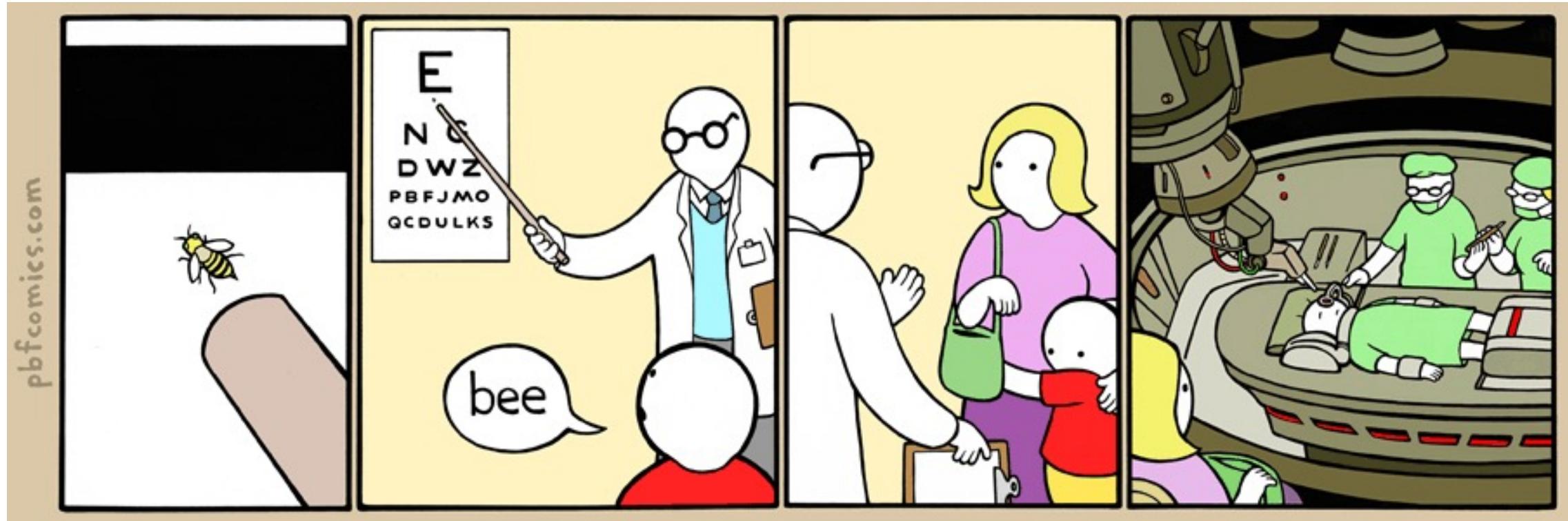


PSYC304:

Neural communication 1

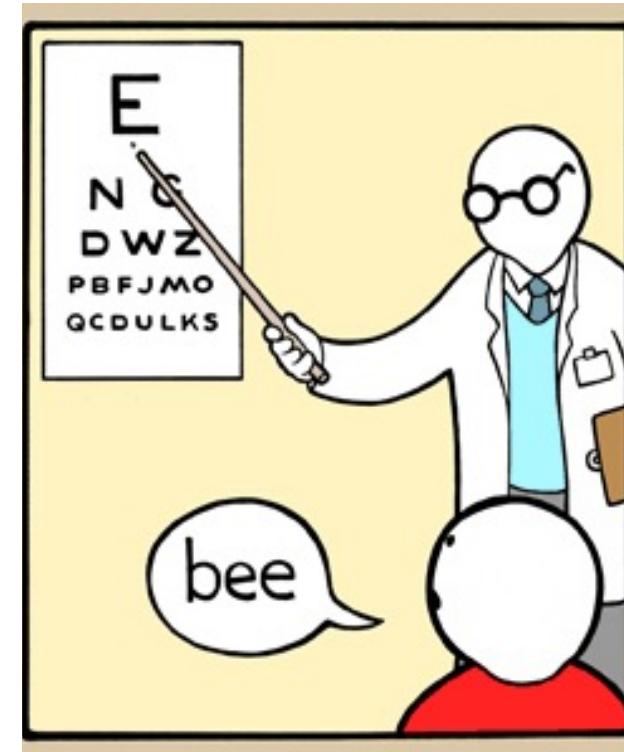
(within cells)

Jay Hosking, PhD



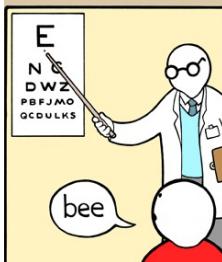
Overview

- A. Introduction to neural communication
- B. The resting membrane potential
- C. Postsynaptic potentials
- D. The action potential
- E. Conduction of the action potential



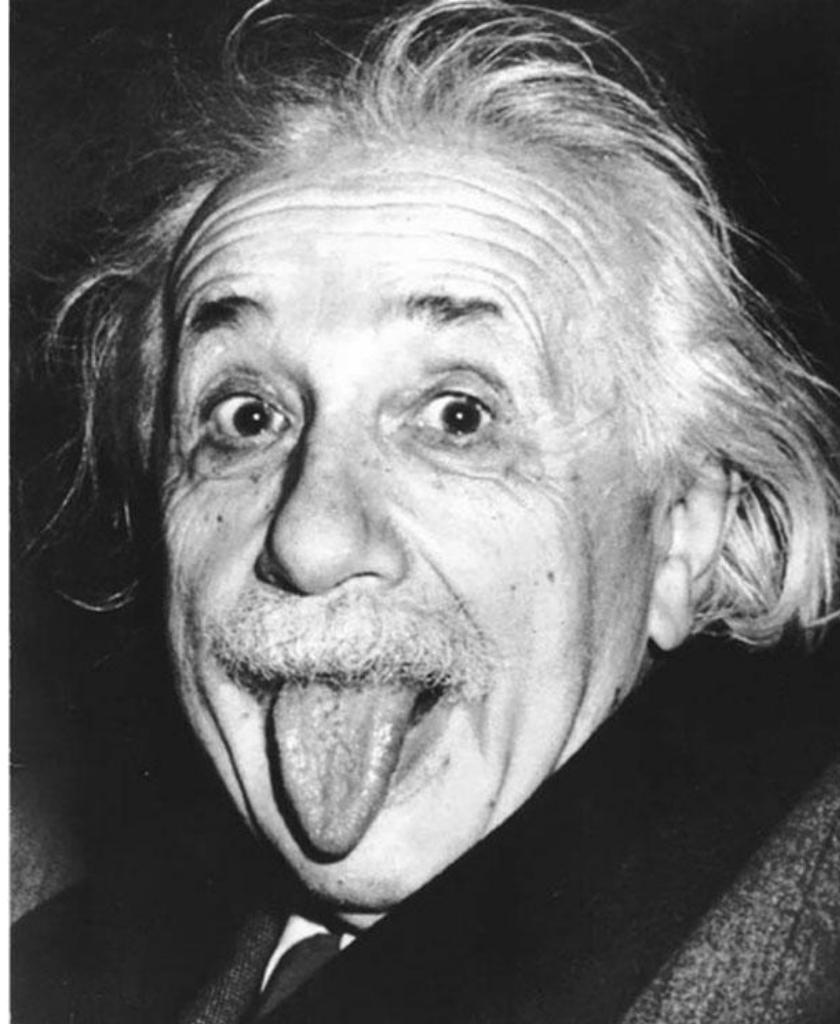
Learning objectives

1. What does it mean to say that neuronal communication is an electrochemical process?
2. Describe the chemical and electrical gradients for a neuron at rest.
3. What two proteins are responsible for the resting membrane potential? How so?
4. Describe how the resting membrane potential is established.
5. What two proteins are responsible for the action potential? How so?
6. Describe how an action potential occurs, including its threshold, stages, and refractory periods.
7. Why does conduction only happen in one direction along the axon? Can you imagine a possibility in which conduction could travel in the opposite direction? (This likely happens in nature.)
8. Describe the differences between conduction in unmyelinated versus myelinated axons.
9. Identify and define four key differences between postsynaptic potentials and action potentials. Additionally, describe where each occurs, and why.



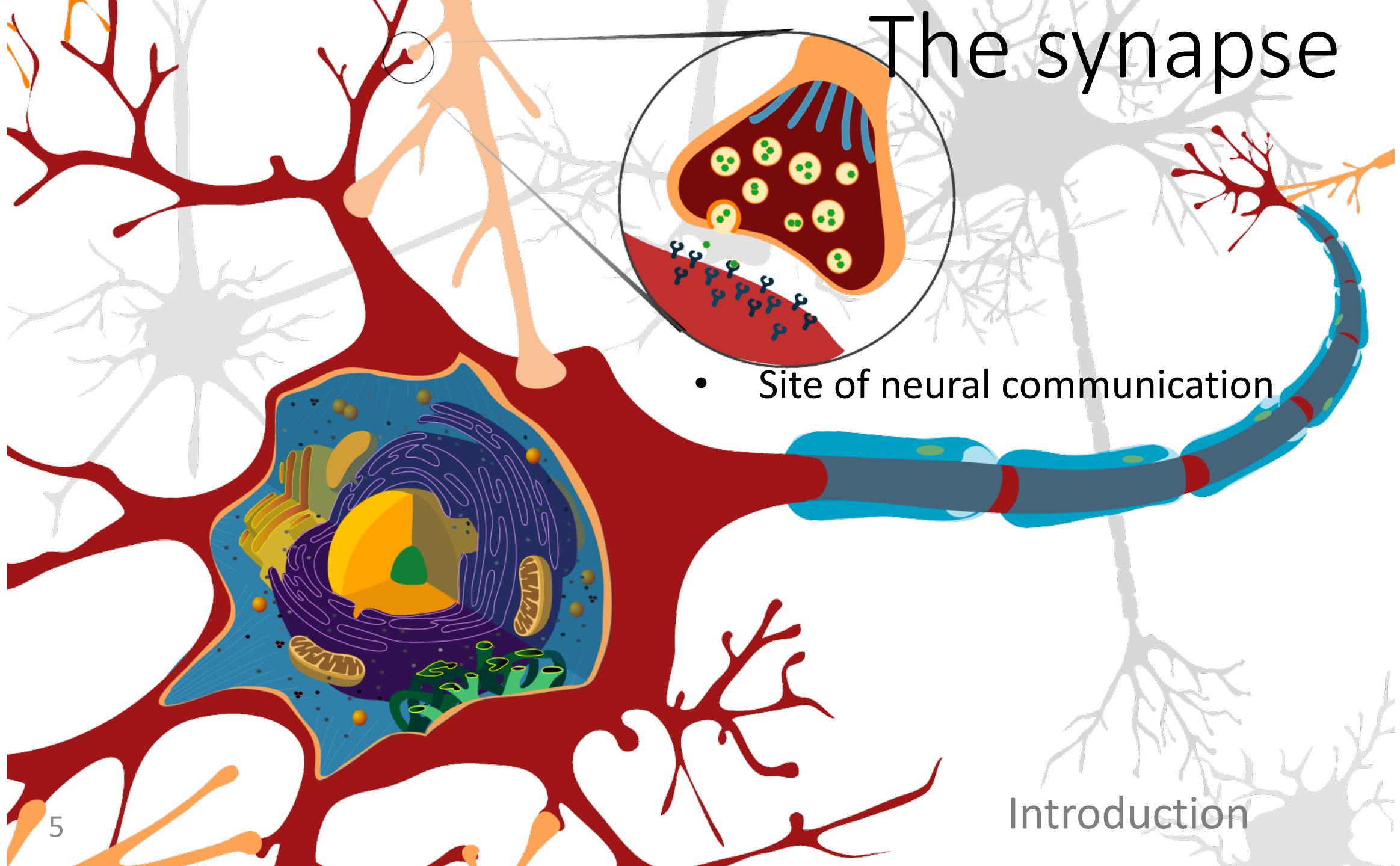
Listen to Einstein(-ish)

“Make things as simple as possible, but no simpler.”

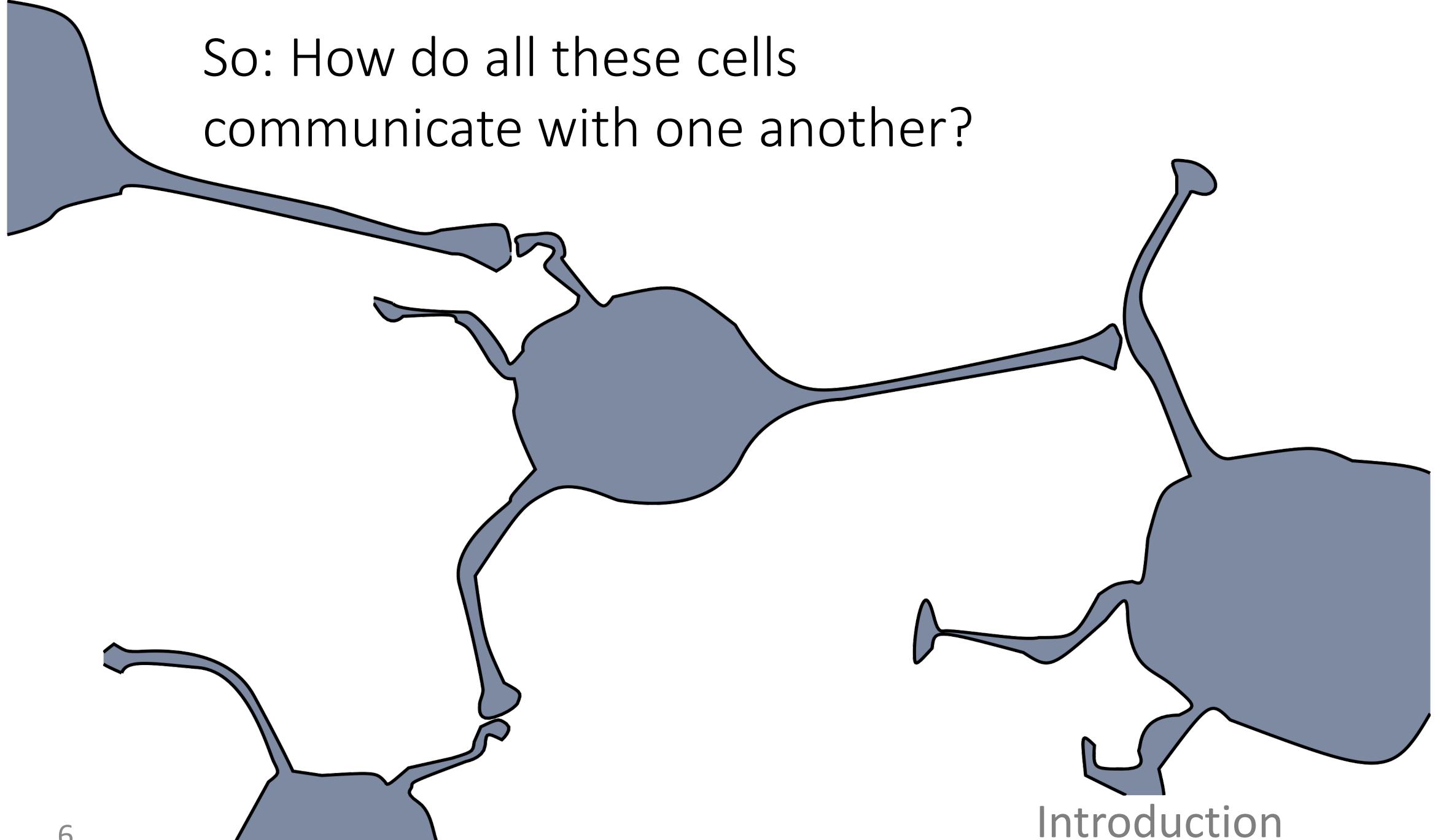


The synapse

- Site of neural communication

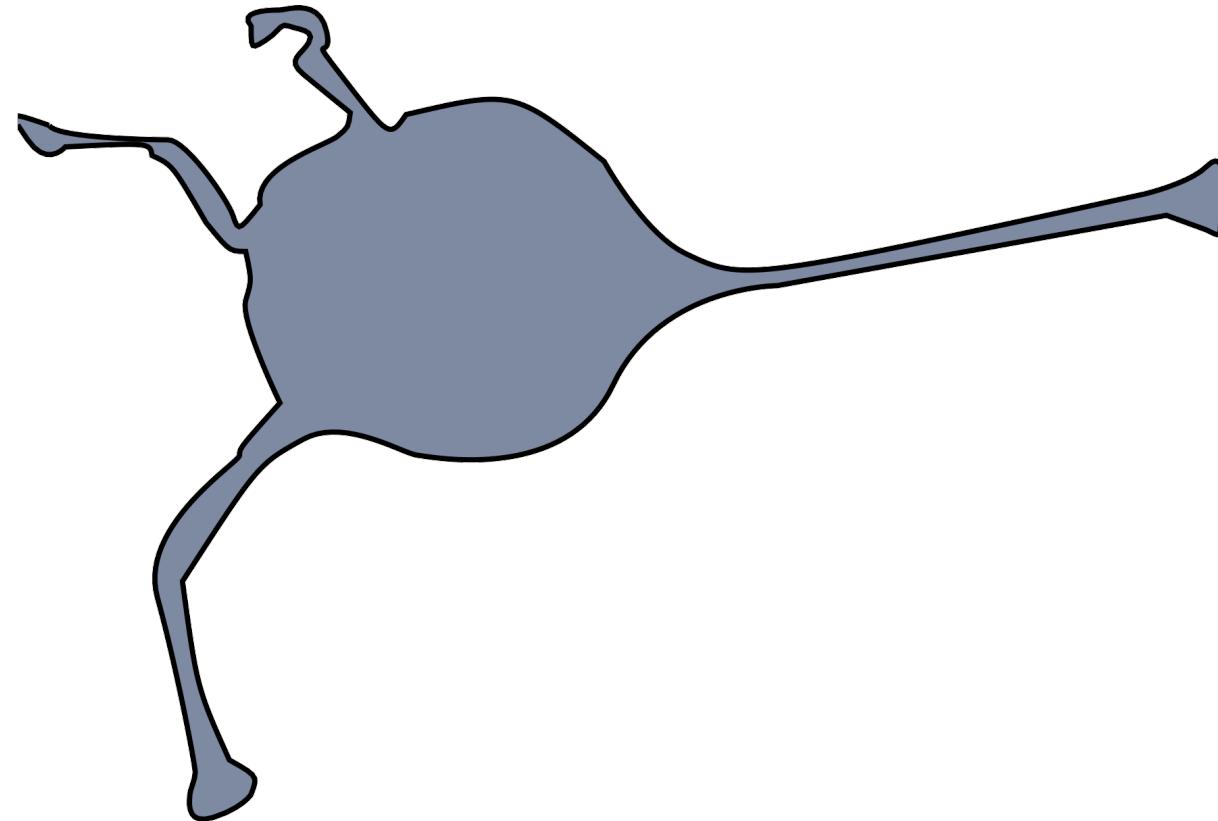


Introduction

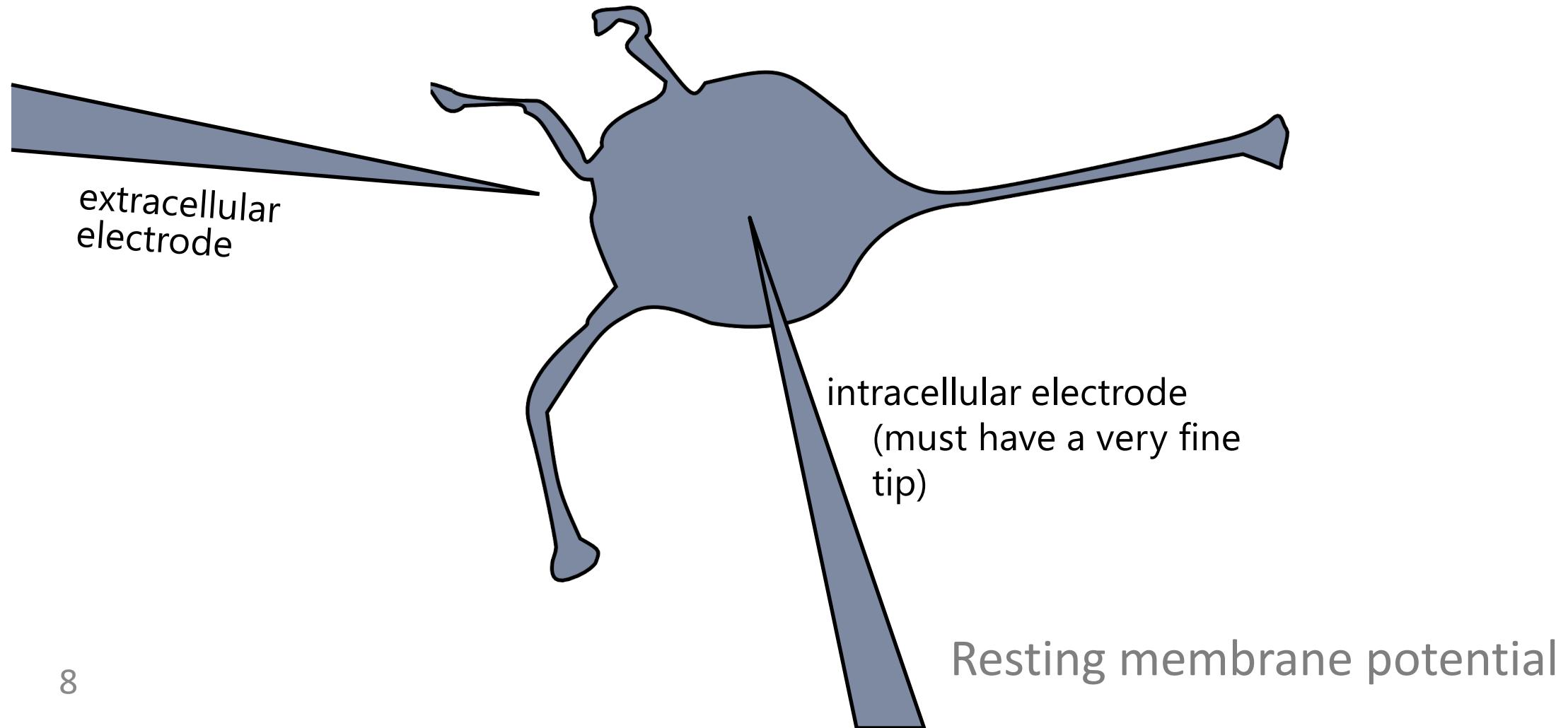


So: How do all these cells
communicate with one another?

As a first step: How does communication occur within a single neuron?

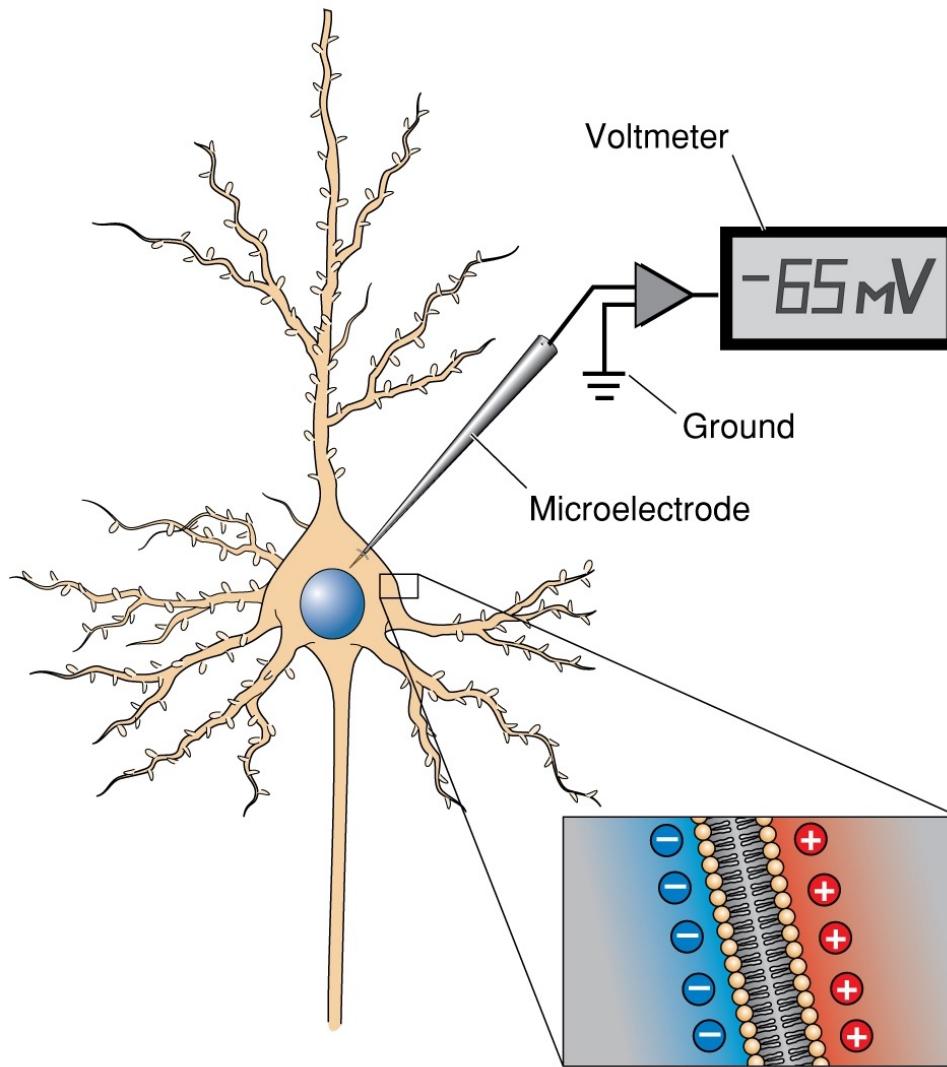


A healthy neuron has a resting membrane potential (or membrane voltage) of between -60 and -80 mV (the voltage inside the neuron is 60-80 mV less than outside the neuron).



The membrane potential

- Originally performed with invertebrates (why?)
- Varies a little from cell to cell / region to region (why?)
- <https://www.youtube.com/watch?v=k48jXzFGMc8>



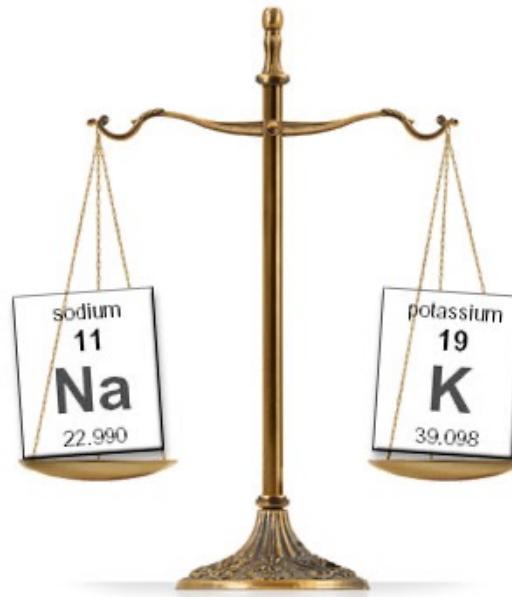
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Resting membrane potential

Neuronal communication is chemical

1. Primarily the result of two ions, sodium (Na^+) and potassium (K^+)
2. Ions move into or out of the cell, but not freely

Periodic Table of the Elements																							
Atomic Number	Symbol		Name		Atomic Mass																		
1	H	Hydrogen	1.008	2	Be	Boron	9.012	3	Li	Lithium	6.941	4	Mg	Magnesium	24.305	5	Al	Aluminum	26.982				
6	Na	Sodium	22.990	7	Ti	Titanium	47.88	8	Cr	Vanadium	51.996	9	Fe	Iron	55.933	10	Co	Cobalt	58.933				
11	K	Potassium	39.098	12	Ca	Calcium	40.078	13	Sc	Scandium	44.956	14	Mn	Manganese	54.938	15	P	Phosphorus	30.974				
16	Rb	Rubidium	84.488	17	Sr	Samarium	87.62	18	Y	Yttrium	88.905	19	Zr	Zirconium	91.224	20	Nb	Molybdenum	92.905				
21	Tc	Technetium	97.905	22	Ta	Tantalum	101.225	23	W	Tungsten	183.85	24	Re	Rhenium	186.207	25	Os	Osmium	190.23				
26	Fe	Iron	55.933	27	Co	Cobalt	58.933	28	Ni	Nickel	58.933	29	Cu	Copper	63.546	30	Zn	Zinc	65.39				
31	Ga	Gallium	69.732	32	Ge	Germanium	72.61	33	As	Arsenic	74.922	34	Se	Selenium	78.00	35	Br	Bromine	79.904				
36	Kr	Krypton	84.80	37	Rb	Rubidium	84.488	38	Sr	Samarium	87.62	39	Y	Yttrium	88.905	40	Tc	Technetium	97.905				
41	Mo	Molybdenum	95.94	42	Tc	Technetium	98.907	43	Rh	Ruthenium	101.07	44	Pd	Palladium	106.42	45	Ag	Silver	107.868				
46	Pd	Palladium	106.42	47	Ag	Silver	107.868	48	Cd	Cadmium	112.411	49	In	Inert Gas	114.818	50	Sn	Tellurium	118.71				
51	Sb	Sb	121.760	52	Te	Te	121.760	53	I	Iodine	126.904	54	Xe	Xenon	131.29	55	Cs	Cesium	132.905				
56	Ba	Barium	137.327	57	La	Lanthanum	138.908	58	Ce	Cerium	140.115	59	Pr	Praseodymium	144.24	60	Nd	Neodymium	140.908				
61	Pm	Promethium	144.913	62	Sm	Samarium	150.36	63	Eu	Europium	151.965	64	Gd	Gadolinium	157.25	65	Tb	Dysprosium	162.50				
66	Dy	Dysprosium	162.50	67	Ho	Holmium	164.930	68	Er	Erbium	167.26	69	Tm	Thulium	168.934	70	Yb	Ytterbium	173.04				
71	Lu	Lutetium	174.967	72	Hf	Hafnium	178.49	73	Ta	Tantalum	180.948	74	W	Tungsten	186.207	75	Re	Rhenium	190.23				
76	Os	Osmium	190.23	77	Ir	Iridium	192.22	78	Pt	Platinum	195.08	79	Au	Gold	196.967	80	Hg	Mercury	200.59				
81	Tl	Thallium	204.383	82	Pb	Lead	207.2	83	Bi	Bismuth	208.950	84	Po	Poison	209.967	85	At	Astatine	209.967				
86	Rn	Radon	222.18	87	Fr	Francium	223.920	88	Ra	Radium	226.025	89-103	Rf	Rutherfordium	[261]	104	Ds	Dubnium	[262]	105	Db	Dubnium	[264]
106	Sg	Seaborgium	[266]	107	Bh	Bohrium	[264]	108	Hs	Hassium	[269]	109	Mt	Mendelevium	[272]	110	Ds	Darmstadtium	[280]	111	Rg	Rutherfordium	[277]
112	Cn	Copernicium	[285]	113	Uut	Ununtrium	[289]	114	F1	Flerovium	[289]	115	Uup	Ununpentium	[289]	116	Lv	Livermorium	[289]	117	Uus	Ununseptium	[289]
118	Uuo	Ununoctium	[289]	119				120				121				122							
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Alkali Metal		Alkaline Earth		Transition Metal		Basic Metal		Semimetal		Nonmetal		Halogen		Noble Gas		Lanthanide		Actinide					



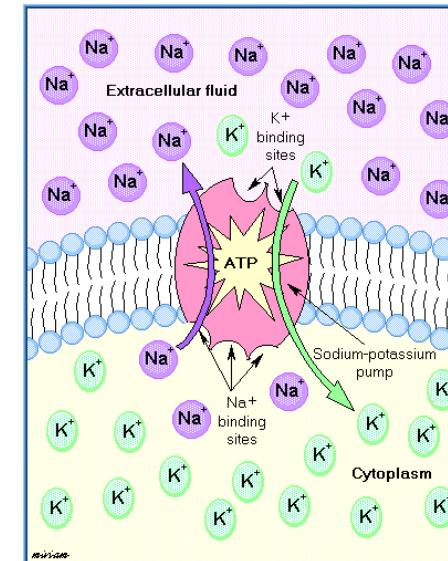
Resting membrane potential

Neuronal communication is electrical

1. Ions are positively and negatively charged (Na^+ and K^+ are both positive, as per "+")
2. As they move into or out of cell, they change the *potential* (voltage) at the membrane

Note: absence of pos. is neg.!

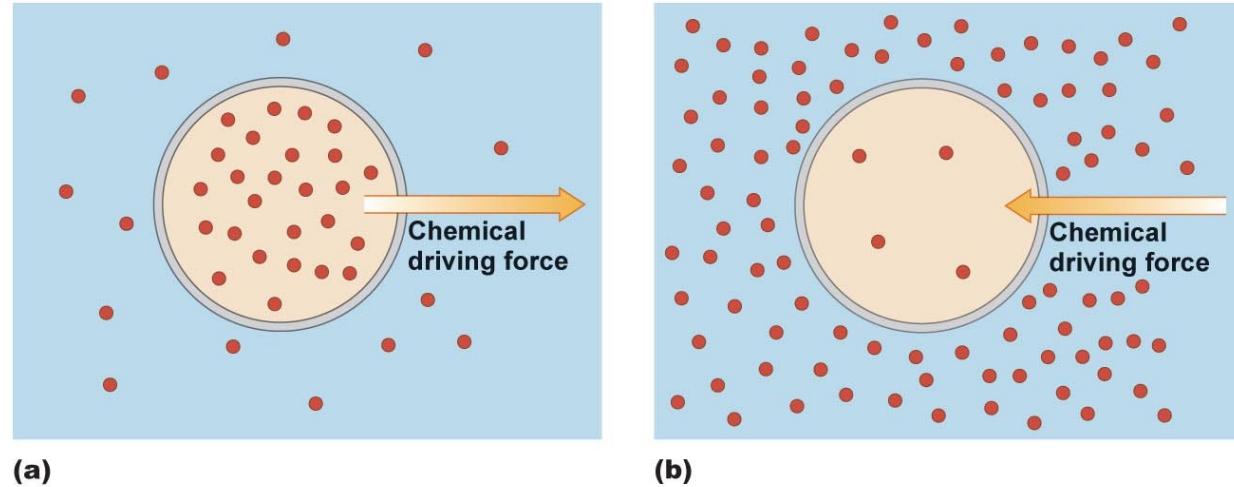
i.e. remove a pos., leave a neg.



Resting membrane potential

Chemical gradients

- Ions want to flow from high concentration to low concentration

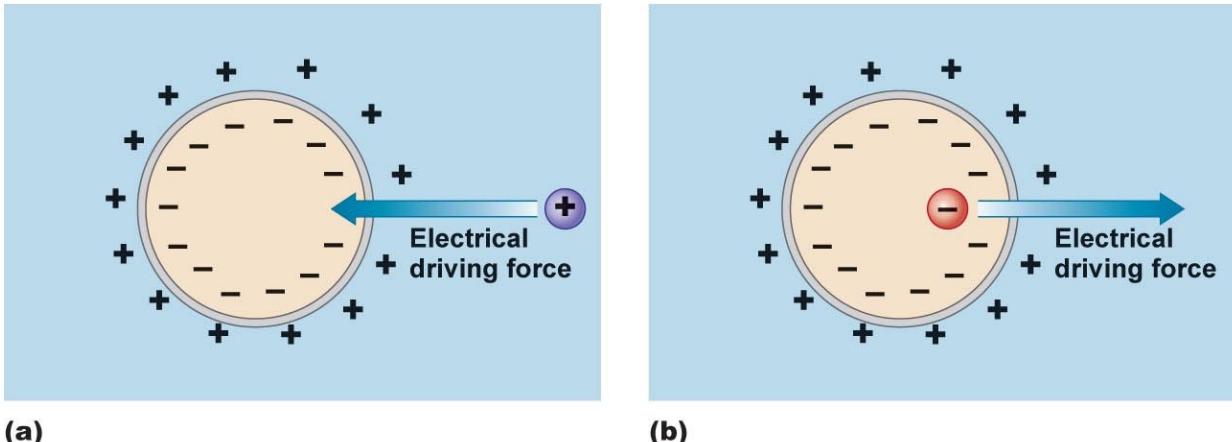


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Resting membrane potential

Electrical gradients

- Charge/potential wants to flow from high concentration to low concentration, too

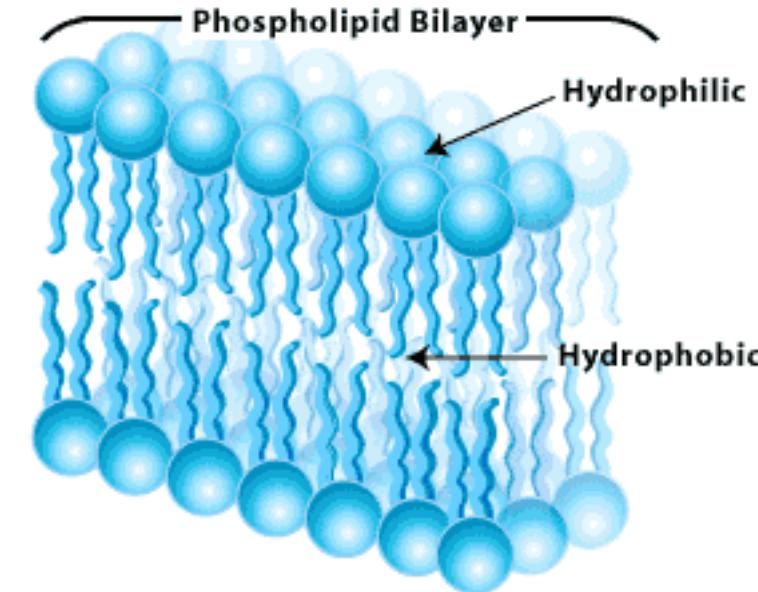
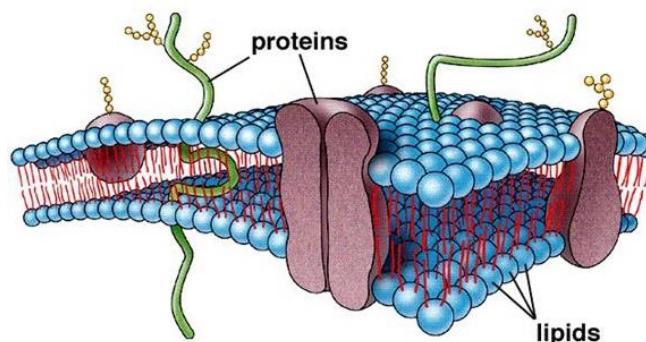
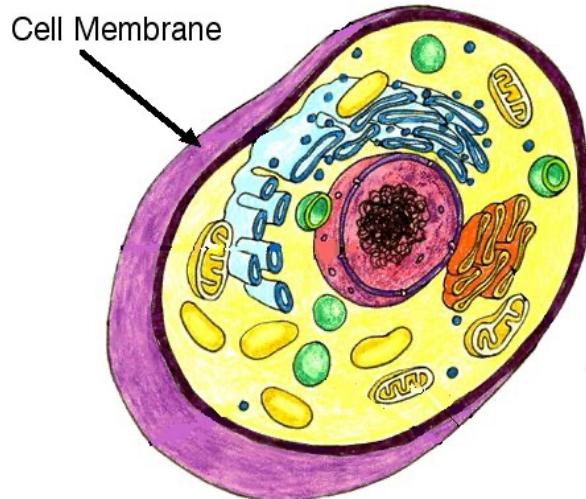


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- Sometimes electrical and chemical gradients are at odds, causing an *equilibrium* that $=/ \approx 0\text{mV}$

The cell membrane - guardian

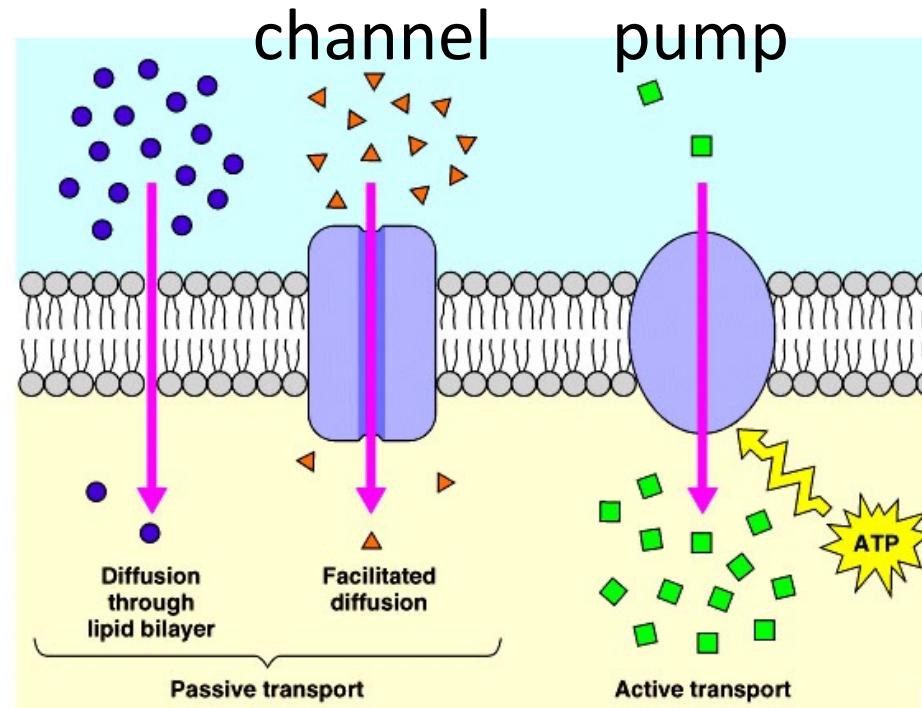
- Lipid bilayer is tightly packed, both hydrophobic and hydrophilic, keeping out all dangerous entities
 - e.g.?



Resting membrane potential

Channels and pumps

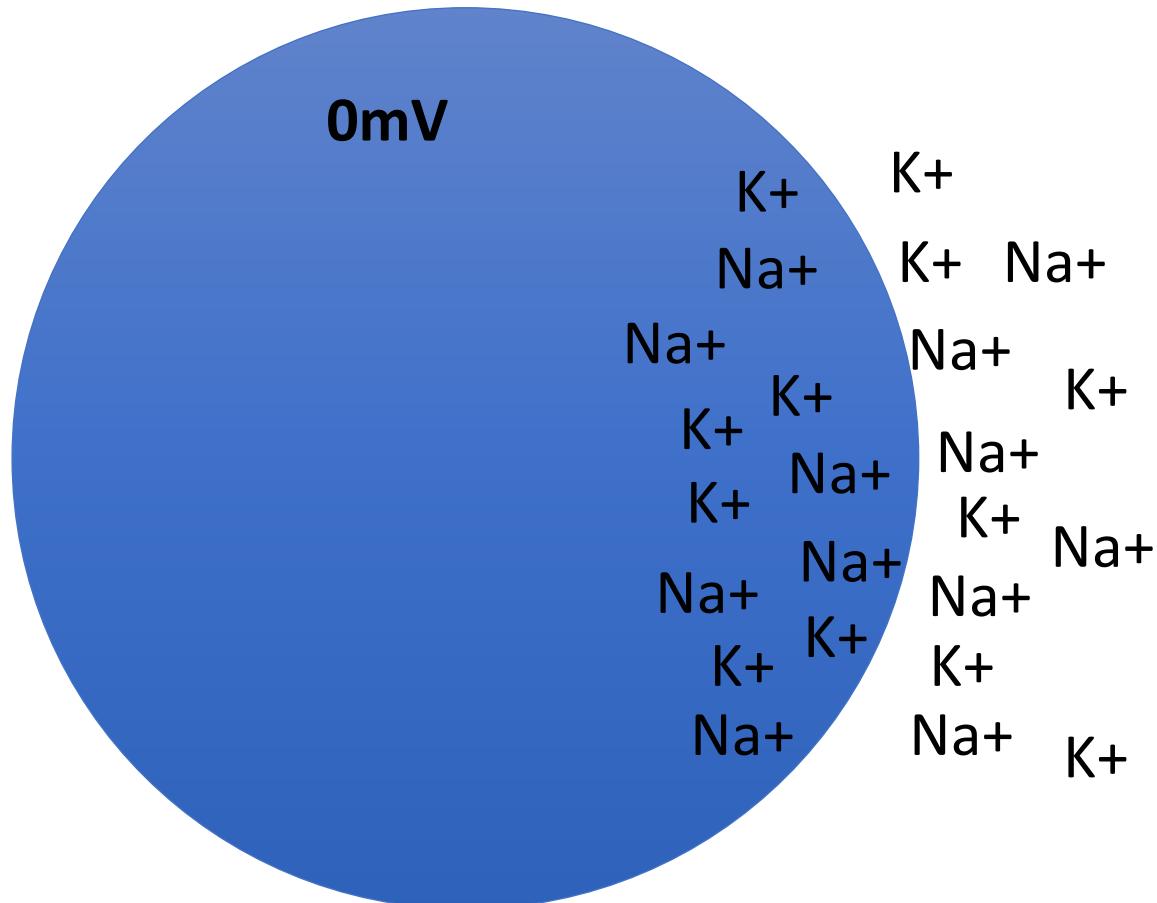
- Only certain molecules and ions permitted via *channels* and *pumps*
 - Channels: allow *passive* diffusion (i.e. along chemical gradient)
 - Pumps: actively push ions against their chemical gradient
 - Requires energy (ATP)



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A cell with no channels or pumps

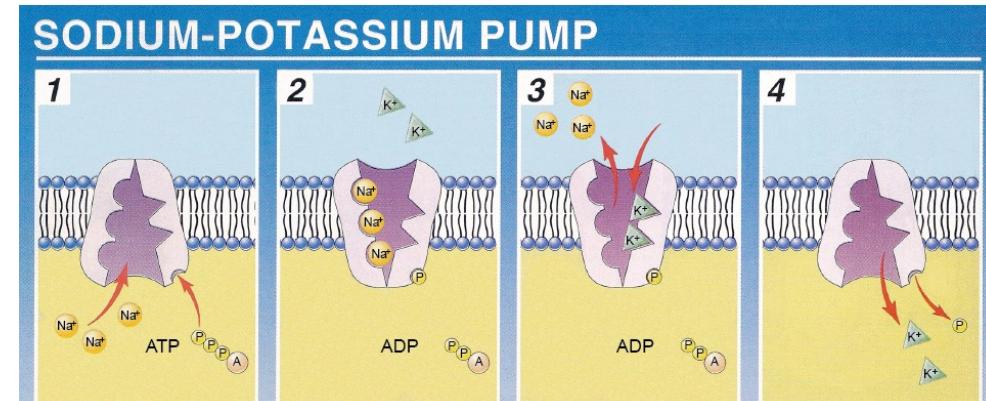
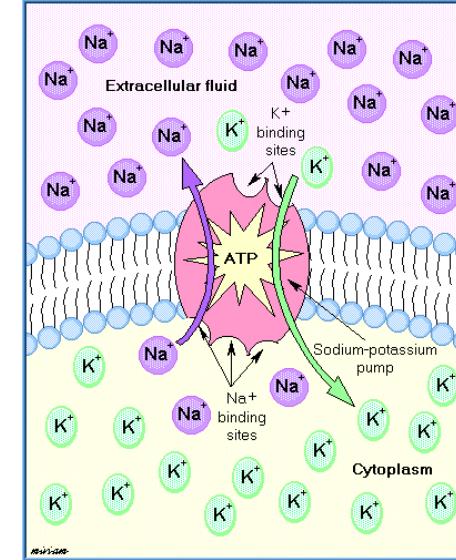
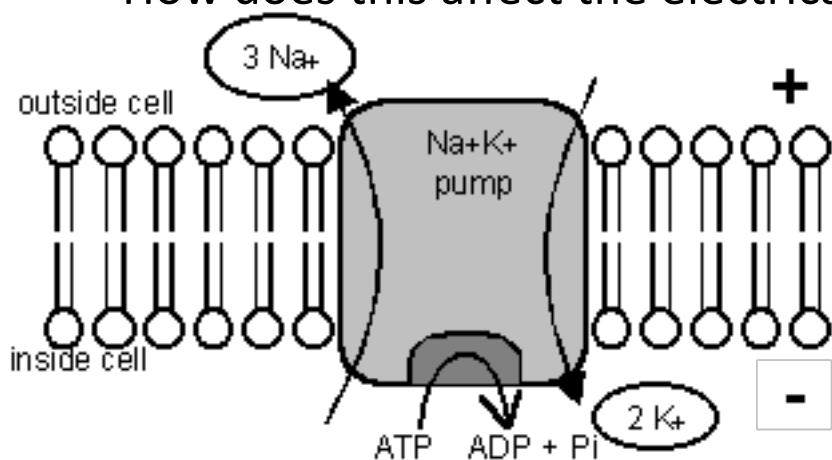
- Nothing moves into or out of the cell



Resting membrane potential

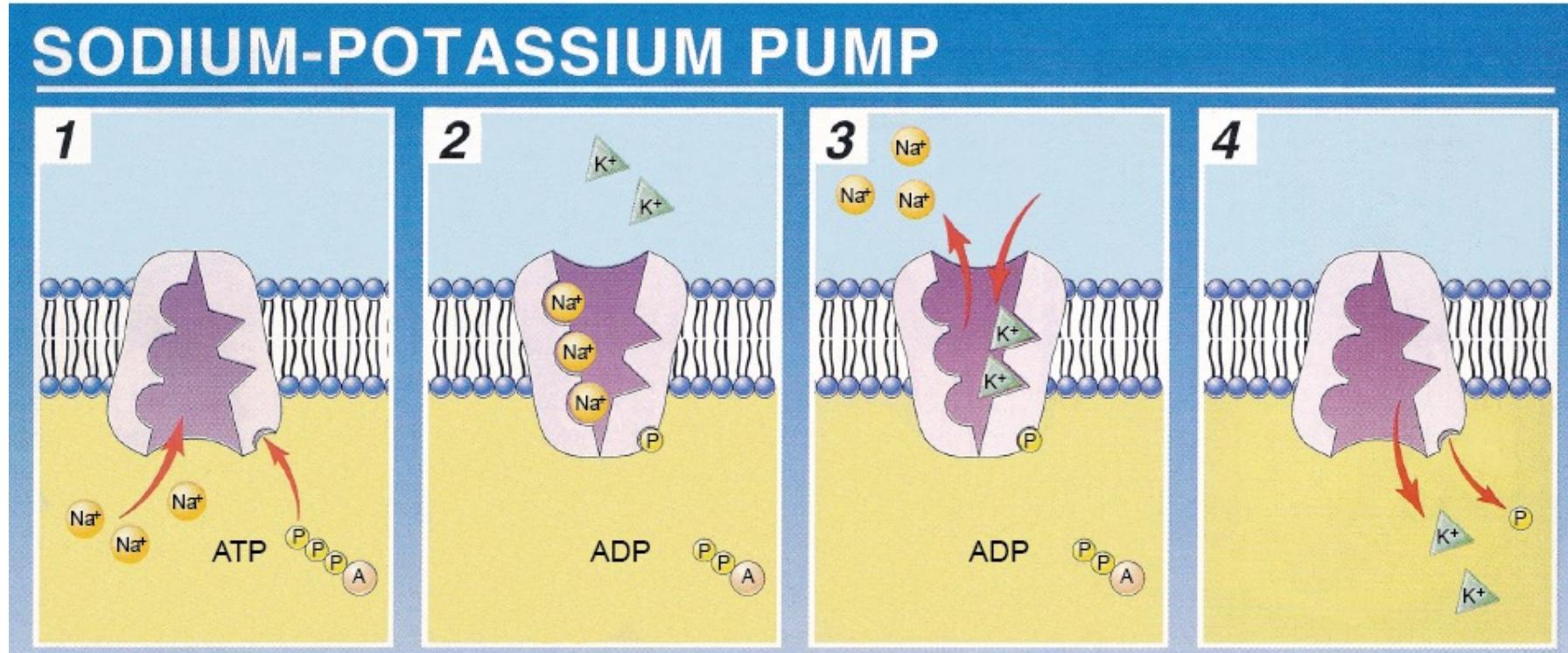
The Sodium-Potassium Pump

- Embedded in cell membrane
- **Extremely** important
 - Consumes 2/3rds of all neuronal energy!
- Pushes 3 Na⁺ out and 2 K⁺ in
 - i.e. Active process that requires energy
- How does this affect the chemical gradients?
- How does this affect the electrical gradient?



Resting membrane potential

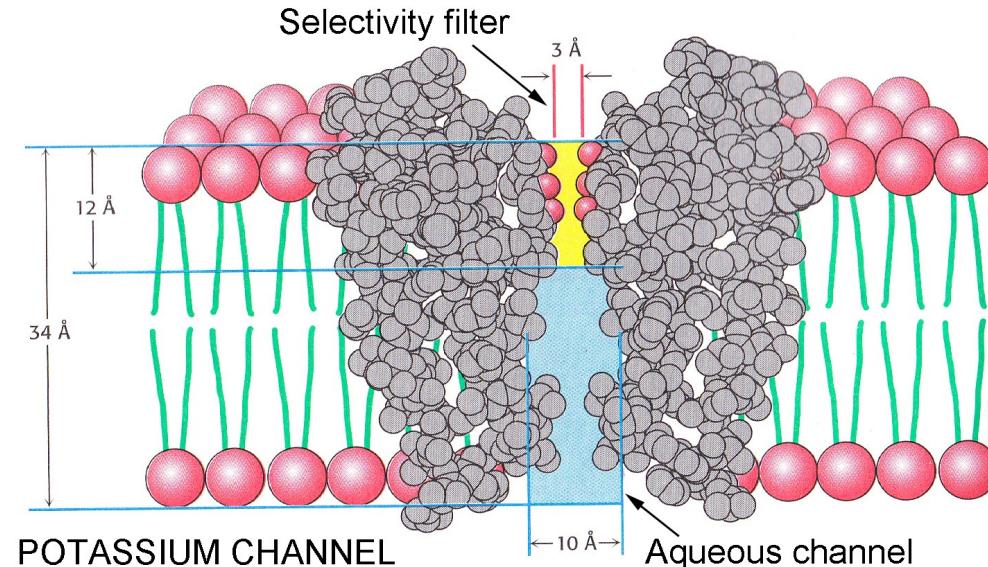
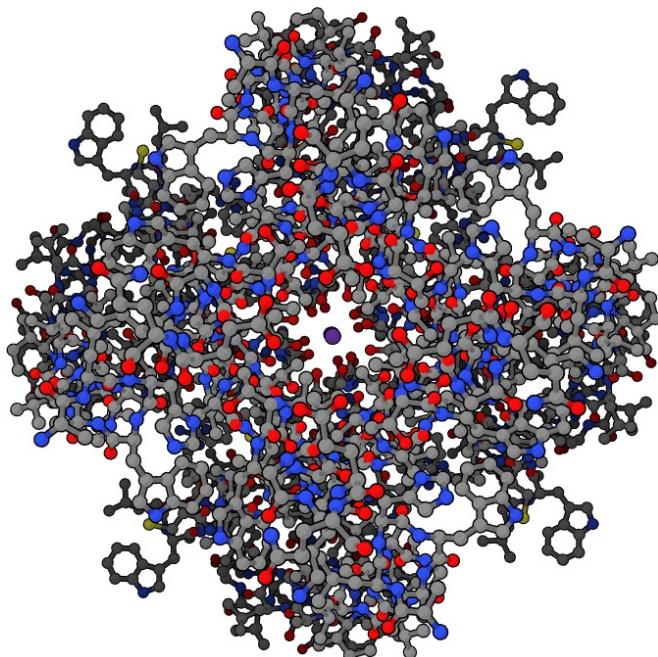
The Sodium-Potassium Pump



Resting membrane potential

Potassium “leak” channels

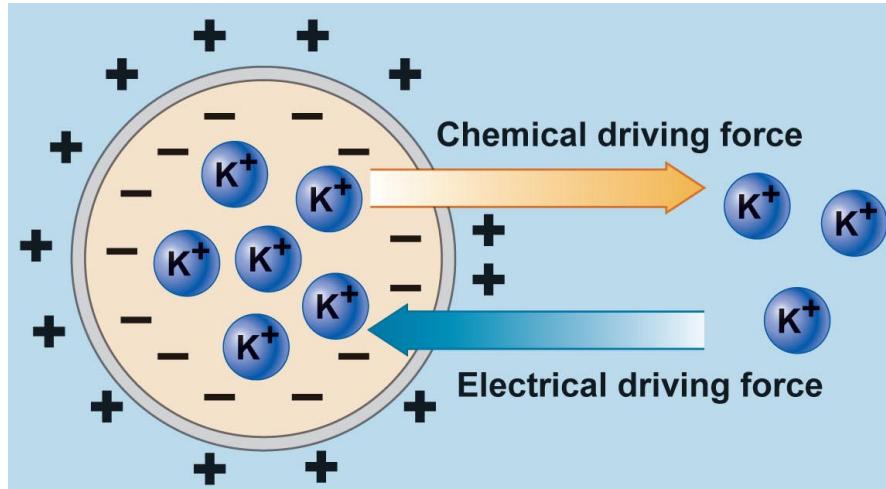
- K⁺ can move freely via K⁺ “leak” channels that are always open
- Na⁺ **cannot** move freely across the membrane
 - It has channels, but they are usually closed



Resting membrane potential

Cells are polarized

- Na⁺/K⁺ pump pushing more Na⁺ out of cell than K⁺ into cell
 - Result: inside of cell slightly more negative than outside
- **But** K⁺ can move freely through its leak channels
 - Result: K⁺ wants to move with chemical gradient, out of the cell
- **But** this moving K⁺ is making the cell even more negative
 - Result: flow of K⁺ stops when force of electrical gradient equals force of chemical gradient
- End result: cell has resting membrane potential of ~-70mV



Resting membrane potential

Cells are *polarized*

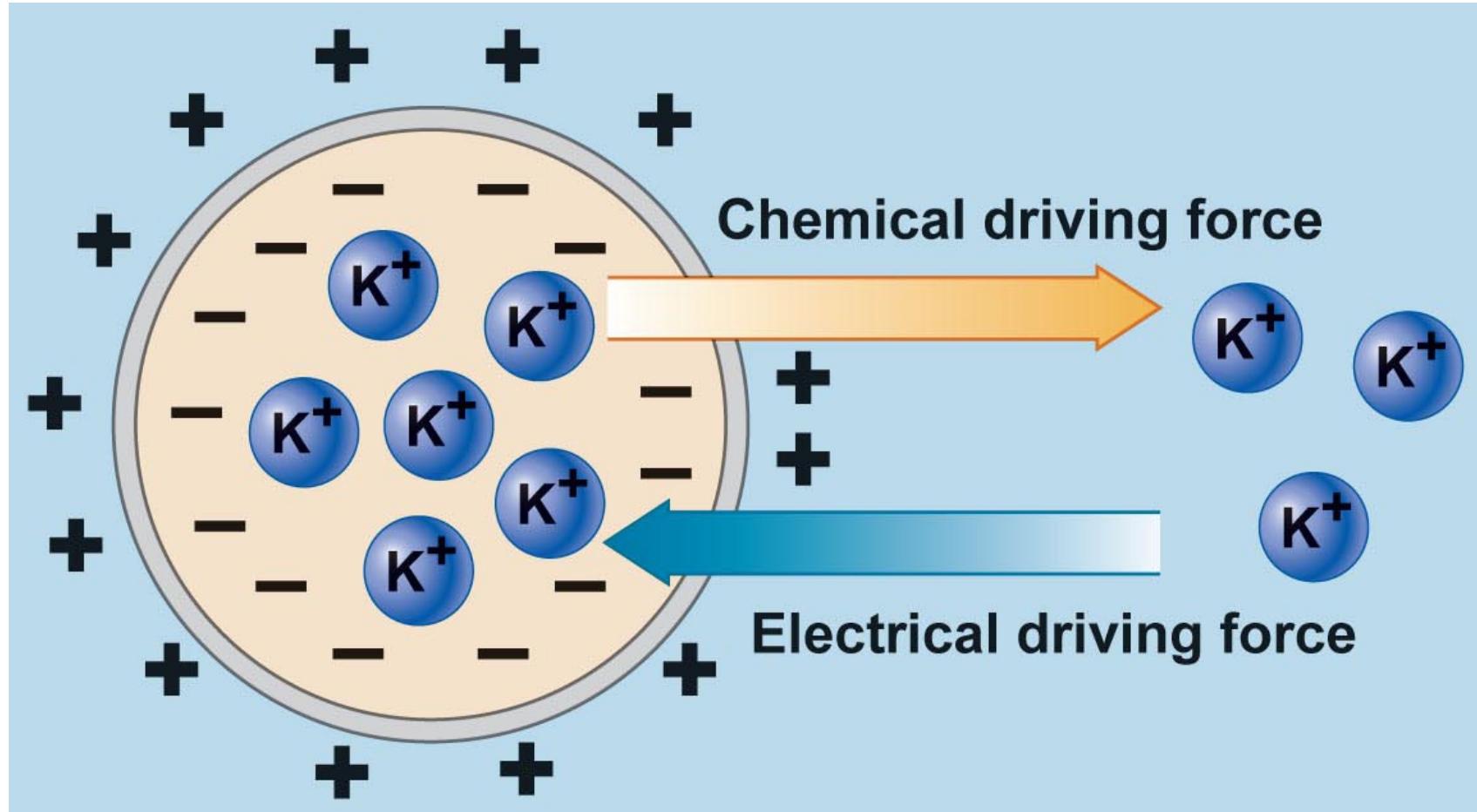
A diagram of a neuron membrane at -70mV . The interior of the cell is shaded blue and labeled -70mV . The exterior is white. On the right side, several potassium ions (K^+) are shown moving from the interior to the exterior through a grey rectangular channel. One sodium ion (Na^+) is also shown moving from the interior to the exterior through an orange rectangular channel.

**Chemical force pushing K⁺ out of the cell
equals**

Electrical force pushing K⁺ into the cell

The diagram illustrates the resting membrane potential of a neuron. On the left, a vertical column of ions is shown: K⁺, Na⁺, Na⁺, Na⁺, Na⁺, Na⁺, Na⁺, K⁺, Na⁺, and K⁺. An orange rounded rectangle labeled "Na⁺/K⁺ pump (always working)" is positioned above the membrane, with arrows indicating movement of K⁺ into the cell and Na⁺ out of the cell. A blue rounded rectangle labeled "K⁺ leak channel (always open)" is also present, with an arrow indicating K⁺ leaking out of the cell. A grey rounded rectangle labeled "Na⁺ channel (closed)" is shown below the membrane. The membrane itself is depicted as a thin grey line separating the intracellular space from the extracellular space.

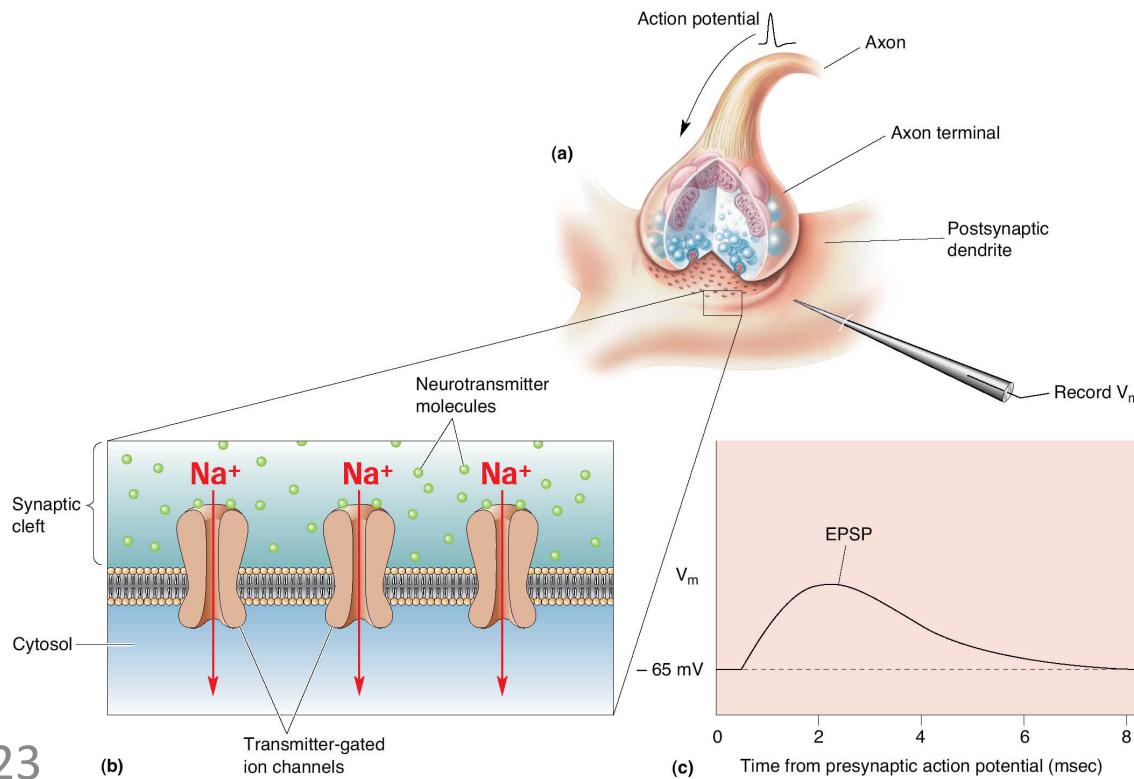
Cells are polarized



Resting membrane potential

When a neurotransmitter molecule binds to a postsynaptic receptor, it can have one of two localized effects:

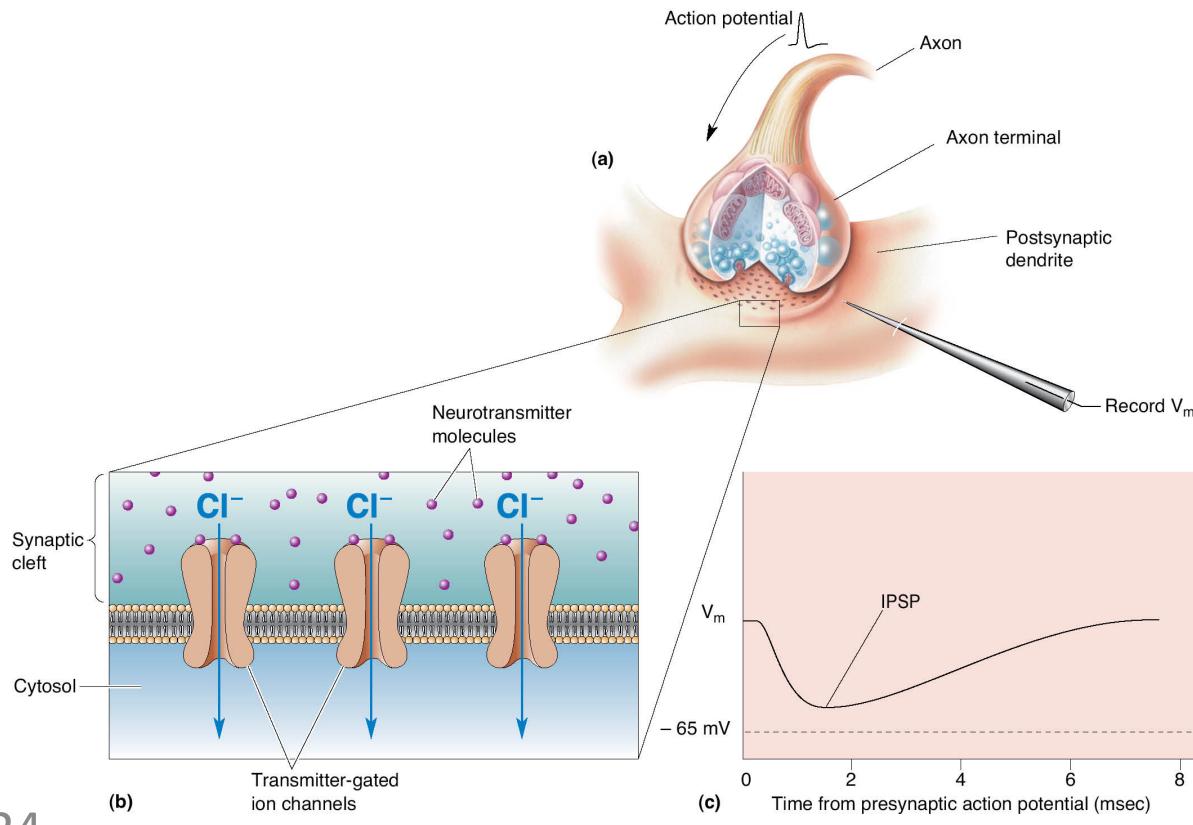
- 1. Depolarize the membrane** (e.g., decrease membrane potential from -70 to -67mV)
- 2. Hyperpolarize the membrane** (e.g., increase the membrane potential from -70 to -72mV)



Postsynaptic potentials

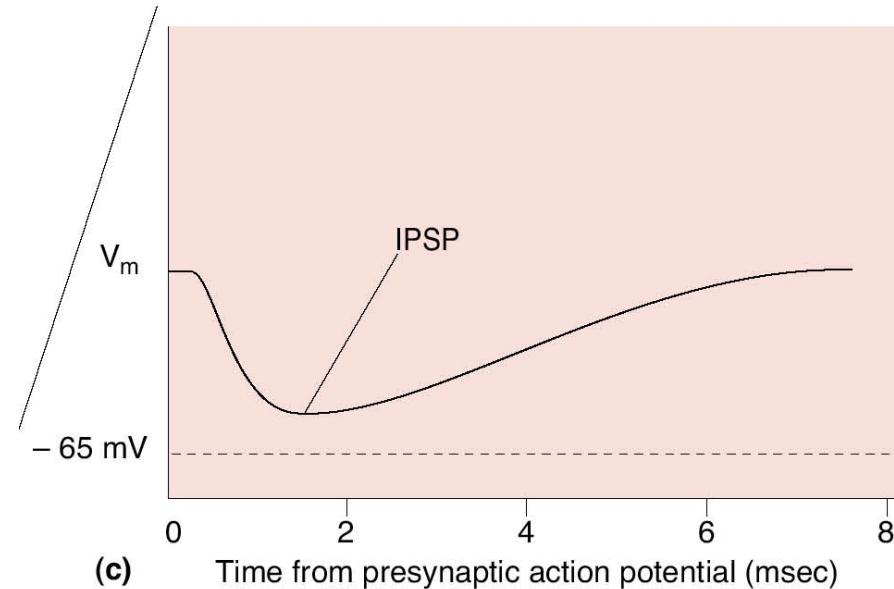
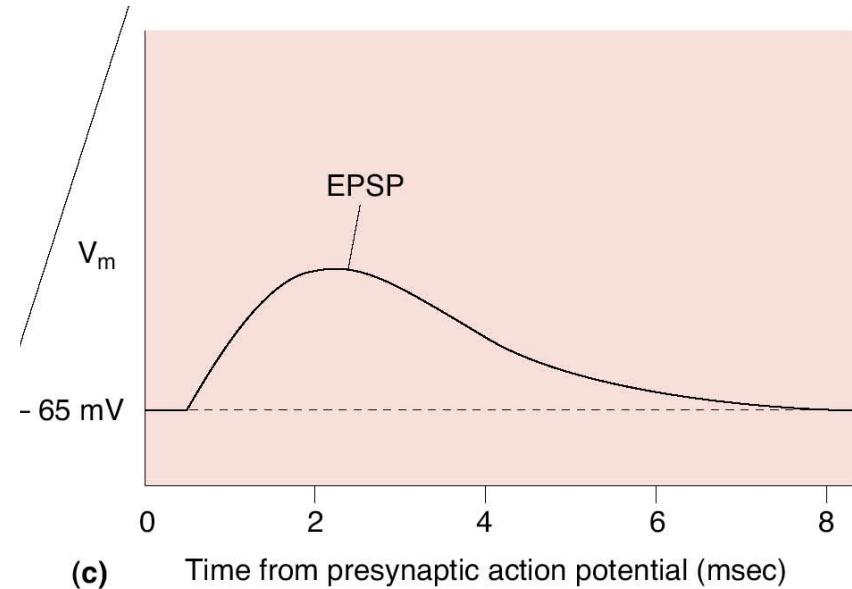
When a neurotransmitter molecule binds to a postsynaptic receptor, it can have one of two localized effects:

1. Depolarize the membrane = **Excitatory postsynaptic potential (EPSP)**
2. Hyperpolarize the membrane = **Inhibitory postsynaptic potential (IPSP)**



When a neurotransmitter molecule binds to a postsynaptic receptor, it can have one of two localized effects:

1. Depolarize the membrane = EPSP = **Increase likelihood that the postsynaptic neuron will fire an action potential (AP)**
2. Hyperpolarize the membrane = IPSP = **Decrease the likelihood that the postsynaptic neuron will fire an AP**



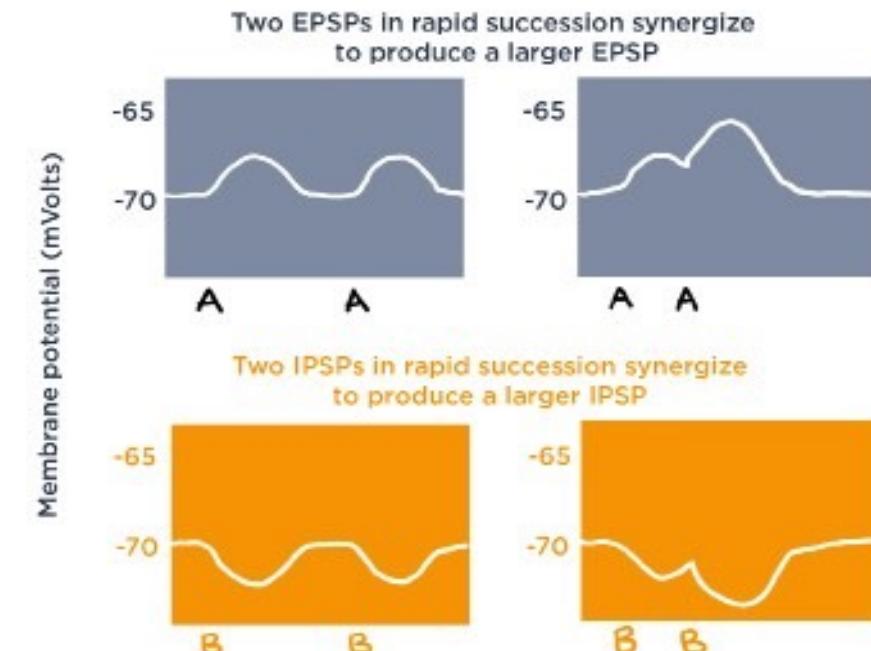
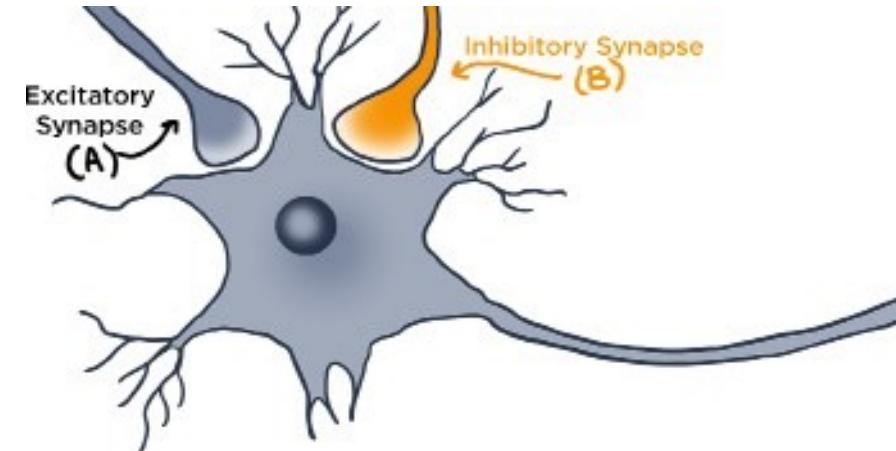
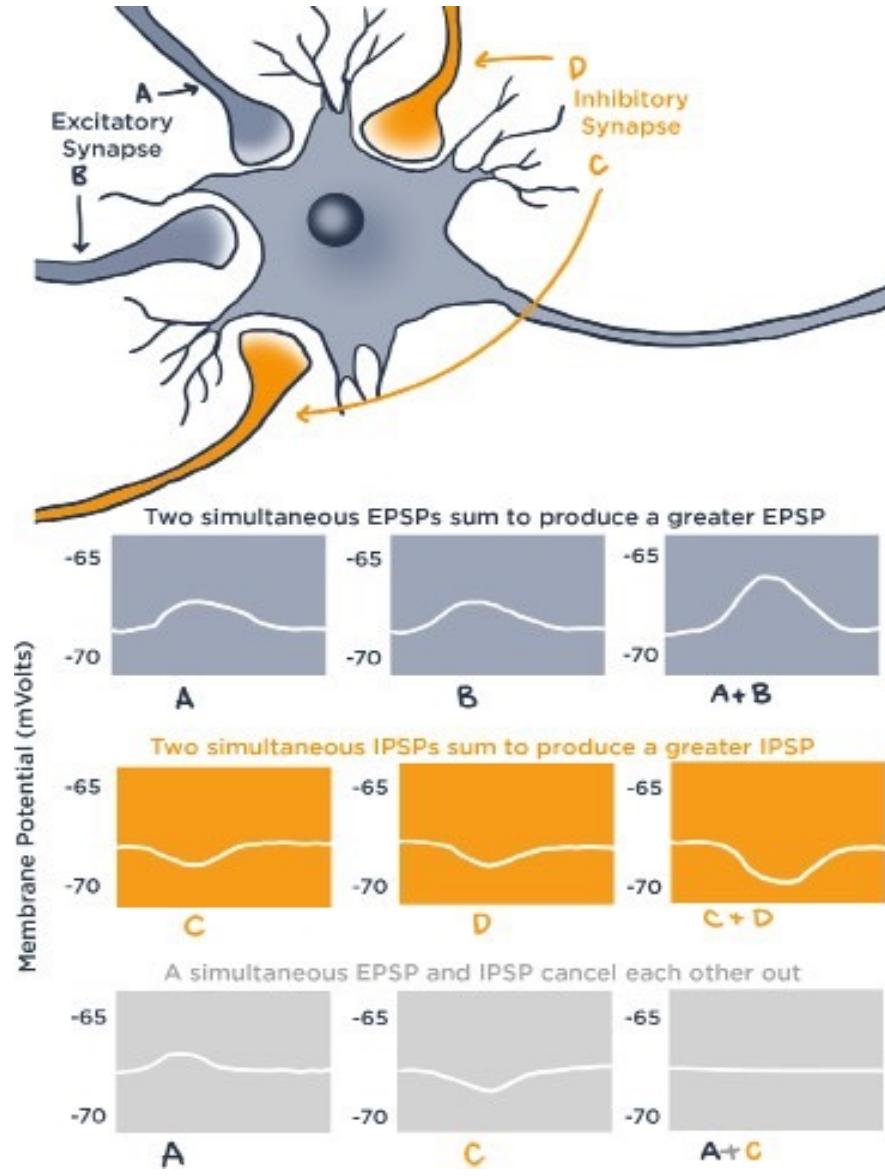
Postsynaptic potentials

When a neurotransmitter molecule binds to a postsynaptic receptor, it can have one of two localized effects:

1. Depolarize the membrane = EPSP = Increase likelihood that the postsynaptic neuron will fire an action potential (AP)
2. Hyperpolarize the membrane = IPSP = Decrease the likelihood that the postsynaptic neuron will fire an AP

The transmission of postsynaptic potentials (PSPs) is **graded, rapid, and decremental**: PSPs travel like an electrical signal along an uninsulated wire.

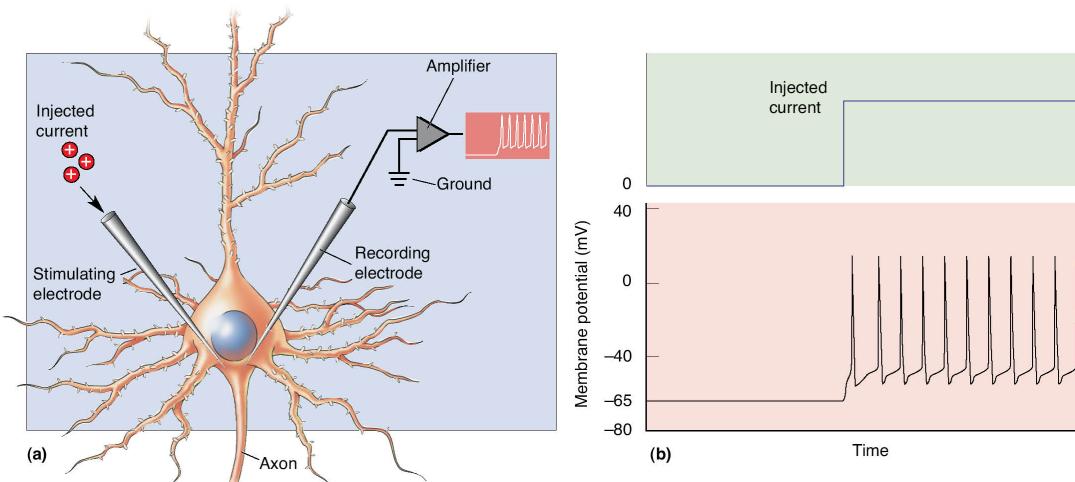
EPSPs and IPSPs sum both spatially and temporally



AP Generation

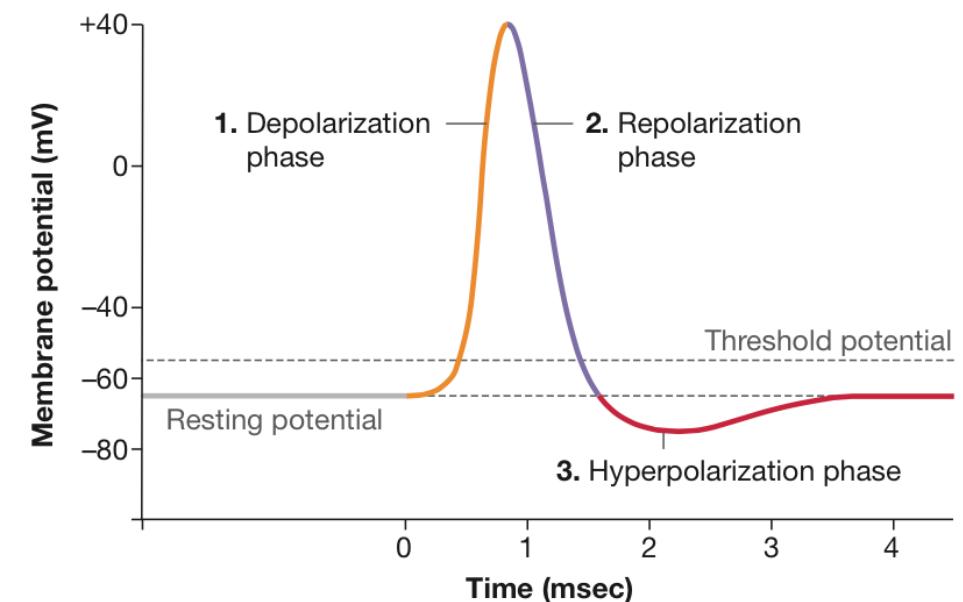
If the sum of the EPSPs and IPSPs that reaches the **axon initial segment** is sufficient to depolarize the membrane there above its **threshold of excitation** (e.g., -55mV) then an **action potential (AP)** is generated

The AP is a massive momentary reversal of the membrane potential (e.g., from -70 to +55 mV)

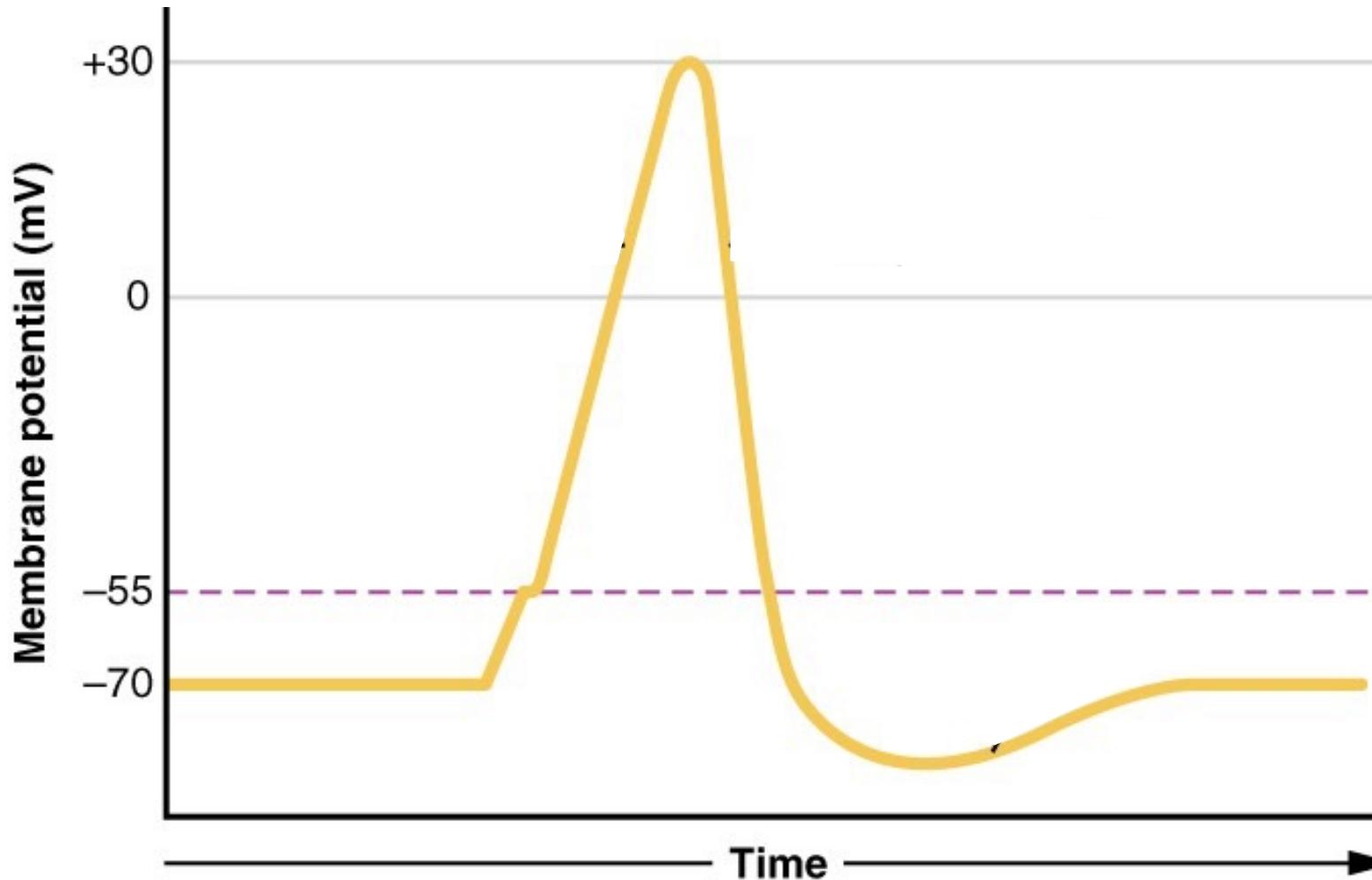


Reverse the polarity!

- *Action potential*: a rapid, brief reversal of the polarity at the membrane, from negative to positive
- **It's the main method of brain communication**
- It's all-or-none (off or on), **not** graded (e.g. 0-100%)
 - i.e. always the same size/shape in a cell
 - How do neurons convey magnitude, then?
- Why does this reversal happen?

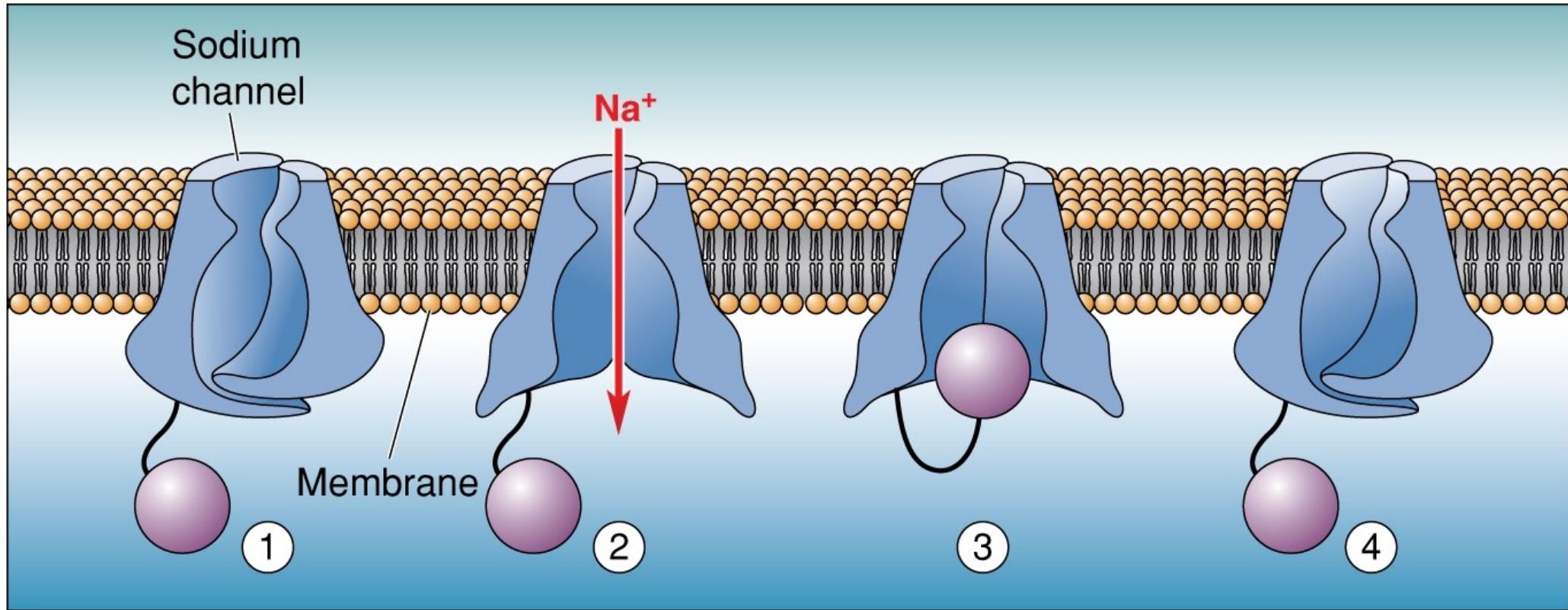


Once the membrane potential reaches a certain threshold, an action potential (AP) can be generated



The action potential

AP generation and conduction are both the result of voltage-activated ion channels (primarily Na_v)

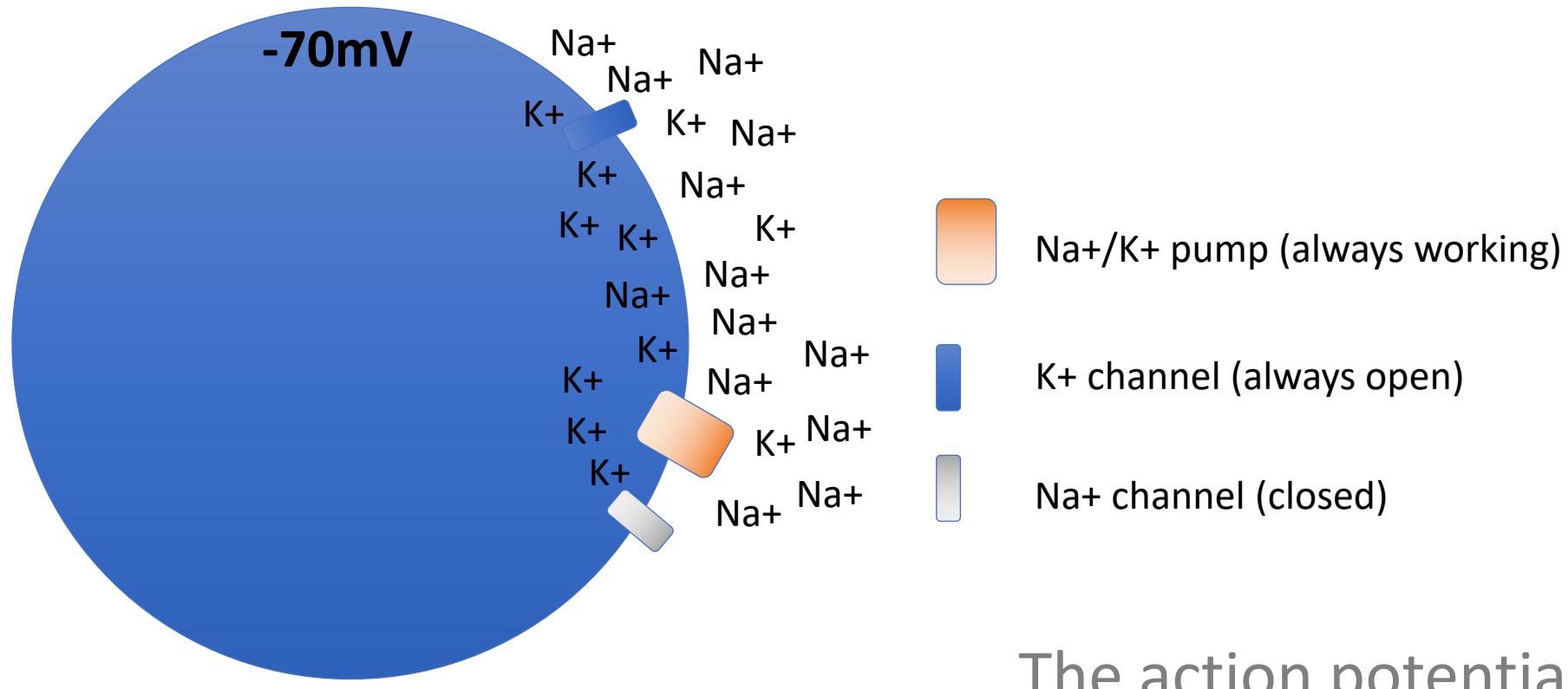


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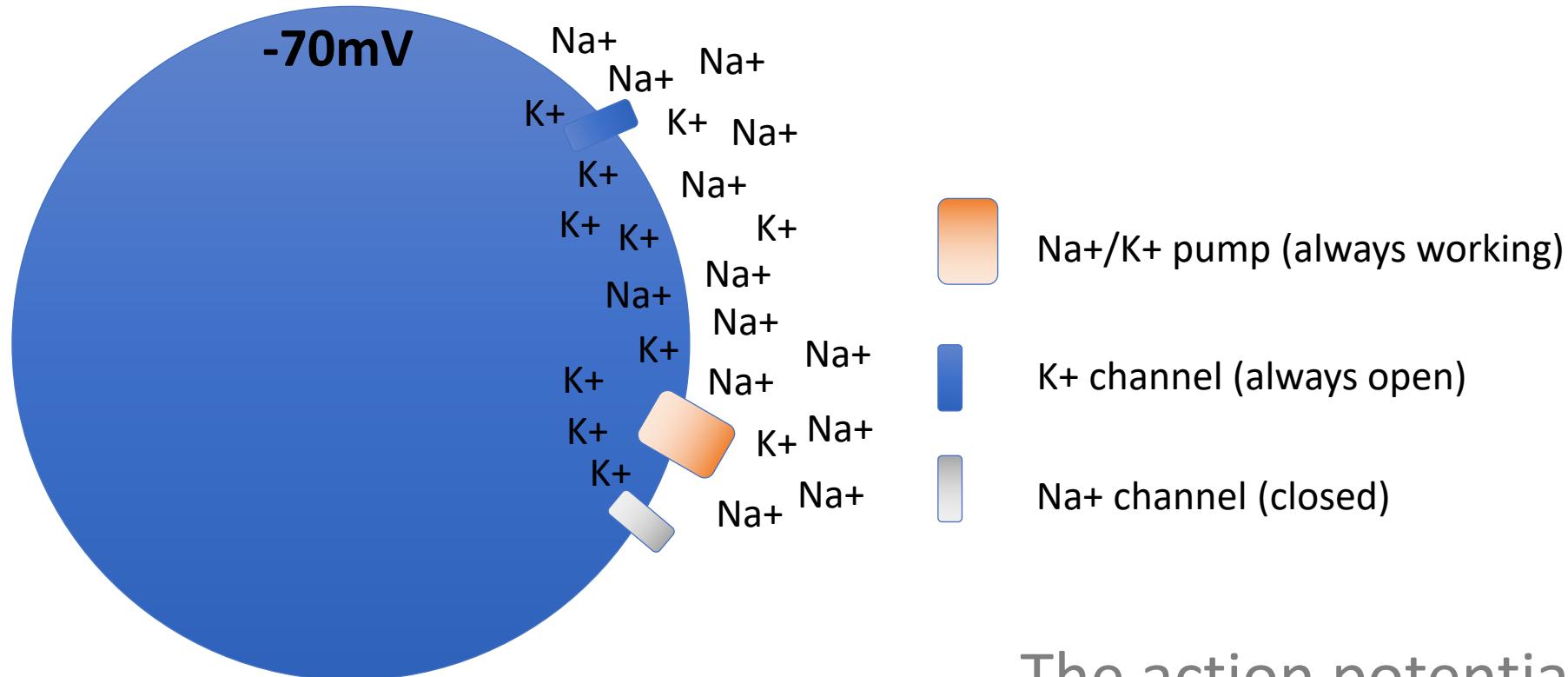
Small depolarizations

- Remember: Na^+ channels usually closed
 - **But** these Na^+ channels are *voltage-gated*, i.e. they open at a certain voltage ($\sim -55\text{mV}$)

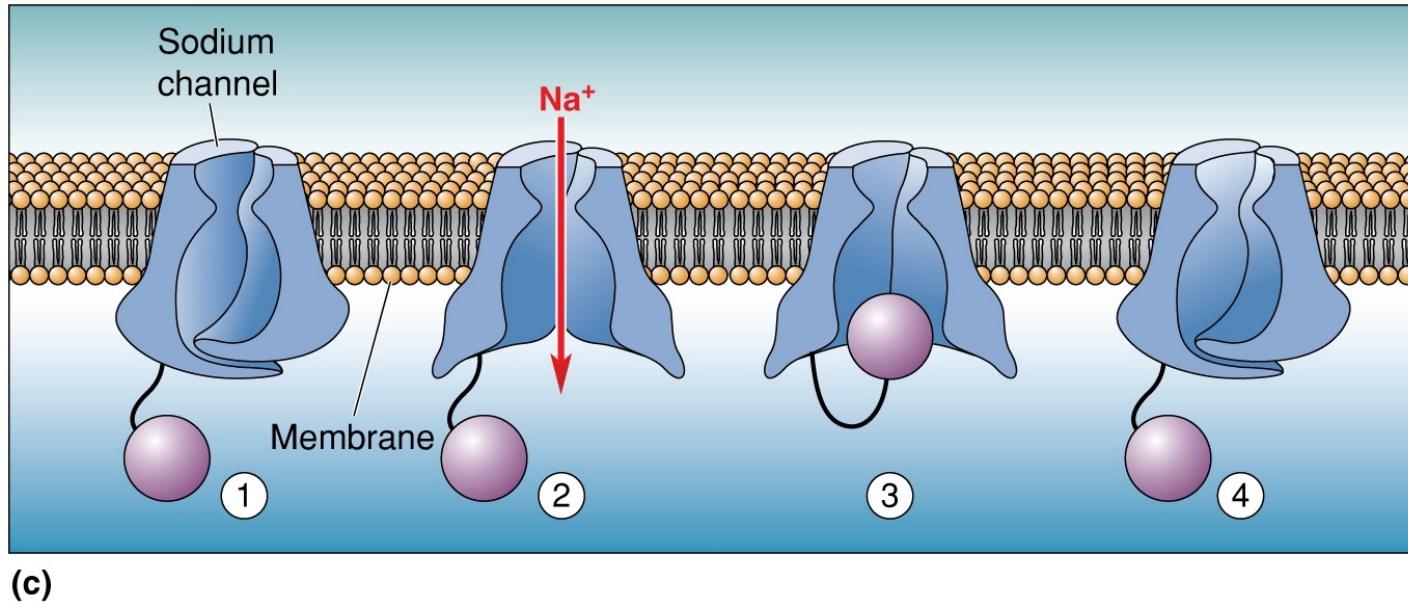


Small depolarizations

- When enough EPSPs arrive at the same time ($\sim 5\text{-}10\text{mV}$), the membrane is depolarized enough to reach the Na^+ channels' voltage threshold (*threshold potential*), and the channels open!
- Which direction does Na^+ want to flow? Why?

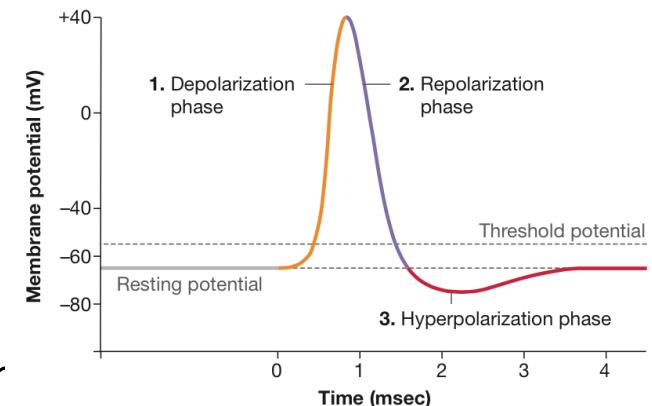


Rapid huge depolarization



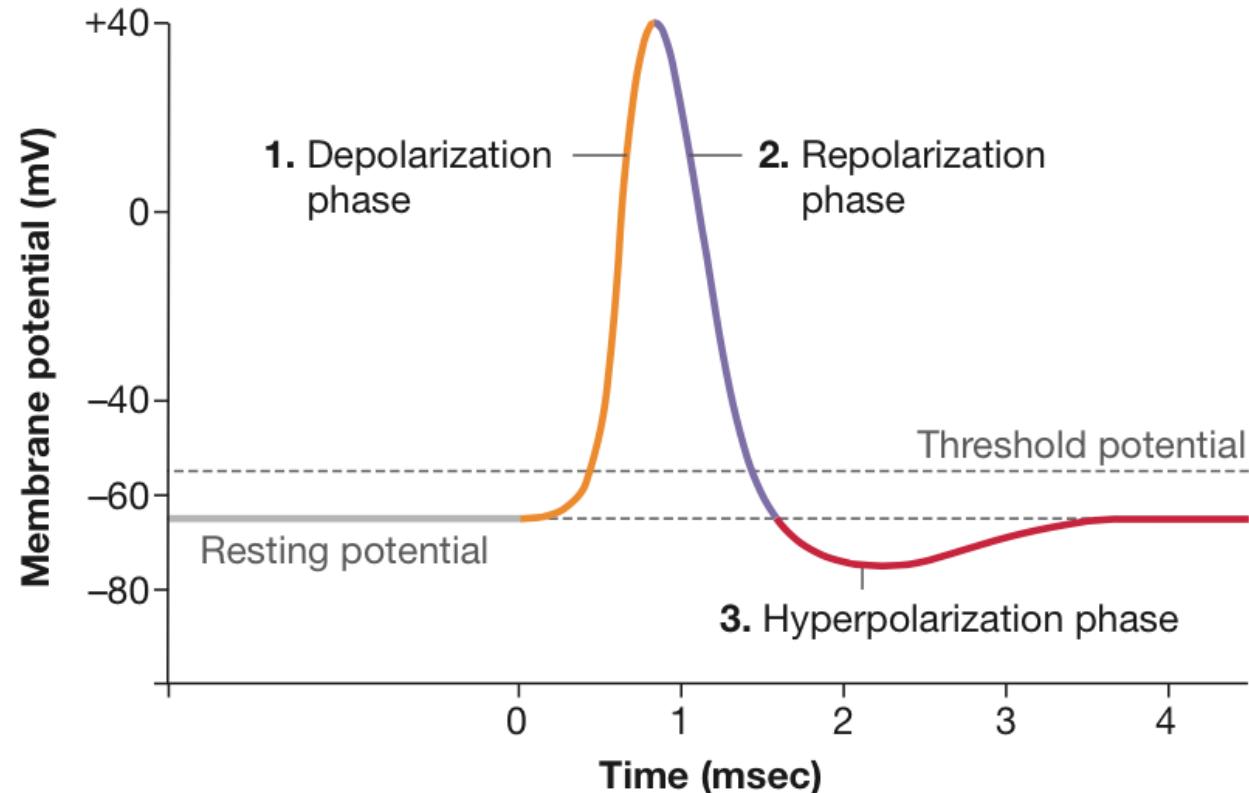
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- Na^+ channels open $\rightarrow \text{Na}^+$ into cell
 - Effect?
- Cell *membrane* flips from neg. to pos.
- BUT Na^+ channels have built-in inactivation
 - Shut-off automatically, after $\sim 1\text{ms}$
- Na^+ channels stay inactivated until membrane goes back to resting poter
 - i.e. No more action potentials until reset!
 - This leads to the **absolute refractory period**

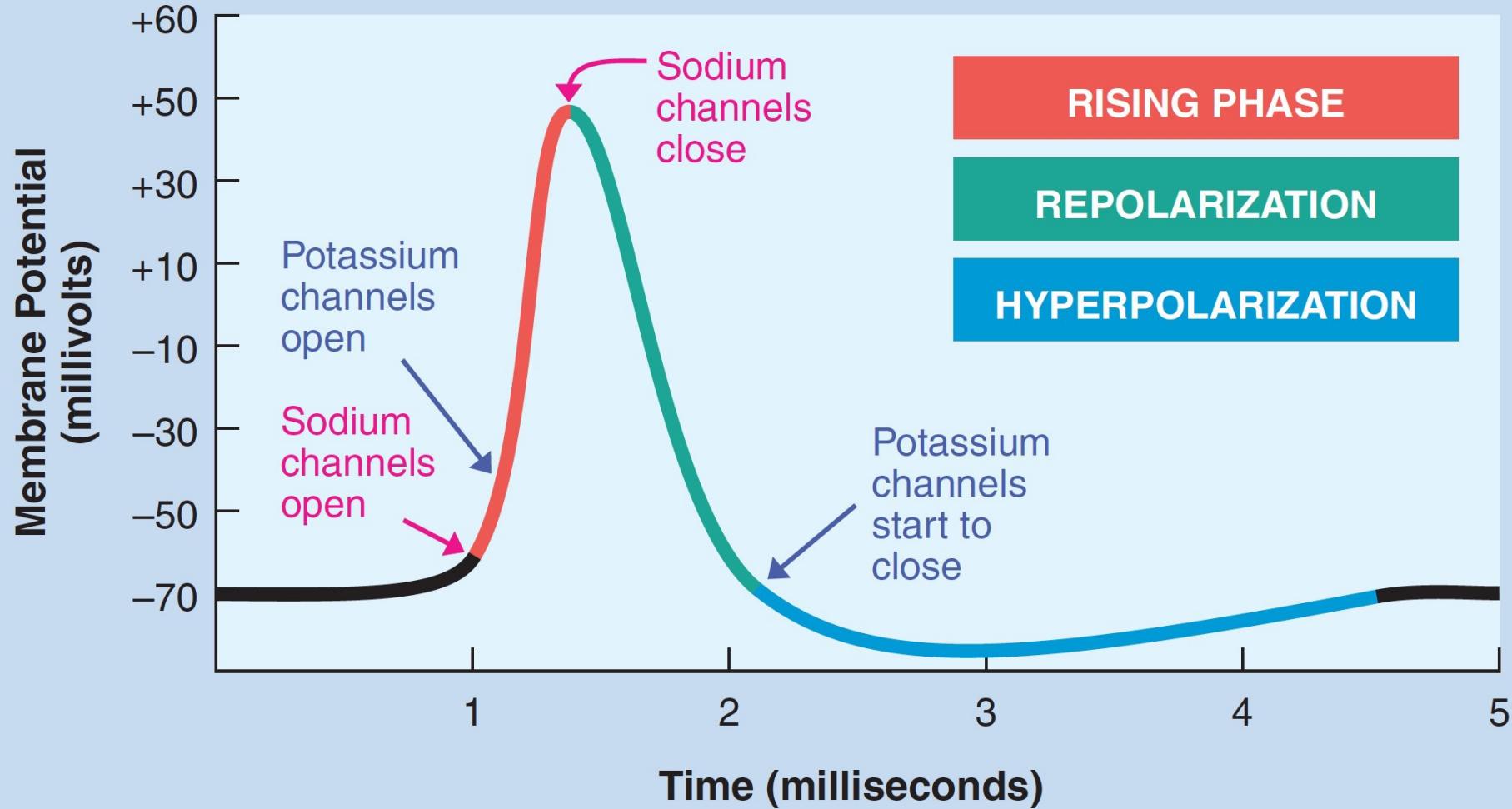


Repolarization

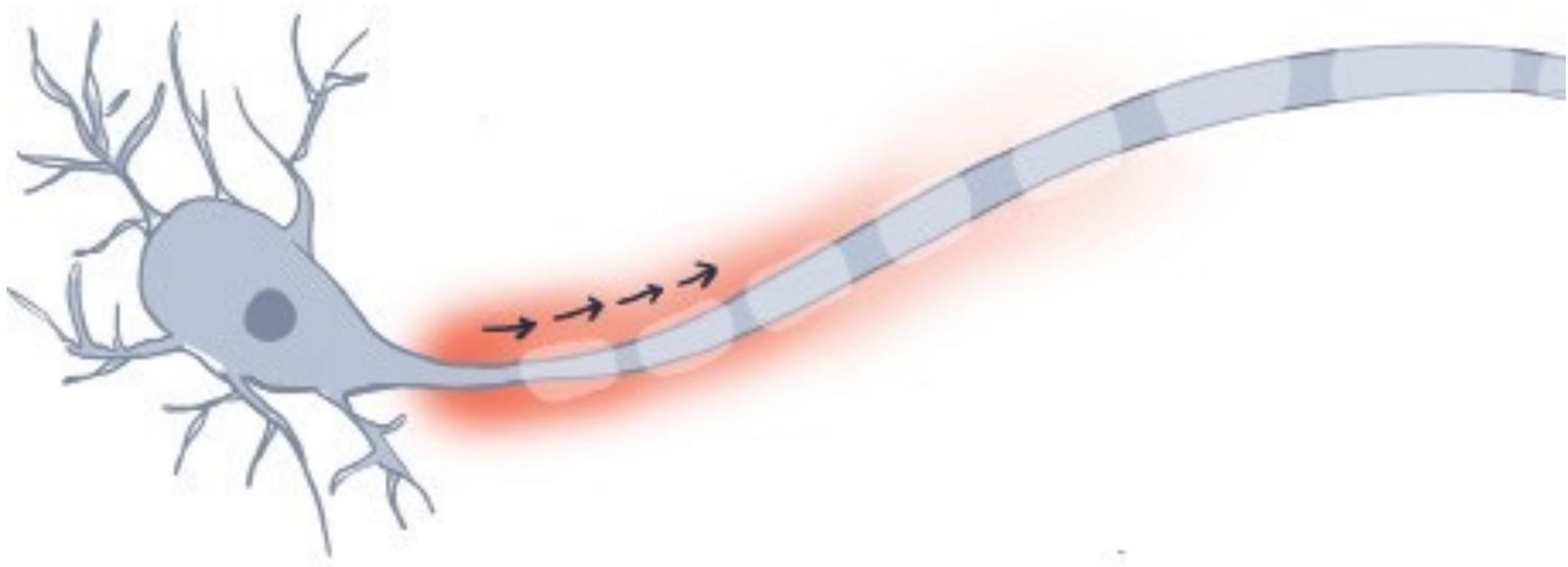
- K⁺ channels, as always, are open
- But even more K⁺ channels open during AP (some others are voltage-gated)
- Membrane is now pos., so which way does K⁺ flow?
 - Effect: return cell to neg. resting membrane potential
- Slow closing of voltage-gated K⁺ channels leads to hyperpolarization phase and the **relative refractory period**
- Na⁺/K⁺ pump restores ion balance over time (slow)



The action potential

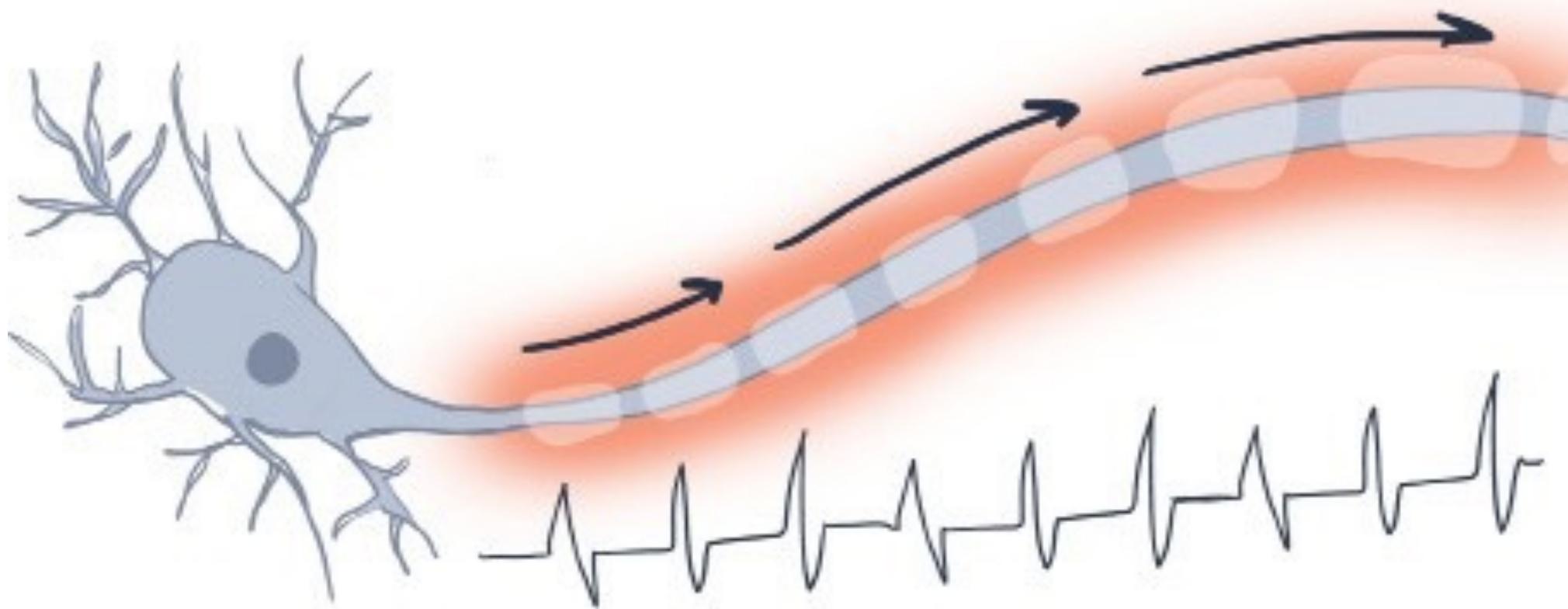


Effect of subthreshold stimulation of an axon:



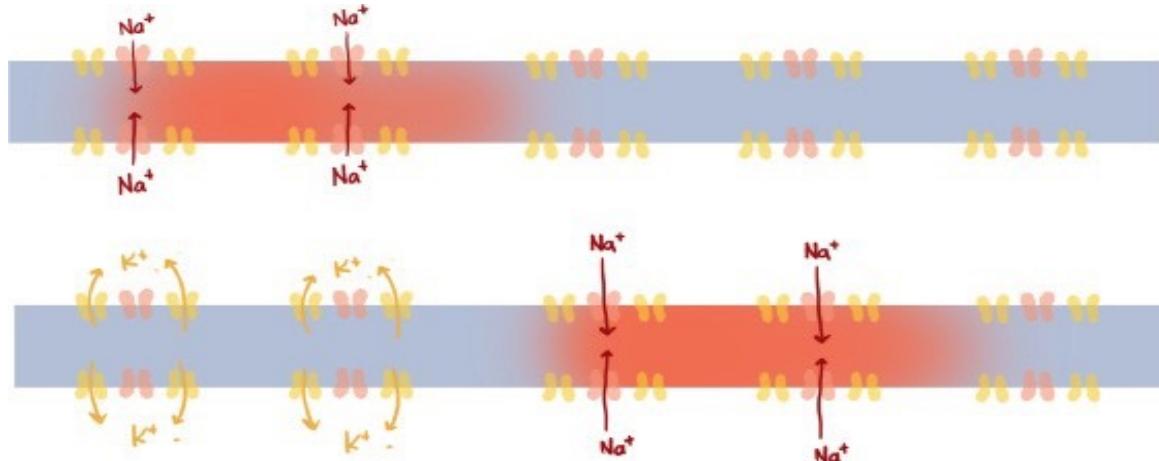
An excitatory potential is produced, but it is not sufficient to elicit an AP

Effect of suprathreshold stimulation of an axon:

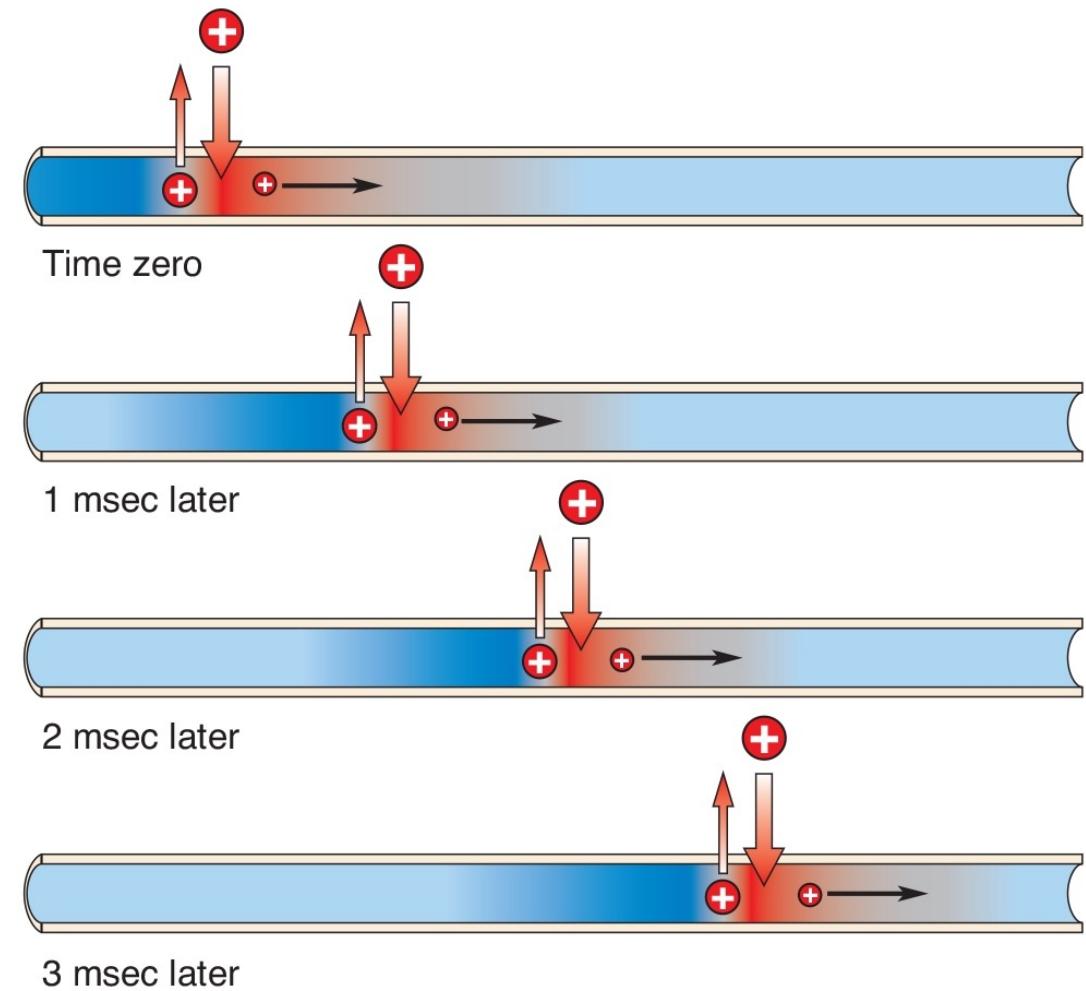


An excitatory potential is produced that exceeds the threshold of excitation and produces an AP that continues undiminished down the axon

Conduction in an Unmyelinated Axon

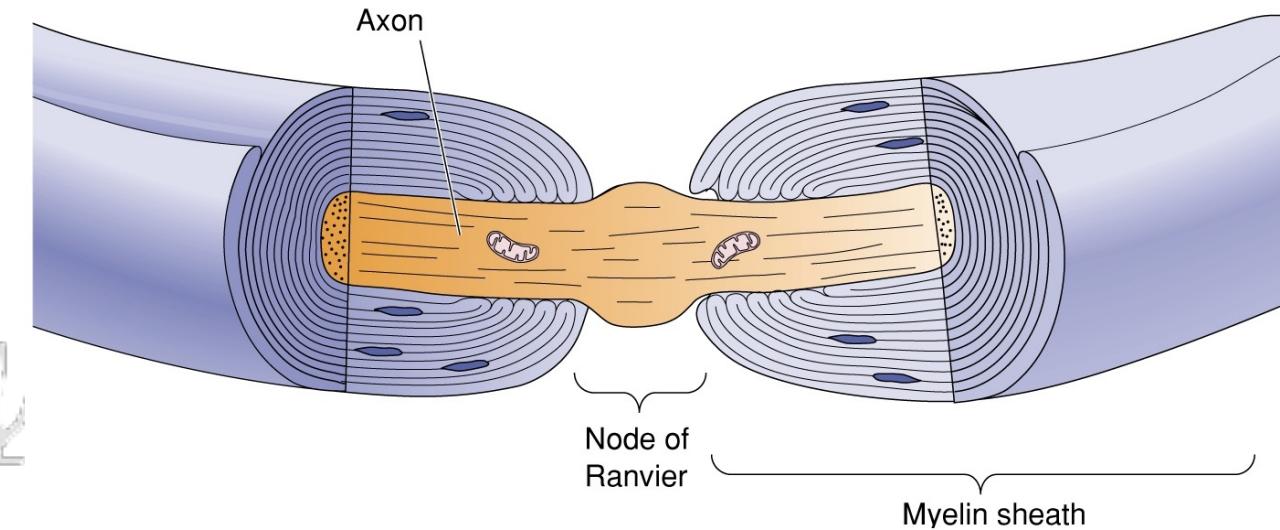
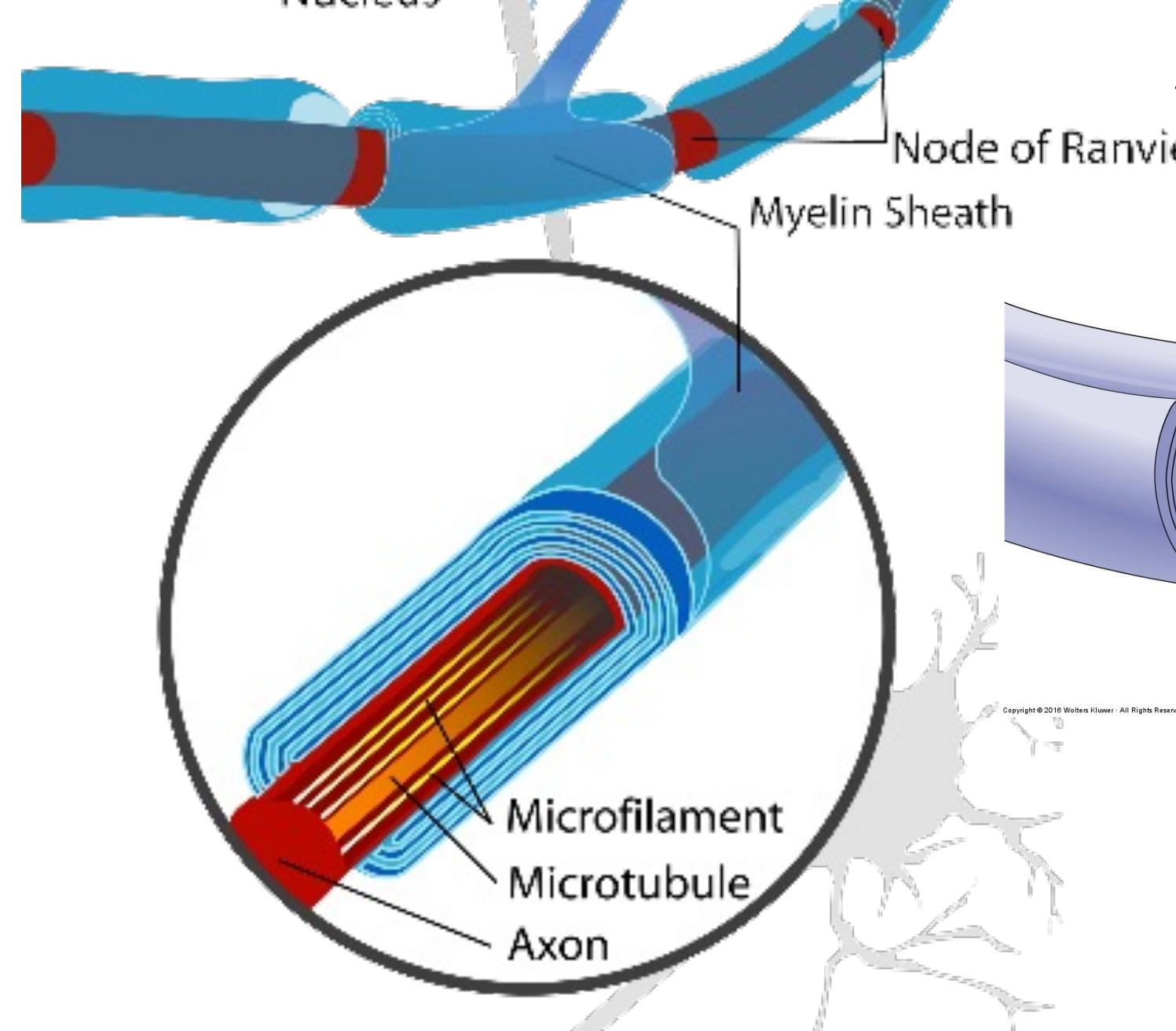


- Na⁺ channels are present all along the axon
- Unmyelinated axons: Na⁺ channels everywhere



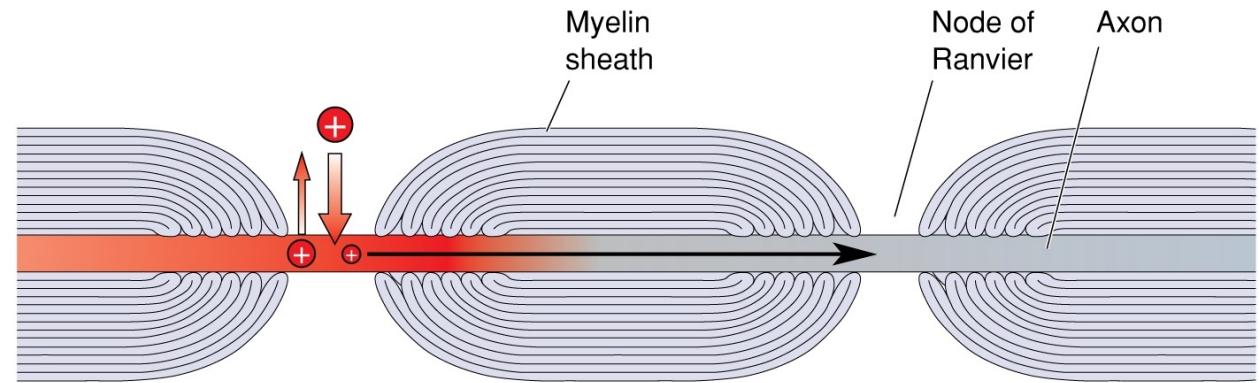
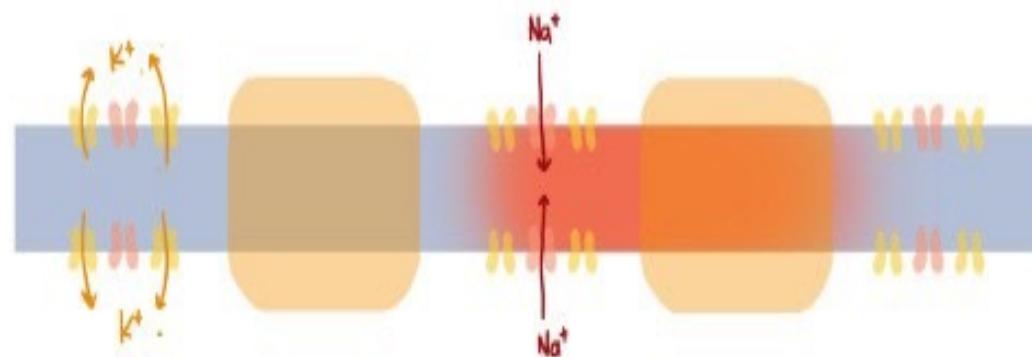
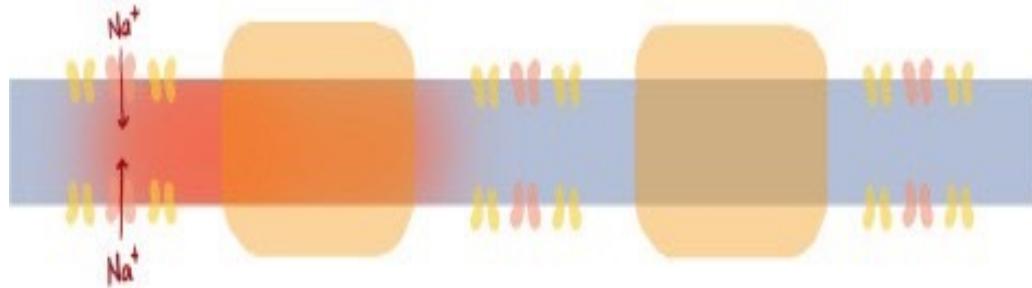
Conduction

Axon Myelination

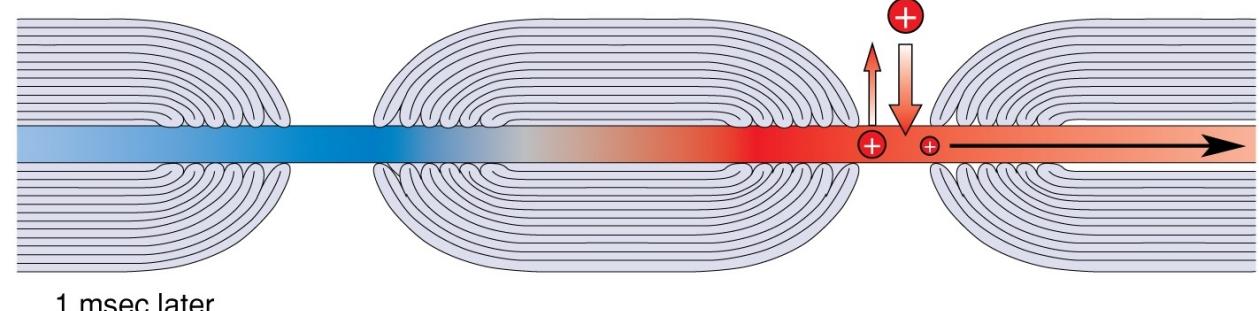


Conduction

Conduction in a Myelinated Axon



Time zero



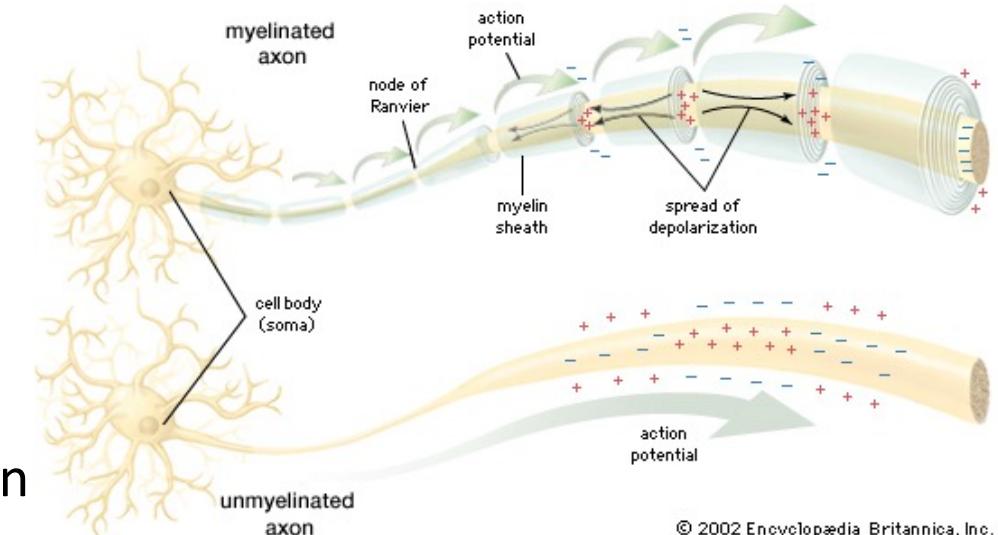
1 msec later

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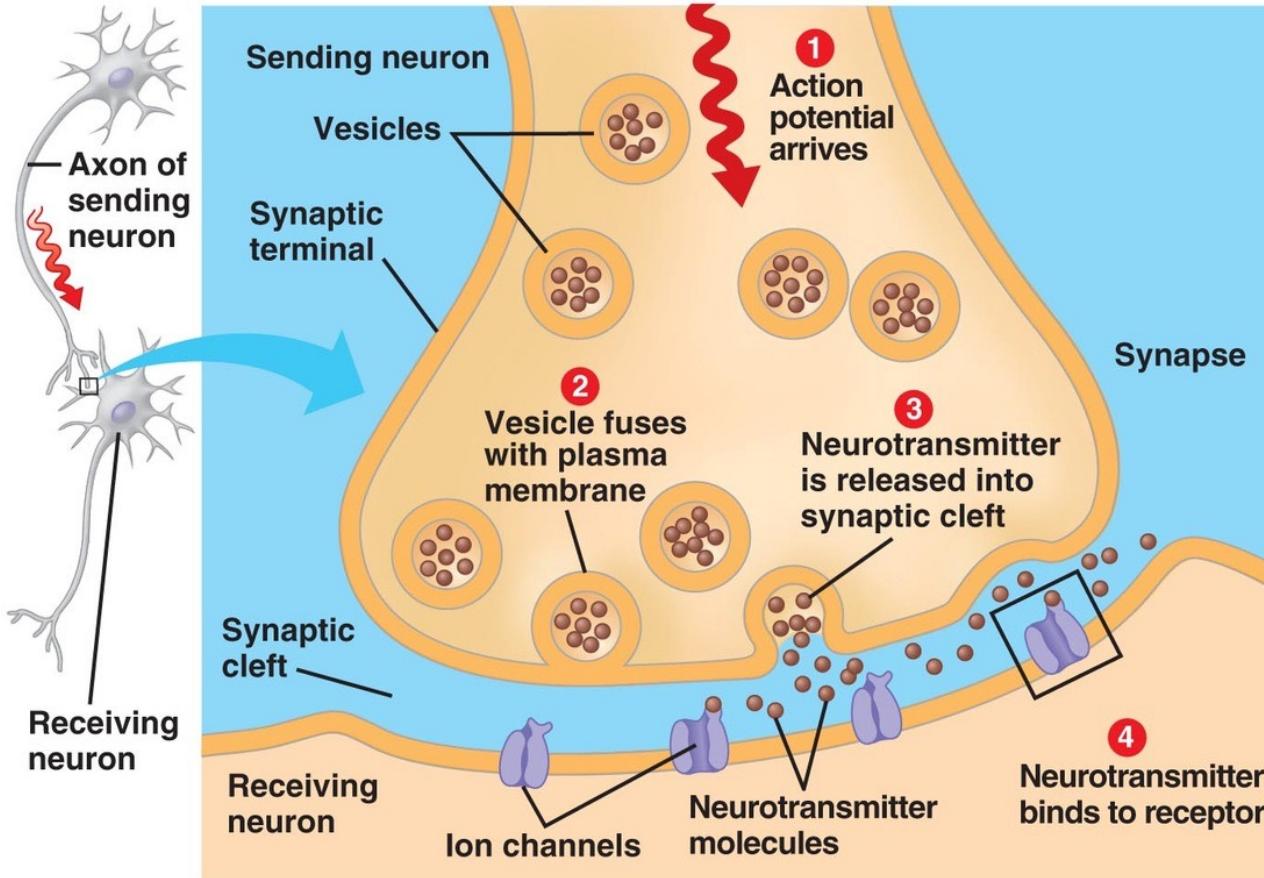
- Na^+ channels are present all along the axon
- Unmyelinated axons: Na^+ channels everywhere
- Myelinated axons: Na^+ channels only at the Nodes of Ranvier

Speed and direction

- Action potential is faster down myelinated axon than unmyelinated axon
 - Why? (Two reasons)
- Action potential only travels in one direction
 - Thanks to Na⁺ channel – why?



End of the line

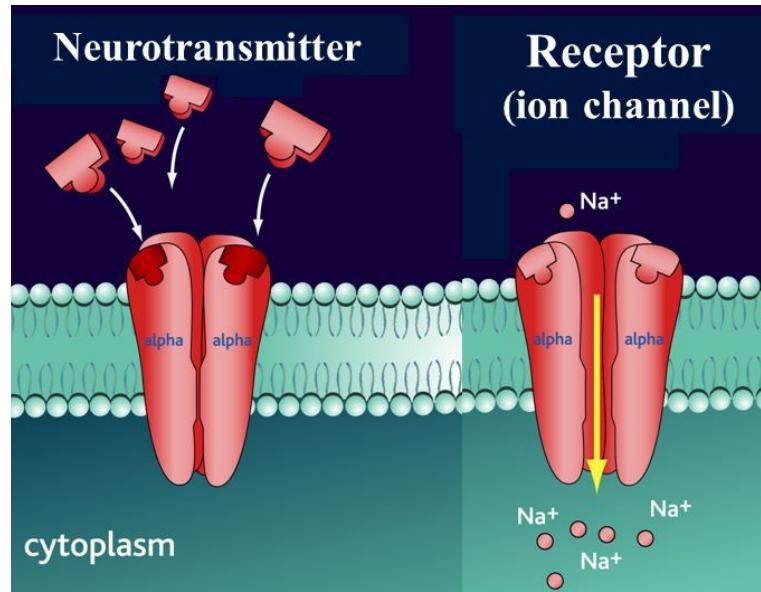
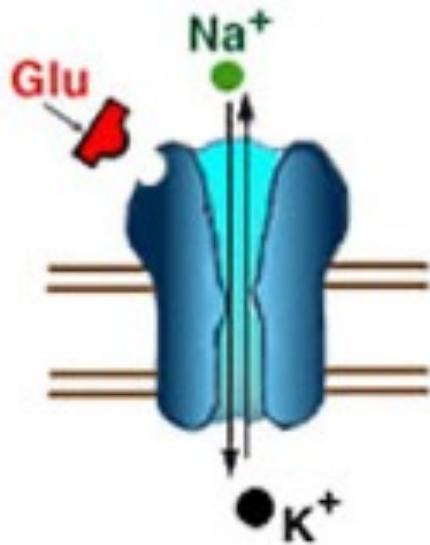


- Axon ends in terminal *boutons* (“buttons”)
- Bouton has *vesicles* (“bubbles”?) filled with *neurotransmitters*
- Action potential depolarizes bouton
 - Causes voltage-gated Ca^{++} channels to open
 - Ca^{++} causes vesicles to fuse with membrane
 - Neurotransmitters released into synapse

Neurotransmission

Welcome to the synapse

- Dendrite membrane has special *receptors* that fit, like lock and key, with the neurotransmitters
- Receptors are often just (closed) channels that open when they bind with neurotransmitter!
 - i.e. *ligand-gated ion channels*



Glu: glutamate, most common excitatory neurotransmitter

Neurotransmission

Types of Potentials

	PSPs	APs
Graded	Yes	No
Strength	AM	FM
Rapid	Yes	Less so
Decremental	Yes	No

A virtual neuron

1. Go to: <https://phet.colorado.edu/en/simulation/neuron> and run the simulation
2. Identify three proteins that we discussed
3. Identify one protein we did not discuss—it is real, but not particularly physiologically relevant for our story of RMPs and APs
4. Describe what's happening at rest (i.e. during resting membrane potential), as regards ionic flow (it helps to zoom in)
5. Describe the order of events when you stimulate the neuron (it helps to slow it down)
6. Turn on the potential chart (bottom right corner). What do you see when you stimulate the neuron? Be specific about voltage changes.
7. Turn on the “Show Concentrations” option (bottom right corner). What do the concentrations tell you at rest? How do those concentrations change when you stimulate the neuron? What do those changes tell you about the effects of an action potential?

