

THE FLUID MOSAIC MODEL

Singer & Nicolson (1972) – Structure of the Plasma Membrane

1. Introduction & Historical Background

In 1972, **S. Jonathan Singer** and **Garth Nicolson** proposed the **fluid mosaic model** to describe the structure and organisation of the plasma membrane. It remains the accepted general model of biological membranes today, refined but not overturned by later discoveries such as lipid rafts and the cytoskeletal “fence and picket” effects.

Earlier membrane models

- **Overton (1899)** – proposed that the membrane is composed of lipids, based on the observation that lipid-soluble substances cross membranes easily.
- **Gorter & Grendel (1925)** – showed, from the surface area of extracted red blood cell lipids, that the membrane is a **lipid bilayer**.
- **Davson & Danielli (1935)** – proposed the “sandwich” or “paucimolecular” model: a lipid bilayer coated on both surfaces by continuous sheets of protein. This model could not explain membrane permeability, protein diversity, or later electron-microscopic and freeze-fracture evidence.
- **Singer & Nicolson (1972)** – replaced the continuous protein sheets with individual, globular proteins *embedded within* a fluid lipid bilayer – the fluid mosaic model.

Quick facts Proposed by: S. J. Singer & G. L. Nicolson | Year: 1972 | Journal: Science | Core idea: lipids form a fluid, two-dimensional solvent in which proteins float as a “mosaic”

2. Main Postulates of the Model

- The membrane is a **fluid** phospholipid bilayer – lipids and proteins are free to move laterally within their own leaflet, giving the membrane the mechanical properties of a two-dimensional fluid rather than a rigid solid.
- Membrane proteins are **globular** and structurally diverse, and are individually inserted into (or embedded within) the lipid bilayer rather than forming continuous surface sheets.
- Proteins are distributed in a **mosaic** pattern – scattered irregularly across the membrane surface, like tiles or icebergs floating in a lipid “sea”.
- The membrane is **amphipathic**: hydrophilic groups of lipids and proteins face the aqueous environment (extracellular fluid / cytoplasm), while hydrophobic groups are buried within the membrane interior, away from water.
- Membrane components are **asymmetrically** distributed – the two leaflets differ in lipid and protein composition, and carbohydrates occur only on the outer (extracellular) surface.

The Fluid Mosaic Model of the Plasma Membrane (Singer & Nicolson, 1972)

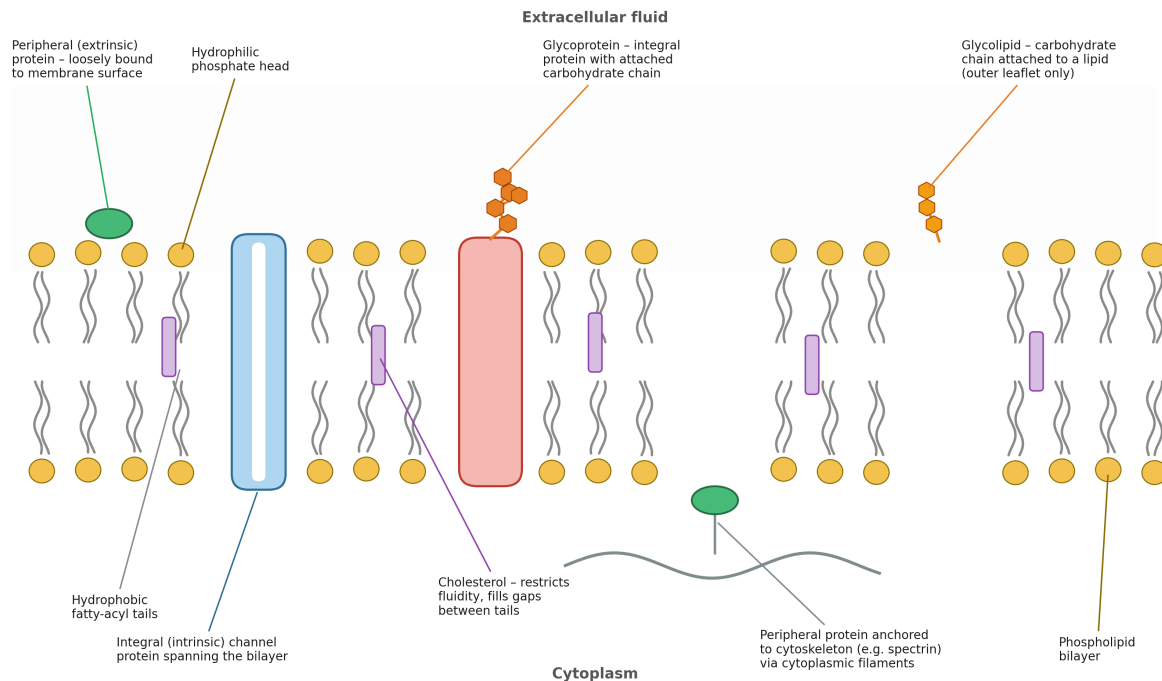


Fig. 1: The fluid mosaic model – a phospholipid bilayer studded with integral and peripheral proteins, cholesterol, glycoproteins, and glycolipids.

3. Components of the Membrane

(a) Phospholipid bilayer

Each phospholipid is **amphipathic**, with a hydrophilic phosphate head and two hydrophobic fatty-acyl tails. In water, phospholipids spontaneously arrange into a bilayer with heads facing the aqueous environments on both sides and tails buried in the interior, minimising contact between the tails and water.

(b) Membrane proteins

Type	Description
Integral (intrinsic) proteins	Embedded within, and often spanning, the bilayer; held in place by hydrophobic interactions with the fatty-acyl tails. Include transmembrane channels, carriers, and receptors. Can only be removed by disrupting the membrane (e.g. with detergent).
Peripheral (extrinsic) proteins	Bound loosely to the membrane surface – either to the polar head groups of lipids or to exposed regions of integral proteins. Can be removed by mild treatments (e.g. changes in pH or ionic strength) without disrupting the bilayer.

(c) Cholesterol

Small, rigid steroid molecules interspersed among the phospholipid tails (mainly in animal cell membranes). Cholesterol acts as a **fluidity buffer**: at high temperature it restrains excessive fluidity by restricting phospholipid movement, while at low temperature it prevents tight packing and so stops the membrane from solidifying.

(d) Glycoproteins and glycolipids

Short branching carbohydrate chains attached to some outer-leaflet proteins (glycoproteins) and lipids (glycolipids) form the **glycocalyx**, a surface “sugar coat” found only on the extracellular face. It functions in

cell–cell recognition, adhesion, and acts as a protective and receptor layer.

4. Fluidity of the Membrane

The word “fluid” in the model's name reflects the fact that individual lipid and protein molecules are not fixed in place but move continuously within the plane of the membrane, giving it the consistency of light machine oil rather than a rigid crystal.

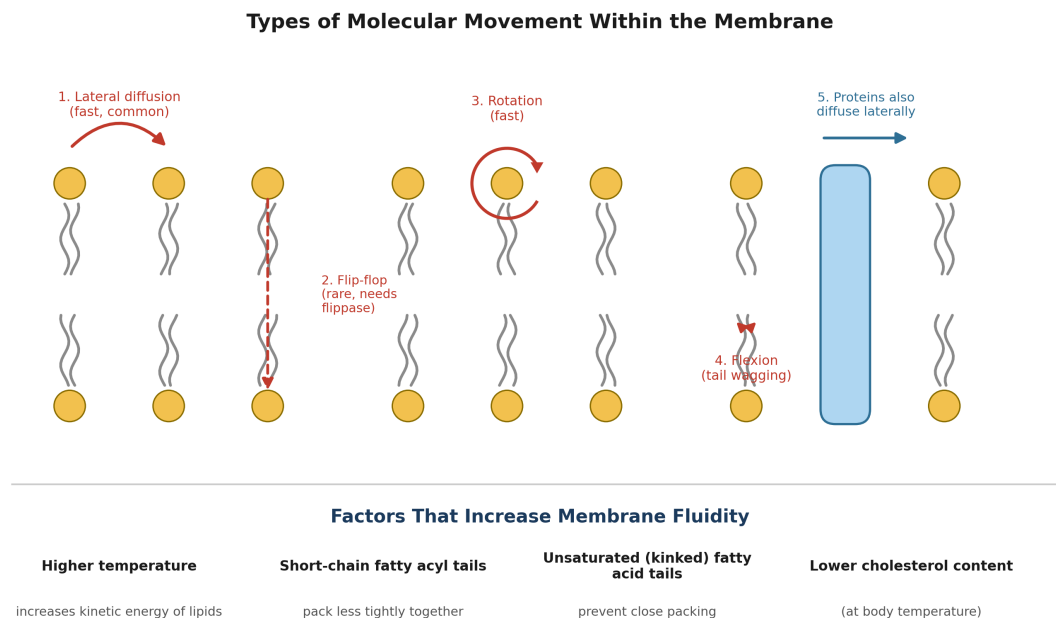


Fig. 2: The main types of molecular movement within the bilayer, and the principal factors that increase membrane fluidity.

- **Lateral diffusion** – the most common movement; a lipid can exchange places with its neighbour roughly 10^7 times per second.
- **Flip-flop** – movement of a lipid from one leaflet to the other; energetically unfavourable and very rare without the help of enzymes called flippases/floppases.
- **Rotation** – spinning of a lipid or protein around its own long axis.
- **Flexion** – flexing/wagging of the hydrophobic tails.
- Integral proteins can also diffuse laterally, although many are restricted or anchored by attachment to the underlying cytoskeleton.

5. “Mosaic” Nature and Membrane Asymmetry

The term “**mosaic**” describes the patchy, irregular arrangement of the many different proteins scattered throughout the lipid bilayer – much like tiles set into a mosaic pattern, or icebergs floating in a fluid lipid “sea”.

The two leaflets of the bilayer are chemically and functionally **asymmetric**:

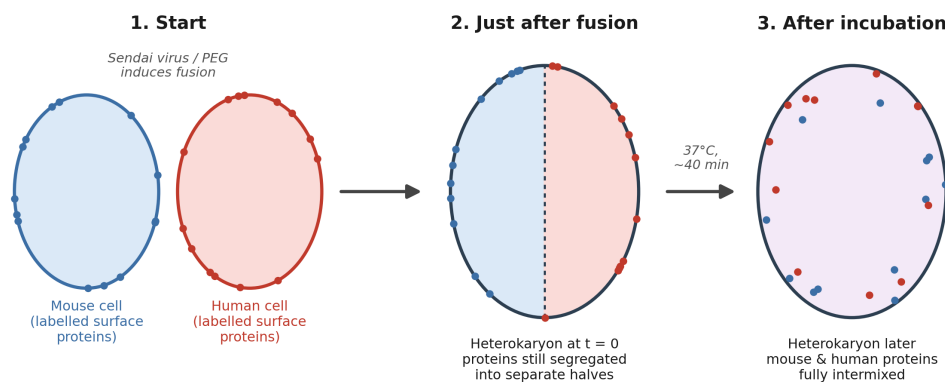
- **Lipid asymmetry** – phosphatidylcholine and sphingomyelin predominate in the outer leaflet, while phosphatidylserine and phosphatidylethanolamine predominate in the inner leaflet.
- **Protein asymmetry** – a given transmembrane protein always has the same orientation; its extracellular and cytoplasmic domains are functionally and structurally distinct.

- **Carbohydrate asymmetry** – glycoproteins and glycolipids occur exclusively on the outer (extracellular) leaflet, forming the glycocalyx.

6. Experimental Evidence for the Model

- **Freeze-fracture electron microscopy** – splits the membrane along the hydrophobic core, revealing randomly scattered globular protein particles studding the exposed lipid faces, consistent with individually embedded (rather than sheet-like) proteins.
- **Frye & Edidin cell fusion experiment (1970)** – classic evidence for lateral protein mobility (see Fig. 3 below).
- **FRAP (Fluorescence Recovery After Photobleaching)** – a small region of fluorescently labelled membrane protein is bleached with a laser; fluorescence recovers within minutes as unbleached labelled molecules diffuse in from surrounding areas, directly demonstrating lateral mobility.

Frye & Edidin (1970) Cell Fusion Experiment - Evidence for Membrane Fluidity



Conclusion: since labelled proteins from the two parent cells intermix within minutes at 37°C, membrane proteins must be able to diffuse freely within the lipid bilayer.

Fig. 3: The Frye & Edidin (1970) mouse–human heterokaryon experiment, showing that surface proteins intermix within minutes at 37°C.

7. Functions of Membrane Proteins

Function	Example
Transport	Channel and carrier proteins move ions/solutes across the membrane
Enzymatic activity	Membrane-bound enzymes catalyse reactions at the membrane surface
Signal transduction (receptor)	Receptors bind hormones/signalling molecules and relay a response inward
Cell–cell recognition	Glycoproteins act as identity markers (e.g. MHC antigens, blood group antigens)
Intercellular joining	Junction proteins (e.g. cadherins, connexins) link adjacent cells
Cytoskeletal attachment	Peripheral proteins anchor the membrane to the cytoskeleton, maintaining cell shape

8. Significance of the Model

- Explains selective permeability, membrane fluidity, and self-sealing behaviour of biological membranes.
- Accounts for the wide functional diversity of membrane proteins (transport, catalysis, signalling, adhesion).
- Provides the conceptual basis for later refinements such as **lipid rafts** (cholesterol- and sphingolipid-rich microdomains) and the **membrane-skeleton “fence” model**, which describe additional constraints on free protein/lipid diffusion.

9. Summary

- Proposed by **Singer & Nicolson in 1972**, replacing the earlier Davson–Danielli “sandwich” model.
- The membrane is a **fluid** phospholipid bilayer in which globular proteins float in a **mosaic** arrangement.
- Components include phospholipids, integral and peripheral proteins, cholesterol, glycoproteins, and glycolipids.
- The membrane shows **fluidity** (lateral diffusion, rotation, rare flip-flop) and **asymmetry** between its two leaflets.
- Supported by freeze-fracture EM, the Frye–Edidin cell fusion experiment, and FRAP studies.

End of notes – The Fluid Mosaic Model