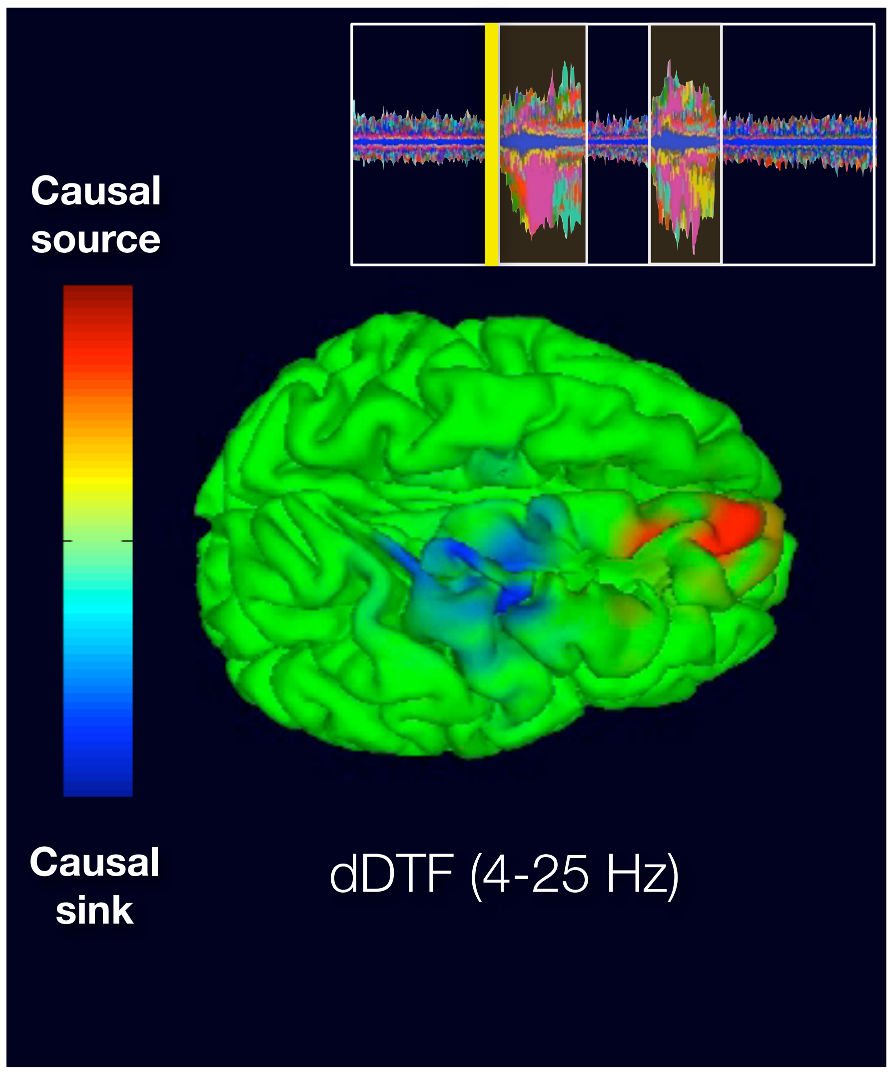
Source-level spatiotemporal dynamics and interactions (in human intracranial EEG)

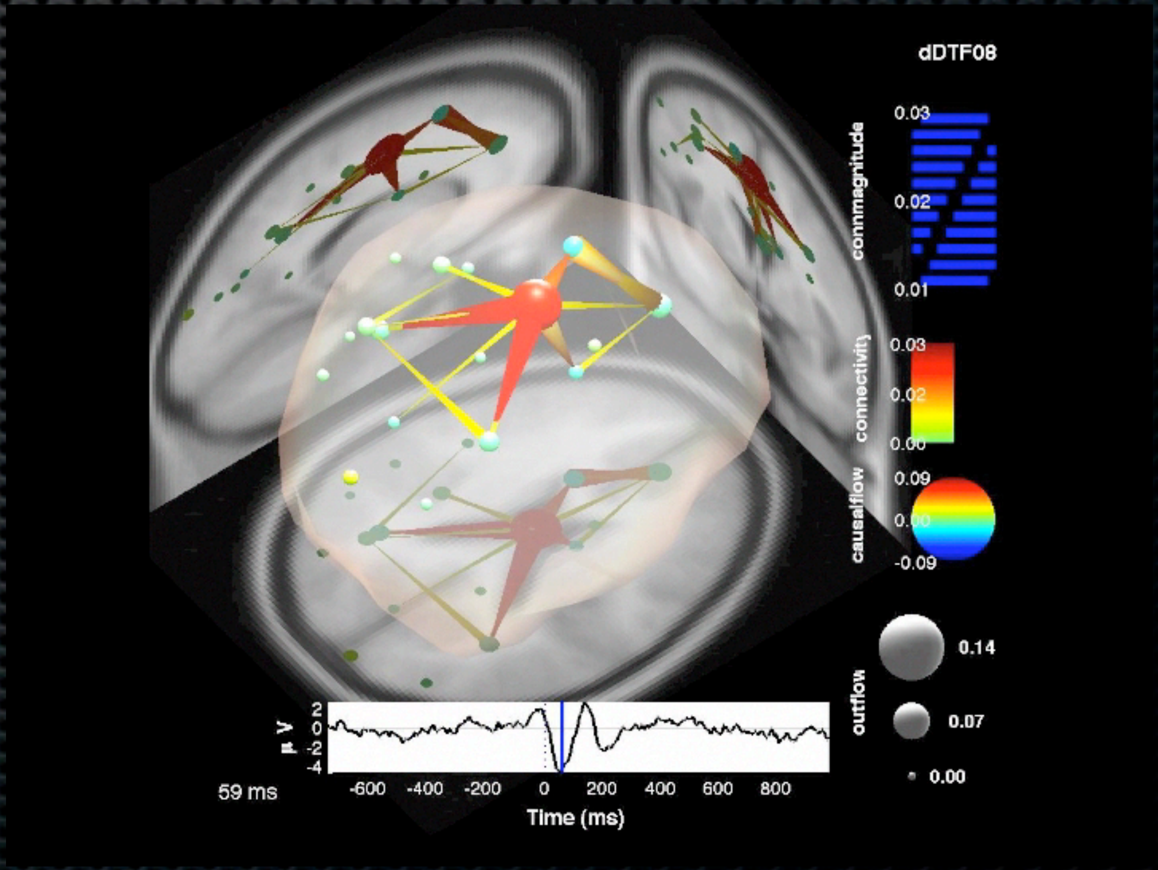
Tim Mullen
Zeynep Akalin Acar
Jason Palmer

2011 Sloan-Swartz Annual Meeting
HHMI Janelia Farm Research Campus



Key Objectives

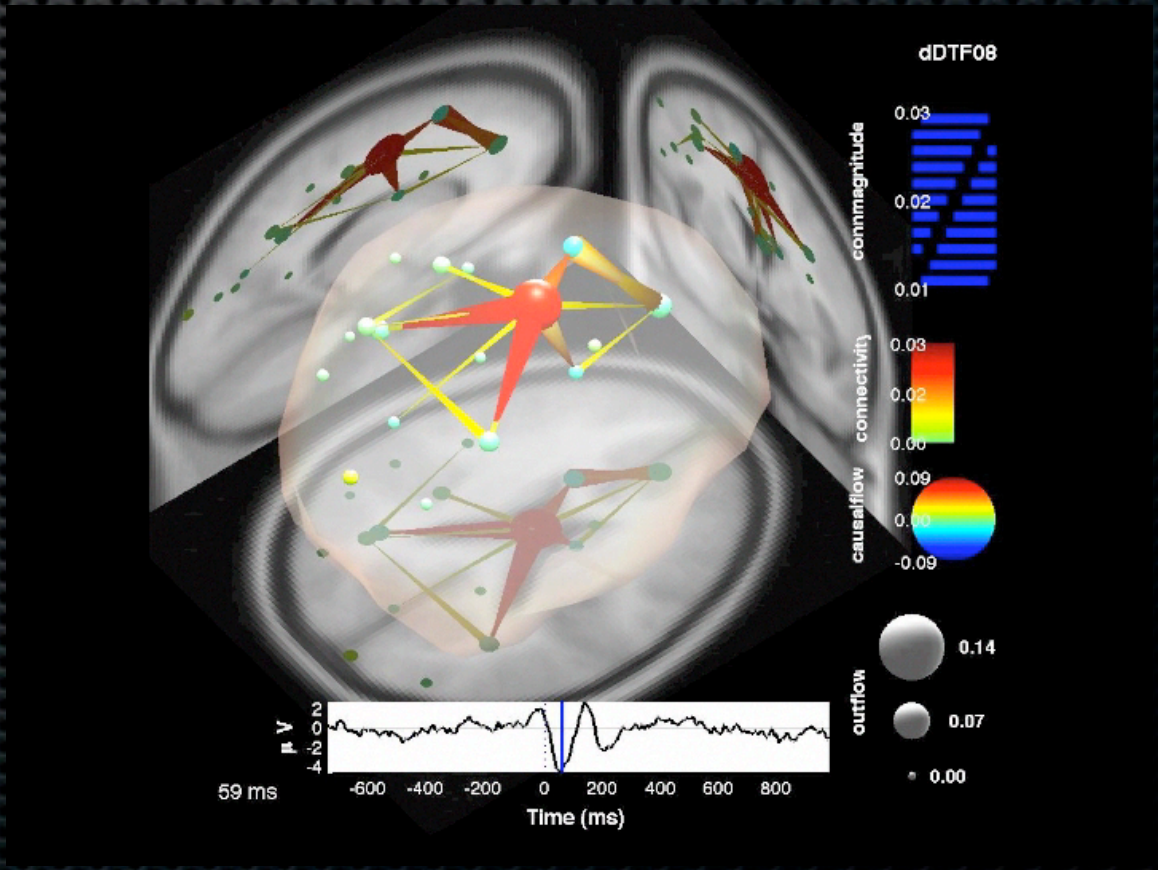
- To measure and visualize **dynamic** changes in neural **activity** and **effective connectivity** between **spatially-localized** cortical structures that **index** and **predict** both **neuropathological states** as well as healthy **cognitive state and behavior**



Key Objectives

- To measure and visualize **dynamic** changes in neural **activity** and **effective connectivity** between **spatially-localized** cortical structures that **index** and **predict** both **neuropathological states** as well as healthy **cognitive state and behavior**

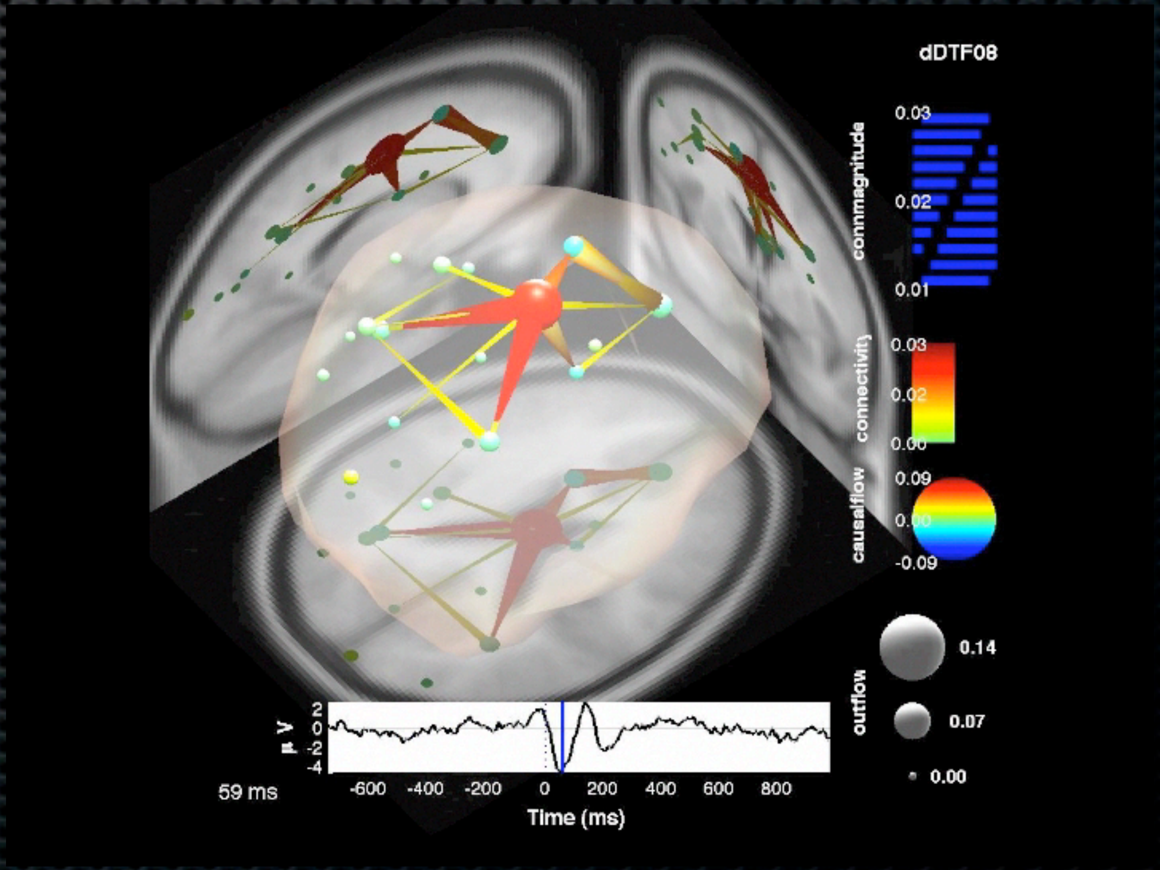
- Important factors:



Key Objectives

- To measure and visualize **dynamic** changes in neural **activity** and **effective connectivity** between **spatially-localized** cortical structures that **index** and **predict** both **neuropathological states** as well as healthy **cognitive state and behavior**

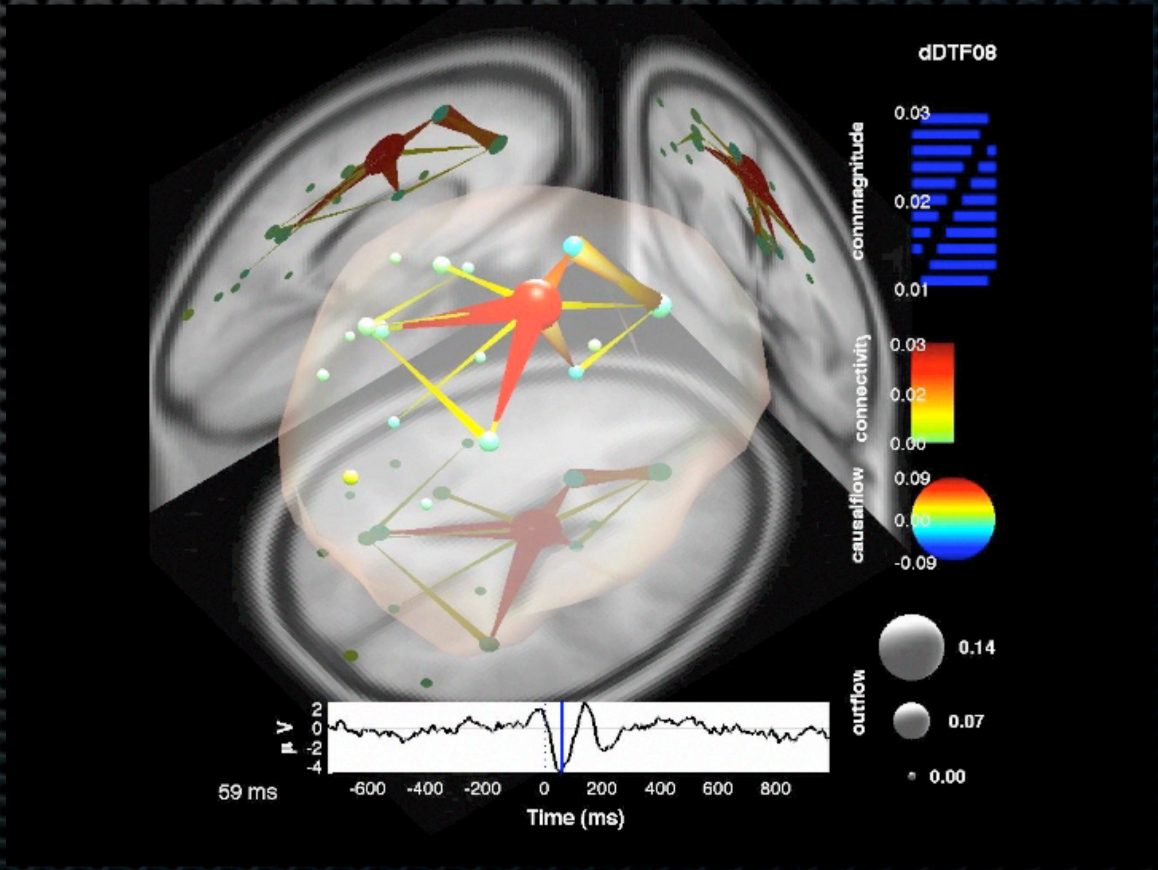
- Important factors:
    - Accuracy and Validity



Key Objectives

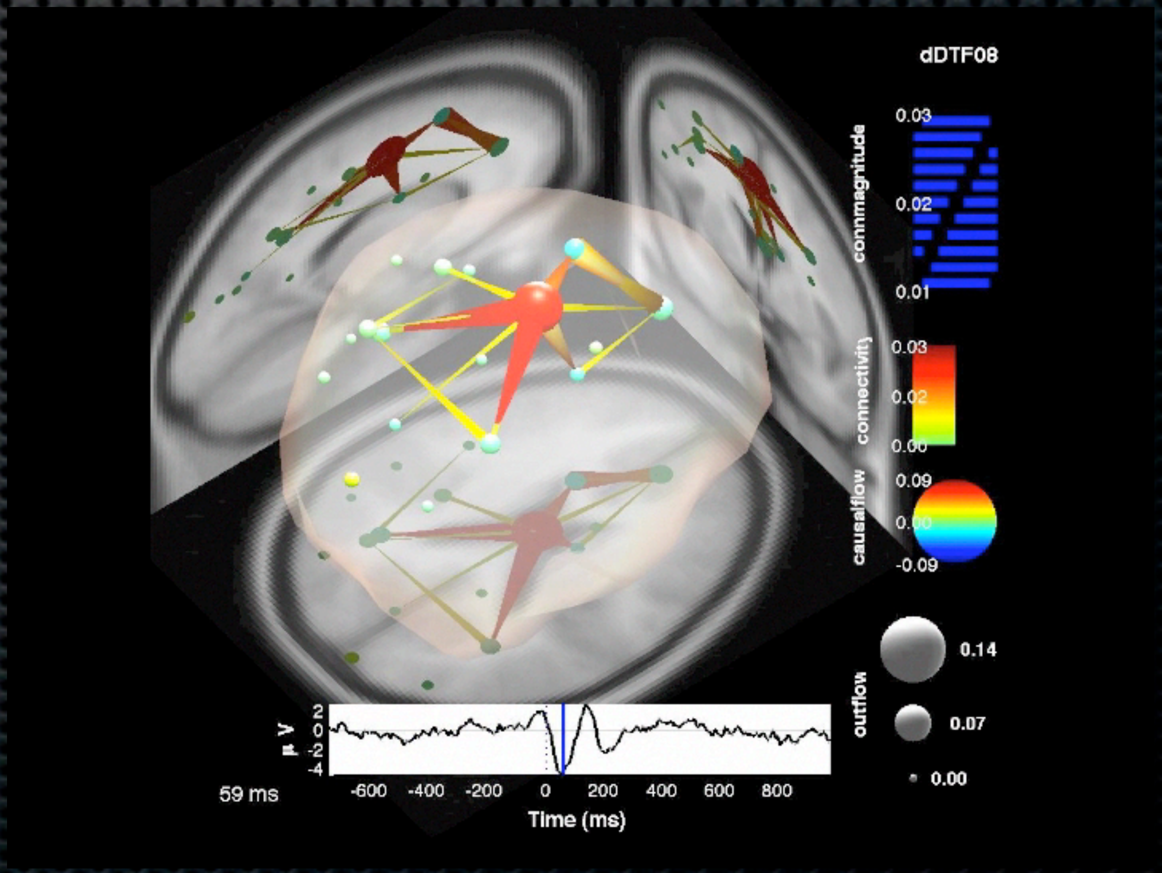
- To measure and visualize **dynamic** changes in neural **activity** and **effective connectivity** between **spatially-localized** cortical structures that **index** and **predict** both **neuropathological states** as well as healthy **cognitive state and behavior**

- Important factors:
  - Accuracy and Validity
  - Spatiotemporal Specificity



Key Objectives

- To measure and visualize **dynamic** changes in neural **activity** and **effective connectivity** between **spatially-localized** cortical structures that **index** and **predict** both **neuropathological states** as well as healthy **cognitive state and behavior**



- Important factors:
  - Accuracy and Validity
  - Spatiotemporal Specificity
  - Scalp and Intracranial EEG

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved) exogenous causes (Guo, 2008a,b; Ge, 2009)

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved) exogenous causes (Guo, 2008a,b; Ge, 2009)
- Equivalent to Transfer Entropy for Gaussian Variables (Seth, 2009)

Estimating Effective Connectivity

Non-Invasive

- *Post-hoc* analyses applied to measured neural activity
- Confirmatory
  - Dynamic Causal Models
  - Structural Equation Models
- Exploratory
  - Granger-Causal methods

- Data-driven
- Simple, but powerful
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or non-stationary systems (Freiwald, 1999; Ding, 2001; Chen, 2004; Ge, 2009)
- Extendable to non-parametric representations (Dhamala, 2009a,b)
- Can be (partially) controlled for (unobserved) exogenous causes (Guo, 2008a,b; Ge, 2009)
- Equivalent to Transfer Entropy for Gaussian Variables (Seth, 2009)
- Flexibly allows us to examine **time-varying** (dynamic) multivariate causal relationships in either the **time** or **frequency** domain

Granger Causality

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

Granger Causality

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

Granger Causality Axioms

Granger Causality

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

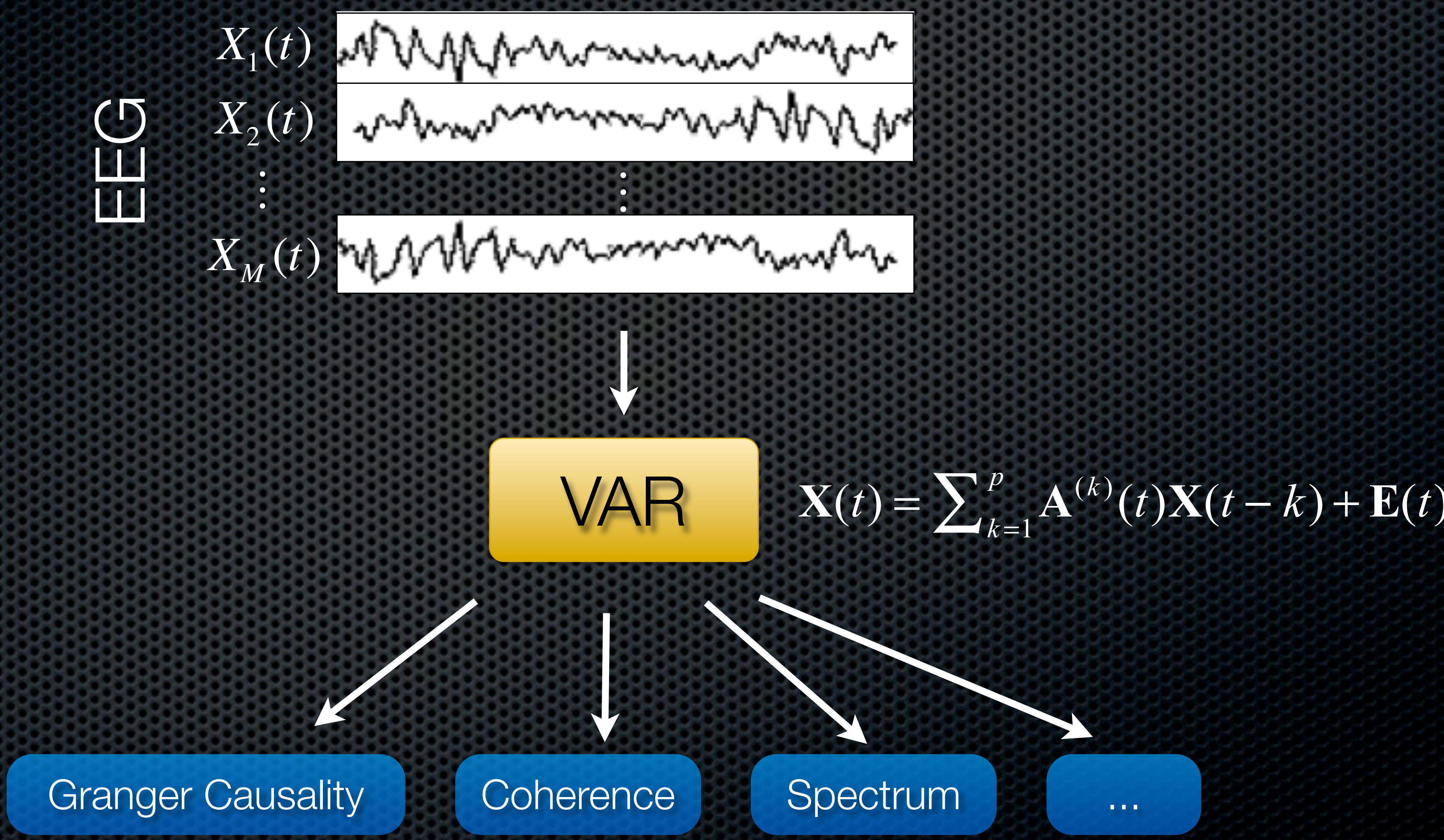
Granger Causality Axioms
1. Causes should precede their effects in time (Temporal Precedence)

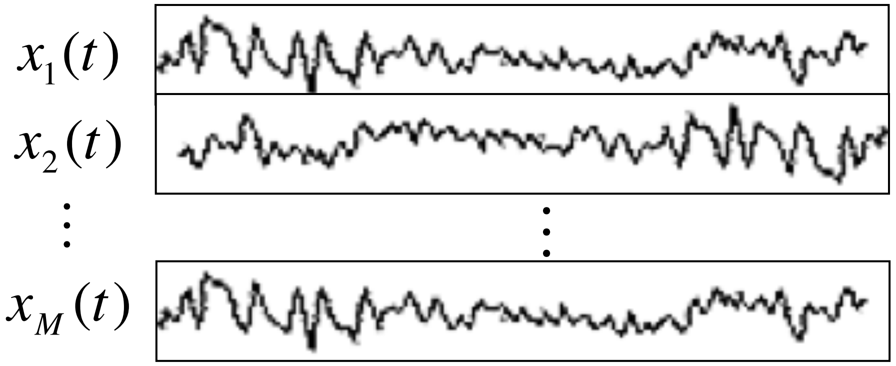
Granger Causality

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

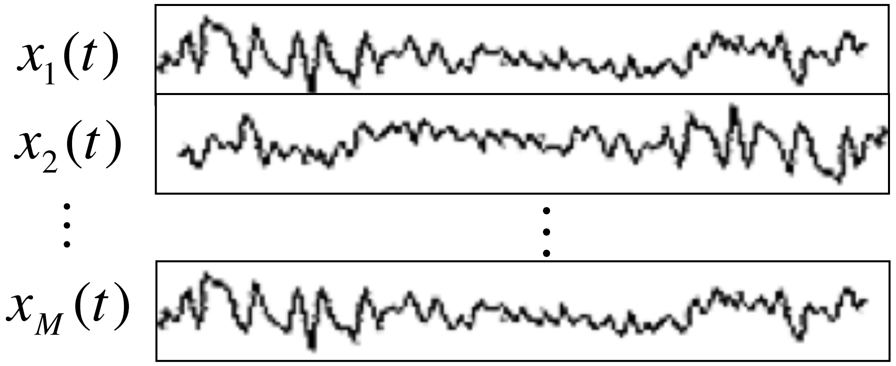
Granger Causality Axioms
1. Causes should precede their effects in time (Temporal Precedence)
2. Information in a cause's past should improve the prediction of the effect, above and beyond the information contained in past of the effect (and other measured variables)

Vector Autoregressive (VAR) Modeling





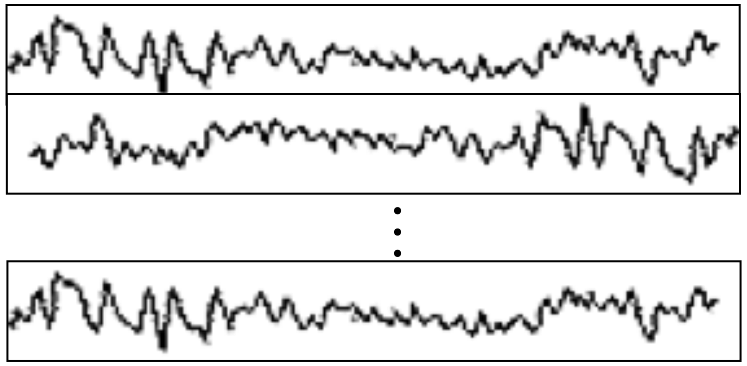
$$\mathbf{X}(t) = \sum_{k=1}^{p} \mathbf{A}^{(k)}(t)\mathbf{X}(t-k) + \mathbf{E}(t)$$



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

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

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



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

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

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

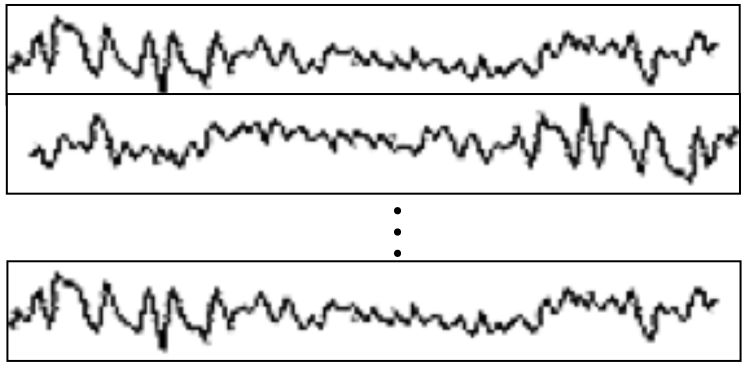
Multivariate Granger Causality

$x_1(t)$

$x_2(t)$

$\vdots$

$x_M(t)$

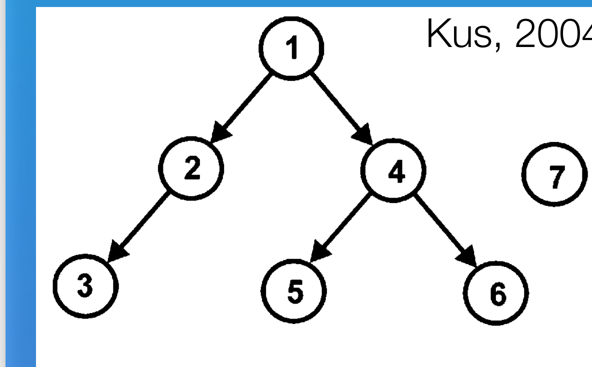


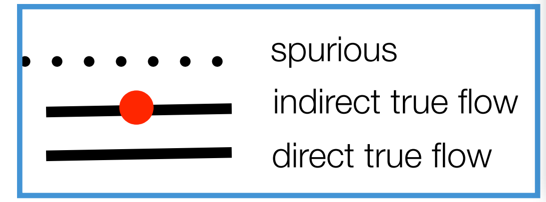
$$\mathbf{X}(t) = \sum_{k=1}^{p} \mathbf{A}^{(k)}(t)\mathbf{X}(t-k) + \mathbf{E}(t)$$

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

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

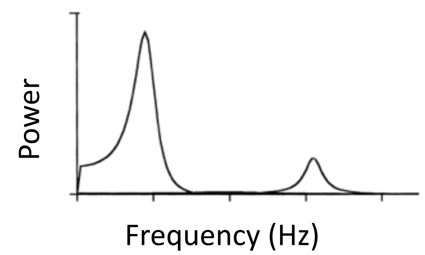
Ground Truth



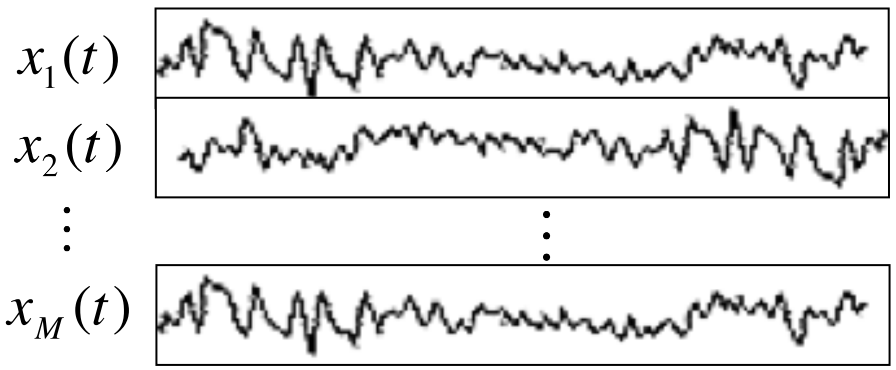


Spectrum

$$S(f,t) = \mathbf{X}(f,t)\mathbf{X}(f,t)^{*}$$
$$= \mathbf{H}(f,t)\Sigma\mathbf{H}(f,t)^{*}$$



Multivariate Granger Causality

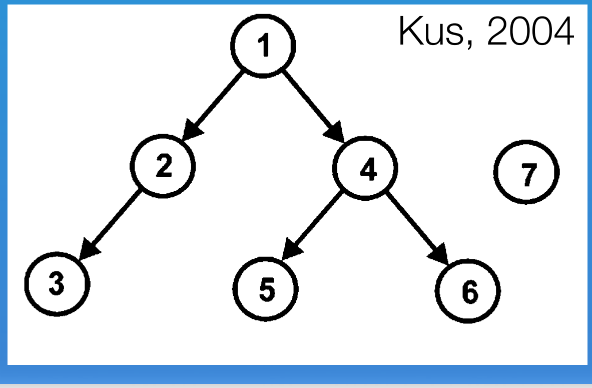


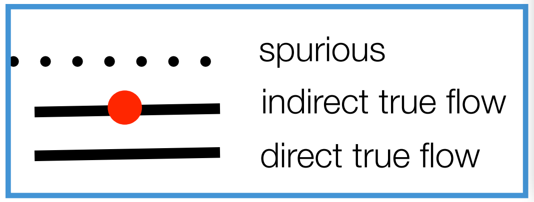
$$\mathbf{X}(t)=\sum_{k=1}^{p}\mathbf{A}^{(k)}(t)\mathbf{X}(t-k)+\mathbf{E}(t)$$

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

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

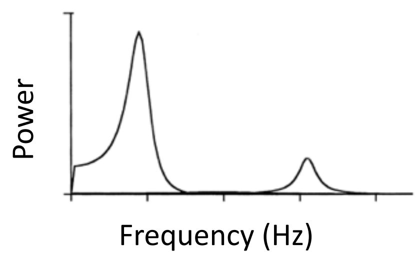
Ground Truth





Spectrum

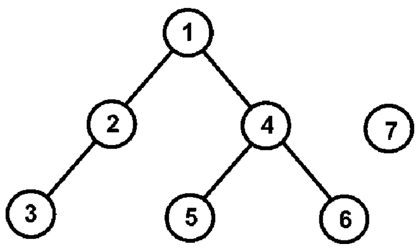
$$S(f,t)=\mathbf{X}(f,t)\mathbf{X}(f,t)^{*}$$
$$=\mathbf{H}(f,t)\Sigma\mathbf{H}(f,t)^{*}$$

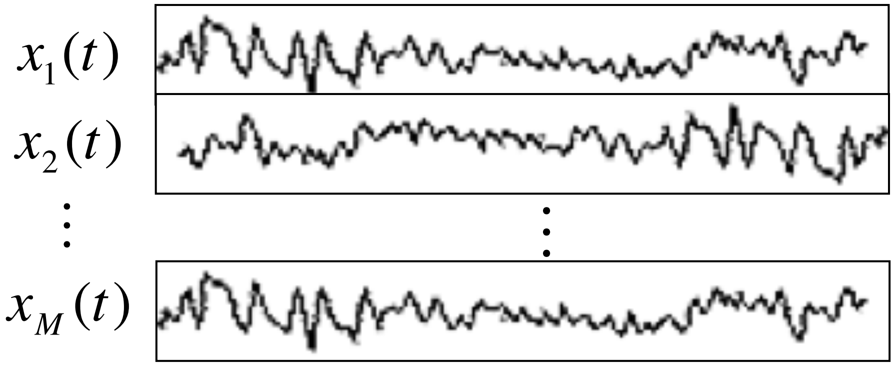


Multivariate Granger Causality

Partial Coherence

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



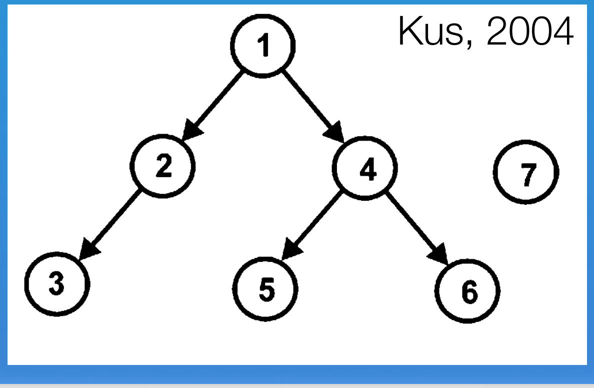


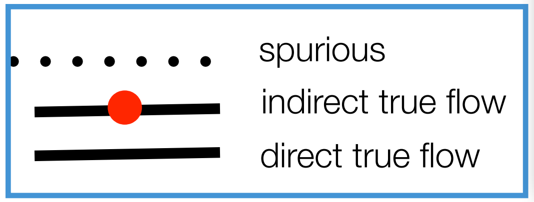
$$\mathbf{X}(t)=\sum_{k=1}^{p}\mathbf{A}^{(k)}(t)\mathbf{X}(t-k)+\mathbf{E}(t)$$

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

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

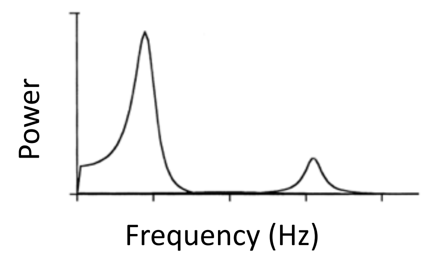
Ground Truth





Spectrum

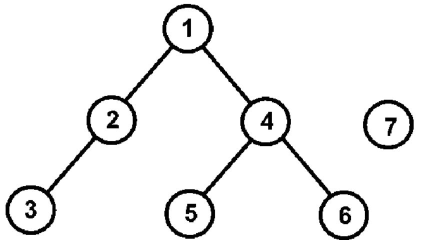
$$S(f,t)=\mathbf{X}(f,t)\mathbf{X}(f,t)^{*}$$
$$=\mathbf{H}(f,t)\Sigma\mathbf{H}(f,t)^{*}$$



Multivariate Granger Causality

Partial Coherence

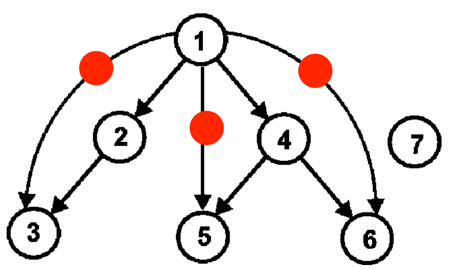
$$P_{ij}(f,t)=\frac{S_{ij}^{-1}(f,t)}{\sqrt{S_{ii}^{-1}(f,t)S_{jj}^{-1}(f,t)}}$$

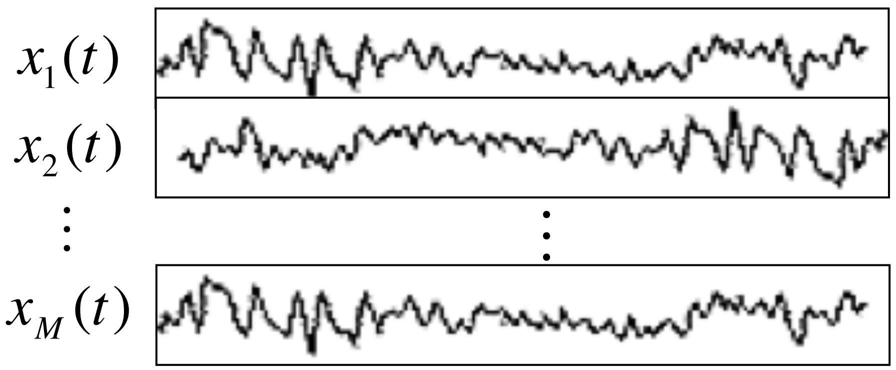


× Full-frequency Directed Transfer Function

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

(Kaminski and Blinowska, 1991, Korzeniewska, 2003)



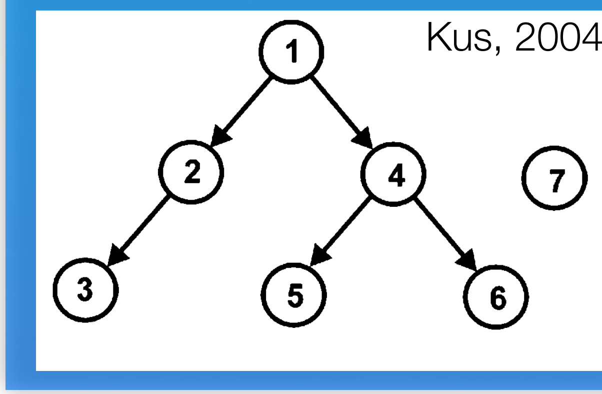


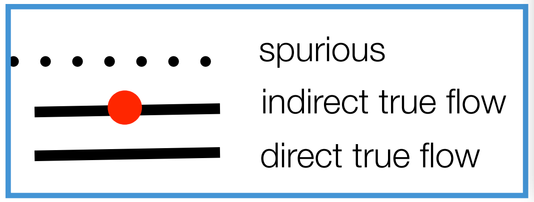
$$\mathbf{X}(t)=\sum_{k=1}^{p}\mathbf{A}^{(k)}(t)\mathbf{X}(t-k)+\mathbf{E}(t)$$

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

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

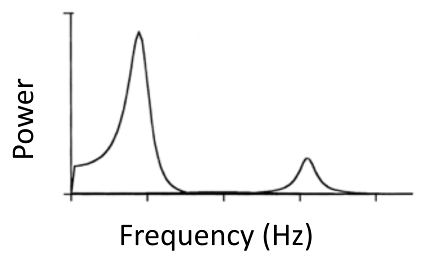
Ground Truth





Spectrum

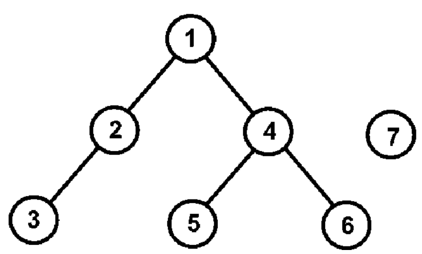
$$S(f,t)=\mathbf{X}(f,t)\mathbf{X}(f,t)^{*}$$
$$=\mathbf{H}(f,t)\Sigma\mathbf{H}(f,t)^{*}$$



Multivariate Granger Causality

Partial Coherence

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

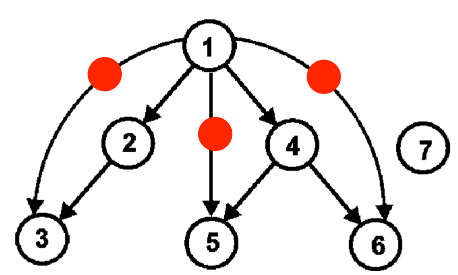


×

Full-frequency Directed Transfer Function

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

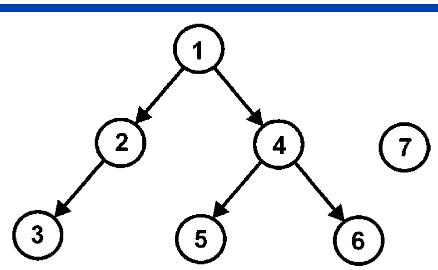
(Kaminski and Blinowska, 1991, Korzeniewska, 2003)



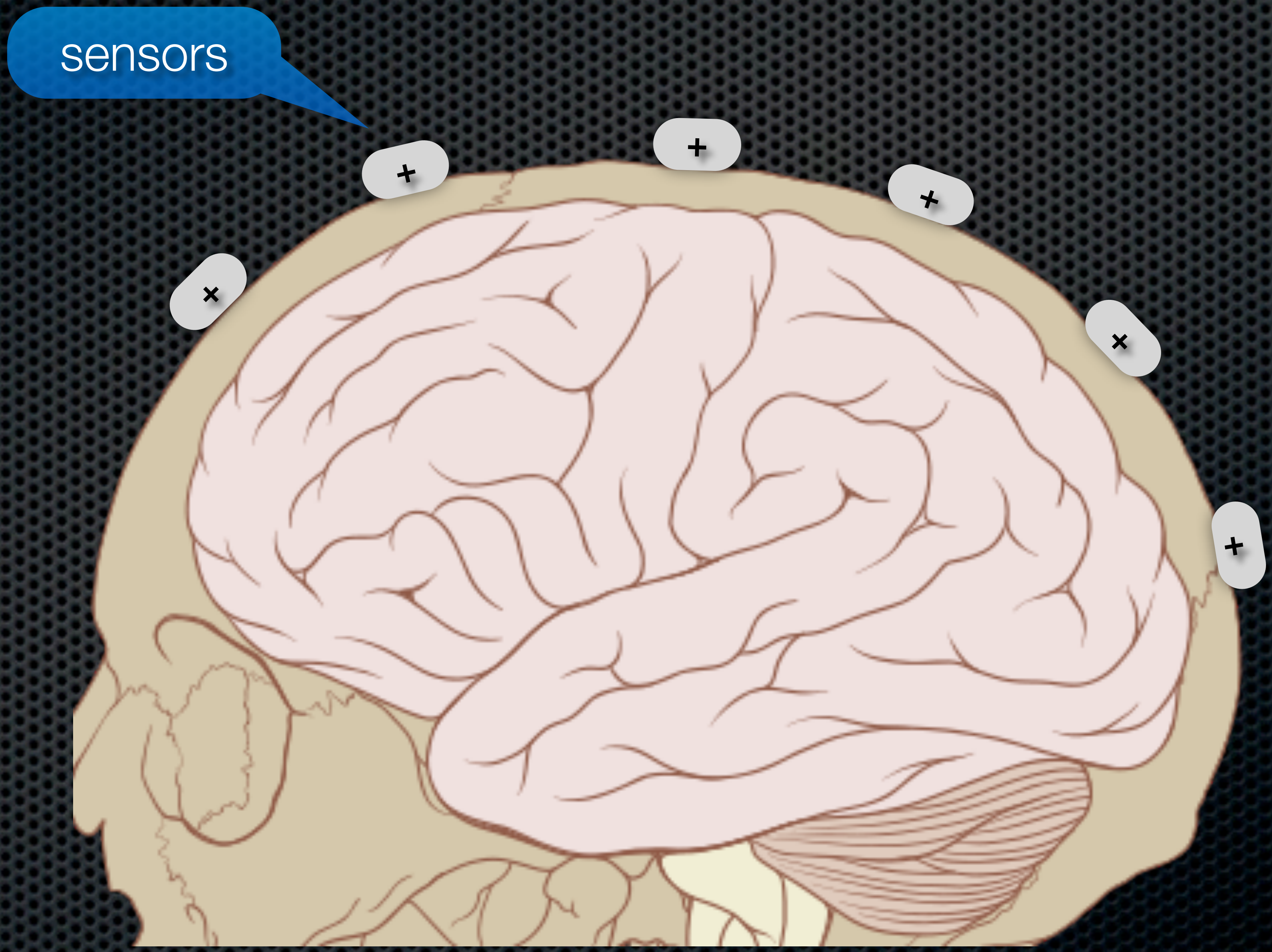
Direct DTF

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

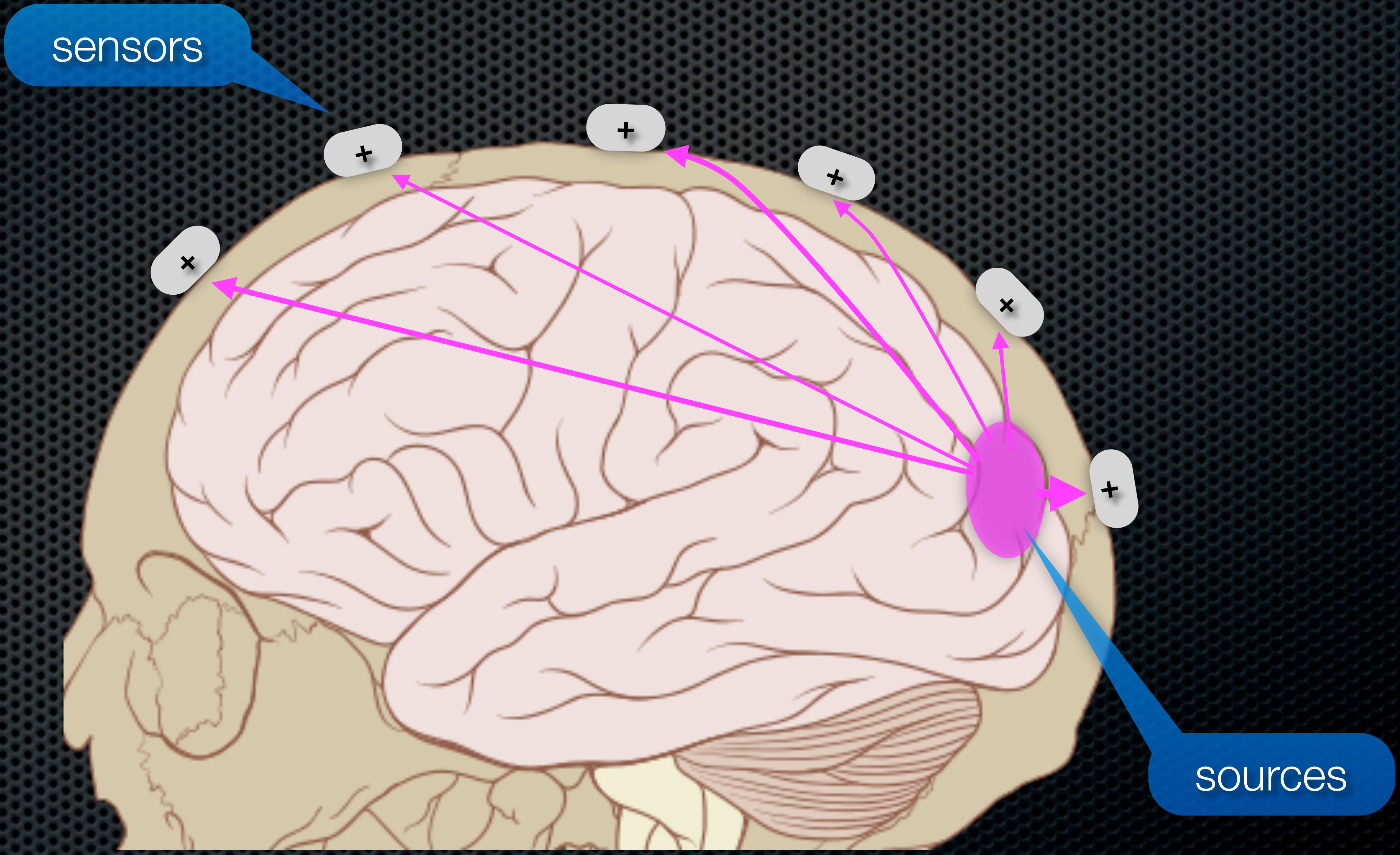
(Korzeniewska, 2003, 2010)



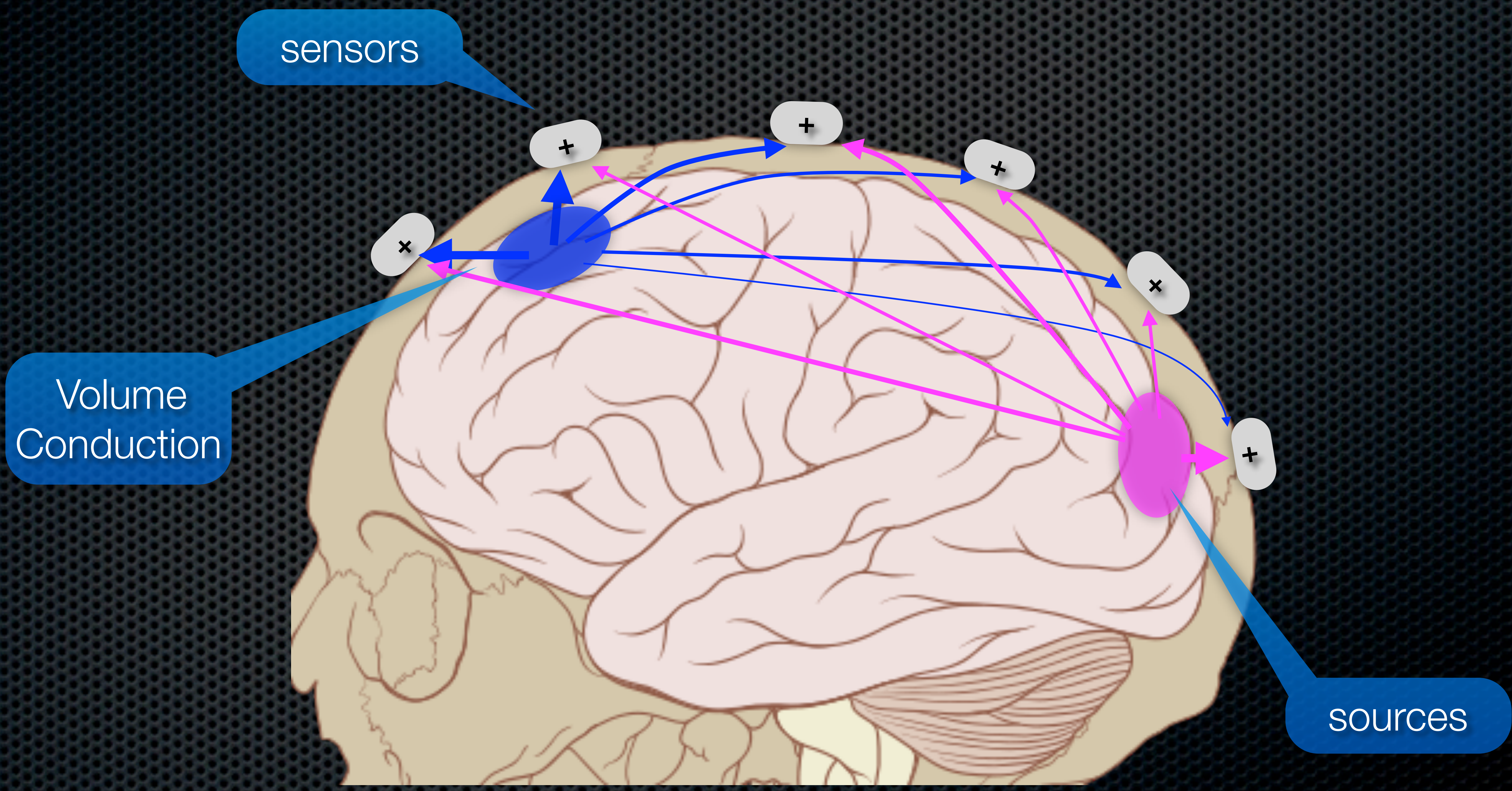
Channel or Source?



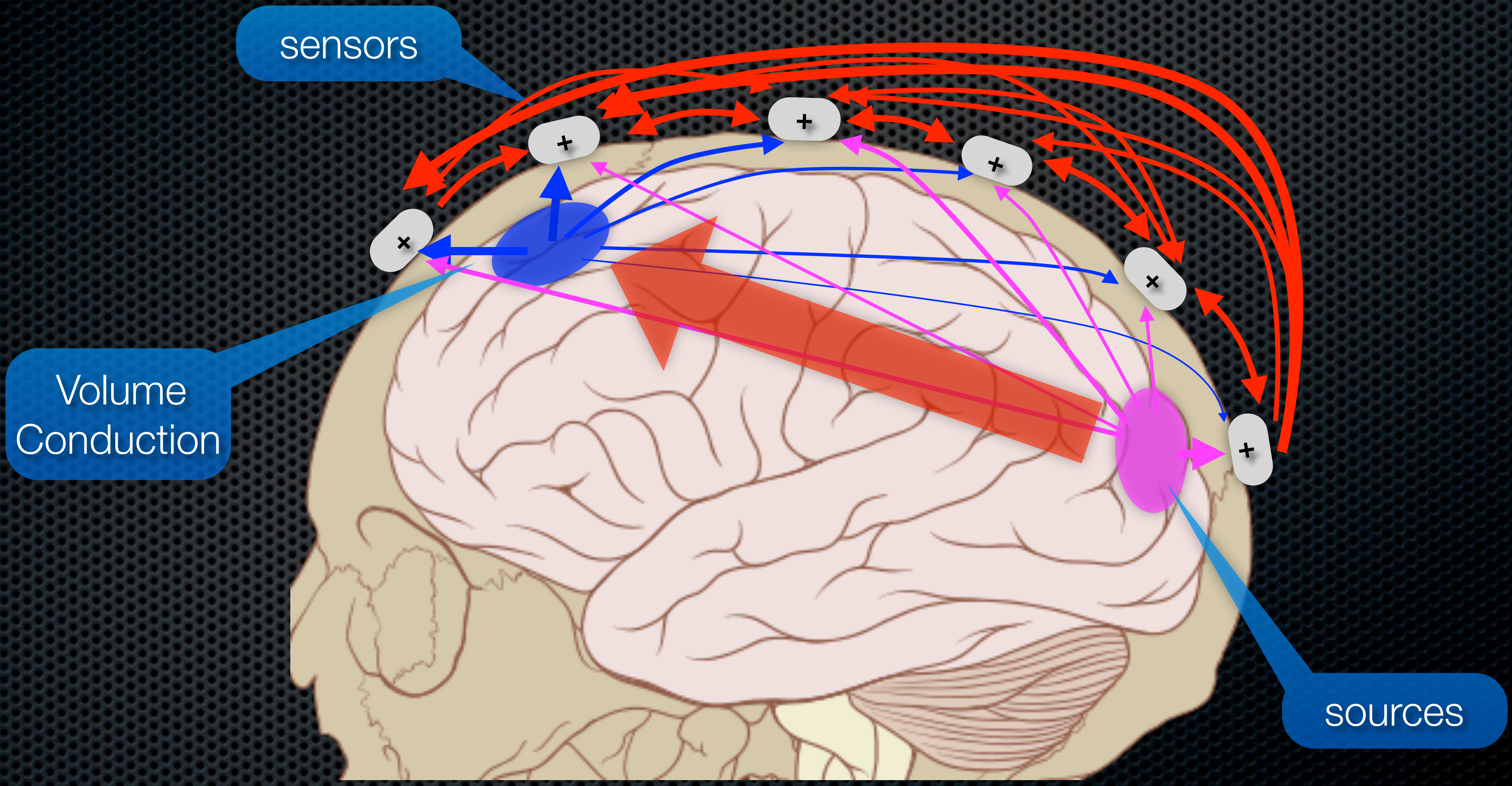
Channel or Source?



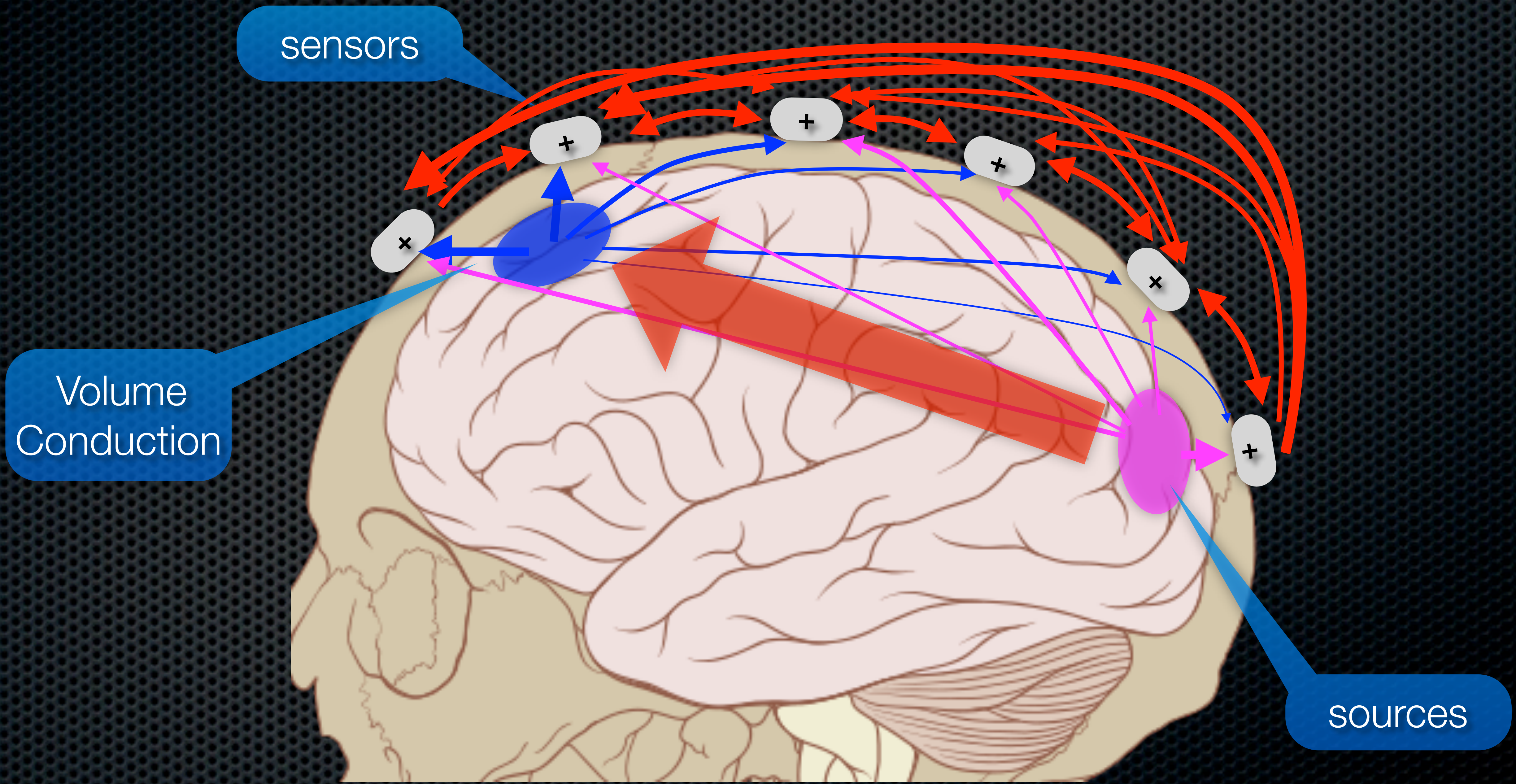
Channel or Source?



Channel or Source?

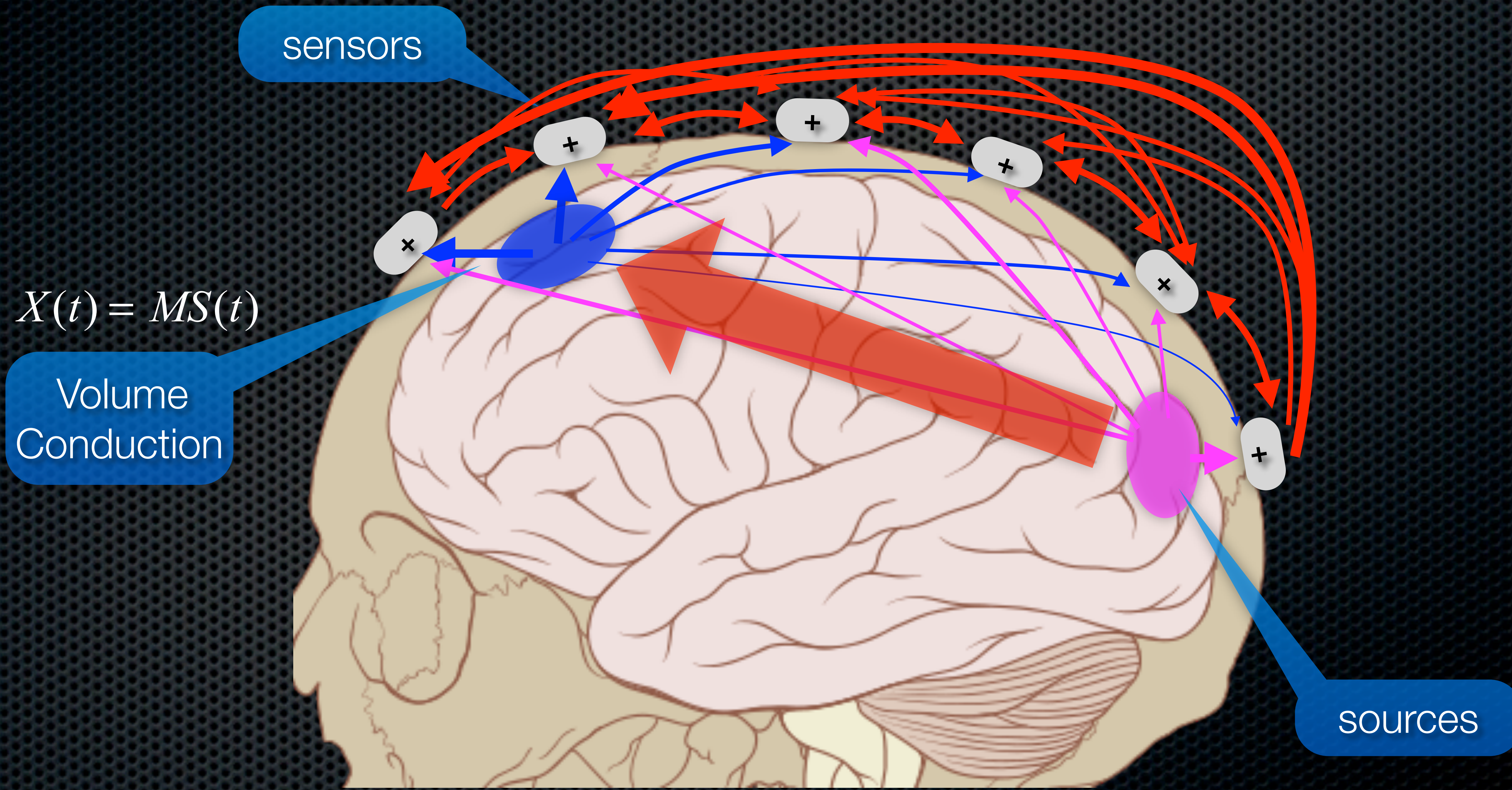


Channel or Source?



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

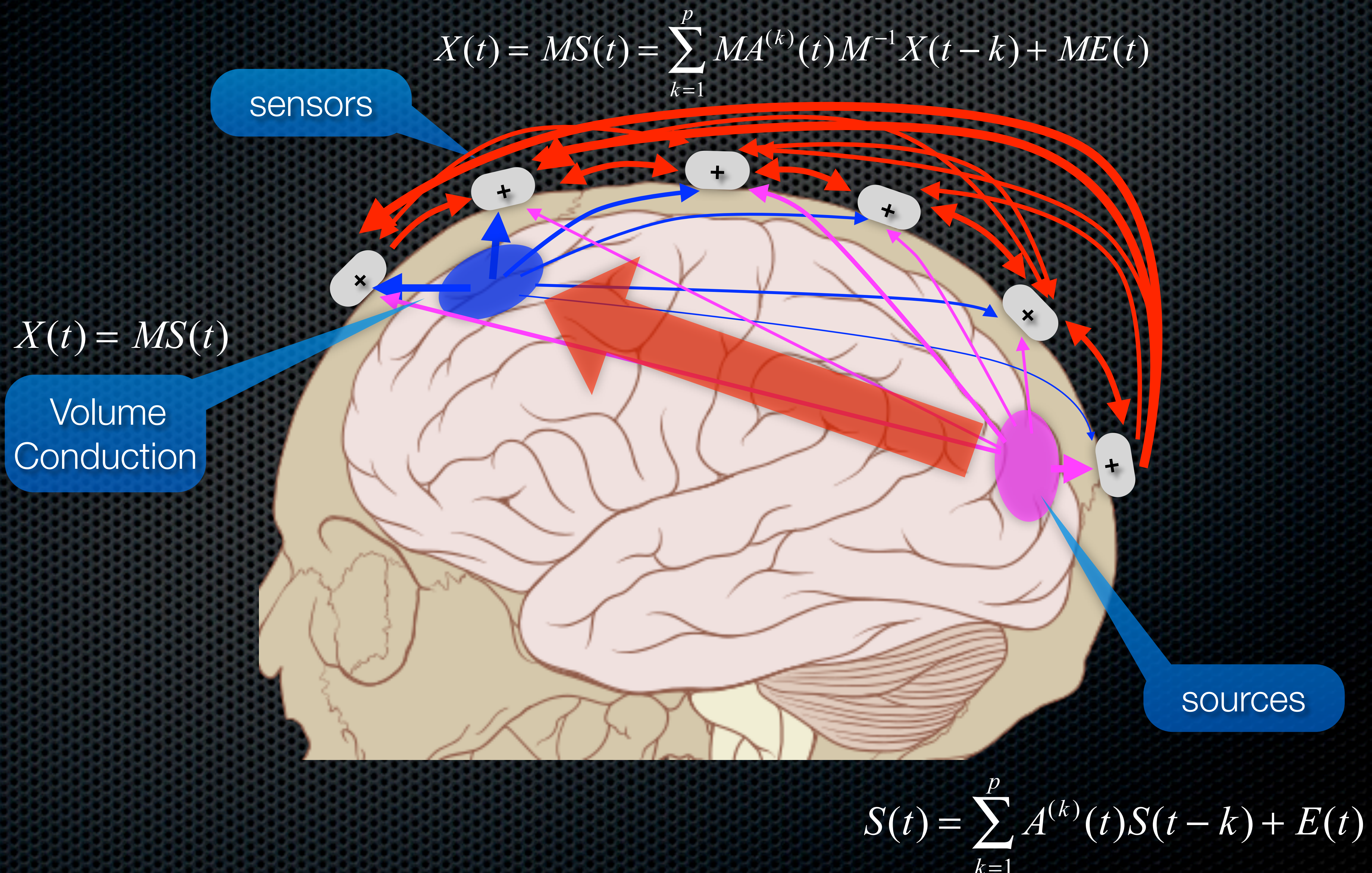
Channel or Source?



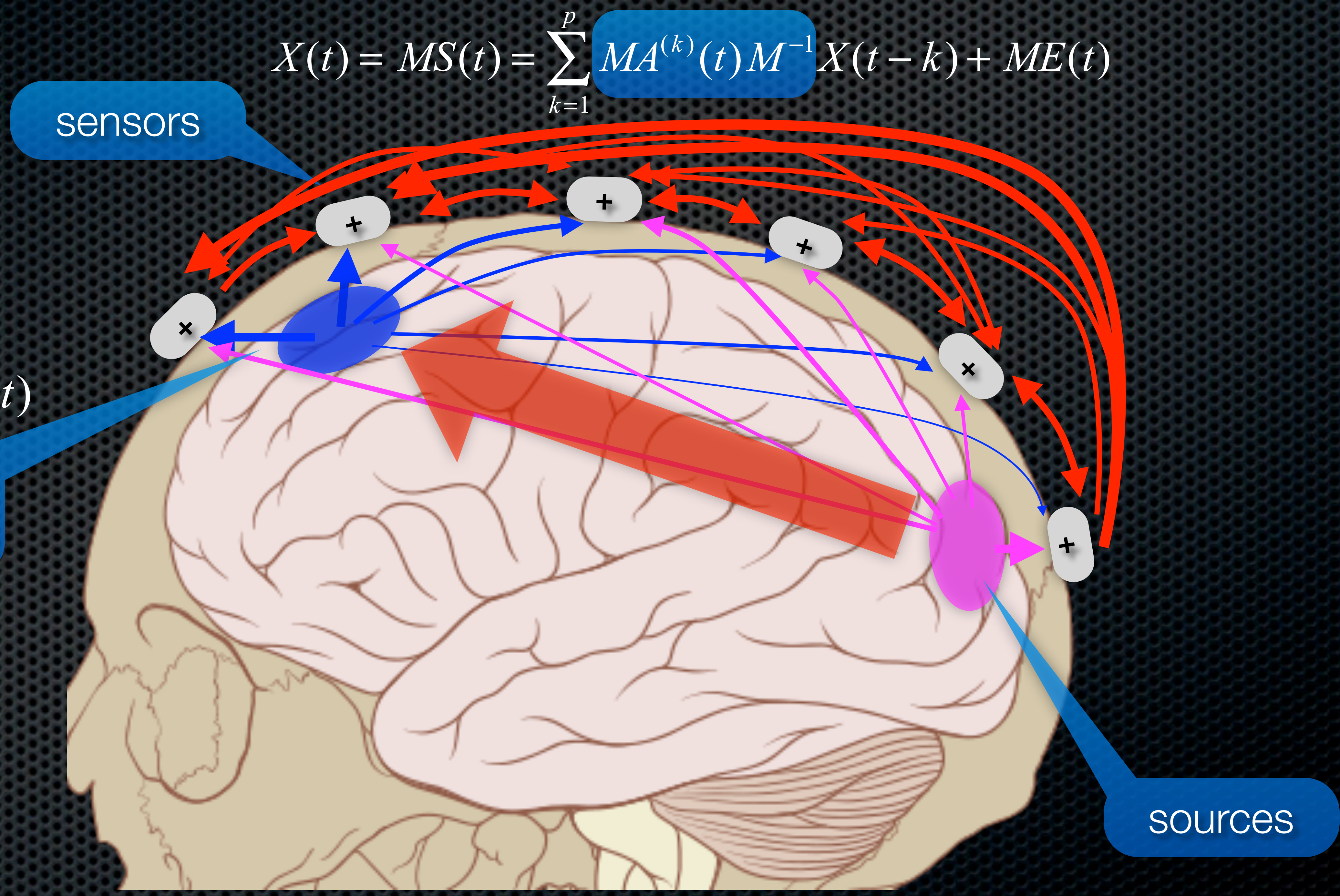
$$X(t) = MS(t)$$

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

Channel or Source?



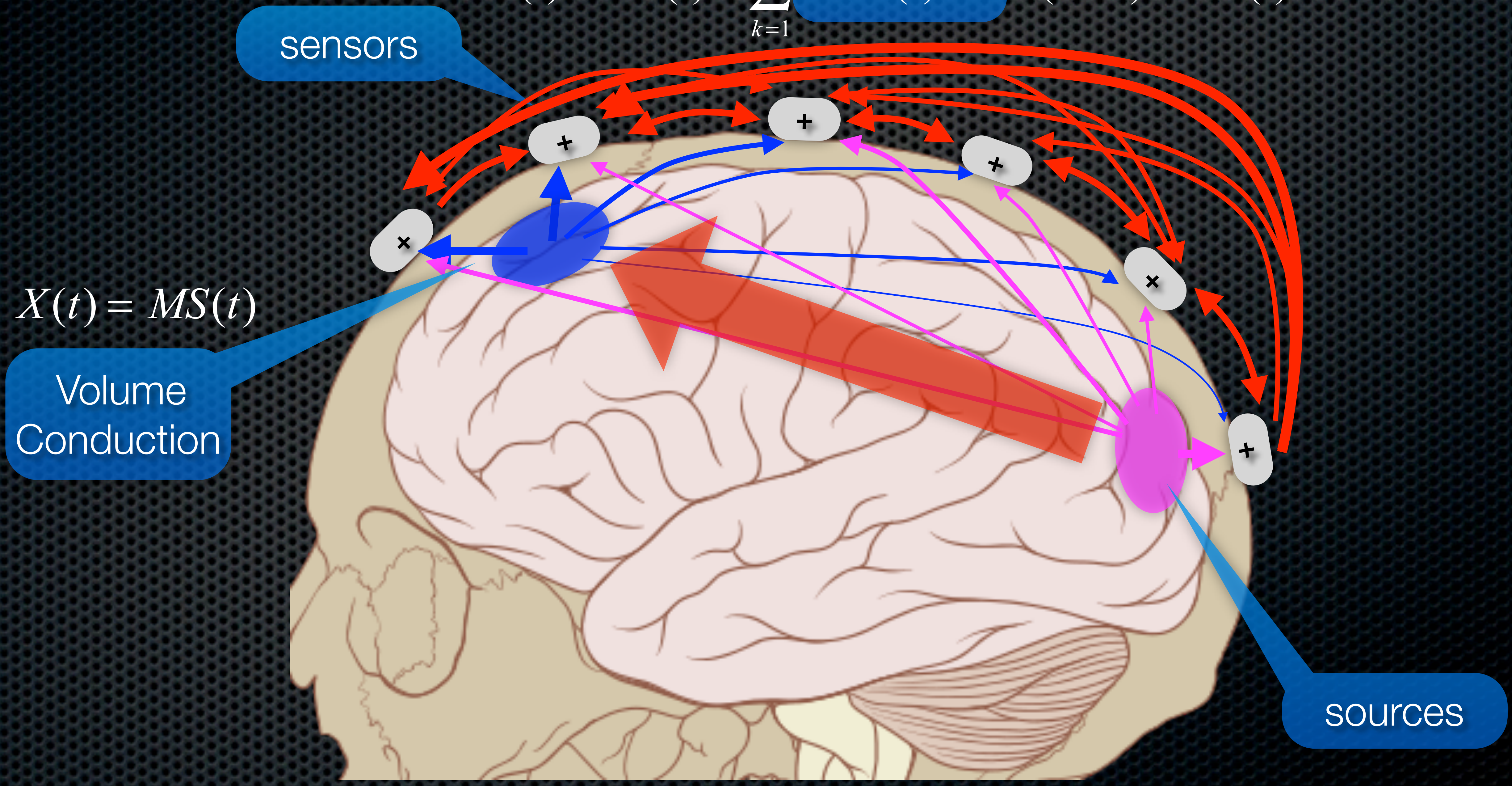
Channel or Source?



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

Channel or Source?

$$X(t) = MS(t) = \sum_{k=1}^{p} \boxed{MA^{(k)}(t)M^{-1}} X(t-k) + ME(t)$$

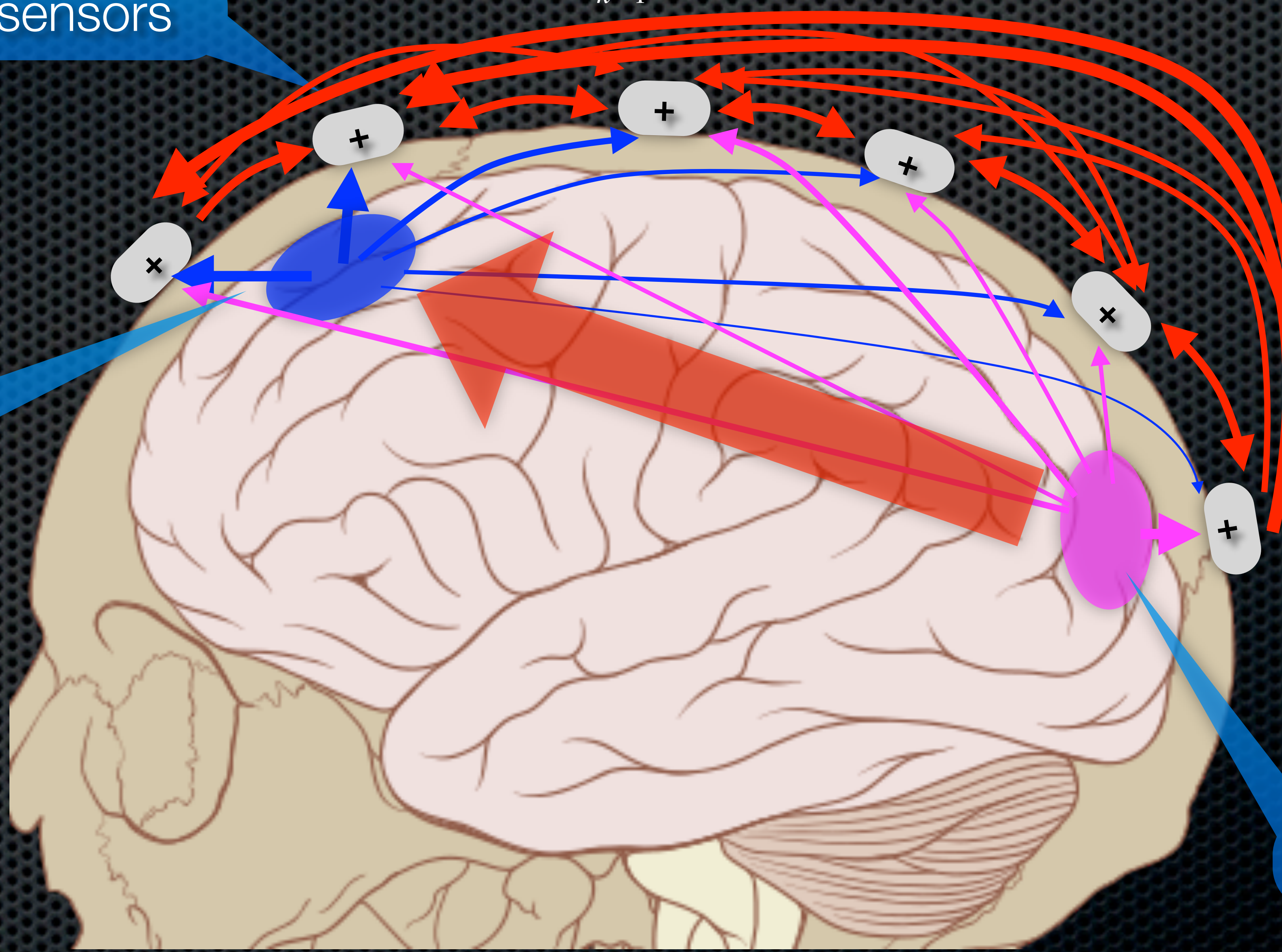


Solution? Source Reconstruction

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

Channel or Source?

$$X(t) = MS(t) = \sum_{k=1}^{p} \boxed{MA^{(k)}(t)M^{-1}} X(t-k) + ME(t)$$



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

Volume Conduction

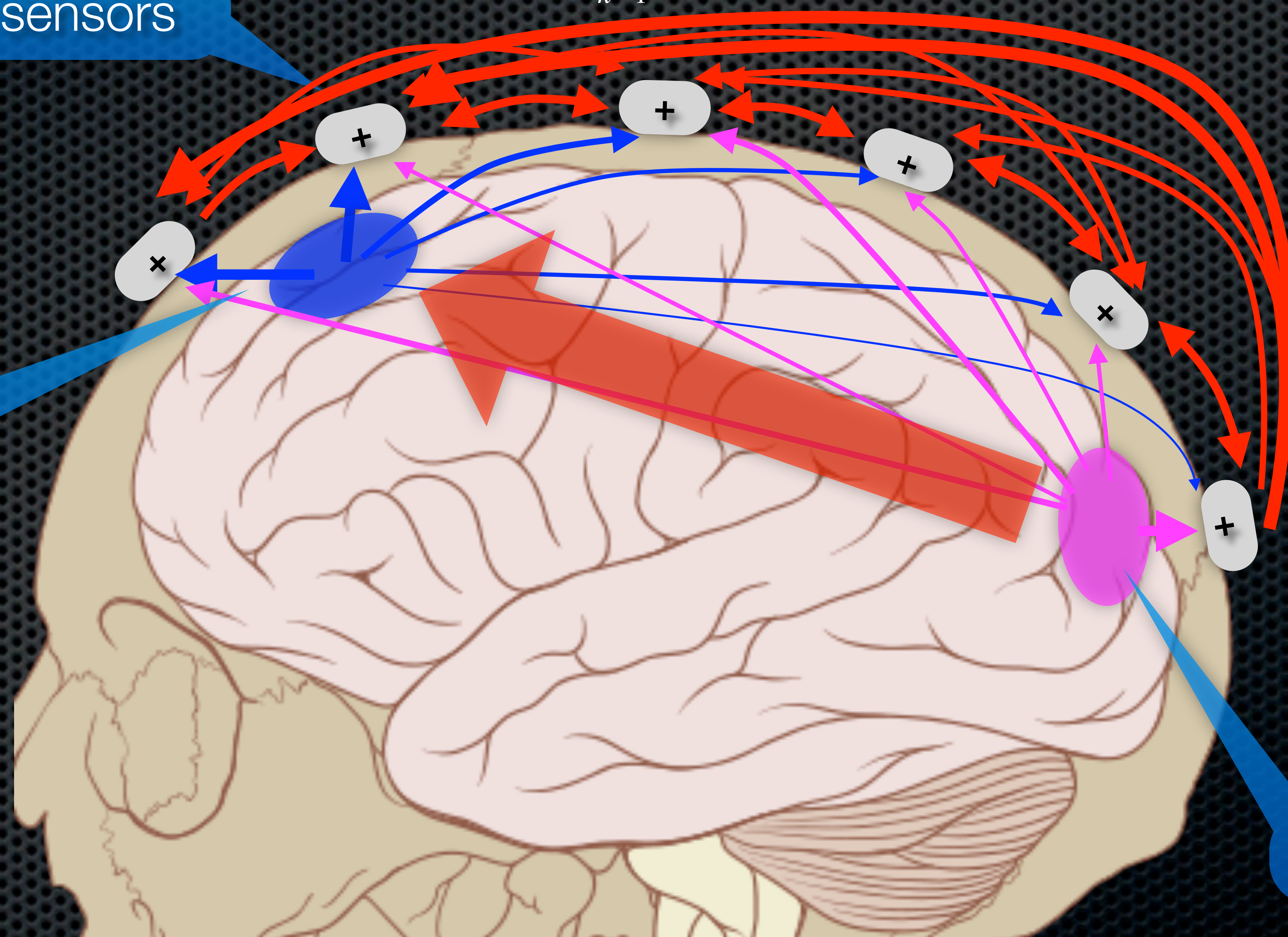
ICA
Sparse Bayesian Learning
Beamforming
Minimum-norm
...

Solution? Source Reconstruction

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

Channel or Source?

$$X(t) = MS(t) = \sum_{k=1}^{p} \boxed{MA^{(k)}(t)M^{-1}} X(t-k) + ME(t)$$



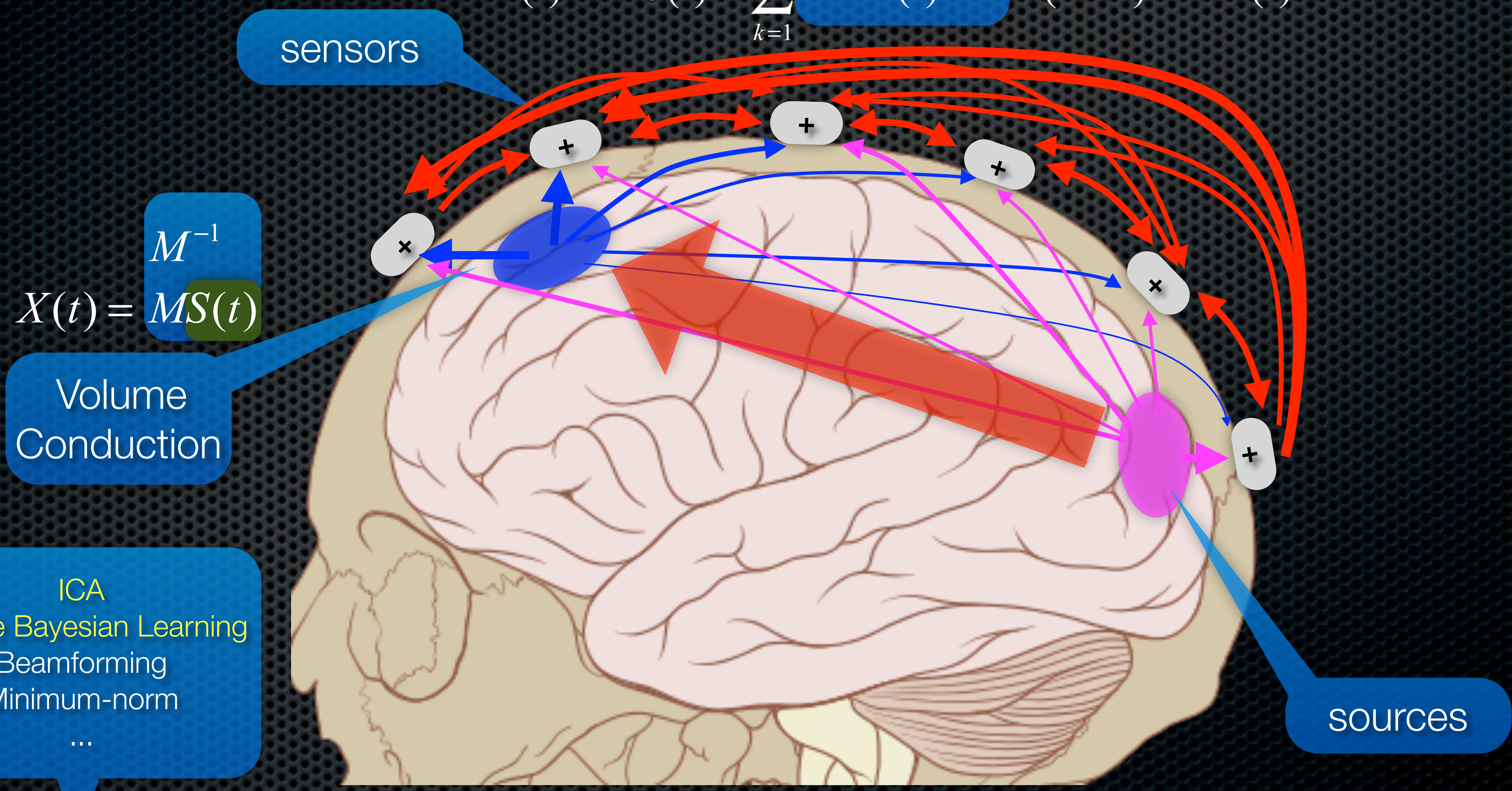
ICA
Sparse Bayesian Learning
Beamforming
Minimum-norm
...

Solution? Source Reconstruction

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

Channel or Source?

$$X(t) = MS(t) = \sum_{k=1}^{p} MA^{(k)}(t)M^{-1}X(t-k) + ME(t)$$

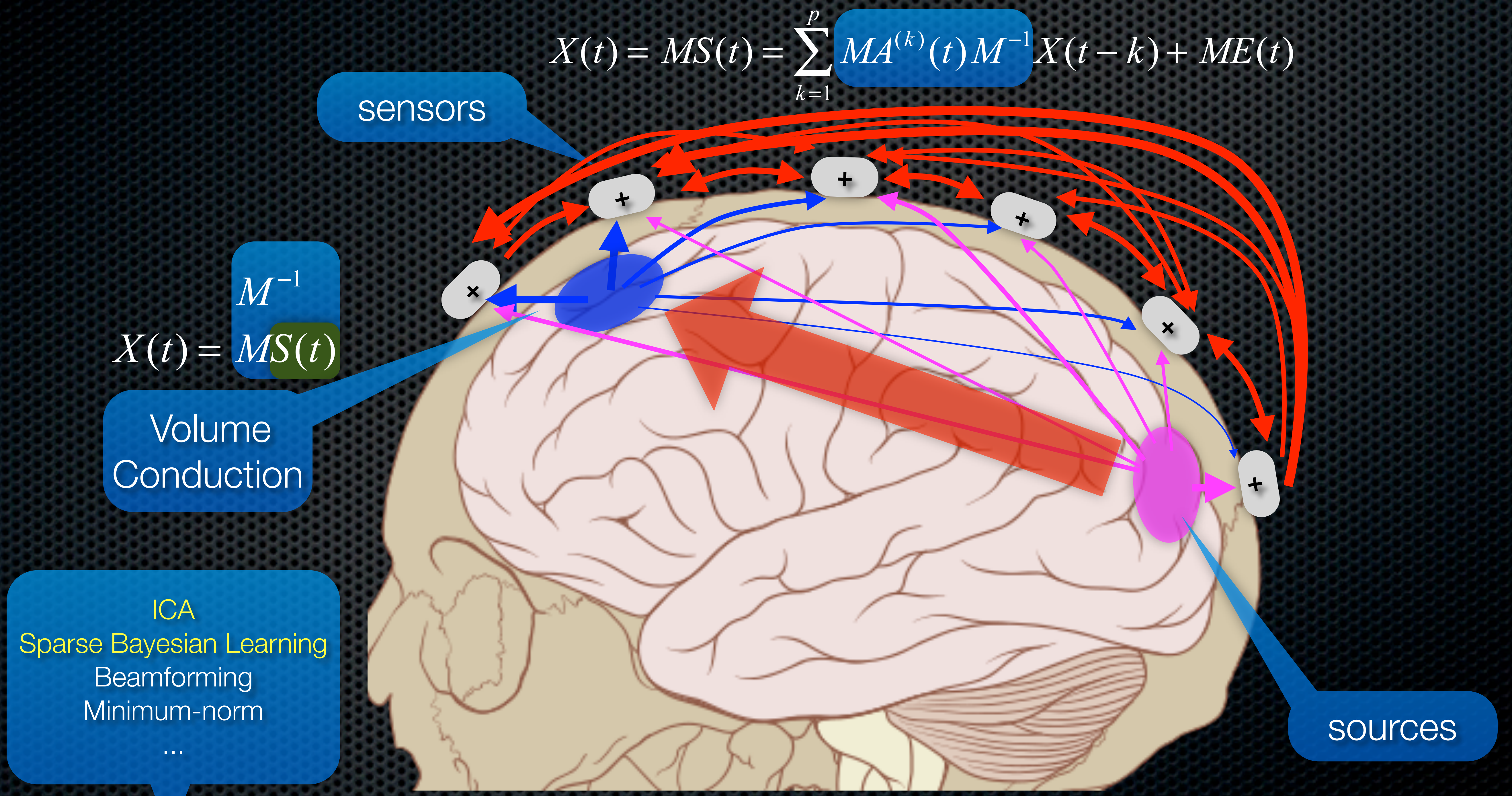


ICA
Sparse Bayesian Learning
Beamforming
Minimum-norm
...

Solution? Source Reconstruction

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

Channel or Source?



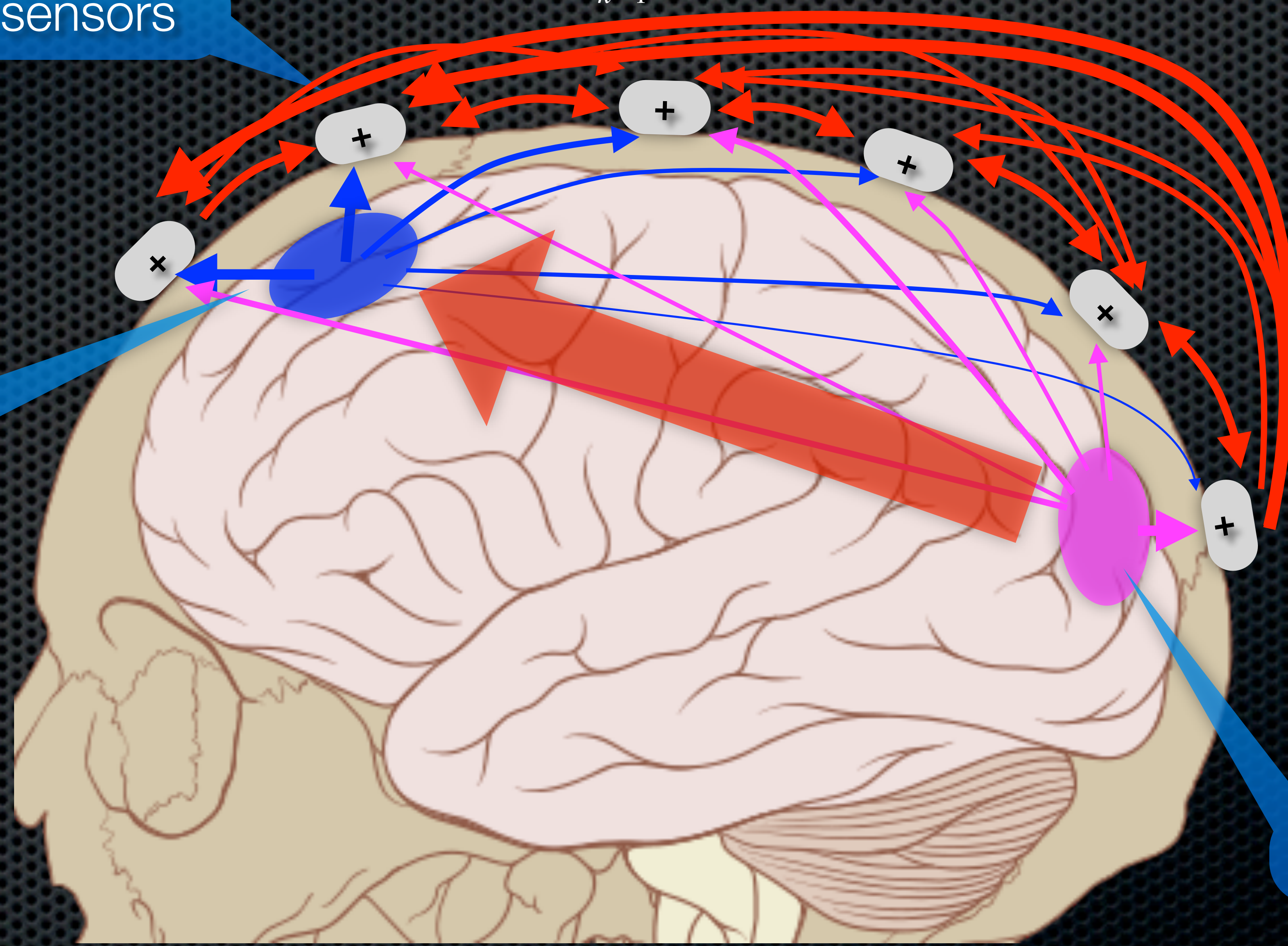
Solution? Source Reconstruction

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

Channel or Source?

Volume conduction exists for ECoG too!
(c.f. Whitmer, Worrell, ... , Makeig, *Frontiers in Neuro*. 2010

$$X(t) = MS(t) = \sum_{k=1}^{p} \boxed{MA^{(k)}(t)M^{-1}} X(t-k) + ME(t)$$



$$X(t) = \boxed{M^{-1}}\ \boxed{MS(t)}$$

ICA
Sparse Bayesian Learning
Beamforming
Minimum-norm
...

Solution? Source Reconstruction

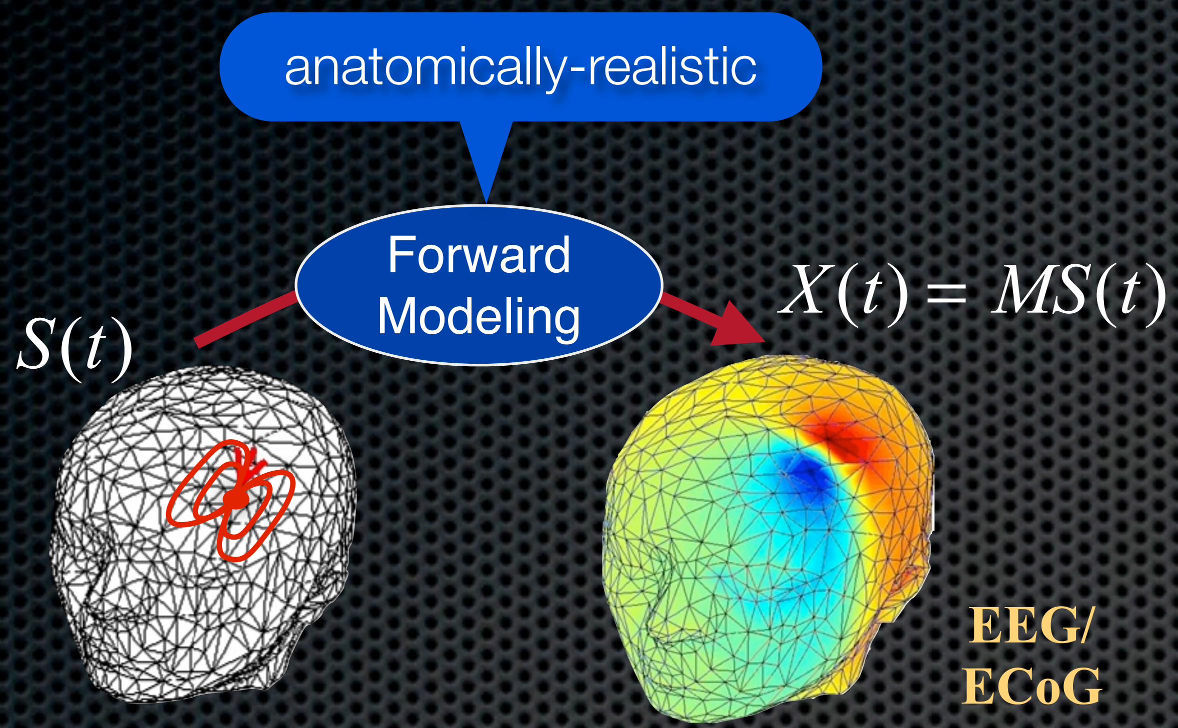
$$S(t) = \sum_{k=1}^{p} \boxed{A^{(k)}(t)} S(t-k) + E(t)$$

Forward/Inverse Modeling

$S(t)$

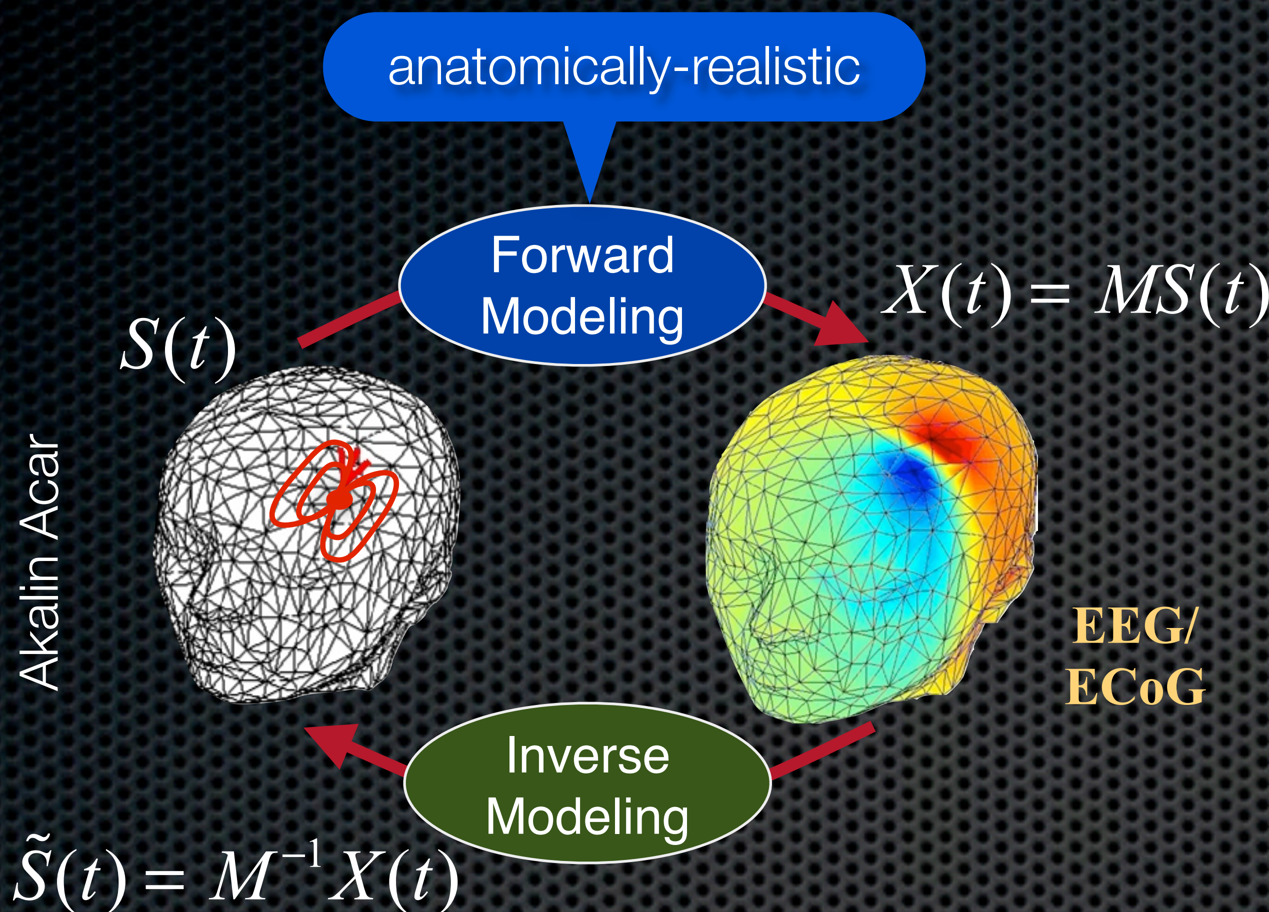
Akalin Acar

Forward/Inverse Modeling

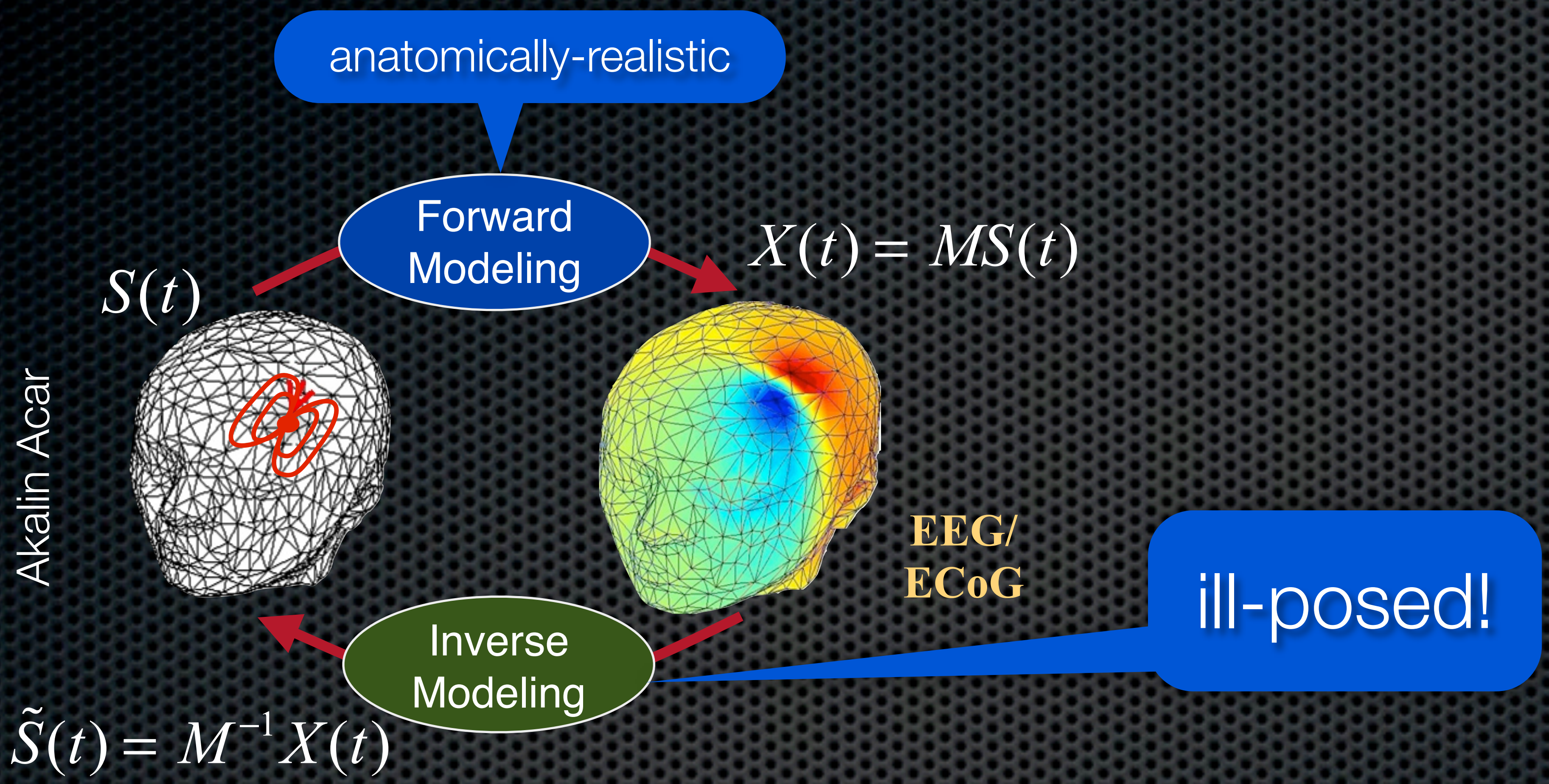


Akalin Acar

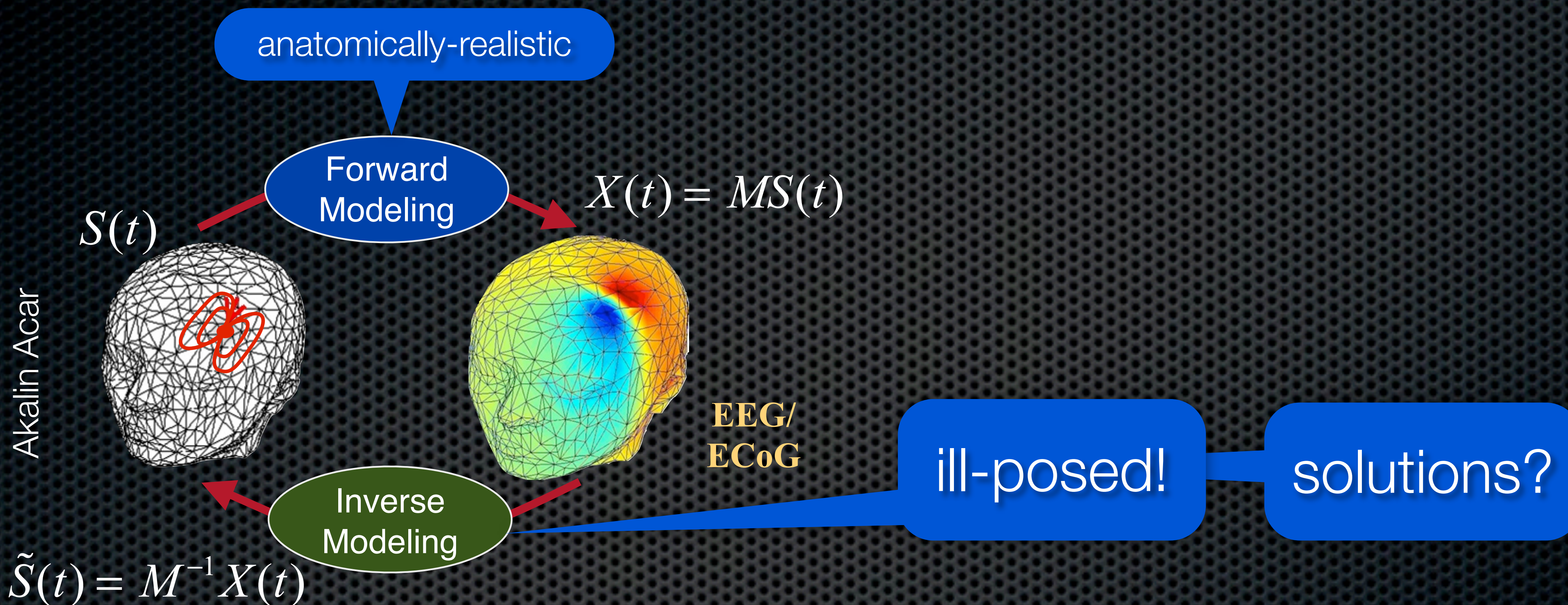
Forward/Inverse Modeling



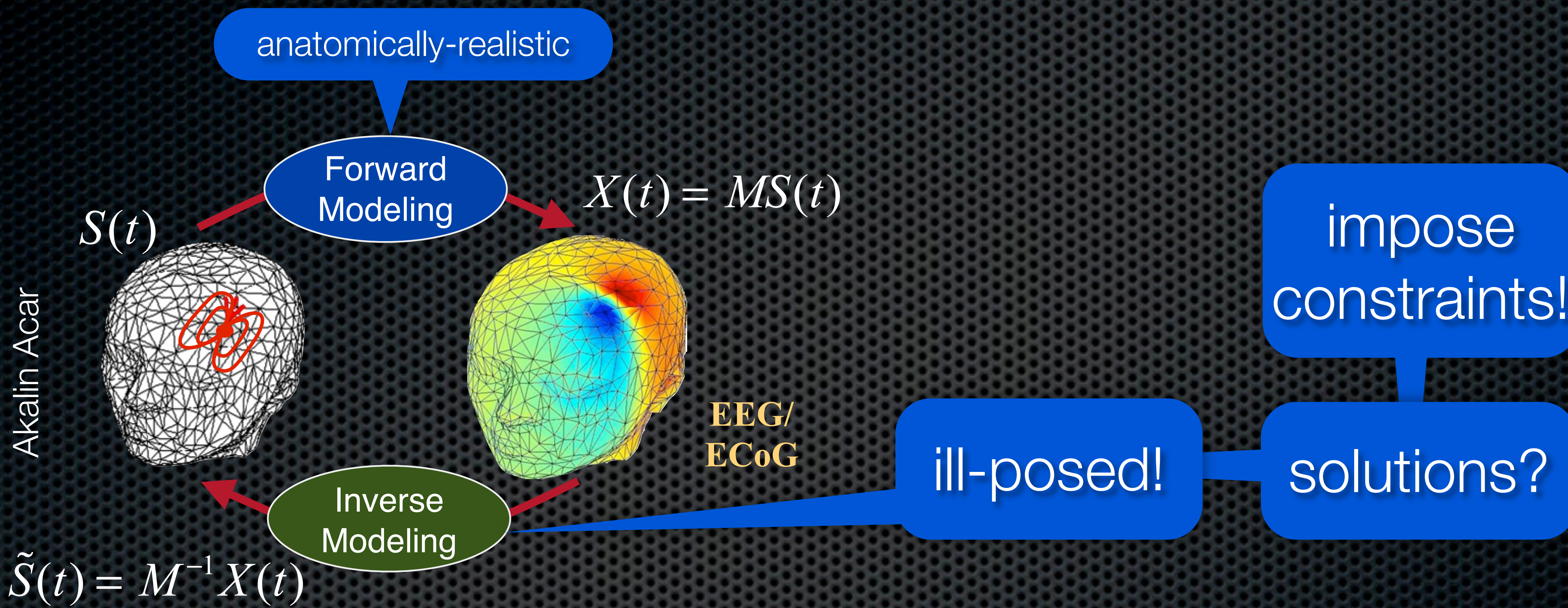
Forward/Inverse Modeling



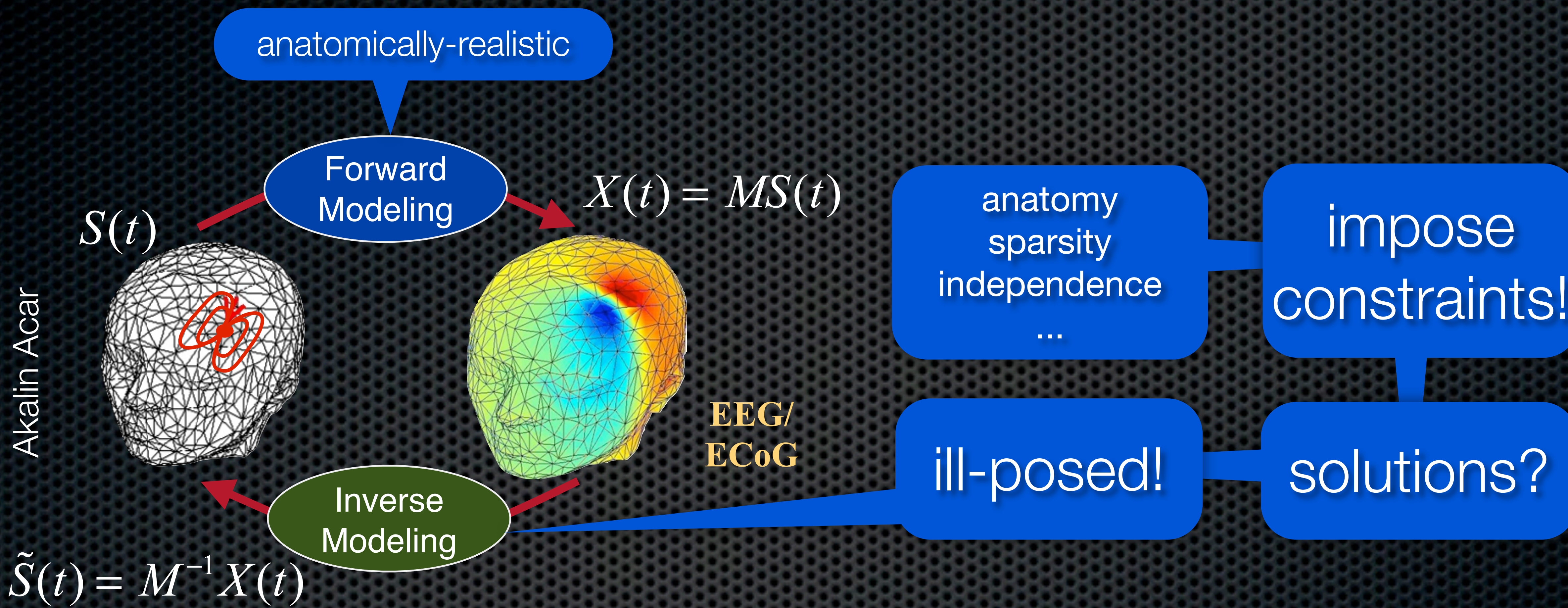
Forward/Inverse Modeling



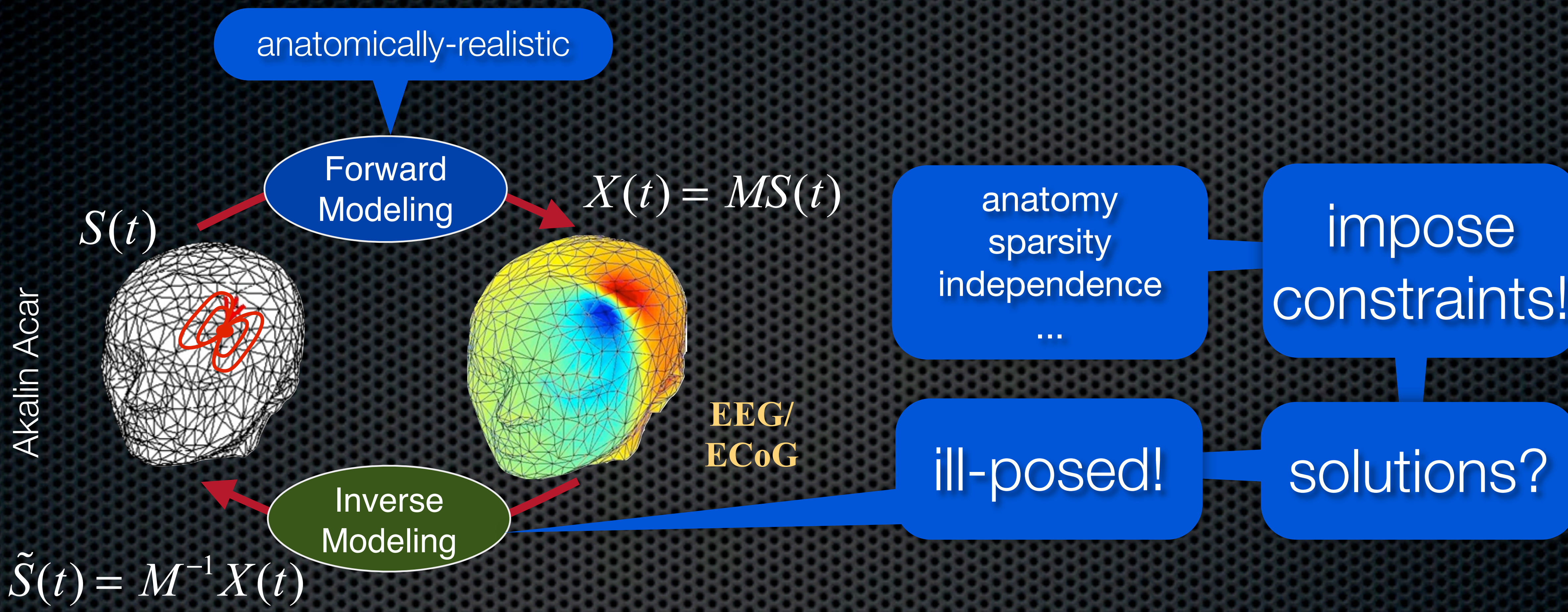
Forward/Inverse Modeling

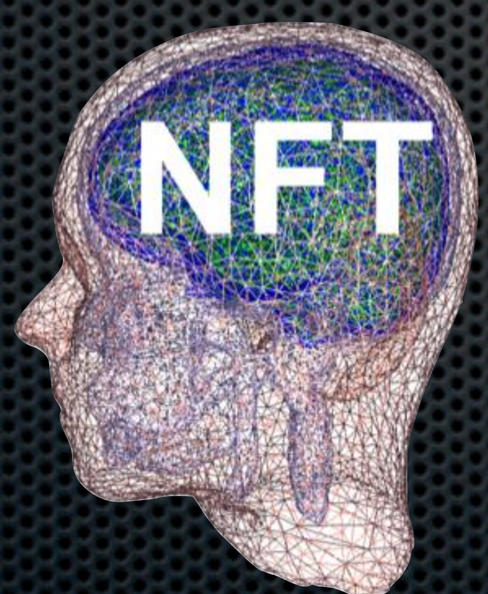


Forward/Inverse Modeling



Forward/Inverse Modeling



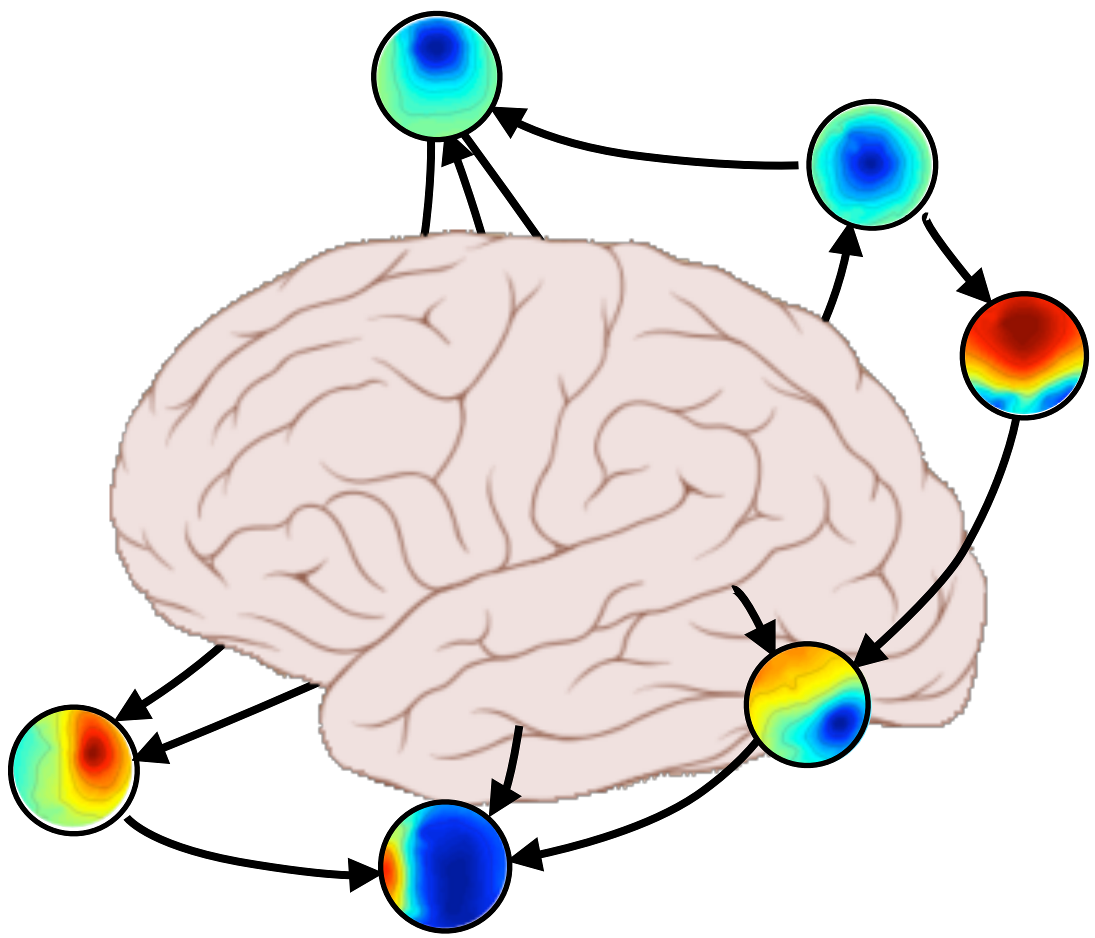


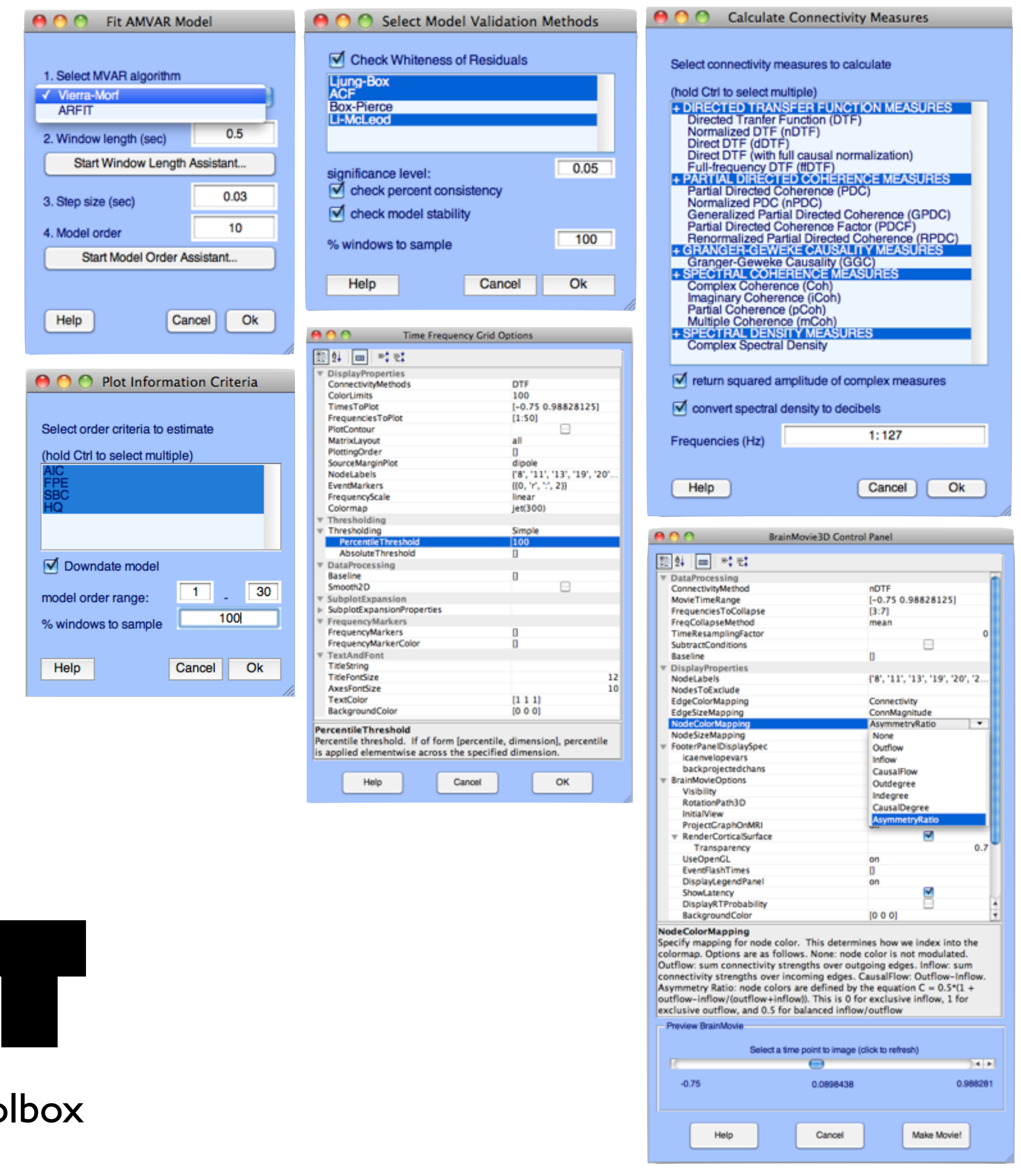
A Recipe for Reducing Errors:

- Anatomically Realistic Forward Model
- Appropriately Constrained Inverse Model

Akalin Acar and Makeig, 2010

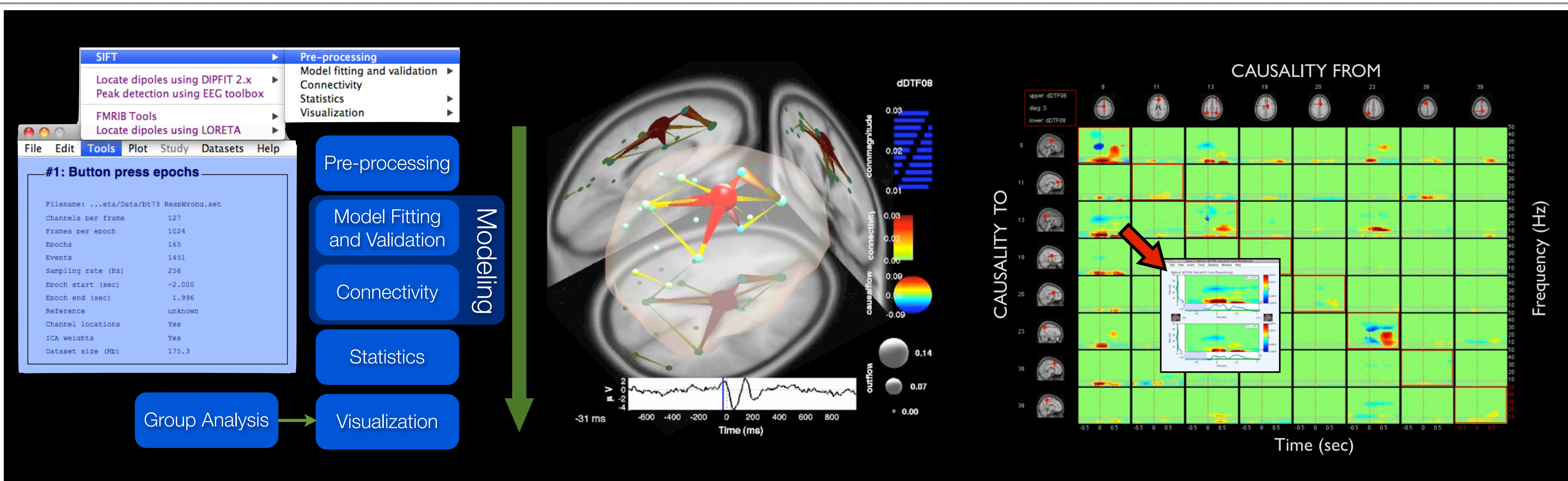
http://sccn.ucsd.edu/wiki/SIFT
Mullen, et al, *Journal of Neuroscience Methods* (in prep, 2011)
Mullen, Delorme, Kothe, Makeig, *Society for Neuroscience*, 2010
Delorme, Mullen, Kothe et al, *Computational Intelligence and Neuroscience*, vol 12, 2011





SIFT

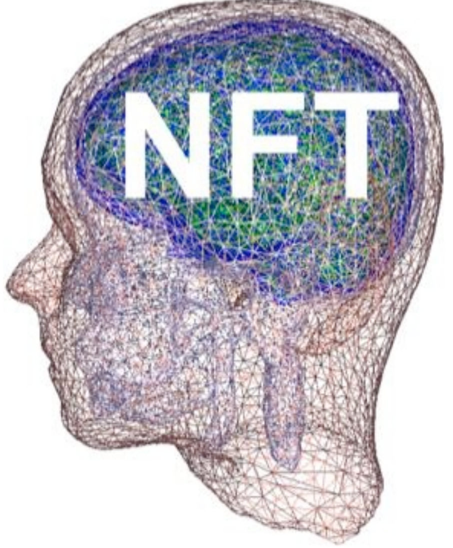
Source Information Flow Toolbox

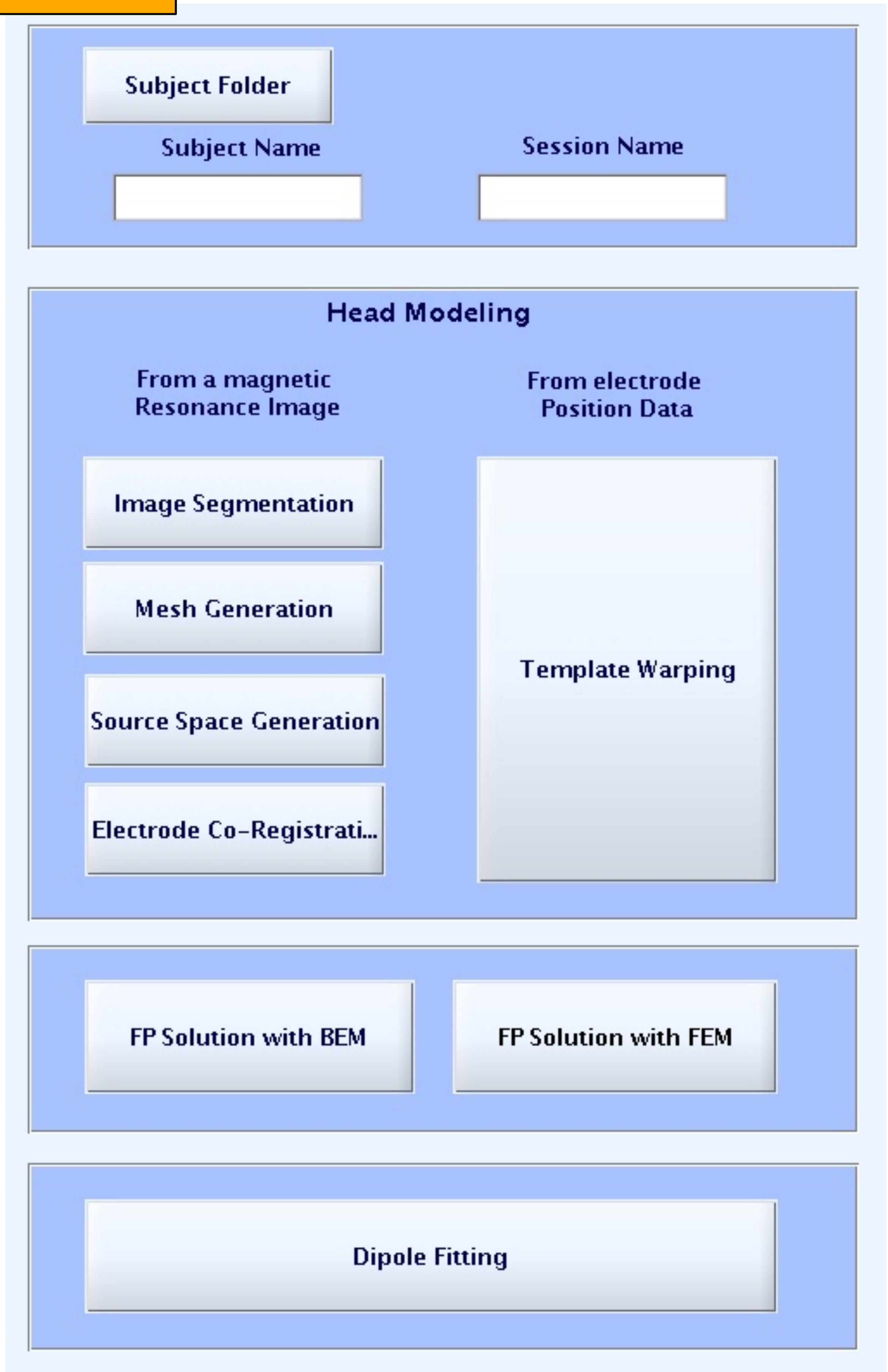


Neuroelectromagnetic Forward Head Modeling Toolbox

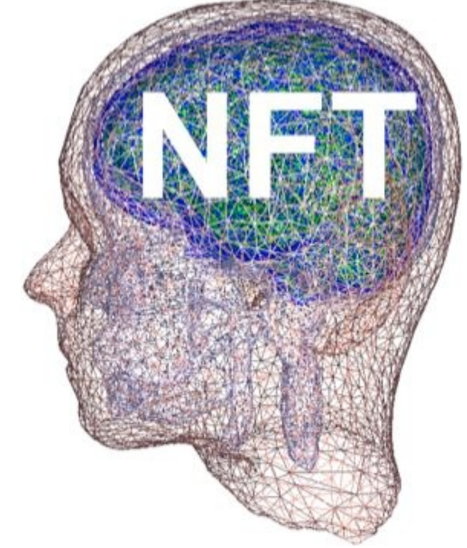
Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



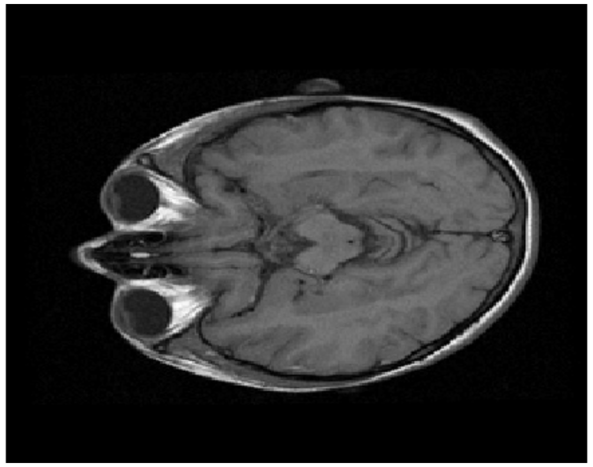


Neuroelectromagnetic Forward Head Modeling Toolbox

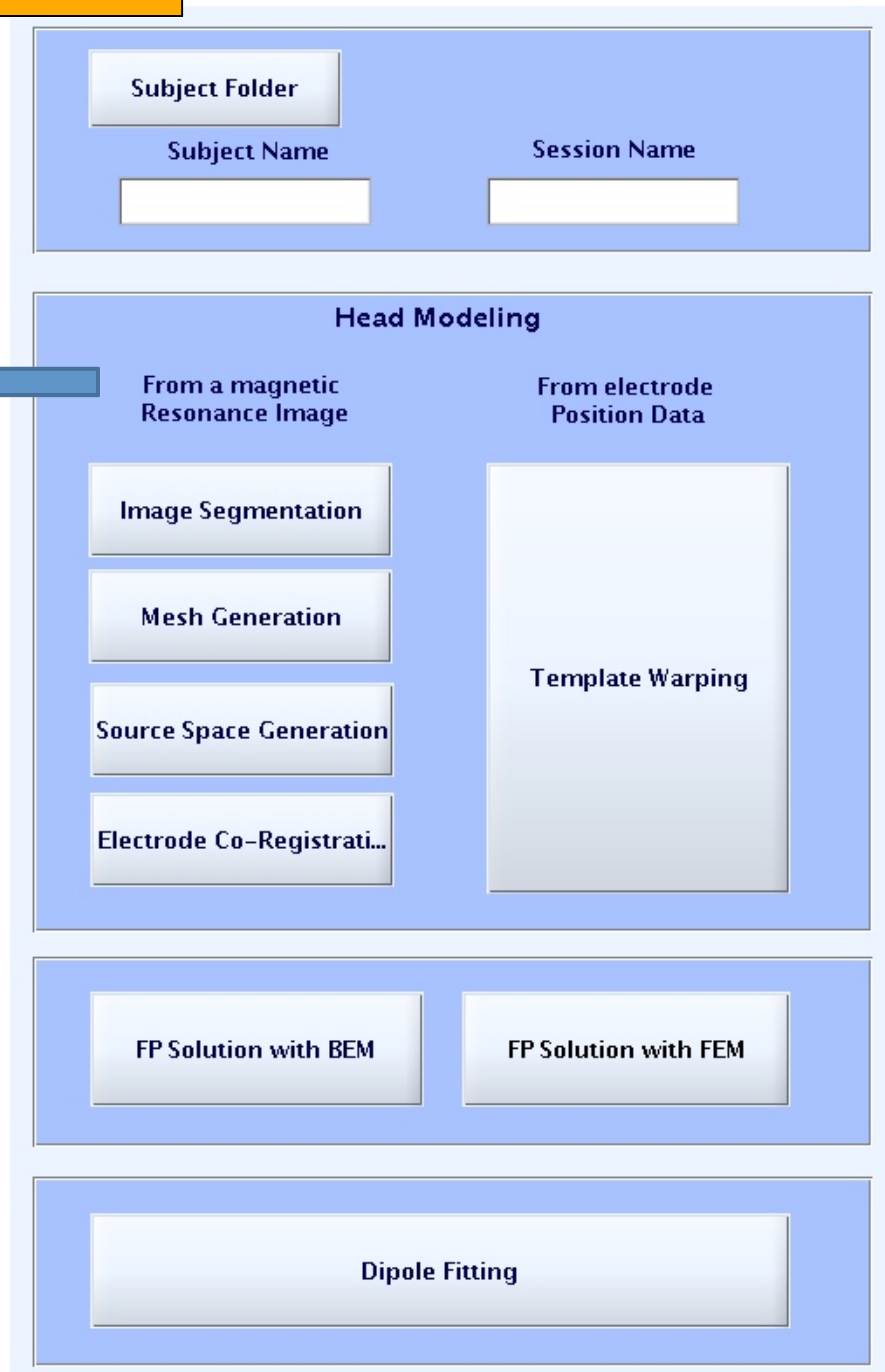


Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



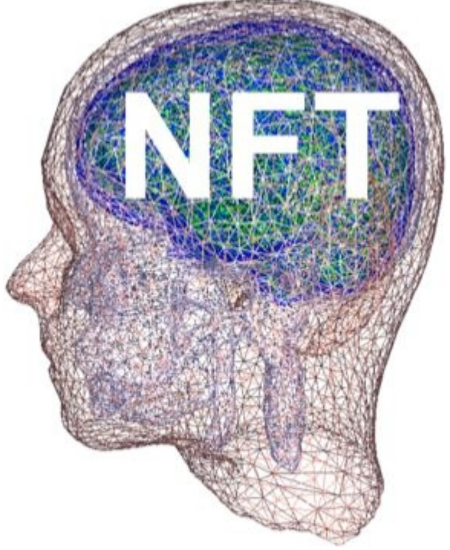
T1-weighted

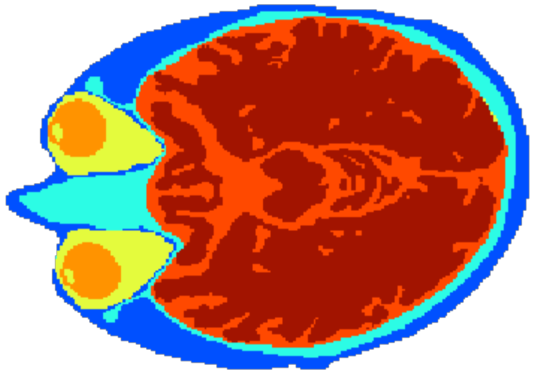


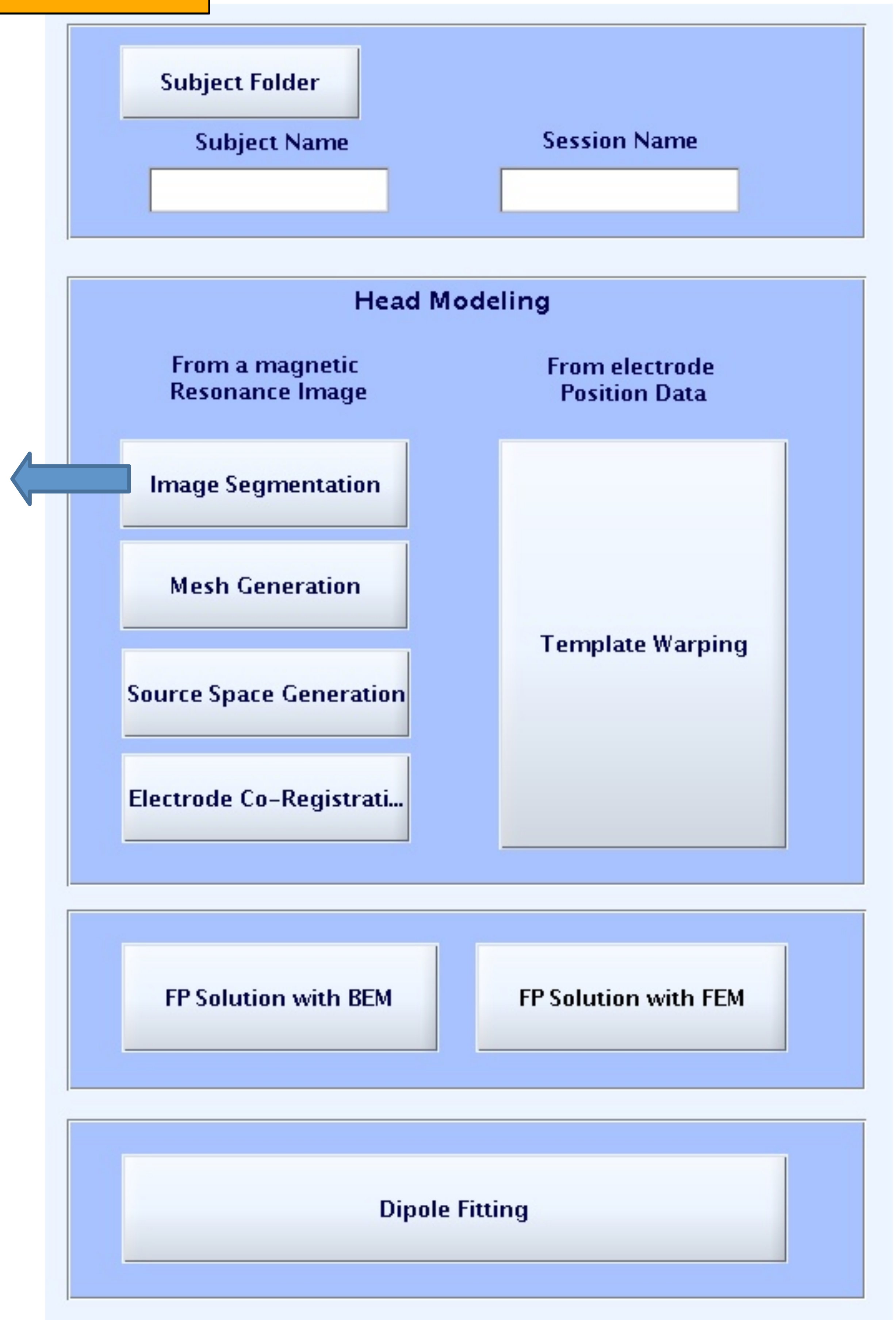
Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



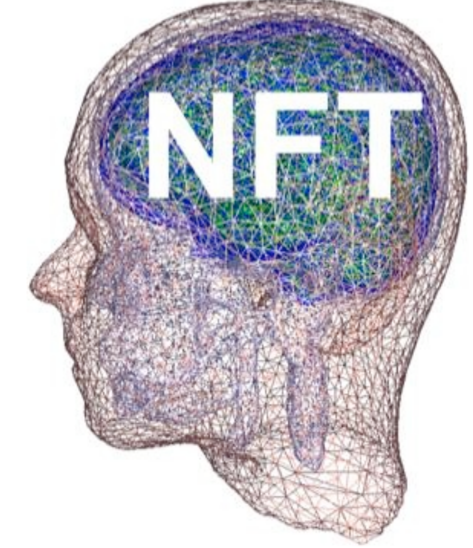


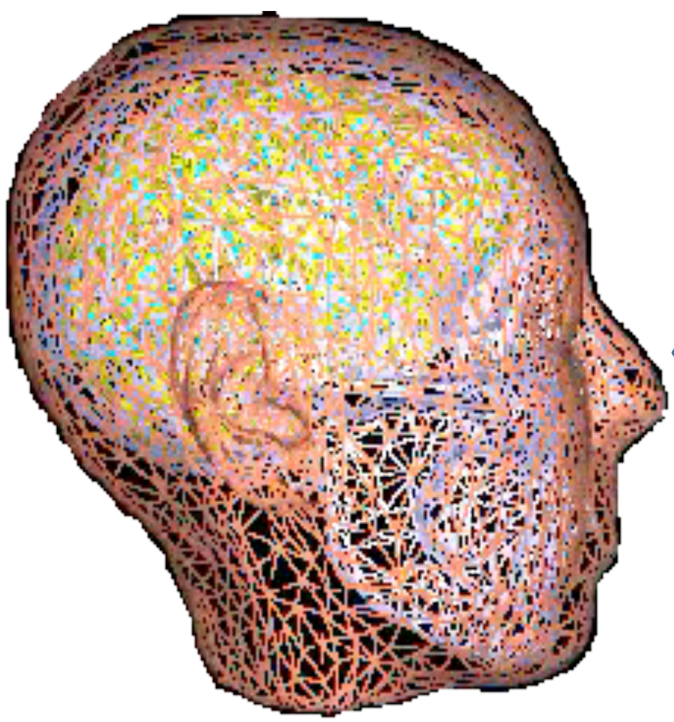


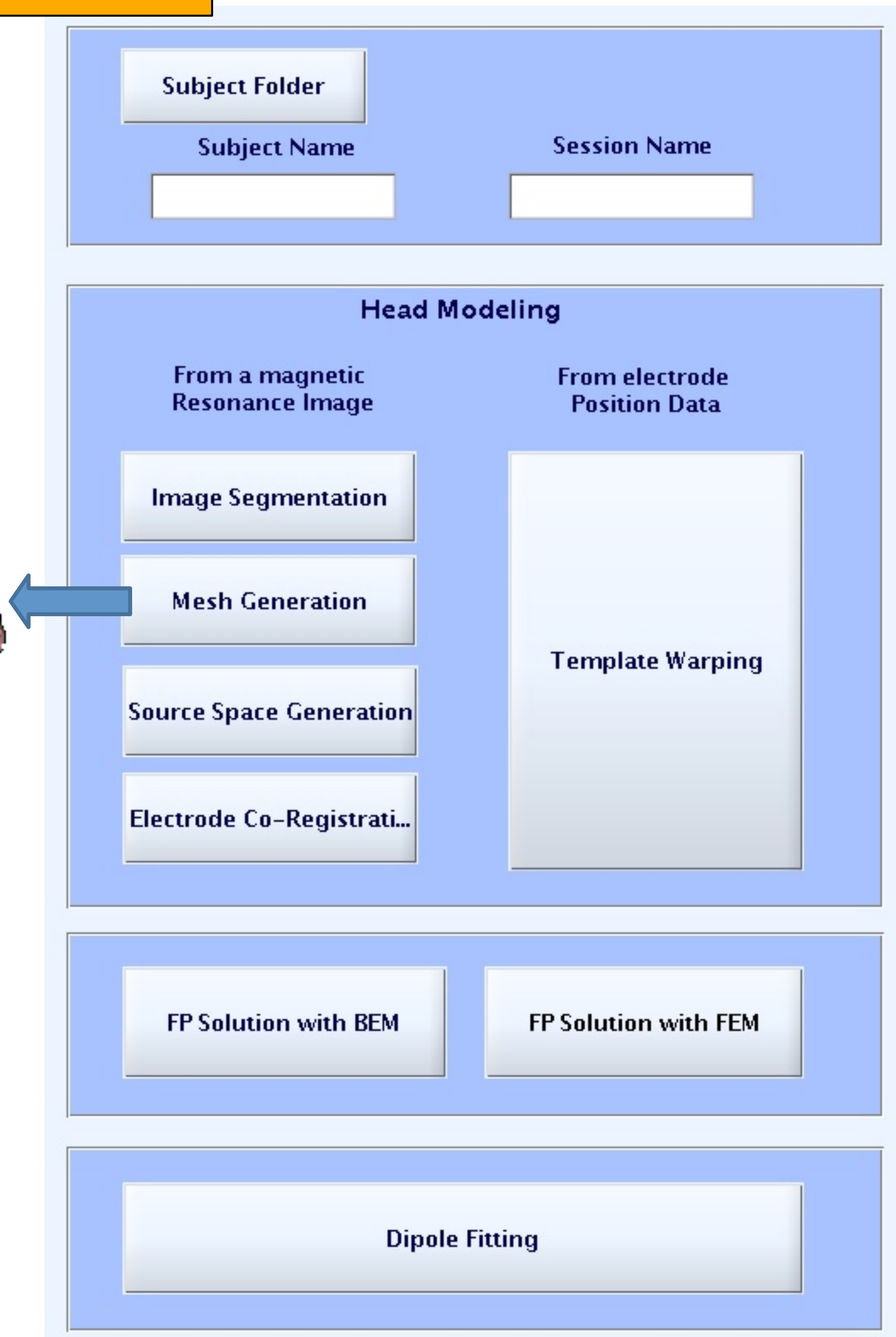
Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



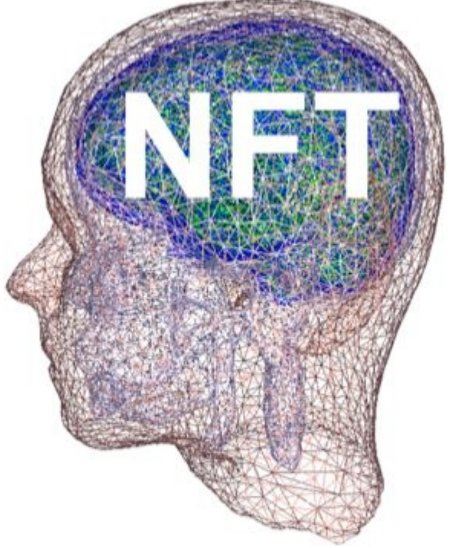


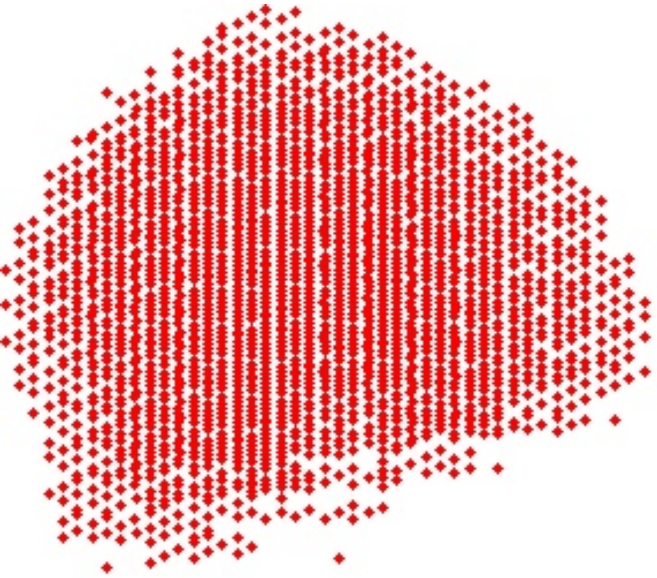


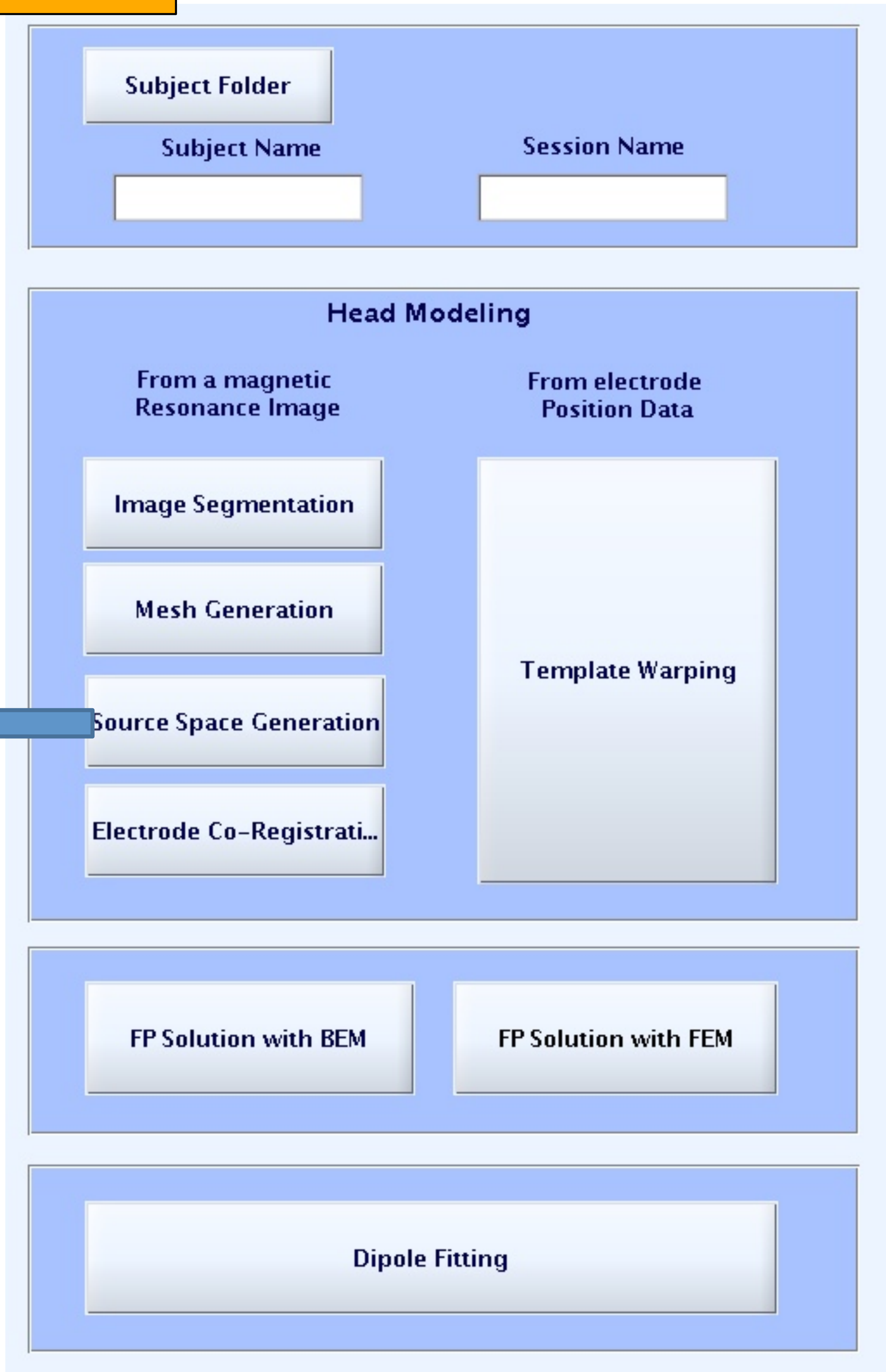
Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

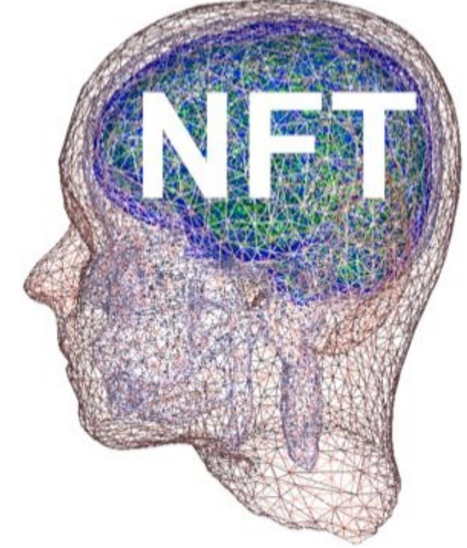
http://sccn.ucsd.edu/nft





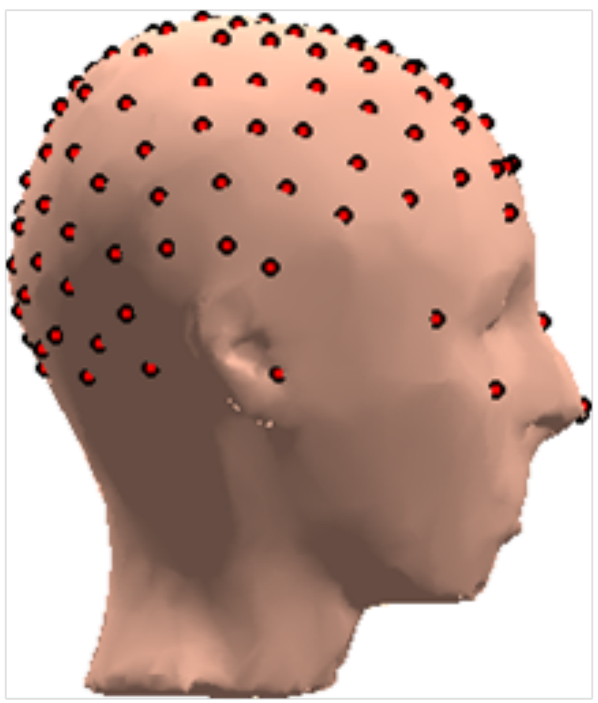


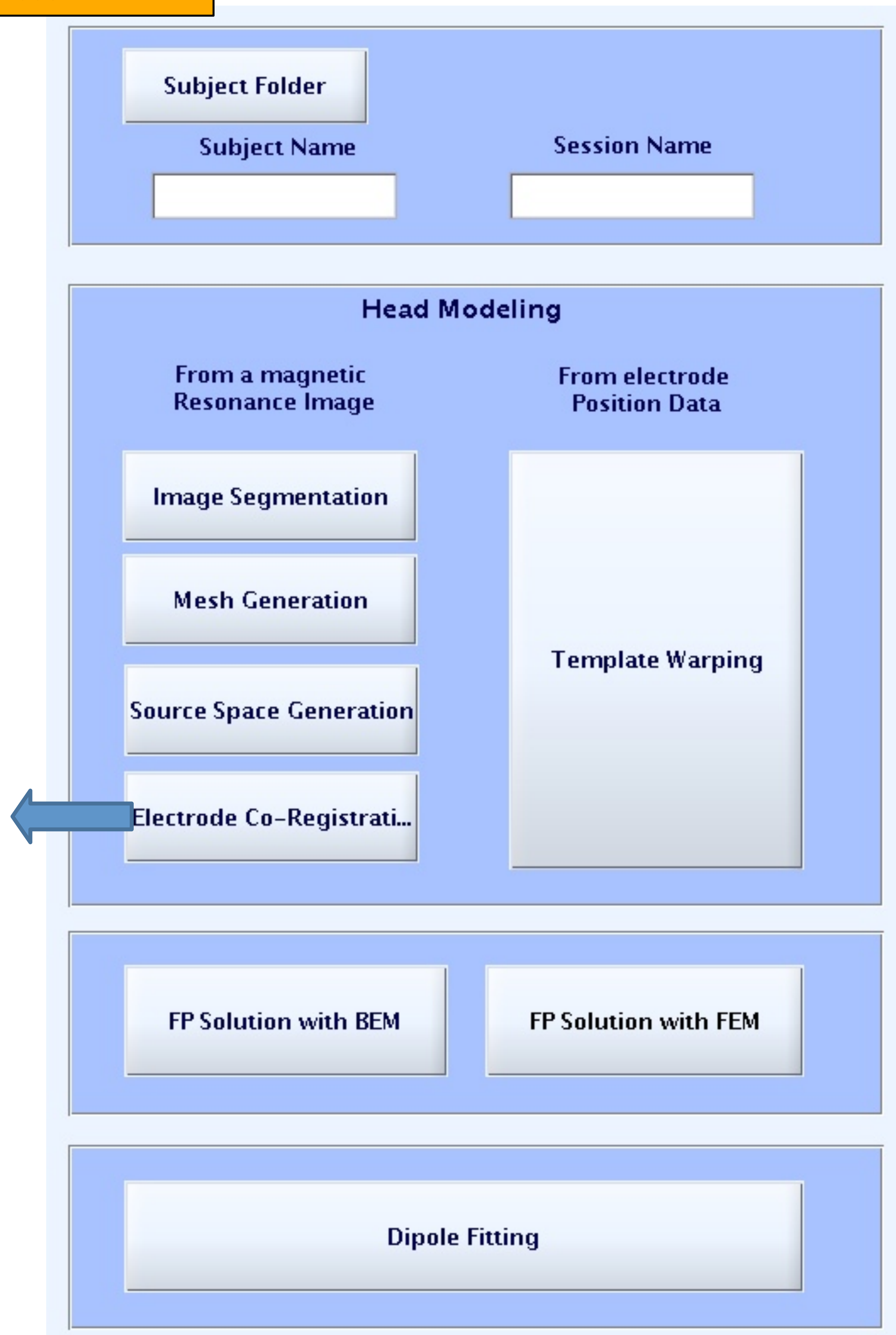
Neuroelectromagnetic Forward Head Modeling Toolbox



Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft

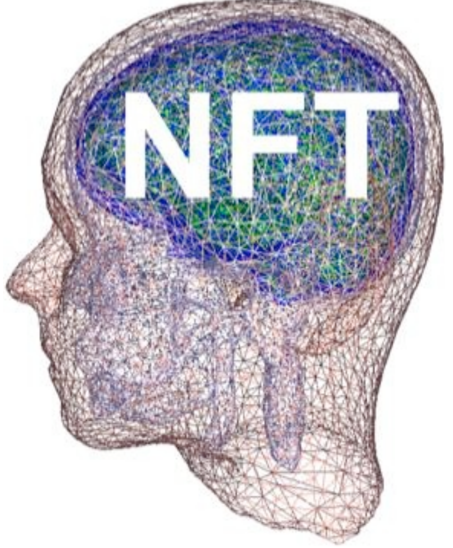


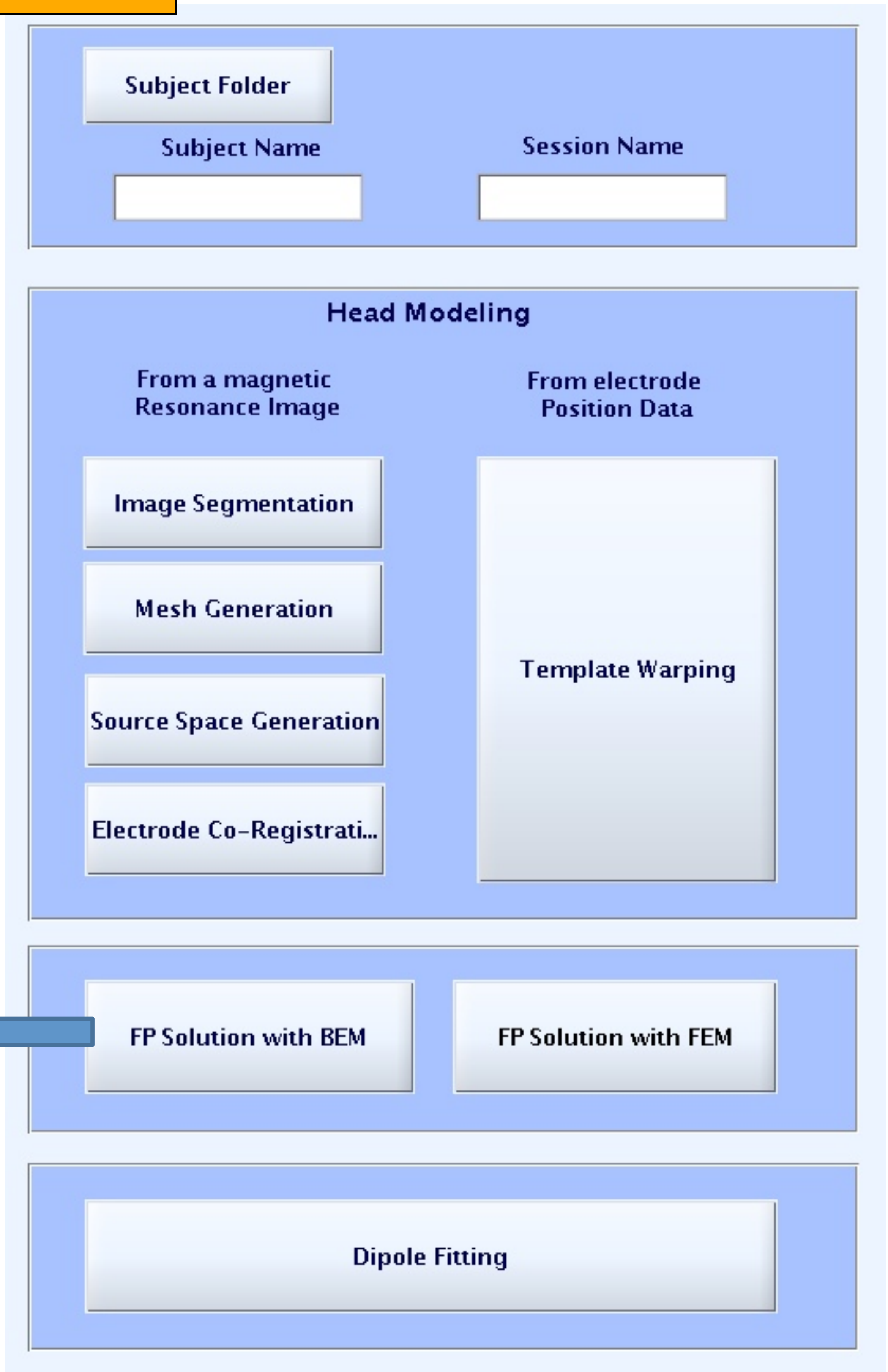


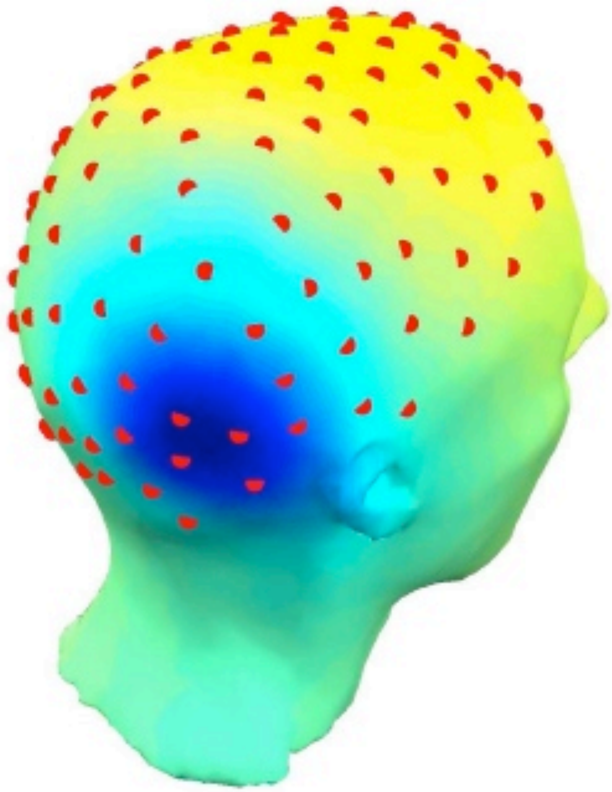
Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



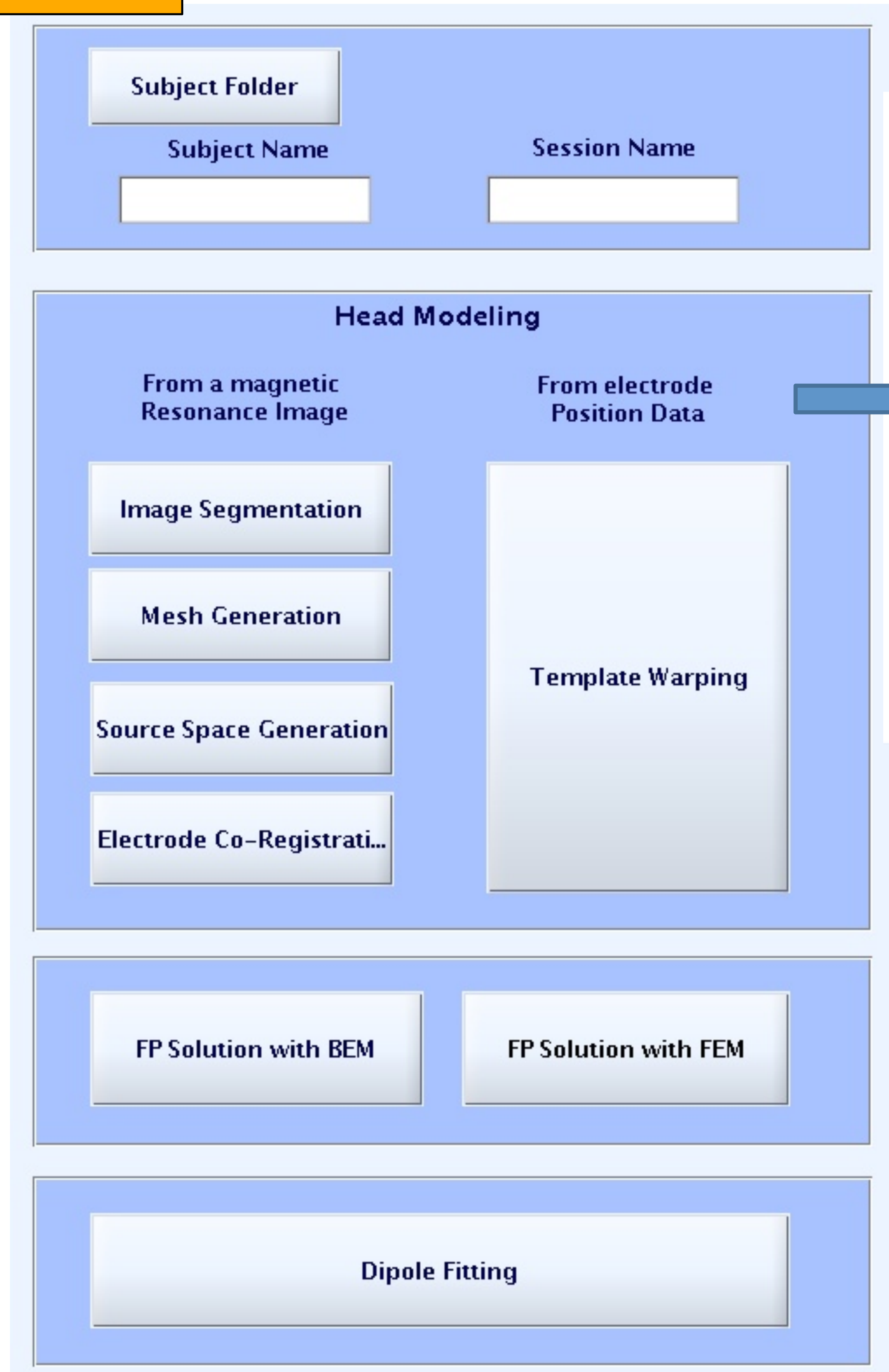


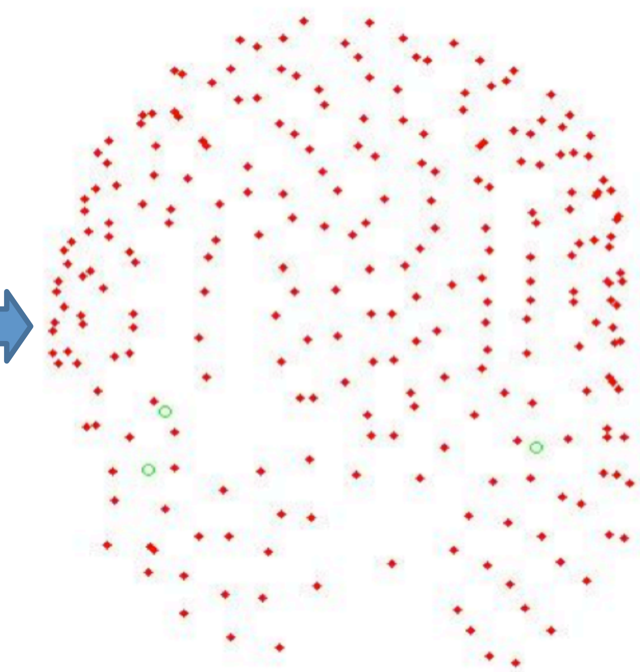


Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



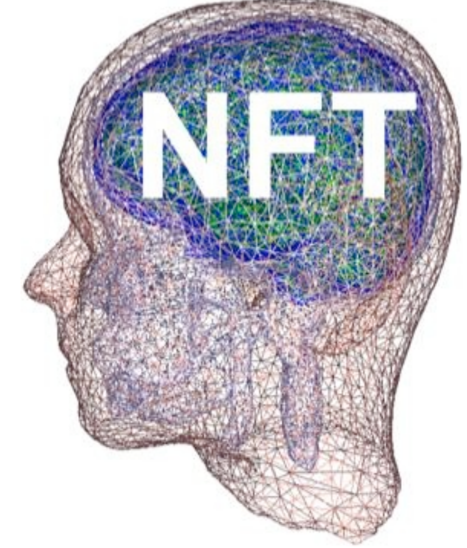


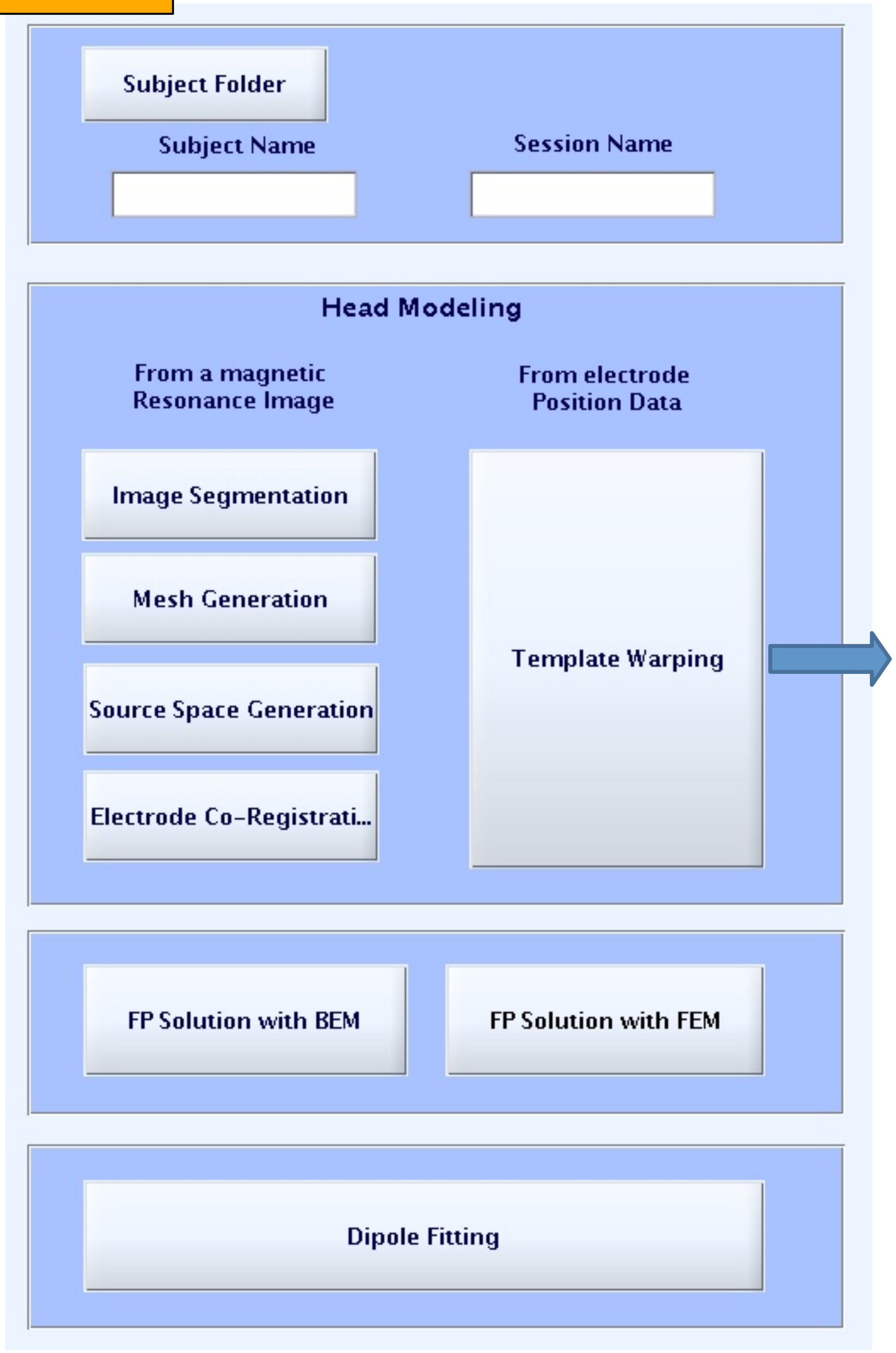
Digitizer locations

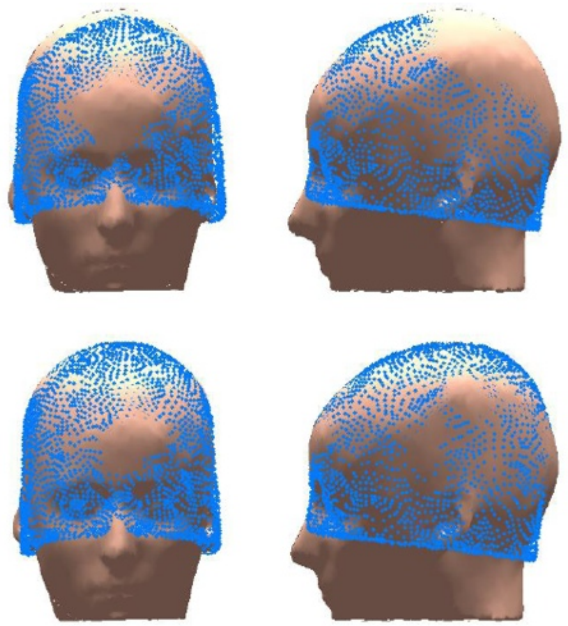
Neuroelectromagnetic Forward Head Modeling Toolbox

Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft



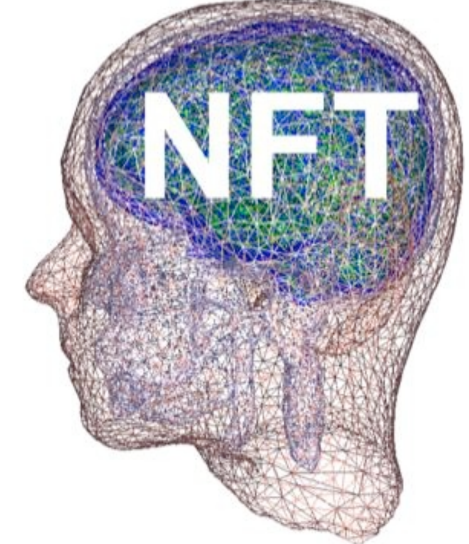


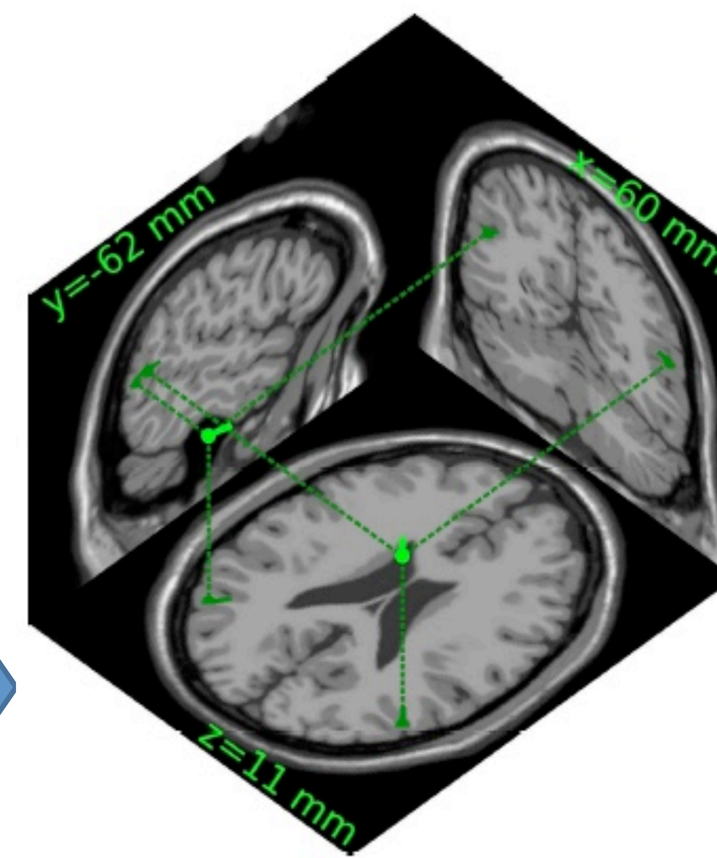


Neuroelectromagnetic Forward Head Modeling Toolbox

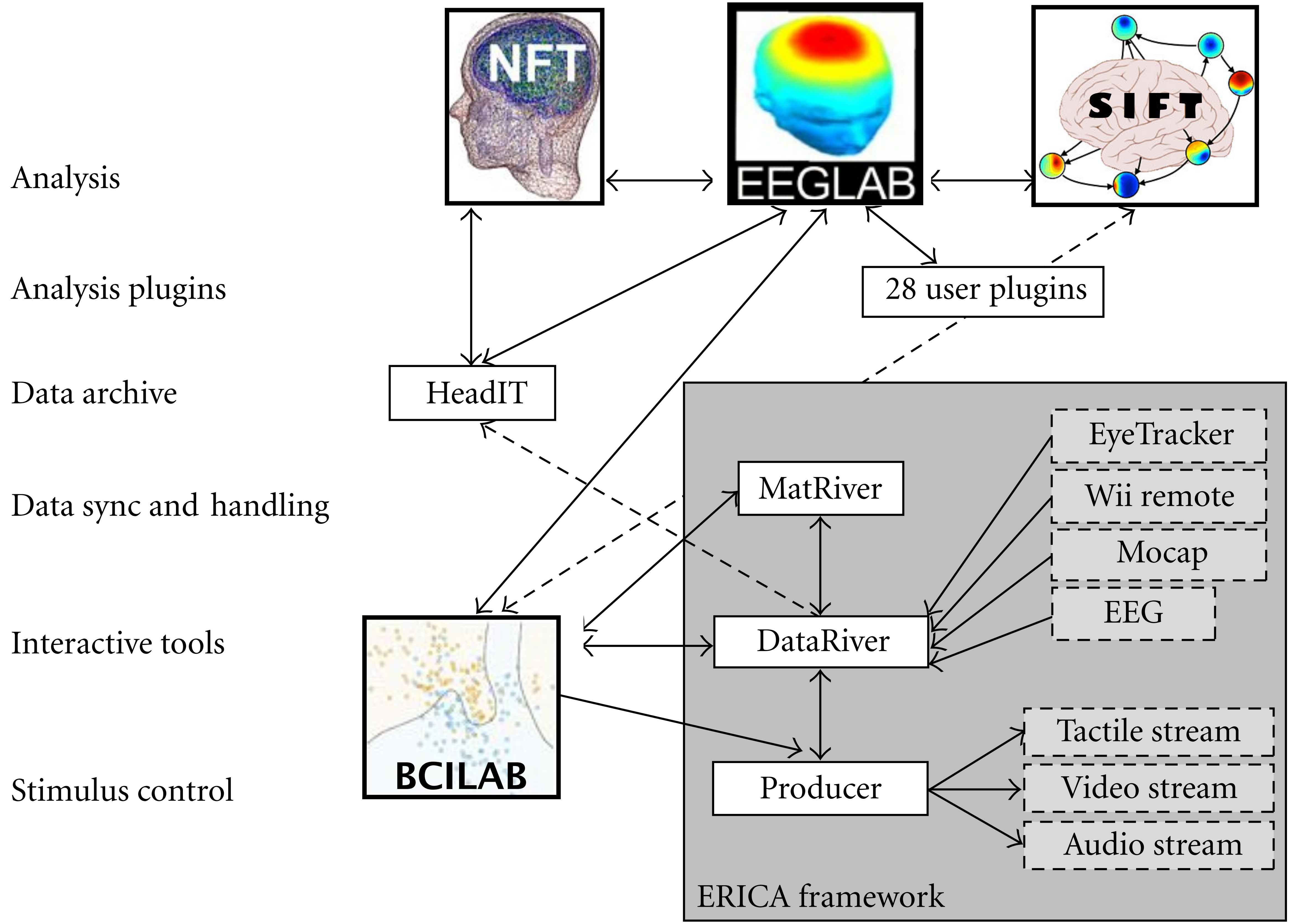
Akalin Acar and Makeig, *J. Neurosci. Methods*, 2010
Akalin Acar and Makeig, *IEEE EMBC*, 2008

http://sccn.ucsd.edu/nft





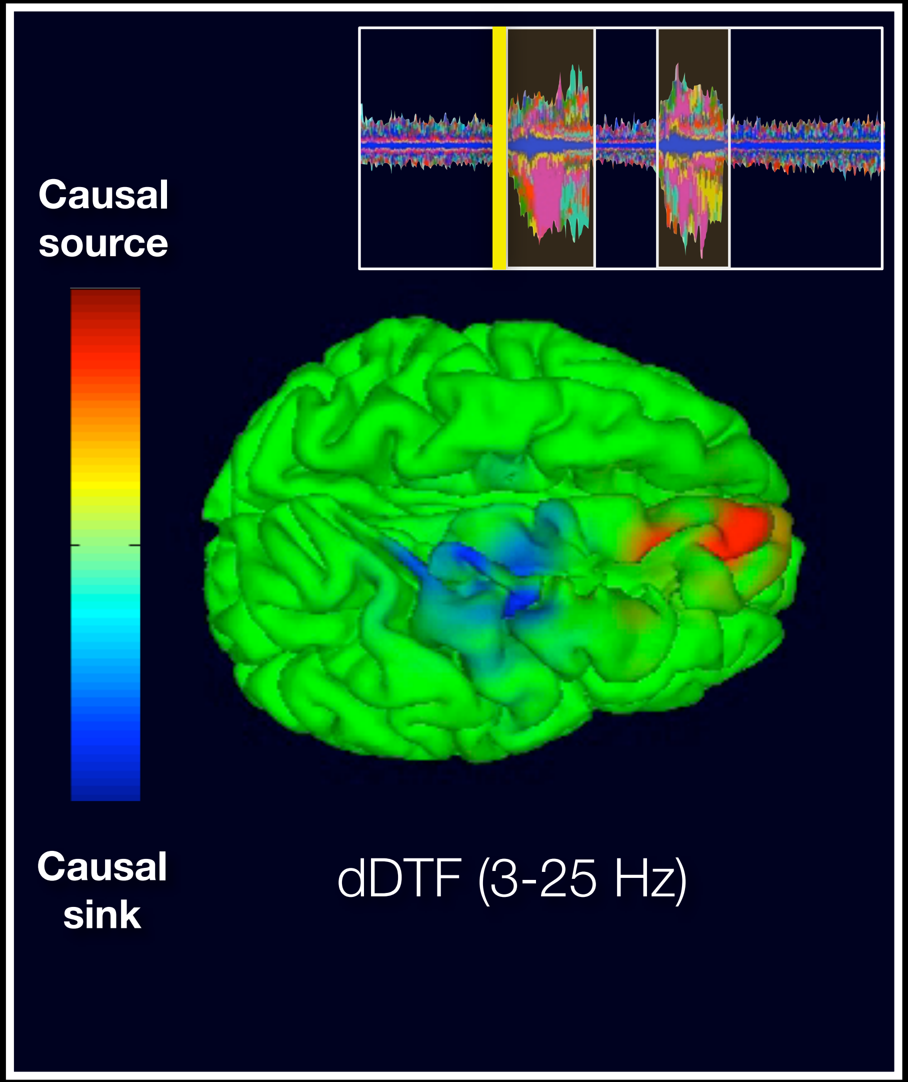
EEGLAB Software framework



Delorme, Mullen, Kothe, Akalin Acar, Bigdely-Shamlo, Vankov, Makeig, *Computational Intelligence and Neuroscience*, vol 12, 2011

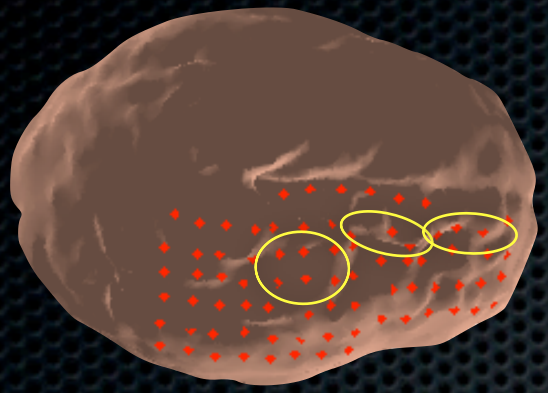
An Application

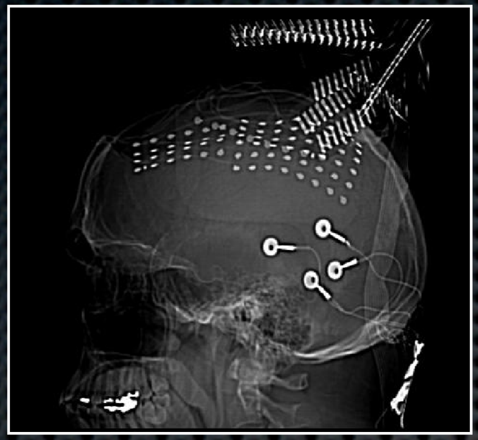
Spatiotemporal modeling of seizure causal hubs and propagation dynamics from intracranial EEG



Mullen et al, *IEEE EMBC*, 2011

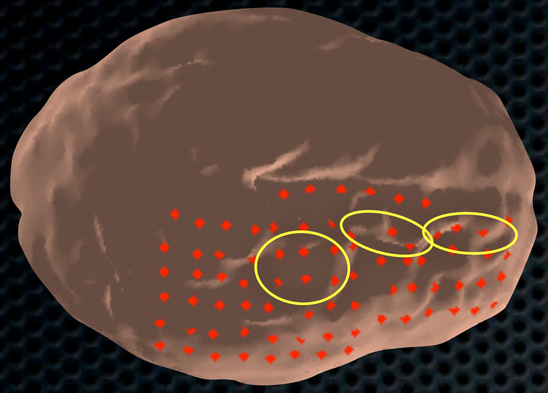
Seizure Data

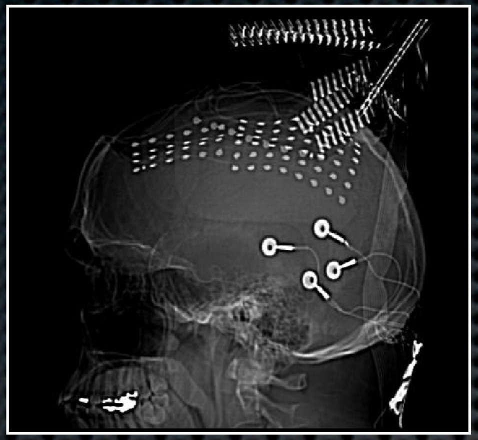




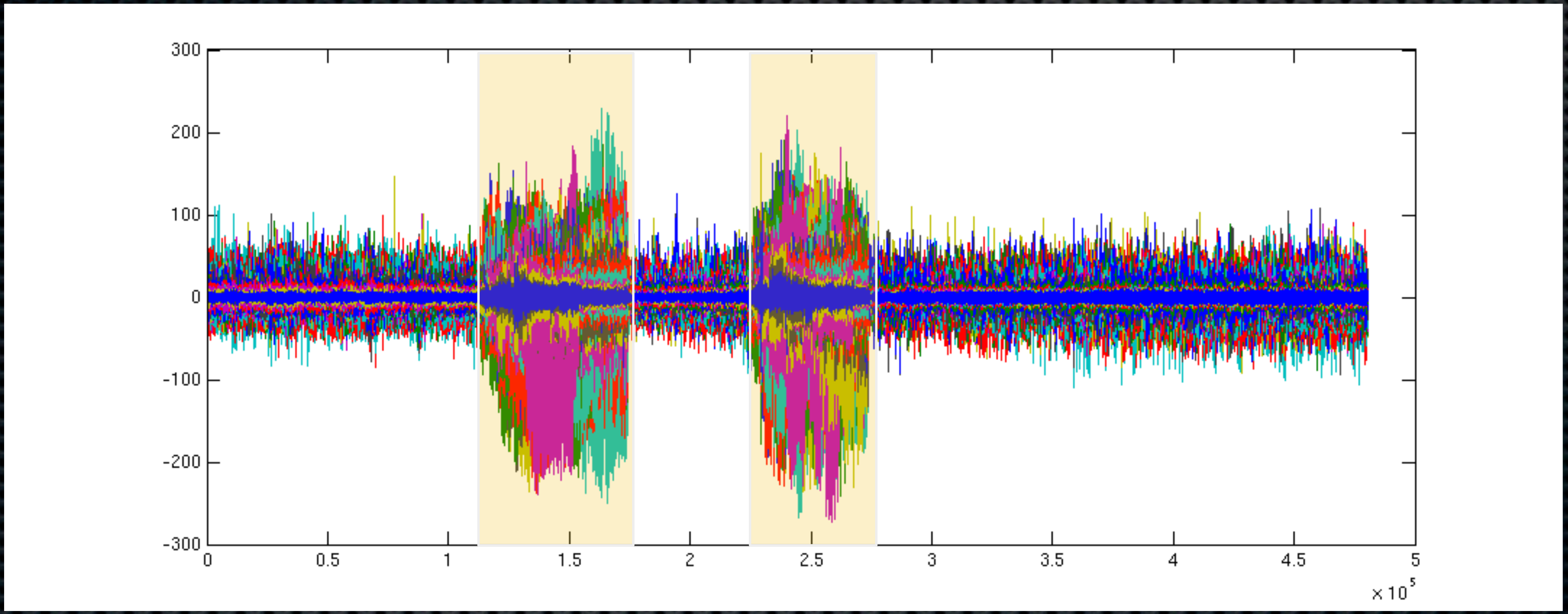
- Pre-Surgical Evaluation
- Rest Data
- 78 ECoG electrodes, 29 Scalp
- Provided by Dr. Greg Worrell, Mayo Clinic

Seizure Data



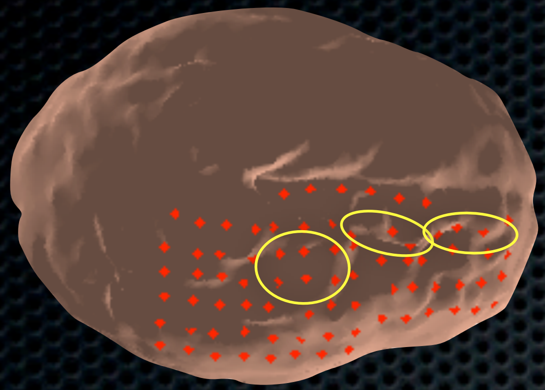


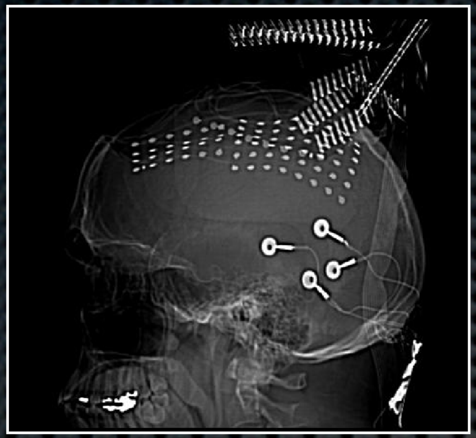
- Pre-Surgical Evaluation
- Rest Data
- 78 ECoG electrodes, 29 Scalp
- Provided by Dr. Greg Worrell, Mayo Clinic

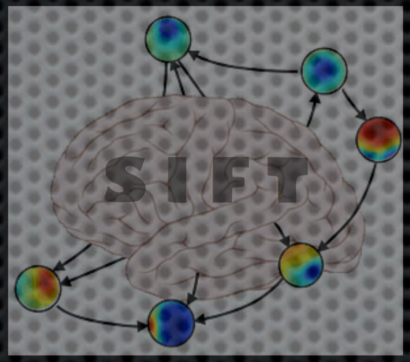


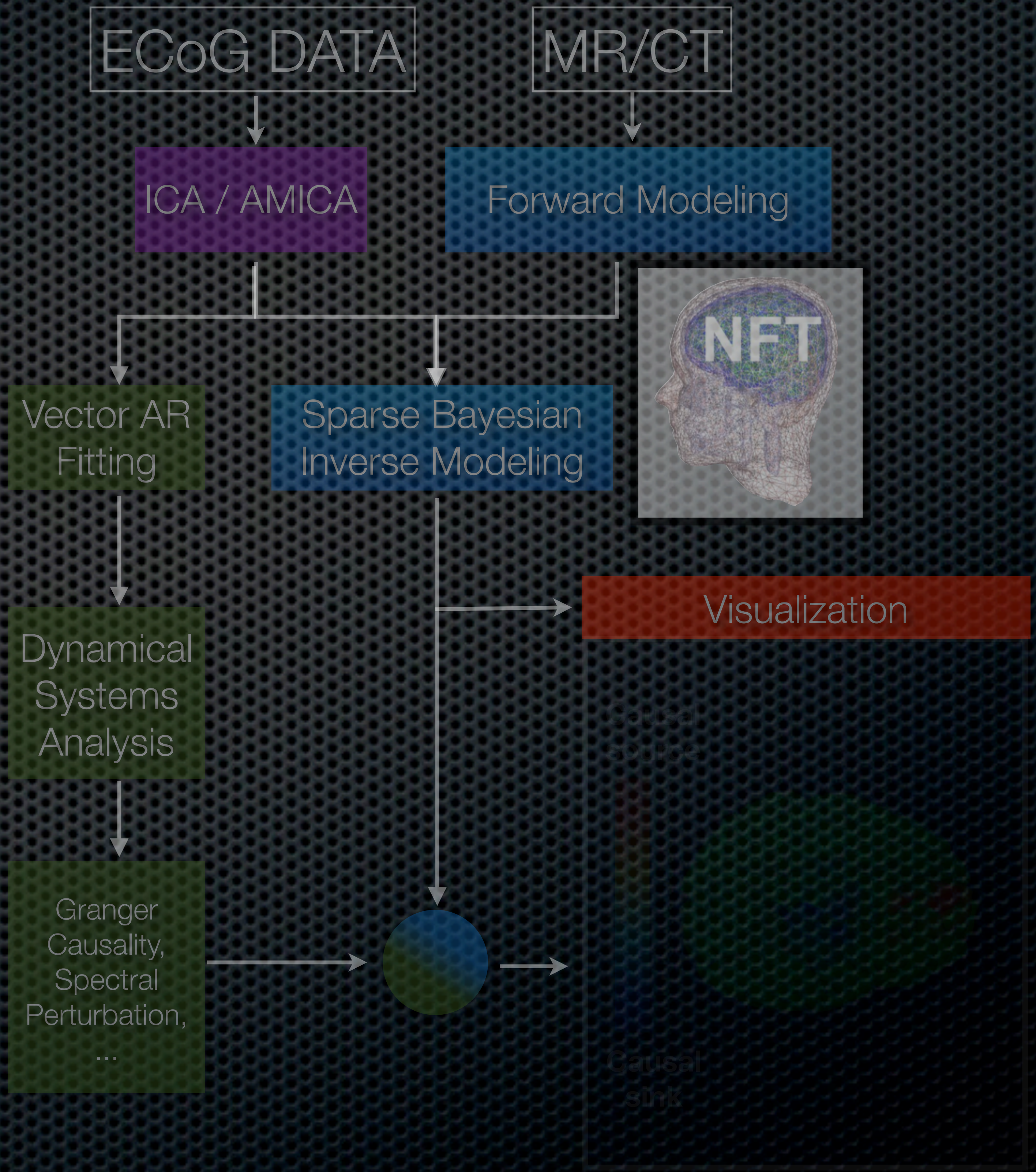
16 minutes ECoG data, 500 Hz
2 seizures (1.9 min + 1.5 min)

Analysis Pipeline



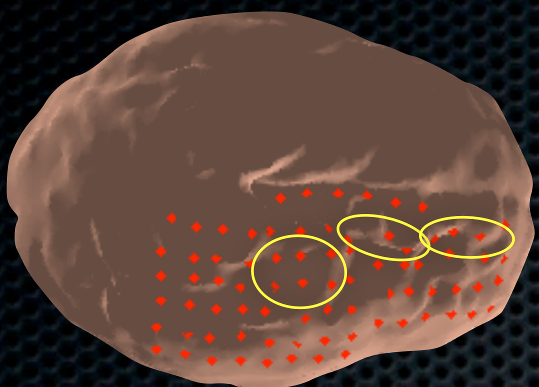


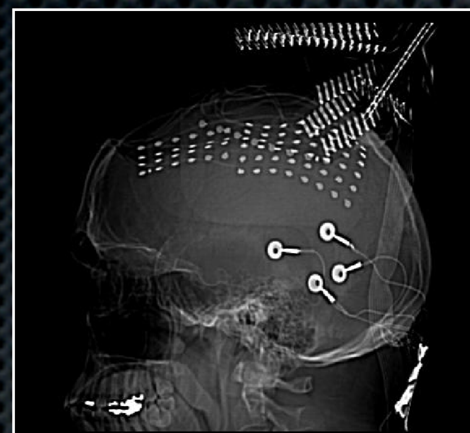




Akalin Acar, Palmer, et al (2011), *IEEE EMBC*
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



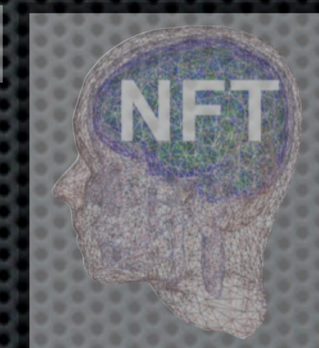


ECoG DATA

ICA / AMICA

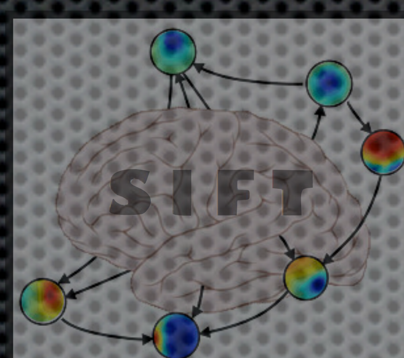
MR/CT

Forward Modeling



Vector AR Fitting

Sparse Bayesian Inverse Modeling



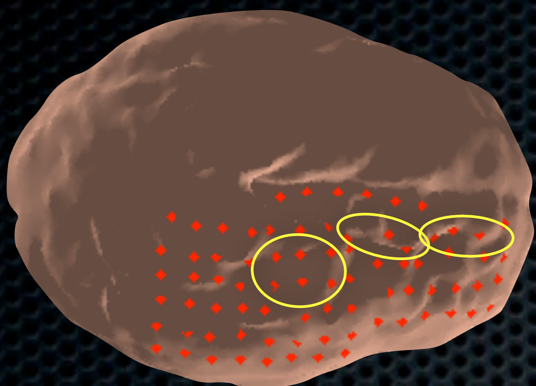
Dynamical Systems Analysis

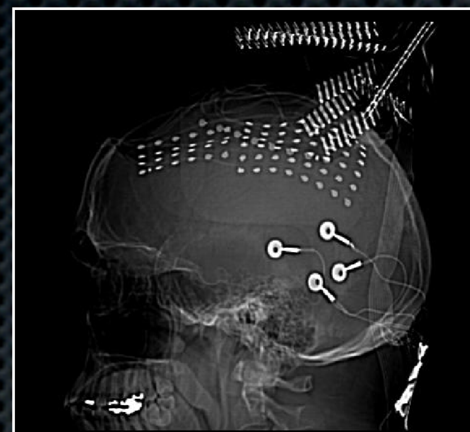
Granger Causality, Spectral Perturbation, ...

Visualization

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



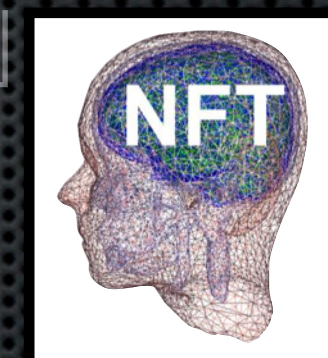


ECoG DATA

MR/CT

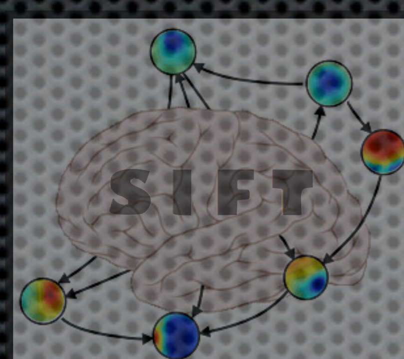
ICA / AMICA

Forward Modeling



Vector AR Fitting

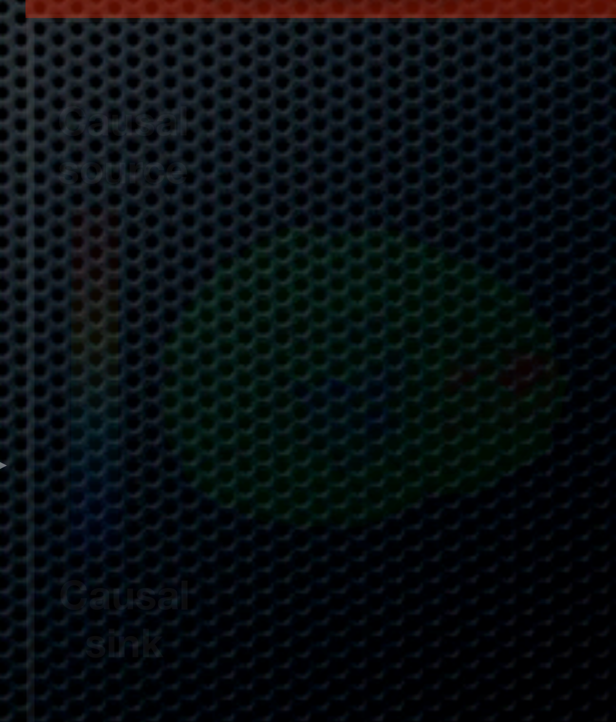
Sparse Bayesian Inverse Modeling



Visualization

Dynamical Systems Analysis

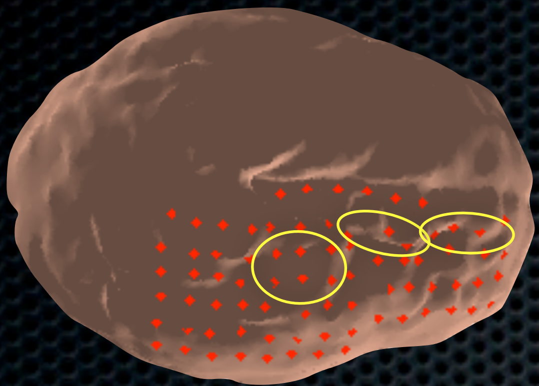
Granger Causality, Spectral Perturbation, ...

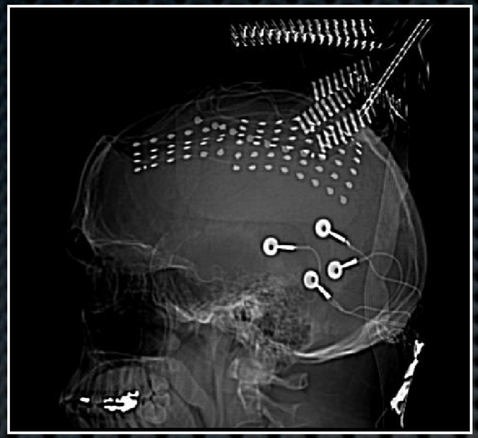


Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



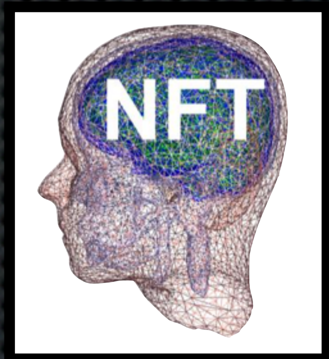


ECoG DATA

MR/CT

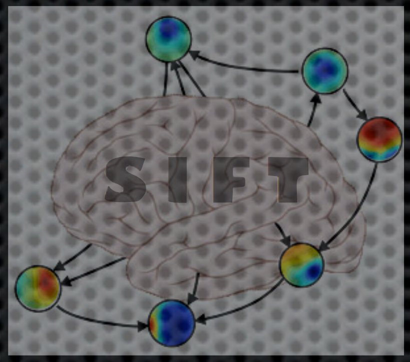
ICA / AMICA

Forward Modeling



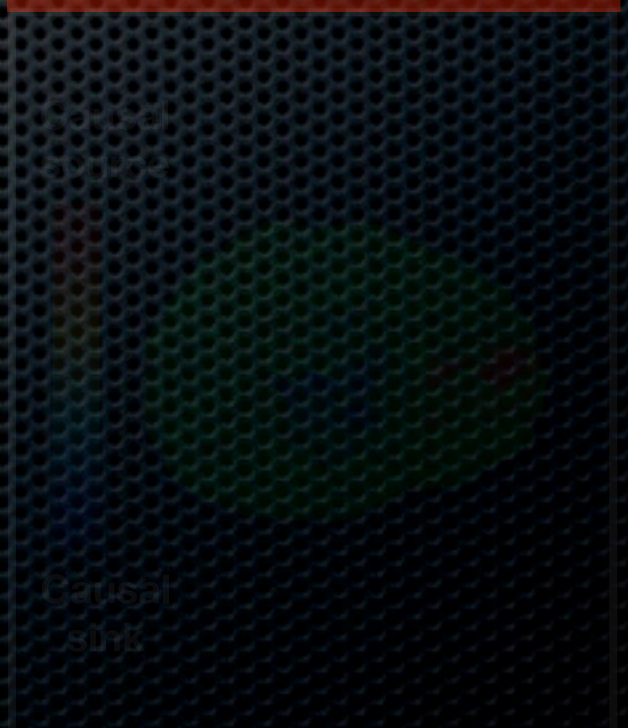
Vector AR Fitting

Sparse Bayesian Inverse Modeling



Dynamical Systems Analysis

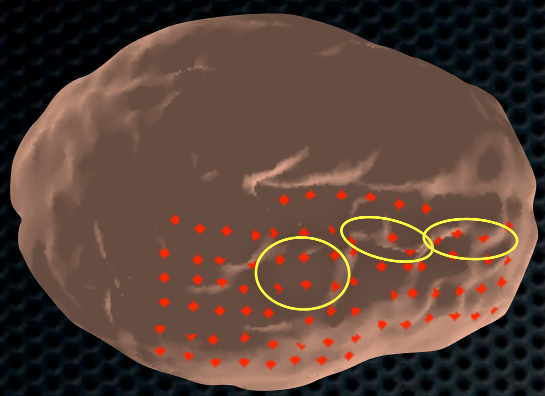
Visualization

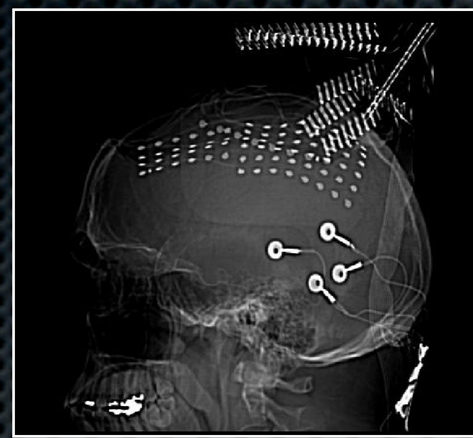


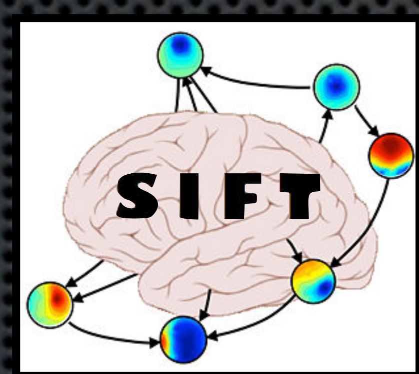
Granger Causality, Spectral Perturbation, …

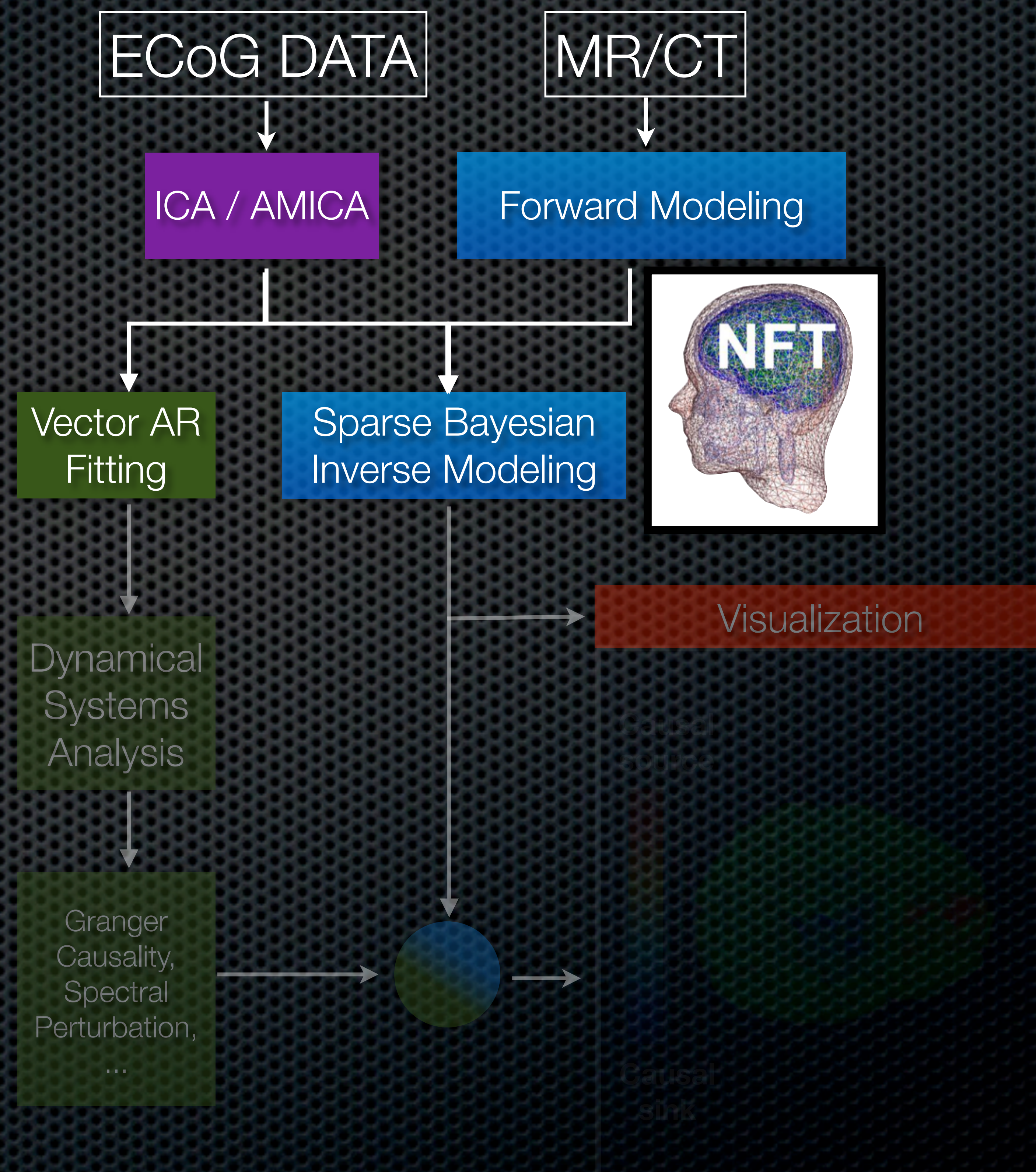
Akalin Acar, Palmer, et al (2011), *IEEE EMBC*
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



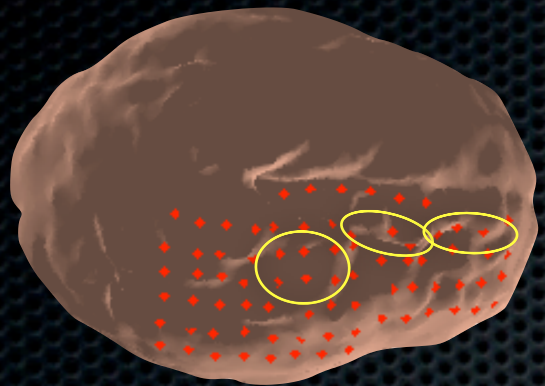


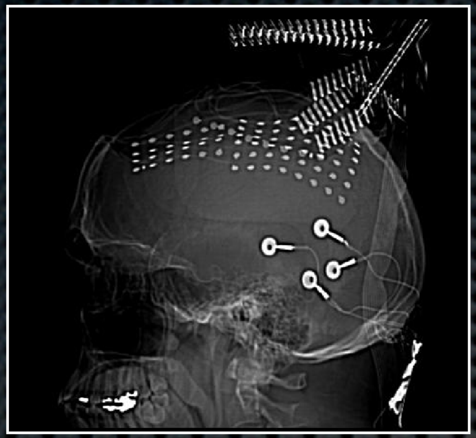




Akalin Acar, Palmer, et al (2011), *IEEE EMBC*
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



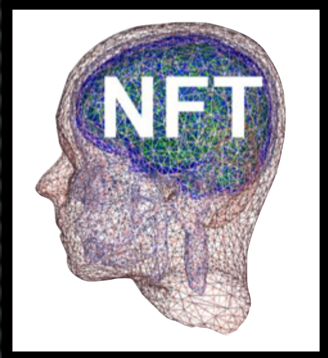


ECoG DATA

MR/CT

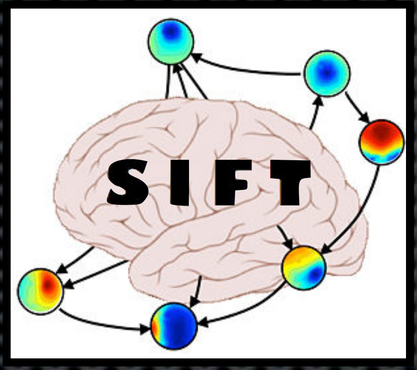
ICA / AMICA

Forward Modeling



Vector AR Fitting

Sparse Bayesian Inverse Modeling



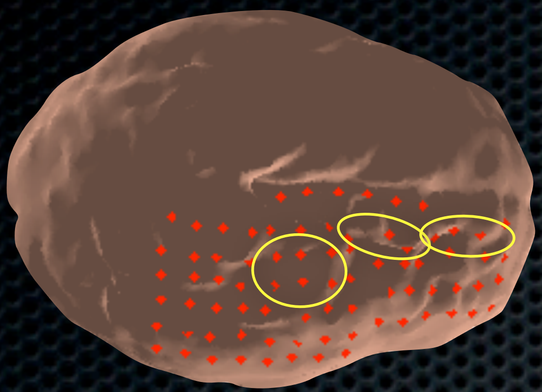
Dynamical Systems Analysis

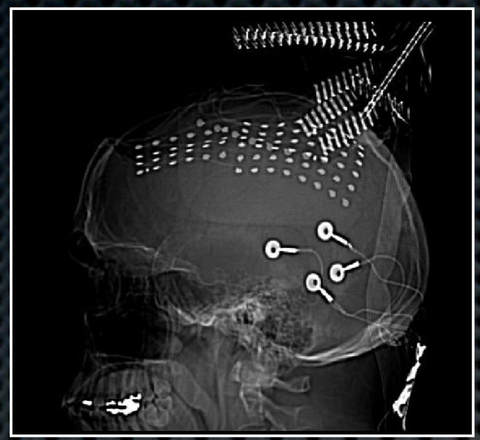
Visualization

Granger Causality, Spectral Perturbation, ...

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



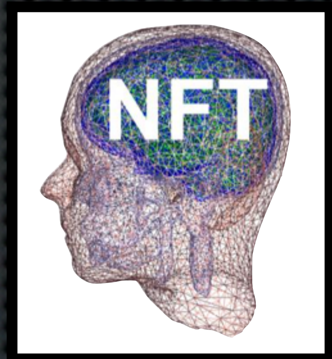


ECoG DATA

MR/CT

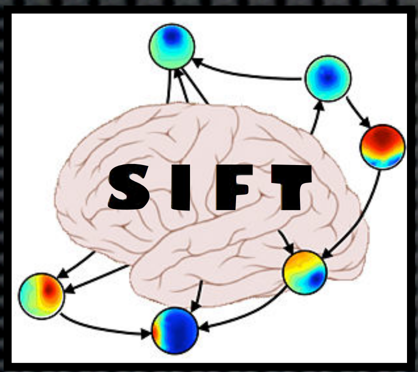
ICA / AMICA

Forward Modeling



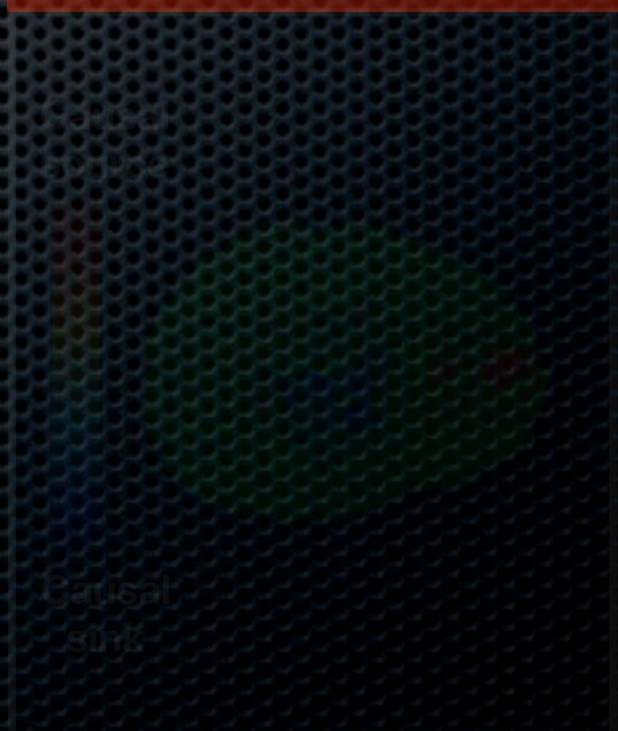
Vector AR Fitting

Sparse Bayesian Inverse Modeling



Dynamical Systems Analysis

Visualization

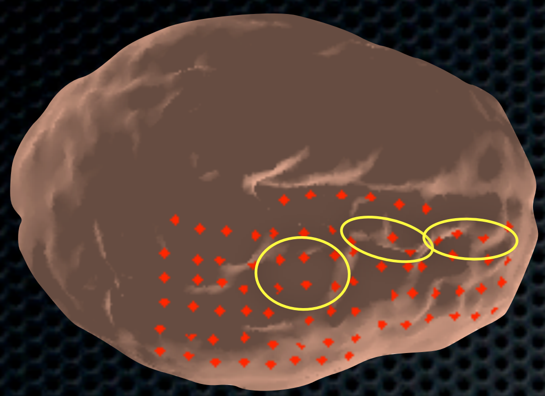


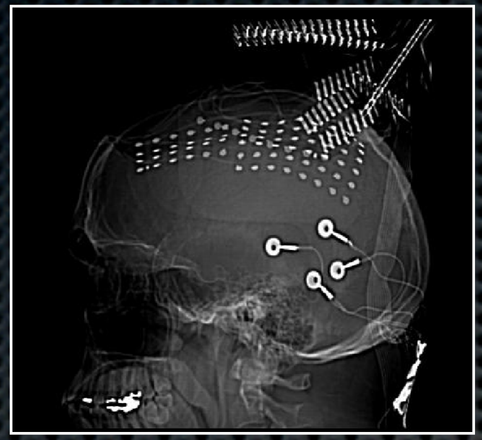
Granger Causality, Spectral Perturbation, ...

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Analysis Pipeline



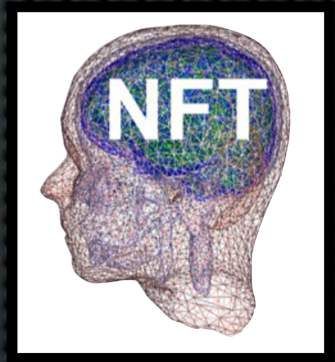


ECoG DATA

MR/CT

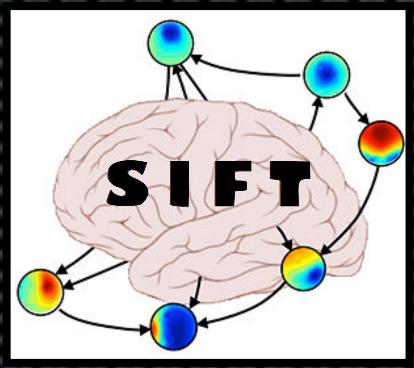
ICA / AMICA

Forward Modeling



Vector AR Fitting

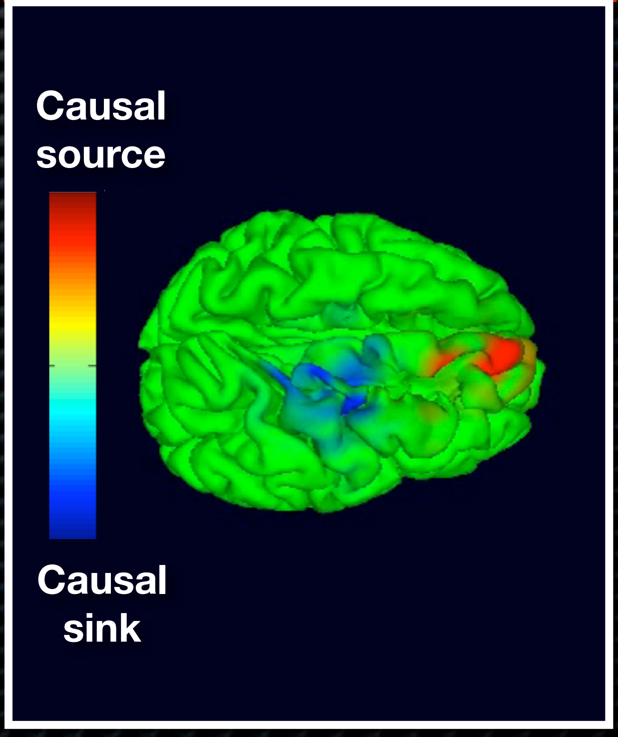
Sparse Bayesian Inverse Modeling



Dynamical Systems Analysis

Granger Causality, Spectral Perturbation, ...

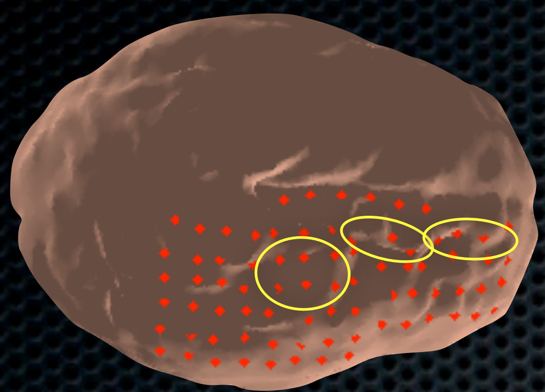
Visualization

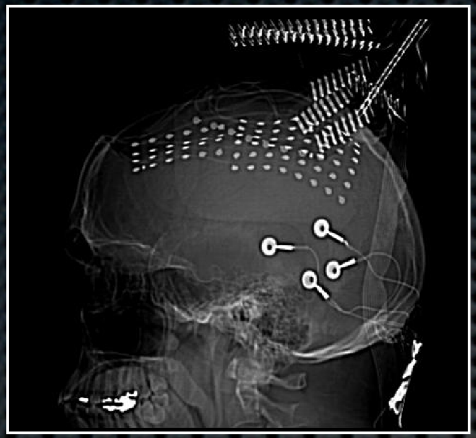


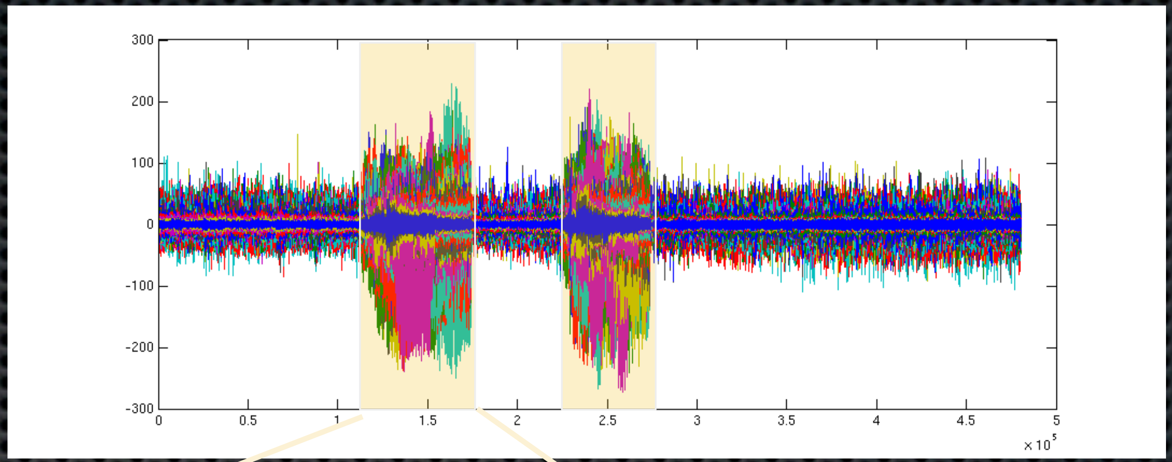
Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

ICA Decomposition

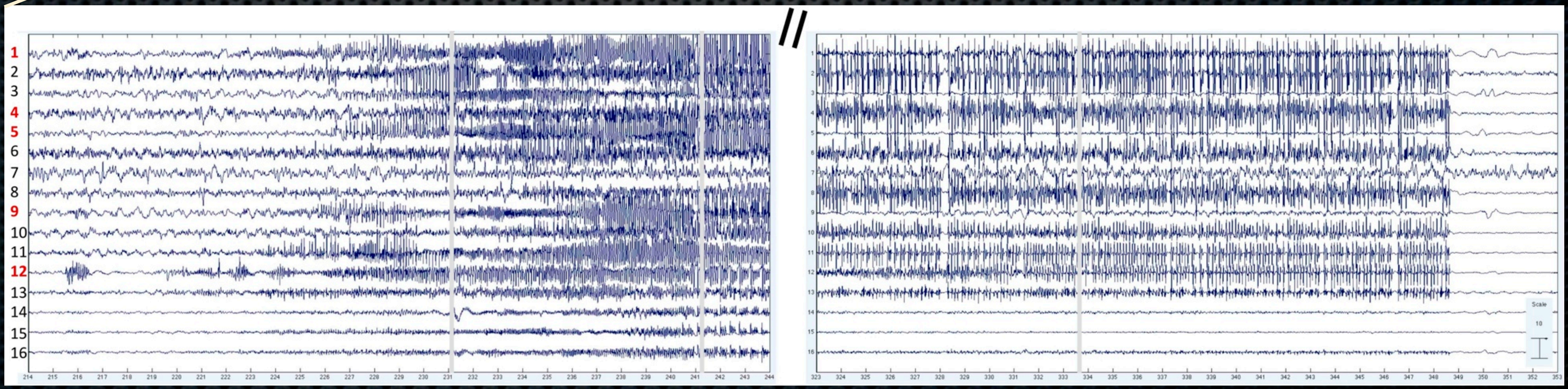






channel voltages

- Extended Infomax ICA Decomposition $X = AS$
- 16 seizure components (ICs) selected



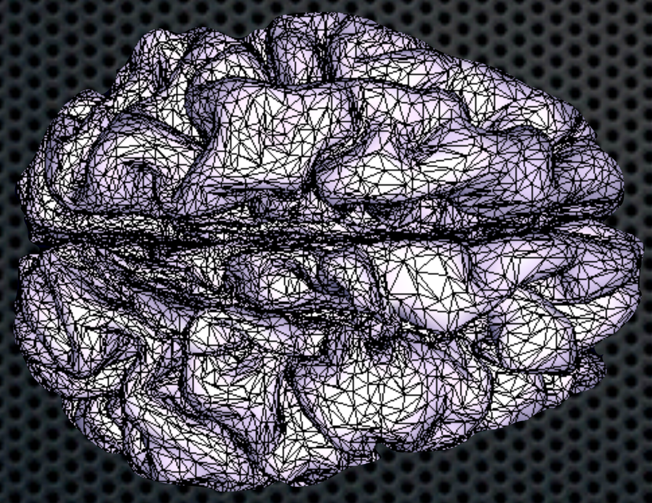
component activations

Forward Modeling

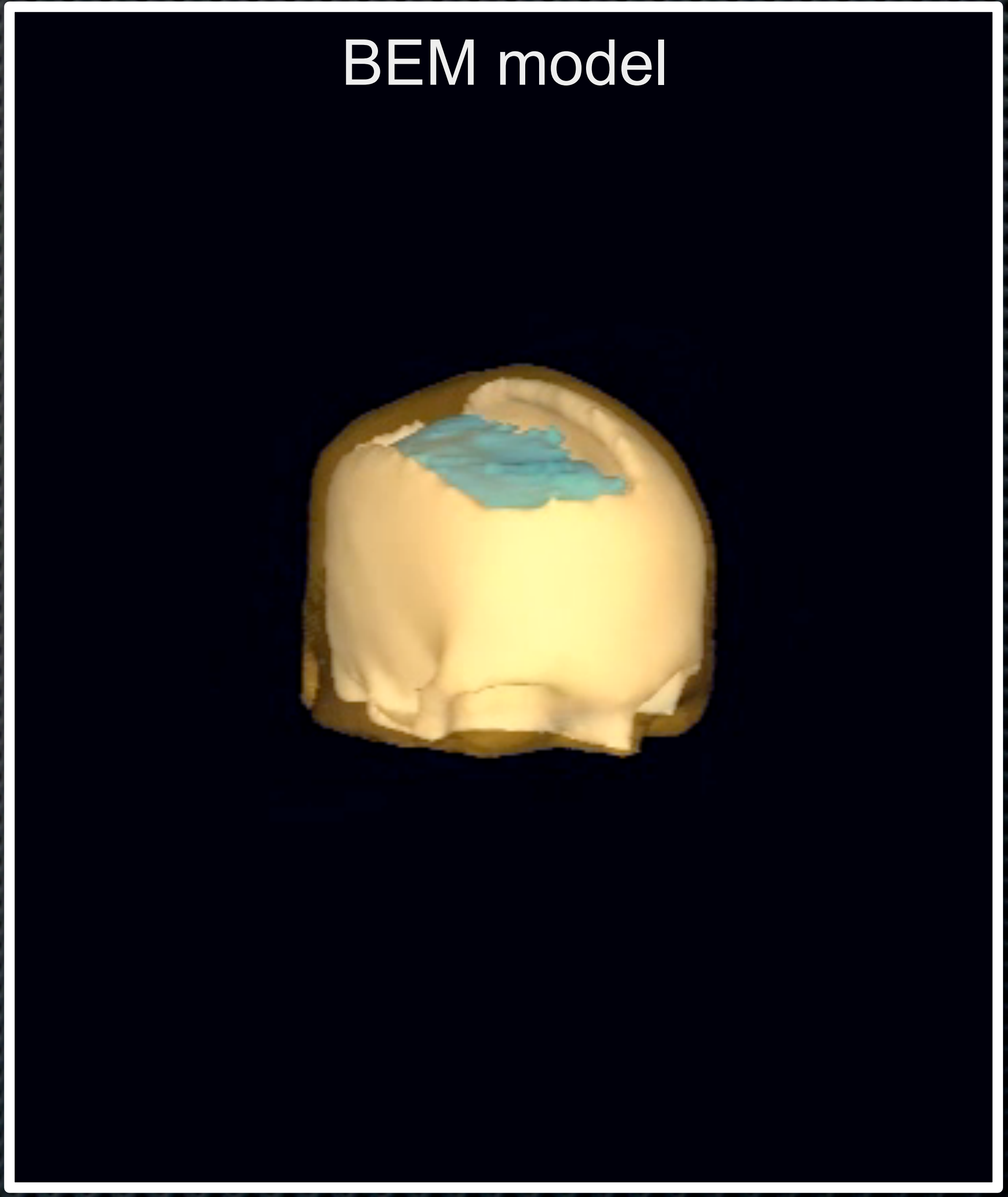
BEM model

- Plastic sheet (grids)
- Skull (with craniotomy hole)
- Scalp

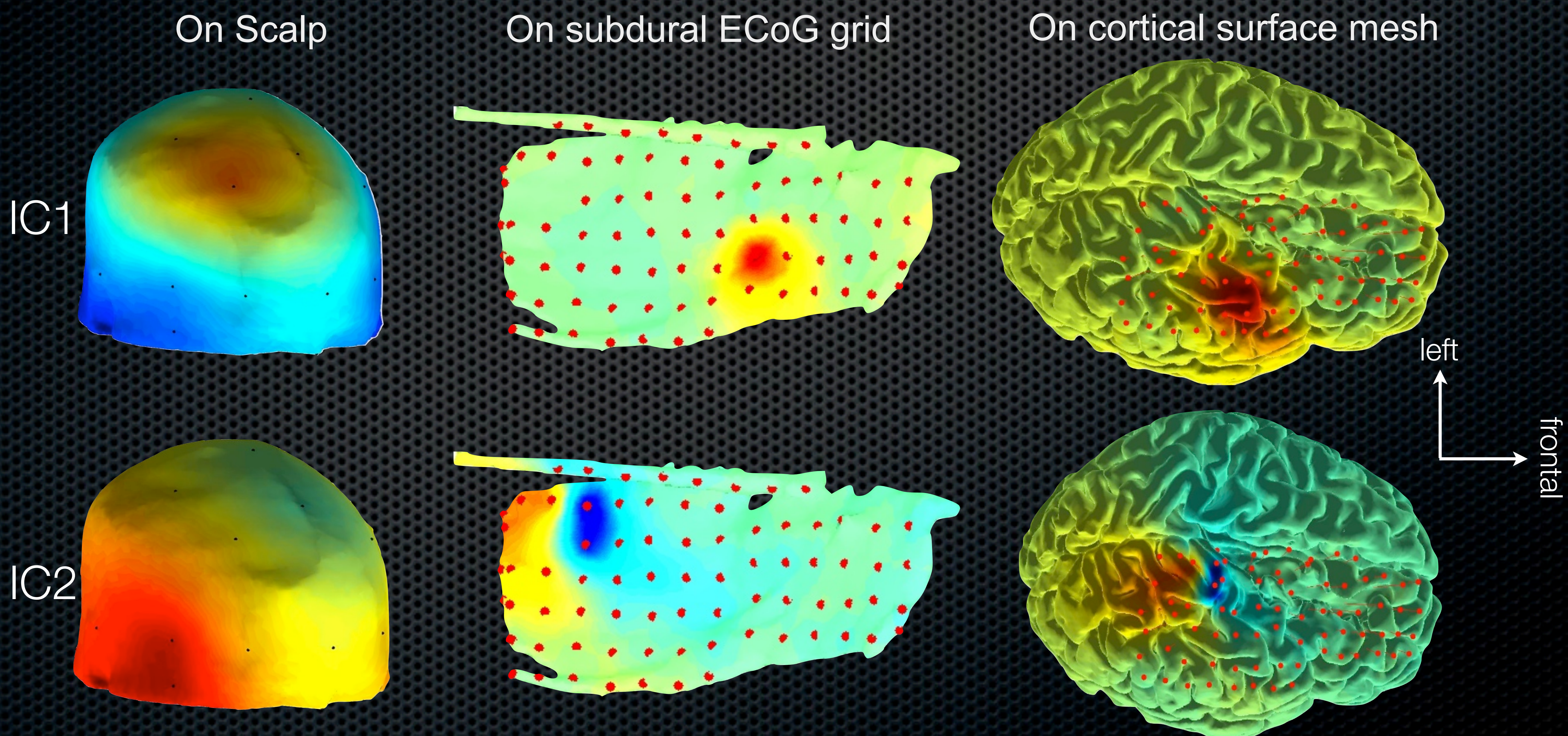
- Cortex



80 000 source vertices



ICA topographic maps on BEM model



Akalin Acar, et al (2008a,2009) *IEEE EMBC*

Multi-scale patch-basis source localization with Sparse Bayesian Learning

Legend	
symb	number of...
m	channels (78)
v	source voxels (80K)
c	ICs (16)
T	time points (120K)

$$D_{ij} = \text{geodesic\_distance}(i, j)$$

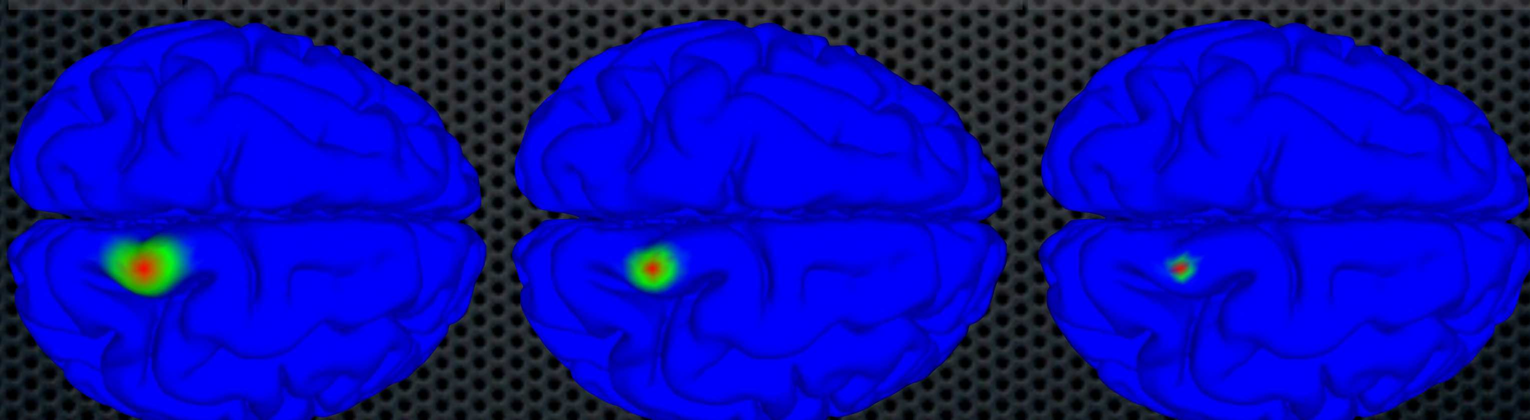
$$D_{ij} = Inf \ \text{ if } D_{ij} > scale$$

$$W_{ij}^{(k)} = gauss(D_{ij}, \sigma_k) = \frac{1}{\sqrt{2\pi\sigma_k^2}} exp\left(-\frac{D_{ij}^2}{2\sigma_k^2}\right)$$

$$\sigma_k = scale / 3$$

Three truncated Gaussian patches of different scales

radius	10 mm	6 mm	3 mm
σ_k	3.33 mm	2 mm	1 mm



Akalin Acar, et al (2008a,2009) *IEEE EMBC*
Ramirez, et al, *HBM*, 2007

Forward Model

$$X = LS$$

$$L := [m \times v]$$ Lead Field Matrix

$$\tilde{L} = [LW^{(1)} \cdots LW^{(3)}]_{m \times 3v}$$

ICA Model

$$X = A\hat{S}$$

$$\hat{S}_q := [1 \times T]$$ q^{th} IC activation

ICA+SBL Inverse Model

$$A_q = \tilde{L}\tilde{M}_q + \epsilon_q$$

$$\tilde{L}^{-1} = \text{SBL}(A_q, \tilde{L})$$

$$\tilde{M}_q = [\tilde{L}^{-1} A_q]_{3v \times 1}$$

$$M_q = reshape(\tilde{M}_q, v \times 3)$$

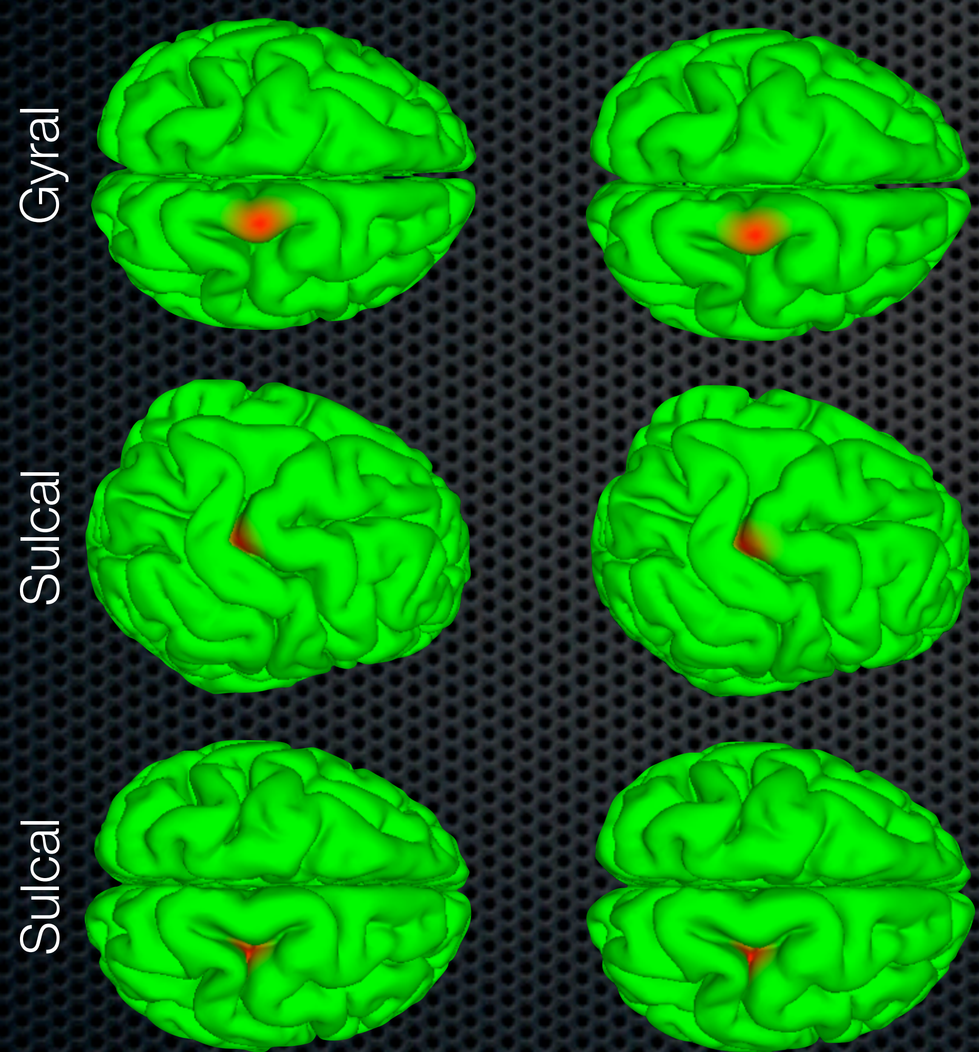
$$M_q = \sum_{i=1}^{3} M_{q(:,i)}$$

$$P_q = M_q \hat{S}_q$$ *[v x T] cortical surface potentials for q^{th} IC*

SBL simulation study with MNI model (SNR=50)

Three examples:

original | reconstructed



Akalin Acar, et al (2009) *IEEE EMBC*

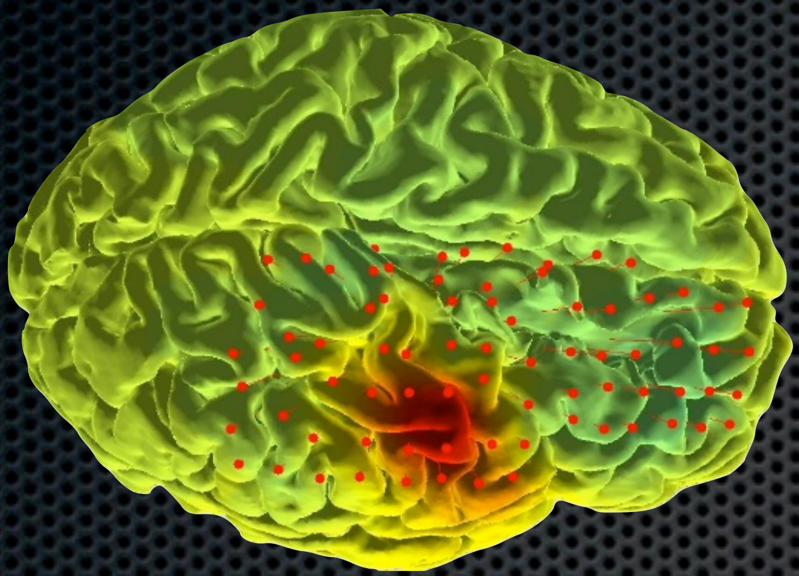
Source (x 15)		Max. dis. (mm)	Energy dif.	DF (%)
Type	Scale (mm)			
Gyral	10	0	1.5	103.8
Sulcul	10	1.01	29.8	101.4
Sulcul	5	2.12	4.1	37.6
Dual	10	11.6	29.3	89.2
Gyral	5	1.01	4.7	41.3
Sulcul	12	1.8	10.6	125.5

Term	Definition
max displacement	geodesic distance between original and reconstructed patch centers
energy difference	|original energy - reconstructed energy|
degree of focalization (DF)	reconstructed energy / original enegy

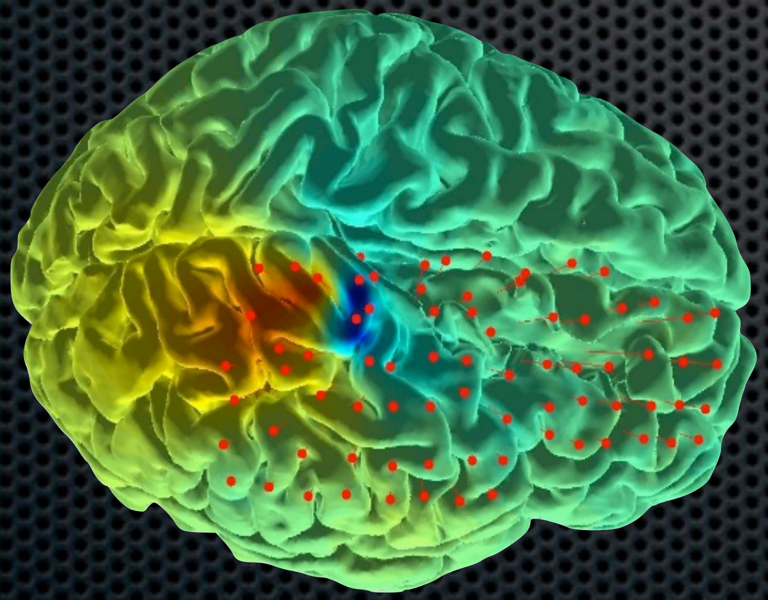
SBL Localization of Epileptogenic IC Sources

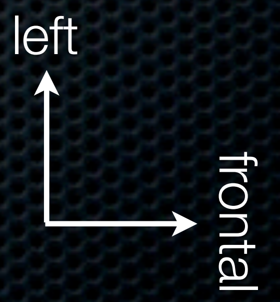
IC maps interpolated on cortical surface mesh

IC1



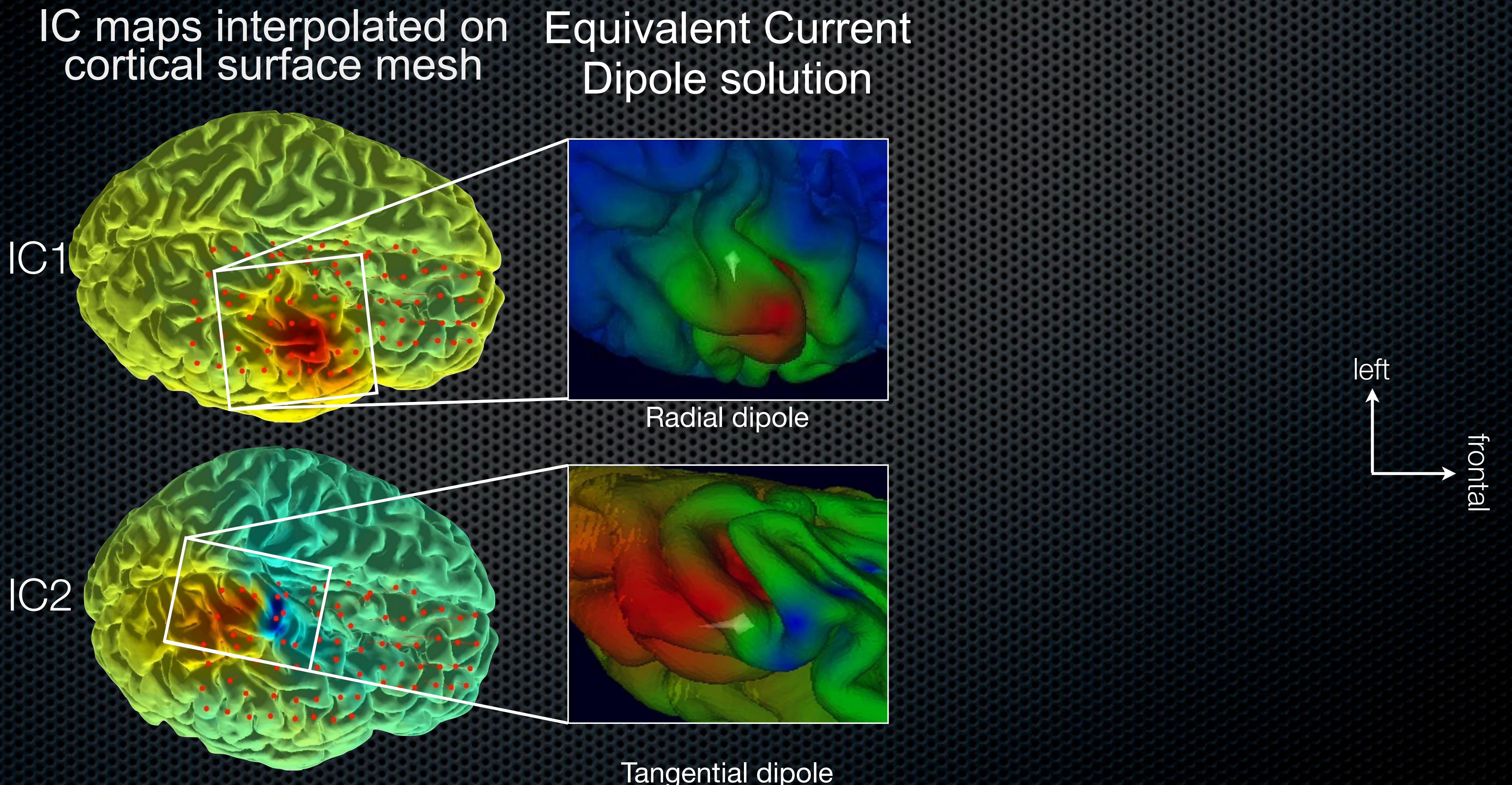
IC2





Akalin Acar, et al (2009) *IEEE EMBC*

SBL Localization of Epileptogenic IC Sources



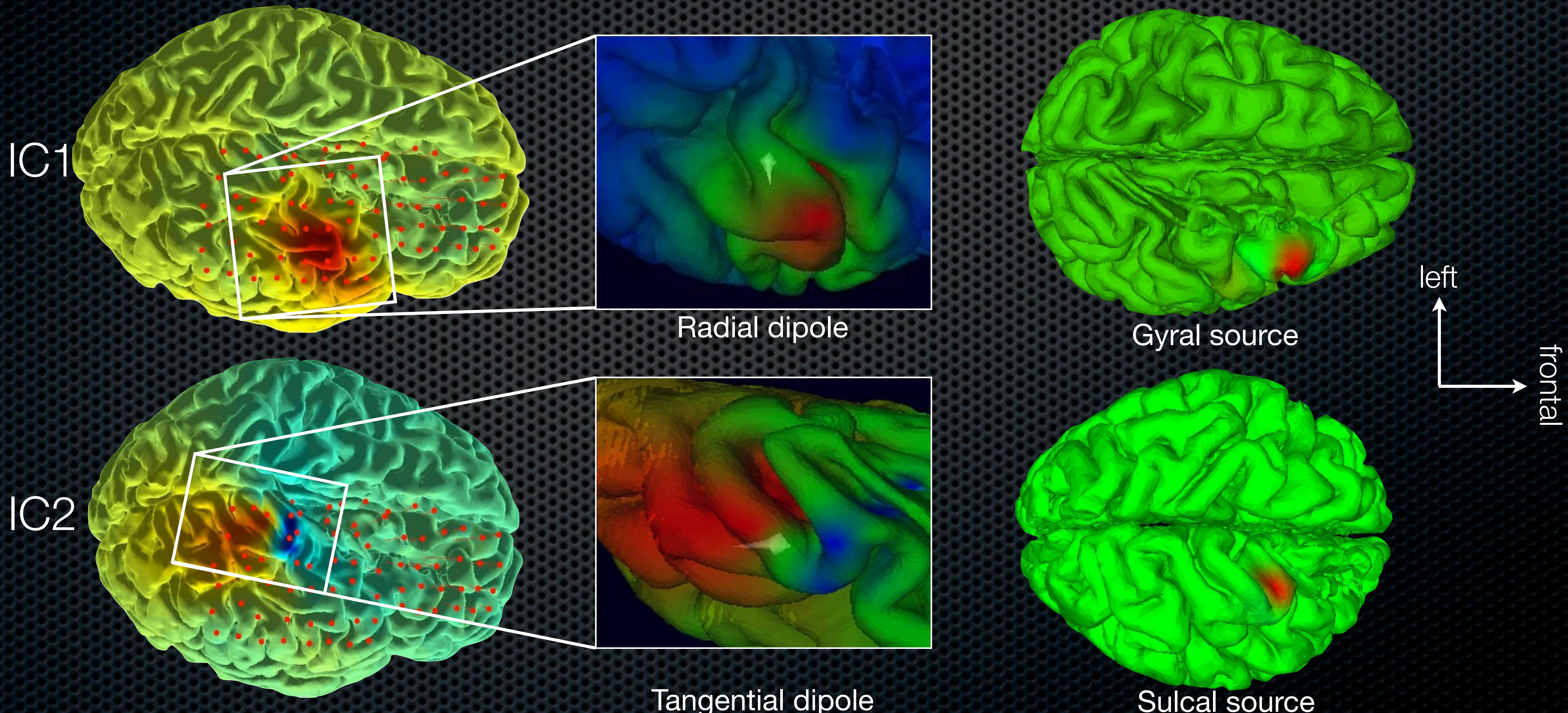
Akalin Acar, et al (2009) *IEEE EMBC*

SBL Localization of Epileptogenic IC Sources

IC maps interpolated on cortical surface mesh

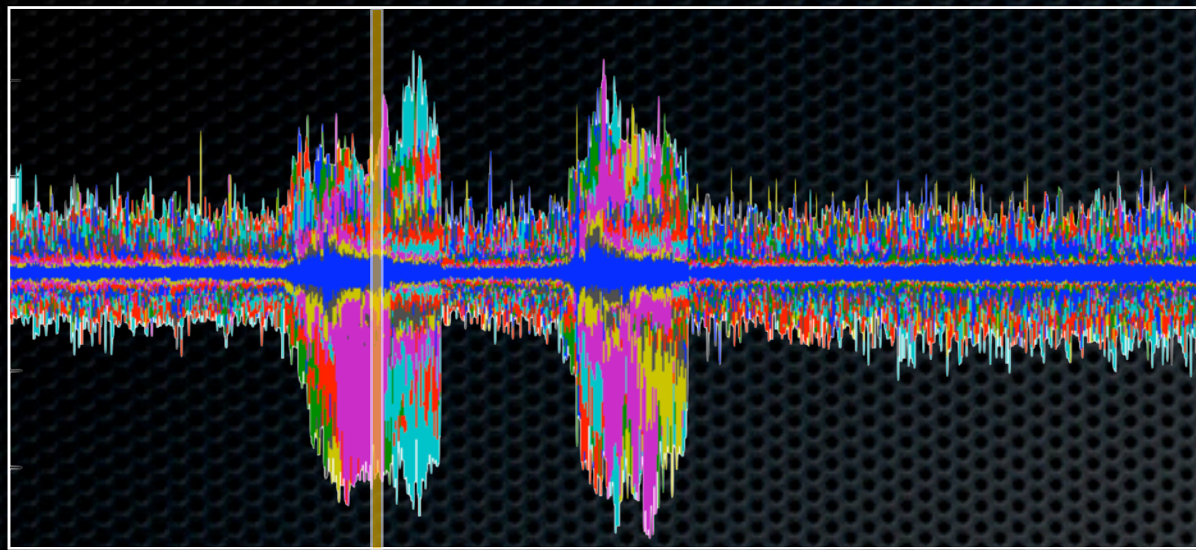
Equivalent Current Dipole solution

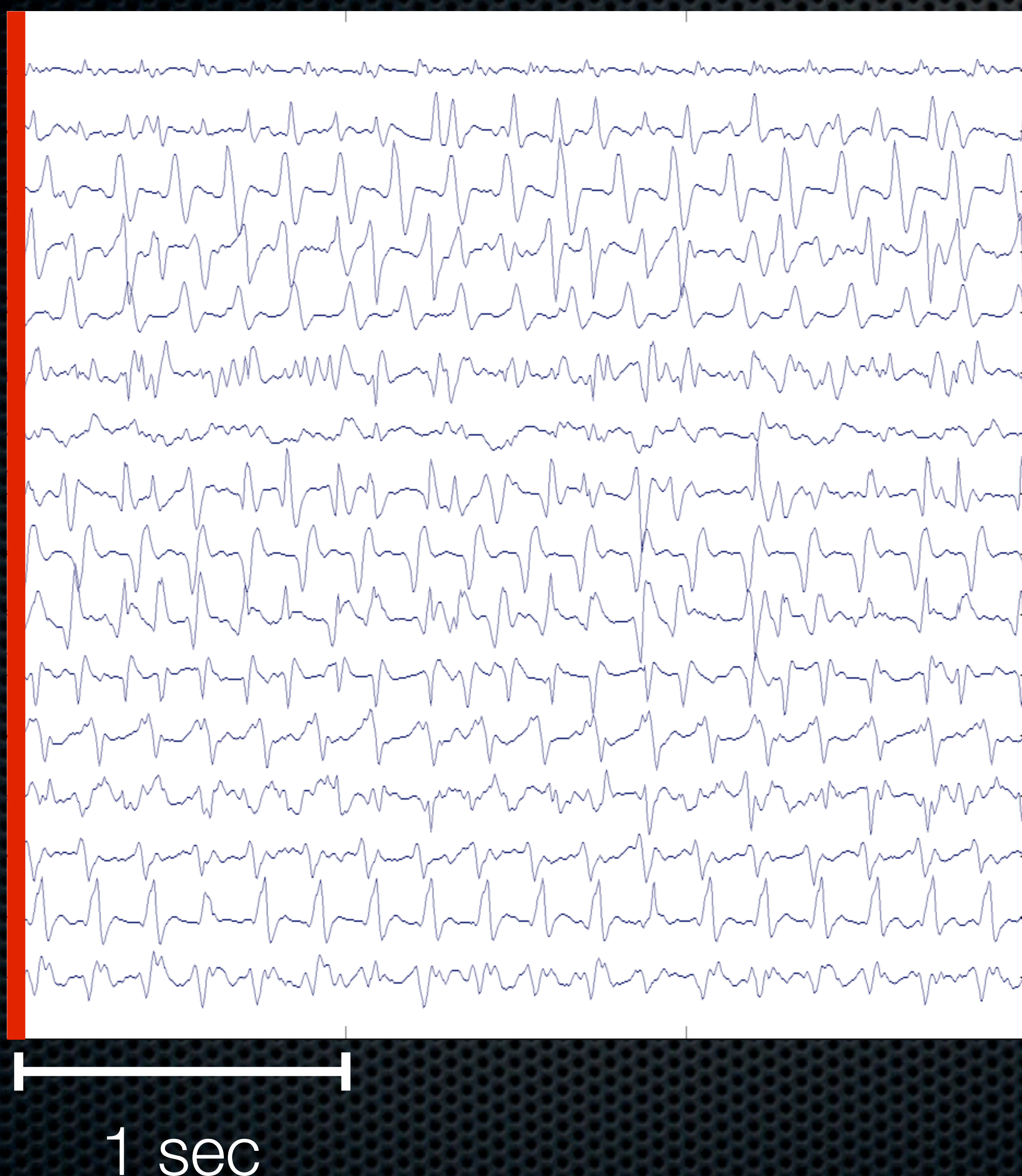
SBL multiscale patch solution

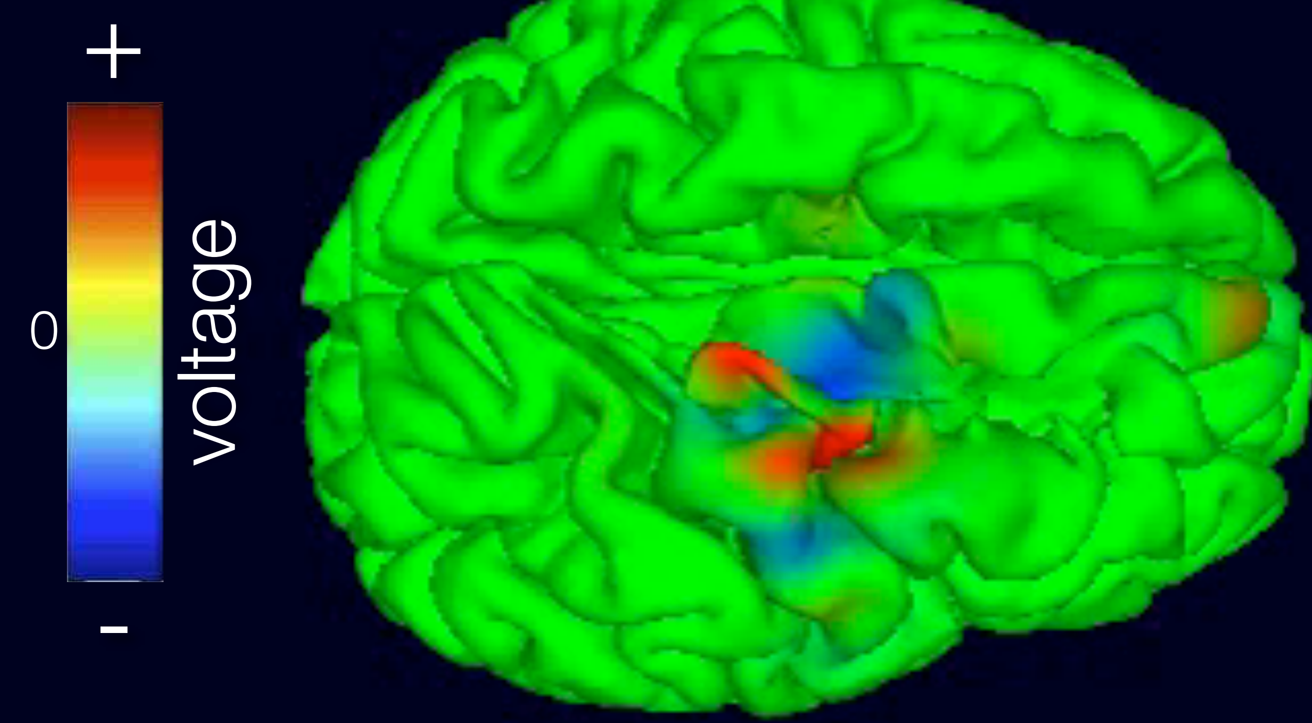


Akalin Acar, et al (2009) *IEEE EMBC*

Cortical surface potentials (16 ICs, SBL solution)







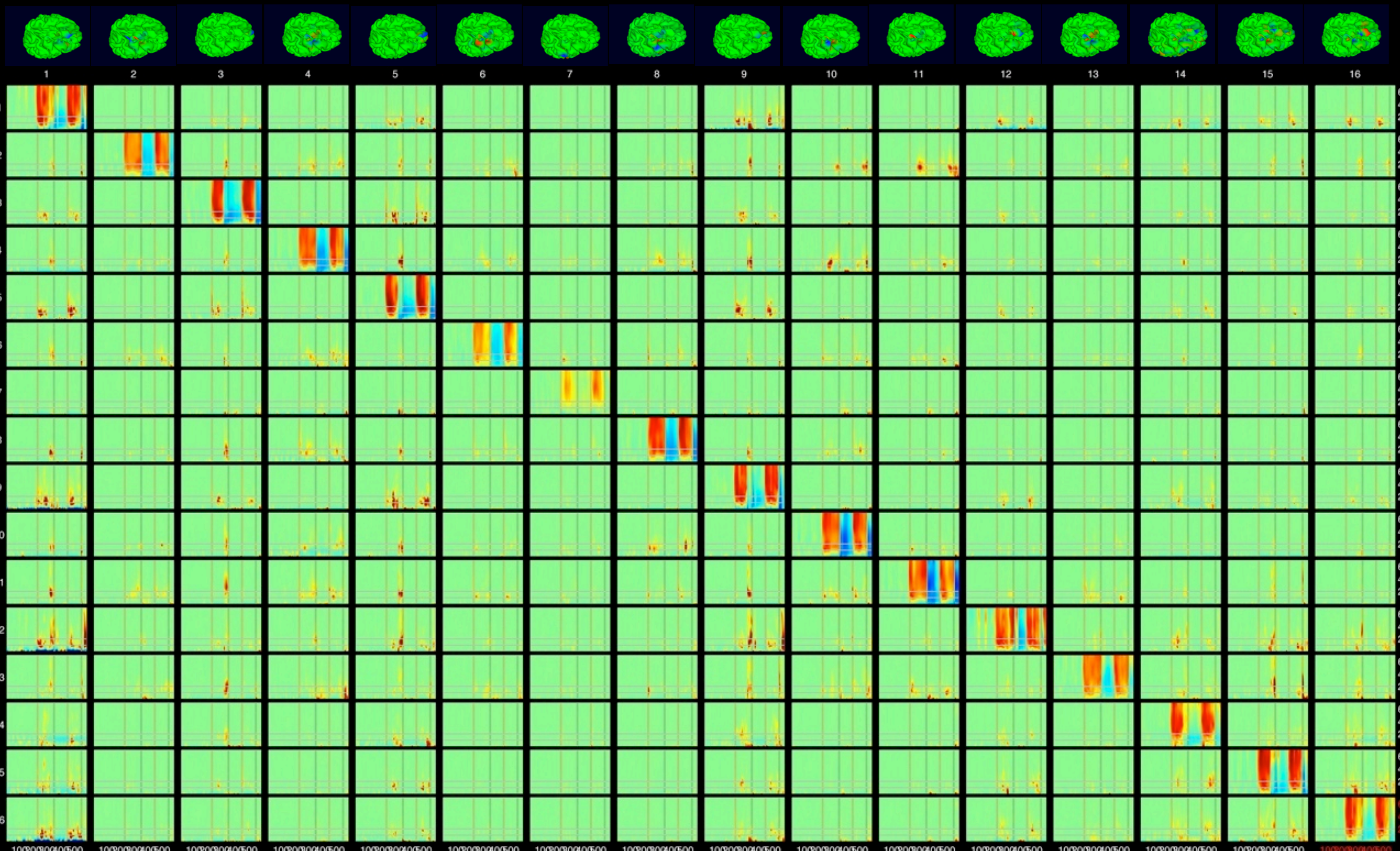
playback at 1/5 actual speed

VAR Model Fitting and Multivariate Granger Causality

- Seizure IC activations down-sampled to 256 Hz
- VAR model of order 7 (selected using Hannan-Quinn information criterion) fit to seizure activations using ARFIT algorithm using a 15-sec sliding window with 1 sec step
- Residual whiteness tests (Portmanteau) and stability analysis
- dDTF and spectral density estimated for each window from 1-70Hz
- Significance determined via phase randomization surrogate test

dDTF (multivariate GC)

FROM



TO

Frequency (Hz)

ERSP (spectrum) on diagonal

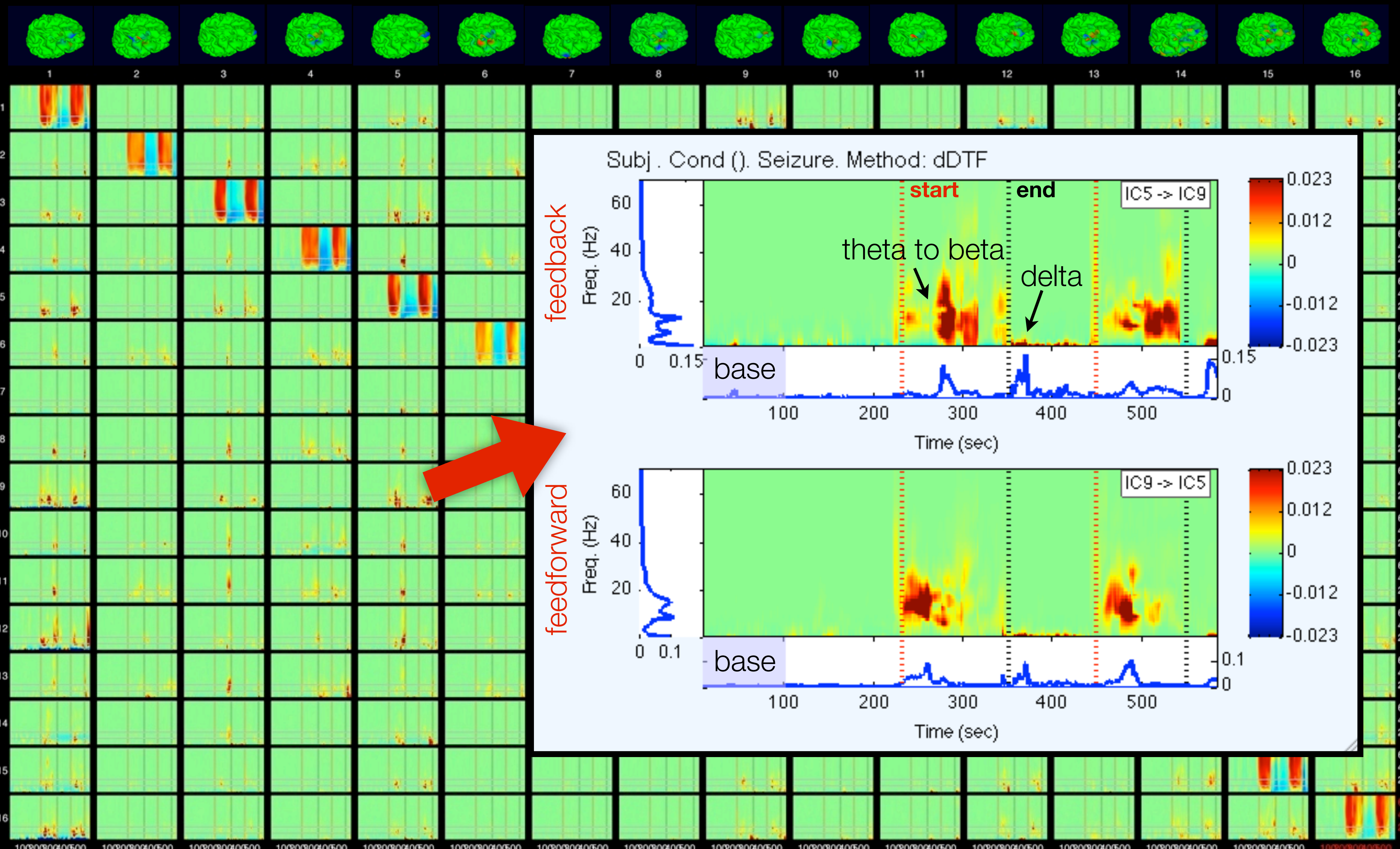
Time (sec)

Mullen, et al (2011)

dDTF (multivariate GC)

FROM

TO



Frequency (Hz)

ERSP (spectrum) on diagonal

Time (sec)

Mullen, et al (2011)

Graph Theoretic Metrics

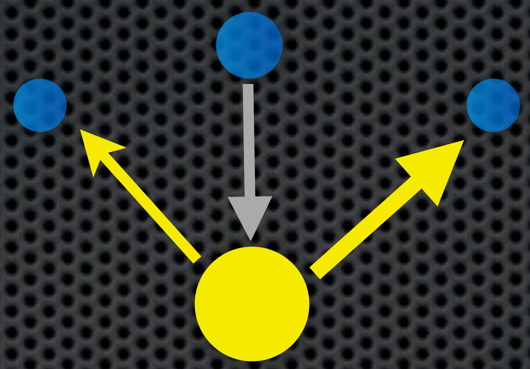
C: Asymmetric (e.g. causal) connectivity matrix

Graph Theoretic Metrics

C: Asymmetric (e.g. causal) connectivity matrix

- Outflow

$$O_j = \sum_{i=1}^{M} C_{ij}$$

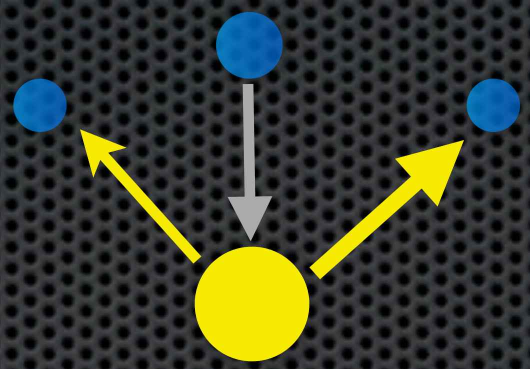


Graph Theoretic Metrics

C: Asymmetric (e.g. causal) connectivity matrix

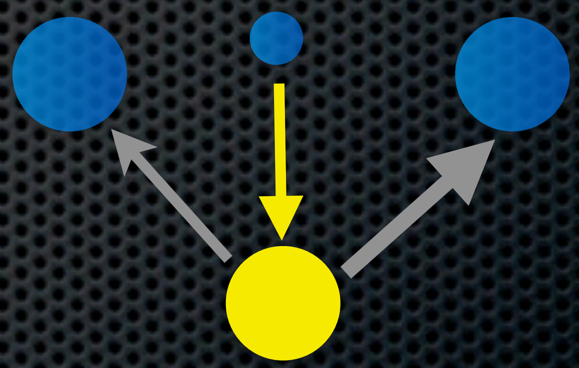
- Outflow

$$O_j = \sum_{i=1}^{M} C_{ij}$$



- Inflow

$$I_i = \sum_{j=1}^{M} C_{ij}$$

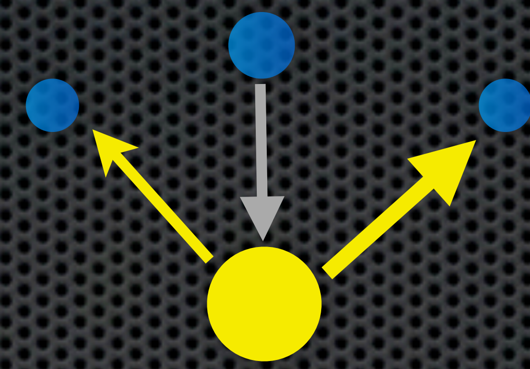


Graph Theoretic Metrics

C: Asymmetric (e.g. causal) connectivity matrix

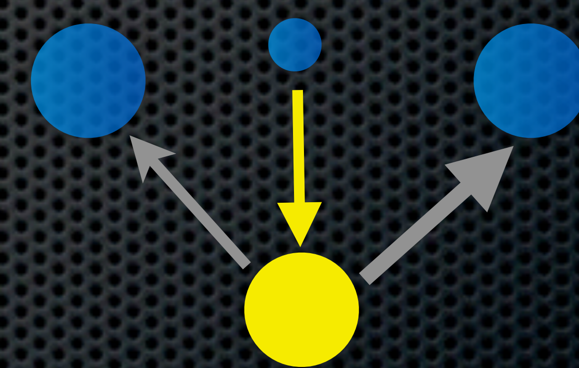
- Outflow

$$O_j = \sum_{i=1}^{M} C_{ij}$$



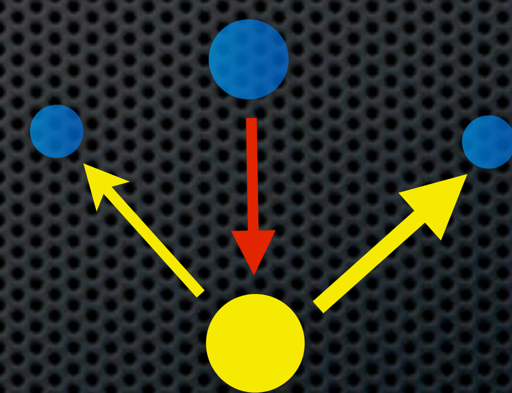
- Inflow

$$I_i = \sum_{j=1}^{M} C_{ij}$$



- Causal Flow

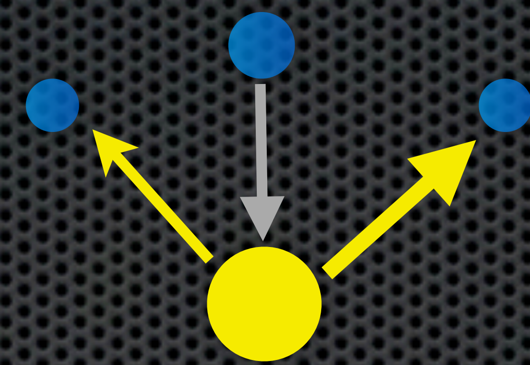
$$F_i = O_i - I_i$$



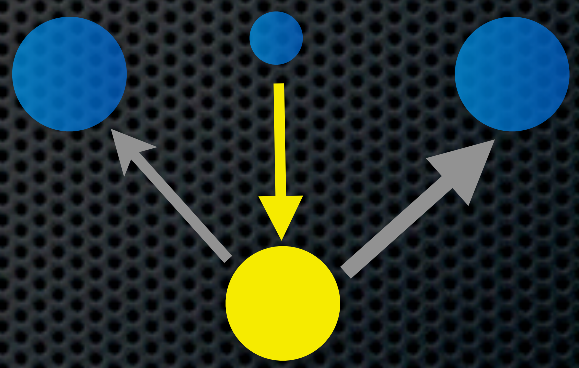
Graph Theoretic Metrics

C: Asymmetric (e.g. causal) connectivity matrix

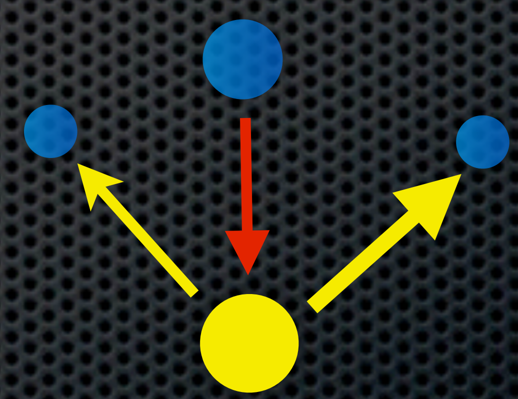
- Outflow $O_j = \sum_{i=1}^{M} C_{ij}$



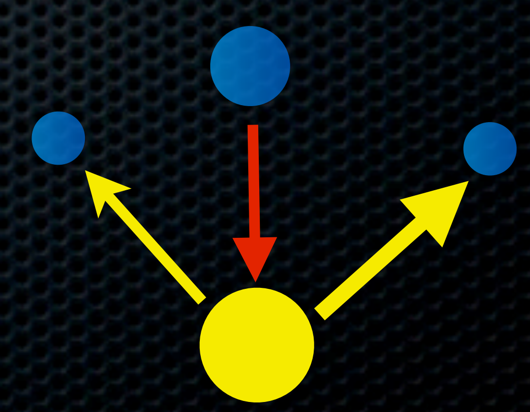
- Inflow $I_i = \sum_{j=1}^{M} C_{ij}$

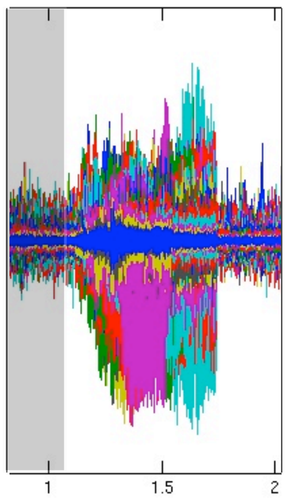


- Causal Flow $F_i = O_i - I_i$



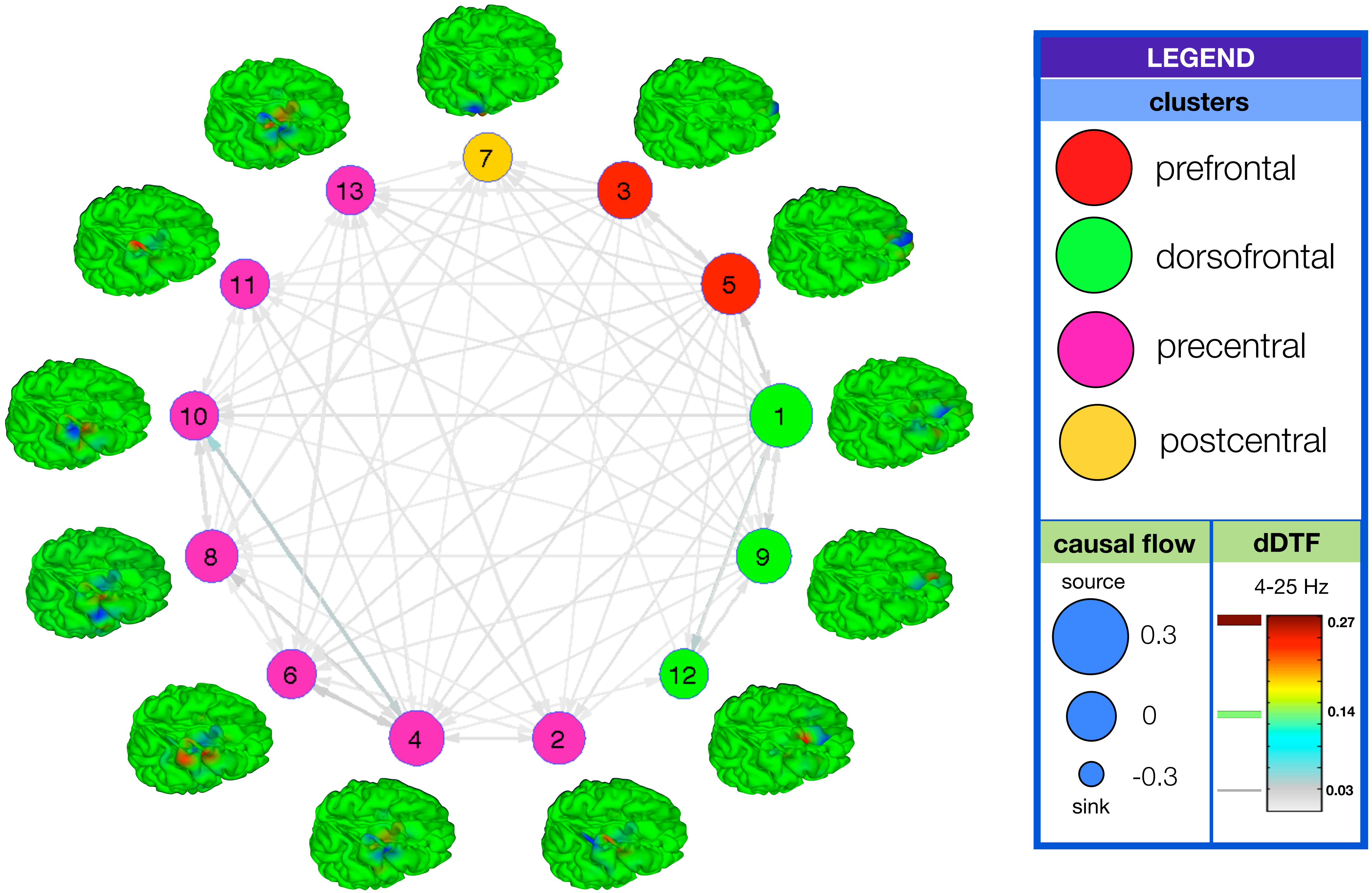
- Asymmetry Ratio $R_i = \dfrac{O_i - I_i}{O_i + I_i}$



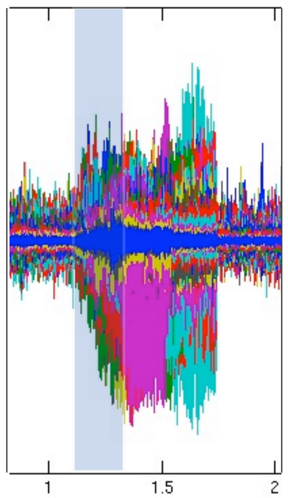


1
1.5
2

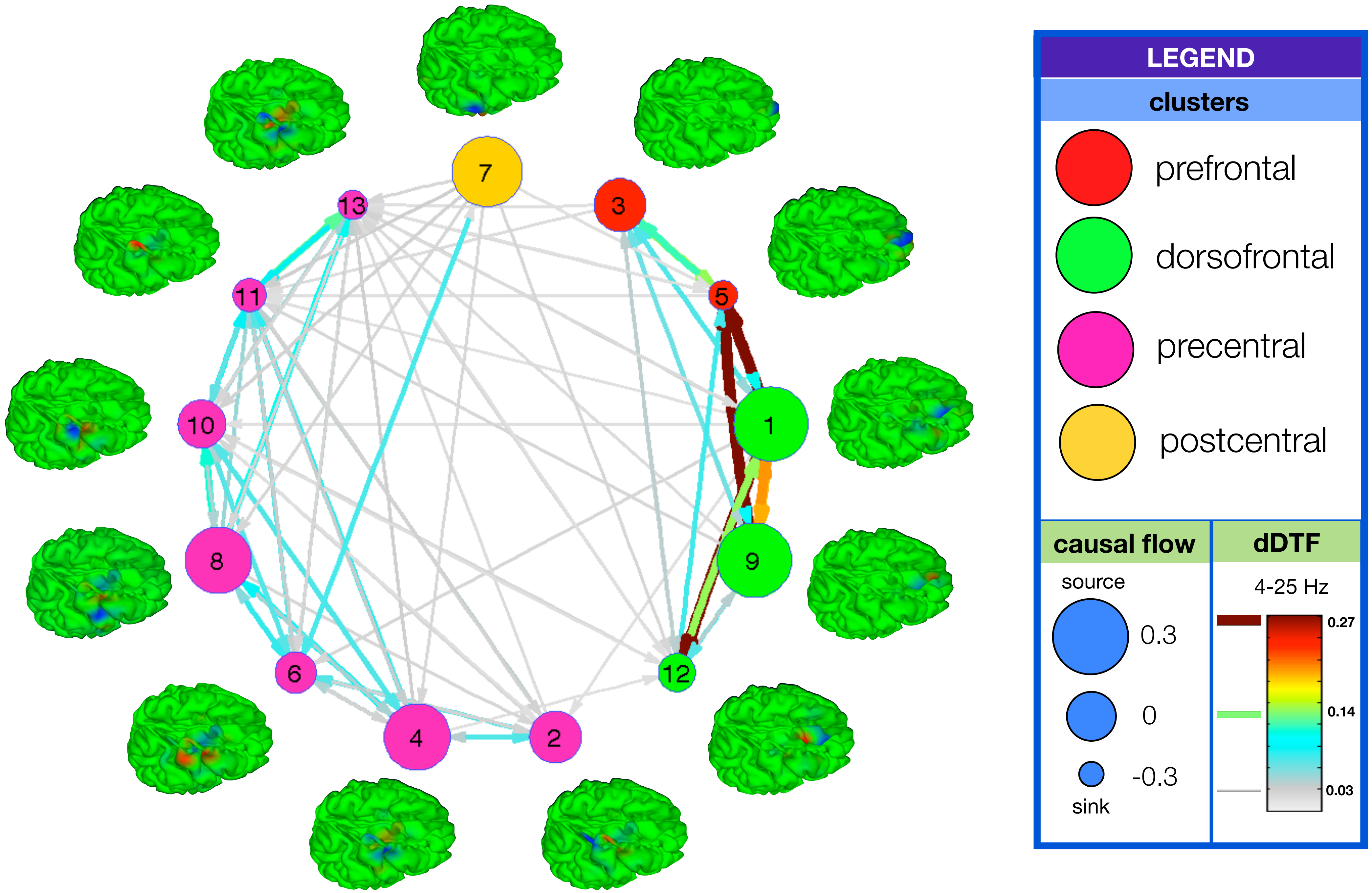
Pre-seizure

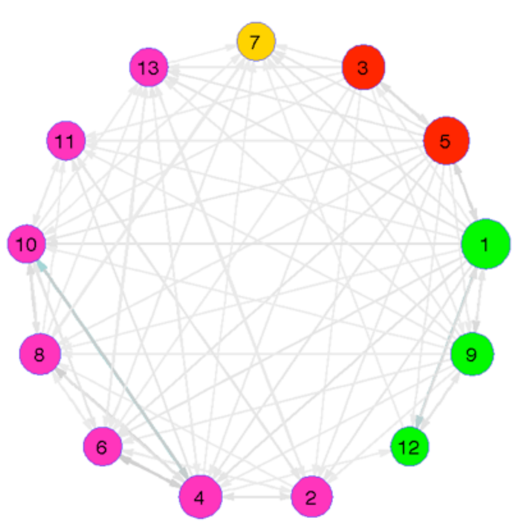


7
13
3
11
5
10
1
8
9
6
12
4
2
LEGEND
clusters
prefrontal
dorsofrontal
precentral
postcentral
causal flow
source
0.3
0
-0.3
sink
dDTF
4-25 Hz
0.27
0.14
0.03

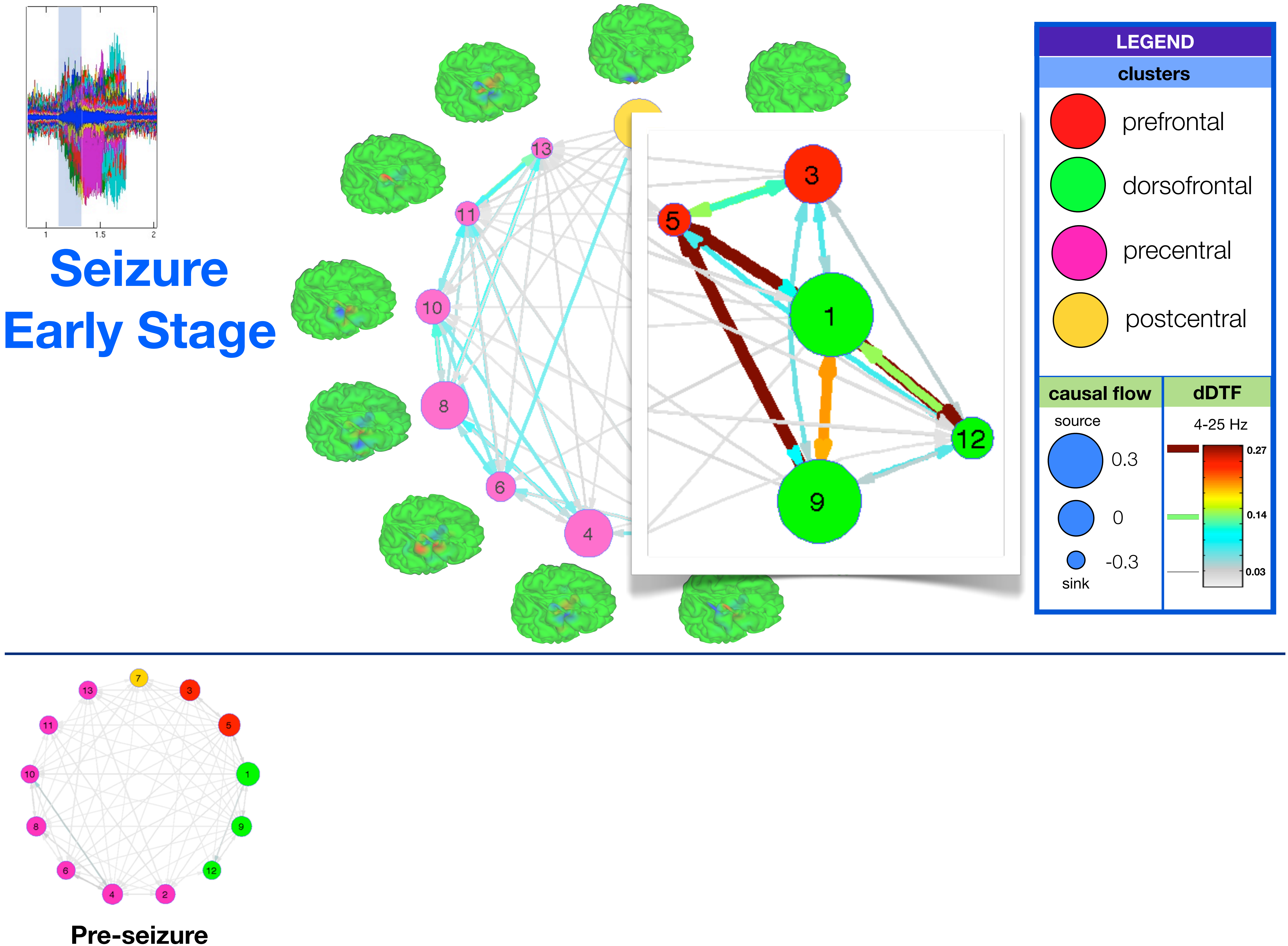


Seizure Early Stage

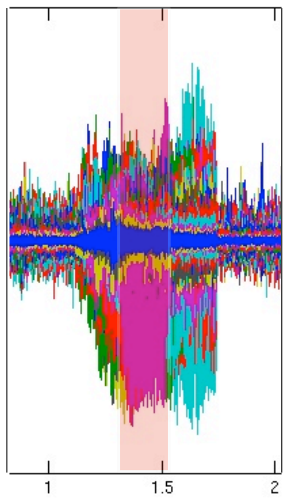




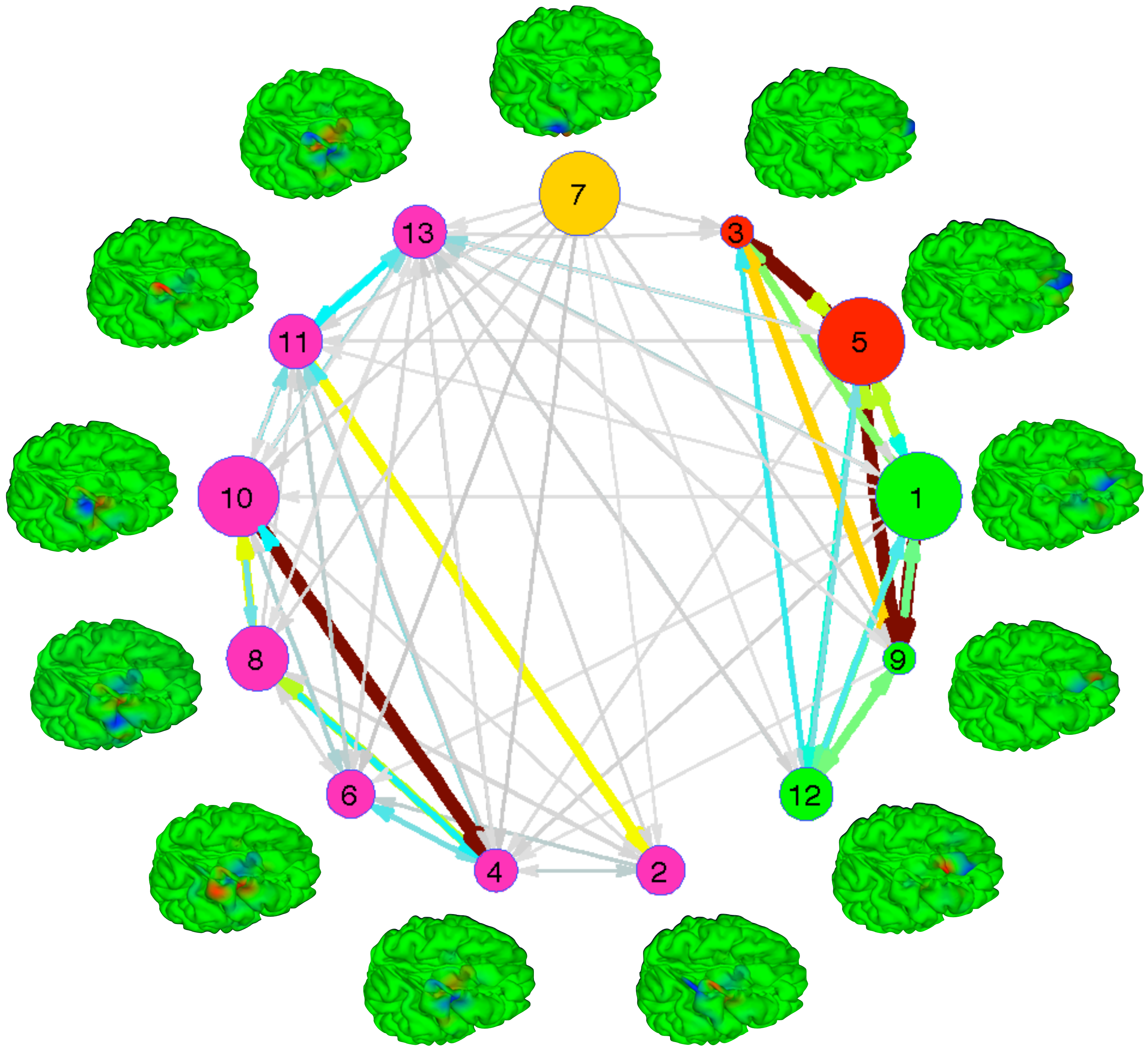
Pre-seizure

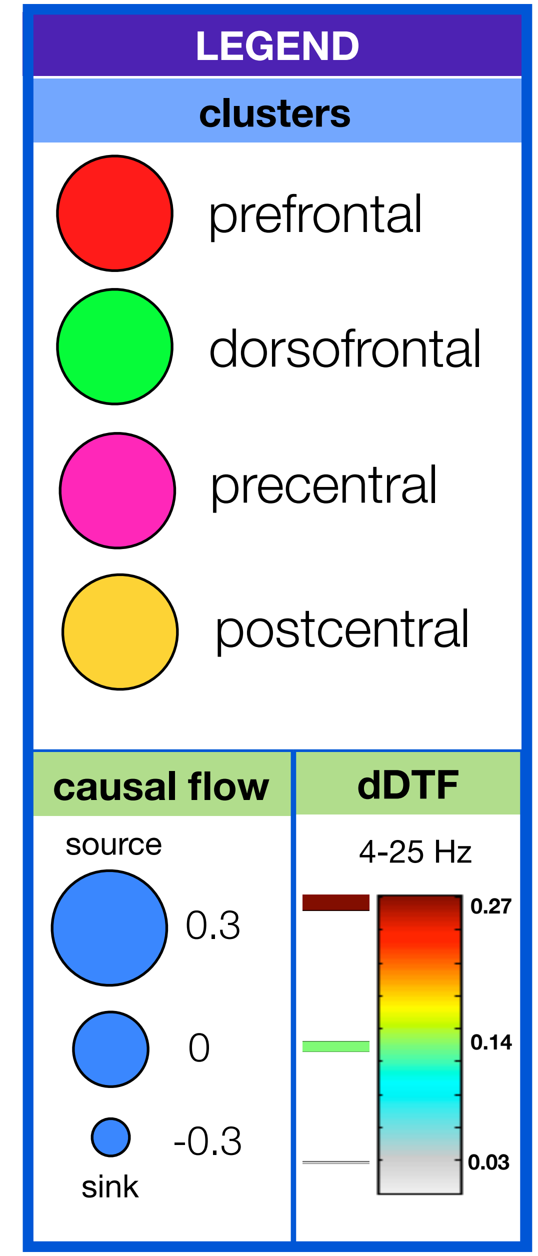


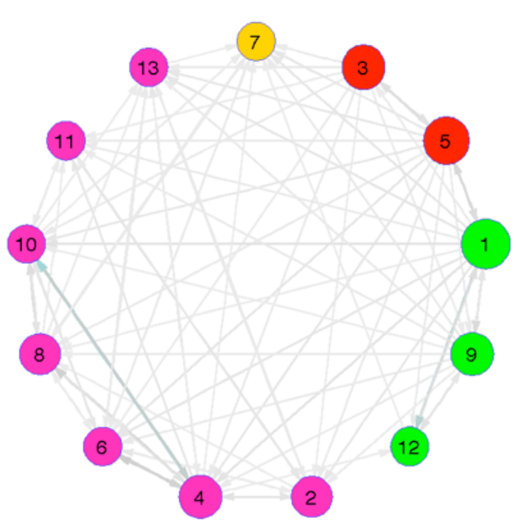
1
1.5
2
Seizure
Early Stage
13
11
10
8
6
4
3
5
1
12
9
LEGEND
clusters
prefrontal
dorsofrontal
precentral
postcentral
causal flow
source
0.3
0
-0.3
sink
dDTF
4-25 Hz
0.27
0.14
0.03
7
2
Pre-seizure



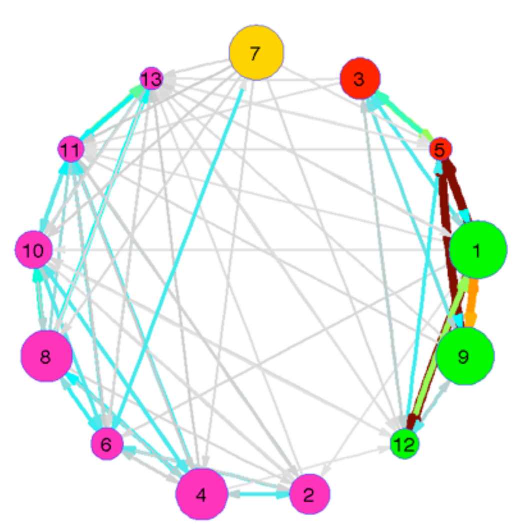
Seizure Mid Stage



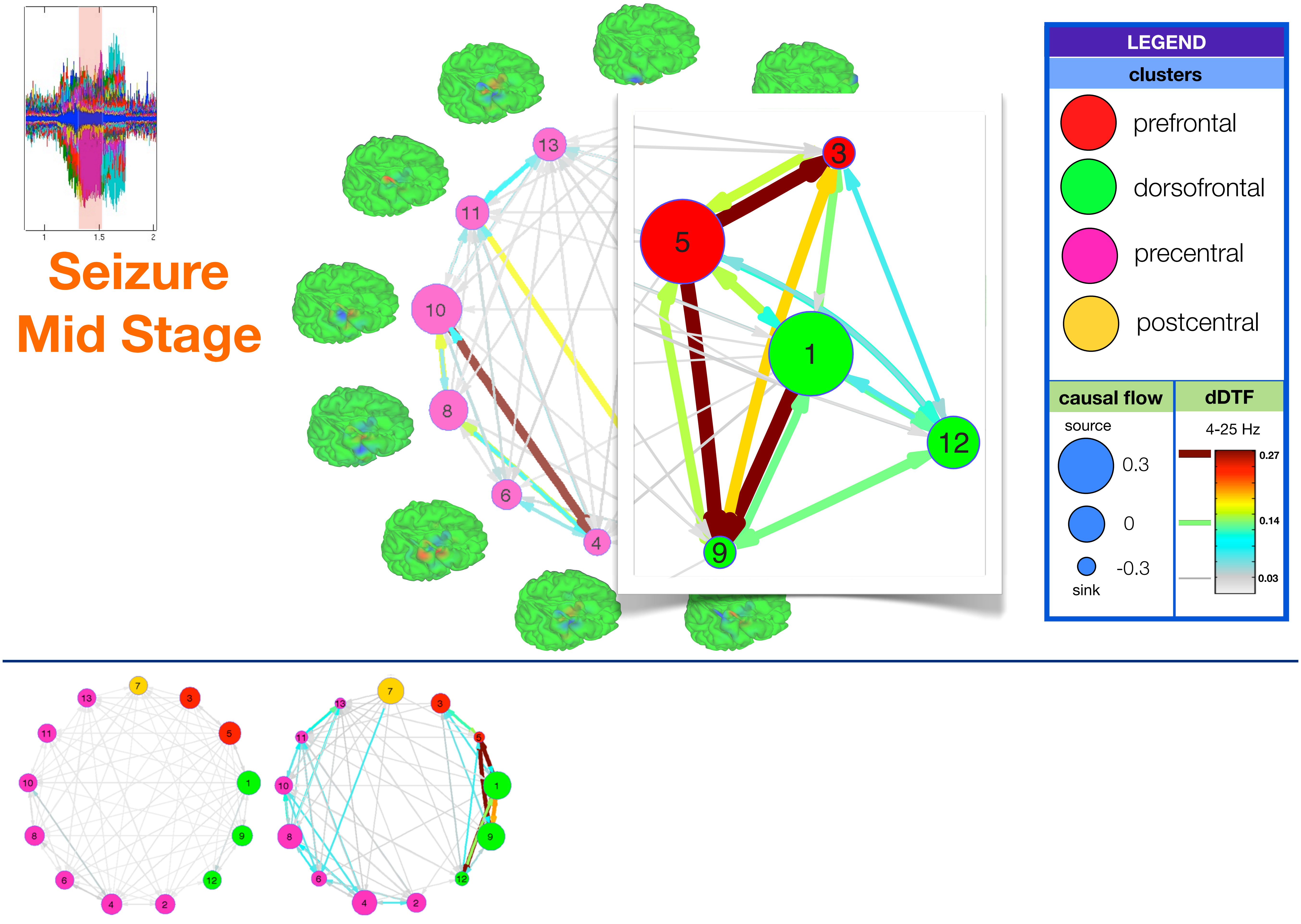




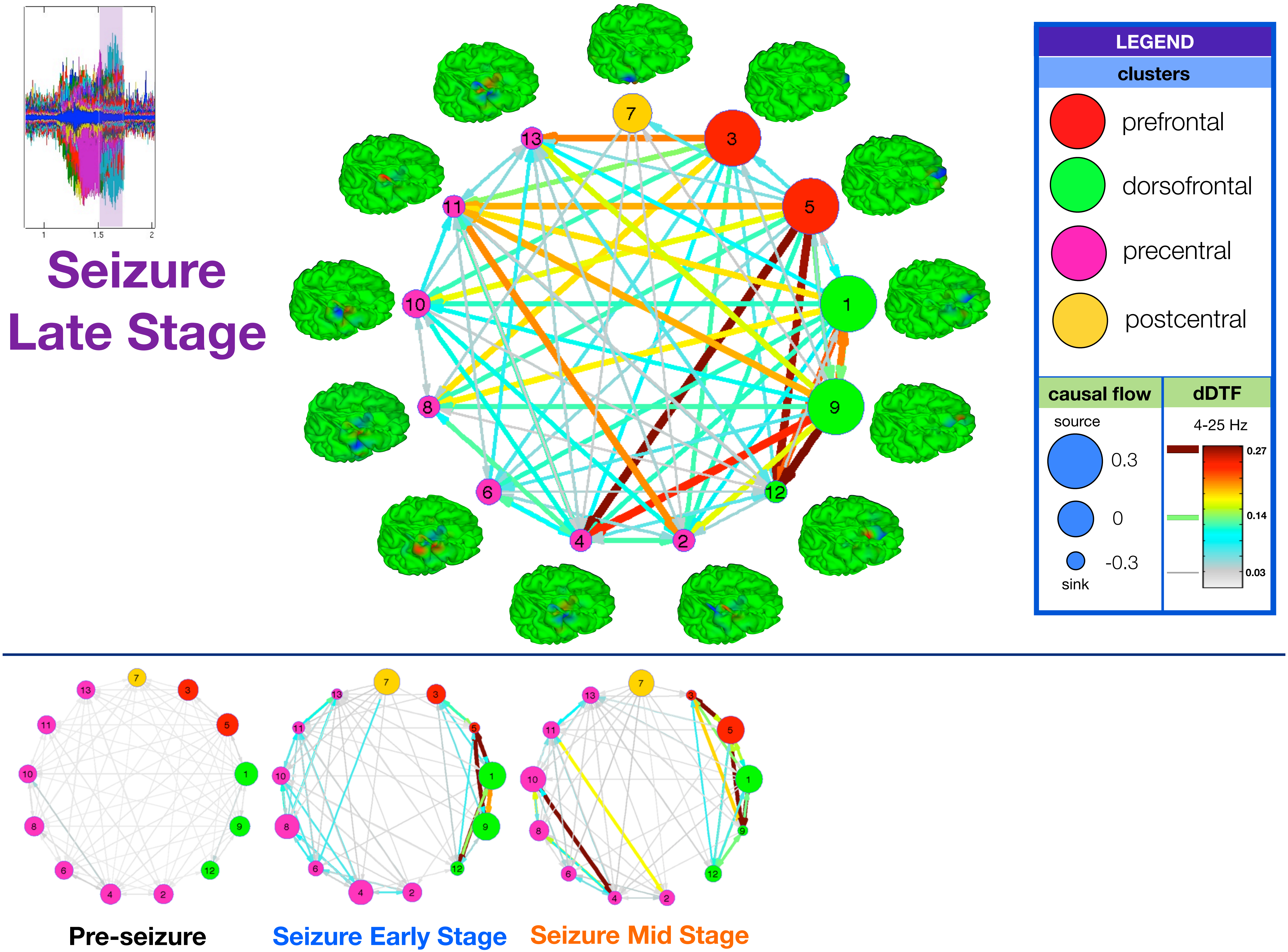
Pre-seizure



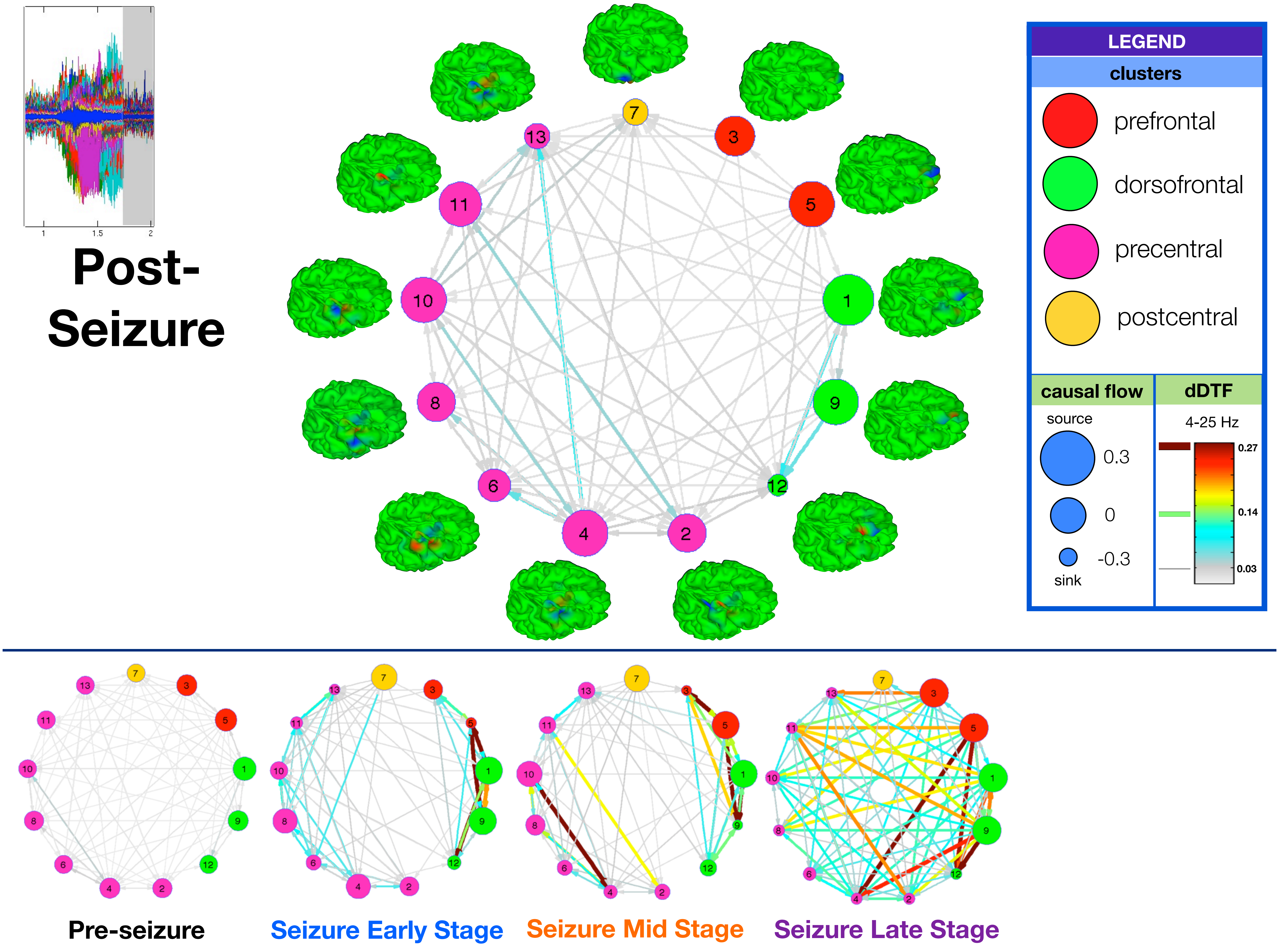
Seizure Early Stage



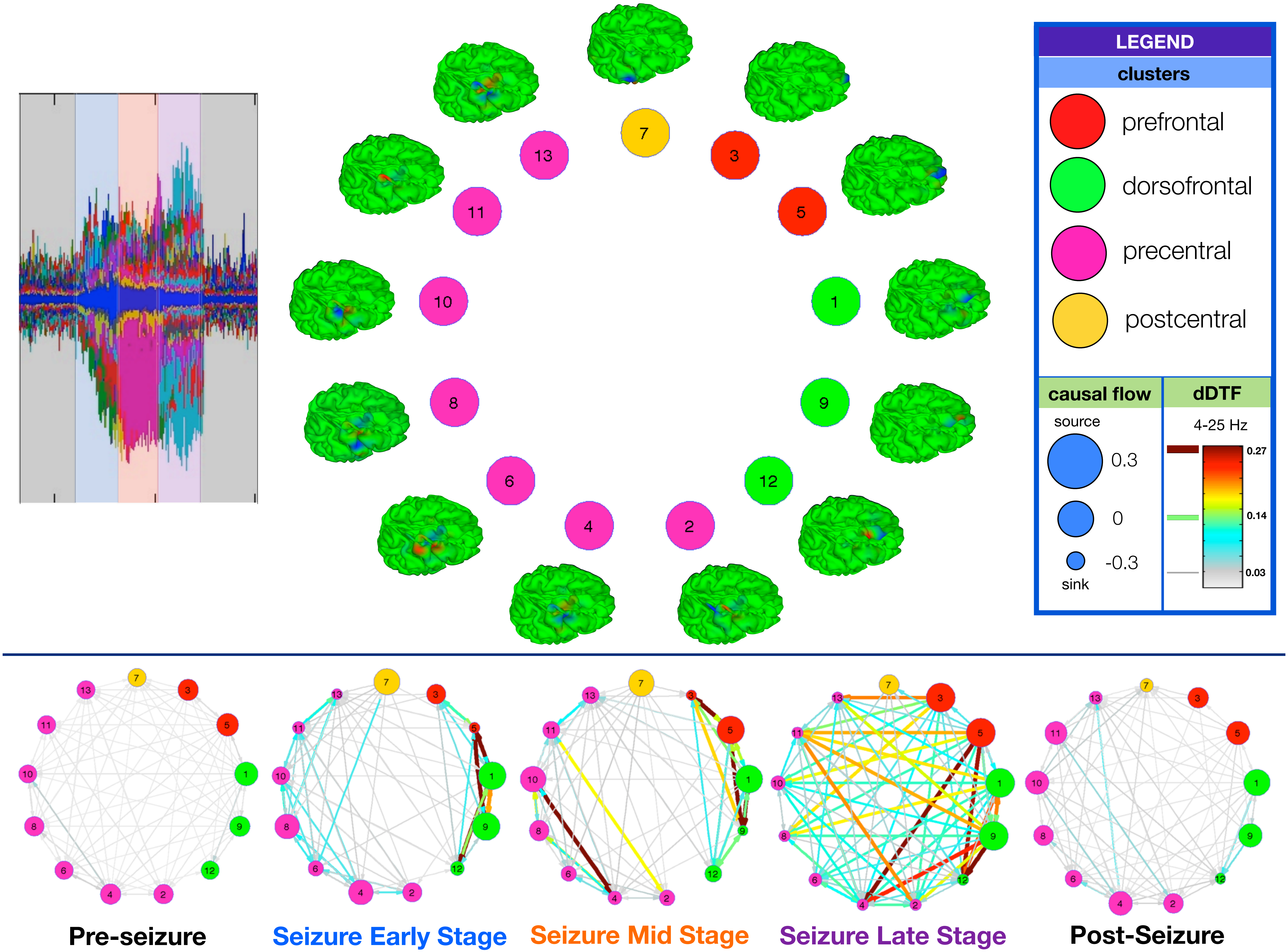
Pre-seizure **Seizure Early Stage**



Seizure
Late Stage
1
1.5
2
LEGEND
clusters
prefrontal
dorsofrontal
precentral
postcentral
causal flow
source
0.3
0
-0.3
sink
dDTF
4-25 Hz
0.27
0.14
0.03
Pre-seizure
Seizure Early Stage
Seizure Mid Stage



Post-Seizure
LEGEND
clusters
prefrontal
dorsofrontal
precentral
postcentral
causal flow
source
0.3
0
-0.3
sink
dDTF
4-25 Hz
0.27
0.14
0.03
Pre-seizure
Seizure Early Stage
Seizure Mid Stage
Seizure Late Stage



LEGEND
clusters
prefrontal
dorsofrontal
precentral
postcentral
causal flow
source
0.3
0
-0.3
sink
dDTF
4-25 Hz
0.27
0.14
0.03
Pre-seizure
Seizure Early Stage
Seizure Mid Stage
Seizure Late Stage
Post-Seizure

Spatiotemporal Visualization of Causal Flow Dynamics

$X = AS$

ICA

FP

$L = [m \times v]$ lead field matrix

$\tilde{L} = [LW^{(1)} \cdots LW^{(3)}]$

VAR

SBL

$A_q = \tilde{L}\tilde{M}_q + \epsilon_q$

$\tilde{L}^{-1} = SBL(A_q, \tilde{L})$

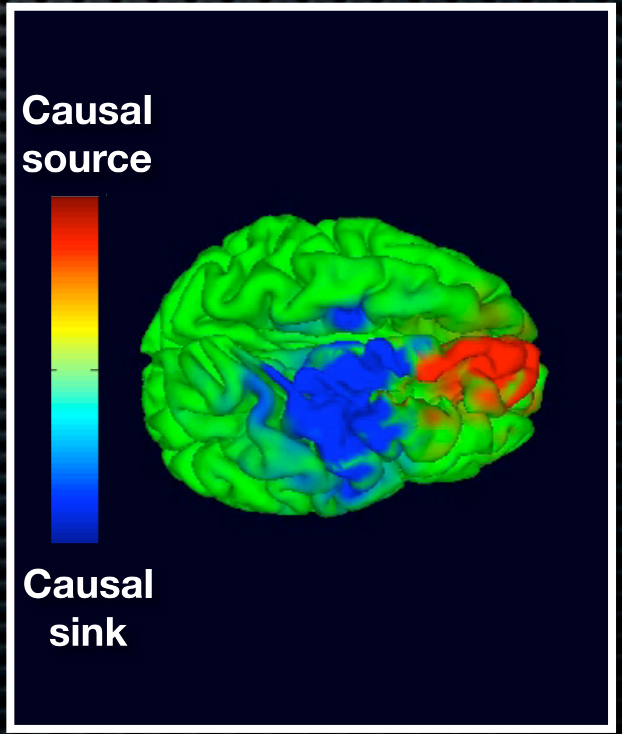
$\tilde{M}_q = \tilde{L}^{-1} A_q$

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

Univariate Metric (Outflow, Causal Flow, Power, ...)

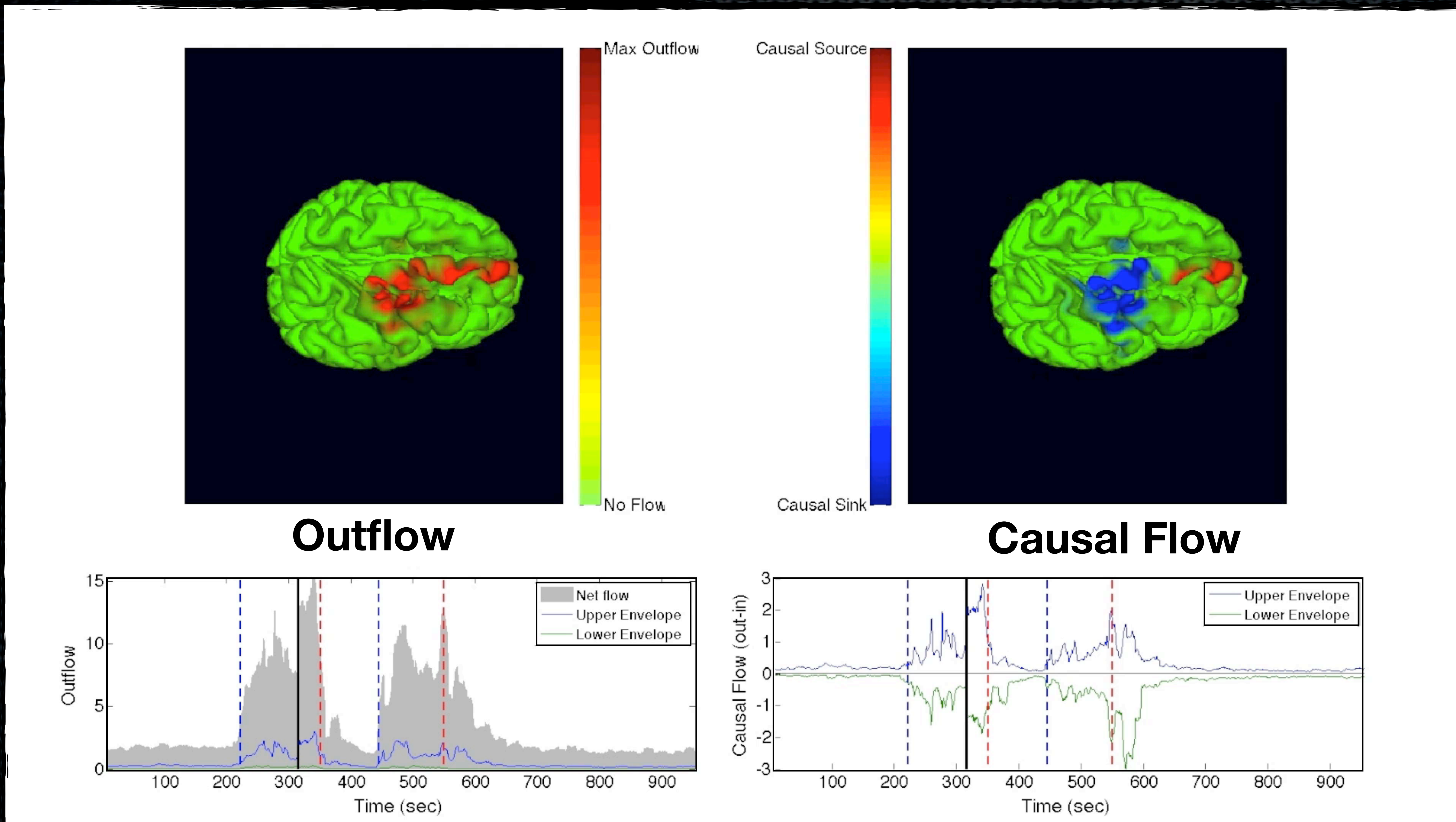
U_q

$P_q = M_q U_q$

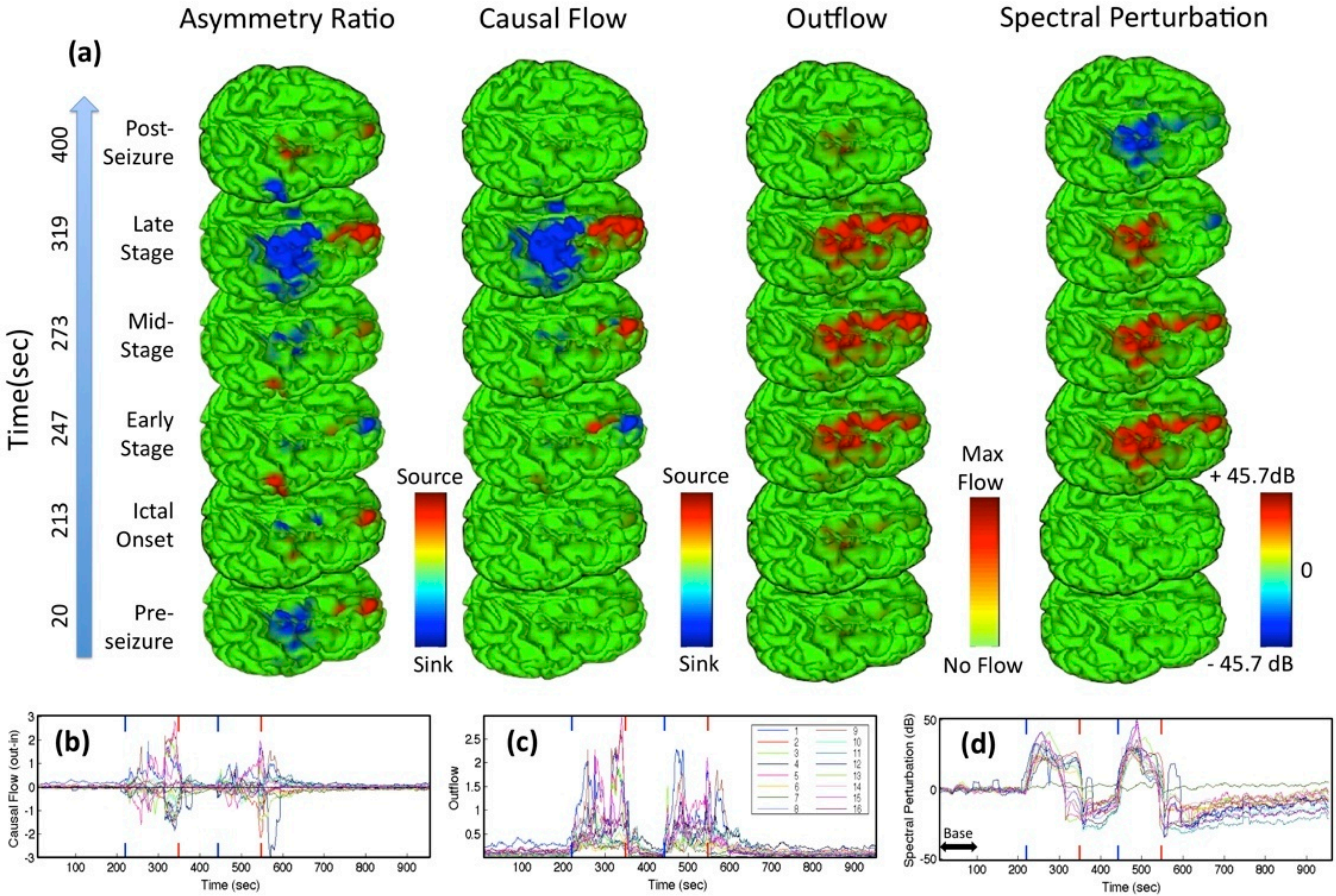


Mullen, Akalin Acar, Worrell, Makeig (2011), *IEEE EMBC*

Causal Flow Dynamics (4-25 Hz)



Mullen, Akalin Acar, Worrell, Makeig (2011), *IEEE EMBC*



Mullen, Akalin Acar, Worrell, Makeig (2011), *IEEE EMBC*

Acknowledgements

Zeynep Akalin Acar
Jason Palmer
Scott Makeig
Arnaud Delorme
Christian Kothe
Nima Bigdely Shamlo
Zhilin Zhang

Wes Thompson

Virginia de Sa
Vicente Malave

Dr. Gregory Worrell
Anonymous Patients

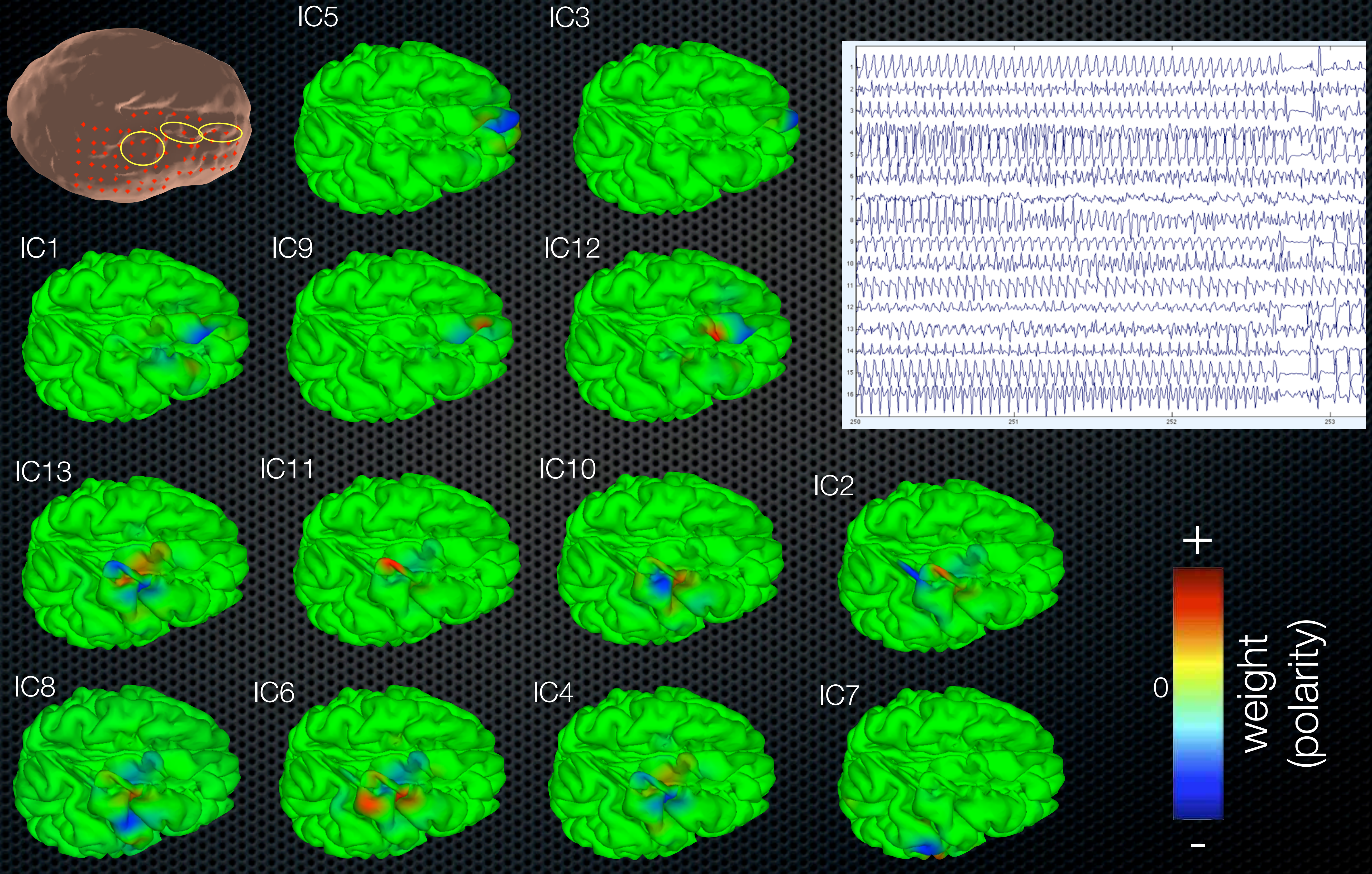
Ken Kreutz-Delgado

Sponsorship

The Swartz Foundation
San Diego Fellowship
Glushko Fellowship

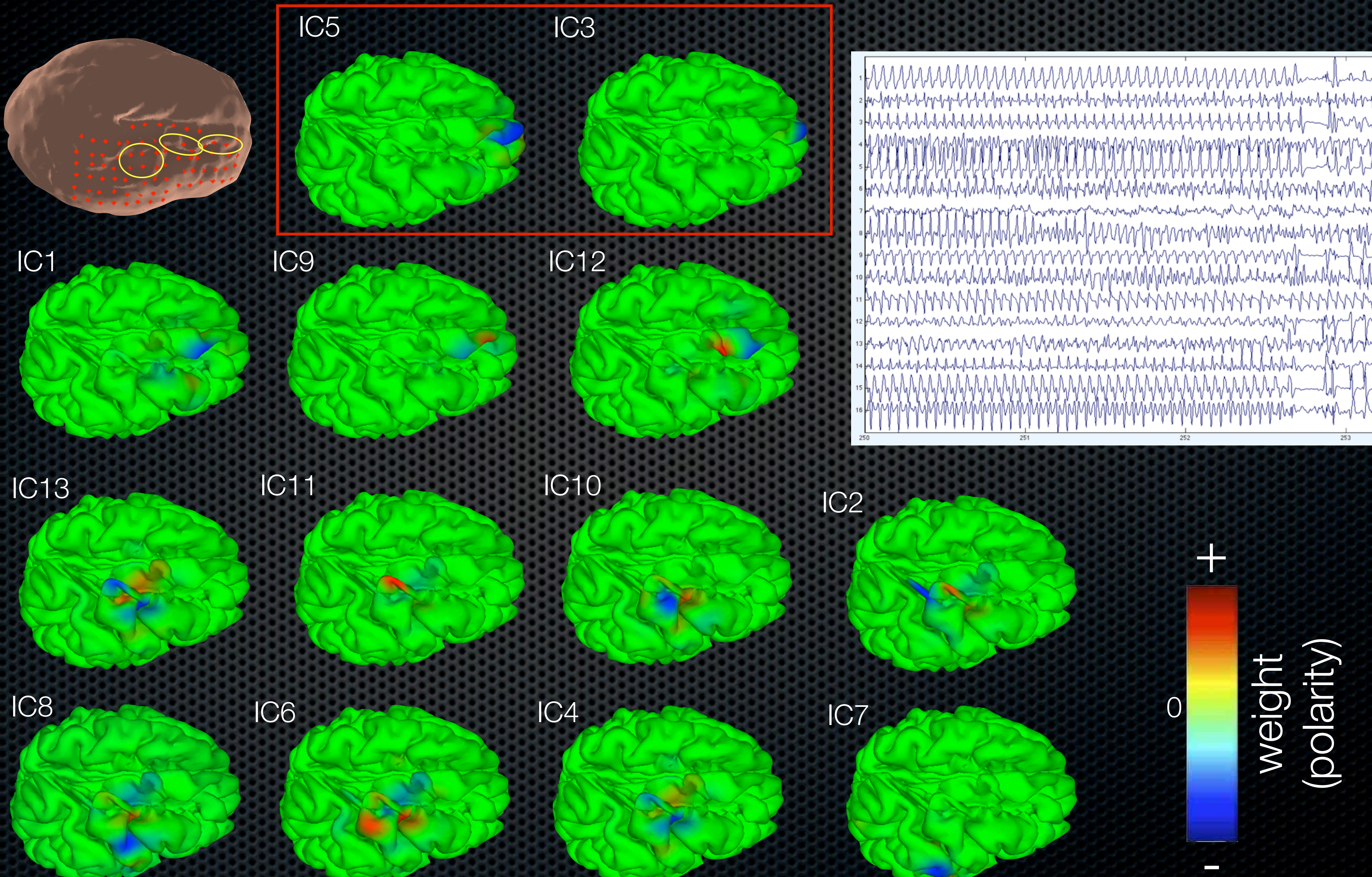
Supplementary Slides

Localized Epileptogenic IC Sources



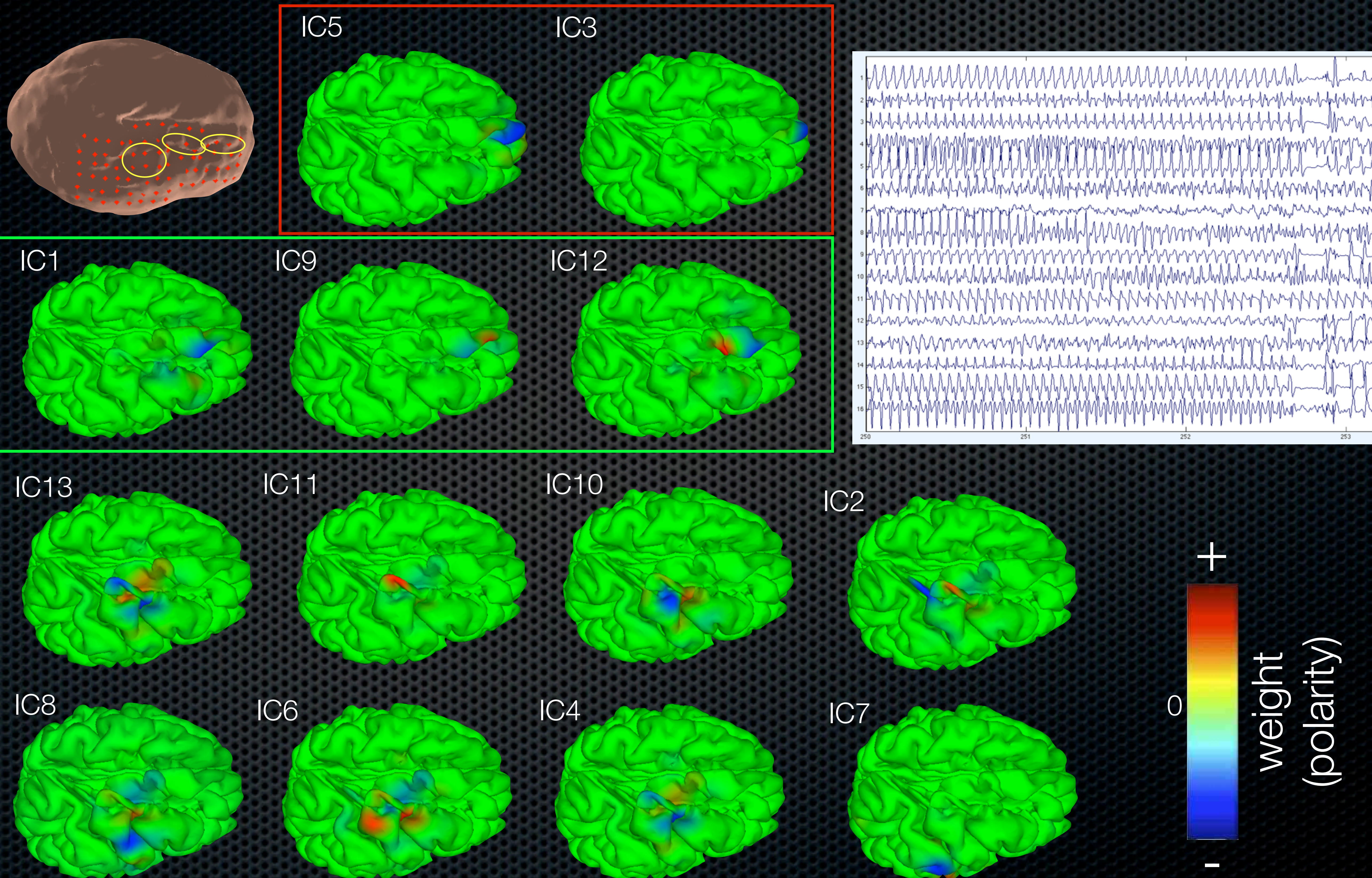
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Localized Epileptogenic IC Sources



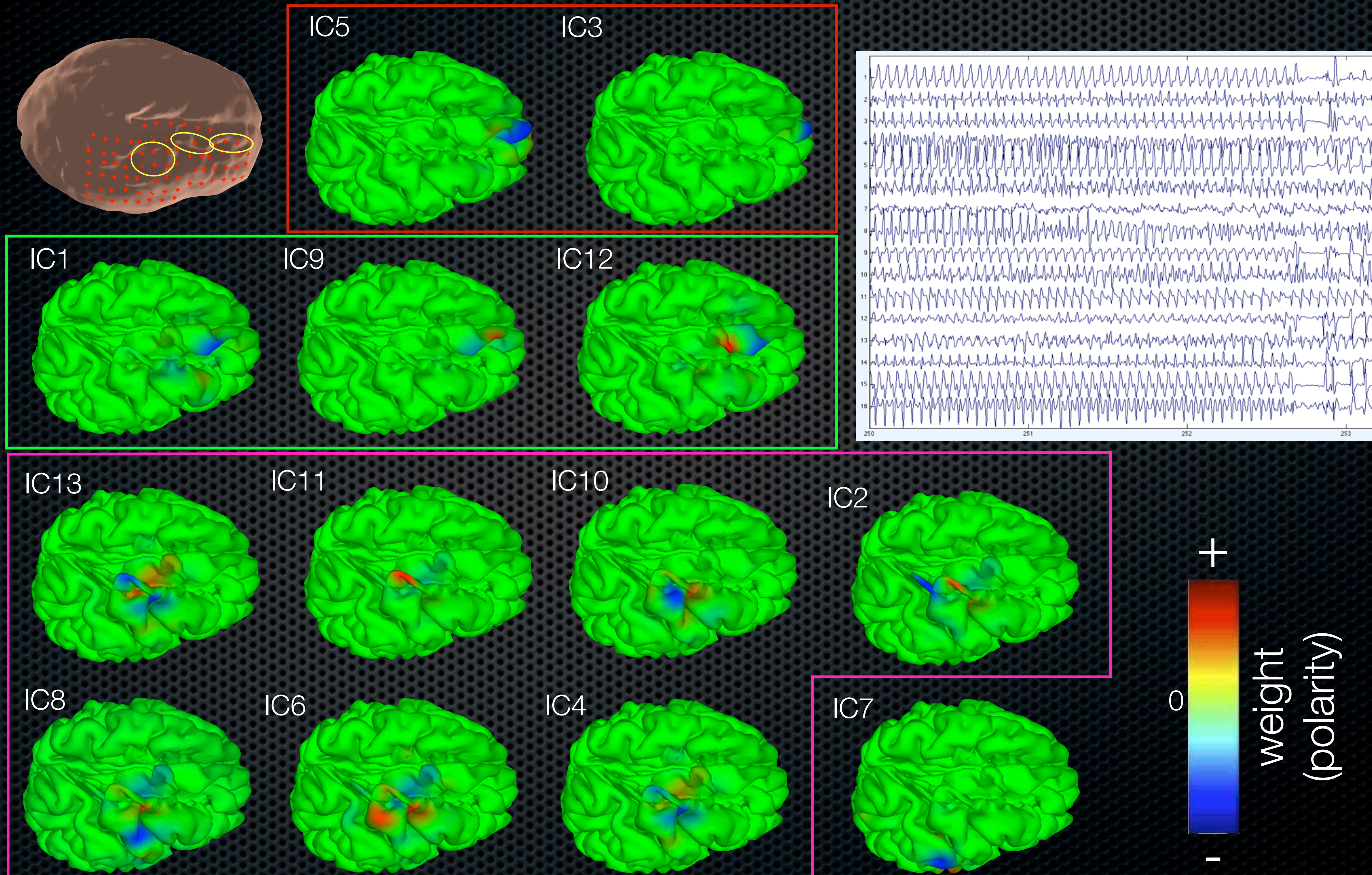
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Localized Epileptogenic IC Sources



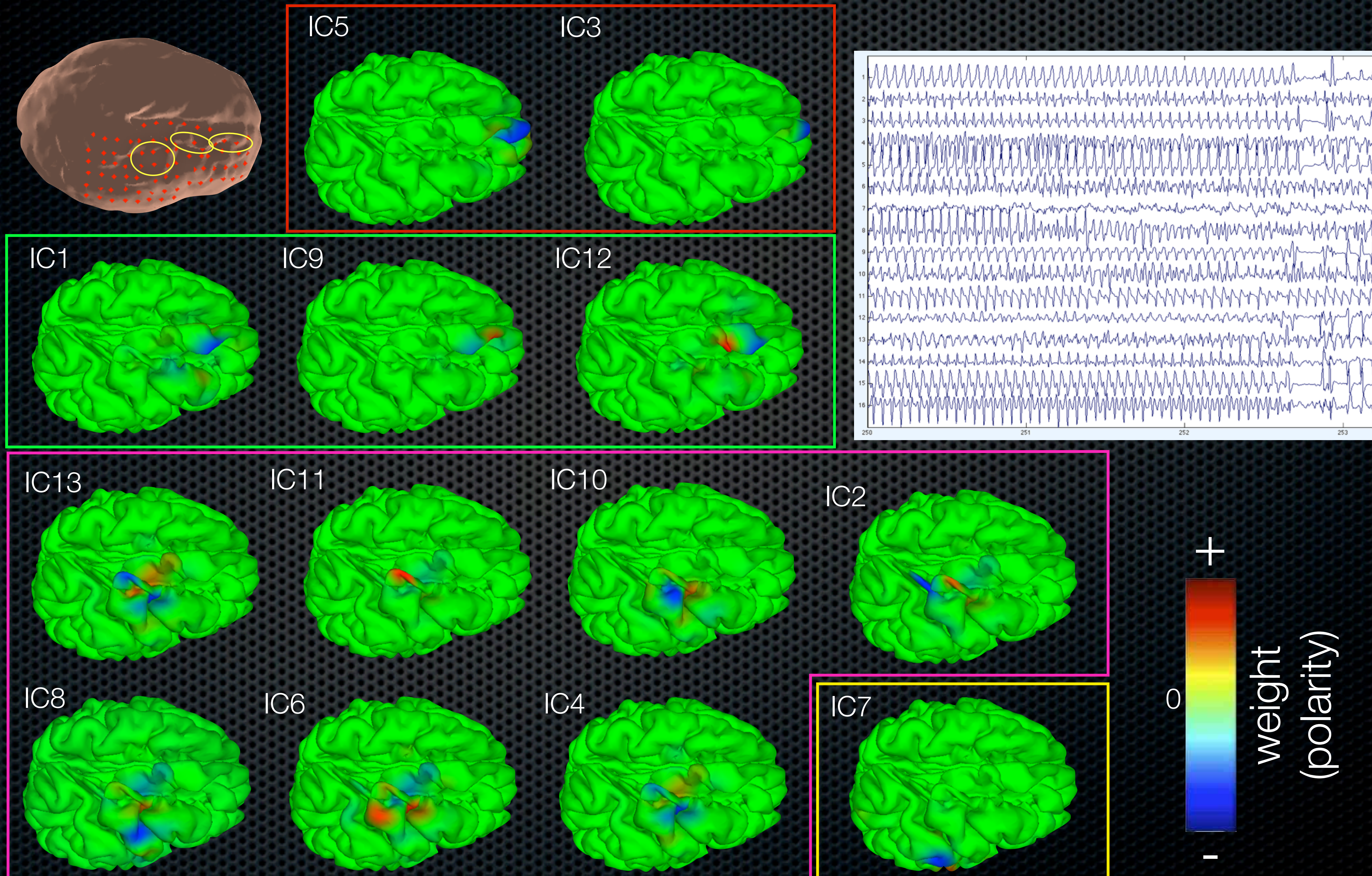
Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Localized Epileptogenic IC Sources



Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Localized Epileptogenic IC Sources



Mullen, Akalin Acar, et al (2011), *IEEE EMBC*

Ongoing Work: AMICA

Adaptive **M**ixture **ICA**

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS,* 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Ongoing Work: AMICA

Adaptive **M**ixture **ICA**

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS,* 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Definitions	
$X(t)$	multivariate data at time t
$A^h(t)$	mixing matrix for h^{th} ICA model
$S^h(t)$	source activations for h^{th} ICA model

Ongoing Work: AMICA

Adaptive **M**ixture **ICA**

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS,* 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Definitions

$X(t)$	multivariate data at time *t*
$A^h(t)$	mixing matrix for h^{th} ICA model
$S^h(t)$	source activations for h^{th} ICA model

AMICA model

$$p(X(t)) = \sum_{h=1}^{K} p(M_h)p(X(t) \mid M_h)$$

$$p(X(t) \mid M_h) = \left|\det A_h^{-1}\right| p_h(A_h^{-1}X(t))$$

$$X(t) = A^h S^h(t)$$

Ongoing Work: AMICA

Adaptive Mixture ICA

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS*, 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Definitions

$X(t)$	multivariate data at time *t*
$A^h(t)$	mixing matrix for h^{th} ICA model
$S^h(t)$	source activations for h^{th} ICA model

AMICA model

mixture model

$$p(X(t)) = \sum_{h=1}^{K} p(M_h)\, p(X(t) \mid M_h)$$

$$p(X(t) \mid M_h) = \left|\det A_h^{-1}\right| p_h(A_h^{-1} X(t))$$

$$X(t) = A^h S^h(t)$$

Ongoing Work: AMICA

Adaptive **M**ixture **ICA**

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS*, 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Definitions

$X(t)$	multivariate data at time *t*
$A^h(t)$	mixing matrix for *h*th ICA model
$S^h(t)$	source activations for *h*th ICA model

AMICA model

mixture model

$$p(X(t)) = \sum_{h=1}^{K} p(M_h)p(X(t) \mid M_h)$$

likelihood function

$$p(X(t) \mid M_h) = \left|\det A_h^{-1}\right| p_h(A_h^{-1}X(t))$$

$$X(t) = A^h S^h(t)$$

Ongoing Work: AMICA

Adaptive **M**ixture **ICA**

(Palmer, Kreutz-Delgado, Rao , Makeig, *ICASS*, 2007)

- Mixture model allowing for robust ICA decomposition of non-stationary processes.
- Affords automated state segmentation based on model likelihoods

Definitions

$X(t)$	multivariate data at time *t*
$A^h(t)$	mixing matrix for h^{th} ICA model
$S^h(t)$	source activations for h^{th} ICA model

AMICA model

mixture model

$$p(X(t)) = \sum_{h=1}^{K} p(M_h)\, p(X(t) \mid M_h)$$

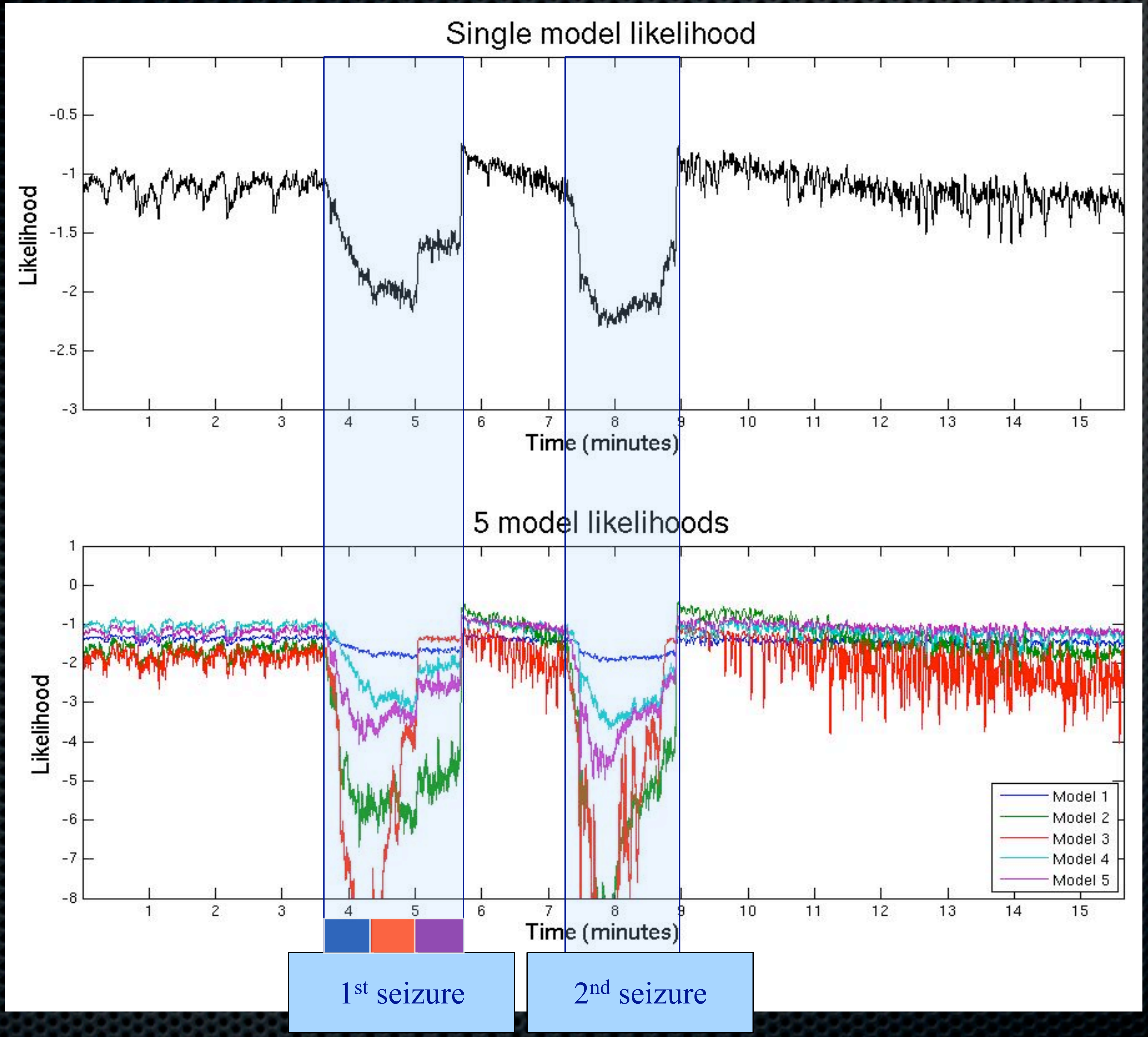
likelihood function

$$p(X(t) \mid M_h) = \left|\det A_h^{-1}\right| p_h(A_h^{-1} X(t))$$

generative model

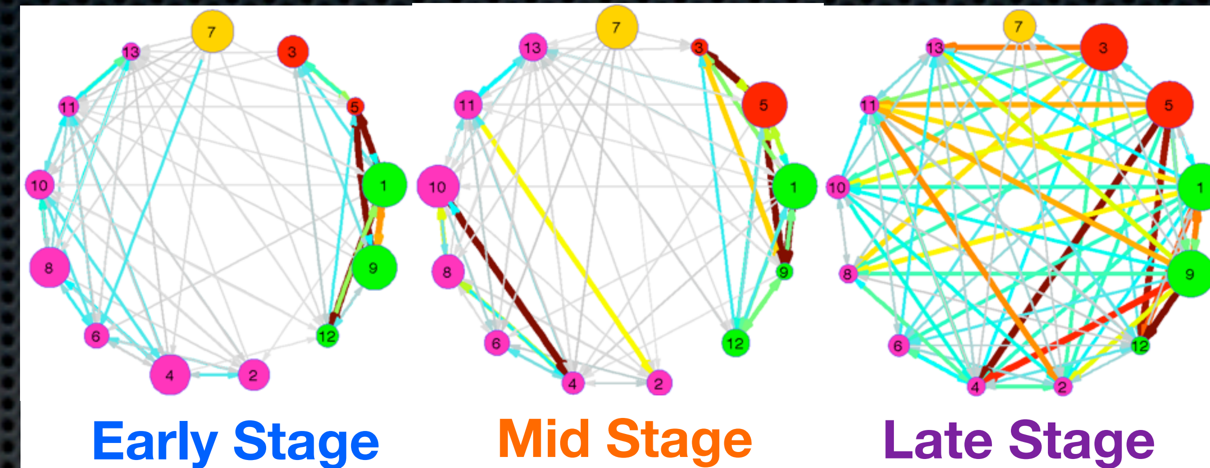
$$X(t) = A^h S^h(t)$$

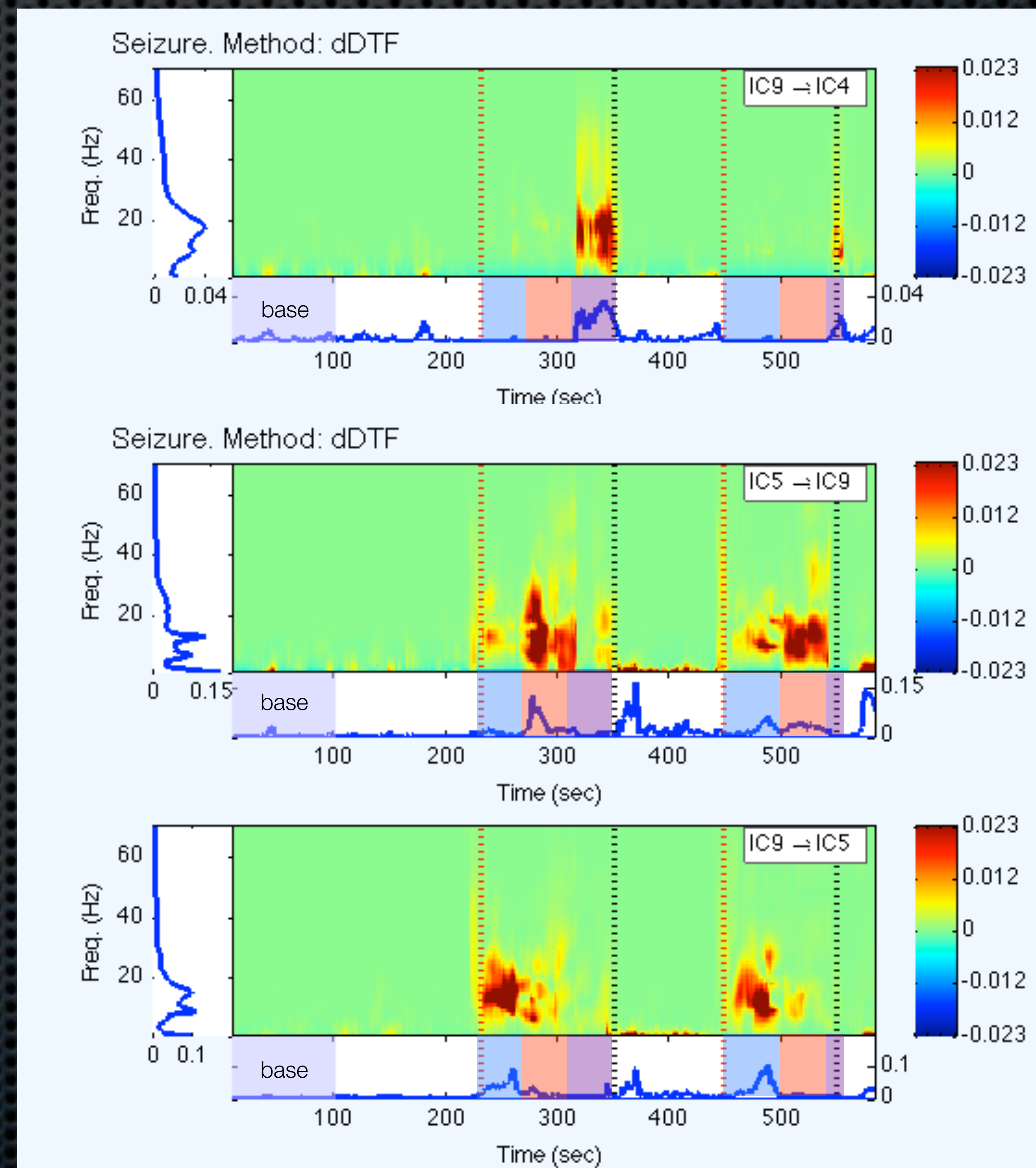
Ongoing Work: AMICA

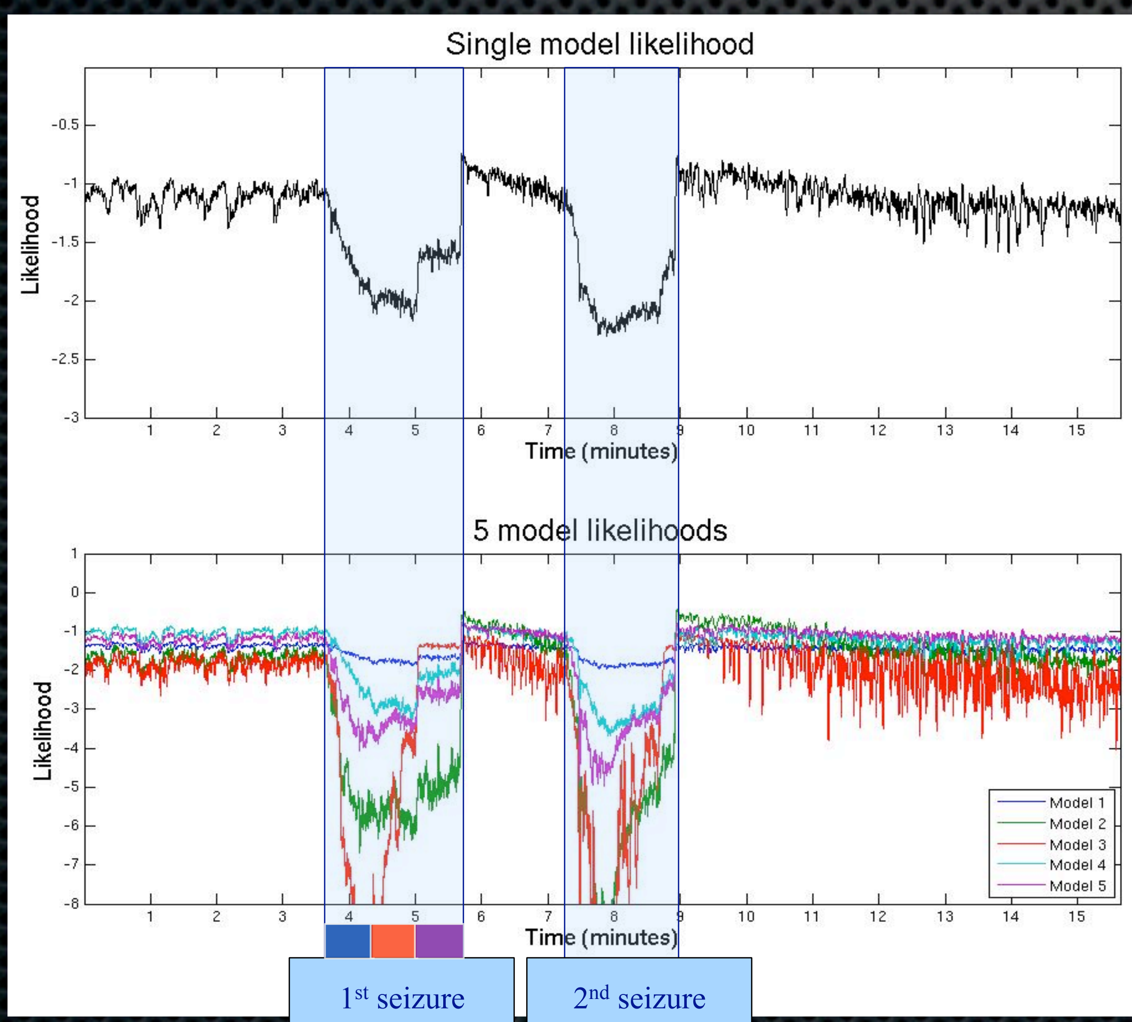


Seizure segmentation using AMICA model likelihoods

Seizure segmentation using AMICA model likelihoods

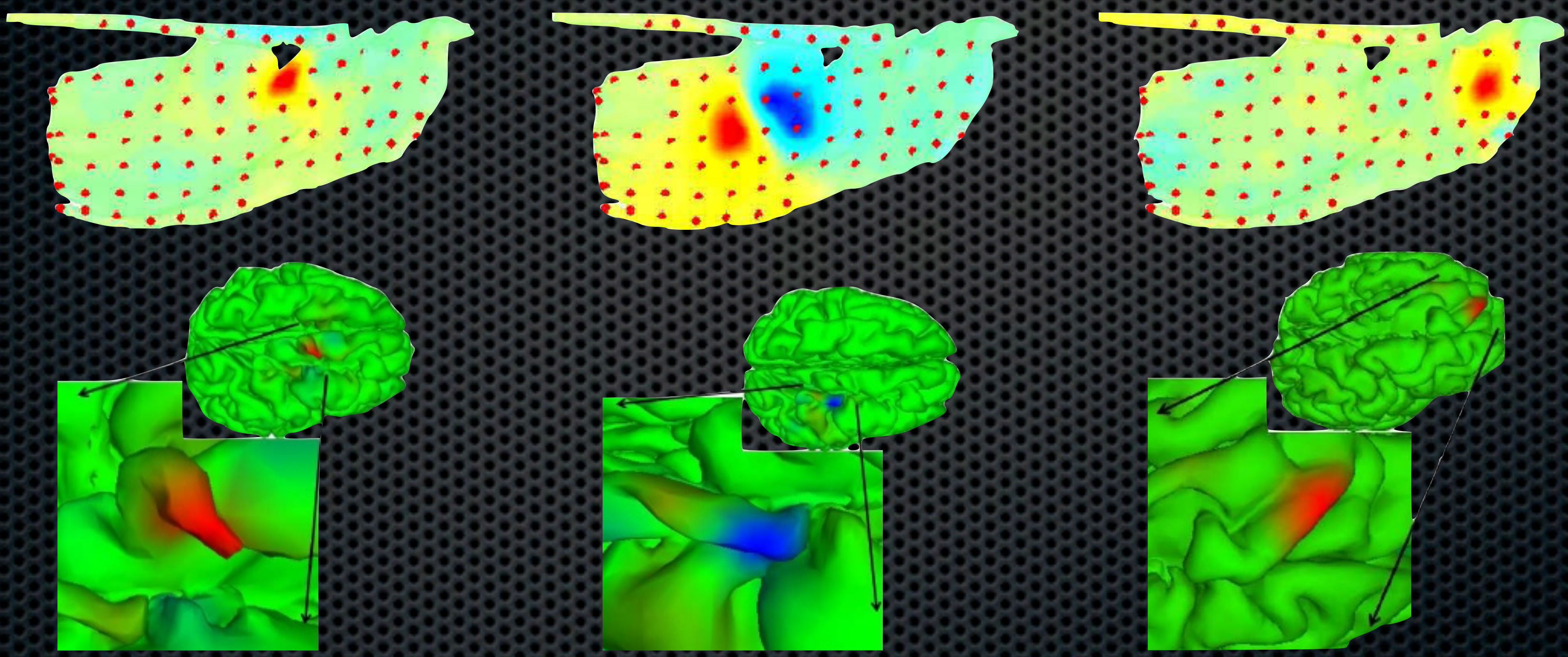






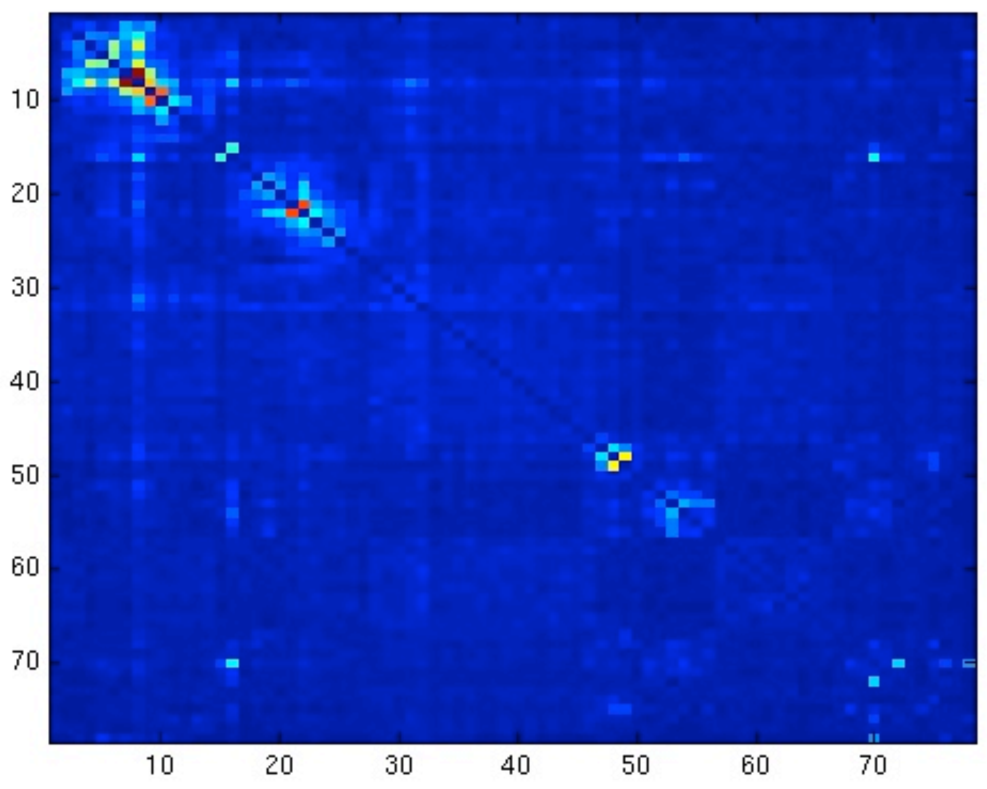
AMICA - SBL Solutions

Representative component maps and SBL solutions from the Amica model which is dominant in late seizure stage



Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

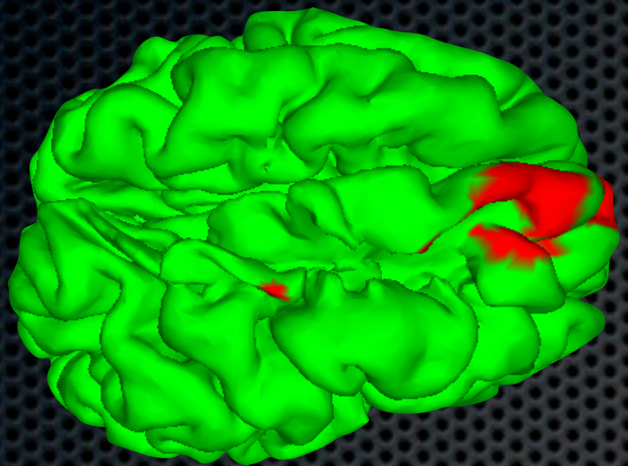
AMICA Dependent Subspace Clusters



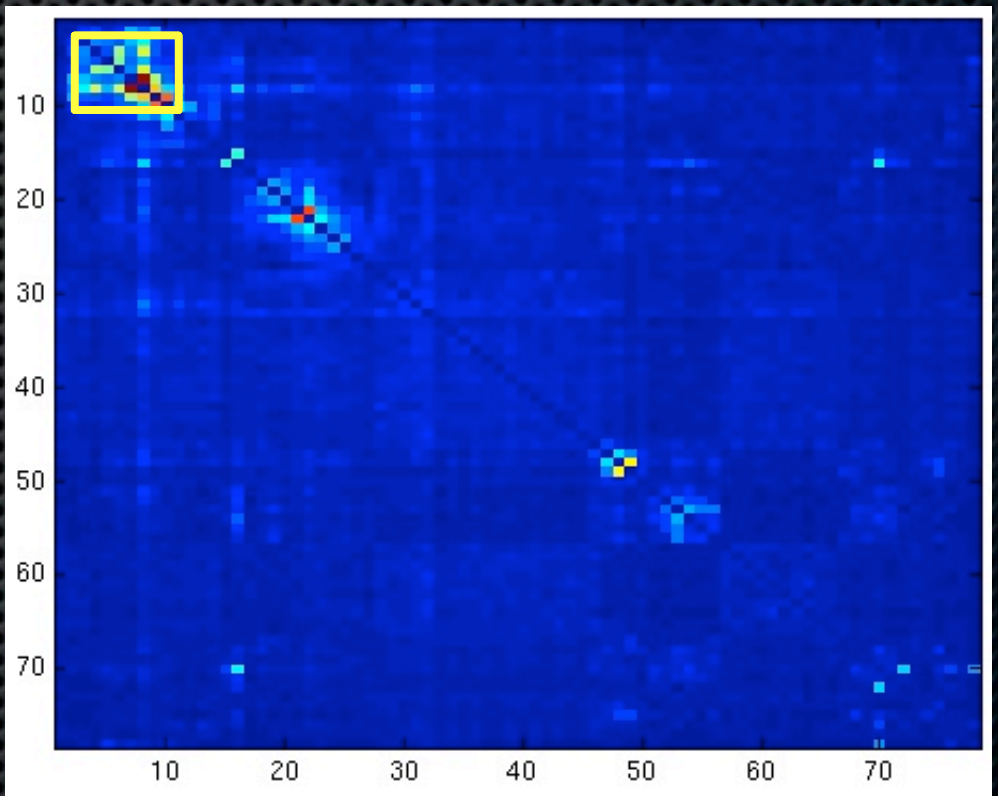
- Pairwise mutual information (PMI) computed for all ICs
- Components clustered using heuristic that promotes a block-diagonal PMI matrix (**Palmer, 2011**)

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

AMICA Dependent Subspace Clusters



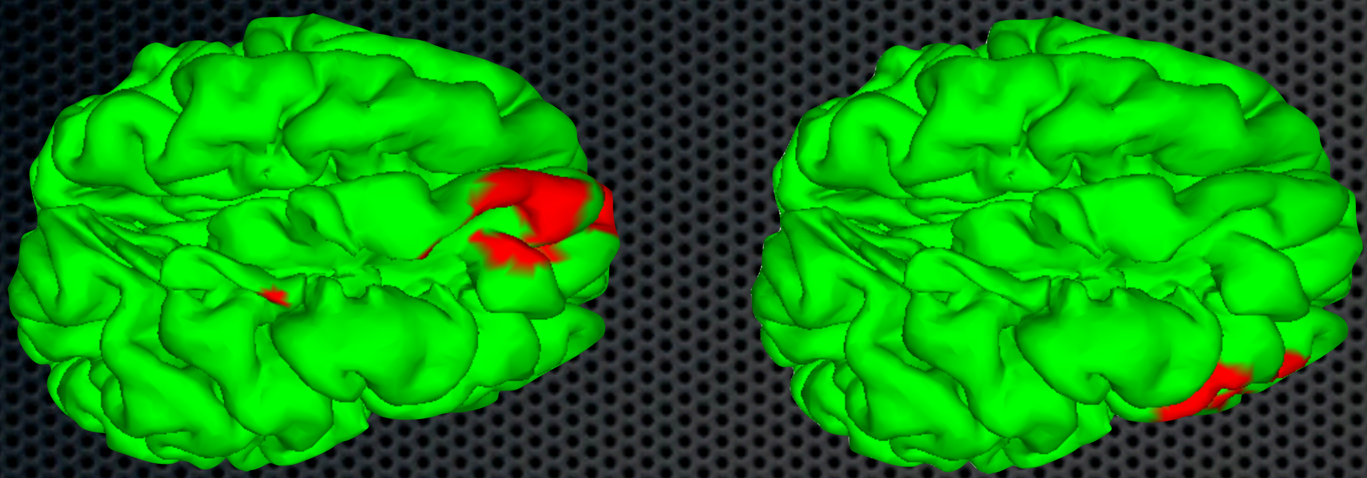
1st cluster



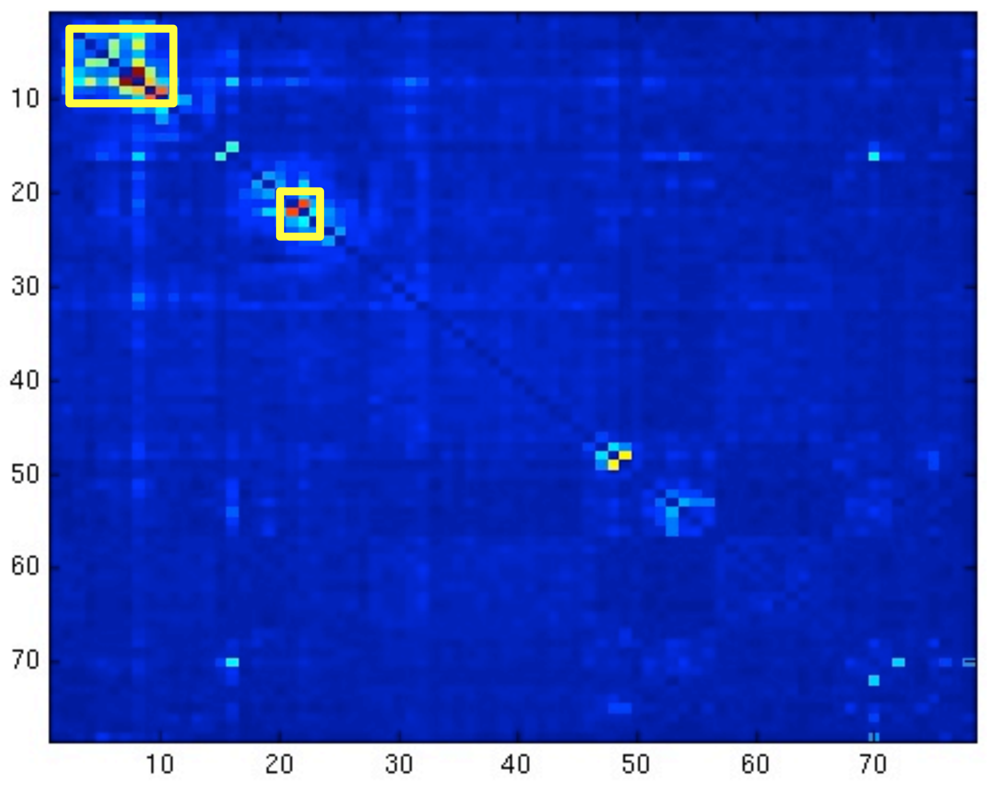
- Pairwise mutual information (PMI) computed for all ICs
- Components clustered using heuristic that promotes a block-diagonal PMI matrix (**Palmer, 2011**)

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

AMICA Dependent Subspace Clusters



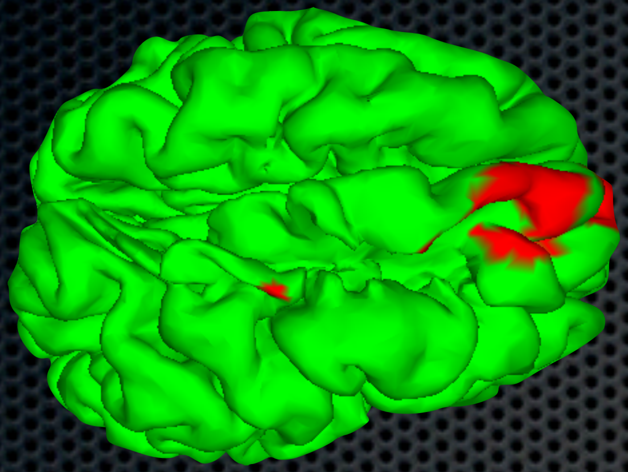
1st cluster   2nd cluster



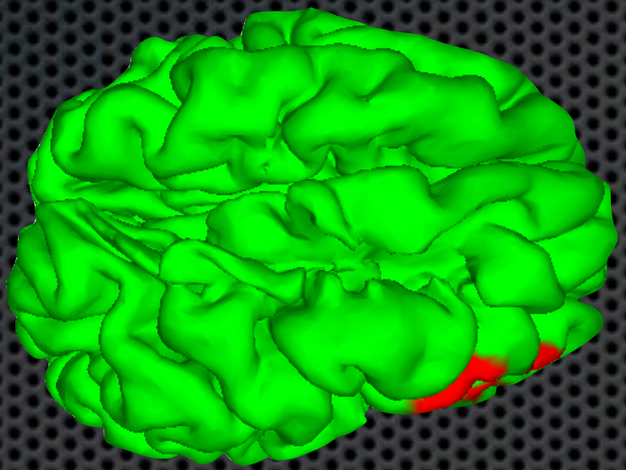
- Pairwise mutual information (PMI) computed for all ICs
- Components clustered using heuristic that promotes a block-diagonal PMI matrix (**Palmer, 2011**)

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

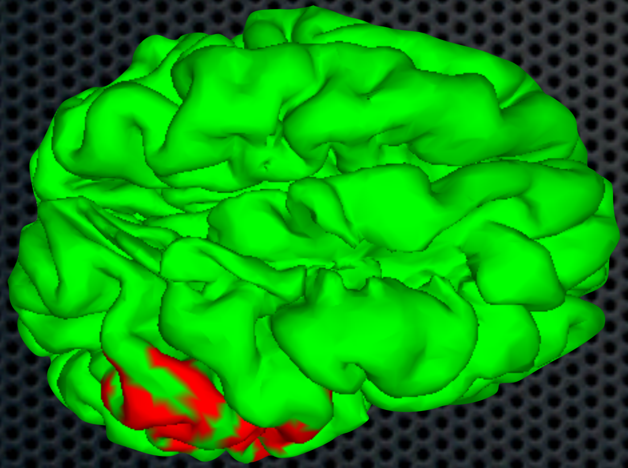
AMICA Dependent Subspace Clusters



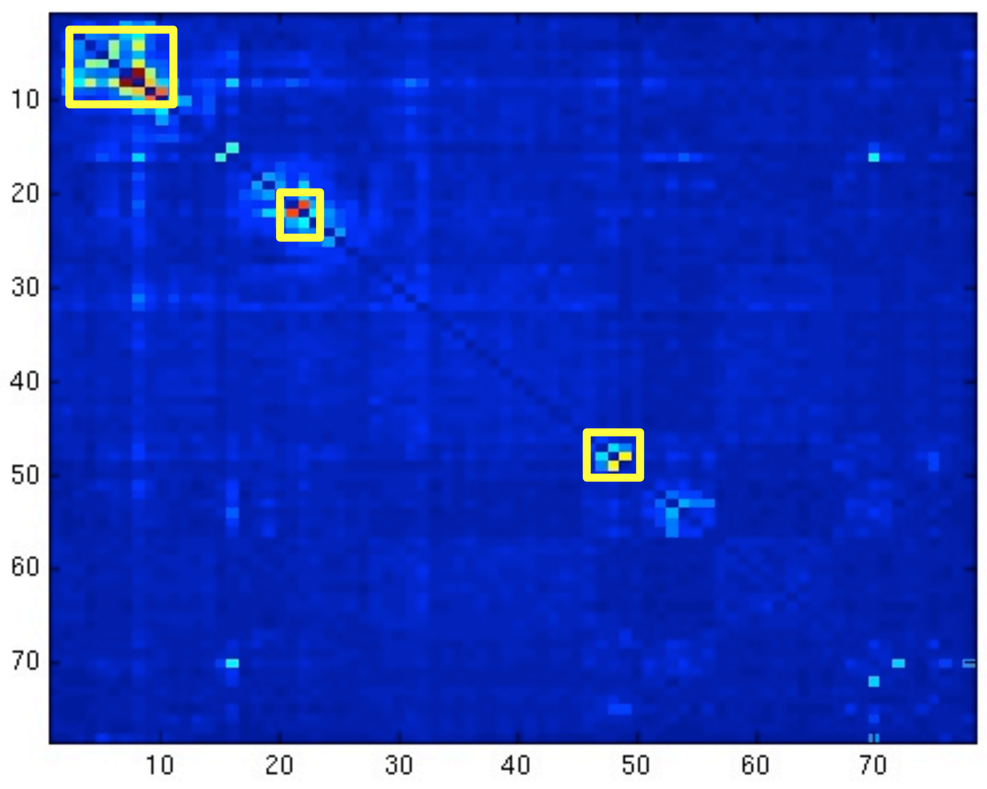
1st cluster



2nd cluster



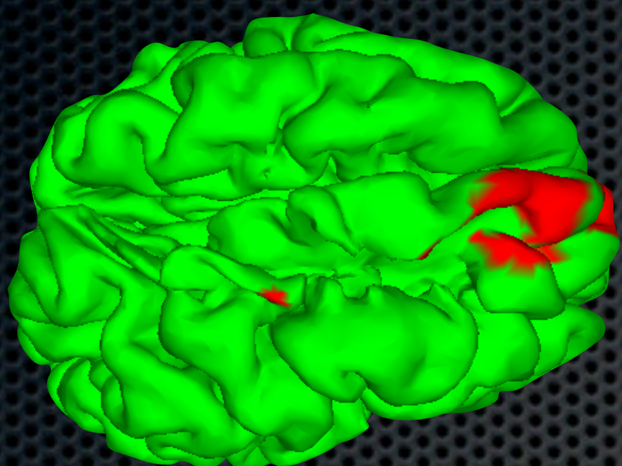
3rd cluster



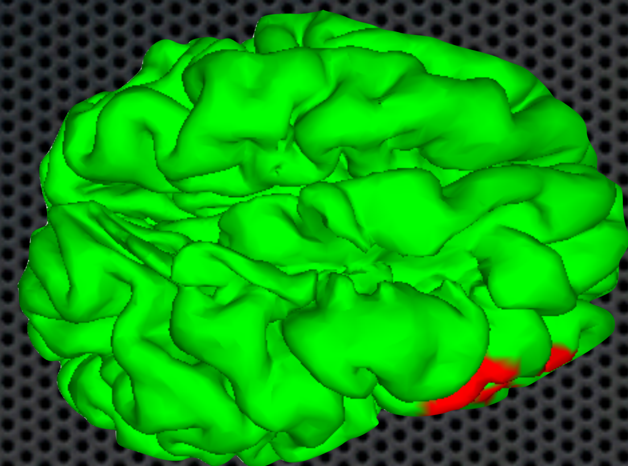
- Pairwise mutual information (PMI) computed for all ICs
- Components clustered using heuristic that promotes a block-diagonal PMI matrix (**Palmer, 2011**)

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

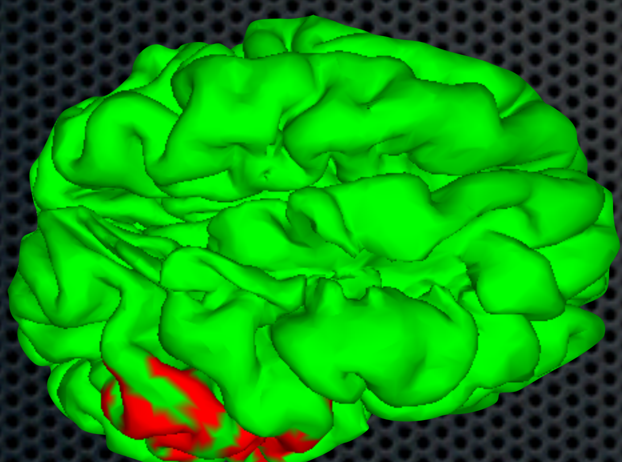
AMICA Dependent Subspace Clusters



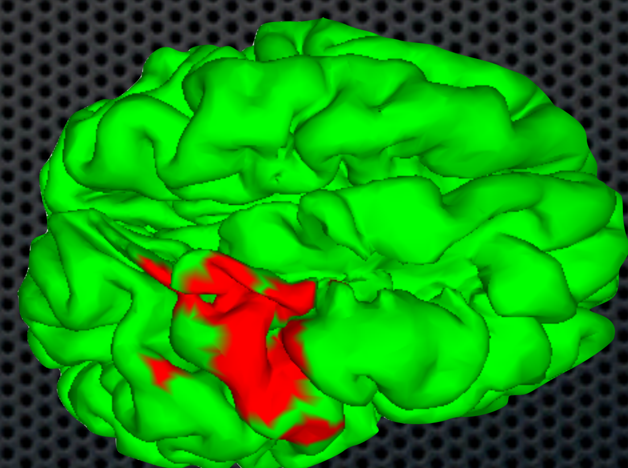
1st cluster



2nd cluster

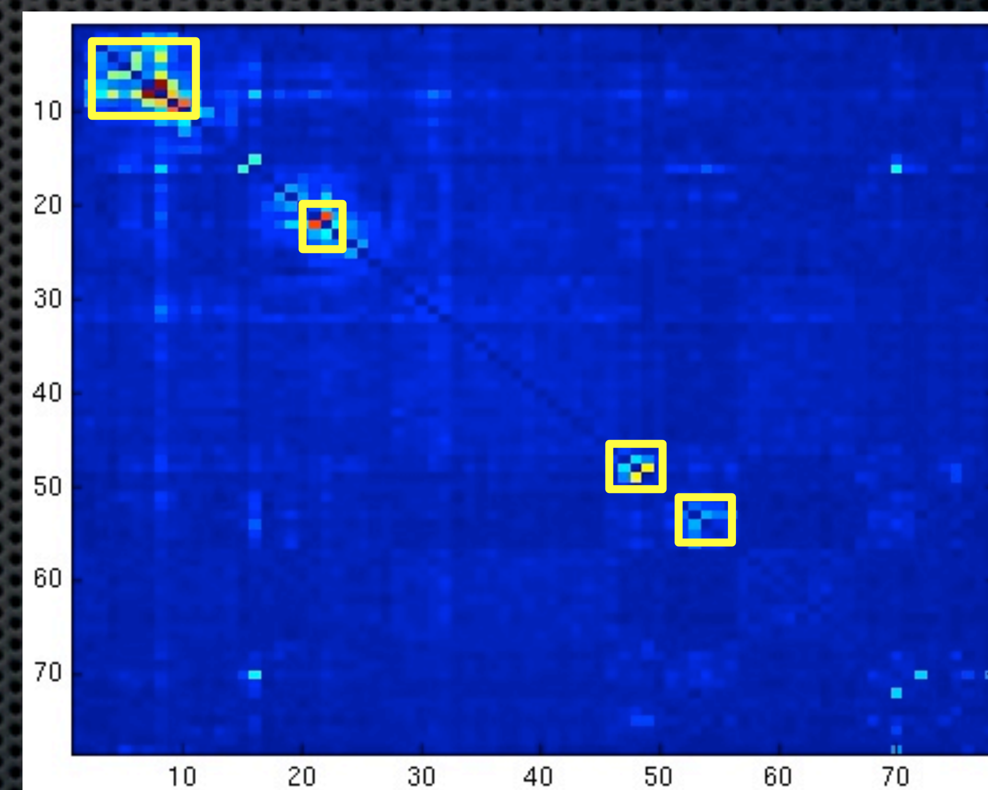


3rd cluster



4th cluster

Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

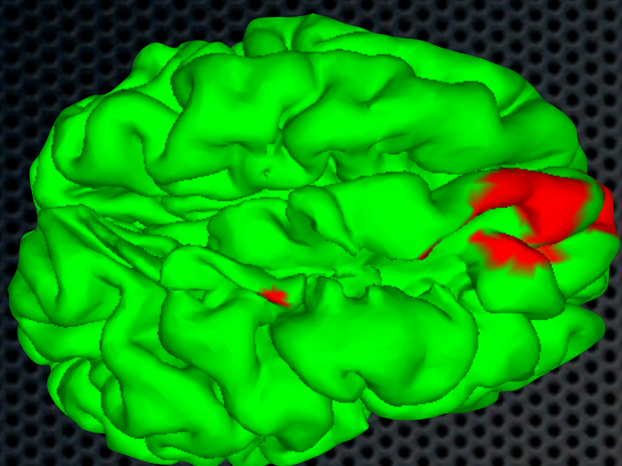


- Pairwise mutual information (PMI) computed for all ICs
- Components clustered using heuristic that promotes a block-diagonal PMI matrix (**Palmer, 2011**)

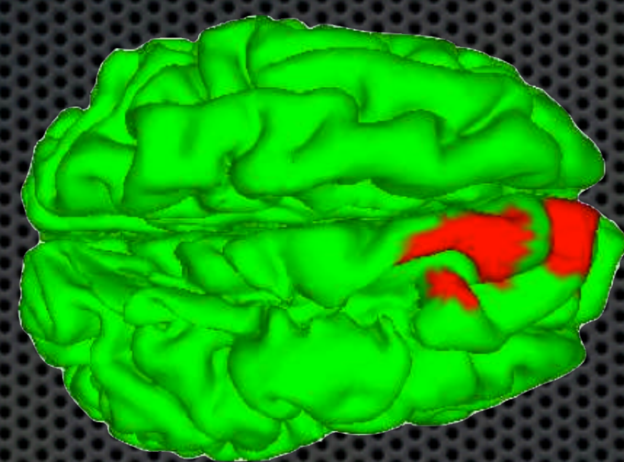
AMICA Dependency Clusters

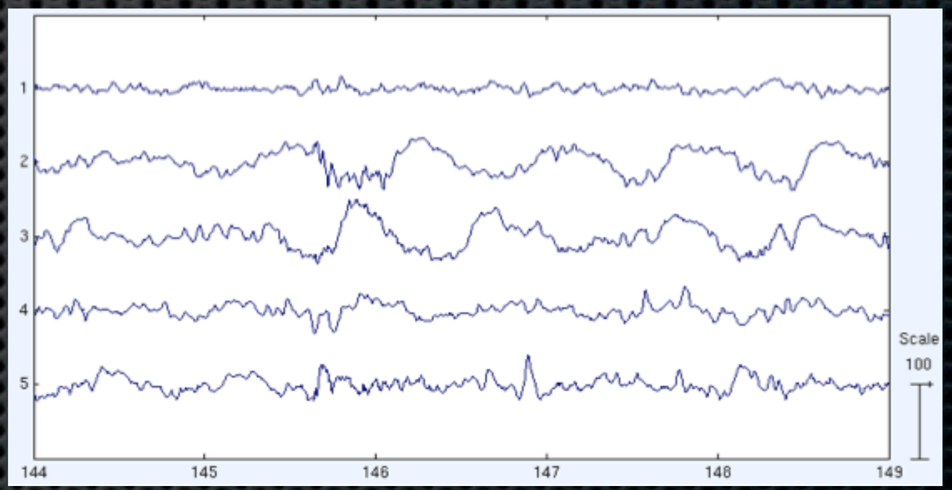
Seizure clusters

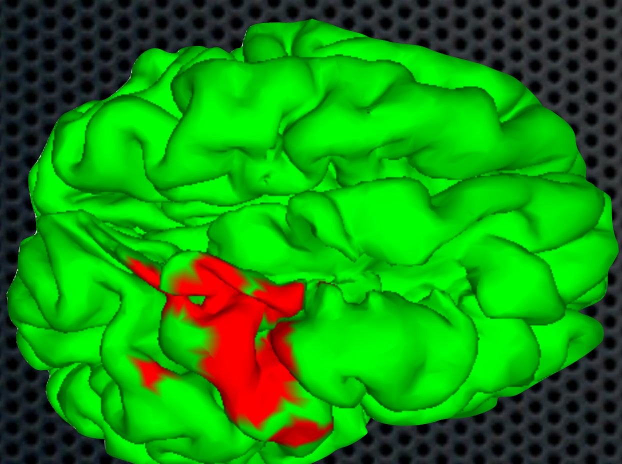
Pre-seizure clusters



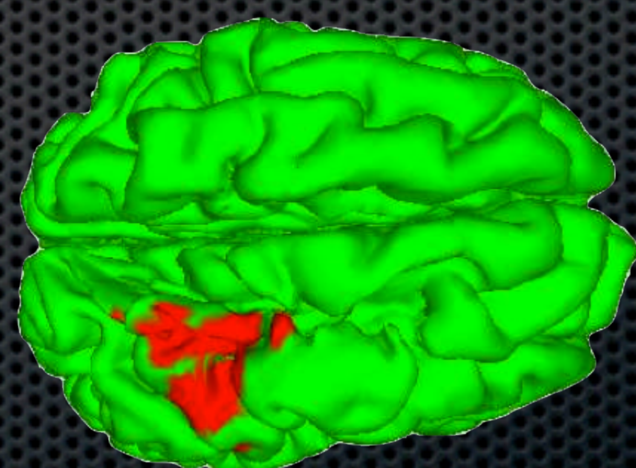
1st cluster

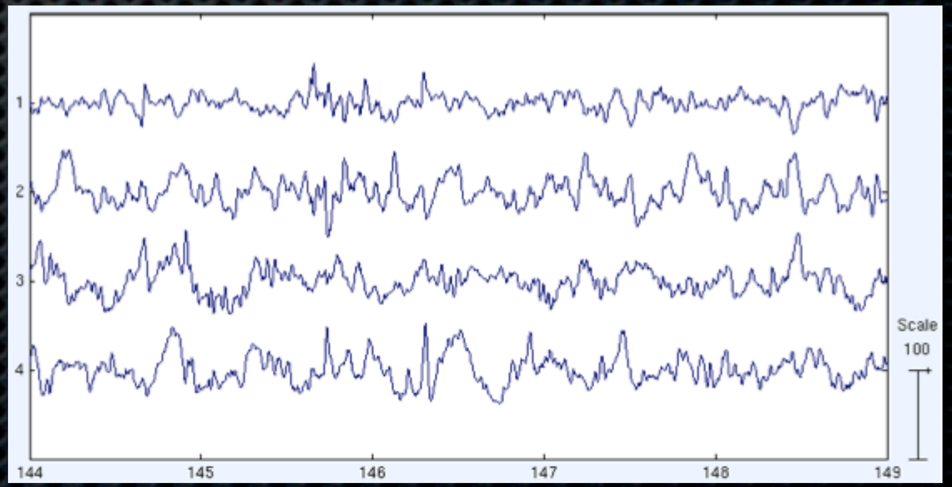






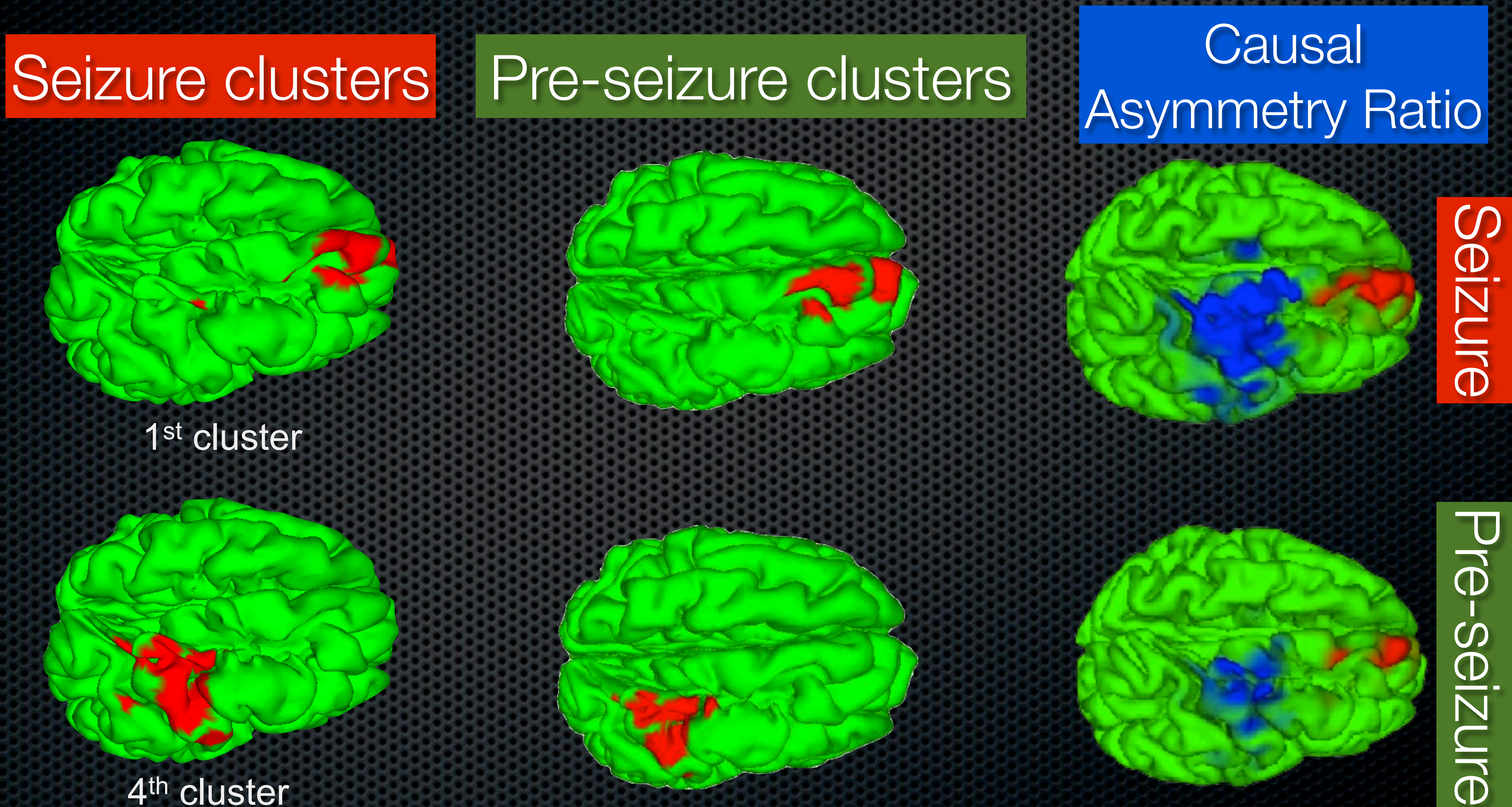
4th cluster





Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

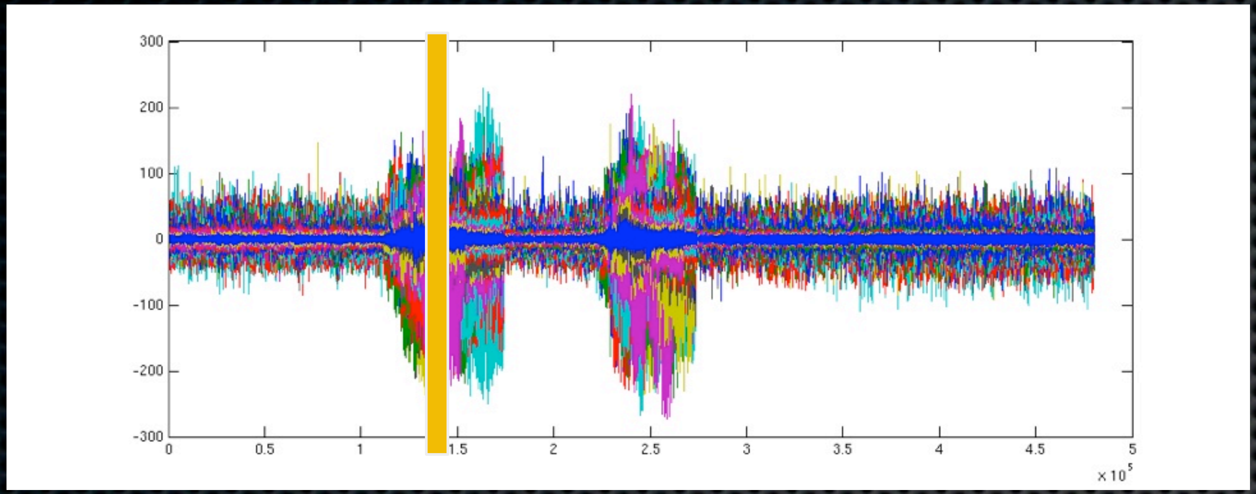
AMICA Dependency Clusters



Akalin Acar, Palmer, et al (2011), *IEEE EMBC*

Mullen, et al (2011) *IEEE EMBC*

AMICA Source Activations



3 seconds data from AMICA model which dominates in second seizure period