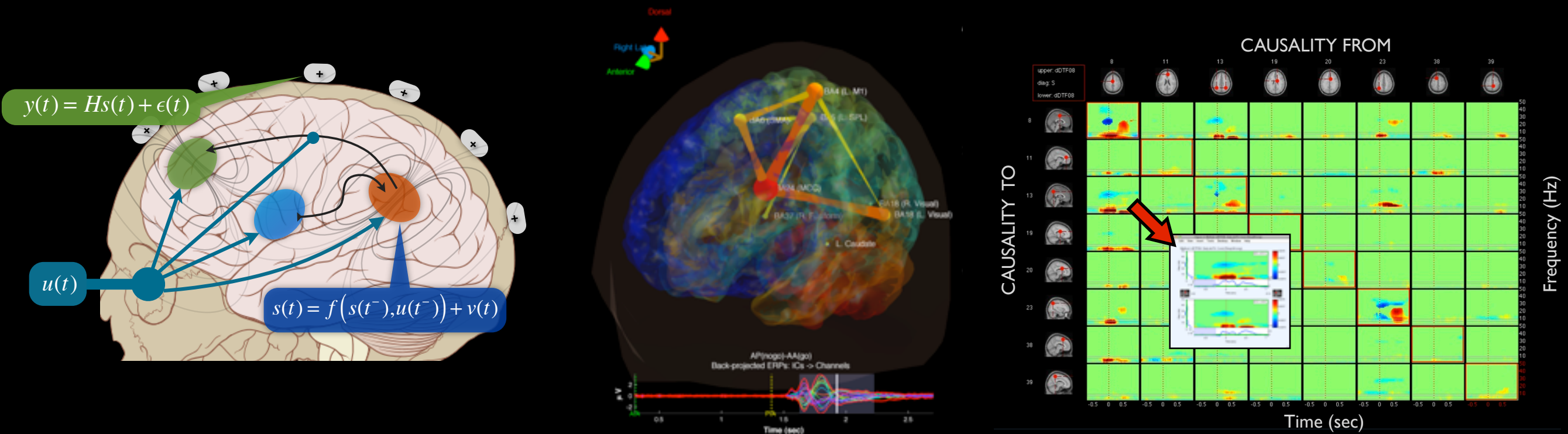


The Dynamic Brain: Modeling Neural Dynamics and Interactions from M/EEG



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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

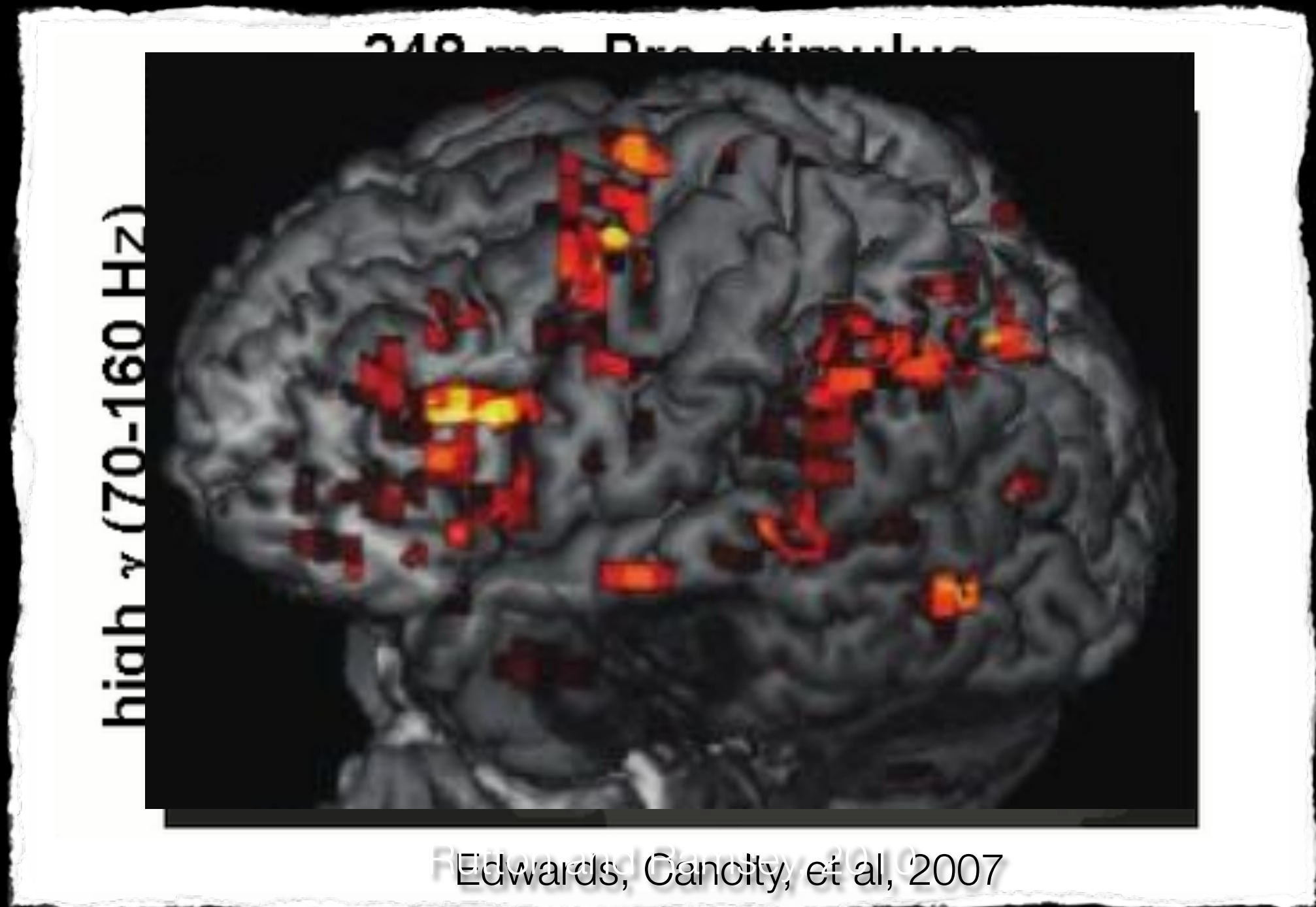
The Source Information Flow Toolbox (SIFT)

Some Applications of SIFT

The Road Ahead

Fin

The Dynamic Brain

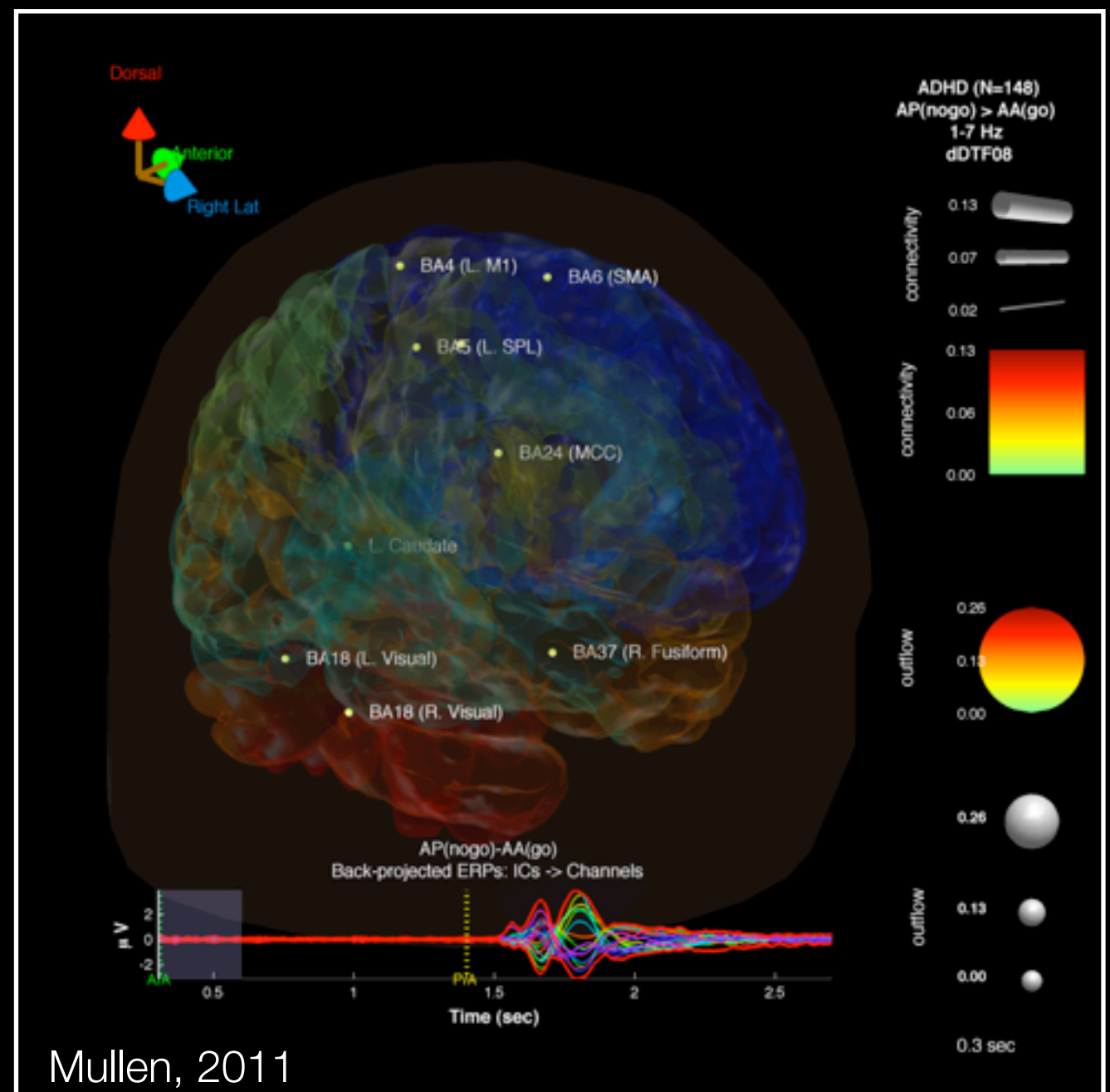


The Dynamic Brain

- 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

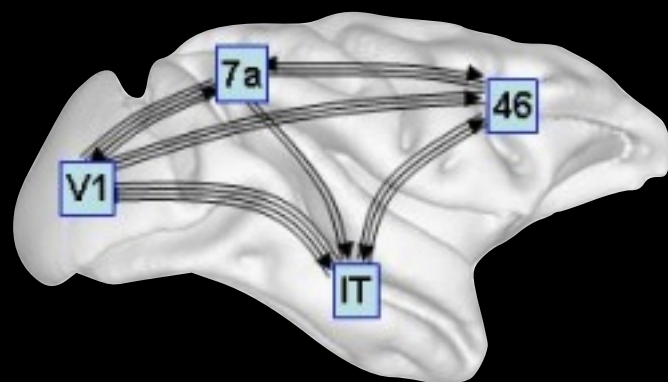
Box and Draper (1987):

“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

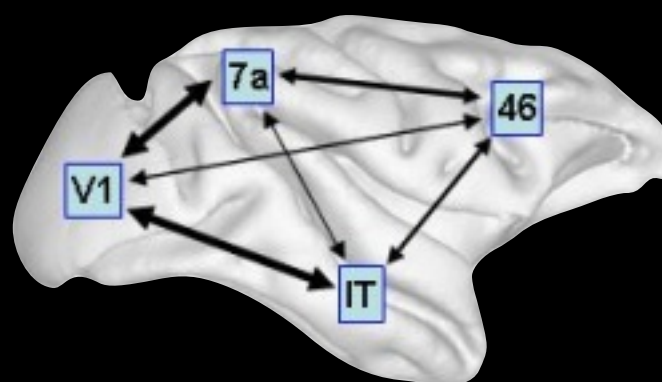
(Bullmore and Sporns, *Nature*, 2009)

Structural



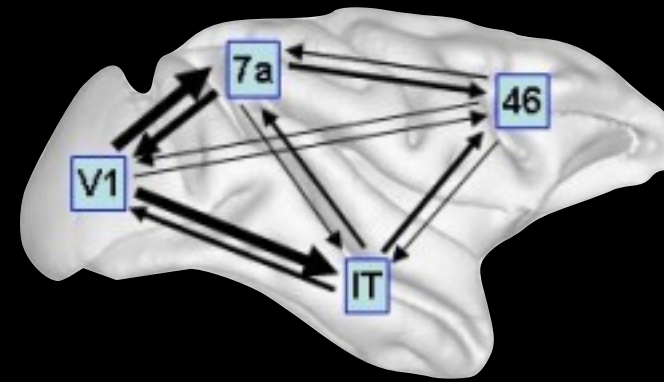
state-invariant,
anatomical

Functional



dynamic, state-dependent,
correlative, symmetric

Effective



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

Hours-Years

milliseconds-seconds

Temporal Scale

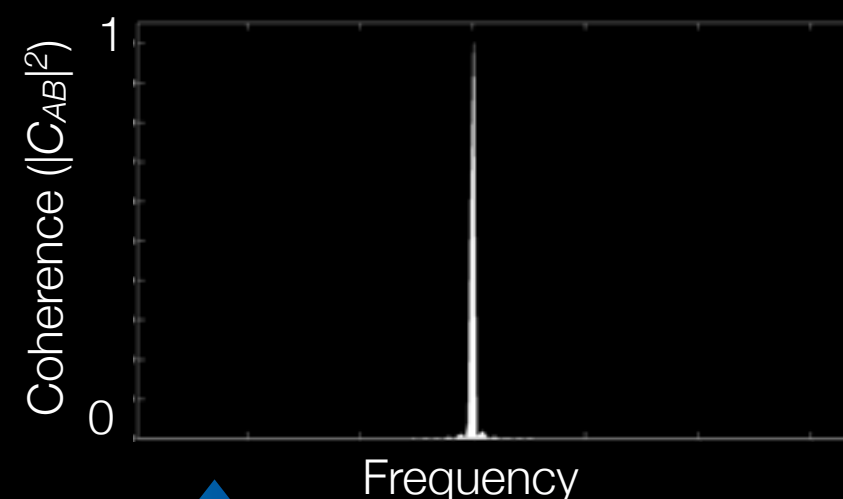
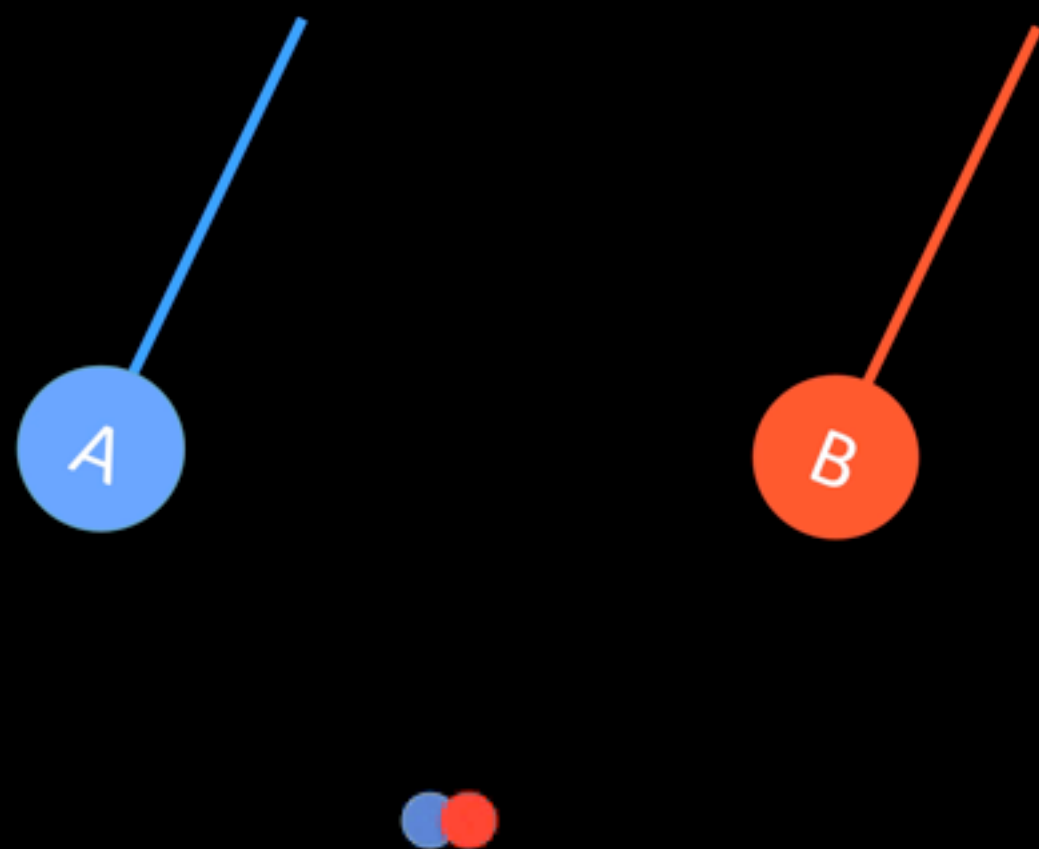
Estimating Functional Connectivity

Popular measures

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

...

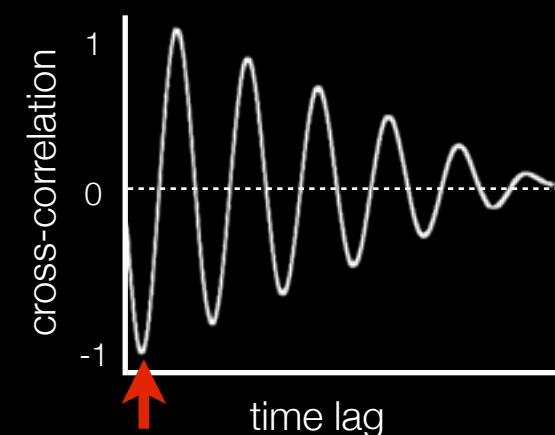
Cross-Correlation and Linear Coherence



DFT

$$C_{AB}(f) = \sum_{k=0}^p \rho_{AB}(k) e^{-i2\pi fk}$$

$$= \frac{S_{AB}(f)}{\sqrt{S_A(f)S_B(f)}}$$



$\rho_{AB}(k)$

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

Phasers

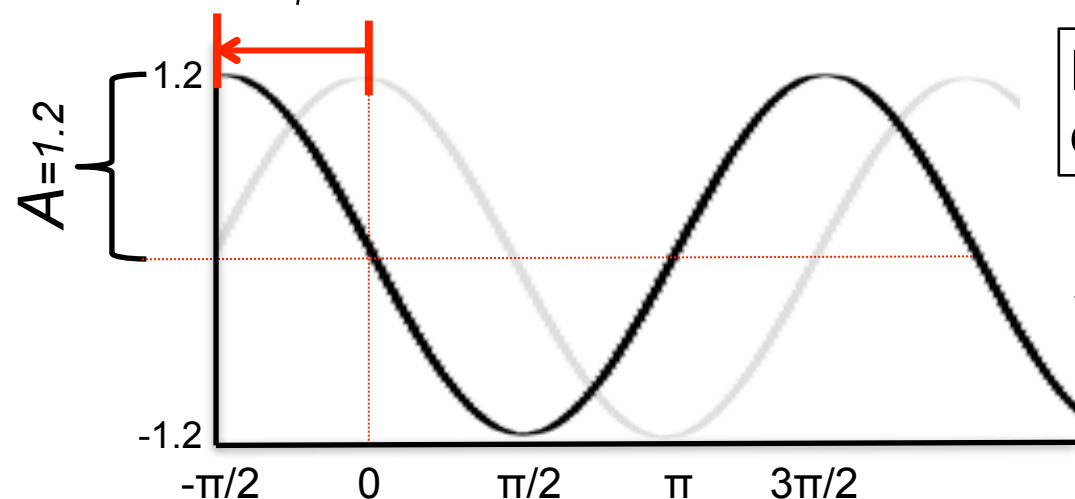


phase shift

$$\phi = \pi / 2$$

angular frequency

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



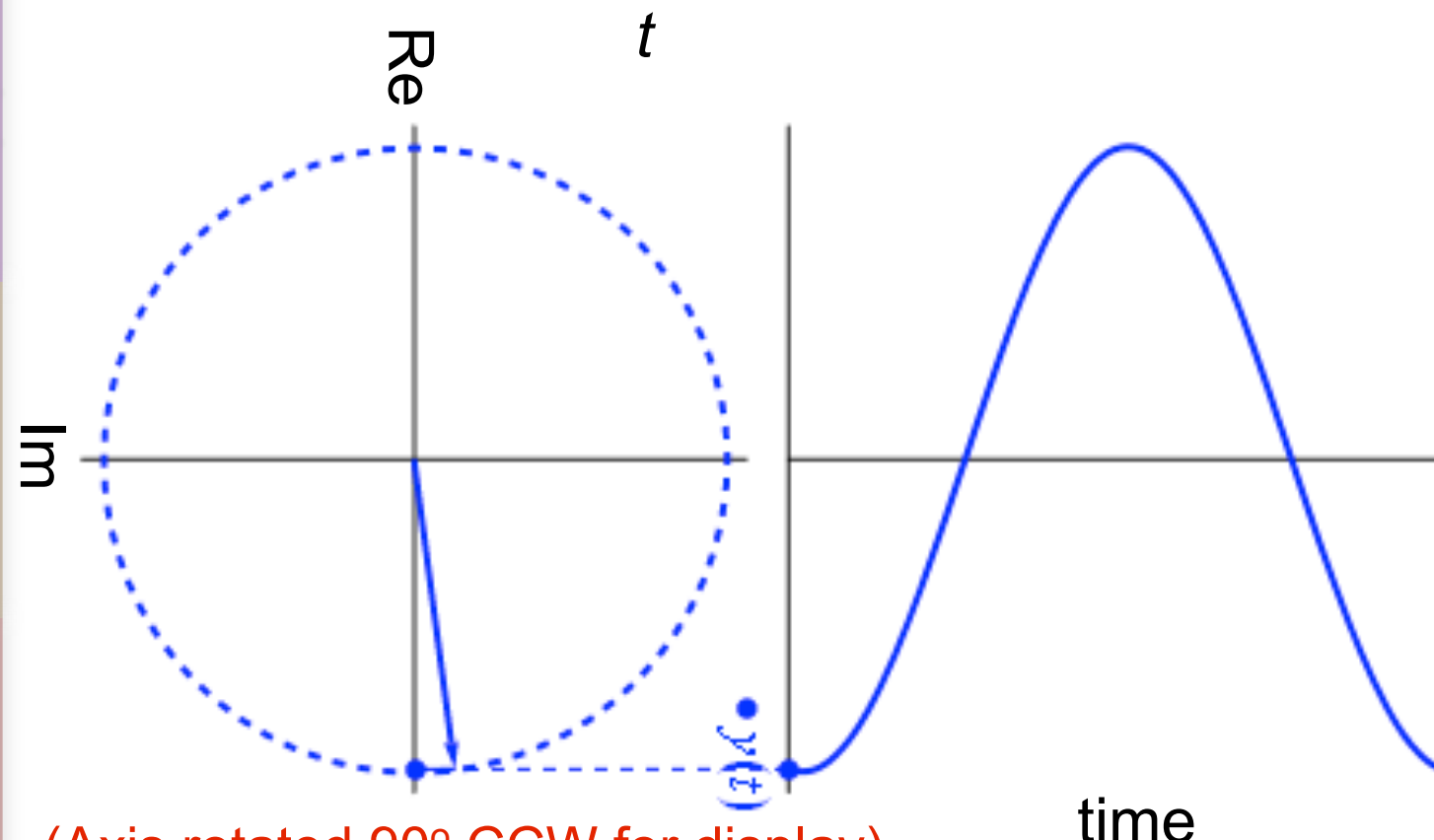
Euler's Formula tells us that any sinusoid can be expressed as the sum of two complex exponentials

$$A \cdot \cos(\omega t + \phi) = \frac{A}{2} e^{i(\omega t + \phi)} + \frac{A}{2} e^{-i(\omega t + \phi)}$$

$$= \text{Re}\{Ae^{i(\omega t + \phi)}\} = \text{Re}\{S(\omega, t)\}$$

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

instantaneous complex amplitude and phase



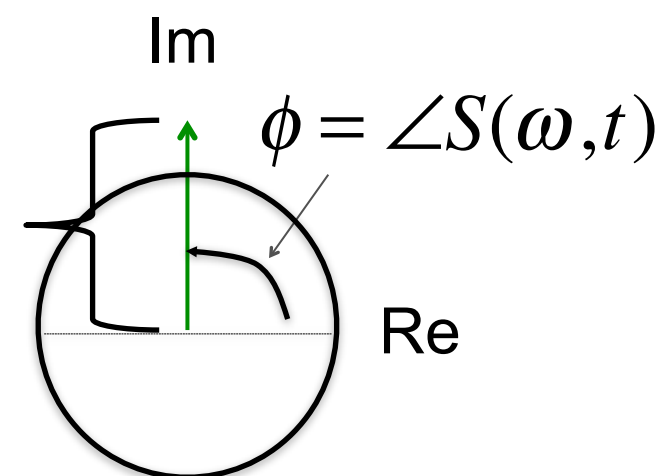
(Axis rotated 90° CCW for display)

Polar animation courtesy Wikipedia

Phasor

(Polar Coords)

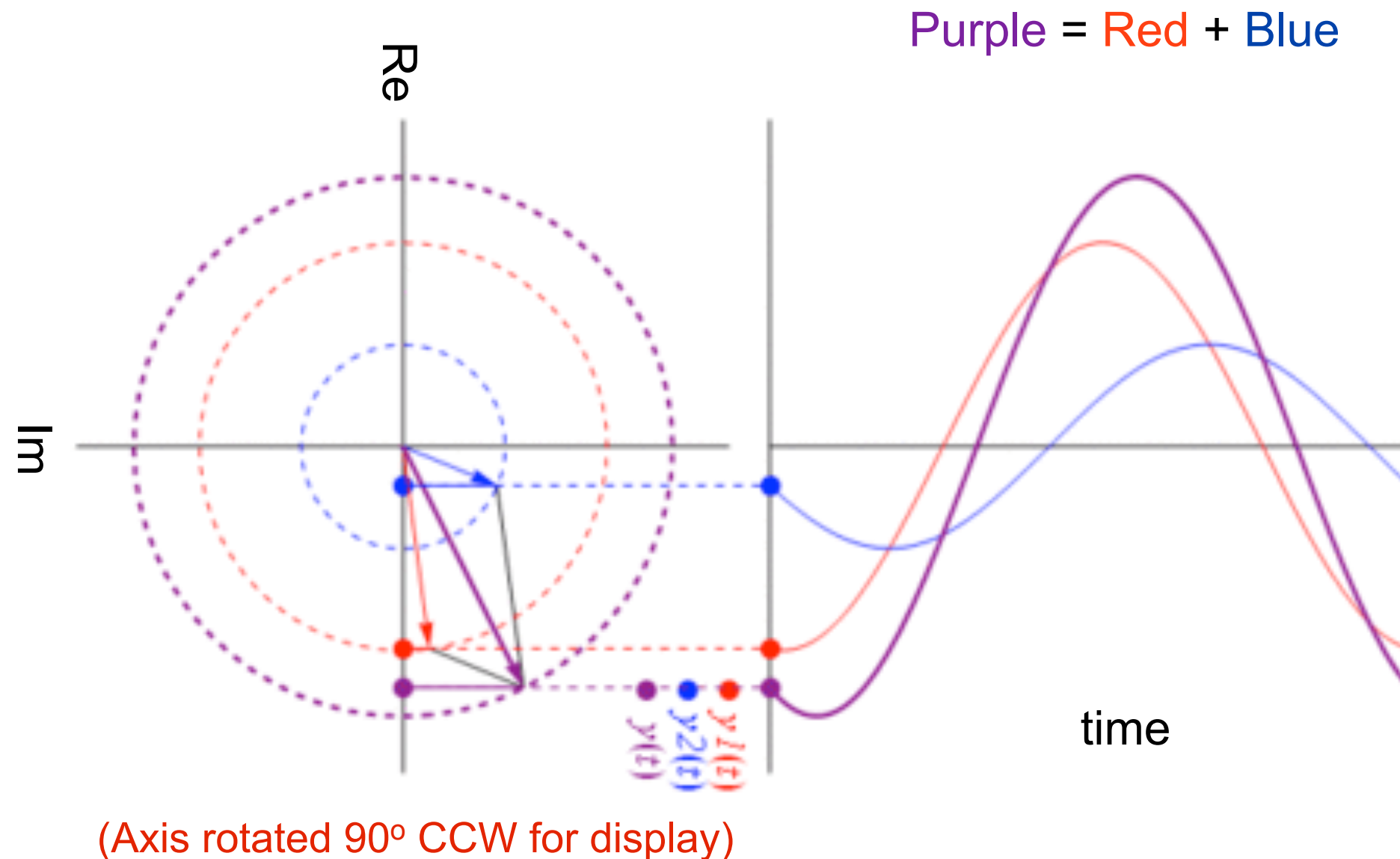
$$|S(\omega, t)| = |A|$$



Shorthand notation: $Ae^{i\phi}$

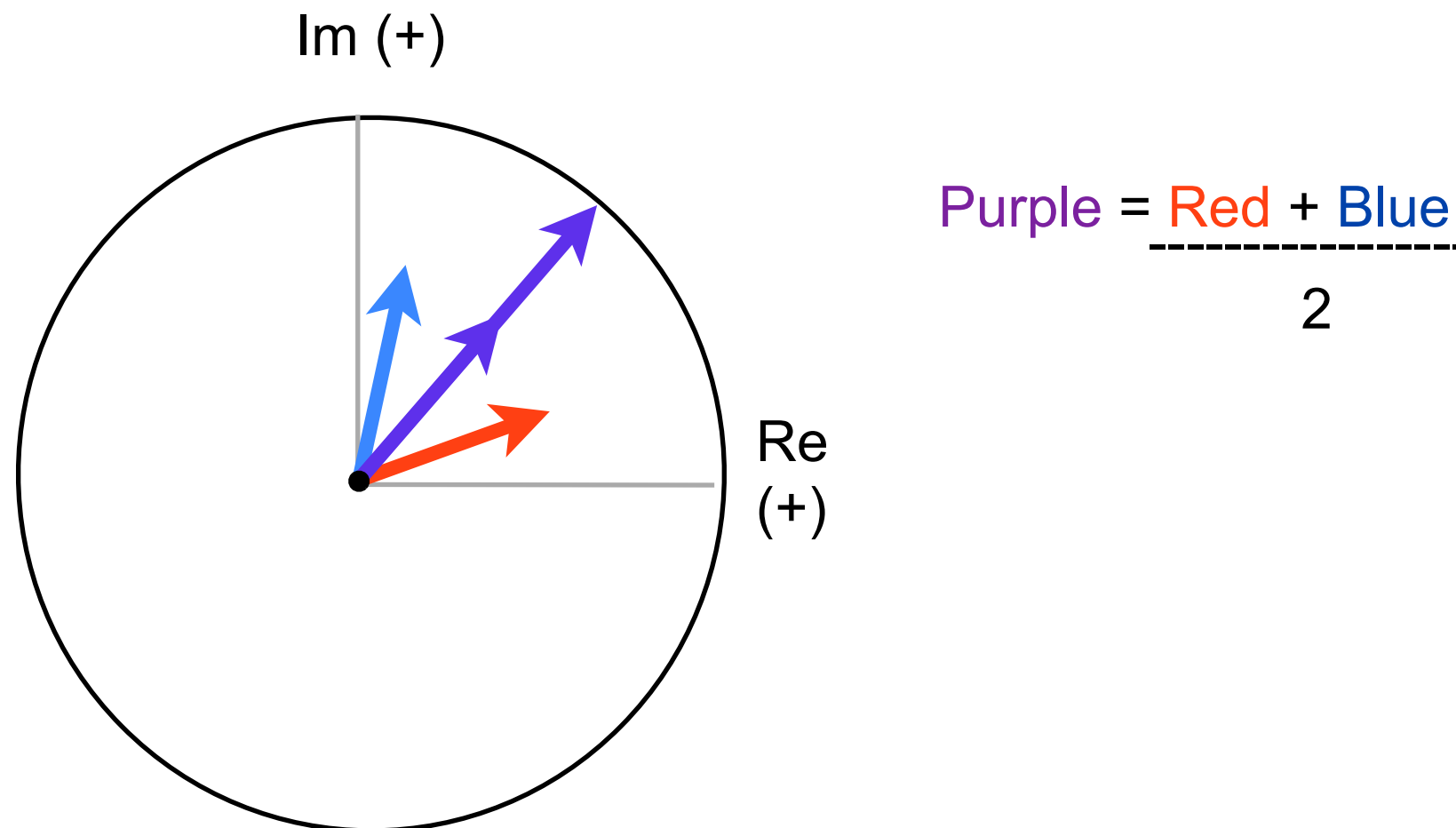
Phasors

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 .

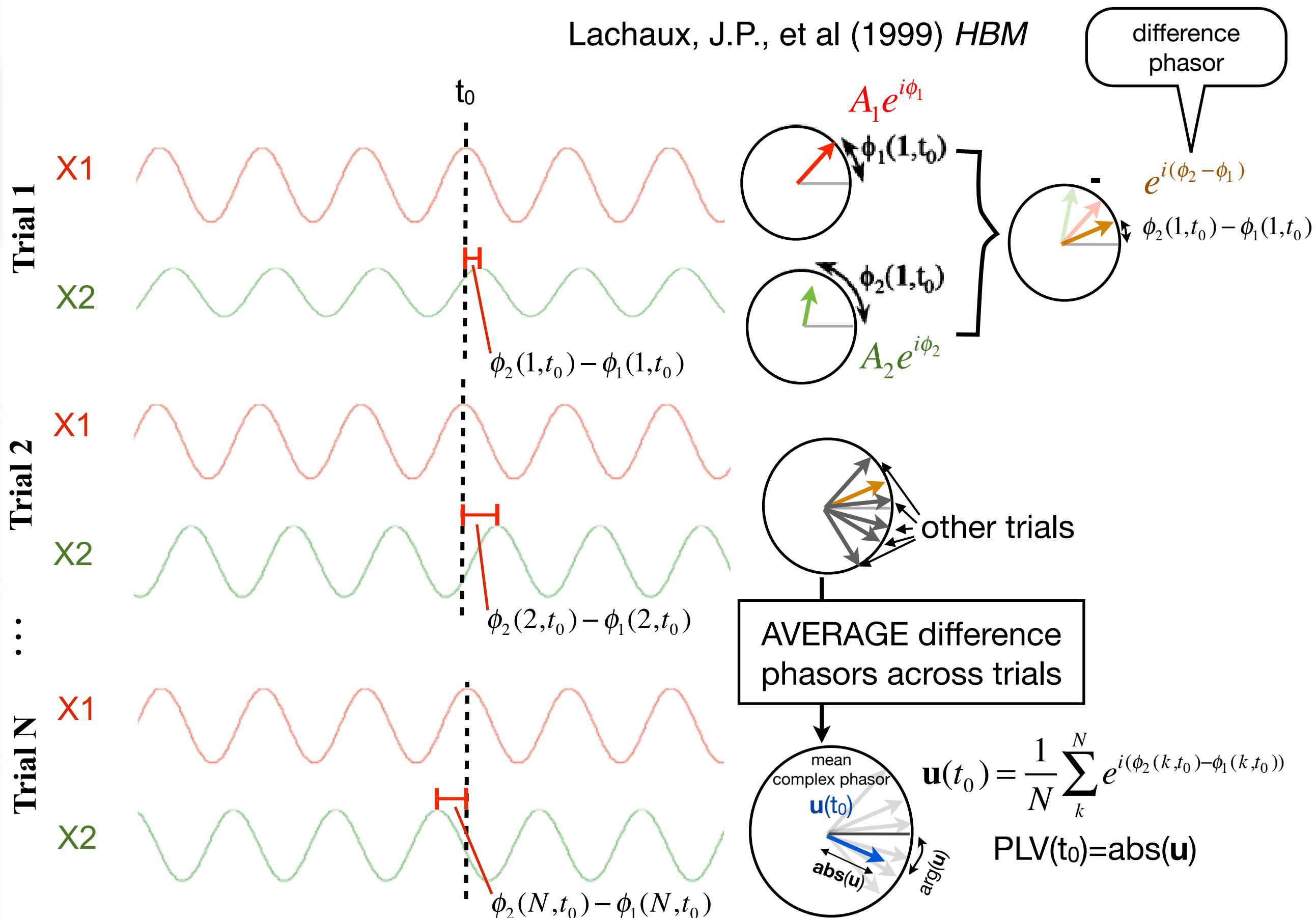


If all **phasors have similar angles**, then vectors will “point” in the same direction and the **length of the mean phasor** will be comparatively **large**.

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)

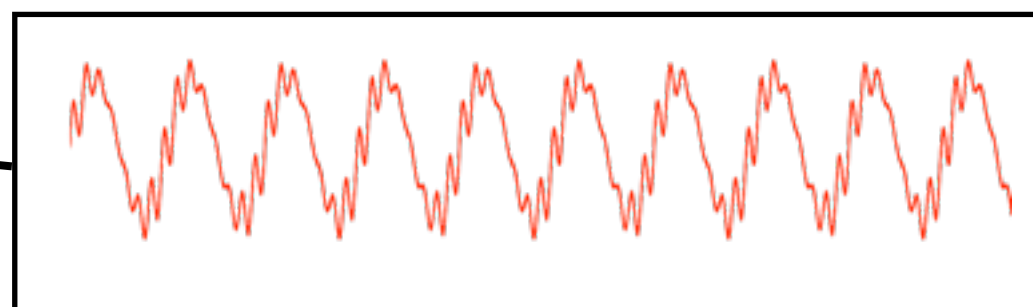
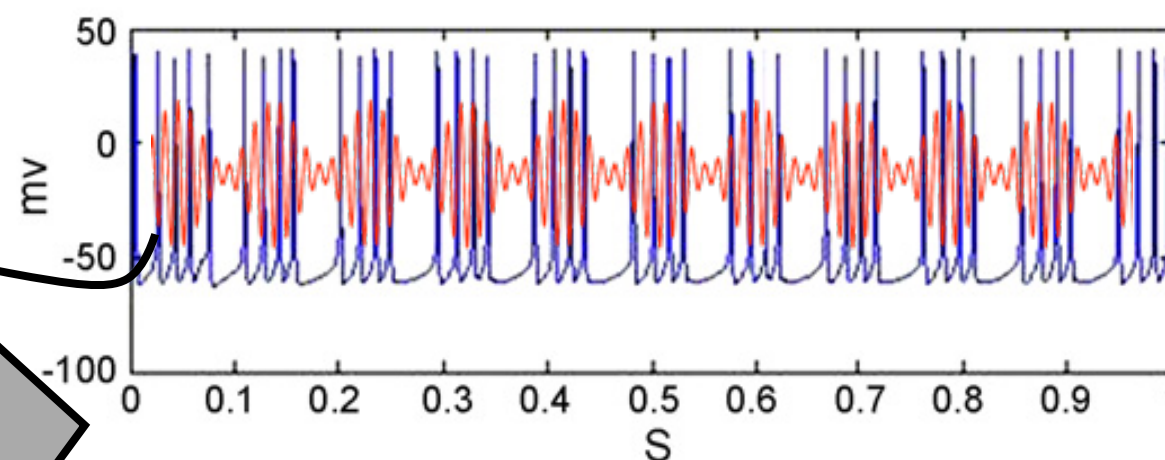
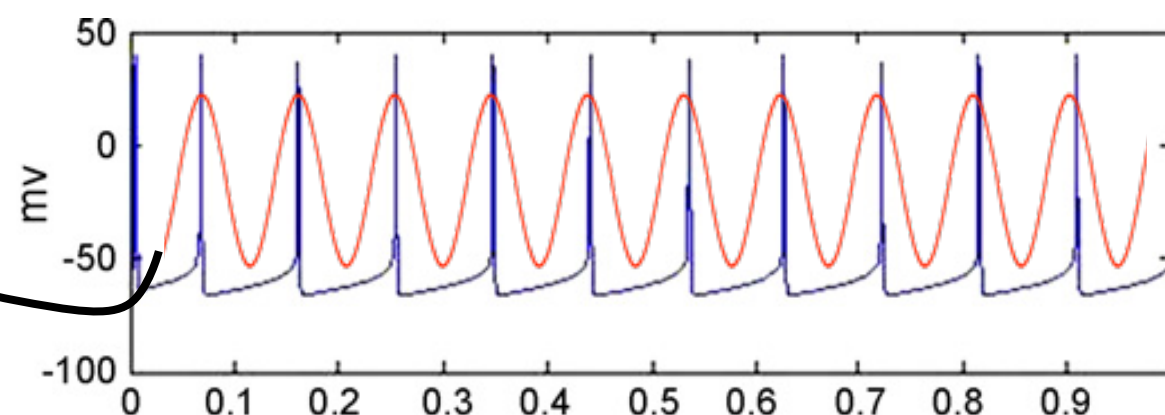
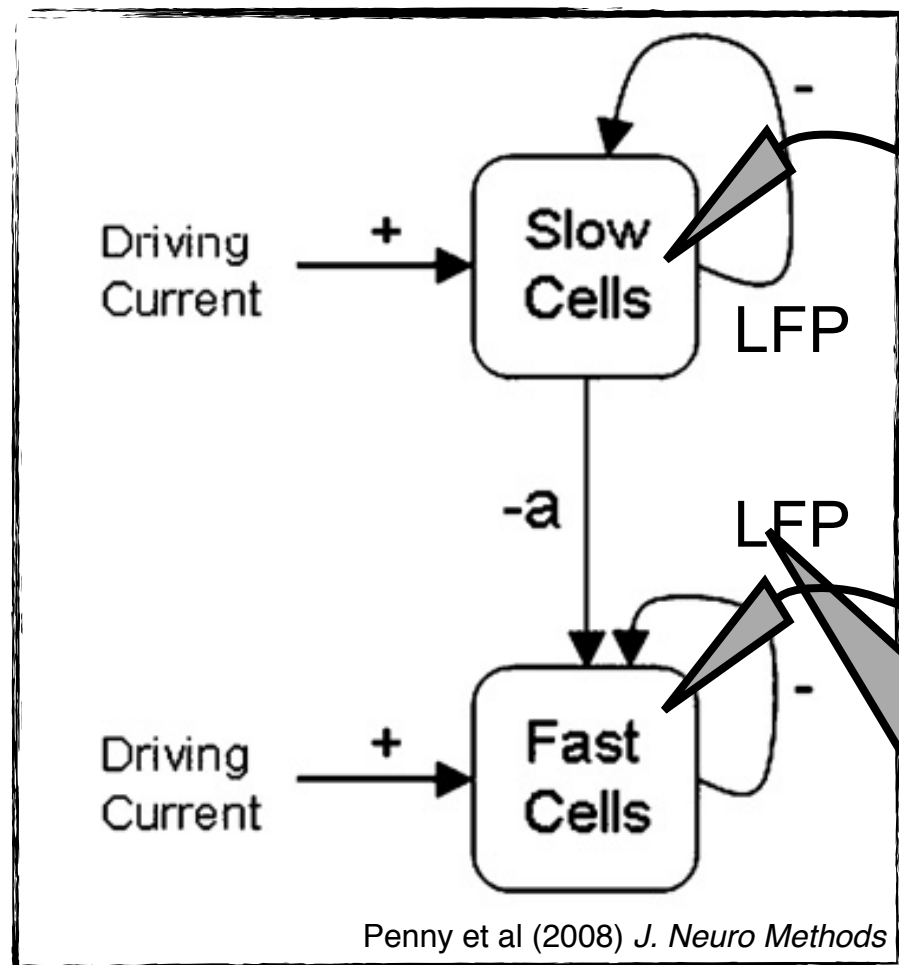
Lachaux, J.P., et al (1999) *HBM*

Computing PLV (“phase coherence”) in EEGLAB:

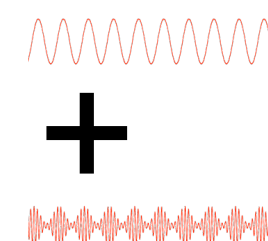
```
pop_newcrossf( . . . , 'type' , 'phase' )
```

Phase-Amplitude Coupling

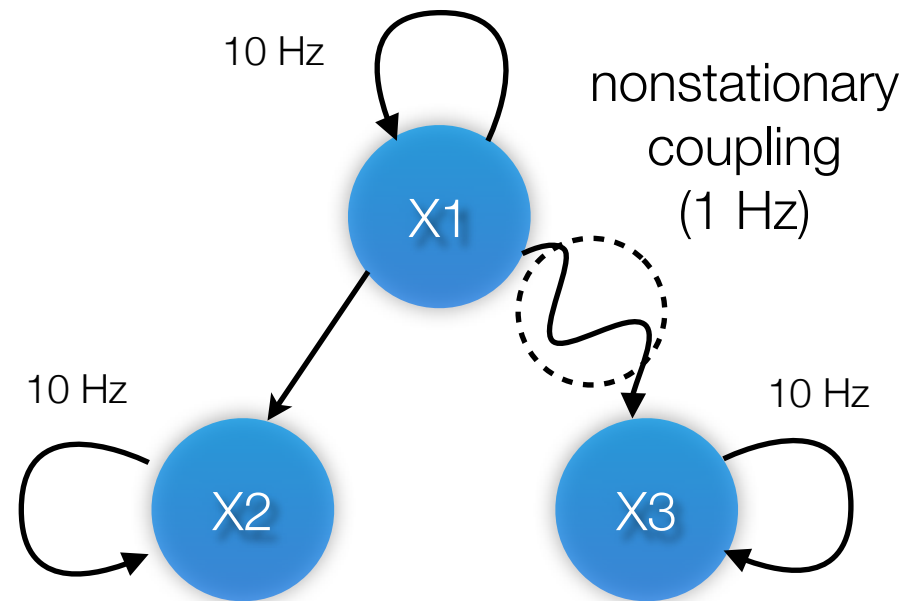
'burst-suppress' oscillators



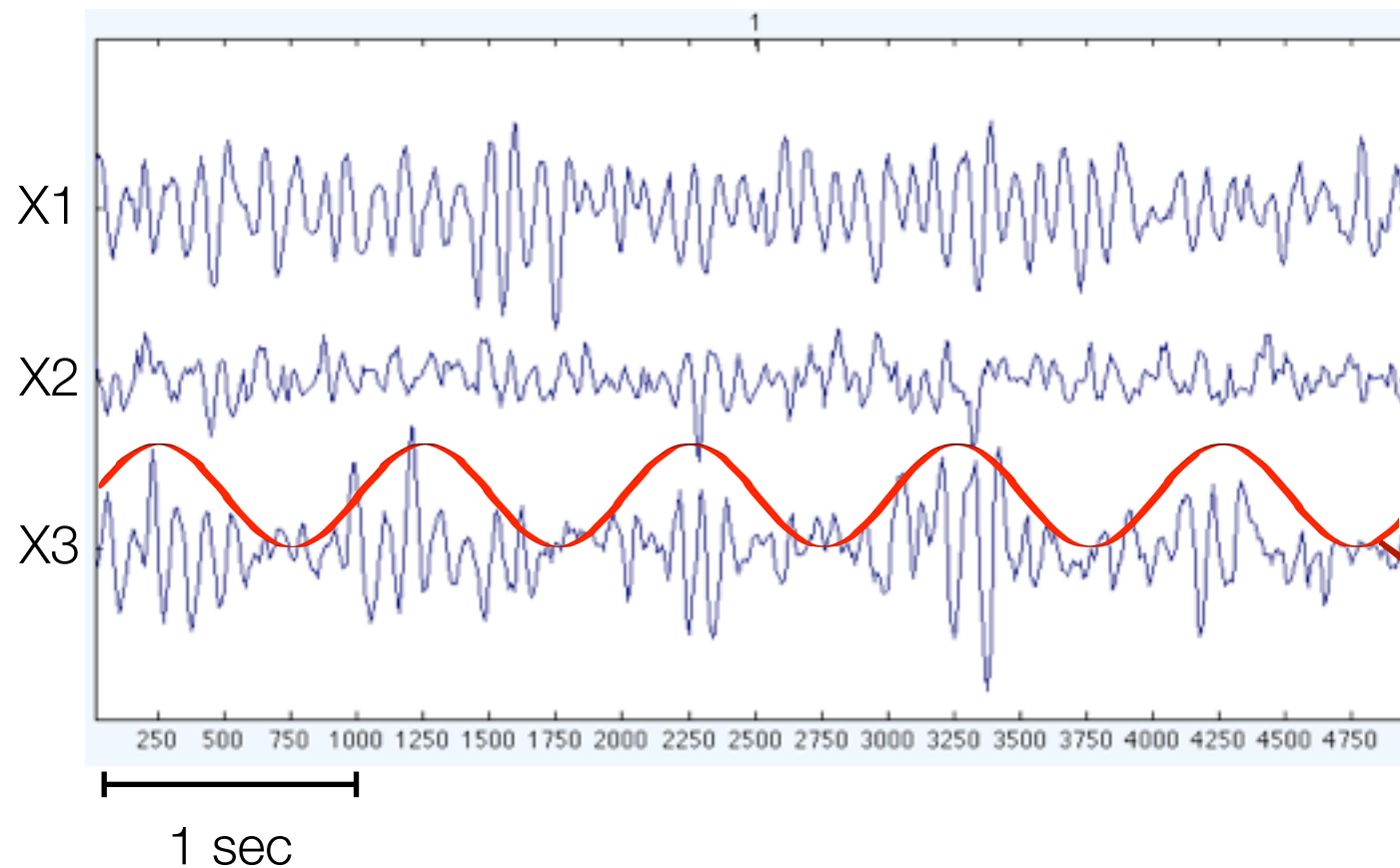
Local Field Potential (Slow + Fast cells)



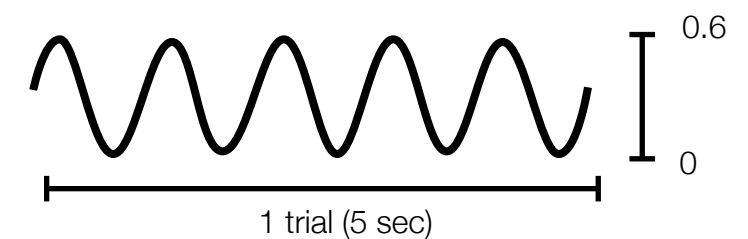
Graphical Model



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



Time-varying $X1 \rightarrow X3$ coupling
(1 Hz modulation)



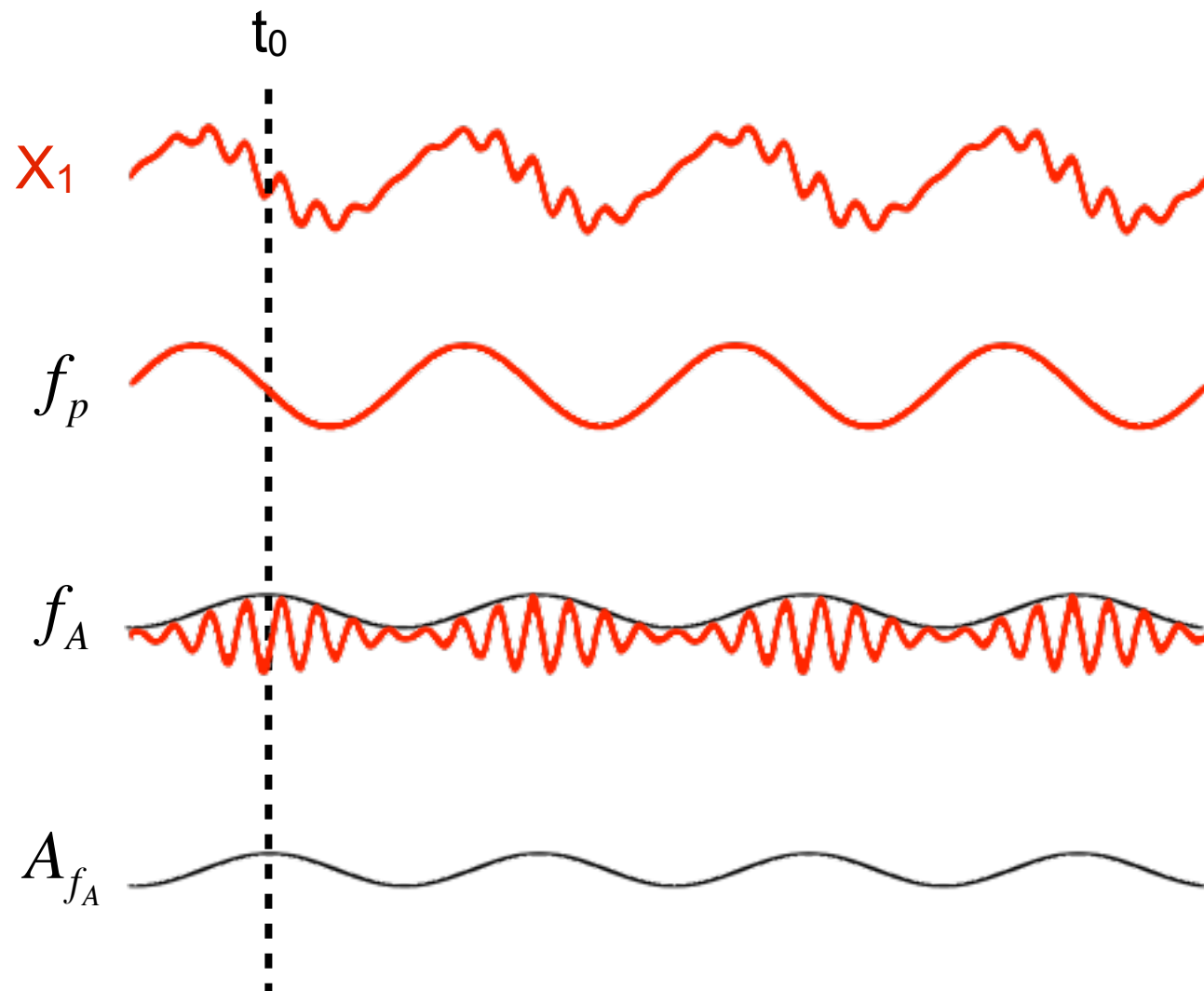
Amplitude Modulation
10Hz amplitude coupled to 1
Hz Phase

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

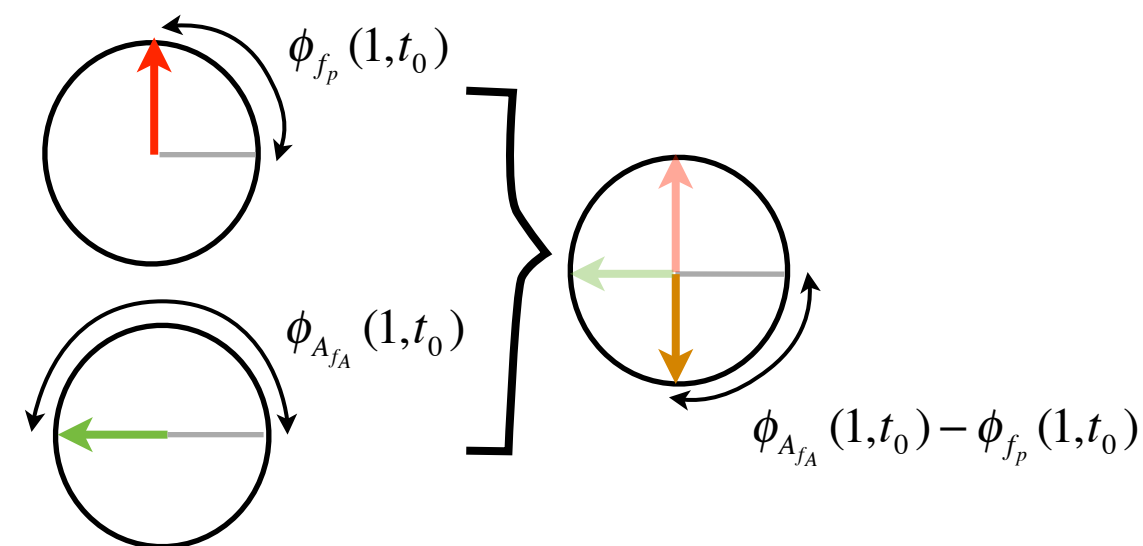
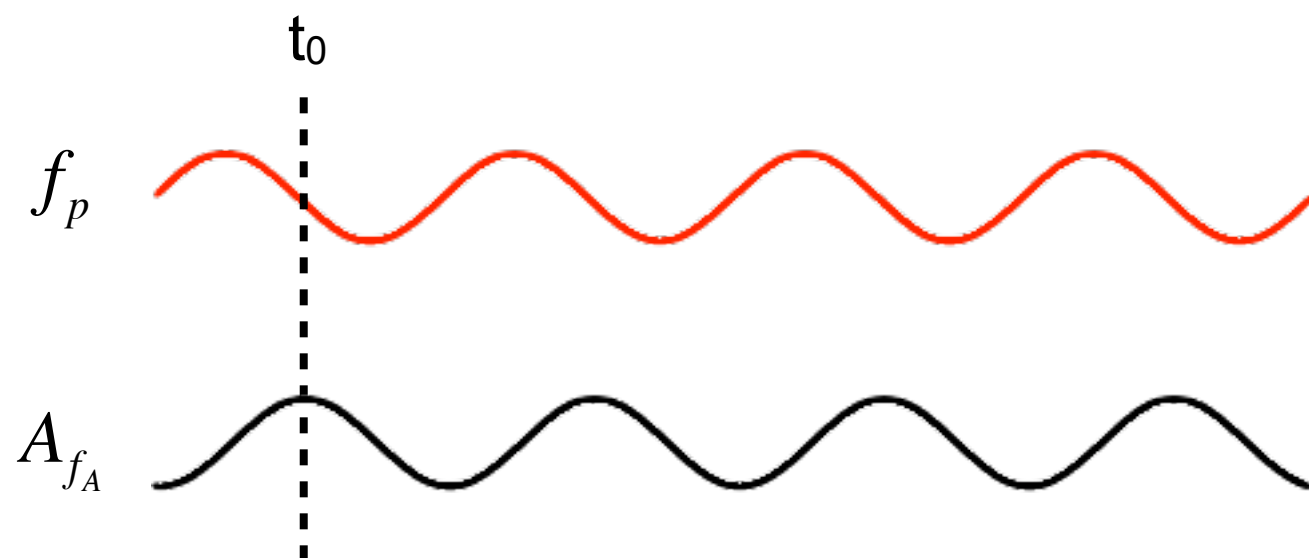
filter X_1 at LFO band (e.g. theta)

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

get amplitude envelope of filtered signal

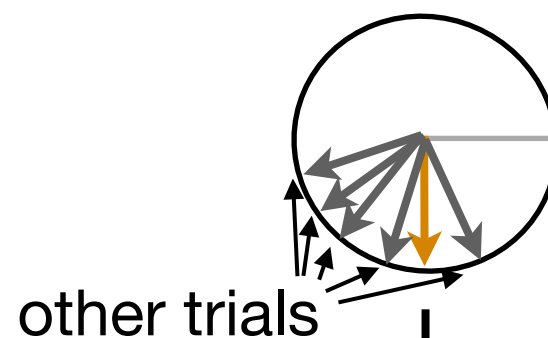
Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) *PNAS*

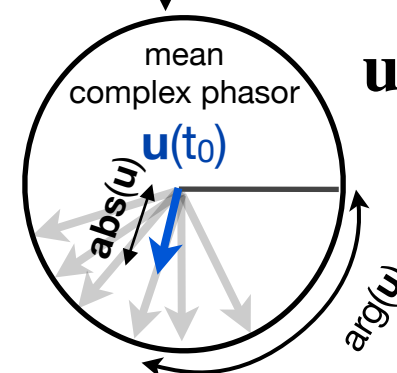


Compute PLV between LFO time-series (f_p) and amplitude envelope of HFO time-series (A_{f_A}).

Significant PLV indicates that the central frequency of f_p modulates the amplitude of the central frequency of f_A



AVERAGE difference phasors across trials



$$\mathbf{u}(t_0) = \frac{1}{N} \sum_k e^{i(\phi_{A_{f_A}}(k, t_0) - \phi_{f_p}(k, t_0))}$$

$$\text{PLV}(t_0) = \text{abs}(\mathbf{u})$$

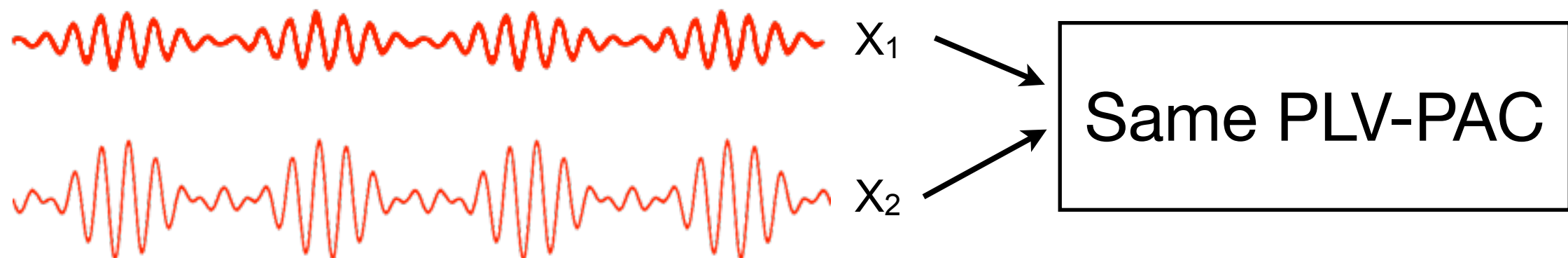
Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) *PNAS*

Problem:

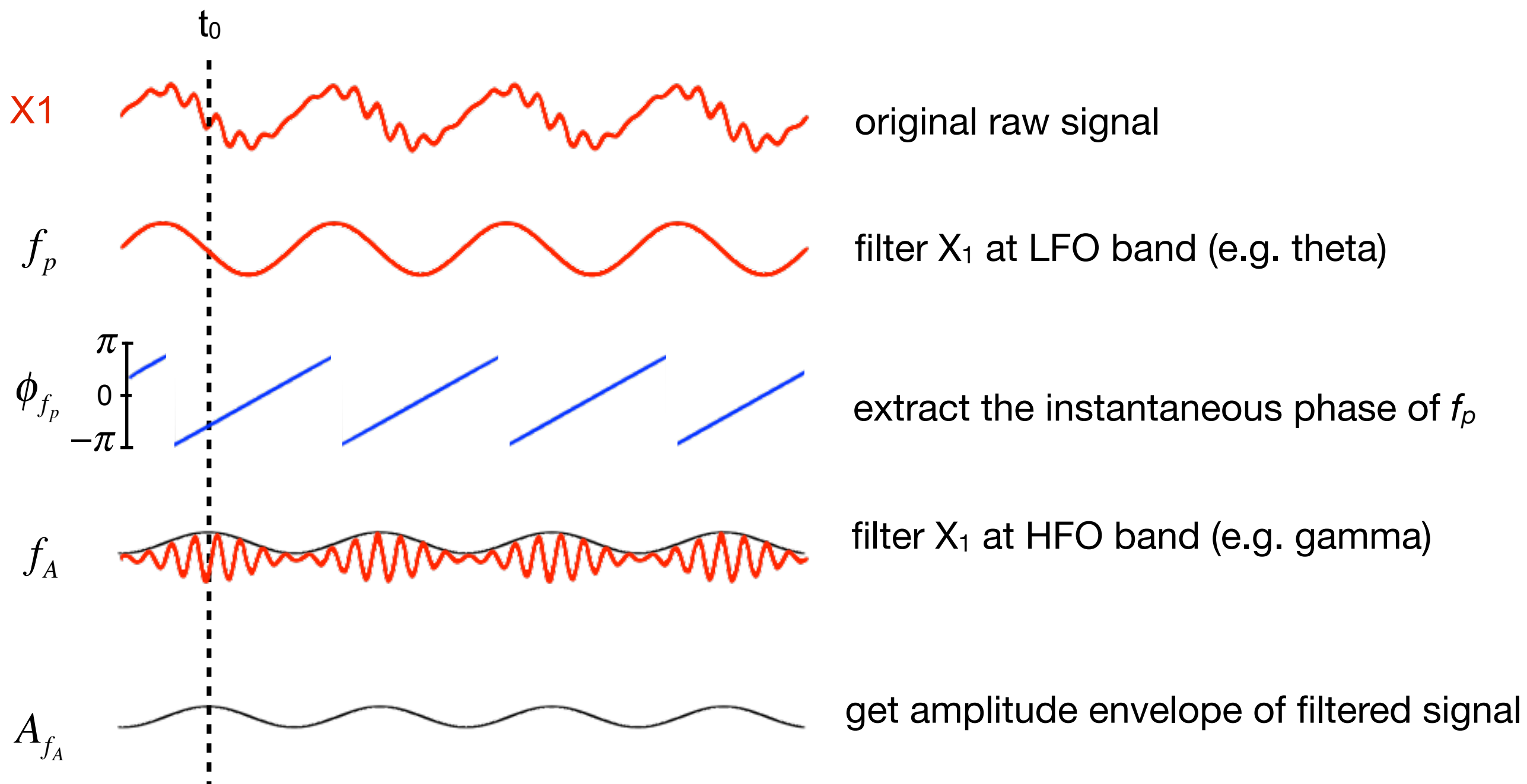
PLV is invariant to differences in amplitude between the two time-series (it only considers phase). Thus PLV-PAC doesn't take into account the *amplitude* of the co-modulation.

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*

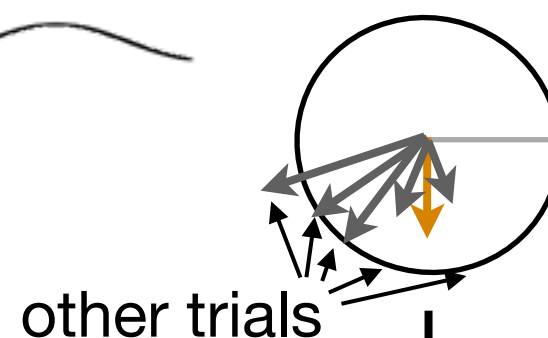
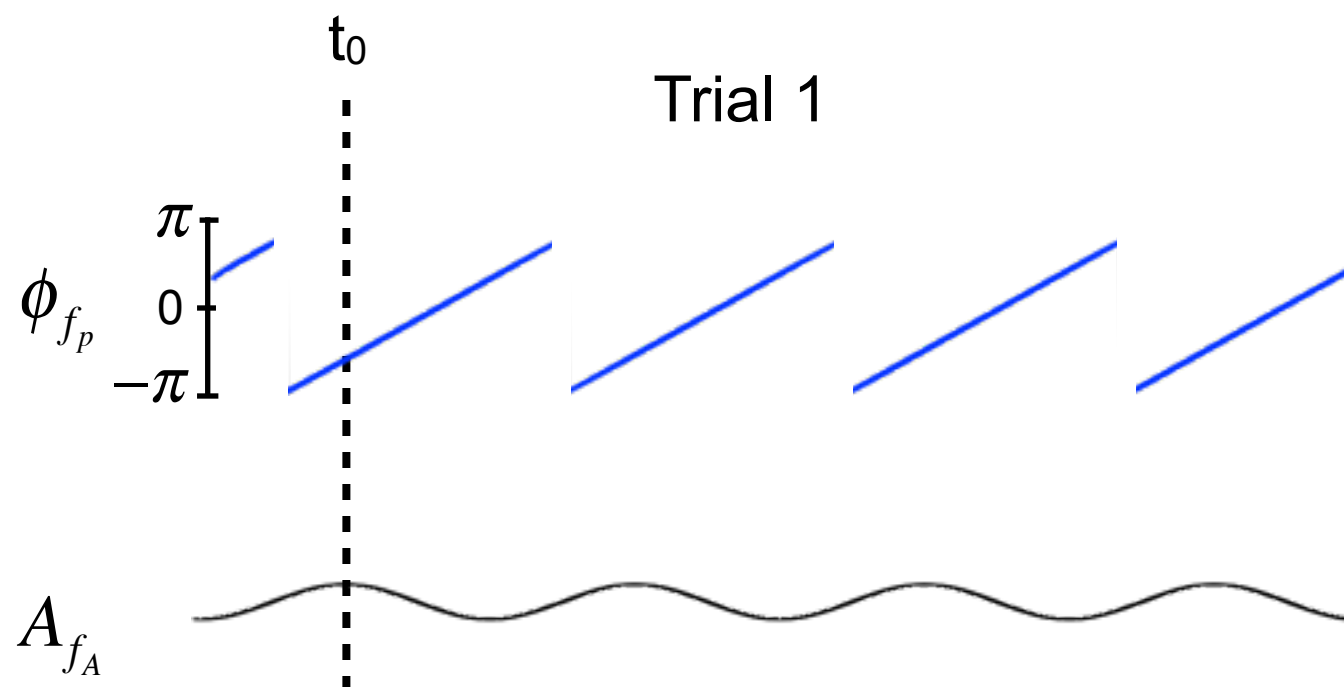
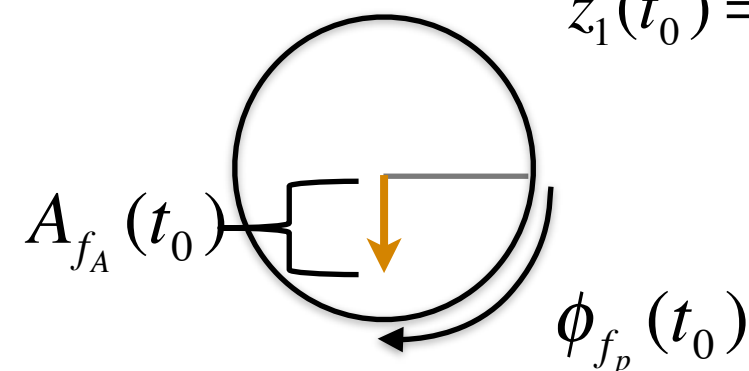


Phase-Amplitude Coupling: Modulation Index Method

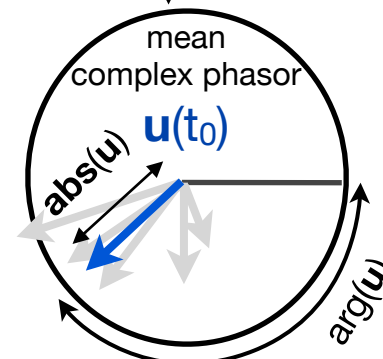
Canolty et al, (2006) *Science*

build complex phasor
with instantaneous
amplitude and phase

$$z_1(t_0) = A_{f_A} e^{i\phi_{f_p}}$$



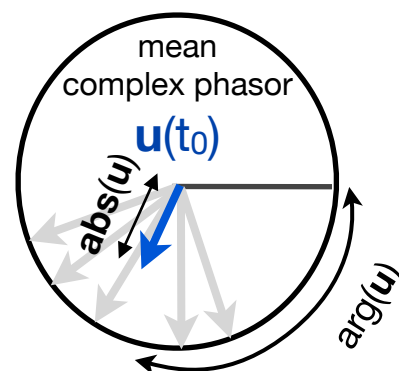
AVERAGE complex
phasors across trials



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

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

Comparison:
PLV-PAC



Phase-Amplitude Coupling: Modulation Index Method

Canolty et al, (2006) *Science*

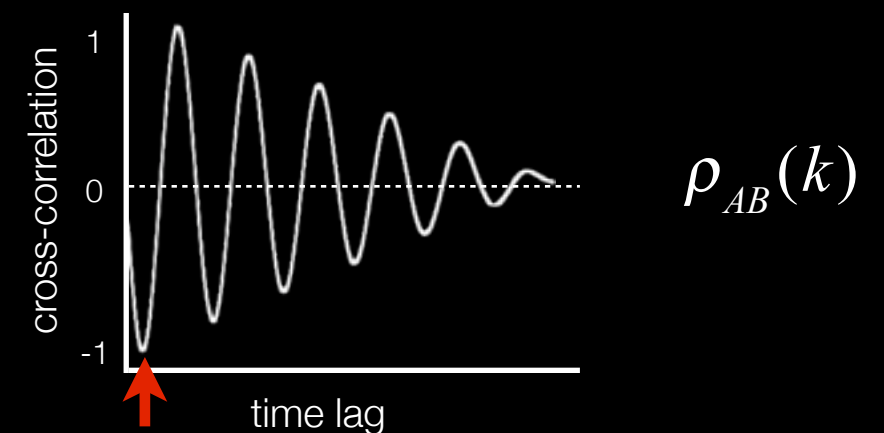
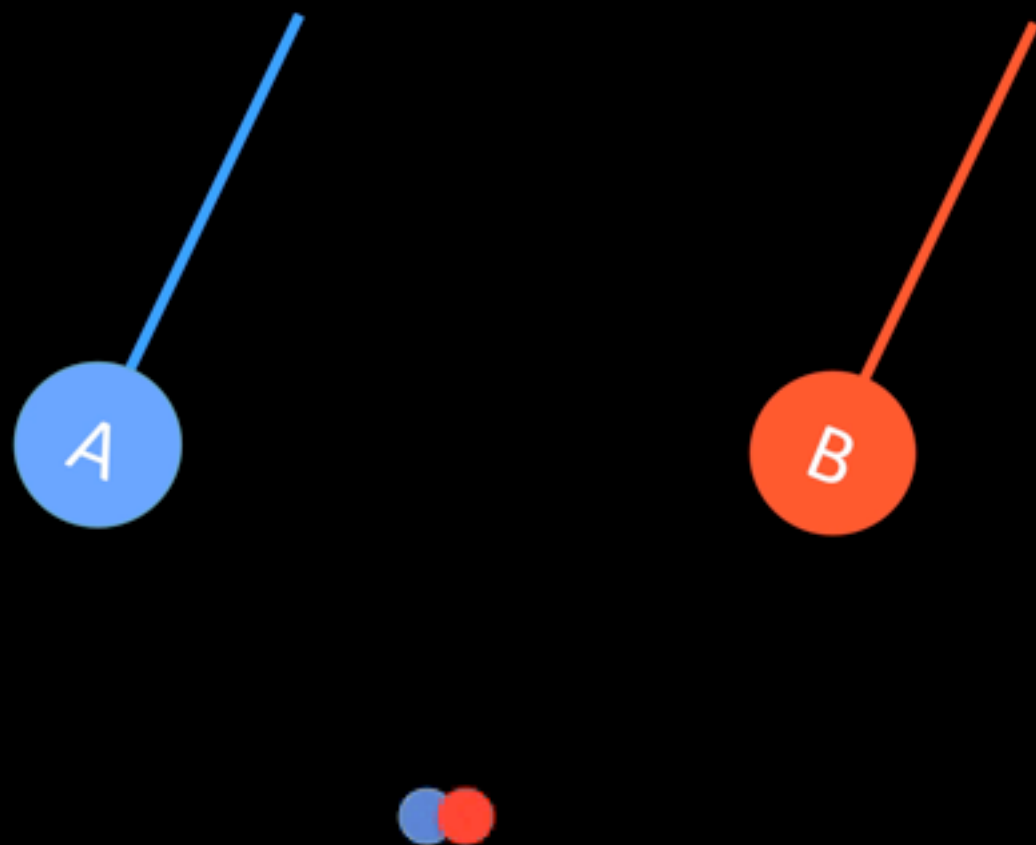
Computing PAC in EEGLAB:

```
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**

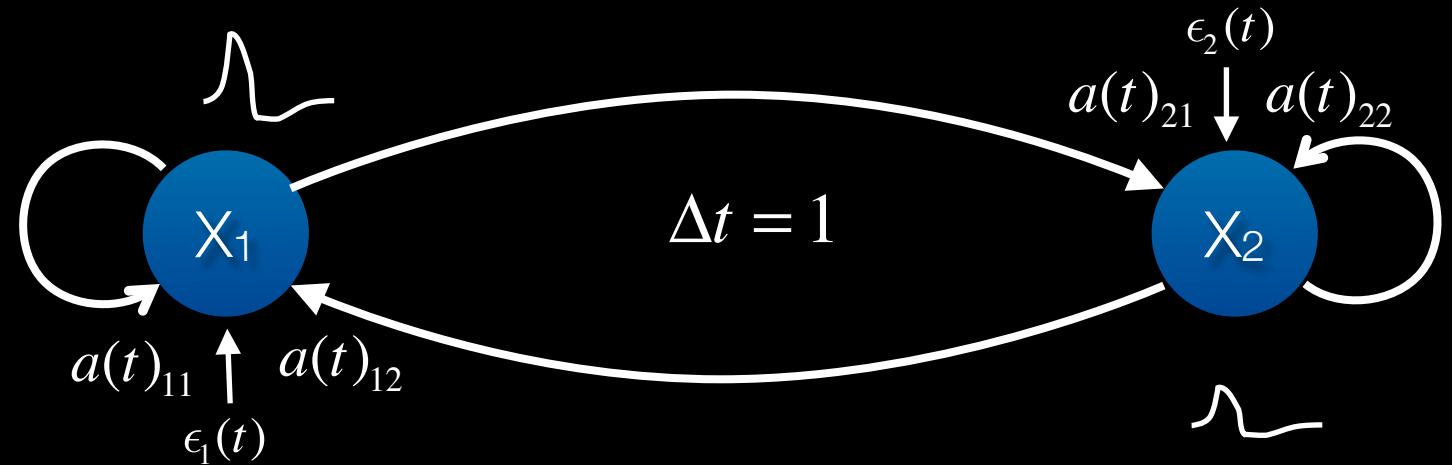
- Data-driven
- Rooted in *conditional predictability*
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved) 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

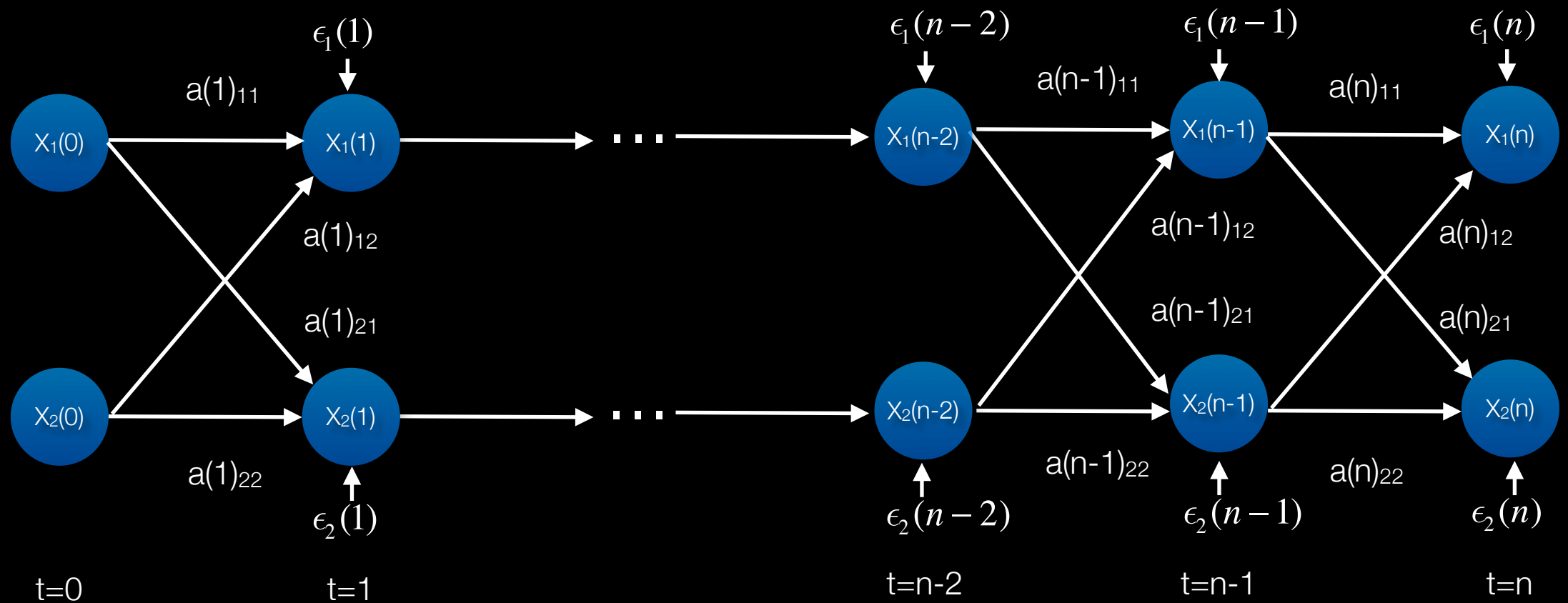
Stochastic Linear Dynamical System

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

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

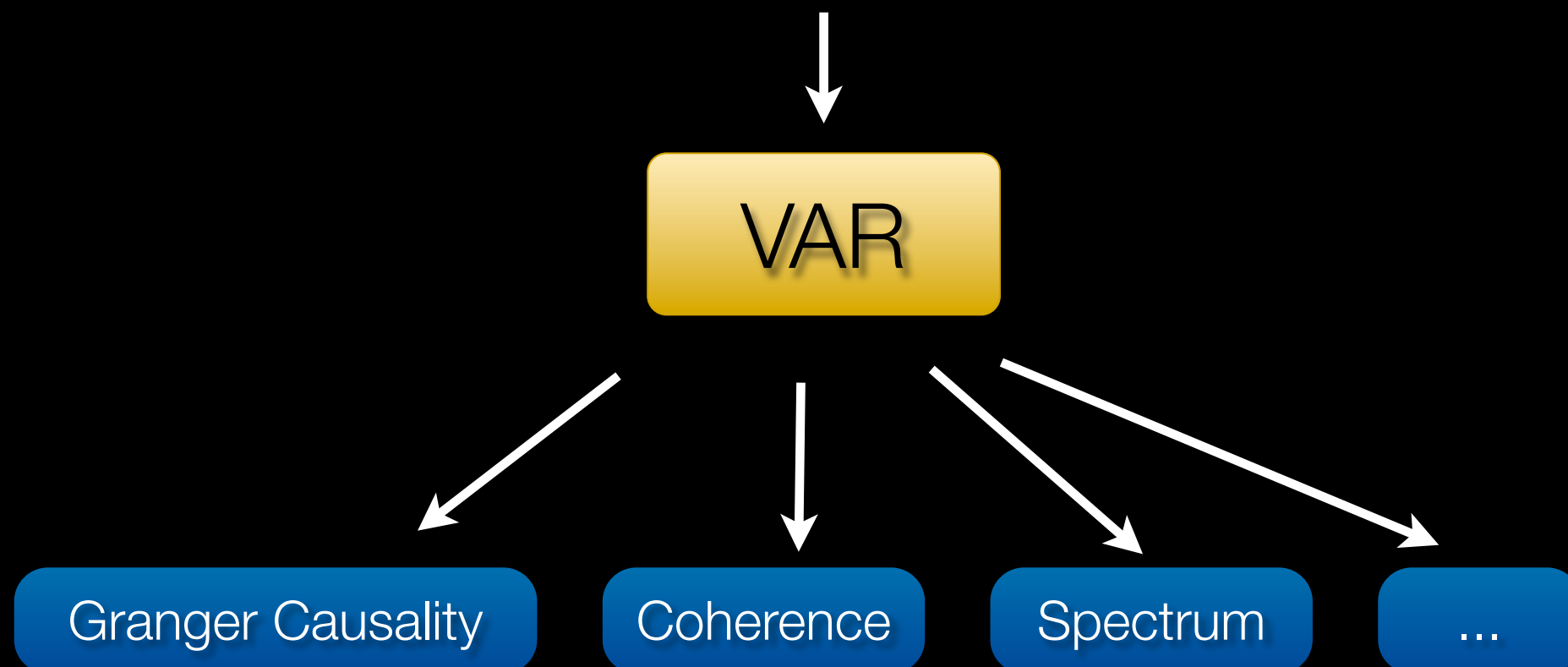
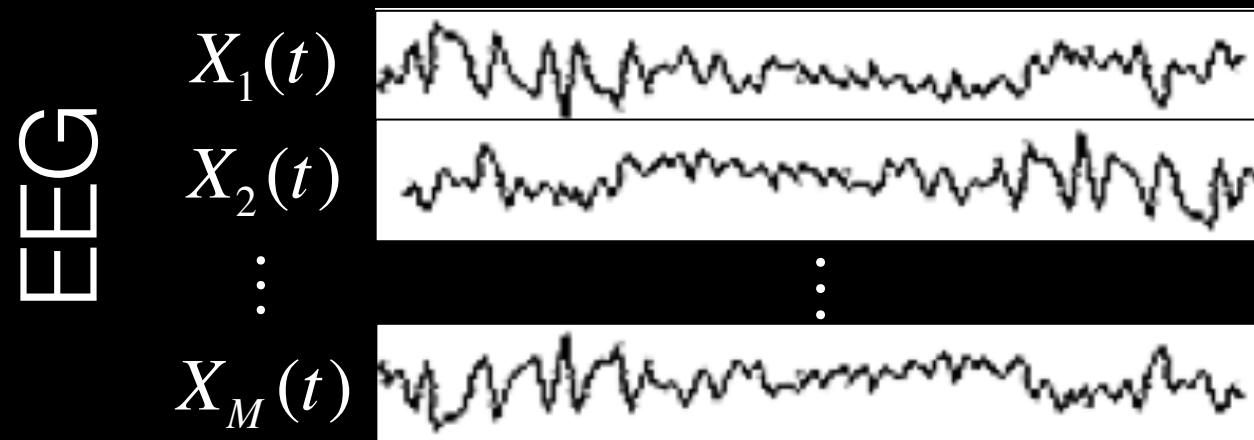


Order 1 Markov Process (VAR[1])



time step

Vector Autoregressive (VAR / MAR / MVAR) Modeling



VAR Modeling: Assumptions

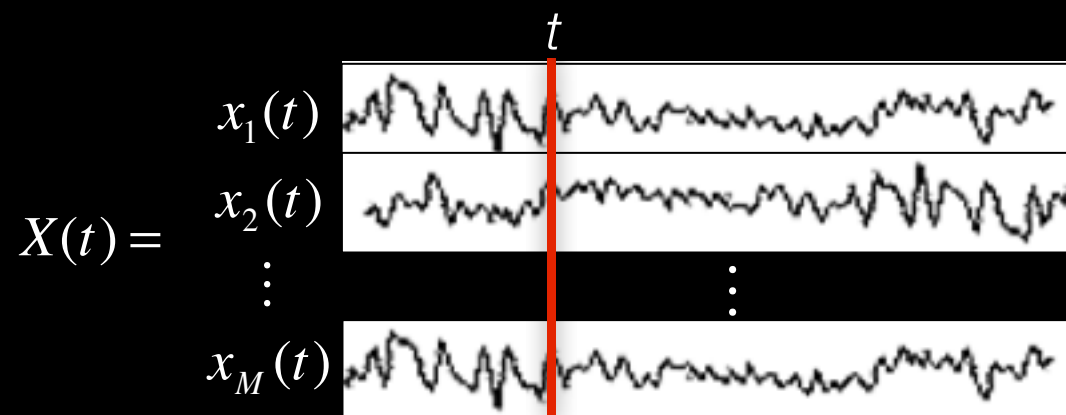
- ✦ **“Weak” stationarity of the data**

- ✦ 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 ≤ 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

random noise process

M-channel data vector
at current time t

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

multichannel data k
samples in the past

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

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

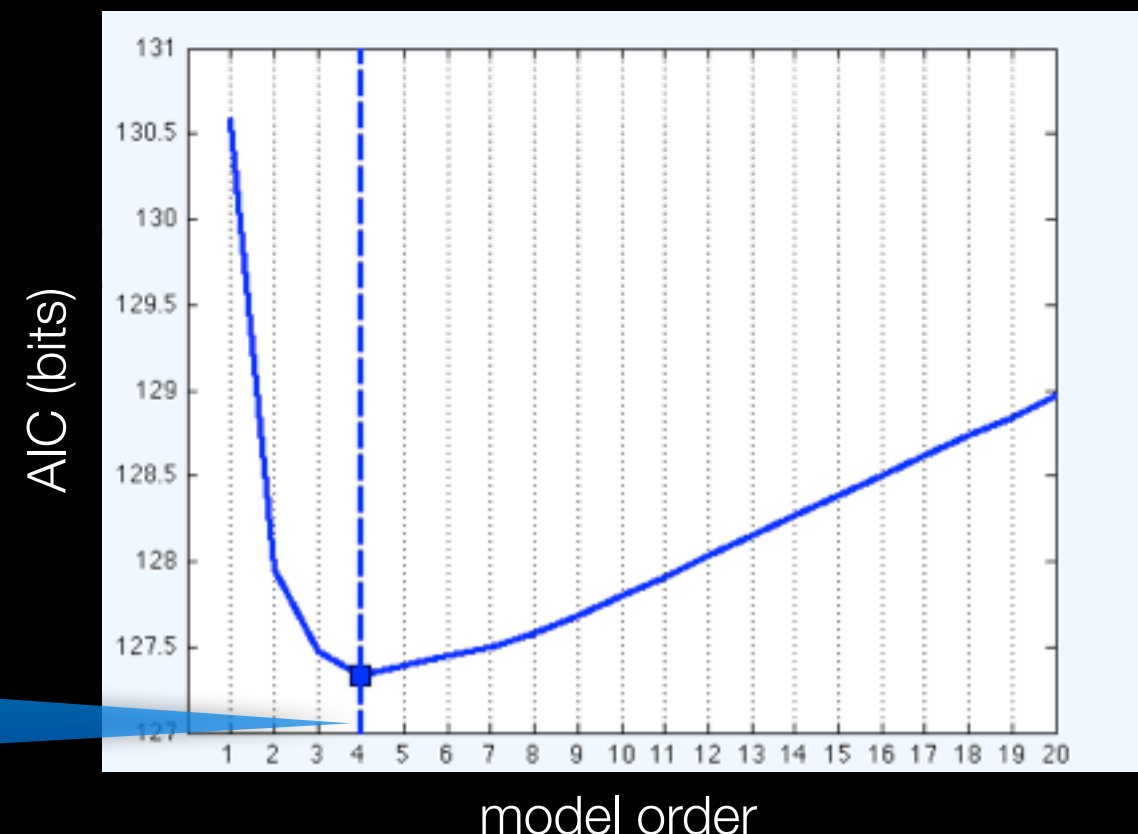
Selecting a VAR Model Order

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

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

Penalizes high model orders (parsimony)

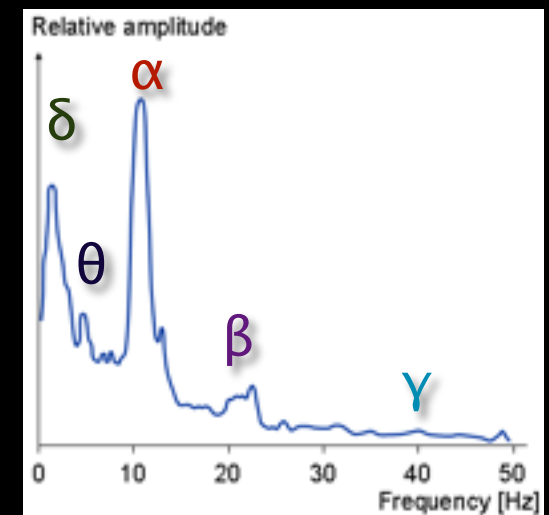
entropy rate (amount of prediction error)



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 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

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

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

autocovariance at lag l / ...

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

with corresponding autocorrelation R

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

$$\mathbf{R}_h = (R_1, \dots, R_h)$$

set of autocorrelations up to lag h

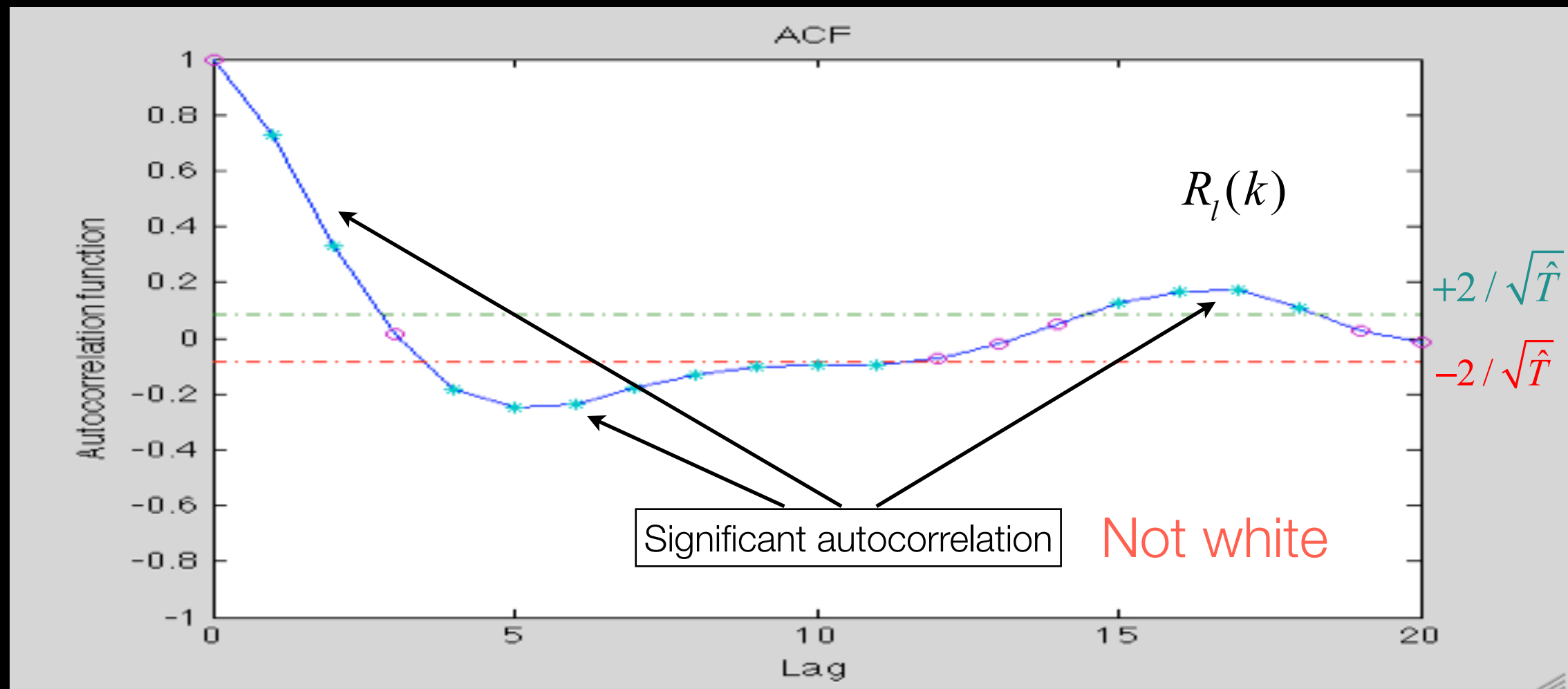
We want to test the null hypothesis $H_0 : \mathbf{R}_h = (R_1, \dots, R_h) = 0$

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 χ^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

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

- 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

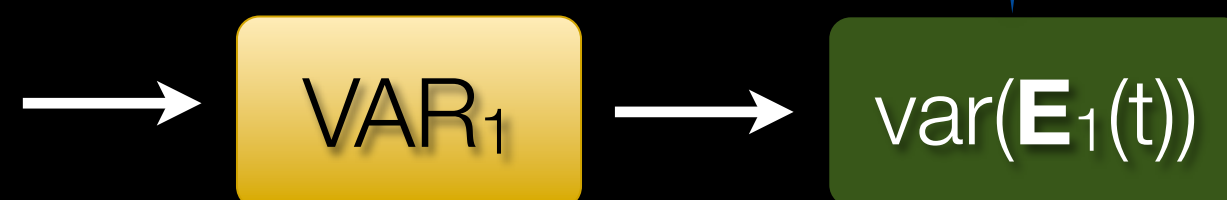
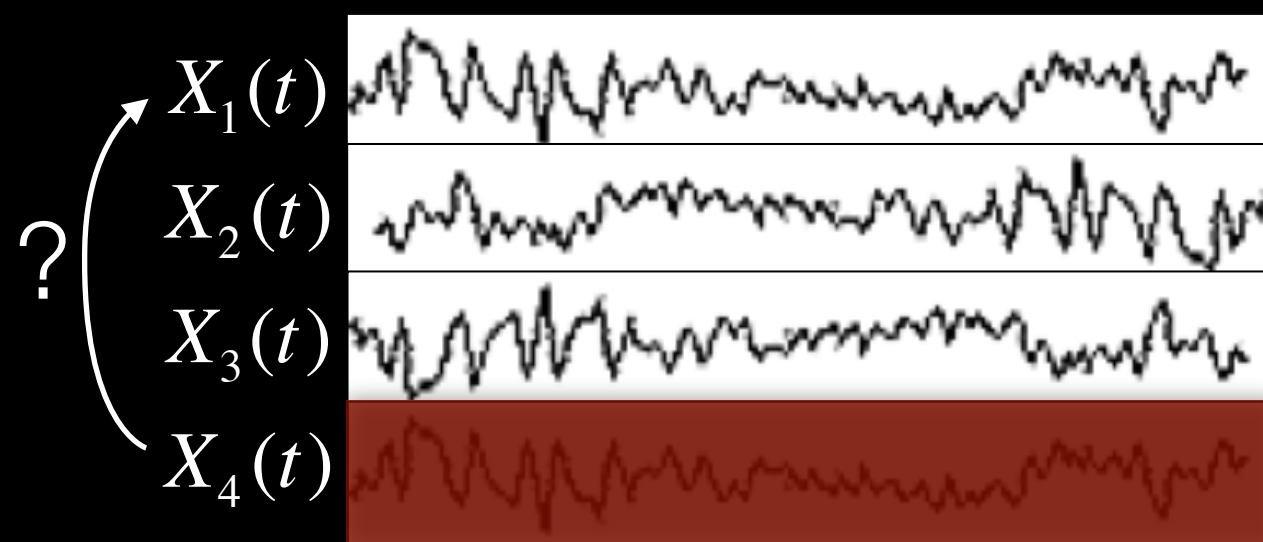
- ✦ First introduced by Wiener (1958). Later reformulated by Granger (1969) in the context of linear stochastic autoregressive models
- ✦ Relies on two assumptions:

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)

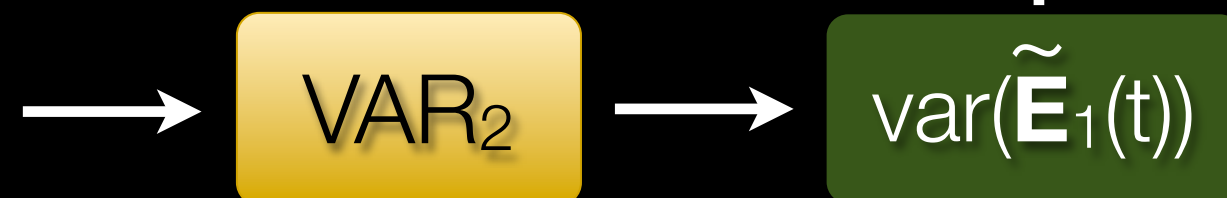
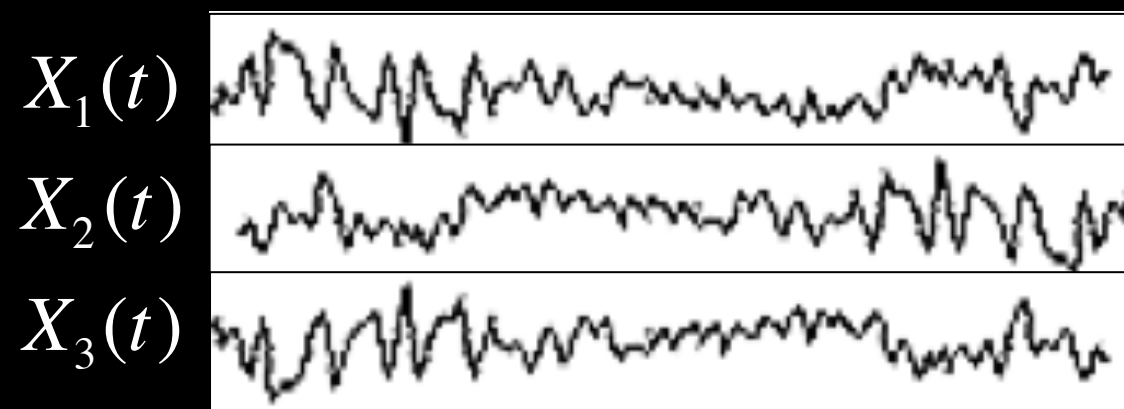
Granger Causality

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



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

= ?



$$\mathbf{X}_{-4}(t) = \sum_{k=1}^p \tilde{\mathbf{A}}^{(k)} \mathbf{X}_{-4}(t-k) + \tilde{\mathbf{E}}(t)$$

prediction error for \mathbf{X}_1
(variance of residuals \mathbf{E}_1)

Granger Causality

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

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

reduced model

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 $\mathbf{A}_{ij}(k) \gg 0$ for some lag $k \in \{1, \dots, p\}$

Granger Causality Quiz

- Example: 2-channel VAR process of order 1

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

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

Which causal structure does this model correspond to?

- a) $\textcircled{1} \rightarrow \textcircled{2}$ b) $\textcircled{1} \leftarrow \textcircled{2}$ c) $\textcircled{1} \leftrightarrow \textcircled{2}$

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:

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

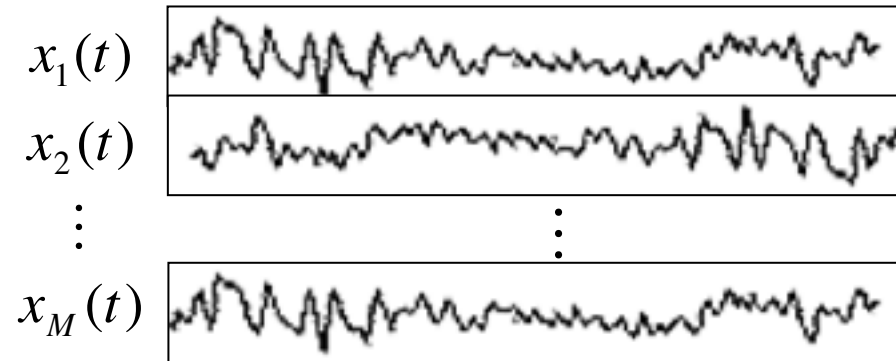
Where $\mathbf{H}(f)$ is the *transfer matrix* of the system.

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 $|\mathbf{A}_{ij}(f)| \gg 0$ for some frequency f

leads to
PDC

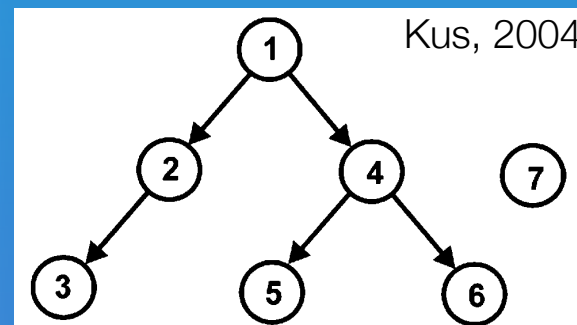


$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

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

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

Ground Truth

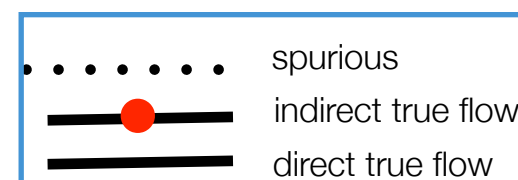
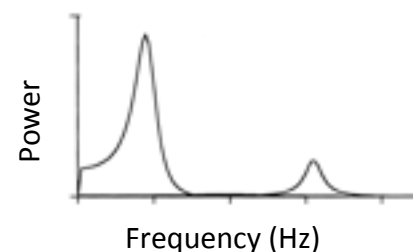


Spectrum

$$S(f) = \mathbf{X}(f) \mathbf{X}(f)^*$$

$$= \mathbf{H}(f) \Sigma \mathbf{H}(f)^*$$

(Brillinger, 2001)



NOTE: time index (t) dropped for convenience

Functional

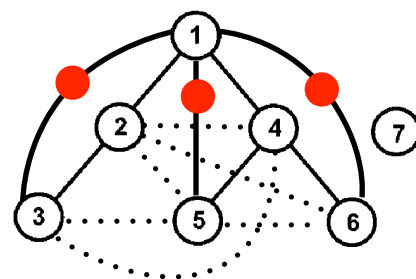
Effective

Bivariate

Coherency

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

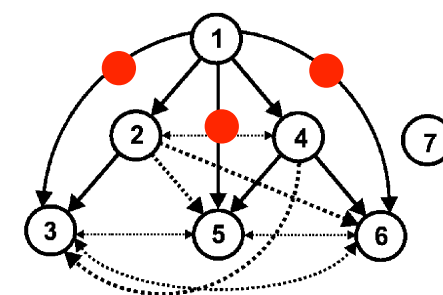
(Bendat and Piersol, 1986)



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)

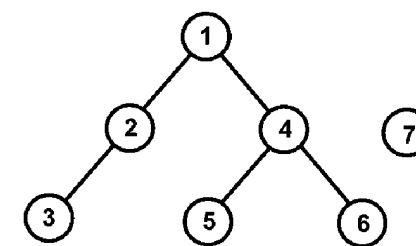


Multivariate

Partial Coherence

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

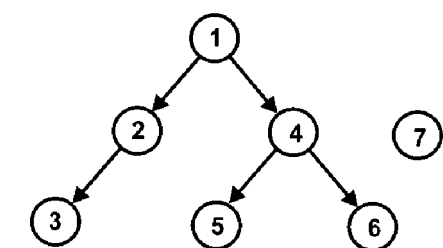
(Bendat and Piersol, 1986; Dalhaus, 2000)



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
Coherence Measures	Spectral Density Matrix	$S(f) = X(f)X(f)^*$ $= H(f)\Sigma H(f)^*$
	Coherency	$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f)S_{jj}(f)}}$ $0 \leq C_{ij}(f) ^2 \leq 1$
	Imaginary Coherence (iCoh)	$iCoh_{ij}(f) = \text{Im}(C_{ij}(f))$
	Partial Coherence (pCoh)	$P_{ij}(f) = \frac{\hat{S}_{ij}(f)}{\sqrt{\hat{S}_{ii}(f)\hat{S}_{jj}(f)}}$ $\hat{S}(f) = S(f)^{-1}$ $0 \leq P_{ij}(f) ^2 \leq 1$
	Multiple Coherence (mCoh)	$G_i(f) = \sqrt{1 - \frac{\det(S(f))}{S_{ii}(f)\mathbf{M}_{ii}(f)}}$ <p>$\mathbf{M}_{ii}(f)$ is the minor of $S(f)$ obtained by removing the i^{th} row and column of $S(f)$ and returning the determinant.</p>

	Estimator	Formula
Partial Directed Coherence Measures	Normalized Partial Directed Coherence (PDC)	$\pi_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{k=1}^M A_{kj}(f) ^2}}$ $0 \leq \pi_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M \pi_{ij}(f) ^2 = 1$
	Generalized PDC (GPDC)	$\bar{\pi}_{ij}(f) = \frac{\frac{1}{\Sigma_{ii}} A_{ij}(f)}{\sqrt{\sum_{k=1}^M \frac{1}{\Sigma_{ii}^2} A_{kj}(f) ^2}}$ $0 \leq \bar{\pi}_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M \bar{\pi}_{ij}(f) ^2 = 1$
	Renormalized PDC (rPDC)	$\lambda_{ij}(f) = Q_{ij}(f)^* V_{ij}(f)^{-1} Q_{ij}(f)$ <p>where</p> $Q_{ij}(f) = \begin{pmatrix} \text{Re}[A_{ij}(f)] \\ \text{Im}[A_{ij}(f)] \end{pmatrix} \text{ and }$ $V_{ij}(f) = \sum_{k,l=1}^p R_{jj}^{-1}(k,l) \Sigma_{ii} Z(2\pi f, k, l) Z(\omega, k, l)$ $= \begin{pmatrix} \cos(\omega k) \cos(\omega l) & \cos(\omega k) \sin(\omega l) \\ \sin(\omega k) \cos(\omega l) & \sin(\omega k) \sin(\omega l) \end{pmatrix}$ <p>R is the $[(Mp)^2 \times (Mp)^2]$ covariance matrix of the VAR[p] process (Lütkepohl, 2006)</p>
Granger-Geweke	Granger-Geweke Causality (GGC)	$F_{ij}(f) = \frac{(\Sigma_{jj} - (\Sigma_{ij}^2 / \Sigma_{ii})) H_{ij}(f) ^2}{S_{ii}(f)}$

	Estimator	Formula
Directed Transfer Function Measures	Normalized Directed Transfer Function (DTF)	$\gamma_{ij}(f) = \frac{H_{ij}(f)}{\sqrt{\sum_{k=1}^M H_{ik}(f) ^2}}$ $0 \leq \gamma_{ij}(f) ^2 \leq 1$ $\sum_{j=1}^M \gamma_{ij}(f) ^2 = 1$
	Full-Frequency DTF (ffDTF)	$\eta_{ij}^2(f) = \frac{ H_{ij}(f) ^2}{\sum_f \sum_{k=1}^M H_{ik}(f) ^2}$
	Direct (dDTF) DTF	$\delta_{ij}^2(f) = \eta_{ij}^2(f) P_{ij}^2(f)$

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

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

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

$H(f)$ Transfer Function

$A(f)$ System Matrix

Σ Noise Covariance Matrix

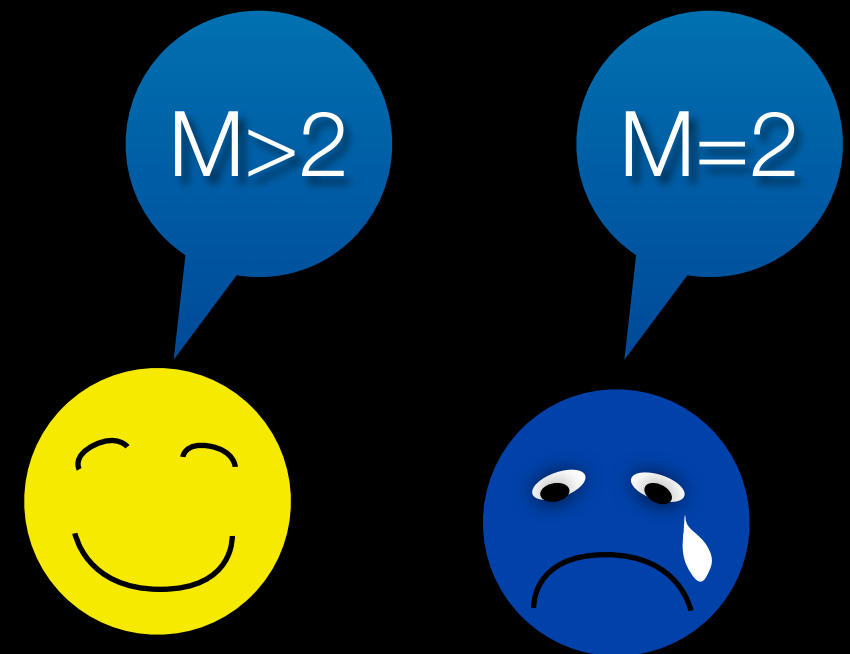
 Variance Stabilization

The image shows a decorative sign for an intermission. It features a central yellow rectangular area with the word "INTERMISSION" written in a dark, serif font. This central area is framed by a wide, ornate border in a light brown or tan color. The border has a repeating pattern of stylized, pointed floral or leaf-like shapes. The entire sign is set against a dark brown background that has a fine, dotted texture. There are some small, light-colored specks scattered around the border, possibly representing dust or light reflections.

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



- ✦ 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

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



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

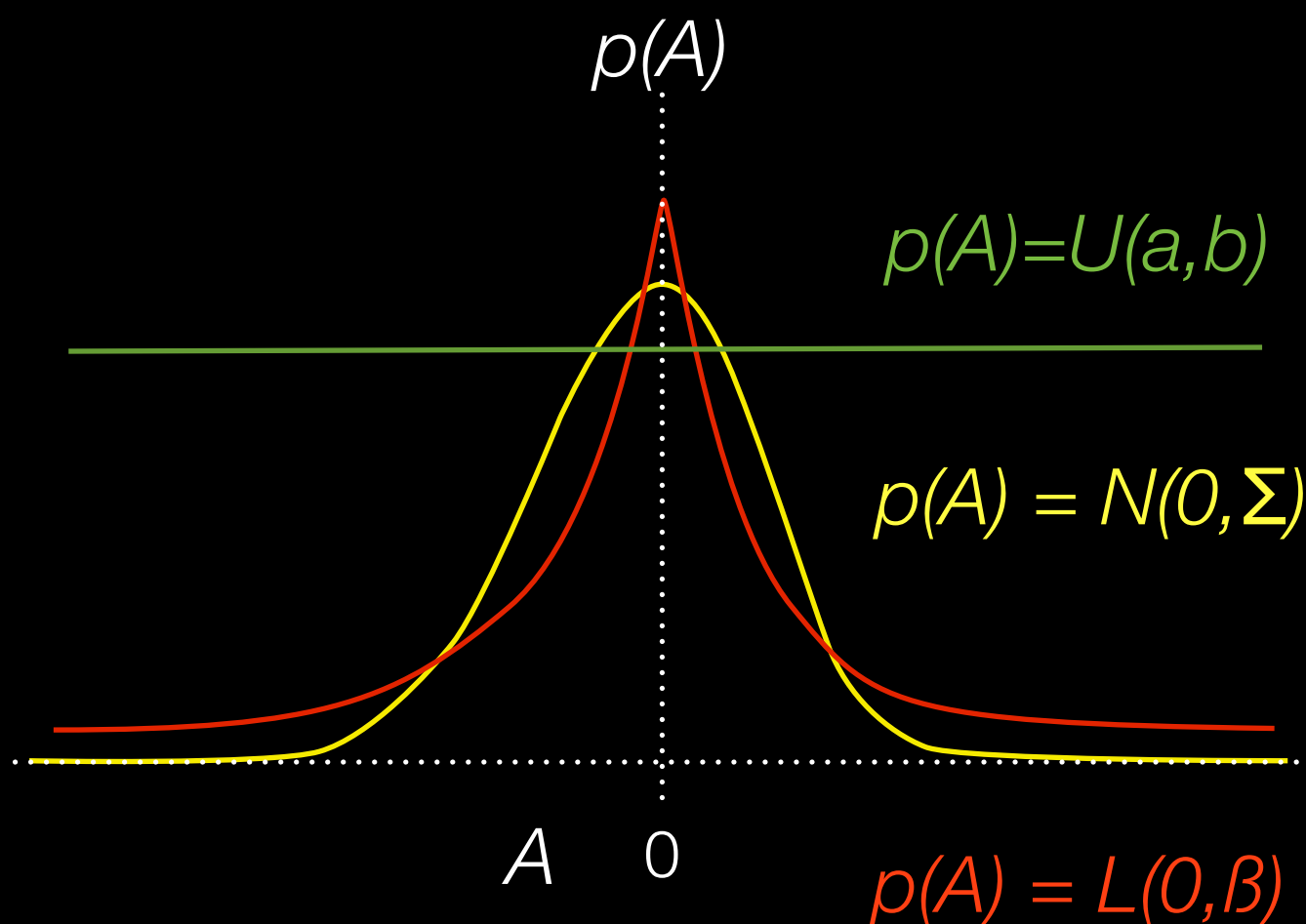
posterior

likelihood

prior

$$\hat{A} = \arg \max_A \{ p(A|D) \cong p(D|A) p(A) \}$$

$M > 2$



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

Smoothness constraints

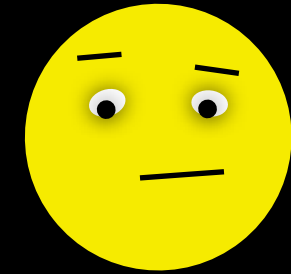
- large differences in values unlikely
- small (non-zero) values most probable. e.g. Normal (gaussian) prior.

Sparsity constraint

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

Smoothness Constraints

- Standard least-squares solution



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

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

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

$$X_k = [X(p+1-k), \dots, X(N-k)]^T$$

$$Z = [X_1, \dots, X_p]$$

$$Y = X_0$$

Rewrite VAR[p] as VAR[1]


Smoothness Constraints

- Ridge Regression
(Tikhonov Regularization, Minimum-(L₂)-Norm Estimation, ...)

$$A(t) = \arg \min_{\hat{A}} \left(\underbrace{\|Y - Z\tilde{A}\|_2^2}_{\text{prediction error}} + \underbrace{\lambda \|\tilde{A}\|_2^2}_{\substack{\text{penalty term,} \\ \text{enforces smoothness}}} \right)$$

λ
regularization

M>2



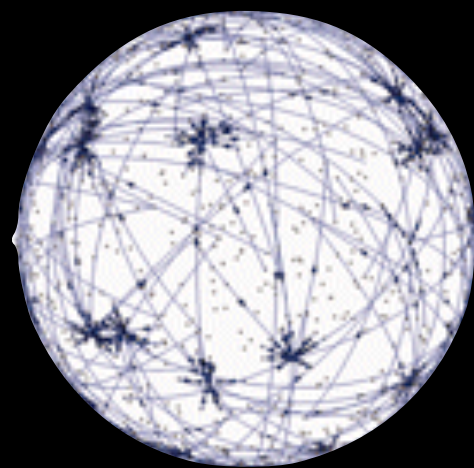
- Equivalent to assuming a Gaussian prior with variance determined by λ
- Large values of A are penalized. The range of allowable values for coefficients is restricted, reducing the *effective* degrees of freedom and allowing us to estimate VAR coefficients with fewer observations.

Sparsity Constraints

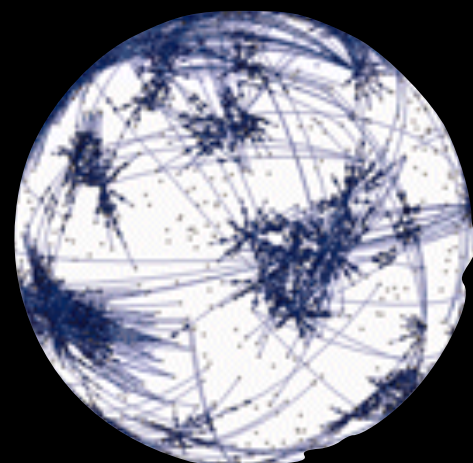
Sparsity

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

It's a small world...

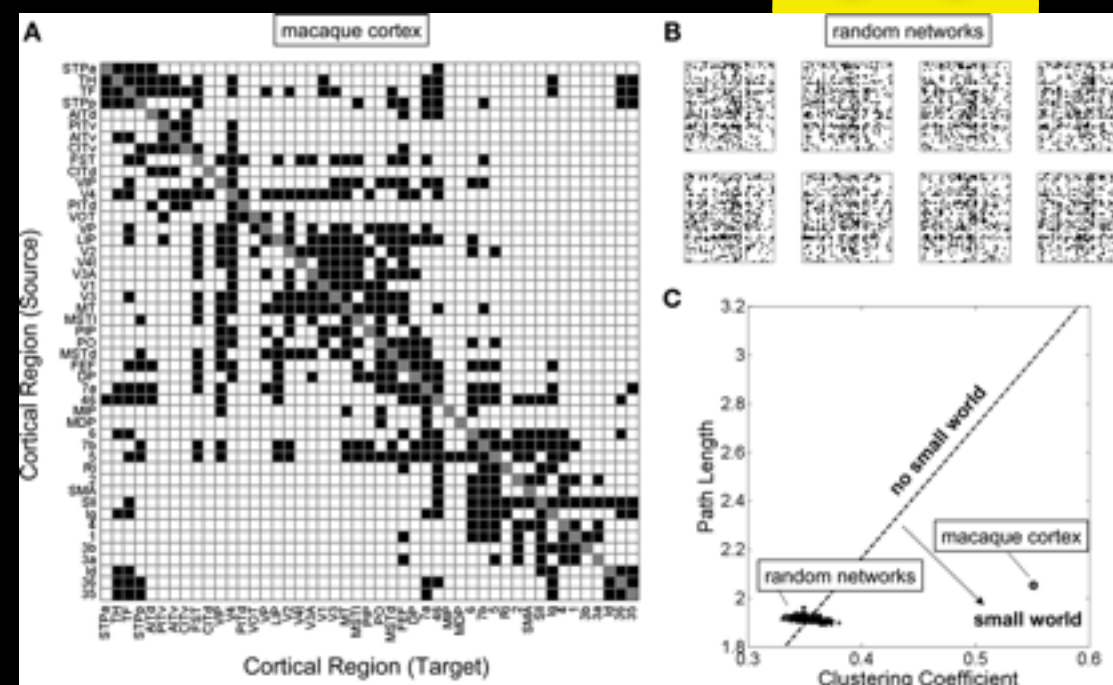


structural
network

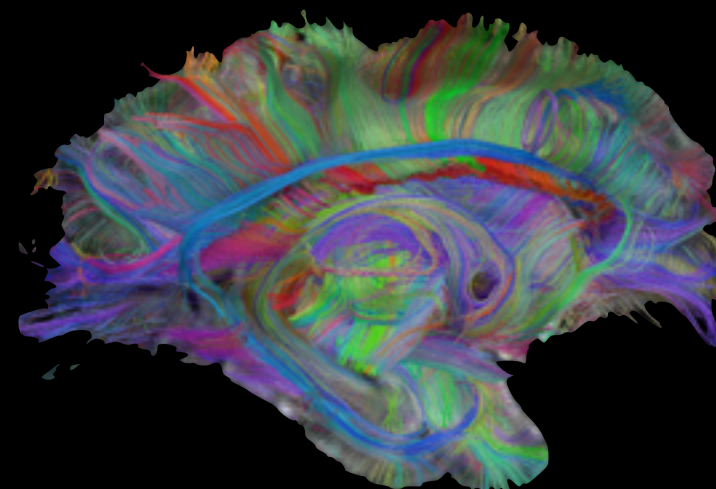


functional
network

Sporns and Honey, *PNAS*, 2006



Sporns, *Frontiers in Computational Neuroscience*, 2011



Structural Connectivity

Sparsity Constraints

- Standard least-squares solution



prediction error

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

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

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

$$X_k = [X(p+1-k), \dots, X(N-k)]^T$$

$$Z = [X_1, \dots, X_p]$$

$$Y = X_0$$

Rewrite VAR[p] as VAR[1]

Sparsity Constraints

$M > 2$

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

$$A(t) = \arg \min_{\hat{A}} \left(\underbrace{\|Y - Z\tilde{A}\|_2^2}_{\text{prediction error}} + \underbrace{\lambda \sum_{ij} \underbrace{\|\tilde{A}_{ij}^{(1)}, \dots, \tilde{A}_{ij}^{(p)}\|_2^2}_{\text{group sparsity (L1)}}}_{\text{regularization}} \right)$$

smoothness (L2)
(preserves spectrum)

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

$M > 2$



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

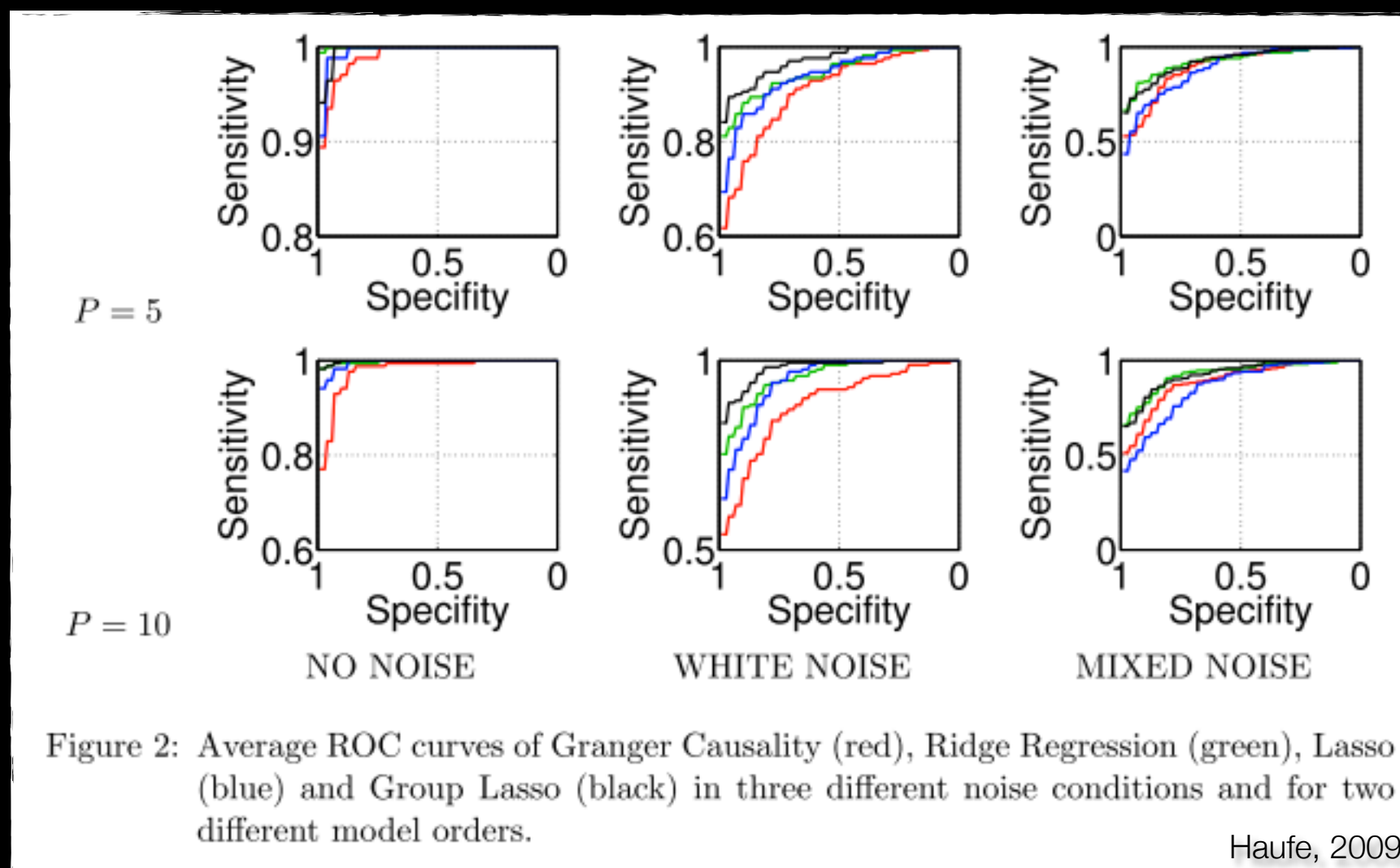
$$N = O\left(K \log(M^2 p / K)\right) \approx O\left(\log M^2 p\right)$$

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

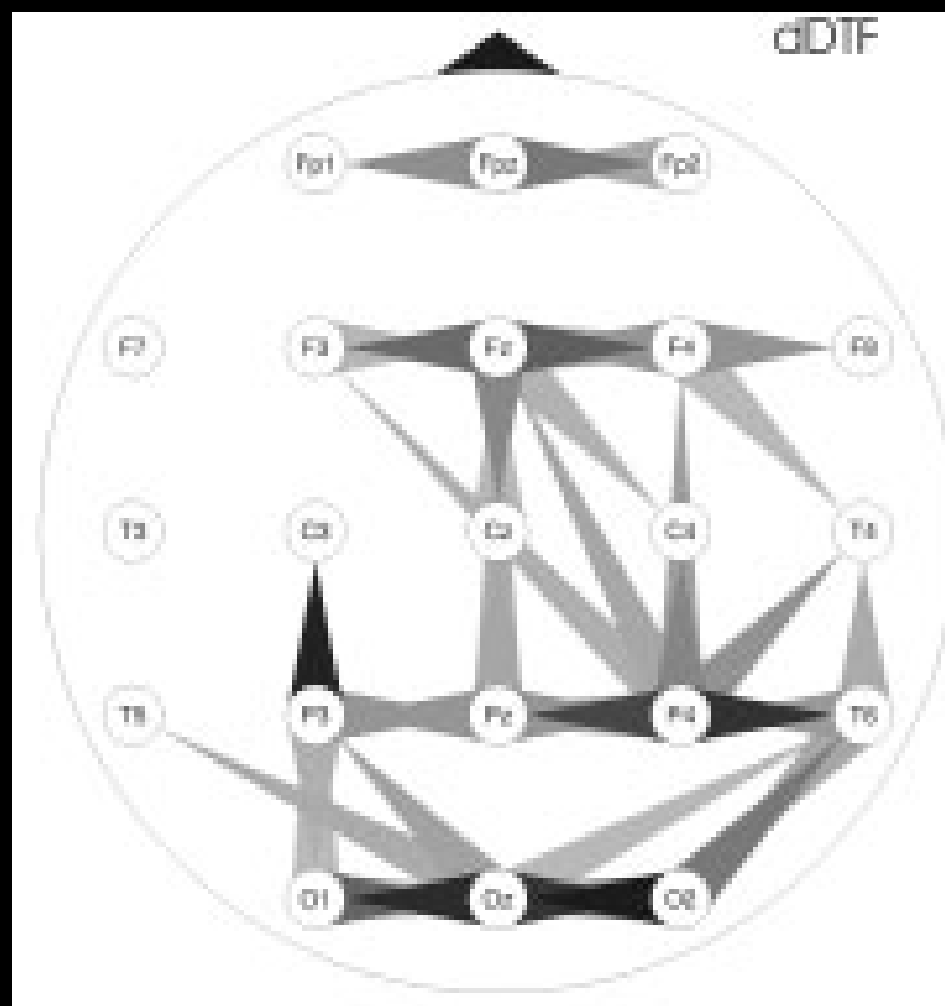
(unconstrained)

Constraints Improve Estimation (if prior assumptions are correct)

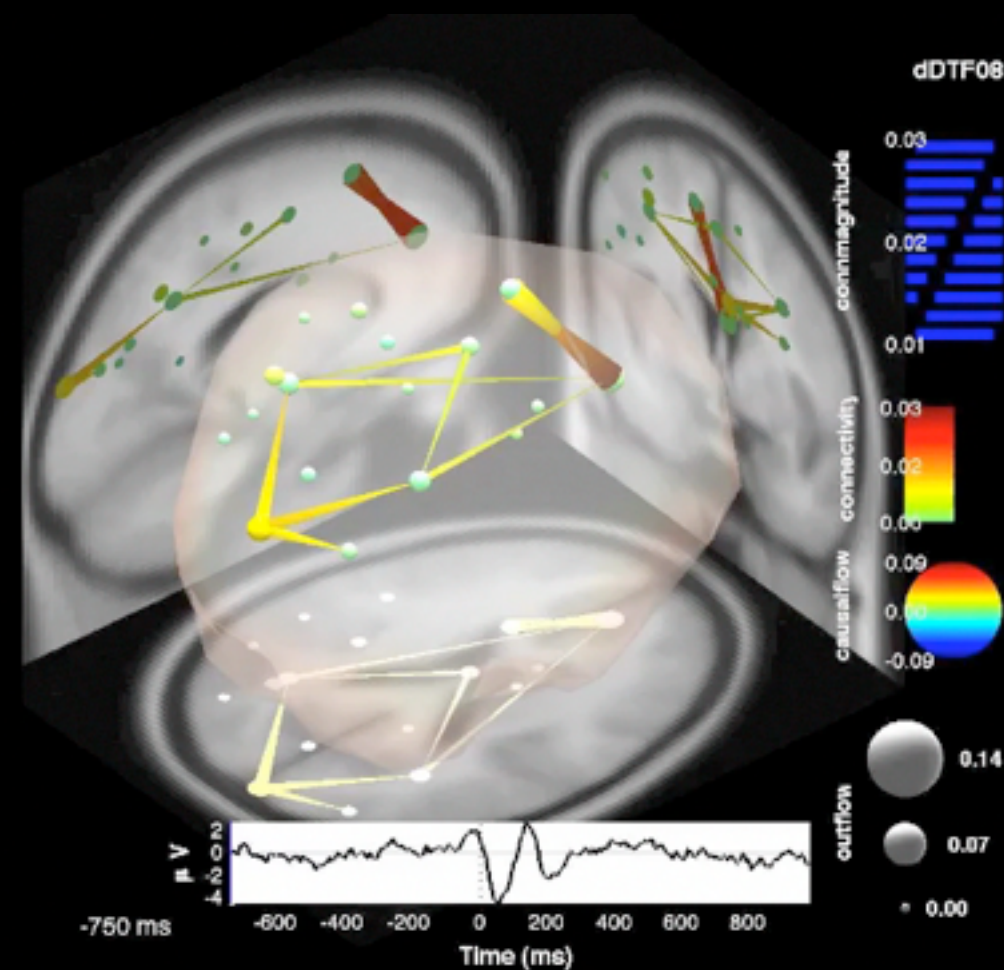
- Significant improvements using smoothness or sparsity assumptions
- (e.g. Haufe et al, 2009, Valdez-Sosa et al, 2009)



Scalp or Source?



or



Scalp or Source?

$$X(t) = HS(t) = \sum_{k=1}^p HA^{(k)}(t)H^{-1}X(t-k) + HE(t)$$

sensors

H^{-1}

$$X(t) = HS(t)$$

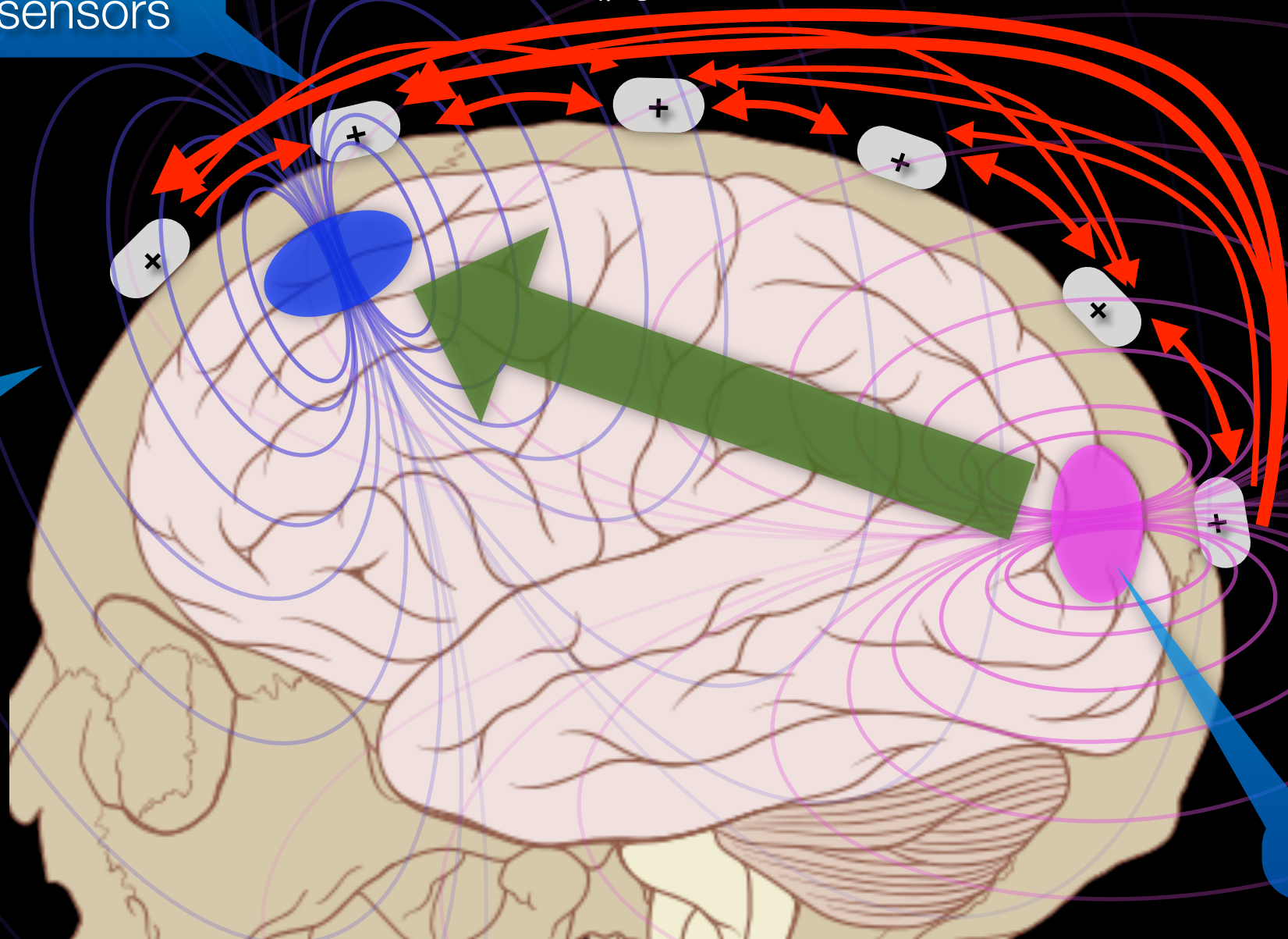
Volume
Conduction

ICA
SBL
Beamforming
Minimum-norm
...

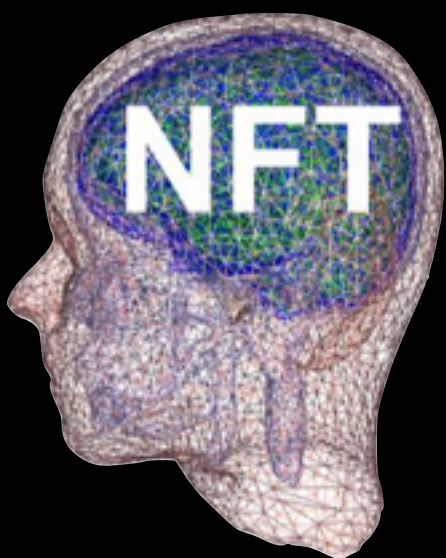
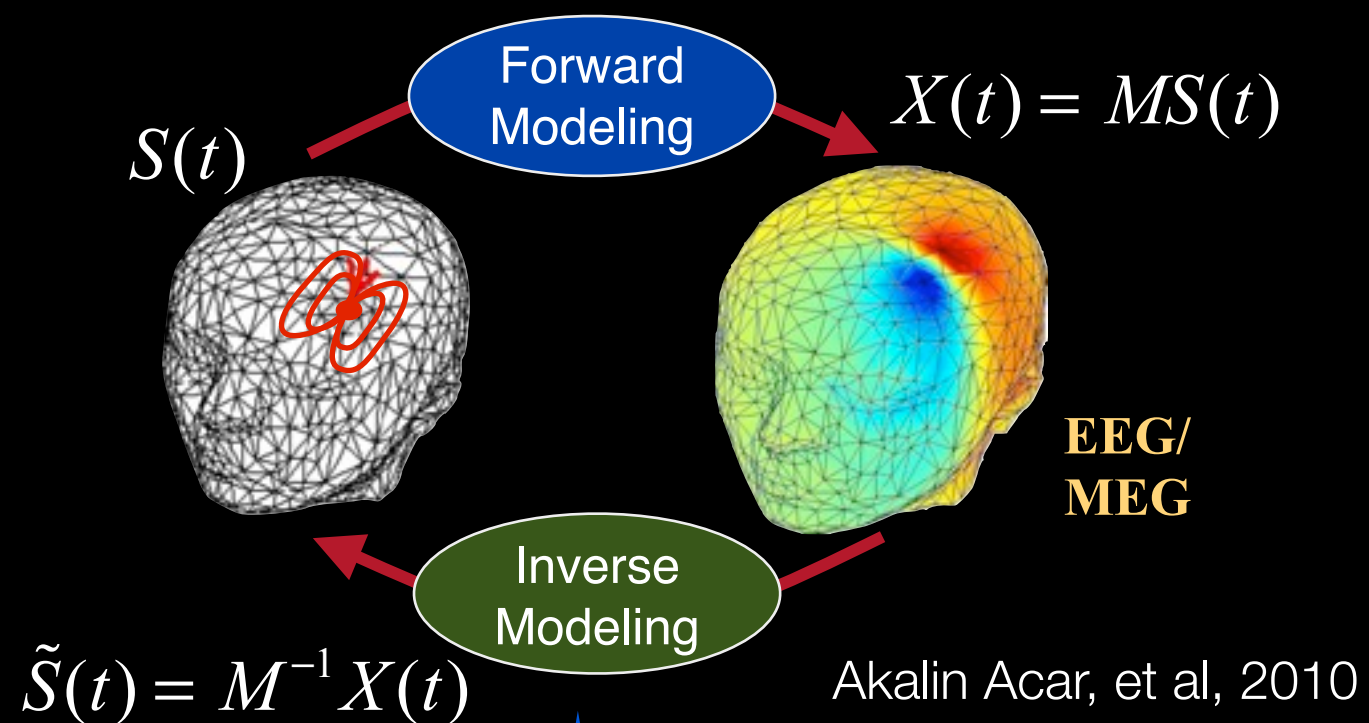
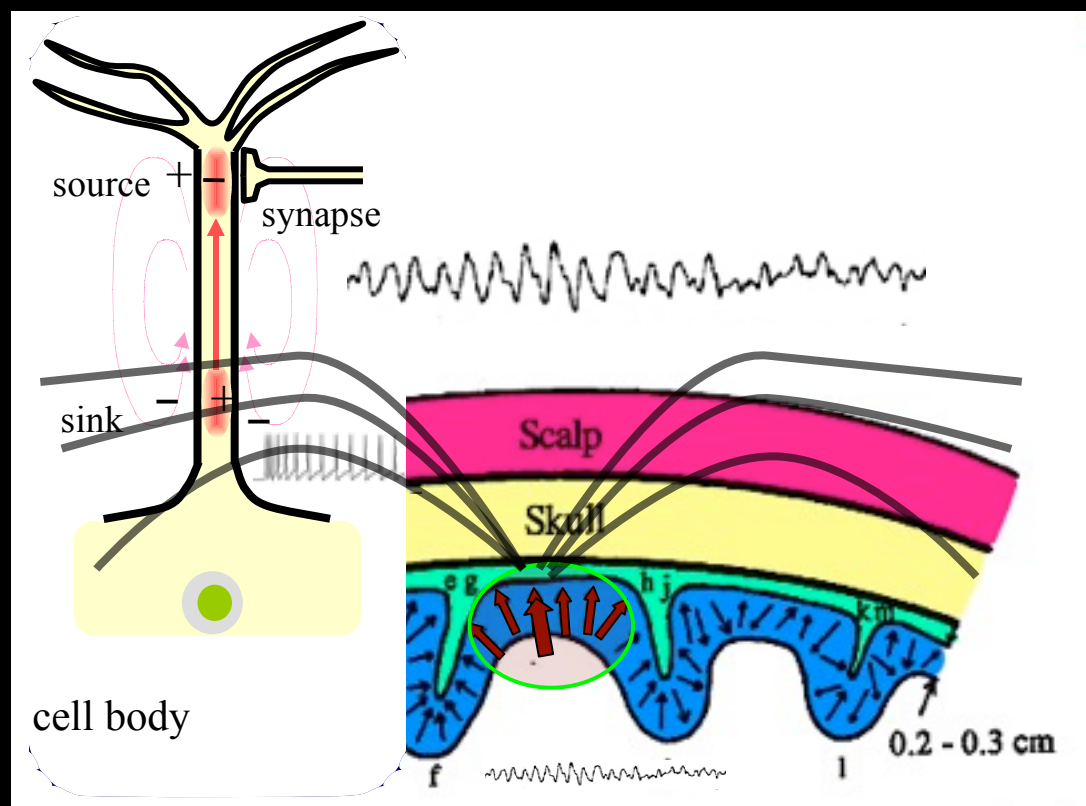
sources

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

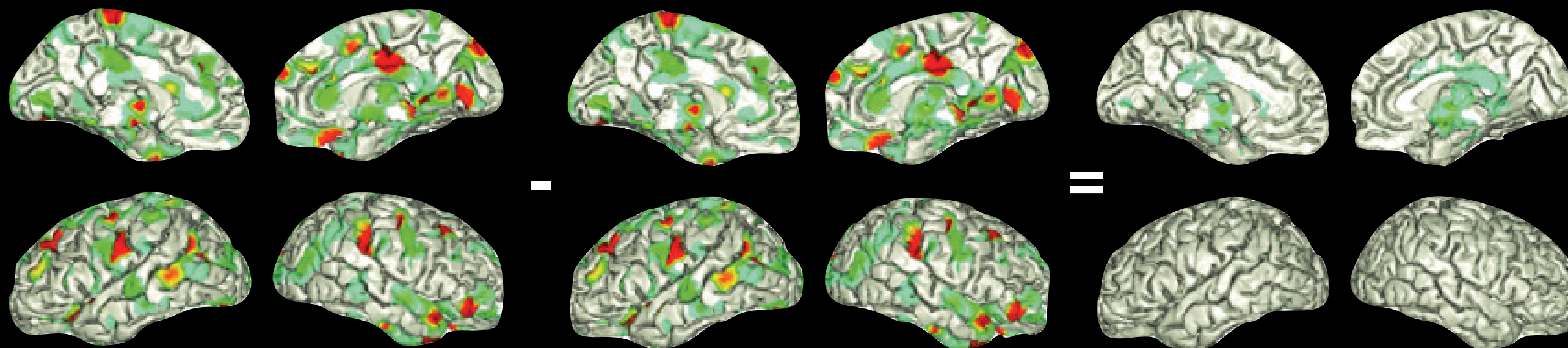
Method	Smoothness	Sparsity	Independence/Orthogonality
MNE	X		
LORETA	X		
dSPM	X		
Beamforming			X
Sparse Bayesian Learning	X	X	
S-FLEX	X	X	
FOCUSS		X	
ICA/PCA/SOBI			X

Source reconstruction with ICA+SBL

simulated

reconstructed

error



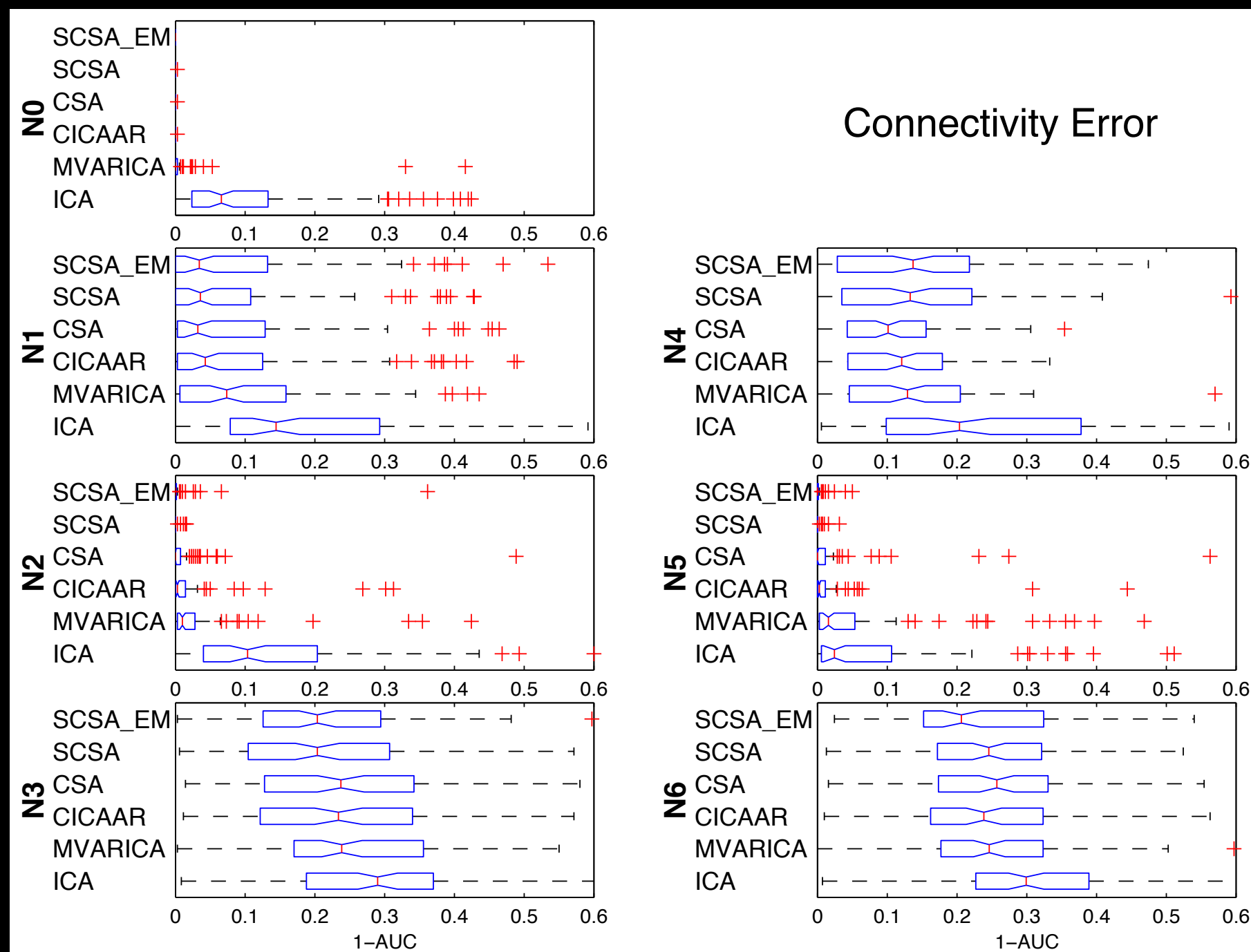
Makeig, Ramirez, Weber, Wipf, Dale, Simpson, *15th Inter. Conf on Biomagnetism* (2006)

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**.

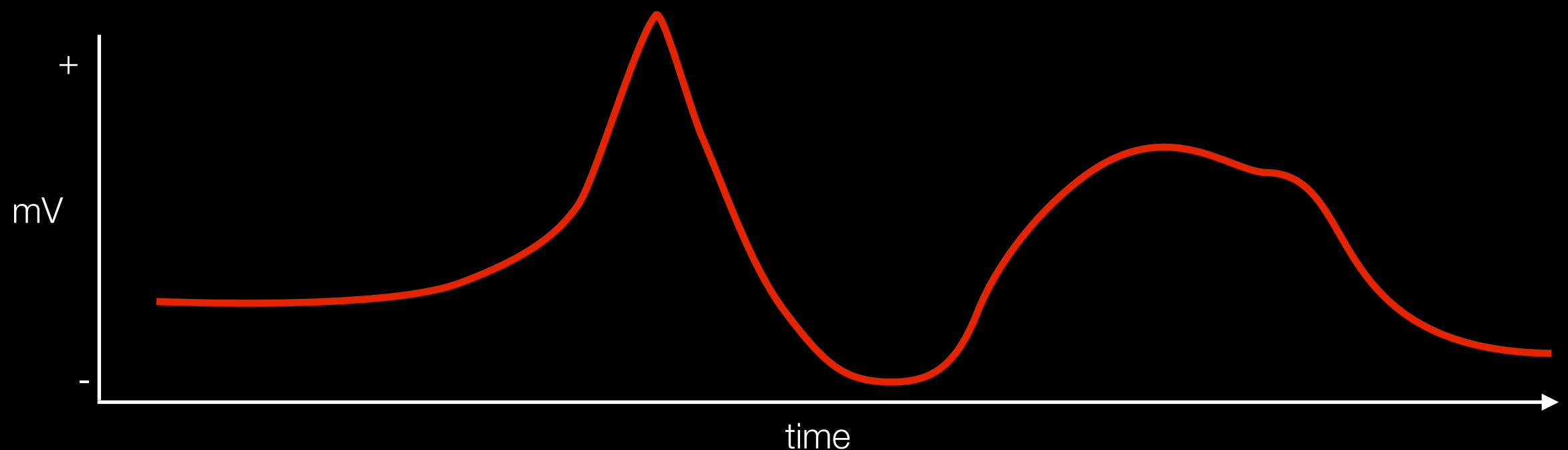
However, the *best* approach is to use an inverse model that explicitly preserves time-delayed dependencies or *jointly* estimates sources (de-mixing matrix) and connectivity (VAR parameters). See Haufe, 2008 IEEE TBME for a good treatment (coming soon to SIFT).

Estimating Dependency of Independent Components ?



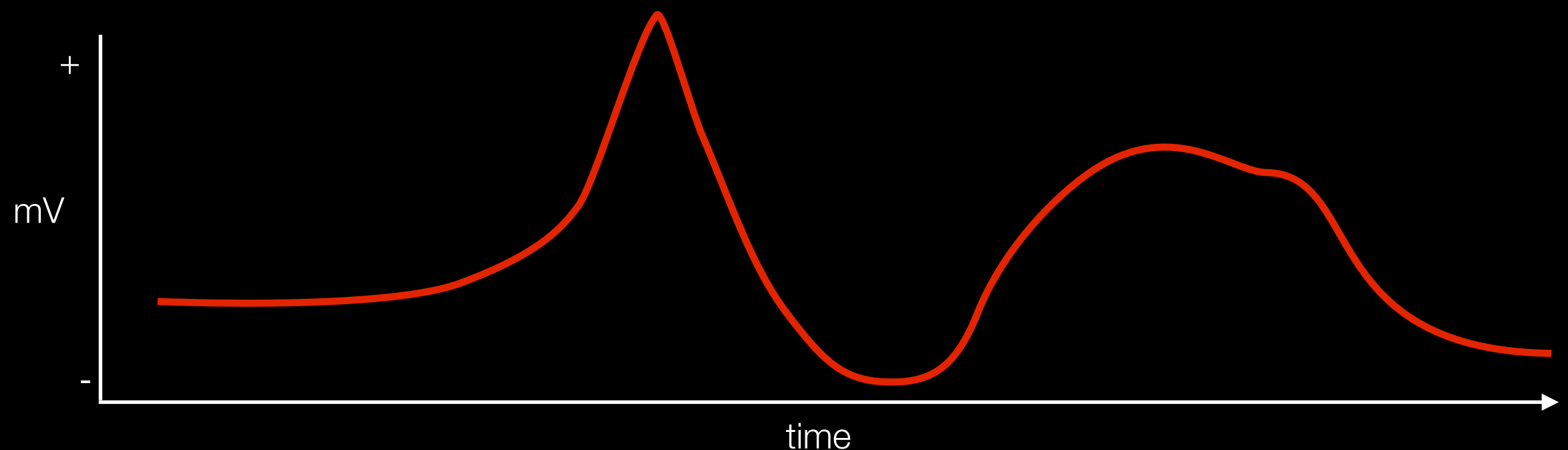
Adapting to Non-Stationarity

- ✦ 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?



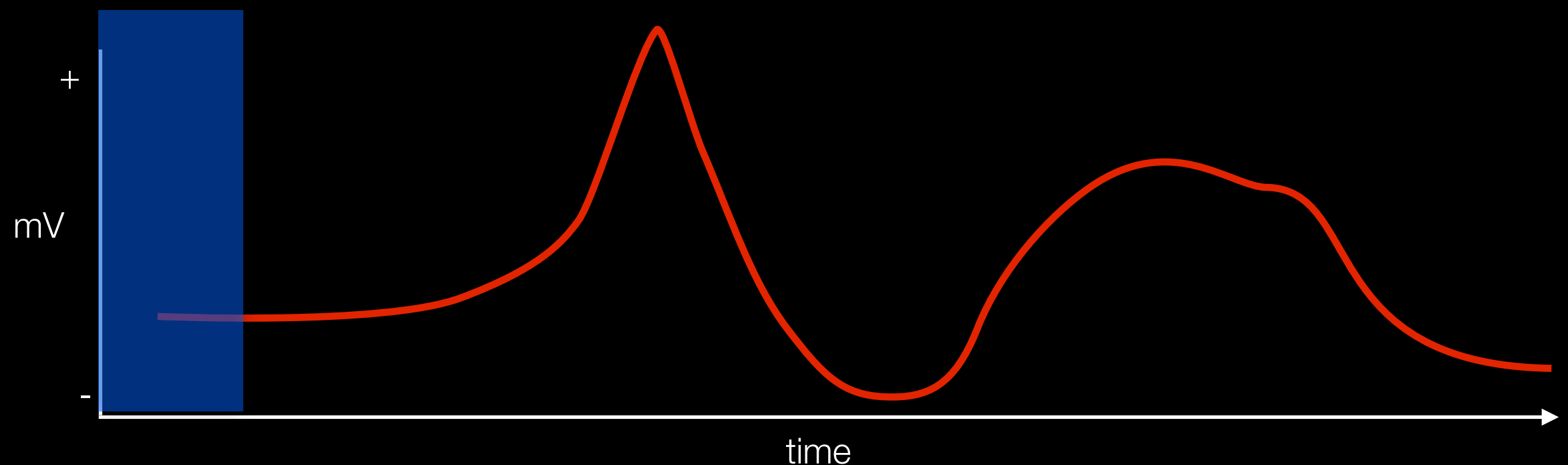
Adapting to Non-Stationarity

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



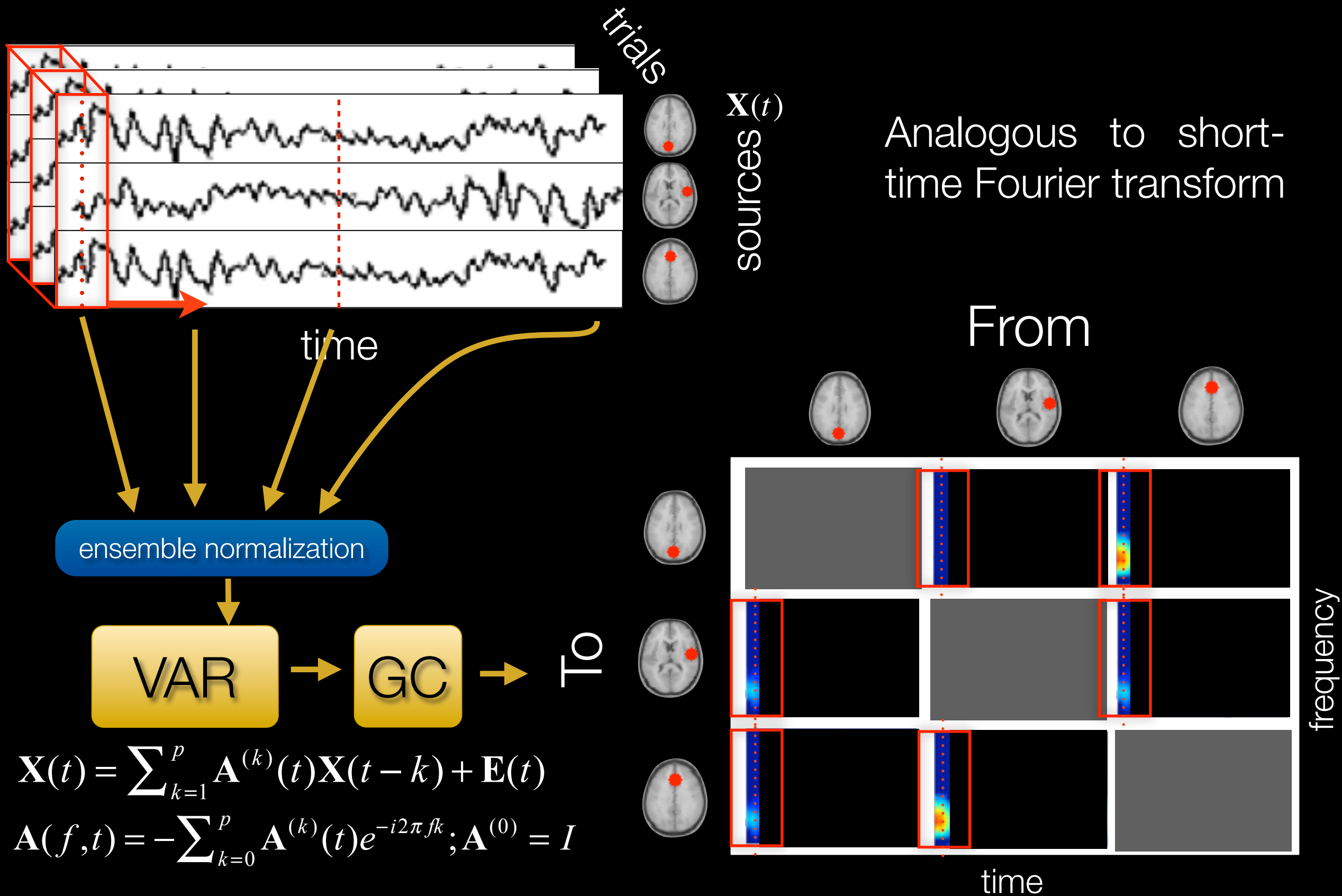
Adapting to Non-Stationarity

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



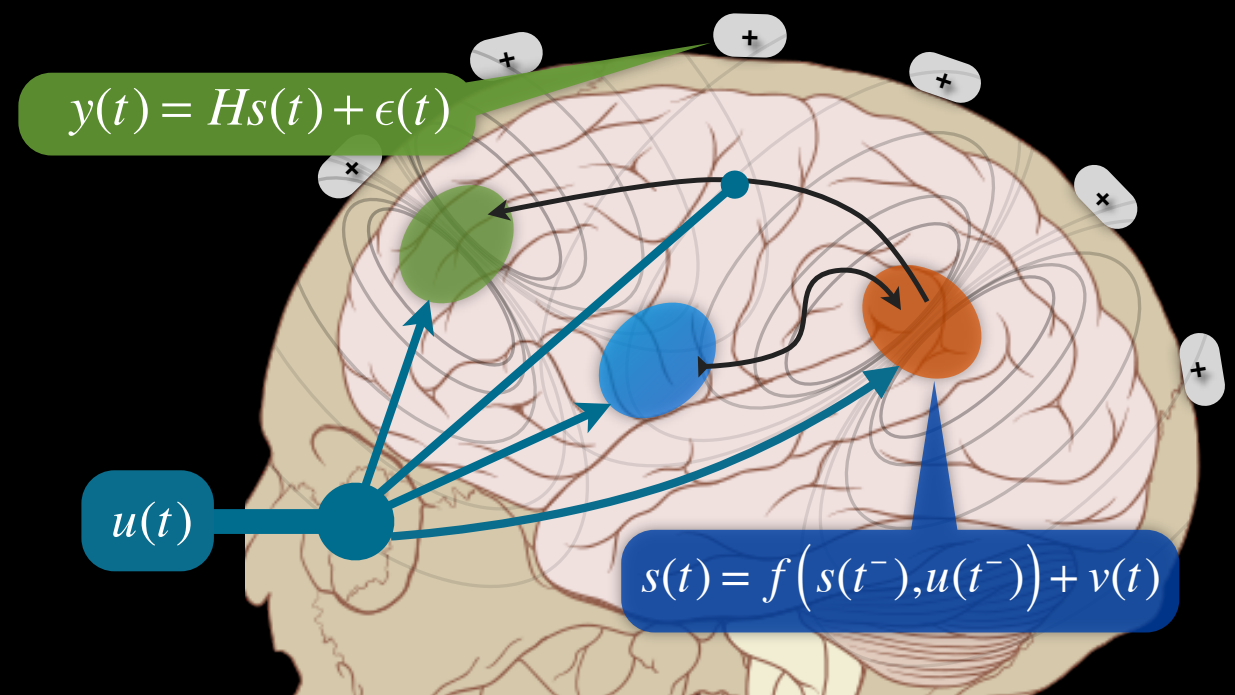
Segmentation-based VAR

(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

Intro

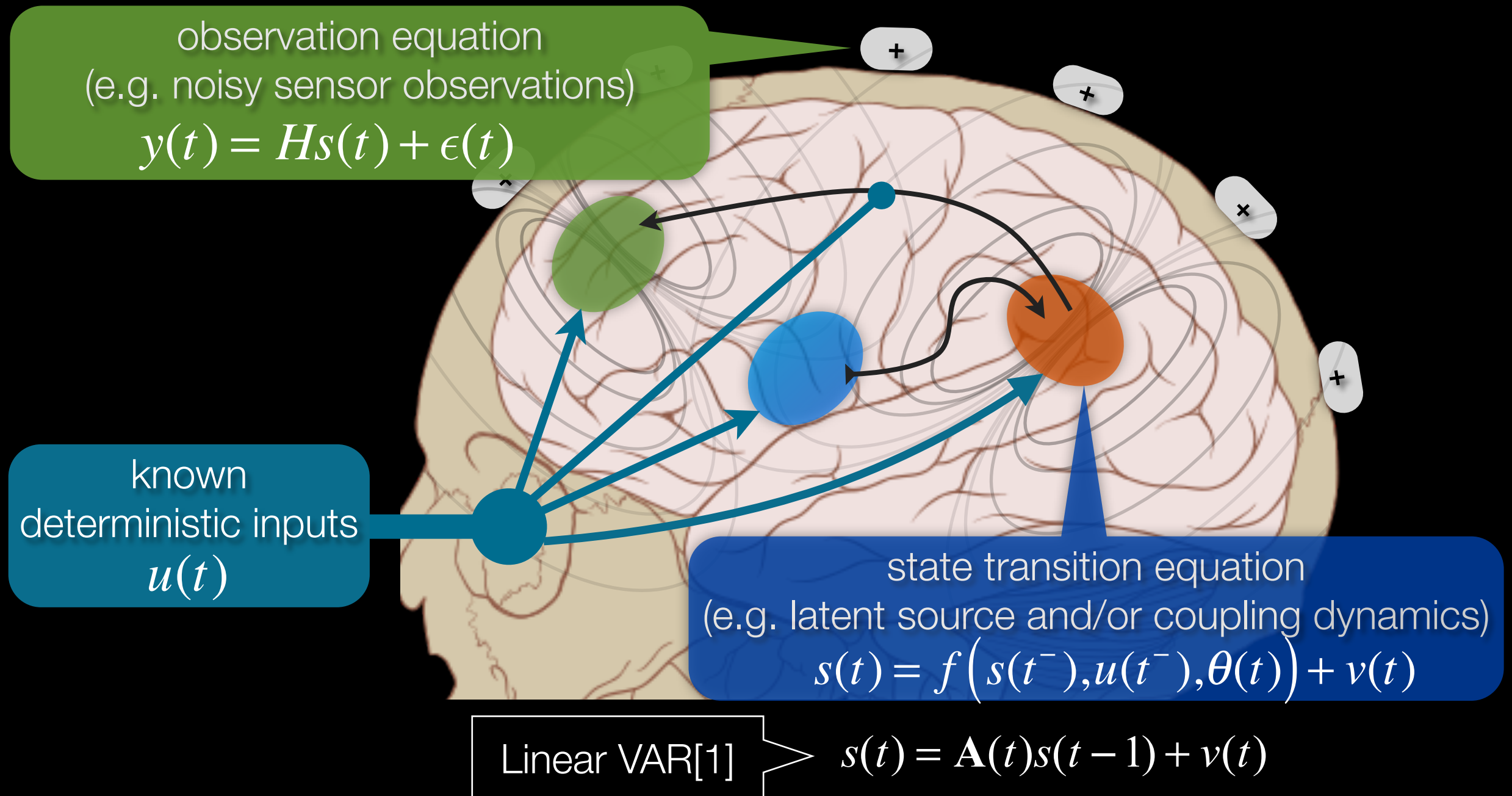
Theory

SIFT

Apps

To-Do

Fin

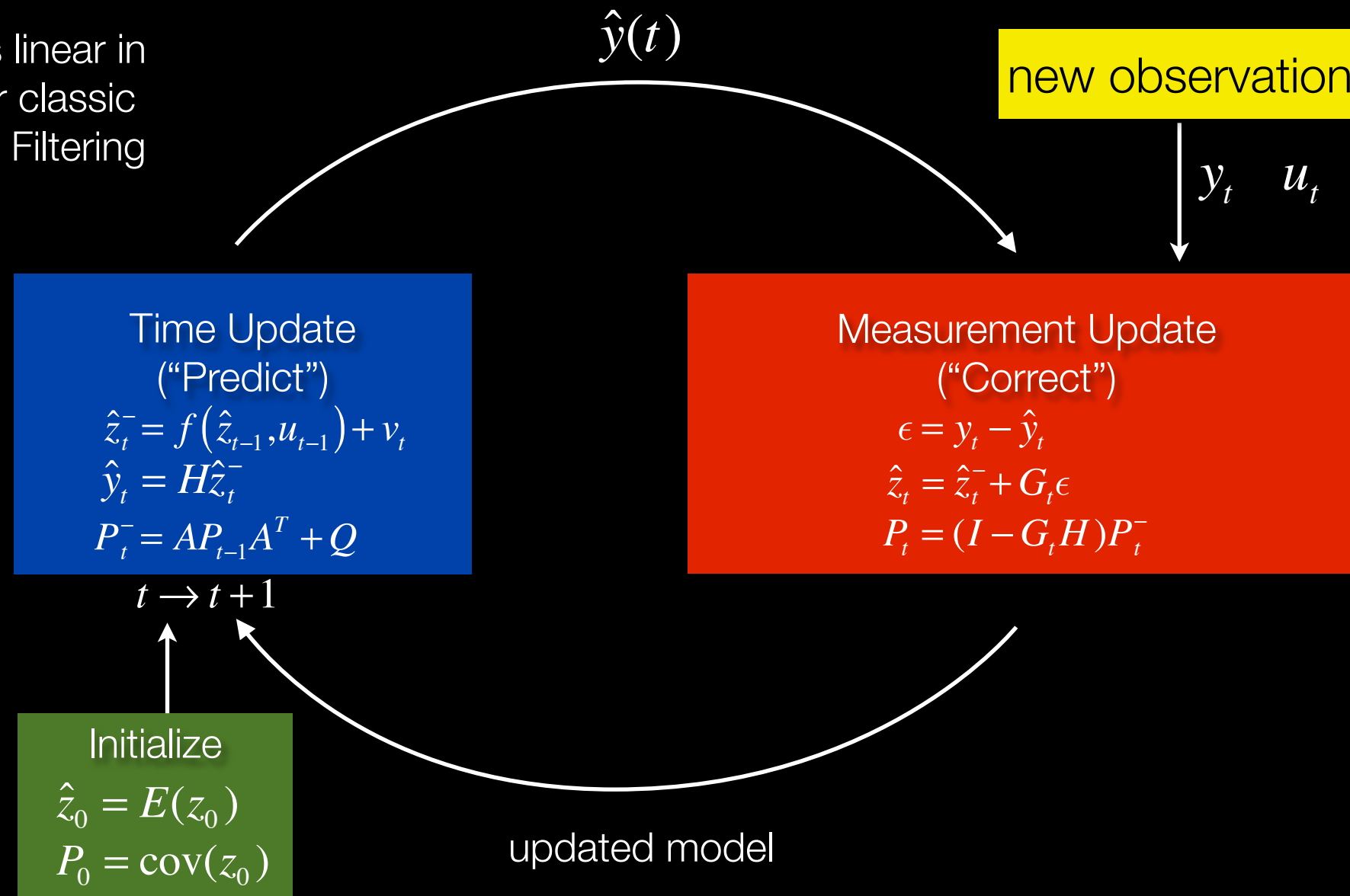


- Dynamical system may be linear or nonlinear, dense or sparse, non-stationary, high-dimensional, partially-observed, and stochastic
- Subsumes discrete Delay Differential Equation (DDE) and Vector Autoregressive (VAR) methods and closely related to Dynamic Causal Modeling (DCM)

Kalman Filtering

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

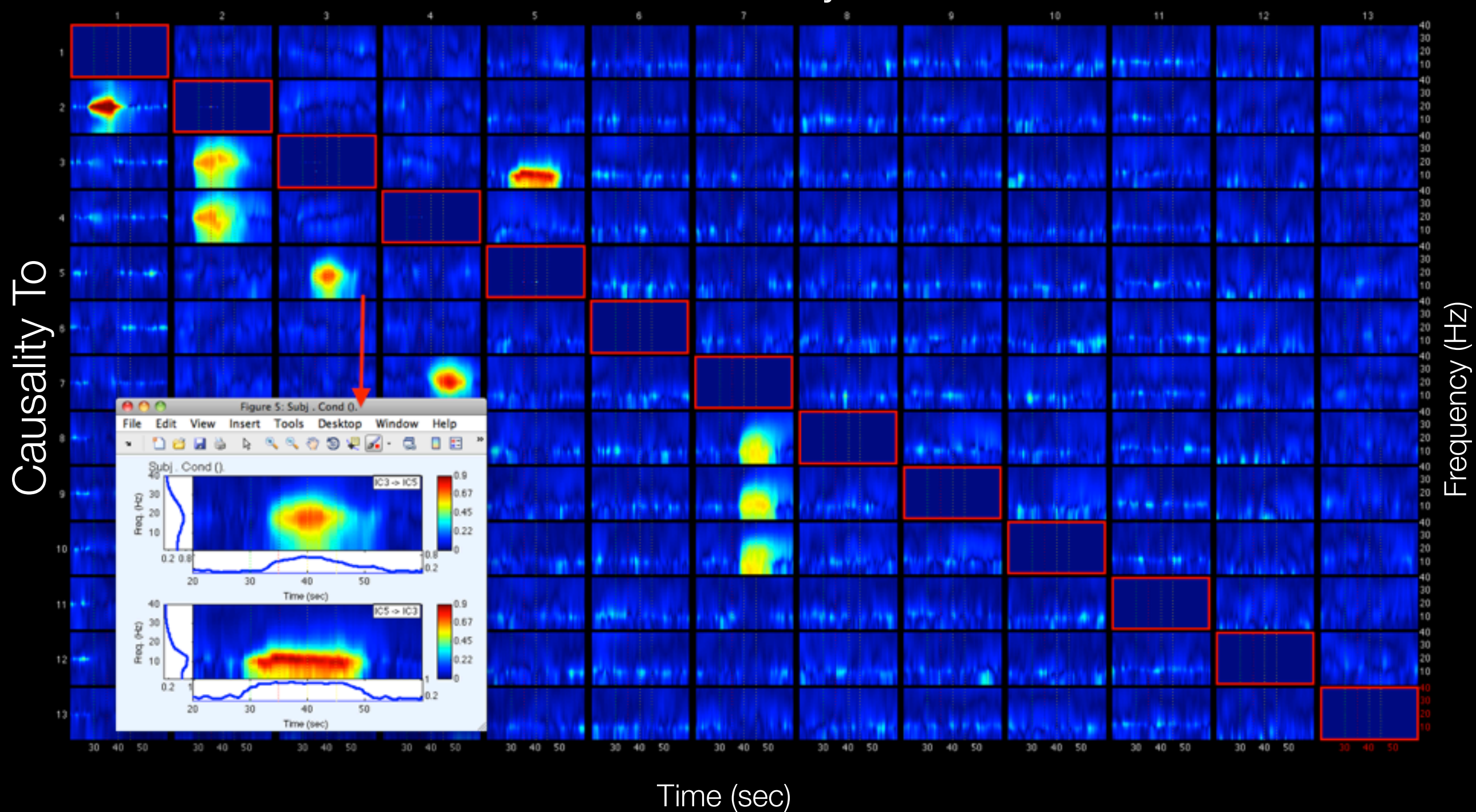
$f(z,u)$ is linear in $\{z,u\}$ for classic Kalman Filtering



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

Kalman Filtering

GPDC Causality From



The image shows a decorative sign for an intermission. It features a central yellow rectangular area with the word "INTERMISSION" written in a dark, serif font. This central area is framed by a wide, ornate border in a light brown or tan color. The border has a repeating pattern of stylized, pointed floral or leaf-like shapes. The entire sign is set against a dark brown background that has a fine, dotted texture. There are small, light-colored circular accents scattered around the border, particularly at the top and bottom edges.

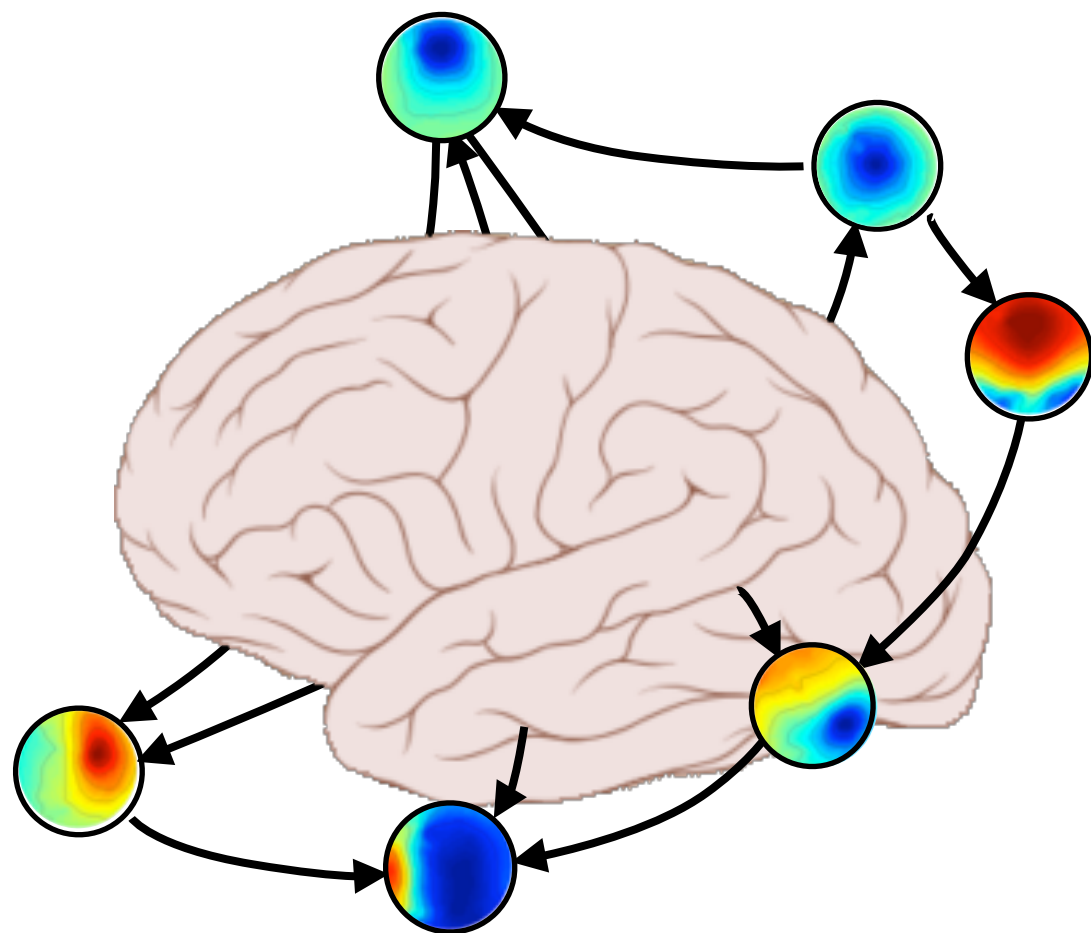
INTERMISSION

<http://sccn.ucsd.edu/wiki/SIFT>

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

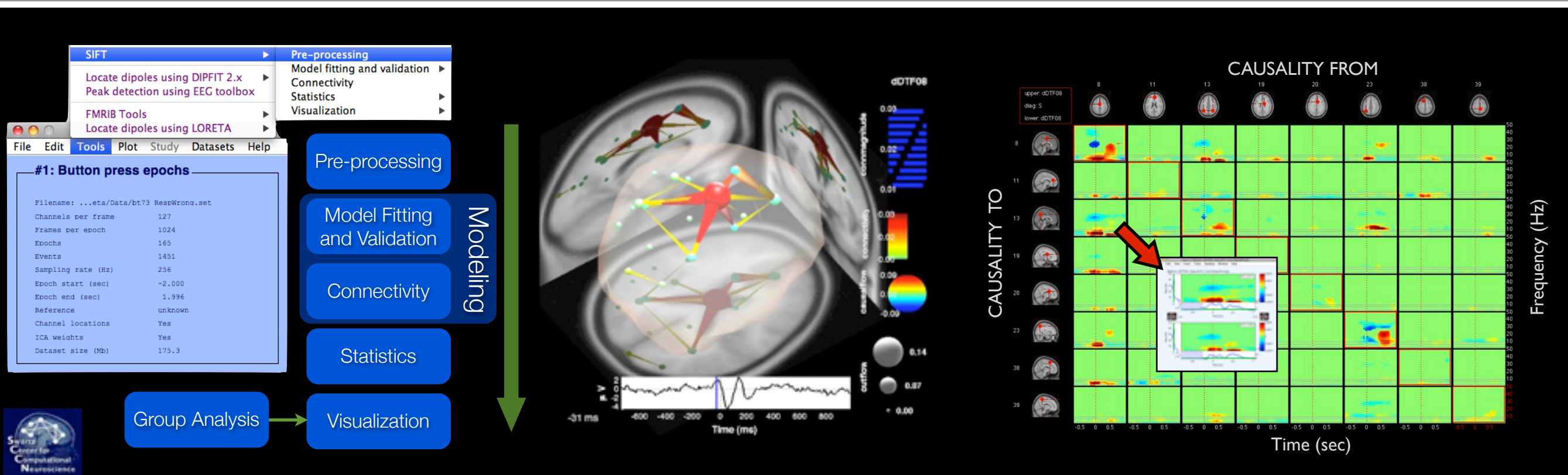
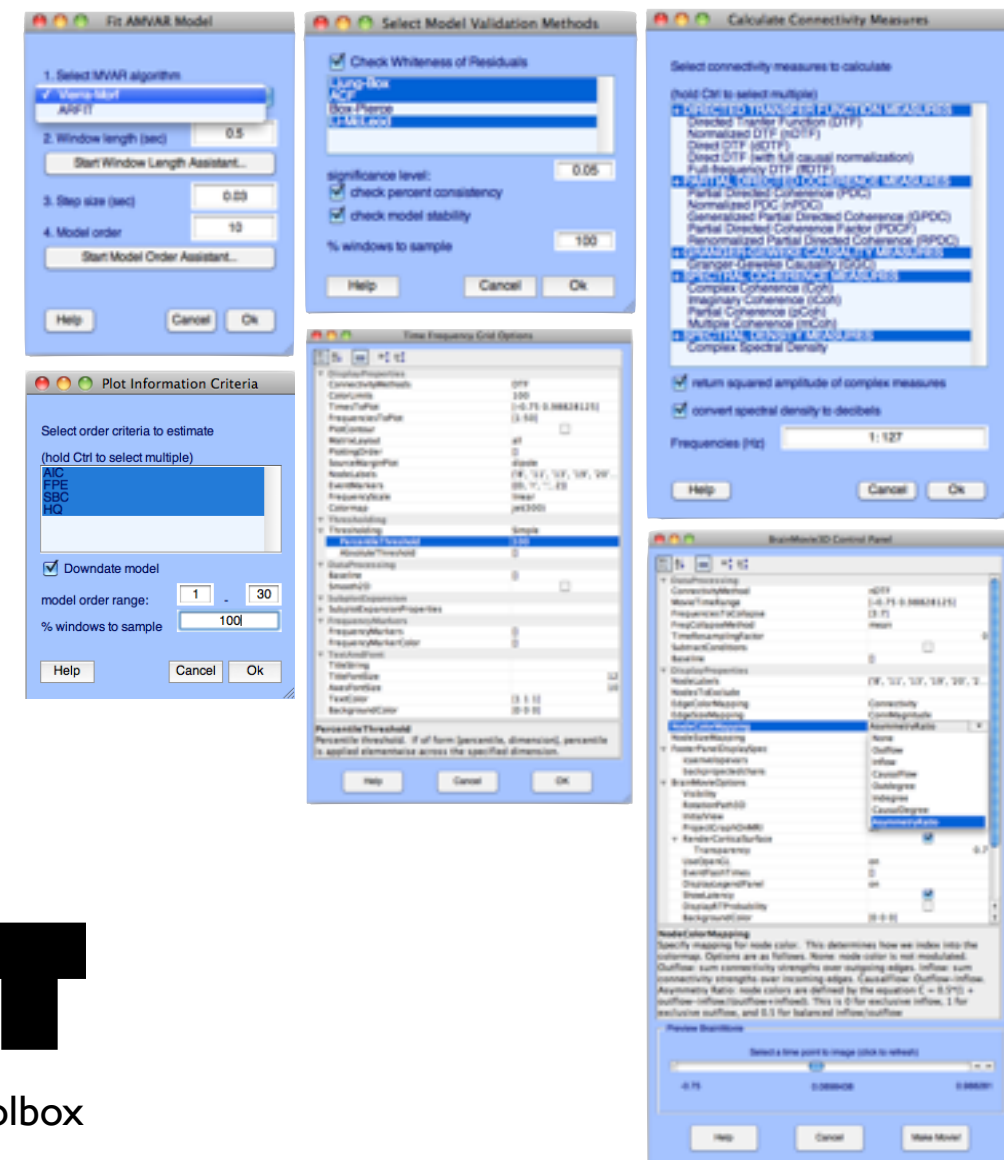
Mullen, et al, *Society for Neuroscience*, 2010

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

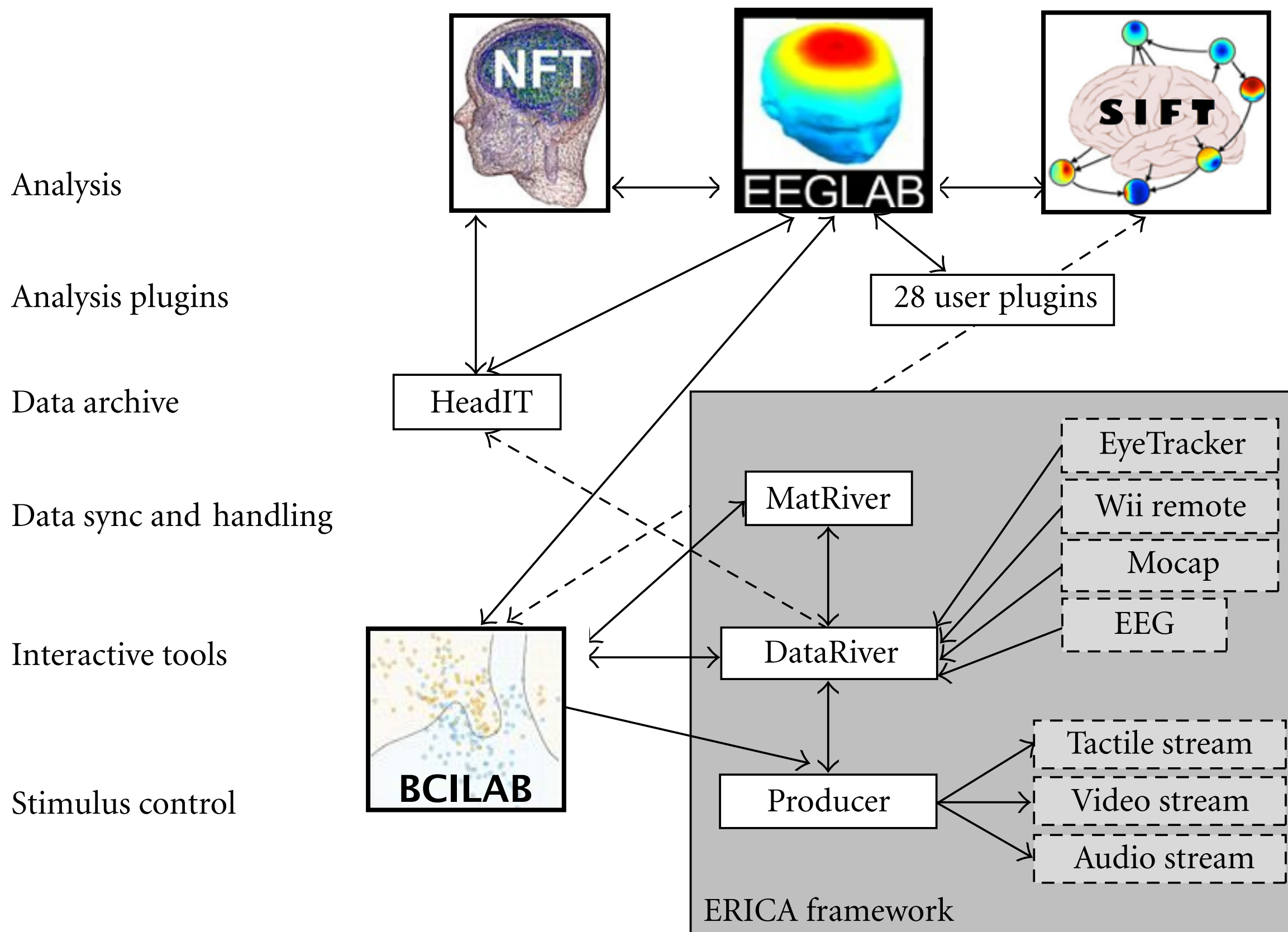


SIFT

Source Information Flow Toolbox

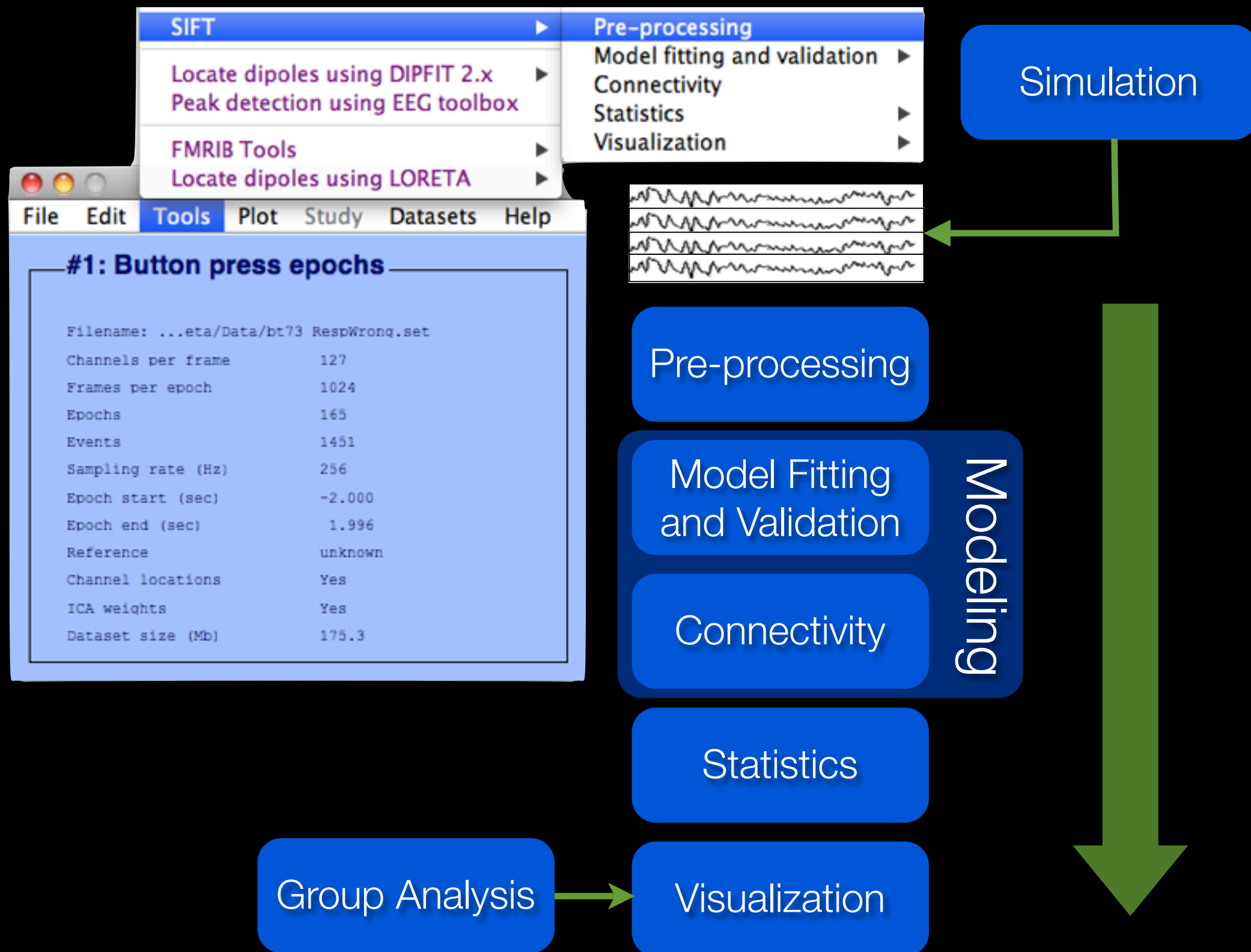


EEGLAB Software framework



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

SIFT

Apps

To-Do

Fin

Preprocessing

Modeling

Statistics

Visualization

- Pre-processing
- Model fitting and validation ▶
- Connectivity
- Statistics ▶
- Visualization ▶

Preprocessing Options

▼ Miscellaneous	
VerbosityLevel	2
SignalType	Components
VariableNames	
ResetConfigs	<input checked="" type="checkbox"/>
▼ Filtering	
DifferenceData	<input type="checkbox"/>
▼ Detrend	
DetrendingMethod	linear
▼ Piecewise	
SegmentLength	0.33
StepSize	0.082
Plot	<input type="checkbox"/>
AmplitudeEnvelope	<input type="checkbox"/>
▼ Normalization	
▼ NormalizeData	
Method	time; ensemble

SignalType
Type of signal to analyze. If 'Components', data in EEG.icaact will be processed. If 'Channels' EEG.data will be processed. If 'Sources' EEG.srcpot will be processed.

Help Cancel **OK**

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

SIFT

Apps

To-Do

Fin

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

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

Modeling Algorithm (2)

Linear

Nonlinear

State-Space Modeling

Linear Kalman Filtering



Dual Extended Kalman Filtering



Cubature Kalman Filtering



Sparsely Connected Components Analysis (SCSA)

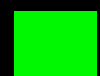


Adaptive Mixture Impulse Response Analysis (AMIRA)



Nonparametric VAR Modeling

Spectral Matrix Factorization



fully implemented



alpha-testing



coming soon

Preprocessing

Modeling

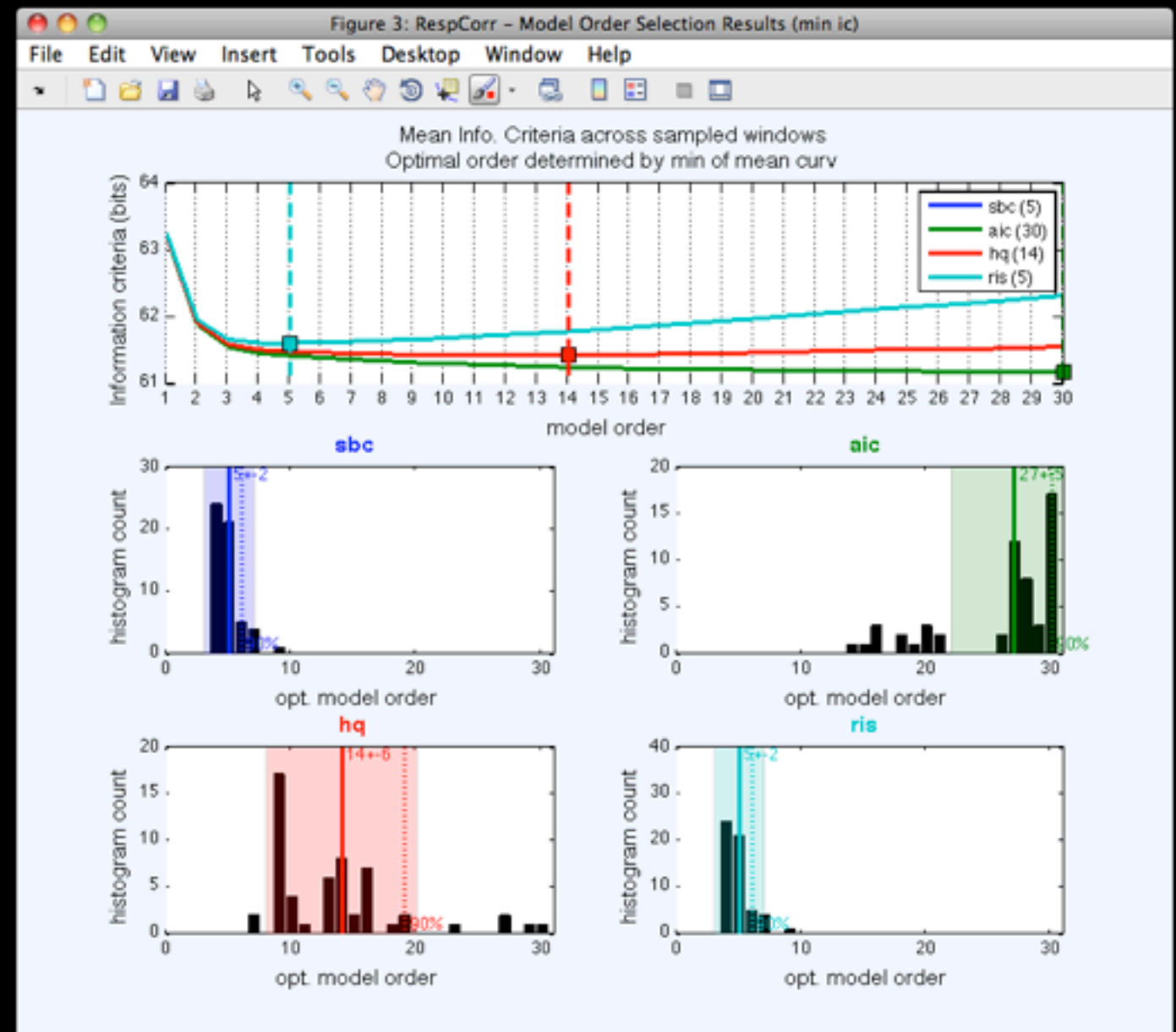
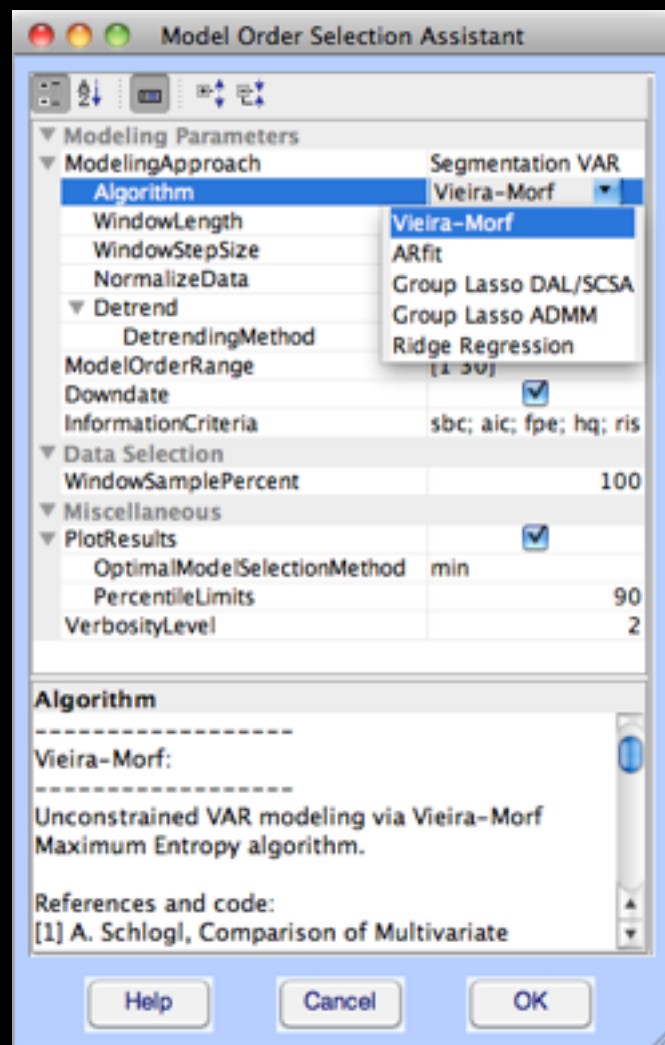
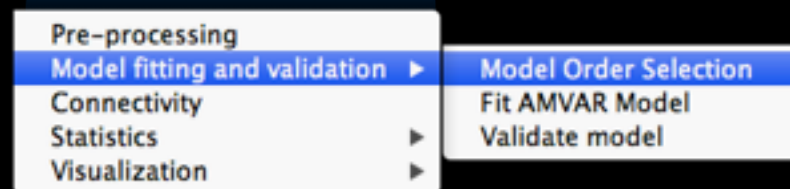
Statistics

Visualization

Model Fitting

Validation

Connectivity



Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

- Pre-processing
- Model fitting and validation ▶
 - Model Order Selection
 - Fit AMVAR Model
 - Validate model
- Connectivity
- Statistics
- Visualization

Autoregressive Model Fitting

Modeling Parameters	
Algorithm	Group Lasso DAL/SCSA
▼ DAL_Options	
RegularizationParam	0.1
ShrinkDiagonal	<input checked="" type="checkbox"/>
LossFunction	HyperbolicSecant
Verbosity	0
DAL_NVP_Args	{}
ModelOrder	18
WindowLength	0.4
WindowStepSize	0.03
EpochTimeLimits	[]
WindowSamplePercent	100
▼ Window Preprocessing	
NormalizeData	<input type="checkbox"/>
▼ Detrend	
DetrendingMethod	constant
▼ Miscellaneous	
Timer	<input type="checkbox"/>
VerbosityLevel	2

Algorithm
 Sparse VAR modeling via Group Lasso.
 This option estimates sparse VAR coefficients using the

Help Cancel OK

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

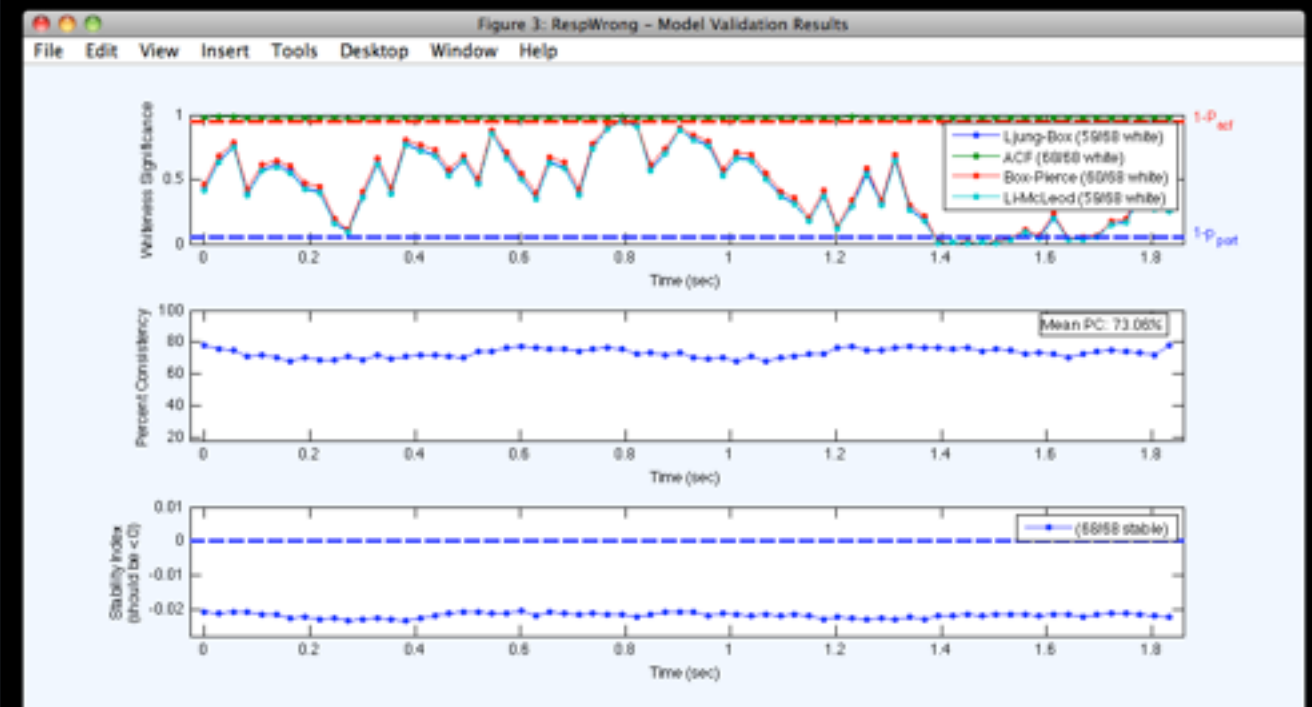
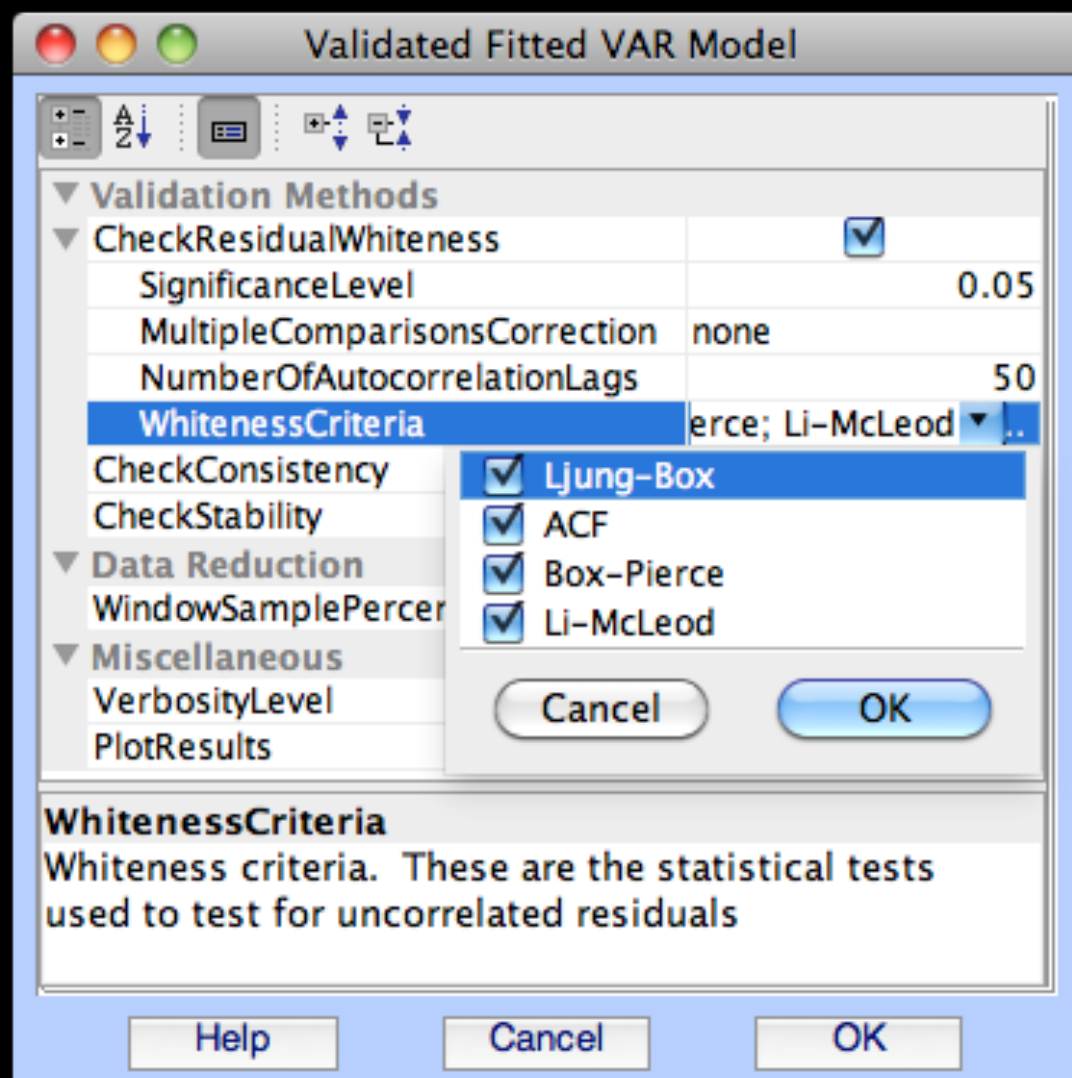
Connectivity

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

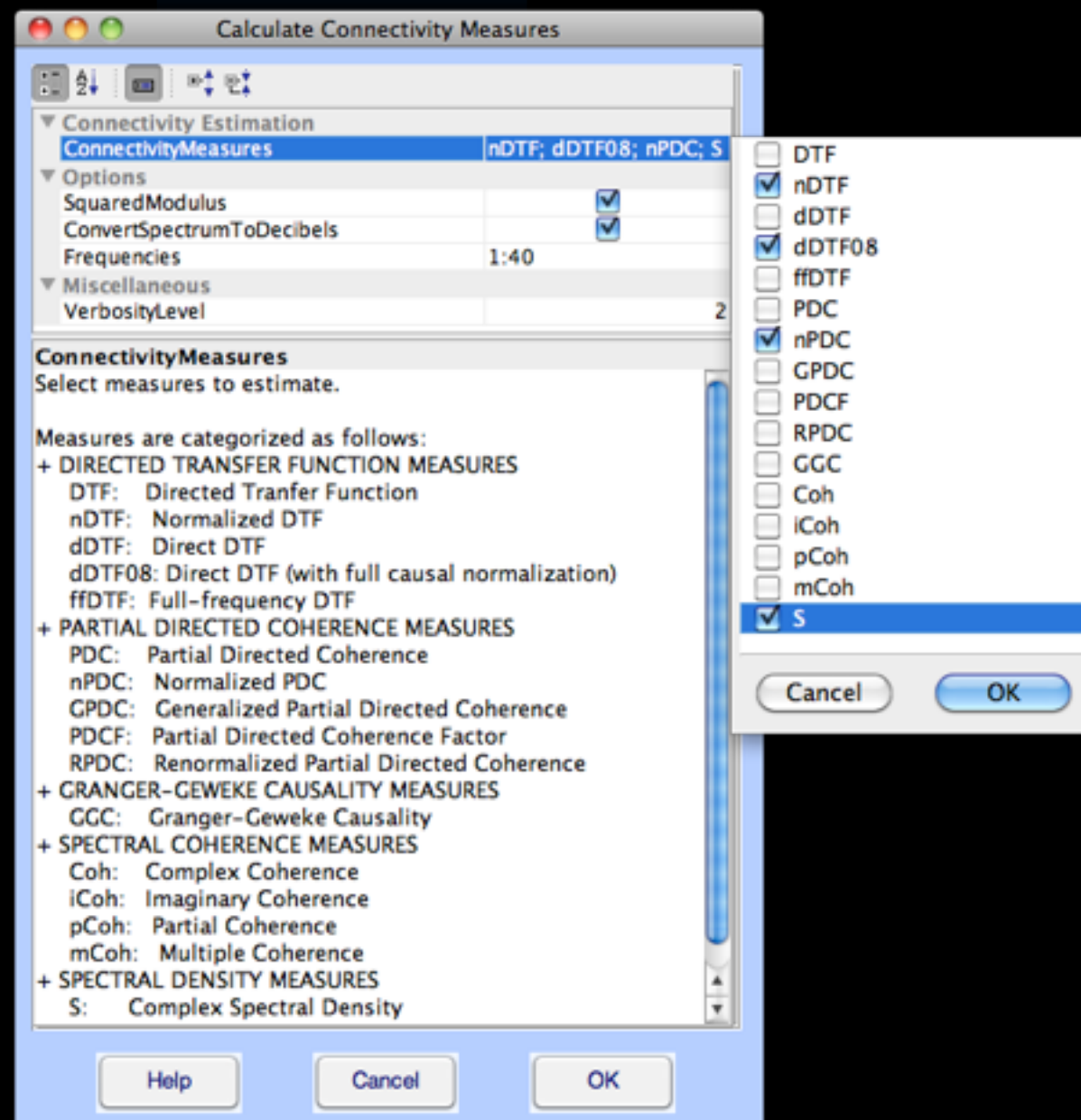
Visualization

Model Fitting

Validation

Connectivity

- 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	$H_{\text{null}}, H_{\text{base}}, H_{\text{AB}}$	✓	
Theiler phase randomization Applies to: all	H_{null}		✓
Bootstrap, Jackknife, Cross-Validation Applies to: all	$H_{\text{AB}}, H_{\text{base}}$		✓
Confidence intervals using Bayesian smoothing splines Applies to: all	$H_{\text{base}}, H_{\text{AB}}$	✓	✓

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

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

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

fully implemented

alpha-testing

coming soon

Preprocessing

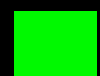
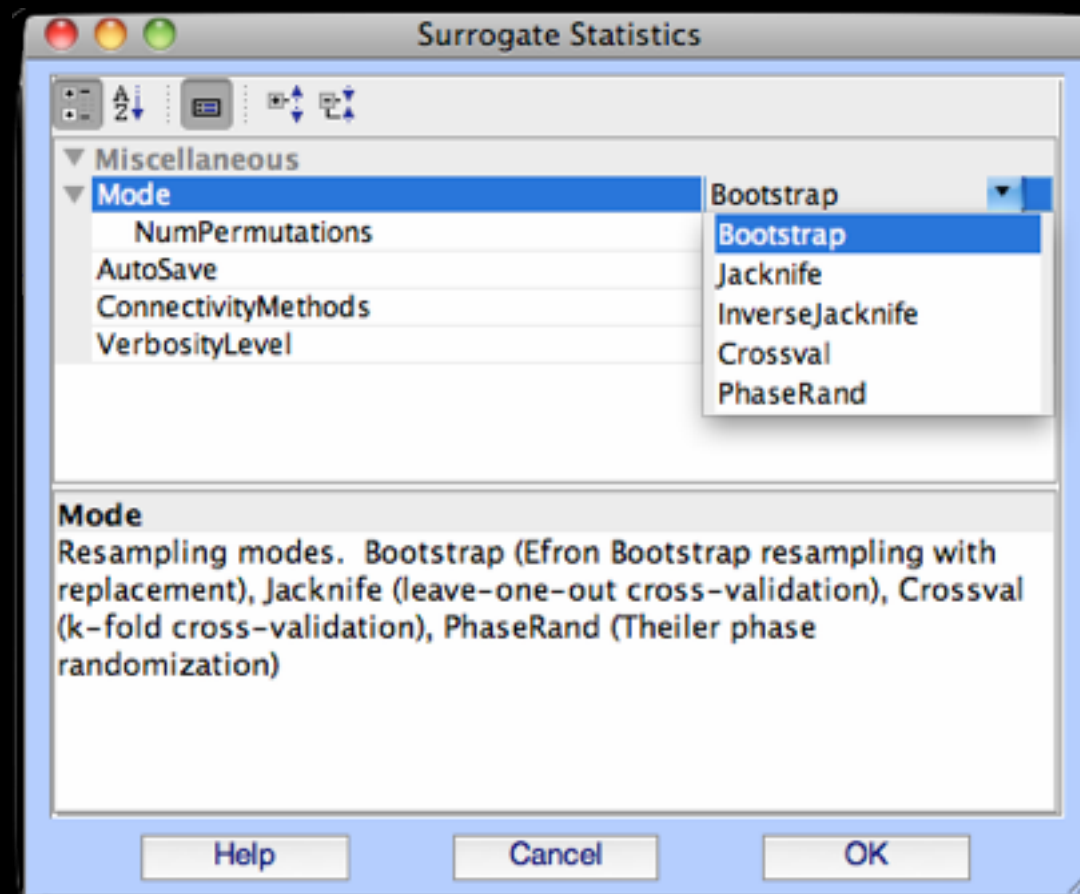
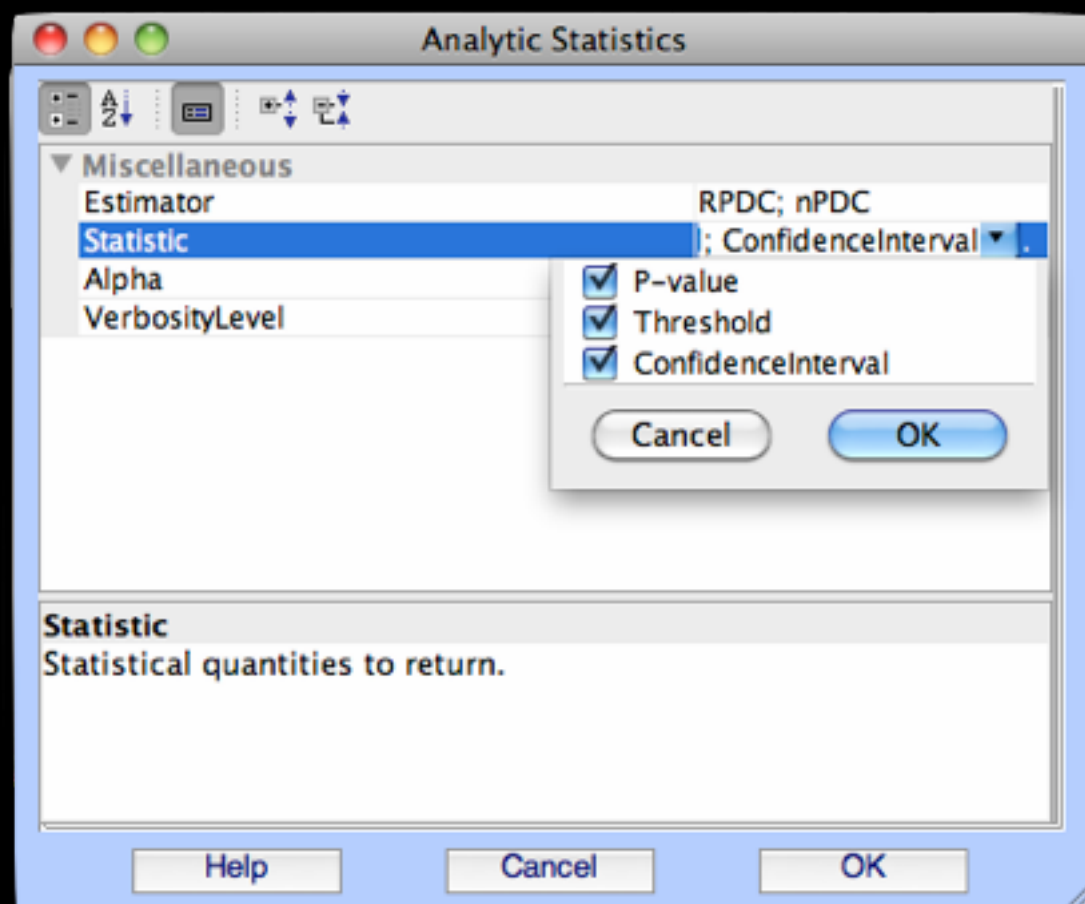
Modeling

Statistics

Visualization

Parametric

Non-parametric



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)

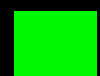
and more ...

SIFT

Apps

To-Do

Fin



fully implemented

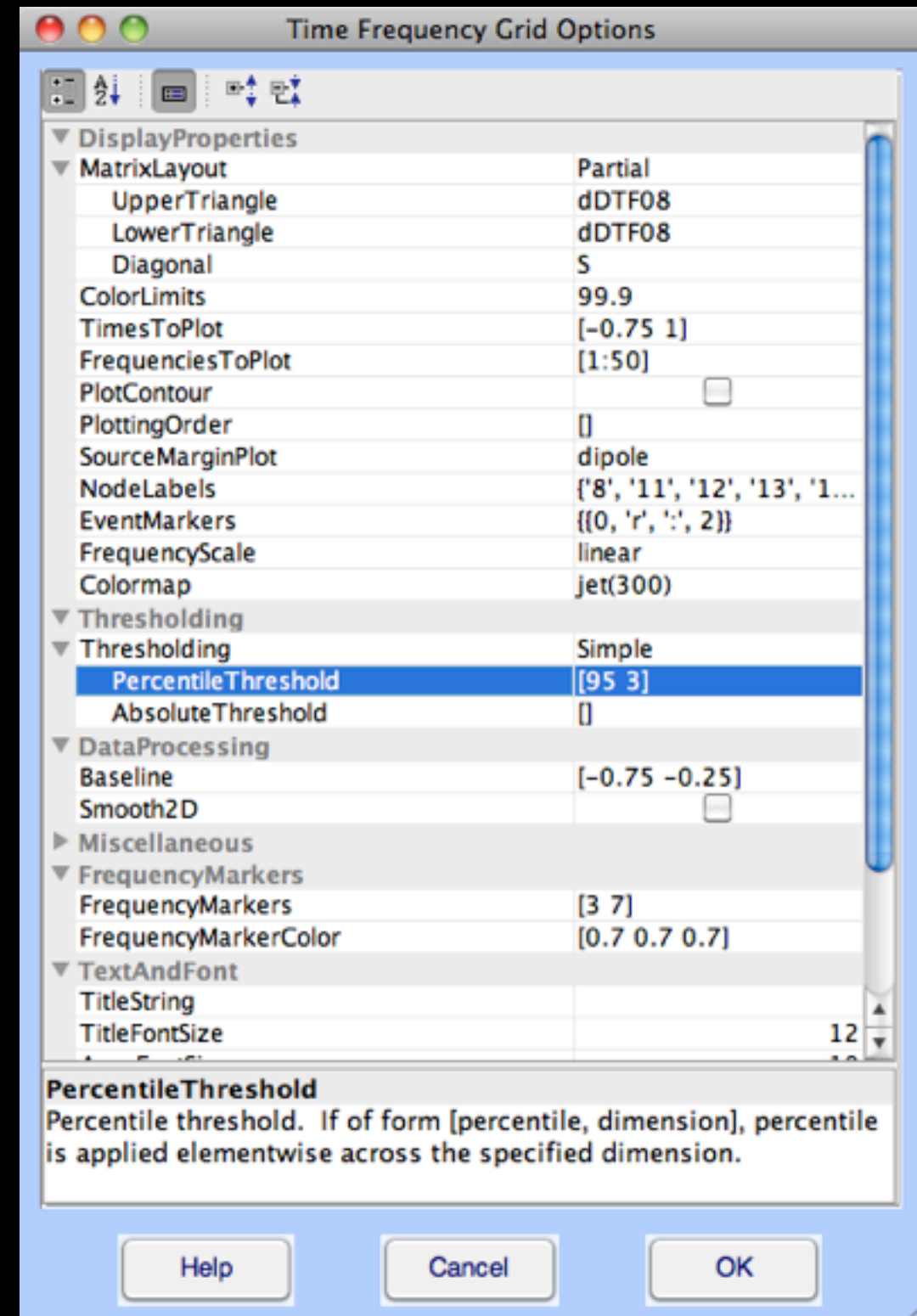
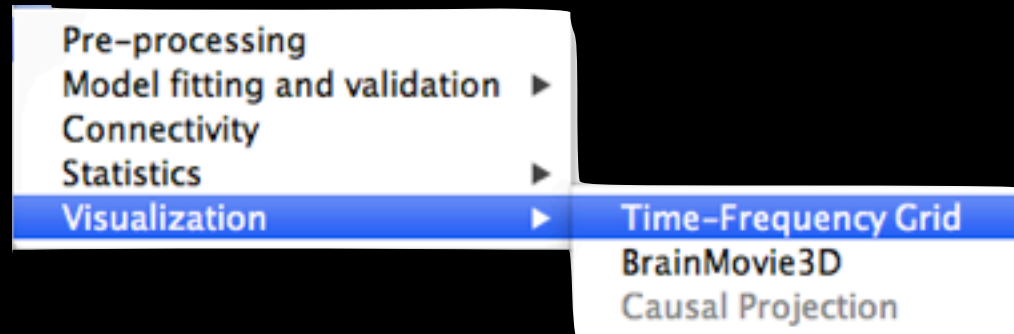


alpha-testing



coming soon

Interactive Time-Frequency Grid



Interactive Time-Frequency Grid

Intro

Theory

SIFT

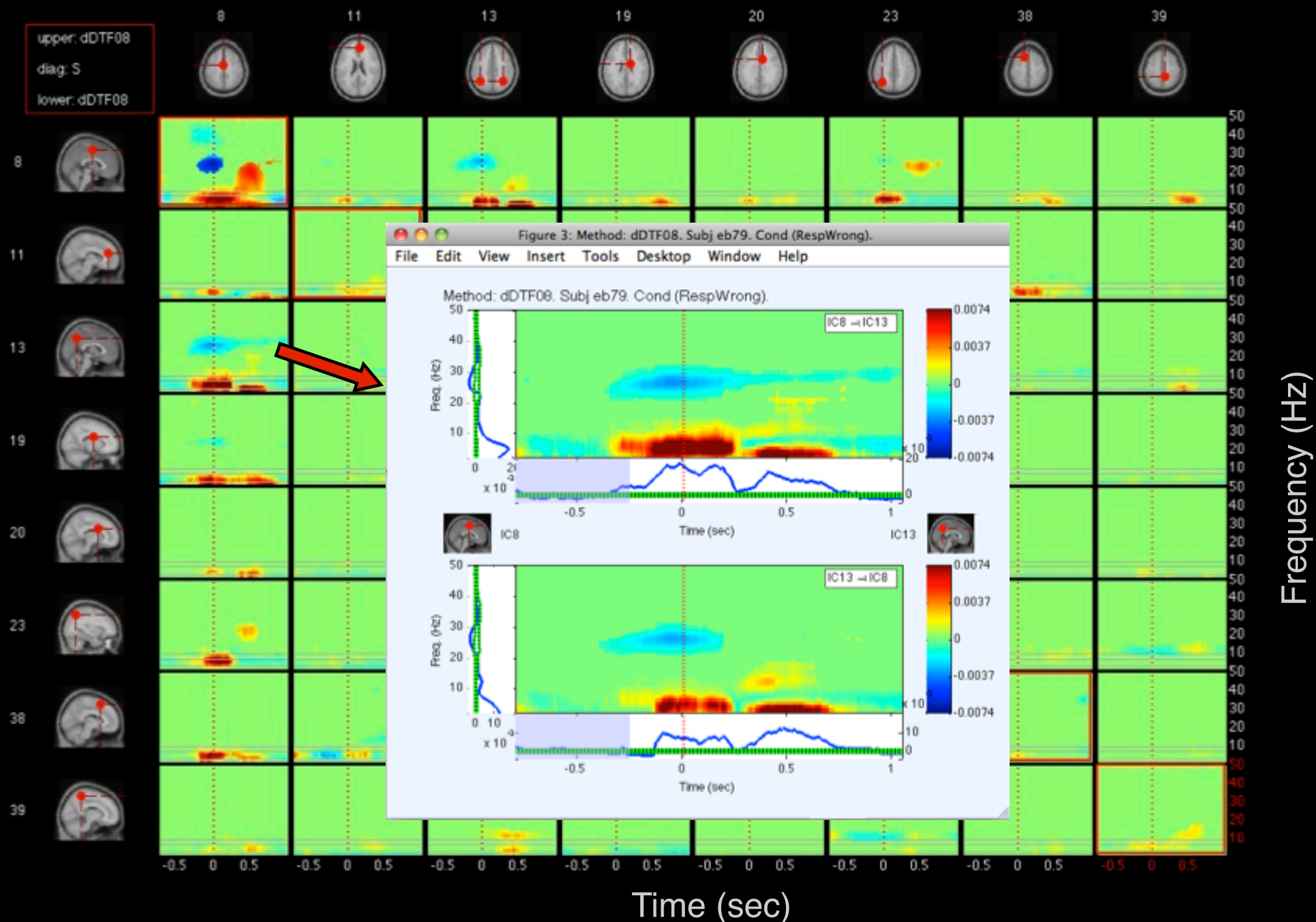
Apps

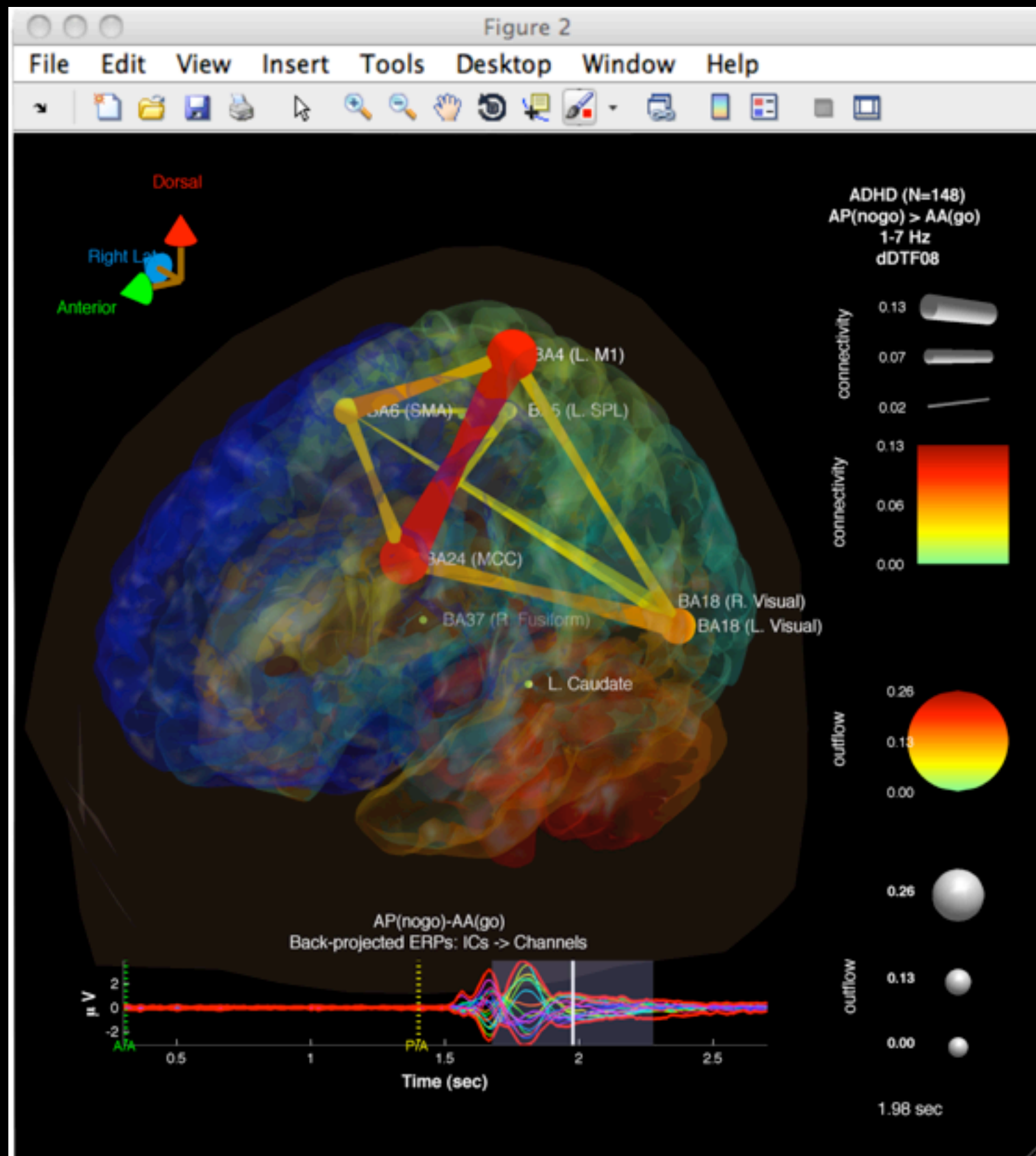
To-Do

Fin

Causality TO

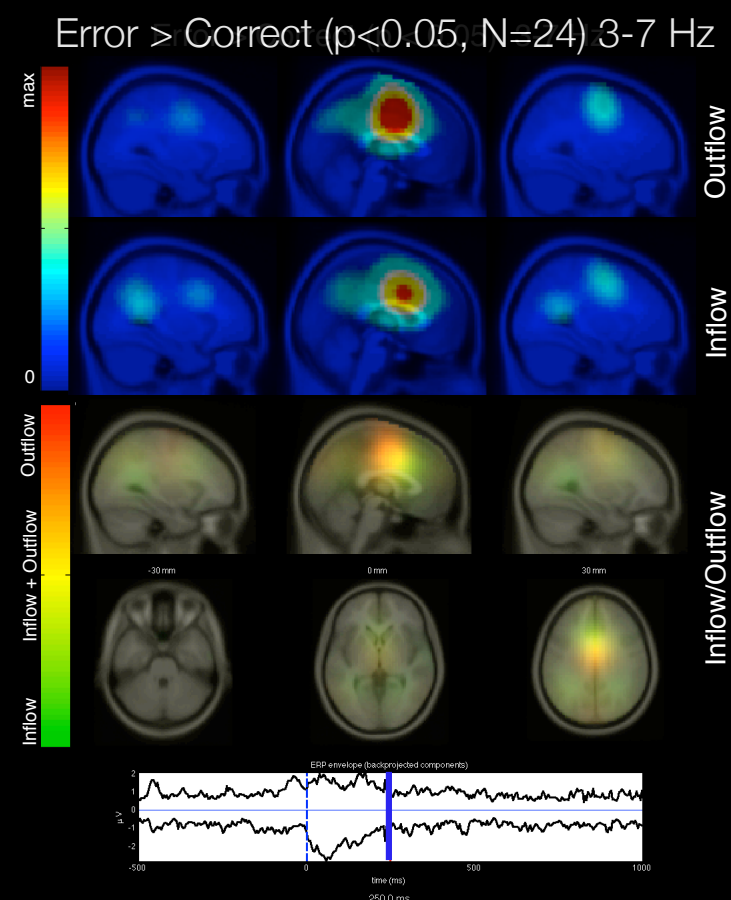
Causality FROM





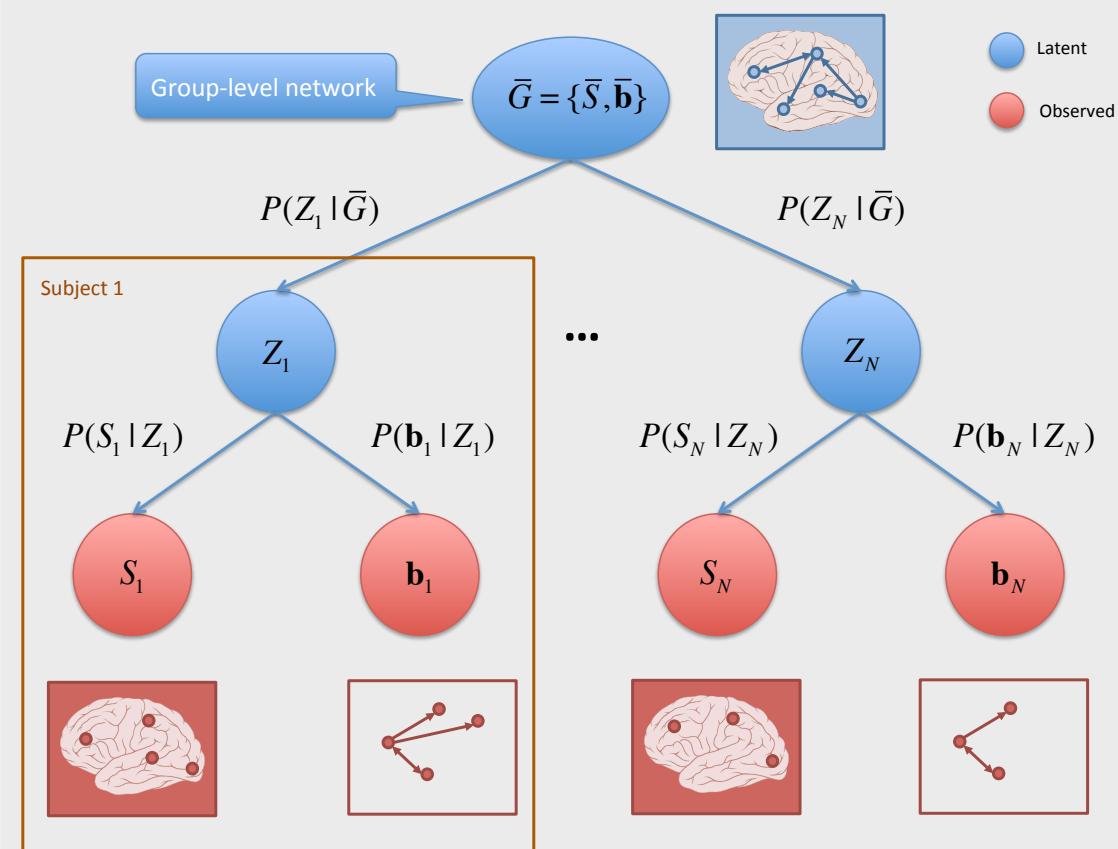
Group Analysis (in prep)

Causal/Measure Projection



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

Bayesian Hierarchical Model



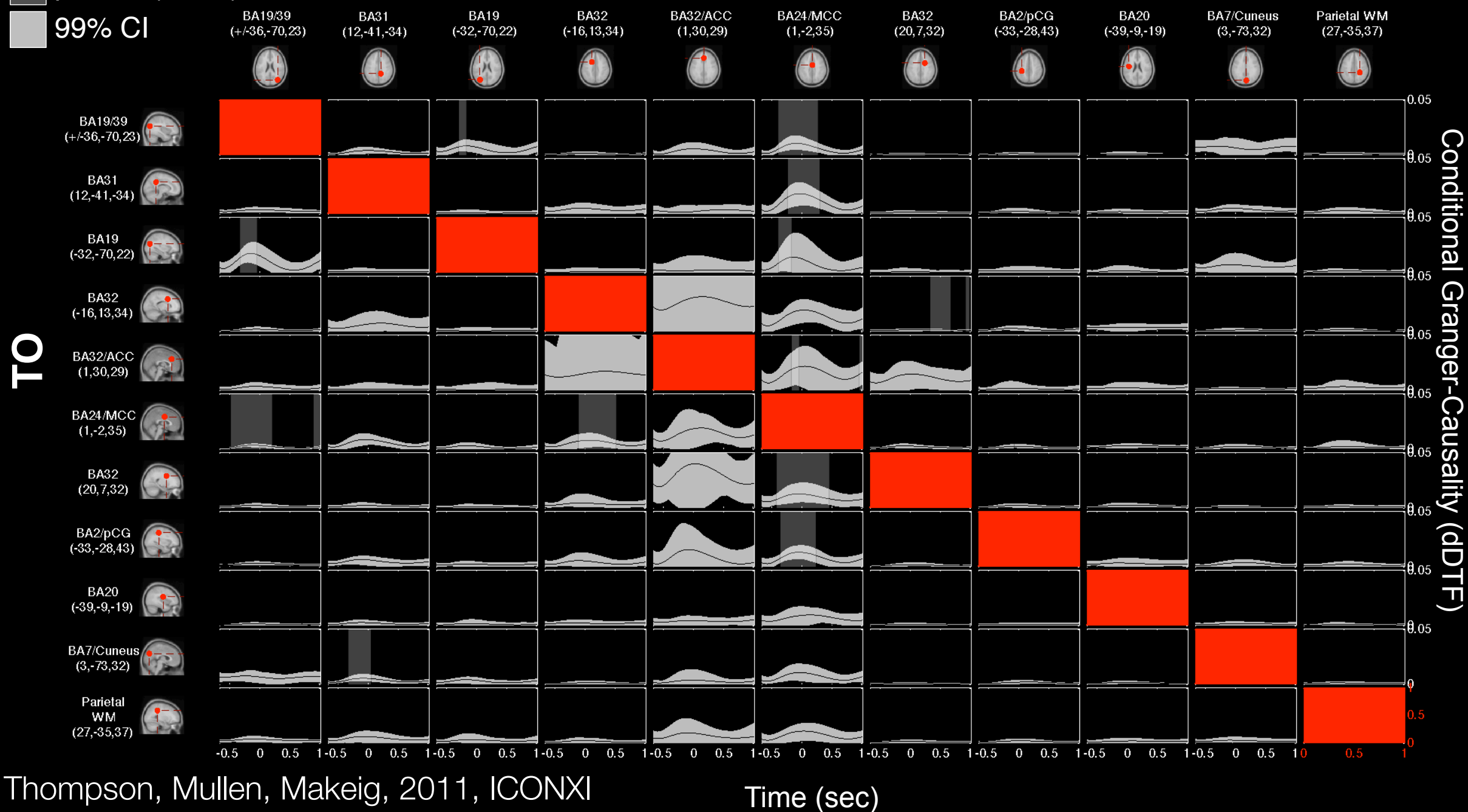
Thompson, Mullen, Makeig, 2011, ICONXI
Thompson, Mullen, Makeig, 2012, *in prep*

Bayesian Multi-Subject Inference

Theta-band (4-8 Hz) dDTF
Response-locked error trials

■ $p < 0.01$ (N=24)
■ 99% CI

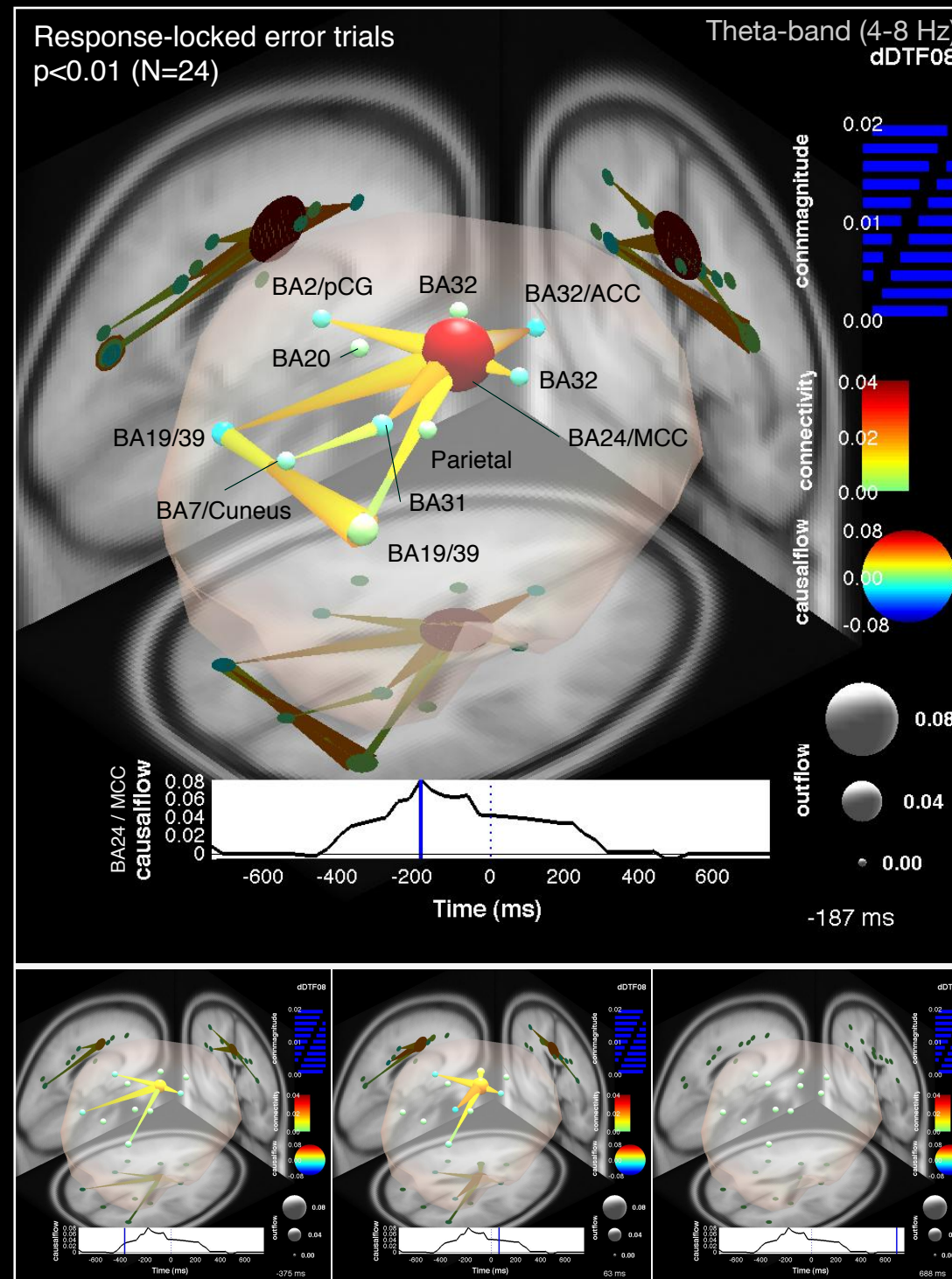
FROM



Thompson, Mullen, Makeig, 2011, ICONXI

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

Bayesian Multi-Subject Inference



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	

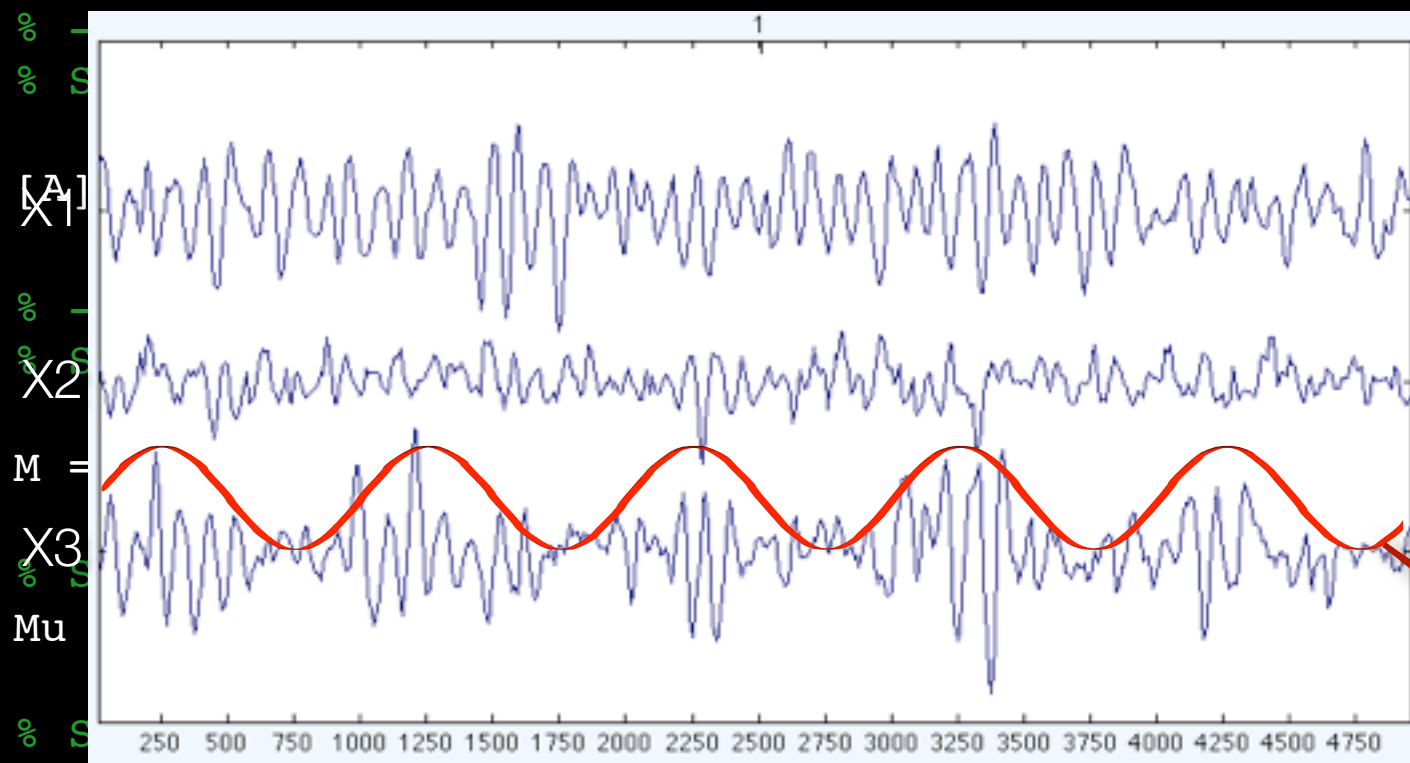
```
% Example: Trivariate damped coupled oscillators with sinusoidally-modulated coupling
```

```
% -----  
% 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)
```

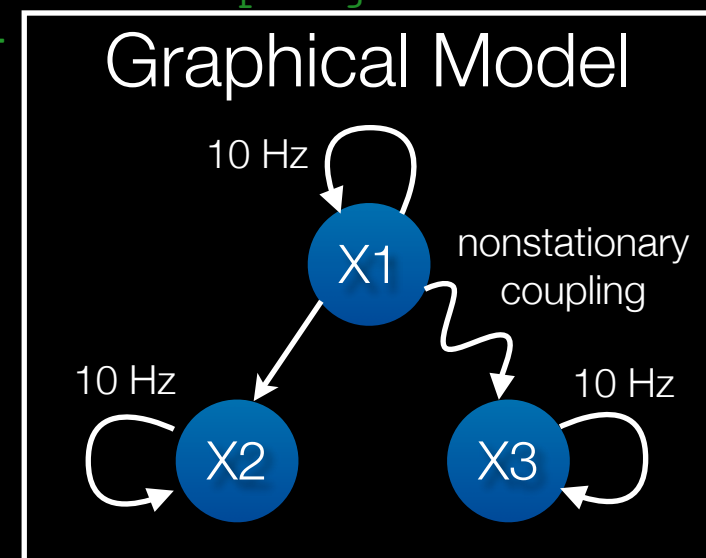
```
expr = {...  
    ['x1(t) = ' sim_dampedOscillator(f0,9,Fs,1) ' + e1(t)'] ...  
    ['x2(t) = ' sim_dampedOscillator(f0,2,Fs,2) ' + -0.1*x1(t-2) + e2(t)'] ...  
    ['x3(t) = ' sim_dampedOscillator(f0,2,Fs,3) ' + {0.3*sin(2*pi*t/100)+0.3}*x1(t-2) + e3(t)'] ...  
};
```

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



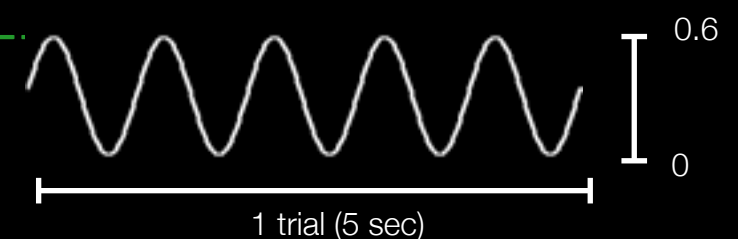
```
sigma = 1;  
E = sigma*eye(M);
```

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



Time-varying X1 → X3 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

Epileptic Seizure

DynamicalEquations

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

ModelOrder

6

SetDynamics

☐

SimParams

SamplingRate

100

TrialLength

5

NumTrials

100

BurnInSamples

1,000

CheckStability

☒

DataGenParams

NoiseCovMat

1

ProcessMean

☐

NoiseDistribution

gengauss

ScaleParam

1

ShapeParam

2

VerbosityLevel

2

OutputFormat

BuildEEGLABStructure

☒

ExportGroundTruth

☐

SetName

Visualization

PlotData

☒

PlotGraphicalModel

☒

Simulation

Select a simulation.

Help

Cancel

OK

Epileptic Seizure

Schelter 2005 Eq 5

Schelter 2009 Eq 3.1

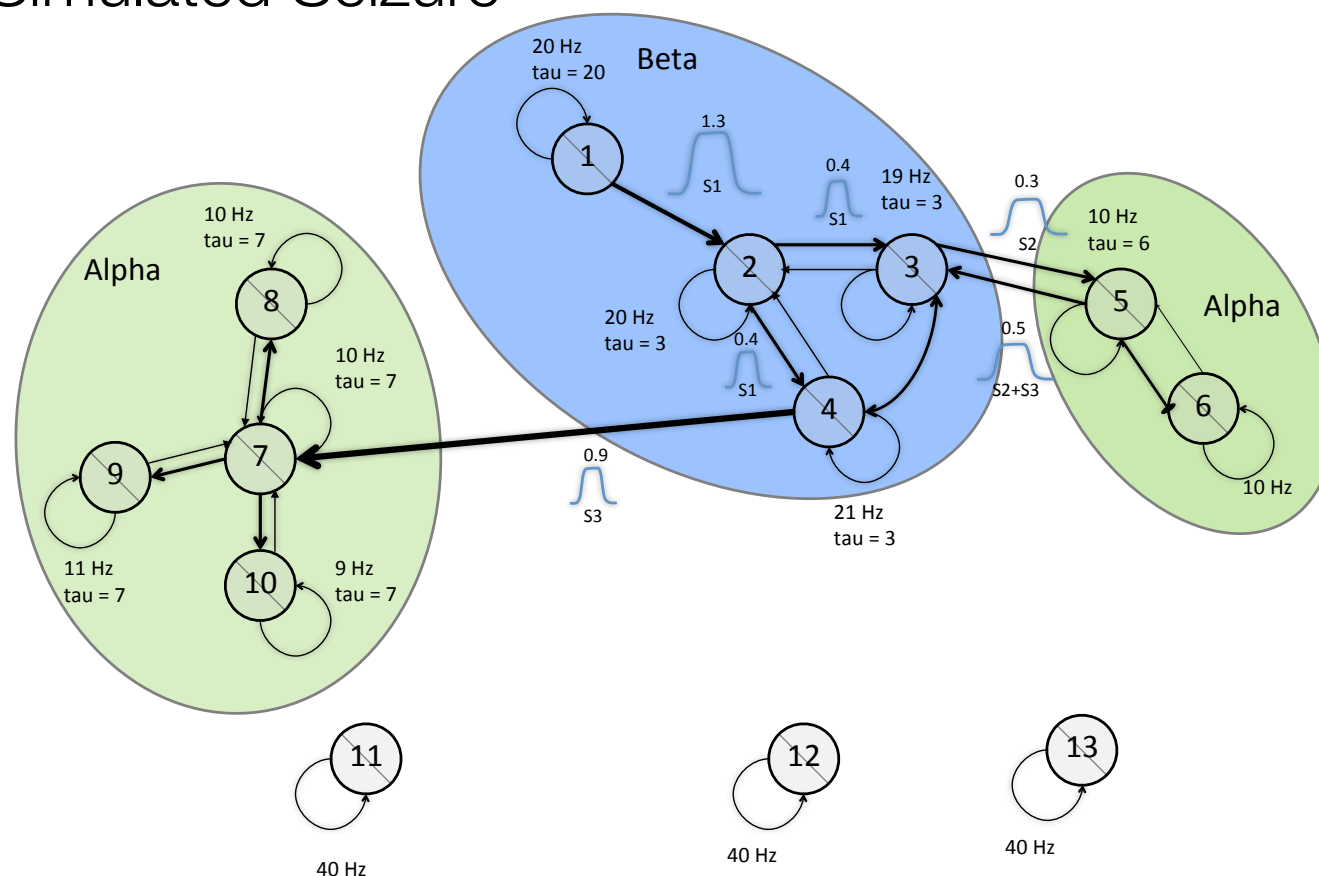
Schelter 2009 Eq 3.2

Bivariate Coupled Oscillator

Trivariate Coupled Oscillator

Simulation

Simulated Seizure

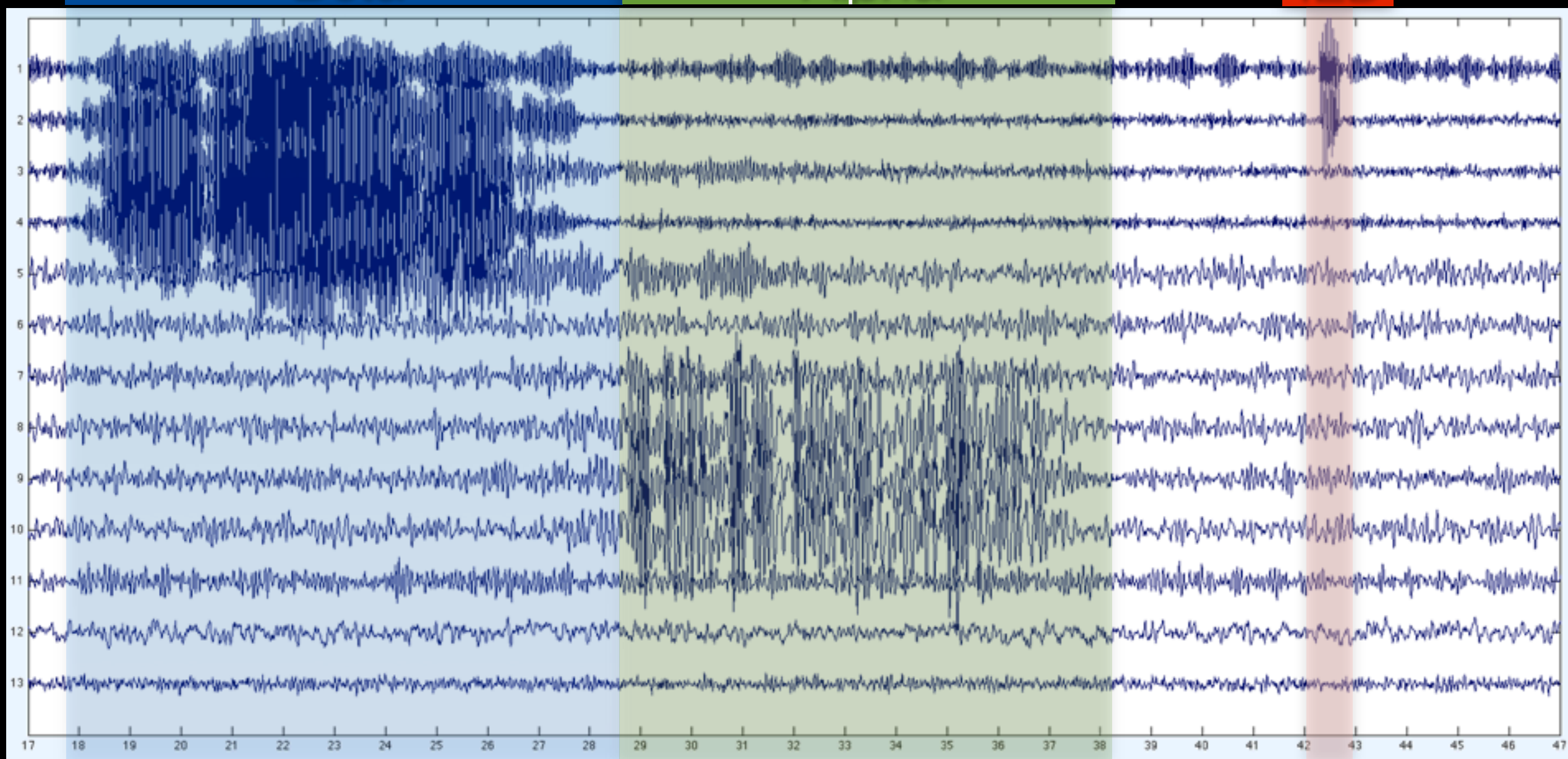


Simulated Seizure Sources

Beta

Alpha

IED



Where do I get SIFT?

sccn.ucsd.edu/wiki/SIFT

SIFT
Source Information Flow Toolbox
Version 0.1-Alpha

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.antilipsi.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

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 - 3.4.1 Segmentation-based Adaptive VAR (AMVAR) 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
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- 4.1. Time-Domain GC
- 4.2. Frequency-Domain GC
- 4.3. A partial list of VAR-based spectral, coherence and GC estimators
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- 4.5. (Cross-) correlation does not imply (Granger-) causation

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- 5.2. Nonparametric surrogate statistics
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 - 6.6.1. Theory: selecting a window length
 - 6.6.1.1. Local Stationarity
 - 6.6.1.2. Temporal Smoothing
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- 6.7. Connectivity Estimation
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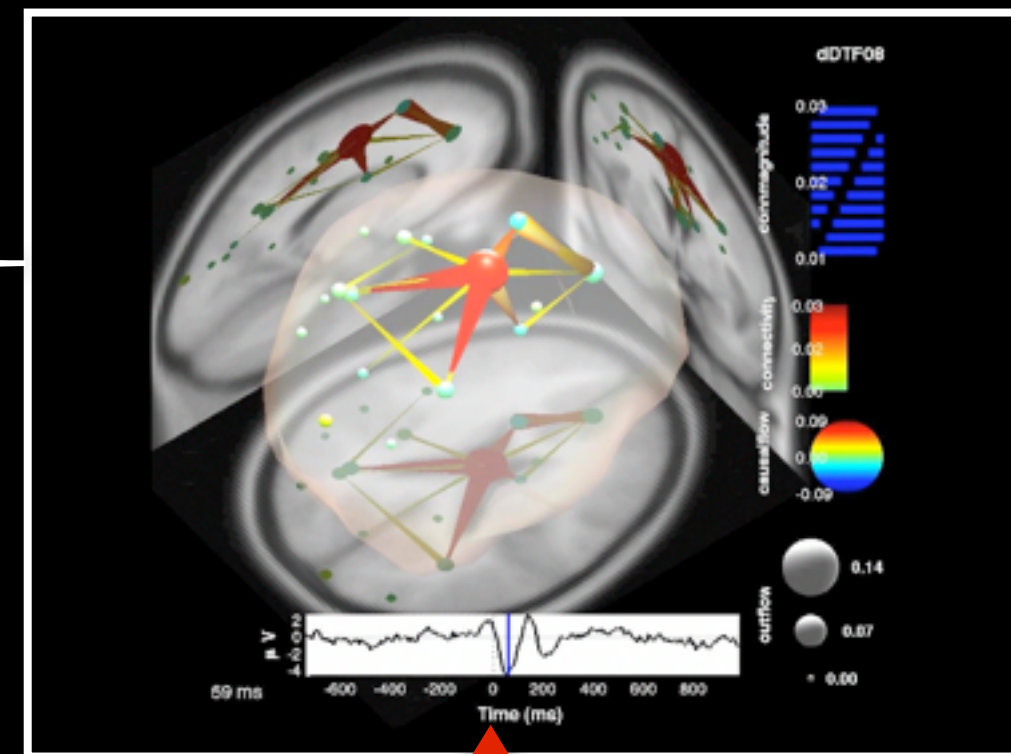
7. Conclusions and Future Work

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)



error event

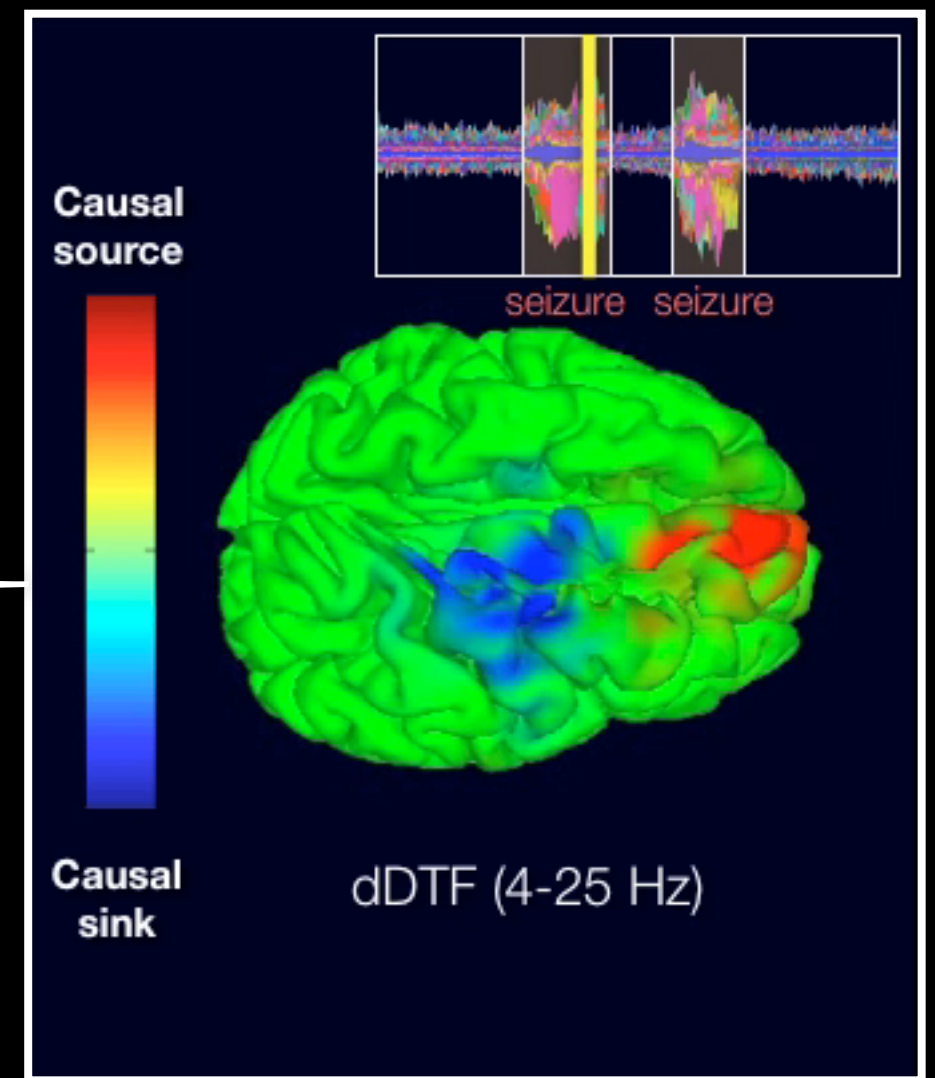
Mullen et al, *HBM*, Barcelona, 2010

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

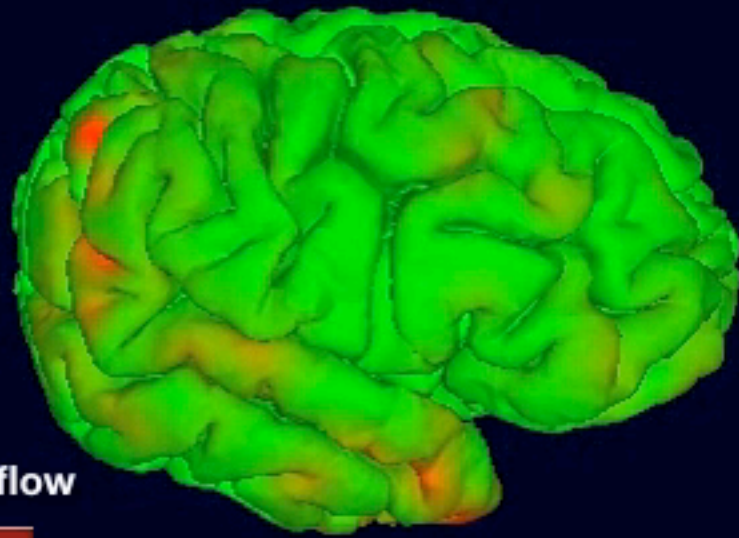
Outflow

Causal Flow

Outflow



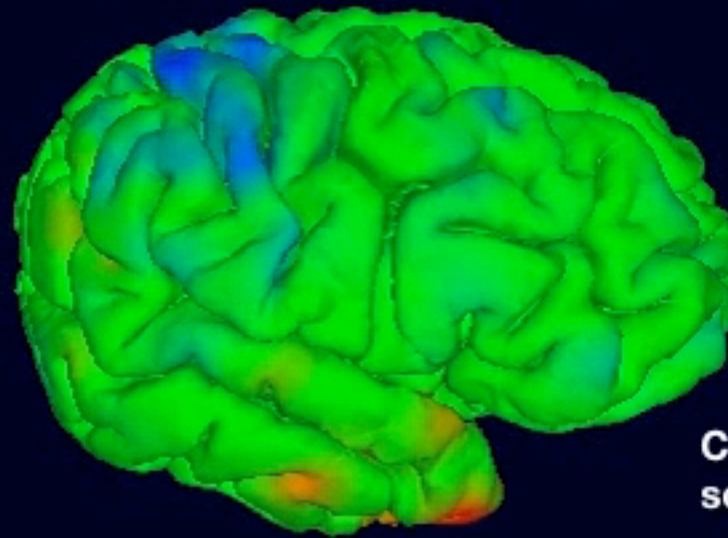
No Flow



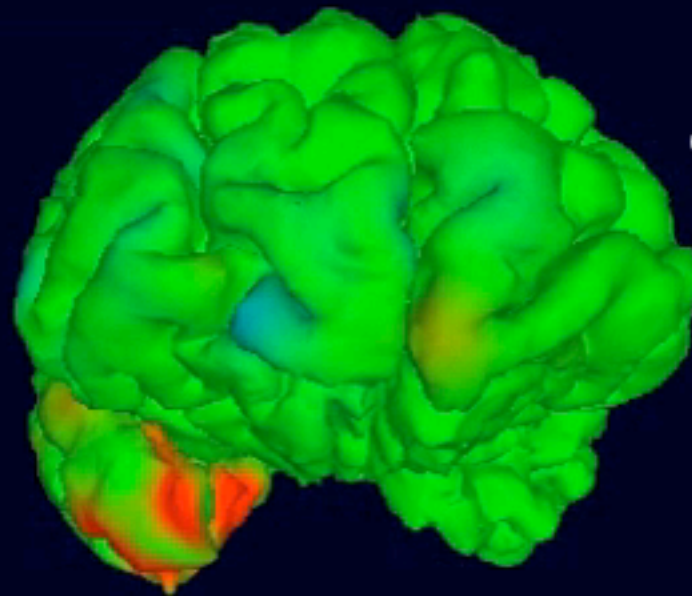
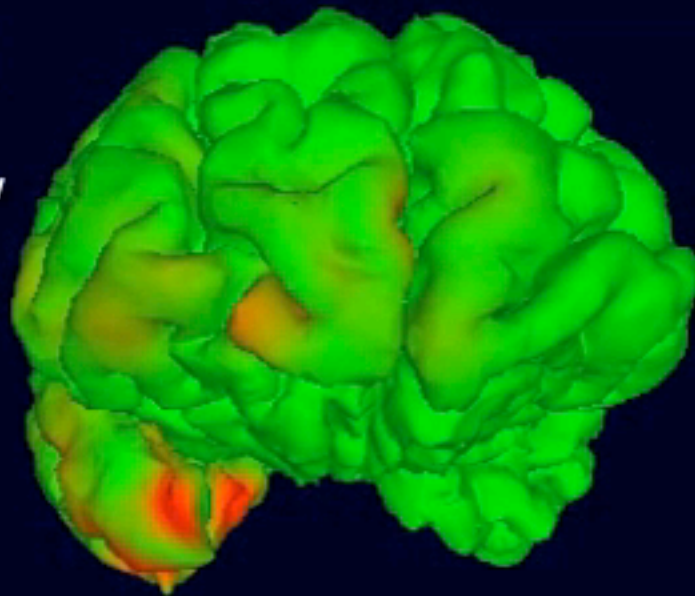
Causal source



Causal sink

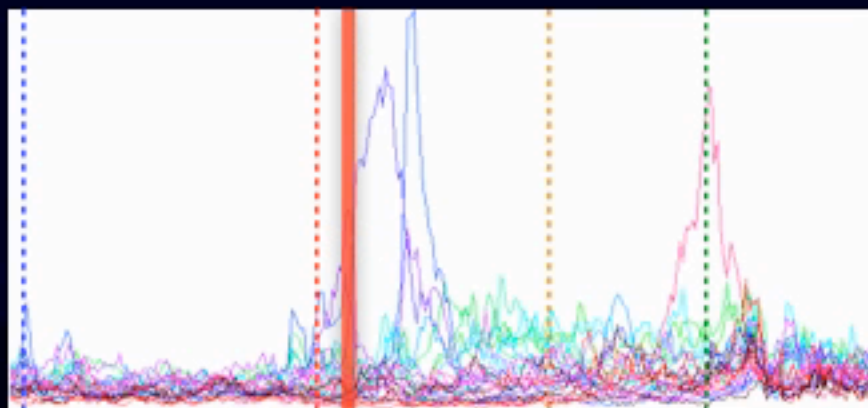


dDTF (2-40 Hz)

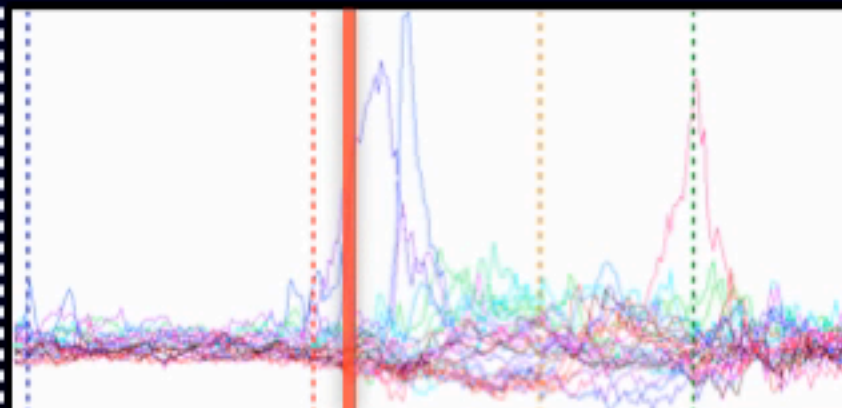


- **ECoG Data**
- 104 ECoG (subdural) electrodes
- Surgical Outcome: Negative
- Provided by Dr. Ashesh Mehta (Feinstein Institute for Clinical Research, NY)
- **Source Reconstruction**
- 5-Model **AMICA** decomposition
- Selection of globally dominant model
- Selection of **29 ICs** comprising independent 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

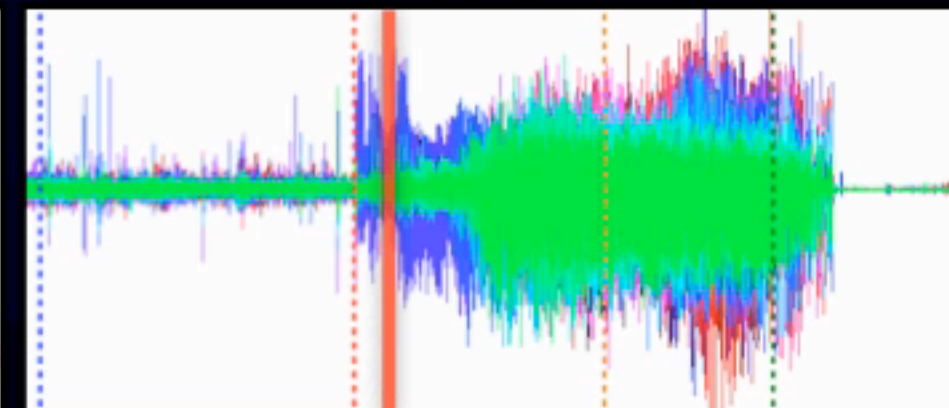
AMICA IC activations



Time (sec)



Time (sec)

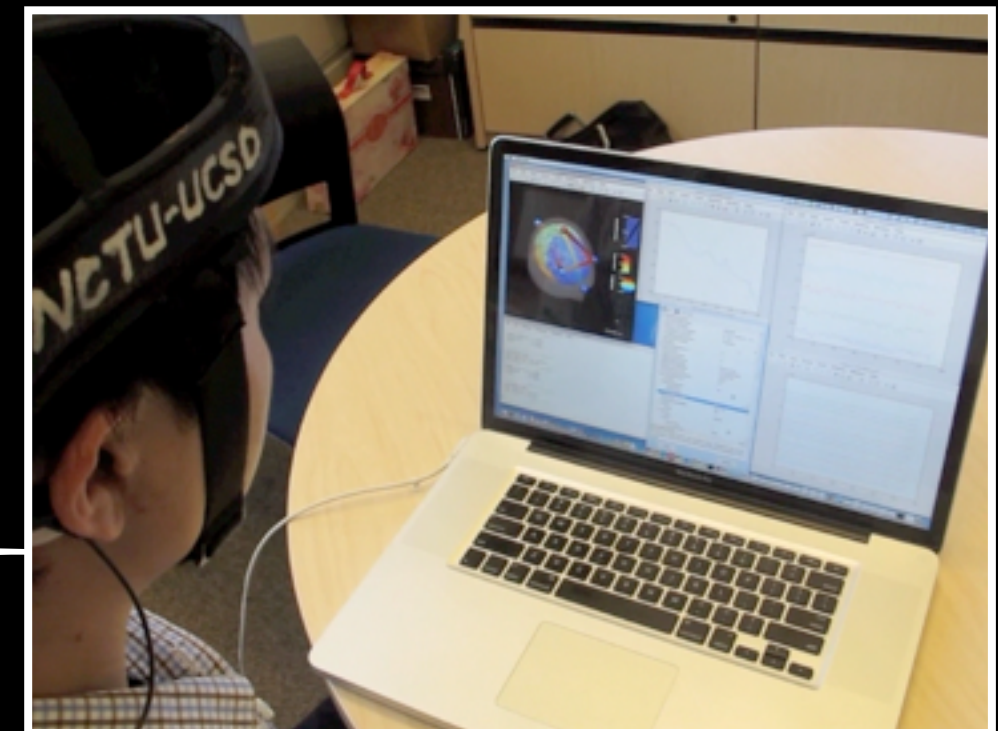
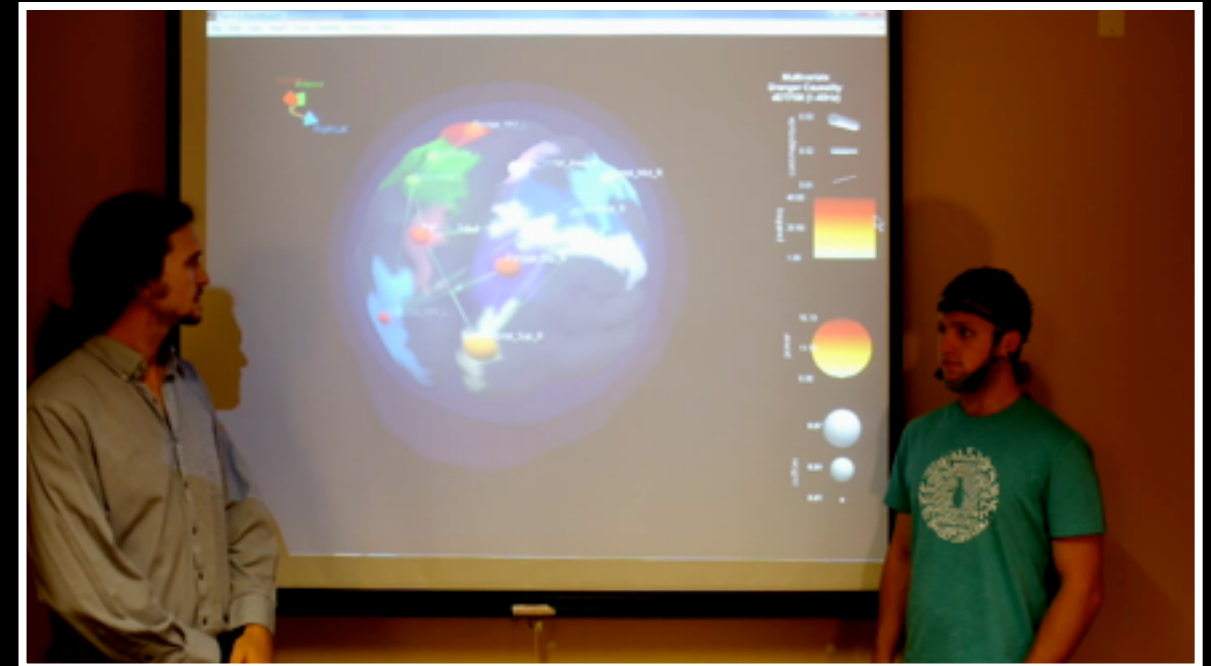
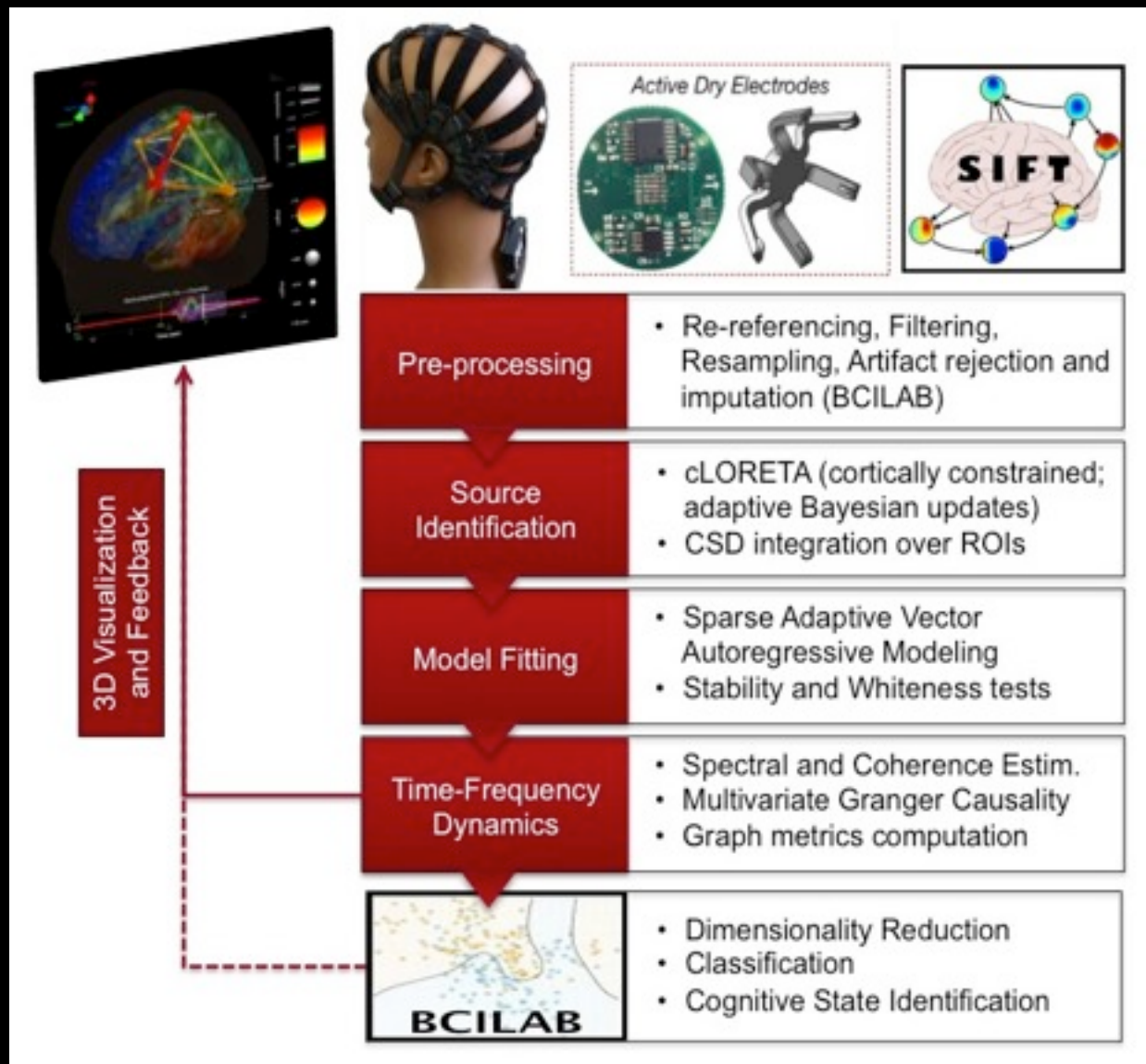


0

Time (sec)

300

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