Continuous Connectomics: An Exploratory Framework for Connectivity Analysis in Brain Imaging

Boris A. Gutman, Neda Jahanshad, Derek Hiber, Cassandra Leonardo, Kristian Eschenburg, Talia Nir, Julio Villalon-Reina, Paul M. Thompson

Imaging Genetics Center, Institute for Neuroimaging & Informatics, University of Southern California, Los Angeles, CA, USA.

Motivation: matching connectomes across different brains

- Structural connectivity may be a better indicator of functional role of brain regions than gross anatomy alone
- Matching connectivity profiles across brains may therefore improve brain surface registration
- Current connectivity analysis assumes a small discrete graph – not flexible enough for connectome matching

Method

1. Pre-processing
   - Tractography with Hough Transform [1]
   - Cortical Surface extraction with Freesurfer

2. Continuous Connectome
   - Treat each fiber as an observation in a connectome space
   - Use kernel density estimation to compute a continuous connectivity profile for each brain:
     \[ K(x, y) = \sum_{1 \leq k \leq N_{\text{fibers}}} G_\sigma(x, p_k) G_\sigma(p_{k, y}). \]

3. Eigen-network matching
   - Eigenfunctions of the connectome kernel (eigen-networks) fully describe the connectome per Mercer’s Theorem: \[ K(x, y) = \sum A_i \epsilon_i(x) \epsilon_i(y). \]
   - By projecting networks of one person’s brain into appropriate eigenspaces of another we can match networks between individual brains.

4. Connectome-based cortical surface registration
   - Registering connectomes reduces to multi-channel registration:
     \[ C(M, f) = \int \sum_{k \in M} \int \left| w_k \right| \left| e_{ik}(x) - e_{j}(f[x]) \right|^2 dx. \]

5. Continuous Connectomics
   - Continuous Nodal degree (connectedness):
     \[ k(x) = \int K(x, y) dy = K(x, x) \]
   - Continuous Clustering Coefficient:
     \[ C(x) = \frac{2d(x)}{\left| \text{deg}(x) \right| \left( \text{deg}(x) - 1 \right)}, \]
     where \( t(x) = \int \left| K(x, y) K(x, z) K(y, z) \right|^{1/3} dydz. \]

References


Data

ADNI 2 dataset: 64-direction DTI images & T1-weighed images for cortical surface extraction. 48 Alzheimer’s patients. 50 age-matched controls.

Results

1. Visualizing individual fiber model contribution to the continuous connectome

2. Matched eigen-networks (right)

3. Connectome registration
   - Spherical fluid framework [2]
   - Connectome mismatch reduced compared to purely anatomical registration:

<table>
<thead>
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<th>Anatomy only</th>
<th>Anatomy + connection</th>
<th>Individual improvement</th>
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<tr>
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<td>0.628</td>
<td>0.43</td>
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<td>kernel</td>
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<td>+/-0.089</td>
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4. Sensitivity of continuous connectomics to Alzheimer’s Disease

Both measures passed False Discovery Rate (FDR) correction. Connectedness: \( q = 1.0 \times 10^{-3} \) for the right hemisphere, and \( q = 1.9 \times 10^{-3} \) for the left. Clustering coefficient: \( q = 1.7 \times 10^{-3} \) for the right hemisphere and \( q = 2.6 \times 10^{-5} \) for the left.

Conclusion

We have presented a framework for fusing connectivity information with cortical surface anatomy for a joint connectivity analysis. There are four distinct contributions: (1) the definition of a continuous connectome space and a method for estimating continuous kernels from fiber models; (2) an algorithm for defining a mutual connectome shared by two brains; (3) a spatial correspondence search between two connectome kernels, directly registering the brains’ structural connectivities; (4) an adaptation of graph theory measures to the continuous setting.