

PSYCH 260/BBH 203

Cellular neuroscience III

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2022-02-08 08:08:07

Today's Topics

- Warm-up
- What good are brains?
- Action potential propagation
- Another take on the resting and action potentials

Warm-up

Which force(s) act to move Na^+ ions *inward* in a neuron at resting potential?

- A. The force of diffusion
- B. The dark side of the force
- C. The electrostatic force
- D. Gravity
- E. Both A. and C.

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What good are brains?

Why brains?

- *Escherichia Coli (E. Coli)*
- *Paramecium*
- *Caenorhabditis Elegans (C. Elegans)*

Sterling & Laughlin, 2015

Escherichia Coli (E. Coli)

- Tiny, single-celled bacterium
- Feeds on glucose
- Chemosensory (“taste”) receptors on surface membrane
- Flagellum for movement
- Food concentration regulates duration of “move” phase
- ~4 ms for chemical signal to diffuse from anterior/posterior



Paramecium

- 300K larger than E. Coli
- Propulsion through coordinated beating of cilia
- Diffusion from head to tail ~40 s!
- Use *electrical* signaling instead
 - Na^+ channel opens (e.g., when stretched)
 - Voltage-gated Ca^{++} channels open, Ca^{++} enters, triggers cilia movement
 - Voltage propagates along cell membrane within ms

Caenorhabditis Elegans (C. Elegans)

- $\sim 10\times$ larger than paramecium
- multi-cellular ($n = 959$ cells total)
- $n = 302$ are neurons & $n = 56$ are glia
- Can swim, forage, mate



Why brains?

- Bigger bodies (need to send specific info)
- For neurons (point to point communication)
- Live longer
- Do more, do it faster, over larger distances & longer time periods

Why chemical & electrical communication?

- Chemical communication : short distances
 - Cheap, energy-efficient, “compute with chemistry”
- Electrical communication : long distances
 - More “expensive”/less energy-efficient

How action potentials propagate

AP propagation

- Propagation
 - move down axon, away from soma, toward axon terminals.
- Unmyelinated axon
 - Each segment “excites” the next

AP propagation is like



AP propagation

- Myelinated axon
 - AP “jumps” between *Nodes of Ranvier* via *saltatory conduction*
 - Nodes of Ranvier == unmyelinated sections of axon
 - voltage-gated Na^+ , K^+ channels exposed
 - Current flows through myelinated segments

Question

- Why does AP flow in one direction, away from soma?
 - Soma does not have (many) voltage-gated Na^+ channels.
 - Soma is not myelinated.
 - Refractory periods mean polarization only in one direction.

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Conduction velocities

WIKIPEDIA

Nerve conduction velocity

Nerve conduction velocity (CV) is an important aspect of nerve conduction studies. It is the speed at which an electrochemical impulse propagates down a neural pathway. Conduction velocities are affected by a wide array of factors, which include; age, sex, and various medical conditions. Studies allow for better diagnoses of various neuropathies, especially demyelinating diseases as these conditions result in reduced or non-existent conduction velocities.

Contents

Normal conduction velocities

Testing methods

Nerve conduction studies

Micromachined 3D electrode arrays

Causes of conduction velocity deviations

Anthropometric and other individualized factors

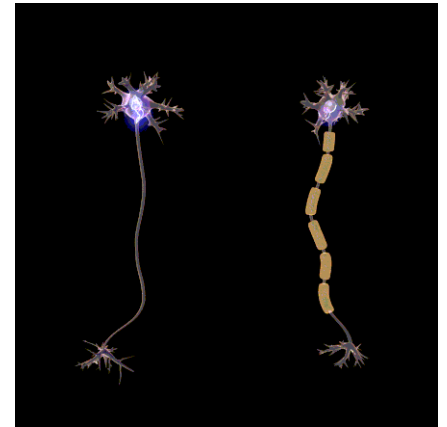
Age

Sex

Temperature

Height

Hand factors



Saltatory conduction

Conduction velocities

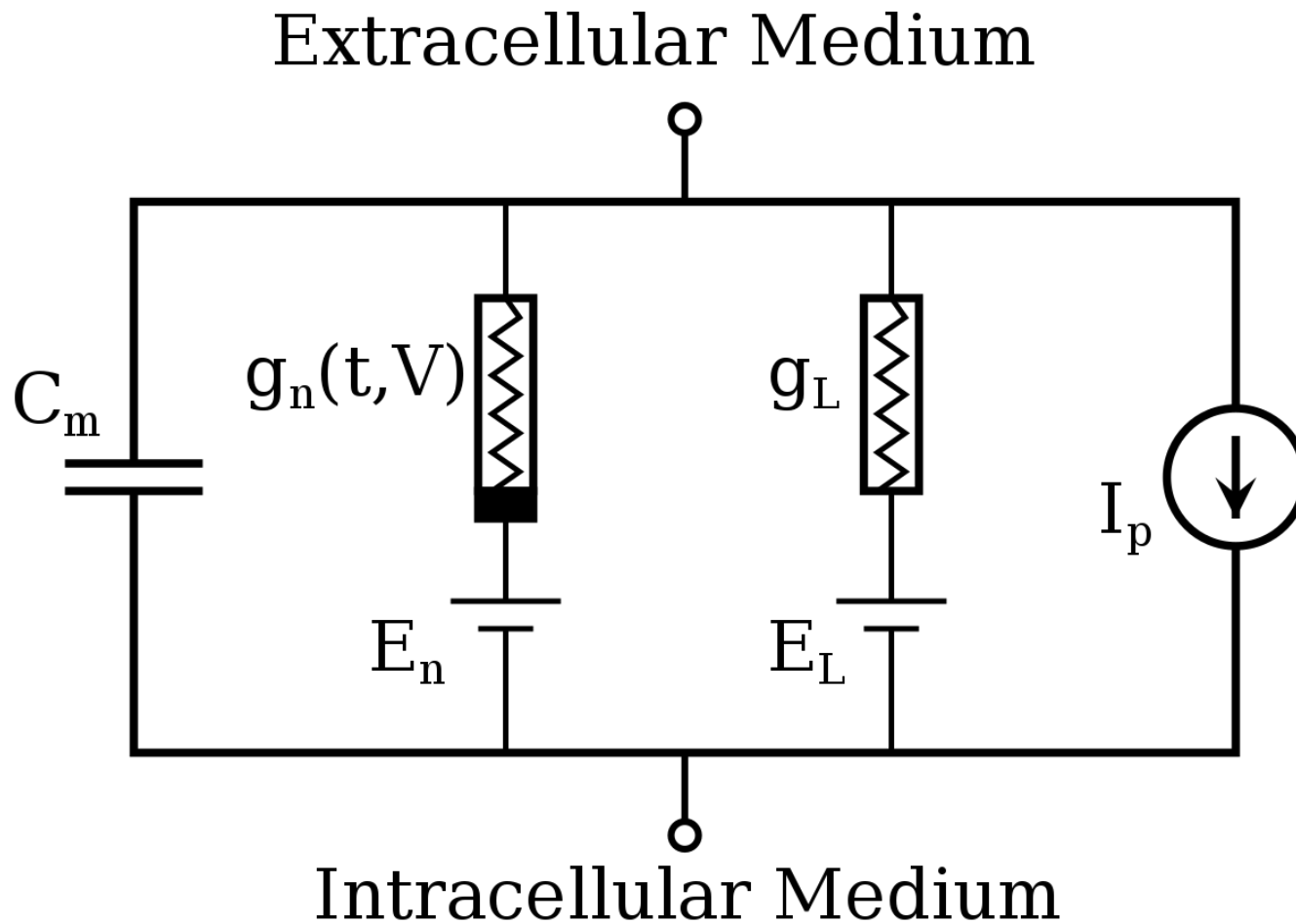
- Axons carry information at different rates
 - More myelin -> faster
 - Larger diameter axon -> faster
- PNS seems to prioritize
 - Somatosensory information & muscle control

Information processing

- AP amplitudes don't vary (much)
 - All or none
 - Na^+/K^+ pumps working all the time
 - $[K^+]$ & $[Na^+]$ don't vary much, so
 - V_{K^+} & V_{Na^+} don't vary much
- AP frequency and timing vary
 - Rate vs. timing codes
 - Neurons use both

Another take...

The Hodgkin-Huxley (HH) model



By [Krishnavedala](#) - Own work, [CC0](#), [Link](#)

HH model: Membrane as simple circuit

- Membrane as capacitor (C): stores charge
- Ion channels: resistors that can vary in conductance ($g = \frac{1}{R}$)
- Ion flows create current (I)
- Ohms Law: $V = \frac{I}{g}$ or $Vg = I$

The K^+ story

- Na^+/K^+ pump pulls K^+ in
- $[K^+]_{in}$ (~150 mM) \gg $[K^+]_{out}$ (~4 mM)
- Outward flow of K^+ through passive/leak channels via force of diffusion
- Outflow stops when *membrane potential*, V_m = *equilibrium potential* for K^+

Equilibrium potential

- Voltage (V_K) that keeps system in equilibrium
 - $[K^+]_{in} \gg [K^+]_{out}$
- Nernst equation
 - $V_K = \frac{RT}{(+1)F} \ln\left(\frac{[K^+]_{out}}{[K^+]_{in}}\right)$
 - $V_K = \sim -90 \text{ mV}$
 - Negative inside/positive outside keeps $[K^+]$ concentration gradient

Equilibrium potential

- K^+ flows out through passive/leak channels
- Most K^+ remains near membrane
- Separation from A^- creates charge $\frac{K+K+K+K+K+}{A-A-A-A-A-}$ along capacitor-like membrane
- V_m (membrane potential) $\rightarrow V_{K^+}$

Equilibrium potentials calculated under typical conditions

Ion	[inside]	[outside]	Voltage
K+	~150 mM	~4 mM	~ -90 mV
Na+	~10 mM	~140 mM	~ +55-60 mV
Cl-	~10 mM	~110 mM	~ - 65-80 mV

$$V_K = \frac{RT}{(+1)F} \ln \frac{[K^+]_o}{[K^+]_i}$$

The Na^+ story

- Na^+/K^+ pump pushes Na^+ out
- $[Na^+]_{in}$ (~ 10 mM) \ll $[Na^+]_{out}$ (~ 140 mM)
- Equilibrium potential for Na^+ , $V_{Na^+} = \sim +55$ mV
 - Inside positive/outside negative to $[Na^+]$ concentration gradient
- If Na^+ alone, $V_m \rightarrow V_{Na}$ ($\sim +55$ mV)

Resting potential

- Sum of outward K^+ and inward Na^+
 - Membrane more permeable to K^+ than Na^+ ,
 $p_{K^+} > p_{Na^+}$
 - Outward flow of K^+ > inward flow of Na^+
 - Resting potential (~ -70 mV) closer to V_{K^+} (-90 mV) than V_{Na^+} ($+55$ mV)

Resting potential

- Goldman-Hodgkin-Katz equation

- $$V_m = \frac{RT}{F} \ln \left(\frac{p_K [K^+]_{out} + p_{Na} [Na^+]_{out}}{p_K [K^+]_{in} + p_{Na} [Na^+]_{in}} \right)$$

“Driving force” and equilibrium potential

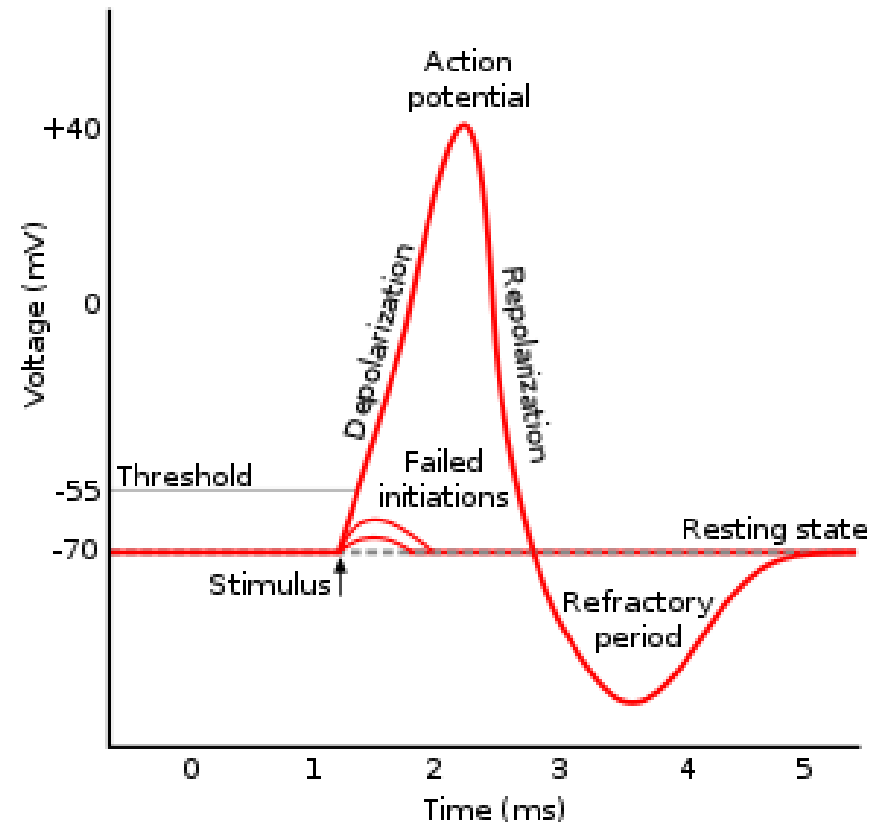
- “Driving Force” on a given ion depends on difference between
 - Equilibrium potential for given ion **AND**
 - Neuron’s current membrane potential (V_m)
 - V_m reflects combined effects of all ions

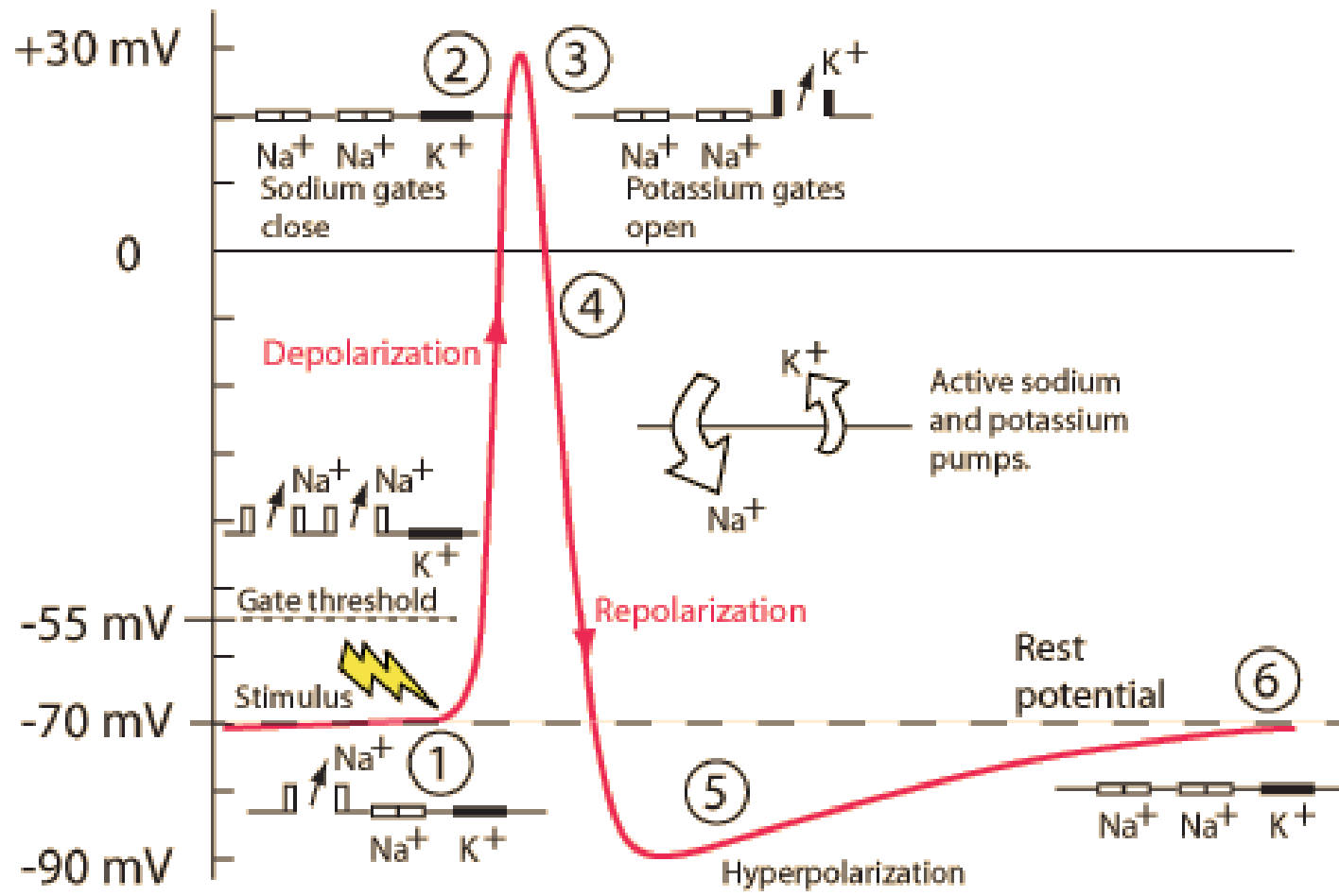
“Driving force” and equilibrium potential

- Anthropomorphic (‘in human form’) metaphor
 - K^+ “wants” to flow out (hyperpolarize neuron)
 - Na^+ “wants” to flow in (depolarize neuron)
 - Strength of that “desire” depends on distance from the equilibrium potential for each ion

- Humans (often) think about causes and effects in psychological terms
 - Ok to do so, as long as we recognize when it's just a metaphor

Action potentials and driving forces



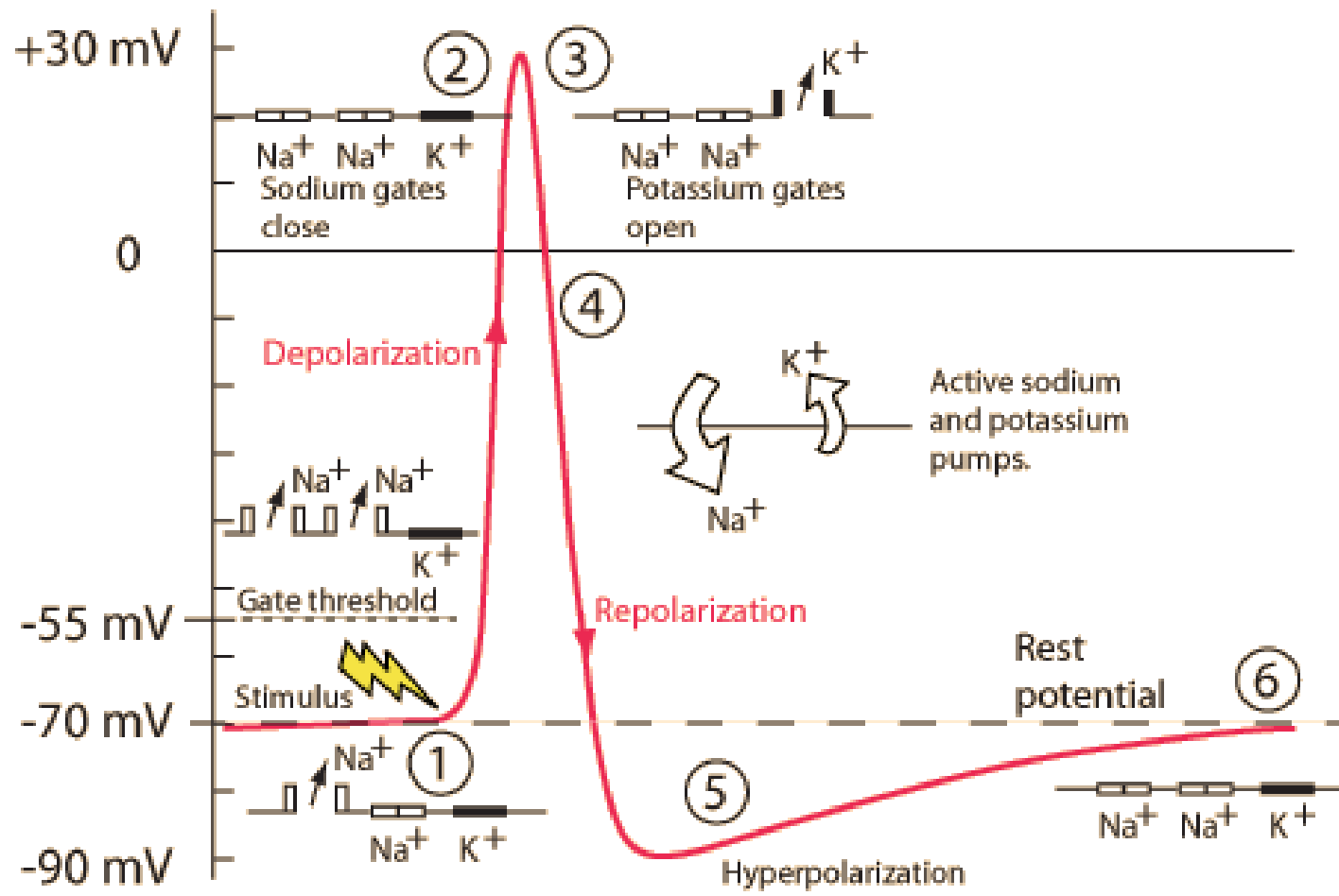


Voltage-gated Na^+ and K^+ channels

- Dynamic elements; change state over time
 - Hodgkin-Huxley (HH) equations describe state changes
- Open and close with changes in voltage
- Voltage-gated Na^+ also *inactivate; de-inactivate* as voltage changes

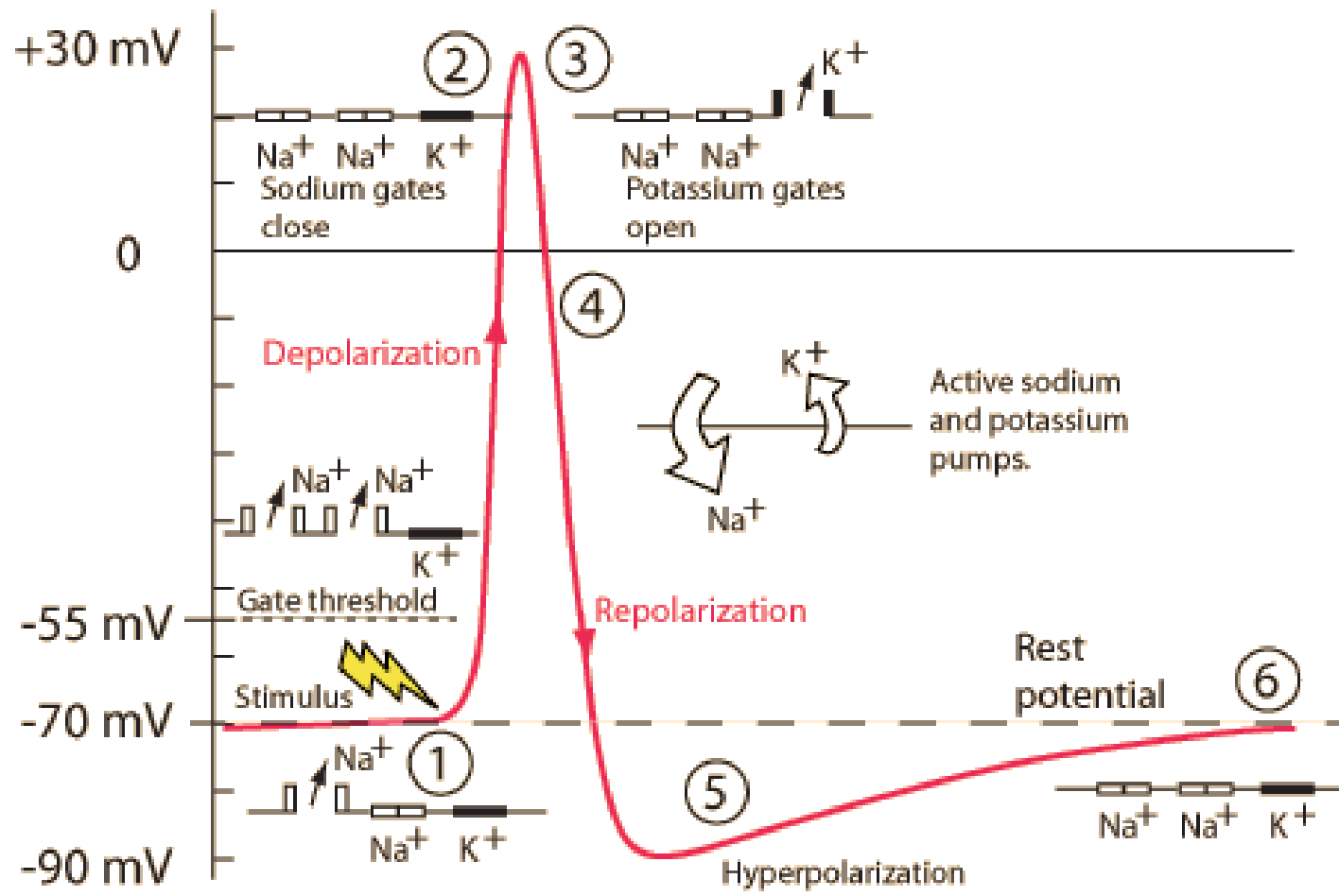
Neuron at rest

- Driving force on K^+ weakly out
 - $-70 \text{ mV} - (-90 \text{ mV}) = +20 \text{ mV}$
- Driving force on Na^+ strongly in
 - $-70 \text{ mV} - (+55 \text{ mV}) = -125 \text{ mV}$
- Na^+/K^+ pump maintains concentrations



Action potential rising phase

- Voltage-gated Na^+ channels open
- Membrane permeability to Na^+ increases
 - Na^+ inflow through passive + voltage-gated channels
 - continued K^+ outflow through passive channels

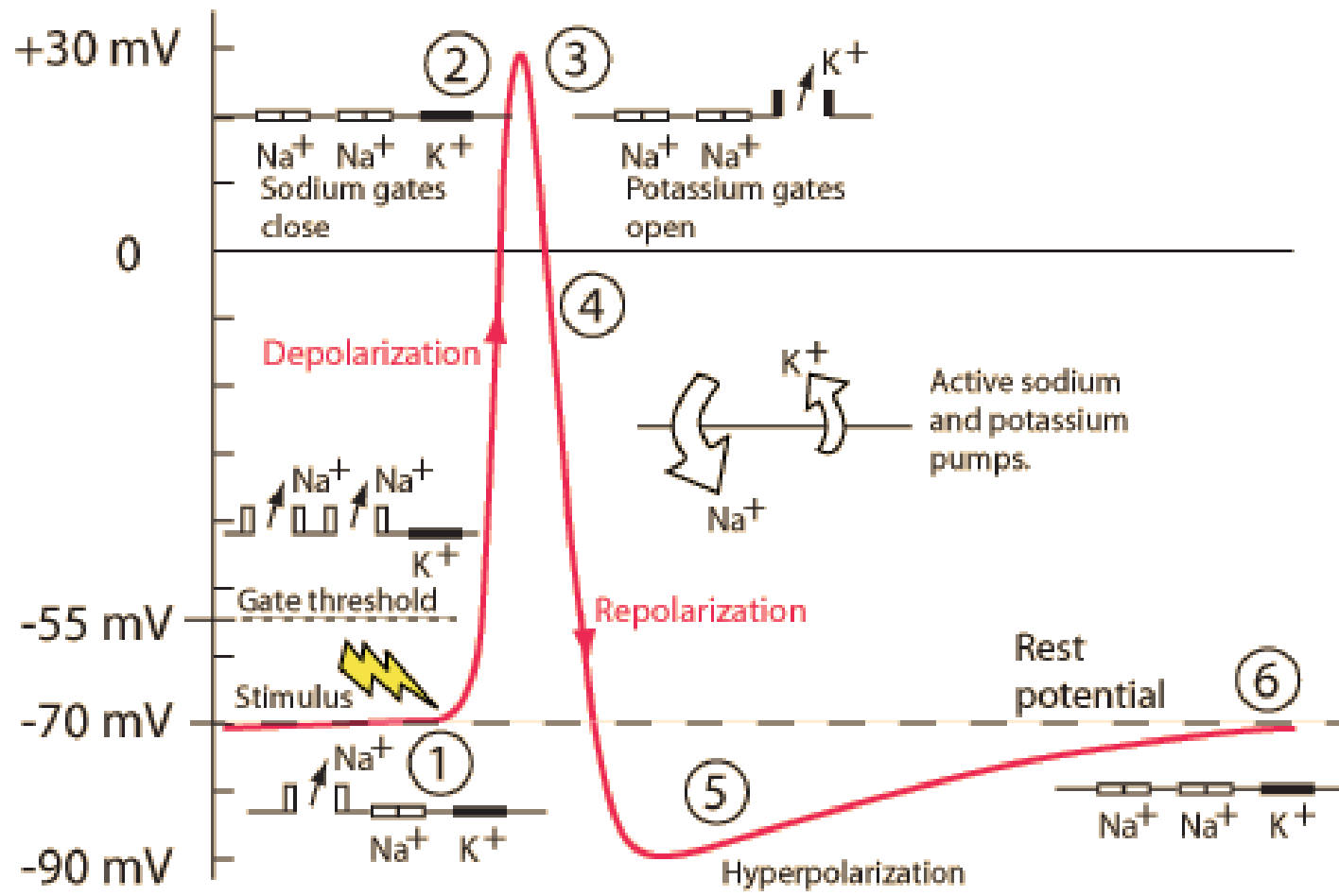


Peak

- Membrane permeability to Na^+ reverts to resting state
 - Voltage-gated Na^+ channels close & inactivate
 - Slow inflow due to small driving force (+30 mV - 55mV = -25 mv)

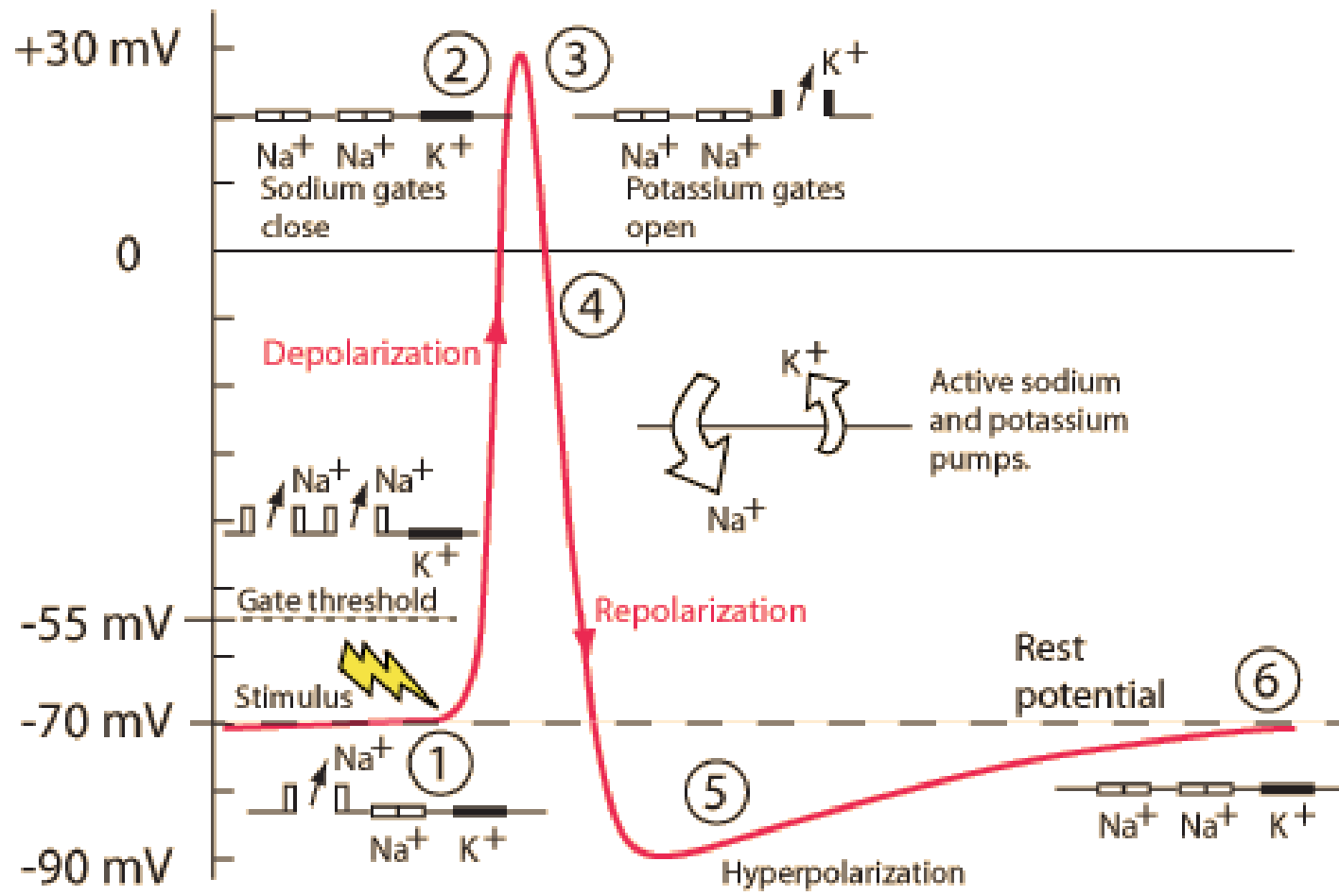
Peak

- Membrane permeability to K^+ increases
 - Voltage-gated K^+ channels open
 - Fast outflow due to strong driving force (+30 mv - (-90 mv) = +120 mV)



Falling phase

- K^+ outflow
 - Through voltage-gated K^+ and passive K^+ channels
- Na^+ inflow
 - Through passive channels only

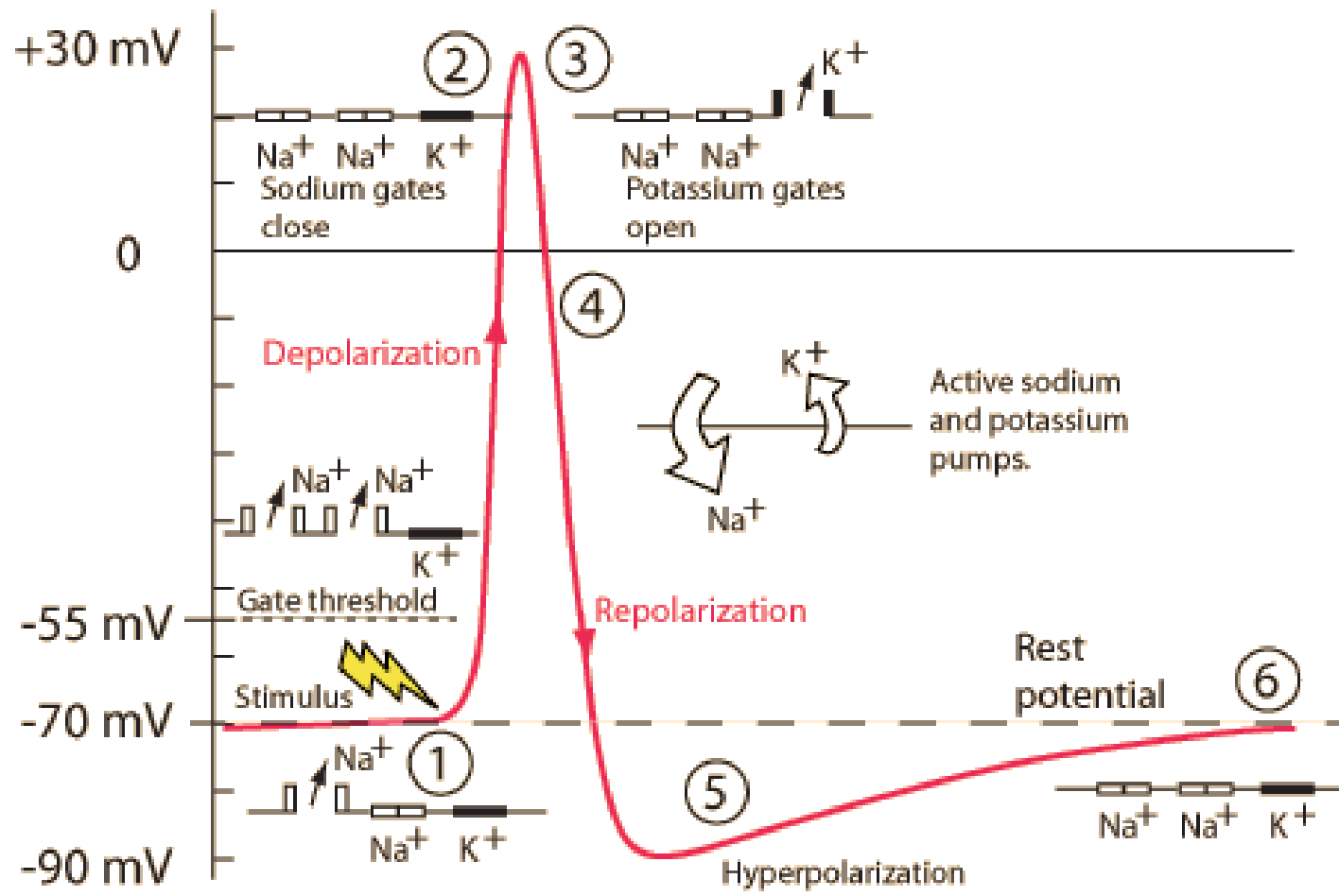


Absolute refractory phase (period)

- Cannot generate action potential (AP) no matter the size of the stimulus
- Membrane potential more negative (~ -90 mV) than at rest (~ -70 mV)
- Voltage-gated Na^+ channels still inactivated
 - Driving force on Na^+ high (-90 mV - 55 mV = -145 mV), but...

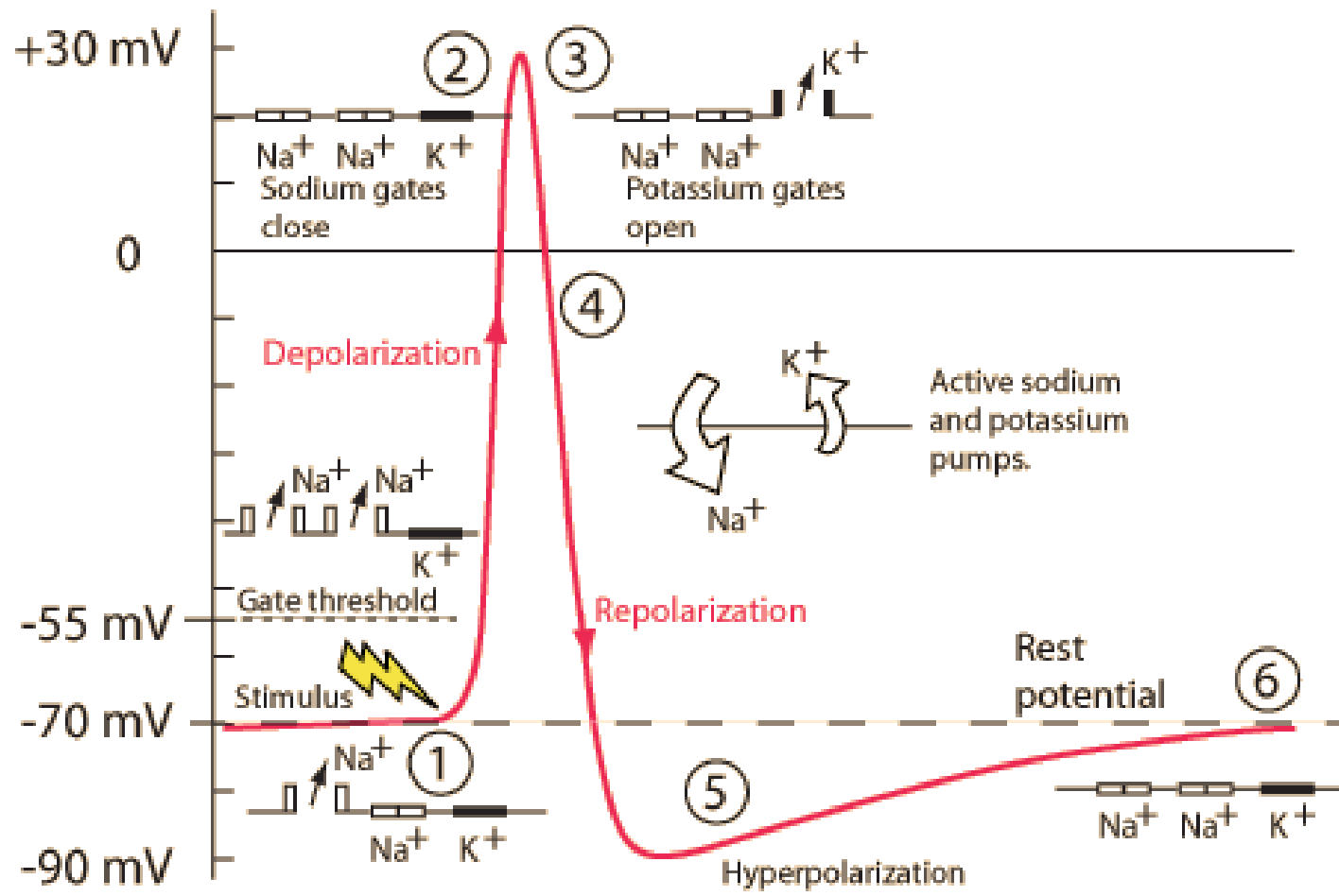
Absolute refractory phase (period)

- Voltage-gated K^+ channels closing
 - Driving force on K^+ tiny or absent
- Na^+/K^+ pump restoring concentration balance



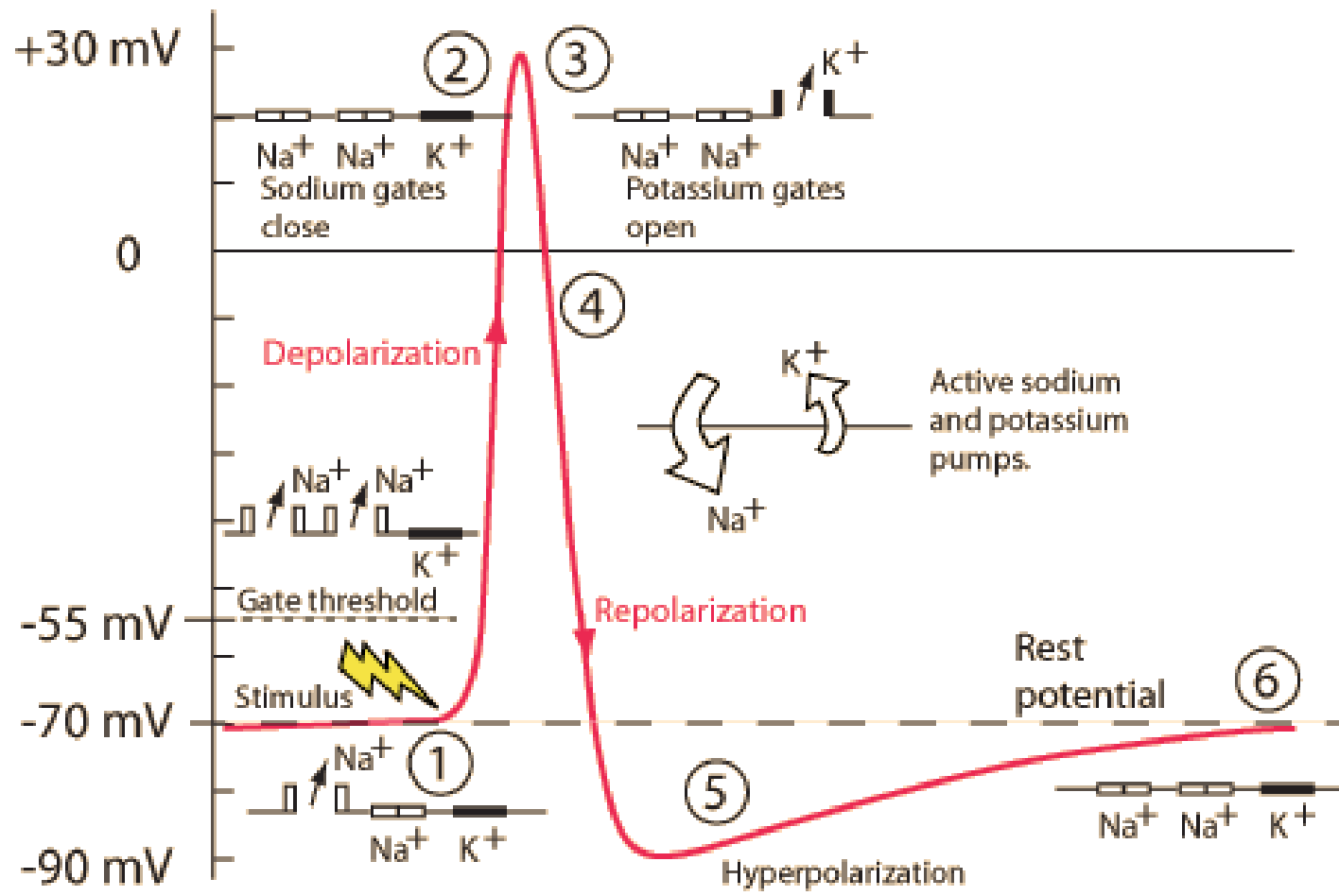
Relative refractory phase (period)

- Can generate AP with larg(er) stimulus
- Some voltage-gated Na^+ 'de-inactivate', can open if
 - Larger input
 - Membrane potential is more negative than resting potential

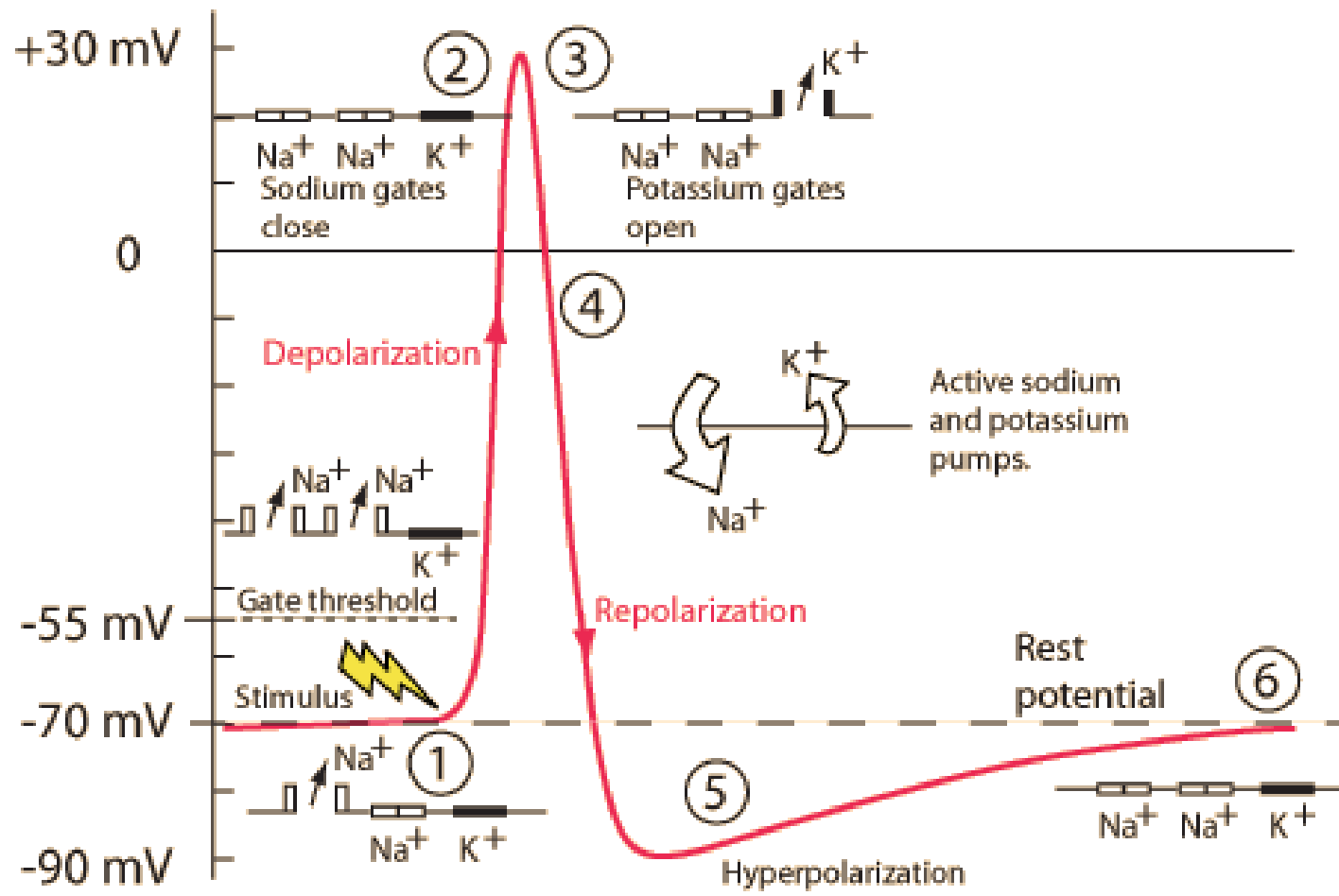


Neuron at rest

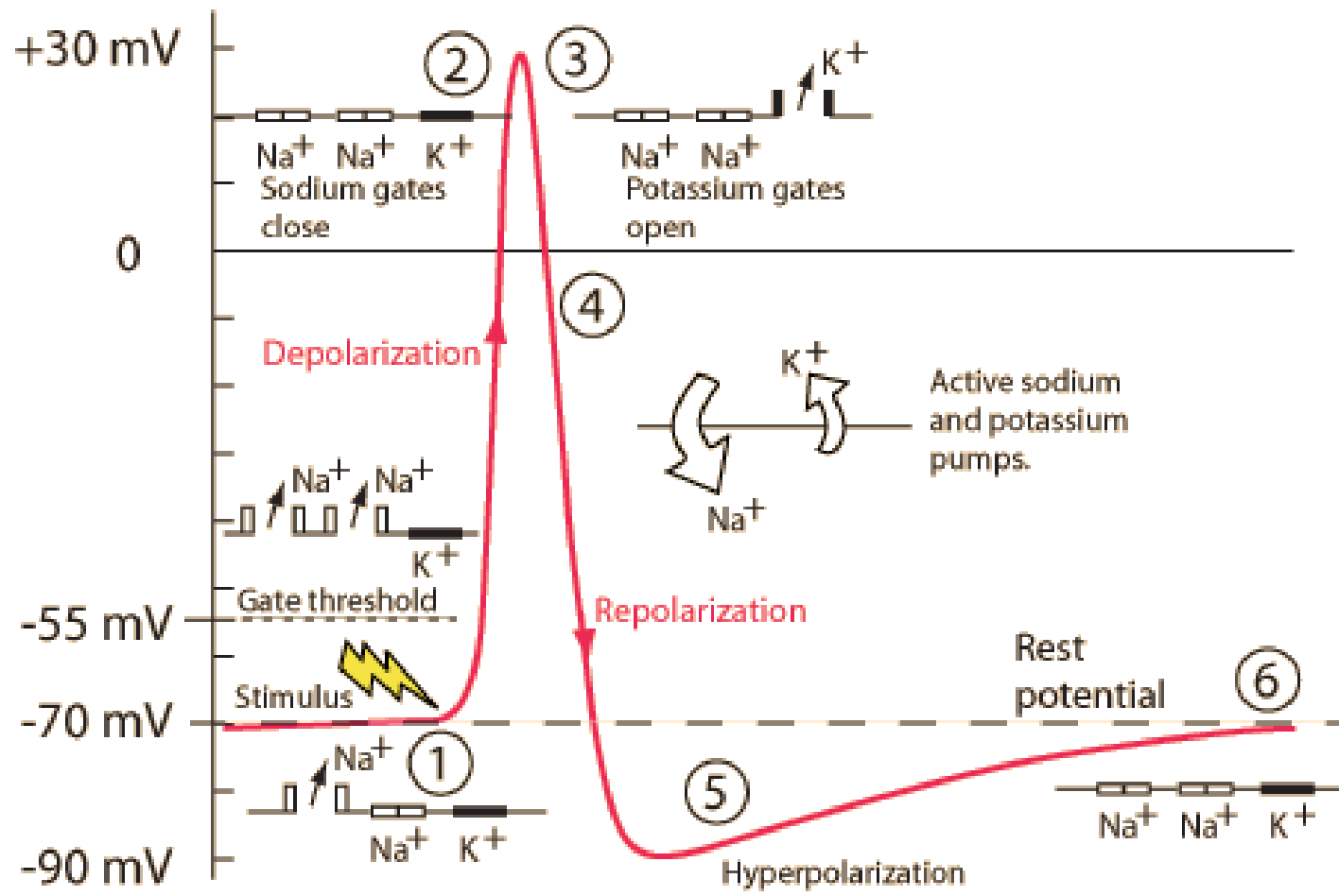
- Voltage-gated Na^+ closed, but ready to open
- Voltage-gated K^+ channels closed, but ready to open
- Membrane potential V_m at rest (~60-75 mV)
- Na^+/K^+ pump still working...



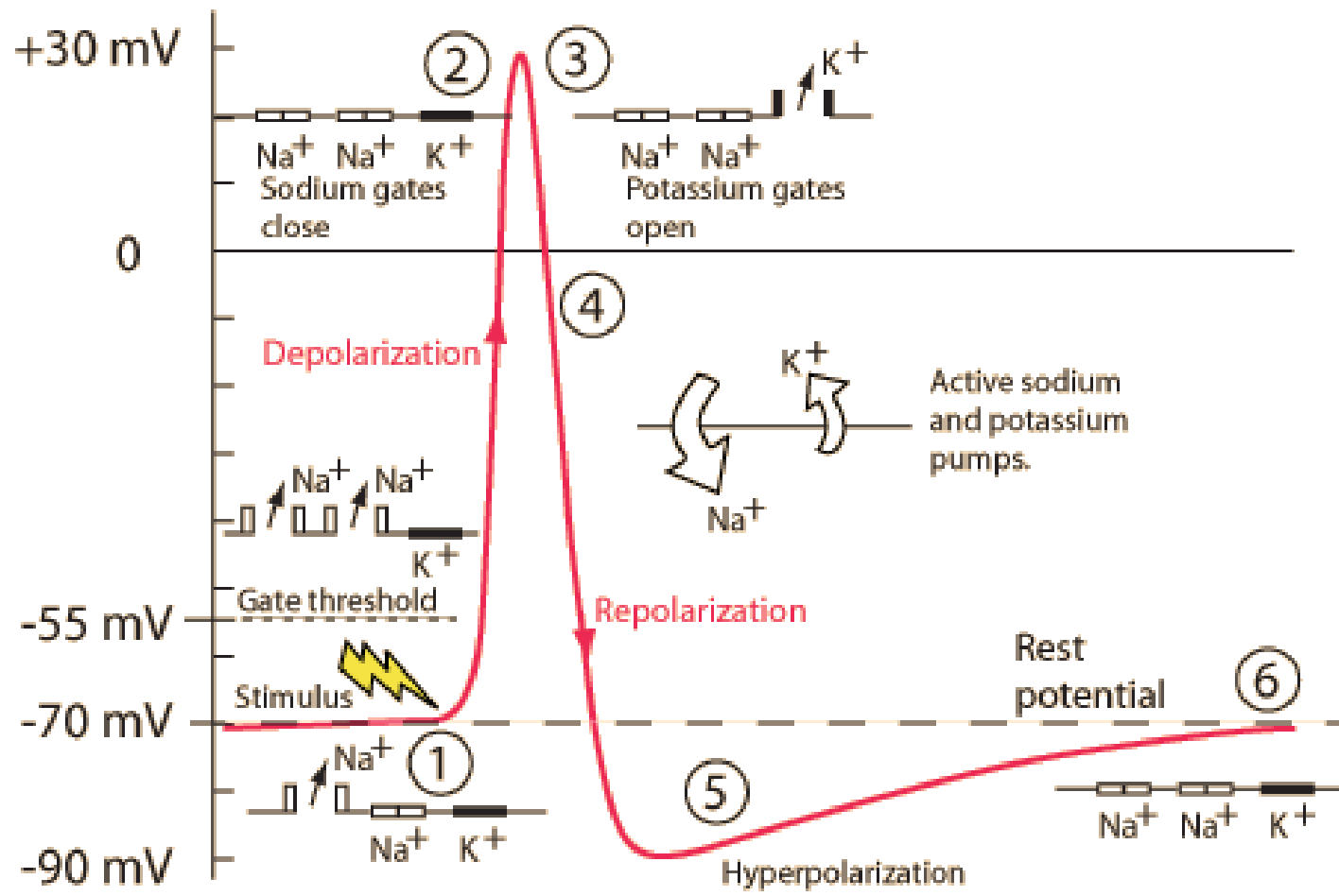
Phase	Ion	Driving force	Flow direction	Flow magnitude
Rest	K ⁺	20 mV	out	small
	Na ⁺	125 mV	in	small



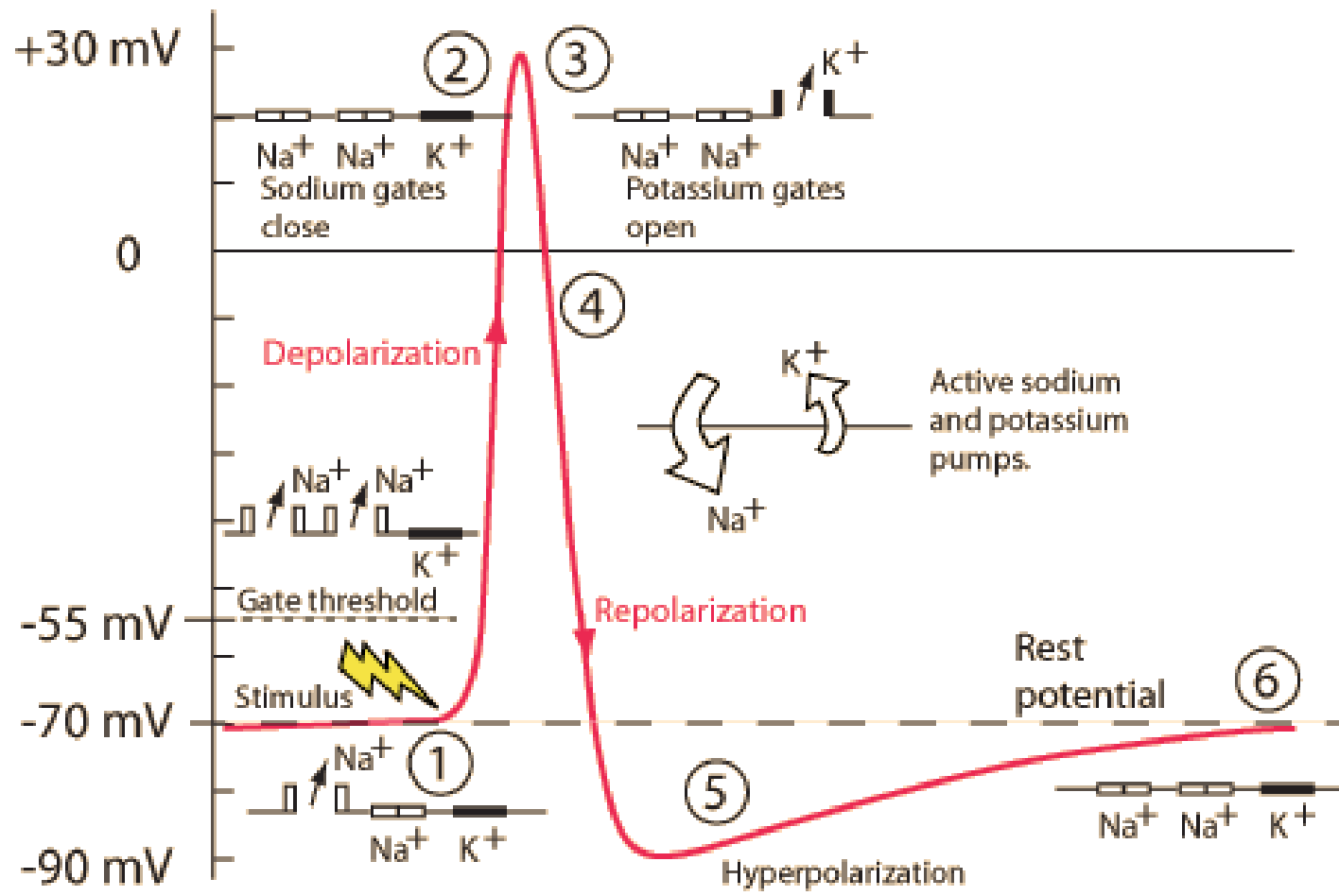
Phase	Ion	Driving force	Flow direction	Flow magnitude
Rising	K ⁺	growing	out	growing
	Na ⁺	shrinking	in	high



Phase	Ion	Driving force	Flow direction	Flow magnitude
Peak	K ⁺	120 mV	out	high
	Na ⁺	20 mV	out	small



Phase	Ion	Driving force	Flow direction	Flow magnitude
Falling	K	shrinking	out	high
	Na ⁺	growing	in	small



Phase	Ion	Driving force	Flow direction	Flow magnitude
Refractory	K	~0 mV	out	small
	Na ⁺	145 mV	in	small

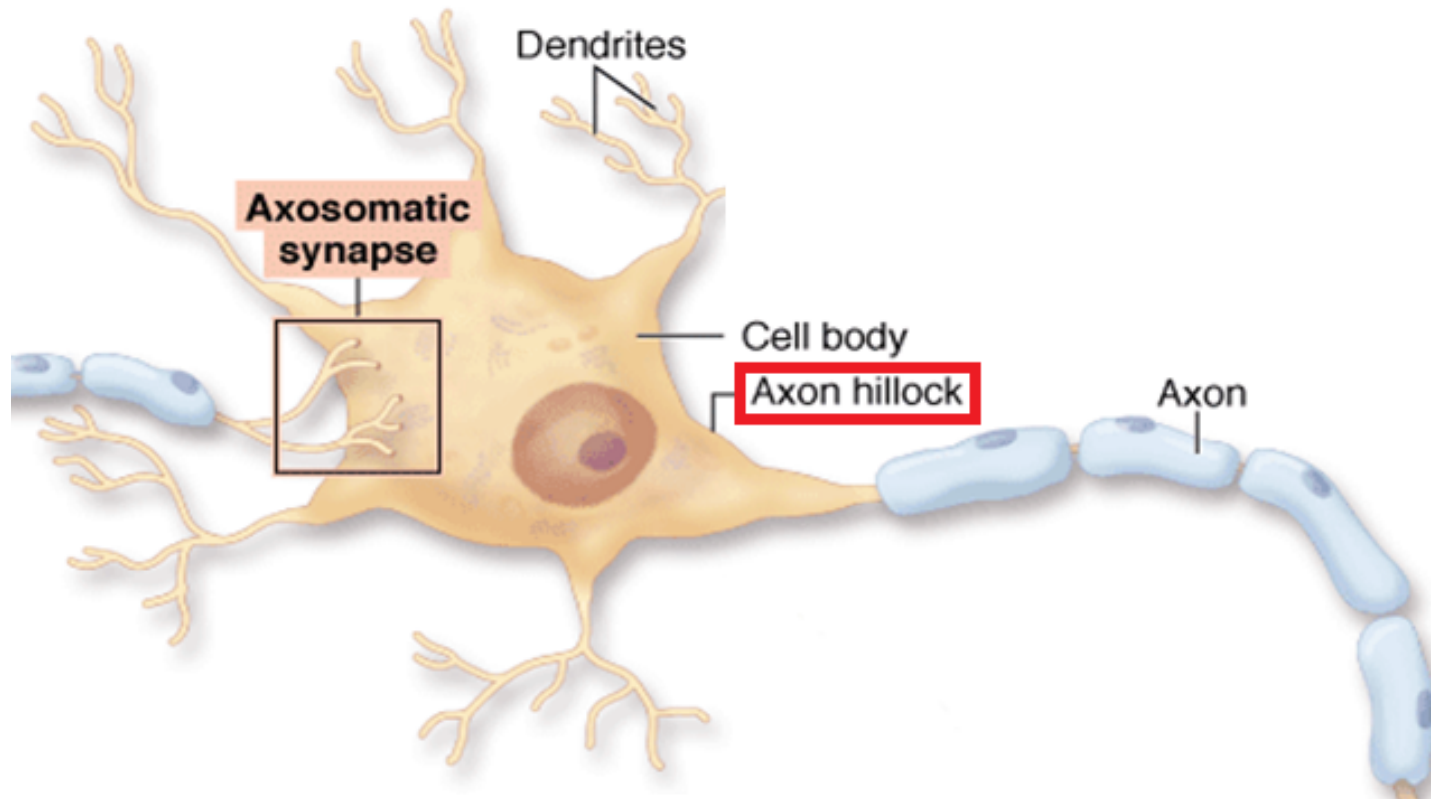
Animation

<https://phet.colorado.edu/sims/html/neuron/latest/neuron>

Generating APs

- *Axon hillock*
 - Portion of soma adjacent to axon
 - Integrates/sums input to soma
- *Axon initial segment*
 - Umyelinated portion of axon adjacent to soma
 - Voltage-gated Na^+ and K^+ channels exposed
 - If sum of input to soma $>$ threshold, voltage-gated Na^+ channels open

Axon hillock, axon initial segment



[Axon Hillock](#) by [M.aljar3i](#) - Own work. Licensed under [CC BY-SA 3.0](#) via [Commons](#)

Next time...

- Exam 1