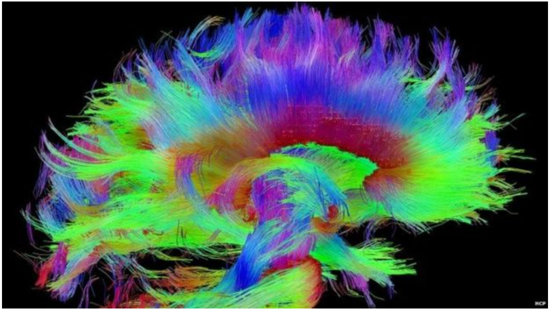
CS 4884: Brain Graphs

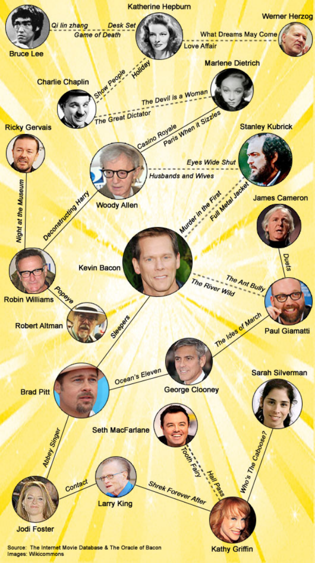
T. M. Murali

January 30, 2020



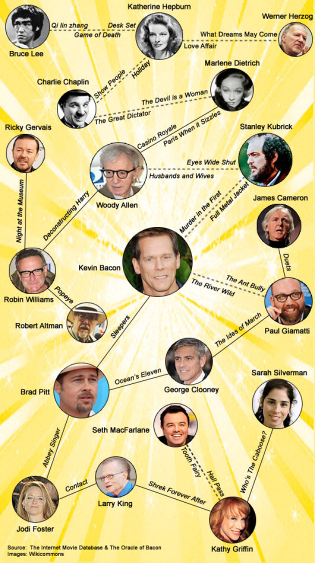
Creating Graphs

Node ≡ , Edge ≡



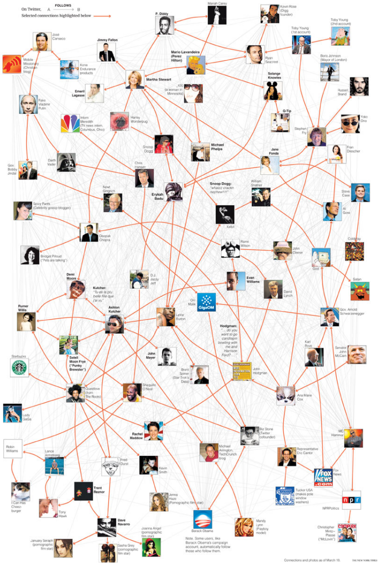
Creating Graphs

Node ≡ Person, Edge ≡ In same movie



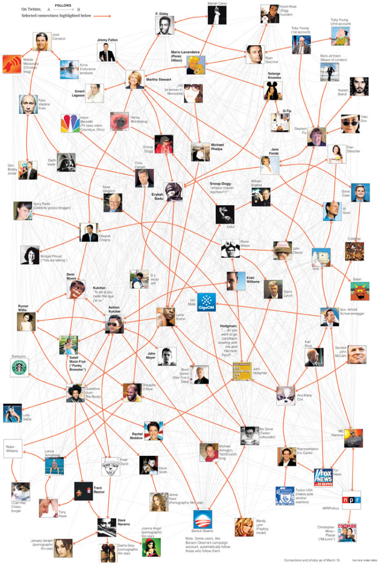
Creating Graphs

Node ≡ , Edge ≡



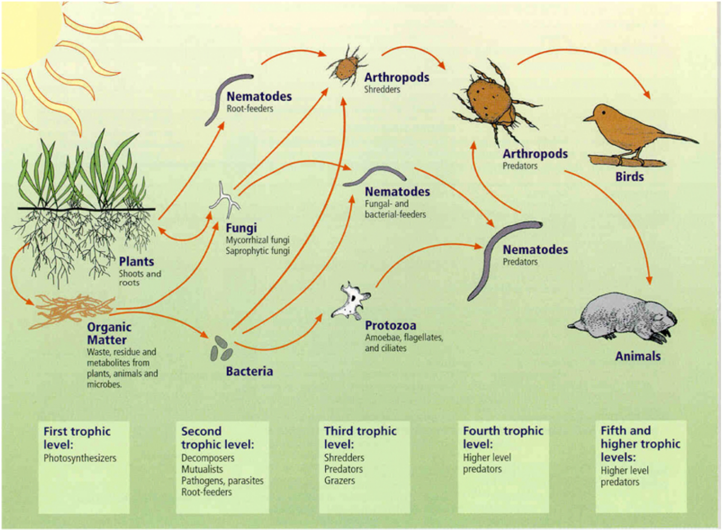
Creating Graphs

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



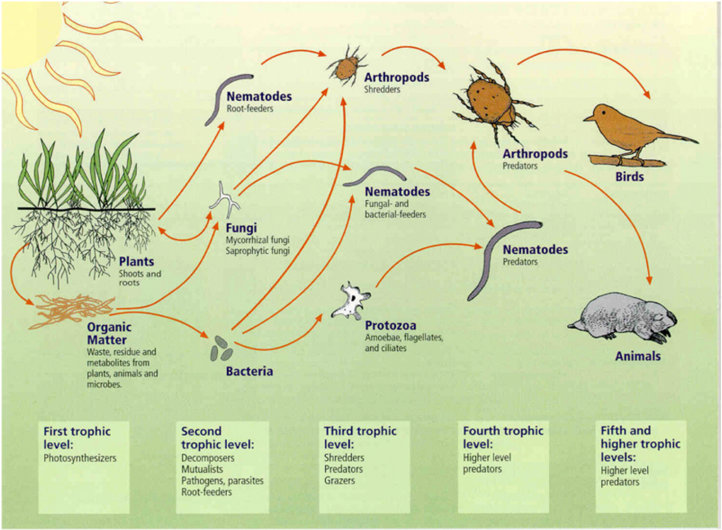
Creating Graphs

Node ≡ , Edge ≡



Creating Graphs

Node ≡ Organism, Edge ≡ Is eaten by

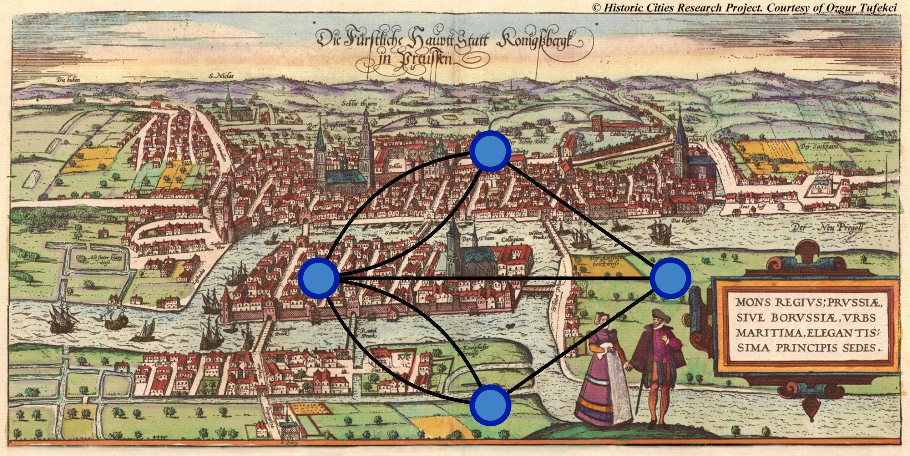


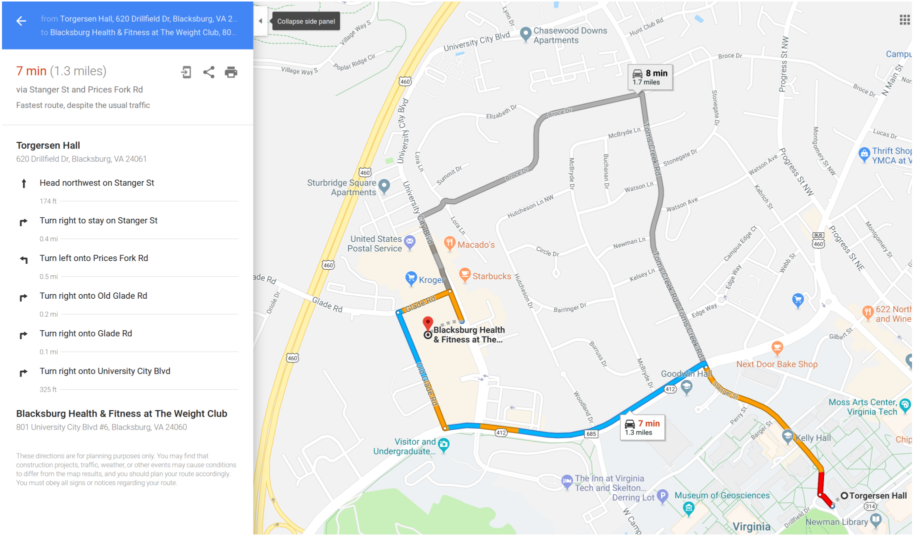
Creating Graphs

Node ≡ , Edge ≡

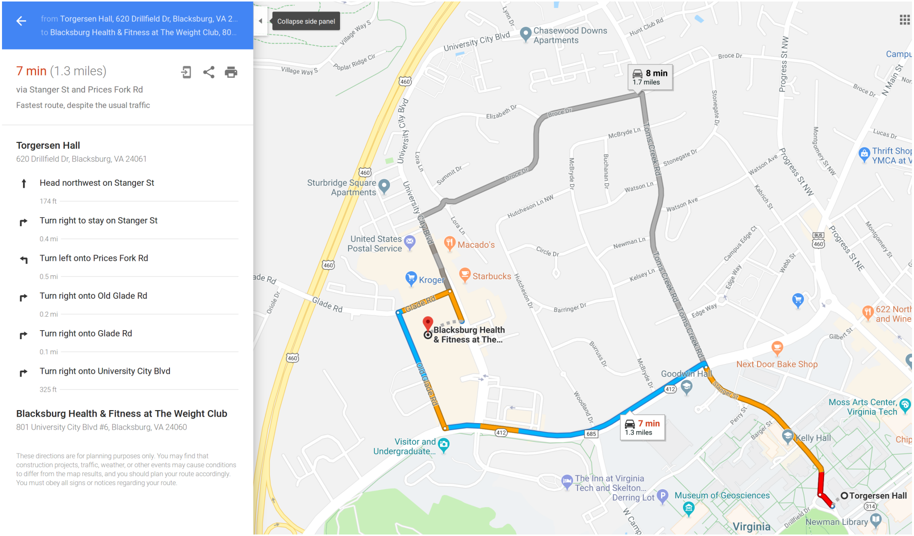
Creating Graphs

Node ≡ Land mass, Edge ≡ Bridge

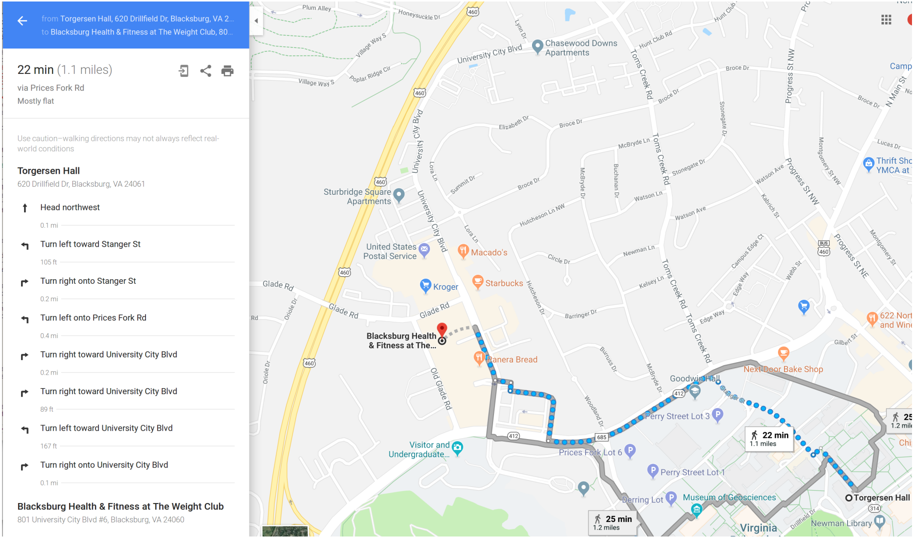




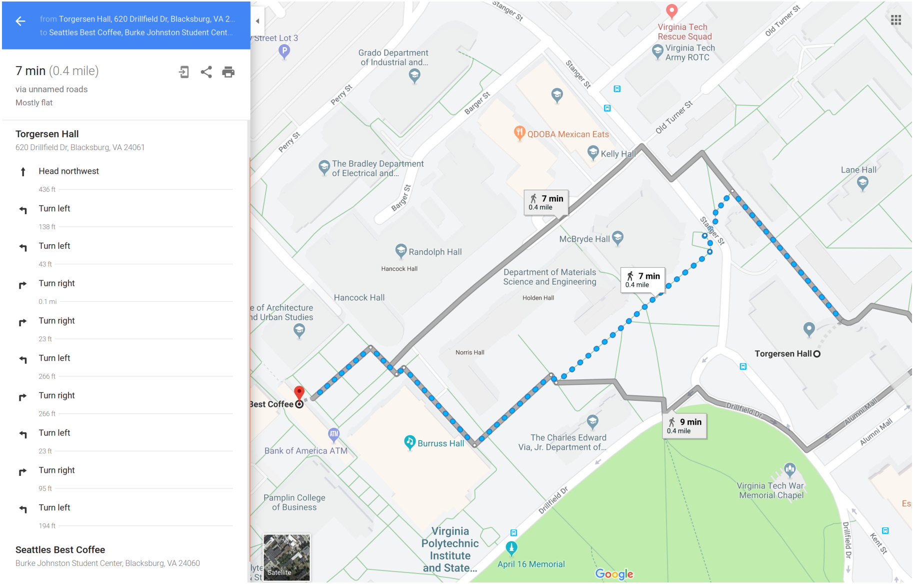
Node $\equiv$, Edge $\equiv$



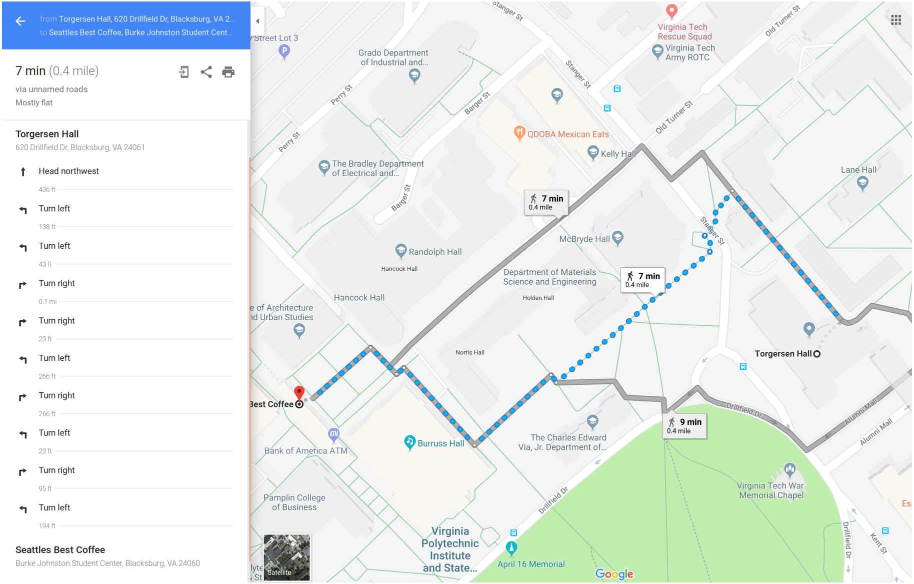
Node ≡ Intersection/Fork, Edge ≡ Street segment



Node $\equiv$, Edge $\equiv$


from Torgersen Hall, 620 Drillfield Dr, Blacksburg, VA 2...
to Seattles Best Coffee, Burke Johnston Student Cent...
7 min (0.4 mile)
via unnamed roads
Mostly flat
Torgersen Hall
620 Drillfield Dr, Blacksburg, VA 24061
Head northwest
436 ft
Turn left
138 ft
Turn left
43 ft
Turn right
0.1 mi
Turn right
23 ft
Turn left
266 ft
Turn right
266 ft
Turn left
23 ft
Turn right
95 ft
Turn left
194 ft
Seattles Best Coffee
Burke Johnston Student Center, Blacksburg, VA 24060
7 min
0.4 mile
7 min
0.4 mile
9 min
0.4 mile
Torgersen Hall
Best Coffee
Randolph Hall
Hancock Hall
McBryde Hall
Kelly Hall
Lane Hall
Burruss Hall
Norris Hall
Holden Hall
QDOBA Mexican Eats
Department of Materials Science and Engineering
The Bradley Department of Electrical and...
Grado Department of Industrial and...
Virginia Tech Rescue Squad
Virginia Tech Army ROTC
The Charles Edward Via, Jr. Department of...
Virginia Tech War Memorial Chapel
Bank of America ATM
Pamplin College of Business
Virginia Polytechnic Institute and State...
April 16 Memorial
Drillfield Dr
Alumni Mall
Old Turner St
Stanger St
Barger St
Perry St
Kent St
Satellite
Google

Node ≡ , Edge ≡



Node ≡ "Intersection", Edge ≡ Walkway/Unnamed road

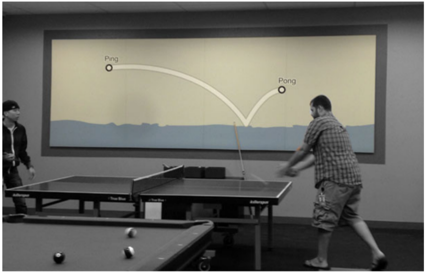
How Do We Create Street Maps?

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

Share Tweet ... TEXT SIZE − +



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 out 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?

Census.gov

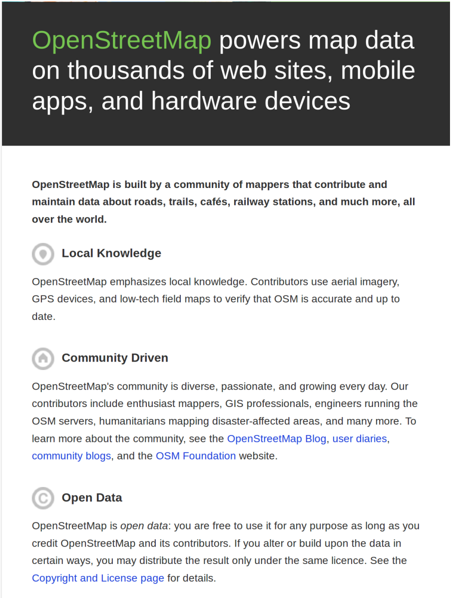
25th Anniversary of TIGER

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?

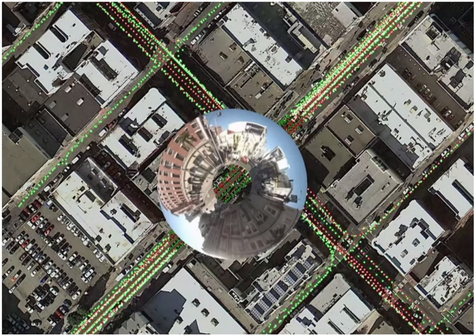
How Do We Create Street Maps?



How Do We Correct Street Maps?

GREG MILLER SCIENCE 12.08.14 06:45 AM

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?

APPS & SOFTWARE

Image Source: Tobermory Press Inc.

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

Yoni Heisler @edibleapple
May 17th, 2016 at 1:12 PM

Share Tweet

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.

How Do We Correct Street Maps?

Waze fixes app after police say it left drivers stranded on unpaved roads 45 miles away from the casino they were trying to reach

By Alisha Ebrahimji, CNN
Updated 7:29 PM ET, Wed January 22, 2020

The Waze navigation app left drivers headed to an Atlantic City, NJ casino stranded and in the middle of Colliers Mills Wildlife Management Area

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.

COMPUTER ANDROID IPHONE & IPAD

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**.

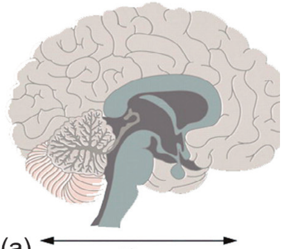
Nodes and Edges

- 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



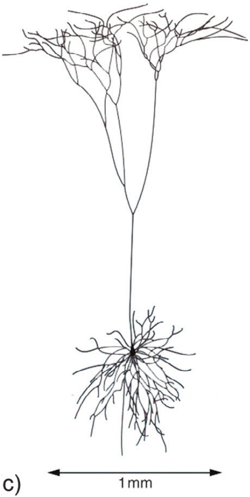
(a) 10 cm

Broad divisions: cortical lobes, cytoarchitectural areas

(b) 1 cm

Neurons aggregate into columns, layers, and cell groups

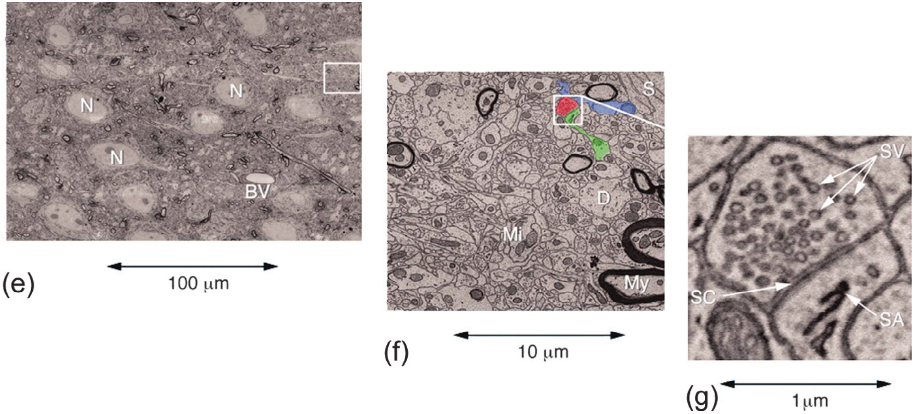
Multiscale Organisation of Brain Anatomy



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.

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.

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.

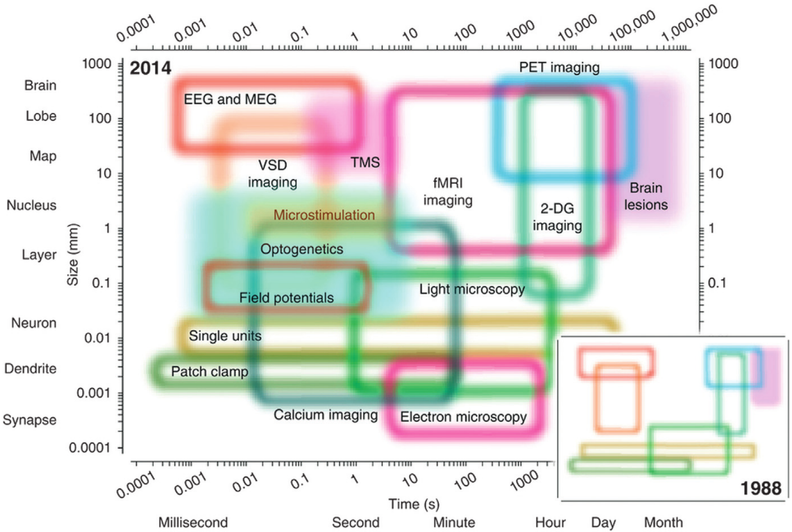
Three Spatial Scales

- *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.

Three Types of Connectivity

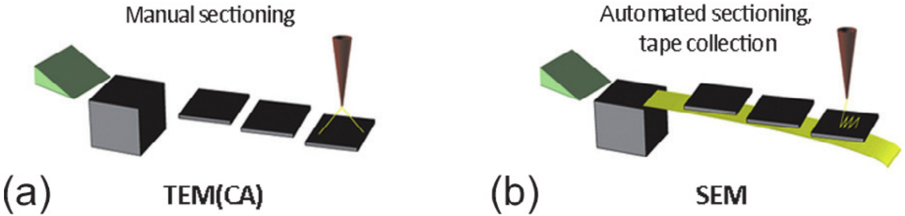
- *Structural*: anatomical connections between neural elements
  - Example: axons and synapses between neurons at the microscale.
  - Example: Large-scale fiber bundles that link cortical areas and subcortical nuclei at meso- and macroscales.
  - Measured using techniques such as electron microscopy (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 on another's activity.

Spatiotemporal Resolution of Measurement Techniques



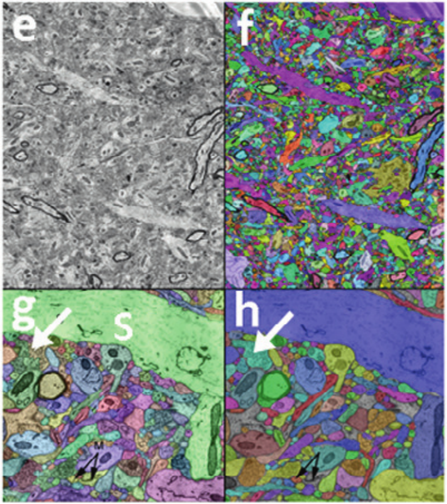
Open areas: measurement, filled areas: perturbation

Structural Connectivity at the Microscale



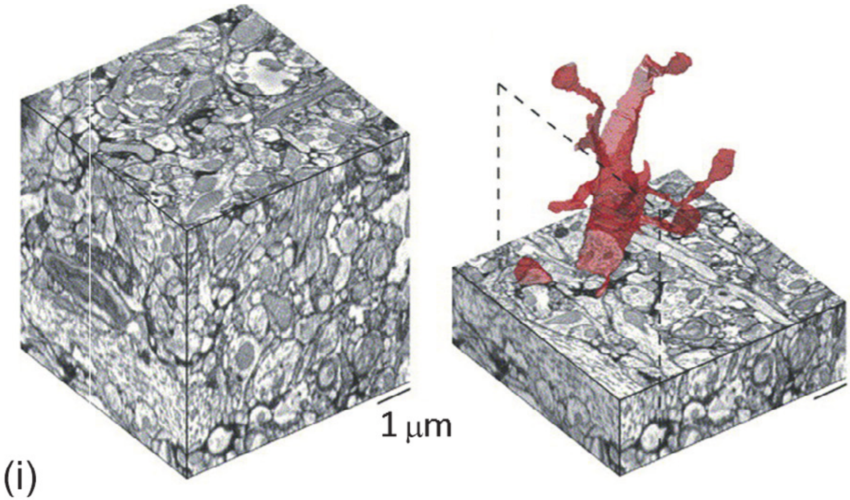
- Transmission electron microscopy (TEM): a beam of electrons is transmitted through a specimen to form an image.
- Scanning electron microscopy (SEM): produce images of a sample by scanning the surface with a focused beam of electrons.

Structural Connectivity at the Microscale



Mouse cortex section: 40 μm $\times$ 20 μm $\times$ 30 nm.

Structural Connectivity at the Microscale



Reconstruction of the Fly Hemi-Brain

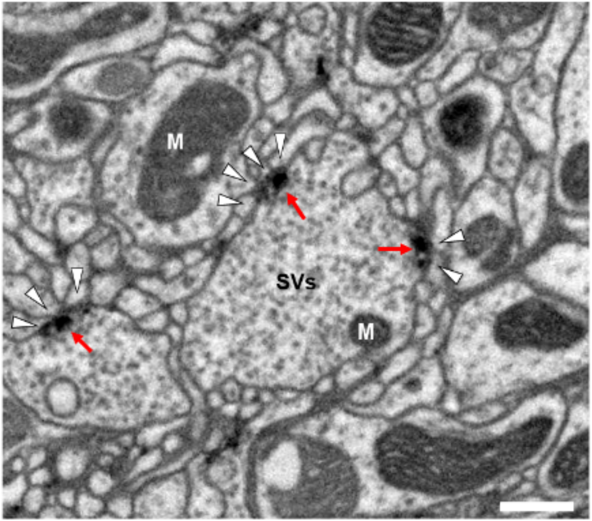
WIRED BUSINESS CULTURE GEAR IDEAS SCIENCE SECURITY MORE SIGN IN SUBSCRIBE

GREGORY BARBER SCIENCE 01.22.2020 11:00 AM

The Most Complete Brain Map Ever Is Here: A Fly's 'Connectome'

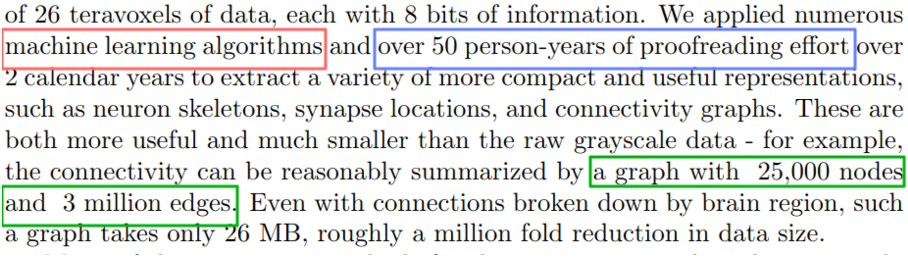
It took 12 years and at least $40 million to chart a region about 250 micrometers across—about the thickness of two strands of hair.

Reconstruction of the Fly Hemi-Brain



(a) *Drosophila* Synapse in EM

Reconstruction of the Fly Hemi-Brain



Reconstruction of the Fly Hemi-Brain

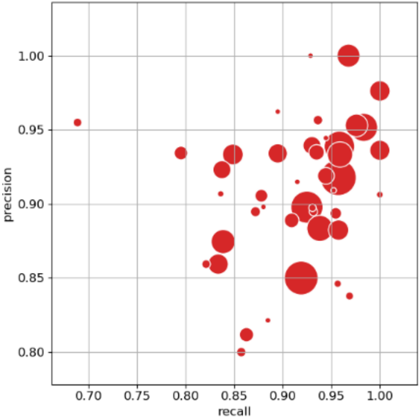
Article | Published: 16 July 2018

High-precision automated reconstruction of neurons with flood-filling networks

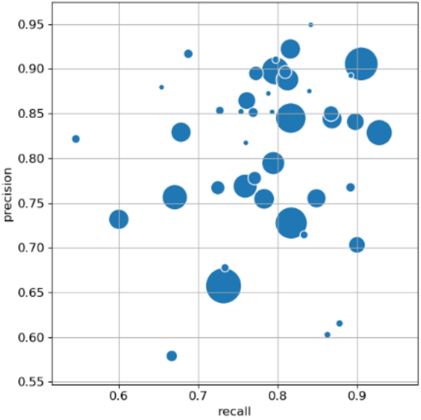
Michał Januszewski, Jörgen Kornfeld, Peter H. Li, Art Pope, Tim Blakely, Larry Lindsey, Jeremy Maitin-Shepard, Mike Tyka, Winfried Denk & Viren Jain

Nature Methods **15**, 605–610(2018) | Cite this article

Reconstruction of the Fly Hemi-Brain



(a) T-bars



(b) PSDs

Reconstruction of the Fly Hemi-Brain

A Connectome of the Adult *Drosophila* Central Brain

C. Shan Xu, Michal Januszewski, Zhiyuan Lu, Shin-ya Takemura, Kenneth J. Hayworth, Gary Huang, Kazunori Shinomiya, Jeremy Maitin-Shepard, David Ackerman, Stuart Berg, Tim Blakely, John Bogovic, Jody Clements, Tom Dolafi, Philip Hubbard, Dagmar Kainmueller, William Katz, Takashi Kawase, Khaled A. Khairy, Laramie Leavitt, Peter H. Li, Larry Lindsey, Nicole Neubarth, Donald J. Olbris, Hideo Otsuna, Eric T. Troutman, Lowell Umayam, Ting Zhao, Masayoshi Ito, Jens Goldammer, Tanya Wolff, Robert Svirskas, Philipp Schlegel, Erika R. Neace, Christopher J. Knecht Jr., Chelsea X. Alvarado, Dennis A. Bailey, Samantha Ballinger, Jolanta A Borycz, Brandon S. Canino, Natasha Cheatham, Michael Cook, Marisa Dreher, Octave Duclos, Bryon Eubanks, Kelli Fairbanks, Samantha Finley, Nora Forknall, Audrey Francis, Gary Patrick Hopkins, Emily M. Joyce, SungJin Kim, Nicole A. Kirk, Julie Kovalyak, Shirley A. Lauchie, Alanna Lohff, Charli Maldonado, Emily A. Manley, Sari McLin, Caroline Mooney, Miatta Ndama, Omotara Ogundeyi, Nneoma Okeoma, Christopher Ordish, Nicholas Padilla, Christopher Patrick, Tyler Paterson, Elliott E. Phillips, Emily M. Phillips, Neha Rampally, Caitlin Ribeiro, Madelaine K Robertson, Jon Thomson Rymer, Sean M. Ryan, Megan Sammons, Anne K. Scott, Ashley L. Scott, Aya Shinomiya, Claire Smith, Kelsey Smith, Natalie L. Smith, Margaret A. Sobeski, Alia Suleiman, Jackie Swift, Satoko Takemura, Iris Talebi, Dorota Tarnogorska, Emily Tenshaw, Temour Tokhi, John J. Walsh, Tansy Yang, Jane Anne Horne, Feng Li, Ruchi Parekh, Patricia K. Rivlin, Vivek Jayaraman, Kei Ito, Stephan Saalfeld, Reed George, Ian Meinertzhagen, Gerald M. Rubin, Harald F. Hess, Louis K. Scheffer, Viren Jain, Stephen M. Plaza

doi: https://doi.org/10.1101/2020.01.21.911859

Reconstruction of the Fly Hemi-Brain

ZL developed sample preparation and fixed and stained the sample; CSX, KJH, HFH developed the imaging hardware and imaged the sample; LS, ETT, DK, KAK, DA and SS aligned, flattened and integrated the slabs into a coherent volume; WK wrote and managed the versioned data system; SB, TZ, PH, LU, TD, DRS, DJO, NN, SP, JC, LS, ET, PS, TK wrote proofreading and analysis software; MJ, JMS, PHL, VJain developed and applied segmentation approaches; TB, LL, JMS developed analysis, visualization and pipeline software; MJ, LL, VJain developed and applied tissue classification approaches; GH developed and applied methods to identify synapses; KS, ST, JG, MI, TW, FL, KI, RP, JAH defined brain regions and cell types; JB and HO did the EM-optical mapping; CXA, DAB, SB, JAB, BSC NC, MC, MD, OD, BE, KF, SF, NF, AF, GPH, EMJ, SK, NAK, JK, SAL, AL, CM, EAM, SM, CM ,MN, OO, NO, Co, NP, CP, TP, EEP, EMP, NR, CR, MKR, JTR, SMR, MS, AKS, ALS, AS CS, KS, NLS, MAS, AS, JS, ST, IT, DT, ET, TT, JJW AND TY performed proofreading; EN and CJK provided proofreading analytics; VJay, IAM, ST, KS, PR, RP, FL, GMR did biological interpretation and analysis; LS, SP did connectivity analysis and wrote the paper; JAH, FL, PR, RP managed proofreading; RG, GMR, SP managed the overall effort.

Graphs from Microscale Structural Connectivity

- Node $\equiv$ neuron, edge $\equiv$ synapse.

Graphs from Microscale Structural Connectivity

- Node $\equiv$ neuron, edge $\equiv$ synapse.
- Reconstructing connectomes in this manner is computationally demanding, time-consuming, and labor intensive.
  - One mm^3 of rat cortex imaged at nanometre resolution: 2PB of data.
  - A complete atlas of rat cortex (vol $\approx 500\ \mathrm{mm}^3$): 1 EB (1000 PB).
  - A complete human cortex will require about 1000 EB.

Graphs from Microscale Structural Connectivity

- Node $\equiv$ neuron, edge $\equiv$ synapse.
- Reconstructing connectomes in this manner is computationally demanding, time-consuming, and labor intensive.
  - One mm^3 of rat cortex imaged at nanometre resolution: 2PB of data.
  - A complete atlas of rat cortex (vol $\approx$ 500 mm^3): 1 EB (1000 PB).
  - A complete human cortex will require about 1000 EB.
  - Reconstructing nervous system of *C. elegans* took over 10 years (White et al., 1986).

Functional Connectivity at the Microscale

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

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 neuron.
  - Coordinated oscillatory activity mediates neuronal communication.

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 neuron.
  - Coordinated oscillatory activity mediates neuronal communication.
- Measure neuronal activity over time.
- Define how to compute similarity or statistical dependence of two time series.

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 neuron.
  - 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.

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 neuron.
  - 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.

From Microscale to Mesoscale

- 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.

From Microscale to Mesoscale

- 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.

Defining Nodes at the Mesoscale

- Goal is to map connectivity between neuronal populations or cell assemblies, rather than individual neurons.
- Exploit aggregation of neurons 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.

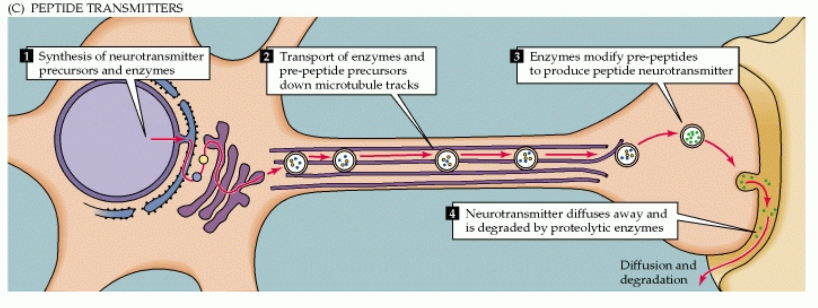
Defining Nodes at the Mesoscale

- Goal is to map connectivity between neuronal populations or cell assemblies, rather than individual neurons.
- Exploit aggregation of neurons 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.
- 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

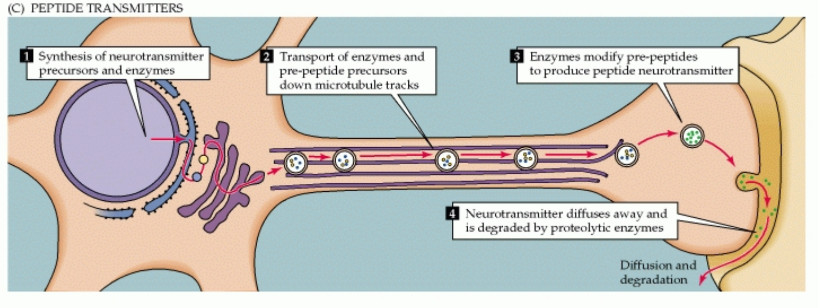
- Invasive tract tracing is the main technique.
- A fluorescent dye or other tracer molecule injected into a specific part of the brain.
- Cellular membranes are permeable to these tracers.
- Once the tracer inside the cell, active axonal transport transfers it from the soma to peripheral axon terminals.
- 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



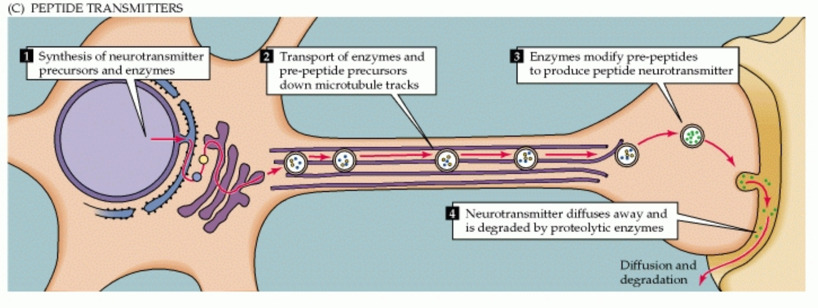
- Direction of transport distinguishes tracers.

Types of Tracers



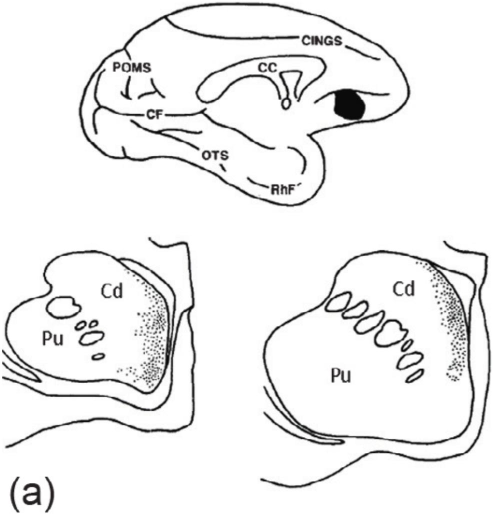
- Direction of transport distinguishes tracers.
- *Anterograde tracers*: transported from the cell body to the axon terminal; used to map the efferent projection sites of an injected area.
- *Retrograde tracers*: transported from the cell periphery to the soma; used to map the upstream sources of afferent projections to the injection site.

Types of Tracers



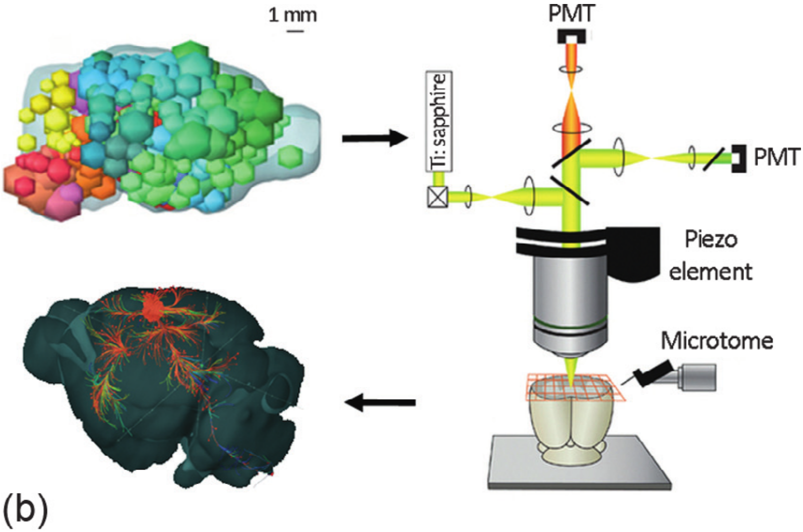
- Direction of transport distinguishes tracers.
- *Anterograde tracers*: transported from the cell body to the axon terminal; used to map the efferent projection sites of an injected area.
- *Retrograde tracers*: transported from the cell periphery to the soma; used to map the upstream sources of afferent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

Structural Connectivity at the Mesoscale: Mouse



Results from a traditional tract tracing experiment

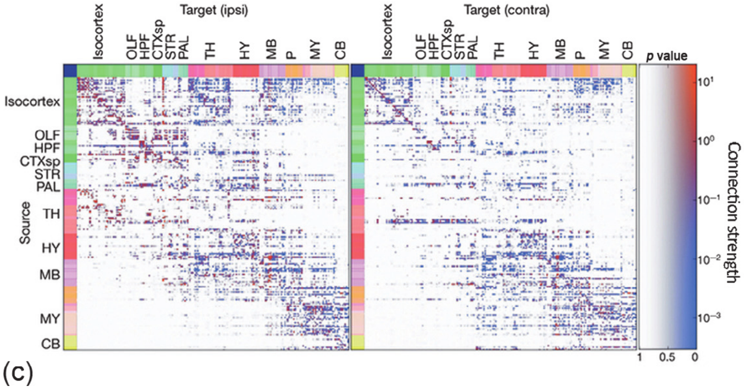
Structural Connectivity at the Mesoscale: Mouse



Modern experimental setup for whole-brain connectivity mapping

469 distinct tracer experiments

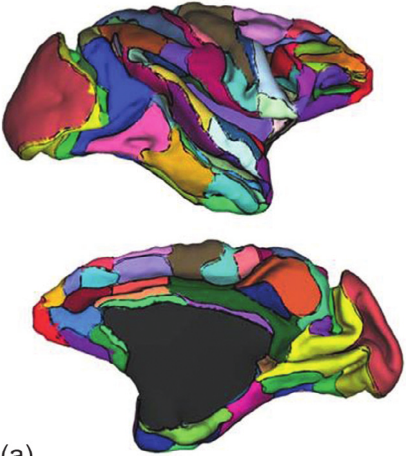
Structural Connectivity at the Mesoscale: Mouse



Example of connectivity matrix.

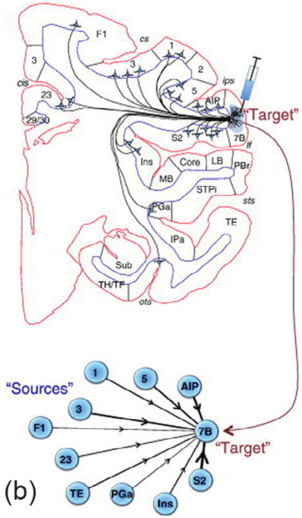
Edge weights range over four orders of magnitude.

Structural Connectivity at the Mesoscale: Macaque


(a)

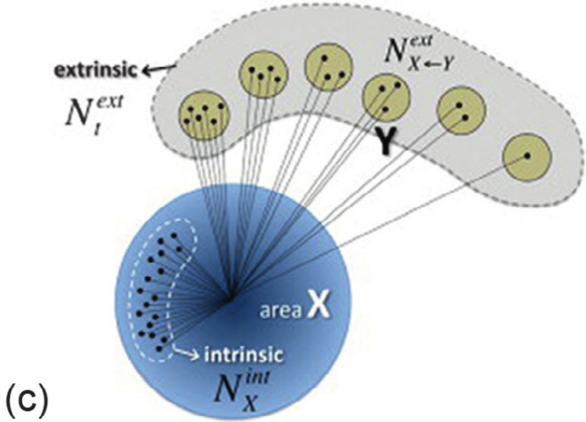
Parcellate the macaque cortex into 91 areas, defined according to cytoarchitecture and sulco-gyral landmarks.

Structural Connectivity at the Mesoscale: Macaque



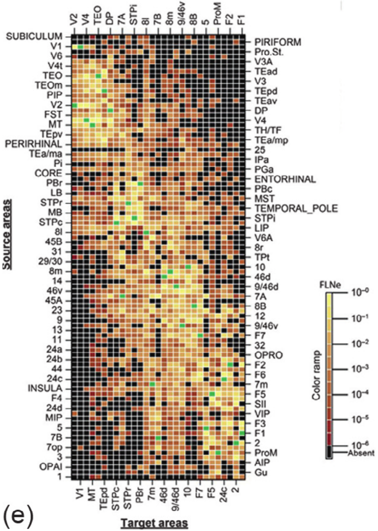
Use retrograde tract tracing. Determine edges coming into node representing area of injection from "labelled" nodes representing neurons that the tracer reaches.

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.

Functional Connectivity at the Mesoscale

Please read Chapter 2.2.2 of the textbook.

From Mesoscale to Macroscale

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

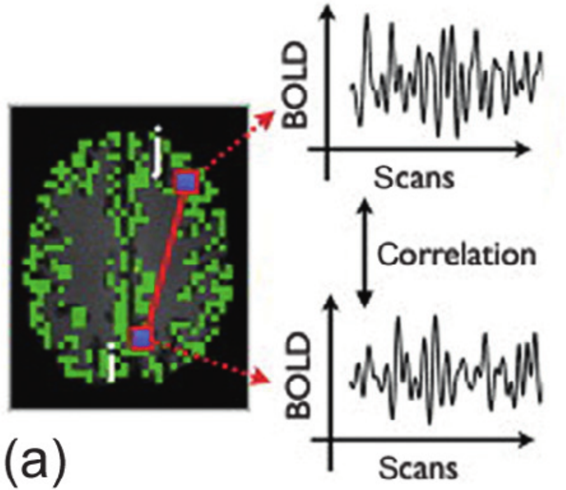
From Mesoscale to Macroscale

- 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.
- 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.
  - Con: Can resolve brain connectivity only at the scale of millimeters and centimeters.
    - 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.

From Mesoscale to Macroscale

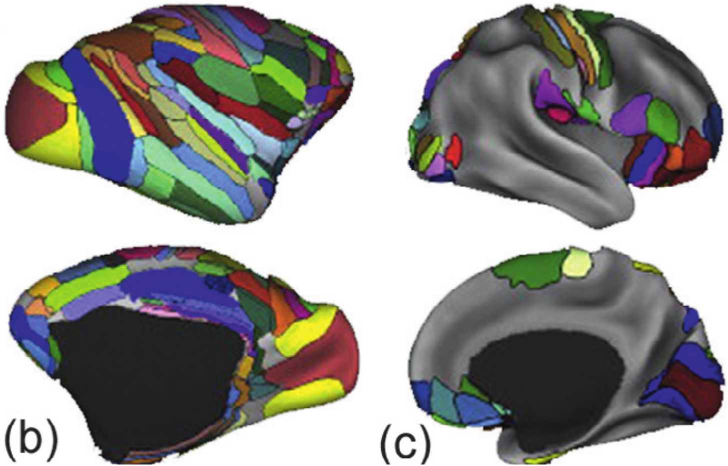
- Experimental methods we have discussed so far for measuring brain connectivity are invasive.
  - Pro: Offer in-depth access to neural structure and function.
  - Con: Difficult to apply across the entire brain, particularly in larger animals and humans.
- Use noninvasive imaging techniques (e.g., MRI, 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.
  - Con: Can resolve brain connectivity only at the scale of millimeters and centimeters.
    - 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.

Defining Nodes at Macroscale



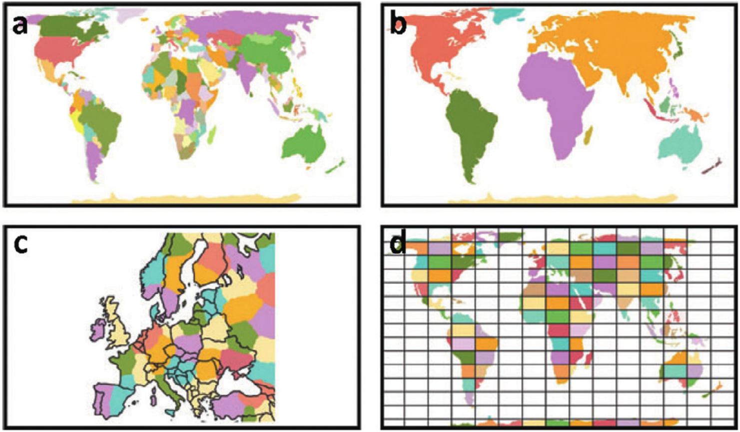
Each voxel is a node. Correlation between measurements for node pairs defines edges.

Defining Nodes at Macroscale

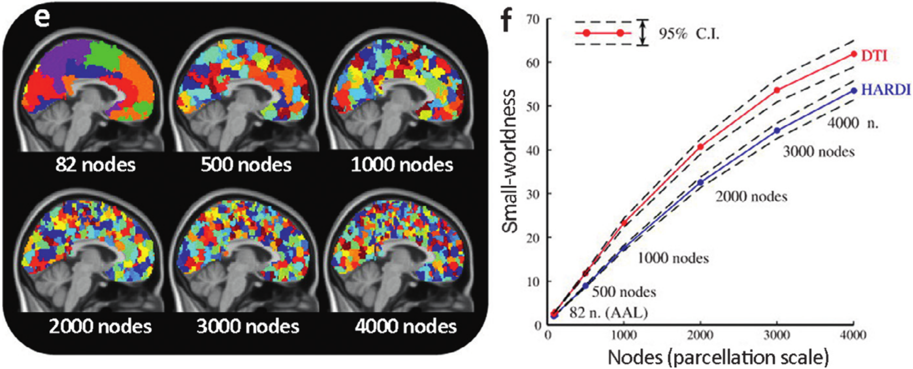


Cytoarchitectural atlases mapped to standard stereotactic space. (b) Macaque brain. (c) Human brain.

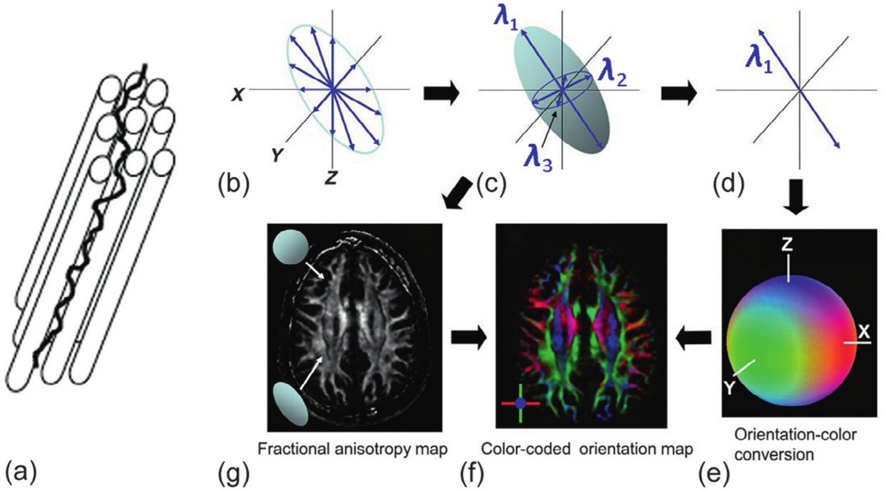
Parcellation Can Affect Network Properties



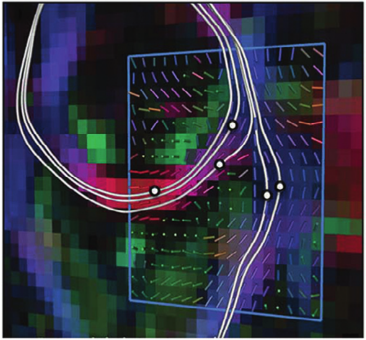
Parcellation Can Affect Network Properties



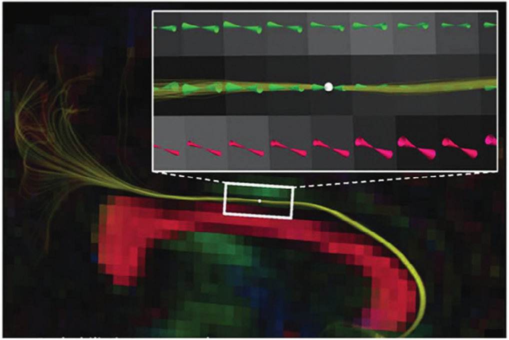
Structural Connectivity at the Macroscale



Structural Connectivity at the Macroscale

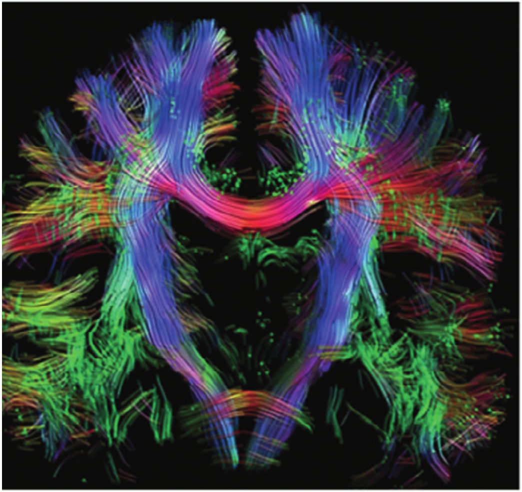


(h) Deterministic

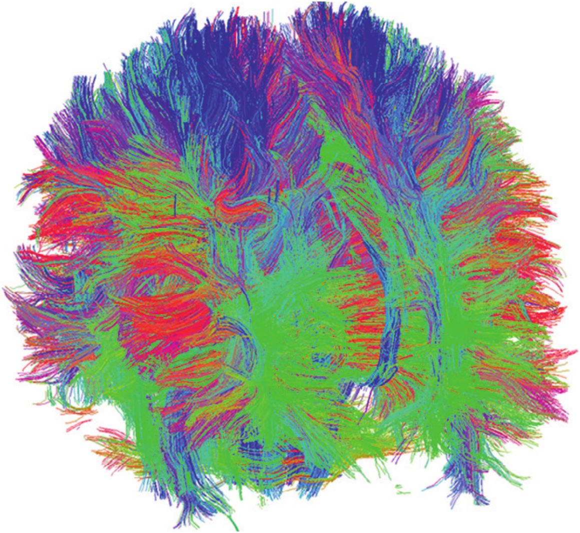


(i) Probabilistic

Structural Connectivity at the Macroscale



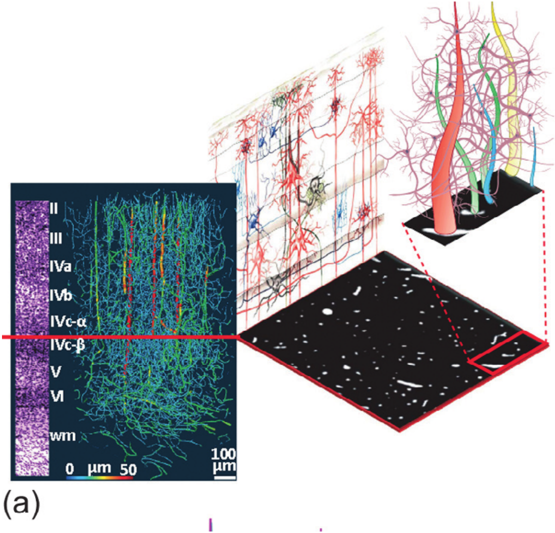
Structural Connectivity at the Macroscale



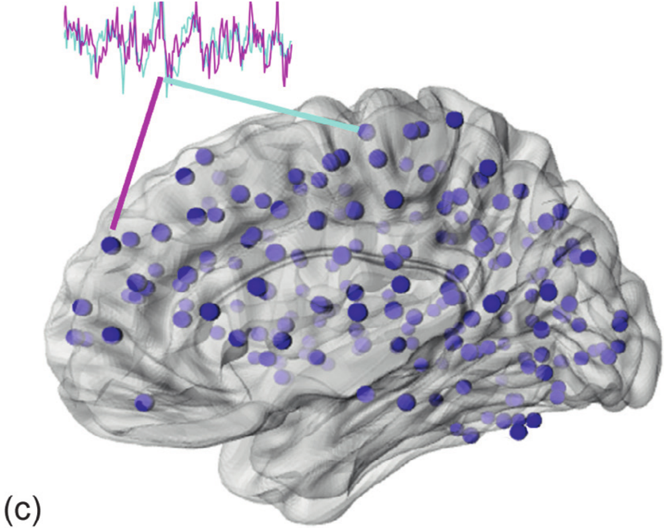
Functional Magnetic Resonance Imaging

fMRI - How it Works and What it's Good For, Video, 6:41"

Functional Connectivity at the Macroscale



Functional Connectivity at the Macroscale



Functional Connectivity at the Macroscale