Supplementary Information: Region-Level Functional and Effective Network Analysis of Human Brain During Cognitive Task Engagement

Authors: Sandeep Avvaru, Noam Peled, Nicole R. Provenza, Alik S. Widge and Keshab K. Parhi

S1 Directed Information (DI)

Directed information is an information-theoretic measure that estimates causal interactions between two jointly distributed sequences (two time-series). It quantifies the amount of causal information in one time-series explained by the other time-series. DI was initially defined for discrete-time, discrete-valued random processes and was later extended to discrete-time continuous-valued processes [1, 2]. Let $X^N$ and $Y^N$ be $N$ samples of continuous-valued sequences $X$ and $Y$. Directed Information from $X^N$ to $Y^N$, denoted $I(X^N \rightarrow Y^N)$, can be written as $I(X^N \rightarrow Y^N) = h(Y^N) - h(Y^N|X^N)$. Here, $h(Y^N)$ and $h(Y^N|X^N)$ represent the differential entropy of the random vector $Y^N$ and the differential entropy of $Y^N$ causally conditioned on $X^N$. The parameter $h(Y^N|X^N)$ is defined as $h(Y^N|X^N) = \sum_{n=1}^{N} h(Y_n|Y_{n-1}, X^n)$.

No particular assumptions are made about their underlying probability distributions or statistical models to estimate the DI between the LFP recordings. In this paper, the signals are downsampled to 200 Hz and their causal interactions are estimated non-parametrically using the data-driven approach developed in [2].

DI not restricted to a particular class of statistical models and is non-parametric [3]. Two widely used causality metrics, Granger causality and transfer entropy, are closely related to DI [4, 5]. If the signals are assumed to originate from an auto-regressive model with Gaussian noise, DI is equivalent to Granger causality [3]. DI can be extended to more general systems than transfer entropy; it is not limited to stationary Markov processes and can quantify the instantaneous causality [6].

S2 Convergent Cross-Mapping (CCM)

Dynamical system theory suggests that each causally linked variable in a dynamical system can be used to estimate the state of another variable since they share a common manifold ($M$). Also, when one variable $X$ drives another variable $Y$, information about the states of $X$ can be recovered from $Y$ but not the other way around. In other words, the ability to predict $X$ from $Y$ is a necessary condition to establish a causal link from $X$ to $Y$. This forms the basis for convergent cross-mapping as an approach to measure causal relationships.

Convergent cross-mapping, introduced by Sugihara in 2012 [7], tests for causation between two time-series $X$ and $Y$ by looking at the (temporal) correspondence between their shadow manifolds. The shadow manifolds, $M_X$ and $M_Y$, are constructed from time-lagged coordinates of the time series values of $X$ and $Y$, respectively. Specifically, CCM measures the extent to which the nearby points in $M_Y$ estimate the states of $X$. This process of estimating states of $X$ from $M_Y$ (or vice-versa) is called cross-mapping.

Consider two time-series of length $L$, $X^L$ and $Y^L$. As a result of time-delayed embedding, the shadow manifold $M_X$ is formed by the time-lagged coordinate vectors $x_t = (x_t, x_{t-\tau}, x_{t-2\tau}, \ldots, x_{t-(E-1)\tau})$ for $t \in [1 + (E-1)\tau, L]$. The embedding thus depends on two parameters: the time delay $\tau$...
and the embedding dimension \( E \). The cross-map of \( x_t \), denoted \( \mathbf{x}_t \| M_Y \) is computed by first identifying \( y_t \) and its \( E + 1 \) nearest neighbors in \( M_Y \), denoted \( \{ y_{t_1}, y_{t_2}, \ldots, y_{t_{E+1}} \} \). As a consequence of Taken’s theorem, \( M_X \) is diffeomorphic to \( M_Y \), i.e., each point in \( M_X \) can be mapped to a unique point in \( M_Y \) [7]. Therefore the neighborhood of \( y_t \) is mapped to a set of points in \( M_X \), represented as \( \{ x_{t_1}, x_{t_2}, \ldots, x_{t_{E+1}} \} \). The weighted mean of \( \{ x_{t_1}, x_{t_2}, \ldots, x_{t_{E+1}} \} \) provides an estimate of \( x_t \) as shown in the equation, \( \mathbf{x}_t \| M_Y = \sum_{i=1}^{E+1} w_i x_{t_i} \).

The weighting \( w_i \) is based on the distance between \( y_t \) and its \( i \)th nearest neighbor \( y_{t_i} \) as given by the equations

\[
w_i = u_i / \sum_{j=1}^{E+1} u_j \quad \text{and} \quad u_i = e^{-d(y_{t_i}, x_{t_i}) / d(y_{t_1}, y_{t})},
\]

where \( d(\cdot, \cdot) \) represents the Euclidean distance.

The cross-mapping was implemented in MATLAB based on the algorithm presented in [8]. A library of \( L \) points is estimated, and the correlation coefficient \( \rho_{xX} \) is used as an indicator of the influence of \( X \) on \( Y \). The causal connection from \( Y \) to \( X \) can also be determined analogously.

**S3 Classification Results Using Mean Region Networks**

This section presents a summary of task vs. non-task classification results using networks computed from averaged time-series in each region. The local field potential signals from all channels with a region of interest are averaged, and the resulting time-series is used to generate the networks. It can be observed that this approach attains about 10% lower classification accuracy compared to MVNM. Results from MVNM and FCHA are also included in Table S1 for comparison.

Table S1: Summary of task vs. non-task classification results. The table presents median and interquartile range values of classification accuracy, sensitivity (task accuracy) and specificity (non-task accuracy) for each of the three network connectivity measures: R, DI and CCM.

| Method | Averaged time-series | MVNM |
|--------|----------------------|------|
| Conn. | FCHA [9] | R | DI | CCM | R | DI | CCM |
| Acc.  | 78.1 ± 7.39 | 75.79 ± 7.59 | 70.04 ± 10.7 | 66.9 ± 8.87 | 82.74 ± 7.45 | 80.85 ± 4.9 | 85.17 ± 5.0 |
| Sens. | 71.0 ± 10.3 | 74.45 ± 11.39 | 69.8 ± 23 | 56.53 ± 26.36 | 84.86 ± 8.57 | 82.58 ± 8.57 | 87.49 ± 8.77 |
| Spec. | 79.2 ± 7.7 | 76.7 ± 14.1 | 67.97 ± 9.6 | 82.89 ± 16.84 | 83.7 ± 9.31 | 79.74 ± 6.38 | 82.12 ± 13.2 |

**S4 Subject-Specific Task Engagement Networks**

Task engagement networks (TENs) for each subject are presented in this section. Fig. S1, Fig. S2 and Fig. S3, respectively, show subject-specific TENs derived using correlation coefficient (R), DI and CCM. By visual inspection, we can observe that dlPFC and the temporal lobe are major hubs in the graphs. This observation is more pronounced in causal networks (DI and CCM). The regions of interest are labelled as follows: Acc– accumbens, Amyg– amygdala, caudate, Hipp– hippocampus, dACC– dorsal anterior cingulate cortex, dlPFC– dorsolateral prefrontal cortex, dIPFC– dorsomedial prefrontal cortex, IOFC– lateral orbitofrontal cortex, mOFC– medial orbitofrontal cortex, parahipp– parahippocampus, postCC– posterior cingulate cortex, rACC– rostral anterior cingulate cortex, temporal lobe, vlPFC– ventral lateral prefrontal cortex.
Figure S1: Task engagement networks derived using inter-region correlational networks.
Figure S2: Task engagement networks derived using inter-region DI networks.
Figure S3: Task engagement networks derived using inter-region CCM networks.
S5  Task Engagement Networks in Left and Right Hemispheres

Task engagement networks for both the hemispheres are shown in Fig. S4. These directed networks were constructed using CCM. The corresponding node centralities are also presented in Fig. S5. The networks depicted in Fig. S6(a) include intrahemispheric (within-hemisphere) and interhemispheric (cross-hemisphere) links. The node centrality values indicate no significant differences in the main hub regions in both hemispheres: dlPFC, temporal and vlPFC. Some interhemispheric links can be observed between the high centrality nodes. However, these connections should not be confused with true information flow or structural connectivity. They may indicate functional correlations or zero-lag interactions between the nodes.

Figure S4: Task engagement networks in left and right hemispheres generated using CCM.

Figure S5: Node centrality of each region in the left and right task engagement networks.
(a) Task engagement network.

(b) Node centrality.

Figure S6: Task engagement network including inter-hemispheric connections.

References

[1] J. L. Massey, “Causality, feedback and directed information,” in Intl. Symposium on Information Theory and its applications (ISITA), 1990.

[2] R. Malladi, G. Kalamangalam, N. Tandon, and B. Aazhang, “Identifying seizure onset zone from the causal connectivity inferred using directed information,” IEEE J. of Selected Topics in Signal Processing, vol. 10, no. 7, pp. 1267–1283, Oct 2016.

[3] P. O. Amblard and O. J. J. Michel, “On directed information theory and granger causality graphs,” J. of Computational Neuroscience, vol. 30, no. 1, pp. 7–16, 2011.

[4] C. W. J. Granger, “Investigating causal relations by econometric models and cross-spectral methods,” Econometrica, vol. 37, no. 3, pp. 424–438, 1969.

[5] T. Schreiber, “Measuring information transfer,” Phys. Rev. Lett., vol. 85, pp. 461–464, Jul 2000.
[6] Y. Liu and S. Aviyente, “The relationship between transfer entropy and directed information,” in *2012 IEEE Statistical Signal Processing Workshop (SSP)*, 2012, pp. 73–76.

[7] G. Sugihara, R. May, H. Ye, C.-h. Hsieh, E. Deyle, M. Fogarty, and S. Munch, “Detecting causality in complex ecosystems,” *Science*, vol. 338, no. 6106, pp. 496–500, 2012.

[8] D. Mønster, R. Fusaroli, K. Tylén, A. Roepstorff, and J. F. Sherson, “Causal inference from noisy time-series data — testing the convergent cross-mapping algorithm in the presence of noise and external influence,” *Future Generation Computer Systems*, vol. 73, pp. 52 – 62, 2017.

[9] N. Provenza, A. Paulk, N. Peled, M. Restrepo, S. Cash, D. Dougherty, E. Eskandar, D. Bor- ton, and A. Widge, “Decoding task engagement from distributed network electrophysiology in humans,” *J. of Neural Engineering*, vol. 16, p. 056015, 08 2019.