Cytology

Introduction

Cell Biology deals with the study of cells. It is also known as Cellular Biology or Cytology.

Important Events/Discoveries **in Cell Biology**

1595 Jansen discovered the first compound microscope.

1665 Robert Hooke described cells in a cork.

1674 Leeuwenhoek discovered Protozoa and saw bacteria some nine years later.

1772 Alfsno Corti observed living matter in cells.

1781 F Fontana discovered nucleolus in the skin cell of an eel.

1833 Brown described cell nucleus in the cells of an orchid.

1835 Dujardin named living matter in cells as sarcode.

1838 Schleiden and Schwann proposed the cell theory.

1839 Purkinje named jelly-like substance in cells as protoplasm.

1840 Albrecht von Roelliker pointed out that sperm cells and egg cells are also cells.

1841 Robert Remark described amitotic cell division in the RBC of a chick's embryo.

1856 N Pingshem observed how a sperm cell penetrates an egg cell.

1857 Kolliker described mitochondria.

1858 Rudlof Virchow gave his conclusion *Omnis cellula e cellula*, that is, cells develop only from pre-existing cells.

1866 Haeckel established that the nucleus is responsible for storing and transmitting hereditary characters.

1861 Schultzee proposed the protoplasm theory.

1873 Anton Schneider described chromosomes.

1875 Van Beneden observed centrioles.

1879 Flemming described the behaviour of chromosomes during mitosis.

1881 Balbiani discovered giant salivary gland chromosomes.

1882 Knock identified bacteria.

1882 Flemming described cell division (mitosis).

1882 W Pfitzner discovered chromomeres.

1883 Schimper named chloroplasts.

1884 Mobius first discovered structures that were later named cell organelles.

1885 Hertwig and Strasburger described the role of nucleus in heredity.

1886 C A Mac Munn discovered cytochrome.

1888 Benden discovered centrosome.

1898 Golgi discovered Golgi apparatus.

1898 Waldeyer described chromosomes.

1902 Mc Clung discovered sex chromosomes.

1905 Farmer coined the term meiosis.

1906 M Tswett discovered chromatography.

1912 A Carrel discovered the technique of tissue culture.

1924 A Feulgen developed the test for identifying DNA in the cell.

1931 W H Lewis discovered pinocytosis.

1931 Ruska built the first Transmission Electron Microscope.

1938 T Svedberg developed the technique for ultracentrifugation.

1938 Behrens used differential centrifugation to separate nuclei from cytoplasm.

1939 First commercial transmission microscope was produced by Siemens.

1945 K R Porter discovered endoplasmic reticulum.

1952 De Duve identified Iysosomes.

1952 Grey and co-workers established a continuous cell line.

1953 Watson and Crick proposed the structure of DNA.

1955 Nutritional need of animal cell was defined by Eagle.

1957 Meselson, Stahl and Vinogard developed density gradient centrifugation in cesium chloride solution for separation of nucleic acids.

1963 Chance and Parsons, Smith and H Fernandez-Moran discovered elementary particles in the mitochondrion.

1965 Cambridge instruments produced the first commercial scanning electron microscope.

1972 Singer and Nicolson proposed the fluid mosaic model.

1974 Claude and Palade described the ultra-structure of a cell.

1976 Keith et al. described the microtrabecular system in the cytoplasm.

1976 Sato and co-workers described that different cell lines have different requirements of a

mixture of hormones and growth factors in serum-free media.
1978 Mitchell discovered chemiosmotic mechanism of ATP synthesis.
1981 Transgenic mice and fruit flies were produced and mouse embryonic stem cell line was established.
1997First sheep cloned.
1998 Mice cloned from stem cells.
1999 Hamilton and Baclcombe discovered SiRNA as post-transcriptional gene silencing in plants.
2001 Hunt and Nurse discovered cell cycle regulation by cyclin and cyclin-dependent kinase.
2007 Craig venter made synthetic chromosome.
2008: Houston-based Introgen developed Advexin (FDA Approval pending), the first gene therapy for cancer and L-Fraumeni , utilizing a form of Adenovirus to carry a replacement gene coding for the p53 protein.
2009: Mike Stratton First complete cancer genome sequenced
2010 Researchers at Northwestern University Feinberg School of Medicine discovered that the gene BOULE is not only responsible for sperm production, it's actually the first known gene to be *required* for sperm production in species ranging from insects to mammals.
2011 Researchers at the University of Pennsylvania find that a major cause of baldness may be related to the inability of some stem cells to grow into full-sized hair follicles.
2011 Gerontologists showed that flushing old, broken-down cells from the bodies of mice indeed slowed their descent into infirmity.
2012 Xue Zhong Liu Mutation in the PRPS1 gene linked to a progressive hearing loss in males
2013 Oregon Health and Science University researchers announced they had cloned human embryos and collected stem cells from them
2014 Genetically modified potatoes capable of resisting blight have been developed by British scientists.
2015 first map of the human epigenome was completed, which can be thought of as the molecular switches which can turn on or silence the individual genes in the DNA
2015 A new human-like species *Homo naledi was* describe for the first time
2016: A genome is sequenced in outer Space for the first time, with NASA astronaut Kate

Rubins using a MinION device aboard the International Space Station

Nucleus

- Nucleus is the largest membrane-bound cell organelle which is known as the 'master cell organelle'.
- It is the first organelle to be discovered.
- It is mainly concerned with the gene expression as well as replication of DNA.
- Nucleus was discovered by Robert Brown (1831) in the orchid root cells.
- Nucleus occupies approximately 10 per cent of the cell volume.
- Nucleus is found in all the eukaryotic cells (except mature mammalian erythrocytes and sieve tubes of seed plants).
- Generally in a cell, there is only one nucleus *(Amoeba).* But there may be two nuclei *(Paramecium)* or there may be many nuclei *(Opalina).*
- A typical nucleus consists of following components:

1. **Nuclear Envelope**
    - Nucleus is surrounded by an envelope called nuclear envelope which isolates it from the cytoplasm.
    - It is a double-membrane structure called outer and inner nuclear membranes.
    - These membranes are lipoprotein membranes.
    - The outer membrane may contain ribosomes and is continuous with the endoplasmic reticulum.
    - The outer membrane bears small pores called nuclear pores.
    - Each nuclear pore is surrounded by a ring-like structure called annulus.
    - The pores and annuli together constitute the pore complex.
    - Through nuclear pores, exchange of material occurs between the cytoplasm and nucleus.
    - In between two membranes, there is a perinuclear space of approximately 10-70 nm.
    - The inner surface of the inner membrane bears mesh work of fibrous protein called nuclear lamina.
    - Nuclear lamina connects inner nuclear membrane with chromatin.
    - Nuclear laminas regulate assembly and disassembly of nuclear membrane during cell

division.

- Nuclear laminas are made up of three principal proteins, viz., laminas A, Band C.
- Nuclear membranes are impermeable to most molecules.
- Nuclear membranes disappear during late prophase and reappear during telophase.

2. **Nucleoplasm**

• Nucleus contains a jelly-like fluid called nucleoplasm.

- Nucleoplasm contains various enzymes involved in metabolic pathways as well as replication of DNA and transcription of RNA.
- Some proteins present in the nucleoplasm are involved in the regulation of chromatin structure and function.

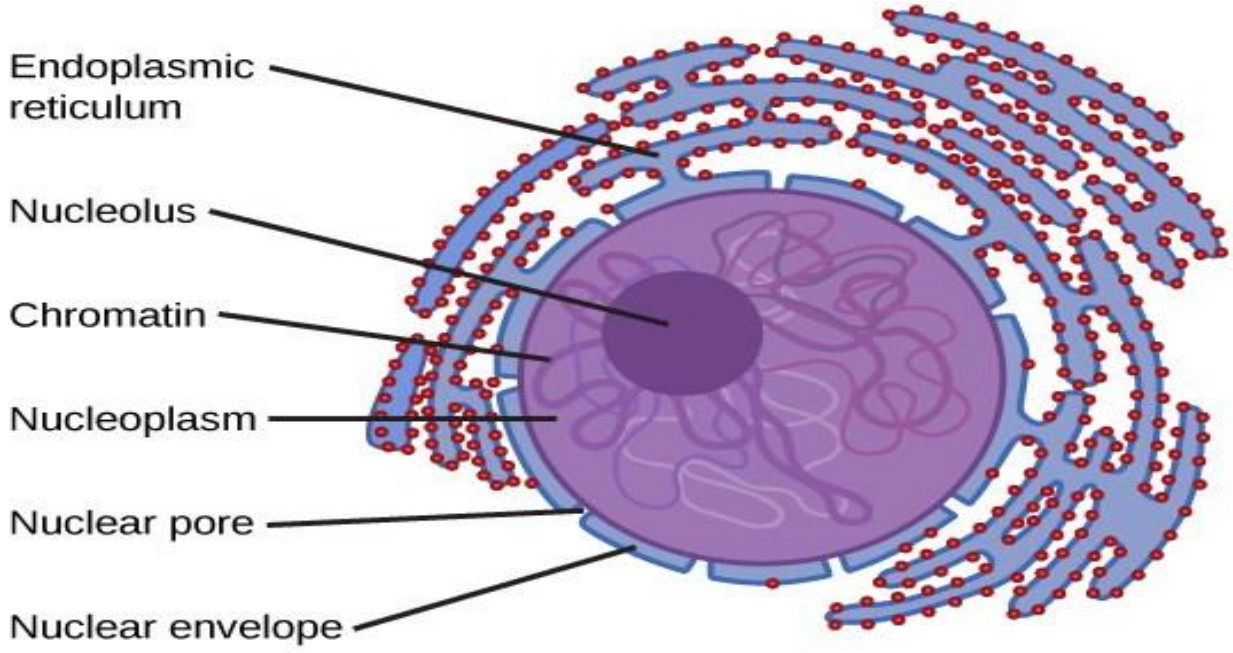
3. **Nucleolus**

- It is a large spherical structure present in the nucleoplasm.
- It was discovered by Fontana (1728) and the term 'nucleolus' was coined by Bowman (1840).
- Nucleolus contains 80 per cent proteins and 20 per cent mixture of DNA and RNA.
- Nucleolus is formed by a special region of the chromosome called 'Nucleolar Organiser Region' (NOR).
- In eukaryotes, nucleolus is the site of synthesis of ribosomes and its assembly.
- A cell may contain up to four nucleoli, but within each species the number of nucleolus is fixed.
- Nucleolus is renewed at each cycle.

4.Chromatin Fibres

- The thread-like filamentous structure present in the nucleoplasm is termed as chromatin fibres.

- Chromatin fibres are complex of DNA and proteins.
- Chromatin fibres are observed at interphase stage.
- During cell division, these chromatin fibres become short and thick thread-like structures called chromosomes.
- Chromatin materials are of two types, viz., euchromatin and heterochromatin.



The basic differences between euchromatin and heterochromatin are as follows:

Euchromatin	*Hetrochromatin*
It stains lightly.	It stains deeply
It is granular.	It is fibrous.
It occurs in the diffused region.	It occurs in the condensed region.
It is genetically active.	It is relatively inert genetically.
It shows normal crossing over.	The frequency of crossing over is less.
It replicates during early S-phase.	It replicates during late S-phase.
It is found in the acetylated form.	It is found in the non-acetylated form.

	It does not exhibit heteropycnosis. It is less affected by temperature, sex, age, etc.	It exhibits heteropycnosis. It is more affected by temperature, sex, age, etc.

Heterochromatin is of two types:

I. **Constitutive Heterochromatin**

- It is found in all cells and all stages of life cycle.
- DNA of this type of chromatin is permanently inactive.
- Constitutive DNA is highly repetitive.
- It remains in condensed state throughout the cell cycle
- It is never transcribed.
- Most of the chromatin occurring around centromere, in the telomeres, in C bands of chromosomes is constitutive heterochromatin.

2. **Facultative Heterochromatin**

- **It** develops during the development of the organisms.
- **It** has no permanent condensation.
- It follows periodic dispersal and in dispersal state it is actively transcribed.
- It may have extra chromosomal inheritance.
- It results from the inactivation of one of the two X chromosomes in females.

Chromosome

- Chromosomes are nuclear components having the power of self-duplication.
- They carry all information for a cell to grow, thrive and reproduce.
- They are popularly known as 'hereditary vehicles' as they carry genetic information from generation to generation.

- A chromosome is not visible in the nucleus when a cell is not dividing.
- The term 'chromosome' was coined by Waldeyer (1898).
- The shape and size of chromosomes are variable. However, the size and number of chromosomes remain constant for a particular species.
- A typical eukaryotic chromosome consists of:
- **Chromonemata:** These are filamentous thread-like structures. They represent chromatids in the early stages of condensation.
- **Chromomeres:** These are bead-like structures which are linearly arranged on the chromosomes.
- These are tightly folded regions of the DNA and more clearly visible in the polytene chromosome.
- They are not visible during metaphase as the chromosome is tightly coiled.

Chromatids

- A chromosome has two symmetrical structures at metaphase called chromatids which are held together by the centromere.
- Chromatids from one mother chromosome are called sister chromatids and chromatids from two different chromosomes are called nonsister chromatids.

Primary Constriction

- It is a narrow and constricted area of the chromosome which contains the centromere.
- Centromere is concerned with the movement of chromosomes during cell division.
- Fibrils of microtubules attach to it during cell division.
- Centromere contains a cup-like structure called kinetochore (0.20--0.25 urn).
- Kinetochore is the implantation site to which spindle microtubules are attached.
- The position of centromere on ,the chromosome is fixed and determines the shape of the chromosomes,

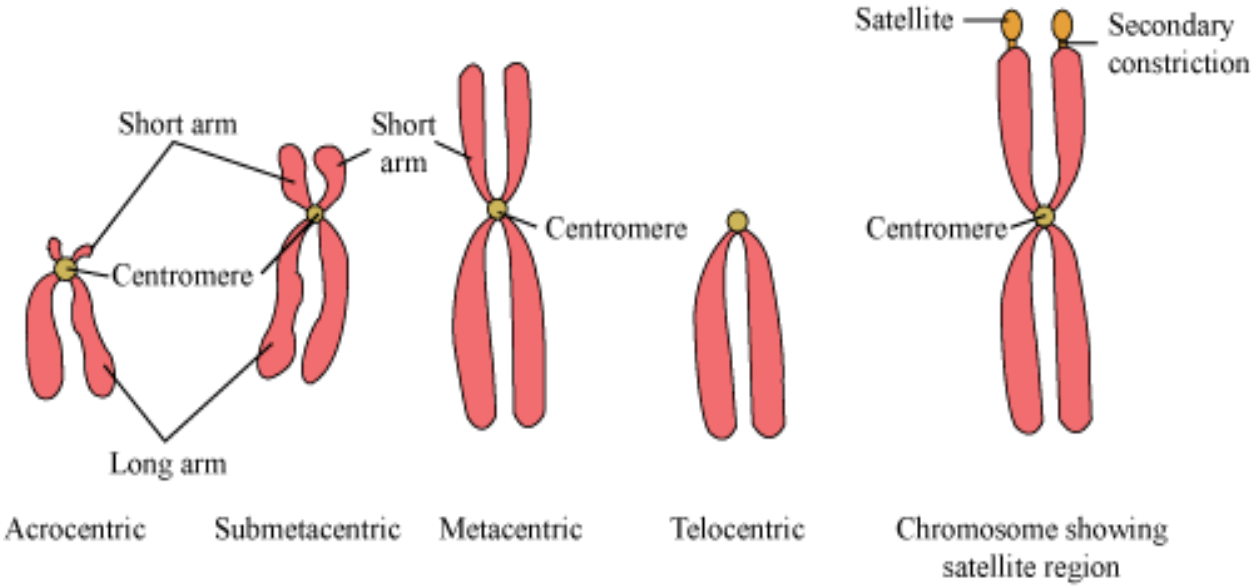
Depending on the position of centromere, a chromosome may be:

(a) **Telocentric**: Centromere is terminal in position.

(b) **Acrocentric**: Centromere is subterminal in position.

(c) M**etacentric**: Centromere is located in the middle of the chromosome.

(d) **Submetacentric:** Centromere is located slightly away from the middle point.



Types of chromosomes

• Depending on the number of centromere, a chromosome may be:

(a) **Acentric**: Without centromere

(b) **Monocentric**: With one centromere

(c) **Dicentric:** With two centromeres

(d) **Polycentric**: With more than two centromeres

(e) **Diffused:** Centromeres are indistinct

Secondary Constriction

- In addition to primary constriction, there is a secondary constriction.
- The difference between primary and secondary chromosomes can be observed during anaphase as a chromosome can bend only at the site of primary constriction.

• Secondary constrictions are constant in position and hence are useful in identifying ~articular chromosome in a set.

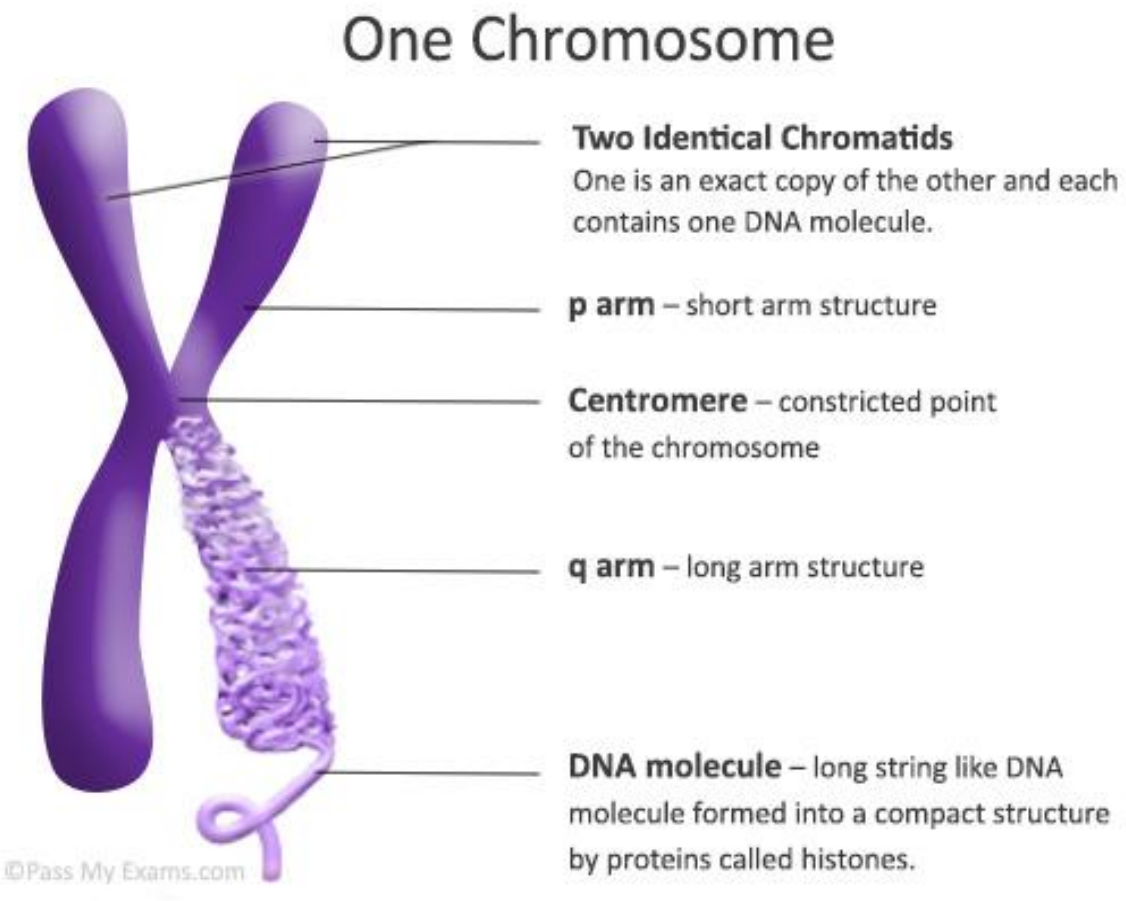
- Secondary constriction may arise because the rRNA genes are transcribed very actively and thus interfere with chromosomal condensation.
- It contains the genes coding for 5.8S, 18S and 28S rRNA which induce formation of nucleolus. Hence, is named as nucleolar organiser region.
- In human beings, chromosomes 13, 14, 15, 21 and 22 are nucleolar chromosomes.

Satellite

- Satellites are round or elongated or knob-like appendages of chromosomes.
- Satellite is produced if secondary constriction is present in the distal region of the chromosome.
- The shape and size of satellites remain constant.
- It i attached with rest of the chromosome by a thin chromatin filament.

Telomercs

- Telomercs are the specialised ends of a chromosome which exhibit structural and physiological polarity.
- They arc nonsticky ends of chromosomes.
- They confer stability to chromosomes.
  - They are synthesised by the enzyme telomerase.
  - Blackburn and Gall (1978) sequenced first telomere from *Tetrahymena thermophilia.*
  - Each species has characteristic telomeric repeat sequences. However, widely divergent species may hay the same telomeric unit.
  - The telomeric DNA in eukaryotic cells is gradually lost in successive generations.



Nucleosome Model

- Under electron microscope, eukaryotic chromosome appears as a series of beads on a string and each bead is known as a nucleosome.
- Nucleosomes are the basic unit structure of eukaryotic chromosomes.
- The beads on the string represent the first level of chromosomal DNA packing.
- The nucleosome is a flat disc-shaped particle having a diameter of 10 urn and length of 5.7 urn.
- Nucleosome is a complex of DNA and histone protein.
- Each nucleosome consists of a histone octamer around which 1.75 turns of the DNA double helix is wrapped, which are 146 nucleotide pairs long.
- Each histone octamer consists of two flat tetramers of H-2A, H-2B, H-3 and H-4.
- Besides H-2A, H-2B, H-3 and H-4, one more histone is found called histone, H-l, which

holds the two ends of the DNA double helix around the histone octamer.

- Histone H-l is not conserved and is tissue-specific.
- H-1 is chemically active and may react with H-l of adjacent nucleosome to assist in coiling.
- Each nucleosome core particle is separated from the next by a region of linker DNA that varies in length from a few nucleotide pairs to 80 nucleotide pairs in different species.
- In each nucleosome, 142 hydrogen bonds are formed between the DNA and the histone core.
- A diploid human cell contains approximately 30 million nucleosomes.
- It has been suggested that the formation of nucleosome converts a DNA molecule into a chromatin thread about one-third of its initial length and this gives a first level of DNA packing.

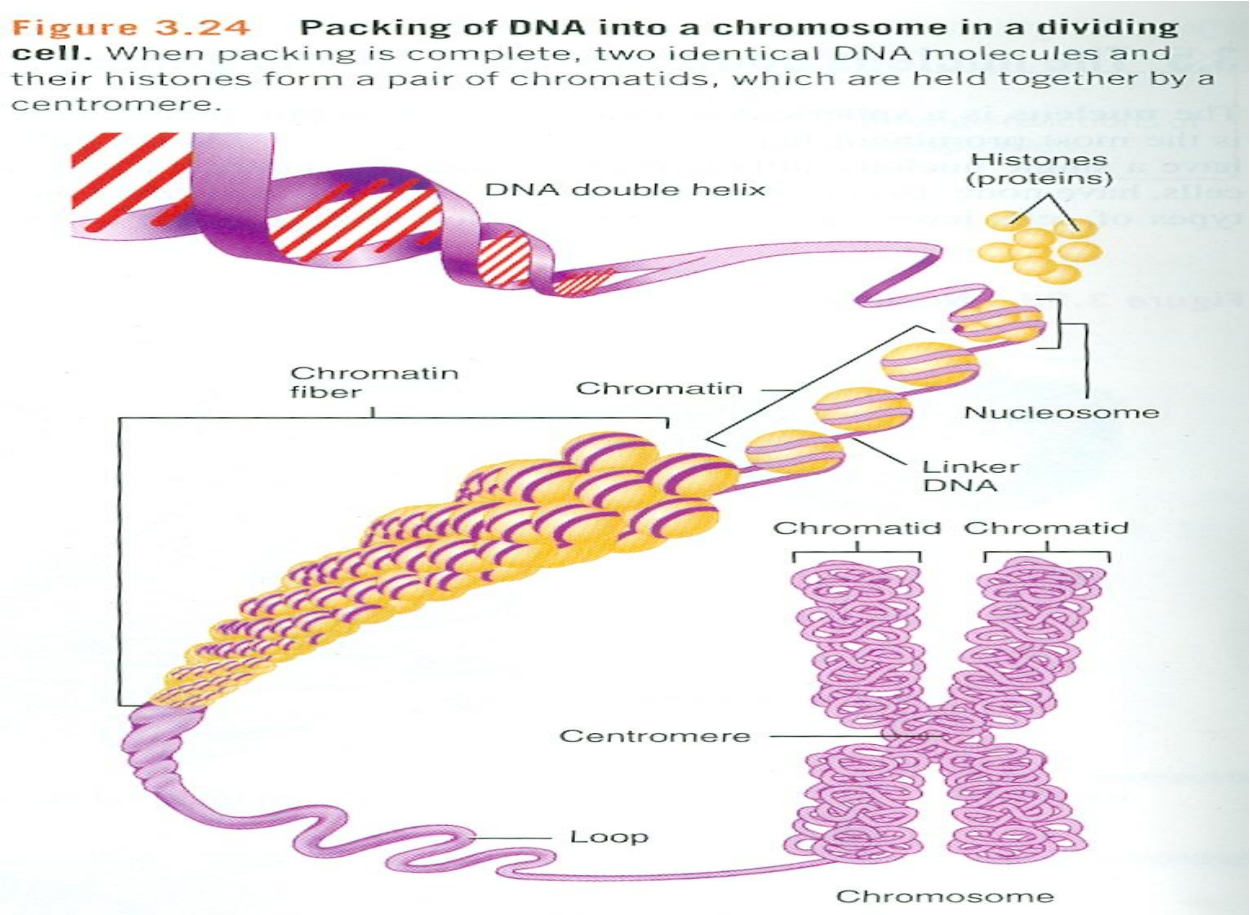


Figure 3.24 Packing of DNA into a chromosome in a dividing cell. When packing is complete, two identical DNA molecules and their histones form a pair of chromatids, which are held together by a centromere.

- **A chromosome is a highly coiled and folded DNA molecule that is**
- Several models have been proposed to explain how nucleosomes are packed in 30 urn chromatin fibre. One of these and the most consistent with the available data is a series of structural variations known as the zigzag model. This model suggests the following:

(a) The 30 urn structure found in chromosome is probably a fluid mosaic of different zigzag variations.

(b) There is variation in the length of linker DNA, and these differences in linker length may introduce further local perturbations into the zigzag structure.

(c) Lastly, the presence of other DNA-binding proteins and DNA sequence that are difficult to fold into nucleosome punctuate the 30 urn fibre with irregular features.

- **Chemical composition:** Chemically, a chromosome is made up of DNA, RNA, histone and nonhistone proteins.
- **Functions**

I. Chromosomes control all cellular activities.

2. They carry transmission of characters from one generation to another.

3. They control development and differentiation of characters.

4. They help in the formation of nucleolus.

5. Any change in the structure or number of chromosome leads to the formation of new characters which acts as raw material for evolution.

Polytene Chromosome

- Polytene chromosomes are the giant chromosomes which are easily visible under light microscope.
- They are found in the tissues of dipteran larvae.
- They were first observed by Balbiani (1882) in the salivary gland of the *Chironomous.*
- They are formed by endomitosis, i.e., duplication of DNA without nuclear division.
- They are visible during interphase.
- The cells of polytene chromosome do not undergo mitosis.
- Polytene chromosomes show somatic pairing, i.e., paternal and maternal chromosomes lie side by side which permits identification of deletions, duplications and inversions.
- All the polytene chromosomes may remain attached to a common chromocentre.
- Polytene chromosomes contain darkly stained dark bands and clear zones of interbands.
- Bands are Feulgen positive and are regions of high DNA concentration.

- Interbands are Feulgen negative and are regions of low DNA concentration.
- There are approximately 5,000 bands and 5,000 interbands in the genome of *Drosophila.*
- The banding patterns of polytene chromosome of *D. melanogaster* were studied by C B Bridges in 1935.
- At certain times, bands become enlarged to form swellings called puffs (Balbiani rings).
- Puffing is due to uncoiling of individual chromosomes in a band.
- Puffs represent active sites of RNA synthesis. Polytene chromosomes are very suitable for *in situ* hybridisation

Lampbrush Chromosome

- Lampbrush chromosomes are found in the diplotene stage of meiosis of all animals and are the largest known chromosome.
- They are so named because of their brush-like appearance.
- They were first observed by Flemming (1882) in the oocytes of salamander and the name Lampbrush was given by Ruckert (1992).
- Lampbrush chromosomes are extensible and elastic. They can be stretched to *2x2* of their original length.
- They are best seen in the oocytes of salamander due to their high DNA content.
- They are present in the form of bivalents in which maternal and paternal chromosomes are held together by chiasmata.
- Each bivalent contains a centromere.
- Each bivalent contains four chromatids which are represented by axial filaments.
- Axial filaments consist of DNA.
- The axial filaments become tightly coiled to form chromomeres.
- Lateral loops come out from chromomeres.
- There are approximately 10,000 loops per chromosome set.
- Loops are symmetrical and each loop appears at constant position.
- Each loop has an axis made up of DNA.
- Loop DNA appears to be thick as it is covered with nonhistone proteins as well as nascent RNA molecules.

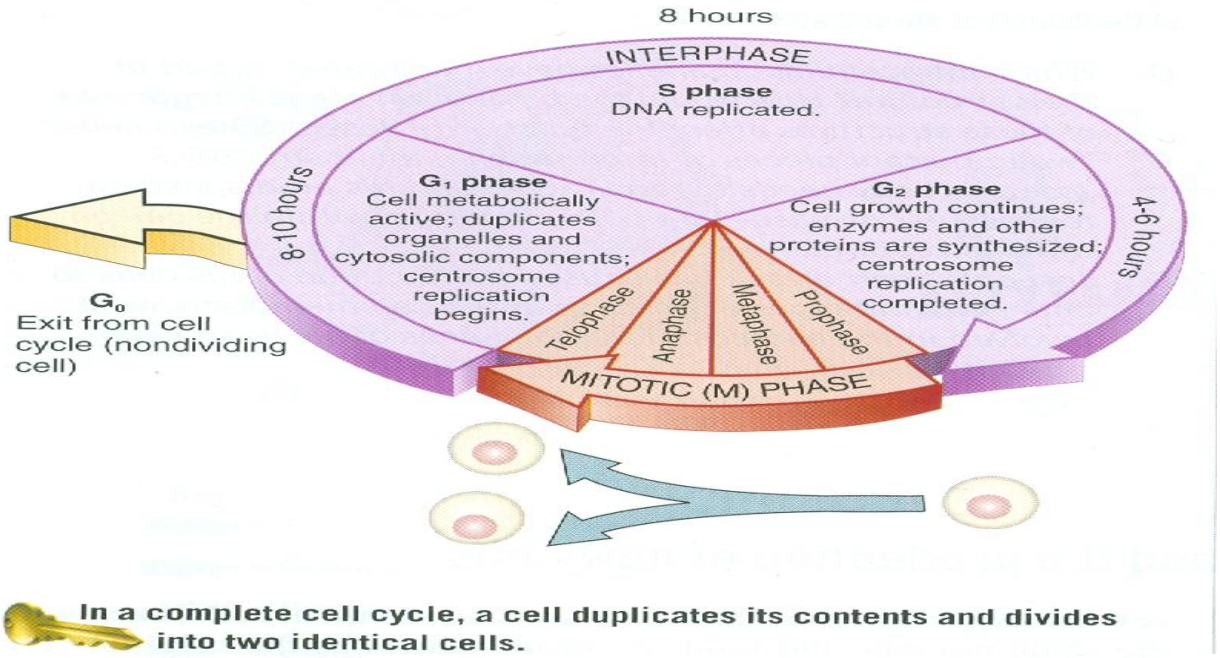
- Telomeres are lacking in lateral loops.
- Lampbrush chromosomes are an excellent material for *in situ* hybridisation of cloned DNA to RNA.
- Loops are the sites of RNA synthesis.

Cell Cycle

- A series of events that occur in a cell and results in its division and duplication is known ascell cycle.
- Each cell has a cell cycle clock which determines that a cell should or should not divide.
- A cell cycle takes 12-24 hours for most mammalian cells and approximately 20-30 minutes in *E. coli* cells.
- Nondividing cells are not considered to be in the cell cycle.
- The time required to complete one cell cycle (from the starting one cell division to the beginning of the next) is known as the generation time.
- The cell cycle is divided into two parts, viz., interphase and dividing phase.

Interphase

- It is the longest phase of the cell cycle and is the period between two consecutive cell divisions.
- Mammalian nerve cells have the longest interphase as they do not divide after birth.
- During interphase, the cell becomes enlarged.
- This phase is characterised by high rate of metabolism.



- Interphase is divided into three phases:

1. **G_1 Phase**

   • It is the first growth phase which is also known as the first gap phase.

- It is a crucial decision point.
- The timing of G, phase is most variable even in different cells of the same species.
- During this phase, synthesis of RNA and proteins takes place.

2. **S Phase**

- It is the synthetic phase during which replication of DNA occurs.
- Histone proteins are synthesised during this phase.
- Duplication of centrioles takes place.
- Each chromosome is made of two chromatids.
- It takes approximately 10 hours to replicate the 3 billion bits of information contained in the nucleus of a single human cell.

3. G_2 Phase

- It is the second growth phase which is also known as the second gap phase or premitotic phase.
- Synthesis of RNA and proteins occurs during this phase.
- Replication of cell organelles and condensation of chromosomes takes place.
- The cell continues to increase in size.
- During G_2 phase, a cell contains two times (4C) the amount of DNA present in the original diploid cell (2C).
- The lengths of S phase and G_2 phase are almost equal.

G_0 State

- A cell after cell division may withdraw from the cell cycle and enter into the resting phase called Go state or it may enter into the G, phase of the cell cycle.
- Cells in the Go state are viable and metabolically active.
- Go cells not only simply represent the absence of signals for mitosis but also an active repression of genes needed for mitosis.
- Most of the lymphocytes in human blood are in the Go state.

- Cells in culture can also be in the Go state.
- Cancer cells cannot enter the Go state.
- On stimulation, G_0 cells enter the G_1 phase.

Cell Cycle Checkpoints

• In a cell cycle, the following three checkpoints have been identified:

I. G_1 Checkpoint

- It is the most important checkpoint in the cell cycle which is also known as restriction point.
- It detects damaged DNA and prevents entry into the S phase.
- G_1 checkpoint blocks entry into the S phase by inhibiting S-Cdk complex.
- p53 levels are increased in damaged cells and block entry into the S phase.
- A p53 mutation is the most frequent mutation that leads to cancer.
- A p27 is a protein that binds to cyclin and CDK blocking entry to the S phase.

2. G_2 Checkpoint
    - It prevents the cell from entering mitosis (M phase).
    - It is triggered by Maturation-Promoting Factor (MPF) which is a cyclin CDK complex.
        - The cdc 2 cyclin B kinase is a key molecule in regulating this transition.
        - Damage to DNA after the S phase inhibits the action of CDK I, thus preventing the cell from proceeding from G_2 to mitosis.
3. Spindle Checkpoint (M-phase Checkpoint)
    - It detects any failure of spindle fibres to attach to kinetochores and arrest the cell in metaphase.
    - It detects incorrect alignment of the spindle itself and blocks cytokinesis.
    - It triggers apoptosis, if the damage is irrepairable.
    - In mammals and in yeast, the spindle checkpoint is inactivated by mutants in MAD and BUB genes.
    - Colchicine, which inhibits spindle assembly, manifests the presence of the spindle check point.
    - A cell cycle is mainly controlled by two classes of regulatory proteins, viz., cyclins and eye dependent kinases. Leland, Hartwell Hunt and Nurse were awarded the Nobel Prize in Physiol Medicine in 1902 for their discovery of these key molecules.

Cell Division

- The process by which a cell divides to form new cells is known as cell division.
- Cell division is the basic feature of life.
- Mature new cells arise from the pre-existing cells, so a cell divides to form new cells.
- Cell divisions take place for growth, reproduction and repair work of the body.
- The main aim of cell division is to maintain the original genome.
- A human body may undergo approximately 10,000 trillion divisions in an entire lifetime.
- Cell division is mainly of two types, viz., mitosis and meiosis.

Mitosis

- Mitosis is a type of cell division in which two daughter cells are formed from a single cell, having the number of the chromosomes as found in the original mother cell.
- Mitosis takes place both in somatic as well as reproductive cells.
- The term 'mitosis' was given by Flemming (1882).
- A cell undergoing mitosis is called mitocyte.
- Mitosis may be acentric (without centromere) as in plants or centric (with centromere) as in animals.
- Generally, the process of mitosis is completed within \-2 hours.
- The steps of mitosis are controlled by different genes and if mitosis is not regulated properly, it may in health problems such as cancer.
- The process of mitosis involves two steps:

1. Karyokinesis
2. Cytokinesis

3. Karyokinesis: Karyokinesis is the division of the nucleus. It involves the following stages:

(a) Prophase

- Prophase is the first and longest stage of mitosis.
- The cell becomes spheroid and there is an increase in viscosity and refractivity.
- Each chromosome consists of two chromatids jointed together by a centromere.
- The two centrioles start to move in opposite poles of the cell.
- Around each centriole, radiating fibres appear called asters.

- Asters are cytoplasmic in origin.
- The two asters are connected by spindle fibres.
- Spindles are formed from microtubules and are made up of tubulin.
- The aster, centrioles and spindle together form the mitotic apparatus.

(b) Metaphase

- Nuclear membrane and nucleolus disappear.
- The chromosome becomes arranged on equatorial prate.
- The chromosomes attain their full contraction.

- Metaphase is the most suitable stage for studying the morphological characterisation, banding and counting of the chromosomes.

(c) Anaphase

- Anaphase is the most dynamic and shortest stage of mitosis.
- The centromere divides. The sister chromatids separate and move towards opposites poles.
- Each chromatid has its own centromere.
- At the end of anaphase, there is a group of chromosomes at each pole.
- Mitotic anaphase has the same number of chromosomes as metaphase but half number of chromatids.
- The chromosomes may assume shape of 'J', 'V' or rod-like.

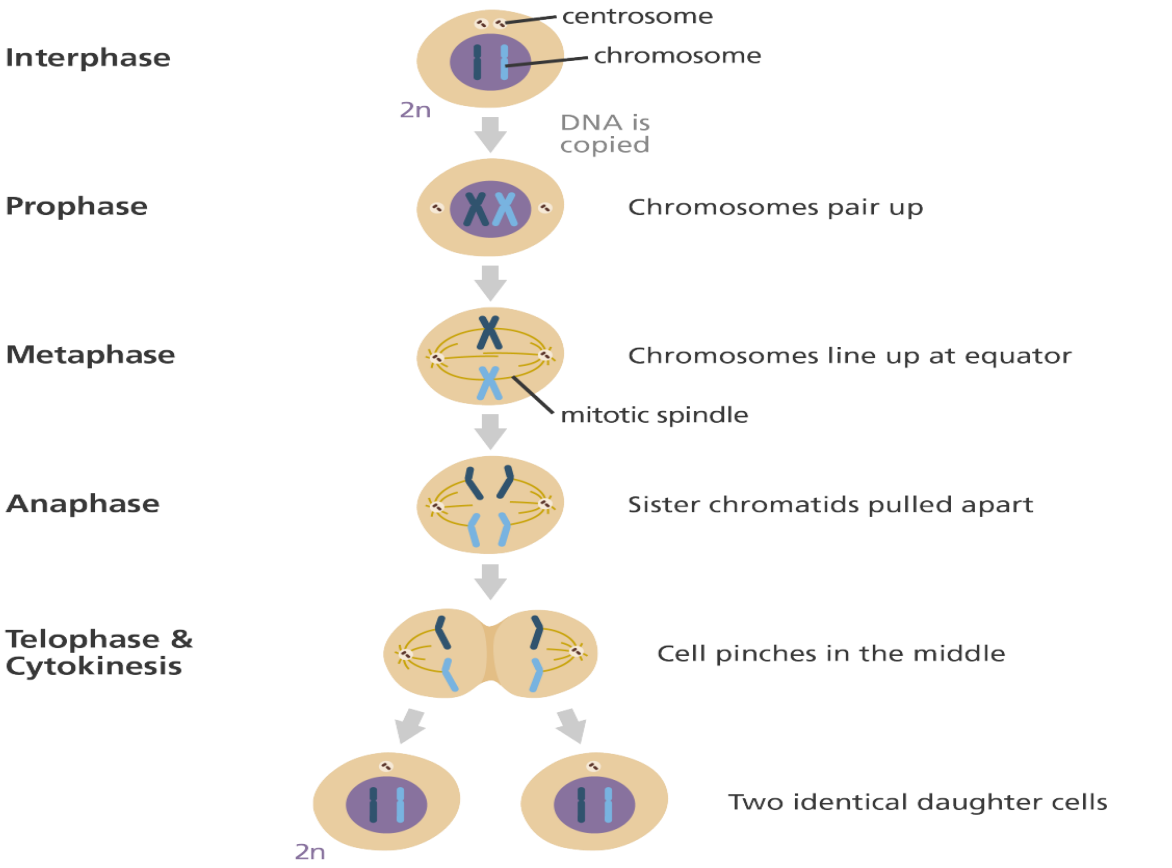
(d) Telophase

- It is the last stage of mitosis.
- Chromosomes at each pole begin to uncoil.
- Nuclear membrane and nucleolus appeared around each group of chromosomes, resulting in the formation of two daughter nuclei.

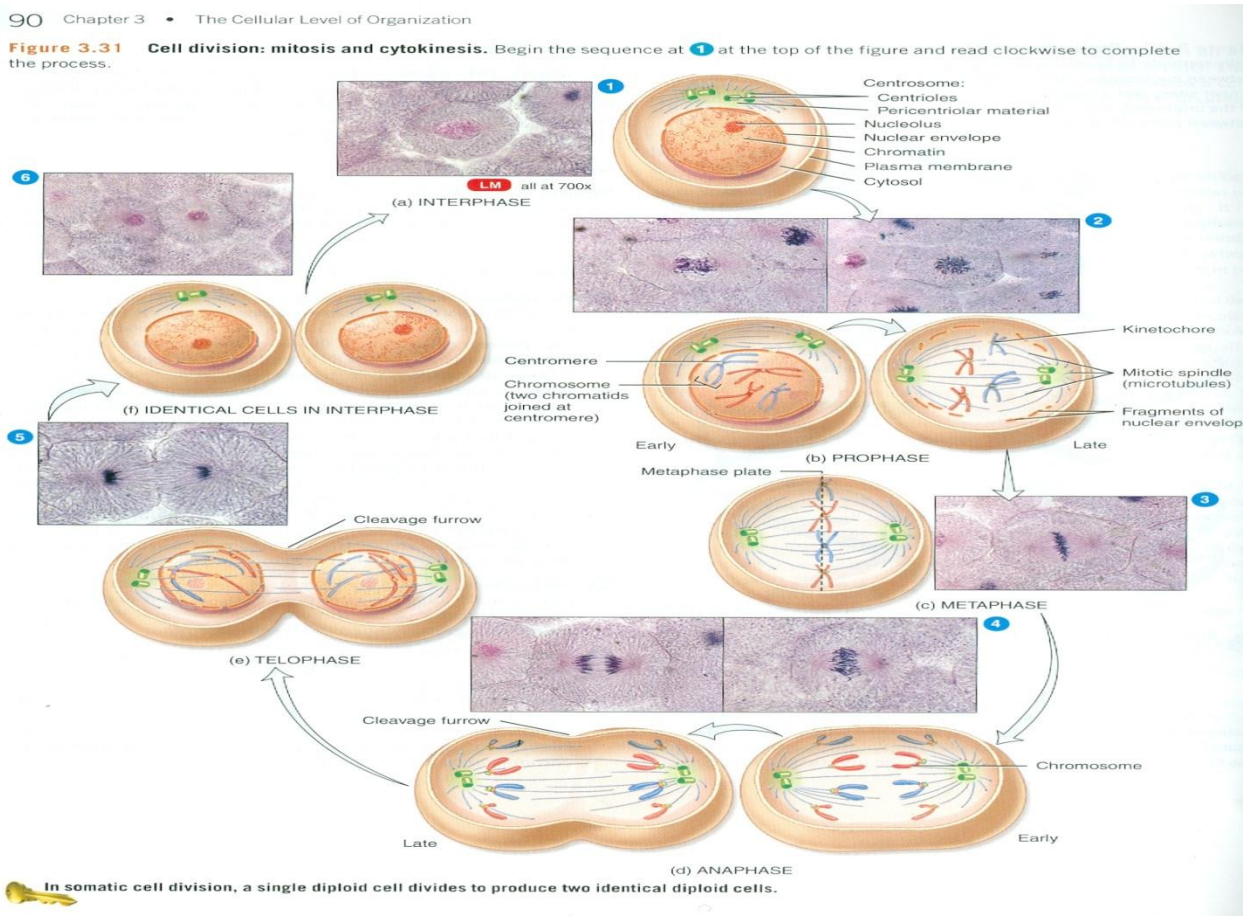
2. Cytokinesis

• Cytokinesis is the division of the cytoplasm

- In animal cells, cytokinesis takes place by cleavage furrow.
- In plant cells, cytokinesis takes place by the formation of cell plates.


Interphase
centrosome
chromosome
2n
DNA is copied
Prophase
Chromosomes pair up
Metaphase
Chromosomes line up at equator
mitotic spindle
Anaphase
Sister chromatids pulled apart
Telophase & Cytokinesis
Cell pinches in the middle
2n
Two identical daughter cells

2n – diploid



Significance

- Mitosis helps in the growth of the organs and the body.
- Mitosis is a means of reproduction in lower organisms.
- It maintains genetic constitution of the organisms.
- Mitosis maintains nucleo-cytoplasmic ratio.
- Mitosis helps in repairing of injured tissues by replacing dead cells by new cells.

Mitotic Poison

- Chemicals that cause anomalies in cell division are known as mitotic poison.
- These chemicals interfere with spindles, centrioles and centrosomes.
- These chemicals produce nondisjunction.
- Colchicine (obtained from the plant *Colchium autumnale)* vinblatine and vincristine inhibit microtubules assembly, whereas diezepam prevents separation of centrioles.
- Microorganisms remain unaffected by mitotic poison as they lack spindle apparatus.

Meiosis

- Meiosis is a special type of cell division as a result of which four daughter cells are formed, in which the number of chromosomes is reduced to half of that in the original cell.
- Meiosis occurs in reproductive cells.
- A cell undergoing meiosis is called meiocytes.
- Meiosis is also known as reductional division as it reduces the chromosome number to half.
- Meiosis involves two nuclear divisions with only one replication of DNA.
- Meiosis is essential for sexual reproduction. -'
- Meiosis was first discovered and described in the eggs of sea urchin by Oscar Hertwig in 1876.
- The term 'meiosis' was coined by Farmer and Moore (1905).
- Bdelloid rotifers have lost the ability to perform meiosis division, while meiosis does not occur in archaea or bacteria.
- Meiosis may be:
- Gametic: It is also known as terminal meiosis. It occurs at the time of gamete formation and is found in animals.
- Zygotic: It is also known as initial meiosis and occurs immediately after zygote formation: It is found in lower plants.
- Sporic: It is also known as intermediate meiosis. Meiosis division occurs in between the formation of zygote and gamete, resulting in the formation of haploid megaspores and microspores. Such type of meiosi is a characteristic of higher plants and some thallophytes.

Meiosis involves two divisions:

1. Heterotypic division: It is the first division as a result of which the chromosome number is reduced to half. It is also known as reduction division.

2.Homotypic division: It is the second division which is totally mitotic in nature.

1. Heterotypic division: It involves the following stages:

(i) Interphase: Before meiosis begins, the genetic material is duplicated.

(ii) Prophase I: It is the longest and most important phase of the meiosis. It is divided into six substages:

(a) Leptotene

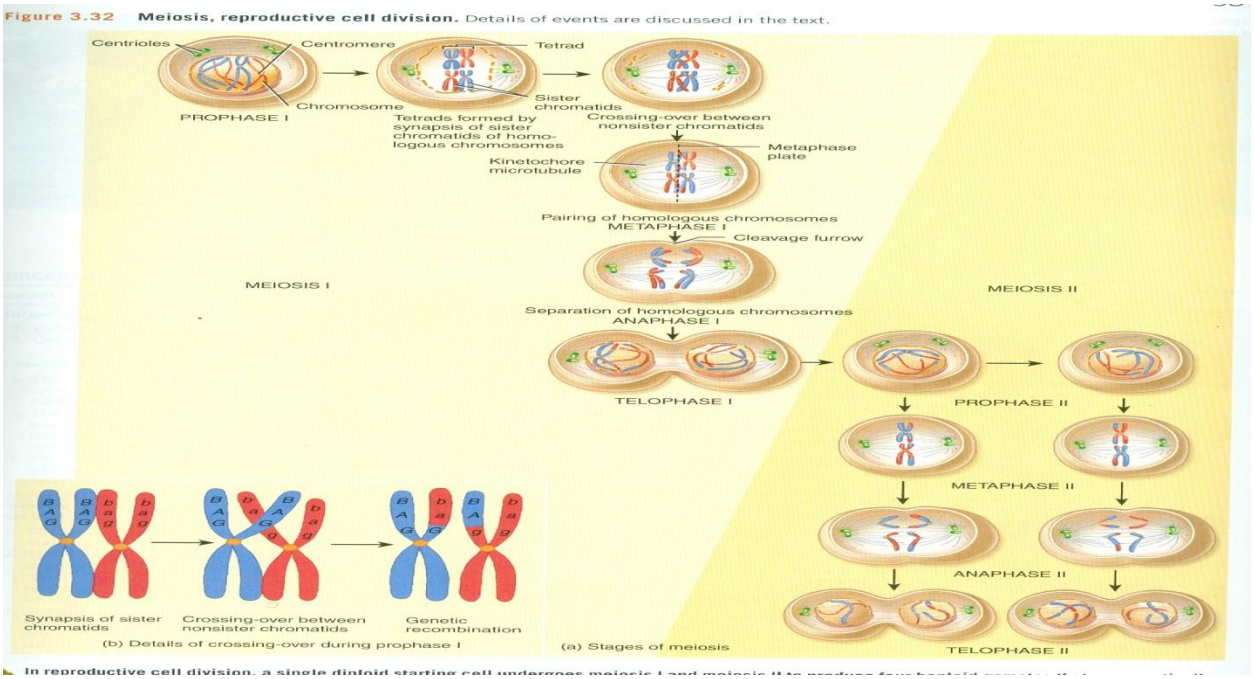
- Chromosomes become more distinct.
- Chromosomes bear bead-like structures called chromomeres.
- The number, size and position of chromomeres are characteristic on a chromosome.
- Chromosome; may develop a basket-like arrangement called bouquet and this stage is called bouquet stage.
- Some plant cells form a tangle of threads called synizetic knot (e.g., *Trillium).*

(b) Zygotene

- Chromosomes become shorter and thicker,
- Pairing of homologus chromosomes takes place.
- Paired chromosomes are called bivalents and the process of pairing is called synpasis.
- The number of bivalents is half of the number of diploid chromosomes.
- The pairing of homologous chromosomes may begin from the centromere (procentric), or from either ends (proterminal), or from anywhere (at random).
- Of the two homologous chromosomes, one is derived from the male parent and other from the female parent.
- As a result of pairing, a tripartite structure is formed called syneptonemal complex.
- Syneptonemal complex first appeared during zygotene.
- Syneptonemal complex is lacking in the meiosis of male diptera.

(c) Pachytene

- Each bivalent splits longitudinally, so in each bivalent the number of chromatids is four (tetravalent). This stage is called tetrad stage.
- Exchange of chromatids takes place between nonsister chromatids. This process of exchange of chromatids is known as crossing over.
- As a result of crossing over, a cross-shaped (X) structure is formed, called chiasmata.
- Pachytene is the longest stage in mammalian spermatogenesis.
- Pachytene may last for days, weeks or even years.



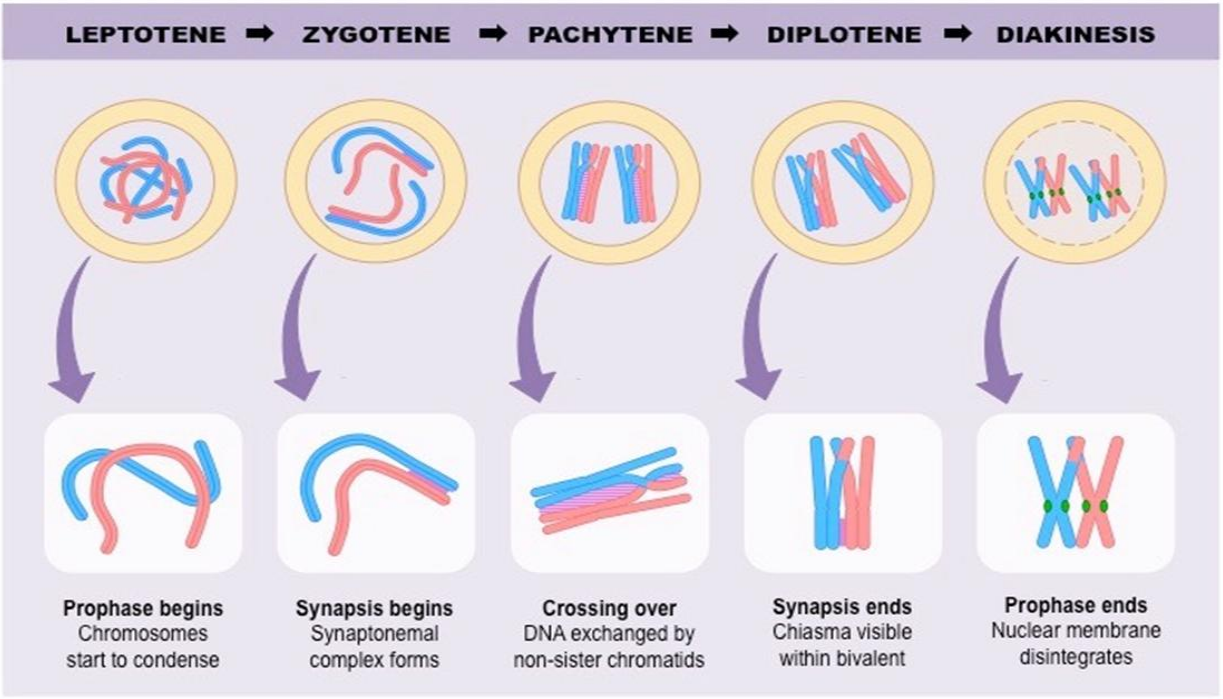
(d) Diplotene

- Separation of homologous chromosomes begins. This process is known as terminalisation.
- Due to contracting tendency of chromosomes, the chiasmata are pulled towards the ends of paired homologous chromosomes.
- Syneptonemal complex begins to break down.
- Diplotene may last for months or

years.

(e) Diakinesis

- The process of terminalisation is completed.
- Chromosomes condense and thicken.
- Nuclear membrane and nucleolus begin to disintegrate.



Metaphase I

- Formation of spindle begins.
  - Bivalents become arranged on equatorial plate.
  - Bivalents are arranged in such a way that their arms lie over the equator while the centromeres are directed towards the poles.
  - There is a 50-50 chance for the daughter cells to get the mother's or father's homologue as orientation is random, with either homologue on a side.

(iv) **Anaphase I**

- The homologous chromosomes separate from each other and move to opposite poles.
- Each pole has haploid number of chromosomes. In this stage, reduction in the number of chromosomes takes place.
- There is no division of centromeres.

(v) **Telophase I**

- Telophase 1 is similar to telophase of mitosis except that there is only one set of (replicated) chromosome in each cell.
- Nuclear membrane and nucleolus reappear around each group of the haploid set of chromosomes at each pole.

- Thus, two daughter haploid nuclei are formed; each with two chromatids.
- Sometimes telophase is absent.

Cytokinesis

• Cytokinesis results in the formation of two daughter cells having haploid number of chromosomes.

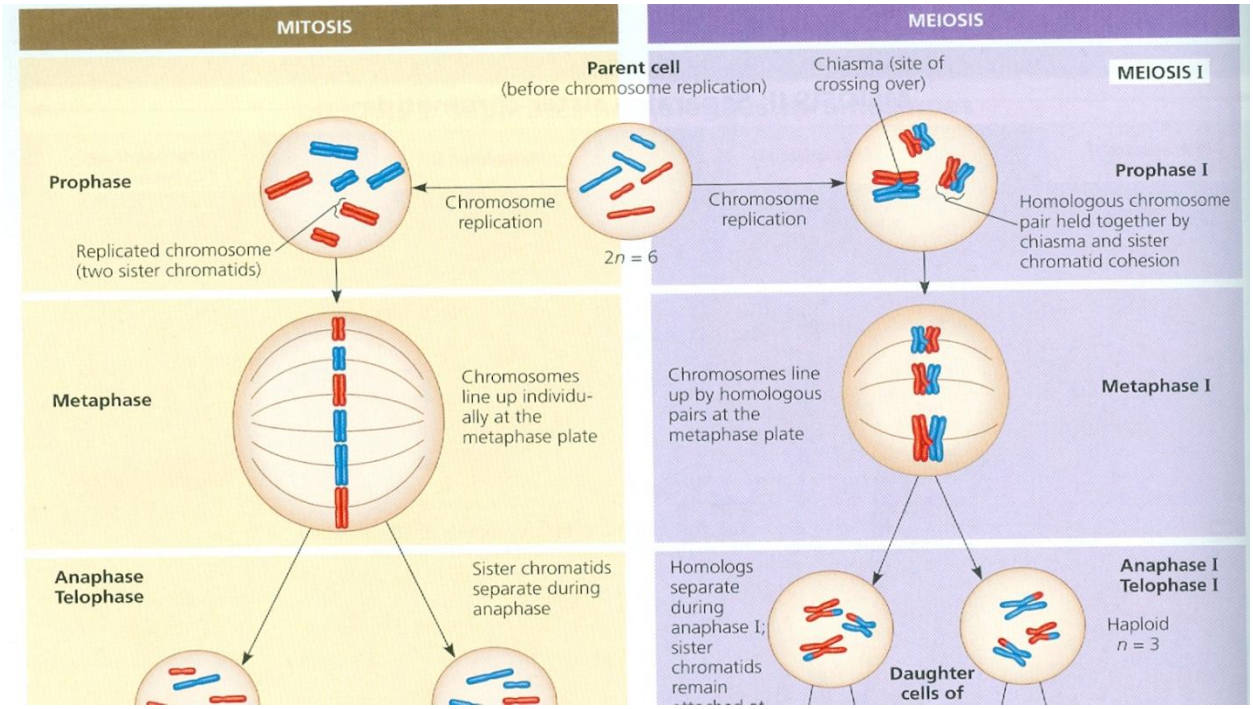
Interkinesis

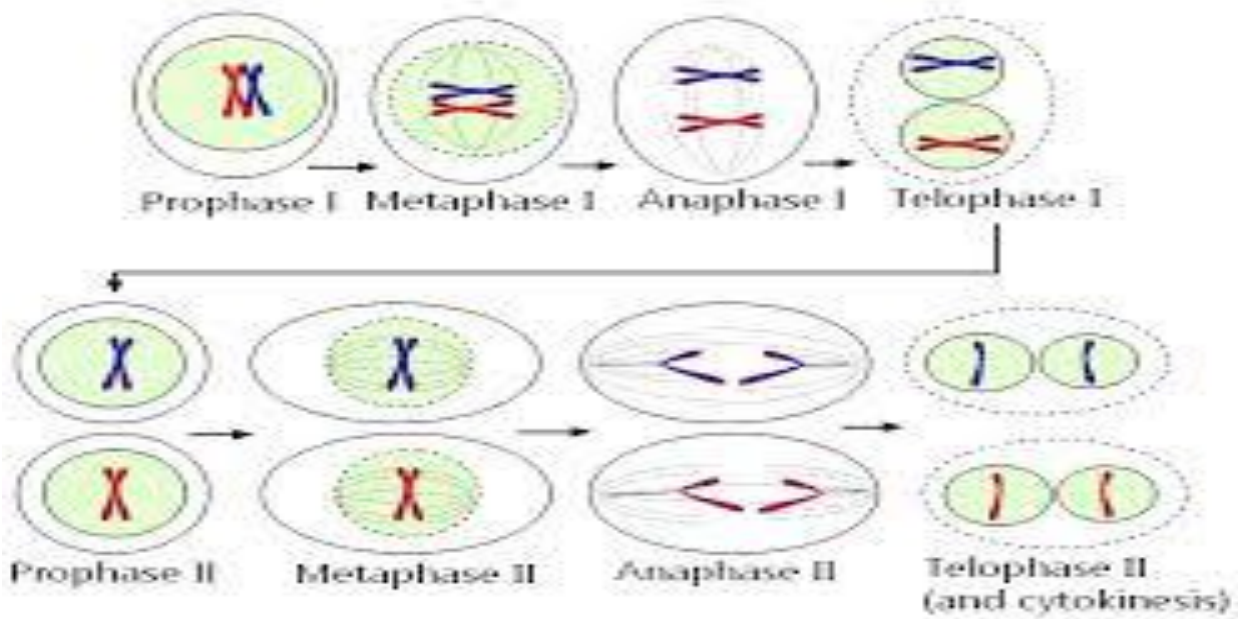
- The period between telophase I and prophase 11 is called interkinesis.
- It is quite a short period or completely absent.
- In *Trillium* and odonata, there is no telophase I and interphase.

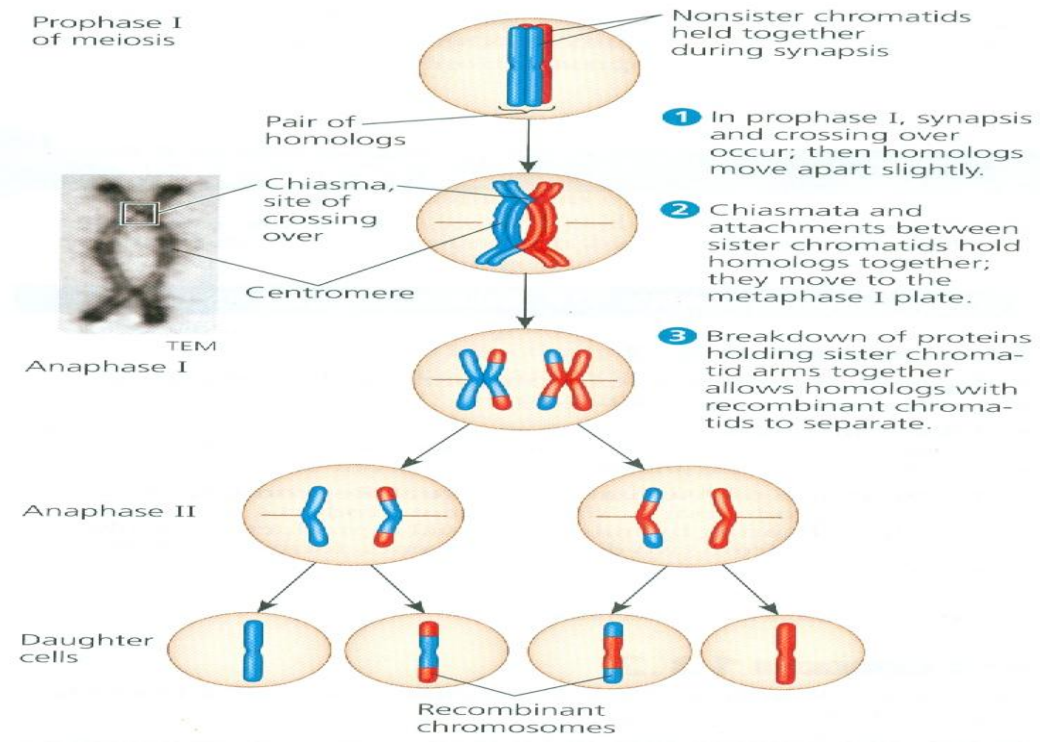
Homotypic Division

It is similar to mitosis but lacks the S phase. It involves the following stages:

1. **Prophase 11**
   - The chromosomes condense and each chromosome consists of two chromatids, viz" one parental and the other recombinant.
   - Nuclear membrane and nucleolus disappear.
   - DNA does not replicate.
2. **Metaphase 11**
   - Spindle fibres are formed.
   - Chromosomes arrange on the equatorial plate.
3. **Anaphase 11**
   - The two chromatids of chromosome separate and move towards the opposite poles.
   - Centromere divides, so each chromatid has its own centromere.
4. **Telophase** 11
   - Nuclear membrane and nucleolus reappear around each group of chromosomes.
   - Thus, four haploid daughter nuclei are formed.
   - Lastly, cytokinesis takes place as a result of which four haploid daughter cells are formed. Meiosis is a means of gametes formation.


MITOSIS
MEIOSIS
Parent cell
(before chromosome replication)
Chiasma (site of crossing over)
MEIOSIS I
Prophase
Chromosome replication
Chromosome replication
Prophase I
Homologous chromosome pair held together by chiasma and sister chromatid cohesion
Replicated chromosome (two sister chromatids)
2n = 6
Metaphase
Chromosomes line up individually at the metaphase plate
Chromosomes line up by homologous pairs at the metaphase plate
Metaphase I
Anaphase
Telophase
Sister chromatids separate during anaphase
Homologs separate during anaphase I; sister chromatids remain
Anaphase I
Telophase I
Haploid
n = 3
Daughter cells of


Prophase I
Metaphase I
Anaphase I
Telophase I
Prophase II
Metaphase II
Anaphase II
Telophase II
(and cytokinesis)



▲ **Figure 13.12** **The results of crossing over during meiosis.**

Significance

- Meiosis is a means of gametes formation
- Meiosis maintains constancy in chromosome number from generation to generation
- It produces genetic variation due to crossing over in organisms which acts as raw material for evolution.

SUMMARY

Property	Mitosis	Meiosis
DNA replication	Occurs during interphase before mitosis begins	Occurs during interphase before meiosis I begins
Number of divisions	One, including prophase, metaphase, anaphase, and telophase	Two, each including prophase, metaphase, anaphase, and telophase
Synapsis of homologous chromosomes	Does not occur	Occurs during prophase I along with crossing over between nonsister chromatids; resulting chiasmata hold pairs together due to sister chromatid cohesion
Number of daughter cells and genetic composition	Two, each diploid ($2n$) and genetically identical to the parent cell	Four, each haploid (n), containing half as many chromosomes as the parent cell; genetically different from the parent cell and from each other
Role in the animal body	Enables multicellular adult to arise from zygote; produces cells for growth, repair, and, in some species, asexual reproduction	Produces gametes; reduces number of chromosomes by half and introduces genetic variability among the gametes

▲ **Figure 13.9 A comparison of mitosis and meiosis in diploid cells.**

DRAW IT *Could any other combination of*