Redux: Group Version of envtopo

NeuroImage: Clinical 6 (2014) 424–437

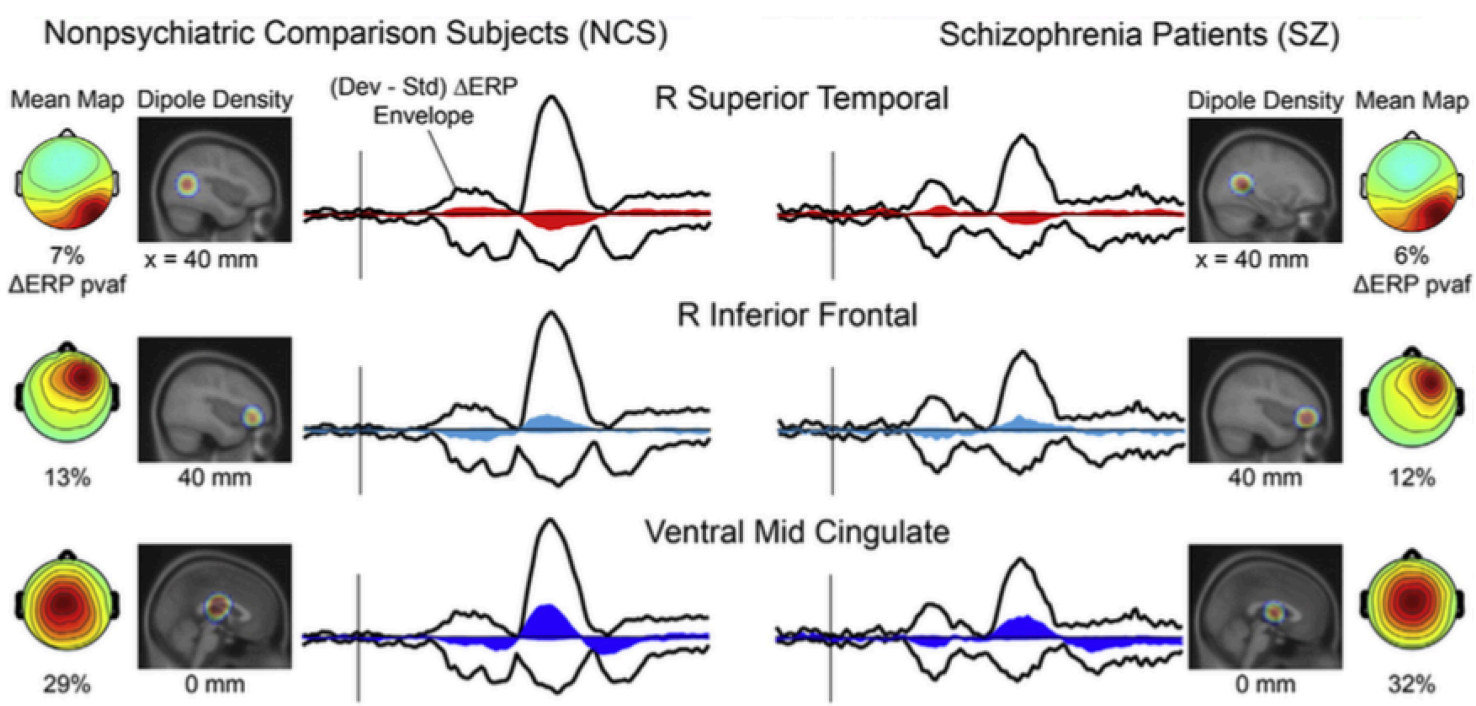
Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Cortical substrates and functional correlates of auditory deviance processing deficits in schizophrenia

Anthony J. Rissling[a], Makoto Miyakoshi[b,c], Catherine A. Sugar[e,f,g], David L. Braff[d,a], Scott Makeig[b], Gregory A. Light[d,a,*]



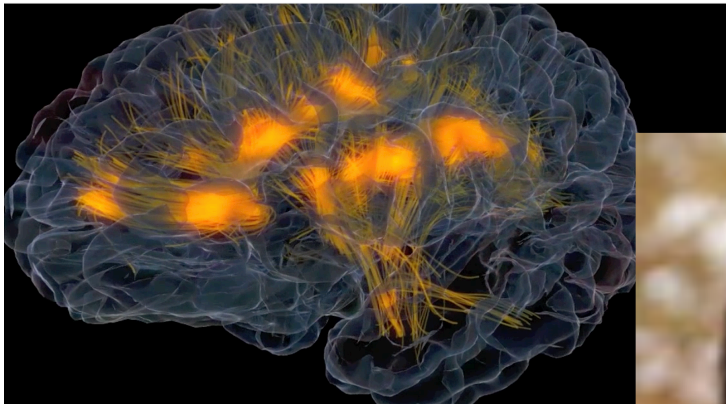
Source information flow and Granger-Causal modeling tools

EEGLAB Workshop XXI

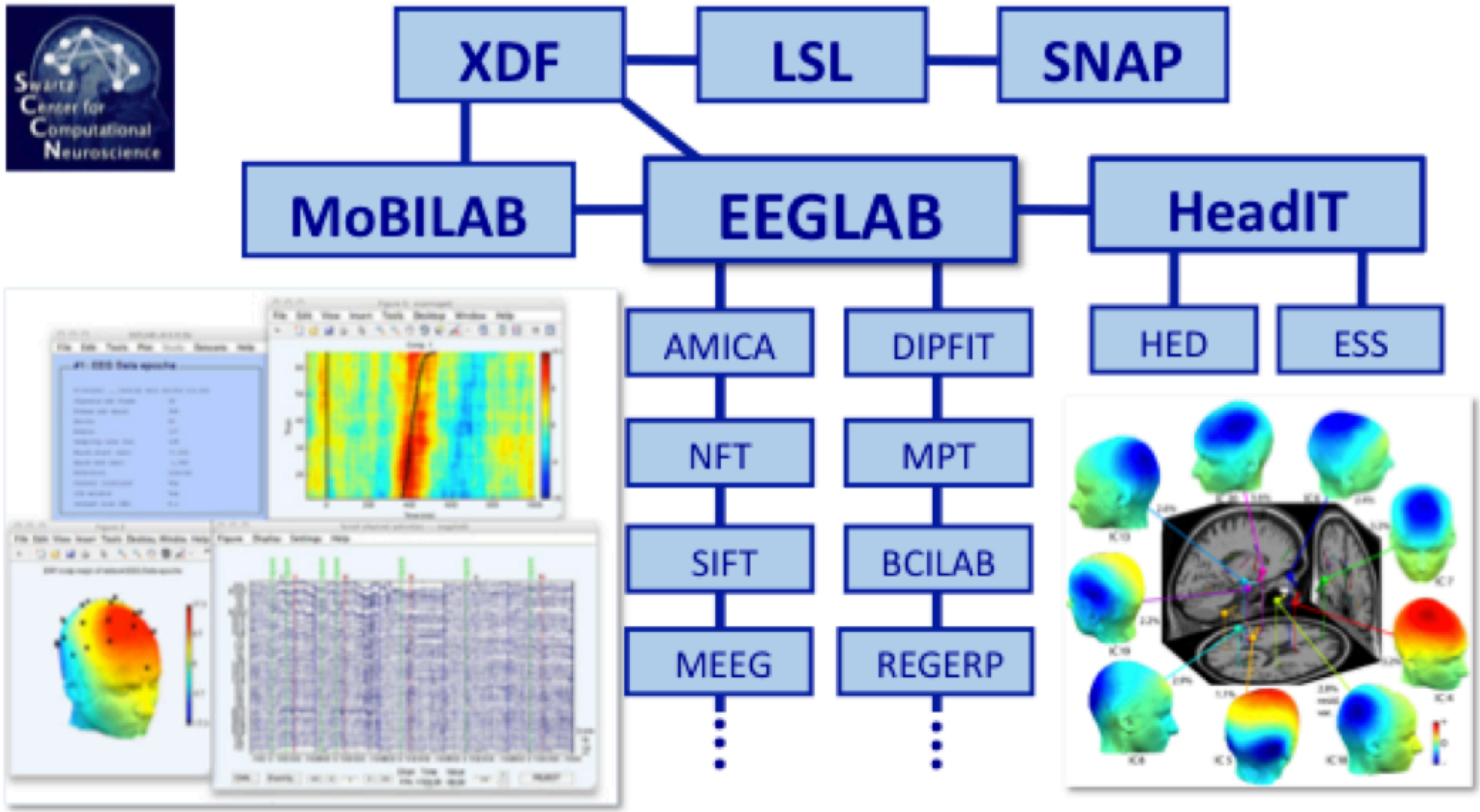
Santa Margherita Ligure, Italy

Day 3

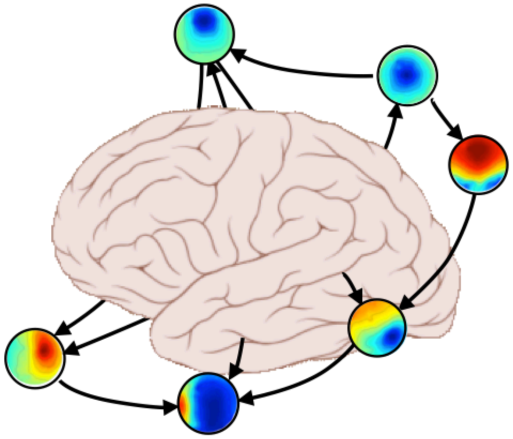
Tim Mullen



EEGLAB Toolset



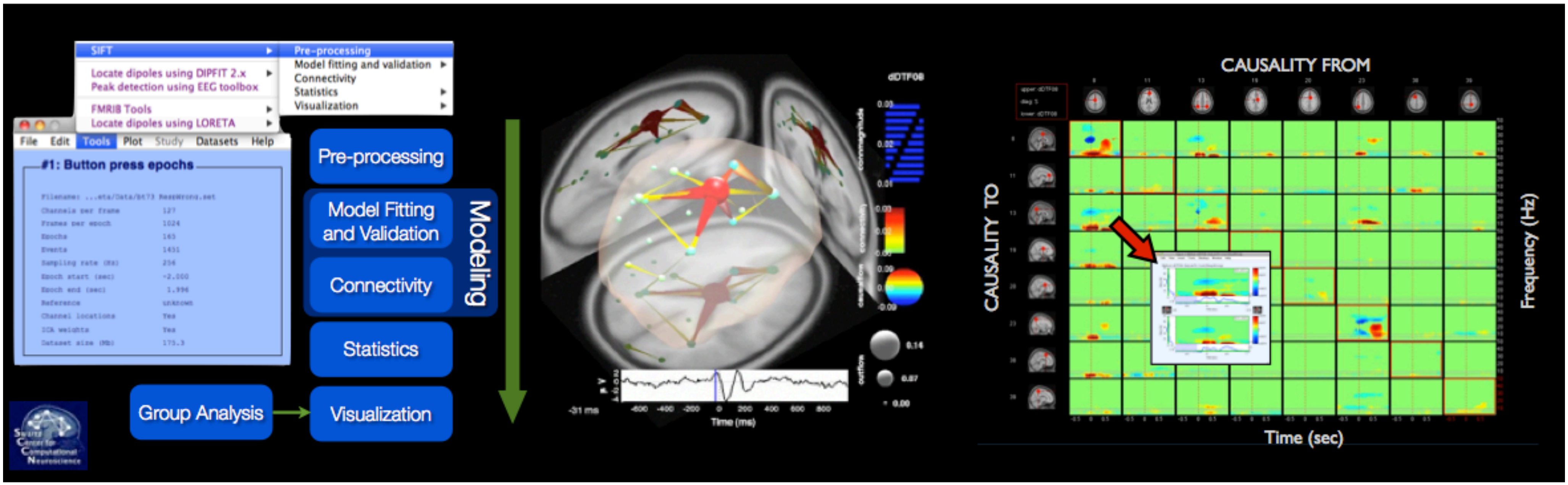
http://sccn.ucsd.edu/eeglab/



SIFT

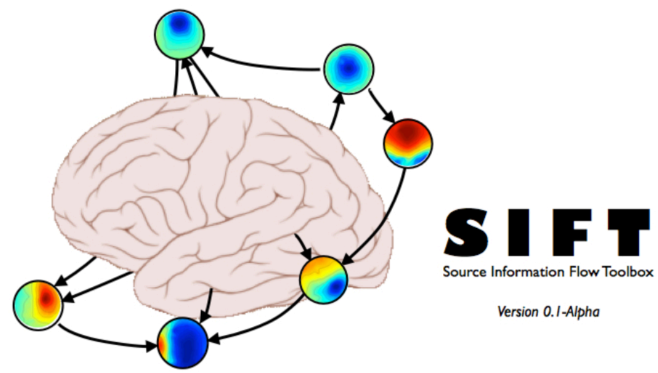
Source Information Flow Toolbox

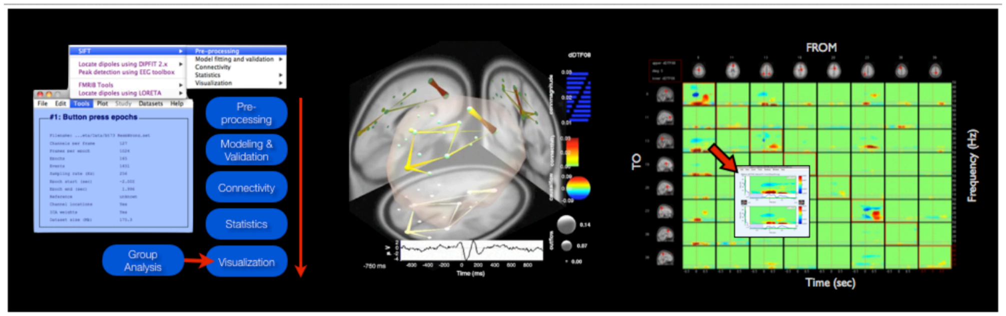
http://sccn.ucsd.edu/wiki/SIFT
Mullen, et al, *Journal of Neuroscience Methods* (in prep, 2012)
Mullen, et al, *Society for Neuroscience*, 2010
Delorme, Mullen, Kothe et al, *Computational Intelligence and Neuroscience*, vol 12, 2011



- 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

SIFT





Contents [hide]

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

Developed and Maintained by: Tim Mullen (SCCN, INC, UCSD)
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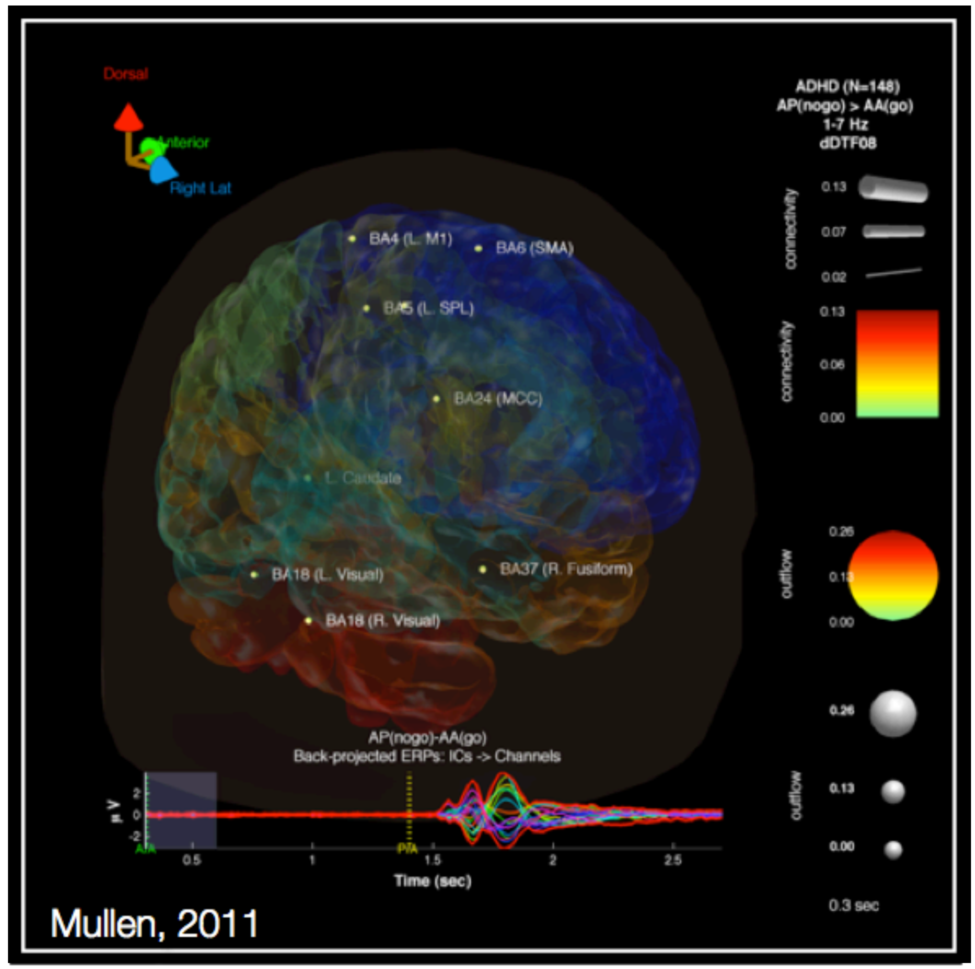
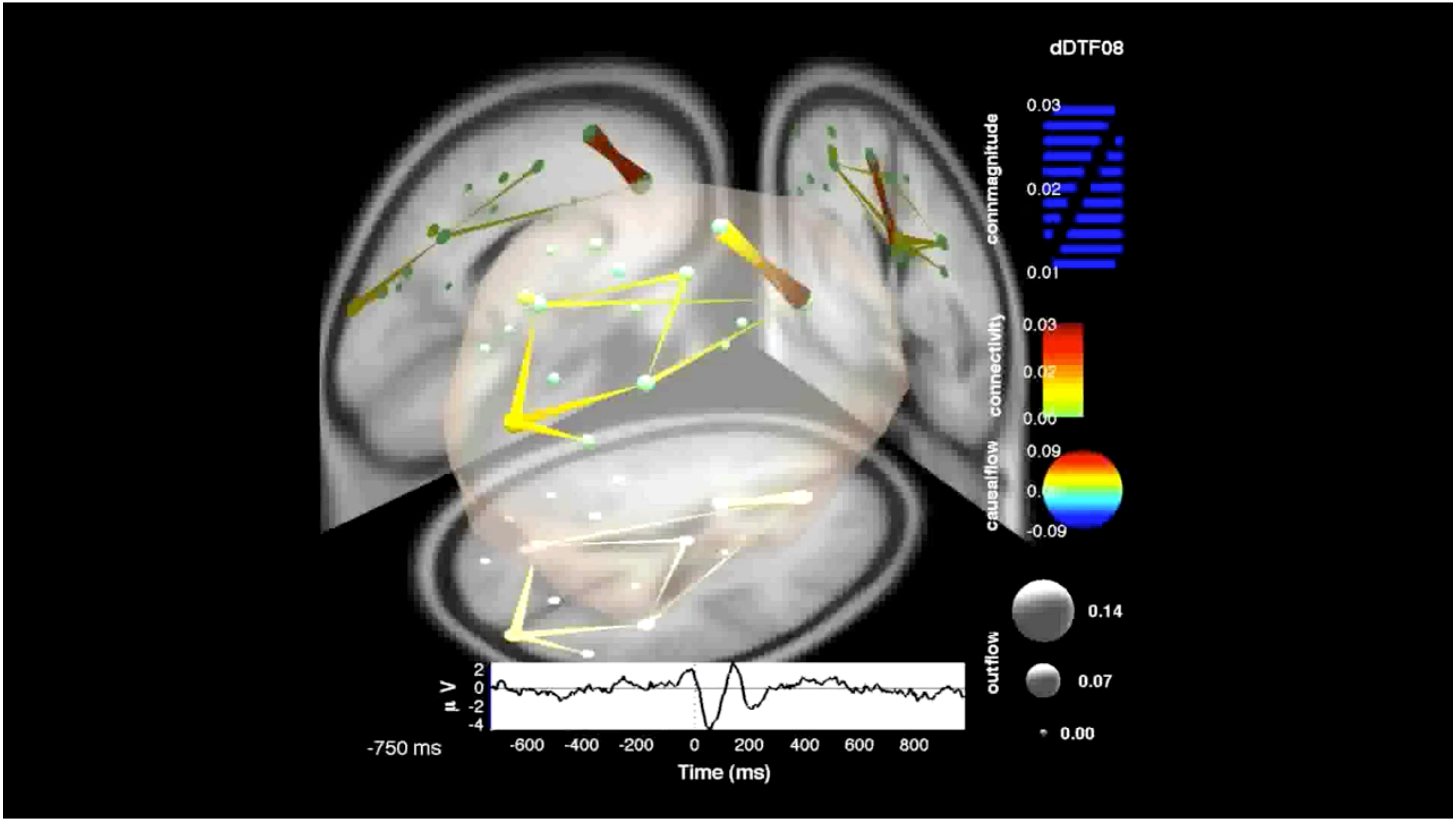
The Dynamic Brain

- 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)



Mullen, 2011

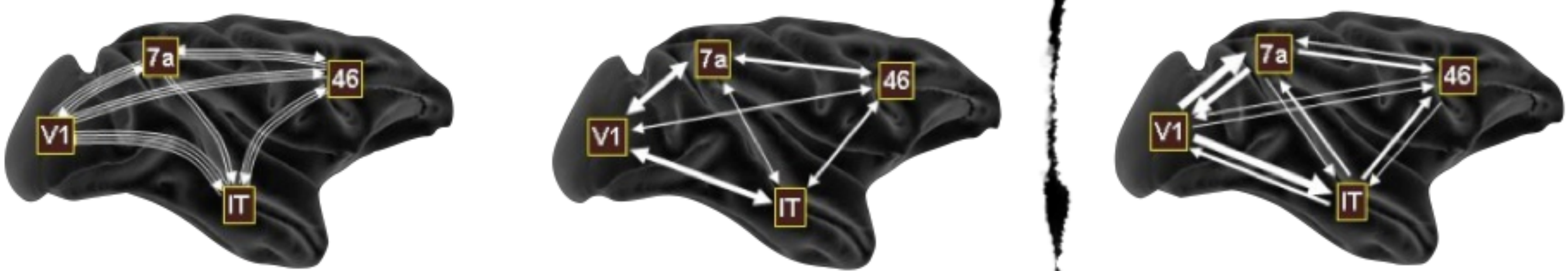

dDTF08
0.03
connmagnitude
0.02
0.01
0.03
connectivity
0.02
0.00
0.09
causalflow
-0.09
0.14
outflow
0.07
0.00
2
0
-2
-4
μ V
-750 ms
-600
-400
-200
0
200
400
600
800
Time (ms)

Tim Mullen

Large-scale brain connectivity

(Bullmore and Sporns, *Nature*, 2009)

Structural | **Functional** | **Effective**



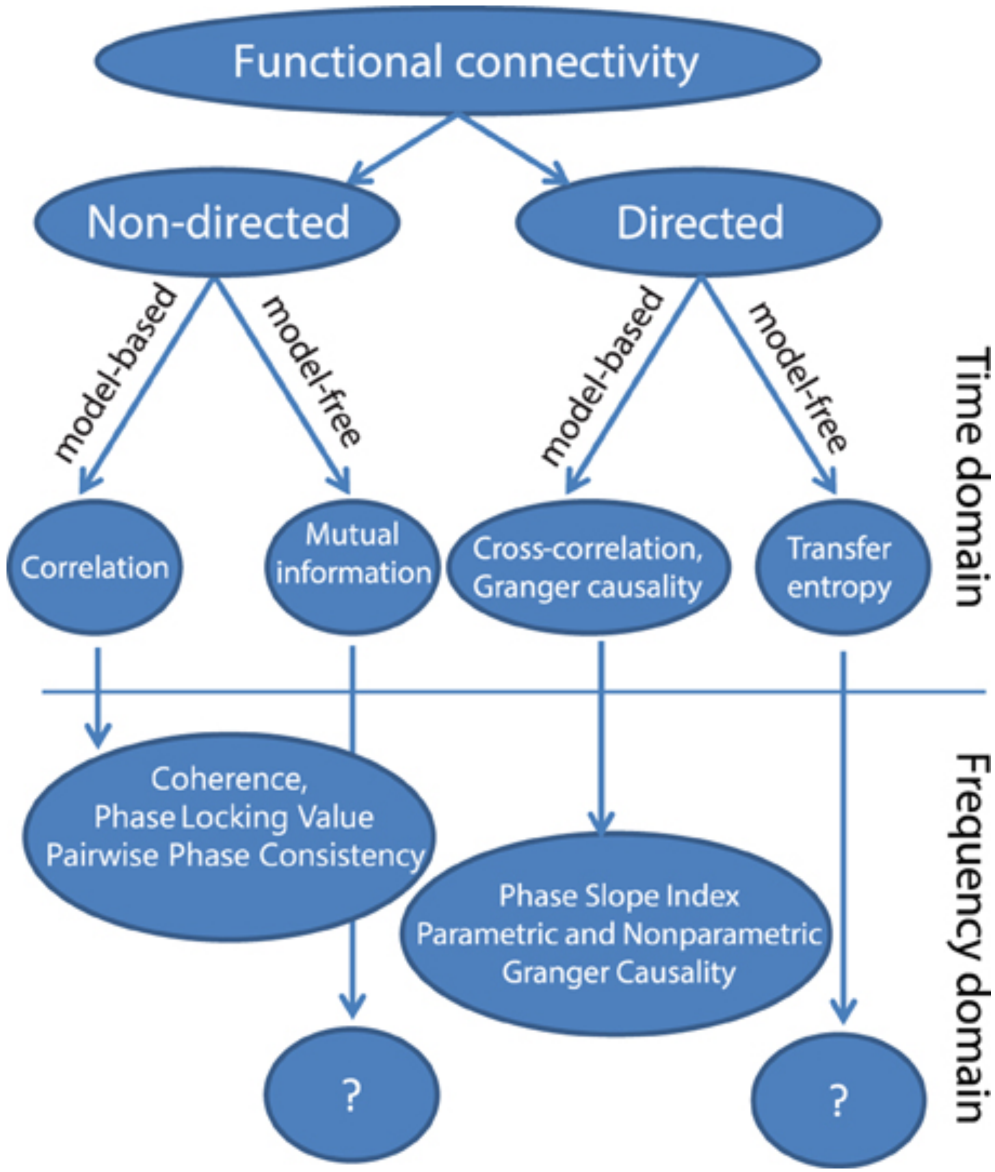
state-invariant, anatomical

dynamic, state-dependent, correlative, symmetric

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

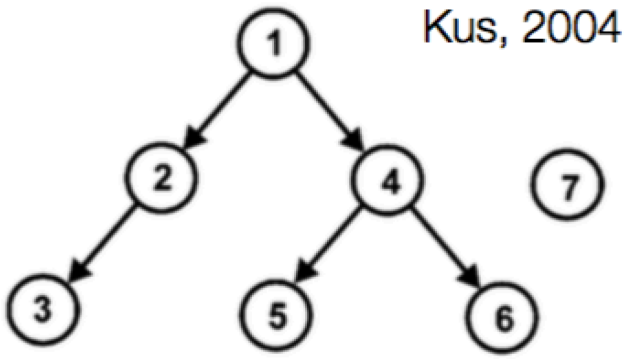
Hours-Years — **milliseconds-seconds**

Temporal Scale



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

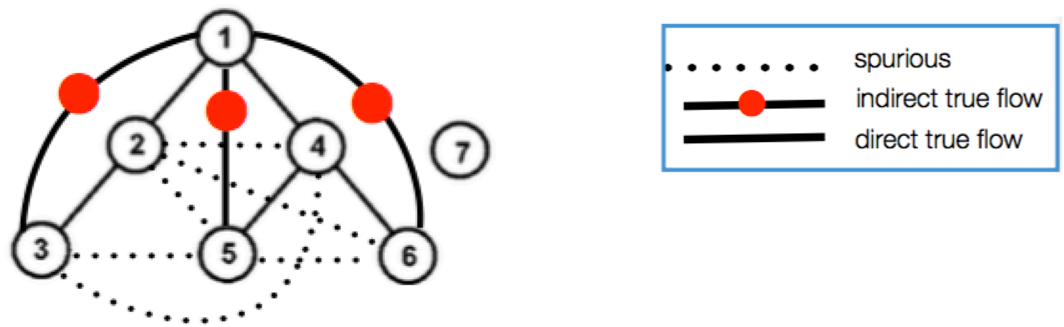


Kus, 2004

Coherency

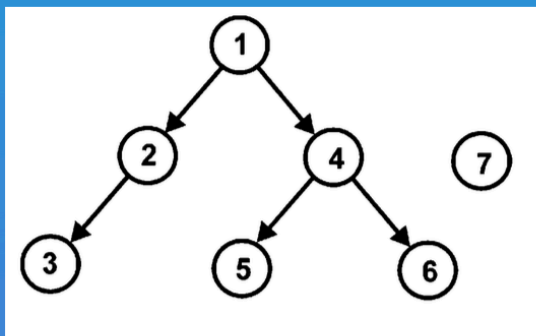
$$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f) S_{jj}(f)}}$$

(Bendat and Piersol, 1986)

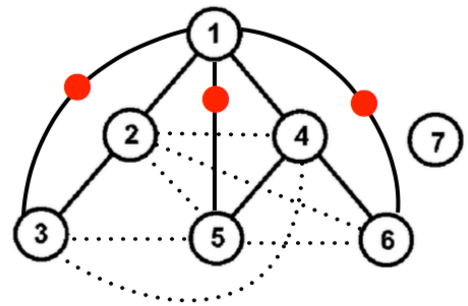


Bivariate measures, such as coherence (but also original GC), find spurious connections between nodes if they share a common input.

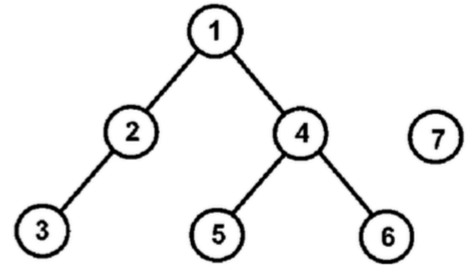
Ground Truth



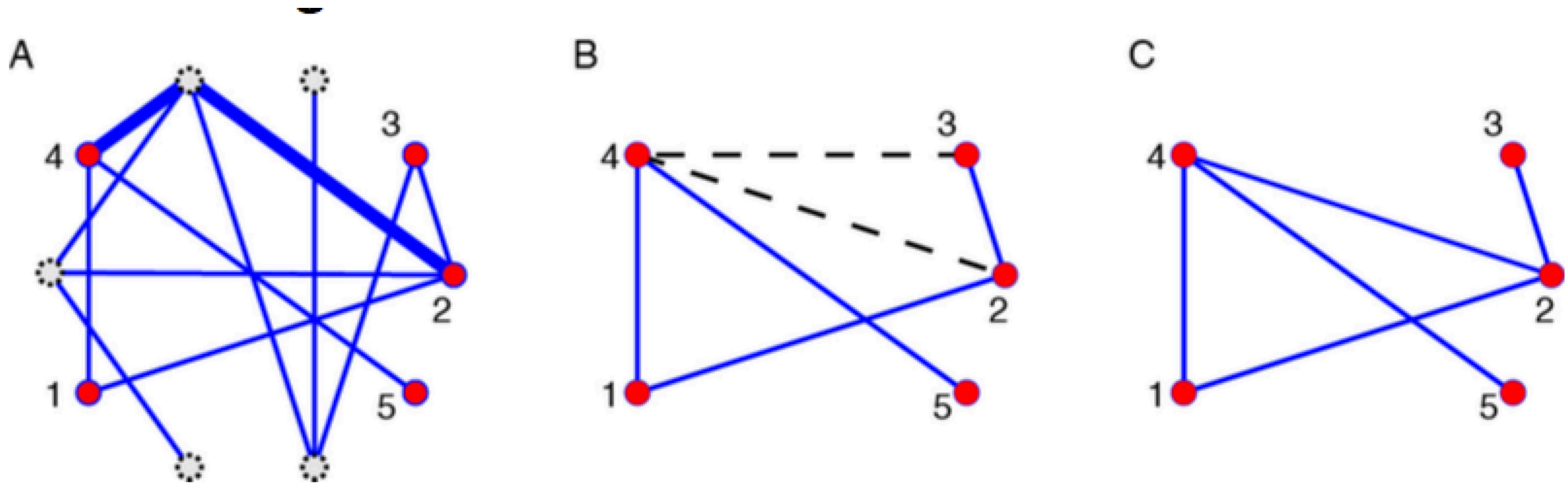
Coherence



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

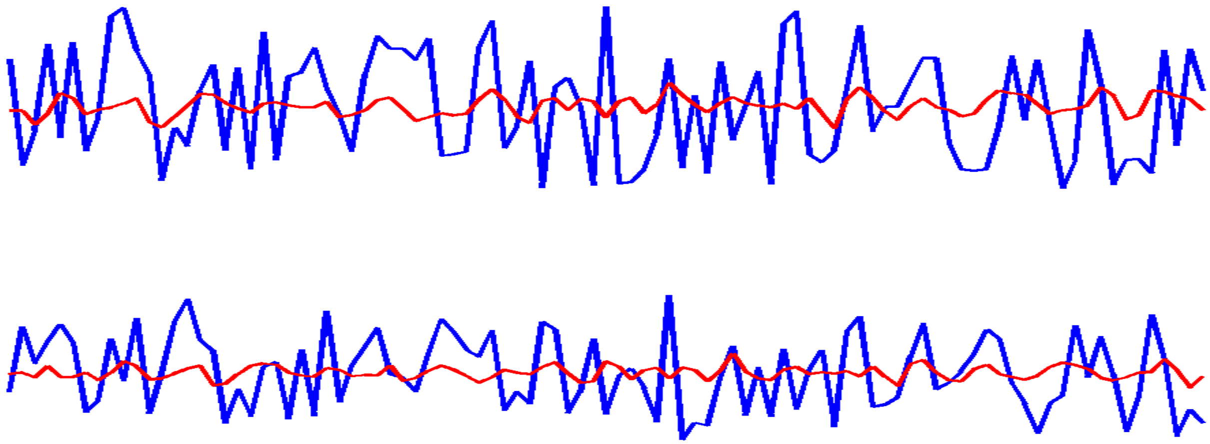
- A measure of *statistical* causality based on prediction.
- Widely used in time-series econometrics.
- Nobel Prize in economics, 2003.

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

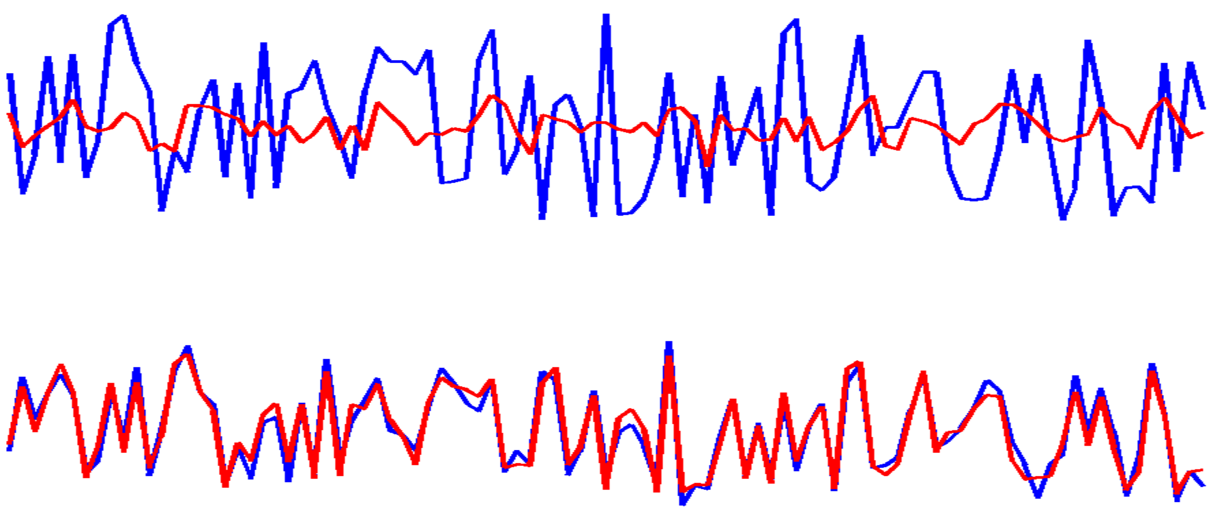
X_2



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

$X_1 | X_2$

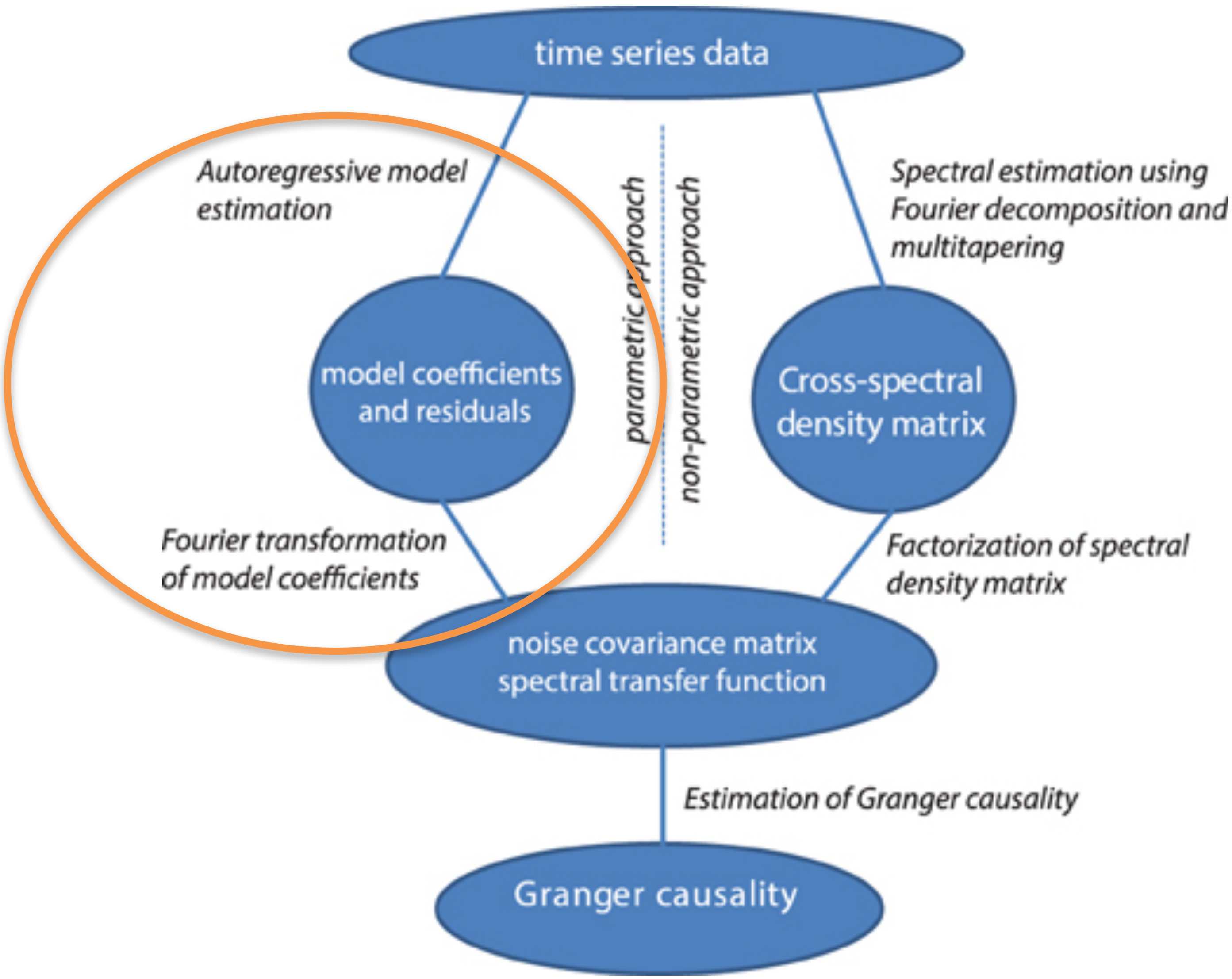
$X_2 | X_1$



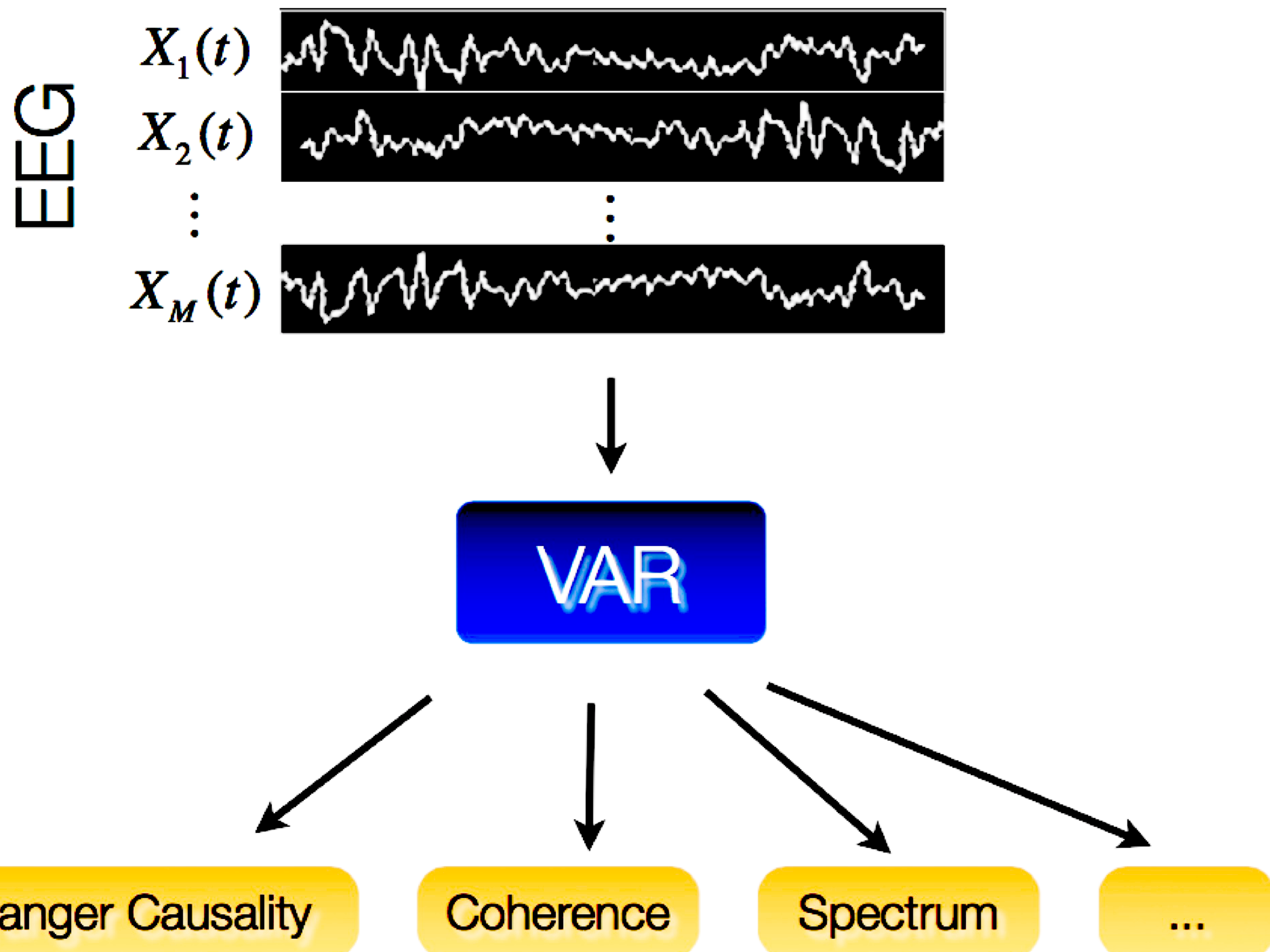
Incorporating information about X_1 improves the prediction of X_2!

We say "X_1 granger-causes X_2"

Calculation of GC



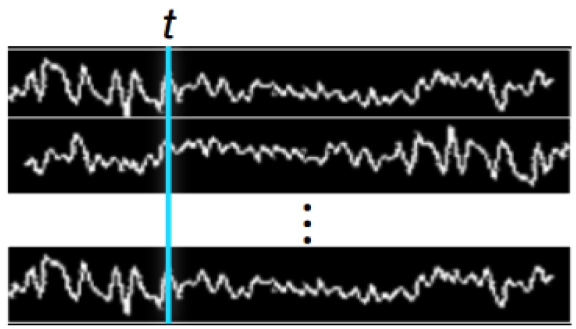
Vector Autoregressive (VAR / MAR / MVAR) Modeling



The Linear Vector Auto-regressive (VAR) Model

Ordinary Least-Squares

$X(t) =$ $x_1(t)$, $x_2(t)$, $\vdots$, $x_M(t)$



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

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

Selecting a VAR Model Order

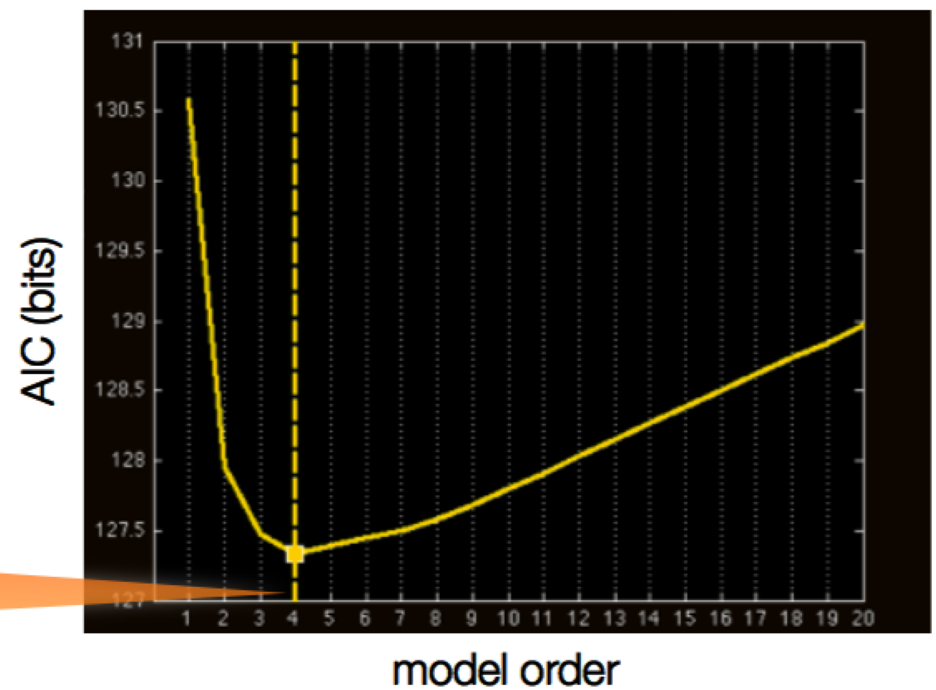
- Model order is typically determined by minimizing information criteria such as Akaike Information Criterion (AIC) for varying model order (p):

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

Penalizes high model orders (parsimony)

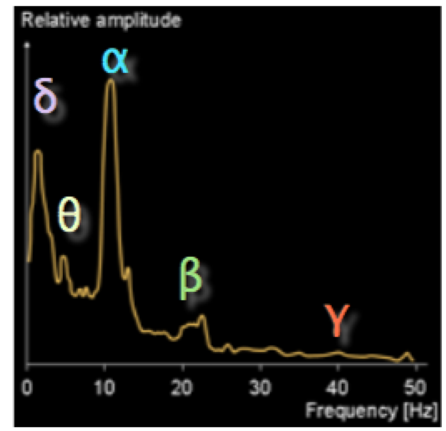
entropy rate (amount of prediction error)

optimal order



Selecting a VAR Model Order

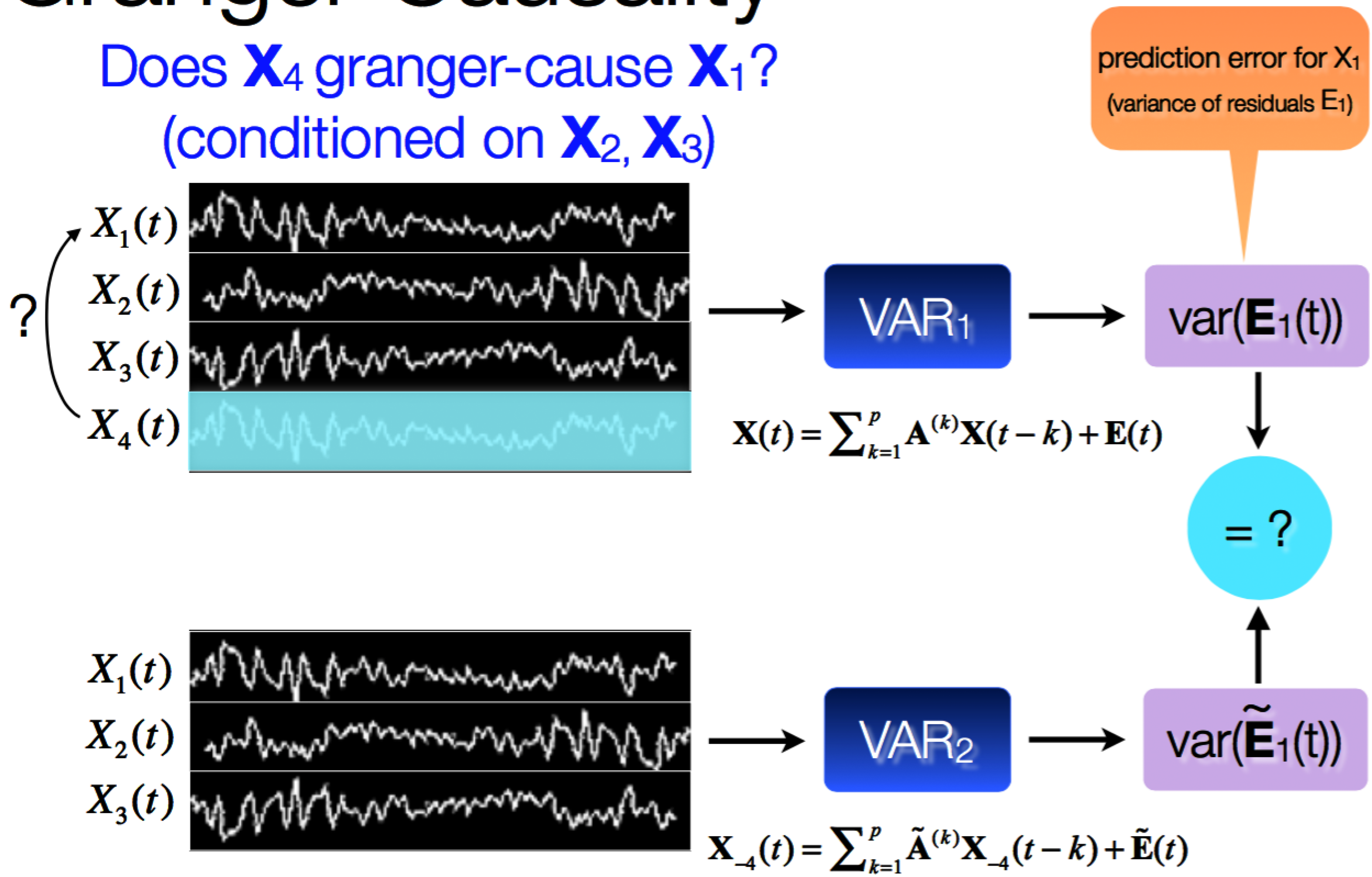
- Other considerations:
  - A M-dimensional VAR model of order *p* has at most *Mp/2* spectral peaks distributed amongst the *M* variables. This means we can observe at most *p/2* peaks in each variables' spectrum (or in the causal spectrum between each pair of variables)



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

Granger Causality

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



Granger Causality

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

$$F_{X_1 \leftarrow X_2} = \ln\left(\frac{\overbrace{var(\tilde{E}_1)}^{\text{reduced model}}}{\underbrace{var(E_1)}_{\text{full model}}}\right) = \ln\left(\frac{var(X_1(t) \mid X_1(\cdot))}{var(X_1(t) \mid X_1(\cdot), X_2(\cdot))}\right)$$

- Alternately, for a **multivariate interpretation** we can fit a single MVAR 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 $\mathbf{A}_{ij}(k) >> 0$ for some lag $k \in \{1, \ldots, p\}$

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

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

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

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

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

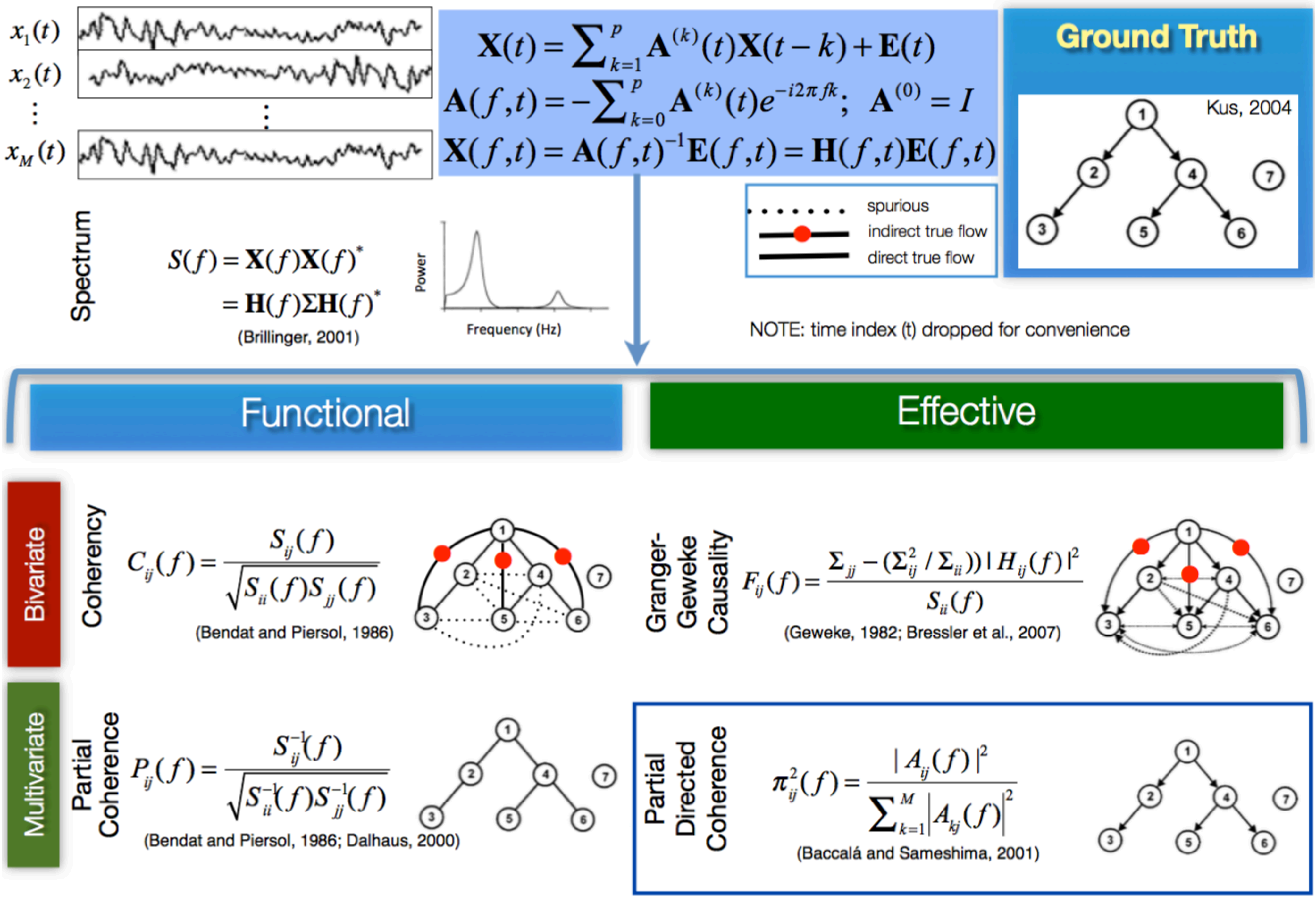
Where $\mathbf{H}(f)$ is the *transfer matrix* of the system.

Definition 2

X_j granger-causes X_i conditioned on all other variables in $\mathbf{X}$

if and only if $|\mathbf{A}_{ij}(f)| >> 0$ for some frequency f

leads to PDC



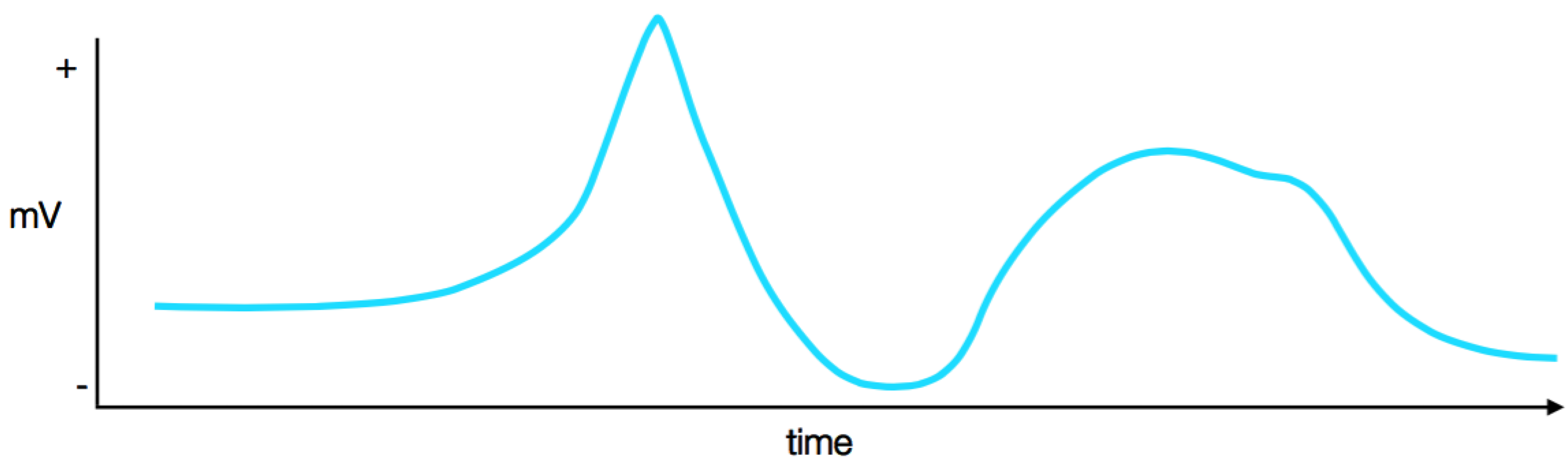
$x_1(t)$
$x_2(t)$
$x_M(t)$
$\mathbf{X}(t) = \sum_{k=1}^{p} \mathbf{A}^{(k)}(t)\mathbf{X}(t-k) + \mathbf{E}(t)$
$\mathbf{A}(f,t) = -\sum_{k=0}^{p} \mathbf{A}^{(k)}(t)e^{-i2\pi fk}; \quad \mathbf{A}^{(0)} = I$
$\mathbf{X}(f,t) = \mathbf{A}(f,t)^{-1}\mathbf{E}(f,t) = \mathbf{H}(f,t)\mathbf{E}(f,t)$
Ground Truth
Kus, 2004
spurious
indirect true flow
direct true flow
Spectrum
$S(f) = \mathbf{X}(f)\mathbf{X}(f)^* = \mathbf{H}(f)\Sigma\mathbf{H}(f)^*$
(Brillinger, 2001)
Power
Frequency (Hz)
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
$\pi_{ij}^2(f) = \frac{|\,A_{ij}(f)\,|^2}{\sum_{k=1}^{M}\left|A_{kj}(f)\right|^2}$
(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?

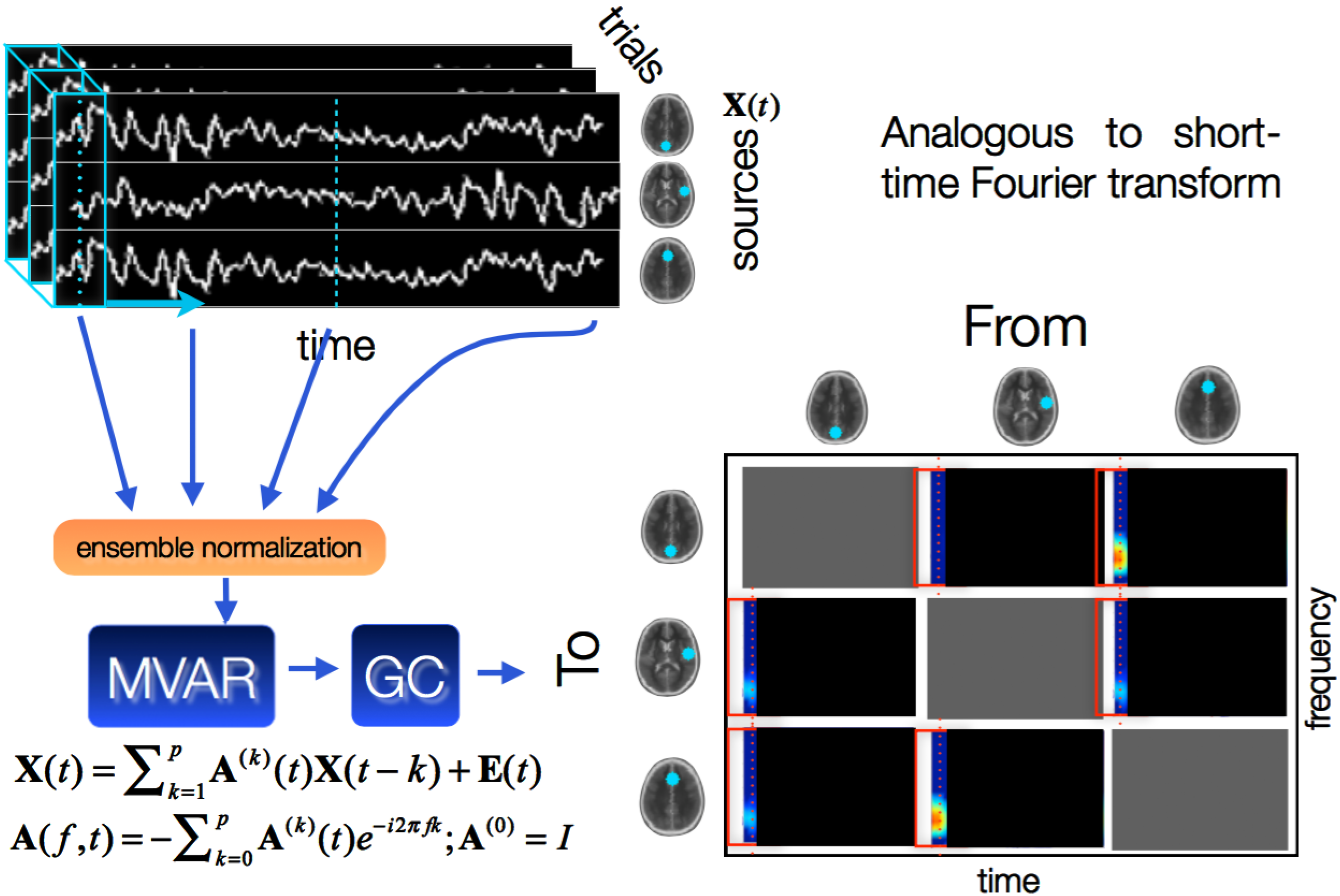


Adapting to Non-Stationarity

- **Many ways to do adaptive VAR estimation**
  - Segmentation-based adaptive VAR estimation
  - Factorization of time-varying spectral density matrices (e.g. from STFTs, Wavelets, etc)
  - State-Space Modeling
  - ...

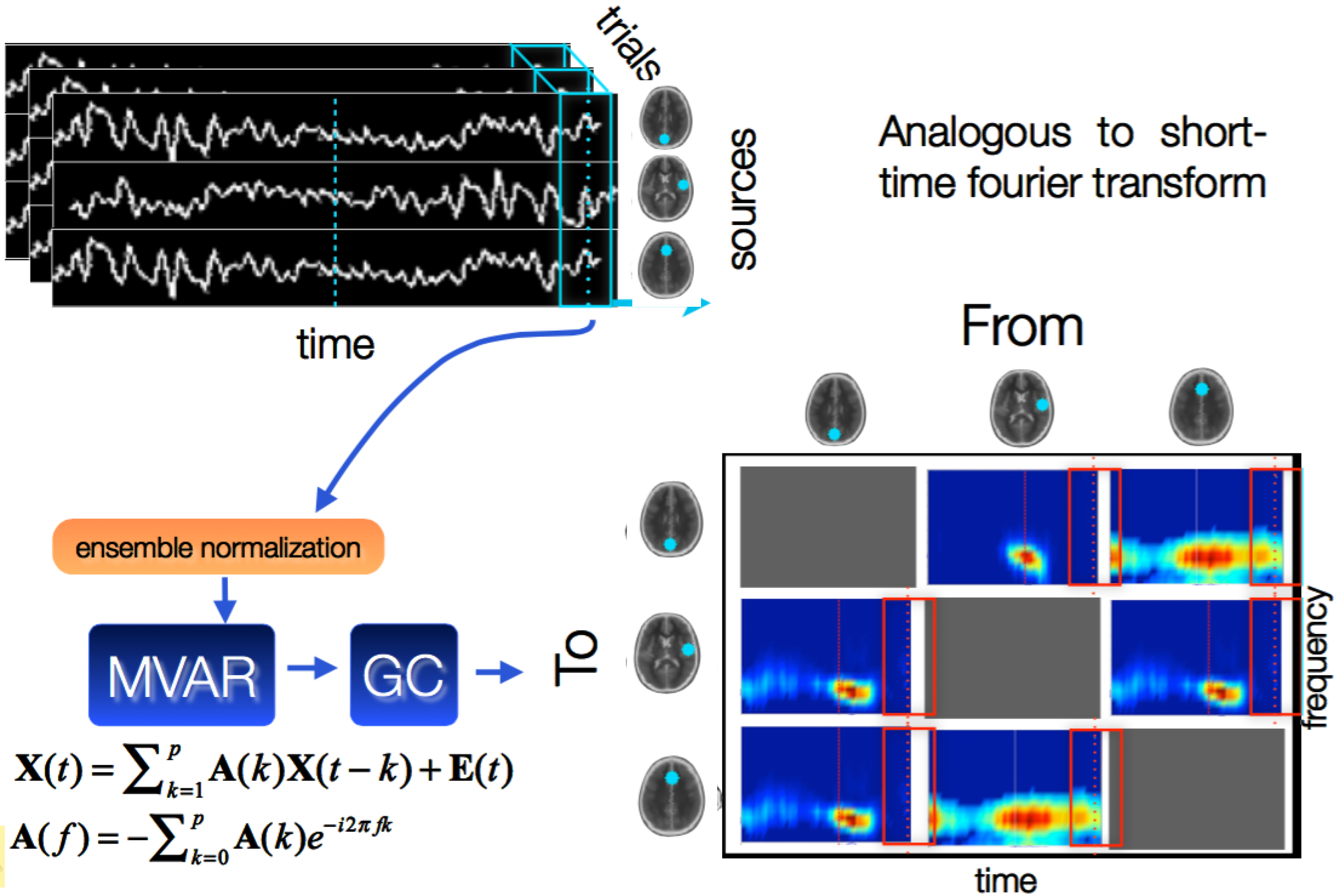
Segmentation-based VAR

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



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

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



Analogous to short-time fourier transform

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

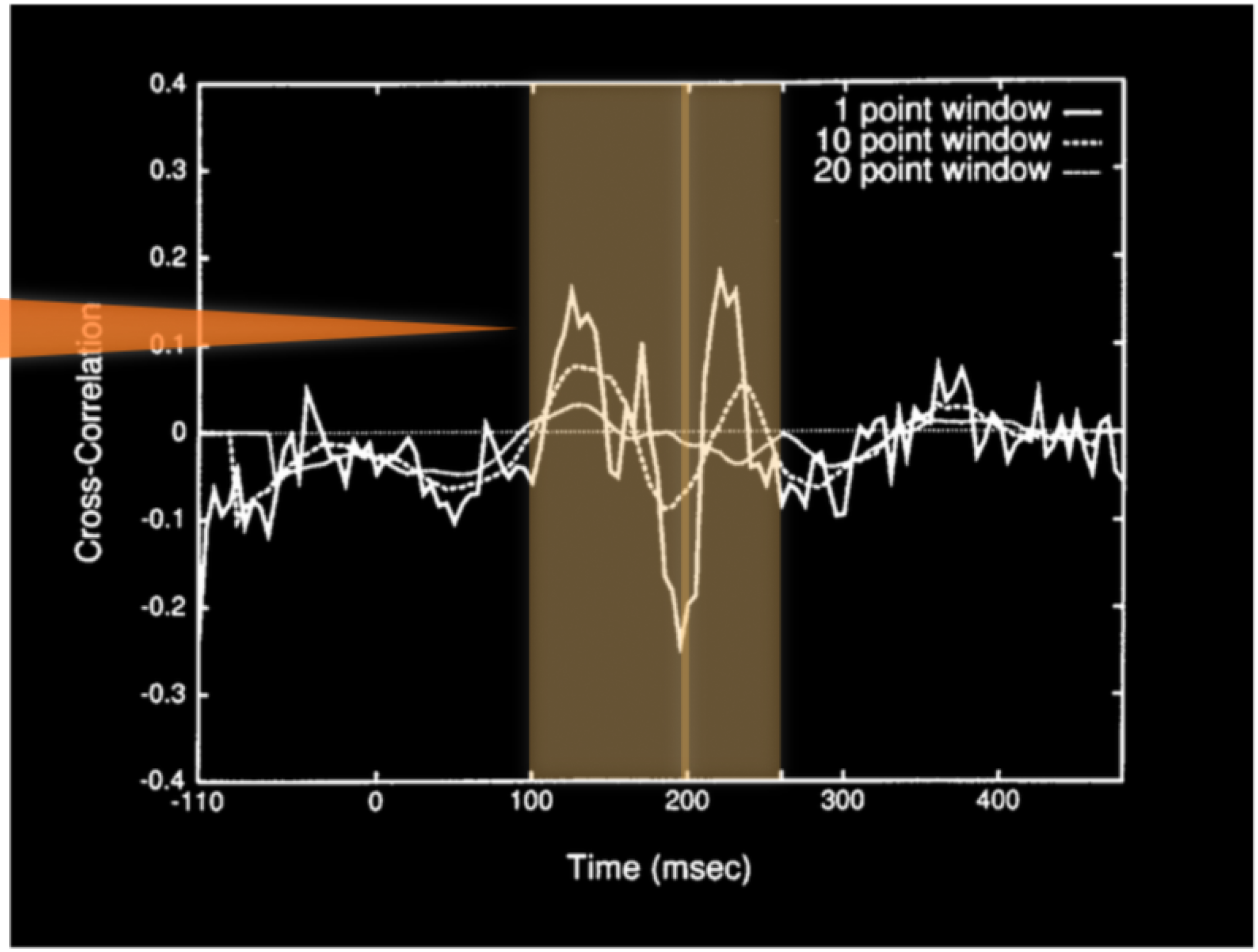
$$\mathbf{A}(f) = -\sum_{k=0}^{p} \mathbf{A}(k) e^{-i2\pi fk}$$

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

Consideration: Local Stationarity

Too-large windows may not be locally-stationary



Consideration: Sufficient data

M = number of variables
p = model order
N_{tr} = number of trials
W = length of each window (sample points)

We have M^2p model coefficients to estimate. This requires a minimum of M^2p independent samples.
So we have the constraint $M^2p <= N_{tr} W$.
In practice, however, a better heuristic is $M^2p <= (1/10)N_{tr} W$.

Or: $\mathbf{W >= 10(M^2p/N_{tr})}$

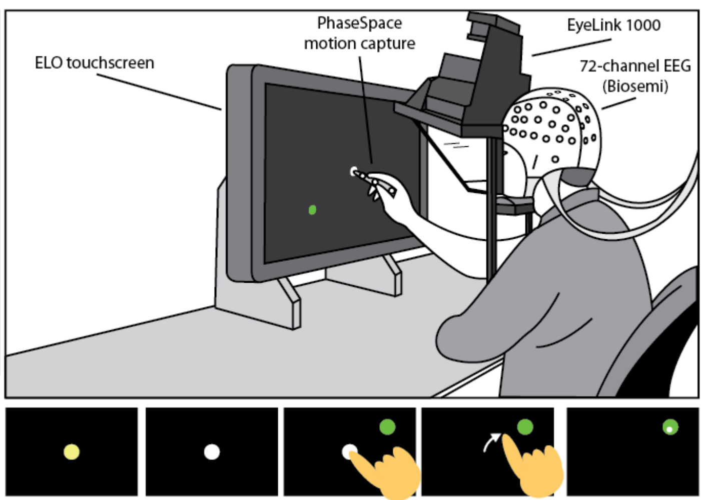
10x more data points than parameters to estimate

SIFT will let you know if your window length is not optimal

Network causal information flow during motor planning and execution

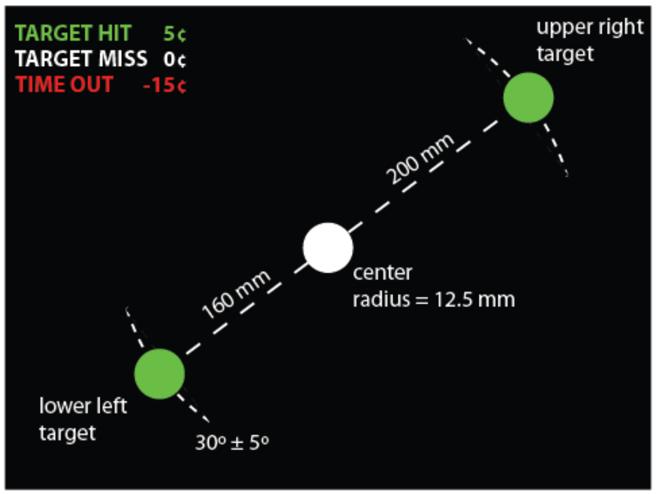
John R. Iversen, Alejandro Ojeda, Tim Mullen, Markus Plank, Joseph Snider,
Gert Cauwenberghs, Howard Poizner

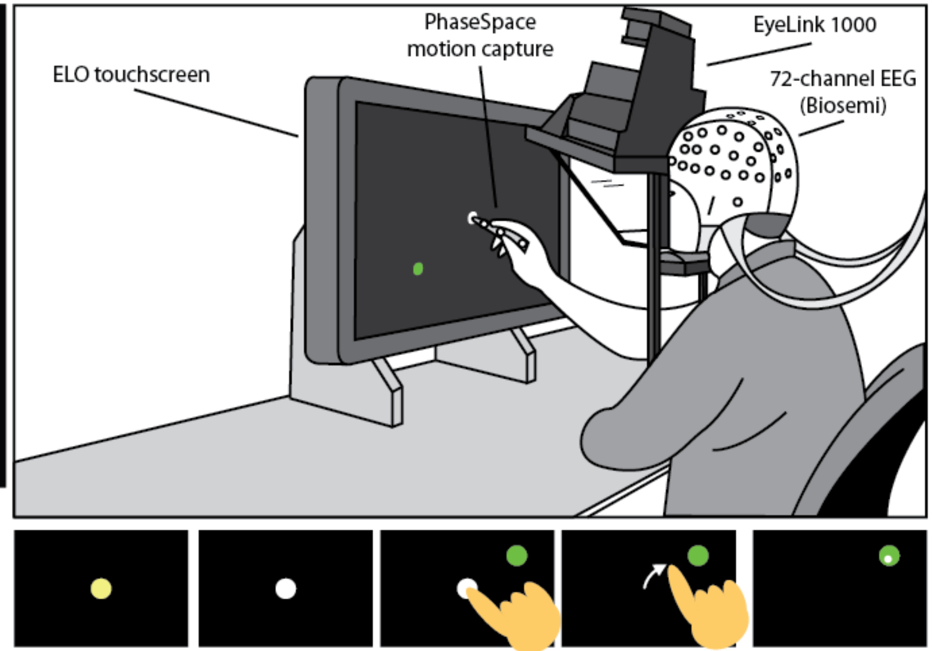
Institute for Neural Computation
Swartz Center for Computational Neuroscience
University of California, San Diego
EMBC 2014

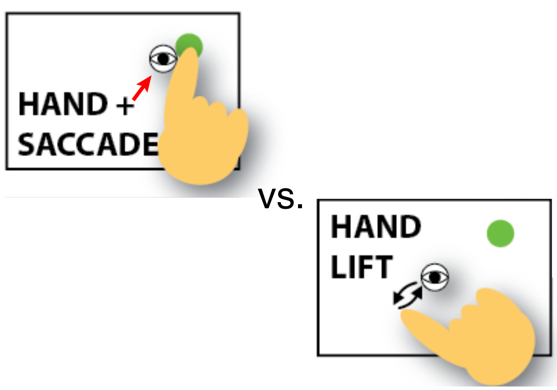


How does brain plan visually guided movements?

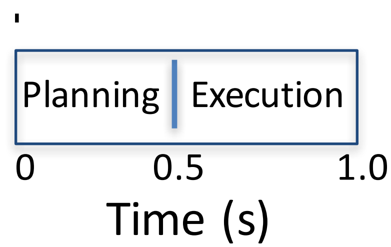
- Pointing Task (Park, et al. 2014, *IEEE Trans Neural Syst Rehabil Eng)*







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)		

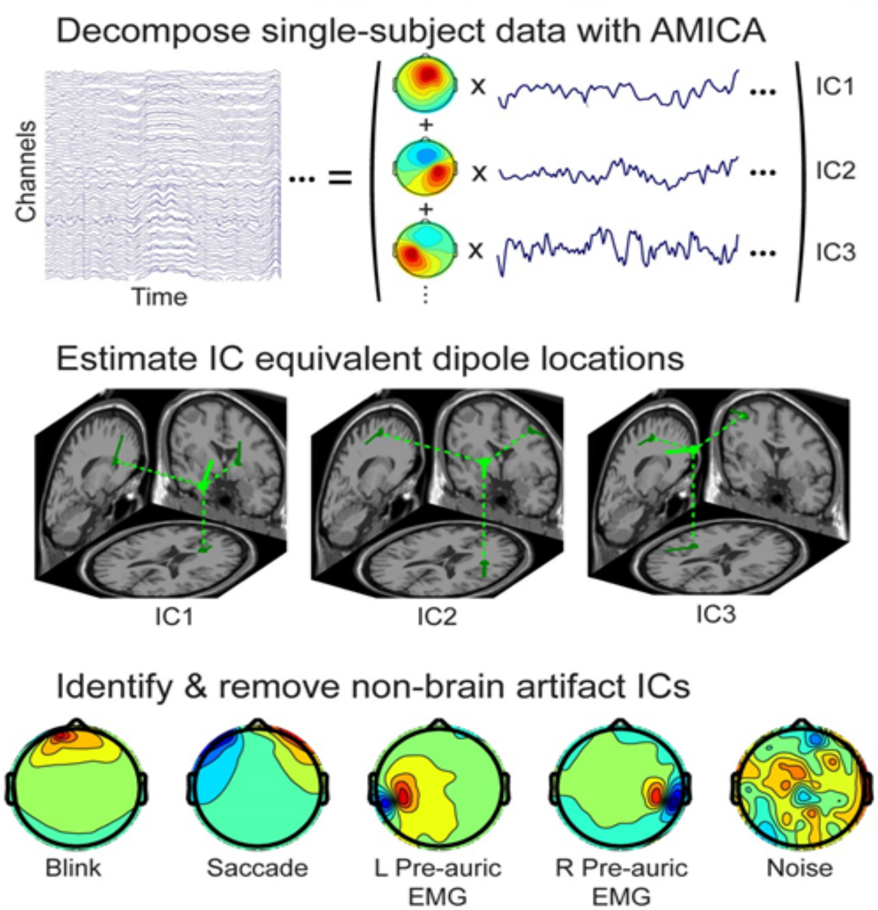


← Analysis Window

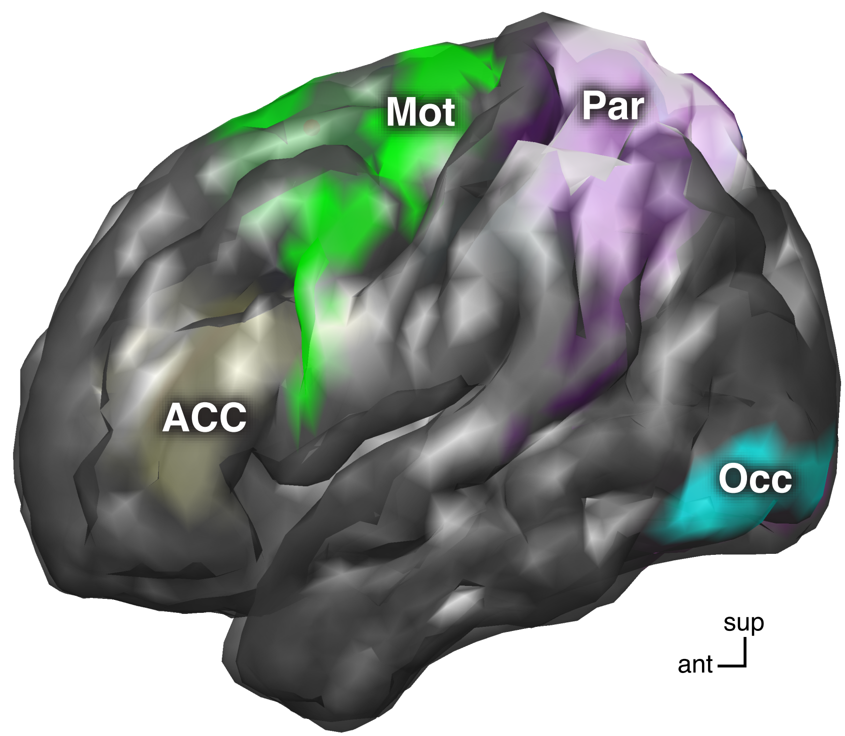
N=10 (right-handed, mean age=21)
70 channel EEG (Biosemi)
512 Hz; 128Hz for connectivity

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*)

Core Analysis Methods I

- Segmentation–based MVAR

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

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

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

$$A(t) = \arg\min_{\hat{A}} \left(\overbrace{\left\| Y - Z\tilde{A} \right\|_2^2}^{\text{prediction error}} + \underbrace{\boxed{\lambda}}_{\text{regularization}} \underbrace{\sum_{ij} \left\| \overbrace{\tilde{A}_{ij}^{(1)}, \ldots, \tilde{A}_{ij}^{(p)}}^{\text{smoothness (L2) (preserves spectrum)}} \right\|_2}_{\text{group sparsity (L1)}} \right)$$

Core Analysis Methods II

- Time-varying SdDTF ("short-time direct directed transfer function")

- Directed measure of direct (unmediated) causal flow between ROIs

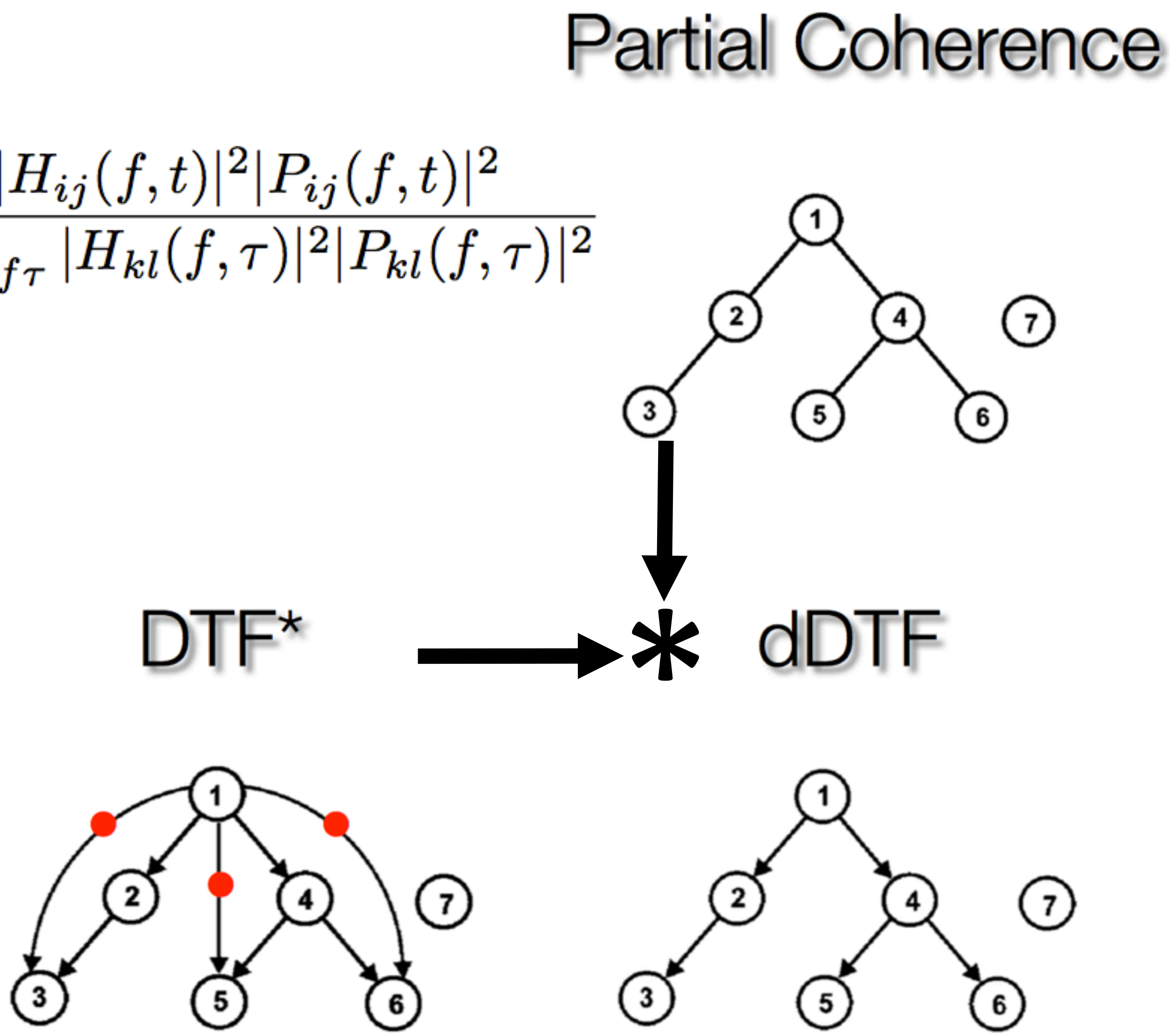
- Combines DTF and partial coherence; windowed (0.5s, 30ms).

$$\eta_{ij}^2(f,t) = \frac{|H_{ij}(f,t)|^2 |P_{ij}(f,t)|^2}{\sum_{klf\tau} |H_{kl}(f,\tau)|^2 |P_{kl}(f,\tau)|^2}$$

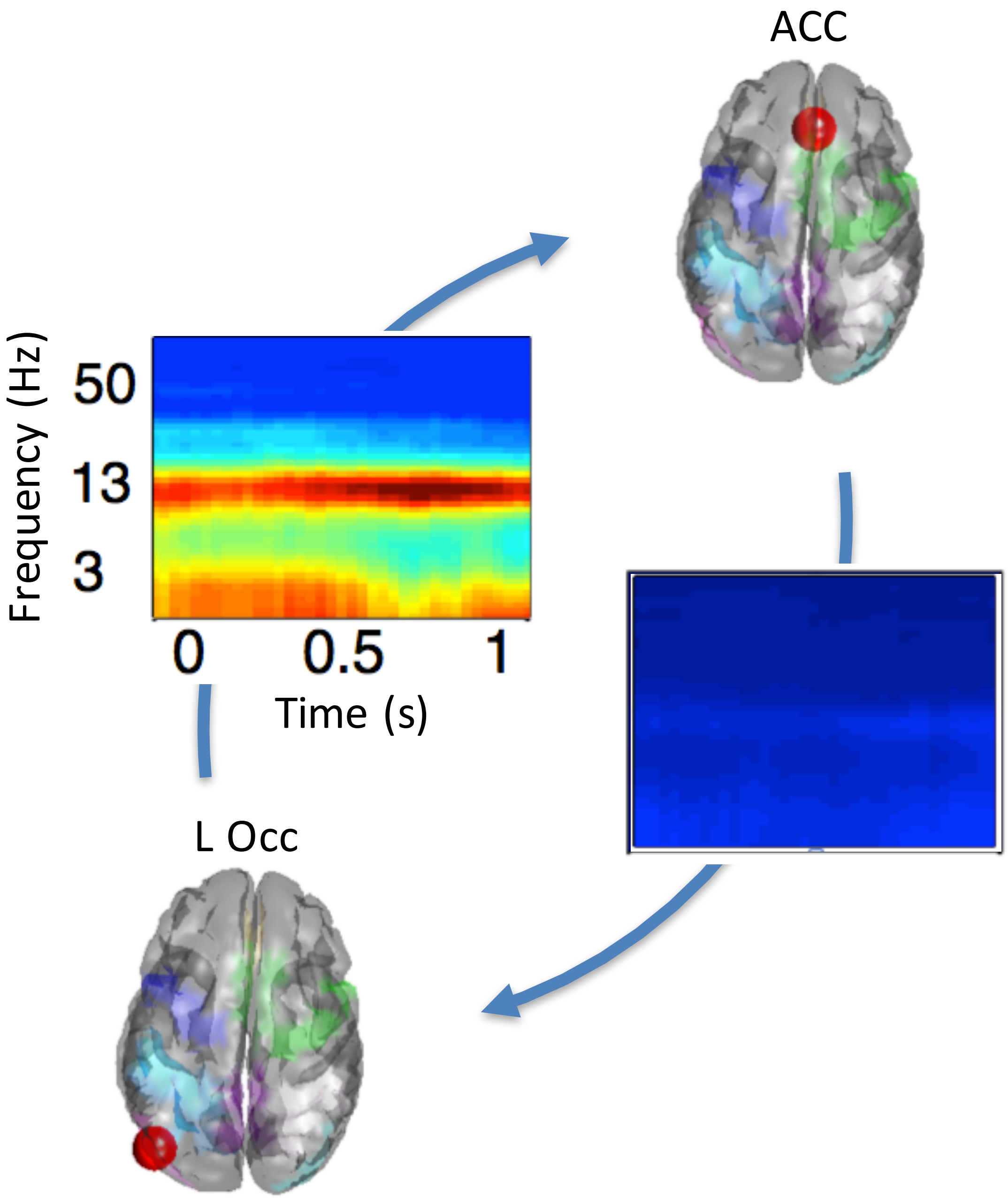
(Korzeniewska, et al. 2008)

dDTF

$$\eta_{ij}^2(f,t) = \frac{|H_{ij}(f,t)|^2 |P_{ij}(f,t)|^2}{\sum_{klf\tau} |H_{kl}(f,\tau)|^2 |P_{kl}(f,\tau)|^2}$$



SIFT Analysis

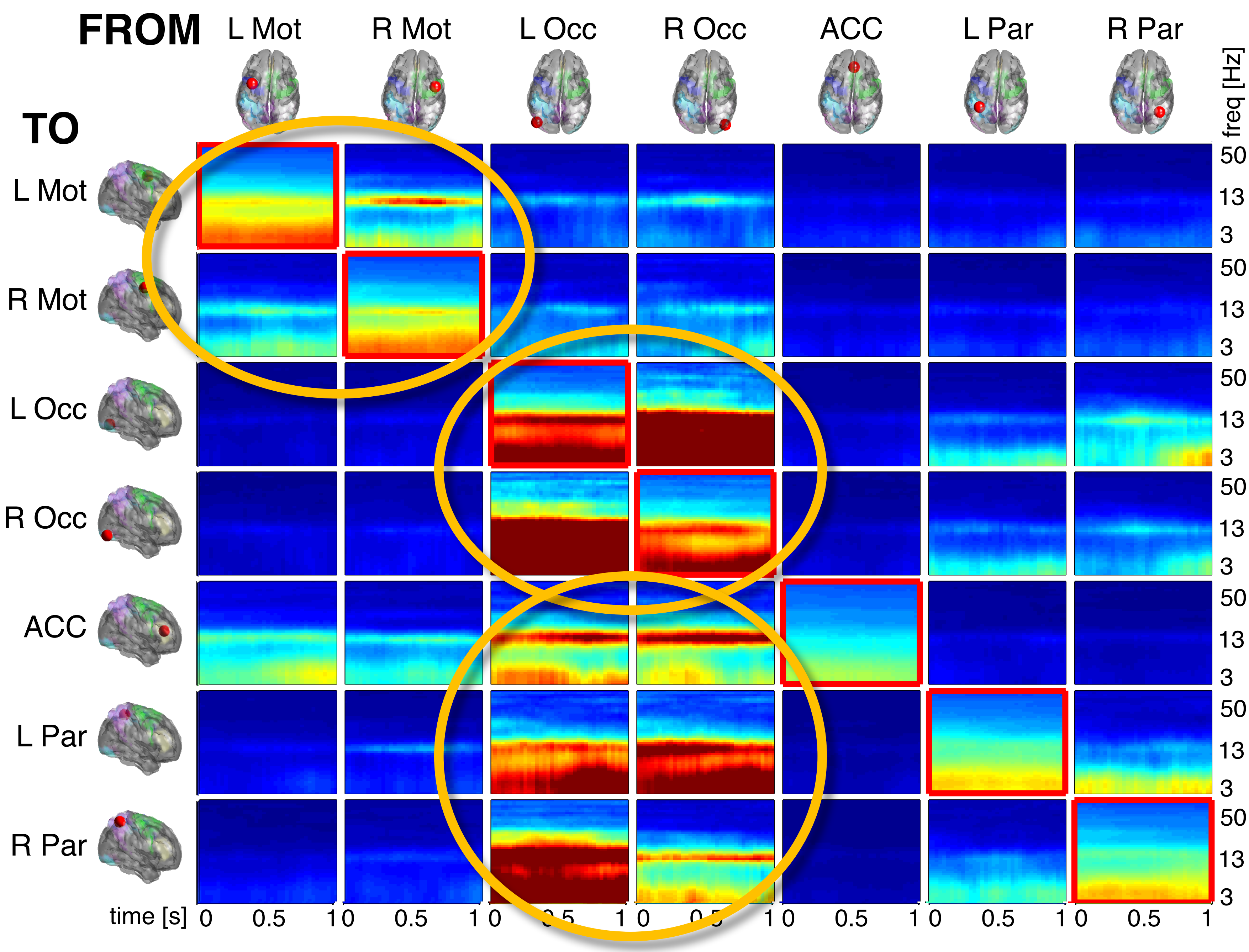


• Time-varying SdDTF

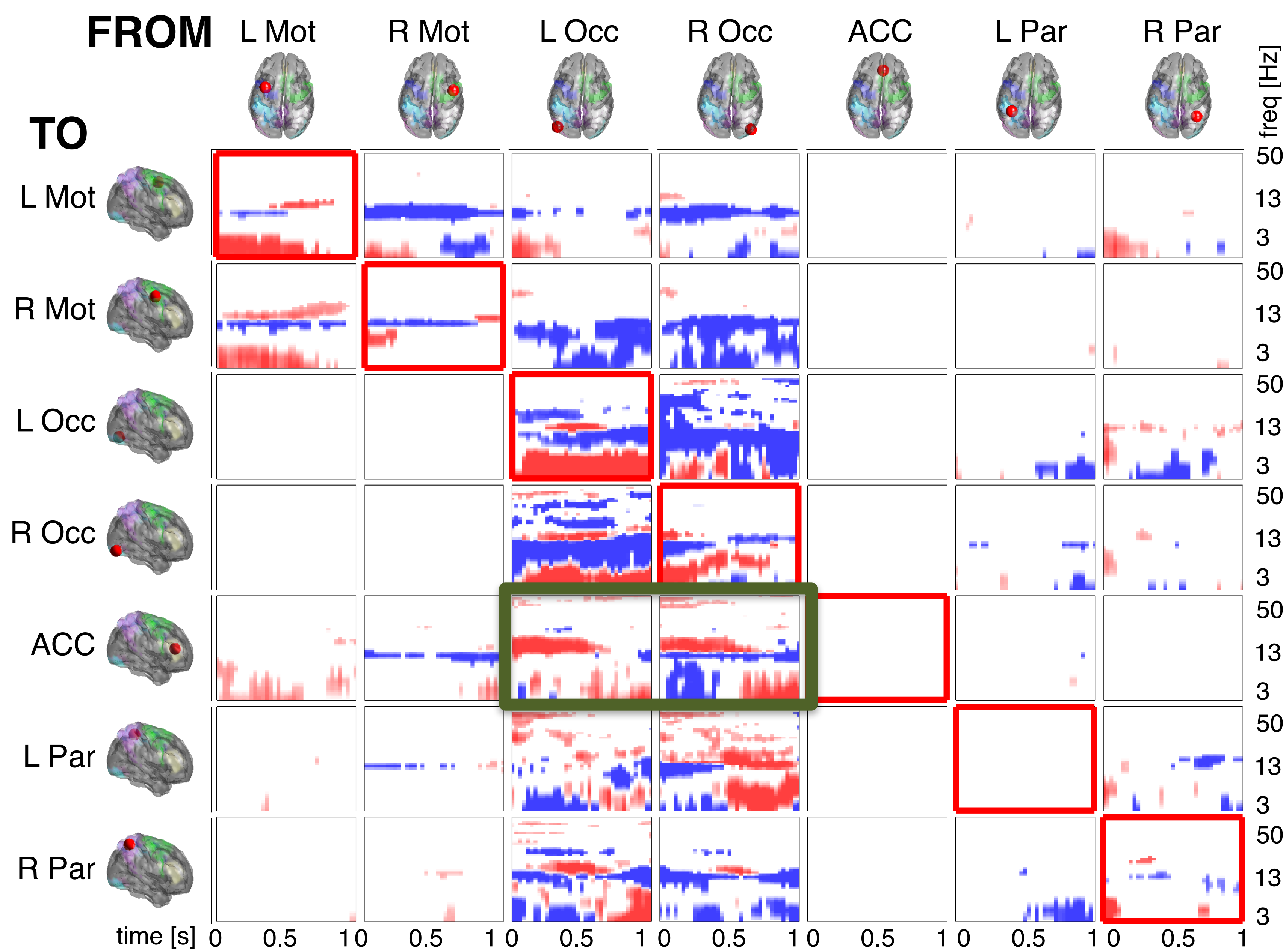
Directed measure of direct causal flow between ROIs

Averaged across subjects

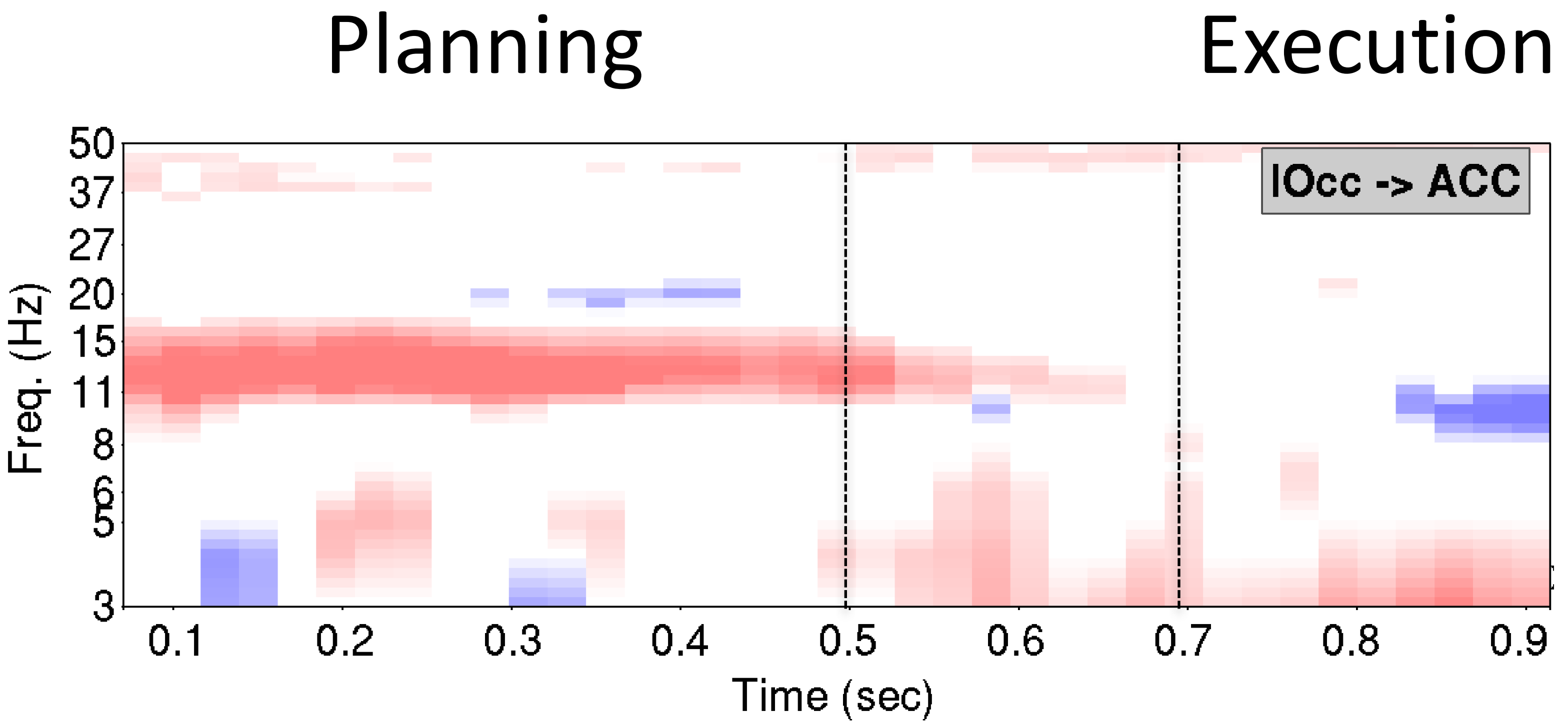
dDTF during reaching



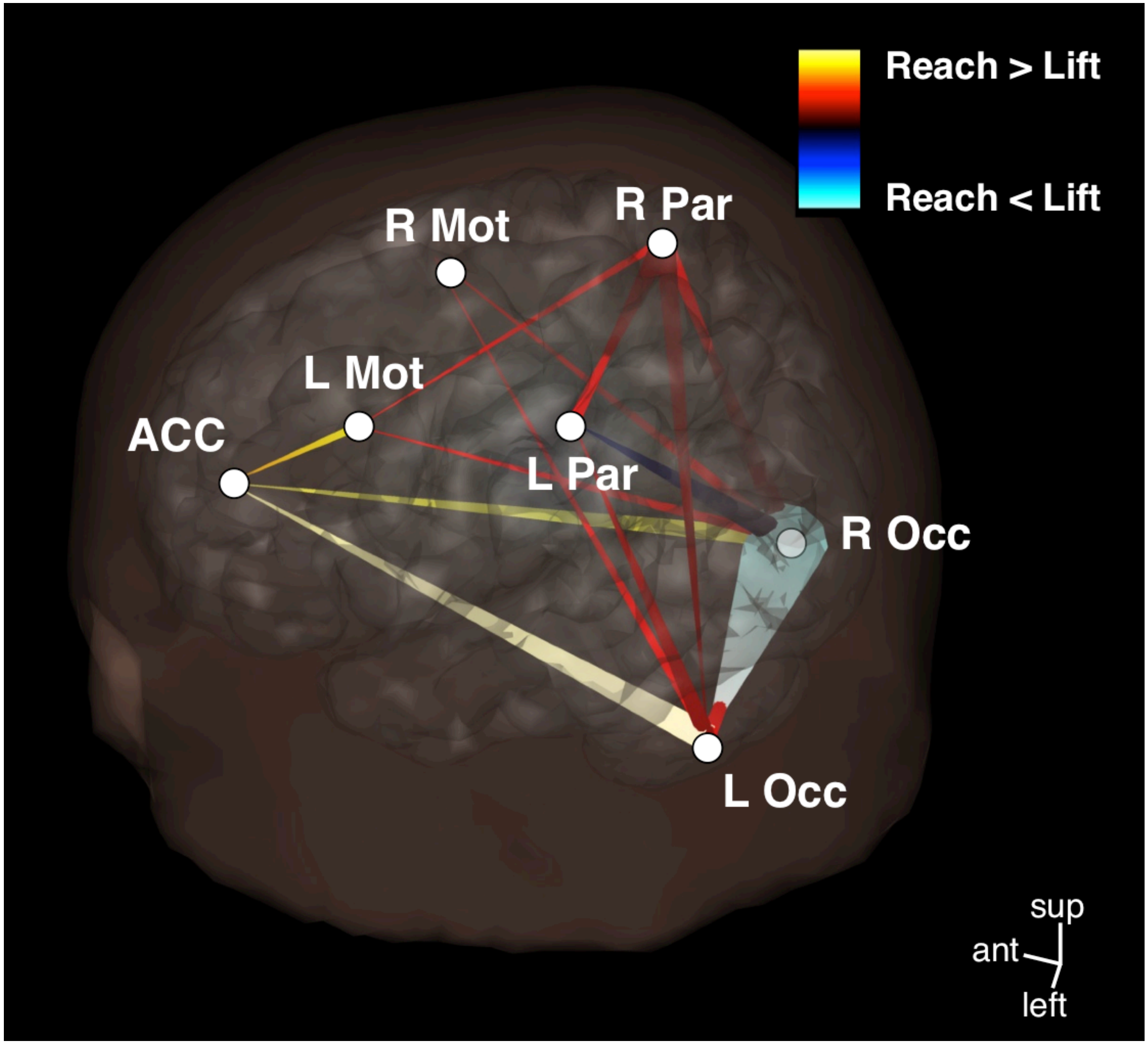
Changed causal flow during reaching



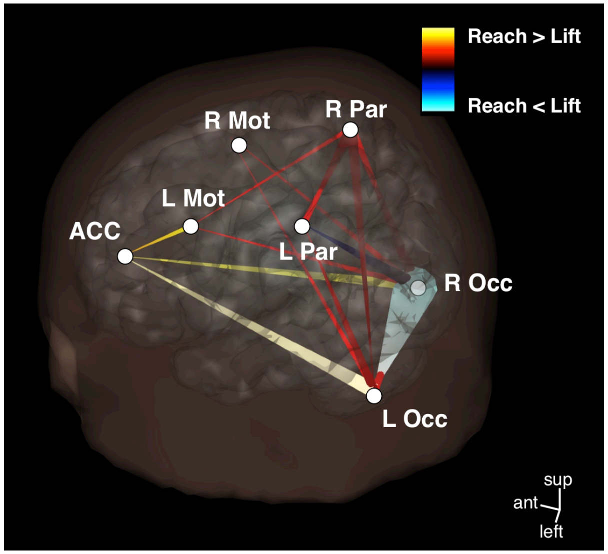
Occipital → ACC



Greater causal flow during movement planning



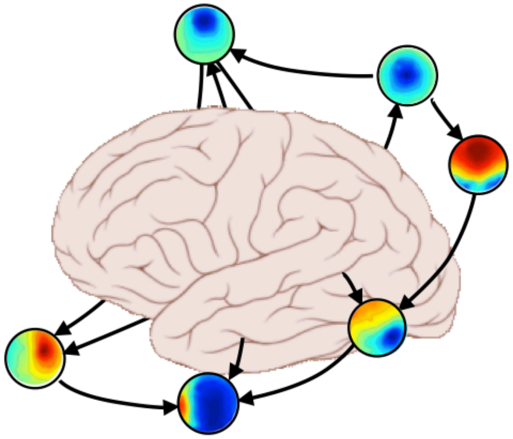
Discussion



- 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

Acknowledgments

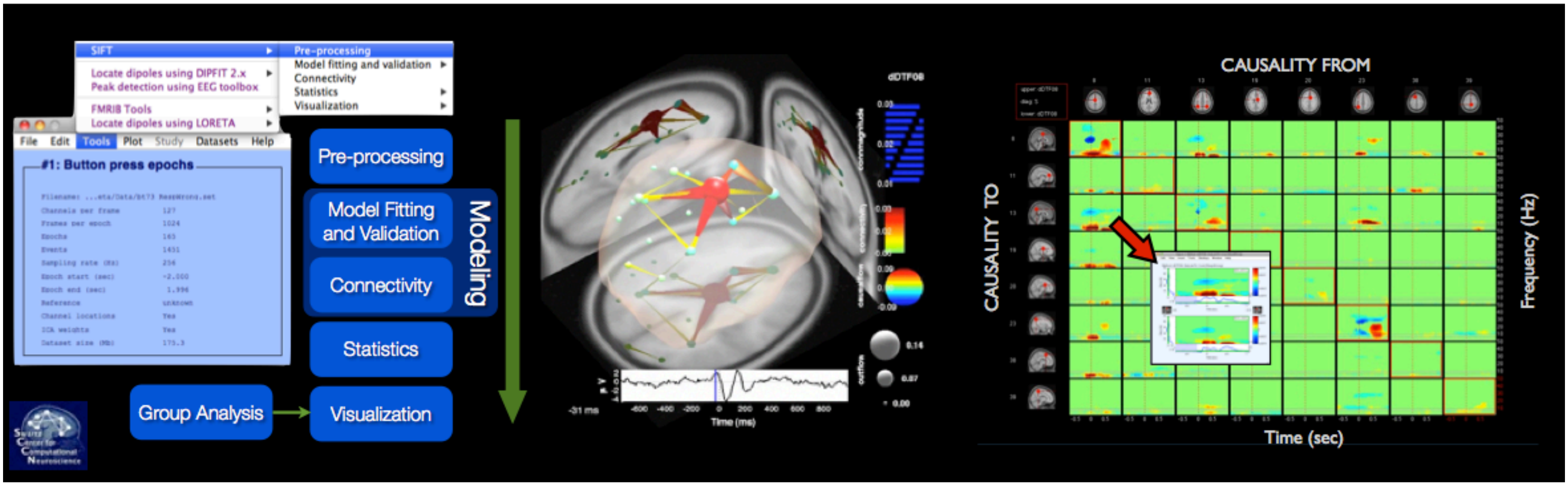
- National Science Foundation grant EFRI-1137279 (M3C: Mind, Machines, and Motor Control).
- NSF SMA-1041755, and ONR MURI Award No. N00014-10-1-0072.
- The Swartz Foundation.



SIFT

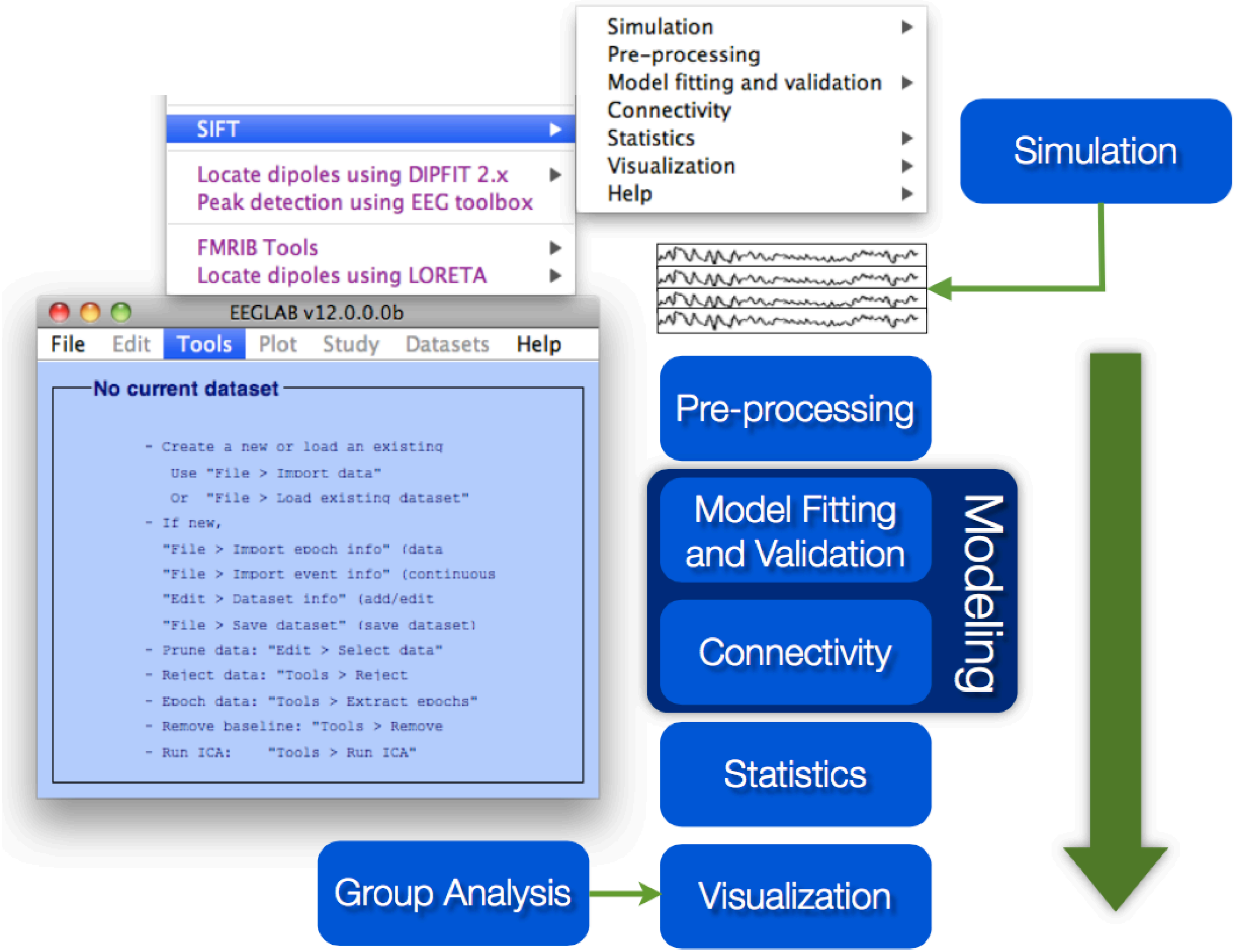
Source Information Flow Toolbox

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

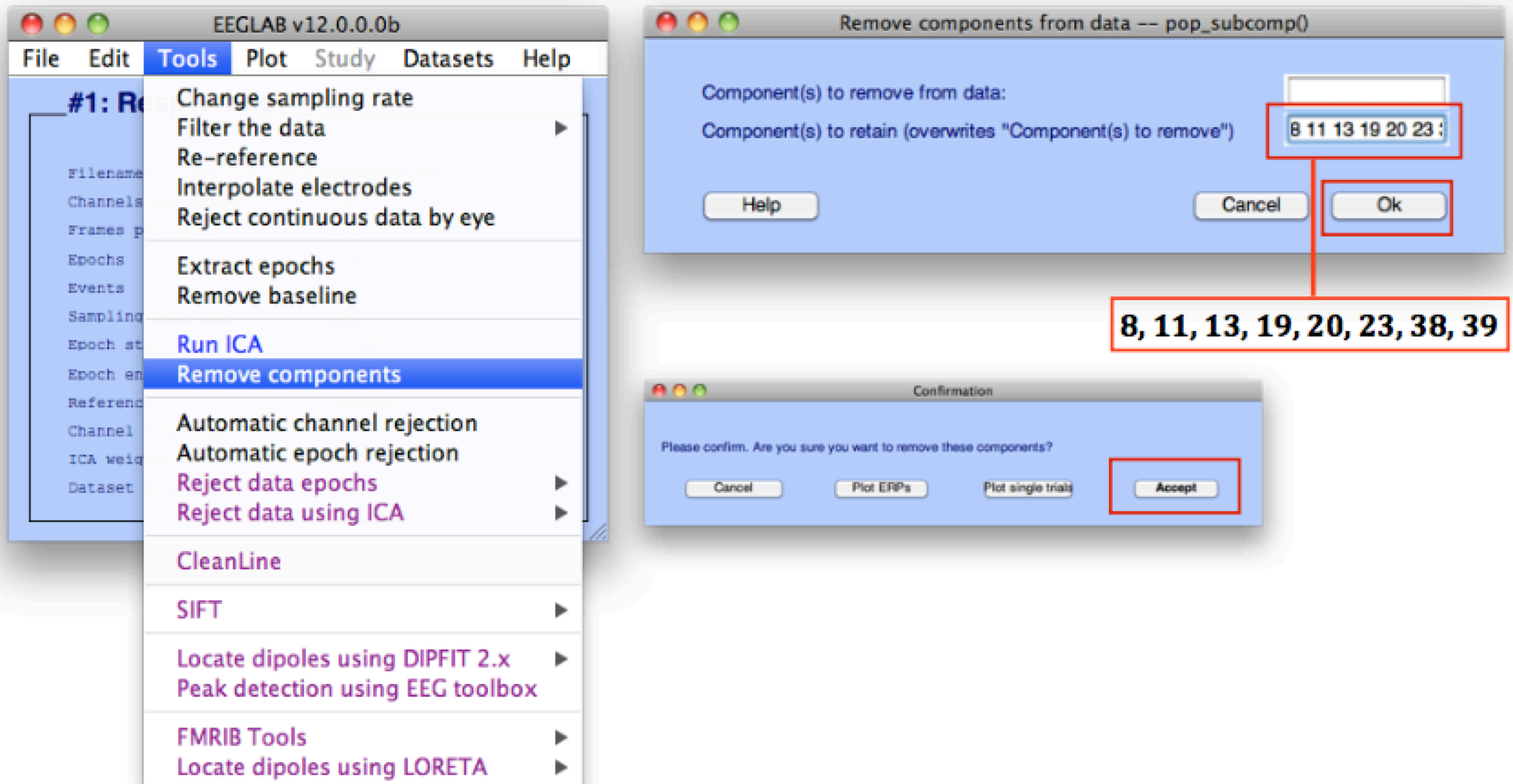


- A toolbox for (source-space) electrophysiological information flow and causality analysis (single- or multi-subject) integrated into the EEGLAB software environment.
- Emphasis on vector autoregression and time-frequency domain approaches
- Standard and novel interactive visualization methods for exploratory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

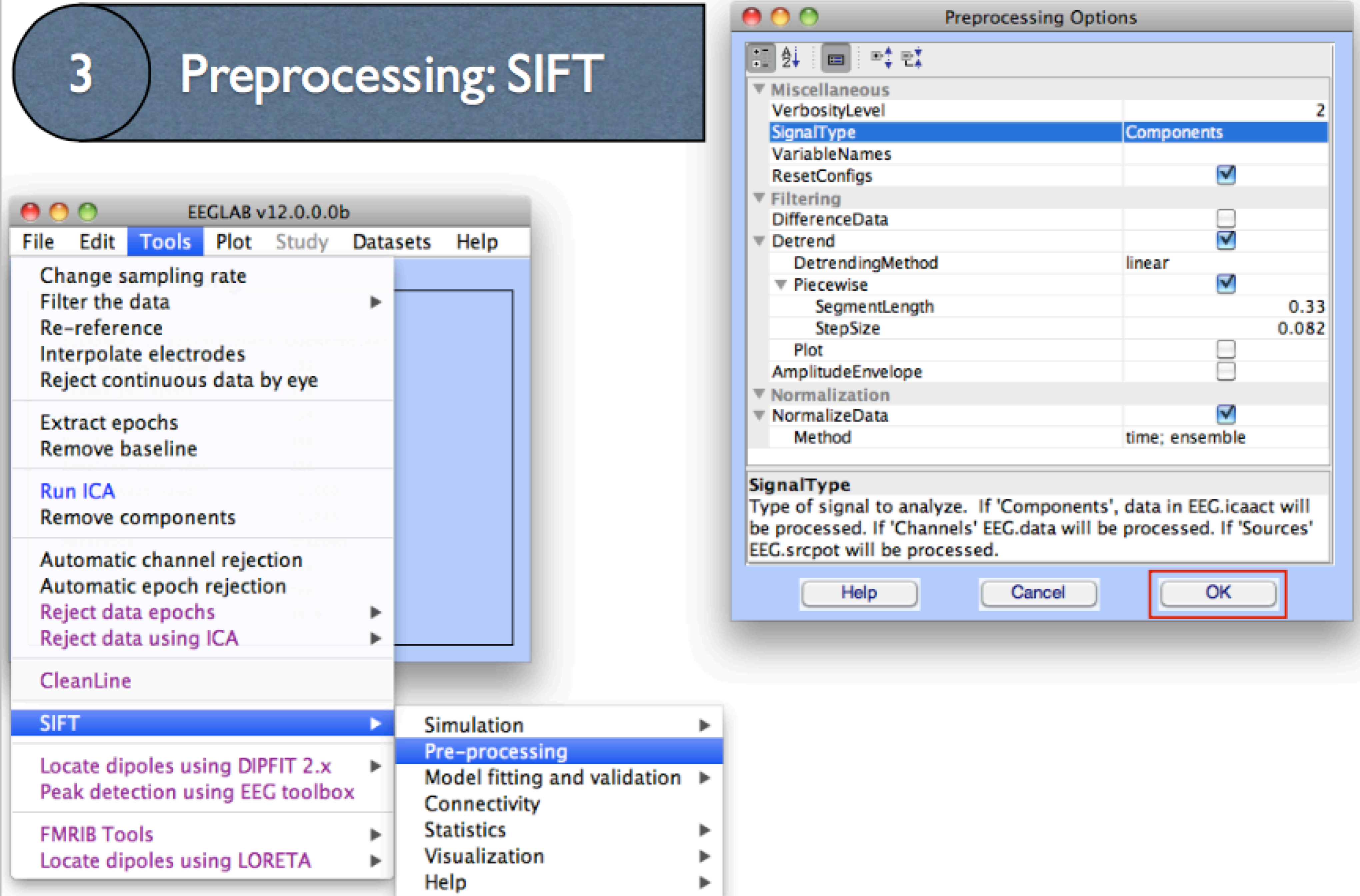
SIFT Workflow



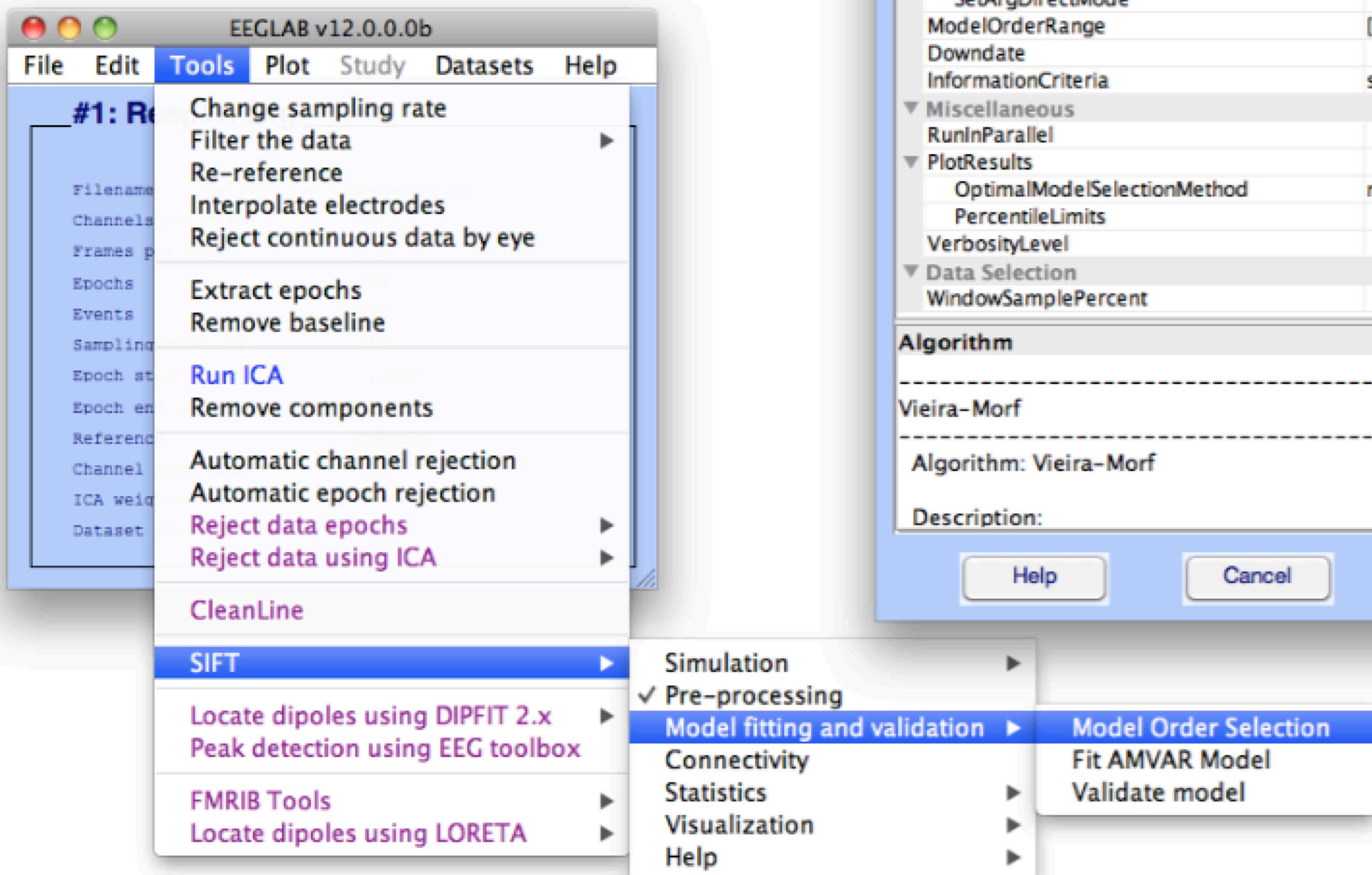
3 Preprocessing: Select Components

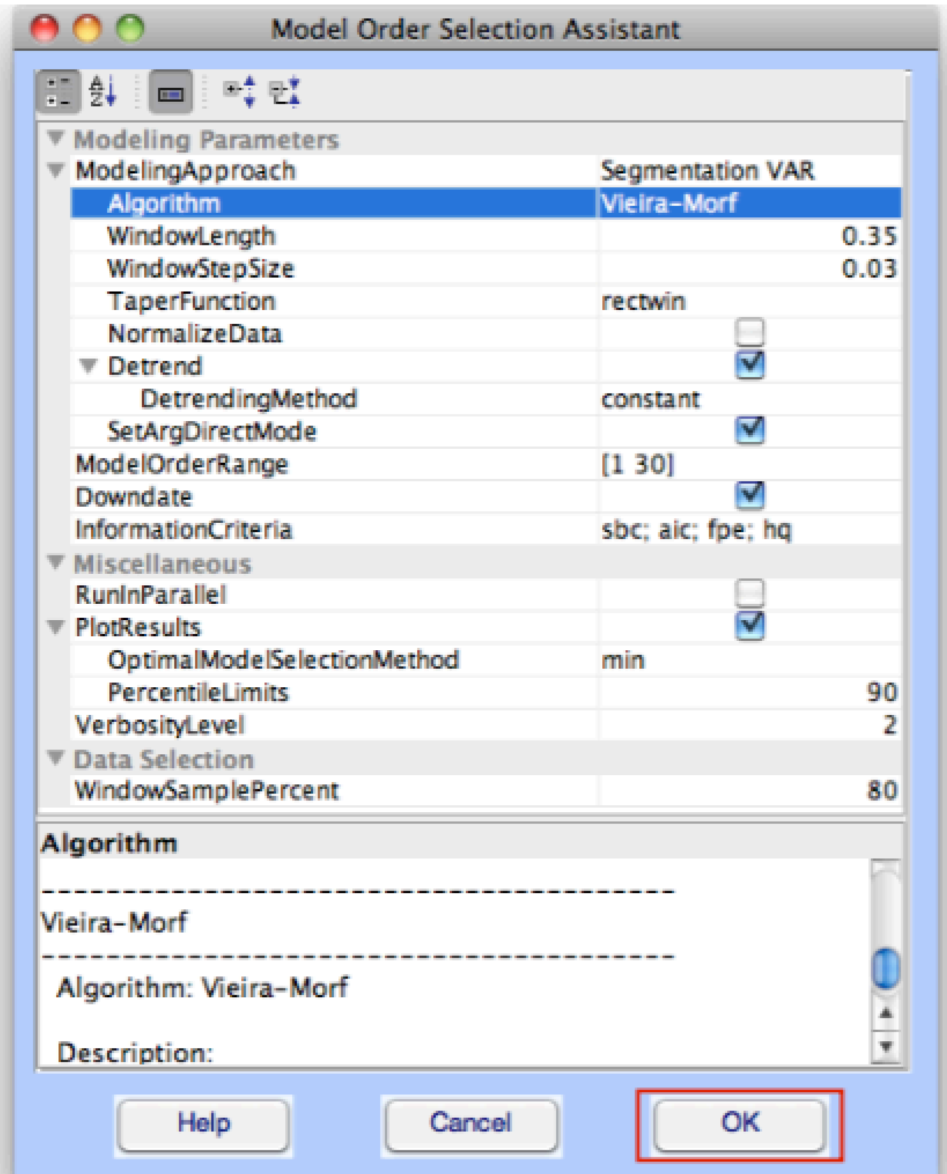


3 Preprocessing: SIFT



4 Model Order Selection





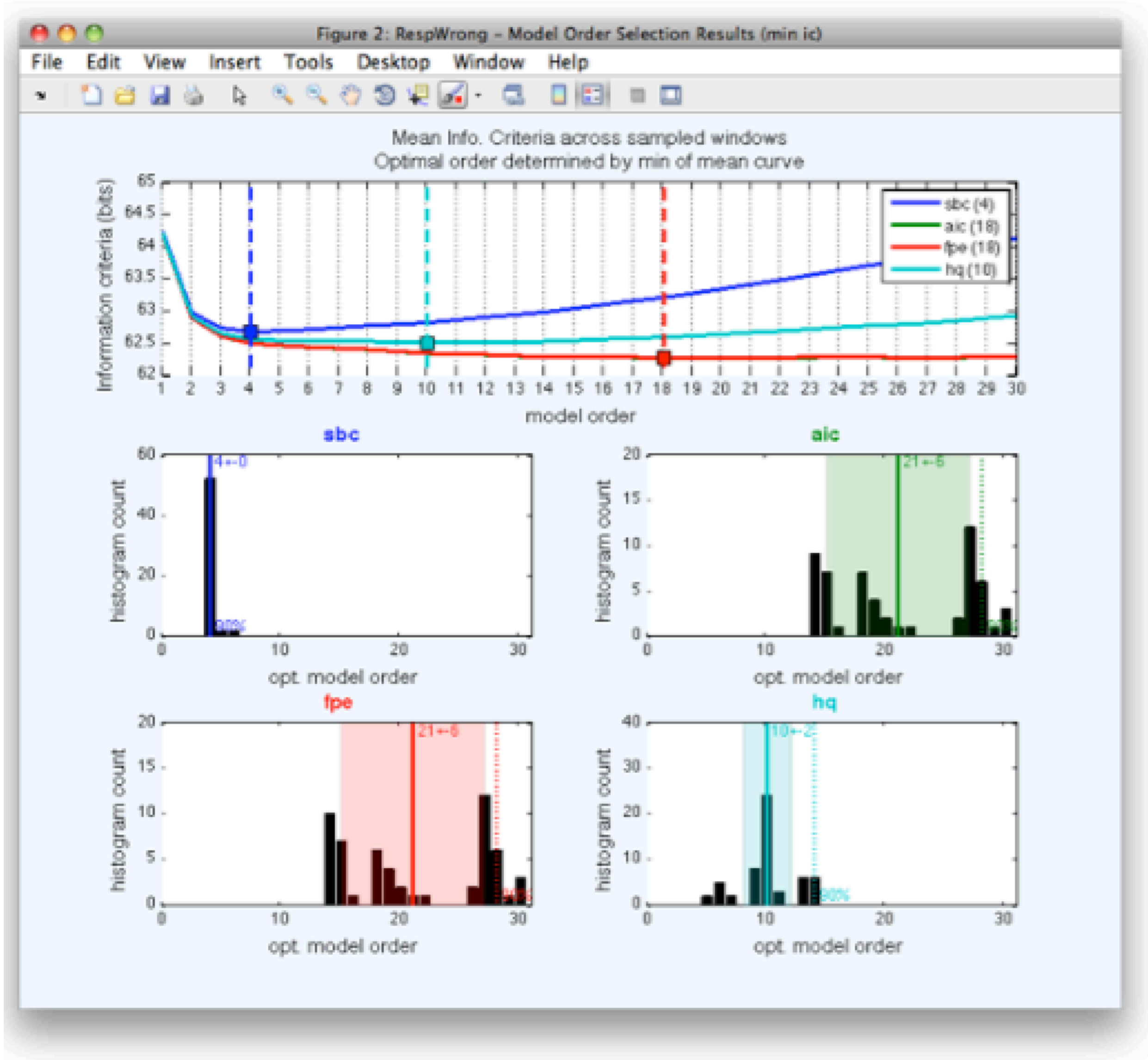
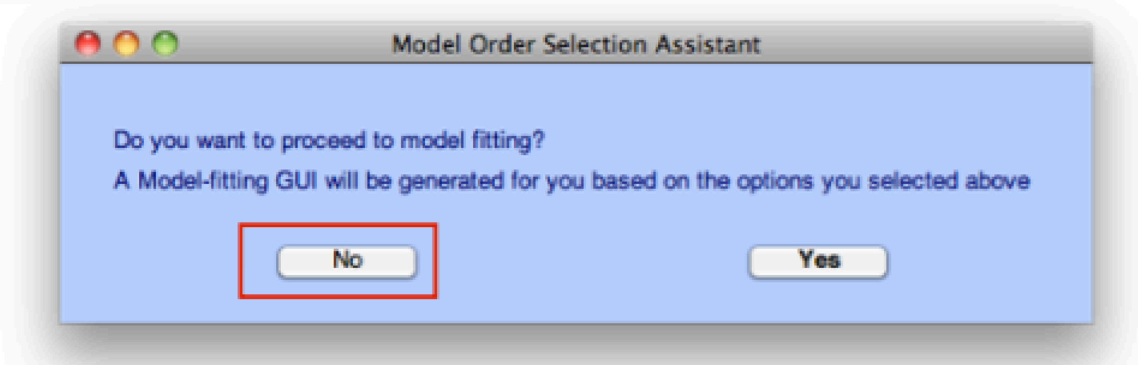
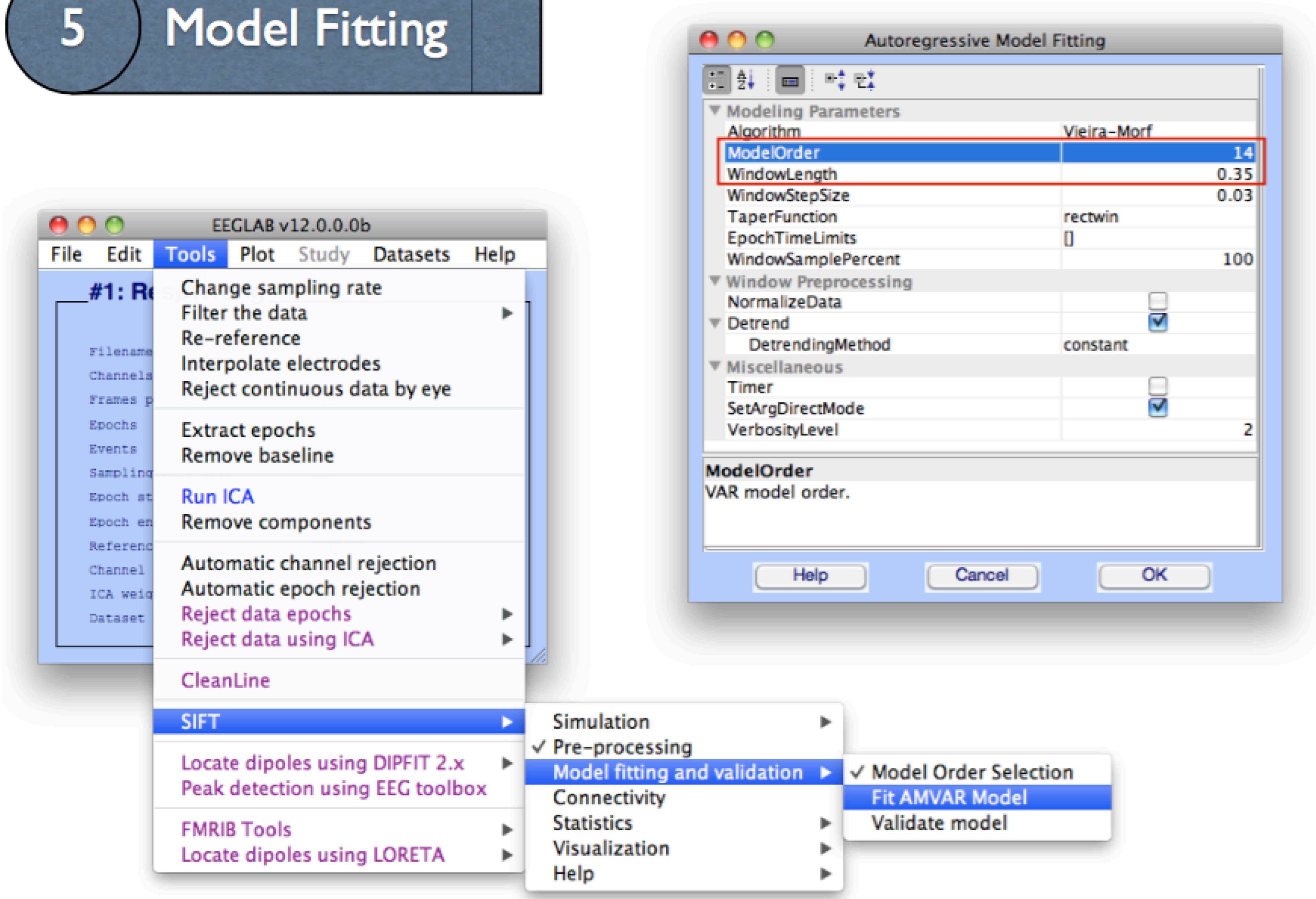


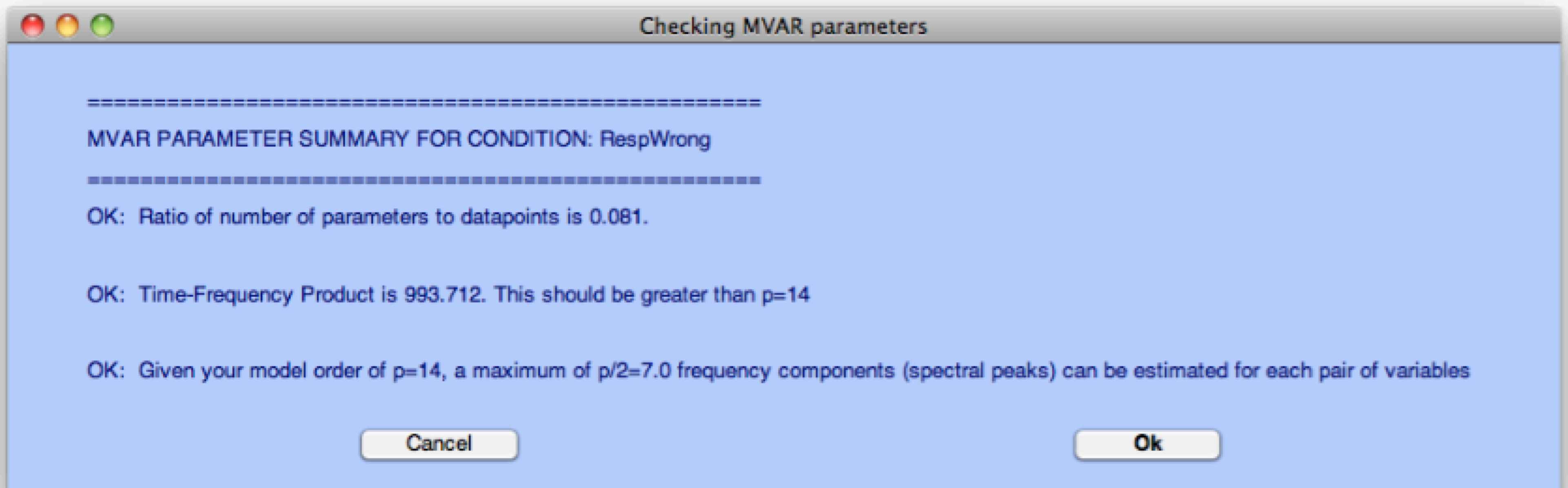
Figure 2: RespWrong - Model Order Selection Results (min ic)
File Edit View Insert Tools Desktop Window Help
Mean Info. Criteria across sampled windows
Optimal order determined by min of mean curve
Information criteria (bits)
model order
sbc (4)
aic (18)
fpe (18)
hq (10)
sbc
aic
fpe
hq
histogram count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


Model Order Selection Assistant
Do you want to proceed to model fitting?
A Model-fitting GUI will be generated for you based on the options you selected above
No
Yes

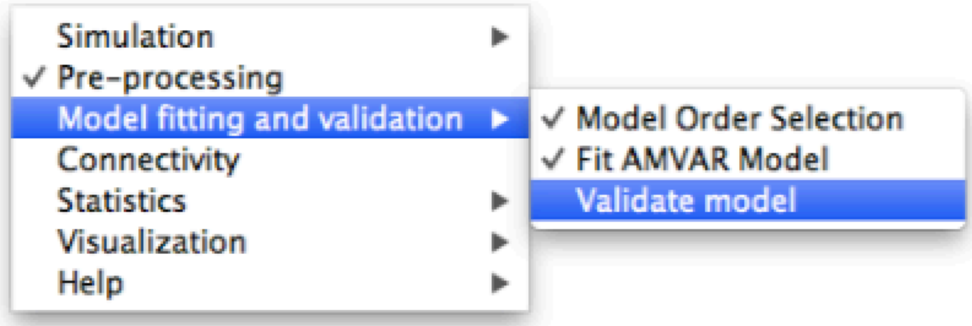
5 Model Fitting

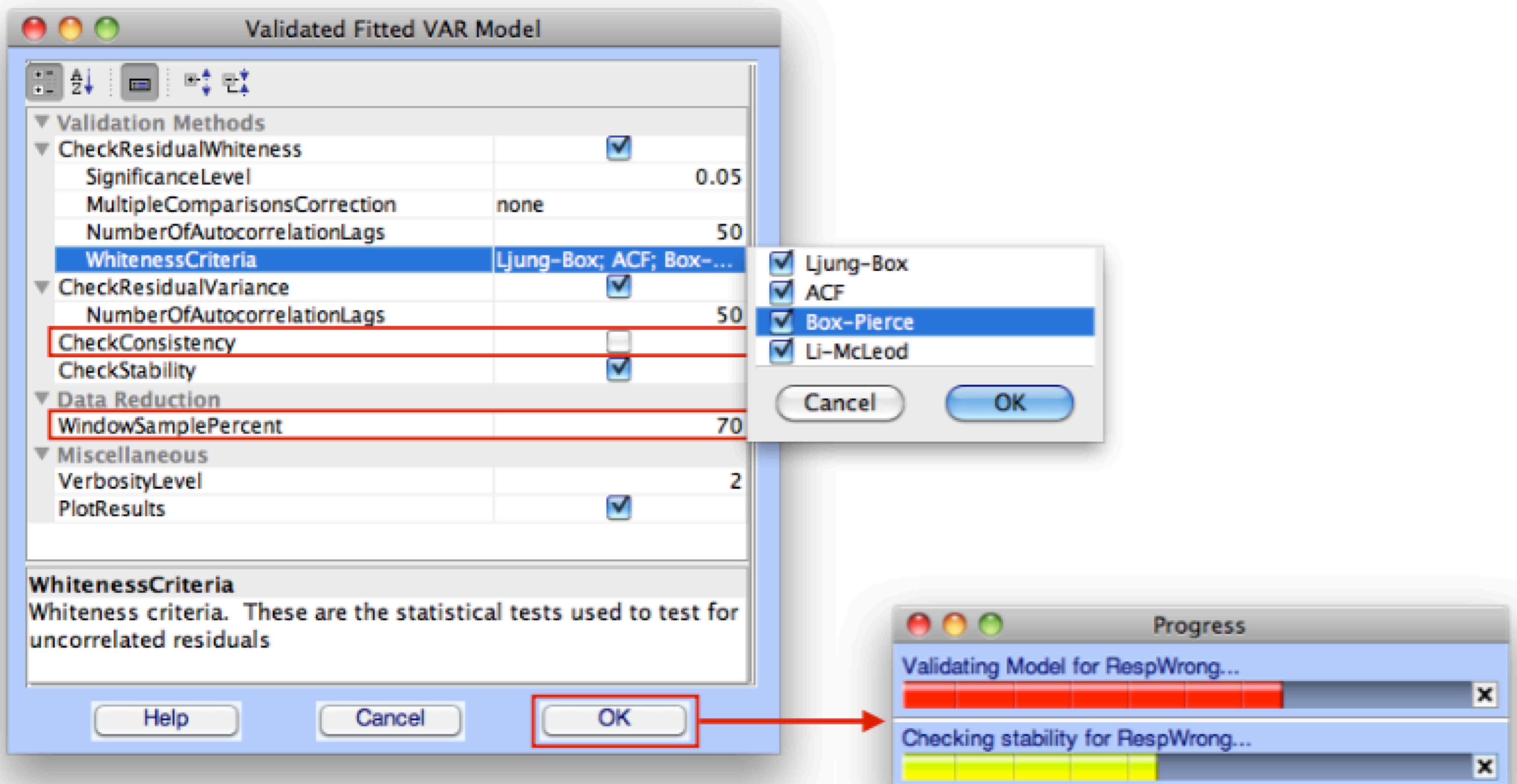


5 Model Fitting

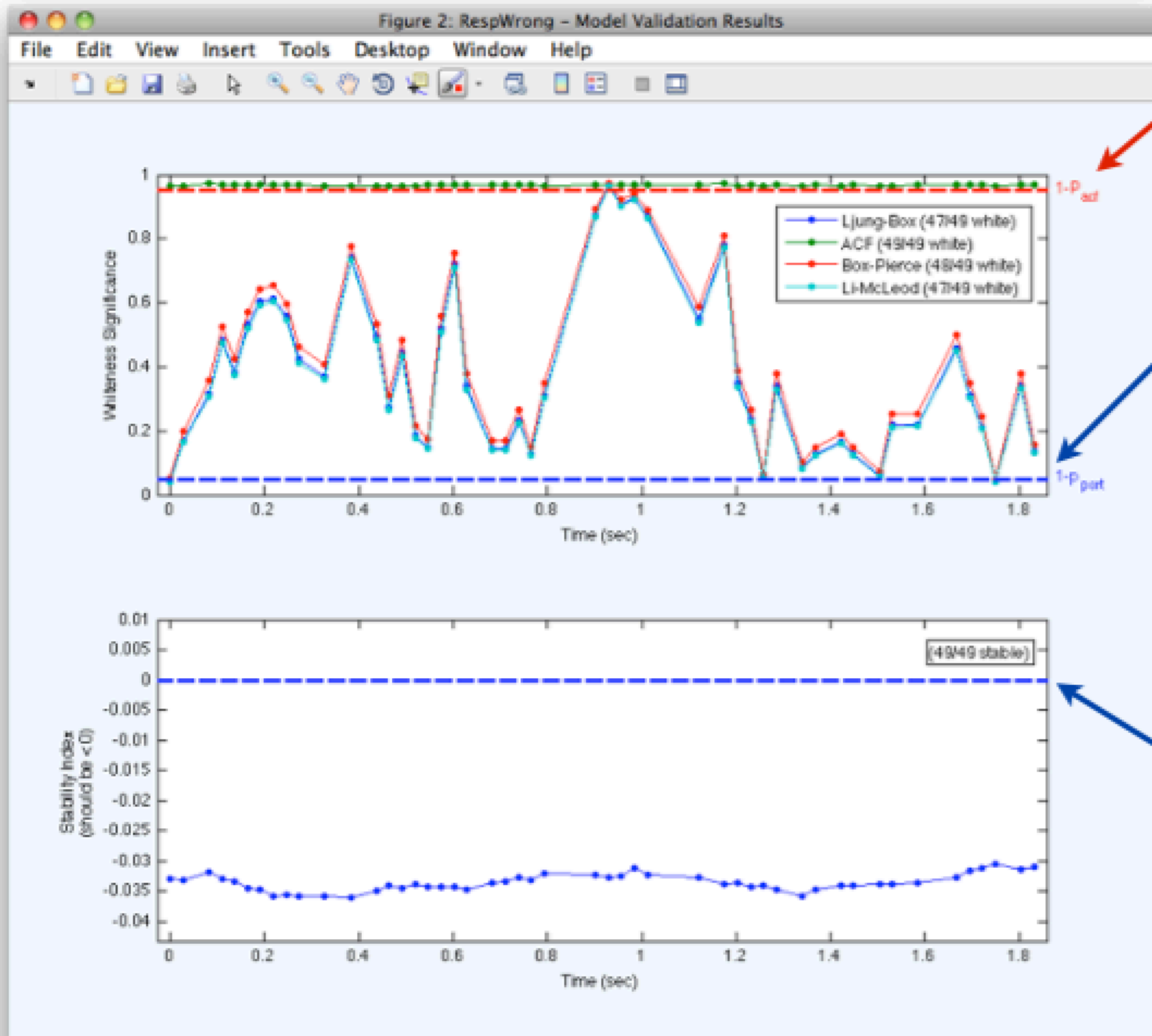


6 Model Validation





6 Model Validation

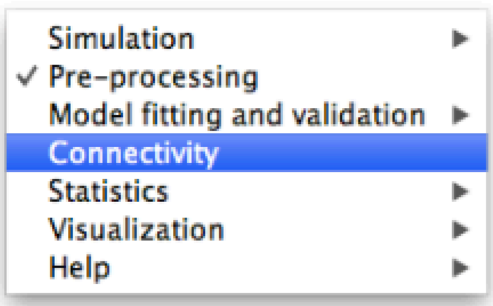


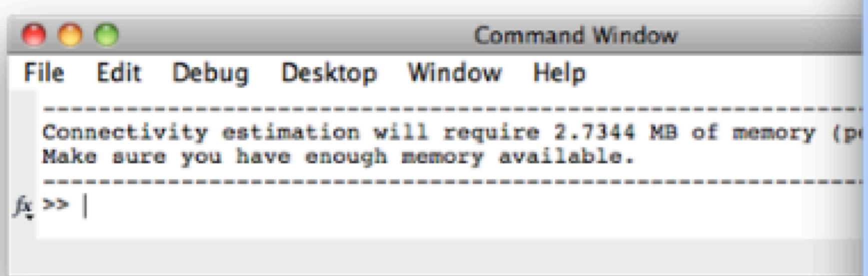
ACF statistic should be above this line

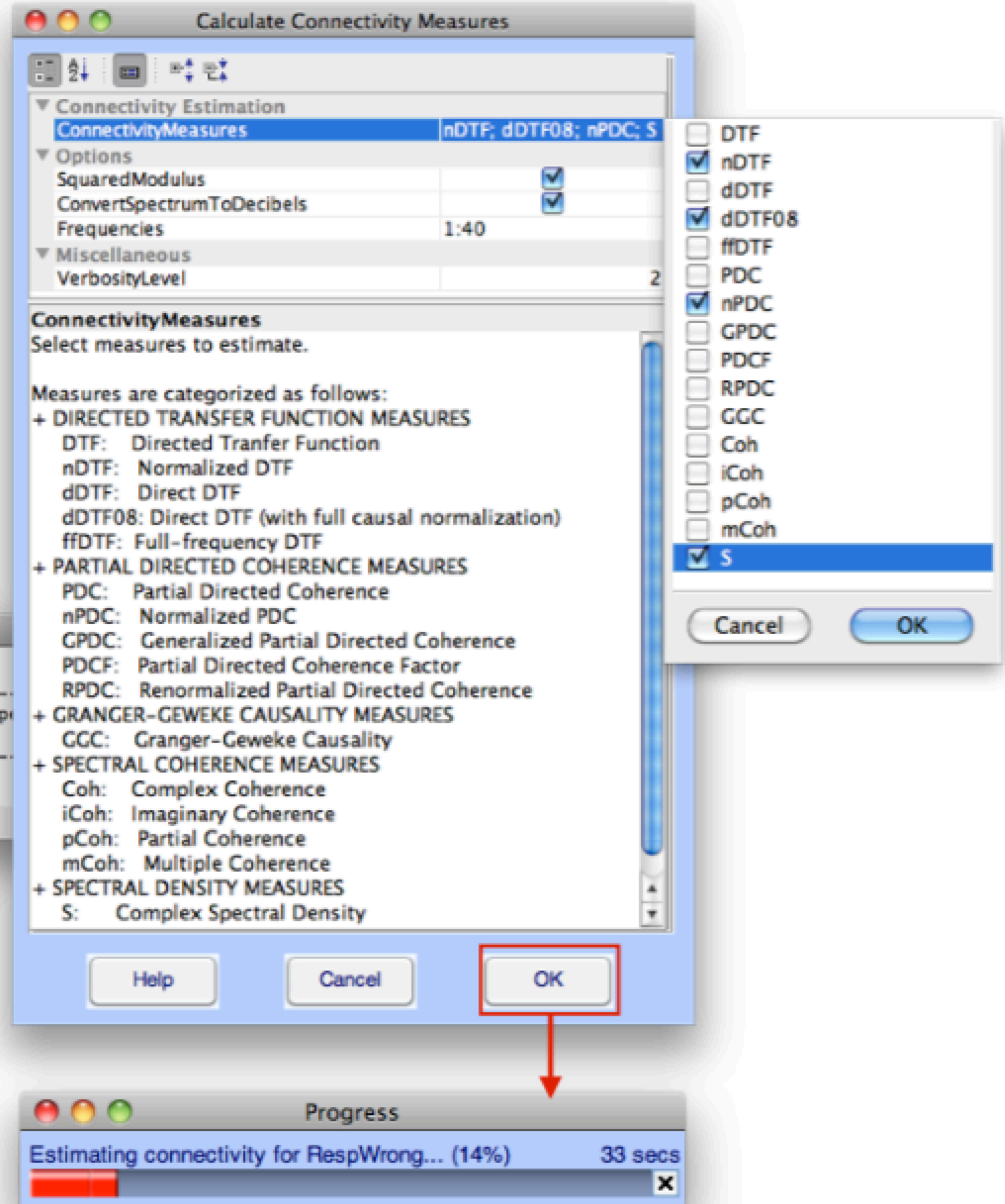
Portmanteau statistics should be above this line

Stability index should be < 0

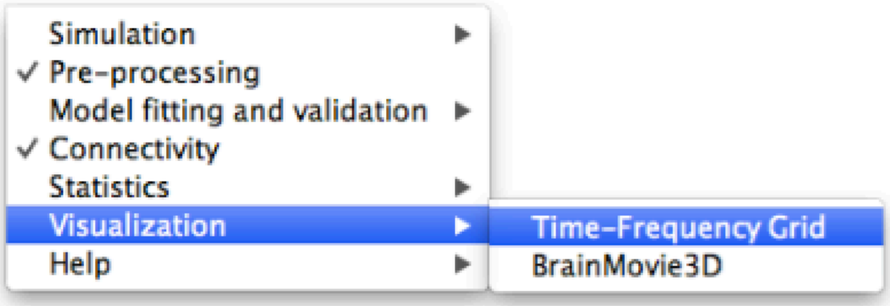
7 Connectivity

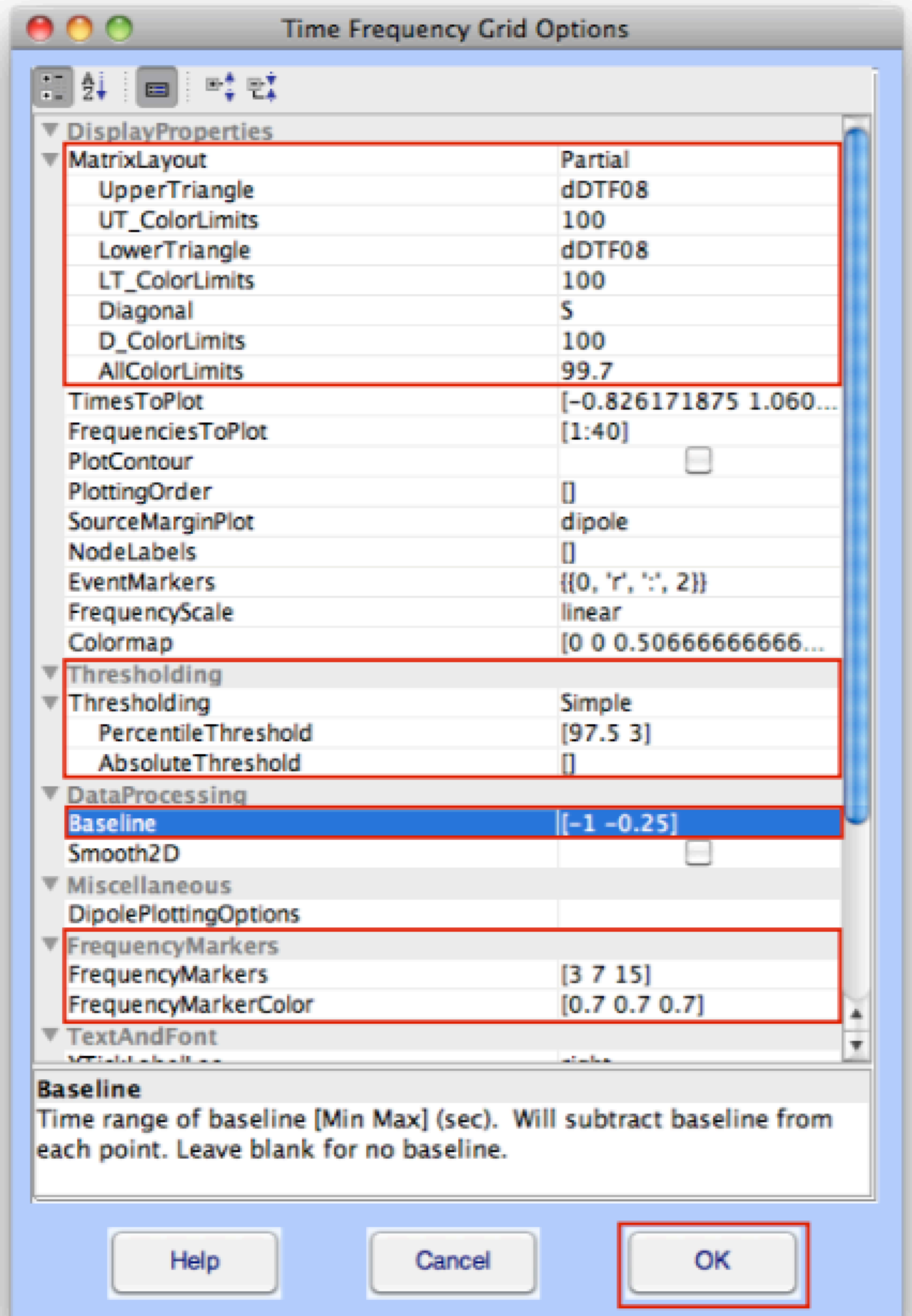






8 Visualization: Time-Frequency Grid





Granger Causality on off-diagonal
ERSP on diagonal

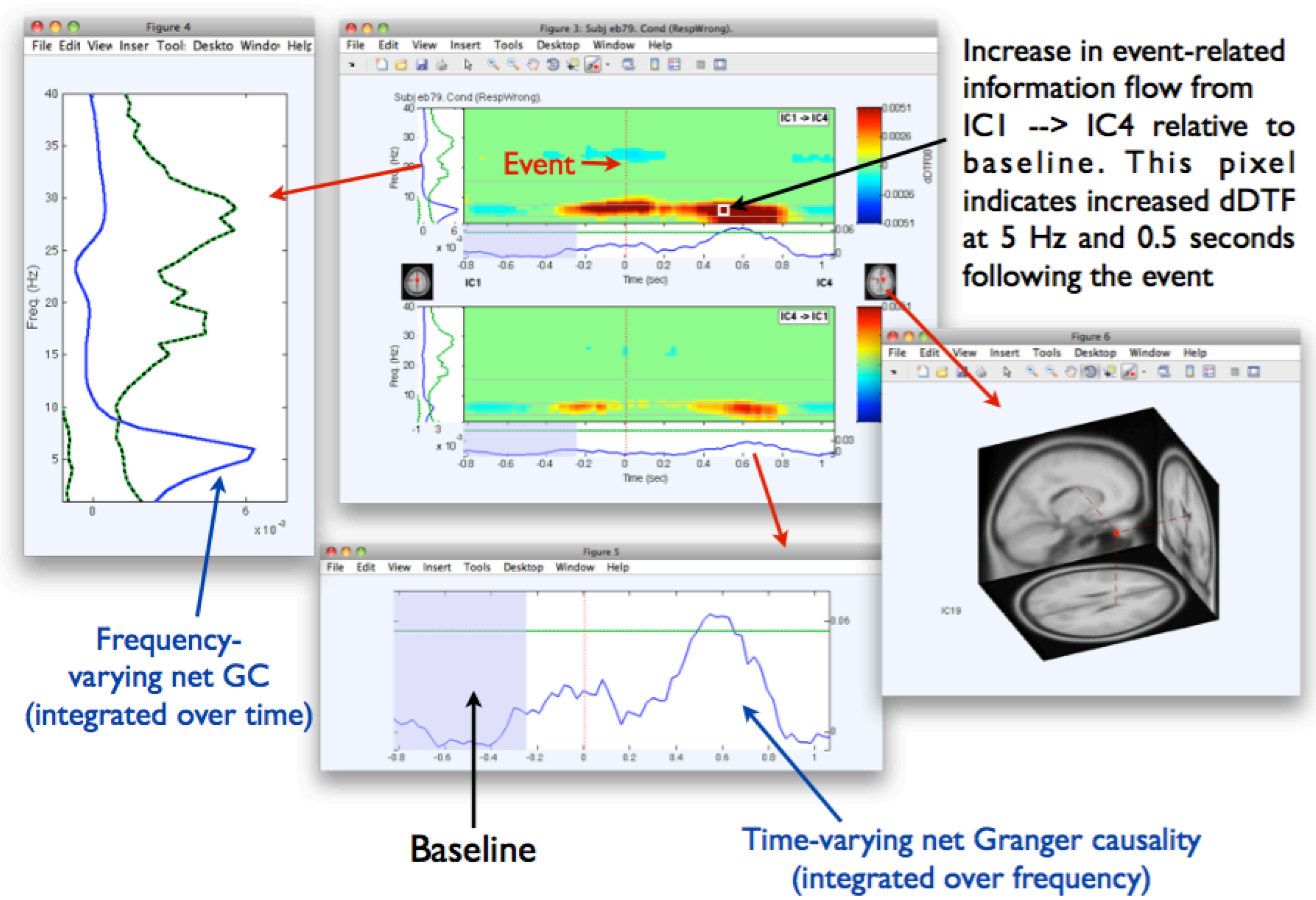
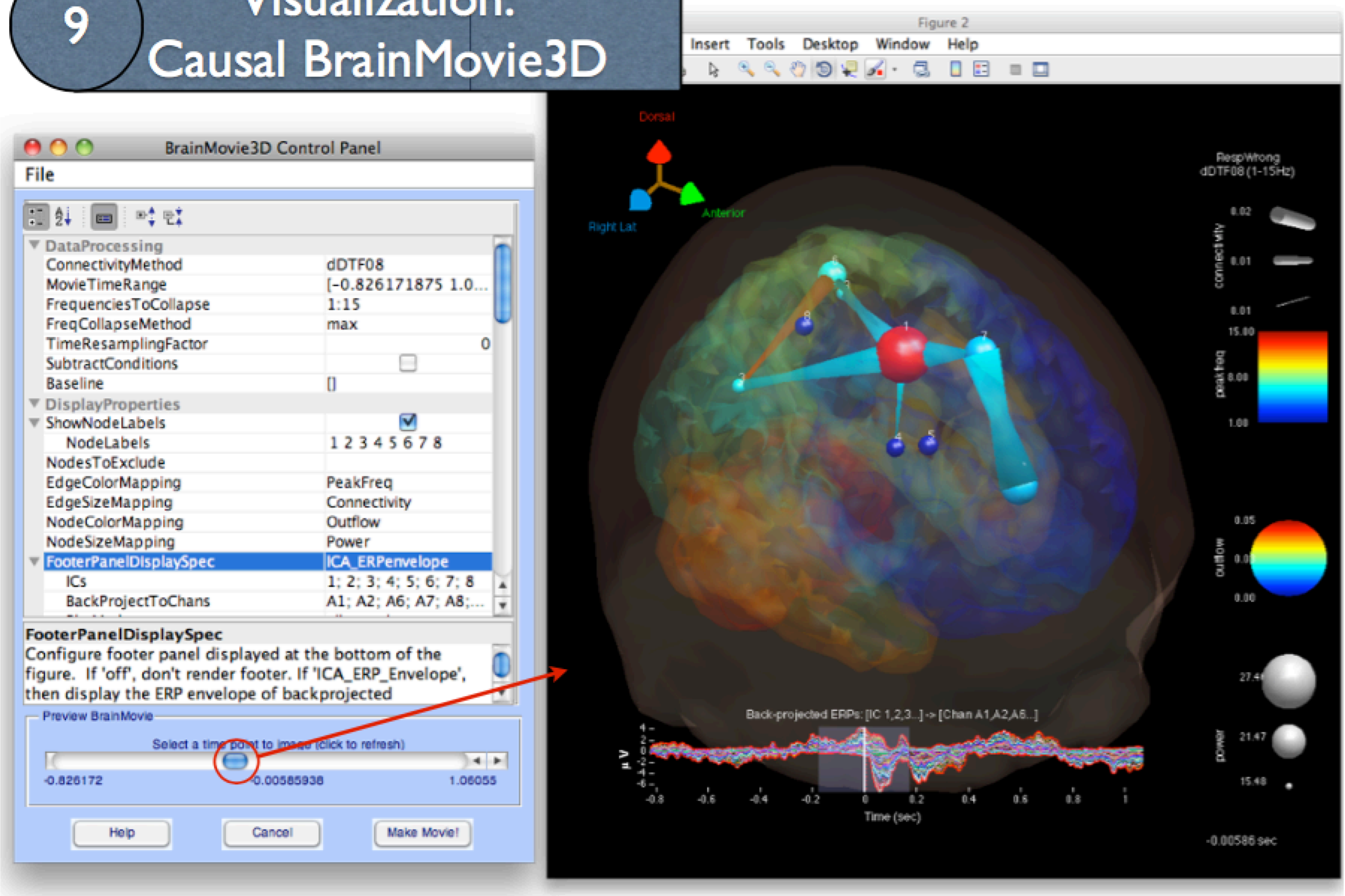


Figure 4
Figure 3: Subj eb79. Cond (RespWrong).
Subj eb79. Cond (RespWrong).
Event
IC1 -> IC4
IC4 -> IC1
IC1
IC4
Figure 5
Figure 6
Increase in event-related information flow from IC1 --> IC4 relative to baseline. This pixel indicates increased dDTF at 5 Hz and 0.5 seconds following the event
Frequency-varying net GC (integrated over time)
Baseline
Time-varying net Granger causality (integrated over frequency)

9 Visualization: Causal BrainMovie3D



History of group-level SIFT

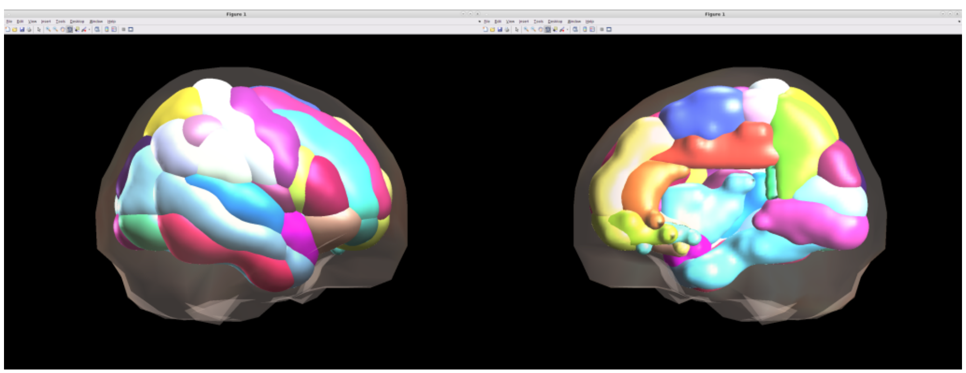
- Approaches
  - Tim Mullen & Wes Thompson (since 2010) ‘**Hierarchical Bayesian Modeling**’ that interpolate missing values (i.e. inconsistency in dipole locations across subjects).
- ROI-based approaches
  - Iversen, et al, 2014: project IC activation onto cortical surface and define activity in anatomically defined cortical ROIs.
  - Nima Bigdely-Shamlo (in his PhD dissertation in 2014) **‘Network Projection’** that uses dipole density and anatomical ROI.

Project groupSIFT

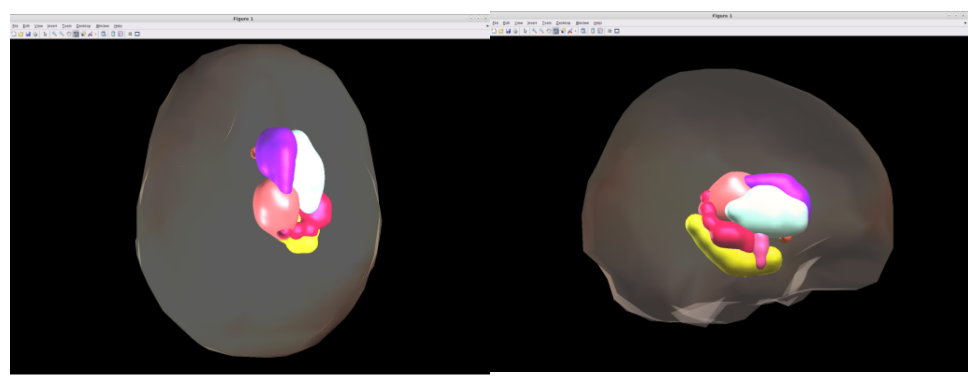
Makoto Miyakoshi
Nima Bigdely-Shamlo

Ongoing development

- Based on Nima's Network Projection
  - It's going to be an extension of his idea
  - Divide Gaussian-smoothed dipole density into anatomical regions of interests (ROIs--used AAL atlas)

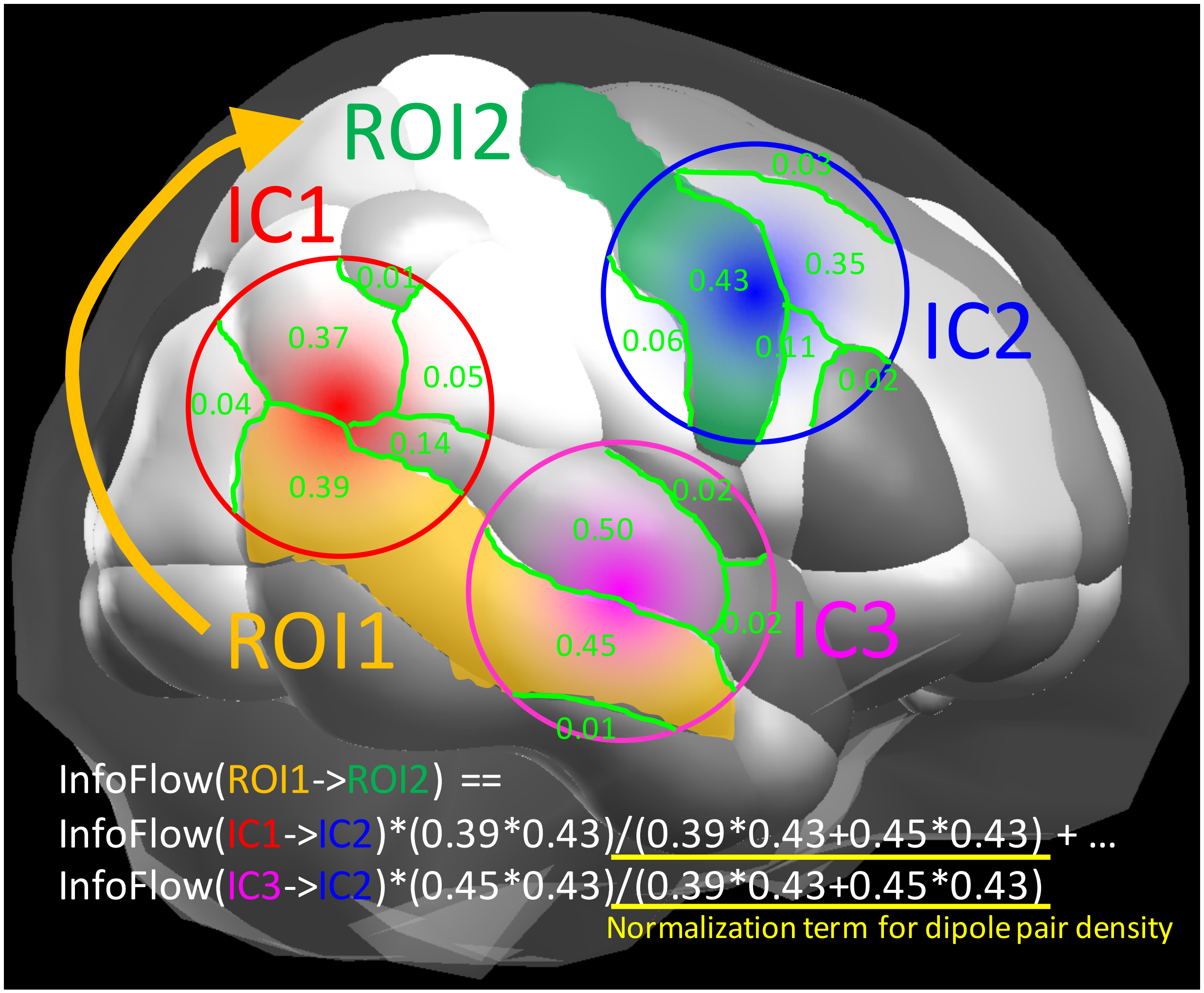


Defines 72 brain regions to include (36 for each hemisphere)



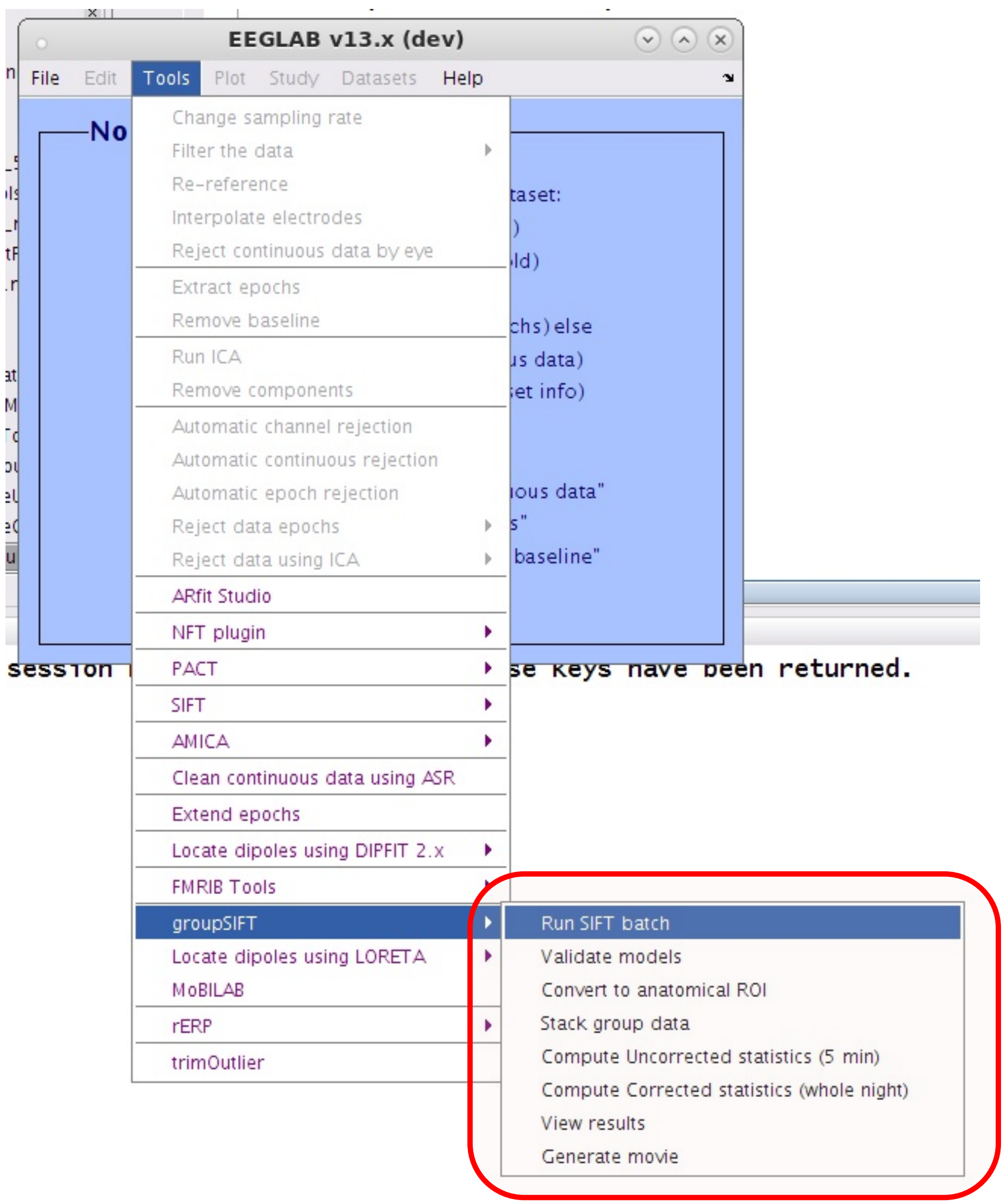
Defines 16 brain regions to exclude (8 for each hemisphere)

How to normalize IC-network to anatomical ROIs

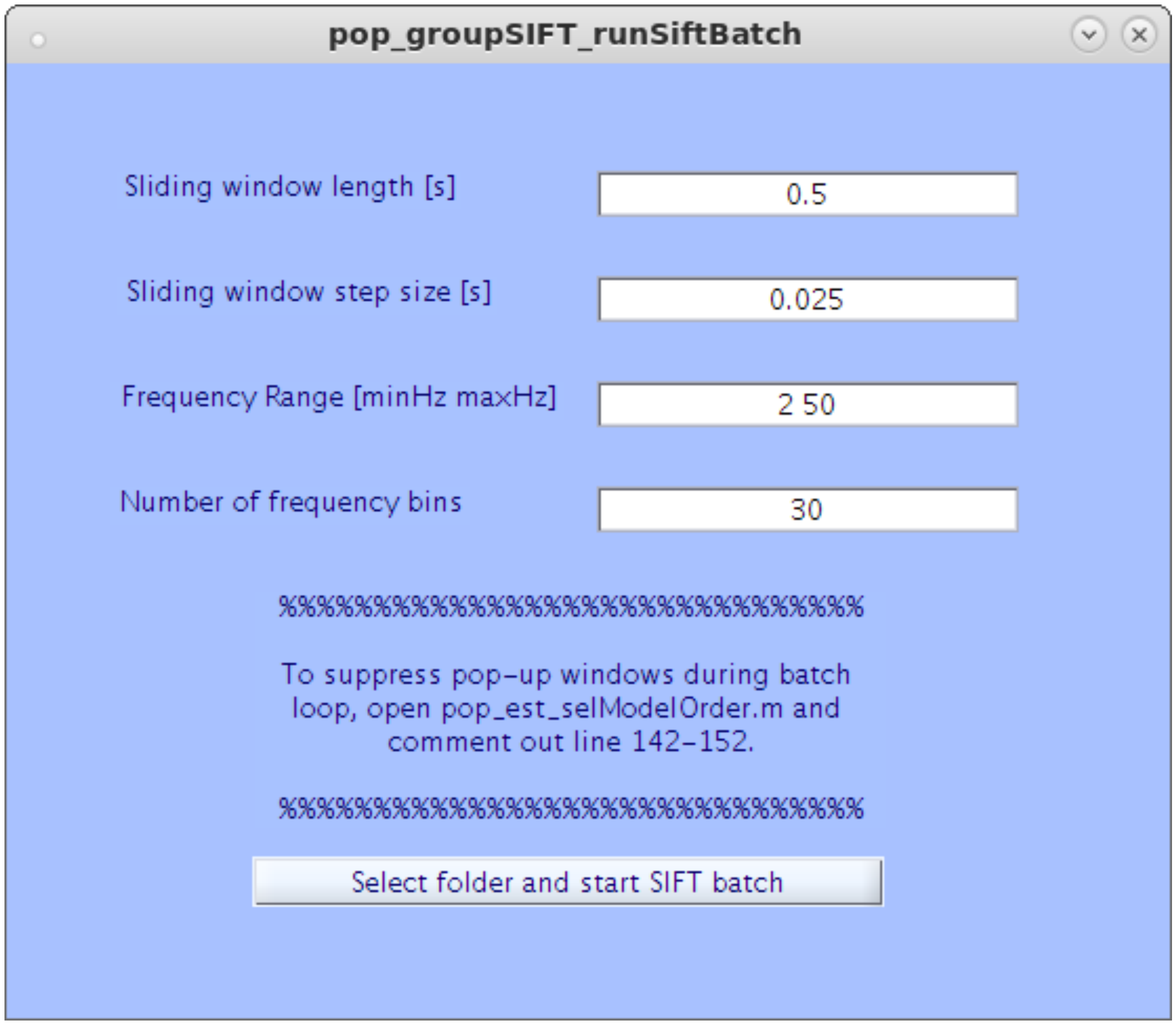


1. Run ICA, DIPFIT, and SIFT.
2. Smooth dipole positions into **dipole density** that is 3-D Gaussian sphere with FWHM == 14.2 mm (for the case of 9.6 mm error in average across all cortex; Akalin Acar et al., 2013.)
3. Compart the dipole density according to Automated Anatomical Labeling Atlas (Tzourio-Mazoyer et al., 2002)
4. Repeat above process for all ICs.
5. For each pair of regions (there are 72 x 72 == 5184 combinations), compute **pairwise dipole density** which is a product of two dipole densities.
6. Multiply info flow measure (rPDC, dDTF, etc) by normalized pairwise dipole density to calculate ROI-to-ROI info flow.

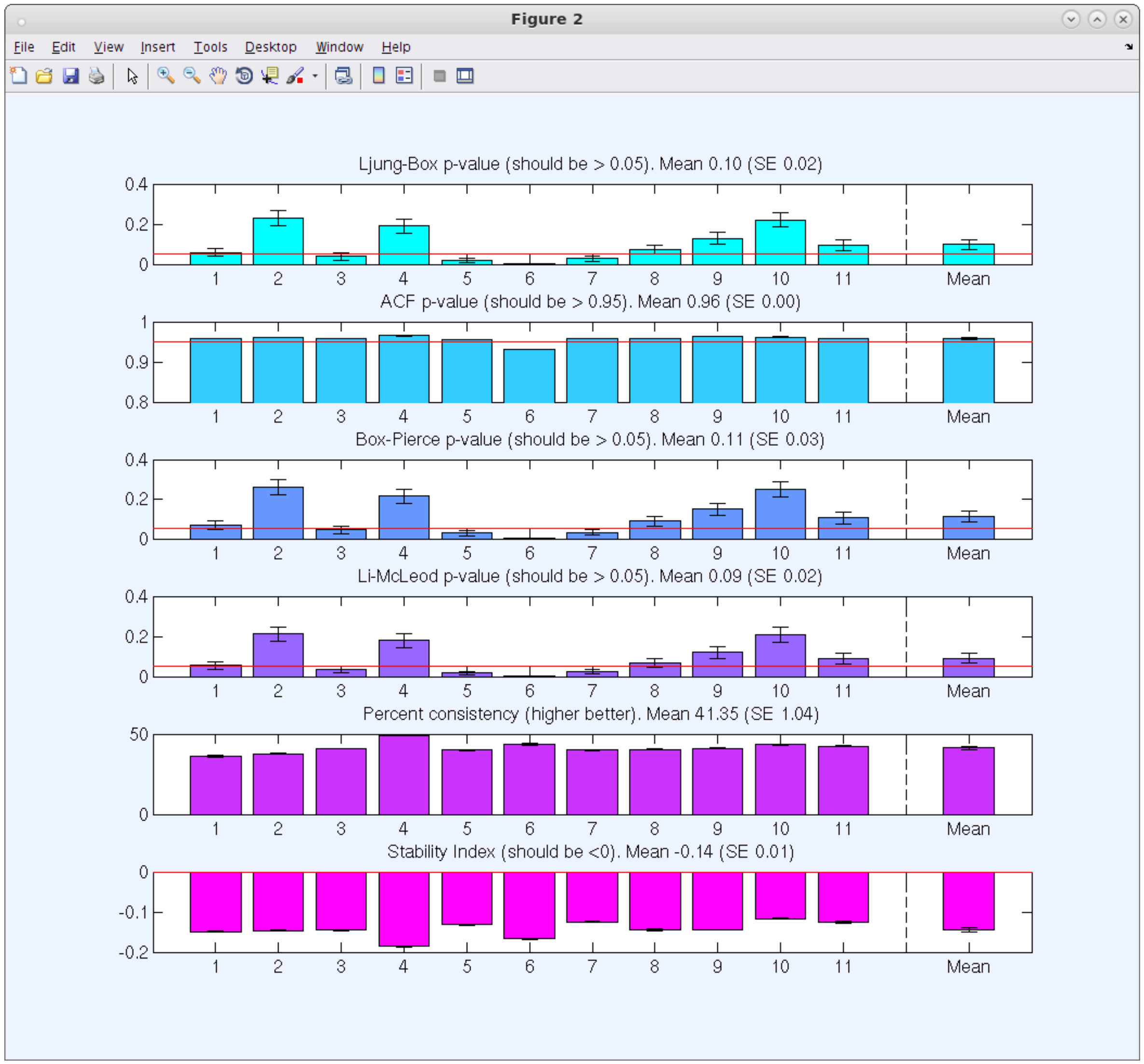
Flow of the process menu



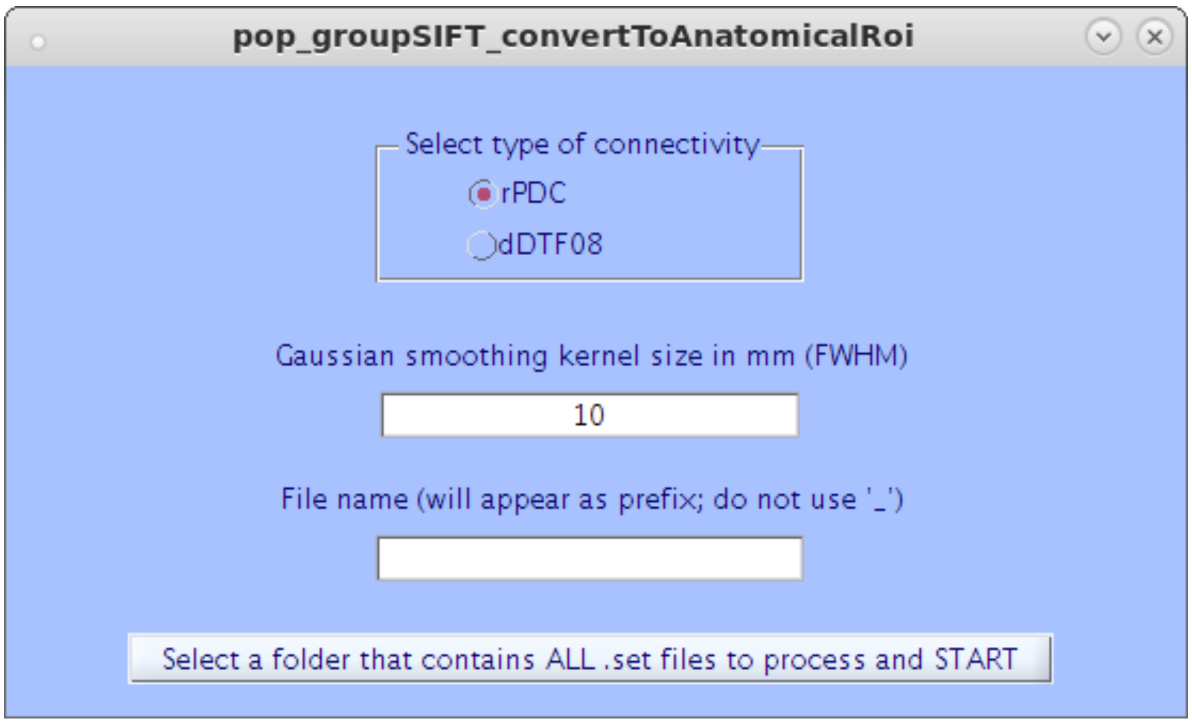
Flow of the process
1. Run SIFT batch



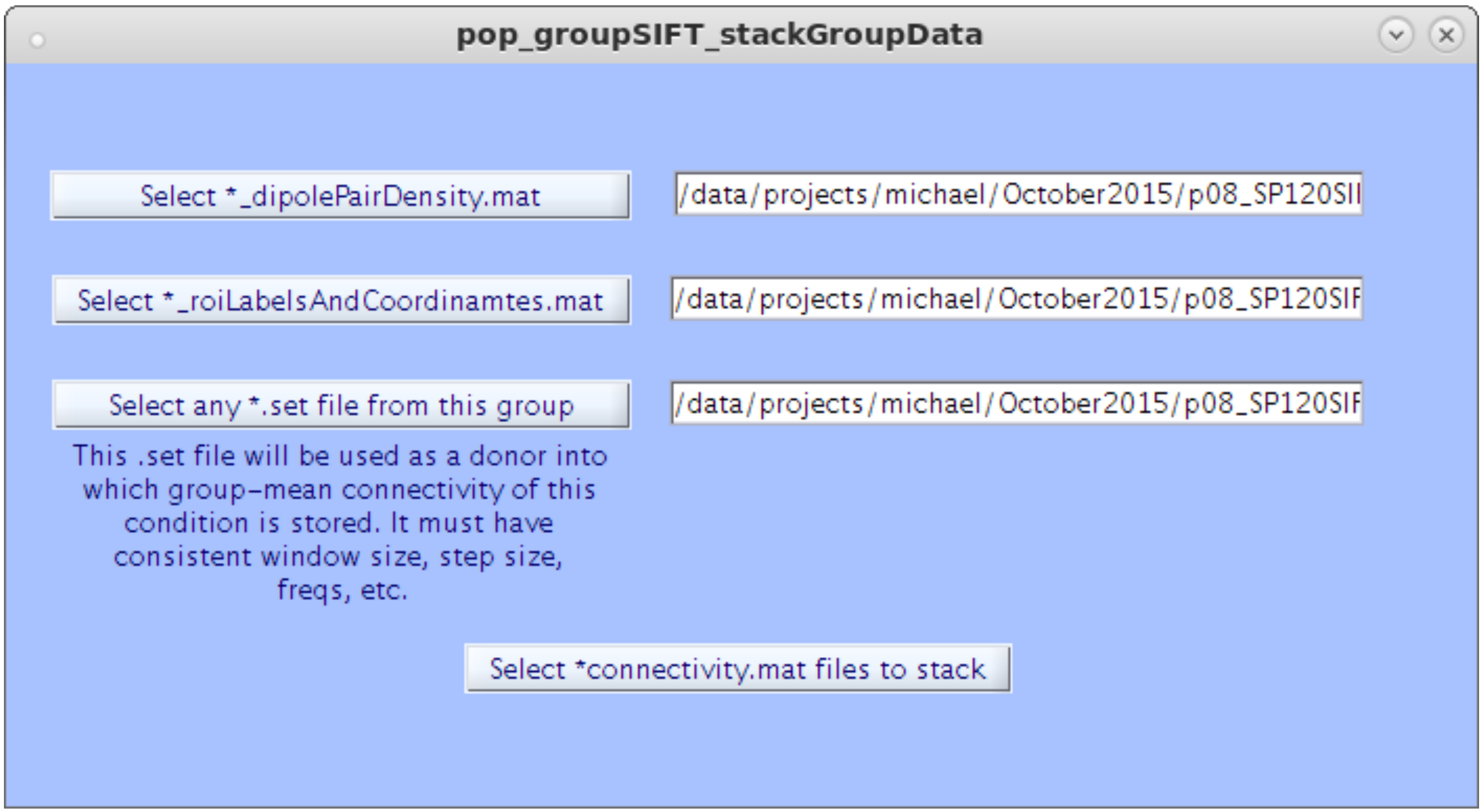
Flow of the process
2. Validate Models



Flow of the process
3. Convert to Anatomical ROI

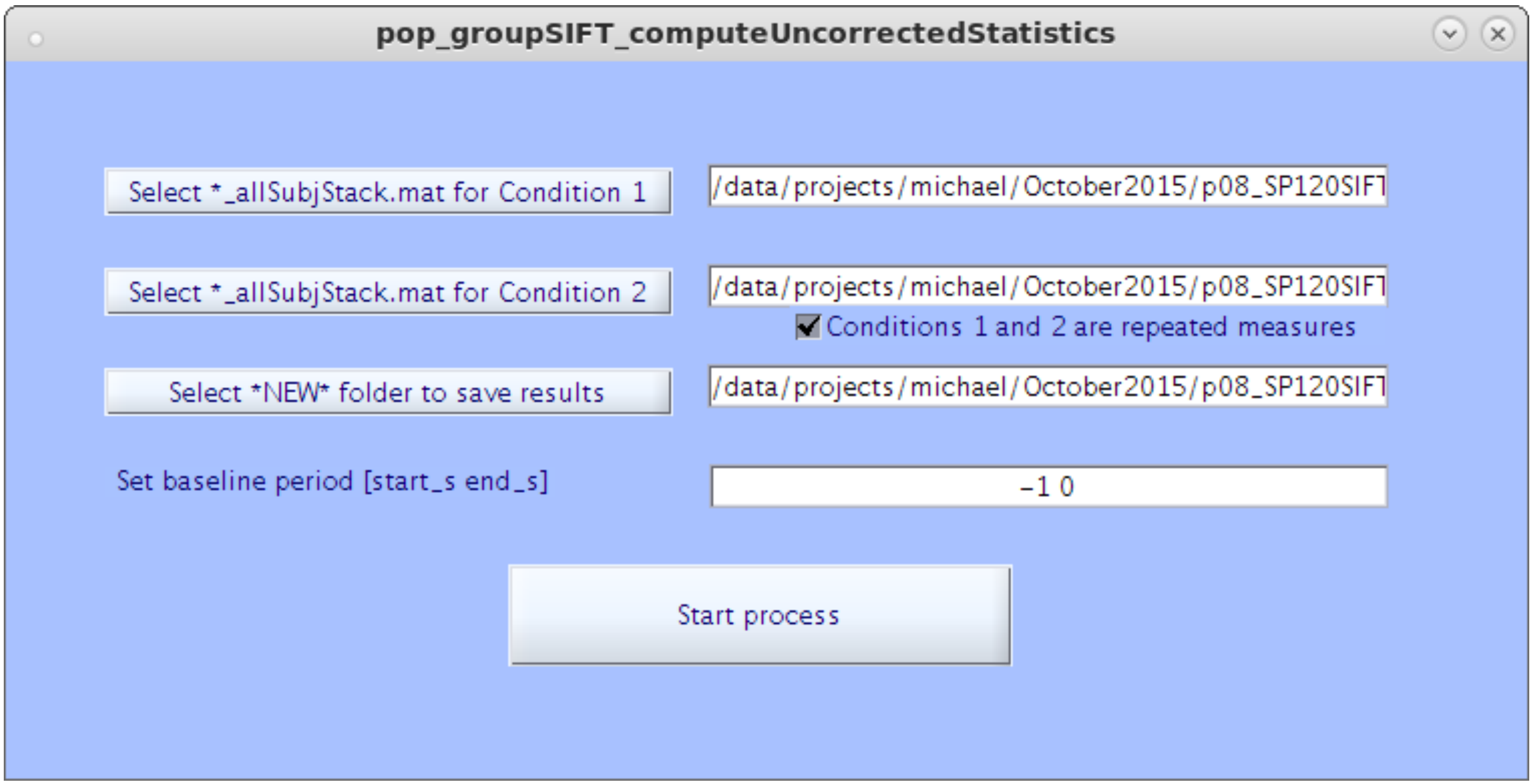


Flow of the process
4. Stack Group Data

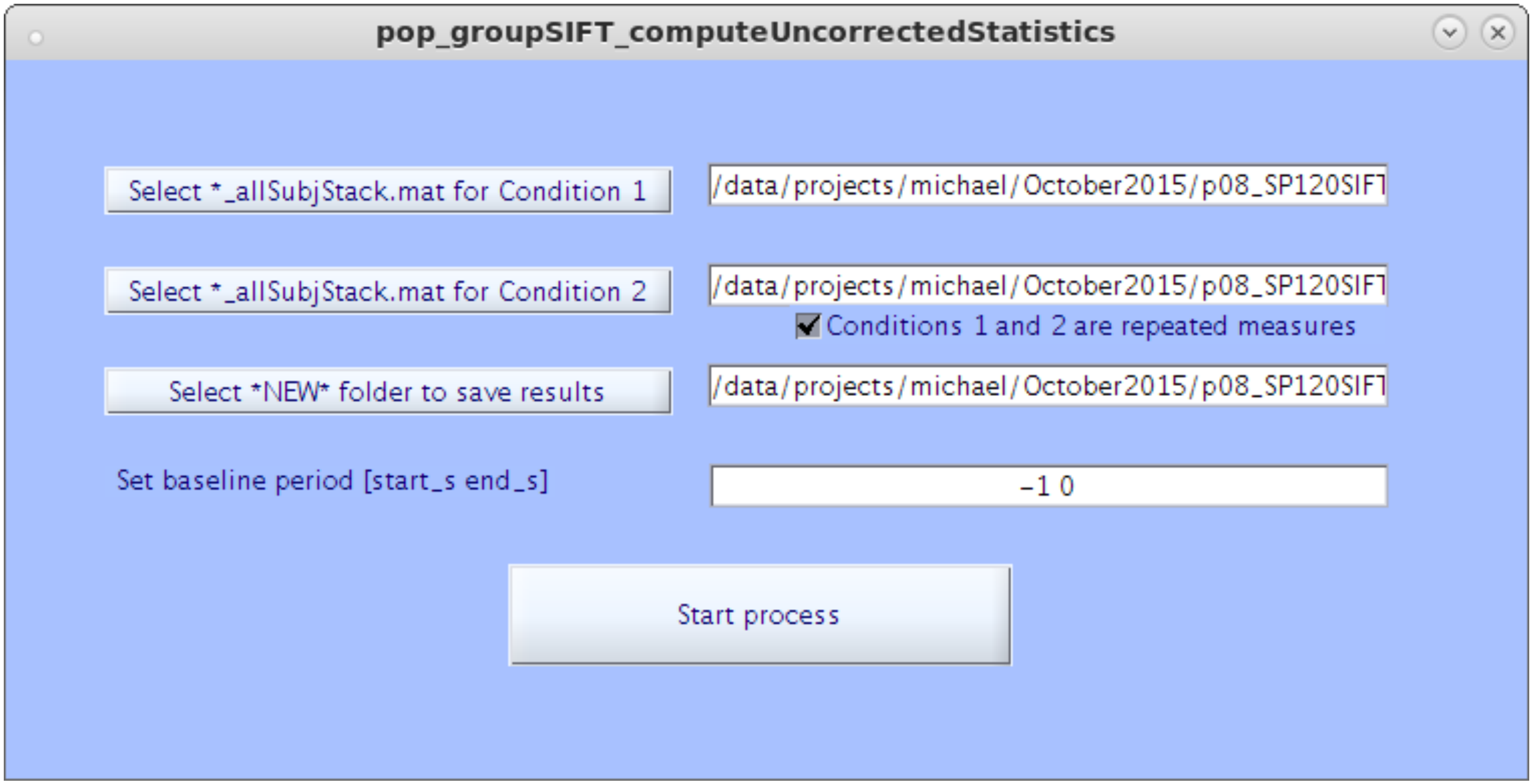


Flow of the process

5. Compute Uncorrected Statistics (5min)

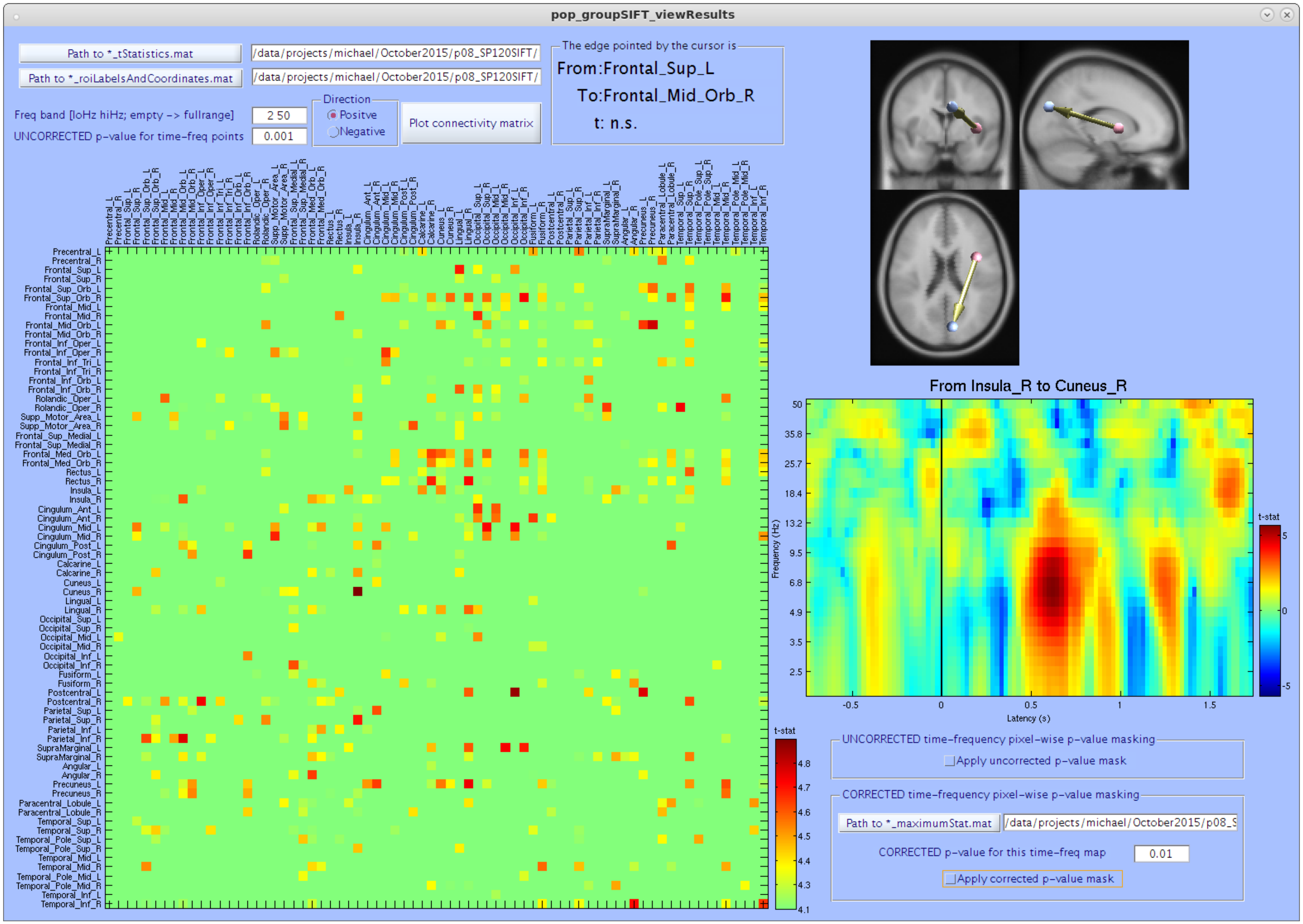


Flow of the process
6. Compute Corrected Statistics (whole night)

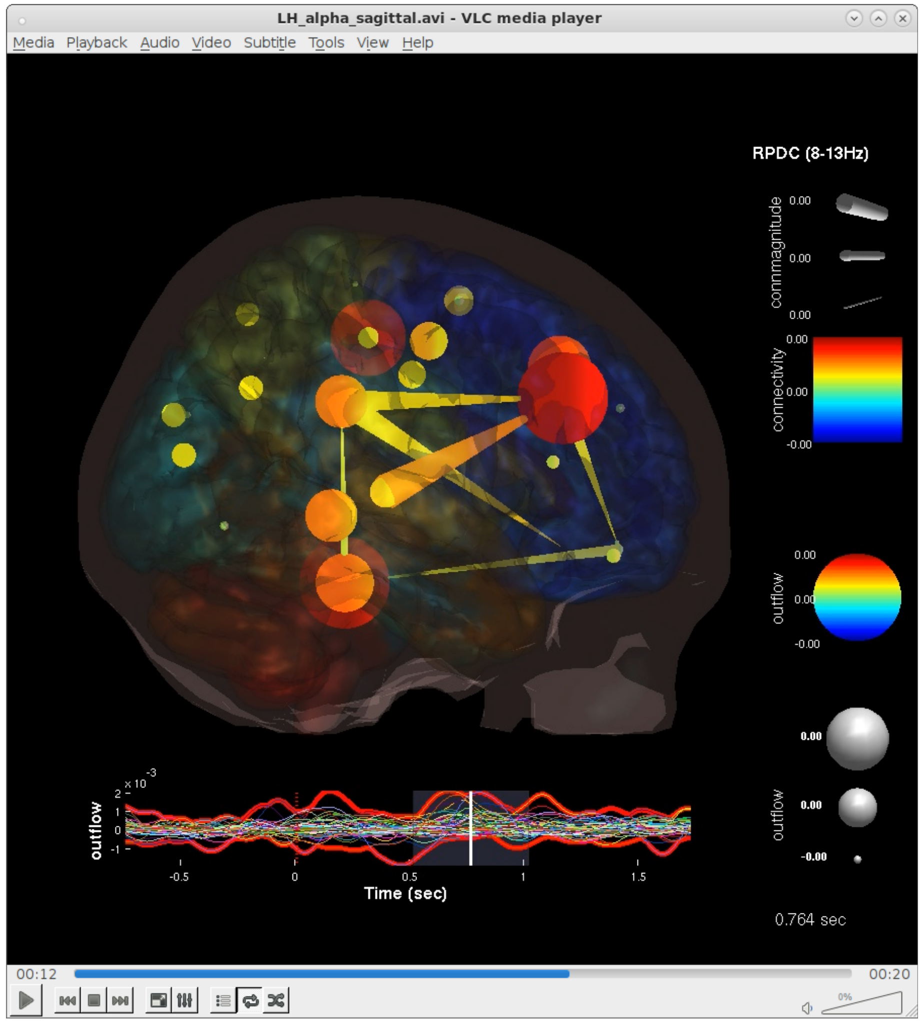


- T-test across 30 (freqs) x 100 (time points) x 72 x 72 (anatomical ROI) x 11 (subjects) x 2 (conditions).
- Single CPU, 17 h; 12 CPU Matlab parfor, 2.4 h.

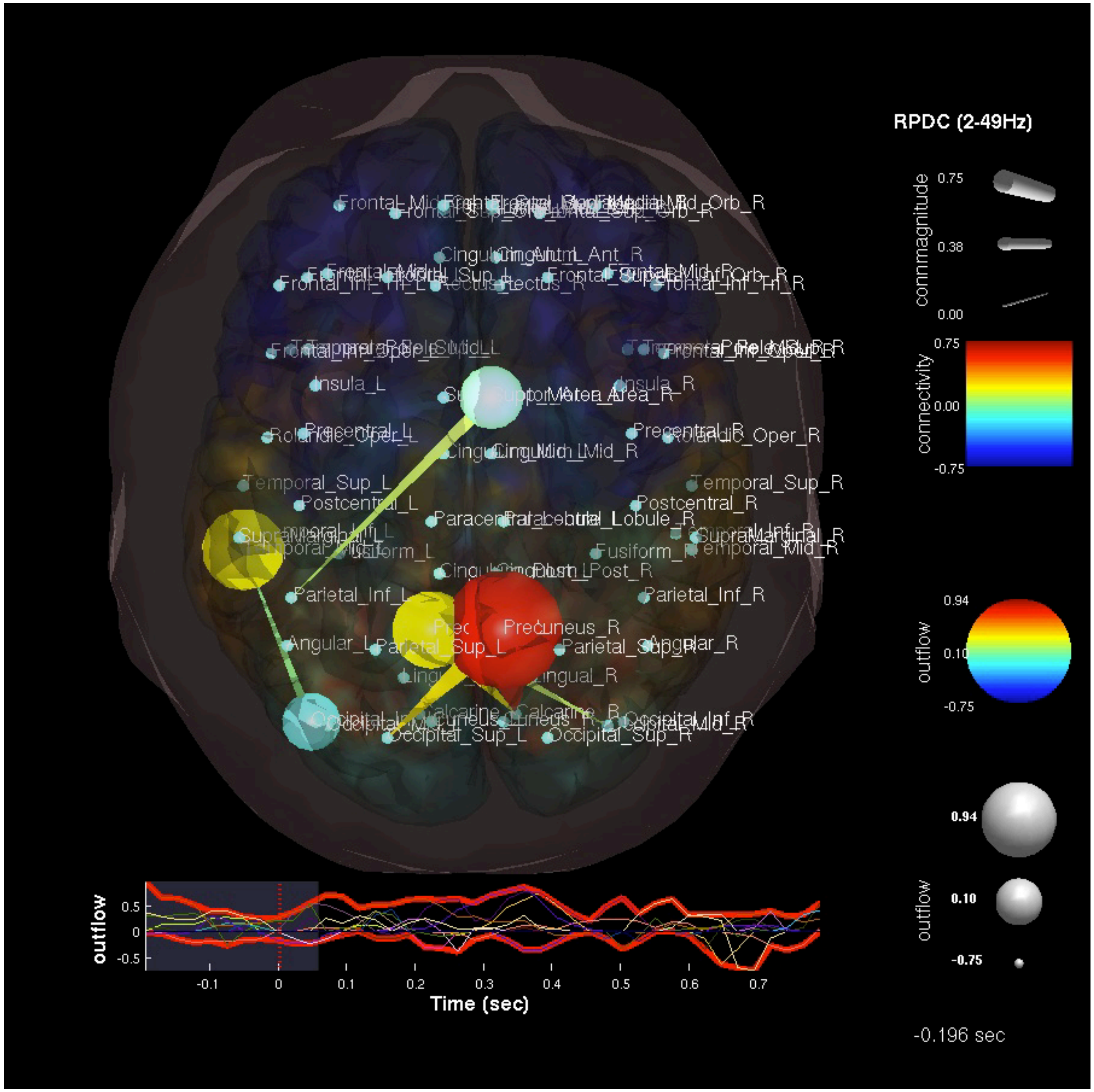
Flow of the process
7. View Results



Flow of the process
8. Generate Movie



- It uses SIFT’s GUI to make the movie by feeding single subject dataset replaced with group-mean data.



RPDC (2-49Hz)
commagnitude
0.75
0.38
0.00
connectivity
0.75
0.00
-0.75
outflow
0.94
0.10
-0.75
outflow
0.94
0.10
-0.75
Insula_L
Insula_R
Temporal_Sup_L
Temporal_Sup_R
Postcentral_L
Postcentral_R
Parietal_Inf_L
Parietal_Inf_R
Angular_L
Precuneus_R
Lingual_R
Occipital_Sup_L
Occipital_Sup_R
Fusiform_R
outflow
0.5
0
-0.5
-0.1
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Time (sec)
-0.196 sec

Current Status

- Alpha test ongoing since March 2016.
- Will be available as a beta version in 2016 Summer!