Biological Membrane Transport

Review of membrane structure and dynamics
Membrane transport
- Energetics
- Types

Membrane Transport

Dr. Kornberg: "The Berlin Wall of the Cell"

Lecture 01.23.17 (21:04-23:56 & 35:27-38:29)-Berlin Wall (3 & 3 min)

[BI422 videos: https://mymedia.bu.edu/channel/BI422/81224851]

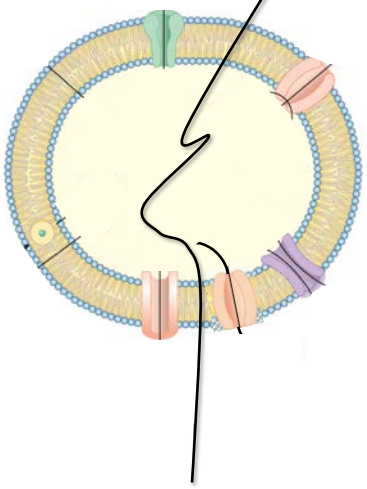
- Cell membranes are permeable to small nonpolar molecules that passively diffuse through the membrane.
- Passive diffusion of polar molecules involves desolvation and thus has a high activation barrier, unless desolvation energy is lowered.
- Transport across the membrane can be facilitated by proteins that provide an alternative diffusion path.
- Such proteins are called transporters or permeases.

Types of Membrane Transport

Non-mediated

$[S]_{out} >> [S]_{in}$

$[S]_{out} << [S]_{in}$



All others are Mediated

Types of Membrane Transport

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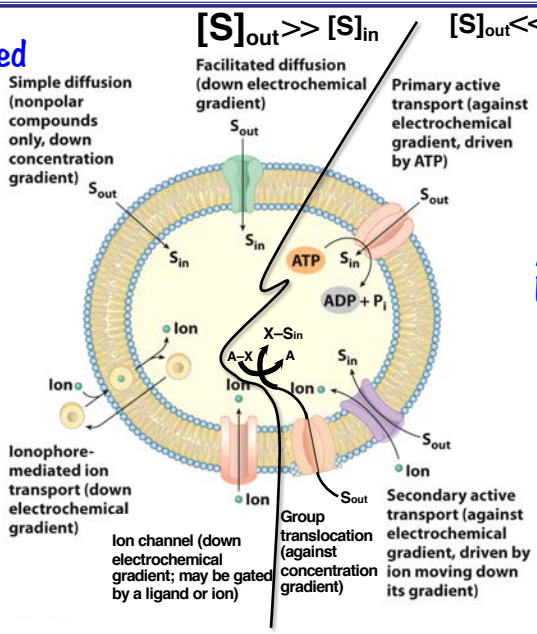

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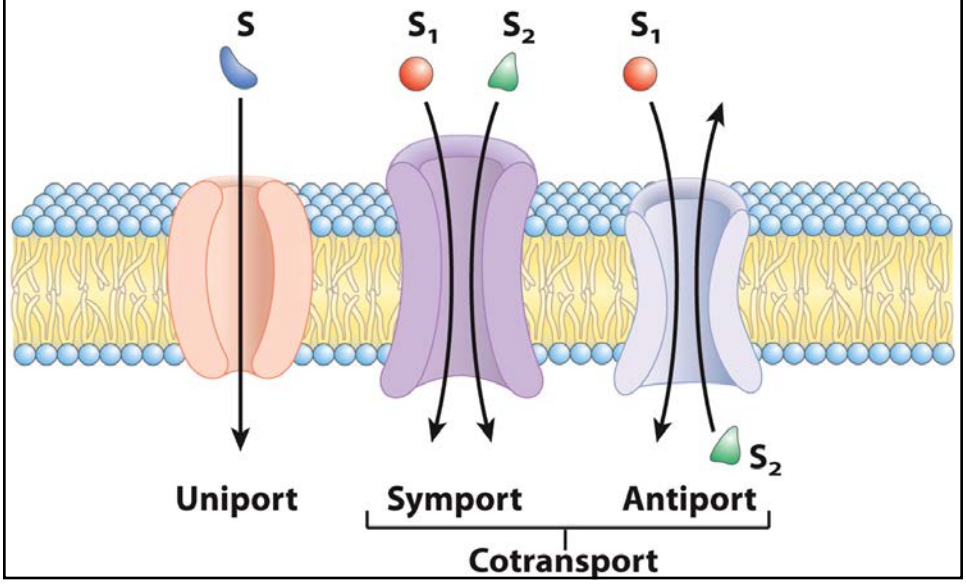
Membrane Transport

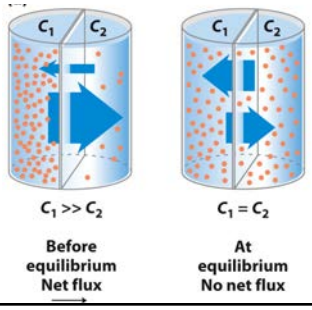
Three Classes of Transport Systems



Membrane Transport

What is this electrochemical gradient?

- Transport across a membrane must be energetically favorable. There are two types of energies at play:
  - Concentration dependence: The solute moves toward chemical equilibrium across the membrane.
  - Electrical dependence: The solute moves toward charge equilibrium across the membrane.



This is why we say "down" or "against" the **electro-chemical** gradient.

How is this gradient quantified?

Membrane Transport

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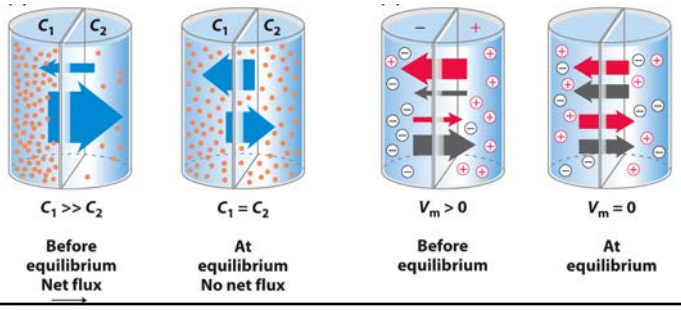


This is why we say "down" or "against" the **electro-chemical** gradient.

How is this gradient quantified?

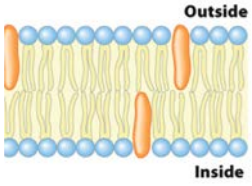
Membrane Transport

Energetics

Transport can be considered like a chemical reaction of S_{out} to S_{in}

$$S_{out} \rightleftharpoons S_{in}$$

[S_{out}]



[S_{in}]

$$\Delta G' = \Delta \boldsymbol{G}^{o'} + RT ln \frac{[S_{in}]}{[S_{out}]}$$

But, $\Delta \boldsymbol{G}^{o'} = \mathbf{0}$ because there is no chemical reaction:

$$\Delta G' = RT ln \frac{[S_{in}]}{[S_{out}]}$$

If $[S_{out}] > [S_{in}]$, $\Delta \boldsymbol{G}'$ is $\ominus$

If $[S_{out}] < [S_{in}]$, $\Delta \boldsymbol{G}'$ is $\oplus$

But, if S is charged, we must account for this:

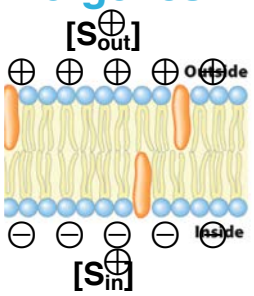
$$\Delta G' = RT ln \frac{[S_{in}]}{[S_{out}]} + z\mathcal{F}\Delta\psi$$

Where "z" is the charge on S, and $\Delta\psi$ is the membrane electrical potential in volts

Membrane Transport

Energetics

$S_{out} \rightleftharpoons S_{in}$



$$\Delta G' = RT\ln\frac{S_{in}}{S_{out}} + z\mathcal{F}\Delta\psi$$

Where "z" is the charge on S, and $\Delta\psi$ is the membrane electrical potential in volts

$\Delta\psi$ = charge difference "in" versus "out"

So, if its more negative in than out, $\Delta\psi$ is $\ominus$ (as depicted)

And, if its more positive in than out, $\Delta\psi$ is $\oplus$

Now, if $\Delta\psi$ is negative, and S has a positive charge (z is +, as depicted), then $z\mathcal{F}\Delta\psi$ makes a negative contribution to $\Delta G'$ making it even more favorable.

As a further consequence, if $\Delta\psi$ is maintained, then at equilibrium $[S_{in}] > [S_{out}]$.

Membrane Transport

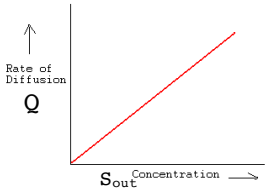
How do you experimentally determine the kind of transport?

Non-mediated — Simple diffusion

Mediated — Facilitated diffusion, ionophore mediated, active transport

Diffusion is governed by **Fick's law of diffusion**:

$$Q = DA\frac{P_1 - P_2}{L}$$



Q = rate of diffusion.

D = diffusion coefficient

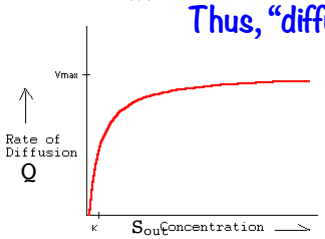
A = area across which diffusion occurs

[S_{out}] and [S_{in}] = concentrations on each side of membrane.

L = thickness of the membrane.

DA/*L* is the permeability coefficient.

Thus, "diffusion" is Non-mediated



Mediated behaves like saturation kinetics

$$C + S_{out} \rightleftharpoons CS \rightleftharpoons C + S_{in}$$

$$Q = \frac{Q_{max}[S_{out}]}{K_d + [S_{out}]}$$

Thus, "diffusion" is Mediated

Membrane Transport

Examples:

- Facilitative Diffusion
  - Ionophore
  - Maltoporins
  - GLUT1 transprter
  - Aquaporin
  - Selective ion channel for potassium (K-channels)
- Active Transport
  - Primary (1°)
    - Na/K
    - ABC
  - Secondary (2°)
    - Na/Glc
    - Bicarb/Cl
  - Group Translocation
    - Bacterial phosphotransferase system (PTS)

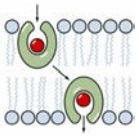
Membrane Transport

Facilitative Diffusion

Membrane Transport

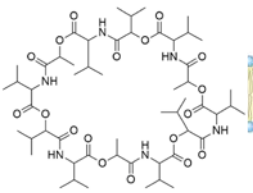
Examples of Facilitative Diffusion

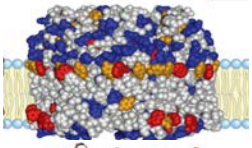
(including ionophore mediated)

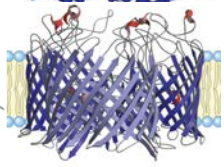


Ionophore

Valinomycin

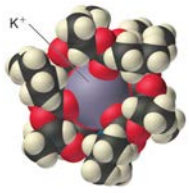




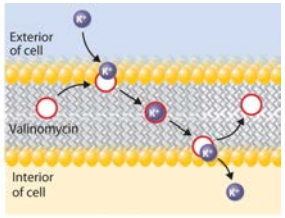


Maltoporin

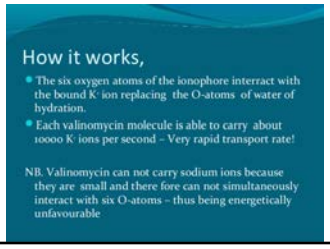
- Proteins of the *E. coli* outer membrane
- Maltoporin (derived from PDB ID 1MAL) is a maltose transporter (a trimer; each monomer consists of 16 β strands).



(a) K^+–valinomycin complex

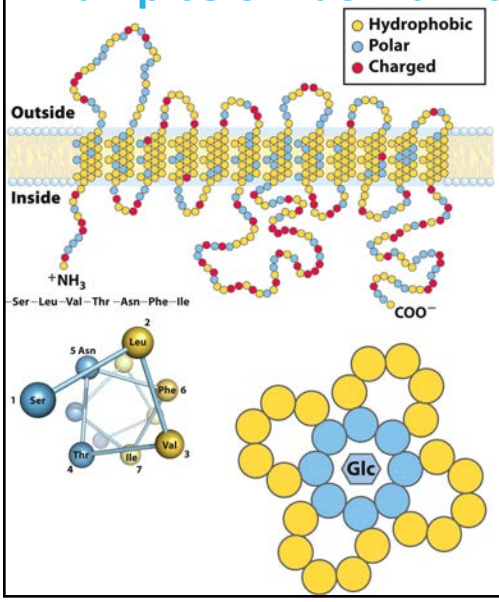


(b) Transport of K^+ across a membrane

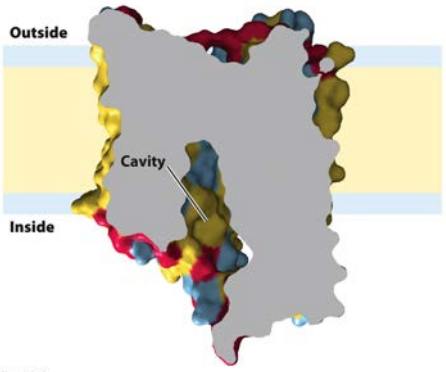


Membrane Transport

Examples of Facilitative Diffusion



Glucose Transporter (GLUT1)



Membrane Transport

Examples of Facilitative Diffusion

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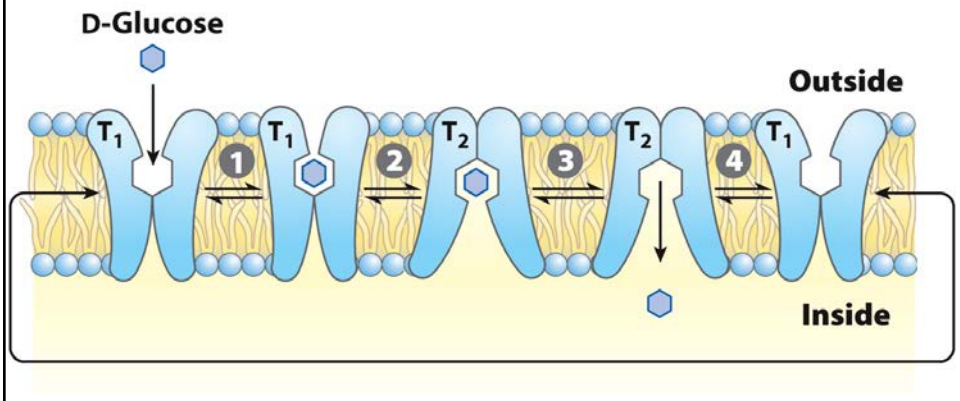
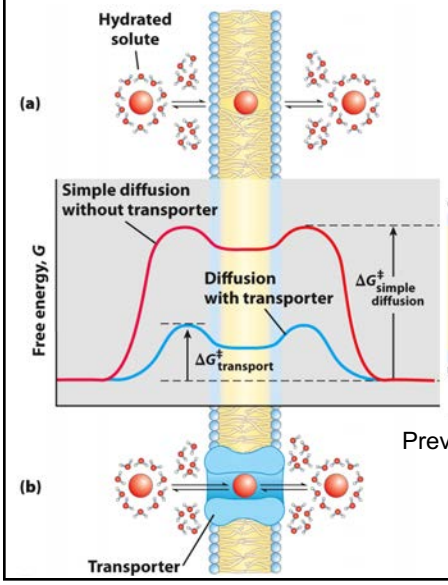
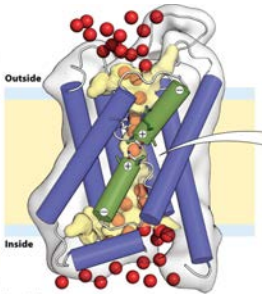


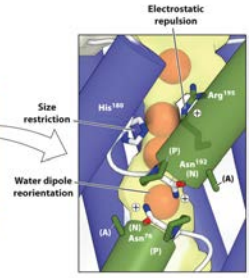
Membrane Transport

Examples of Facilitative Diffusion

Aquaporins Allow Rapid Water Passage Through Membranes







Prevention of proton ($^{+}H_3O$) transport:

- role of His180 – Gates the size of pore at 2.8 Å
- role of Arg195 – Repels hydronium ions
- role of NPA – Positive poles at ends of helices repels hydronium ions, but also breaks up network of water molecules

Membrane Transport

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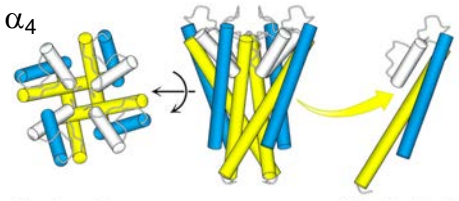
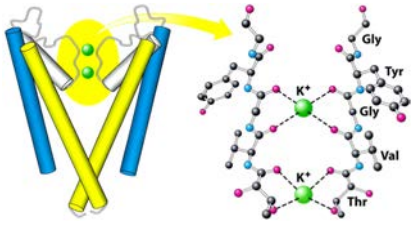
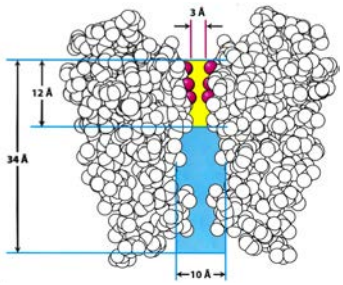
Membrane Transport

Examples of Facilitative Diffusion



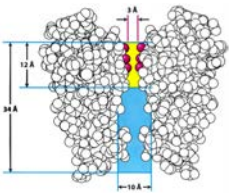


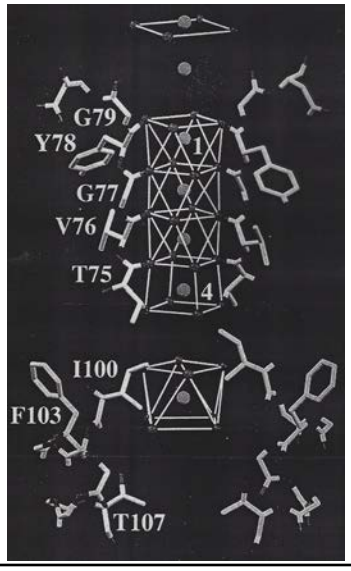
Potassium Channel KcsA K+ allows specific passage of this ion through membranes



Membrane Transport

Examples of Facilitative Diffusion



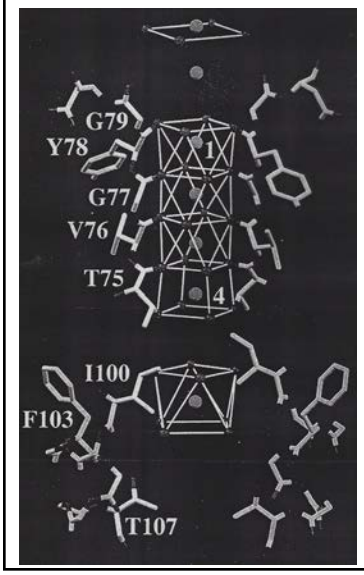


How is the >100X specificity for K^+ achieved?

Ion	Radius (Å)
Li^+	0.6
Na^+	1.0
K^+	1.3
Rb^+	1.5
Cs^+	1.7

Membrane Transport

Examples of Facilitative Diffusion



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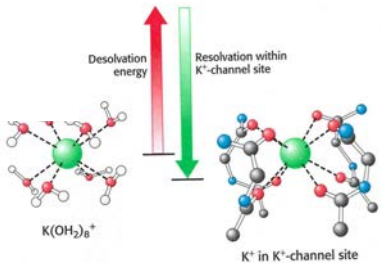
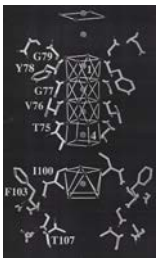
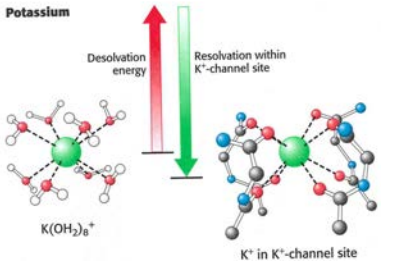


Membrane Transport

Examples of Facilitative Diffusion



Ion	Radius (Å)	Energy of dehydration (kcal/mole)
Li^+	0.6	– 98
Na^+	1.0	– 72
K^+	1.3	– 55
Rb^+	1.5	– 51
Cs^+	1.7	– 47



While specificity for Na^+ over K^+ can be achieved by the size of the binding site, that won't work the other way around. To get specificity of K^+ over Na^+, the protein takes advantage of the higher (30%) energy of dehydration. It takes more energy to dehydrate Na^+ than K^+ and the protein doesn't make as good bonds to Na^+ ion as does water shell (see off-set oxygens in polygon).