Rich-Club Organization of the Human Connectome

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September 13, 2016
Motivation: To map out both the subcortical and neocortical hubs of the brain and ...
Introduction

Motivation: To map out both the subcortical and neocortical hubs of the brain and examine their mutual relationship, particularly their structural linkages in terms of

- Rich-club organization
- s-core computation
- Modularity and network perturbations
- Various other graph metrics
- Discuss functional implications of the rich-club organization
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![Network Diagrams](a) (b)
“Rich-club” phenomenon in networks is said to be present when the *hubs of a network* tend to be more densely connected among themselves than nodes of a lower degree.

Which of the following networks do you observe the rich-club phenomenon?

- Observed in power-grids
Datasets

- Diffusion tensor imaging (DTI) data of 21 healthy individuals [mean age (SD), 29.95 (8.3) years; 15 males, 6 females]
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- What is DTI?
Diffusion Tens or Imaging

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- Diffusion Tensor Imaging (DTI) uses six or more such DWIs oriented in different directions in the 3D-space to compute a diffusion tensor. We compute the D matrix for each voxel.

\[
D = \begin{bmatrix}
D_{xx} & D_{xy} & D_{xz} \\
D_{yx} & D_{yy} & D_{yz} \\
D_{zx} & D_{zy} & D_{zz}
\end{bmatrix}
\]
• There are multiple ways in which we can go from diffusion tensors to white matter fibers, most commonly used technique is ”Fractional Anisotropy”
Diffusion Tensor Imaging

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\[ D = \lambda_1 e_1 \cdot e_1 + \lambda_2 e_2 \cdot e_2 + \lambda_3 e_3 \cdot e_3 \]

\[ e_i = \begin{bmatrix} e_{ix} \\ e_{iy} \\ e_{iz} \end{bmatrix} \]
There are multiple ways in which we can go from diffusion tensors to white matter fibers, most commonly used technique is "Fractional Anisotropy".

Fractional anisotropy (FA) is a scalar value between zero and one that describes the degree of anisotropy of a diffusion process. (Isotropic diffusion is one where the magnitude of diffusion is same along any direction.)

**Isotropic diffusion:**
\[ \lambda_1 \approx \lambda_2 \approx \lambda_3 \]

**Anisotropic diffusion:**
\[ \lambda_1 \gg \lambda_2 \approx \lambda_3 \]
Diffusion Tensor Imaging

- FA measures the fraction of the diffusion that is anisotropic. This can be thought of as the difference of the tensor ellipsoid’s shape from that of a perfect sphere. FA is basically a normalized variance of the eigenvalues.

- Alternate ways exist, but FA gives better contrast

\[
\begin{align*}
\lambda_1 &= \text{longitudinal (axial) diffusivity (AD)} \\
\frac{\lambda_2 + \lambda_3}{2} &= \text{radial diffusivity (RD)} \\
\frac{\lambda_1 + \lambda_2 + \lambda_3}{3} &= \text{mean diffusivity (MD)} \\
\sqrt{\frac{1}{2} \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}} &= \text{fractional anisotropy (FA)}
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Diffusion Tensor Imaging

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We can then track the axon fibers using the diffusion tensors and map the white matter in the brain. It **does not** map individual axons, it only maps the axon bundles!
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- The brain was segmented into 82 brain regions, consisting of 68 cortical regions (34 in each hemisphere) and 14 subcortical regions (7 in each hemisphere)
Datasets

- Generated four connectivity matrices for nodes from parcellation and edges from DTI data. Of the reconstructed fiber streamlines 53% connected different brain regions.

- Unweighted network - $M_{unw}$

- Weighted by streamline count - $M_{w}^{nos}$

- Weighted by streamline count, corrected for ROI volume - $M_{w}^{nosROI}$

- Weighted by FA - $M_{w}^{FA}$: for each of the existing connections between region $i$ and region $j$ the average FA was computed as the mean of the FA values of all included streamlines

- Generated group averaged networks
  - Unweighted: By selecting all connections that were present in at least 75% of the group of subjects
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- Alternate parcellation with 1170 nodes (unweighted)
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• Are all these graphs directed or undirected?
**Strength & Betweenness**

- **Strength,** $k_i$, of a node $i$: sum of edge-weights of the edges incident up on node $i$. Equivalent to ‘degree of a node in an unweighted network’.

![Graphs showing examples of degree and strength calculations.](image)
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• Betweenness centrality: Calculate the shortest path between each pair of nodes. Then for each node, calculate how many of the computed shortest paths go through that node (excluding the paths to or from that node).
Results - strength & betweenness

node specific graph metrics (NOS weighted)
Path length & Centrality

- Avg. path length of a node: Avg. of all shortest path lengths from a node to every other node in the network
Path length & Centrality

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• Clustering coefficient $C(v) = \frac{2}{k_i(k_i-1)} \sum_{j,k \in N_v} (w_{ij}w_{ik}w_{jk})^{1/3}$
  • Where, $k_i$ is the strength of a node
Results - Path length & Centrality

path length

c

clustering

d
Rich-club coefficient - Unweighted Network

• For a given graph $M$, determine the degree of each node $i$ in the network
Rich-club coefficient - Unweighted Network

- For a given graph $M$, determine the degree of each node $i$ in the network
- Rich-club coefficient $\phi(k) = \frac{2E_{>k}}{N_{>k} (N_{>k} - 1)}$
  - where, $E_{>k}$ is the number of edges in $M$ between nodes of degree greater than $k$
  - $N_{>k}$ is the number of nodes with degree greater than $k$

Why are we normalizing it?
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• Rich-club coefficient $\phi(k) = \frac{\sum_{i=1}^{E_{>k}} W_i}{\sum_{i=1}^{E_{>k}} W_i}$

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  - where, \( E_{>k} \) is the number of connections between the nodes with a degree greater than \( k \)
- Compute \( \phi_{\text{norm}}(k) = \frac{\phi(k)}{\phi_{\text{random}}(k)} \)
  - How do we generate weighted random networks? Is the ‘weighted degree distribution’ preserved?
Example - Rich-club coefficient

\[ E_{>3} = 3 \]

\[ W_{>3} = 4 + 2 + 2 = 8 \]

\[ \sum_{l} W_{i}^{r} = 4 + 4 + 2 = 10 \]

\[ \Phi(3) = \frac{8}{10} = 0.8 \]
Example - Rich-club coefficient

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\[ W_{>3} = 2 + 1 + 1 = 4 \]

\[ \sum_{i}^{E_{>3}} W_i^r = 4 + 4 + 2 = 10 \]

\[ \Phi(3) = \frac{4}{10} = 0.4 \]
Results - Rich-club coefficient

a

b

c

d
Results - Rich-club coefficient, Group Averaged, NOS-weighted
Results: High-Resolution Connectome

(a) rich-club high resolution
1170 regions

(b) $\Phi_{ND, \text{weighted}}$

(c) $k$

(d) $\Phi_{\text{norm}}$
A $k$-core of an unweighted graph $G$ is a maximal connected subgraph of $G$ in which all vertices have degree at least $k$. Equivalently, it is one of the connected components of the subgraph of $G$ formed by *repeatedly* deleting all vertices of degree less than $k$. 
$k$-core and $s$-core

$G$ is its own 0-core.

The 1-core of $G$.

The 2-core of $G$.

The 3-core of $G$ is $2K_4$.

Figure 1: An example of the cores of a graph.
$k$-core and $s$-core

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- The $s$-core of a weighted graph $G$ is the subgraph of nodes of $G$ in which all connections show a summed weight of $s$ or higher.

- For each node $i$ in the network its core-level can be determined, as the maximal $s$-core node $i$ is participating in.

- Do you think the ‘rich’ nodes are in the $s$-core (for some large value of $s$)?
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Results: $s$-core, Group Averaged, NOS-weighted
Global Efficiency (GE)

- Global efficiency measures the rate at which information is passed through the network

\[ GE = \frac{1}{n} \left( \sum_{i=1}^{n} \sum_{j \neq i} d_{ij} \right) \]

where, 
- \( i \) and \( j \) are nodes in \( G \)
- \( d_{ij} \) is the shortest path length between two nodes
Global Efficiency (GE)

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\[ E_G = \frac{1}{n(n-1)} \sum_i \sum_{j \neq i} \frac{1}{d_{ij}} \]

- Where, \( i \) and \( j \) are nodes in \( G \).
- \( d_{ij} \) is the shortest path length between two nodes \( i \) and \( j \).
- It is a measure comparable to inverse of avg. path length.
Rich club in targeted and random attack

• “Network attack”
Rich club in targeted and random attack

- “Network attack”
- In this paper they reduced the edge weights (to 50% and 100% of their original value) for:
  - Edges interconnecting rich-club nodes
  - Edges connecting rich-club nodes to other nodes in the network
  - Randomly chosen edges
  - Computed GE before and after the perturbation for $M_{w_{nos}}$
  - Analyzed the normalized GE wrt the GE value before perturbation
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Rich club in targeted and random attack

a) Toy network

- RC connection
- Hub connection
- Other
- Rich-club nodes
- Non rich-club

b) Percentage of total GE

- Random attack
- Random attack hub connections
- Targeted RC attack

p < 0.0001

50%

100%

c) Total damage to network

- 50%
- 100%
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Rich club centrality

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  - 89% of all shortest paths between all non-rich-club regions in the network passed through one or more of the rich-club nodes
  - Almost 66% of the shortest paths between any two non-rich-club nodes in the network were found to pass through one or more of the rich-club edges (i.e., using at least two RC nodes). For randomly chosen edges, this number was only 4% on average.
  - Rich-club nodes and edges are central!
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  - Almost 66% of the shortest paths between any two non-rich-club nodes in the network were found to pass through one or more of the rich-club edges (i.e., using at least two RC nodes). For randomly chosen edges, this number was only 4% on average.

- Rich-club nodes and edges are central!
How did the authors identify network modules in this paper?

The four network modules in this paper are based on brain anatomy (two anterior and two posterior).

Analyzed nodes for their 'participation in the modules' $P_{\text{index}, i} = \frac{1}{N_{\text{mod}}} (k_{im} k_i)$

where, $k_{im}$ is the strength of the edges from node $i$ to module $m$.

When is $P_{\text{index}, i} = 0$ and what is the maximum value it can take?

Connector Nodes: if $P_{\text{index}, i} > 0$.

Provincial Nodes: if $P_{\text{index}, i} \leq 0$.

The threshold 0.5 marks the top 15% of the node-specific $P_{\text{index}}$ values across the 82 nodes of the network.
Modularity, provincial and connector hubs

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Modularity of a Network

- Designed to measure the strength of division of a network into modules

\[
\text{Modularity (unweighted), } Q = \frac{1}{m} \sum_{i,j} (a_{ij} - d_i d_j) \left( \frac{m_i m_j}{m} \right)
\]

- Where, \(2m\) is the sum of all node degrees
- \(d_i\) is the degree of node \(i\)
- \(\left( \frac{m_i m_j}{m} \right) = 1\) if \(m_i = m_j\) (i.e., nodes are in the same module)

The formula computes “difference between the actual and expected number of edges connecting nodes of the same type”.

The modularity takes positive values if there are more edges between same-type vertices than expected, and negative values if there are less.
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- Networks with high modularity have dense connections between the nodes within modules but sparse connections between nodes in different modules

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  • In social networks, nodes tend to be connected with other nodes with similar degree values
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• A measure of assortativity is the number of edges that run between vertices of the same type minus the number of such edges we would expect to find if the edges were positioned at random while preserving the vertex degrees
Graph Metrics Summary

Table 1. Graph metrics of group-averaged connectome and individual networks

<table>
<thead>
<tr>
<th>Graph measures</th>
<th>Group-averaged network</th>
<th>Individual networks&lt;sup&gt;a&lt;/sup&gt;</th>
<th>1170 nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unweighted</td>
<td>NOS weighted</td>
<td>NOS-ROI weighted</td>
</tr>
<tr>
<td>Clustering coefficient</td>
<td>0.57</td>
<td>208.9</td>
<td>0.017</td>
</tr>
<tr>
<td>Path length</td>
<td>2.33</td>
<td>0.0044</td>
<td>62.7</td>
</tr>
<tr>
<td>g</td>
<td>3.3</td>
<td>3.6</td>
<td>3.68</td>
</tr>
<tr>
<td>λ</td>
<td>1.17</td>
<td>1.21</td>
<td>1.40</td>
</tr>
<tr>
<td>Global efficiency&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.5017</td>
<td>303</td>
<td>0.022</td>
</tr>
<tr>
<td>Degree/strength</td>
<td>12</td>
<td>5.7 × 10&lt;sup&gt;3&lt;/sup&gt;</td>
<td>0.048</td>
</tr>
<tr>
<td>Assortativity</td>
<td>−0.036</td>
<td>0.070</td>
<td>0.154</td>
</tr>
<tr>
<td>Modularity</td>
<td>0.44</td>
<td>0.49</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Graph metrics validate the existence of the small-world topology of the connectome.

<sup>a</sup>Values represent mean ± SD.

<sup>b</sup>Non-normalized values.

- What are $g$ and $\lambda$?
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Conclusions

- The authors study the existence of rich-club organization in the human connectome. However observe that,
  - Upper and lower-bounds for rich-club phenomenon exist (shaded regions in rich-club plots)
  - Upper bounds actually mean there is no existence of rich-club phenomenon!
  - Due to DTI data collection, directionality information is missing
  - Different parcellations might result in different conclusions
  - Failure of a hub can have a severe effect on the level of global communication efficiency of a network, due to its central role in the network
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Fin. Thank YOU!