CS 4884: Brain Graphs

T. M. Murali

January 31, 2019
Creating Graphs

Node \equiv \text{Person}, \quad \text{Edge} \equiv \text{In same movie}
Creating Graphs

Node ≡ Person, Edge ≡ In same movie

Source: The Internet Movie Database & The Oracle of Bacon
Creating Graphs

Node $\equiv$, Edge $\equiv$
Creating Graphs

Node $\equiv$ Person, Edge $\equiv$ Follows on Twitter
Creating Graphs

Node $\equiv$, Edge $\equiv$
Creating Graphs

Node $\equiv$ Organism, Edge $\equiv$ Is eaten by

First trophic level:
- Photosynthesizers

Second trophic level:
- Decomposers
- Mutualists
- Pathogens, parasites
- Root-feeders

Third trophic level:
- Shredders
- Predators
- Grazers

Fourth trophic level:
- Higher level predators

Fifth and higher trophic levels:
- Higher level predators
Creating Graphs

Node ≡ , Edge ≡
Creating Graphs

Node ≡ Land mass, Edge ≡ Bridge
Graphs

Multiscale Brain

Microscale

Mesoscale

Macroscale

Node ≡ Intersection/Fork, Edge ≡ Street segment

T. M. Murali January 31, 2019 CS 4884: Computing the Brain
Node ≡ Intersection/Fork, Edge ≡ Street segment
Node ≡ \text{Intersection}, \quad \text{Edge} ≡ \text{Walkway/Unnamed road}
Graphs Multiscale Brain Microscale Mesoscale Macroscale

Node ≡ , Edge ≡

T. M. Murali January 31, 2019 CS 4884: Computing the Brain
Node ≡ “Intersection”, Edge ≡ Walkway/Unnamed road
How Do We Create Street Maps?

How Google Builds Its Maps—and What It Means for the Future of Everything

An exclusive look inside Ground Truth, the secretive program to build the world's best accurate maps

ALEXIS C. MADRIGAL | SEP 6, 2012 | TECHNOLOGY
How Do We Create Street Maps?

I was slated to meet with Gupta and the engineering ringleader on his team, former NASA engineer Michael Weiss-Malik, who'd spent his 20 percent time working on Google Mars, and Nick Volmar, an "operator" who actually massages map data.

"So you want to make a map," Weiss-Malik tells me as we sit down in front of a massive monitor. "There are a couple of steps. You acquire data through partners. You do a bunch of engineering on that data to get it into the right format and conflate it with other sources of data, and then you do a bunch of operations, which is what this tool is about, to hand massage the data. And out the other end pops something that is higher quality than the sum of its parts."

This is what they started with, the TIGER data from the US Census Bureau (though the base layer could and does come from a variety of sources in different countries).
How Do We Create Street Maps?

25th Anniversary of TIGER

TIGER is celebrating its 25th anniversary. The **Topologically integrated Geographic Encoding and Referencing** database—the first nationwide digital map of roads, boundaries, and other features—was initially created for the 1990 Census to modernize the once-a-decade head count. However, its impact went well beyond its initial purpose by offering common map data in electronic form that powers the geographic information system (GIS) industry today. Through its TIGER/Line products, the Census Bureau has provided the common geospatial framework for use in linking statistical and other data in GIS.

The idea for TIGER developed within the Census Bureau. In the 1970s mathematicians, geographers, and software developers designed a spatial data handling system that resembled one big spreadsheet. Custom-built solutions were the norm for most GIS software companies in the two decades leading up to TIGER's release. TIGER was like a giant
How Do We Create Street Maps?
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OpenStreetMap powers map data on thousands of web sites, mobile apps, and hardware devices.

OpenStreetMap is built by a community of mappers that contribute and maintain data about roads, trails, cafés, railway stations, and much more, all over the world.

Local Knowledge

OpenStreetMap emphasizes local knowledge. Contributors use aerial imagery, GPS devices, and low-tech field maps to verify that OSM is accurate and up to date.

Community Driven

OpenStreetMap’s community is diverse, passionate, and growing every day. Our contributors include enthusiast mappers, GIS professionals, engineers running the OSM servers, humanitarians mapping disaster-affected areas, and many more. To learn more about the community, see the OpenStreetMap Blog, user diaries, community blogs, and the OSM Foundation website.

Open Data

OpenStreetMap is open data: you are free to use it for any purpose as long as you credit OpenStreetMap and its contributors. If you alter or build upon the data in certain ways, you may distribute the result only under the same licence. See the Copyright and License page for details.
How Do We Correct Street Maps?

THE HUGE, UNSEEN OPERATION BEHIND THE ACCURACY OF GOOGLE MAPS

Inside Atlas, Google's map-editing program, operators can see where Street View cameras have captured images (colored dots), and zoom in with a spyglass tool. 📈 GOOGLE MAPS
How Do We Correct Street Maps?

Report an error on the map

If we need to add roads to Google Maps, or something on the map isn't right, you can tell us. Let us know if you notice errors in Google Maps such as:

- Incorrect road names
- Wrong info about one-way and two-way roads
- Incorrectly drawn road
- Road closures
- A road on the map doesn't exist
- Missing roads
- Wrong addresses or marker locations

Notes:

- To edit info about a business or landmark, you can suggest an edit.
- To update your business in Google Maps, you can edit the business listing.
- Learn how to set or change your address in Google Maps.
- You can only help us correct an error in Maps in some countries and regions.

Tell us about an error

1. On your computer, open Google Maps. Make sure you're signed in.
2. In the top left, click Menu > Send feedback > Edit the map.
3. Follow the instructions.
4. Click Submit.
How Do We Correct Street Maps?

People are still driving into lakes because their GPS tells them to

We’ve seen the “GPS directions gone awry” scenario play out on TV shows any number of times, but perhaps the most well-known example comes from an old episode of The Office where Michael and Dwight both ignore their common-sense instincts and instead blindly drive a car into a lake.

Recently, and rather unfortunately, a Canadian woman on the road had her own Michael Scott moment when, in the midst of a rainstorm and accompanying fog with low visibility, she followed her GPS’s driving directions — only to find herself in the middle of a freezing cold lake in Ontario.
Nodes and Edges

- Nodes and edges are elemental building blocks of networks.

What are the nodes and edges of brain graphs?

- Multiscale architecture of brain makes the answer challenging.
- There is no single, privileged scale for the analysis of brain networks.
- No single technology that can measure brain networks over all biologically relevant scales of space or time.
Multiscale Organisation of Brain Anatomy

Broad divisions: cortical lobes, cytoarchitectural areas

Neurons aggregate into columns, layers, and cell groups
Multiscale Organisation of Brain Anatomy

Neuronal processes such as dendritic trees and axons

Structure of individual fibers and dendritic spines
Multiscale Organisation of Brain Anatomy

N: neuron, BV: blood vessel, 
S: soma (cell body), Mi: mitochondria, My: myelinated axon, D: dendrite, 
Blue: glial processes, Red: presynaptic terminal, Green: dendritic spines, 
SV: synaptic vesicles, SC: synaptic cleft, SA: spine apparatus
Three Spatial Scales

- **Microscopic scale**: properties that are too small to resolve with the naked eye.
  - Require the use of microscopic techniques for visualization.
  - Scale that is synonymous with networks reconstructed at the level of individual neurons and synapses.

- Macroscopic scale: properties that can be resolved without the aid of microscopic methods.
  - Most commonly refers to analyses of structural and functional interactions between large-scale populations of neurons.
  - Characterized with MRI, MEG or EEG.

- Mesoscopic scale bridges the microscopic and macroscopic.
  - Analyses at this scale combine microscopic and macroscopic techniques.
  - Goal is to understand neuronal connectivity with high precision across the brain.

Techniques used at each scale constrain the way in which nodes and edges are defined.
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Three Types of Connectivity

- **Structural**: anatomical connections between neural elements
  - Example: axons and synapses between neurons at the microscale.
  - Example: Large-scale fiber bundles that link cortical areas and subcortical nuclei at meso- and macroscales.
  - Measured using techniques such as electron microscopy (micro), axonal tract-tracing (meso), and diffusion MRI (macro).

- **Functional**: statistical dependence between physiological recordings that have been acquired from distinct neural elements.
  - Example: Correlation between spiking output of two neurons.
  - Measured by mathematical definitions of correlations.

- **Effective**: direct, causal influence that one neural element exerts another's activity.
Spatiotemporal Resolution of Measurement Techniques

Open areas: measurement, filled areas: perturbation
Transmission electron microscopy (TEM): a beam of electrons is transmitted through a specimen to form an image.

Scanning electron microscopy (SEM): produce images of a sample by scanning the surface with a focused beam of electrons.
Structural Connectivity at the Microscale

Mouse cortex section: 40 μm × 20 μm × 30 nm.
Structural Connectivity at the Microscale
Structural Connectivity at the Microscale

Segmented neurons

Layout graph

Soma:
- Neuron ID,
- three-dimensional coordinates, type

Axonal branch:
- Neuron ID,
- three-dimensional coordinates, diameter

Dendritic branch:
- Neuron ID,
- three-dimensional coordinates, diameter

Synaptic junction:
- Pre- and postneuron ID,
- three-dimensional coordinates, number of vesicles

Connectivity graph
Graphs from Microscale Structural Connectivity

- Node $\equiv$ neuron, edge $\equiv$ synapse.
Graphs from Microscale Structural Connectivity

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- Reconstructing connectomes in this manner is computationally demanding, time-consuming, and labor intensive.
  - One cubic millimeter of rat cortex imaged with a resolution of a few nanometers will create 2PB of data.
  - A complete atlas of rat cortex ($\text{vol} \approx 500$ cubic mm) will require around 1 EB (1000 PB).
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  - Reconstructing nervous system of *C. elegans* took over 10 years (White et al., 1986).
  - State-of-the-art acquisition methods require 800 h to reconstruct 1 cubic mm of neural tissue.
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  - Accurate segmentation and annotation is difficult and tedious.
**Functional Connectivity at the Microscale**

- Why is functional connectivity (based on statistical dependence) important?

- **Cell assembly**: representation of multiple, distinct features of a stimulus as a coherent entity through the joint activity of distributed, interconnected neurons.

- Coordinated oscillatory activity mediates neuronal communication.

- Measure neuronal activity over time.
  - Classic method: Insert electrodes distinct parts of the brain to record the spiking activity of either individual or multiple cells.
  - Multi-electrode arrays: neurons cultured in vitro, i.e., in the lab.
  - Calcium imaging can map neuronal interactions across large distances with cellular resolution.
    - Measures intracellular calcium levels by introducing specific molecules.
    - Can sample only a restricted, superficial patch of cortex at any time.

- Define how to compute similarity or statistical dependence of two time series.
  - Pearson’s correlation coefficient. Read Box 2.2 on pages 50–51.
  - Rank correlation coefficients.
  - Mutual information.
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Microscale connectomics

- **Pro:** offers unparalleled precision for resolving synaptic connectivity and spiking activity of individual neurons
- **Con:** Techniques are not scalable to large-scale neural systems.
- **Con:** High plasticity of synaptic connectivity makes it difficult to distinguish stable characteristics of neuronal networks from more transient features.

Mesoscale connectomics

- **Pro:** Can smooth out some variability.
- **Pro:** Offers a more robust means for characterizing time-invariant aspects of brain architecture.
- **Con:** Not at the level of individual neurons.
- **Con:** Depends on the parcellation.
From Microscale to Mesoscale

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Defining Nodes at the Mesoscale

- Goal is to map connectivity between neuronal populations or cell assemblies, rather than individual neurons.
- Exploit aggregation of neurons that aggregate into populations that perform the same or related functions and are spatially proximal.
- Treat each volume as a node.
  - A volume may contain thousands or millions of cells.
  - Size of volume can which can range in size from cortical columns to larger cytoarchitectural areas and subcortical nuclei.
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  - A volume may contain thousands or millions of cells.
  - Size of volume can which can range in size from cortical columns to larger cytoarchitectural areas and subcortical nuclei.
- No gold standard for defining nodes; use approximations based on cytoarchitecture and anatomical landmarks.
- Coarse approach to defining nodes that results in the loss of information.
- Counterbalanced by an improved ability to map network structure over long distances.
Tracers for Structural Connectivity at the Mesoscale

- Invasive tract tracing is the main technique.
- A fluorescent dye or other tracer molecule injected into a specific part of the brain.
- Cellular membranes are permeable to these tracers.
- Once the tracer inside the cell, active axonal transport transfers it from the soma to peripheral axon terminals.
- After the tracer has had sufficient time to fill the entire extent, sacrifice the animal, dissect the brain, and determine sites of tracer uptake.
Types of Tracers

- Direction of transport distinguishes tracers.
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- **Anterograde tracers**: transported from the cell body to the axon terminal; used to map the efferent projection sites of an injected area.
- **Retrograde tracers**: transported from the cell periphery to the soma; used to map the upstream sources of afferent projections to the injection site.
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Viral tracers can cross synaptic junctions, allowing the mapping of polysynaptic pathways.
Structural Connectivity at the Mesoscale: Mouse

(a)

Results from a traditional tract tracing experiment
Modern experimental setup for whole-brain connectivity mapping
469 distinct tracer experiments

(b)
Structural Connectivity at the Mesoscale: Mouse

Example of connectivity matrix. Edge weights range over four orders of magnitude.
Parcellate the macaque cortex into 91 areas, defined according to cytoarchitecture and sulco-gyral landmarks.
Structural Connectivity at the Mesoscale: Macaque

Use retrograde tract tracing. Determine edges coming into node representing area of injection from “labelled” nodes representing neurons that the tracer reaches.
Structural Connectivity at the Mesoscale: Macaque

Injection is at $X$: $w(Y, X) = \frac{\text{number of neurons labelled in } Y}{\text{total number of labelled neurons}}$
Structural Connectivity at the Mesoscale: Macaque

Example of connectivity matrix. Edge weights range over six orders of magnitude.
Please read Chapter 2.2.2 of the textbook.
Experimental methods we have discussed so far for measuring brain connectivity are invasive.

- **Pro:** Offer in-depth access to neural structure and function.
- **Con:** Difficult to apply across the entire brain, particularly in larger animals and humans.
From Mesoscale to Macroscale

- Experimental methods we have discussed so far for measuring brain connectivity are invasive.
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- Use noninvasive imaging techniques (e.g., MRI, EEG, and MEG) at the macroscale.
  - Pro: Can map connectivity across the entire brain, *in vivo*, in animals and in humans.
  - Pro: Clinically safe, can be used for studies across lifespan and for brain disorders.

- Typical MRI has a voxel resolution of 1 cubic mm, which contains an estimated 20,000–30,000 neurons and billions of synapses.
- EEG and MEG have even lower resolution.
- Coarse spatial resolution means we must aggregate measurements over ever-larger populations of neurons, axons, and synapses.
- Reduces precision of node and edge definition.
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Defining Nodes at Macroscale

Each voxel is a node. Correlation between measurements for node pairs defines edges.
Defining Nodes at Macroscale

Cytoarchitectural atlases mapped to standard stereotactic space. (b) Macaque brain. (c) Human brain.
Parcellation Can Affect Network Properties
Parcellation Can Affect Network Properties

82 nodes, 500 nodes, 1000 nodes, 2000 nodes, 3000 nodes, 4000 nodes

Small-worldness

Nodes (parcellation scale)
Structural Connectivity at the Macroscale
Structural Connectivity at the Macroscale

(h) Deterministic

(i) Probabilistic
Structural Connectivity at the Macroscale
Structural Connectivity at the Macroscale
Functional Magnetic Resonance Imaging

fMRI - How it Works and What it’s Good For, Video, 6:41”
Functional Connectivity at the Macroscale
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(d)