The Evolution of the Fluid-Mosaic Model of Membrane Structure
Evolution of Membrane Models

(a) Lipid nature of membrane
(b) Lipid monolayer
(c) Lipid bilayer
(d) Lipid bilayer plus protein sheets
(e) Unit membrane
(f) Fluid mosaic
(g) Membrane protein structure

Overton
Langmuir
Gorter and Grendel
Davson and Danielli
Robertson
Singer and Nicolson
Unwin and Henderson

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Davson and Danielli – model 1 (1935)

A role for proteins
• surface tension

**Fig. 1** Schema of molecular conditions at the cell surface.
Davson and Danielli – model 1 (1935)

Evidence to support their model:

- surface tension of oil droplets is high

- surface tension of cell membranes is low
  (using starfish eggs)

- surface tension of oil droplets coated with protein is...

  LOW!!!

  surface tension of cell membranes that have been heat treated
  to denature proteins...???
Davson and Danielli model 2 (1952)

Realized that there was a problem with the Davson/Danielli model 1

*what might this problem be?*

- Transport of things into and out of the cell!!!

So, the model was revised to allow for pores…

Verification by EM?!
This was believed to confirm the Davson/Danielli model of the plasma membrane structure.
Fluid Mosaic Model Of Membrane Structure


fluid = all components are free to diffuse in the plane of the membrane

mosaic = heterogeneity in the membrane – proteins and lipids interspersed AND, because of fluidity, randomly distributed

- lipid bilayer retained
- protein coat lost
  - proteins now believed to be discontinuous particles

But what evidence did Singer and Nicholson present to support their model??
What is the Evidence that the Membrane is Fluid?

used fluorescently labeled antibodies…

IgG (immunoglobulin class G) antibody:

![Diagram of IgG antibody, antigen, protein A, fluorophore, and Fc domain]
Frye and Edidin (1970)

1. Human cell
2. Addition of Sendai (fusing) virus
3. Mouse cell
4. 40 minutes

(a)
Frye and Edidin (1970)

**Explanations:**

1. Proteins are free to diffuse in the membrane.

2. Newly synthesized membrane proteins are inserted into the membrane.

3. An active (i.e. ATP dependent) process is responsible for intermixing.

Controls???
Is protein synthesis of new membrane proteins responsible for intermixing?

- Add protein synthesis inhibitor (cyclohexamide)

  Intermixing Still Occurred

Is an active (ATP dependent) process responsible for intermixing?

- Block ATP synthesis:
  add dinitrophenol (DNP), cyanide

  Intermixing Still Occurred
### Frye and Edidin (1970)

![Diagram of antigen spread](image)

#### Table 2. Time course of antigen spread

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<th>Incubation time at 37°C (min)</th>
<th>$M_{1/2}-H_{1/2}$</th>
<th>$M_{1/2}-H_1$</th>
<th>$M_1-H_{1/2}$</th>
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</table>

**Note:** Experiment done at 37°C
Membranes are ‘Fluid’

Factors that Affect Fluidity

- Degree of hydrocarbon saturation
- Cholesterol
- Temperature
If intermixing is due to membrane fluidity, then intermixing should be temperature dependent.
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What is the Experimental Evidence That The Membrane is a ‘Mosaic’?

Technique: Freeze-Fracture
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Exceptions/Modifications?
Measuring Movement in Membranes

FRAP
Fluorescence Recovery After Photobleaching

- Measures lateral diffusion of molecules (lipids/proteins) in cell membranes
- Method allows us to look at populations of molecules.
- Information obtained addresses whether components are, in fact, free to diffuse

From: Molecular Biology of the Cell, 4th ed. Alberts et. al.,