



# Lecture 3: Passive Electrical Properties

- Reading assignment from Kandell, Schwartz & Jessell:
  - Chapter 6 – Local Signaling: Passive Electrical Properties of the Neuron
- We are now equipped to calculate  $V_m$  for any set of:
  - ionic concentration gradients and
  - membrane permeabilities
  - (using Goldman equation or equivalent circuit model).
- We now must understand how  $V_m$  changes in response to stimuli.
  - What determines rate of  $V_m$  change?
  - Will a brief synaptic current always produce the same  $V_m$  change?
  - How does the size of the post-synaptic cell affect things?
  - What determines whether a stimulus will produce an action potential?



# Three Key Electrical Parameters of Interest

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- Three passive electrical properties important to electrical signaling:
  - Resting membrane resistance.
  - Membrane capacitance.
  - Intracellular axial resistance along axons and dendrites.
- These elements provide return pathway to complete electrical circuit when active currents flow into/out of the cell.
- Thus they determine the time course and amplitude of the synaptic potential change generated by synaptic current.
- They also determine whether a synaptic potential generated at the dendrite will result (at the axon-hillock trigger zone) in an action potential.
- Finally, passive properties influence the speed of action potential conduction.

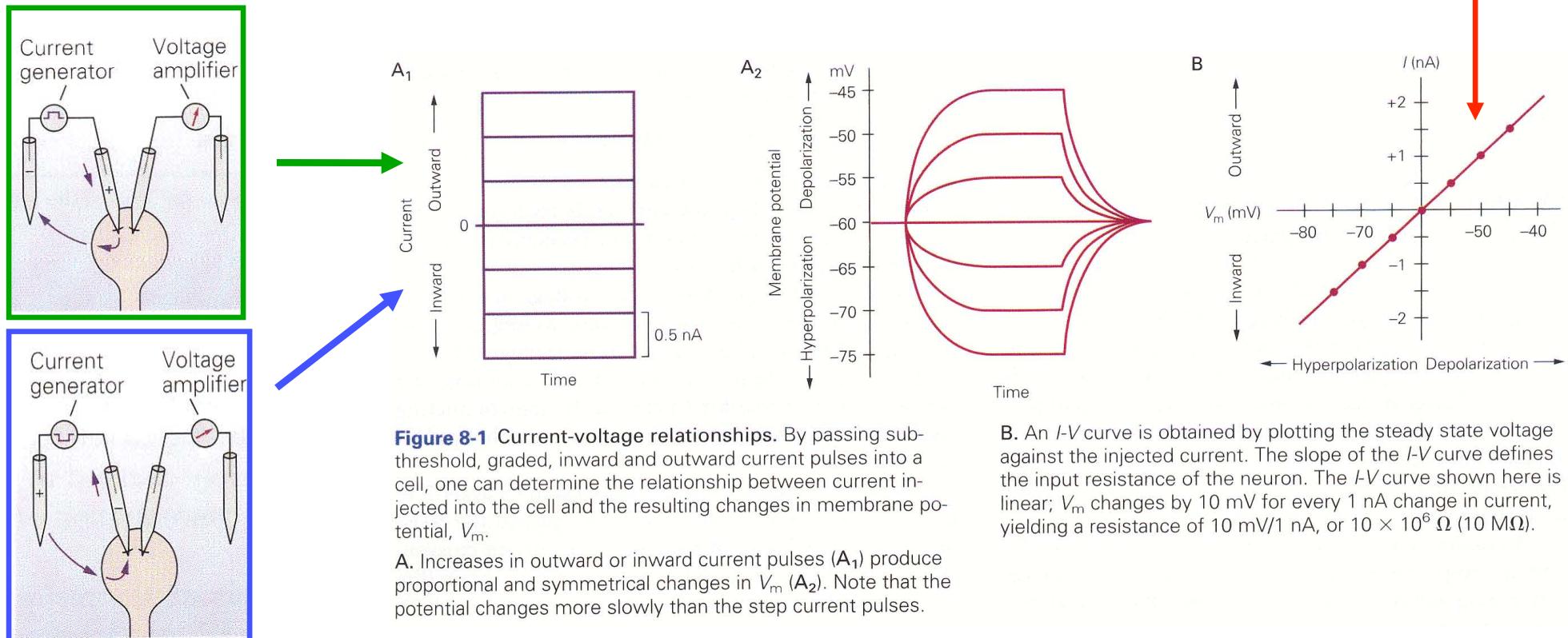


# Input Resistance and $\Delta V_m$

- Inject **negative** charge into cell  $\rightarrow V_m$  more negative (**hyperpolarize**).
- Inject **positive** charge into cell  $\rightarrow V_m$  more positive (**depolarize**).
- Linear relationship between current injected and steady state  $V_m$ .
  - Assuming hyperpolarization or subthreshold depolarization.
- This is the **input resistance**,  $R_{in}$ .
- So, a steady current drive changes  $V_m$ :  $\Delta V_m = I \times R_{in}$ .

$$\text{Slope} = 1/R_{in}$$

(e.g., 10 MΩ)





# Input Resistance and $\Delta V_m$

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- A given synaptic input current will produce a larger  $|\Delta V_m|$  the larger  $R_{in}$ .
- But what controls  $R_{in}$ ?
- For a spherical neuron w/o processes,  $R_{in}$  increases as:
  - Conductance of resting ion channels decreases.
  - Number of resting ion channels / unit surface area decreases.
  - Neuron size, and thus surface area, decreases.
- Specific membrane resistance ( $R_m$ ) = resistance of a unit area of membrane [ $\Omega \text{ cm}^2$ ].
- For a spherical neuron:  
where  $a$  is the radius. 
$$R_{in} = \frac{R_m}{4\pi a^2}$$



# Input Capacitance and $\Delta V_m$

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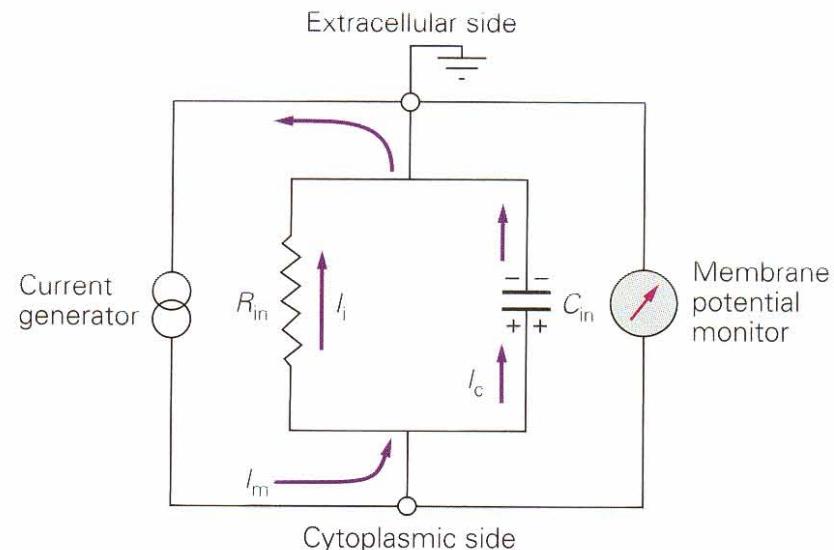
- The membrane voltage step response is not instantaneous (Fig. 6-15).
- For  $R_{in}$  we only considered steady state response (independent of C).
- For time course we must consider membrane capacitance (C).
- Straightforward to calculate and relate parameters:
  - $V_m = Q / C$
  - $\Delta V_m = \Delta Q / C$
  - $I_c = \Delta Q / \Delta t$
  - Thus, assuming constant current and no resistance:  $\Delta V_m = (I_c \Delta t) / C$
- $C = \epsilon A/d$  (parallel plate capacitor)
- $d \approx 4 \text{ nm}$
- $C_m \approx 1 \mu\text{F/cm}^2$  (specific capacitance per unit area)
- Thus, total input capacitance ( $C_{in}$ ) for a spherical neuron:

$$C_{in} = C_m \cdot 4\pi a^2$$



# RC Behavior of $\Delta V_m$

- Actually,  $R_{in}$  and  $C_{in}$  are in parallel.
- $I_m = I_i + I_c$
- $I_i$  – ionic membrane current.
- $I_c$  – capacitive membrane current.



**Figure 8-2** A simplified electrical equivalent circuit is used to examine the effects of membrane capacitance ( $C_{in}$ ) on the rate of change of membrane potential in response to current flow. All resting ion channels are lumped into a single element ( $R_{in}$ ). Batteries representing the electromotive forces generated by ion diffusion are not included because they affect only the absolute value of membrane potential, not the rate of change. This equivalent circuit represents the experimental setup shown in Box 7-1 (Figure 7-2C), in which pairs of electrodes are connected to the current generator and the membrane potential monitor.





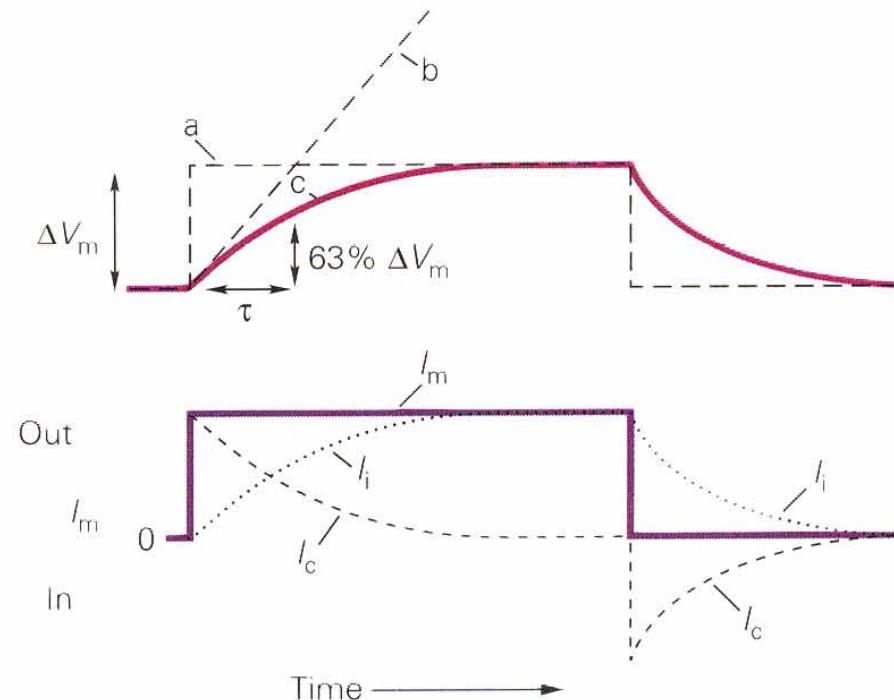
# RC Behavior of $\Delta V_m$

- In sum, simple RC circuit:

$$\Delta V_m(t) = I_m R_{in} (1 - e^{-t/\tau})$$

where

$$\tau = R_{in} C_{in}.$$



**Figure 8-3** The rate of change in the membrane potential is slowed by the membrane capacitance. The response of the membrane potential ( $\Delta V_m$ ) to a step current pulse is shown in the upper plot. The actual shape of the response (red line c) combines the properties of a purely resistive element (dashed line a) and a purely capacitive element (dashed line b). The lower plot shows the total membrane current ( $I_m$ ) and its ionic ( $I_i$ ) and capacitive ( $I_c$ ) components ( $I_m = I_i + I_c$ ) in relation to the current pulse. The time taken to reach 63% of the final voltage defines the membrane time constant,  $\tau$ . The time constants of different neurons typically range from 20 to 50 ms.



# Signal Conduction

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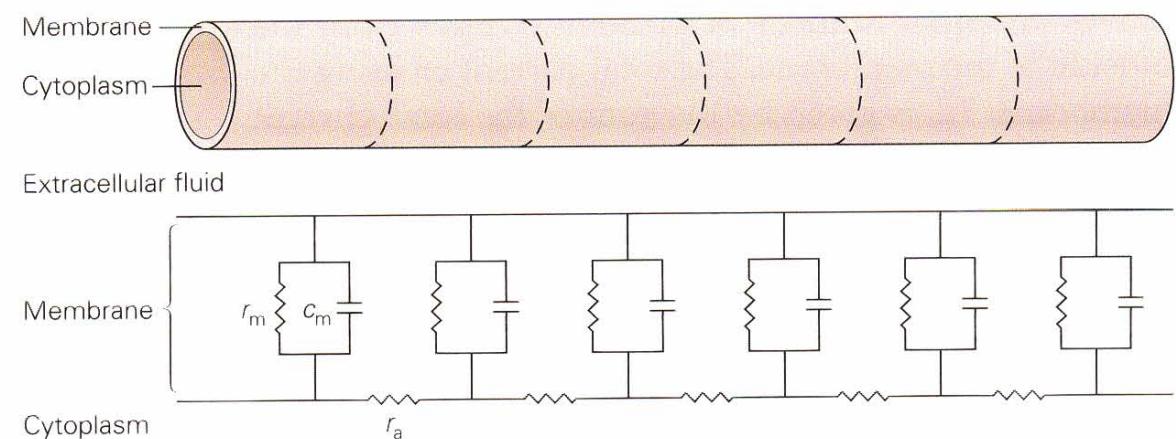
- So far we have considered  $V_m$  in/around the cell body (spherical).
- Now we consider signaling along axons and dendrites (distance matters).
- Consider synaptic potentials at dendrites conducting toward the cell body and trigger zone (where they could trigger an action potential):
  - Cytoplasmic core is highly resistive.
  - Longitudinal flow particularly so, due to small cross-sectional area.
  - Resistance due to ions colliding with other molecules  
**(akin to electron scattering in semiconductors).**
- What we need is an **incremental-length equivalent circuit**:
  - Each segment has own measurable membrane resistance ( $r_m$ ).
  - Each segment has own membrane capacitance ( $c_m$ ).
  - Each segment has own axial resistance within cytoplasmic core ( $r_a$ ).
  - **(Akin to electromagnetic transmission line models).**



# Signal Conduction – Equiv. Ckt. Model

- With this equivalent circuit model it is possible to solve for  $V_m(x,t)$  as a function of injected current  $I(x,t)$  and  $r_m$ ,  $c_m$  and  $r_a$ .
- Computational simulation packages (e.g., Neuron, Genesis) allow one to specify parameters, and solve for  $V_m(x,t)$ .  
**(akin to SPICE/SUPREM circuit/devices simulators).**
- We'll now consider special (simple, but important) cases.

**Figure 8-4** A neuronal process can be represented by an electrical equivalent circuit. The process is divided into unit lengths. Each unit length of the process is a circuit with its own membrane resistance ( $r_m$ ) and capacitance ( $c_m$ ). All the circuits are connected by resistors ( $r_a$ ), which represent the axial resistance of segments of cytoplasm, and a short circuit, which represents the extracellular fluid.

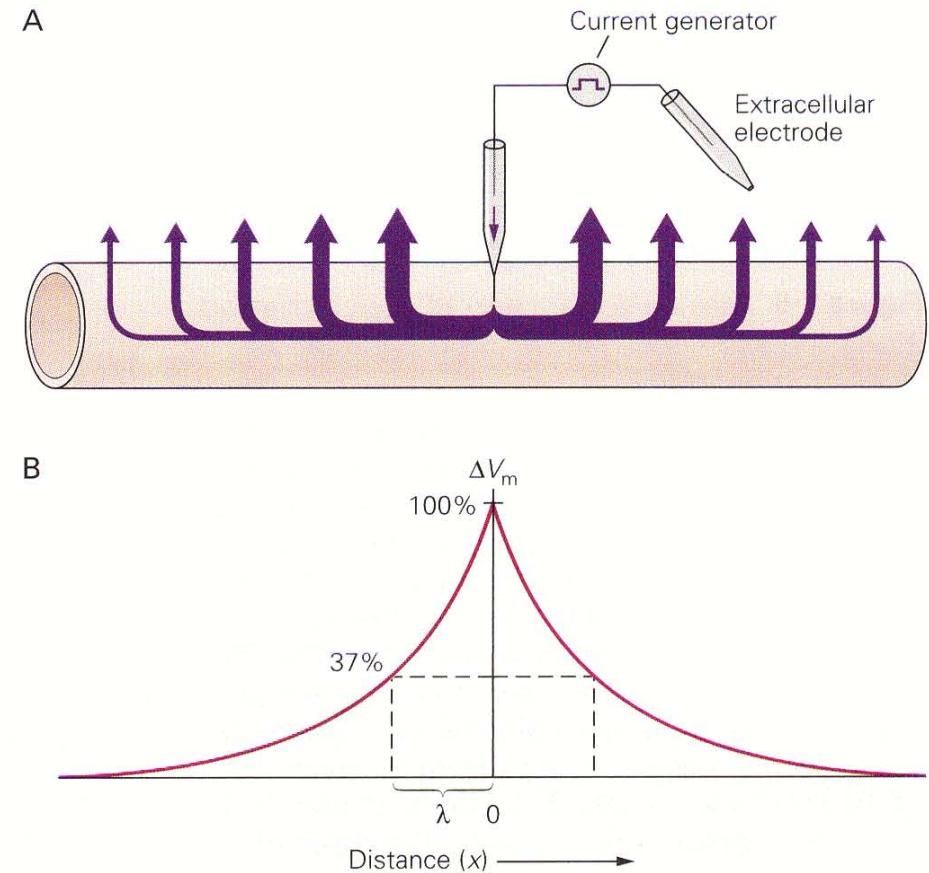




# Signal Conduction – Constant Input

- Constant current on for  $t \gg \tau$ .
- Thus, steady state ( $I_c = 0$ ;  $I_m = I_i$ ).
- Thus, potential distribution depends on relative values of  $r_m$  and  $r_a$ .
- Axial resistance at point  $x$  is:  
 $r_x = r_a x$ .
- Membrane resistance at point  $x$  is:  
 $r_m = r_m$ .
- $V_m(x) = I_m r_m$
- Thus, current-injection induced change in membrane potential decays with distance:

$$\Delta V(x) = \Delta V_o e^{-x/\lambda}$$
$$\lambda = \sqrt{r_m/r_a}$$



**Figure 8-5** The voltage response in a passive neuronal process decays with distance due to electronic conduction. Current injected into a neuronal process by a microelectrode follows the path of least resistance to the return electrode in the extracellular fluid (A). The thickness of the arrows represents membrane current density at any point along the process. Under these conditions the change in  $V_m$  decays exponentially with distance from the site of current injection (B). The distance at which  $\Delta V_m$  has decayed to 37% of its value at the point of current injection defines the length constant,  $\lambda$ .



# Signal Conduction – Geometry

$$\Delta V(x) = \Delta V_o e^{-x/\lambda}$$

$$\lambda = \sqrt{r_m/r_a}$$

- $\lambda$  is a length constant
- Better membrane insulation increases  $r_m$ .
- Better inner core conduction decreases  $r_a$ .
- Both increase  $\lambda \rightarrow$  current able to spread farther along before leaking.
- For a cylindrical dendrite of radius  $a$ :

$$r_a = \rho / \pi a^2$$

$$r_m = R_m / 2\pi a$$

$$\lambda = \sqrt{\frac{R_m}{\rho} \cdot \frac{a}{2}}$$

- Thus thicker axons and dendrites transmit “electrotonic” signals farther.
- Typical  $\lambda = 0.1 - 1.0$  mm



# Signal Conduction & Neural Function

- Electrotonic conduction efficiency has two effects on neural function:
  - **Spatial summation** – synaptic potentials generated in different regions of the neuron are added together at the trigger zone.

*Neuron geometry/structure, and thus how electrotonic signals are combined, is a fundamental aspect of neural computation.*

- **Propagation** – local depolarization (region of action potential) spreads electrotonically down the axon, causing adjacent regions of the membrane to reach threshold.

*Neurons with longer length constants have greater electrotonic spread → action potentials propagate more rapidly.*

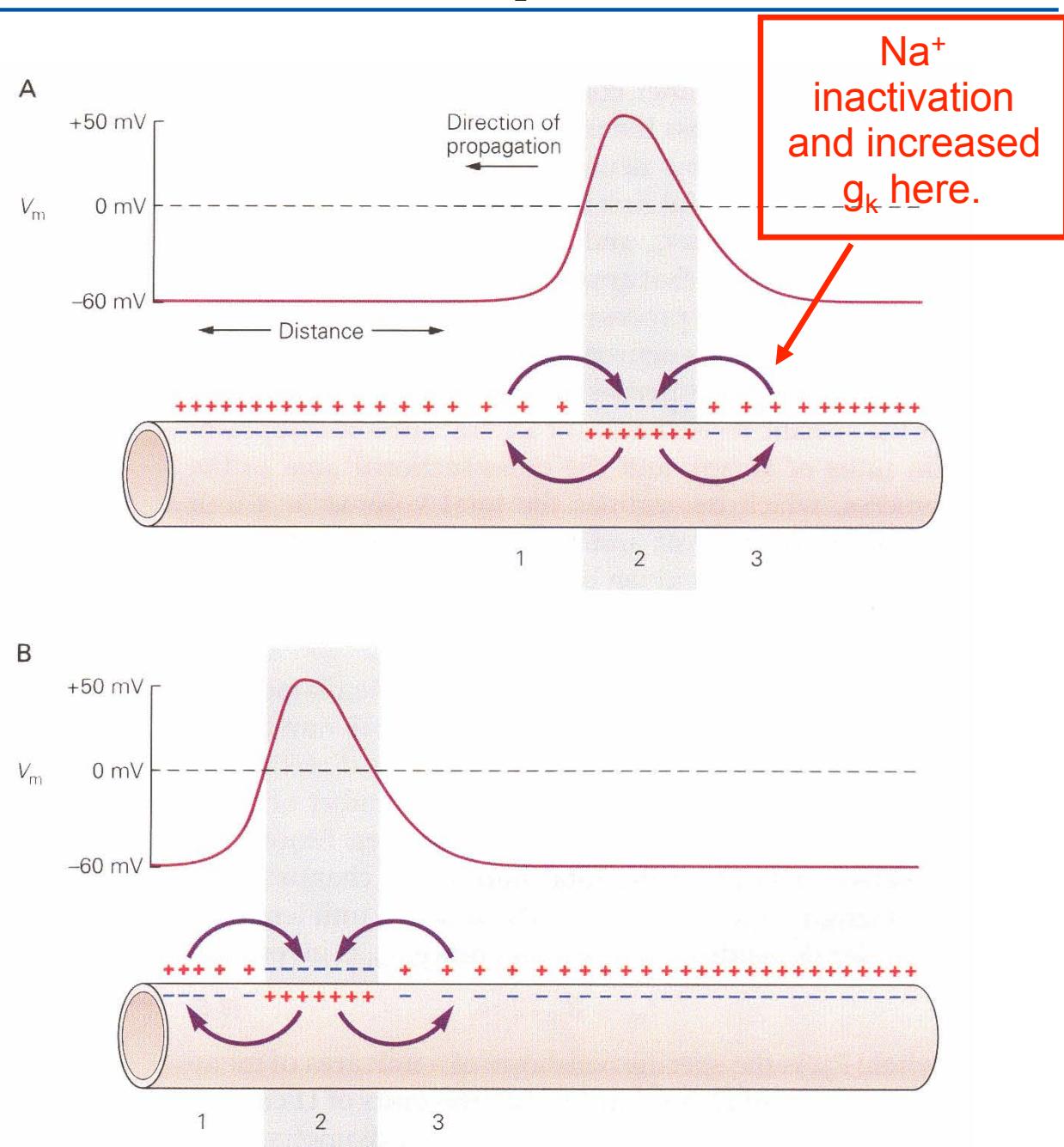


# Passive Conduction of Depolarization

**Figure 8-6** Passive conduction of depolarization along the axon contributes to propagation of the action potential.

**A.** The waveform of an action potential propagating from right to left. The difference in potential along the length of the axon creates a local-circuit current flow that causes the depolarization to spread passively from the active region (**2**) to the inactive region *ahead* of the action potential (**1**), as well as to the area *behind* the action potential (**3**). However, because there is also an increase in  $g_K$  in the wake of the action potential (see Chapter 9), the buildup of positive charge along the inner side of the membrane in area **3** is more than balanced by the local efflux of  $K^+$ , allowing this region of membrane to repolarize.

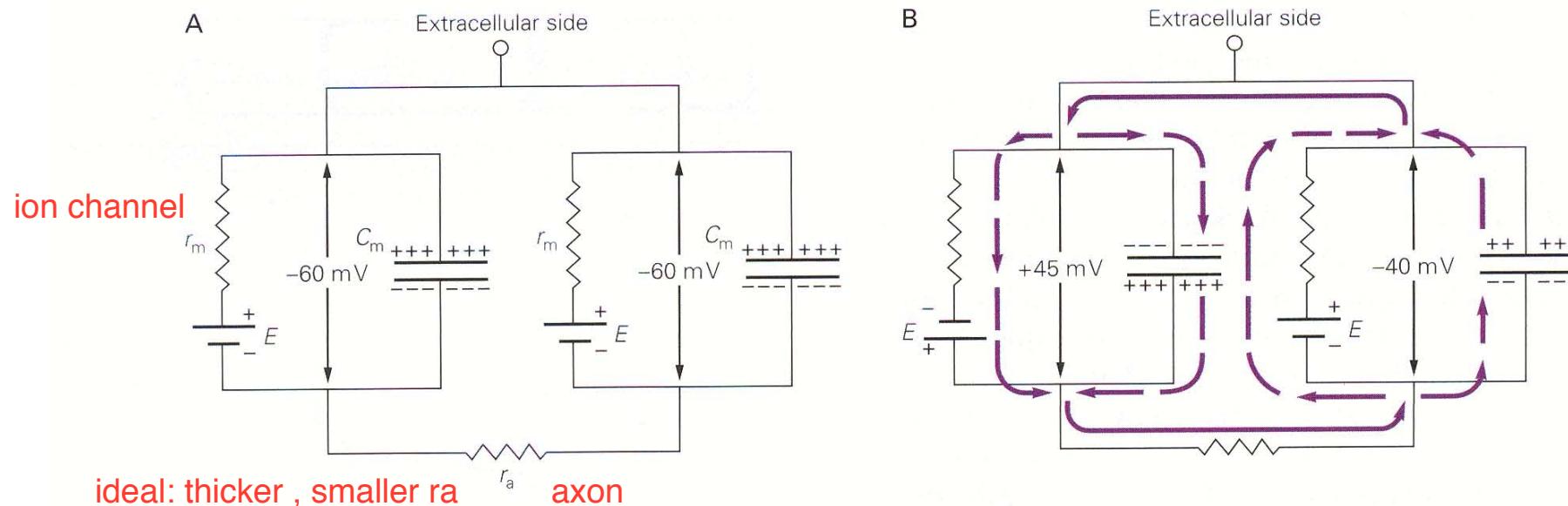
**B.** A short time later the voltage waveform and the current distributions have shifted down the axon and the process is repeated.





# Action Potential Velocity

- Larger  $C_m$  requires more charge to change  $V_m \rightarrow$  thus slower.
- Larger  $r_a$  limits current passing from one segment to next  $\rightarrow$  thus slower.



**Figure 8-7** Axial resistance and membrane capacitance limit the rate of spread of depolarization during the action potential.

A. The electrical equivalent circuit represents two adjacent segments of the resting membrane of an axon connected by a segment of axoplasm ( $r_a$ ).

B. An action potential is spreading from the membrane segment on the **left** to the segment on the **right**. Purple lines indicate pathways of current flow.



# Action Potential Velocity

- It is important to have fast action potentials.
- Action potential speed  $\propto \frac{1}{r_a c_m}$  r<sub>a</sub>\*cm time constant
- Two mechanisms have evolved to increase speed:
  - Increase diameter of axon core:  
 $r_a \propto \frac{1}{\text{diameter}^2}$  and  $c_m \propto \text{diameter}$   
thus  $r_a c_m \propto \frac{1}{\text{diameter}}$  → speed  $\propto \text{diameter}$ .  
cin = cm \* A  
cylinder : cin = cm \* 2 \* pi \* radius
  - Myelination of the axon (glial cell wrapping) effectively increases membrane thickness (up to 100x).

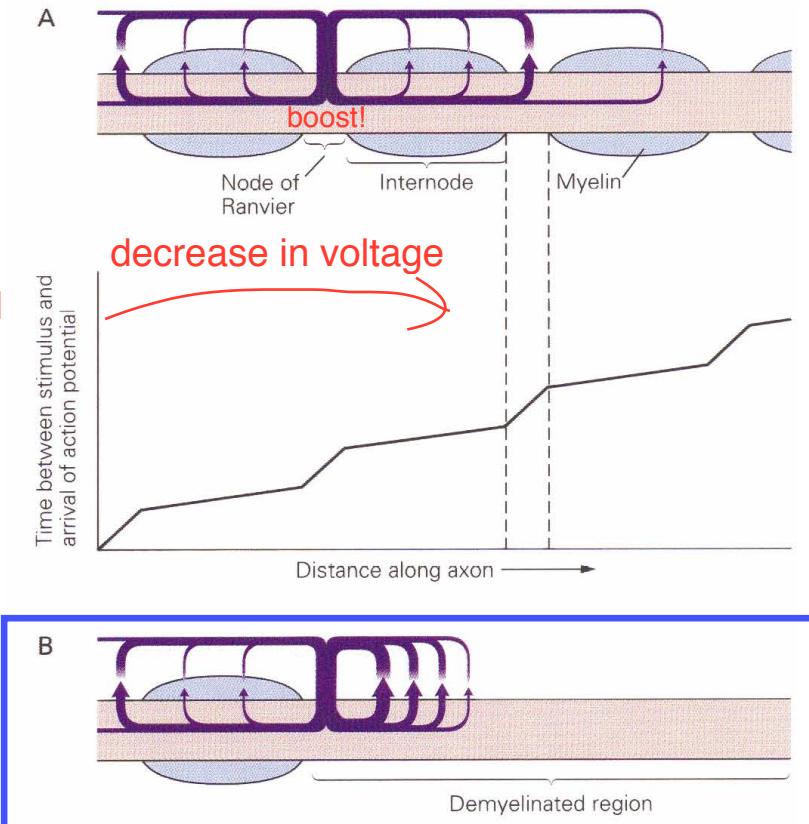
$c_m \propto \frac{1}{\text{thickness}}$   
thus  $r_a c_m \propto \frac{1}{\text{thickness}}$  → speed  $\propto \text{thickness}$ .

different term: diameter and thickness



# Nodes of Ranvier

- For neurons w/ myelinated axon, action potentials (APs) triggered at nonmyelinated segment of membrane at axon hillock.
  - This current can discharge capacitance of myelinated axon segment ahead of it.
  - Myelin sheath interrupted every 1-2 mm by bare patches (~2  $\mu\text{m}$  in length).
  - These Nodes of Ranvier are dense in voltage-gated  $\text{Na}^+$  channels → boost amplitude of APs and keep them from dying out.
- Multiple sclerosis is caused by demyelination.



**Figure 8-8** Action potentials in myelinated nerves are regenerated at the nodes of Ranvier.

- A. In the axon capacitive and ionic membrane current densities (membrane current per unit area of membrane) are much higher at the nodes of Ranvier than in the internodal regions. The density of membrane current at any point along the axon is represented by the thickness of the arrows. Because of the higher capacitance of the axon membrane at the unmyelinated nodes, the action potential slows down as it approaches each node and thus appears to skip rapidly from node to node.
- B. In regions of the axon that have lost their myelin, the spread of the action potential is slowed down or blocked. The local-circuit currents must charge a larger membrane capacitance and, because of the low  $r_m$ , they do not spread well down the axon.



# Propagated Signals – Action Potentials

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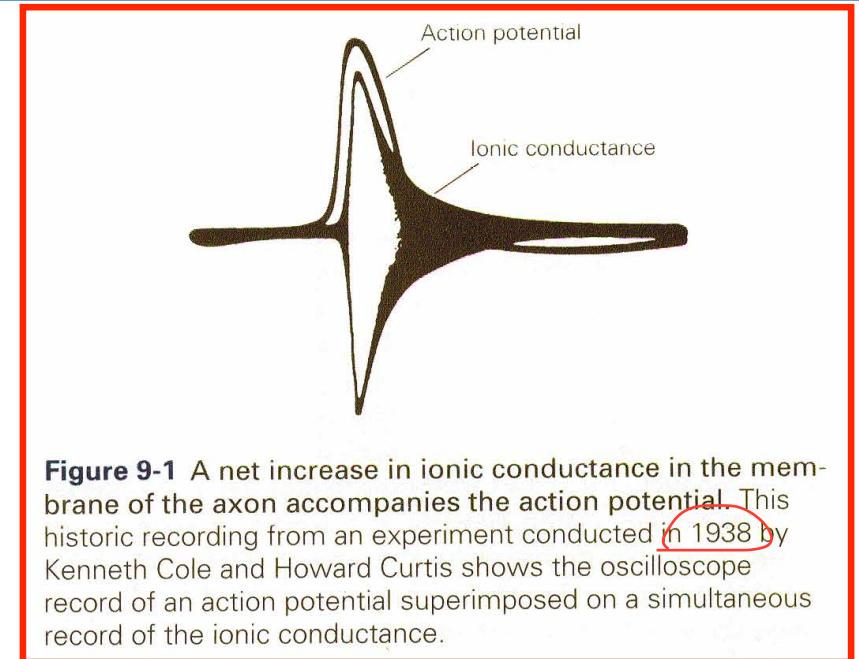
- Reading assignment from Kandell, Schwartz & Jessell:
  - Chapter 7 – Propagated Signaling: The Action Potential
- Neurons can carry information long distances b/c of action potentials.
- Action potentials (APs or “spikes”) – regenerative electrical signal whose amplitude does not attenuate as it moves down the axon.
  - Chap. 6 – APs arise from sequential changes in membrane’s selectivity for  $\text{Na}^+$  and  $\text{K}^+$ .
  - Chap. 6 – membrane’s passive properties influence AP propagation speed.
  - Chap. 7 – here we consider voltage-gated ion channels, which are critical for generating and propagating APs.



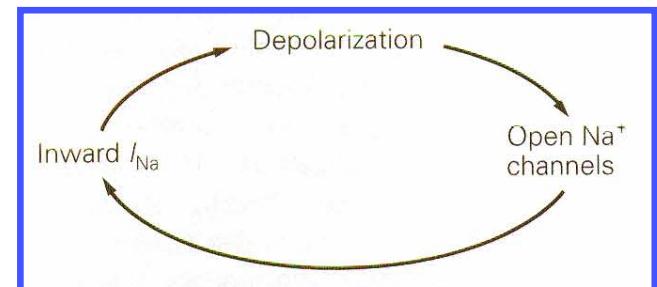
# APs and Ion Flow Through Voltage-Gated Channels

- How are APs generated?
- Ion conductance **HIGH** during AP.
- 1<sup>st</sup> evidence that AP result from change in ion flux through 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:  $V_m$  and ion conductance coupled.
- Solution: The Voltage Clamp.



**Figure 9-1** A net increase in ionic conductance in the membrane of the axon accompanies the action potential. This historic recording from an experiment conducted in 1938 by Kenneth Cole and Howard Curtis shows the oscilloscope record of an action potential superimposed on a simultaneous record of the ionic conductance.



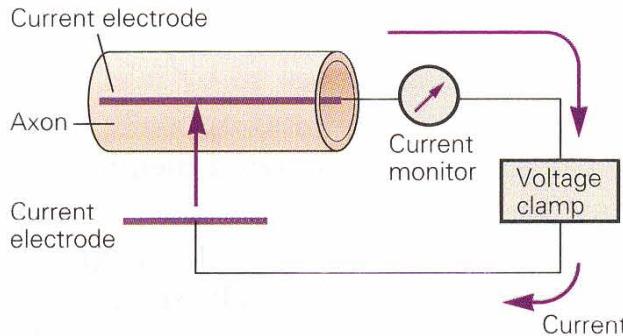


# The Voltage Clamp

- “Voltage clamp” decouples  $V_m$  and the opening / closing of voltage-gated ion channels.
- Injects current into axon that is equal and opposite to current flowing through voltage-gated ion channels.
- Thus, membrane charge and  $V_m$  do not change.
- The current supplied by the voltage clamp is a direct measure of current flowing across membrane.
- Hodgkin & Huxley used voltage clamp to provide 1<sup>st</sup> complete description of ionic mechanisms underlying APs.
- A brief aside – How important was this work?
  - The Nobel Prize in Physiology or Medicine 1963, Hodgkin
  - The Nobel Prize in Physiology or Medicine 1963, Huxley
  - The Nobel Prize in Physiology or Medicine 1970, Katz



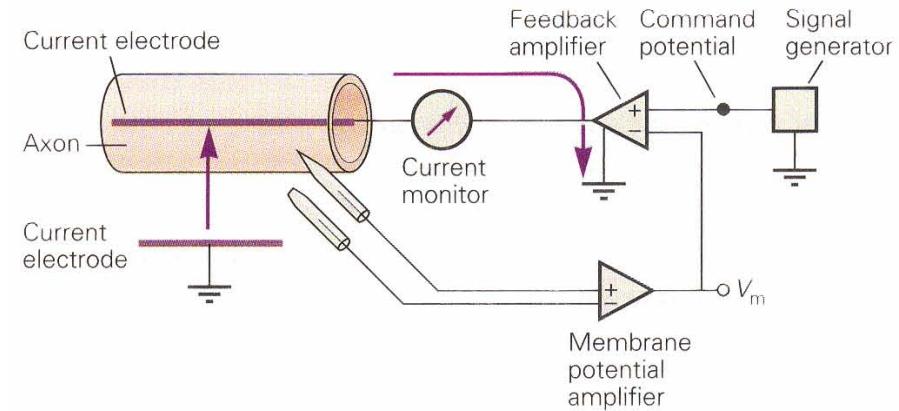
# The Voltage Clamp



**Figure 9-2 A**

The voltage clamp is a current generator that is connected to a pair of electrodes. It is used to change the charge separation, and thus the electrical potential difference, across the membrane. Monitoring the additional current that is passed to clamp the membrane potential at its new value then provides a measure of the membrane current passing through the ion channels in the membrane.

- 1) Step  $V_m$  to level of depolarization.
  - 2) Voltage-gated  $\text{Na}^+/\text{K}^+$  open.
  - 3) V-clamp sources equal and opposite  $I$  to maintain  $V_m$ .
- Developed by Kenneth Cole (1949).
  - Patch clamp similar, but more advanced, allowing measurement of single-channel currents.



**Figure 9-2 B**

The negative feedback mechanism by which the voltage clamp operates. Membrane potential is measured by one amplifier connected to an intracellular electrode and to an extracellular electrode in the bath. The membrane potential signal is displayed on an oscilloscope and is also fed into one terminal of the "feedback" amplifier. This amplifier has two inputs, one for membrane potential ( $V_m$ ) and the other for the command potential. The command potential, which comes from a signal generator, is selected by the experimenter and can be of any desired amplitude and waveform. The feedback amplifier subtracts the membrane potential from the command potential. Any difference between these two signals is amplified several thousand times at the feedback amplifier. The output of this amplifier is connected to a current electrode, a thin wire that runs the length of the axon. To accurately measure the current-voltage relationship of the cell membrane, the membrane potential must be uniform along the entire surface of the axon. This is achieved by using a highly conductive current electrode, which short circuits the axoplasmic resistance, reducing the axial resistance to zero (see Chapter 8). This low-resistance pathway within the axon eliminates all potential differences along the axon core.



# Voltage Clamp Experiments

A) 10 mV depolarizing step w.r.t. resting value:

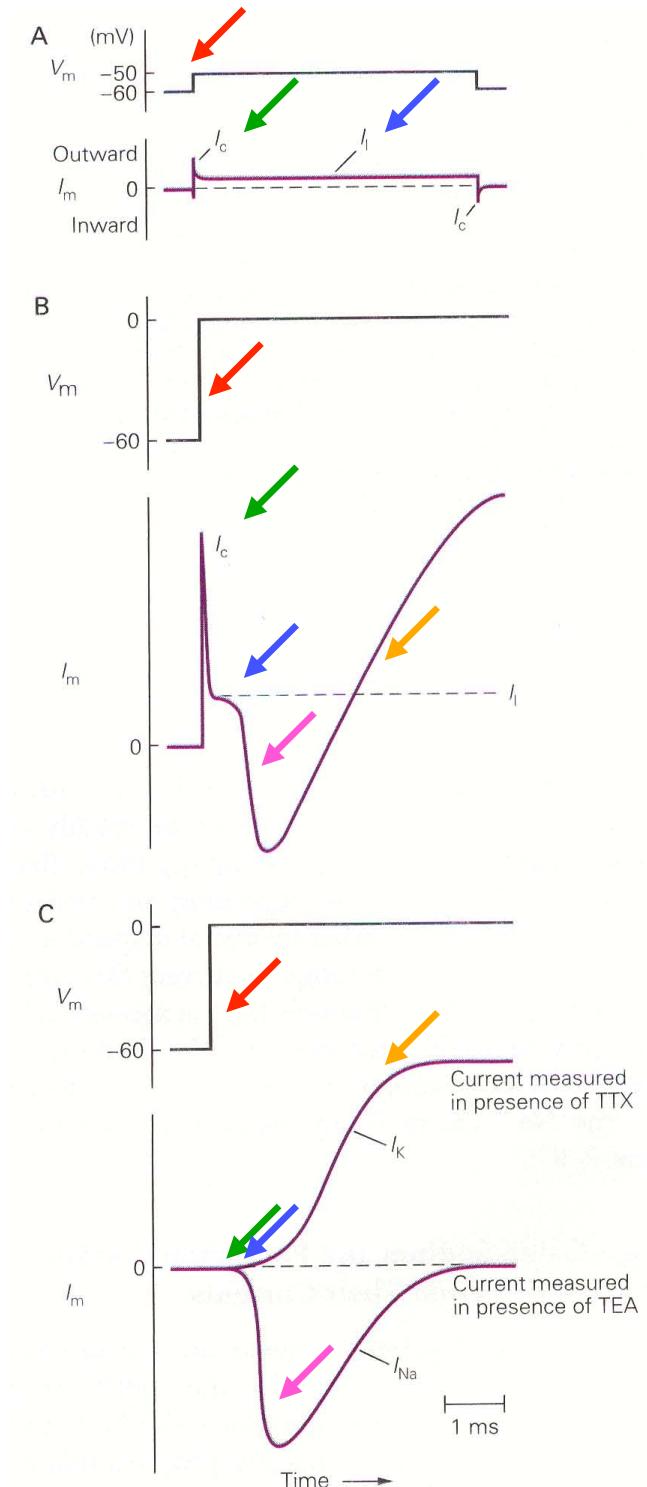
- Brief capacitive current ( $I_c$ ) discharges membrane capacitance.
- Sustained ionic current termed leakage ( $I_l$ ).

B) 60 mV depolarizing step w.r.t. resting value:

- Larger  $I_c$  and  $I_l$  now.
- Short time later, large inward current.
- Shortly after that, large outward current.

C) 60 mV depolarizing step w.r.t. resting value:

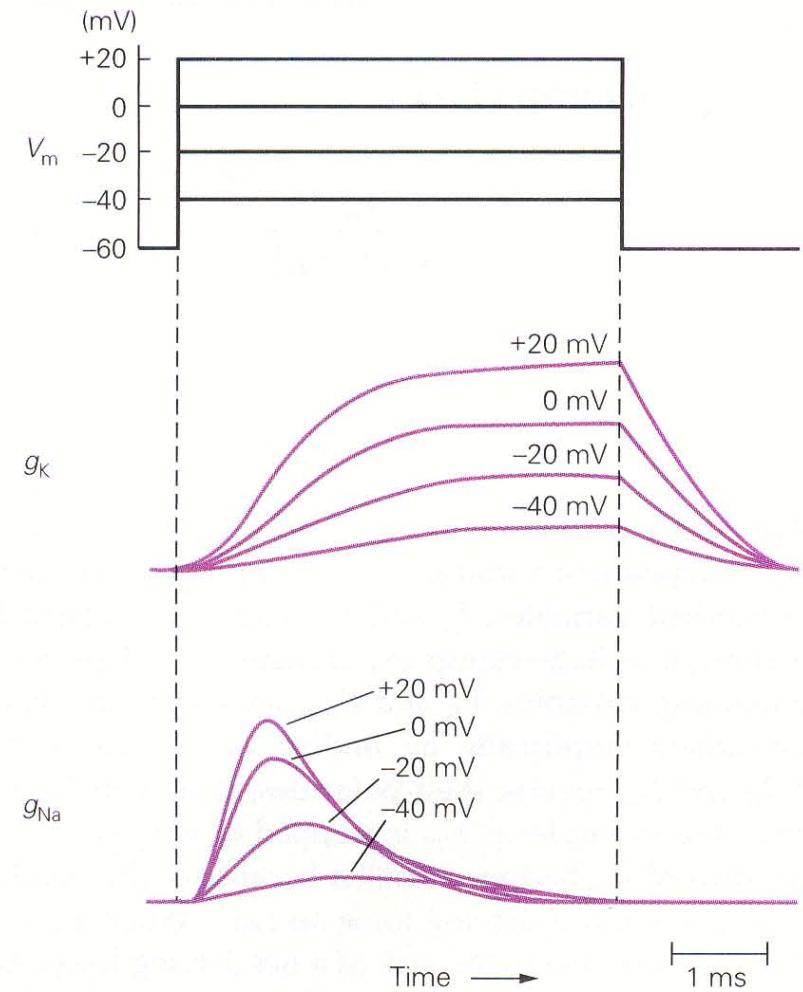
- Subtract stereotyped  $I_c$  and  $I_l$  from traces.
- Tetraethylammonium (TEA) blocks voltage-gated  $K^+$  channels, revealing  $I_{Na}$  component.
- Tetrodotoxin (TTX) blocks voltage-gated  $Na^+$  channels, revealing  $I_K$  component.





# Channel Conductance Kinetics

- Repeat V-Clamp experiments – step to a range of  $V_M$ 's.
- $\text{Na}^+$  and  $\text{K}^+$  conductance **similarities**:
  - Depolarizing  $V_M$  steps → channels open ( $g$  **UP**).
  - Larger depolarizing steps → probability and rate of opening increases (rise times **DOWN**).
- $\text{Na}^+$  and  $\text{K}^+$  conductance **differences**:
  - Rates of opening:  $\text{Na}^+ > \text{K}^+$ .
  - Responses to prolonged depolarization:  $\text{Na}^+$  **opens and closes (inactivation)**;  $\text{K}^+$  stays **open**.



**Figure 9-6** Voltage-clamp experiments show that  $\text{Na}^+$  channels turn on and off more rapidly than  $\text{K}^+$  channels over a wide range of membrane potentials. The increases and decreases in the  $\text{Na}^+$  and  $\text{K}^+$  conductances ( $g_{\text{Na}}$  and  $g_{\text{K}}$ ) shown here reflect the shifting of thousands of voltage-gated channels between the open and closed states.



# Short-term vs. Long-term Depolarization

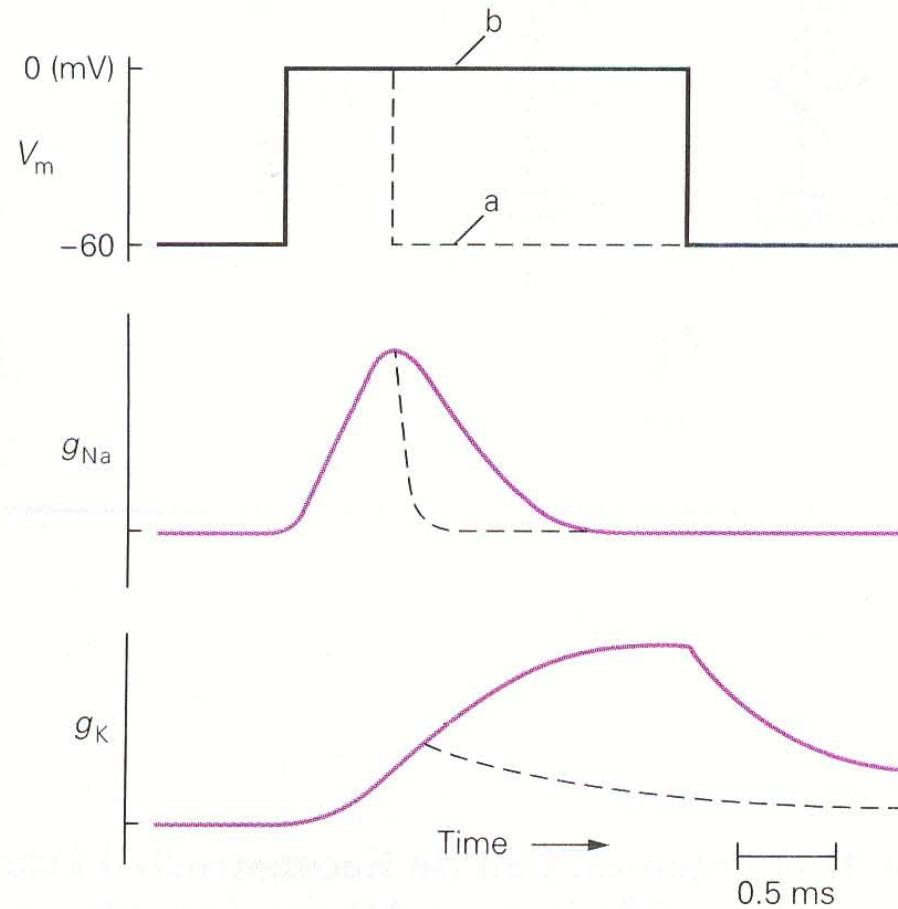
## a) Short-term depolarization

allows  $\text{Na}^+$  and  $\text{K}^+$  channels to return to their resting states.

## b) Long-term depolarization

cause  $\text{Na}^+$  channels to enter inactive state.

- Once inactivated, repolarization required to transit  $\text{Na}^+$  channels back to resting state.
- This takes some time.

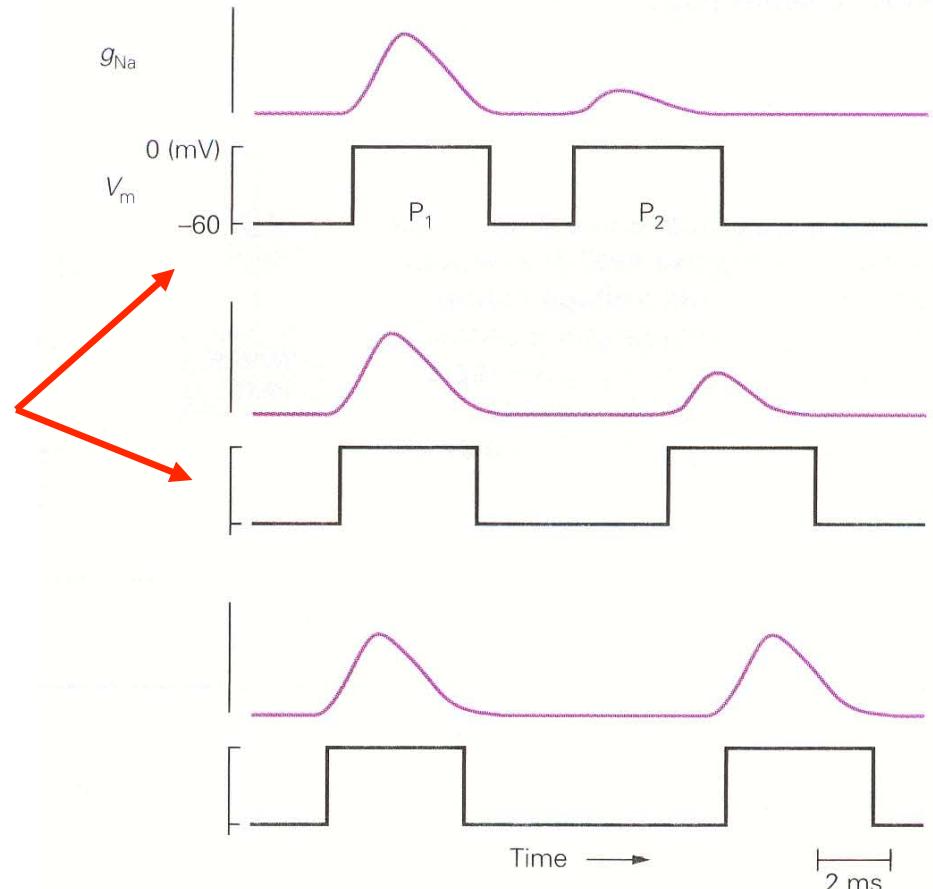


**Figure 9-7** Sodium and potassium channels respond differently to long-term depolarization. If the membrane is repolarized after a brief depolarization (line a), both  $g_{\text{Na}}$  and  $g_{\text{K}}$  return to their initial values. If depolarization is maintained (line b), the  $\text{Na}^+$  channels close (or inactivate) before the depolarization is terminated, whereas the  $\text{K}^+$  channels remain open and  $g_{\text{K}}$  increases throughout the depolarization.



# Na<sup>+</sup> Channel Inactivation Timecourse

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

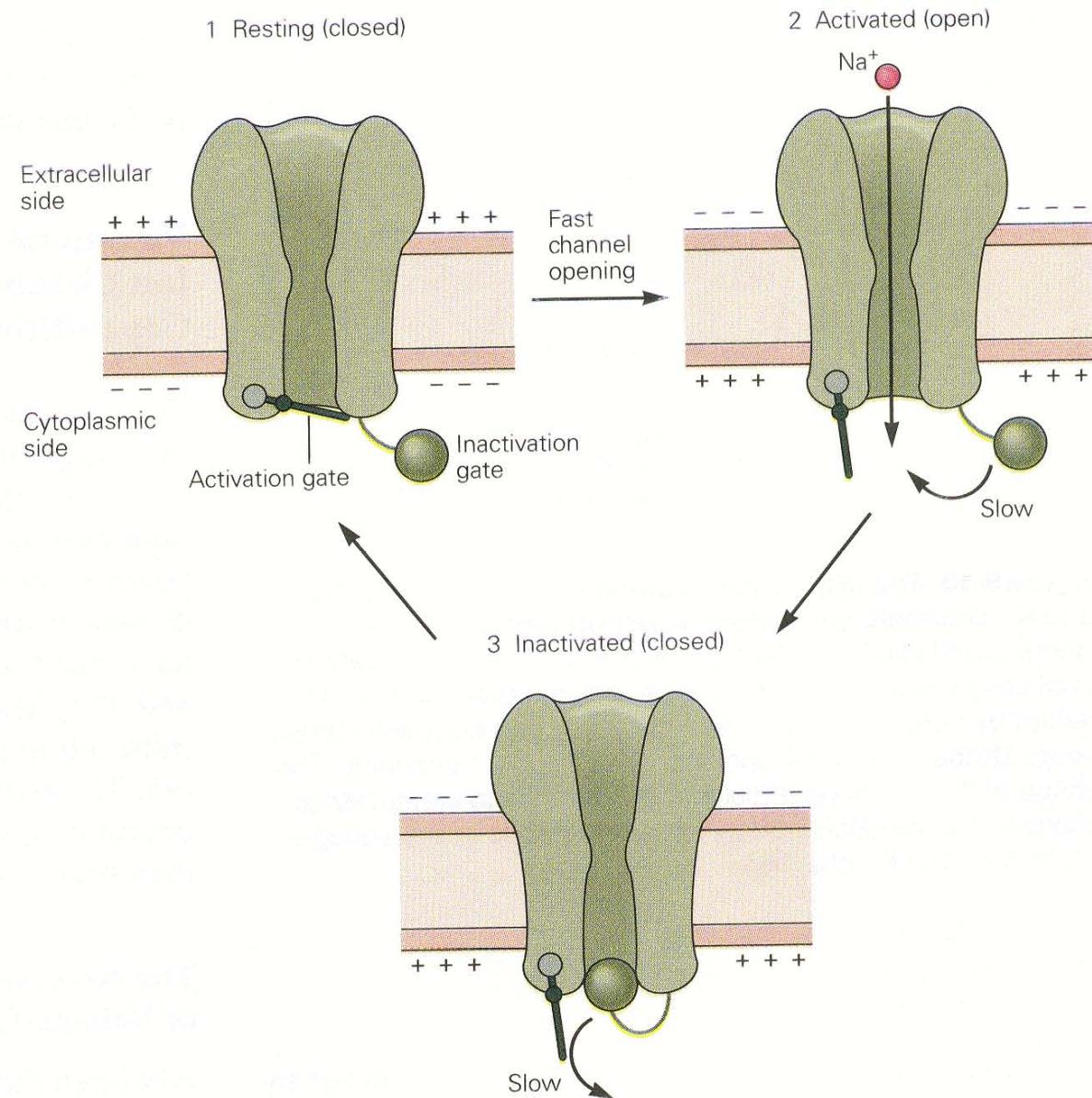


**Figure 9-8** Sodium channels remain inactivated for a few milliseconds after the end of a depolarization. Therefore if the interval between two depolarizing pulses (P<sub>1</sub> and P<sub>2</sub>) is brief, the second pulse produces a smaller increase in  $g_{\text{Na}}$  because many of the Na<sup>+</sup> channels are inactivated. The longer the interval between pulses, the greater the increase in  $g_{\text{Na}}$ , because a greater fraction of channels will have recovered from inactivation and returned to the resting state when the second pulse begins. The time course of recovery from inactivation contributes to the time course of the refractory period.



# Activation Gate (fast) and Inactivation Gate (slow)

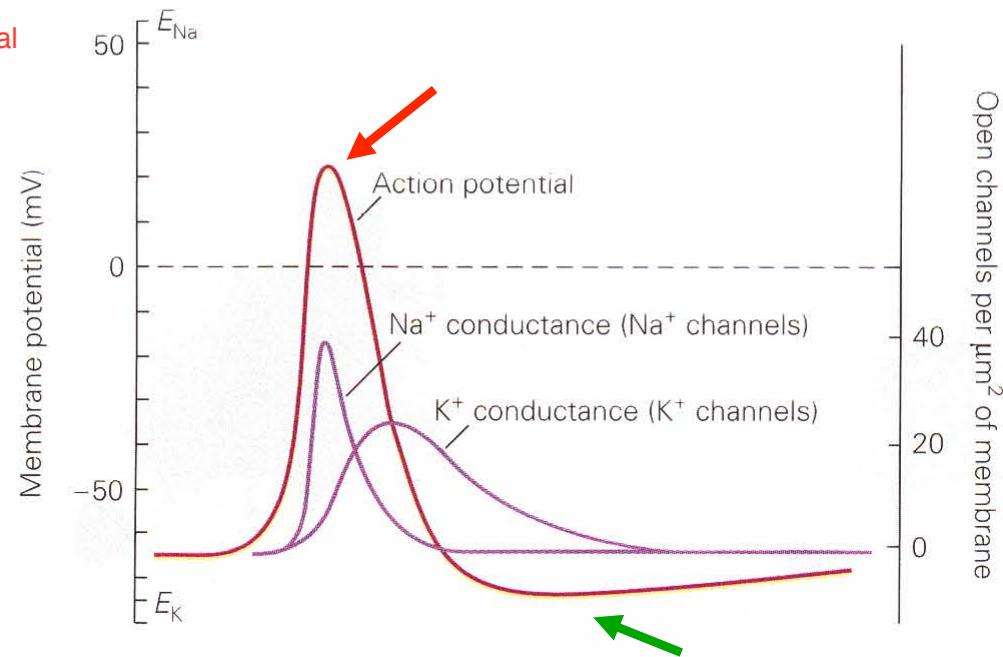
**Figure 9-9** Voltage-gated  $\text{Na}^+$  channels have two gates, which respond in opposite ways to depolarization. In the resting (closed) state the activation gate is closed and the inactivation gate is open (1). Upon depolarization a rapid opening of the activation gate allows  $\text{Na}^+$  to flow through the channel (2). As the inactivation gates close, the  $\text{Na}^+$  channels enter the inactivated (closed) state (3). Upon repolarization, first the activation gate closes, then the inactivation gate opens as the channel returns to the resting state (1).





# Hodgkin-Huxley Measurements & Model Explain APs

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



**Figure 9-10** The sequential opening of voltage-gated  $\text{Na}^+$  and  $\text{K}^+$  channels generates the action potential. One of Hodgkin and Huxley's great achievements was to separate the total conductance change during an action potential, first detected by Cole and Curtis (see Figure 9-1) into separate components attributable to the opening of  $\text{Na}^+$  and  $\text{K}^+$  channels. The shape of the action potential and the underlying conductance changes can be calculated from the properties of the voltage-gated  $\text{Na}^+$  and  $\text{K}^+$  channels.



## Further Notes on Action Potentials

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- All-or-nothing behavior of APs:
  - Once  $V_m$  depolarization crosses a particular value (threshold)...
  - Positive feedback takes over and ...
  - The rest of the AP waveform unfolds.
- APs in the giant squid axon result from just two type of voltage-gated channels, but many other types of voltage-gated channels are found in the nervous system:
  - Voltage-gated  $\text{Ca}^{2+}$ ,  $\text{Cl}^-$  channels.
  - Fast / very-slow voltage-gated  $\text{K}^+$  channels.
  - This channel variety increases complexity of possible neural information processing.
  - Beyond the scope of this course.
- $\text{Ca}^{2+}$  influx is important (e.g., can modulate gating of  $\text{K}^+$  channels).
  - Beyond the scope of this course.



## Further Notes on Action Potentials

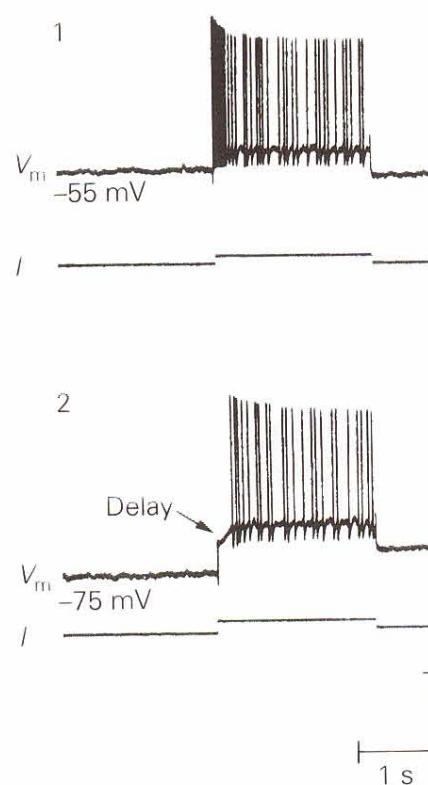
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- Different regions of the neuron perform specific signaling tasks, e.g.:
  - Axon – carries signals over long distances (relay line).
  - Input, integrative regions – lots of complex computations (processor).
  - These functions depend on the particular set of ion channels present.
- Excitability properties vary among neurons:
  - Computing power greater w/ range of functional properties.
  - It's still true that neural function is largely determined by its connectivity, the biophysical properties of cells also critical.
  - How a neuron responds to synaptic input depends on different types and proportions of voltage-gated channels in integrative and trigger zones.
  - Same input could result in single AP, constant frequency train of APs or even accelerating/decelerating train of APs.
  - Some examples are shown on next slide; we'll look at specific response characteristics when we study specific sensory or motor regions of the brain.

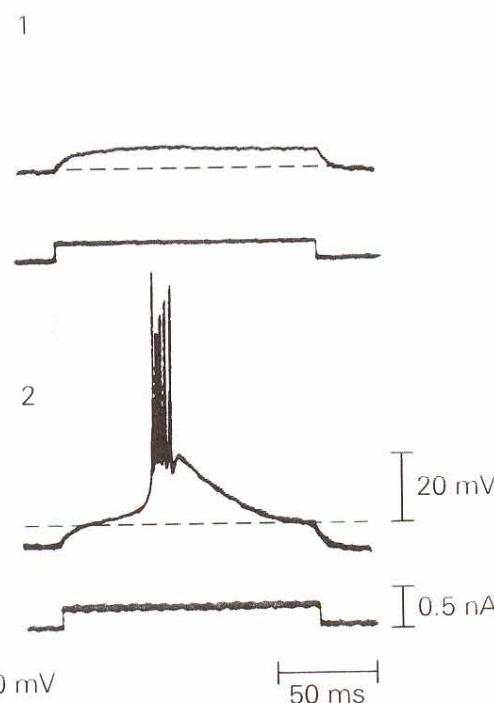


# Different Voltage-Gated Channels → Different Firing Properties

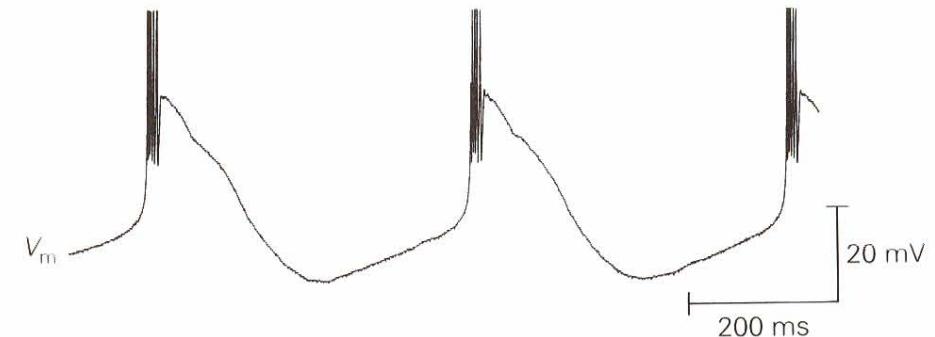
A Delayed firing



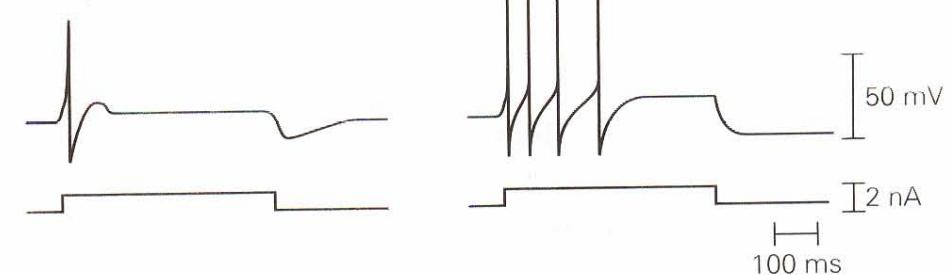
B Potential-dependent excitability



C Bursting neuron



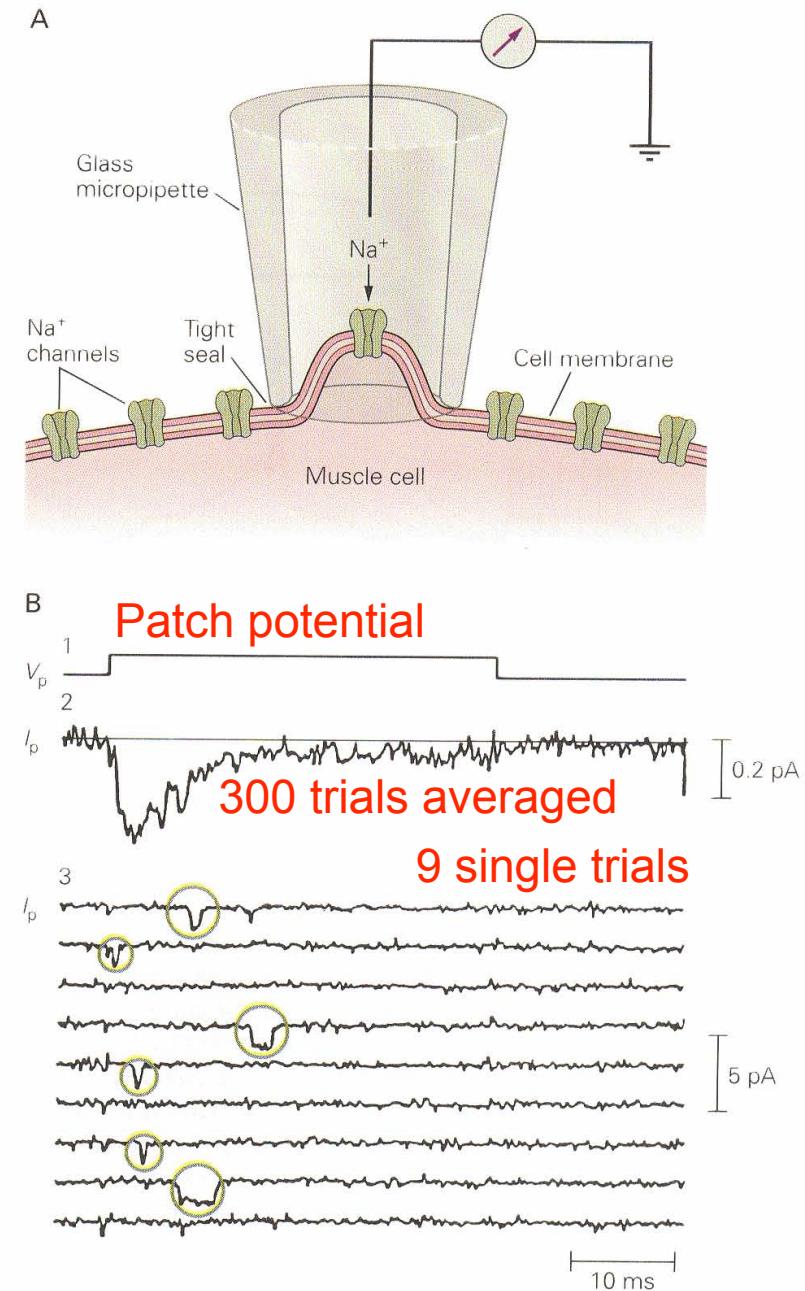
D Spike accommodation





# Patch-Clamp Experiments (Single Channels)

- Voltage-clamp experiments can not measure single-channel current flow:
  - Measures large patch of membrane w/ 1000s of channels opening/closing randomly.
  - Background noise created by passive membrane channels.
- Patch-clamp experiments isolate very small patch of membrane:
  - Voltage-gated channels open or closed, not partially open.
  - Thus current through single-channel is variable duration, not variable amplitude.





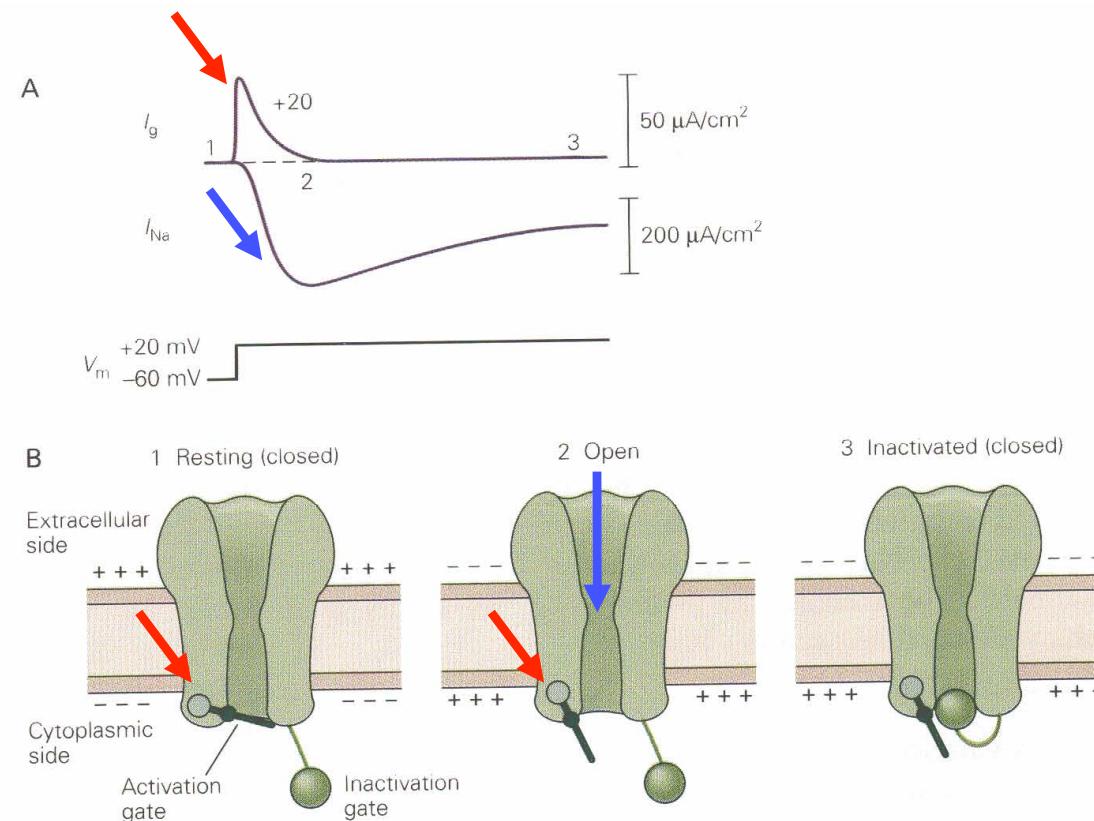
# Gating Current

- Patch-clamp experiments are sensitive enough to measure *gating current*.
- Gating current caused by movement of + charge associated with activation gate within channel protein.

**Figure 9-13** Gating currents directly measure the changes in charge distribution associated with  $\text{Na}^+$  channel activation.

A. When the membrane is depolarized the  $\text{Na}^+$  current ( $I_{\text{Na}}$ ) first activates and then inactivates. The activation of the  $\text{Na}^+$  current is preceded by a brief outward gating current ( $I_g$ ), reflecting the outward movement of positive charge within the  $\text{Na}^+$  channel protein associated with the opening of the activation gate. To detect the small gating current it is necessary to block the flow of ionic current through the  $\text{Na}^+$  and  $\text{K}^+$  channels and mathematically subtract the capacitive current due to charging of the lipid bilayer.

B. Illustration of the position of the activation and inactivation gates when the channel is at rest (1), when the  $\text{Na}^+$  channels have been opened (2), and when the channels have been inactivated (3). It is the movement of the positive charge on the activation gate through the membrane electric field that generates the gating current.





## Rest of Chapter 7

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- We've covered topics in Chapter 7 up to, but not including, the section titled, "Genes encoding the potassium, sodium, and calcium channels stem from a common ancestor."
- We will not cover this section or beyond.
- Feel free to read if you are interested in learning more.