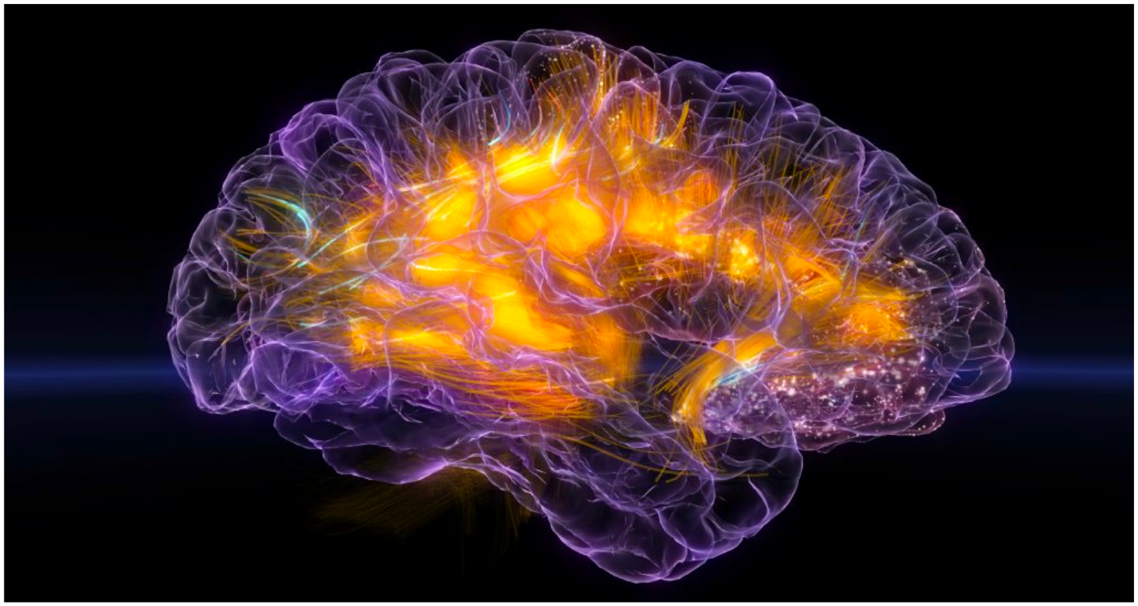
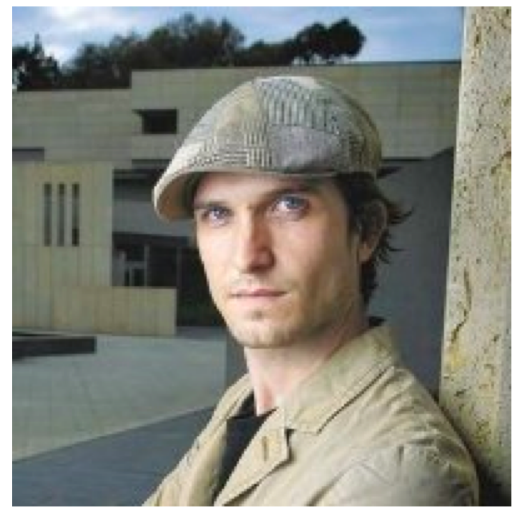
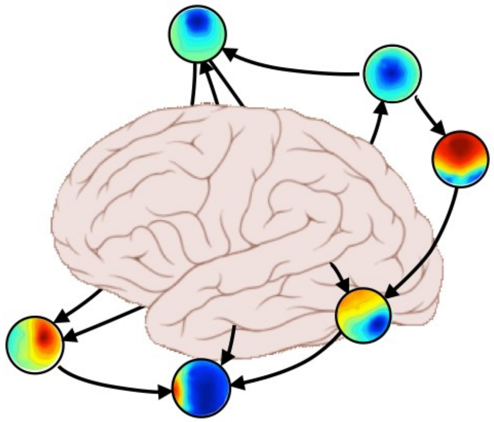
Brain connectivity



Tim Mullen



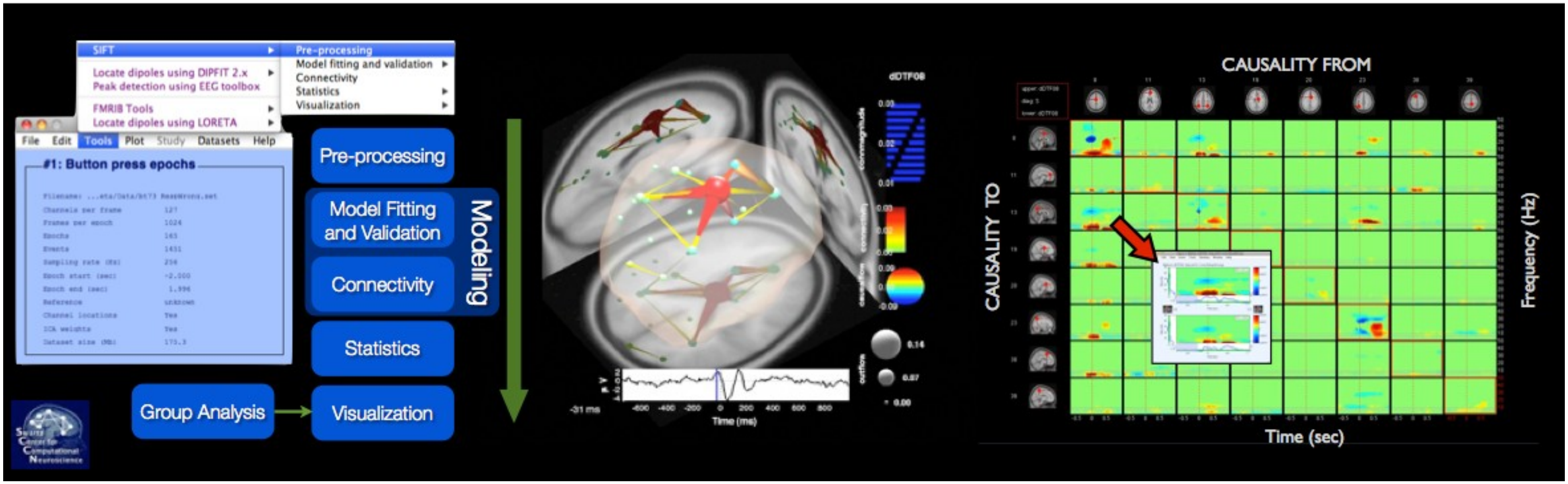
intheon



SIFT

Source Information Flow Toolbox

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



- A toolbox for (source-space) electrophysiological information flow and causality analysis (single- or multi-subject) integrated into the EEGLAB software environment.
- Emphasis on vector autoregression and time-frequency domain approaches
- Standard and novel interactive visualization methods for exploratory analysis of connectivity across time, frequency, and spatial location

Swartz Center for Computational Neuroscience

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- MoBI Lab Wiki
- SCCN Wiki Home

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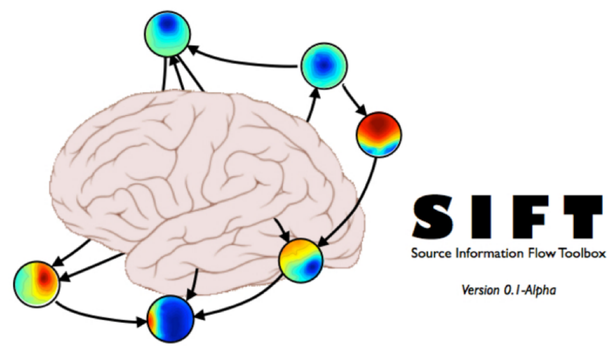
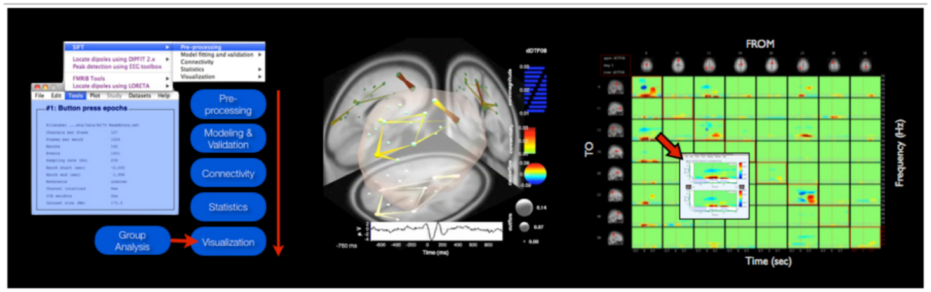
SIFT





Contents [hide]

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

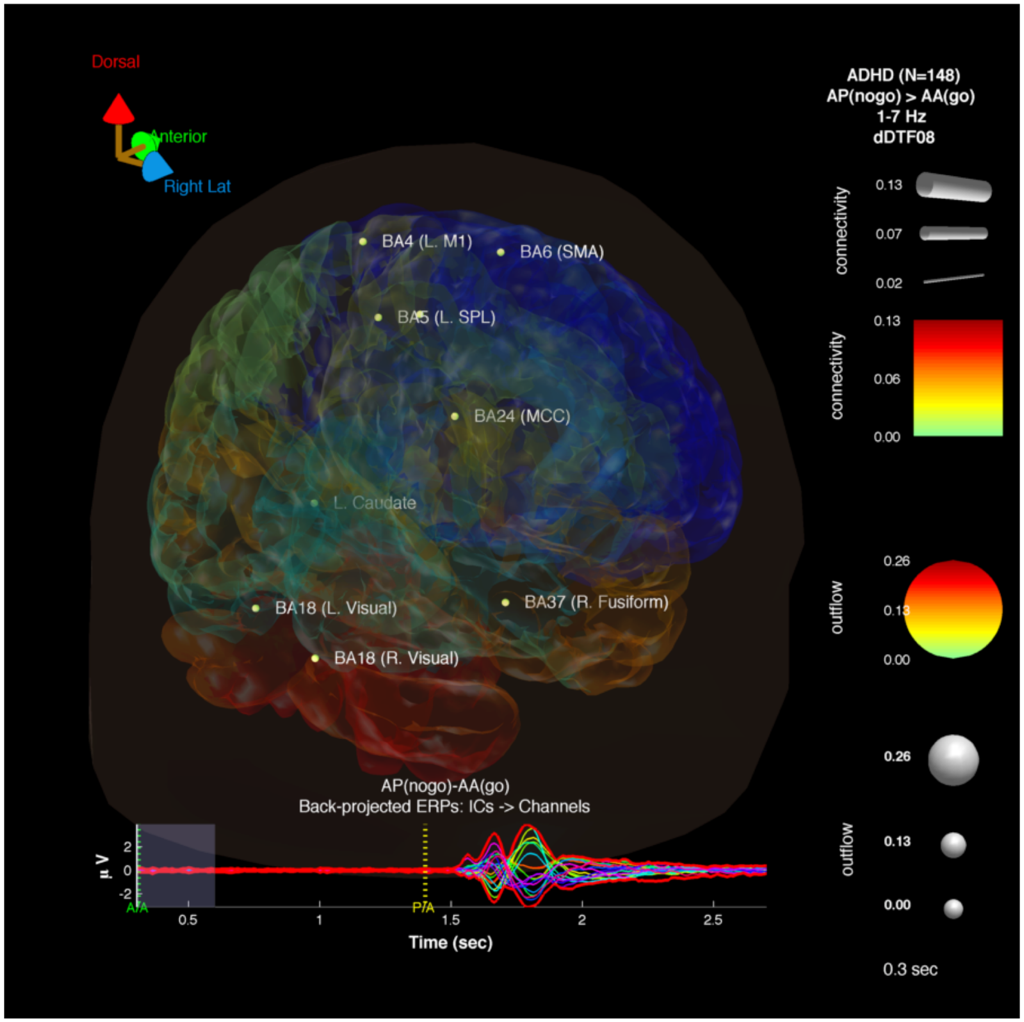
Developed and Maintained by: Tim Mullen (SCCN, INC, UCSD)
Web: http://www.antillipsi.net
Email: <Tim's first name> (at) sccn (dot) ucsd (dot) edu

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

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

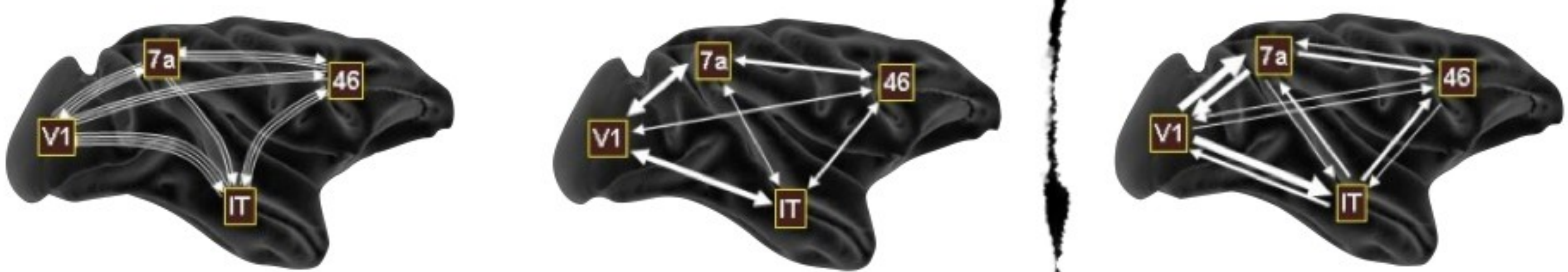
- Open Challenges:
  - Non-invasive measures (source inference)
  - Robustness and Validity (constraints statistics)
  - Scalability (multivariate)
  - Temporal Specificity / Non stationarity / Single-trial (dynamics)
  - Multi-subject Inference
  - Usability and Data Visualization (software)



Large-scale brain connectivity

(Bullmore and Sporns, *Nature*, 2009)

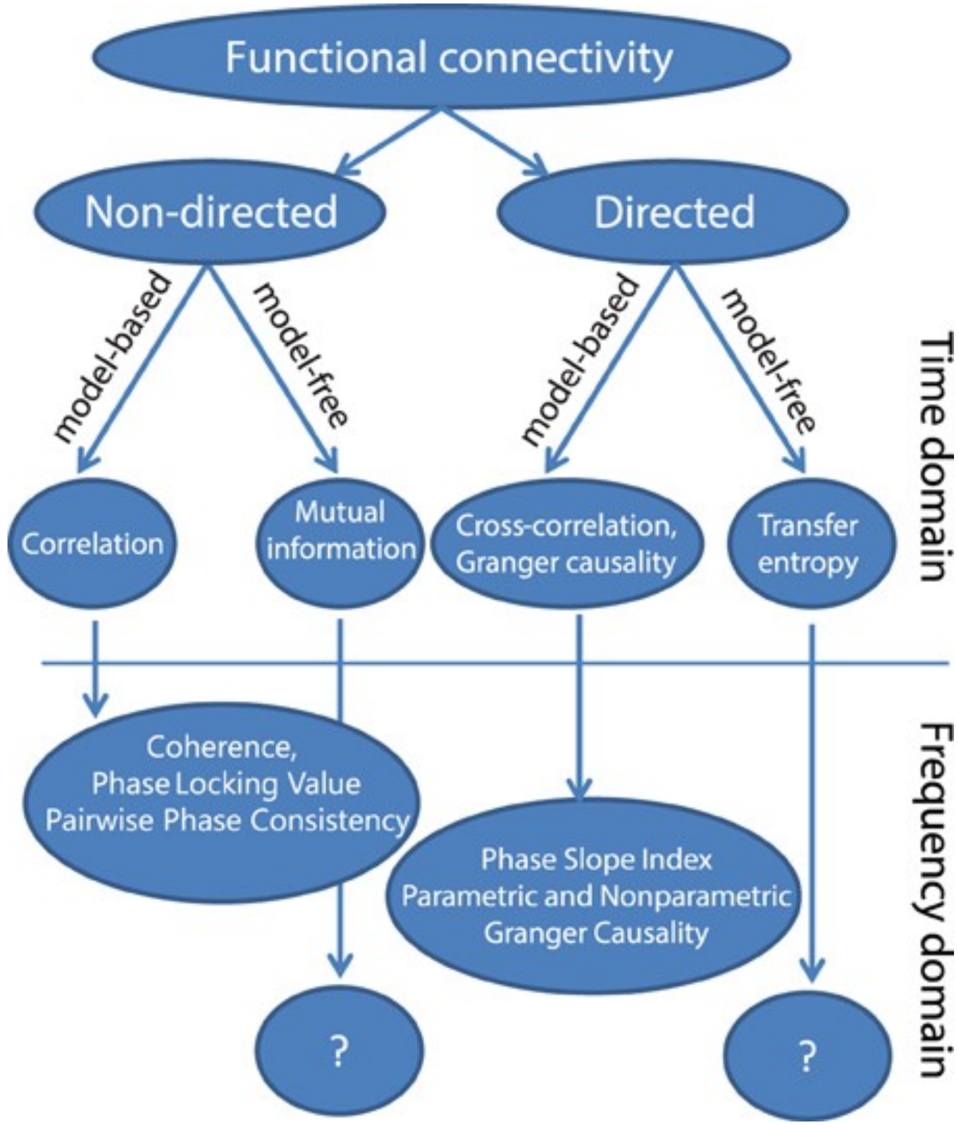
Structural	**Functional**	**Effective**



Structural	Functional	Effective
state-invariant, anatomical	dynamic, state-dependent, correlative, symmetric	dynamic, state-dependent, asymmetric, causal, information flow

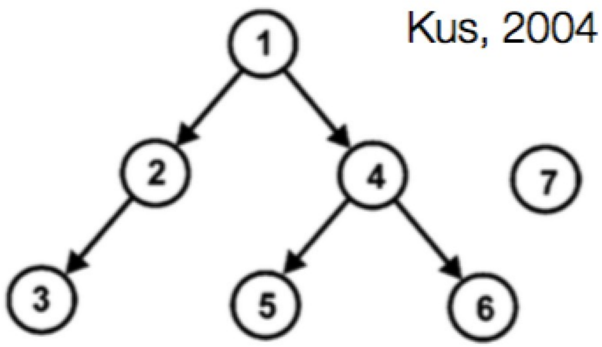
Hours-Years **milliseconds-seconds**

Temporal Scale



Bastos AM, Schoffelen J-M: **A Tutorial Review of Functional Connectivity Analysis Methods and Their Interpretational Pitfalls**. *Front Sys Neurosci* 2016, **9**:413.

The problem of spurious connectivity

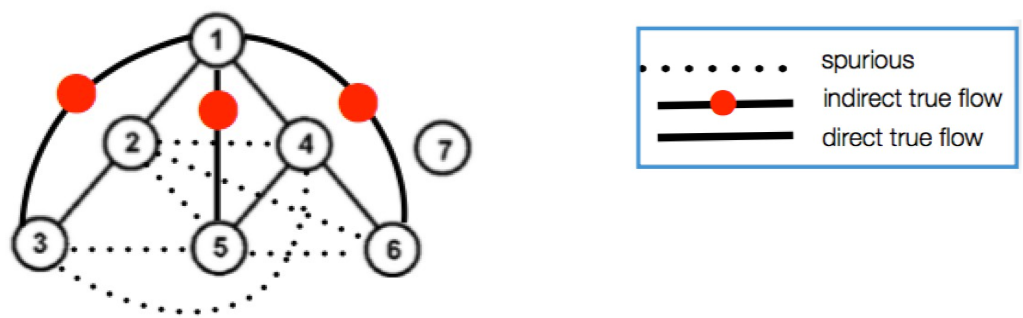


Kus, 2004

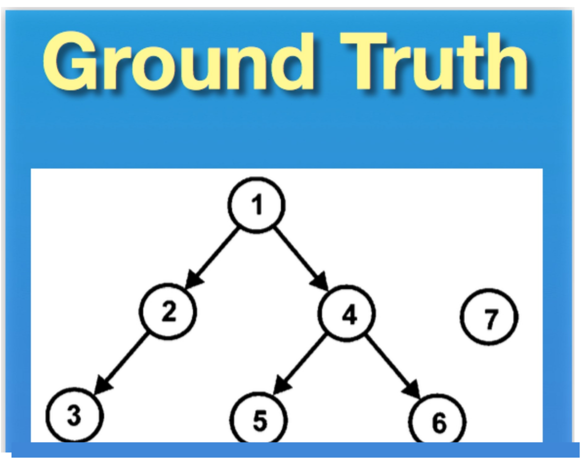
Coherency

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

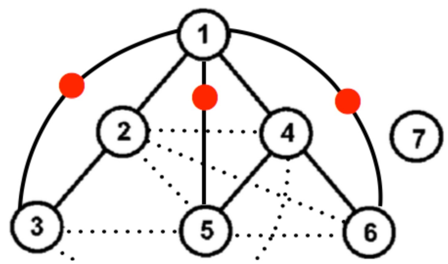
(Bendat and Piersol, 1986)



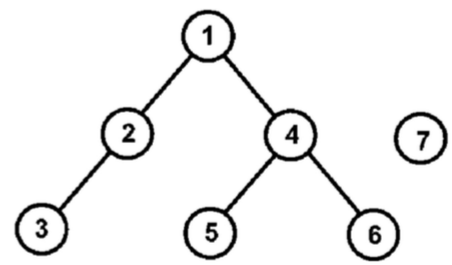
Bivariate measures such as coherence (but also original GC), find spurious connections between nodes if they share a common input.



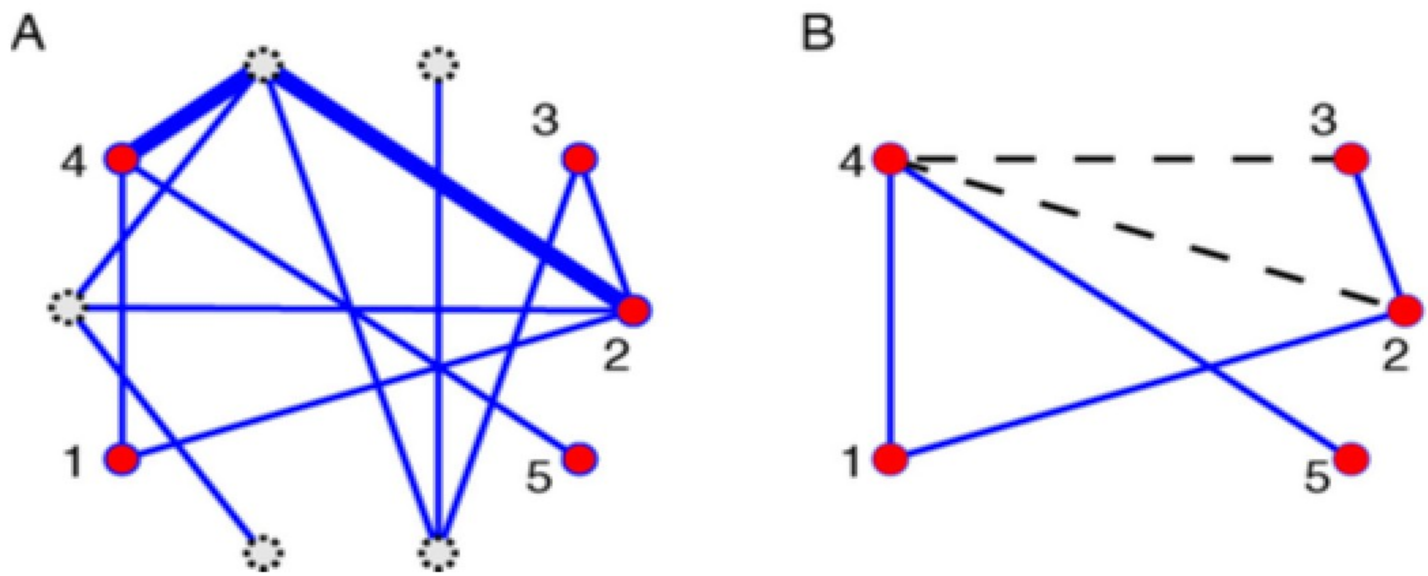
Coherence



Partial coherence



A deeper problem – unobserved nodes



With EEG, it's unavoidable that there will be contributing network nodes (e.g. thalamus) that we cannot observe.

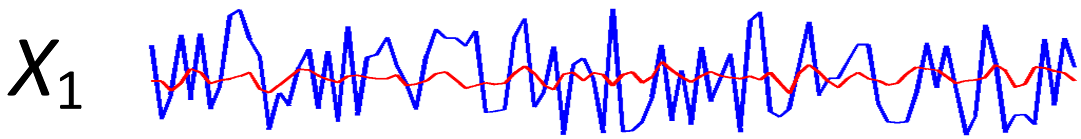
We also can't be sure ICA will identify all important sources…

Granger-causality

- A measure of *statistical* causality based on prediction.
- Widely used in time-series econometrics.
- Nobel Prize in economics, 2003.

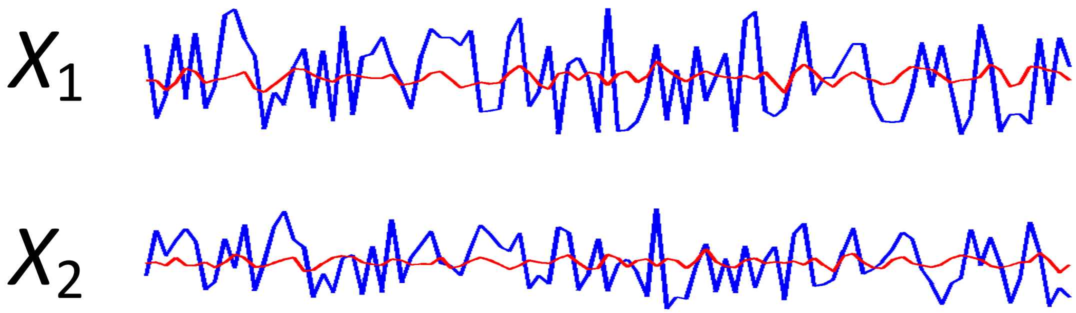
If a signal A causes a signal B, then knowledge of the past of both A and B should improve the predictability of B, as compared to knowledge of B alone.

AR Models (prediction of future of a signal by its past)

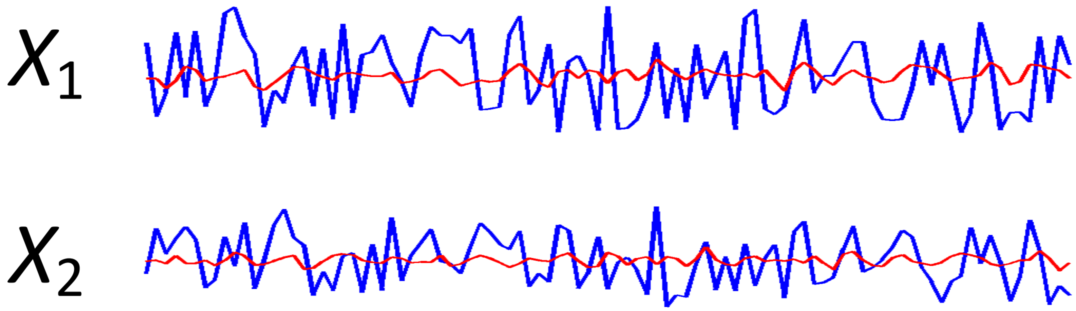


$$X_1(t) = -0.5X_1(t-1) + 0.3X_1(t-2) + 0.1X_1(t-3) \ldots$$

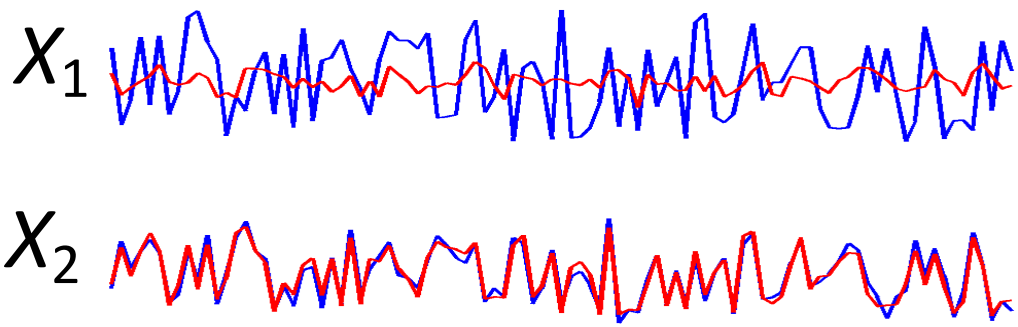
AR Models (prediction of future of a signal by its past)



AR Models (prediction of future of a signal by its past)

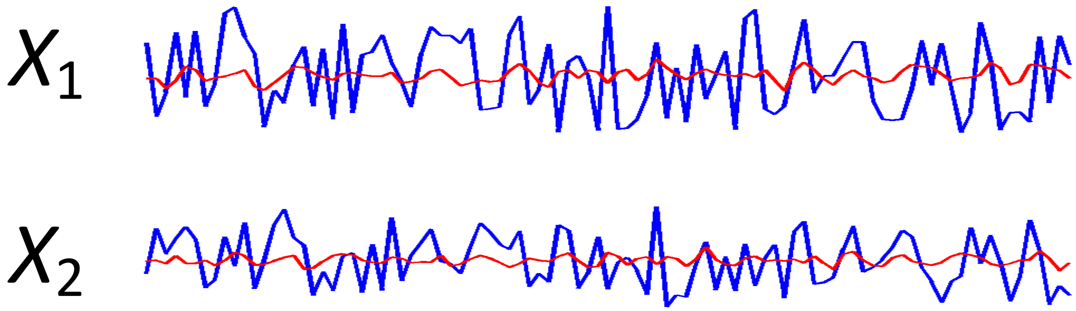


VAR Models (prediction of future of a signal by its past + the other signal's past)



Incorporating information about X_1 improves the prediction of X_2! We say "X_1 granger causes X_2"

AR Models (prediction of future of a signal by its past)



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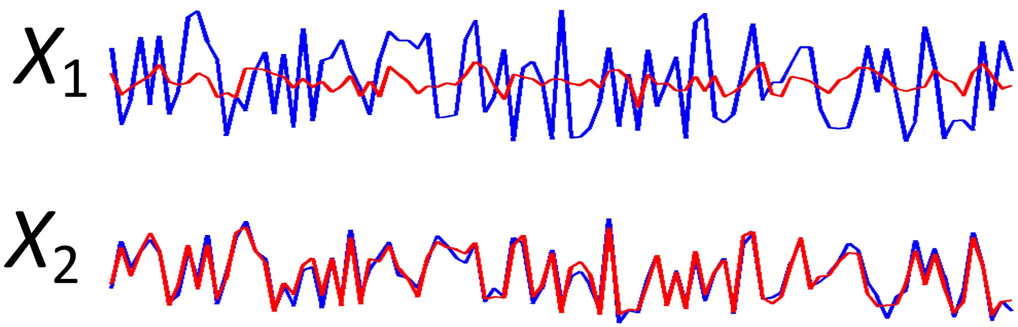
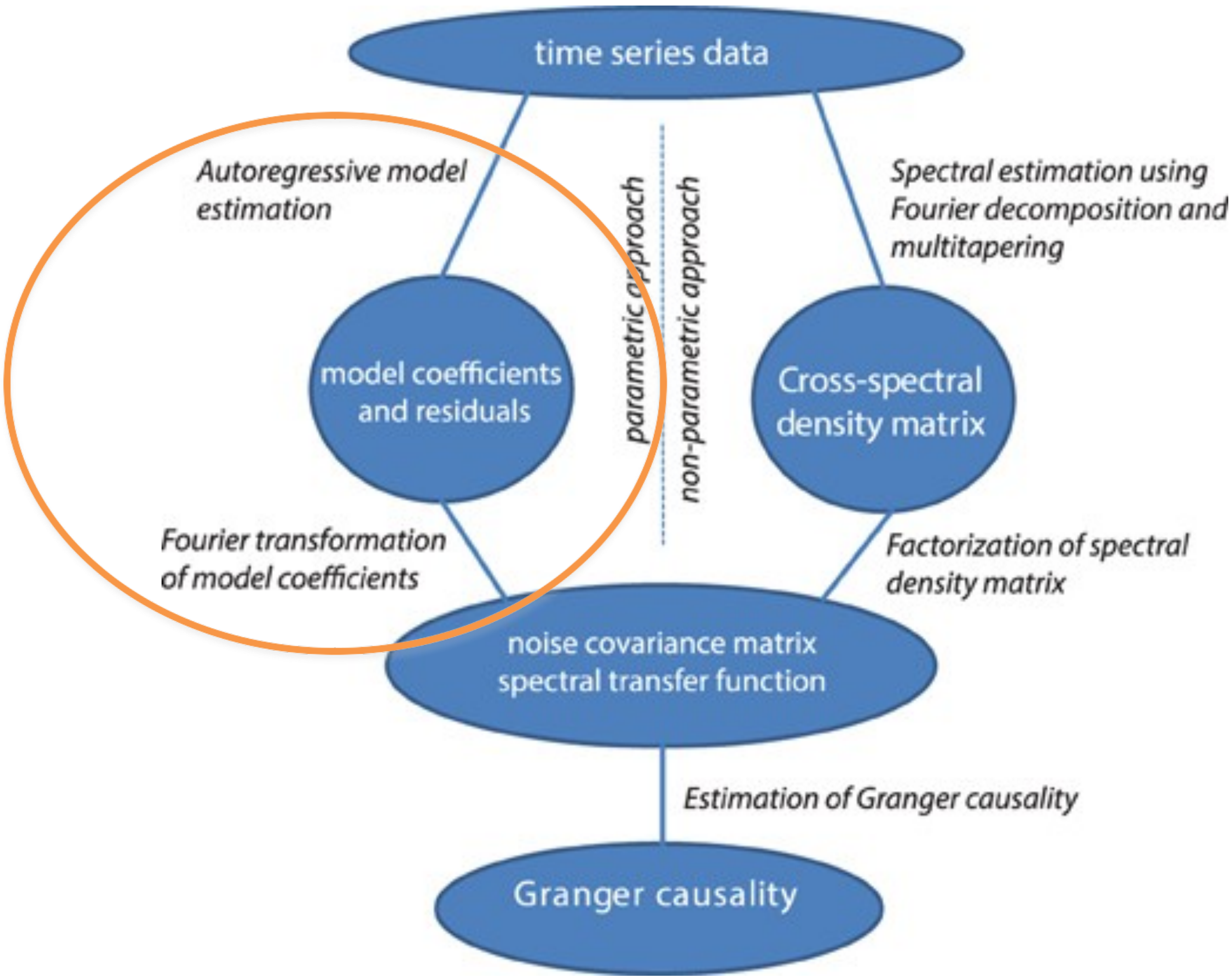


$X_1(t) = -0.5X_1(t-1) + 0.3X_2(t-1) + \ldots$

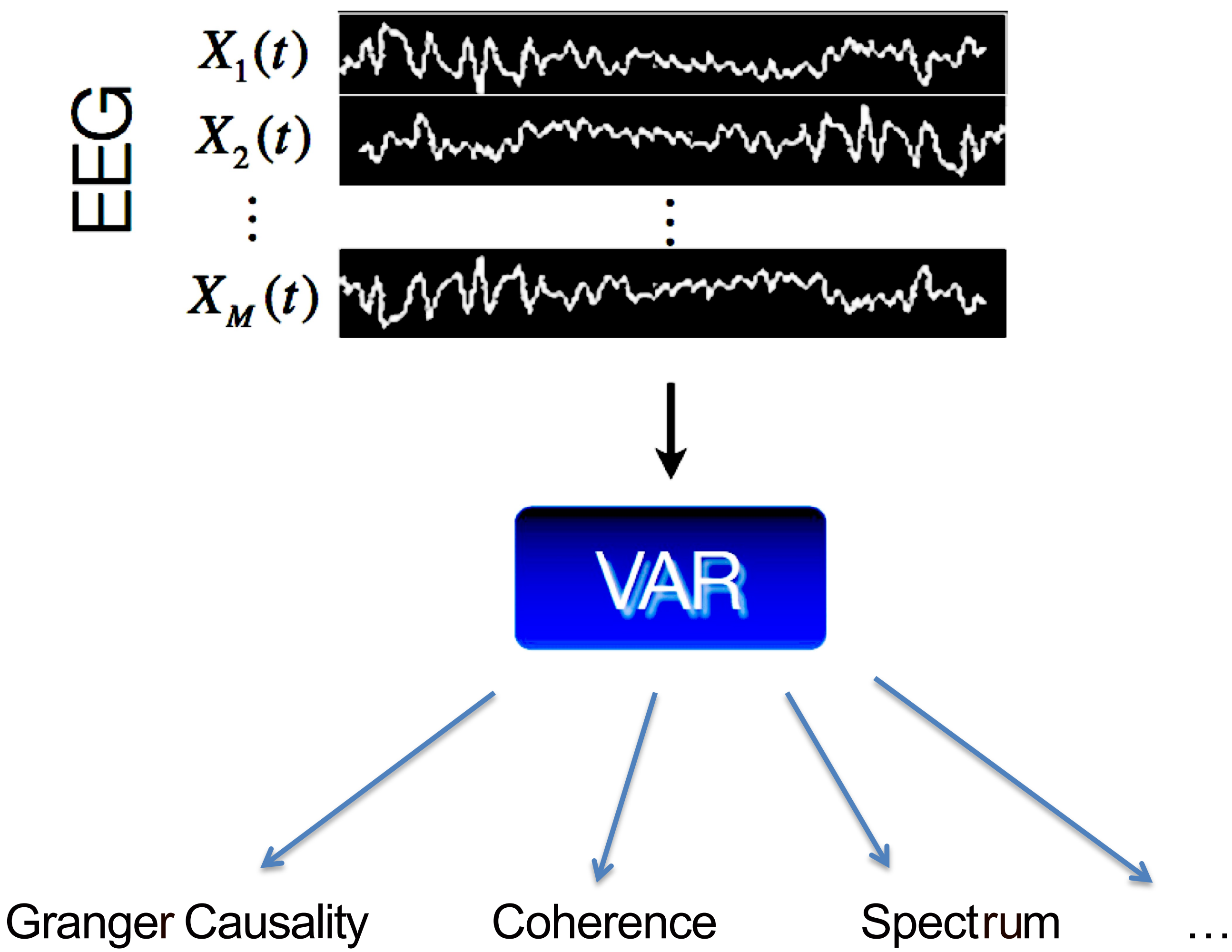
$X_2(t) = -5X_1(t-1) - 0.1X_2(t-1) + \ldots$

Incorporating information about X_1 improves the prediction of X_2! We say "X_1 granger causes X_2"

Calculation of GC

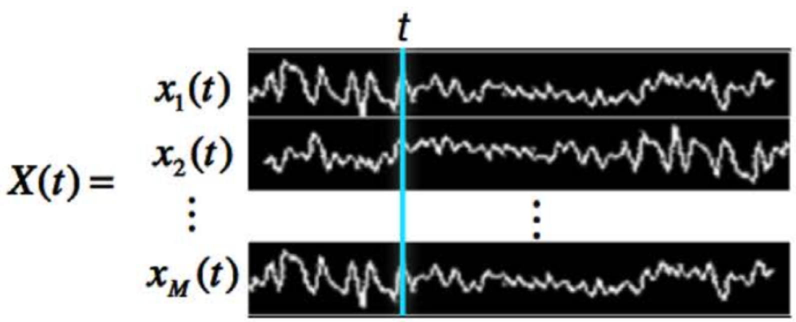


Vector Autoregressive (VAR / MAR / MVAR) Modeling



The Linear Vector Auto-regressive (VAR) Model

Ordinary Least-Squares



VAR[*p*] model

model order

random noise process

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

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

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

Selecting a VAR Model Order

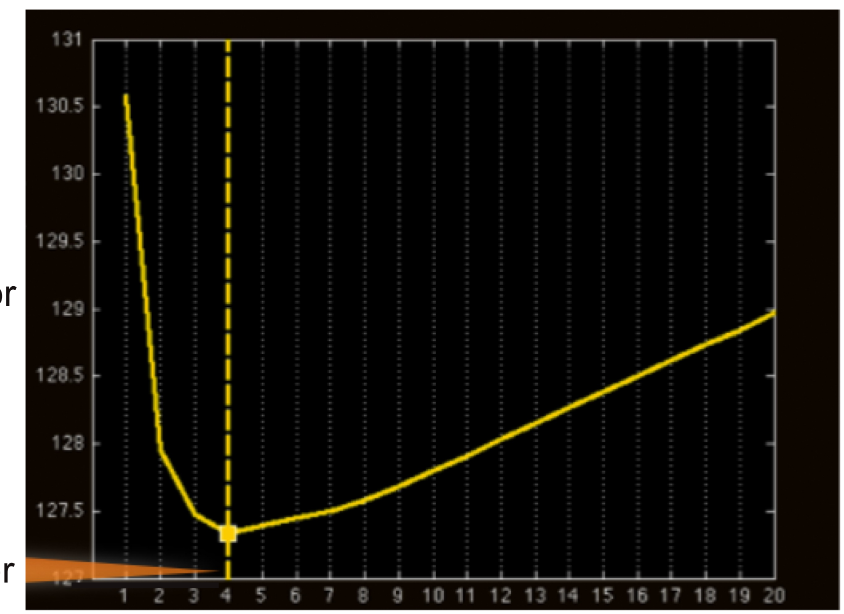
- Model order is typically determined by minimizing information criteria such as Akaike Information Criterion (AIC) for varying model order (p):

$$AIC(p) = 2\log(\det(V)) + M2p/N$$

Penalizes high model orders (parsimony)

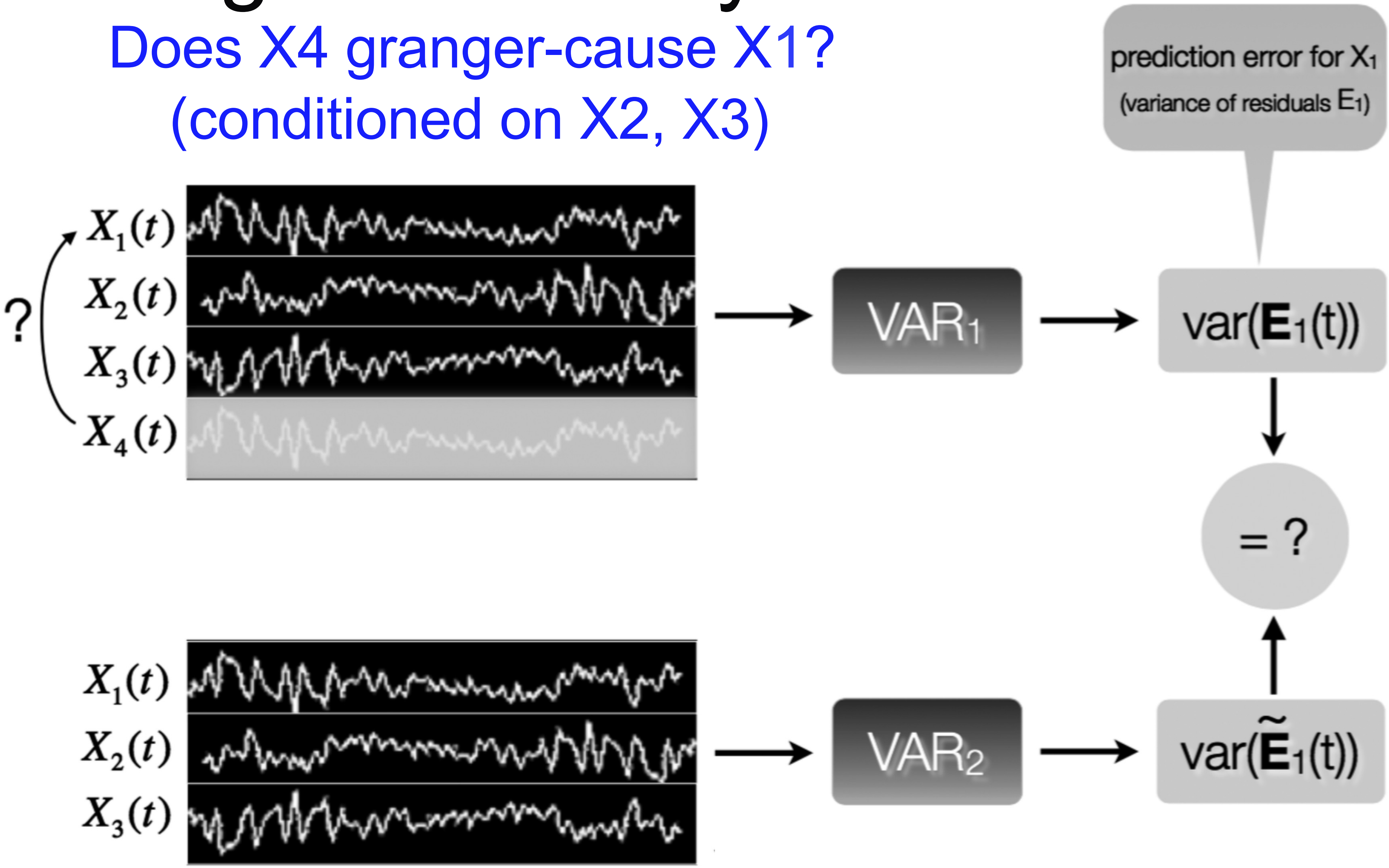
entropy rate (amount of prediction error)

- Optimal model order depends on sampling rate (higher sampling rate often requires higher model orders)



Granger Causality

Does X4 granger-cause X1?
(conditioned on X2, X3)

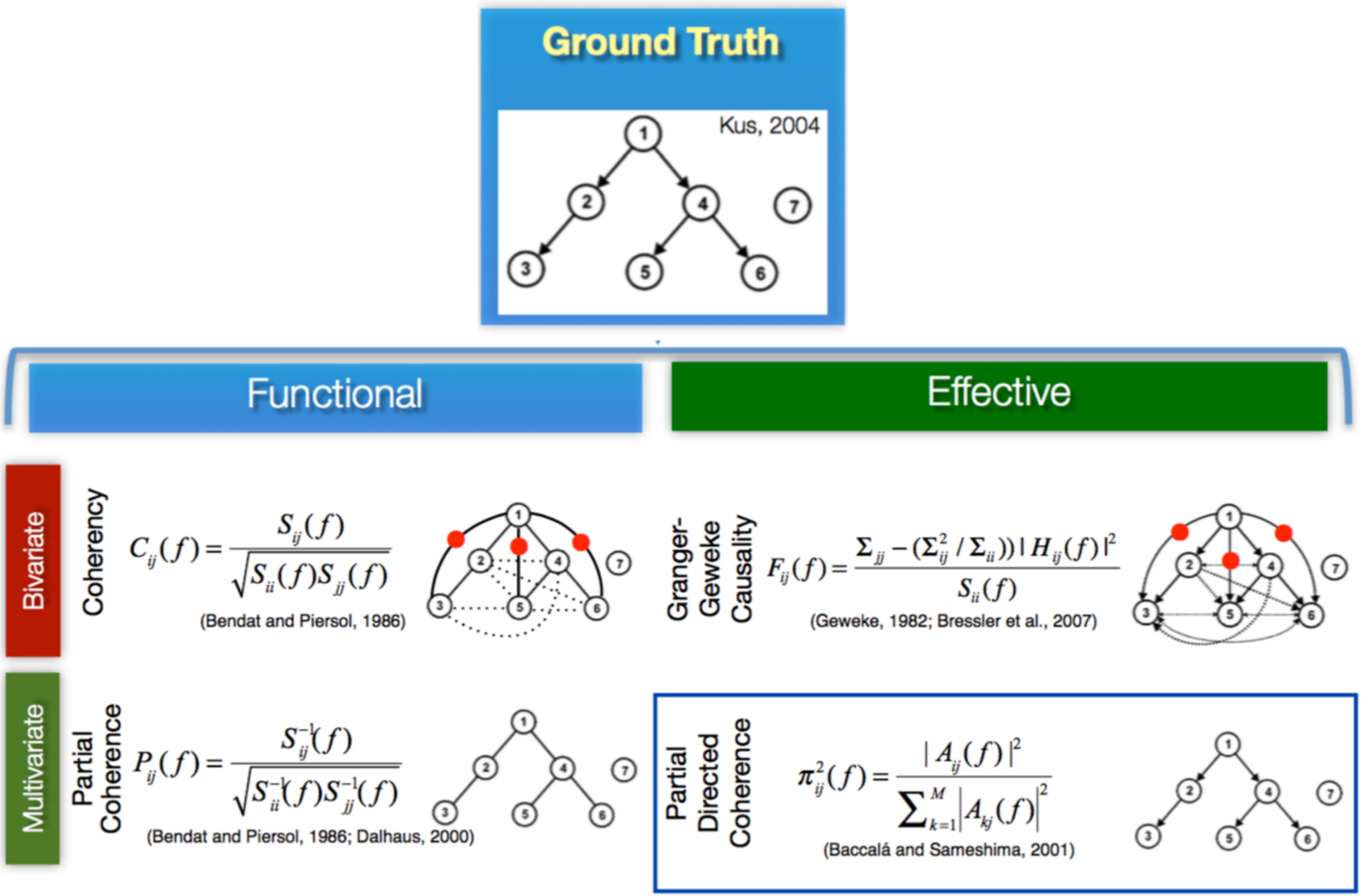


Granger-causality quiz

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

Which causal structure does this model correspond to?

a) $1 \rightarrow 2$ b) $1 \leftarrow 2$ c) $1 \leftrightarrow 2$



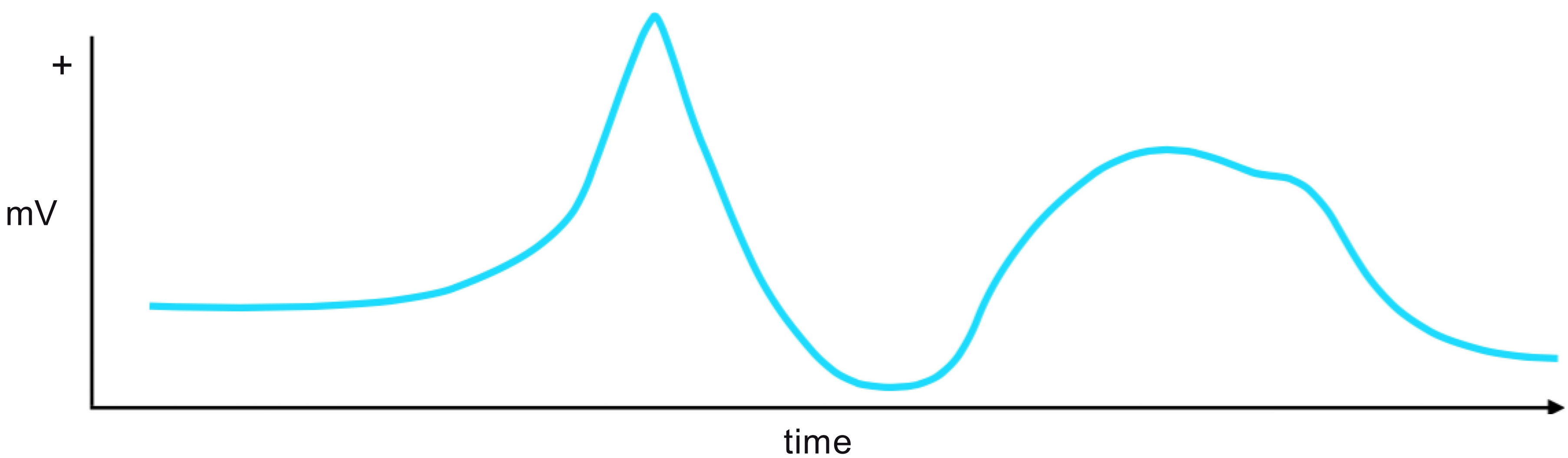
Ground Truth
Kus, 2004
Functional
Effective
Bivariate
Multivariate
Coherency
$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f)S_{jj}(f)}}$
(Bendat and Piersol, 1986)
Granger-Geweke Causality
$F_{ij}(f) = \frac{\Sigma_{jj} - (\Sigma_{ij}^2 / \Sigma_{ii}))|H_{ij}(f)|^2}{S_{ii}(f)}$
(Geweke, 1982; Bressler et al., 2007)
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
$\pi_{ij}^2(f) = \frac{|A_{ij}(f)|^2}{\sum_{k=1}^{M} \left|A_{kj}(f)\right|^2}$
(Baccalá and Sameshima, 2001)

Time-Frequency GC

- Brain network dynamics often change rapidly with time
  - event-related responses
  - transient network changes during sequential information processing
- Electrophysiological processes often exhibit oscillatory phenomena, making them well-suited for frequency domain analysis

Adapting to Non-Stationarity

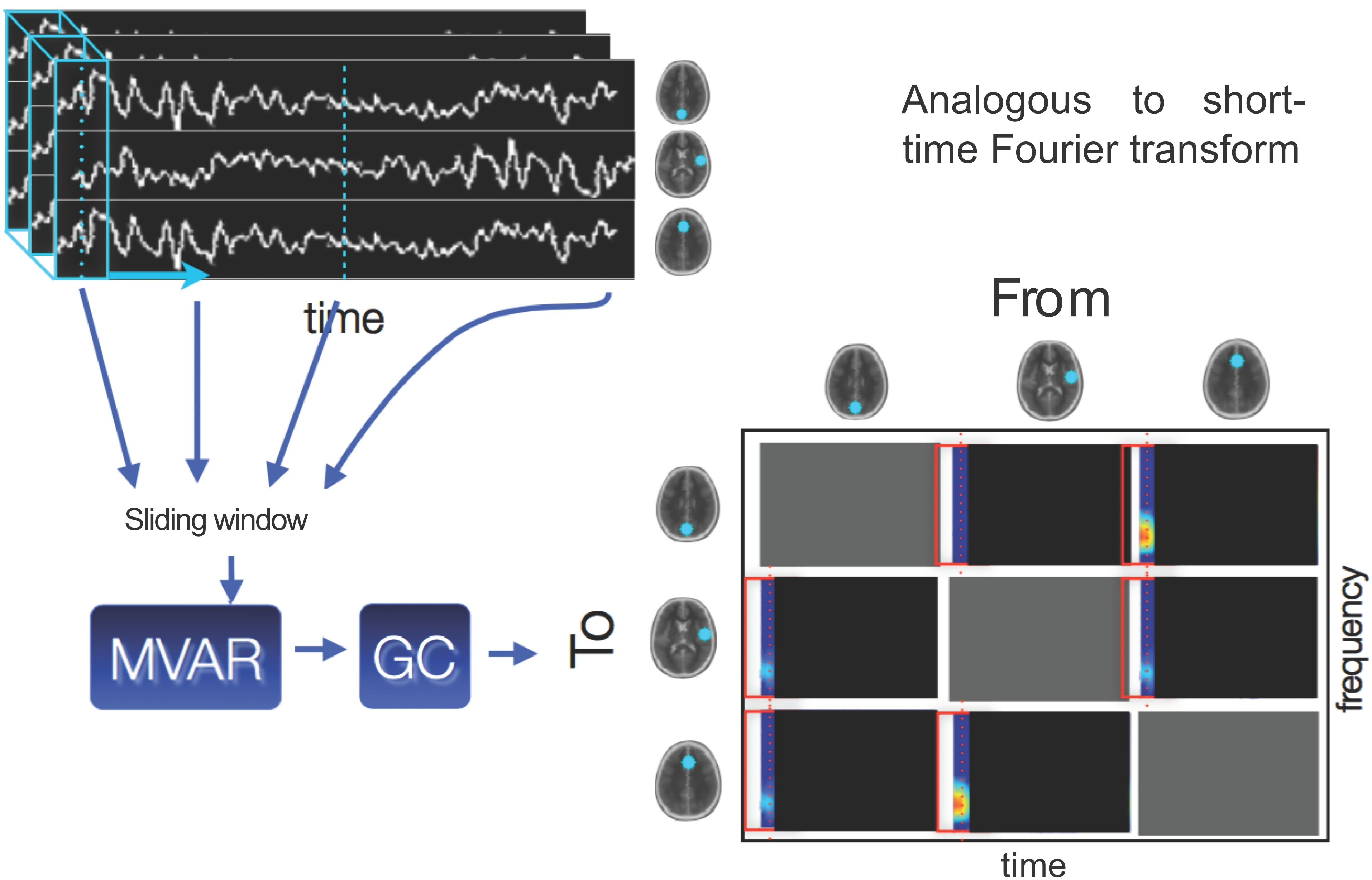
- The brain is **a dynamic system** and measured brain activity and coupling can change rapidly with time (non-stationarity)
  - event-related perturbations (ERSP, ERP, etc)
  - structural changes due to learning/feedback
- How can we adapt to non-stationarity?



Segmentation-based VAR

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

Analogous to short-time Fourier transform



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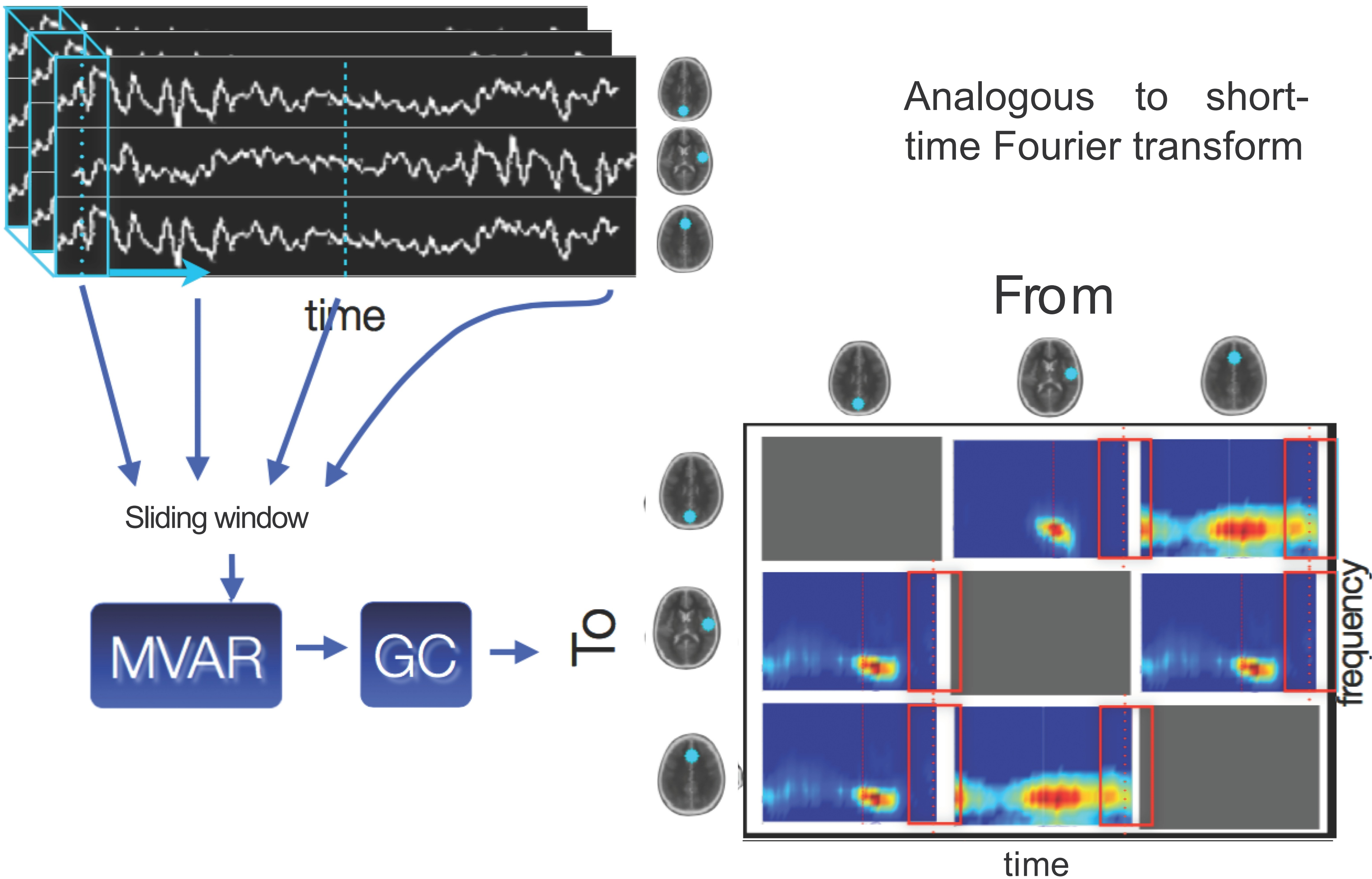


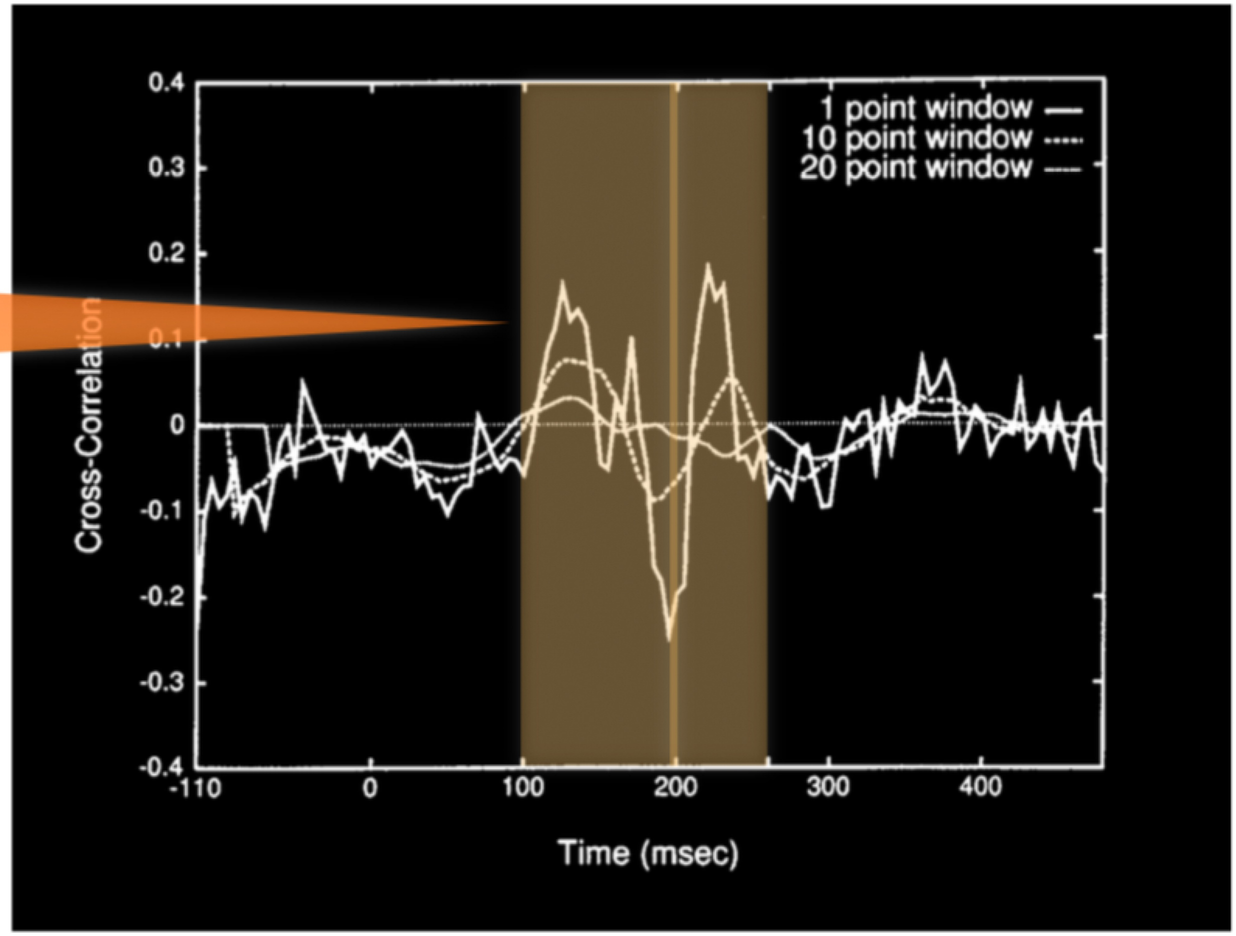
Important Choices

- Model Order
  - Determines complexity of spectrum you can model
  - Larger orders need more data

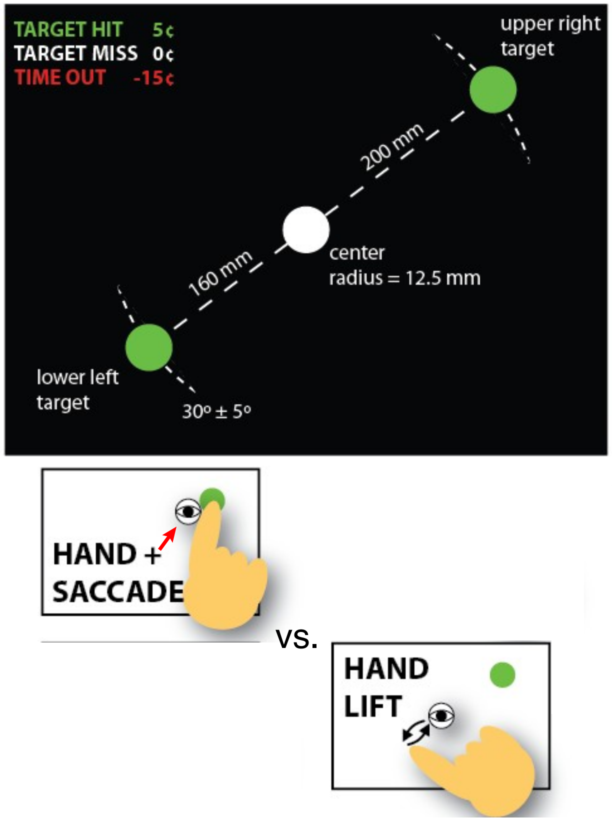
- Window Length
  - Window must be long enough to contain sufficient data for your chosen model order
  - Must be long enough to encompass the time-scale of interactions
  - Yet not too long as to smear temporal dynamics or include non-stationary data
  - *If trials are present, can optimize AR model over trials*

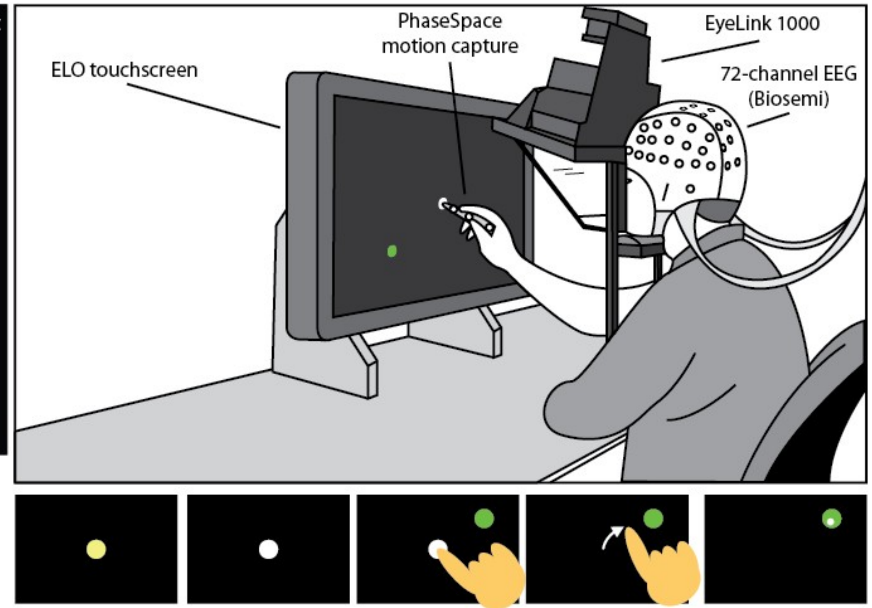
Consideration: Local Stationarity

Too-large, windows may not be locally-stationary



How does brain plan visually guided movements?





1	2	3	4	5
hold	target onset hold	center offset	eye/hand initiation	eye/hand arrival, feedback
500 - 700	500 - 700	< time window (e.g., 450 ms)		

Planning | Execution

0 0.5 1.0

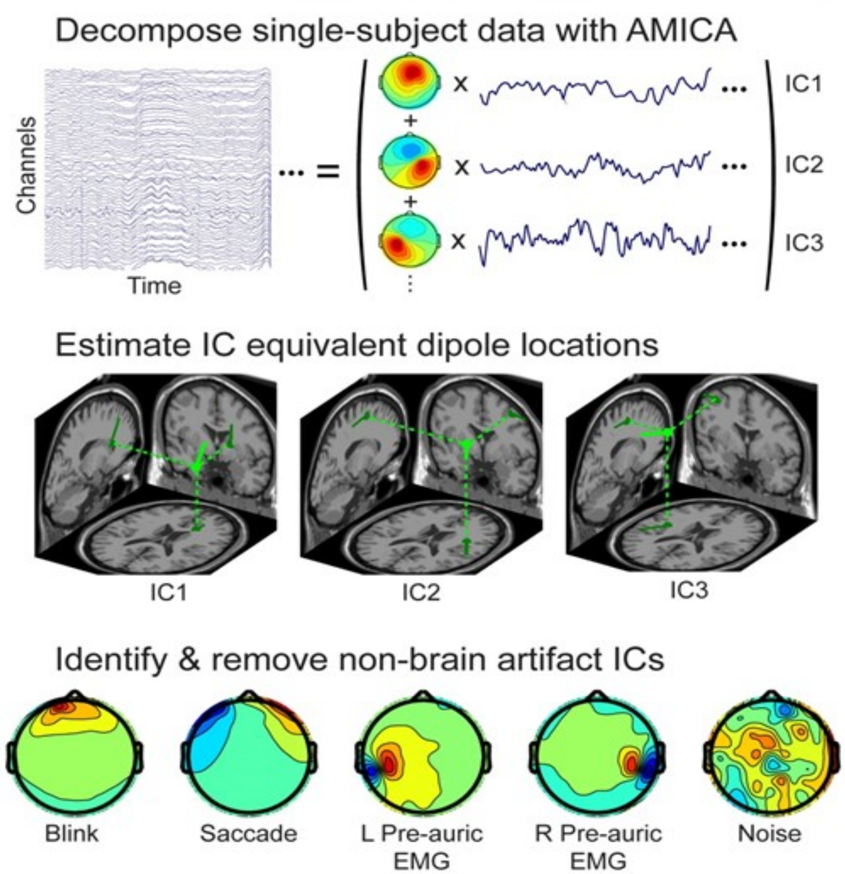
Time (s)

N=10 (right-handed, mean age=21) 70 channel EEG (Biosemi) 512 Hz; 128Hz for connectivity

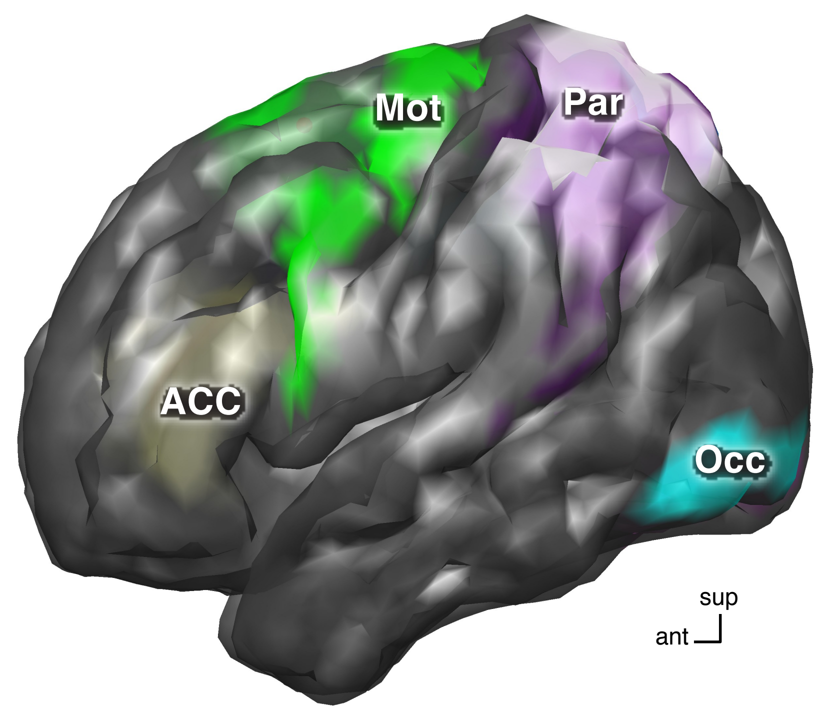
Network causal information flow during motor planning and execution (2014) John R. Iversen, Alejandro Ojeda, Tim Mullen, Markus Plank, Joseph Snider, Gert Cauwenberghs, Howard Poizner. EMBC 2014.

ICA source space analysis

Independent Component Analysis

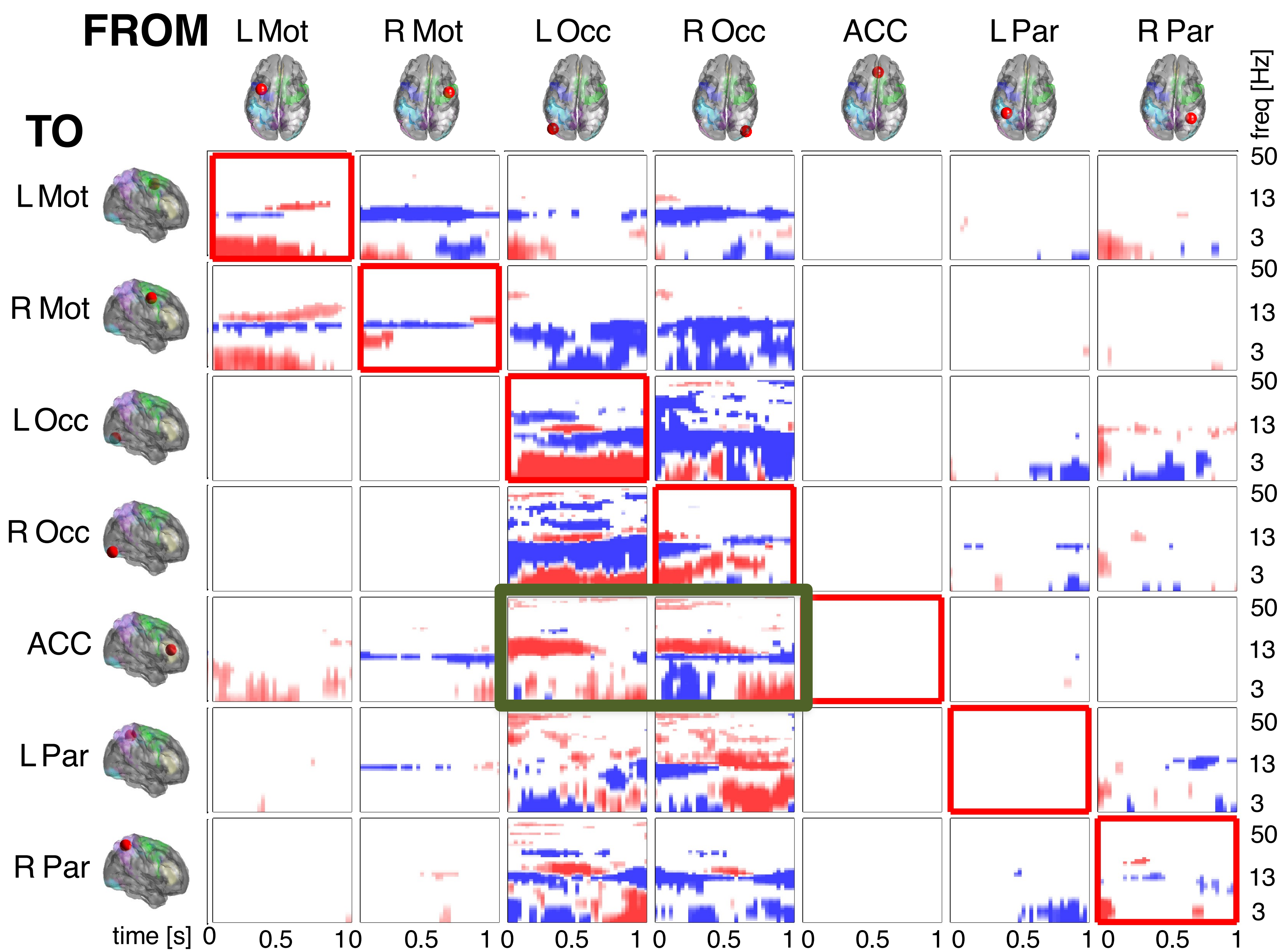


Cortical ROIs



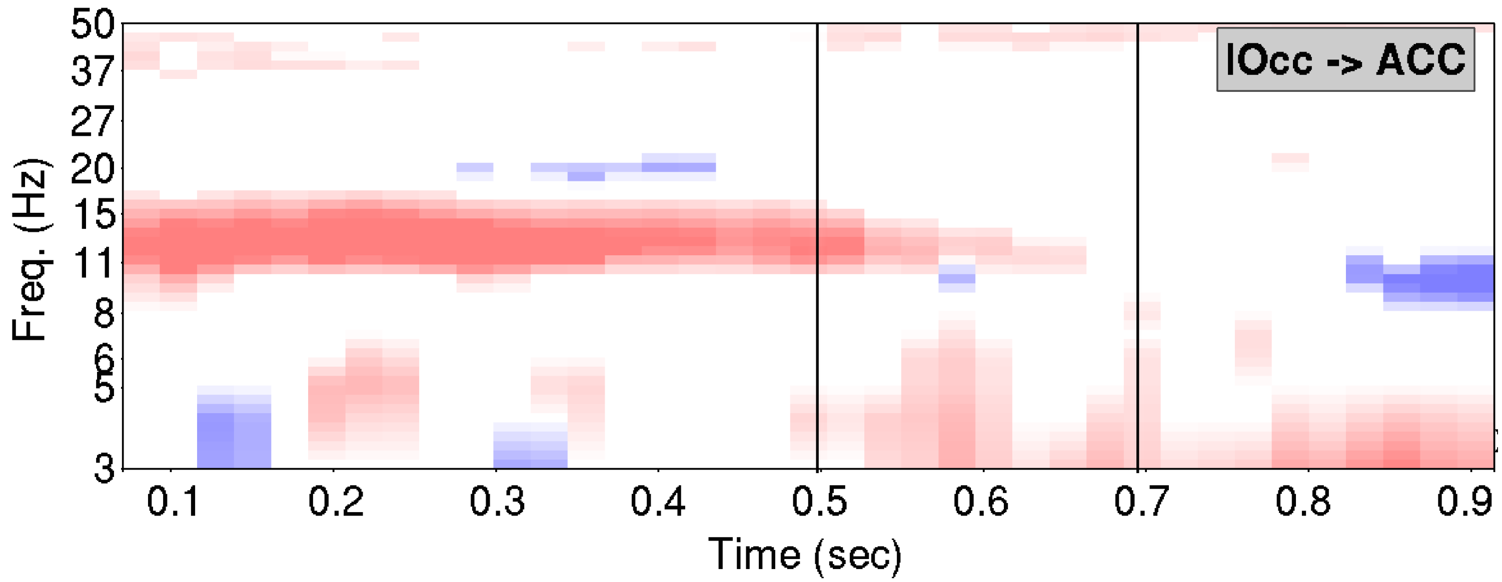
Group SIFT: Project ICs onto cortical surface using LORETA; extract ROI time series. Advantage: Same ROIs for all subjects enables statistical comparison. (*Use BCILAB srcpot*)

Changed causal flow during reaching

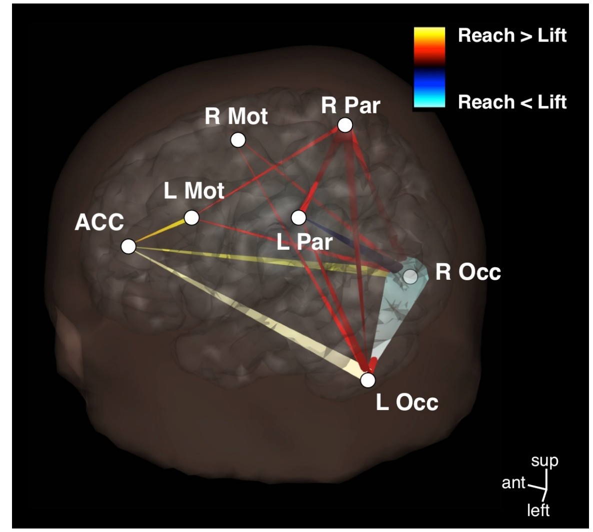


Occipital -> ACC

Planning Execution

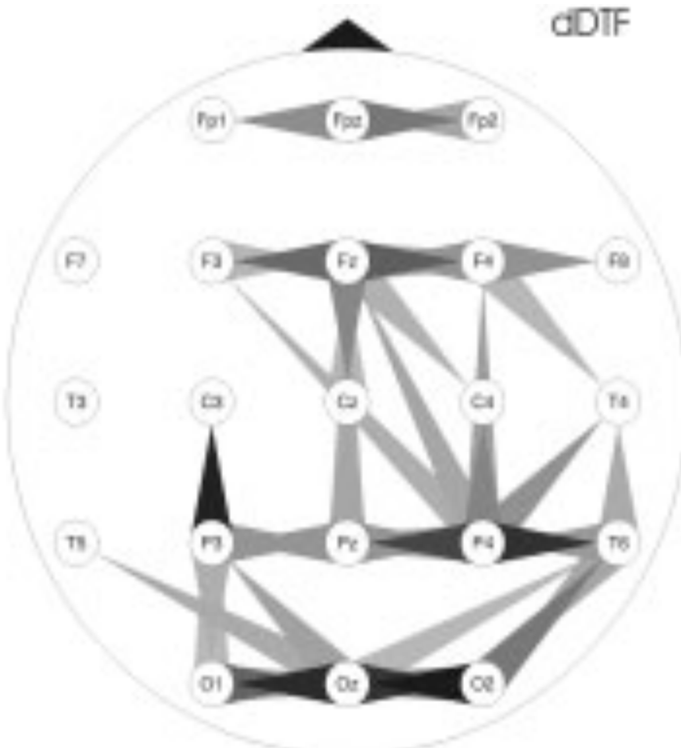


Result discussion

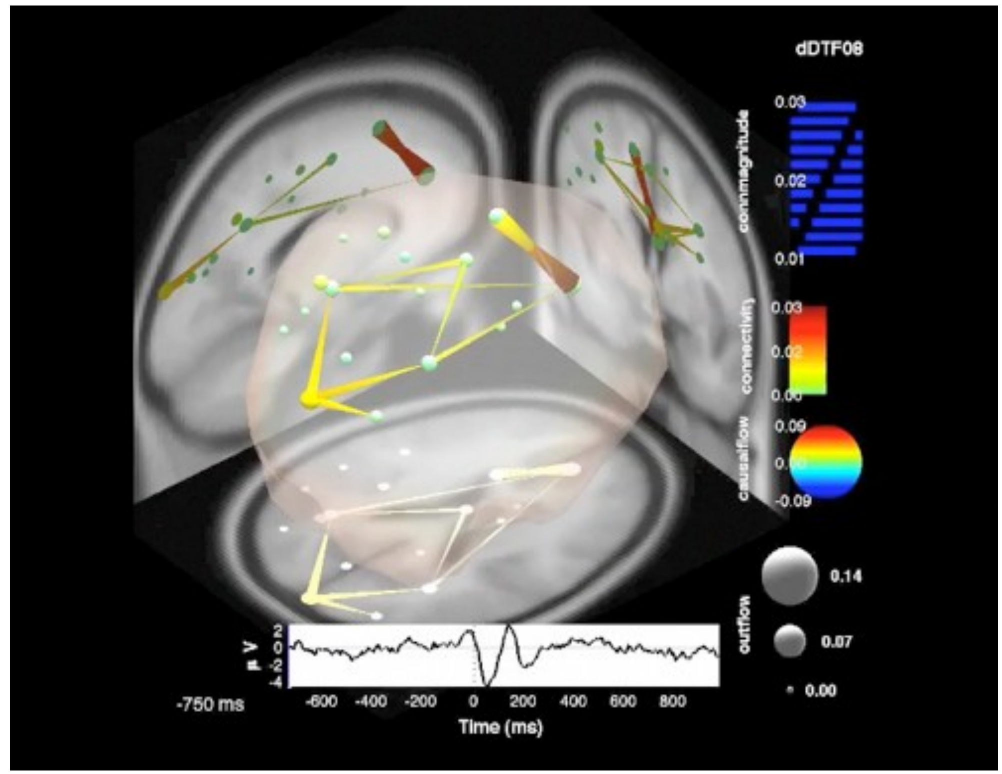


- SIFT is a capable toolkit for causal dynamical analysis at source level
- Parietal network expected for visually guided action (e.g. Heider, et al., 2010)
- ACC more strongly driven by Occipital   Motor. Locus for translation of intention into action (Paus, 2001; Srinivasan, et al. 2013). ACC drives SMA (not shown).
- Causal network results depend on the number of nodes
  - E.g. Occipital " ACC could be mediated by region not included in model
  - There will always be a tradeoff between network size and amount of data needed to fit the model.
  - Regularization

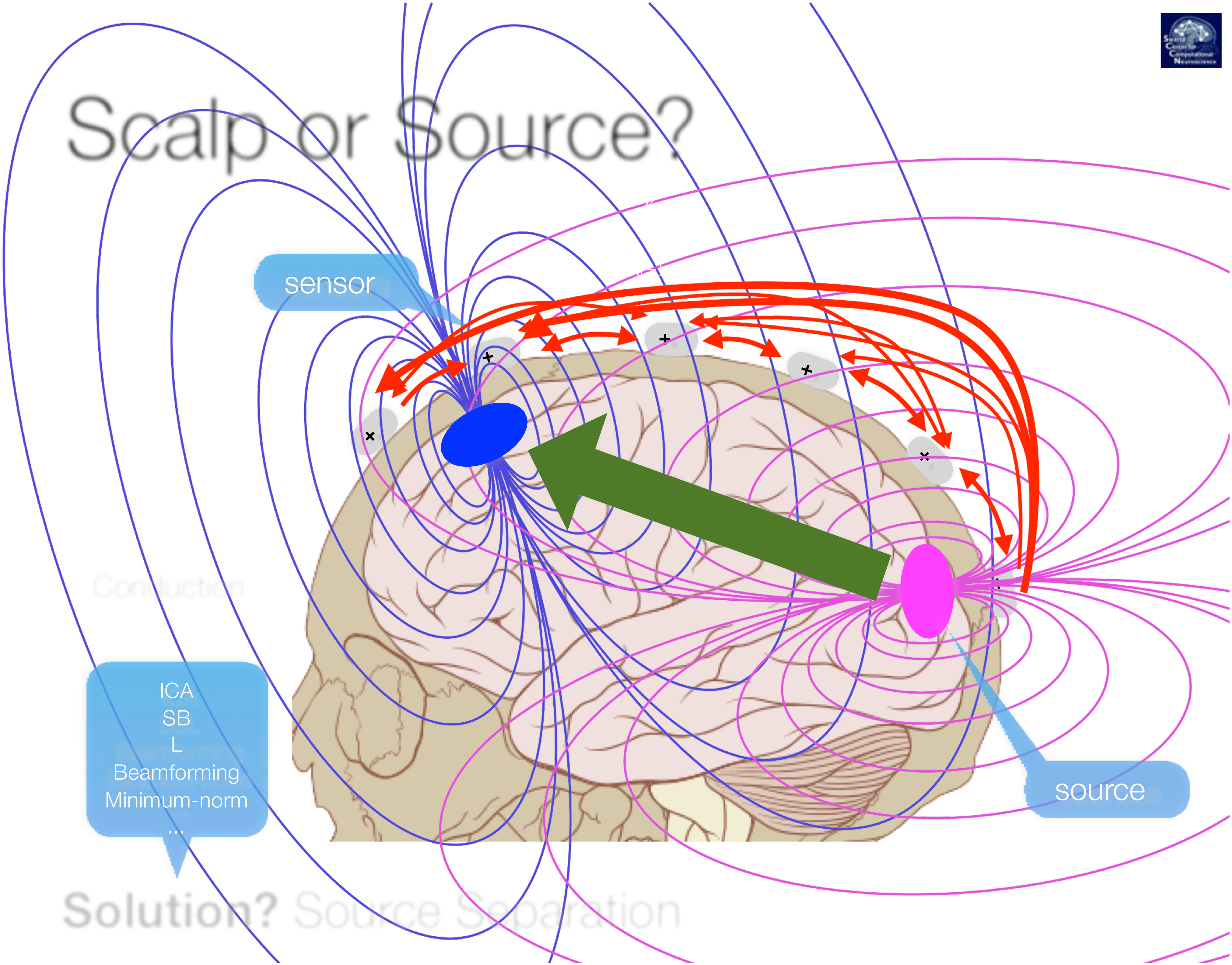
Scalp or Source?



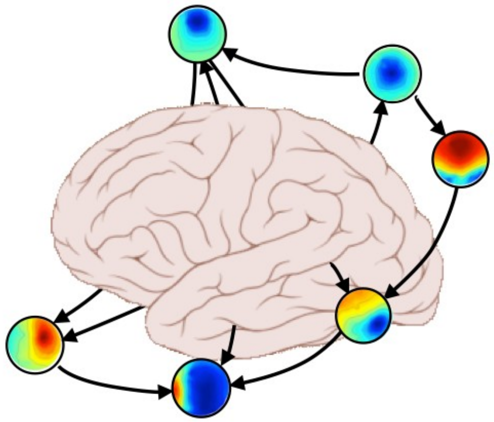
or



Scalp or Source?



Solution? Source Separation



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Mullen, et al, *Journal of Neuroscience Methods* (in prep, 2012)
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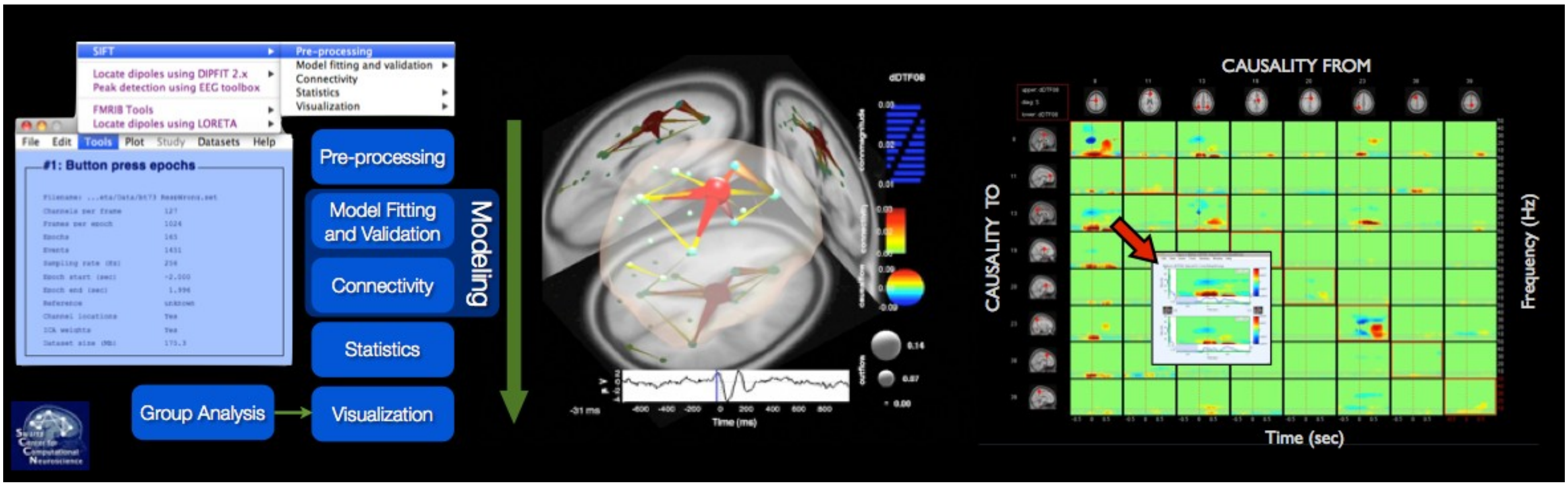
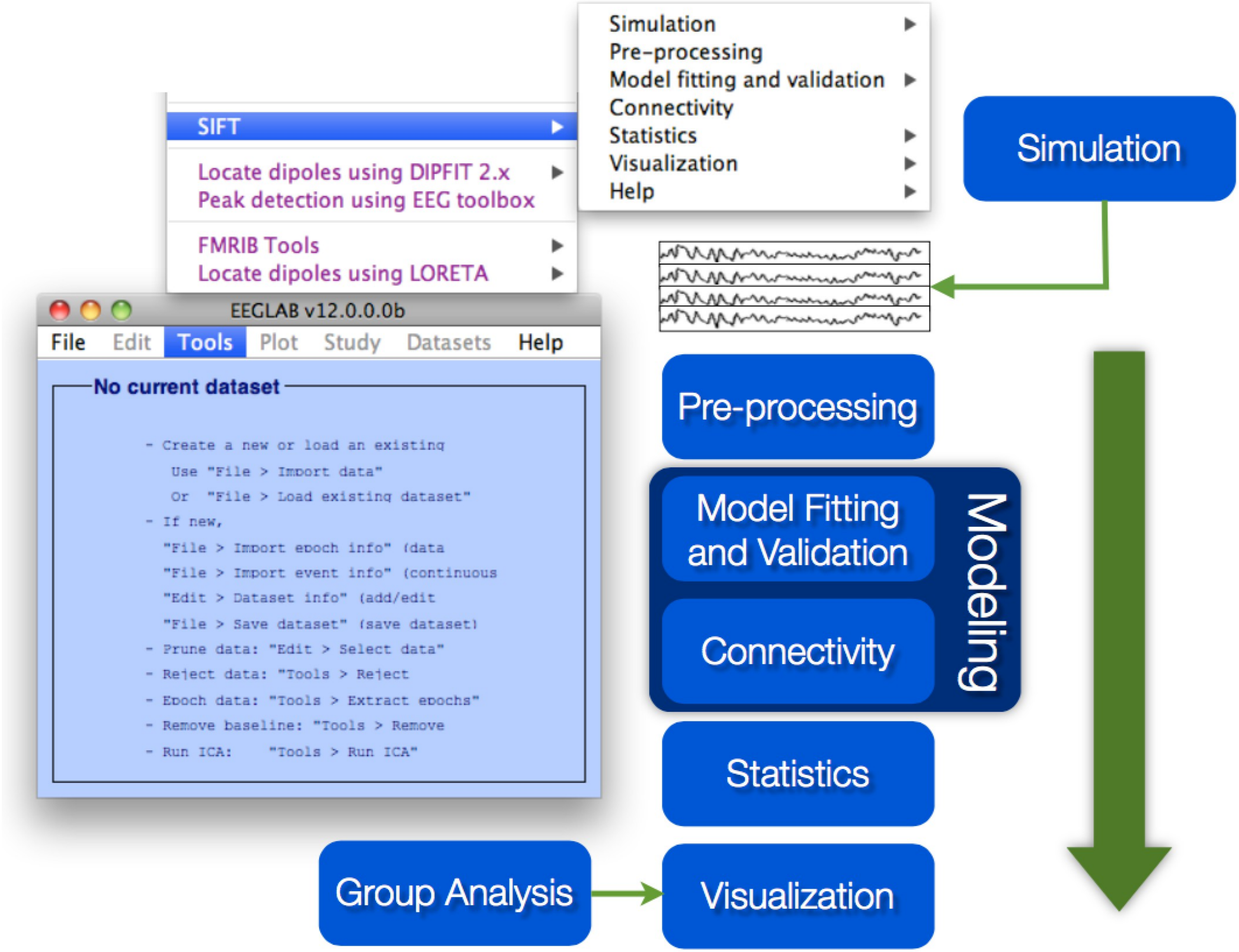
Delorme, Mullen, Kothe et al, *Computational Intelligence and Neuroscience*, vol 12, 2011



- A toolbox for (source-space) electrophysiological information flow and causality analysis (single- or multi-subject) integrated into the EEGLAB software environment.
- Emphasis on vector autoregression and time-frequency domain approaches
- Standard and novel interactive visualization methods for exploratory analysis of connectivity across time, frequency, and spatial location

SIFT Workflow



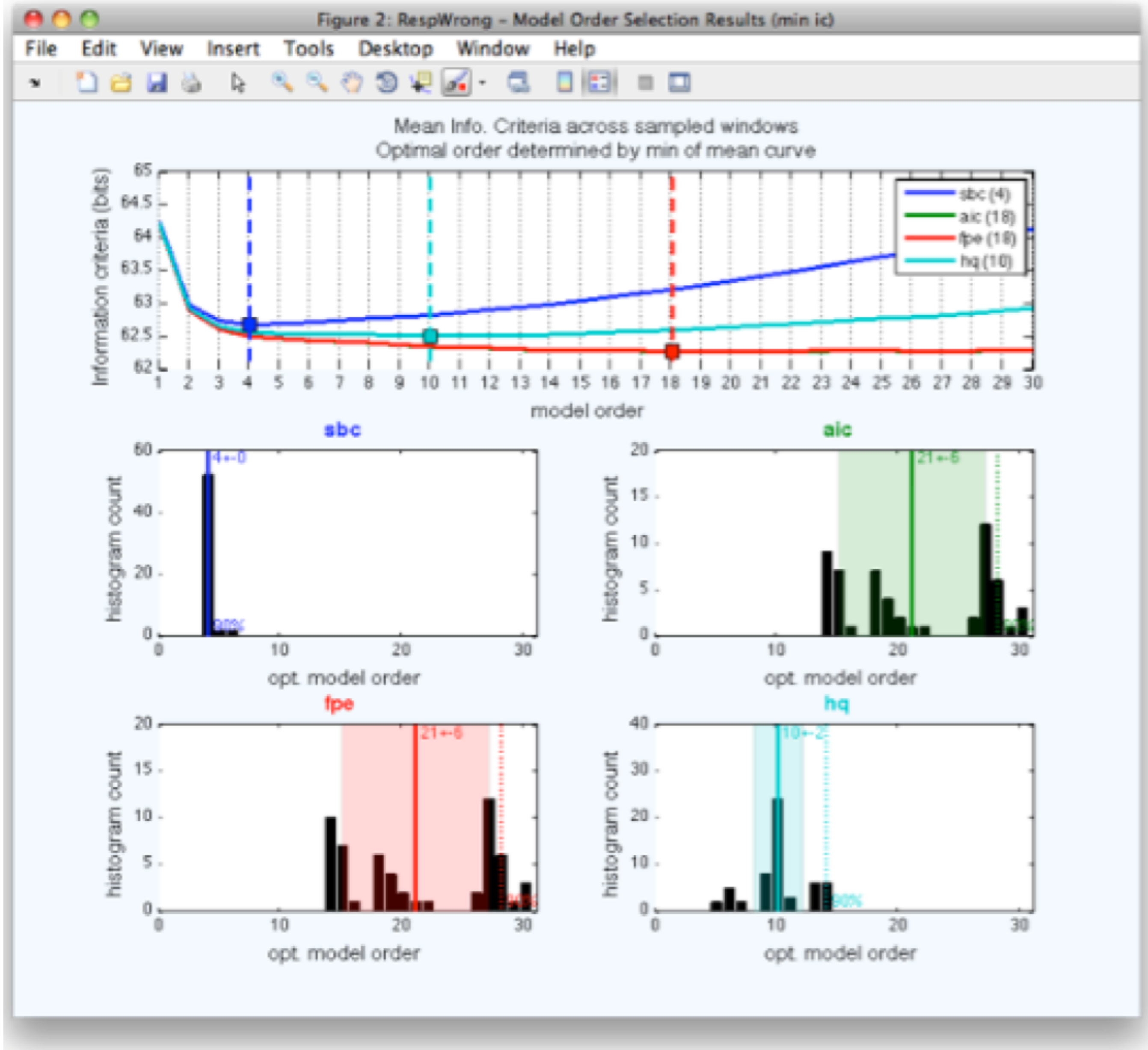
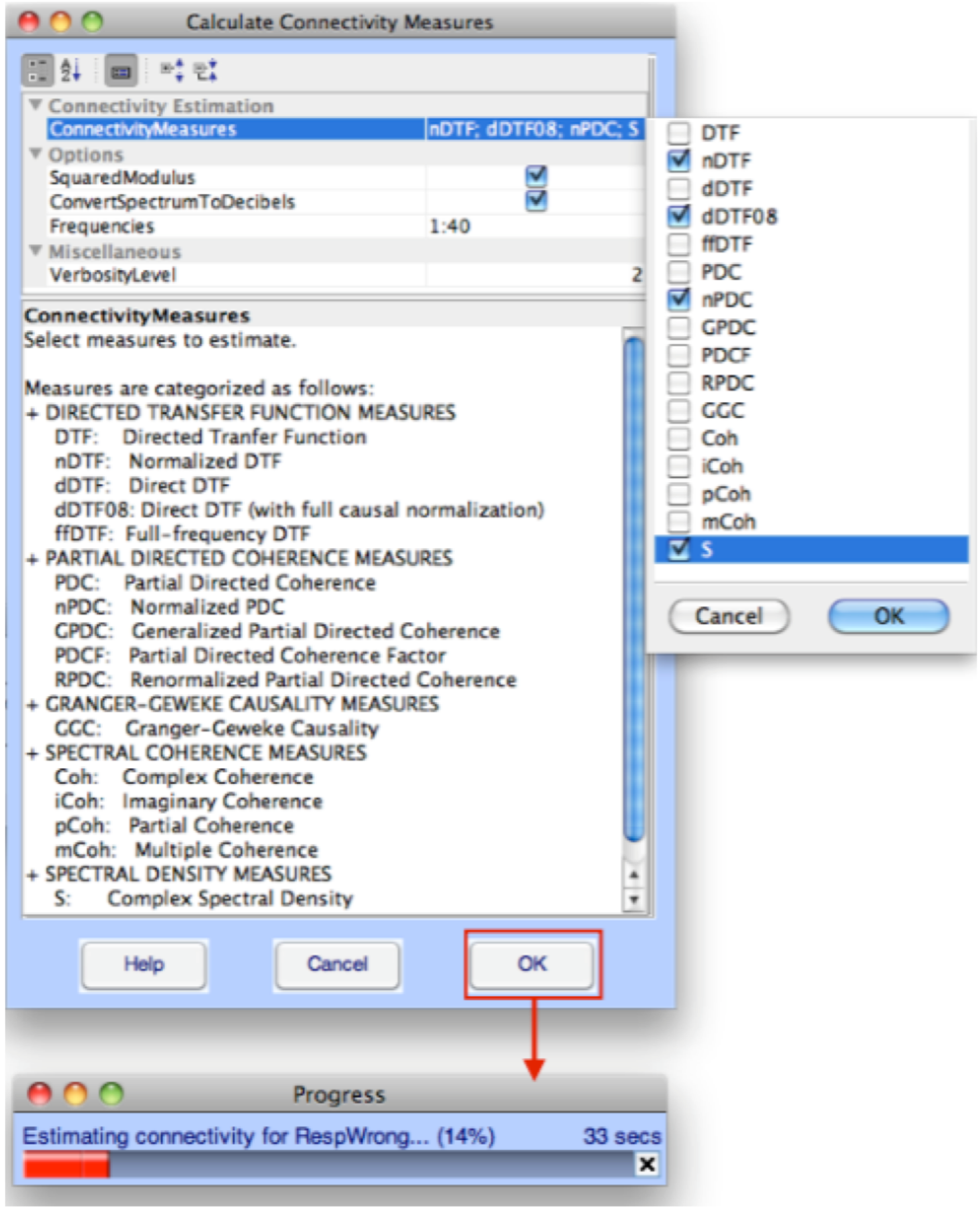
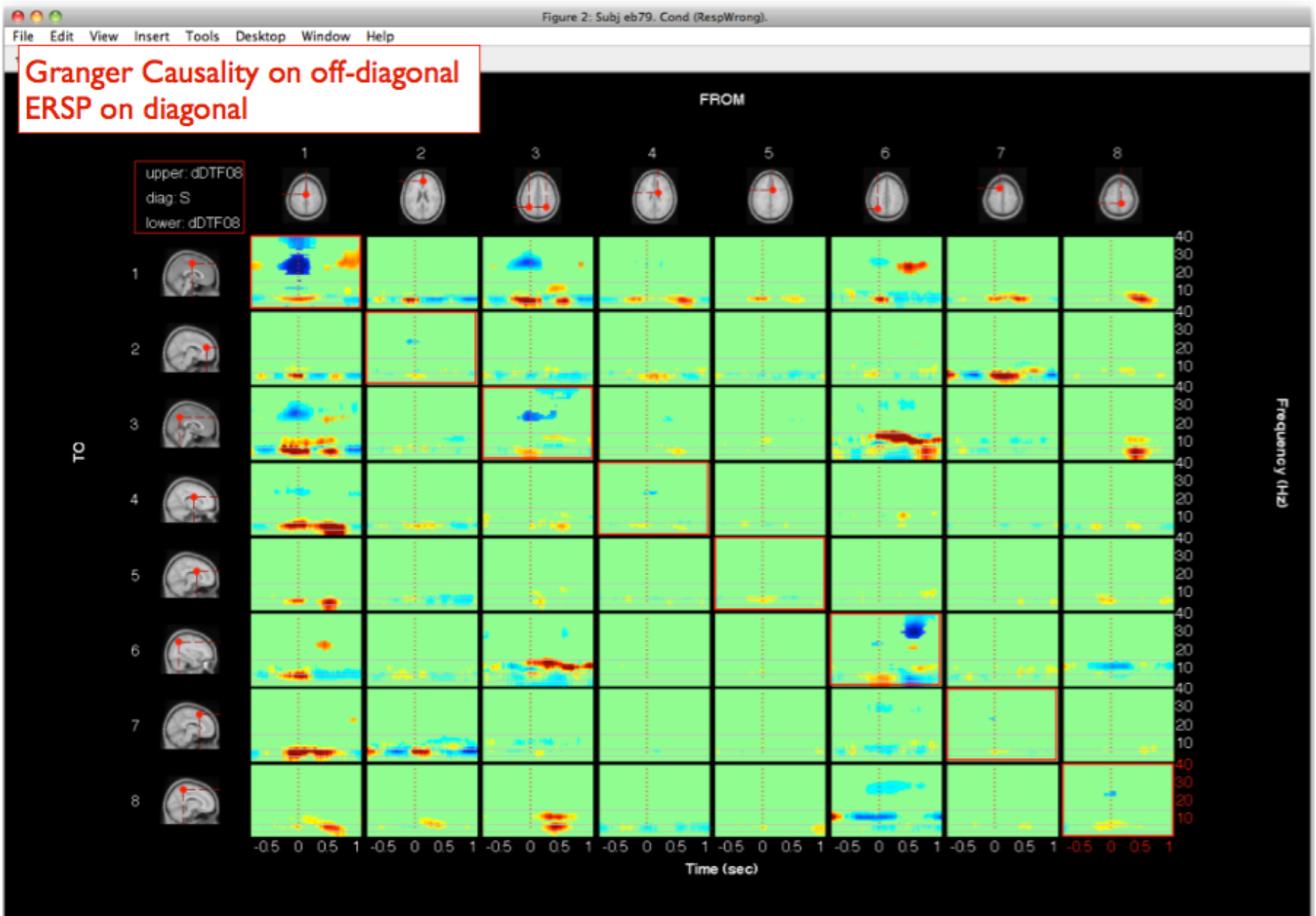


Figure 2: RespWrong - Model Order Selection Results (min ic)
File Edit View Insert Tools Desktop Window Help
Mean Info. Criteria across sampled windows
Optimal order determined by min of mean curve
Information criteria (bits)
model order
sbc (4)
aic (18)
fpe (18)
hq (10)
sbc
aic
fpe
hq
histogram count
opt. model order
4+-0
21+-6
10+-2



Calculate Connectivity Measures
Connectivity Estimation
ConnectivityMeasures
nDTF; dDTF08; nPDC; S
Options
SquaredModulus
ConvertSpectrumToDecibels
Frequencies
1:40
Miscellaneous
VerbosityLevel
2
ConnectivityMeasures
Select measures to estimate.
Measures are categorized as follows:
+ DIRECTED TRANSFER FUNCTION MEASURES
DTF: Directed Tranfer Function
nDTF: Normalized DTF
dDTF: Direct DTF
dDTF08: Direct DTF (with full causal normalization)
ffDTF: Full-frequency DTF
+ PARTIAL DIRECTED COHERENCE MEASURES
PDC: Partial Directed Coherence
nPDC: Normalized PDC
GPDC: Generalized Partial Directed Coherence
PDCF: Partial Directed Coherence Factor
RPDC: Renormalized Partial Directed Coherence
+ GRANGER-GEWEKE CAUSALITY MEASURES
GGC: Granger-Geweke Causality
+ SPECTRAL COHERENCE MEASURES
Coh: Complex Coherence
iCoh: Imaginary Coherence
pCoh: Partial Coherence
mCoh: Multiple Coherence
+ SPECTRAL DENSITY MEASURES
S: Complex Spectral Density
Help
Cancel
OK
DTF
nDTF
dDTF
dDTF08
ffDTF
PDC
nPDC
GPDC
PDCF
RPDC
GGC
Coh
iCoh
pCoh
mCoh
S
Cancel
OK
Progress
Estimating connectivity for RespWrong... (14%)
33 secs

Granger Causality on off-diagonal
ERSP on diagonal



9 Visualization: Causal BrainMovie3D