Reproducibility of graph metrics of human brain structural networks

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Neuroinformatics with the Insight ToolKit

ABSTRACT

Recent interest in the human connectome has led to the application of graph theoretical analysis to human brain structural networks, in particular white matter connectivity inferred from diffusion imaging and fiber tractography. While these methods have been used to study a variety of patient populations, there has been less examination of the reproducibility of these methods. These graph metrics typically derive from fiber tractography, however a number of tractography algorithms exist and many of these are known to be sensitive to user-selected parameters. The methods used to derive a connectivity matrix from fiber tractography output also influence the resulting graph metrics. Here we examine how these algorithm and parameter choices influence the reproducibility of proposed graph metrics.

Keywords: Structure Tractography Connectivity Brain Network Reproducibility

1 INTRODUCTION

Test retest of functional graph metrics via MEG (Deuker et al., 2009)
Test retest of functional graph metrics via fMRI (Telesford et al., 2010)
Test retest of structural graph metrics via DTI (Owen et al., 2013)
Test retest of structural graph metrics via DTI and DSI with multiple labeling schemes (Bassett et al., 2011)
Intra and inter subject variability of structural graph metrics via DTI for binary and weighted networks (Cheng et al., 2012)
Correlations between pairs of regions using a variety of structural measures (Irimia and Van Horn, 2012)

Novel contributions

1. Public data and fully open source
2. In-depth examination of deterministic tractography parameters
3. Probabilistic tractography extensions
4. In-depth analysis of streamline-to-matrix conversion
5. Provides plug-and-play framework for evaluation of new methods and/or alternate data sets
6. Easy to extend to functional study (BOLD and ASL)

Table 1. Descriptions and references for graph metrics examined in this study.

Node metrics	Description	Reference
Degree	Number of connections for a node	
Clustering coefficient	Local neighborhood connectivity	(Watts and Strogatz, 1998)
Path length	Average shortest path to all other nodes	(Watts and Strogatz, 1998)
Global efficiency	“Closeness” to all other nodes	(Latora and Marchiori, 2001)
Local efficiency	“Closeness” to local nodes	
Whole-graph metrics		
Small-world		(Watts and Strogatz, 1998)
Synchronizability		(Motter et al., 2005)
Assortativity		(Newman, 2002)
Hierarchy		(Ravasz and Barabási, 2003)
Cost efficiency		(Achard and Bullmore, 2007)
Rich-club coefficient	Degree to which high-degree nodes preferentially inter-connect	(Colizza et al., 2006)
Network similarity measures		
Network overlap		(van Wijk et al., 2010)
Edge overlap	Percentage of common edges in constant density networks	(**?**)

Table 2. Formulas for node metrics.

Degree	$K_i = \sum_{j=1}^{n} A_{ij}$
Clustering coefficient	$C_i = 2 * e_i / K_i(K_i - 1)$
Path length	$L = 1/N(N-1) \sum_{ij \in n, i \neq j} d_{ij}$
Global efficiency	$E_{glob} = E(G) = 1/N(N-1) \sum_{i \neq j \in G} 1/d_{ij}$
Local efficiency	$E_{loc} = 1/N \sum_{i \in n} E(G_i)$

2 MATERIAL & METHODS

Provide an overview of what we are examining here

2.1 NODE METRICS

For more details on the node metrics see (Rubinov and Sporns, 2010).

2.2 WHOLE-GRAPH METRICS

More formulas go here.

2.3 NETWORK SIMILARITY

Use these to examine methods that extract sub-networks such as rich-club and constant density networks.

2.4 TRACTOGRAPY

Algorithms, parameters

2.5 MATRIX DERIVATION

Turning streamlines into nice N x N matrices

2.6 NEUROIMAGING DATA

The Multi-Modal MRI Reproducibility Resource (Landman et al., 2011) provides a test-retest data set consisting of 21 subjects with two time points each for which T1-weighted anatomical images and diffusion tensor images were acquired. Other image types, not examined here, were also acquired making this data useful for future examinations of structure and function. A population averaged template and manually defined cortical labels for one time point for each subject are available as part of the Mindboggle-101 dataset (Klein and Tourville, 2012).

2.7 IMAGE ANALYSIS

Minimal processing

1. Intra-subject registration for label transfer
2. B0-T1 registration
3. DTI reconstruction
4. MTR ?

For each subject, cortical labels were manually defined on the T1-weighted image from a single time-point. In order to label the addtional time-point, we use the ANTs Toolkit to find an affine mapping between the T1-weighted images using the cross-correlation metric. The cortical labels are then mapped into the unlabeled image using nearest-neighbor interpolation.

Optional processing

1. Registration to template (for additional label sets)

Future processing

1. Cortical thickness
2. BOLD / ASL / etc

3 RESULTS

Overview of what we found

4 DISCUSSION

4.1 DATA SHARING

DISCLOSURE/CONFLICT-OF-INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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SUPPLEMENTAL DATA

Maybe need this, maybe not

REFERENCES

Deuker, L., Bullmore, E. T., Smith, M., Christensen, S., Nathan, P. J., Rockstroh, B., et al. (2009) Reproducibility of graph metrics of human brain functional networks. *Neuroimage* 47 1460–1468.

Telesford, Q. K., Morgan, A. R., Hayasaka, S., Simpson, S. L., Barret, W., Kraft, R. A., et al. (2010) Reproducibility of graph metrics in fmri networks. *Frontiers in neuroinformatics* 4.

Owen, J. P., Ziv, E., Bukshpun, P., Pojman, N., Wakahiro, M., Berman, J. I., et al. (2013) Test-retest reliability of computational network measurements derived from the structural connectome of the human brain. *Brain Connect* 3 160–176. doi:10.1089/brain.2012.0121.

Bassett, D. S., Brown, J. A., Deshpande, V., Carlson, J. M., and Grafton, S. T. (2011) Conserved and variable architecture of human white matter connectivity. *Neuroimage* 54 1262–1279. doi:10.1016/j.neuroimage.2010.09.006.

Cheng, H., Wang, Y., Sheng, J., Kronenberger, W. G., Mathews, V. P., Hummer, T. A., et al. (2012) Characteristics and variability of structural networks derived from diffusion tensor imaging. *Neuroimage* 61 1153–1164. doi:10.1016/j.neuroimage.2012.03.036.

Irimia, A. and Van Horn, J. D. (2012) The structural, connectomic and network covariance of the human brain. *Neuroimage* 66C 489–499. doi:10.1016/j.neuroimage.2012.10.066.

Watts, D. J. and Strogatz, S. H. (1998) Collective dynamics of 'small-world' networks. *Nature* 393 440–442. doi:10.1038/30918.

Latora, V. and Marchiori, M. (2001) Efficient behavior of small-world networks. *Physical review letters* 87 198701.

Motter, A. E., Zhou, C., and Kurths, J. (2005) Enhancing complex-network synchronization. *EPL (Europhysics Letters)* 69 334.

Newman, M. E. (2002) Assortative mixing in networks. *Physical review letters* 89 208701.

Ravasz, E. and Barabási, A.-L. (2003) Hierarchical organization in complex networks. *Physical Review E* 67 026112.

Achard, S. and Bullmore, E. (2007) Efficiency and cost of economical brain functional networks. *PLoS Comput Biol* 3 e17. doi:10.1371/journal.pcbi.0030017.

Colizza, V., Flammini, A., Serrano, M. A., and Vespignani, A. (2006) Detecting rich-club ordering in complex networks. *Nature physics* 2 110–115.

van Wijk, B. C. M., Stam, C. J., and Daffertshofer, A. (2010) Comparing brain networks of different size and connectivity density using graph theory. *PLoS One* 5 e13701. doi:10.1371/journal.pone.0013701.

Rubinov, M. and Sporns, O. (2010) Complex network measures of brain connectivity: uses and interpretations. *Neuroimage* 52 1059–1069. doi:10.1016/j.neuroimage.2009.10.003.

Landman, B. A., Huang, A. J., Gifford, A., Vikram, D. S., Lim, I. A. L., Farrell, J. A. D., et al. (2011) Multi-parametric neuroimaging reproducibility: a 3-t resource study. *Neuroimage* 54 2854–2866. doi:10.1016/j.neuroimage.2010.11.047.

Klein, A. and Tourville, J. (2012) 101 labeled brain images and a consistent human cortical labeling protocol. *Front Neurosci* 6 171. doi:10.3389/fnins.2012.00171.