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Faculty of Veterinary and Agricultural Sciences

Cells to Systems Lecture 9: Transport of molecules across cell membranes Video 1

VETS30015 / VETS90121

Dr Laura Dooley
Senior Lecturer

laura.dooley@unimelb.edu.au

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Lecture 9: ILOs

- Describe the composition of the cell membrane and explain how the distribution of phospholipids and proteins influences the membrane permeability to ions, hydrophilic and hydrophobic compounds, and cell-cell communication
- Describe how cells regulate the movement of substances across their membranes and the role of diffusion, facilitated diffusion, and primary and secondary active transport mechanisms
- Explain how energy from the Na+ and K+ electrochemical gradients across the plasma membrane are maintained

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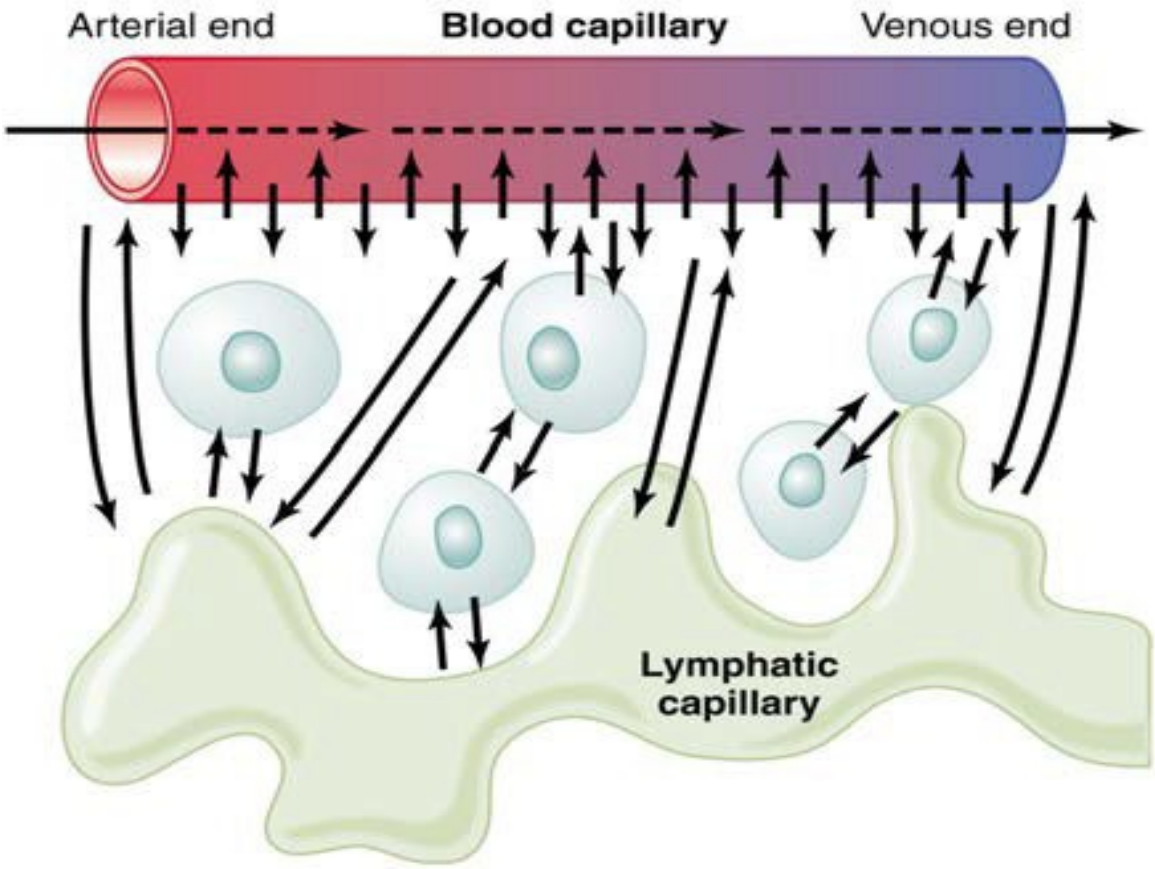
Transport of fluid and molecules across cell membranes

- Movement of fluid and solutes from blood to interstitial fluid (L8)
  - Diffusion, osmosis
  - Bulk flow and Starling' Forces
- Movement of fluid and solutes from interstitial fluid into cells (L9)
  - Diffusion
  - Facilitated Diffusion
  - Active Transport
  - Co-transport



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Key functions of biological membranes

1. Selective Barrier

- Regulates flow of material into and out of the cell

2. Organization

- Form compartments (e.g. organelles)
- Help maintain separate and distinct molecular environments

3. Transport

- Contain specific molecular pumps and channels for transporting solutes

4. Controlling information flow

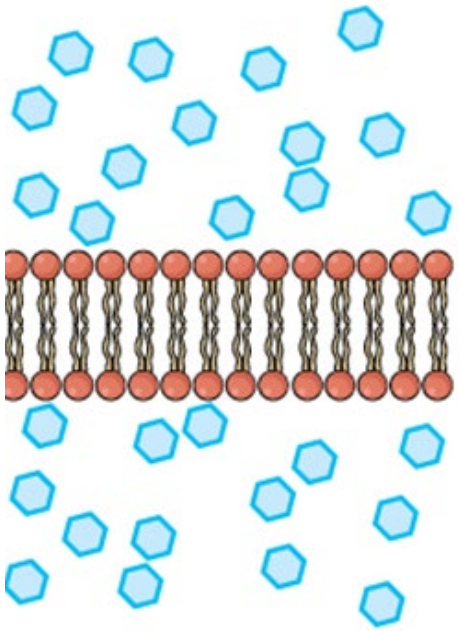
- Specific receptors for external signalling
- Generate chemical & electrical signals

5. Cell-cell interactions

- Cell recognition
- Cell adhesion

6. Reactions

- Enzyme activity



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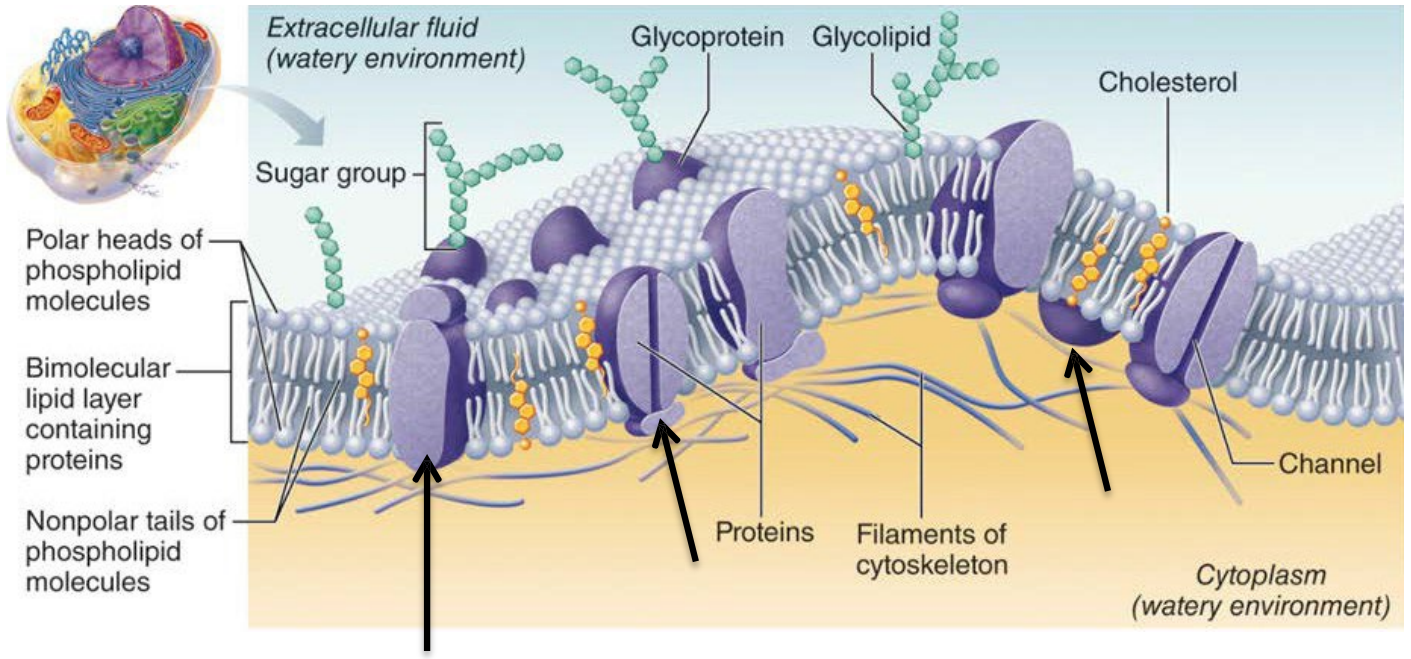
Cell membrane structure and composition

The cell membrane is composed of a phospholipid bilayer that regulates entry and exit of fluid and molecules

- Plasma membrane Structure:
  - Phospholipid bilayer
  - Proteins
    - Integral, surface
  - Cholesterol
  - Carbohydrates linked to proteins & lipids

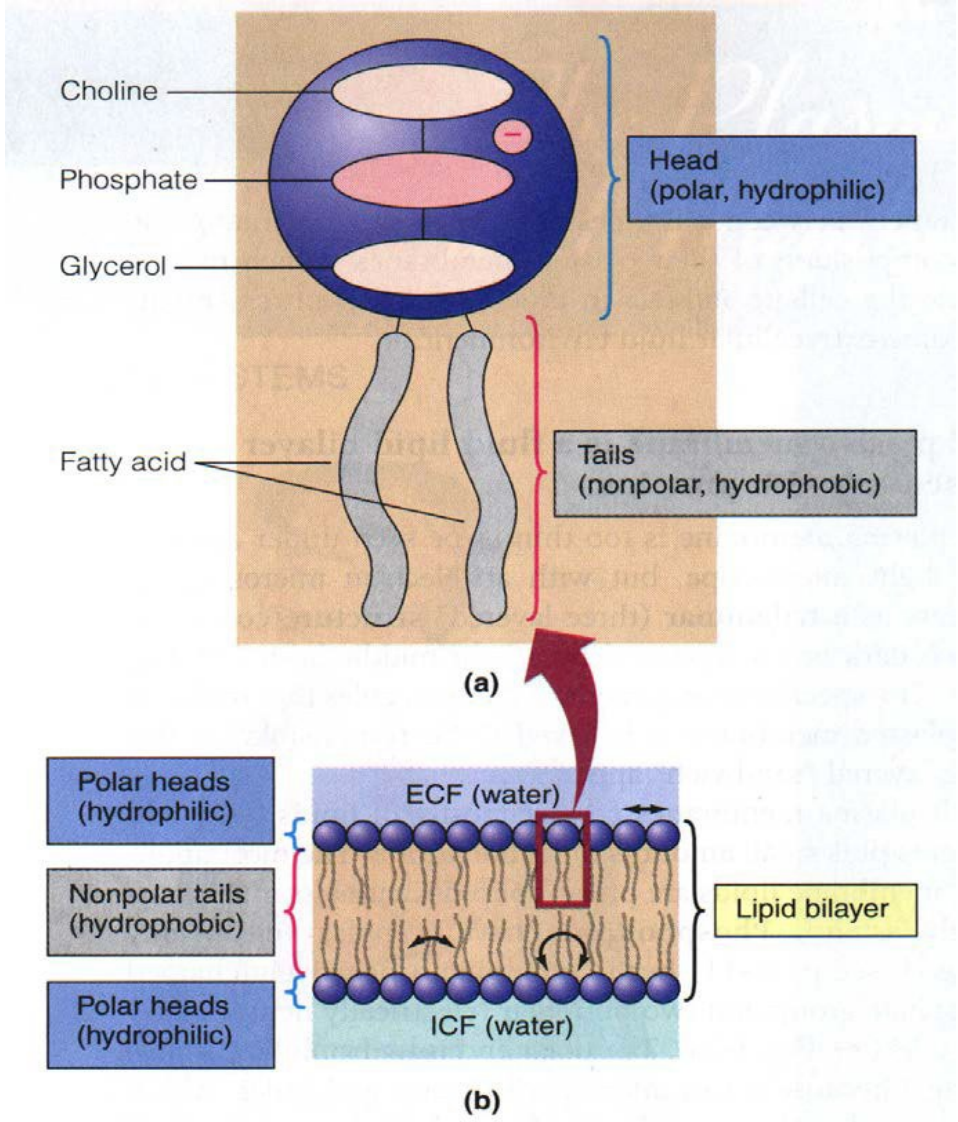


- Fluid mosaic model:
  - Membrane proteins move freely in the lipid layer
  - Ever-changing pattern of proteins
  - Cytoskeleton can restrict proteins to specific areas of cell membrane

Phospholipid bilayer

- Lipid bilayer
- Phospholipids
  - Have a hydrophilic
    - Polar ‘head group’
    - Attracted to water
  - Hydrophobic
    - Non polar ‘tail’ region
    - Fatty acids

- Cholesterol molecules are tucked between phospholipid molecles – support membrane fluidity



Lipid bilayer permeability: determined by size & solubility in lipid

Hydrophobic (lipid soluble)

Diffuses quickly

Hydrophilic (lipid insoluble)

Hydrophilic (polar) substances in membrane are sparingly soluble

1. Nonpolar molecules

   Pass freely e.g., fatty acids, steroid hormones, CO_2, & O_2 (act as nonpolar – because they are linear)

2. Small uncharged polar molecules

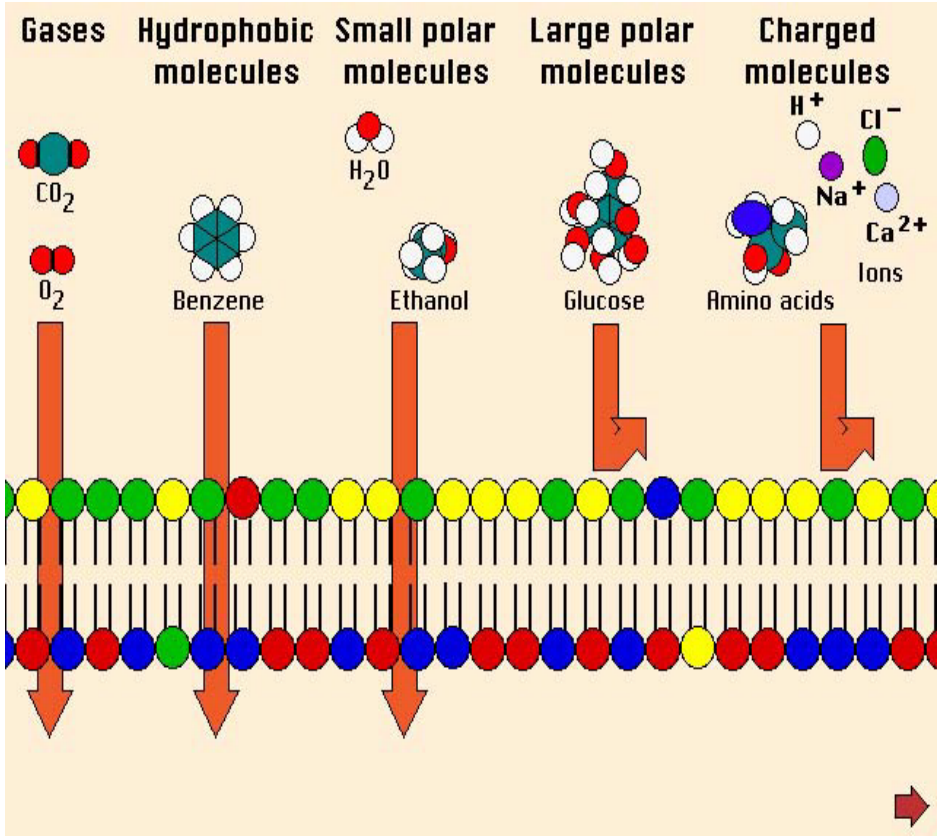
   Pass freely but more slowly than nonpolar molecules e.g., H_2O

3. Large polar molecules & ions

   Don't pass freely (e.g. glucose, Na^{+})

4. Macromolecules

   Don't pass (e.g. proteins, polysaccharides, nucleic acids)



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Plasma Membrane Proteins: integral and peripheral

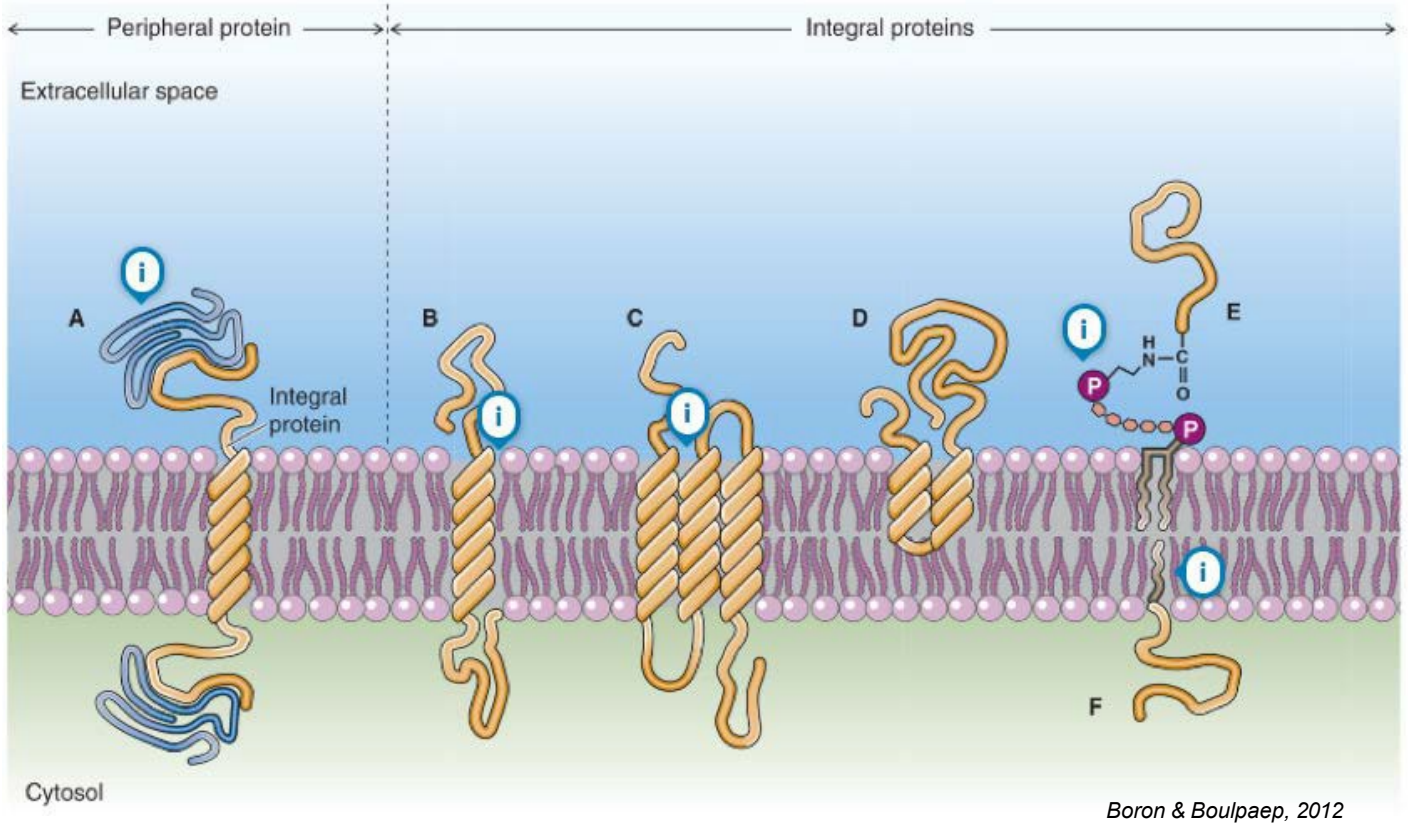
Integral membrane protein: permanently attached to the cell membrane lipid bilayer

- Some span the entire membrane (e.g. ion channels, hormone receptors

-Others are embedded (e.g. enzymes)

Peripherally associated membrane proteins: not permanently attached to the cell membrane lipid bilayer

- Non-covalently bound, often attached to integral proteins (e.g. regulatory proteins, transporter proteins, enzymes)



Boron & Boulpaep, 2012

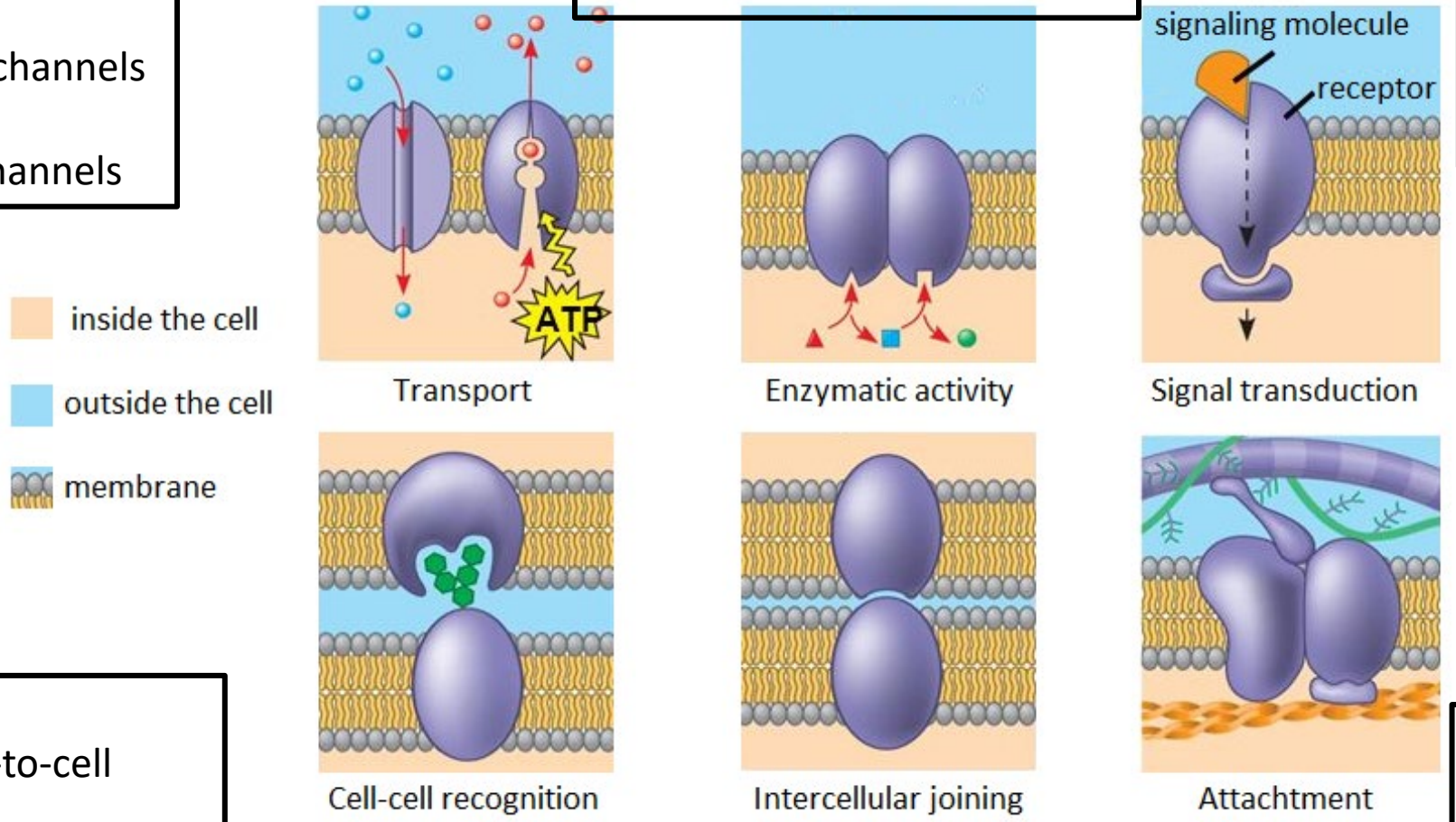
A: peripheral protein, B: α helix, single span C: α helix, triple span, D:embedded, but not spanning membrane,E: Linked to phospholipid by an oligosaccharide,F: Direct link to a fatty acid

Functions of the membrane proteins

Transport:
- Form hydrophilic channels across lipid bilayer
- Highly selective channels

Enzymatic activity:
- Control chemical reactions inside or outside cell

Signal transduction
- Receptor proteins that receive external signals



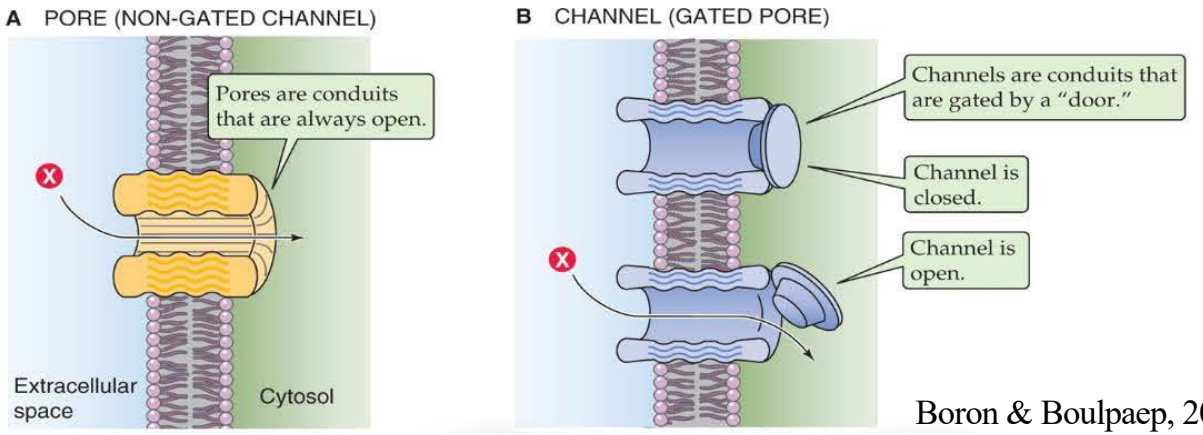
Cell recognition:
- Facilitate cell-to-cell interactions
- Cell's ability to recognise 'self'

Intercellular joining
- Cell adhesion molecules
- Form loops or hooks to grip other cells

Attachment
- Proteins that connect the cell to extracellular matrix

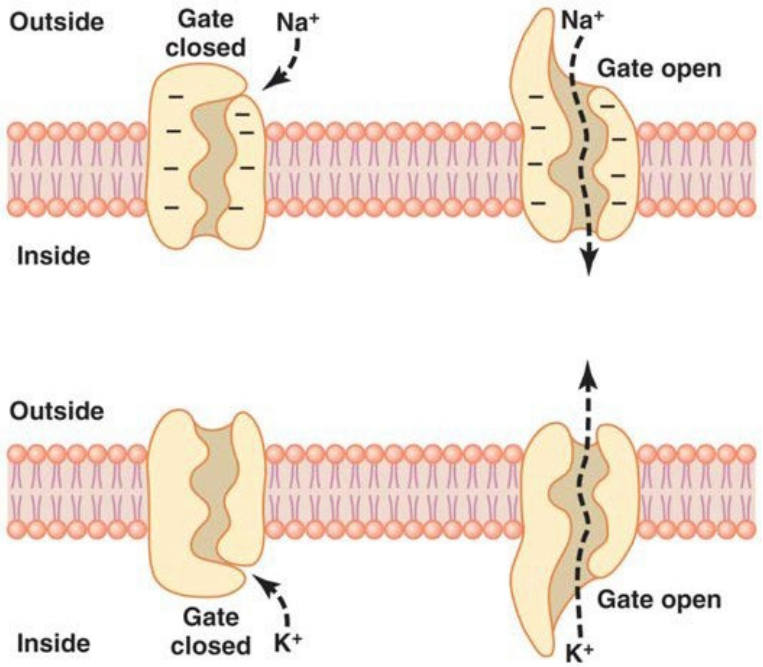
Membrane channels

- The protein transmembrane channels that permit simple diffusion:
  - pores and channels (gated)



Boron & Boulpaep, 2012

- Types of gated ion channels
  - voltage-gated, e.g. Na^+ or K^+ (specific channel for each)
  - Chemical or ligand-gated, e.g. acetylcholine
  - mechanically-gated, e.g. sound waves in inner ear open ion channels



Guyton and Hall, 2011

Transport across biological membranes

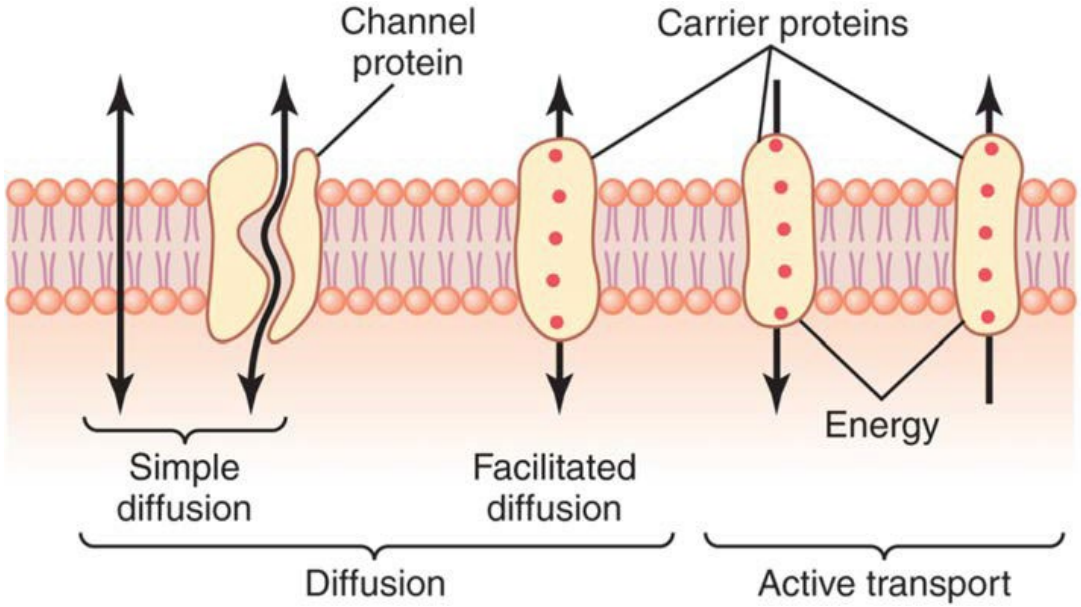
1. Simple diffusion

Down a concentration or electrical gradient

- Through membrane (lipid-soluble molecules)
- Through pores – integral cell membrane protein, e.g. aquaporin for water
- Through protein channels – selectively permeable, may be gated, eg ion channels

2. Facilitated Diffusion

- Down a concentration or electrical gradient
  - Carrier mediated - need integral membrane protein
  - Transporter is specific for the molecule
  - Rate limited by binding and conformational change in carrier protein; eg glucose, amino acids



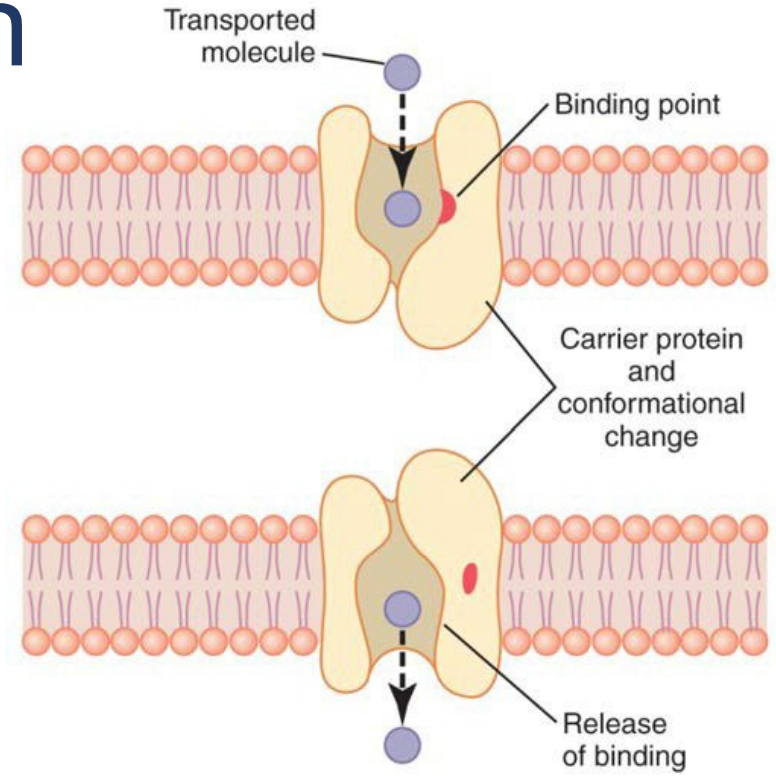
Guyton and Hall, 2011

3. Active transport

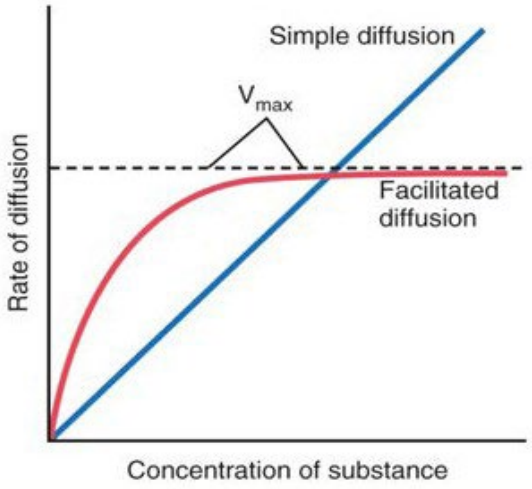
- Up a concentration or electrical gradient
  - Carrier mediated and energy dependent

Facilitated diffusion

- Use of a carrier protein to facilitate transfer across membrane, down a concentration gradient
- Molecule binds to a receptor within the carrier protein
- Binding triggers a shape (conformation) change of carrier protein allowing entry to the opposite side of the membrane
- Release returns carrier protein's shape to the original or unoccupied state.
- Carrier proteins demonstrate specificity
- Transport rate is limited by concentration of molecule and number of channels (receptors become saturated)
- Examples: glucose (*in most cells*) and amino acids



Guyton and Hall, 2011



Comparison of simple and facilitated diffusion Hall, 2016

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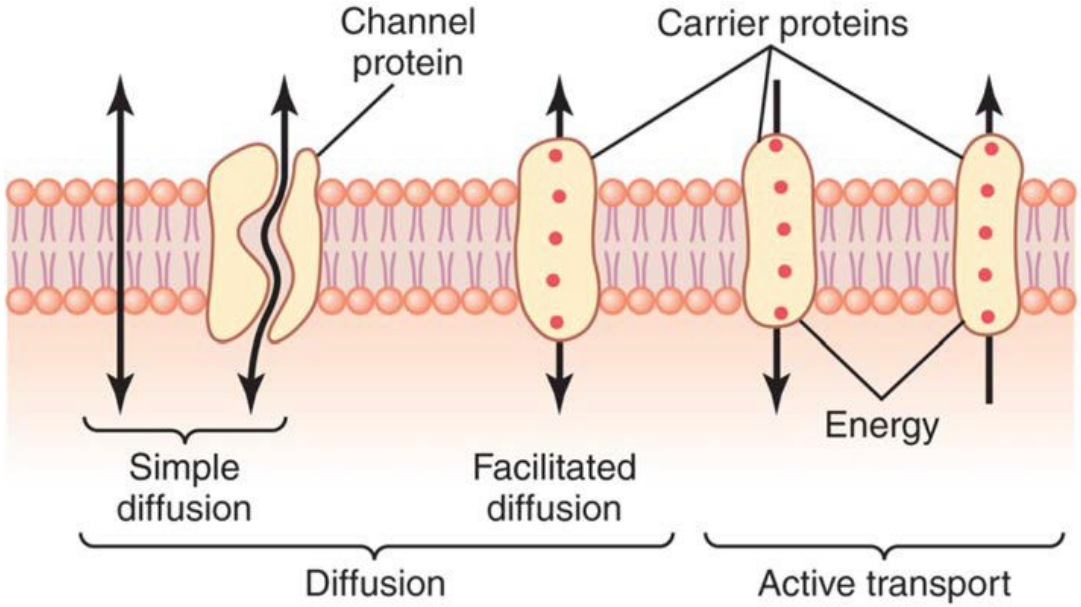

Guyton and Hall, 2011

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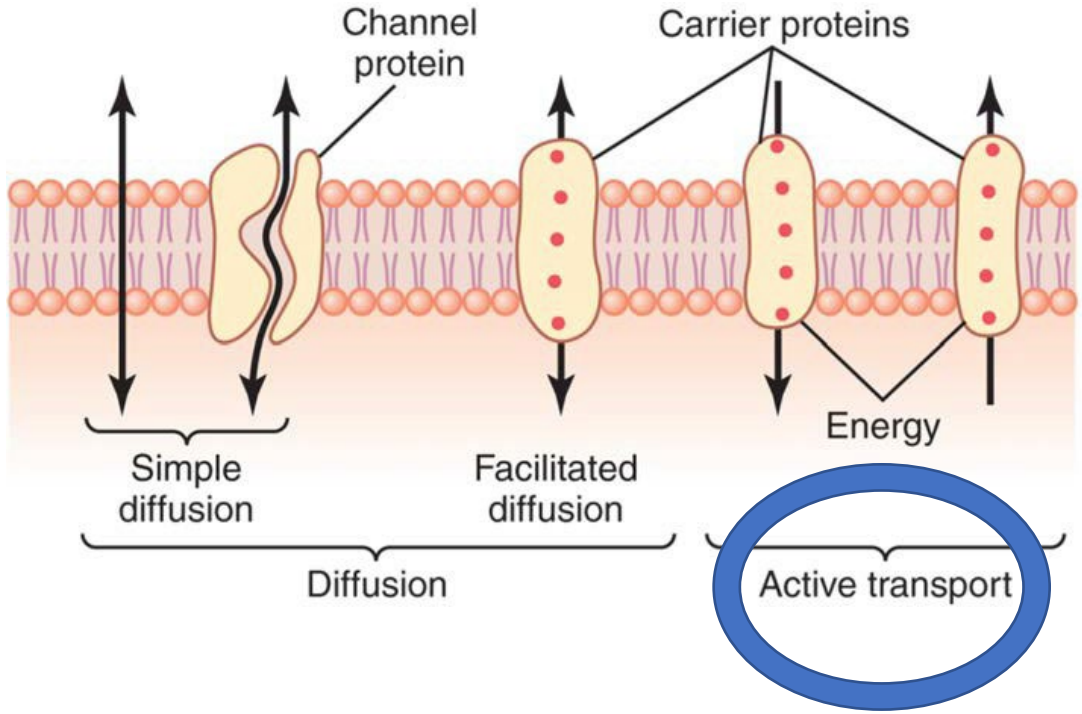
Active transport

- Use of protein carrier to carry a specific substance
- Transported against concentration or electrochemical gradient
- Requires expenditure of energy (in the form of ATP) to drive carrier

- Active transport mechanisms are often called ‘pumps’
- **Primary active transport** directly uses chemical energy (primarily ATP) to move molecules
- **Secondary active transport** uses an electrochemical gradient – generated by active transport – as an energy source to move molecules against their gradient. It does not directly require a chemical source of energy such as ATP.

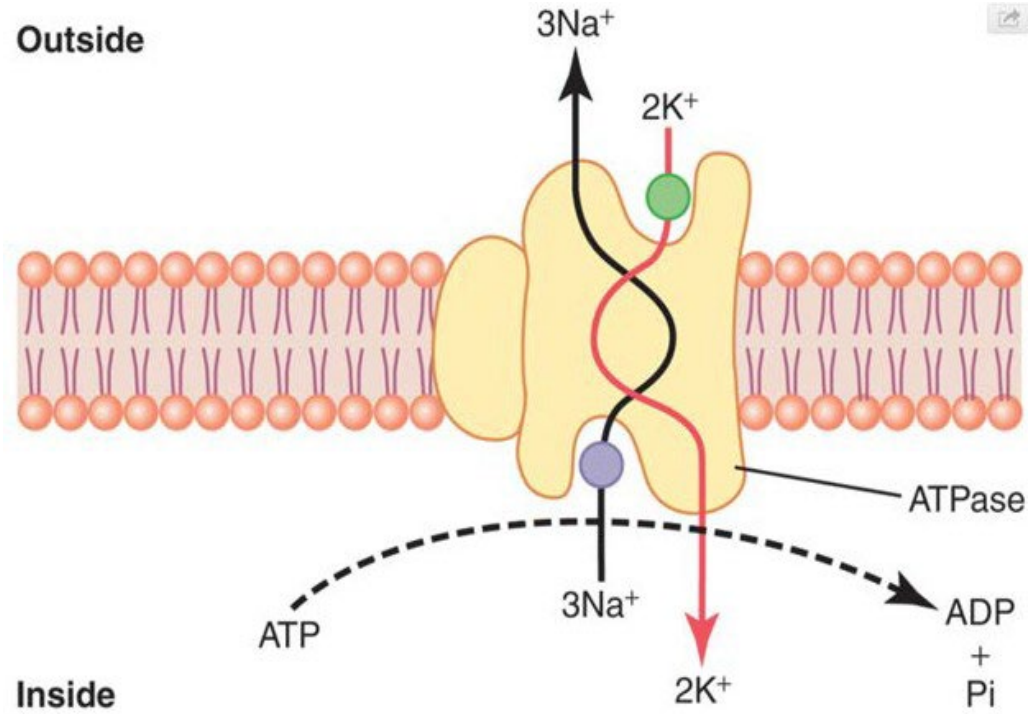


Guyton and Hall, 2011

Primary active transport example: Na^+-K^+ ATPase pump

- Membrane of all cells contains an active Na^+-K^+ ATPase pump
- Functions to concentrate Na^+ in the ECF and K^+ in the ICF
- 3 receptors for Na^+ inside cell & 2 receptors for K^+ outside cell
- ATPase activated when ions bind → cleaves 1 molecule of ATP

- Liberated energy causes conformational change in carrier which flips the ions across the membrane



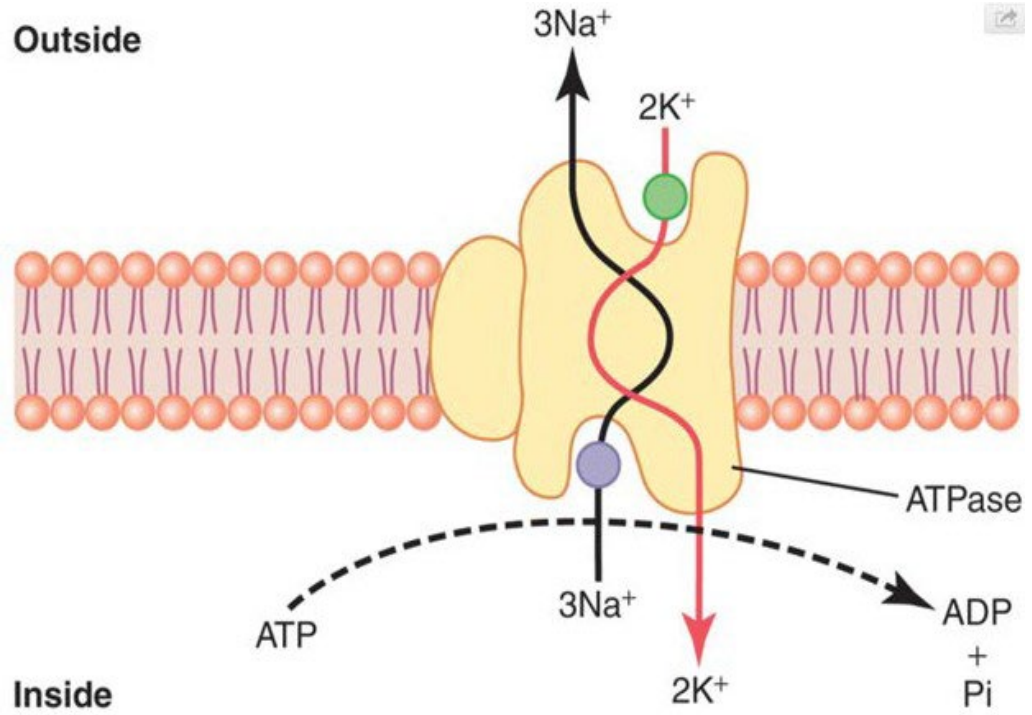
Guyton and Hall, 2011

Primary active transport example: Na^+-K^+ ATPase pump

Functions:

1. Establishes Na^+ and K^+ concentration gradients across the cell membrane → interior of cell negative with respect to exterior → critical for propagation of action potentials in nerves and for muscle contraction
2. Regulates cell volume by controlling solute concentrations– minimise osmotic effects that would induce swelling/shrinking of cell
3. Energy used also indirectly serves as energy source for cotransport of glucose and amino acids through *secondary active transport*

- Similar primary active transport pumps for Ca^{2+} and H^+



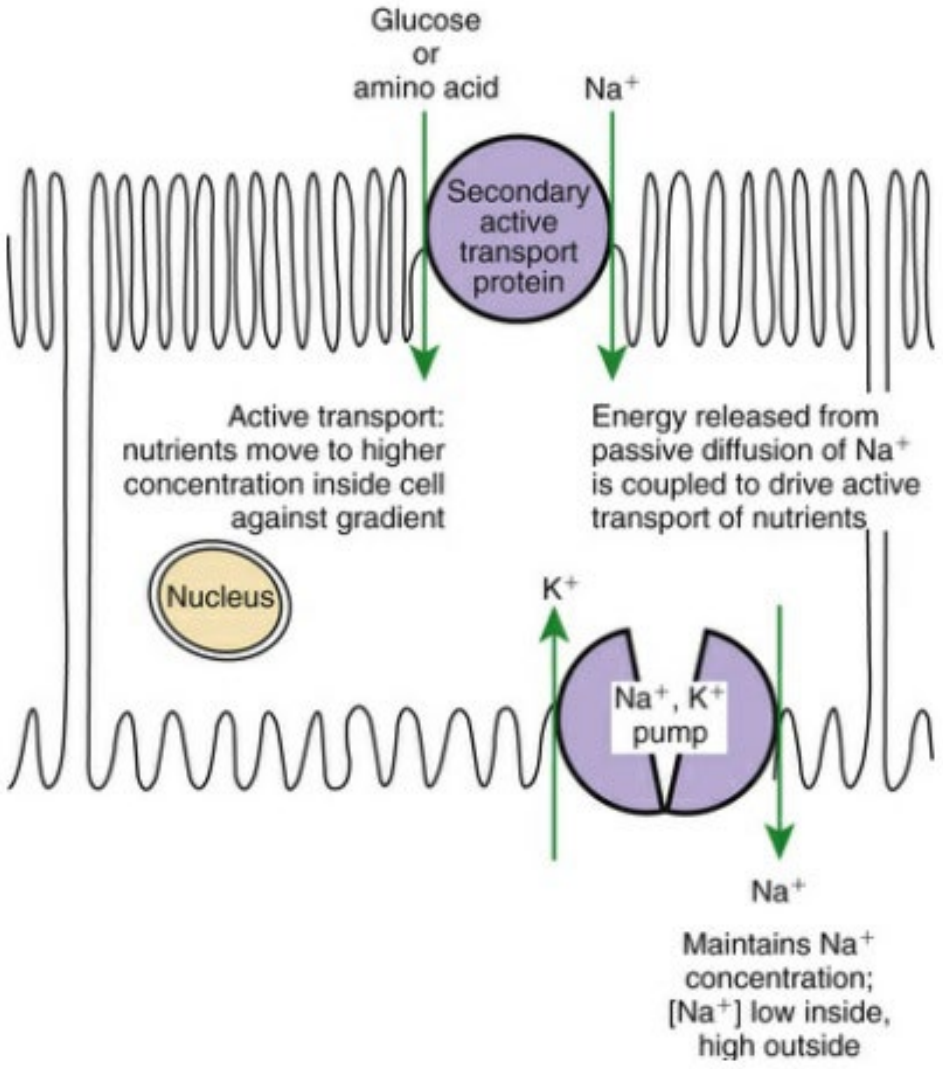
Guyton and Hall, 2011

Secondary active transport

Secondary active transport uses an electrochemical gradient – generated by active transport – as an energy source to move molecules against their gradient.

For example:

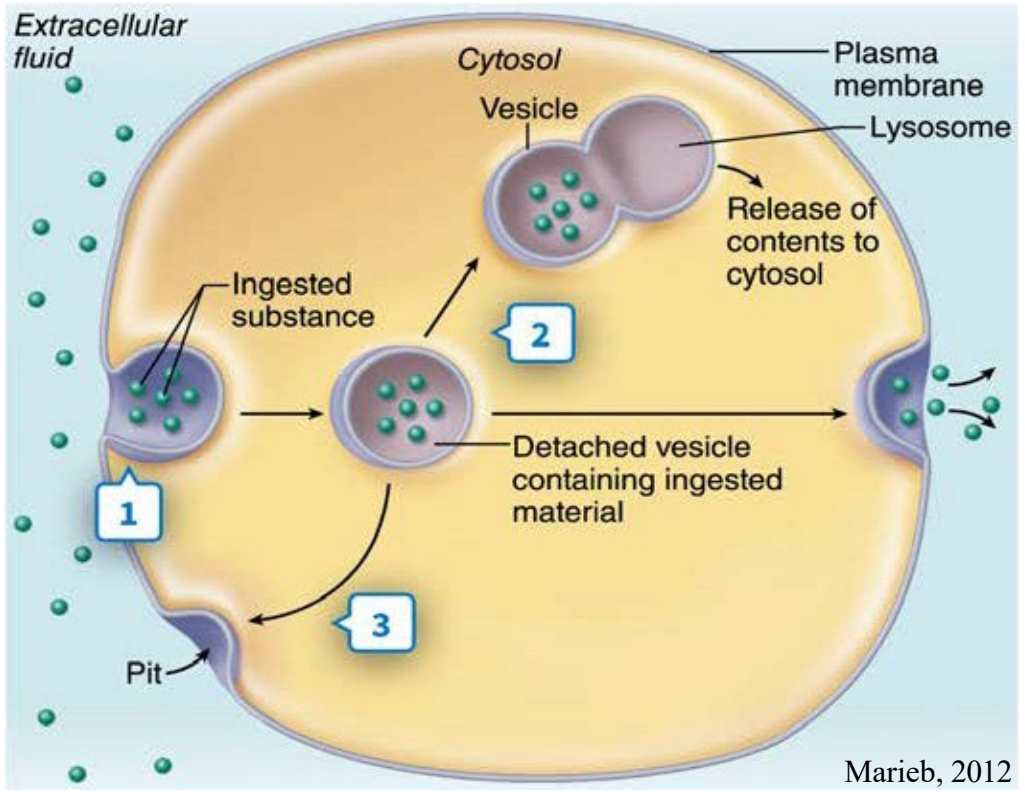
- Intestinal and kidney cells actively transport glucose and amino acids up their concentration gradients
- Co-transport carriers have two binding sites – one for Na^+ an the other for the nutrient molecule (e.g. glucose)
- When both glucose and Na^+ are bound to the carrier, it changes shape and opens to the inside of the cell – both Na^+ and glucose are released into the ICF
- Released Na^+ is quickly pumped out again by the Na^+-K^+ ATPase pump, to keep the intracellular Na^+ low (maintaining Na^+ concentration gradient across membrane)



Cunningham, 2010

Vesicular transport

- Some large molecules/multimolecular materials are too large for channels and carriers
- They are transferred in a membrane-enclosed vesicle → vesicular transport
- Vesicular transport requires energy → active transport mechanism
- Transport into the cell = endocytosis; Transport out of cell = exocytosis
- Three forms of endocytosis:
  1. pinocytosis – non-selective uptake of ECF
  2. receptor-mediated endocytosis (large molecule)
  3. phagocytosis (multimolecular particles)



1. Vesicle buds off from plasma membrane
2. Vesicle transported intact, releasing contents to exterior by exocytosis or fuses with a lysosome
3. Membrane components recycled to the plasma membrane

Membrane potential

- All cell membranes have a membrane potential due to difference in the relative number of cations and anions in the ICF and ECF
- The ions primarily responsible are Na+, K+, and negatively charged intracellular proteins
- Negatively charged intracellular proteins cannot permeate the membrane → unbalanced distribution → ICF is more negative than ECF

- 20% of membrane potential is generated by the Na+-K+ ATPase pump (active transport mechanism)
- The rest is generated through the passive diffusion of Na+ and K+ down concentration gradients

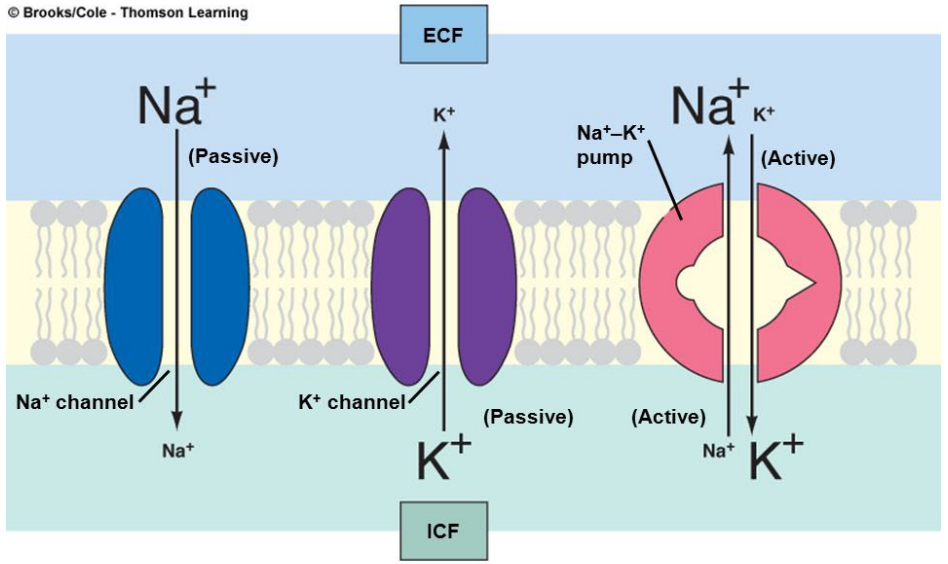
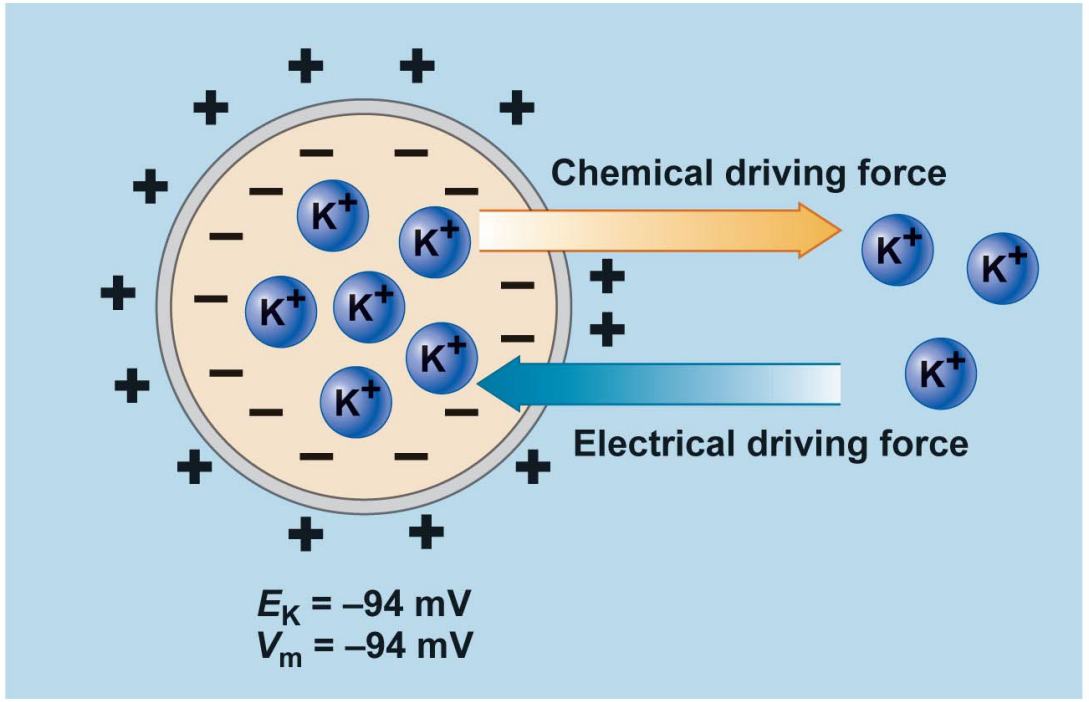


Fig. 3-23, p. 79

Ion concentrations and electrochemical gradients

Extracellular fluid		Intracellular fluid
Blood plasma	Interstitial fluid	Intracellular fluid
1.0 litre*	3 litre*	8 litres*
[Na+]= 153 mM	[Na+]= 145 mM	[Na+]= 10-15 mM
[K+]= 4.7 mM	[K+]= 4.5 mM	[K+]= 120-140 mM
[Cl-]= 110 mM	[Cl-]= 116 mM	[Cl-]= 20 mM Range 3-30mM

- For K+, the concentration gradient would tend to move the ion out of the cell, but the electrical gradient would tend to move K+ into the cell
  →K^+ diffuses out of the cell down its concentration gradient until electrical forces prevent further net diffusion
- More diffusion (leak) channels for K^+ than Na^+ → so more K^+ leaves than Na^+ enters
- Negative ions that can't easily diffuse remain in ICF
  → Results in a net **negative** charge within the cell



(a)

Membrane potential

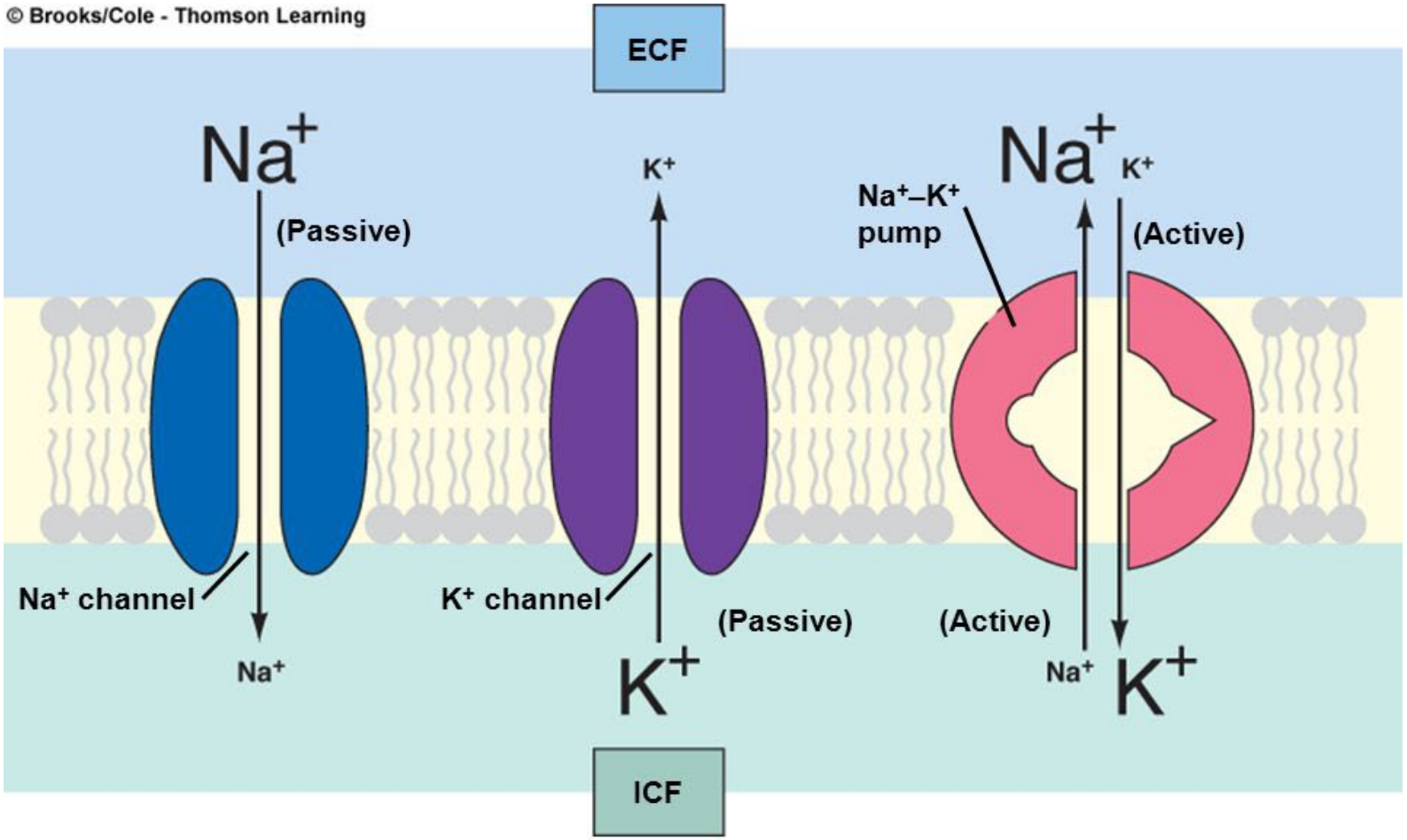


Fig. 3-23, p. 79

At resting membrane potential:

- Passive leaks of Na+ and K+ down their electrochemical gradients
- This is counterbalanced by the Na+-K+ ATPase pump
- No net movement of Na+ and K+ → membrane potential remains constant

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