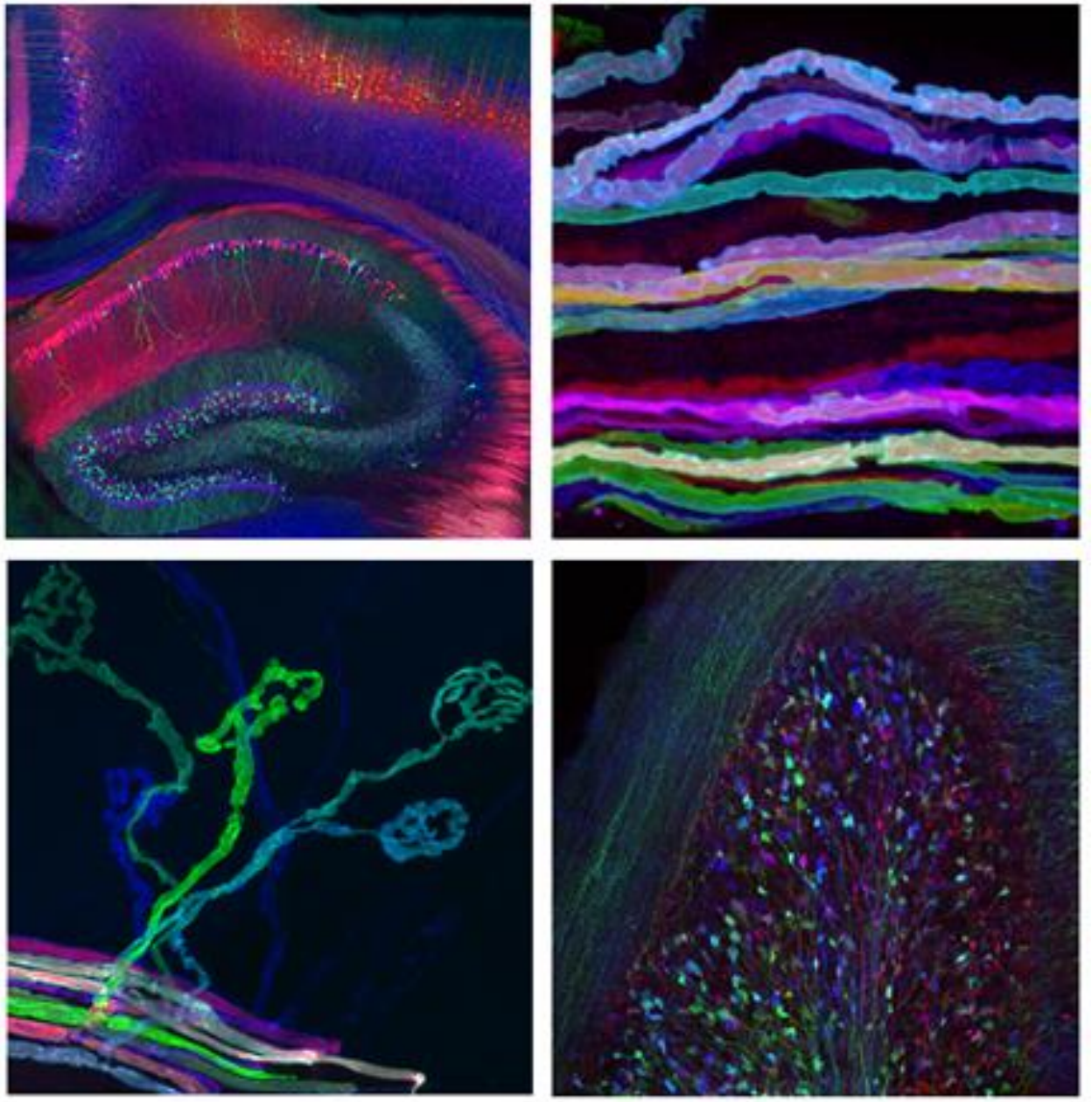
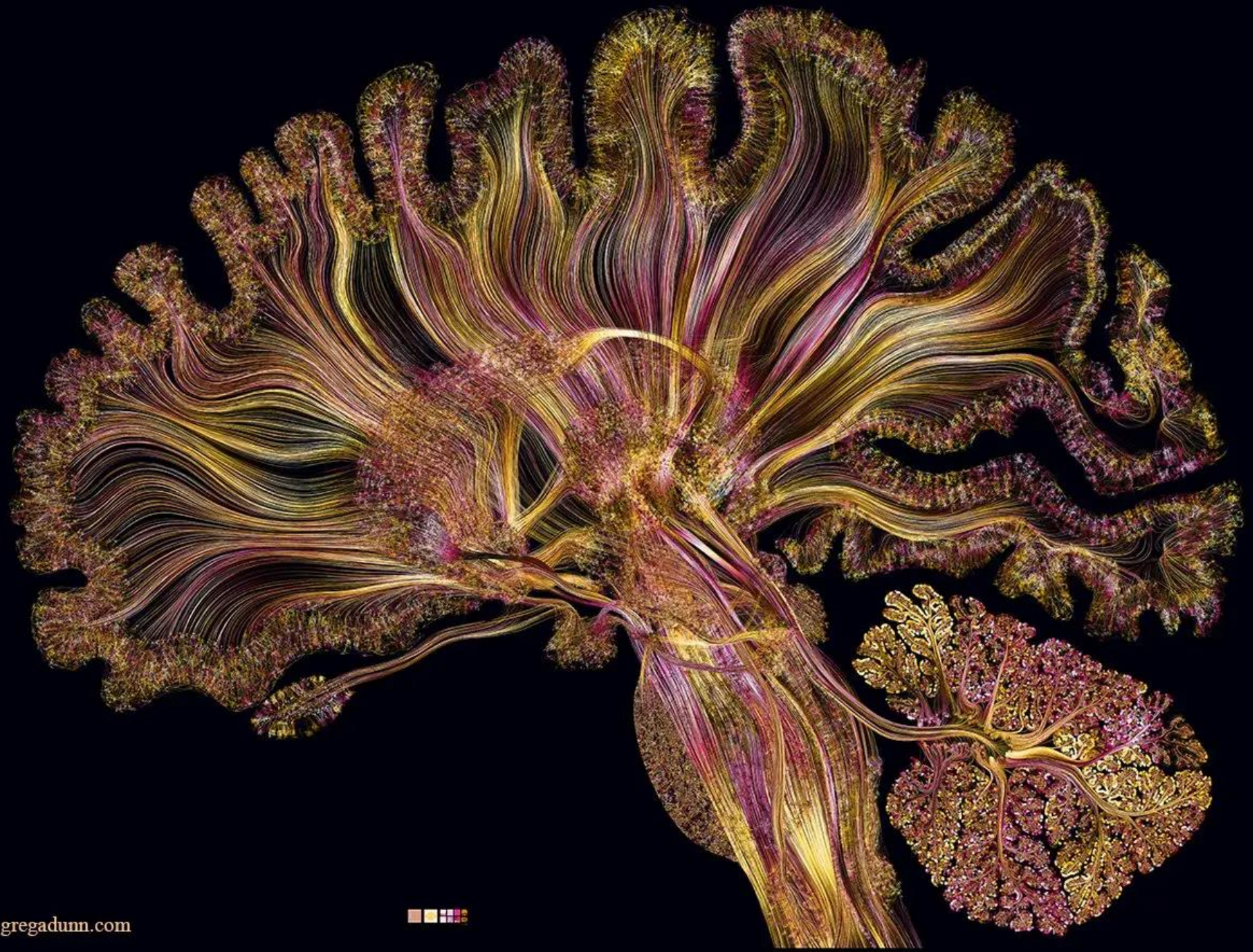
BIO-311: Introduction to Neuroscience

Course instructor:
Prof. Mackenzie Mathis, PhD

Material in this course was developed over the years by Mackenzie Mathis, Pavan P Ramdya, & Ralf Schneggenburger

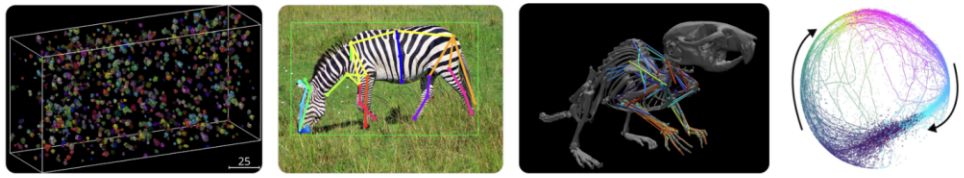


Top left: Cerebral cortex and hippocampus (Gonzales E, Weissman TA and Lichtman JW)
Top right: Motor neuron axons (Livet J, Sanes JR and Lichtman JW)
Bottom left: Motor axons synapsing onto muscle at the neuromuscular junction (Draft RW, Livet J, Sanes JR and Lichtman JW)
Bottom right: Cells in the cerebellum (Weissman TA, Livet J, Sanes JR Sanes, and Lichtman JW)


gregadunn.com

Prof. Mackenzie Weygandt Mathis, PhD
Bertarelli Foundation Chair of Integrative Neuroscience
PhD: Harvard University
Fellow: Rowland Institute at Harvard
http://mackenziemathislab.org
SV 2811 – Mondays, Campus Biotech otherwise (Geneva)

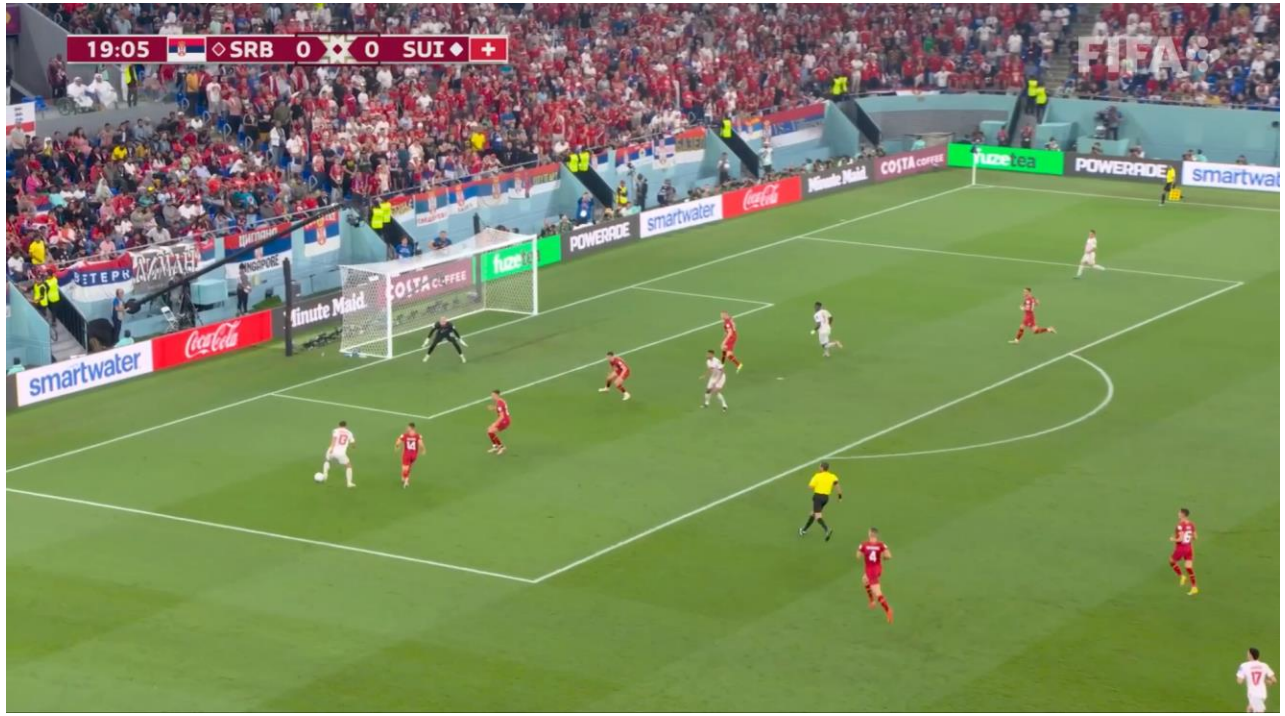
Mathis Laboratory of Adaptive Intelligence | EPFL



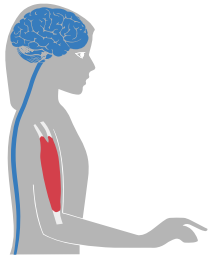
Our world is always changing: how do our brains adapt? We aim to understand the mechanisms underlying adaptive sensorimotor behavior in intelligence systems, aka "adaptive intelligence", and develop new machine learning methods that enable us to do so.

Merging artificial intelligence & neuroscience

Biological Intelligence

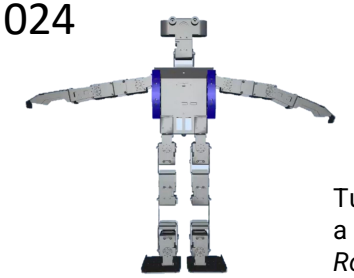


World Cup 2022 CH



Artificial Intelligence

DeepMind 2024

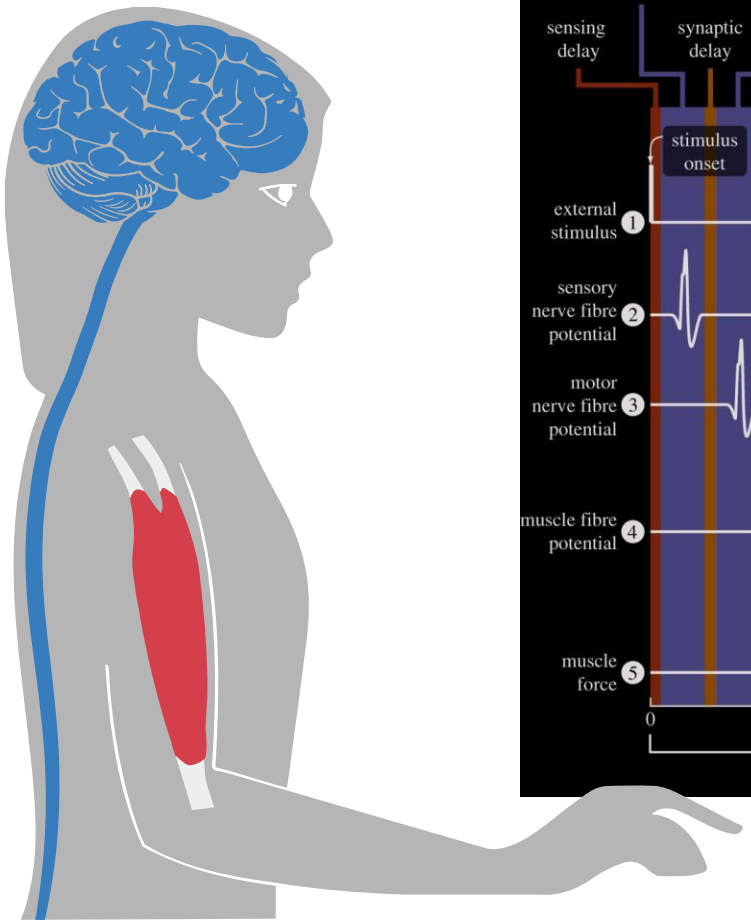


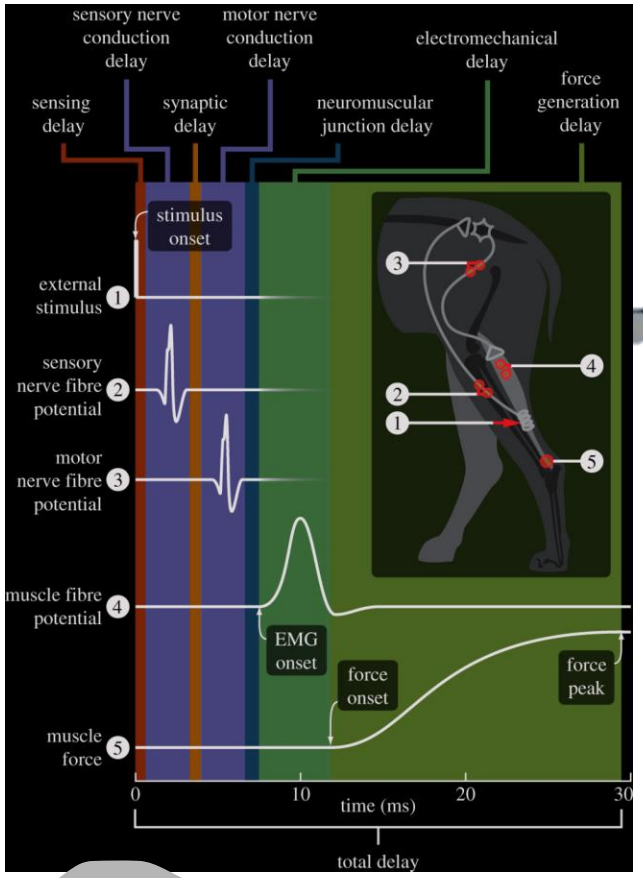
Tuomas Haarnoja *et al*. Learning agile soccer skills for a bipedal robot with deep reinforcement learning. *Sci. Robotics* (2024).

Boston Dynamics

Biological Intelligence

our nervous system is slow!

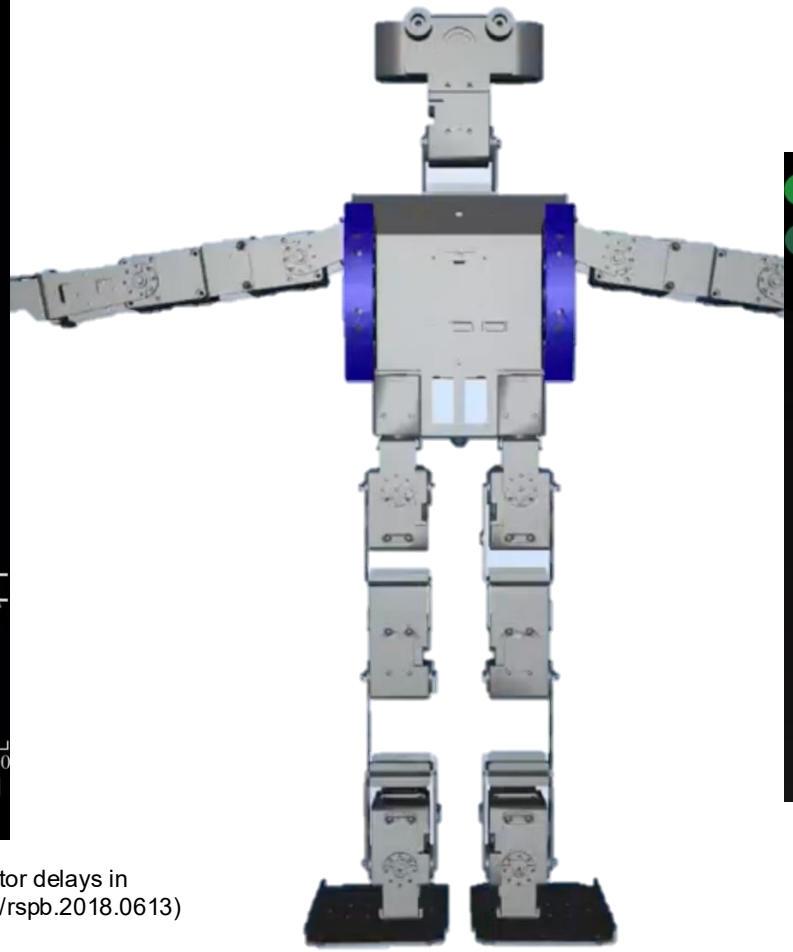


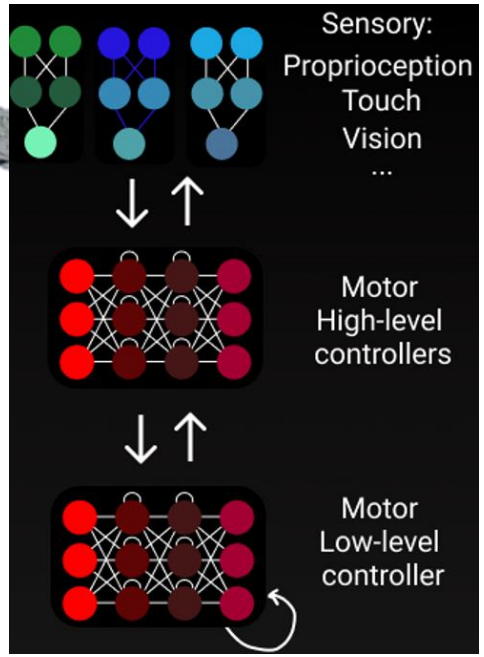


Adapted from Scaling of sensorimotor delays in terrestrial mammals. DOI: (10.1098/rspb.2018.0613)

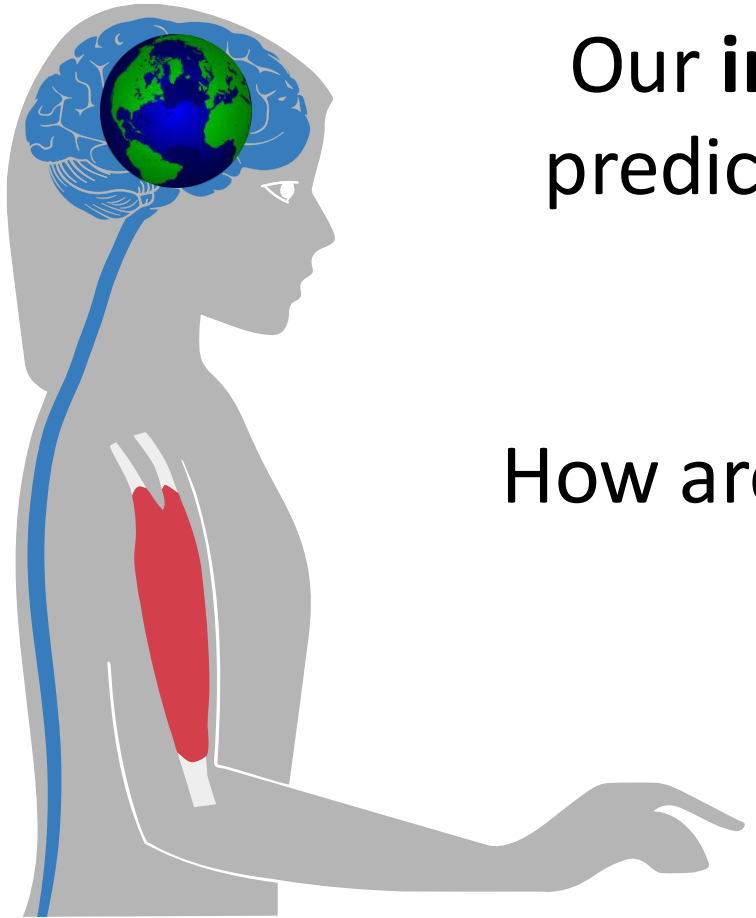
Artificial Intelligence

electronics are fast!



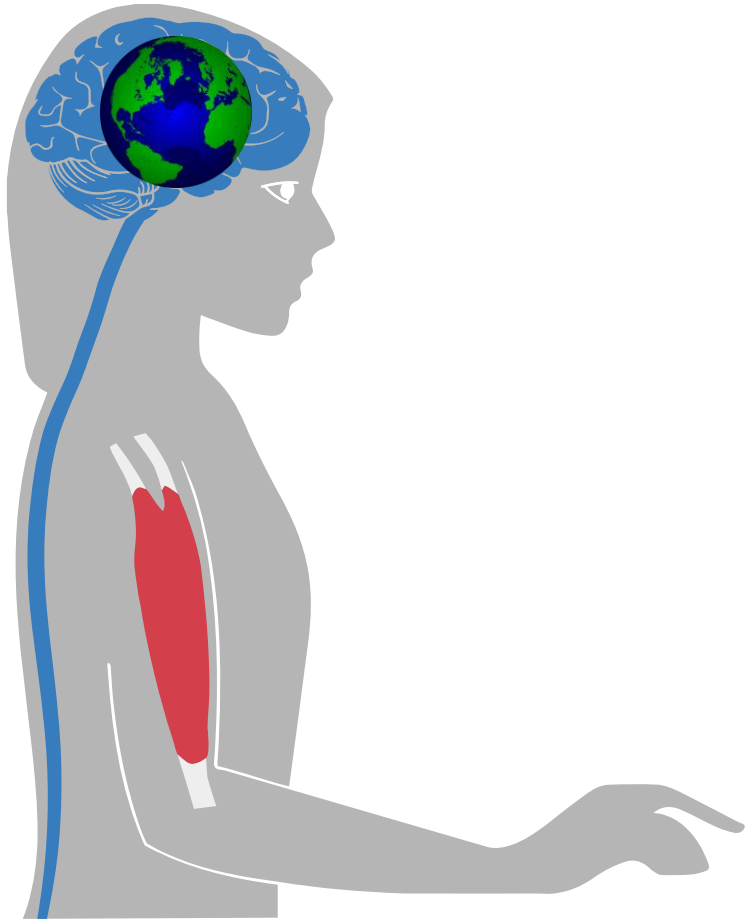


Adapted from Hausmann … Mathis 2021



Our **internal models** enable us to make predictions and rapidly adapt to changes

How are they encoded in neural dynamics?

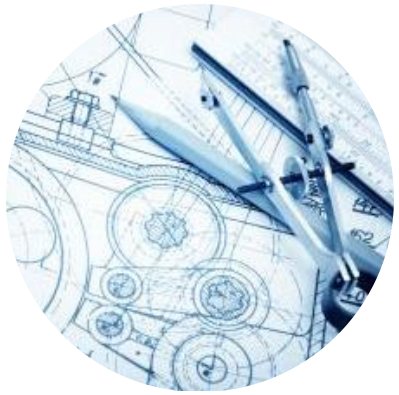



L. WITTGENSTEIN

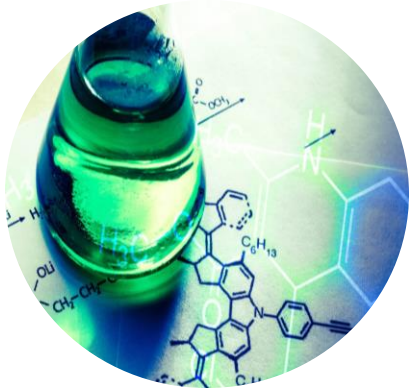
What is Neuroscience?

Wiki:

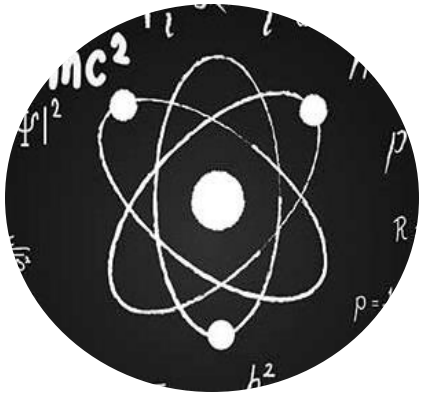
“Neuroscience is the scientific study of the nervous system (the brain, spinal cord, and peripheral nervous system) and its functions.”



Engineering

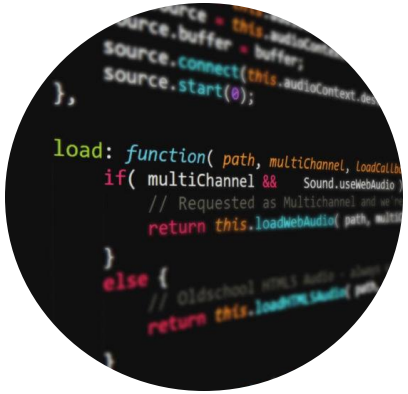


Chemistry

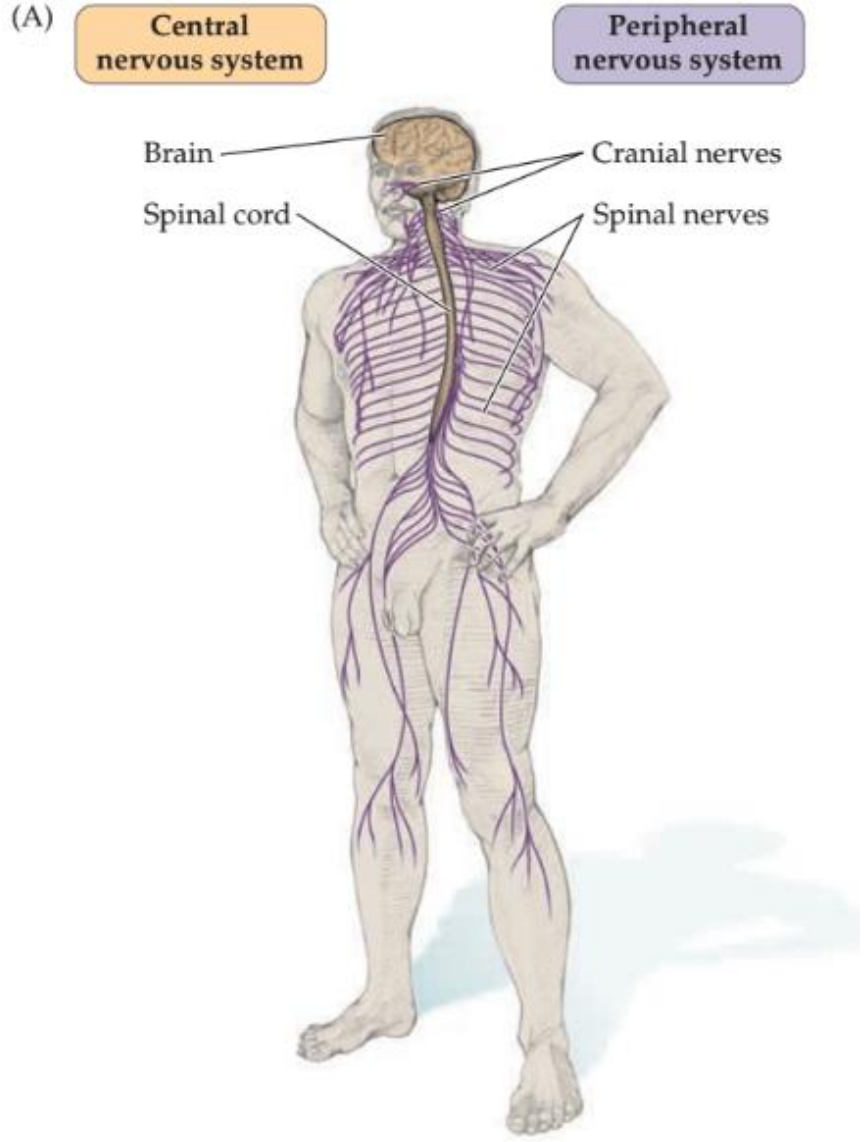


Physics

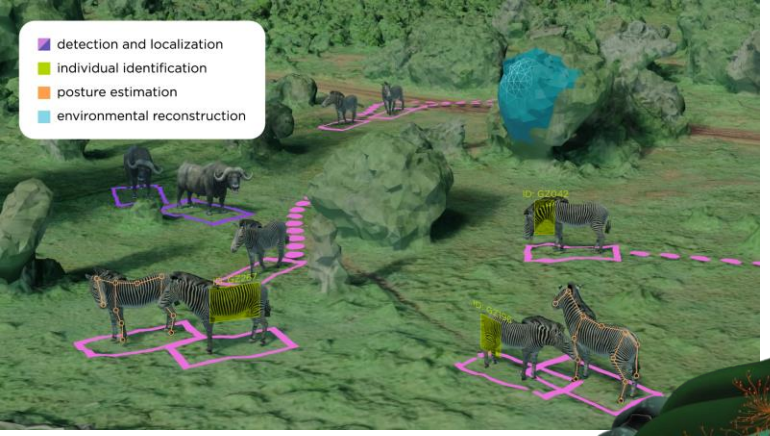
Biology

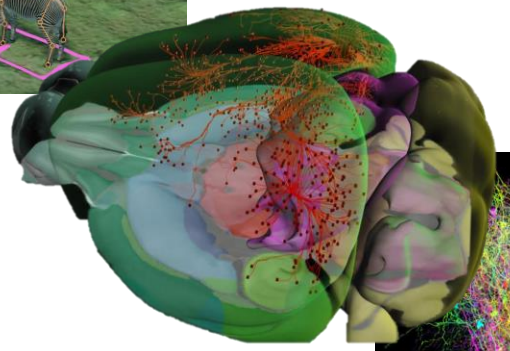


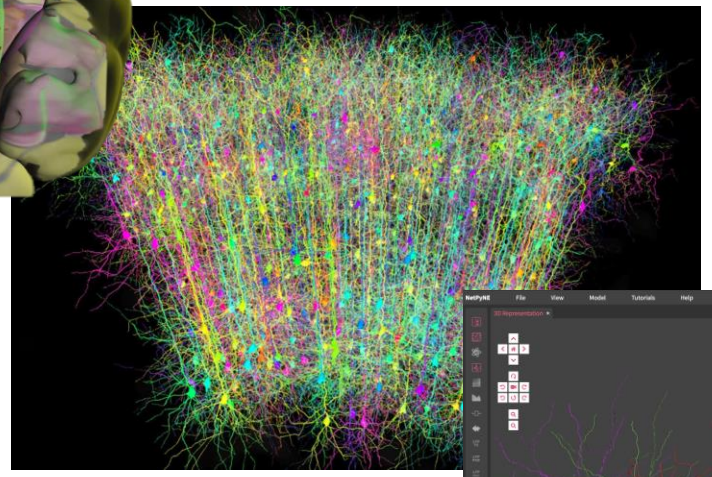
Computer Science

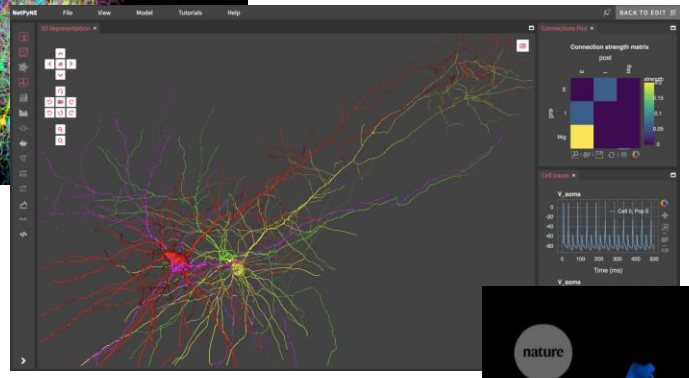


Neuroscience across scales…

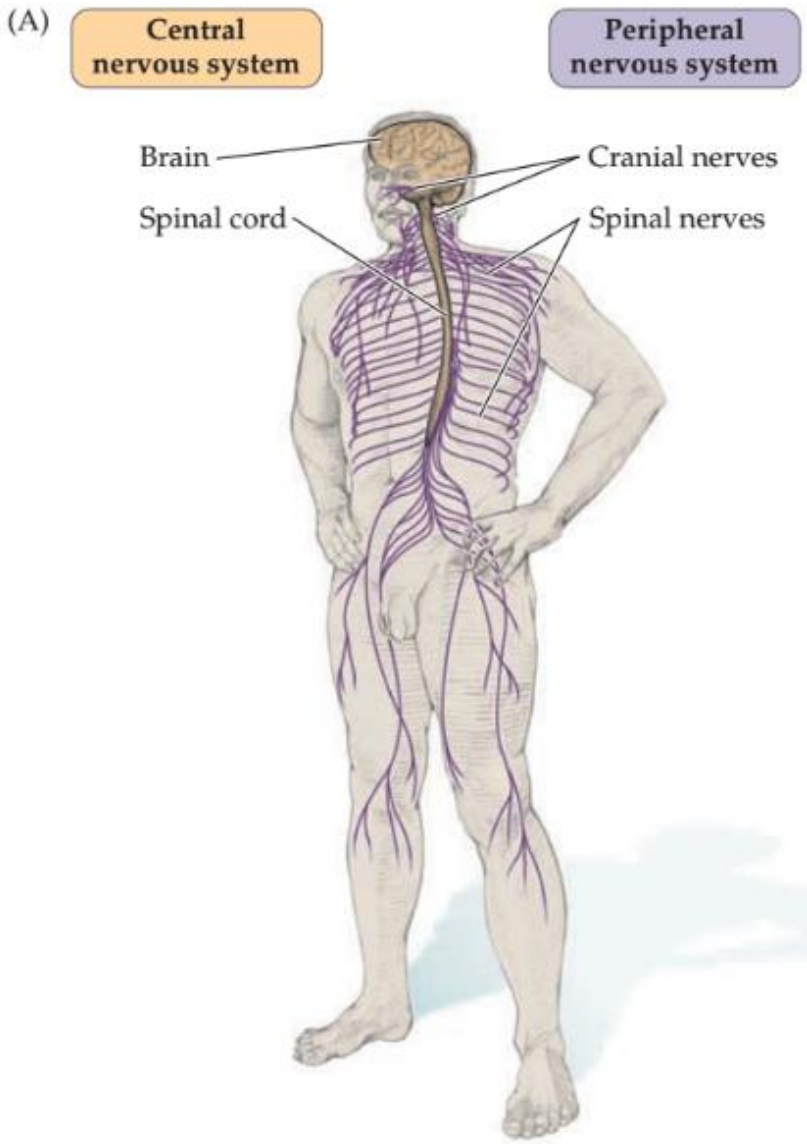


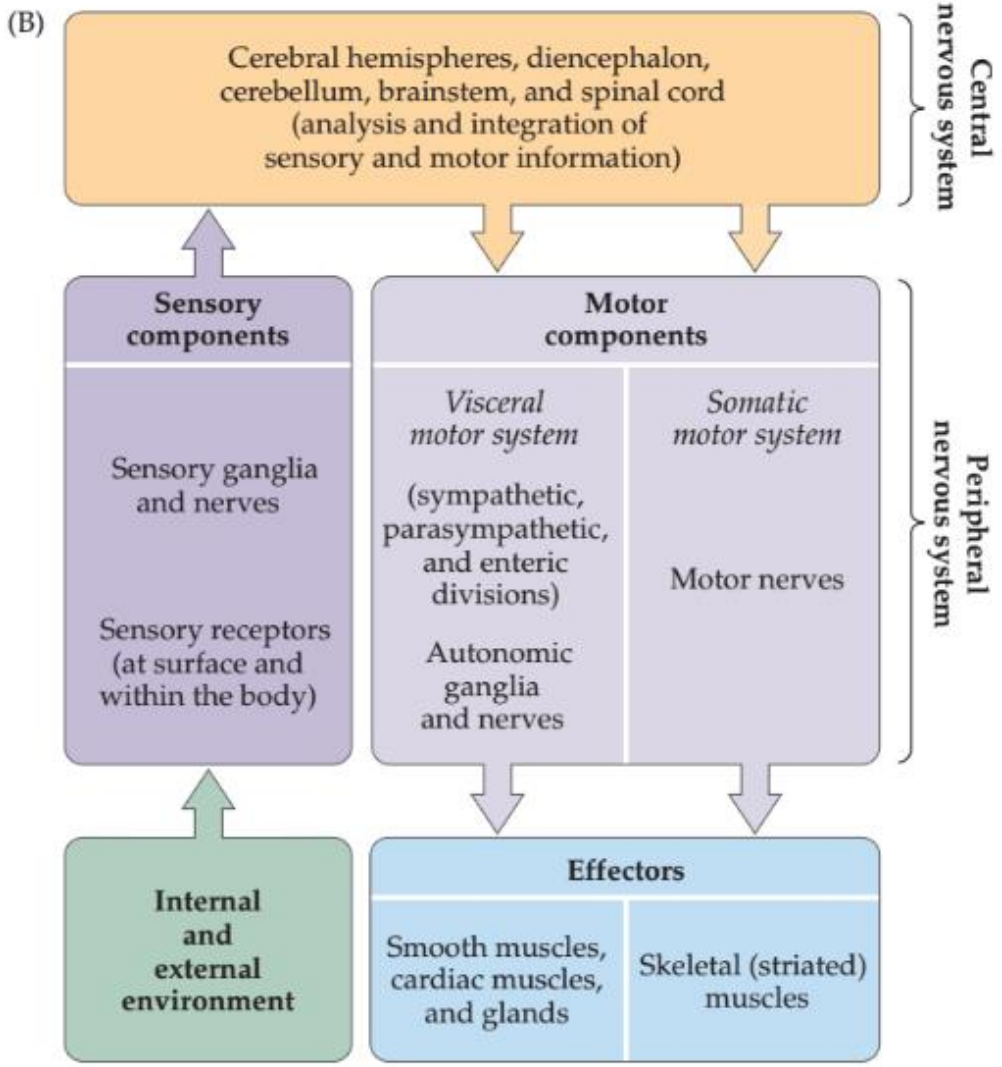






The Nervous System





Neurons & Glia

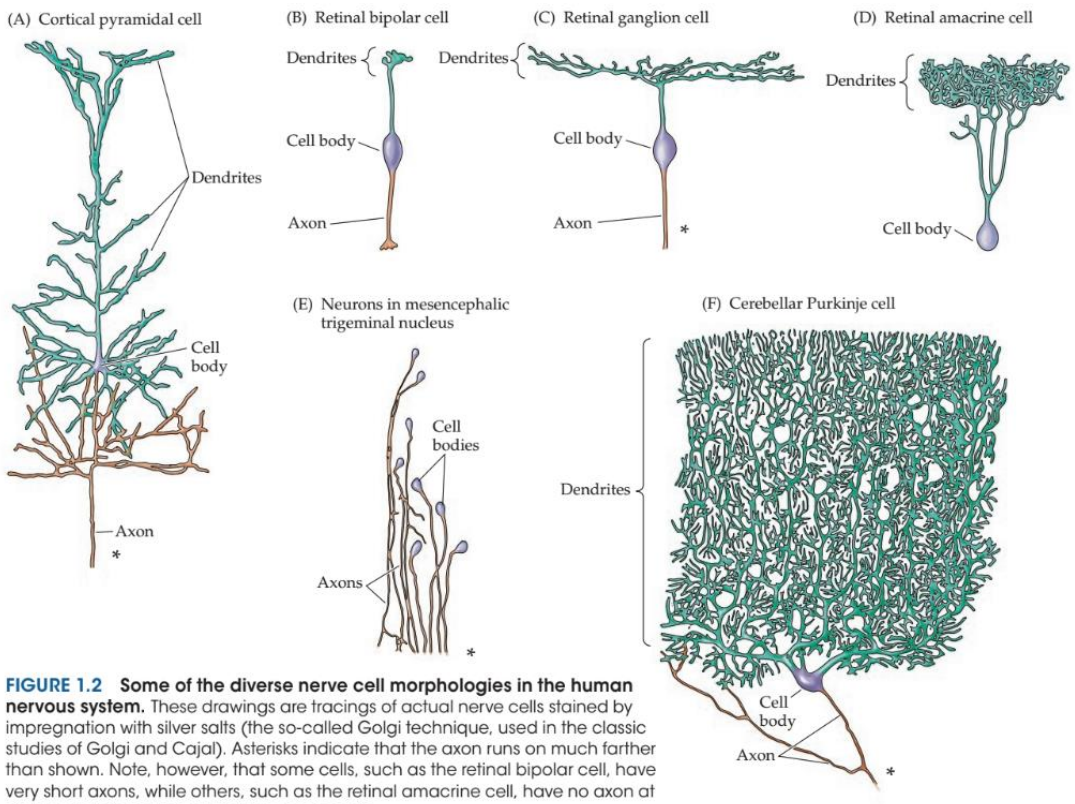
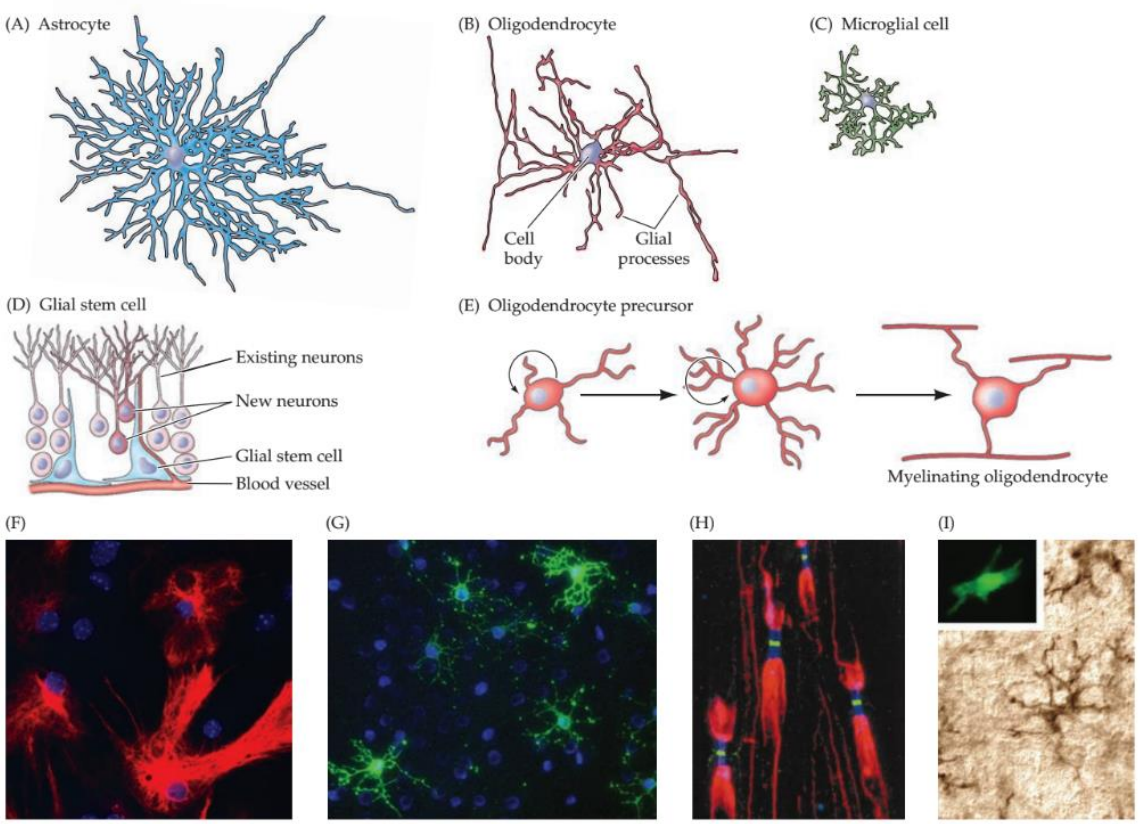


FIGURE 1.2 Some of the diverse nerve cell morphologies in the human nervous system. These drawings are tracings of actual nerve cells stained by impregnation with silver salts (the so-called Golgi technique, used in the classic studies of Golgi and Cajal). Asterisks indicate that the axon runs on much farther than shown. Note, however, that some cells, such as the retinal bipolar cell, have very short axons, while others, such as the retinal amacrine cell, have no axon at all. The drawings are not all at the same scale.



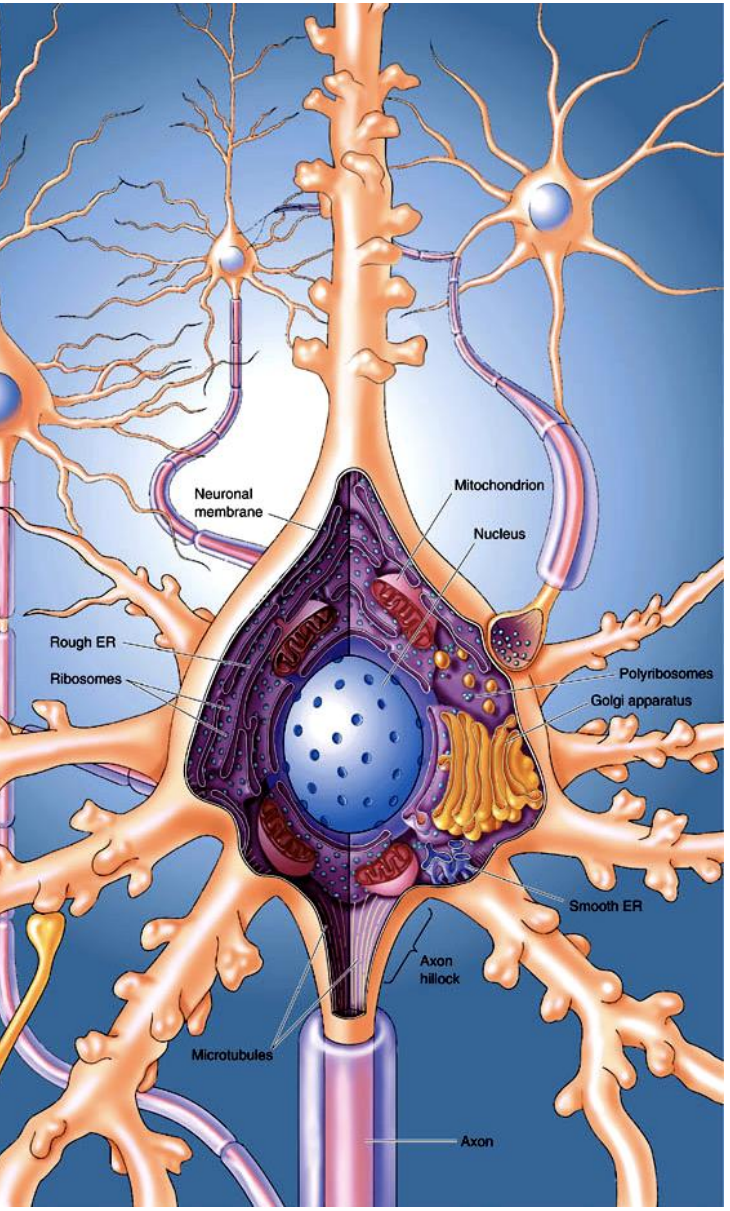
Neurons

- From Greek: *neûron* sinew, cord, nerve
- Limited regeneration (olfactory)
- Hundreds (maybe more) of types
- The “neuron doctrine”: the single neuron constitutes the structural and functional unit of the CNS (Golgi, 1906)

Glia or glial cells

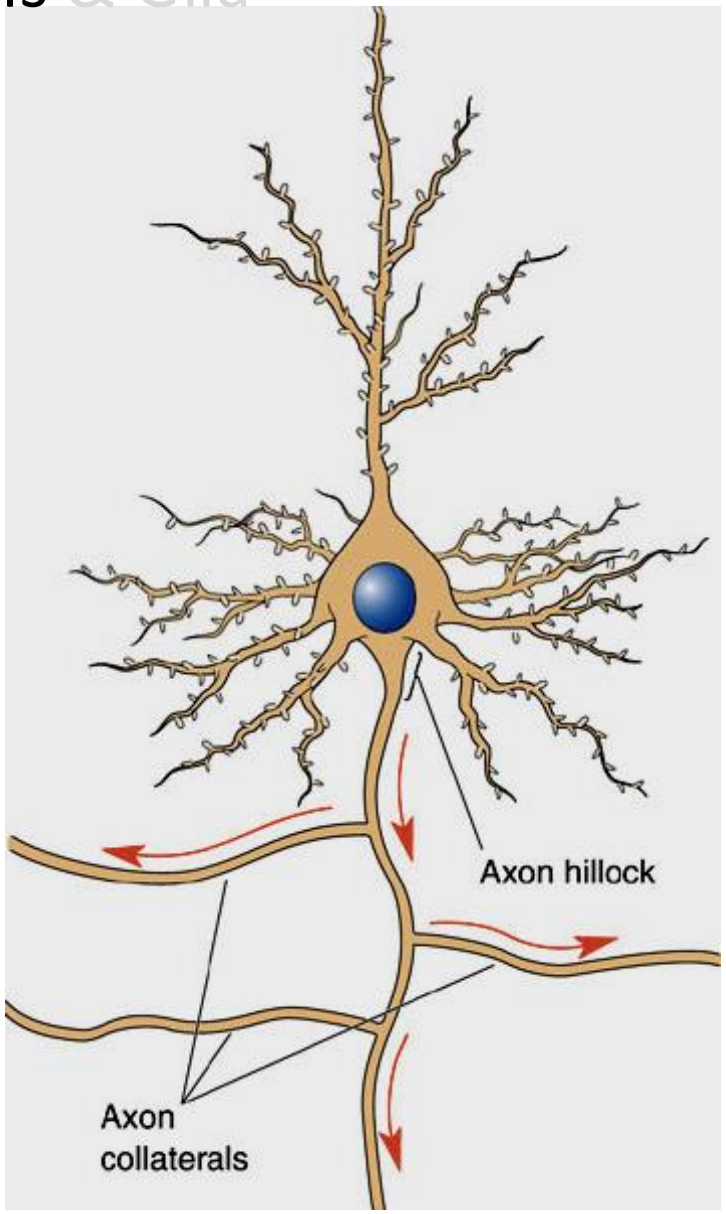
- From latin: “glue”
- Unlike neurons, they are proliferative (glial scars), only a few types
- Called the “support cells,” but do much more!
- Major types: astrocytes, myelinating glia (oligodendrites, Schwann cells)

Neurons & Glia



Soma (cell body)

Cytoplasm contains
– the 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)
• Separated from outside by the cell membrane or plasmalemma



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 µms 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 later in the course.

Useful Terms to Know

*for reading later 😎

Terms

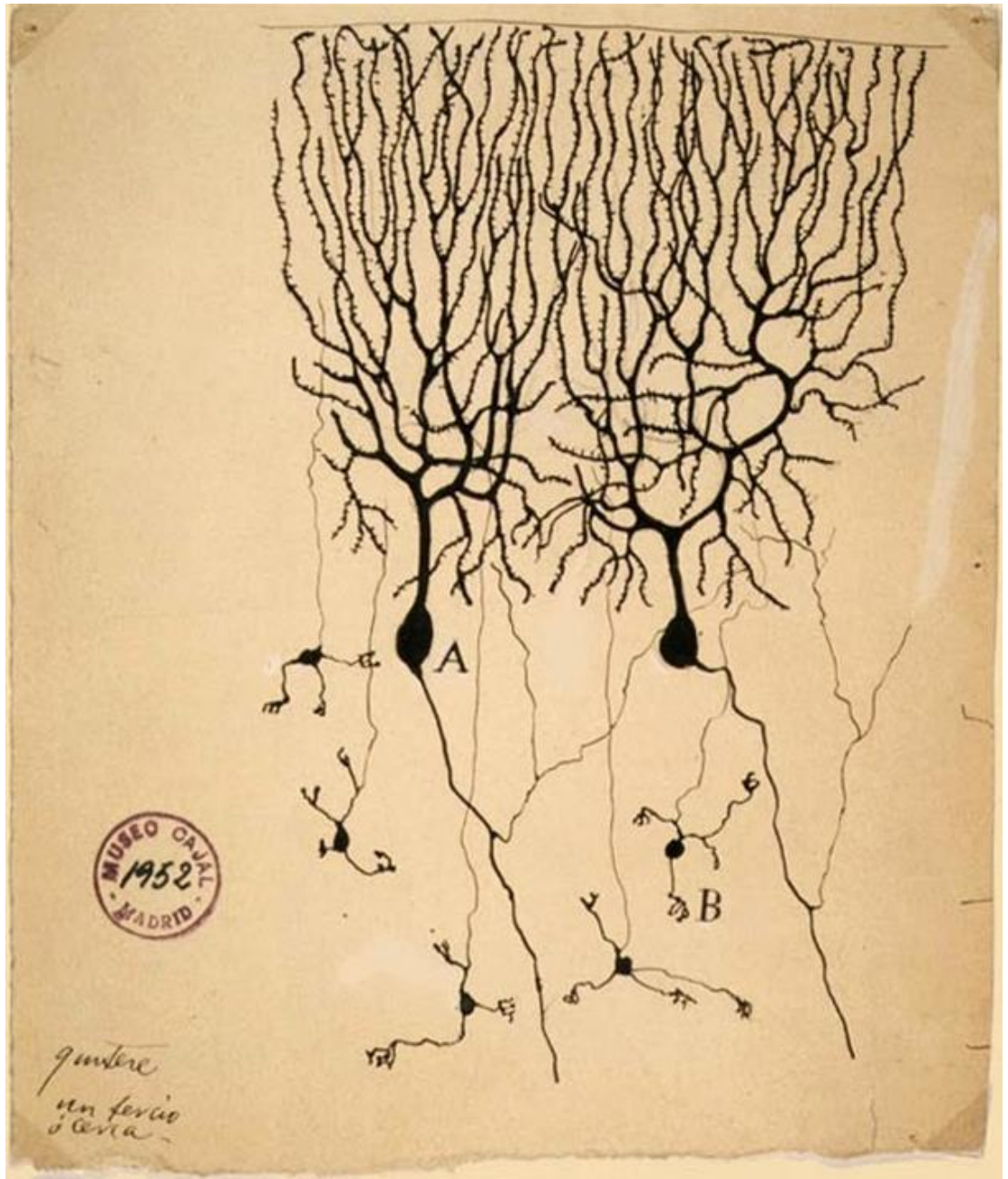
Table 7.1 Collections of Neurons

NAME	DESCRIPTION AND EXAMPLE
Gray matter	A generic term for a collection of neuronal cell bodies in the CNS. When a freshly dissected brain is cut open, neurons appear gray.
Cortex	Any collection of neurons that form a thin sheet, usually at the brain's surface. *Cortex* is Latin for "bark." Example: *cerebral cortex*, the sheet of neurons found just under the surface of the cerebrum.
Nucleus	A clearly distinguishable mass of neurons, usually deep in the brain (not to be confused with the nucleus of a cell). *Nucleus* is from the Latin word for "nut." Example: *lateral geniculate nucleus*, a cell group in the brain stem that relays information from the eye to the cerebral cortex.
Substantia	A group of related neurons deep within the brain, but usually with less distinct borders than those of nuclei. Example: *substantia nigra* (from the Latin for "black substance"), a brain stem cell group involved in the control of voluntary movement.
Locus (plural: loci)	A small, well-defined group of cells. Example: *locus coeruleus* (Latin for "blue spot"), a brain stem cell group involved in the control of wakefulness and behavioral arousal.
Ganglion (plural: ganglia)	A collection of neurons in the PNS. *Ganglion* is from the Greek for "knot." Example: the *dorsal root ganglia*, which contain the cells bodies of sensory axons entering the spinal cord via the dorsal roots. Only one cell group in the CNS goes by this name: the *basal ganglia*, which are structures lying deep within the cerebrum that control movement.

Table 7.2 Collections of Axons

NAME	DESCRIPTION AND EXAMPLE
Nerve	A bundle of axons in the PNS. Only one collection of CNS axons is called a nerve: the *optic nerve*.
White matter	A generic term for a collection of CNS axons. When a freshly dissected brain is cut open, axons appear white.
Tract	A collection of CNS axons having a common site of origin and a common destination. Example: *corticospinal tract*, which originates in the cerebral cortex and ends in the spinal cord.
Bundle	A collection of axons that run together but do not necessarily have the same origin and destination. Example: *medial forebrain bundle*, which connects cells scattered within the cerebrum and brain stem.
Capsule	A collection of axons that connect the cerebrum with the brain stem. Example: *internal capsule*, which connects the brain stem with the cerebral cortex.
Commissure	Any collection of axons that connect one side of the brain with the other side.
Lemniscus	A tract that meanders through the brain like a ribbon. Example: *medial lemniscus*, which brings touch information from the spinal cord through the brain stem.

Anatomy

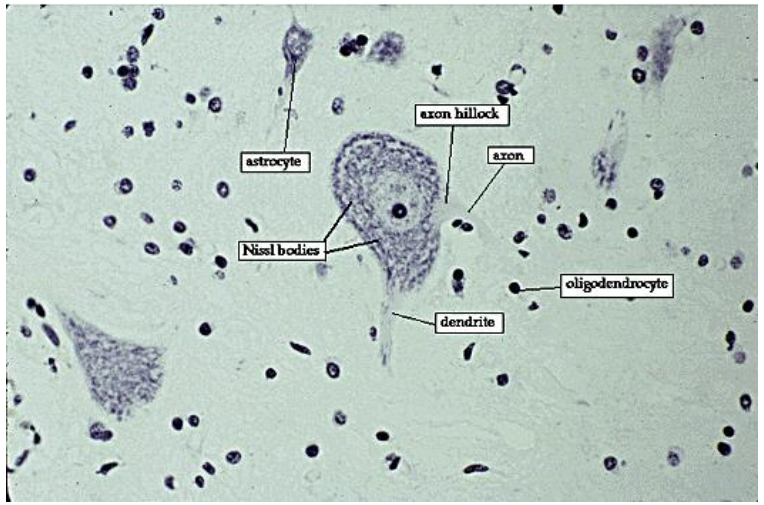


Classifying Neurons

• About 86-100 hundred billion neurons in human brain, 300 in a little worm

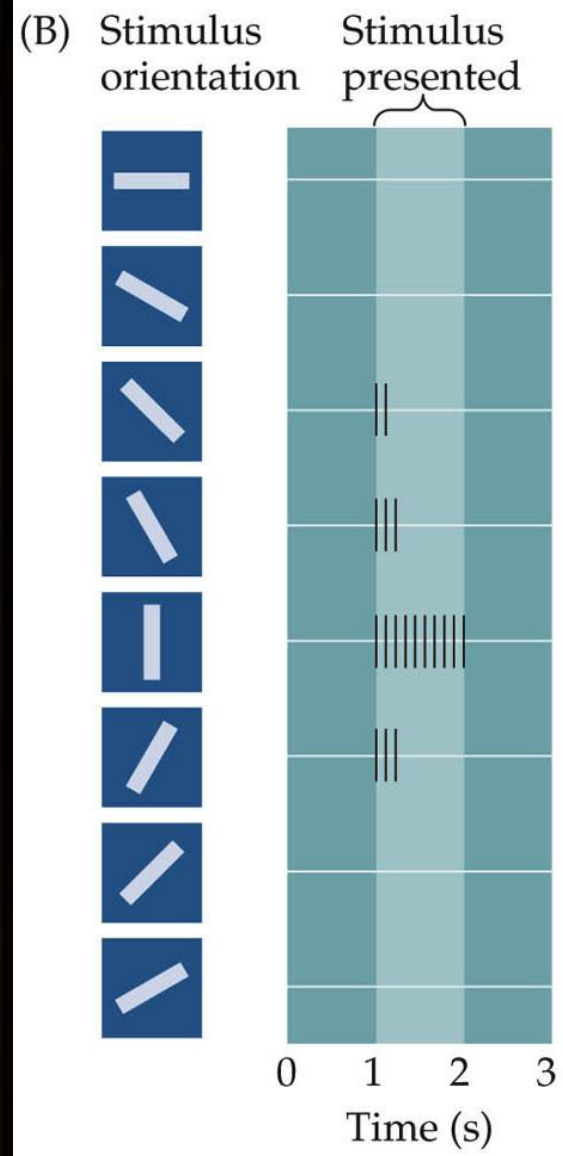
• Can be classified in many different ways including:

1. Based on number of “neurites”
2. Based on dendrites
3. Based on connections or function
4. Based on axon length
5. Based on neurotransmitter, typically one neurotransmitter per neuron
6. Named cells



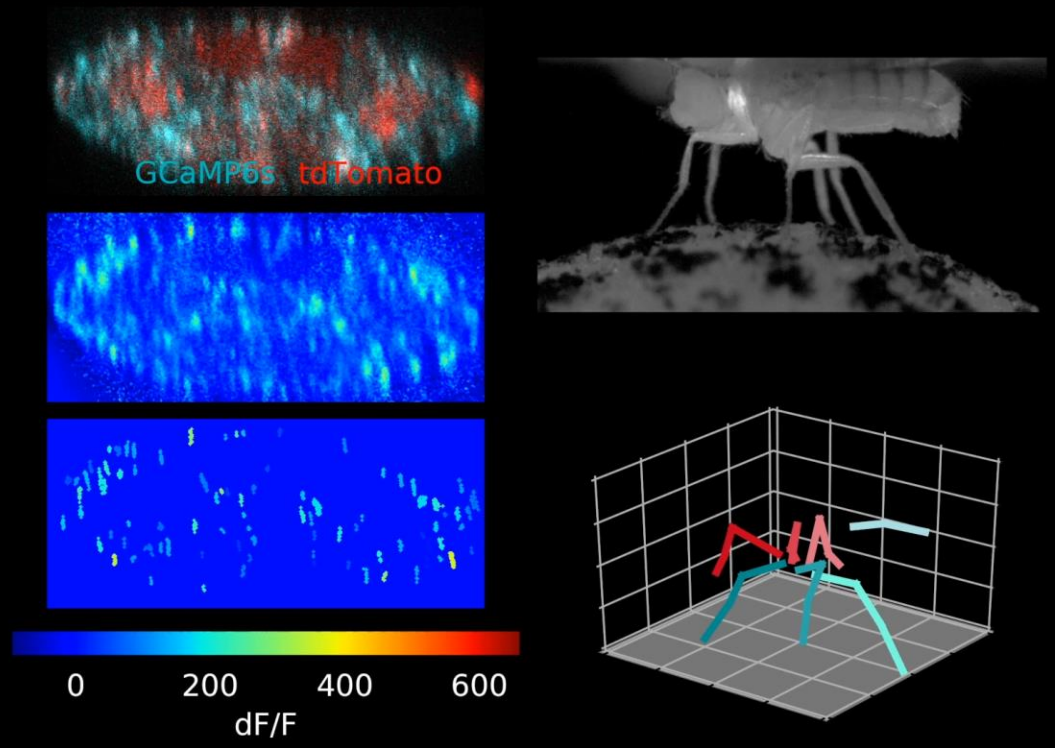
Function

Hubel & Wiesel

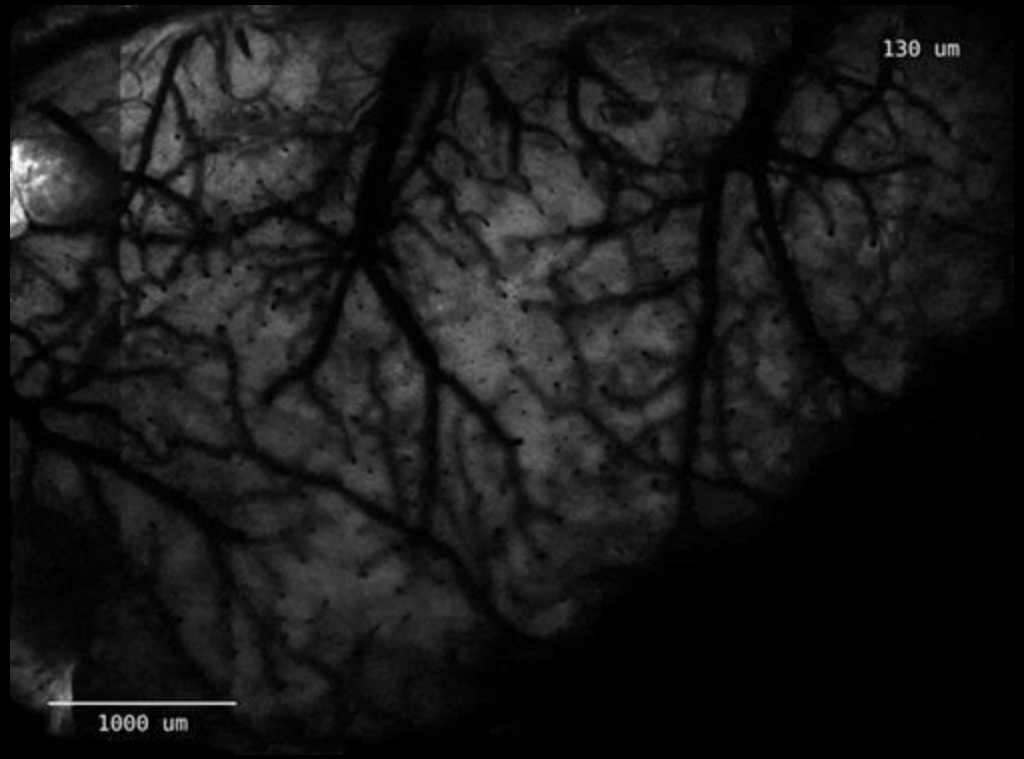


Purves Fig. 12.8

Function: modern techniques



[Chen, Hermans et al., ***Nature Communications*** 2018]

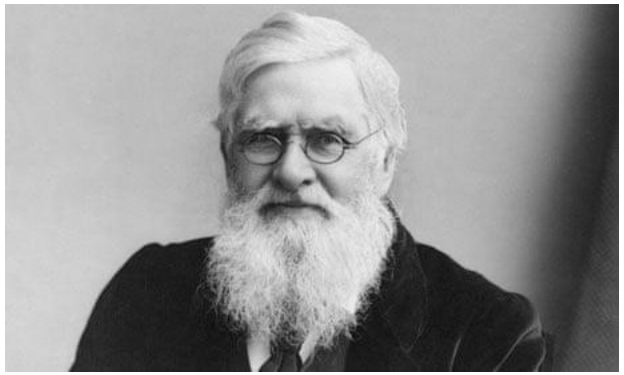


Sofroniew et al 2016 eLife

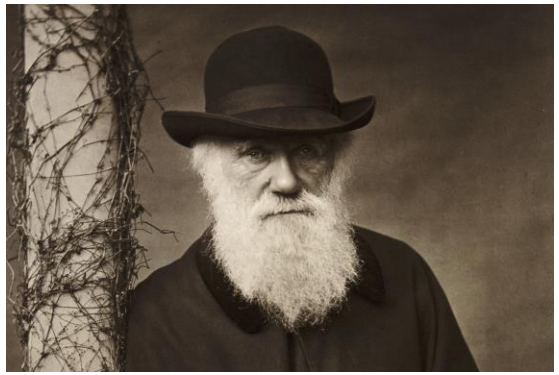
Evolution & Development

Modern humans evolved 300-30K years ago, and this gave rise to symbolic thinking (philosophy, religion, science, logic)

Our brains are the key to our evolutionary success 🧠 ….

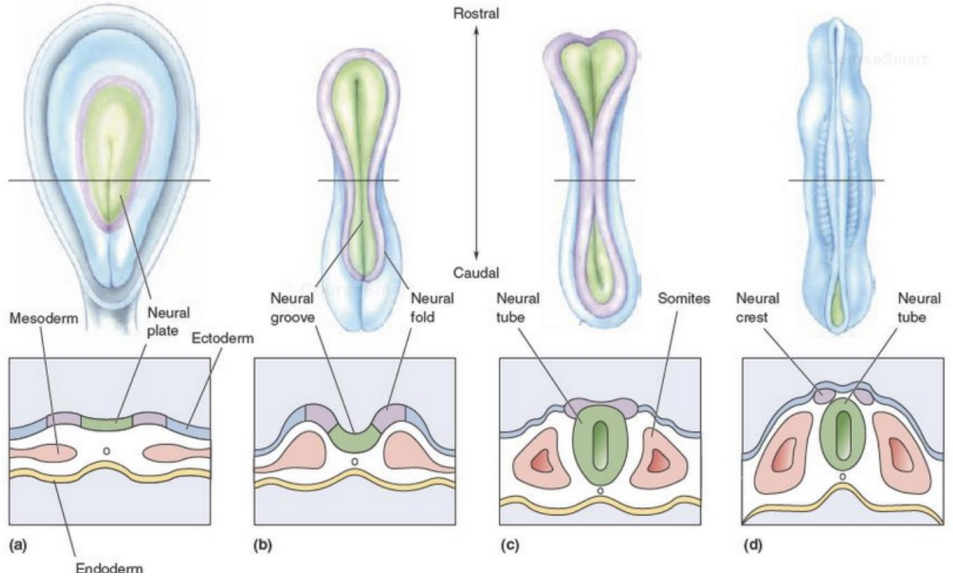


Alfred Wallace

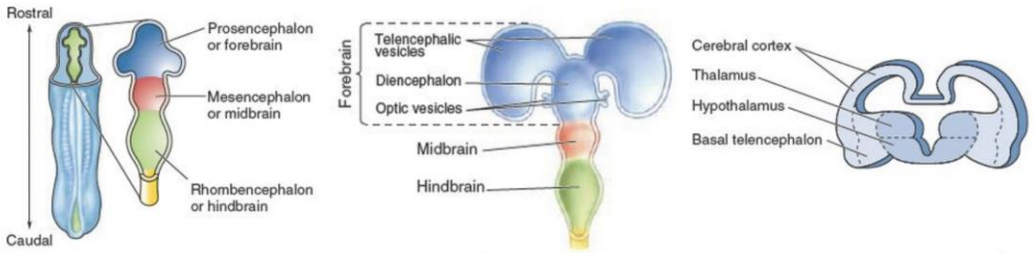


Charles Darwin

Step 1: Neuralation



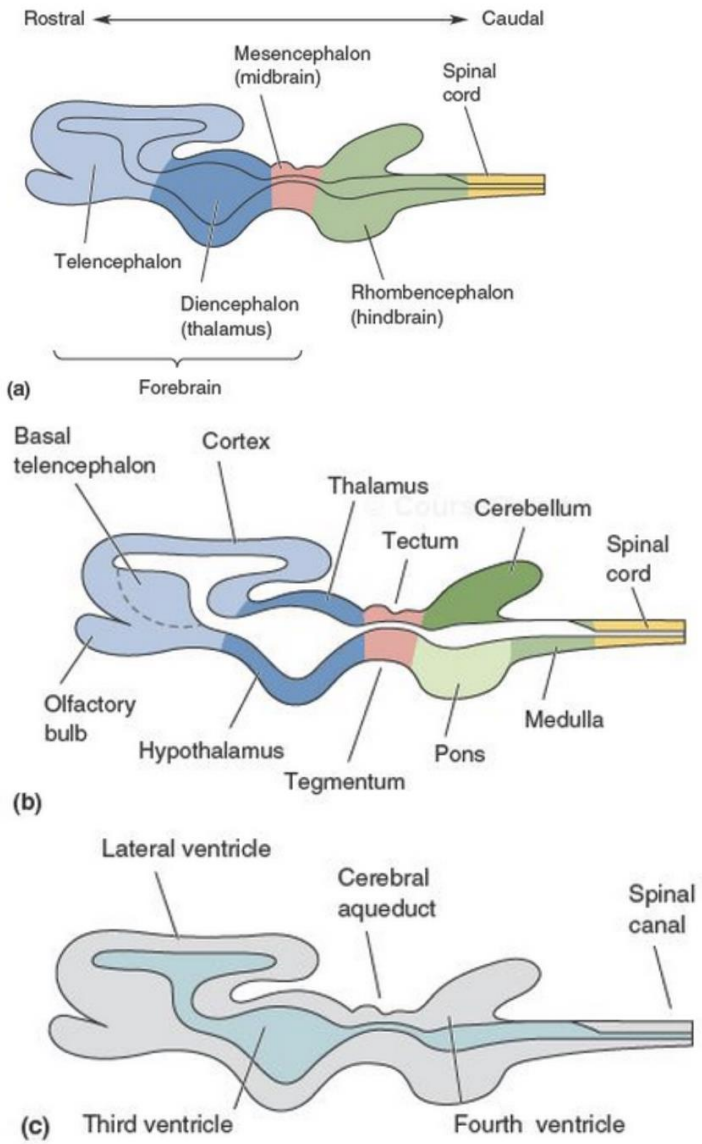
Step 2: Regionalization



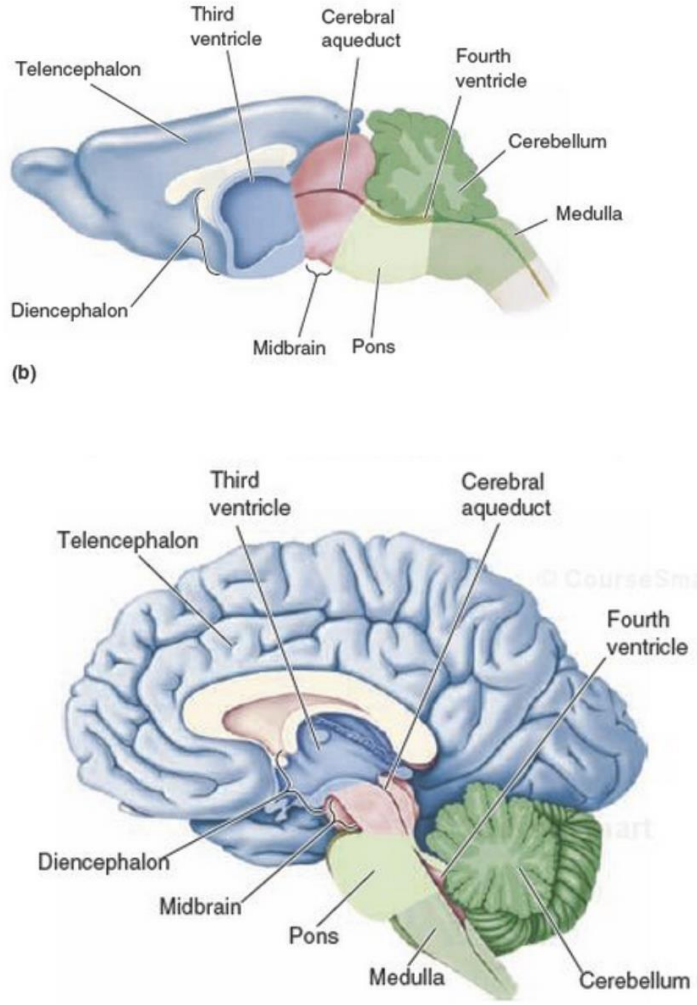
Primary brain vesicles	Secondary vesicles (or other subdivisions)	Structures in mature brain	Ventricular system
Prosencephalon (Forebrain)	Telencephalon	Cerebral cortex, Basal telencephalon	Lateral ventricles
	Diencephalon	Thalamus, Hypothalamus	3rd ventricle
	Optic cup and optic stalk	Retina, Optic nerve	
Mesencephalon (midbrain)	Tectum (above cerebral aquaduct	Superior colliculus, Inferior colliculus	Cerebral aqueduct
	Tegmentum (below cerebral aquaduct)	Substantia nigra, Red nucleus, etc.	
Rhombencephalon (hindbrain)	Metencephalon	Cerebellum, Pons	4th ventricle
	Myelencephalon	Medulla oblongata	

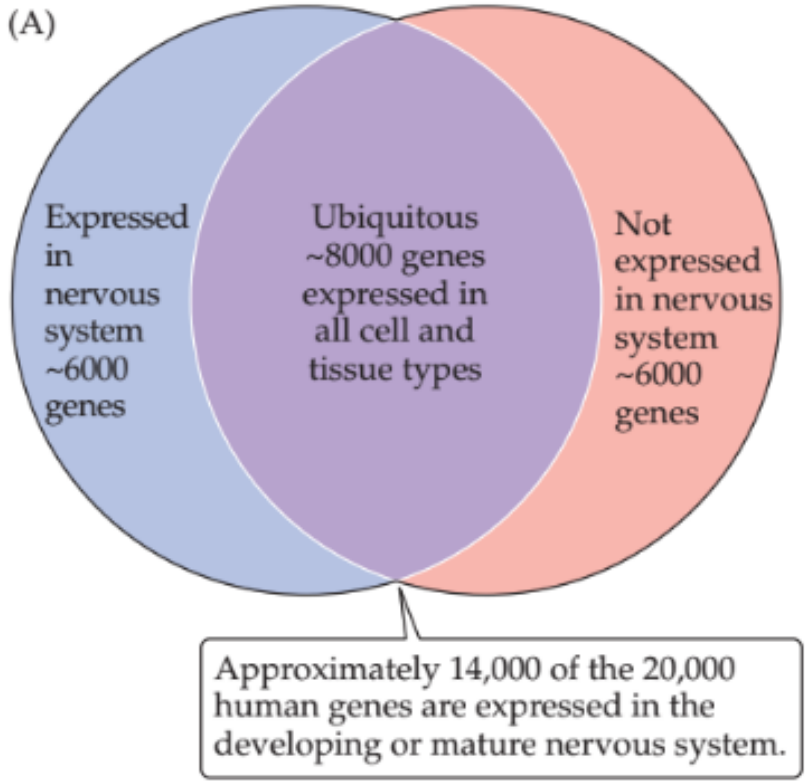
Evolution & Development

Developing brain



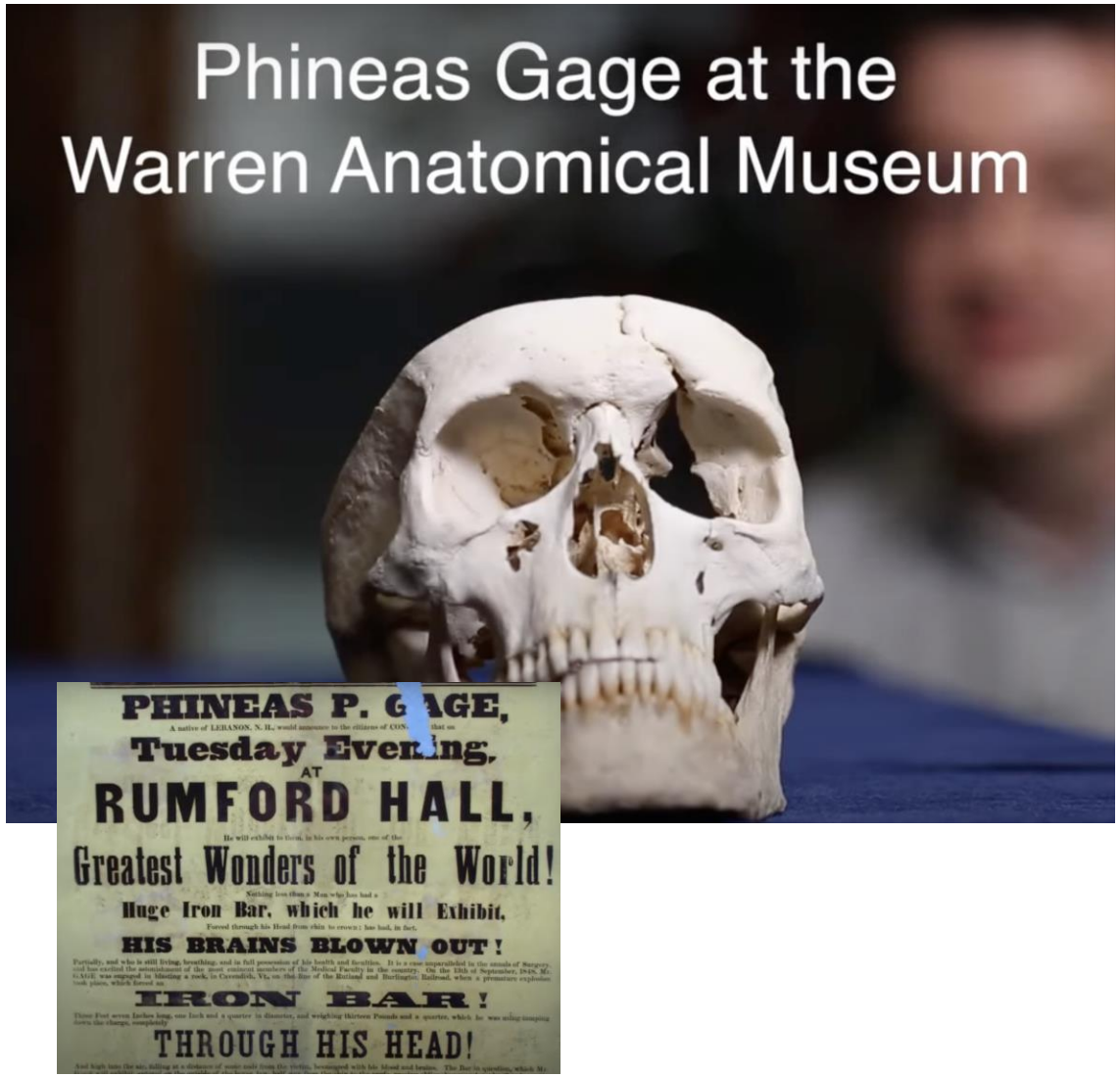
Mature brain





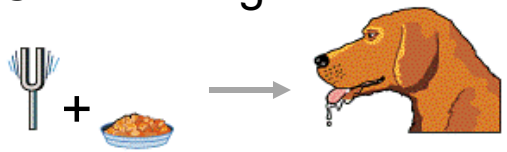
Behavior…

and how changes in behavior can tell us about the brain (learning, damage, illness)

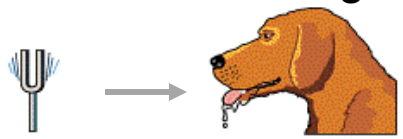


https://www.youtube.com/watch?v=0mf_Nf7fKIQ

1. Conditioning



2. After conditioning



3. 2nd conditioning

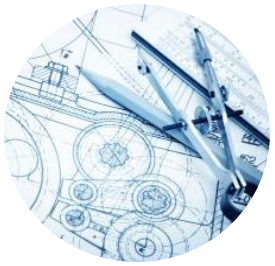
predicts food already.
No surprise…

4. Test

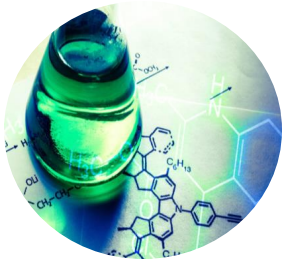
Blocking

Pavlov Conditioning &
Kamin's blocking experiment (1969)

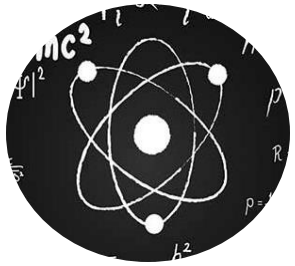
Tools & technology to study neuroscience



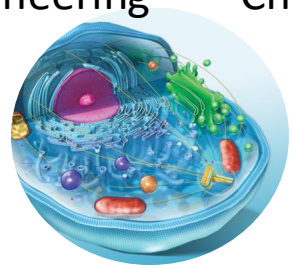
Engineering



Chemistry

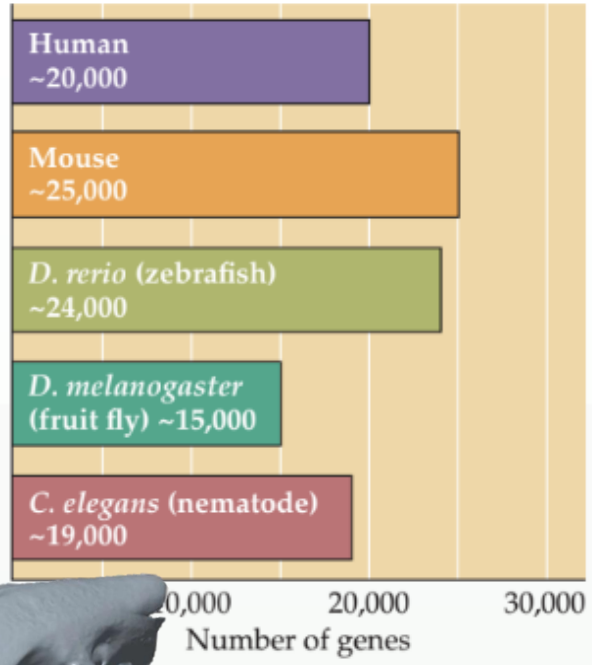


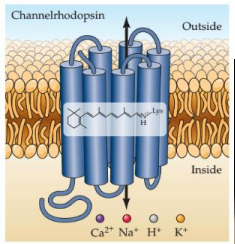
Physics



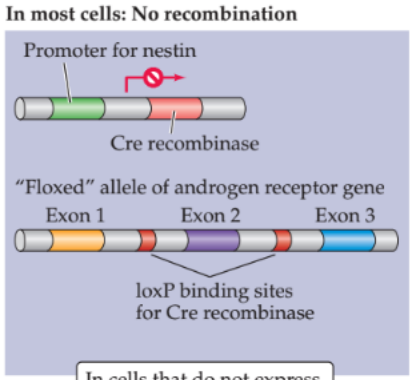
Biology

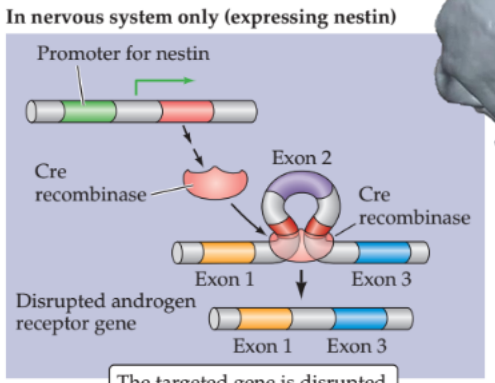
Computer Science

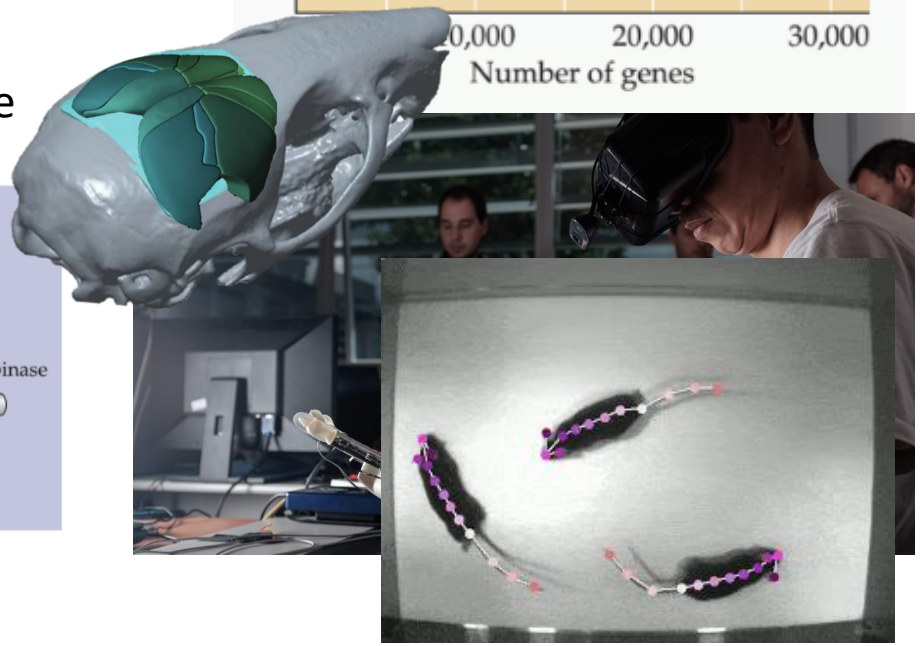


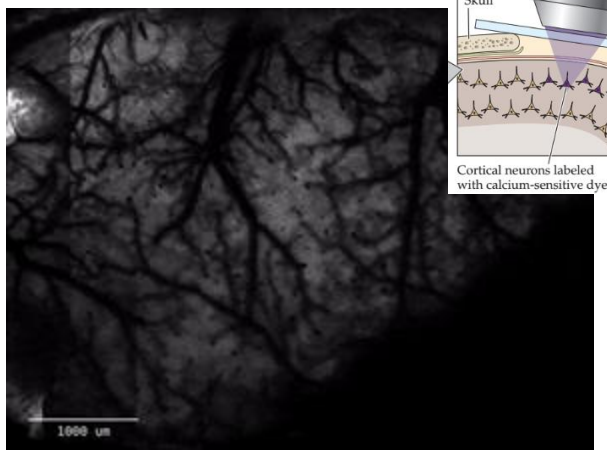


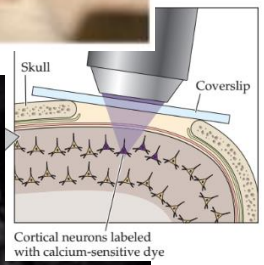
Optogenetics.org





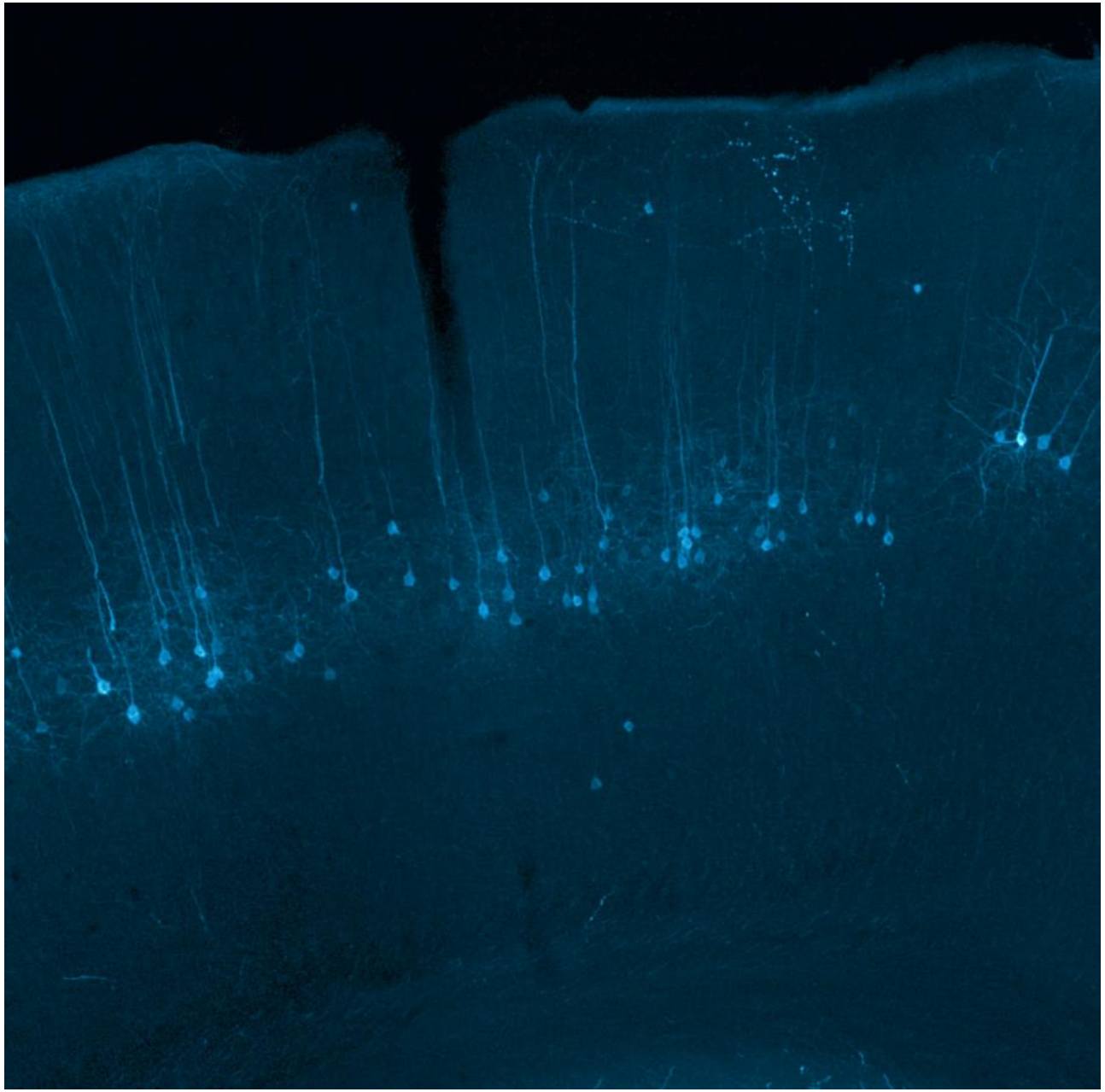






Sofroniew et al 2016 eLife

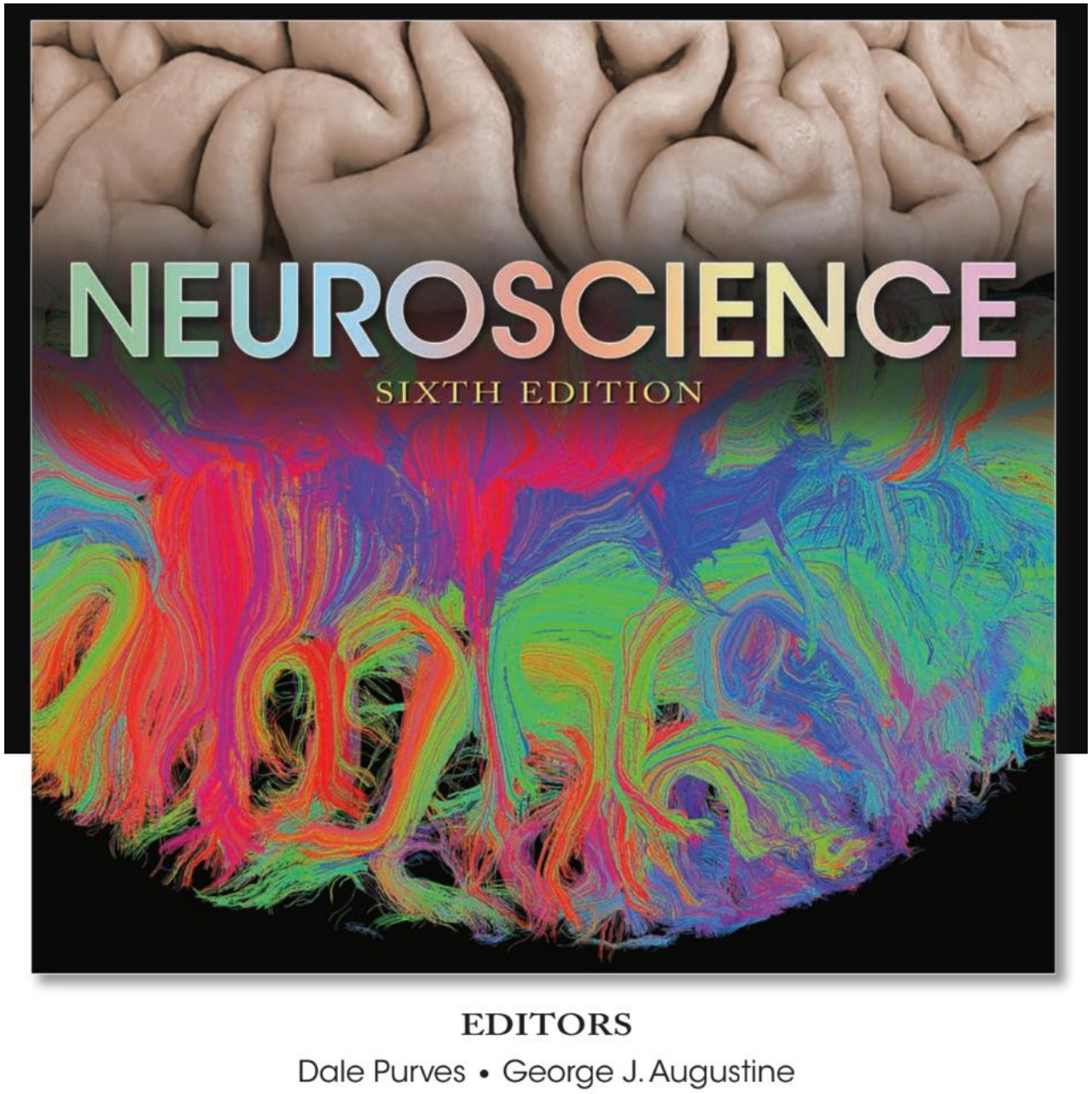
What you should get from this course



The course starts with high-level overview of neuroscience, and takes you through fundamentals of **electrical and chemical signaling** in neurons to **decision-making**. Students learn how neurons in the brain receive and process **sensory** information, and how other neurons **control the behavior** of an animal. Furthermore, **learning**, **memory**, and **brain disorders** will be introduced.

The course is organized around **UNITS**. These units are designed for you to learn about neuroscience from a holistic perspective - how the core units of the brain--the neuron--work and are utilized across systems and behaviors.

How to learn in this course



- 📖😳 Please check Moodle for the **assigned readings** (and link to textbook). We ask you read this before exercises!
- **Ask questions** ⁉️🙋🙋 Both in lecture & exercises, and/or reach out to meet with us!
- ✍️📝 **Attend exercises**: they include a mini-overview & recap of critical concepts, group problems to solve, and a short quiz (which count for 20% of your grade).

How to learn in this course

Course Syllabus

Collapse all

Welcome to BIO-311! 🧠 Intro to Neuroscience | Fall 2025

Your head instructor is Prof. Mackenzie Mathis

You will be supported by several excellent teaching assistants (TAs): Yasmine, Maelys, Louis, Laurine, Celia

NOTE: If you have a scheduling conflict or no biology background consider the course: "BIOENG-310: Neuroscience foundations for engineers" offered in the Spring

What is the goal?

The course starts with high-level overview of neuroscience, and takes you through fundamentals of electrical and chemical signaling in neurons to decision-making. Students learn how neurons in the brain receive and process sensory information, and how other neurons control the behavior of an animal. Furthermore, learning, memory, and brain disorders will be introduced.

The course is organized around **Units**. These units are designed for you to learn about neuroscience from a "bottom-up" perspective - how the core units of the brain--the neuron--work and are utilized across systems and behaviors.

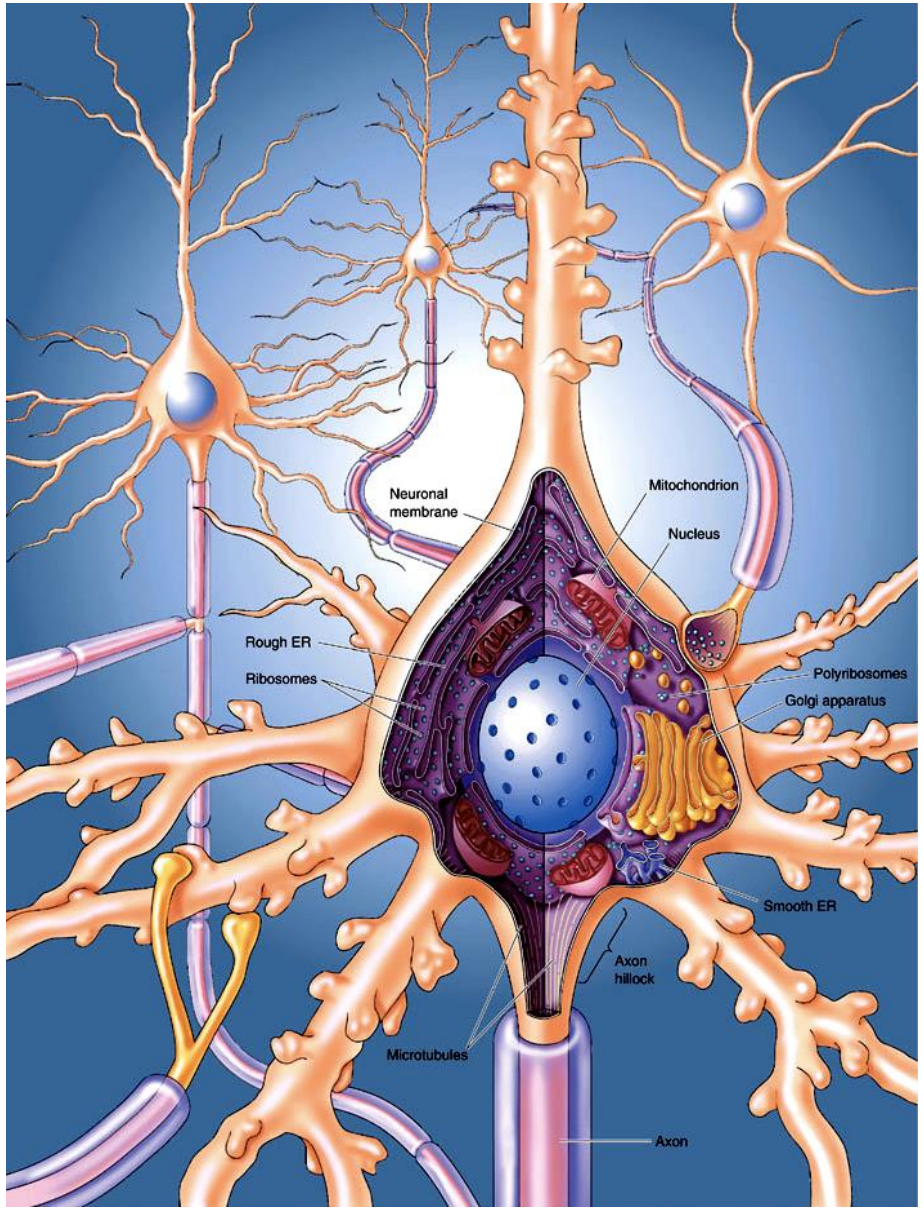
The UNITS:

- Unit 1: Intro to Neuroscience: the neuron & neuronal basics
- Unit 2: Brain Anatomy & the Action Potential
- Unit 3: Synaptic Transmission & Neurotransmitters
- Unit 4: Vision: the retina
- Unit 5: Vision: systems
- Unit 6: Somatosensation
- Unit 7: Neural Control of Movement – spinal cord & cerebellum
- Unit 8: Neural Control of Movement – motor cortex & basal ganglia
- Unit 9: TBA
- Unit 10: Modern Techniques in Neuroscience
- Unit 11: Disorders of the Nervous System
- Unit 12: Decision Making

- You will find: assigned reading, slides, and exercises
- **Please check Moodle before lectures**
- Please have access to Moodle during Monday Exercises!

GRADING:

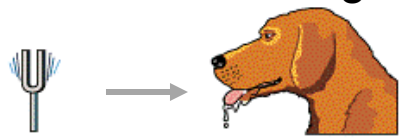
- 80% from Final exam
- 20% from Quizzes held during exercises!



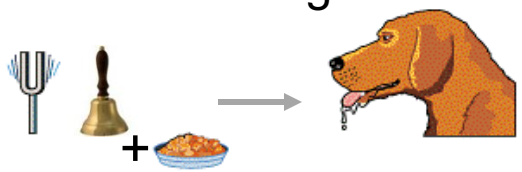
There is a huge gap between the neuron and control of behavior

1. Conditioning

2. After conditioning



3. 2nd conditioning



4. Test

What is the mind?

If I say of myself that it is only from my own case that I know what the word "pain" means - must I not say the same of other people too? And how can I generalize the *one* case so irresponsibly?

Now someone tells me that *he* knows what pain is only from his own case!

Suppose everyone had a box with something in it: we call it a "beetle". No one can look into anyone else's box, and everyone says he knows what a beetle is only by looking at *his* beetle.

Here it would be quite possible for everyone to have something different in his box.

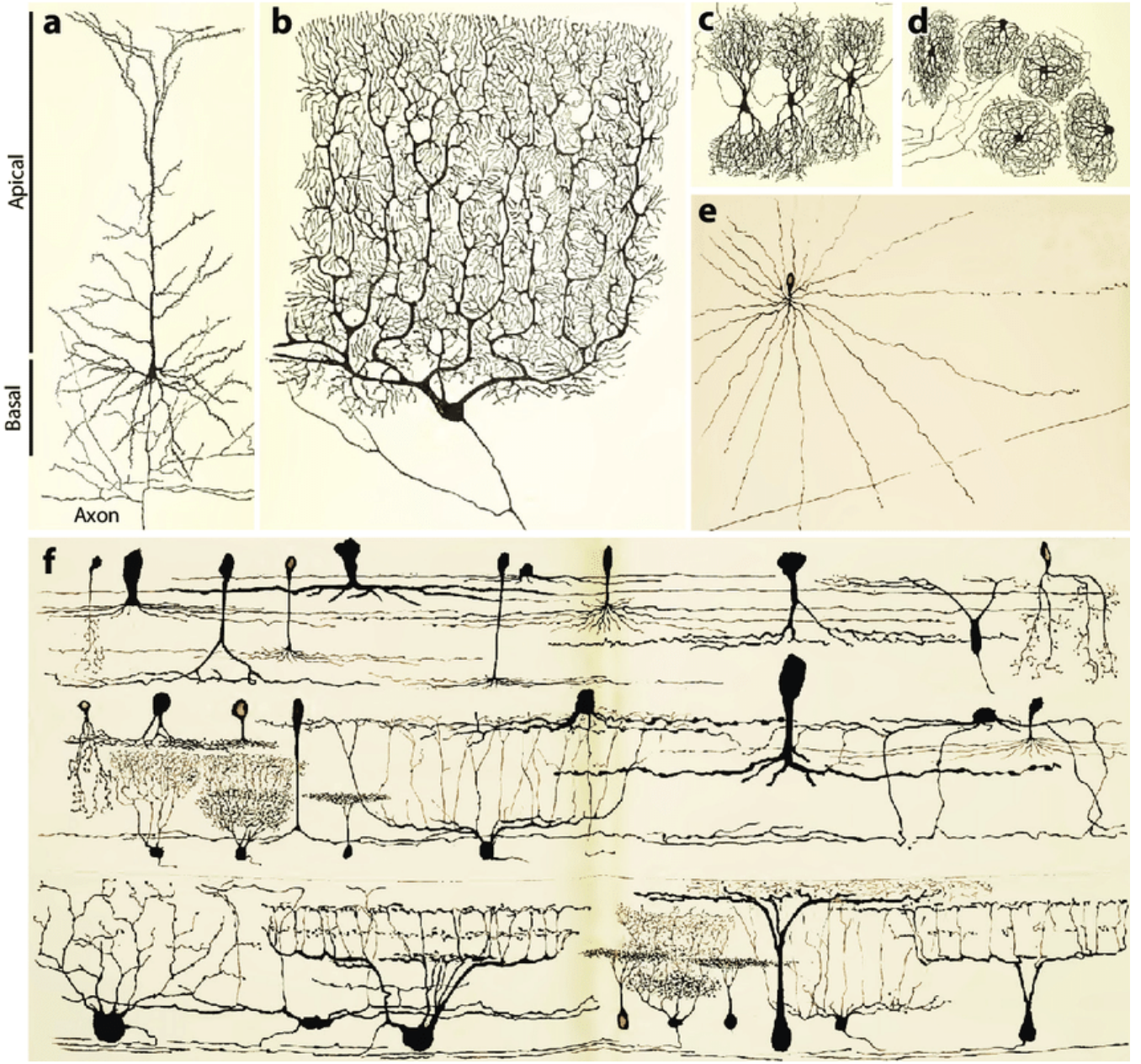
One might even imagine such a thing constantly changing. But suppose the word "beetle" had a use in these people's language? If so it would not be used as the name of a thing. The thing in the box has no place in the language-game at all; not even as a *something:* for the box might even be empty. No, one can 'divide through' by the thing in the box; it cancels out, whatever it is.

That is to say: if we construe the grammar of the expression of sensation on the model of 'object and designation' the object drops out of consideration as irrelevant.

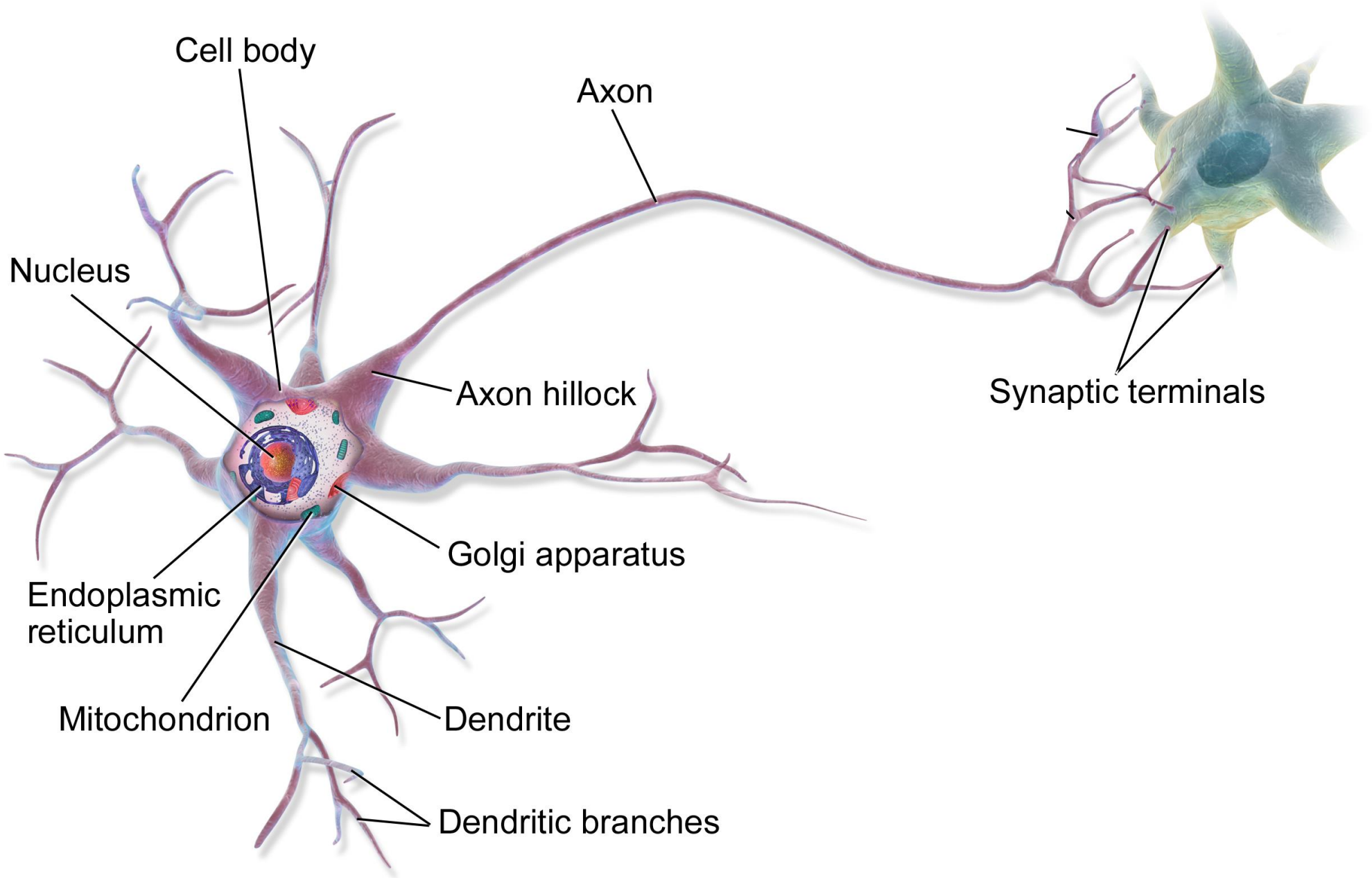
Philosophical Investigations, Sec. 293 **by L. Wittgenstein**

What is a neuron?

Santiago Ramón y Cajal

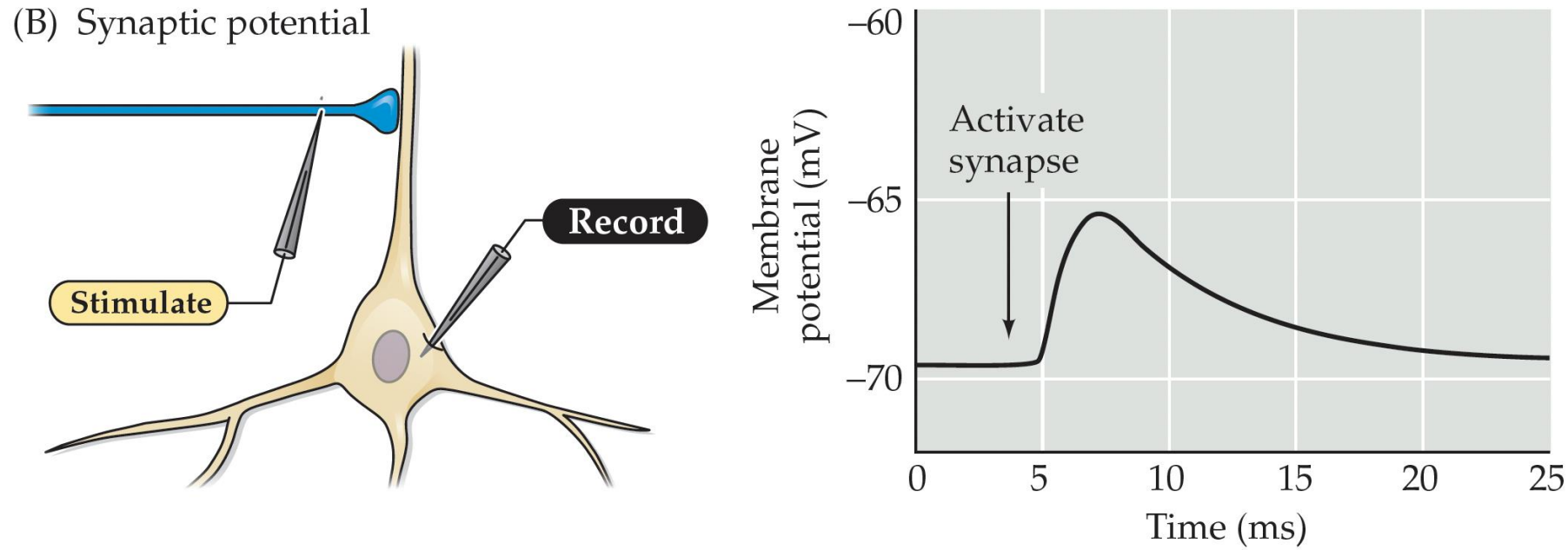


What is a neuron?



Wikipedia

Neurons have a negative "resting" membrane potential

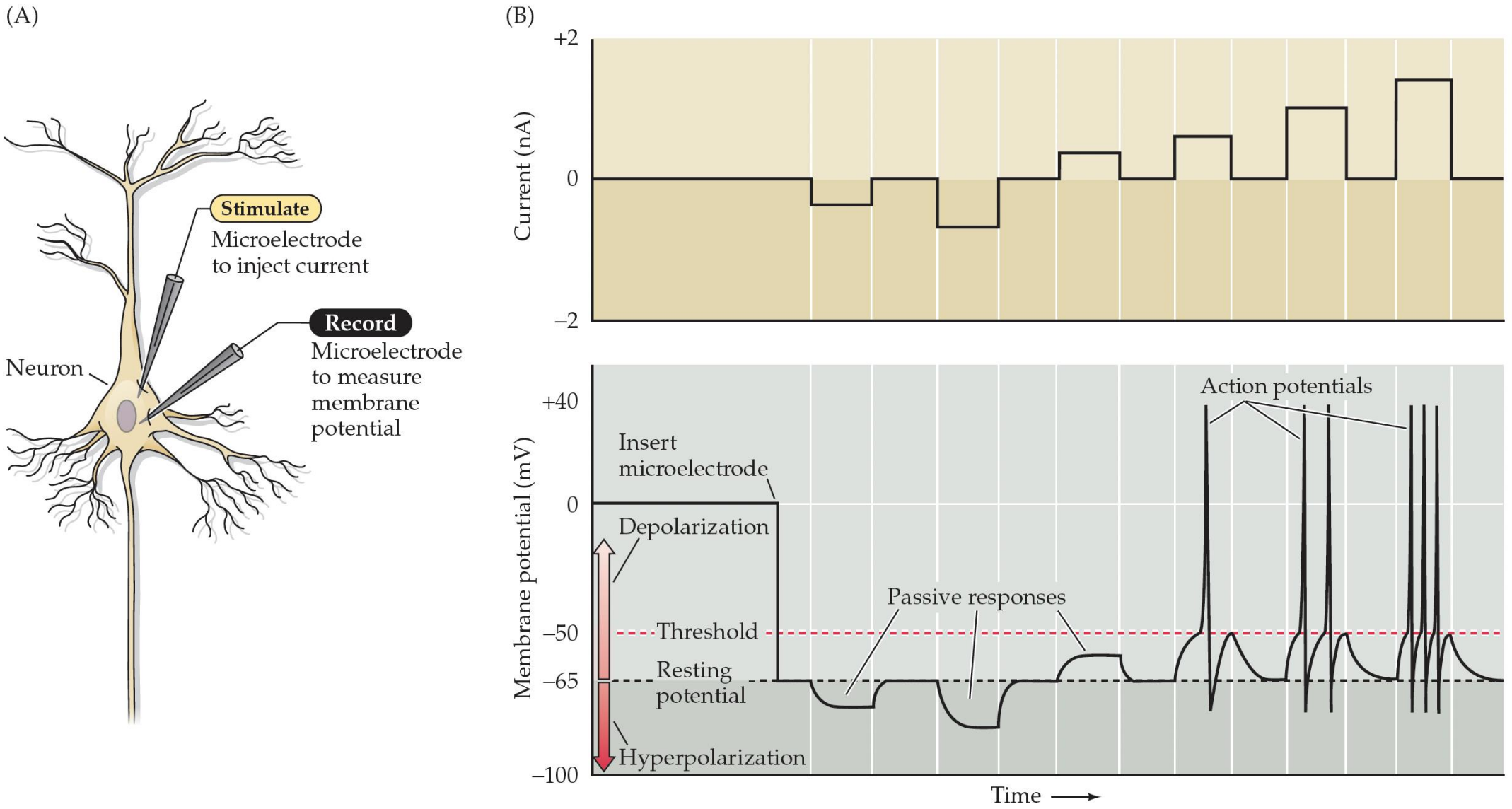


- Here a **microelectrode** is inserted into a neuron
- The neuron has a ***negative*** resting membrane potential, ~ -70 mV before stimulation
- The resting V_m is usually between -60 mV and - 80 mV
- Stimulation of an excitatory synaptic connection causes a small EPSP: a graded change in V_m

V_m = membrane potential whose unit is [V], usually [mV]

Purves, Figure 2.1

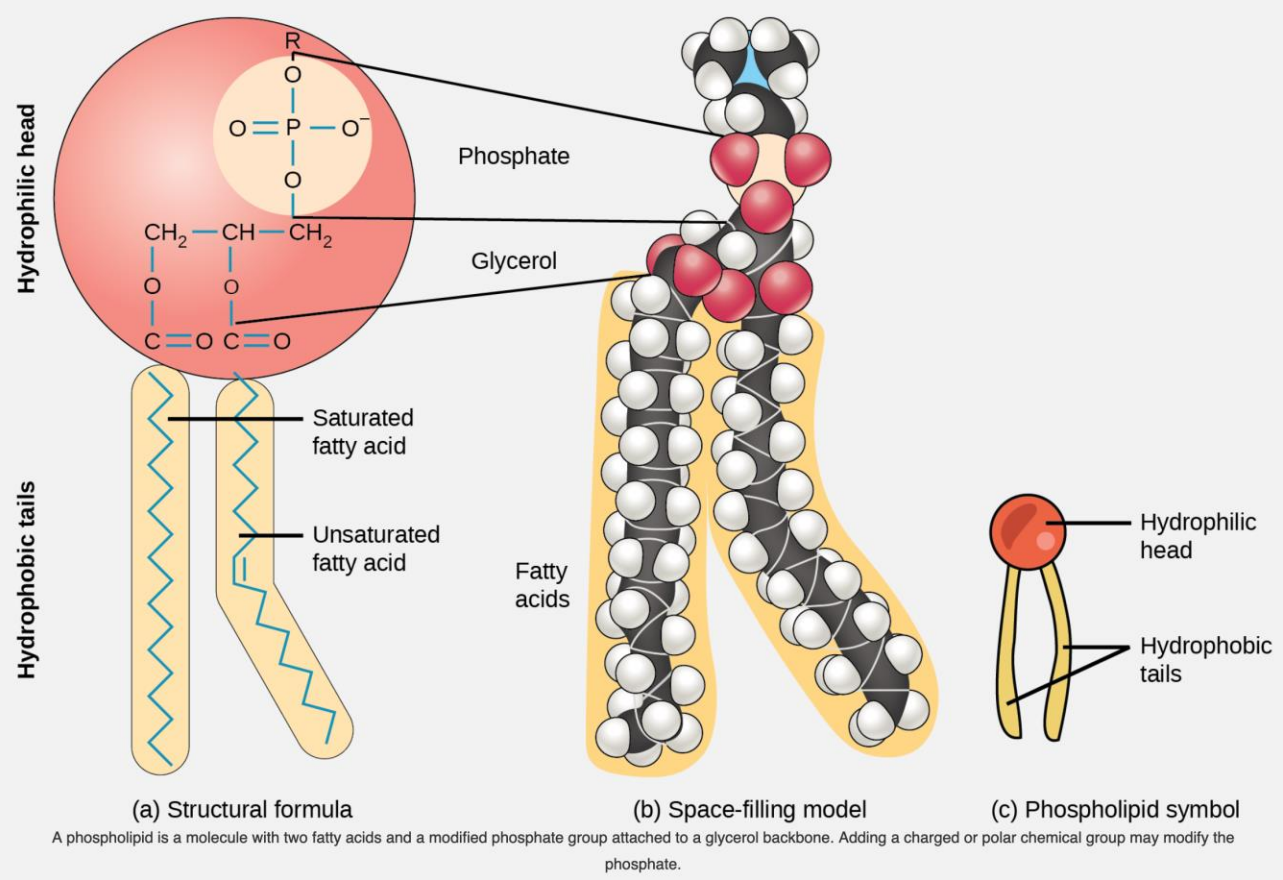
Current stimulation of a neuron drives passive or active responses in V_m

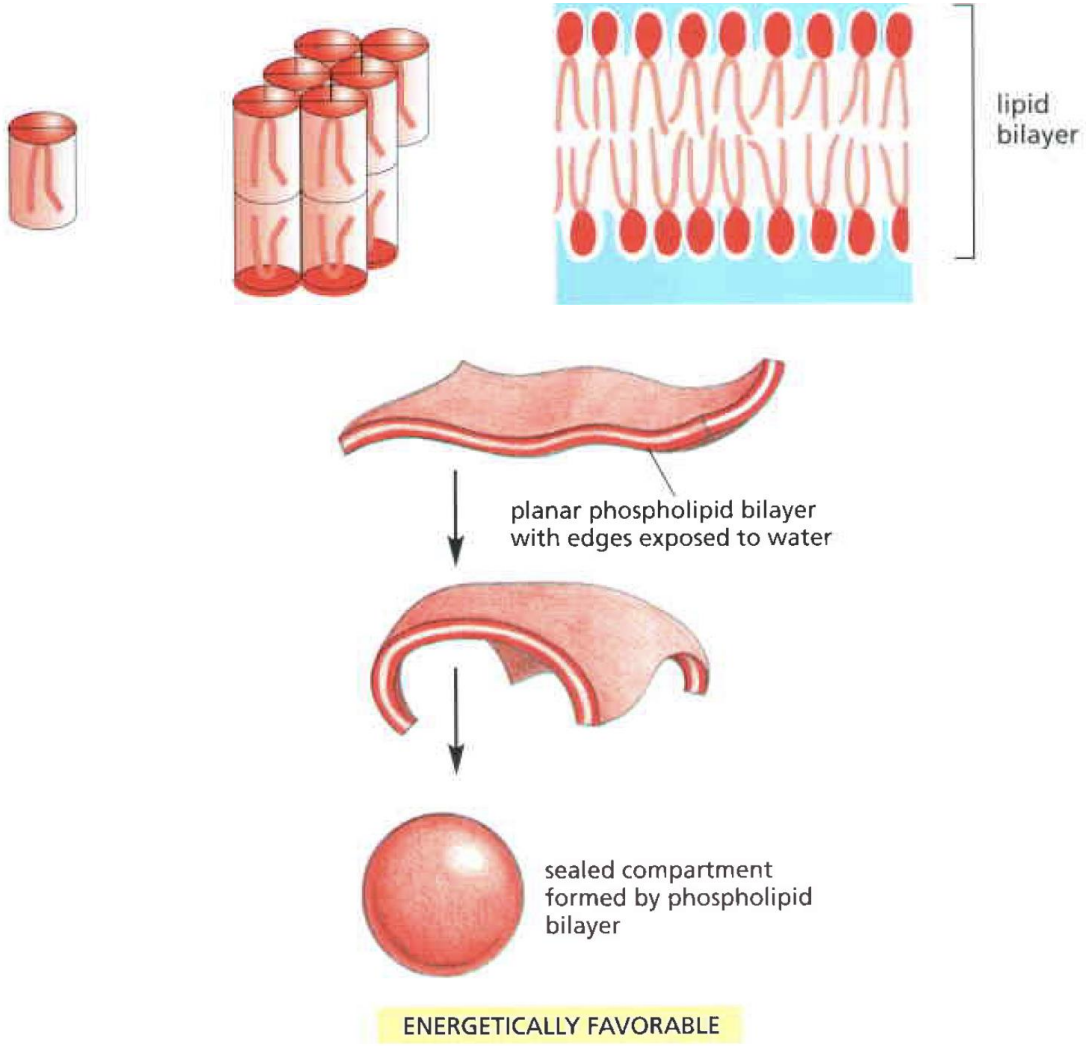


Purves, Figure 2.2

- A drop in V_m is observed when a microelectrode is inserted into the neuron ("resting V_m")
- The neuron is then stimulated by rectangular current injections using a second electrode

Passive electrical properties of the cell: Permeability of phospholipid bilayer





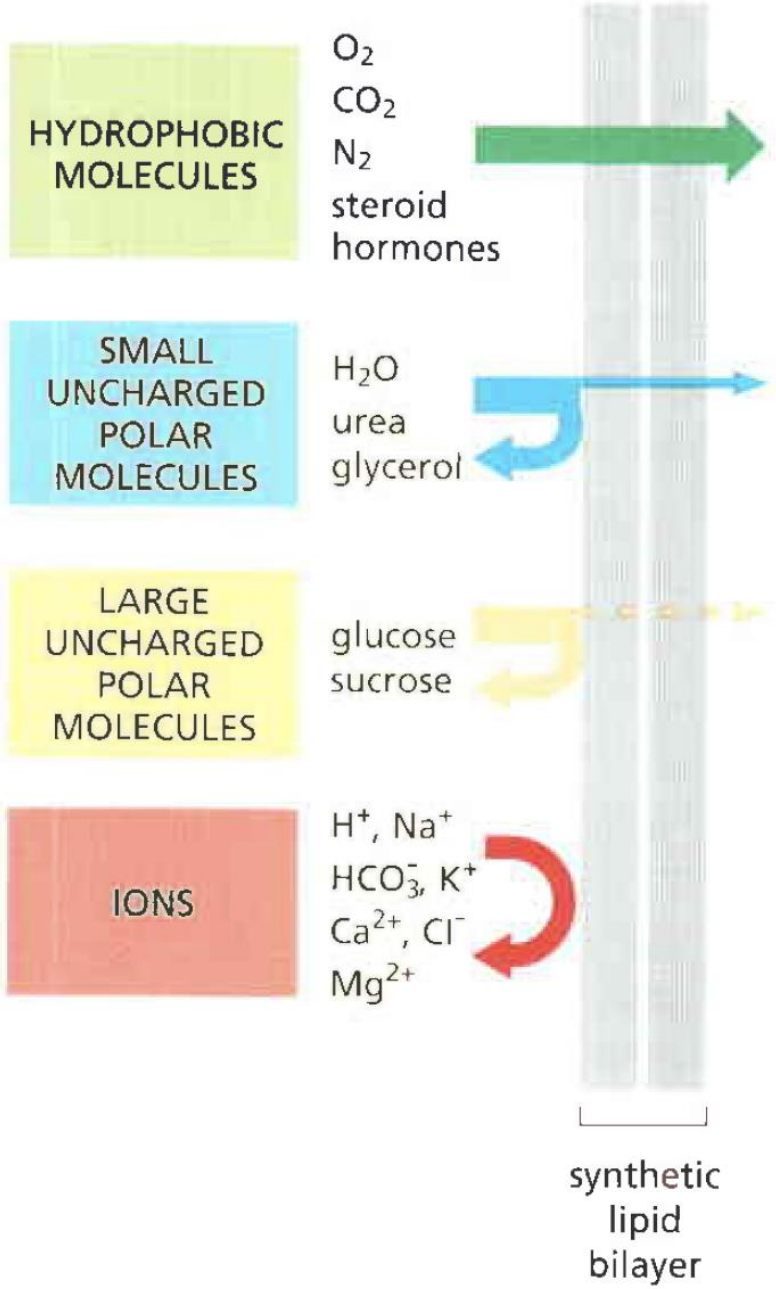
- Cells are surrounded by a phospholipid bilayer membrane
- Phospholipids spontaneously form micelles and lipid bilayers in water

Alberts et al. Molecular Biology of the Cell

Passive electrical properties of the cell: Permeability of phospholipid bilayer

Rapid diffusion occurs for molecules which

- are smaller in size
- associate less strongly with water (important)



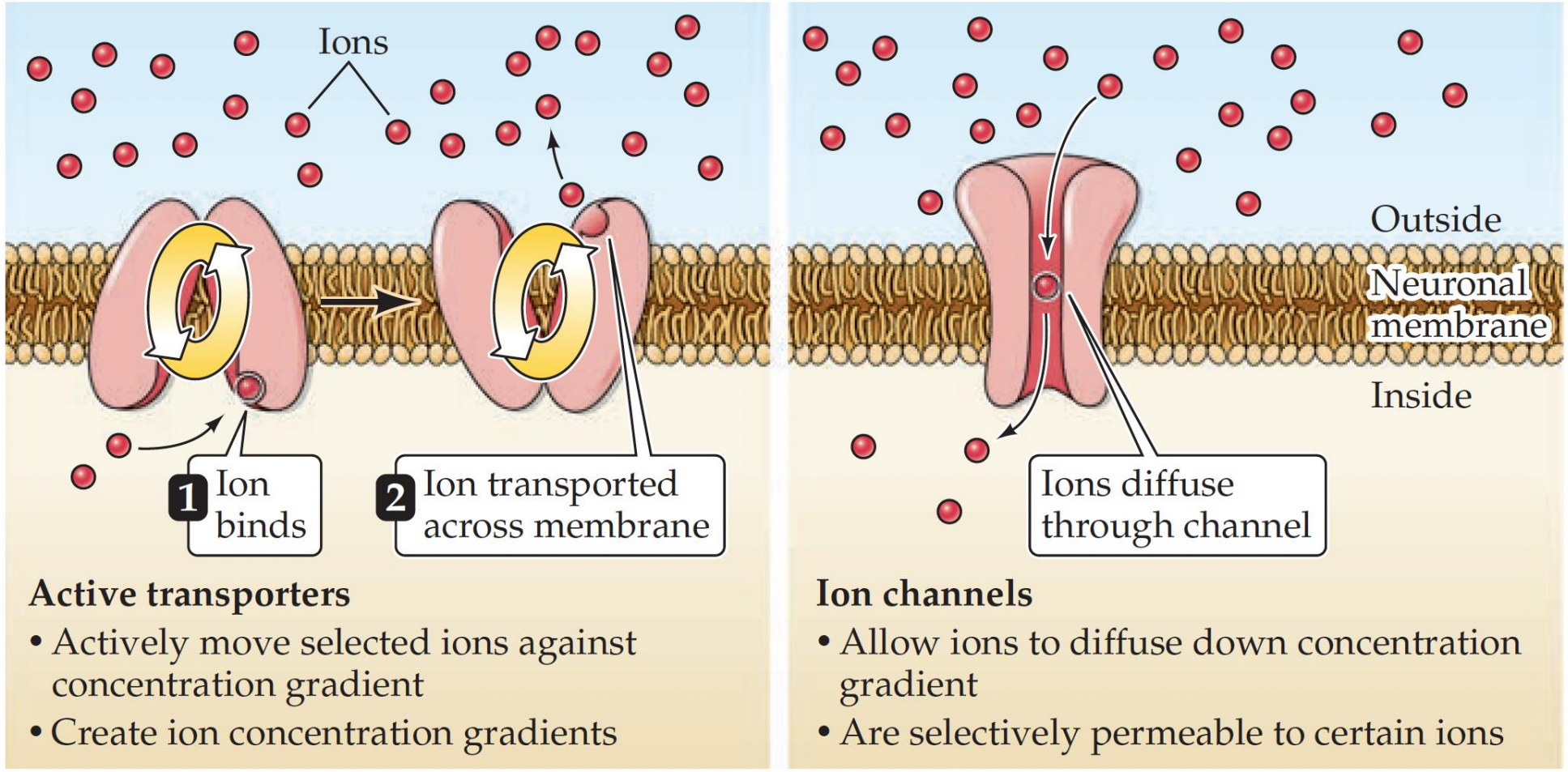
High permeability (gases, ethanol)

Intermediate permeability: H_2O

Impermeable: Ions!

Alberts et al.

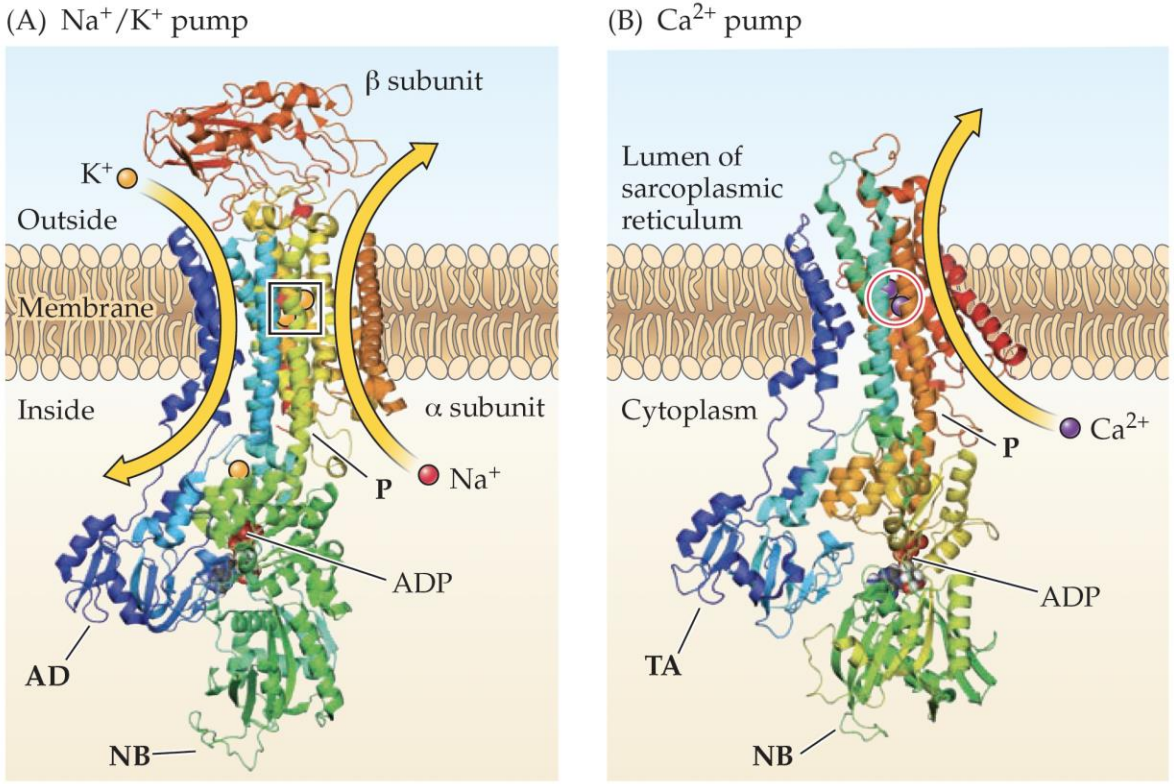
A biological signal (e.g., bound ligand, or V_m) can change *open probability*



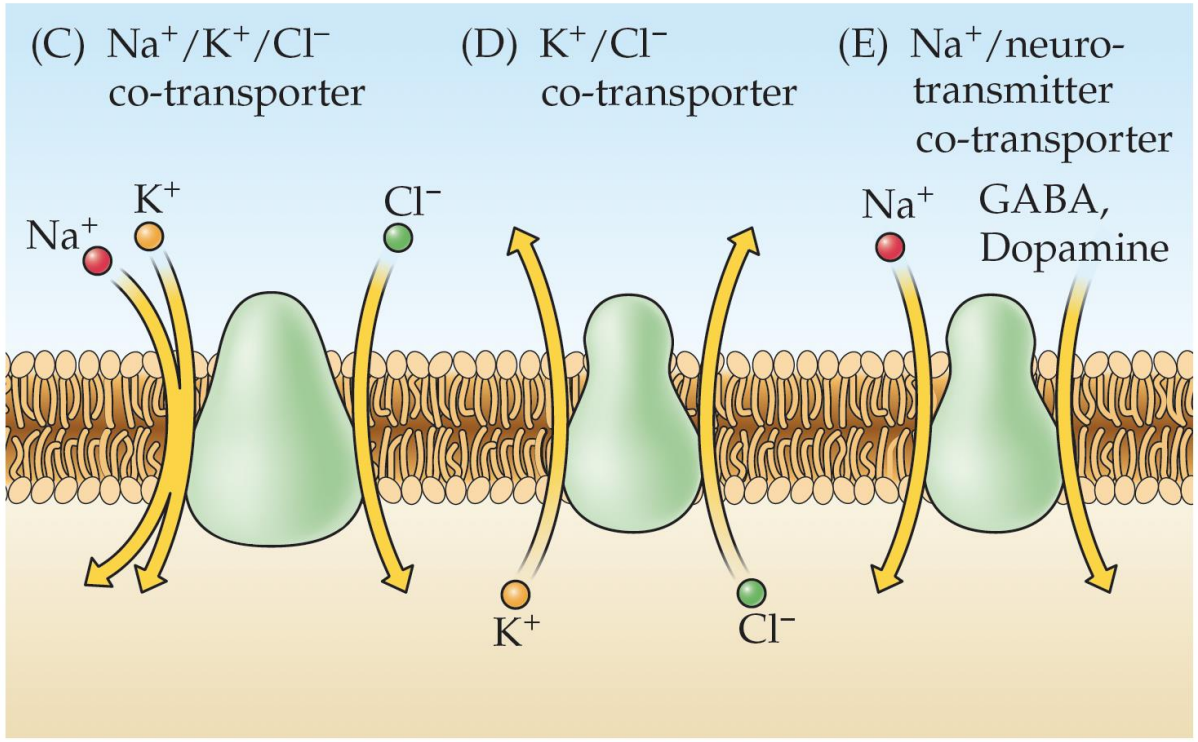
Purves, Figure 2.4

Examples of active transporters

ATPase pumps

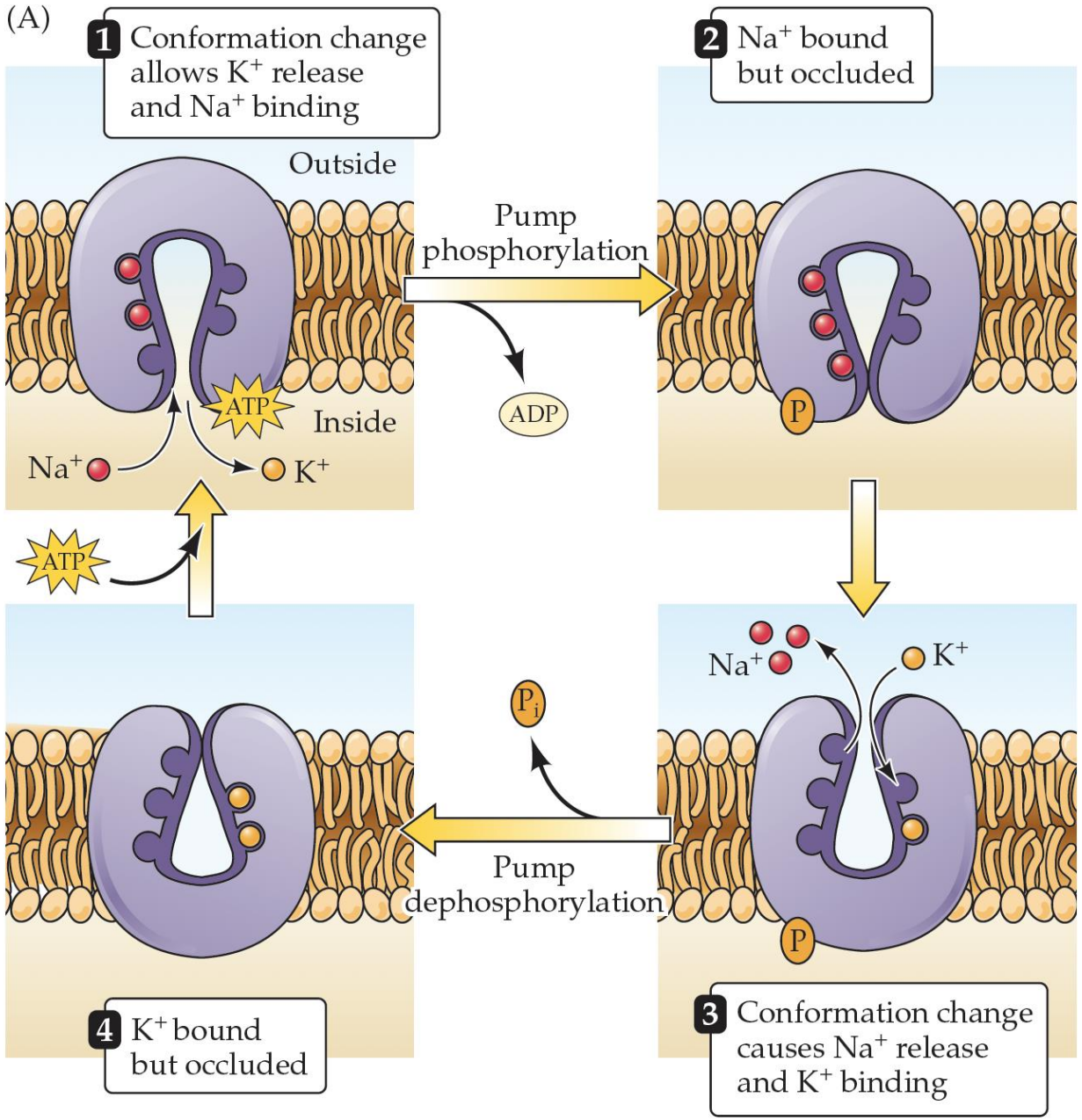


Co-transporters



Purves, Figure 4.10 / 4.13

Na^+/K^+ ATPase creates the principal ion gradients over all cell membranes



Purves, Figure 4.12

1 transport cycle:

- Stoichometry:

2 K^+ in for each **3 Na^+** out,

- Energy consumption:

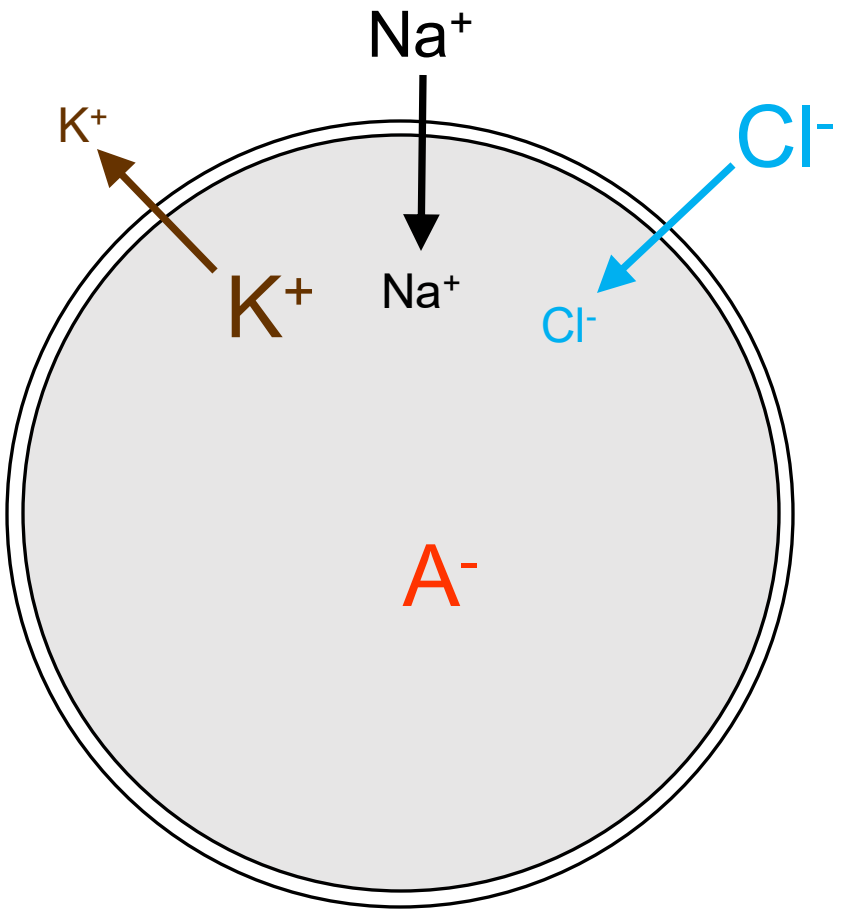
1 ATP -> ADP + Pi

- The Na^+/K^+ ATPase, when working continuously, will create a characteristic distribution of $[Na^+]$ and $[K^+]$ inside and outside of all mammalian cells:

Inside: $[K^+]$, **high** $[Na^+]$ low

Outside: $[K^+]$, low $[Na^+]$ **high**

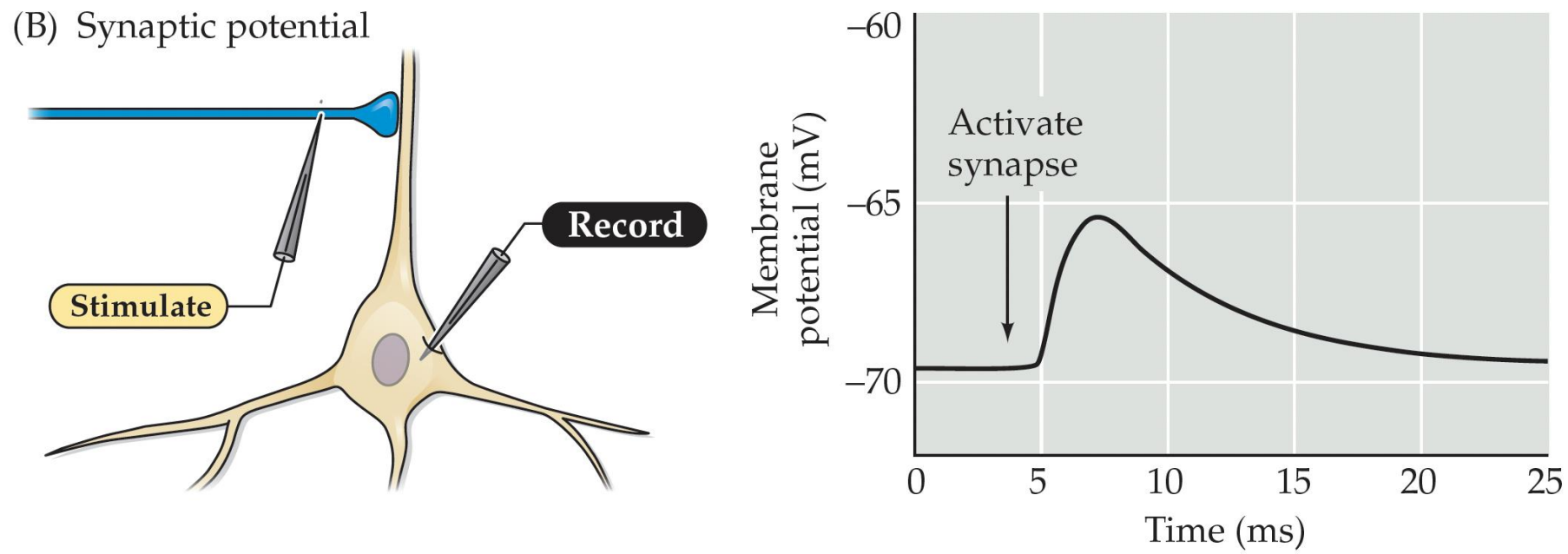
The distribution of major anions and cations *inside* (cytoplasm) and *outside* (extracellular fluid; blood plasma) of a mammalian cell



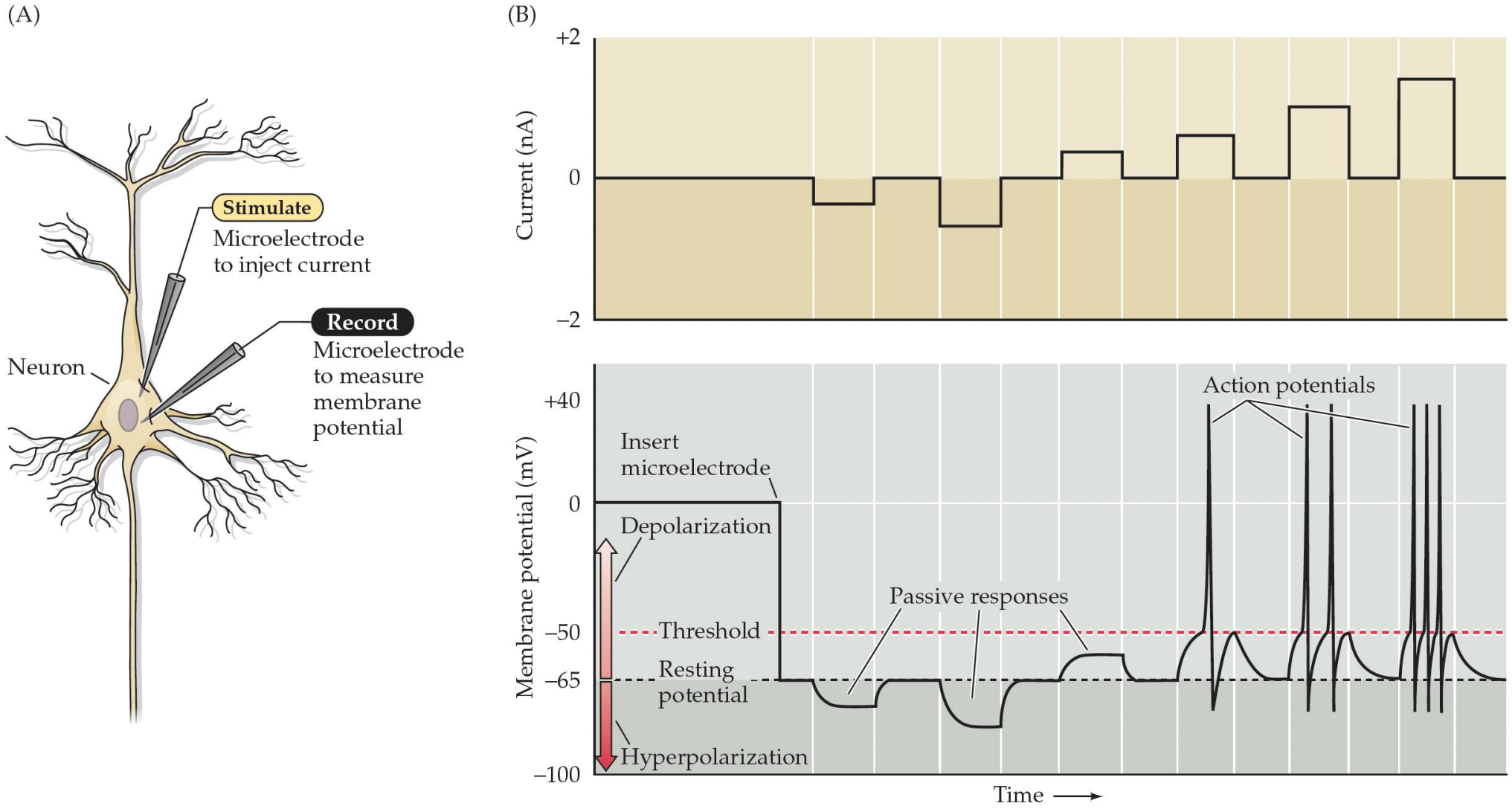
Ion	***Intra*cellular Concentration (mM)**	***Extra*cellular Concentration (mM)**
K^+	140	~3
Na^+	5-15 (~10)	145
Cl^-	4-30	110
Ca^{2+}	10^{-4} M	1-2

Electroneutrality holds true : The sum of all positive charges (contributed by cations) and the sum of all negative charges (anions; Cl^-; negatively charged metabolites like ATP, glutamate and many others called A^-) = **0**

How is the resting membrane potential ($V_{m,\ rest}$) generated?



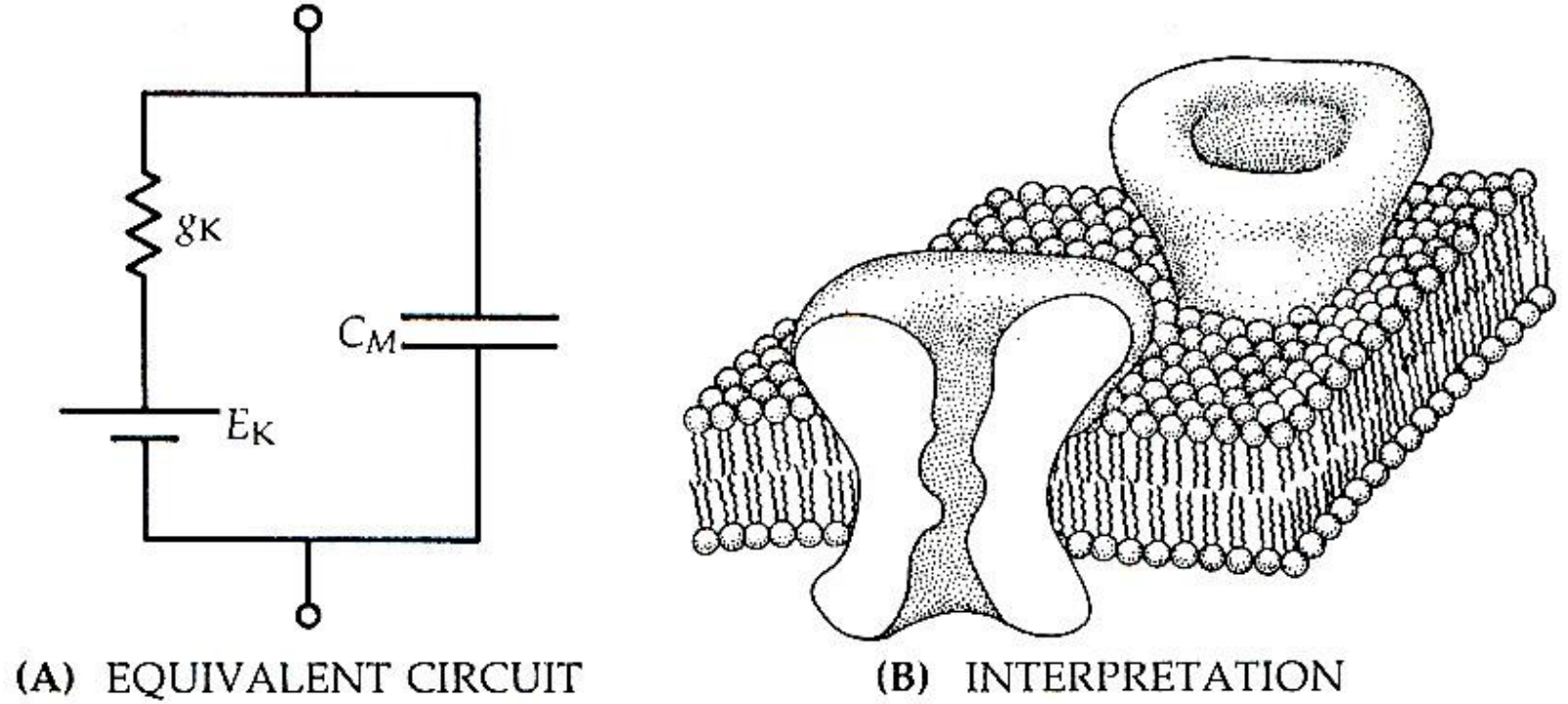
Passive membrane potential (V_m) response to current injection



The temporal filter of the passive V_m response is related to the properties of the **phospholipid bilayer** as an **electrical capacitor**

Purves, Figure 2.2

Membrane permeability to K^+ ions creates the negative resting membrane potential, $V_{m,\ rest}$



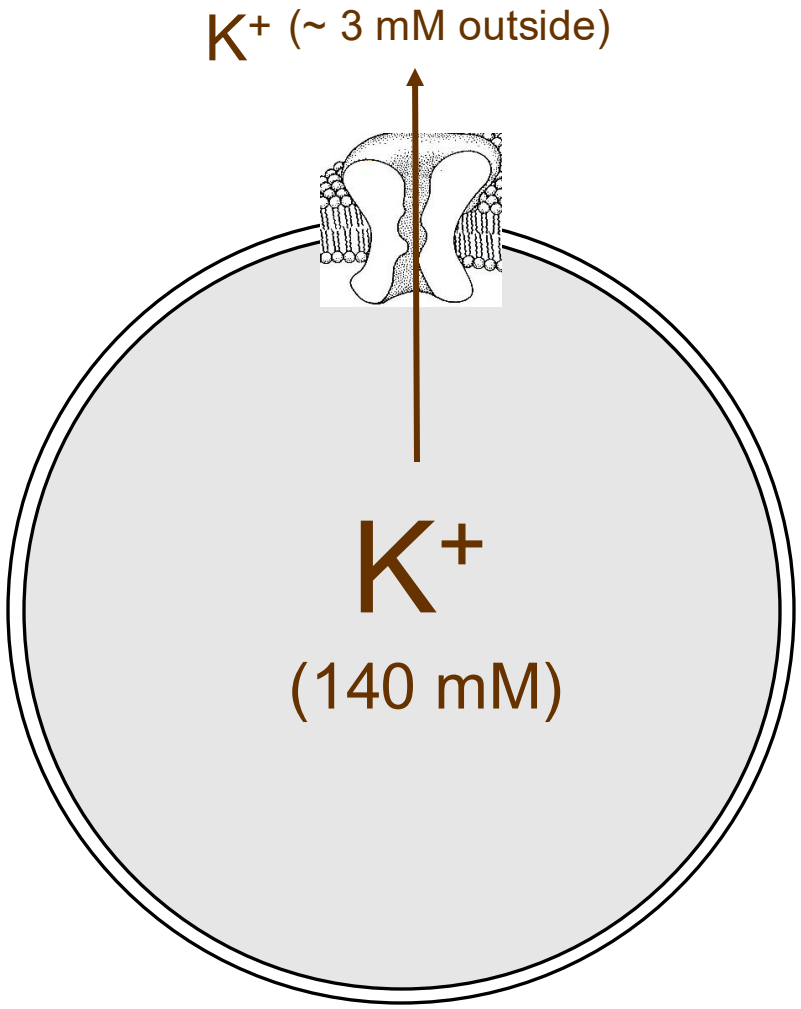
(A) EQUIVALENT CIRCUIT (B) INTERPRETATION

TWO VIEWS OF A K^+-SELECTIVE MEMBRANE

- Concept of *selective permeability* of the membrane

Hille

The negative resting membrane potential ($V_{m,\ rest}$) is determined by "leak" channels **only permeable to K+** and <u>not</u> by the Na^+/K^+ ATPase



<u>"Thought experiment"</u>:

At t = 0, V_m = 0 mV, and a K^+ channel opens…

… K^+ ions start passing through the K^+ channel …

… until an equilibrium potential (V_K or E_K) for K^+ ions is reached:

$$E_K = \frac{RT}{zF} \ln \frac{[K^+]_{outside}}{[K^+]_{inside}}$$

Nernst equation

The Nernst Equation: Equilibrium potential for a given ion species, X+

Nernst equation

$$E_X = \frac{RT}{zF} \ln \frac{[X^+]_{outside}}{[X^+]_{inside}}$$

In the case of K^+ :

$$E_K = \frac{RT}{zF} \ln \frac{[K^+]_{outside}}{[K^+]_{inside}}$$

Physical constants and units

Gas constant: $R = 8.314\ J\ K^{-1}\ mol^{-1}$

T is in Kelvin (deg Celsius + 273.15) e.g., body temp = 310.15 K

Faraday's constant $F = 9.648 * 10^4\ C\ mol^{-1}$

z is valence of ionic species (for $K^+ = +1$)

Remember:

Joule = Coulomb Volt

Avogadro's number $N = 6.022 * 10^{23}\ mol^{-1}$

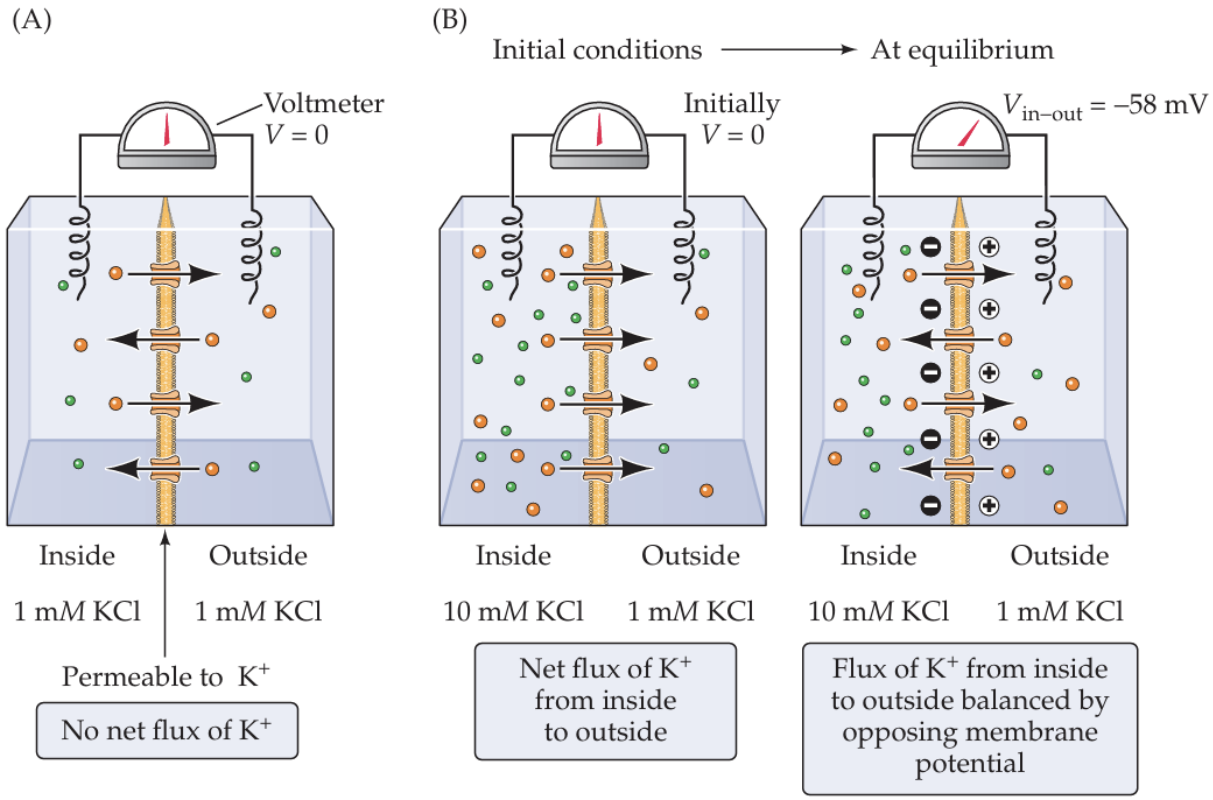
Elementary charge $e = 1.602 * 10^{-19}\ C$

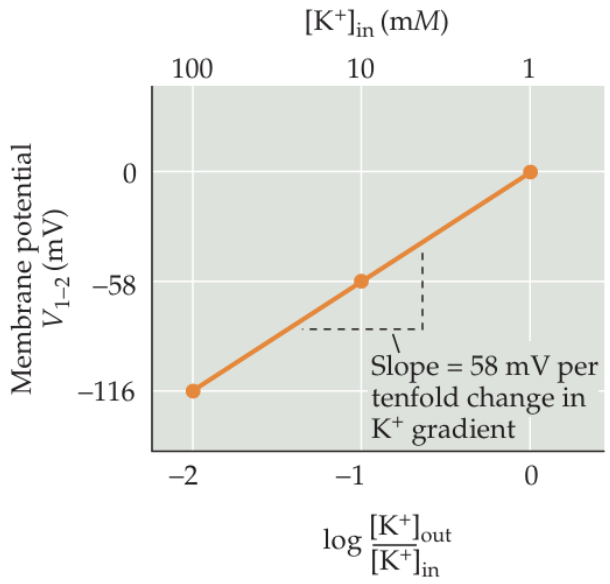
Exercise: Calculate the equilibrium potentials for K^+

(V_K) E_K ~ - 100 mV

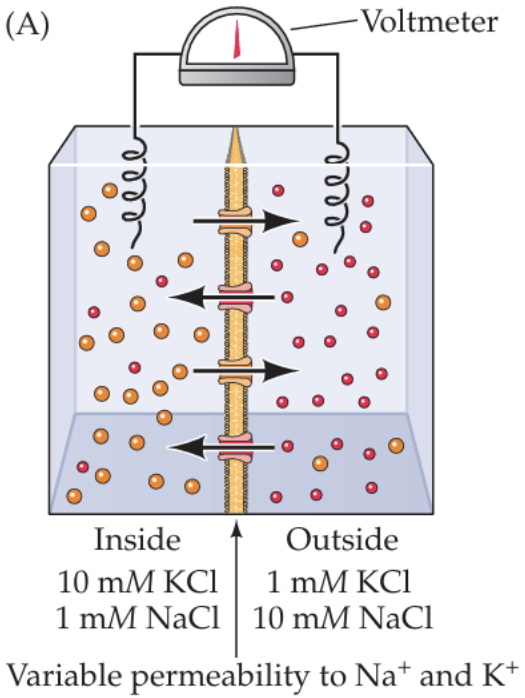
If only permeable to K^+

simple model system:





If permeable to Na^+ and K^+



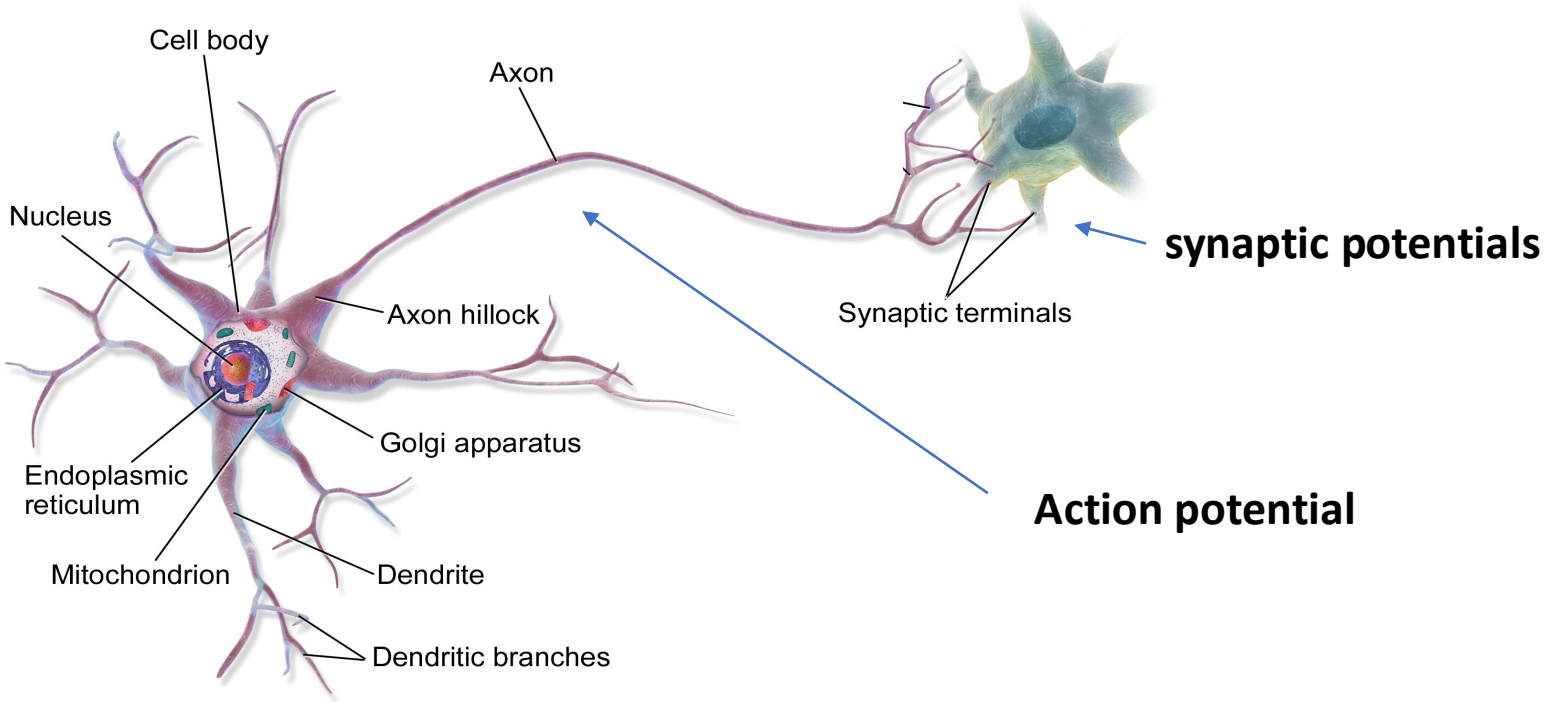
What would happen if 10 mM K+ and 1 mM Na+ were present inside, and 1 mM K+ and 10 mM Na+ were present outside? If the membrane were permeable only to K+, the membrane potential would be –58 mV; if the membrane were permeable only to Na+, the potential would be +58 mV. But what would the potential be if the membrane were permeable to both K+ and Na+?

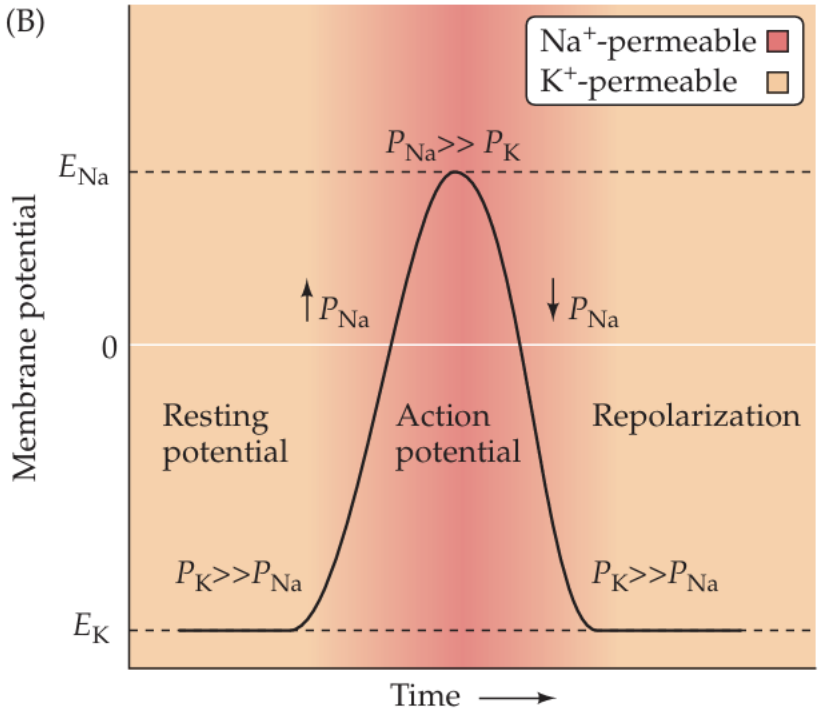
there is no permeability term in the Nernst equation, which considers only the simple case of a single permeant ion species, a more elaborate equation is needed.

This equation must take into account both the concentration gradients of the permeant ions and the relative permeability of the membrane to each permeant species

Such an equation was developed by David Goldman in 1943. For the case most relevant to neurons, in which K^+, Na^+, and Cl^- are the primary permeant ions at room temperature, the **Goldman equation** is written

$$V_m = 58 \log \frac{P_K[K]_{out} + P_{Na}[Na]_{out} + P_{Cl}[Cl]_{in}}{P_K[K]_{in} + P_{Na}[Na]_{in} + P_{Cl}[Cl]_{out}}$$





Summary: Important concepts and keywords

- Anatomy of a neuron
- Synaptic potential, action potential
- Phospholipid bilayer permeability
- Concentrations of major ions (anions & cations)
  inside & outside of the cell
- Na^+/K^+ ATPase
- Equilibrium potential for an ion X; Nernst equation
- Goldman Equation
- Resting membrane potential:
  - how is it measured?
  - how is it generated? (K^+ channel)
- Terminology:
  - depolarization, hyperpolarization
  - threshold