BIOELECTRIC POTENTIALS-3
Action Potential

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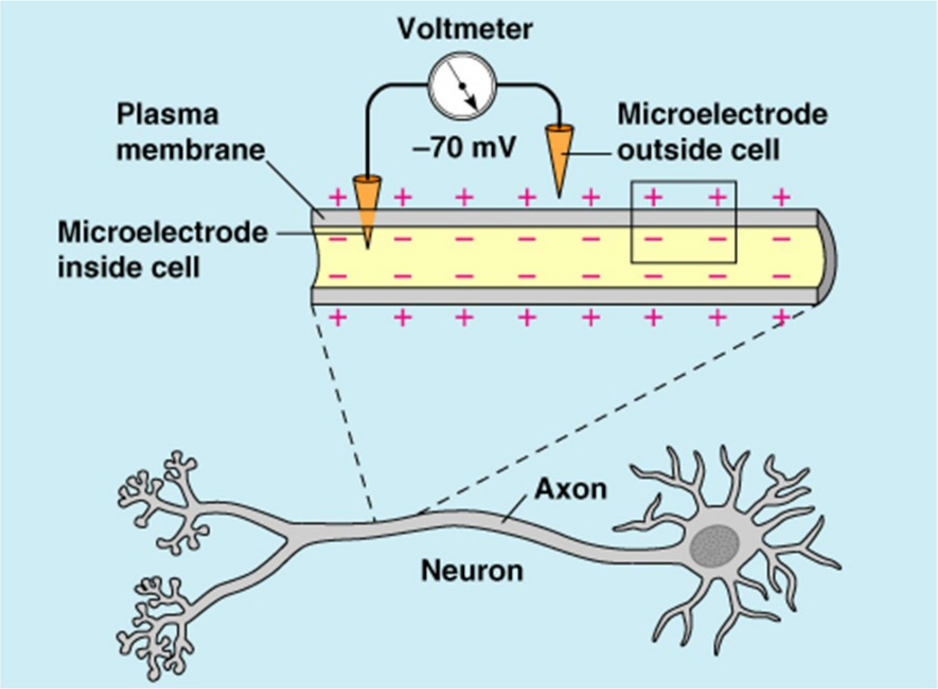
Resting Potential

- All cells (not just excitable cells) have a resting potential
- The size of the resting potential varies
  - in excitable cells runs about -65/-80/-100 mV



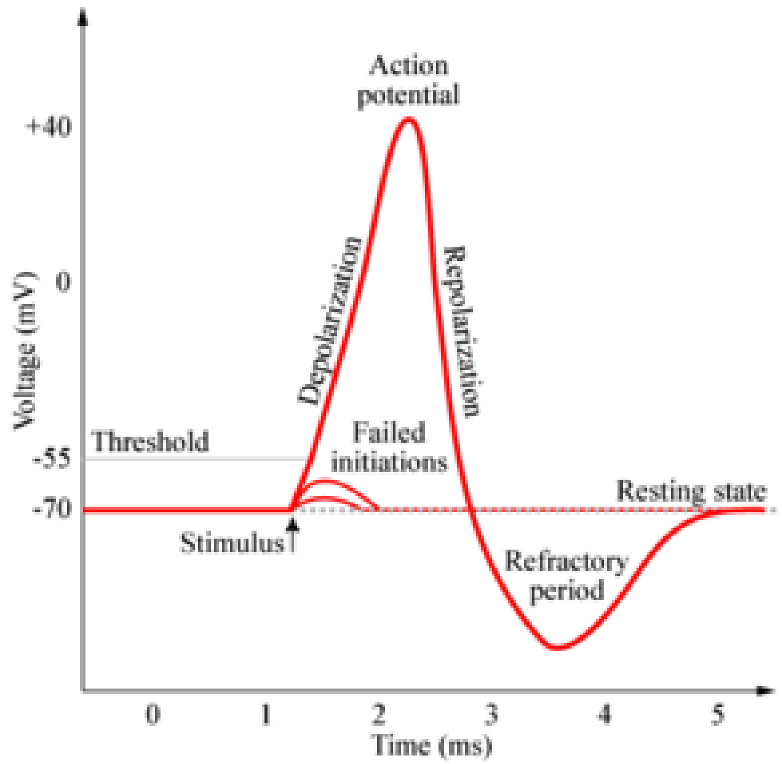
Excitable Cells

- Neuron
- Muscle Cells
- Endocrine Cells

Could be stimulated by appropriate chemical and physical stimuli

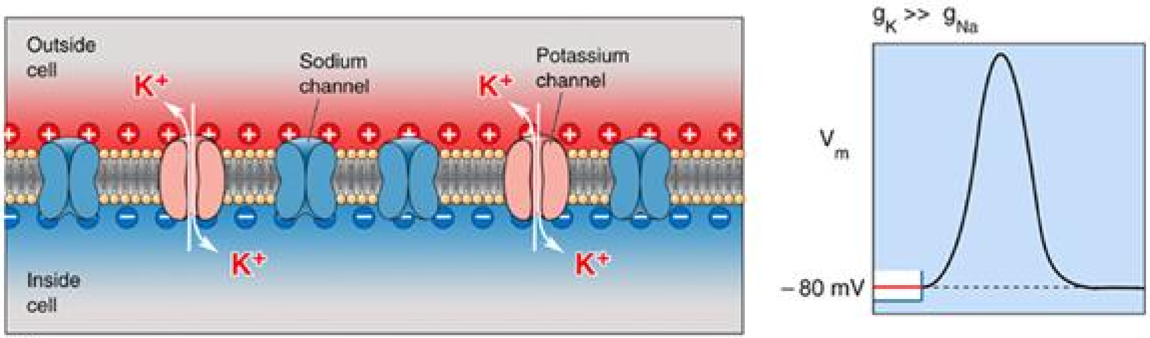
Action Potential

- In response to the appropriate stimulus, the cell membrane of an excitable cell goes through a sequence of depolarization from its rest state followed by repolarization to that rest state.



Action Potential

- The main electrical activity of excitable cells.
- In neurons, they play a central role in cell-to-cell communication
- Their main function is to activate intracellular processes
  - In muscle cells;an action potential is the first step in the chain of events leading to contraction.
  - In beta cells of the pancreas, they provoke release of insulin.



(a)

- At resting potential the membrane is more permeable to K^+ ions than Na^+ ions.

$$V_m = 58 \log \frac{K_o + (p_{Na}/p_K)\,Na_o + (p_{Cl}/p_K)\,Cl_i}{K_i + (p_{Na}/p_K)\,Na_i + (p_{Cl}/p_K)\,Cl_o}$$

Axon of Squid (-70 mV)

Ion	Extracellular Concentration	Intracellular Concentration
Na^+	460	50
K^+	10	400
Cl^-	540	40

Concentrations are in mM/l

p_K: 1.0, p_{Na}: 0.03, p_{Cl}: 0.1

$$V_m = 58\log\frac{K_o + (p_{Na}/p_K)\,Na_o + (p_{Cl}/p_K)\,Cl_i}{K_i + (p_{Na}/p_K)\,Na_i + (p_{Cl}/p_K)\,Cl_o}$$

$$= 58\log\frac{10 + (0.03)460 + (0.1)40}{400 + (0.03)50 + (0.1)540} = 58\log\frac{10 + 13.8 + 4}{400 + 1.5 + 54} = -70mV$$

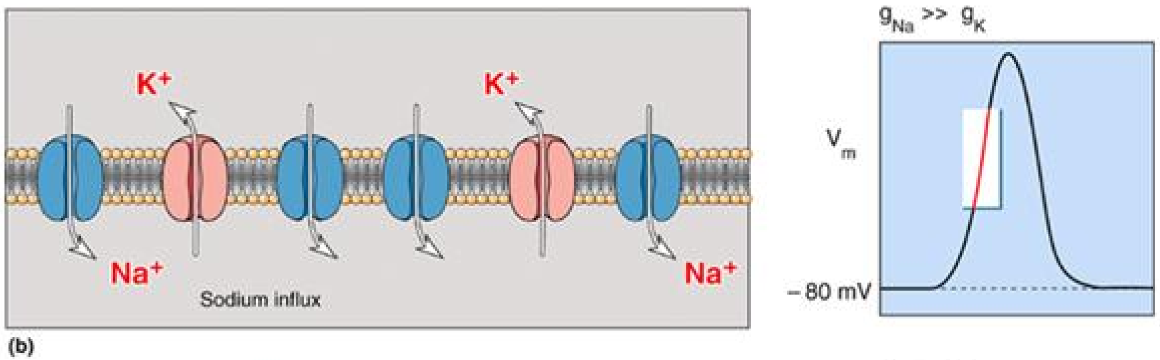
Equlibrium Potential of $K^{\pm}$

E_K=(RT/zF) 2,303 log(K_o/K_i) Nernst Equation

E_K=((8,31x293)/(1x96500))x 2,303x log(10/400)

=58,1 x log (0.025)

=-93 mV



- When the cell is stimulated the sodium permeability of the membrane increases suddenly and allows tremendous numbers of positively charged sodium ions to diffuse to the interior of the cell.
- The normal "polarized" state of -80 millivolts is immediately neutralized by the inflowing positively charged sodium ions, with the potential rising rapidly in the positive direction.
- This is called ***depolarization.***

Axon of Squid

Ion	Extracellular Concentration	Intracellular Concentration
Na^+	460	50
K^+	10	400
Cl^-	540	40

Concentrations are in mM/l

During resting state p_K: 1.0, p_{Na}: 0.03, p_{Cl}: 0.1

During action potential p_K: 1.0, p_{Na}: 15, p_{Cl}: 0.1

$$V_m = 58 \log \frac{K_o + (p_{Na}/p_K)\,Na_o + (p_{Cl}/p_K)\,Cl_i}{K_i + (p_{Na}/p_K)\,Na_i + (p_{Cl}/p_K)\,Cl_o}$$

$$= 58 \log \frac{10 + (15)460 + (0.1)40}{400 + (15)50 + (0.1)540} = +44mV$$

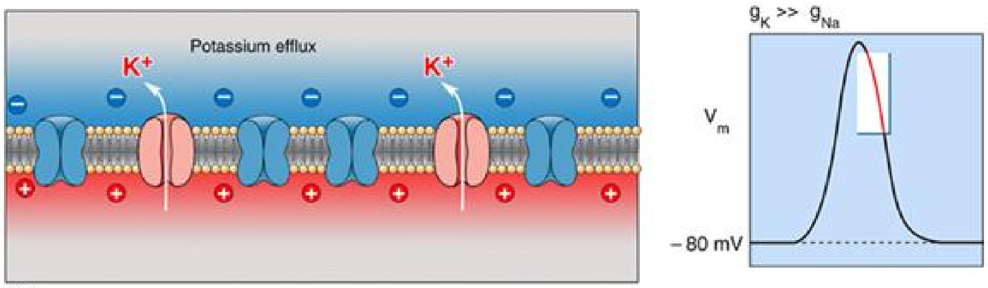
Equlibrium Potential of $Na^{\pm}$

E_{Na}=(RT/zF) 2,303 log(Na_o/Na_i)   Nernst Equation

E_{Na}=((8,31x293)/(1x96500))x 2,303x log(460/50)

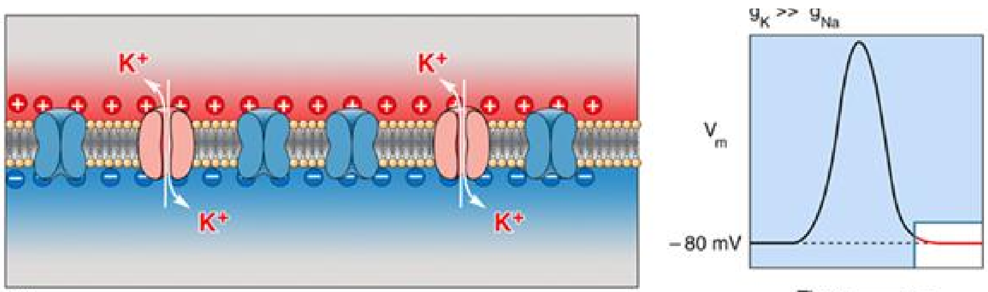
=58,1 x log (9.2)

=56 mV



(c)

- Within a few 10,000ths of a second after the membrane becomes highly permeable to sodium ions, the sodium channels begin to close and the potassium channels open more than normal.



(d)

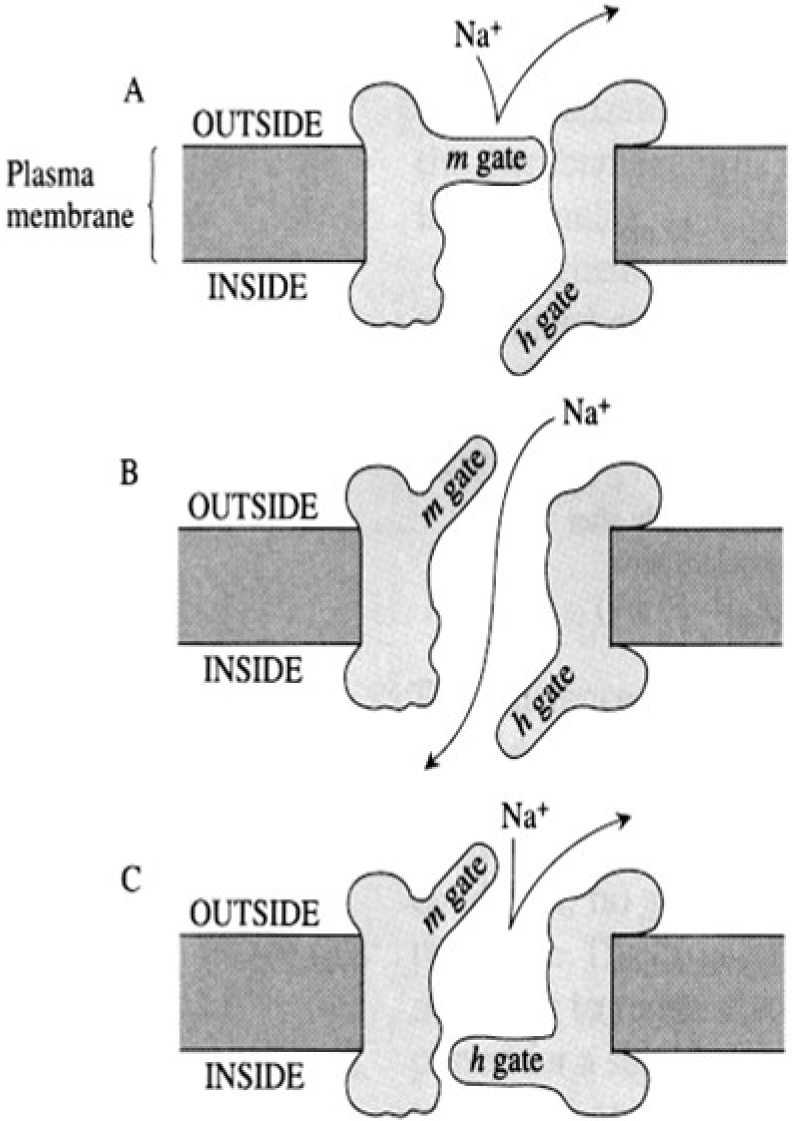
- Then, rapid diffusion of potassium ions to the exterior re-establishes the normal negative resting membrane potential.
- This is called ***repolarization*** of the membrane.

Two other types of transport channels through the nerve membrane: **<u>the voltage-gated sodium and potassium channels</u>**

- The necessary actor in causing both depolarization and repolarization of the nerve membrane during the action potential is the *voltage-gated sodium channel.*

- A *voltage-gated potassium channel* also plays an important role in increasing the rapidity of repolarization of the membrane.

Voltage –gated Na+ Channels

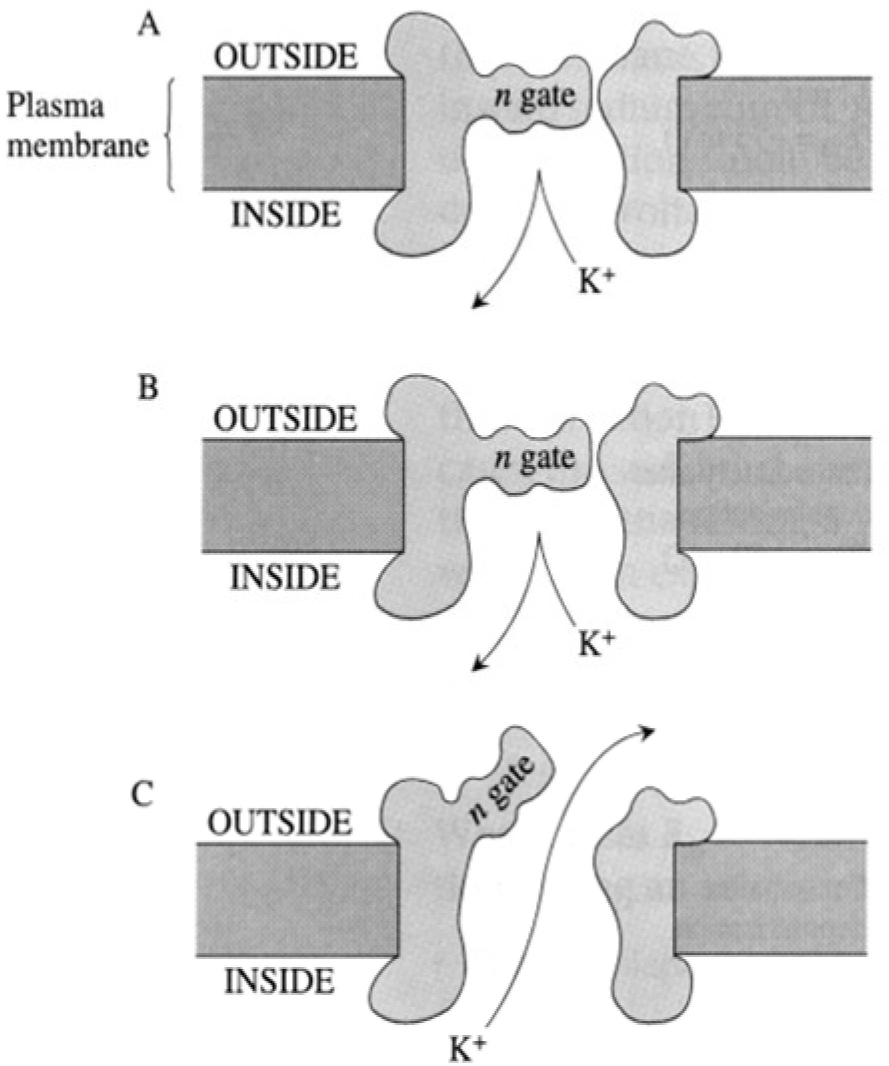


- In resting state, activation gates closed, inactivation gates are open.
- As a result of the stimulus (which exceeds the threshold value) both gates are activated
  - Activation gate opens -rapid process
  - Inactivation gate starts closing -slow process
- Till the inactivation gate is closed Na^+ ions that enter the cell are depolarized the cell.

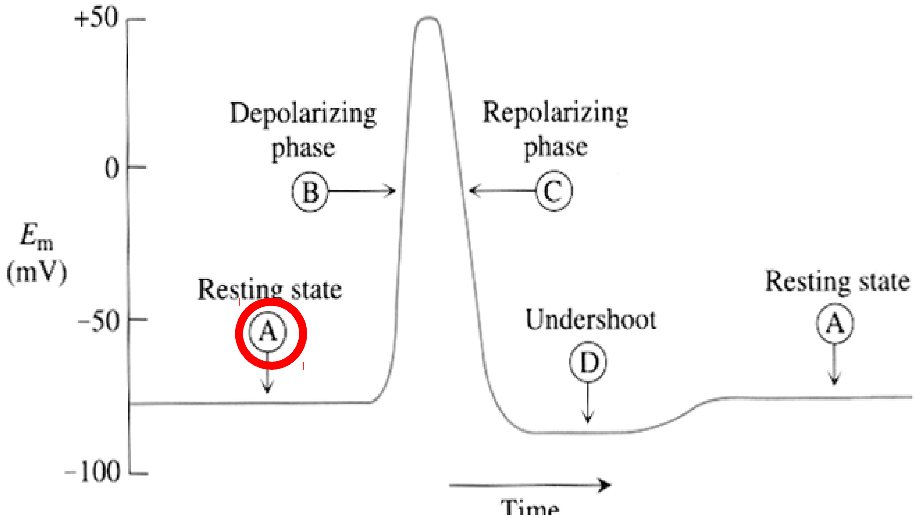
Voltage –gated Na^+ Channels

- Another important characteristic of the sodium channel inactivation process is that the inactivation gate will not reopen until the membrane potential returns to or near the original resting membrane potential level.
- Therefore, it is usually not possible for the sodium channels to open again without first repolarizing the nerve fiber.

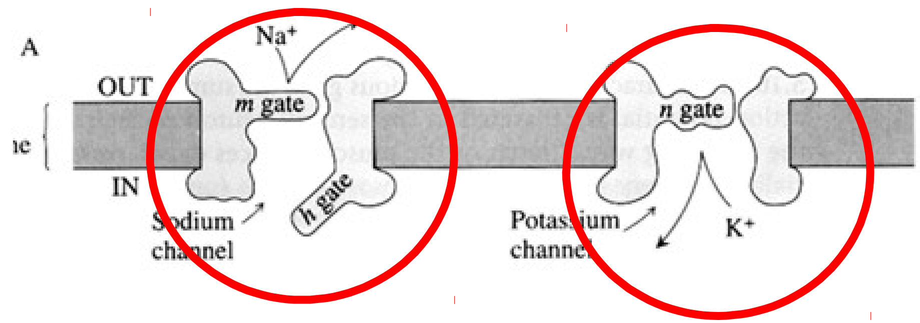
Voltage –gated K^+ Channels



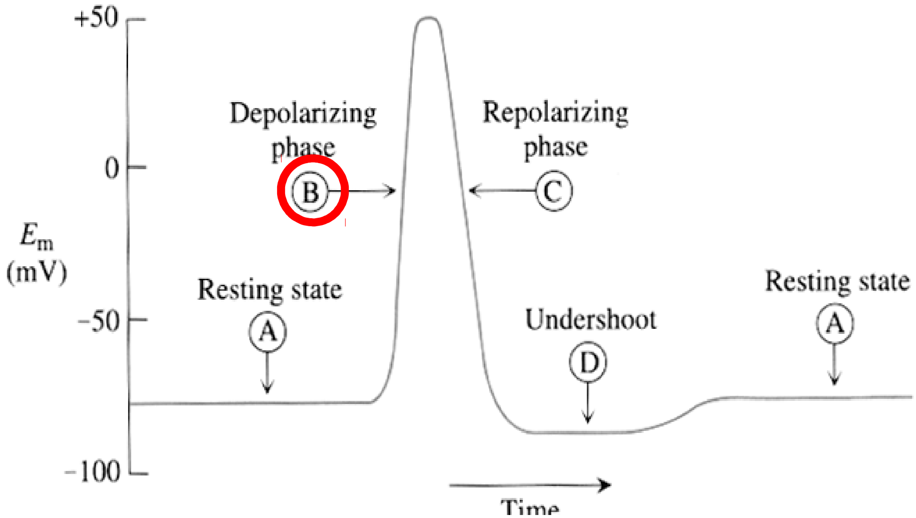
- When the cell is at rest
  - Gate closed
- At threshold voltage
  - Gate starts opening -slow process
- At peak positivity level
  - Gate opens
  - Remains open till resting membrane potential is restored
- During repolarization
  - Gate starts to close -slow process



+50
0
-50
-100
E_m
(mV)
Depolarizing phase
Repolarizing phase
Resting state
Undershoot
Resting state
A
B
C
D
A
Time



A
OUT
IN
Na+
m gate
h gate
Sodium channel
n gate
K+
Potassium channel


+50
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Depolarizing phase
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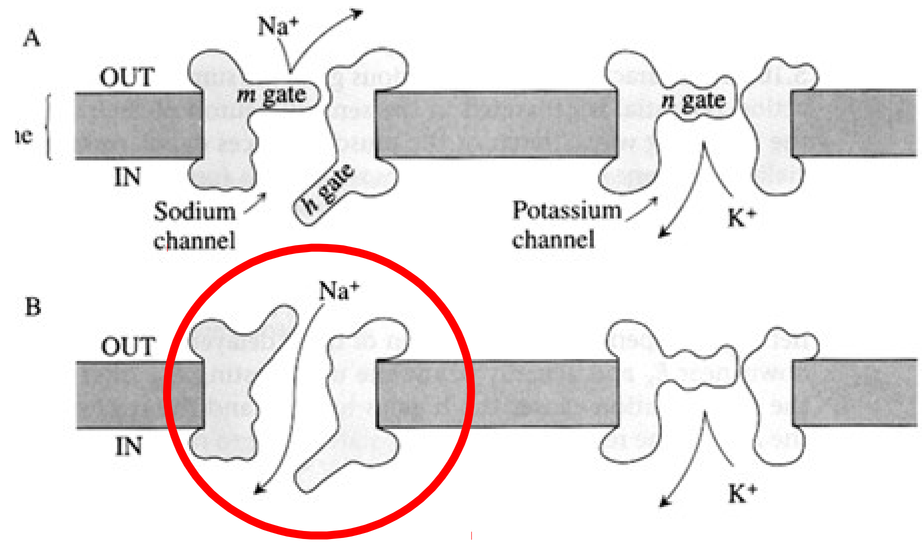
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Na+
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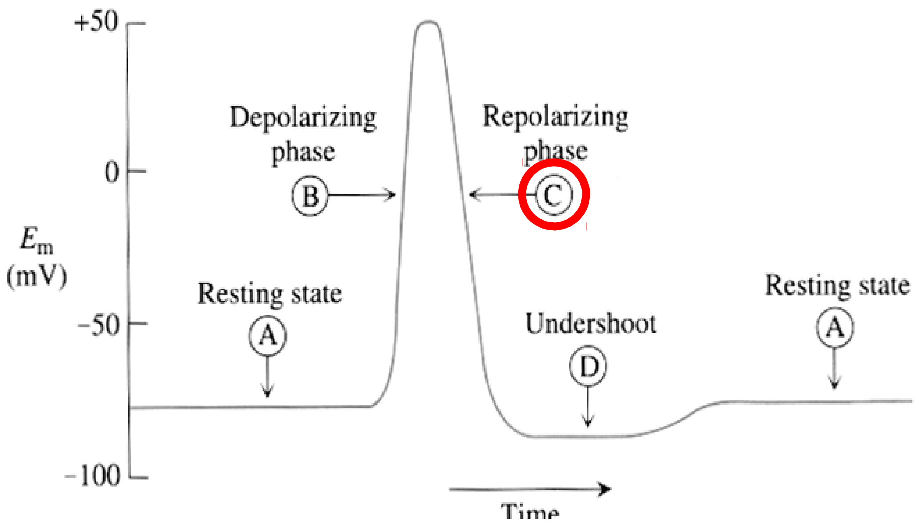
Sodium channel
Potassium channel
K+
B
Na+
OUT
IN
K+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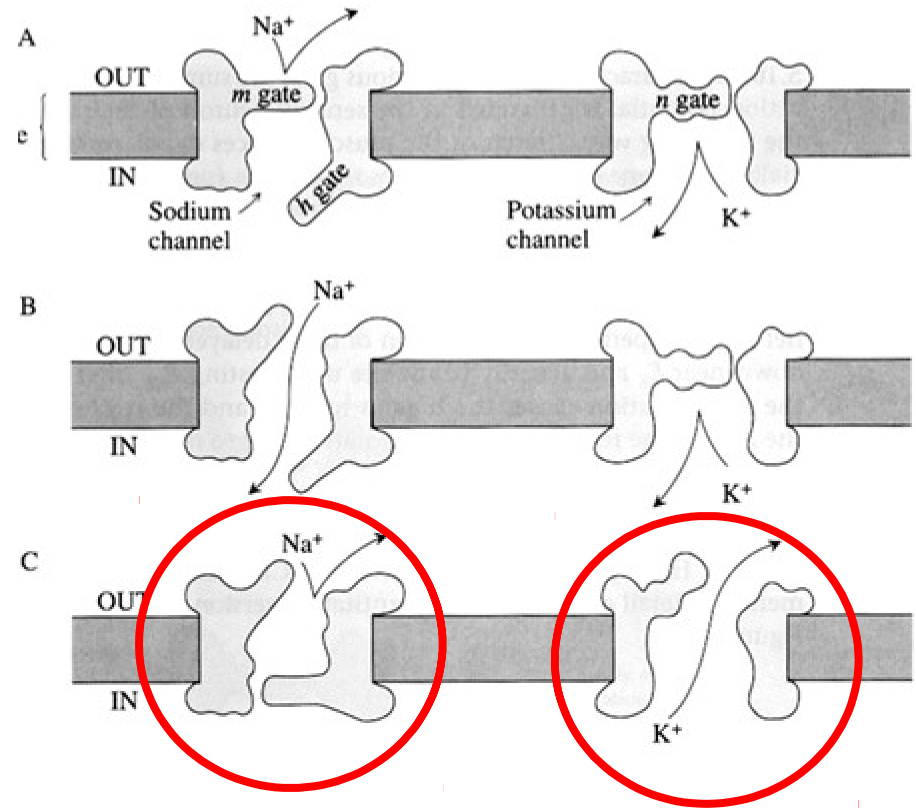
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K+
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IN
Na+
K+
C
OUT
IN
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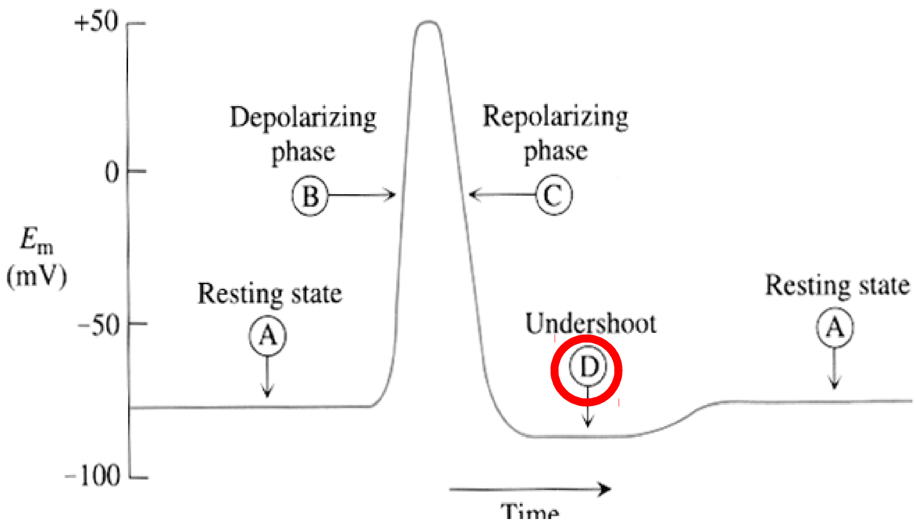
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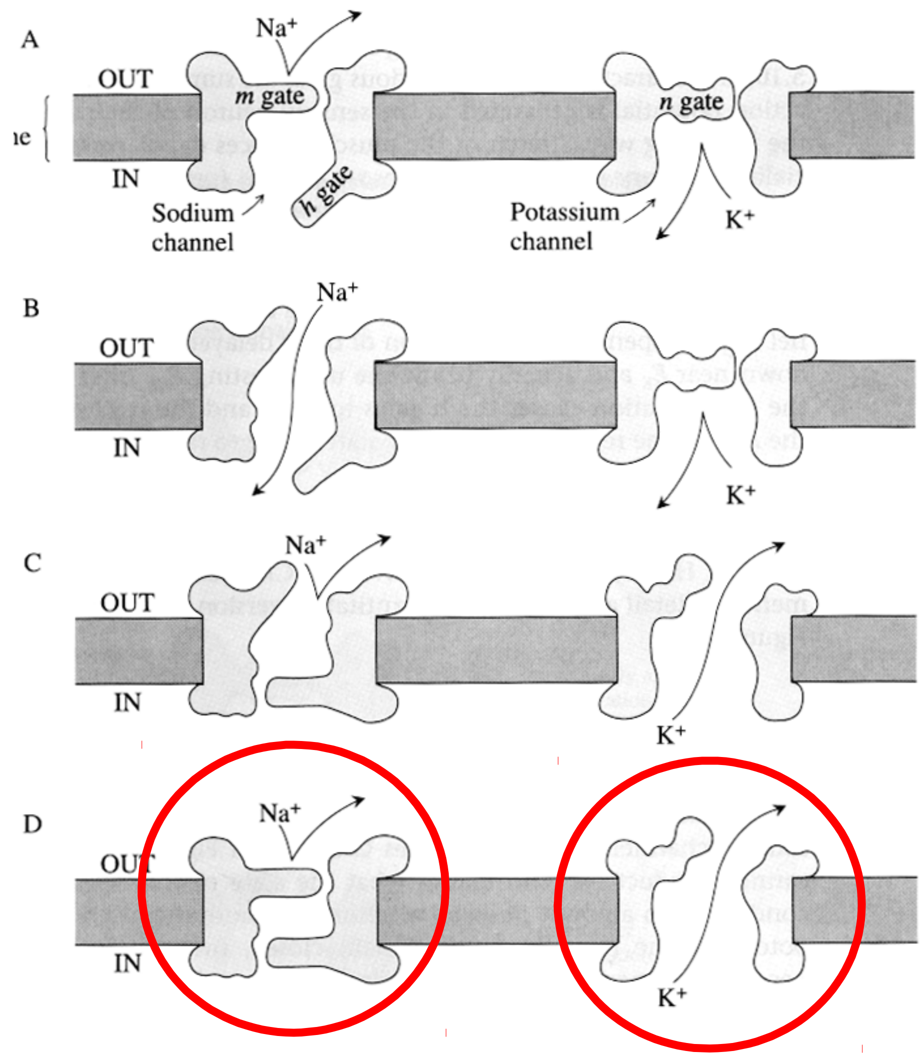
A
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IN
Na+
K+
D
OUT
IN
Na+
K+

A Positive-Feedback Cycle Opens the Sodium Channels

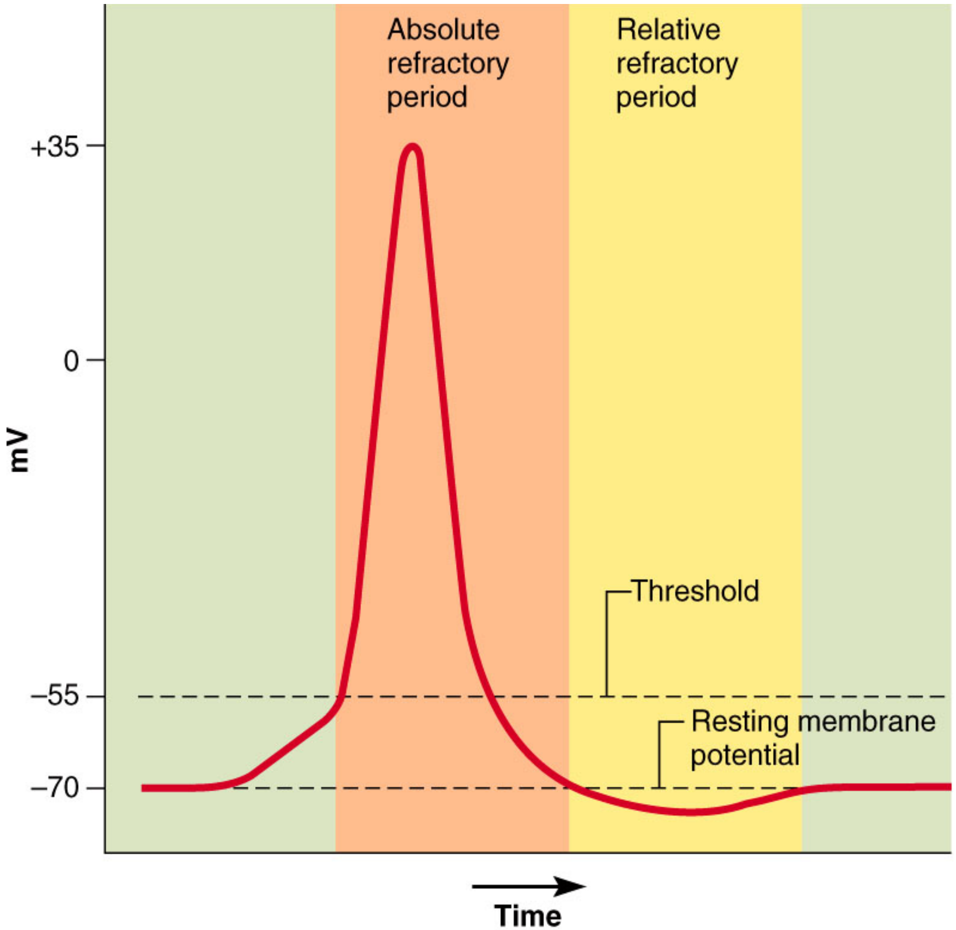
- if any event causes enough initial rise in the membrane potential from -90 millivolts toward the zero level, the rising voltage itself causes many voltage-gated sodium channels to begin opening.
- This allows rapid inflow of sodium ions, which causes a further rise in the membrane potential, thus opening still more voltage-gated sodium channels and allowing more streaming of sodium ions to the interior of the fiber.
- This process is a positive-feedback cycle that, once the feedback is strong enough, continues until all the voltage-gated sodium channels have become activated (opened).

All or none principle

- Action potential will either be generated or not…
  no gradations or intensities possible
- **Suprathreshold** stimulus will elicit same action potential as elicited by threshold stimulus
- **Subthreshold** stimulus will not elicit action potential

Refractory period

- A new action potential cannot occur as long as the membrane is still depolarized from the preceding action potential
- shortly after the action potential is initiated, the sodium channels become inactivated and no amount of excitatory signal applied to these channels at this point will open the inactivation gates.
- The only condition that will allow them to reopen is for the membrane potential to return to or near the original resting membrane potential level.
- Then, within another small fraction of a second, the inactivation gates of the channels open and a new action potential can be initiated.



Refractory period

1. Absolutely refractory period

Period during which a 2nd action potential can not be generated.

- After closure, the inactivation gates do not reopen until RMP is restored

2. Relative refractory period

Period during which 2nd action potential can be generated but with stronger than normally required stimulus.

- Some voltage gated Na^+channels regain their resting configuration
- During this period K^+efflux continues.