

Reproducibility of graph metrics of human brain structural networks

Jeffrey T. Duda^{1,*}, Philip A. Cook¹ and James C. Gee¹

¹Penn Image Computing and Science Laboratory, University of Pennsylvania, Department of Radiology, Philadelphia, PA, USA

Correspondence*:

Jeffrey T. Duda

Penn Image Computing and Science Laboratory, University of Pennsylvania, Department of Radiology, 3600 Market Street, Suite 370, Philadelphia, PA, USA, jtduda@seas.upenn.edu

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

Prior work Bassett et al. (2011); Cheng et al. (2012); Irimia and Van Horn (2012); Owen et al. (2013)

2 MATERIAL & METHODS

Science goes here

2.1 ORIGINAL RESEARCH ARTICLES, CLINICAL TRIAL ARTICLES, AND TECHNOLOGY REPORTS

For Original Research Articles, Clinical Trial Articles, and Technology Reports the following sections are mandatory:

- Introduction: Succinct, with no subheadings.
- Materials and Methods: This section may be divided by subheadings. This section should contain sufficient detail so that when read in conjunction with cited references, all procedures can be repeated.
- Results: This section may be divided by subheadings. Footnotes should not be used and have to be transferred into the main text.
- Discussion: This section may be divided by subheadings. Discussions should cover the key findings of the study: discuss any prior art related to the subject so to place the novelty of the discovery in

Table 1. Resolution Requirements for the figures

Image Type	Description	Format	Color Mode	Resolution
Line Art	An image composed of lines and text, which does not contain tonal or shaded areas.	TIFF, EPS, JPEG	RGB, Bitmap	900 - 1200 dpi
Halftone Combination	A continuous tone photograph, which contains no text. Image contains halftone + text or line art elements.	TIFF, EPS, JPEG TIFF, EPS, JPEG	RGB, Grayscale RGB, Grayscale	300 dpi 600 - 900 dpi

This is a footnote

the appropriate context; discuss the potential short-comings and limitations on their interpretations; discuss their integration into the current understanding of the problem and how this advances the current views; speculate on the future direction of the research and freely postulate theories that could be tested in the future.

Please note that the Material and Methods section can be placed in any of the following ways: before Results, before Discussion or after Discussion.

Figure 1. Enter the caption for your figure here. Repeat as necessary for each of your figures.

2.2 CLINICAL CASE STUDIES

For Clinical Case Studies the following sections are mandatory:

- Introduction: Include symptoms at presentation, physical exams and lab results.
- Background: This section may be divided by subheadings. Include history and review of similar cases.
- Results: This section may be divided by subheadings. Include diagnosis and treatment.
- Concluding Remarks

Please note that the Material and Methods section can be placed in any of the following ways: before Results, before Discussion or after Discussion.

3 RESULTS

Frontiers requires figures to be submitted individually, in the same order as they are referred to in the manuscript. Figures will then be automatically embedded at the bottom of the submitted manuscript. Kindly ensure that each table and figure is mentioned in the text and in numerical order. Permission must be obtained for use of copyrighted material from other sources (including the web). Please note that it is compulsory to follow figure instructions. Figures which are not according to the guidelines will cause substantial delay during the production process.

$$\sum x + y = Z \quad (1)$$

Table1 shows the resolution requirements for the figures. The figures must be legible:

1. The smallest visible text is no less than 8 points in height, when viewed at actual size.
2. Solid lines are not broken up.
3. Image areas are not pixelated or stair stepped.
4. Text is legible and of high quality.
5. Any lines in the graphic are no smaller than 2 points width.

Figure 2. Enter the caption for your figure here. Repeat as necessary for each of your figures.

4 DISCUSSION

51 Text
52 Text Text Text Text. Additional Requirements:

4.1 CORRECTIONS

53 Minor corrections to published articles can be communicated to the Frontiers Production Office at
54 production.office@frontiersin.org. If you need to communicate important changes to an article please
55 submit a General Commentary. Submit the article with the title Erratum: Original Title of Article.

4.2 COMMENTARIES ON ARTICLES

56 At the beginning of your manuscript provide the citation of the article commented on.

4.3 FOCUSED REVIEWS

57 For Tier 2 invited Focused Reviews the sections Introduction, Material and Methods, Results, and
58 Discussion are recommended. In addition the authors must submit a short biography of the corresponding
59 author(s). This short biography has a maximum of 600 characters, including spaces.
60 A picture (5 x 5 cm, in *.tif or *.jpg, min 300 dpi) must be submitted along with the biography in the
61 manuscript and separately during figure upload. Focused Reviews highlight and explain key concepts
62 of your work. Please highlight a minimum of four and a maximum of ten key concepts in bold in your
63 manuscript and provide the definitions/explanations at the end of your manuscript under Key Concepts.
64 Each definition has a maximum of 400 characters, including spaces.

4.4 HUMAN SEARCH AND ANIMAL RESEARCH

65 All experiments on live vertebrates or higher invertebrates must be performed in accordance with
66 relevant institutional and national guidelines and regulations. In the manuscript, authors must identify
67 the committee approving the experiments and must confirm that all experiments conform to the relevant
68 regulatory standards. For manuscripts reporting experiments on human subjects, authors must identify the
69 committee approving the experiments and must also include a statement confirming that informed consent
70 was obtained from all subjects. In Original Research Articles and Clinical Trial Articles these statements
71 should appear in the Materials and Methods section.

4.5 CLINICAL TRIAL REGISTRATION

72 Clinical trials should be registered in a public trials registry in order to become the object of a publication
73 at Frontiers. Trials must be registered at or before the start of patient enrollment. A clinical trial is defined
74 as "any research study that prospectively assigns human participants or groups of humans to one or more
75 health-related interventions to evaluate the effects on health outcomes." (www.who.int/ictcp/en).
76 A list of acceptable registries can be found at www.who.int/ictcp/en and www.icmje.org.

4.6 INCLUSION OF PROTEOMICS DATA

77 Authors should provide relevant information relating to how the peptide/protein matches were undertaken,
78 including methods used to process and analyze data, false discovery rates (FDR) for large-scale studies
79 and threshold or cut-off rates for peptide and protein matches. Further information could include
80 software used, mass spectrometer type, sequence database and version, number of sequences in database,
81 processing methods, mass tolerances used for matching, variable/fixed modifications, allowable missed
82 cleavages, etc.
83 Authors should provide as supplementary material information used to identify proteins and/or peptides.
84 This should include information such as accession numbers, observed mass (m/z), charge, delta mass,
85 matched mass, peptide/protein scores, peptide modification, miscleavages, peptide sequence, match rank,
86 matched species (for cross species matching), number of peptide matches, ambiguous protein/peptide
87 matches should be indicated, etc. For quantitative proteomics analyses authors should provide information
88 to justify the statistical significance including biological replicates, statistical methods, estimates of

89 uncertainty and the methods used for calculating error.
90 For peptide matches with biologically relevant post-translational modifications (PTM) and for any protein
91 match that has occurred using a single mass spectrum, authors should include this information as raw data,
92 annotated spectra or submit data to an online repository (recommended option). Authors are encouraged
93 to submit raw or matched data and 2-DE images to public proteomics repositories. Submission codes
94 and/or links to data should be provided within the manuscript.

4.7 DATA SHARING

95 Frontiers supports the policy of data sharing, and authors are advised to make freely available any
96 materials and information described in their article, and any data relevant to the article (while not
97 compromising confidentiality in the context of human-subject research) that may be reasonably requested
98 by others for the purpose of academic and non-commercial research. In regards to deposition of data and
99 data sharing through databases, Frontiers urges authors to comply with the current best practices within
100 their discipline.

DISCLOSURE/CONFLICT-OF-INTEREST STATEMENT

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

ACKNOWLEDGEMENT

[illegible]

105 *Funding:* Text Text Text Text Text Text Text Text.

SUPPLEMENTAL DATA

[illegible]

REFERENCES

- 108 Bassett, D. S., Brown, J. A., Deshpande, V., Carlson, J. M., and Grafton, S. T. (2011) Conserved and
109 variable architecture of human white matter connectivity. *Neuroimage* 54 1262–1279. doi:10.1016/j.
110 neuroimage.2010.09.006.
- 111 Cheng, H., Wang, Y., Sheng, J., Kronenberger, W. G., Mathews, V. P., Hummer, T. A., et al.
112 (2012) Characteristics and variability of structural networks derived from diffusion tensor imaging.
113 *Neuroimage* 61 1153–1164. doi:10.1016/j.neuroimage.2012.03.036.
- 114 Irimia, A. and Van Horn, J. D. (2012) The structural, connectomic and network covariance of the human
115 brain. *Neuroimage* 66C 489–499. doi:10.1016/j.neuroimage.2012.10.066.
- 116 Owen, J. P., Ziv, E., Bukshpun, P., Pojman, N., Wakahiro, M., Berman, J. I., et al. (2013) Test-
117 retest reliability of computational network measurements derived from the structural connectome of
118 the human brain. *Brain Connect* 3 160–176. doi:10.1089/brain.2012.0121.