This is a lesson aimed at helping students to develop their understanding of the role of theoretical models in science, using models of the structure of cell membranes as an example.

**Resources for students**

Downloaded from www.nuffieldfoundation.org/aboutscience

OHP B0.1 Aims of the lesson
Sheet B1.1 Structural models of cell membranes
Sheet B1.2 Time line
Sheet B1.3 Lipid layer evidence
Sheet B2.1 Electronmicrograph evidence
Sheet B2.2 Danielli and Davson model
Sheet B2.3 Robertson model
Sheet B3.1 Freeze fracture electronmicrograph evidence
Sheet B3.2 NMR and X-ray diffraction evidence
Sheet B3.3 Singer and Nicholson model
Sheet B3.4 Plasticine model

**Teachers’ notes** *(separate download)*

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Aims of the lesson

In this lesson you are learning about the following.

• When scientists produce theoretical models, they use their imagination and creativity to think about data in new ways. The theoretical models that they produce are therefore more than careful descriptions of the data.

• Because the models go beyond the data, more than one theoretical model can be supported by the available evidence.

• In some cases new evidence is gathered which shows one model to be better than another.
THEORETICAL MODELS: CELL MEMBRANES

STRUCTURAL MODELS OF MEMBRANES

In this lesson you will respond to a number of pieces of evidence which will be provided in the sequence in which they were discovered.

The time line will help you to see the order of events as they actually happened.
You will need to respond to the questions using all the evidence you have been provided with at each stage.

Task 1

You should have a copy of sheet B1.3 ‘Lipid layer evidence’.

1.1 From looking at the data in the table, would you agree with the conclusions of Gorter and Grendel?

1.2 What aspects of the membrane structure is there no evidence for in this data?

Task 2

You should have been given sheet B2.1 ‘Electronmicrograph evidence’ and a description of two different models.

2.1 For each of the models, state how the evidence you have supports or undermines the model.

2.2 Describe what you think led to each model being devised.

Task 3

You should now also have sheets:
B3.1 ‘Freeze fracture electronmicrograph evidence’,
B3.2 ‘NMR and X-ray diffraction evidence’ and
B3.3 ‘Singer and Nicholson’s model’.

The time line will help you see the order these pieces of evidence and models came in.

3.1 How is each of the models, including Singer and Nicholson’s, supported or undermined by all the evidence now available?

3.2 Which do you think is the most useful model? Justify your answer.
B Theoretical Models: Cell Membranes

Time Line

1920
- Gorter and Grendel publish their paper indicating the possibility of a bilayer of lipids (1924)

1930
- Danielli and Davson propose their original model of the membrane (1935)

1940
- First electronmicroscope images of cell membranes produced

1950
- Danielli and Davson publish a revised version of their model (1954)
- J.D. Robertson proposes his model based on Danielli and Davson’s

1960
- The structure of a protein (haemoglobin) was identified for the first time (1959)
- Freeze etching techniques developed giving images of membrane faces

1970
- Singer and Nicholson publish fluid mosaic model (1972)
- NMR and X-ray diffraction techniques are developed sufficiently to provide evidence about the movement of lipids in the membrane

1980

1990

2000
- Gunther Blobel receives a Nobel Prize for his pioneering work on the mechanisms by which proteins integrate with the membrane (1999)
  ????
**LIPID LAYER EVIDENCE**

Data from the experiment which laid the foundations for a model of membrane structure is summarised in the table below. Gorter and Grendel obtained the membranes of red blood cells. They calculated the area of the red blood cell membrane and then extracted the lipids that were present. These were dissolved in petroleum ether and allowed to spread into a layer one molecule thick on a surface of water and the area was measured.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Total surface area of the red blood cell membrane (A) Sq. μ</th>
<th>Surface area occupied by the lipids extracted (B) Sq. μ</th>
<th>Factor B/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>31.3</td>
<td>62</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>6.2</td>
<td>12.2</td>
<td>2</td>
</tr>
<tr>
<td>Sheep</td>
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<td>6.2</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>2.65</td>
<td>5.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Rabbit</td>
<td>5.46</td>
<td>9.9</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>5.46</td>
<td>8.8</td>
<td>1.6</td>
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<td>2</td>
</tr>
<tr>
<td></td>
<td>4.9</td>
<td>9.8</td>
<td>2</td>
</tr>
<tr>
<td>Guinea-pig</td>
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<td>1.02</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0.52</td>
<td>0.97</td>
<td>1.9</td>
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<tr>
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<td>2</td>
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<tr>
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<td>0.63</td>
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<tr>
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<td>0.92</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0.47</td>
<td>0.89</td>
<td>1.9</td>
</tr>
</tbody>
</table>

From these results they concluded:

‘It is clear that all our results fit in well with the supposition that the erythrocytes (red blood cells) are covered by a layer of fatty substances that is two molecules thick.’

(From Gorter, E. and Grendel, F. *Bimolecular layers of lipoids on the chromocytes of the blood*, 1924.)
THEORETICAL MODELS: CELL MEMBRANES

ELECTRONMICROGRAPH EVIDENCE

During the late 1930s and early 1940s, electronmicroscopy techniques were developed which provided much more detailed resolution of the structure of a cell. Early micrographs were obtained by staining a very thin section of tissue with heavy metal salts. These are absorbed in different amounts by different parts of the cell, giving contrasting degrees of electron scattering. The parts that take up the most stain appear the darkest on the image.

Electron microscope images of the cell membrane such as this one give us clues as to its basic structure.

### THEORETICAL MODELS: CELL MEMBRANES

#### DANIELLI AND DAVSON MODEL

Danielli and Davson proposed their initial model in 1935 and refined it as in the diagram below in 1954.

The model consists of

- A lipid bilayer where two layers of polar lipid molecules are arranged with their hydrophilic heads outward.

- A layer of protein covering the surfaces of the membrane. Note that the protein layer is embedded in the layer of lipids, holding them in place.

In this model, the lipids are **not** free to move around.
**B THEORETICAL MODELS: CELL MEMBRANES**

**ROBERTSON MODEL**

The model proposed by J.D. Robertson in 1959 is a development of the Danielli and Davson model with the following exceptions.

The protein layer is formed from a monolayer of polypeptide chains rather than whole protein molecules. (Polypeptides are the long chain molecules that proteins are made from.)

The polypeptide layer is on the exterior of the membrane. It is not embedded in it so the lipids are not held in place.

Robertson proposed that the inner layer could be either polypeptide or polysaccharide (a long chain sugar molecule).

![Diagram of the Robertson Model](image-url)
THEORETICAL MODELS: CELL MEMBRANES

FREEZE FRAC TURE ELECTRONMICROGRAPH EVIDENCE

In the freeze fracture technique, the sample is frozen and then cut with a microtome knife to split the cell. This exposes the membrane’s layered structure showing the outer and inner layers.

This electron micrograph image shows a red blood cell treated in this way. Note the presence of globular particles on the top surface of the inner membrane layer which would be within the intact membrane.

The second picture shows a similarly treated cell that has first had 70% of the protein removed. There are very few of the globular structures that appear in the membrane of the untreated cell.

**Theoretical models: Cell membranes**

**NMR and X-ray diffraction evidence**

NMR stands for Nuclear Magnetic Resonance. By exposing the molecules of the membrane to a static and an oscillating magnetic field, scientists have been able to show that the **lipids** in the membrane, which have a characteristic magnetic ‘spin’, **move** over distances of up to 50 nm during the duration of the measurement (5 to 10 seconds).

X-ray diffraction has shown that, at higher temperatures, the hydrocarbon chains of the **lipids** give off diffraction patterns **similar** to those of **liquid** paraffins. However at low temperatures this movement is lost.
**Singer and Nicholson Model**

Singer and Nicholson’s ‘fluid mosaic model’ (1972) was again a development of Danielli and Davson’s model but with more significant differences than in the Robertson model.

The key differences are as follows.

The proteins **do not form a structural layer** holding the lipids in place so the **lipid component of the membrane is not rigid but fluid**.

The proteins **are not attached to the outside of the lipid layer but embedded within it**, in some cases extending through the thickness of the membrane.
**THEORETICAL MODELS: CELL MEMBRANES**

**PLASTICINE MODEL**

In pilot studies, student feedback suggested that a simple model was helpful in understanding the evidence presented on the freeze fracture sheet.

In freeze fracture preparation, the sample is frozen and then cut with a microtome knife in a way which exposes the interior of cell organelles.

In the electronmicrographs shown on sheet B3.1, the membrane has been fractured in a way which exposes the interior of the membrane bilayer.

The simple model described here helps to illustrate this.

*Roll out a flattened doughnut of plasticine and superimpose it on a roughly circular sheet of a contrasting colour.*

This surface represents the outer face of the inner layer of the membrane.

This surface represents the outer face of the upper layer of the membrane.

**Current membrane research**

Studies of cell surface protein receptors in T-cells has shown a link between tumour necrosis factor (TNF), which attacks cancer cells, and the ageing process. (1999)

Work on molecules that bind with specific receptors on membranes is enabling new drugs to be developed. (2000)