Fig. 1. Modular design of the cell. Schematic view of eucaryotic cell composed of modules with well defined functions. These include: The nucleus, N, (the site of information storage); the endoplasmatic reticulum, ER, with associated ribosomes (the location of protein and lipid synthesis); the Golgi apparatus, G, (serving the modification and sorting of newly synthesized proteins and lipids and their directed distribution to other compartments or membranes); the mitochondria, M, (organelles where ATP is produced); the lysosomes, L, (specialized for intracellular digestion). V denotes a whole palette of vesicles (e.g., endosomes) which are required for the molecular transport within the cell and between the cell and its environment. The plasma membrane (PM) forms a selective filter and regulates communication between cells. The intracellular compartments are embedded in the cytoskeleton: a soft network of protein filaments (not shown). The cytoskeleton helps to establish some order within the cytoplasm and, together with the plasma membrane, determines the mechanical stability of the cell. The membranes create three subspaces: the lumina inside of the compartments, the cytosol which is the zone between the compartments, and the extracellular space.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Fig. 2. Coarse and fine structure of plasma membranes: a stratified composite material. 

(a) Schematic coarse grained structure of cell plasma membrane and associated networks. The caricature shows the three layered composite build-up from the lipid/protein bilayer forming the center, the glyocalix facing the extracellular space and the bilayer-coupled cytoskeleton facing the cytosol. The latter may again closely couple to the three-dimensional actin network and the glyocalix may attach to the extracellular matrix (e.g., a collagen IV network). Note that the lipid/protein bilayer and the glyocalix are enlarged in thickness by a factor of about 300 compared to the macromolecular networks.

(b) Simplified high resolution cartoon of the plasma membrane of an erythrocyte with associated spectrin-actin network. Note the asymmetric distribution of the lipids between two monolayers and that the proteins are surrounded by clouds of specific lipid. For details of the fine structure of cytoskeleton see fig. 6.

From: "Handbook of Biological Physics", Lipowsky and Sackmann 
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Modell system: erythrocyte

Life data of human erythrocytes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production rate</td>
<td>$2.4 \cdot 10^6$ per sec</td>
</tr>
<tr>
<td>Daily loss</td>
<td>$2.1 \cdot 10^{11}$ cells</td>
</tr>
<tr>
<td>Total number of RBC's</td>
<td>$2.5 \cdot 10^{13}$ cells</td>
</tr>
<tr>
<td>Distance travelled during 120 day life-time</td>
<td>400 km</td>
</tr>
<tr>
<td>Cell weight</td>
<td>$3 \cdot 10^{-11}$ g</td>
</tr>
<tr>
<td>Cell surface</td>
<td>$140 \mu m^2$</td>
</tr>
<tr>
<td>Cell volume</td>
<td>$110 \mu m^3$</td>
</tr>
</tbody>
</table>


Fig. 4. Formation of erythroblast (red blood cell with nucleus) from megacyte and simultaneous expulsion of the nucleus (cf. arrow) which is taken up by the mother cell (cf. fig. 22 below).

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Figure 10-31. The spectrin-based cytoskeleton on the cytosolic side of the human red blood cell membrane. The structure is shown (A) schematically and (B) in an electron micrograph. The arrangement shown in the drawing has been deduced mainly from studies on the interactions of purified proteins in vitro. Spectrin dimers are linked together into a netlike meshwork by junctional complexes (enlarged in the box on the left) composed of short actin filaments (containing 13 actin monomers), band 4.1, adducin, and a tropomyosin molecule that probably determines the length of the actin filaments. The cytoskeleton is linked to the membrane by the indirect binding of spectrin tetramers to some band 3 proteins via ankyrin molecules, as well as by the binding of band 4.1 proteins to both band 3 and glycophorin (not shown). The electron micrograph shows the cytoskeleton on the cytosolic side of a red blood cell membrane after fixation and negative staining. The spectrin meshwork has been purposely stretched out to allow the details of its structure to be seen. In a normal cell, the meshwork shown would be much more crowded and occupy only about one-tenth of this area. (B, courtesy of T. Byers and D. Branton, Proc. Natl. Acad. Sci. USA 82:6153–6157, 1985. © National Academy of Sciences.)

From: Alberts et al "Molecular Biology of the cell"
Fig. 8. Major classes of membrane lipids of animal cells. The major classes of two-chain lipids are distinguished by the structure (i) of the fatty acid chains (number of C-atoms and double bonds), (ii) the semipolar backbone and (iii) the head group. The phospholipids (a) exhibit a glycerol-backbone while that of sphingomyelins and glycolipids (cerebrosides, gangliosides) is a so-called sphingosine (b). The four major classes of phospholipids: phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS) and phosphatidylinositol (PI) differ only in the hydrophilic group esterified to the phosphate group. The sphingomyelin (SPHM) exhibits a phosphocholine head group (as PC), the cerebrosides a single sugar residue (glucose, galactose) and the gangliosides a complex (branched or linear) oligosaccharide. The ganglioside shown in (b) represents the antigen specifying blood group A.

Note: Each two-chain lipid may be transformed into a one chain lipid (lyso lipid) and fatty acid.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
## Composition of different membranes

Table 2
Summary of lipid composition of various cellular organelles of mammalian liver cells and erythrocyte plasma membrane. Values are given in percentages by mass of total lipids. (Source: Jinnemion and Robinson, [41].)

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Plasmamembrane</th>
<th>Endoplasmic Reticulum</th>
<th>Golgi</th>
<th>Lysosome</th>
<th>Nuclear Membrane</th>
<th>Mitochondria</th>
<th>Nerve Cells</th>
<th>Myelin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid</td>
<td>human erythrocyte</td>
<td>rat liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphatidylcholine</td>
<td>20</td>
<td>18</td>
<td>48</td>
<td>25</td>
<td>23</td>
<td>44</td>
<td>38</td>
<td>48</td>
</tr>
<tr>
<td>phosphatidyldiethanolamine</td>
<td>18</td>
<td>12</td>
<td>19</td>
<td>9</td>
<td>13</td>
<td>17</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>phosphatidylethanolamine</td>
<td>7</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>phosphatidylserine</td>
<td>3</td>
<td>3</td>
<td>8</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>sphingomyelin</td>
<td>18</td>
<td>12</td>
<td>5</td>
<td>7</td>
<td>23</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>cardiolipin</td>
<td></td>
<td></td>
<td>5</td>
<td>7</td>
<td>23</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>glycolipid</td>
<td>3</td>
<td>8</td>
<td>traces</td>
<td>0</td>
<td>traces</td>
<td>traces</td>
<td>3</td>
<td>29</td>
</tr>
<tr>
<td>others</td>
<td>11</td>
<td>21(1)</td>
<td>10(2)</td>
<td>4(3)</td>
<td>16(4)</td>
<td>15</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>cholesterol</td>
<td>20</td>
<td>19</td>
<td>6</td>
<td>8</td>
<td>14</td>
<td>10</td>
<td>3</td>
<td>11</td>
</tr>
</tbody>
</table>

Footnotes: 1) These include 6% free fatty acid, 2.5% lyso PC, 2.5% cholesterol esters, 7% triglycerides.
2) These include 5% triglycerides.
3) These include 3% triglycerides.
4) These include 10% triglycerides, 18% free fatty acid and 5% cholesterol esters.
5) These include 3% triglycerides and 8% cholesterol esters.
6) Average lipid composition of rat brain neurons.
7) Bovin brain myelin.
8) Essentially ceramides.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
A typical membrane protein: Band III

Fig. 9. a) Distribution of amino acids with hydrophobic and hydrophilic side chain along polypeptide chain of anion exchange (band III) protein of erythrocytes (called hydrophobicity plot). The built-up from a predominantly hydrophilic (first 420 amino acids of NH2-terminus) to strongly hydrophobic (= membrane spanning) is obvious. The latter has a quasi-periodicity of ten. Source: R.R. Kopito and H.F. Lodish, Nature 316, 234 (1985), [6]. b) Model of molecular architecture of band III protein as suggested by periodicity of hydrophobicity-plot and lengths of the ten hydrophobic stretches of the membrane spanning part. The hydrophobic band b comprises 38 amino-acids which can form two antiparallel and amphipathic helices facing each other with polar surfaces. Also the domain j can form an amphipathic cylinder. The orientation of the last domain (second half of hydrophobic band j) is unclear. It could either penetrate the bilayer or extend into the cytosol. Note that one amino-acid contributes 0.15 nm to the length of an -helix.

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http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
A small membrane protein: Glycophorin

Fig. 10. Schematic structure of glycophorins: an example of a small membrane anchored receptor. The glycoprotein is composed of 131 amino acids with a large head group (61–74 amino acids) pointing into the extracellular space and a smaller (36 amino acids long) C-terminal extending into the cytosol. Remarkably, the segment formed by amino acids 62 to 74 could form a hairpin-like loop (reminiscent of α-pleated structure) penetrating into the bilayer with the 2 pairs of acidic and basic segments forming ion pairs. The positively charged segments, 96, 97, 100, 101, could link the cytoplasmatic domain to the anionic lipids of the cytoplasmatic monolayer inducing simultaneously local phase segregation (cf. chapter 5).

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Ion pumps control ionic concentrations

Fig. 11a. Schematic view of quartenary structure of Na\(+\)K\(+\)-ATPase: an $\alpha_2\beta_2$-heterodimer; $\alpha$ denotes a 120 kD protomer consisting of 7 membrane spanning helices. The domains extending into the aqueous phases contain the binding site for the promotor ATP at one side and that for regulating steroids at the opposite one. The $\beta$-dimer is supposed to form the channel. The $\alpha$-domain denotes the associated glycoprotein with molecular weight of 40 kD. It consists of about four membrane spanning helices and is supposed primarily to maintain the correct orientation of the protein within the bilayer.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Sodium-Potassium Antiporter

Fig. 12. Model of mechanism of Na⁺–K⁺-antitransport by P-type ATPases. E1 and E2 are two conformational states of the protein and the E1 → E2 transition is triggered by phosphorylation. The uptake of Na⁺ and detachment of K⁺ at one side is due to the high (low) affinity of E1 for Na⁺ (for K⁺) and the reverse behaviour for the E2-conformation. The E1 → E2 transformation is associated with the turn-over of both binding sites on the protein from one site of the membrane to the other.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Finding a ligand is faster in 2D

Time to hit a target of size $a$ from a distance $b$:

Three dimensions:

$$\tau_R^{(3)} \approx \frac{b^3}{3Da}$$

Two dimensions:

$$\tau_R^{(2)} \approx \frac{b^2}{2D} \ln \frac{b}{a}$$

$D$: diffusion constant of ligand

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Many signal processes involve G-proteins

Fig. 26a. Schematic model of hormone signal transduction and amplification by machinery consisting of three proteins: (1) the β-adrenergic receptor, (2) the GTP-regulated G-protein and (3) the adenylate cyclase (AC). The receptor consists of an integral protein spanning the membrane with seven helices. The G-protein is a trimer composed of an $\alpha$, $\beta$ and $\gamma$ unit of which two are coupled to the bilayer by lipid anchors. The binding site of the G-protein to the receptor is located at the cytosolic loop between helix number 5 and 6. Receptor and G-protein are similar in visual signal transducer of rod cells.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbb
Figure 10-44. The cell coat, or glycocalyx. This electron micrograph of the surface of a lymphocyte stained with ruthenium red emphasizes the thick carbohydrate layer surrounding the cell. (Courtesy of Audrey M. Glauert and G.M.W. Cook.)

Figure 10-45. Simplified diagram of the cell coat (glycocalyx). The cell coat is made up of the oligosaccharide side chains of glycolipids and integral membrane glycoproteins and the polysaccharide chains on integral membrane proteoglycans. In addition, adsorbed glycoproteins and adsorbed proteoglycans (not shown) contribute to the glycocalyx in many cells. Note that all of the carbohydrate is on the noncytosolic surface of the membrane.

From: Alberts et al "Molecular Biology of the cell"
Leukocyte Rolling

From:
The molecular basis of leukocyte adhesion to and migration through vascular endothelium
Guy Cinamon, Oren Dwir, Sara Feigelson, Revital Shamri, Ronen Alon
Immunology and Hematopoiesis pp 207
Fig. 20. Model of receptor mediated import of iron and membrane receptor recycling. Iron is bound to transferrin (two ions per ligand) and couples to the transferrin receptor which induces its accumulation in the coated pits. After budding and pinch-off of the coated vesicle the clathrin coat is detached. The naked vesicle (= endosome) fuses with acidic decoupling vesicles (= CURL vesicle or pre-lysosomes), resulting in dissociation of iron. This hybrid vesicle undergoes fission into an iron containing and a receptor enriched part. The latter re-fuses with the plasma membrane and the neutralization of the aqueous milieu causes dissociation of transferrin; thus closing the cycle. The cycle time is about 15 minutes. The dissociation of clathrin from the vesicle is triggered by binding of a cytosolic protein (a relative of the family of heat shock enzymes; cf. review J.F.Rothman and S.L.Schmid, Cell 16, 5–9 (1980)).

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/content/home1.html
Phagocytosis requires adhesion between membrane and particles

Fig. 21a. Electron micrograph showing one invagination and pinch-off of clathrin coated vesicle.

Fig. 21b. Model of coated pit formation by selective binding of clathrin to the receptor via adaptin followed by lateral phase separation. Note that a selective lipid fraction comes with the protein.

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
**Phagocytosis**

Figure 24-24. Antibody-activated phagocytosis. (A) An IgG-antibody-coated bacterium is efficiently phagocytosed by a macrophage or neutrophil, which has cell-surface receptors that bind the tail (Fc) region of IgG molecules. The binding of the antibody-coated bacterium to these Fc receptors activates the phagocytic process. The tail of an antibody molecule is called an Fc region because, when antibodies are cleaved with the proteolytic enzyme papain, the fragments containing the tail region readily crystallize. (B) Electron micrograph of a neutrophil phagocytosing an IgG-coated bacterium, which is in the process of dividing. (B, courtesy of Dorothy F. Bainton, from R.C. Williams, Jr. and H.H. Fudenberg, Phagocytic Mechanisms in Health and Disease. New York: Intercontinental Book Corporation, 1971.)

Figure 25-46. Phagocytosis. This scanning electron micrograph shows a macrophage in the midst of consuming five red blood cells that have been coated with an antibody against a surface glycoprotein. (From E.S. Gold et al., J Exp. Med. 190:1849–1856, 1999. © The Rockefeller University Press.)
Phagocytosis

From: Scott C. Kuo, Johns Hopkins University
http: www.bme.jhu.edu/~skuo
Ion concentrations in an erythrocyte

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html

Fig. 13a. Equilibrium concentrations of major ions in the cytosol of erythrocytes and in blood plasma in mM. The membrane potential is $V_m = -6$ mV with the inside negative.
Erythrocyte shapes

Fig. 14. Various shapes of erythrocytes. Transition between the various shapes can be triggered biochemically by metabolic defects or diseases. The discocyte in the center represents the resting state.

From: "Handbook of Biological Physics", Lipowsky
http://www1.elsevier.com/homepage/sak/hbbiophy
Shape transitions in vesicles: Budding

Figure 3: Typical budding transition (type 1) of a DMPC vesicle in pure water. The temperatures, the volume, and the values for the area are given below the figures. In the temperature regime between 27.2°C and 40.9°C the vesicle shapes are stable. At 41.0°C the vesicle shape becomes unstable going over into the budded limiting shape. From 98 examined DMPC vesicles 35 vesicles showed this behavior. This transition happens if lateral stress is exerted to the vesicle before heating.

From: Shape transitions and shape stability of giant phospholipid vesicles in pure water induced by area-to-volume changes.
J Käs and E Sackmann
Biophys J. 1991 October; 60(4): 825-844.
Shape transitions in vesicles: Budding


Figure 5 Shape transition caused by cooling an outside budded vesicle. Starting at 52.6°C the neck between the bleb and the mother vesicle opens transiently for the first time at 49.6°C which is shown in the first three pictures and again at three lower temperatures, namely 45.7°C, 41.4°C, and 35.3°C. The bleb disappears at 31.7°C.
Shape transitions in vesicles: 
Budding

FIGURE 6 Discocyte-stomatocyte transition of a DMPC vesicle in pure water observed at increasing temperature. The temperature was varied from 41.9°C to 42.4°C at a rate of 0.02°C per image. The set of images starts at the left top and ends at the right bottom. The area varies from 1,370 μm² at 41.9°C to 1,380 μm² at 42.4°C and the volume is 3,200 μm³. In a separate stepwise heating cycle we found that all the shapes are stable up to a temperature of 42.3°C. We observed this type of transitions with 31 vesicles.

From: Shape transitions and shape stability of giant phospholipid vesicles in pure water induced by area-to-volume changes.  
J Käs and E Sackmann  
Curvature: \[ H = \frac{1}{R_1} + \frac{1}{R_2} \] / 2

Gaussian Curvature: \[ K = \frac{1}{R_1 R_2} \].

Bending Energy: \[ f_1 = \frac{\kappa}{2}(2H - C_0)^2 + \kappa_G K \]

\( C_0 \) is spontaneous curvature, e.g. in case of asymmetric membranes

\( \kappa \) is the bending modulus

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/content/home1.html
Total energy of a vesicle's membrane

\[ F = \left(\frac{\kappa}{2}\right) \int dA \ (2H - C_0)^2 + \kappa_G \int dA \ K + \left(\frac{k}{2}\right) \int dA \ \left(\phi/\phi_0 - 1\right)^2 \]

Bending Energy \hspace{1cm} Bending Energy \hspace{1cm} Elastic Energy
(Gaussian curvature) \hspace{1cm} (k is compressional modulus)

Usually the total area \(A_0\) and the enclosed volume \(V_0\) are usually constrained, but can be modified by temperature, osmotic stress, etc.

\[ F = \left(\frac{\kappa}{2}\right) \int dA \ (2H - C_0)^2 + \kappa_G \int dA \ K + \left(\frac{k}{2}\right)(A - A_0)^2/A_0 \]

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Shapes of minimal energy

reduced volume

\[ v = \frac{V}{\left[\frac{4\pi R_0^2}{3}\right]} \]

enters, where

\[ A = 4\pi R_0^2 \]

Fig. 6. Shapes of lowest bending energy for spontaneous curvature \( C_0 = 0 \) and several values of the reduced volume \( v \). \( D \) and \( D^{sto} \) denote the discontinuous prolate/oblate and oblate/stomatocyte transition, respectively. All shapes have the same area [9].

From: "Handbook of Biological Physics", Lipowsky and Sackmann
http://www1.elsevier.com/homepage/sak/hbbiophys/contenthome1.html
Membranes define cellular compartments

Fig. 10: Phase diagram of the ADE model. Shown are the shapes of lowest energy as a function of the reduced volume $v$ and the scaled preferred area-difference $m_0$ for $= 1:4$. The capital letters denote shape transitions, limiting lines and special points. The region of stable starfish vesicles lies at smaller $v$ [13].