Granger causality: theory and applications to neuroscience data

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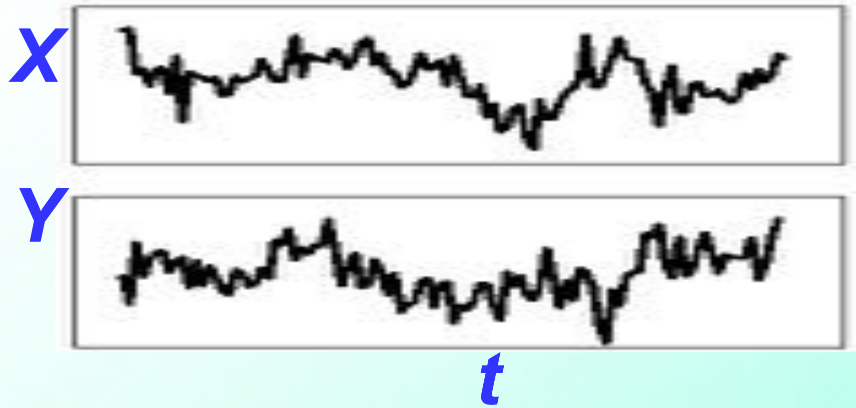
Overview

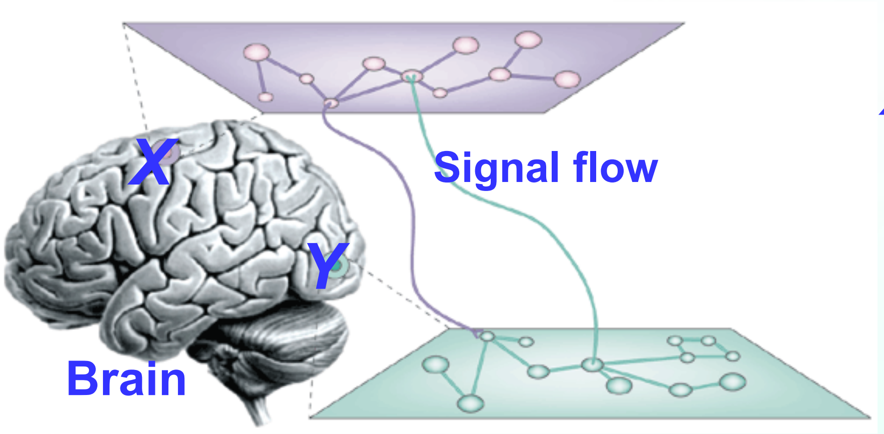
- **Granger Causality (GC):**
  - **Time and frequency domain versions**
- **Estimation approaches:**
  - **Parametric (P) and Nonparametric (NP)**
  - **Validation/demonstration with synthetic data**
  - **P and NP comparisons/limitations**
- **Applications to: LFPs, EEG, iEEG and rfMRI**

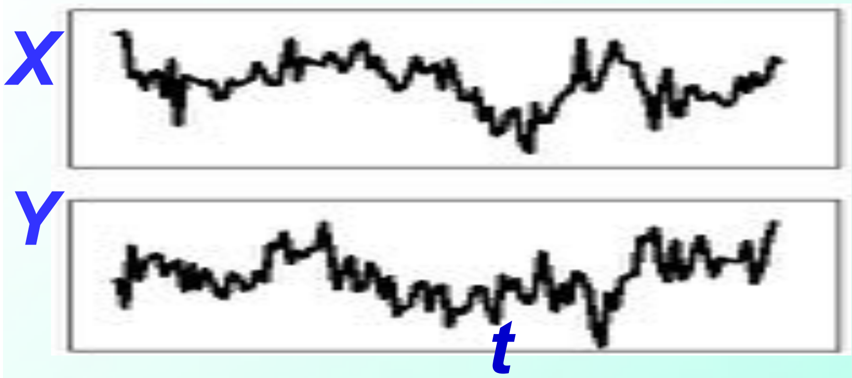


Granger causality: X $\overset{?}{\longleftrightarrow}$ Y

$$F_{Y \to X} = \int M_{Y \to X}(f)\,df$$

Time Series, Oscillations and Spectral Measures





- **Oscillatory features in *X* and *Y*?** ***Power***
- **Interdependence between *X* and *Y*?** ***Coherence***
- **Information flow between *X* and *Y*?**
  Granger Causality
- **In multiple time series, network flow patterns?**
  Granger Causality (Pairwise & Conditional)

Estimation of Spectral Measures

Methods	Spectral Measures
Parametric (Vector Autoregressive, State Space Modeling)	**Power, Coherence, Granger Causality** (Geweke, 1982; 1984; Ding et. al., 2006; Barnett and Seth, 2014; Solo, 2015)
Nonparametric (Fourier & Wavelet Methods)	**Power, Coherence, Granger causality** (Dhamala, et. al., 2008a; 2008b)

Spectral interdependency:

$$M_{x,y} = M_{x \to y} + M_{y \to x} + M_{x.y}$$

$$M_{x,y}(f) = -\ln(1 - C(f))$$

$$F_{Y \to X} = \int M_{Y \to X}(f)\,df$$

(Geweke, 1982; 1984; Dhamala, 2014)

Granger causality:
a subset of spectral interdependency measures

Spectral interdependency: $$\mathrm{M}_{x,y} = \mathrm{M}_{x\to y} + \mathrm{M}_{y\to x} + \mathrm{M}_{x.y}$$

(Geweke, 1982; Hosoya, 1991)

$$M_{x,y}(f) = -\ln(1 - C(f))$$

$$C(f) = \frac{|S_{xy}(f)|^2}{S_{xx}(f)S_{yy}(f)}$$

$$S(f) = H(f)\Sigma H^*(f)$$

$$M_{y\to x}(f) = -\ln \frac{S_{xx}(f) - \left(\Sigma_{yy} - \frac{\Sigma_{xy}^2}{\Sigma_{xx}}\right)|H_{xy}(f)|^2}{S_{xx}(f)}$$

Encyclopedia of Computational Neuroscience
DOI 10.1007/978-1-4614-7320-6_420-1

Spectral Interdependency Methods

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Who is Granger?

"Rebel Without a Causal Model"

C. W. J. Granger

2003 Nobel Laureate

in Economics

(1934 – 2009)

Concept of Granger Causality

- **For two simultaneously measured time series, the first series is called causal to the second series if the second series can be predicted better by using the knowledge of the first one (Wiener, 1956).**

Wiener (1894-1964)

On Causality and the Brain

In the study of brain waves we may be able to obtain electroencephalograms more or less corresponding to electrical activity in different parts of the brain. **Here the study of the coefficients of causality running both ways and of their analogues for sets of more than two functions (*two processes*) may be useful in determining what part of the brain is driving what other part of the brain *in its normal activity*.**

Norbert Wiener, The Theory of Prediction, 1956

Granger Causality: Statistical Definition

- **Given:**

$$X: \quad x_1, x_2, \ldots, x_n, \ldots$$

$$Y: \quad y_1, y_2, \ldots, y_n, \ldots$$

Clive J. Granger
2003 Nobel Laureate
Economics

- **Linear Prediction Models:**

Model 1: $x_n = a_1 x_{n-1} + \ldots + a_m x_{n-m} + \ldots + e_x$

Model 2: $x_n = b_1 x_{n-1} + \ldots + b_k x_{n-k} + \ldots$

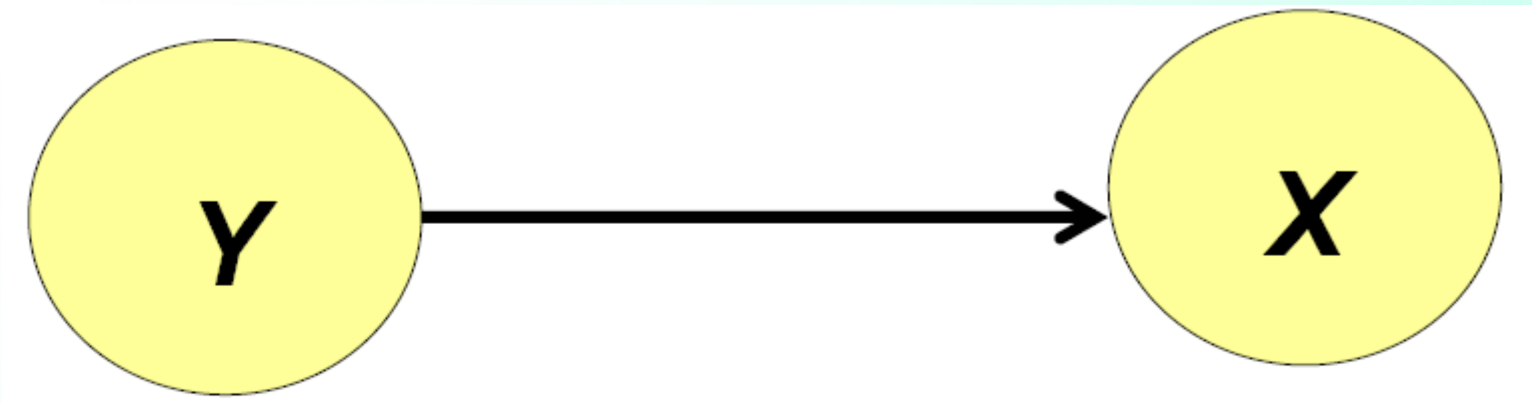
$$+ c_1 y_{n-1} + \ldots + c_k y_{n-k} + \ldots + e_{x|y}$$

- **Granger Causality (1969):**

If $var(e_{x|y}) < var(e_x)$, then
Y is said to exert a causal influence on X.

Granger Causality: Representation

Granger causality from *Y* to *X*: $F_{Y \to X}$



$F_{Y \to X}$ = log (var(e_x)/var($e_{x|y}$))

(time-domain Granger causality (GC))

Granger Causality: Spectral Version
(often referred as Granger-Geweke causality (GGC))

- **Geweke (1982) introduced a spectral representation of time-domain Granger causality:**

John Geweke
Univ of Iowa

$$F_{Y \to X} = \frac{1}{2\pi} \int I_{Y \to X}(f)\, df$$

where $I_{Y \to X}(f)$ **is Granger causality spectra.**

- **Statistical meaning:** spectral decomposition

total *power* = *intrinsic power* + *causal power*

I = log (total power/intrinsic power)

Granger Causality: Parametric Estimation

- **Given:** $\mathbf{X}(t) \equiv [x_1(t), x_2(t), \ldots, x_M(t)]^T$
- **Multivariate Autoregressive Models:**

time domain

$$\sum_{k=0}^{p} \mathbf{B}_k \mathbf{X}(t-k) = \mathbf{E}(t); \qquad \mathbf{E}(t) \equiv N(0, \Sigma)$$

frequency domain

$$\mathbf{X}(f) = \mathbf{H}(f)\mathbf{E}(f) \quad ; \quad \mathbf{H}(f) = \left(\sum_{k=0}^{p} \mathbf{B}_k \, e^{-ik2\pi f} \right)^{-1}$$

- **Spectral density matrix:**

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

Granger Causality: Parametric Estimation (cont'd)

- **Spectral matrix:** $$S(f) = \begin{pmatrix} S_{11}(f) & \cdots & S_{1M}(f) \\ \cdots & \cdots & \cdots \\ S_{M1}(f) & \cdots & S_{MM}(f) \end{pmatrix}$$

- **Power: diagonal terms**

- **Coherence spectra: normalized magnitude of off-diagonal terms**

- **Granger causality:**

$$I_{2\to 1}(f) = \ln \frac{S_{11}(f)}{S_{11}(f) - (\Sigma_{22} - \Sigma_{12}^{2} / \Sigma_{11}) \, | H_{12}(f) |^{2}}$$

(H and Σ needed)

Nonparametric Methods

- **Fourier and wavelet methods are first used to estimate the spectral density** *($S_{lm}(f) = \langle X_l(f) X_m(f)^* \rangle$)*:

$$S(f) = \begin{pmatrix} S_{11}(f) & \cdots & S_{1M}(f) \\ \cdots & \cdots & \cdots \\ S_{M1}(f) & \cdots & S_{MM}(f) \end{pmatrix}$$

- **We need *H* and Σ to calculate Granger causality**

Granger Causality: Nonparametric Estimation

- **Spectral density matrix factorization** (Wiener and Masani 1957; Wilson 1972):

$$S = \Psi\Psi^* \quad \text{where} \quad \Psi = \sum_{k=0}^{\infty} A_k e^{ik2\pi f}$$

- **Derivation of *H* and Σ:**

$$H = \Psi A_0^{-1} \; ; \; \Sigma = A_0 A_0^T \quad \text{such that} \quad \Psi\Psi^* = H\Sigma H^*$$

- **Granger causality:**

$$I_{2\to1}(f) = \ln \frac{S_{11}(f)}{S_{11}(f) - (\Sigma_{22} - \Sigma_{12}^2/\Sigma_{11})|H_{12}(f)|^2}$$ (frequency domain)

$$F_{2\to1} = (2\pi)^{-1} \int I_{2\to1}(f)\, df$$ (time domain)

(Dhamala, et. al., PRL 2008; NeuroImage, 2008)

Demonstrations with Simulated Time Series

Fourier Transform-Based Granger Causality

- **Model System:**

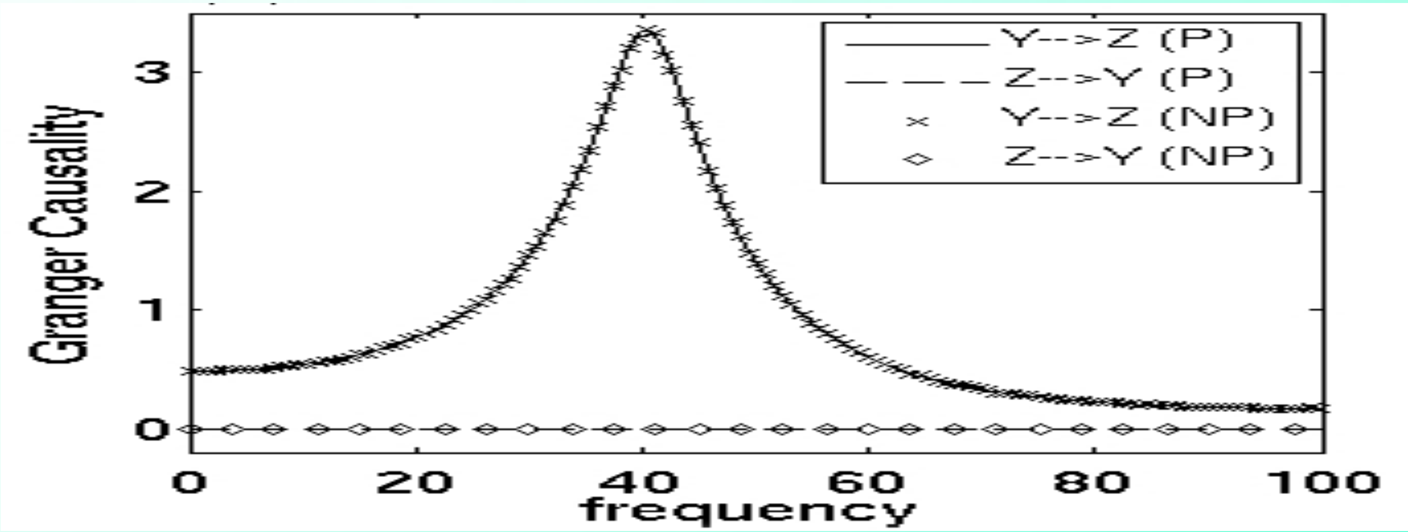
$$Y(t) = 0.53\,Y(t-1) - 0.8\,Y(t-2) + \xi(t)$$

$$Z(t) = 0.5\,Z(t-1) - 0.2\,Z(t-2) + 0.5\,Y(t-1) + \varepsilon(t)$$

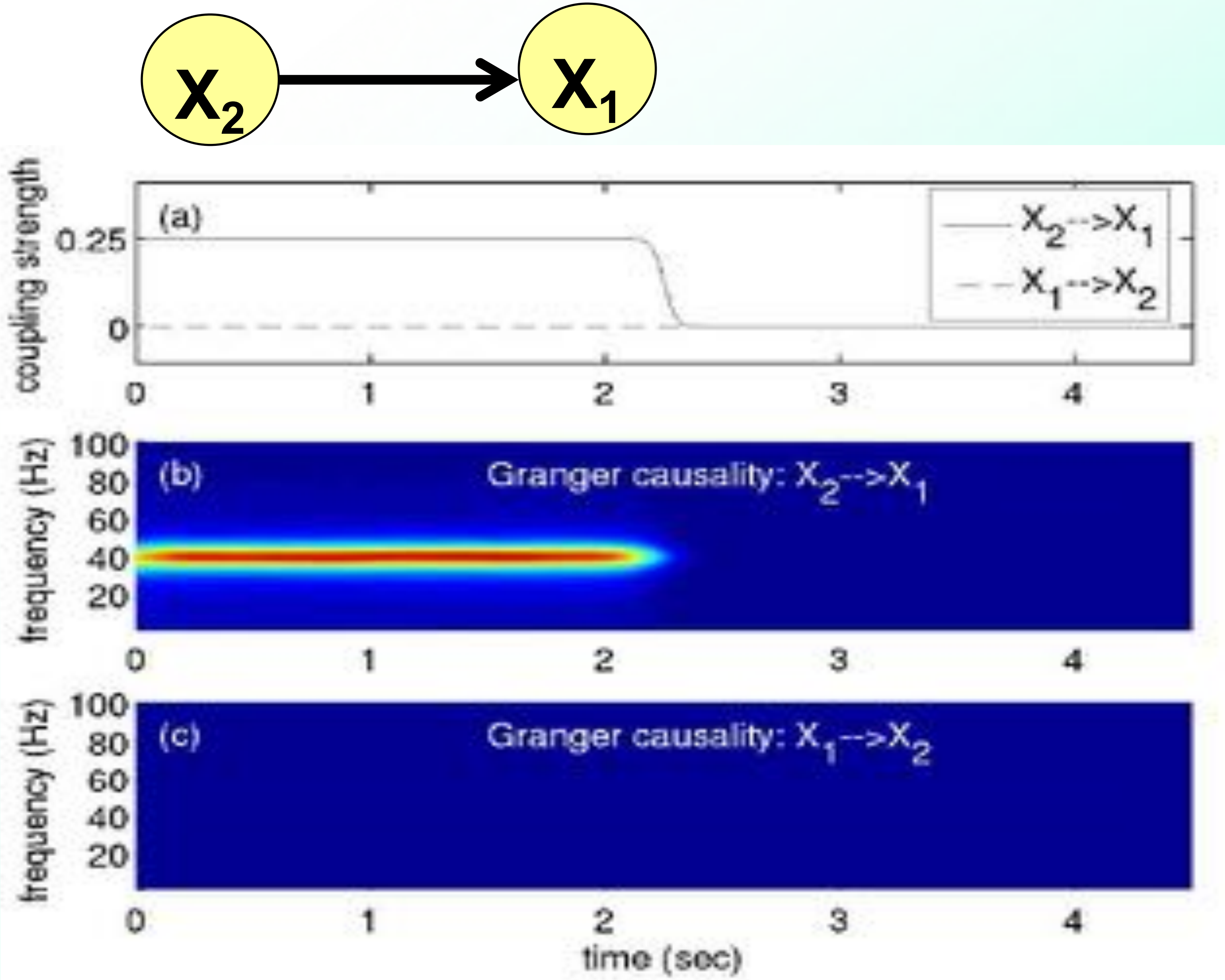
Power and Coherence spectra have peaks at 40 Hz

(considering f_s = 200 Hz).

- **Causality Spectra:**



Wavelet Transform-Based Granger Causality



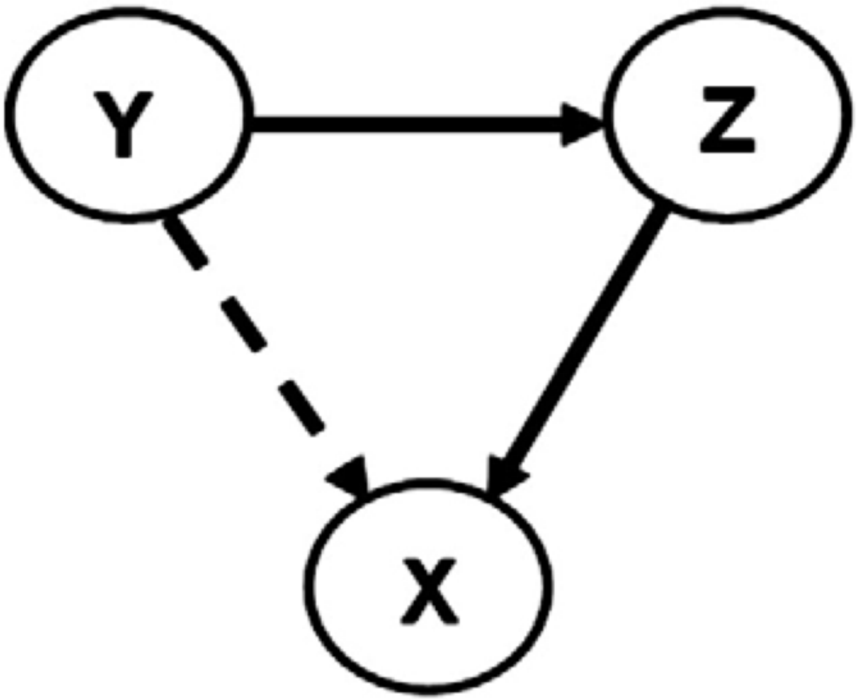
Conditional (Multivariate) Granger causality and its demonstrations with simulated data

Conditional Causality: direct or indirect?

Conditional causality:

$$F_{Y \to X|Z} = \ln \frac{\Sigma_{xx}(X,Z)}{\Sigma_{xx}(X,Y,Z)}$$

$$I_{Y \to X|Z}(f) = \ln \frac{\mathrm{var}(x_t)}{|Q_{xx}(f)\hat{\Sigma}_{xx}Q_{xx}(f)^*|}$$

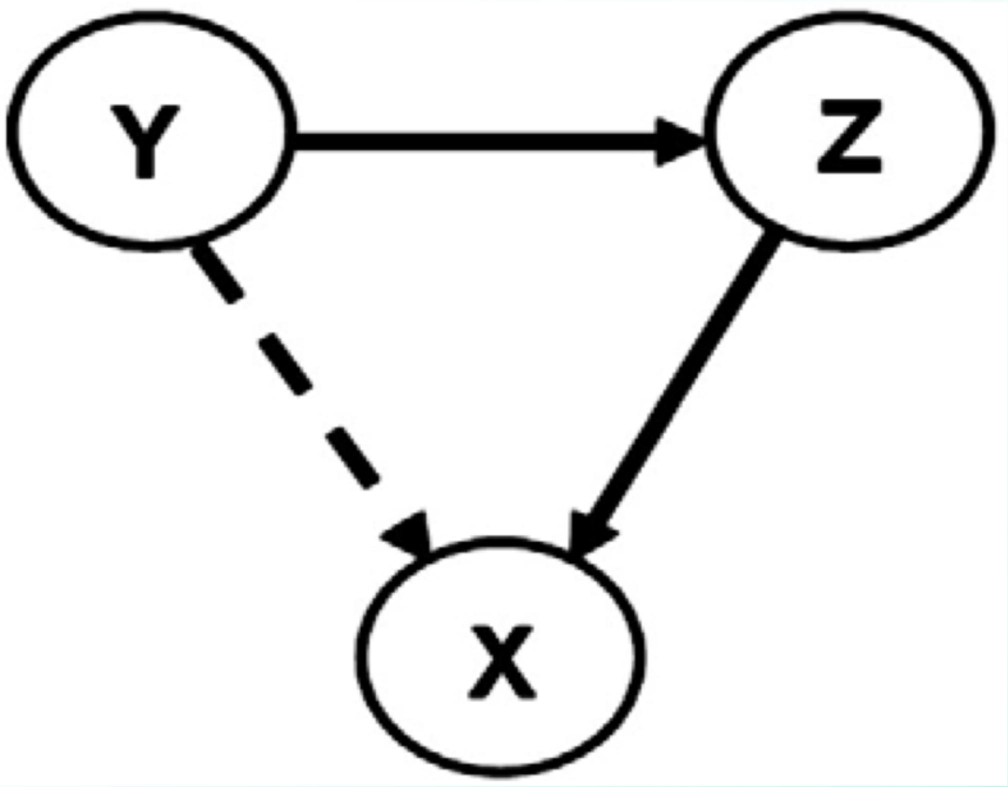


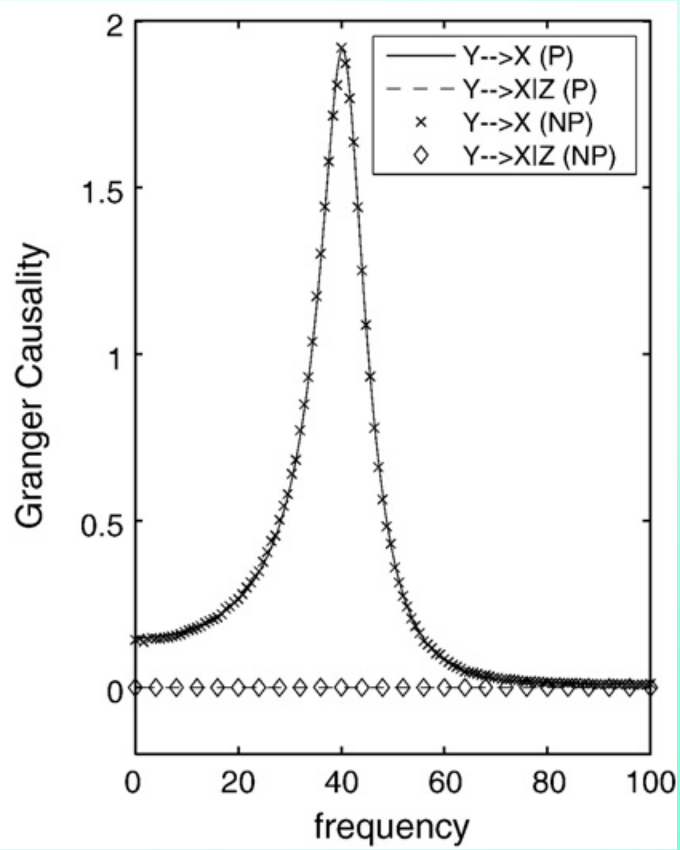
$$\mathbf{F}_{Y \to X|Z} = \mathbf{F}_{YZ \to X} - \mathbf{F}_{z \to x}$$
$$= \mathbf{F}_{YZ^* \to X^*}$$

Y indirectly influences X

(Geweke,1984)

Example 1: Conditional Granger causality





Y indirectly influences X

(Dhamala, et. al., NeuroImage, 2008)

Example 2: Conditional Granger causality

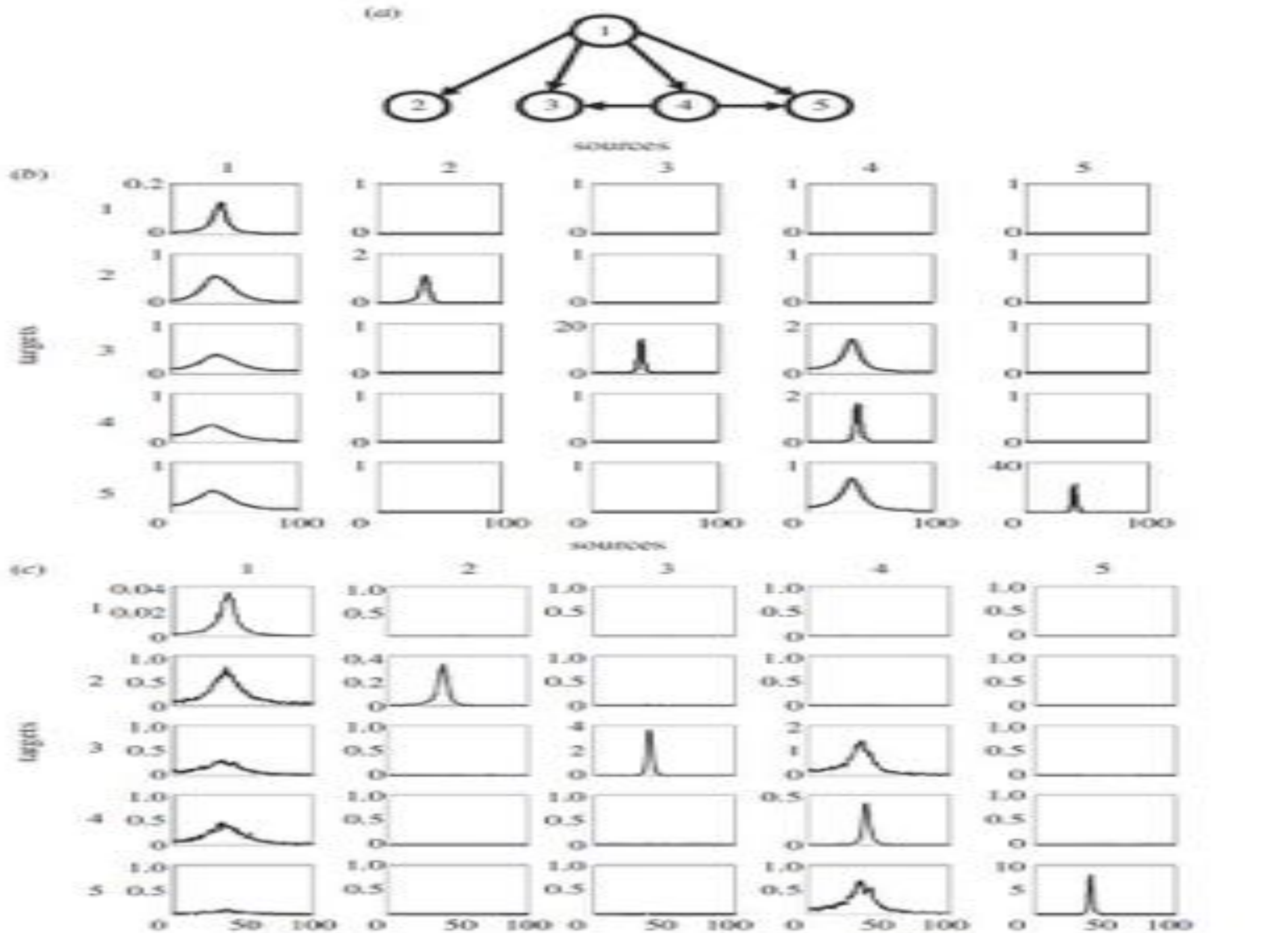
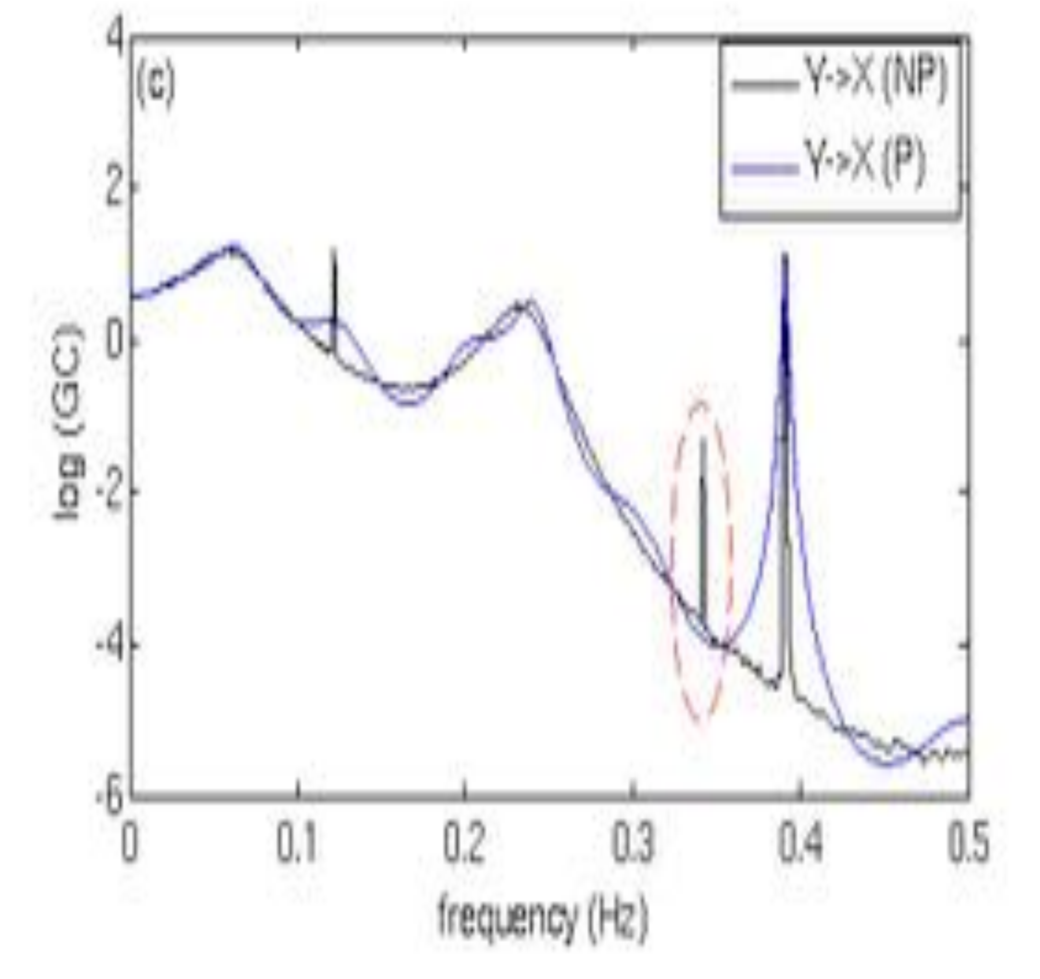


Figure 2. Simulation example 2. (a) Schematic of the network topology, (b) power and conditional Granger causality results from a multivariate parametric analysis and (c) results from a non-parametric analysis.

(Wen, et. al., Phil. Trans. R. Soc. A, 2013)

Parametric Approach: difficulty and limitation

- **Uncertainty in model order selection**
- **Sharp oscillatory spectral features often not captured**

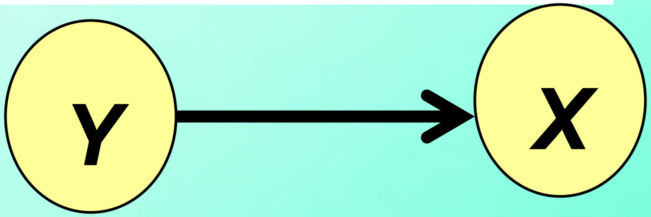


$$y_t = \sum_{k=1}^{4} a_k y_{t-k} + \varepsilon_t$$

$$Y_t = y_t + \sum_{k=1}^{3} A_k \sin(2\pi f_k t + \phi_k)$$

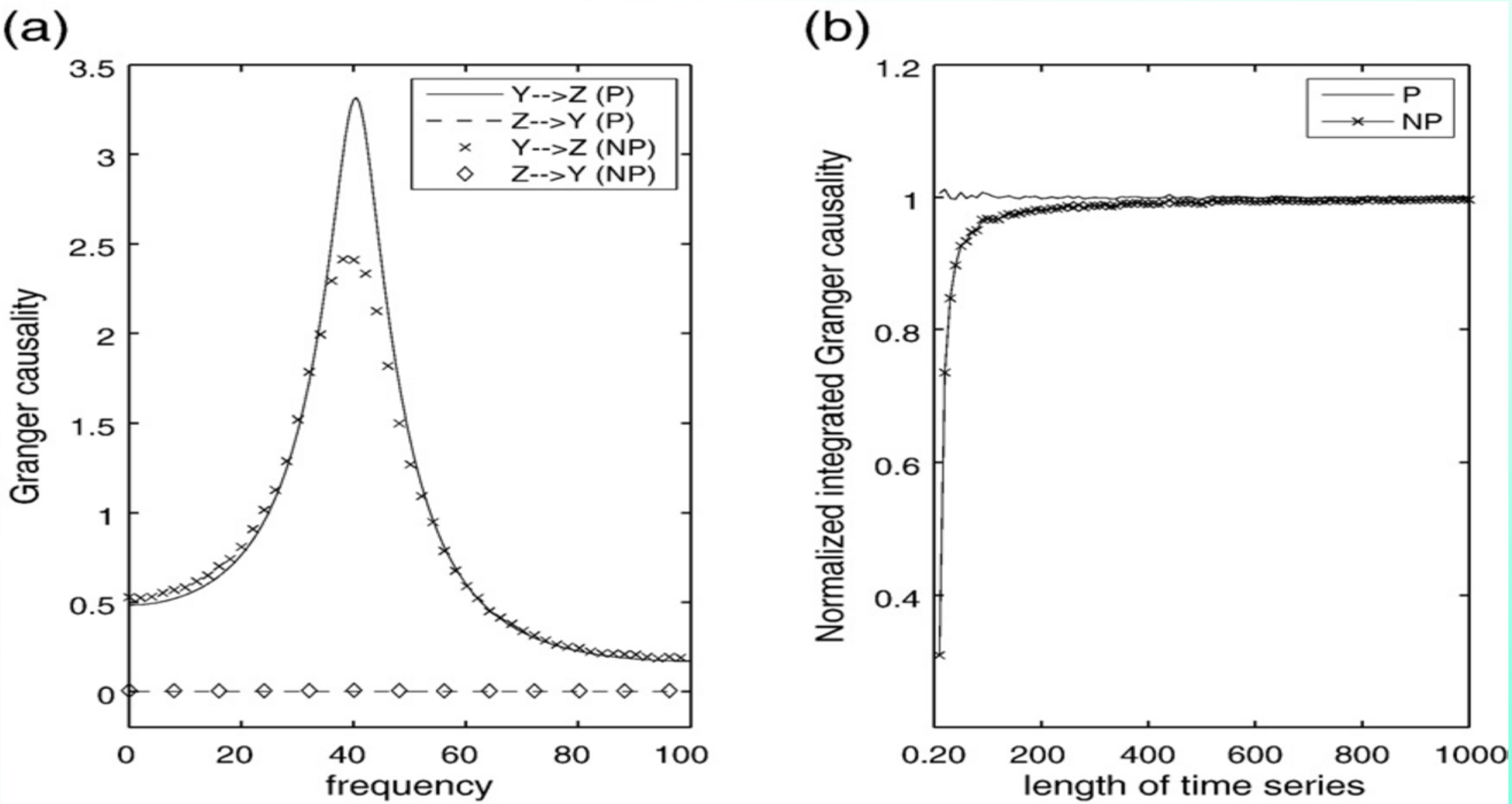
$f_k = (0.122, 0.391, 0.342)$

$$X_t = \sum_{k=1}^{4} a_k X_{t-k} + cY_{t-1} + \eta_t$$



(Dhamala, et. al., NeuroImage, 2008)

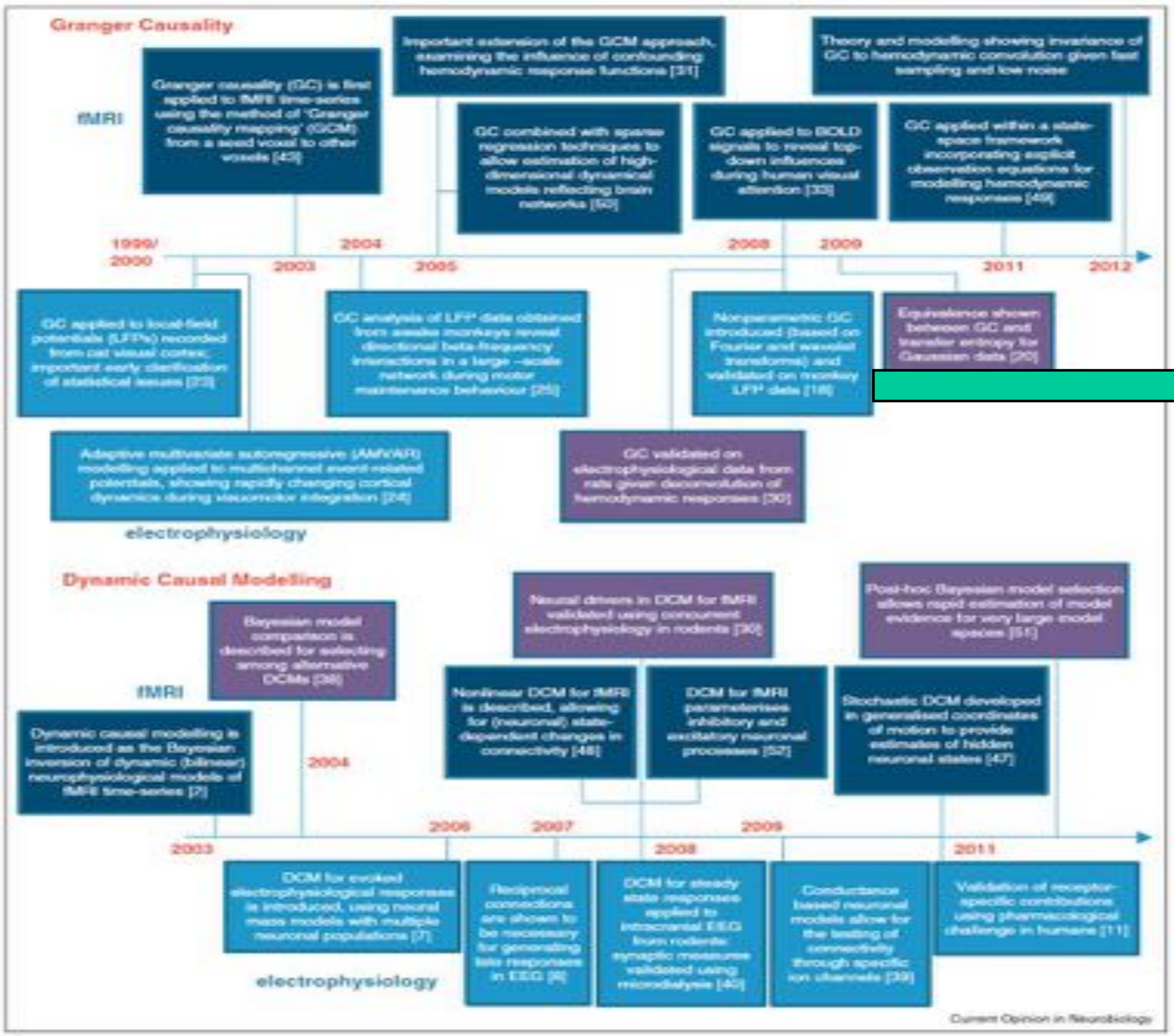
Nonparametric Approach: limitation



- **Effect of data length**

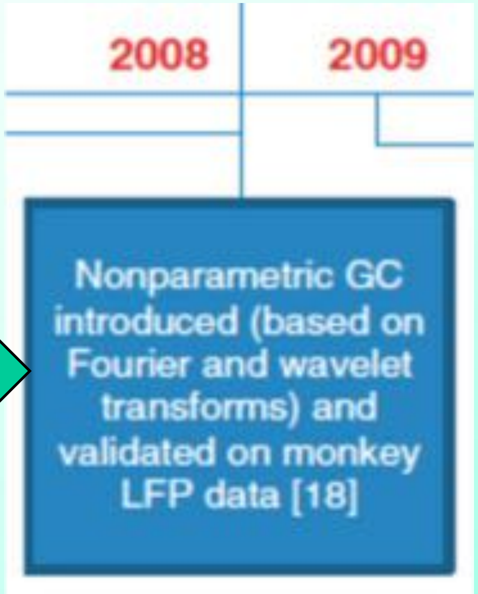
  short data: lower estimates, but correct directions

Granger Causality in neuroscience



A timeline of recent advances in Granger causality (top panel) and dynamic causal modelling (bottom panel). Entries above the time lines pertain to functional magnetic resonance imaging (fMRI) and those below the lines report specific developments for electrophysiology.

Current Opinion in Neurobiology 2013, 23:172–178 www.sciencedirect.com



18. Dhamala M, Rangarajan G, Ding M: **Analyzing information flow in brain networks with nonparametric Granger causality.** *Neuroimage* 2008, **41**:354-362.

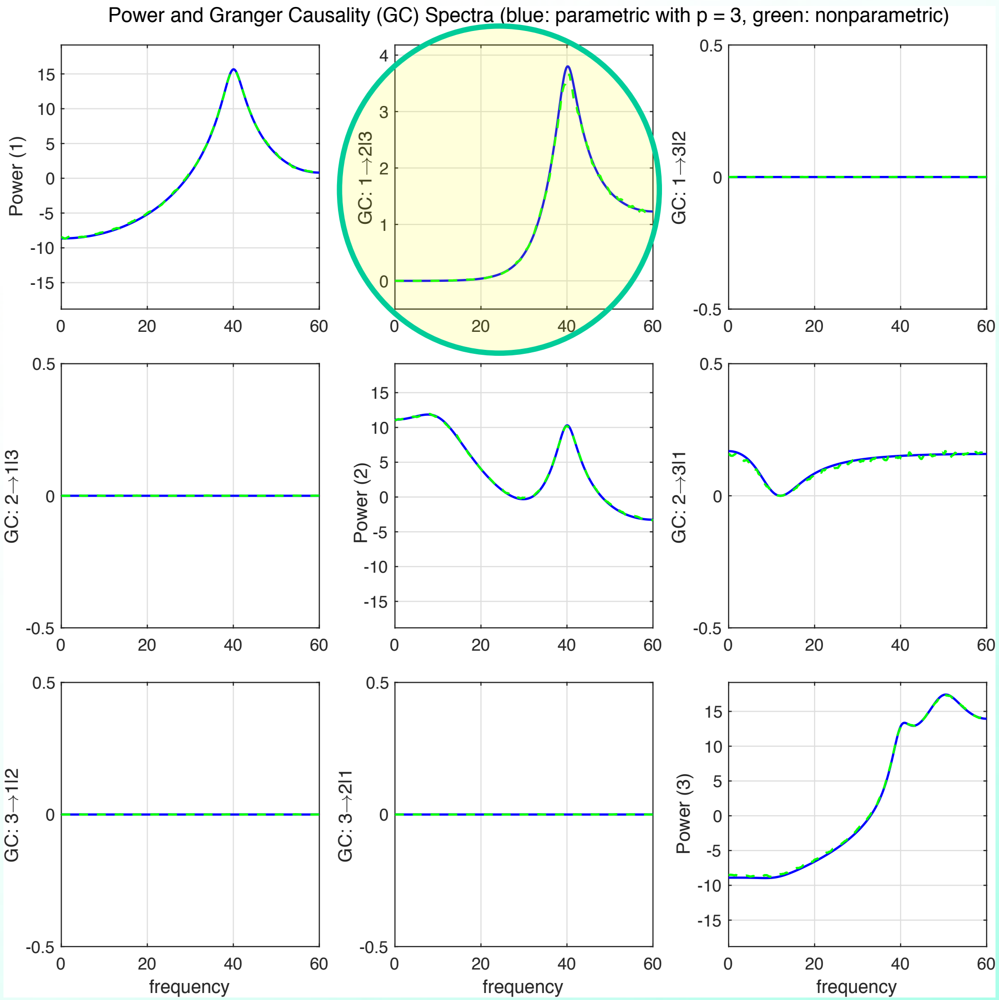
2014: State-space approach to Granger causality

(Barnett and Seth, 2014)

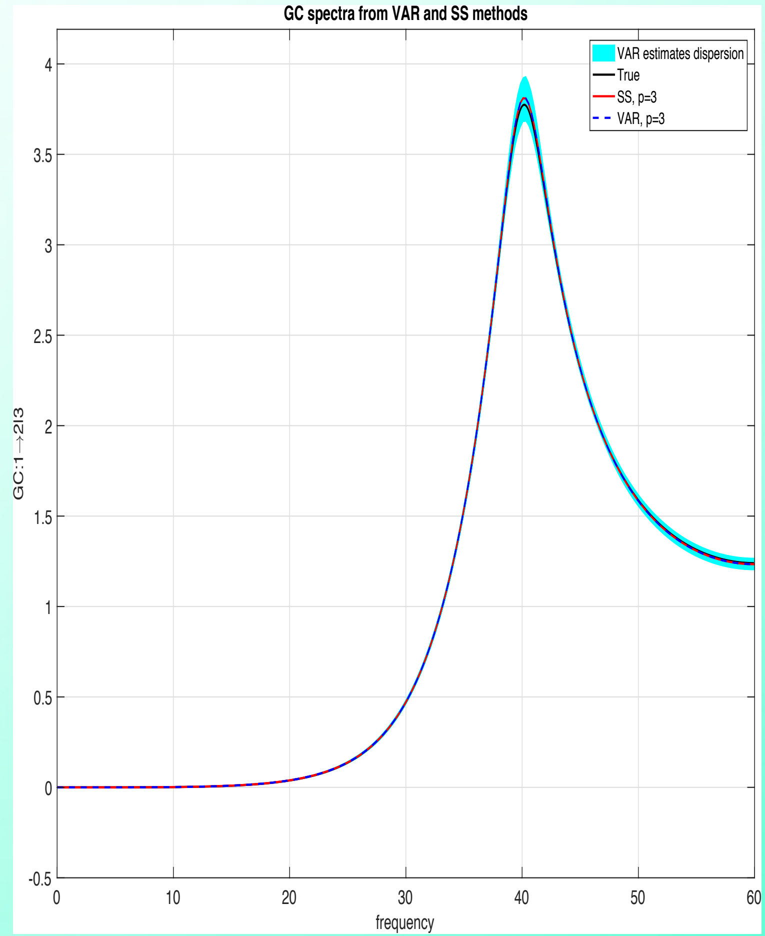
(Friston, Moran, Seth, Current Opinion in Neurobiology, 2013)

Granger-Geweke causality (GGC) problematic? No!

- PNAS article by Stokes and Purdon, 2017
- Commentaries by (i) Barnett et al., (ii) Faes et al., and (iii) reply by Stokes and Purdon, 2017



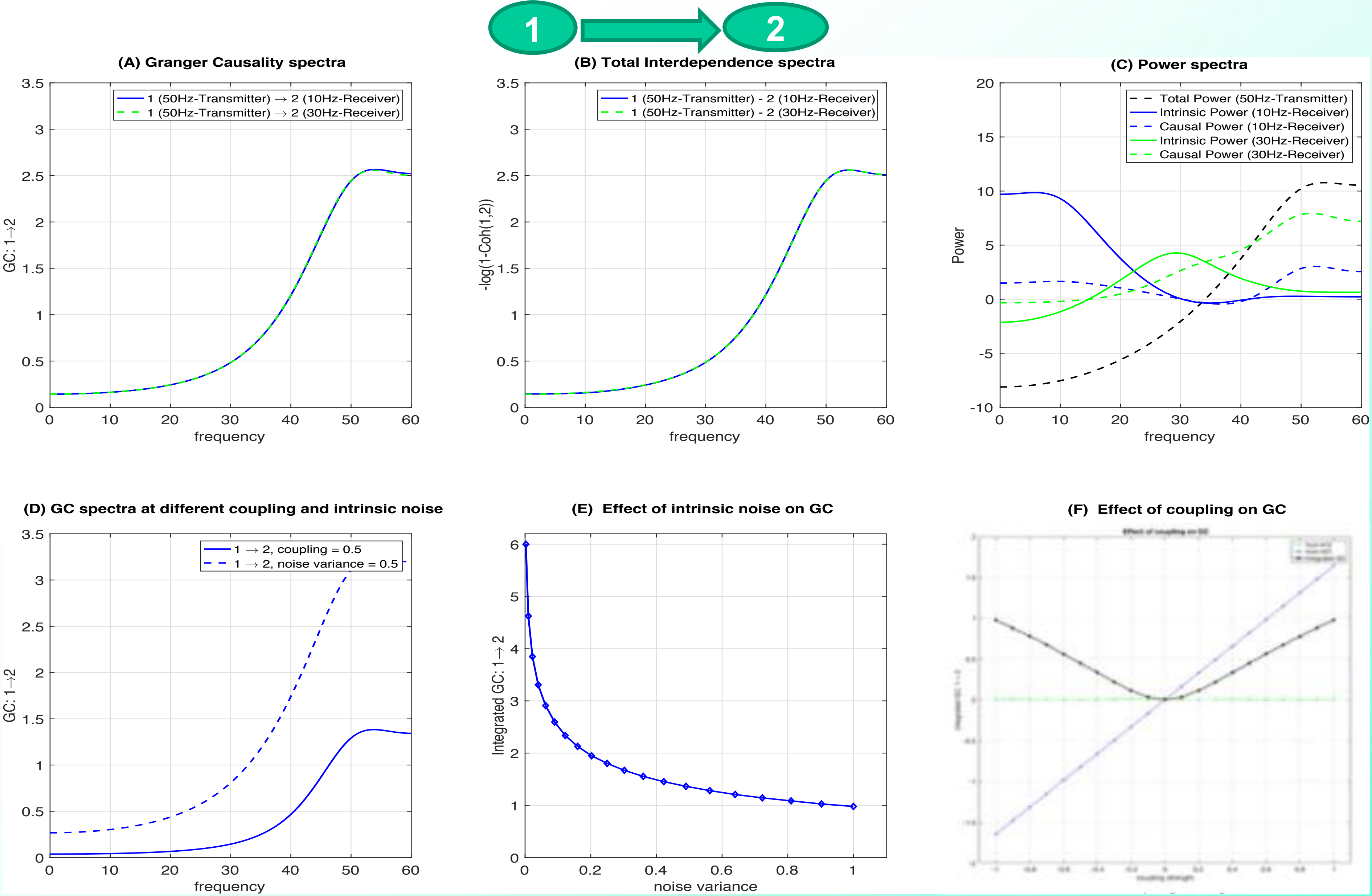
Excellent agreement between VAR and SS!



Parametric (VAR) and Nonparametric Methods

Parametric: VAR and SS

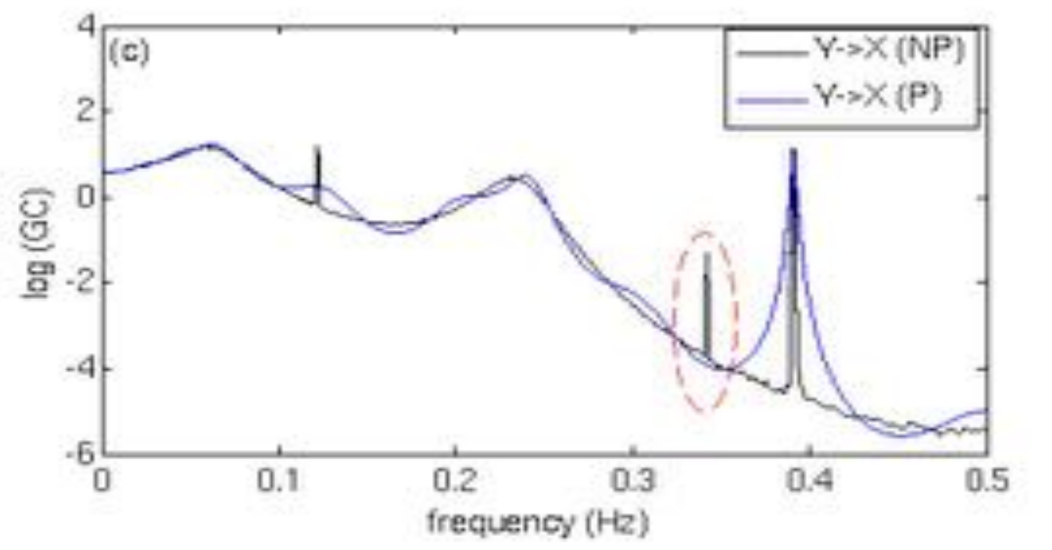
(Dhamala, et al., *NeuroImage*, 2018; includes codes)



- ❖ GGC consistent with other interdependency measures **(not problematic at all!)**
- ❖ GGC definition allows for intrinsic and causal power estimation
- ❖ GGC depends on intrinsic noise and coupling strength

(Dhamala, et al., *NeuroImage*, 2018; includes codes)

Parametric and Nonparametric Methods on Sinusoidal Driving



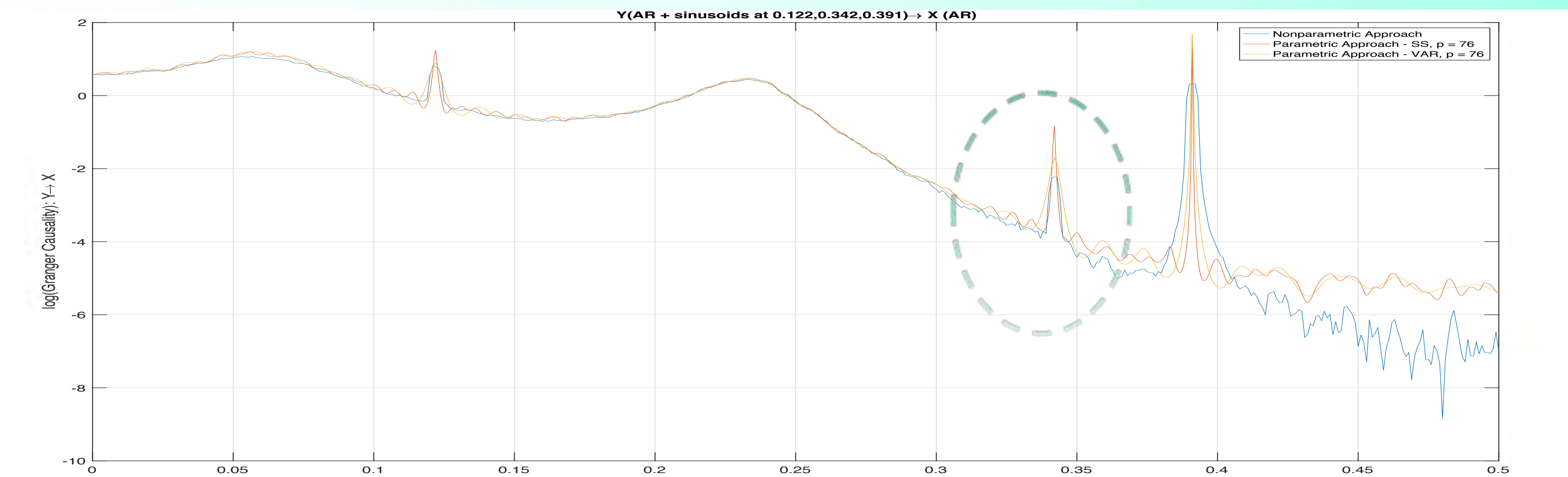
$$y_t = \sum_{k=1} a_k y_{t-k} + \varepsilon_t$$

$$Y_t = y_t + \sum_{k=1}^{3} A_k \sin(2\pi f_k t + \phi_k)$$

f_k = (0.122, 0.342, 0.391)

$$X_t = \sum_{k=1}^{4} a_k X_{t-k} + cY_{t-1} + \eta_t$$

(Dhamala, et. al., NeuroImage, 2008)

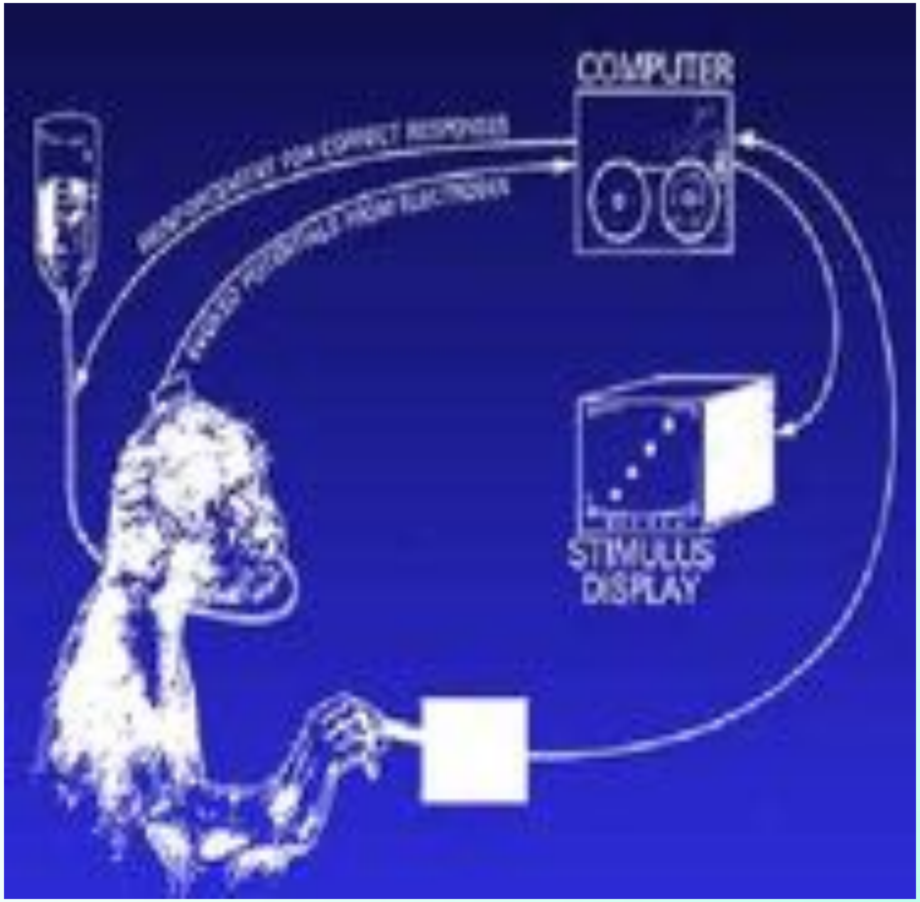


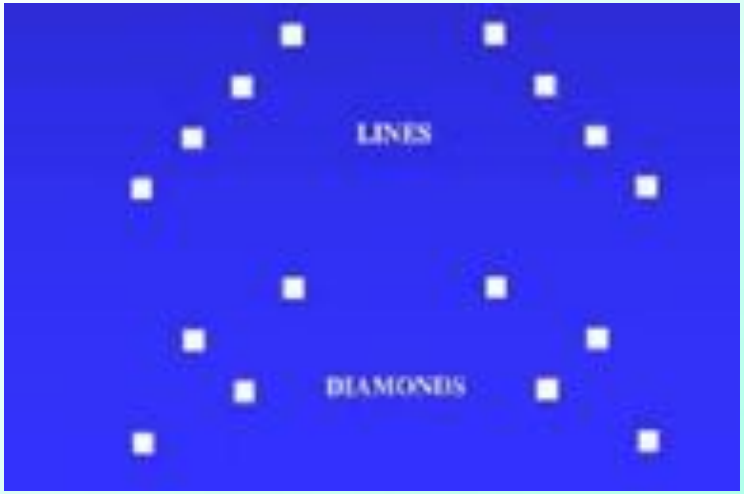
❖ **The nonparametric approach works better in recovering complex spectral features!**

Application to Local Field Potentials (Monkeys)

(Bressler, et. al. 1993; Brovelli, et. al. 2004; Dhamala, et ., 2008)

Experiment: Sensorimotor Task with Go/No-Go

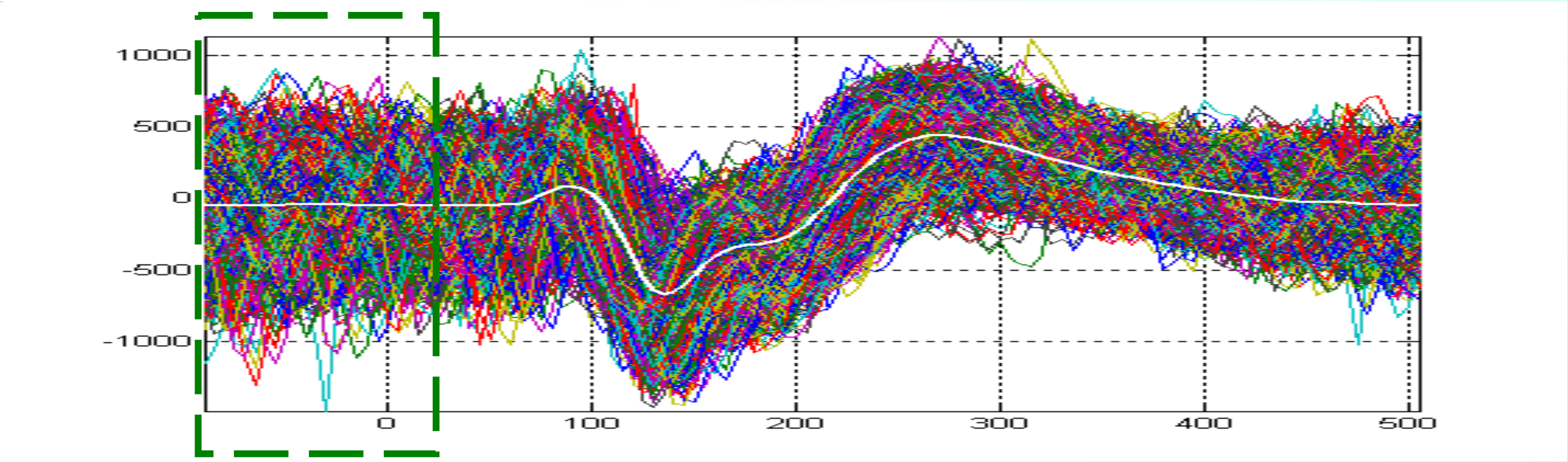




- **Subject depressed a hand lever**
- **Released for Go-stimuli**

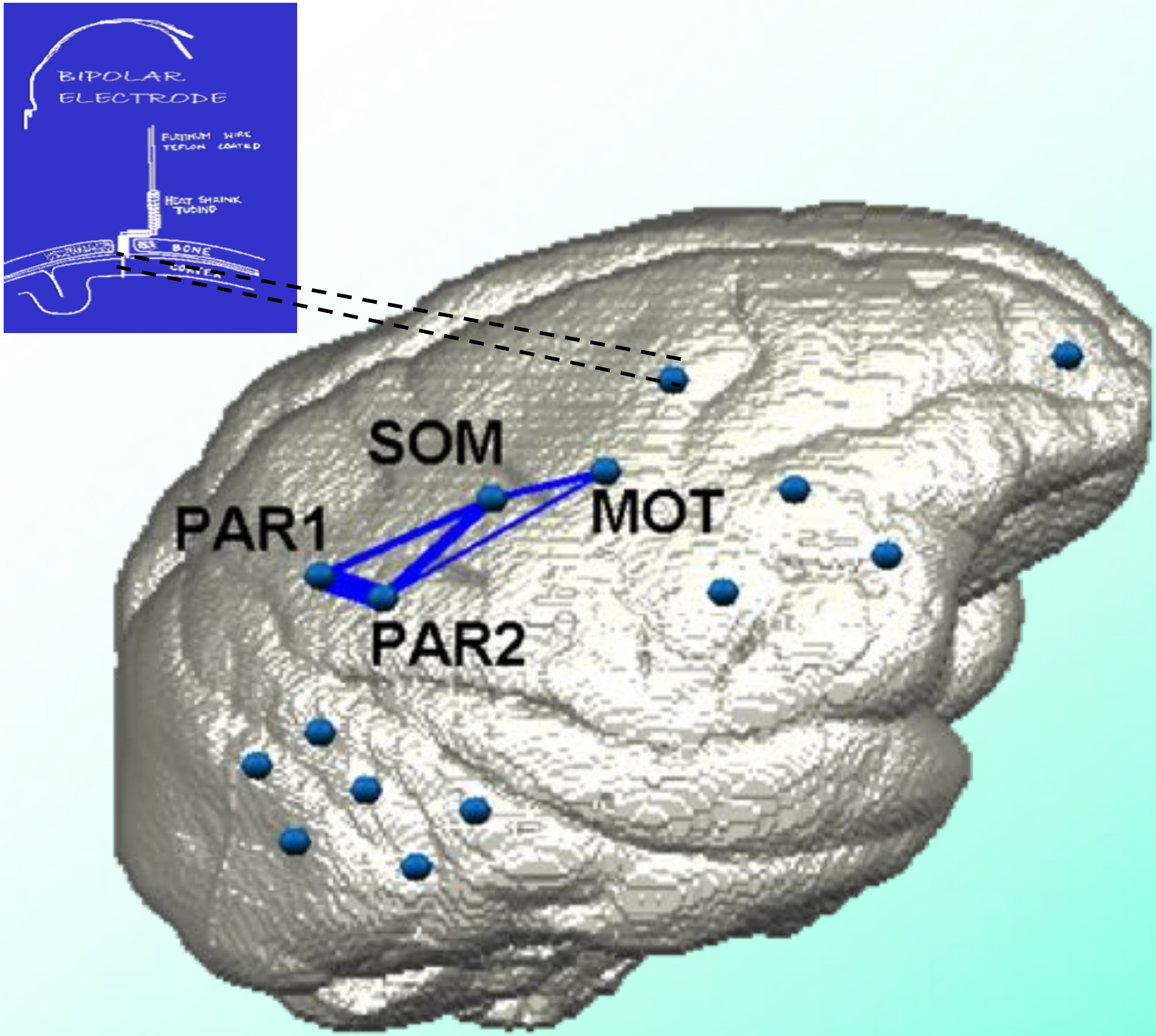
Experiments conducted by Dr. Nakamura at NIMH (Bressler, et.al. 1993; Brovelli, et. al. 2004)

Network Analysis Segment of LFPs



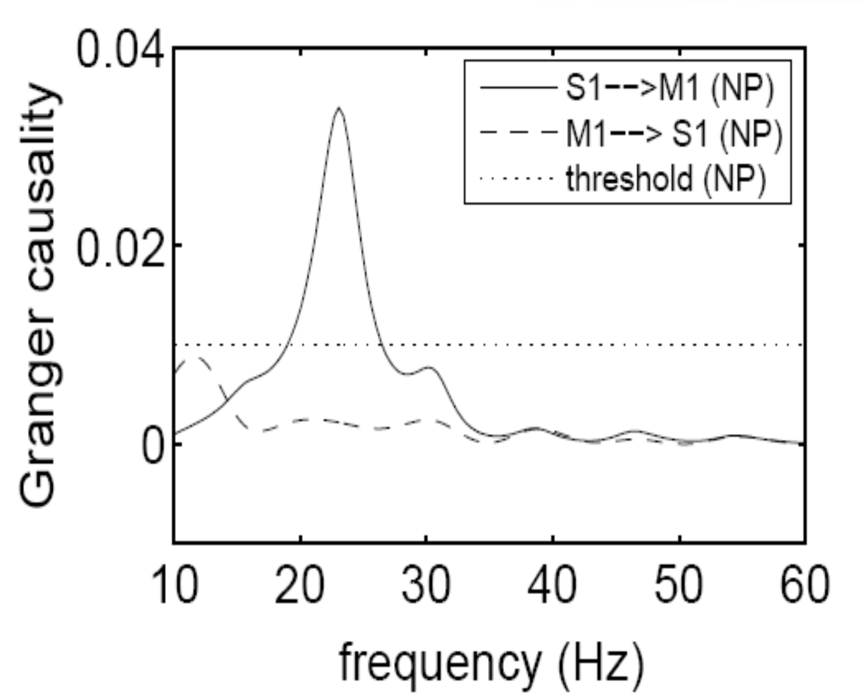
- <u>-100 to 20 ms</u> = Network Analysis Segment during which hand pressure on the lever was maintained

Sensorimotor Beta (14 – 30 Hz) Network



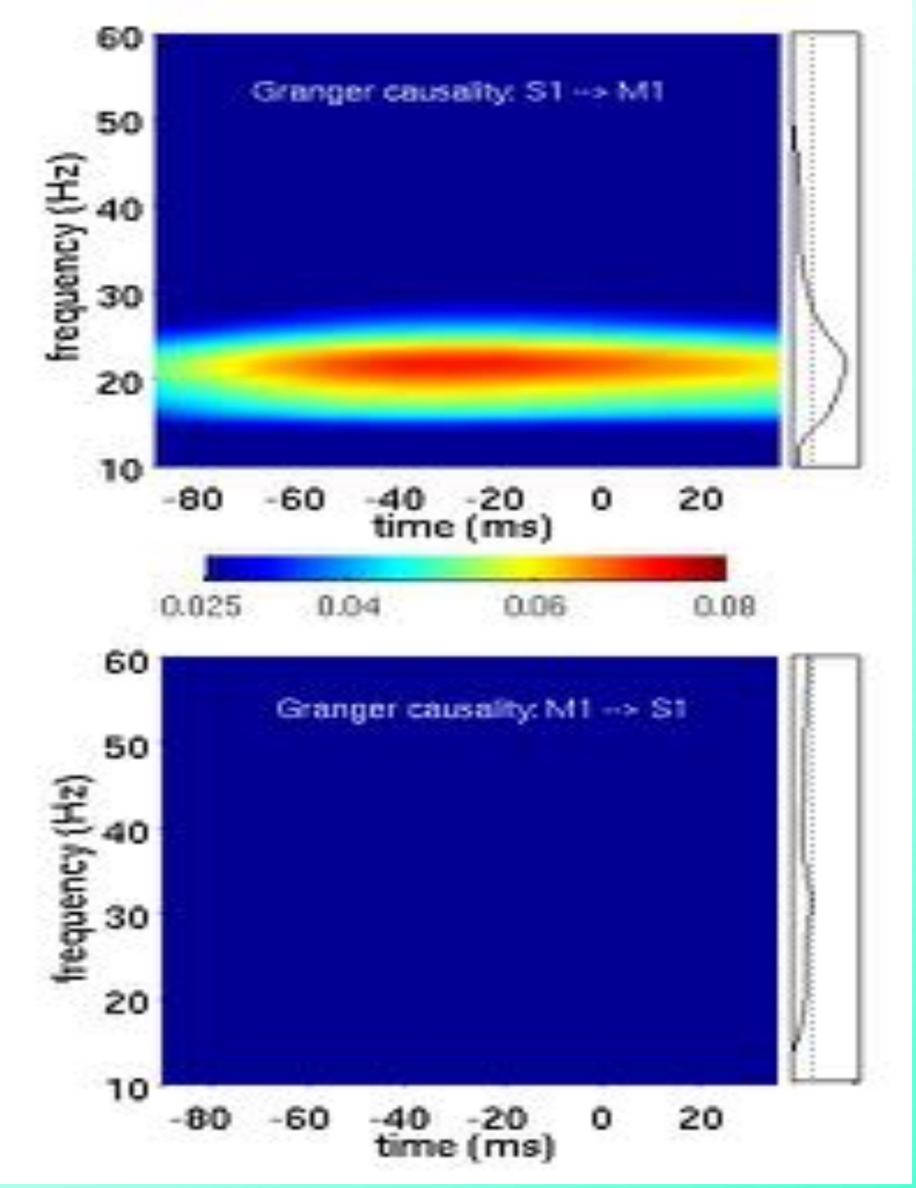
(Brovelli, et. al. 2004)

Nonparametric Granger Causality Spectra



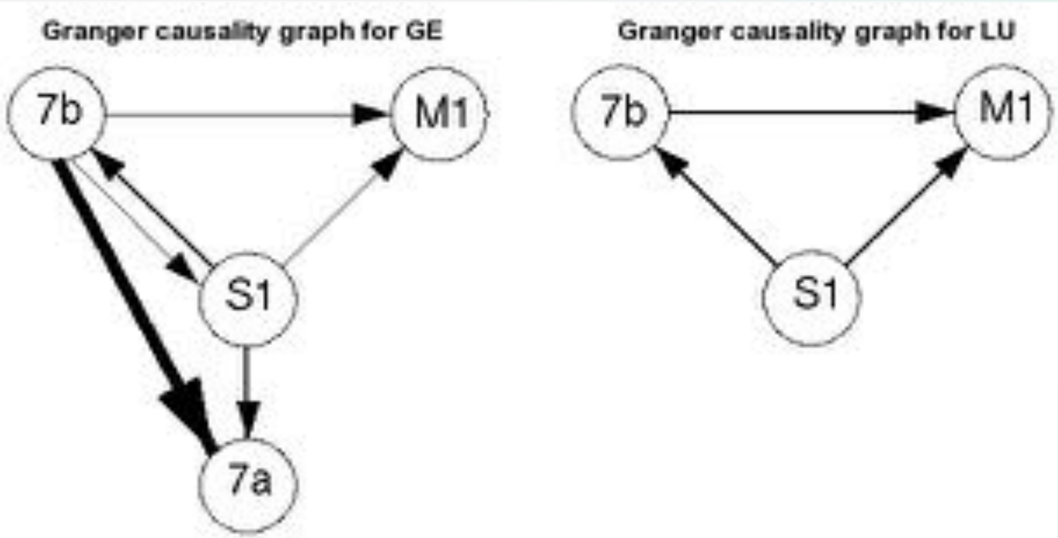
Fourier-Based Granger Causality

- **S1→M1 consistent with the known role of S1 for a sustained motor output.**

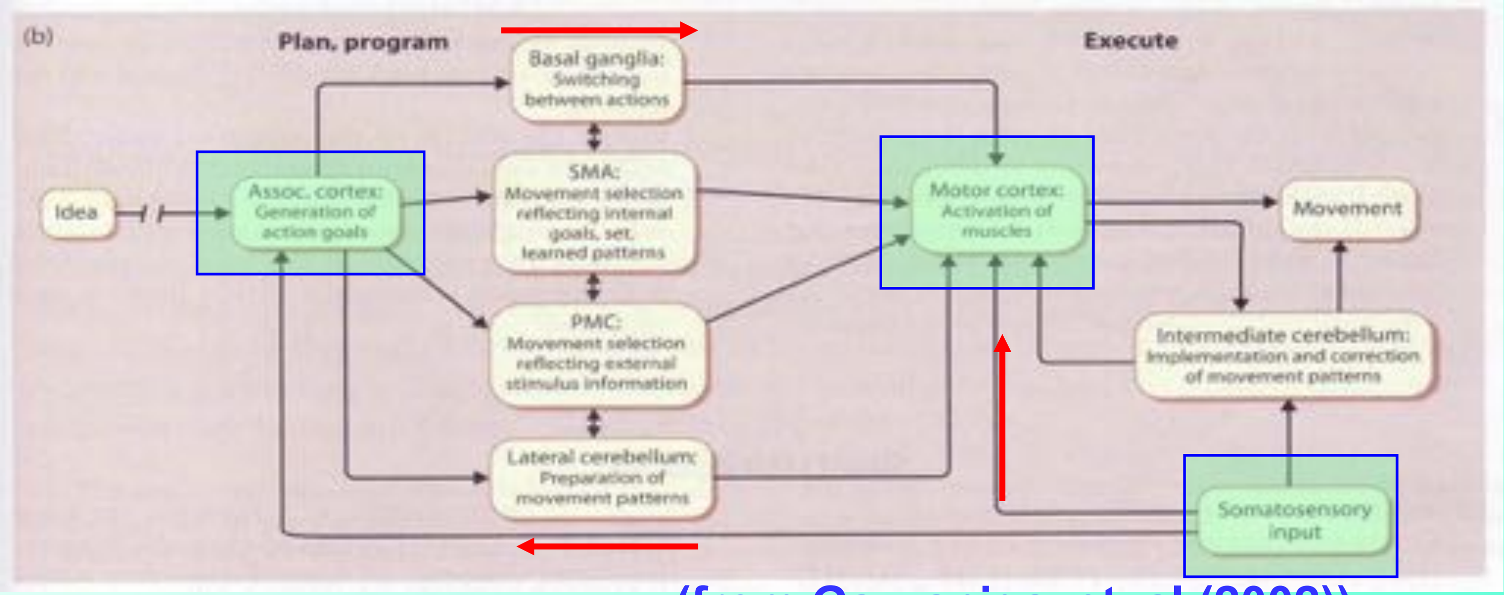


Wavelet-Based Granger Causality

Sensorimotor Granger Causality Network Graph

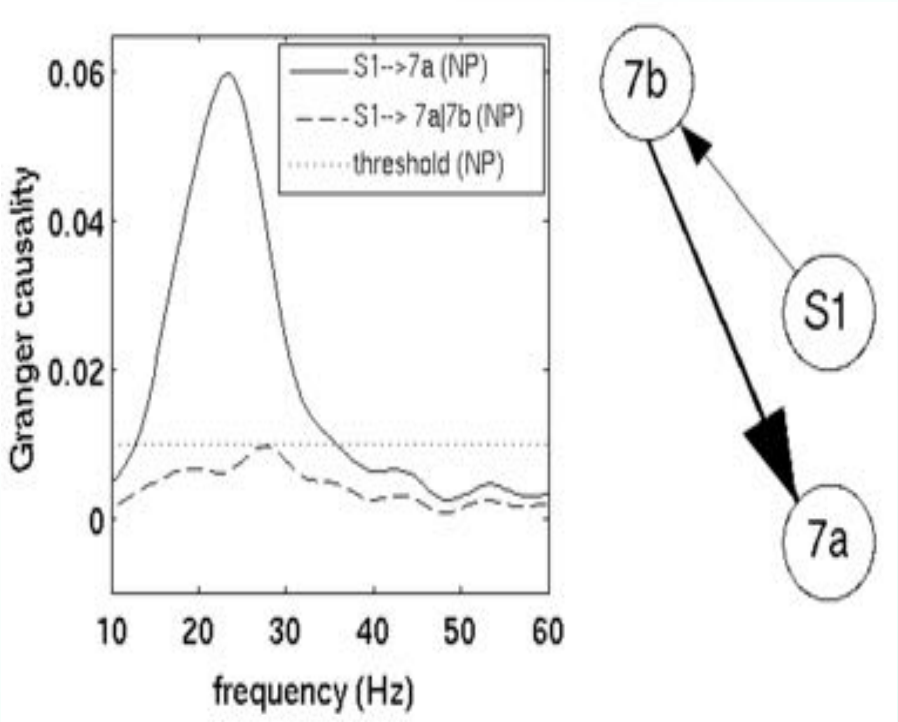


- **Neural Substrate of Motor Control:**

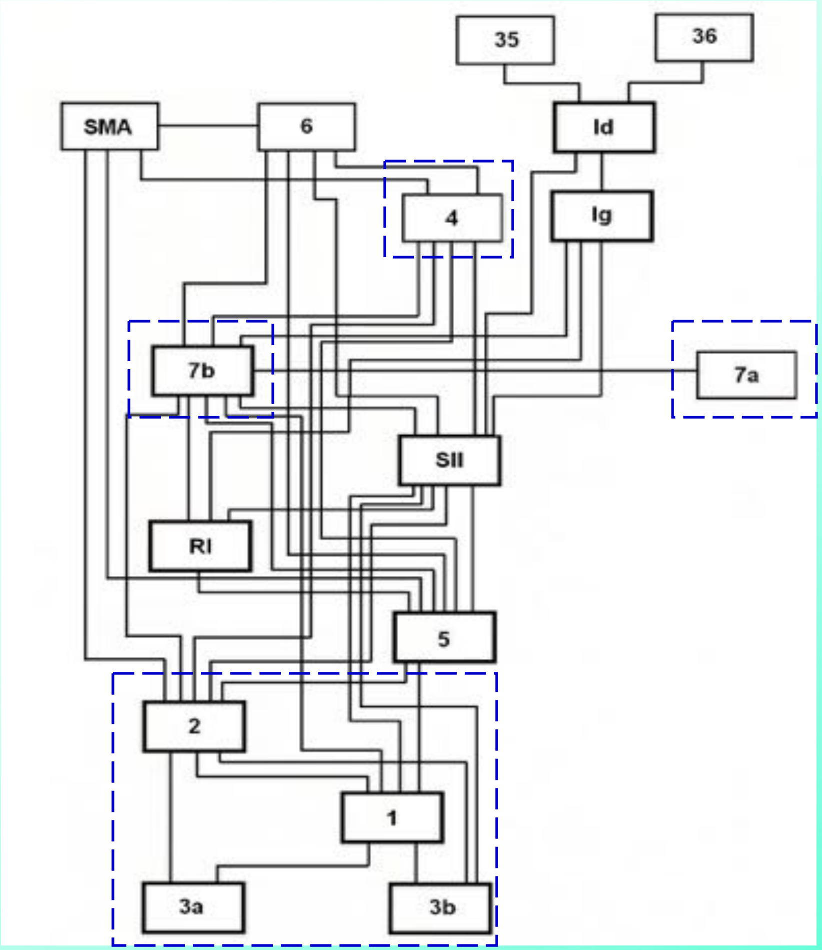


(from Gazzaniga, et. al.(2002))

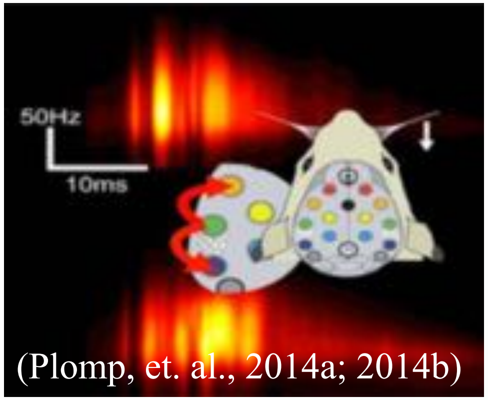
S1→7a is not direct, but mediated by 7b



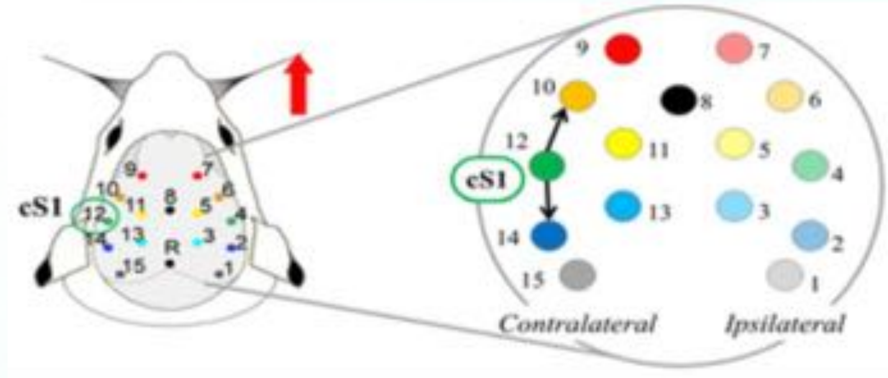
- Consistent with the anatomical connections.



Anatomical Connections
(Felleman and Van Essen, 1991)



(Plomp, et. al., 2014a; 2014b)



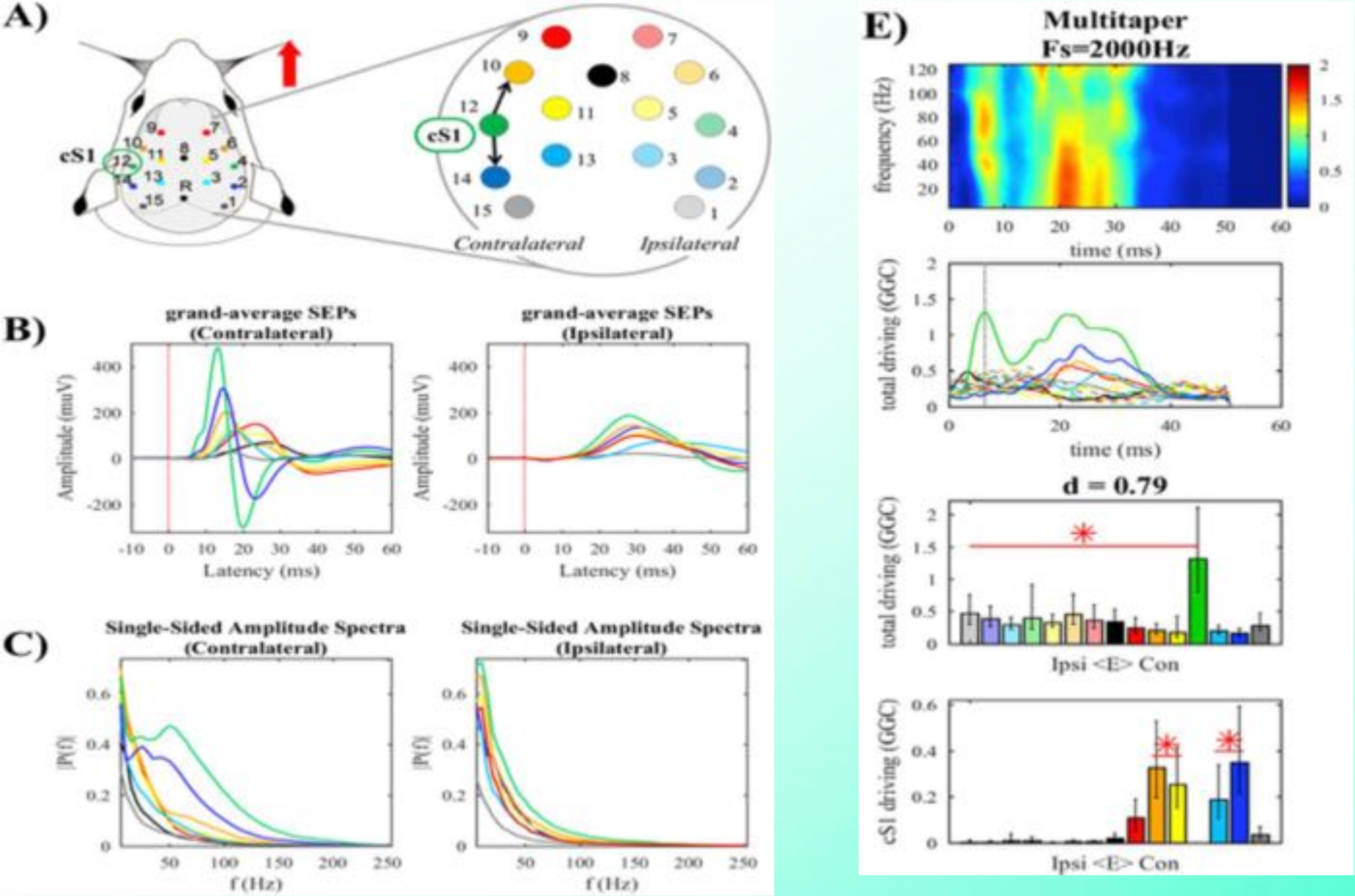
Application to Epicranial EEG

- ✧ M. F. Pagnotta, M. Dhamala, G. Plomp, "Benchmarking nonparametric Granger causality: Robustness against downsampling and influence of spectral decomposition parameters", *NeuroImage 183, 478-494 (2018)*.
- ✧ M. F. Pagnotta, M. Dhamala, G. Plomp, "Assessing the performance of Granger-Geweke causality: Benchmark dataset and stimulation framework", *Data in Brief 21, 833-851 (2018). (Data and Matlab codes included)*

Mattia Pagnota
(Univ of Fribourg)

Gijs Plomp
(Univ of Fribourg)

Stimulation, Electrode Locations, SEPs, Power and GGC



(Pagnotta, et al., NeuroImage 183, 478-494 (2018))

Application to iEEG of human epilepsy patients

- ✧ B. Adhikari, C. Epstein, M. Dhamala, "Localizing epileptic seizures with Granger causality", *Physical Review E 88, 030701 (Rapid Communications) (2013)*.
- ✧ C. Epstein, B. Adhikari, R. Gross, J. Willie, M. Dhamala, "High-frequency Granger causality in analysis of intracranial EEG and in surgical decision-making", *Epilepsia 55, 2038 (2014)*.

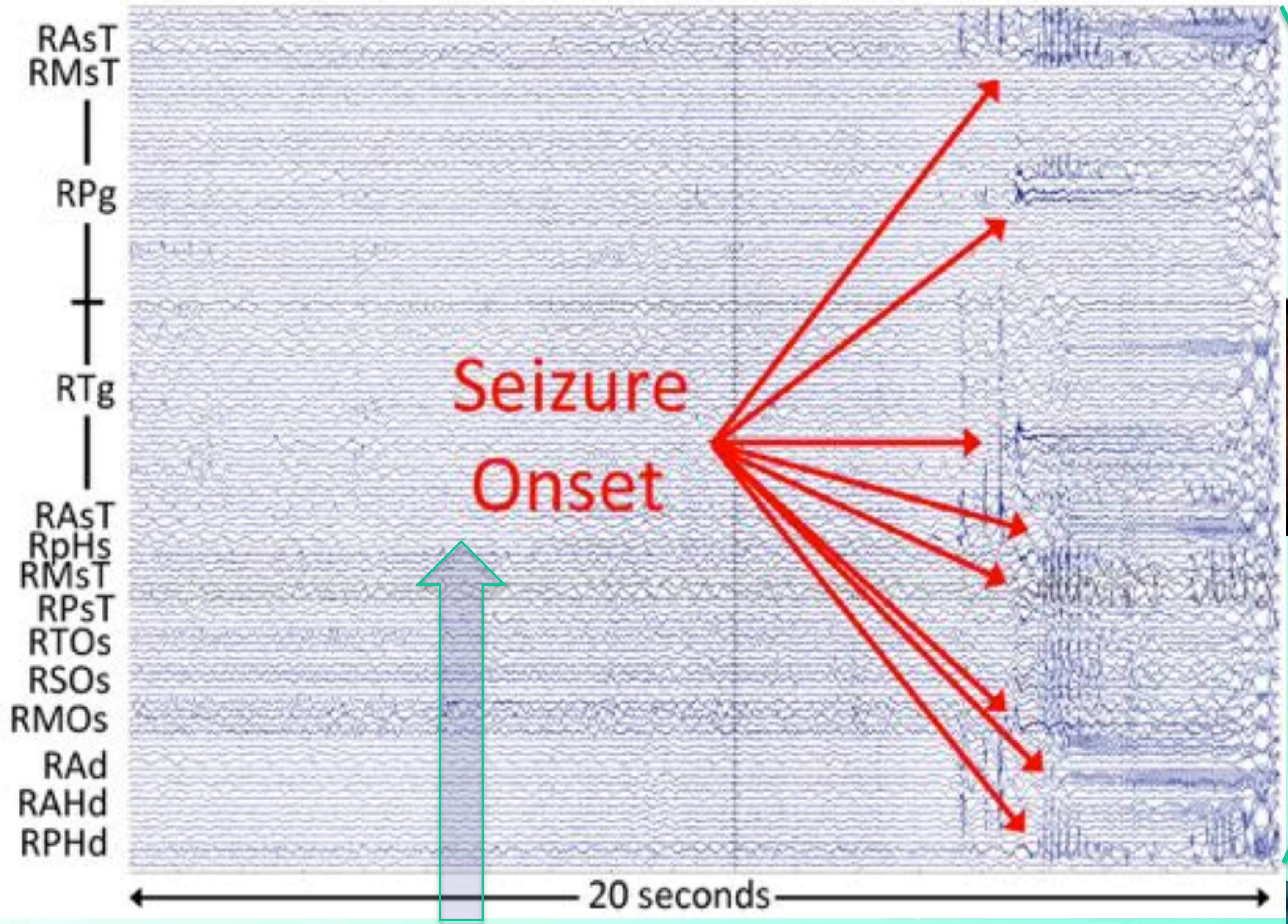
Bhim Adhikari (Physics, Georgia State Univ)

Charles Epstein (Neurophysiologist, Emory Univ)

Robert Gross (Neurosurgeon, Emory Univ)

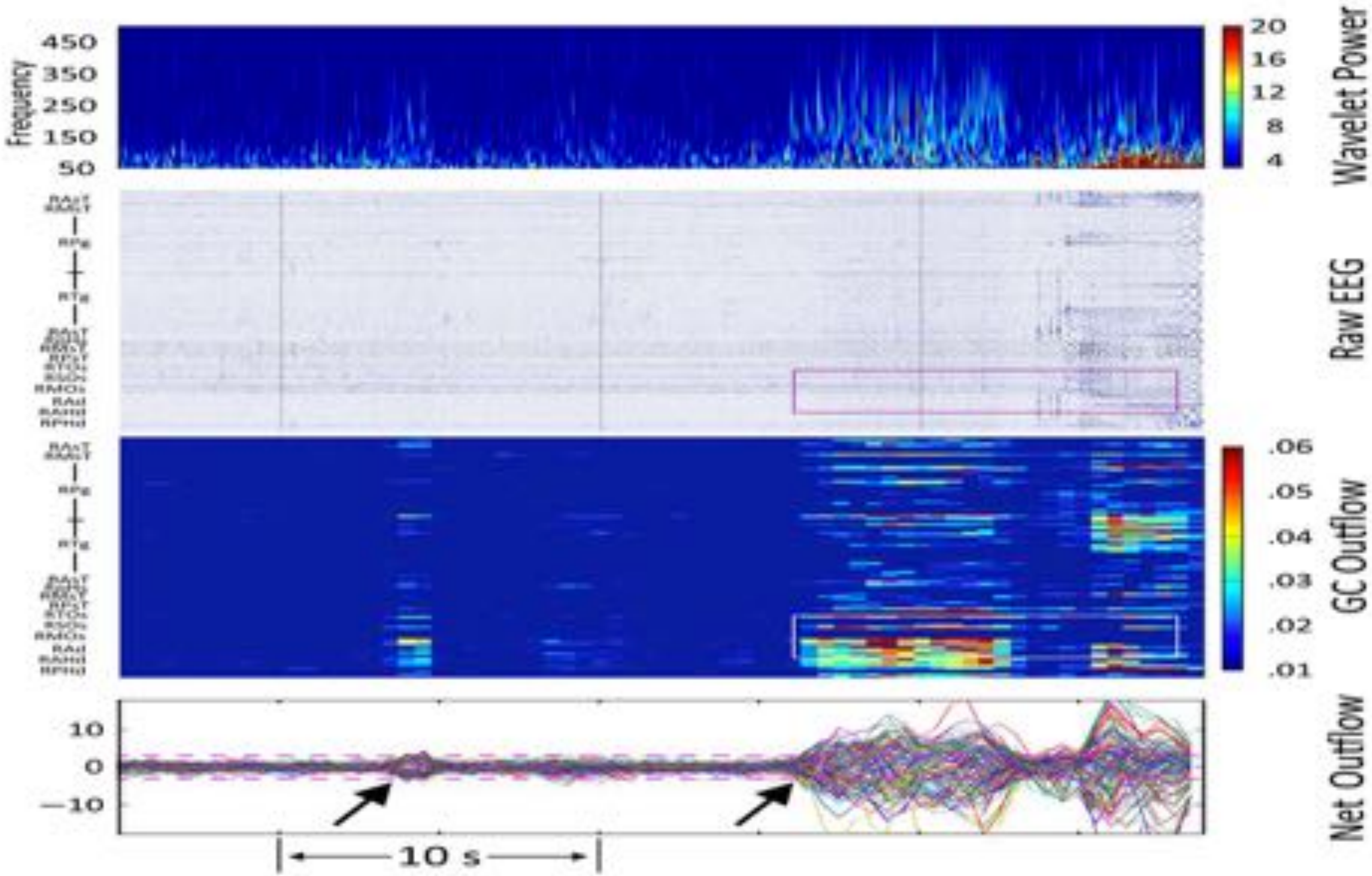
Jon Willie (Neurosurgeon, Emory Univ)

iEEG data and Seizure Origin



Where and when does it start?
Can GGC help to localize the onset?

High-Frequency Network Activity in One Patient



High-frequency network activity (up to 250 Hz) with GGC can assist in the localization of epileptic seizures.

Application to fMRI

- S. Bajaj, B. M. Adhikari, K. J. Friston, M. Dhamala, "Briding the gap: dynamic causal modling and Granger causality analysis of resting state functional magnetic resonance imaging". Brain Connectivity (2016).
- K. Dhakal, M. Norgaard, B. M. Adhikari, K. S. Yun, M. Dhamala, "Higher Node Activity with Less Functional Connectivity During Musical Improvisation". Brain Connectivity (2019).

GC and DCM to rfMRI

BRAIN CONNECTIVITY
Volume 6, Number 8, 2016
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Bridging the Gap: Dynamic Causal Modeling and Granger Causality Analysis of Resting State Functional Magnetic Resonance Imaging

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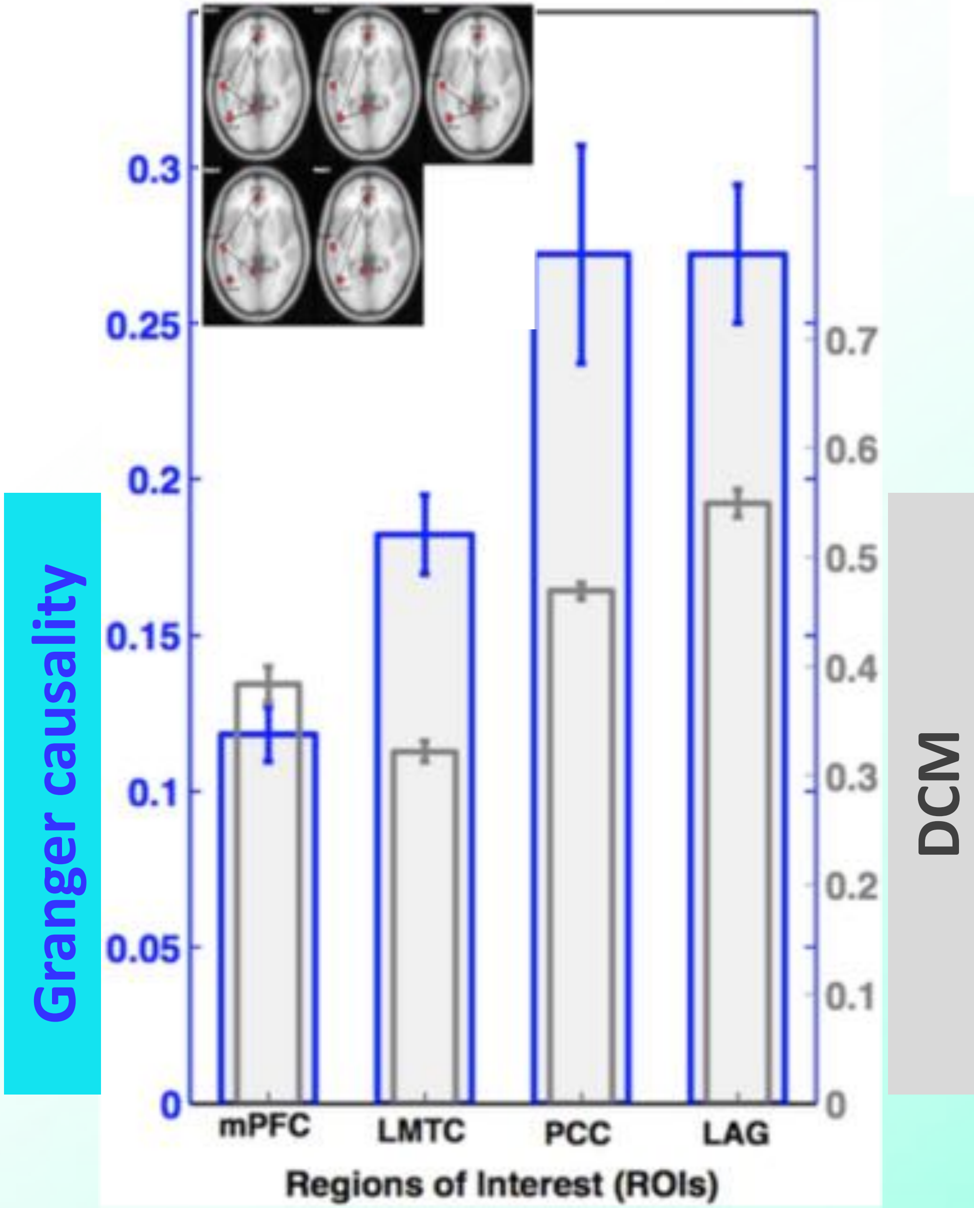
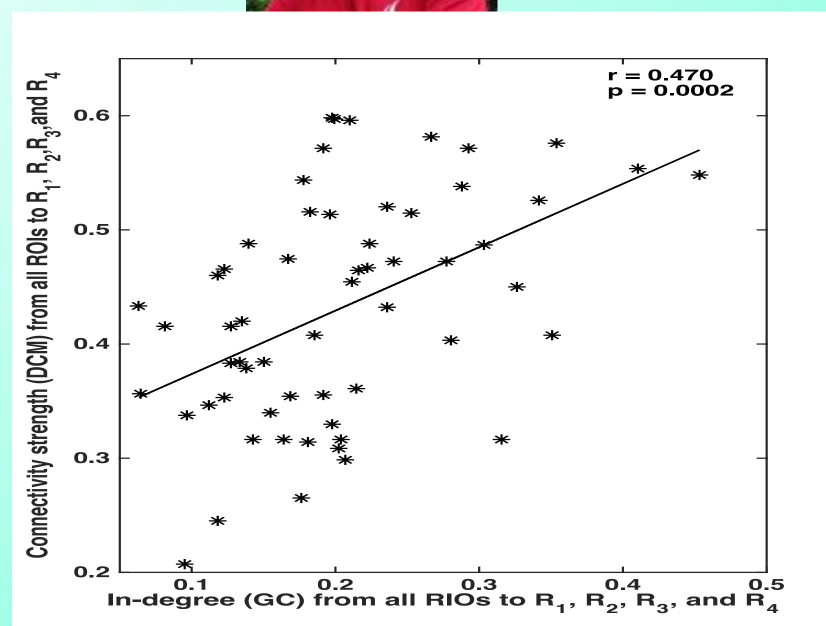




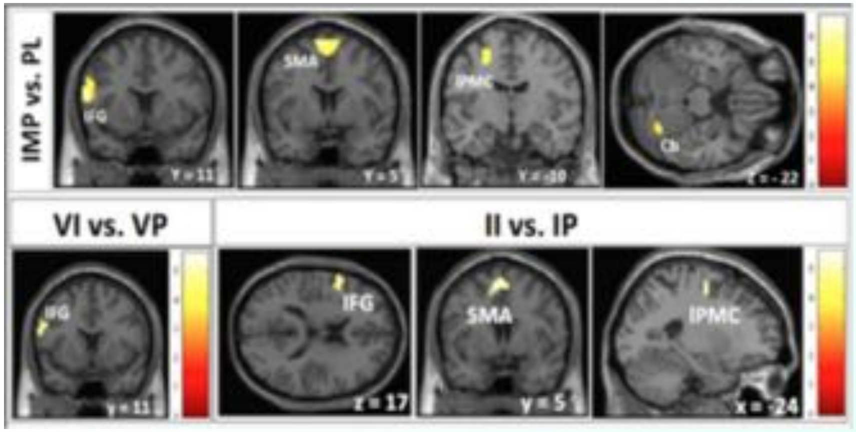
(Bajaj et al., 2016)

GC to task-based fMRI

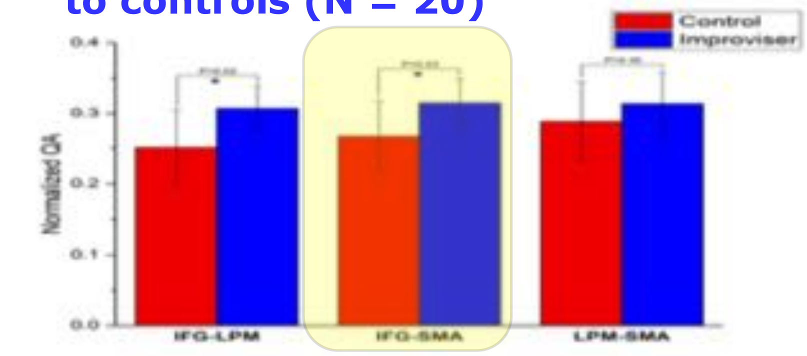
Kiran Dhakal

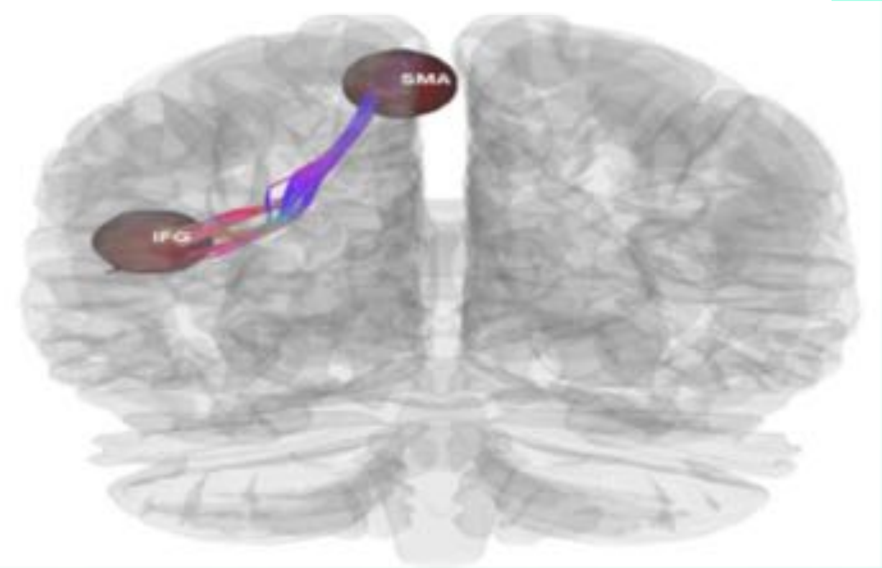
fMRI activation Analysis

N = 20, p < 0.0005, k > 20

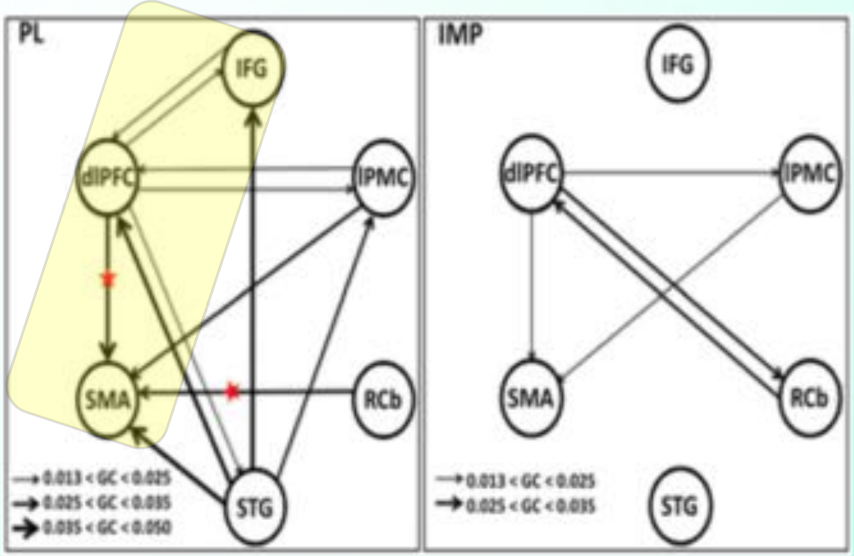


Anatomical basis: fiber tracts enhanced for expert musicians (N=20) compared to controls (N = 20)





Directional connectivity Granger Causality



(Dhakal, et. al., Brain Connectivity (2019); Dhakal, et al., *in preparation*)

Summary

- Granger causality techniques are useful to test hypotheses about information flow or to explore information flow from time series data.

- There are two estimation approaches: parametric (modeling based) and nonparametric (Fourier- and wavelet-transforms based), which can be complementary to each other.

- Granger causality methods are applicable to a variety of neuroscience data: LFP, iEEG, fMRI, fNIR, EEG, MEG.

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Thank you!
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