

# Chapter 1

## Cells and Viruses

Cells are the smallest structural component of all known living organisms capable of self-maintenance and reproduction. Although cells vary greatly in their appearance or size, their structure is basically similar. Even the plant and animal cells show a significant degree of similarity in their overall organization.

There are two types of cells: **eukaryotic** and **prokaryotic**. The main difference between them is the method of genetic material storage: in eukaryotic cells — in an isolated nucleus, in prokaryotic cells — directly in the cytoplasm (there is no nucleus). Prokaryotic cells are usually independent (unicellular), while eukaryotic cells are often found in multicellular organisms.

Eukaryotic organisms are organisms composed of eukaryotic cells. We classify here: animals, plants, fungi, and protists (including organisms that do not fit into the remaining groups). A new classification of prokaryotic organisms distinguishes archaea (formerly known as archaebacteria) and bacteria (formerly eubacteria). Both are single cell organisms. Archaea live in extreme environments. They are divided into three main groups on the basis of living environment: **extreme thermophiles** (live in high-temperature environments, rich in sulfur compounds and low pH, such as hot springs and geysers), **extreme halophiles** (live in environments with high concentrations of NaCl, such as the Dead Sea), and **methanogens** (live in anaerobic environments such as swamps, produce methane and do not tolerate oxygen).

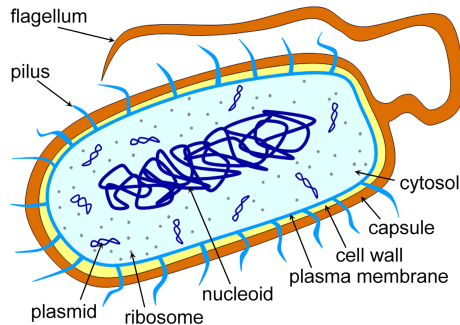
### 1.1 Cell Structure

All cells contain cytoplasm, cell membrane, and DNA (the carrier of genetic information). The cytoplasm is the liquid filling of the cell, with high density, holding all the cell's internal sub-structures (called the organelles), except for the nucleus. It contains also insoluble substances (so called cytoplasmic inclusions) and free ribosomes. A cell membrane surrounds the cytoplasm and

isolates cell from the environment. The cell membrane is composed of the phospholipid bilayer, which contains proteins and carbohydrates. The phospholipid bilayer is also the basic component of other biological membranes. DNA (deoxyribonucleic acid) is the genetic material. Eukaryotic cells possess several pieces of DNA, located in organelles surrounded by a phospholipid membrane (in the nucleus and mitochondria). Prokaryotic cells possess a single DNA molecule, directly in the cytoplasm.

### 1.1.1 Prokaryotic Cell Structure

A prokaryotic cell is simpler and smaller than an eukaryotic cell. A typical bacterial cell is  $5\mu\text{m}$  long and  $1\mu\text{m}$  wide. There are also smaller bacteria ( $0.5\mu\text{m}$  in diameter), or bigger. A prokaryotic cell contains DNA, cytoplasm, plasma membrane, and also some of the following components: cell wall, capsule, slime, flagellum and fimbriae/pili (Fig 1.1). It does not contain organelles. Prokaryotes are always single-cell organisms; however most are capable of forming stable aggregate communities. When such communities are encased in a stabilizing polymer matrix (“slime”), they may be called “biofilms”. Bacterial biofilms may be 100 times more resistant to antibiotics than free-living unicells and may be nearly impossible to remove from surfaces once they have colonized them.



**Fig. 1.1** Generalized structure of the prokaryotic cell

A bacterial cell wall contains a unique structure called peptidoglycan. Archaea do not have peptidoglycan, which means that they are resistant to many antibiotics interacting with the cell wall. Due to differences in cell wall structure and the effect of staining by the Gram dye, bacteria can be divided into two groups: Gram-negative and Gram-positive. The cell wall of Gram-negative bacteria consists of three layers: the periplasmic space, which is an open area on the outside of the plasma membrane, then a thin layer of peptidoglycan, and an outer membrane surrounding the peptidoglycan.

In the cell wall of Gram-positive bacteria, there is no periplasmic space and outer membrane, while the peptidoglycan layer is thicker. As a result, they are more sensitive to the lysozyme (an enzyme that is naturally present e.g. in saliva or tears and is able to hydrolyze bacteria cell wall), and penicillin (antibiotic derived from fungi).

Capsule and slime form hydrophilic surrounding of the cell wall in most bacteria. Capsule sticks more closely to the wall than slime. Flagellum is a tail-like projection that protrudes from the cell body. It facilitates the movement of mobile bacteria. Fimbriae and pili are structures similar to short hairs. They attach cells to other cells, which is important when infecting other organisms.

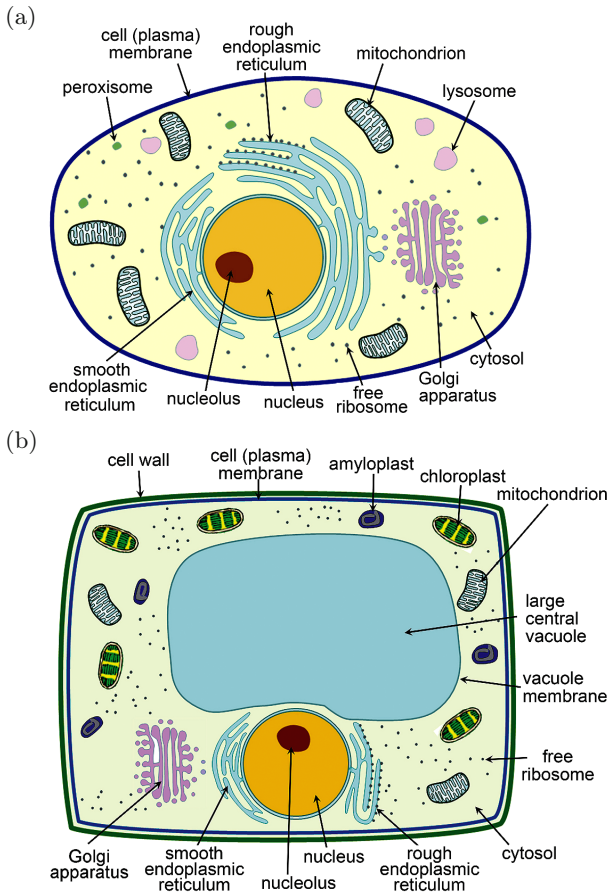
Spores are small, haploid and unicellular structures used for reproduction. They can be found in plants, algae, fungi, protozoa and bacteria. Bacteria spores have thick wall, which allows them to survive in wide range of temperatures, humidity and other unfavorable conditions, which kills vegetative forms exhibiting normal life activity.

All information essential for the bacteria survival (in the environment typical for it) are saved in the chromosome (bacterial nucleoid). Bacterial chromosome is usually large, circular piece of DNA, but sometimes linear chromosomes and several copies of them occur. Bacteria may have also plasmids. These are (usually) circular DNA molecules that are replicated independently of the chromosome. Plasmids often contain genes that could be very useful, for example include information how to use a compound present in environment. If this compound is in the environment, the bacteria gain an obvious advantage over other bacteria, which do not have the ability to decompose that compound. Plasmids can be different in sizes, from tiny to megaplasmids exceeding the size of the genomes of some bacteria. Plasmids are natural vectors, by which continuous exchange of genetic information among bacteria (sometimes even completely unrelated) occurs. For example, many antibiotic resistance genes reside on plasmids, facilitating their transfer. Plasmids serve as important tools in bioengineering, where they are commonly used to multiply or express particular genes.

### *1.1.2 Eukaryotic Cell Structure*

Eukaryotic cells contain organelles, which are defined as membrane-enclosed structures (such as nucleus, mitochondria, chloroplasts, endoplasmic reticulum, Golgi apparatus, lysosomes, vacuoles or peroxisomes). Animal cell is surrounded only by the plasma membrane, while the plant cell has an additional layer called the cell wall, which is formed from cellulose and other polymers (Fig. 1.2). Typical size of eukaryotic cells varies from 5 to 50  $\mu\text{m}$ .

The nucleus is the largest structure in the eukaryotic cell. It is not part of the cytoplasm, which can be defined as everything that is surrounded by a



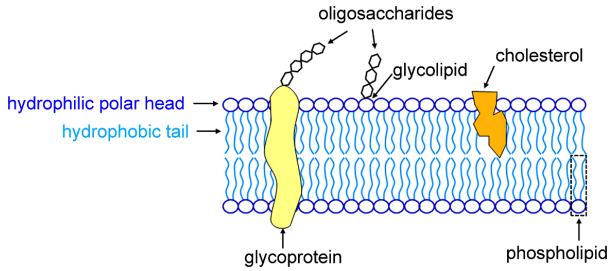
**Fig. 1.2** A typical eukaryotic cell illustration: (a) animal; (b) plant

cell membrane, excluding the nucleus. The term “cytoplasm” is however often used in the narrower sense, meaning only the cytosol. **Cytosol** is the cytoplasm after exclusion of all organelles. It is a liquid, water colloid containing proteins (suspended or dissolved), lipids, fatty acids, free amino acids and minerals (e.g. calcium, magnesium, sodium). Complex network of protein fibrils (microfilaments) and microtubules, forming the **cytoskeleton** (which allows the cell to maintain its shape and size), is also an important component of the cytoplasm.

## 1.2 Biological Membranes and Their Lipid Component

All biomembranes (cell membrane and membranes of all intracellular organelles) are highly selective permeable barriers, setting out the boundaries

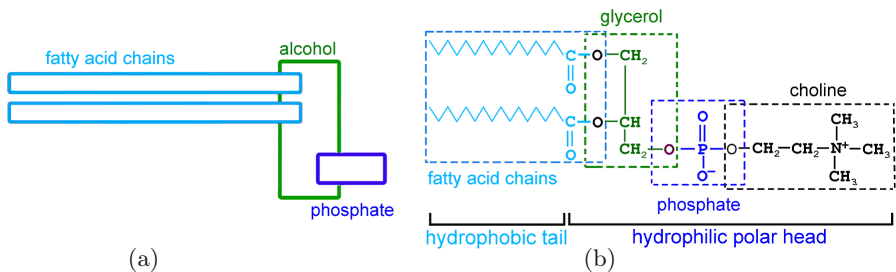
of cells and organelles. They are built from lipids and proteins. The lipids existing in biological membranes there are mainly phospholipids and cholesterol. Carbohydrates may be attached to proteins and phospholipids present in the membranes — forming respectively glycoproteins and glycolipids (Fig. 1.3). The membranes are liquid layered structures: the majority of lipid and proteins molecules can move fast along the membranes. It is worth noting that the lipids, besides cell membrane building function, can also be used as “fuel particles”, energy storing molecules and as signaling molecules (ch. 8).



**Fig. 1.3** Scheme of a typical biological membrane (lipid-protein bilayer)

### 1.2.1 Phospholipids

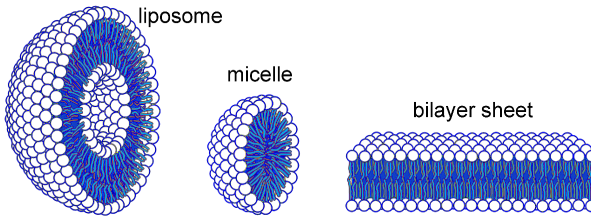
Phospholipid molecule is composed of hydrophilic (with high affinity for water) polar group, so-called “head”, and hydrophobic (with low affinity for water) “tail”. Hydrophobic tail is made up of two fatty acid chains (Fig. 1.4). Most polar phospholipids are phosphoglycerides that contain glycerol connecting the head with the tail. For example phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine or phosphatidylinositol belong to this group. Chains of fatty acids in biological membranes usually contain an even number of carbon atoms, generally from 14 to 24. There are saturated (the neighboring carbon atoms are linked by a single bond) or unsaturated fatty



**Fig. 1.4** The chemical structure of phospholipids: (a) general model, (b) structure of phosphatidylcholine

acids (when some of the neighboring carbon atoms are connected by a double bond). The chain length and degree of saturation of fatty acids in lipids has significant influence on the fluidity of biological membranes.

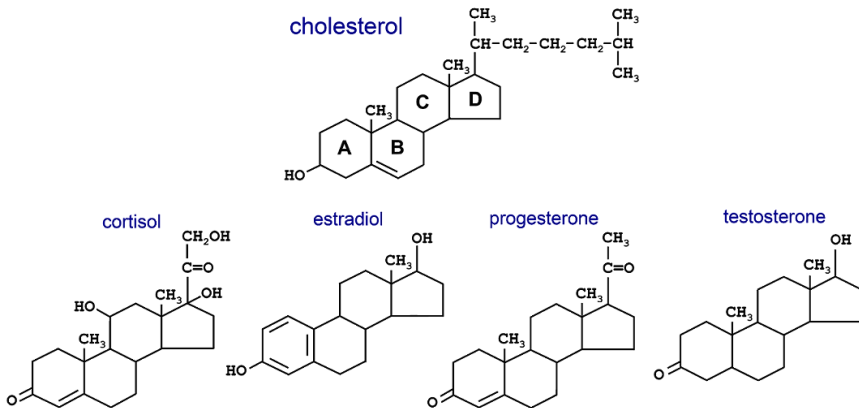
When phospholipid molecules are placed in water, the hydrophilic heads are oriented facing the water and the hydrophobic tails avoid water. As result, the structure called the bilayer sheet, liposome, or micelle may be formed (Fig. 1.5).



**Fig. 1.5** The structures formed by phospholipids in aqueous solutions. The figure presents a section through the liposome and micelle and a fragment of the bilayer sheet. Altered from: [http://upload.wikimedia.org/wikipedia/commons/c/c6/Phospholipids\\_aqueous\\_solution\\_structures.svg](http://upload.wikimedia.org/wikipedia/commons/c/c6/Phospholipids_aqueous_solution_structures.svg)

### 1.2.2 Cholesterol and Steroids

Cholesterol does not exist in most prokaryotic cells, whereas it is a common component of mammalian cell membranes. It fulfills a critical role in the regulation of membrane fluidity. Also synthesis of steroid hormones is based on

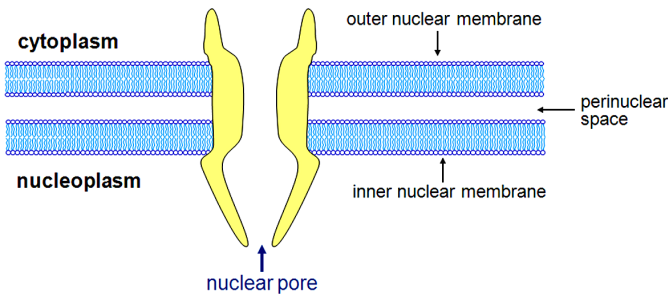


**Fig. 1.6** The structure of cholesterol and other important steroids. They are characterized by the presence of four hydrocarbon rings, marked here as A, B, C and D. Due to the presence of the hydroxyl group (-OH) cholesterol has amphipathic properties (it has hydrophobic and hydrophilic parts).

cholesterol (Fig. 1.6; ch. 8.1). Accumulation of cholesterol in an artery wall plays a key role in atherosclerosis — disorder, which can lead to heart attack or stroke.

## 1.3 Nucleus

The nucleus consists of a nuclear envelope (constructed from two membranes; Fig. 1.7), the nucleolus and nucleoplasm. The outer nuclear membrane is continuous with the membrane of the rough endoplasmic reticulum (RER). The space between the membranes (perinuclear space) is continuous with the RER lumen. With the inner face of the nuclear envelope the nuclear lamina is associated, which is built from fibrous proteins called lamins. The nuclear lamina binds inner nuclear membrane with genetic material. The genetic material formed in the chromatin/chromosomes is located mainly in nucleoplasm. However, the parts of various chromosomes, which contain groups of genes encoding rRNA (ch. 3.3.3), could be concentrated in one region forming the nucleolus. Its main role is the production of rRNA.



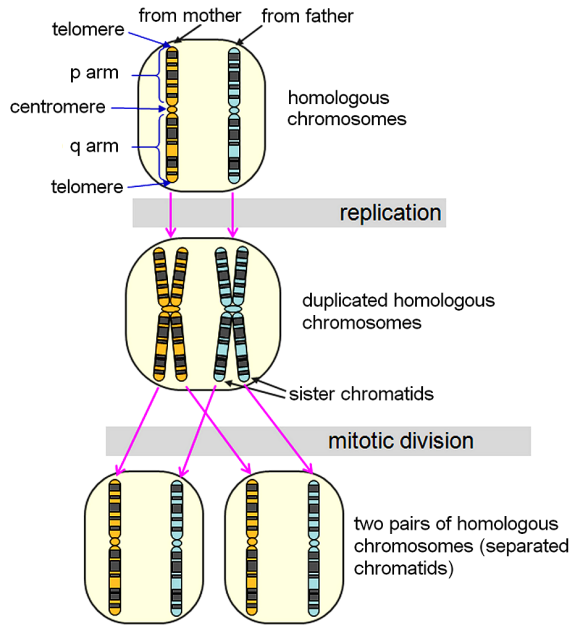
**Fig. 1.7** Scheme of a nuclear envelope which is built from two layers of double lipid membrane. In the nucleus of mammals there are about 4,000 nuclear canals (pores) present, each composed of more than 100 various proteins.

### 1.3.1 Chromosomes and Karyotype

Chromosome is condensed structure, which is formed from a single DNA molecule and associated proteins. In cells which are not dividing at the moment, chromosomes are not visible in light microscope, because DNA together with accompanying proteins (i.e. chromatin) is loosely spreaded across the nucleus. During cell division, in the stage of metaphase (see ch. 7), chromatin condenses and becomes visible in the form of chromosomes.

Each chromosome has the short and long arm (designated as p, from the “petit” and q, from the “queue”). The arms are separated by narrow region

called the centromere (Fig. 1.8). The chromosomes of the same shape and size, containing similar genetic information (i.e. genes) are called homologous chromosomes. In diploid cells, one of them comes from the mother and the other from the father. During cell division, at metaphase, replicated chromosomes contain two sister chromatids linked with centromere. Sister chromatids are identical copies of the chromosome: they contain the same genes and the same alleles (i.e. versions of genes in a particular location — locus — on the homologous chromosome). However, homologous chromosomes contain the same genes, but alleles can vary. During cell division pairs of chromosomes are separated into two daughter cells.



**Fig. 1.8** Homologous chromosomes during mitotic cell division

Chromosomes are visible under the microscope only after staining. Then, they look like strings with dark and light transverse stripes. A set of chromosomes present in the cell during metaphase is called a **karyotype**. Human germ cells (egg or sperm) contain one set of chromosomes (haploid cell,  $1n$ ), that is 23 pieces: 22 autosomes and the X or Y. Somatic cells (remaining cells of the body) normally contain two homologous sets of chromosomes, i.e. 46 chromosomes (diploid,  $2n$ ). One set comes from mother, the other — from father. In other species the number of chromosomes varies from 1 to 1260.

Human somatic cells contain two chromosomes that determine sex: XX in females and XY in males. In germ cells there is only one sex chromosome: in female it is always X chromosome, in male — X or Y.

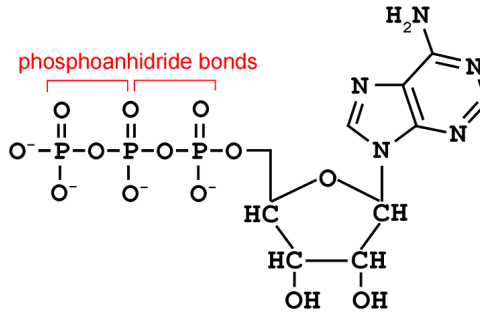


## 1.4 Cytoplasmic Organelles

Organelles can be defined as intracellular, bounded by membrane, protein-lipid structures (the cell nucleus is also an organelle). In cytoplasm there are present mitochondria, chloroplasts, endoplasmic reticulum, Golgi apparatus, peroxisomes, lysosomes, vacuoles, and glyoxysomes.

### 1.4.1 Mitochondria

Eukaryotic cells have a lot of mitochondria — they can be up to a quarter of the cytoplasm volume. They are elongated organelles with a diameter ranging from 0.5 to 10  $\mu\text{m}$  (the size corresponds to a bacterial cell). Mitochondria are composed from two membranes: outer and inner, which is strongly folded. Mitochondria have their own DNA (defined as the mtDNA) coding for proteins and RNA. However the majority of mitochondrial proteins are encoded by nuclear DNA.



**Fig. 1.9** Chemical structure of ATP (adenosine triphosphate)

The main task of mitochondria is the production of ATP (adenosine triphosphate), which provides source of energy for most cellular processes (Fig. 1.9). Energy is stored in phosphate bonds and can be released during the hydrolysis of ATP to ADP (adenosine diphosphate) and AMP (adenosine monophosphate).

In animal cells, the catabolism (degradation of glucose and fatty acids) is the main source of energy for ATP synthesis. The production of ATP takes place in the inner mitochondrial membrane. Energy is transferred from electron transport chain to the ATP synthase by movements of protons across this membrane. As a result of disturbances in electron transport, the free radicals (and other reactive oxygen species) can be generated, which can lead to damage of cell structures and to cell senescence.

### 1.4.2 *Chloroplasts*

Chloroplasts, like mitochondria, are composed from inner and outer membrane. Chloroplasts also have their own DNA, but most of their proteins are encoded by nuclear DNA. The inner membrane of the chloroplast forms thylakoids, that contain chlorophyll. It absorbs light necessary for the light reaction of photosynthesis. In this stage, thanks to the energy absorbed from light quanta, oxygen molecule and hydrogen ions are formed from two water molecules. This results in forming of the concentration gradient in the thylakoid membrane. The flow of ions through the membrane is connected with the synthesis of ATP. Stroma is the liquid component of the chloroplast, in which, using the energy from ATP,  $\text{CO}_2$  is assimilated and synthesis of saccharides occurs (dark reactions of photosynthesis).

### 1.4.3 *Endoplasmic Reticulum and Golgi Complex*

Endoplasmic reticulum (ER) forms an irregular network of cisternae, vesicles and tubules inside the cell isolated from the cytosol by biological membranes. It exists in two forms: smooth and rough. The main role of the rough endoplasmic reticulum is to process the newly synthesized proteins, so it is associated with ribosomes (ch. 6.2.1). Smooth endoplasmic reticulum is involved in the synthesis and metabolism of lipids. It appears in highest quantities in liver cells (hepatocytes).

After the initial processing of proteins in rough endoplasmic reticulum, they are closed in transport vesicles and directed to other membranous structures — the Golgi apparatus (ch. 6.2.2). These structures are the main place of sorting and modifications of proteins and lipids. Here, glycoproteins are produced and they are transported further to their destinations. Golgi apparatus is also a place of synthesis of polysaccharides and mucopolysaccharides.

### 1.4.4 *Peroxisomes, Lysosomes, Vacuoles, and Glyoxysomes*

Peroxisomes contain enzymes, which allow degradation of amino acids and fatty acids. In these reactions the hydrogen peroxide is formed, which is harmful to cells. It is converted to water and oxygen by an enzyme called catalase.

The main function of lysosomes is degradation of unnecessary macromolecules. Macromolecules are hydrolyzed by the respective enzymes: nucleic acids (DNA and RNA) by **nucleases**, proteins by **proteases**, and lipids by **lipases**. Lysosomes are present only in animal cells. In plant cells their functions are performed by the vacuoles.

Vacuoles store water, ions, saccharides, amino acids and other small molecules. They can also store unnecessary cell products, which can undergo degradation here. Vacuoles usually fill about 30% of the cell volume, but can increase its volume up to 90%.

Glyoxysomes are found mainly in plant seeds. Their main function is to convert fatty acids into acetyl-CoA molecules, which in glyoxylate cycle are converted into monosaccharides. This mechanism is important in the use of fat reserves of oilseeds. It occurs during germination and when it is necessary to launch a non-carbohydrate energy reserves in plants. Glyoxysomes and peroxisomes are also called microbodies.

## 1.5 Viruses, Bacteriophages, and Virophages

Viruses are macromolecular complexes built from proteins and nucleic acids. Viruses are not able to replicate by themselves — so they can not be treated as living organisms. Replication of viruses is possible only within other cells, using enzymes from infected cells. Because of that viruses are intracellular parasites. Most viruses have a diameter between 10 and 300 nm (but discovered in 2013 Pandoraviruses have a size approaching  $1\mu m$ ). The molecule of the virus (**virion**) consists of one or more molecules of DNA or RNA (as a carrier of genetic information of the virus) and a protein shell called a **capsid**. Some viruses have an additional lipid envelope which surrounds the capsid. Most viruses are pathogens — after penetration into living cells they cause the diseases. Various viruses specifically attack different types of cells (e.g. the HIV virus attacks only the immune cells, mainly T lymphocytes). When a virus encounters “his” cell, it attaches to the cell membrane using specific receptors (proteins on the surface of host cells, which normally have other functions). Then, it can inject its genetic material into the cell or whole virus is absorbed entirely by the cell. Inside the cell, based on the information contained in the genetic material of the virus, there are created new virus molecules. They can remain in the cell for a long latent phase, or leave after the cell destruction. It sometimes happens, that the virus remains in the cell in form of genetic material integrated with the host genome.

Viruses can also infect bacteria. Such viruses are called bacteriophages (or commonly phages). Bacteriophages can be used for treating bacterial infections as an alternative to antibiotics. In biotechnology and genetic engineering, phages and other viruses are used to transfer genetic information between cells (as so-called “vectors”).

There are also viruses that infect other viruses. The first known, called Sputnik, was discovered in 2008. It is a subviral agent that reproduces in amoeba cells which are already infected by a certain helper virus.

Sputnik uses the helper virus's machinery for reproduction and inhibits replication of the helper virus. Viruses that depend on co-infection of the host cell by helper viruses are known as satellite viruses. They act as a parasite of helper viruses. In analogy to the term bacteriophage they were called virophages.

The risk associated with viral infections may be very different. Many viral infections do not cause diseases, for example, most people are infected with cytomegalovirus (CMV), however, do not show symptoms of the disease. There are also viruses that often lead to death of the organism, such as coronavirus which cause Severe Acute Respiratory Syndrome (SARS) or the HIV virus causing AIDS.

### 1.5.1 *Classification of Viruses*

The classification of viruses could be based on the type of genetic material held by the virus and on strategy of genetic material replication (the Baltimore classification). Besides double-stranded DNA, the carrier of genetic information in prokaryotic and eukaryotic cells, also single-stranded DNA or RNA can be a genetic material in viruses. Viruses were divided into seven classes (ds — double strand, ss — single strand):

- I. dsDNA viruses — contain double-stranded DNA;
- II. ssDNA viruses — contain single-stranded DNA;
- III. dsRNA viruses — contain double-stranded RNA;
- IV. ssRNA(+) viruses — contain single-stranded RNA, (+) sense;
- V. ssRNA (-) viruses — contain single-stranded RNA, (-) sense;
- VI. RNA viruses that use virally encoded reverse transcriptase to produce DNA from the initial virion RNA genome;
- VII. DNA viruses that use virally encoded reverse transcriptase.

The last two classes of viruses are known as retroviruses. Rewriting of the genetic information from RNA to DNA is an essential part of their replication cycle. This reaction is catalyzed by reverse transcriptase — an enzyme encoded by the virus genome (ch. 5.9).

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