Applied Neuroscience

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

Introduction to Applied Neuroscience

Logistics

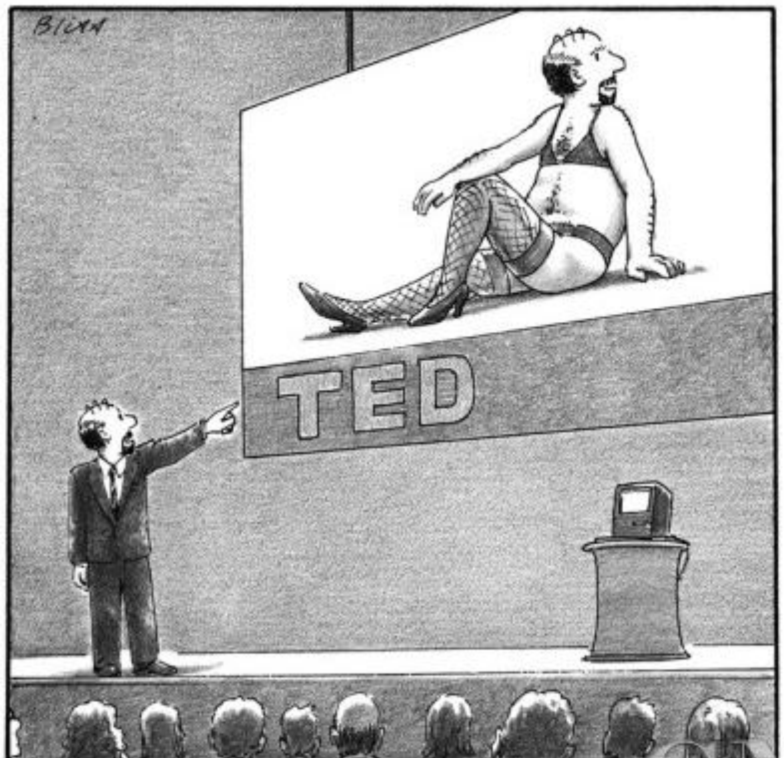
1. Maximum of **4 Absences**
2. For an excused absence, e-mail shpattendance@columbia.edu and ng2410@columbia.edu
3. Two 10 minute breaks at 11:00 AM and 12:00 PM
4. Joe’s Coffee in Northwest Corner Building
5. Do not hesitate to ask questions
6. Do request topics of interest for course
7. No exams

Introduction to Applied Neuroscience

Objective: Fundamentals of Neuroscience

Agenda:

1. Logistics
2. Computational Neuroscience
3. Neurobiology

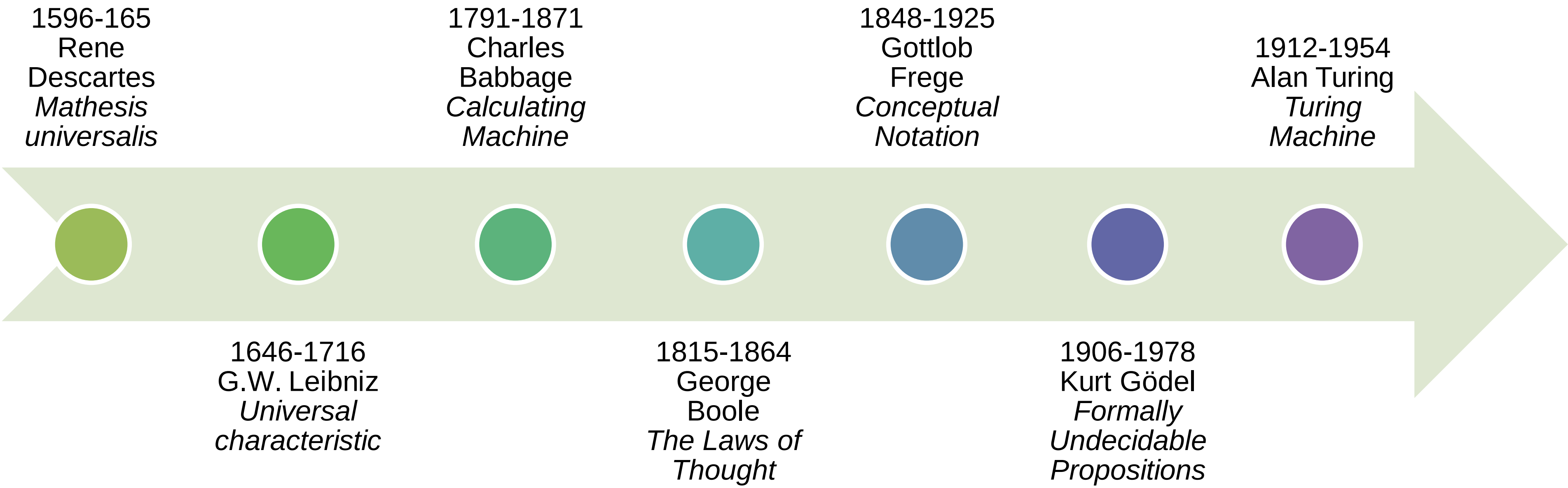


"As an icebreaker, let's all share one interesting thing about ourselves. I'll start."

- Name
- Grade
- Location
- What is something you would like to learn in this class?
- Share one interesting thing about yourself.

Philosophical Questions on Computers

1. What is *intelligence?* What is *thought?*
2. Are these functions that a machine can have?
3. If machines can display thought or intelligence, does this imply that human cognition is a type of computational ability?
4. If human cognition is a computation, does this imply that the human mind is a machine?



Introduction to Applied Neuroscience

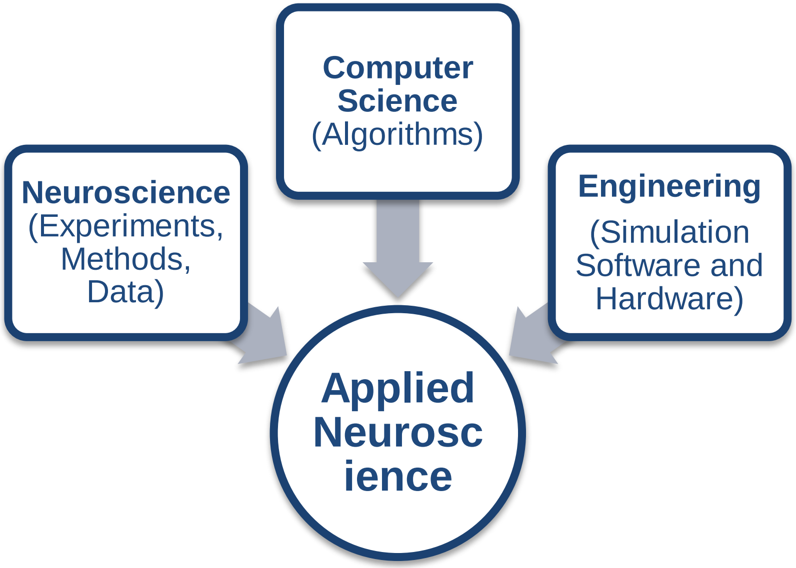
- ***Descriptive Models of the Brain***
  - How is information about the external world *encoded* in neurons and networks?
  - How can we *decode* neural information?
- ***Mechanistic Models of Brain Cells and Circuits***
  - How can we reproduce the behavior of a *single neuron* in a computer simulation?
  - How do we model a *network* of neurons?
- ***Interpretive Models of the Brain***
  - Why do brain circuits operate the way they do?
  - What are the *computational principles* underlying their operation?

Course Objectives

1. To be able to *quantitatively describe* what a given component of a neural system is doing based on experimental data
2. To be able to *simulate on a computer* the behavior of neurons and networks in a neural system
3. To be able to *formulate specific computational principles* underlying the operation of neural systems

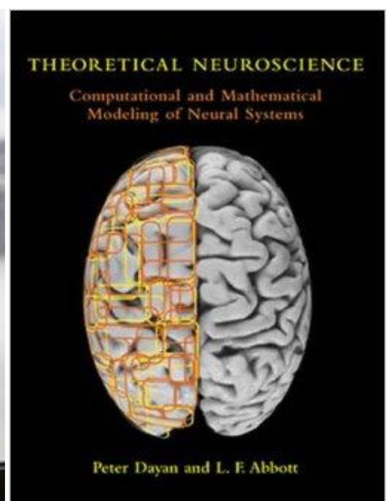
Introduction to Applied Neuroscience

How can we reproduce the behavior of a *single neuron* in a computer simulation?



Computational neuroscience provides tools and methods for “characterizing *what* nervous systems *do*, determining *how* they function, and understanding *why* they operate in particular ways” (Dayan and Abbott)

1. Description Models (*What*)
2. Mechanistic Models (*How*)
3. Interpretive Models (*Why*)



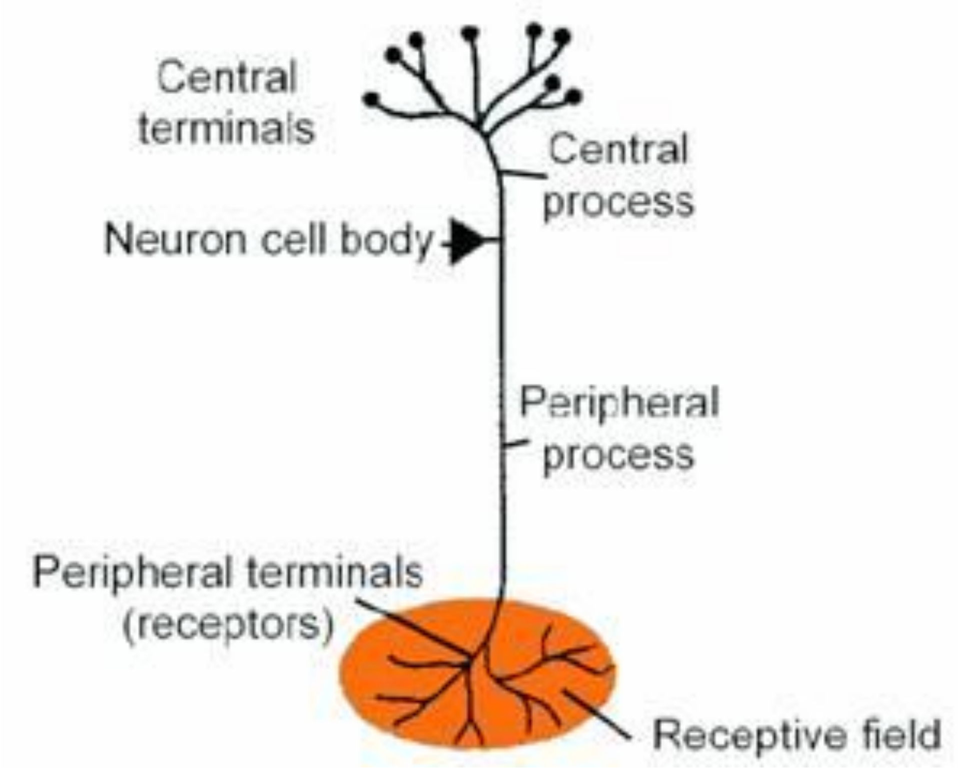
Professor Larry Abbott
Center for Theoretical Neuroscience
Columbia University

An Example: Cortical Receptive Fields

What is the *receptive field* of a brain cell?

Classical Definition: the region of sensory space that activates a neuron (Hartline, 1938)

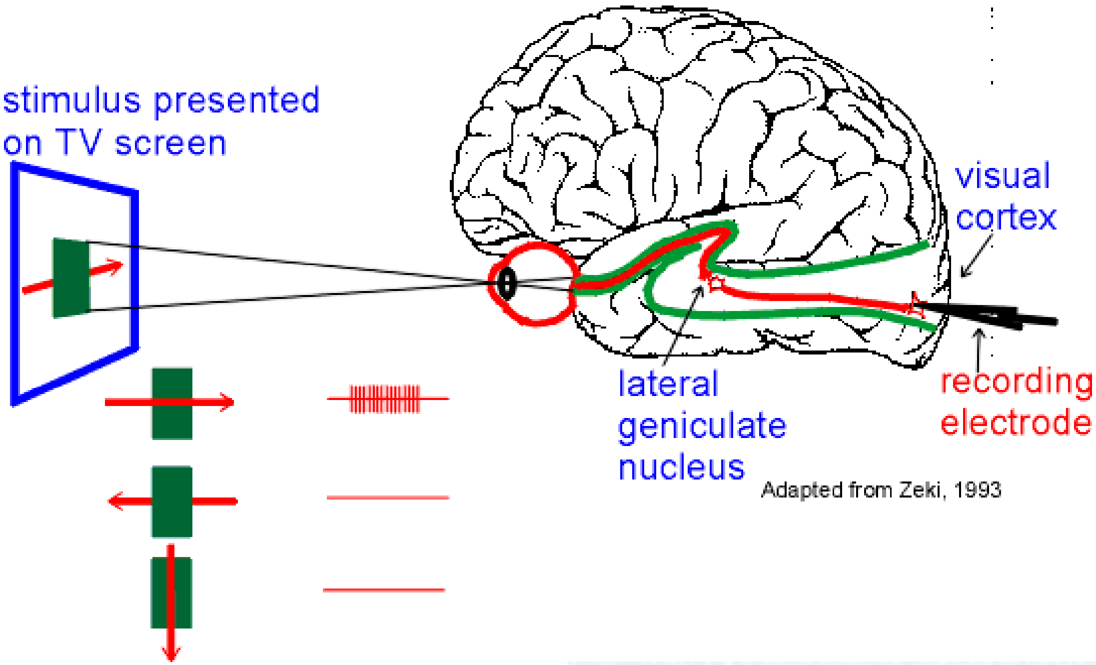
Example: Region of the retina where a spot of light activates a retinal cell

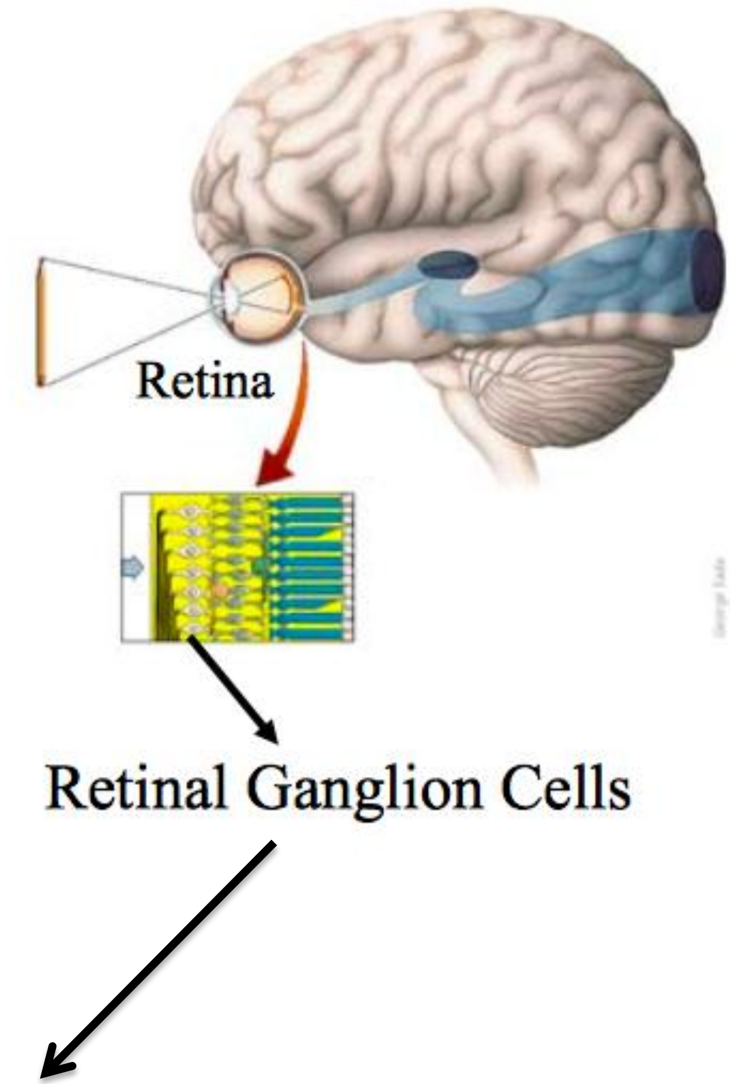


Let's look at:

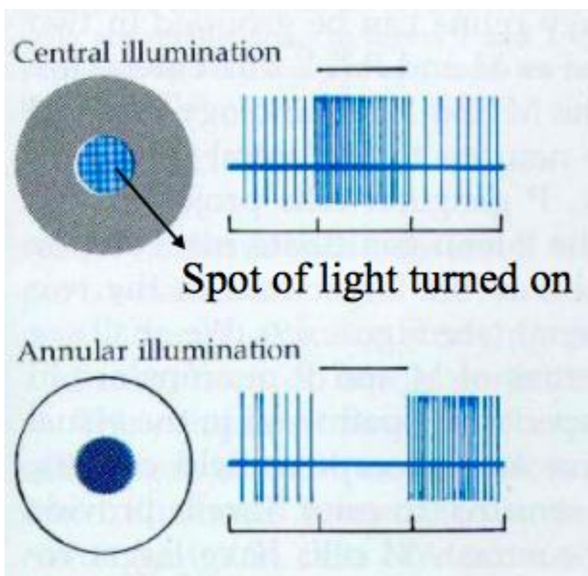
I. A *Descriptive Model* of Receptive Fields
II. A *Mechanistic Model* of Receptive Fields
III. An *Interpretive Model* of Receptive Fields

I. Descriptive Model of Receptive Fields



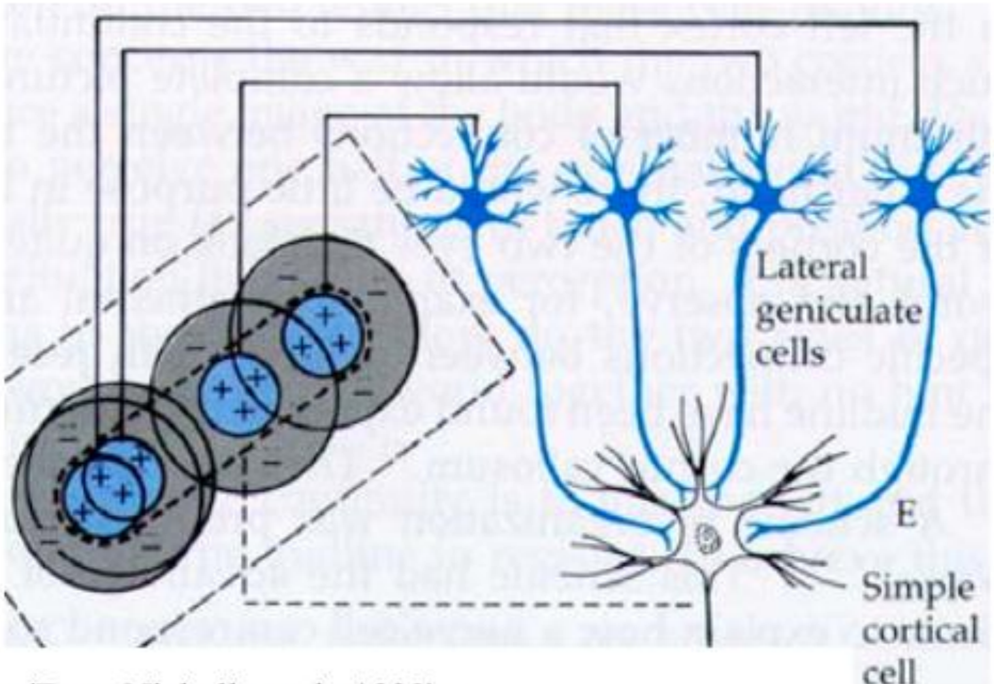


Output Responses (Spike Trains) from a Retinal Ganglion Cell

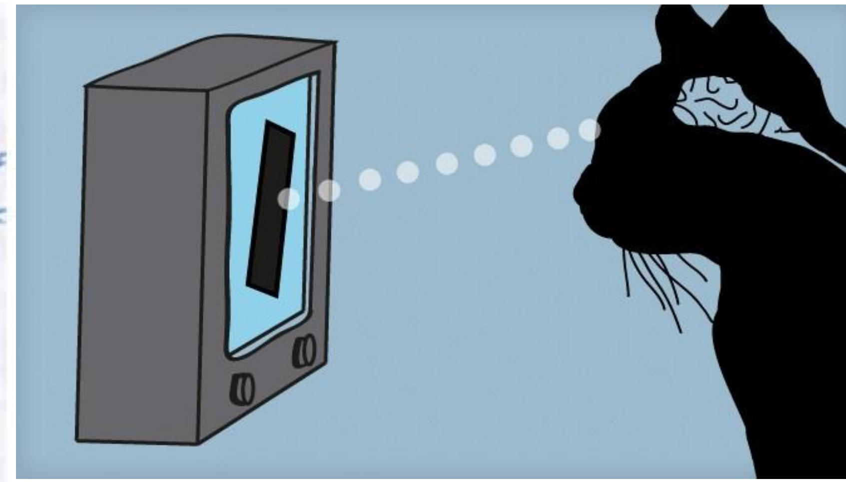


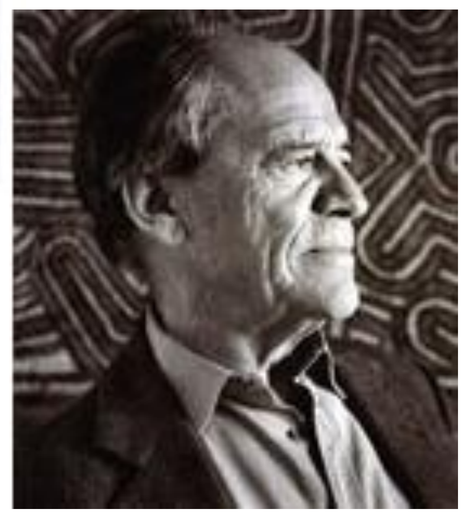
II. Mechanistic Model of Receptive Fields

The Question: *<u>How</u>* are receptive fields constructed using the neural circuitry of the visual cortex?



(From Nicholls et al., 1992)





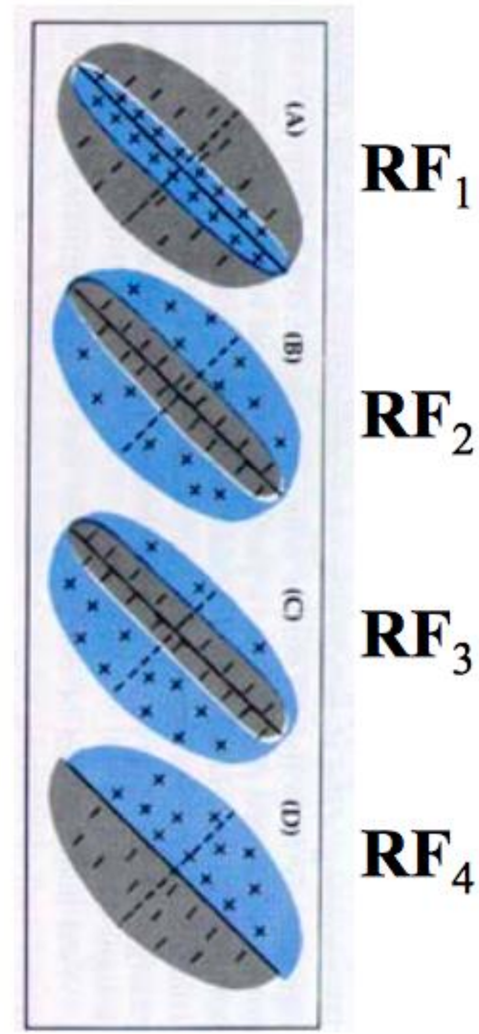
Model suggested by Hubel and Wiesel in 1960s: V1 Receptive Fields are created from converging LGN inputs

III. Interpretive Model of Receptive Fields

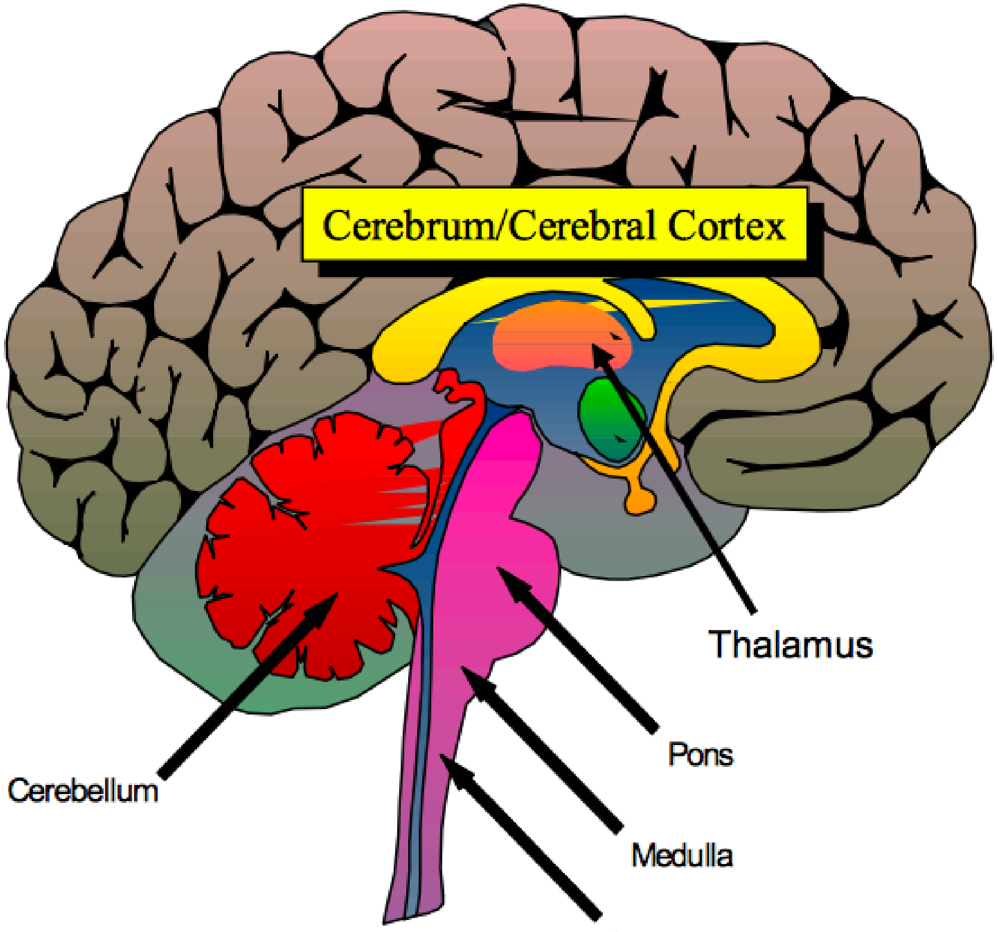
The Question: *Why* are receptive fields in V1 shaped in this way?

What are the computational advantages of such receptive fields?

Computational Hypothesis: How can the image **I** be represented as faithfully and efficiently as possible using neurons with receptive fields $\mathbf{RF_1}$, $\mathbf{RF_2}$, … $\mathbf{RF_n}$



The Human Brain



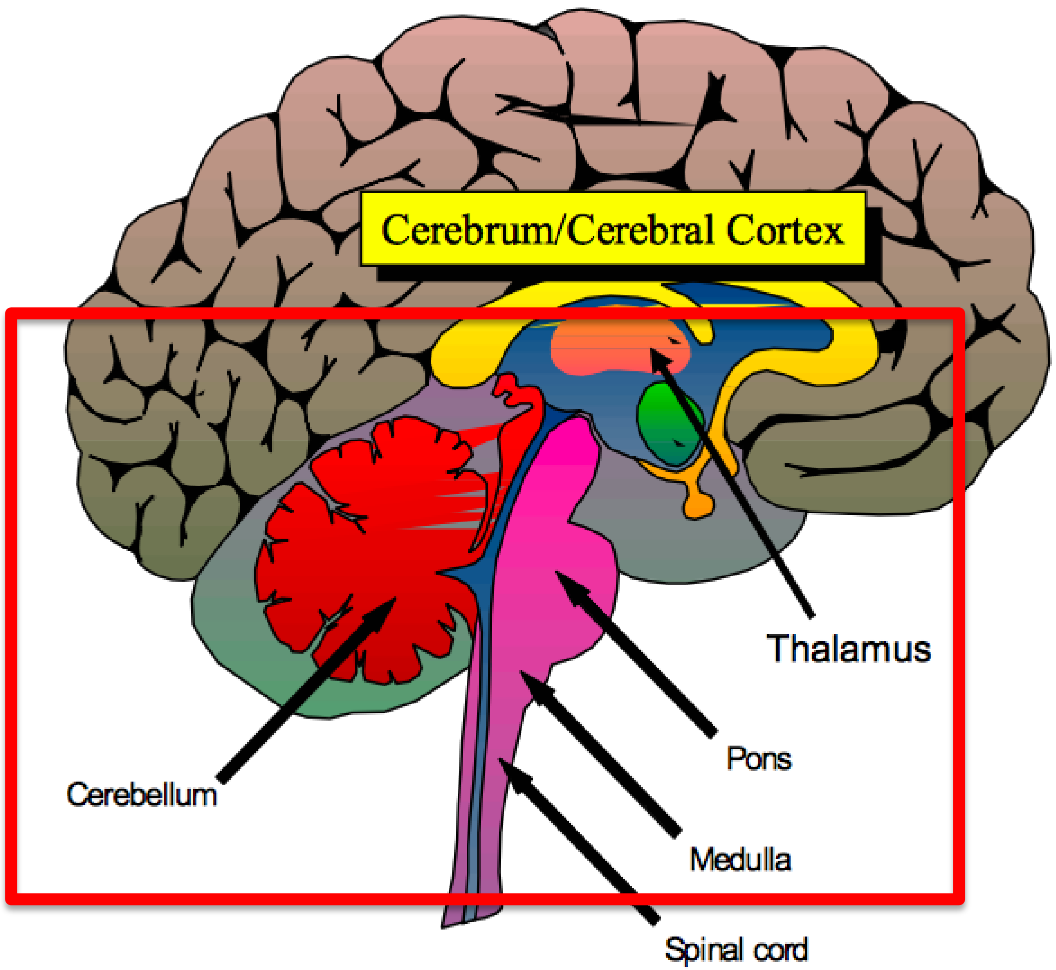
THE BRAIN is wider than the sky,
For, put them side by side,
The one the other will include
With ease, and you beside.

The brain is deeper than the sea,
For, hold them, blue to blue,
The one the other will absorb,
As sponges, buckets do.

The brain is just the weight of God,
For, lift them, pound for pound,
And they will differ, if they do,
As syllable from sound.

Emily Dickinson

Major Brain Regions: Brain Stem and Cerebellum

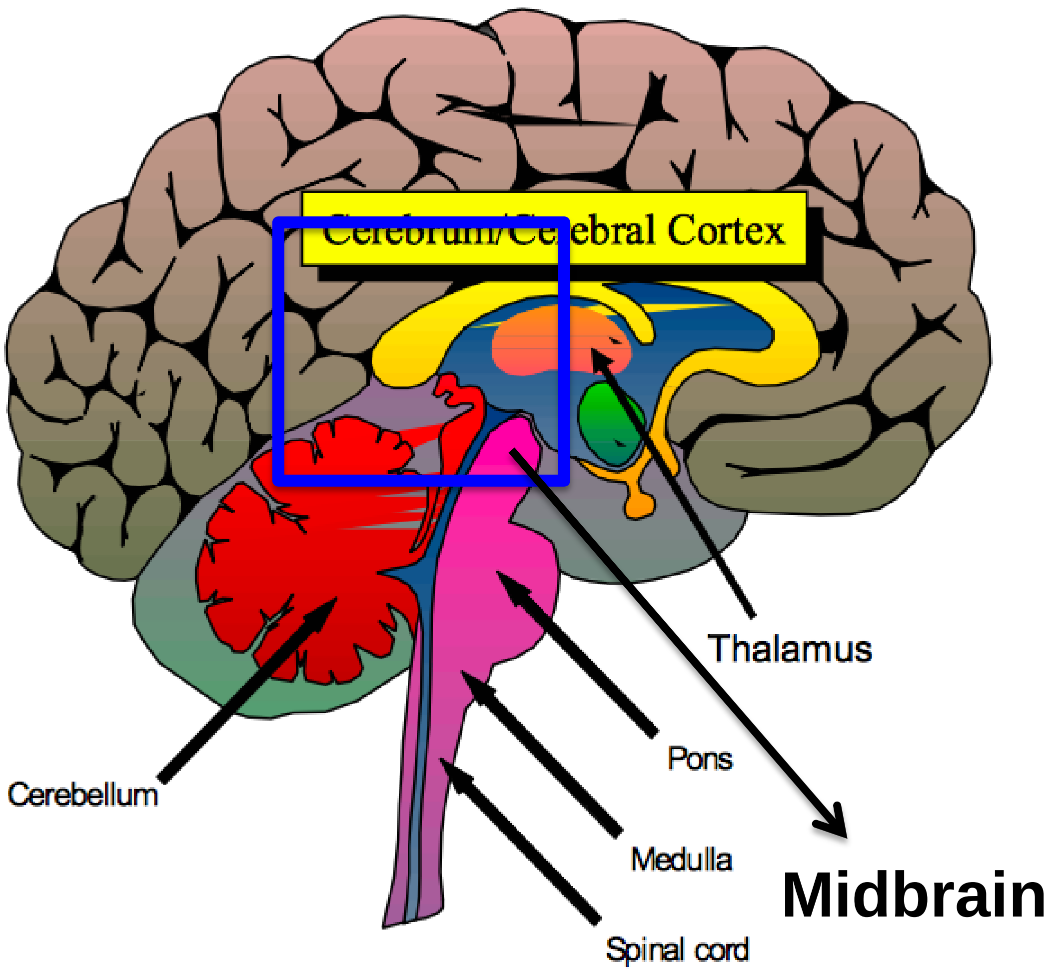


Cerebellum:
Coordination of voluntary movements and sense of equilibrium

Pons:
Connects brainstem with cerebellum and involved in sleep and arousal

Medulla:
Breathing, muscle tone, and blood pressure

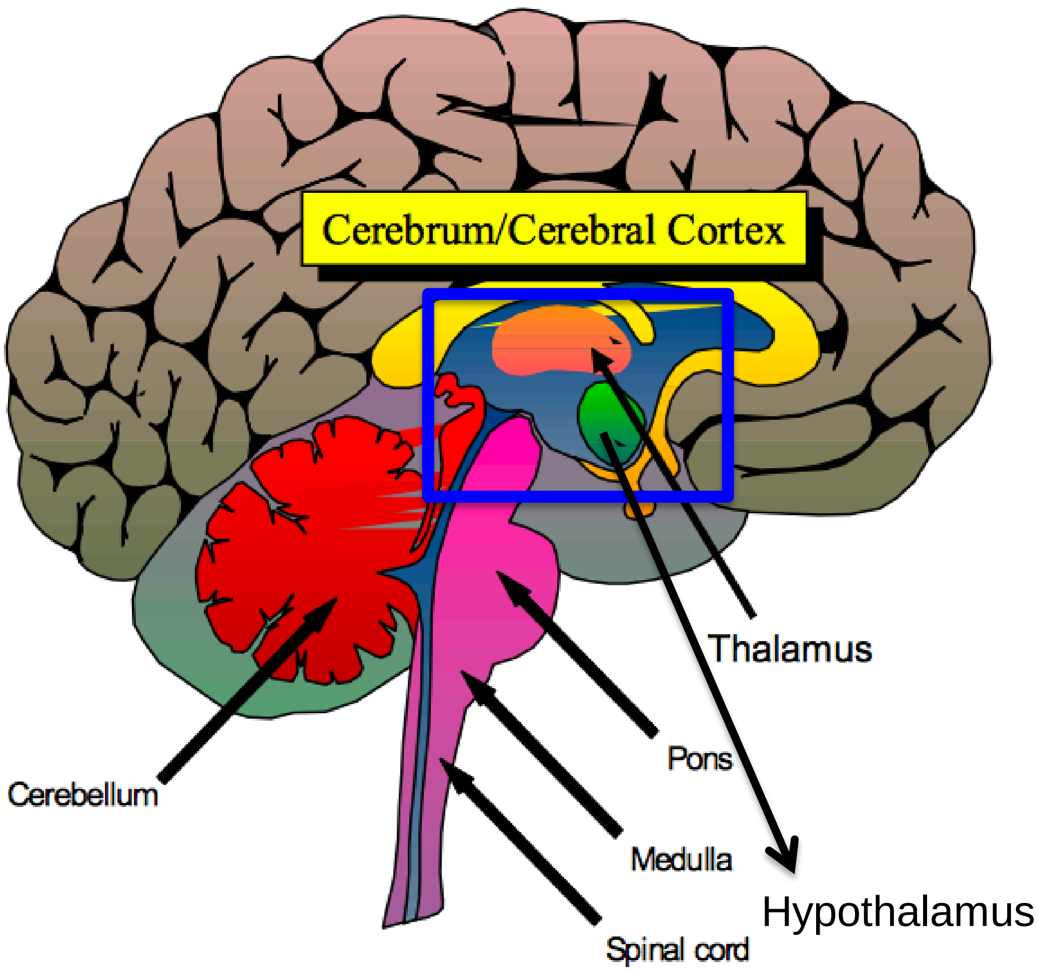
Major Brain Regions: Midbrain and Reticular Formation



Midbrain:
Eye movements, visual, and auditory reflexes

Reticular Formation:
Modulates muscle reflexes, breathing, and pain perception.
Regulates sleep, wakefulness, and arousal.
Not anatomically well-defined (set of nuclei in brainstem).

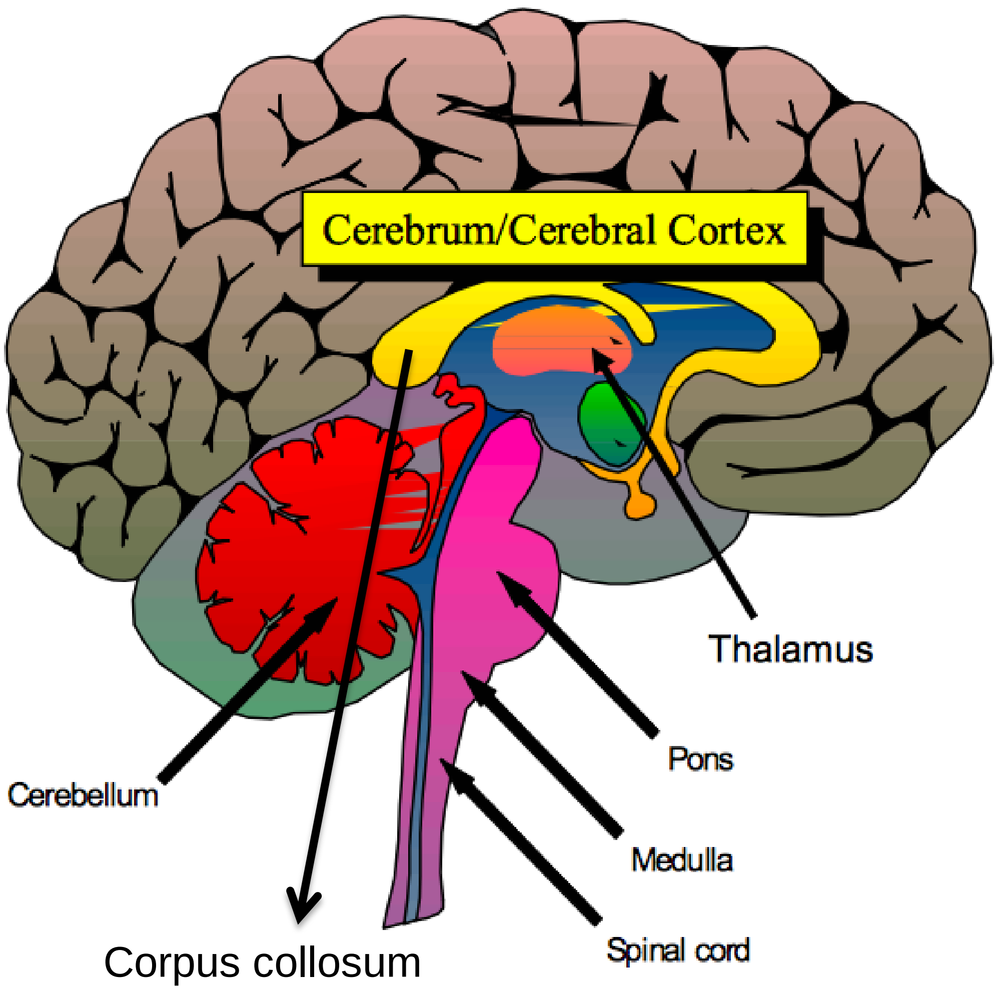
Major Brain Regions: Thalamus and Hypothalamus



Thalamus:
"Relay station" for all sensory information (except smell) to the cortex

Hypothalamus:
Regulates basic needs including fighting, fleeing, feeding, and mating

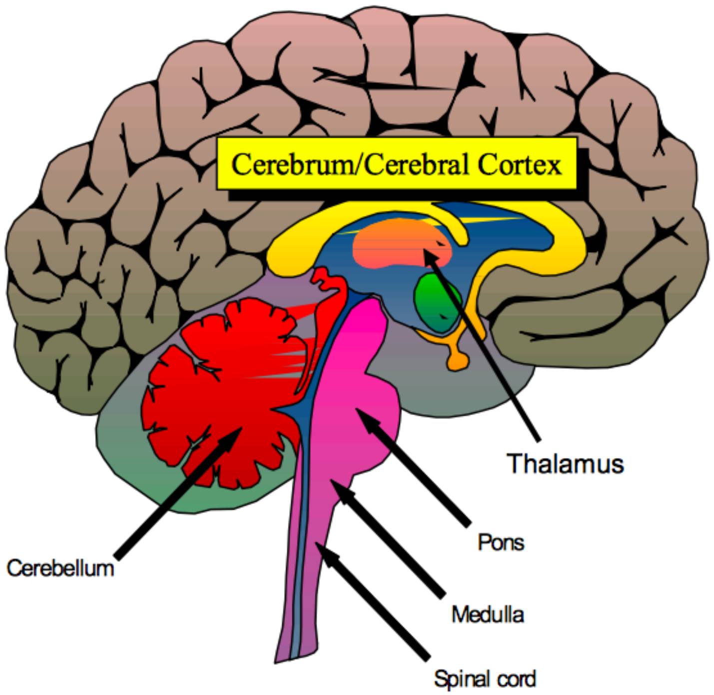
Major Brain Regions: Cerebral Hemispheres

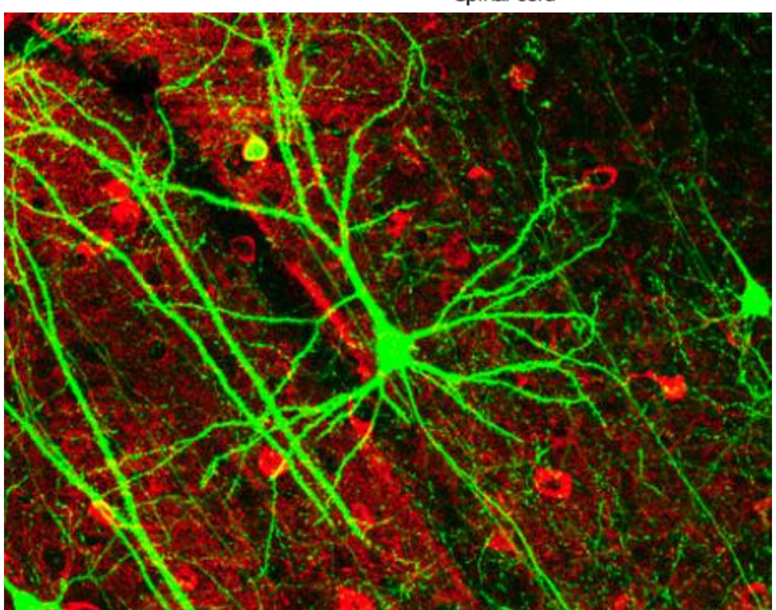


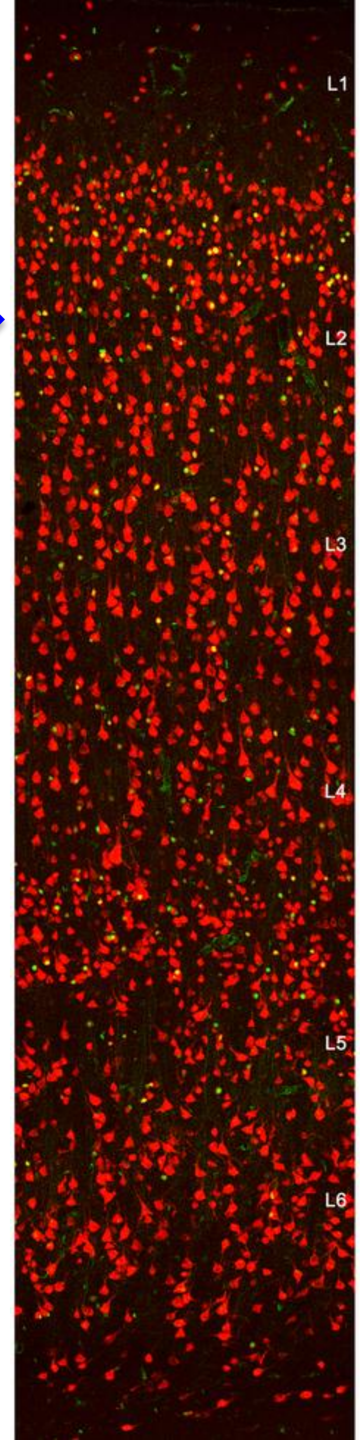
Consists of: cerebral cortex, basal ganglia, hippocampus, and amygdala

Involved in:
Perception and motor control, cognitive functions, emotion, memory and learning

The Neuron



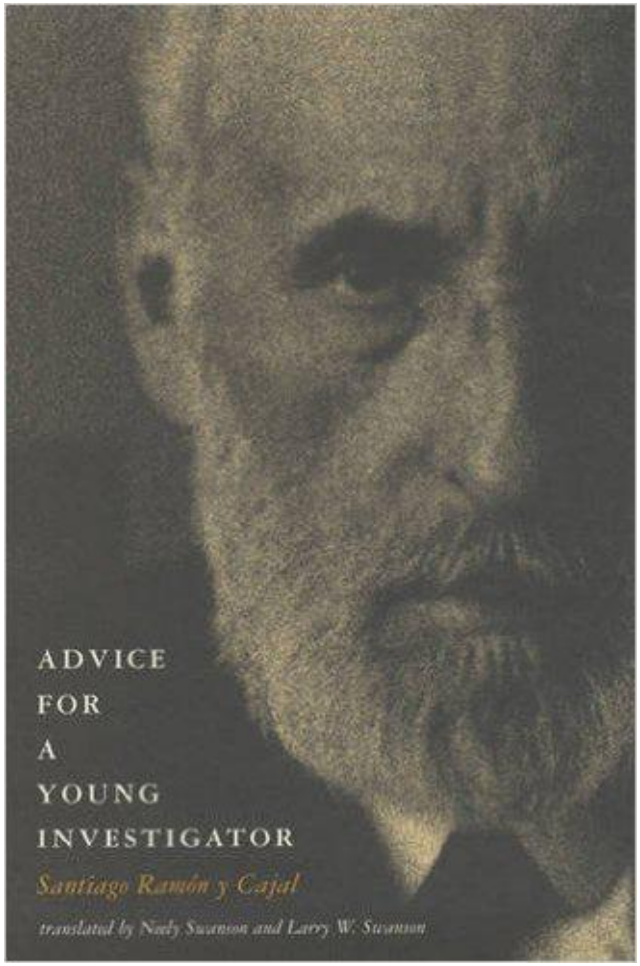


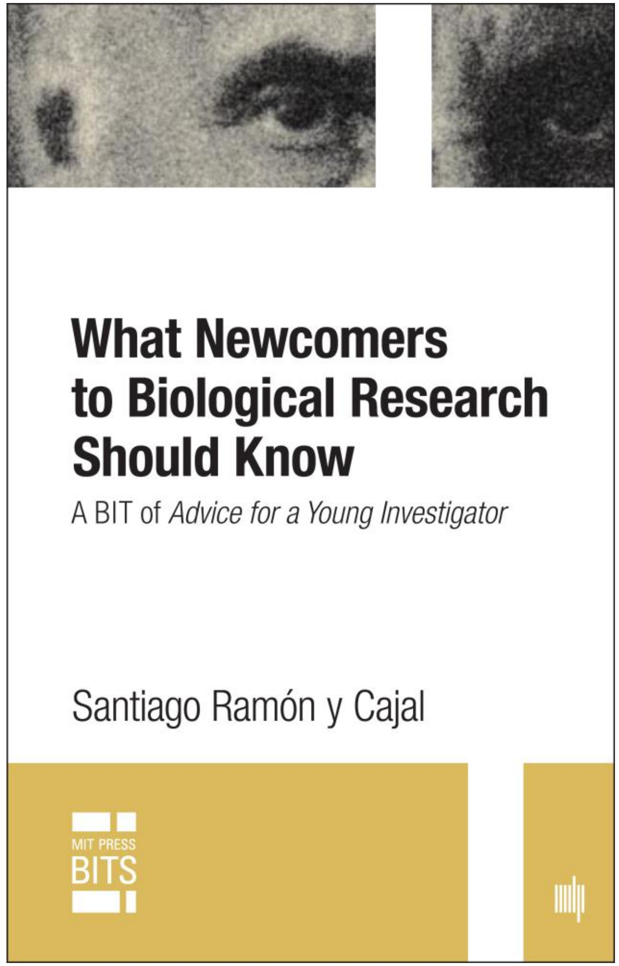


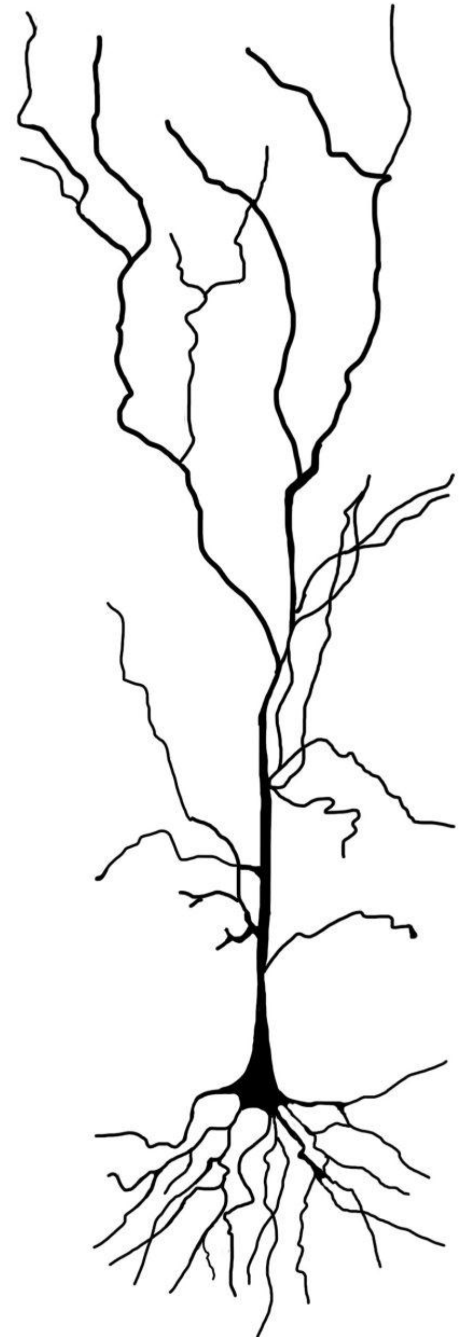
Neo-cortex:
Part of cerebral cortex concerned with sight and hearing in mammals, regarding as the site of higher intelligence
The neo-cortex has six layers of tissue.

Pyramidal neuron:
Primary component of cortical tissue and named for triangular cell body (soma)

The Neuron Doctrine

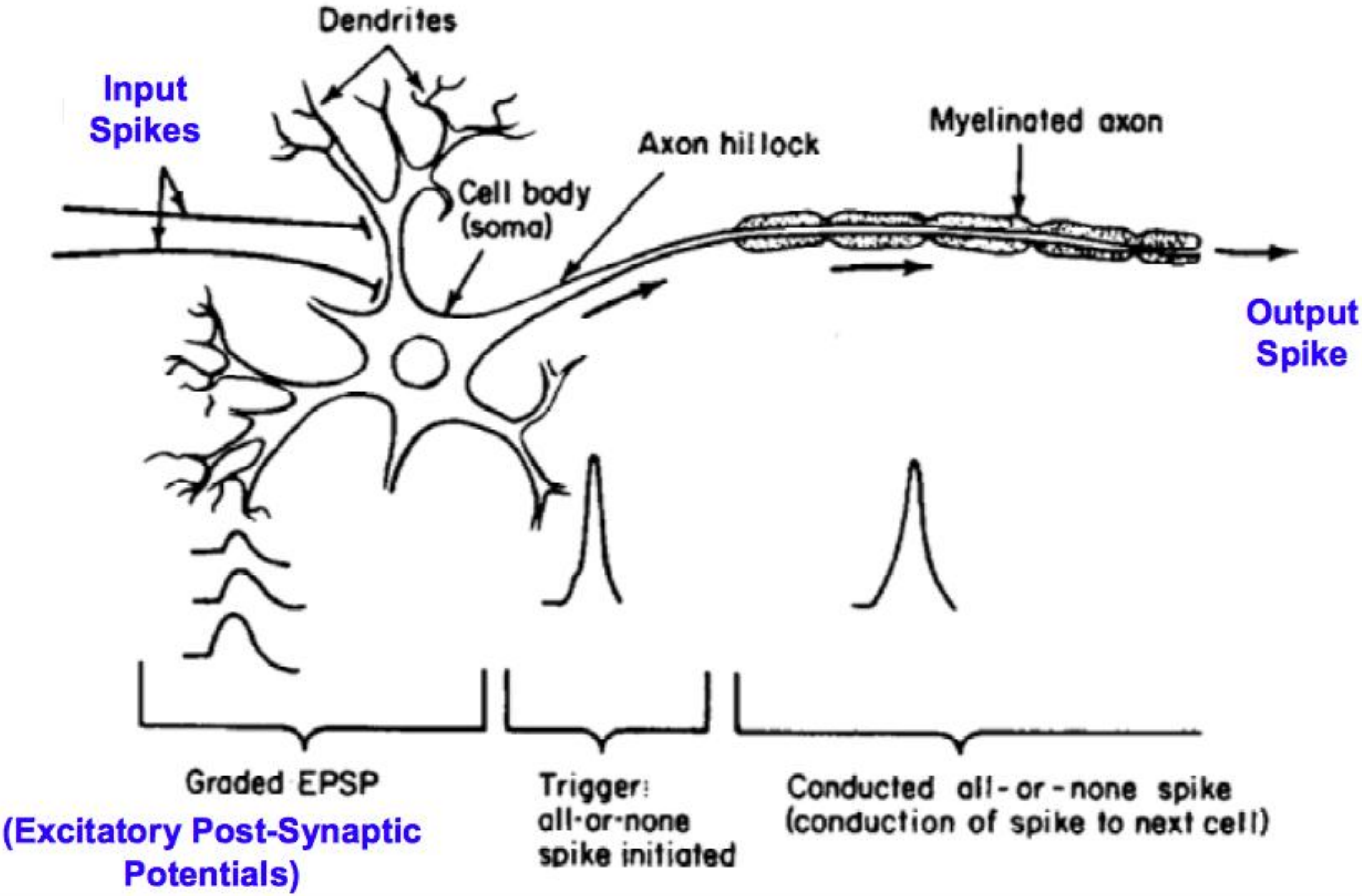






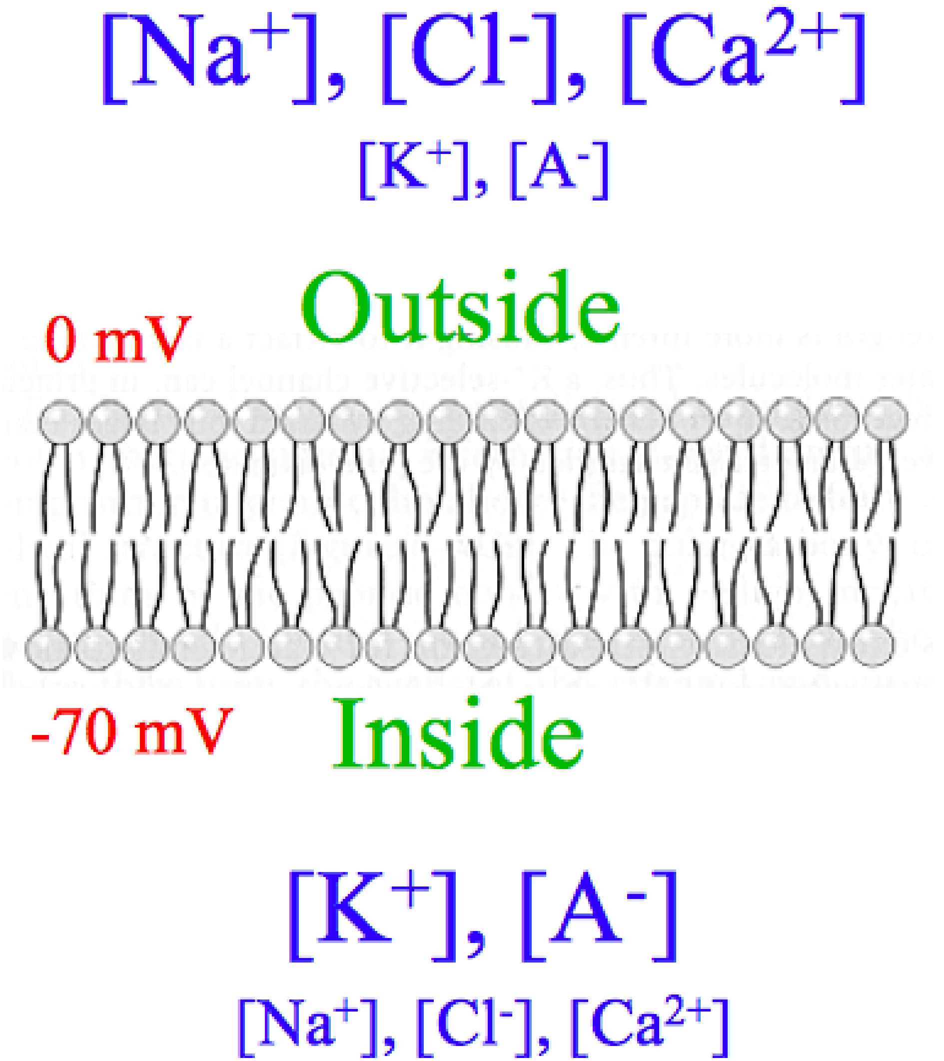
"The neuron is the appropriate basis for understanding the computational and functional properties of the brain" (1891)

The Neuron

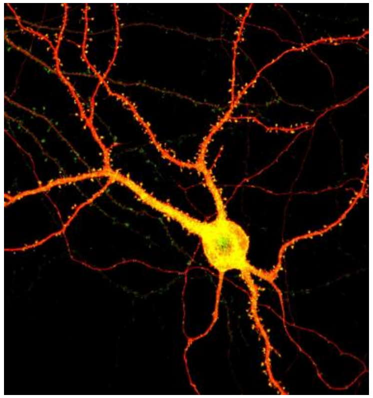

Dendrites
Input Spikes
Axon hillock
Myelinated axon
Cell body (soma)
Output Spike
Graded EPSP
(Excitatory Post-Synaptic Potentials)
Trigger: all-or-none spike initiated
Conducted all-or-none spike (conduction of spike to next cell)

Properties of a Neuron

- Contents of the neuron enclosed within a *cell membrane*, which is a *lipid bilayer*
- The bilayer is impermeable to charged ions
- Each neuron maintains a *potential difference* across its membrane
  - Inside is -70 to -80 mV relative to outside
  - *Ionic pump* maintains -70 mV difference by expelling Na^+ out and allowing K^+ ions in



Electrophysiology of a Neuron

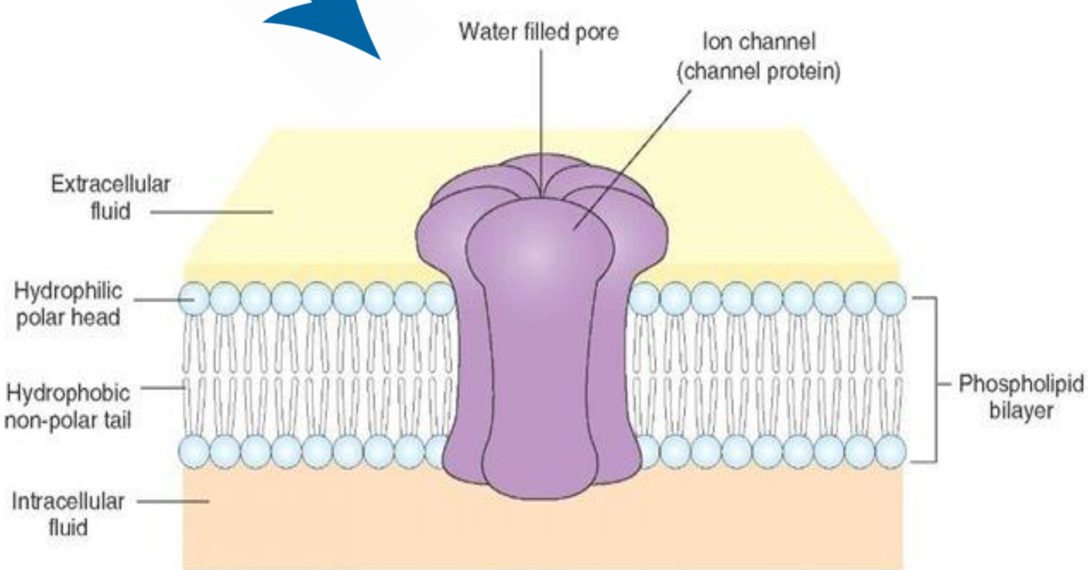


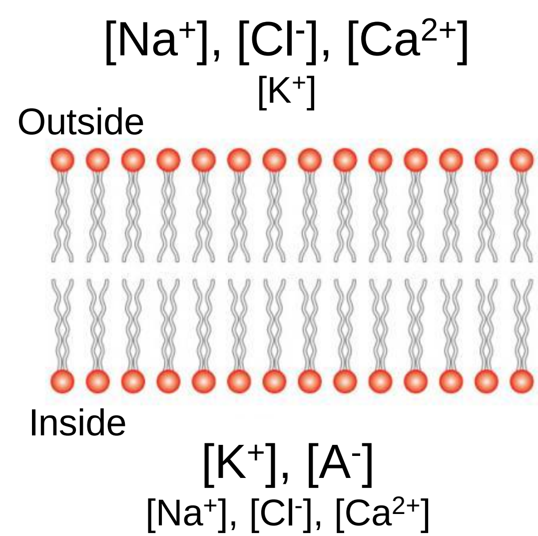
Nernst Equation

E = Membrane Potential at which current flow due to diffusion of ions is balanced by electric forces

$$E = \frac{RT}{zF} \ln\left(\frac{[outside]}{[inside]}\right)$$

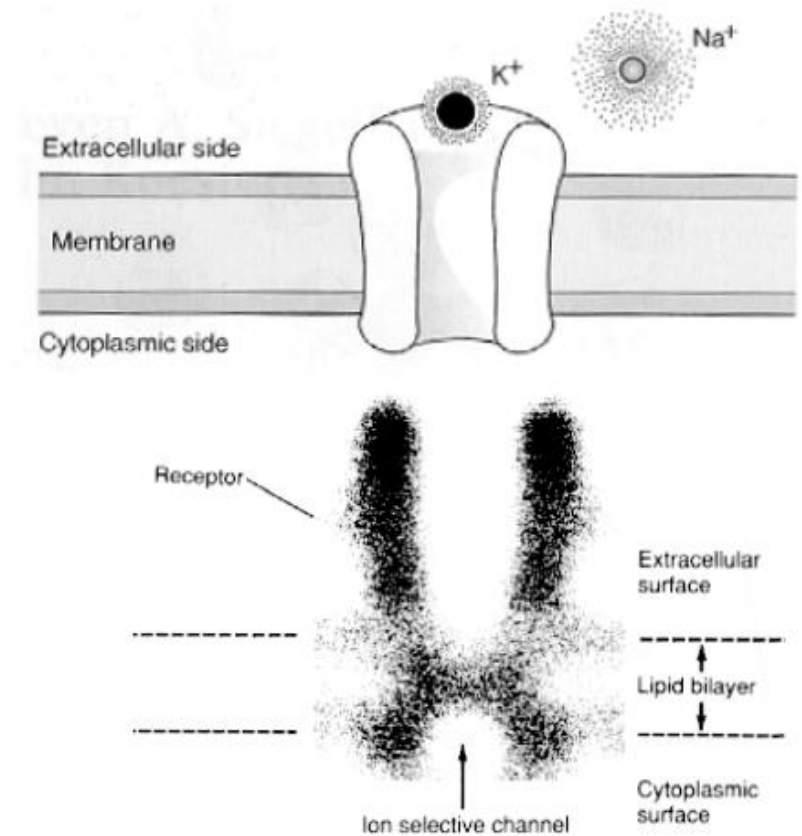
Cell Membrane





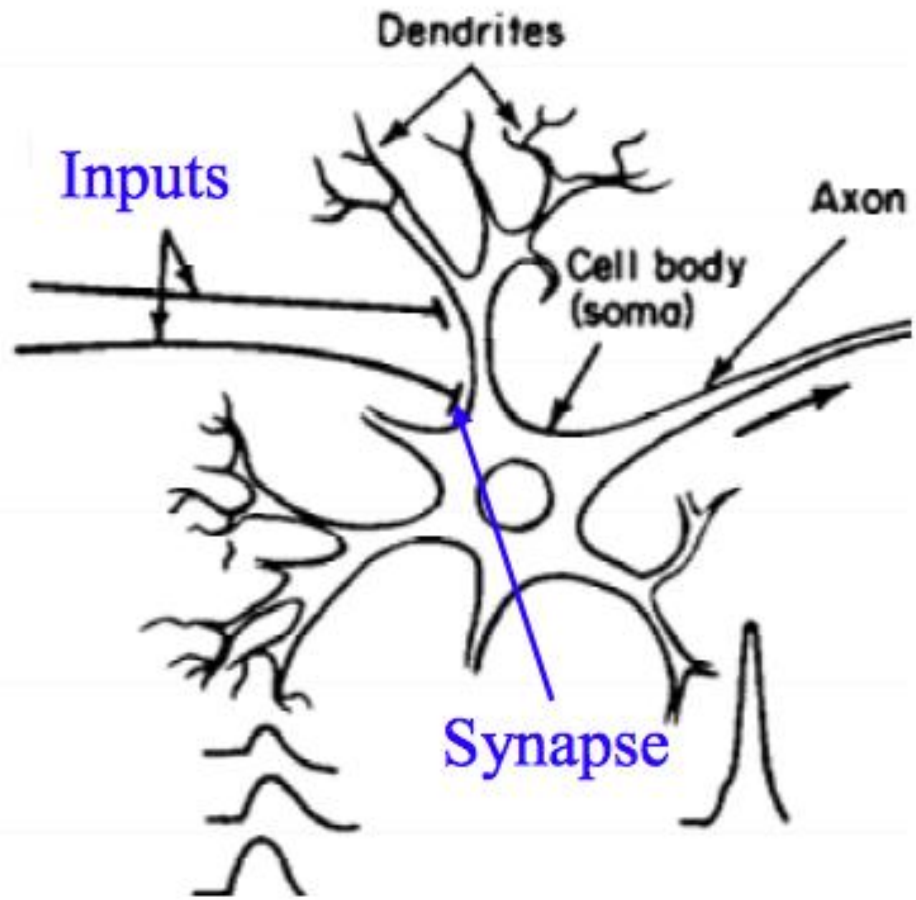
Membrane Proteins: The Gatekeepers

- Properties in membranes act as pores or channels that are ion-specific
- Ionic channels are *gated*
  - Voltage-gated: Probability of opening depends on membrane voltage
  - Chemically-gated: Binding to a chemical causes channel to open (neurotransmitters)
  - Mechanically-gated: Sensitive to pressure or stretch (sensory neurons)



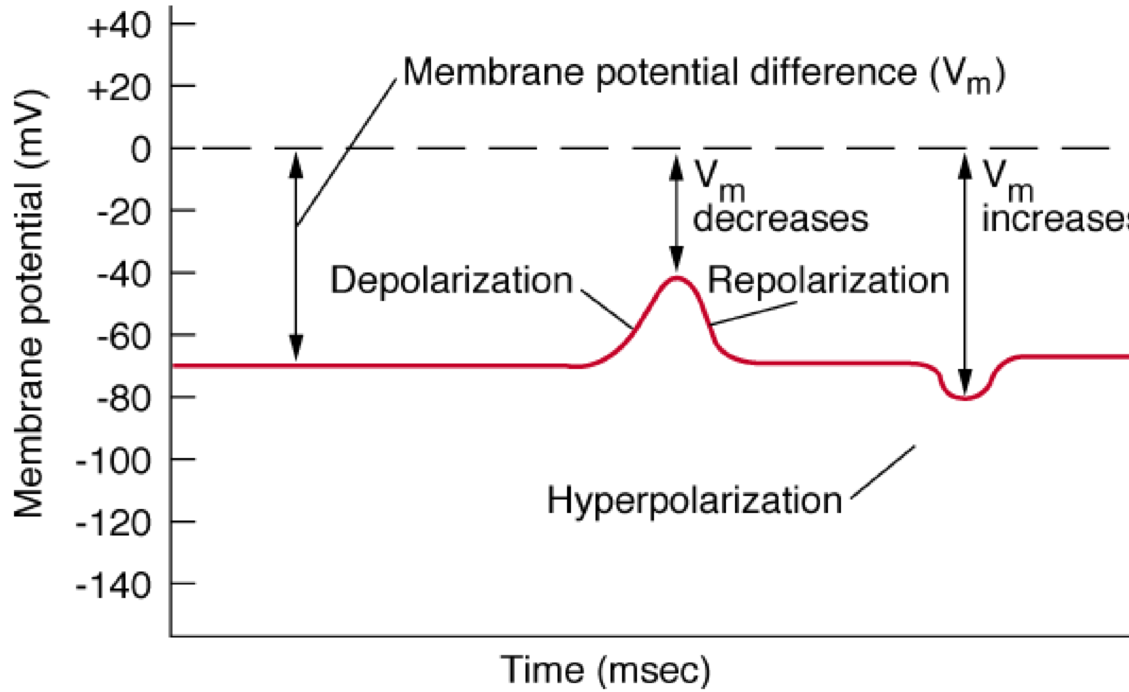
Neuronal Signaling

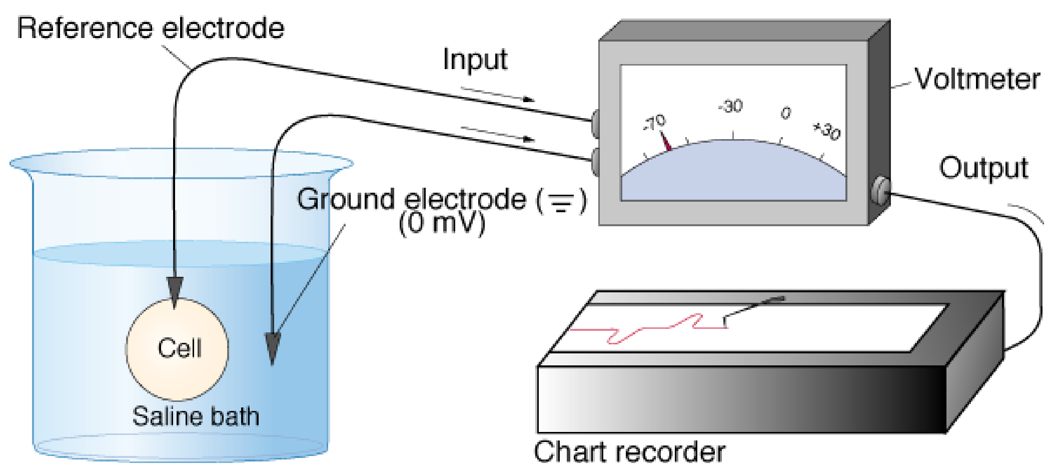
- Different types of gated channels are involved in neuronal signaling
  - Graded Potentials: travel over <u>short distances</u> and are activated by the opening of <u>mechanically or chemically gated channels</u>
  - Action Potentials: travel over <u>long distances</u> and are generated by the opening of <u>voltage-gated channels</u>



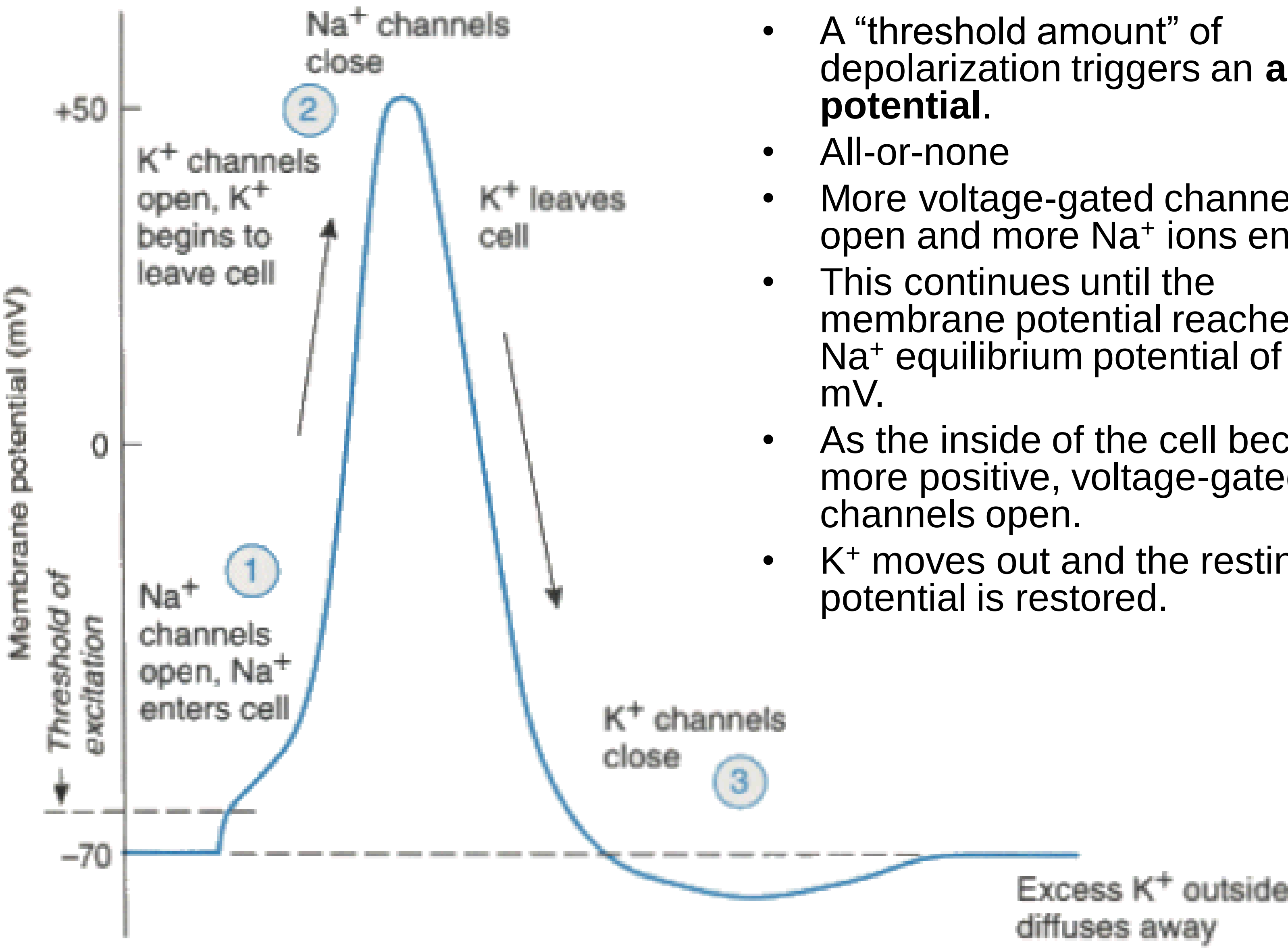
Action Potential

- Depolarization: a decrease in the potential difference between the inside and outside of the cell
- Hyperpolarization: an increase in the potential difference between the inside and outside of the cell
- Repolarization: returning to the resting membrane potential from either direction





Action Potential



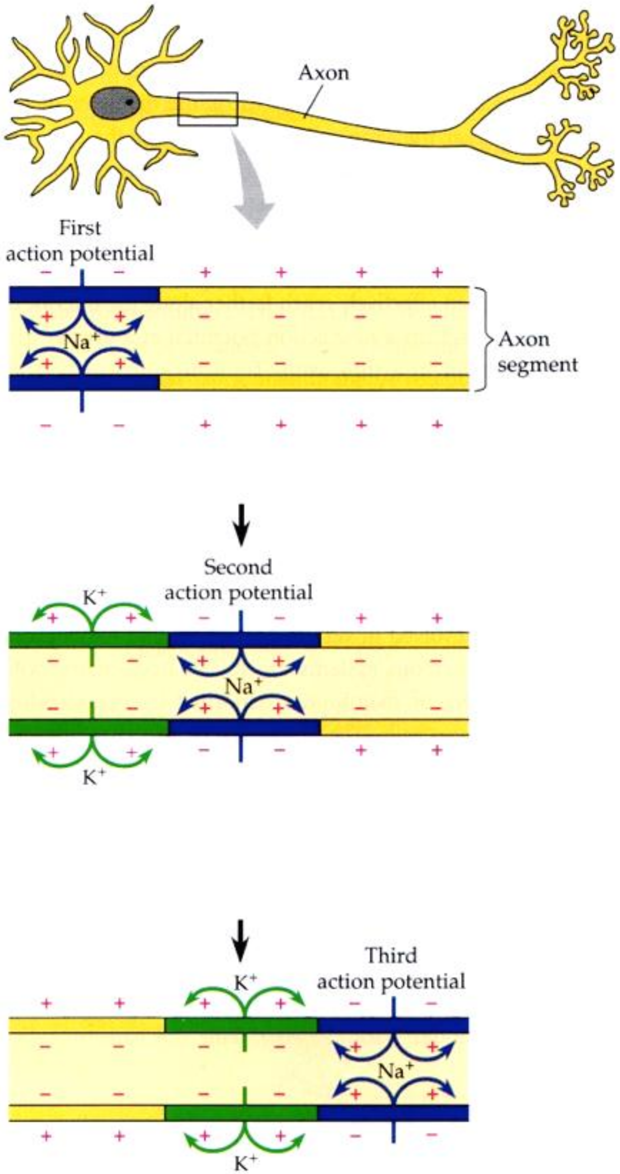
- A “threshold amount” of depolarization triggers an **action potential**.
- All-or-none
- More voltage-gated channels open and more Na^+ ions enter.
- This continues until the membrane potential reaches the Na^+ equilibrium potential of +50 mV.
- As the inside of the cell becomes more positive, voltage-gated K^+ channels open.
- K^+ moves out and the resting potential is restored.

Action Potential Propagation

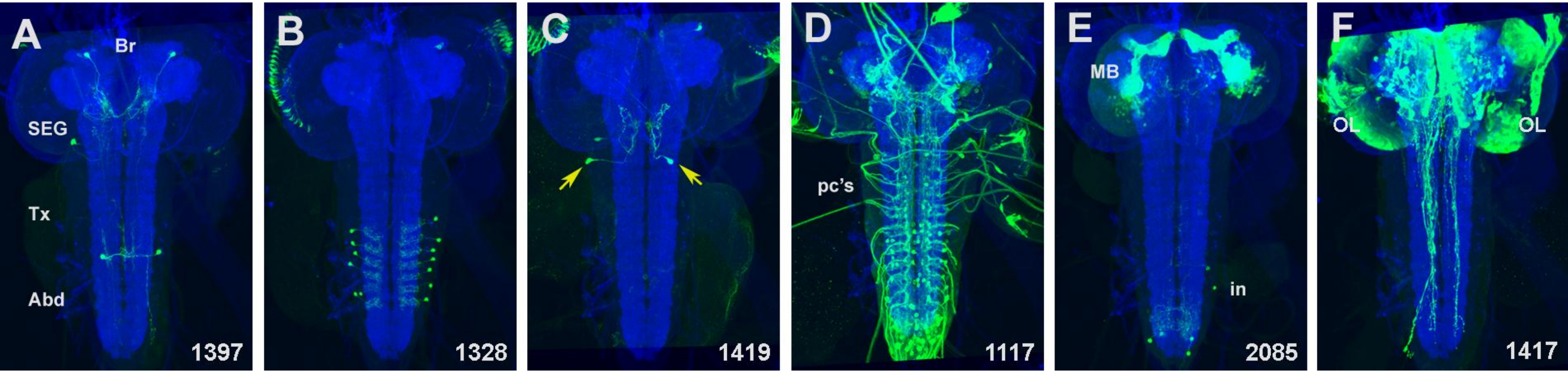
The action potential is propagated along the axon of the neuron

Voltage-gated sodium channels

Voltage-gated potassium channels



Neural Circuits in Drosophila Larval Brain



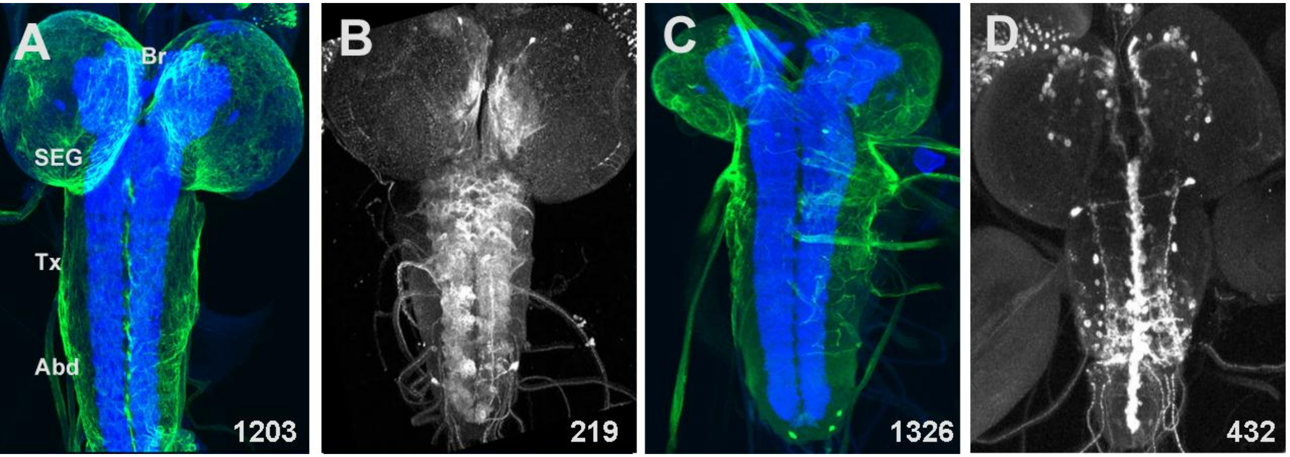


Figure (Top)

Z- Projections of Confocal Stacks of Larval Nervous Systems Illustrating Selected Expression Patterns in the InSITE Collection

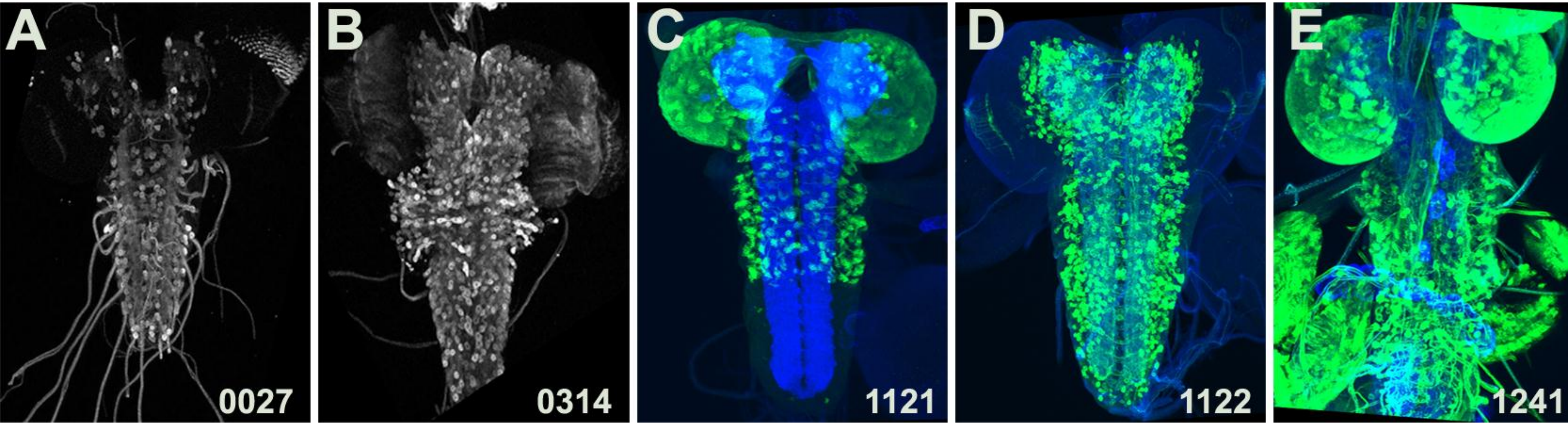
A and B. Extremely sparse lines with expression in **(A)** the brain and **(B)** the abdominal neurons. ***C and D.*** Lines with expression in clusters of post-embryonic neurons (pc). Arrows show sparse expression pattern. ***E.*** Strong expression in mushroom bodies (MB) and abdominal interneurons (in). ***F.*** Expression in the optic lobes (OL) and post-embryonic neurons. Abd, abdomen; Br, brain; Tx, thorax.

Figure (Bottom)

Examples of Glial Expression in the InSITE Collection

A. Perineurial and subperineurial glia ***B.*** Ensheathing glia. ***C.*** Astrocyte-like glia ***D.*** Midline Glia. Abd, abdomen; Br, brain; Tx, thorax.

Lineage Lines in Drosophila Larval Brain



Figure

Examples of Cell-Type Expression in Lineage Groups in the InSITE Collection

A, D, and E. All of the members of the post-embryonic lineages express GFP from the NBs to the oldest neurons. ***B.*** Expression in NBs and GMCs. ***C.*** Lineage expression exclusive to brain and thorax. NB, neuroblast; GMC; ganglion mother cell.

Introduction to Image Registration

What is registration?

Registration is the determination of geometrical transformation that aligns points in one view of an object with corresponding points in another view of that object or another object

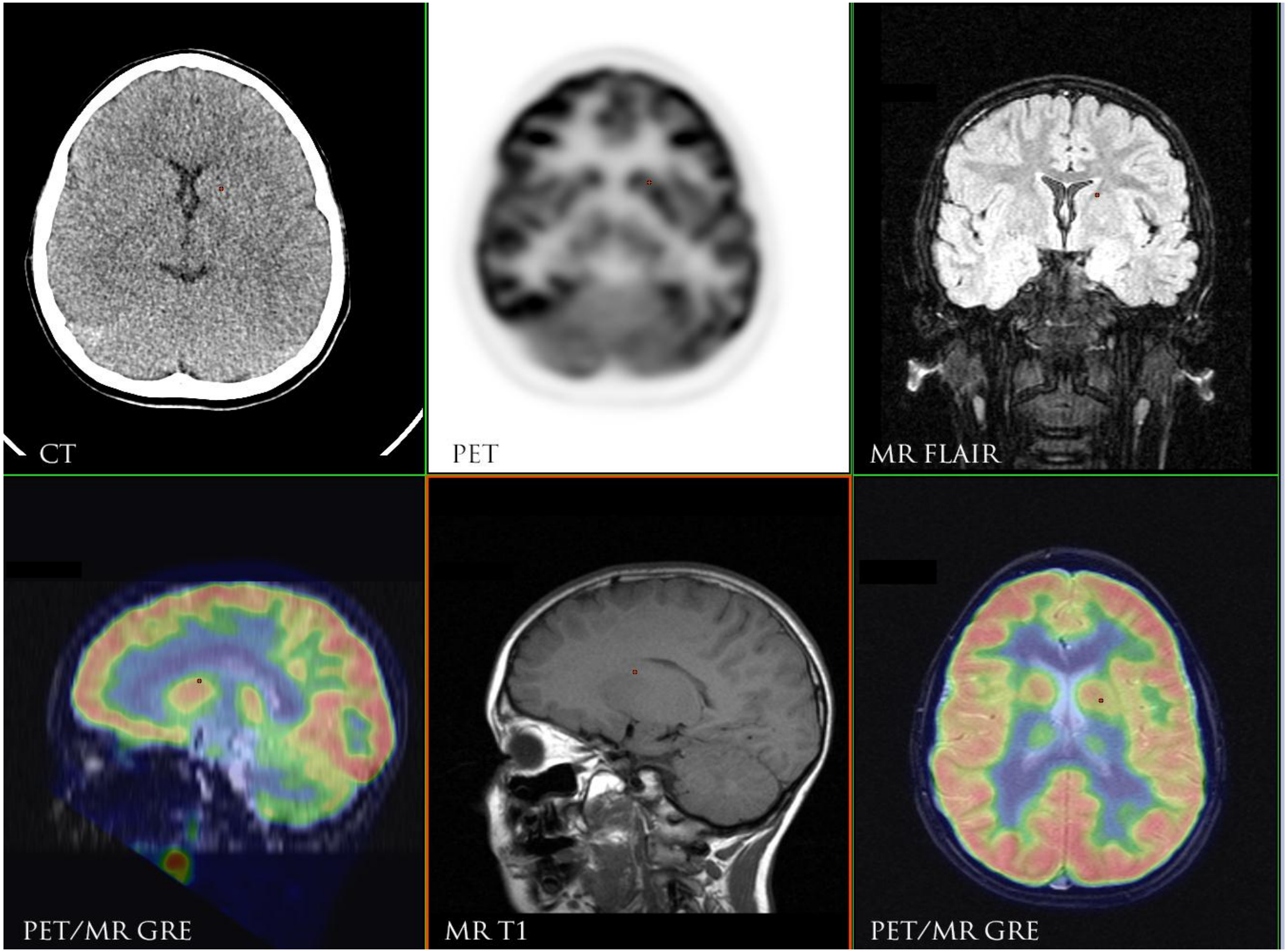
“View” refers to the physical arrangement of an object in space (a 3-D or 2-D Image)

Inputs of Image Registration: 2 Views to be Registered

- Target/Source
- Fixed/Moving

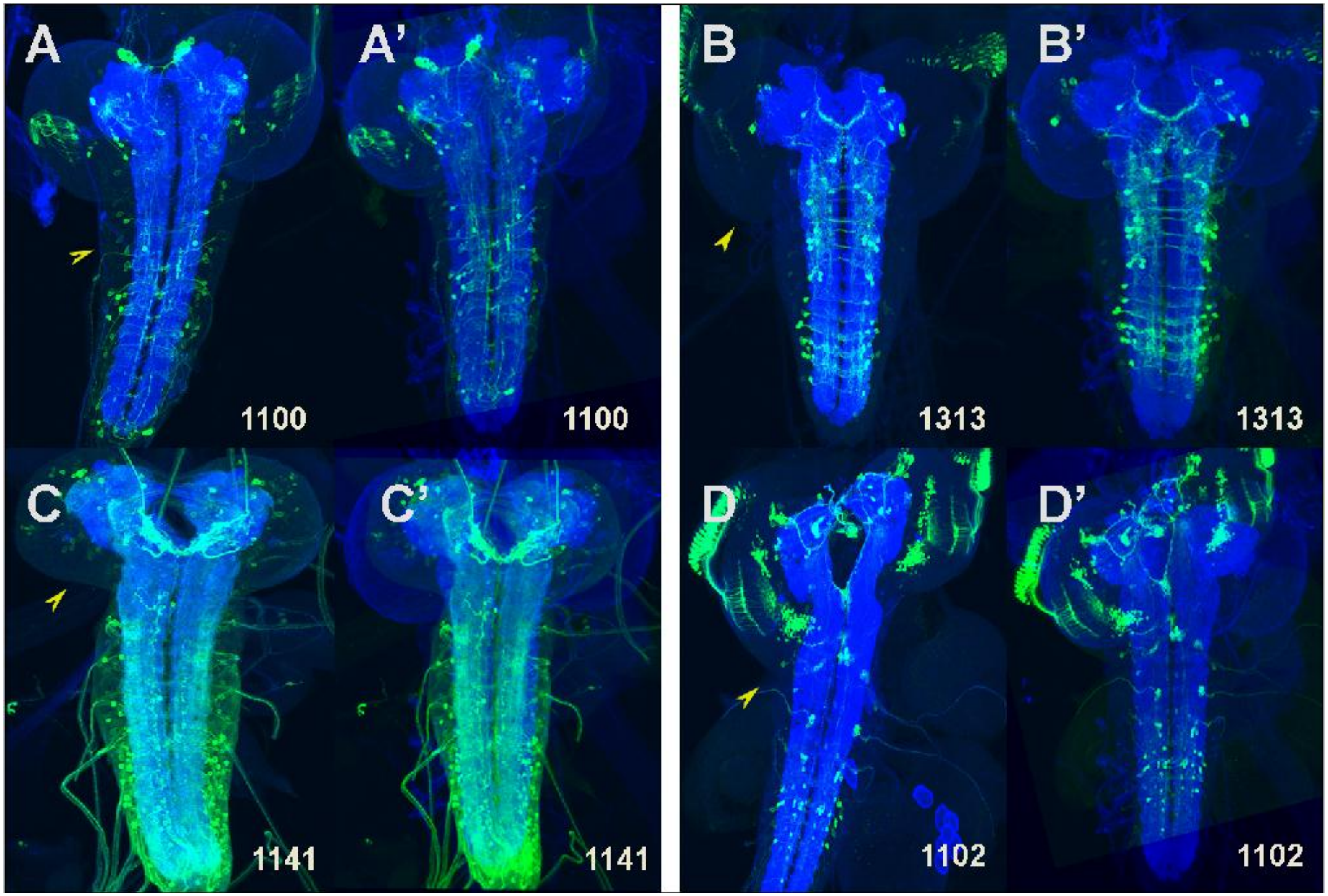
Output of Image Registration: Geometrical Transformation (a mathematical mapping of points in one view to points in the second view)

Example of Image Registration



Note: *Image Fusion* is not the same as *Image Registration*

Image Registration to Standardized Template



Figure

(A, A') and (D,D') Correction for Bending Larval Body.

(B,B') and (C,C') Correction for Mushroom Body Size. *Arrows indicate regions for correction.*

Identified Issues in Image Registration

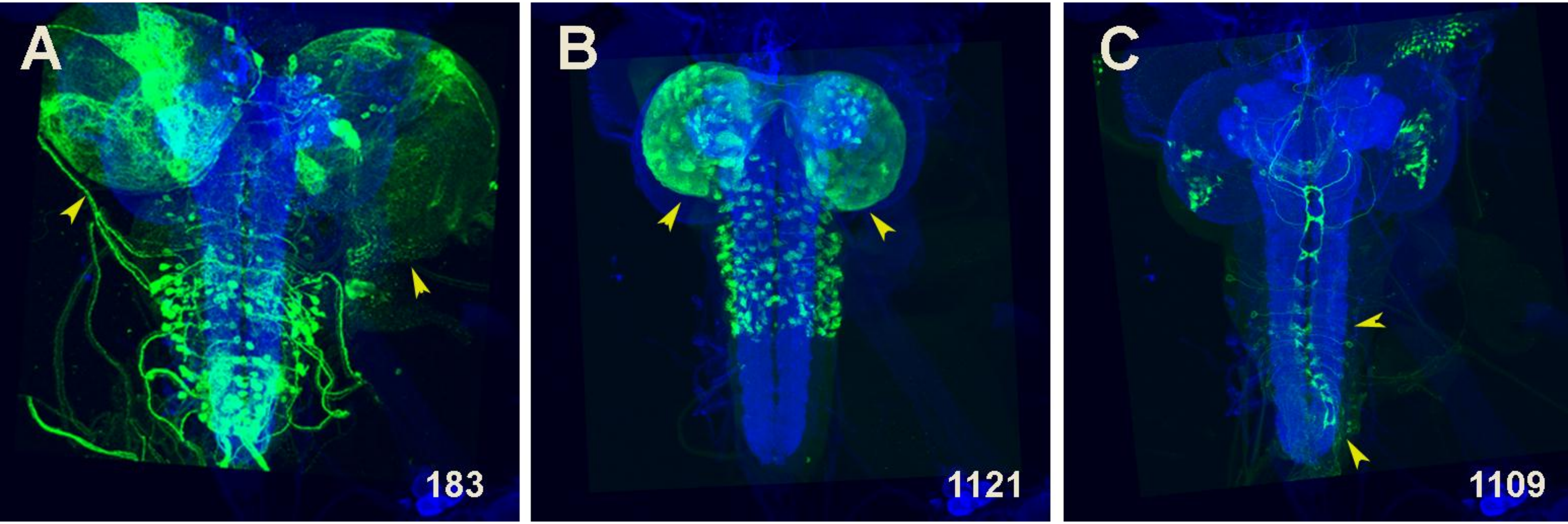


Figure
A. Expression pattern larger than template (Scaling Issue)
B. Expression pattern smaller than template (Scaling Issue)
C. Expression pattern twisted (Motion Correction Issue)
Arrows indicate regions of misalignment.

Scaling Correction Method in Image Registration

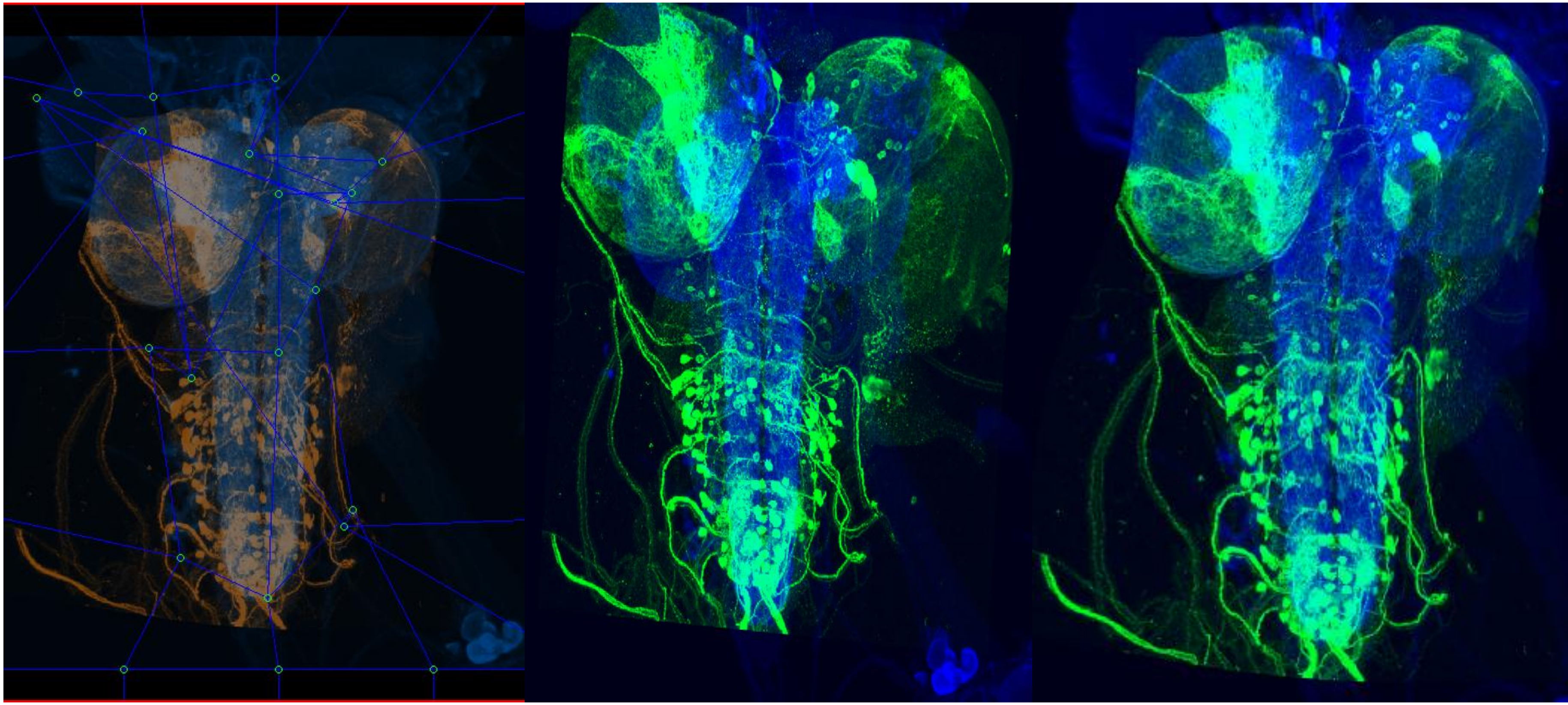


Figure
Scaling Correction Method by Manual B-Spline Deformation

Motion Correction Method in Image Registration

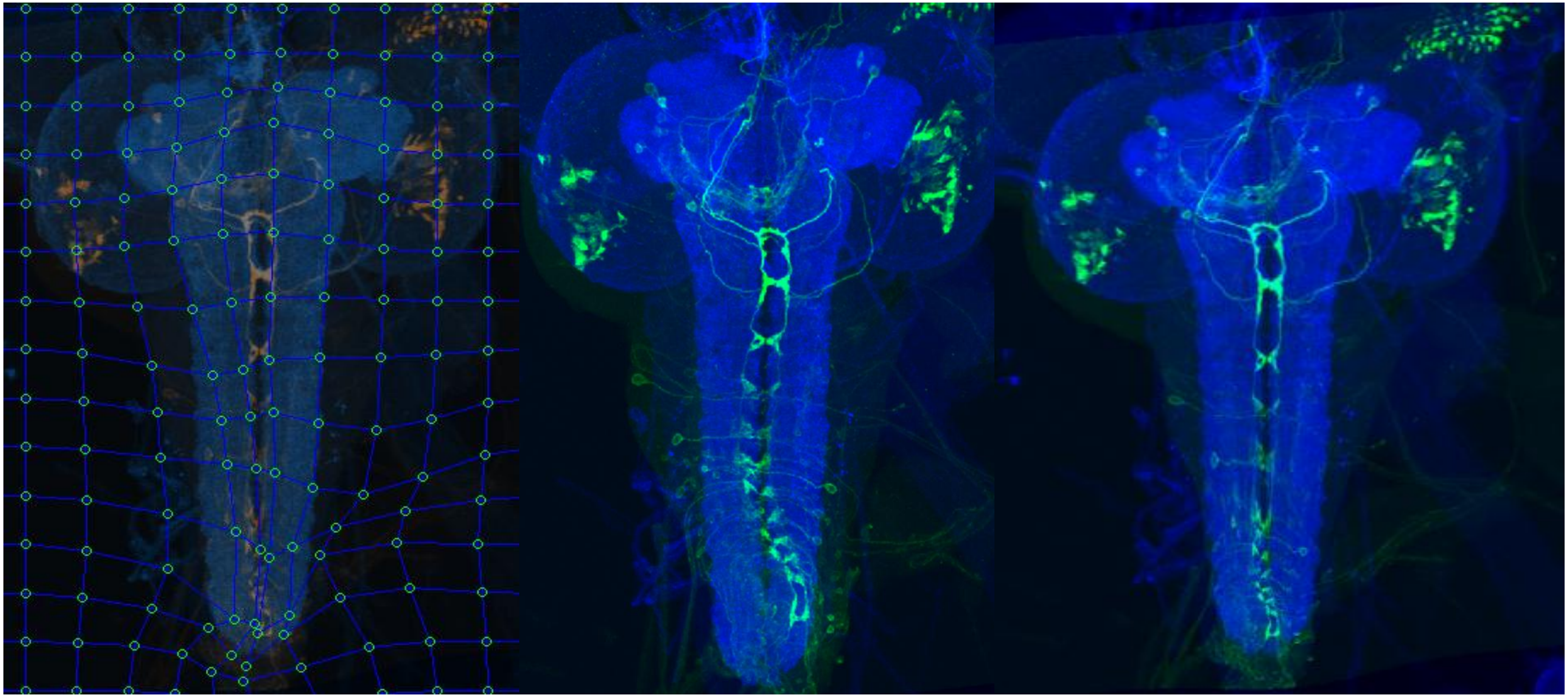
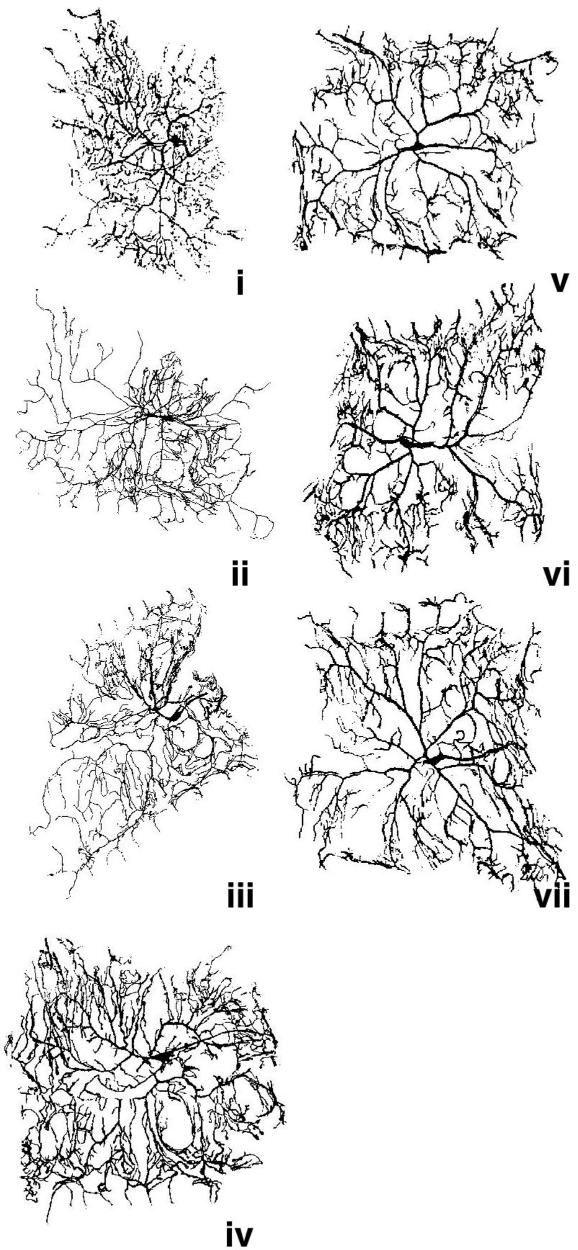
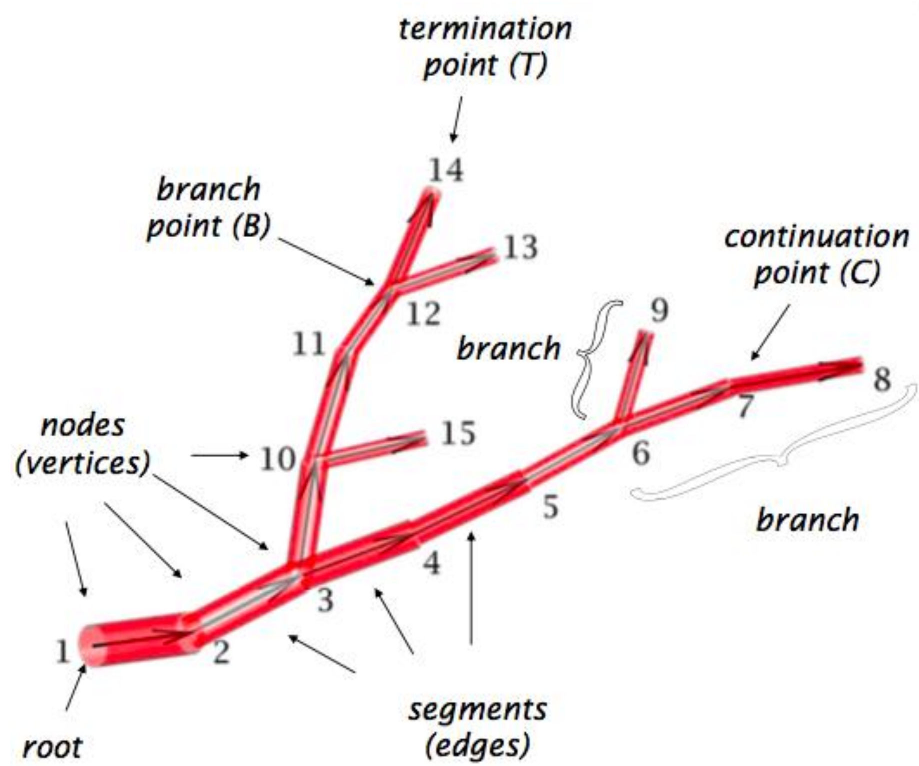


Figure
Motion Correction Method by Manual B-Spline Deformation

Dendrite Morphology Analysis

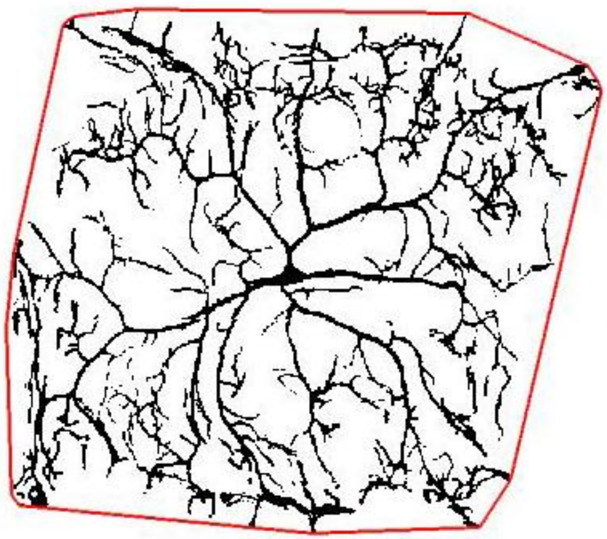




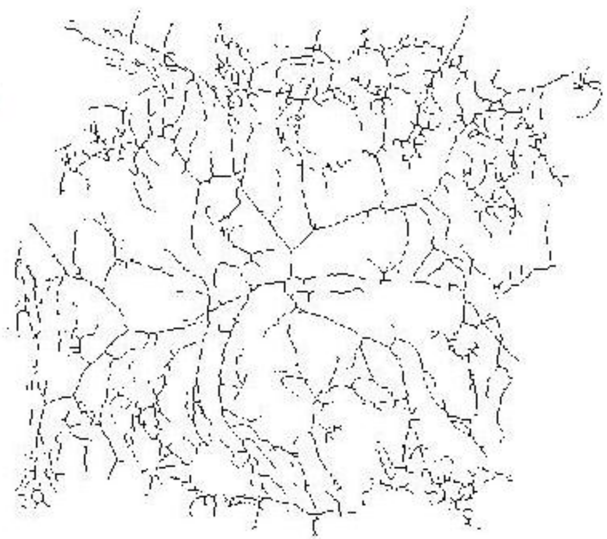
Graph Theory in Neuroscience

A dendritic tree is represented by a set of nodes connected by edges. Branch order begins at the root (node with an index of 1). All edges lead away from the root. This defines their directionality uniquely.

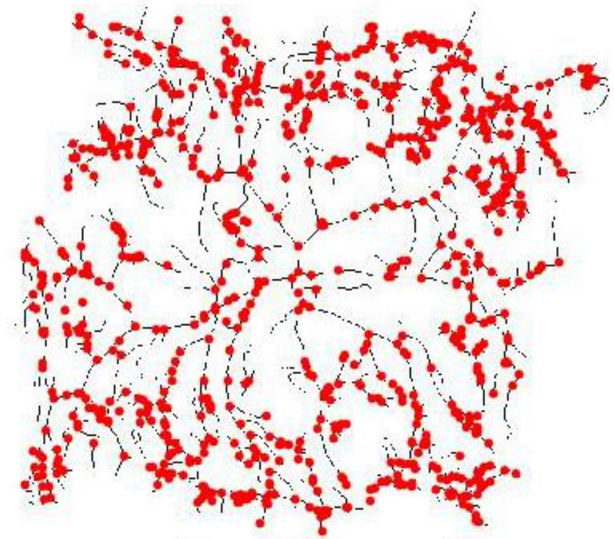
Dendrite Morphology Analysis



Dendritic Tree Area



Total Dendritic Length



Total Branch Point Number

Dendritic Tree Area: area circumscribed by convex hull
Total Dendritic Length: sum of all dendritic segments identified in a skeletonization of the arbor
Total Branch Point Number: sum of branch points identified in a skeletonized rendition of the arbor

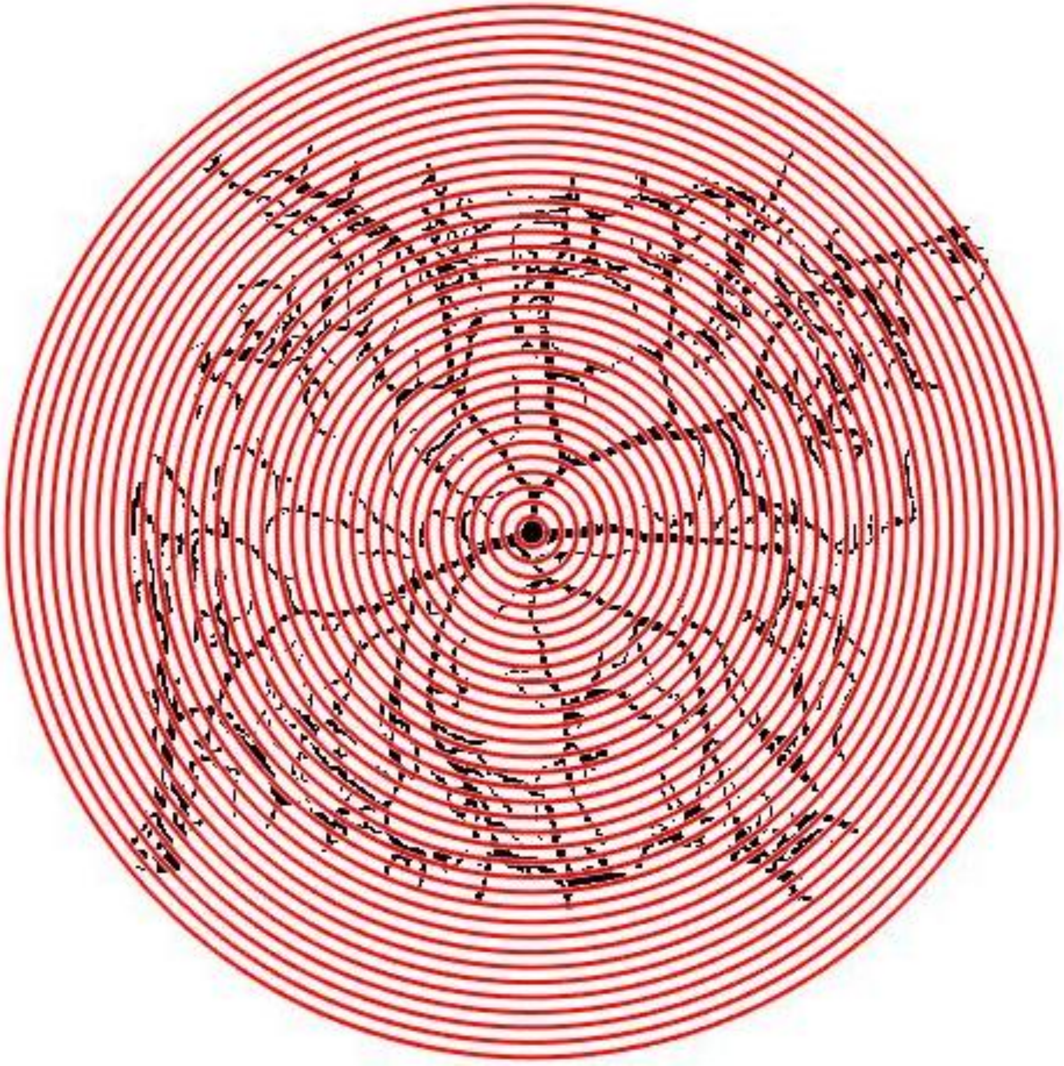
Sholl Analysis

Sholl Analysis:

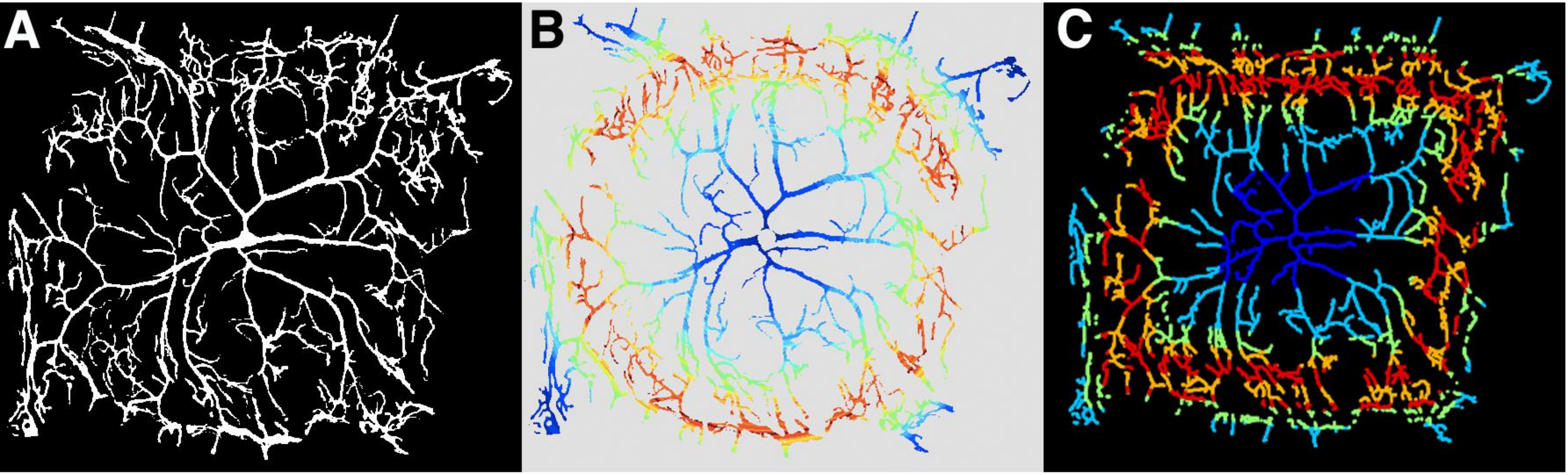
Technique to describe neuronal arbors and quantify morphological complexity

How does it work?

Sholl Analysis creates a series of concentric shells around a neuronal arbor, and counts how many times connected voxels defining the arbor intersect the sampling shells.

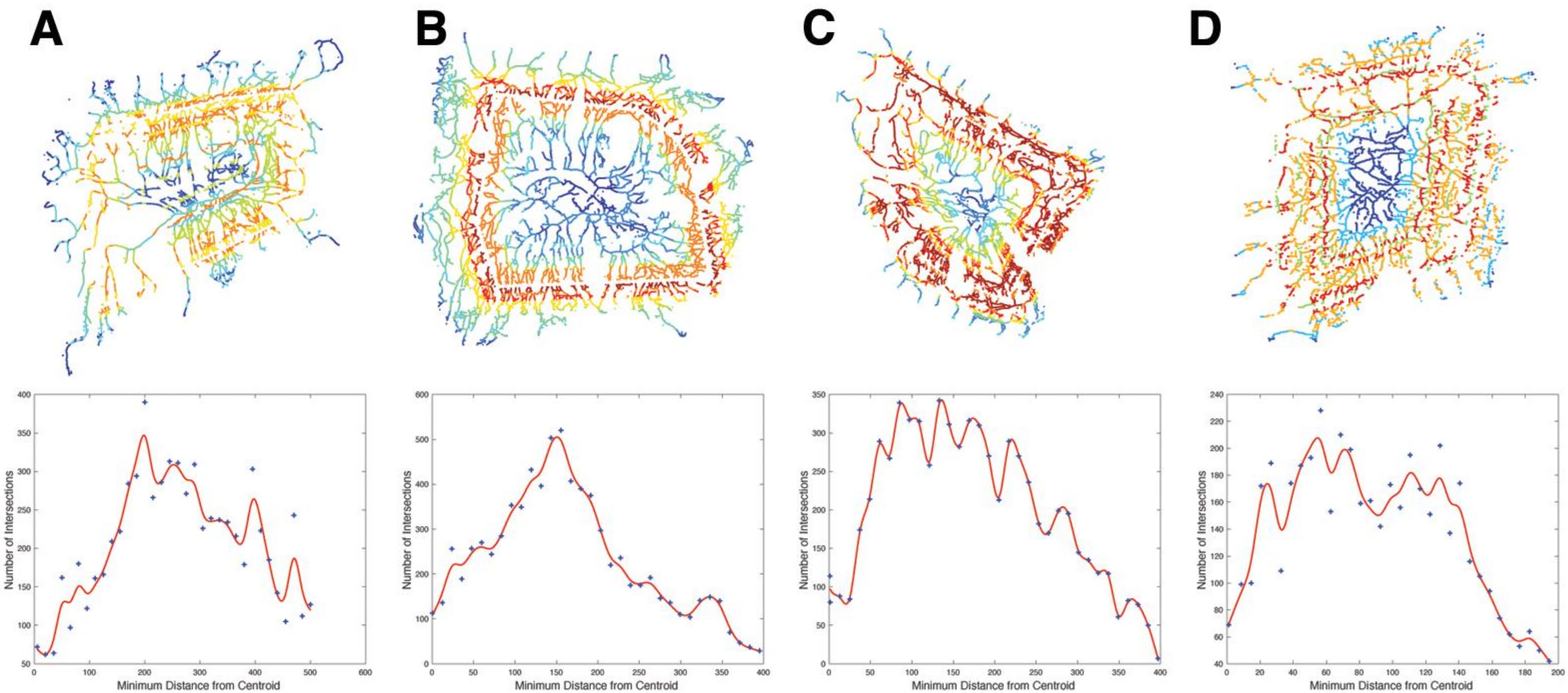


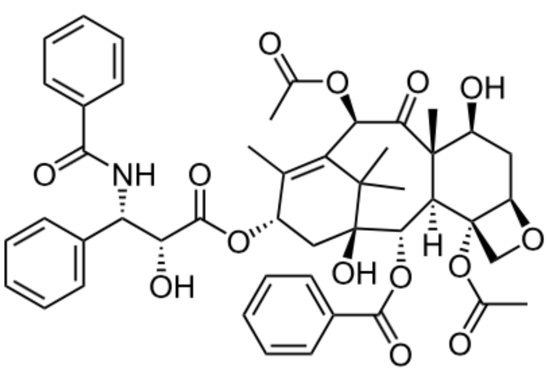
Motivation to Modify Sholl Analysis



A. Binary Image of *Drosophila* Class IV neuron
B. A Sholl plot visualization showing the number of intersections of the dendritic tree with circles of increasing radius from the center of the dendritic arbor
C. A Modified Sholl plot visualization using concentric irregular polygons

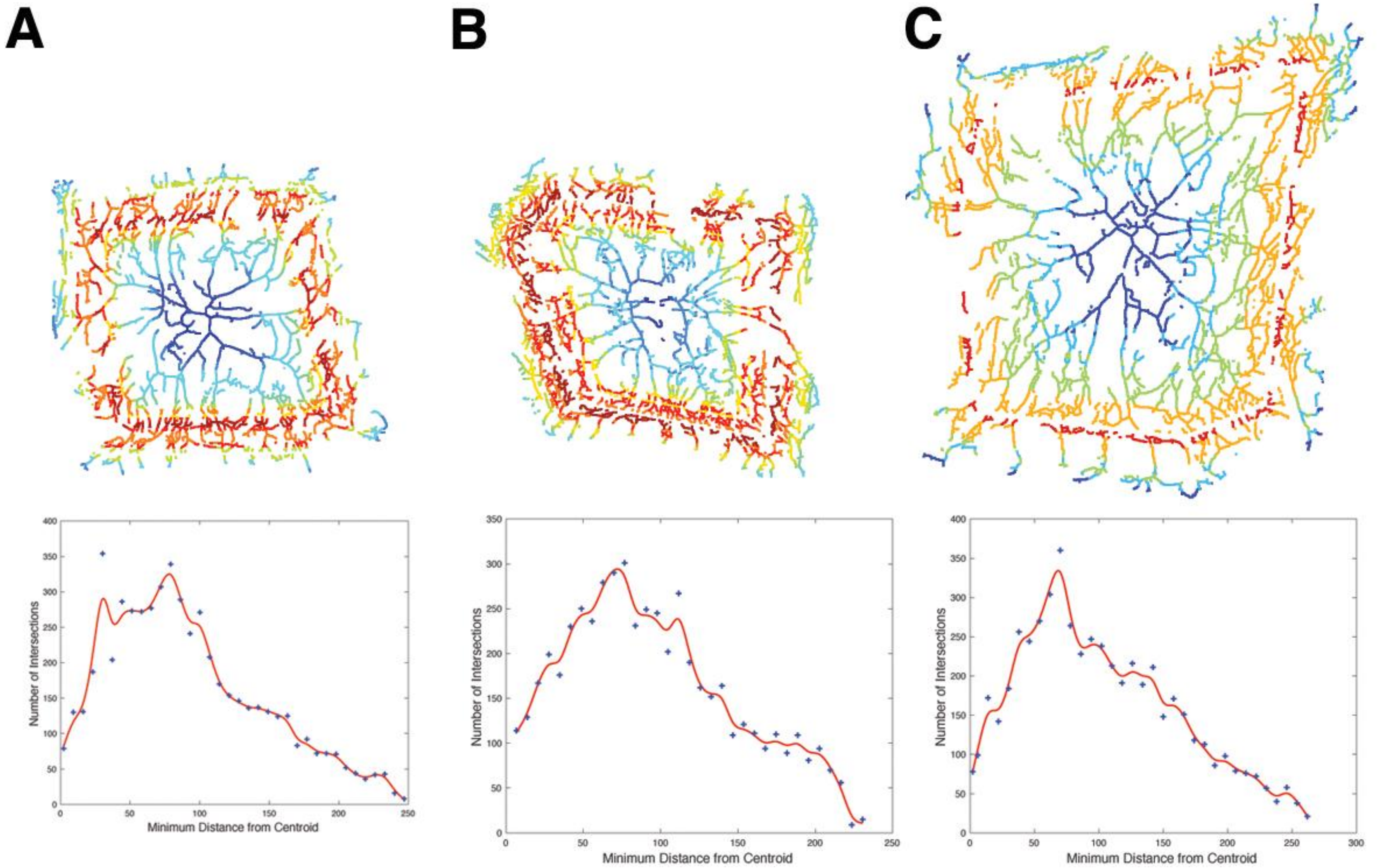
Results of Modified Sholl Analysis





Analysis of Paclitaxel Treated Class IV *Drosophila* sensory neurons

Results of Modified Sholl Analysis



Analysis of Class IV *Drosophila* sensory neurons

Next Time:
Single-Neuron Models