Chem 452 – Lecture 9
Pumps and Channels
Part 1

Question of the Day: What two factors about a molecule influence the change in its free energy as it moves across a membrane?

Introduction

- Membrane proteins function as
  - Pumps (Chapter 13)
  - Channels (Chapter 13)
  - Signal transducers (Chapter 14)
  - Energy transducers (Chapter 18 & 19)

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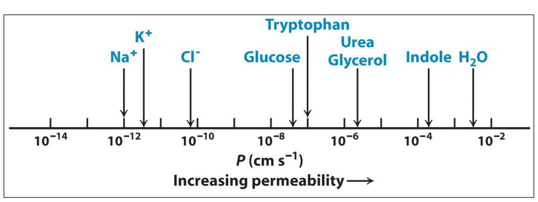
Membrane Lipids and Water

- Lipid membranes display a wide range of permeability's to small molecules.



Introduction

- Pumps and Channels move substances across membranes.
  - Pumps move substances from regions of low concentration to high concentration.
    - Requires a source of energy (**active transport**)
  - Channels allow substances to move from regions of high concentration to low concentration.
    - Does not require an outside source of energy (**passive transport**)
    - If passive transport requires a channel it is called **facilitated diffusion**.

Introduction

- Some pumps couple transport to the hydrolysis of ATP (**primary transport)**
  - P-Type ATPases
  - ATP-binding cassette (ABC) transporters
- And some pumps couple transport to a second concentration gradient (**secondary transport**)

Introduction

- Transporters are used to regulate the metabolic in different tissues across an organism.
  - e.g. Glucose Transporters

TABLE 16.4 Family of glucose transporters

Name	Tissue location	K_M	Comments
GLUT1	All mammalian tissues	1 mM	Basal glucose uptake
GLUT2	Liver and pancreatic β cells	15–20 mM	In the pancreas, plays a role in the regulation of insulin In the liver, removes excess glucose from the blood
GLUT3	All mammalian tissues	1 mM	Basal glucose uptake
GLUT4 brane	Muscle and fat cells	5 mM	Amount in muscle plasma mem- increases with endurance training
GLUT5	Small intestine	—	Primarily a fructose transporter

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Which tissue is last in line to take up glucose from the blood?

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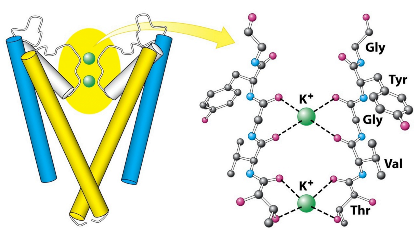
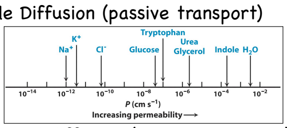
- Gated channels, while not requiring energy for transport, can be highly specific.



The Potassium Channel

Active versus Passive Transport

- Transport across membranes
  - Simple Diffusion (passive transport)



  - Facilitated diffusion (passive transport)
  - Requires energy (active transport)
- For all kinds of transport, the ΔG for the process must be < 0.

Active versus Passive Transport

- The free energy change for moving a species across a membrane depends on
  - The concentration differences for that species
  - Voltage differences across the membrane, if the species carries a charge

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

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Concentration

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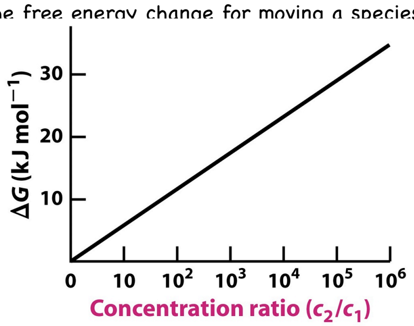

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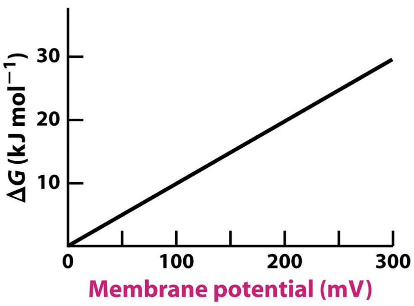

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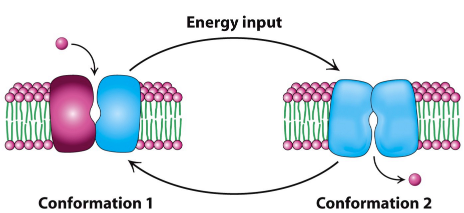
ATPase Pumps (Active Transport)

- P-type ATPases
- ATP-Binding Cassette Transporters



Conformational changes are coupled to ATP hydrolysis

ATPase Pumps (Active Transport)

- P-type ATPases
- ATP-Binding Cassette Transporters

Table 15.1 Standard free energies of hydrolysis of some phosphorylated compounds

Compound	kJ mol^{-1}	kcal mol^{-1}
Phosphoenolpyruvate	−61.9	−14.8
1,3-Bisphosphoglycerate	−49.4	−11.8
Creatine phosphate	−43.1	−10.3
ATP (to ADP)	−30.5	− 7.3
Glucose 1-phosphate	−20.9	− 5.0
Pyrophosphate	−19.3	− 4.6
Glucose 6-phosphate	−13.8	− 3.3
Glycerol 3-phosphate	− 9.2	− 2.2

Conformational changes are coupled to ATP hydrolysis

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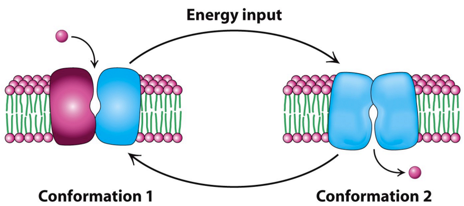

Conformational changes are coupled to ATP hydrolysis

ATPase Pumps

- P-type ATPases
  - Na^+/K^+ ATPase
    - Pumps 3 Na^+ out while pumping 2 K^+ in.
  - Gastric H^+/K^+ ATPase
  - Sarcoplasmic Ca^{2+}ATPase (SERCA)

ATPase Pumps

- The energetics of active transport
  - Na^+/K^+ ATPase
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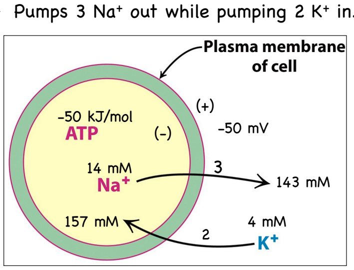


ATPase Pumps

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

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

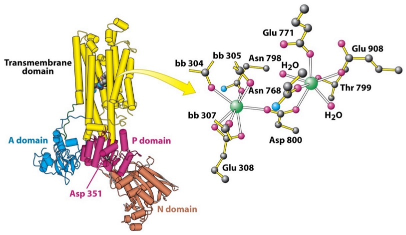
$$= \left(8.314 \text{ x } 10^{-3}\ \frac{\text{kJ}}{\text{mol•K}}\right)(310\text{ K})\ln\left(\frac{(0.143)^3(0.157)^2}{(0.014)^3(0.004)^2}\right) + (+1)\left(96.5\ \frac{\text{kJ}}{\text{mol•V}}\right)(+0.050\text{V})$$

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

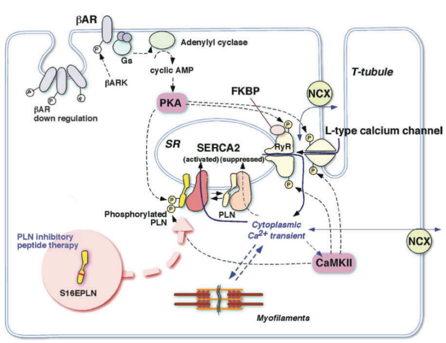
$$= 41.7\ \frac{\text{kJ}}{\text{mol}}$$

ATPase Pumps

- SERCA (Sarcoplasmic Reticulum Ca^{2+} ATPase)
  - Have crystal structure for each step in pumping cycle



ATPase Pumps



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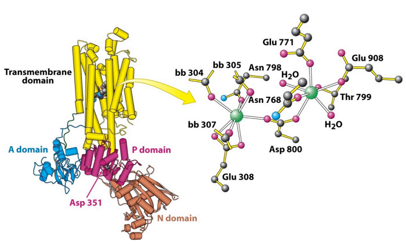
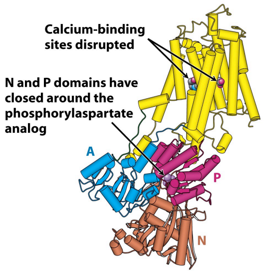


ATPase Pumps

- SERCA
  - Phosphorylation of an aspartate (A351) causes a conformational change that disrupts the Ca^{2+} binding sites.



ATPase Pumps

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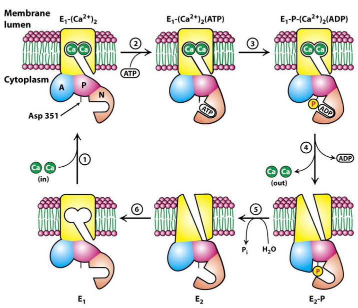
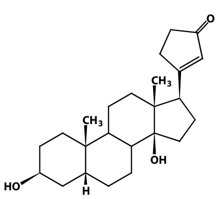


ATPase Pumps

- The drug digitoxigenin (digitalis), which is used to treat congestive heart failure, inhibits the Na^+/K^+ ATPase.



Digitoxigenin

ATPase Pumps

- The P-type pumps are homologous.
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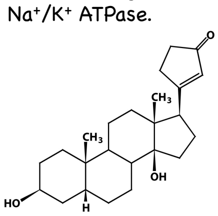

Digitoxigenin

$$E_2{-}P + H_2O \not\longrightarrow E_2 + P_i$$

Inhibited by cardiotonic steroids

ATPase Pumps

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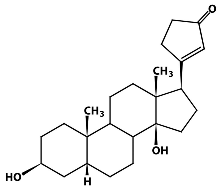
Foxglove (Digitalis purpurea)

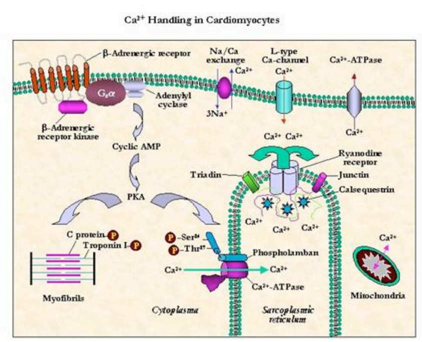


Digitoxigenin

ATPase Pumps

- The P-type pumps are homologous.
- The drug digitoxigenin (digitalis), which is used to treat congestive heart failure, inhibits the Na^+/K^+ ATPase.
- With higher cellular Na^+ levels, the Ca^{2+} pump is slower to remove the Ca^{2+} from the cytoplasm, leading to a stronger contraction.

ATPase Pumps



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  - Yeast contain 16 examples
    - H^+
    - Ca^{2+}
    - Na^+
    - Cu^{2+}
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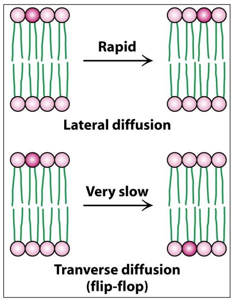
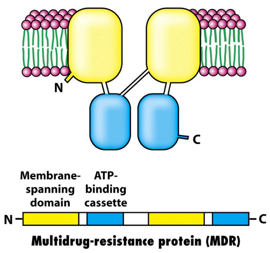


ATPase Pumps

- The ATP-binding (ABC) Transporter.
  - Uses a slightly different strategy from the P-type ATPases.



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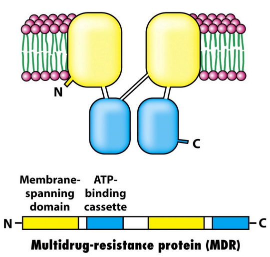
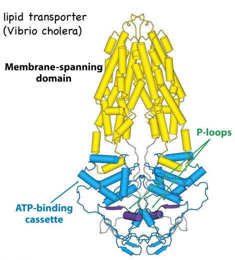


lipid transporter (Vibrio cholera)



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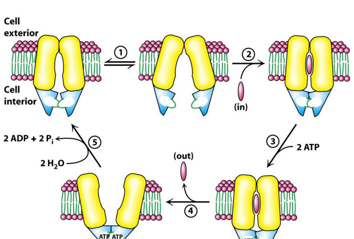
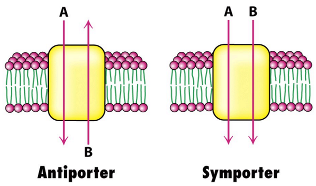


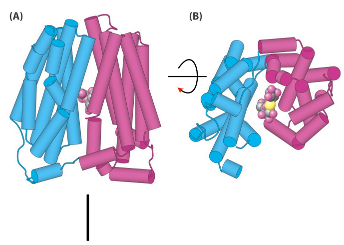
Secondary Transporters

- Secondary transporters are active transport systems that do not derive their energy directly from the hydrolysis of ATP
  - Instead, the active transport is coupled to the passive transport of a second metabolite



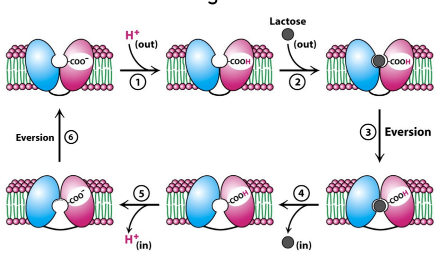
Secondary Transporters

- Lactose Permease is a well-studied example.



Secondary Transporters

- The transport of lactose up a concentration gradient is coupled to the transport of protons down a concentration gradient.



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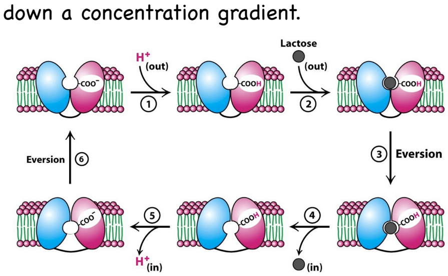

Next up

- Unit V, Lecture 9, con'd - Membrane Channels and Pumps. (Chapter 13)
  - K^+ channel and the action potential