Modeling Distributed Brain Network Dynamics

Tim Mullen

12th EEGLAB Workshop
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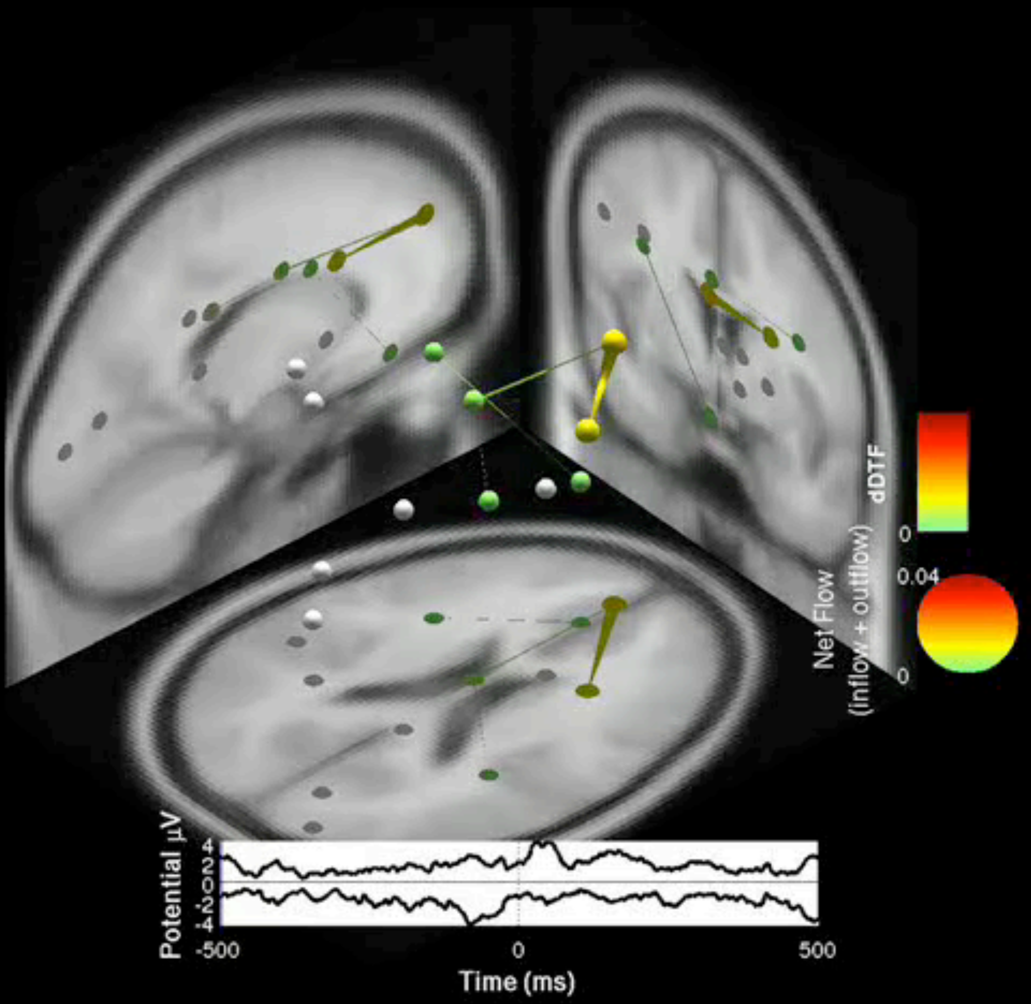

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Different types of connectivity

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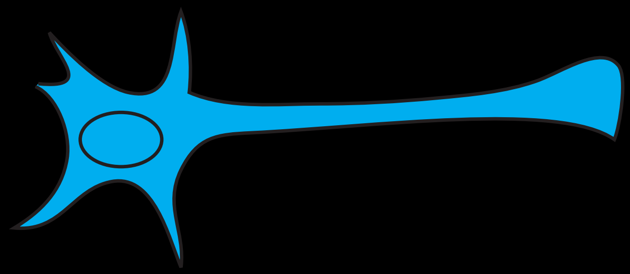
- **Structural Connectivity**
  - anatomical



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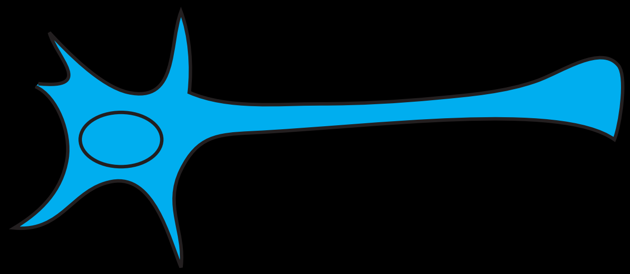

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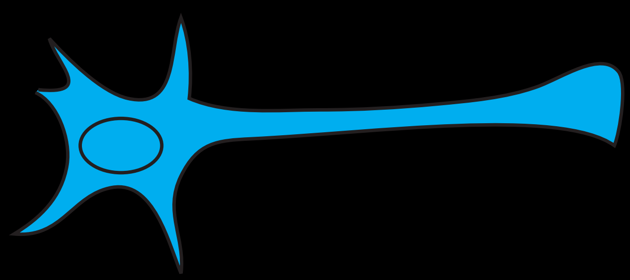

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  - symmetric, correlative

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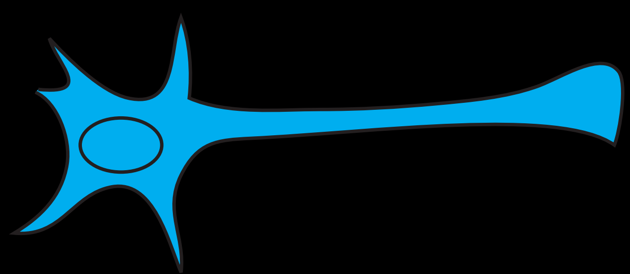

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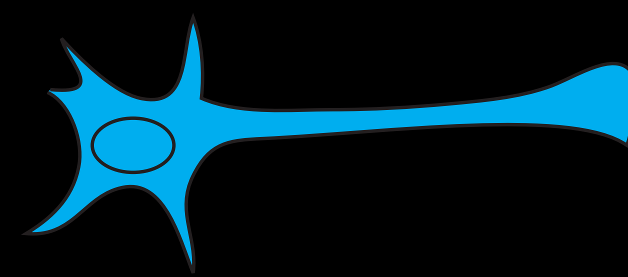

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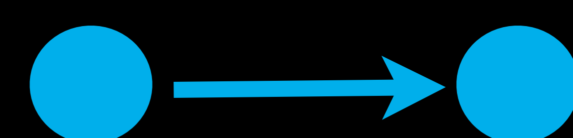
  - asymmetric, causal, information flow



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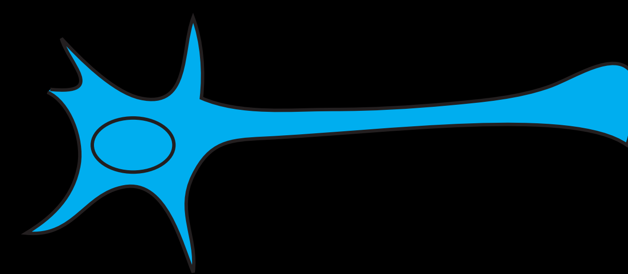

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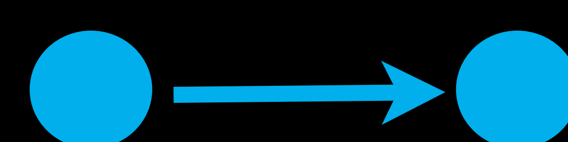

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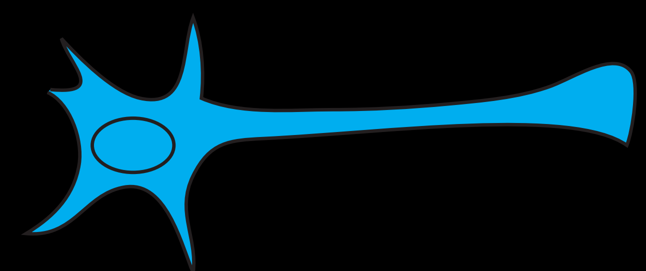

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Many ways to model effective connectivity in EEG

- Coherence, Phase-locking value
- Cross-correlation
- Transfer Entropy
- Dynamic Causal Models
- Structural Equation Models
- Granger-Causal methods

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Granger Causality

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

  1. causes should precede their effects in time
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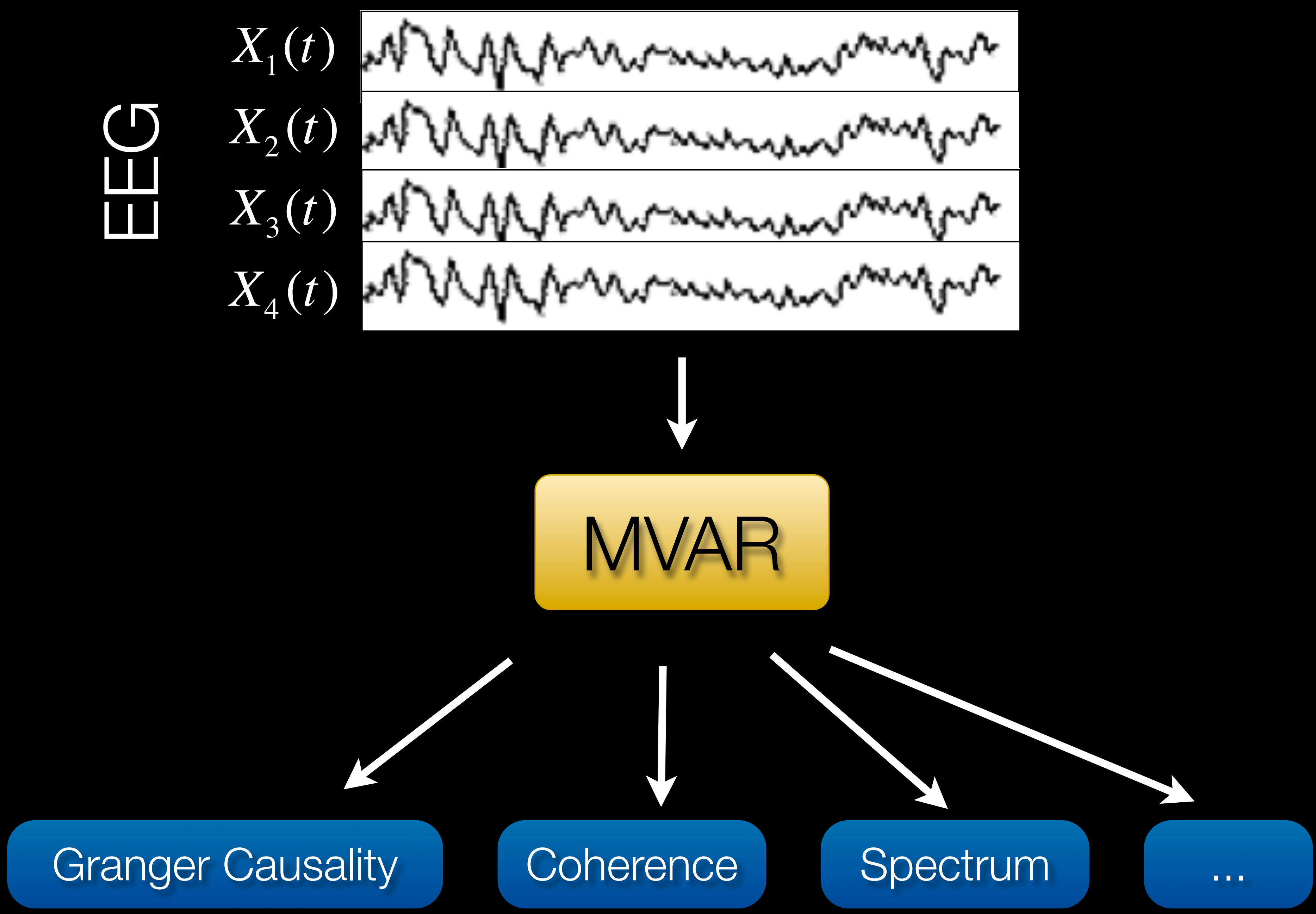
This is **not** the same as (cross-)correlation!

Multivariate Autoregressive (MVAR) Modeling



Multivariate Autoregressive (MVAR) Modeling

- We have M variables (e.g., EEG channels or source activations): $\mathbf{X}(t) = [\mathbf{X}_1(t), \mathbf{X}_2(t), \ldots, \mathbf{X}_M(t)]^T$

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

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random noise process

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

Multivariate Autoregressive (MVAR) Modeling

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

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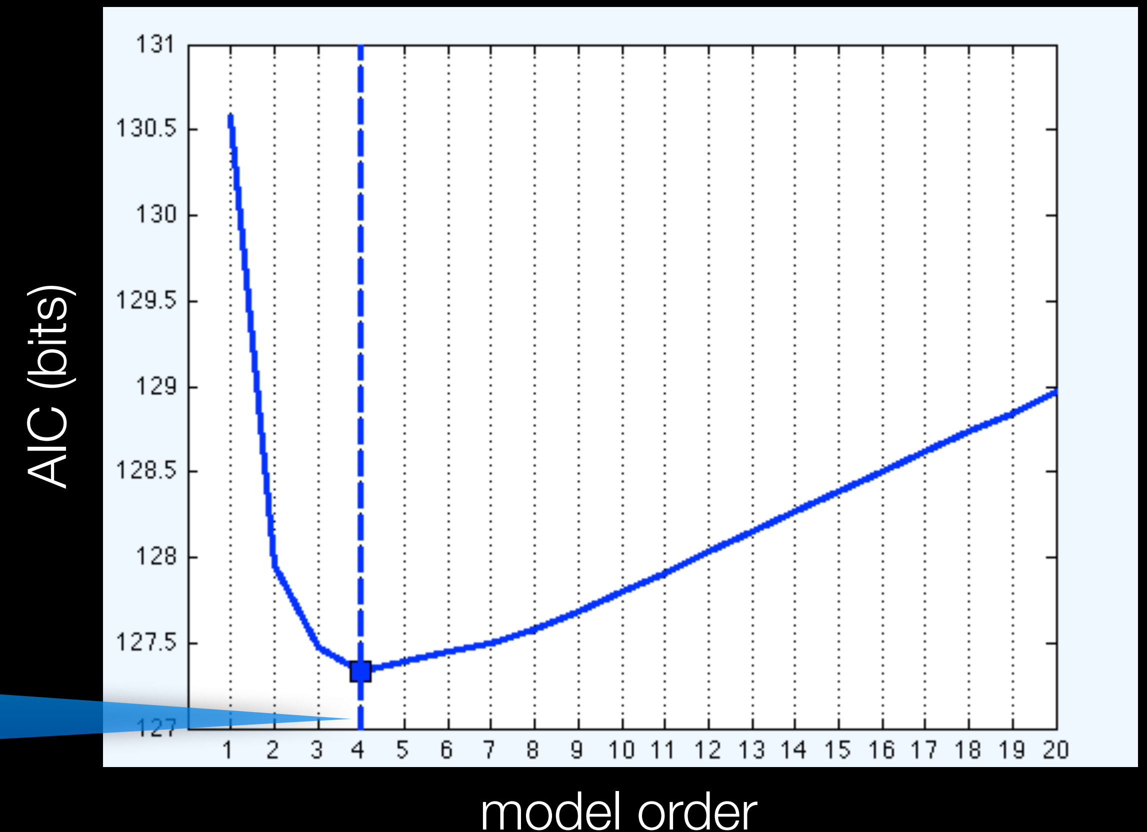

optimal order

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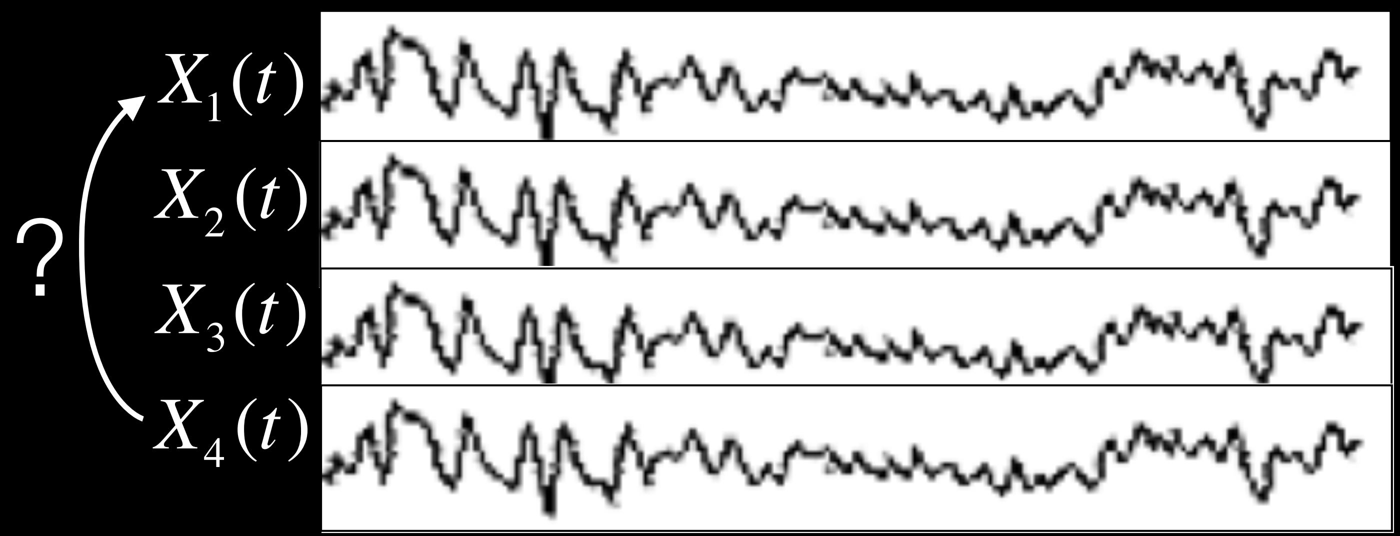
- **Stability**
  - Technically, an MVAR process is stable if the reverse characteristic polynomial of the process has all roots outside the complex unit circle (all eigenvalues of **A** have modulus less than 1)
  - Importantly, stability implies stationarity and SIFT provides you techniques for verifying the stability

Granger Causality

Test: Does **X**$_4$ granger-cause **X**$_1$?



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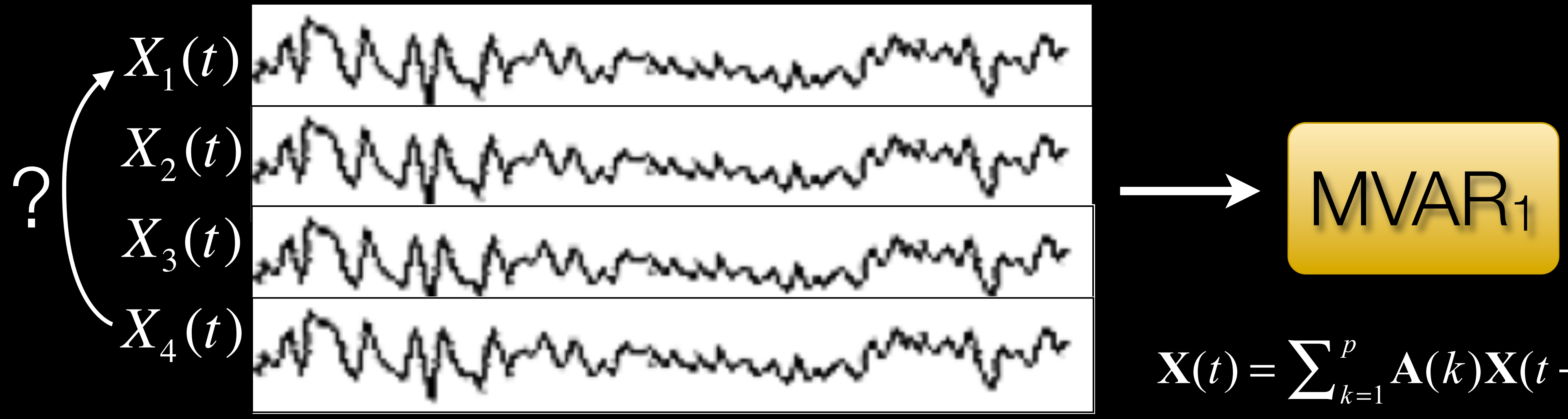

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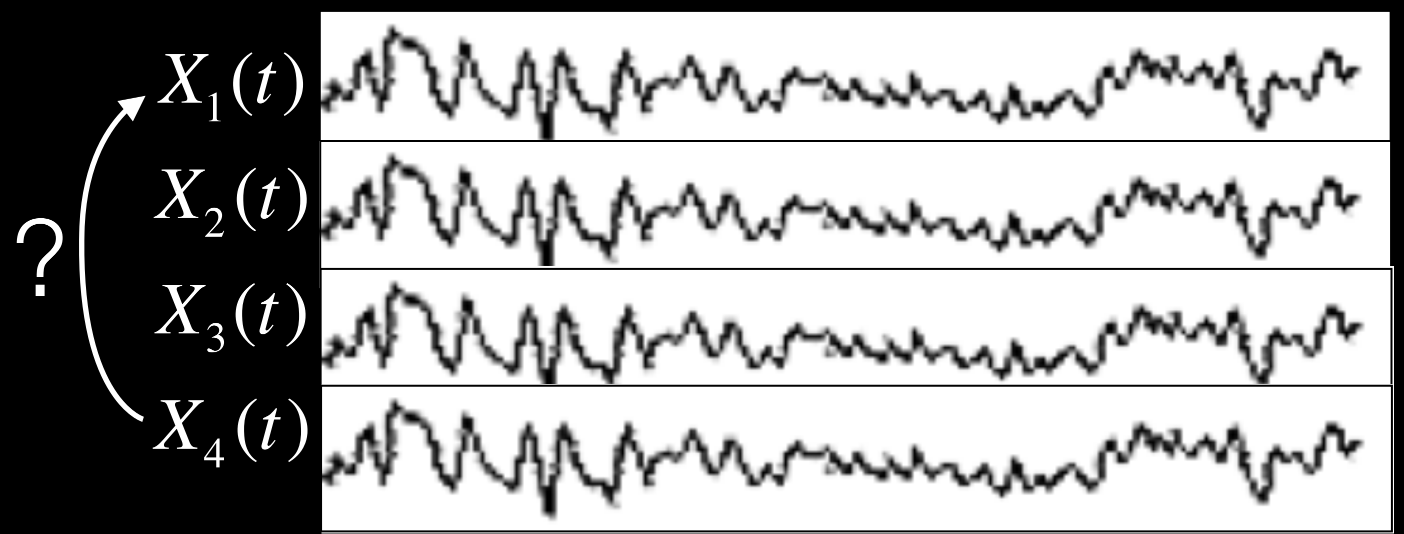
prediction error for X_1



→ MVAR_1 → $\text{var}(\mathbf{E}_1(t))$

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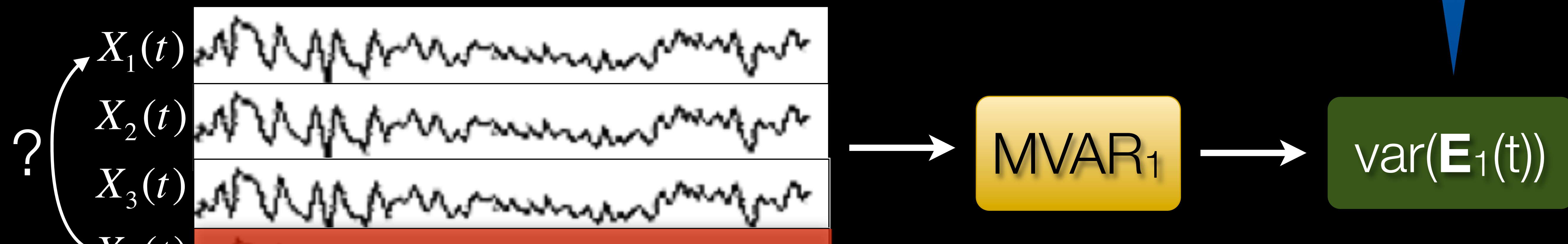

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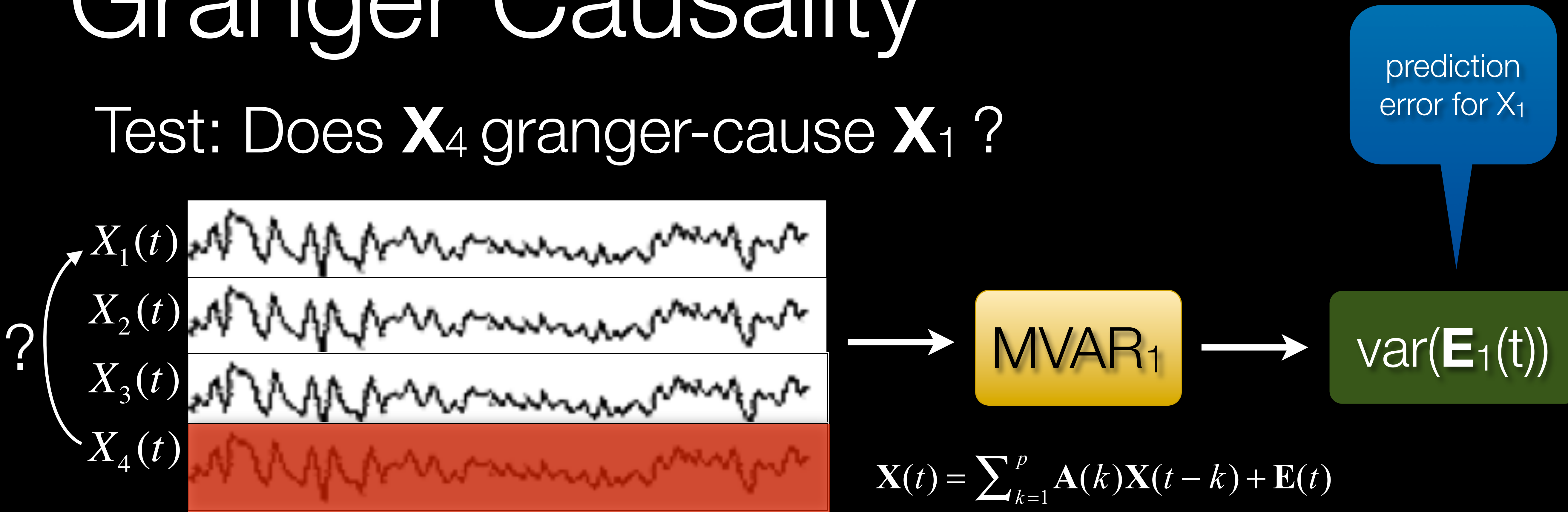

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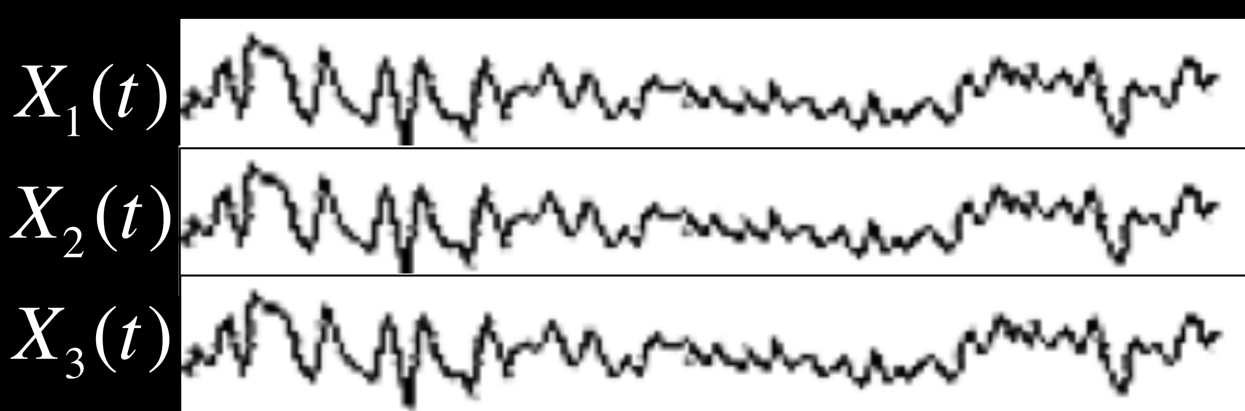

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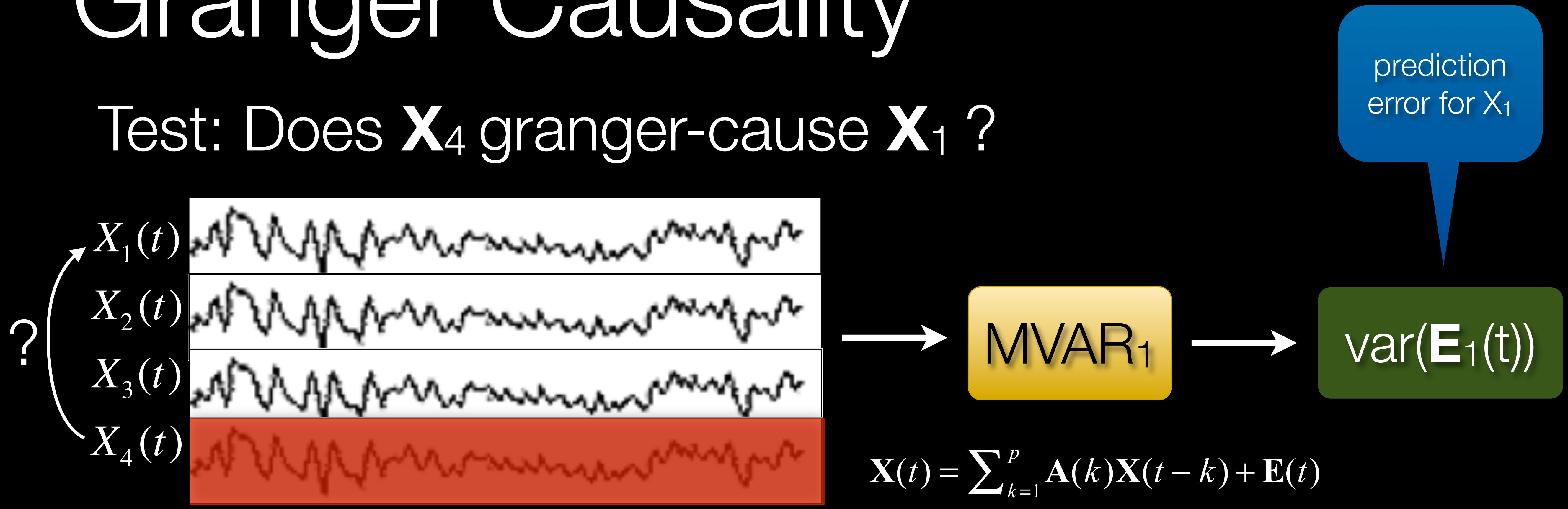

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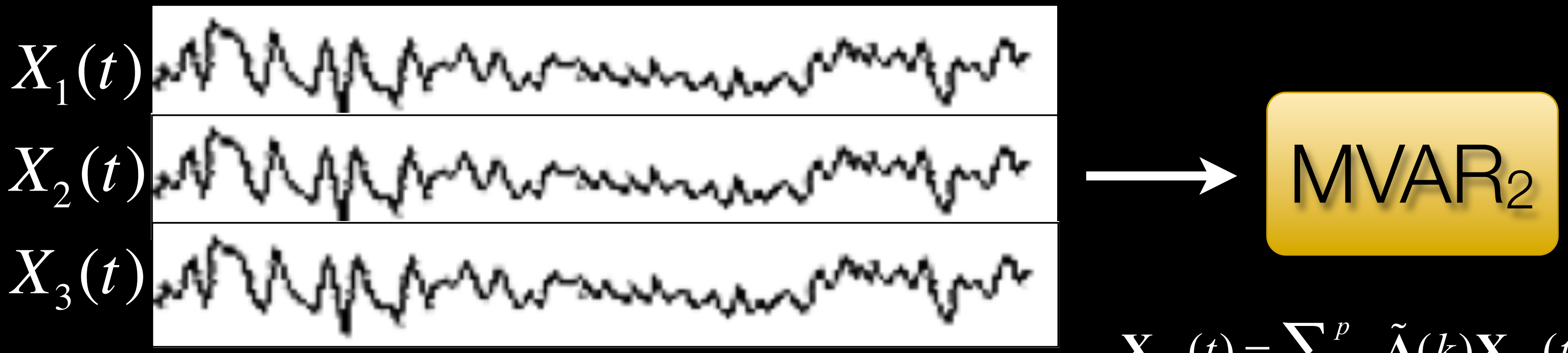

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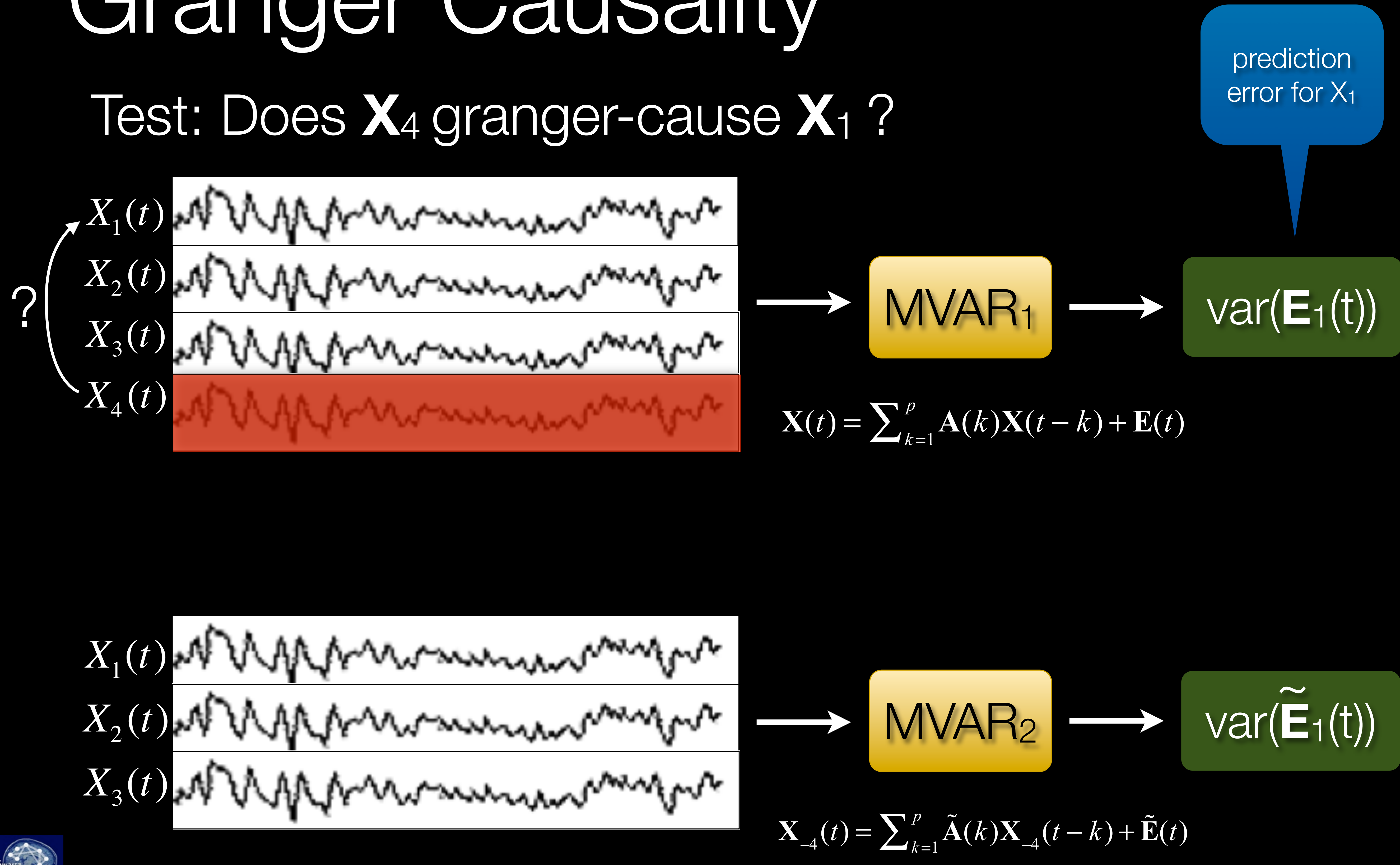

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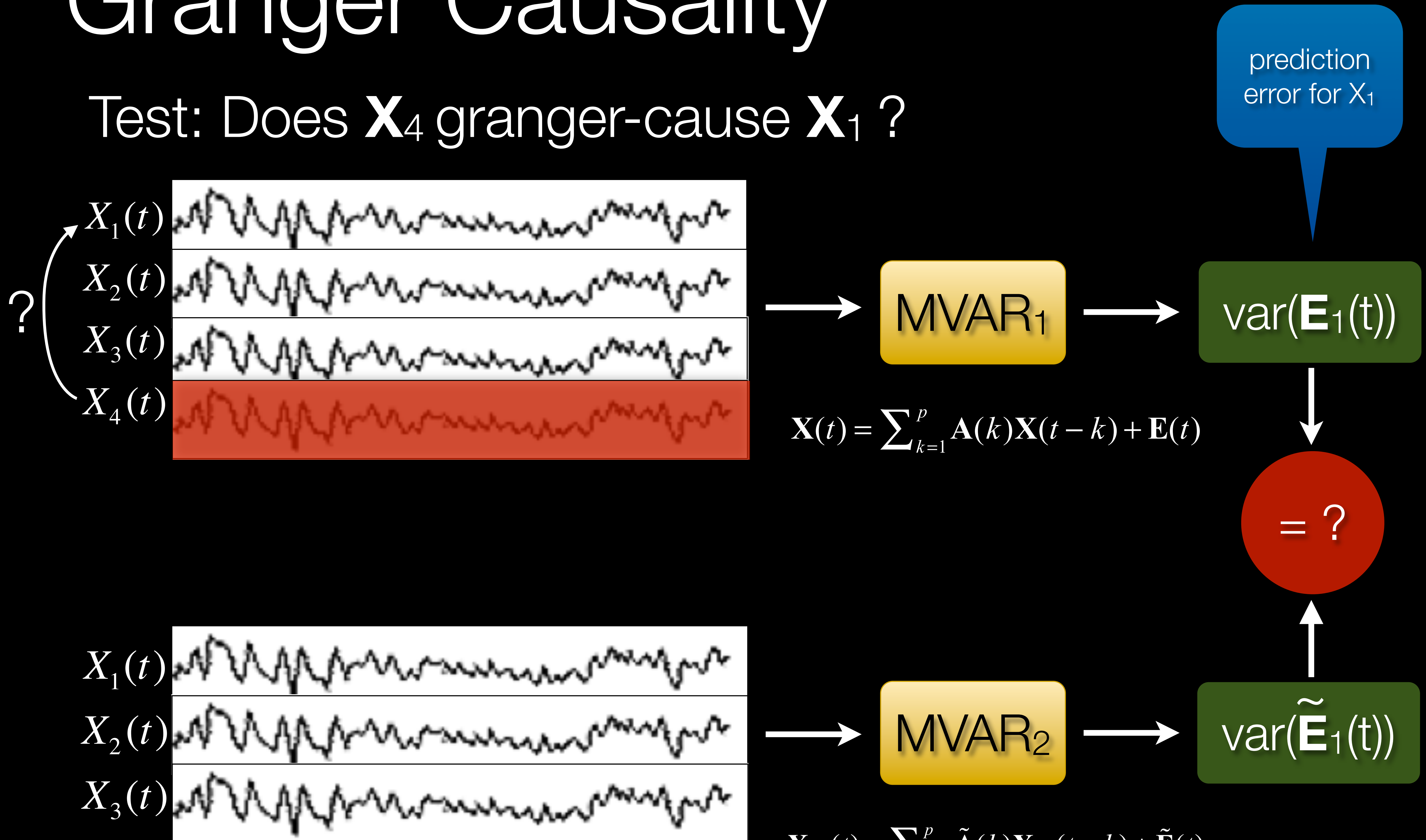

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- Granger (1969) quantified this definition for bivariate processes in the form of an F-ratio:

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

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

X_j granger-causes X_i condition on all other variables in **X**

if and only if $\mathbf{A}_{ij}(k) >> 0$ for some lag $k \in \{1, \ldots, p\}$

Granger Causality Quiz

- Example: 2-channel MVAR process of order 1

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

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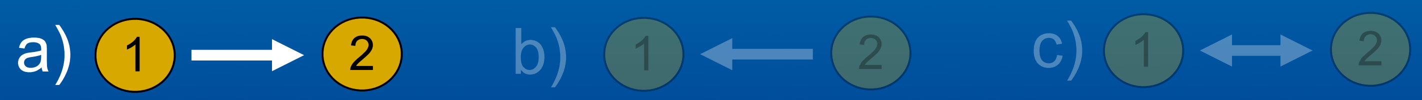

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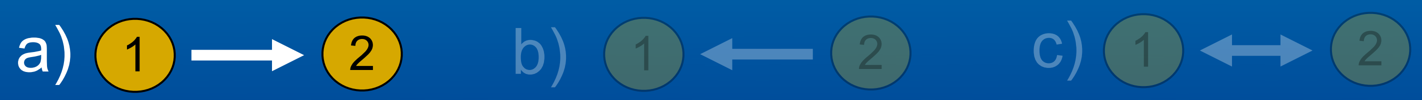

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a) 1 → 2 b) 1 ← 2 c) 1 ↔ 2

Granger Causality – Frequency Domain

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

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Fourier-transforming A(k) we obtain

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

Likewise, **X**(f) and **E**(f) correspond to the fourier transforms of the data and residuals, respectively

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We can then define the spectral matrix **X**(*f*) as follows:

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

Where **H**(*f*) is the *transfer matrix* of the system.

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Definition: If $|\mathbf{A}_{ij}(f)|$ is significantly non-zero, then X_j *granger-causes* X_i (at frequency *f*) conditioned on all other vars in **X**

Granger Causality – Frequency Domain Estimators

- (some) Coherence measures

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

Coherence

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

Partial coherence

$$G_i(f) = \sqrt{1 - \frac{\det(\mathbf{S}(f))}{S_{ii}(f)\mathbf{M}_{ii}(f)}}$$

Multiple coherence

S(*f*)= **X**(*f*)**X**(*f*)***** is the **spectral density matrix** of **X**

Granger Causality – Frequency Domain Estimators

- (some) GC measures

$$\theta_{ij}^2(f) = \left|H_{ij}(f)\right|^2$$

(non-normalized) Directed Transfer Function (DTF)

$$\gamma_{ij}^2(f) = \frac{\left|H_{ij}(f)\right|^2}{\sum_{k=1}^{M}\left|H_{ik}(f)\right|^2}$$

Normalized DTF

$$\delta_{ij}^2(f) = \eta_{ij}^2(f) P_{ij}^2(f) \quad \text{where} \quad \eta_{ij}^2(f) = \frac{\left|H_{ij}(f)\right|^2}{\sum_f \sum_{k=1}^{M}\left|H_{ik}(f)\right|^2}$$

ffDTF

partial coherence

Direct DTF

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

Normalized Partial Directed Coherence (PDC)

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Time-Frequency GC

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- Brain network dynamics often change rapidly with time
  - event-related responses
  - transient network changes during sequential information processing

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- How can we perform time-varying, frequency-domain analysis of network dynamics?

Time-Frequency GC

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- **Many ways to do time-varying MVAR estimation**

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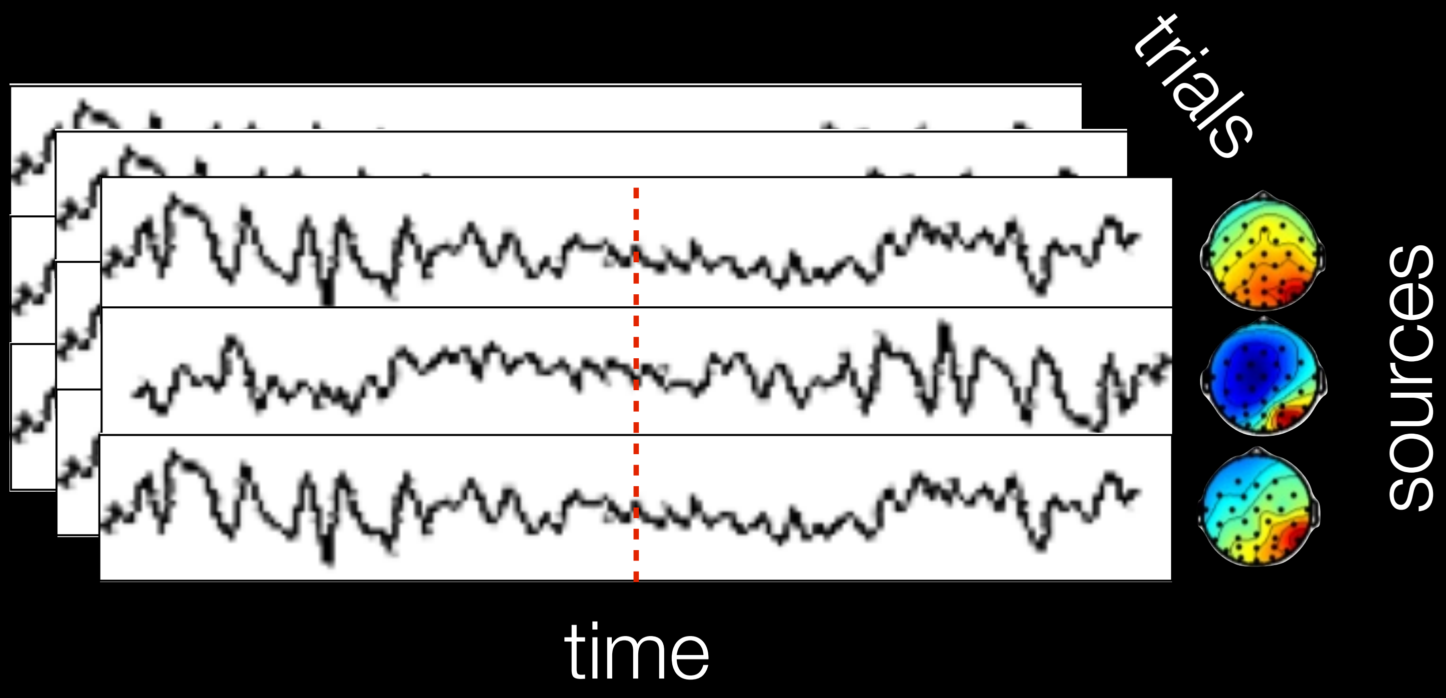
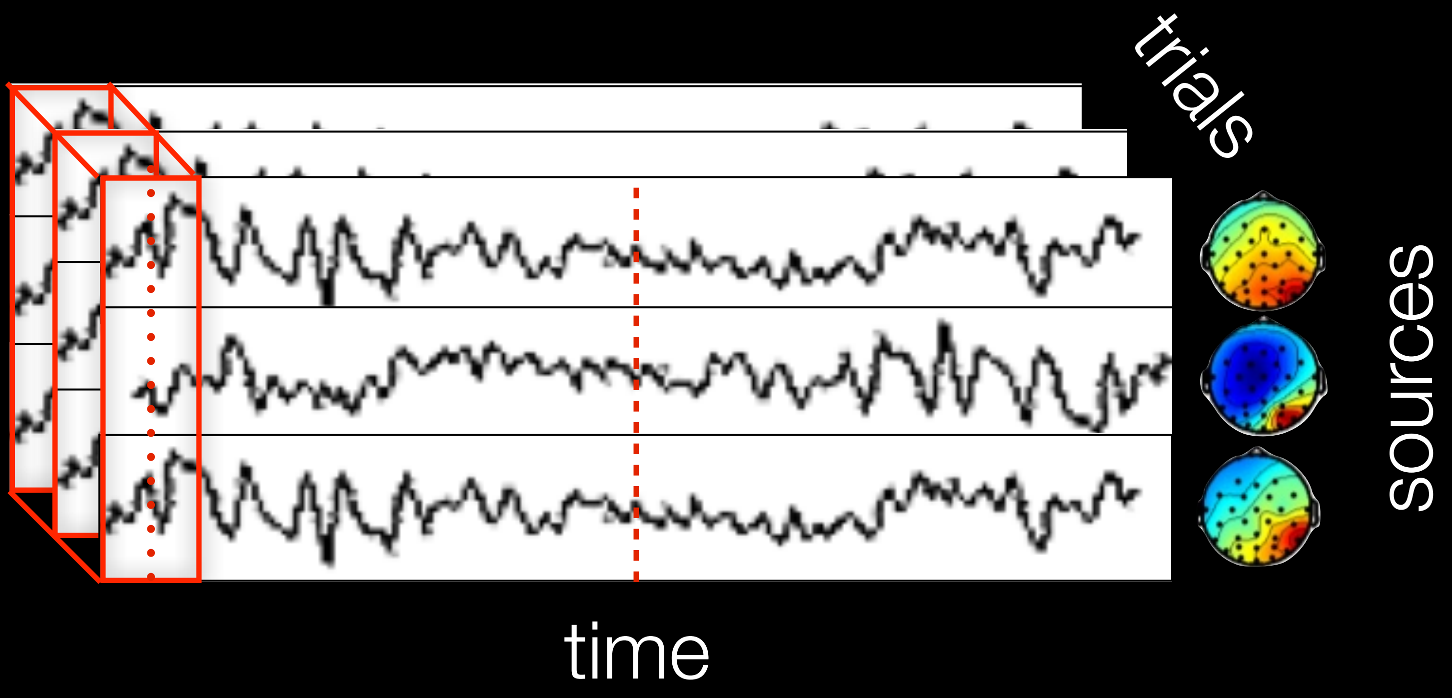


Analogous to short-time fourier transform

Time-Frequency GC



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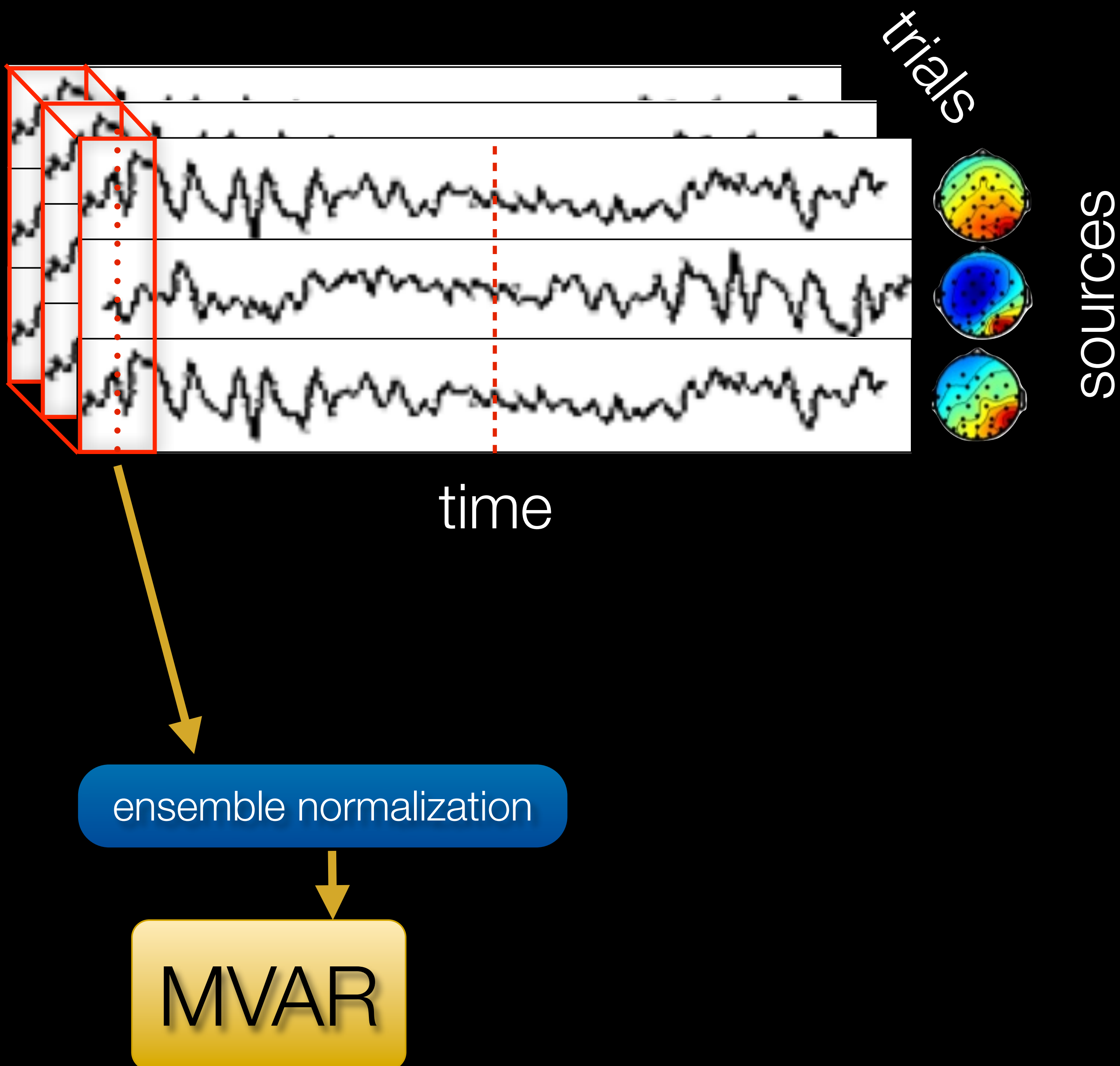

Analogous to short-time fourier transform

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

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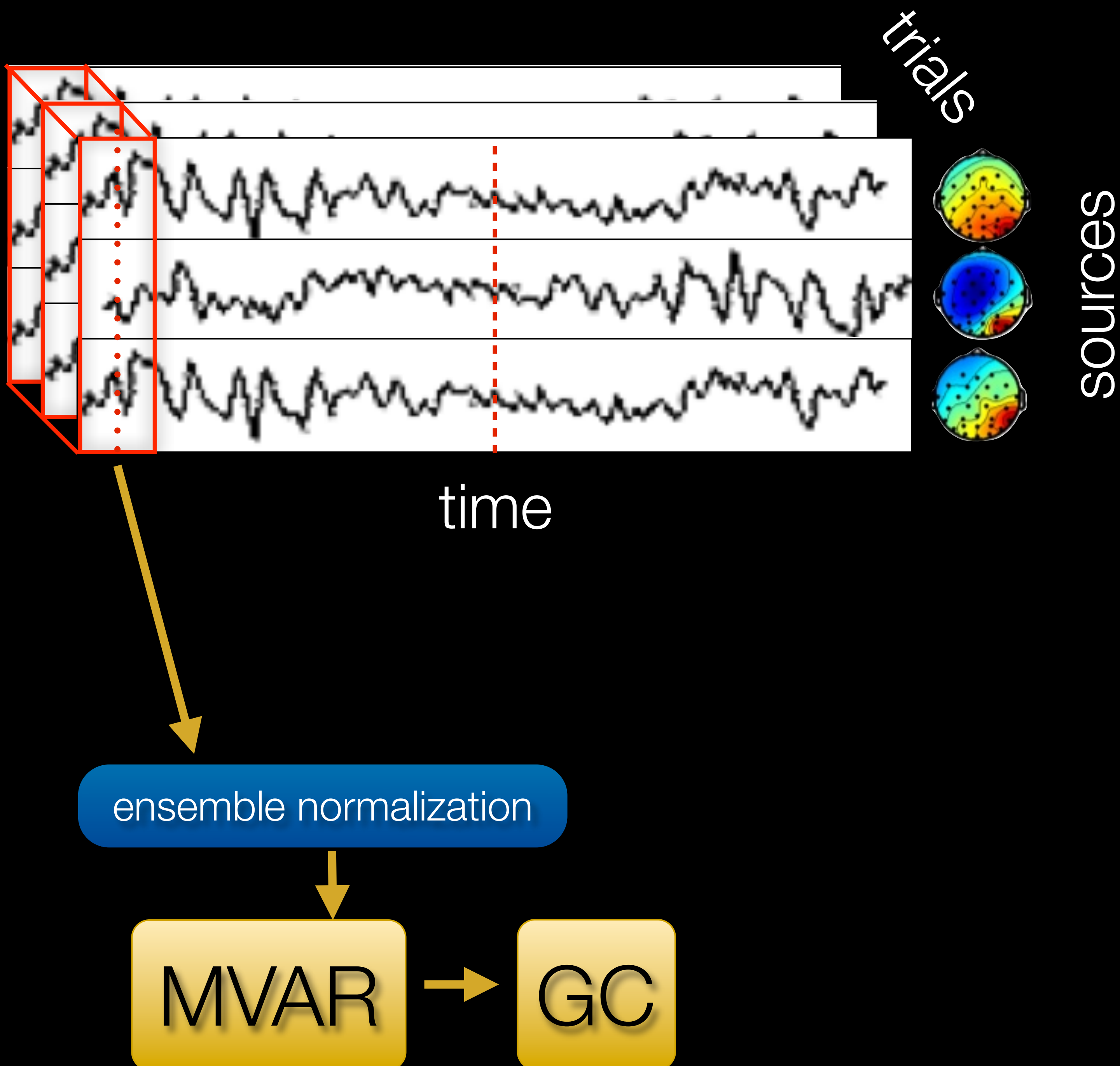

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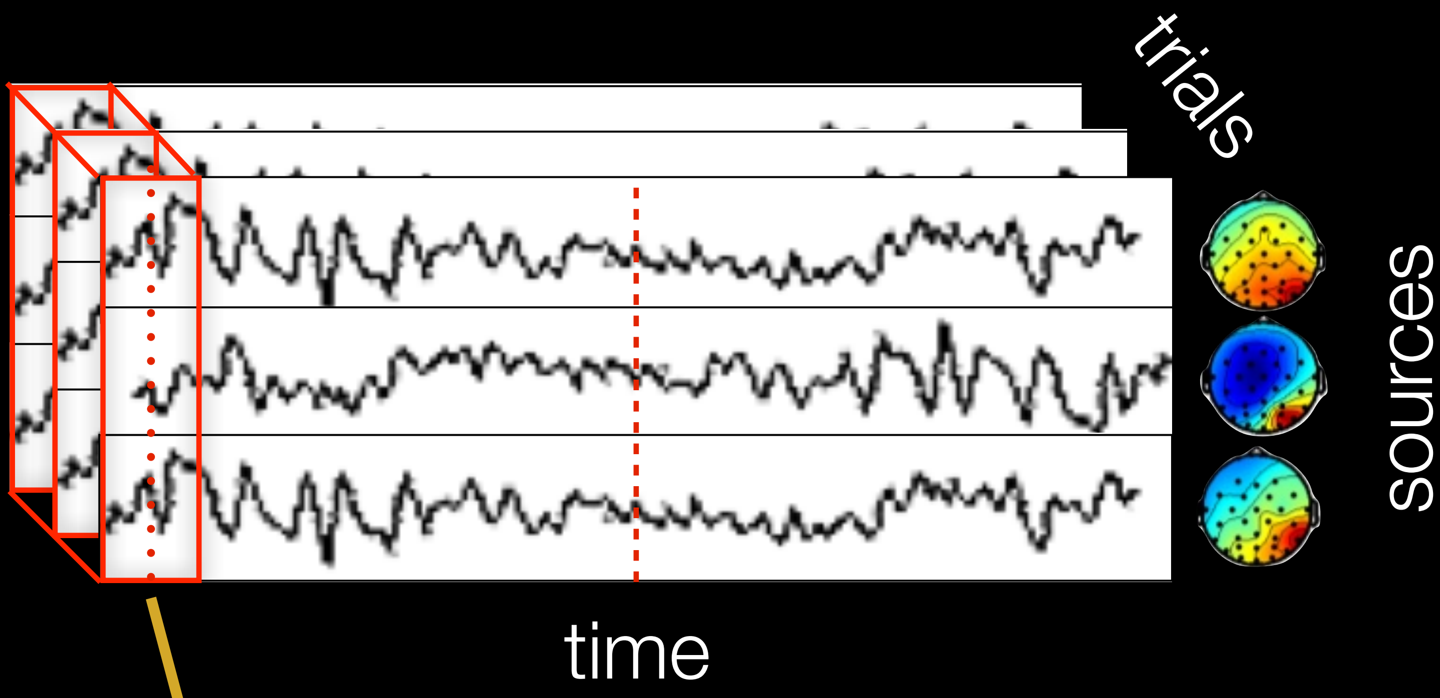

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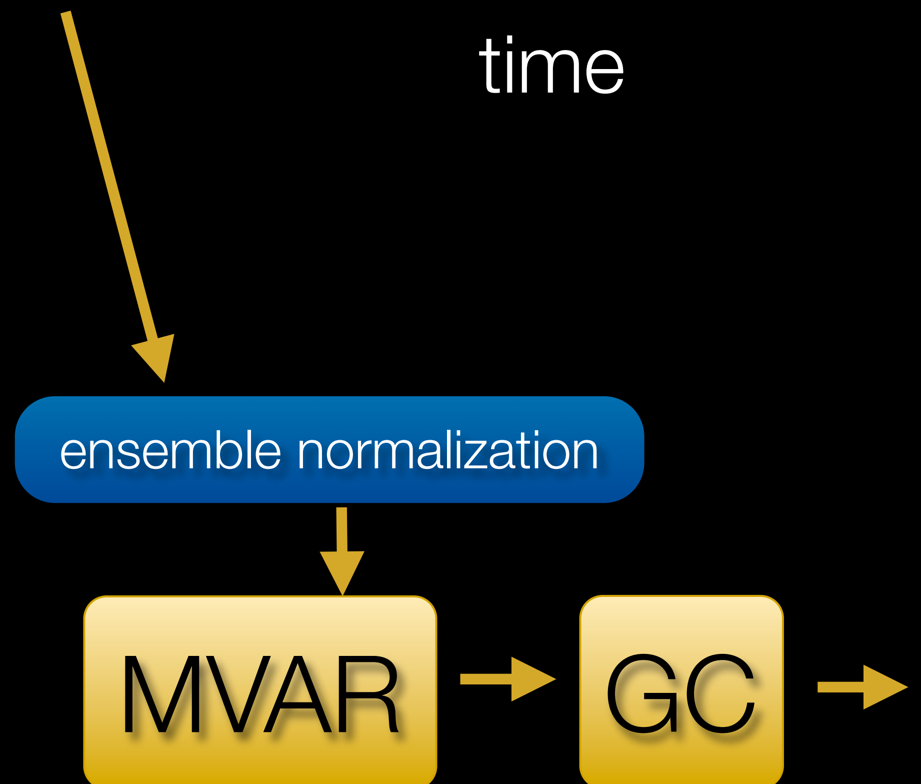

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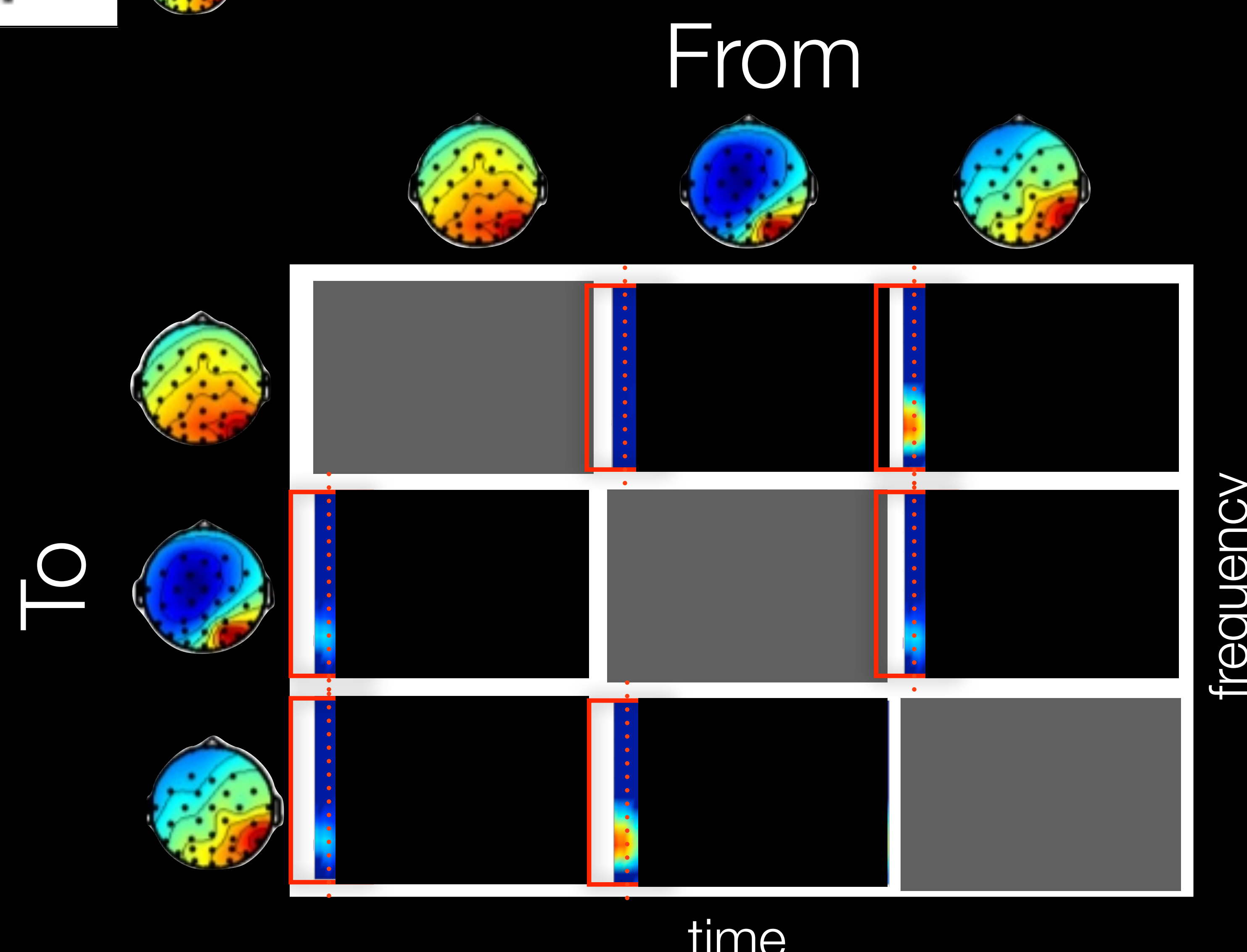

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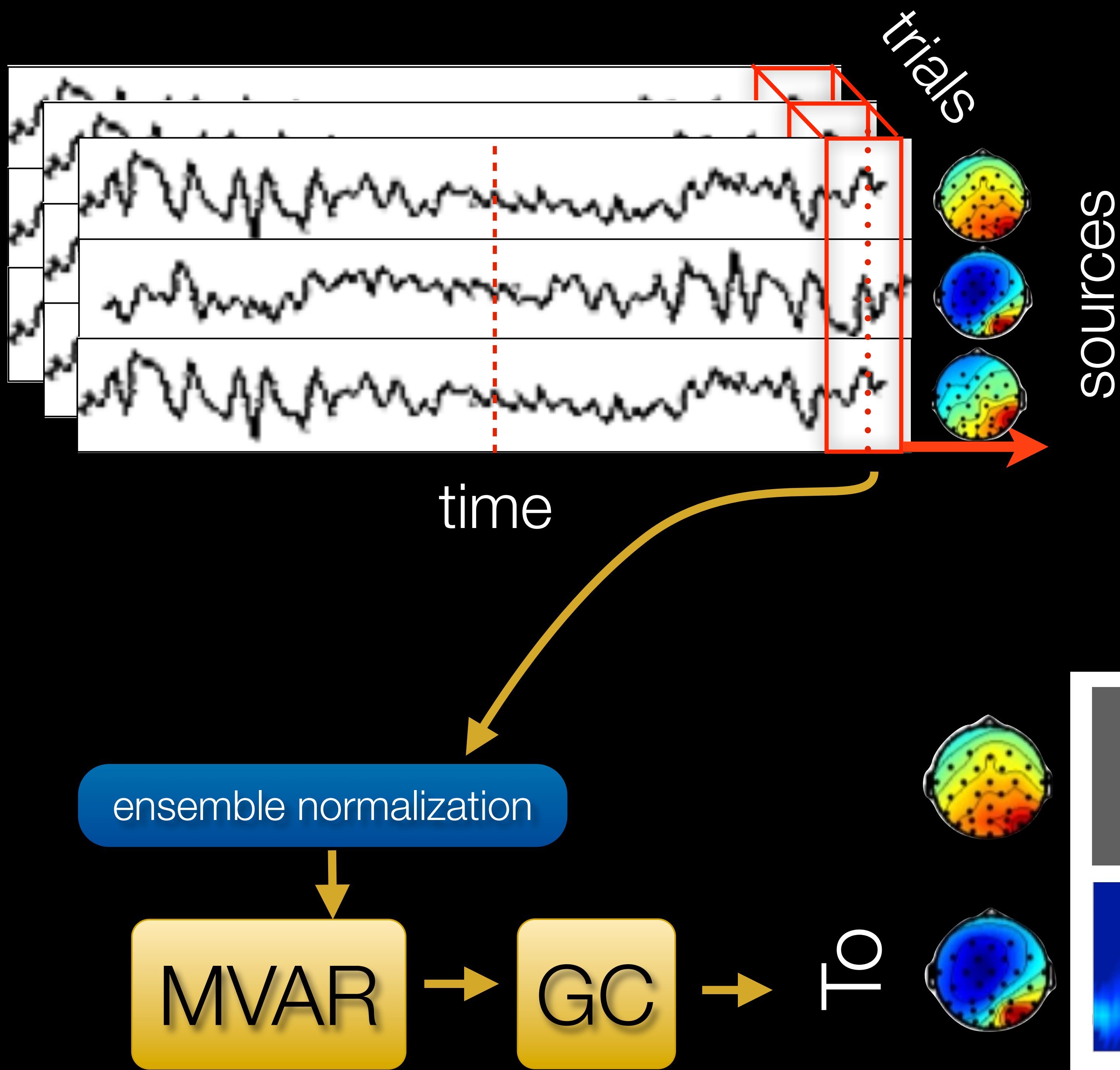
Time-Frequency GC



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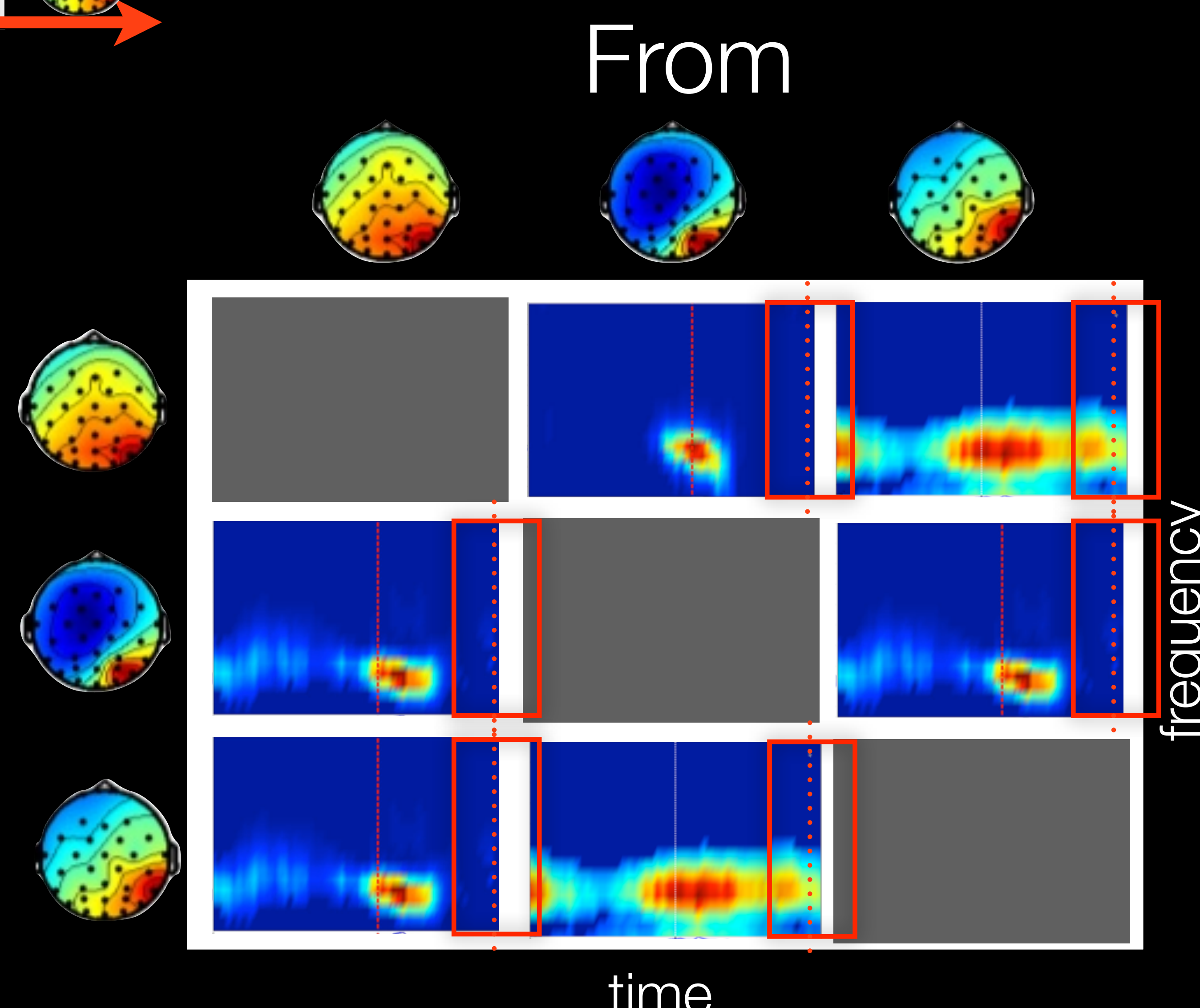

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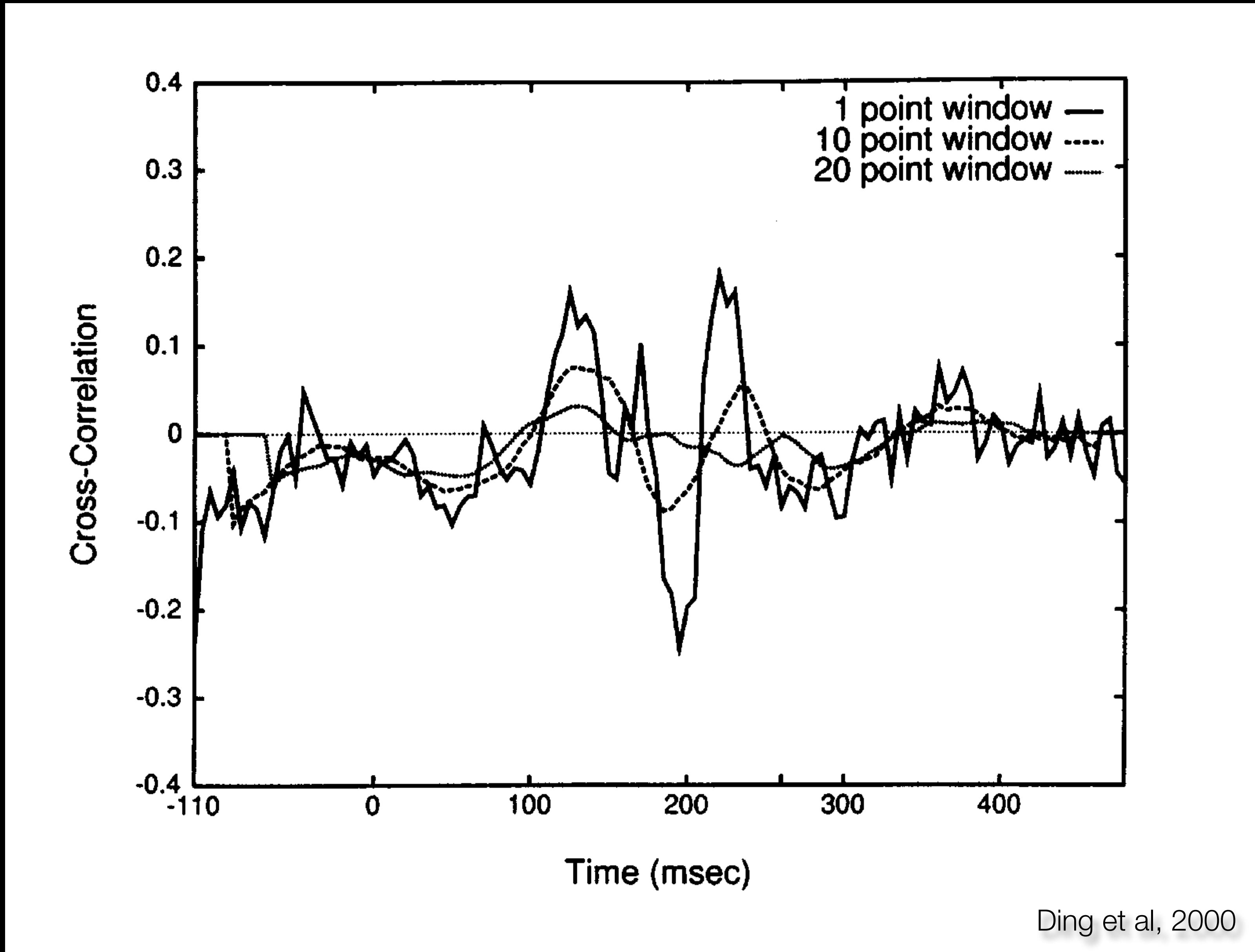
Time-Frequency GC

Consideration: Temporal Smoothness

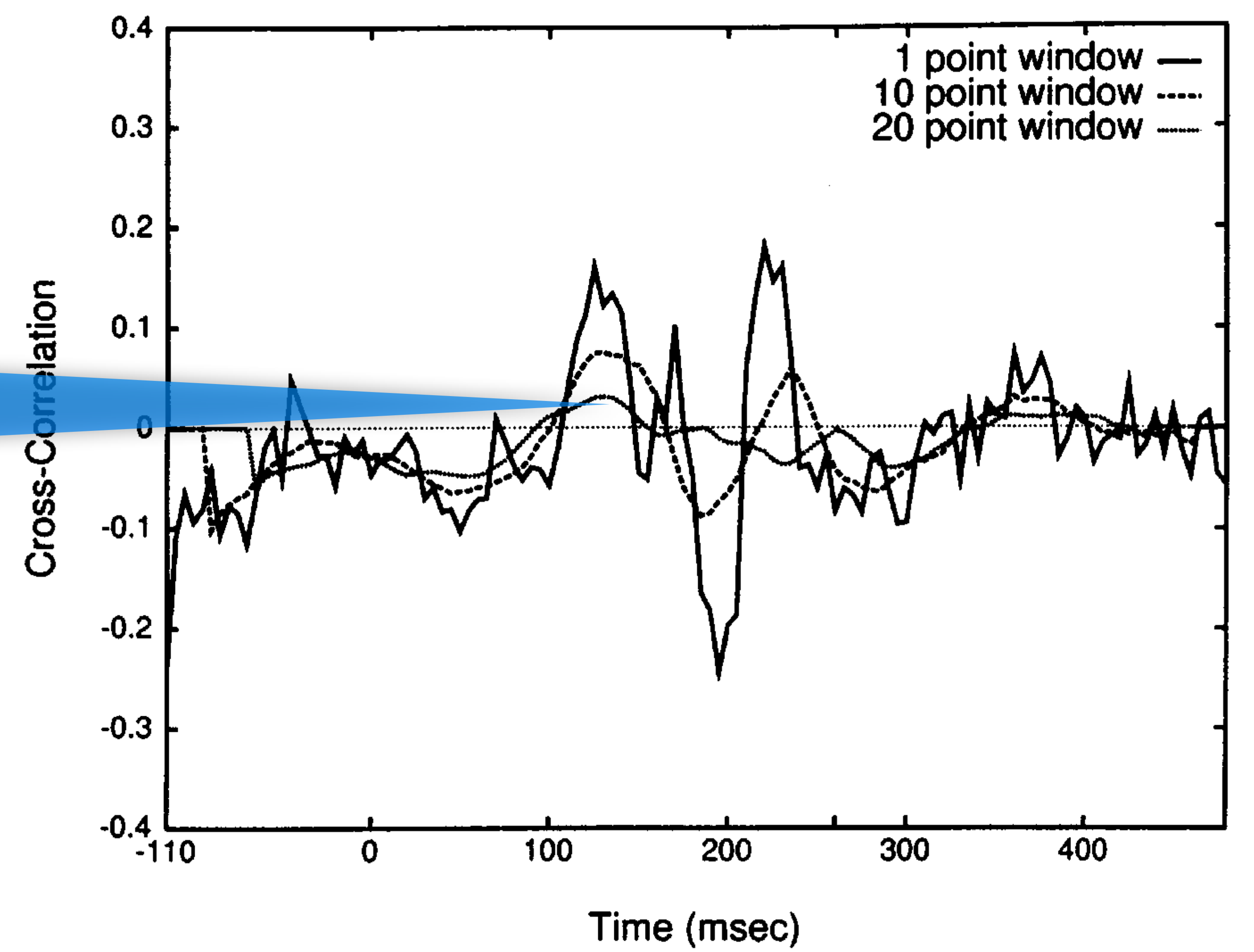


Ding et al, 2000

Time-Frequency GC

Consideration: Temporal Smoothness

Too-large windows may smooth out interesting transient dynamic features.



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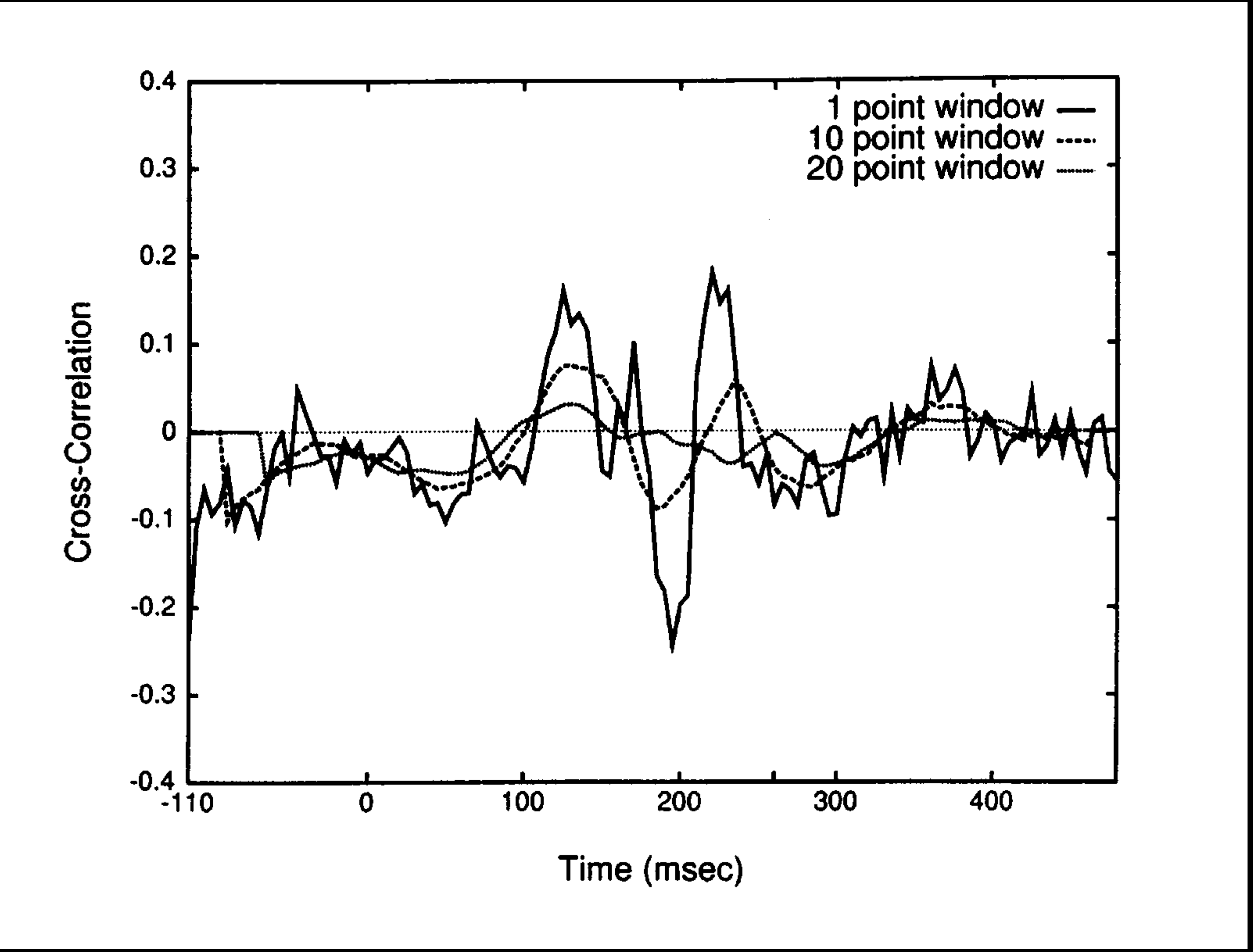
Time-Frequency GC

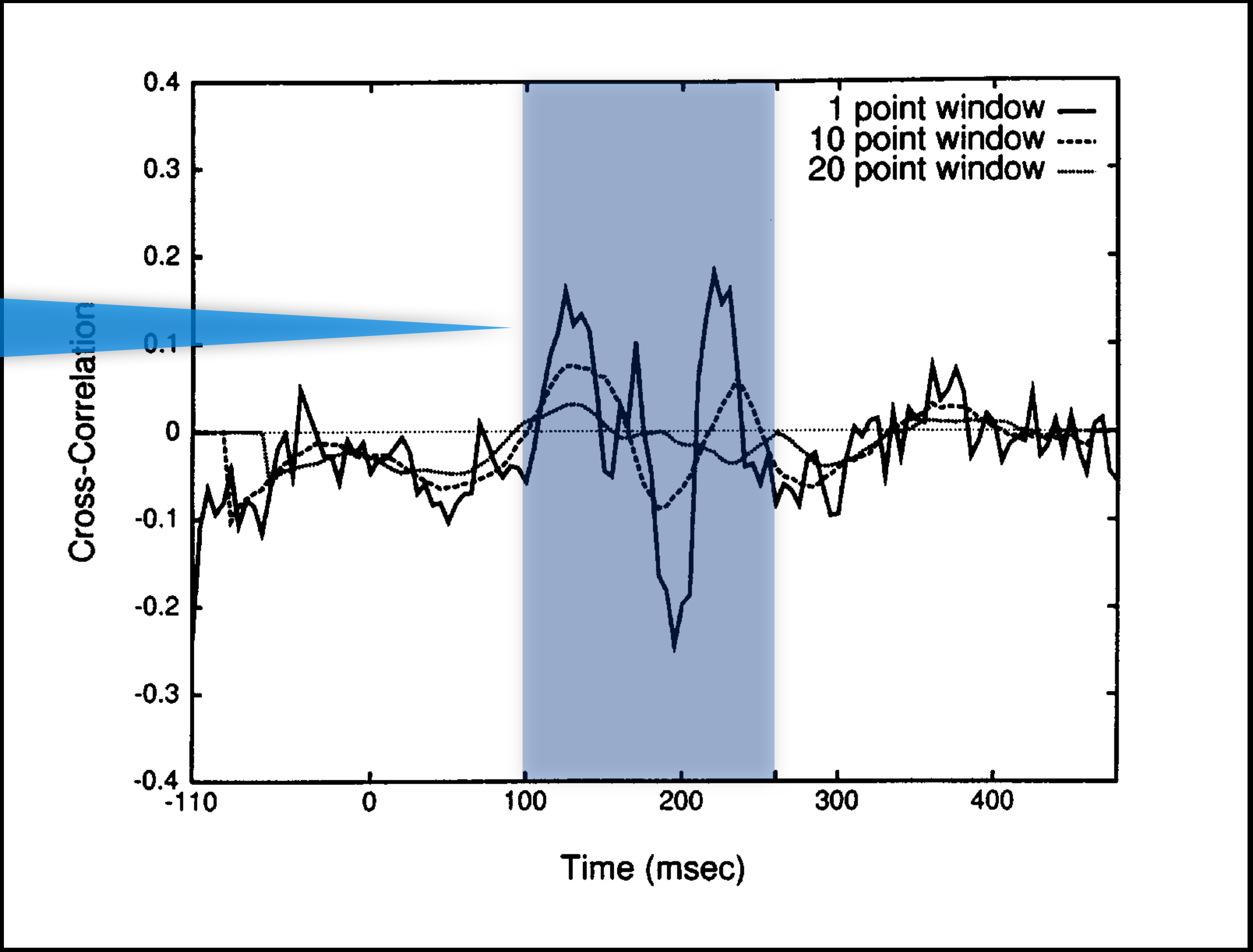
Consideration: Local Stationarity



Time-Frequency GC

Consideration: Local Stationarity

Too-large windows may not be locally-stationary



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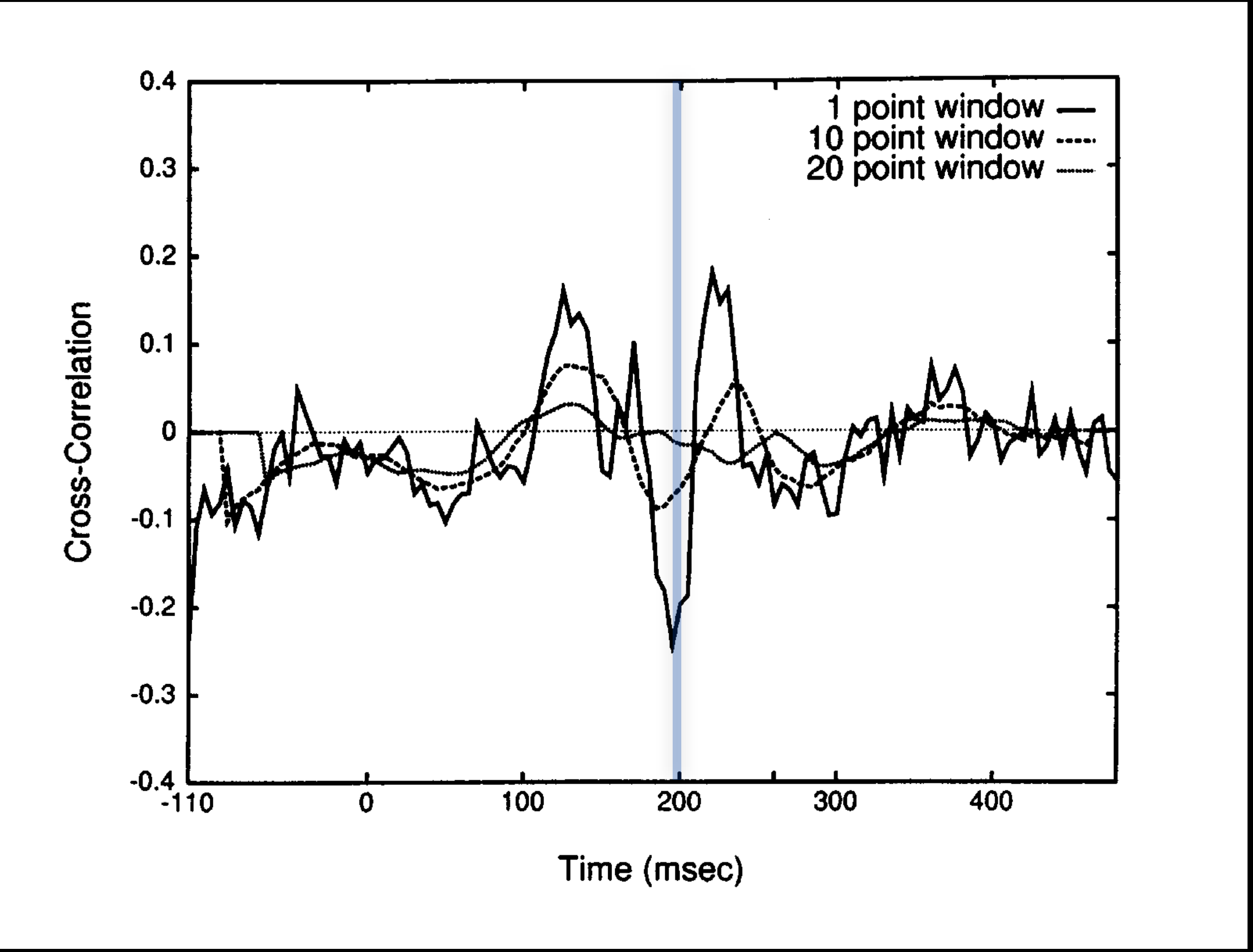

Time-Frequency GC

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Consideration: Sufficient data

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

10x more data points than parameters to estimate

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

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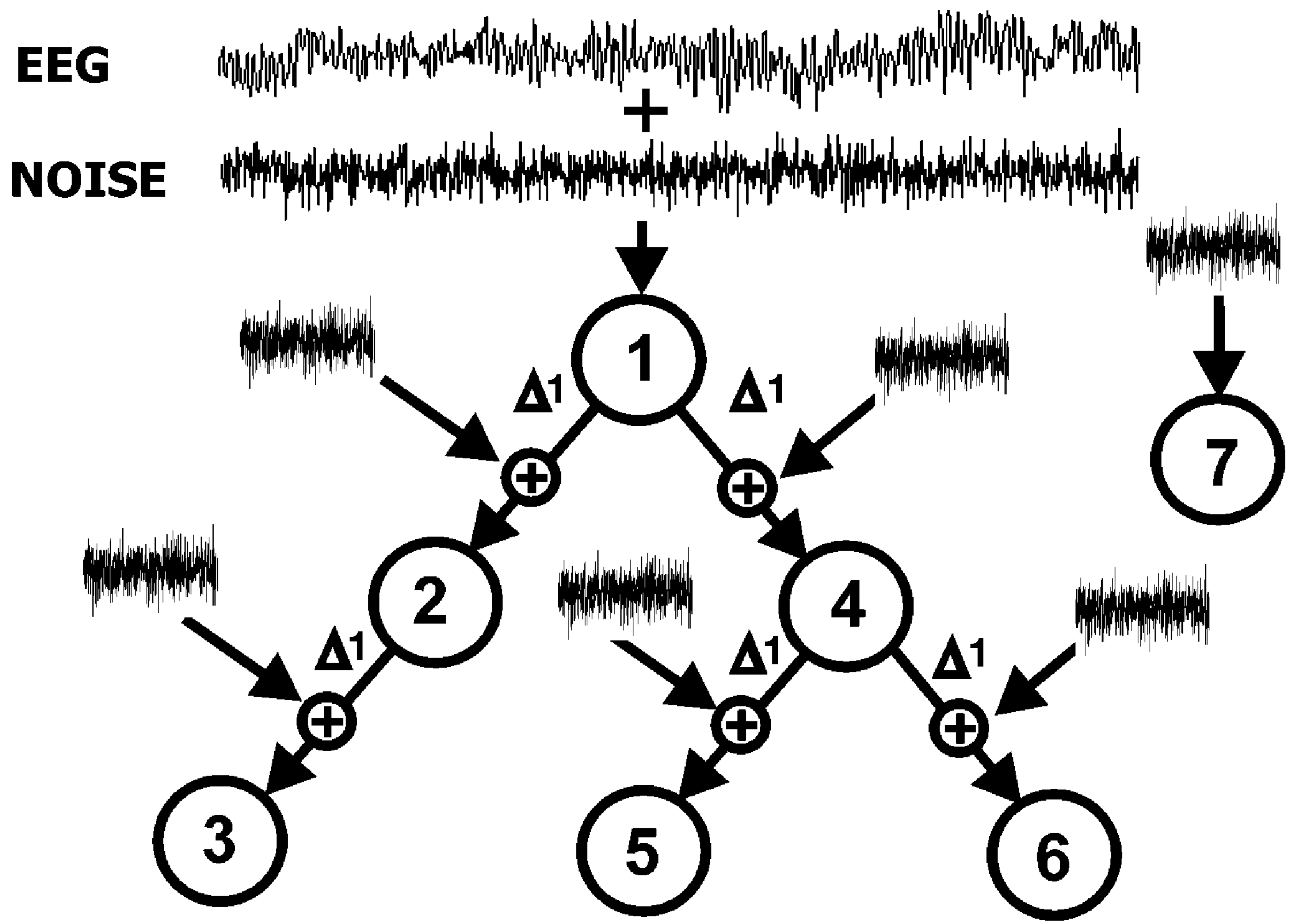
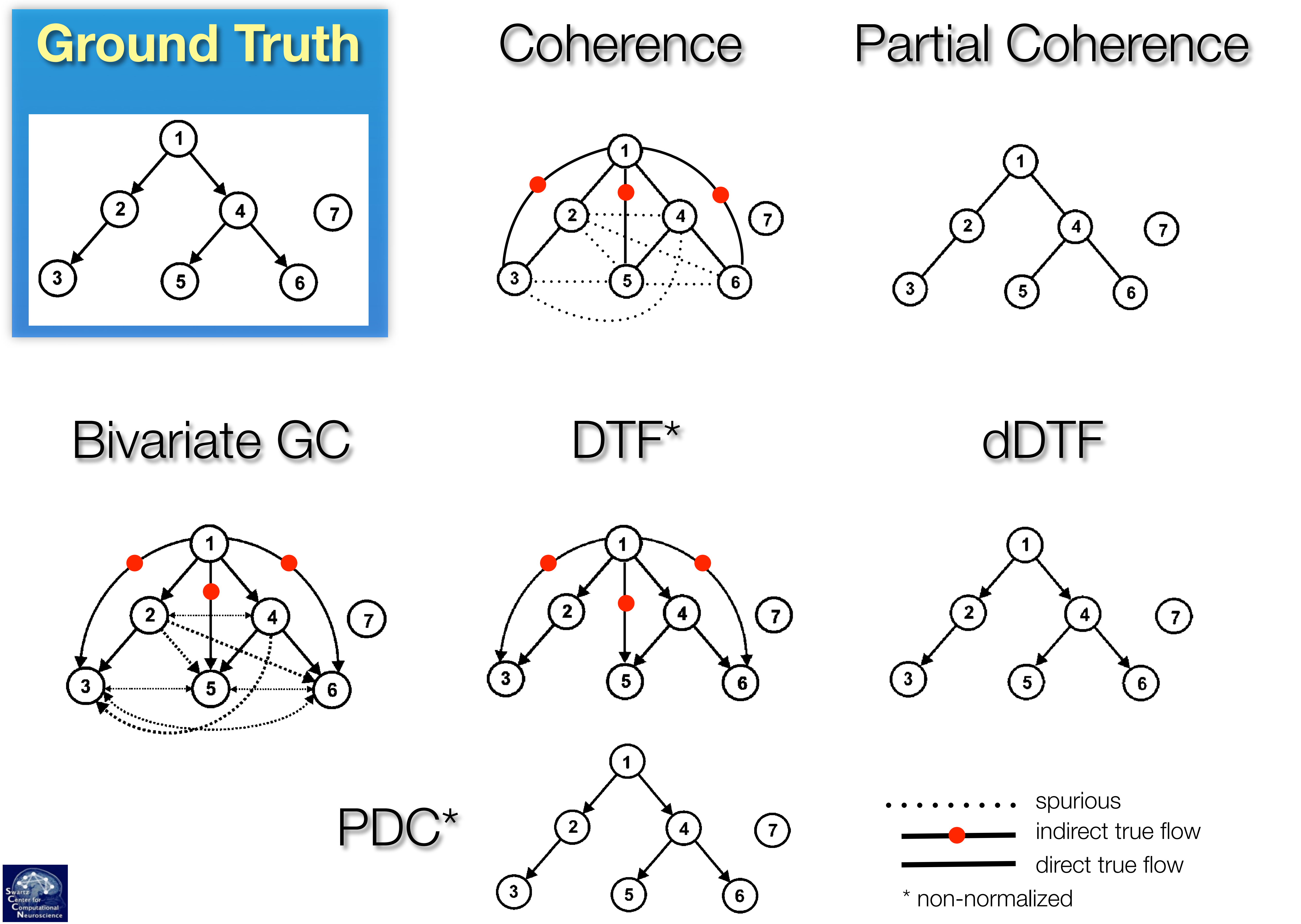
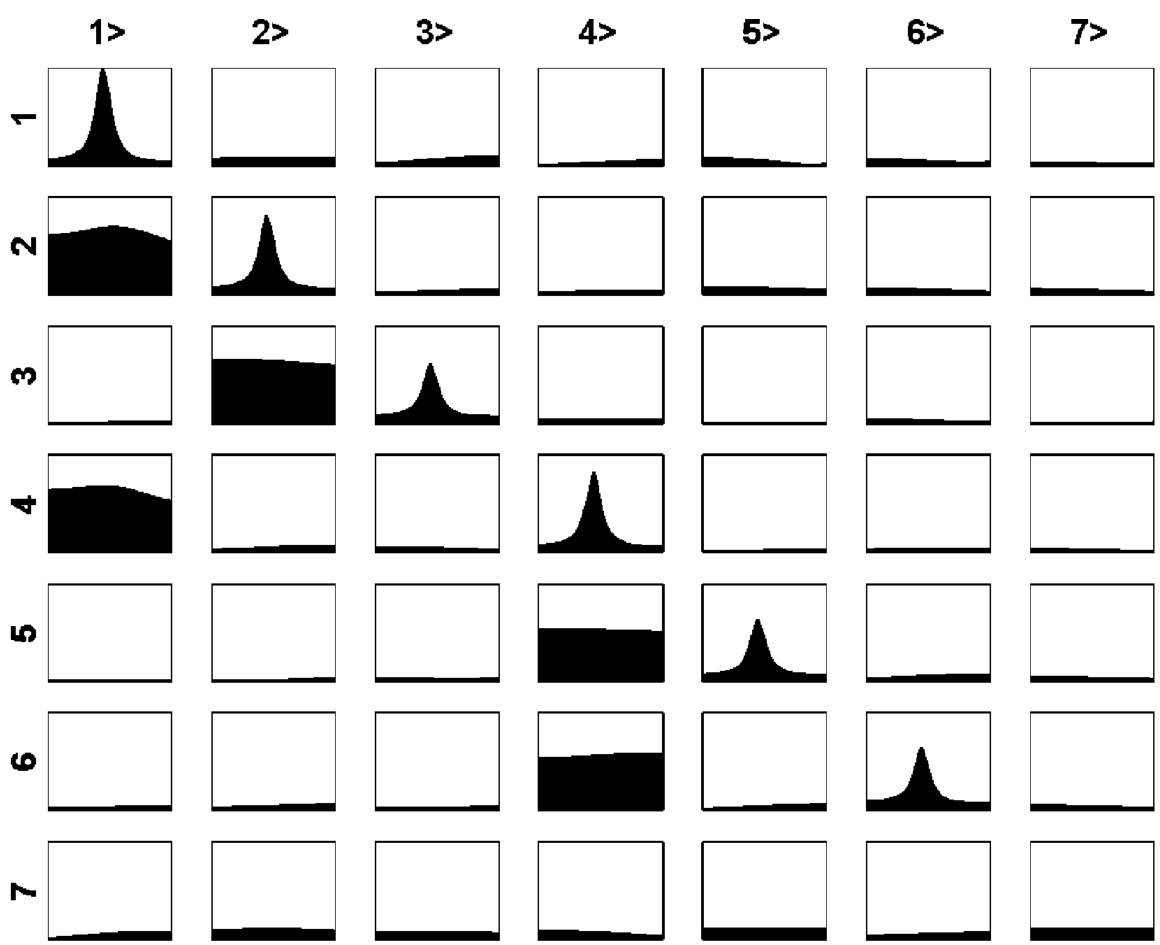
Which Measure to Use?



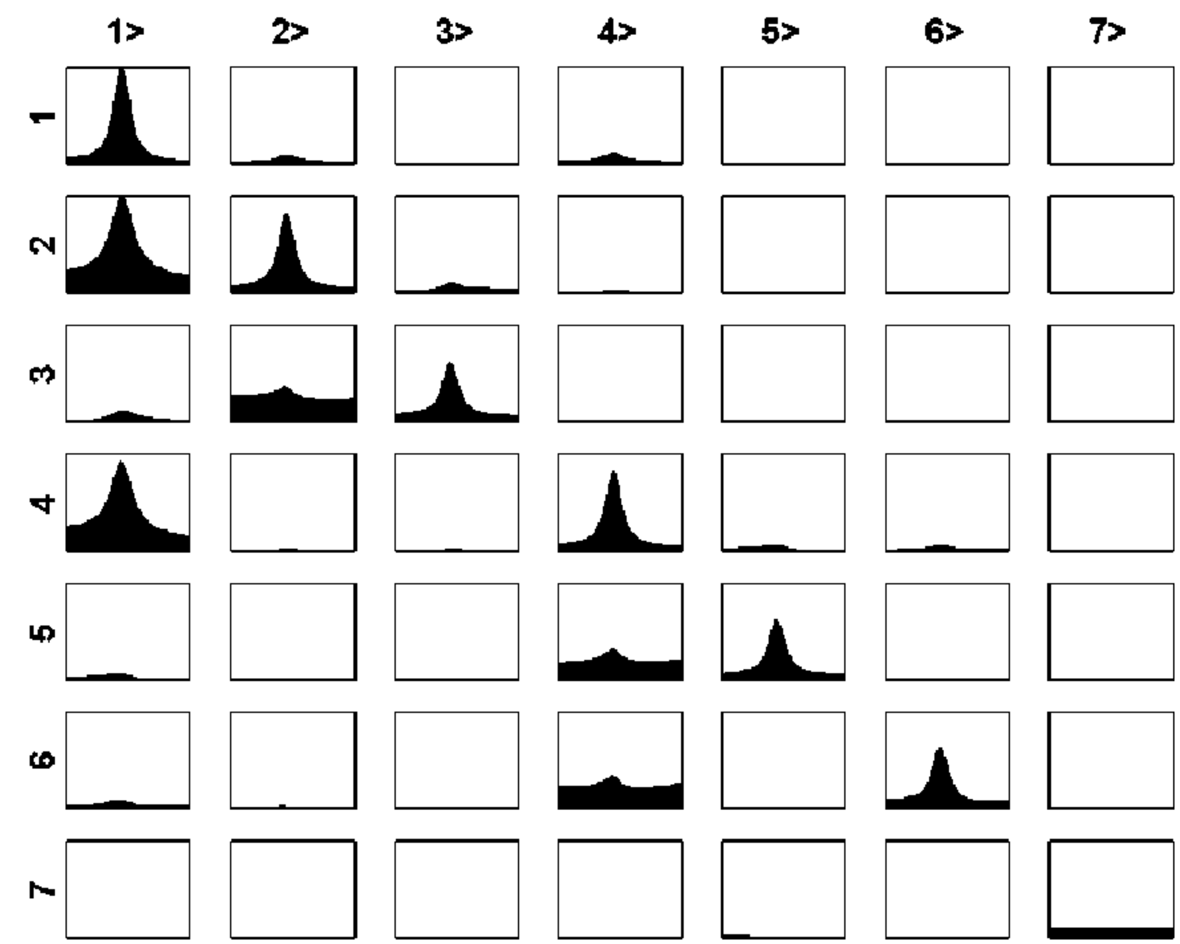
Kus et al, 2004


Ground Truth
Coherence
Partial Coherence
Bivariate GC
DTF*
dDTF
PDC*
spurious
indirect true flow
direct true flow
* non-normalized

PDC versus DTF methods (spectral considerations)

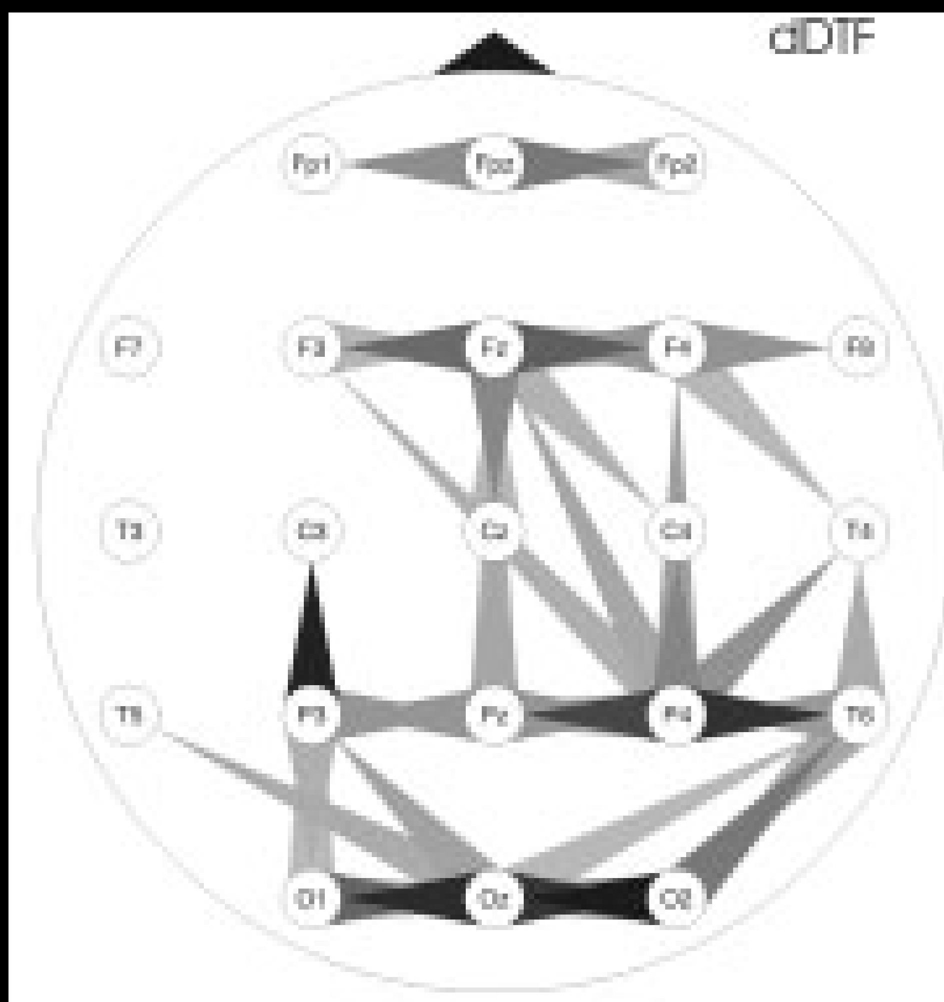


PDC

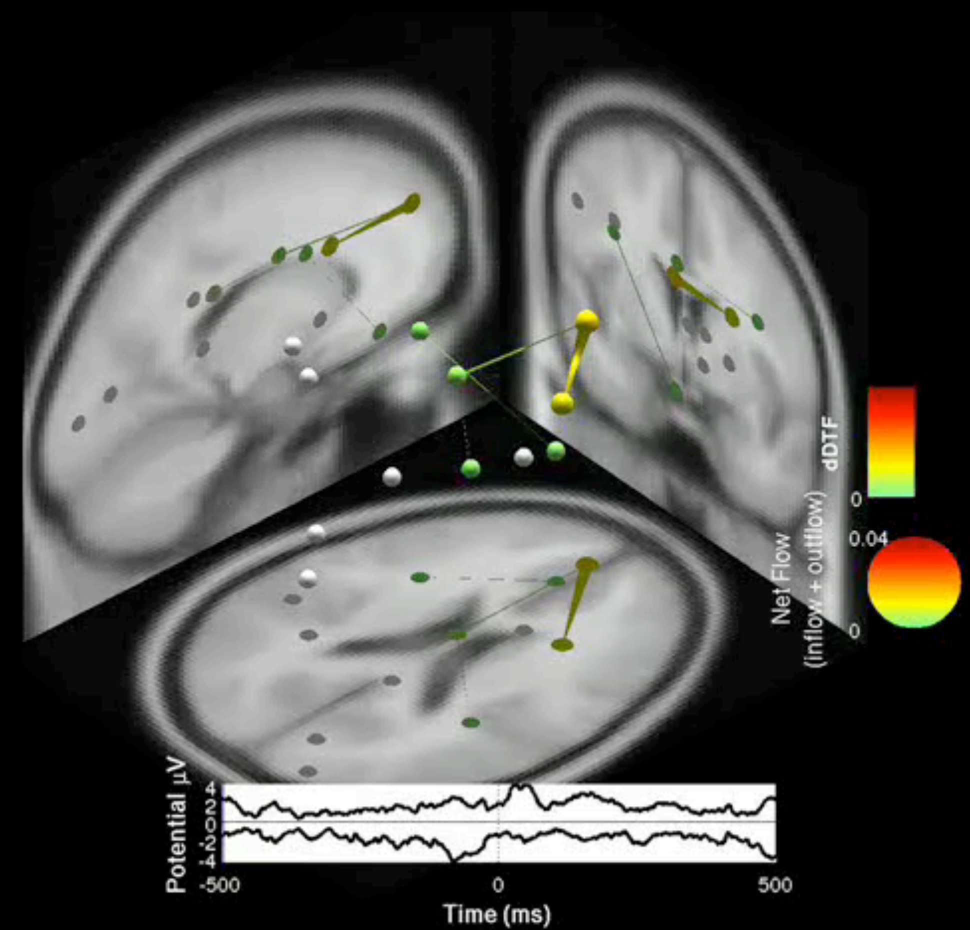


dDTF

Scalp or Source?



or



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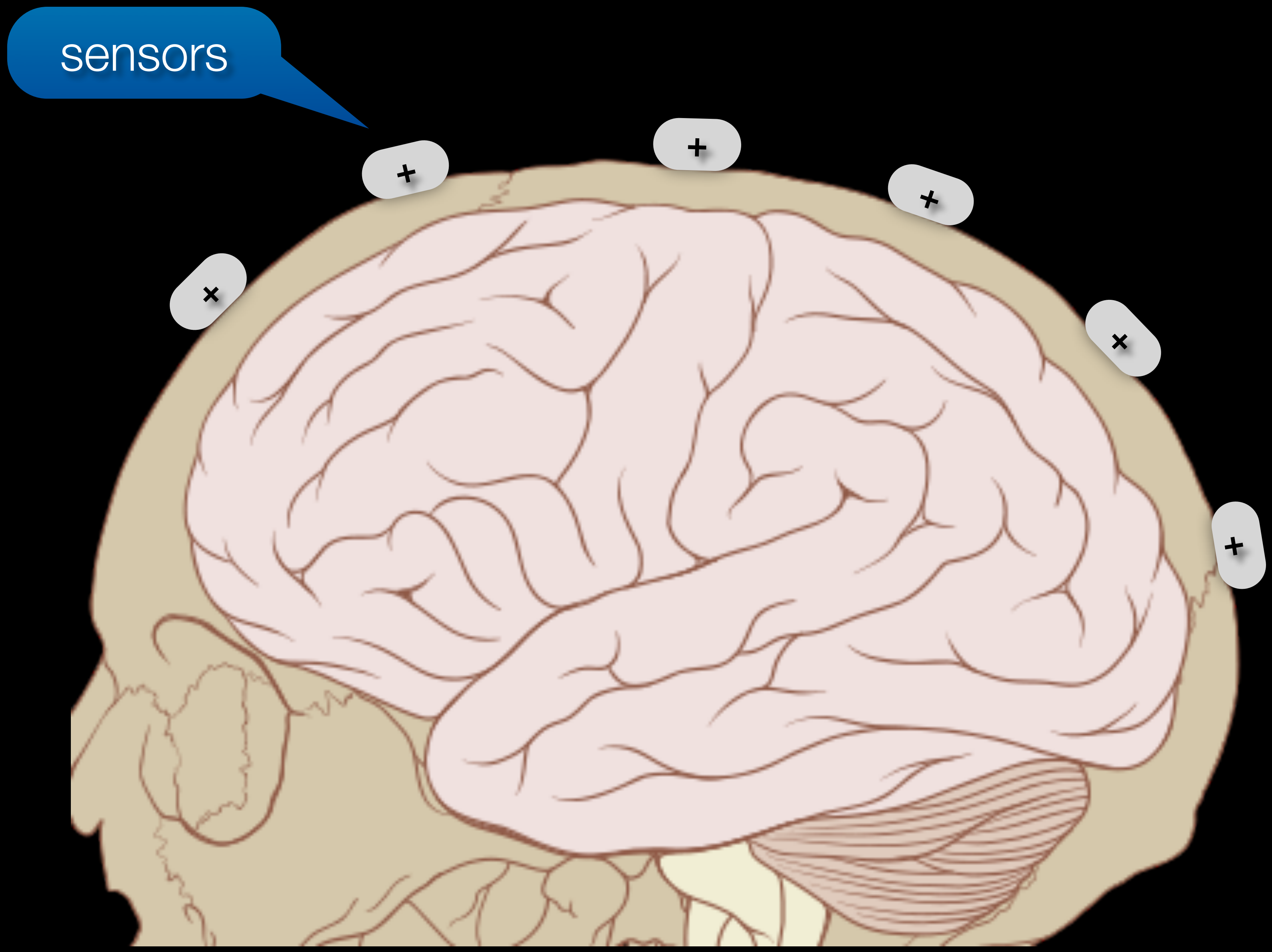

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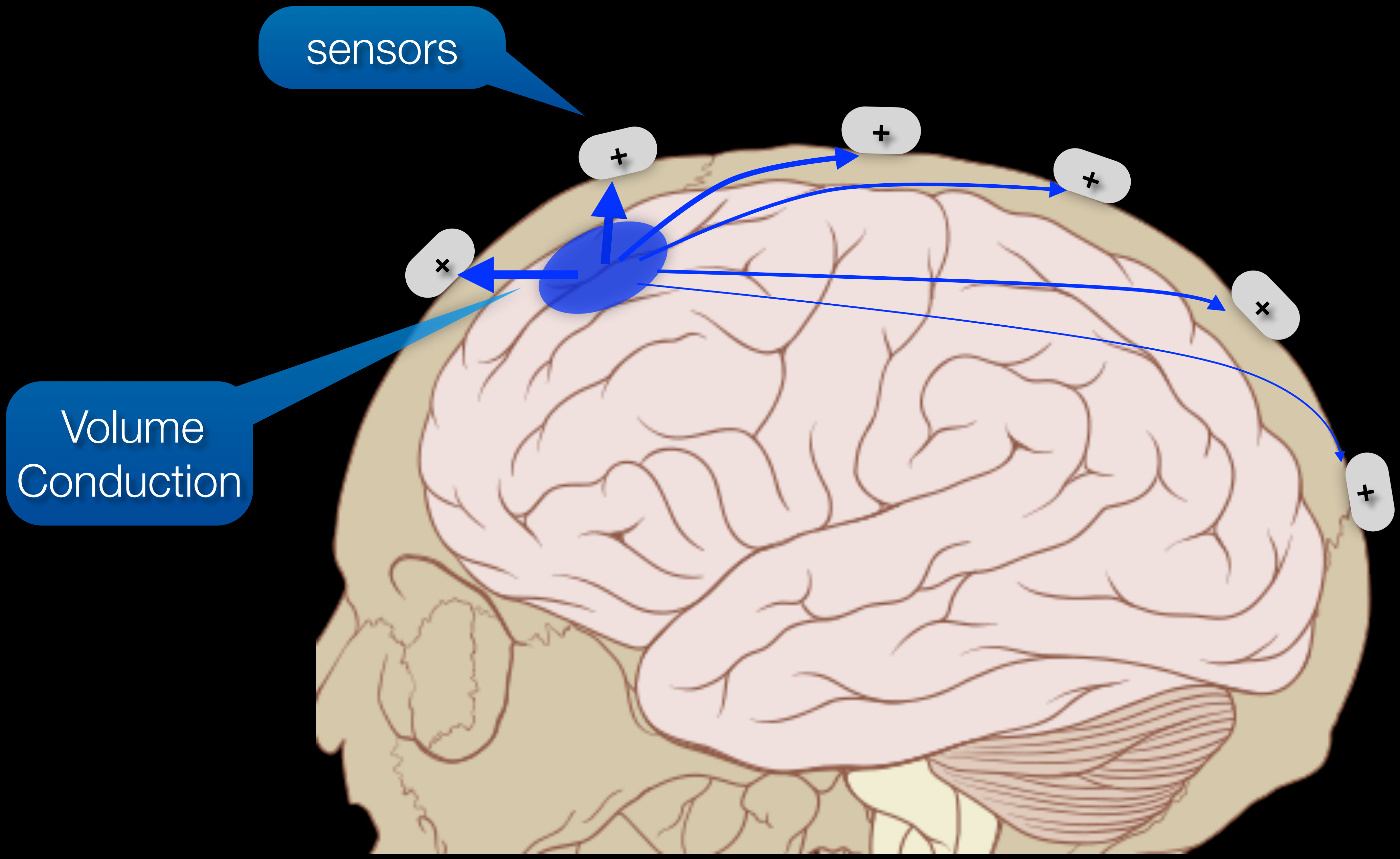

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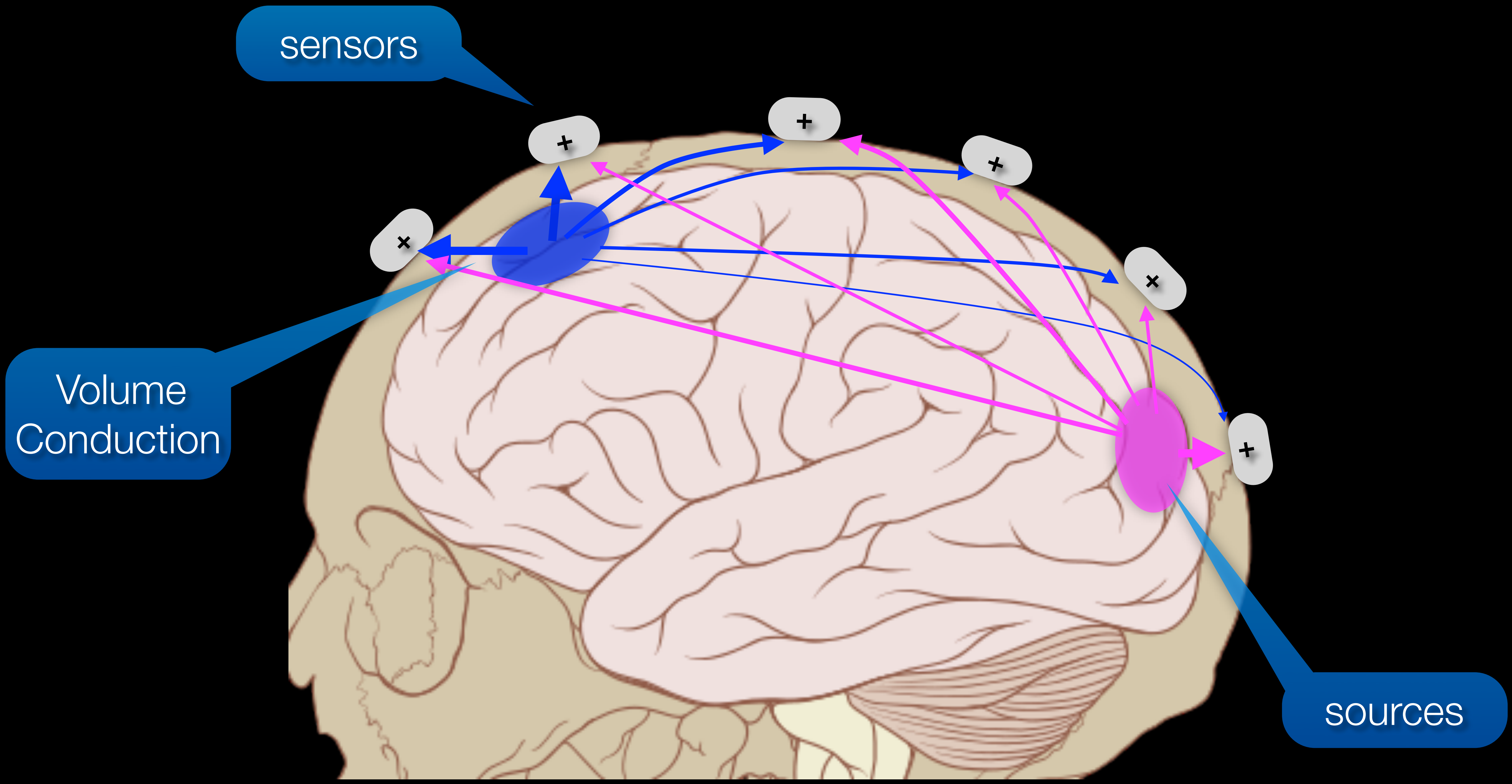

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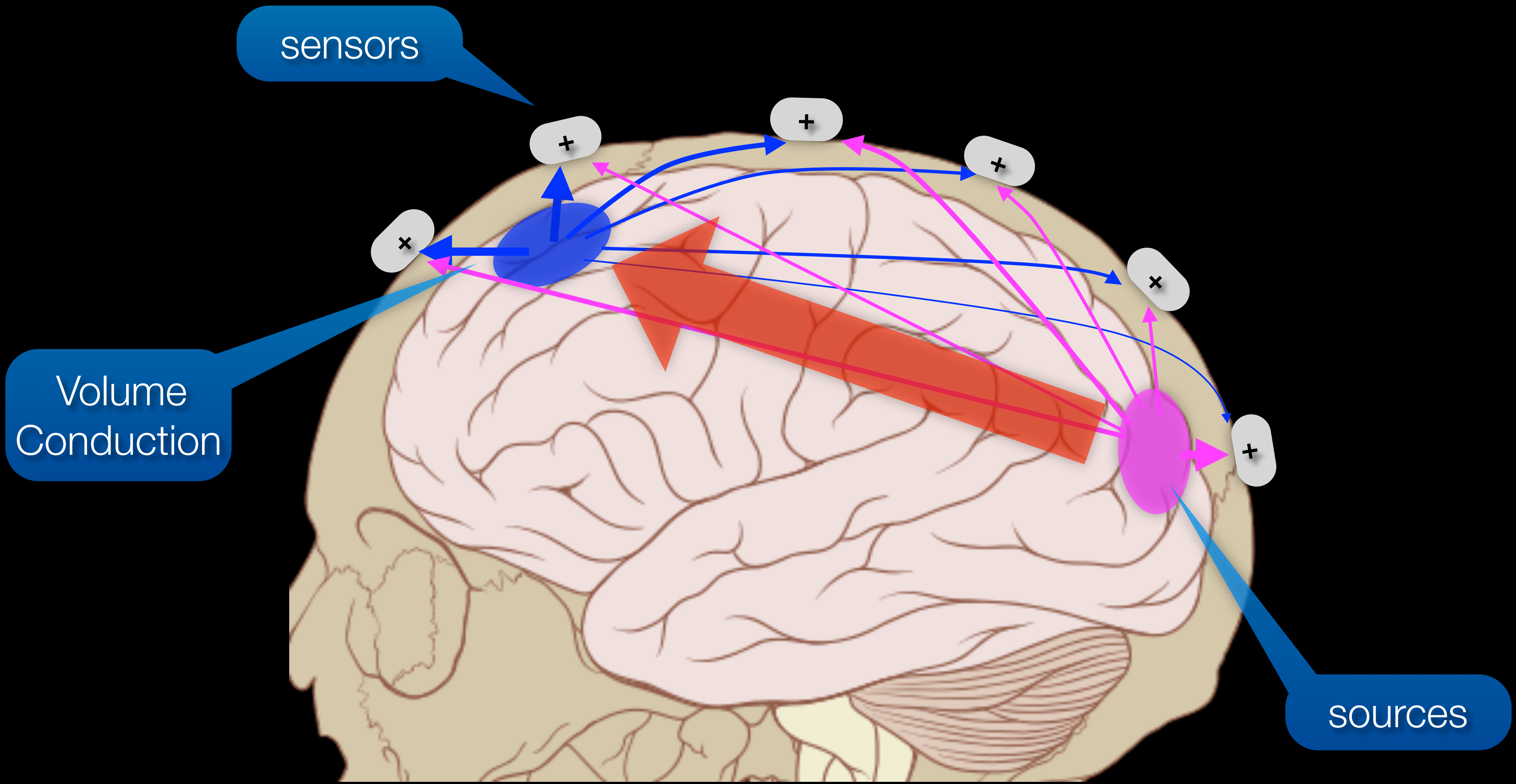

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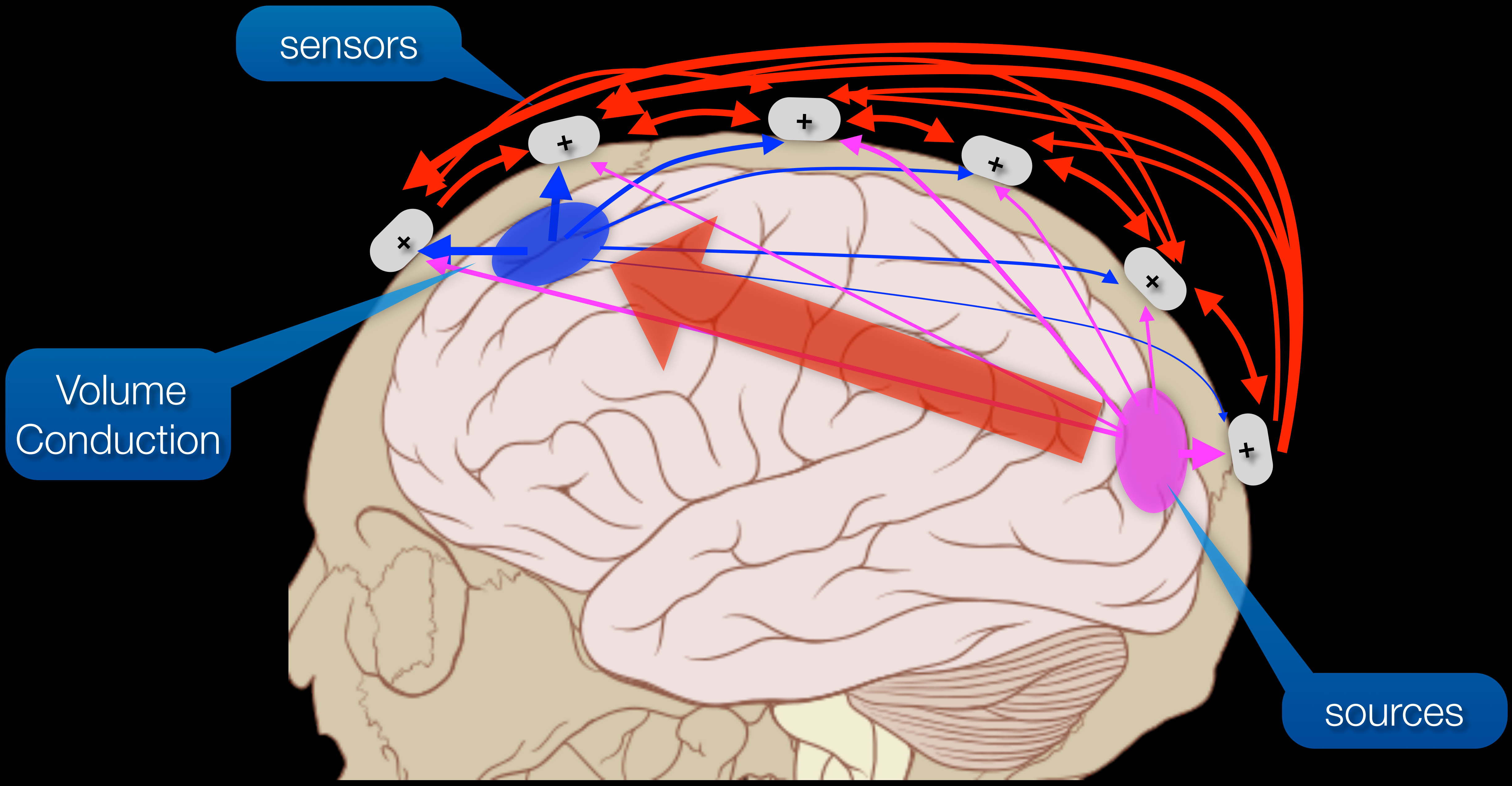

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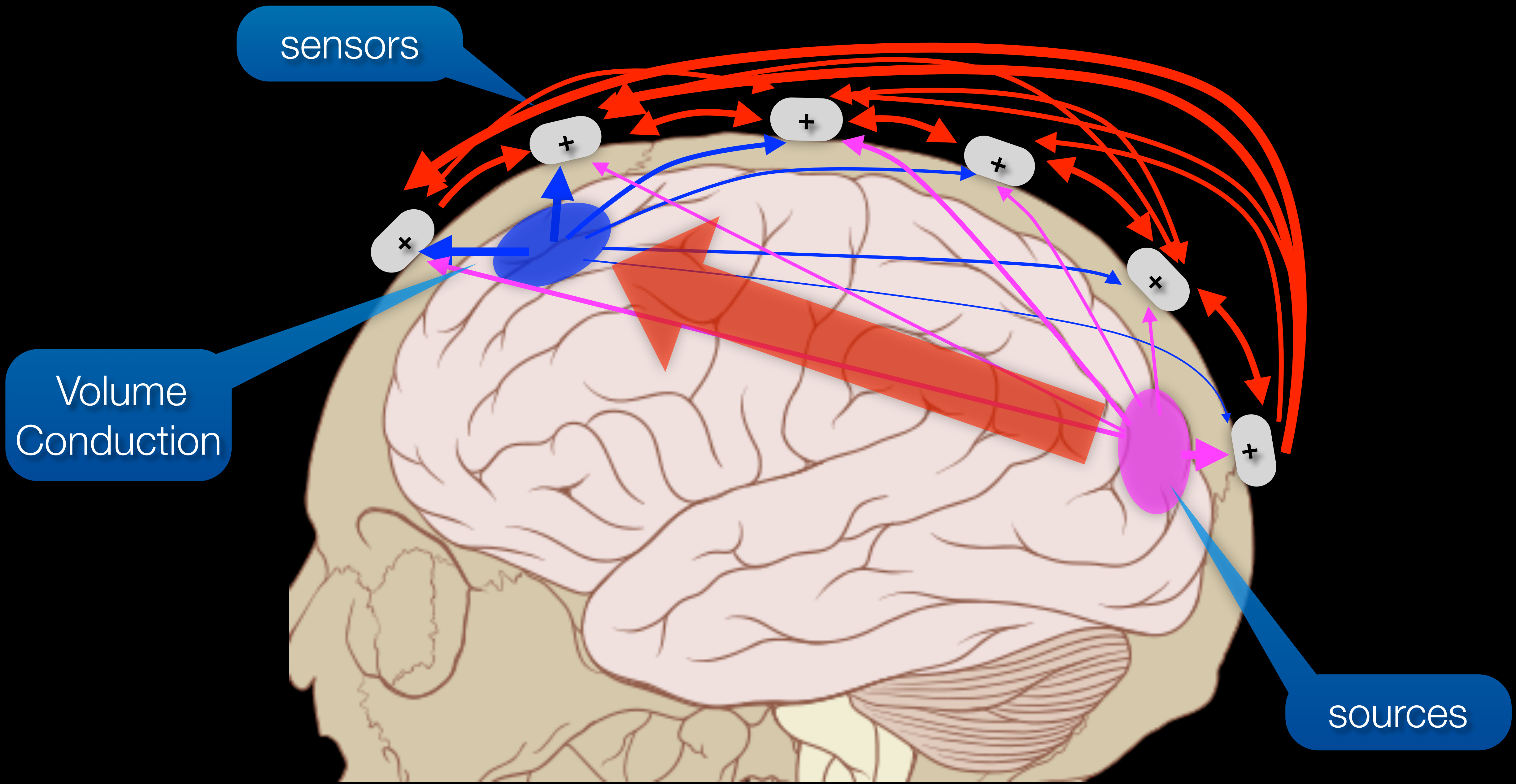
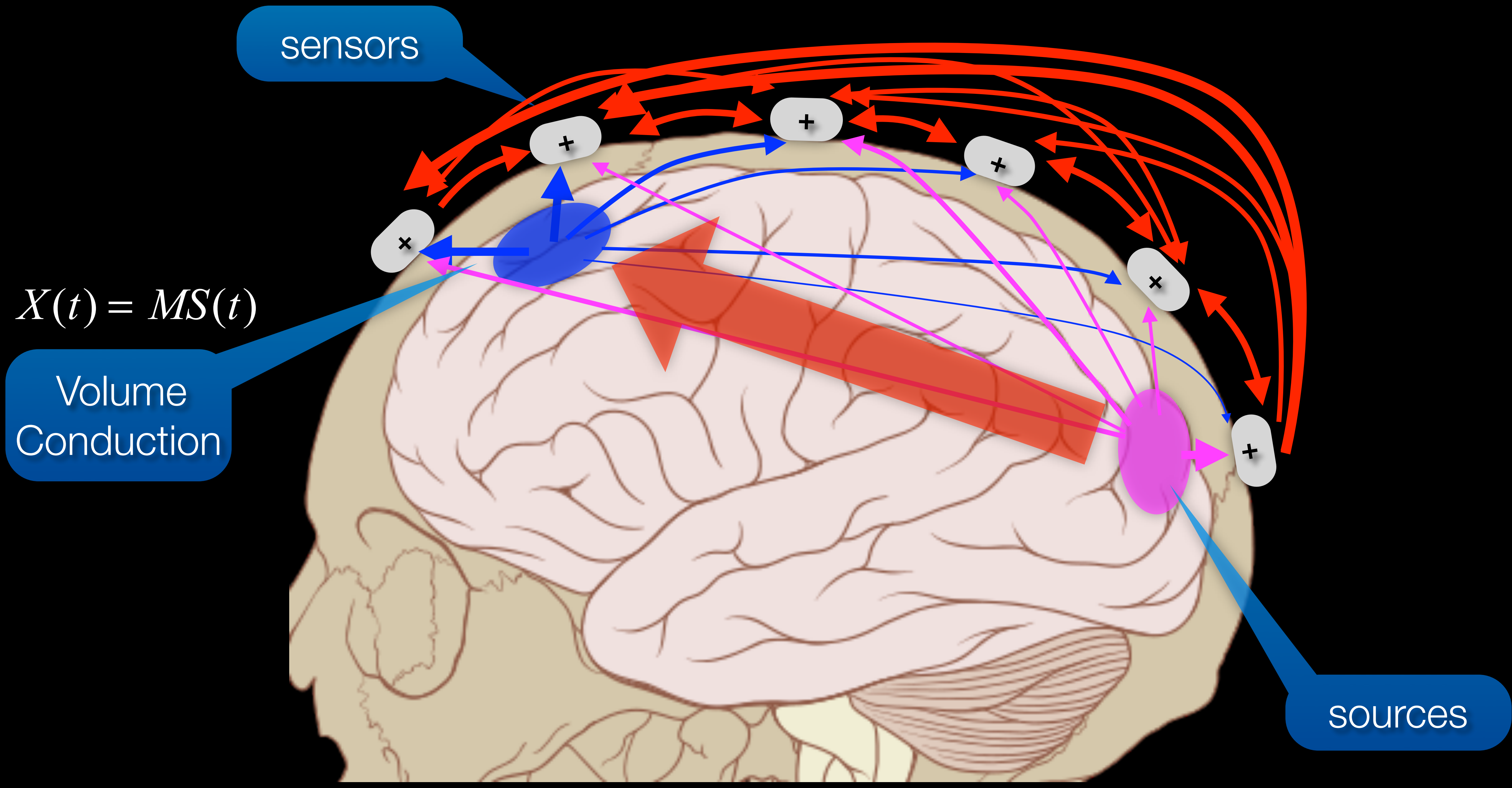


$$S(t) = \sum_{k=1}^{p} A(k)S(t-k) + E(t)$$

Scalp or Source?



$$X(t) = MS(t)$$

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Scalp or Source?

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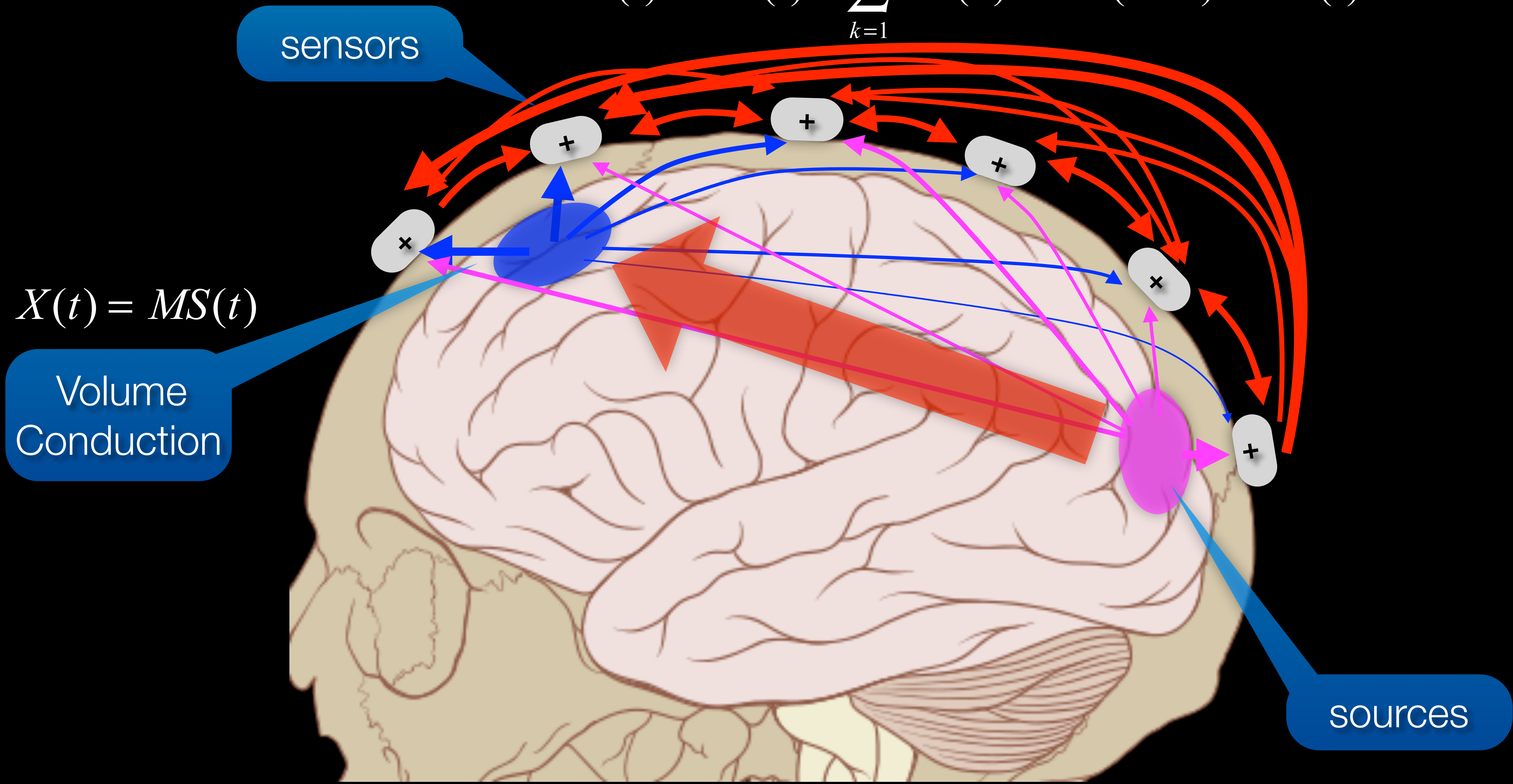

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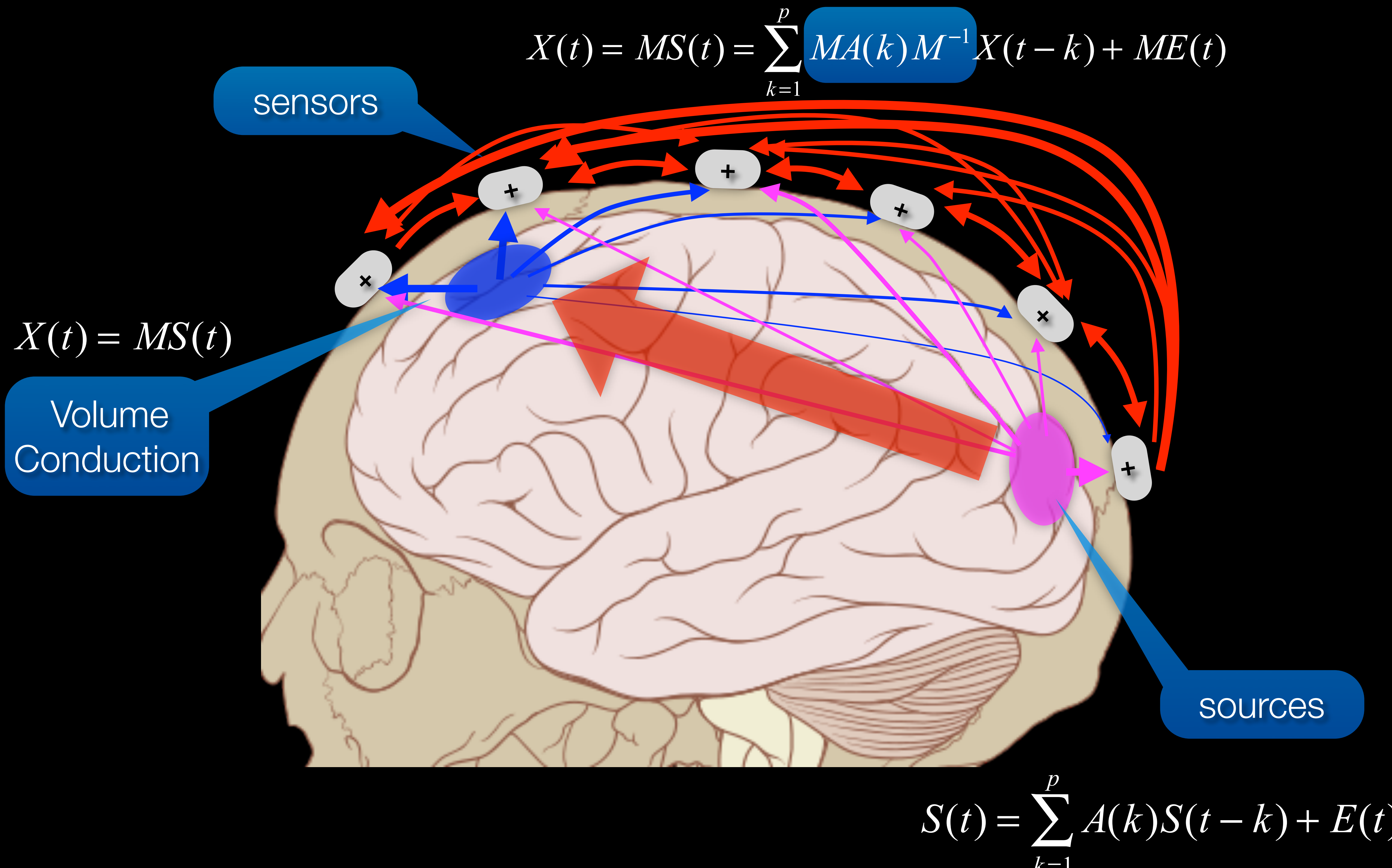

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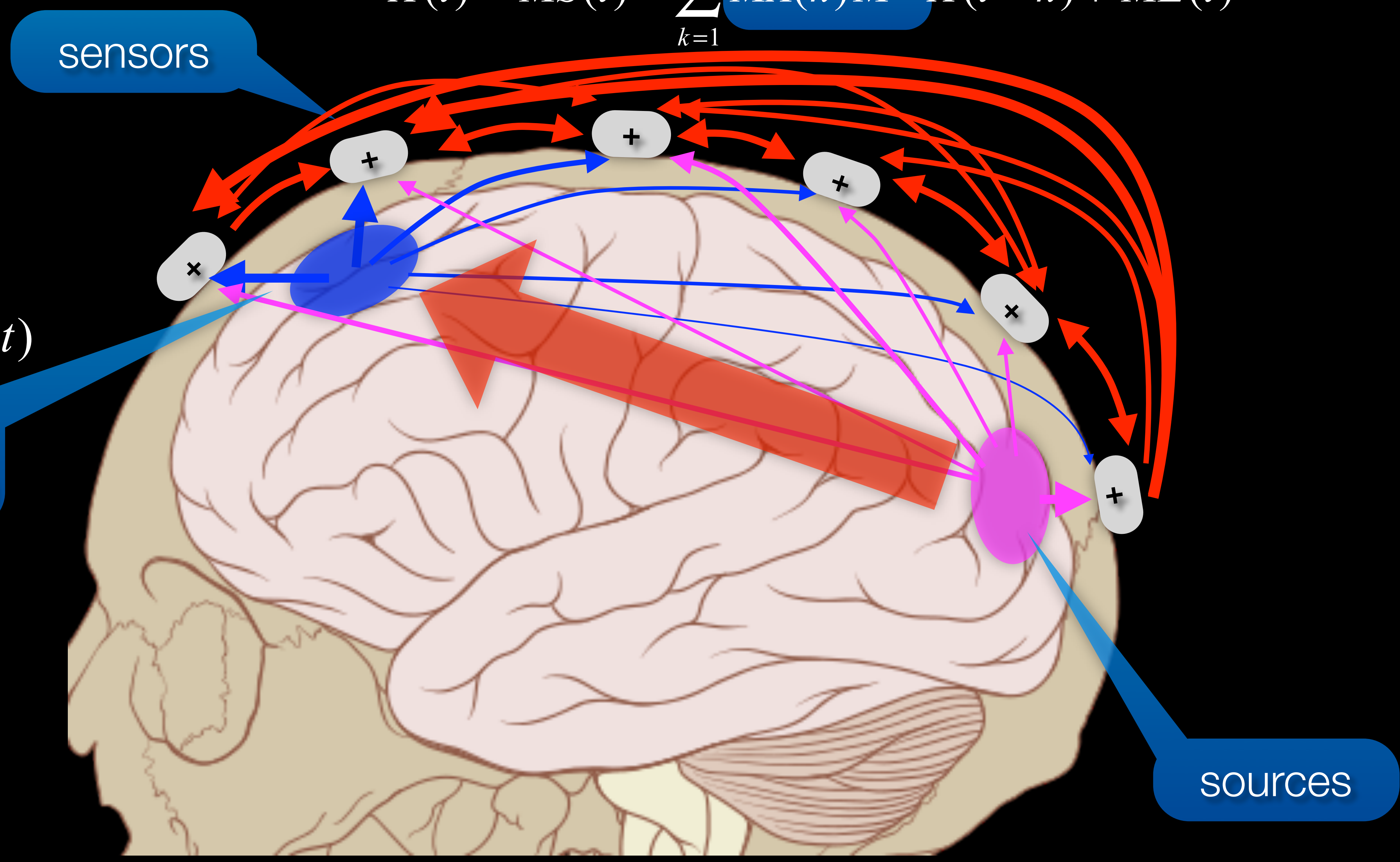

Solution? Source Separation

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Estimating Dependency of Independent Components ?

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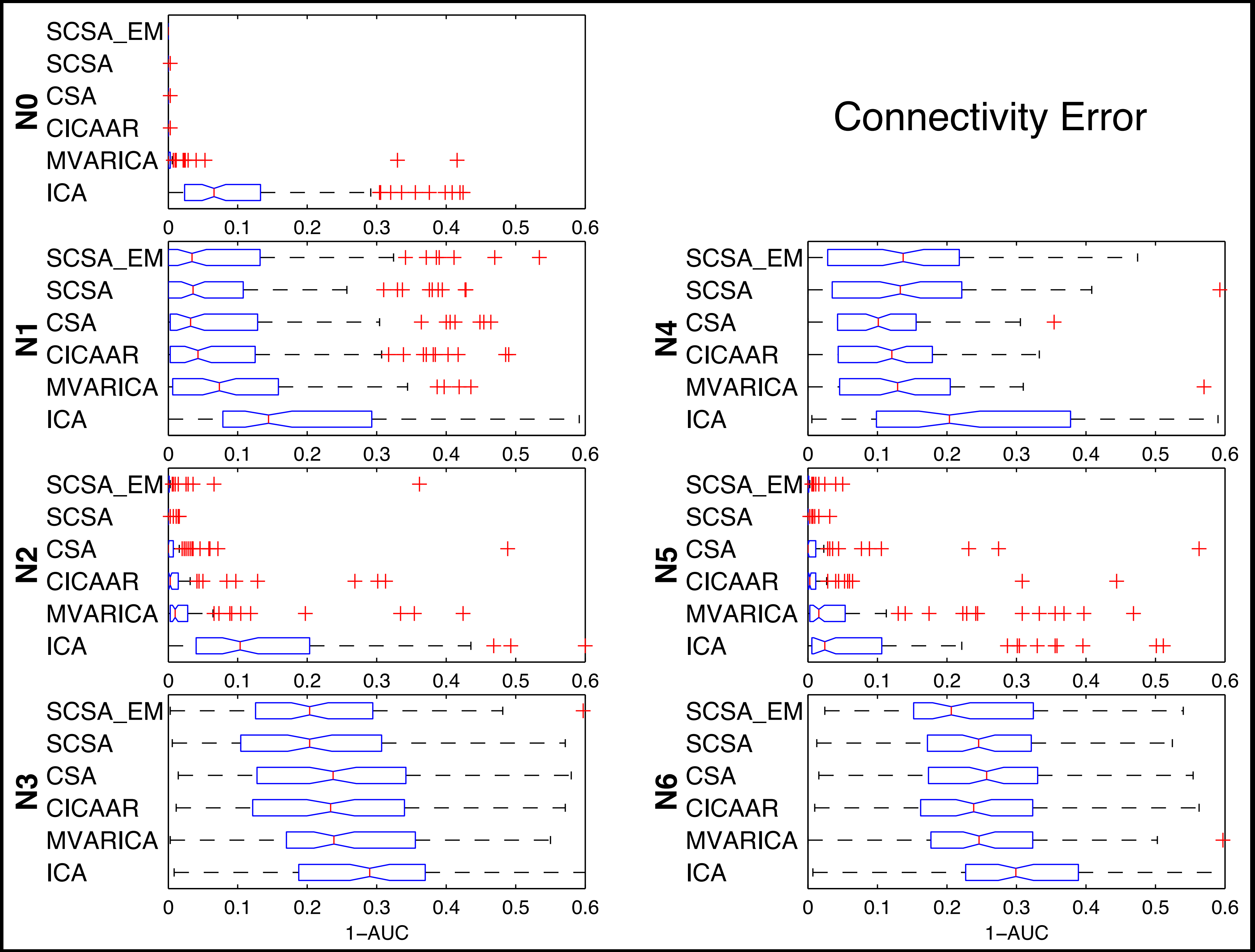
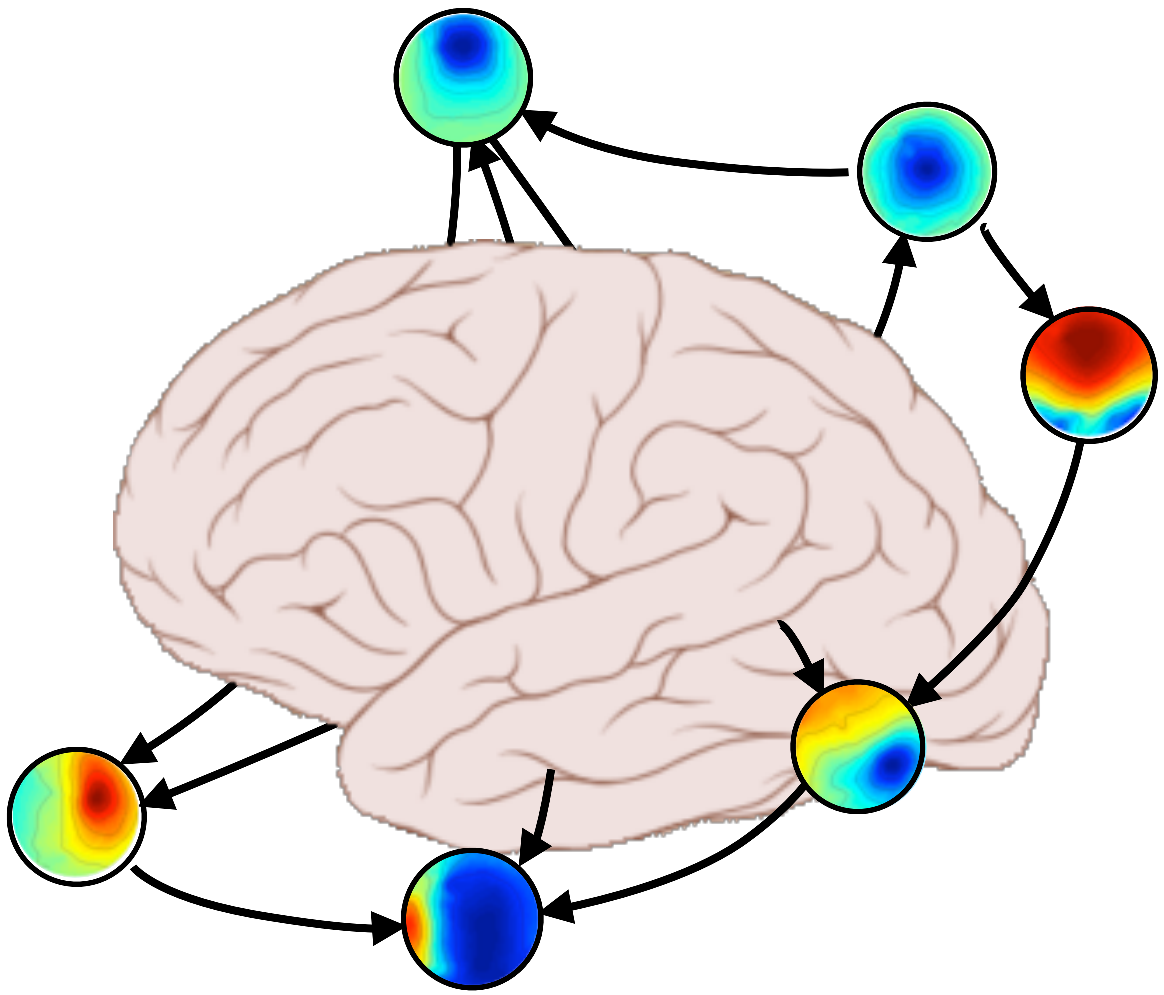
Estimating Dependency of Independent Components ?



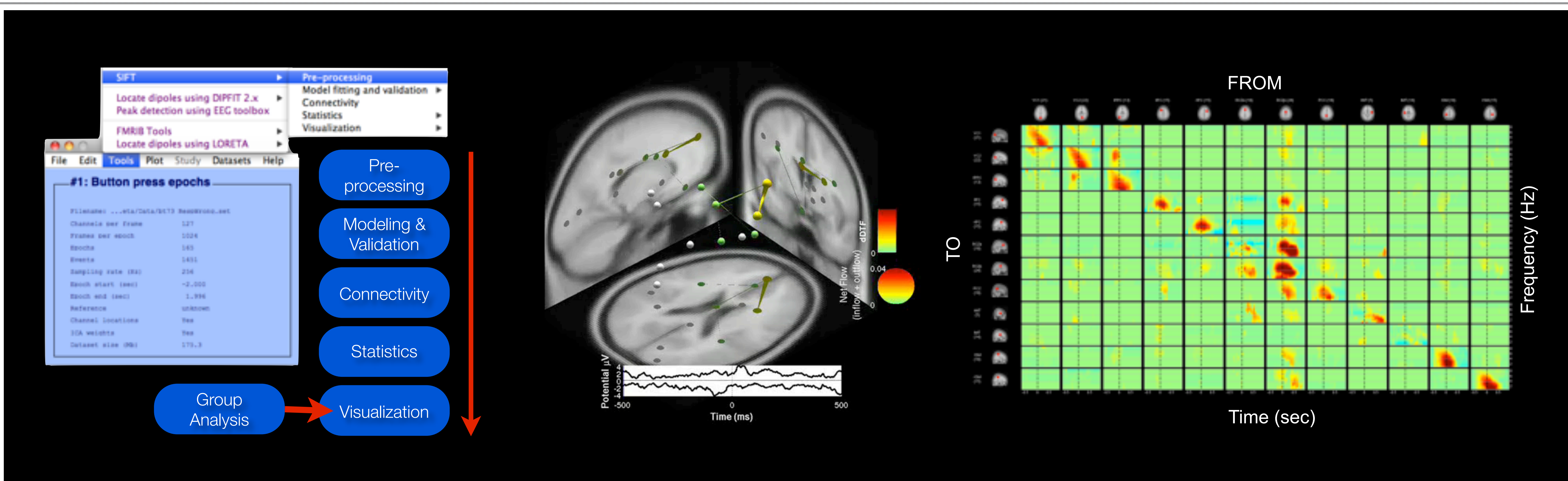
Haufe et al, 2008



SIFT

Source Information Flow Toolbox

Version 0.1-Alpha



Source Information Flow Toolbox (SIFT) 0.1-alpha

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- A new (alpha) toolbox for source-space electrophysiological information flow and causality analysis (single-subject or group analysis) integrated into the EEGLAB software environment

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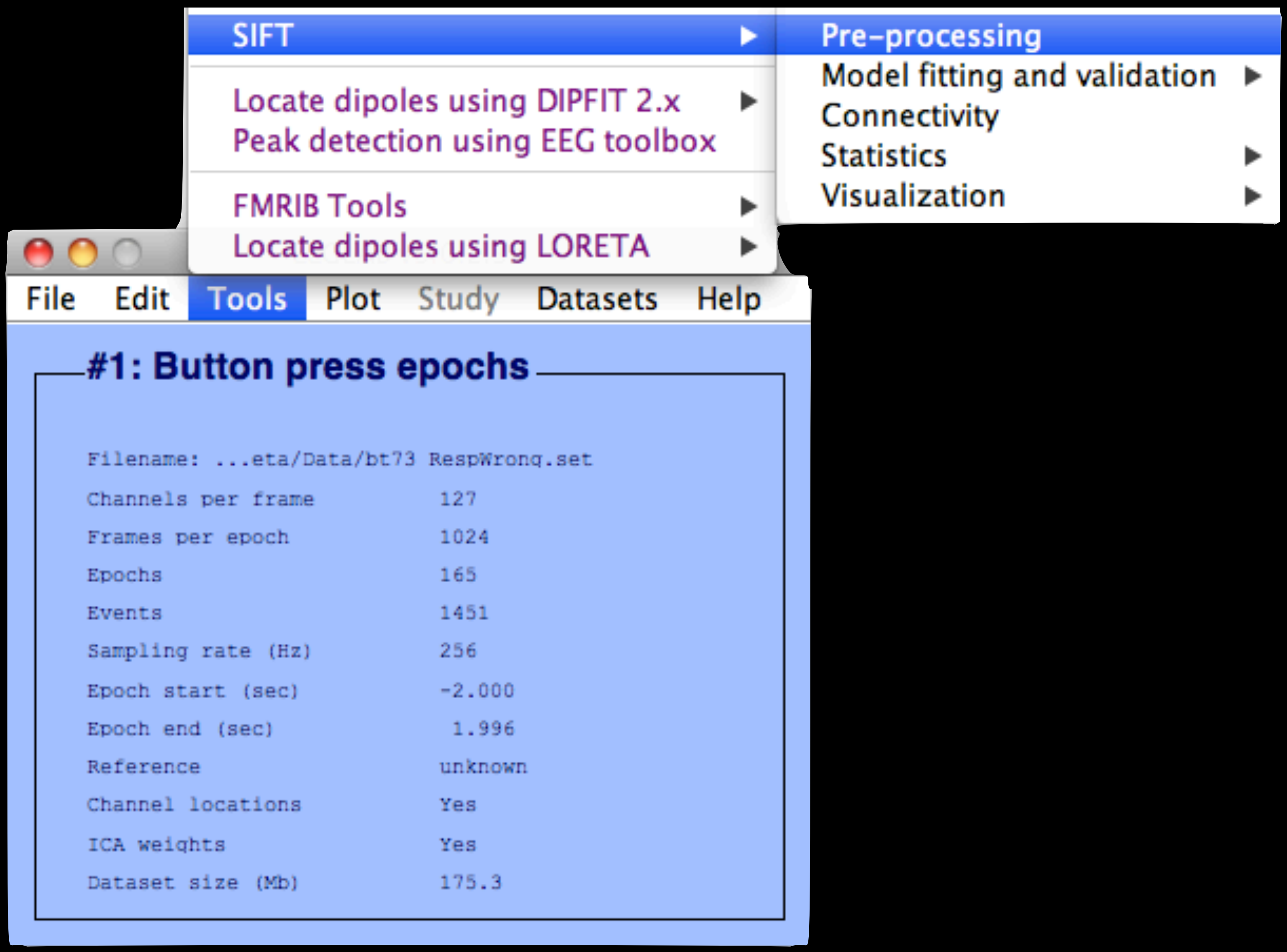
- Novel interactive visualization methods for exploratory analysis of connectivity across time, frequency, and spatial location
- Requirements: EEGLAB, MATLAB™ 2008b, Signal Processing Toolbox, Statistics Toolbox (the latter two dependencies may be removed in the future)

SIFT: Acknowledgements

- Arnaud Delorme
- Scott Makeig
- Christian Kothe
- Nima Bigdely-Shamlo
- Wes Thompson
- SCCN


SIFT
Locate dipoles using DIPFIT 2.x
Peak detection using EEG toolbox
FMRIB Tools
Locate dipoles using LORETA
Pre-processing
Model fitting and validation
Connectivity
Statistics
Visualization
File
Edit
Tools
Plot
Study
Datasets
Help
#1: Button press epochs
Filename: ...eta/Data/bt73 RespWrong.set
Channels per frame 127
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Epochs 165
Events 1451
Sampling rate (Hz) 256
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ICA weights Yes
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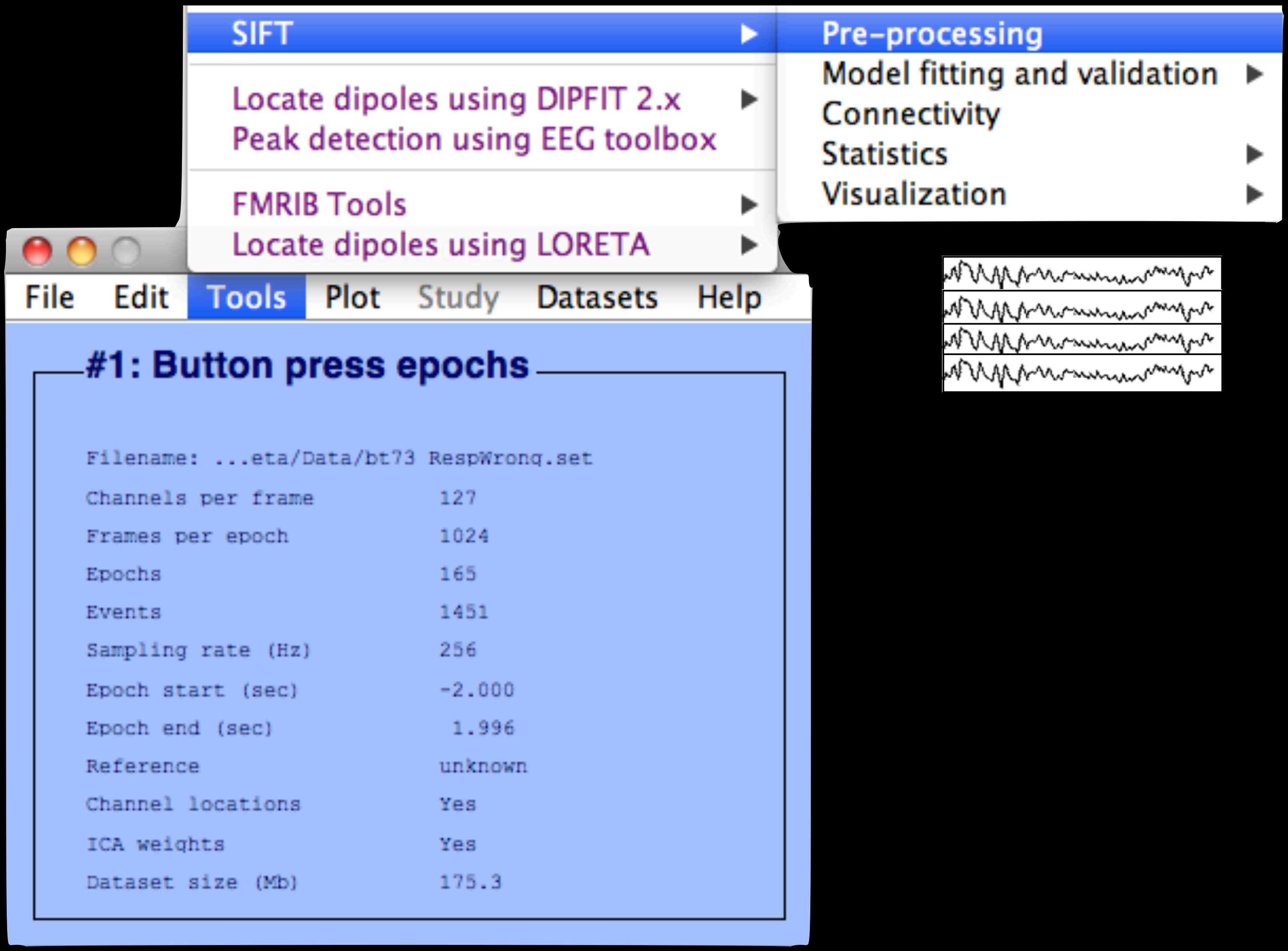
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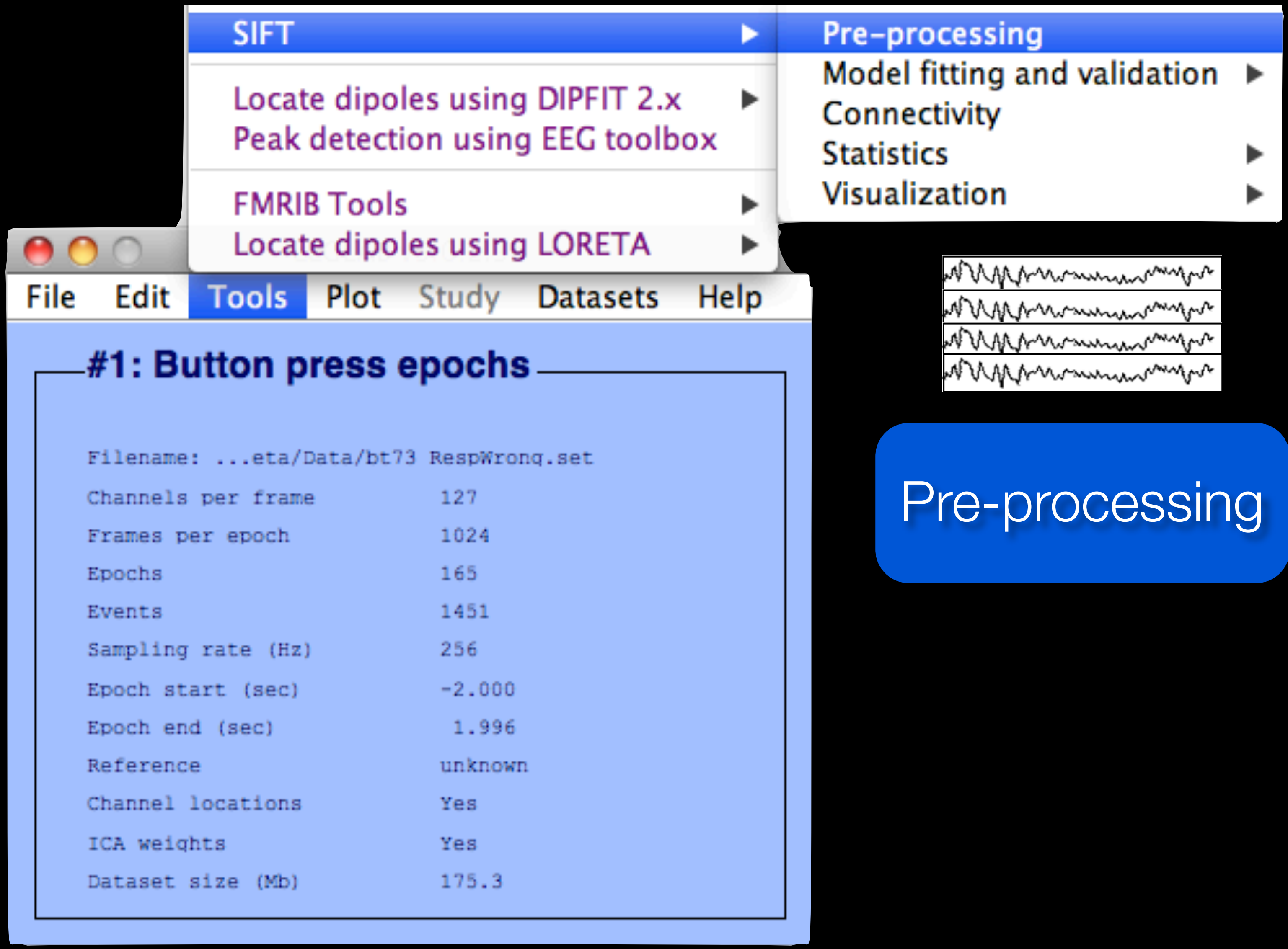

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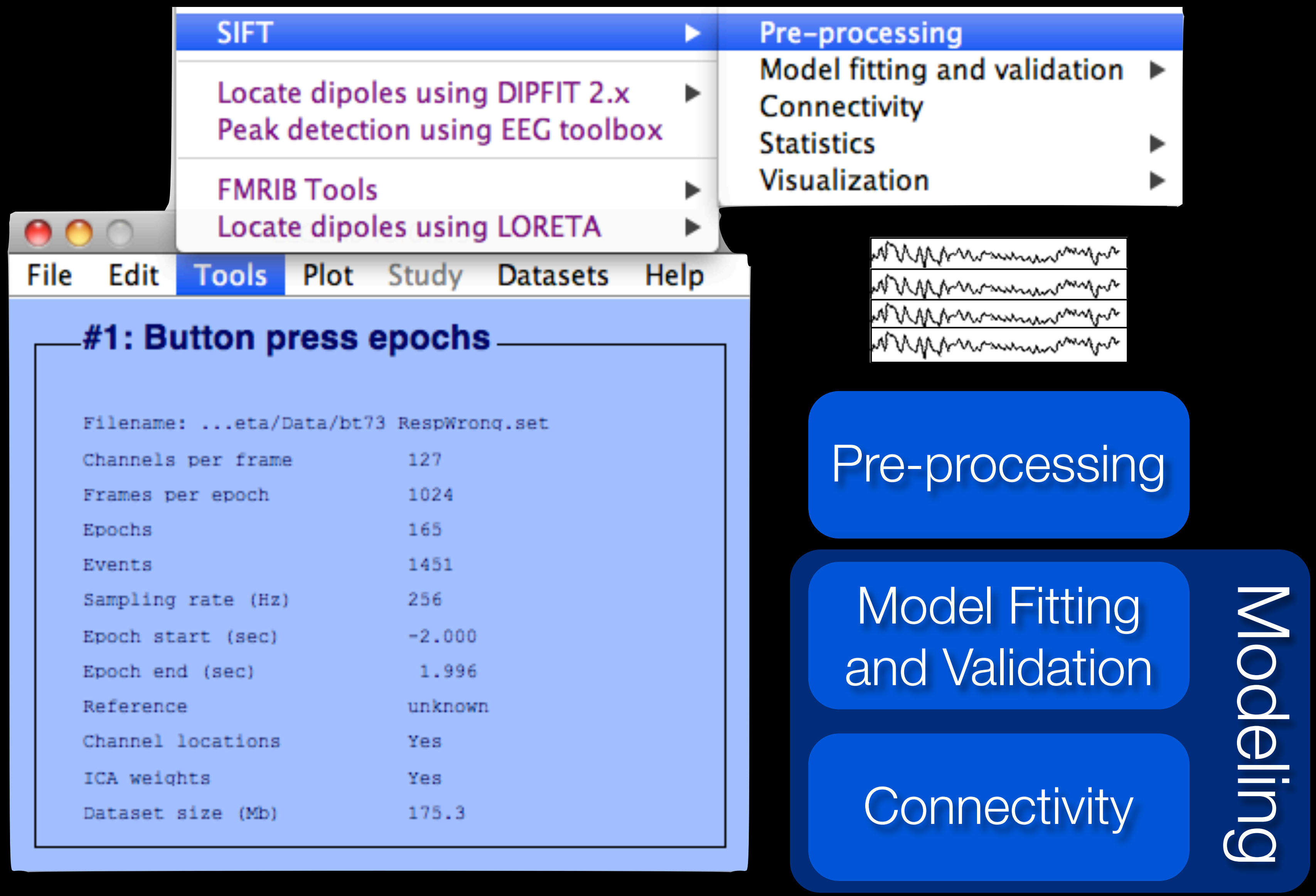
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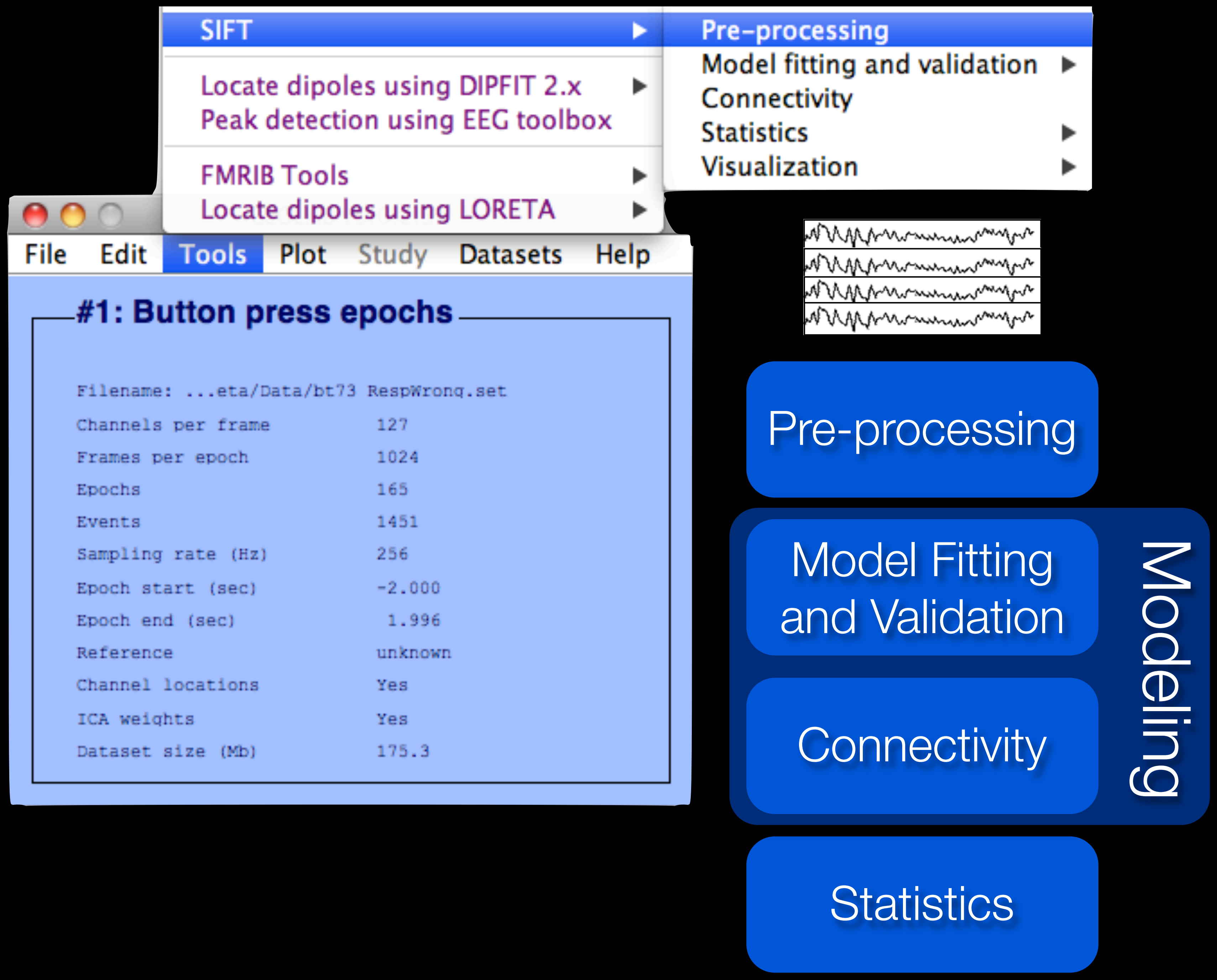
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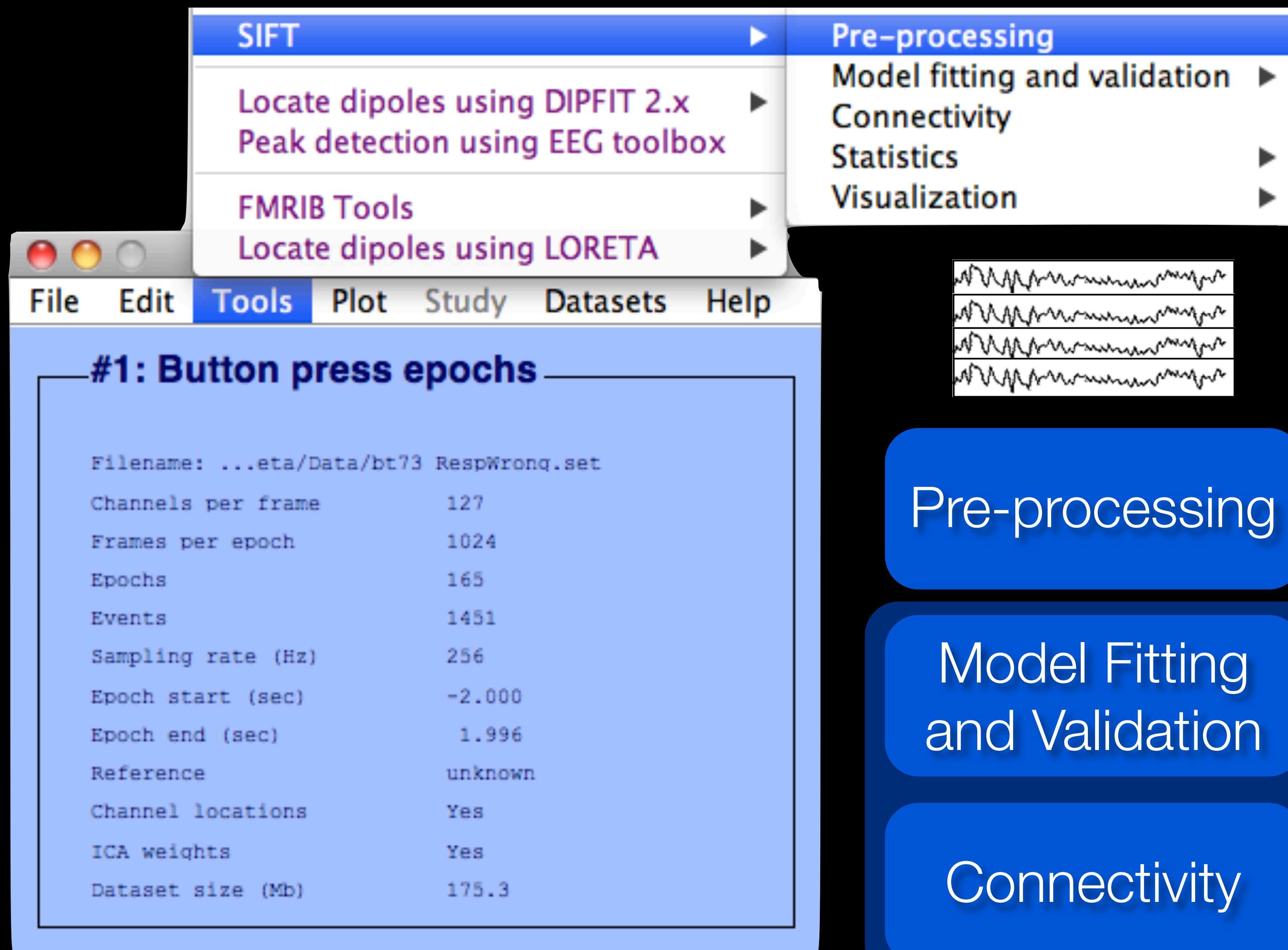
Peak detection using EEG toolbox
FMRIB Tools
Locate dipoles using LORETA
Pre-processing
Model fitting and validation
Connectivity
Statistics
Visualization
File
Edit
Tools
Plot
Study
Datasets
Help
#1: Button press epochs
Filename: ...eta/Data/bt73 RespWrong.set
Channels per frame 127
Frames per epoch 1024
Epochs 165
Events 1451
Sampling rate (Hz) 256
Epoch start (sec) -2.000
Epoch end (sec) 1.996
Reference unknown
Channel locations Yes
ICA weights Yes
Dataset size (Mb) 175.3
Pre-processing
Model Fitting and Validation
Connectivity
Modeling
Statistics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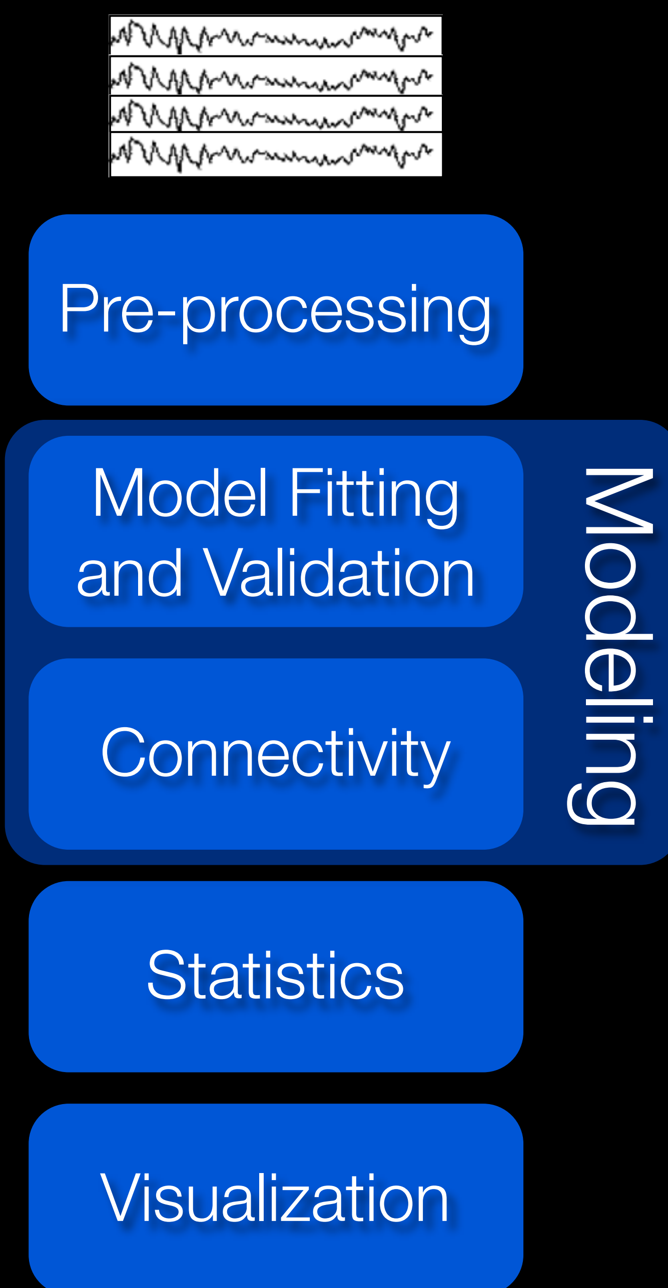
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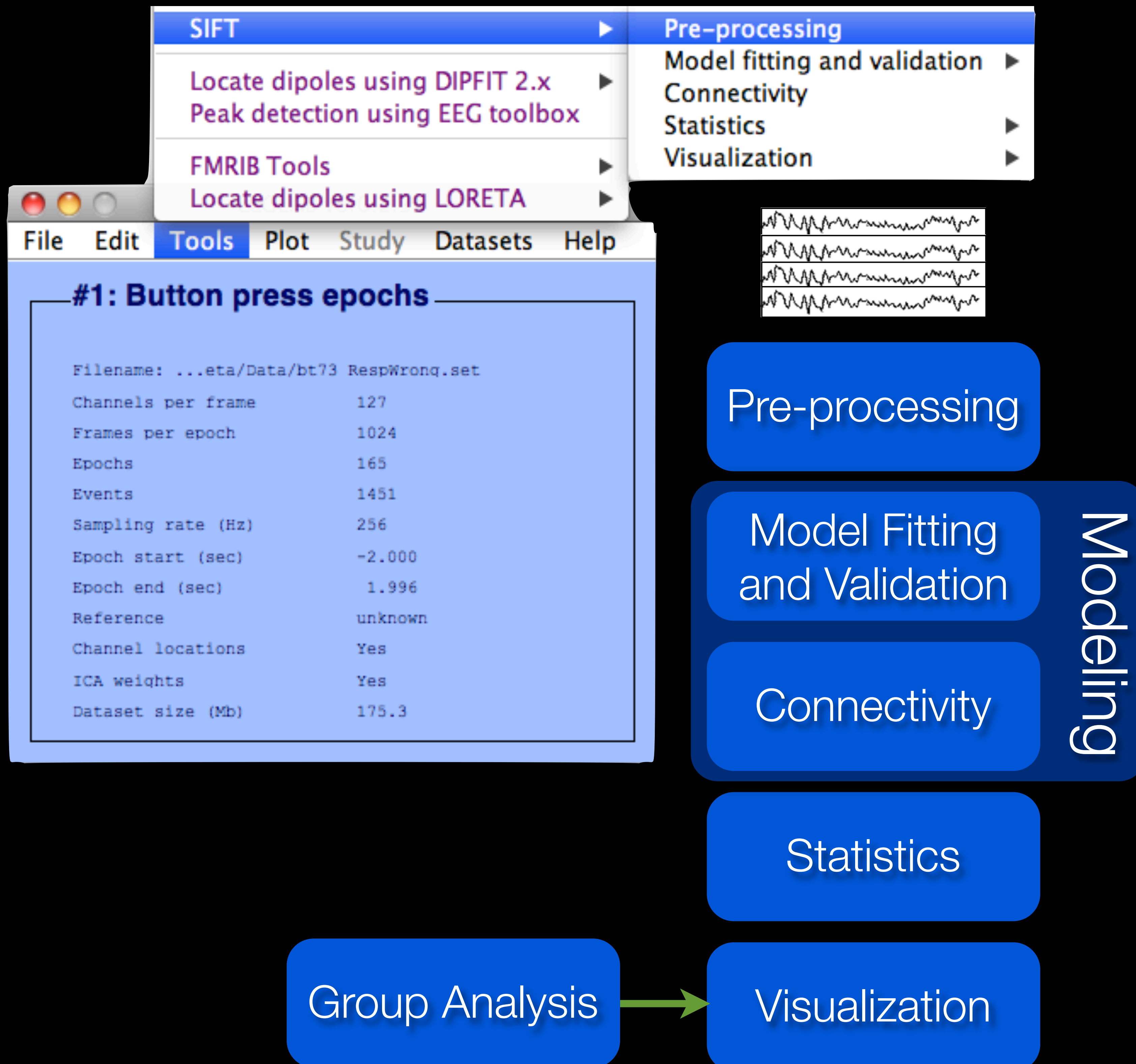
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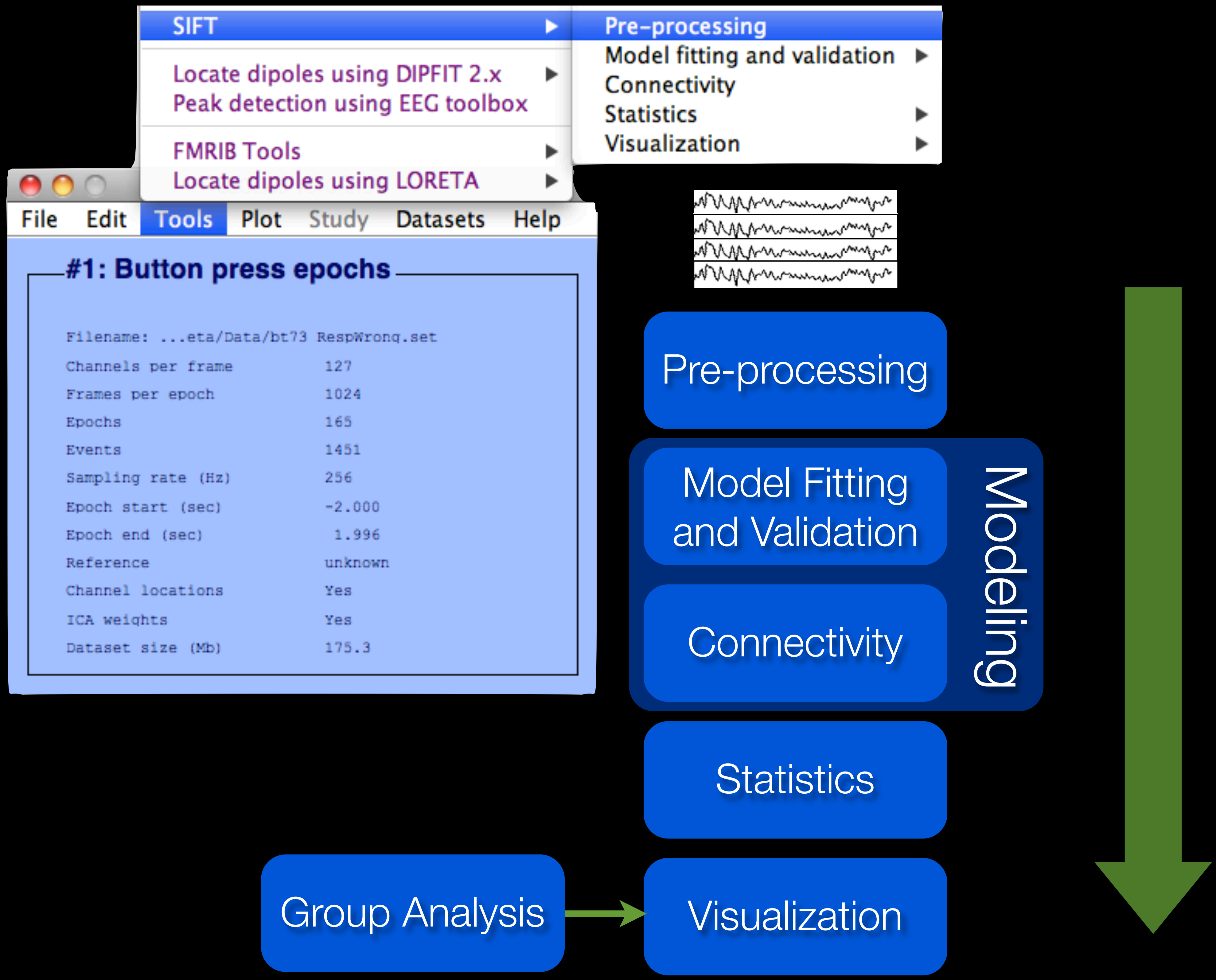
Group Analysis
Visualization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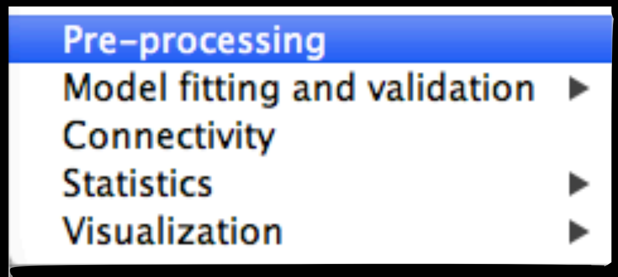
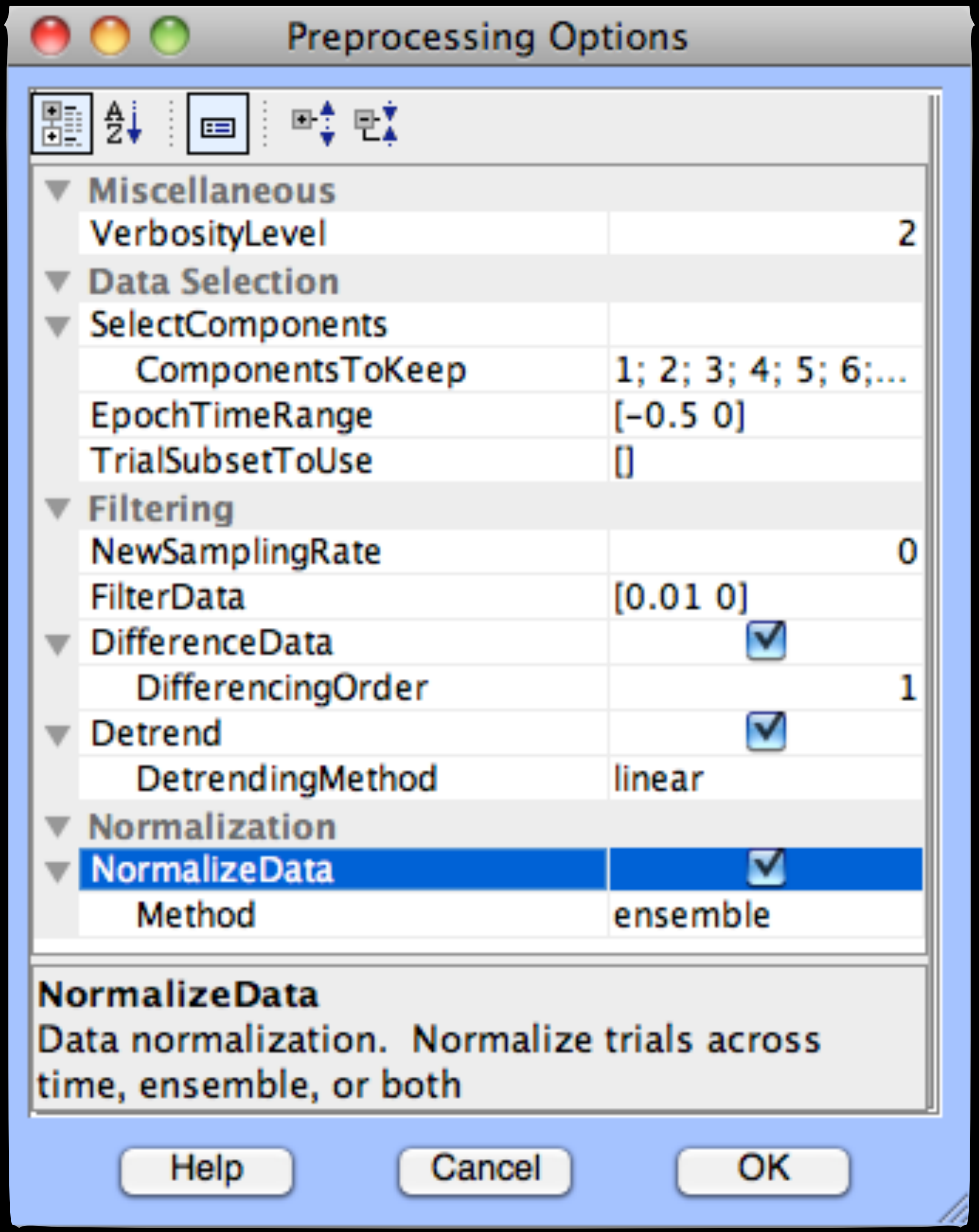
Preprocessing | Modeling | Statistics | Visualization

- **Source-separation and localization**
  (performed externally using EEGLAB or other toolboxes)
- Filtering/Detrending
- Downsampling
- Differencing
- Normalization (temporal or ensemble)
- Trial balancing
- Tests for stationarity of the data (linear methods)

...

Preprocessing | Modeling | Statistics | Visualization





Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

Preprocessing

Modeling

Statistics

Visualization

Model Fitting

Validation

Connectivity

Preprocessing | **Modeling** | Statistics | Visualization

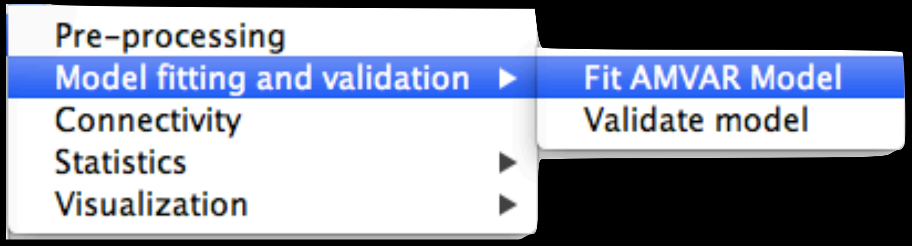
Model Fitting | Validation | Connectivity

	Linear	Nonlinear/Nonstationary
Parametric	MVAR Modeling Sparse MVAR Bayesian MVAR Kalman Filtering	Dual Extended Kalman Filtering
Nonparametric	Nonparametric MVAR (minimum-phase spectral factorization) Multivariate phase distribution	Transfer Entropy

fully implemented — partially-developed — coming soon

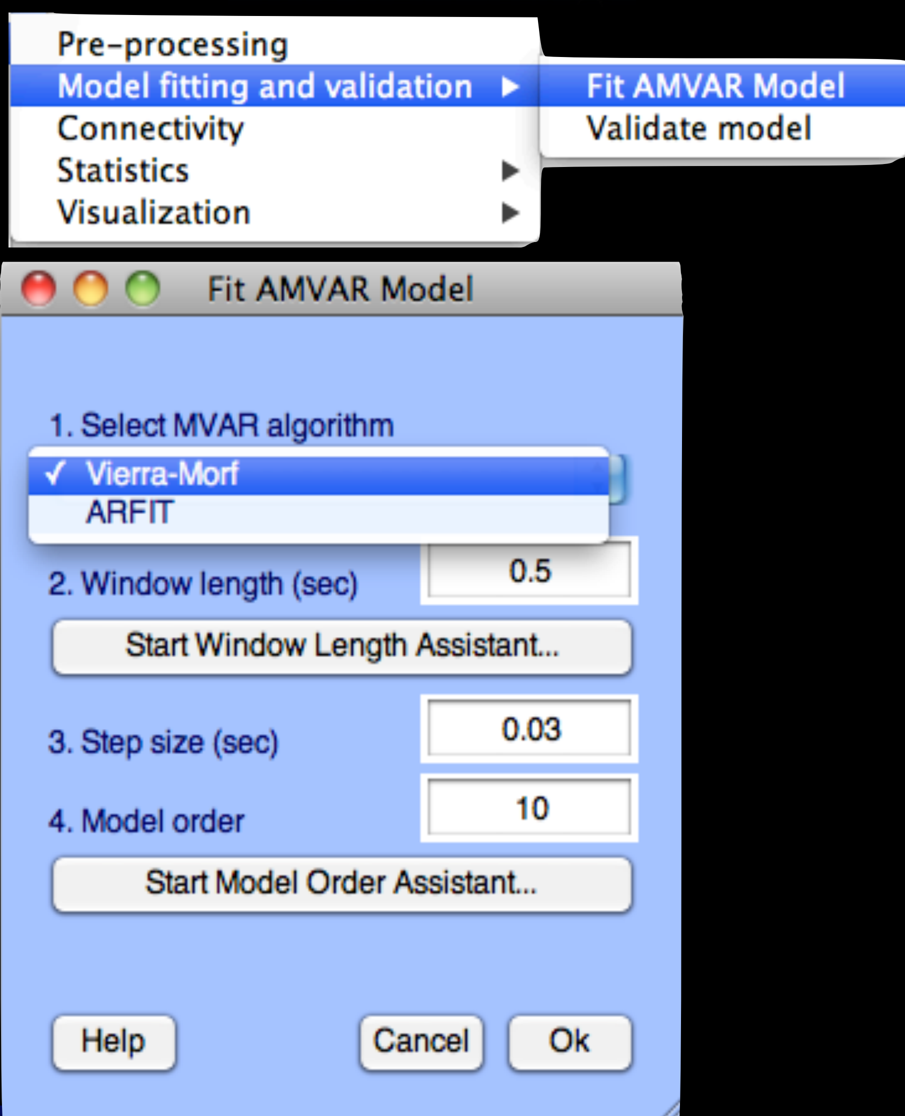
Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | Connectivity



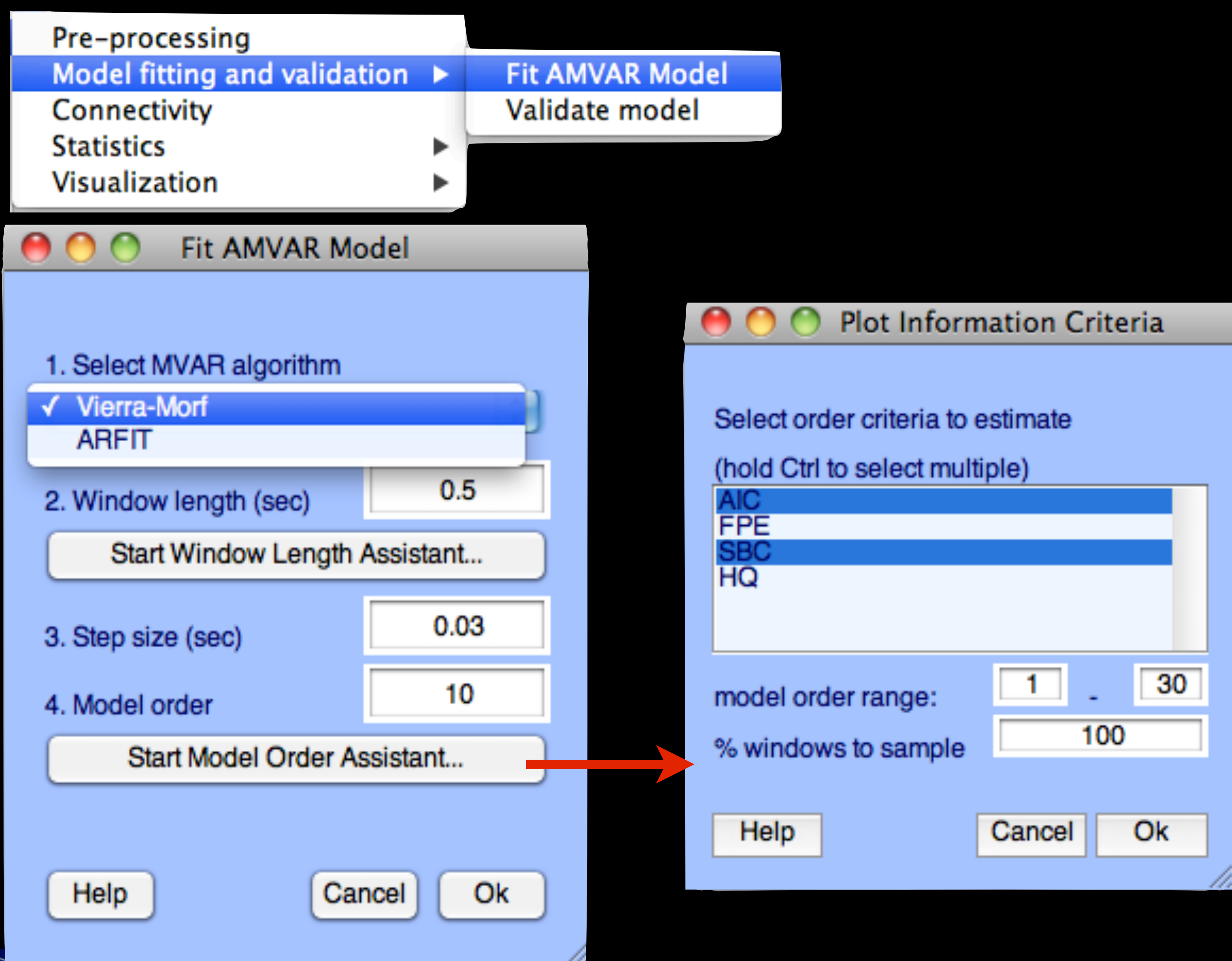
Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | Connectivity



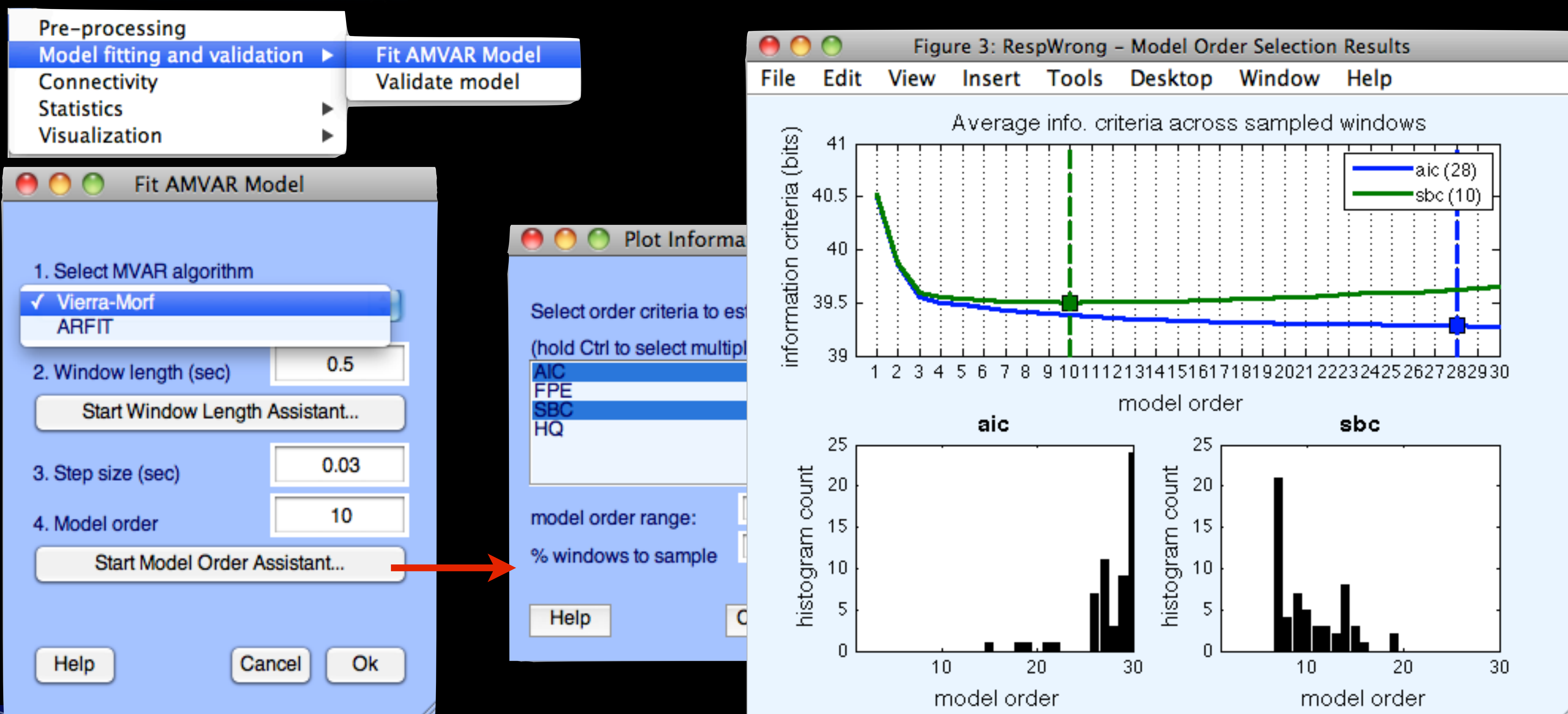
Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | Connectivity



Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | Connectivity



Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | **Validation** | Connectivity

- Whiteness of Residuals
  - Portmanteau tests
  - Autocorrelation function
- Model Consistency
- Model Stability

fully implemented | partially-developed | coming soon

Preprocessing

Modeling

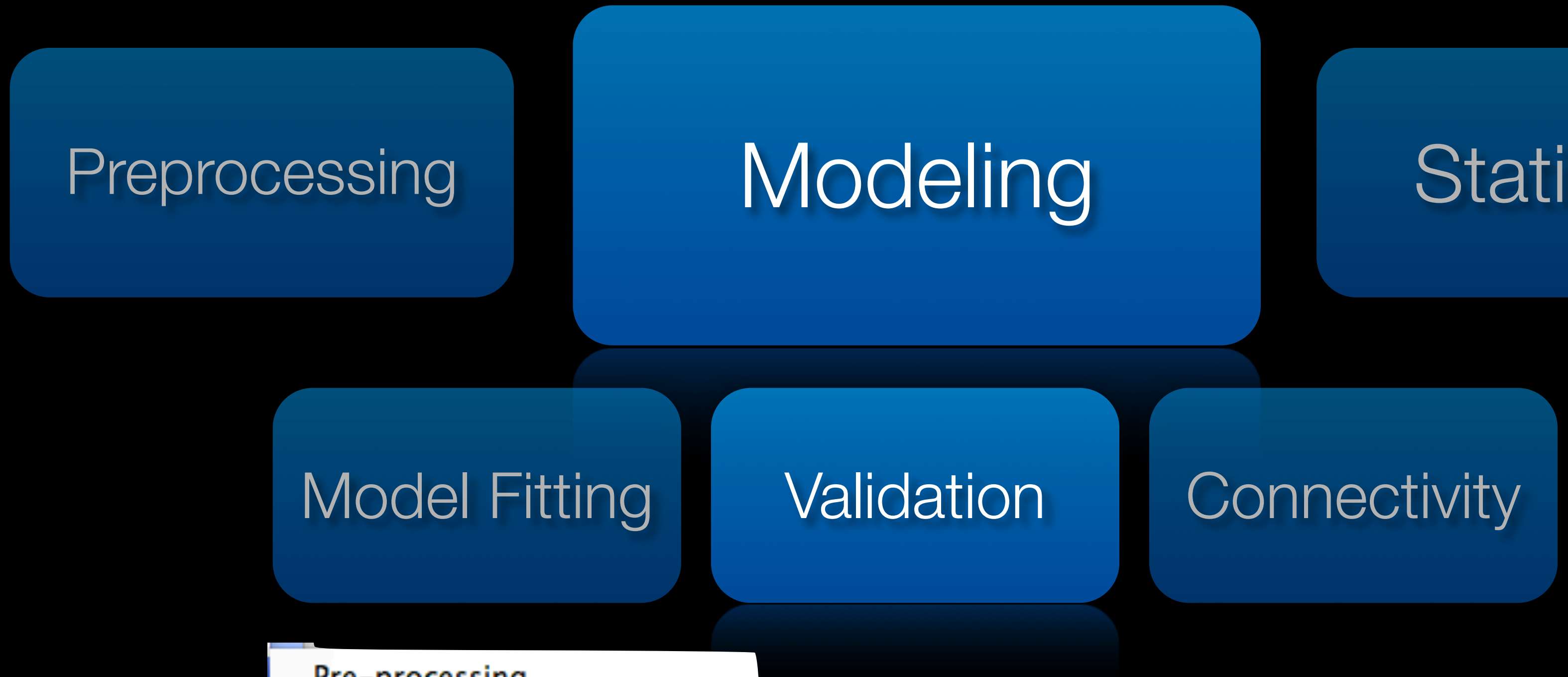
- Model Fitting
- **Validation**
- Connectivity

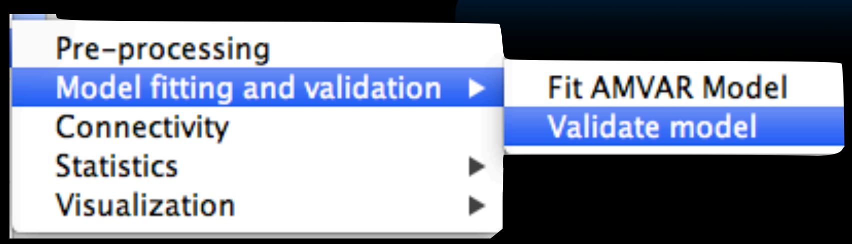
Statistics

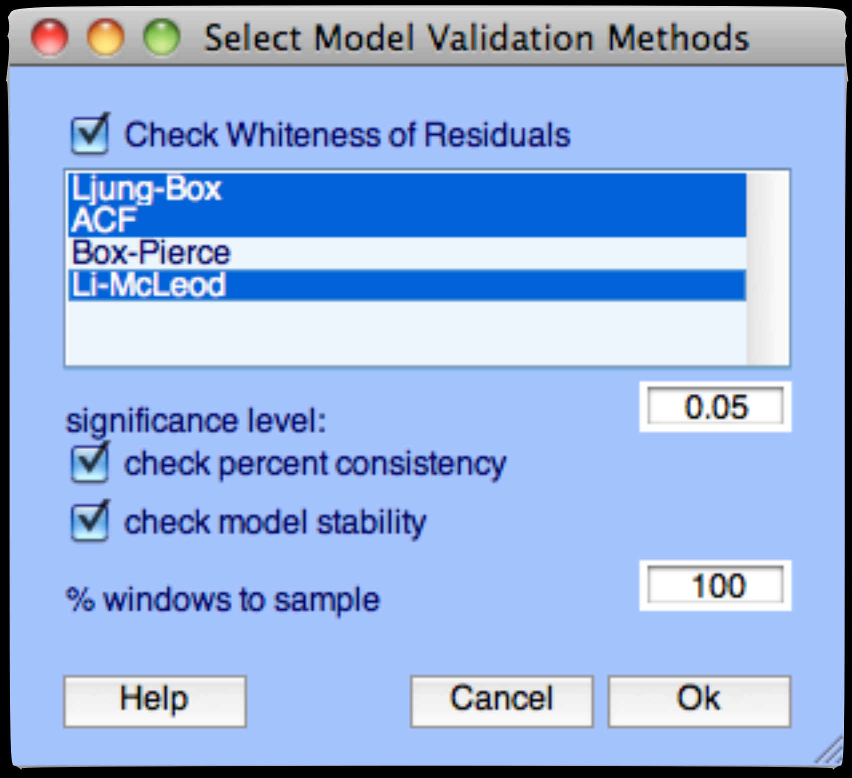
Visualization

Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | **Validation** | Connectivity

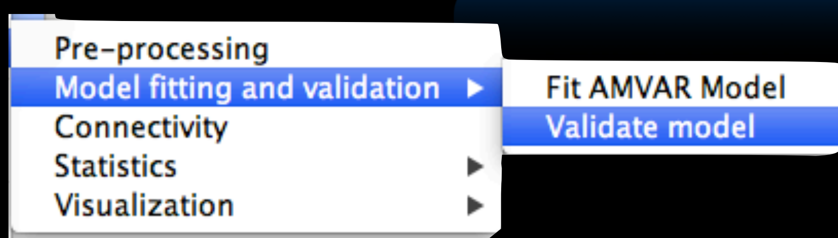

Preprocessing
Modeling
Statistics
Visualization
Model Fitting
Validation
Connectivity

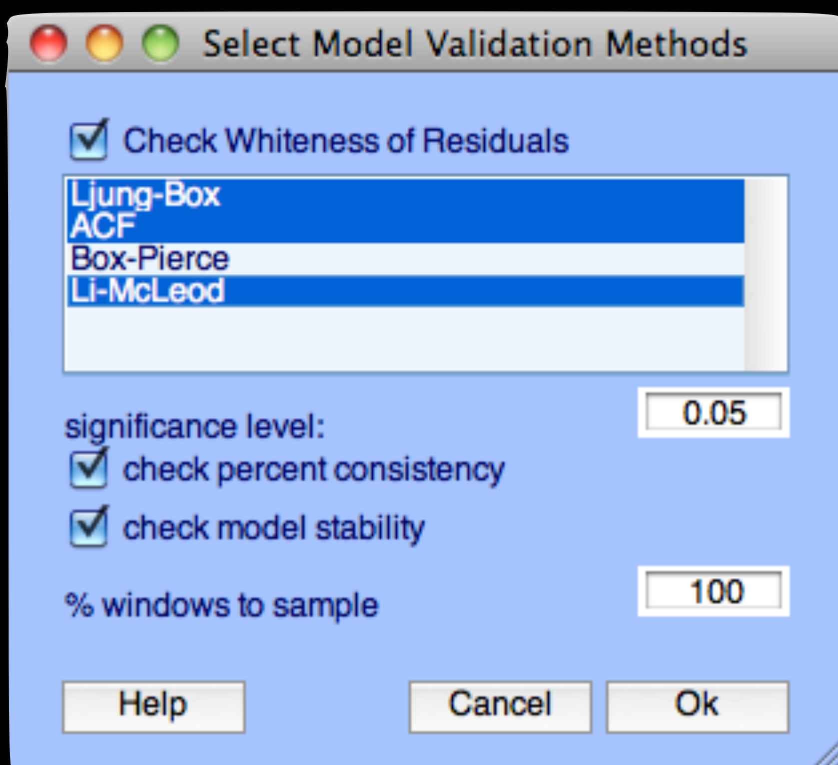

Pre-processing
Model fitting and validation
Connectivity
Statistics
Visualization
Fit AMVAR Model
Validate model

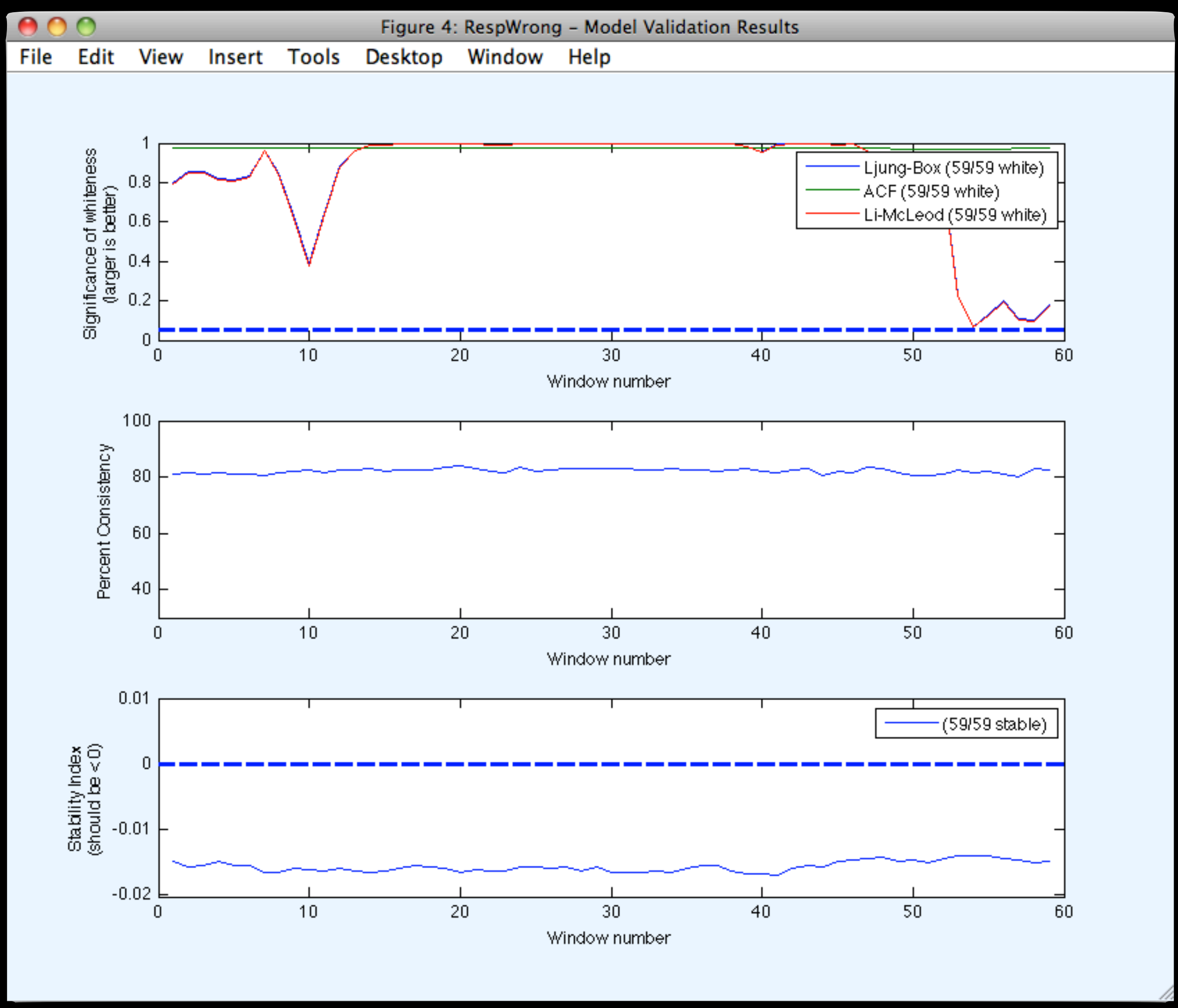

Select Model Validation Methods
Check Whiteness of Residuals
Ljung-Box
ACF
Box-Pierce
Li-McLeod
significance level:
0.05
check percent consistency
check model stability
% windows to sample
100
Help
Cancel
Ok

Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | **Validation** | Connectivity







Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | **Connectivity**

MVAR	Other
-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) -Granger-Geweke Causality (GGC) -Conditional GGC -Blockwise GGC *	-Transfer Entropy * -Multivariate phase-locking value (mPLV) *

fully implemented | partially-developed | coming soon

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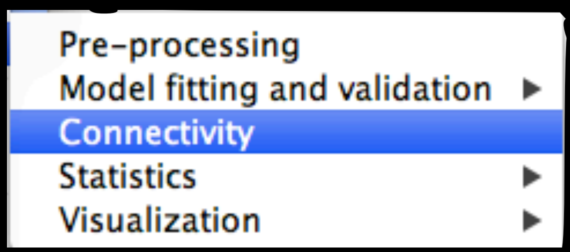
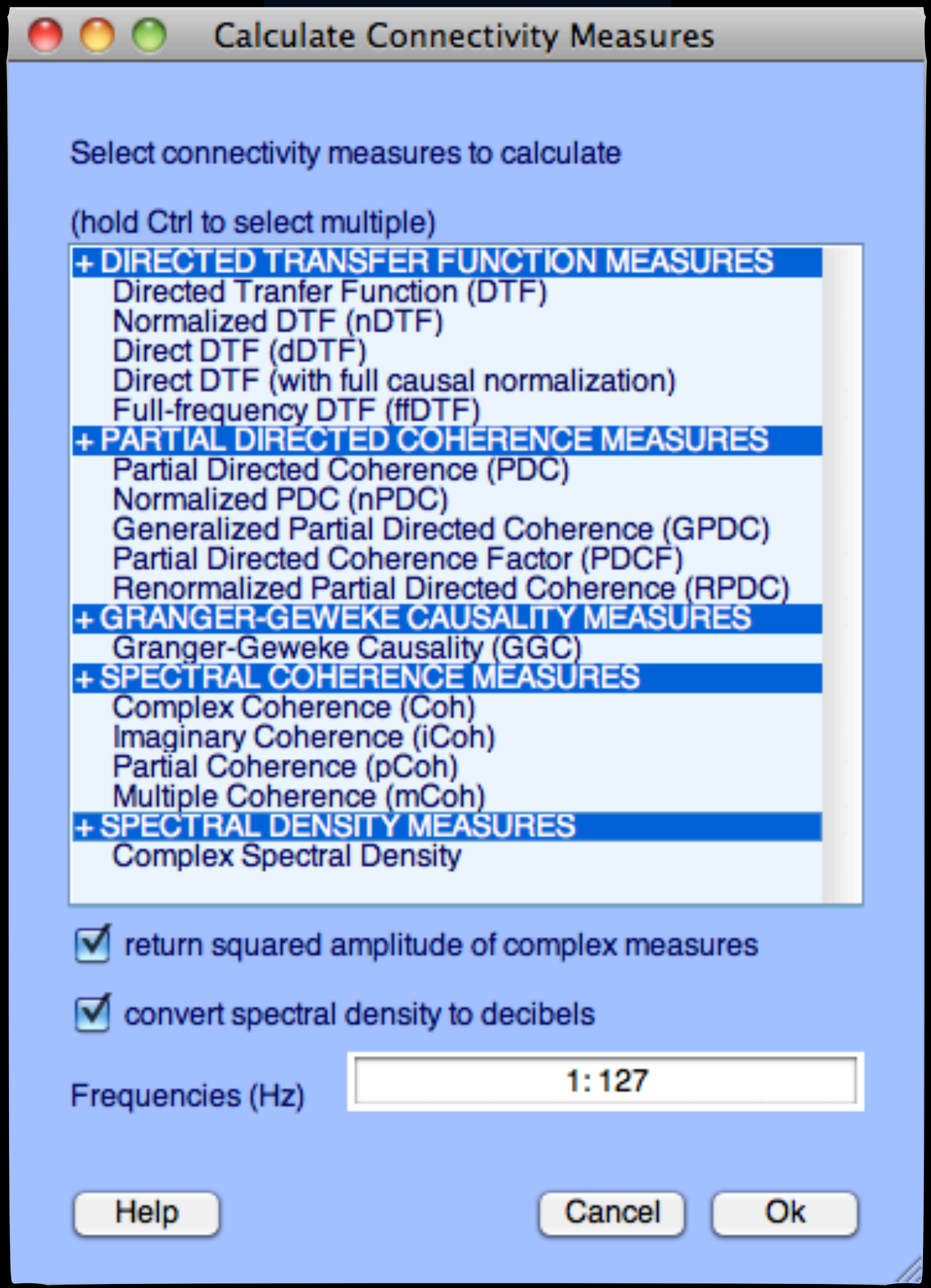
Preprocessing | **Modeling** | Statistics | Visualization

Model Fitting | Validation | **Connectivity**





Preprocessing | Modeling | **Statistics** | Visualization

Preprocessing | Modeling | **Statistics** | Visualization

Parametric

Asymptotic analytic estimates of confidence intervals

- Applies to: PDC, nPDC, DTF, nDTF, rPDC
- Tests: H_{null}, H_{base}, H_{AB}

Confidence intervals using thin-plate smoothing splines

- Applies to: dDTF
- Tests: H_{base}, H_{AB}

$H_{null}: \mathbf{C}_{ij} \leq \mathbf{C}_{null}$ $\quad H_{base}: \mathbf{C}_{ij} \leq \mathbf{C}_{baseline}$ $\quad H_{AB}: \mathbf{C}^{A}_{ij} = \mathbf{C}^{B}_{ij}$

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | **Statistics** | Visualization

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Asymptotic analytic estimates of confidence intervals
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Confidence intervals using thin-plate smoothing splines
- Applies to: dDTF
- Tests: H_{base}, H_{AB}

Non-parametric

Phase-randomization
- Applies to: all
- Tests: H_{null}

Permutation Tests
- Applies to: all
- Tests: H_{AB}, H_{base}

Bootstrap and Jacknife
- Applies to: all
- Tests: H_{AB}, H_{base}

H_{null} : $\mathbf{C}_{ij} \leq \mathbf{C}_{null}$ $\quad$ H_{base}: $\mathbf{C}_{ij} \leq \mathbf{C}_{baseline}$ $\quad$ H_{AB}: $\mathbf{C}^{A}_{ij} = \mathbf{C}^{B}_{ij}$

fully implemented | partially-developed | coming soon

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Preprocessing | Modeling | Statistics | **Visualization**

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Swartz Center for Computational Neuroscience

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Density Movie

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Density Movie

Directed Graphs on anatomicals (ECoG)

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Density Movie

Directed Graphs on anatomicals (ECoG)

and more...

fully implemented | partially-developed | coming soon

Preprocessing | Modeling | Statistics | **Visualization**

Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Density Movie

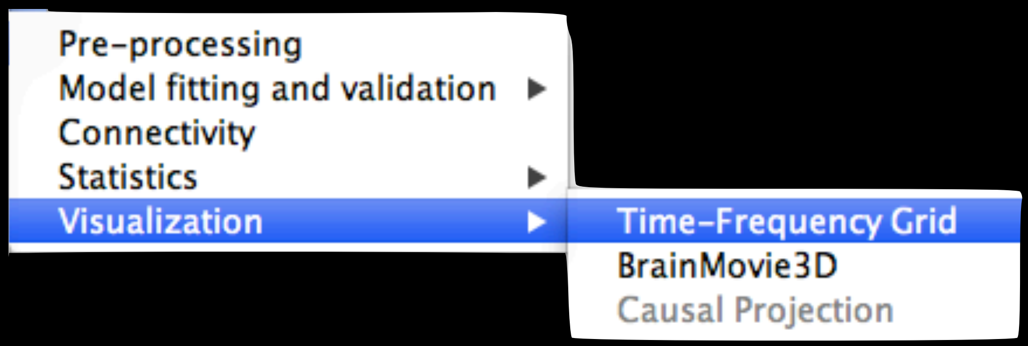
Directed Graphs on anatomicals (ECoG)

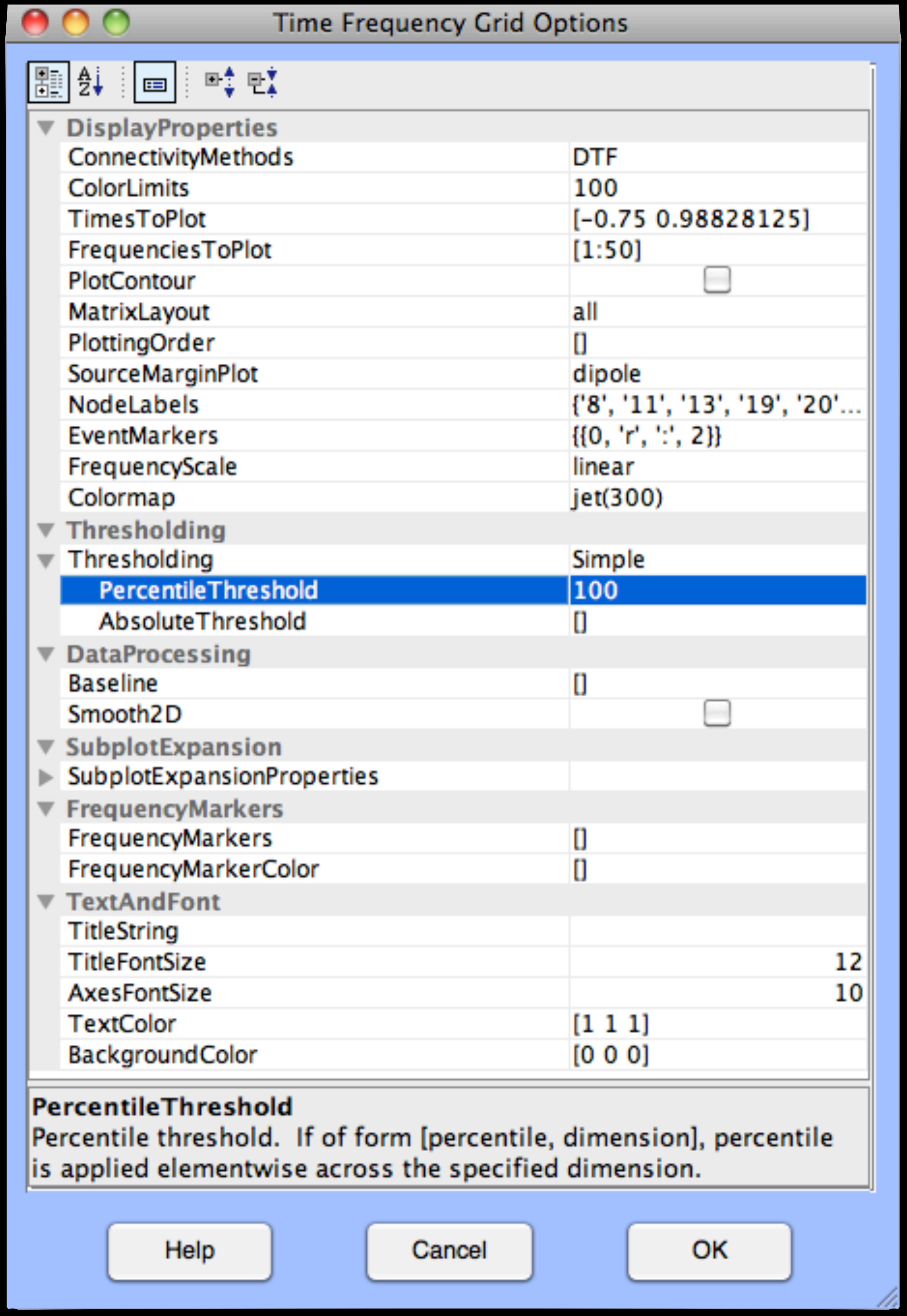
and more...

All of these currently support single-subject or (in beta version) group analysis
ROI connectivity analysis can currently be performed using dipole clustering

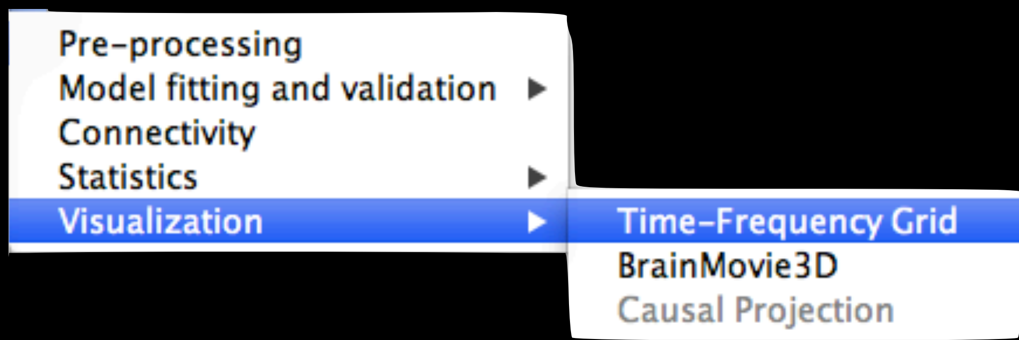
fully implemented | partially-developed | coming soon

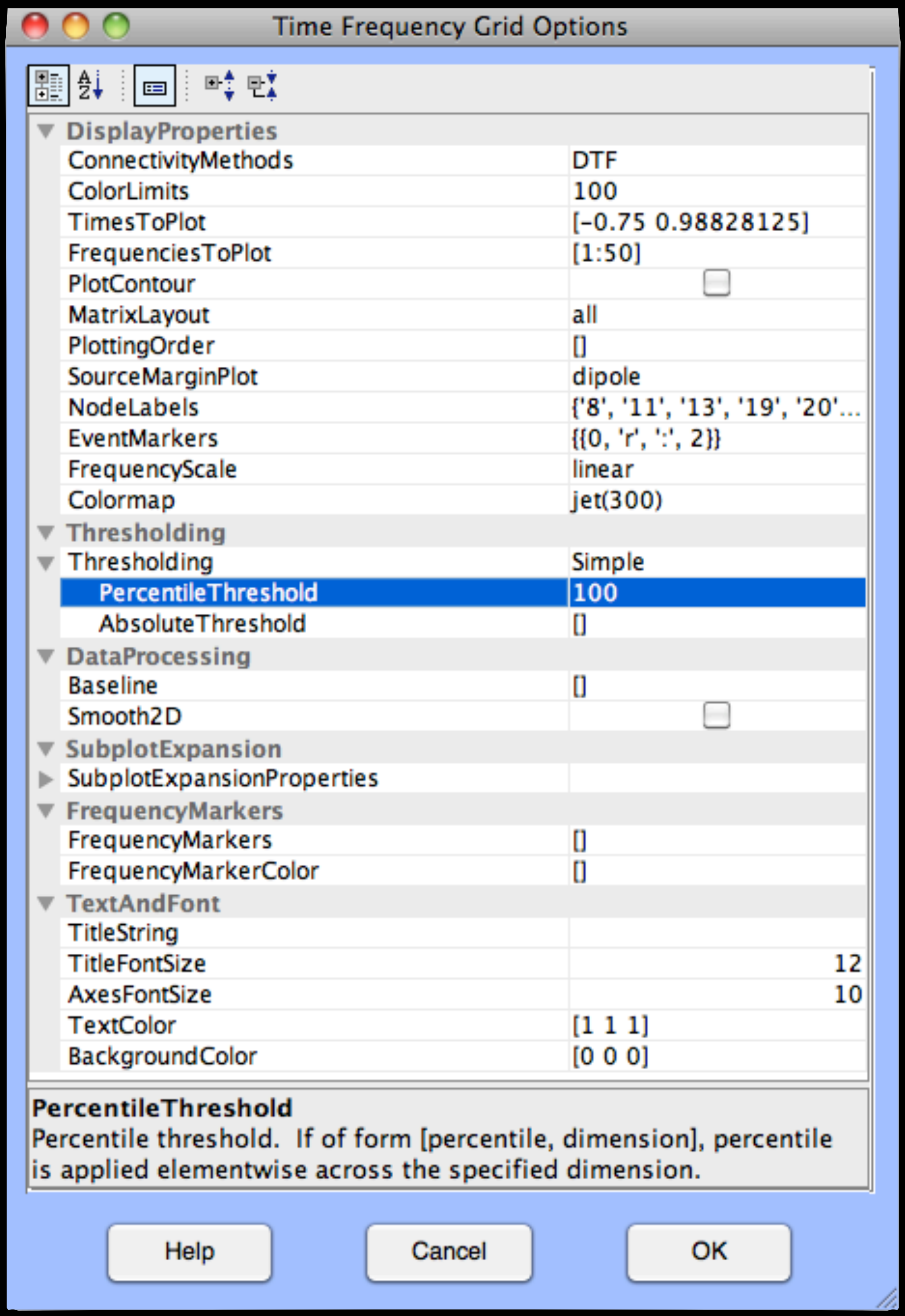
Interactive Time-Frequency Grid



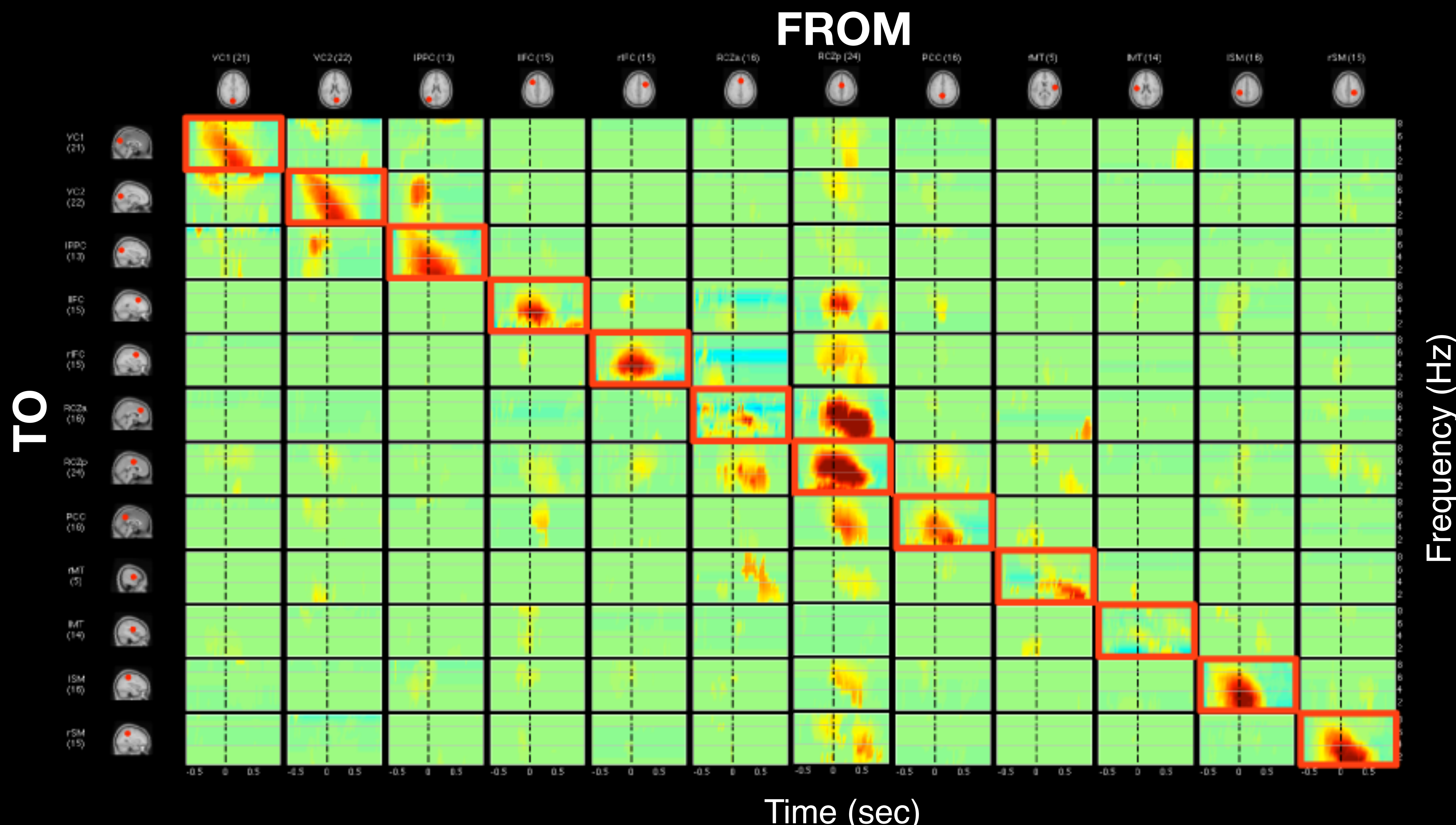


Interactive Time-Frequency Grid





Causal Time-Frequency Grid



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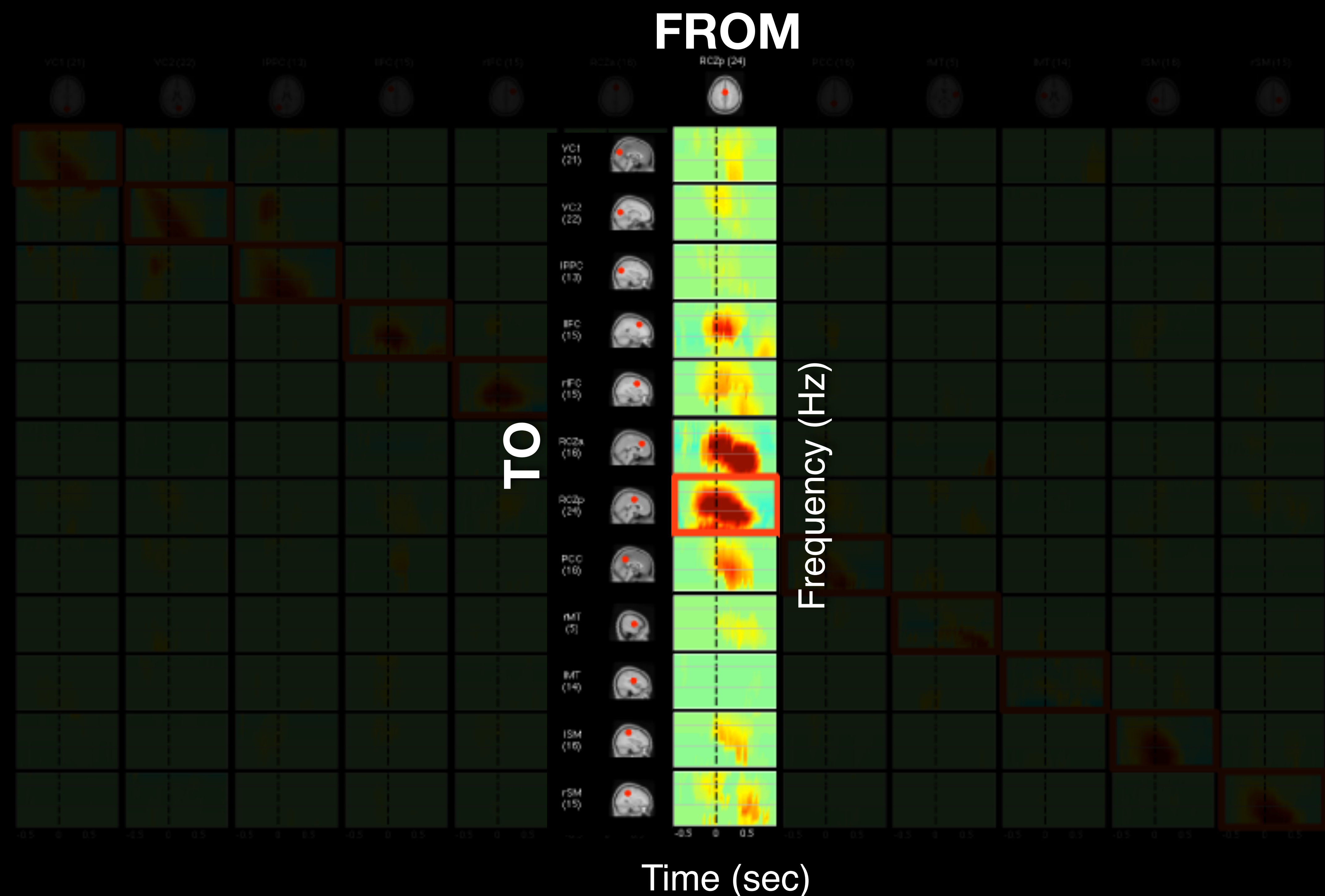

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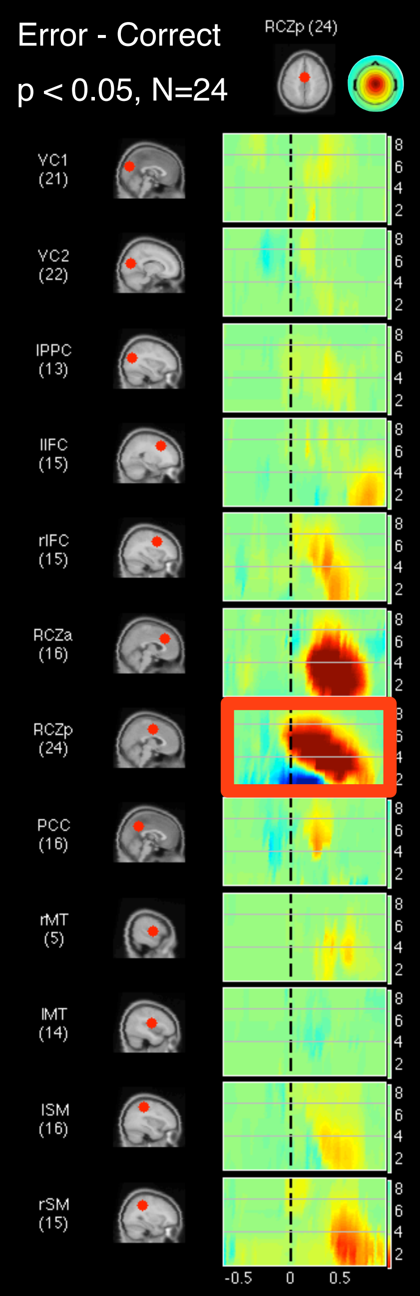

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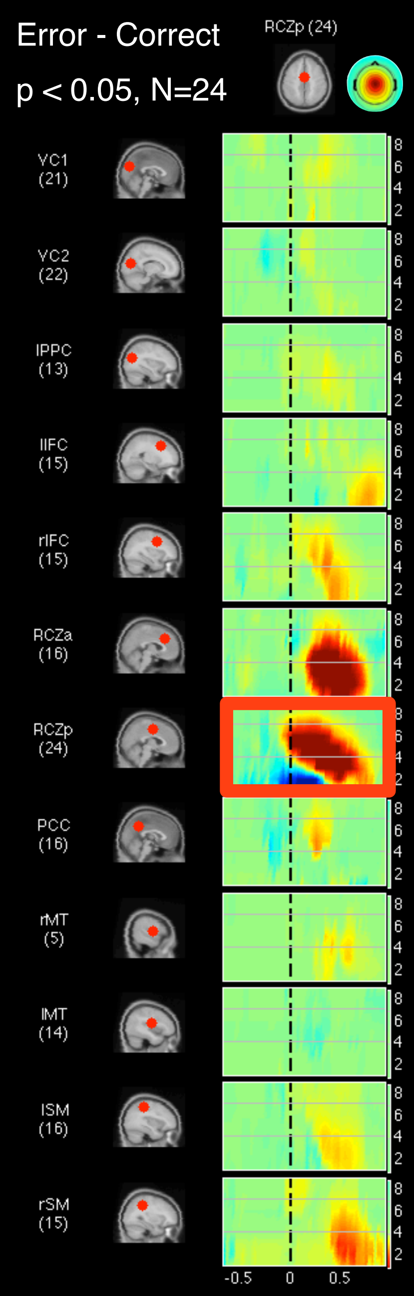

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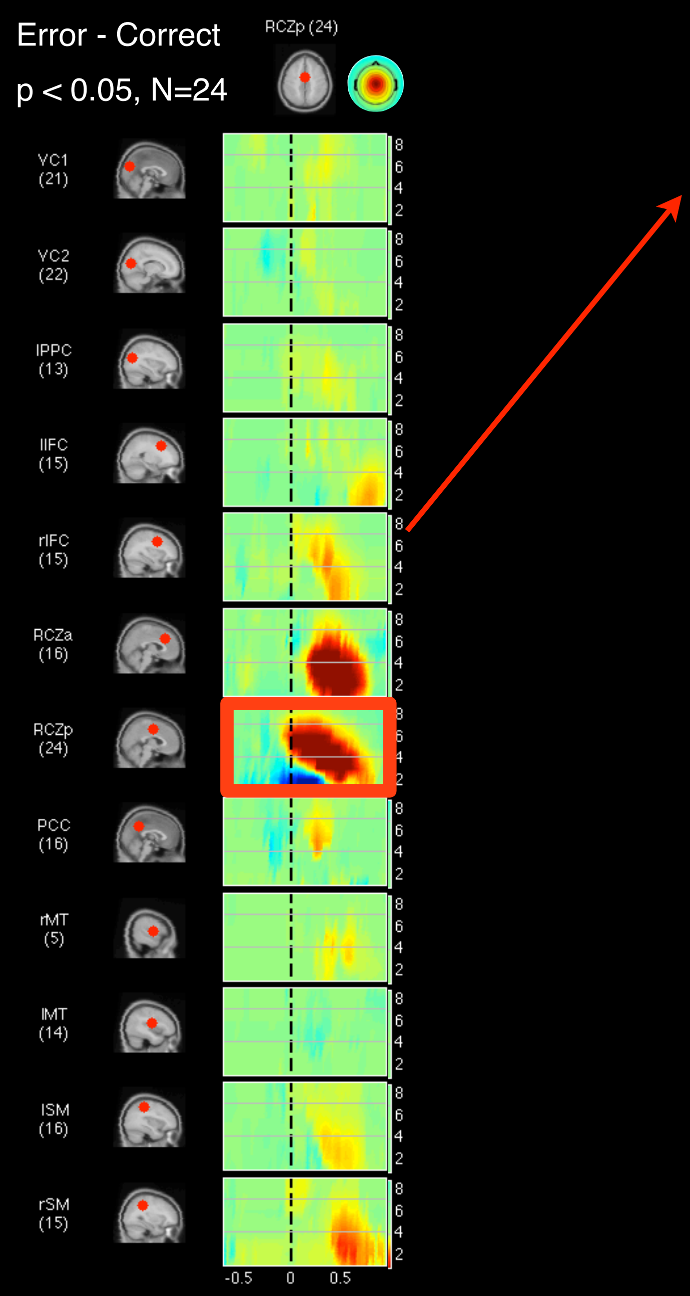

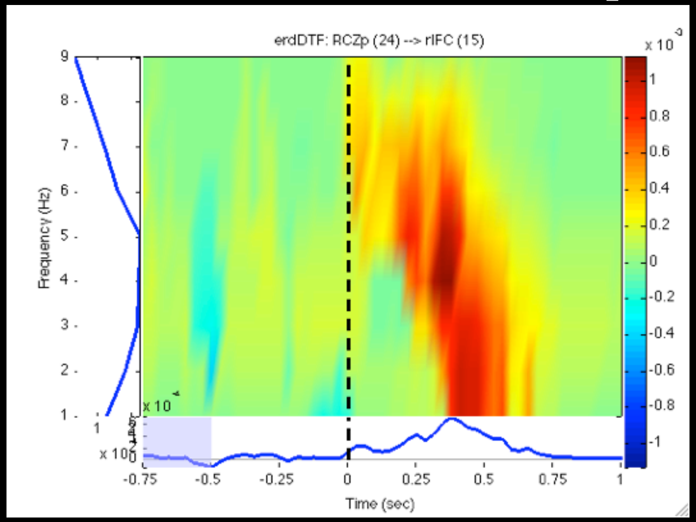

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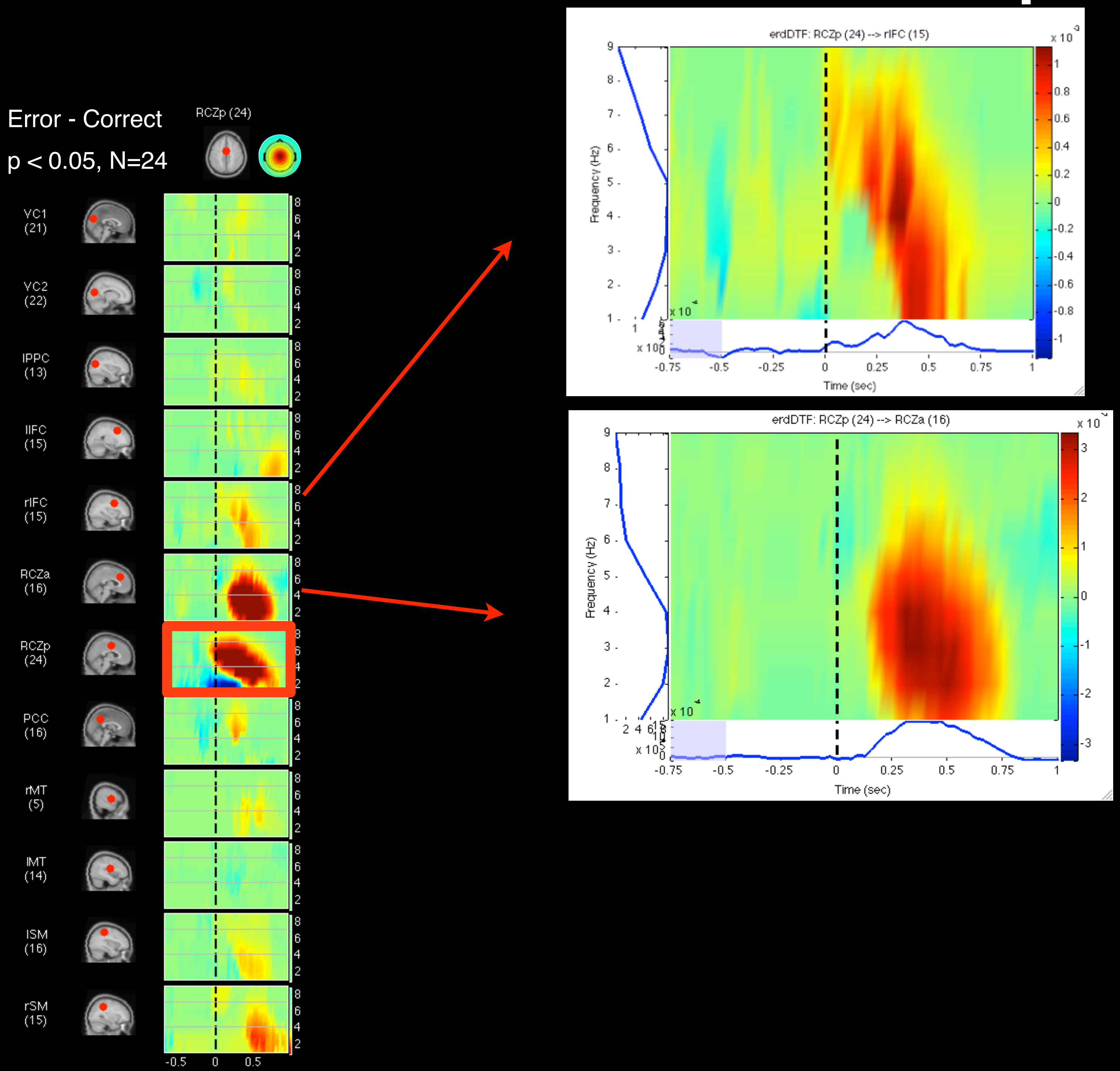

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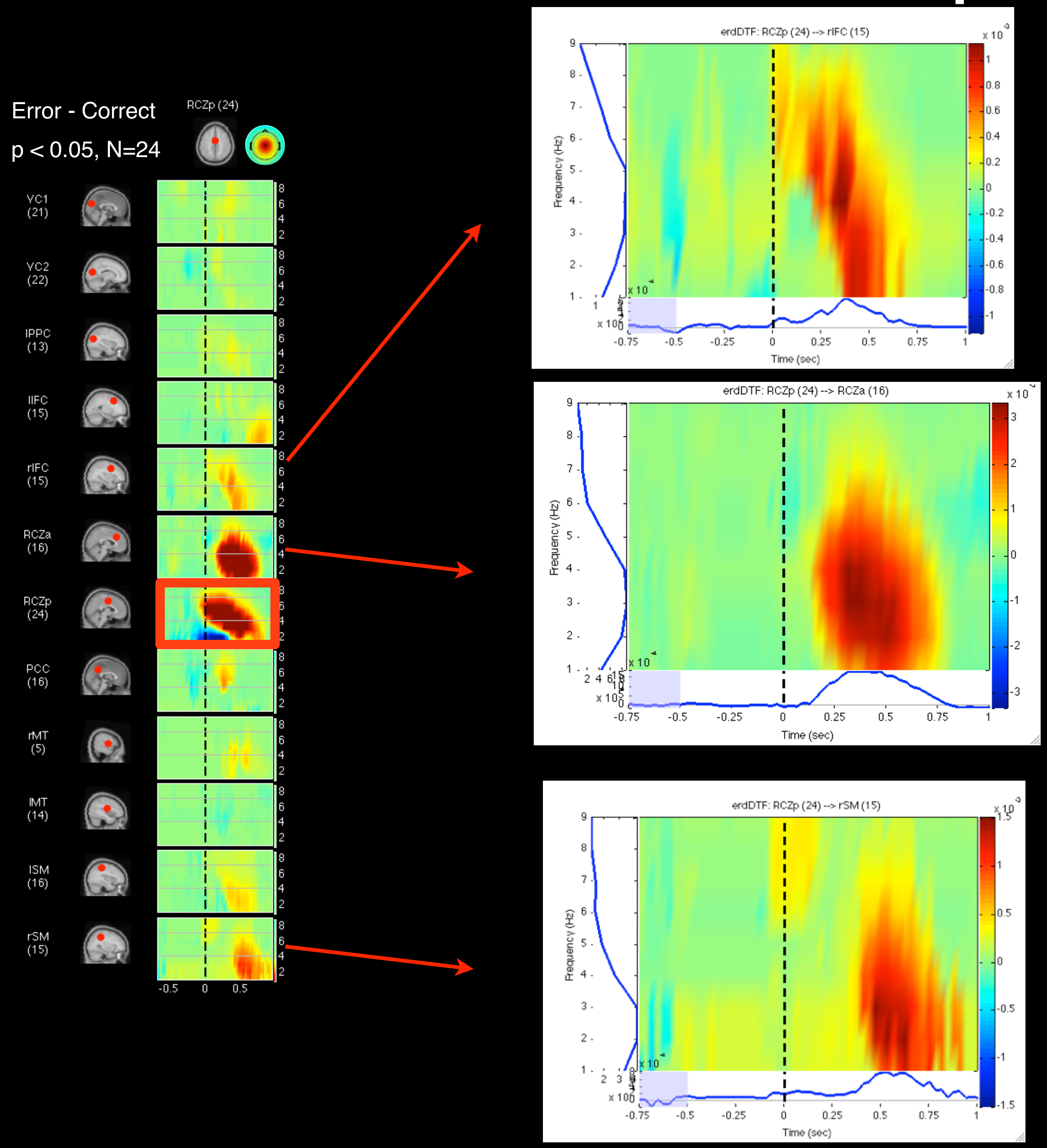
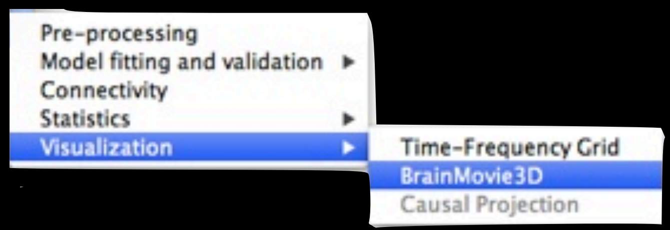
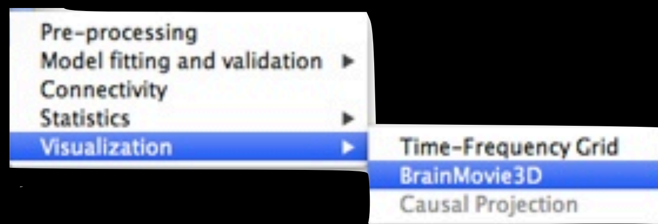
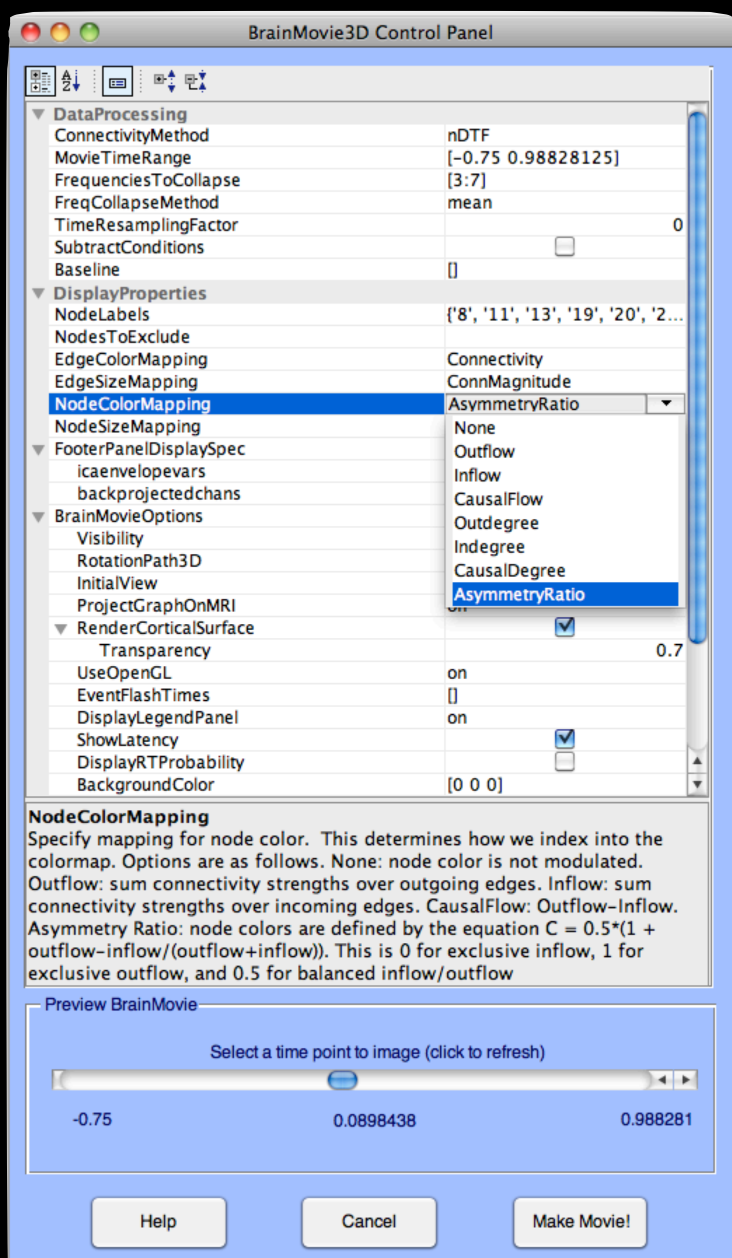


Interactive BrainMovie3D



Interactive BrainMovie3D





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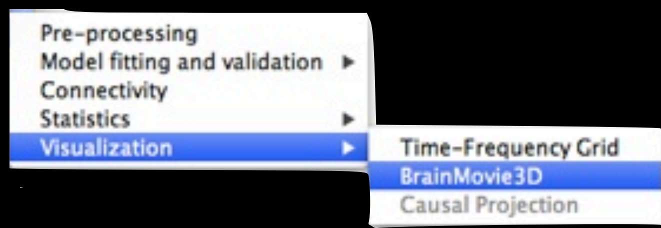
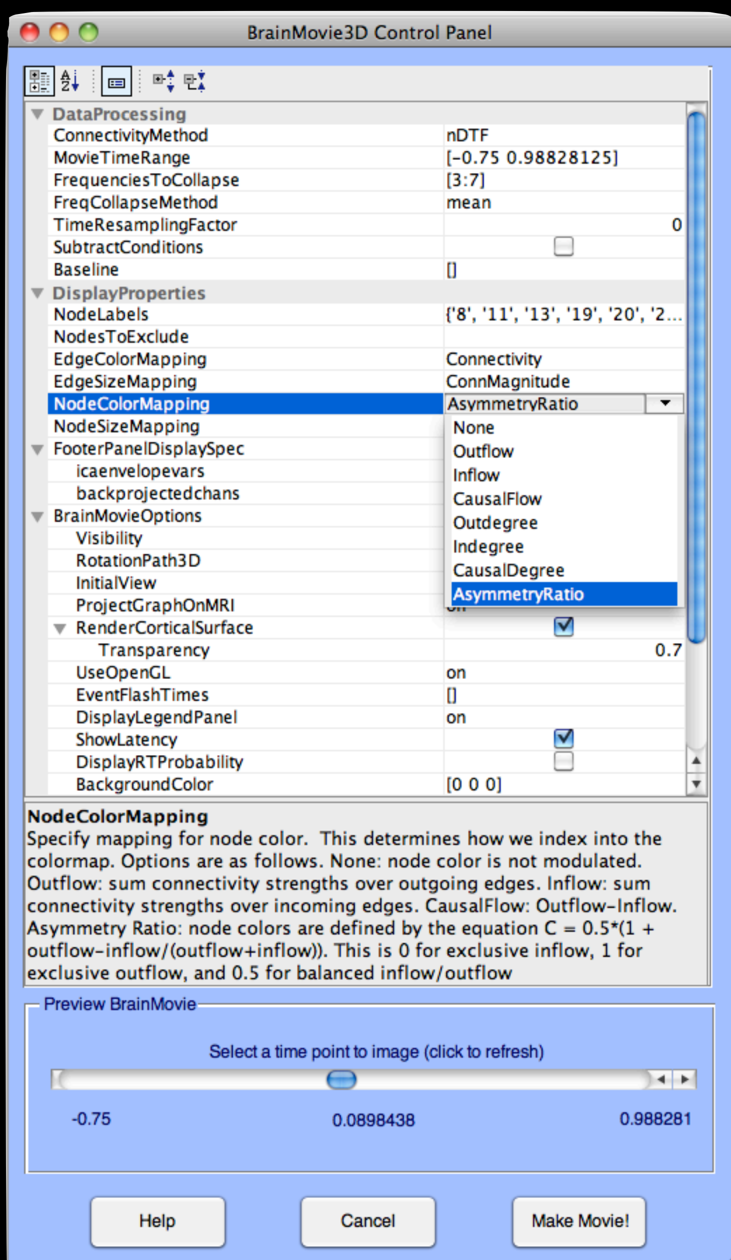
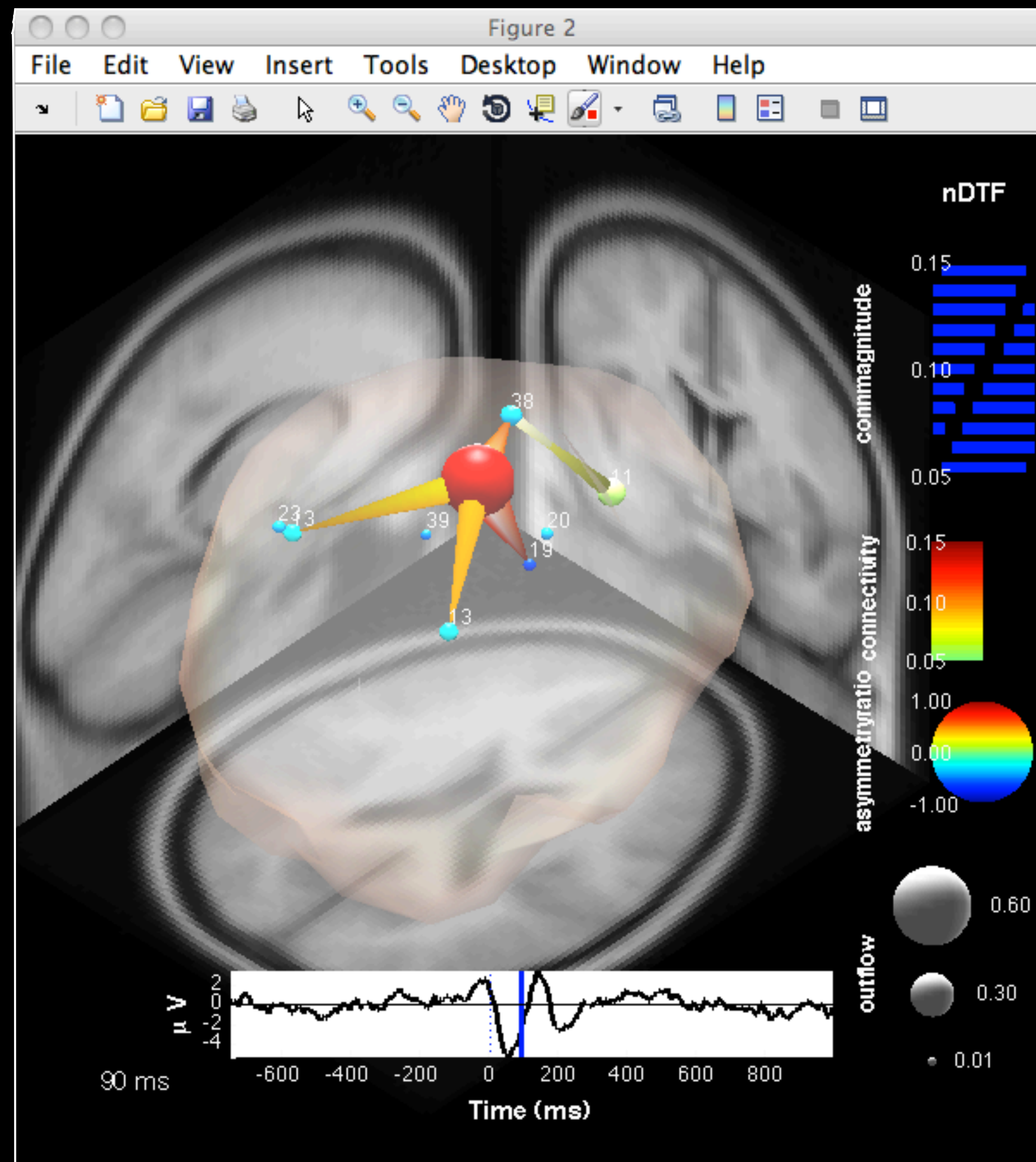




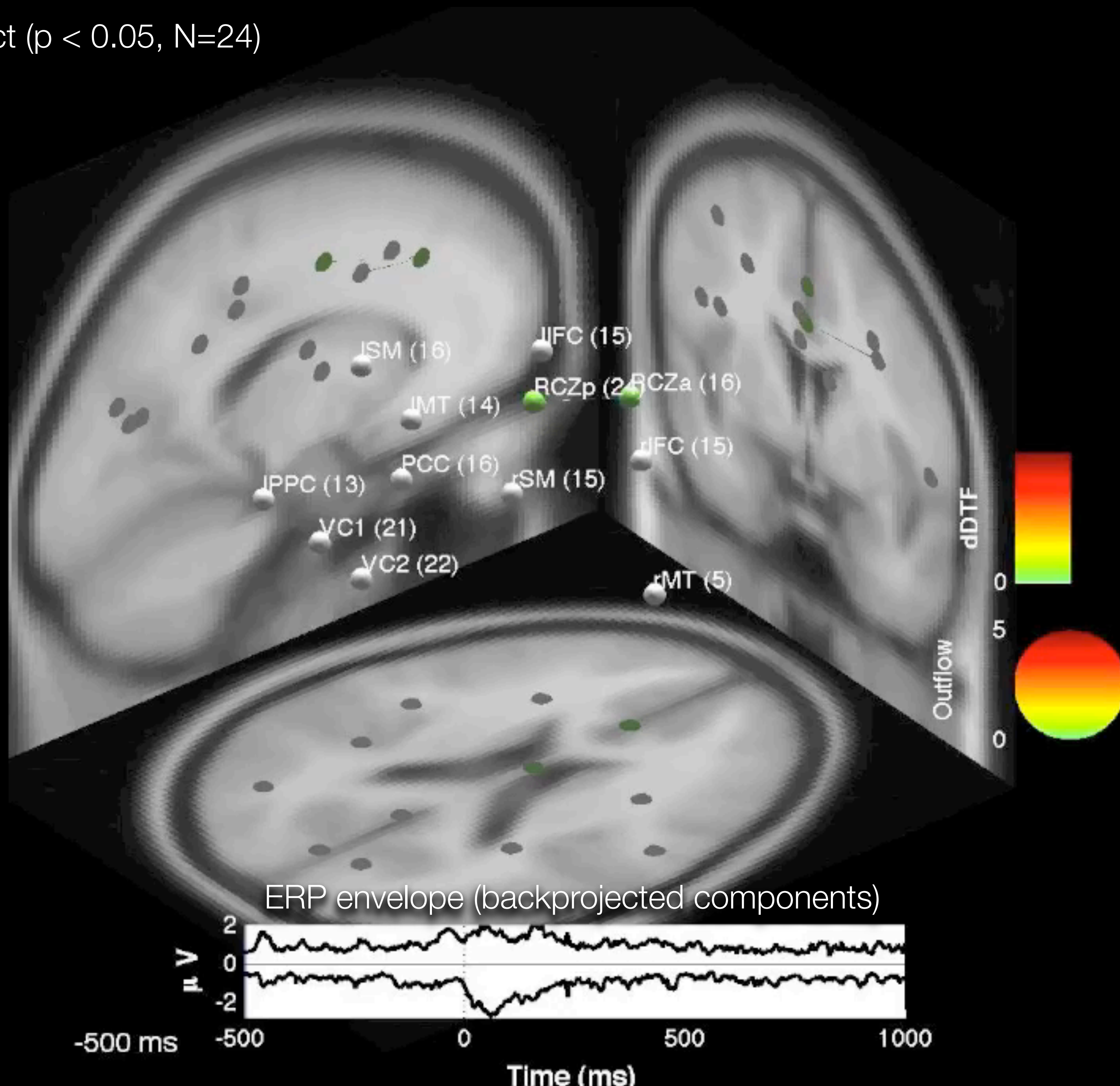


Interactive BrainMovie3D

Error > Correct ($p < 0.05$, N=24)

dDTF

3-7 Hz

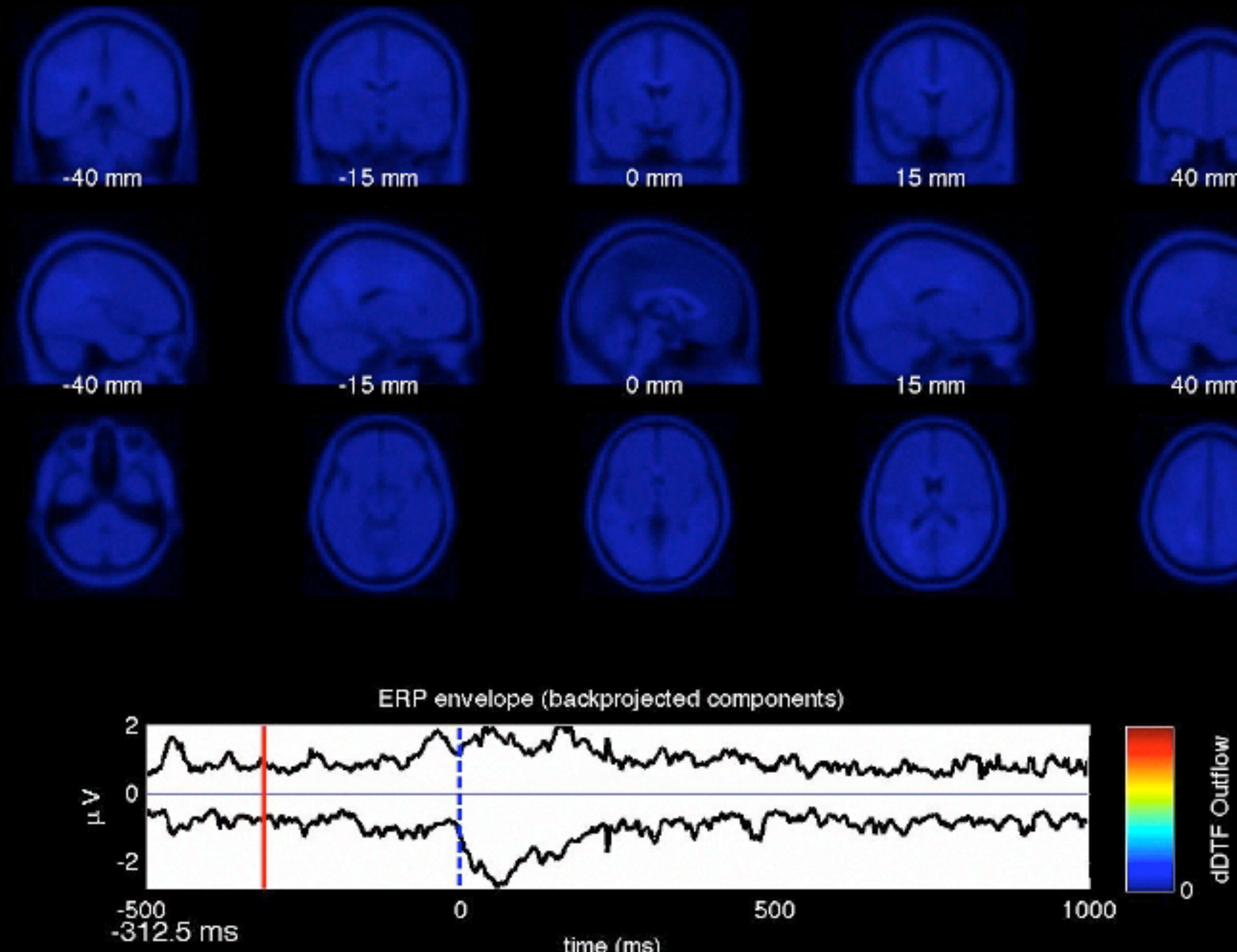


Causal Density Movie

Error > Correct ($p < 0.05$, N=24)

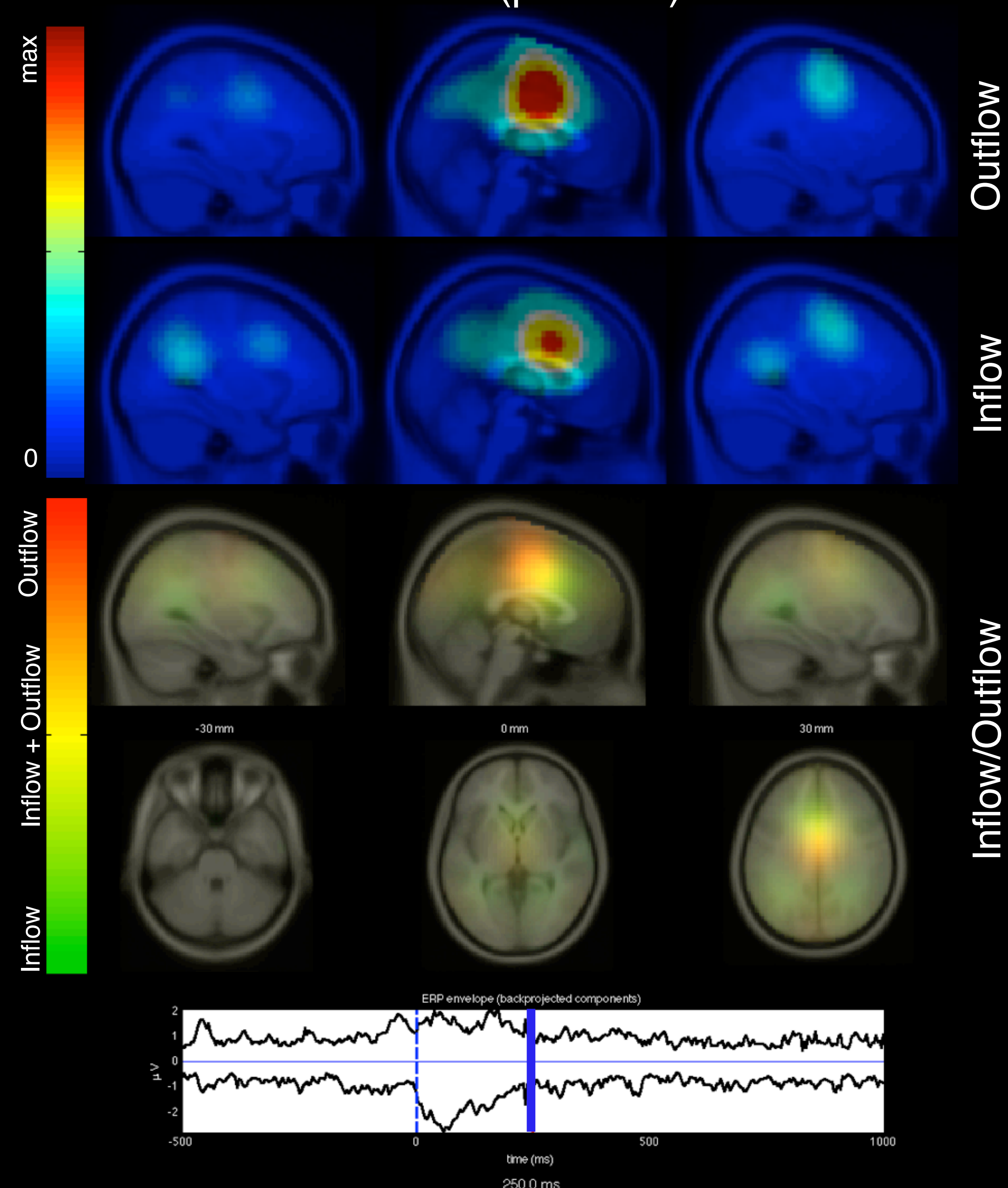
dDTF

3-7 Hz



Causal Density Movie

Error > Correct ($p < 0.05$) 3-7 Hz



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Group Analysis

partially-developed

Group Analysis

Disjoint Clustering

This approach adopts a 3-stage process:
1. Identify K ROI's (clusters) by affinity clustering of sources across subject population using EEGLAB's Measure-Product clustering.
2. Average all incoming and outgoing statistically significant connections between each pair of ROIs to create a [K X K [x freq x time]] group connectivity matrix.
3. Visualize the results using any of SIFTs visualization routines. This method suffers from low statistical power when subjects do not have high agreement in terms of source locations (missing variable problem).

partially-developed

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Bayesian Mixture Model

A more robust approach (in development with Wes Thompson and to be released in SIFT 1.0b) uses smoothing splines and Monte-Carlo methods for joint estimation of posterior probability (with confidence intervals) of cluster centroid location and between-cluster connectivity. This method takes into account the "missing variable" problem inherent to the disjoint clustering approach and provides robust group connectivity statistics.

partially-developed

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Future Work

- Improvement of architecture, GUI, and EEGLAB integration
- Ongoing implementation/incorporation of state-of-the-art methods for effective connectivity analysis and visualization
- Improved group statistics
- Evaluation of relative suitability of various source-separation algorithms when combined with MVAR modeling

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