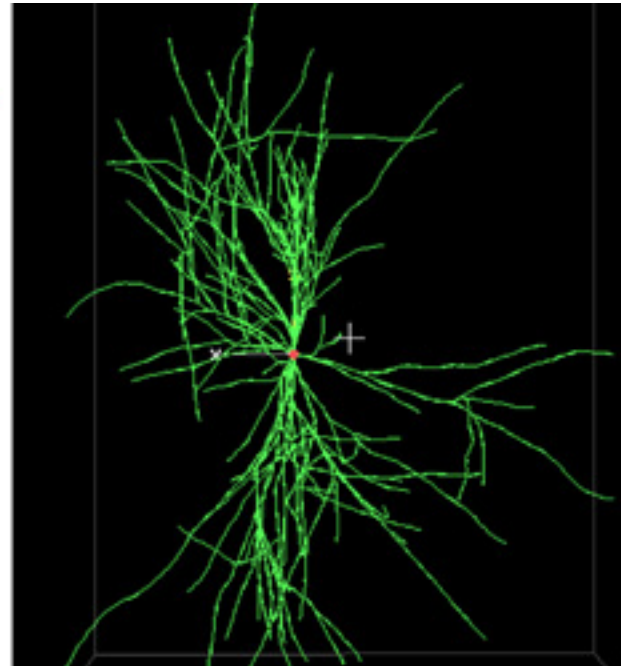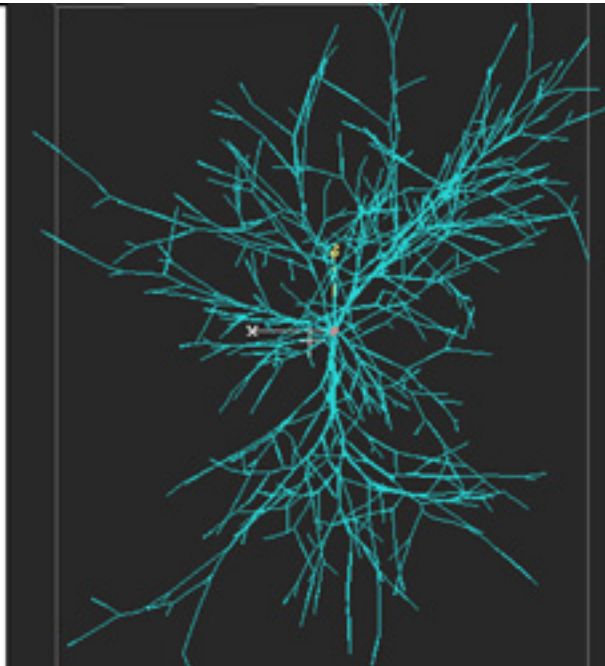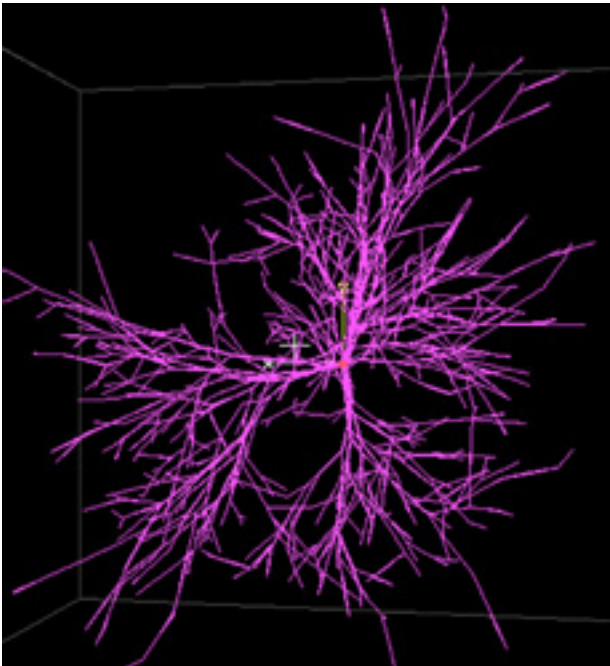# Applied Neuroscience

**Columbia
Science
Honors
Program**
<u>**Spring 2017**</u>

Glia and Neurons

Glia and Neurons

Objective: Role of Glia in Nervous System
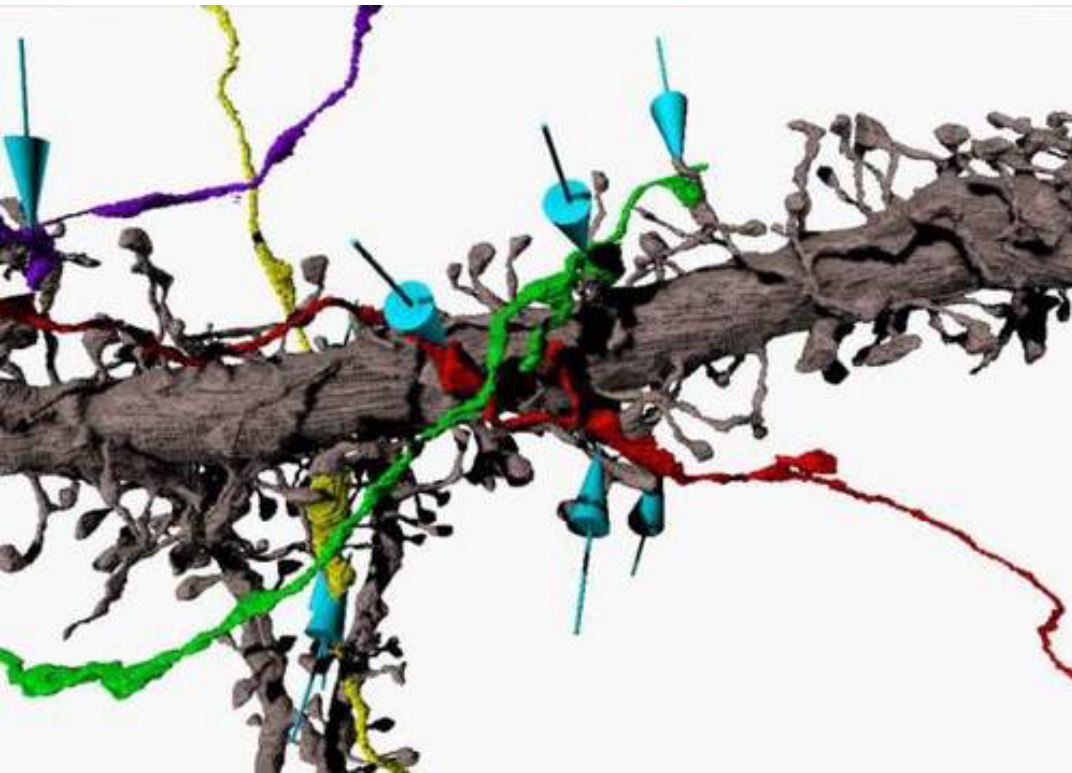
Agenda:
1. Glia
   - Guest Lecture by Dr. Jennifer Ziegenfuss
2. Machine Learning
   - Applications in Neuroscience

Connectomics

A connectome is a comprehensive map of neural connections in the brain *(wiring diagram).*

- Fails to illustrate how neurons behave in real-time (neural dynamics)
- Fails to show how a behavior is generated
- Fails to account for glia

A Tiny Piece of the Connectome
Serial EM Reconstruction of Axonal Inputs (various colors) onto a section of apical dendrite (grey) of a pyramidal neuron in mouse cerebral cortex. Arrows mark functional synapses.
*Lichtman Lab (Harvard)*

Neuroscience: Map the other brain

R. Douglas Fields

Scaling up efforts to map neural connections is unlikely to deliver the promised benefits such as understanding:

- how the brain produces memories
- Perception
- Consciousness
- Treatments for epilepsy, depression, and schizophrenia

While glia have been neglected in the quest to understand neuronal signaling, they can sense neuronal activity and control it.
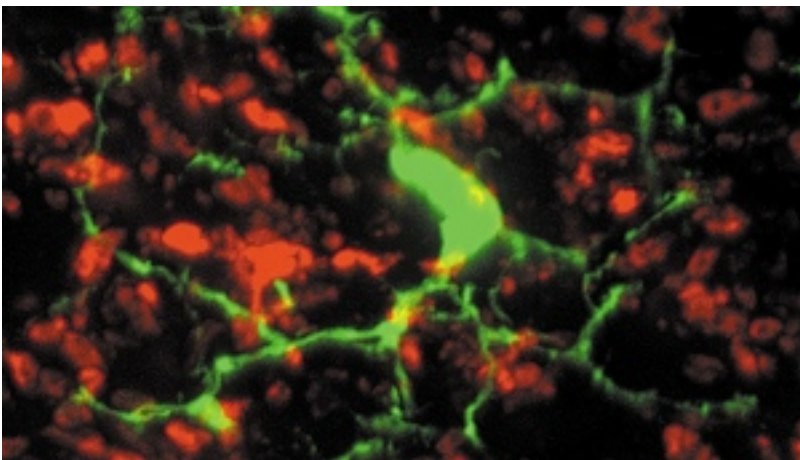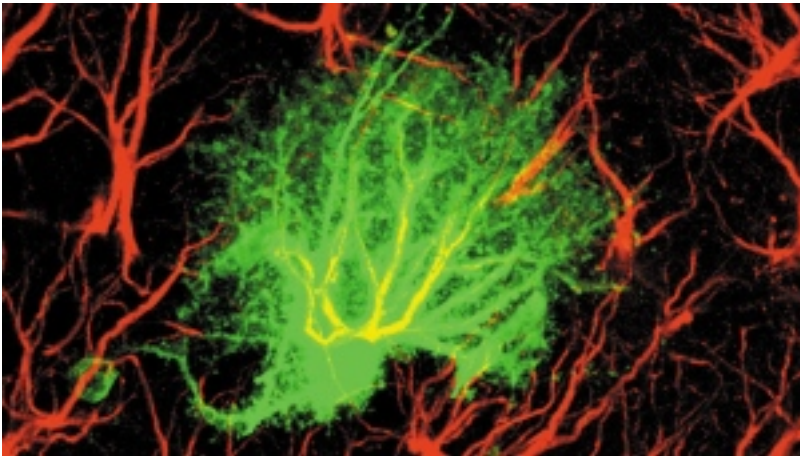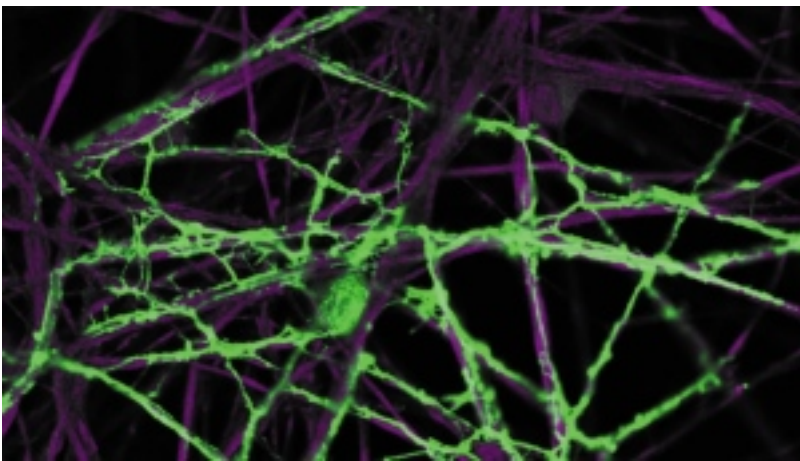
Are Glia the Genius Cells?

Structure-Function Divide in Brain

The function of a neural network is critically dependent upon its interconnections. Only *C. elegans* has a complete connectome.

In neuroscience:

- many common diseases and disorders have no known histological trace
- debates how many cell types there are
- questionable plan to image whole volumes by EM
- complexity of structure
    How is the brain's function related to its complex structure?
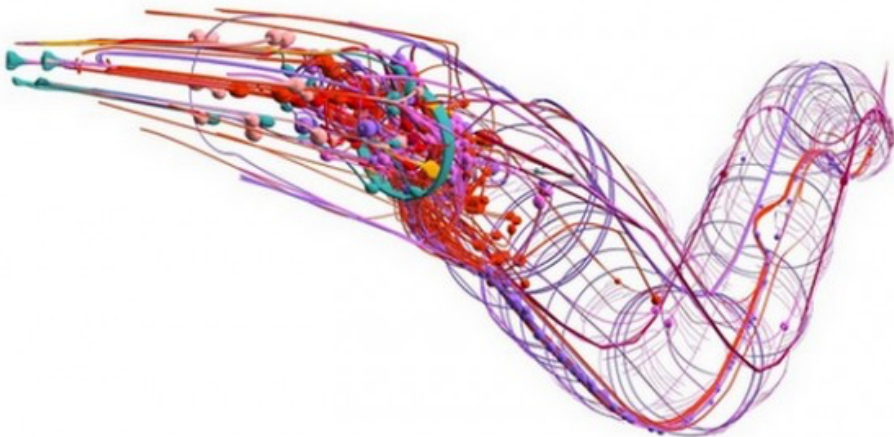
Worm Connectome
Dots are individual neurons and lines represent axons.

C. elegans

*Caenorhabditis elegans* (*C. elegans)* is a transparent nematode commonly used in neuroscience research.

They have a simple nervous system: 302 neurons and 7000 synapses.

Advantages of using *C. elegans* in research:
- Acts as a model for neuronal development and function
- Powerful genetic studies can be conducted
- Small
- Completely sequenced genome
- Can be frozen and preserved
- Invariant cell lineage
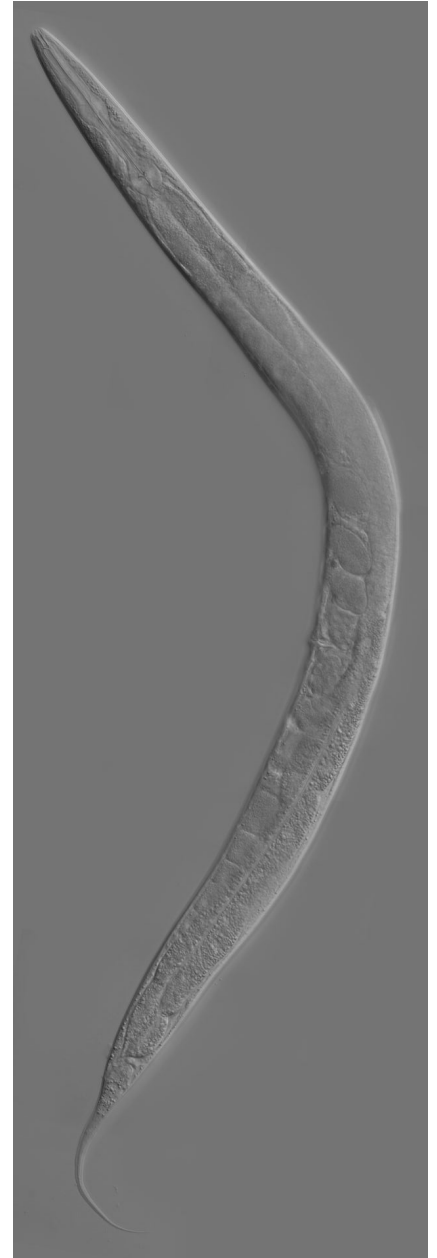
History of the *C. elegans* connectome

1970s: Sydney Brenner and colleagues preserved *C. elegans* in agar and osmium fixative, prepared slices and imaged the cells using an electron microscope.
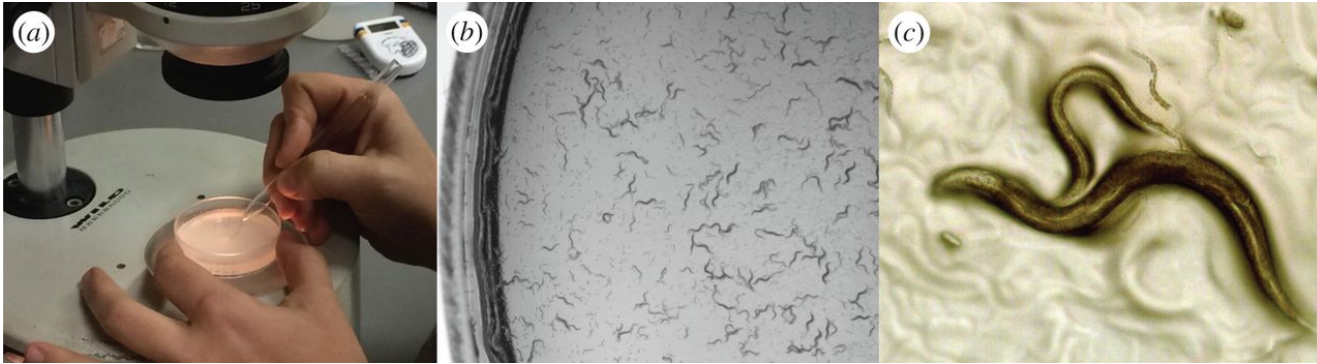
Sydney Brenner

1986: Brenner published a near complete draft of the wiring diagram of *C. elegans*

2000s: Dmitri Chklovskii published a more comprehensive connectome of *C. elegans*
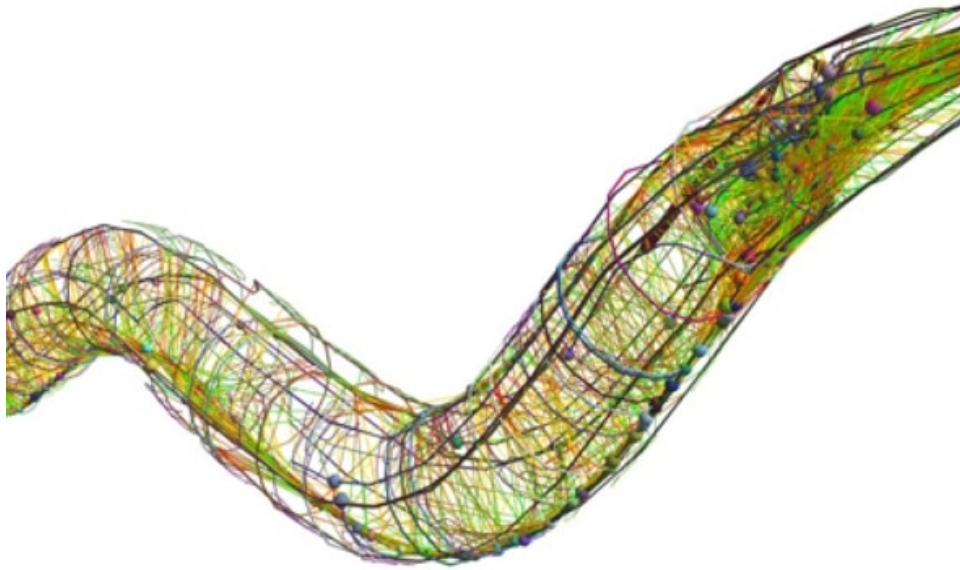 *What is the difference between the old and new C. elegans connectome?*

Dmitri Chklovskii

The *C. elegans* connectome

Obtaining this connectome was tedious:
- 12 years for completion
- Every neuron was individually identified, its precise location determined, and its projections to other neurons traced
- Tracings done manually

The Connectome Debate: Is Mapping the Mind of a Worm Worth It?

Scientists have mapped a tiny roundworm's entire nervous system. Did it teach them anything about its behavior?

TED Talk by Sebastian Seung

What is Machine Learning?

- *"Learning denotes changes in a system that… enable a system to do the same task… more efficiently the next time" Herbert Simon*
- *"Learning is constructing or modifying representations of what is being experienced" Rysard Michalski*
- *"Learning is making useful changes in our minds" Marvin Minsky*
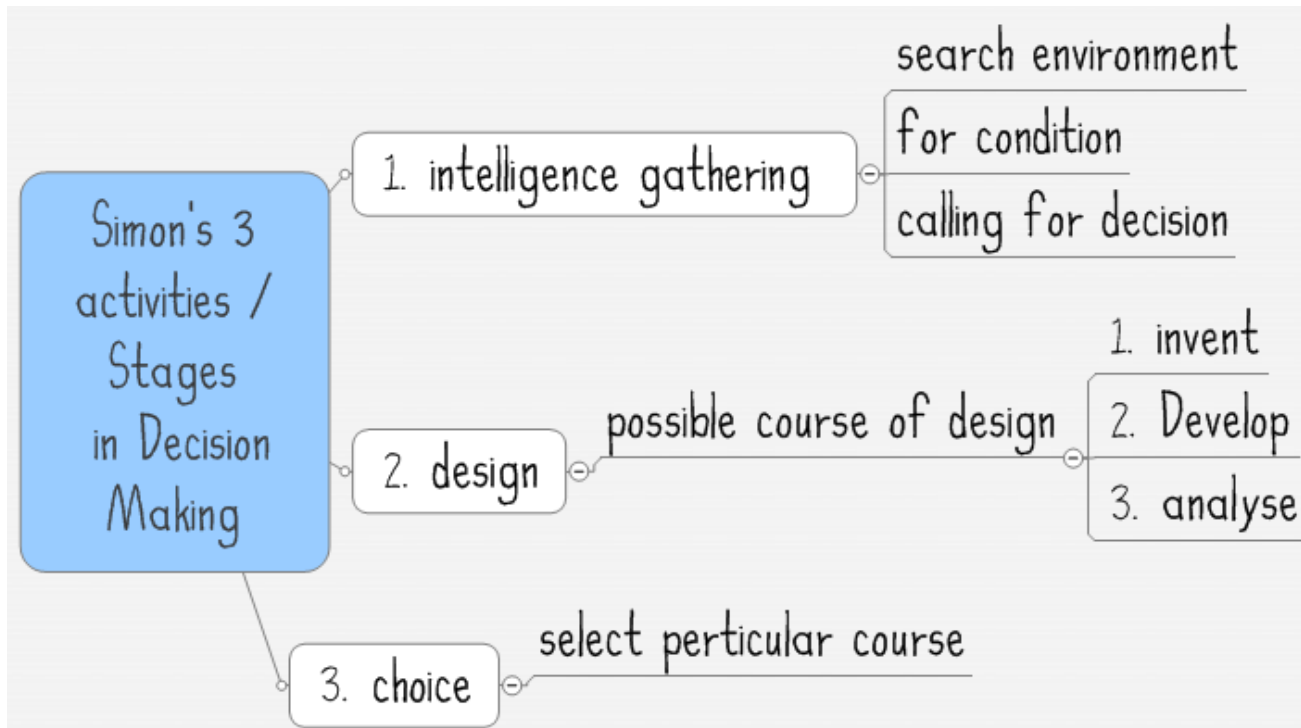
Machine Learning

Machine learning is the study of algorithms that improve their performance at some task with experience

"Machine learning refers to a system capable of autonomous acquisition and integration of knowledge"

Role of Statistics: Inference from a sample

Role of Computer Science:

Efficient algorithms to represent and evaluate the model for inference

Machine learning is used in:
- Speech Recognition
- Computer Vision
- Robotics
- **Computational Neuroscience**

Why Machine Learning?

- No human experts
  - Industrial/manufacturing control
  - Mass spectrometer analysis, drug design, astronomic discovery
- Black-box human expertise
  - Speech recognition
  - Autonomous vehicles
- Rapidly changing phenomena
  - Credit scores
  - Financial models
  - Clinical diagnosis
  - Fraud detection
- Need for customization
  - Personalized news reader
  - Video recommendations

Why Machine Learning?

The primary role of machine learning is to form data-driven hypotheses:

> *"Machine learning sits at the intersection of data engineering and mathematical modeling. The thing that makes it different from statistics traditionally, is far more focus on building algorithms." Chris Wiggins*

Why The New York Times Hired A Biology Researcher As Its Chief Data Scientist

To help make sense of the massive troves of data produced by people clicking around its website, the *Times* made a (very) nontraditional hire—Chris Wiggins, a biology researcher with a PhD in theoretical physics. If you can map the human genome, maybe you can even fix journalism.

Machine Learning

Machine learning methods include:
- Classification
- Cluster Analysis
- Regression
- Dimensional Reduction

Computational neuroscience involves:
- Classification by Morphology and Electrophysiology
- Cluster Analysis of Neurons
- Regression Models of Neural Imaging Data
- Dimensional Reduction of Large-Scale Neural Recordings

Classification of Cortical Cells in Visual System

1. Single-Cell Gene Expression Profiling through use of Transgenic Mouse Lines
2. Unsupervised Cluster Analysis of Genetic Data

Allen Institute of Brain Sciences
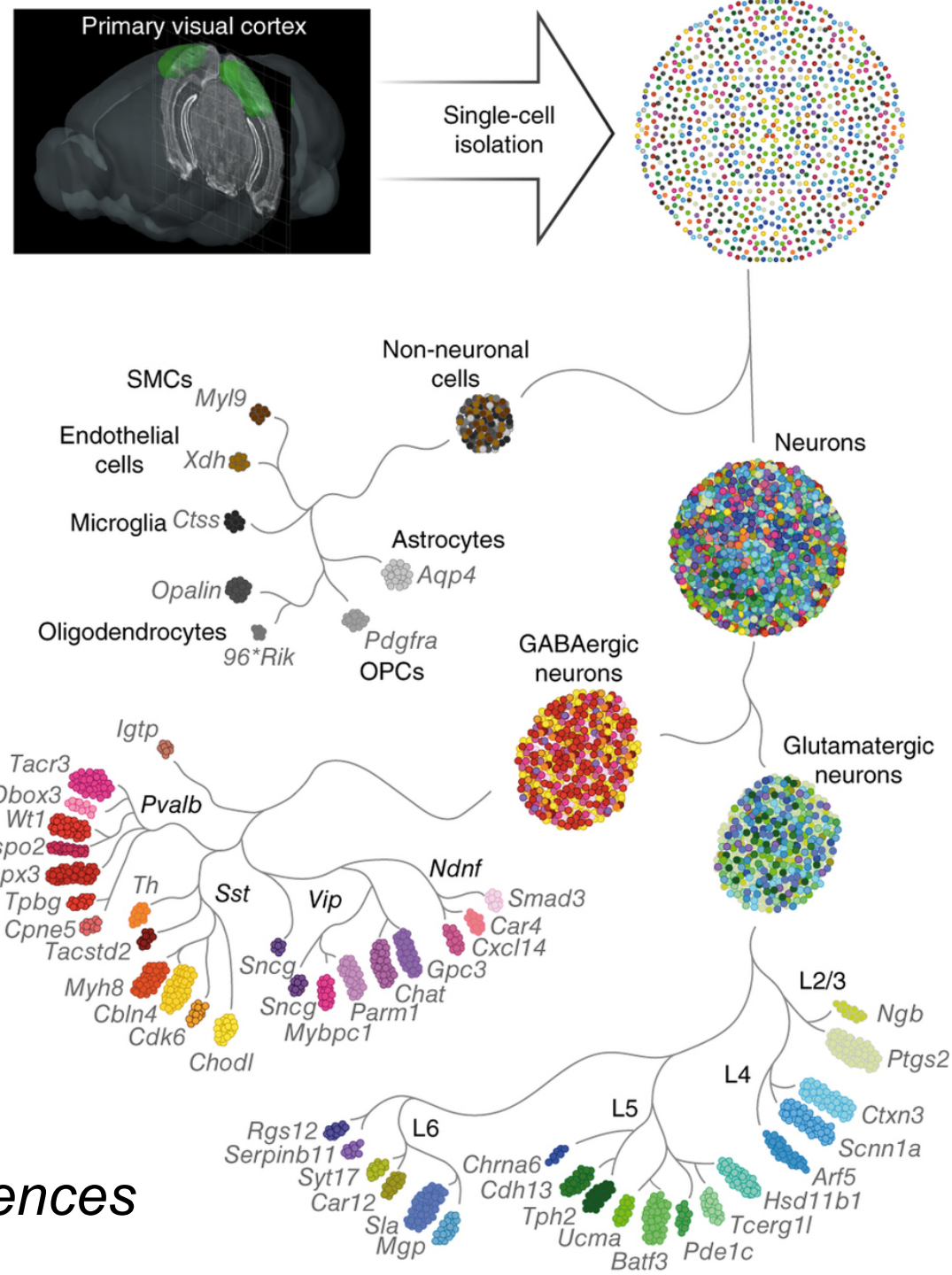
Next Time:
Sensory Systems
and Neural Circuits I