PSYCH 260/BBH 203

Cellular neuroscience III

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2022-02-15 08:10:21

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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At the (positive voltage) *peak* of the action potential, which force(s) act to move K+ ions *outward*?

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At the (positive voltage) *peak* of the action potential, which force(s) act to move K+ ions *outward*?

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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)

- $\sim 10x$ larger than paramecium
- multi-cellular ($n = 959$ cells total)
- $n = 302$ are neurons & $n = 56$ are glia
- nervous system 37% of cells vs. ~0.5% in humans
- Can swim, forage, mate

Why brains?

- Bigger bodies (need to process specific info, move through water, air, on land)
- 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

Axon is like an electrical cable

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knitr::include_graphics("http://pittmedneuro.com/img/Cable.jpg")
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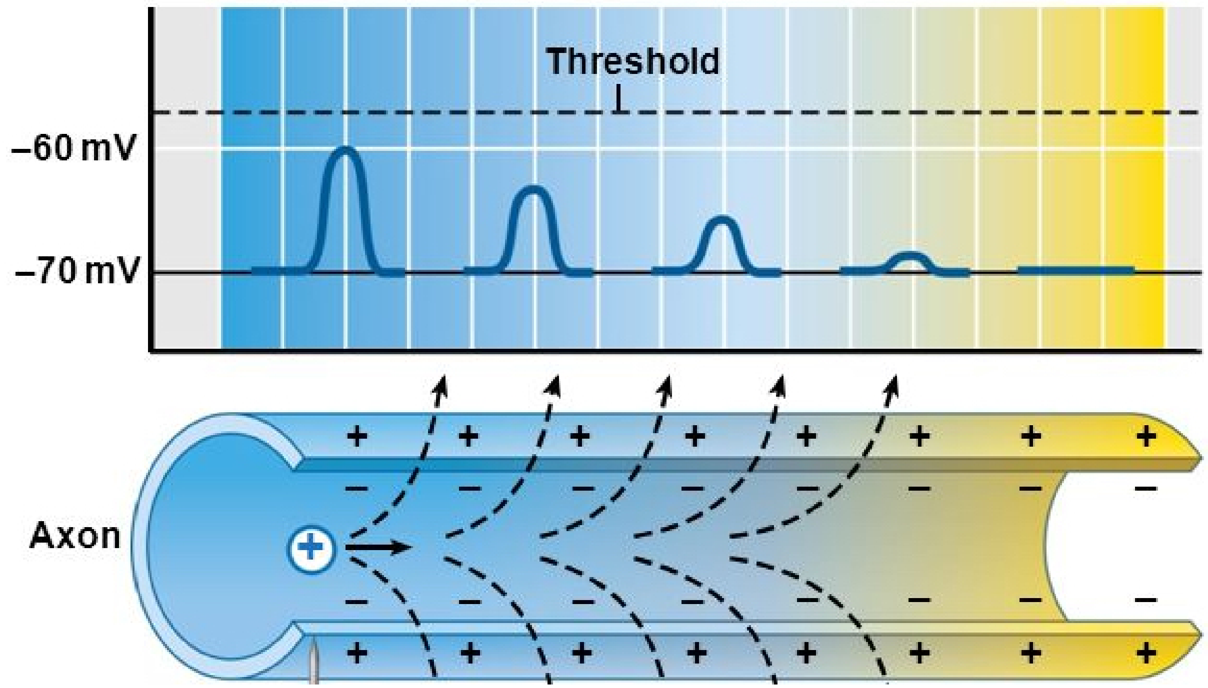


http://pittmedneuro.com/synaptic.html

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.

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.**

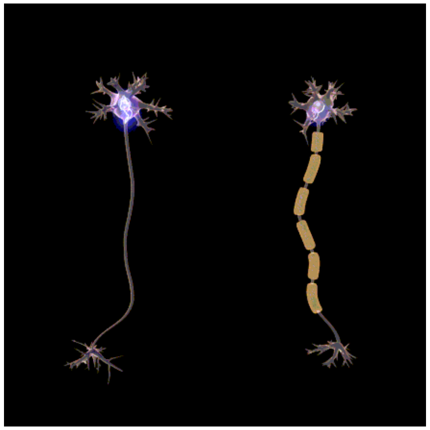
Conduction velocities

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



Saltatory conduction

Conduction velocities

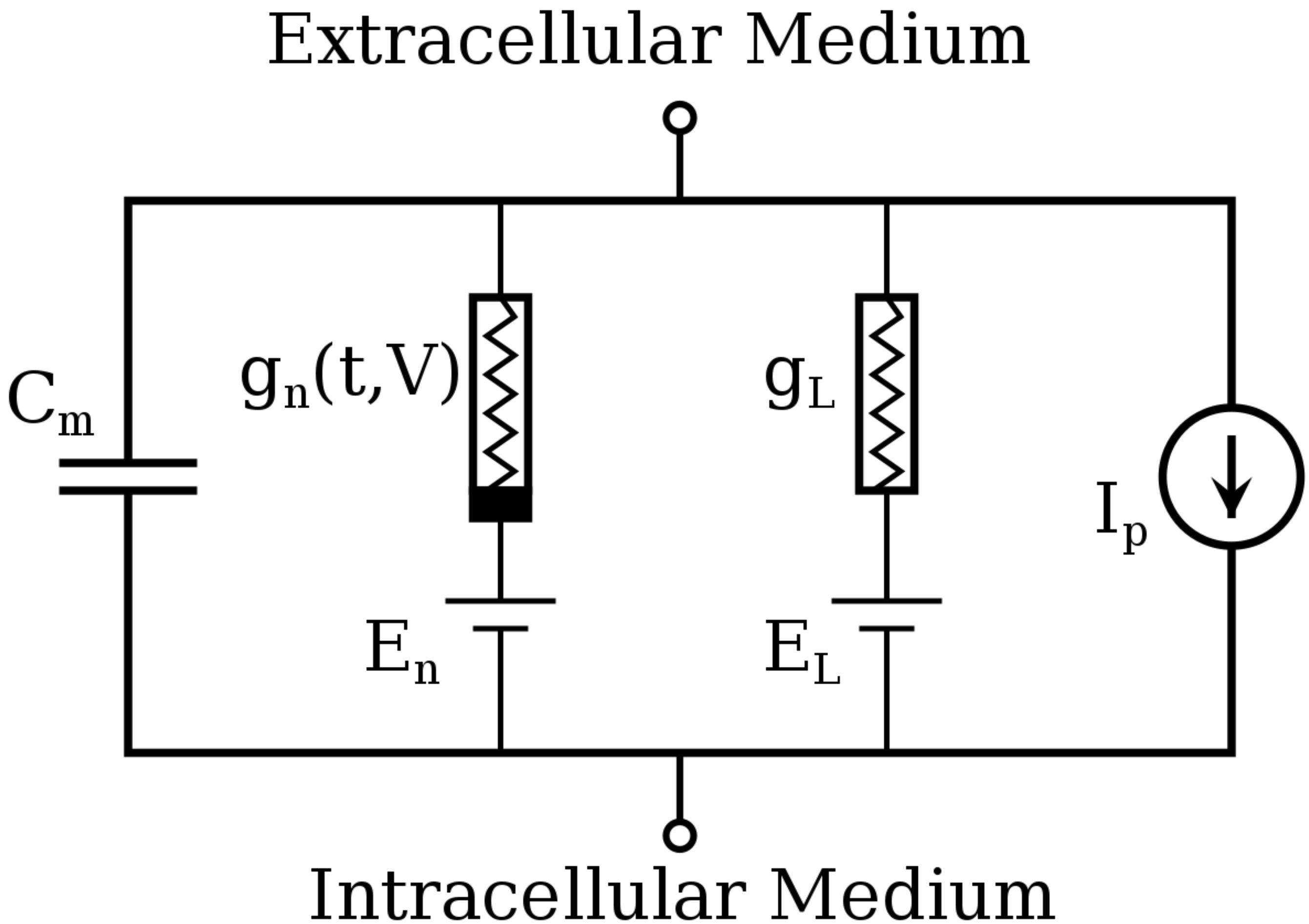
- Axons carry information at different rates
  - More myelin -> faster
  - Larger diameter axon -> faster
- PNS seems to prioritize
  - Somatosensory information & muscle control

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



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) >> $[K^+]_{out}$ (~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
  - $[K^+]_{in} >> [K^+]_{out}$
- Nernst equation
  - $V_K = \frac{RT}{(+1)F} ln(\frac{[K^+]_{out}}{[K^+]_{in}})$
  - V_K = ~ -90 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) –> 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) << $[Na^+]_{out}$ (~140 mM)
- Equilibrium potential for Na^+, V_{Na^+} = ~ +55 mV
    - Inside positive/outside negative to $[Na^+]$ concentration gradient
- If Na^+ alone, V_m –> V_{Na} (~ +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
  - $V_m = \frac{RT}{F} ln(\frac{p_K[K^+]_{out} + p_{Na}[Na^+]_{out}}{p_K[K^+]_{in} + p_{Na}[Na^+]_{in}})$

“Driving force” and equilibrium potential

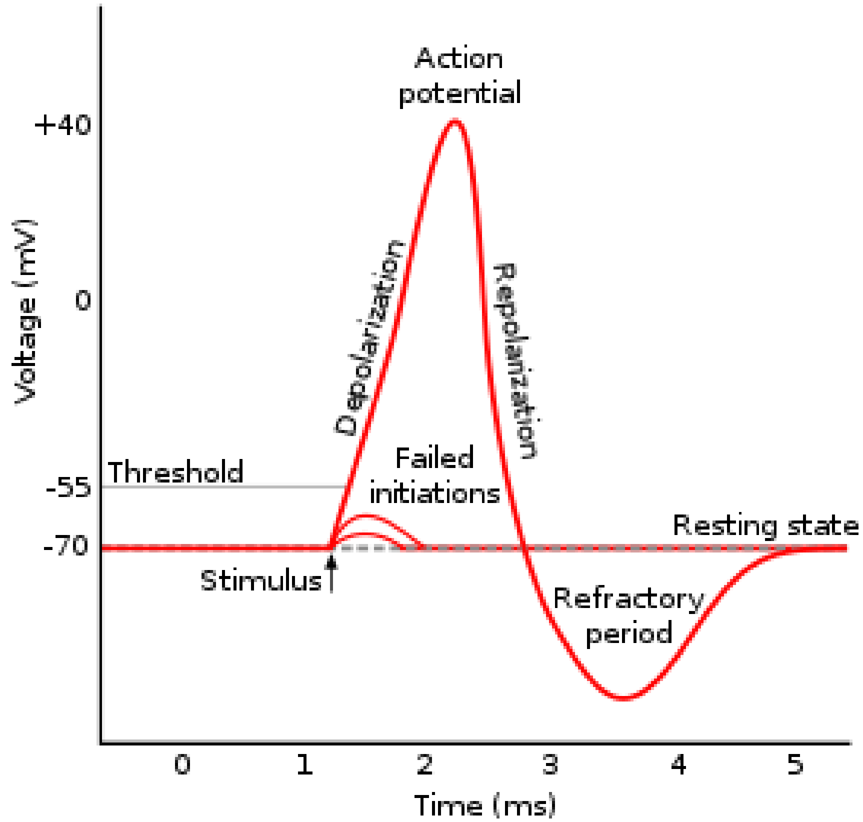
- “Driving Force” on a given ion depends on difference between
    - Equilibrium potential for given ion **AND**
    - Neuron’s current membrane potential (V_m)
    - V_m reflects combined effects of all ions

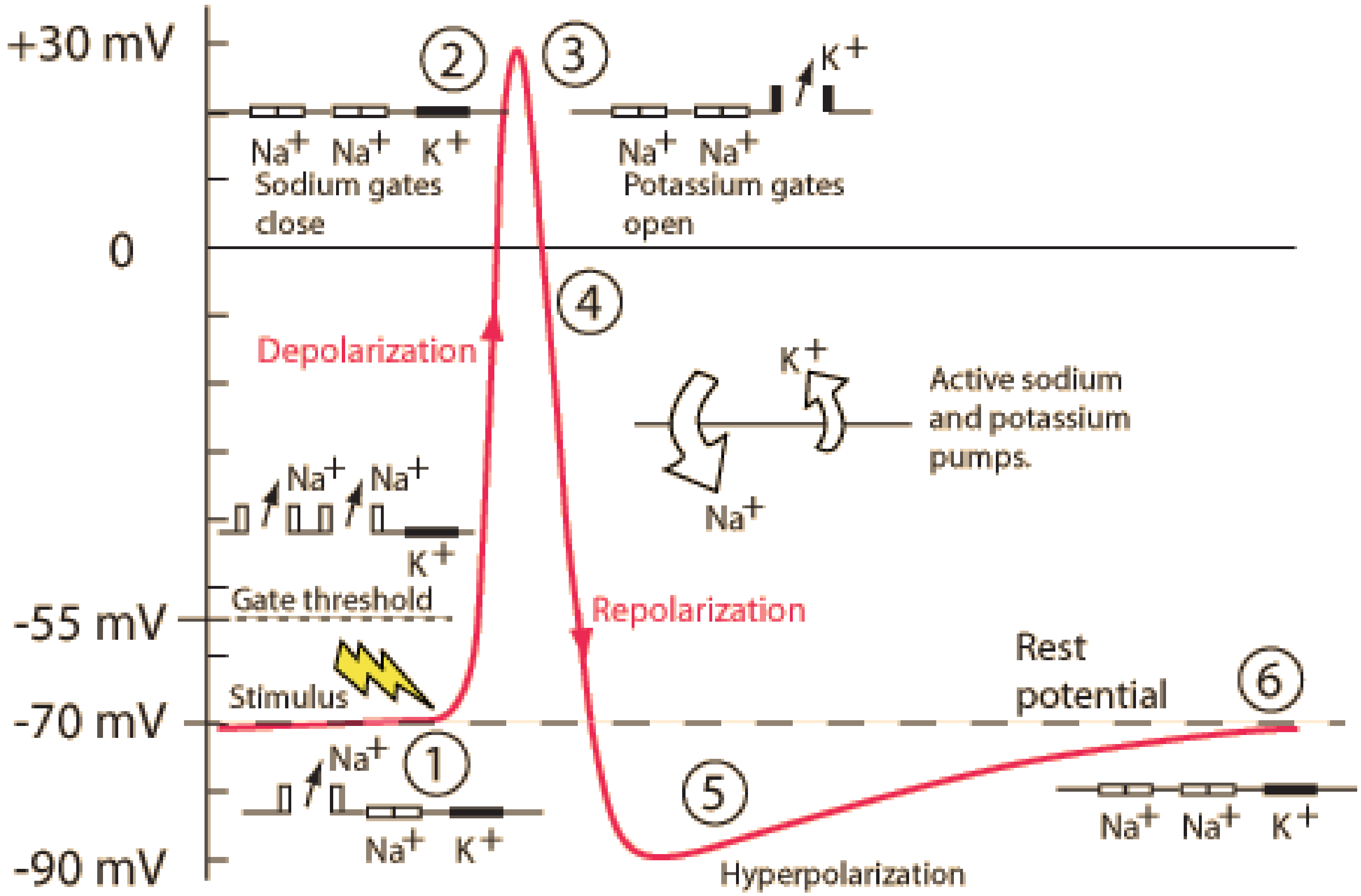
“Driving force” and equilibrium potential

- 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





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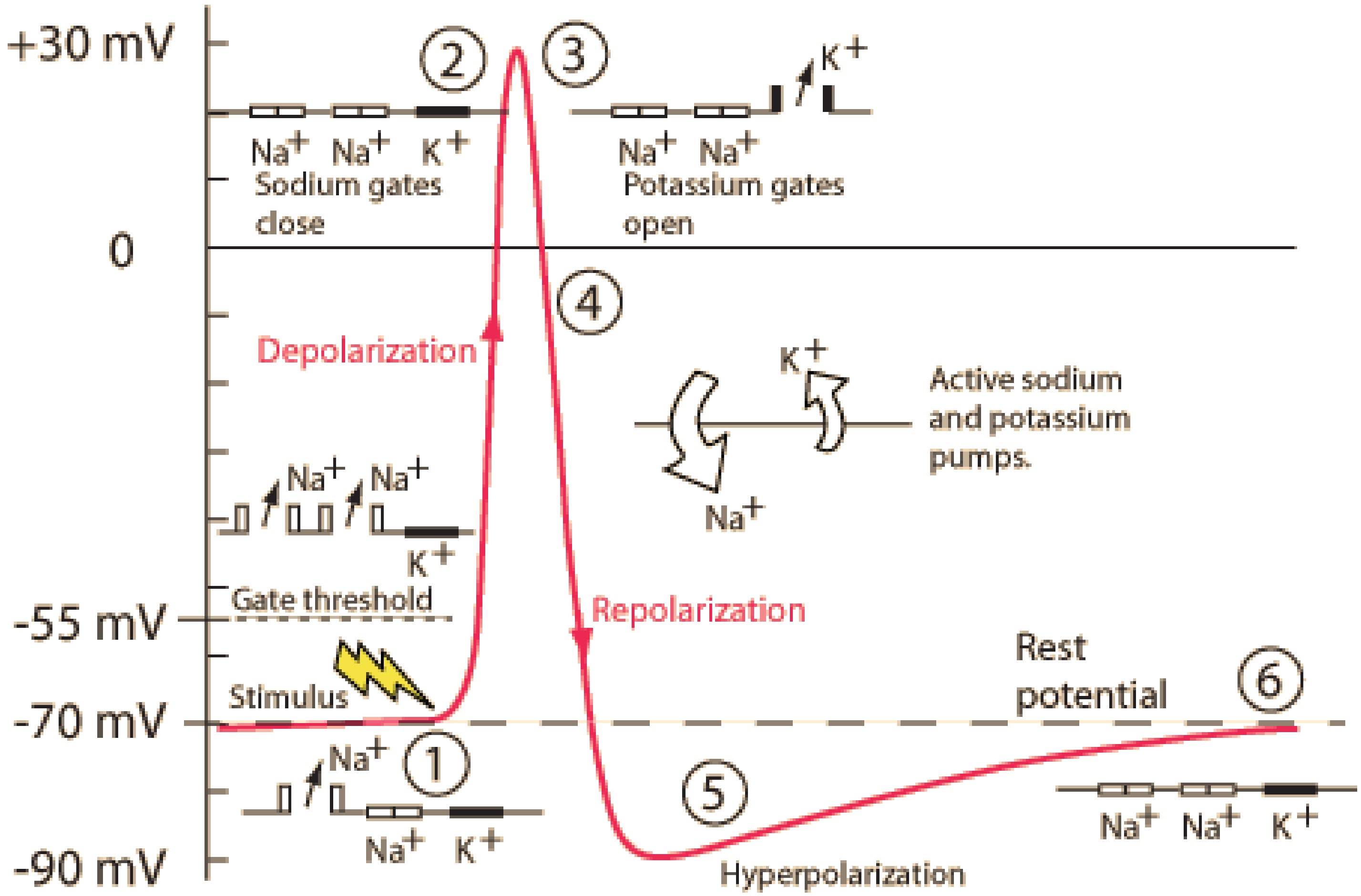
Voltage-gated Na^+ and K^+ channels

- 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 mV - (-90 mV) = +20 mV
- Driving force on Na^+ strongly in
    - -70 mV - (+55 mV) = -125 mV
- Na^+/K^+ pump maintains concentrations



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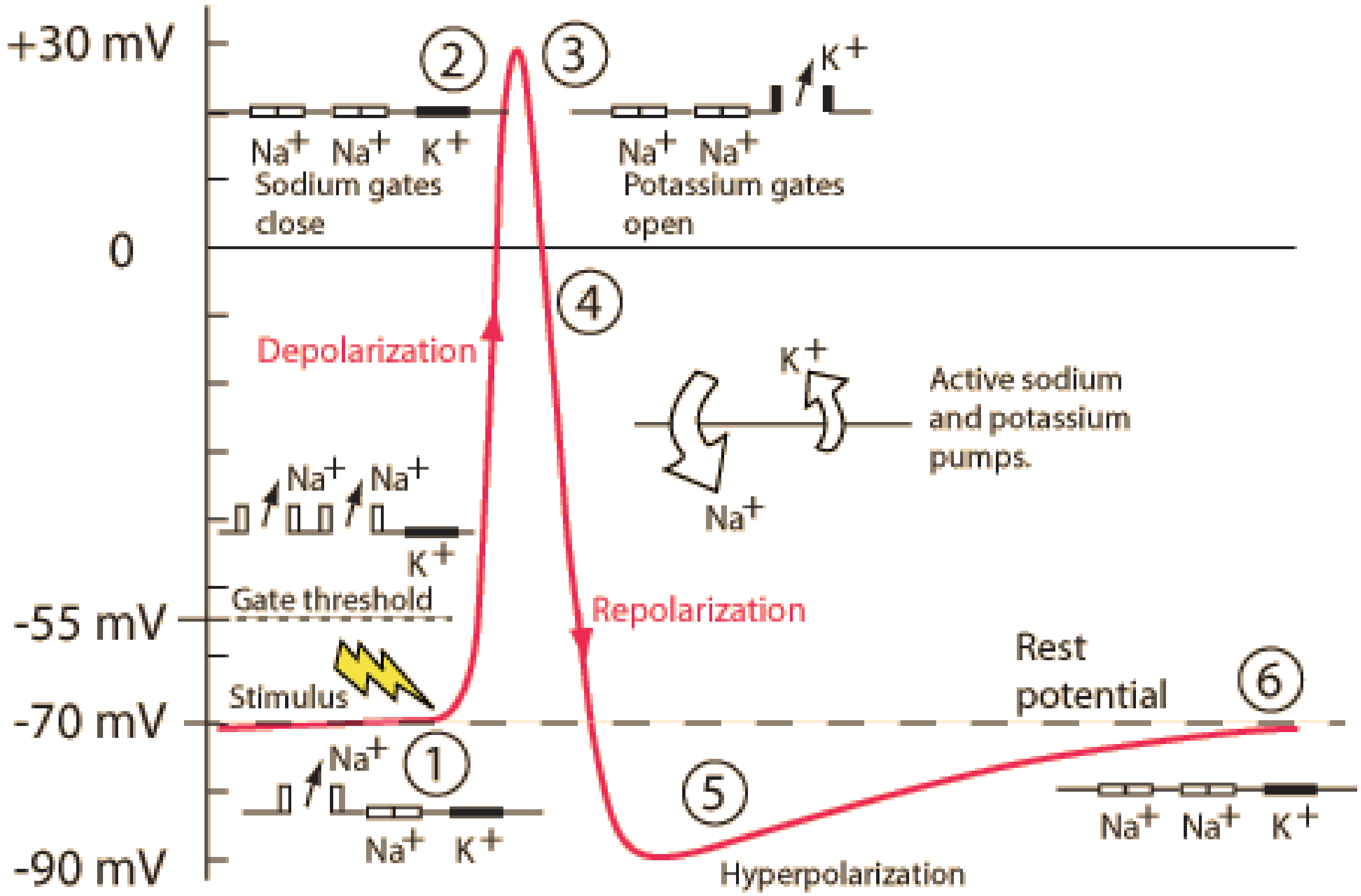
Action potential rising phase

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



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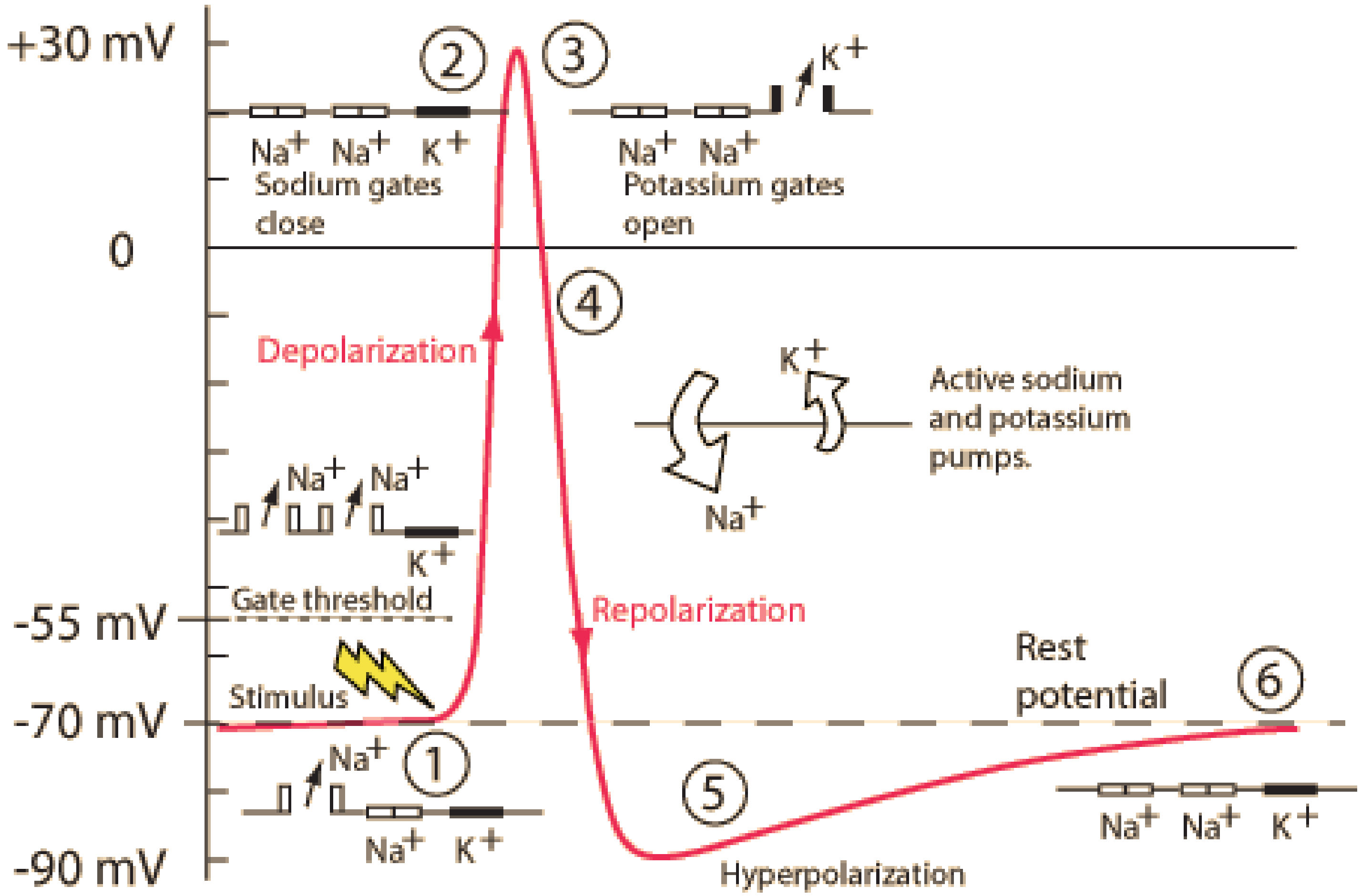
Peak

- 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)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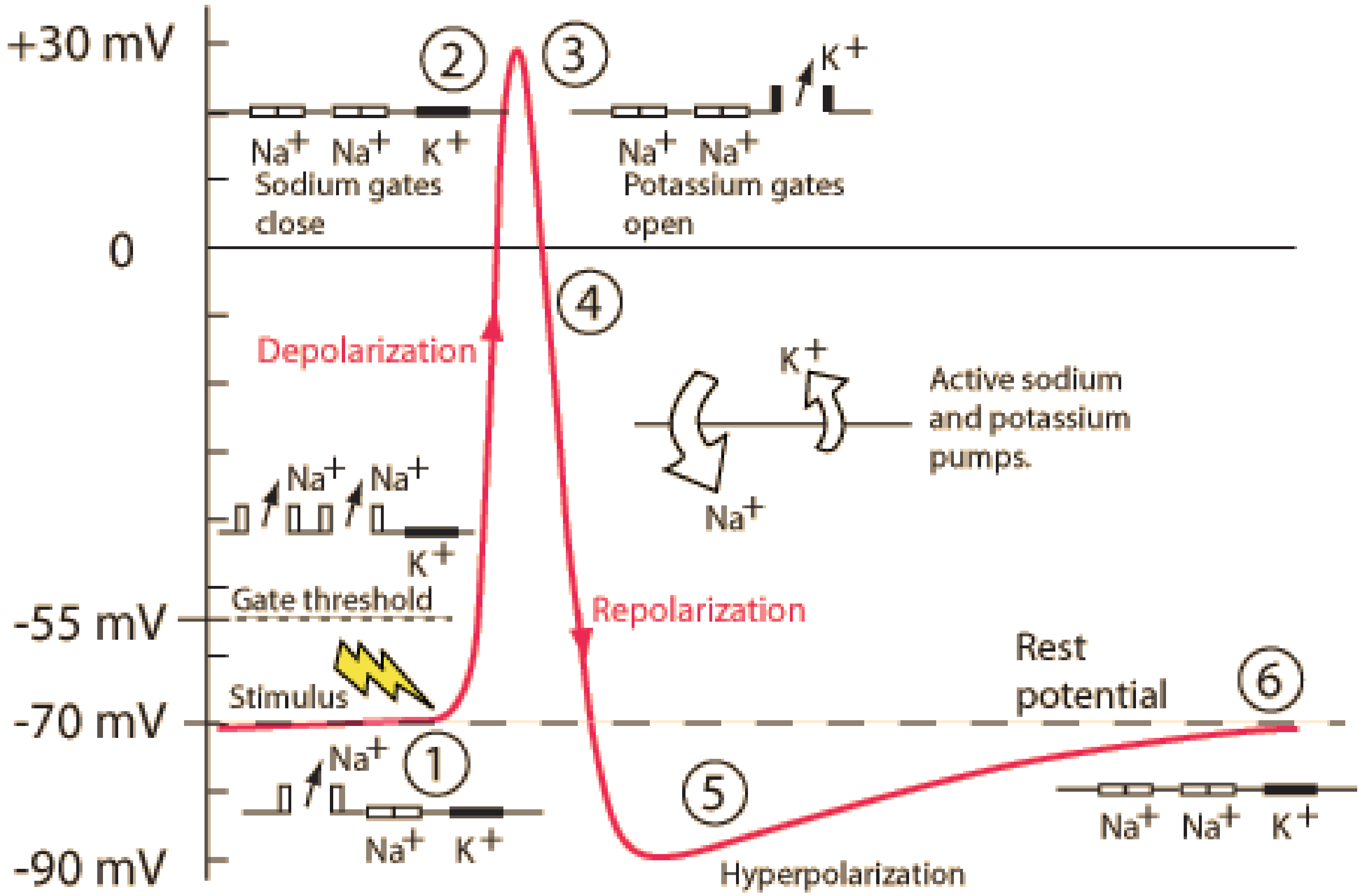
Hyperpolarization

Falling phase

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



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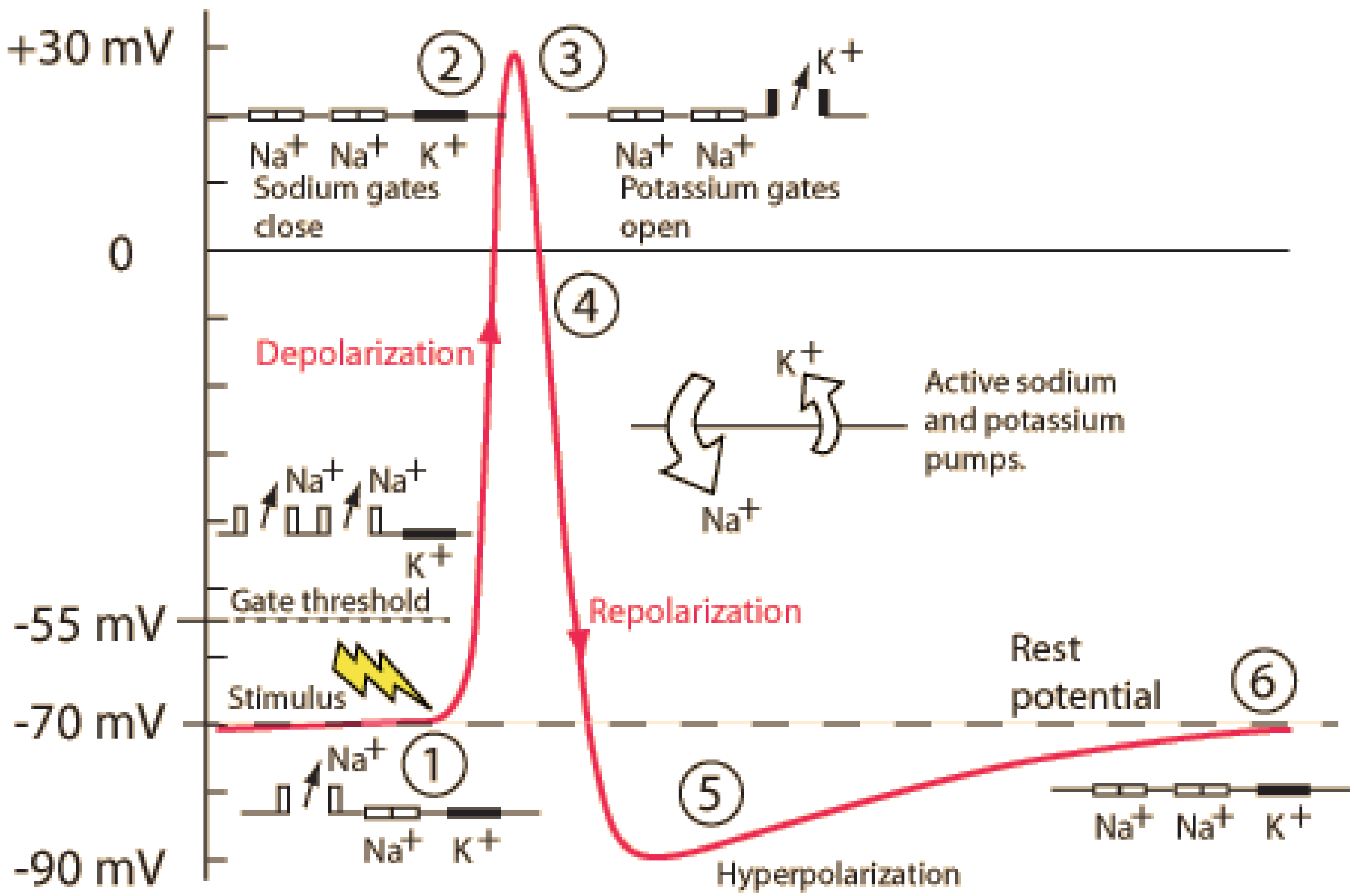
Absolute refractory phase (period)

- 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



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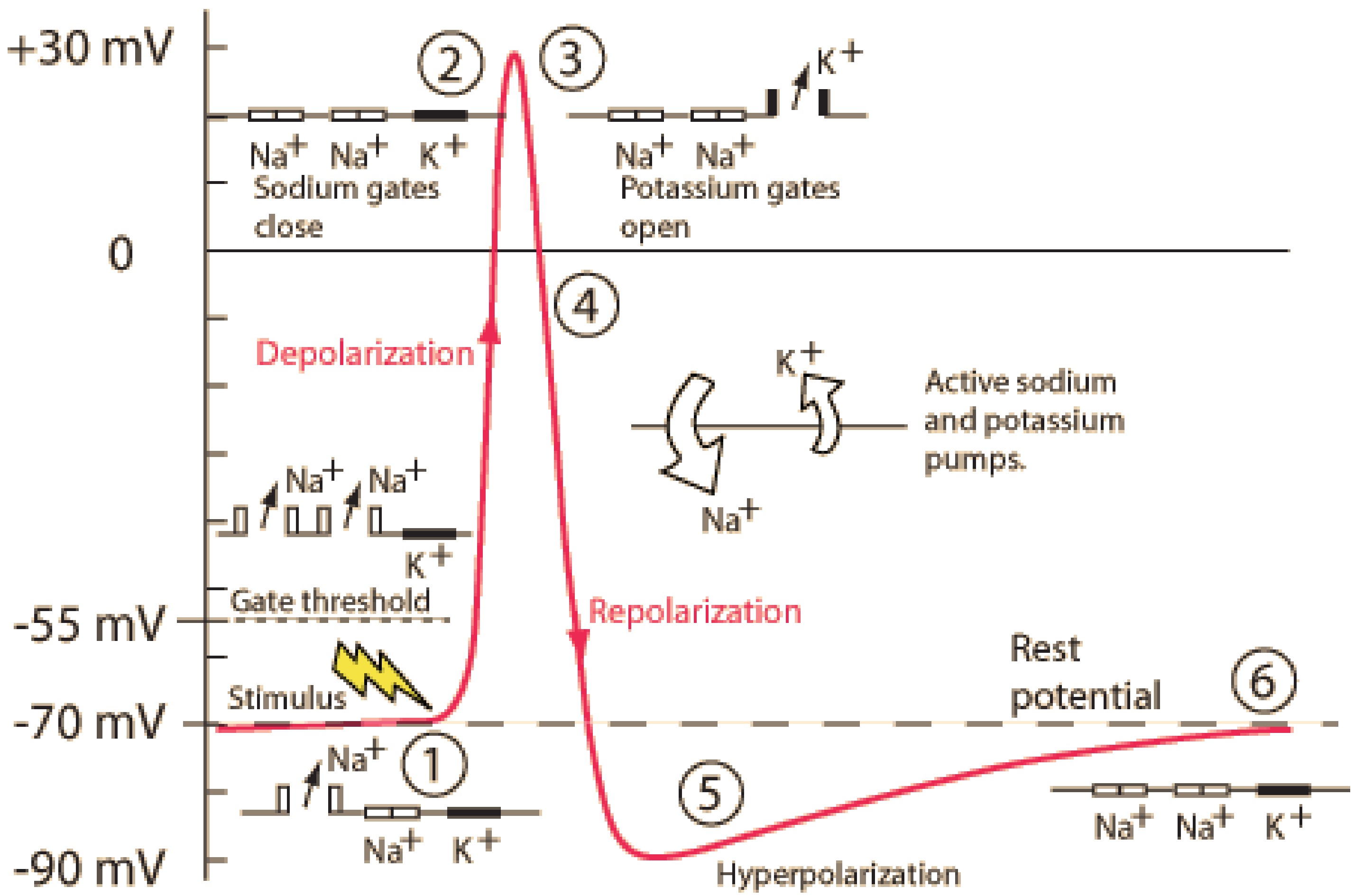
Hyperpolarization

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



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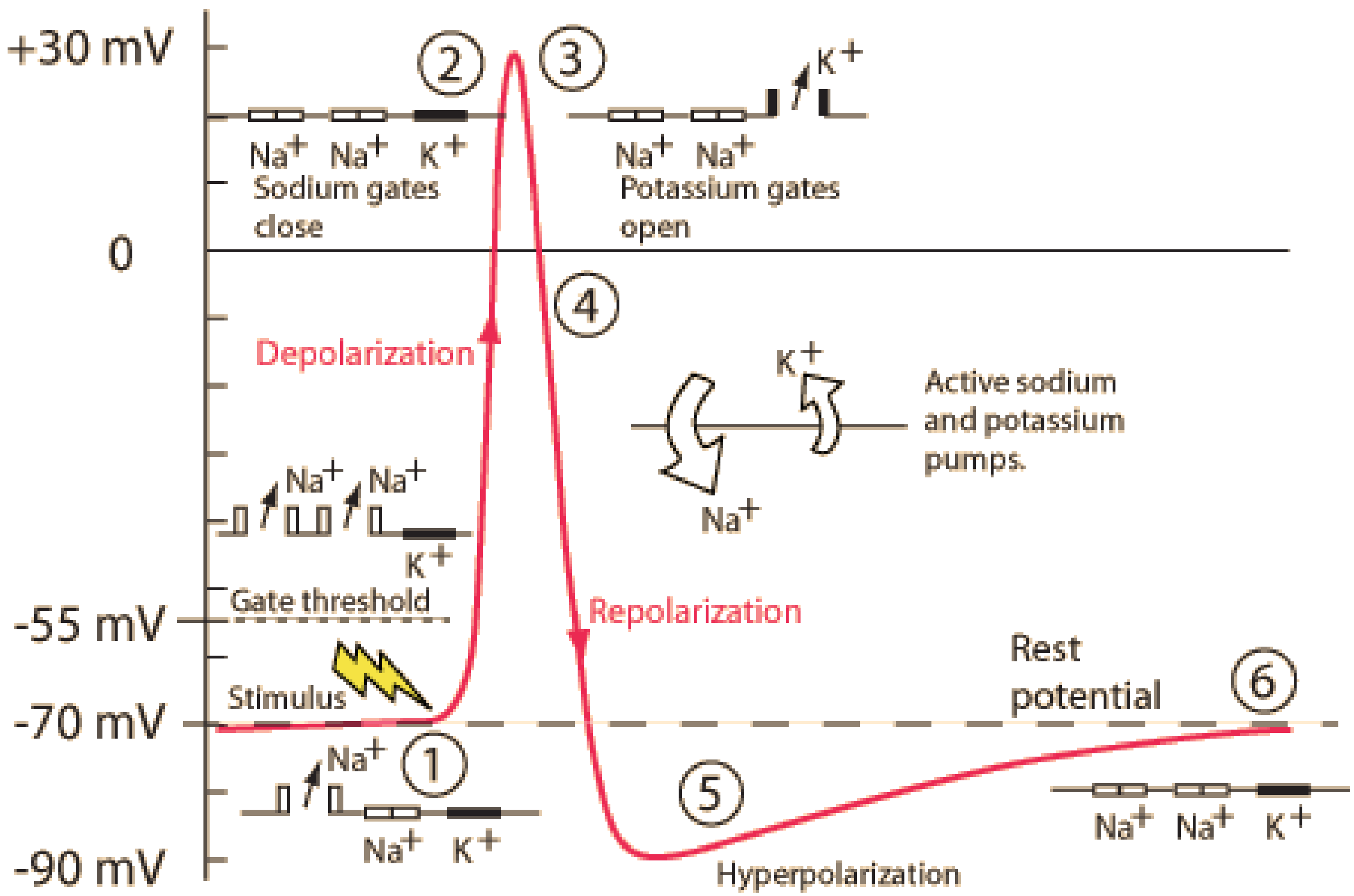
Hyperpolarization

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…



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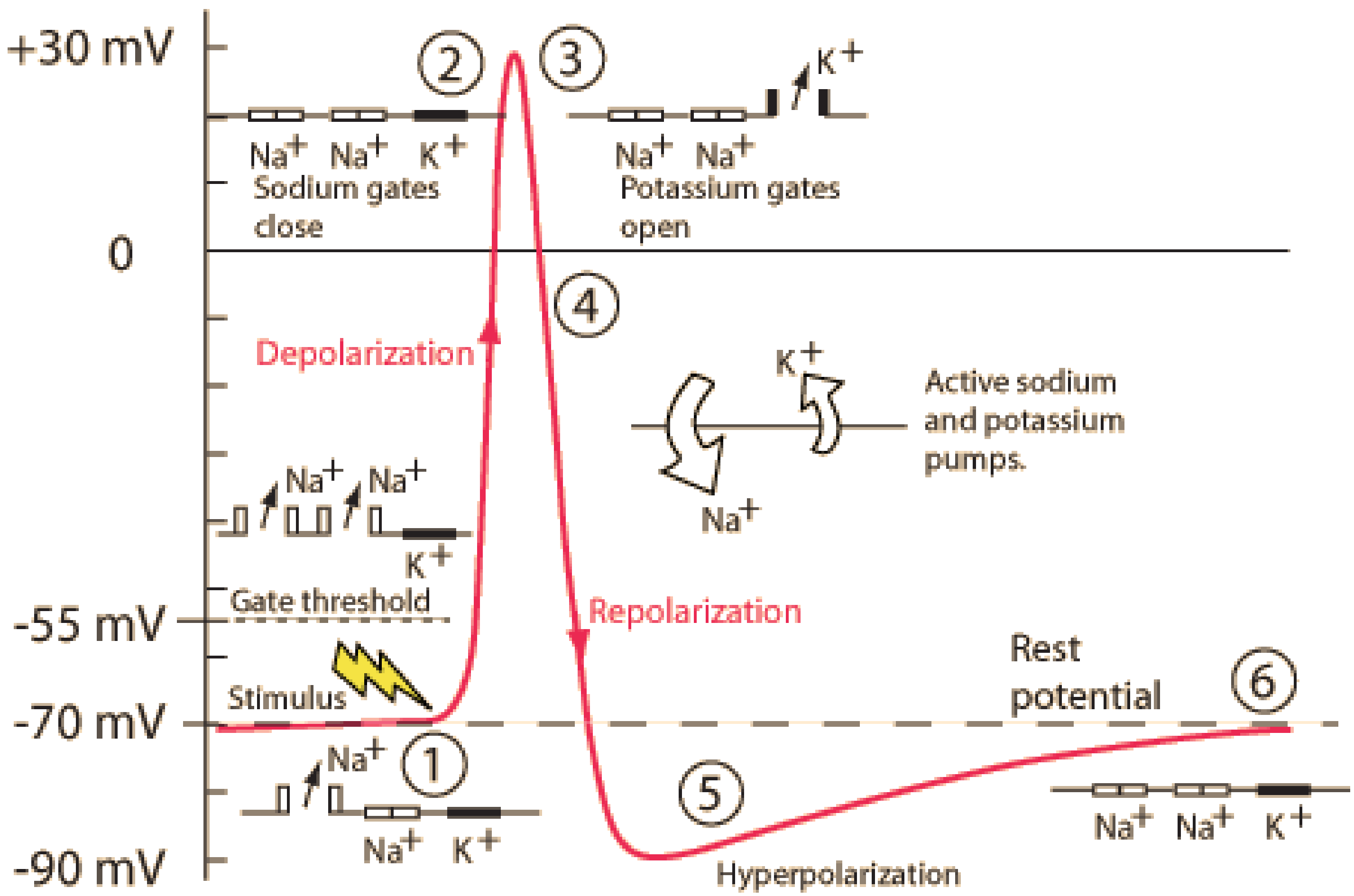
Phase	Ion	Driving force	Flow direction	Flow magnitude
Rest	K+	20 mV	out	small
	Na+	125 mV	in	small



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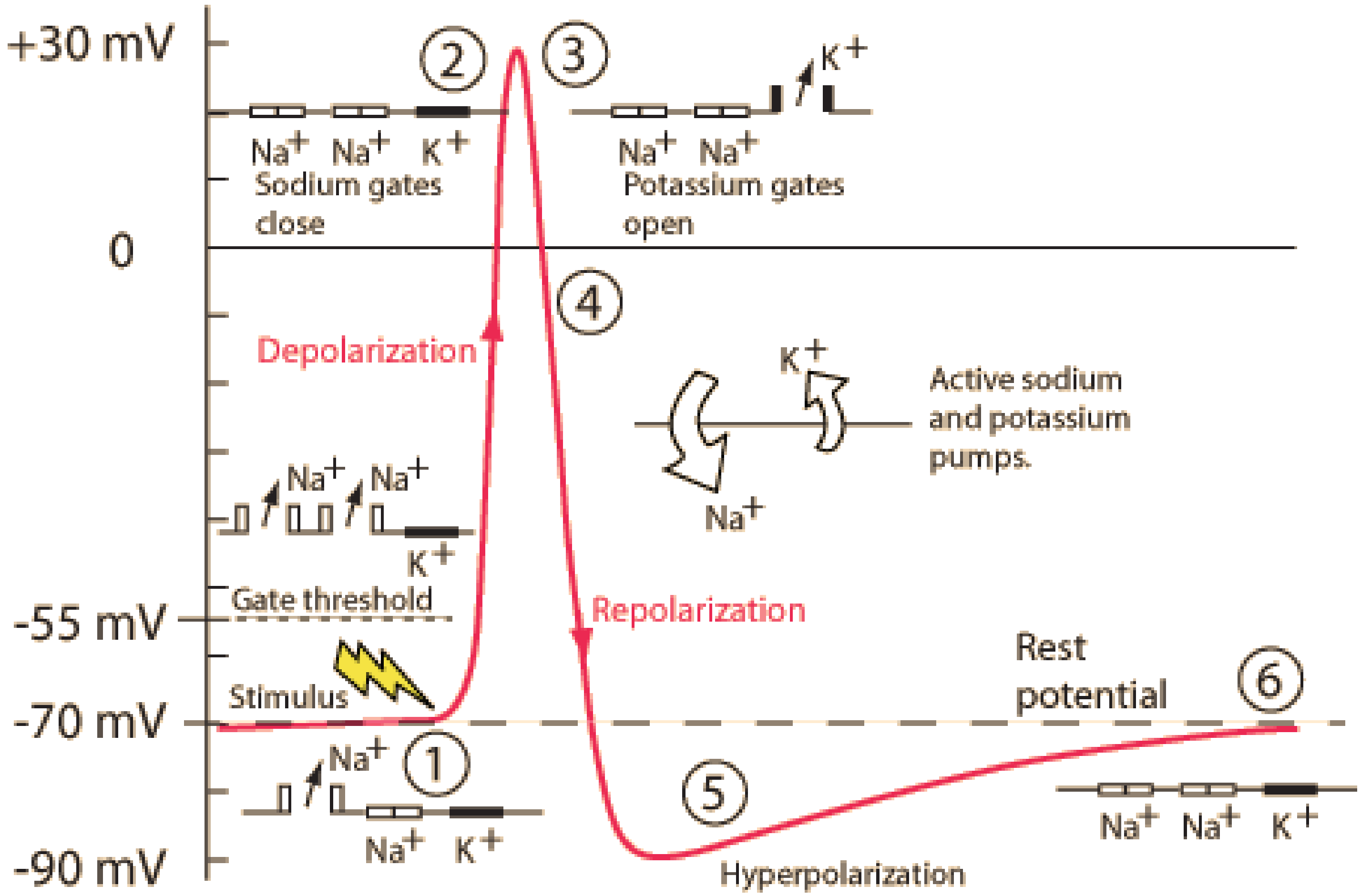
Phase	Ion	Driving force	Flow direction	Flow magnitude
Rising	K+	growing	out	growing
	Na+	shrinking	in	high



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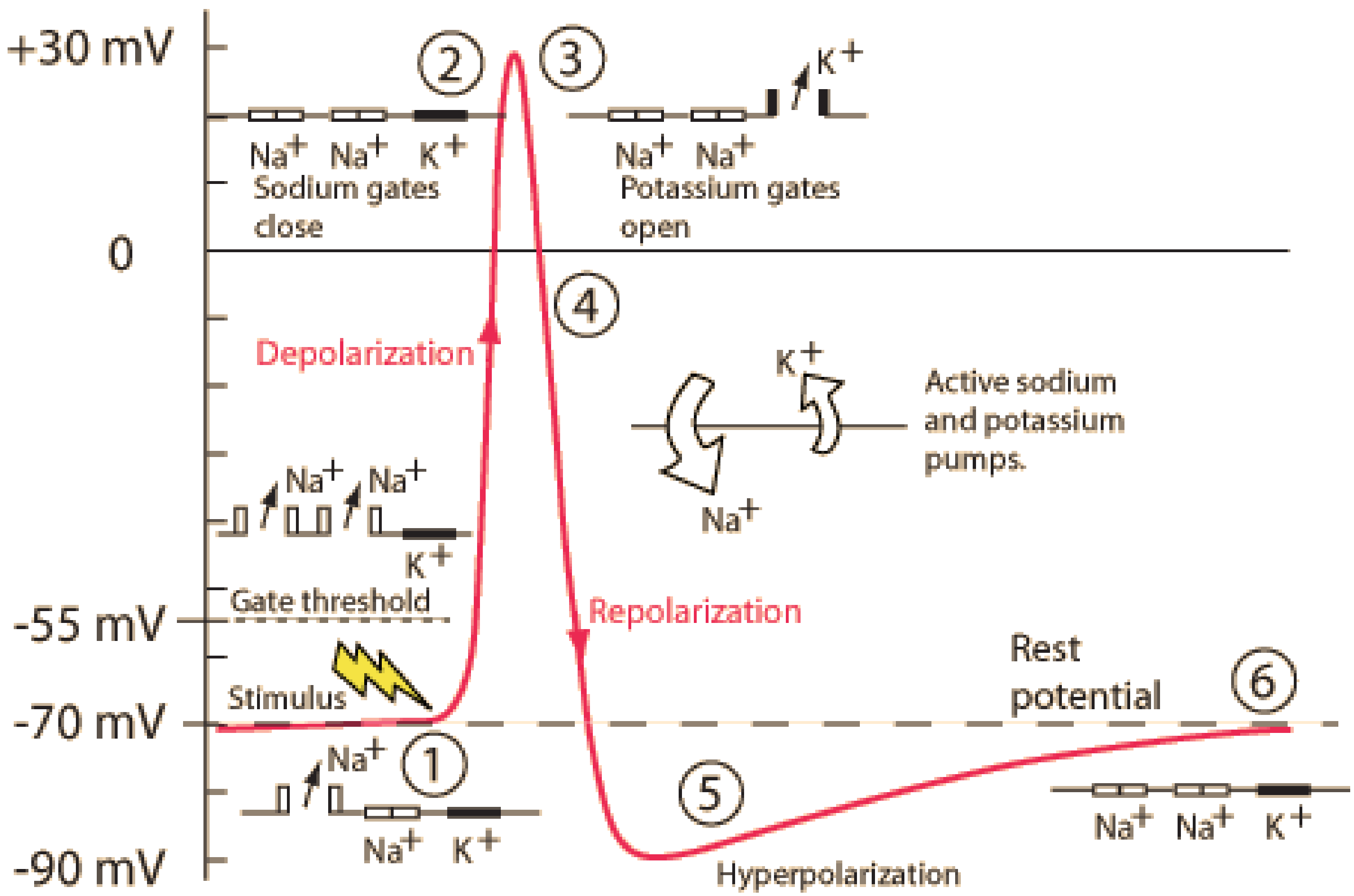
Phase	Ion	Driving force	Flow direction	Flow magnitude
Peak	K+	120 mV	out	high
	Na+	20 mV	out	small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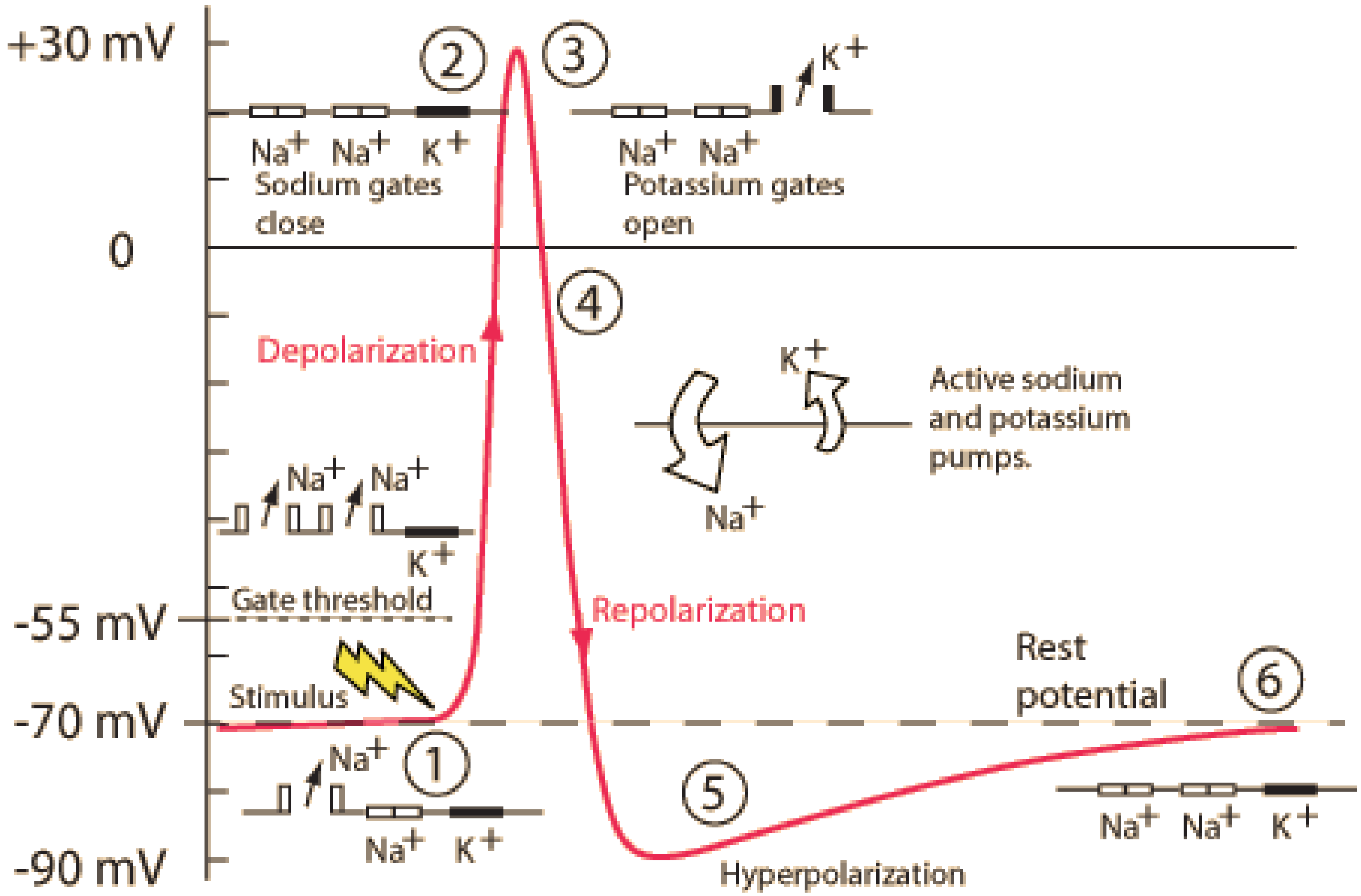
Phase	Ion	Driving force	Flow direction	Flow magnitude
Falling	K	shrinking	out	high
	Na+	growing	in	small



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Hyperpolarization

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

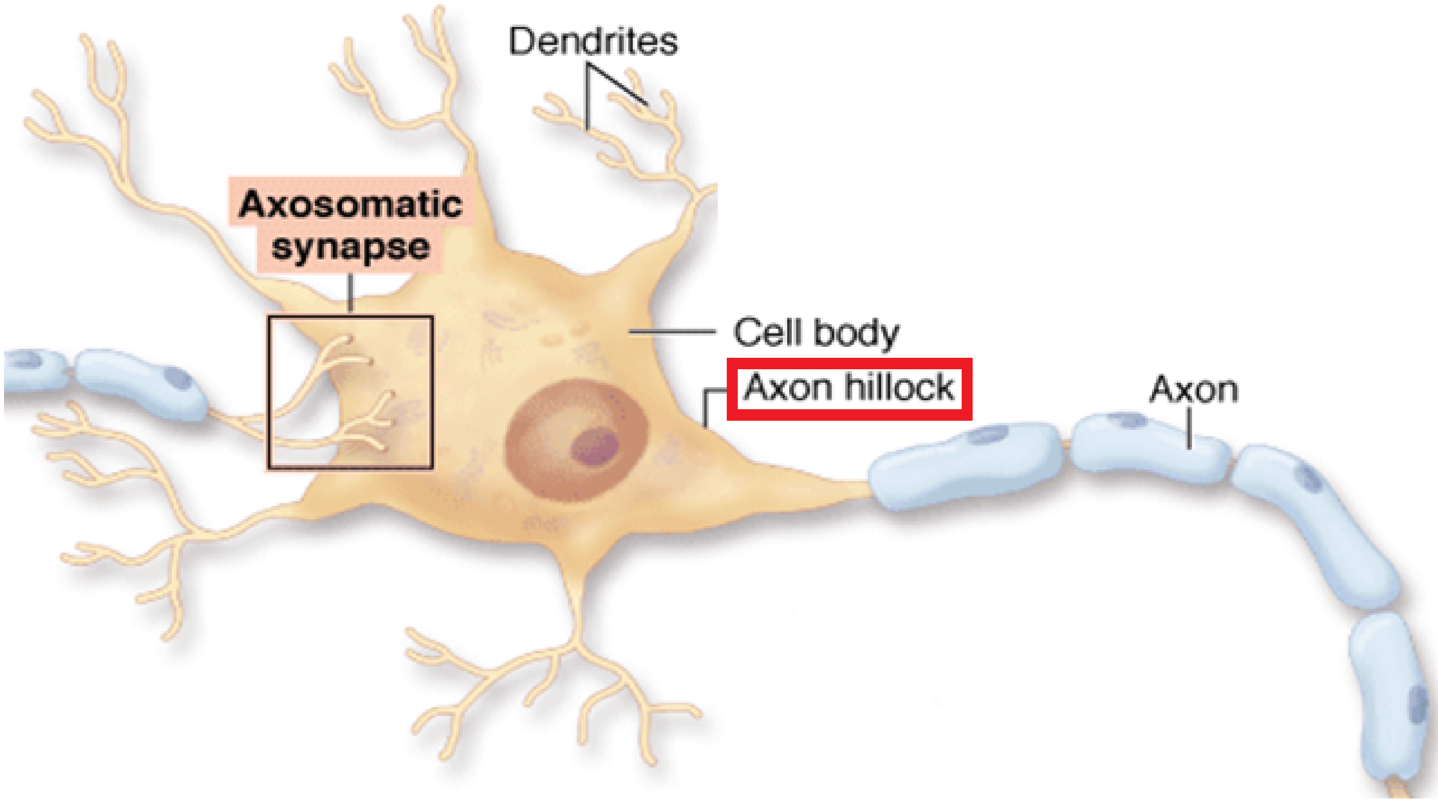
Animation

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



Next time…

- Exam 1