

# Nerv 80 Lecture 2

Sept 9, 2019

OH w/ faculty: Fri 12:30 - 1:30  
email for different times

## How does a car work?

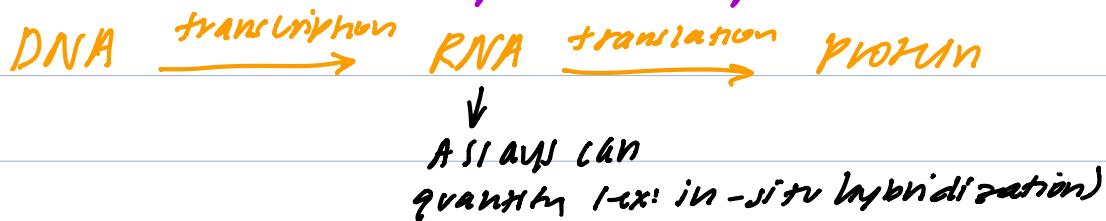
- figure out function by studying components: deconstruction
- What is the "right" level of decomposition?
- What is the function?

## The Brain

- neurobiologists seek to understand how the brain works at 3 levels:
  1. Systems (visual, auditory, etc)
  2. Cells (neurons)
  3. Molecules (particularly gene products)

## Motivation

Gene Expression: Gene synthesizes protein @ times & places



- In Nature 2007: where are all the genes expressed in the brain
- small genetic changes → big consequences
- neuronal heterogeneity
  - no gene is unique to one neuron

# HOW does the brain work?

Motivus  $\xrightarrow{\text{make}}$  CNS  $\xrightarrow{\text{make}}$  Systems  $\xrightarrow{\text{decide}}$  Behavior

## • Celluar Microbiology

Camillo Golgi, Santiago Ramón y Cajal

✓  
Reticular  
Theory  
all connected  
parts

↓  
Neuron Theory  
discrete parts

## • Golgi Stain

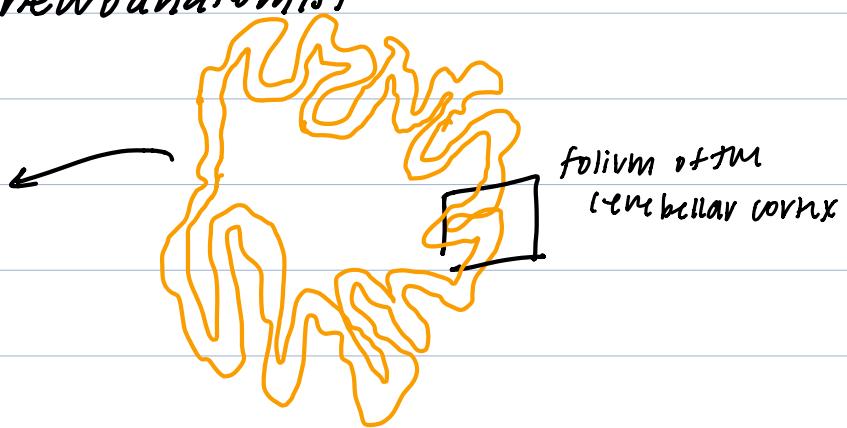
"black reaction": tissue is slowly fixed, bathed in silver nitrate  $\rightarrow$  makes silver dichromate  
 $\sim 1\%$  of CNS are stained

## • Ramón y Cajal

• Discovered many fundamental principles of the nervous system's organization

• likely greatest neuroanatomist

climbing fibers  
mosaic fiber  
more tissue types



## • Golgi's drawing

- No individual cellular entities
- diffuse neural network
- his detailed drawing

# Nervous Doctrine

- Nerves are the basic structure and functional unit of the nervous system
- Not proven till 1950s
- Cytology anatomy of the brain is not modular

What makes a cell a neuron?

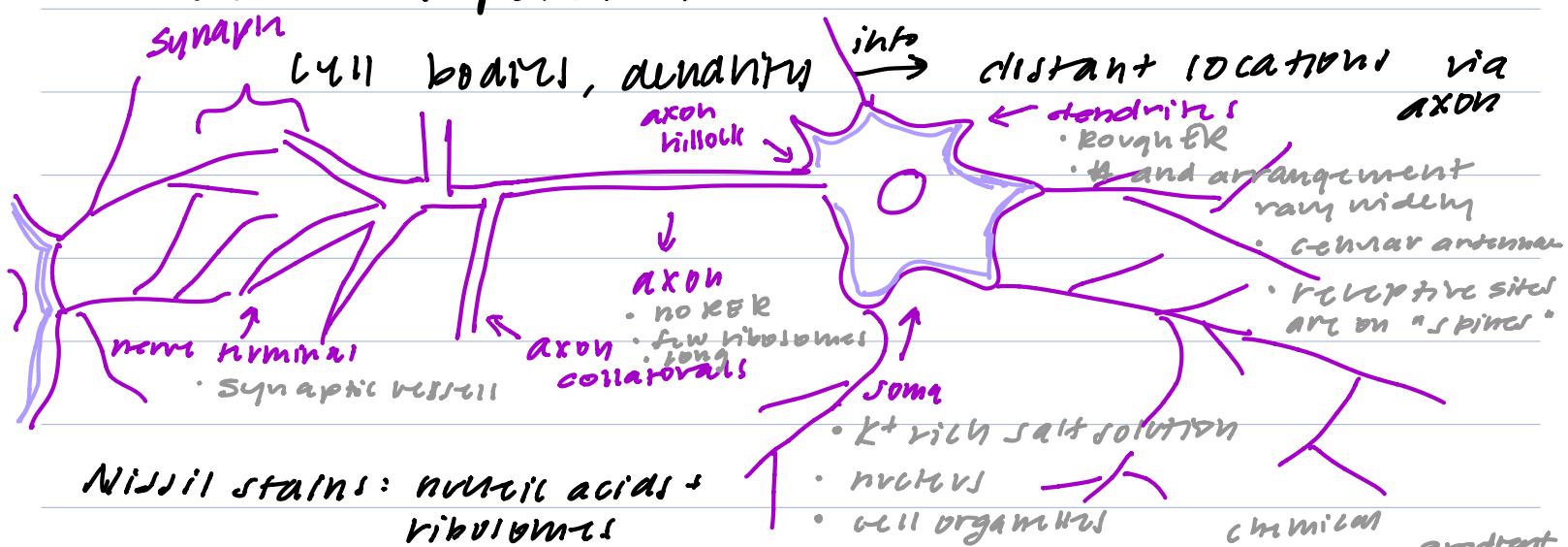
- converts into to/ from neurons
- common features

1. Compartmentalization: receptive region, integration, output
2. Electrical excitability
3. Synaptic connections
4. Nearly all neurons are non-replicating (post-mitotic)

Cajal's second idea: Law of Dynamic Polarization

Dynamic polarization

- Cells are polarized



Nissl stains: nucleic acids + ribosomes

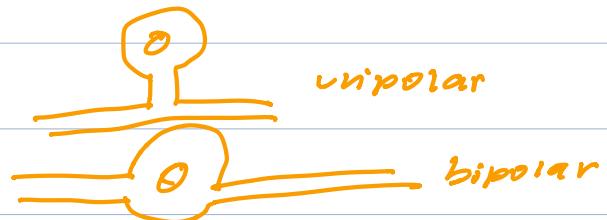
- Axoplasmic transport
  - Wallerian degeneration (cell degenerates after you cut axon)
- Anterograde (towards terminals): Kinesin
- Retrograde (towards soma): Dynein
- Membrane vesicles w/ motor proteins walk along microtubules (organelles) can be transported too
- Axons vs. Dendrites

Note: there will be exceptions to these rules

	<u>Axon</u>	<u>Dendrites</u>
Designed to	Conduct APs	Integrating and filtering inputs
#	One leaves soma	Many
Shape	Cylindrical	Tapered with spines
Myelinated?	Often ( $>0.2 \mu\text{m}$ )	No
Ribosomes?	No	Yes, both RER and cytoplasmic
APs?	Yes, generated at the axon hillock and conducted away from the soma	Not usually.
Branching?	Yes, at right or obtuse angles	Yes, at acute angles

## Classifying Nerves

- # of neurons (# of inputs)
- based on shape
- based on connections or function
  - sensory vs motor
  - CNS vs PNS
  - Intrinsic
  - Autonomic (sympathetic or para or enteric)
- Axon length
  - Long axons (projection neurons e.g. pyramidal)
  - Shorter axons
- Neurotransmitter type



Brains are densely connected

- Spiny pyramidal cell offshoots
- Glial cells: not many subtypes
  - proliferate
  - inexcitable
- Astrocytes :
  - most numerous, structural support
  - form BBB
  - regular chemical content of extracellular space around synapses
- Myelinating glia : ensheathe axons to prevent leak
  - Oligodendroglia (CNS)
  - Schwann cells (PNS) wrap entire cell body
- Microglia: phagocytosis (debris from damage)

Classical types / functions

What activity at the neuro fair on Friday did you like best?

Structure and Function  
of Brain Regions

Model Organism Zoo

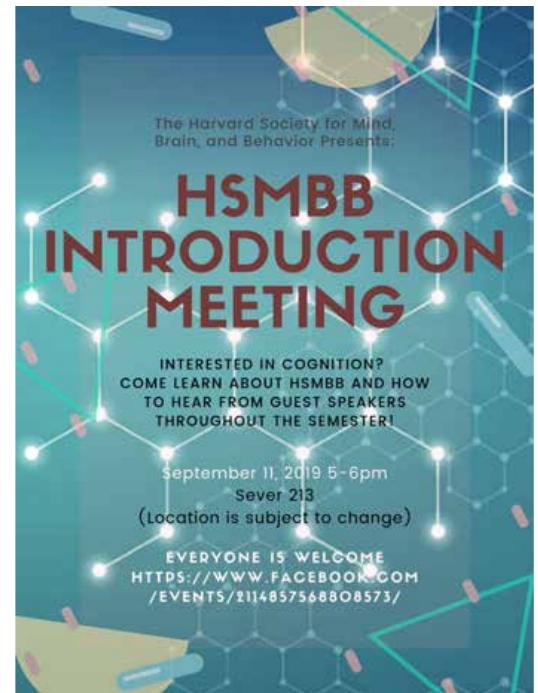
Microscopy

Muscle electrical  
activity

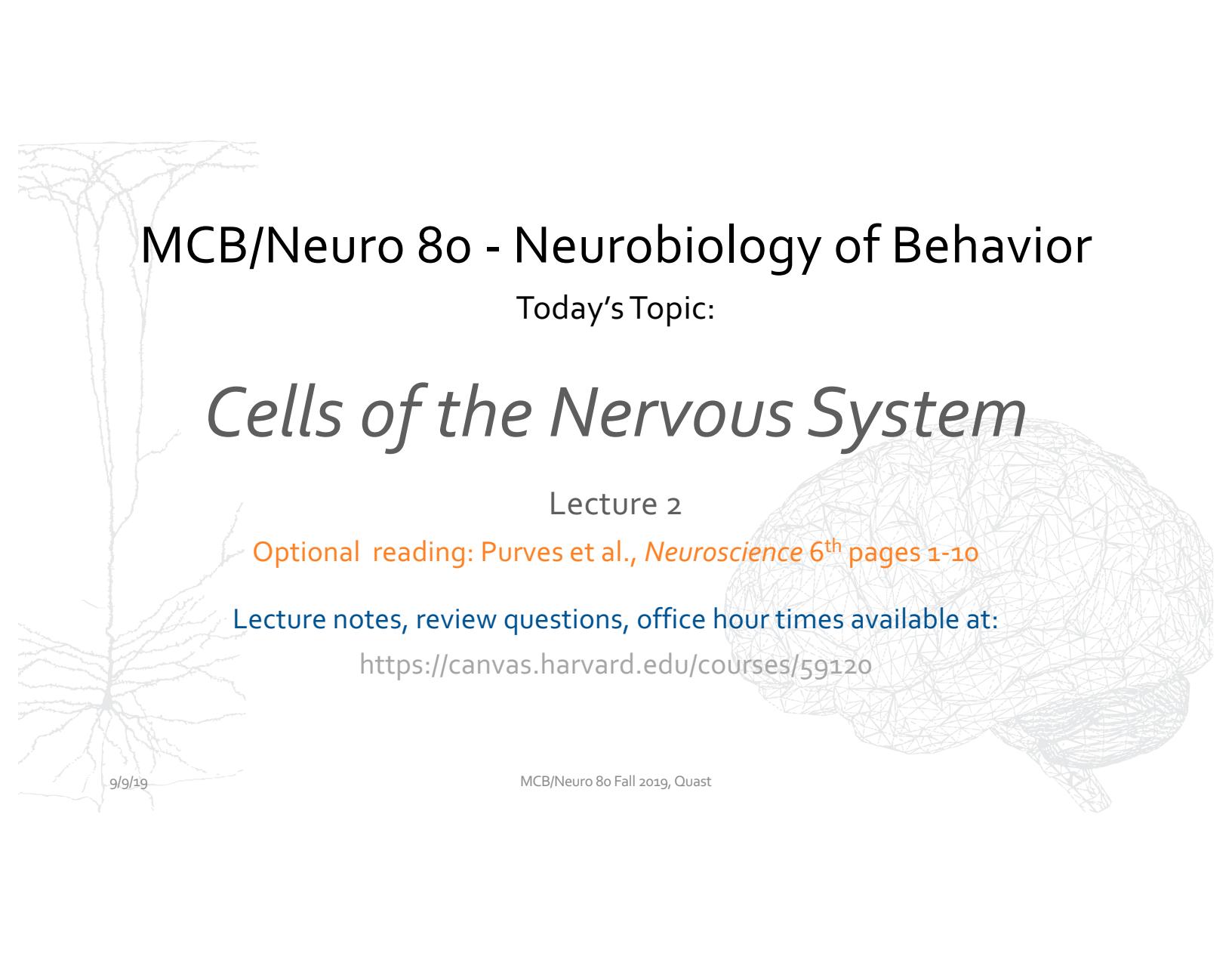
Start the presentation to see live content. Still no live content? Install the app or get help at Pollify.com/app

Total Results

9/9/19



1



# MCB/Neuro 8o - Neurobiology of Behavior

Today's Topic:

## *Cells of the Nervous System*

Lecture 2

Optional reading: Purves et al., *Neuroscience* 6<sup>th</sup> pages 1-10

Lecture notes, review questions, office hour times available at:

<https://canvas.harvard.edu/courses/59120>

# Logistic Announcements

- Registration issues...
- Section preferences – submit poll by midnight tonight!
- Office hours with faculty
  - Come! (times will be listed on course web site this week!)
  - No need to prepare
  - Ask any questions you have about the material or any other questions about neuroscience.
  - If you can't make the scheduled office hours email us and we can set up special meetings.
  - Talking one on one with faculty should be fun and illuminating for you.

## How does a car work?



## How does a brain work?



- Figure out function by studying the components: deconstruction
- But what is the “right” level of deconstruction:
  - subatomic particles
  - atoms
  - molecules
  - macroscopic structures
  - ensembles of structures?
- What is the function?

## Why is the brain harder to understand than an automobile?

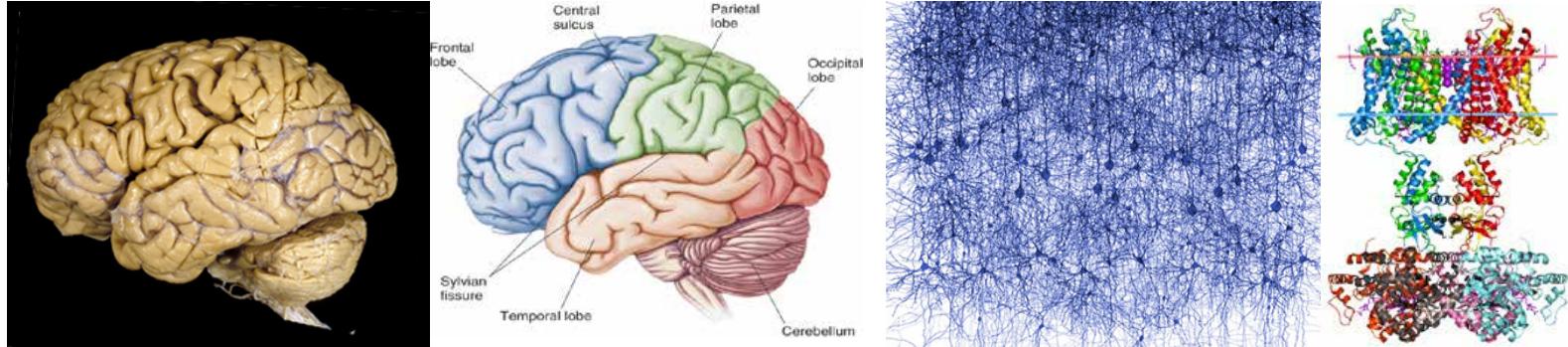
Many more parts and connections

Not obvious what is the right level of deconstruction

Humans didn't design it

A brain can't understand itself

Another answer



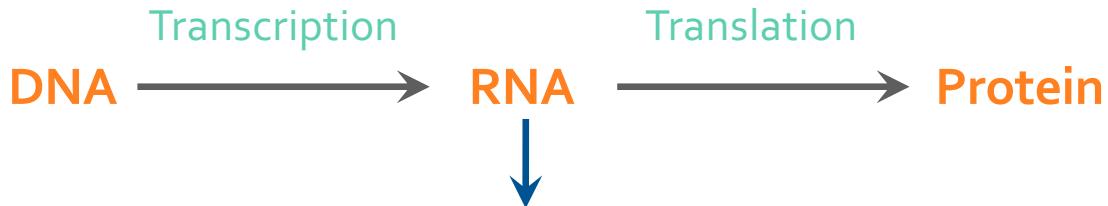
- Neurobiologists seeking to understand how the brain works scrutinize the nervous system at three different levels of deconstruction:
  - **Systems** such as visual, motor, autonomic etc
  - **Cells** particularly neurons and their parts
  - **Molecules** particularly gene products.

Let's start here

# The central dogma of molecular biology

“Gene expression”:

Each gene (DNA) is used to synthesize a particular gene product (usually a particular protein) at particular times and places in the body.



Assays (such as “in situ hybridization”) reveal in which cells particular messenger RNAs (mRNA) are being transcribed and thus tell scientists which genes are expressed, that is, which proteins are synthesized in which particular cells

# Where all the genes (20,000) are expressed in the brain!



9/9/19

nature

Vol 445 | 11 January 2007 | doi:10.1038/nature05453

## ARTICLES

### Genome-wide atlas of gene expression in the adult mouse brain

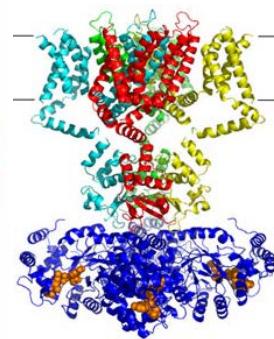
Ed S. Lein<sup>1\*</sup>, Michael J. Hawrylycz<sup>1\*</sup>, Nancy Ao<sup>2</sup>, Mikael Ayres<sup>1</sup>, Amy Bensinger<sup>1</sup>, Amy Bernard<sup>1</sup>, Andrew F. Boe<sup>1</sup>, Mark S. Boguski<sup>1,†</sup>, Kevin S. Brockway<sup>1</sup>, Emi J. Byrnes<sup>1</sup>, Lin Chen<sup>1</sup>, Li Chen<sup>2</sup>, Tsuey-Ming Chen<sup>2</sup>, Mei Chi Chin<sup>1</sup>, Jimmy Chong<sup>1</sup>, Brian E. Crook<sup>1</sup>, Aneta Czaplinska<sup>2</sup>, Chinh N. Dang<sup>1</sup>, Suvro Datta<sup>1</sup>, Nick R. Dee<sup>1</sup>, Aimee L. Desaki<sup>1</sup>, Tsega Desta<sup>1</sup>, Ellen Diep<sup>1</sup>, Tim A. Dolbear<sup>1</sup>, Matthew J. Donelan<sup>1</sup>, Hong-Wei Dong<sup>1</sup>, Jennifer G. Dougherty<sup>1</sup>, Ben J. Duncan<sup>1</sup>, Amanda J. Ebbert<sup>1</sup>, Gregor Eichler<sup>3</sup>, Lili K. Estin<sup>1</sup>, Casey Faber<sup>1</sup>, Benjamin A. Facer<sup>1</sup>, Rick Fields<sup>1</sup>, Shanna R. Fischer<sup>1</sup>, Tim P. Fliss<sup>1</sup>, Cliff Frenzley<sup>1</sup>, Sabrina N. Gates<sup>1</sup>, Katie J. Glattfelder<sup>1</sup>, Kevin R. Halverson<sup>1</sup>, Matthew R. Hart<sup>1</sup>, John G. Hohmann<sup>1</sup>, Maureen P. Howell<sup>1</sup>, Darren P. Jeung<sup>1</sup>, Rebecca A. Johnson<sup>1</sup>, Patrick T. Karr<sup>1</sup>, Reena Kawai<sup>1</sup>, Jolene M. Kidney<sup>1</sup>, Rachel H. Knapik<sup>1</sup>, Chihchau L. Kuan<sup>1</sup>, James H. Lake<sup>1</sup>, Annabel R. Laramee<sup>1</sup>, Kirk D. Larsen<sup>1</sup>, Christopher Lau<sup>1</sup>, Tracy A. Lemon<sup>1</sup>, Agnes J. Liang<sup>2</sup>, Ying Liu<sup>2</sup>, Lon T. Luong<sup>1</sup>, Jesse Michaels<sup>1</sup>, Judith J. Morgan<sup>1</sup>, Rebecca J. Morgan<sup>1</sup>, Marty T. Mortrud<sup>1</sup>, Nerick F. Mosqueda<sup>1</sup>, Lydia L. Ng<sup>1</sup>, Randy Ng<sup>1</sup>, Geraldyn J. Orta<sup>1</sup>, Caroline C. Overly<sup>1</sup>, Tu H. Pak<sup>1</sup>, Sheana E. Parry<sup>1</sup>, Sayan D. Pathak<sup>1</sup>, Owen C. Pearson<sup>1</sup>, Ralph B. Puchalski<sup>1</sup>, Zackery L. Riley<sup>1</sup>, Hannah R. Rockett<sup>1</sup>, Stephen A. Rowland<sup>1</sup>, Joshua J. Royall<sup>1</sup>, Marcos J. Ruiz<sup>2</sup>, Nadia R. Sarno<sup>1</sup>, Katherine Schaffnit<sup>1</sup>, Nadiya V. Shapovalova<sup>1</sup>, Taz Sivisay<sup>1</sup>, Clifford R. Slaughterbeck<sup>1</sup>, Simon C. Smith<sup>1</sup>, Kimberly A. Smith<sup>1</sup>, Bryan I. Smith<sup>1</sup>, Andy J. Sodt<sup>1</sup>, Nick N. Stewart<sup>1</sup>, Kenda-Ruth Stumpf<sup>1</sup>, Susan M. Sunkin<sup>1</sup>, Madhavi Sutram<sup>1</sup>, Angelene Tam<sup>2</sup>, Carey D. Teemer<sup>1</sup>, Christina Thaller<sup>2</sup>, Carol L. Thompson<sup>1</sup>, Lee R. Varnam<sup>1</sup>, Axel Visel<sup>3,†</sup>, Ray M. Whitlock<sup>1</sup>, Paul E. Wohynckta<sup>1</sup>, Crissa K. Wolkey<sup>1</sup>, Victoria Y. Wong<sup>1</sup>, Matthew Wood<sup>2</sup>, Murat B. Yayaoglu<sup>2</sup>, Rob C. Young<sup>1</sup>, Brian L. Youngstrom<sup>1</sup>, Xu Feng Yuan<sup>1</sup>, Bin Zhang<sup>2</sup>, Theresa A. Zwingman<sup>1</sup> & Allan R. Jones<sup>1</sup>

Molecular approaches to understanding the functional circuitry of the nervous system promise new insights into the relationship between genes, brain and behaviour. The cellular diversity of the brain necessitates a cellular resolution approach towards understanding the functional genomics of the nervous system. We describe here an anatomically comprehensive digital atlas containing the expression patterns of ~20,000 genes in the adult mouse brain. Data were generated using automated high-throughput procedures for *in situ* hybridization and data acquisition, and are publicly accessible online. Newly developed image-based informatics tools allow global genome-scale structural analysis and cross-correlation, as well as identification of regionally enriched genes. Unbiased fine-resolution analysis has identified highly specific cellular markers as well as extensive evidence of cellular heterogeneity not evident in classical neuroanatomical atlases. This highly standardized atlas provides an open, primary data resource for a wide variety of further studies concerning brain organization and function.

# Small genetic changes can have big consequences



Huntington's disease:  
a neurodegenerative disorder

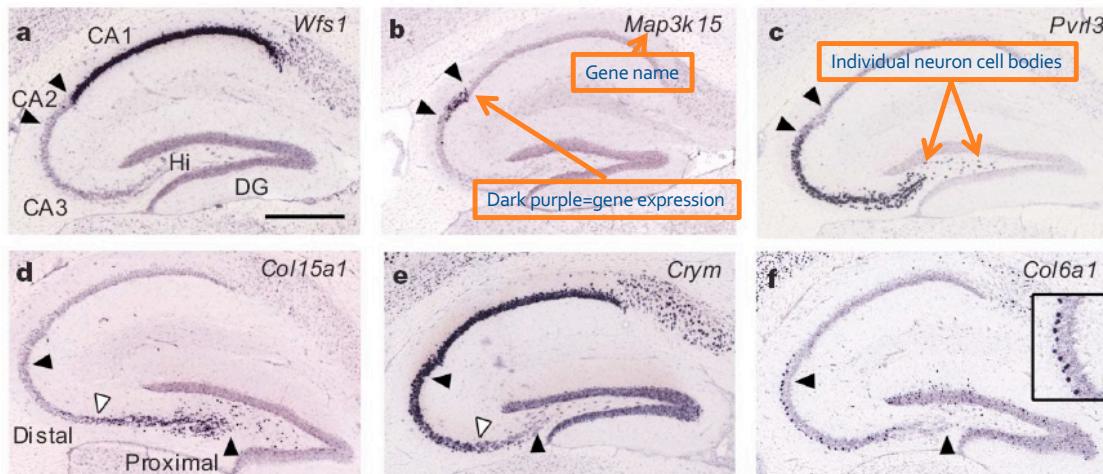


Channel mutations:  
absence of pain



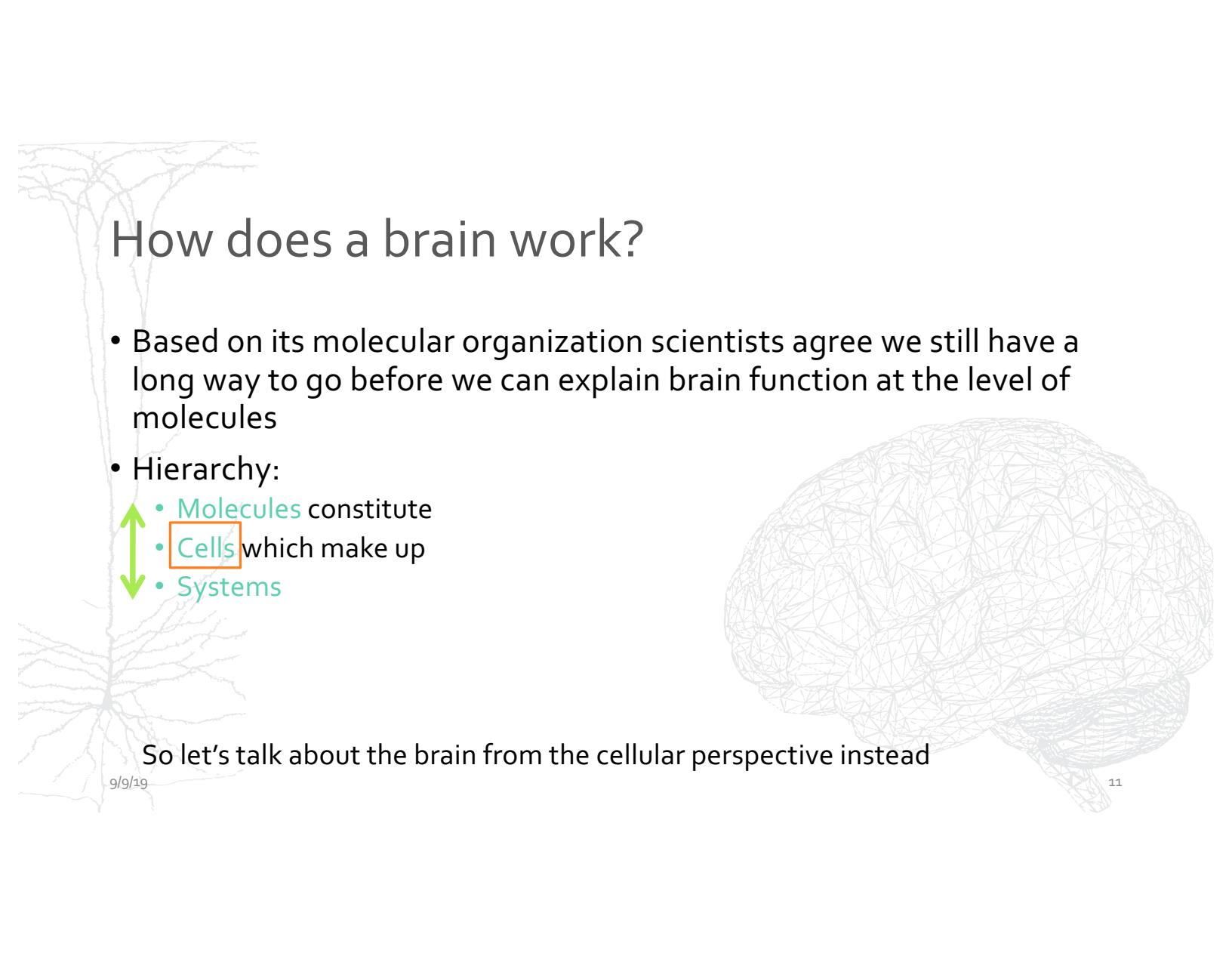
Leptin deficiency: obesity

# *In situ* hybridizations demonstrate neuronal heterogeneity



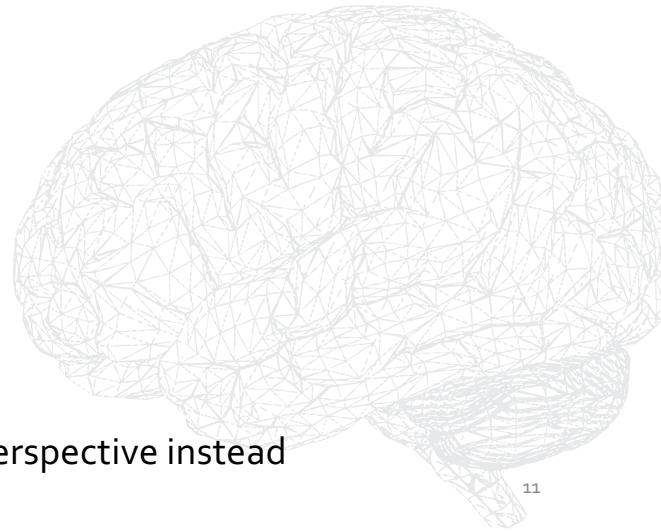
**Figure 7 | Heterogeneity of hippocampal gene expression.** Classically defined hippocampal subregions (black arrowheads) are delineated by gene expression: **a**, *Wfs1* in CA1; **b**, *Map3k15* in CA2; **c**, *Pvr13* in CA3. Heterogeneous expression within hippocampal subfields: proximal–distal (*Col15a1*, **d**) and distal–proximal (*Crym*, **e**) gradients in CA3 (white arrowheads mark approximate expression boundaries); selective expression of *Col6a1* in the outer band of cells in CA3 (**f**); differential expression in dorsal (*Dsp*,

- No genes unique to one cell type
- Maybe a combinatorial code? (i.e., Gene A + B + Q makes a cell type)
- Very complicated and not understood at present.



# How does a brain work?

- Based on its molecular organization scientists agree we still have a long way to go before we can explain brain function at the level of molecules
- Hierarchy:
  - Molecules constitute
  - Cells which make up
  - Systems



So let's talk about the brain from the cellular perspective instead

# The birth of cellular neurobiology

Camillo Golgi

and

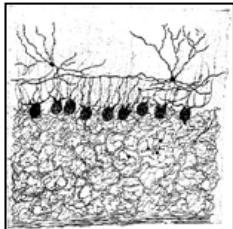
Santiago Ramón y Cajal

1843-1926

Reticular theory



Italy



9/9/19

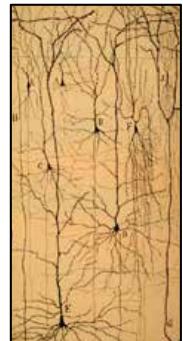
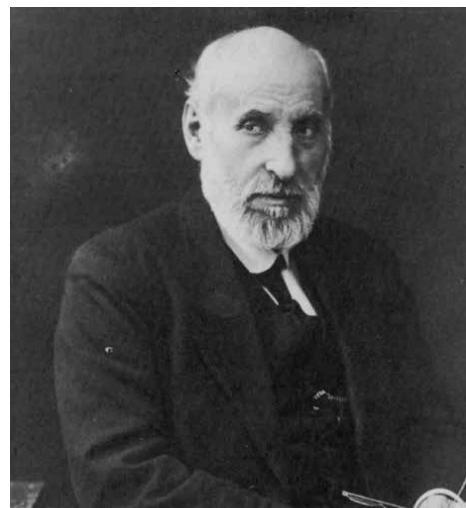


1852-1934

Neuron doctrine



Spain



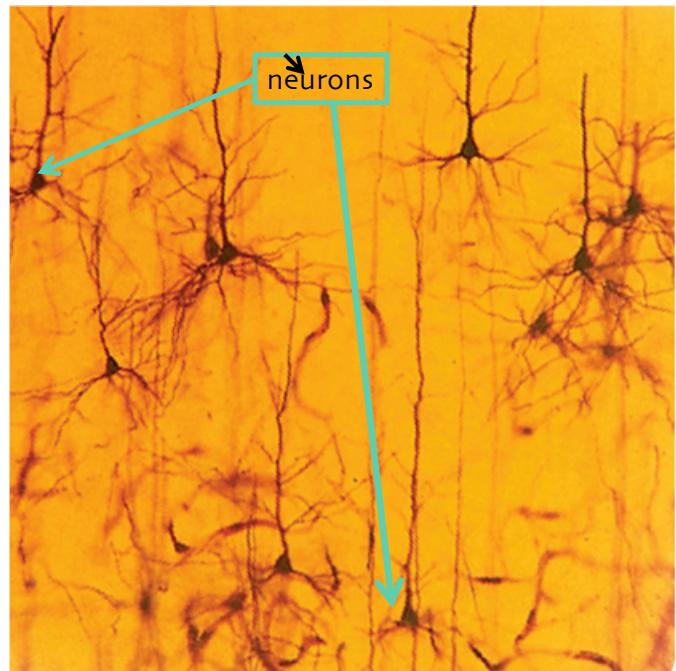
They both used the Golgi Stain to reach their opposite conclusions

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# The Golgi Stain

The “black reaction” was invented in 1873 by Camillo Golgi (1843-1926). It was the first technique to reveal neurons in their entirety.

- Tissue is slowly “fixed” (i.e. hardened)
- Then tissue is bathed in silver nitrate solution
- ~1% of nerve cells are completely stained, while other cells are **not** stained at all



## Why would it be much less useful if the Golgi stain labelled all the cells in the brain?

Too expensive (so much silver would be needed)

Too heavy (the stained samples would weigh too much and break the microscope)

Too dark (the brain would be just a brown lump)



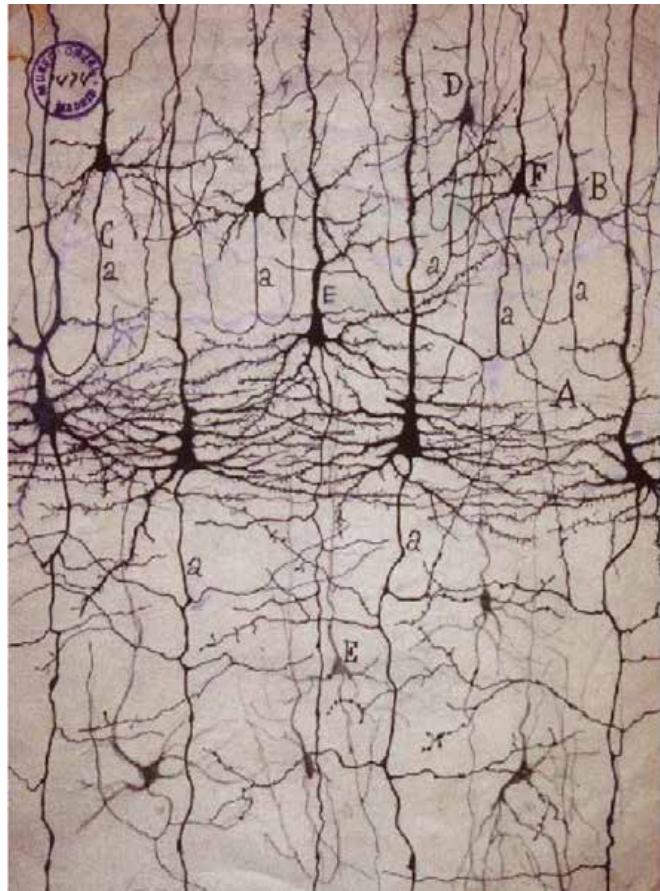
another answer

# Santiago Ramón y Cajal

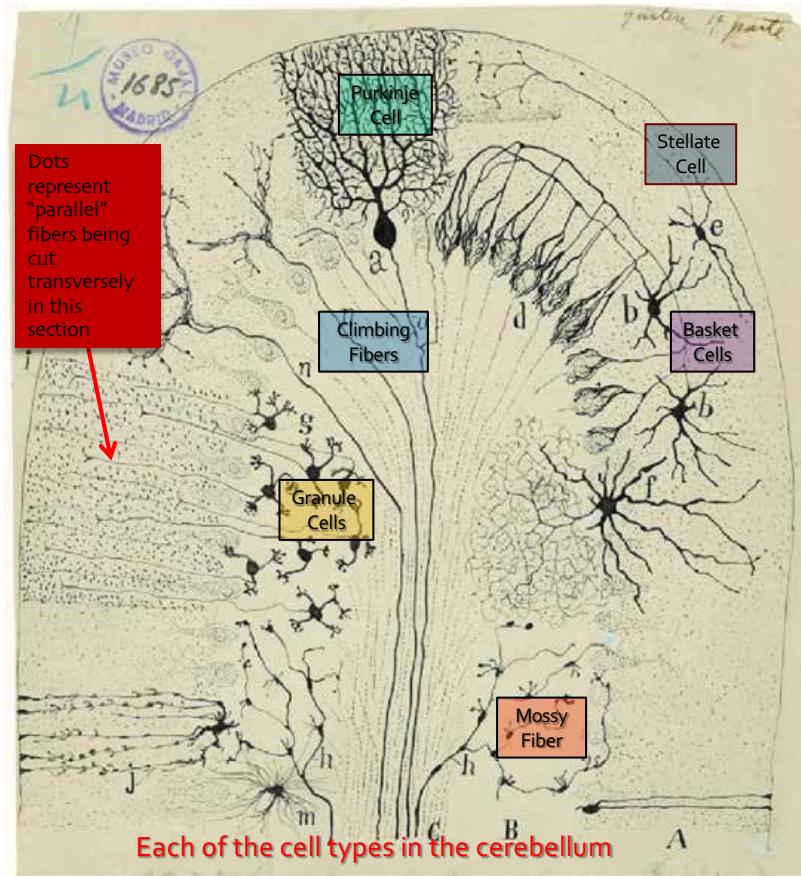
- 1852-1934
- Used Golgi stain to study the nervous system
- Discovered many fundamental principles of the nervous system's organization
- Likely the greatest neuro-anatomist ever lived.



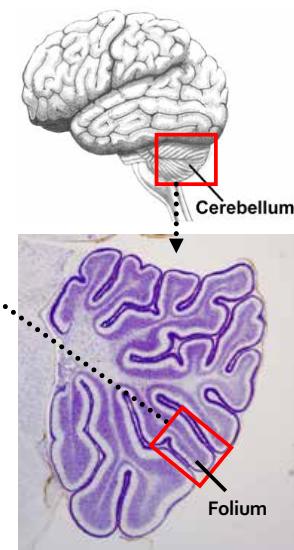
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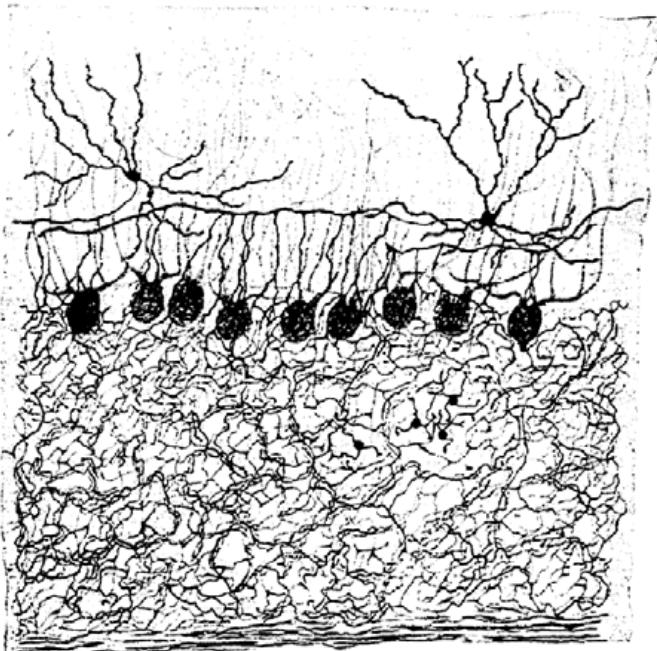


Cajal's drawing of the  
Folium of the  
cerebellar cortex



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# Golgi's drawing of the cerebellum



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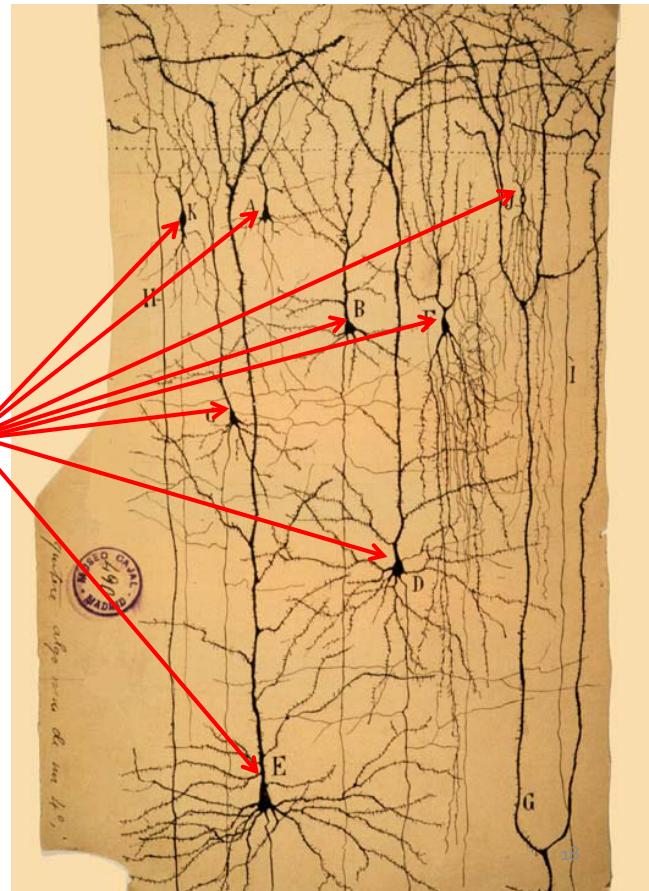
- The reticular theory:
  - No individual cellular entities rather a single continuous network
  - the nervous system is a net-like structure: *rete nervosa diffusa* 'diffuse neural network'
- Golgi's drawings are less detailed than Cajal's

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# Neuron Doctrine

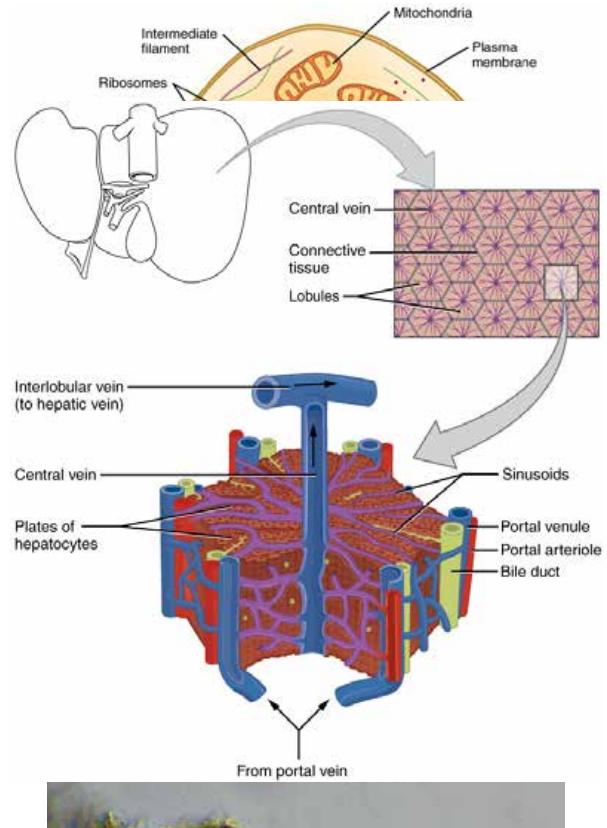
- The first of Cajal's great ideas
- "The neuron doctrine" which states that **neurons are the basic structural and functional unit of the nervous system**
- Not proven definitively until the 1950s

Different kinds of neurons



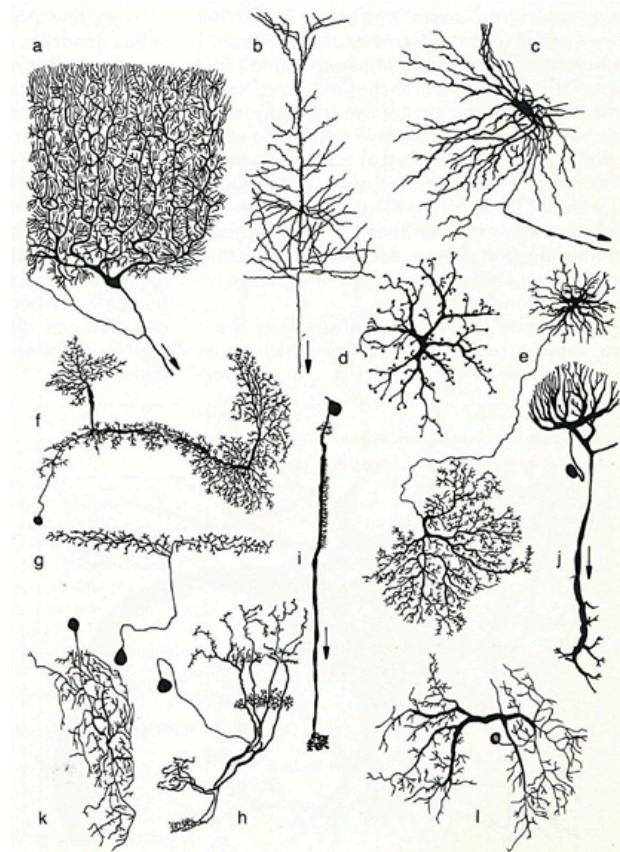
# What is a cell?

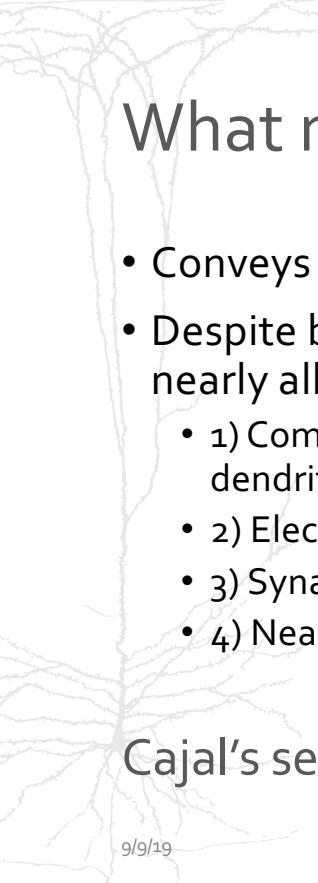
- The basic structural and functional unit of all “multicellular” organisms
- They may also exist as independent units of life (as in protozoa swimming in a pond) – smallest living things.
- Surrounded by a membrane and usually have a nucleus (containing genetic material)
- Cells are the building blocks of organs - Most organs have a simple, repetitive structure that are built from a small number of different cell types.



# Cellular anatomy of the brain is not modular!

- We still don't know the number of cell types in the brain: a few hundred or a few billion?





# What makes a cell a neuron?

- Conveys information to and/or from other neurons
- Despite being more variable than cells of any other organ system, nearly all of them have certain features in common including:
  - 1) Compartmentalization of structure and function: receptive regions (mostly dendrites) integration (cell body or soma) and output (axon)
  - 2) Electrical excitability
  - 3) Synaptic connections
  - 4) Nearly all are non-replicating (post-mitotic)

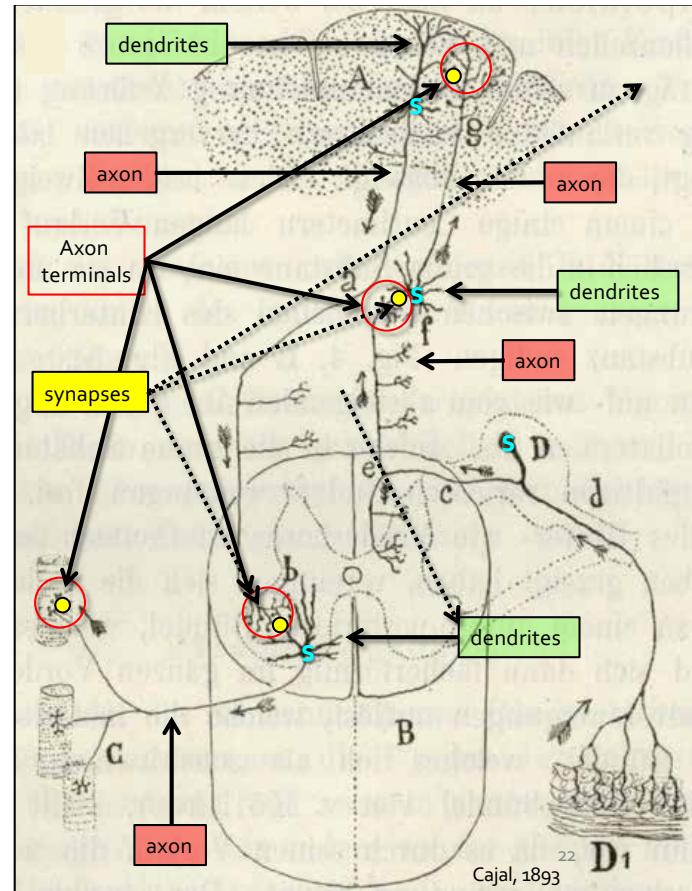
Cajal's second great idea: "the law of dynamic polarization"

# Dynamic Polarization

- Cells are polarized
  - They receive information on their cell bodies and dendrites and conduct information to distant locations through axons

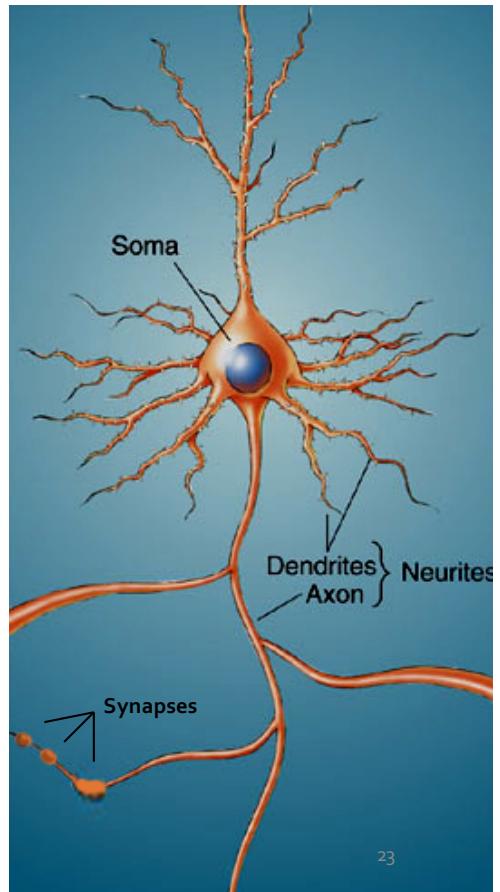


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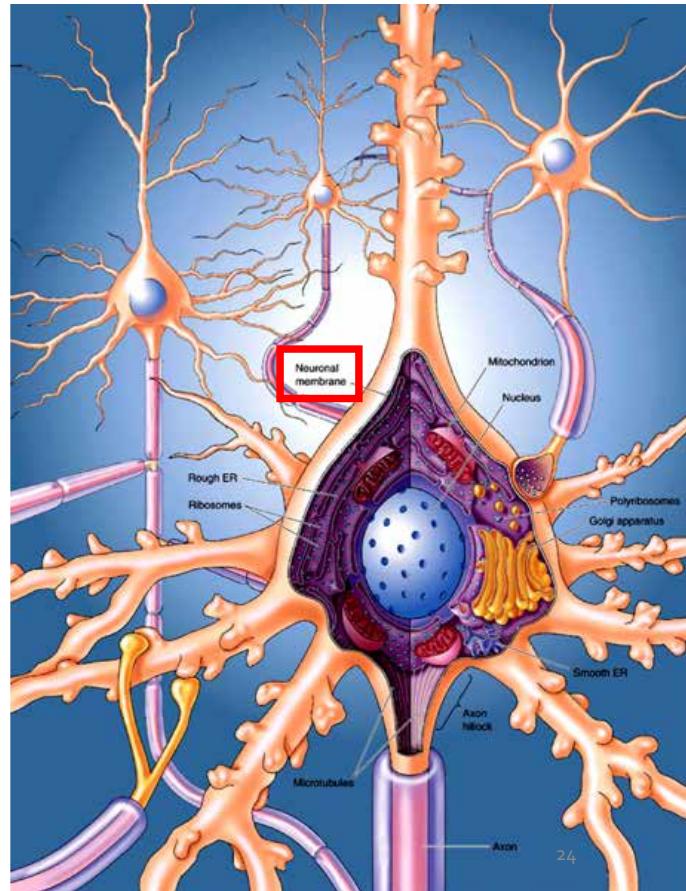
# 4 Compartments of a neuron

- soma
- axons
- synapses
- dendrites



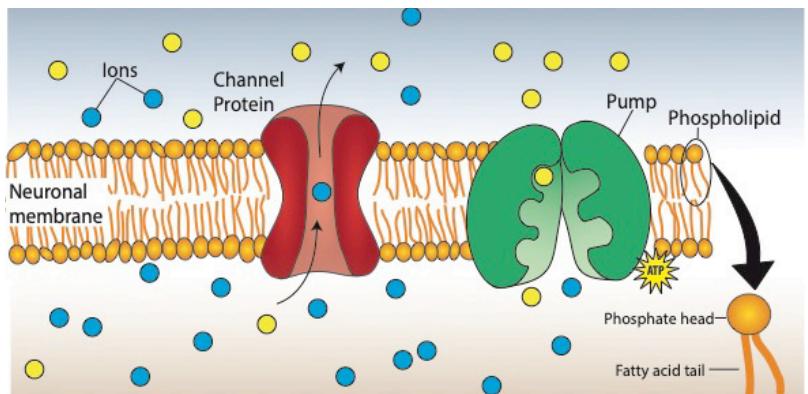
# 1. Soma (cell body)

- Cytoplasm contains
  - a potassium ( $K^+$ ) rich salt solution (same in axon and dendrites)
  - The nucleus (genes)
  - Other organelles
    - Golgi apparatus (sorts proteins for axons and dendrites)
    - Mitochondria (make the energy molecule: ATP)
    - Ribosomes (protein synthesis)
    - Cytoskeleton (structure and transport functions)

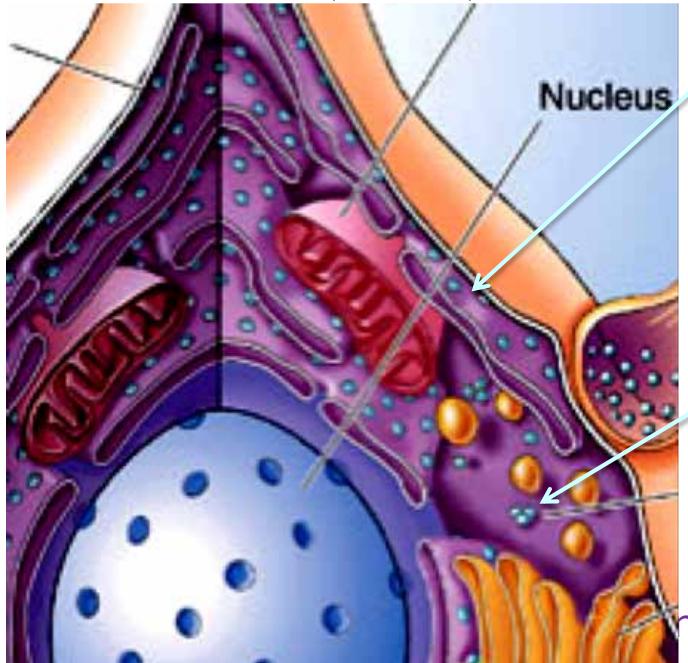


# Cell membrane

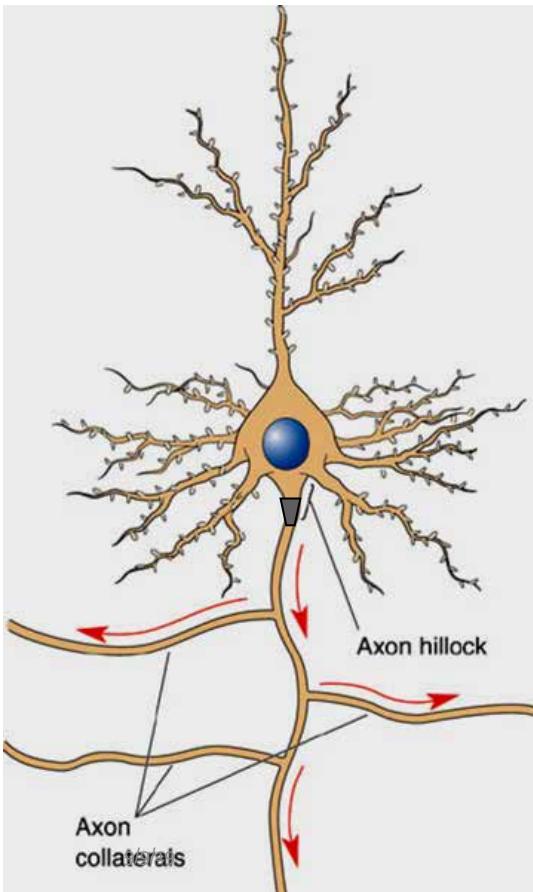
- Separates the cytoplasm from the outside
- Maintains chemical and electrical differences
- Contains many important transmembrane proteins
  - ion channels
  - pumps
  - intracellular signaling receptors



# Ribosomes on “rough” endoplasmic reticulum (RER) makes proteins for axons



- More RER in neurons than most other cell types: “Nissl” substance or bodies.
- Because RER synthesizes nearly all proteins for the axon (in some neurons a huge volume)
- Free polyribosomes make proteins for cytoplasm.

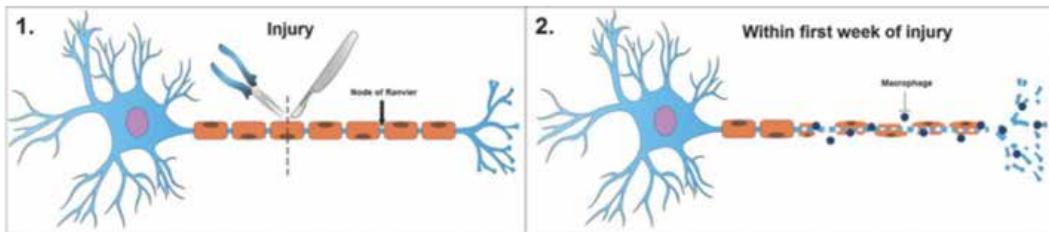


## 2. The Axon

- Unique to neurons
- Origin is axon hillock (initial segment)
- Two features distinguish axon from soma
  - No RER
  - Few polyribosomes
  - Hence little or no protein synthesis in axon so almost all proteins must come from the soma
  - Axons can be very long (meters in a giraffe)
- Axon diameter (caliber) ranges from 0.1-25 mm in mammals. (The squid giant axon is 1 mm wide!) The fatter the axon, the faster is electrical conduction -- we will have more to say about this in later lecture.
- The VAST majority of a neuron's volume is in its axon

# Axoplasmic transport

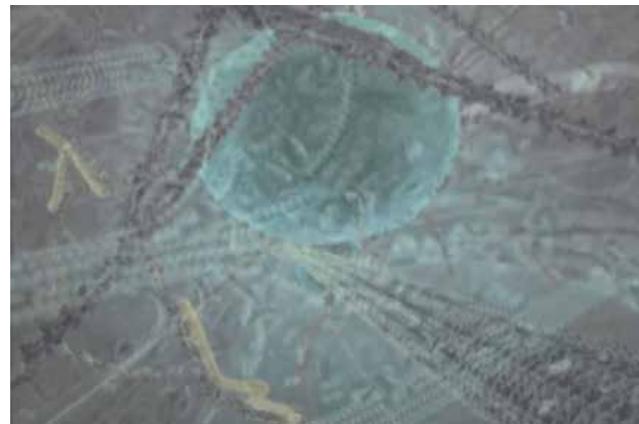
- Because they can't make proteins axons are dependent on their cell bodies for their entire life
  - 12-18 hrs after cutting an axon, Wallerian degeneration occurs distal to the cut site (the part of the axon that is separated from the soma by the cut)



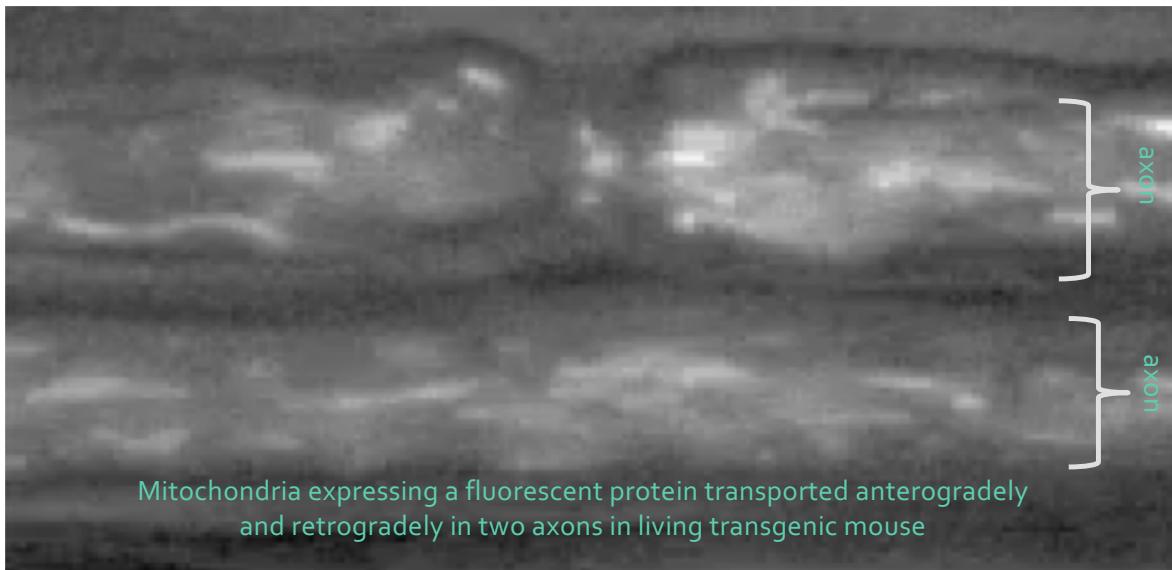
- Proteins diffusing from the cell body would take years to reach nerve terminals so there are specialized transport mechanisms that are thousands of times faster

# Mechanism of axoplasmic transport

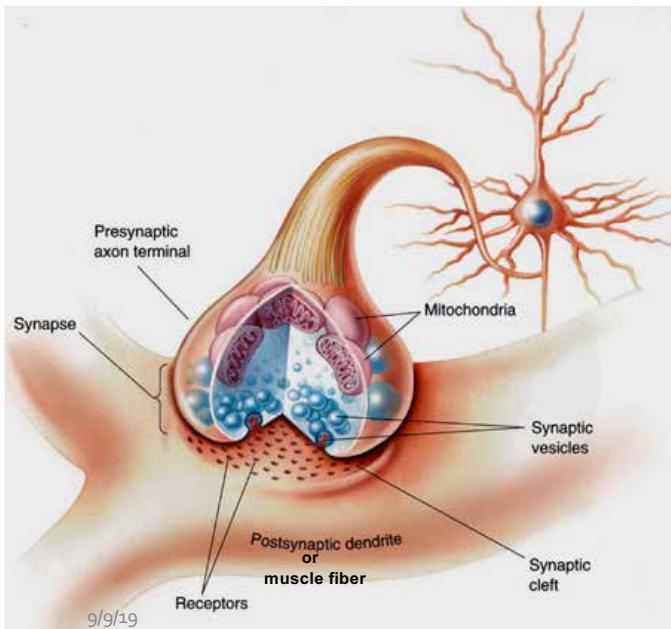
- Distinct anterograde (towards nerve terminals) and retrograde (towards soma) transport machines
- In both cases material enclosed in membrane vesicles walk along microtubules (part of cytoskeleton) in the axon
- Motor proteins tethered to the vesicles crawl along the microtubules via an ATP (energy-requiring) dependent mechanism. Kinesin is the name of the anterograde motor protein and Dynein is the retrograde motor



# Organelles are also transported along microtubules in axons



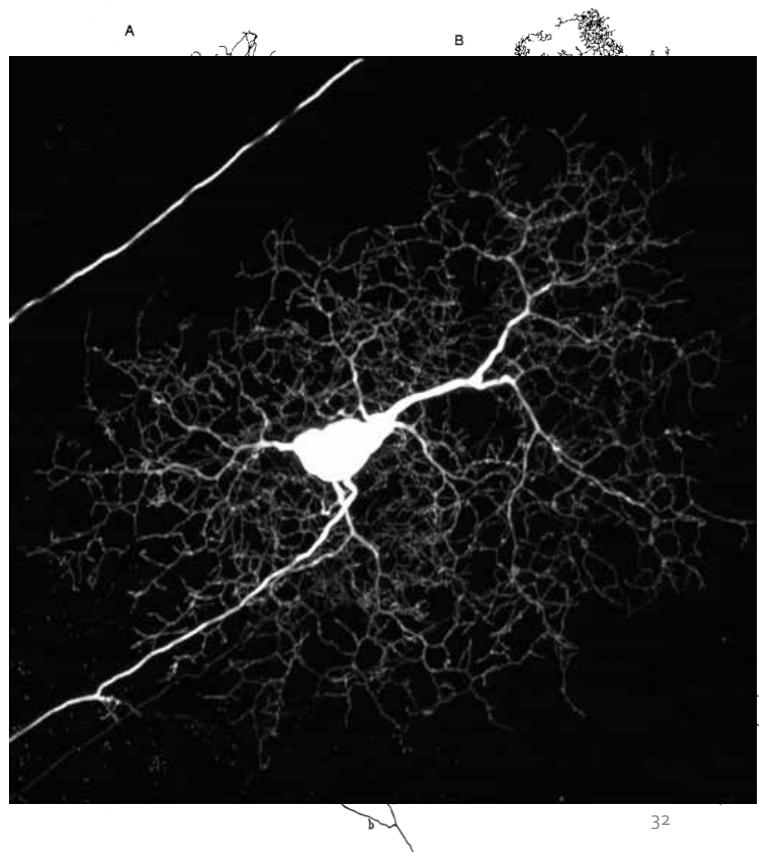
### 3. The nerve terminal (a.k.a. the presynaptic part of a synapse)



- Axon typically contains many collateral branches to innervate many postsynaptic cells (one such connection is shown at the left)
- Highly specialized “presynaptic” machinery (vesicles etc)--much more on this structure in later lectures....

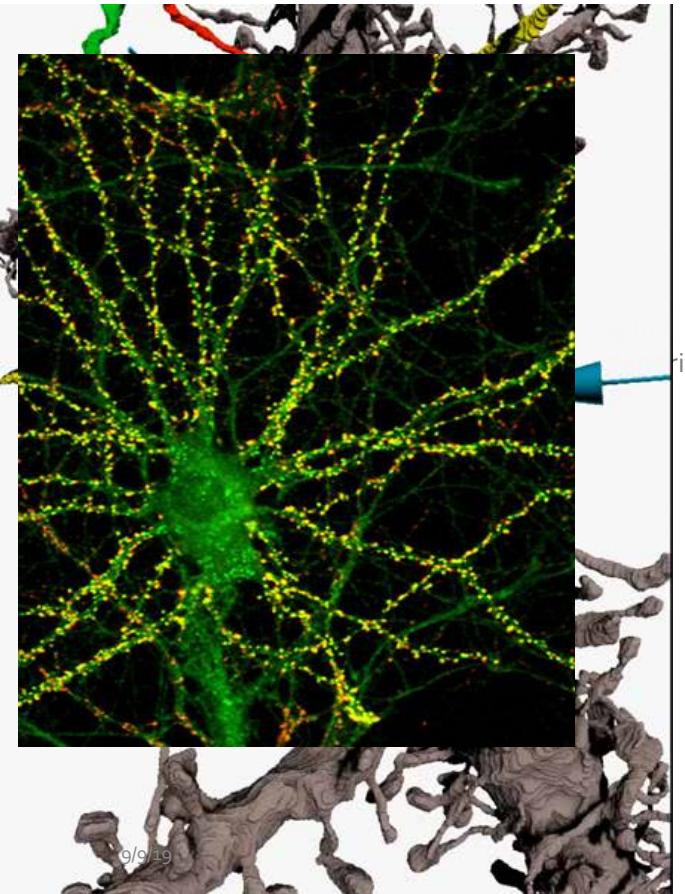
## 4. Dendrites

- Dendrite from Greek for “tree”
- Whereas one axon leaves soma, typically many dendrites do
- Number and arrangement varies widely between neuron types

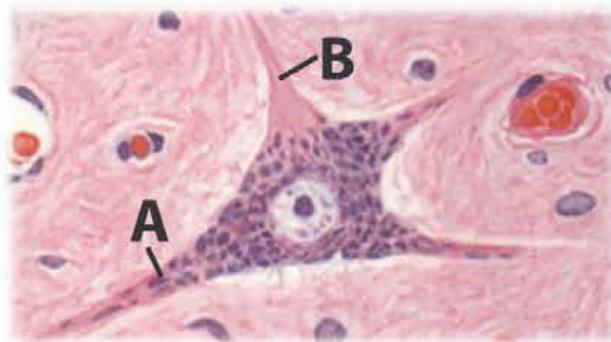


## Dendrites (cont.)

- Function as cell's antennae, studded with many synaptic terminals from other neurons' axons (yellow in figure).
- Receptive sites on dendrites are sometimes on little thorny extensions known as "spines"
- Shown is a spiny dendrite of a pyramidal neuron and a few (colored) axons innervating spines at arrows



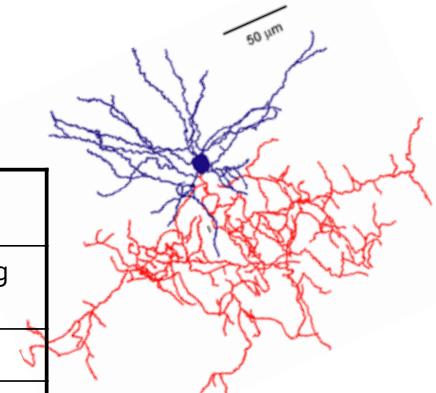
## Which is the axon?

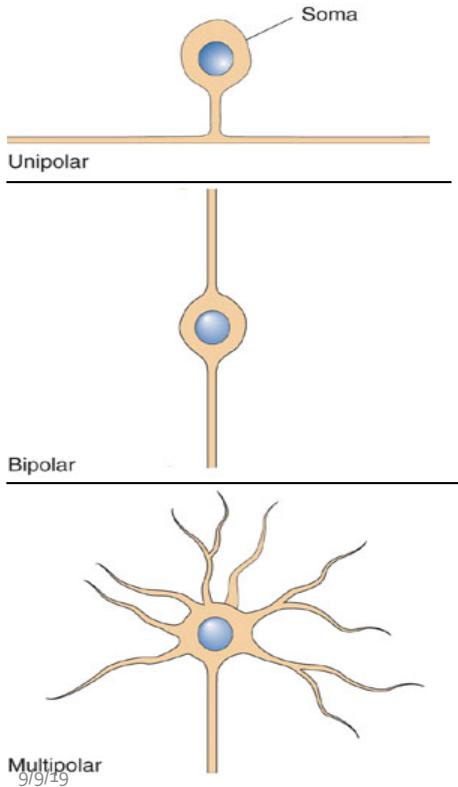


# Axons vs. Dendrites

**Note:** there will be exceptions to these rules

	<u>Axon</u>	<u>Dendrites</u>
<b>Designed to</b>	Conduct APs	Integrating and filtering inputs
<b>#</b>	One leaves soma	Many
<b>Shape</b>	Cylindrical	Tapered with spines
<b>Myelinated?</b>	Often ( $>0.2 \mu\text{m}$ )	No
<b>Ribosomes?</b>	No	Yes, both REF and cytoplasmic
<b>APs?</b>	Yes, generated at the axon hillock and conducted away from the soma	Not usually.
<b>Branching?</b>	Yes, at right or obtuse angles	Yes, at acute angles



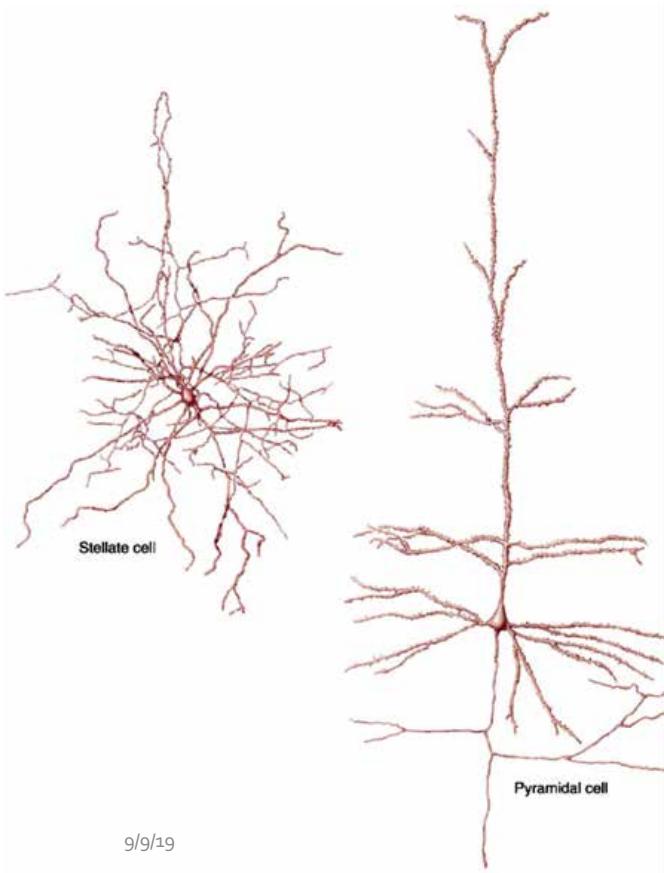


# Classifying Neurons

- About one hundred billion neurons in human brain, but only 300 in a little worm
- Can be classified in many different ways including
  - Based on number of “neurites”

# Classifying Neurons

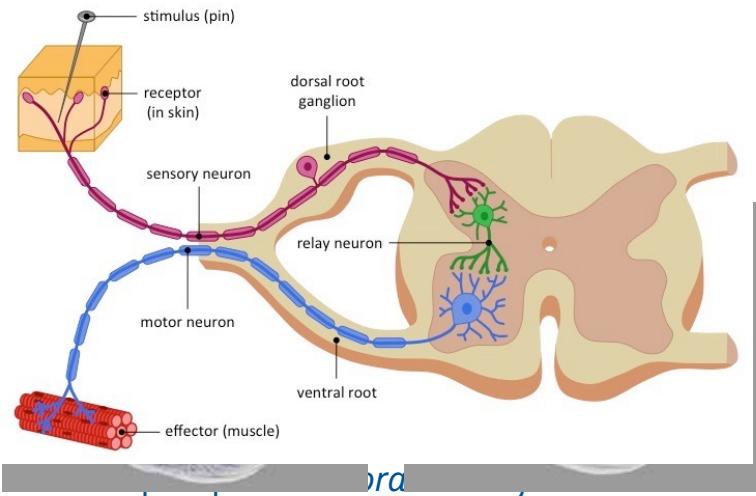
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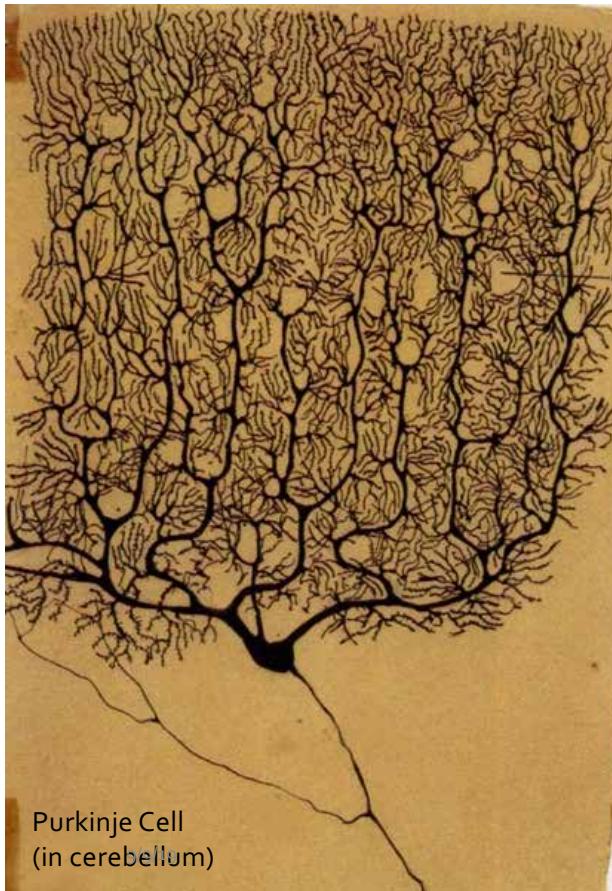


- Sensory or Motor
- Interneurons
- CNS or PNS
- Autonomic (sympathetic or parasympathetic or enteric)

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  - Based on connections or function
  - Based on axon length
  - Based on neurotransmitter, typically one neurotransmitter per neuron





Purkinje Cell  
(in cerebellum)

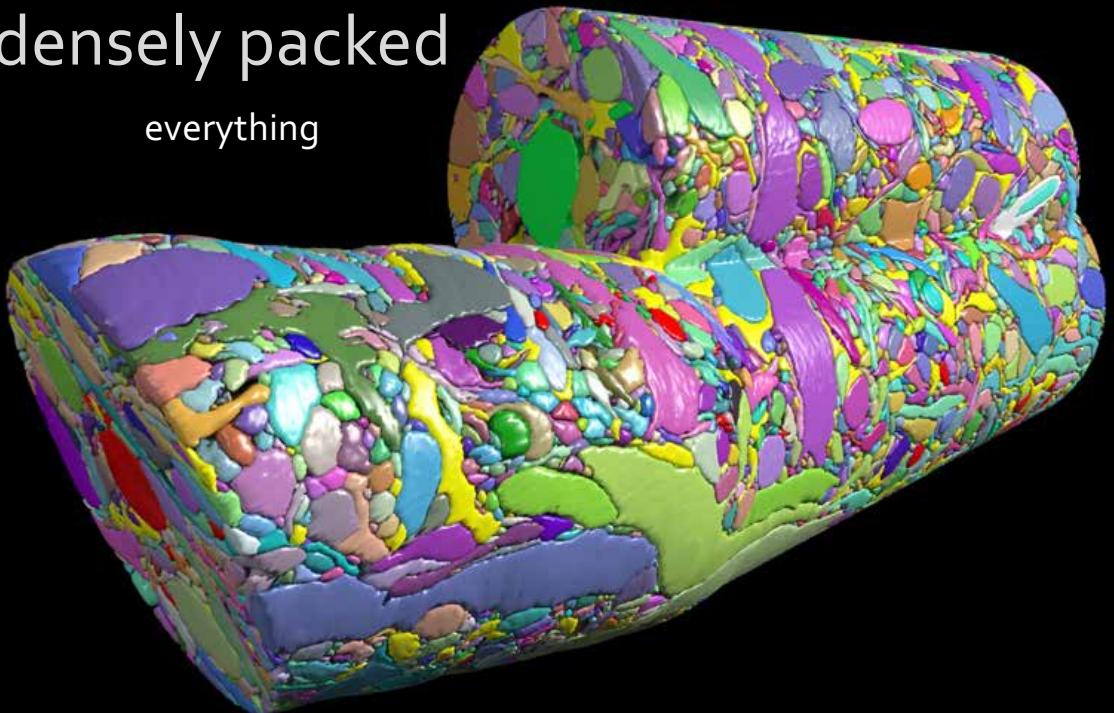
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  - Named cells

# Brains are densely packed

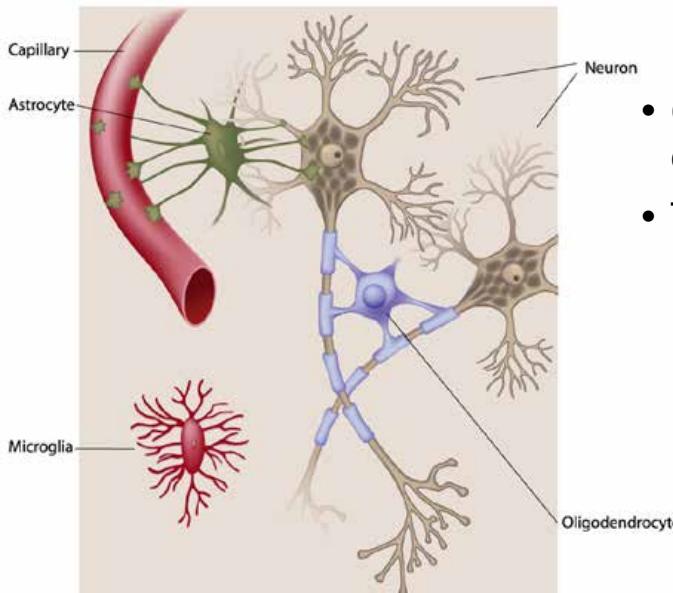
everything

- Spiny apical dendrites of pyramidal cells
- Brains are made up of lots of kinds of cells packed at extraordinary high density



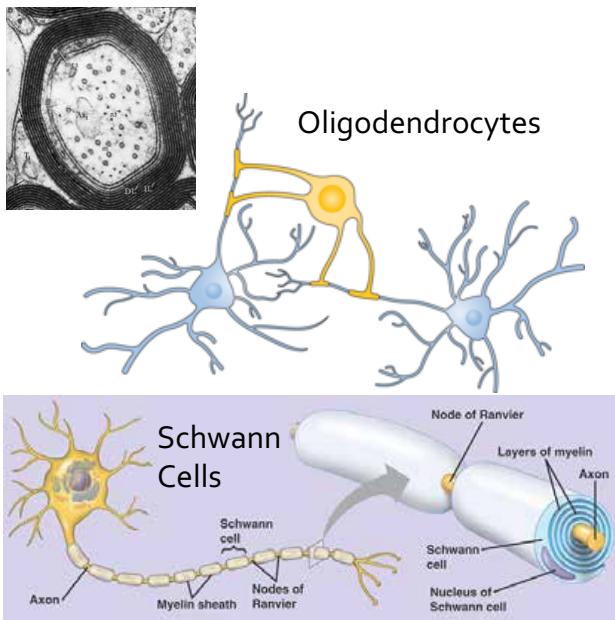
# Glia or Glial Cells

## Cells of the Central Nervous System



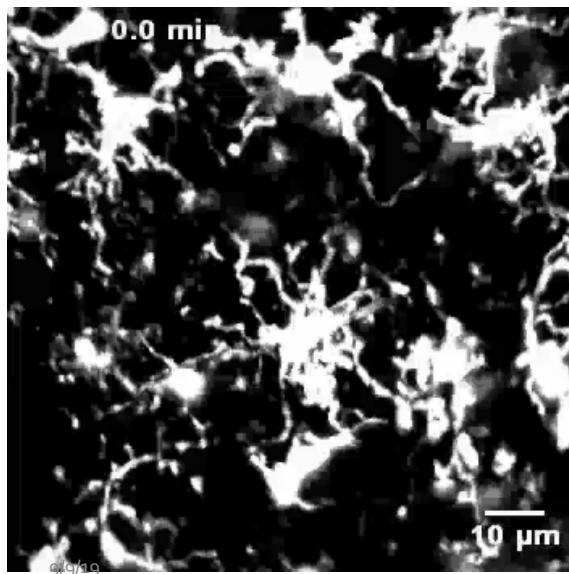
- From latin “glue” Unlike neurons they are:
  - Proliferative: glial scars
  - Inexcitable (?)
  - Of only a few types
- Called supporting cells, or space filling but do much more than that
- Three categories
  - Astrocytes- most numerous
    - form the blood-brain barrier
    - regulate chemical content of extracellular space

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  - Microglia- function as phagocytes (remove debris from sites of damage)

**One type of glia has been implicated in neuronal plasticity by "pruning" or removing synapses. Which type do you think it is?**

Astrocytes

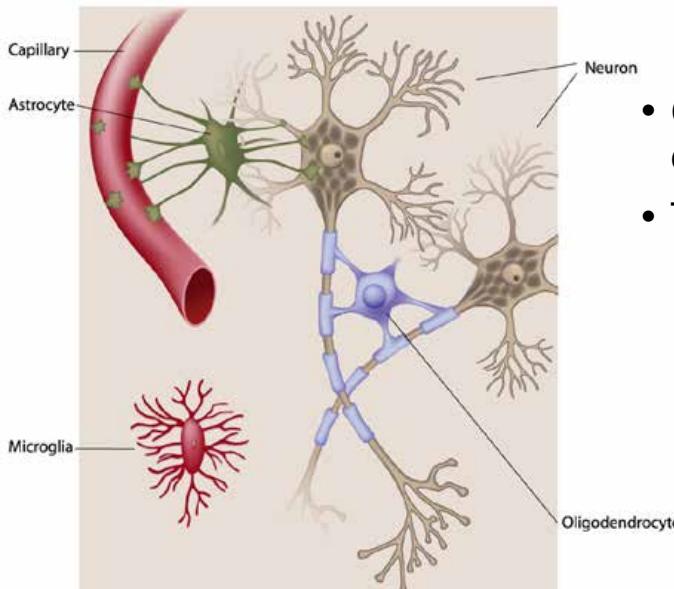
Myelinating  
glia

Microglia



# Glia or Glial Cells

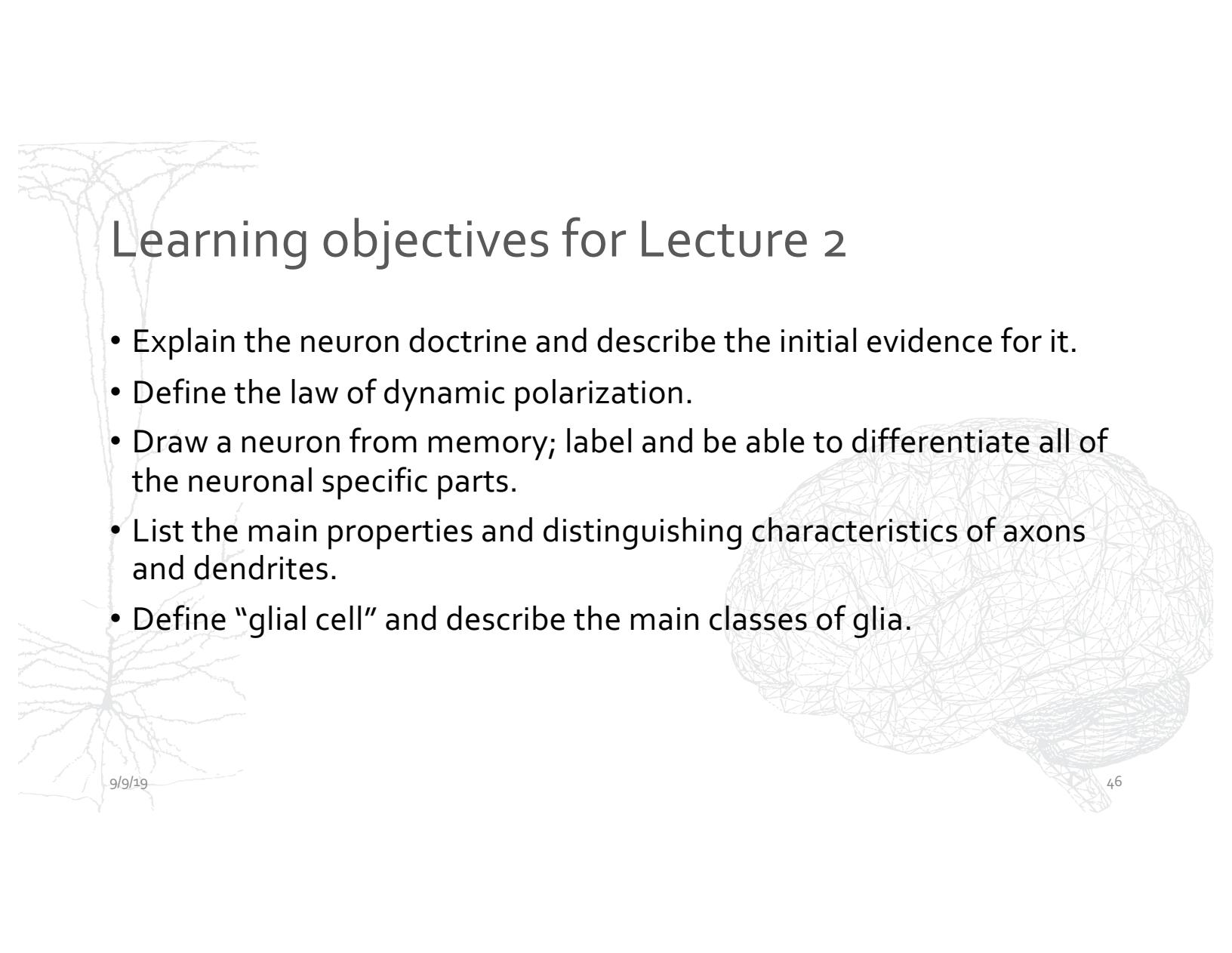
## Cells of the Central Nervous System



9/9/19

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# Learning objectives for Lecture 2

- Explain the neuron doctrine and describe the initial evidence for it.
- Define the law of dynamic polarization.
- Draw a neuron from memory; label and be able to differentiate all of the neuronal specific parts.
- List the main properties and distinguishing characteristics of axons and dendrites.
- Define “glial cell” and describe the main classes of glia.

## Lecture 2 - Cells of the nervous system

Pre-class notes for September 9, 2019

Reading: *Neuroscience* by Purves et al., pages 1-10

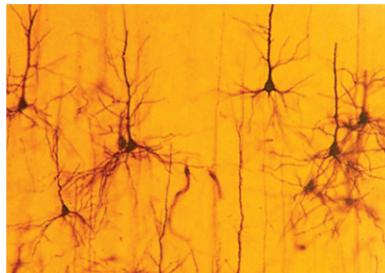
The modern study of neuroscience can be traced back to studies around the beginning of the 20th century by the anatomists Camillo Golgi and Santiago Ramón y Cajal. Golgi invented the Golgi stain which allows the visualization of individual neurons in their entirety. Santiago Ramón y Cajal used the Golgi stain to study the nervous system and elucidate many fundamental principles of the nervous system's organization. Cajal promoted two great ideas:

**Neuron Doctrine** - the concept that the nervous system carries out its functions by passing information from one cell to the next. These cells are called **neurons** and they are the basic structural and functional unit of the nervous system. **Neurites** (see below) of different neurons are not continuous and communicate by contact (i.e. **synapses**), not continuity.

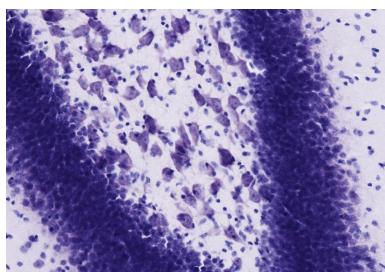
**Law of dynamic polarization** - the concept that information arrives from inputs (axons of neurons) and flows within neurons from dendrites, through the cell body to the axon and to its axon terminals.

Today, modern methods allow for the study of the nervous system at different levels of deconstruction: **molecules** (particularly gene products), **cells** (particularly neurons and their parts), and **systems** (networks/groups of connected neurons such as the visual, motor or autonomic). Some of the important methods for studying neuroscience today include:

**in situ hybridization** - histological method that localizes the expression (presences of mRNA) of specific genes (nucleotide sequences) in fixed tissue.



**Golgi stain** - histological method in which fixed nervous tissue is bathed in silver nitrate and potassium dichromate, which react to form silver chromate that stochastically accumulates in a small fraction of neurons. The Golgi method stains the entire neuron including any neuronal processes (dendrites and axons). The Golgi method labels only a small fraction of the population of cells within the sample, while leaving most of the surrounding tissue unstained.



**nissl stain** - histological method that stains the nucleus and surrounding material within a neuron. Traditionally cresyl violet is used to stain nucleic acids (DNA and RNA). **Nissl bodies** refers to the rough ER staining, which is prominent in long axon neurons.

Today there are a variety of approaches to label and visualize neurons, including antibody staining, fluorescent dyes, and transgenic animals expressing fluorescent proteins in genetically defined cell populations.

**electrophysiology** - experimental approach that measure the electrical activity of a living neuron. *Extracellular recordings* are when an electrode is placed near the cell of interest whereas *intracellular recordings* place the electrode inside the cell.

**MRI** - *magnetic resonance imaging*, a noninvasive method for visualizing the structure of the brain in detail. Differentiating white (myelinated axons) from gray matter (neuronal cell bodies)

**fMRI** - *functional MRI* - noninvasive methods for visualizing changes in blood flow in the brain. When a brain area is activated by a specific task, it begins to use more oxygen and within seconds, there is an increased flow of oxygen-rich blood to the active area.

The **Central Dogma** explains how genetic information flows within an organism. DNA is copied into RNA in a process called transcription, and RNA is used to create proteins in a process called translation. Within a given cell, not all genes will be made into protein. **Gene expression** refers to the particular times and places a gene will be transcribed.

Neurons are the fundamental cell type of the nervous system. Many of the structures are typical features of all cells, while there are also several specialized features, that are particular to neurons.

**Soma** - the cell body of a neuron which contains the nucleus and where most protein synthesis occurs and where other organelles (specialized structures) also reside.

**Cytosol** - the protein rich liquid that fills the cell, also referred to as *intracellular fluid* (oppose to *extracellular fluid*, that surrounds the cell).

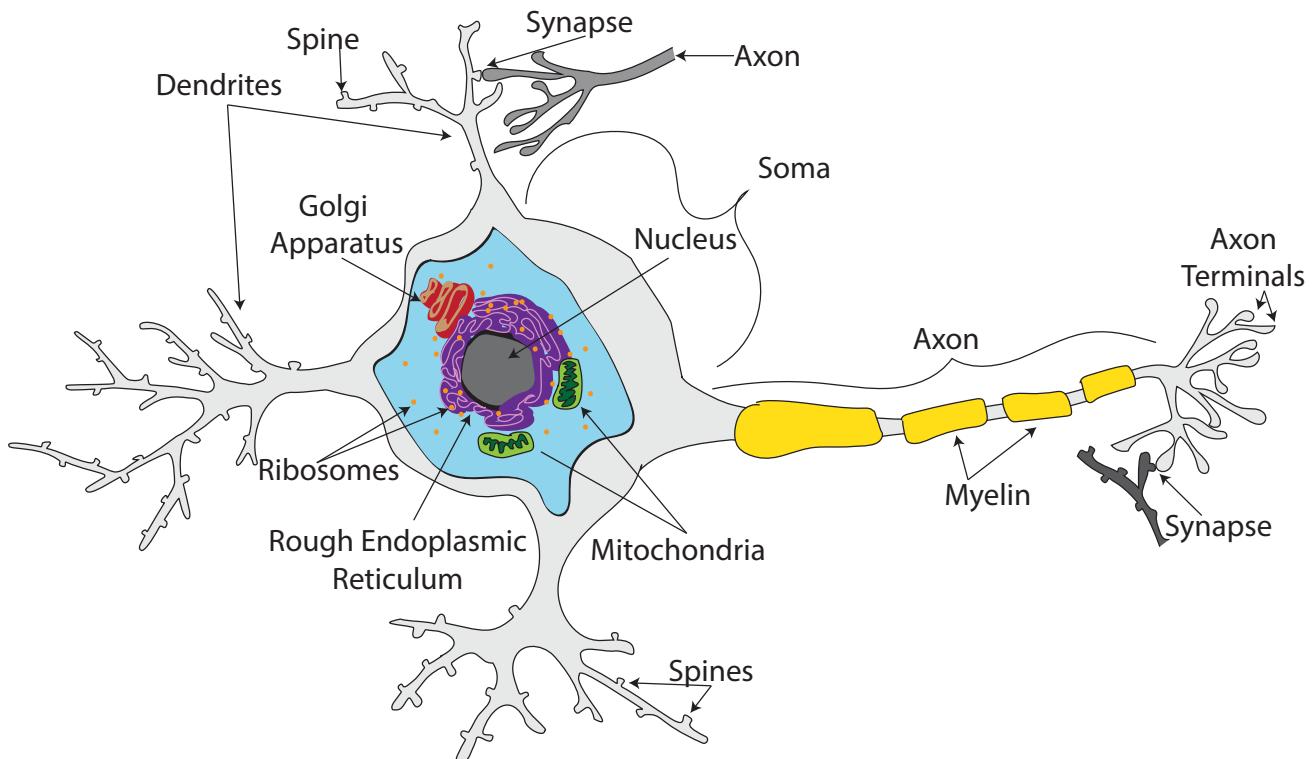
**Nucleus** - double membrane bound organelle that contains the DNA and is the site of transcription (DNA to mRNA) within the cell.

**Ribosome** - small organelle responsible for assembling protein from amino acids according to the mRNA sequence (code) in a process known as *translation*.

**Rough endoplasmic reticulum (ER)** - a system of membrane stacks with many ribosomes attached. The rough endoplasmic reticulum is responsible for the synthesis of proteins and is enriched in neurons with long axons compared to other cell types.

**Golgi apparatus** - organelle consisting of many folded membranes and vesicles that is involved in the secretion and transport of proteins.

**Mitochondria** - organelles involved in energy production. Within a mitochondrion, the energy stored in glucose bonds is broken down to form ATP in oxygen dependent reactions.



**Neurite** - a neuronal process or projection that arises from the cell body, either an axon or a dendrite.

**Dendrite** - type of neurite, usually branched and shorter than the axon, that receives much of the synaptic input to that neuron.

**Dendritic spines** - a small protrusion on a dendrite of some neurons (especially excitatory cells) that receives a synaptic connection from axon terminals and compartmentalizes the chemical and electrical signals.

**Axon** - long neurite that extends from the soma. Although an axon often branches extensively, a neuron usually has only 1 axon that originates from the cell body. Axons lack rough ER and thus there is little or no local protein synthesis. Since axons can be very long (possibly meters long), cytoskeletal networks such as **microtubules** provide structural support and provide a mechanism for transport.

**Anterograde** - directional term, meaning toward the axon terminal.

**Retrograde** - directional term, meaning toward the cell body.

**Axon initial segment** - site of action potential initiation, close to the origin of the axon.

**Axon terminal** - specialized endings of the axon that makes synaptic contacts with other cells (often with dendrites/spines)

**Synapse** - a junction, typically between the axon of one cell and a dendrite of another cell, that permits signals to transfer from a neuron to another cell.

In addition to neurons the nervous system is also made up of **glia (glial cells)**, which is a collective term for several different types of non-neuronal cells in the nervous system, each of which is specialized for particular functions.

**Astrocyte** - type of glial cell located in the central nervous system (CNS) which aids in maintaining the appropriate chemical environment of the brain including formation of the blood brain barrier and removing chemicals from the extracellular fluid surround synapses.

**Oligodendrocyte** - type of glial cell responsible for myelinating axons within the CNS. A single oligodendrocyte wraps part of its membrane many times around segments of multiple axons.

**Schwann cell** - type of glial cell responsible for myelinating axons within the peripheral nervous system (PNS) . A single Schwann cell wraps itself many times around a single segment of one axon.

**Microglia** - type of glial cell that has many immune response properties including removal of cellular debris, modulating local inflammation and influencing neuronal survival.

**Learning Objectives:** (By the end of Lecture 2 you should be able answer the following)

1. Define the neuron doctrine and describe the initial evidence for it.
2. Define the law of dynamic polarization.
3. Draw a neuron from memory; label and be able to differentiate all of the neuronal specific parts.
4. List the main properties and distinguishing characteristics of axons and dendrites.
5. Define “glial cell” and describe the main classes of glia.