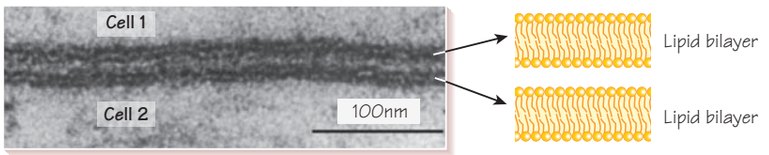
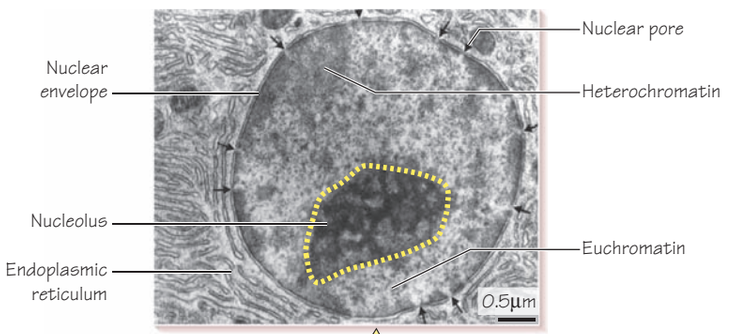
5 The cell and its components

(a) Plasma membrane (electron micrograph)

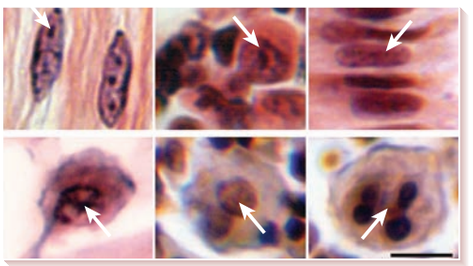


Electron microscopy shows the plasma membranes of two adjacent cells

(b) The nucleus (electron micrograph)



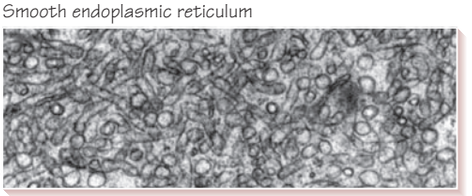
(c) Appearance of nuclei in H&E stained sections



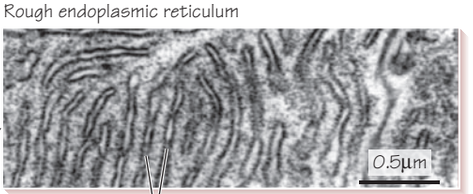
Nuclei (arrowed) in histological sections have a variable appearance. Chromatin can be condensed (dark staining) or non-condensed (lighter staining) and nucleoli can be prominent or difficult to see.

(d) Electron micrographs of:

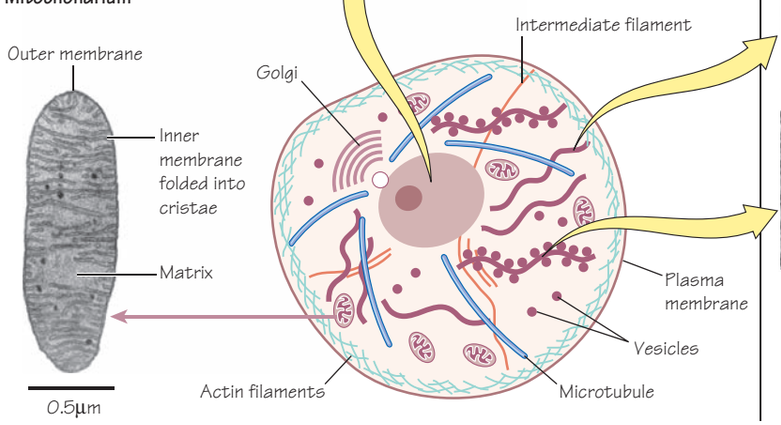
Smooth endoplasmic reticulum



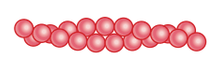
Rough endoplasmic reticulum



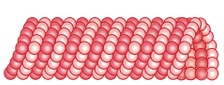
(f) Mitochondrium



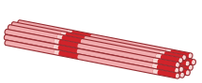
(g) Cytoskeleton (in electron micrographs and diagrams)



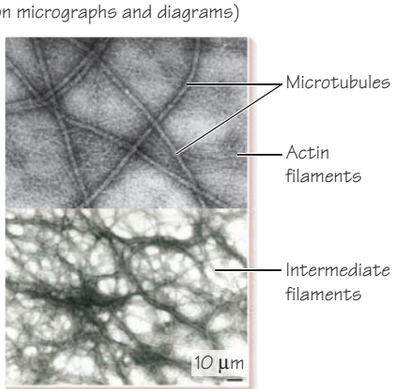
Actin filaments
7nm in diameter



Microtubules
25nm in diameter

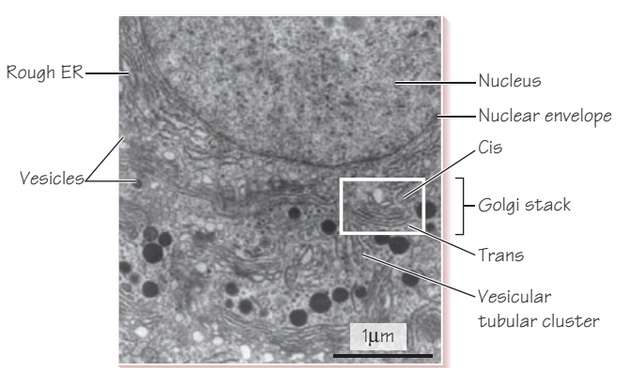


Intermediate filaments
10nm in diameter



EMs reproduced with permission courtesy of Vic Small, from http://cellix.imba.oeaw.ac.at/cytoskeleton/

(e) Organelles in the cell (electron micrograph)



Figures 5a, 5b and 5e reproduced from an *Atlas of Fine Structure: The Cell*

The plasma membrane

The plasma membrane (Fig. 5a) is the boundary between the cell and its exterior environment.

It consists of a lipid bilayer, seen by electron microscopy as two parallel electron-dense (dark) lines with a narrow gap between them.

The plasma membrane is only 8–10 nm thick, and cannot be seen by light microscopy without special dyes.

The nucleus

The nucleus (Fig. 5b), about 10 μm in diameter, is enclosed by a nuclear envelope, which forms a barrier between it and the cytoplasm. The nuclear envelope consists of both an outer and an inner nuclear membrane (lipid bilayer). Nuclear pores within the nuclear envelope control which proteins and RNA can pass between the nucleus and the cytoplasm.

Light patches of staining, known as euchromatin, contain DNA that is being actively transcribed. Darker staining patches of heterochromatin contain DNA that is not being actively transcribed. The nucleolus is where ribosomal RNA is processed and assembled into ribosome subunits.

The nucleus and the nucleoli can be seen in sections by light microscopy (Fig. 5c). The appearance of nuclei varies between cells and cell types, and depends on the activity of the cells.

Cellular organelles

Endoplasmic reticulum

The endoplasmic reticulum (ER; Fig. 5d) is a single internal membrane system that extends throughout the cytoplasm, and makes up about 10% of the total cell volume. Its membrane is continuous with the outer nuclear membrane. The ER synthesizes lipids and proteins, generating the membranes of most of the organelles in the cell, and it stores Ca^{2+}. Some proteins are internalized into its lumen and sent to the Golgi to be modified.

Rough ER (Fig. 5d) is organized into parallel layers of flattened sacs and covered with ribosomes. Its lumen is 20–30 nm wide. The cytoplasm of cells rich in rough ER stains a darker pink, or blue/purple with H&E due to the high amounts of RNA in the many ribosomes, which are acidic, and therefore stain blue/purple with hematoxylin. Rough ER synthesizes secretory proteins and lysosomal enzymes.

Smooth ER (Fig. 5d) is not covered with ribosomes. It is branched and has a wider lumen than rough ER (30–60 nm).

Golgi apparatus

The **Golgi apparatus** (Fig. 5e) is found close to the nucleus. It glycosylates proteins received from the ER and packages them for transport to the plasma membrane. It also retrieves and recycles proteins.

It consists of 3 to 7 flattened discs of membranes, called cisternae.

The receiving face of the Golgi is called the 'cis' (receiving, forming, or entry) face.

Proteins exit via the trans (maturing or exit) face.

Vesicles

Cells contain a large number of vesicles (Fig. 5e).

- **Secretory vesicles:** These travel from the Golgi to the plasma membrane.
- **Endocytic vesicles:** These travel from the plasma membrane inwards. Cells endocytose membrane proteins and extracellular material to bring them into the cell. Endocytic vesicles are called endosomes. Once inside the cell, these can fuse with vesicles called lysosomes, which break down the contents of endocytic vesicles. Cells can also endocytose fluids in larger vesicles (macropinosomes) and some cells are specialized to endocytose bacteria (phagocytosis).
- **Peroxisomes:** These degrade fatty acids by oxidation and synthesize cholesterol, and are particularly abundant in the kidney and the liver.

Vesicles are 50–200 nm in diameter and are difficult to see by light microscopy, without using special stains or immunostaining.

Mitochondria

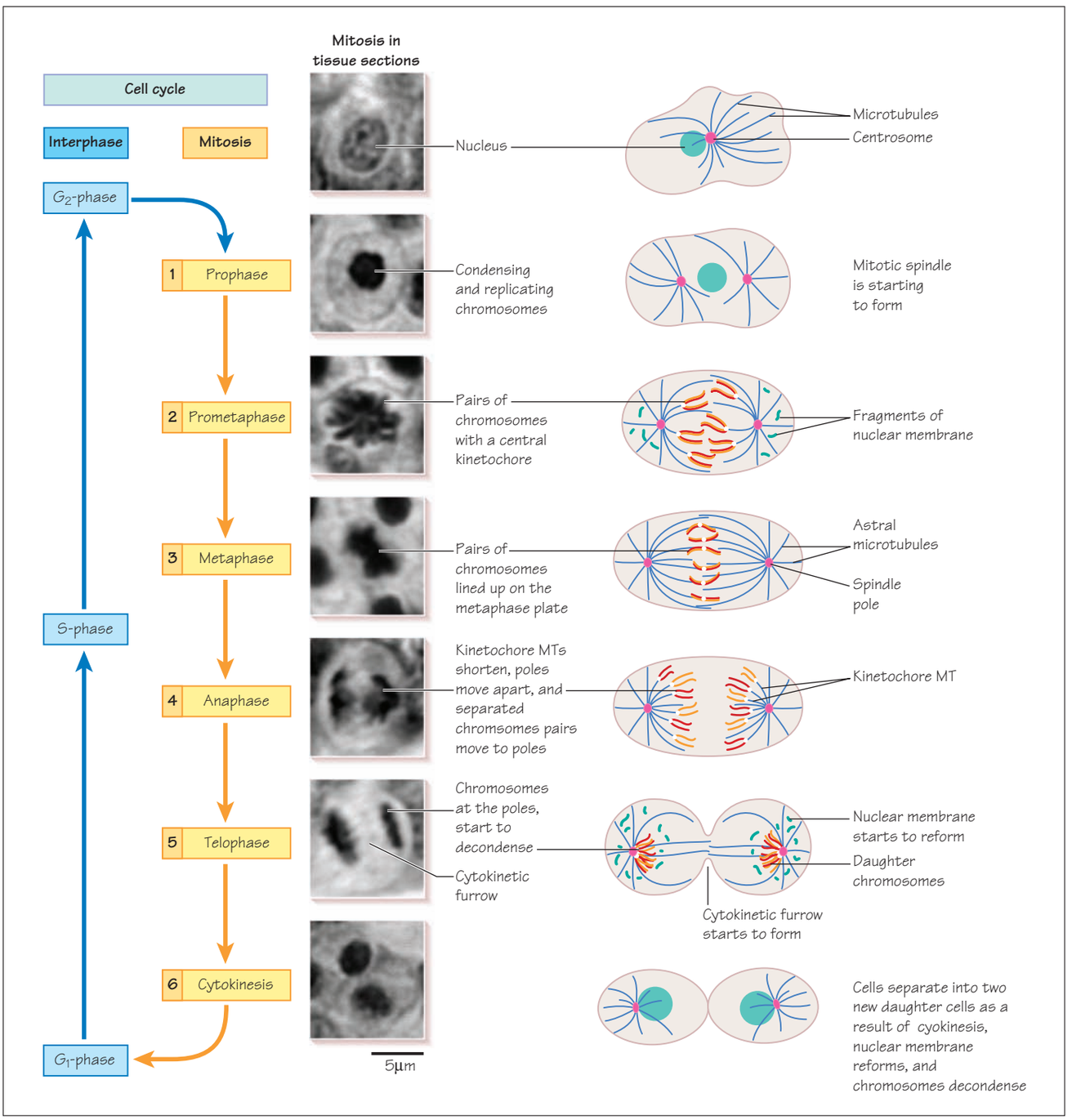
Mitochondria (Fig. 5f; singular, mitochondrion) provide energy for the cell in the form of adenosine triphosphate (ATP). Mitochondria contain a smooth outer membrane and an inner membrane that is folded into 'christae'. Mitochondria migrate throughout the cell, can fuse, undergo fission, and can be degraded. Their appearance varies between different tissues/cells.

Cytoskeleton

There are three main types of filament in the cytoskeleton (Fig. 5g).

- **Actin filaments** (the smallest in diameter) have many cellular functions. They act as tracks for motor proteins (myosins). They facilitate cell–cell adhesion by linking the cytoskeleton to tight junctions and adherens junctions (see Chapter 7), which connect cells to each other. In addition they are key components of cellular protrusions such as microvilli.
- **Intermediate filaments** (intermediate in diameter) maintain the structural integrity of cells and facilitate cell–cell adhesion through their linkage to desmosomes and hemidesmosomes (focal adhesions; see Chapter 7). Nuclear lamins preserve the integrity of the nucleus. The type of intermediate filament is cell-type specific.
- **Microtubules** (the largest in diameter) grow out from the centrosome. These filaments act as tracks for motors (kinesins, dynein), which traffic (move) vesicles around in cells. They are also key components of cilia and flagella, and they are essential for building the mitotic (and meiotic) spindle in cell division.

6 Cell division



In the cell cycle, cells spend most of their time in interphase (phase between each mitosis). Interphase is divided up into three phases:

- G_1 (growth 1): growth phase 1;
- S (synthesis): DNA replication;
- G_2 (growth 2): growth phase 2.

Following G_2, the cells can then enter mitosis.

Some cells enter G_0 after mitosis: a resting/quiescent/senescent stage, in which cells have stopped dividing.

Many cells in the body are terminally differentiated, and do not divide, an example being skeletal muscle. Therefore, you will not commonly find examples of dividing cells in tissue sections, but they can be seen occasionally, depending on the tissue.

Mitosis

Each cell contains two pairs of chromosomes, one of which is paternally, and one maternally derived.

Cell division occurs about once every 24–48 hours in cells that have not yet terminally differentiated. Cell division only takes about 30–60 minutes. Dividing cells can sometimes be observed in tissue sections and are often called 'mitotic figures'. The different phases of cell division can be identified in tissue sections (Fig. 6).

Prophase

In prophase (Fig. 6, stage 1), the centrosome duplicates and the two resultant centrosomes move apart to form the poles of the mitotic spindle. The replicated chromosomes condense, and associate (sister chromatids). They are held together along their length. Pairs of paternal and maternal chromosomes remain separate.

Prometaphase

In prometaphase (Fig. 6, stage 2), the nuclear membrane breaks down, and the spindle is formed. There are three main types of microtubules.

- Astral microtubules: These grow out from the poles to towards the plasma membrane anchoring the spindle in the center of the cell.
- Kinetochore microtubules: These grow out from the poles and attach to the kinetochores of the chromosomes.
- Spindle microtubules: These can attach to the arms of chromosomes.

Chromosome movement is highly dynamic during this stage.

Metaphase

In metaphase (Fig. 6, stage 3), all the chromosomes become aligned on the metaphase plate. Each chromosome pair is attached to kinetochore microtubules from each of the two poles.

Anaphase

In anaphase (Fig. 6, stage 4), when each pair of chromosomes is aligned on the metaphase plate (spindle checkpoint), the kinetochore microtubules rapidly shorten, and together with molecular motors (kinesin and dynein) the pairs of chromosomes are separated. Each half of the pair (daughter chromosome) is moved apart to the poles very rapidly. In the second stage of anaphase, the poles move outwards towards the plasma membrane. This phase is very rapid (takes a few minutes).

Telophase

In telophase (Fig. 6, stage 5), the pairs of chromosomes have fully separated. The daughter chromosomes are found at the poles of the spindle. The nuclear envelope starts to reform, and the cytokinetic furrow starts to form.

Cytokinesis

In cytokinesis (Fig. 6, stage 6), the cytokinetic furrow pinches off the two cells from each other. The nuclear envelope has reformed, and the DNA in the chromosomes has condensed.

Mitosis is exquisitely controlled. In particular, the metaphase checkpoint is used to make sure all the pairs of chromosomes are lined up at the metaphase plate, before they are separated. Problems in mitosis can result in cells that contain an abnormal number of chromosomes, either losing or gaining chromosomes (aneuploidy). This can result in pre-cancerous cells (cancer 'stem' cells).

Meiosis

Meiosis is similar to mitosis but with several important differences (not shown here).

- There are two sets of meiotic divisions, resulting in 4 haploid cells, rather than one division resulting in 2 diploid cells.
- Prophase I: In prophase of the first meiotic division, pairs of homologous chromosomes (maternal and paternal) adhere together to form bivalents (In mitosis, each pair of homologous chromosomes remains separate.)
- During this stage, crossovers between maternal and paternal chromosomes can occur. About 2–3 crossovers per chromosome occur in humans. This process is important for generating genetic diversity.
- Metaphase I: The bivalents line up on the metaphase plate.
- Anaphase I: Sister chromatids separate and chromosomes are segregated into daughter cells, such that one cell will inherit the paternal homolog and the other the maternal homolog, for each chromosome.
- Meiosis II: A second meiotic division separates the sister chromatids, resulting in haploid cells.