Cortical Connectivity Changes Under Difficult Listening Conditions Revealed by Network Localized Granger Causality

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Introduction

- Cortical connectivity may change under difficult listening conditions
- Connectivity characterized by the temporal predictability of activity across brain regions via Granger causality (GC)
- Challenges with M/EEG: the data are low-dimensional, noisy, and linearly-mixed versions of the true source activity
- Conventional methods:

E/MEG Data → Source Localization → GC Inference

- Drawbacks: bias propagation, spatial leakage

- Goal: *directly* localize GC influences without an intermediate source localization step
- Method: Network Localized Granger Causality (NLGC)
- Source dynamics as latent multivariate autoregressive model

E/MEG Data → *(Sparse)* Parameter Estimation → GC *Statistical* Inference

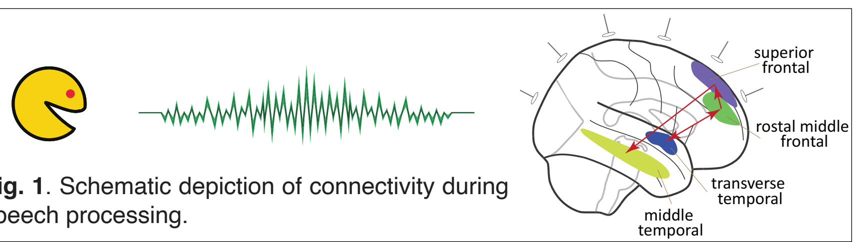

Fig. 1. Schematic depiction of connectivity during speech processing.

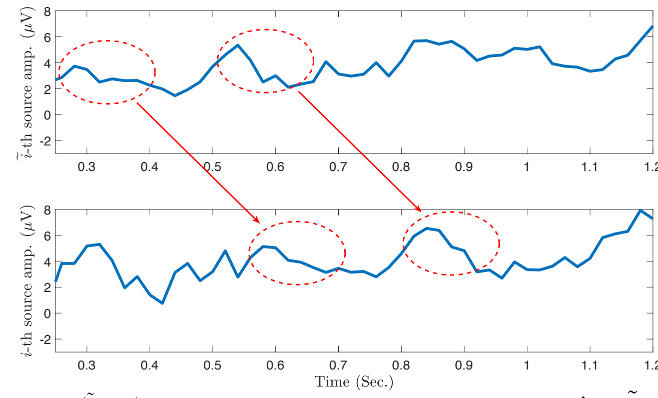

Fig. 2. GC link $(\tilde{i} \to i)$ implies temporal predictability of source i by $\tilde{i}$.

Model

- MEG observation model

$$\mathbf{y}_t = \mathbf{C}\mathbf{x}_t + \mathbf{n}_t, \quad t = 1, 2, \cdots, T$$

$\mathbf{y}_t \in \mathbb{R}^M$ MEG sensor data,
$\mathbf{C} \in \mathbb{R}^{M\times N}$ Lead field matrix,
$\mathbf{x}_t \in \mathbb{R}^N$ Source activity,
$\mathbf{n}_t \in \mathbb{R}^M$ Measurement noise.

- Source dynamics model

$$\mathbf{x}_t = \sum_{k=1}^{q} \mathbf{A}_k \mathbf{x}_{t-k} + \mathbf{w}_t, \quad t = 1, 2, \cdots, T$$

$\mathbf{A}_k \in \mathbb{R}^{N\times N}$ Coefficient matrix,
$\mathbf{w}_t \in \mathbb{R}^N$ Noise process.

Granger Causality

- Consider link $(\tilde{i} \to i)$

\- Can source $\tilde{i}$ improve temporal predictability of i ?

full model

$$\mathbf{x}_t^{(i)} = \sum_j \sum_k a_{i,j,k} \mathbf{x}_{t-k}^{(j)} + \mathbf{w}_t^{(i)}, \quad \mathbf{w}_t^{(i)} \sim \mathcal{N}(0, \sigma_i^2)$$

reduced model

$$\mathbf{x}_t^{(i)} = \sum_{j\neq\tilde{i}} \sum_k a'_{i,j,k} \mathbf{x}_{t-k}^{(j)} + \mathbf{w}'^{(i)}_t, \quad \mathbf{w}'^{(i)}_t \sim \mathcal{N}(0, \sigma^2_{i\setminus\tilde{i}})$$

- Granger Causality

$$\mathcal{F}_{(\tilde{i}\to i)} = \log\left(\frac{\sigma^2_{i\setminus\tilde{i}}}{\sigma^2_i}\right)$$

relative predictive variance explained

- $\mathcal{F}_{(\tilde{i}\to i)} \gg 0$: GC link exists

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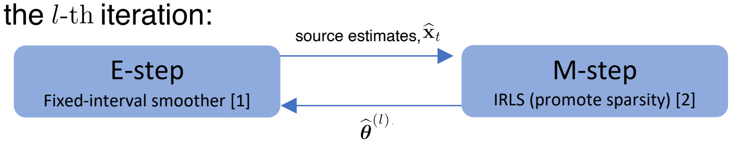
Parameter Estimation

- Objective: to estimate dynamic source model parameters

$$\boldsymbol{\theta} = (\mathbf{A}_k, k = 1, \cdots, q; \mathrm{diag}(\mathbf{Q}))$$

- Challenge: source activities are unknown
- Solution: Expectation Maximization (EM)
- At the l-th iteration:



- Perform the EM parameter estimation for full/reduced model corresponding to every source pair

Statistical Inference

- Test statistic, the *debiased deviance* for link $(\tilde{i} \rightarrow i)$ [3]

$$\mathcal{D}_{(\tilde{i} \mapsto i)} = 2\big(\ell_i(\widehat{\boldsymbol{\theta}}_i^F) - \ell_i(\widehat{\boldsymbol{\theta}}_i^R)\big) - B(\widehat{\boldsymbol{\theta}}_i^F, \widehat{\boldsymbol{\theta}}_i^R)$$

log-likelihood of the i-th source; bias term; full and reduced model parameters

- Hypothesis test, distributional results [4]

Null: $\boldsymbol{\theta}_i = \boldsymbol{\theta}_i^R$ (i.e., no GC influence); $\mathcal{D}_{(\tilde{i} \mapsto i)} \xrightarrow{d} \chi^2(q)$

Alternative: $\boldsymbol{\theta}_i = \boldsymbol{\theta}_i^F$ (i.e., GC influence); $\mathcal{D}_{(\tilde{i} \mapsto i)} \xrightarrow{d} \chi^2(q, \nu_{(\tilde{i} \mapsto i)})$

- False discovery rate (FDR) control

- Reject null hypothesis at a confidence level and control FDR via BY procedure [5]

- Test strength characterization

- Calculate Youden's J-statistic for all links

$$J_{(\tilde{i} \mapsto i)} = 1 - \alpha - F_{\chi^2(q, \widehat{\nu}_{(\tilde{i} \mapsto i)})}(F^{-1}_{\chi^2(q)}(1-\alpha))$$

- $J_{(\tilde{i} \mapsto i)} \approx 1$ (≈ 0) implies high (low) statistical confidence

- The GC map $\boldsymbol{\Phi}$: $[\boldsymbol{\Phi}]_{i,\tilde{i}} = \begin{cases} J_{(\tilde{i} \mapsto i)}, & i \neq \tilde{i} \\ 0, & \text{otherwise} \end{cases}$

Simulation Results

-100 sources, 50 sensors
-FDR controlled at 2%
-MNE procedure results in numerous spuriously detected links

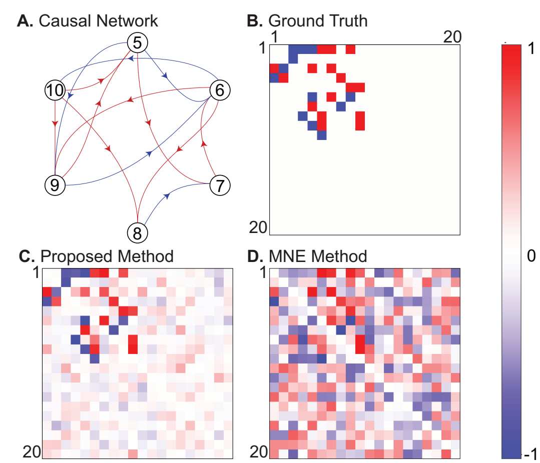


Fig. 3. **A.** The GC network corresponding to sources {5, 6, . . . , 10}. **B.** Ground truth GC map corresponding to 20 sources. **C.** Estimated GC map using the proposed method. **D.** Estimated GC map based on the two-stage procedure.

[1] Anderson, et al., "Optimal Filtering", 2012.
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[3] Soleimani et al., "Granger Causal Inference from Indirect Low-Dimensional Measurements with Application to MEG Functional Connectivity Analysis", *CISS, 2020*.
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[5] Benjamini, et al., "The control of the false discovery rate in multiple testing under dependency", *Ann. Stat.*, 2001.

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Difficult Listening Experiment

- Task (see poster #71 [6]): 1-minute long speech segments from an audio book in two conditions:
  - -Clean: male/ female narration
  - -Mixed speech: two talker speech, male vs. female speaker
- Mixed speech task: attend to pre-specified speaker
- We analyzed the data from the first trials of these conditions

Model Specifications

- Band-passed between 0.1 – 4.5 Hz (delta band)
- Head model: morph 'fsaverage' source space, Desican-Killiany atlas to identify 68 ROIs [6]
- Analyzed ROIs (in both hemispheres)

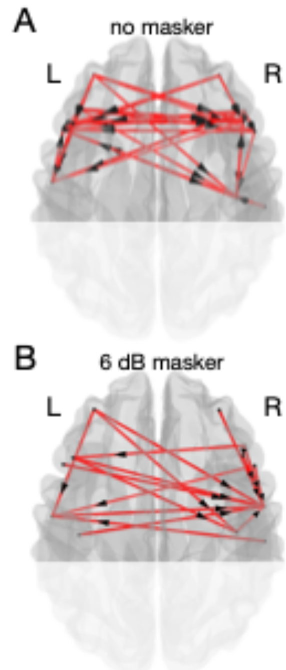
Temporal lobe
'superiortemporal', 'middletemporal', 'transversetemporal

Frontal lobe
'rostralmiddlefrontal', 'caudalmiddlefrontal', 'parsopercularis', 'parstriangularis'

- We summarize the contribution of each ROI by the leading eigenvectors within the ROI
- The measurement noise covariance: empty room recordings
- 155 MEG sensors
- Model order $q = 6$ (to fully capture the delta band)
- Sampling frequency: 25 Hz

Application to MEG Data

Fig. 4. NLGC estimates of neural connectivity for sites in the frontal and temporal lobes, during the last 40 s of each continuous speech listening trial, for either clean or masked speech (only significant links shown; arrows indicate direction of GC influence; N=4, FDR=1%).



- While listening to clean speech, about half (48%) of the significant causal links are frontal→frontal and about a third (32%) are top- down frontal→temporal (out of 31 significant links).
- In contrast, while listening to masked speech, almost two thirds (65%) of the 17 significant causal links are now top-down frontal→temporal, and only 12% are frontal→frontal (out of 17 significant links).

[6] Poster #71: I.M. Dushyanthi Karunathilake, et al. "Effects of Aging on the Cortical Representation of Continuous Speech".

[7] Desikan, et al., "An Automated Labeling System for Subdividing the Human Cerebral Cortex on MRI Scans into Gyral based Regions of Interest", *NeuroImage*, 2006.