ECE 498LV – Network Science
Lecture 3

January 23, 2018
How does the brain work?
Analogies to Technology

- Mechanical devices like pianos, steam engine governors, water systems, city, enchanted loom
- Telephone exchange

- Electrical devices like phonographs, telegraphrepeaters, diodes, triodes, multi-vibrators, amplifiers
- Computer

Neuron Doctrine

• The neuron doctrine is the concept that the nervous system is made up of discrete individual cells
• Nerve cells are connected by sites of contact and not cytoplasmic continuity
Allometric Scaling

• Allometry studies the relationship between body size to shape. Goes back to D'Arcy Thompson’s *On Growth and Form* (1917)

• In neurobiology, one can look at allometric scaling relationships:
  – across different species with similar brain architectures [evolution],
  – scaling relationships for different individuals of same species [growth],
  – properties of the brain within the same individual [structure]

• The relationship between the two measured quantities is usually expressed as a power law equation:

  \[ y = kx^\alpha \]

  where \( \alpha \) is the scaling exponent of the law.

• How should we interpret superlinear \( (\alpha > 1) \) or sublinear \( (\alpha < 1) \) scaling?
Allometric Scaling

Encephalization quotient

\( E = CS^2 \), where \( E \) and \( S \) are body and brain weights
Allometric Scaling

Fig. 1. Brain weights of guinea pigs (*Cavia cobaya*)

Allometric Scaling

Scaling of the total basal cerebral metabolism with brain volume. The least-square fit line for the log – log plot yields the following. (A) For the total oxygen consumption rate, the scaling exponent was $0.86 \pm 0.04$ ($y = 0.86x - 1.02$, $R^2 = 0.989$, $p < 10^{-4}$, $n = 7$), and its 95% confidence interval was 0.75 to 0.96. (B) For the total glucose utilization rate, an identical exponent $0.86 \pm 0.03$ was found ($y = 0.86x - 0.09$, $R^2 = 0.994$, $p < 10^{-4}$, $n = 10$) and its 95% confidence interval was 0.80 to 0.91.

Are there common allometric scalings among different kinds of networks?
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<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Variable for City Highways</th>
<th>City Highway System Exponent</th>
<th>Variable for Neocortex</th>
<th>Neocortex Exponent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area</td>
<td>Land area</td>
<td>1</td>
<td>Total convoluted surface area</td>
<td>1</td>
</tr>
<tr>
<td>(a) No. of conduits</td>
<td>No. of highways</td>
<td>0.759 (± 0.083)</td>
<td>No. of pyramidal neurons</td>
<td>3/4 = 0.75</td>
</tr>
<tr>
<td>(b) Total no. of leaves</td>
<td>Total no. exits</td>
<td>1.138 (± 0.072)</td>
<td>Total no. of synapses</td>
<td>9/8 = 1.125</td>
</tr>
<tr>
<td>(c) No. of leaves per conduit</td>
<td>No. of exits per highway</td>
<td>0.379 (± 0.064)</td>
<td>No. of synapses per neuron</td>
<td>3/8 = 0.375</td>
</tr>
<tr>
<td>(d) Diameter of conduit</td>
<td>No. of highway lanes</td>
<td>0.174 (± 0.038)</td>
<td>Diameter of white matter axon</td>
<td>1/8 = 0.125</td>
</tr>
<tr>
<td>(e) Propagation velocity</td>
<td>Velocity of cross-city travel</td>
<td>0.108 (± 0.021)</td>
<td>Propagation velocity of white matter axon</td>
<td>1/8 = 0.125</td>
</tr>
<tr>
<td>(f) Total surface area of conduits</td>
<td>Total surface of highways</td>
<td>1.433 (± 0.096)</td>
<td>Total surface area of white matter axons</td>
<td>11/8 = 1.375</td>
</tr>
<tr>
<td>(g) No. of compartments</td>
<td>Population</td>
<td>1.462 (± 0.141)</td>
<td>Total volume of white matter axons</td>
<td>3/2 = 1.5</td>
</tr>
<tr>
<td></td>
<td>No. of concentric ring regions</td>
<td>0.390 (± 0.055)</td>
<td>No. of cortical areas</td>
<td>3/8 = 0.375</td>
</tr>
</tbody>
</table>
(Human) Connectomics
• A key challenge is that basic structural elements of the human brain, in terms of network nodes and connections, are difficult to define.
  – Parcellation

• Different kinds of structural descriptions could target at least three rather distinct levels of organization.
  – Microscale - the level of single neurons and synapses
  – Mesoscale - the level of neuronal groups or populations
  – Macroscale - the level of anatomically distinct brain regions and inter-regional pathways

• It is important to determine which level of description is the most appropriate for a given connectome application
Microscale

• With single neurons as the basic element, the size of the connectome is several orders of magnitude larger than of the genome, comprising roughly $10^{11}$ neurons and $10^{15}$ connections between them.

• Alterations of single synapses have not been shown to have macroscopic effects; human cognitive functions depend on the activity and coactivity of large populations of neurons in distributed networks.

• Individual neurons and connections are subject to rapid plastic changes, including synaptic weights as well as structural remodeling of dendritic spines and presynaptic boutons.
Macroscale

• Brain areas and neuronal populations are difficult to delineate: No single universally accepted parcellation scheme currently exists for human brain regions.

• Feasible to actually determine human connectome at this organizational level, but insufficient for a complete understanding of the human brain’s functional dynamics and information processing capabilities.

Diffusion Tensor Imaging (DTI) is an MRI-based neuroimaging technique which makes it possible to estimate the location, orientation, and anisotropy of the brain's white matter tracts.
Anatomical and Functional Connectivity
Pregnancy causes substantial changes in brain structure, primarily reductions in gray matter (GM) volume in regions subserving social cognition.

Changes were selective for the mothers and highly consistent, correctly classifying all women as having undergone pregnancy or not in-between sessions.

Speculate that the female brain undergoes a maturation or specialization of the neural network subserving social cognition during pregnancy.
The neuroscience of human intelligence differences

Ian J. Deary, Lars Penke and Wendy Johnson

Abstract | Neuroscience is contributing to an understanding of the biological bases of human intelligence differences. This work is principally being conducted along two empirical fronts: genetics — quantitative and molecular — and brain imaging. Quantitative genetic studies have established that there are additive genetic contributions to different aspects of cognitive ability — especially general intelligence — and how they change through the lifespan. Molecular genetic studies have yet to identify reliably reproducible contributions from individual genes. Structural and functional brain-imaging studies have identified differences in brain pathways, especially parieto-frontal pathways, that contribute to intelligence differences. There is also evidence that brain efficiency correlates positively with intelligence.
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Network efficiency
Describes short mean path lengths for parallel information transfer — as provided by a small-world network structure, for example.

In a resourceful use of the 79 healthy adults from REF. 82, Li and colleagues combined DT-MRI tractography and MRI with graph analysis to construct a global brain network. They found significant correlations between intelligence and parameters that reflect white matter network efficiency, indicating that not only the integrity, but also the organizational efficiency, of white matter is important for higher intelligence.
Speech Graphs Provide a Quantitative Measure of Thought Disorder in Psychosis

Natalia B. Mota¹,²,³, Nivaldo A. P. Vasconcelos¹,⁴,⁵, Nathalia Lemos¹, Ana C. Pieretti¹, Osame Kinouchi⁶, Guillermo A. Cecchi⁷, Mauro Copelli⁸, Sidarta Ribeiro¹
I walked into a place, and I found my grandma. I hugged her strongly, I woke up.

About dreaming
About waking

C

Schizophrenia

Control

Mania
Breakdown of Brain Connectivity Between Normal Aging and Alzheimer’s Disease: A Structural $k$-Core Network Analysis

Madelaine Daianu,$^1$ Neda Jahanshad,$^1$ Talia M. Nir,$^1$ Arthur W. Toga,$^1$ Clifford R. Jack, Jr.,$^2$ Michael W. Weiner,$^3,4$ and Paul M. Thompson,$^1$ for the Alzheimer’s Disease Neuroimaging Initiative$^*$
Brain connectivity analyses show considerable promise for understanding how our neural pathways gradually break down in aging and Alzheimer’s disease (AD). Even so, we know very little about how the brain’s networks change in AD, and which metrics are best to evaluate these changes. To better understand how AD affects brain connectivity, we analyzed anatomical connectivity based on 3-T diffusion-weighted images from 111 subjects (15 with AD, 68 with mild cognitive impairment, and 28 healthy elderly; mean age, 73.7 ± 7.6 SD years). We performed whole brain tractography based on the orientation distribution functions, and compiled connectivity matrices showing the proportions of detected fibers interconnecting 68 cortical regions. We computed a variety of measures sensitive to anatomical network topology, including the structural backbone—the so-called “k-core”—of the anatomical network, and the nodal degree. We found widespread network disruptions, as connections were lost in AD. Among other connectivity measures showing disease effects, network nodal degree, normalized characteristic path length, and efficiency decreased with disease, while normalized small-worldness increased, in the whole brain and left and right hemispheres individually. The normalized clustering coefficient also increased in the whole brain; we discuss factors that may cause this effect. The proportions of fibers intersecting left and right cortical regions were asymmetrical in all diagnostic groups. This asymmetry may intensify as disease progressed. Connectivity metrics based on the k-core may help understand brain network breakdown as cognitive impairment increases, revealing how degenerative diseases affect the human connectome.
Research article

Search for computational modules in the *C. elegans* brain

Markus Reigl¹, Uri Alon² and Dmitri B Chklovskii*¹
Figure 5. Subnetwork distributions for the gap junction network.

http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1001066
Triad Significance Profile

Normalized Z score

[Graph showing various subgraphs and significance profiles for different networks, including Transcriptional Networks, Signaling Networks, and Web Graphs.]

[Ron Milo, Shalev Itzkovitz, Nadav Kashtan, Reuven Levitt, Shai Shen-Orr, Inbal Ayzenshtat, Michal Sheffer, Uri Alon, “Superfamilies of Evolved and Designed Networks,” Science, 2004.]
Matrix methods for calculating the triad census

James Moody *

CB# 31210, Department of Sociology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
Connectomics

- Experimental phase: map out the wiring diagrams of neuronal networks
  - Electron micrographs to determine synaptic connections between neurons
  - In *C. elegans*, gap junction and chemical synapse connections
  - Unlike genomics, only a few individual *C. elegans* have been mapped

- Theoretical phase: try to infer function from structure
  - Compute several graph-theoretic functionals and determine statistical significance under various generative models
  - Apply systems-theoretic analysis
**Linear Systems Analysis**

- System stores energy (and information) in only one form and location: represent by linear, constant-coefficient differential equation

For single state variable $V_i$, canonical first-order, linear, constant-coefficient differential equation is:

$$\tau \frac{dV_i(t)}{dt} + L_{ii}V_i(t) = M(t),$$

where $\tau$ and $L_{ii}$ are fixed constants and $M(t)$ is some signal.

Natural (unforced) response of system is:

$$V_i(t) = V_0 e^{-L_{ii}/\tau t},$$

where $-L_{ii}/\tau$ is the eigenvalue determining decay time.
Linear Systems Analysis

Vector of states, $V(t) = [V_1(t) \quad V_2(t) \quad \cdots \quad V_N(t)]^T$:

\[
\tau \frac{dV_1(t)}{dt} + L_{11} V_1(t) + L_{12} V_2(t) + \cdots + L_{1N} V_N(t) = M_1(t)
\]

\[
\tau \frac{dV_2(t)}{dt} + L_{21} V_1(t) + L_{22} V_2(t) + \cdots + L_{2N} V_N(t) = M_2(t)
\]

\[
\vdots
\]

\[
\tau \frac{dV_N(t)}{dt} + L_{N1} V_1(t) + L_{N2} V_2(t) + \cdots + L_{NN} V_N(t) = M_N(t)
\]

which can be written in matrix-vector form as

\[
\tau \frac{dV(t)}{dt} + LV(t) = M(t).
\]
Linear Systems Analysis

Natural response with initial condition $V(t = 0) = V_0$ is vector:

$$V(t) = V_0 e^{(-L/\tau)t}.$$

- To examine, decouple system dynamics through eigendecomposition of $L$
- System moves in direction of eigenvectors with speed governed by eigenvalues
- Faster eigenvectors associated with larger eigenvalues
- Slower (more interesting) eigenvectors associated with smaller eigenvalues
  - Different from PCA/KLT in population genetics (Patterson, Price, and Reich, 2006), model selection (Hoyle, 2008), or denoising (Donoho, 1995).
A fast eigenvector shows that a left-right pair acts as a single unit on a timescale of 0.2ms.
A slow eigenvector (timescale 10ms) suggests the dynamics of a functional hub-and-spoke circuit mediating pheromone attraction, oxygen sensing, and social behavior (Macosko, Pokala, Feinberg, Chalasani, Butcher, Clardy, and Bargmann, 2009).
Closing Comments on \textit{C. elegans}

- Presented the beginnings of a theoretical phase to connectomics
- Introduced linear systems eigenanalysis as a principled methodology to infer functional circuits purely from structure