BIOCHEMISTRY 3

Contents

Chapter 11

Biological Membranes and Transport

- Membranes define the external boundaries ofcells and regulate the molecular traffic across thatboundary; in eukaryotic cells, they divide the internal space into discrete compartments to segregate processes and components **(p 385,Fig. 11–1)**.
- They organize complex reaction sequences and are central to both biological energy conservation and cell-to-cell communication.

11.1 The Composition and Architecture of Membranes

- The molecular components of membranes:
  - proteins and polar lipids, which account for almostall the mass of biological membranes,
  - and carbohydrates,present as part of glycoproteins and glycolipids.

Each Type of Membrane Has CharacteristicLipids and Proteins

- The relative proportions of protein and lipid varywith the type of membrane, reflecting the diversity of biological roles**(p 386, Table 11–1)**.
- Each membrane has a characteristic set of membrane lipids **(p 386,Fig. 11–2)**.

All Biological Membranes Share Some Fundamental Properties

- Membranes are impermeable to most polar or chargedsolutes, but permeable to nonpolar compounds.
- Physical studies of permeability and the motionof individual protein and lipid molecules within membranes, led to the development of the **fluid mosaic model** for the structure of biological membranes **(p 387, Fig. 11–3)**.
  - The fattyacyl chains in the interior of the membrane form a fluid, hydrophobicregion.
  - Integral proteins float in this sea of lipid, held by hydrophobicinteractions with their nonpolar amino acid side chains.

- Both proteinsand lipids are free to move laterally in the plane of the bilayer, butmovement of either from one leaflet of the bilayer to the other is restricted.
- The carbohydrate moieties attached to some proteins andlipids of the plasma membrane are exposed on the extracellular surface.

A Lipid Bilayer Is the Basic Structural Element of Membranes

- Glycerophospholipids, sphingolipids, and sterols are insoluble in water.
- When they are mixed with water, they spontaneously form microscopic lipid aggregates, clustering together, with their hydrophobic moieties in contact with each other and their hydrophilic groups interacting with the surrounding water.
- Three types of lipid aggregate can form**(p 388, Fig.11–4)**.
  - **Micelles** are spherical structures.There is no water in the hydrophobic interiorand their hydrophilic head groups at the surface.
  - **Bilayer** has two lipid monolayers (leaflets).The hydrophobic portions in each monolayer, excluded from water, interact with each other.Thehydrophilic head groups interact with water at each surface of the bilayer.
  - When a two-dimensional bilayer foldson itself, it forms a closed bilayer, a three-dimensional hollow **vesicle** (liposome) enclosing an aqueous cavity.
- Plasma membrane lipids are asymmetrically distributedbetween the two monolayers of the bilayer,

Three Types of Membrane Proteins Differ in Their Association with the Membrane

- **Integral membrane proteins** are associated with the lipid bilayer, and are removable only by agents that interfere with hydrophobic interactions, such as detergents, organic solvents, or denaturants **(p 389,Fig. 11–7)**.
- **Peripheral membrane proteins** associatewith the membrane through electrostatic interactions and hydrogen bonding with the hydrophilic domains of integral proteins and with the polar head groups of membrane lipids. They can be released by relatively mild treatments that interfere with electrostatic interactions or break hydrogen bonds; a commonly used agent is carbonate at high pH.
- **Amphitropic proteins** are found both in the cytosol and in association with membranes.Their affinity for membranesresults in some cases from the protein's

noncovalent interaction with a membrane protein or lipid, and in other cases from the presence of one or more lipids covalently attached to the amphitropic protein.Generally, the reversible association ofamphitropic proteins with the membrane is regulated; for example, phosphorylation or ligand binding can force a conformational change in the protein.

Integral Proteins Are Held in the Membrane by Hydrophobic Interactions with Lipids

- The firm attachment of integral proteins to membranes isthe result of hydrophobic interactions between membrane lipids and hydrophobic domains of the protein.
- For known proteins ofthe plasma membrane, the spatial relationships of protein domains to the lipid bilayer fall into six categories**(p 391,Fig. 11–9)**.
  - Types I and II have a singletransmembrane helix; the amino-terminal domain is outside the cell in type I proteins and inside in type II.
  - Type III proteins have multipletransmembrane helices in a single polypeptide.
  - In type IV proteins,transmembrane domains of several different polypeptides assemble to form a channel through the membrane.
  - Type V proteins are held to thebilayer primarily by covalently linked lipids.
  - TypeVI proteins have both transmembrane helices and lipid anchors.

11.2Membrane Dynamics

- Lipids in a biological membrane can exist in liquid-ordered (regular geometry) or liquid-disordered states (no regular organization) **(p 395,Fig. 11–16)**.
- Fluidity is affected by temperature, fatty acid composition, and sterol (such as cholesterol) content.

Transbilayer Movement of Lipids Requires Catalysis

- At physiological temperatures, uncatalyzed transbilayer (flip-flop) diffusion of a lipid molecule from one leaflet of the bilayer to the other occurs very slowly, although uncatalyzed lateral diffusion *in the plane* of the bilayer is very rapid **(p 396, Fig. 11–16a,b).**

- Several families of proteins, including the flippases, floppases, and scramblases, facilitate the transbilayer movement of lipids, providing a path that is energetically more favorable and much faster than the uncatalyzed movement**(p 396,Fig. 11–16c)**.

Lipids and Proteins Diffuse Laterally in the Bilayer

- Individual lipid molecules can move laterally in theplane of the membrane by changing places with neighboring lipid molecules.
- Many membrane proteins moveas if afloat in a sea of lipids.

Integral Proteins of the Plasma Membrane Are Involved in Surface Adhesion, Signaling, and Other Cellular Processes

- Several families of integral proteins in the plasma membraneprovide specific points of attachment between cells or between a cell and extracellular matrix proteins.
- Integral membrane proteins play roles in many other cellular processes.
  - They serve as transporters and ionchannels and as receptors forhormones, neurotransmitters, and growth factors.
  - They are central to oxidative phosphorylation and photophosphorylation and to cell-cell and cell-antigen recognition in the immune system.
  - Integral proteins are also important players in the membrane fusion (the entry of many types of viruses into host cells).

11.3Solute Transport across Membranes

- Every living cell must acquire from its surroundings theraw materials for biosynthesis and for energy production, and must release the byproducts of metabolism to its environment.
- A few nonpolar compounds can dissolve inthe lipid bilayer and cross the membrane unassisted, but for transmembrane movement of any polar compound or ion, a membrane protein is essential.
- In some cases amembrane protein simply facilitates the diffusion of a solute down its concentration gradient, but transport can also occur against a gradient of concentration, electrical charge, or both, in which case the process requires energy **(p 403, Fig. 11–26)**.

Passive Transport Is Facilitated by Membrane Proteins

- When two aqueous compartments containing unequalconcentrations of a soluble compound or ion are separated by a permeable membrane,
  - the solute moves by **simple diffusion** from the region of higher concentration, through the membrane, to the region of lower concentration, until the two compartments have equal solute concentrations **(p 403, Fig. 11–26a)**.
- When ions of opposite charge are separated by a permeable membrane,
  - there is a transmembrane electrical gradient, a membrane potential, Vm (expressed in millivolts). This membrane potential produces a force opposing ion movements that increase Vm and driving ion movements that reduce Vm **(p 403, Fig. 11–26b)**.
- Thus, the direction in which a charged solute tends to move spontaneously across a membrane depends on both the chemical gradient (the difference in solute concentration) and the electrical gradient (Vm) across the membrane.
- Together, these two factors are referred to as the **electrochemical gradient** or **electrochemical potential**.
- Membrane proteins lower the activation energy fortransport of polar compounds and ions across the membrane for specific solutes**(p 404, Fig. 11–28a, b)**.
- Some transporters simply facilitate passive diffusion across the membrane from the side with higher concentration to the side with lower. Others transport solutes against an electrochemical gradient; this requires a source of metabolic energy
- Membrane proteins are called **transporters** or **permeases**.

Transporters and Ion Channels Are Fundamentally Different

- There are probably a thousand or more different proteins that allow molecules and ions to cross membranes.
- These proteins fall within two very broad categories: **transporters** and **channels(p 404, Fig. 11–29a, b)**.
- In an ion channel, a transmembrane pore is either open or closed, depending on the position of the single gate. When it is open, ions move.

- Transporters (pumps) have two gates, and they are never both open. Movement of a substrate (an ion or a small molecule) through the membrane is limited for one gate to open and close (on one side of the membrane) and for the second gate to open.
- These transporters are called the passive transporters. Energy is not required.

The Glucose Transporter of Erythrocytes Mediates Passive Transport

- The glucose transporter of erythrocytes (called GLUT1) is a type III integral protein.
- The steps of glucose transport are summarized in **(p 406, Fig. 11–32)**.
- Twelve glucose transporters are encoded in the human genome, each with its unique kinetic properties, patterns of tissue distribution, and function **(p 407, Table 11–3)**.

The Chloride-Bicarbonate Exchanger Catalyzes Electroneutral Cotransport of Anions across the Plasma Membrane

- The **chloride-bicarbonate exchanger**, also called the **anion exchange (AE) protein,** mediates the simultaneousmovement of two anions: for each HCO^-_3 ion that moves in one direction, one Cl^- ion moves in the opposite direction,with no net transfer of charge; the exchange is **electroneutral**.
- The anion exchanger is called **cotransport systems**, that simultaneously carry two solutes across a membrane.
- There are three general classes of transport systems.Transporters differ in the number of solutes (substrates) transported and the direction in which each solute moves**(p 409, Fig. 11–34)**.
  - Thetwo substrates move in opposite directions, the process is **antiport**.
  - In **symport**, two substrates are moved simultaneouslyin the same direction.
  - Transporters thatcarry only one substrate, such as the erythrocyte glucose transporter, are known as **uniport** systems.

Active Transport Results in Solute Movement against a Concentration or Electrochemical Gradient

- Active transport is thermodynamicallyunfavorable (endergonic) and takes place only when coupled (directly or indirectly) to an exergonic process such as the absorption of sunlight, an oxidation reaction, the breakdown of ATP.
- There are two types of active transport**(p 409, Fig. 11–35)**.
  - In **primary active transport**, solute accumulation is coupled directly to an exergonic chemical reaction, such as conversion of ATP to ADP + P_i.
  - In **secondary active transport**, a gradient of ion X (S_1) (often Na^+) has been established by primary active transport. Movement of X down its electrochemical gradient now provides the energy to drive cotransport of a second solute (S_2) against its electrochemical gradient.

Aquaporins Form Hydrophilic Transmembrane Channels for the Passage of Water

- The aquaporinsprovide channels for rapid movement of water molecules across all plasma membranes**(p 419, Table 11-5)**.