The Source Information Flow Toolbox

An Electrophysiological Information Flow Toolbox for EEGLAB



Tim Mullen



15th EEGLAB Workshop June 16, 2012 Tsinghua University, Beijing, China Introduction

Theory				
Functional and Effective Connectivity				
Linear Dynamical Systems and Vector Autoregressive Modeling				
Granger Causality and Related Multivariate Connectivity Measures				
Scalp or Source?				
Adapting to Time-Varying Dynamics				
The Source Information Flow Toolbox (SIFT)				
Some Applications of SIFT				
The Road Ahead				
Fin				

The Dynamic Brain

- A key goal: To measure temporal changes in neural dynamics and information flow that index and predict task-relevant changes in cognitive state and behavior
- Important factors:
 - Accuracy and Validity
 - Temporal Specificity
 - Non-invasive measures



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Categorizations of Large-Scale Brain Connectivity Analysis

(Bullmore and Sporns, *Nature*, 2009)



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Modeling Brain Connectivity

 Model-based approaches mitigate the 'curse of dimensionality' by making some assumptions about the structure, dynamics, or statistics of the system under observation

Box and Draper (1987):

"Essentially, all models are wrong, but some are useful [...] the practical question is how wrong do they have to be to not be useful"

"The map is not the territory"

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Estimating Functional Connectivity

Popular measures

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



Coherence/CC/PLV indicate *functional*, but not *effective* connectivity

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Estimating Effective Connectivity

Non-Invasive

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

- Data-driven
- Rooted in conditional predictability
- Scalable (Valdes-Sosa, 2005)
- Extendable to nonlinear and/or nonstationary 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 timevarying (dynamic) multivariate causal relationships in either the time or frequency domain



Linear Dynamical Systems



time step

Vector Autoregressive (VAR / MAR / MVAR) Modeling



Intro

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VAR Modeling: Assumptions • "Weak" stationarity of the data

"Weak" stationarity of the data

- mean and variance do not change with time
- An EEG trace containing prominent evoked potentials is a classic example of a non-stationary time-series

Stability

- A stable process will not "blow up" (diverge to infinity)
- Importantly, stability implies stationarity

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The Linear Vector Autoregressive (VAR) Model



M x M matrix of (possibly time-varying) model coefficients indicating variable dependencies at lag k

multichannel data k samples in the past

$$\mathbf{A}^{(k)}(t) = \left(\begin{array}{ccc} a_{11}^{(k)}(t) & \dots & a_{1M}^{(k)}(t) \\ \vdots & \ddots & \vdots \\ a_{M1}^{(k)}(t) & \cdots & a_{MM}^{(k)}(t) \end{array}\right)$$

at current time t

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

/AR[p] mode

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Selecting a VAR Model Order

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

 $AIC(p) = 2log(det(V)) + M^2p/N$

Penalizes high model orders (parsimony)

entropy rate (amount of prediction error)





Selecting a VAR Model Order

• Other considerations:

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



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



Granger Causality

- 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)
- 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)

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Granger Causality

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

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

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

Definition 1

- X_j granger-causes X_i conditioned on all other variables in X
- if and only if $A_{ii}(k) >> 0$ for some lag $k \in \{1, ..., p\}$

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Granger Causality Quiz

Example: 2-channel MVAR process of order 1

$$\begin{pmatrix} X_{1}(t) \\ X_{2}(t) \end{pmatrix} = \begin{pmatrix} -0.5 & 0 \\ 0.7 & 0.2 \end{pmatrix} \begin{pmatrix} X_{1}(t-1) \\ X_{2}(t-1) \end{pmatrix} + \begin{pmatrix} E_{1}(t) \\ E_{2}(t) \end{pmatrix}$$

$$\begin{pmatrix} X_{1}(t) = -0.5X_{1}(t-1) + 0X_{2}(t-1) + E_{1}(t) \\ X_{2}(t) = 0.7X_{1}(t-1) + 0.2X_{2}(t-1) + E_{2}(t) \end{pmatrix}$$

Which causal structure does this model correspond to?

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b)

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a) (1

Intro Granger Causality – Frequency Domain Theory

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

Fourier-transforming $\mathbf{A}^{(k)}$ we obtain

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

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

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

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

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

Definition 2

 X_i granger-causes X_i conditioned on all other variables in X if and only if $|\mathbf{A}_{ii}(f)| >> 0$ for some frequency f

leads to PDC

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Scalp or Source?



Volume conduction exists for ECoG too!

(c.f. Whitmer, Worrell, ..., Makeig, Frontiers in Neuro. 2010



Solution? Source Separation

 $I^{(k)}(t)\overline{S(t-k)} + \overline{E(t)}$

S(t) =

Adapting to Non-Stationarity

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

mV

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Adapting to Non-Stationarity

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

Fin

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time

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Fin

Time-Frequency GC

What is a good window length?

- Considerations:
 - Temporal smoothing
 - Local stationarity
 - Sufficient amount of data
 - Process dynamics

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

Too-large windows may not be locally-stationary



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Time-Frequency GC

Consideration: Sufficient data

M = number of variables

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

We have M²p model coefficients to estimate. This requires a minimum of M²p independent samples. So we have the constraint M²p <= N_{tr} W. In practice, however, a better heuristic is M²p <= (1/10)N_{tr} W.

Or: W >= 10(M²p/N_{tr})

10x more data points than parameters to estimate

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

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Time-Frequency GC Consideration: Process dynamics

Consideration: Process dynamics

- Your window must be larger than the maximum expected interaction time lag between any two processes.
- Your window should be large enough to span ~1 cycle of the lowest frequency of interest (remember the Heisenberg uncertainty principle)



Time-Frequency GC • Many ways to do time-varying VAR e

Many ways to do time-varying VAR estimation

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

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Discrete State-Space Model (SSM) for Electrophysiological Dynamics

observation equation (e.g. noisy sensor observations) $y(t) = Hs(t) + \epsilon(t)$

known deterministic inputs u(t)

state transition equation (e.g. latent source and/or coupling dynamics) $s(t) = f(s(t^-), u(t^-), \theta(t)) + v(t)$

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Linear VAR[1] $> s(t) = \mathbf{A}(t)s(t-1) + v(t)$

- Dynamical system may be linear or nonlinear, dense or sparse, non-stationary, highdimensional, partially-observed, and stochastic
- Subsumes discrete Delay Differential Equation (DDE) and Vector Autoregressive (VAR) methods and closely related to Dynamic Causal Modeling (DCM)

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Kalman Filtering

optimal estimator (in terms of minimum variance) for the state of a linear dynamical system



Kalman Filtering

GPDC Causality From



Time (sec)

Intro

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EEGLAB Software framework





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

Theory

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To-Do



Source Information Flow Toolbox (SIFT)

- A toolbox for (source-space) electrophysiological information flow and causality analysis (single- or multi-subject) integrated into the EEGLAB software environment.
- Modular architecture intended to support multiple modeling approaches
- Emphasis on vector autoregression and SSMs and time-frequency domain approaches
- Standard and novel interactive visualization methods for exploratory analysis of connectivity across time, frequency, and spatial location
- **Requirements**: EEGLAB, MATLABTM 2008a+, Signal Processing Toolbox, Statistics Toolbox (for some functions -- may be removed in the future)

Theory

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Preprocessing

Modeling

Statistics

Visualization

Source reconstruction (performed externally using EEGLAB or other toolboxes)
Filtering or Local Detrending
Downsampling
Differencing
Normalization (temporal or ensemble)
Trial balancing



Preprocessing

Modeling

Statistics

Visualization

Pre-processing
Model fitting and validation
Connectivity
Statistics
Visualization

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Statistics

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opt. model order

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Visualization

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Model Fitting

Connectivity

Visualization

Algorithm

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Downdate

▼ Miscellaneous

VerbosityLevel

Unconstrained VAR modeling via Vieira-Morf

[1] A. Schlogl, Comparison of Multivariate

Cancel

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Maximum Entropy algorithm.

References and code:

Help

PlotResults

Algorithm

Vieira-Morf:

Statistics

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opt. model order

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Preprocessing	Modeling	Statistics	Visualization
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To-Do

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Validation

Statistics



Model Fitting

Connectivity







ocessing	Modeling	Stati	stics	Visualization	
Model Fitti	ing Validation	Connectivity			
	VAR-based Measures				
Power spec	Power spectrum (ERSP)				
Coherence (Coh), Partial Coherence (pCoh), Multiple Coherence (mCoh)					
Partial Directed Coherence (PDC)					
Generalized	Generalized PDC (GPDC)				
Partial Direc	ted Coherence Factor	(PDCF)			
Renormalize	ed PDC (rPDC)				
Directed Tra	Insfer Function (DTF)				
Direct Direc ⁻	Direct Directed Transfer Function (dDTF)				
Bivariate Gr	Bivariate Granger-Geweke Causality (GGC)				
Conditional	Conditional GGC				
Blockwise G	Blockwise GGC				
fully	implemented	alpha-testing		comina soon	

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To-Do Apps

Fin

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Validation

Connectivity

Model Fitting

SIFT

Pre-processing	
Model fitting and validation	►
Connectivity	
Statistics	۲
Visualization	►

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PDC: Partial Directed Coherence nPDC: Normalized PDC GPDC: Generalized Partial Directed Coherence PDCF: Partial Directed Coherence Factor RPDC: Renormalized Partial Directed Coherence + GRANGER-GEWEKE CAUSALITY MEASURES GGC: Granger-Geweke Causality + SPECTRAL COHERENCE MEASURES Coh: Complex Coherence iCoh: Imaginary Coherence pCoh: Partial Coherence pCoh: Partial Coherence mCoh: Multiple Coherence + SPECTRAL DENSITY MEASURES S: Complex Spectral Density							
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Statistics

Visualization

Parametric

Non-parametric

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Asymptotic analytic estimates of confidence intervals Applies to: PDC, nPDC, DTF, nDTF, rPDC Tests: Hnull, Hbase, HAB

Confidence intervals using Bayesian smoothing splines Applies to: all Tests: H_{base}, H_{AB}

Phase-randomization

Applies to: all Tests: H_{null}

Bootstrap, Jacknife, Cross-Validation

> Applies to: all Tests: H_{AB}, H_{base}



fully implemented



alpha-testing



coming soon

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Preprocessing

Modeling

Statistics

Visualization

Parametric

Non-parametric

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Miscellaneous Estimator Statistic Alpha VerbosityLevel Statistic Statistic Statistic	Analytic Statistics
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Visualization

Interactive Visualizers



Interactive Time-Frequency Grid

Interactive 3D Causal Brainmovie

Causal Projection Movie

Directed Graphs and Graph Theoretic Analysis (Bioinformatics Toolbox Interface)

and more ...



fully implemented



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coming soon

Interactive Time-Frequency Grid

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Interactive Time-Frequency Grid



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Interactive Causal BrainMovie3D



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BrainMovie3D Control Panel

NodeColorMapping

Specify mapping for node color. This determines how we index into the colormap. Options are as follows. None: node color is not modulated. Outflow: sum connectivity strengths over outgoing edges. Inflow: sum connectivity strengths over incoming edges. CausalFlow: Outflow-Inflow. Asymmetry Ratio: node colors are defined by the equation C = 0.5*(1 + outflow-inflow/(outflow+inflow)). This is 0 for exclusive inflow, 1 for exclusive outflow, and 0.5 for balanced inflow/outflow





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Bioinformatics Toolbox IFace



Interactive Directed Graphs

Radial, Hierarchical, or Customized Node Layout

Graph-Theoretic Analysis (SCCs, Shortest-Path, MaxFlow, etc)

Assignment of useful quantities to Node and Edge size/color



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Group Analysis

Causal/Measure Projection Bayesian Hierarchical Model

Error > Correct (p<0.05, N=24) 3-7 Hz



Mullen, Onton, et al, 2010, HBM, Barcelona Bigdely-Shamlo, Mullen, et al, 2012, *in review*



Thompson, Mullen, Makeig, 2011, ICONXI Thompson, Mullen, Makeig, 2012, *in prep*



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Causal Projection

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

3-7 Hz

dDTF

SIFT

Intro

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Fin



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Causal Projection

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





Mullen, et al, 2010, HBM, Barcelona

Theory Intro

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Bayesian Multi-Subject Inference



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Bayesian Multi Subject Inference



Thompson, Mullen, Makeig, 2011, ICONA Thompson, Mullen, Makeig, 2012, *in prep*

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Simulation

Dynamical System Simulation Workbench

Systems of linear stochastically-forced damped coupled oscillators

Support for arbitrary time-varying (non-stationary) coupling dynamics

Intuitive equation-based scripting environment

Support for generalized gaussian or hyperbolic secant innovations

Nonlinear Dynamical Systems

Rössler and Lorenz Systems

Apps



fully implemented







Simulated Seizure



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Simulated Seizure Sources

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JOOL

Where do I get SIFT?





Some Applications of SIFT

Identification of event-related shifts in effective connectivity which index and predict behavior



Single-trial spatiotemporal modeling of seizure propagation dynamics

To-Do

Brain-Computer Interfaces: Error correction/prediction Neural Prostheses



Mullen et al, HBM, Barcelona, 2010

Some Applications of SIFT

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Apps

To-Do

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Mullen, et al IEEE EMBC, 2011



Some Applications of SIFT



Brain-Computer Interfaces: Error correction/prediction Neural Prostheses





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Theory

Apps

The Road Ahead

- Public release of alpha-testing methods (SIFT 1.0-beta ... being released at <u>sccn.ucsd.edu/wiki/SIFT</u> in the next week)
- Ongoing development of sparse/regularized VAR and state-space models as well as nonlinear SSMs
- Improved Group Analysis and Statistics
- Integration with other toolboxes: Transfer Entropy (TRENTOOL), Dynamic Causal Modeling (SPM), Brain-Computer Interfaces (BCILAB)
- Incorporation of structural constraints on dynamic connectivity (e.g. from DTI, anatomical priors, etc)

Theory

SIF

Apps

To-Do

SIFT

Apps

To-Do

Fin

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