Small-world property of functional connectivity revisited

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Motivation

The small-world property of brain networks has been extensively discussed, however even random timeseries give rise to small-world functionl connectivity graphs. So is this small-world property of fMRI FC just a methodological artifact?

Introduction

Brain can be characterized by using graph theory [Bullmore].
Small-world property [Watts], defined by short paths together with high clustering of the network, is one of the most discussed and studied [Bassett]. Representative network commonly given by functional connectivity (FC). Most used FC measure is correlation coefficient, especially when the data can be deemed close to Gaussian [Hlinka, 2011]. FC matrices provide upwardly biased estimates of small-world, leading even to small world properties of connectivity graphs estimated from independent or randomly connected dynamical systems [Hlinka, 2012; Zalesky; Bialonski].

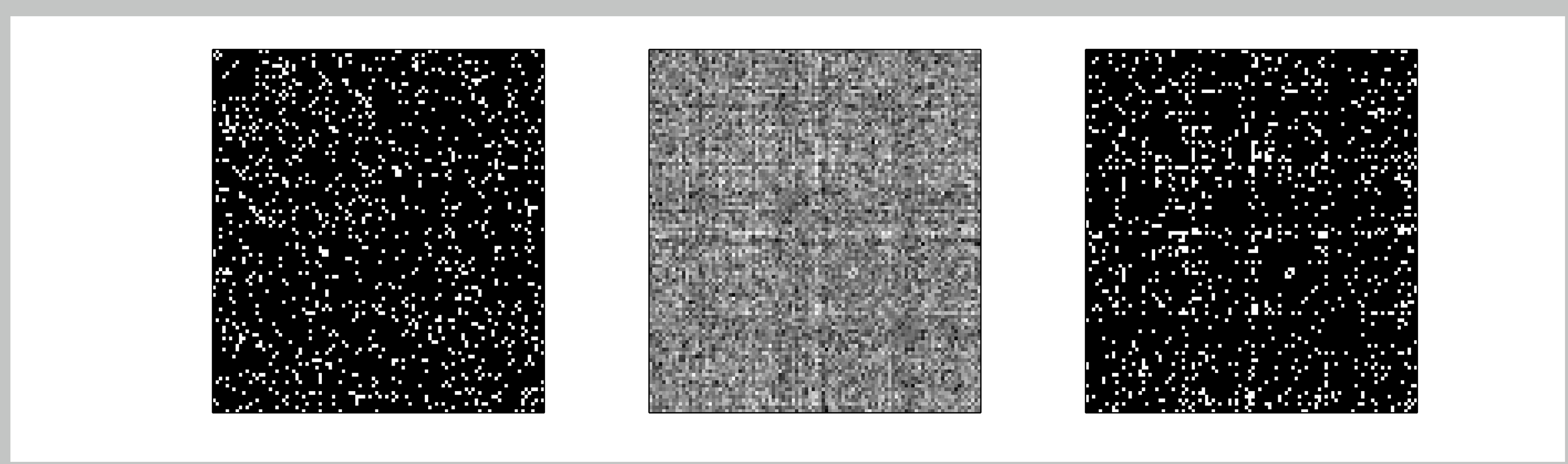

Figure 1: Example binary functional connectivity matrix (right) generated from random structural connectivity matrix (left) by thresholding the correlation matrix of VAR-model-based time series (center). Note that the FC matrix shows a specific structure for random input.

To what extent may this bias explain the observed small-world property in resting state fMRI functional connectivity graphs?

Data

- 10 minutes, 240 volumes of resting state fMRI (BOLD)
- 84 (48 males, mean age ± SD: 30.83 ± 8.48) healthy volunteers
- 3T Siemens Trio scanner (GE-EPI, TR/TE=2500/30 ms, voxel=3x3x3mm)
- A 3D high-resolution T1-weighted image was used for anatomical reference.
- slice-timing correction, motion correction, spatial normalization to MNI
- 90 parcels from the Automated Anatomical Labeling (AAL) atlas
- orthogonalized wrt motion parameters, white matter and CSF signal
- linear detrending, band-pass filtering (Butterworth filter 0.01 - 0.08 Hz)
- FC matrix computed by correlation and binarized to 20 percent density

Methods

- The average path length and the clustering coefficient are defined as:

$$L = \frac{1}{N\cdot(N-1)}\cdot\sum_{i,j} d_{i,j}, \qquad C = \frac{1}{N}\sum_{i\in V} c_i, \qquad c_i = \frac{\sum_{j,\ell} a_{i,j}a_{j,\ell}a_{\ell,i}}{k_i(k_i-1)}$$

  where $a_{i,j}$ denotes the link between nodes i, j, c_i the local clustering coefficient and $d_{i,j}$ the length of shortest path among nodes i, j.
- Small-world property is quantified by small-world index [Humphries]

$$\sigma = \frac{\gamma}{\lambda} \gg 1, , \text{ where } \lambda = \frac{L}{L_{rand}} \gtrsim 1, \gamma = \frac{C}{C_{rand}} \gg 1$$

  are relative average path length and clustering coefficient wrt random graph.

Methods II: comparison of data and randomly connected process

- Small-world indices were computed in the same way for data and a 'scrambled interaction' time series. This was modeled by fitting an vector autoregressive (VAR) process of order 1 to the BOLD time series:

$$X_t = c + AX_{t-1} + e_t, \qquad (1)$$

  (where c is a $N \times 1$ vector of constants, A is a $N \times N$ matrix and e_t is a $N \times 1$ vector of error terms) and subsequently randomly scrambling A.
- To control for the effects of approximation by a VAR process, a realization of the fitted VAR model with scrambling omitted was also analyzed.

Results

Small-world properties observed: mean small-world index = 2.33
For the linear VAR model: mean small-world index = 2.32
For randomly linked VAR model: mean small-world index = 2.18
The small-world property is driven by the clustering coefficient

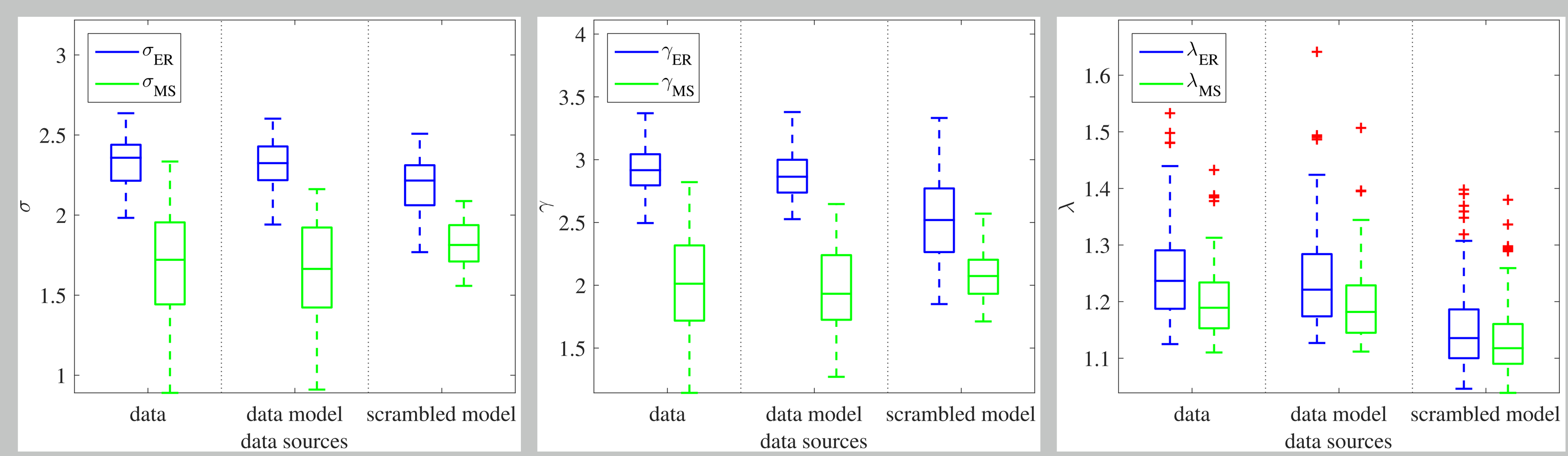

Figure 2: Left: small-world index (median, quartiles, extremes, outliers) for data, VAR model and randomized VAR model. Middle: relative clustering. Right: relative mean path length.

The difference between the real and modeled data is almost negligible ($p > 0.05$). The difference between the real and scrambled interaction data is also quite small, albeit statistically significant ($p < 0.05$).

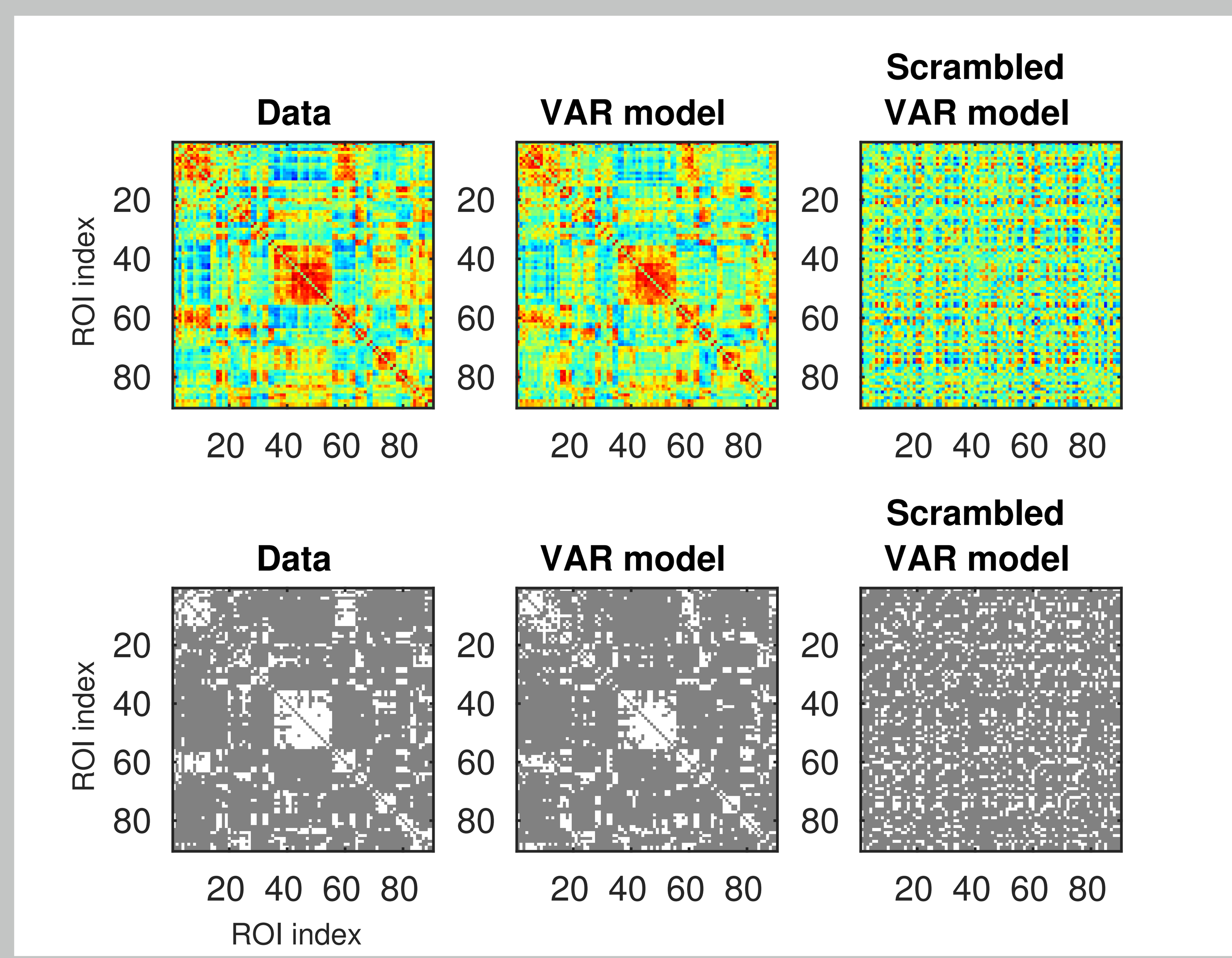

Figure 3: Example FC matrices. Top: raw. Bottom: thresholded to density 0.2.

Results generalize across atlases, not fully to other FC measures!

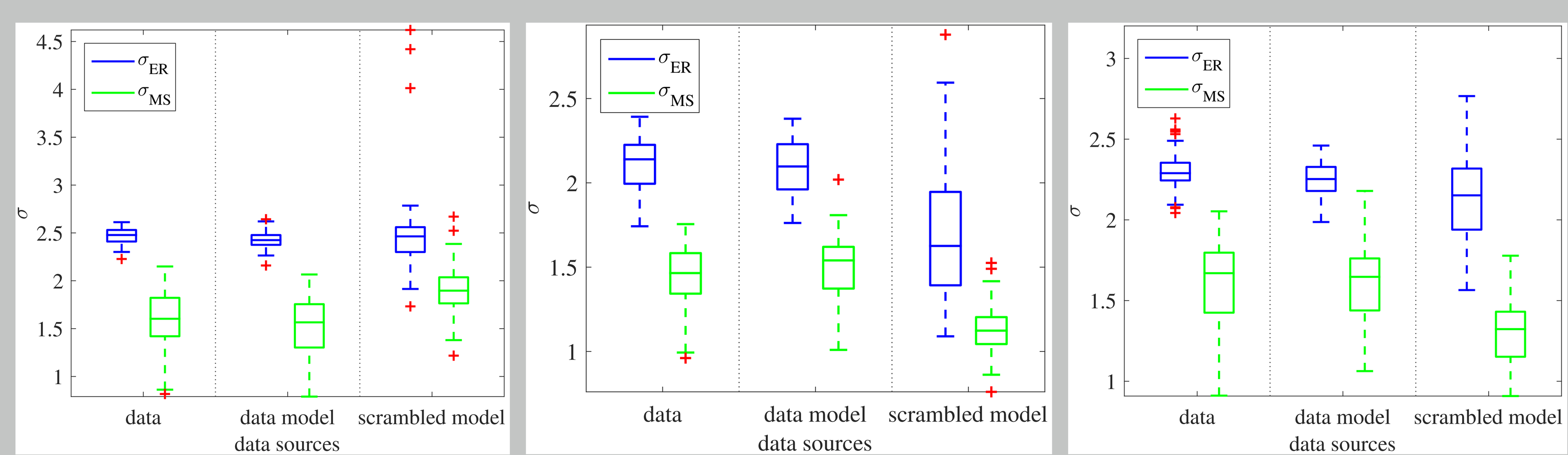

Figure 4: Left: small-world indices for alternative atlas (Craddock atlas with 200 ROIs); Middle: FC quantified by absolute correlation; Right: FC quantified by mutual information.

Discussion and conclusions

- **The small-world properties of fMRI FC graph is virtually reproduced by a matching randomly connected multivariate autoregressive process [Hlinka, 2017].**

References

Bassett, D. S. and Bullmore, E. (2006) 'Small-world brain networks' Neuroscientist vol. 12, pp. 512-523
Bialonski, S. et al. (2010) 'From brain to earth and climate systems: Small-world interaction networks or not?' Chaos, vol. 20, pp. 013134
Bullmore, E. and Sporns, O. (2009) 'Complex brain networks: graph theoretical analysis of structural and functional systems' Nature Reviews Neuroscience, vol. 10, pp. 186-198
Hlinka, J. et al. (2011) 'Functional connectivity in resting-state fMRI: Is linear correlation sufficient?' NeuroImage, vol. 54, pp. 2218-2225
Hlinka, J. et al. (2012) 'Small-world topology of functional connectivity in randomly connected dynamical systems.', Chaos, vol 22. no. 3, 033107
Hlinka, J. et al. (2017) 'Small-world bias of correlation networks: From brain to climate', Chaos, vol 27, 035812
Humphries, M. D. and Gurney, K.(1998) 'Network 'Small-World-Ness': A Quantitative Method for Determining Canonical Network Equivalence', PLoS One, vol. 3, e0002051.
Watts, D. & Strogatz, S. (1998) 'Collective dynamics of 'small-world' networks', Nature, 393, pp. 440-442
Zalesky, A. et al. (2012) 'On the use of correlation as a measure of network connectivity', Neuroimage, vol.60, pp. 2096-2106

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