

lipid component of membrane and the lipid bilayer is the fluid backbone but the mosaic part is the unique complement of proteins that give the membrane its function these proteins fall into 3: integral, peripheral and lipid-anchored

- most of the proteins are floating around and are less fluid than the lipids because larger (not easy to move around) and some are anchored in place
- a number of membrane proteins linked to the cytoskeleton or extracellular environment are not nearly as free to move around as other proteins
- proteins are more variable in mobility in the membrane than lipids are

**Membrane proteins**

- The 'mosaic' component of the fluid mosaic model
- Functions include
  - Transport
  - Enzymes
  - Signal transduction
  - Attachment/recognition
- 3 types: integral, peripheral, lipid-anchored

Fig. 5.1

-some proteins cannot move around freely because of certain structures in the cell like

tight junctions

-proteins are mobile but more variable than lipids

'Mosaic' Component of Fluid Mosaic Model, 3 Types: Integral, Peripheral, Lipid-anchored  
The membrane is depicted as mosaic because like a mosaic that is made up of many different parts the plasma membrane is composed of different kinds of macromolecules, such as integral proteins, peripheral proteins, glycoproteins, phospholipids, glycolipids, and in some cases cholesterol, lipoproteins.

A number of membrane proteins linked to the cytoskeleton or extracellular environment are not nearly as free to move around as other proteins. Some proteins are more variable in mobility in the membrane than lipids.

Some proteins cannot move around freely because of certain structures in the cell like tight junctions. Some proteins are mobile but more variable than lipids.

### Three types of Membrane Proteins

Integral membrane proteins which are permanently bound to the lipid bilayer

Peripheral membrane proteins that are temporarily associated with lipid bilayer or with integral membrane proteins

Lipid-anchored proteins bound to lipid bilayer bound through lipidated amino acid residues

**Membrane proteins**

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e.g. Na<sup>+</sup>K<sup>+</sup>-ATPase    e.g. Electron transport chain    e.g. B-adrenoreceptor    e.g. connexin

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Fig. 5.8

-many membranes are specialized for enzyme functions (distinguish mitochondrial membranes from cell membranes by the given enzymes present -proteins and electrons involved in electron transport chains)

-proteins distinguished by their receptors, most receptors are membrane proteins

-the proteins that allow

-transport proteins (Na K ATP's that move K and Na ions across)

-proteins that allow recognitions between themselves, connections

-variety of different proteins within the membrane (they allow membrane to carry out particular functions and they characterize the membrane)

- Integral membrane proteins
  - Amphipathic with one or more hydrophobic regions
  - Usually transmembrane (single or multipass)
  - Transmembrane regions typically  $\alpha$ -helix of 20-30 hydrophobic aa residues

Fig. 5.9

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Fig. 5.10

-proteins that go right through the membrane (transmembrane), some are buried within the membrane without extending the whole way across, hydrophobic regions for those that extend right across the membrane (region for an alpha helix structure, centered in the core of the aa) and some hydrophilic areas loops of either side of transmembrane domains (water friendly)

-they are transmembrane proteins that simply pass thru the membrane so N terminus on one side and C terminus on the other side and they are known as single path transmembrane proteins

-multipath transmembrane proteins with several to many transmembrane domains and protein weaves back and forth through the membrane

-placed in the membrane in the hydrophilic areas of these transmembrane domain and so are difficult to dislodge from that place (difficult to isolate unless destroy the membrane)

### Integral membrane proteins

A protein molecule (or assembly of proteins) that is permanently attached or firmly anchored in the plasma membrane via its hydrophobic domains interacting with the membrane phospholipids.

Integral membrane proteins may be classified into two major groups:

1. transmembrane proteins - are protein that spans the entire biological membrane
2. integral monotopic proteins - are permanently attached to the membrane from one side

The more common type is the transmembrane protein.

There are transmembrane proteins that simply pass thru the membrane so N terminus on one side, and C terminus on the other side. They are known as single path transmembrane proteins.

Multipath transmembrane proteins with several to many transmembrane domains and proteins weave back and forth through the membrane.

Placed in the membrane in the hydrophilic areas of these transmembrane domain and so are difficult to dislodge from that place (difficult to isolate unless destroy the membrane).

Peripheral membrane proteins

Peripheral membrane proteins are proteins that adhere only temporarily to the biological membrane with which they are associated. These molecules attach to integral membrane proteins or penetrate the peripheral regions of the lipid bilayer. They are held by non-covalent interactions by phospholipids or other membrane proteins on the surfaces of the membrane. As they are held by non-covalent interactions and proteins are on surfaces of membrane then they are much easier to get off of the membrane than integral proteins (changing pH or changing the ionic strength of the solution). As they have a dynamic relationship with the membrane in the cell, they are usually the proteins that can be detached and attracted to another membrane as part of a signaling pathway.

- Peripheral membrane proteins
  - Membrane-associated through non-covalent interactions
  - Dynamic relationship with membrane
- Lipid-anchored membrane proteins
  - Membrane-associated through covalent linkages to phospholipids
  - Fatty-acid anchored
    - Intracellular orientation
  - GPI anchor (glycosylphosphatidylinositol)
    - extracellular orientation
    - can be cleaved with phospholipase C
    - e.g. type IV carbonic anhydrase

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IV... :

-enzyme found in blood vessels in lungs, it allows ventilation to be matched for gas exchange, its a GPI anchored protein that can be removed using phospholipase C enzyme

-on surfaces of the membranes held by non covalent interactions by phospholipids or other membrane proteins

-non covalent interactions and proteins are on surfaces of membrane then they are much easier to get off of the membrane than integral proteins (changing pH or changing the ionic strength of the solution)

-they have a dynamic relationship with the membrane in the cell so they are proteins that can be detached and attracted to a membrane as part of a signalling pathway

-examples: number of proteins that help anchor the cytoskeleton to the plasma membrane (help support the membrane)

3) lipid anchored proteins held together by covalent interactions with membrane lipids

-protein covalently linked to fatty acid chains (found on the inner leaflet of membrane)

-GPI anchored (glycosyl = carbohydrate group, phosphatidylinositol = membrane phospholipid, protein linked to carbohydrate group. (anchors portion to membrane)

-covalent association that can be broken down by particular enzymes (enzyme of phospholipase category can be used to cleave the GPI anchor, if cleaved the proteins is freely floating and can be removed from membrane)

### Movement across membranes

- Overview
  - Importance of size, polarity/charge, gradient
  - How?
    - Passive transport
      - Simple diffusion
      - Facilitated diffusion
    - Active transport
      - Primary
      - Secondary

BIO 1140 – SLIDE 5 Fig. 5.12

2 main routes for solutes crossing a membrane

1) passive transports :diffusion

3) active transport: carrier protein and expenditure of energy

-which route the solute takes depends on its size, polarity or charge of the solute and gradient for its movement (against gradient requires energy with the gradient = passive)

-small solutes move through membrane more easily than larger ones

-small hydrophobic molecules move most easily (O, CO2-relatively small, lipid soluble, simply diffuse through without transport pathways) small polar molecules like H2O and glycerol can pass through reasonably well without transport pathways, adding a pathway will speed up the transport such as water but can move against the membrane without pathways, glycerol can cross the membrane fairly easily (below 100 daltons) glucose needs a specialized transport pathway because higher 100,

anything charged can't pass through membrane because charged molecules attract to them a sphere of water molecules and become very large causing it to be cut off

which requires energy

Passive Transport

A kind of transport by which ions or molecules move along a concentration gradient, which means movement from an area of higher concentration to an area of lower concentration.

Since the movement of substances is by passive transport, this process does not require chemical energy (in contrast to active transport).

In moving substances across a biological membrane, a passive transport may or may not need the assistance of a membrane protein.

### Movement across membranes

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    - Active transport
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BIO 1140 – SLIDE 6 Fig. 12-4, Alberts et al. 2004

Types of pathways:

1) simple diffusion - with diffusion gradient for molecules that can pass through membrane

2) facilitated diffusion - with gradient and help of a protein transporter

3) active transport - against gradient with the expenditure of energy

passive :

simple diffusion

A type of passive transport, therefore, it is a net movement of molecules in and out of the cell across the cell membrane along a concentration gradient.

facilitated diffusion

Transport of substances across a biological membrane from an area of higher concentration to an area of lower concentration by means of a carrier molecule. Since the substances move along the direction of their concentration gradients, energy is not required.

-filtration and -osmosis

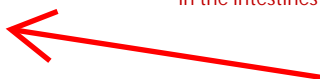
Active Transport

Active transport is the movement of a substance against its concentration gradient (from low to high concentration). In all cells, this is usually concerned with accumulating high concentrations of molecules that the cell needs, such as ions, glucose, and amino acids. If the process uses chemical energy, such as from adenosine triphosphate (ATP), it is termed primary active transport. Secondary active transport involves the use of an electrochemical gradient. Active transport uses energy, unlike passive transport, which does not use any type of energy. Active transport is a good example of a process for which cells require energy. Examples of active transport include the uptake of glucose in the intestines in humans and the uptake of mineral ions into root hair cells of plants.

There are two major types of active transport:

-primary active transport: also called direct active transport, directly uses energy to transport molecules across a membrane.

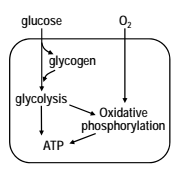
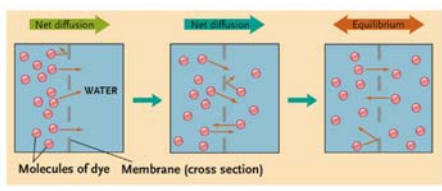
-secondary active transport or co-transport, in contrast to primary active transport, there is no direct coupling of ATP; instead, the electrochemical potential difference created by pumping ions out of the cell is used.



**Passive transport**

□ Diffusion

- Spontaneous; based on random movements
- Driven by diffusion gradient (downhill)
  - For solutes without a charge → concentration gradient
  - For gases → partial pressure gradient
  - For ions → electrochemical gradient
  - For water → osmotic gradient

BIO 1140 - SLIDE 7 Fig. 5.11

-diffusion is based on movement of individual molecules that undergo random thermal movements and tend to move from areas where they are abundant to areas where they are less abundant (move down a diffusion gradient which drives their movement)

-a solute without a charge where movement is given by a concentration gradient (semi-permeable membrane and a dye next to it, the dye will diffuse across the membrane until you have equal concentrations on both sides of membrane (at this point individual molecules can pass back and forth but no longer any net movement))

-movement of glucose (cells use glucose to produce ATP) glucose move into the cell and the gradient is maintained by the cells use of glucose

-oxygen and CO2 movements are driven by partial pressure gradient set by the cells use of their material (CO2 diffuses out of the cell and O into the cell)

-charge and concentration is considered when ions are being transported (electrochemical gradients)

-water by simple diffusion is driven by osmotic gradients, different than other solutes cuz it moves from concentrations of low solutes to high solute concentrations (osmotic does this= low concentration to high)

Passive Transport  
 Classifications of Passive Transport  
 Gases Partial pressure gradient  
 Ions Electrochemical gradient  
 Water Osmotic gradient

**Hypotonic vs Hypertonic vs Isotonic:**

**Hypertonic Solution:**

Greater concentration of solute outside of cell than inside  
 Water potential is higher; osmotic potential is lower  
 Net movement of water from the cell to the solution across a semi-permeable membrane  
 In excess, causes crenation in animal cells and plasmolysis in plant cells

**Hypotonic Solution:**

Greater concentration of solute inside cell than outside  
 Water potential is low (0 in distilled water); osmotic potential is higher  
 Net movement of water into the cell from the solution across a semi-permeable membrane  
 A pure water solution (DH2O) can cause lysis (bursting) in animal cells and turgor pressure in plant cells

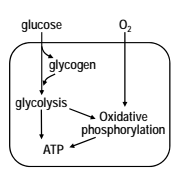
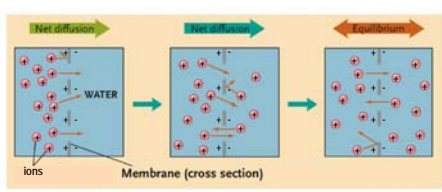
**Isotonic Solution:**

Concentration inside cells is equal to that of the solution  
 No net movement of water across a semi-permeable membrane (although there is osmosis)  
 Cell is at equilibrium (what it strives for)

**Passive transport**

□ Diffusion

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- Driven by diffusion gradient (downhill)
  - For solutes without a charge → concentration gradient
  - For gases → partial pressure gradient
  - For ions → electrochemical gradient
  - For water → osmotic gradient

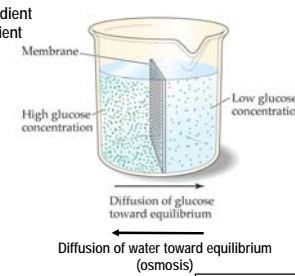



BIO 1140 - SLIDE 8 Fig. 5.11

**Passive transport**

□ Diffusion

- Spontaneous; based on random movements
- Driven by diffusion gradient (downhill)
  - For solutes without a charge → concentration gradient
  - For gases → partial pressure gradient
  - For ions → electrochemical gradient
  - For water → osmotic gradient



BIO 1140 - SLIDE 9 Fig. 3.2 Hill et al. 2004

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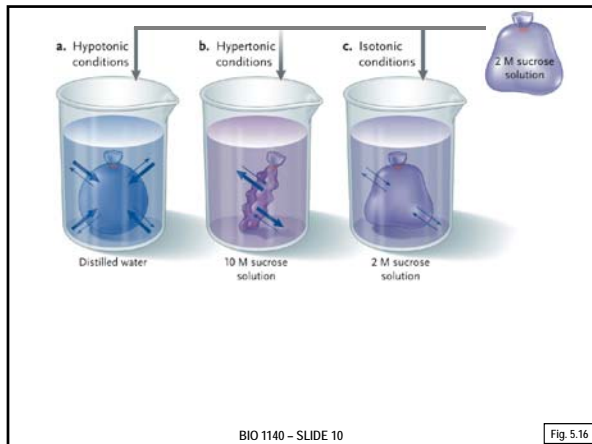
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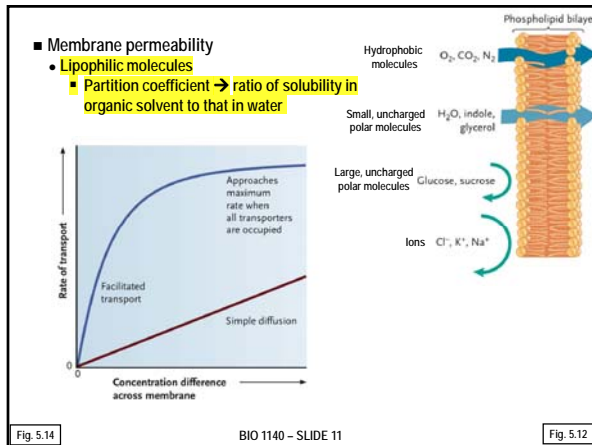
-if we take a fake cell (dialysis tubing permeable to water but not glucose with 2M sucrose) put it in solution of 2M sucrose, water will move freely back and forth across membrane but no net movement of water because concentrations are same at both membranes = isotonic

-isotonic conditions= cell shape doesn't change

-put in 10M sucrose solution, water will move from fake cell into environment and so cell shrivels up = hypertonic (more concentrated than cell contents)

-put in distilled water so no sucrose= hypotonic solution (lower) and so water moves into the cell (higher salt concentration within the cell) which causes it to burst

-these cell changes occur as environment changes



-gradient determines the direction of diffusion

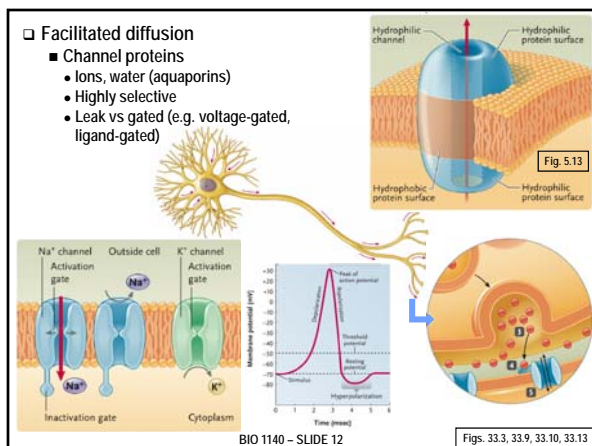
-based on the partition coefficient (lipophilic and cross membrane very easily)

-small molecules with high partition coefficient are lipophilic and cross the membrane easily

-large molecules have trouble getting across membrane even if lipid soluble

-diffusion rate is proportional to diffusion gradient

**Membrane Permeability**  
 Membrane permeability is a quality of a cell's plasma membrane that allows substances to pass in and out of the cell, so that the cell can expel waste products and ship out the chemicals it assembles for the body. At the same time, the nutrients that the cell needs can pass through the membrane to the inside. Cell membranes have selective permeability, meaning that the membrane will allow certain substances to pass while forming a barrier against others.



-non lipophilic molecule cannot cross membrane without help (transporter or channels)

-integral membrane proteins (channels) have hydrophobic regions on external surface of protein that anchor them in place and have a hydrophilic channel down the central of the protein that gives a route to particular solutes to get through the membrane without interacting with the hydrophobic environment

-they provide a water filled channel across the membrane (hydrophilic channel)

-transmembrane

-movement in the channel is directed in the same direction as the diffusion gradient

-leak channels opened)

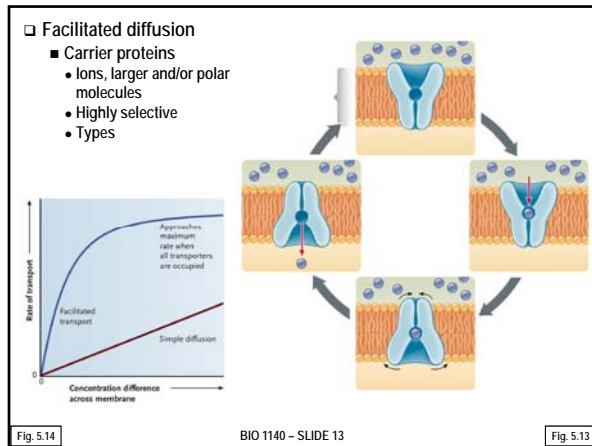
-gated (only open in response to specific signals: 1) changes in membrane potential- voltage gated channel 2) binding of a particular chemical- ligand gated channel

-in neurons the signal that travels down is an action potential- a rapid depolarization and then goes back down, occurs because of gates Na and K channels

-at the end of neuron there will be interaction with muscle cells (ligand gated channels found there that open or close in response to binding of a chemical), voltage acting along the length of the neuron and ligand gated channels that respond to the muscles of the neurons

**Facilitated Diffusion**  
 Facilitated diffusion (also known as facilitated transport or passive-mediated transport) is a process of passive transport, facilitated by integral proteins. Facilitated diffusion is the spontaneous passage of molecules or ions across a biological membrane passing through specific transmembrane integral proteins. The facilitated diffusion may occur either across biological membranes or through aqueous compartments of an organism. Polar molecules and charged ions are dissolved in water but they can not diffuse freely across the plasma membrane due to the hydrophobic nature of the fatty acid tails of phospholipids that make up the lipid bilayers.

Only small non-polar molecules, such as oxygen can diffuse easily across the membrane. All polar molecules are transported across membranes by proteins that form transmembrane channels. These channels are gated so they can open and close, thus regulating the flow of ions or small polar molecules. Larger molecules are transported by transmembrane carrier proteins, such as permeases that change their conformation as the molecules carried through, for example glucose or amino acids. Non-polar molecules, such as retinol or fatty acids are poorly soluble in water. They are transported through aqueous compartments of cells or through extracellular space by water-soluble carriers as retinol binding protein. The metabolites are not changed because no energy is required for facilitated diffusion. Only permease changes its shape in order to transport the metabolites. The form of transport through cell membrane which modifies its metabolites is the group translocation Transportation.



-example of a protein with 2 stable conformations, start in an initial stable conformation in which a particular solute binds to them causing the solute to be released by a conformation change on the other side of the membrane and the carrier goes back to its original starting point

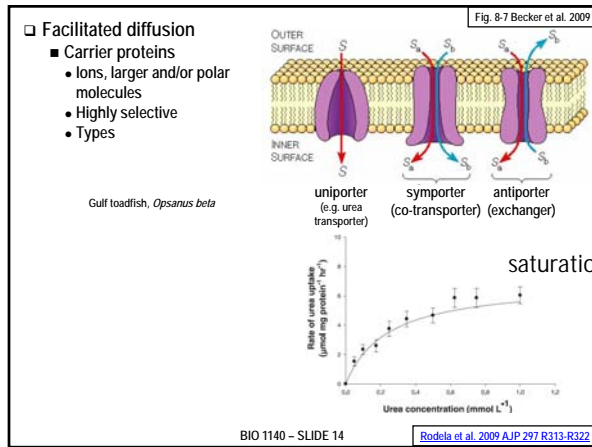
-net affect is to move the solute that binds to it through the membrane

-highly selective

-move ions and sometimes larger molecules such as aa, glucose

-the rate of diffusions of solutes shows saturation of kinetics (rate of transport depends on the diffusion gradient and the number of transport proteins present, rate of transport increases with diffusion gradient to a maximum it reaches in which all carrier proteins are being used = saturation kinetics)

-inhibitors affect channels and carrier proteins (can be blocked from carrying its solute/inhibition of movement) inhibitor conditions distinguishes between passive and facilitated diffusion



any transport that involves a transport protein = saturation kinetics

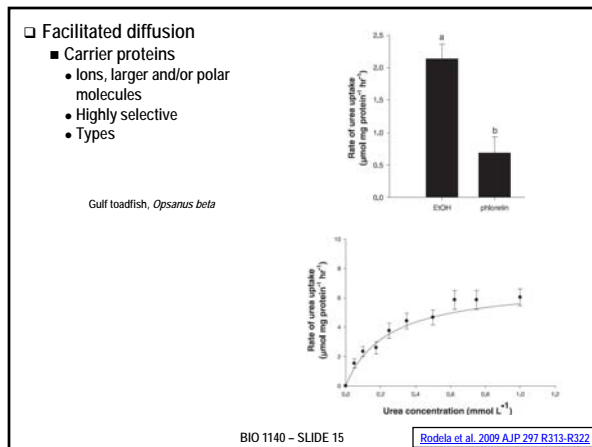
-uniporters: transfer a single solute across membrane

-symporter: transfers 2 solutes across the membrane in same direction

-antiporter: 2 solutes again but moving in opposite direction

-solute is moving according to its diffusion gradient

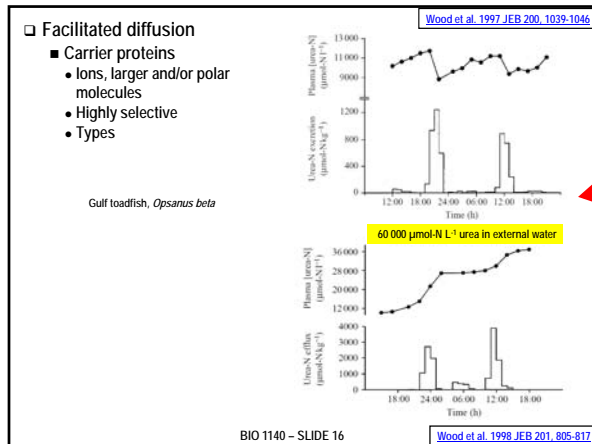
-kinetics show saturation rather than linear



-adding drugs that affect protein function have no impact on the transport if its just simple diffusion

-how to know if its a facilitated diffusion mechanism or active transport?

-facilitated and simple diffusion: the movement is driven by diffusion gradient so if we reverse gradient we can reverse the transport



-if this is facilitated diffusion then we should be able to reverse the mechanism

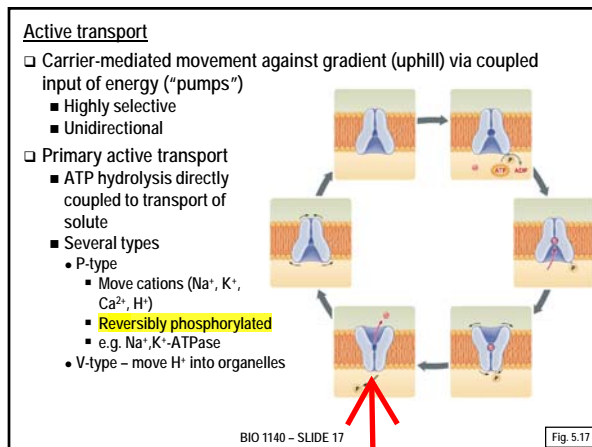
transport by reversing the gradient

-direction of transport is reversed when diffusion is reversed

### Primary Active Transport

Primary active transport, also called direct active transport, directly uses energy to transport molecules across a membrane.

Most of the enzymes that perform this type of transport are transmembrane ATPases. A primary ATPase universal to all cellular life is the sodium-potassium pump, which helps to maintain the cell potential. Other sources of energy for Primary active transport are redox energy and photon energy (light). An example of primary active transport using Redox energy is the mitochondrial electron transport chain that uses the reduction energy of NADH to move protons across the inner mitochondrial membrane against their concentration gradient.



phosphate group detaches

often called pumps because they are moving their solutes against the

gradients with the use of energy, involves carrier proteins that can utilize

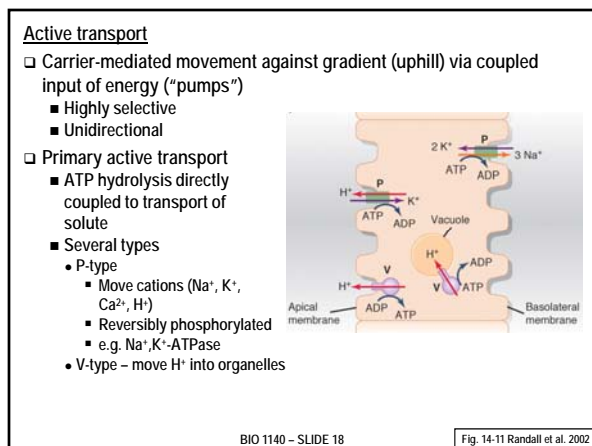
ATP to provide energy and move against gradient, only particular solutes

can bind to, transporter and pumps and unidirectional (only pump in one

direction, even if u reverse they will pump in one direction)

-primary: ATP hydrolysis is used to move solute across membrane,

-exchange in pump



move protons into vacuoles, into a variety of organelles, they occur on cell

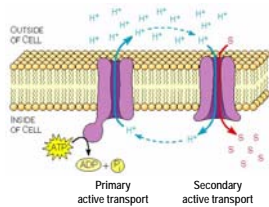
membrane as well, V-types pumps are in conjunction with the vacuole

## Secondary Active Transport

Simultaneous transport of two solutes. Downhill transport along gradient established by 1<sup>o</sup> active transport allows uphill transport of second solute. It is also known as a coupled transport. In animal cells its normally the Na<sup>+</sup> pump that established the gradient whereas in plant cells its a H<sup>+</sup> pump.

### □ Secondary active transport

- Simultaneous transport of two solutes. Downhill transport along gradient established by 1<sup>o</sup> active transport allows uphill transport of second solute.
  - Na<sup>+</sup> gradient in animal cells
  - H<sup>+</sup> gradient in plant cells



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Fig. 8-9 Becker et al. 2009

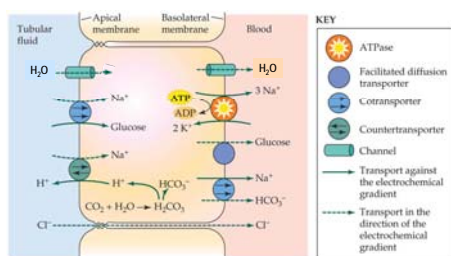
-coupled transport

-in animal cells its normally the Na pump that established the gradient where

as in plant cells its a proton pump

### □ Transport in the mammalian kidney

- Filtration followed by reabsorption
- Transport maximum for glucose and diabetes mellitus
- Structural specialization – mitochondria & microvilli



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Fig. 27.16 Hill et al. 2004

-transport capacity of these kidney cells are maxed out and so sugar gets

transported out in urine

### Transport in the Mammalian Kidney

Mammalian kidney function involves two processes, ultrafiltration and active transport. Ultrafiltration is filtration under pressure in which blood is squeezed to separate a fluid called "glomerular filtrate" or simply called "the filtrate." Active transport modifies the filtrate, secreting some substances and reabsorbing others according to the needs of the body. The result is that blood flows back into the body without much of its harmful waste. This waste is a solution containing urea, salts and various other chemicals which is known as urine.

### □ Transport in the mammalian kidney

- Filtration followed by reabsorption
- Transport maximum for glucose and diabetes mellitus
- Structural specialization – mitochondria & microvilli

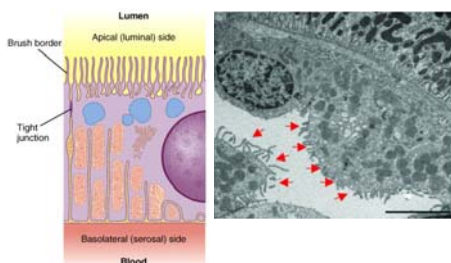


Fig. 14-19 Randall et al. 2002

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Blomqvist et al. 2004 J Clin Invest 113, 1560-1570