

Chapter 8

Cell Membranes

Lecture Presentations by Nicole Tunbridge and Kathleen Fitzpatrick

Life at the Edge

- The plasma membrane is the boundary that separates the living cell from its surroundings
- The plasma membrane exhibits **selective permeability**, allowing some substances to cross it more easily than others
- Transport proteins are often responsible for controlling passage across cellular membranes

Potassium ion channel protein

Concept 8.1: Cellular membranes are fluid mosaics of lipids and proteins

- Phospholipids are the most abundant lipid in the plasma membrane
- Phospholipids are **amphipathic** molecules, containing hydrophobic ("water-fearing") and hydrophilic ("water-loving") regions
- The hydrophobic tails of the phospholipids are sheltered inside the membrane, while the hydrophilic heads are exposed to water on either side

De Some proteins are amphipathic as well having polar parts to the outer sides are

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- In the **fluid mosaic model**, the membrane is a mosaic of protein molecules bobbing in a fluid bilayer of phospholipids
- Proteins are not randomly distributed in the

membrane

So They are Associated in long-lesting specialized

potches where they carry out common functions. O lipid rafts are specific lipids found in Patches [similar to the above @]
So still not sure about whether they are really

The Fluidity of Membranes

- Membranes are held together mainly by weak hydrophobic interactions
- Most of the lipids and some proteins can move sideways within the membrane
- Rarely, a lipid may flip-flop across the membrane, from one phospholipid layer to the other

Data from L. D. Frye and M. Edidin, The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons, *Journal of Cell Science* **7:319 (1970).**

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- **(A)** some proteins in the membrane are chiven along
extosleted fibers in an ordered monner.
 As temperatures cool, membranes switch from a
- fluid state to a solid state
- The temperature at which a membrane solidifies depends on the types of lipids
- Membranes rich in unsaturated fatty acids are more fluid than those rich in saturated fatty acids
- \bullet Membranes must be fluid to work properly; membranes are usually about as fluid as salad oil

E 2 permeability

E survility of protein -> their functioning spots. 4 Over-Fluidity is no good either.

- The steroid cholesterol has different effects on the membrane fluidity of animal cells at different temperatures
- At warm temperatures (such as 37°C), cholesterol restrains movement of phospholipids
- At cool temperatures, it maintains fluidity by preventing tight packing
- Though cholesterol is present in plants, they use related steroid lipids to buffer membrane fluidity

Figure 8.5

(a) Unsaturated versus saturated hydrocarbon tails

(b) Cholesterol within the animal cell membrane

Cholesterol reduces membrane fluidity at moderate temperatures, but at low temperatures hinders solidification.

Evolution of Differences in Membrane Lipid Composition

- Variations in lipid composition of cell membranes of many species appear to be adaptations to specific environmental conditions
- Ability to change the lipid compositions in response to temperature changes has evolved in organisms that live where temperatures vary
 F_{x}

Eramples: SOML unusual lipids preventing
over-fluidity. (A) Bactevia & Archaea high proportion of unsaturated (B) V. cold water Fish hydrocarbon tails preventing tight packing. O 2018 Pearson Education Ltd. Unsolutated Fets

Membrane Proteins and Their Functions

- Somewhat like a tile mosaic, a membrane is a collage of different proteins, often clustered in groups, embedded in the fluid matrix of the lipid bilayer
- Phospholipids form the main fabric of the membrane
- Proteins determine most of the membrane's functions
 \bigoplus_{more} RBC's (red blood cells) e.g. have been found to have

move them 50 different kinds of proteins.

Figure 8.UN01

often to the exposed parts of
integral proteins.

- **Peripheral proteins** are bound to the surface of the membrane single-side penetration = no "sperial" name.
- **Integral proteins** penetrate the hydrophobic core
- Integral proteins that span the membrane are called transmembrane proteins
- The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acids, often coiled into α helices typically $20 - 30$

a. acidy

SIDE

@ To support the munifyane framework : Some membrane proteins are bound to: (a) cytoskeletal fibers (b) extracellular matrix e.g. integrins [integral,
bond to, ECM e.g. fibro-
materials in the nucting (see ch. 7.6)

CYTOPLASMIC SIDE

- Cell-surface membranes can carry out several functions:
	- **Transport**
	- Enzymatic activity
	- Signal transduction
	- Cell-cell recognition
	- Intercellular joining
	- Attachment to the cytoskeleton and extracellular matrix (ECM)

Figure 8.7

HIV: Human Immunodeficiency Virus
AIDS: Acquired Immune Deficiency Syndrome.

- Cell-surface proteins are important in the medical field
	- cell
enths sells of model ● For example, HIV must bind to the immune cellsurface protein CD4 and a "co-receptor" CCR5 in order to infect a cell
	- HIV cannot enter the cells of resistant individuals who lack CCR5
	- Drugs are now being developed to mask the CCR5
	- protein
e.g. mavavivoc (by Selzentry) approved in 2007.

(a) HIV can infect a cell with CCR5 on its surface, as in most people.

(b) HIV cannot infect a cell lacking CCR5 on its surface, as in resistant individuals. gune alteration. due to

The Role of Membrane Carbohydrates in Cell-Cell Recognition in an embryonic animal
an important eg is in the differentiation of cells into tissues

- Cells recognize each other by binding to molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane
often short branched l_{15}^{es} sugar units.
- Membrane carbohydrates may be covalently bonded to lipids (forming **glycolipids**) or, more commonly, to proteins (forming **glycoproteins**)
- Carbohydrates on the extracellular side of the plasma membrane vary among species, individuals, and even cell types in an individual

 O, A, B, AB

 $RBC's$

Synthesis and Sidedness of Membranes

- Membranes have distinct inside and outside faces
- The asymmetrical distribution of proteins, lipids, and associated carbohydrates in the plasma membrane is determined when the membrane is built by the ER and Golgi apparatus $\left[\begin{array}{c} \bot \text{ w} \text{ p} \text{ o} \text{ r} \text{ t} \text{ w} \end{array}\right]$

V Figure 8.9 Synthesis of membrane components and their orientation in the membrane.
The cytoplasmic (orange) face of the plasma membrane differs from the extracellular (aqua) face. The latter arises from the inside face of ER, Golgi, and vesicle membranes.

Concept 8.2: Membrane structure results in selective permeability

- A cell must exchange materials with its surroundings, a process controlled by the plasma membrane
- Plasma membranes are selectively permeable, regulating the cell's molecular traffic Etake in materials such as O_2 , sugars, A. acids...
Earpell woste products such as CO_2 ...
Engulate the concentrations of inorganic ions
such as Nat, CI , k^+ , Ca^{2+} ...

The Permeability of the Lipid Bilayer

• Hydrophobic (nonpolar) molecules, such as \mathcal{I} hydrocarbons, can dissolve in the lipid bilayer and pass through the membrane rapidly selective permeability (1).

 $+ \{O_2, CO_2\}$

- Hydrophilic molecules including ions and polar molecules do not cross the membrane easily
- Proteins built into the membrane play key roles in regulating transport

Transport Proteins

- **Transport proteins** allow passage of hydrophilic substances across the membrane
- Some transport proteins, called channel proteins, have a hydrophilic channel that certain molecules or ions can use as a tunnel
- Channel proteins called **aquaporins** greatly facilitate the passage of water molecules

8 Aquaporius => Quaternary (4 identical sub units) each having a channel for water passage Allowing = 3 billion H20 molecules per Second.

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- Other transport proteins, called carrier proteins, bind to molecules and change shape to shuttle them
across the membrane \rightarrow selective permubility (2). across the membrane
- A transport protein is specific for the substance it moves

e.g. Glucose Carrier proteins speed up movement membrane of RBC's by a factor of 50.000.
These corrier proteins are so specific that they reject fructose. a structural isomer © 2018 Pearson Education Ltd.

- **Concept 8.3: Passive transport is diffusion of a substance across a membrane with no energy investment**
	- **Diffusion** is the tendency for molecules to spread out evenly into the available space
	- Although each molecule moves randomly, diffusion of a population of molecules may be directional
	- At dynamic equilibrium, as many molecules cross the membrane in one direction as in the other

Et e.g. O2 that is dissolved in water Heeps
moving into cells performing cellular respiration as it (02) is continuously being EDUCATION LANGER AND COLL.
Figure 8.10

Molecules of dye Membrane (cross section) WATER Net diffusion Equilibrium Net diffusion (a) Diffusion of one solute $\mathbf{\Omega}$ \bullet O \bullet \bullet **Net diffusion Net diffusion Equilibrium Net diffusion Net diffusion Equilibrium**

(b) Diffusion of two solutes

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- Substances diffuse down their **concentration gradient**, the region along which the density of a chemical substance increases or decreases
- No work must be done to move substances down the concentration gradient
- The diffusion of a substance across a biological membrane is **passive transport** because no energy is expended by the cell to make it happen

Effects of Osmosis on Water Balance

- **Osmosis** is the diffusion of water across a selectively permeable membrane
- Water diffuses across a membrane from the region of lower solute concentration to the region of higher solute concentration until the solute concentration is equal on both sides

1 free

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Water Balance of Cells Without Cell Walls

- **Tonicity** is the ability of a surrounding solution to cause a cell to gain or lose water
- The tonicity of a solution depends on its concentration of solutes that cannot cross the membrane relative to that inside the cell

$$
for this topic, Solutes \equiv Non-penerating Solutesas other solutes do not matter (one even).
$$

- **Isotonic** solution: Solute concentration is the same as that inside the cell; no *net* water movement across the plasma membrane
- **Hypertonic** solution: Solute concentration is greater than that inside the cell; cell loses water
- **Hypotonic** solution: Solute concentration is less than that inside the cell; cell gains water
- Cells without cell walls will shrivel in hypertonic solution and lyse (burst) in a hypotonic solution

seawater is TSOTONIC to most \bigoplus

marine vertebrates.

O Cells of most terrestrial animals are battud in

- Hypertonic or hypotonic environments create osmotic problems for organisms that have cells without rigid walls
- **Osmoregulation, the control of solute** concentrations and water balance, is a necessary adaptation for life in such environments protist (specifying).
	- For example, the unicellular eukaryote *Paramecium*, which is hypertonic to its pond water environment, has a contractile vacuole that acts as a pump

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● Bacteria and archaea that live in hypersaline (excessively salty) environments have cellular mechanisms to balance internal and external solute concentrations

Water Balance of Cells with Cell Walls pressure by Cell walls help maintain water balance A plant cell in a hypotonic solution swells until the wall opposes uptake; the cell is now **turgid** (firm) • If a plant cell and its surroundings are isotonic, there is no net movement of water into the cell; the cell becomes **flaccid** (limp) $\frac{1}{1}$ il t.s.

• In a hypertonic environment, plant cells lose water

• The membrane pulls away from the cell wall, causing the plant to wilt, a potentially lethal effect called **plasmolysis**

> Bacteria and Fungi
also empurience plasmolysis in HYPERTONIC Conditions.

Facilitated Diffusion: Passive Transport Aided by Proteins

- In **facilitated diffusion**, transport proteins speed the passive movement of molecules across the plasma membrane
- Transport proteins include channel proteins and carrier proteins

- Channel proteins provide corridors that allow a specific molecule or ion to cross the membrane
- Aquaporins facilitate the diffusion of water
- **Ion channels** facilitate the transport of ions
- Some ion channels, called **gated channels**, open or close in response to a stimulus for chemical stimulus by
	- For example, in nerve cells, ion channels open in response to electrical stimulus \blacksquare

(b) A carrier protein

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- Carrier proteins undergo a subtle change in shape that translocates the solute-binding site across the membrane
- This change in shape can be triggered by the binding and release of the transported molecule

Concept 8.4: Active transport uses energy to move solutes against their gradients

- Facilitated diffusion is still passive because the solute moves down its concentration gradient, and the transport requires no energy
- Some transport proteins, however, can move solutes against their concentration gradients

The Need for Energy in Active Transport

- **Active transport** requires energy, usually in the form of ATP hydrolysis, to move substances against their concentration gradients
- All proteins involved in active transport are carrier proteins -> Important.

- Active transport allows cells to maintain concentration gradients that differ from their surroundings
	- For example, an animal cell has a much higher potassium $(K+)$ and a much lower sodium (Na+) concentration compared to its surroundings
	- This is controlled by the **sodium-potassium pump**, a transport protein that is energized by transfer of a phosphate group from the hydrolysis of ATP

Status (0): non-phosphorylated -> High affinity for Na^+ (3ions) \Box open to the inside]
Status (1): Phosphorylated -> High offinity for K^+ (2ions) \Box open to the outside].

Figure 8.16 The sodium-potassium pump: a specific case of active transport.

This transport system pumps ions against steep concentration gradients. The pump oscillates between two shapes in a cycle that moves Na⁺ out of the cell (steps \bigcirc - \bigcirc) and K⁺ into the cell (steps $\left(-6\right)$. The two shapes have different binding
affinities for Na⁺ and K⁺. **ATP hydrolysis powers** the shape change by transferring a phosphate group to the transport protein (phosphorylating the protein).

VISUAL SKILLS For each ion (Na⁺ and K^+), describe its concentration inside the cell relative to outside. How many Na⁺ are moved out of the cell and how many K^+ moved in per cycle?

Mastering Biology Animation: Active Transport

5

Cytoplasmic Na⁺ binds to the sodium-potassium pump with high affinity when the protein has this shape.

2 Binding of 3 Na⁺ ions stimulates phosphorylation by a kinase, using ATP.

AD Phosphorylation leads to
a change in protein shape,
reducing its affinity for Na⁺: 3 Na⁺ are released outside

6 2 K⁺ are released; affinity for Na⁺ is high again, and the cycle repeats.

G Loss of the phosphate group restores the protein's original shape, which has a lower affinity for K⁺.

4 The new shape has a high affinity for K⁺; 2 K⁺
bind on the extracellular side, triggering release of the phosphate group.

Passive transport Active transport

Aow Ion Pumps Maintain Membrane Potential

- **Membrane potential** is the voltage across a membrane
- Voltage is created by differences in the distribution of positive and negative ions across a membrane
- The cytoplasmic side of the membrane is negative in charge relative to the extracellular side

MEM. Potential $\widetilde{\in}$ [-200,-50] mv. V_{cyc}
MEM. Potential = V_{cyc} plasm = V_{cscide} The negative number indicates that Vat. < V Fr cide

- Two combined forces, collectively called the **electrochemical gradient**, drive the diffusion of ions across a membrane
	- A chemical force (the ion's concentration gradient)
	- An electrical force (the effect of the membrane

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Diffusion of ions (+/-) across the plasma membrane M Chemical: Concentration (simple diffusion).
2 Electrical: wrt the membrane potential (3) inwards The combination of both gradients is called The Electrochemical gradient. in neuve alls. Ele C can act together as in the case of Na^{tions} when the gates facilitate Vor against each other [active transport may be needed].

- An **electrogenic pump** is a transport protein that generates voltage across a membrane
- The sodium-potassium pump is the major electrogenic pump of animal cells
- The main electrogenic pump of plants, fungi, and bacteria is a **proton pump**, which actively transports hydrogen ions (H+) out of the cell
- Electrogenic pumps help store energy that can be used for cellular work in the form of Voltage différence.

C.J. CD ATP synthesis

Cotransport: Coupled Transport by a Membrane Protein

- **Cotransport** occurs when active transport of a solute indirectly drives transport of other substances
- The diffusion of an actively transported solute down its concentration gradient is coupled with the transport of a second substance against its own concentration gradient \mapsto Important.

Figure 8.18

plants load sucrose into cells in the veins of leaves non-photosynkitic organs.

Figure 8.19 Cotransport: active transport driven by a
 Figure 8.19 Cotransport: A carrier protein, such as this H⁺/sucrose
 concentration gradient. A carrier protein, such as this H⁺/sucrose

cotransporter in a p **Such the cell wall is not shown.) Although not technically** of sucrose. (The cell wall is not shown.) Although not technically or sucrose. Cotransport process, an ATP-driven proton pump is shown here (bottom), which concentrates H⁺ outside the cell. The resulting H⁺ gradient represents potential energy that can be used
for active transport—of sucrose, in this case. Thus, ATP hydrolysis for active transport—of sucrose, in this case. These the space

A similar cotransporter in animals transports Na⁺ into
intestinal cells together with glucose, which is moving down its concentration gradient into the cell. (The Na⁺ is then pumped out of the cell into the blood on the other side by Na⁺/K⁺ pumps; see Figure 8.16.) Our understanding of Na⁺/ glucose cotransporters has helped us find more effective treatments for diarrhea, a serious problem in developing countries. Normally, sodium in waste is reabsorbed in the colon, maintaining constant levels in the body, but diarrhea expels waste **+ +** patients are given a solution to drink containing high concen- \mathbf{d} $\frac{1}{2}$ **hreatening con
Ik containing h**i **+ H + + H +**

Concept 8.5: Bulk transport across the plasma membrane occurs by exocytosis and endocytosis

- Small molecules and water enter or leave the cell through the lipid bilayer or via transport proteins
- Large molecules, such as polysaccharides and proteins, cross the membrane in bulk via vesicles
- Bulk transport requires energy
 \circledast but is <u>not</u> named "active transport".

Exocytosis

● In **exocytosis**, transport vesicles migrate to the membrane, fuse with it, and release their contents outside the cell specific oppositions in both membranes • Many secretory cells use exocytosis to export arrangument. their products) such as poncreatic cells (secrete insulin). 2 release of neurotransmitters for signals. 23 relevre of necessary carbonydrates and other materials when building cell walls.

Endocytosis

- In **endocytosis**, the cell takes in macromolecules by forming vesicles from the plasma membrane
- Endocytosis is a reversal of exocytosis, involving different proteins
- There are three types of endocytosis
	- Phagocytosis ("cellular eating")
	- Pinocytosis ("cellular drinking")
	- Receptor-mediated endocytosis

V Figure 8.21 Exploring Endocytosis in Animal Cells

in hnn:

ä

FLUID

 \bullet

 \bullet

 σ

Pseudonodium

Ennd vacuole

CYTOPLASM

In **phagocytosis**, a cell engulfs a particle by extending pseudopodia (singular, *pseudopodium*) around it and packaging it within a membranous sac called a food vacuole. The particle will be digested after the hydrolytic enzymes (see Figure 7.13a).

In **pinocytosis**, a cell continually "gulps" droplets of extracellular fluid into tiny vesicles, formed by infoldings of the plasma membrane. In this way, the cell obtains molecules dissolved in the droplets. Because any and all solutes are taken into the cell, pinocytosis as shown here is nonspecific for the substances it transports. In many cases, the parts of the plasma membrane that form vesicles are lined on their cytoplasmic side by food vacuole fuses with a lysosome containing a fuzzy layer of coat protein; the "pits" and resulting vesicles are called *coated pits*.

Receptor-mediated endocytosis is a specialized type of pinocytosis that enables the cell to acquire bulk quantities of specific substances, even though those substances may not be very concentrated in the extracellular fluid. Embedded in the plasma membrane are proteins with receptor sites exposed to the extracellular fluid. Specific solutes bind to the receptors. The receptor proteins then cluster in coated pits, and each coated pit forms a vesicle containing the bound molecules. The diagram shows only bound molecules (purple triangles) inside the vesicle, but other molecules from the extracellular fluid are also present. After the ingested material is liberated from the vesicle, the emptied receptors are recycled to the plasma membrane by the same vesicle (not shown).

An amoeba engulfing a green algal cell via phagocytosis (TEM).

Pinocytotic vesicles forming (TEMs).

Plasmamembrane SA
loss by endocytosis is Balanced
by exocytosis. Phagocytosis
Pinocytosis
are not specific
<u>unlike</u> R.M. Endocytosis.

- Human cells use receptor-mediated endocytosis to take in cholesterol, which is carried in particles called low-density lipoproteins (LDLs) $\frac{100}{\alpha}$ a complex of lipids and
- Individuals with the disease familial hypercholesterolemia have missing or defective LDL receptor proteins

Using to high [LDL's] in blood
\nthus *constring early atterosclusis*
$$
\equiv
$$
 Light's with closed
\nthus *early atterosclusis* \equiv *Light's with closed*
\n*in isaturated*
\n*and trans-fats. heat change*

Glucose Uptake over Time in Guinea Pig Red Blood Cells

Data from T. Kondo and E. Beutler, Developmental changes in glucose transport of guinea pig erythrocytes, *Journal of Clinical Investigation* **65:1–4 (1980).**

