Overview of Transport Across Biological Membranes

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Roles of Membrane Transport

- Nutrient uptake
- Waste product removal
- Bioenergetics
- Signal transduction
- Compartmentation

5 – 10% of genes in most genomes encode membrane transporters
## Nobel Prizes in Membrane Transport

<table>
<thead>
<tr>
<th>Year</th>
<th>Name(s)</th>
<th>Achievement</th>
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<tbody>
<tr>
<td>1978</td>
<td>Peter Mitchell (UK)</td>
<td>Concept of chemiosmotic coupling</td>
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<td>1988</td>
<td>Johan Deisenhofer (D)</td>
<td>Structure of electron-translocating photosynthetic reaction centre</td>
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<td>Robert Huber (D)</td>
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<td>Hartmut Michel (D)</td>
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<td>1991</td>
<td>Erwin Neher (D)</td>
<td>Patch clamp technique for single channel recording</td>
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<td>Bert Sakmann (D)</td>
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<td>1997</td>
<td>Jens-Christian Skou (DK)</td>
<td>Mechanisms of ATP-driven ion translocation</td>
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<td>Paul Boyer (USA)</td>
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<td></td>
<td>John Walker (UK)</td>
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<tr>
<td>2004</td>
<td>Peter Agre (USA)</td>
<td>Structure of water- and ion-channels</td>
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<td>Rod MacKinnon (USA)</td>
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### Reading

A basic introduction, good for this lecture and many others following:

Aims: By the end of the lecture you should understand...

- That \( H^+ \) and/or \( Na^+ \) transport systems comprise the “currency” for energy transduction across biological membranes;
- That *pumps* have fairly slow turnover rates and are normally abundant membrane proteins;
- That *carriers* have moderate turnover rates and can be energised by coupling transport of specific solutes to that of ions;
- That *channels* dissipate ion potentials but are nevertheless specific for their ionic substrates and are highly regulated.
Transport at “Energy-Coupling” Membranes

ATP synthesis → inner mîto; thylakoid; Bacteria, Archaea

P  membrane  N = matrix; stroma; cytosol

H+ pumps (diverse)  Lectures 10, 11

Reduced substrate or light

ATP synthase (ubiquitous)  Reversed pump  Lecture 12

H+  →  ADP + Pi  →  ATP
Transport Strategies and Classes of Transport System at “Non-Energy-Coupling” Membranes

Lectures 13-16

i.e. those membranes not involved in ATP synthesis

We’ll consider Animals Plants Fungi

• Plasma membrane
• Endomembranes:
  • Lysosomes/vacuoles
  • ER
  • Golgi ……
Transport Processes in an Idealized Eukaryotic Cell

Plasma membrane

energy-coupling

light/redox

H^+

ADP

+ Pi

ATP

D^+ = "driver ion"

storage, waste products

nutrients

D^+

Cations^+

Anions^−

Cations^+

Anions^−
There are Three Classes of Transport System

1. Primary pumps [Lecture 13]:

   - Normally (but not exclusively) fuelled by ATP in intracellular and plasma membranes;
   - Set up electrochemical potential differences for ions and other solutes;
   - If pumping ions, they are normally (but not exclusively) “electrogenic”:
     They carry electrical current in the form of ions and have the capacity to set up a transmembrane voltage ($\Delta \psi$).
2. **Carriers: (for solute, S) [Lecture 14]**:

- Can be energized by electrochemical potentials for ions:
  - a. “Symport” or “Cotransport”
  - b. “Antiport” or “Countertransport”

- or not energized at all:
  - c. “Uniport” or “Facilitated Diffusion”
3. **Channels (for ions and water)**
[Lectures 15, 16] :

- Transport is thermodynamically dissipative (downhill), so not energised
- Exhibit Open/Shut kinetics ("Gating")
- Normally for specific ions: i.e. not just molecular sieves
Animal Cell Plasma Membranes Run an “Na⁺ Economy”

1. The dominant PRIMARY PUMP: A (Na⁺/K⁺)–ATPase
   Expels Na⁺ from the cell, imports K⁺ in stoichiometry
   \[ 3 \text{Na}^+ : 2 \text{K}^+ : 1 \text{ATP} \]
   Sets up a “sodium-motive force”

2. Solute Carriers: For many mammalian cells, bathed in fluid in which solute concentrations are homeostatically regulated, solute (e.g. glucose) entry is via facilitated diffusion.

3. However, in some specialized cells (e.g. gut, kidney) solutes are accumulated from dilute media via Na⁺ symport. Furthermore, H⁺ excretion via H⁺/Na⁺ antiport.
3. **Channels**: $K^+$ (dominant), $Na^+$, $Ca^{2+}$, $Cl^-$

Summary

The University of York
Plant and Fungal Cell Plasma Membranes Run a “H+ Economy”

1. Dominant PRIMARY PUMP: An H⁺-ATPase
   Expels H⁺ from cell in stoichiometry 1 H⁺: 1 ATP
   Sets up a protonmotive force

2. Solute Carriers  In contrast to many mammalian cells, plant and fungal cells cannot rely on environment for maintenance of high [nutrient]. Most plant and fungal cells exhibit energized uptake of nutrients.
   Driver ion for symport is H⁺
3. **Channels** $K^+$ (dominant) $Ca^{2+}$, $Cl^-$ - but not $Na^+$
Bacterial Cell Membranes Run (Dominantly) an “H⁺-Economy”, with Hints of an “Na⁺-Economy”

1. Dominant 1° PUMPS
   - in most bacteria metabolizing oxidatively:
     A respiratory chain with great similarities to that of mitos.
   - in photosynthetic bacteria:
     A light-driven redox chain like that in chloroplasts.
     Classic “energy-coupling” membranes, pumping H⁺ out.

2. Carriers: like plants and fungi, bacteria must, in many environments, absorb nutrients from dilute solution.
   Uptake of many nutrients via H⁺-symport.
   H⁺/Na⁺ antiport also sets up inwardly-directed “sodium motive force” which can be used to drive other solute uptake systems
3. Channels exist, e.g. for K⁺; others ??

Summary

- redox or light

- K⁺
- K⁺
- H⁺
- H⁺

- Na⁺

- solutes e.g. lactose
- solutes e.g. melibiose
Non-Energy Coupling Intracellular Membranes

1. Dominant $1^\circ$ PUMP:

   - an H$^+$-ATPase
   - stoichiometry 2 H$^+$: 1 ATP
   - pumps H$^+$ into the intracellular compartment, resulting in cytoplasm-negative $\Delta \psi$

   Sets up a protonmotive force directed into the cytoplasm
2. Carriers:

Their nature is highly dependent on organellar function e.g…

- chromaffin granules (adrenal medulla) store high concs. of catecholamines (neurotransmitter) – up to 0.6 M
- vacuoles (higher plants) accumulate Ca^{2+}
- vacuoles (yeast) accumulate amino acids

All these are cytoplasmic export systems driven by H^{+} antiport (as for export across plasma membrane)
3. **Channels** for $K^+$, anions, $\text{Ca}^{2+}$

Summary

- $K^+$
- anions
- $\text{Ca}^{2+}$
- $\text{H}^+$
- ATP
- $2\text{H}^+$
- solutes, ions
Turnover Rate and Protein Density

PRIMARY PUMPS AND CARRIERS: turnover rates are those of slowish enzymes $\approx 100 \text{ s}^{-1}$ and $1000 \text{ s}^{-1}$, respectively.

By contrast, CHANNELS catalyse very rapid ion movement, approaching the limits set by diffusion. Typically, $10^6 - 10^8 \text{ ions s}^{-1}$.

In addition, $1^\circ$ pumps must translocate all of the driver ions used for setting up an ion gradient to drive a wide range of selective carriers.

Therefore pump density must be high

Density of carriers will be lower

Density of channels will be even lower
Some numbers on protein density...

- In kidney epithelium – a tissue with specific transport requirements, the density of the (Na\(^+\)/K\(^+\))-ATPase pump approaches 10,000 protein molecules/\(\mu\)m\(^2\) membrane.

- By contrast, a typical density of channels is only 1 channel molecule/\(\mu\)m\(^2\)

This has significant implications for characterization of the PROTEIN CHEMISTRY of transport systems: 1° pumps are easy to work with and purify from native systems, channels are not!
SUMMARY

1. Light or redox-powered H\(^+\) pumping at energy-coupling membranes sets up PMF which drives (a) ATP synthesis and (b) transport processes (in the mitochondrion and bacteria).

2. Transport systems can be classified into Pumps, Carriers and Channels.

3. Animal cell plasma membranes run a “Na\(^+\) economy” in which the Na\(^+\) gradient is used to drive transport of other solutes.

4. Other membranes run a “H\(^+\) economy”.

5. Pumps have low turnover rates, while channels turnover very fast.

6. Turnover rates have a profound influence on the abundance of transport systems.