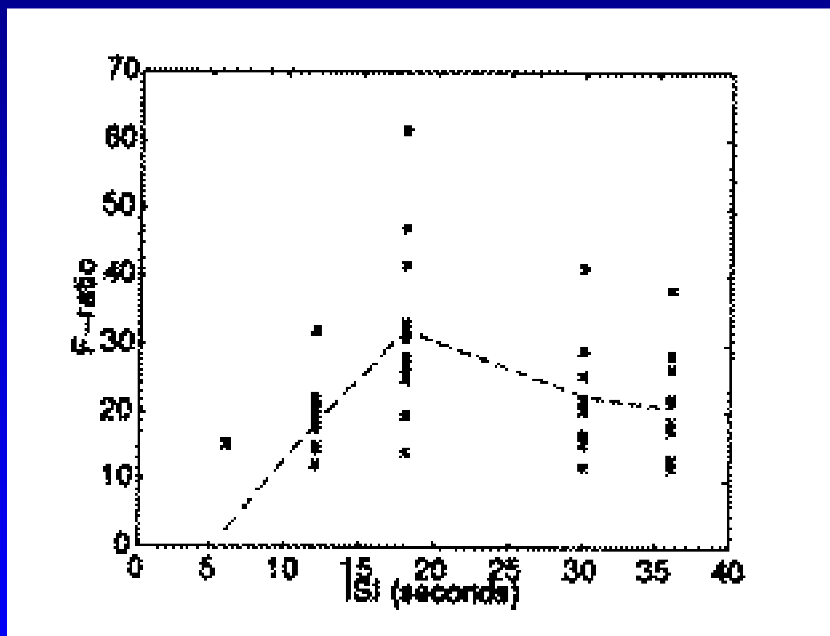
Rapid Event-Related:



Temporal Overlap of Event-Related Responses

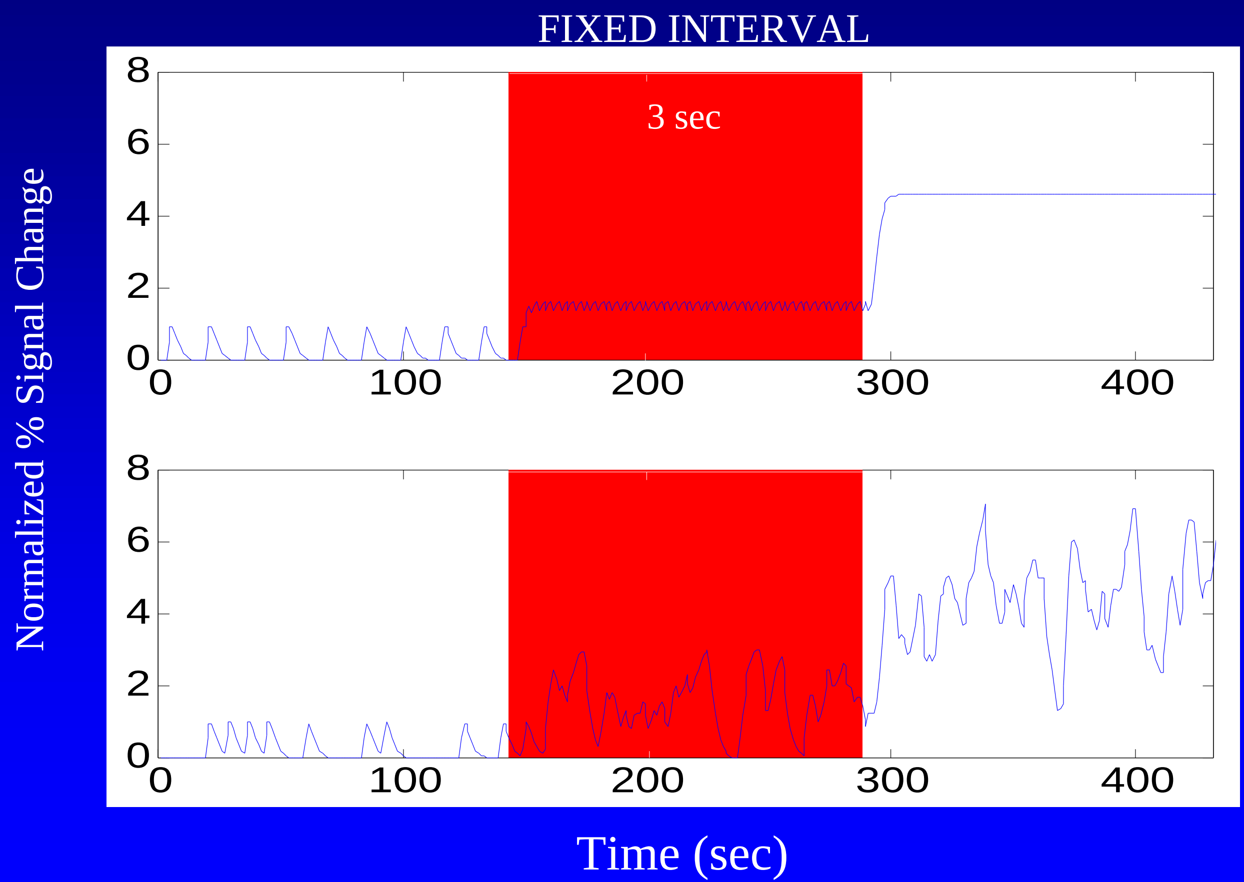


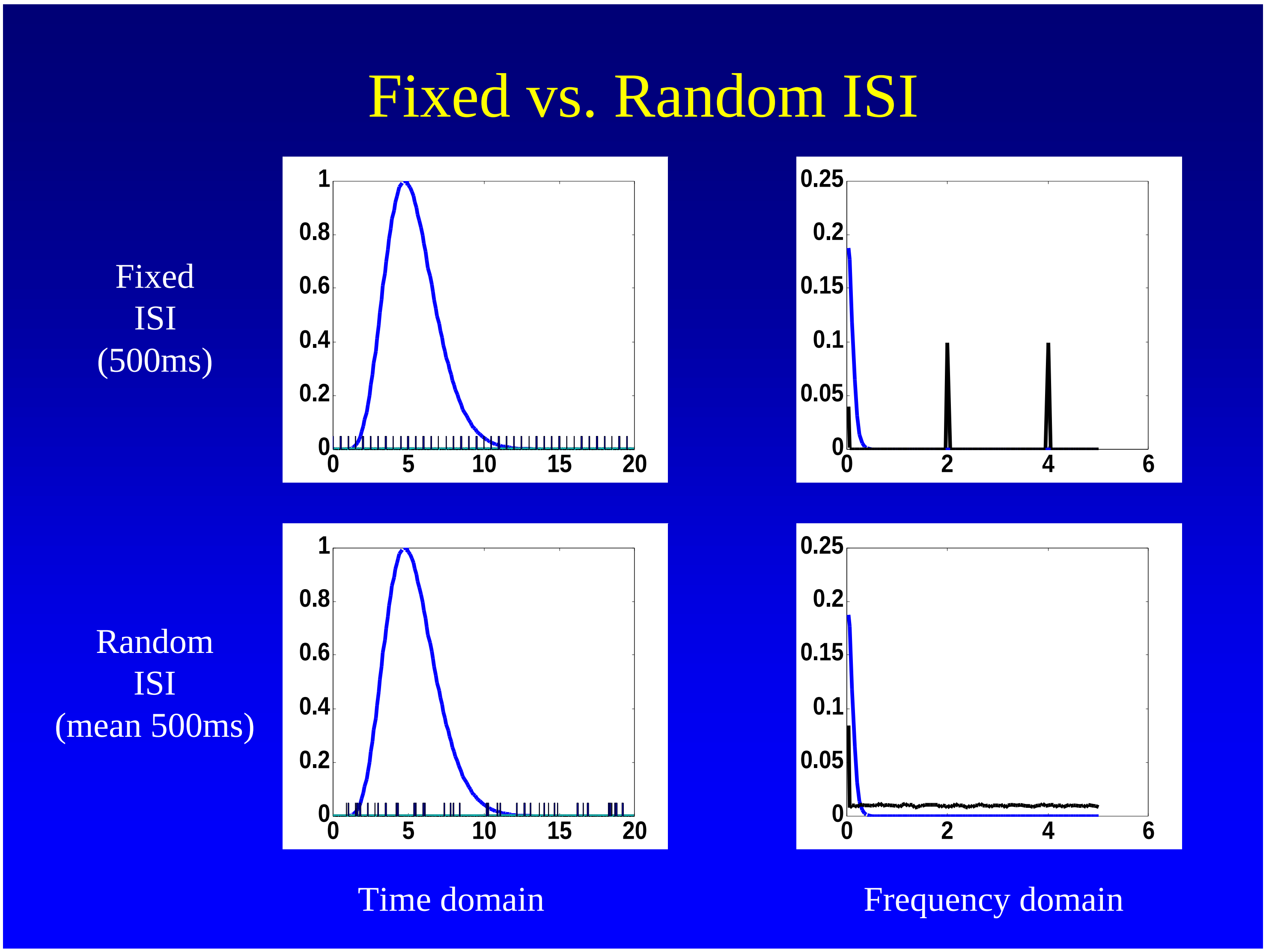
Optimal Presentation Rate for Event-Related fMRI Experiments



18 sec: Hutton, Howseman, Josephs, Friston & Turner, 1998
15 sec: Cox & Bandettini, 1998

Fixed Interval vs. Randomized Event-Related Simulated Timecourses




Fixed vs. Random ISI
Fixed
ISI
(500ms)
Random
ISI
(mean 500ms)
0 0.2 0.4 0.6 0.8 1
0 5 10 15 20
0 0.05 0.1 0.15 0.2 0.25
0 2 4 6
Time domain
Frequency domain

Optimal Experimental Design

Predicted Estimation Error:

$$\operatorname{var}\left(\hat{\mathbf{h}}_{ML}\right) = \left(\mathbf{X}^{T}\ddot{\mathbf{E}}^{-1}\mathbf{X}\right)^{-1}$$

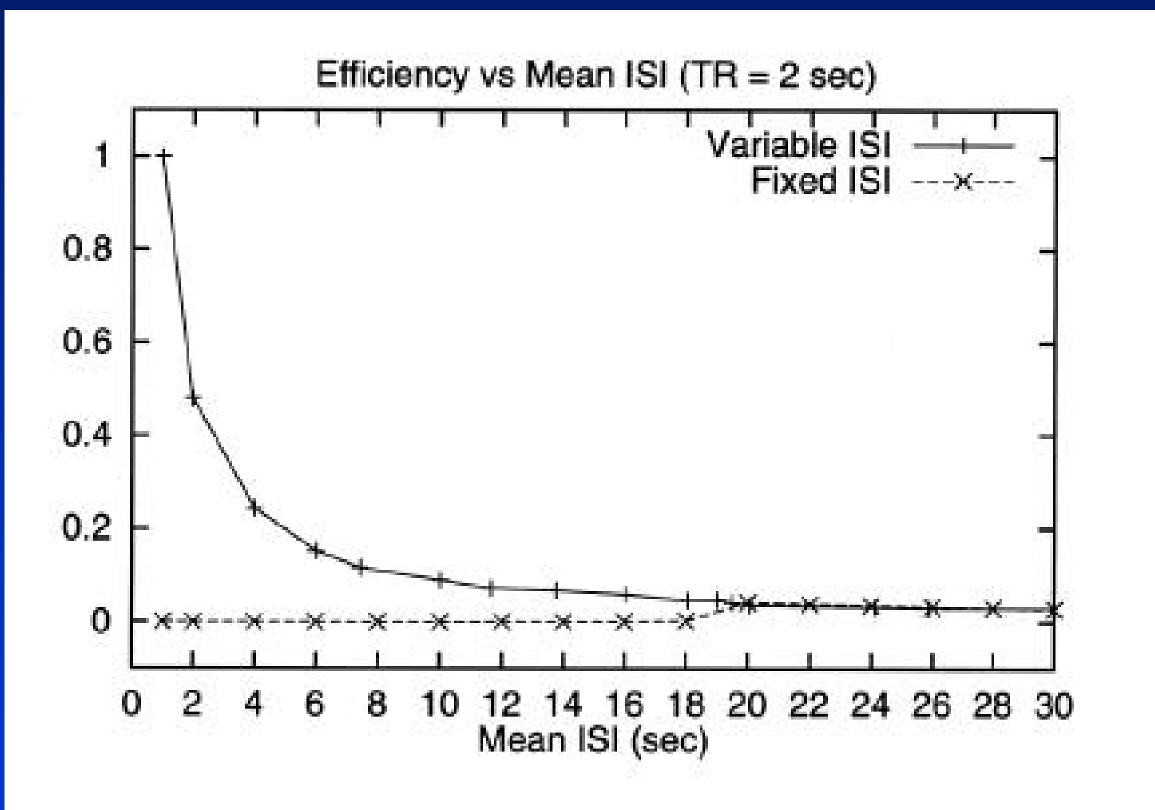
Efficiency:

$$E = \left\langle \left\| \hat{\mathbf{h}} - \mathbf{h} \right\|^{2} \right\rangle^{-1} = trace\left(\operatorname{var}\left(\hat{\mathbf{h}}\right)\right)^{-1}$$

Optimal Experimental Design:

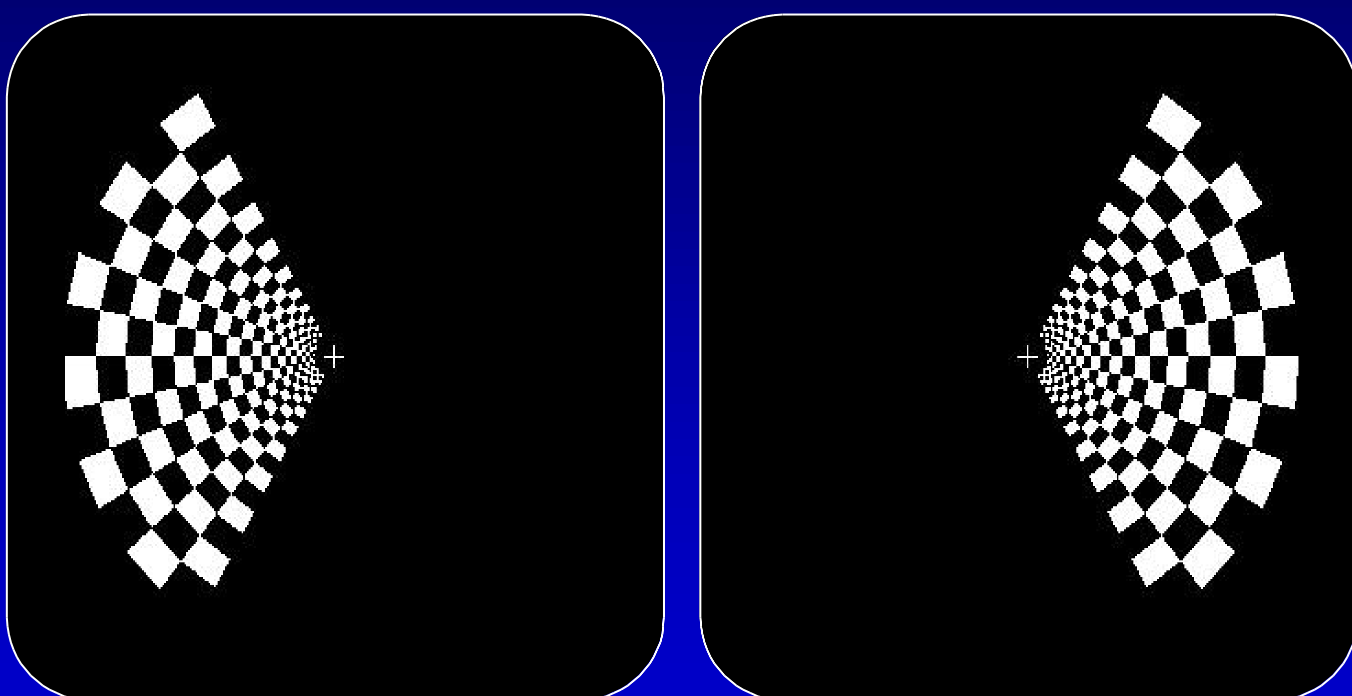
Find $\mathbf{X}$ which maximizes E

Estimation Efficiency Event-Related fMRI

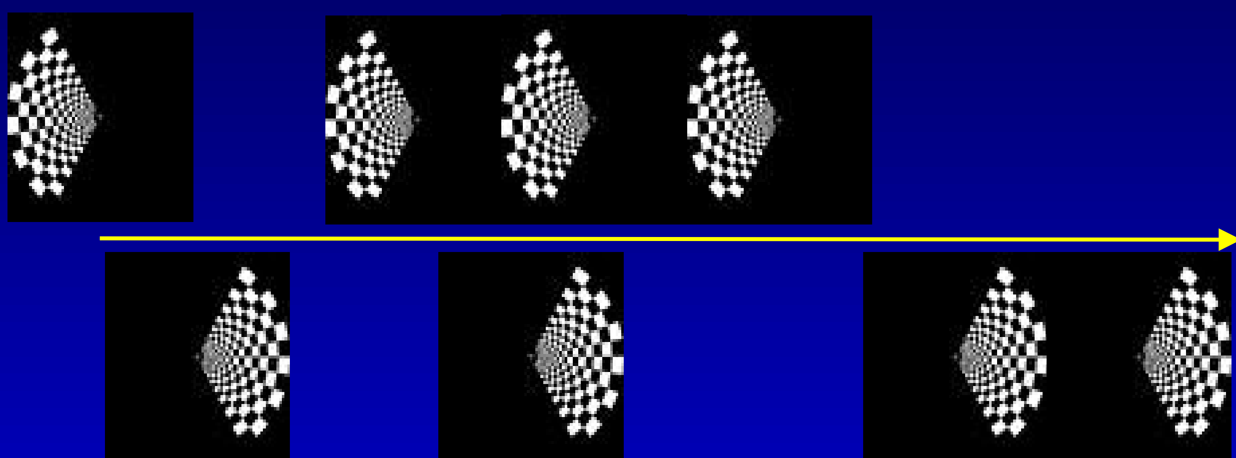


Visual Activation Paradigm - Two Trial Types

Left Hemifield | **Right Hemifield**

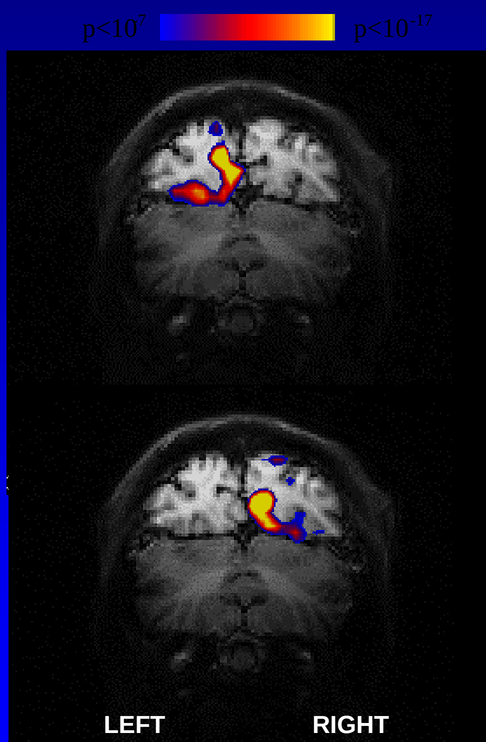


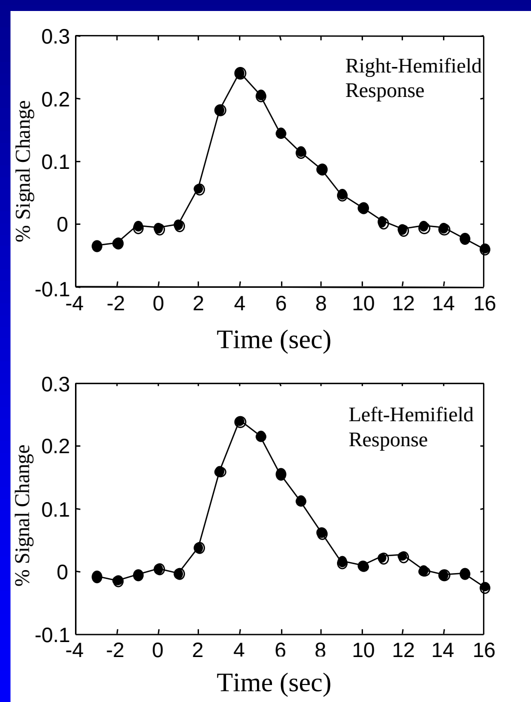
Sub-TR Visual Activation Paradigm



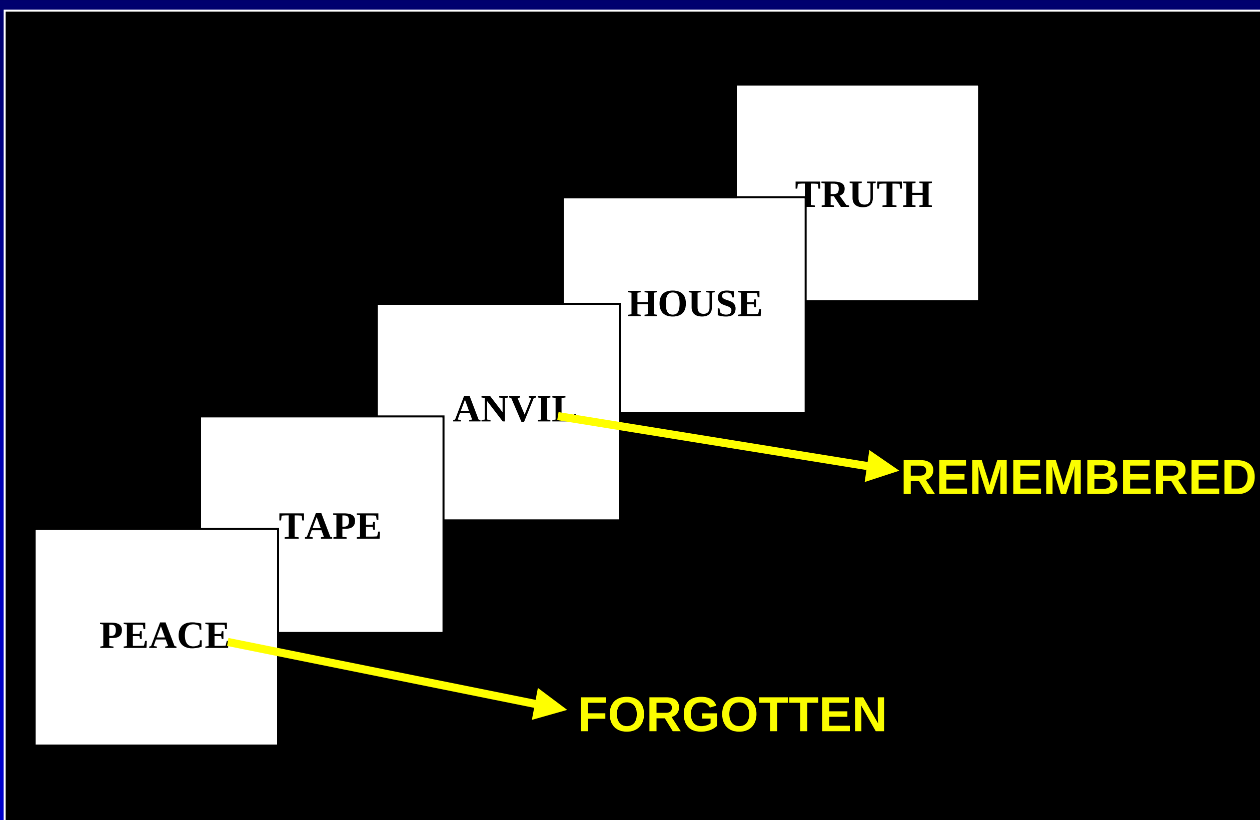
Trials randomly presented <u>500</u> msec apart

Estimated fMRI Response (500 ms ISI)

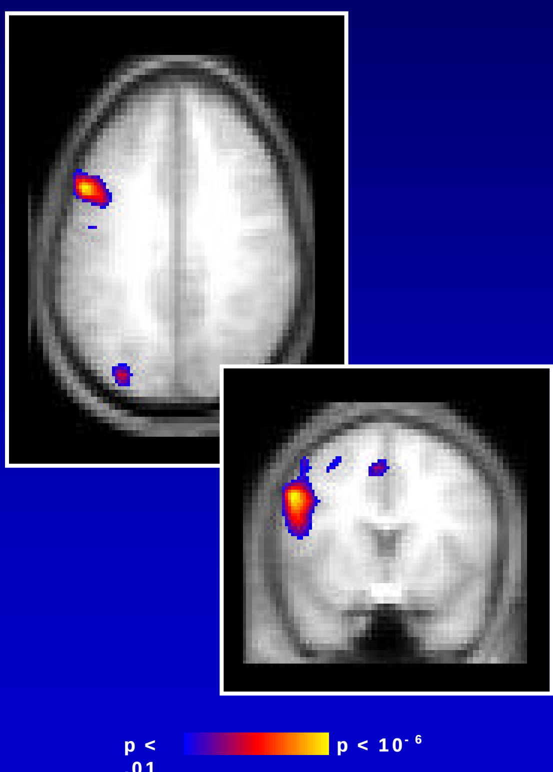


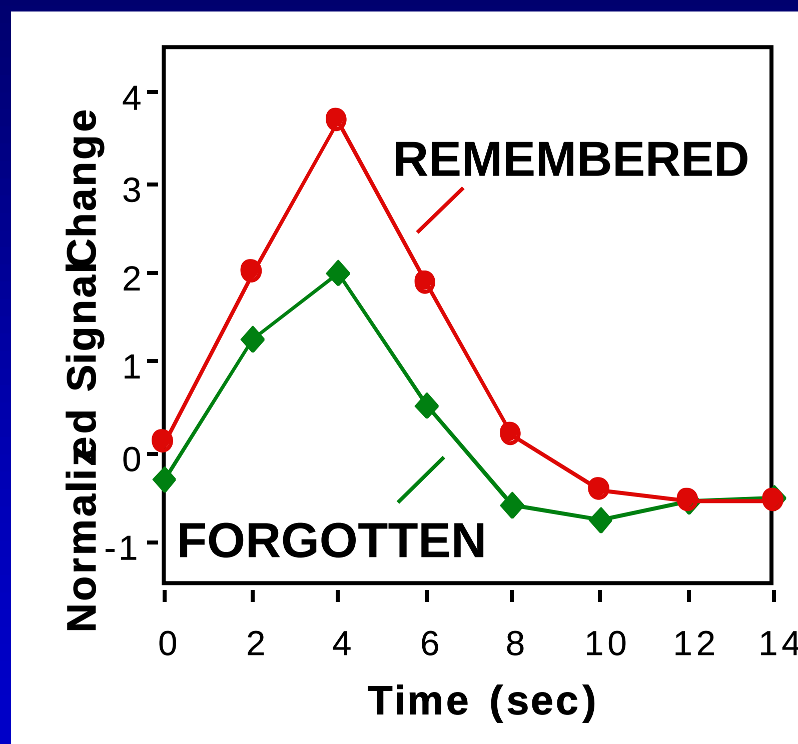


Sorting Based on Subsequent Memory Performance



Sorting Based on Subsequent Memory Performance





Wagner et al., *Science*, 1998