3. Reproduction of cells

Multiplication (division) of the cell belongs to its primary functions. Cell division is a part of subsequent processes, known as **cell cycle.** In multicellular organisms it is not only way how to increase number of cells, but include also structural and functional specialization of cells – via differentiation. If particular cell will continue in cell cycle toward its division, depends on many factors – extracellular and intracellular, stimulating or inhibiting.

In regard to course of division and its result, we recognize generally three types of cell division – amitosis, mitosis and meiosis.

Amitosis (direct division) happens immediately after replication of DNA. In form of "binary fission" is typical for bacterial cells. Multiplication of intracellular endosymbiont organelles (mitochondria and chloroplast) termed as "endoreduplication" or fission.

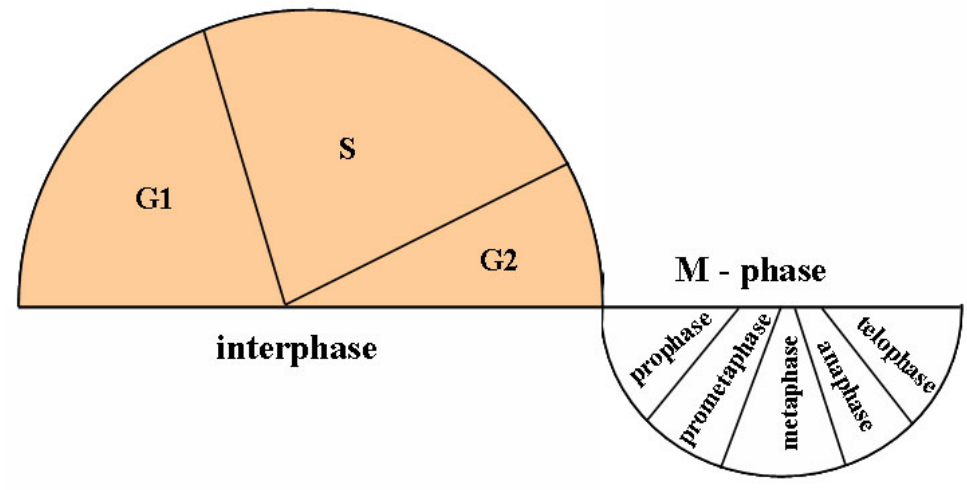
Mitosis is indirect division, because between replication of DNA (S-phase of cell cycle) is intermission (gap) – G2 phase of cell cycle. Mitosis is for multicellular organisms standard mode of cell division, because it guarantees genetic identicalness (concordance) of daughter cells.

Meiosis (reductive division) is essential precondition to gametes origin – e.g. haploid cells having single chromosome of each type. Fertilization of gametes recreates original – species-specific (diploid) number o chromosomes.

In the world of protozoa, especially parasitic ones, does exist many extraordinary ways of cell division, but these out of range of this text.

3.1 Cell cycle of eukaryotic cells

The cell cycle consists of two main phases, which are **interphase** and **M-phase** (mitosis phase). The individual phases of the cell cycle proceed after each other (Fig. 28). The process is regulated by a complex of regulatory proteins, which are coded by tumor suppressor genes (they have a control function) and protooncogenes (stimulating division). A failure of their normal function can cause deregulation of the cell cycle and a consecutive malign transformation of the cell, meaning a change to a cancer cell.



● **Figure 28.** Scheme of the cell cycle

The time duration of the cell cycle is genetically determined and is connected with the telomeres of chromosomes, but is also effected by different signal molecules from the environment and by the cell itself (look up part 2 – chapter 10). It differs, depending on the cell type of various tissues.

Interphase is a time between two divisions and is made up of G_1, S a G_2 phase. The duration of the phases differs and depends on the type of the cell and the life period of the individual.

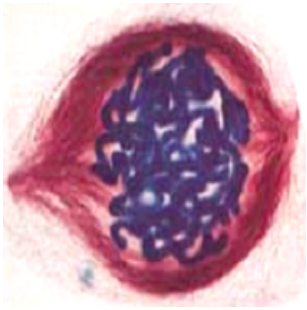
G_1 phase begins after the end of the previous mitosis. It is characterized by an intensive synthesis of proteins, and usually also growth and of new cell. During this process, in the so called **G_0 phase**, the cell differentiates, to fulfill specialized functions for organism. Time duration of G_0 phase is the most variable component of the interphase. In embryonic cells it is short, while with older individuals it is longer. In case that the cell will not divide (e. q. a mature human erythrocyte) this phase is the final one. At the end of the G1 phase is the so called **main checkpoint**, in which it is decided weather the cycle will continue or not. If it will, it is necessary to find and repair mutations in DNA. If the number of mutations is higher then can be repaired in a given time limit, the protection mechanisms evoke a „silent"cell death (**apoptosis**). This step is an important protection of the organism against the accumulation of mutations and the consecutive formation of cancer cells.

S phase (synthetic) is a time during which the duplication (semiconservative replication) of the nuclear DNA occurs. Considering the length of the DNA in the nucleus (in women around 2 m) and the processes of their repeating control and the repair of defects, it is the longest phase of the cell cycle, even tough the replication takes place at numerous places simultaneously. At its end each chromosome is doubled, meaning it consists of two chromatids connected by Scc1 and Scc3 proteins – cohensins.

G_2 phase is a relatively short period of preparation for mitosis and it contains another checkpoint of the cell cycle. After replication it is important for the cell to check the DNA and repair the potential mistakes. It is also important to prepare the necessary proteins, mainly tubulin, as well as sufficient sources of energy. During this phase the duplication of the centrosome occurs (made up of centrioles). At the same time, on the second centrosome, a so called astral complex and the basis of non-kinetochore microtubules are formed.

M phase - mitosis is a part of the cell cycle, during which the division of the nucleus occurs (karyokinesis) and consecutively the division of the whole cell (cytokinesis) happens. It was first described and named by Walther Flemming (1887 – 1880).

Mitosis is divided into five phases – prophase, prometaphase, metaphase, anaphase and telophase.



During **prophase** (Fig. 29) the condensation of chromatin (chromosomes) begins. Continue elongation of the non-kinetochore microtubules, from each centrosome toward another one. These fibrils slide on each other, which starts the movement of centrosomes towards the opposite cell sides (poles). An early division spindle is formed. Starts the process of nuclear envelope disorganization and when it "disappears" finishes prophase.

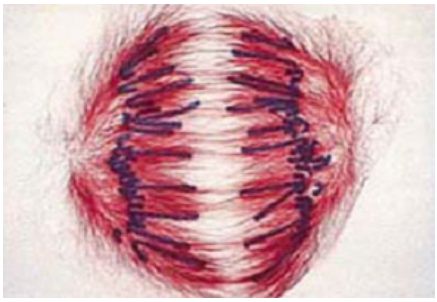
● **Figure 29.** Prophase in plant cell

During **prometaphase** the movement of the centrosomes towards the poles continues. The condensation of the chromosomes goes ahead and they can be observed as stick-like formations. The process of chromatid separation from the end part of the chromosomes (telomeres) begins. On the outer side of each chromatid centromere functional kinetochores are formed. At the same time, kinetochore microtubules (KMT) "grow out" from each centrosome (elongated by polymerization of tubulin dimers) and enter the area of the former nucleus – "searching" for connection to kinetochores. When kinetochore microtubules connect to both kinetochores of particular doubled chromosome, they begin to elongate and shorten (by depolymerization), to transport the chromosome to the central (equatorial) plain of the cell. This takes a certain amount of time, making prometaphase the longest period of mitosis.

Metaphase (Fig. 30) is a relatively short period during which the duplicated chromosomes are located in the equatorial plain of the cell. The centrosomes are pushed to the opposite sites of the cell – spindle body is finished. All the kinetochores are occupied by kinetochore microtubules. Cohesins, except for the parts between centromeres of sister chromatids, are destroyed. This is why the metaphase chromosomes have the shape of the letter X. By this, all the conditions for the activation of the so called anaphase promotion complex (**APC**) are fulfilled and mitosis can continue to anaphase – chromatids are separated and transfer of daughter chromosomes can start. The mechanism is described in detail in chapter 10 of the second part of the text-book.

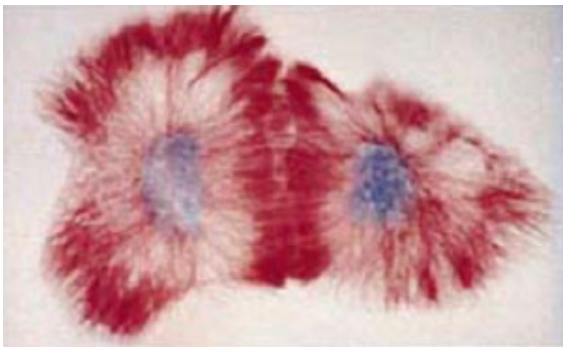
● **Figure 30.** Metaphase in a plant cell

During **anaphase** (Fig. 31) two parallel processes take place. Anaphase A is characterized by the shortening of the KMT, which is responsible for transporting ("pulling") of the individual daughter chromosome, to the centrosomes. In anaphase B the elongation of the non-kinetochore microtubules continues which elongates the whole cell and creates the space for cytokinesis. Both processes are supported by the activity of the so called motor proteins – dyneins and kinesins.



● **Figure 31.** Anaphase in a plant cell

During **telophase** (Fig. 32) the nucleus is reformed close to each centrosome. The formation of two new nuclei in the cell is called **karyokinesis**. Chromosomes decondense and the functional organization of the nuclei is renewed. Parallelly – the cell divides (**cytokinesis**) and two new identical daughter cells are formed – in animal cell by "cleavage" and plant cell by building of septum "from inside". Important is, that each of the two daughter cells retains one centrosome near the nucleus with the base of the non-kinetochore microtubules – new cell keeps the essential components necessary for the next division. If the cytokinesis doesn't take place, a so called syncytium is formed.



● **Figure 32.** Telophase (cytokinesis) in a plant cell

Mitosis makes up only about 5 – 10 % of the cell cycle duration. This is the reason why – even within very intensively proliferating tissues – it is difficult to find cells undergoing a certain phase of mitosis. Because of this, phenomena connected with the division of somatic cells are studied mainly on tissue cultures during *in vitro* cell cultivations (see chapter 4).