# PSYCH 260/BBH 203

## Cellular neuroscience III

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2022-02-08 14:39:12

# 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.

**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.

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

A. The force of diffusion
B. The dark side of the force
C. The electrostatic force
D. Gravity
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## At the (positive voltage) *peak* of the action potential, which force(s) act to move K+ ions *outward*?

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

# 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

# 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

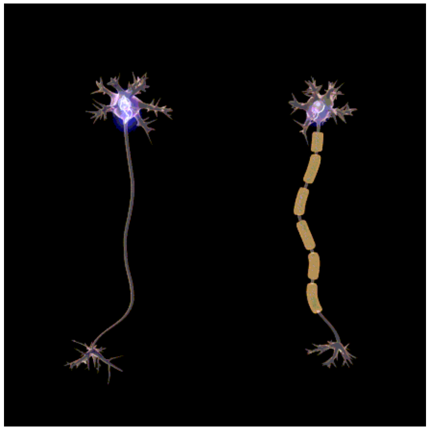
WIKIPEDIA

## 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

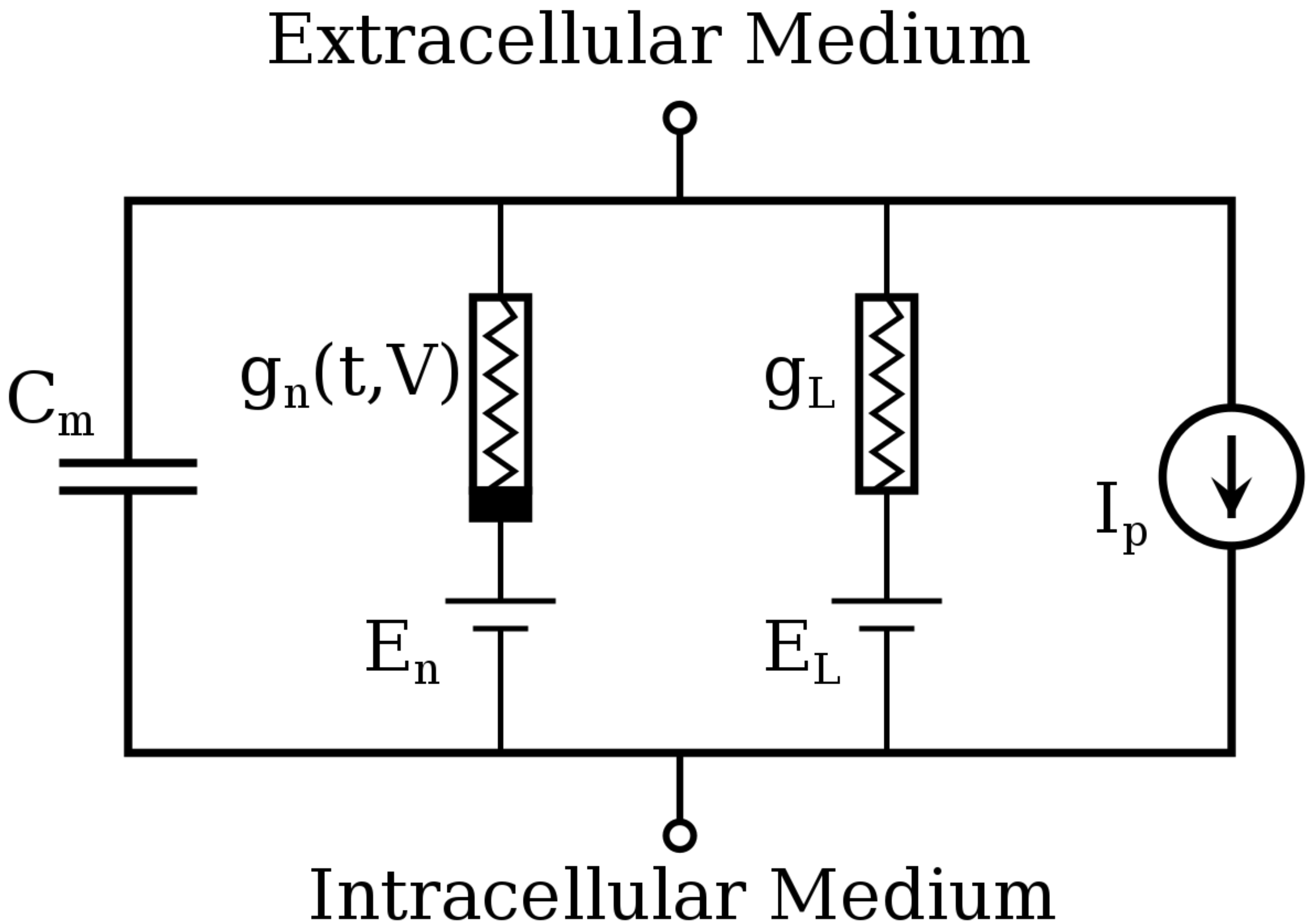
- Axons carry information at different rates
    - More myelin -> faster
    - Larger diameter axon -> faster
- PNS seems to prioritize
    - Somatosensory information & muscle control

# 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 |

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

# 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

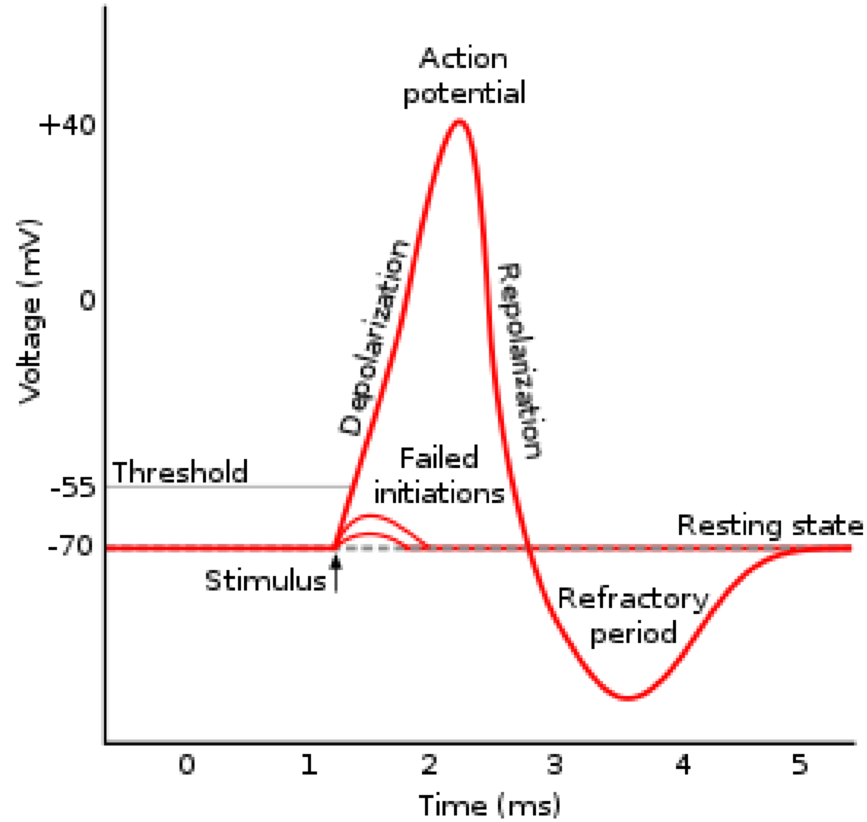
- “Driving Force” on a given ion depends on difference between
    - Equilibrium potential for given ion **AND**
    - Neuron’s current membrane potential ($V_m$)
    - $V_m$ reflects combined effects of all ions

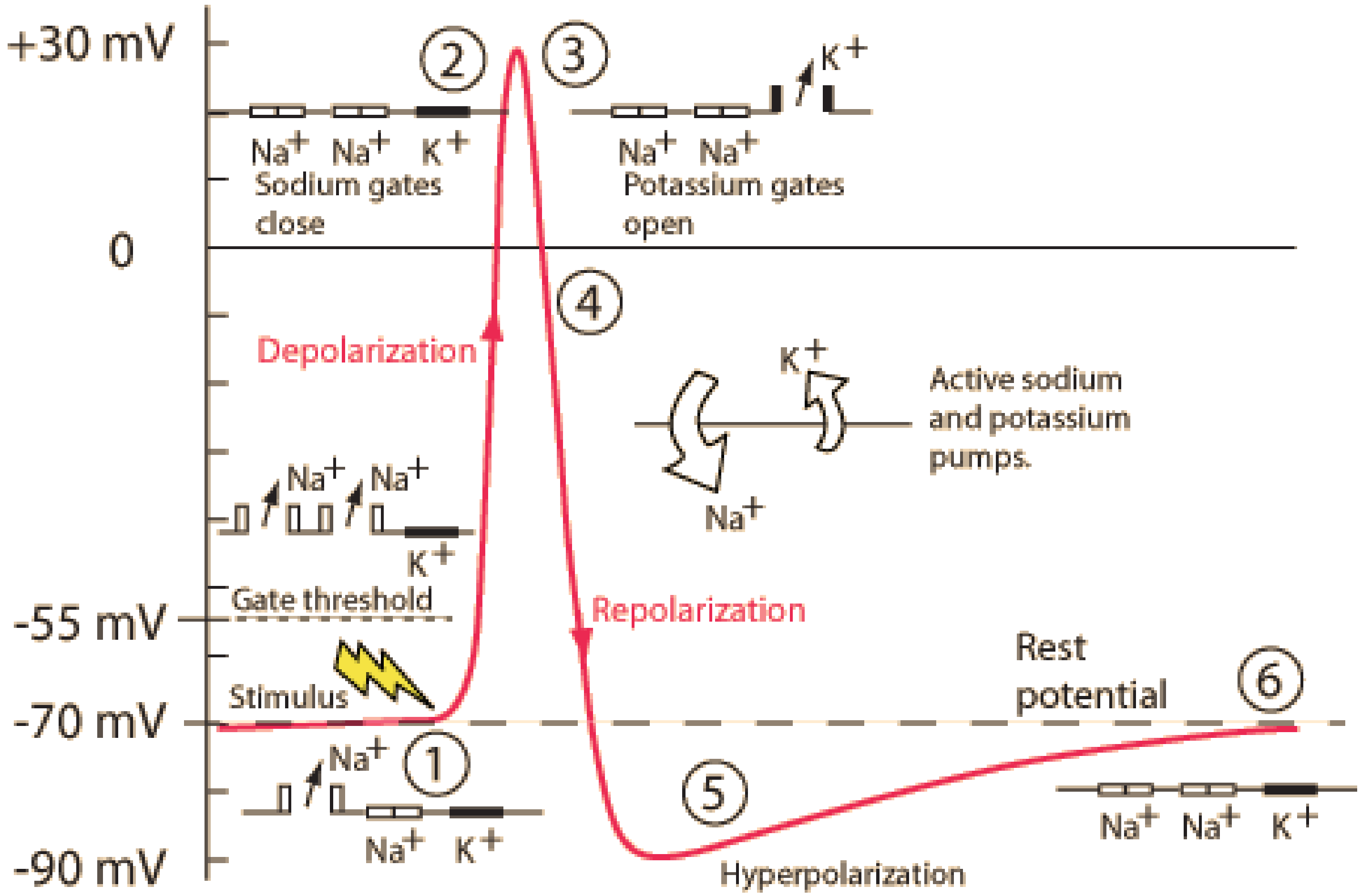
# “Driving force” and equilibrium potential

- 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





+30 mV
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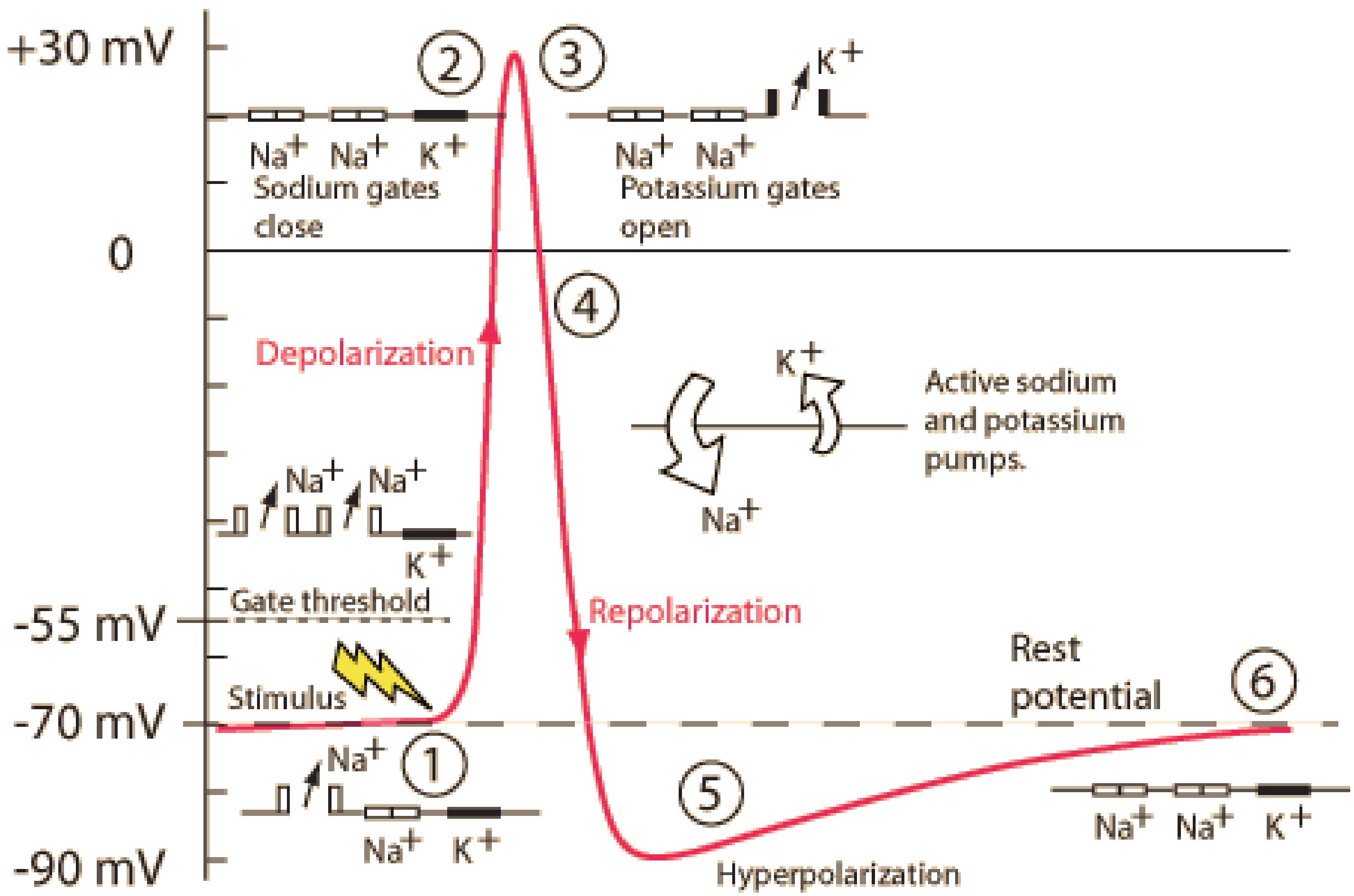
Hyperpolarization

# 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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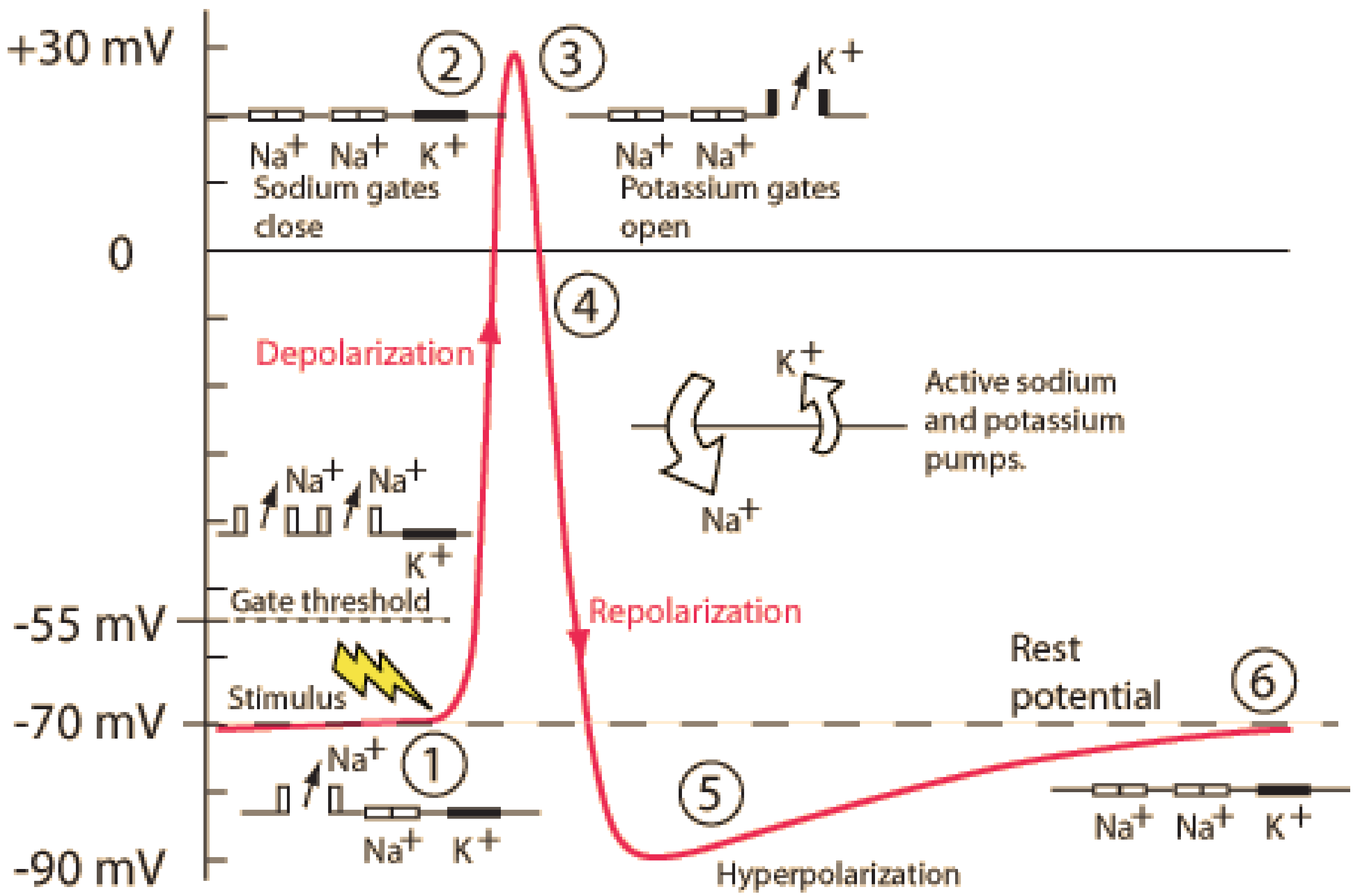
# Action potential rising phase

- 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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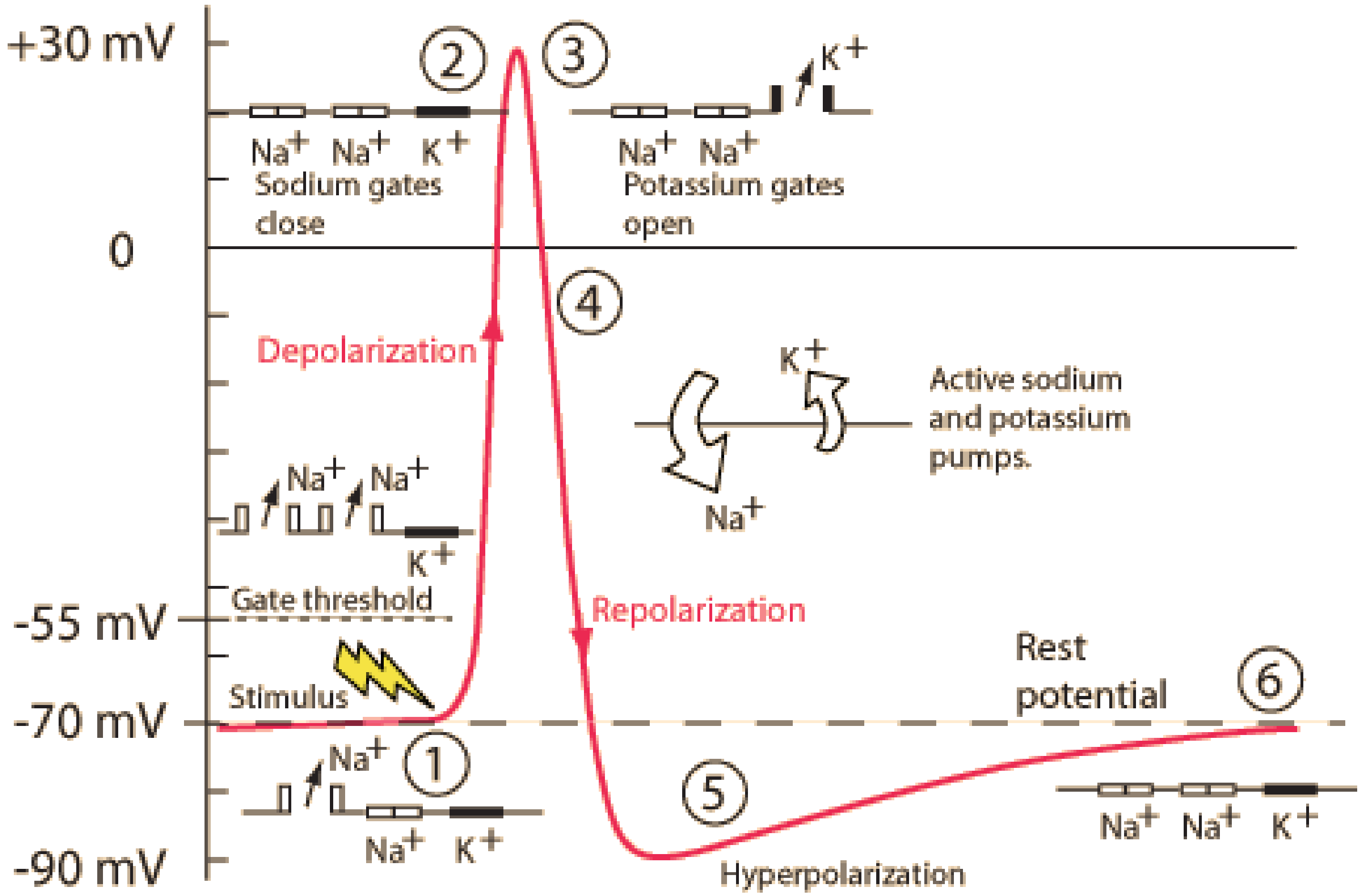
# Peak

- 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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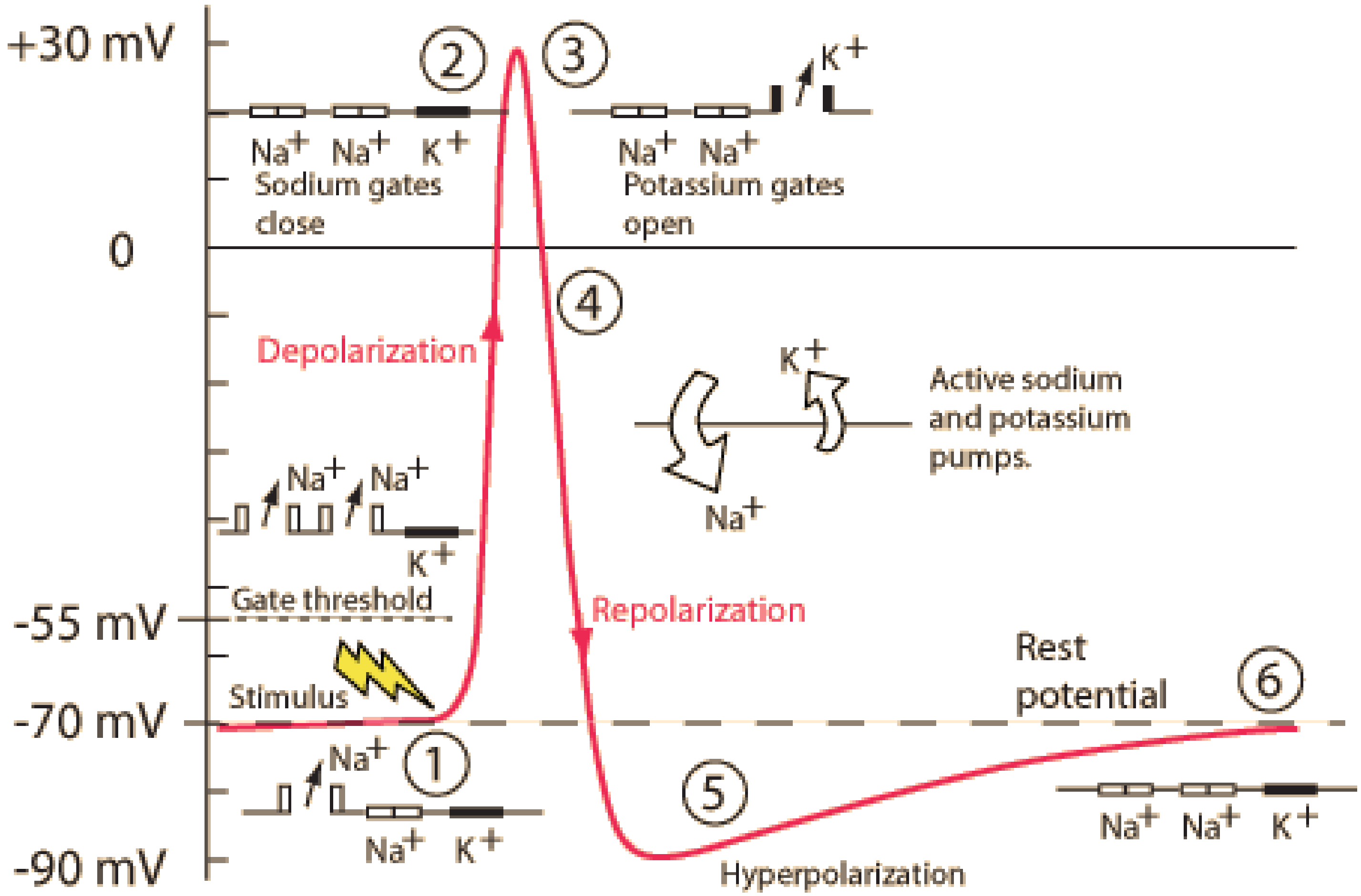
# Falling phase

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



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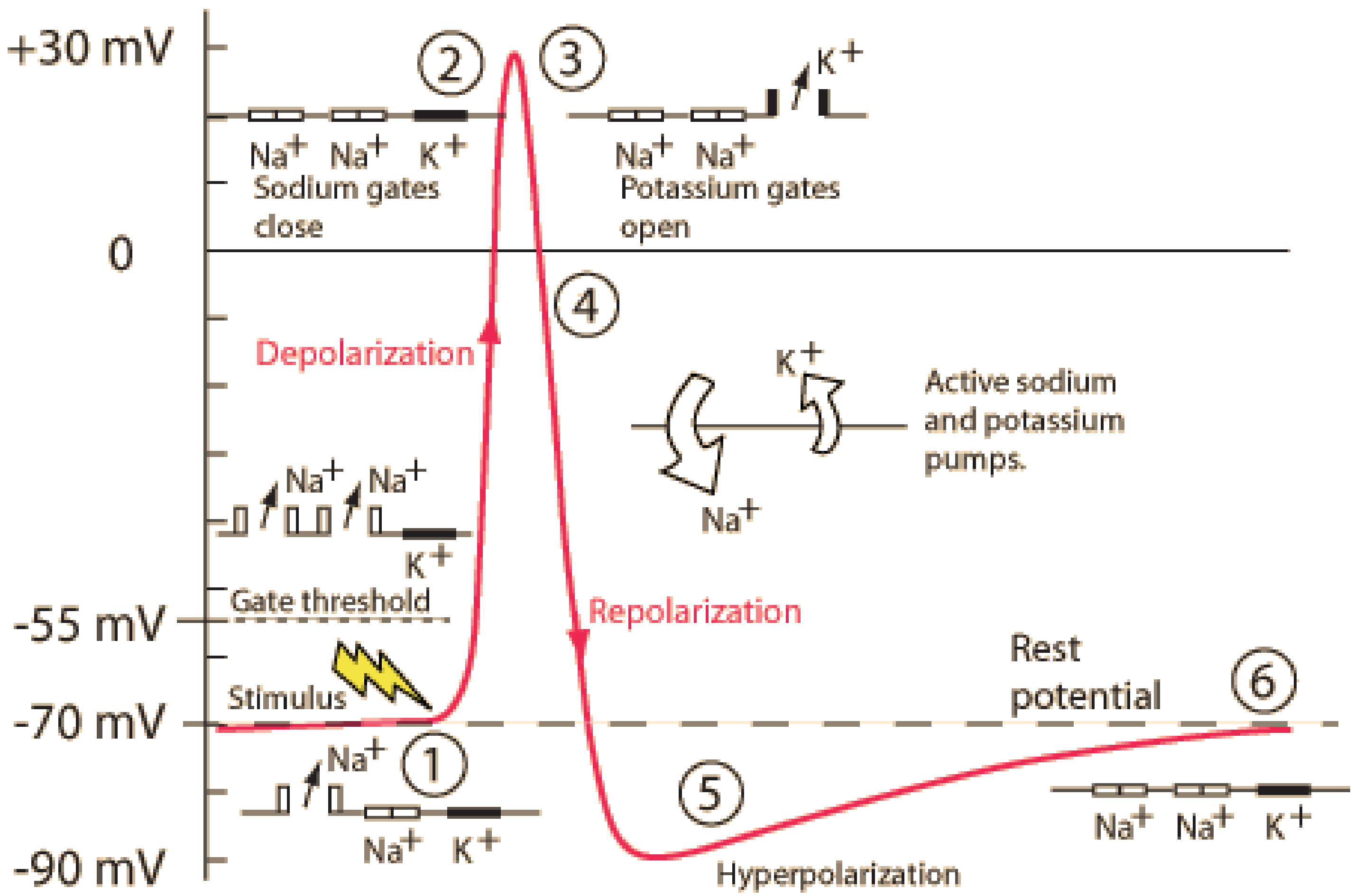
# Absolute refractory phase (period)

- 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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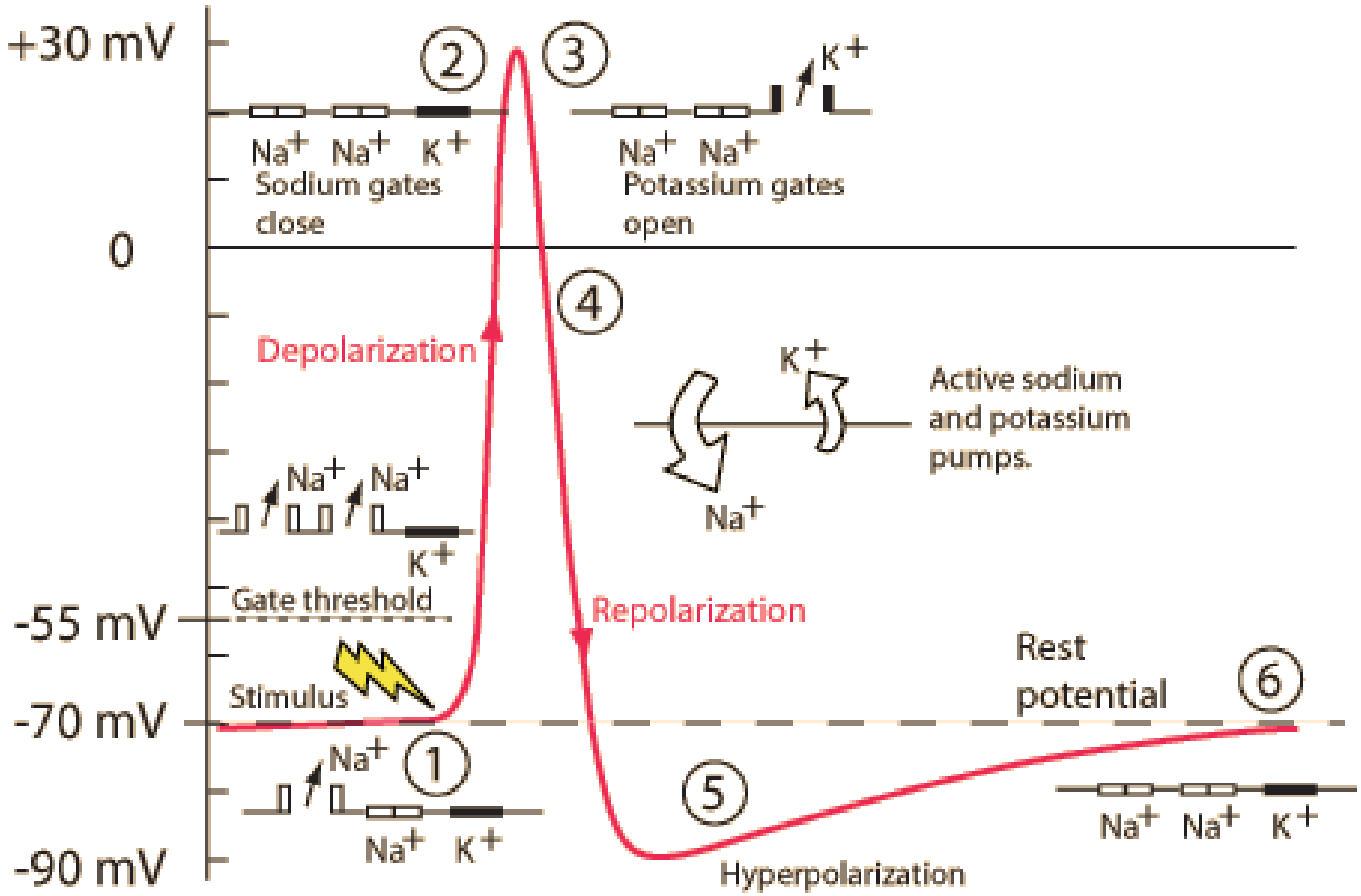
# *Relative* refractory phase (period)

- 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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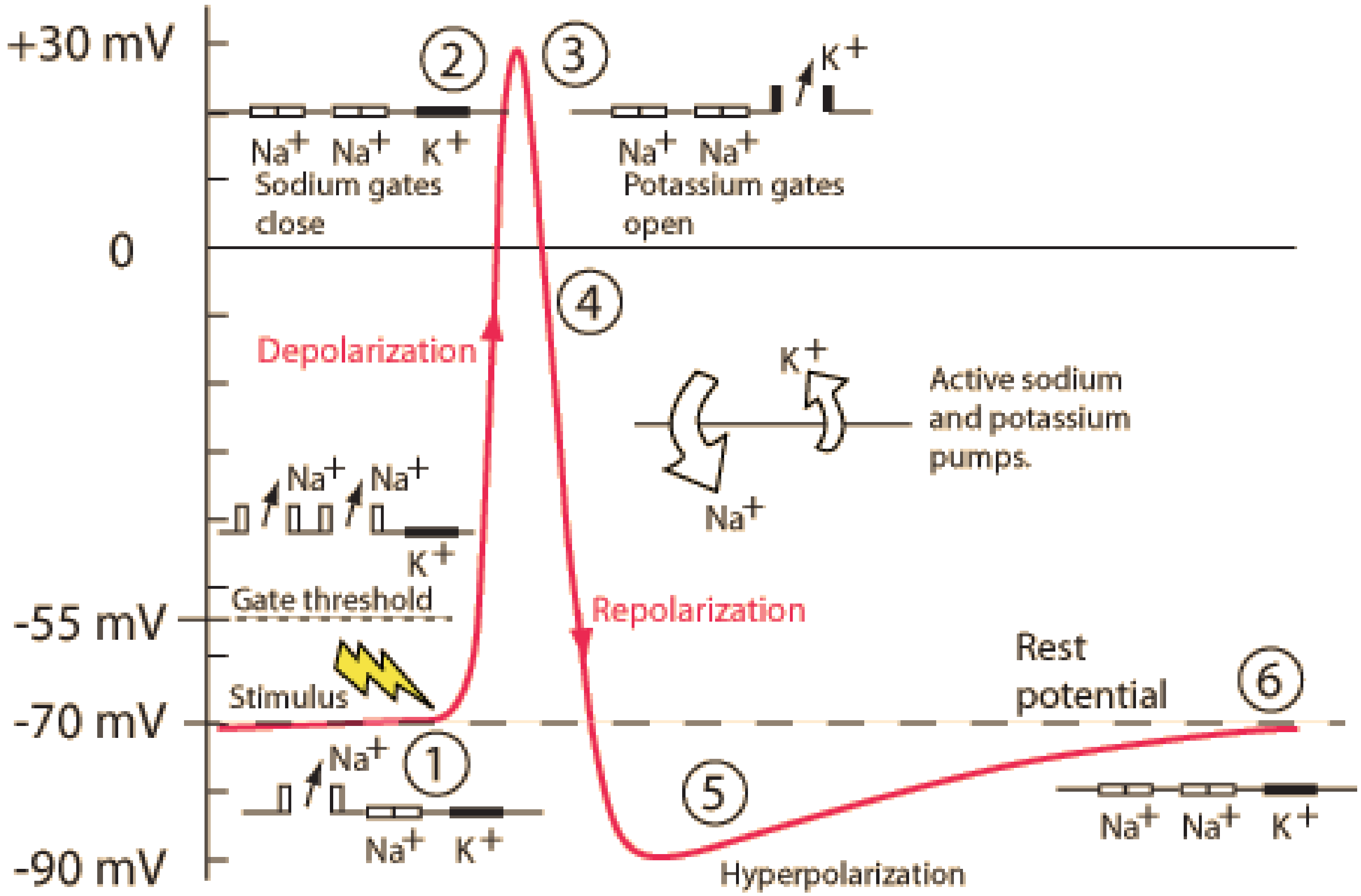
# Neuron at rest

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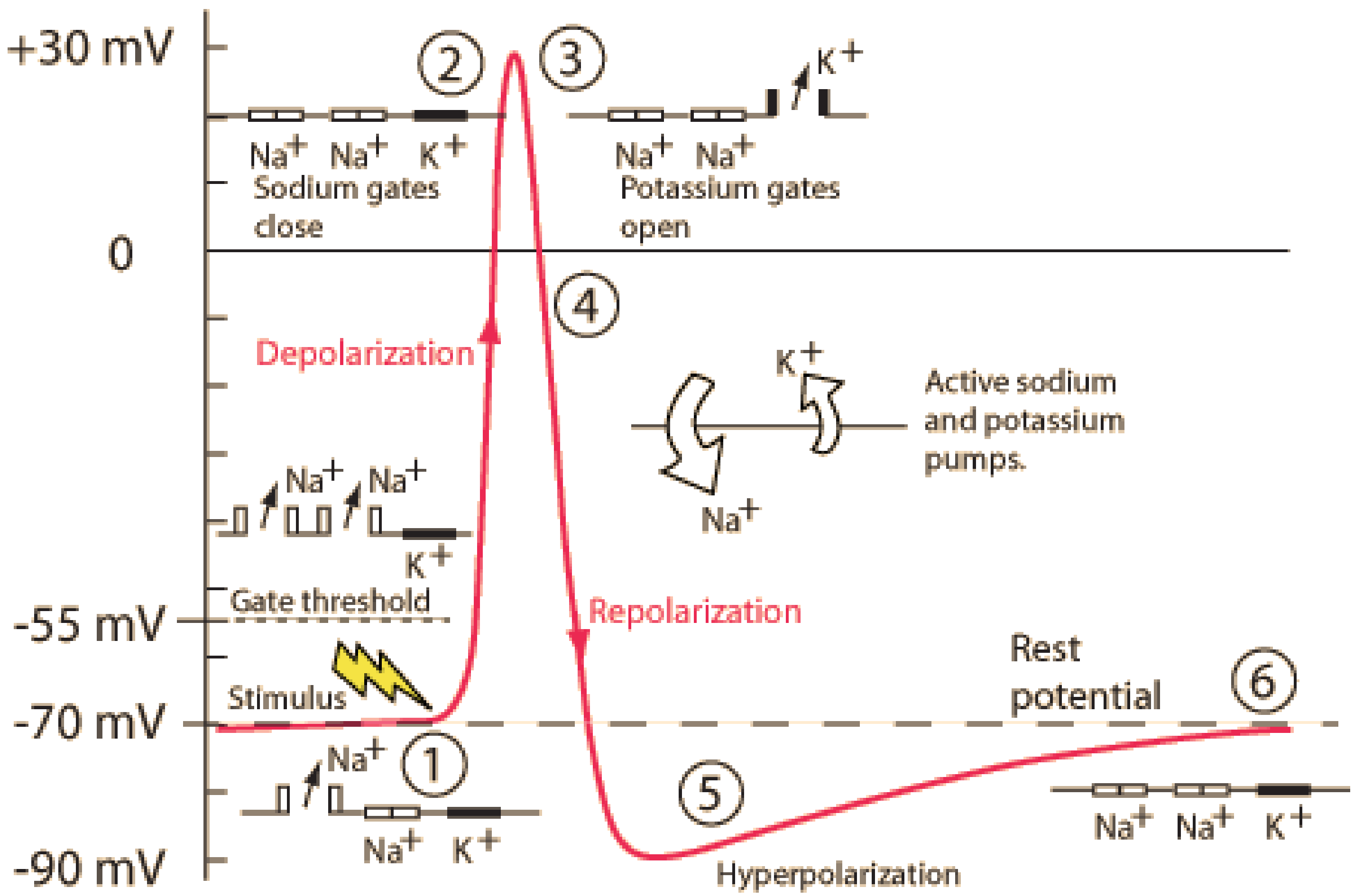
| Phase | Ion | Driving force | Flow direction | Flow magnitude |
|---|---|---|---|---|
| **Rest** | K+ | 20 mV | out | small |
| | Na+ | 125 mV | in | small |



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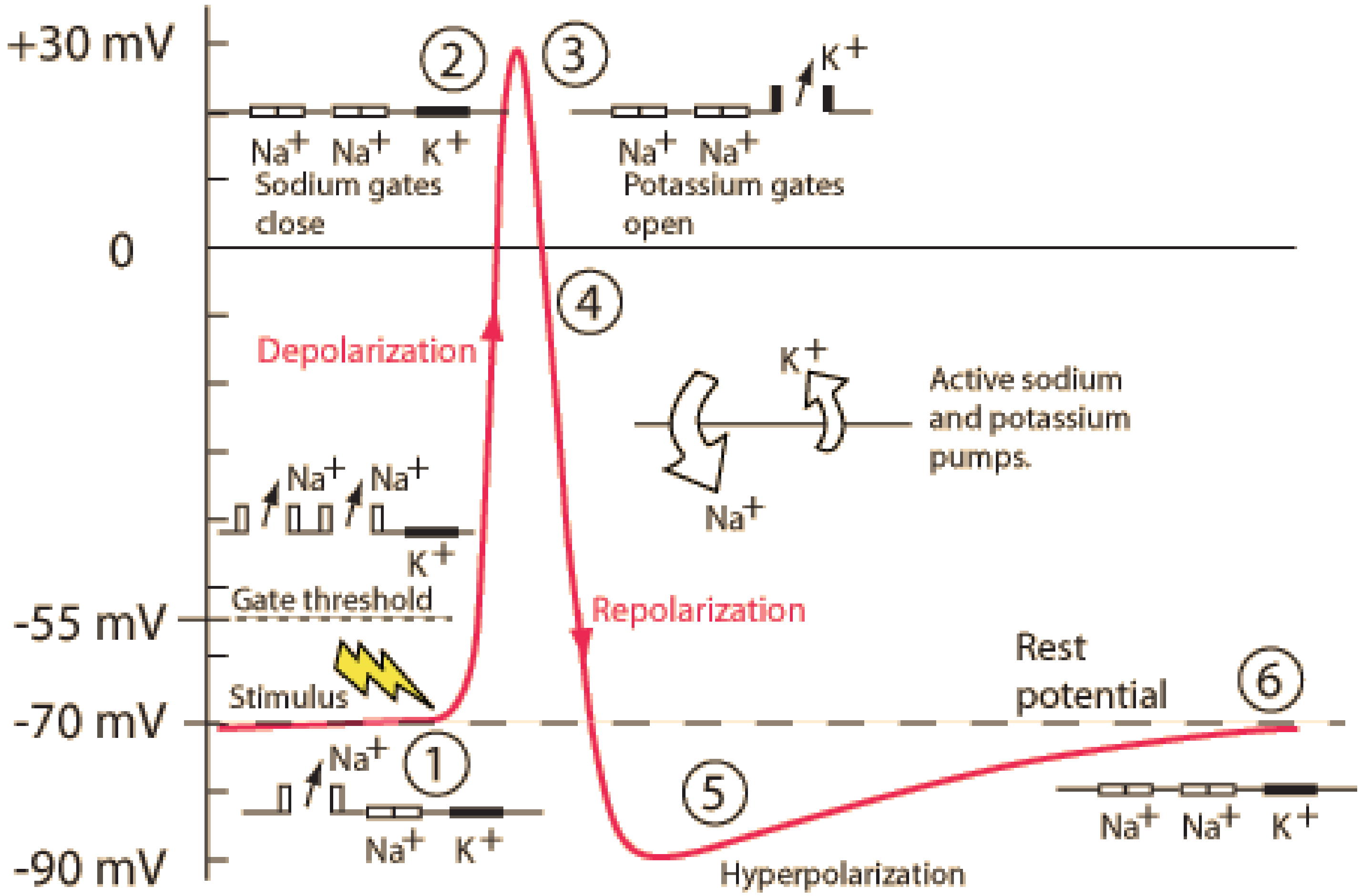
Hyperpolarization

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



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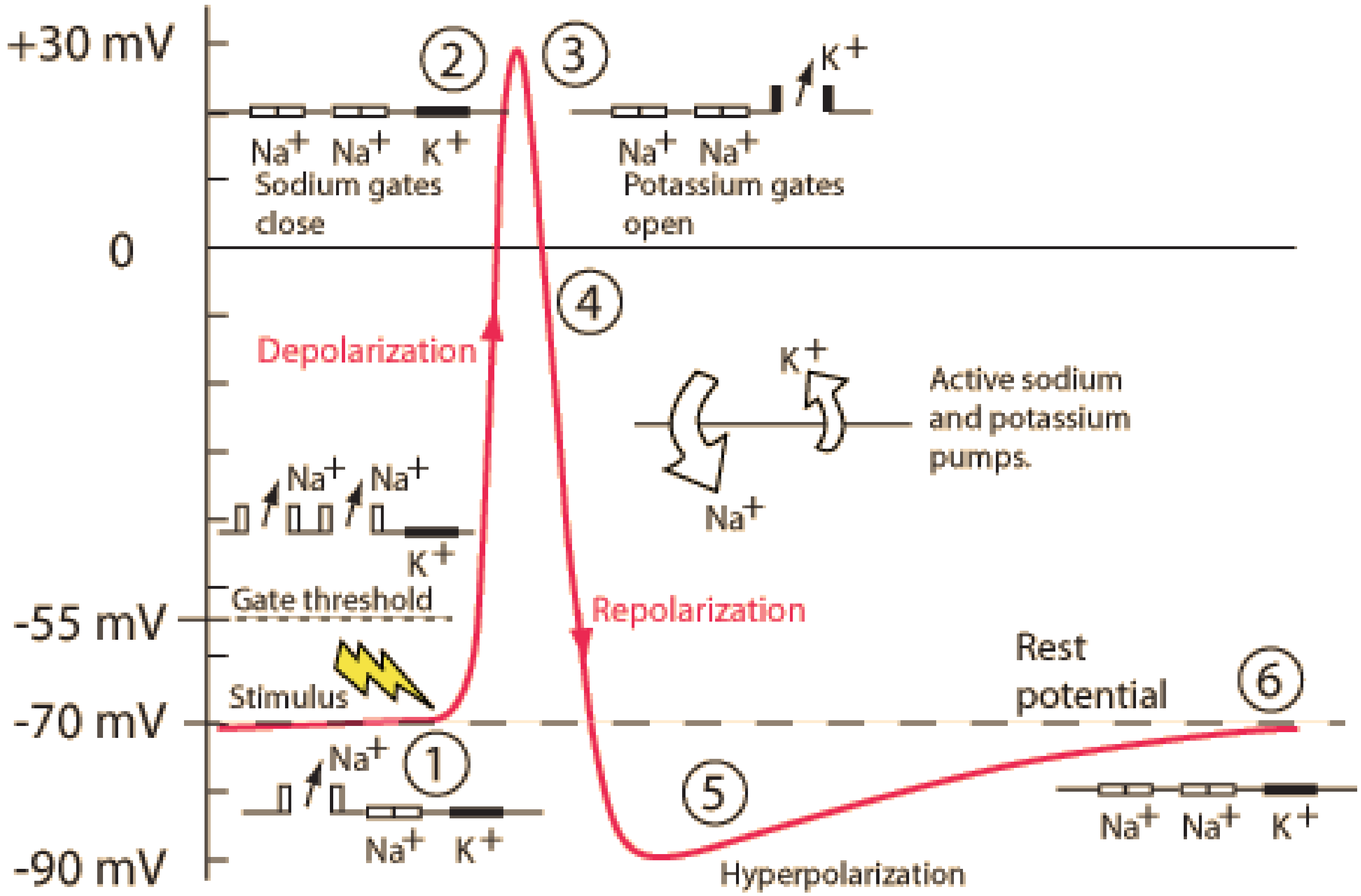
Hyperpolarization

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



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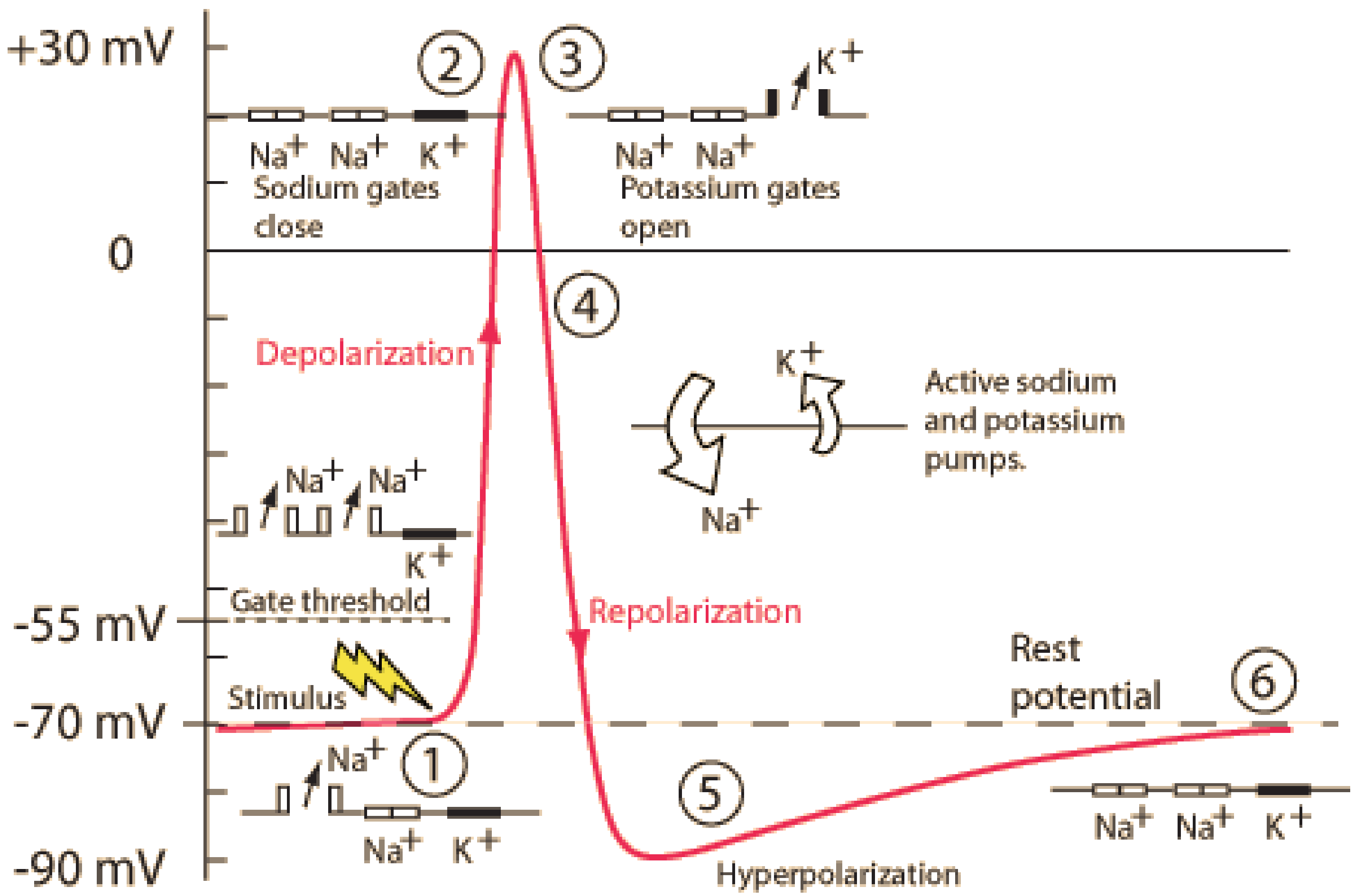
| Phase | Ion | Driving force | Flow direction | Flow magnitude |
| --- | --- | --- | --- | --- |
| **Falling** | K | shrinking | out | high |
| | Na+ | growing | in | small |



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Hyperpolarization

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

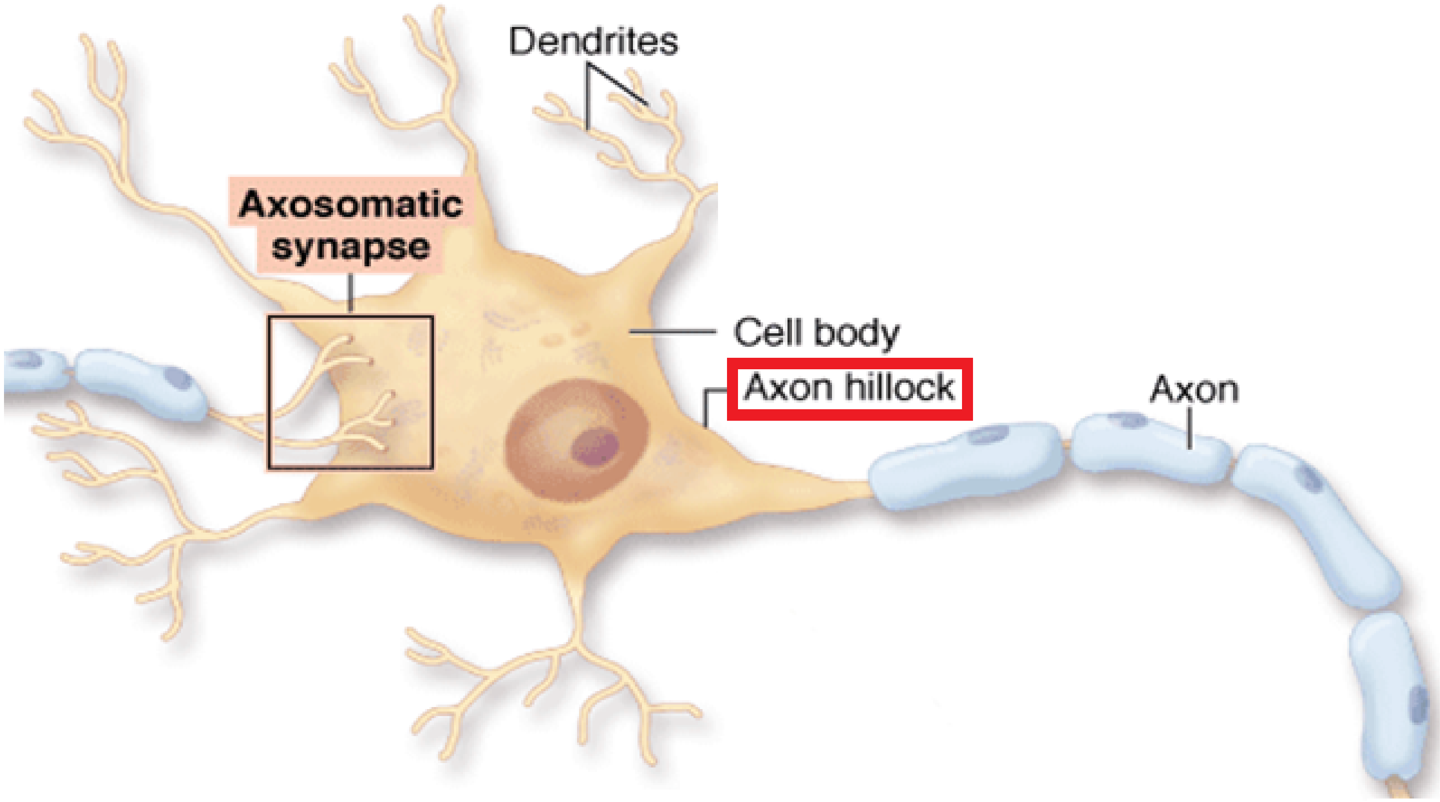
# Animation

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