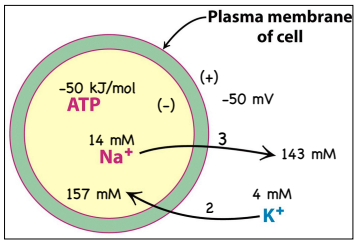
Chem 452 - Lecture 9
Pumps and Channels
111123

With this lecture we begin a unit a that looks at proteins as complex machines. We will look first at the intrinsic membrane proteins that are responsible for moving material across membranes. Those that require a source of free energy to carry out the transport are called active transport systems. Some of these are directly coupled to the hydrolysis of ATP, while others are coupled to a second concentration gradient that flows across the cell in a favorable direction. We will also look at gated passive transport systems, which, while requiring no external source of free energy, are far from from being just simple channels.

ATPase Pumps

- The energetics of active transport
  - Na^+/K^+ ATPase
    - Pumps 3 Na^+ out while pumping 2 K^+ in.



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$$\Delta G = RT\ln\left(\frac{c_2}{c_1}\right) + ZF\Delta V$$

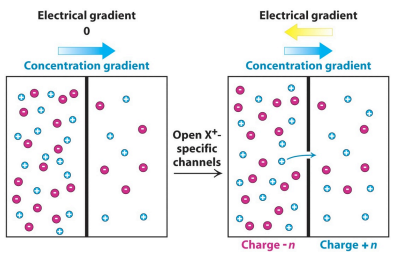
$$= \left(8.314 \text{ x } 10^{-3}\ \frac{\text{kJ}}{\text{mol•K}}\right)(310\text{ K})\ln\left(\frac{(0.143)^3(0.157)^2}{(0.014)^3(0.004)^2}\right) + (+1)\left(96.5\ \frac{\text{kJ}}{\text{mol•V}}\right)(+0.050\text{V})$$

$$= 36.9\ \frac{\text{kJ}}{\text{mol}} + 4.8\ \frac{\text{kJ}}{\text{mol}}$$

$$= 41.7\ \frac{\text{kJ}}{\text{mol}}$$

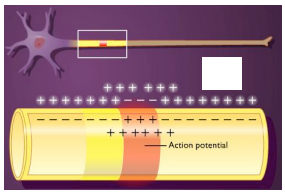
Channels and the Action Potential

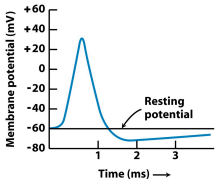
- Due to a small movement of K^+ ions, the resting nerve fiber has a resting membrane potential of -60mV



Channels and the Action Potential

- When a nerve fires, the membrane potential inverts in a wave that move along the axon of the nerve fiber.





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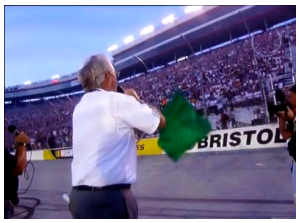

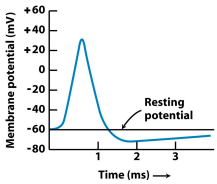

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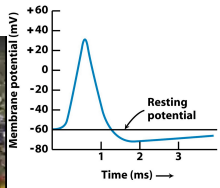

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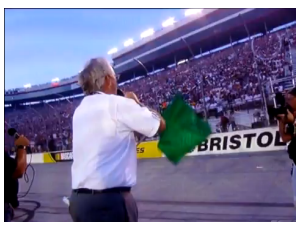
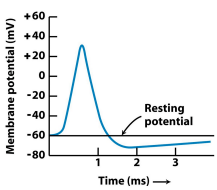
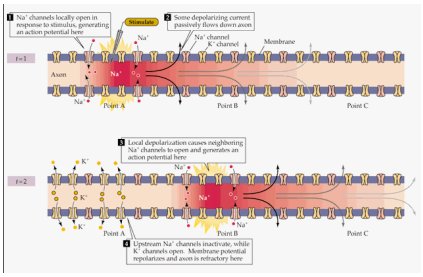




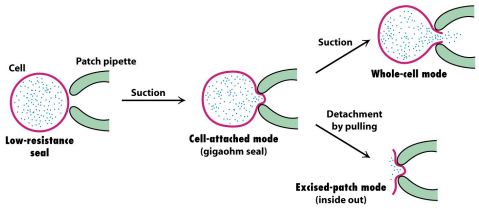
Channels and the Action Potential

- The action potential is due to the sequential opening of a Na^+ and a K^+ channel.



Channels and the Action Potential

- Channels can be studied using the patch-clamp technique.



Channels and the Action Potential

- The Na^+ channel was the first to be isolated and structurally characterized.

  - 260 kDa chain
  - 4 internal repeats
  - Hydrophobicity profiles indicates 5 hydrophobic rageions (S1, S2, S3, S5, S6)
  - S4 is highly positively charged
    - Proposed these acted as voltage sensors.

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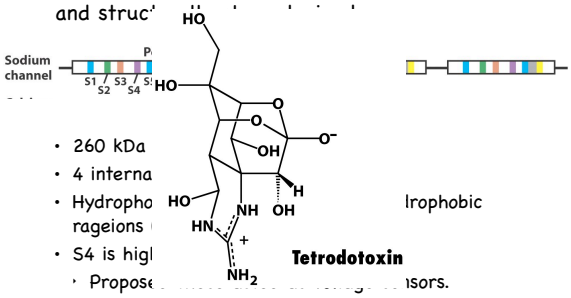

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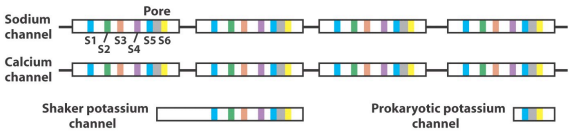
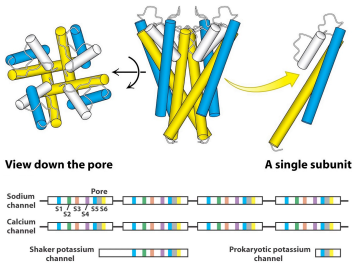
Channels and the Action Potential

- The K^+ channel was more difficult to isolate and structurally characterize.



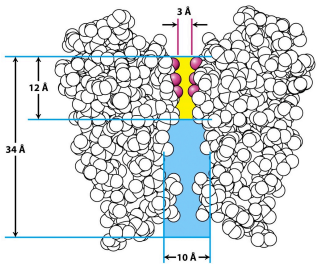
Channels and the Action Potential

- The basic channel is illustrated by bacterial K^+ channel.



Channels and the Action Potential

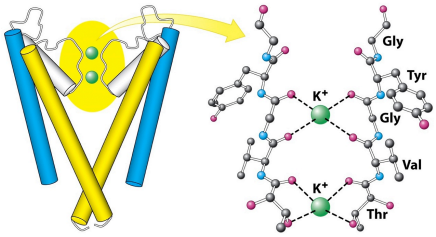
- K^+ channel illustrates ion selectivity.



K^+ must give up waters of hydration to pass through the narrow opening in the channel.

Channels and the Action Potential

- K^+ channel illustrates ion selectivity.
  - The sequence Thr-Val-Gly-Tyr-Gly is highly conserved.



Channels and the Action Potential

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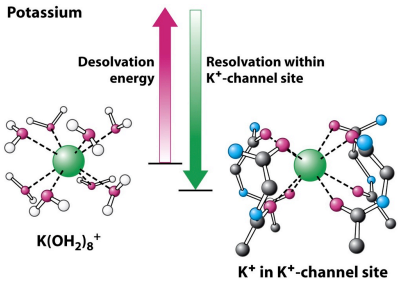


Channels and the Action Potential

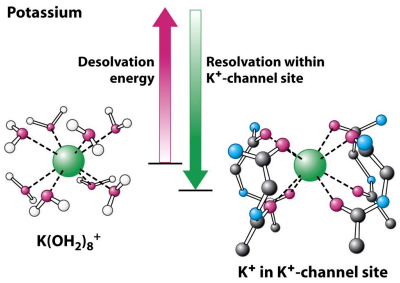
- K^+ channel illustrates ion selectivity.

TABLE 13.1 Properties of alkali cations

Ion	Ionic radius (Å)	Hydration free energy in kJ mol^{-1} (kcal mol^{-1})
Li^+	0.60	−410 (−98)
Na^+	0.95	−301 (−72)
K^+	1.33	−230 (−55)
Rb^+	1.48	−213 (−51)
Cs^+	1.69	−197 (−47)

Channels and the Action Potential

- K^+ channel illustrates ion selectivity.



Channels and the Action Potential

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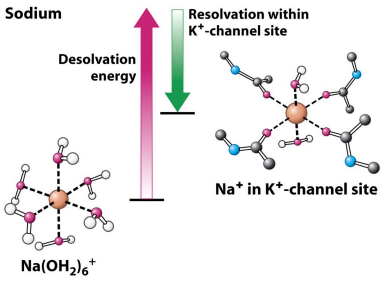
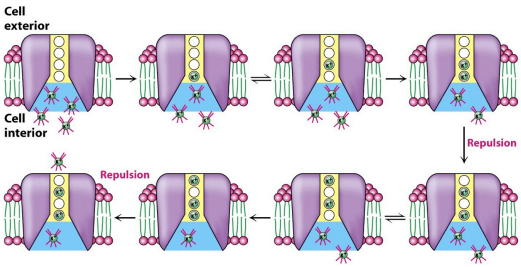


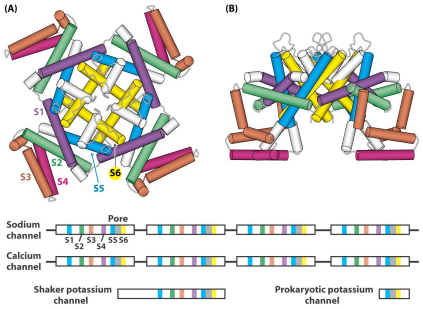
Channels and the Action Potential

- K^+ channel illustrates basis for rapid transport.
  - Charge repulsion increases the rate of flow



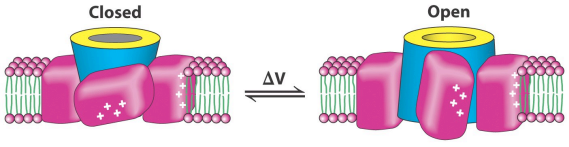
Channels and the Action Potential

- The voltage-gated K^+ channel of nerve cells.



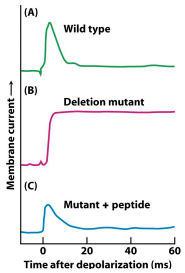
Channels and the Action Potential

- The voltage-gated K^+ channel of nerve cells.
  - Voltage rise opens channel



Channels and the Action Potential

- Transport is abruptly halted by a plug



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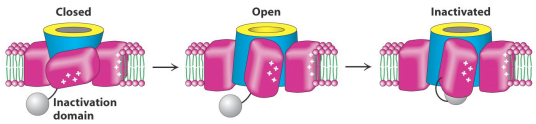
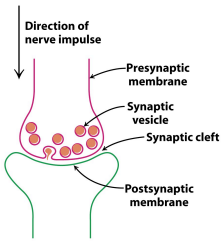


Channels and the Action Potential

- Neurotransmitters from neighboring nerve cells trigger the action potential.



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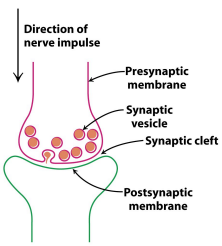
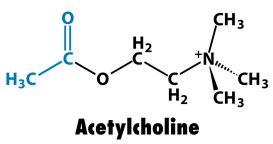


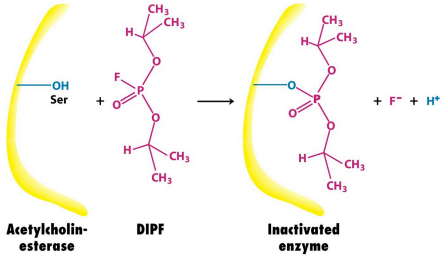


Acetylcholine

Acetylcholine is an example of a neurotransmitter

Enzyme Inhibition

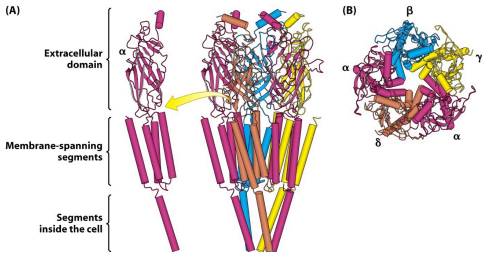
- Irreversible Inhibition



DIPF is related to the poison Sarin gas

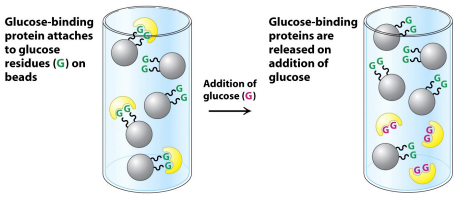
Channels and the Action Potential

- Acetylcholine triggers a ligand-gated channel.



Channels and the Action Potential

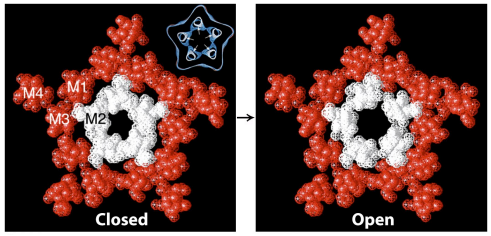
- The Acetylcholine receptor can be isolated with affinity chromatography using cobratoxin as the ligand.



Affinity Chromatography

Channels and the Action Potential

- The binding of acetylcholine to the he acetylcholine opens the flow to Na^+ and K^+ ions.



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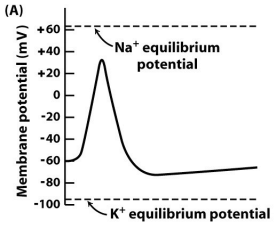

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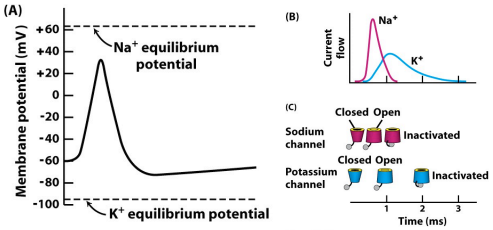
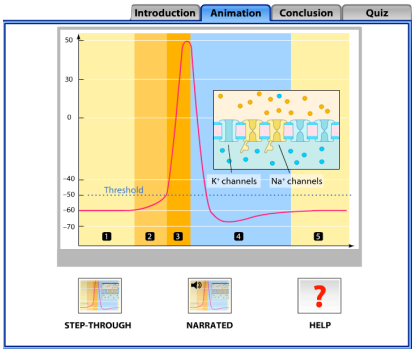


Channels and the Action Potential



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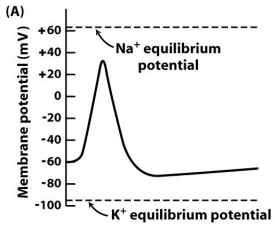

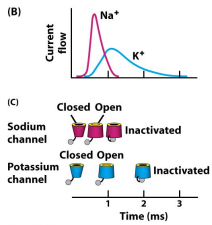

Next up

- Lecture 9, con'd - Membrane Channels and Pumps. (Chapter 13)
- Lecture 10, Signal Transduction. (Chapter 14)