4 Cell cycle and division

Candidates should be able to:

(a) understand the importance of cell division in growth and reproduction.

(b) recognize the various stages of cell cycle.

(c) outline and compare the processes mitosis and meiosis.

4.1 Cell cycle

Define

Cell cycle is the reproductive cycle of the cell whereby well-coordinated sequence of events occurs between the formation of a cell and its division into daughter cells.

- Cells reproduce by duplicating their contents followed by dividing into two. This pattern of growth and division increases cell numbers in living things. Therefore, the cell cycle is fundamental in all living organisms for propagation.

- The duration of the cell cycle varies greatly from one cell type to another. However, all cell cycles require the essential processes of cell reproduction to be fulfilled.

- These essential processes of cell reproduction that must occur in order for the cell cycle to progress are:

  - *DNA replication*.
  - *segregation of replicated chromosome* into two separate daughter cells.

- These two processes are related to checkpoints in the cell cycle. Checkpoints can be thought as brakes where the cell cycle is stopped or arrested to ensure that essential processes hves been performed before continuing the cycle.

  - G_2 checkpoint: This ensures all *DNA* are replicated before progressing to *M phase* (M = mitotic).
  - Metaphase checkpoint: This checks whether all *chromosomes* are aligned on spindles before proceeding through Anaphase.

Stages and phases of cell cycle

- In a typical eukaryotic cell, the cell cycle consists of three stages:

  - *Interphase*: Cells do not normally divide continuously. Interphase is the non-dividing period in the cell cycle that elapses between two divisions.
    - The long Interphase accounts for 90% of the cell cycle, where there is cell growth and intense metabolic activity. The duration of Interphase is variable depending on the function of the cell.
    - Growth at a cellular level is accomplished by the synthesis of nucleic acids, carbohydrates, proteins, lipids and other biological molecules.
    - Interphase has three sub-phases: G_1, S and G_2 phases.
  - *Mitosis*
  - *Cytoplasmic division*

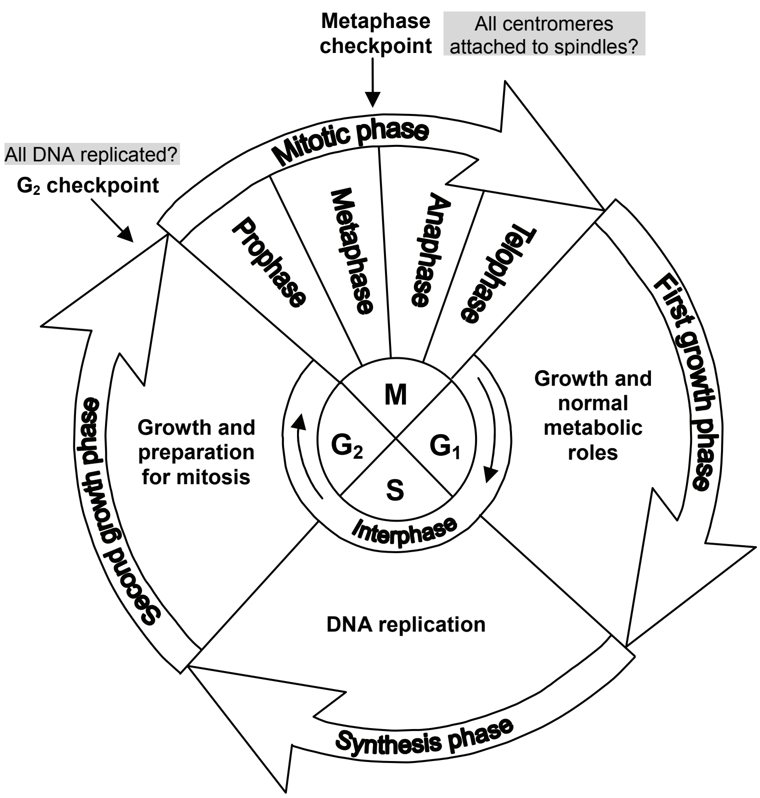


Figure 4.1.1 A typical cell cycle

Table 4.1.1 The four successive phases of a typical eukaryotic cell cycle.

Stage	Phase	Events within the cell

Interphase	G_1
	(G = Gap)
		Growth and normal metabolic roles:
		• Intensive cellular synthesis:
		  o organelles synthesis
		  o ATP synthesis
		  o RNA synthesis in nucleolus
		  o protein (both structural and functional) synthesis
		• Increase in cytoplasm results in cell growth. When growth exceeds a certain size, cell progresses to the S phase for DNA replication.
		• Substances produced in this phase will stimulate or inhibit the onset of the next phase.

	S (S = Synthesis)	DNA replication occurs: • Histones are synthesized. • DNA content of the cell doubles when DNA strands replicate. DNA strands coil around the histones to form chromatin. • Cells in the Interphase contain mostly chromatin in relatively decondensed form, known as *euchromatin*.

	G_2
	(G = Gap)
		Growth and preparation for mitosis:
		• Intensive cellular synthesis:
		  o organelles replication e.g. mitochondria and chloroplasts in plants divide.
		  o ATP synthesis to increase the energy store for cell division.
		  o synthesis of histones and spindle proteins.
		  o centrioles in animal cells replicate. Cells of higher plants lack centrioles.

Mitosis	M	Four phases of nuclear division: • Prophase • Metaphase • Anaphase • Telophase
Cytokinesis	M	Equal distribution of organelles and cytoplasm into each daughter cell.

Worked Examples

Fundamental

(a) Define cell cycle.

(b) Name the four phases of the cell cycle. State the corresponding stage of the cell cycle to each phase.

Solution:

(a) Cell cycle is the reproductive cycle of the cell whereby well-coordinated sequence of events occurs between the formation of a cell and its division into daughter cells.

(b) G_1, S, G_2 and M phases. Interphase consists of the G_1, S and G_2 phases. Mitosis and cytokinesis (cytoplasmic division) are in the M phase.

Challenging

The duration of the cell cycle varies greatly from one cell type to another. The early embryonic cell cycle is one that has a cycle time that is exceptionally rapid. The main function of the large egg cell is to subdivide into many smaller cells as fast as possible.

(a) Account, in contrast to the typical eukaryotic cell cycle, for the short cycle time in the early embryonic cell cycle.

(b) State two prominent events within such a large egg cell.

Solution:

(a) When the large egg cell subdivides into many smaller cells, no growth is involved. Therefore in the early embryonic cell cycle, only the S phase and M phase alternate. Unlike the typical eukaryotic cell cycle where there are four phases, in the sequence of G_1, S, G_2 and M phases, there are no intervening G_1 and G_2 phases.

(b) DNA replication and nuclear division/chromosome segregation.

4.2 Nuclear division (Mitosis)

Define

Mitosis is the process of nuclear division that results in two daughter cells each having a nucleus containing the same number and genetically identical chromosomes as the parent cell.

- Mitosis happens exclusively in eukaryotic cells (animals and plants).
- The genetic material exists in the form of DNA.
  - **Chromatins**: Complexes of DNA tightly coiled around proteins called histones. Chromatins are dispersed throughout the nucleus during Interphase and cannot be seen easily under a microscope.
  - **Chromosomes**: *Chromatins* condense to form chromosomes during mitosis and meiosis that are visible structures under a microscope. Each chromosome has one *centromere*.
  - **Sister chromatids**: Replicated form of chromosomes joined by a centromere. One sister chromatid consists of one DNA molecule with its associated proteins. Both sister chromatids are identical since they are replicated from the same DNA molecule.

Phases of mitosis

- In a typical eukaryotic cell, mitosis can be divided into four principle stages after Interphase (refer to Table 4.1.1):
  - *Prophase*:
    - In early Prophase, *chromatin* in the nucleus begins to condense and becomes visible as *chromosomes* (double stranded). The replicated centrioles begin to move to opposite ends of the cell.
    - In late Prophase, the nucleolus disappears and nucleus membrane disassembles. Spindle fibers form from microtubules, extending from the centrioles. Some fibers cross the cell to form the *mitotic spindle*.
  - *Metaphase*: Spindles that are completely formed attach to the kinetochores at the centromere region of chromosomes. Contraction of spindle fibers aligns the chromosomes along the equator of spindles, also known as *metaphase plate*.
  - *Anaphase*: Centromeres divide and the paired chromosomes separate. Spindle fibers pull each daughter centromere, thus separating each sister chromatid to opposite poles of the cell.

- *Telophase*:
  - Chromosomes (single stranded) arrive at opposite poles of cell, and a new membrane forms around each daughter nucleus. The chromosomes decondense. The spindle fibers disintegrate.
  - *Cytokinesis* or the partitioning of the cell begins immediately after this stage.

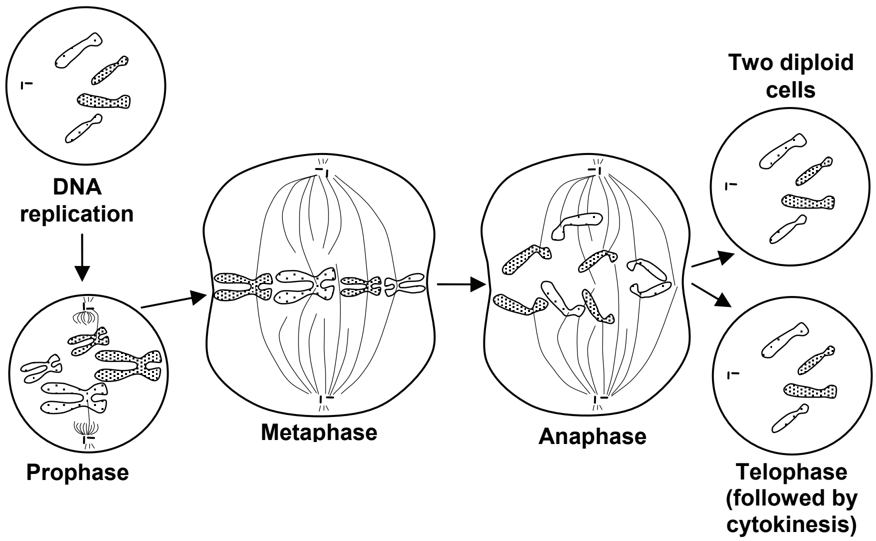


Figure 4.2.1 Mitosis

Importance of mitosis

- Ensures genetic stability within the population of cells derived from parental cells.
  - Mitosis produces two daughter cells which have same number of chromosomes and are genetically identical to their parental cell. Therefore, mitosis does not introduce genetic variation.
  - Advantage: Favourable traits can be passed down from generation to generation.
  - Disadvantage: Genetic variation increases the probability of survival. Without genetic variation, an entire population can be wiped out when there is a change in the environment.
- Multicellular growth: Mitosis results in an increase in the number of cells found in an organism without altering the genetic content.

- In tissue/cell replacement, mitosis ensures that during the repair of damaged tissues, the damaged cells are replaced by exact copies of the original cells. Such repair will restore the function of the tissue. Regeneration of tissue can occur at varying extents in multicellular organisms.

- *Asexual reproduction*: This occurs when a single parent produces offspring that are genetically identical to itself.

  - Asexual reproduction can be advantageous under a stable environment. The offspring can receive exactly the same set of genetic material from the parent to survive and subsequently reproduce under the same conditions. Such population can reproduce rapidly with ideal conditions for its genes.

Worked Examples

Fundamental

(a) Explain the significance of each phase of mitosis.

(b) What are the important features of mitosis that ensure the production of genetically identical cells?

Solution:

(a) Prophase:
Chromatin condenses into compact, visible chromosomes. This allows chromosomes to move and separate easily without entanglement. The disappearance of nucleolus and nuclear membrane allows spindle fibers to form across the cell between the poles. The formation of spindle fibers organizes chromosome movement and alignment in the later stages of mitosis.

Metaphase:
Each chromosome with a pair of sister chromatids is aligned along the equator of spindles. This alignment ensures that when centromeres split, the spindle fibers will pull one sister chromatid of each pair to opposite poles. As a result, equal division of chromosomes is ensured and each daughter cell will have a complete copy of genetic material of the parent cell.

Anaphase:
Equal distribution of chromosomes (single stranded DNA) into each daughter cell ensures genetic stability.

Telophase:
In this stage, new nucleolus and nucleus membrane are formed. This prepares each daughter nucleus for normal activities in each daughter cell.

(b) The fine control of DNA replication of the parent cell during Interphase ensures that twice the amount of genetic material exists before M phase. The arrangement of the chromosomes on the spindle during metaphase and contraction of the spindle pulling the chromosomes to the opposite poles, ensure even distribution of chromosomes in daughter cells. Since the sister chromatids that are separated to the opposite poles are identical (both replicated from the same DNA), the resultant daughter cells are genetically identical.

Challenging

Briefly explain how cancer arises due to uncontrolled cell division.

Solution:

Cancer is a disease in which cells begin dividing excessively resulting in the formation of a mass of cancerous cells called tumour. It occurs when the cells escape the control mechanism of the cell cycle that normally limit their growth, thus leading to uncontrolled cell growth. In cancerous cells, mutations have occurred in the genes that control cell division. Genes (proto-oncogenes) that normally promote normal cell growth and division can become mutated (oncogenes). Genes (tumour suppressors) that function to suppress cell growth and division can also become mutated.

4.3 Nuclear division (Meiosis)

Define

Meiosis is the process of nuclear division that gives rise to four reproductive cells (gametes), each with half the chromosome number of the parent cell.

- **Diploid cell** is a cell with two sets of chromosomes, one paternally and other maternally derived. Chromosomes are in homologous pairs. A somatic cell is *diploid*.

- **Haploid cell** is a cell with one set of chromosomes and there are no homologous pairs. **Gametes** or sex cells (e.g. eggs and sperms) are *haploid*.

- **Somatic cell** is any plant or animal cell other than a germ cell.

- **Germ cell** is a precursor cell that gives rise to a *gamete*. Union of a haploid egg and sperm during fertilization produces a diploid embryo.

- **Homologous chromosome** is a pair of chromosomes, one maternal and one paternal, that have relatively similar structures (e.g. length and centromere position) and gene (allele might be different).

    - During *Metaphase I*, each duplicated chromosome will pair with its homologous partner to form a **bivalent** which contains four chromatids.

- *Meiosis* occurs only in the process of **gametogenesis,** i.e. formation of gametes.

- Sexual reproduction promotes *variation* because each gamete (sperm or egg) contains a mixture of genes from two different parents.

Phases of meiosis

- Meiosis consists of two successive nuclear divisions – Meiosis I (reduction in chromosome number) and Meiosis II (division).

- Phases of Meiosis I:

    - *Interphase I*: Same as mitosis (Refer to Table 4.1.1).

- *Prophase I*:
  - The pairing of homologous chromosomes (each homolog is double stranded) to form bivalents. This event is also known as **synapsis**. Bivalents further condense.
  - Chiasmata formation and crossing over (refer to Figure 4.3.2) may occur.
  - Other events are similar to the Prophase of mitosis – chromatin condenses into chromosomes, the nucleolus disappears, nuclear membrane disassembles, centrioles move to opposite ends of the cell and spindles form.
- *Metaphase I*:
  - Spindles are completely formed and microtubules of spindle attach to the kinetochores at the centromere region of chromosomes.
  - Homologous chromosomes are still closely associated.
  - Bivalents align along the equator of the spindle by dynamic contraction of spindle fibres.
- *Anaphase I*: Homologous chromosomes separate, and are drawn to opposite poles by the spindle fibers that are attached to the centromeres. The centromeres in *Anaphase I* remain intact.
- *Telophase I*: This is similar to telophase of mitosis, except that only one set of (double stranded) chromosomes is in each daughter cell. Depending on species, new nuclear envelope may or may not form. Nucleolus reforms.

✍ In plants, cytokinesis does not occur after Telophase I.

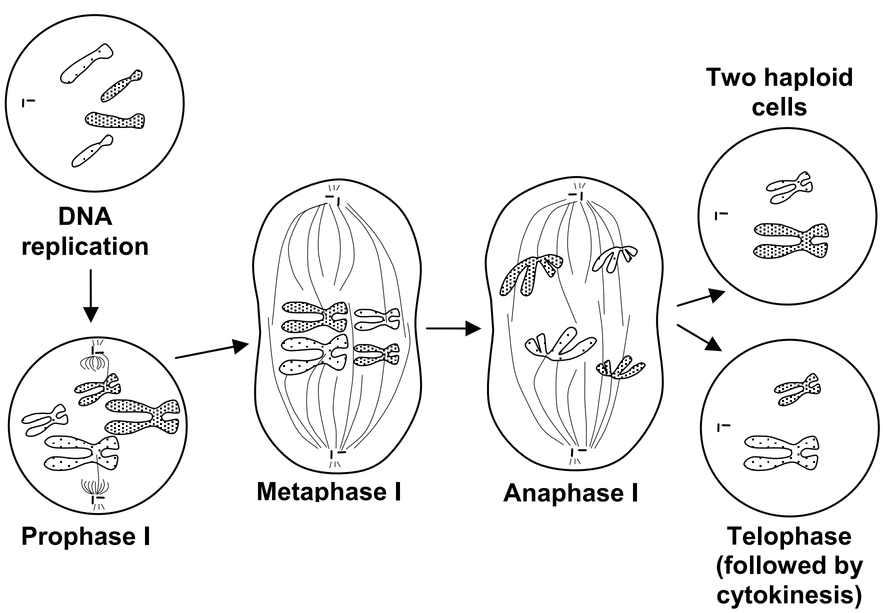


Figure 4.3.1 Meiosis I without Chiasmata formation and crossing over.

- Interphase II where replication of centrioles but <u>no</u> replication of DNA may occur before Meiosis II. Phases of Meiosis II are similar to those of mitosis:
    - Prophase II
    - Metaphase II
    - Anaphase II
    - Telophase II

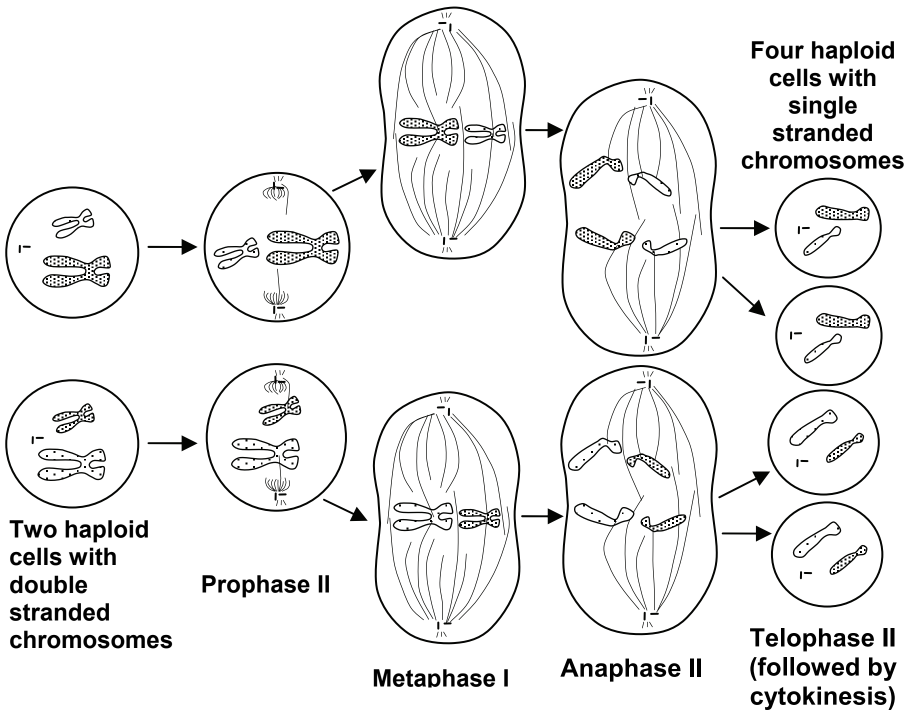


Figure 4.3.2 Meiosis II

Importance of meiosis

- Ensures <u>genetic stability</u> generation after generation by keeping the chromosome number in each species <u>constant</u>.
    - Meiosis produces *haploid* (n) gametes (egg and sperm) for sexual reproduction. During fertilization, the nuclei of male and female gametes fuse to produce a zygote with *diploid* (2n) number of chromosomes. As a result, the diploid condition of cells is <u>restored</u>.
    - The zygote develops into the embryo, then into the multicellular organism with *diploid* (2n) number of chromosomes in <u>all</u> the *somatic* cells in the body. One set of chromosomes from the mother (egg) and the other from the father (sperm).

- Consequence if meiosis does not occur:

  Fusion of male and female gametes will result in doubling of the number of chromosomes for every successive sexually reproduced generation.

Genetic variation is made possible by two events in meiosis:

- *Genetic crossing over*: The breakage and rejoining between non-sister chromatids of a *bivalent* result in the exchange of alleles.

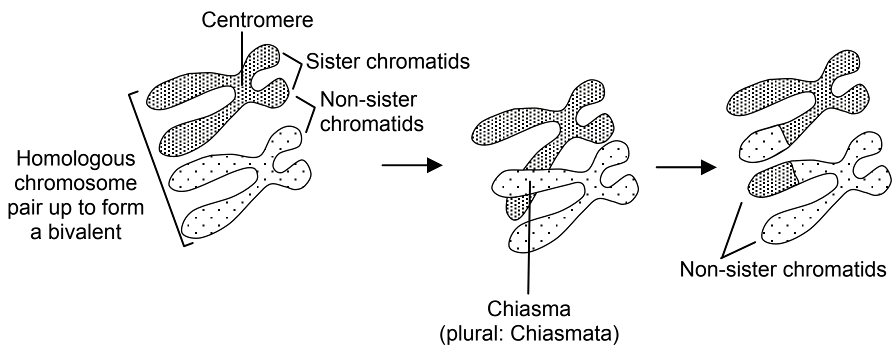


Figure 4.3.3 Non-sister chromatids of a bivalent twist around each other to form a contact point called chiasma. Then crossing over occurs where there is reciprocal exchange of alleles to form recombinant chromosomes.

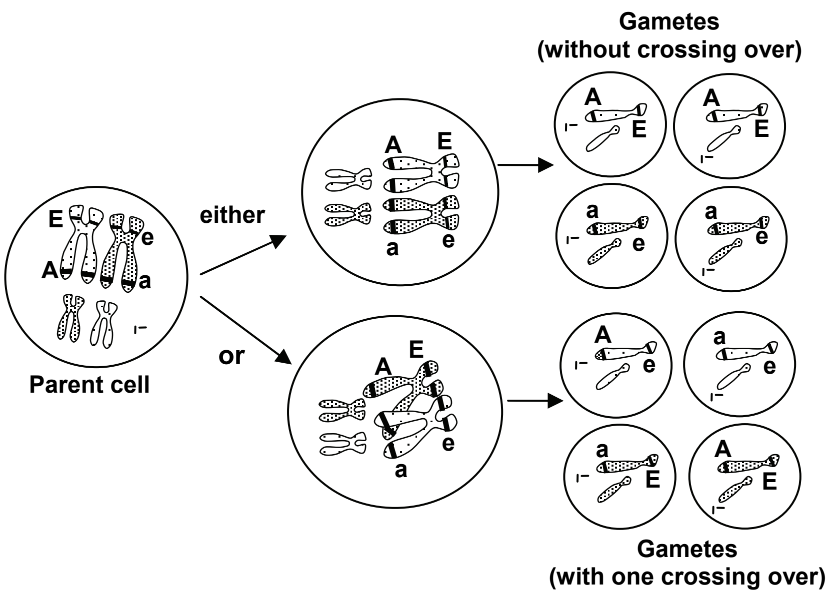


Figure 4.3.4 Possible genetic combinations with crossing over.

- *Independent assortment of chromosomes* that results in different combinations of chromosomes in the daughter cells:
    - During M*etaphase I*, the homologous chromosomes are randomly aligned at the equator. The arrangement of one pair of homologous chromosome at the equator is independent of other pairs of homologous chromosome.
    - During *Anaphase I*, the chromosomes of one homologous pair separates independently of other pairs.
    - 2^n possible combinations where n = haploid number. For humans, each somatic cell has 46 chromosomes and each gamete has 23 chromosomes. Therefore n = 23, resulting in 2^{23} possible combinations of maternal and paternal chromosomes.

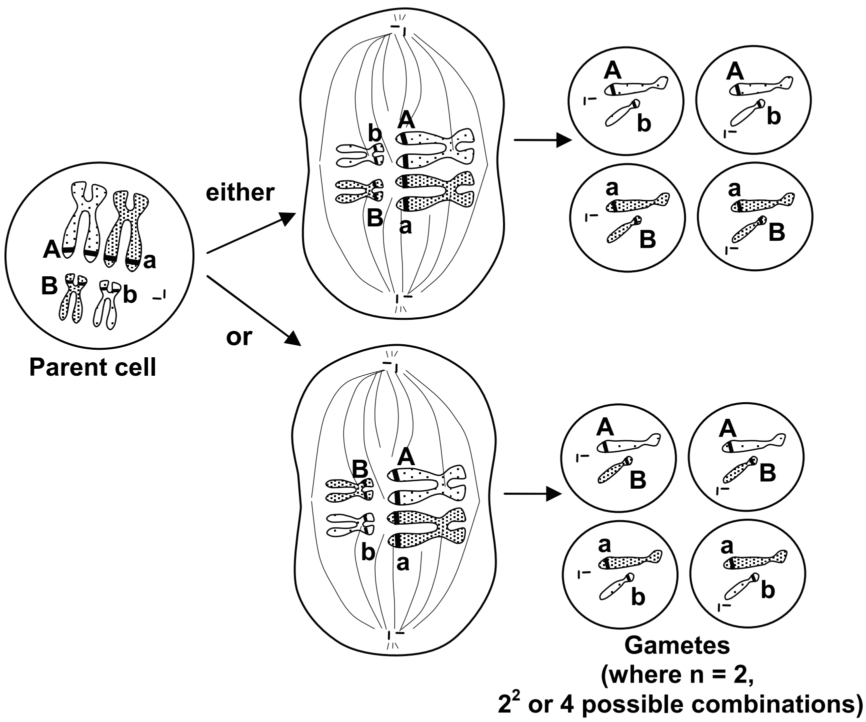


Figure 4.3.5 Possible genetic combinations with independent assortment.

Table 4.3.1 The differences between mitosis and meiosis.

	Mitosis	Meiosis
Number of divisions	• One • Consists of prophase, metaphase, anaphase and telophase	• Two • Meiosis **I** (reduction phase) • Meiosis **II** (mitotic phase)

Prophase	• No pairing of homologous chromosomes
	• No chiasmata formation
	• No crossing over
		• *Prophase I*:
		  ○ Homologous chromosomes pair up to form bivalents.
		  ○ Chiasmata formation between non-sister chromatids of homologous chromosomes
		  ○ Crossing over (of complementary alleles) may occur
		• *Prophase II*:
		  ○ Similar to mitosis

Metaphase	• Individual chromosomes, each with two sister chromatids, align at the equator of the spindles.	• During *Metaphase I*, *bivalents* align at the equator of the spindles. • During *Metaphase II*, individual pairs of chromatids align at the equator of the spindles.
Anaphase	• Centromeres divide and sister chromatids separate to opposite poles.	• During *Anaphase I*, centromeres do not divide and homologous chromosomes separate to opposite poles. • During *Anaphase II*, centromeres divide and chromatids separate to opposite poles.

Telophase	• Two daughter cells are formed. Each contains the same number of chromosomes as the parent cell.
	• Both homologous chromosomes are present in each daughter nuclei (i.e. diploid).
	• Each chromosome is single stranded.
		• *Telophase I*:
		  ○ Two daughter cells are formed. Each contains half the number of chromosomes of the parent cell.
		  ○ Only one of each pair of homologous chromosomes is present in each daughter nuclei (i.e. haploid).
		  ○ Each chromosome is double stranded.

		• *Telophase II:* ◦ <u>Four</u> *haploid* daughter cells are formed. ◦ Each chromosome is single stranded.
Occurrence	• May occur in haploid, diploid or polyploidy cells and during the formation of <u>somatic</u> cells. • In plant meristematic cells e.g. root and shoot tips for growth. • In animal epithelium cells for repair and replacement of worn out cells. • In eukaryotic unicellular organism e.g. amoeba.	• <u>Only</u> occurs in diploid or polyploidy cells and during the formation of <u>gametes</u> or <u>spores</u>. • In plant sex organs e.g. pollen sacs and ovaries. • In animal sex organs e.g. testes and ovaries.

Worked Examples

Fundamental

(a) Distinguish between the terms:

(i) haploid and diploid; and

(ii) centromere and centriole.

(b) Describe how genetic variations in gametes arise.

(c) What is the importance of genetic variation in a population?

Solution:

(a) (i) Haploid (n) is to have half the original number of chromosomes. This haploid cell has only one of each homologous pair of chromosomes (one set) and thus no homologous pairs.

Diploid (2n) is to have the complete pairs of homologous chromosomes (two sets).

(ii) Centromere is the localized region which joins two sister chromatids together and where kinetochore forms to capture spindle fiber.

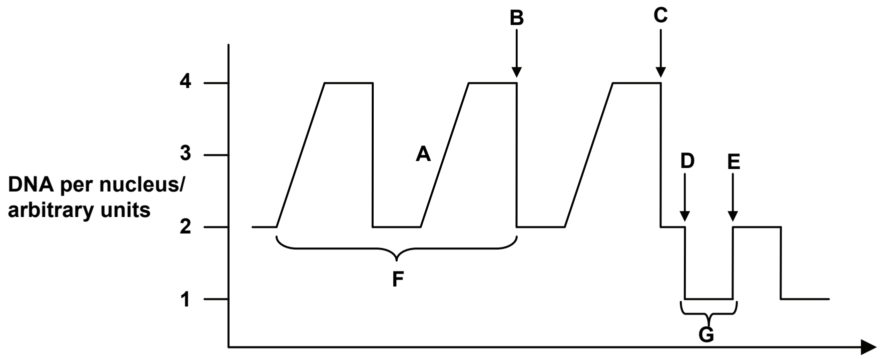
Centriole is a pair of short rod structures that are positioned at right angles to each other. Centrioles are found in animal cells, located in the centrosome of the cell.

(b) In Prophase I, there is *crossing over* through the physical breakage and rejoining of non-sister chromatids of homologous chromosomes. Subsequently, *independent assortment* of chromosomes will result in random and independent arrangement of bivalents along the equator in Metaphase I. This is followed by independent separation of homologous chromosomes in Anaphase I to result in different combinations of double stranded chromosomes at the end of meiosis I. Genetic variation is further enhanced with independent assortment of non-sister chromatids in Metaphase II and Anaphase II.

(c) Ensures the survival of species or population in a dynamic environment.

Challenging

The figure below represents the relative amounts of DNA per nucleus during several cell divisions in a plant tissue.



(a) (i) From the graph, state the letter (A, B, C, D or E) that represents the point where the cell enters haploidy. Name the stage.

(ii) Explain your answer in (i).

(b) State what is occurring at the points marked A, B, C and E.

(c) What types of cells are produced at F and G?

(d) Down syndrome is the most frequently occurring chromosomal disorder. Individuals with Down syndrome have an extra chromosome 21 in their genetic make-up. Suggest and explain the stage(s) at which meiosis can be disrupted to give rise to the chromosome disorder.

Solution:

(a) (i) C. Telophase I

(ii) The amount of DNA in each nucleus decreases from 4 to 2 units. This corresponds to the first nuclear division. During meiosis I, there is separation of homologous chromosomes of a bivalent. Each daughter cell would contain one (n) set of chromosomes but each chromosome is double stranded.

(b) A: replication of DNA

B: Telophase of mitosis

C: Telophase I of meiosis

E: fertilization/fusion of gametes

(c) F: diploid cell

G: haploid cell

(d) The error could have occurred at Anaphase I when the homologous chromosomes failed to separate. The error could have also arisen at Anaphase II when the sister chromatids failed to divide, resulting in a haploid daughter cell with two chromosome 21 and another daughter cell without chromosome 21. The fusion of the gametes with two chromosome 21 and a normal gamete will give rise to Down syndrome.