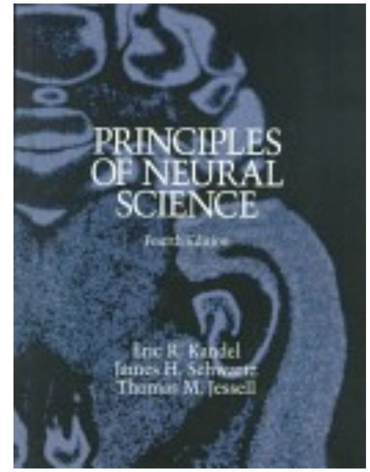
PNS Chapter 9

Propagated Signaling: Action Potential 1

Plan of Action



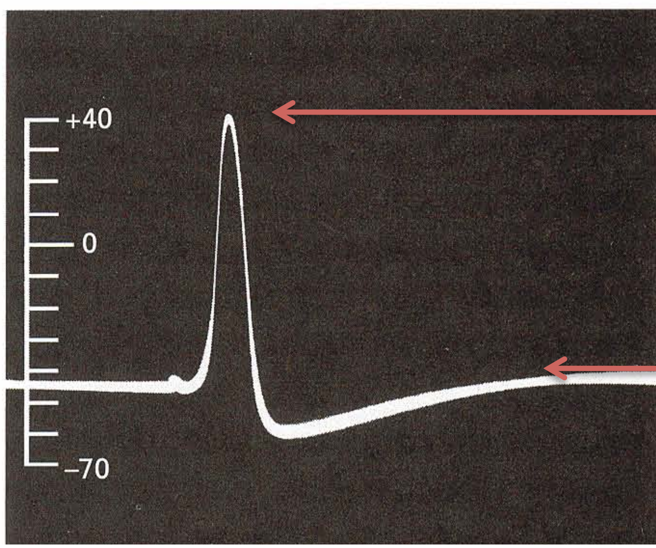
- Introduction to neuroscience
  - Chapter 1 – *The brain and behavior*
  - Chapter 2 – *Nerve cells and behavior*
- How are neural signals generated?
  - Chapter 7 – *Membrane potential*
  - Chapter 9 – *Propagated signaling: the action potential*
- How do neurons communicate with each other?
  - Chapter 10 – *Overview of synaptic transmission*
  - Chapter 12 – *Synaptic integration*

Dynamic range of action potential waveform

Table 7-1 Distribution of the Major Ions Across a Neuronal Membrane at Rest: the Giant Axon of the Squid

Species of ion	Concentration in cytoplasm (mM)	Concentration in extracellular fluid (mM)	Equilibrium potential[1] (mV)
K^+	400	20	−75
Na^+	50	440	+55
Cl^-	52	560	−60
A^- (organic anions)	385	—	—

[1]The membrane potential at which there is no net flux of the ion species across the cell membrane.



Near E_{Na}

Near E_K

Action Potentials

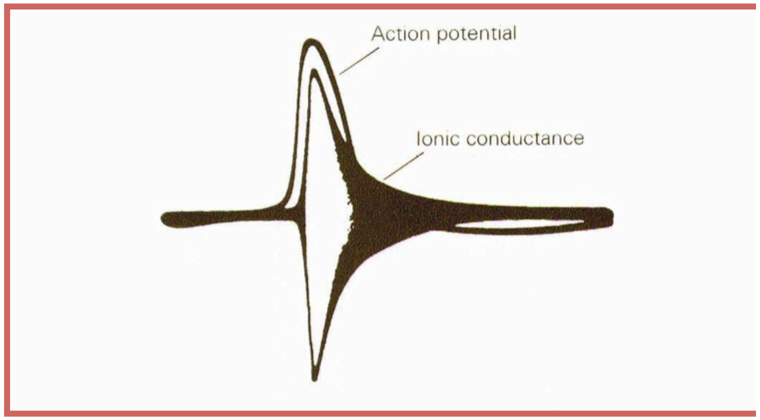
- Neurons can carry information long distances because of action potentials.
- Action potential (AP or "spike") – regenerative electrical signal whose amplitude does not attenuate as it moves down the axon.
  - Chap. 7 – APs arise from sequential changes in membrane's selectivity for Na+ and K+.
  - Chap. 9 – here we consider voltage-gated ion channels, which are critical for generating and propagating APs.

Geyser eruption:
an explosive, all-or-nothing event

Geyser Strokker, Iceland

- There are no half-eruptions. It's all or nothing.
- One eruption cannot directly follow another (minimum 5 minute gap) because it takes time for pressure to build.

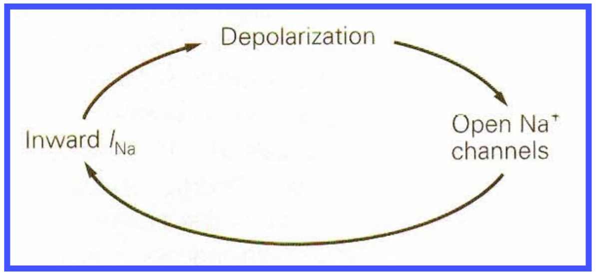
APs and Ion Flow Through Voltage-Gated Channels



- How are APs generated?
- Ion conductance **HIGH** during AP.
- 1st evidence that AP result from change in ion flux though membrane channels.

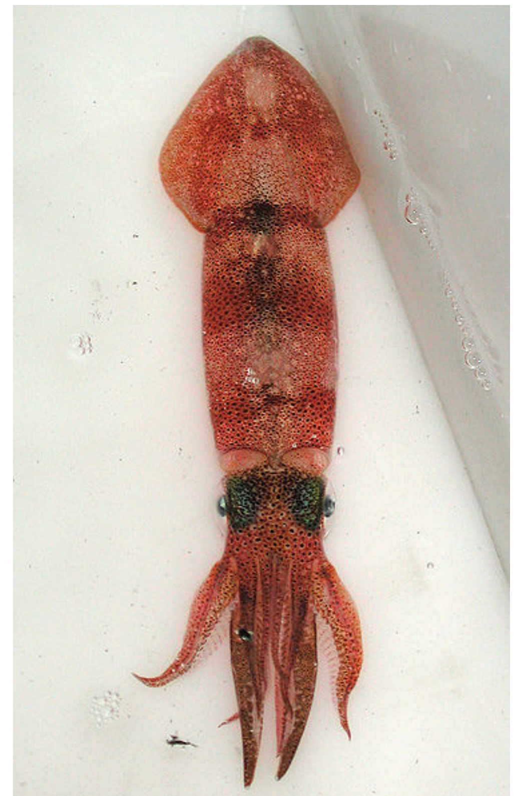
- But which ions?
- Big clue: if extracellular [Na^+] **LOW**, then AP amplitude **LOW**.
- Thus Na^+ responsible for rising edge of AP.
- Hodgkin's & Katz's data also pointed to K^+ involved w/ falling edge of AP.
- To test these hypotheses, need to measure Na^+ and K^+ conductance as a function of membrane potential (V_m).

- Problem: V_m cannot be held steady.
- Solution: The Voltage Clamp.



The Squid Giant Axon

- First “discovered” by J.Z. Young in 1936
- Controls water jet propulsion during the escape response
- 1 mm in diameter
- Unmyelinated
- The cytoplasm can be squeezed out and can be replaced with artificial medium
- So large that a glass capillary can be inserted down the length of the cell for recording membrane potentials

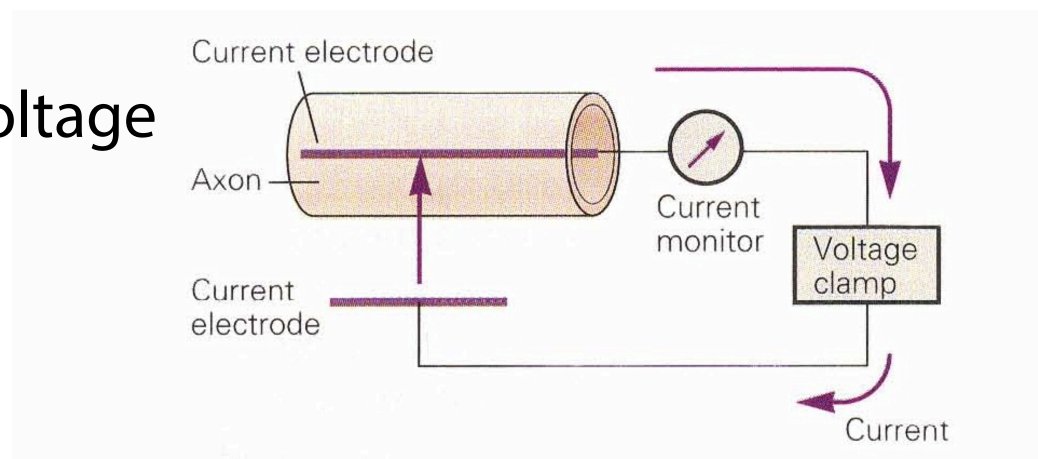


The Voltage Clamp

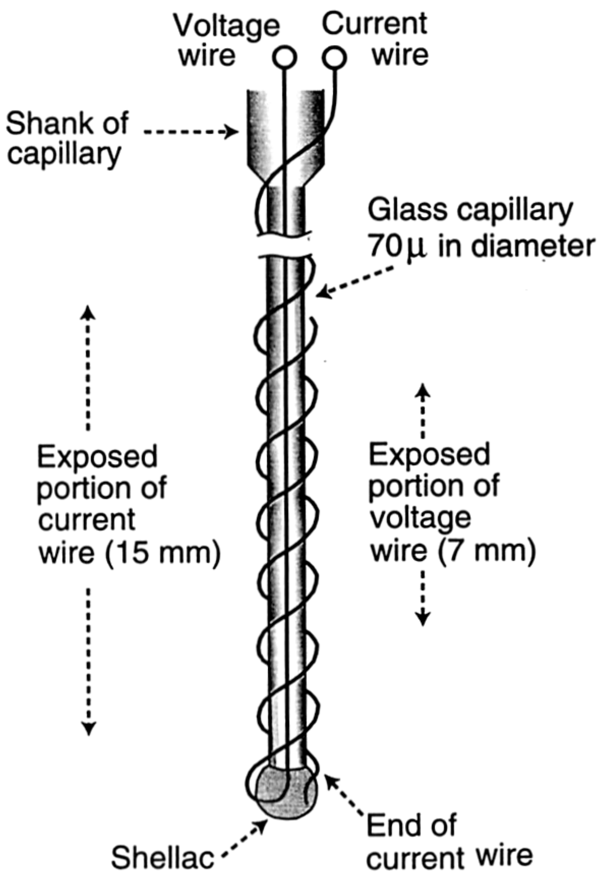
<u>Basic idea</u>:

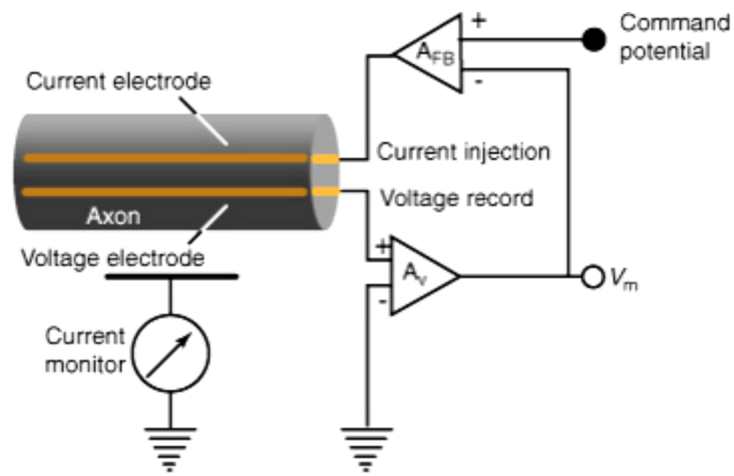
1) Voltage clamp fixes the membrane potential by passing current into or out of neuron, thereby preventing the charge separation across the membrane from changing.
2) Because the membrane potential is fixed, so is the ionic conductance.
3) The amount of current needed for 1) allows one to compute the ionic conductance:

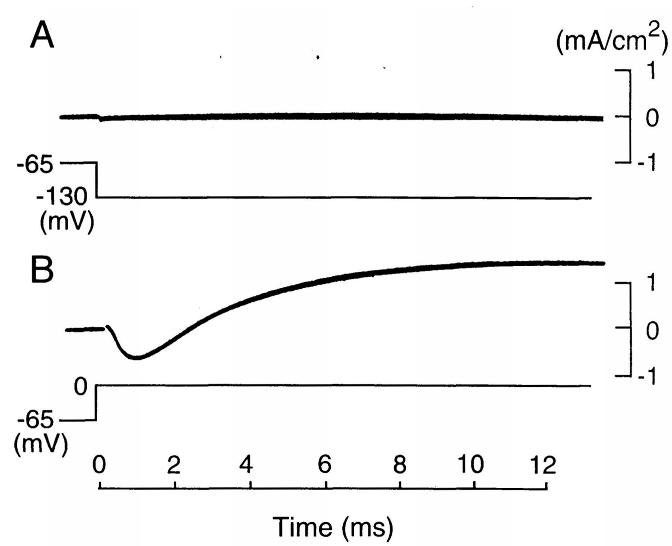
Conductance = Current / Voltage



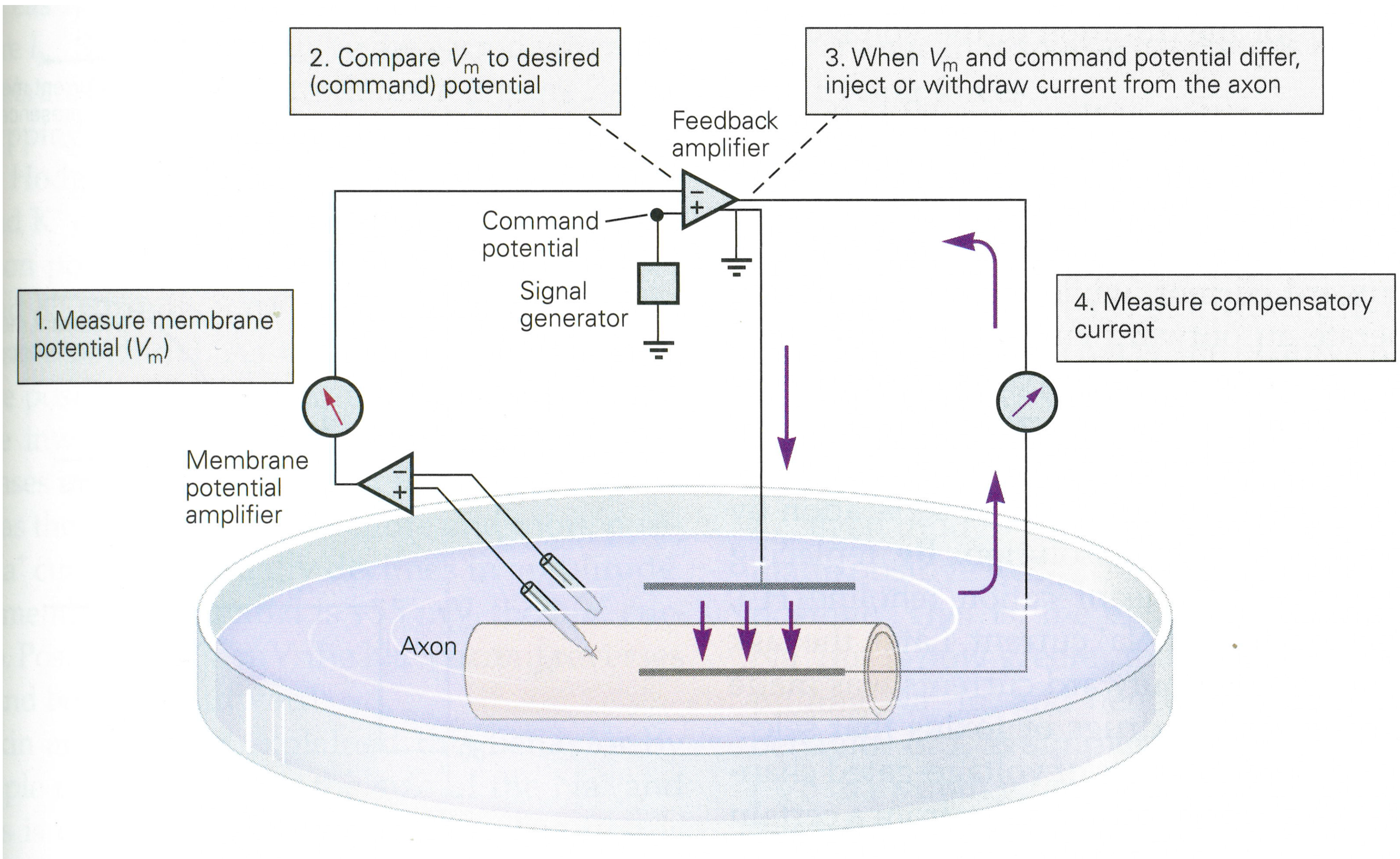
Voltage Clamp







The Voltage Clamp



Voltage Clamp Equivalent Circuit

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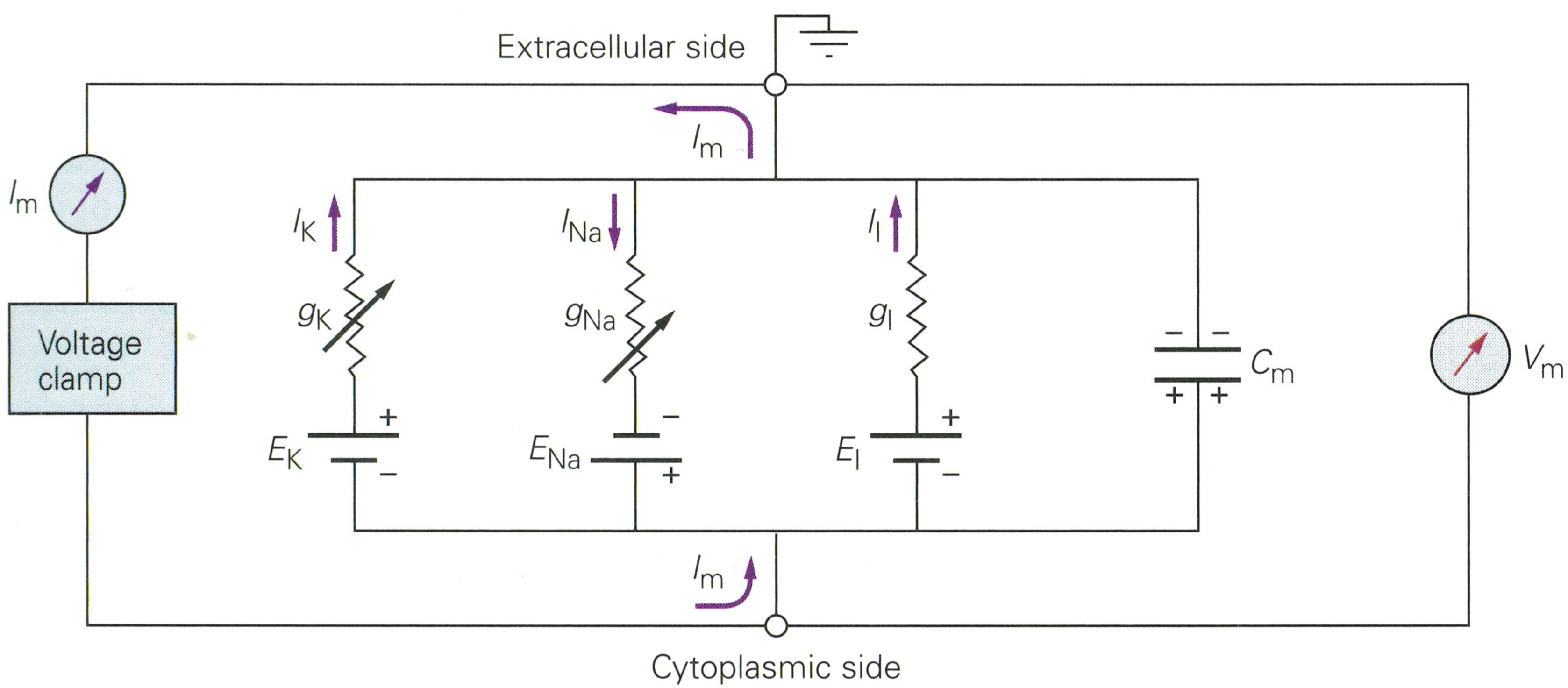
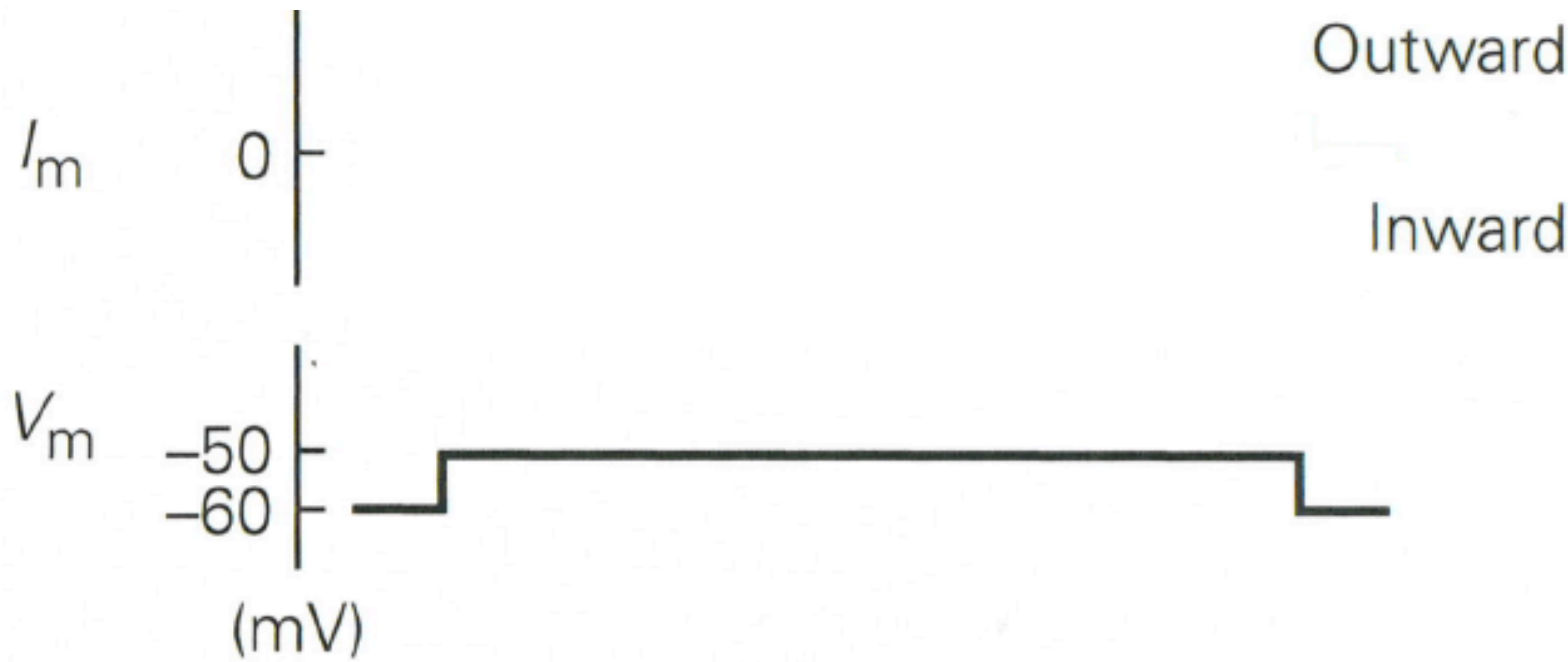
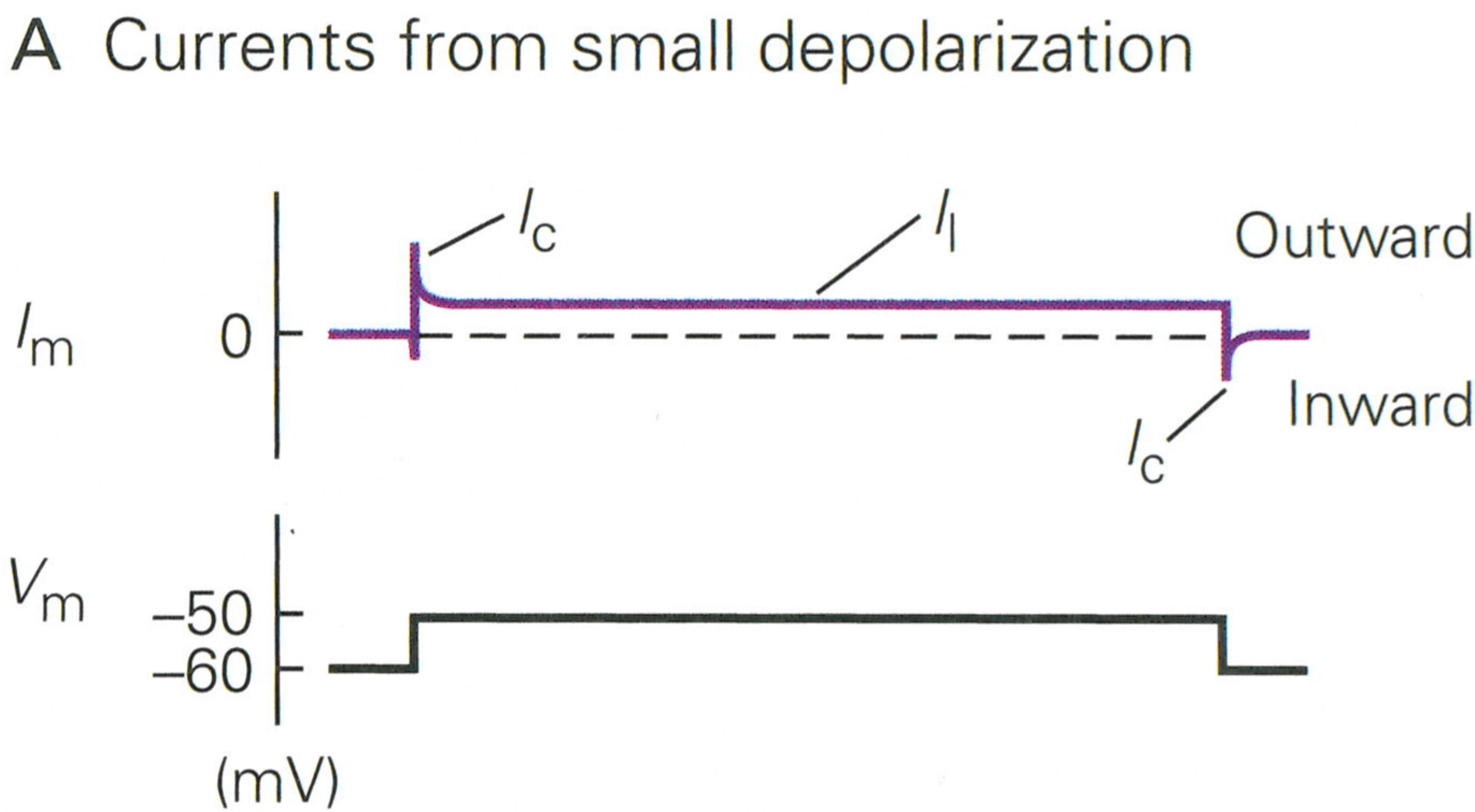


Voltage Clamp Currents

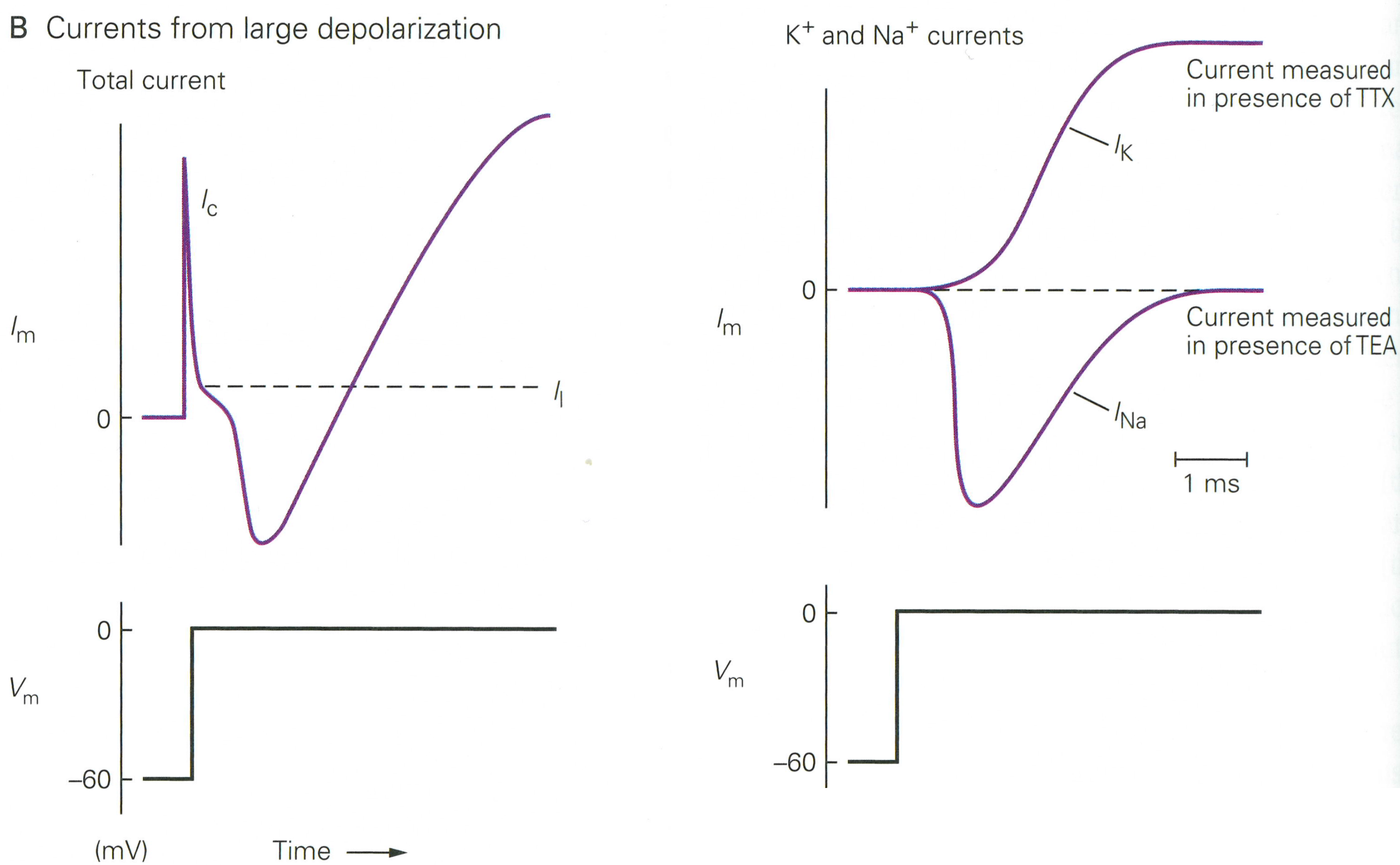
- What will the current for a small depolarization look like?



Voltage Clamp Currents



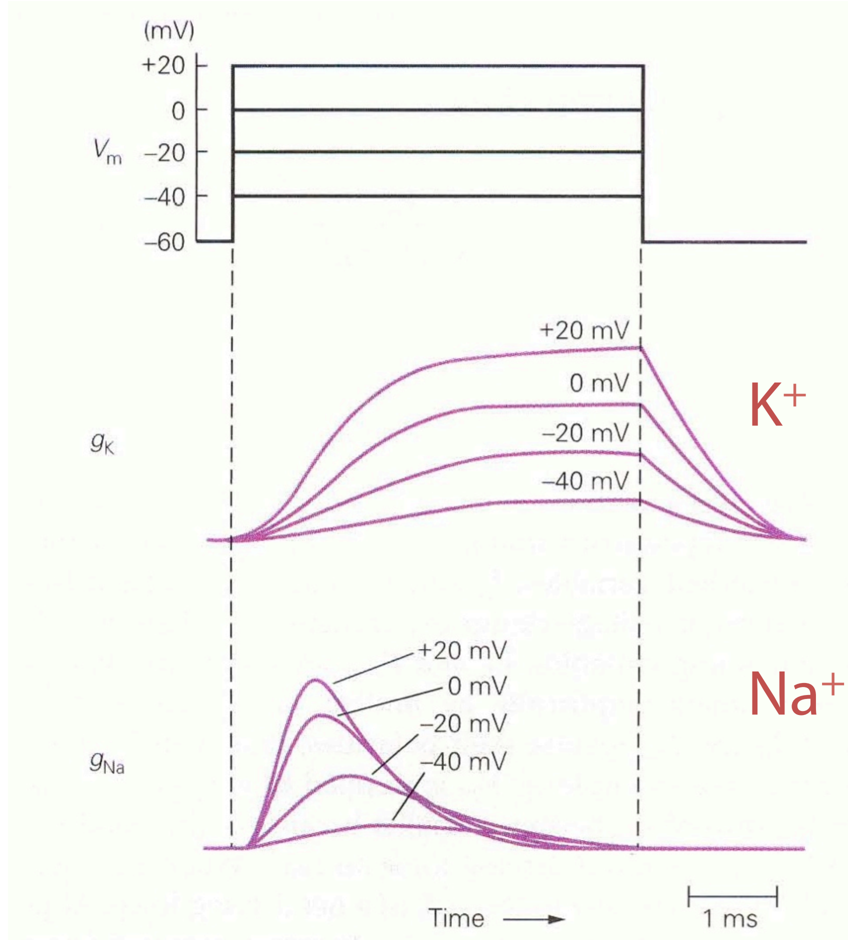
Action Potential Currents



How Would Resting Potential Affect Currents?

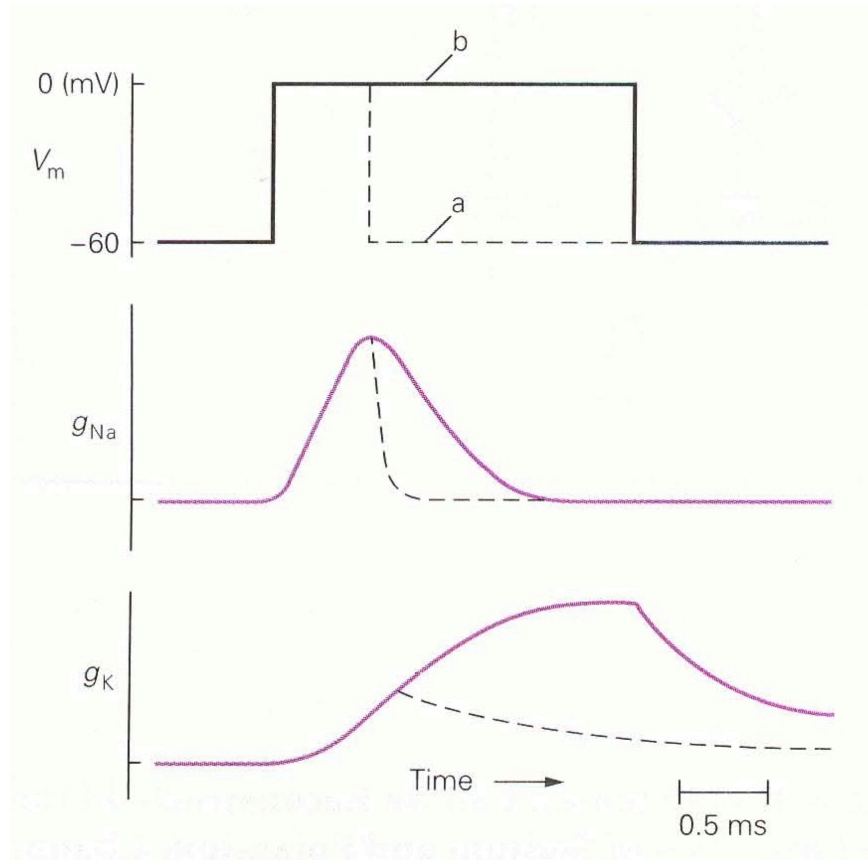
Channel Conductance Kinetics

- Na^+ and K^+ conductance similarities:
  - Depolarizing V_m steps ⇒ channels open (larger g).
  - Larger depolarizing steps ⇒ probability and rate of opening increases (g rises faster).
- Na^+ and K^+ conductance differences:
  - Rates of opening: $Na^+ > K^+$.
  - Responses to prolonged depolarization: Na^+ opens and closes (inactivation); K^+ stays open.



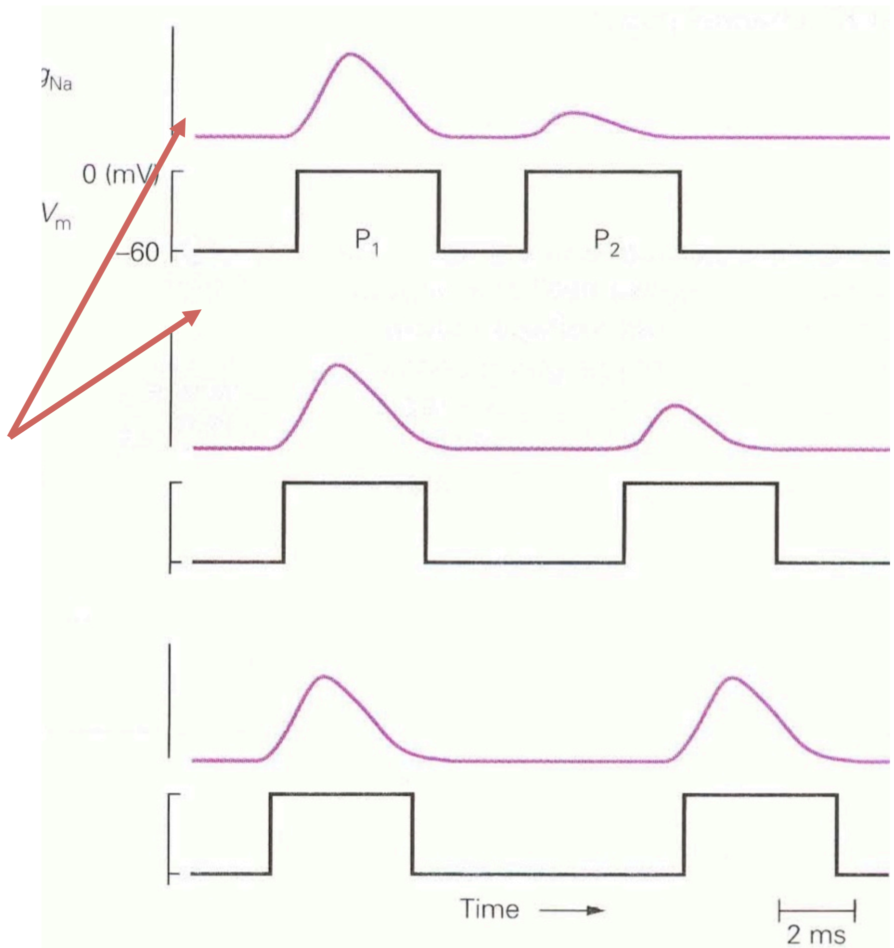
Short-term vs. Long-term Depolarization

- Short-term depolarization allows Na^+ and K^+ channels to return to their resting states.
- Long-term depolarization cause Na^+ channels to enter inactive state. K^+ channels remain open.

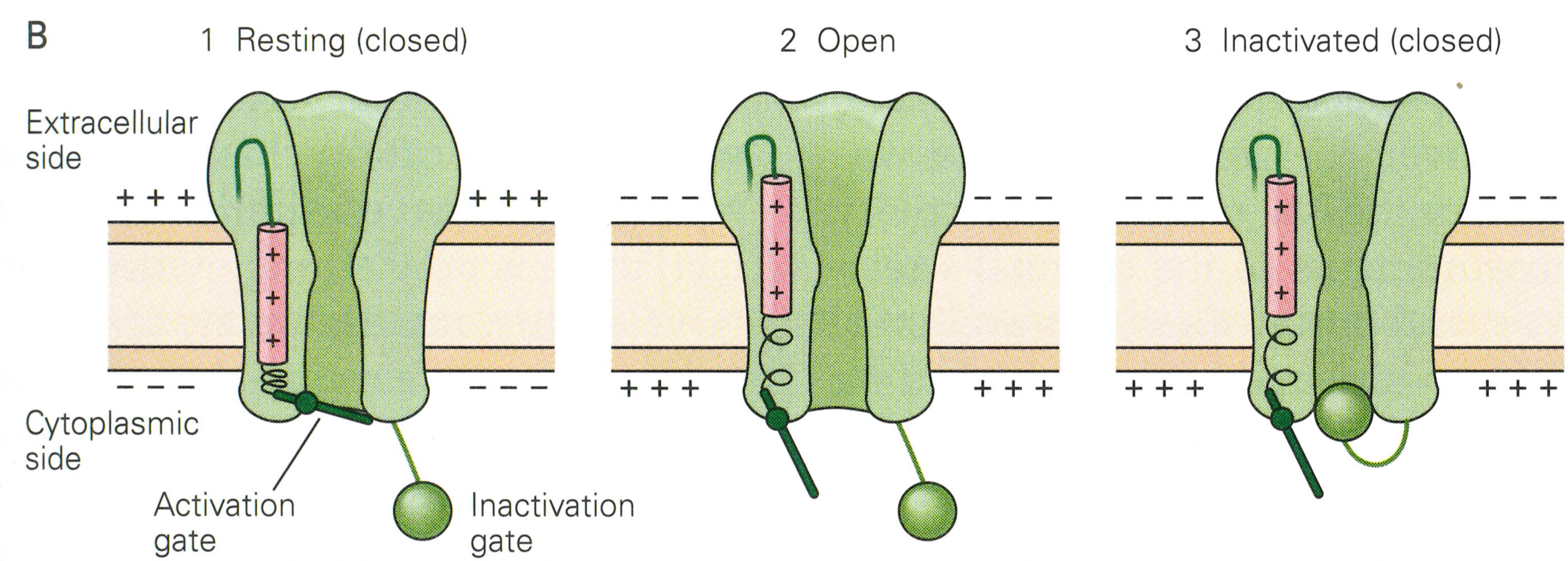


Na+ Channel Inactivation Timecourse

- Once inactivated, Na+ channels must be repolarized for a few ms in order to return to the resting state.
- If the membrane is depolarized prematurely, g_{Na} will not increase appreciably (channel still inactivated).
- Inactivation time course underlies the *refractory period*.

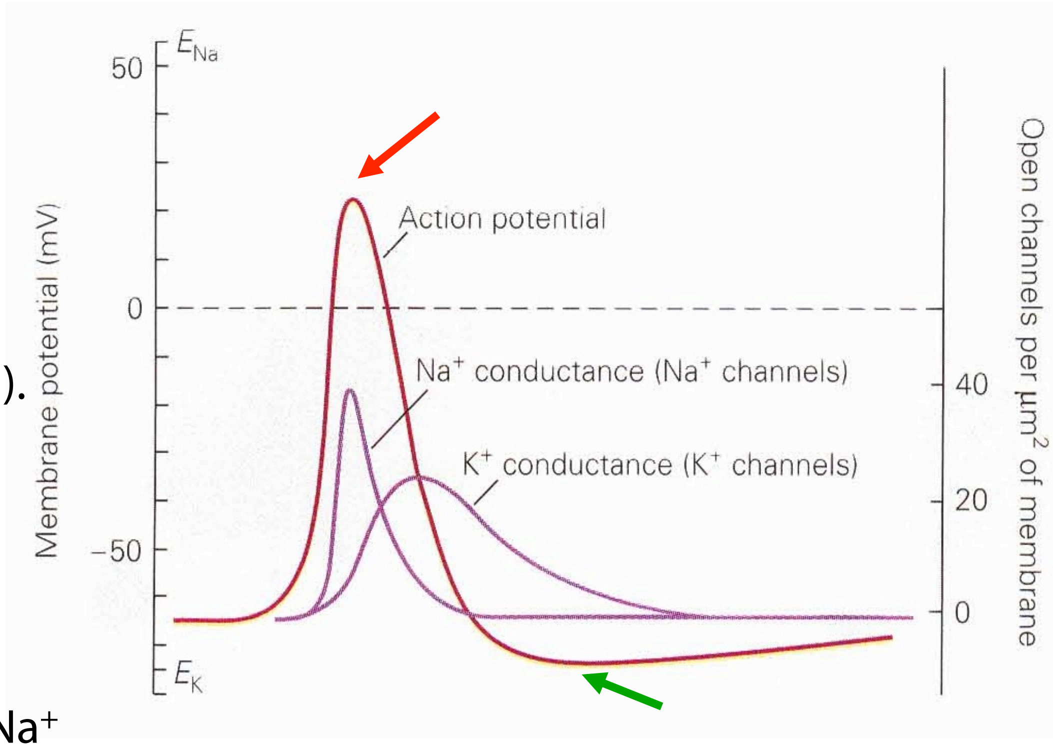


Activation Gate (fast) and Inactivation Gate (slow)



Hodgkin-Huxley Measurements & Model Explain APs

1) Depolarization event.
2) Na^+ channels open fast (g_{Na} **UP**).
3) Inward Na^+ current.
4) Further depolarization.
5) Further Na^+ channels open.
6) Positive feedback continues…
7) $V_m \Rightarrow E_{Na}$.
8) Na^+ channels inactivate (g_{Na} **DOWN**).
9) K^+ channels start opening (g_K **UP**).
10) Outward current decreases V_m.
11) $V_m \Rightarrow E_K$. Hyperpolarizes beyond resting potential (*after potential*).
12) Absolute refractory period (due to Na^+ inactivation).
13) Relative refractory period (due to increased opening of K^+).

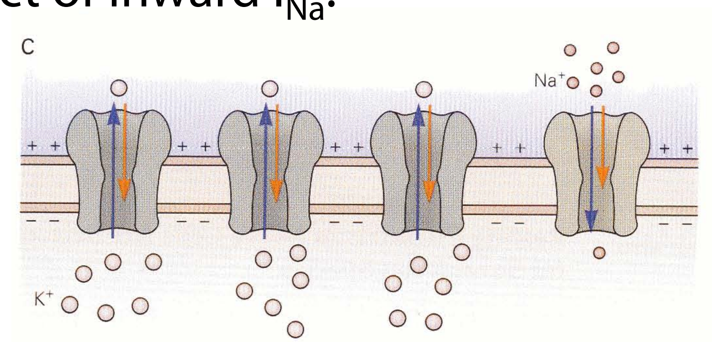


"Threshold"

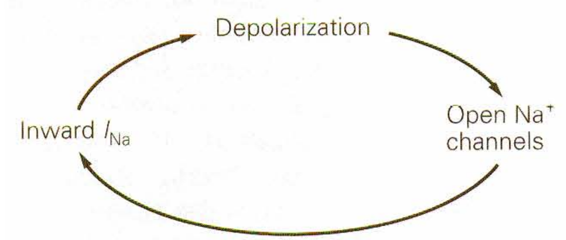
- Both Na and K currents are increasing when membrane potential is depolarized!
- What would threshold voltage be in terms of currents?

All-or-nothing behavior of APs

- Before V_m crosses a particular value (threshold), outward I_K resists depolarizing effect of inward I_{Na}.



- Threshold is the membrane voltage where inward I_{Na} exceeds outward I_K.
- At this point, **positive feedback** takes over



- and the rest of the AP waveform unfolds.