Mitosis, development, regeneration and cell differentiation

**Mitosis** is a type of cell division by binary fission (splitting in two) which occurs in certain eukaryotic cells.

Mitosis generates new body cells (somatocytes) for renewal and repair.

New cells in the developing embryo are produced by mitosis. These cells then differentiate often losing the ability to undergo further mitosis at some stage

**Differentiation**: the process by which cells develop into specific cell types by taking on shapes and expressing the specific enzymes required for their different roles within the body. E.g. cells in the embryo may develop into skin, gut, blood, muscle or nerve cells, etc. Often differentiation occurs in stages, e.g. stem cells in the bone marrow may undergo mitosis and some of the daughter cells become new stem cells, whilst others become differentiated into myeloid and lymphoid stem cells, which then differentiate into the various types of blood cell:

- **Multipotential stem cell in bone marrow**
  - **Myeloid progenitor cell**
    - Red blood cell
    - Platelet progenitor
      - Platelets
  - **Mast cell**
  - **Granulocyte progenitor**
  - **Lymphoid progenitor cells**
    - T lymphocytes
    - NK cells
    - B lymphocytes
  - Neutrophils
  - Basophils
  - Eosinophils
  - Monocytes
  - Macrophages

The most basic stem cells are multipotent (or pluripotent) meaning they have many potential fates through differentiation. The fertilised egg cell is totipotent (possessing within it all the possible cell fates). Cells like neutrophils are terminally differentiated – they have no ability to undergo mitosis and will eventually die.

Cancer cells are immortalised since they can undergo mitosis indefinitely.
The Cell Cycle

Cell cycle: the life-cycle of the cell. Cells in multicellular animals, like humans, cycle between two phases: interphase (I phase), the interval between mitosis, and mitosis (M phase) itself. Most cells are in interphase most of the time.

Interphase (I phase): cells in interphase are metabolically active, they grow and synthesise enzymes, especially those enzymes required for DNA replication (like DNA polymerase) as they prepare for mitosis. In most mammalian cells, interphase occupies ~18-20 h of the 24 h cycle. Interphase is subdivided into the: G₁, S and G₂ phases.

G₁ and G₂ are gaps or growth phases. G₁ is often the longest phase (~ 10 h / 24 h) as the cells use this as an opportunity to resume growth following mitosis. It is here that the cell prepares for DNA replication.

S phase (~ 5-6 h / 24 h): this is the DNA synthesis phase. The cell’s DNA replicates (duplicates) during this phase.

G₂ (~ 3-4 h / 24 h): a short gap between DNA synthesis and the onset of mitosis.

Cells may exit the cell cycle, usually at G₁, and enter a phase called G₀. G₀ cells may be quiescent (resting) cells, they may be busy performing other tasks (like metabolising glucose in the liver) or their DNA might be too damaged to enable them to replicate. Terminally differentiated cells have left the cell cycle permanently. Some differentiated cells are not in terminal stages, and can be induced to re-enter the cell cycle. For example, damage to the liver and kidneys can induce liver and kidney cells to re-enter the cycle in order to replace those cells that have been destroyed (regeneration). Most cells in the nervous system, especially the central nervous system (CNS) are terminally differentiated.
Mitosis (copy division): the process whereby a cell divides into two, such that each daughter cell receives a full copy of the genome (the two daughter cells are genetic clones).

Centriole: a short cylinder of 9 triplets of microtubules

1. Interphase cell
   • Metabolically active: growing, performing work
   • Preparing for mitosis
   • Chromosomes diffuse (not visible with light microscope)
   • Nucleolus visible within nucleus
   • A pair of microtubule-organising centres MTOCs (centrosomes in animal cells)
   • Each chromosome duplicates (DNA synthesis)

Centrosome: a pair of centrioles

Cell skeleton (cytoskeleton)
Made up of protein fibres (filaments and tubules) of 3 principle types:
- Microfilaments (thin (~8 nm diameter) actin filaments)
- Microtubules (thicker (~20 nm diameter), made of tubulin)
- Intermediate filaments (intermediate thickness, e.g. keratin in skin cells)

Maintains cell shape, gives the cell strength and toughness, moves the cell and its organelles

Q. What is the nucleolus and what is its function?
Stages of mitosis:

2. **Prophase**

- Cell rounds up into a ball
- Chromatin begins to condense
- Nucleolus disappears
- Centrioles begin to move to opposite poles of the cell
- Microtubules (MTs) dissolve and reassemble (polymerise) around the centrosomes, from which they extend.

3. **Prometaphase**

- Chromosomes condensed and arranged in sister pairs (*chromatids*)
- Chromosomes begin to move
- Centrioles begin to move to opposite poles of the cell
- Microtubules have formed the **mitotic spindle**; proteins attach to the centromeres to form kinetochores; spindle MTs attach to kinetochores and pull on chromosomes
- Nuclear envelope disperses

3. **Metaphase**

- Paired chromatids align along the **cell equator** (or midline of the nucleus) by the mitotic spindle
- This (imaginary) midline is called the mitotic plate
5. **Anaphase**

- Paired chromosomes separate at their kinetochores and move to opposite poles (the kinetochores move along the microtubules)

6. **Telophase**

- Chromosomes arrive at opposite poles
- New nuclear envelopes form around each daughter nucleus
- Mitotic spindle disperses
- Chromosomes disperse as their chromatin becomes diffuse (and invisible under the light microscope)

7. **Cytokinesis**

- A ring of actin filaments forms around the cell equator (beneath the cell membrane) and contracts, pinching the cell into two new daughter cells
- At some point each centrosome duplicates
- Each daughter cell returns to interphase and prepares for the next mitotic division
Q. What is a chromosome?

Q. What is chromatin?

Q. What is a chromatid?
Meiosis

Meiosis is a reduction division in which the number of chromosomes is halved from the normal diploid state to the haploid condition.

In diploid organisms, such as human beings, there are two sets of chromosomes in each cell – one paternal set (23 chromosomes) and one maternal set (23 chromosomes). For each paternally derived chromosome there is an homologous maternally derived chromosome with the same genes but different alleles. Thus, there are 46 chromosomes in total (23 homologous pairs).

Homologous: similar in structure or function.

The haploid number of chromosomes: \( n = 23 \)

The diploid number of chromosomes: \( 2n = 46 \)

Prior to meiosis the DNA duplicates, giving the cell \( 2 \times 2n \) chromosomes. The daughter cells must end up with the haploid \( n \) chromosomes and so the parent cell divides twice, resulting in 4 haploid daughters:

**Meiosis:**

![Meiosis Diagram]

Human beings exhibit a gametic life cycle: in which the organism is diploid.

• The body contains two principle cell lineages: the germ cell line, which leads to the reproductive gametes and the somatic cell line which produces the tissues of the body.

• The diploid germ-line stem cells undergo meiosis to create haploid gametes (spermatozoa and ova), which fertilize to form the diploid zygote.

• The diploid zygote undergoes repeated cellular division by mitosis to grow into the organism. Mitosis creates two cells that are genetically identical to the parent cell.

• Mitosis creates somatic cells and meiosis creates germ cells (gametes).
Spermatocyte: 2n

Oocyte: 2n

Meiosis

Egg (ovum)

Polar bodies

4 haploid cells (n)

Fertilisation

Zygote (diploid 2n)

Mitosis

Adult (2n)

Gametogenesis

Male: spermatogenesis

Female: oogenesis

Germ-line stem cells

Males never run out of sperm because spermatocytes are produced by mitosis from spermatogonia.

Human males produce approximately 1000 sperm per second (30 billion/year).

Each ejaculation should contain 200 - 300 million sperm.

Meiosis in human females begins before birth but stops and does not resume until after puberty.

Each month, approximately 1000 oocytes will mature but most will die.

Ovulation occurs about once every 28 days. Females ovulate approximately 400 times during their lifetime.

The second meiotic division occurs only after fertilisation.