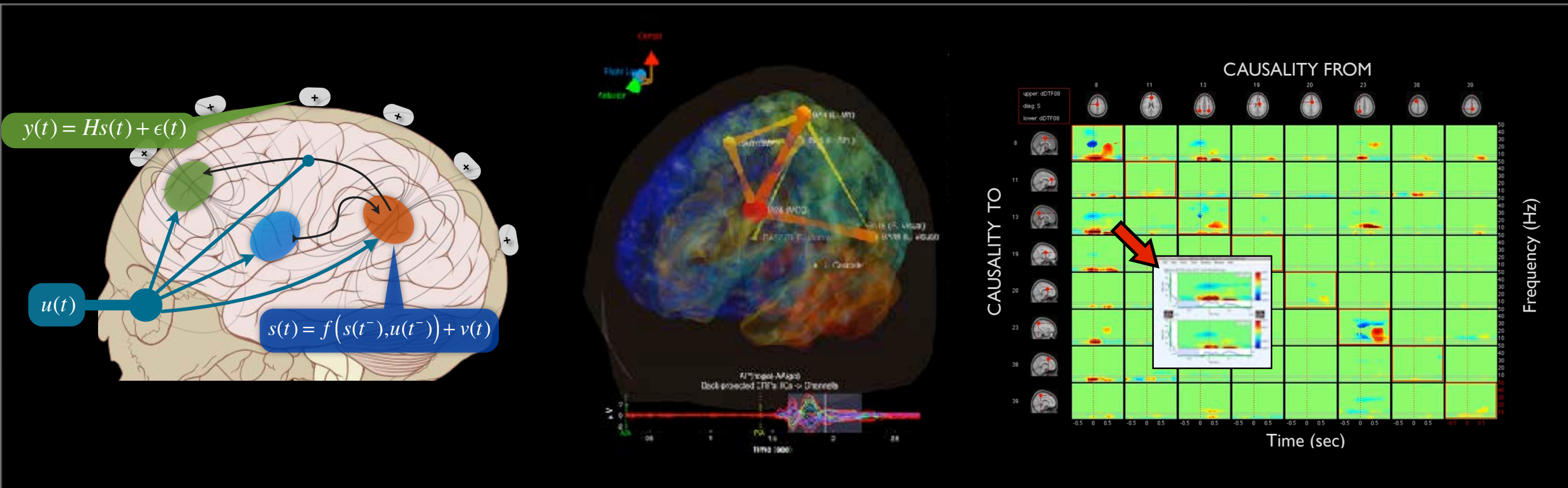


The Dynamic Brain I: Modeling Neural Dynamics and Interactions from M/EEG



Tim Mullen, PhD

Outline

Theoretical Foundations I

- Functional Connectivity Measures (PLV, PAC, Coherence)
- Linear Dynamical Systems and the VAR model
- Granger Causality and Effective Connectivity Measures
- Scalp versus Source
- Adapting to Time-Varying Dynamics

Practicum: Hands-On Walkthrough of SIFT

Preview Outline (Sunday)

Theoretical Foundations II



Model Validation



Multivariate vs. Bivariate



Imposing Constraints



Single-trial Estimation and State-Space Models



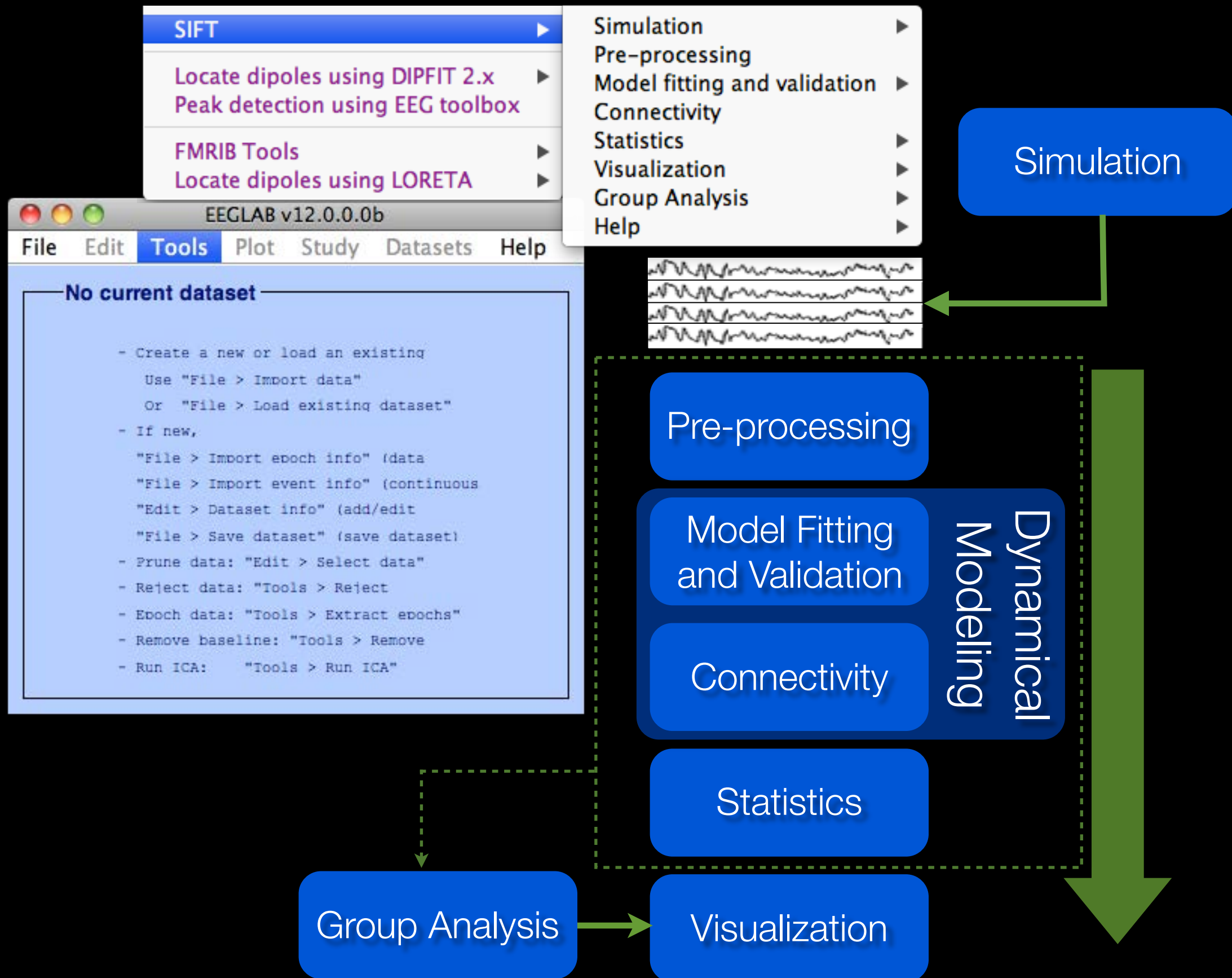
Statistical Testing

Practicum: Hands-On Simulation-based training

Source Information Flow Toolbox (SIFT)

- ✦ **Requirements:** EEGLAB, MATLAB 2008b+
- ✦ Some functions leverage: Signal Processing Toolbox, Statistics Toolbox

DOWNLOAD SIFT FROM THE EEGLAB EXTENSION
MANAGER (File—>Manage EEGLAB Extensions—>Data
Processing Extensions)

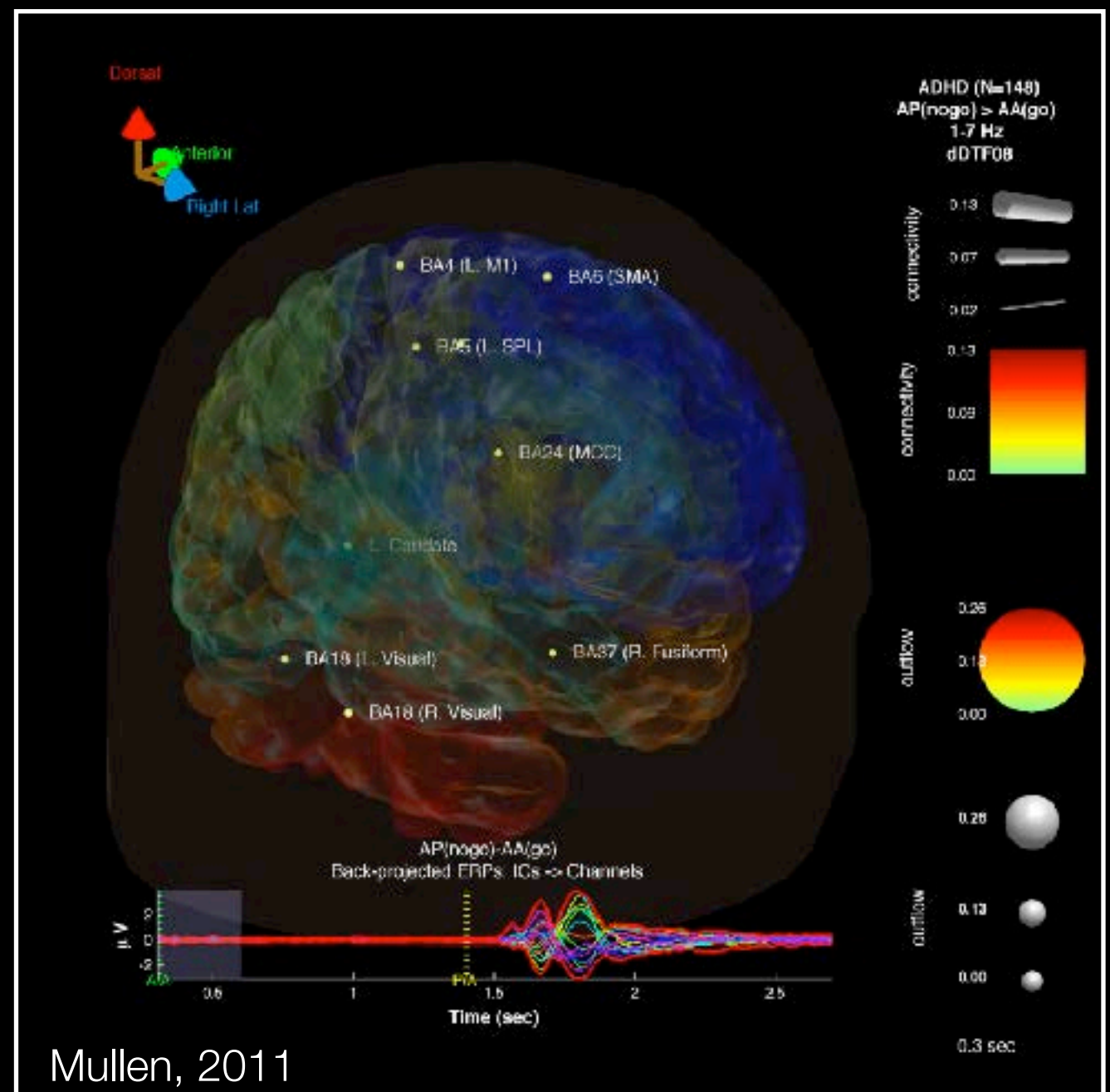


The Dynamic Brain



Tim Mullen

- ✦ 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

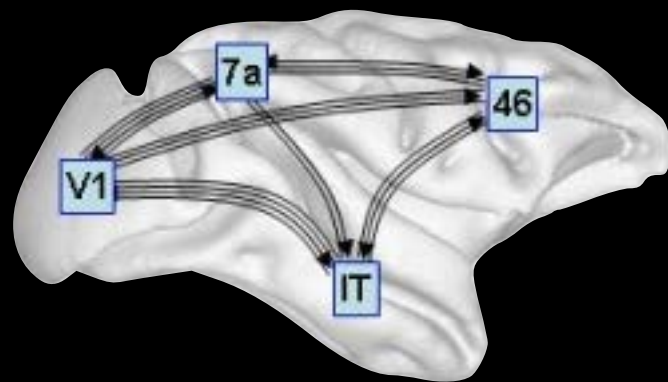
Box and Draper (1987):

“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

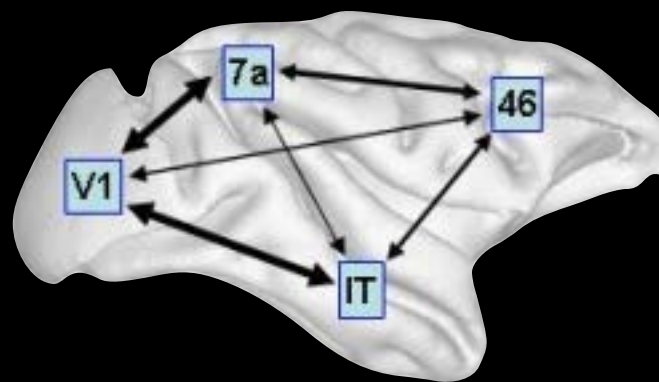
(Bullmore and Sporns, *Nature*, 2009)

Structural



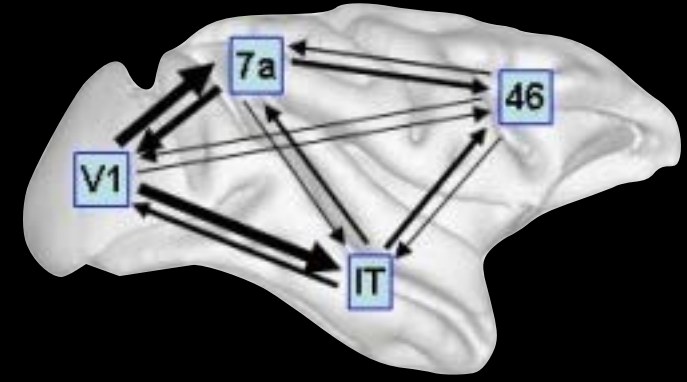
state-invariant,
anatomical

Functional



dynamic, state-dependent,
correlative, symmetric

Effective



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

Hours-Years

milliseconds-seconds

Temporal Scale

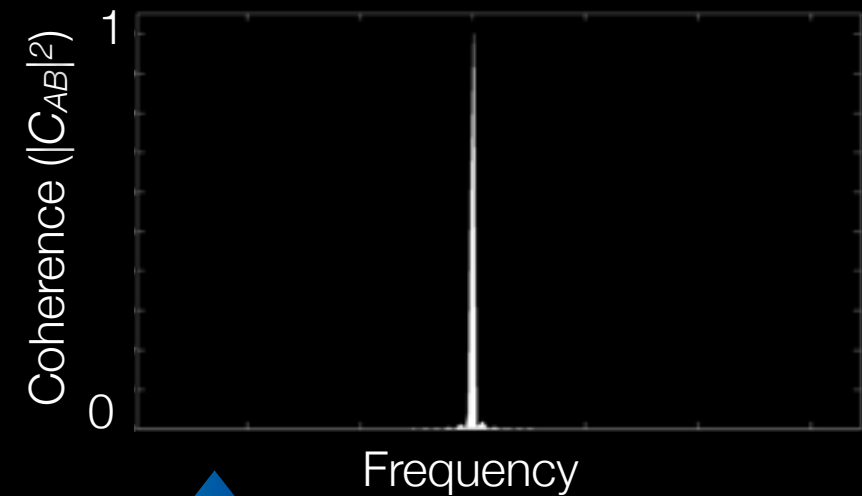
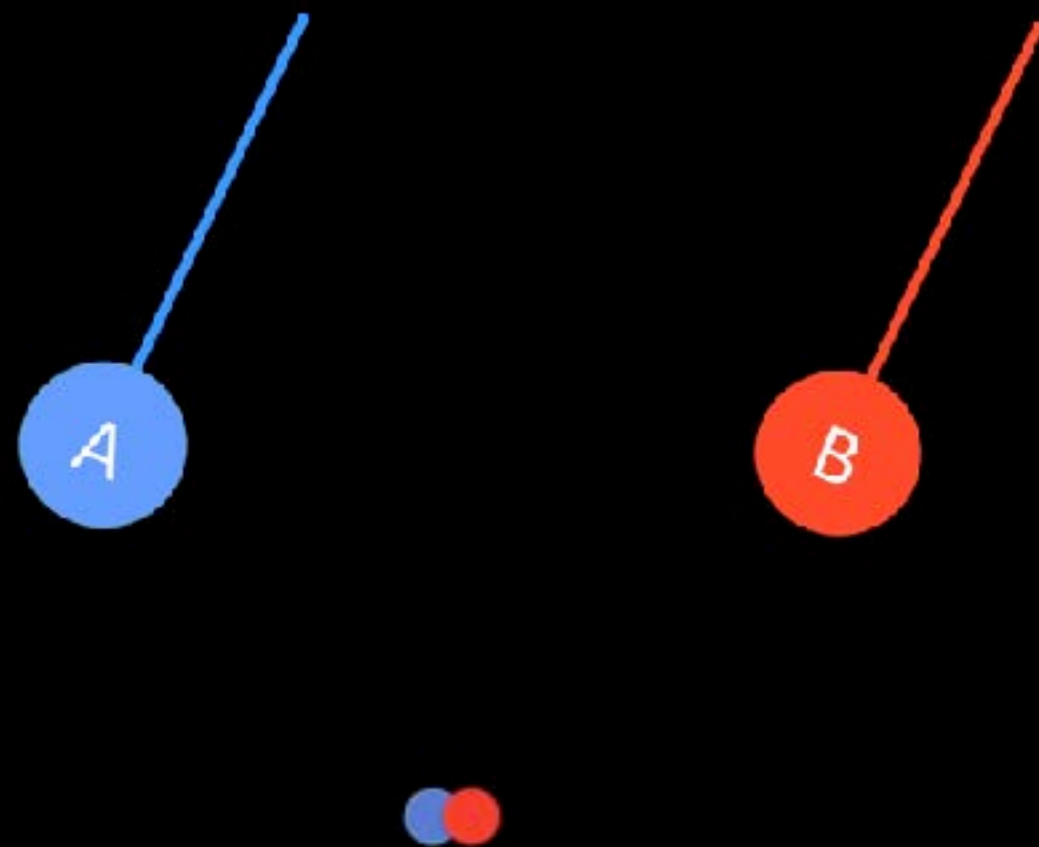
Estimating Functional Connectivity

Popular measures

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

...

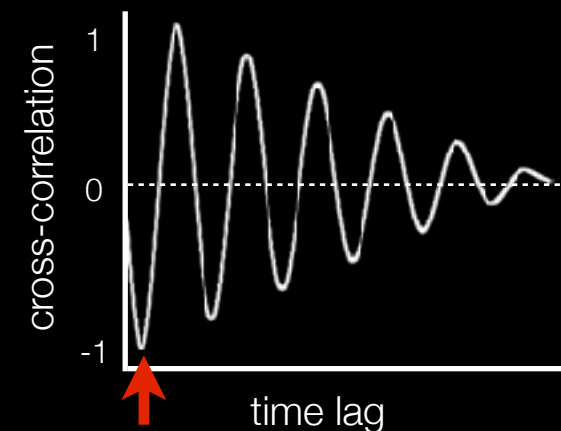
Cross-Correlation and Linear Coherence



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

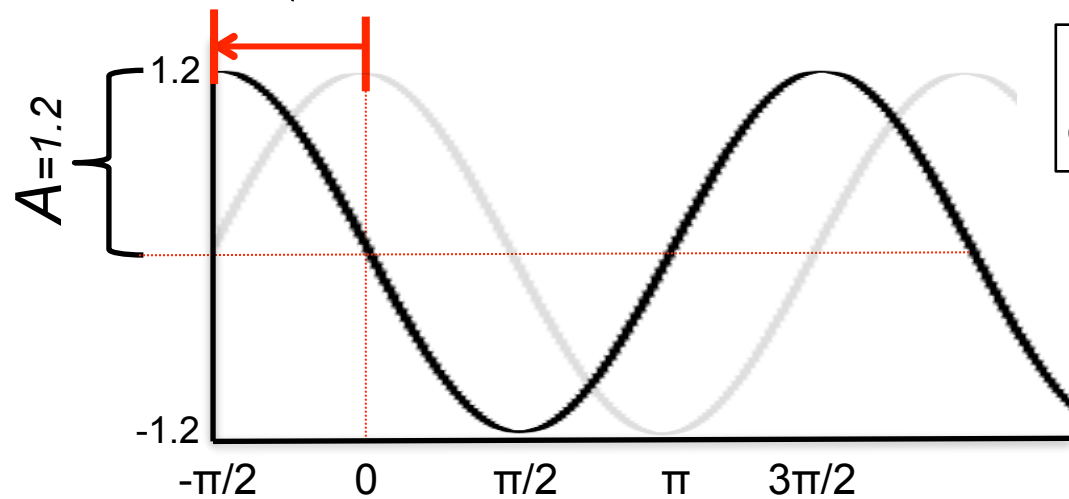


phase shift

$$\phi = \pi / 2$$

angular frequency

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



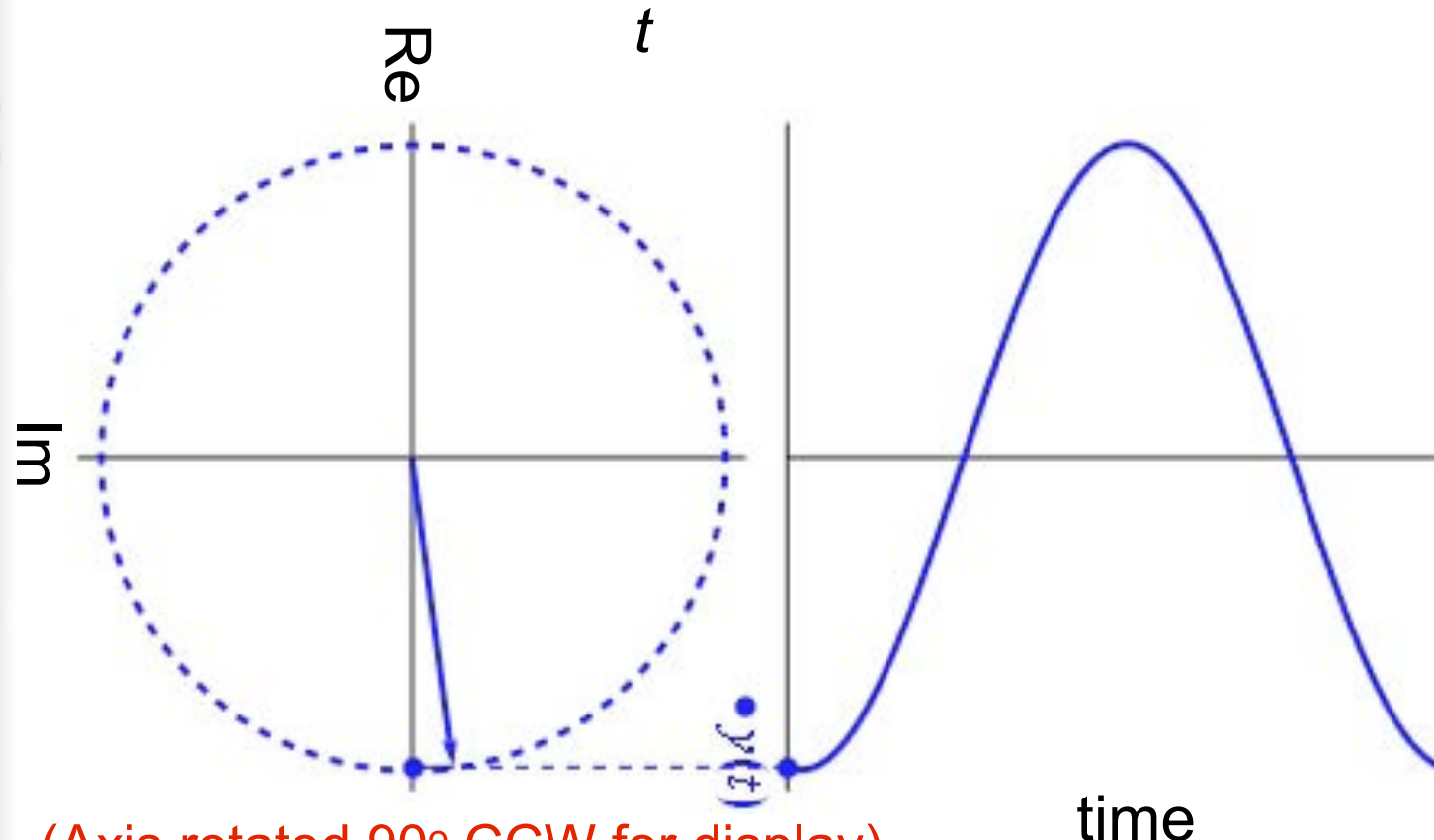
Euler's Formula tells us that any sinusoid can be expressed as the sum of two complex exponentials

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

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

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

instantaneous complex amplitude and phase



(Axis rotated 90° CCW for display)

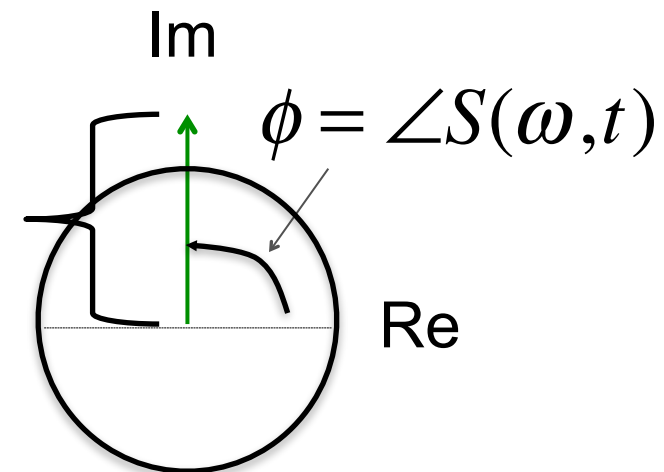
Polar animation courtesy Wikipedia

time

Phasor

(Polar Coords)

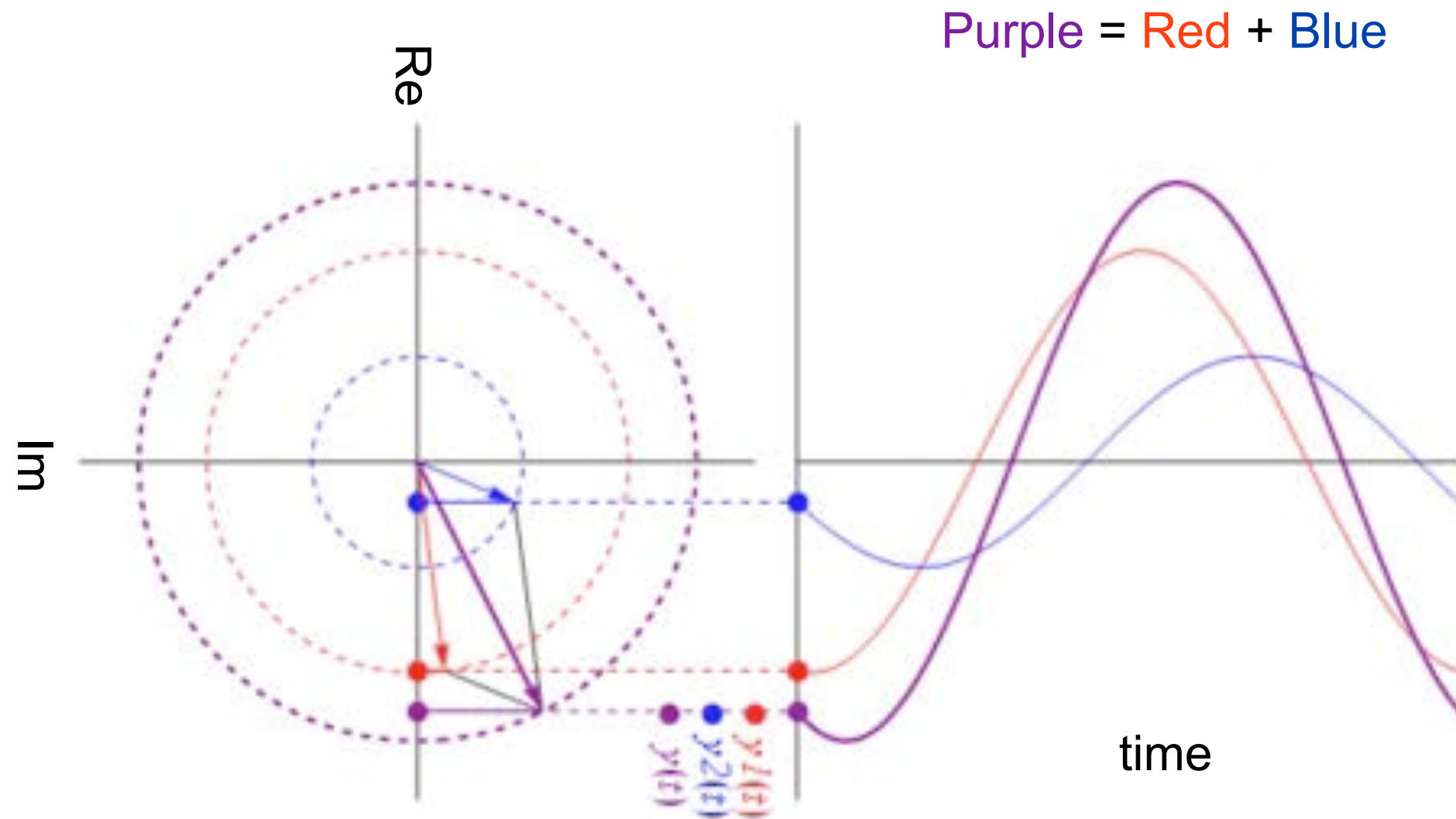
$$|S(\omega, t)| = |A|$$



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

Phasors

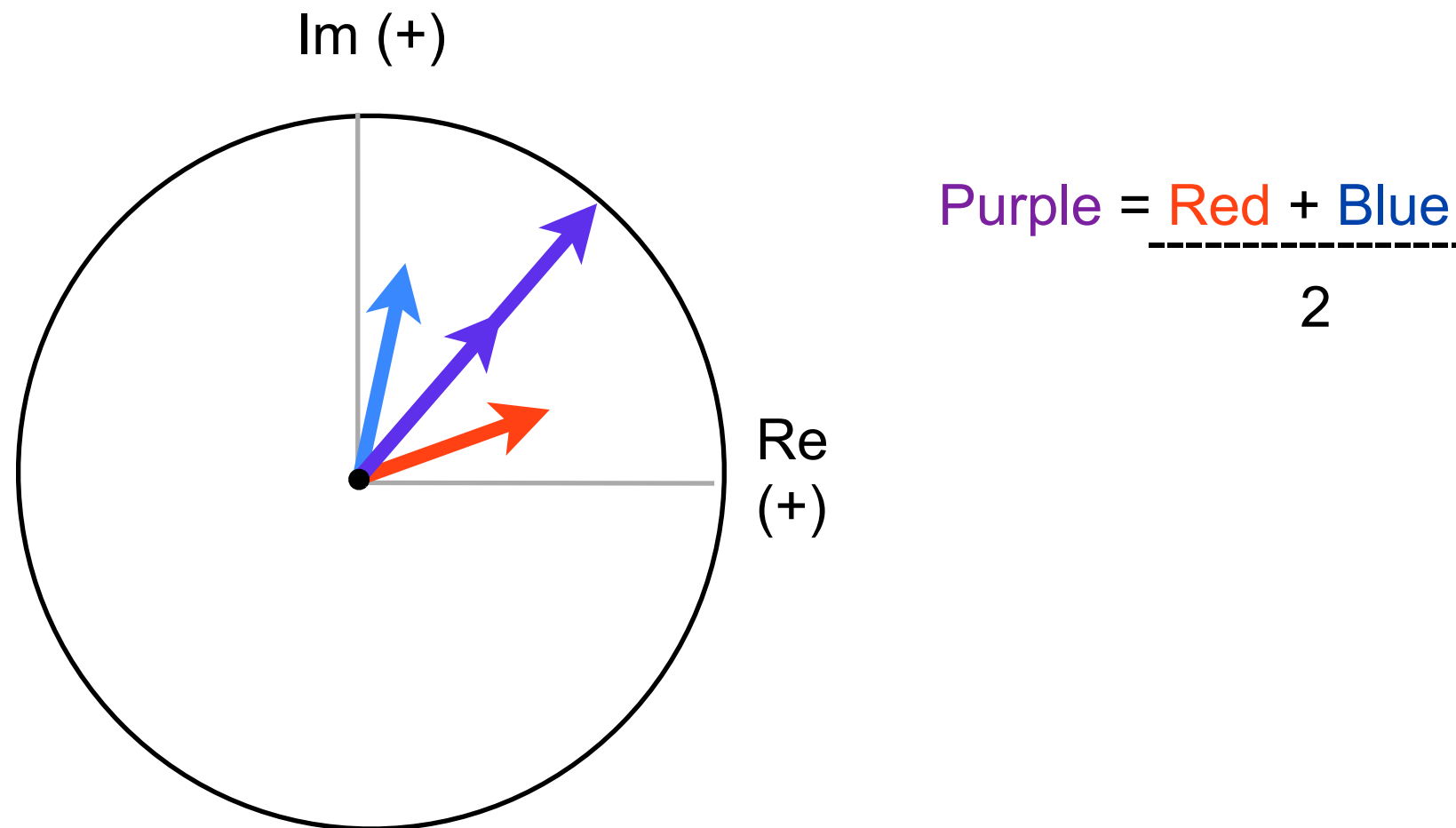
If we want to examine oscillatory dynamics or relationships between oscillatory signals, analysis in the time domain (i.e. cartesian coordinates) is equivalent to (simpler) operations involving phasors in Fourier space (i.e. polar coordinates).



(Axis rotated 90° CCW for display)

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 .

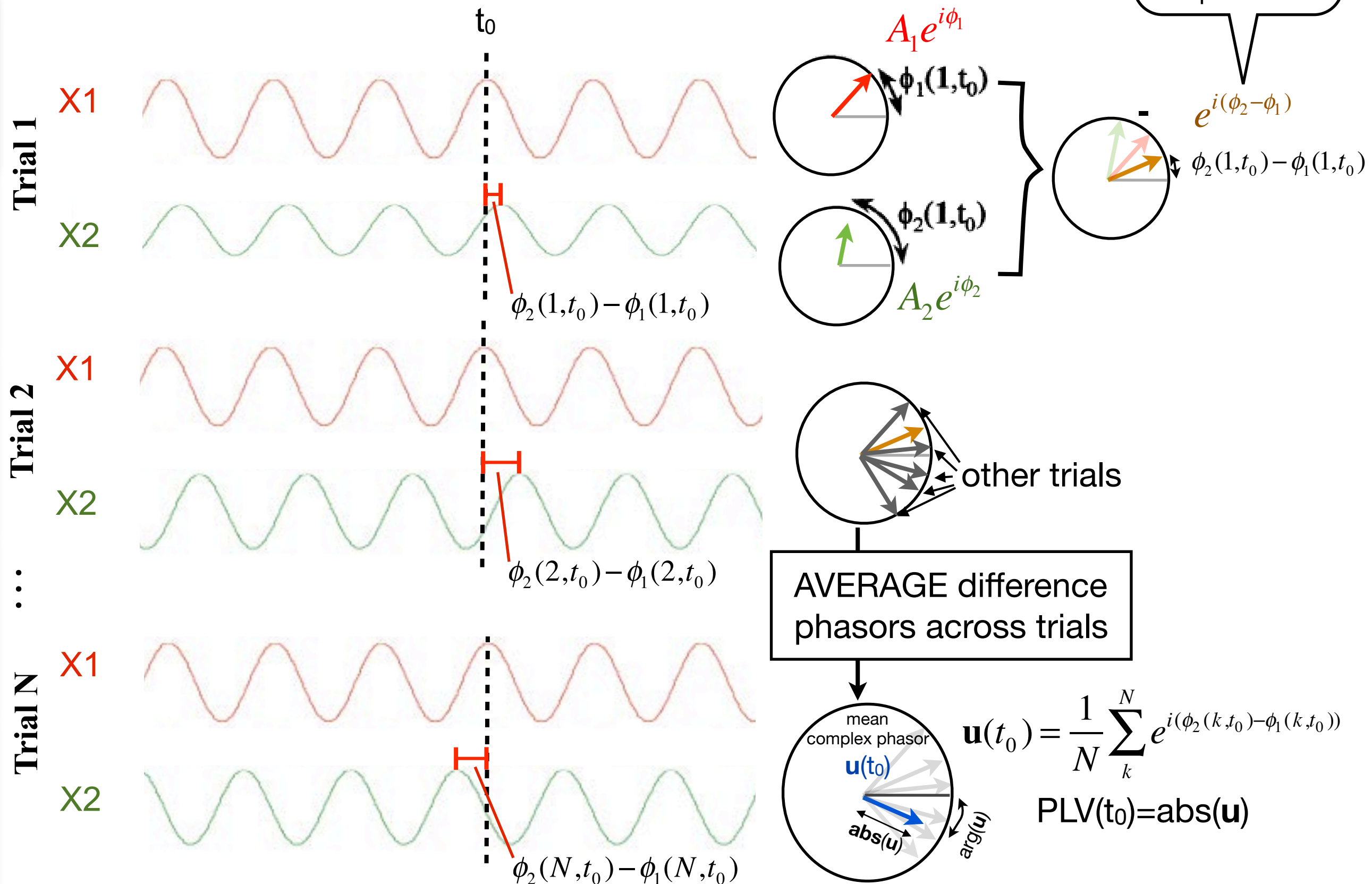


If all **phasors have similar angles**, then vectors will “point” in the same direction and the **length of the mean phasor** will be comparatively **large**.

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:

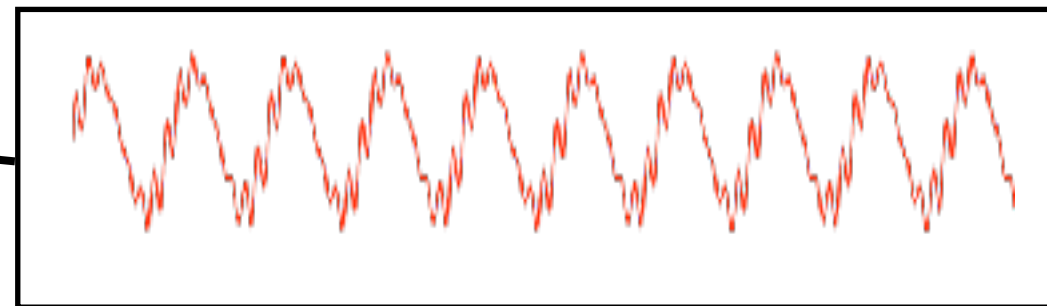
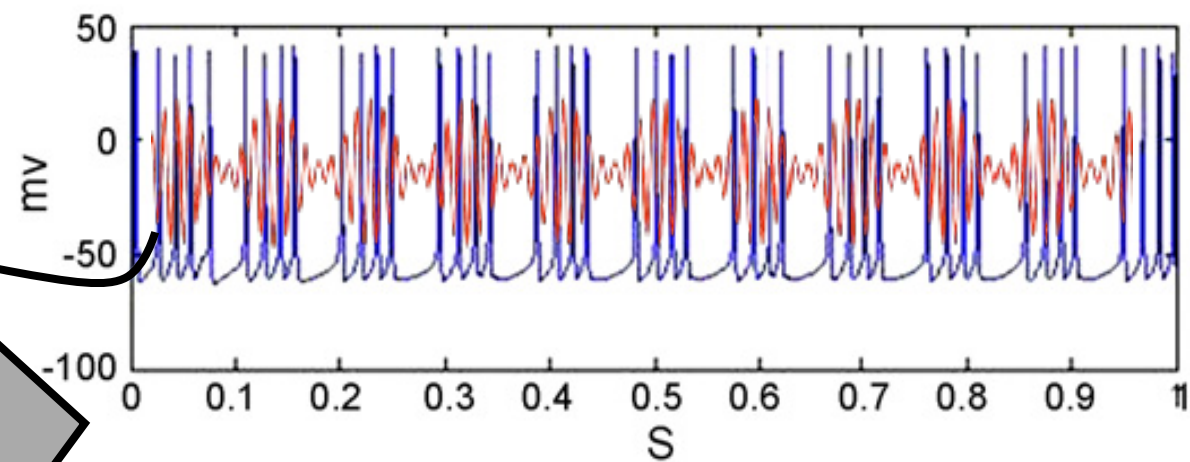
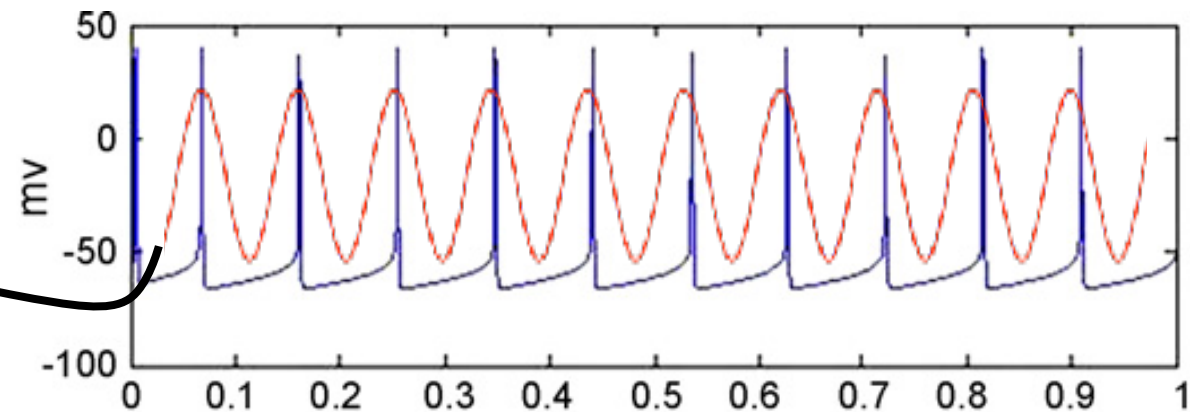
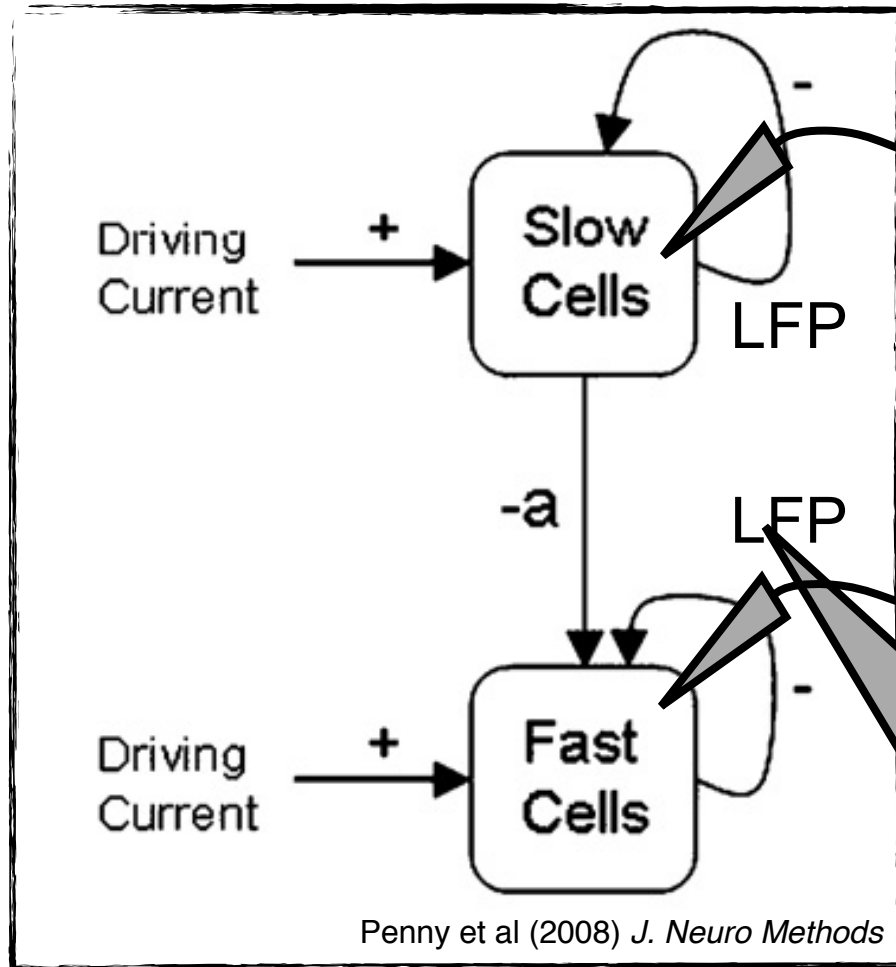
```
pop_newcrossf( . . . , 'type', 'phase' )
```

Phase-Amplitude Coupling

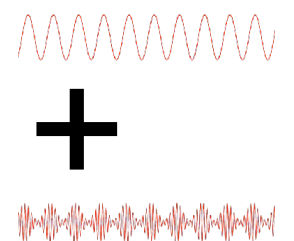
- May present a functional role in execution of cognitive functions (Axmacher et al. 2010; Cohen et al. 2009a,b; Lakatos et al. 2008; Tort et al. 2008, 2009; Canolty et al, 2006).
- Suggested involvement in **sensory signal detection** (Handel and Haarmeier 2009), **attentional selection** (Schroeder and Lakatos 2009), **memory processes** (Axmacher et al. 2010; Tort et al. 2009; and **neurodegenerative disorders** (Swann et al, 2015)

Phase-Amplitude Coupling

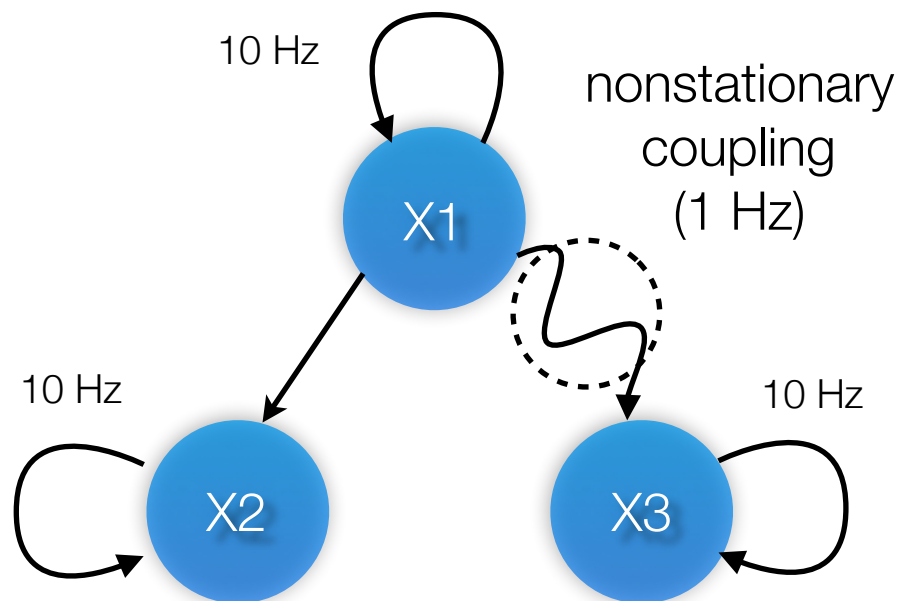
'burst-suppress' oscillators



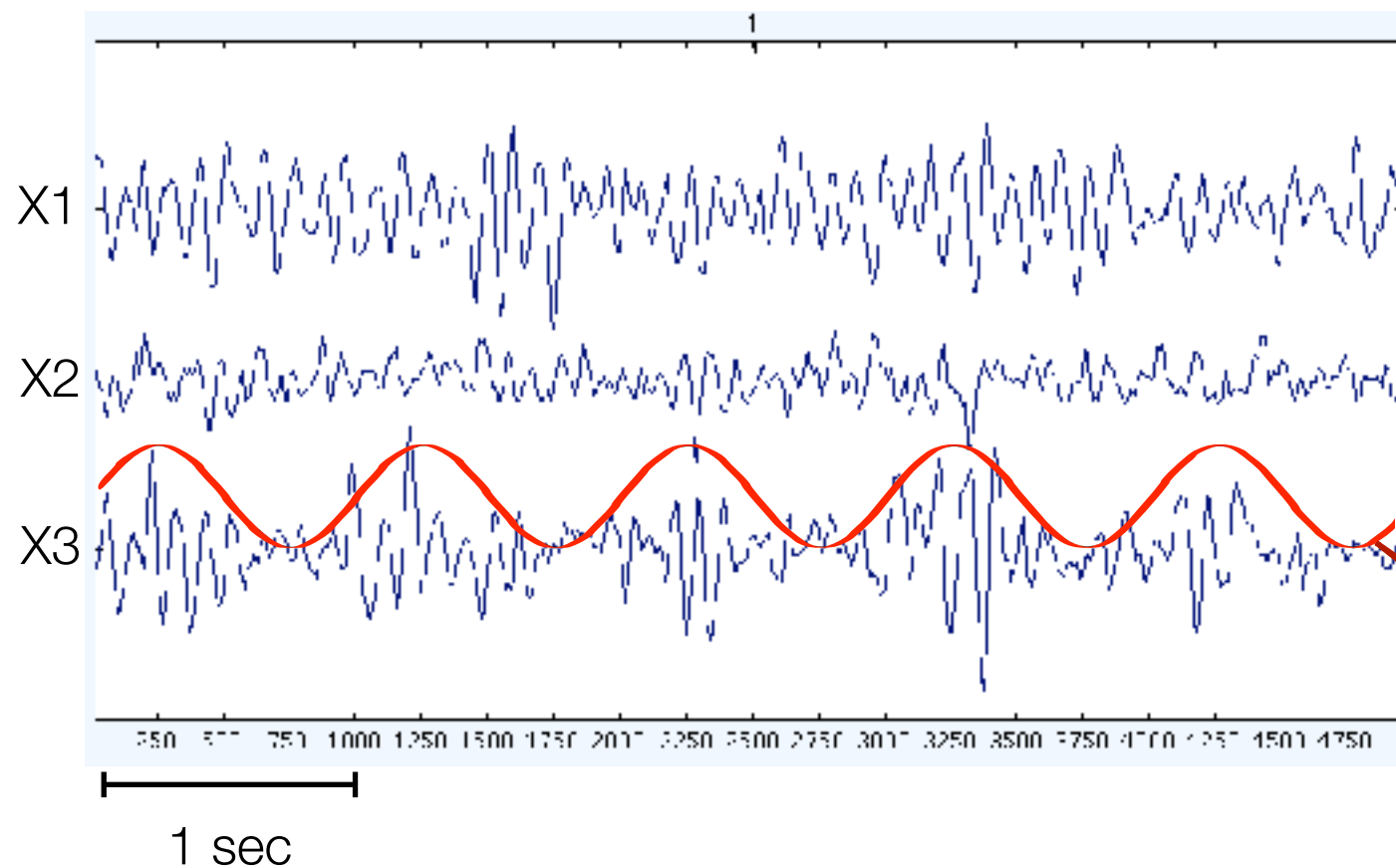
Local Field Potential (Slow + Fast cells)



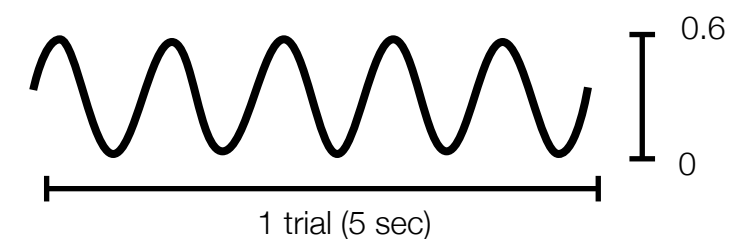
Graphical Model



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



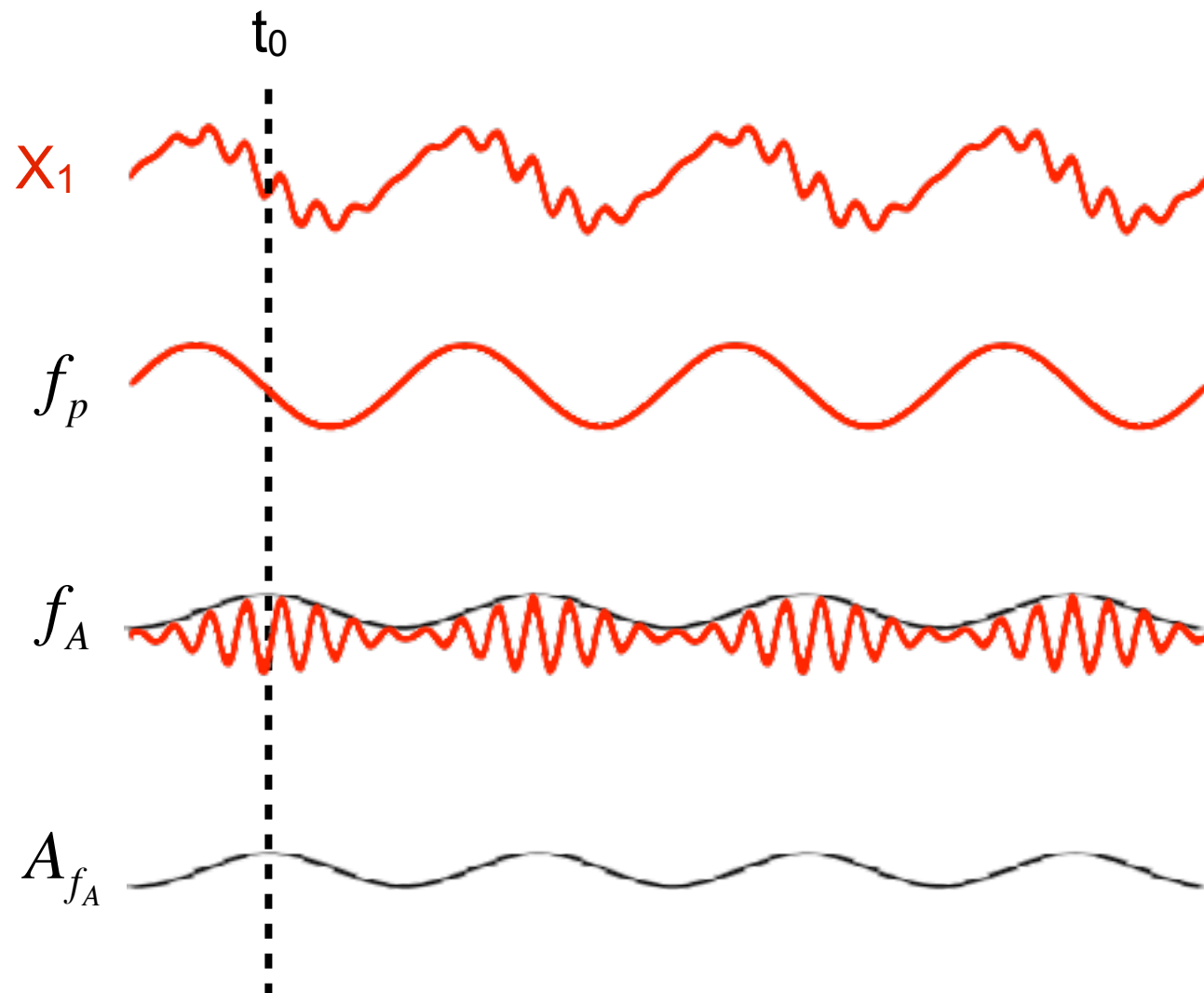
Time-varying $X1 \rightarrow X3$ coupling
(1 Hz modulation)



Amplitude Modulation
10Hz amplitude coupled to 1
Hz Phase

Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) *PNAS*



original raw signal

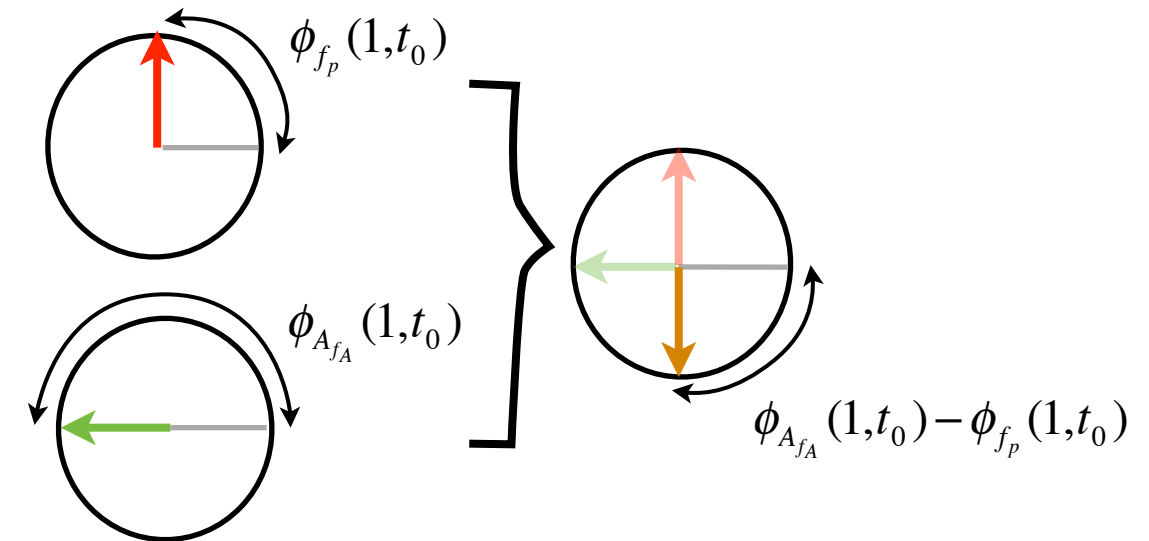
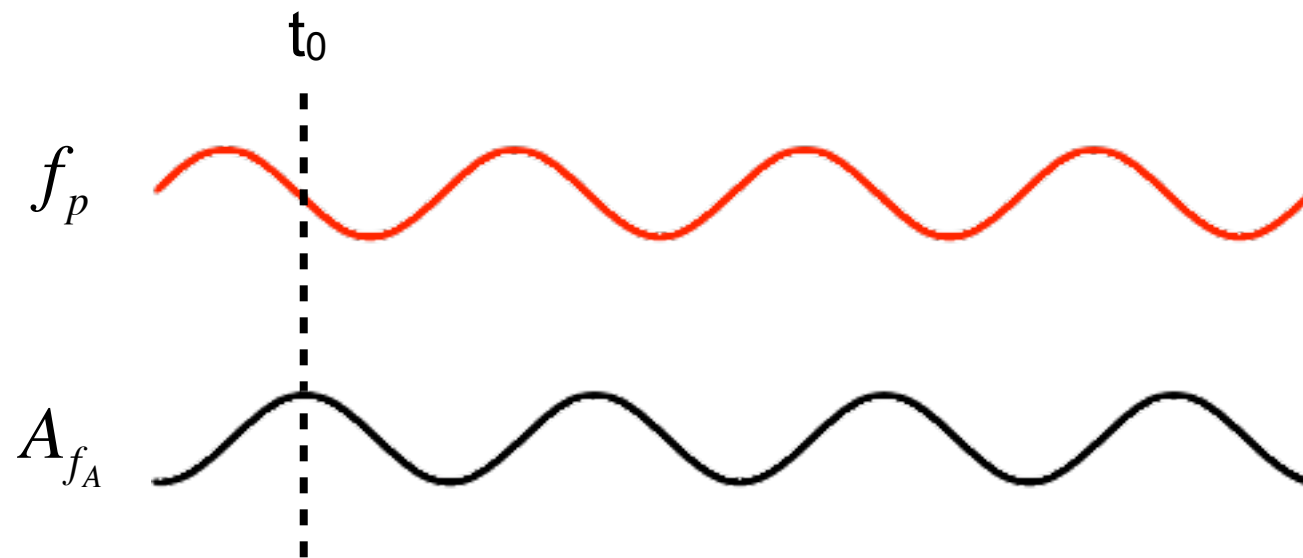
filter X_1 at LFO band (e.g. theta)

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

get amplitude envelope of filtered signal

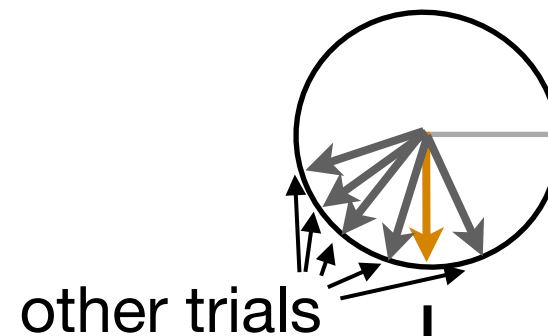
Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) *PNAS*

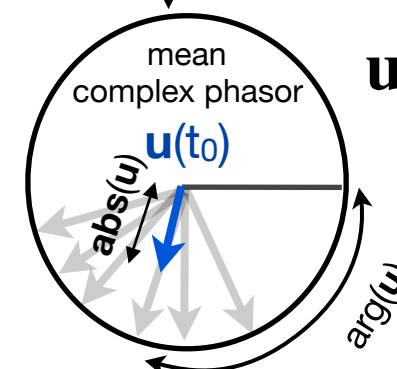


Compute PLV between LFO time-series (f_p) and amplitude envelope of HFO time-series (A_{f_A}).

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



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

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

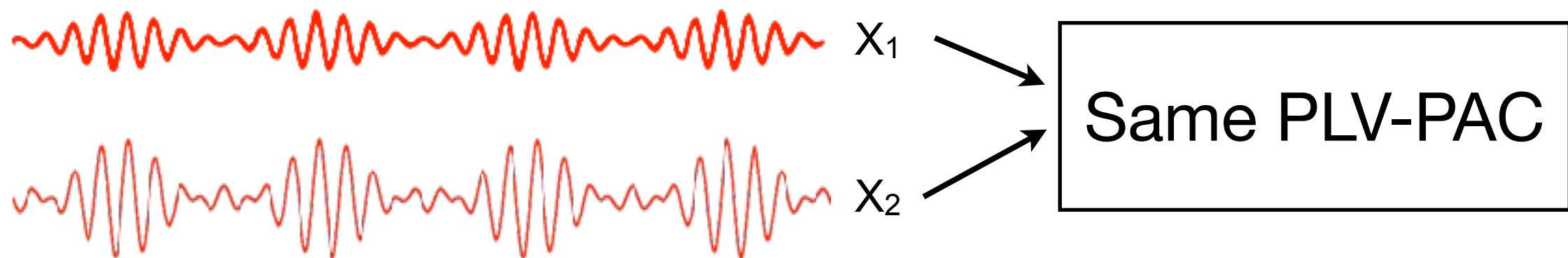
Phase-Amplitude Coupling: PLV Method

Vanhatalo, S et al (2004) *PNAS*

Problem:

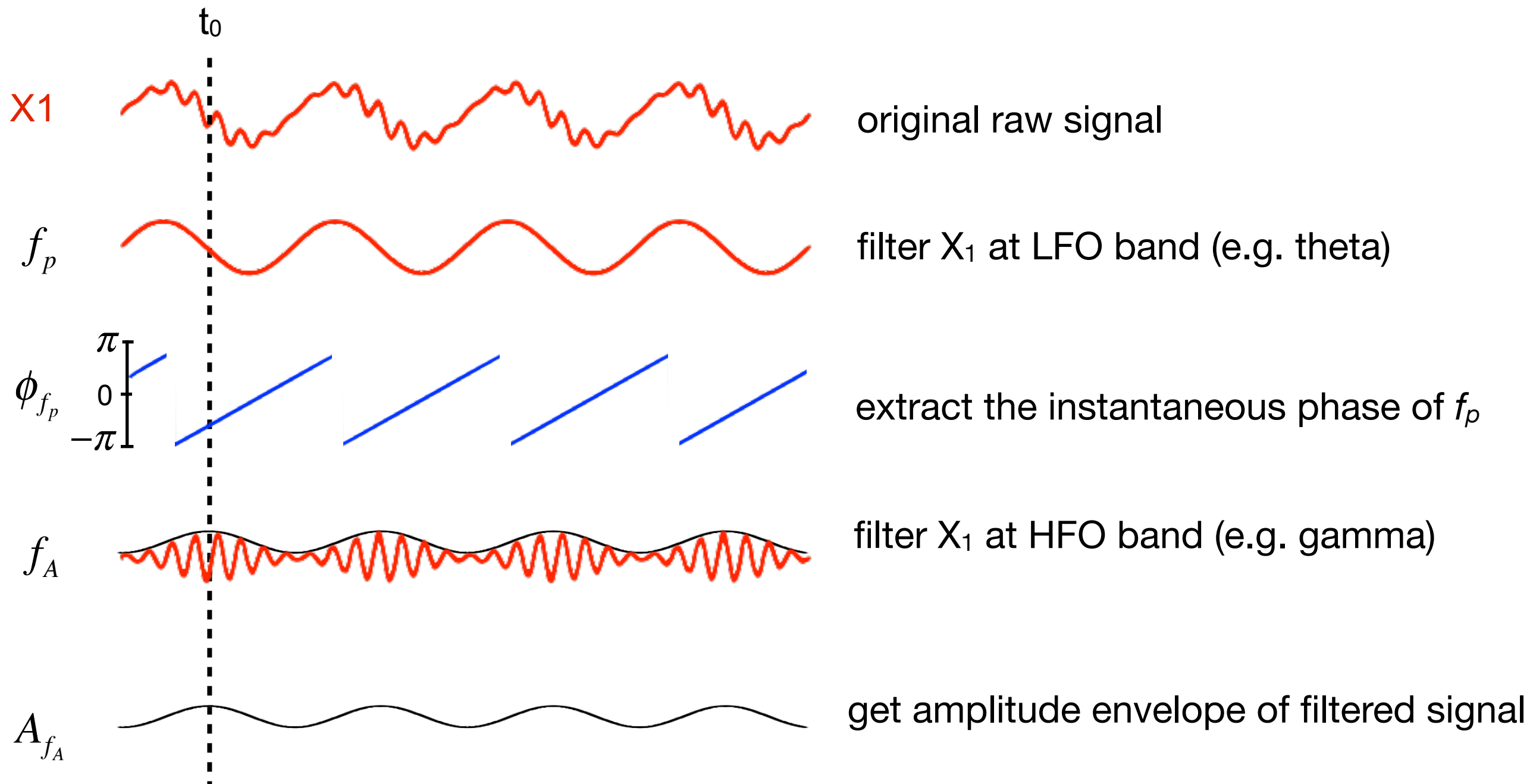
PLV is invariant to differences in amplitude between the two time-series (it only considers phase). Thus PLV-PAC doesn't take into account the *amplitude* of the co-modulation.

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*

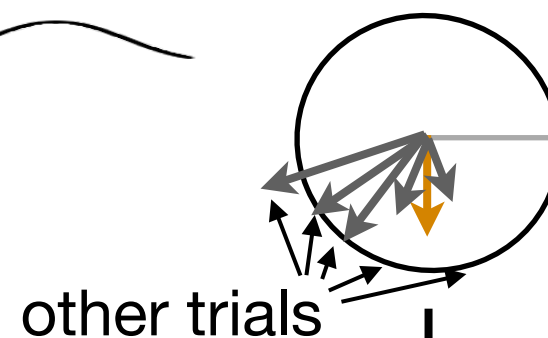
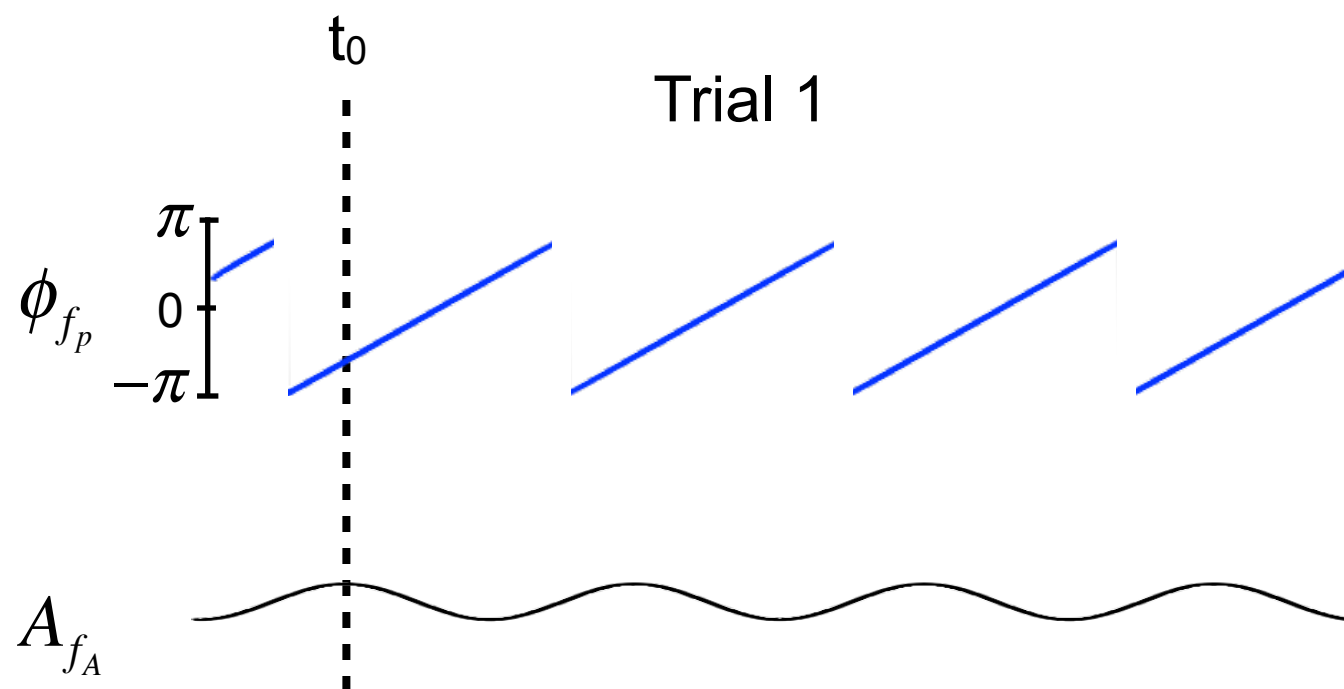
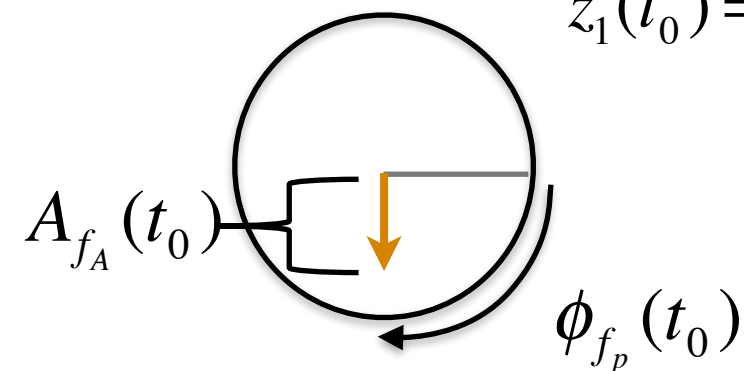


Phase-Amplitude Coupling: Modulation Index Method

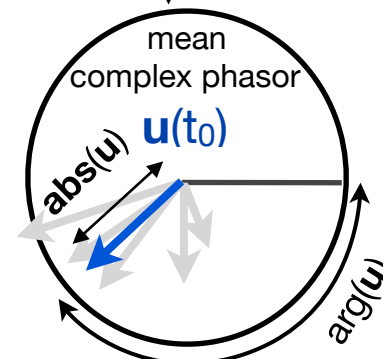
Canolty et al, (2006) *Science*

build complex phasor
with instantaneous
amplitude and phase

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



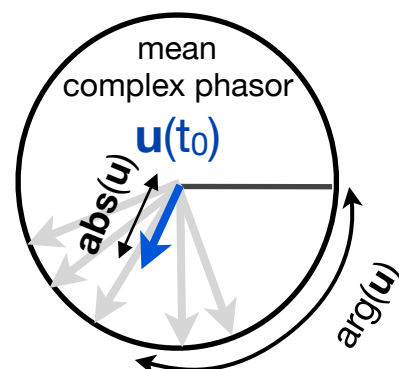
AVERAGE complex
phasors across trials



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

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

Comparison:
PLV-PAC



Phase-Amplitude Coupling: Modulation Index Method

Canolty et al, (2006) *Science*

Computing PAC in EEGLAB:

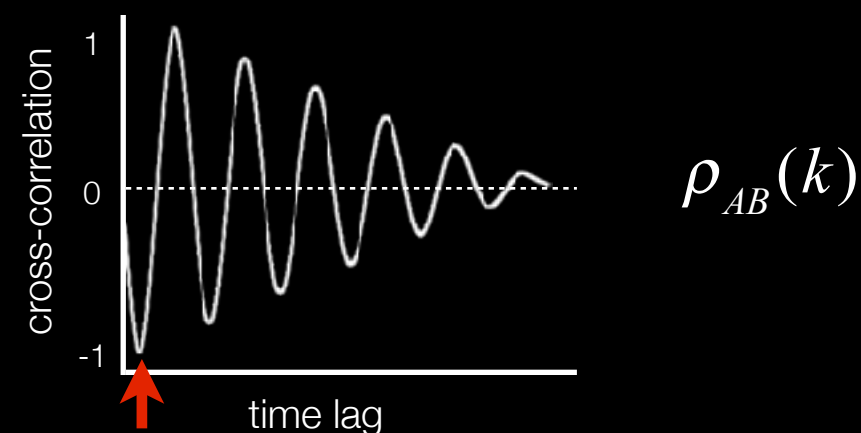
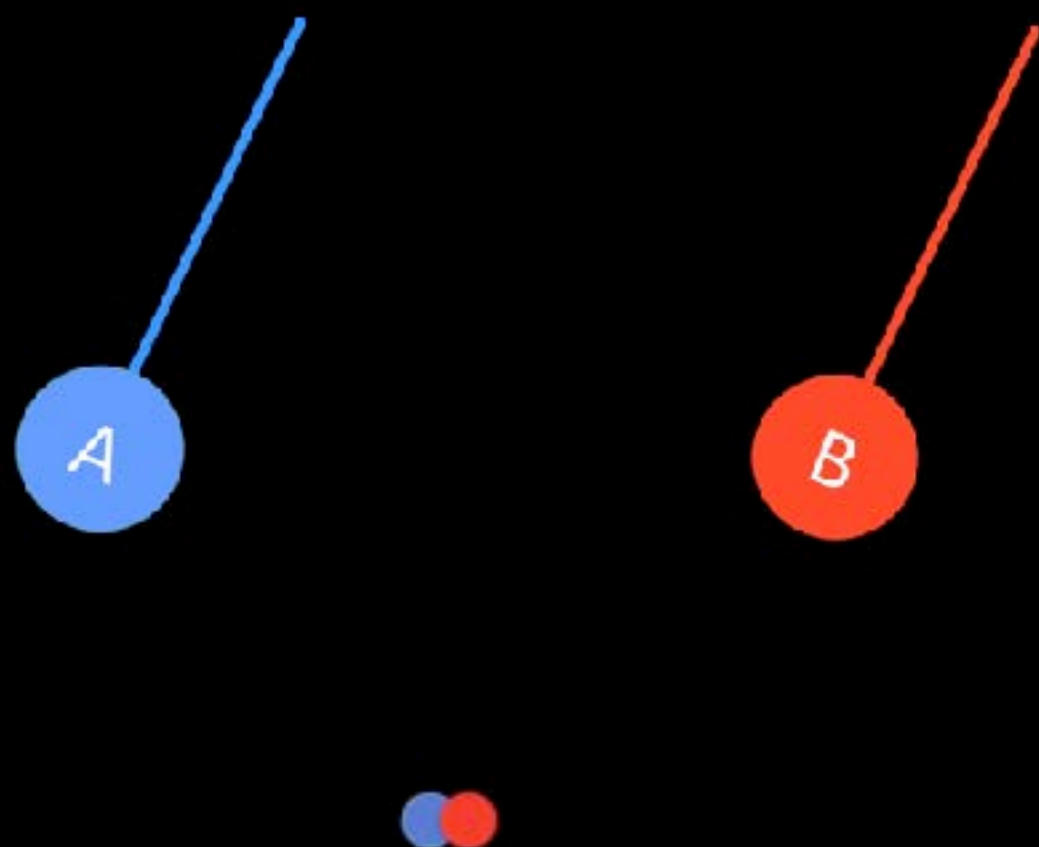
```
pac(IC1, IC2, ..., 'method', 'mod')
```

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)

Also see PACT plugin for EEGLAB by
Miyakoshi et al
(<http://sccn.ucsd.edu/wiki/PACT>)

(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**

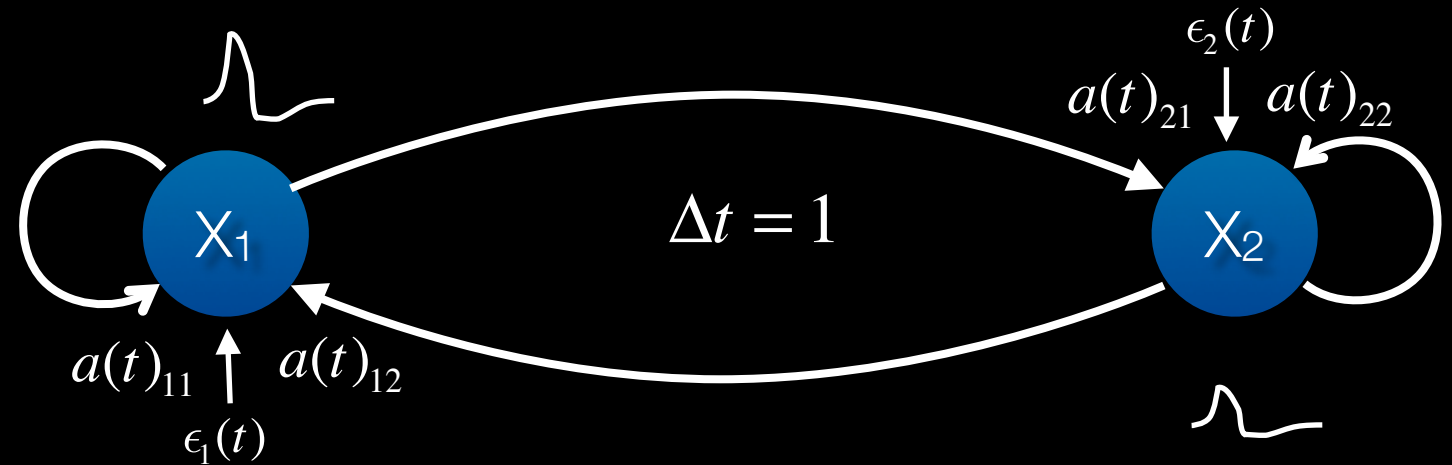
- Data-driven
- Rooted in *conditional predictability*
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved)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

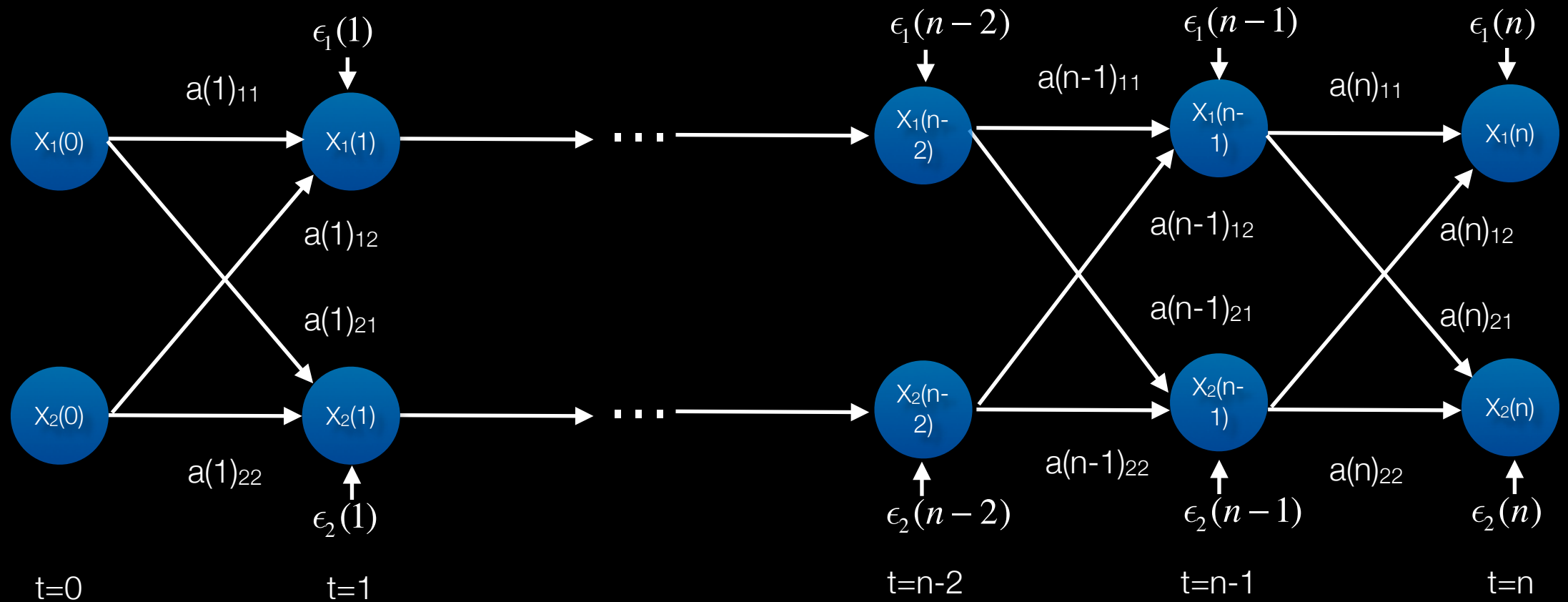
Stochastic Linear Dynamical System

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

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

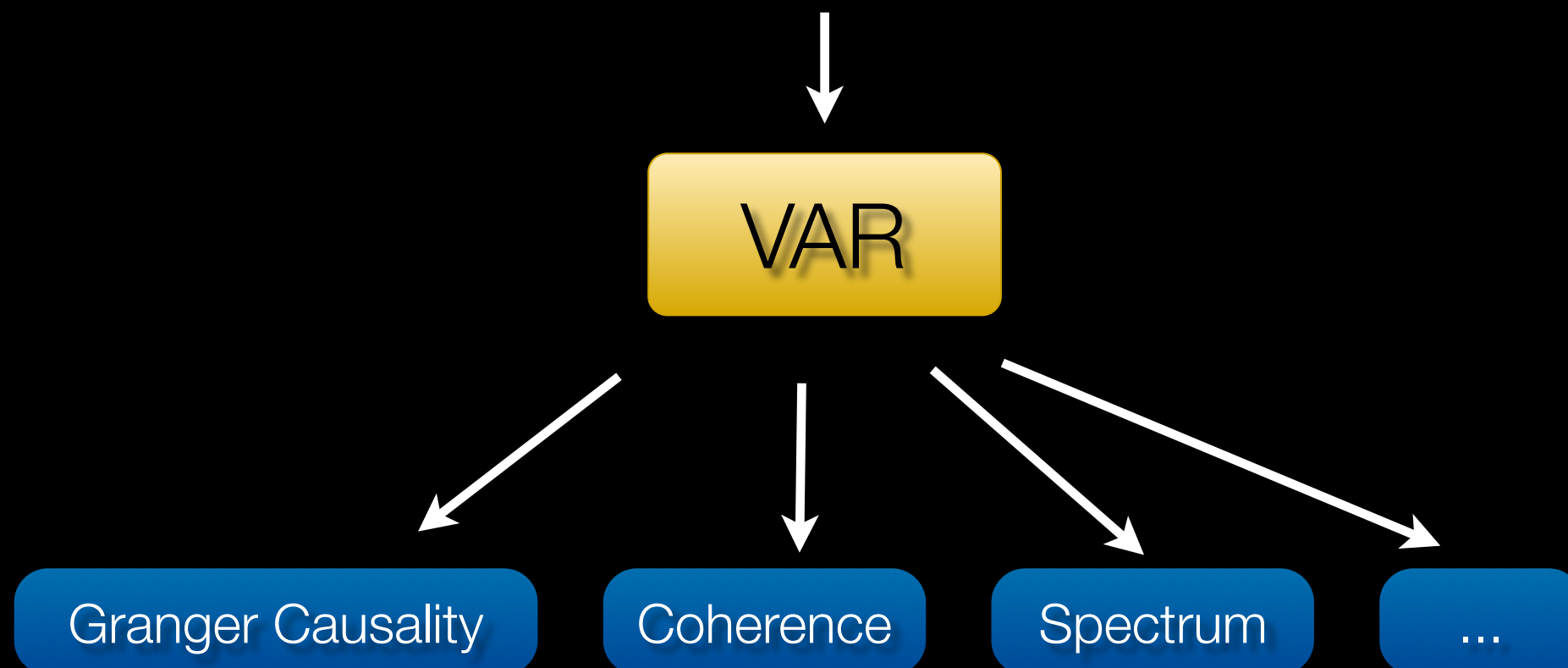
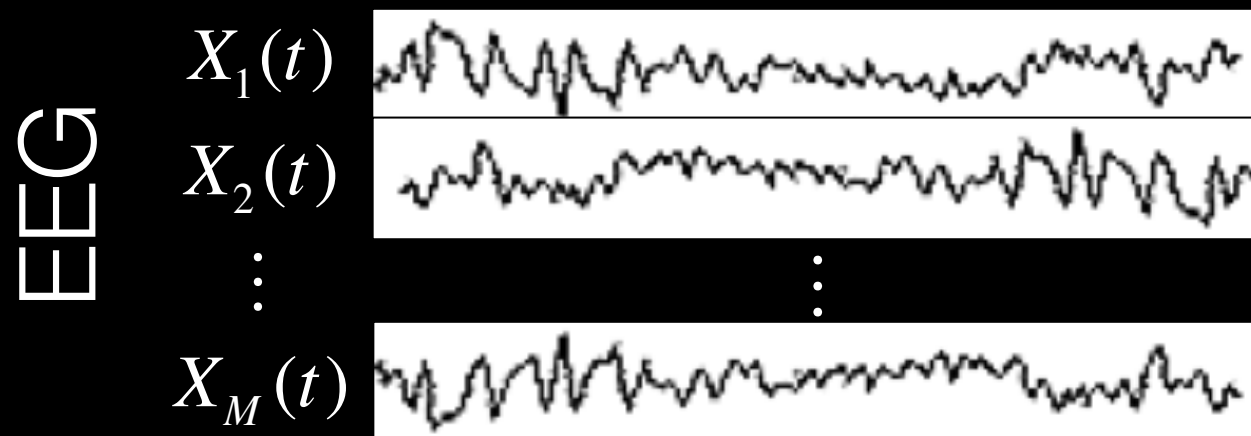


Order 1 Markov Process (VAR[1])



time step

Vector Autoregressive (VAR / MAR / MVAR) Modeling



VAR Modeling: Assumptions

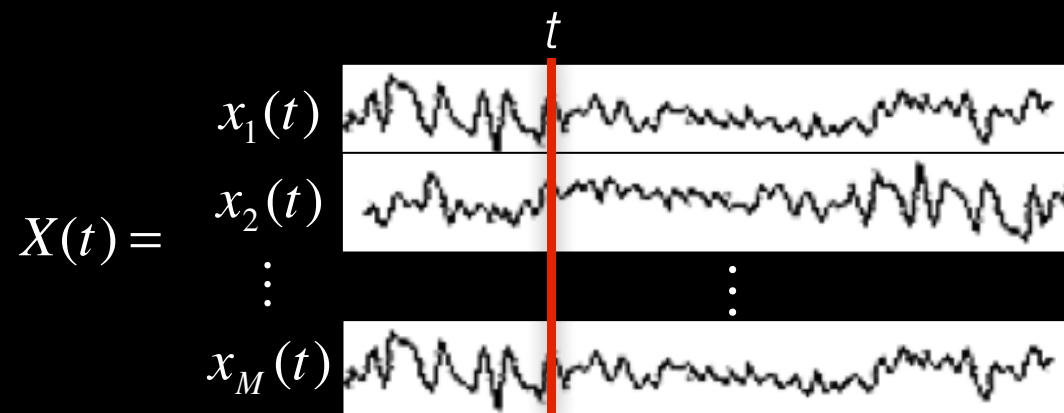
- ✦ **“Weak” stationarity of the data**

- ✦ 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

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

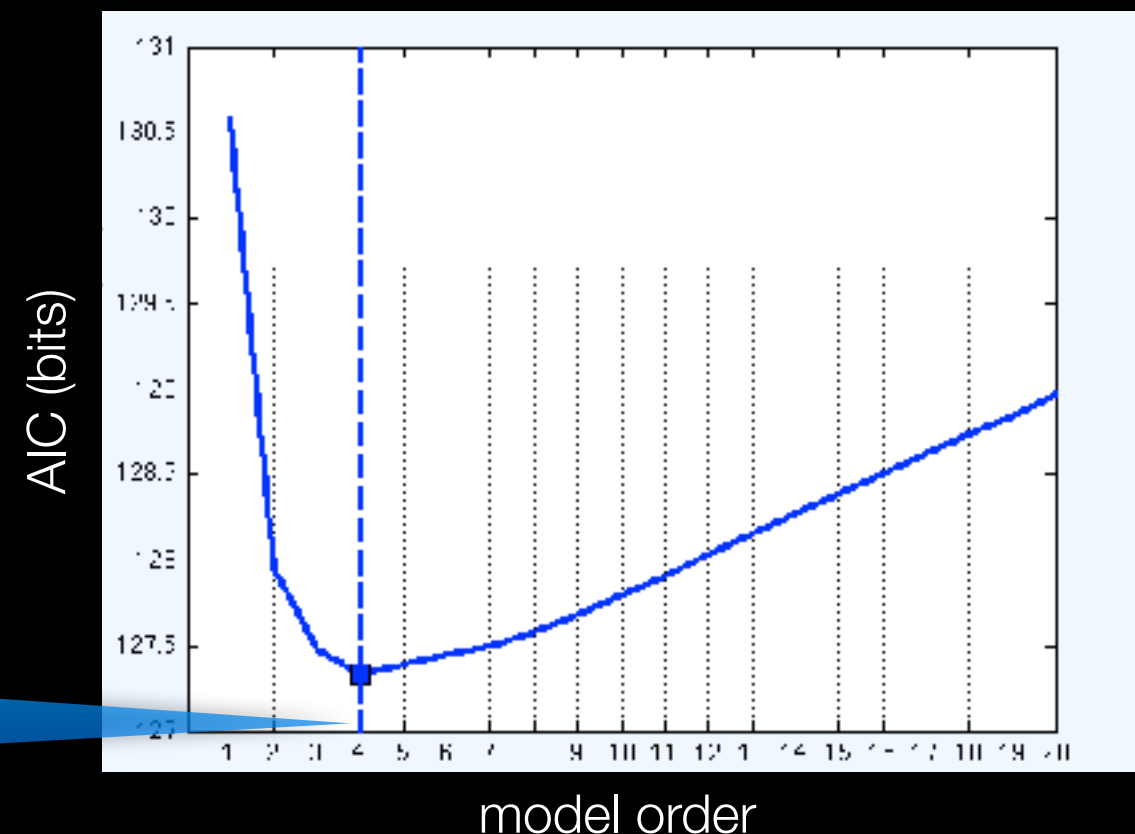
Selecting a VAR Model Order

- 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

Model Order Selection Criteria

More
Conservative

Schwarz-Bayes Criterion
(Bayesian Information Criterion)

$$SBC(p) = \ln |\tilde{\Sigma}(p)| + \frac{\ln(\hat{T})}{\hat{T}} p M^2$$

Akaike Information Criterion

$$AIC(p) = \ln |\tilde{\Sigma}(p)| + \frac{2}{\hat{T}} p M^2$$

Less
Conservative

Akaike's Final Prediction Error

$$FPE(p) = |\tilde{\Sigma}(p)| + \left(\frac{\hat{T} + Mp + 1}{\hat{T} - Mp - 1} \right)^M$$

and its logarithm (used in SIFT)

$$\ln(FPE(p)) = \ln |\tilde{\Sigma}(p)| + M \ln \left(\frac{\hat{T} + Mp + 1}{\hat{T} - Mp - 1} \right)$$

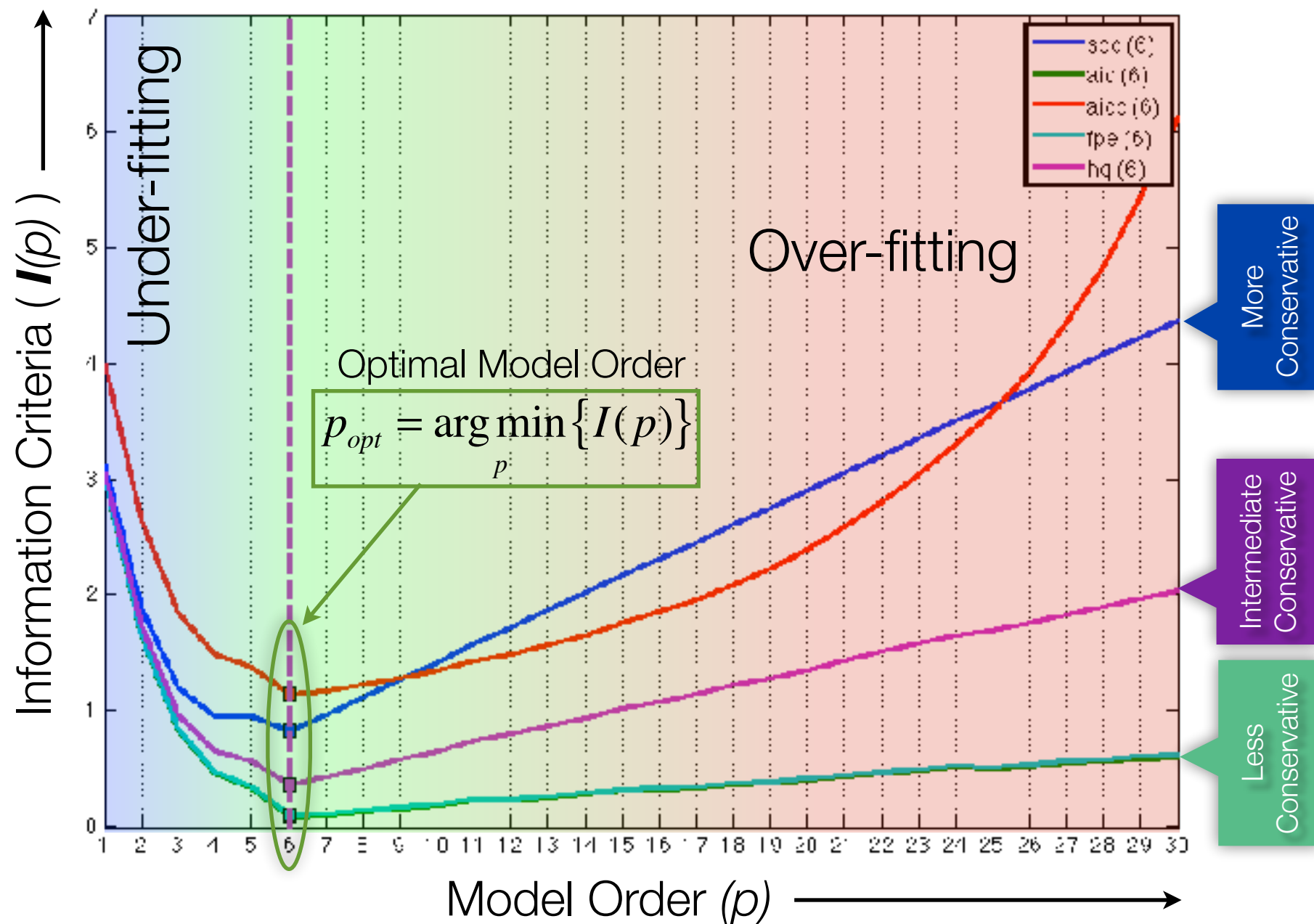
Intermediate
Conservative

Hannan-Quinn Criterion

$$HQ(p) = \ln |\tilde{\Sigma}(p)| + \frac{2 \ln(\ln(\hat{T}))}{\hat{T}} p M^2$$

Model Order Selection Criteria

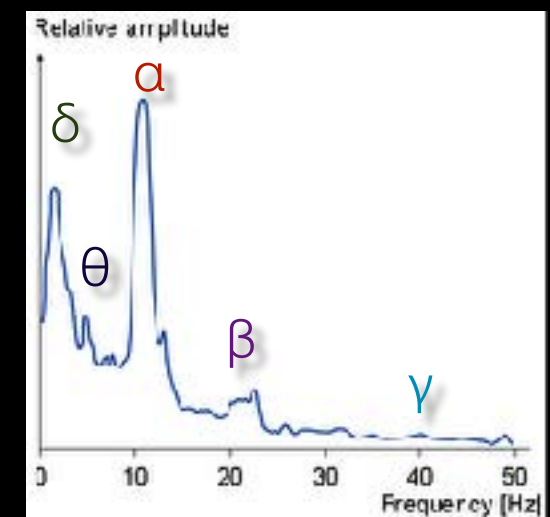
$$I(p) = [\text{Prediction Error}] + [\text{Overfitting Penalty}]$$



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.

We'll discuss these further in Part 2 (Sunday)

Granger Causality

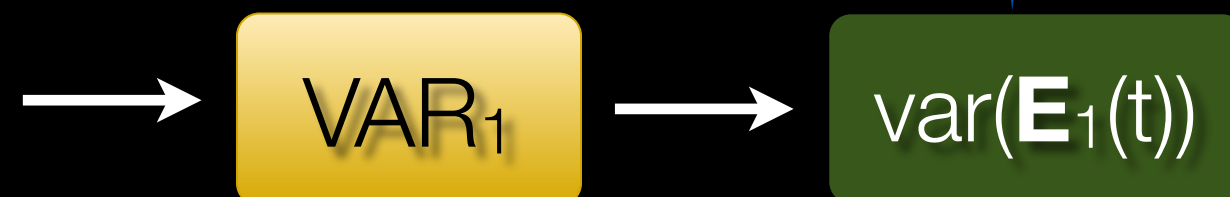
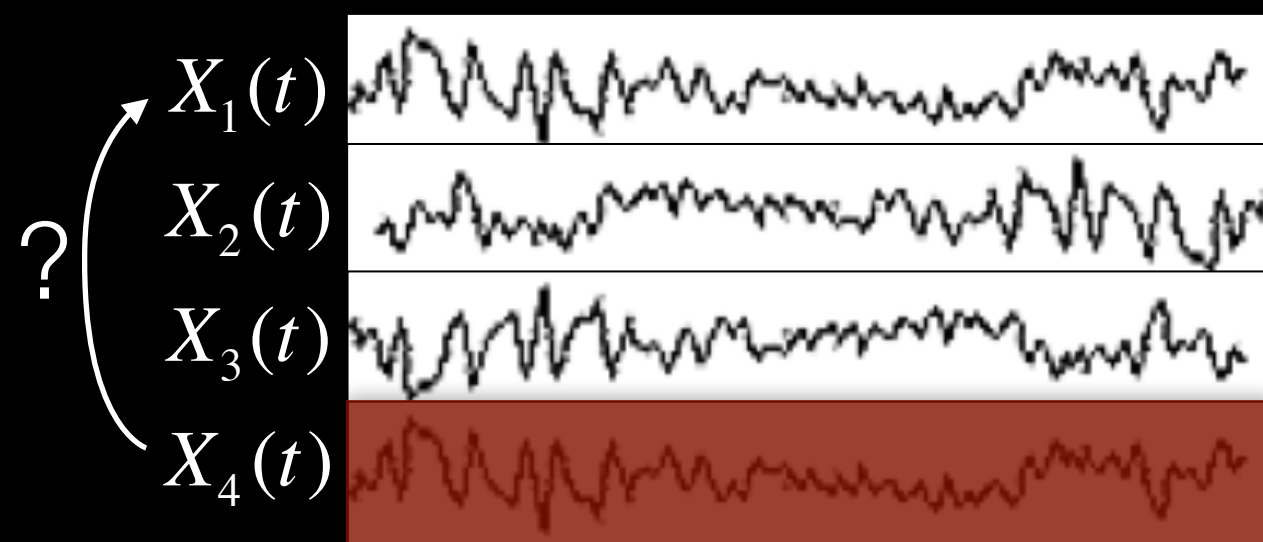
- ✦ First introduced by Wiener (1958). Later reformulated by Granger (1969) in the context of linear stochastic autoregressive models
- ✦ Relies on two assumptions:

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)

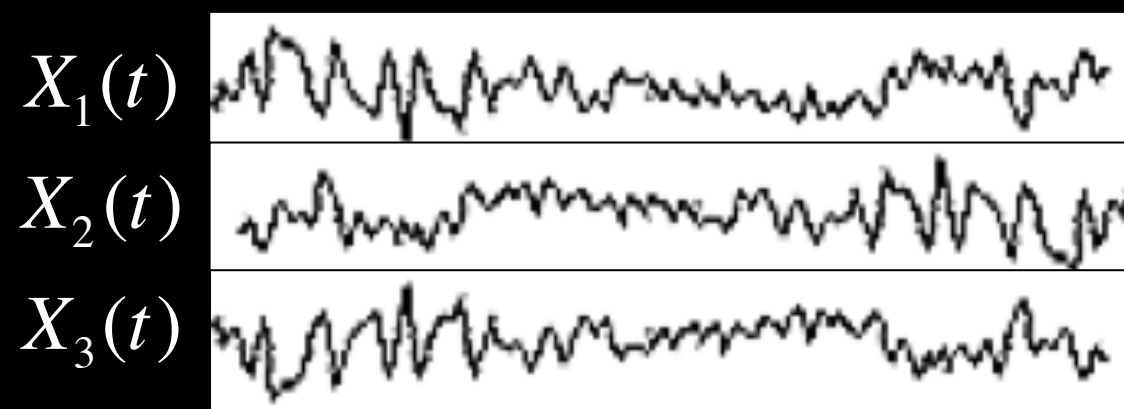
Granger Causality

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

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

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

Diagram illustrating the causal structure: A red arrow points from $X_2(t-1)$ to $X_1(t)$ (labeled with a red 'X'), and a green arrow points from $X_1(t-1)$ to $X_2(t)$.

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

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

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

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

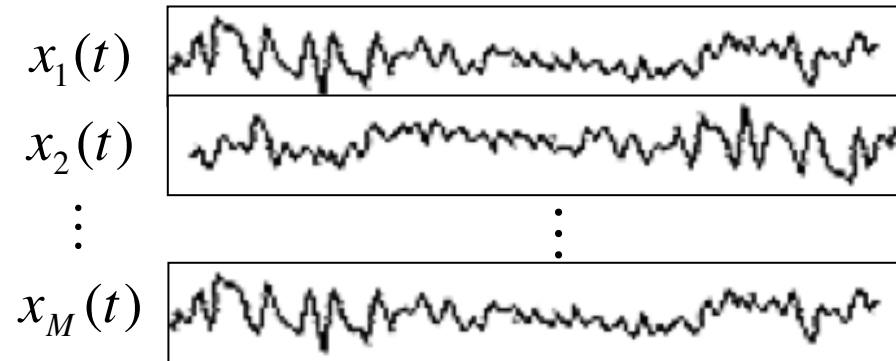
Where $\mathbf{H}(f)$ is the *transfer matrix* of the system.

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

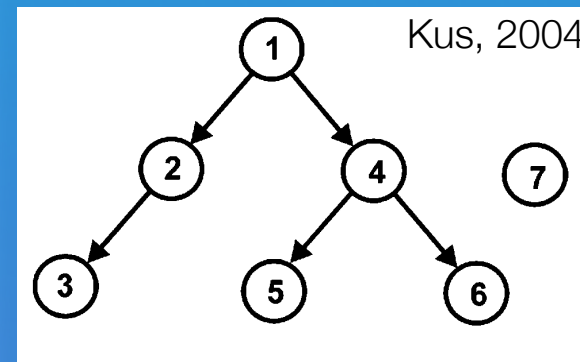


$$\mathbf{X}(t) = \sum_{k=1}^p \mathbf{A}^{(k)}(t) \mathbf{X}(t-k) + \mathbf{E}(t)$$

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

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

Ground Truth

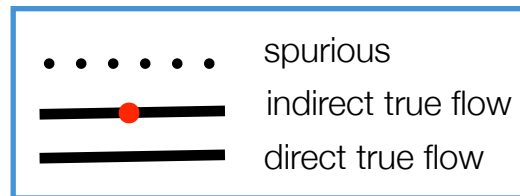
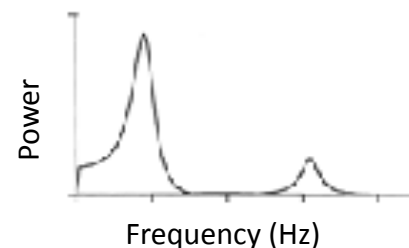


Spectrum

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

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

(Brillinger, 2001)



NOTE: time index (t) dropped for convenience

Functional

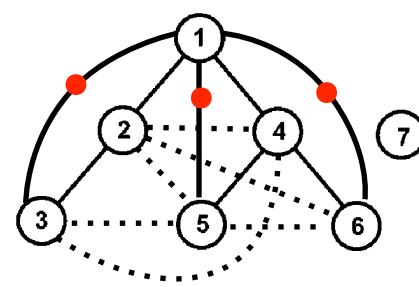
Effective

Bivariate

Coherency

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

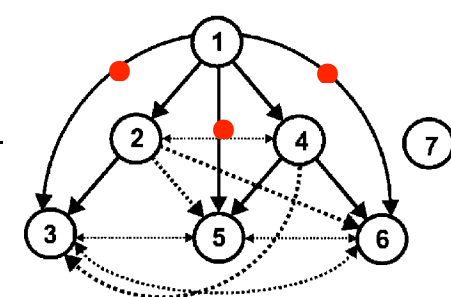
(Bendat and Piersol, 1986)



Granger-Geweke Causality

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

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

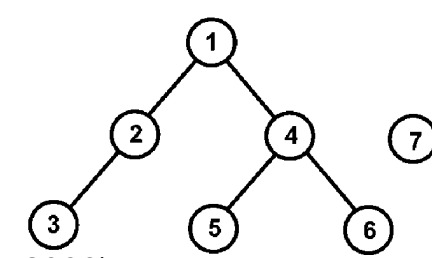


Multivariate

Partial Coherence

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

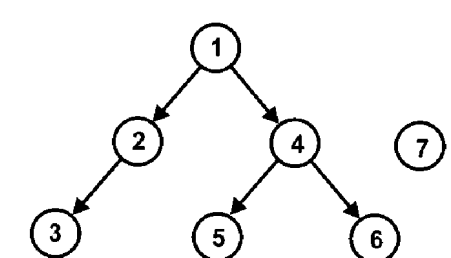
(Bendat and Piersol, 1986; Dalhaus, 2000)



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	$\delta_{ij}^2(f) = \eta_{ij}^2(f) P_{ij}^2(f)$

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

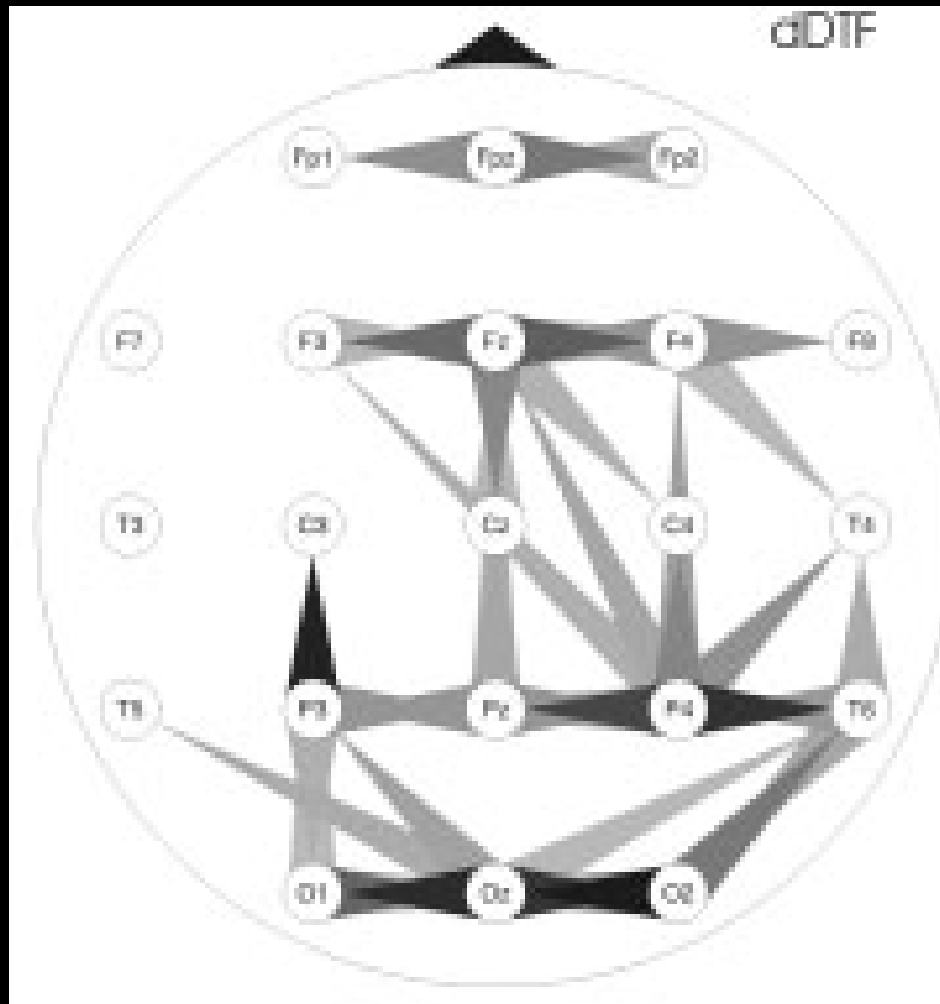
$$\mathbf{A}(f, t) = -\sum_{k=0}^p \mathbf{A}^{(k)}(t) e^{-i2\pi f k}; \quad \mathbf{A}^{(0)} = I$$

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

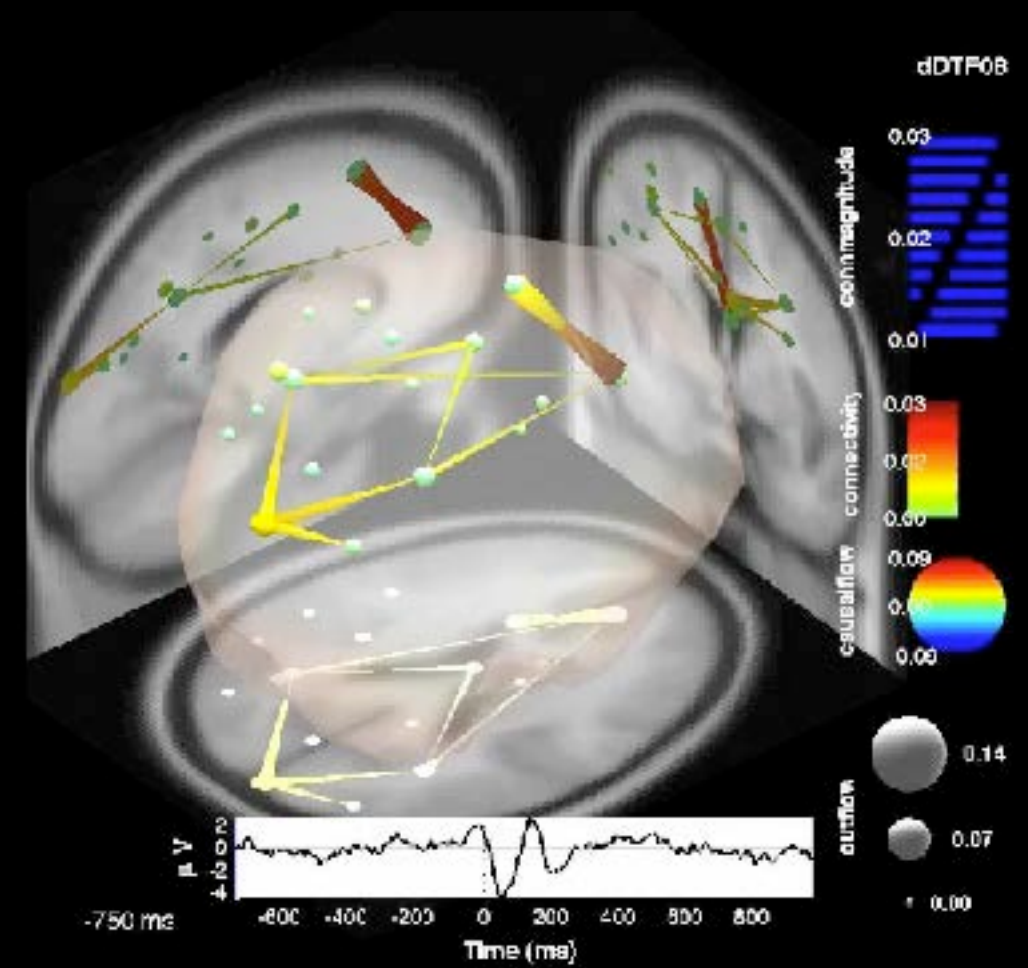
$H(f)$ Transfer Function
 $A(f)$ System Matrix
 Σ Noise Covariance Matrix

Variance Stabilization

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}

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

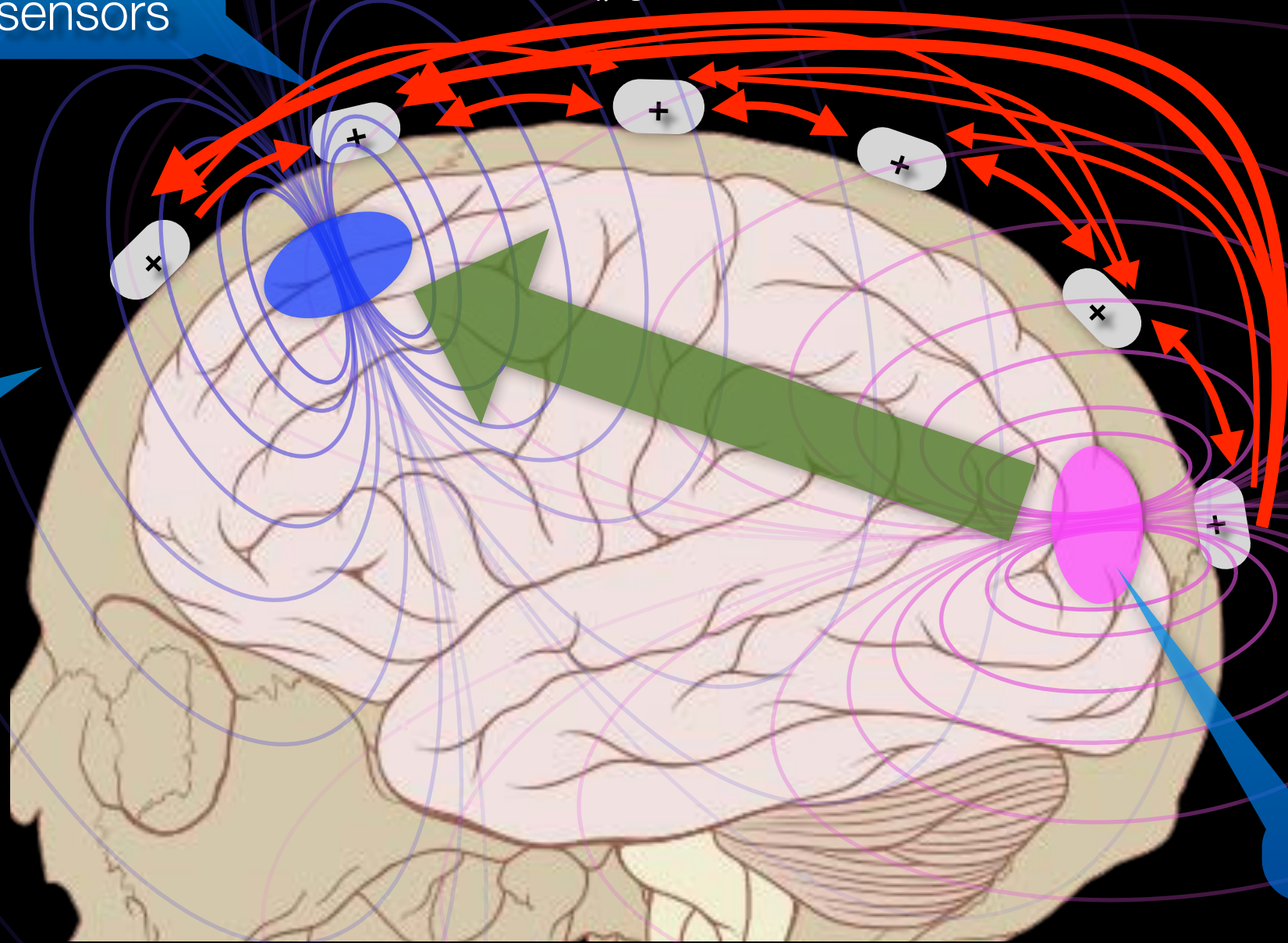
Volume
Conduction

ICA
SBL
Beamforming
Minimum-norm
...

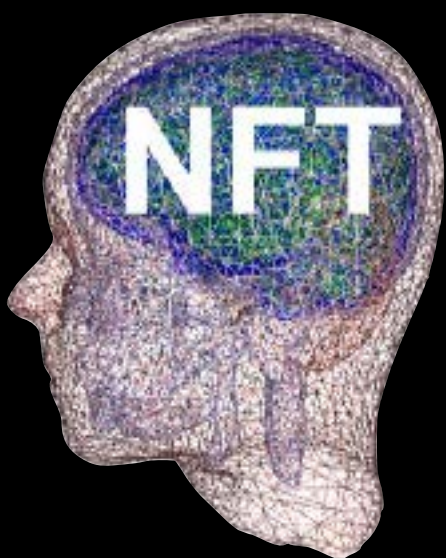
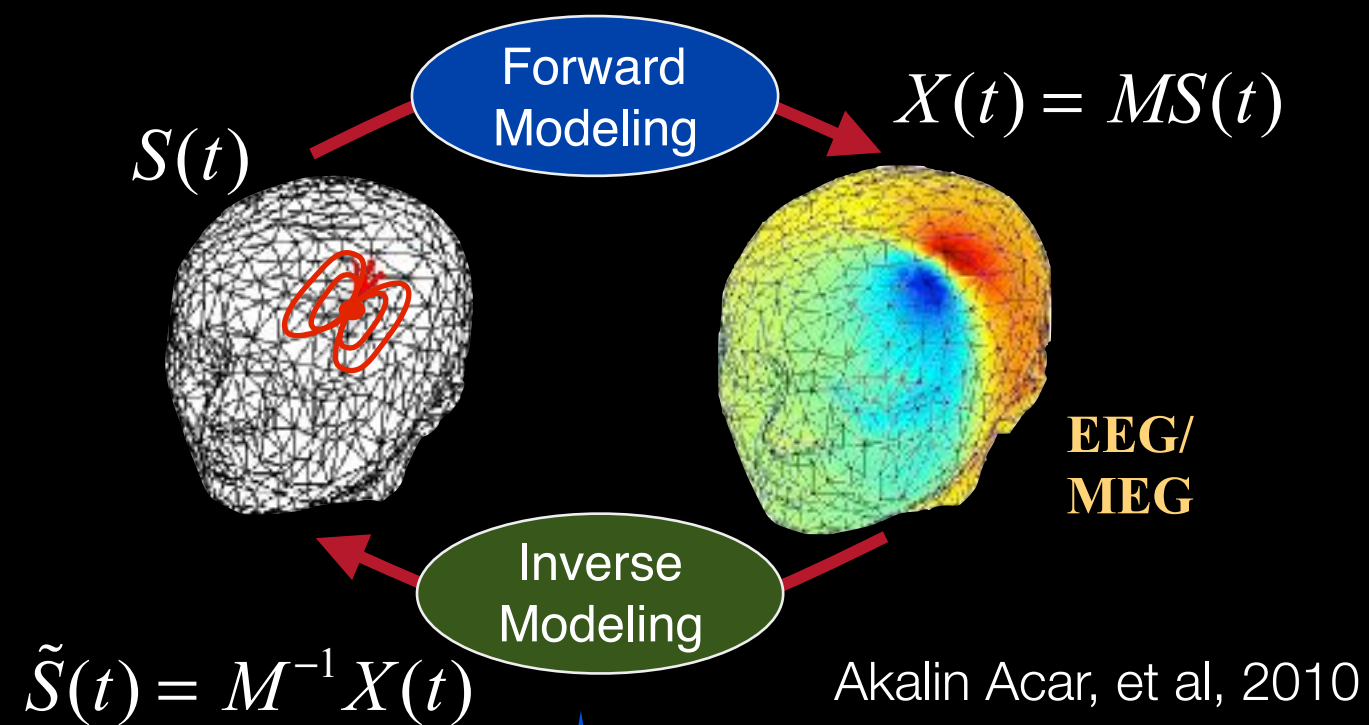
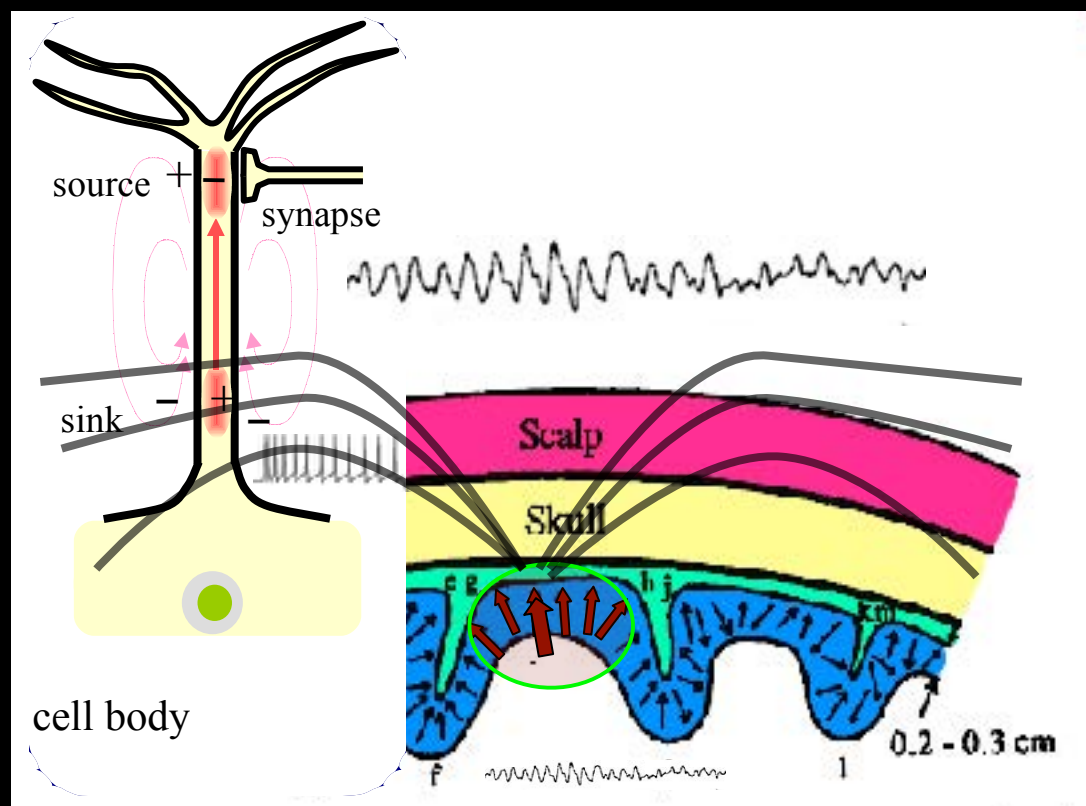
sources

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

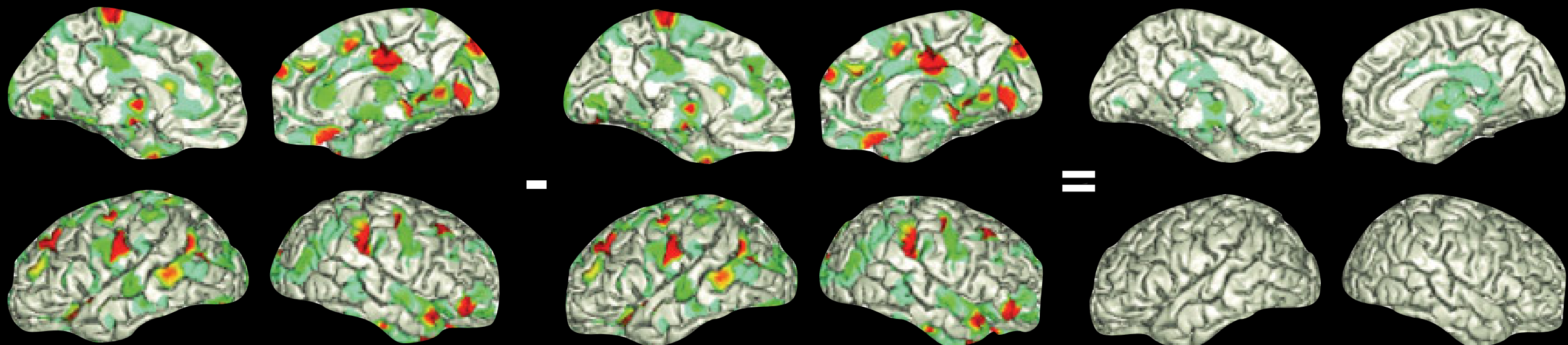
Method	Smoothness	Sparsity	Independence/Orthogonality
MNE	X		
LORETA	X		
dSPM	X		
Beamforming			X
Sparse Bayesian Learning	X	X	
S-FLEX	X	X	
FOCUSS		X	
ICA/PCA/SOBI			X

Source reconstruction with ICA+SBL

simulated

reconstructed

error



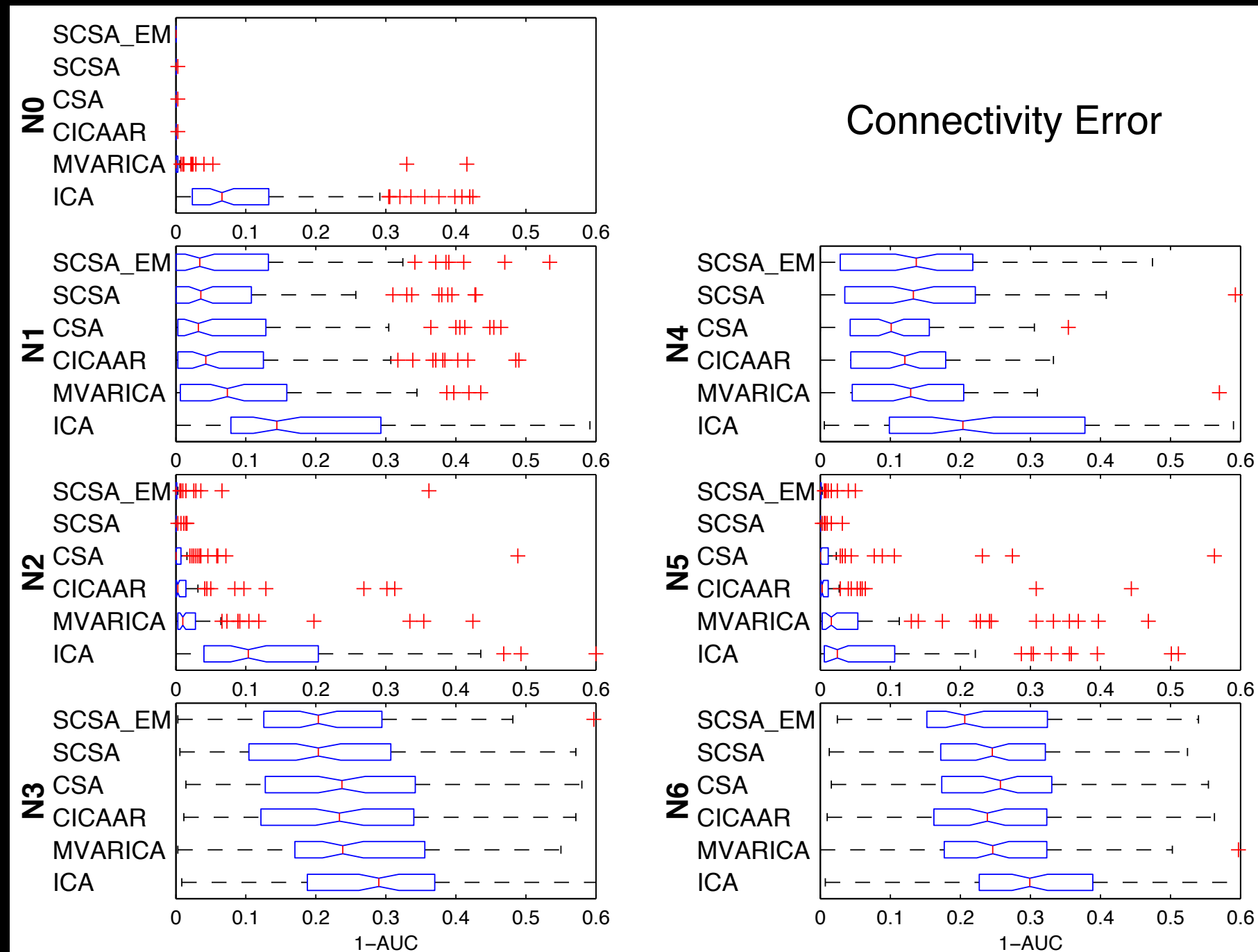
Makeig, Ramirez, Weber, Wipf, Dale, Simpson, *15th Inter. Conf on Biomagnetism* (2006)

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**.

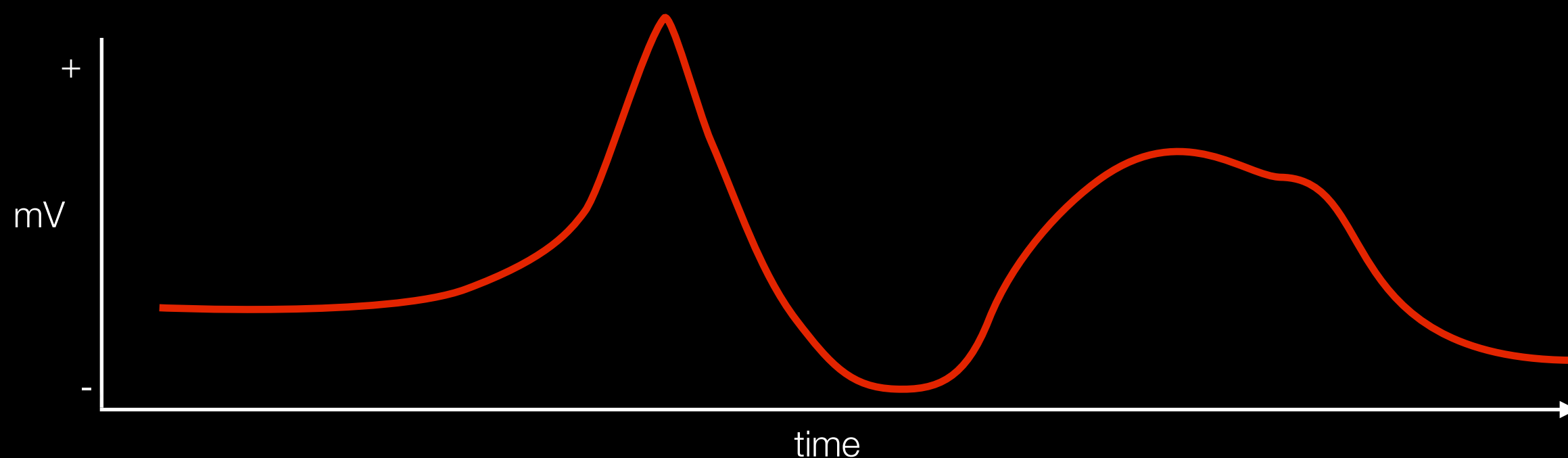
However, the *best* approach is to use an inverse model that explicitly preserves time-delayed dependencies or *jointly* estimates sources (de-mixing matrix) and connectivity (VAR parameters). See the Sparsely Coupled Sources Analysis method (Haufe, 2008 IEEE TBME), available in SIFT.

Estimating Dependency of Independent Components ?



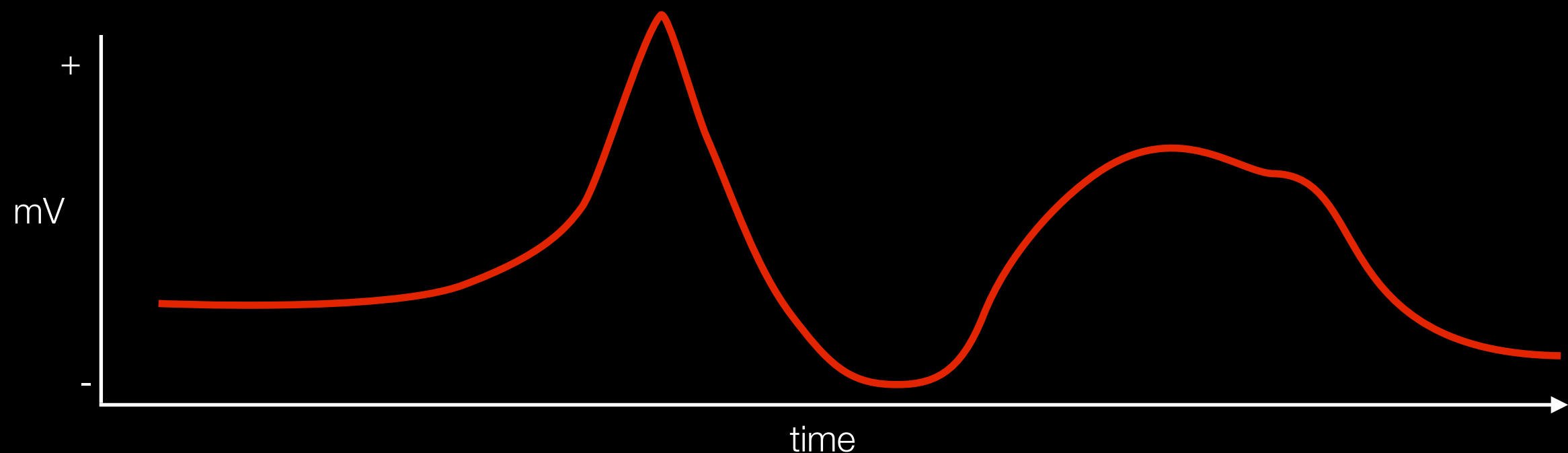
Adapting to Non-Stationarity

- ✦ 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?



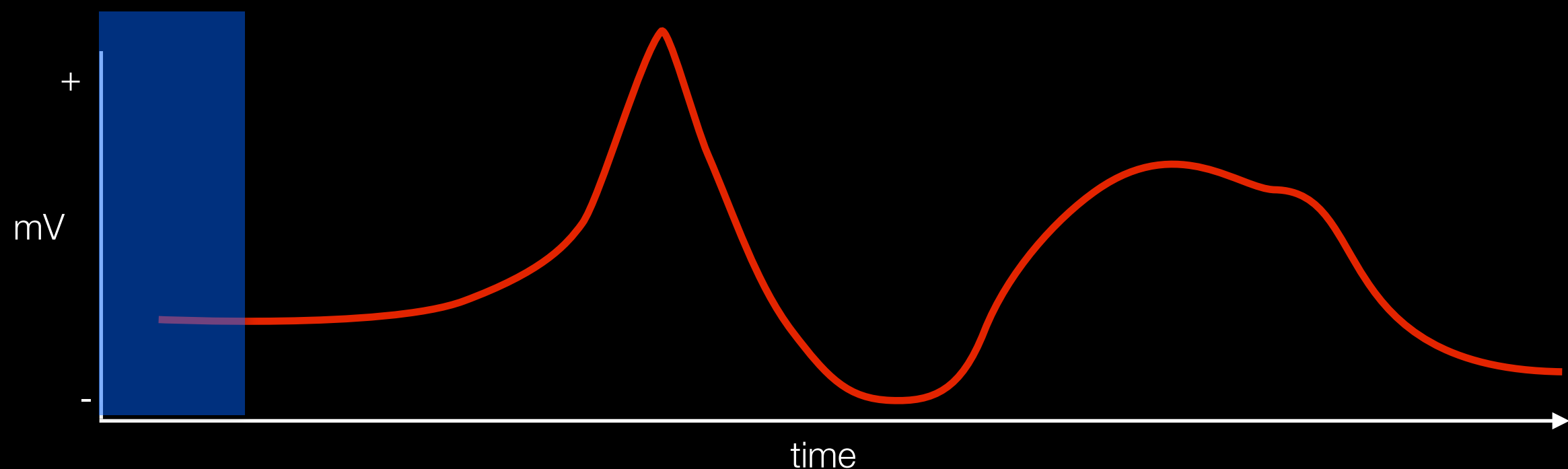
Adapting to Non-Stationarity

- ✦ **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)

