What is the best method for robust statistical inference on connectomic graph metrics?

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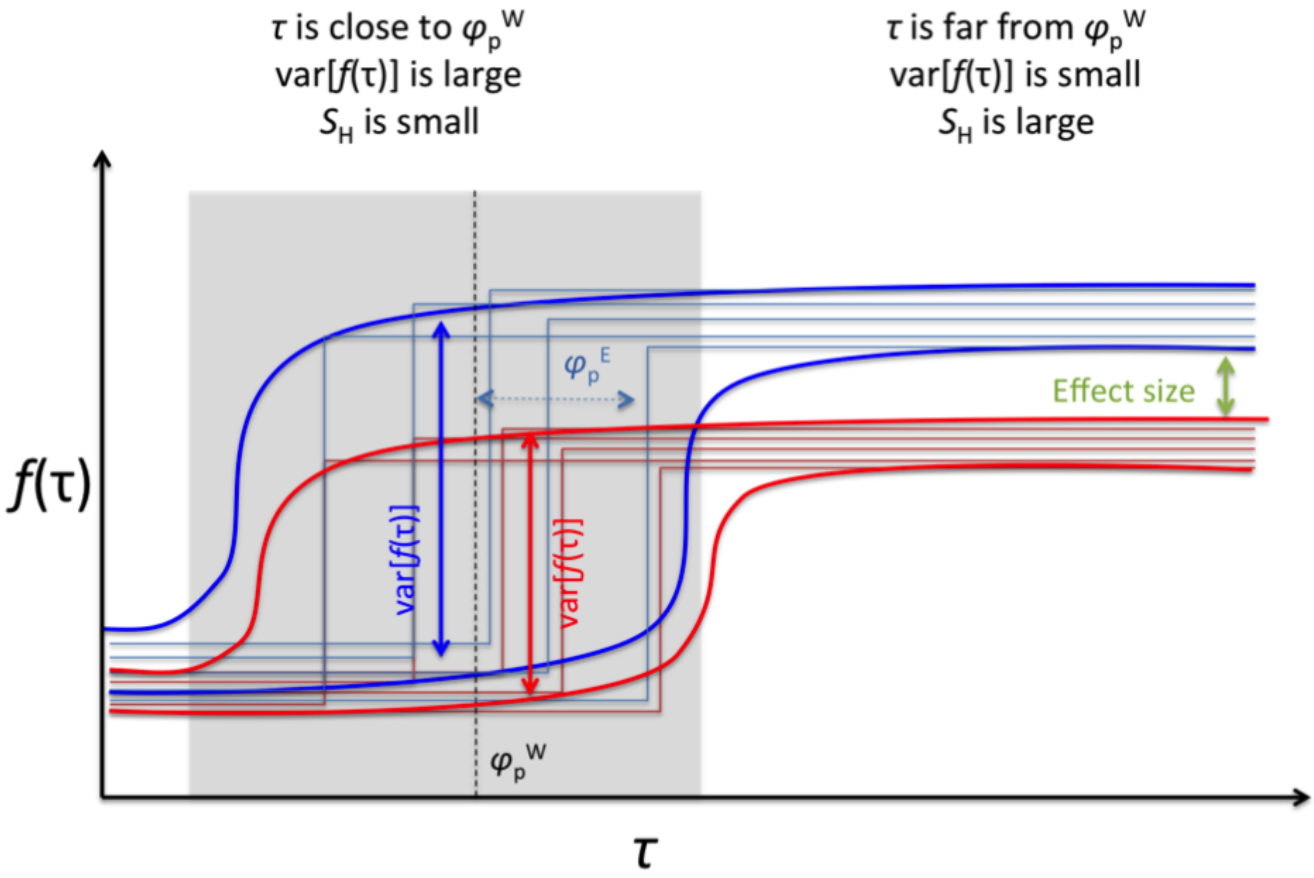
E-Poster

Introduction:

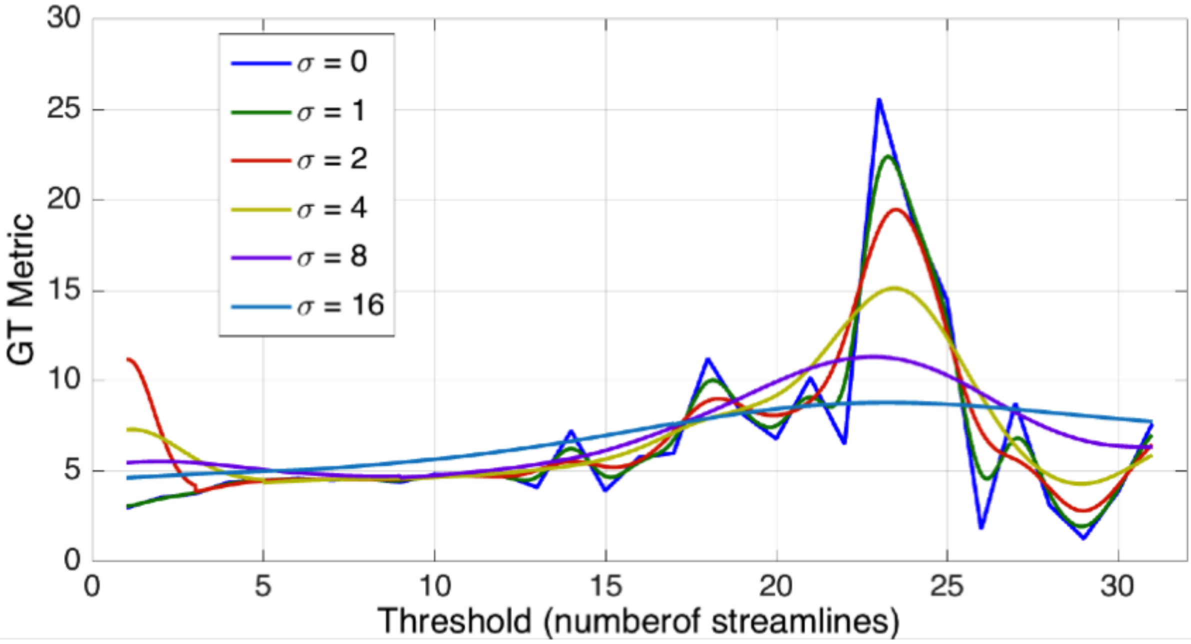
Network, or graph theoretical, analyses are a powerful and increasingly utilised tool for studying brain connectomics (1). However, graph metrics are highly sensitive to various parameters and as such are highly unstable (2–4). Large phase transitions in topology can lead to instability and regions of high variance across thresholds (fig. 1) (4,5). A common approach to analysing graph metrics is to compute the area under the curve (AUC) across thresholds, e.g. (6). However, this can dilute inferred effects if true effects only manifest in narrow threshold ranges, which is often the case (4). A more recent development is multi-threshold permutation correction (MTPC) (4), which agnostically identifies limited but sustained effects across different threshold levels. However, this method is computationally expensive. A potentially less costly approach is to compute smoothed AUCs (smAUCs). Theoretically, this will smooth out narrow effects across a wider range of thresholds while also reducing the high variance around phase transitions. However, this approach is yet to be tested.



·Fig.1. Toy example of the effect of phase transitions ϕ on inferential statistics across thresholds (τ) for two groups (red and blue). Around such transition, the graph metric f(τ) has high variance.

Methods:

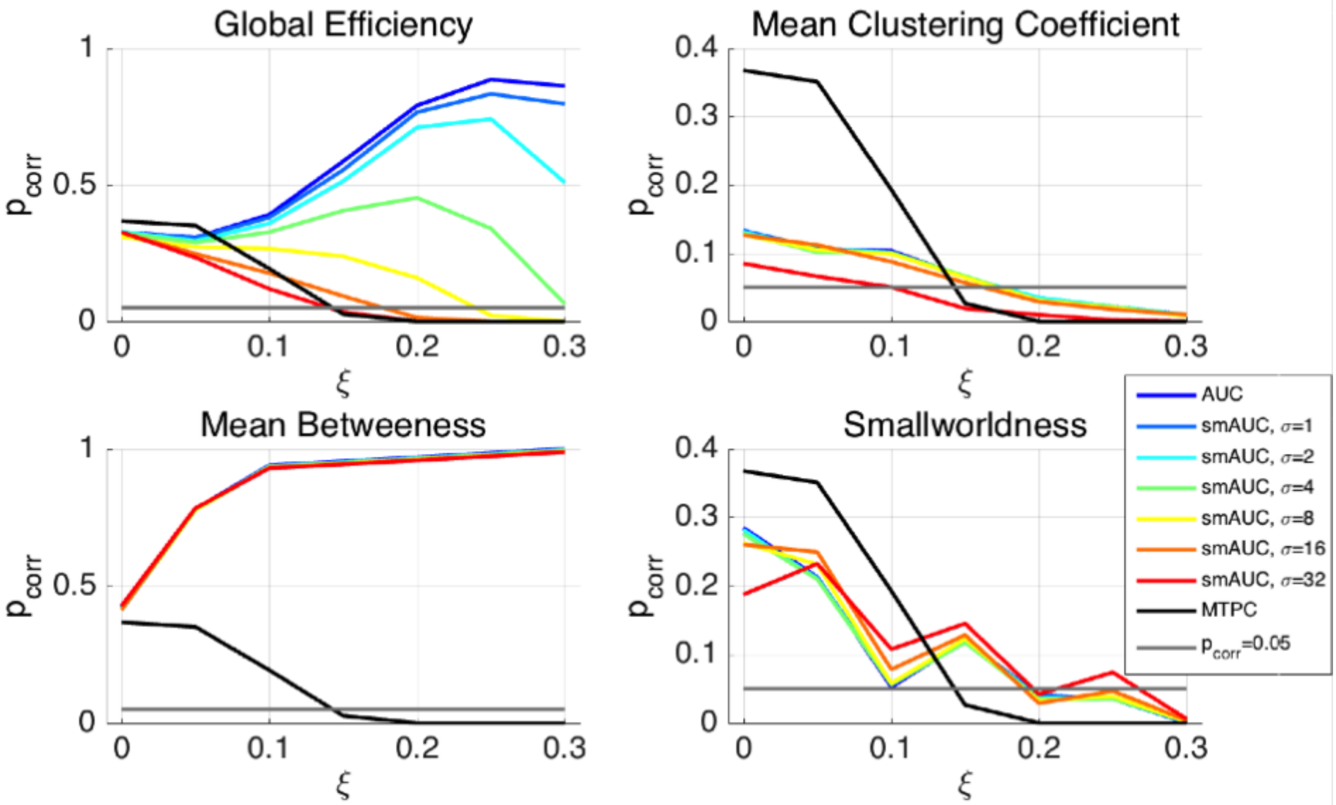
Connectomes for 248 subjects were constructed with deterministic tractography with the damped Lucy-Richardson algorithm (7) (step size = 1mm, angle threshold = 45°, seed point resolution = 2mm², length threshold=20–500mm, FOD threshold = 0.05, β =1.77, λ = 0.0019, η = 0.04), from 60 direction HARDI acquisition (cardiac gated, b=1200s/mm², TE=87 ms, 60 slices, FoV=230×230mm, acquisition matrix=96×96, 2.4mm³ isotropic resolution). Connectivity was inferred between cortical regions of the automated atlas labelling (AAL) atlas (8), with additional a priori anatomical constraints to eliminate spurious streamlines. The datasets were randomly assigned to a 'healthy' or a 'lesioned' group. In the lesioned group a proportion of inter-hemispheric streamlines were removed from the connection (Gaussian distribution with standard deviation ξ, ranged from 0:0.05:0.3). The larger ξ is, the larger the effect size. Four graph metrics were tested: global efficiency, mean clustering coefficient, mean betweenness and smallworldness. Graph metrics were computed across streamline counts of 0:1:30. smAUCs were computed with Gaussian smoothing kernels with FWHMs of σ = 0, 1, 2, 4, 8, 16 and 32 (fig. 2). Permutation-corrected p-values (p_{corr}) were obtained from 500 randomisations. MTPC was also performed across the same threshold range and the same randomisation indices. The sensitivity of each method was assessed from the minimum value for ξ at which $p_{corr}<0.05$. ···



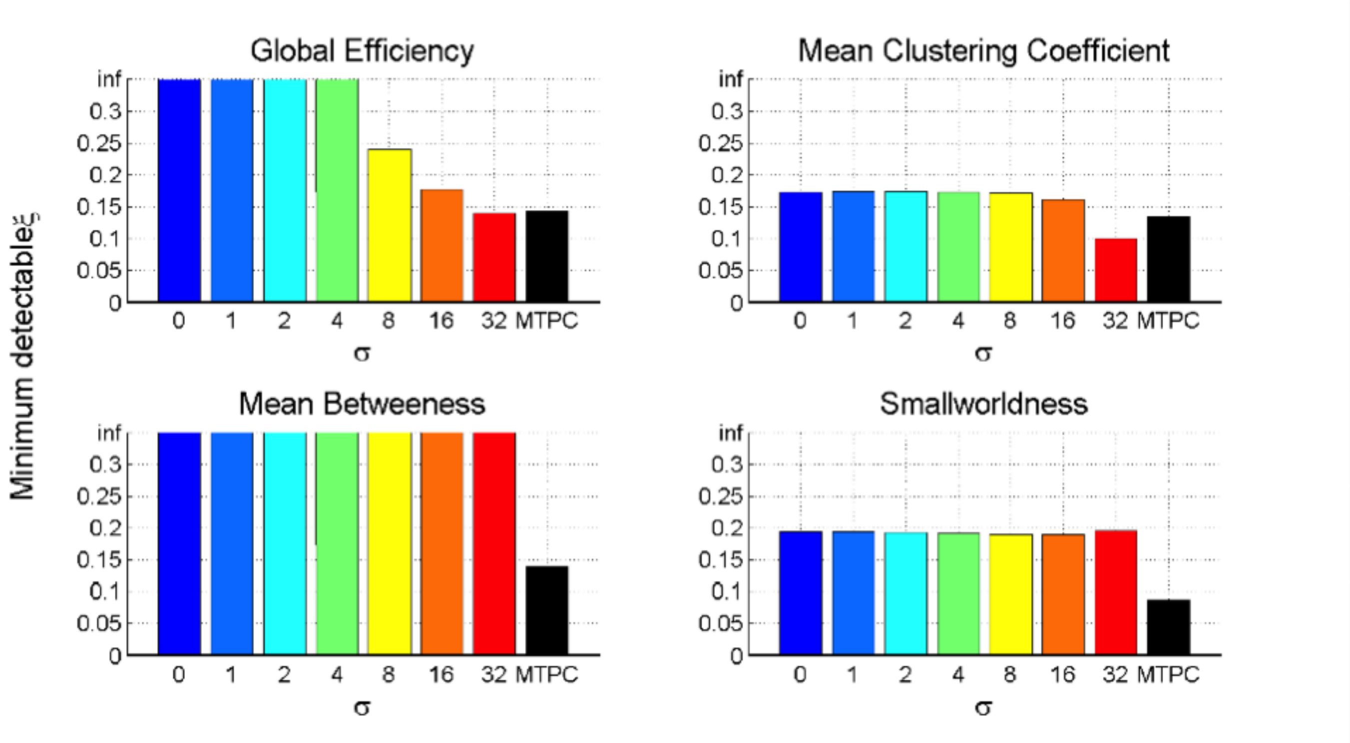
·Fig.2. Examples of smoothing kernels (with FWHM σ) applied to graph metrics across thresholds.

Results:

In most cases, the MTPC method was sensitive to similar or smaller ξ than the smAUC method (fig. 3, 4). The only exceptions is mean clustering coefficient where the smAUC with σ=32 was more sensitive. In most cases, the smoothing kernel made no improvement compared to the standard AUC method, although it does have an effect of increased sensitivity for global efficiency.



·Fig.3. p_corr values across ξ for the four graph metrics and inference methods (smAUC and MPTC) tested.



·Fig.4. Minimum detectable ξ (at p_corr<0.05) for the smAUCs across smoothing kernels and MTPC. For any comparisons where no threshold satisfies _corr <0.05, minimum debatable ξ is treated as infinite.

Conclusions:

MTPC provides robust testing of statistical effect on graph metrics, allowing the identification of sustained but restricted effects across thresholds. The smAUC theoretically does the same smoothing localised effect across larger ranges of thresholds but without the computational demands of MTPC. However, smAUC does not prevent dilution of the true effect by regions where true effects are hidden due to high variance and does not provide consistently comparable performance compared to MTPC. smAUC shows comparable performance with Global efficiency. This may be explained by this metric being less susceptible to phase transition effects. This indicates that the effect of phase transitions cannot be effectively overcome with smoothing and a more exhaustive search of the threshold space is still required. These results have implications for statistical connectomic network analyses of neuroimaging data, especially in comparison where differences in network topology are expected to be subtle.

Imaging Methods:

Diffusion MRI [2]

Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis [1]

Poster Session:

Poster Session - Monday

Keywords:

Data analysis
Statistical Methods
Tractography
Other - Graph theory, connectomics, network analysis

[1|2]Indicates the priority used for review

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Please indicate which methods were used in your research:

Diffusion MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL
Other, Please list - ExploreDTI

Provide references in author date format

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