Alberts • Johnson • Lewis • Raff • Roberts • Walter

Molecular Biology of the Cell

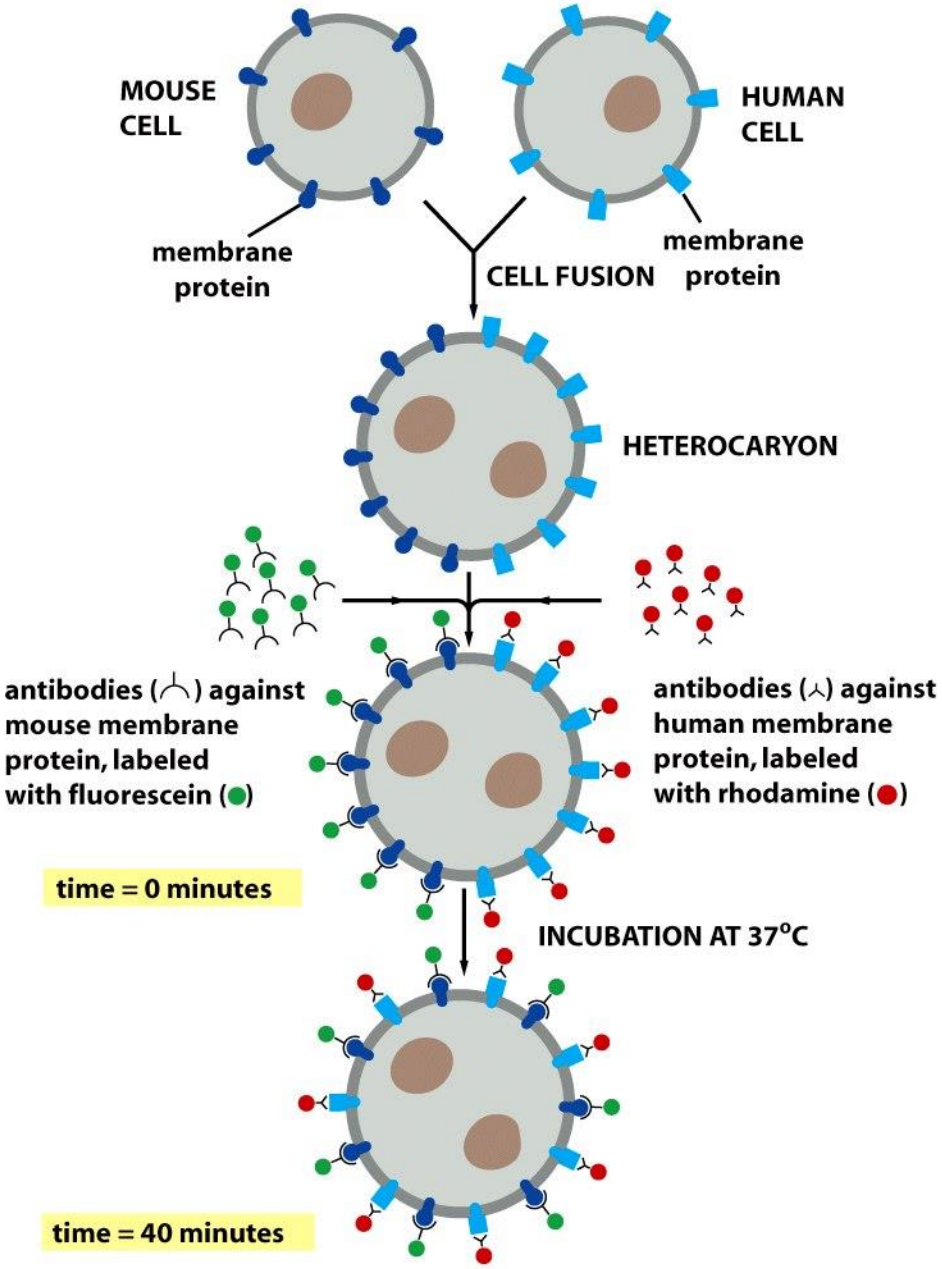
Fifth Edition

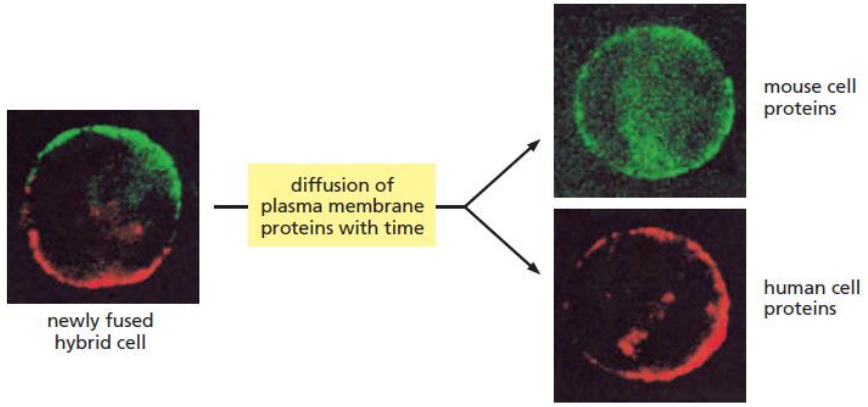
Chapter 10

Membrane Structure

Cell cortex

Many Membrane Proteins Diffuse in the Plane of the Membrane



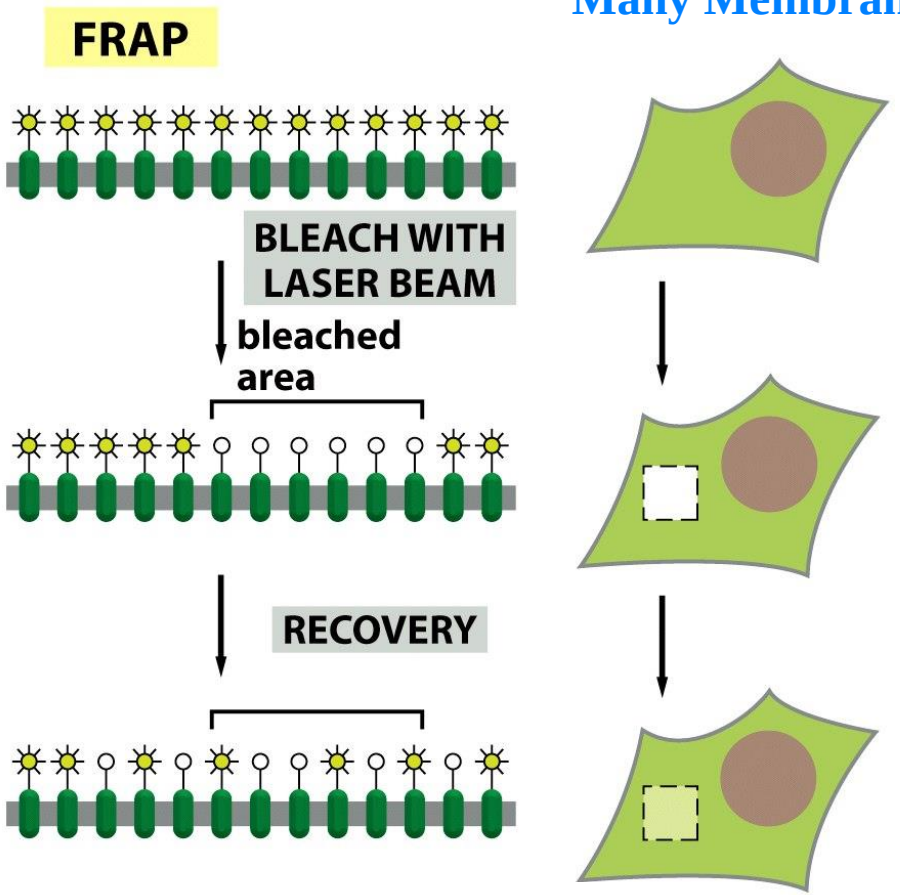


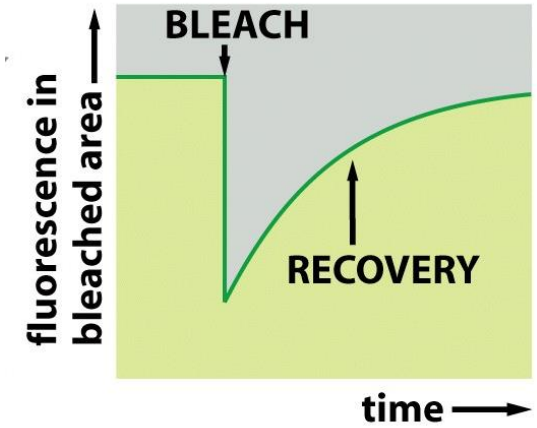
✓ Membrane proteins do not tumble (*flip-flop*) across the lipid bilayer, but they do rotate about an axis perpendicular to the plane of the bilayer (*rotational diffusion*).

Many membrane proteins are able to move laterally within the membrane (*lateral diffusion*).

✓ An experiment in which mouse cells were artificially fused with human cells to produce hybrid cells (***heterokaryons***) provided the first direct evidence that some plasma membrane proteins are mobile in the plane of the membrane: Two differently labeled antibodies were used to distinguish selected mouse and human plasma membrane proteins.

Many Membrane Proteins Diffuse in the Plane of the Membrane





- The lateral diffusion rates of membrane proteins can be measured by using the technique of *fluorescence recovery after photobleaching* (*FRAP*).
- The method usually involves marking the membrane protein of interest with a specific fluorescent group.
- The fluorescent group is then bleached in a small area of membrane by a laser beam, and the time taken for adjacent membrane proteins carrying unbleached ligand or GFP to diffuse into the bleached area is measured.
- From FRAP measurements, we can estimate the **diffusion coefficient** for the marked cell-surface protein.
- The values of the diffusion coefficients for different membrane proteins in different cells are highly variable, because **interactions with other proteins impede the diffusion of the proteins to varying degrees**.
- Measurements of proteins that are minimally impeded in this way indicate that cell membranes have a viscosity comparable to that of olive oil.

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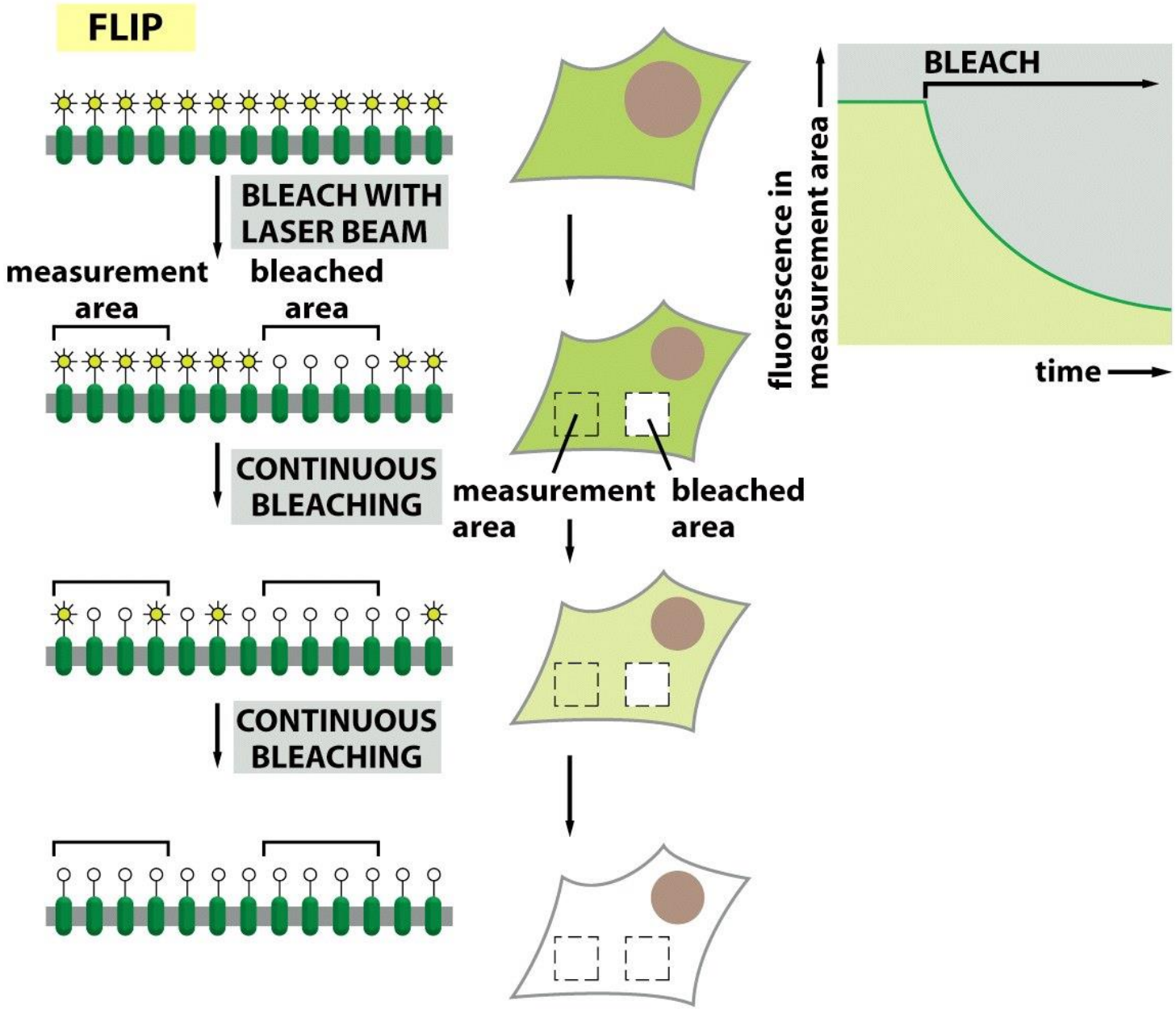
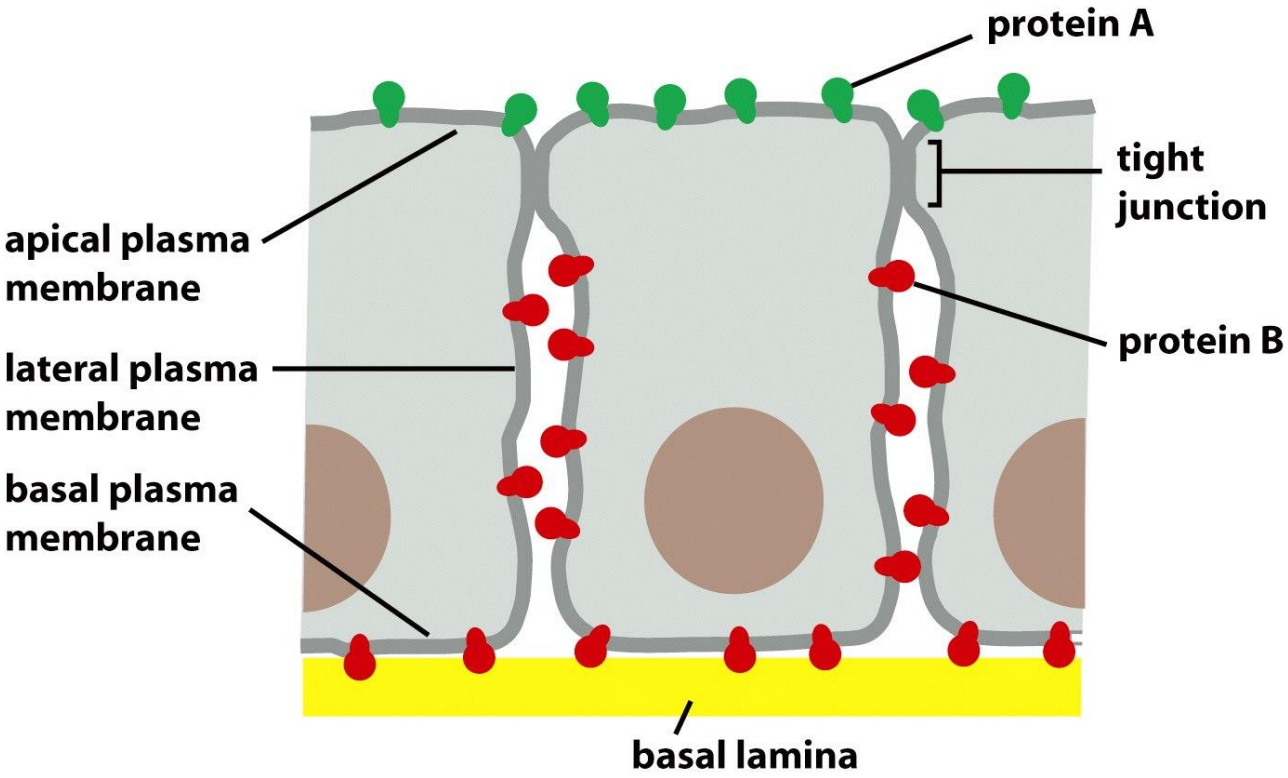


Cells Can Confine Proteins and Lipids to Specific Domains Within a Membrane



- In epithelial cells, such as those that line the **gut** or the tubules of the **kidney**, certain plasma membrane enzymes and transport proteins are confined to the **apical surface** of the cells, whereas others are confined to the **basal** and **lateral surfaces**.

- This **asymmetric distribution of membrane proteins** is often essential for the function of the epithelium.

- The lipid compositions of these two membrane domains are also different, demonstrating that epithelial cells can prevent the diffusion of lipid as well as protein molecules between the domains.

- The barriers set up by a specific type of **intercellular junction** (called a ***tight junction***) maintain the separation of both protein and lipid molecules.

- Clearly, the membrane proteins that form these intercellular junctions cannot be allowed to diffuse laterally in the interacting membranes.

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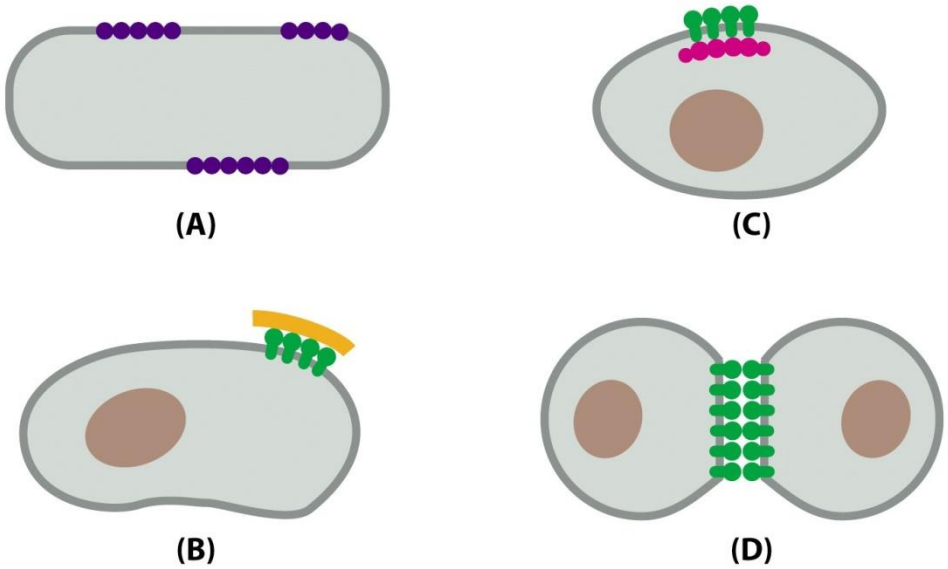


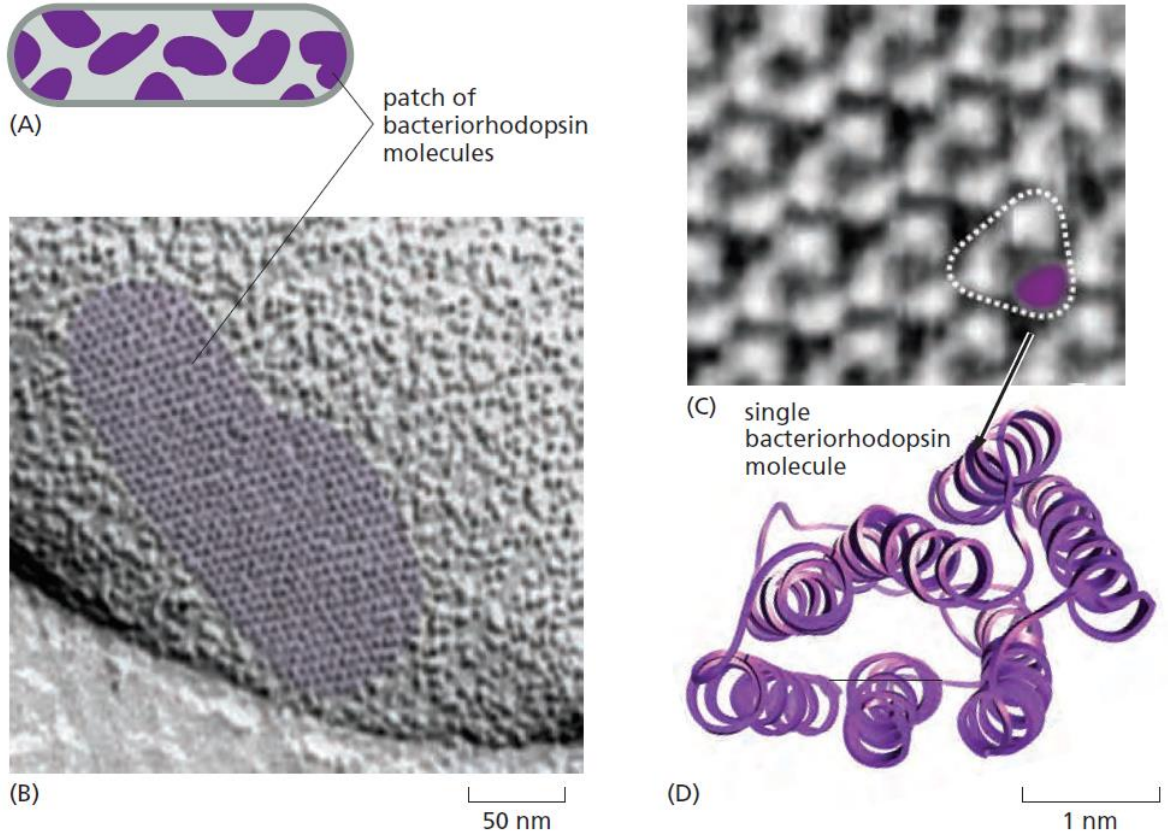
four common ways of immobilizing specific membrane proteins through protein–protein interactions

Some of the membrane molecules are able to diffuse freely within the confines of their own domain.

The molecular nature of the “fence” that prevents the molecules from leaving their domain is not known.

Many other cells have similar membrane fences that confine membrane protein diffusion to certain membrane domains:
The plasma membrane of nerve cells, contains a domain enclosing the **cell body and dendrites**, and another enclosing the **axon**; it is thought that a **belt of actin filaments** tightly associated with the plasma membrane at the cellbody–axon junction forms part of the barrier.

Bacteriorhodopsin Is a Light-driven Proton (H+) Pump That Traverses the Lipid Bilayer as Seven α Helices



- The "purple membrane" of the archaeon *Halobacterium salinarum* is a specialized patch in the plasma membrane that contains a single species of protein molecule, **bacteriorhodopsin**. The protein functions as a **light-activated H+ pump** that transfers H+ out of the archaeal cell.
- Because the bacteriorhodopsin molecules are **tightly packed** and arranged as a **planar two-dimensional crystal**, it was possible to determine their three-dimensional structure by x-ray crystallography.

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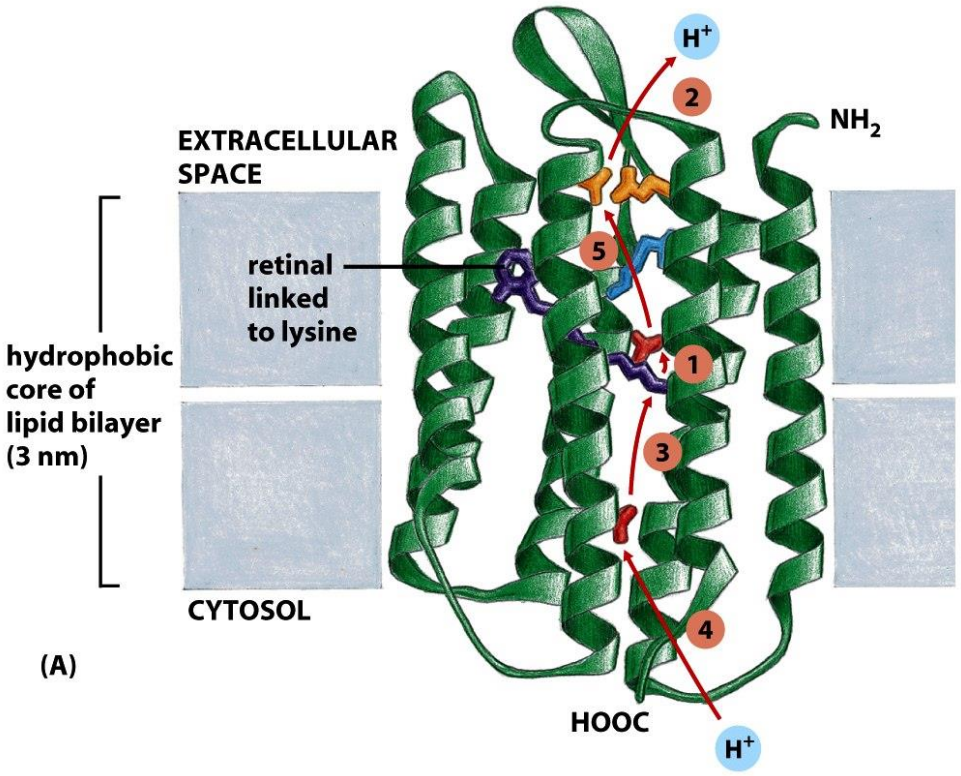
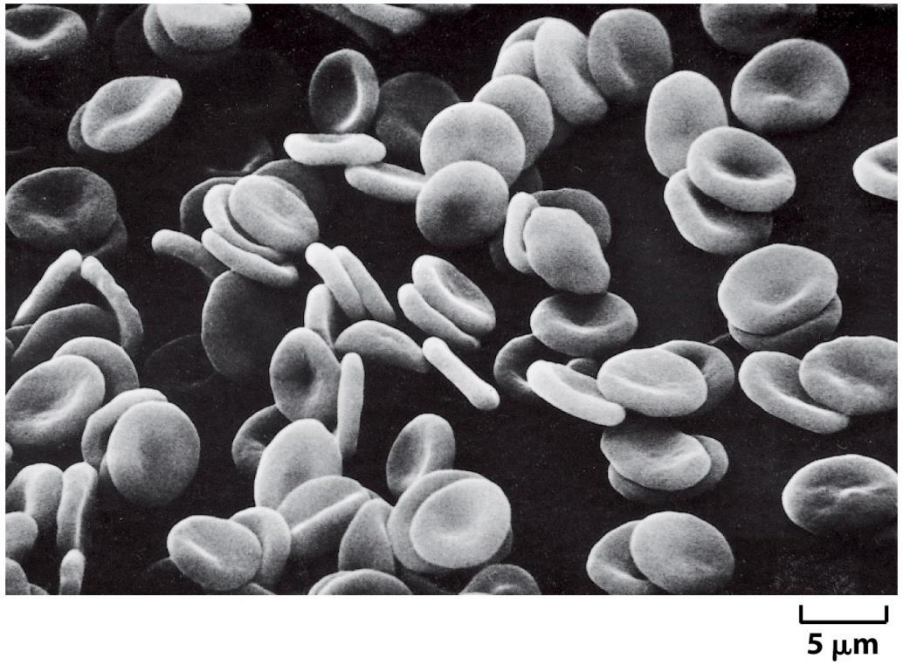
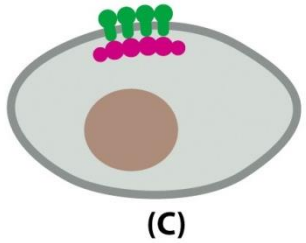


- Each bacteriorhodopsin molecule is folded into seven closely packed transmembrane α helices and contains a single light-absorbing group, or chromophore (*retinal*), which gives the protein its purple color.
- Retinal is vitamin A in its aldehyde form.
- Retinal is identical to the chromophore found in ***rhodopsin*** of the photoreceptor cells of the vertebrate eye.
- Retinal is covalently linked to a lysine side chain of the bacteriorhodopsin protein.
- When activated by a single photon of light, the excited chromophore changes its shape and causes a series of small conformational changes in the protein, resulting in the transfer of one H+ from the inside to the outside of the cell.
- In bright light, each bacteriorhodopsin molecule can pump several hundred protons per second.
- The light-driven proton transfer establishes an H+ gradient across the plasma membrane, which in turn drives the production of ATP by a second protein in the cell's plasma membrane.

- **Thus, bacteriorhodopsin converts solar energy into a H+ gradient, which provides energy to the archaeal cell.**

The Cortical Cytoskeleton Gives Membranes Mechanical Strength and Restricts Membrane Protein Diffusion





- A common way in which a cell restricts the lateral mobility of specific membrane proteins is to tether them to macromolecular assemblies on either side of the membrane.
- The characteristic biconcave shape of a red blood cell, for example, results from interactions of its plasma membrane proteins with an underlying *cytoskeleton*, which consists mainly of a meshwork of the filamentous protein **spectrin**.
- Spectrin is a long, thin, flexible rod about 100 nm in length.
- As the principal component of the red cell cytoskeleton, it maintains the structural **integrity** and **shape** of the plasma membrane, which is the red cell's only membrane, as the cell has no nucleus or other organelles.
- The spectrin cytoskeleton is riveted to the membrane through various membrane proteins.
- **The final result is a deformable, netlike meshwork that covers the entire cytosolic surface of the red cell membrane**.
- This spectrin-based cytoskeleton enables the red cell to **withstand the stress** on its membrane as it is forced through narrow capillaries.
- Mice and humans with genetic abnormalities in spectrin are anemic and have red cells that are spherical and fragile.
- the severity of the anemia increases with the degree of spectrin deficiency.

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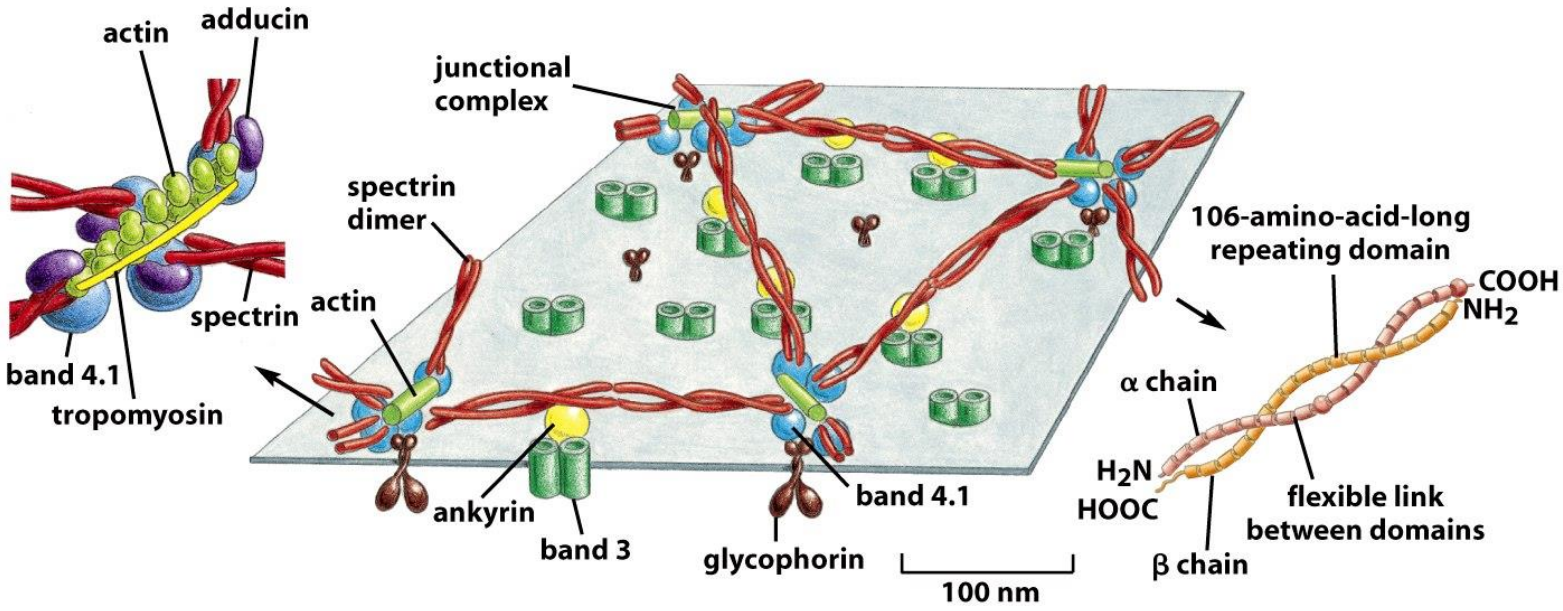
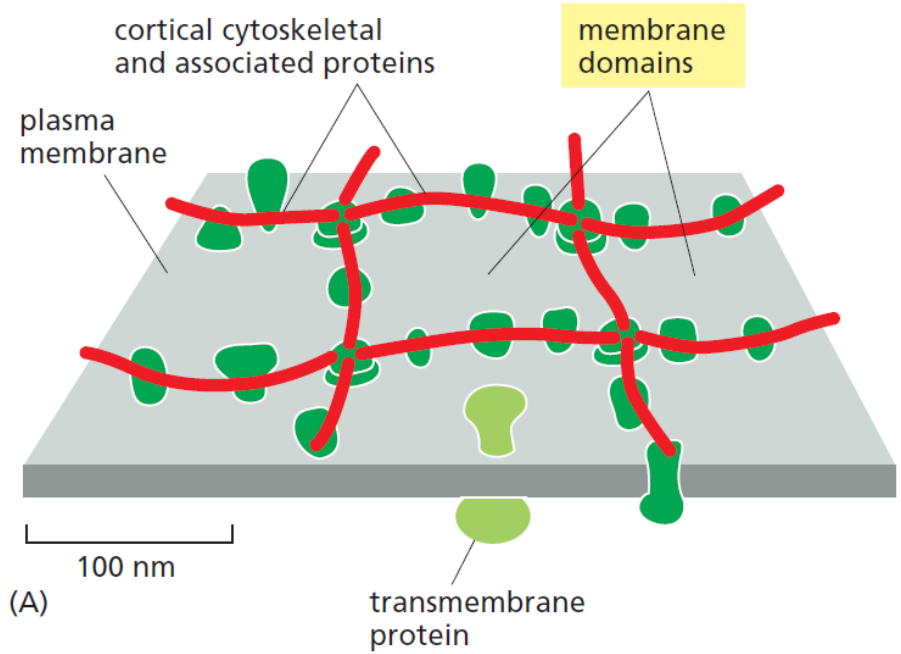


Spectrin heterodimers are linked together into a netlike meshwork by "**junctional complexes**".

Each spectrin heterodimer consists of two antiparallel, loosely intertwined, flexible polypeptide chains called α and β. The two spectrin chains are attached noncovalently to each other at multiple points, including at both ends. Both the α and β chains are composed largely of repeating domains. Two spectrin heterodimers join end-to-end to form tetramers.

The junctional complexes are composed of short actin filaments (containing 13 actin monomers) and these proteins—*band 4.1*, *adducin*, and a *tropomyosin*.

The cytoskeleton is linked to the membrane through two transmembrane proteins—a multipass protein called ***band 3*** and a single-pass protein called ***glycophorin***. The spectrin tetramers bind to some band 3 proteins via *ankyrin* molecules, and to glycophorin and band 3 via band 4.1 proteins.



Corralling plasma membrane proteins by cortical cytoskeletal filaments. The filaments are thought to provide diffusion barriers that divide the membrane into small domains, or corrals.

- An **analogous** but much more elaborate and highly dynamic cytoskeletal network exists beneath the plasma membrane of most other cells in our body. This network, which constitutes the cortex of the cell, is rich in actin filaments, which are attached to the plasma membrane in numerous ways.

- The dynamic remodelling of the cortical actin network provides a driving force for many essential cell functions, including cell movement, endocytosis, and the formation of transient, mobile plasma membrane structures such as filopodia and lamellopodia.

- The cortex of nucleated cells also contains proteins that are structurally homologous to spectrin and the other components of the red cell cytoskeleton.

- The cortical cytoskeletal network restricts diffusion of not only the plasma membrane proteins that are directly anchored to it. Because the cytoskeletal filaments are often closely apposed to the cytosolic surface of the plasma membrane, they can form mechanical barriers that obstruct the free diffusion of proteins in the membrane.
- These barriers partition the membrane into small domains or ***corrals***.

- The extent to which a transmembrane protein is confined within a corral depends on its association with other proteins and the size of its cytoplasmic domain:
- Proteins with a large cytosolic domain will have a harder time passing through cytoskeletal barriers. When a cell-surface receptor binds its extracellular signal molecules, for example, large protein complexes build up on the cytosolic domain of the receptor, making it more difficult for the receptor to escape from its corral.
- It is thought that **corralling** helps concentrate such signaling complexes, increasing the speed and efficiency of the signaling process.