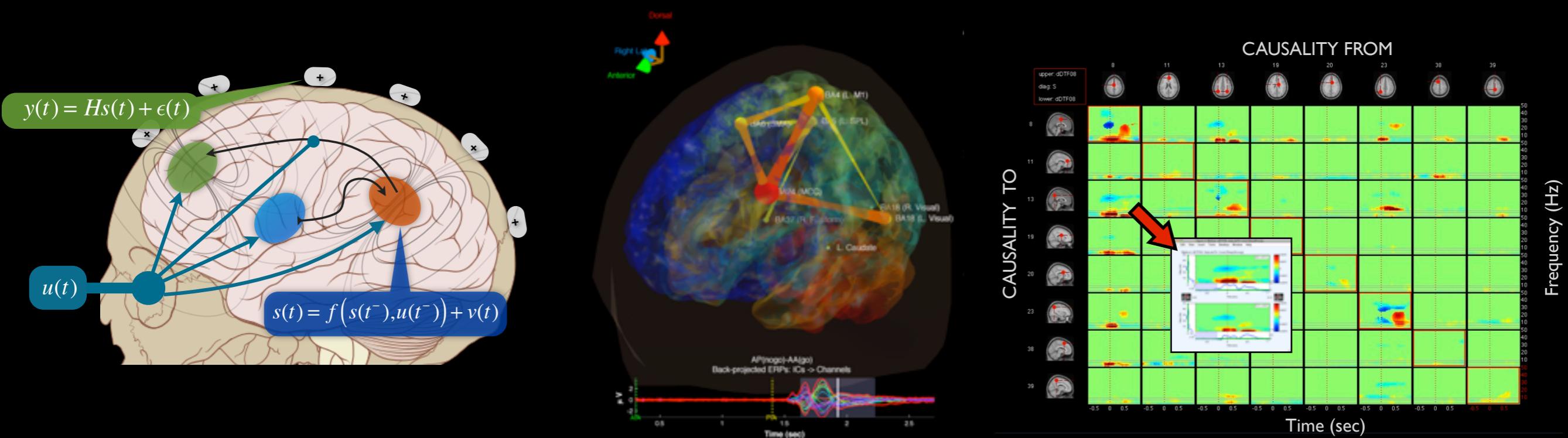


# The Dynamic Brain: Modeling Neural Dynamics and Interactions from M/EEG



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Institute for Neural Computation  
Dept. of Cognitive Science  
UC San Diego



# Outline

Introduction

Theory

Functional Connectivity Measures (PLV, PAC, Coherence)

Linear Dynamical Systems and Vector Autoregressive Modeling

Granger Causality and Related Effective Connectivity Measures

Multivariate versus Bivariate Estimation / Imposing Constraints

Scalp or Source?

Adapting to Time-Varying Dynamics

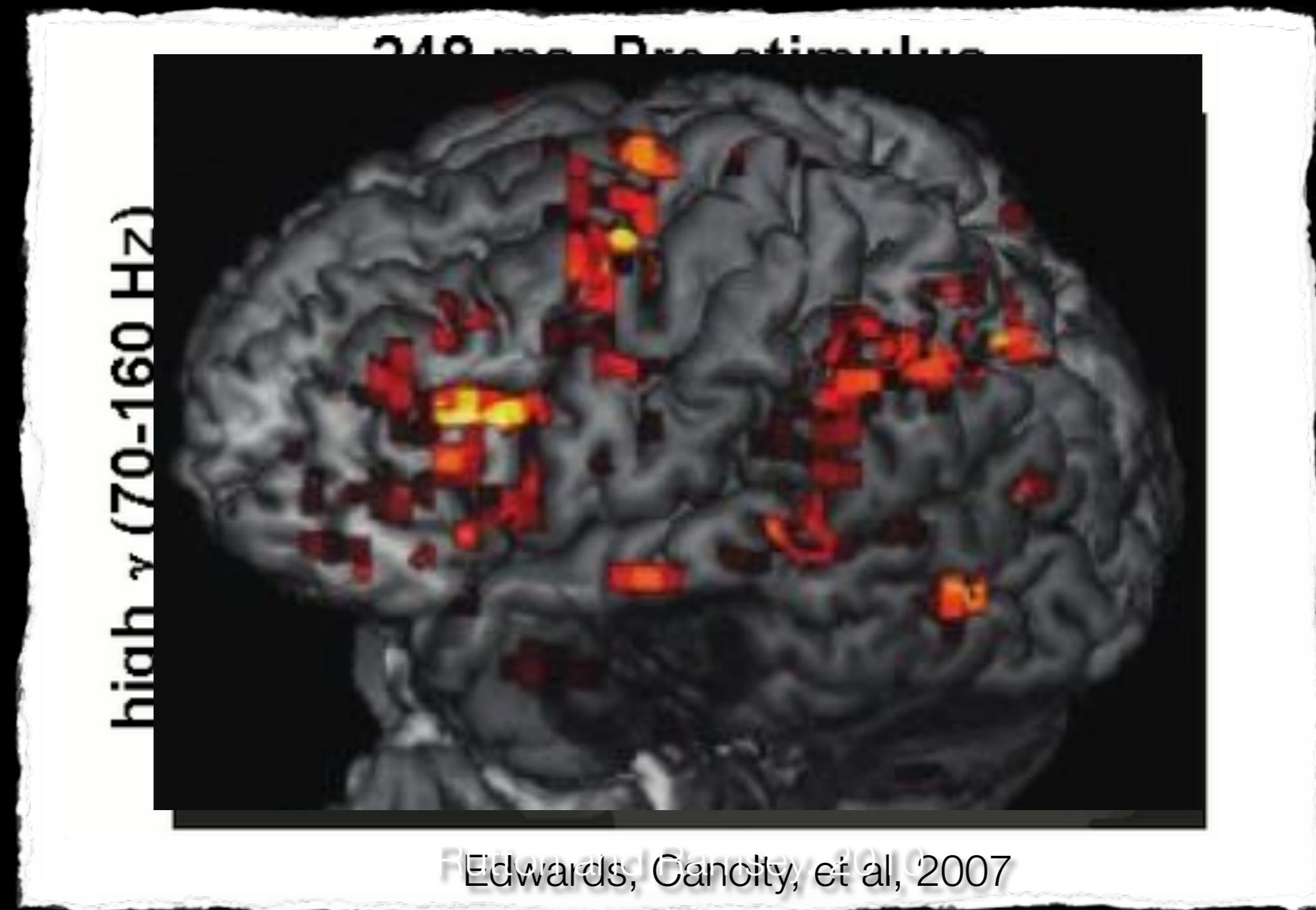
The Source Information Flow Toolbox (SIFT)

Some Applications of SIFT

The Road Ahead

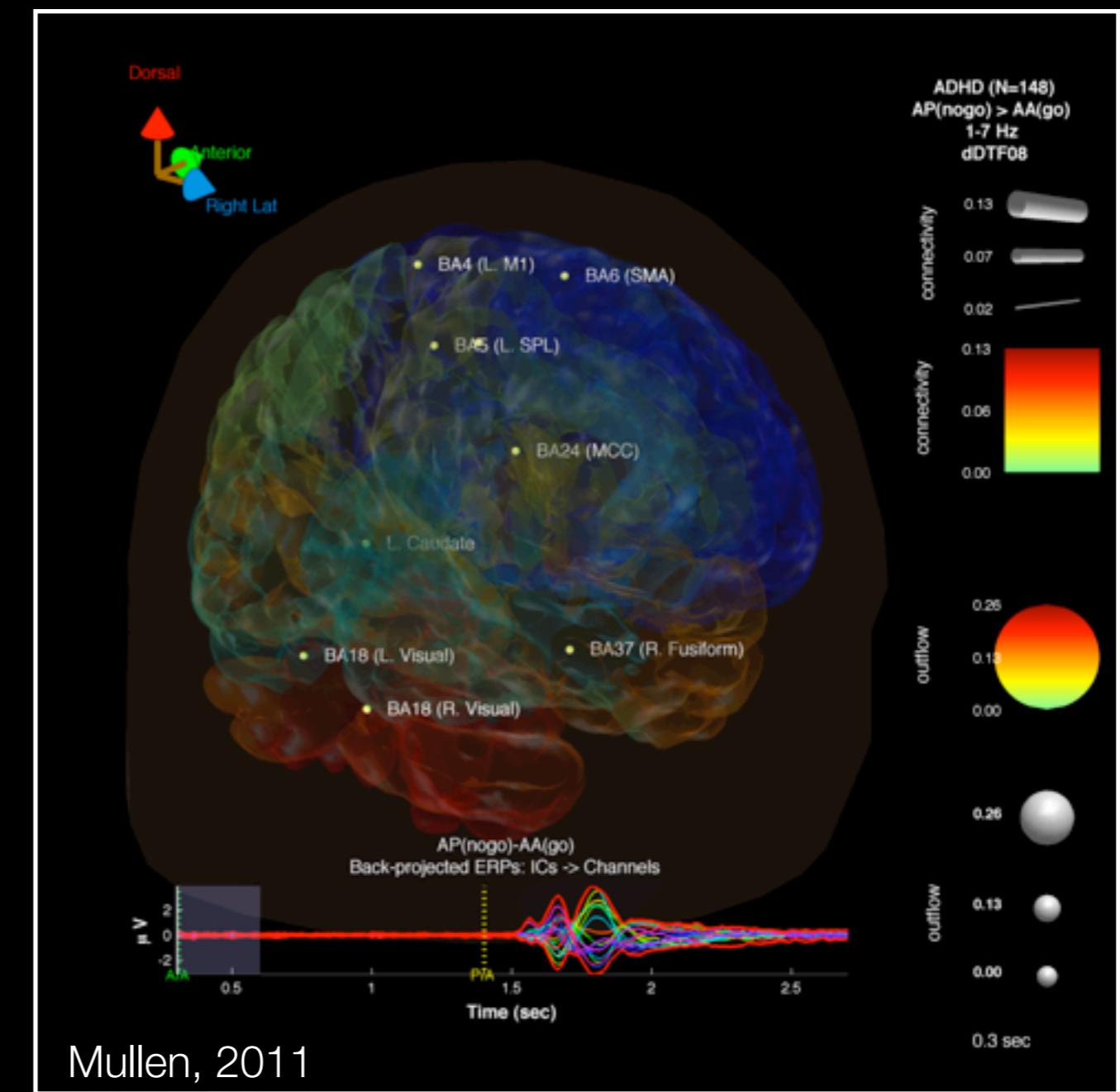
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# The Dynamic Brain



# The Dynamic Brain

- A key goal: To model temporal changes in neural **dynamics** and **information flow** that **index** and **predict** task-relevant changes in cognitive state and behavior
- **Open Challenges:**
  - Non-invasive measures (source inference)
  - Robustness and Validity (constraints & statistics)
  - Scalability (multivariate)
  - Temporal Specificity / Non-stationarity / Single-trial (dynamics)
  - Multi-subject Inference
  - Usability and Data Visualization (software)



# Modeling Brain Connectivity

- Model-based approaches mitigate the ‘curse of dimensionality’ by making some assumptions about the structure, dynamics, or statistics of the system under observation

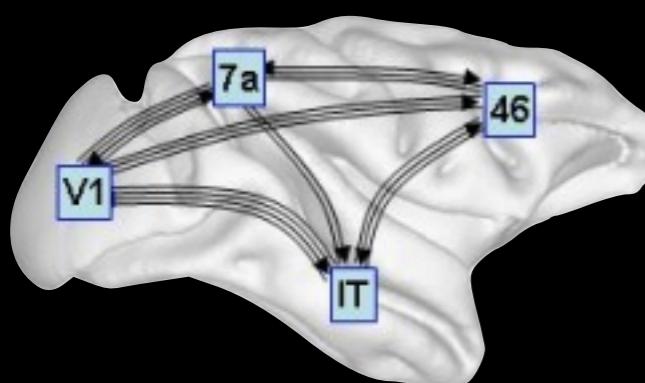
Box and Draper (1987):

“Essentially, all models are wrong, but some are useful [...] the practical question is how wrong do they have to be to not be useful”

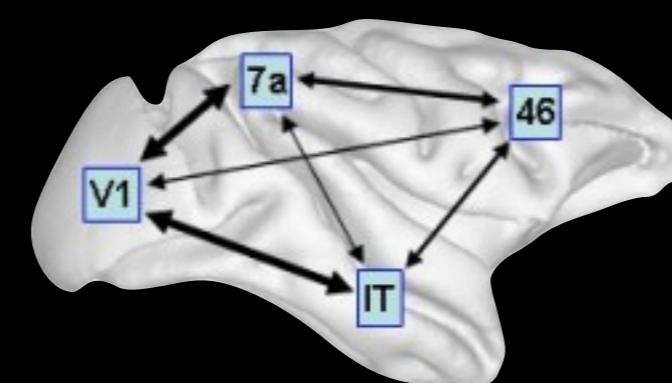
# Categorizations of Large-Scale Brain Connectivity Analysis

(Bullmore and Sporns, *Nature*, 2009)

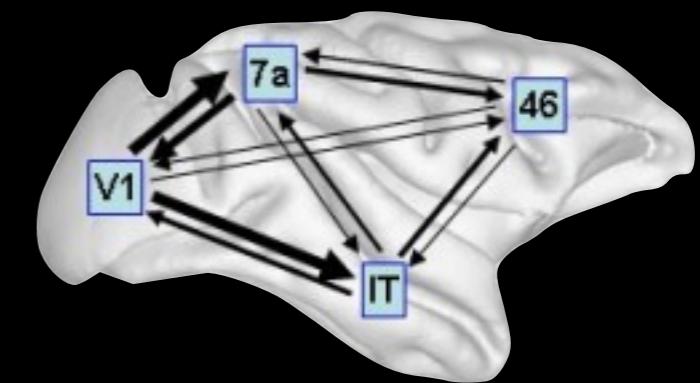
## Structural



## Functional



## Effective



state-invariant,  
anatomical

dynamic, state-dependent,  
correlative, symmetric

dynamic, state-dependent,  
asymmetric, causal,  
information flow

Hours-Years

milliseconds-seconds

Temporal Scale

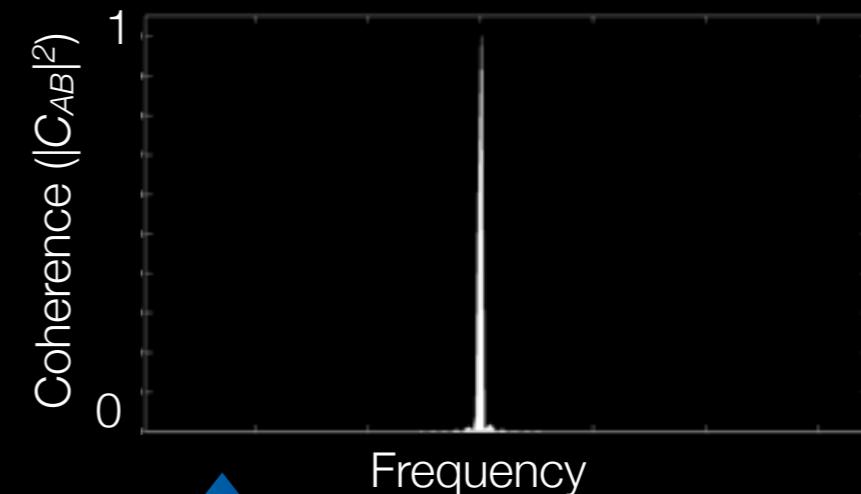
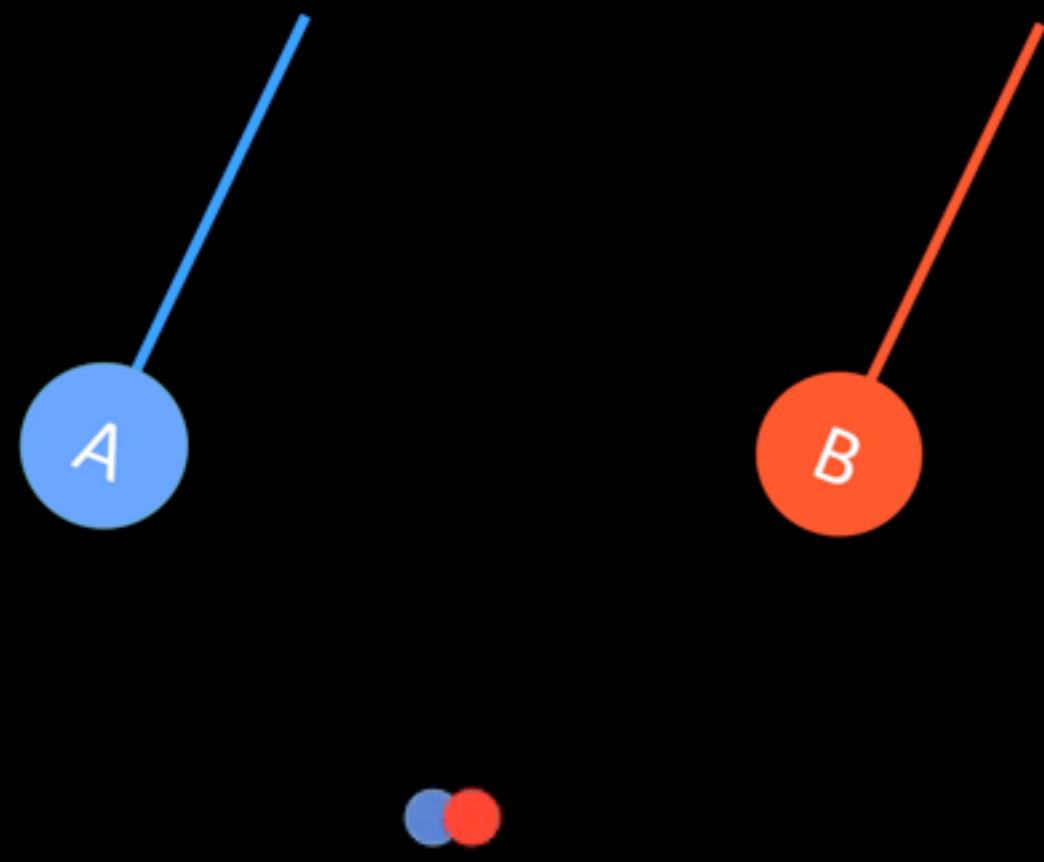
# Estimating Functional Connectivity

## Popular measures

- Cross-Correlation
- Coherence
- Phase-Locking Value
- Phase-amplitude coupling

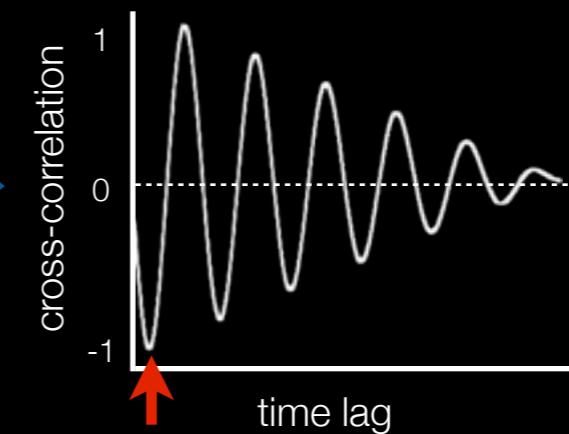
...

# Cross-Correlation and Linear Coherence



DFT

$$\begin{aligned} C_{AB}(f) &= \sum_{k=0}^p \rho_{AB}(k) e^{-i2\pi fk} \\ &= \frac{S_{AB}(f)}{\sqrt{S_A(f)S_B(f)}} \end{aligned}$$



$\rho_{AB}(k)$

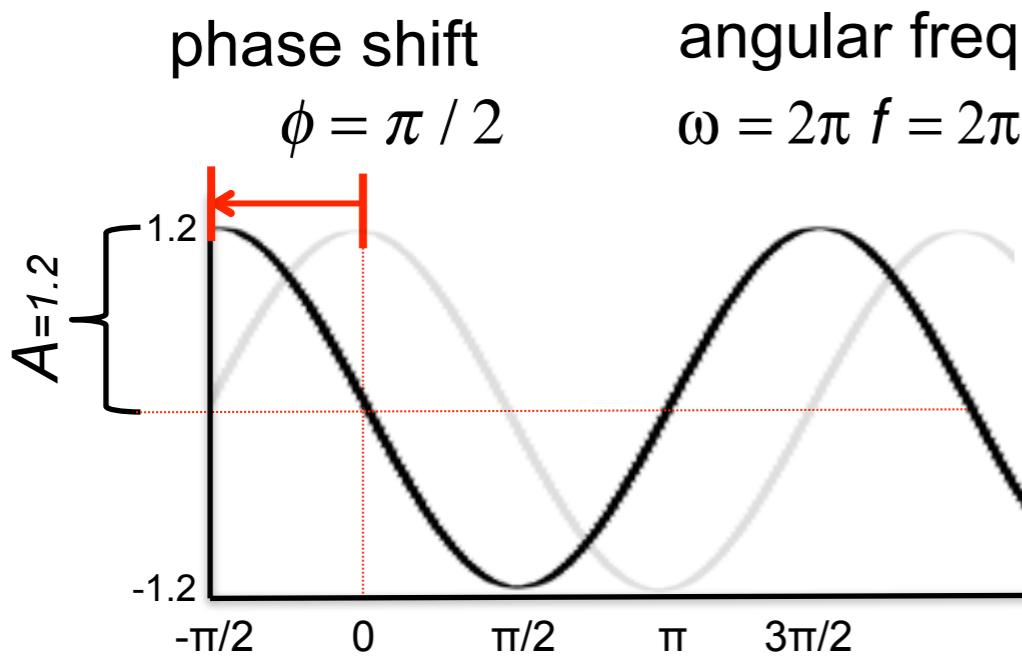
Issue: Linear coherence is biased by auto-power (just as the cross-correlation is biased by strong autocorrelation in individual time series)

# Phasers



phase shift

$$\phi = \pi / 2$$



angular frequency

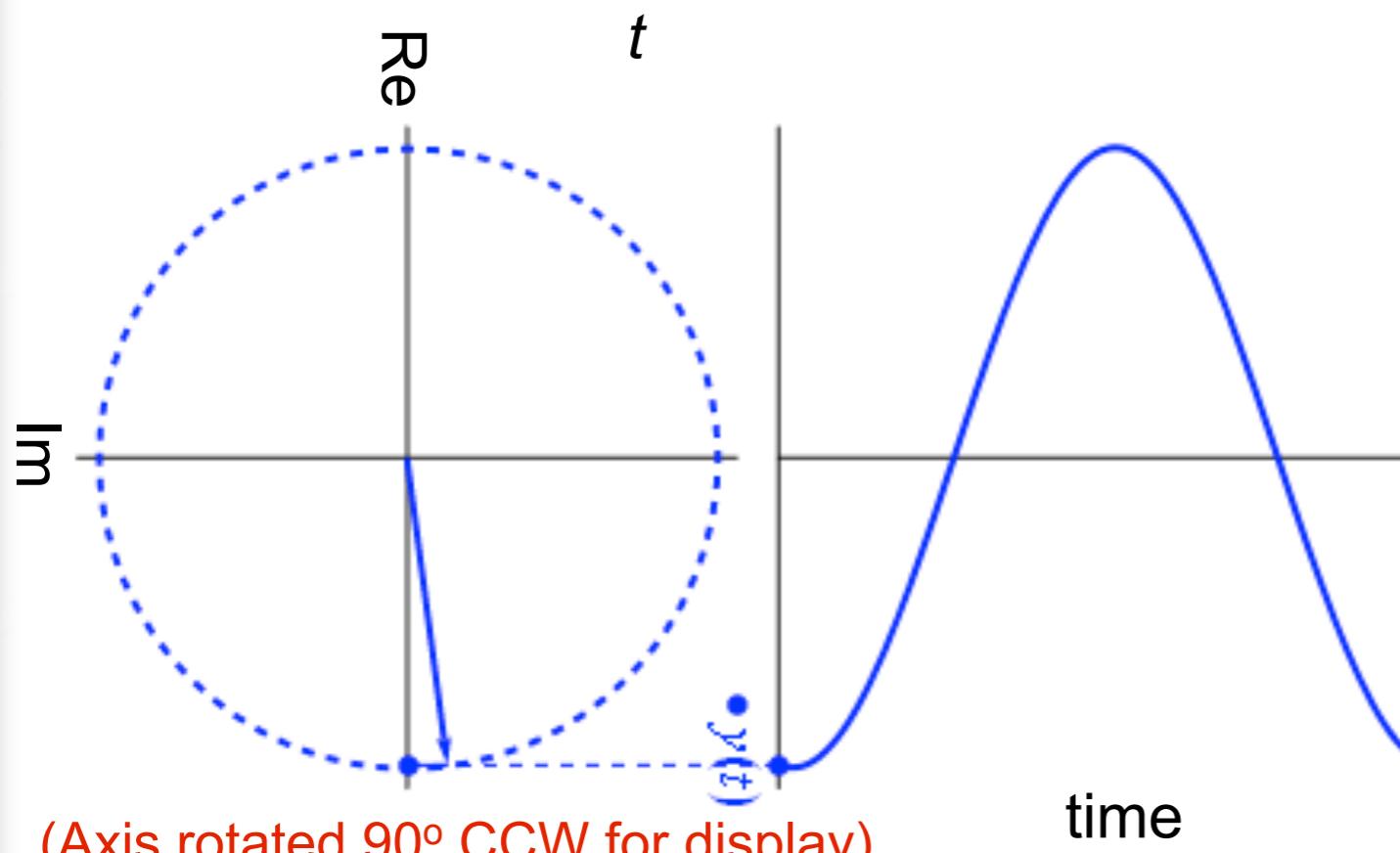
$$\omega = 2\pi f = 2\pi \text{ rad/sec}$$

Euler's Formula tells us that any sinusoid can be expressed as the sum of two complex exponentials

$$\begin{aligned} A \cdot \cos(\omega t + \phi) &= \frac{A}{2} e^{i(\omega t + \phi)} + \frac{A}{2} e^{-i(\omega t + \phi)} \\ &= \operatorname{Re}\{A e^{i(\omega t + \phi)}\} = \operatorname{Re}\{S(\omega, t)\} \end{aligned}$$

... or (if real-valued) as the real part of a single complex exponential

instantaneous complex amplitude and phase

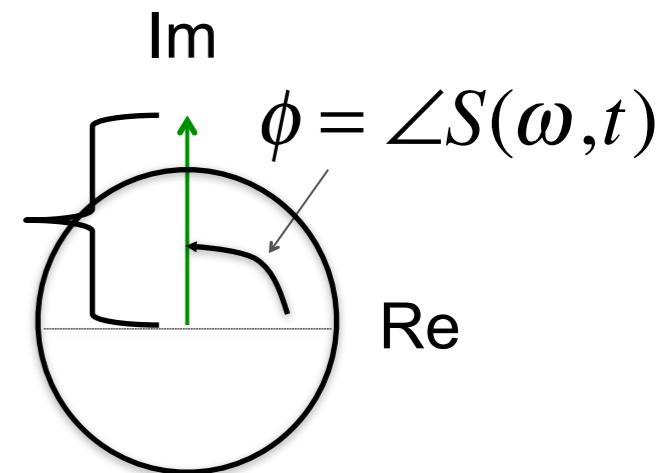


Polar animation courtesy Wikipedia

**Phasor**

(Polar Coords)

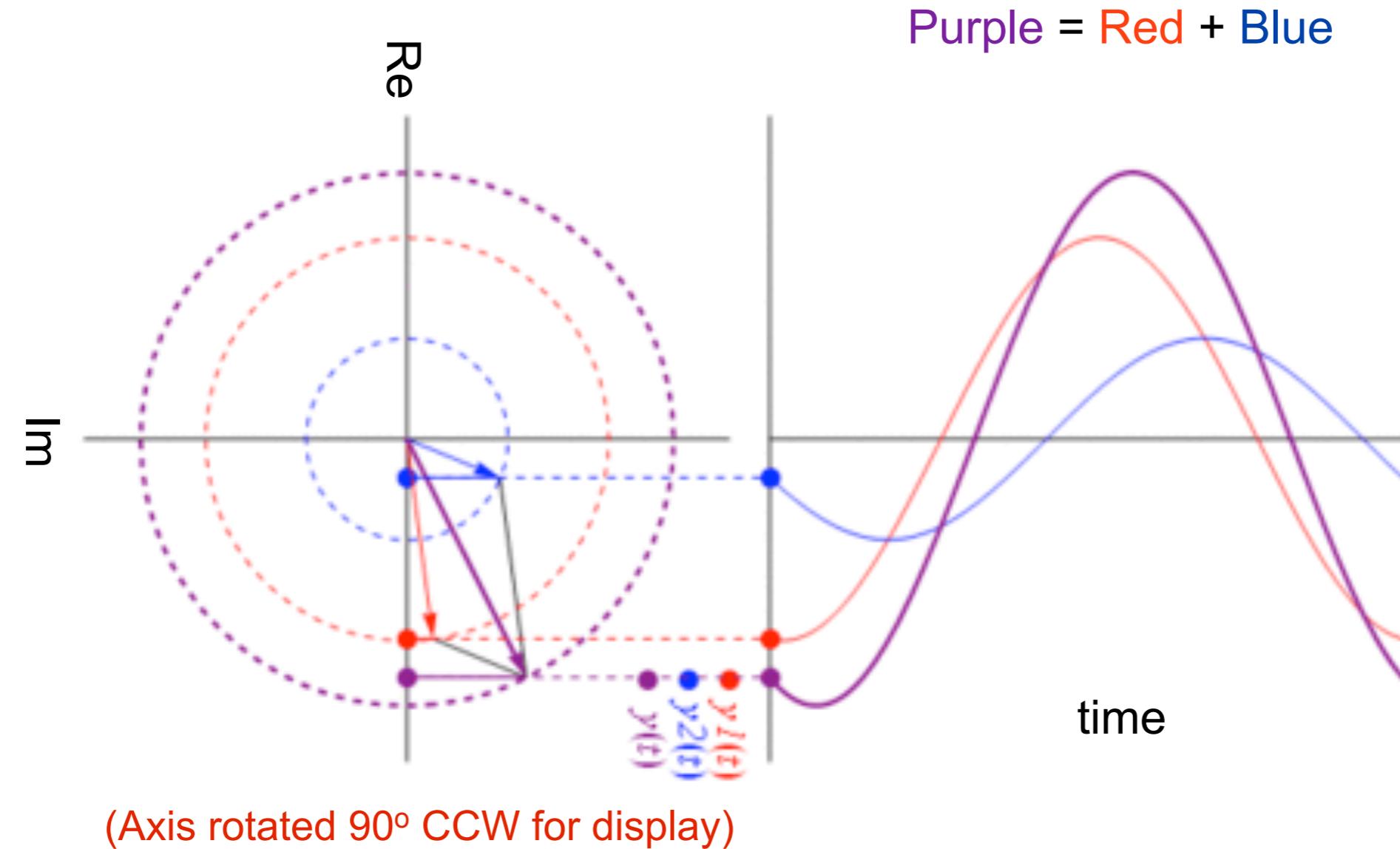
$$|S(\omega, t)| = |A|$$



Shorthand notation:  $A e^{i\phi}$

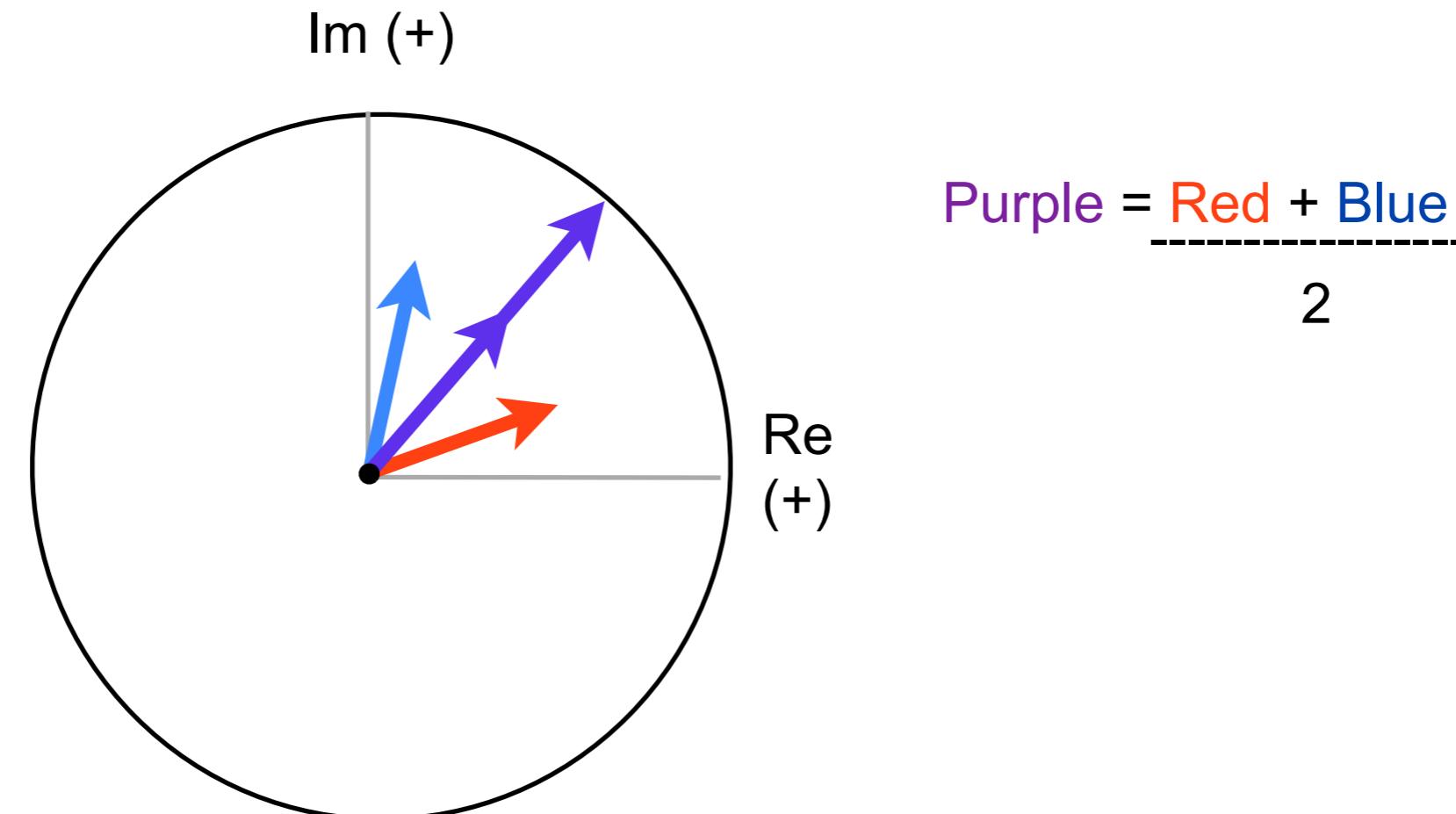
# Phasors

If we want to examine oscillatory dynamics or relationships between oscillatory signals, analysis in the time domain (i.e. cartesian coordinates) is equivalent to (simpler) operations involving phasors in Fourier space (i.e. polar coordinates).



# The Mean Phasor

The average of  $k$  phasors is a new phasor constructed by adding up the original vectors and dividing the length of the resultant vector by  $k$ .

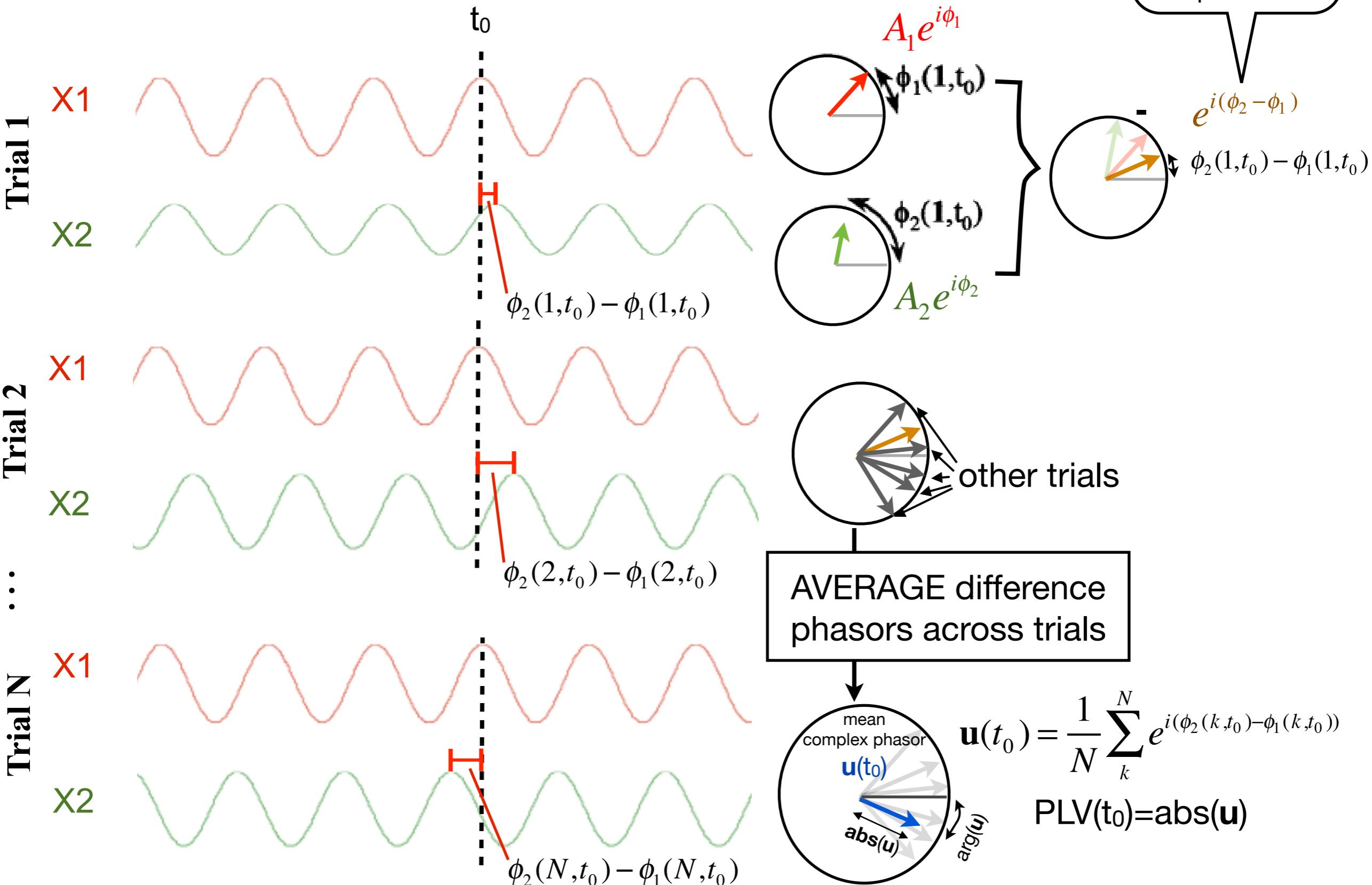


If all **phasors have similar angles**, then vectors will “point” in the same direction and the **length of the mean phasor** will be comparatively **large**.

If **phasor angles are random**, then vectors will point in random directions and the **length of the mean phasor** will be close to **zero**

# Phase-Locking Value (PLV)

Lachaux, J.P., et al (1999) *HBM*



# Phase-Locking Value (PLV)

Lachaux, J.P., et al (1999) *HBM*

Computing PLV (“phase coherence”) in EEGLAB:

```
pop_newcrossf( . . . , 'type', 'phase' )
```

# Phase-Amplitude Coupling

Intro

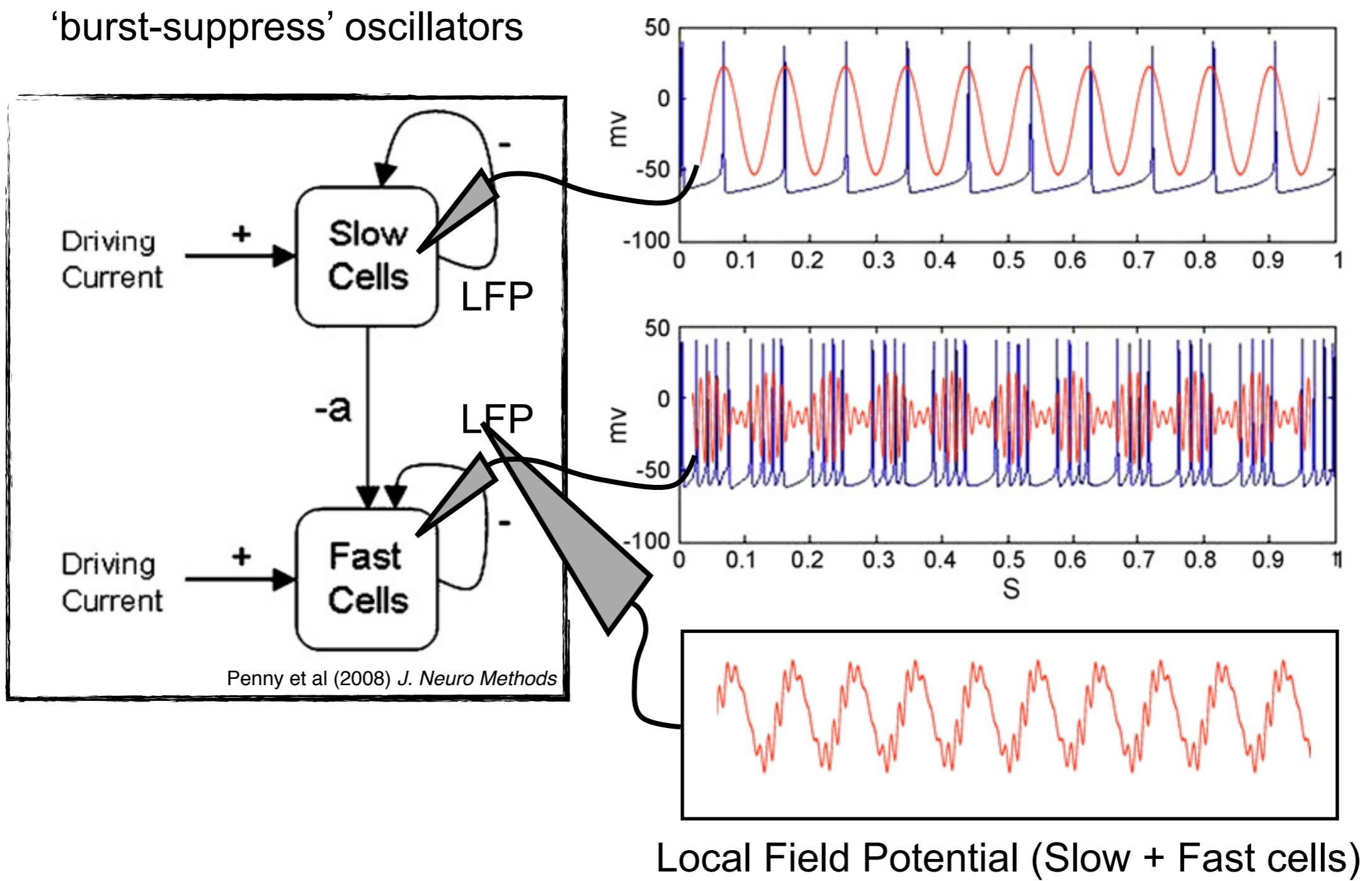
Theory

SIFT

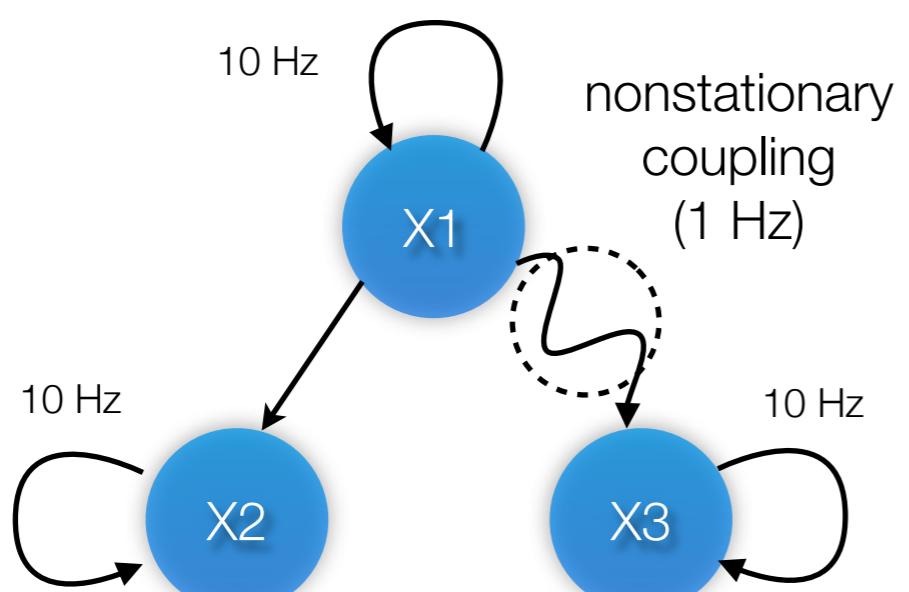
Apps

To-Do

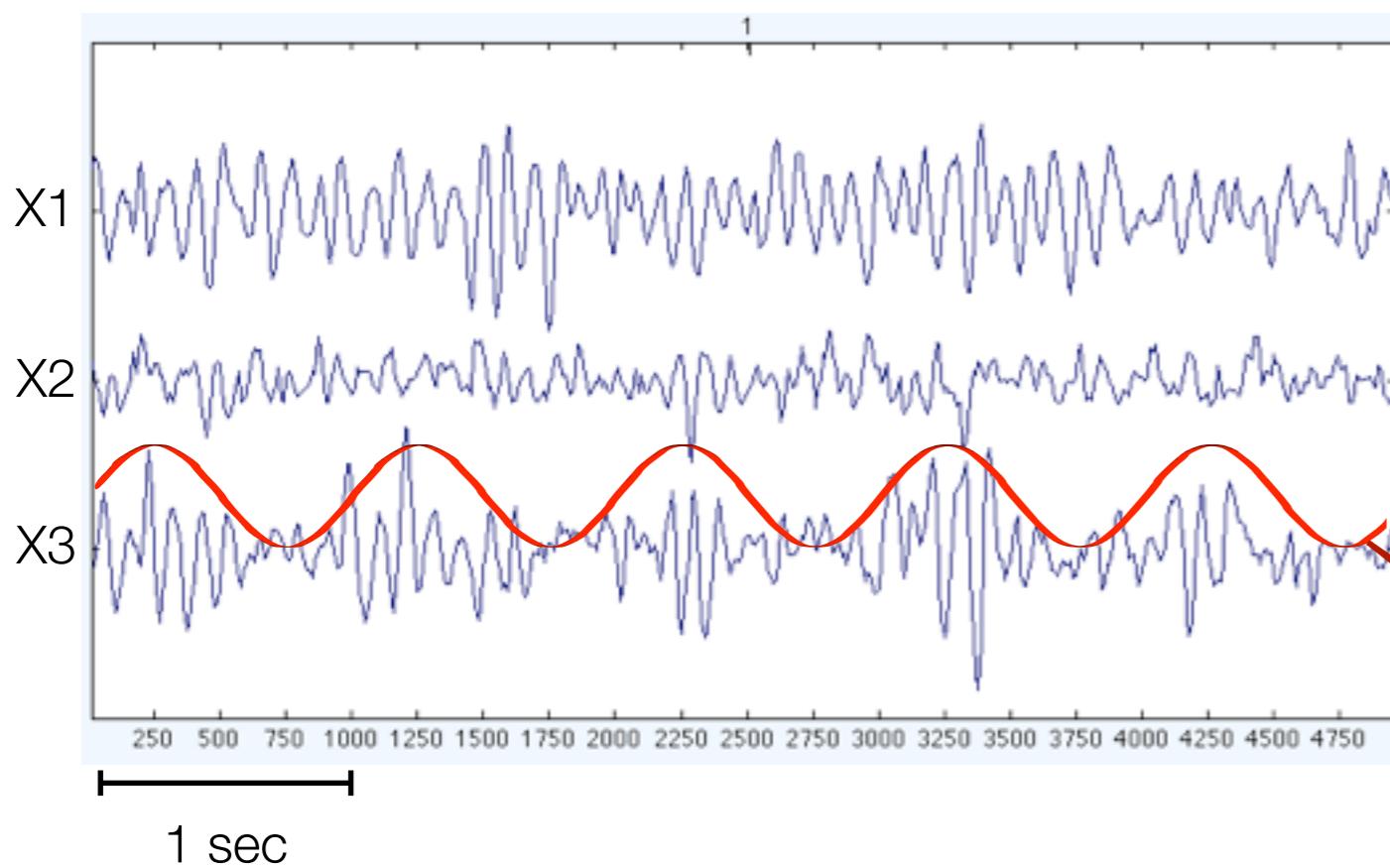
Fin



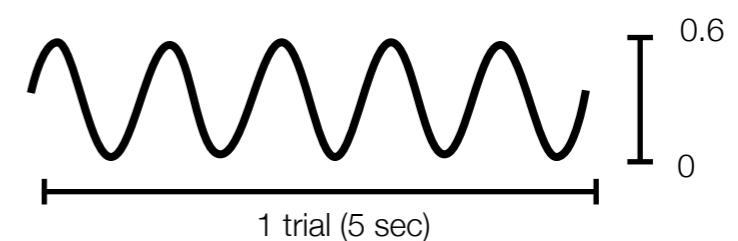
## Graphical Model



PAC may reflect non-stationary or non-linear network dynamics



Time-varying  $X_1 \rightarrow X_3$  coupling  
(1 Hz modulation)



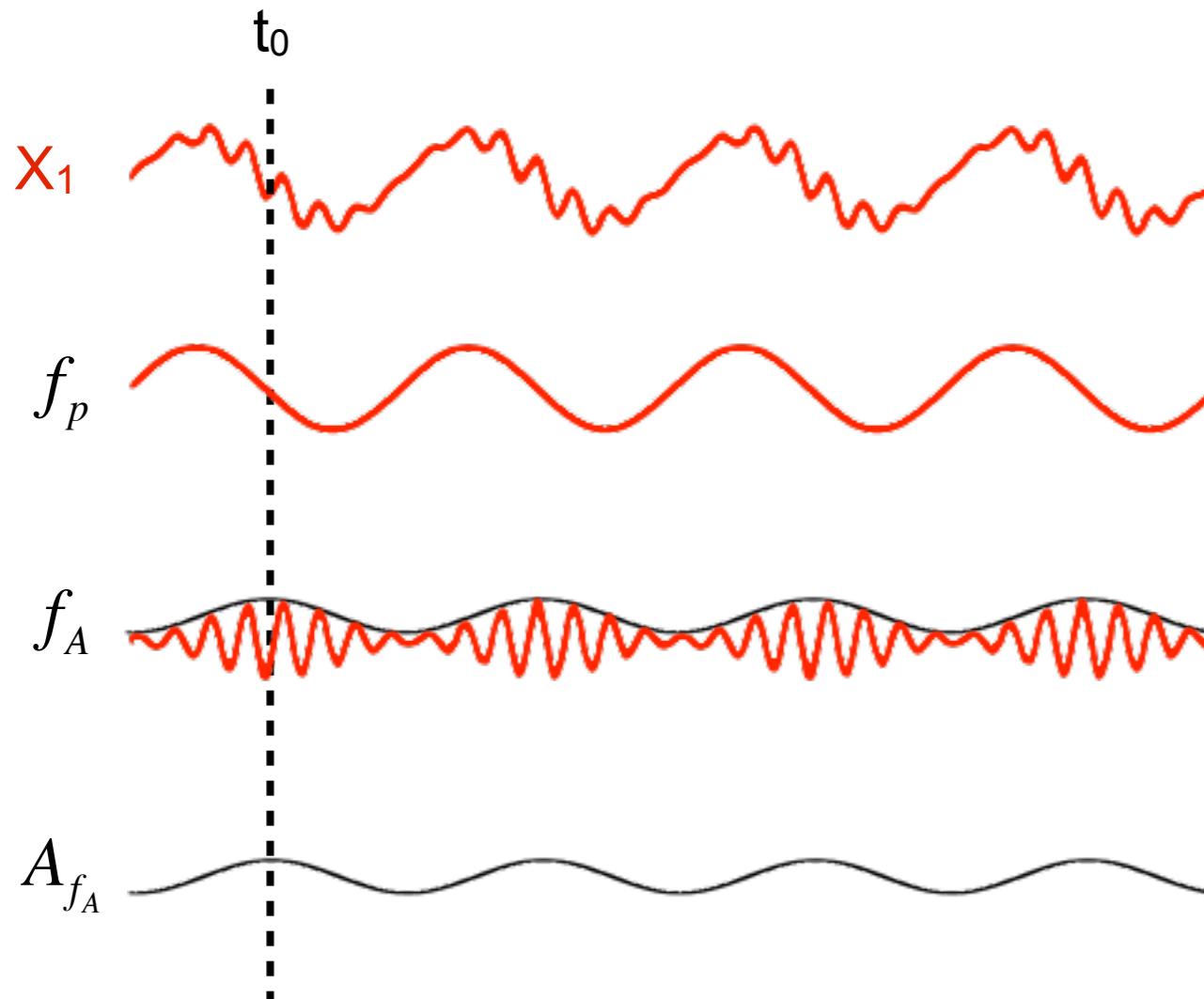
Amplitude Modulation  
10Hz amplitude coupled to 1  
Hz Phase

# Phase-Amplitude Coupling

- May present a functional role in execution of cognitive functions (Axmacher et al. 2010; Cohen et al. 2009a,b; Lakatos et al. 2008; Tort et al. 2008, 2009).
- Suggested involvement in **sensory signal detection** (Handel and Haarmeier 2009), **attentional selection** (Schroeder and Lakatos 2009), and **memory processes** (Axmacher et al. 2010; Tort et al. 2009)

# Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) PNAS



original raw signal

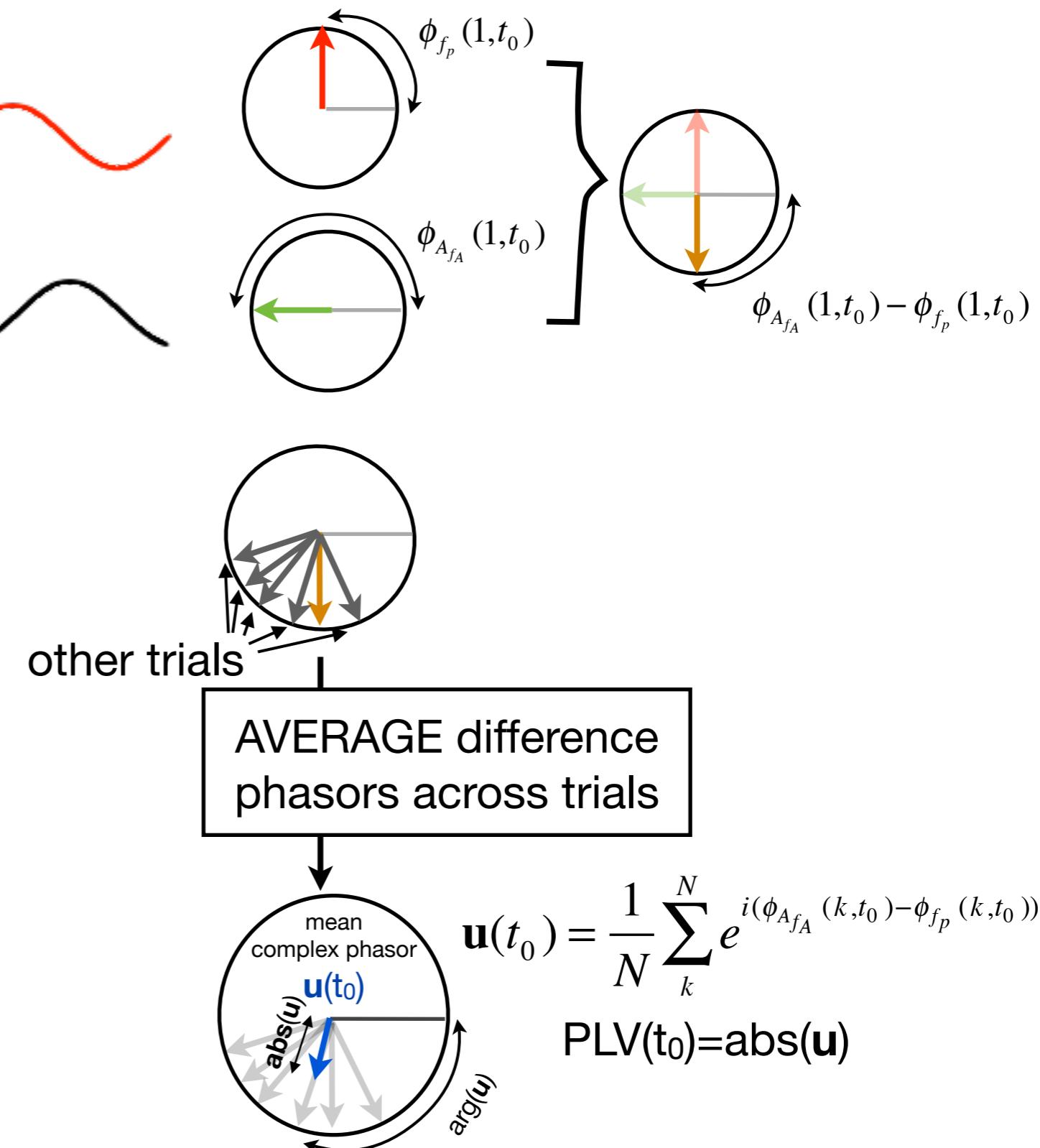
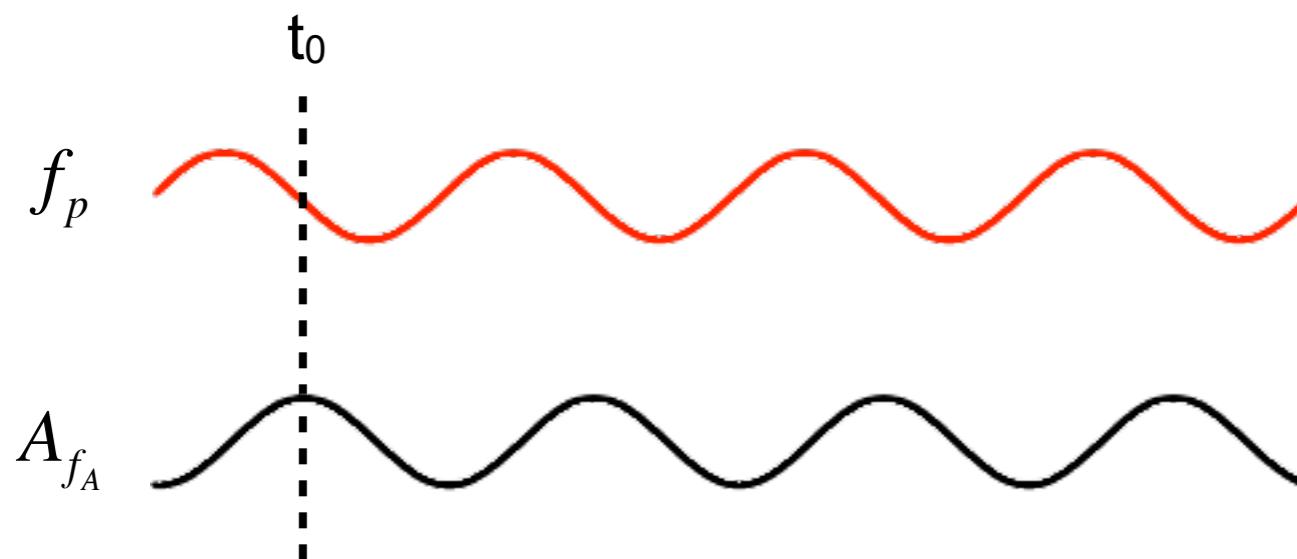
filter  $X_1$  at LFO band (e.g. theta)

filter  $X_1$  at HFO band (e.g. gamma)

get amplitude envelope of filtered signal

# Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) PNAS



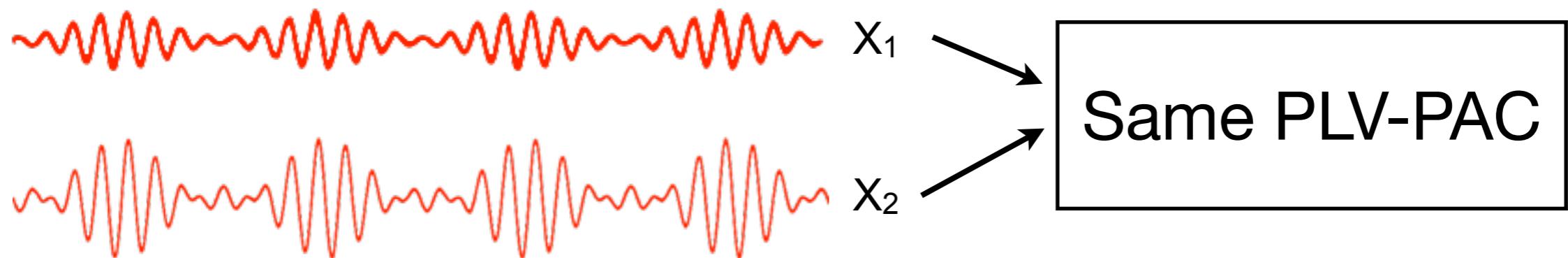
# Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) PNAS

## Problem:

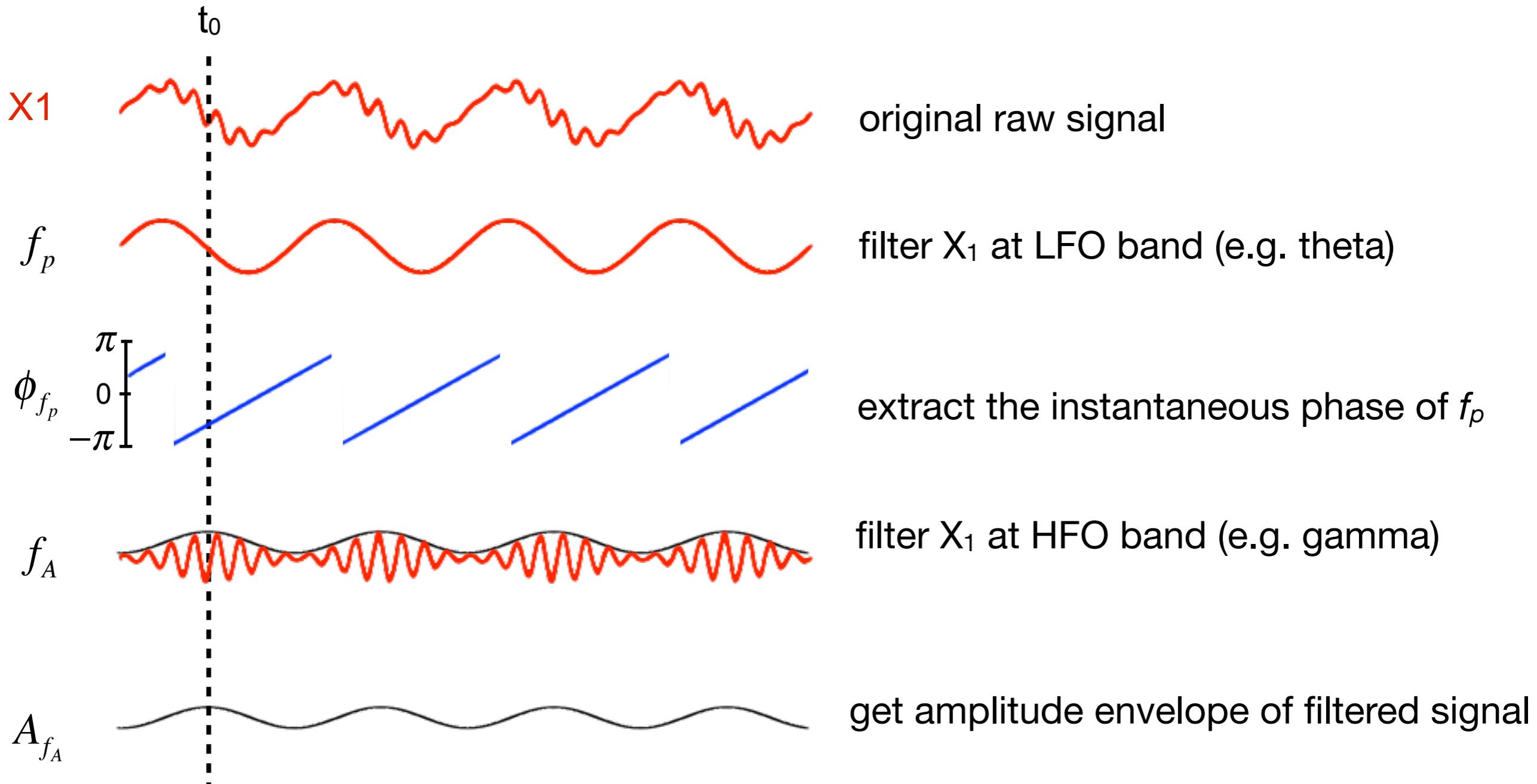
PLV is invariant to differences in amplitude between the two time-series (it only considers phase). Thus PLV-PAC doesn't take into account the *amplitude* of the co-modulation.

In the example below,  $X_1$  and  $X_2$  both would produce the same PAC, even though the high-frequency amplitude of  $X_2$  clearly is more strongly modulated by the low-frequency rhythm.



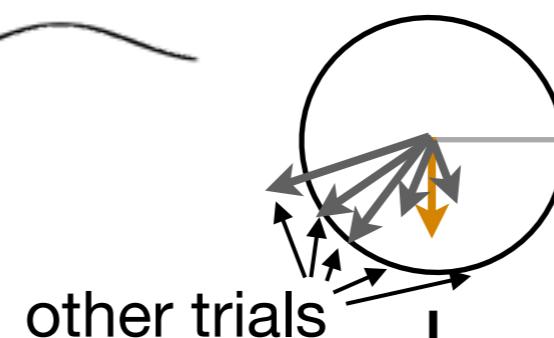
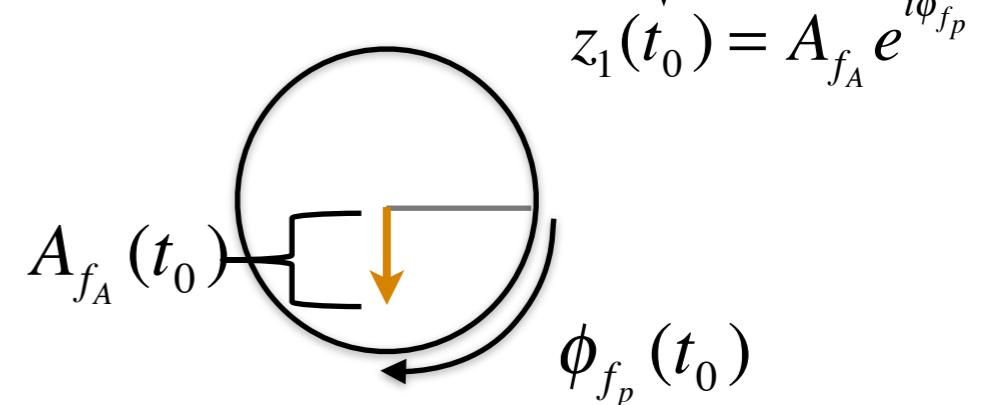
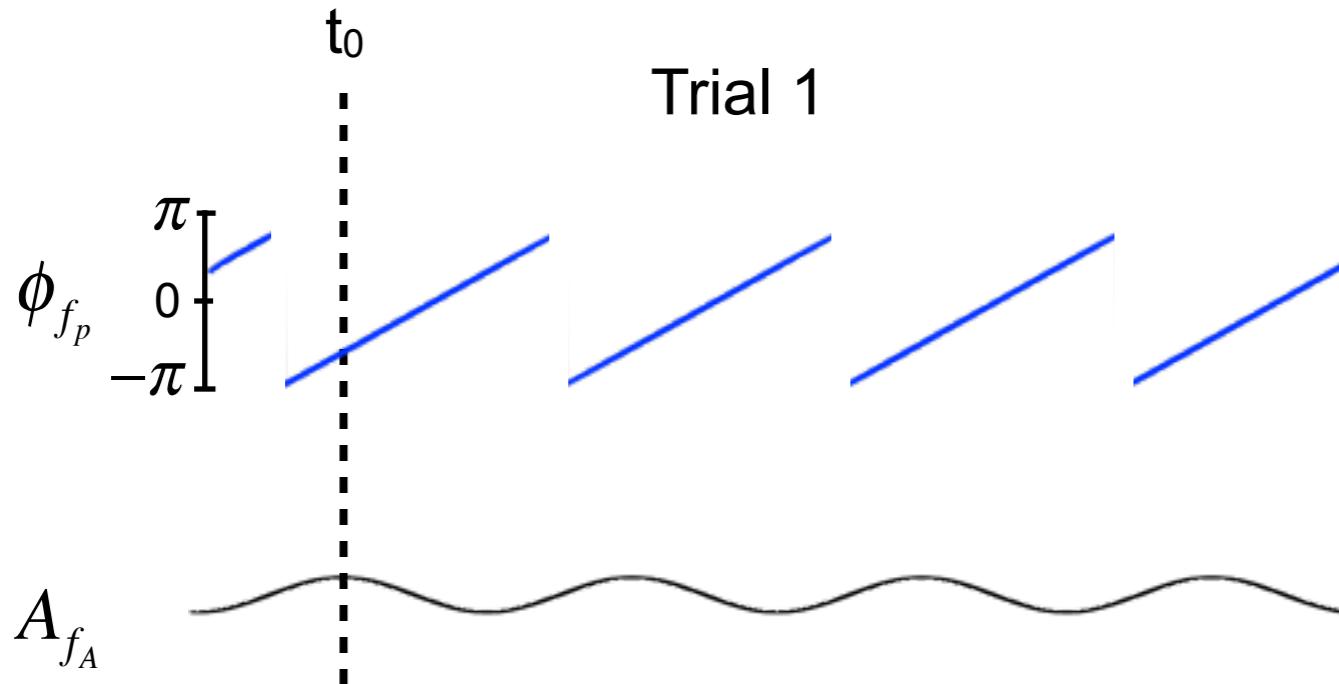
# Phase-Amplitude Coupling: Modulation Index Method

Canolty et al, (2006) *Science*

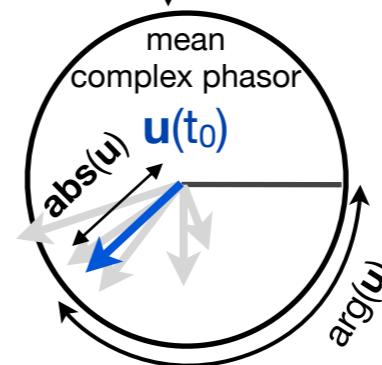
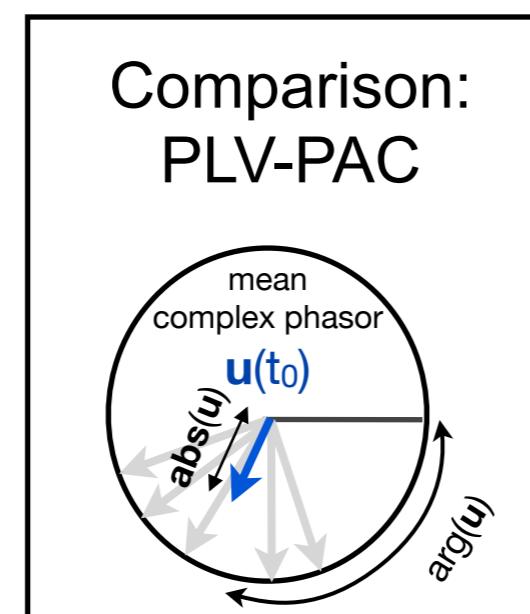


# Phase-Amplitude Coupling: Modulation Index Method

Canolty et al, (2006) *Science*



AVERAGE complex  
phasors across trials



$$\mathbf{u}(t_0) = \frac{1}{N} \sum_k^N z_k(t_0)$$

$$PAC(t_0) = abs(\mathbf{u})$$

# Phase-Amplitude Coupling: Modulation Index Method

Canolty et al, (2006) *Science*

## Computing PAC in EEGLAB:

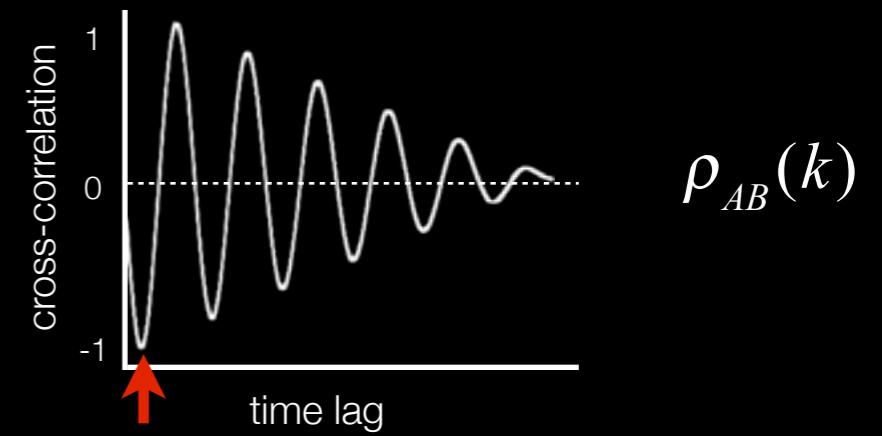
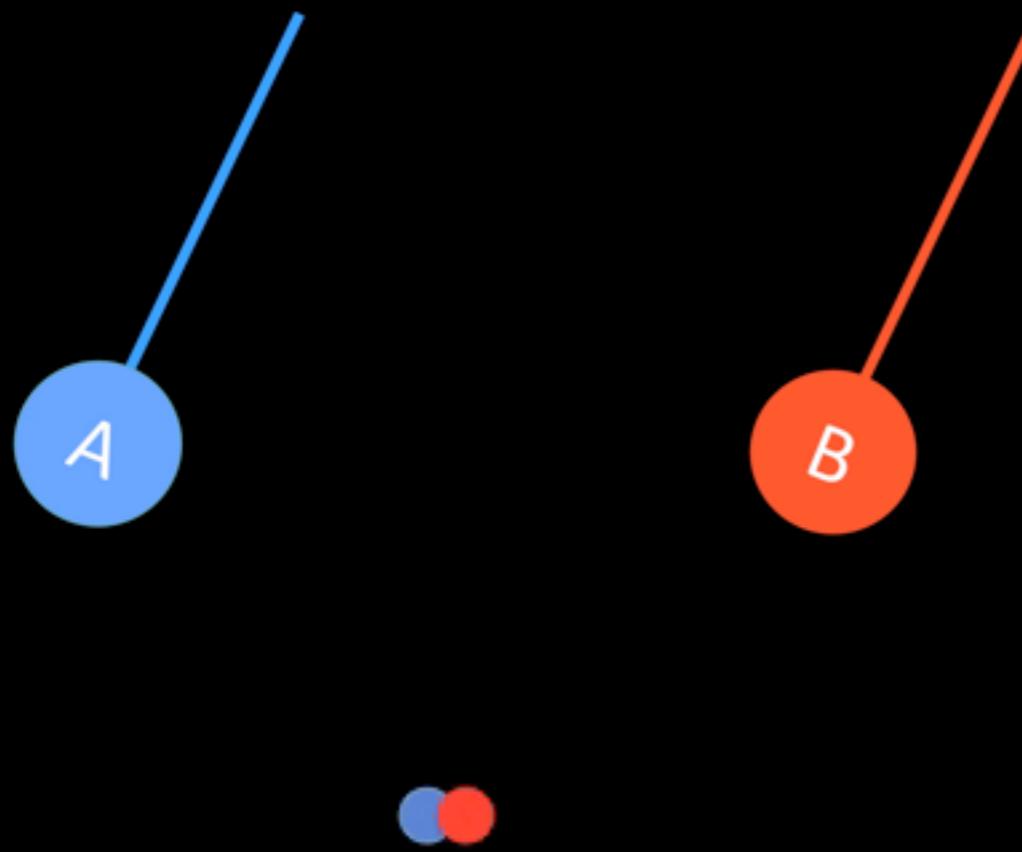
```
pac (IC1, IC2, ..., 'method', 'mod' )
```

PAC can also be applied *between* sources/channels (e.g. determine whether the phase of oscillation at freq.  $w_p$  in IC1 modulates the amplitude of oscillation at freq.  $w_A$  in IC2. This leads to a measure of cross-frequency (non-linear) functional connectivity.



For Modulation Index method  
(other modes also available)

# (Cross)-Correlation $\neq$ Causation



Coherence/CC/PLV indicate ***functional***, but not ***effective*** connectivity

# Estimating Effective Connectivity

## Non-Invasive

- Post-hoc analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

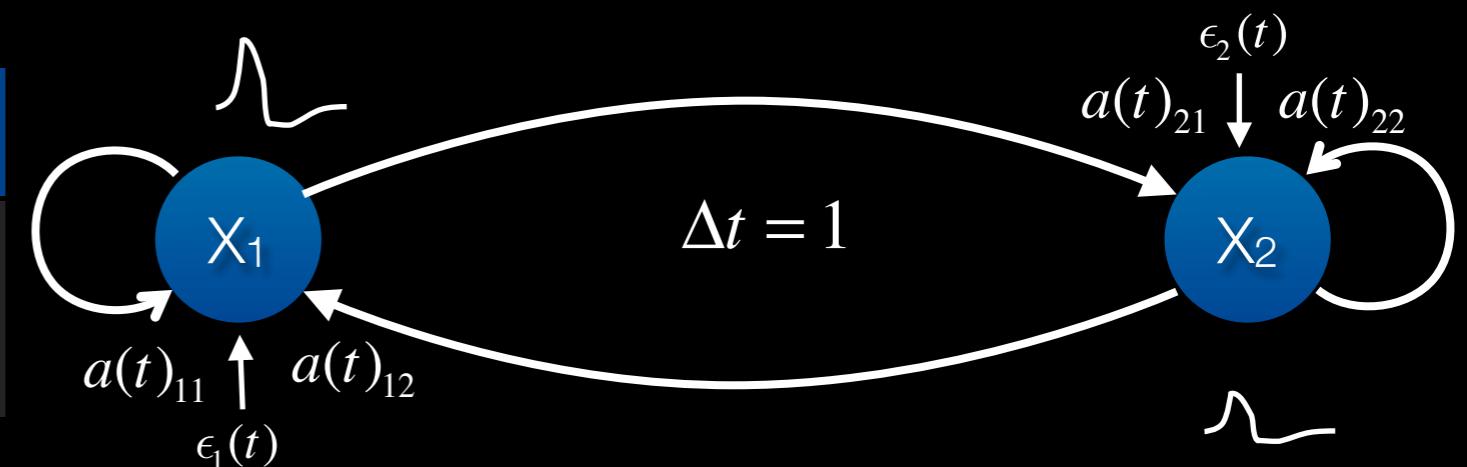
- Data-driven
- Rooted in *conditional predictability*
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved) exogenous causes (Guo, 2008a,b; Ge, 2009)
- Equivalent to Transfer Entropy for Gaussian Variables (Seth, 2009)
- Flexibly allows us to examine **time-varying** (dynamic) multivariate causal relationships in either the **time** or **frequency** domain

# Linear Dynamical Systems

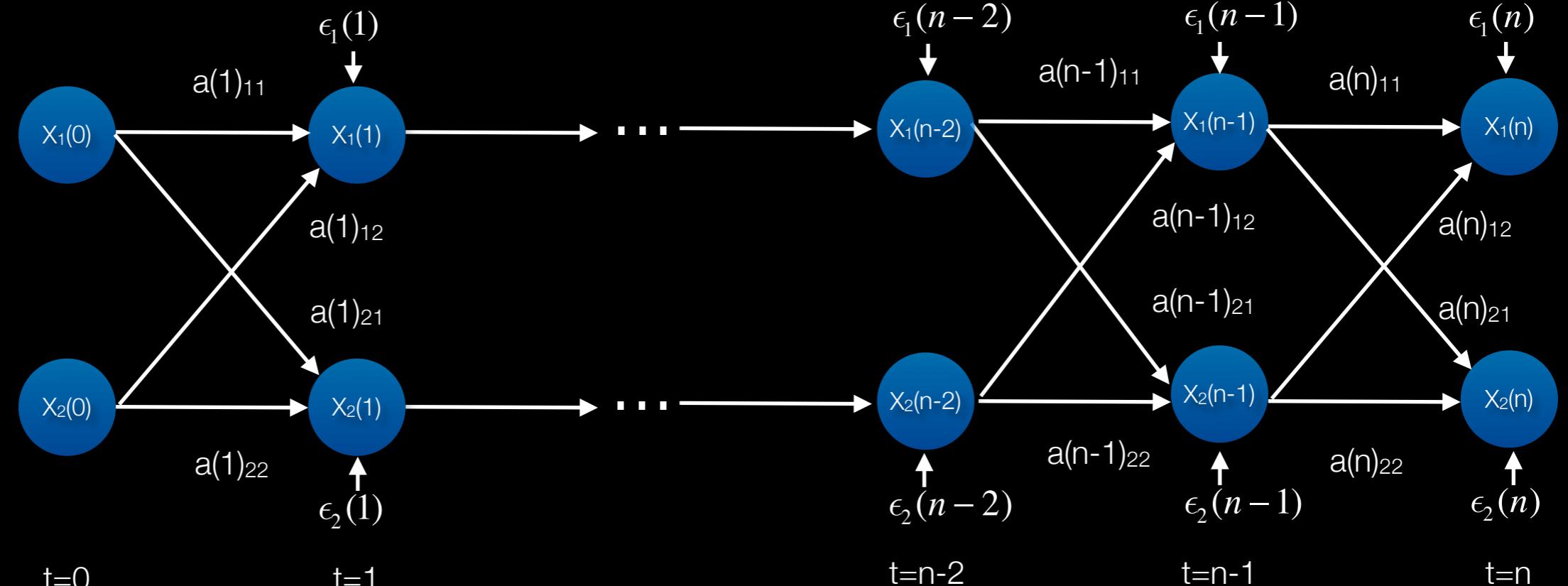
## Stochastic Linear Dynamical System

$$X_1(t) = a(t)_{11}X_1(t-1) + a(t)_{12}X_2(t-1) + \epsilon_1(t)$$

$$X_2(t) = a(t)_{22}X_2(t-1) + a(t)_{21}X_1(t-1) + \epsilon_2(t)$$

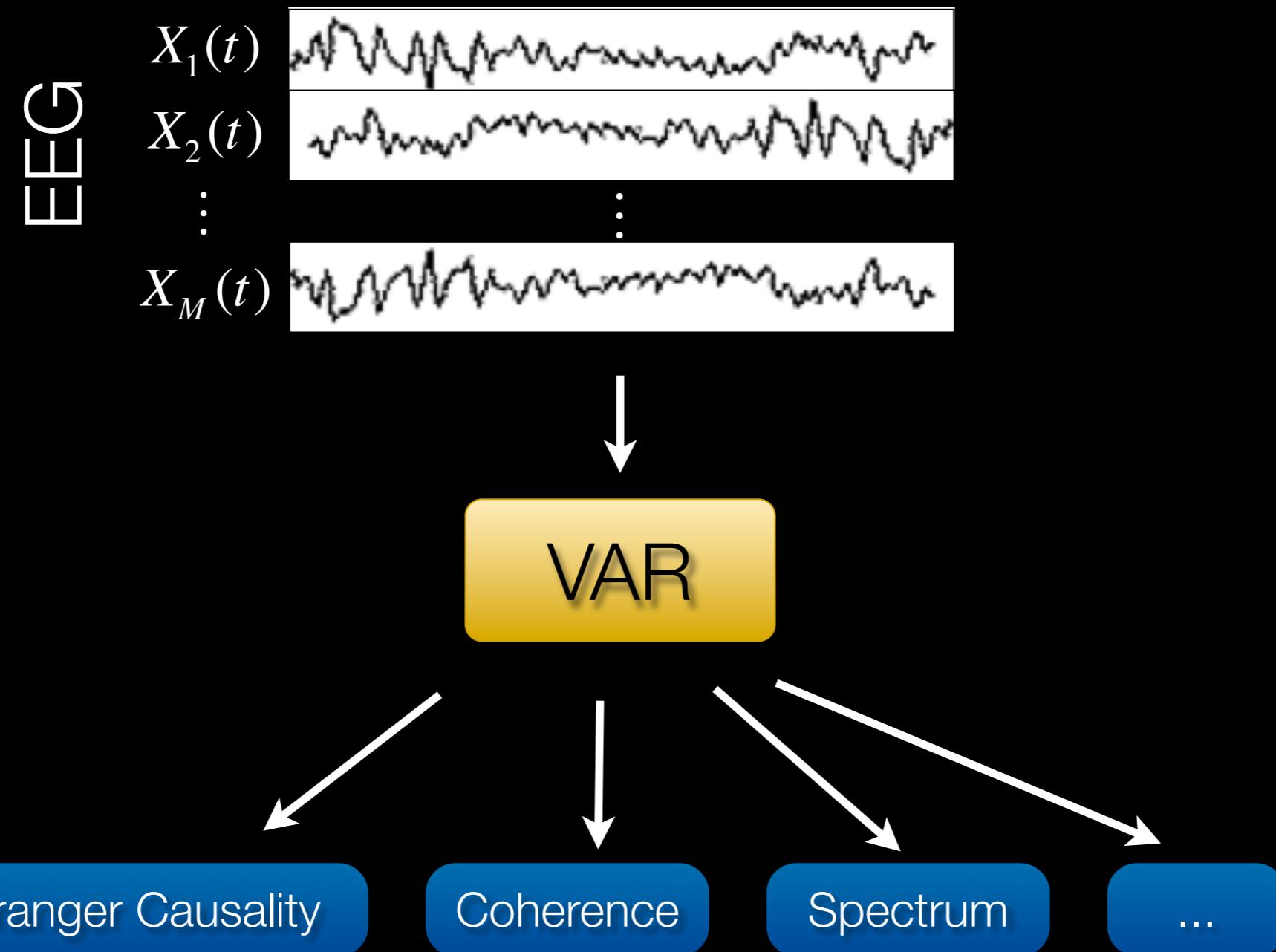


## Order 1 Markov Process (VAR[1])



time step

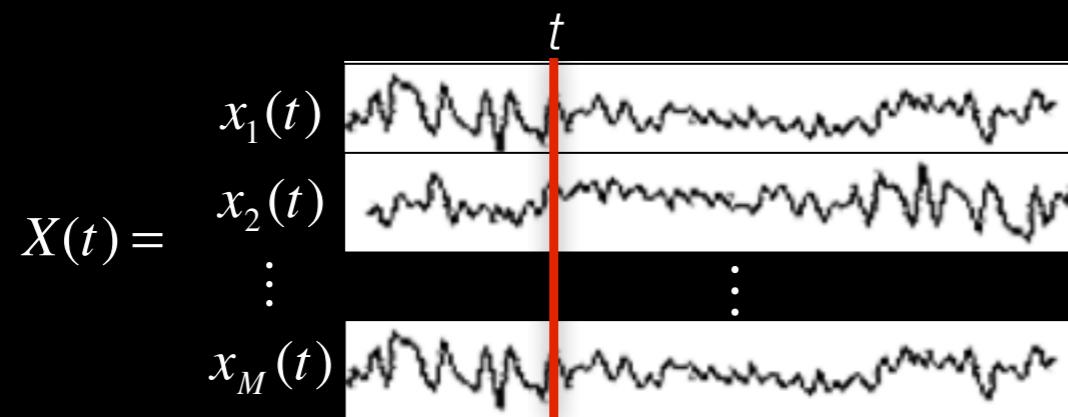
# Vector Autoregressive (VAR / MAR / MVAR) Modeling



# VAR Modeling: Assumptions

- **“Weak” stationarity of the data**
  - mean and variance do not change with time
  - An EEG trace containing prominent evoked potentials is a classic example of a non-stationary time-series
- **Stability**
  - All eigenvalues of the system matrix are  $\leq 1$
  - A stable process will not “blow up” (diverge to infinity)
  - A stable model is always a stationary model (however, the converse is not necessarily true). If a stable model adequately fits the data (white residuals), then the data is likewise stationary

# The Linear VAR Model



Ordinary Least-Squares  
 Lattice Filters  
 Kalman Filtering  
 Bayesian Methods  
 Sparse methods  
 ...

## VAR[p] model

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

model order

M-channel data vector at current time  $t$

$M \times M$  matrix of (possibly time-varying) model coefficients indicating variable dependencies at lag  $k$

random noise process

multichannel data  $k$  samples in the past

$$\mathbf{A}^{(k)}(t) = \begin{pmatrix} a_{11}^{(k)}(t) & \dots & a_{1M}^{(k)}(t) \\ \vdots & \ddots & \vdots \\ a_{M1}^{(k)}(t) & \dots & a_{MM}^{(k)}(t) \end{pmatrix} \quad \mathbf{E}(t) = N(\mathbf{0}, \mathbf{V})$$

# Selecting a VAR Model Order

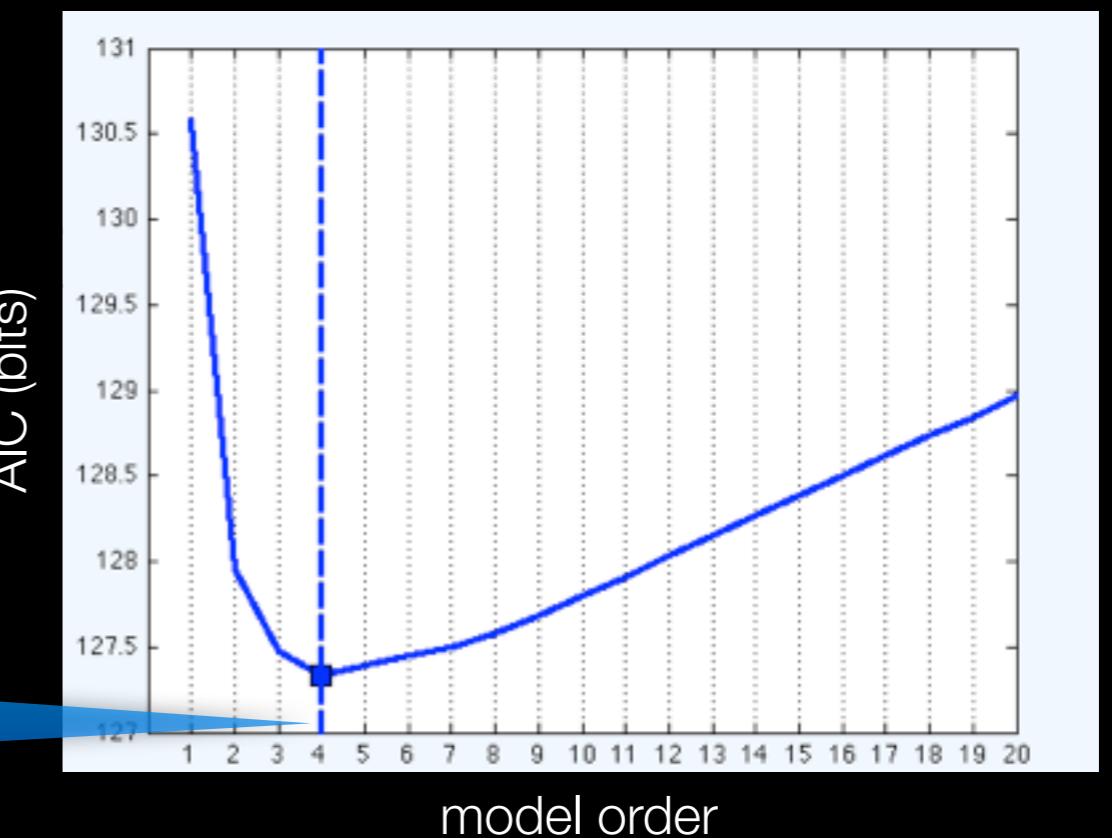
- Model order is typically determined by minimizing information criteria such as Akaike Information Criterion (AIC) for varying model order ( $p$ ):

$$AIC(p) = 2\log(\det(\mathbf{V})) + M^2 p / N$$

Penalizes high model orders (parsimony)

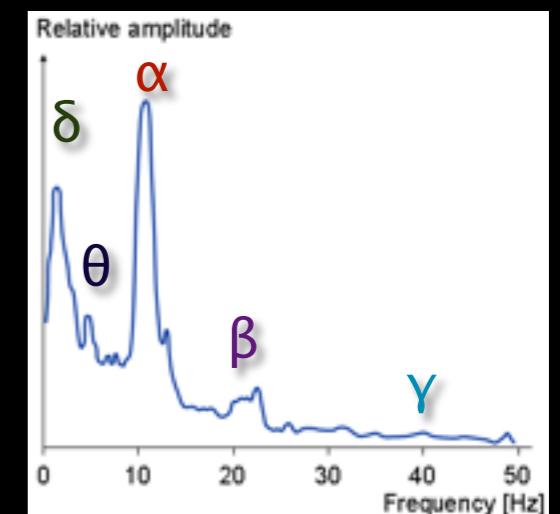
entropy rate (amount of prediction error)

optimal order



# Selecting a VAR Model Order

- Other considerations:
  - A  $M$ -dimensional VAR model of order  $p$  has at most  $Mp/2$  spectral peaks distributed amongst the  $M$  variables. This means we can observe at most  $p/2$  peaks in each variables' spectrum (or in the cross spectrum between each pair of variables)
  - Optimal model order depends on sampling rate. Higher sampling rate often requires higher model orders.



# Model Validation

- If a model is poorly fit to data, then few, if any, inferences can be validly drawn from the model. There are a number of criteria which we can use to determine whether we have appropriately fit our VAR model. Here are three commonly used categories of tests:
- **Whiteness Tests:** checking the residuals of the model for serial and cross-correlation
- **Consistency Test:** testing whether the model generates data with same correlation structure as the real data
- **Stability Test:** checking the stability/stationarity of the model.

# Whiteness Tests

- We can regard the VAR[p] model coefficients  $\mathbf{A}^{(k)}$  as a filter which transforms innovations (random white noise),  $\mathbf{E}(t)$ , into observed, structured data  $\mathbf{X}(t)$ :

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

- Consequently, for coefficient estimates  $\hat{\mathbf{A}}^{(k)}$ , we can obtain the residuals

$$\hat{\mathbf{E}}(t) = \mathbf{X}(t) - \sum_{k=1}^p \hat{\mathbf{A}}^{(k)}(t) \mathbf{X}(t-k)$$

- If we have adequately modeled the data, the residuals should be small and uncorrelated (white). Correlation structure in the residuals means there is still some correlation structure in the data that has not been described by our model.
- Checking the whiteness of residuals typically involves testing whether the residual **autocorrelation** coefficients up to some desired lag  $h$  are sufficiently small to ensure that we cannot reject the null hypothesis of white residuals at some desired significance level.

# Whiteness Tests

$$\mathbf{E}(t) = N(0, \mathbf{V})$$

$$C_l = \langle \hat{\mathbf{E}}(t)\hat{\mathbf{E}}'(t-l) \rangle$$

$$R_l = D^{-1} C_l D^{-1}$$

$$D = \text{diag}\left(\sqrt{\text{diag}(C_0)}\right)$$

$$R_h = (R_1, \dots, R_h)$$

autocovariance at lag  $l$  ...

with corresponding autocorrelation  $R$

set of autocorrelations up to lag  $h$

We want to test the null hypothesis  $H_0 : \mathbf{R}_h = (R_1, \dots, R_h) = 0$

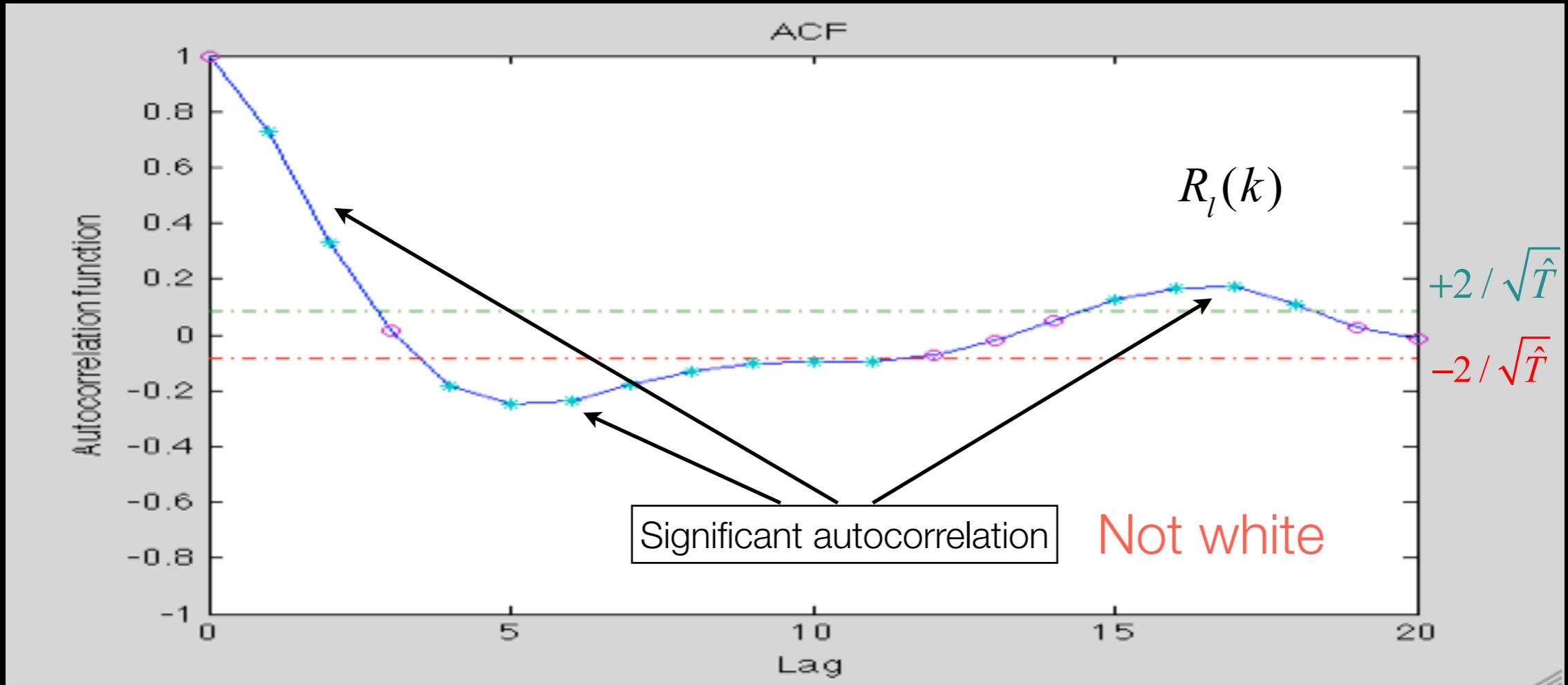
against the alternative:

$H_1 : \mathbf{R}_h \neq 0$

Two possible ways to do this:

- Autocorrelation function test
- Portmanteau tests

# Whiteness Tests: ACF



Under the null hypothesis that  $\hat{\mathbf{E}}(t)$  is Gaussian white noise, we expect approximately  $1/20=5\%$  of a.c.f. coefficients to exceed the threshold  $\pm 2/\sqrt{\hat{T}}$ . This gives us a p-value for rejecting  $H_0$

$$\rho = \frac{\text{count}(|\mathbf{R}_h| > 2/\sqrt{\hat{T}})}{\text{count}(\mathbf{R}_h)} = \frac{\text{count}(|\mathbf{R}_h| > 2/\sqrt{\hat{T}})}{M^2(h+1)-M}$$

If  $p < 0.05$  then we cannot reject  $H_0$  at the 5% level and we accept that residuals  $\hat{\mathbf{E}}(t)$  are white

# Whiteness Tests: Portmanteau

**Table 3. Popular portmanteau tests for whiteness of residuals, implemented in SIFT. Here  $\hat{T} = TN$  is the total number of samples used to estimate the covariance**

Portmanteau Test	Formula (Test Statistic)	Notes
Box-Pierce (BPP)	$Q_h := \hat{T} \sum_{l=1}^h \text{tr}(C_l' C_0^{-1} C_l C_0^{-1})$	The original portmanteau test. Potentially overly-conservative. Poor small-sample properties.
Ljung-Box (LBP)	$Q_h := \hat{T}(\hat{T} + 2) \sum_{l=1}^h (\hat{T} - l)^{-1} \text{tr}(C_l' C_0^{-1} C_l C_0^{-1})$	Modification of BPP to improve small-sample properties. Potentially inflates the variance of the test statistic. Slightly less conservative than LMP with slightly higher (but nearly identical) statistical power.
Li-McLeod (LMP)	$Q_h := \hat{T} \sum_{l=1}^h \text{tr}(C_l' C_0^{-1} C_l C_0^{-1}) + \frac{M^2 h(h+1)}{2\hat{T}}$	Further modification of BPP to improve small-sample properties without variance inflation. Slightly more conservative than LBP. Probably the best choice in most conditions.

Mullen, 2010 (SIFT Manual)

These test statistics are asymptotically  $\chi^2$  distributed with  $M^2(h-p)$  d.f.

# Consistency Tests

- A well-fit model should be able to generate data that has the same correlation structure as the original data.
- One test of this is *percent consistency* (Ding et al, 2000)
- Here we generate simulated data from our fitted model (feeding it white noise) and calculate auto- and cross-correlations up to a fixed lag for both simulated data ( $\mathbf{R}_s$ ) and real data ( $\mathbf{R}_r$ ).
- The percent consistency (PC) is then given by

$$PC = \left( 1 - \frac{\|\mathbf{R}_s - \mathbf{R}_r\|_2}{\|\mathbf{R}_r\|_2} \right) \times 100$$

- A PC value near 100% indicates that the model is able to generate data that has a nearly identical correlation structure as the original data. A PC value near 0% indicates a complete failure to model the data.

# Granger Causality

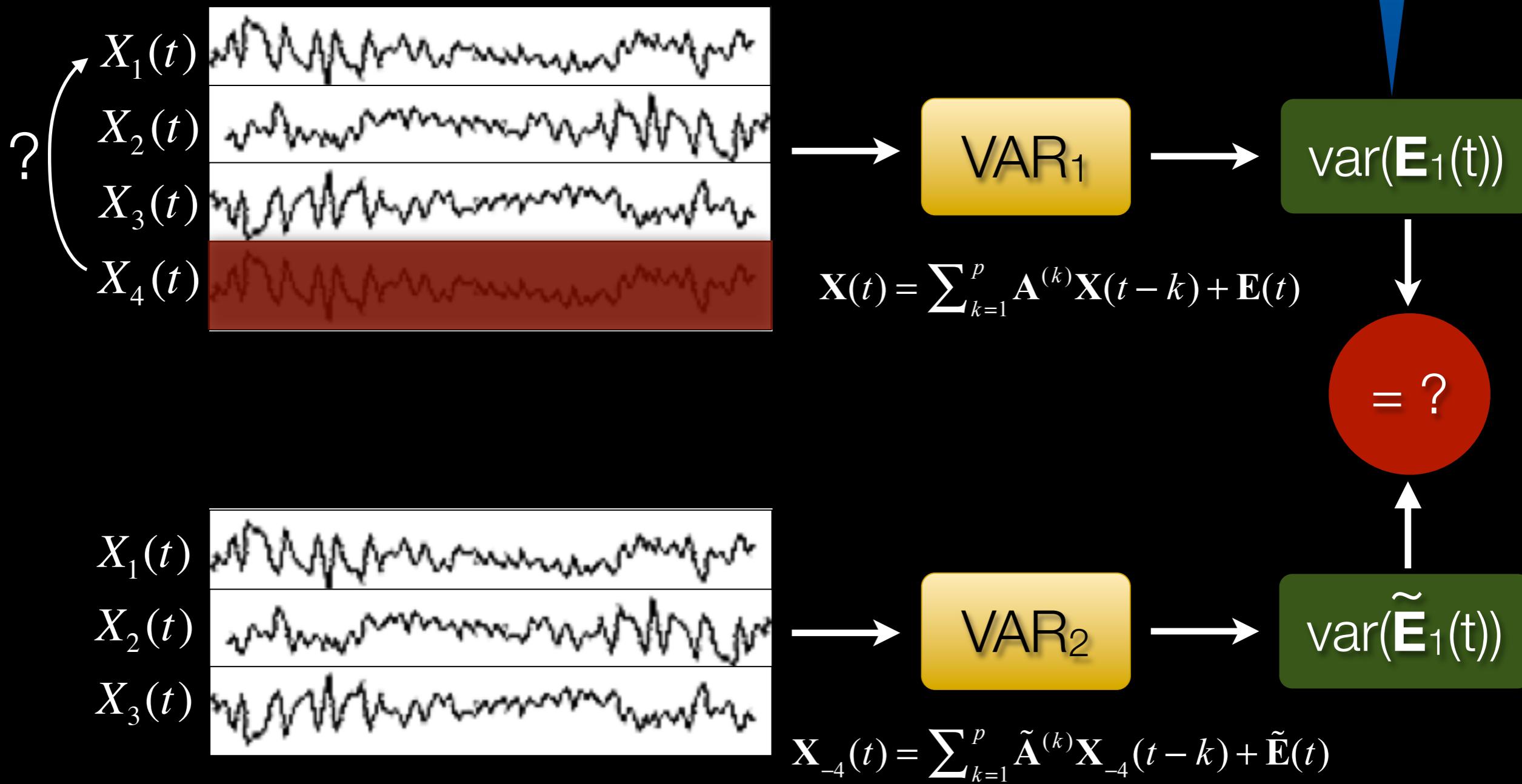
- First introduced by Wiener (1958). Later reformulated by Granger (1969) in the context of linear stochastic autoregressive models
- Relies on two assumptions:

## Granger Causality Axioms

1. Causes should precede their effects in time (Temporal Precedence)
2. Information in a cause's past should improve the prediction of the effect, above and beyond the information contained in past of the effect (and other measured variables)

# Granger Causality

Does  $\mathbf{X}_4$  granger-cause  $\mathbf{X}_1$ ?  
(conditioned on  $\mathbf{X}_2, \mathbf{X}_3$ )



# Granger Causality

- Granger (1969) quantified this definition for **bivariate** processes in the form of an F-ratio:

$$F_{X_1 \leftarrow X_2} = \ln \left( \frac{var(\tilde{E}_1)}{var(E_1)} \right) = \ln \left( \frac{var(X_1(t) | X_1(\cdot))}{var(X_1(t) | X_1(\cdot), X_2(\cdot))} \right)$$

full model

- Alternately, for a **multivariate interpretation** we can fit a single VAR model to all channels and apply the following definition:

## Definition 1

$X_j$  granger-causes  $X_i$  *conditioned on all other variables in  $\mathbf{X}$*   
if and only if  $A_{ij}(k) >> 0$  for some lag  $k \in \{1, \dots, p\}$

# Granger Causality Quiz

- Example: 2-channel VAR process of order 1

$$\begin{pmatrix} X_1(t) \\ X_2(t) \end{pmatrix} = \begin{pmatrix} -0.5 & 0 \\ 0.7 & 0.2 \end{pmatrix} \begin{pmatrix} X_1(t-1) \\ X_2(t-1) \end{pmatrix} + \begin{pmatrix} E_1(t) \\ E_2(t) \end{pmatrix}$$

$$X_1(t) = -0.5X_1(t-1) + 0X_2(t-1) + E_1(t)$$
$$X_2(t) = 0.7X_1(t-1) + 0.2X_2(t-1) + E_2(t)$$

Which causal structure does this model correspond to?

a) →

b) ←

c) ↔

# Granger Causality – Frequency Domain

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)} \mathbf{X}(t - k) + \mathbf{E}(t)$$

Fourier-transforming  $\mathbf{A}^{(k)}$  we obtain

$$\mathbf{A}(f) = -\sum_{k=0}^p \mathbf{A}^{(k)} e^{-i2\pi fk}; \mathbf{A}^{(0)} = I$$

We can then define the spectral matrix  $\mathbf{X}(f)$  as follows:

$$\mathbf{X}(f) = \mathbf{A}(f)^{-1} \mathbf{E}(f) = \mathbf{H}(f) \mathbf{E}(f)$$

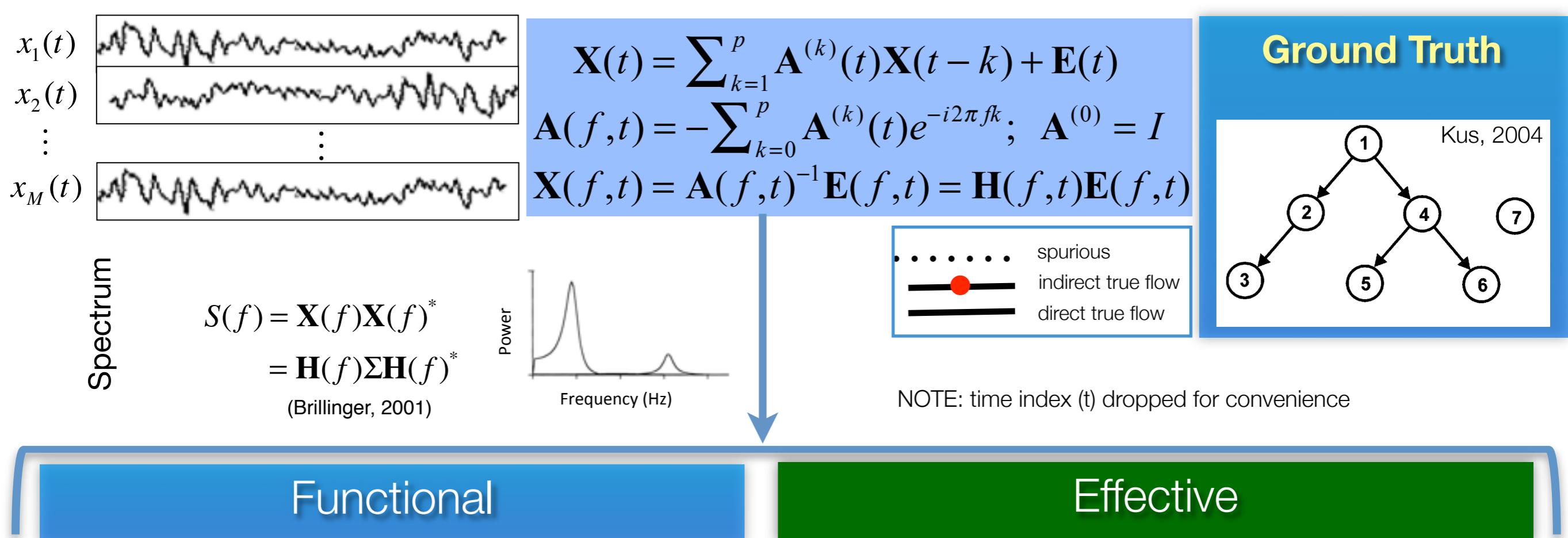
Where  $\mathbf{H}(f)$  is the *transfer matrix* of the system.

Likewise,  $\mathbf{X}(f)$  and  $\mathbf{E}(f)$  correspond to the fourier transforms of the data and residuals, respectively

## Definition 2

$X_j$  granger-causes  $X_i$  *conditioned on all other variables in  $\mathbf{X}$*   
if and only if  $|\mathbf{A}_{ij}(f)| >> 0$  for some frequency  $f$

leads to  
PDC



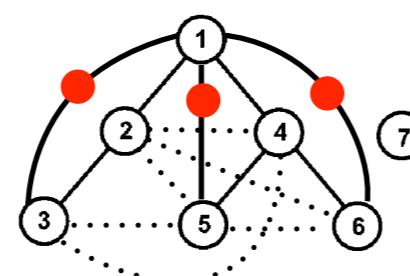
## Functional

## Effective

### Bivariate Coherency

$$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f)S_{jj}(f)}}$$

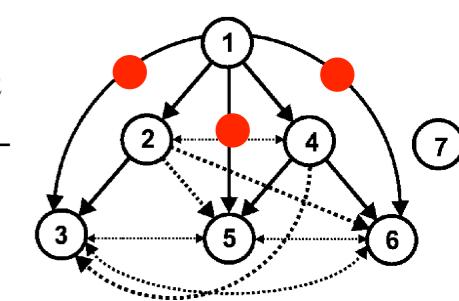
(Bendat and Piersol, 1986)



### Granger-Geweke Causality

$$F_{ij}(f) = \frac{\Sigma_{jj} - (\Sigma_{ij}^2 / \Sigma_{ii}) |H_{ij}(f)|^2}{S_{ii}(f)}$$

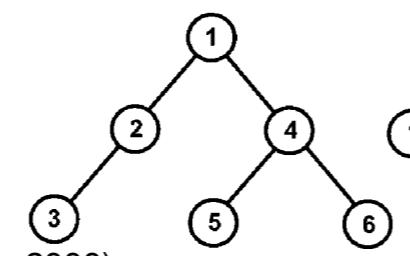
(Geweke, 1982; Bressler et al., 2007)



### Multivariate Partial Coherence

$$P_{ij}(f) = \frac{S_{ij}^{-1}(f)}{\sqrt{S_{ii}^{-1}(f)S_{jj}^{-1}(f)}}$$

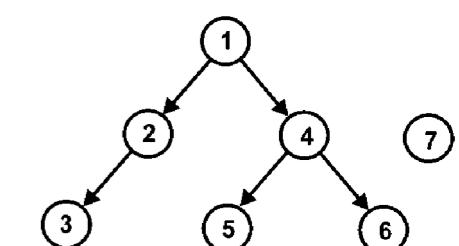
(Bendat and Piersol, 1986; Dalhaus, 2000)



### Partial Directed Coherence

$$\pi_{ij}^2(f) = \frac{|A_{ij}(f)|^2}{\sum_{k=1}^M |A_{kj}(f)|^2}$$

(Baccalá and Sameshima, 2001)



	Estimator	Formula		Estimator	Formula		Estimator	Formula
Spectral M.	Spectral Density Matrix	$S(f) = X(f)X(f)^*$ $= H(f)\Sigma H(f)^*$	Partial Directed Coherence Measures	Normalized Partial Directed Coherence (PDC)	$\pi_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{k=1}^M  A_{kj}(f) ^2}}$ $0 \leq  \pi_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M  \pi_{ij}(f) ^2 = 1$	Directed Transfer Function Measures	Normalized Directed Transfer Function (DTF)	$\gamma_{ij}(f) = \frac{H_{ij}(f)}{\sqrt{\sum_{k=1}^M  H_{ik}(f) ^2}}$ $0 \leq  \gamma_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M  \gamma_{ij}(f) ^2 = 1$
Coherence Measures	Coherency	$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f)S_{jj}(f)}}$ $0 \leq  C_{ij}(f) ^2 \leq 1$	Generalized PDC (GPDC)	$\bar{\pi}_{ij}(f) = \frac{\frac{1}{\Sigma_{ii}} A_{ij}(f)}{\sqrt{\sum_{k=1}^M \frac{1}{\Sigma_{ii}^2}  A_{kj}(f) ^2}}$ $0 \leq  \bar{\pi}_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M  \bar{\pi}_{ij}(f) ^2 = 1$	Full-Frequency DTF (ffDTF)	$\eta_{ij}^2(f) = \frac{ H_{ij}(f) ^2}{\sum_f \sum_{k=1}^M  H_{ik}(f) ^2}$		
Imaginary Coherence (iCoh)	$iCoh_{ij}(f) = \text{Im}(C_{ij}(f))$		Renormalized PDC (rPDC)	$\lambda_{ij}(f) = Q_{ij}(f)^* V_{ij}(f)^{-1} Q_{ij}(f)$ where $Q_{ij}(f) = \begin{pmatrix} \text{Re}[A_{ij}(f)] \\ \text{Im}[A_{ij}(f)] \end{pmatrix}$ and $V_{ij}(f) = \sum_{k,l=1}^p R_{jj}^{-1}(k,l) \Sigma_{ii} Z(2\pi f, k, l)$ $Z(\omega, k, l) = \begin{pmatrix} \cos(\omega k) \cos(\omega l) & \cos(\omega k) \sin(\omega l) \\ \sin(\omega k) \cos(\omega l) & \sin(\omega k) \sin(\omega l) \end{pmatrix}$ $R$ is the $[(Mp)^2 \times (Mp)^2]$ covariance matrix of the VAR[p] process (Lütkepohl, 2006)	Direct (dDTF)	$\delta_{ij}^2(f) = \eta_{ij}^2(f) P_{ij}^2(f)$		
Partial Coherence (pCoh)	$P_{ij}(f) = \frac{\hat{S}_{ij}(f)}{\sqrt{\hat{S}_{ii}(f)\hat{S}_{jj}(f)}}$ $\hat{S}(f) = S(f)^{-1}$ $0 \leq  P_{ij}(f) ^2 \leq 1$	Granger-Geweke	$G_i(f) = \sqrt{1 - \frac{\det(S(f))}{S_{ii}(f)\mathbf{M}_i(f)}}$ $\mathbf{M}_i(f)$ is the <b>minor</b> of $S(f)$ obtained by removing the $i^{\text{th}}$ row and column of $S(f)$ and returning the determinant.	$F_{ij}(f) = \frac{(\Sigma_{jj} - (\Sigma_{ij}^2 / \Sigma_{ii}))  H_{ij}(f) ^2}{S_{ii}(f)}$				
Multiple Coherence (mCoh)								

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

$$\mathbf{A}(f, t) = -\sum_{k=0}^p \mathbf{A}^{(k)}(t) e^{-i2\pi fk}; \quad \mathbf{A}^{(0)} = I$$

$$\mathbf{X}(f, t) = \mathbf{A}(f, t)^{-1} \mathbf{E}(f, t) = \mathbf{H}(f, t) \mathbf{E}(f, t)$$

$H(f)$  Transfer Function  
 $A(f)$  System Matrix  
 $\Sigma$  Noise Covariance Matrix

■ Variance Stabilization

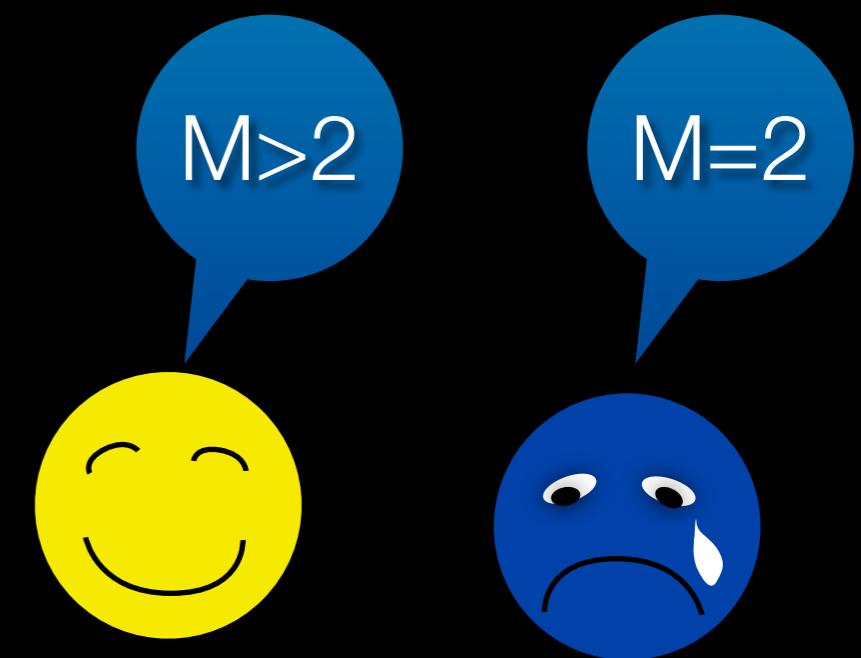
INTERMISSION

# Multivariate versus Bivariate

- Exclusion of processes that may exert causal influence on modeled processes increases the risk of causal mis-identification. (c.f. Pearl, *Causality: Models, Inference and Reasoning*, 2009)

- Multivariate approaches are generally superior to bivariate approaches

- allow detection of direct versus indirect dependence, reducing false positives
- allow us to partially control for exogenous/unobserved causes (e.g. Guo, et al., J. Neuro. Methods, 2008)



- In the absence of *a priori* knowledge concerning causal structure, it is advisable to include as many processes as possible in a causal model (*within data/modeling limitations*)

# Multivariate Models: Limitations

M>2



- However, multivariate methods come with a cost:
  - More parameters + limited data = higher risk of **over-fitting** or worse yet....
  - ...the problem becomes *ill-posed* or *under-determined*. There are insufficient observations to uniquely determine a solution to the system of equations defining our model.

# Multivariate Models: Limitations

M&gt;2



How many samples do we need?

- $N$  = number of samples required
- $M$  = number of variables/sources
- $T$  = number of trials/realizations
- $p$  = model order
- We have  $M^2p$  model coefficients to estimate. So our ordinary least-squares solution requires a *minimum* of  $M^2p$  samples.

$$N = O(M^2p)$$

- Back-of-envelope:  $M=20, p=10, T=1$  We need  $20^2 \times 10 = 4000$  samples -- 20 second epoch at sampling rate of 200Hz!

Ensemble aggregation ( $T > 1$ )?

- $M=20, p=10, T=50$ :  $4000/50$  samples/trial  $\rightarrow 20/50 = 0.4$  sec epoch

# Multivariate Models: Constraints

M>2



## Solutions?

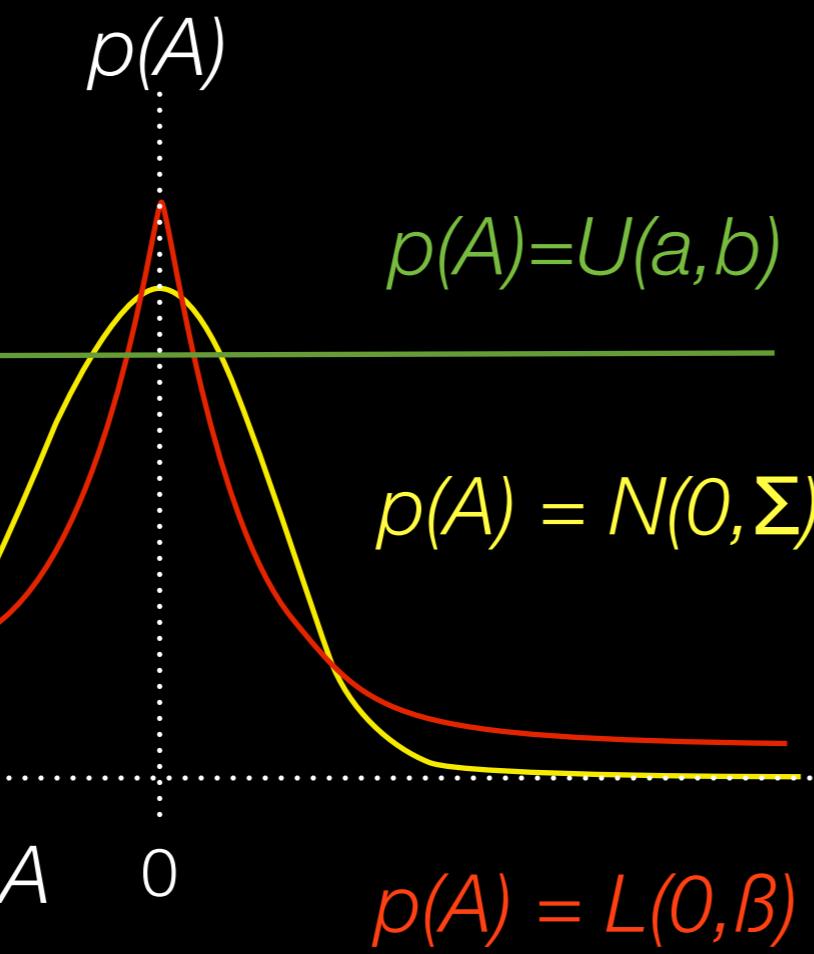
### **Make assumptions (impose constraints)**

We want to *a priori* restrict the range of allowable values for our parameters -- transforming the problem from one with infinite number of solutions in the original parameter space to one with a unique (“best”) solution in the new parameter space

In a Bayesian context, this corresponds to making assumptions about the *prior distribution* of the parameters (Gaussian, Laplacian, ...)

# Multivariate Models: Constraints

$$\hat{A} = \arg \max_A \left\{ p(A|D) \equiv p(D|A) \boxed{p(A)} \right\}$$

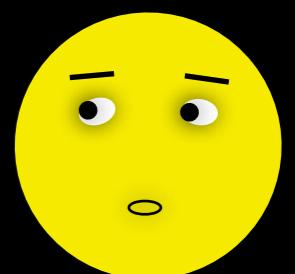


posterior

likelihood

prior

M&gt;2



Unconstrained (all values equally probable). e.g. Uniform distribution

Smoothness constraints

- large differences in values unlikely
- small (non-zero) values most probable. e.g. Normal (gaussian) prior.

Sparsity constraint

- many values small or exactly zero with occasional large values e.g. Laplacian prior

# Smoothness Constraints

- Standard least-squares solution



$$A(t) = \arg \min_{\hat{A}} \left( \|Y - Z\tilde{A}\|_2^2 \right)$$

prediction error

A blue brace is drawn from the top of the equation to the right side of the error term, highlighting the prediction error.

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

$$\tilde{\mathbf{A}} = [A^{(1)}(t), \dots, A^{(p)}(t)]^T$$

$$\mathbf{X}_k = [X(p+1-k), \dots, X(N-k)]^T$$

$$\mathbf{Z} = [X_1, \dots, X_p]$$

$$Y = X_0$$

Rewrite VAR[p] as VAR[1]

# Smoothness Constraints

- Ridge Regression  
(Tikhonov Regularization, Minimum-(L<sub>2</sub>)-Norm Estimation, ...)

$$A(t) = \arg \min_{\hat{A}} \left( \|Y - Z\tilde{A}\|_2^2 + \lambda \|\tilde{A}\|_2^2 \right)$$

prediction error

penalty term,  
enforces smoothness

M>2



regularization

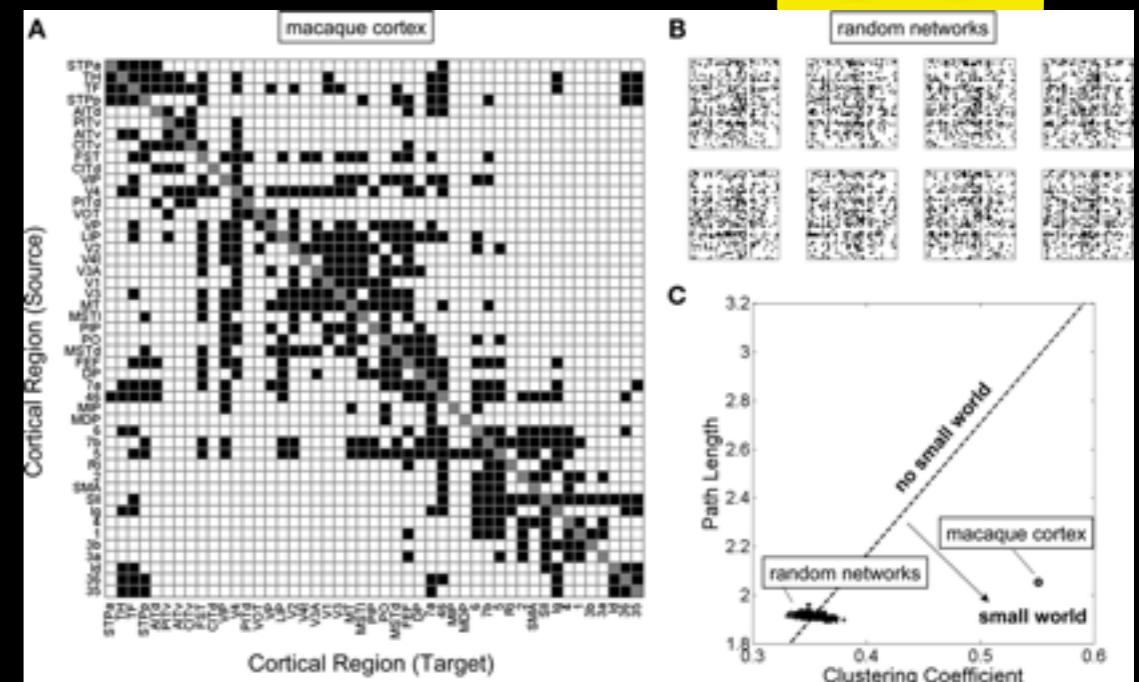
- Equivalent to assuming a Gaussian prior with variance determined by  $\lambda$
- Large values of  $A$  are penalized. The range of allowable values for coefficients is restricted, reducing the *effective* degrees of freedom and allowing us to estimate VAR coefficients with fewer observations.

# Sparsity Constraints



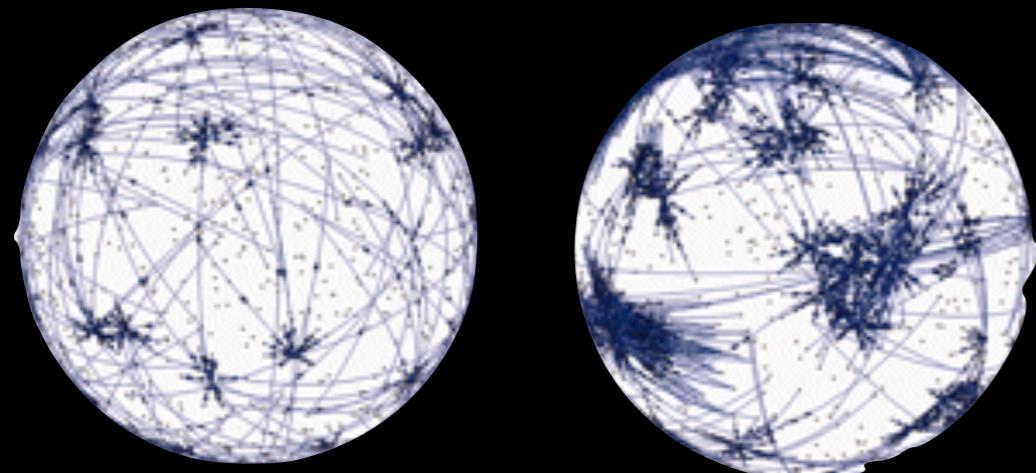
# Sparsity

- Relatively low probability of a *direct* connection between any two anatomical functional units. This probability decreases with distance



Sporns, *Frontiers in Computational Neuroscience*, 2011

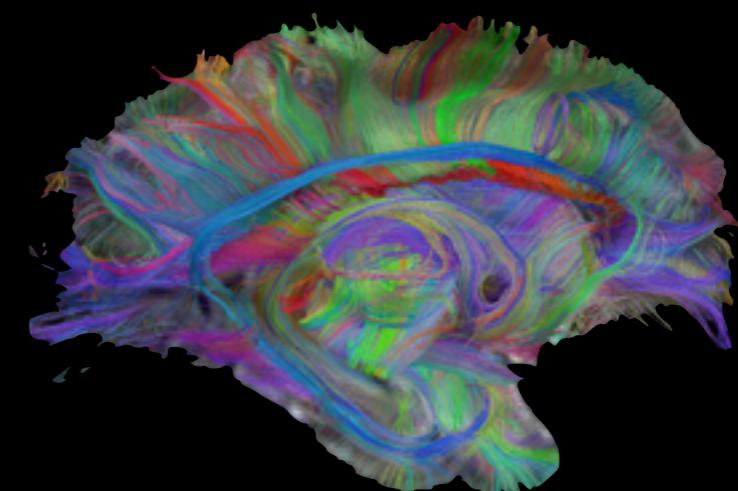
# It's a small world...



# structural network

## functional network

Sporns and Honey, PNAS, 2006



# Structural Connectivity

# Sparsity Constraints

- Standard least-squares solution



$$A(t) = \arg \min_{\tilde{A}} \left( \|Y - Z\tilde{A}\|_2^2 \right)$$

prediction error

$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

$$\tilde{\mathbf{A}} = [A^{(1)}(t), \dots, A^{(p)}(t)]^T$$

$$\mathbf{X}_k = [X(p+1-k), \dots, X(N-k)]^T$$

$$\mathbf{Z} = [X_1, \dots, X_p]$$

$$Y = X_0$$

Rewrite VAR[p] as VAR[1]

# Sparsity Constraints

M&gt;2

- Group Lasso ( $L_{1,2}$  norm)



$$\hat{A}(t) = \arg \min_{\hat{A}} \left( \|Y - Z\tilde{A}\|_2^2 + \lambda \sum_{ij} \left\| \tilde{A}_{ij}^{(1)}, \dots, \tilde{A}_{ij}^{(p)} \right\|_2^2 \right)$$

prediction error

smoothness (L2)  
(preserves spectrum)

regularization

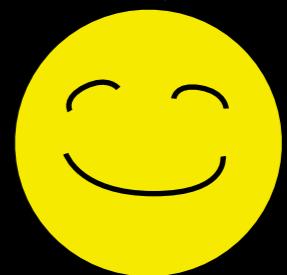
group sparsity (L1)

ADMM  
DAL

- Equivalent to assuming a Gaussian prior over coefficients within groups and a Laplacian prior over the groups themselves
- Entire groups of coefficients are jointly pruned (set *exactly* to zero) while remaining groups. Allowing us to estimate VAR coefficients with fewer observations.

# Sparsity Constraints

M&gt;2



## Compressive Sensing

- The process of acquiring and reconstructing a quantity that is underdetermined but known to be sparse (compressible) in some basis

## How many samples do we need?

- $N$  = number of samples required
- $M$  = *number of variables/sources*,  $p$  = *model order*

$$N = O\left(K \log(M^2 p / K)\right) \approx O(\log M^2 p)$$

$$N = O(M^2 p)$$

(unconstrained)

# Constraints Improve Estimation (if prior assumptions are correct)

- Significant improvements using smoothness or sparsity assumptions
- (e.g. Haufe et al, 2009, Valdez-Sosa et al, 2009)

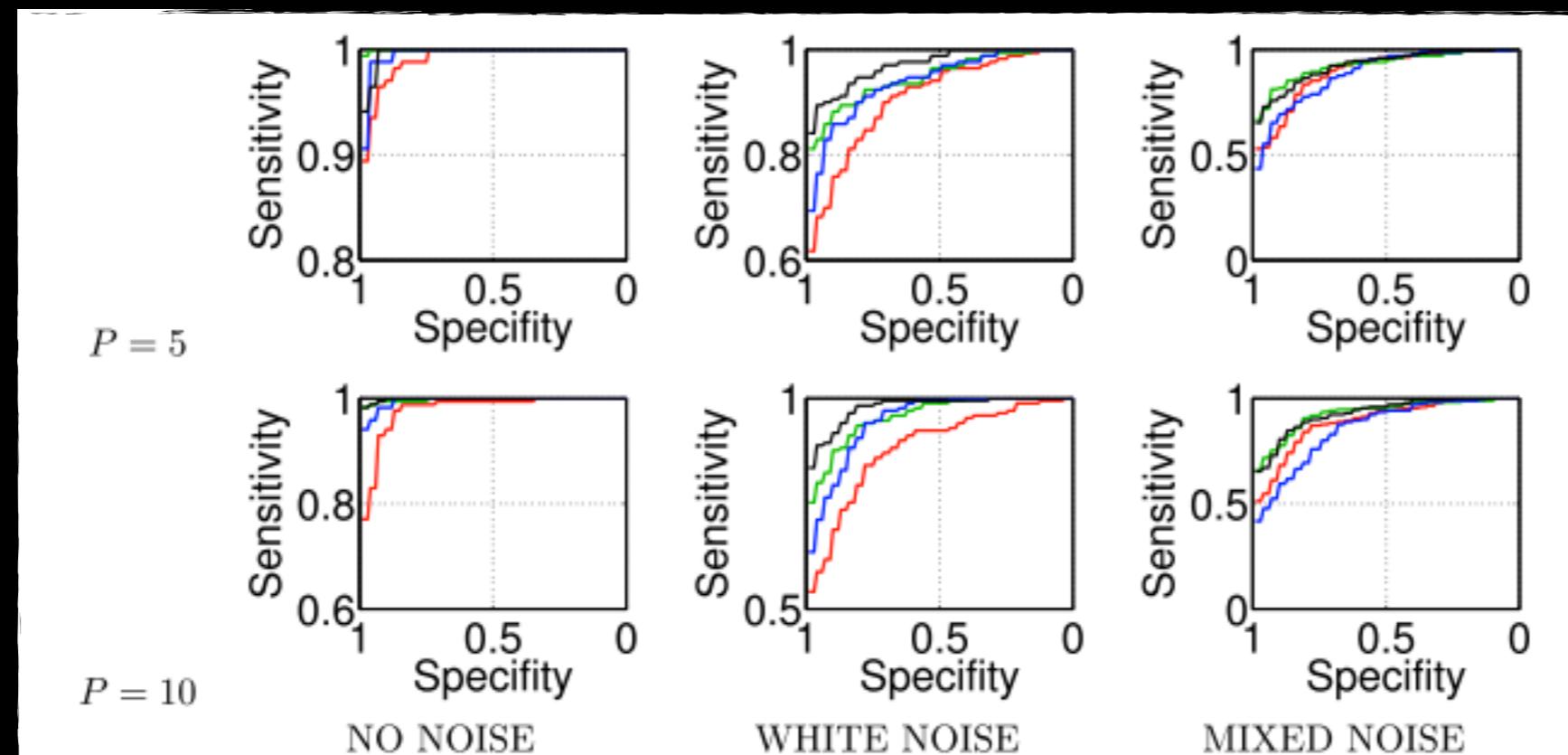
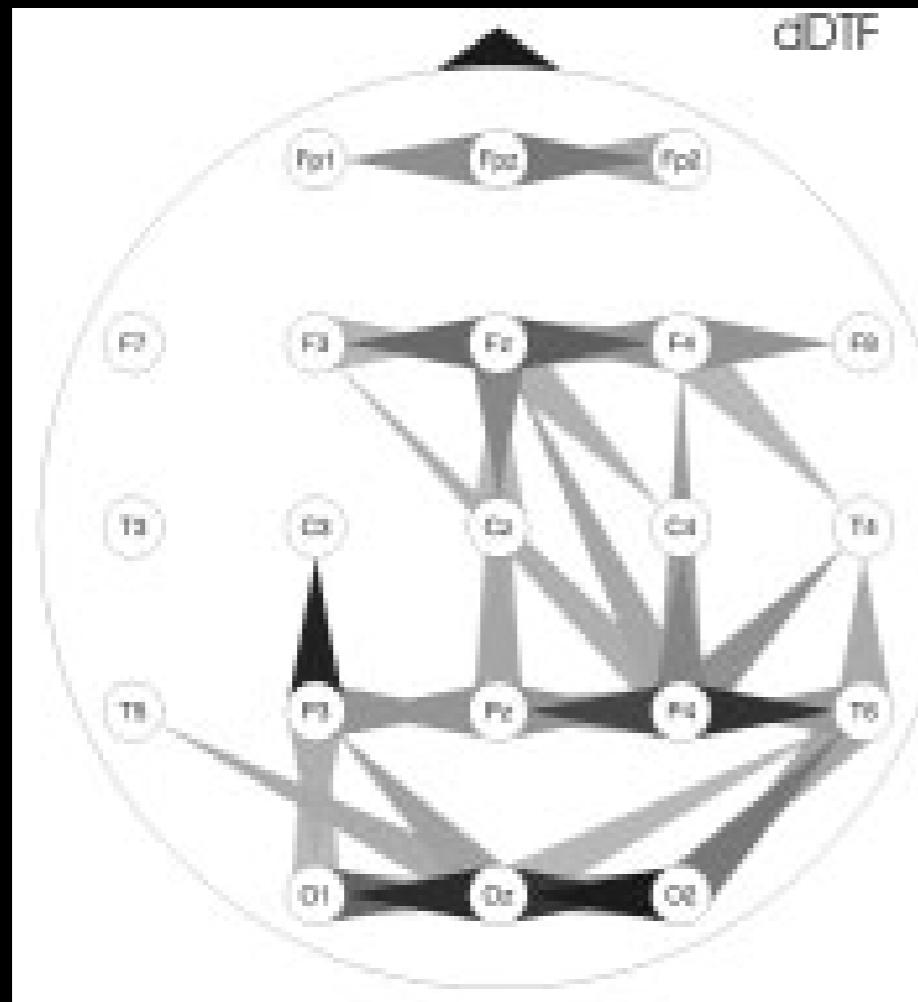


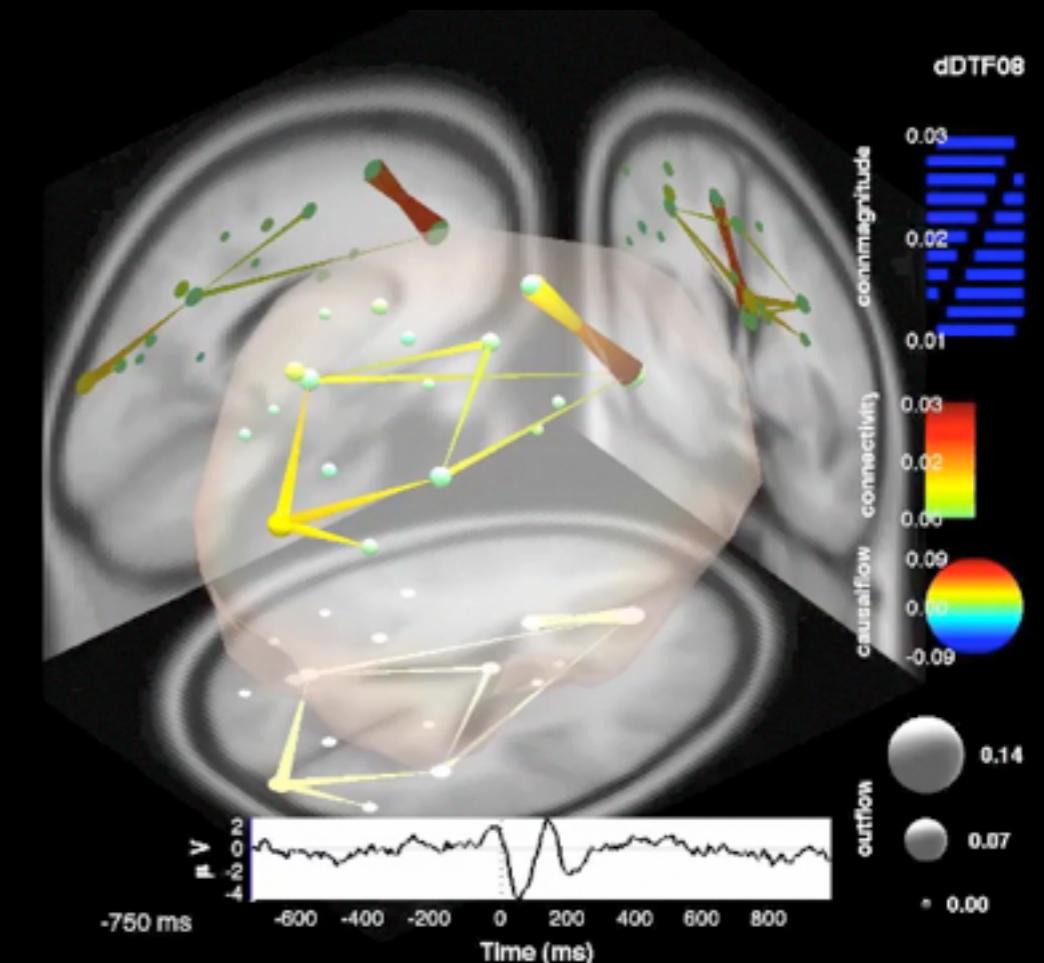
Figure 2: Average ROC curves of Granger Causality (red), Ridge Regression (green), Lasso (blue) and Group Lasso (black) in three different noise conditions and for two different model orders.

Haufe, 2009

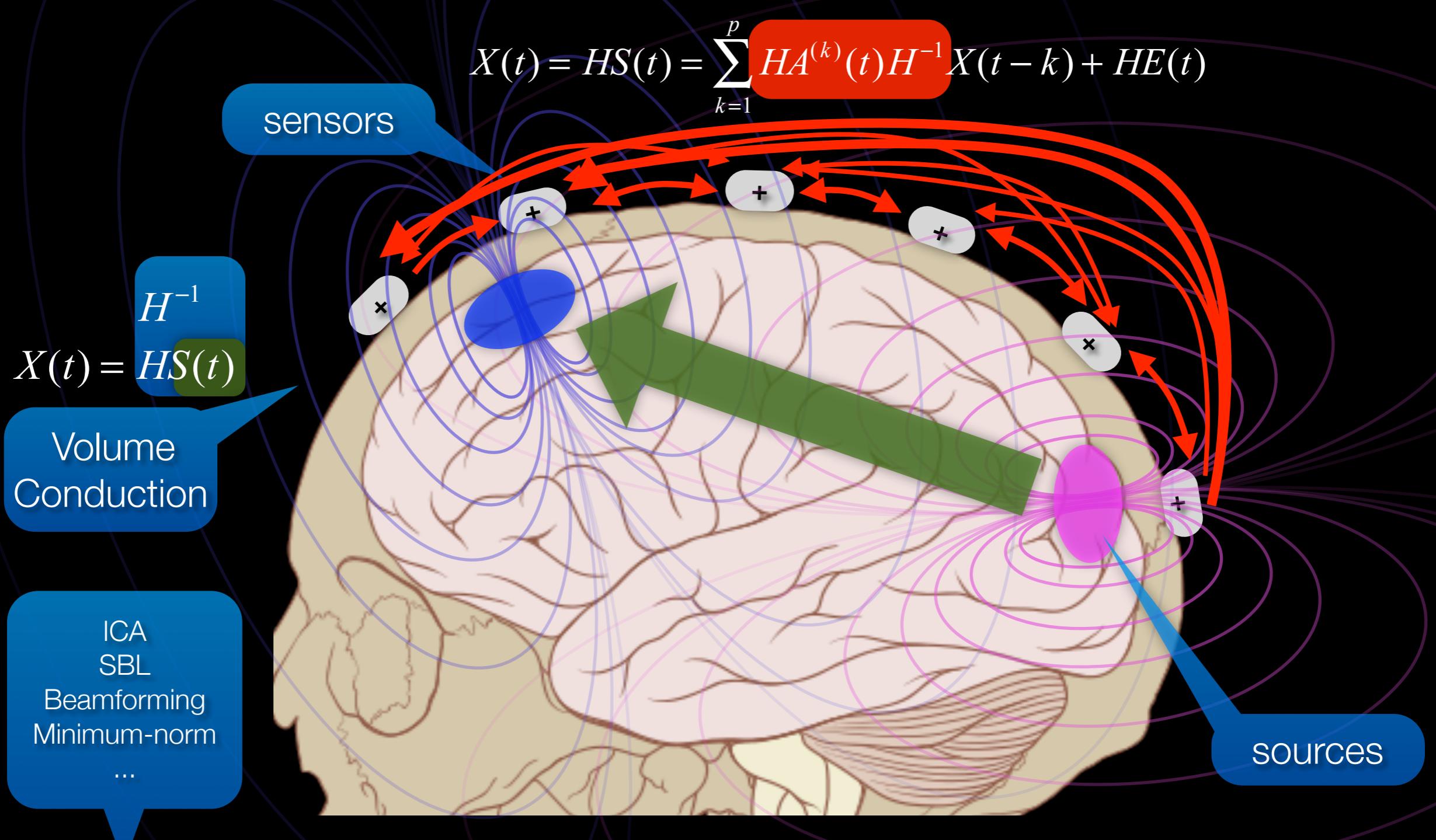
# Scalp or Source?



or



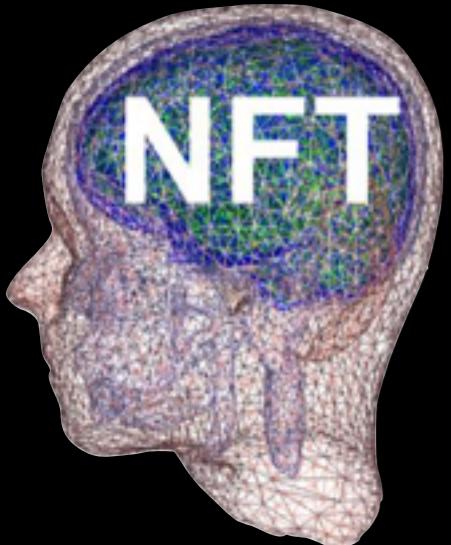
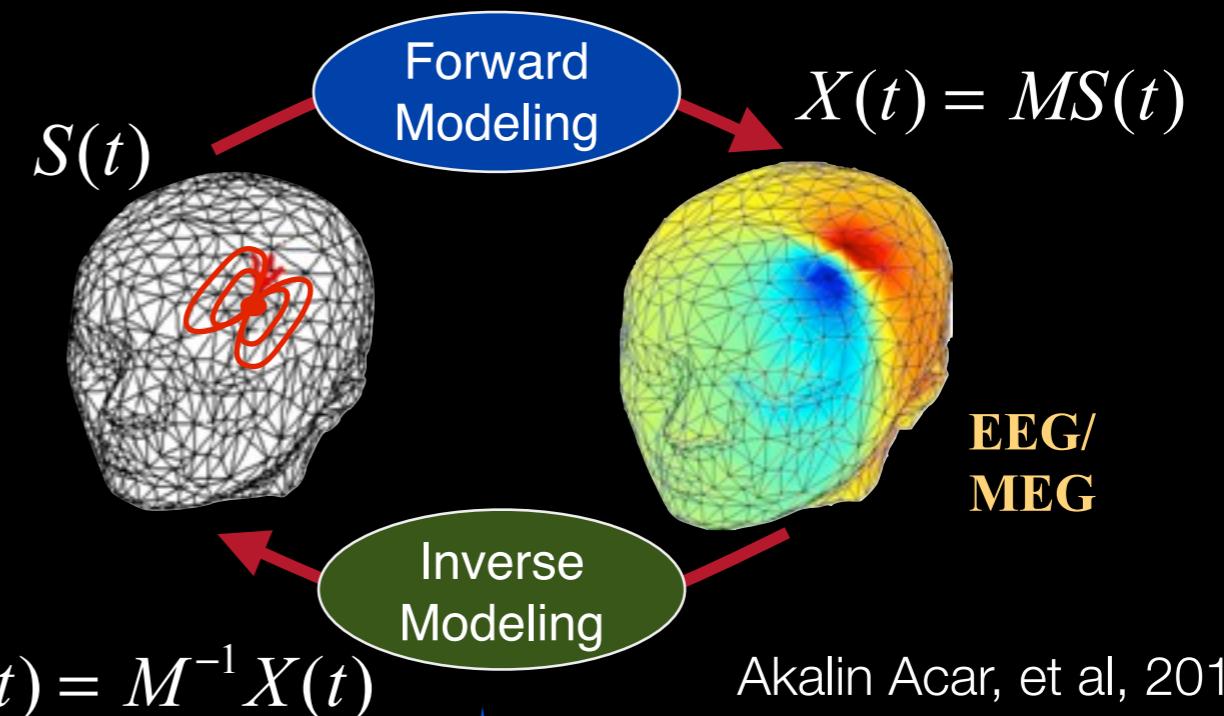
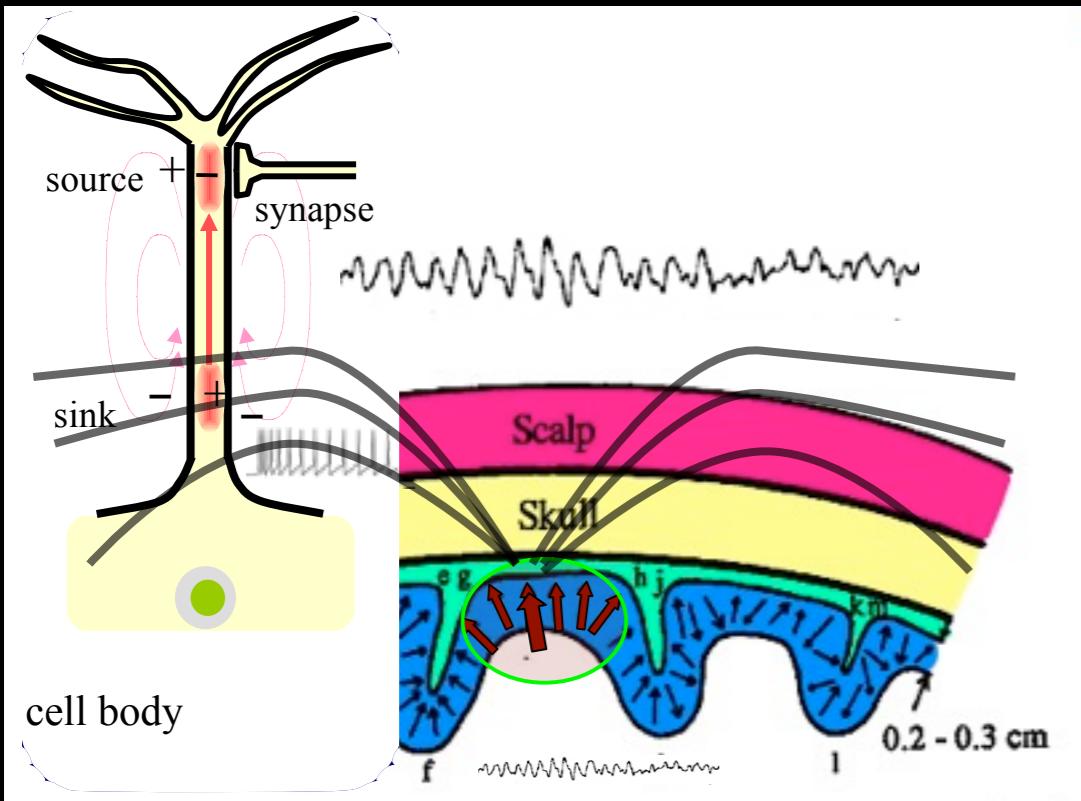
# Scalp or Source?



**Solution? Source Separation**

$$S(t) = \sum_{k=1}^p A^{(k)}(t)S(t-k) + E(t)$$

# Forward/Inverse Modeling



## A Recipe for Reducing Errors:

- Realistic Forward Model
- Appropriately Constrained Inverse Model

Akalin Acar and Makeig, 2009

ill-posed!

solutions?

sparse/smooth  
independence  
anatomy  
...

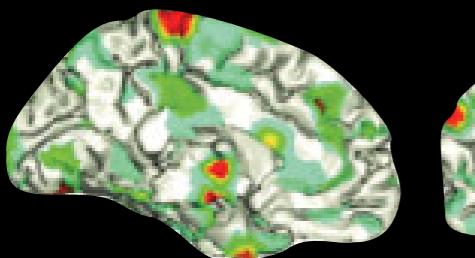
impose  
constraints!

# Forward/Inverse Modeling

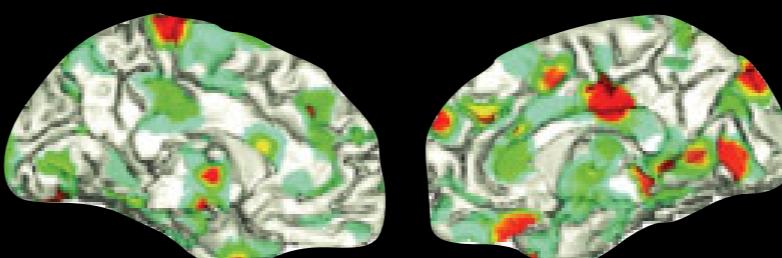
Method	Smoothness	Sparsity	Independence/Orthogonality
MNE	X		
LORETA	X		
dSPM	X		
Beamforming			X
Sparse Bayesian Learning	X	X	
S-FLEX	X	X	
FOCUSS		X	
ICA/PCA/SOBI			X

## Source reconstruction with ICA+SBL

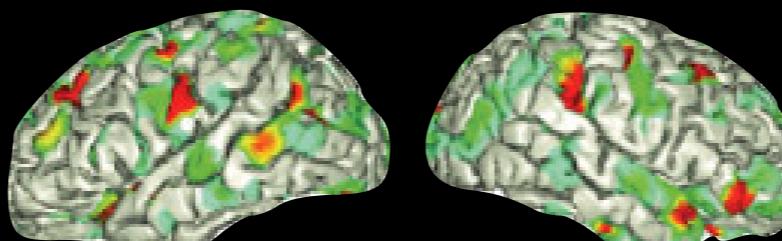
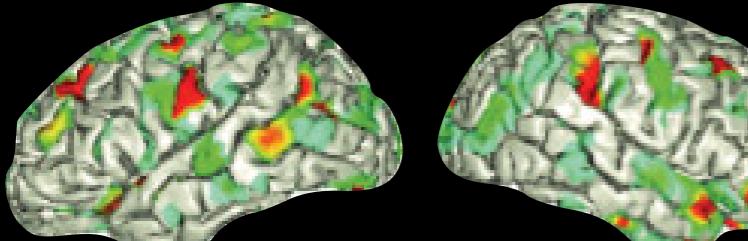
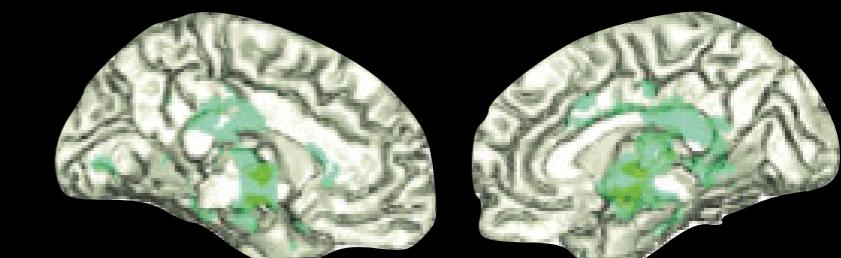
simulated



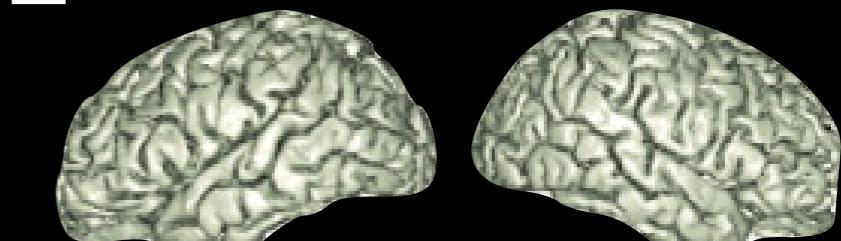
reconstructed



error



-



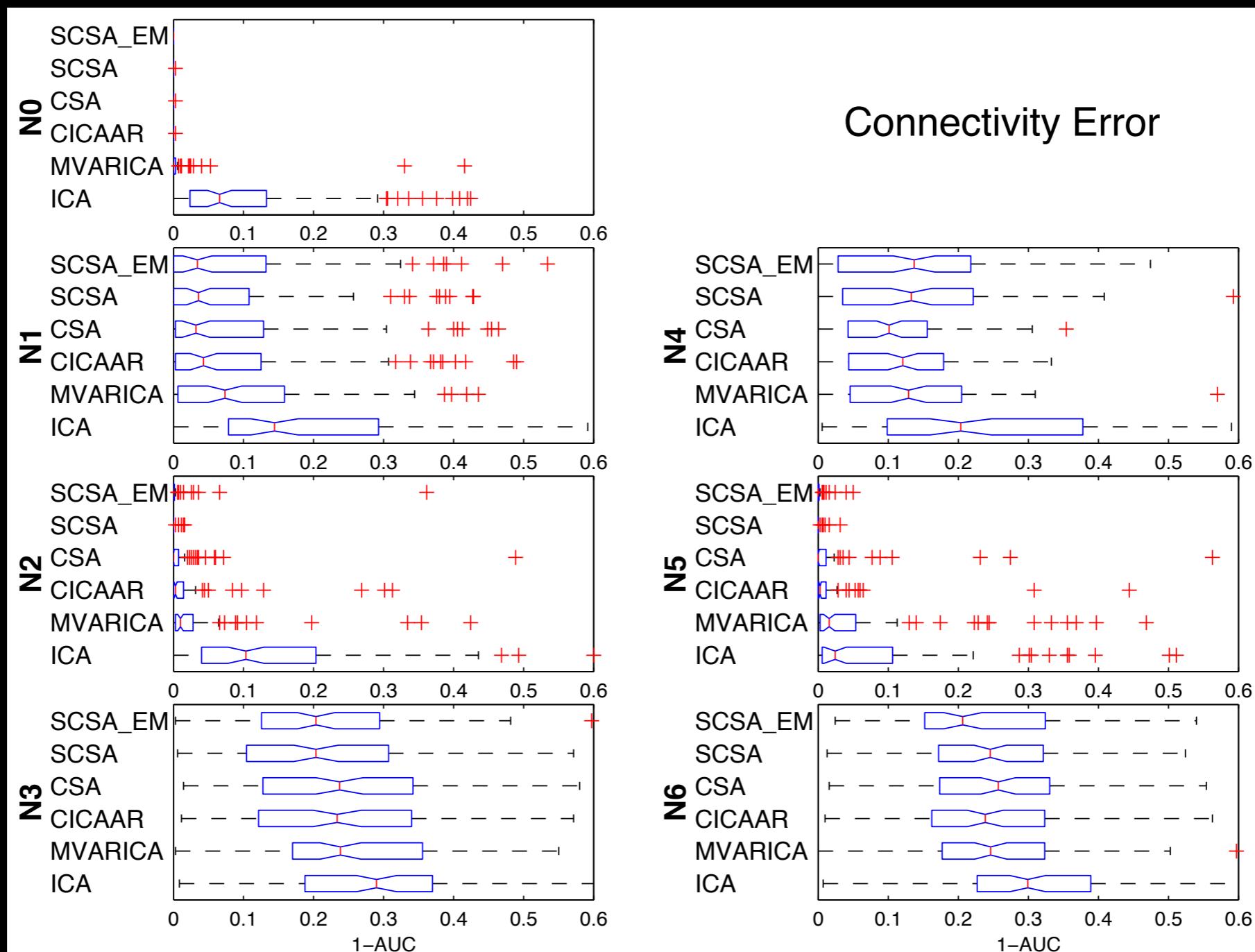
Makeig, Ramirez, Weber, Wipf, Dale, Simpson, 15th Inter. Conf on Biomagnetism (2006)

# Estimating Dependency of Independent Components ?

- Isn't it a contradiction to examine dependence between Independent/Uncorrelated Components?
- Instantaneous (e.g., Infomax) ICA only explicitly seeks to maximize *instantaneous* independence. Time-delayed dependencies may be preserved.
- Infomax ICA seeks to maximize *global* independence (over entire recording session), transient dependencies may be preserved.
- Independence is a very strict criterion that cannot be achieved *in general* by a linear transformation (such as ICA). Instead, dependent variables will form a **dependent subspace**.

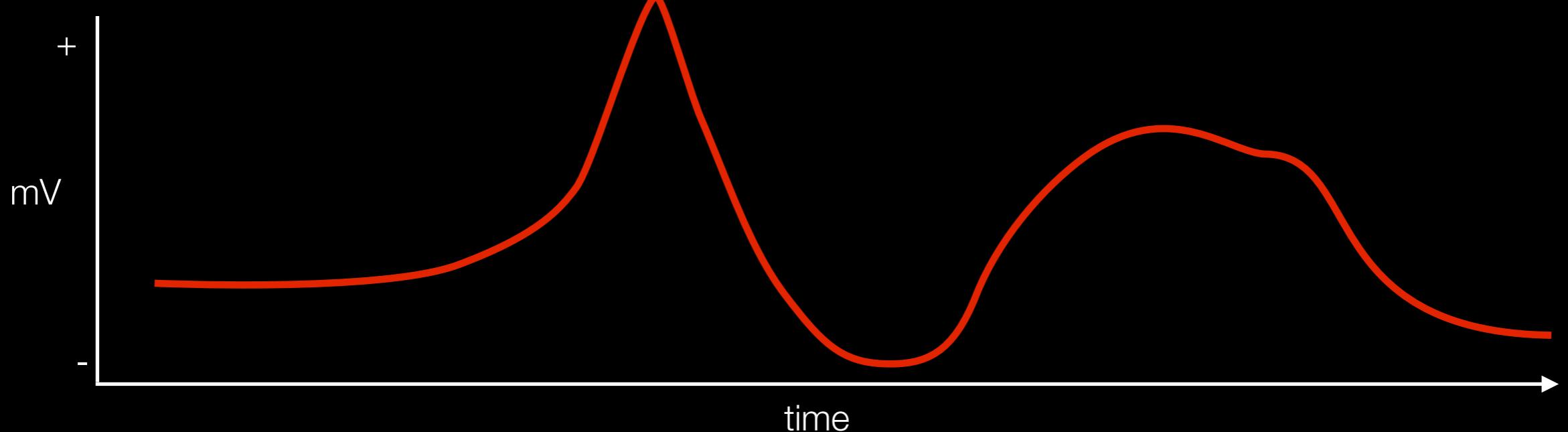
However, the *best* approach is to use an inverse model that explicitly preserves time-delayed dependencies or *jointly* estimates sources (de-mixing matrix) and connectivity (VAR parameters). See Haufe, 2008 IEEE TBME for a good treatment (coming soon to SIFT).

# Estimating Dependency of Independent Components ?



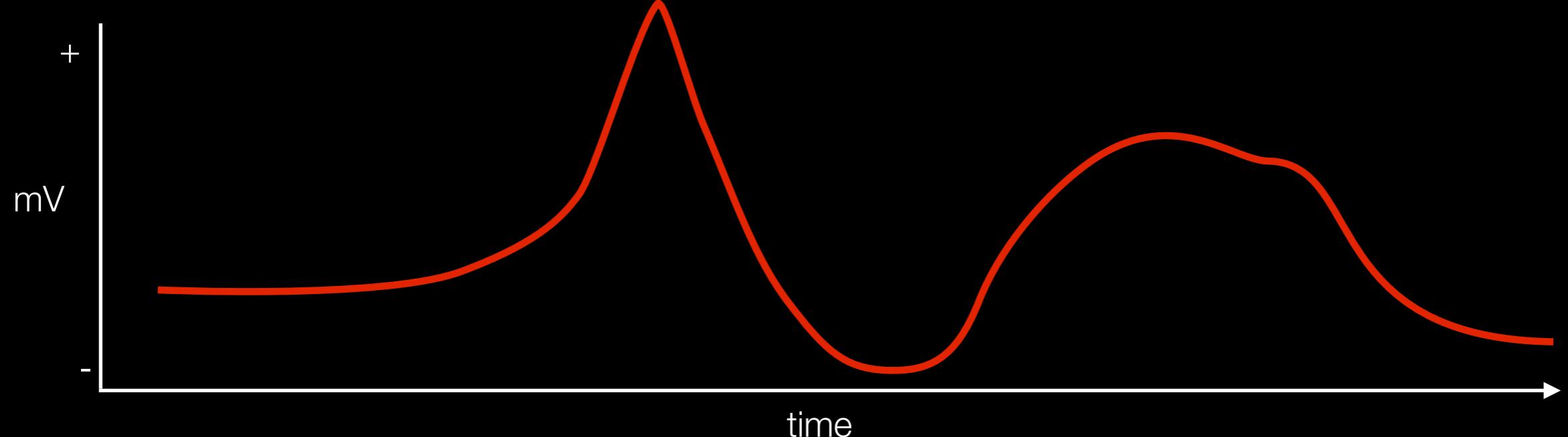
# Adapting to Non-Stationarity

- The brain is a **dynamic system** and measured brain activity and coupling can change rapidly with time (non-stationarity)
  - event-related perturbations (ERSP, ERP, etc)
  - structural changes due to learning/feedback
- How can we adapt to non-stationarity?



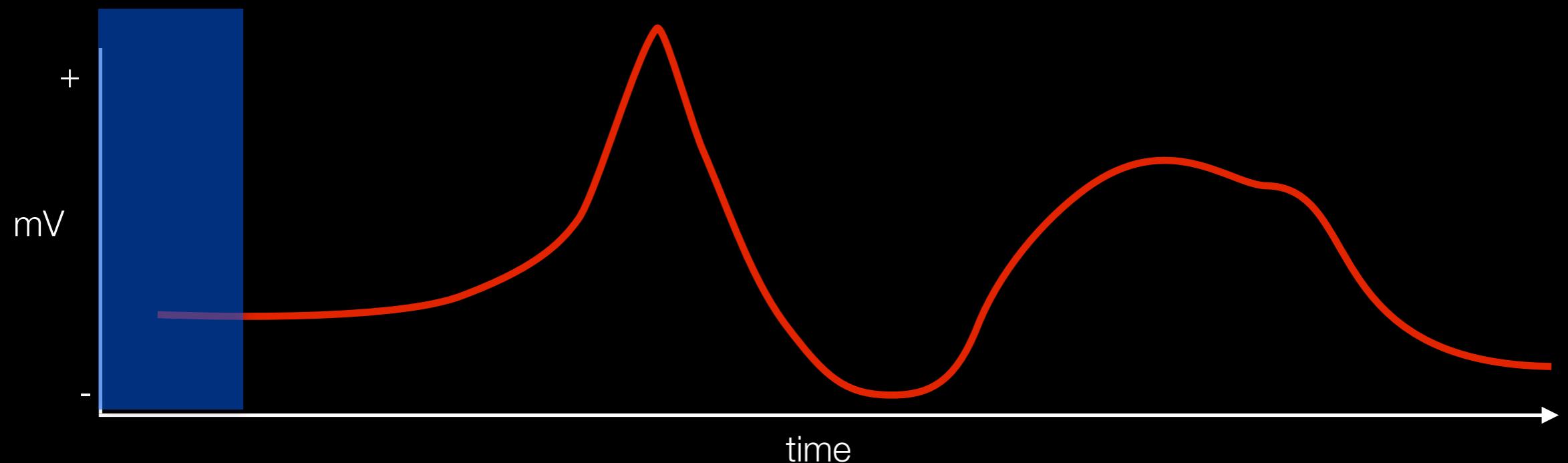
# Adapting to Non-Stationarity

- **Many ways to do adaptive VAR estimation**
- Two popular approaches (adopted in SIFT):
  - Segmentation-based adaptive VAR estimation  
(assumes local stationarity)
  - State-Space Modeling



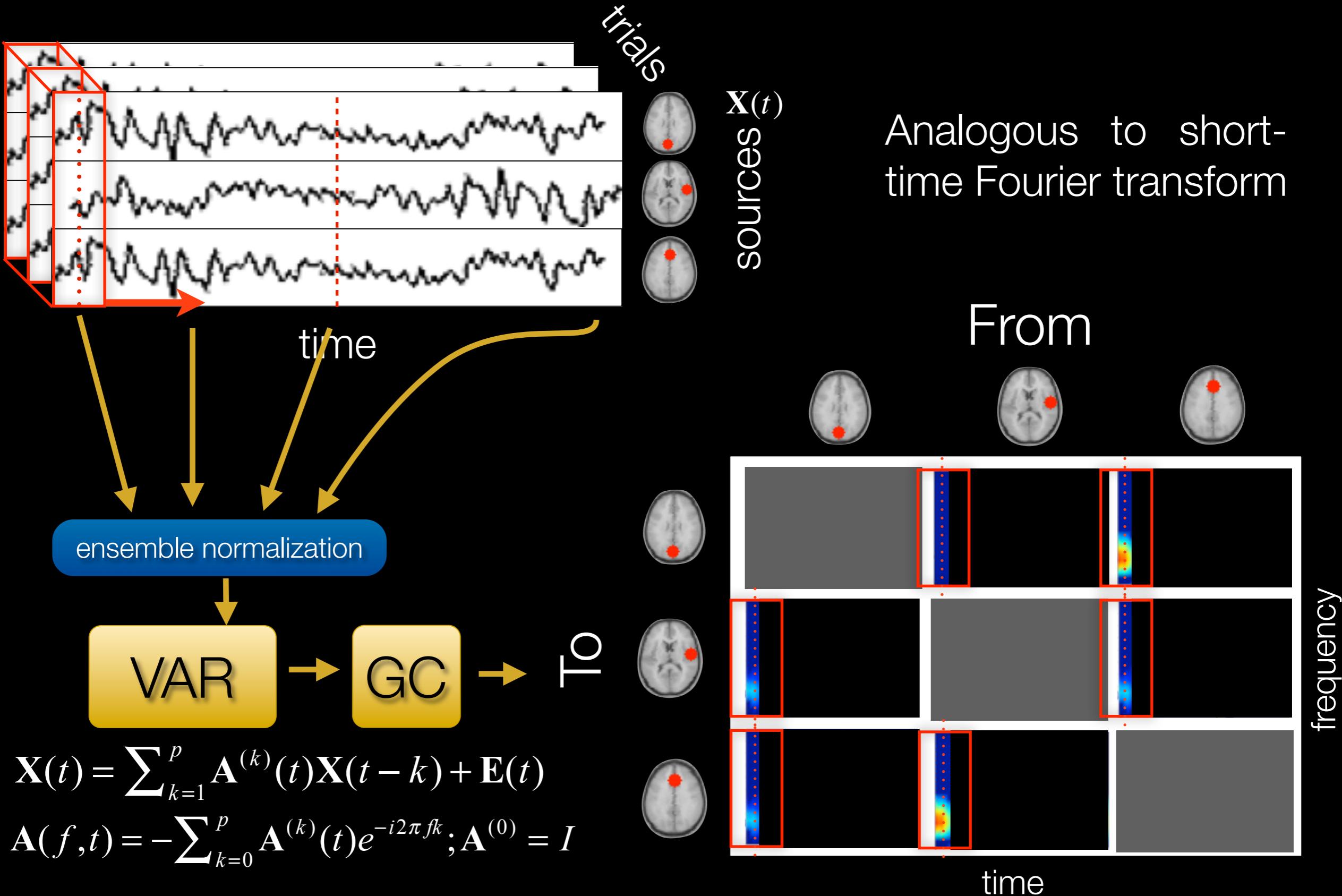
# Adapting to Non-Stationarity

- Many ways to do adaptive VAR estimation
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# Segmentation-based VAR

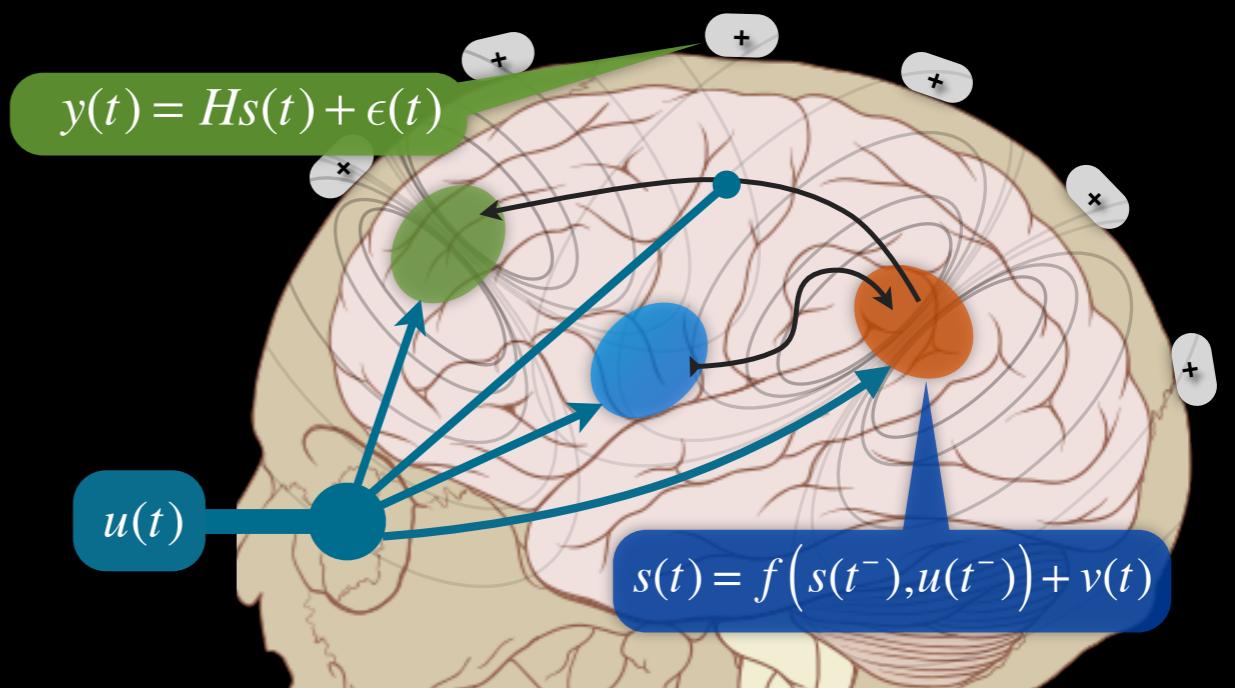
(Jansen et al., 1981; Florian and Pfurtscheller, 1995; Ding et al, 2000)



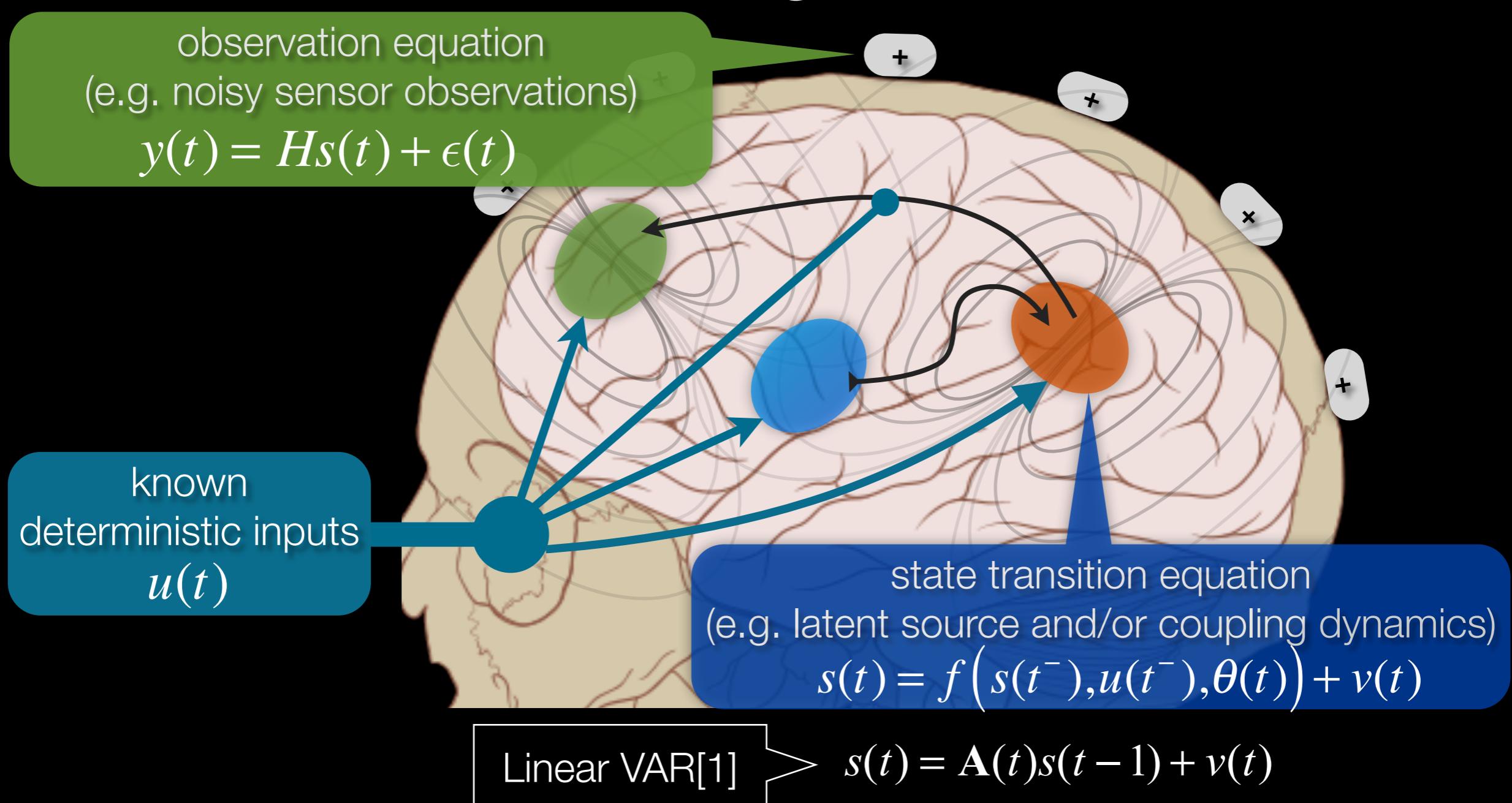
# Adapting to Non-Stationarity

- Many ways to do adaptive VAR estimation
- Two popular approaches (adopted in SIFT):
  - Segmentation-based adaptive VAR estimation (assumes local stationarity)
- **State-Space Modeling**

Kalman Filtering and extensions



# Discrete State-Space Model (SSM) for Electrophysiological Dynamics

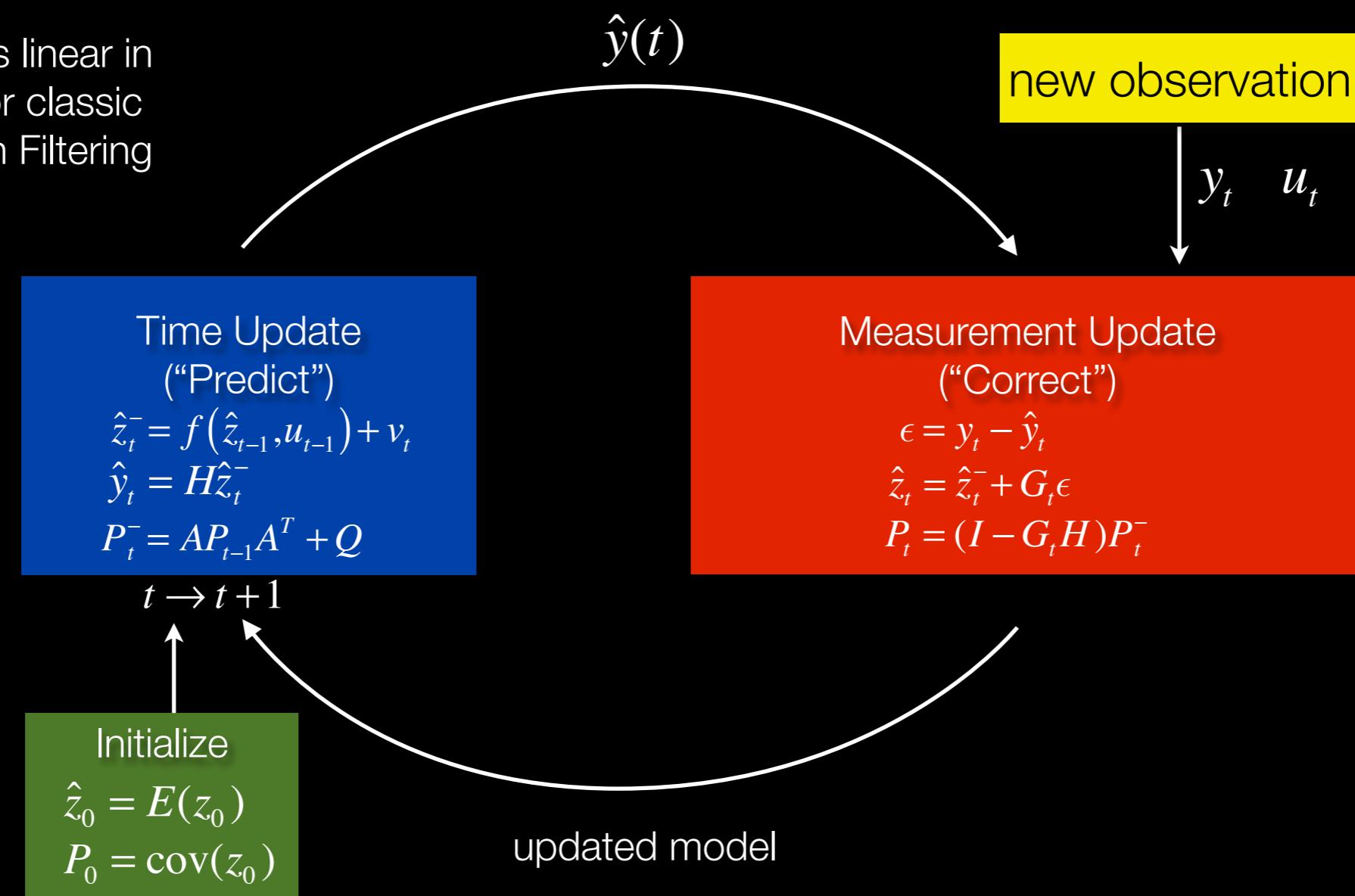


- Dynamical system may be linear or nonlinear, dense or sparse, non-stationary, high-dimensional, partially-observed, and stochastic
- Subsumes discrete Delay Differential Equation (DDE) and Vector Autoregressive (VAR) methods and closely related to Dynamic Causal Modeling (DCM)

# Kalman Filtering

optimal estimator (in terms of minimum variance) for the state of a linear dynamical system

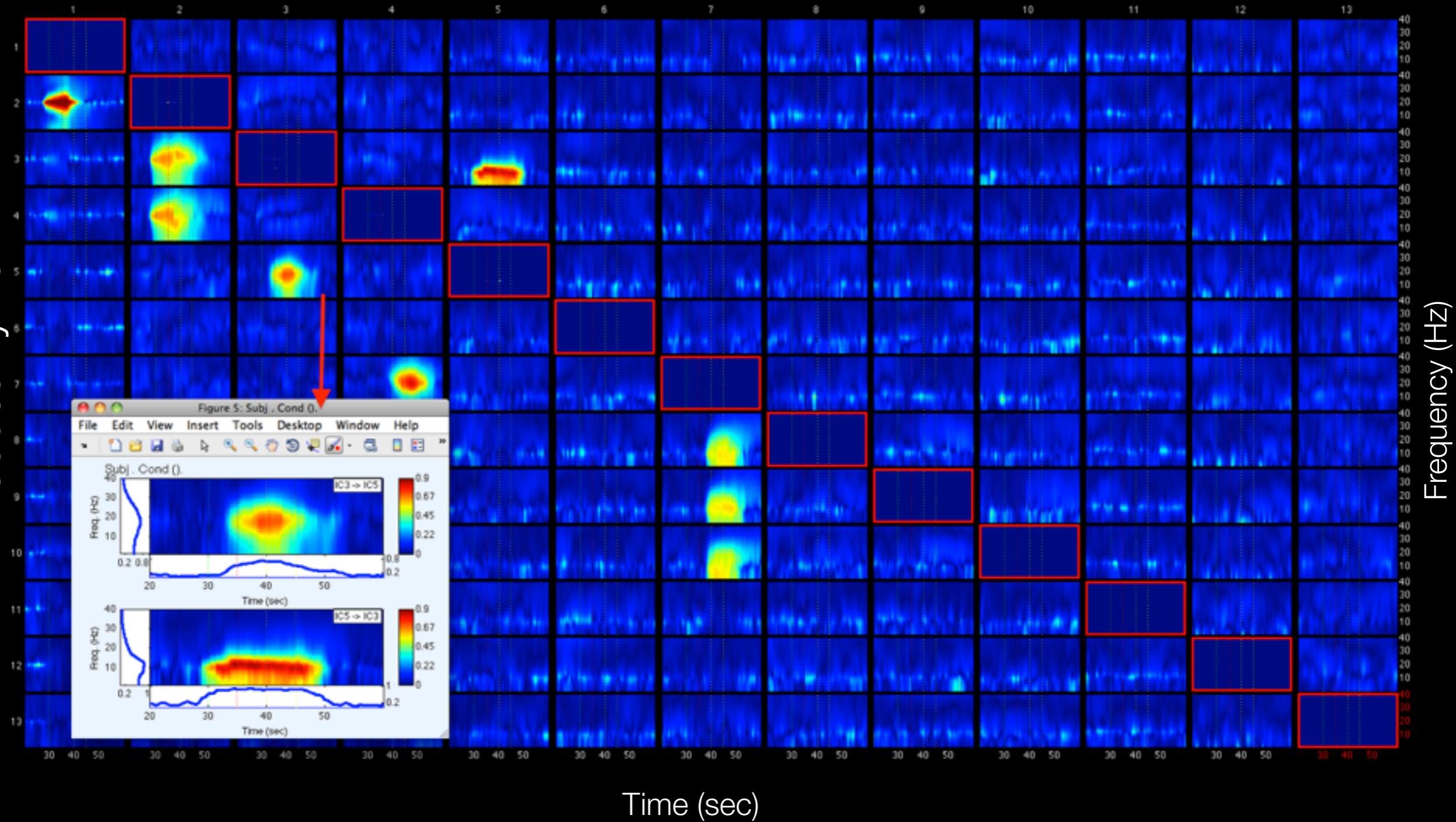
$f(z,u)$  is linear in  $\{z,u\}$  for classic Kalman Filtering



$z_t :=$  unknown state vector at time  $t$   
e.g. delay-embedding of sources and/or coupling (VAR) parameters

# Kalman Filtering

GPDC Causality From

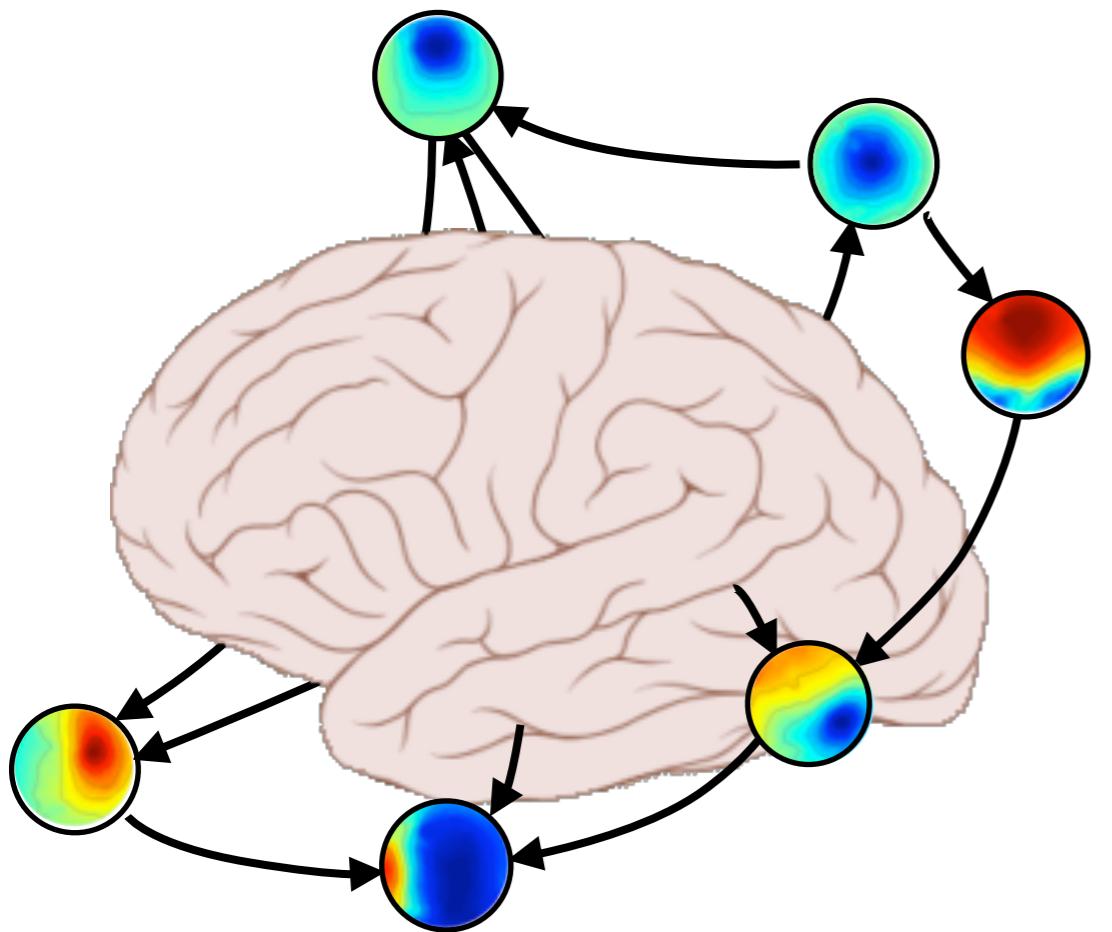


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Mullen, et al, *Journal of Neuroscience Methods* (in prep, 2012)

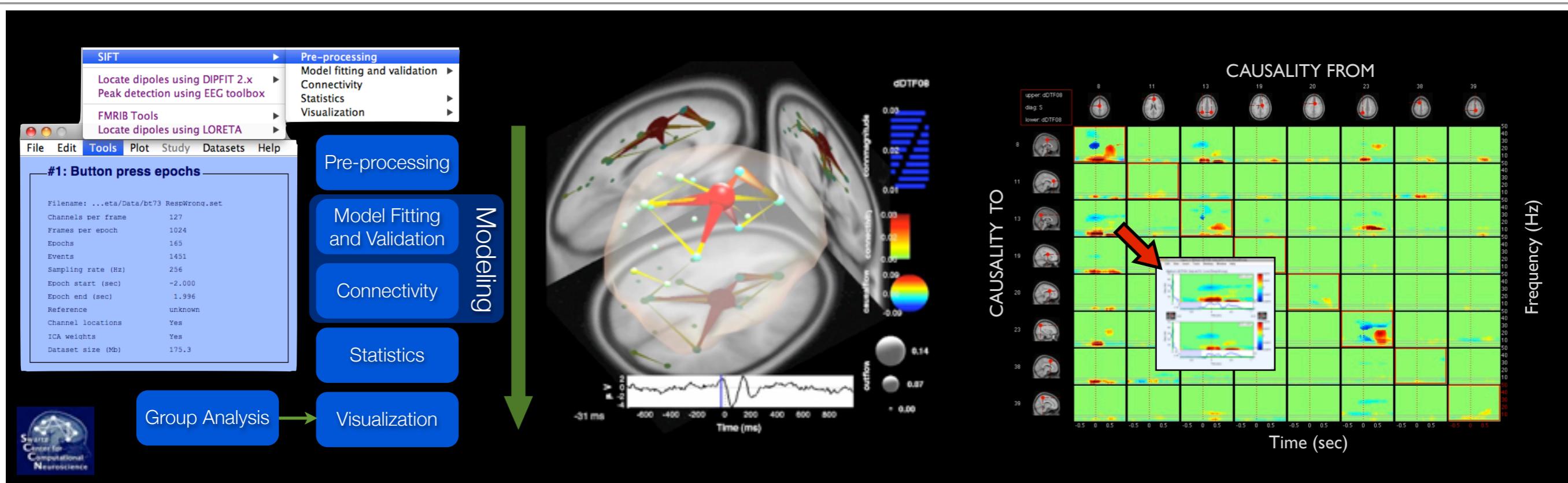
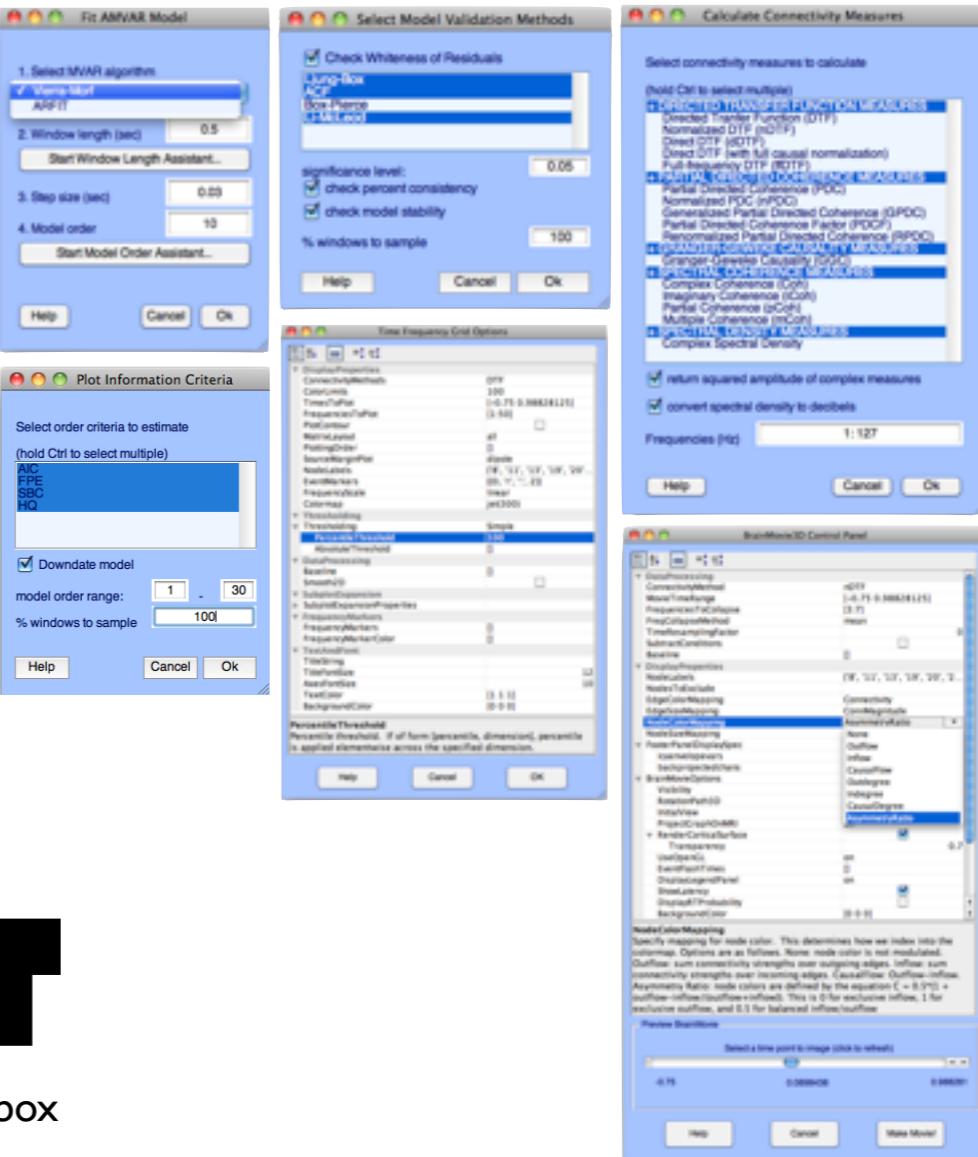
Mullen, et al, Society for Neuroscience, 2010

Delorme, Mullen, Kothe et al, *Computational Intelligence and Neuroscience*, vol 12, 2011



# SIFT

Source Information Flow Toolbox



# EEGLAB Software framework

Intro

Theory

SIFT

Apps

To-Do

Fin

Analysis

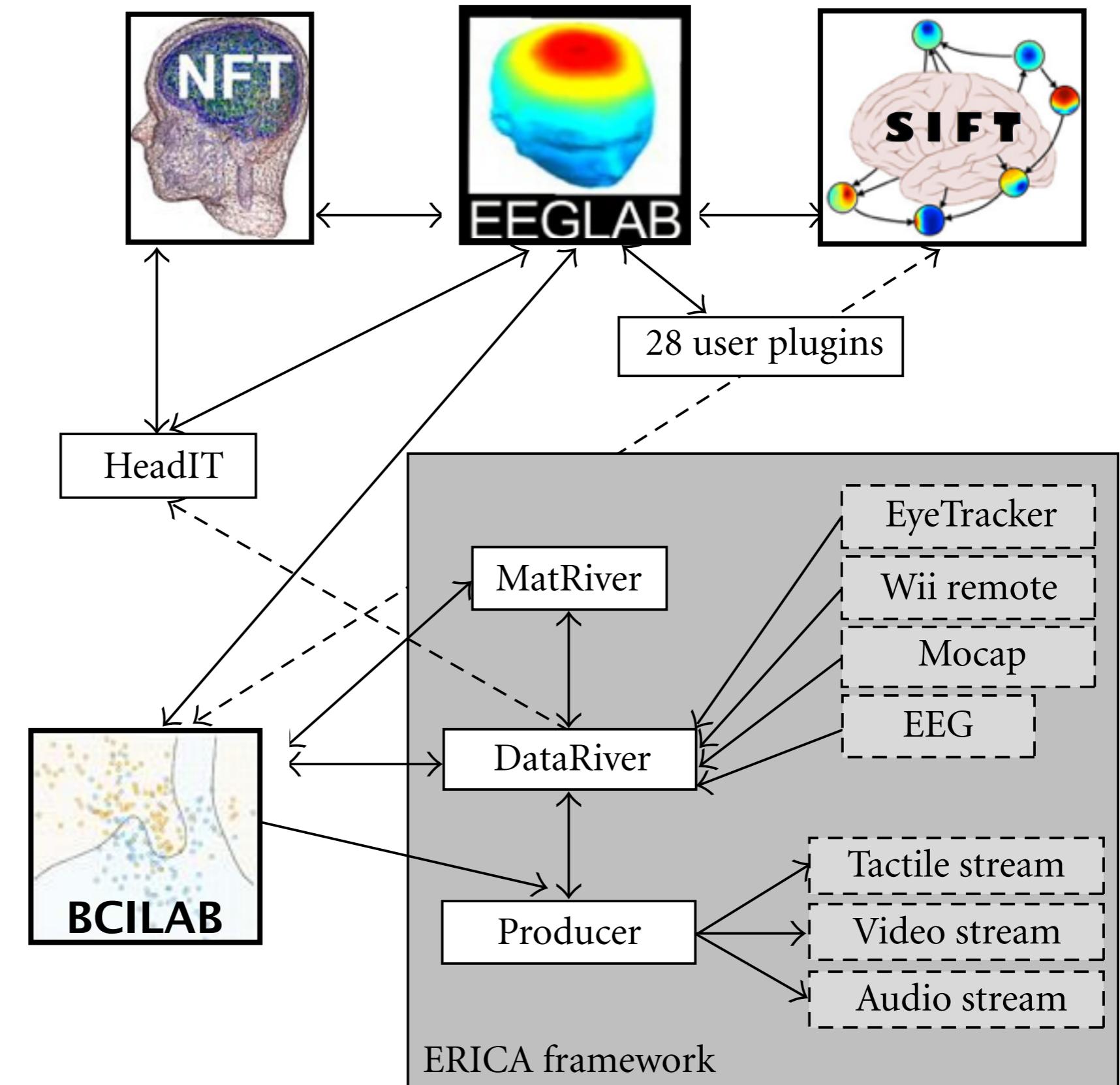
Analysis plugins

Data archive

Data sync and handling

Interactive tools

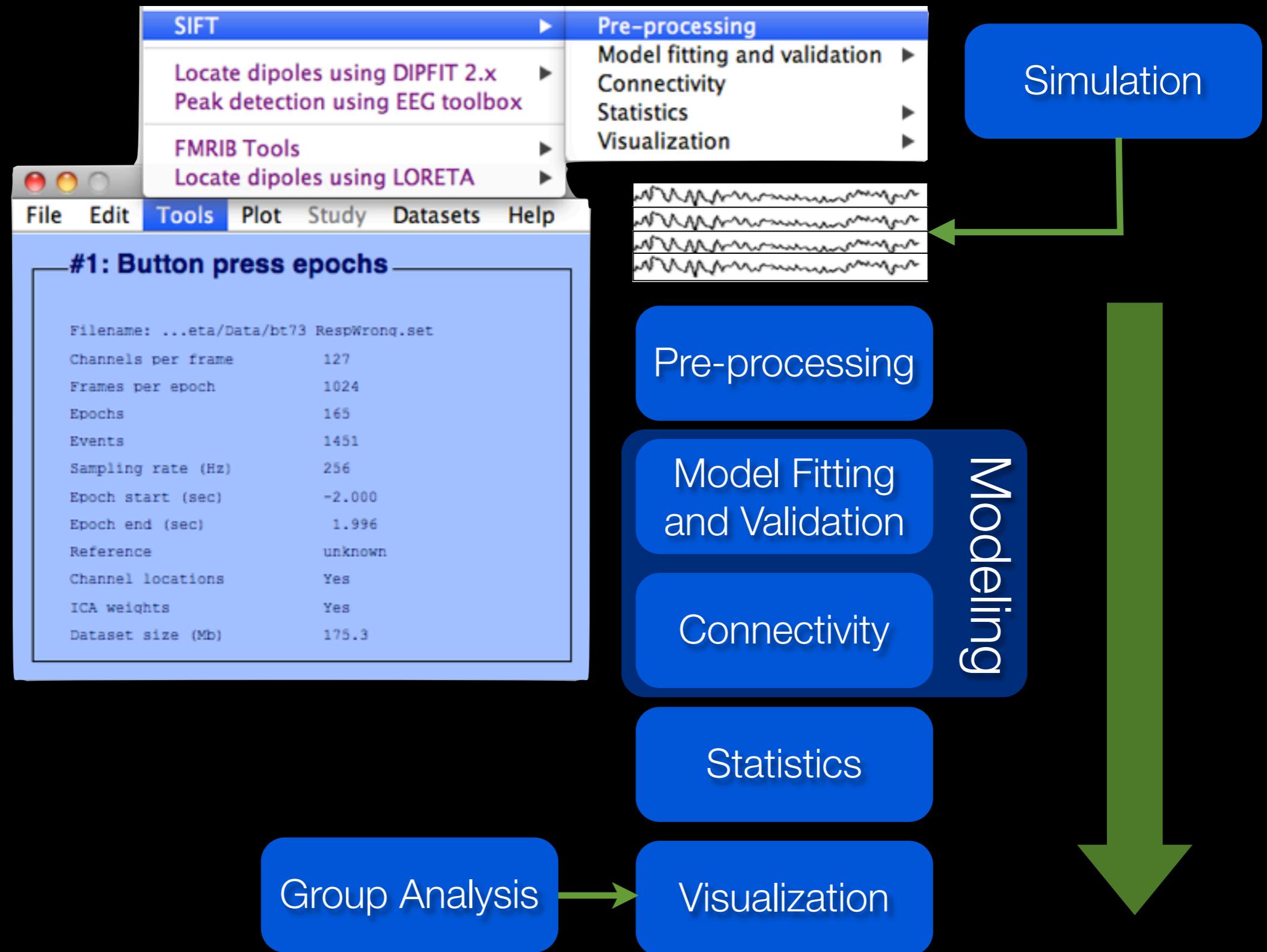
Stimulus control



# Source Information Flow

## Toolbox (SIFT)

- A toolbox for (source-space) electrophysiological information flow and causality analysis (single- or multi-subject) integrated into the EEGLAB software environment.
- Modular architecture intended to support multiple modeling approaches
- Emphasis on vector autoregression and SSMs and time-frequency domain approaches
- Standard and novel interactive visualization methods for exploratory analysis of connectivity across time, frequency, and spatial location
- **Requirements:** EEGLAB, MATLAB™ 2008a+, Signal Processing Toolbox, Statistics Toolbox (for some functions -- may be removed in the future)



Preprocessing

Modeling

Statistics

Visualization

## Source reconstruction

(performed externally using EEGLAB or other toolboxes)

Filtering or Local Detrending

Downsampling

Differencing

Normalization (temporal or ensemble)

Trial balancing

## Preprocessing

## Modeling

## Statistics

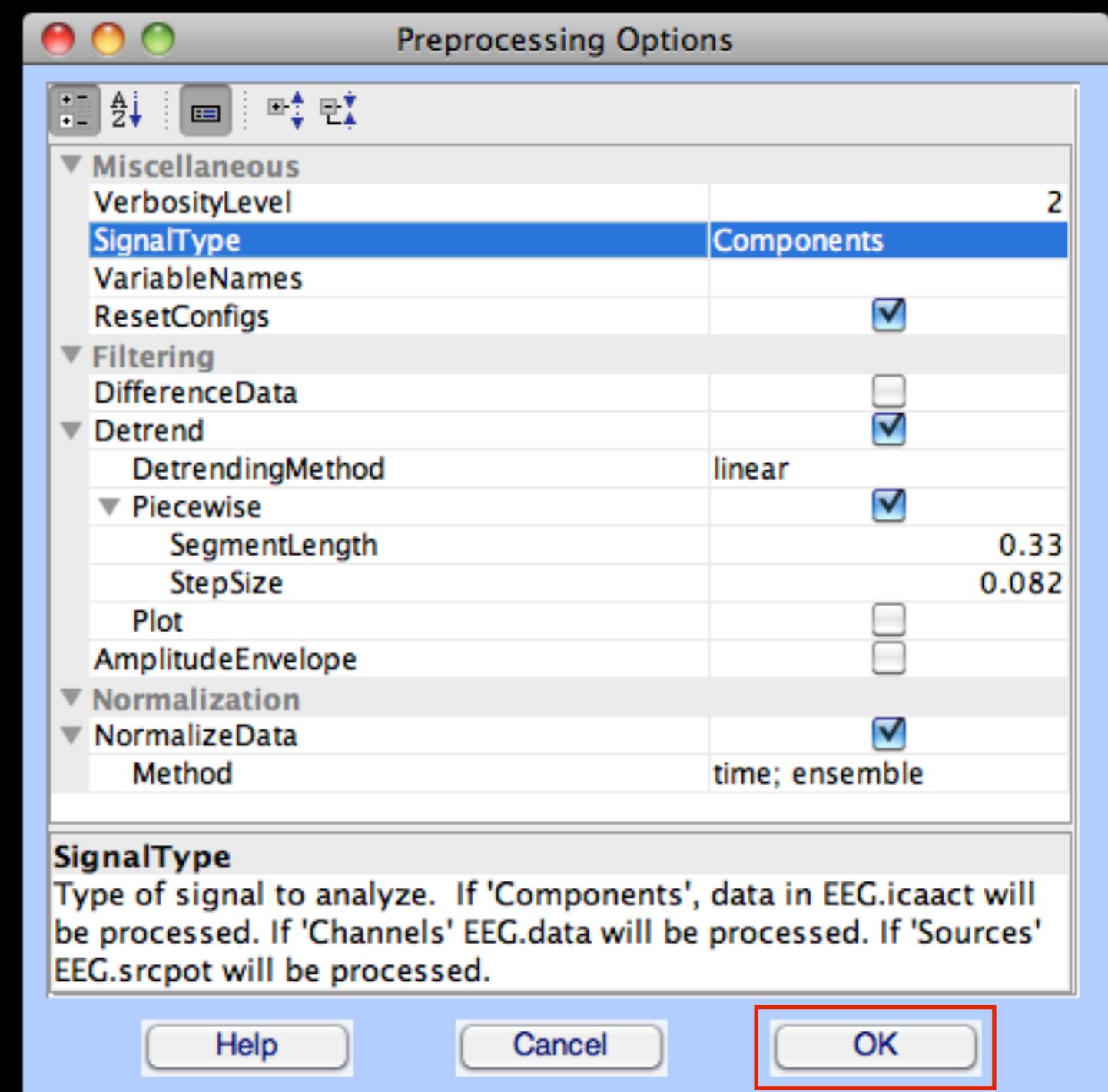
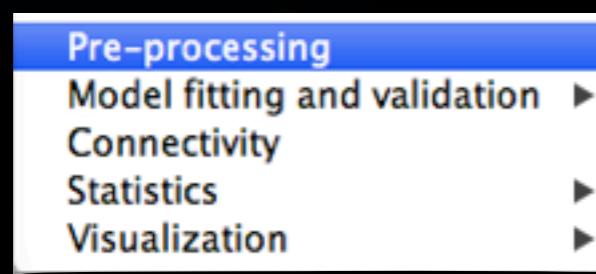
## Visualization

SIFT

Apps

To-Do

Fin



Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

SIFT

Apps

To-Do

Fin

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

SIFT

Apps

To-Do

Fin

Modeling Algorithm (1)	Linear	Nonlinear
Segmentation VAR (Sliding Window)		
Unconstrained		
Vieira-Morf	✓	
ARfit	✓	
Regularized		
Ridge Regression ( $L_2$ )	✓	
Group Lasso ( $L_{1,2}$ )		
ADMM, DAL	✓	
Elastic Net ( $L_1L_2$ )	✓	
Sparse Bayesian Learning ( $L_p$ )		
TMSBL, BSBL	✓	



fully implemented



alpha-testing



coming soon

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

SIFT

Apps

To-Do

Fin

Modeling Algorithm (2)	Linear	Nonlinear
State-Space Modeling		
Linear Kalman Filtering	✓	
Dual Extended Kalman Filtering		✓
Cubature Kalman Filtering		✓
Sparsely Connected Components Analysis (SCSA)	✓	
Adaptive Mixture Impulse Response Analysis (AMIRA)	✓	
Nonparametric VAR Modeling		
Spectral Matrix Factorization	✓	



fully implemented



alpha-testing



coming soon

## Preprocessing

## Modeling

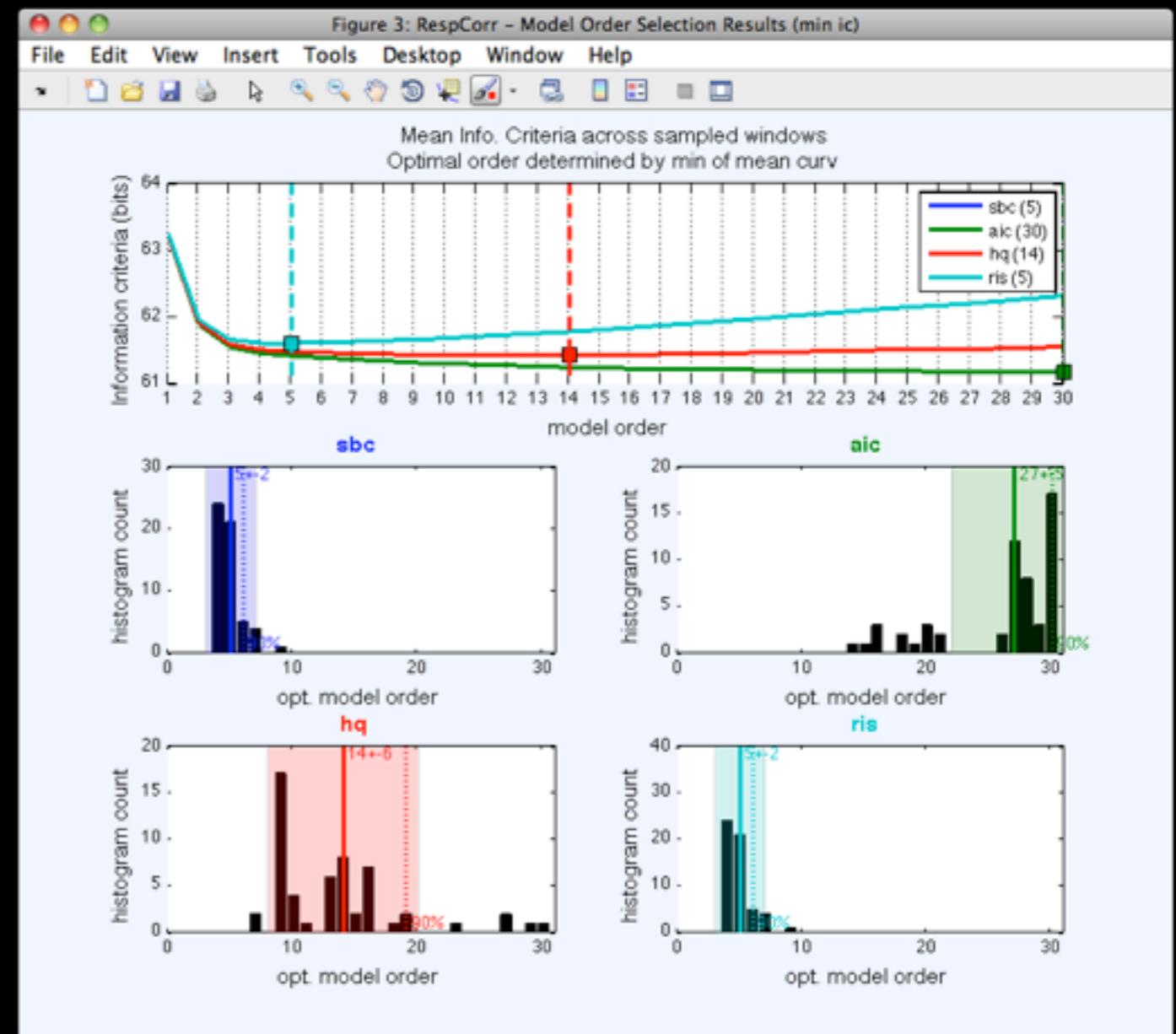
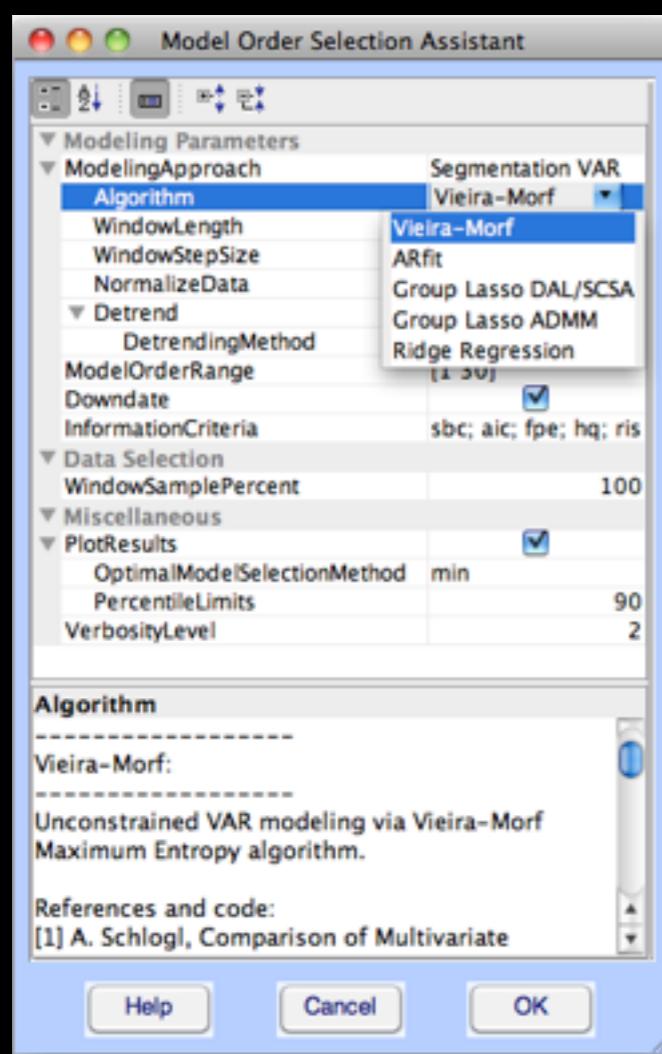
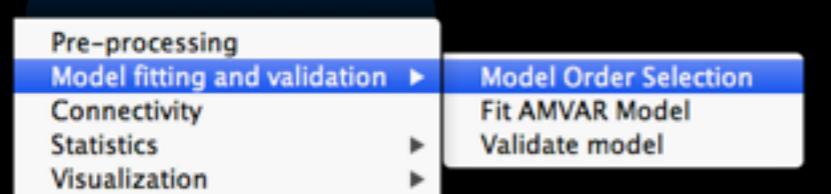
## Statistics

## Visualization

### Model Fitting

### Validation

### Connectivity



Preprocessing

Modeling

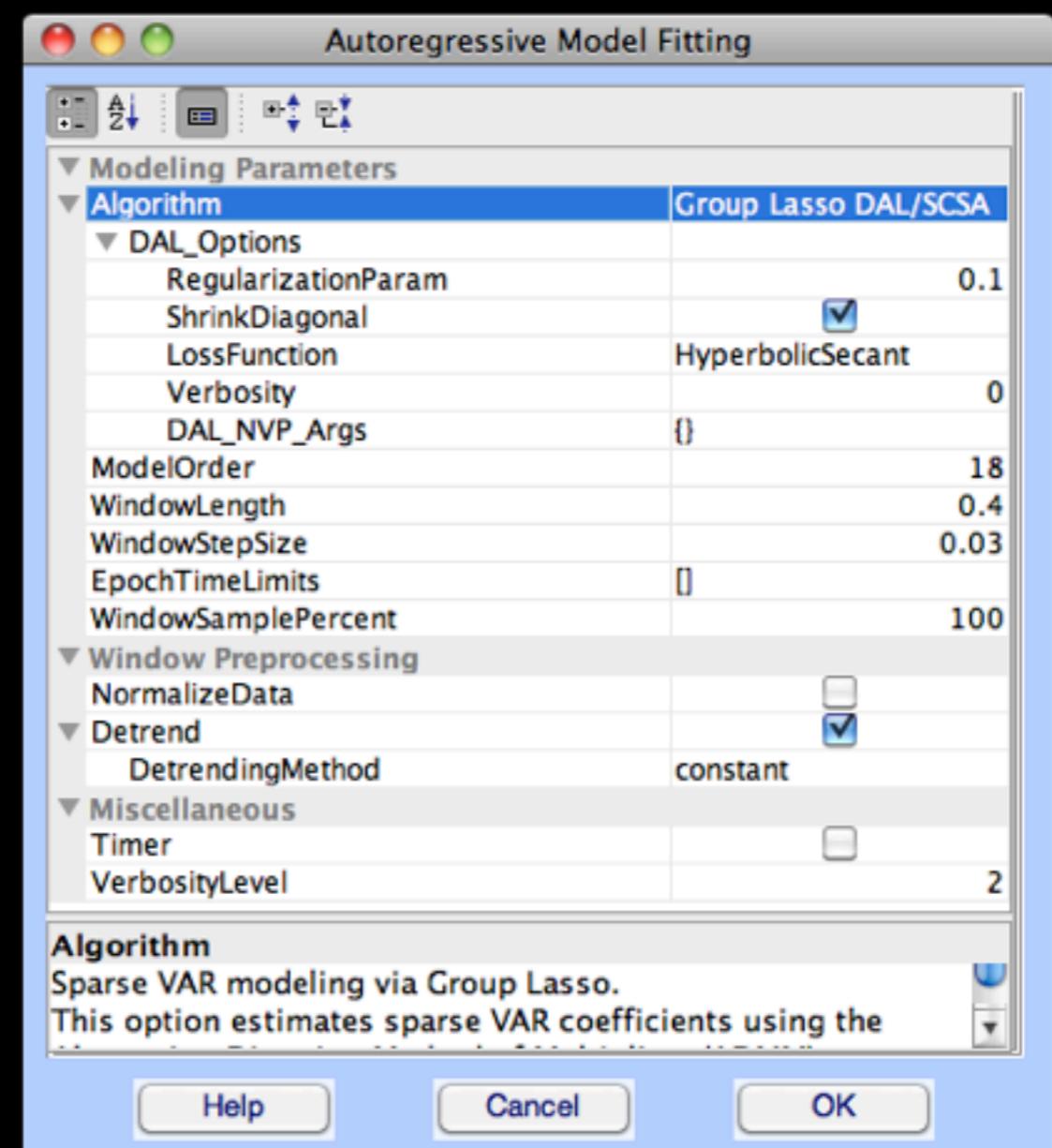
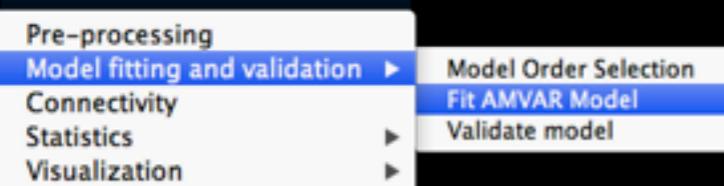
Statistics

Visualization

Model Fitting

Validation

Connectivity



Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

## VAR Model Validation

Residual ‘Whiteness’ Tests

Multivariate portmanteau tests

Residual autocorrelation probability test

Model Consistency

Model Stability

Nonparametric Spectral/Coherence Correlation



fully implemented



alpha-testing



coming soon

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

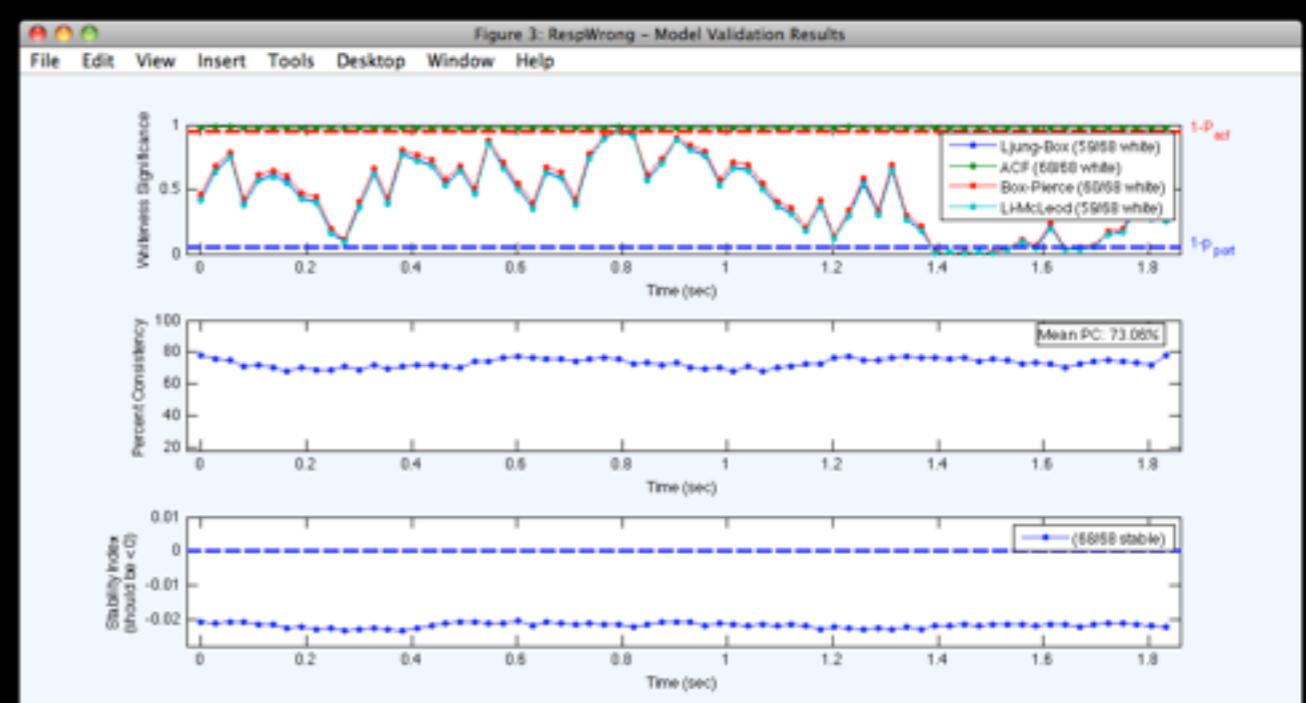
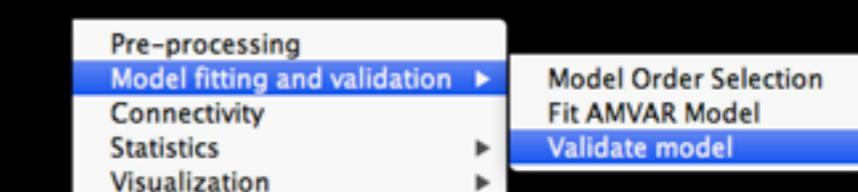
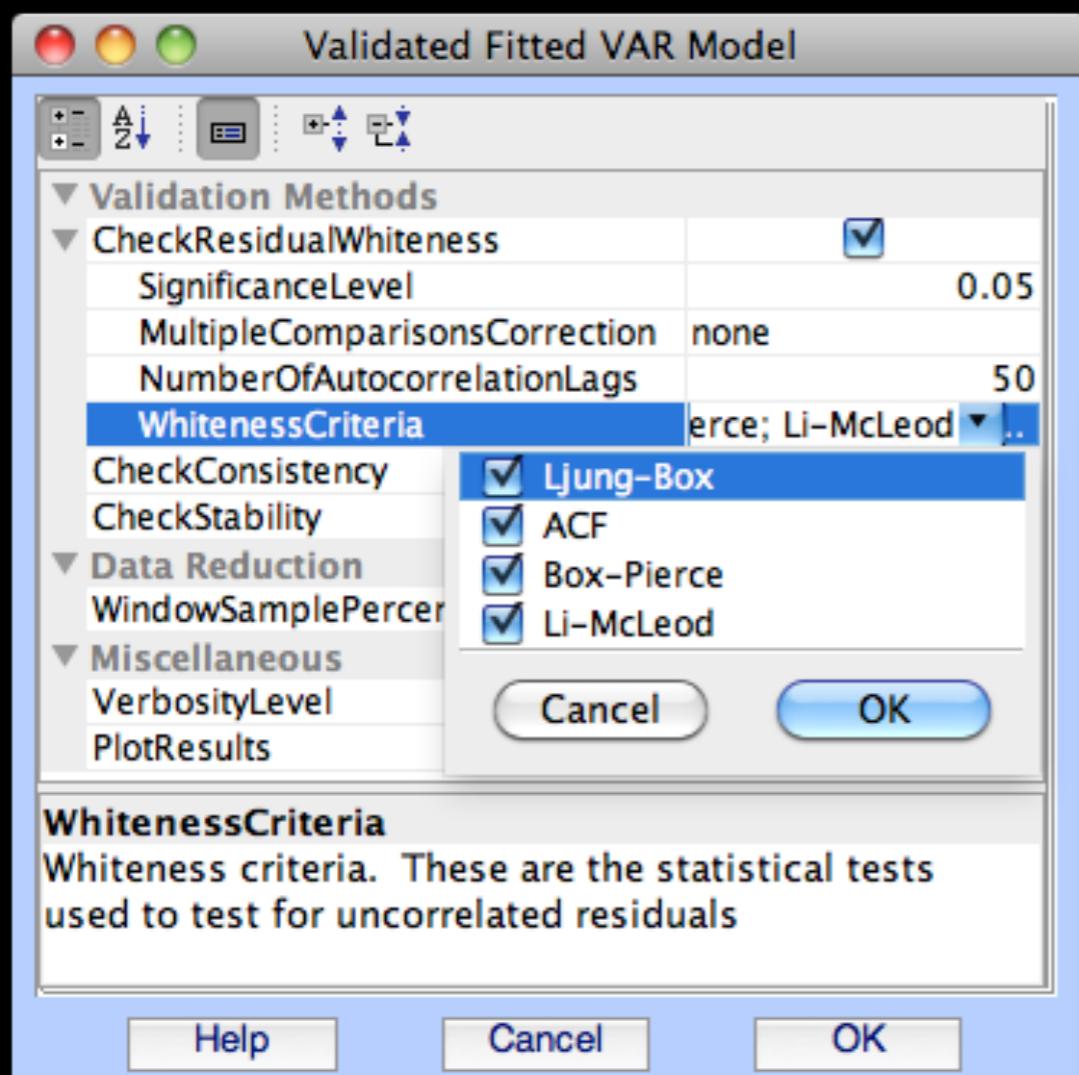
Connectivity

SIFT

Apps

To-Do

Fin



Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

## VAR-based Measures

Power spectrum (ERSP)

Coherence (Coh), Partial Coherence (pCoh), Multiple Coherence (mCoh)

Partial Directed Coherence (PDC)

Generalized PDC (GPDC)

Partial Directed Coherence Factor (PDCF)

Renormalized PDC (rPDC)

Directed Transfer Function (DTF)

Direct Directed Transfer Function (dDTF)

Bivariate Granger-Geweke Causality (GGC)

Conditional GGC

Blockwise GGC



fully implemented



alpha-testing



coming soon

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

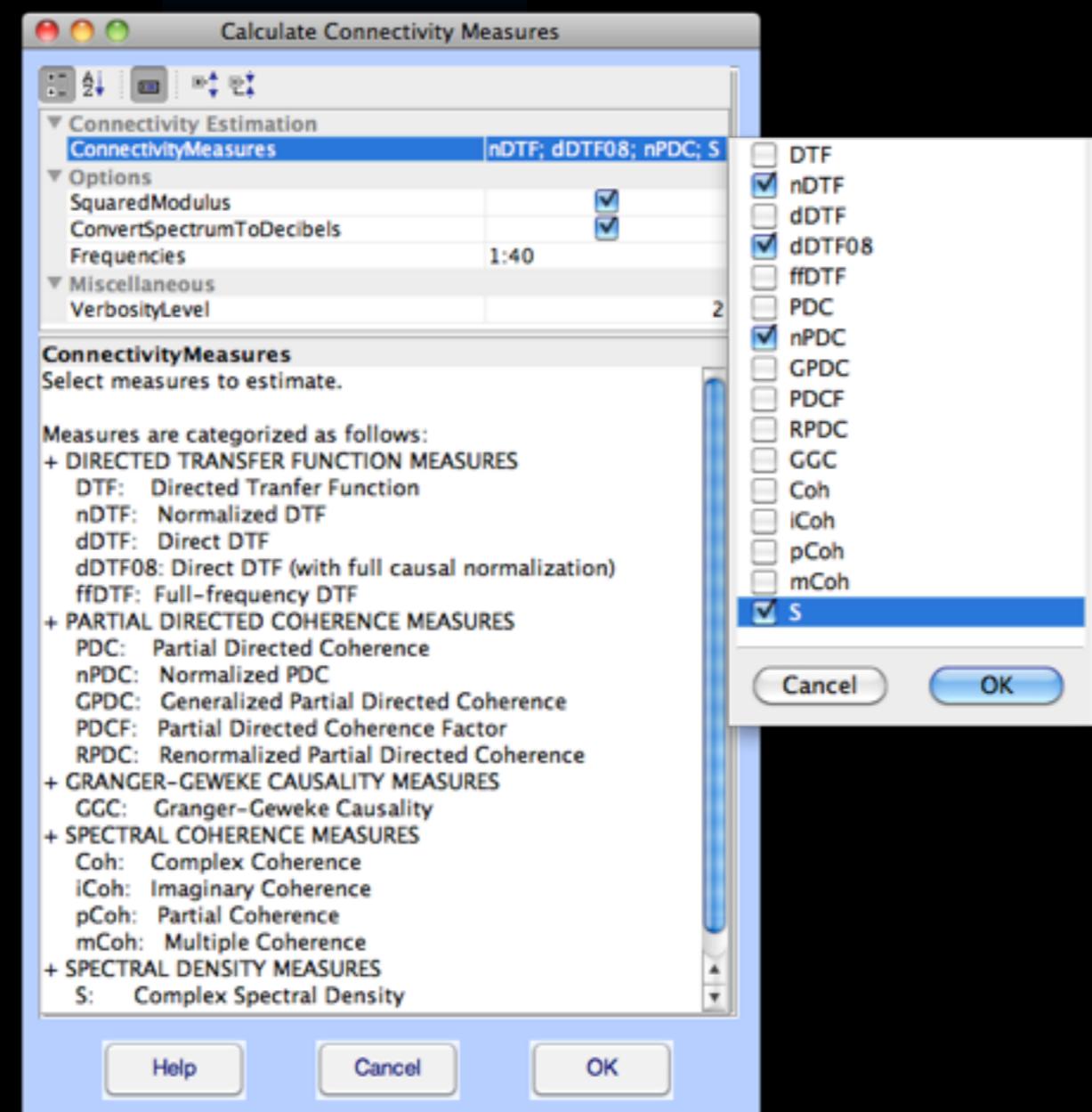
SIFT

Apps

To-Do

Fin

Pre-processing  
Model fitting and validation ►  
**Connectivity**  
Statistics  
Visualization



Preprocessing

Modeling

Statistics

Visualization

SIFT

Apps

To-Do

Fin

Statistical Approach	Test	Parametric	Nonparam.
Asymptotic analytic estimates of confidence intervals. Applies to: PDC, nPDC, DTF, nDTF, rPDC	$H_{\text{null}}$ , $H_{\text{base}}$ , $H_{\text{AB}}$	<input checked="" type="checkbox"/>	
Theiler phase randomization Applies to: all	$H_{\text{null}}$		<input checked="" type="checkbox"/>
Bootstrap, Jackknife, Cross-Validation Applies to: all	$H_{\text{AB}}$ , $H_{\text{base}}$		<input checked="" type="checkbox"/>
Confidence intervals using Bayesian smoothing splines Applies to: all	$H_{\text{base}}$ , $H_{\text{AB}}$	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

$$H_{\text{null}} : \mathbf{C}_{ij} = 0$$

$$H_{\text{base}} : \mathbf{C}_{ij} = \mathbf{C}_{\text{baseline}}$$

$$H_{\text{AB}} : \mathbf{C}_{ij}^A = \mathbf{C}_{ij}^B$$

 fully implemented

 alpha-testing

 coming soon

Preprocessing

Modeling

Statistics

Visualization

Parametric

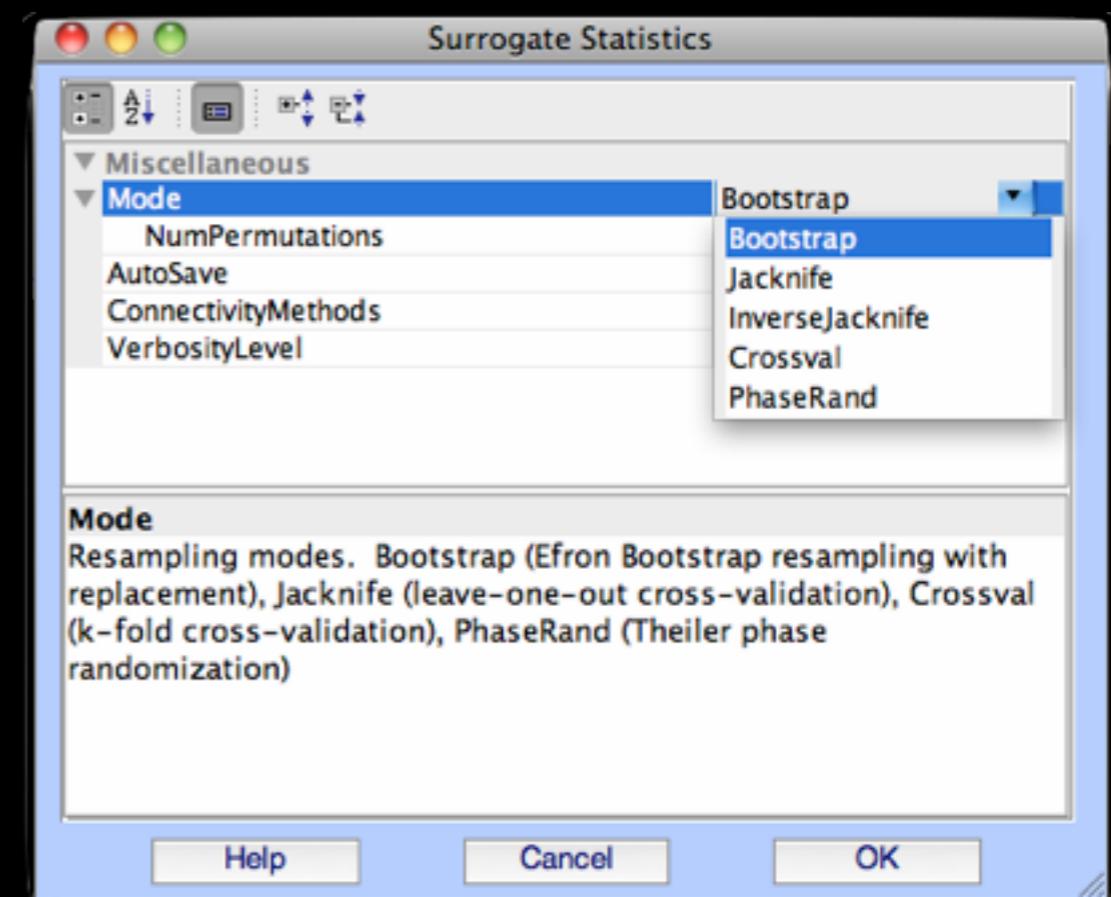
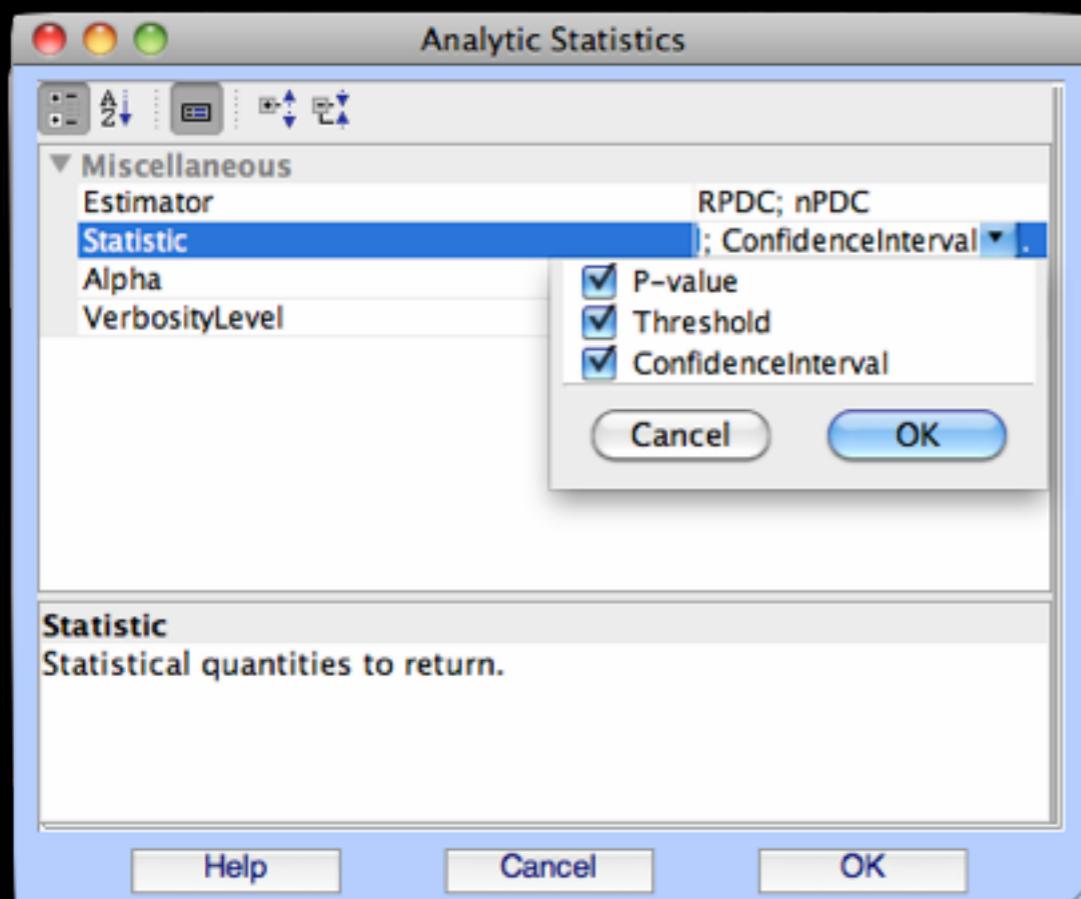
Non-parametric

SIFT

Apps

To-Do

Fin



fully implemented



alpha-testing



coming soon

Preprocessing

Modeling

Statistics

Visualization

## Interactive Visualizers

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Projection Movie

Directed Graphs and Graph Theoretic Analysis  
(Bioinformatics Toolbox Interface)

and more ...



fully implemented

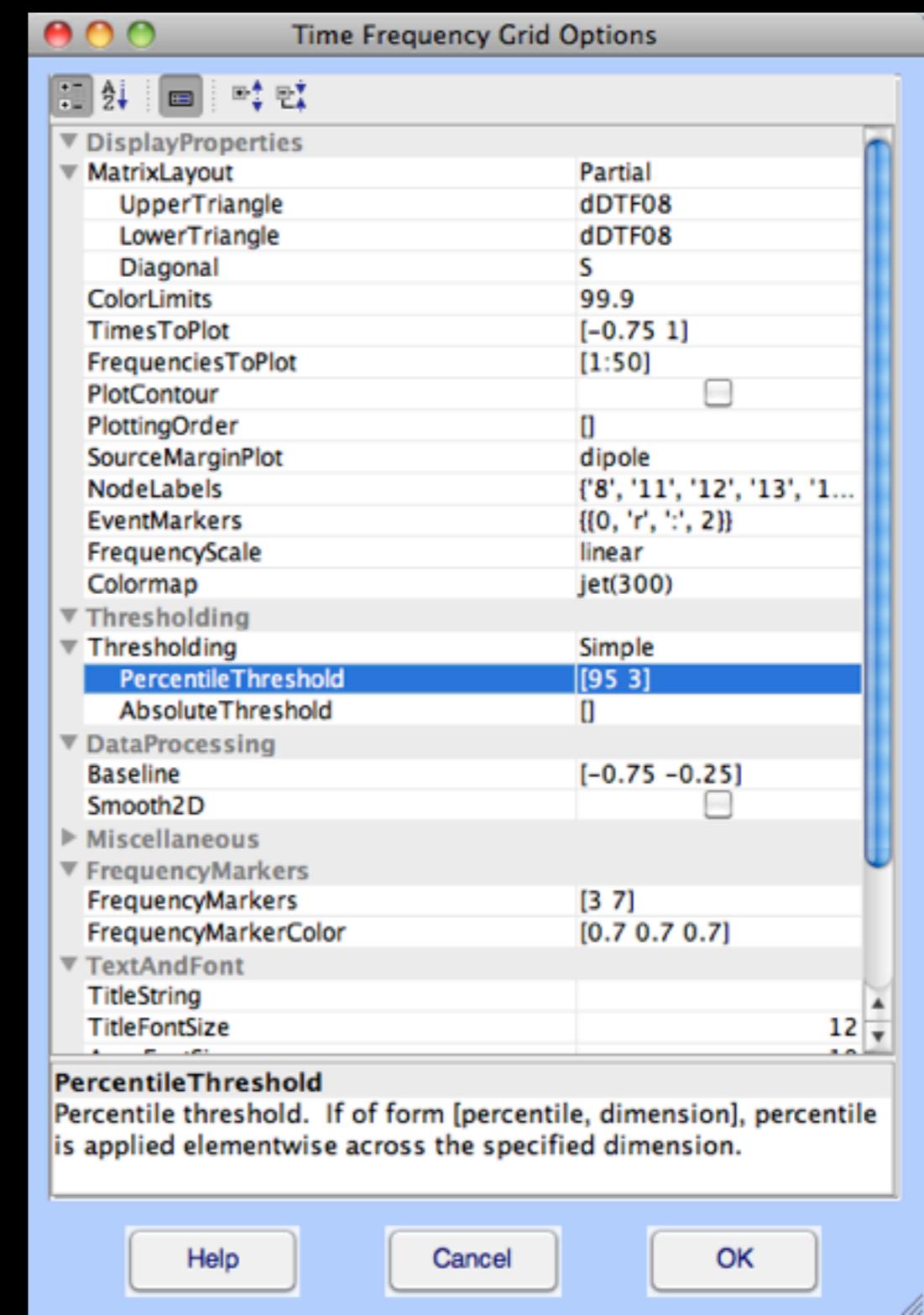
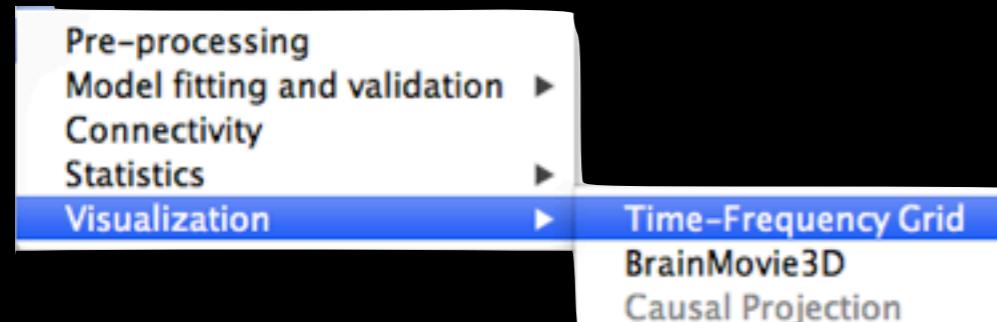


alpha-testing



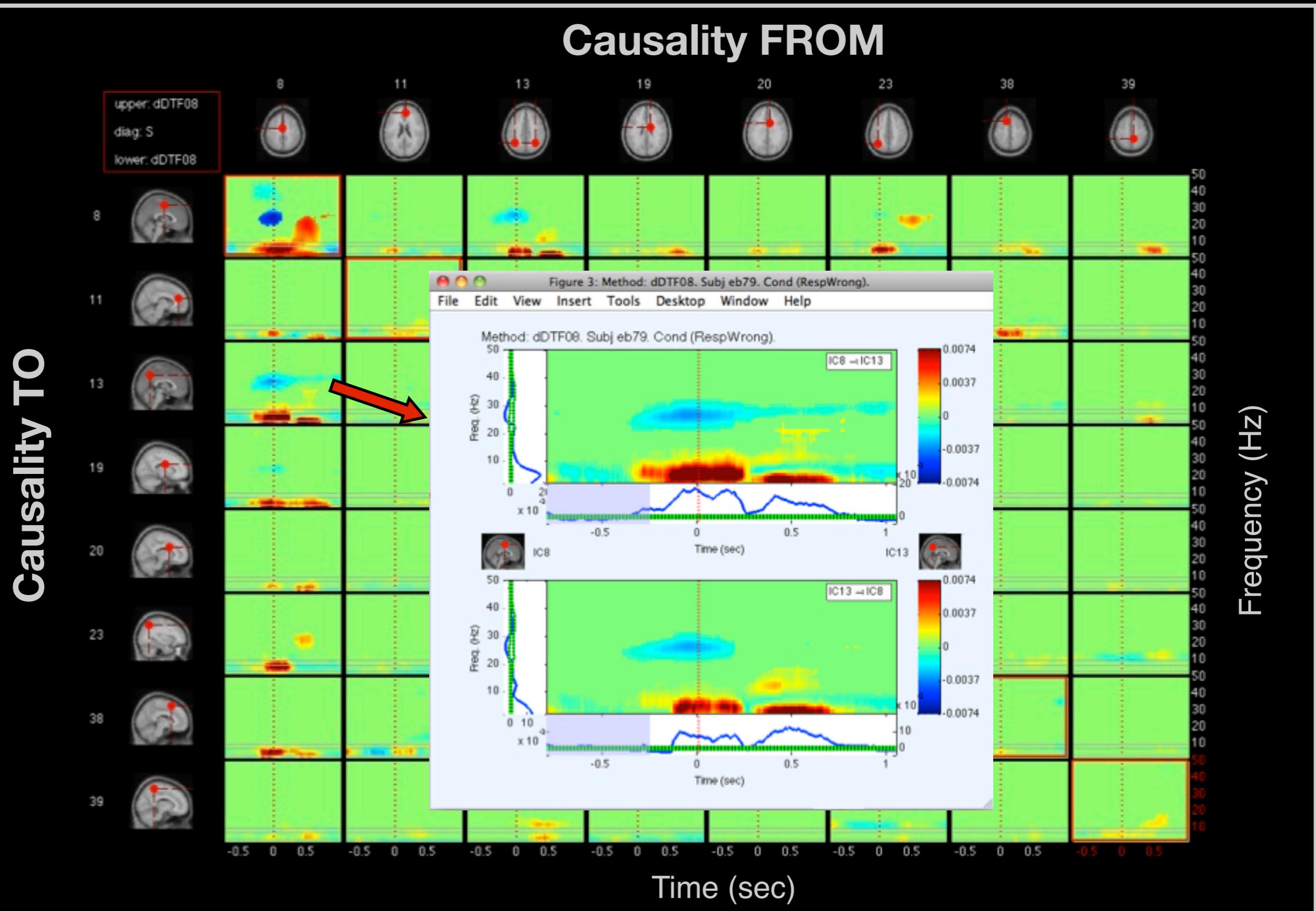
coming soon

# Interactive Time-Frequency Grid



# Interactive Time-Frequency Grid

Intro | Theory | SIFT | Apps | To-Do | Fin



# Interactive Causal BrainMovie3D

Intro

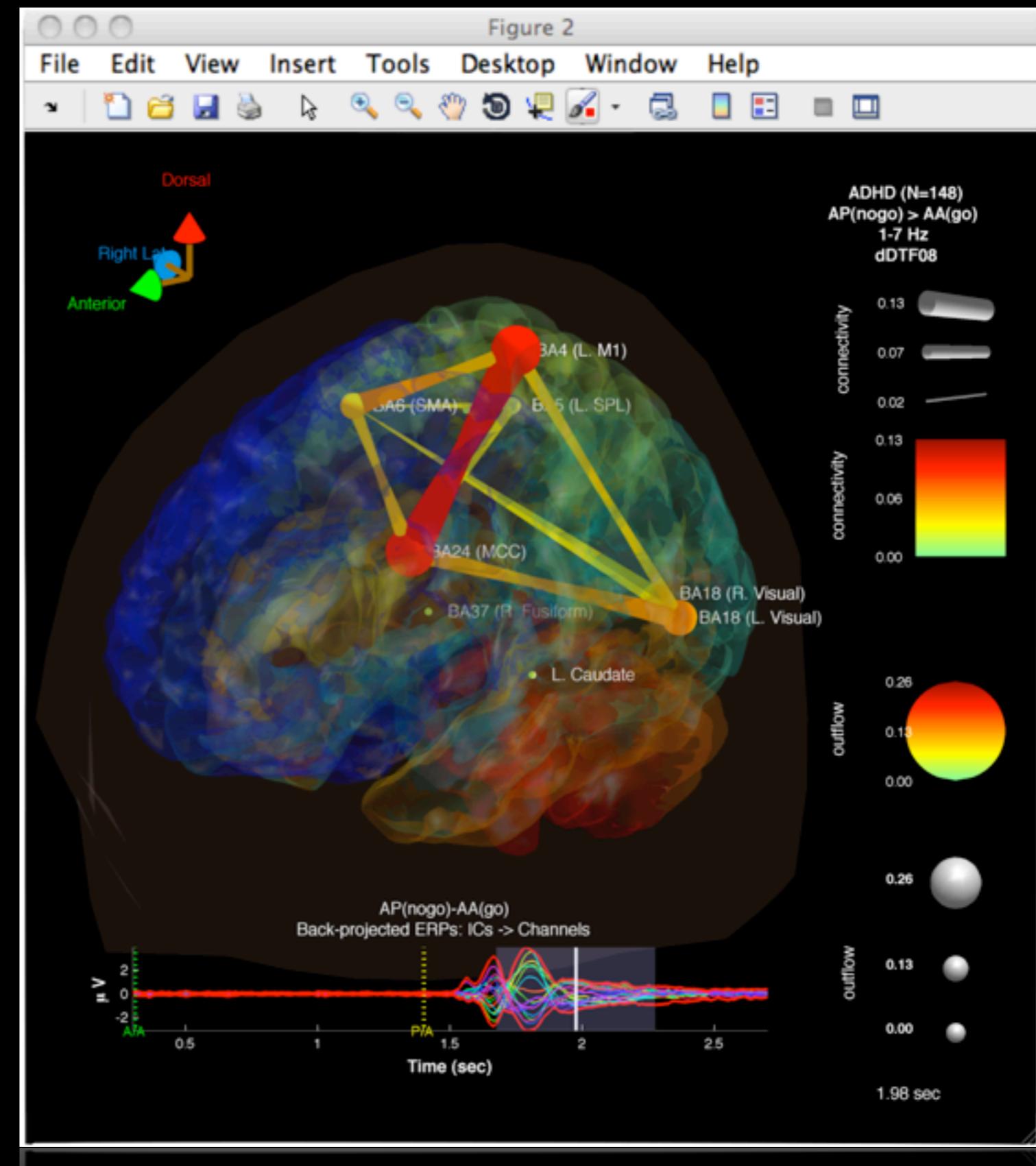
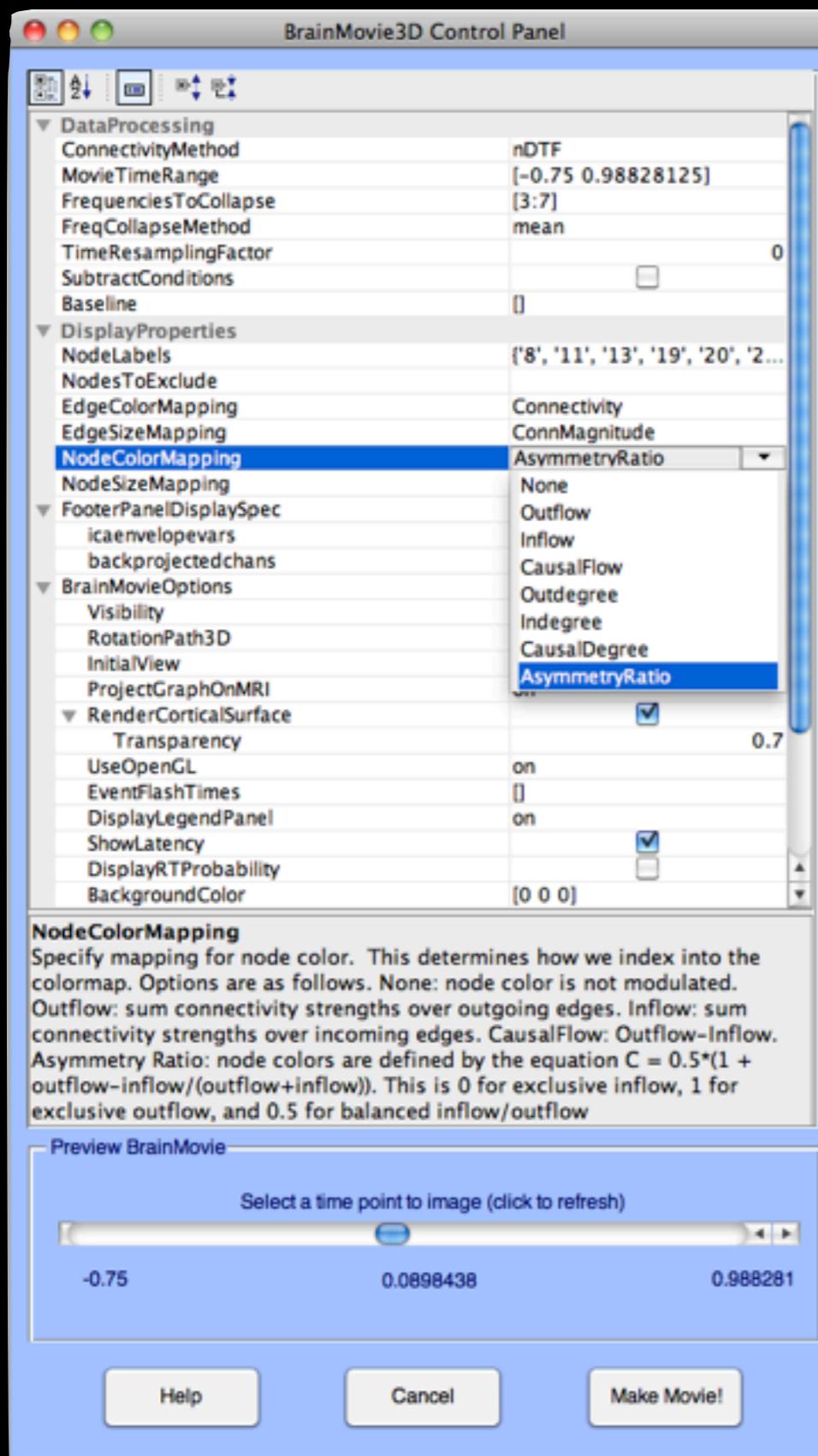
Theory

118

Após

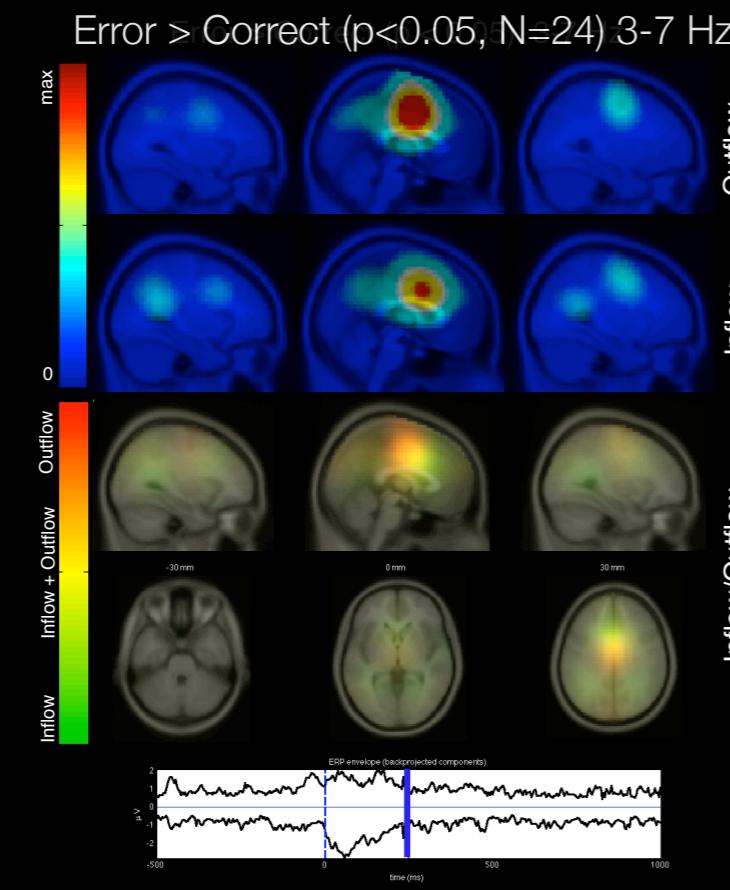
To-Do

卷之三



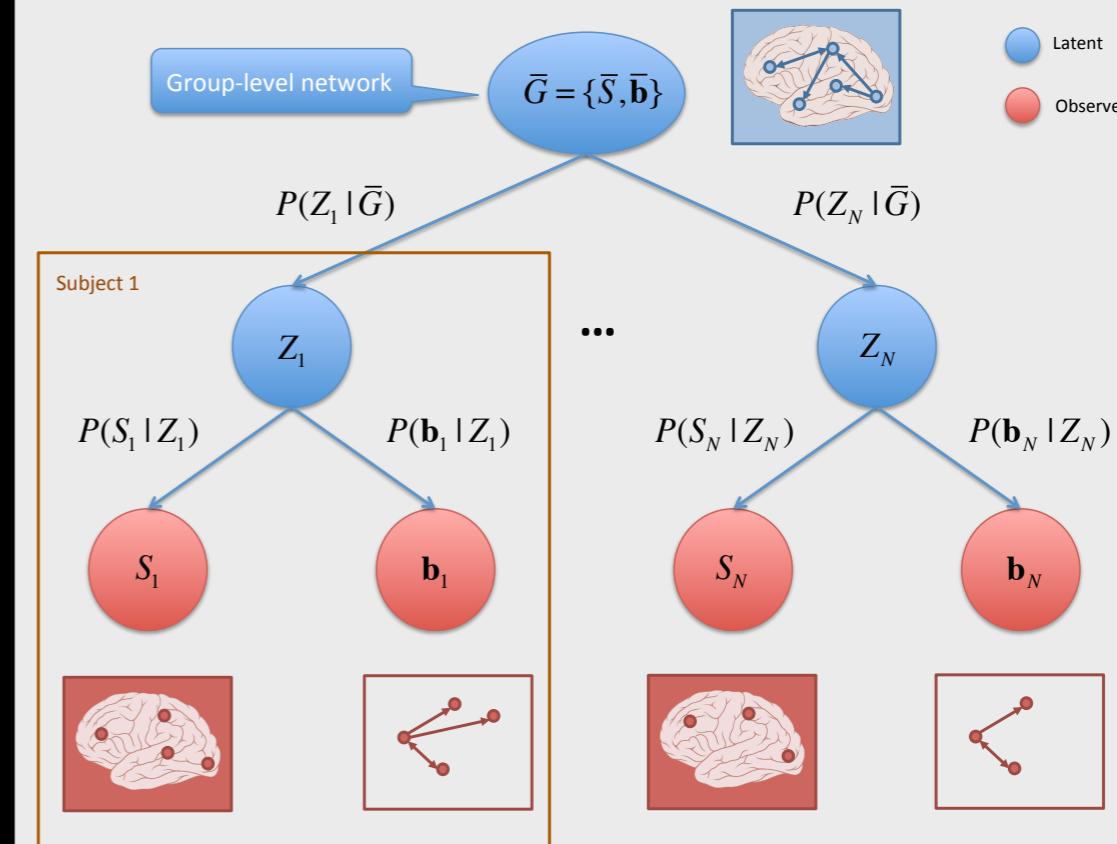
# Group Analysis (in prep)

## Causal/Measure Projection



Mullen, Onton, et al, 2010, HBM, Barcelona  
Bigdely-Shamlo, Mullen, et al, 2012, *in review*

## Bayesian Hierarchical Model



Thompson, Mullen, Makeig, 2011, ICONXI  
Thompson, Mullen, Makeig, 2012, *in prep*



alpha-testing

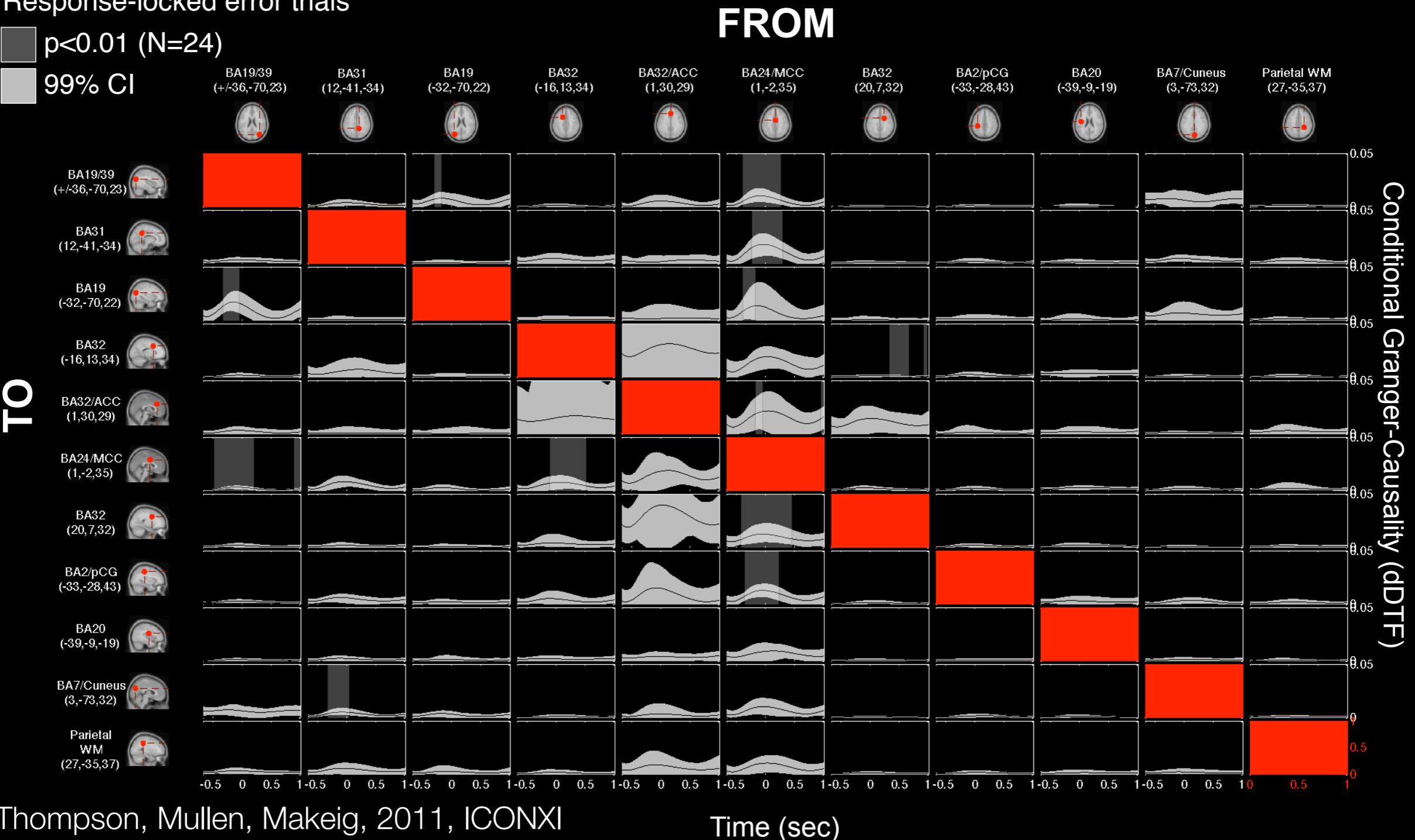
# Bayesian Multi-Subject Inference

Theta-band (4-8 Hz) dDTF

Response-locked error trials

p<0.01 (N=24)

99% CI



Thompson, Mullen, Makeig, 2011, ICONXI

Thompson, Mullen, Makeig, 2012, *in prep*

# Bayesian Multi-Subject Inference

Intro

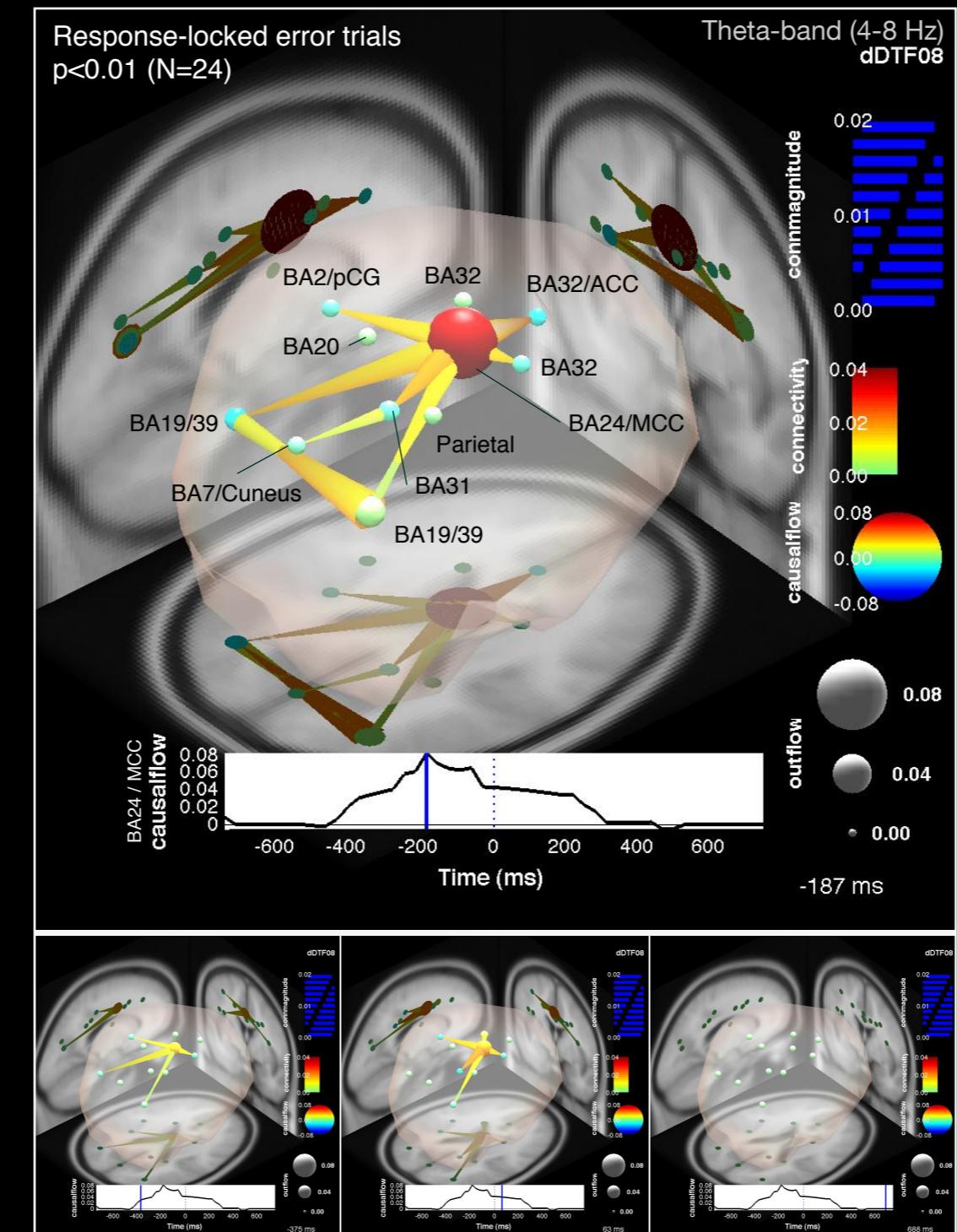
## Theory

THE  
S

Abs

TODAY

三



Thompson, Mullen, Makeig, 2011, ICONXI  
Thompson, Mullen, Makeig, 2012, *in prep*

## Simulation

### Dynamical System Simulation Workbench

Systems of linear stochastically-forced damped coupled oscillators

Support for arbitrary time-varying (non-stationary) coupling dynamics

Intuitive equation-based scripting environment

Support for generalized gaussian or hyperbolic secant innovations

Nonlinear Dynamical Systems

Rössler and Lorenz Systems



fully implemented



alpha-testing



coming soon

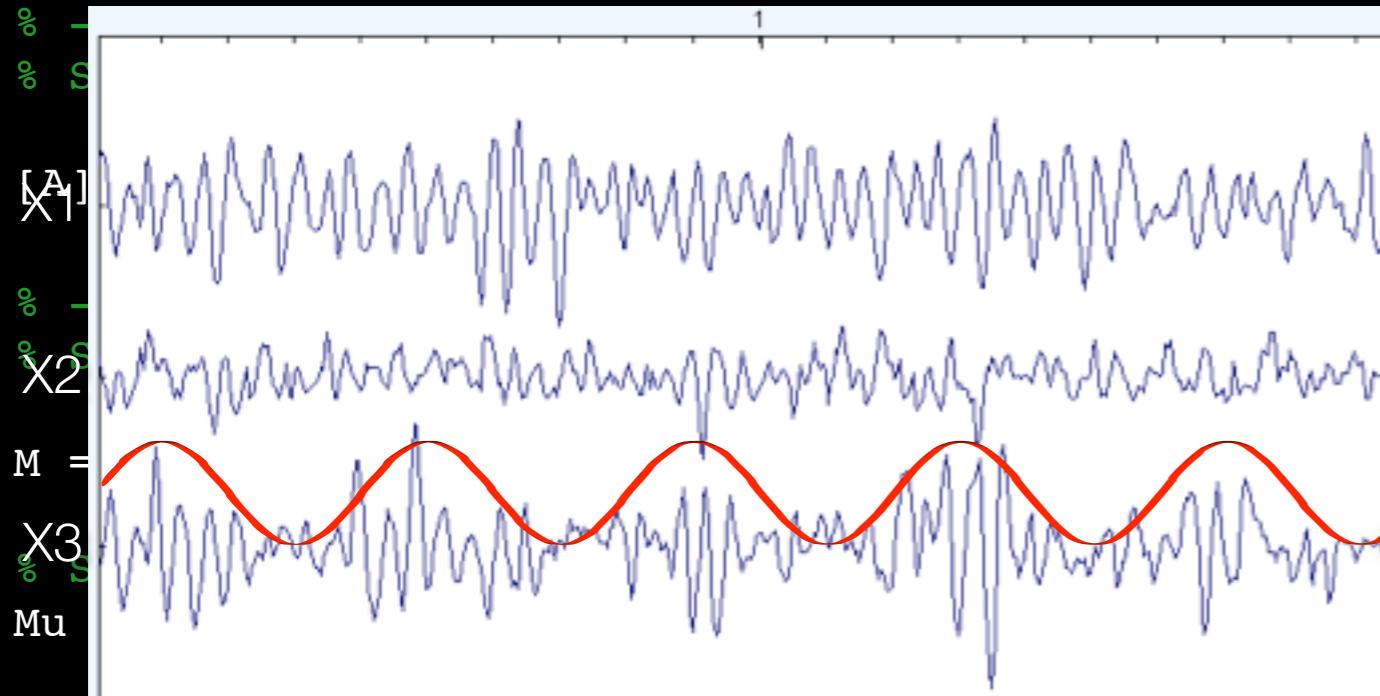
```
% Example: Trivariate damped coupled oscillators with sinusoidally-modulated coupling
```

```
% -----
% STEP 1: create prototype VAR structure
```

```
Fs = 100; % Sampling Rate (Hz)
Nl = 500; % length of each epoch (samples)
Nr = 100; % number of trials (realizations)
ndisc = 1000; % number of startup samples to discard
ModelOrder = 2; % model order
f0 = 10; % central oscillation frequency (Hz)
```

```
expr = { ...
    ['x1(t) = ' sim_dampedOscillator(f0,9,Fs,1) ' + e1(t)'] ...
    ['x2(t) = ' sim_dampedOscillator(f0,2,Fs,2) ' + -0.1*x1(t-2) + e2(t)'] ...
    ['x3(t) = ' sim_dampedOscillator(f0,2,Fs,3) ' + {0.3*sin(2*pi*t/100)+0.3}*x1(t-2) + e3(t)'] ...
};
```

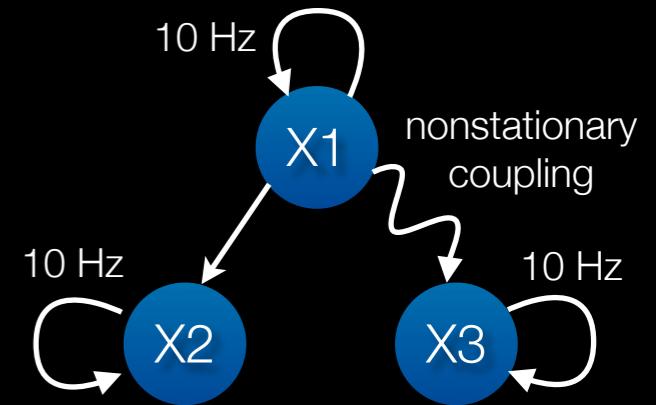
```
Aproto = sim_genVARModelFromEq(expr,ModelOrder);
```



```
sigma = 1;
E = sigma*eye(M);
```

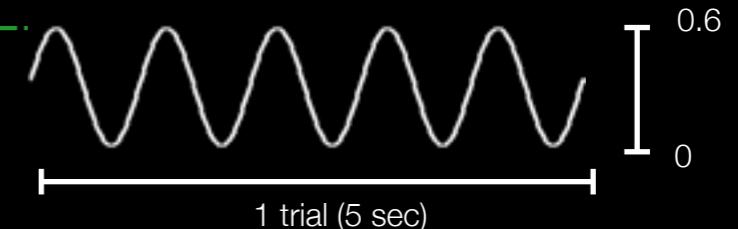
```
% generate simulated data with laplacian (supergaussian) innovations
data = sim_tvarsim(Mu,A,E,[Nl Nr],ndisc,1,1,'gengauss');
```

## Graphical Model



Time-varying  $X_1 \rightarrow X_3$  coupling  
(1 Hz modulation)

```
Verbose',true);
```



Amplitude Modulation (PAC)

**Simulation****Linear Dynamical System****Vector Autoregressive Process**

- ✓ Pre-processing
- Model fitting and validation
- ✓ Connectivity



Simulate Autoregressive Data

**Miscellaneous****Simulation**

DynamicalEquations

**Epileptic Seizure** $x1(t) = \{2 * \exp(-1/(0.2 * t))\}$ 

ModelOrder

SetDynamics

**SimParams**

SamplingRate

100

TrialLength

5

NumTrials

100

BurnInSamples

1,000

CheckStability

**DataGenParams**

NoiseCovMat

1

ProcessMean

[]

**NoiseDistribution**

ScaleParam

1

ShapeParam

2

VerbosityLevel

2

**OutputFormat****BuildEEGLABStructure**

ExportGroundTruth



SetName

**Visualization**

PlotData



PlotGraphicalModel

**Simulation**

Select a simulation.

**Epileptic Seizure**

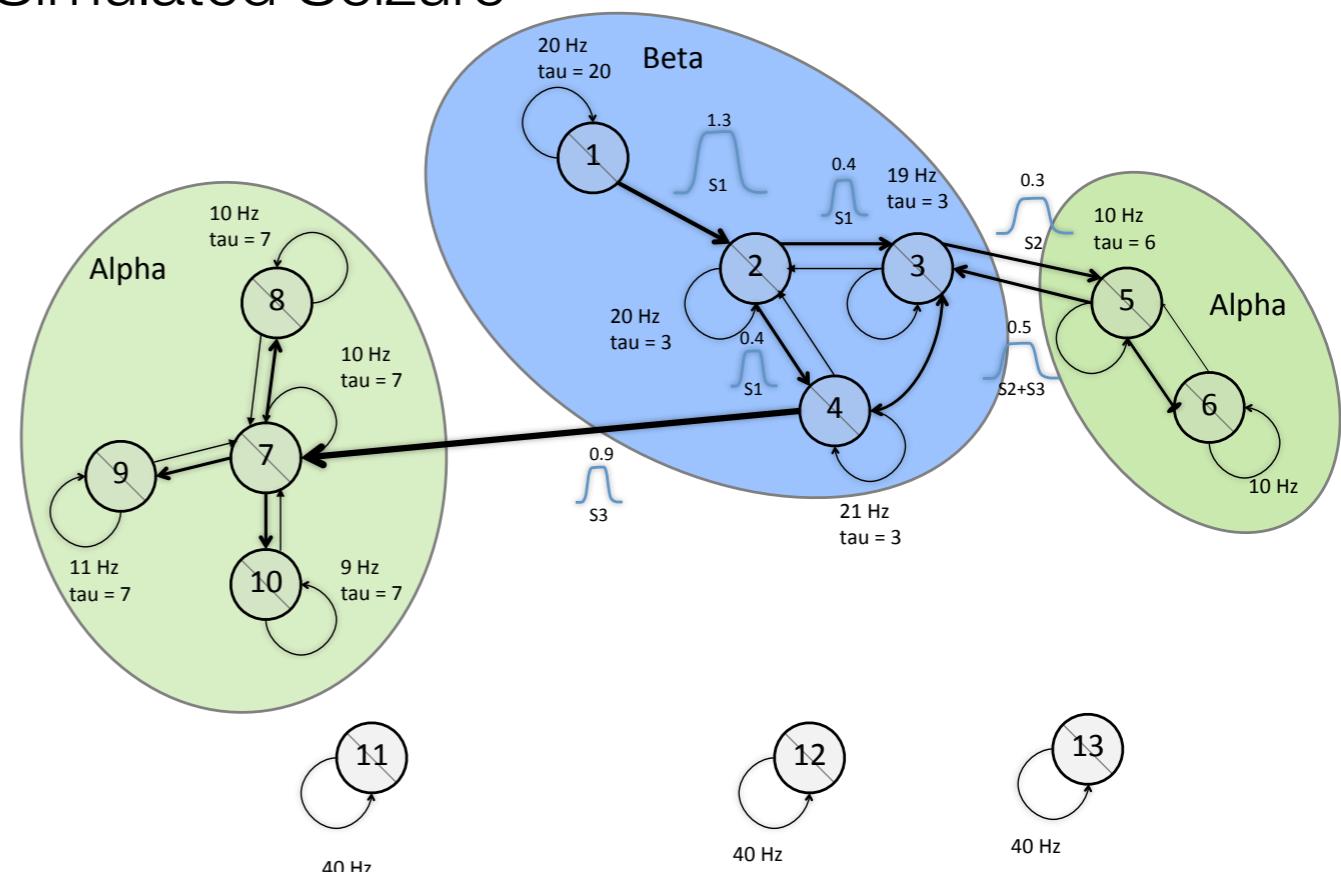
Schelter 2005 Eq 5

Schelter 2009 Eq 3.1

Schelter 2009 Eq 3.2

Bivariate Coupled Oscillator

Trivariate Coupled Oscillator

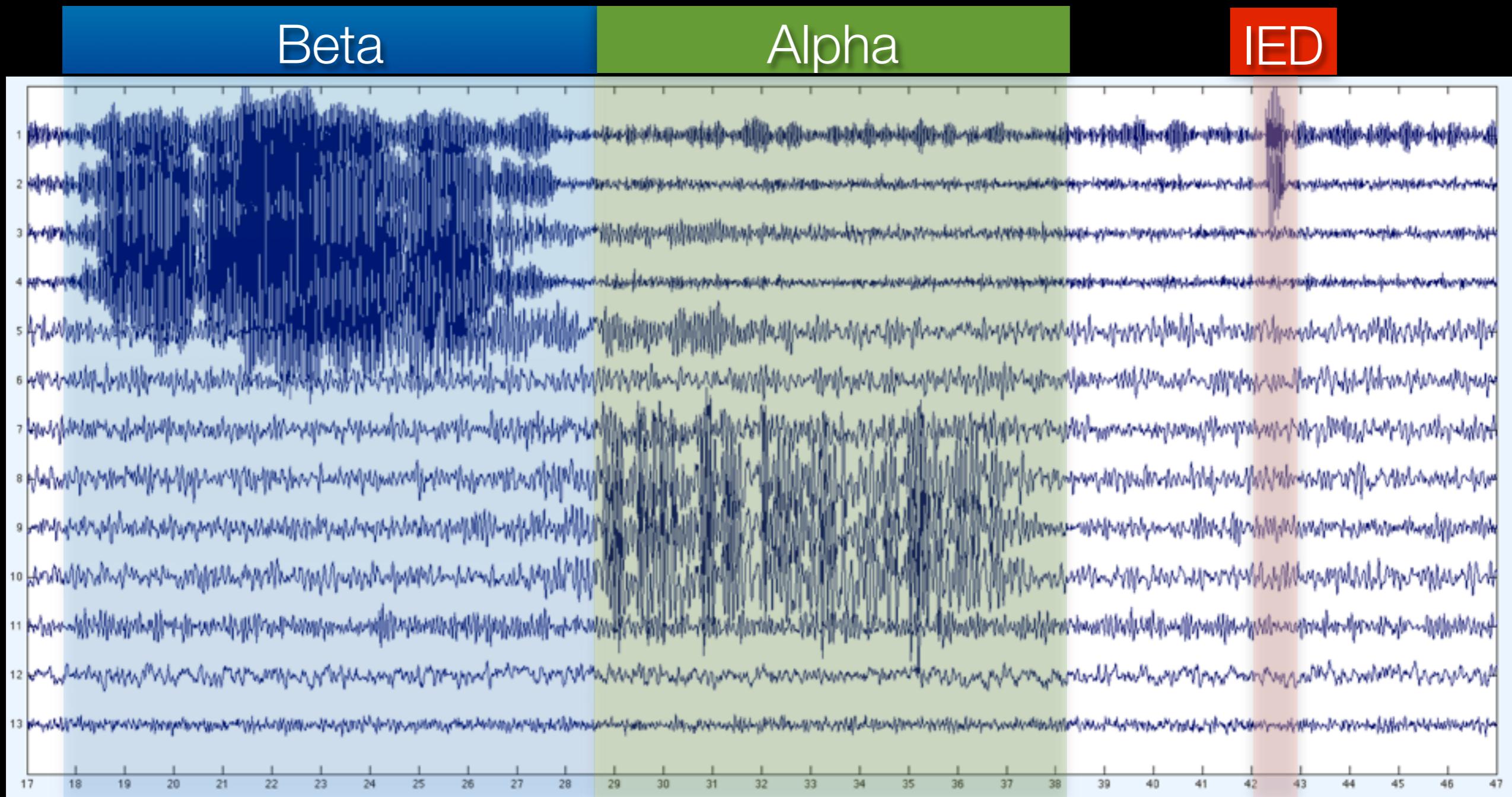
**Simulation****Simulated Seizure**

Help

Cancel

OK

# Simulated Seizure Sources



# Where do I get SIFT?

[sccn.ucsd.edu/wiki/SIFT](http://sccn.ucsd.edu/wiki/SIFT)

The screenshot shows the SIFT repository page on the SCCN wiki. It features a large brain diagram with colored nodes representing different regions, and arrows indicating connectivity between them. The SIFT logo is prominently displayed with the text "Source Information Flow Toolbox Version 0.1-Alpha". Below the diagram is a screenshot of the SIFT software interface, showing a 3D brain model with connectivity paths and a time-frequency spectrogram.

**Contents [hide]**

- Welcome to the repository for the Source Information Flow Toolbox (SIFT)
  - SIFT Downloads
  - Citing SIFT
- SIFT Online Handbook and User Manual

**Welcome to the repository for the Source Information Flow Toolbox (SIFT)**

Developed and Maintained by: Tim Mullen (SCCN, INC, UCSD)  
 Web: <http://www.antillipsi.net>  
 Email: <Tim's first name> (at) sccn (dot) ucsd (dot) edu

SIFT is an EEGLAB-compatible toolbox for analysis and visualization of multivariate causality and information flow between sources of electrophysiological (EEG/ECOG/MEG) activity. It consists of a suite of command-line functions with an integrated Graphical User Interface for easy access to multiple features. There are currently four modules: data preprocessing, model fitting, and connectivity estimation, statistical analysis, and visualization.

## SIFT Online Handbook and User Manual

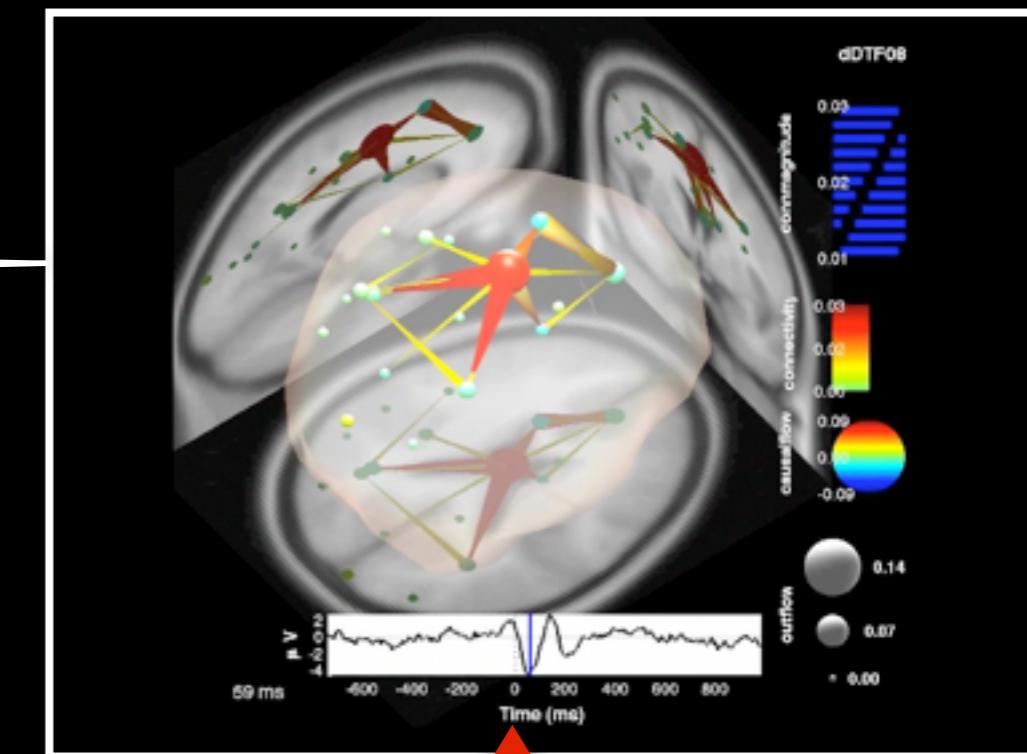
A video-lecture on the (very) basic theory of application of SIFT to modeling distributed brain dynamics in EEG is available here

Table of Contents	[hide]
<a href="#">2. Introduction</a>	
<a href="#">3. Multivariate Autoregressive Modeling</a>	
3.1. Stationarity and Stability	
3.2. The Multivariate Least-Squares Estimator	
3.3. Frequency-Domain Representation	
3.4. Modeling non-stationary data using adaptive VAR models	
3.4.1 Segmentation-based Adaptive VAR (AMVAP) models	
3.5. Model order selection	
3.6. Model Validation	
3.6.1 Checking the whiteness of the residuals	
3.6.1.1 Autocorrelation Function (ACF) Test	
3.6.1.2 Portmanteau Tests	
3.6.2 Checking the consistency of the model	
3.6.3 Checking the stability and stationarity of the model	
3.6.4 Comparing parametric and nonparametric spectra and coherence	
<a href="#">4. Granger Causality and Extensions</a>	
4.1. Time-Domain GC	
4.2. Frequency-Domain GC	
4.3. A partial list of VAR-based spectral, coherence and GC estimators	
4.4. Time-Frequency GC	
4.5. (Cross-) correlation does not imply (Granger-) causation	
<a href="#">5. Statistics</a>	
5.1. Asymptotic analytic statistics	
5.2. Nonparametric surrogate statistics	
5.2.1. Bootstrap resampling	
5.2.2. Phase Randomization	
<a href="#">6. Using SIFT to analyze neural information flow dynamics</a>	
6.1. System Requirements	
6.2. Configuring EEGLAB	
6.3. Loading the data	
6.4. The SIFT analysis pipeline	
6.5. Preprocessing	
6.5.1. Theory: preprocessing	
6.5.1.1. Component Selection	
6.5.1.2. Epoching	
6.5.1.3. Filtering	
6.5.1.4. Downsampling	
6.5.1.5. Differencing	
6.5.1.6. Detrending	
6.5.1.7. Normalization	
6.6. Model Fitting and Validation	
6.6.1. Theory: selecting a window length	
6.6.1.1. Local Stationarity	
6.6.1.2. Temporal Smoothing	
6.6.1.3. Sufficient amount of data	
6.6.1.4. Process dynamics and neurophysiology	
6.6.2. Selecting the model order	
6.6.3. Fitting the final model	
6.6.4. Validating the fitted model	
6.7. Connectivity Estimation	
6.8. Statistics	
6.9. Visualization	
6.9.1. Interactive Time-Frequency Grid	
6.9.2. Interactive Causal BrainMovie3D	
6.9.3. Causal Projection	
6.10. Group Analysis	
6.10.1. Disjoint Clustering	
6.10.2. Bayesian Mixture Model	
<a href="#">7. Conclusions and Future Work</a>	

# Some Applications of SIFT

**Identification of event-related shifts in effective connectivity which index and predict behavior**

Single-trial spatiotemporal modeling of seizure propagation dynamics



Brain-Computer Interfaces  
(Cognitive State Assessment)

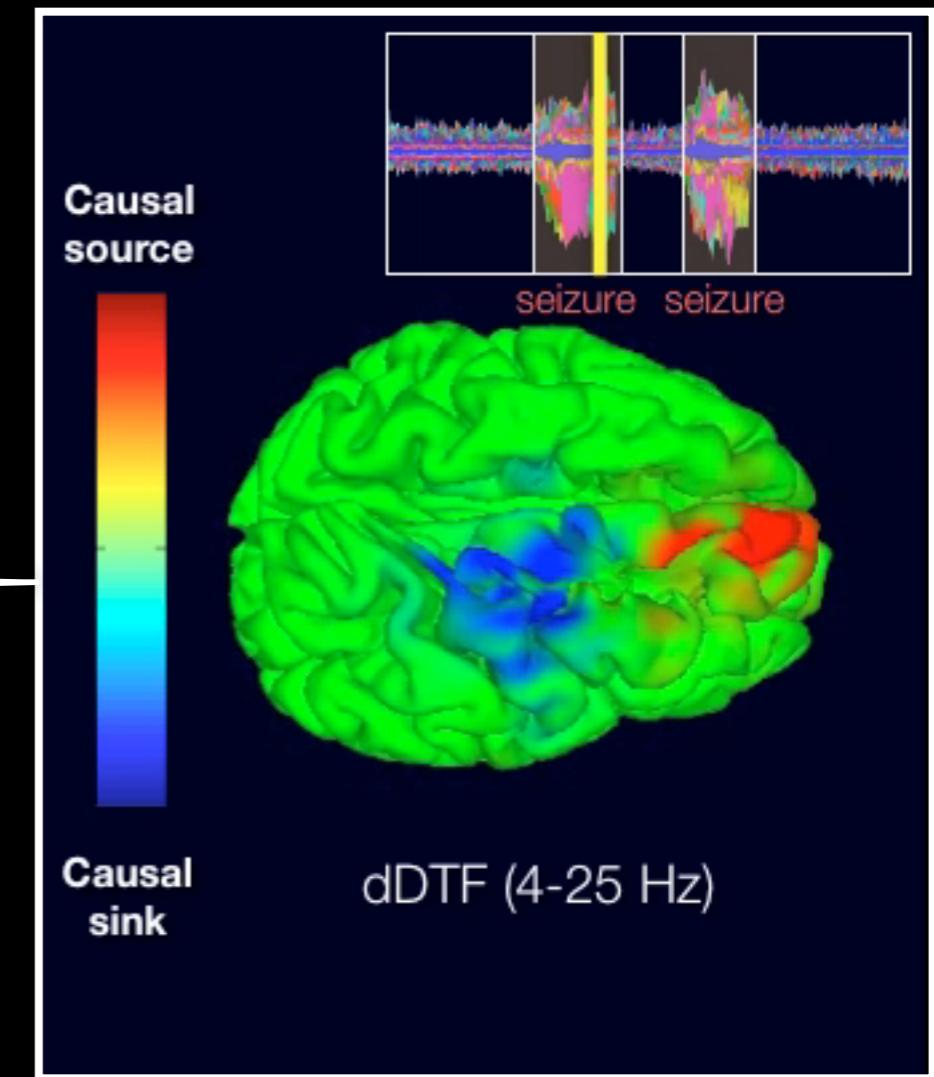
Mullen et al, *HBM*, Barcelona, 2010

# Some Applications of SIFT

Identification of event-related shifts in effective connectivity which index and predict behavior

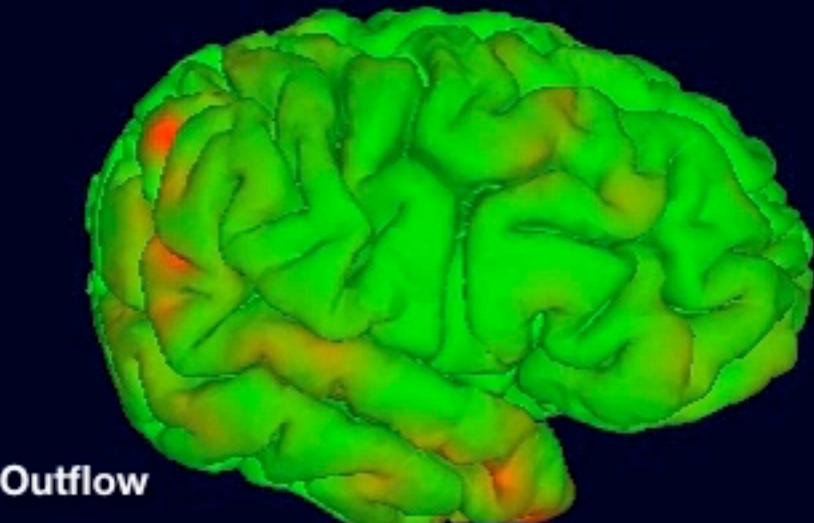
**Single-trial spatiotemporal modeling of seizure propagation dynamics**

Brain-Computer Interfaces  
(Cognitive State Assessment)

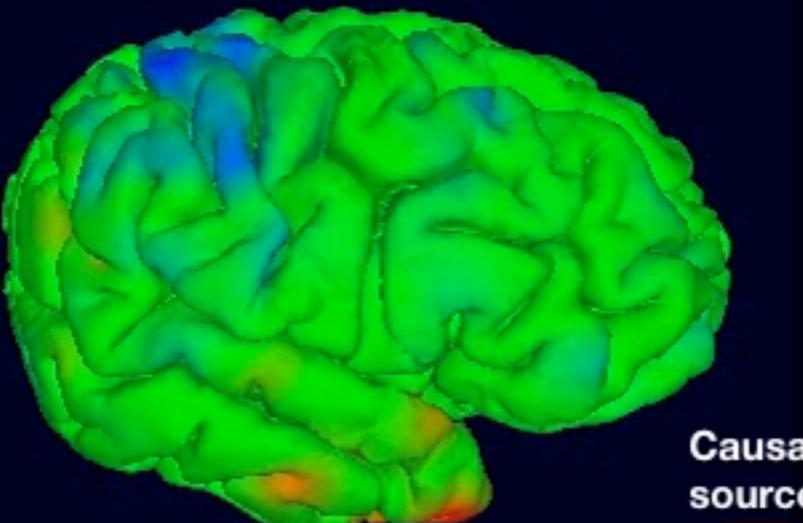


Mullen, Akalin Acar, et al *IEEE EMBC*, 2011

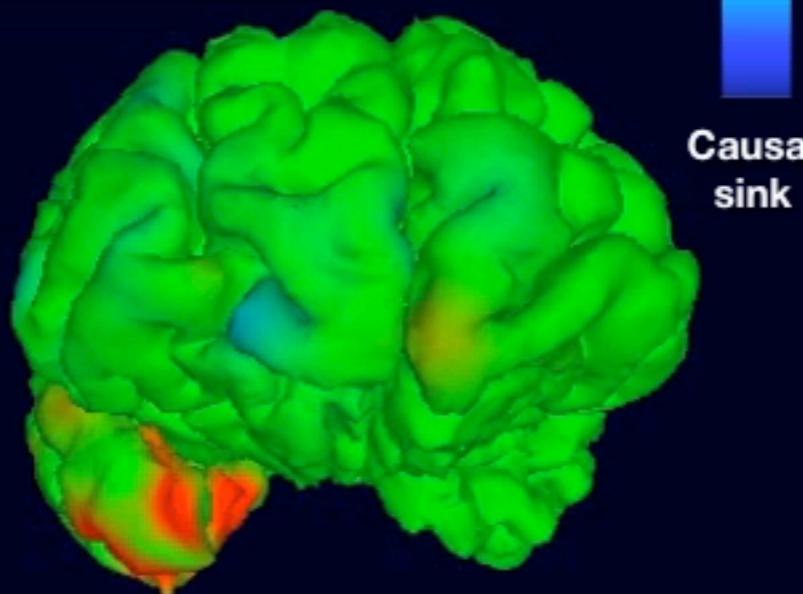
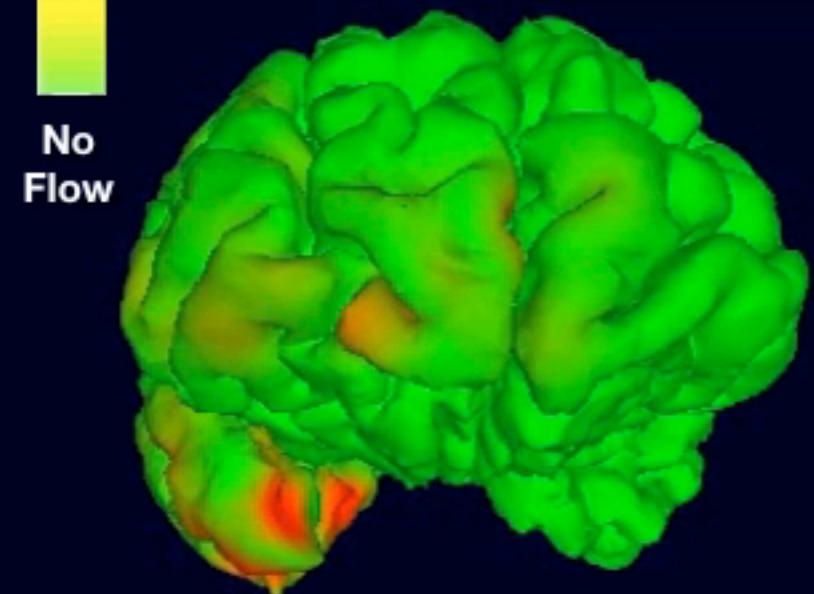
# Outflow



# Causal Flow



dDTF (2-40 Hz)



- **ECoG Data**
- 104 ECoG (subdural) electrodes
- Surgical Outcome: Negative
- Provided by Dr. Ashesh Mehta (Feinstein Institute for Clinical Research, NY)

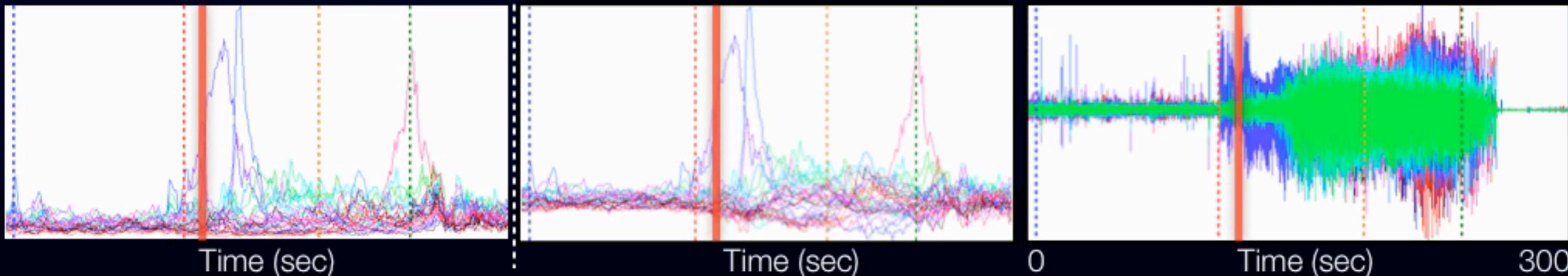
- **Source Reconstruction**

- 5-Model **AMICA** decomposition
- Selection of globally dominant model
- Selection of **29 ICs** comprising independent subspaces
- Component localization via multiscale patch basis **Sparse Bayesian Learning**

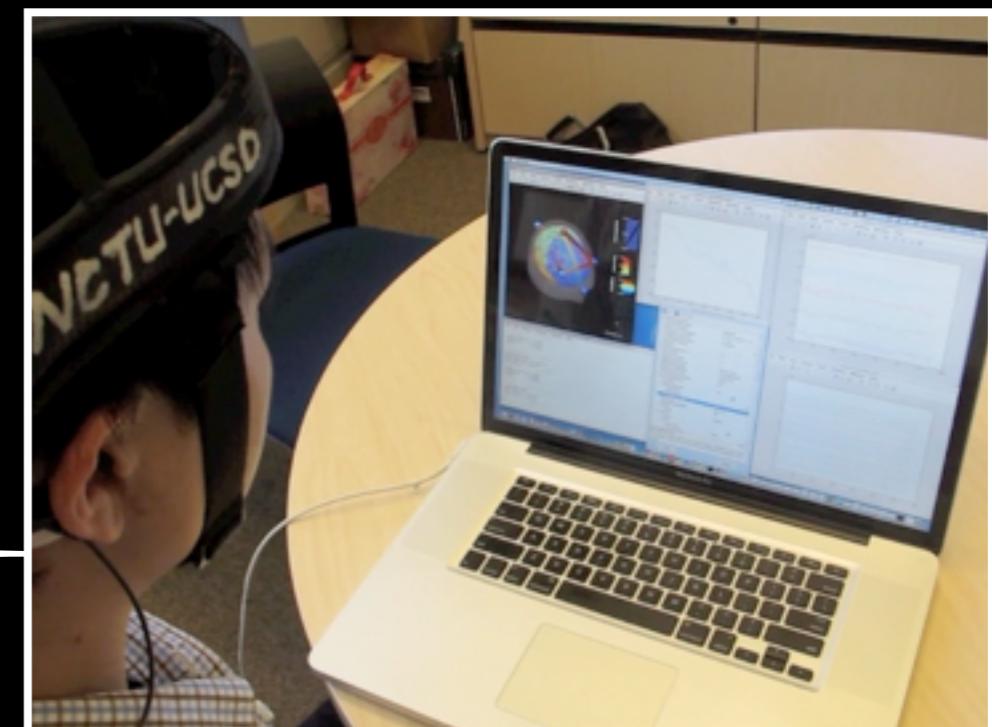
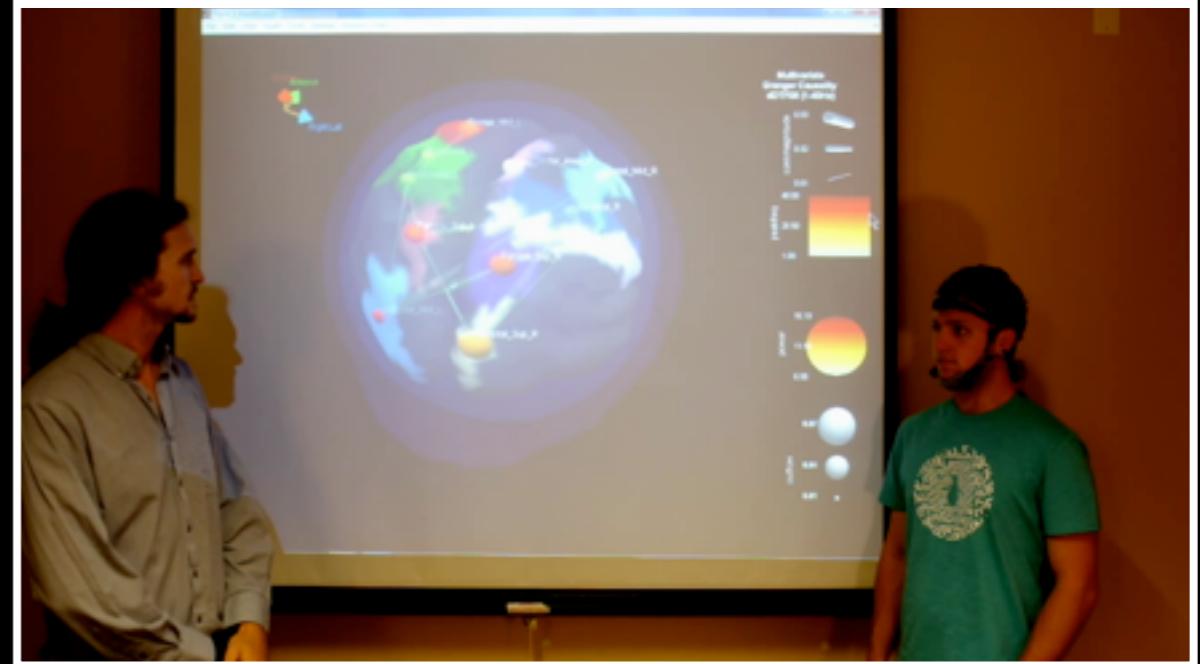
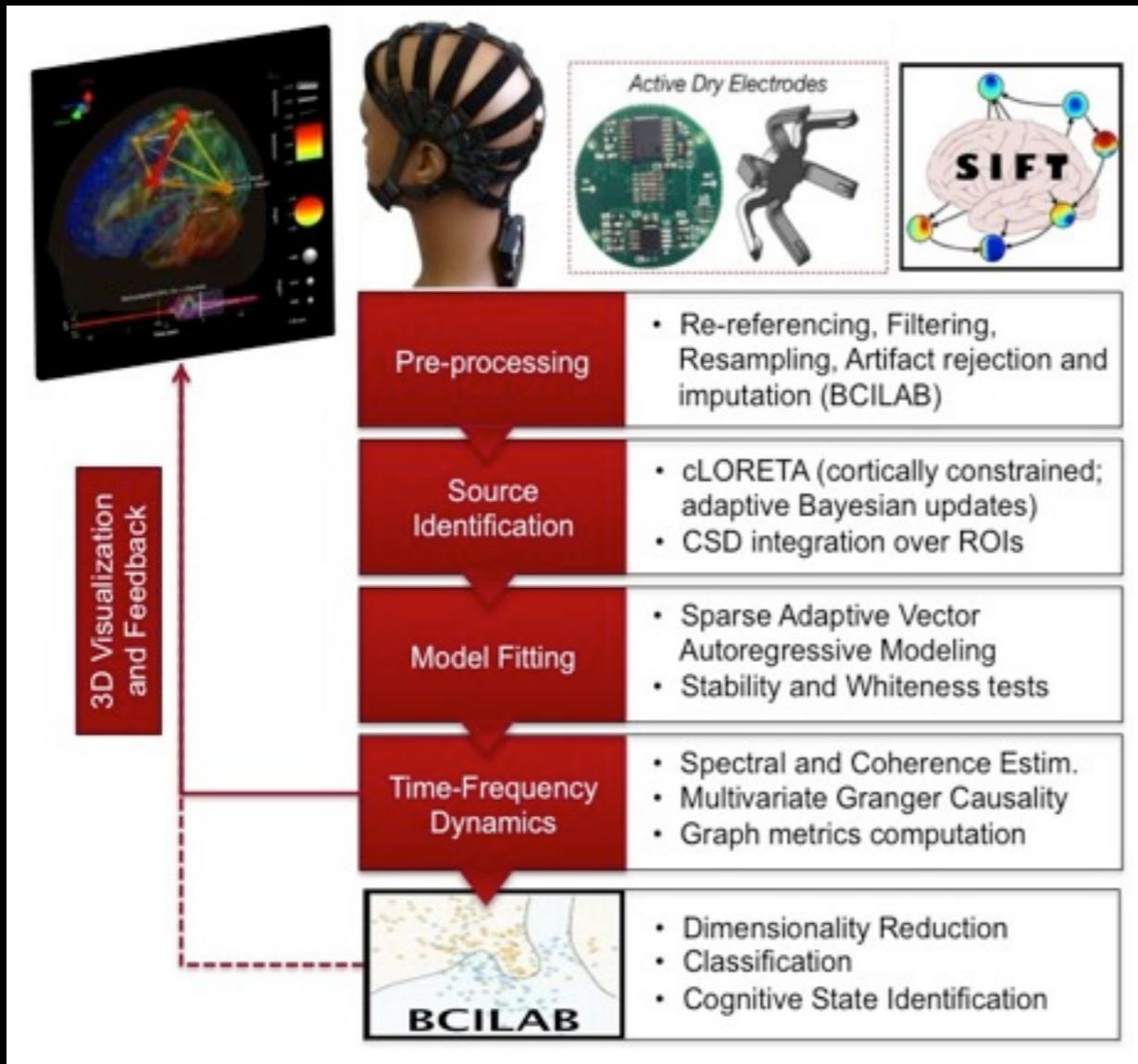
- **Sparse VAR Model Fitting**

- 29-dimensional VAR[12] model
- Group Lasso (ADMM solver)
- 5-second windows, 1-sec step
- Model Order = 12
- Adaptive regularization selection (step-down from 0.013)
- direct DTF method of causality

## AMICA IC activations



# Some Applications of SIFT



**Brain-Computer Interfaces:**  
(Cognitive State Assessment)

Mullen, T., Kothe, C., Chi, Y.M., Ojeda, A., Makeig, S., Cauwenberghs, G., Jung, T-P. (2013). Real-Time Modeling and 3D Visualization of Source Dynamics and Connectivity Using Wearable EEG. *IEEE EMBC*

# The Road Ahead

- Public release of new **alpha-testing** methods with updated online Handbook
- Ongoing incorporation/improvement of sparse VAR, and linear/nonlinear state-space models (Cubature Kalman Filter, EGCA, SCSA, AMIRA)
- Facilitate specification of constraints/priors on dynamic connectivity (e.g. from DTI, anatomy, etc)
- Release and further development of Group Analysis module with multi-subject Bayesian inference and comprehensive statistics (EEGLAB STUDY framework).
- Interfaces with other toolboxes: TRENTOOL (Transfer Entropy), SPM (Dynamic Causal Modeling), Fieldtrip, BCILAB (Brain-Computer Interfaces)
- Improved 2D/3D/4D interactive visualization suite