Membrane Structure & Dynamics

Chapter 12, L. Stryer
MEMBRANE STRUCTURE & DYNAMICS

INTRODUCTION

• Why are membranes important
• Common features
• Basic experiments
• Thermodynamics of bilayer formation
• Membrane protein folding
• Molecular motions in a bilayer
Electron micrograph of plasma membrane from red blood cell
Important Functions of Membranes

- Transport
- Energy storage
- Immune response
- Information transduction
COMMON FEATURES OF BIOLOGICAL MEMBRANES

- Sheetlike structures & closed boundaries
- Major components: Lipids & proteins (carbohydrates)
- Lipids are amphiphilic: They form closed bilayers
- Specific proteins mediate distinct functions
- Noncovalent assemblies
- Asymmetric
- Fluid structures = 2D solutions
- Electrically polarized
Phospholipids

Membrane lipids (polar)

Phospholipids

Glycerophospholipids

Glycerol

Fatty acid

Fatty acid

PO₄

Alcohol

Sphingolipids

Sphingosine

Fatty acid

PO₄

Choline

Glycolipids

Sphingolipids

Sphingosine

Fatty acid

Mono- or oligosaccharide
Schematic structure of a phospholipid
<table>
<thead>
<tr>
<th>Number of</th>
<th>Number of</th>
<th>Common name</th>
<th>Systematic name</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
<td>Laurate</td>
<td>n-Dodecanoate</td>
<td>CH$_3$(CH$<em>2$)$</em>{10}$COO$^-$</td>
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<tr>
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<td>0</td>
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<td>n-Tetradecanoate</td>
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<td>16</td>
<td>0</td>
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<td>n-Hexadecanoate</td>
<td>CH$_3$(CH$<em>2$)$</em>{14}$COO$^-$</td>
</tr>
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<td>0</td>
<td>Arachidate</td>
<td>n-Eicosanoate</td>
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<td>CH$_3$(CH$<em>2$)$</em>{20}$COO$^-$</td>
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<tr>
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<td>0</td>
<td>Lignocerate</td>
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<td>CH$_3$(CH$<em>2$)$</em>{22}$COO$^-$</td>
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<tr>
<td>16</td>
<td>1</td>
<td>Palmitoleate</td>
<td>cis-$\Delta^9$-Hexadecenoate</td>
<td>CH$_3$(CH$<em>2$)$</em>{15}$CH═CH(CH$<em>2$)$</em>{7}$COO$^-$</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>Oleate</td>
<td>cis-$\Delta^9$-Octadecenoate</td>
<td>CH$_3$(CH$<em>2$)$</em>{17}$CH═CH(CH$<em>2$)$</em>{7}$COO$^-$</td>
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<td>cis,cis-$\Delta^9$,$\Delta^{12}$-Octadecadienoate</td>
<td>CH$_3$(CH$<em>2$)$</em>{14}$(CH═CHCH$_2$)$_2$(CH$_2$)$_6$COO$^-$</td>
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<tr>
<td>18</td>
<td>3</td>
<td>Linolenate</td>
<td>all-cis-$\Delta^9$,$\Delta^{12}$,$\Delta^{15}$-Octadecatrienoate</td>
<td>CH$_3$CH$_2$(CH═CHCH$_2$)$_3$(CH$_2$)$_6$COO$^-$</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
<td>Arachidonate</td>
<td>all-cis-$\Delta^5$,$\Delta^8$,$\Delta^{11}$,$\Delta^{14}$-Eicosatetraenoate</td>
<td>CH$_3$(CH$_2$)$_4$(CH═CHCH$_2$)$_4$(CH$_2$)$_2$COO$^-$</td>
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</table>
Phosphatidyl serine

Phosphatidyl choline

Phosphatidyl ethanolamine

Phosphatidyl inositol

Diphosphatidyl glycerol (cardiolipin)
Lipids can include carbohydrates

Cerebroside (a glycolipid)

Fatty acid unit

Sugar unit

glucose or galactose
Steroids

Cholesterol is the main steroid in mammalian cells
- present in plasma membranes
- has an important effect on the properties (fluidity) of membranes
Archaeal membranes are built of ether lipids with branched chains

Ether bonds are more resistant to hydrolysis than ester bonds

Branched hydrocarbons make membranes more rigid
Models of phospholipids

(A)

Phosphoglyceride

Sphingomyelin

Archaecal lipid

(B)

Shorthand depiction
Selfassembly of lipids

General structure of membrane components

HYDROPHOBIC  HYDROPHILIC

In water the amphipatic membrane components segregate \textit{spontaneously} driven by \textit{entropy}. This process is called \textit{self assembly}

$\Rightarrow$ flexible
$\Rightarrow$ dynamic
$\Rightarrow$ self healing
Lipid bilayer

Individual units are cylindrical (cross-section of head equals that of side chain)

Micelle

Individual units are wedge-shaped (cross-section of head greater than that of side chain)
Lipid bilayer

Interactions:

• Hydrophobic
• Van der Waals
• Electrostatic
Distribution of lipids between inner & outer monolayers in cell membranes

<table>
<thead>
<tr>
<th>Membrane phospholipid</th>
<th>Percent of total membrane phospholipid</th>
<th>Distribution in membrane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphatidylethanolamine</td>
<td>30</td>
<td>Inner monolayer</td>
</tr>
<tr>
<td>Phosphatidylcholine</td>
<td>27</td>
<td>Outer monolayer</td>
</tr>
<tr>
<td>Sphingomyelin</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylserine</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylinositol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphatidylinositol 4-phosphate</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylinositol 4,5-bisphosphate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphatidic acid</td>
<td></td>
<td></td>
</tr>
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</table>
Lateral distribution of lipids in cell membranes
Cryomicroscopy

Visualisation membrane proteins by freeze fracture cell membranes
The fluid mosaic model of a cellular membrane
Architecture of cellular membranes

Kusumi (Nagoya, Japan)
Membrane proteins

30 % of all human proteins are membrane proteins
Protein composition in different membranes

SDS-polyacrylamid gel

erythrocytes
Retinal rod cells
Sarcoplasmic reticulum
membrane of muscle cells

Retinal rod cells
Integral membrane proteins

- One transmembrane segment
- Several transmembrane segments
- Several transmembrane proteins assemble
Some proteins associate with membranes through covalently attached lipids

S-Palmitoylcysteine

C-terminal S-farnesylcysteine methyl ester

Carboxyl terminus

Glycosyl phosphatidylinositol (GPI) anchor
Polypeptide chain

Polypeptide backbone (black)
Amino acid side chains (green)
Structures secondaires

- Motif dans une membrane:
  - 3 nm: épaisseur membrane
  - Dans une hélice α: 0.15 nm / acide aminé
    - 20 - 25 acides aminés par hélice transmembranaire
Water-soluble proteins fold into compact 3D structures: e.g. myoglobin

Ball-and-stick model of all nonhydrogen atoms

Scheme of helices & heme group
Distribution of amino acids in myoglobin

Hydrophobic (yellow)    Charged (blue)    Others (white)
Prediction of transmembrane helices from sequence

### TABLE 12.2 Polarity scale for identifying transmembrane helices

<table>
<thead>
<tr>
<th>Amino acid residue</th>
<th>Transfer free energy kcal mol(^{-1}) (kJ mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phe</td>
<td>3.7 (15.5)</td>
</tr>
<tr>
<td>Met</td>
<td>3.4 (14.3)</td>
</tr>
<tr>
<td>Ile</td>
<td>3.1 (13.0)</td>
</tr>
<tr>
<td>Leu</td>
<td>2.8 (11.8)</td>
</tr>
<tr>
<td>Val</td>
<td>2.6 (10.9)</td>
</tr>
<tr>
<td>Cys</td>
<td>2.0 (8.4)</td>
</tr>
<tr>
<td>Trp</td>
<td>1.9 (8.0)</td>
</tr>
<tr>
<td>Ala</td>
<td>1.6 (6.7)</td>
</tr>
<tr>
<td>Thr</td>
<td>1.2 (5.0)</td>
</tr>
<tr>
<td>Gly</td>
<td>1.0 (4.2)</td>
</tr>
<tr>
<td>Ser</td>
<td>0.6 (2.5)</td>
</tr>
<tr>
<td>Pro</td>
<td>−0.2 (−0.8)</td>
</tr>
<tr>
<td>Tyr</td>
<td>−0.7 (−2.9)</td>
</tr>
<tr>
<td>His</td>
<td>−3.0 (−12.6)</td>
</tr>
<tr>
<td>Gln</td>
<td>−4.1 (−17.2)</td>
</tr>
<tr>
<td>Asn</td>
<td>−4.8 (−20.2)</td>
</tr>
<tr>
<td>Glu</td>
<td>−8.2 (−34.4)</td>
</tr>
<tr>
<td>Lys</td>
<td>−8.8 (−37.0)</td>
</tr>
<tr>
<td>Asp</td>
<td>−9.2 (−38.6)</td>
</tr>
<tr>
<td>Arg</td>
<td>−12.3 (−51.7)</td>
</tr>
</tbody>
</table>


Note: The free energies are for the transfer of an amino acid residue in an α helix from the membrane interior (assumed to have a dielectric constant of 2) to water.

1 transmembrane segment
Polypeptide chain

Polypeptide backbone  (black)
Amino acid side chains (green)
Bacteriorhodopsin

7 transmembrane segments
Bacterial porins are membrane proteins built entirely of beta strands.
Architecture of a cellular membrane
Lateral diffusion in membranes

FRAP: fluorescence recovery after photobleaching

\[ S = (2D t)^{1/2} \]
Model Membranes for studying the properties of

- lipid bilayers
- individual membrane proteins
Solubilisation of membrane proteins

- Peripheral protein
- Integral protein (hydrophobic domain coated with detergent)
- Change in pH; chelating agent; urea; \( \text{CO}_3^{2-} \)
- \( \text{Ca}^{2+} \)
- Détergent
Liposomes

Miniaturized containers

50 nm - 100µm diameter
Preparation of liposomes containing cargo

1. Glycine in \( \text{H}_2\text{O} \)
2. Phospholipid
3. Sonication
4. Gel filtration
5. Glycine trapped in lipid vesicle
Planar bilayers to measure electrical conductance

Diagram showing a setup with electrode, aqueous compartments, and bilayer membrane.
Diffusion of lipids in membranes

Lateral diffusion

Rapid

Very slow

Tranverse diffusion (flip-flop)
Phase transition in synthetic lipid membranes
<table>
<thead>
<tr>
<th>Number of carbons</th>
<th>Number of double bonds</th>
<th>Fatty acid</th>
<th>Common name</th>
<th>Systematic name</th>
<th>$T_m$ (°C)</th>
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<tbody>
<tr>
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<td>Behenate</td>
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<td>n-Octadecanoate</td>
<td>75</td>
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<td>Stearate</td>
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<td>58</td>
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<tr>
<td>16</td>
<td>0</td>
<td>Palmitate</td>
<td>n-Hexadecanoate</td>
<td>n-Hexadecanoate</td>
<td>41</td>
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<tr>
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