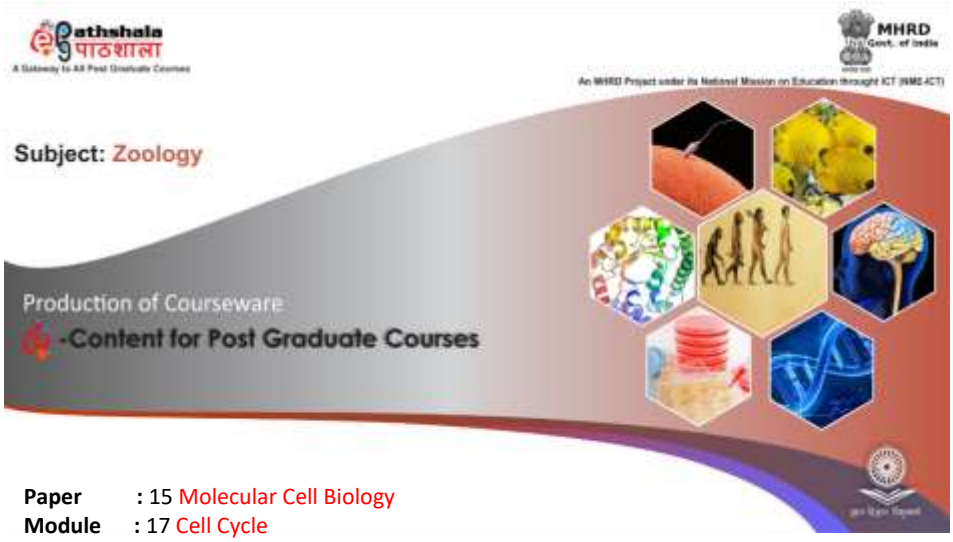

Paper : 15 Molecular Cell Biology
Module : 17 Cell Cycle

athshala पाठशाला MHRD

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Description of Module	
Subject Name	ZOOLOGY
Paper Name	Molecular Cell Biology; Zool 015
Module Name/Title	Cellular energetic and regulatory mechanisms
Module Id	M17: Cell Cycle
Keywords	Chromosomes, Cell division, Crossing over, Mitosis, Meiosis

CONTENTS

1. Learning Outcomes

After studying this module, you shall be able to

- Know how a single cell zygote can give rise to a multi cellular organism i.e., how a cell arise from a pre-existing cell.
- Learn about various phases of cell cycle.
- Identify various stages of mitosis and meiosis under microscope
- Evaluate the importance of regulation of cell cycle.
- Analyze that any loss of cell cycle regulation will lead to cancerous growth.

2. Introduction

We are aware that all living organisms are composed of CELL – The Basic Unit of Life. All living beings start their life from a single cell (Zygote). Zygote formed as a result of fertilization undergoes countless division giving rise to a multi cellular organism. The multi cellular organism has astonishing cellular complexity & body organization. Cell proliferation creates two daughter cells from a single parent cell. It involves two major processes:

(1) Cell Growth - Increasing cell size up to a certain stage.

(2) Cell Division - Emergence of two or more daughter cells (in meiosis four daughter cells are formed) from a single parent cell.

Certain cells continue to divide even after the organism attains maturity, but few cells lose their ability to divide and enter in Quiescent phase (Example - Nerve cells).

Cell Cycle is a well-organized series of events that leads to cell division and creation of two daughter cells identical to their parental cells. It is a highly regulated process necessary for the normal cell (growth). Any loss in the control of cell cycle may lead to cancer. Despite of the deeply intrigued scientific community for the cure of this menace, one-sixth of the world's population is hunted by the same. All living organisms show cell division, but it occurs in different ways in prokaryotes and eukaryotes. Prokaryotic cells are simple in structure, lack nuclear membrane and have a simplistic genome (only one circular chromosome). Therefore, it divides through binary fission. Chromosome duplication takes

place prior to division followed by its attachment to opposite side of cell membrane. Cytokinesis is through physical separation of the cell. A eukaryotic cell divides by Mitosis and sometimes by Meiosis. In short in prokaryotes cell division is called AMITOSIS (unsymmetrical cell division) and in eukaryotes either it is mitosis or meiosis, equal separation of cellular material in 2 or 4 daughter cells. We will discuss eukaryotic cell division in detail.

Advent of various new biochemical and genetic techniques has strengthened our understanding of various events of the eukaryotic cell cycle. From these studies it is evident that the cell division is principally controlled by regulating two major phases:

(1) DNA replication phase

(2) Cell division phase

The main regulators of cell cycle events are a variety of heterodimer protein kinase having a regulatory subunit- Cyclin and catalytic subunit –Cdk (cyclin –dependent kinase). Kinase regulates the activity of many proteins involved in the major events of cell cycle (DNA replication & mitosis) by phosphorylation at their specific regulatory sites. It is also involved in activating some & inhibiting others to coordinate the activities of these proteins.

Major events that occur before and during cell cycle:

(1) Signal to induce cell proliferation.

(2) DNA replication and replication of important cell components.

(3) DNA which is being duplicated is equally distributed in the daughter cells.

(4) Cell membrane (in case of plants-cell wall) distinct the two newly formed cells by cytokinesis.

3. Historical Aspect of Cell Cycle

Since the discovery of Third tenet of cell cycle proposed by **Rudolf Ludwig Karl Virchow** (Fig: 3.1) “New cells arise from pre-existing cells”, cell cycle became the subject of intensive research. Many microscopists and embryologists tried but couldn’t speculate the underlining mechanism of cell cycle regulation.

After the discovery of double helical structure of DNA in 1953, scientists started focusing on process of DNA replication.

http://php.med.unsw.edu.au/cellbiology/index.php?title=2009_Group 5Project

3.1 - Image of Rudolf Ludwig Karl Virchow

Discovery of cell cycle phases - In 1970, general mechanism of regulating the onset of cell cycle phases were recognized. G_o phase was identified.

Mechanism of cell cycle regulation - Pardee (1974) focused on the regulating mechanism of cell cycle. He uncovered the mechanism of cell switching between proliferative & G_o phase of the cell cycle.

Discovery of cell cyclins and function of centromere - In 1980 scientists discovered how centromere helped in chromosome segregation & isolated a functional centromere of budding Yeast. They discovered changes in levels of cyclins in a cyclic manner during cell cycle.

Discovery of cell cycle checkpoints and their control mechanisms – In 1980, origin of replications sites were identified. The checkpoints of the cell cycle were identified and their control mechanisms were understood, whole mechanism- how damaged DNA arrest cell cycle by regulation at checkpoint and P53 was discovered.

1990 – Cyclin dependent kinase (new class of protein) was identified. Scientists identified new classes of Cyclin C, D, E and discovery of CDK inhibitors.

In year 2001, Leland Hartwell, Tim Hunt and Paul Nurse were jointly awarded Nobel Prize in Physiology or Medicine for their discoveries of "key regulators of the cell cycle". They identified the molecules CDK and cyclin that controls cell cycle in a eukaryotic cell. It was magnificent discovery in biology and medicine.

Five noble prizes in physiology and medicine have been awarded in understanding of cell cycle & its regulation. Currently scientists are focusing on specific treatments at different phases & disease related to cell cycle.

4. Phases of Cell Cycle

The cell cycle is divided into two basic phases (In a typical eukaryotic cell):

Interphase – The period between end of first cell divisions and beginning of second cell division, cell is majorly involved in cell growth and in diverse metabolic activities.

M Phase (Mitosis phase) – actual division phase. (Refer to Fig: 4.1)

The interphase is further divided into three phases: (Refer to Fig: 4.1)

G_1 phase (Gap 1) – During this phase, cells synthesize RNAs and proteins and get prepared for DNA replication and chromosome replication. During the G_1 phase, cell is metabolically active and continuously grows but does not replicate its DNA.

S phase (Synthesis) – It is a period involving DNA synthesis. The amount of DNA doubles per cell though number of chromosomes remains the same.

G_2 phase (Gap 2) – During this phase proteins are synthesized for mitosis. The cell growth continues.

M - Phase Includes – The dividing phase. It consists of:

Prophase
Metaphase
Anaphase
Telophase

It is important to note that a human cell growing in a cell culture medium completes cell cycle in the average duration of 24 hour and cell division lasts for only about an hour. The interphase lasts more than 95% of the duration of cell Cycle.

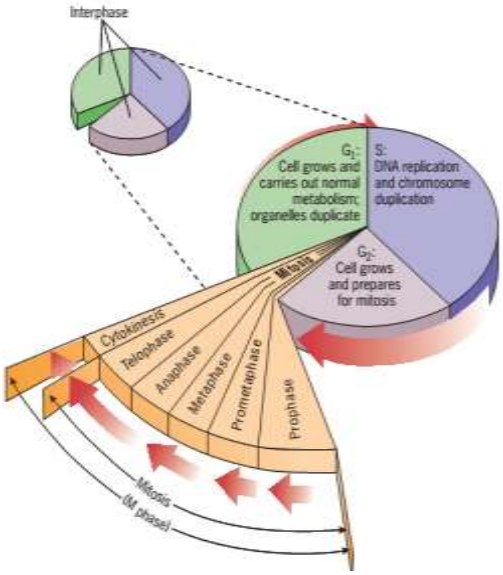
1. Cell growth is one of the significant events of G_1 phase. G_1 phase is most variable in terms of its duration in cell cycle.

2. The transition from G_1 to S is the critical control point in the cell cycle.

3. G_2 (gap between S and M). This gap phase is utilized for proofreading of the genetic material (DNA) to ensure DNA is properly replicated and packaged.

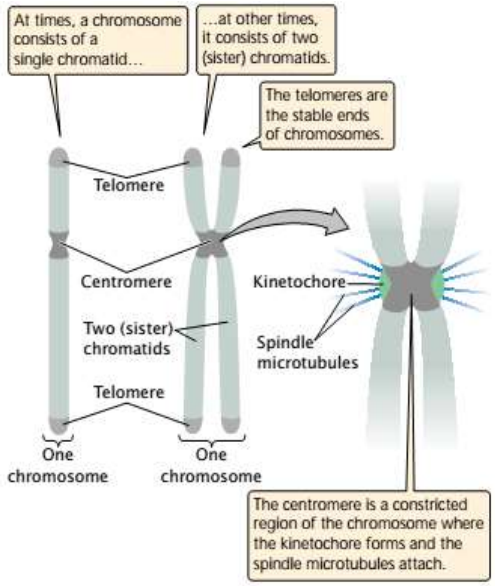
4. G_0 or quiescence (Quiscent phase) occurs when cells stop dividing and exit the cell cycle due to the lack of growth-promoting signals or presence of prodifferentiation signals. They can survive for days, weeks or in some cells lifetime (eg: nerve cells, cells of eye lens).

Most differentiated cells "exit" the cell cycle. The systematic progress through each phase is intricately regulated through both positive and negative regulatory signaling molecules.



http://www.amazon.com/Cell-Molecular-Biology-Concepts-Experiments/dp/1118206738

4.1- An Overview of Eukaryotic Cell Cycle: This diagram of the cell cycle indicates the stages through which a cell passes from one division to the next.



http://www.amazon.com/Genetics-Conceptual-Approach-Benjamin-Pierce/dp/1429251697

4.2 - Structure of a Eukaryotic Chromosome

Three essential elements of a eukaryotic chromosome: (Refer Fig: 4.2)

- Centromere - Site of attachment of spindle microtubule on chromosome. Kinetochore (a protein structure), assemble on chromosome before cell division.
- A pair of Telomeres – Natural tips of chromosomes (ends) to provide stability.
- Origin of Replication – Site where DNA synthesis begins.

The kinetochore (a mutiprotein complex) assembles at each centromere during metaphase. The kinetochores of sister chromatids then associate with microtubules coming from opposite spindle poles. During the anaphase, sister chromatids separate and move at opposite poles and get distributed in two daughter cells.

5. Mitosis

Microscopic and biochemical research on animals and plants has provided immense information about the M- phase of cell cycle. The name described the thread like chromosomes that mystifyingly appeared in animal cells just before their division.

Mitosis is a process of cell reproduction involving faithful segregation of replicated DNA molecules into two daughter nuclei. The genetic content of two daughter cells arising as a result of mitosis and cytokinesis possess a genetic content identical to the mother cell from which they arose. During mitosis cell devotes nearly all of its energy to single activity- chromosome segregation. It was discovered by Strasburger (1875AD) in plant cells & by W. Flemming (1879AD) in animal cells. It occurs both in somatic cells as well as germ cells.

Mitosis is generally divided into five stages:

Prophase
Prometaphase
Metaphase
Anaphase
Telophase

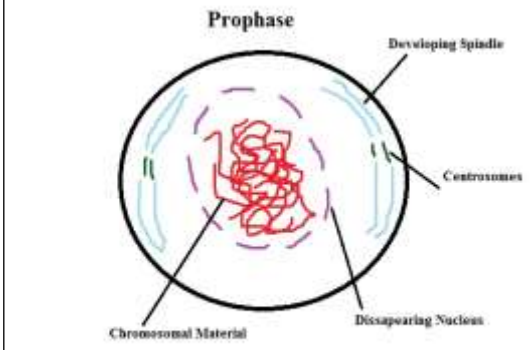
5.1 PROPHASE (Refer Fig: 5.1)

During Prophase

The duplicated chromosomes are prepared for segregation.

The mitotic machinery is assembled.

The chromatin of an interphase cell is organized into fibers approximately 30 nm in diameter.



http://biologyblock.com/?p=111

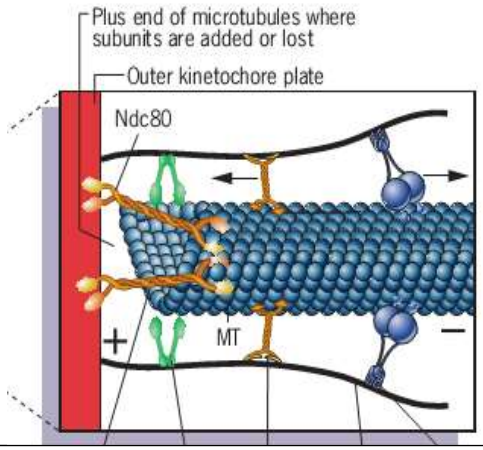
5.1 Cell in Prophase Stage of Cell Cycle

Compaction of chromosome during prophase does not alter the nature of the chromatin fiber. It alters the packaging of chromatin fiber.

Condensin (multiprotein complex) proteins associate with the chromosomes during their compaction (DNA codensation).

In the presence of a topoisomerase and ATP, condensin is able to bind to DNA in vitro and curl the DNA into positively supercoiled loops.

Condensin – Cause chromosome compaction by forming a ring around supercoiled loops of DNA within chromatin. (Refer Fig: 5.2)



http://www.amazon.com/Cell-Molecular-Biology-Concepts-Experiments/dp/1118206738

5.2 - The Kinetochore

Cohesin molecules hold the DNA of sister chromatids together.

Before replication, the DNA of each interphase chromosome becomes associated at sites along its length with a multiprotein complex called cohesin. After DNA replication, cohesin holds the two sister chromatids together through G_2 and into mitosis when they are ultimately separated.

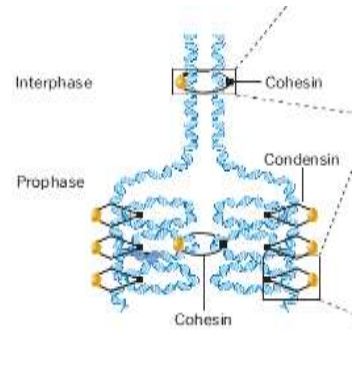
The chromatids of each mitotic chromosome are held together loosely along their extended arms, but much more firmly at their centromeres.

<u>Centromeres and Kinetochores</u>:

Centromere is the residence of highly repeated DNA sequences.

Kinetochore - Proteinaceous, button-like structure, at the outer surface of the centromere of each chromatid. The kinetochore functions as:

Site of attachment of the chromosome to the dynamic



http://www.amazon.com/Cell-Molecular-Biology-Concepts-

5.3 - Model for the roles of condensin and cohesin in the formation of mitotic chromosomes.

microtubules of the mitotic spindle.

Residence of several motor proteins involved in chromosome motility.

In the signaling pathway of an important mitotic checkpoint.

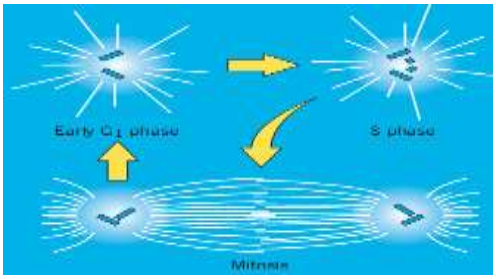
How Kinetochores are able to maintain their attachment to microtubules that are continually growing and shrinking at their plus end?

Ndc80 is an essential kinetochore protein that forms fibrils that appear to reach out and bind the surface of the adjacent microtubule. **CENP-E,** which is a member of the kinesin superfamily, has been the most strongly associated as a potential microtubule coupler. (Refer Fig: 5.3)

5.1.1 Formation of the Mitotic Spindle:

With the commencement of DNA replication in the nucleus at the onset of S phase, each centriole of the centrosome initiates its "replication" in the cytoplasm.

The centrosome splits into two adjacent centrosomes, each comprising a pair of mother–daughter centrioles. (Fig 5.4)



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5.4 - The Centrosome Cycle of an Animal Cell

The formation of additional centrioles can lead to abnormal cell division and contribute to the development of cancer.

Journey of Mitotic spindle begins with the appearance of microtubules in a "sun-burst" arrangement, or aster, around each centrosome during early prophase, followed by separation of the centrosomes from one another. This is followed by its movement around the nucleus towards opposite ends of the cell.

A number of different types of animal cells (including those of the early mouse embryo) lack centrosomes, cells of higher plants also lack centrosome, and still all of these cells can form a bipolarmitotic spindle and undergo a somewhat typical mitosis. In all of these cells without

centrosome, nucleation of the microtubules of the mitotic spindle starts near the chromosomes. It starts near the pole in those cells where centrosome resides at poles.

5.1.2. The Dissolution of the Nuclear Envelope and Partitioning of Cytoplasmic Organelles

The interaction between the spindle and chromosomes is made conceivable by the break-down of the nuclear envelope at the end of prophase.

All of these processes are thought to be initiated by phosphorylation of key substrates by mitotic kinases, particularly cyclin B–Cdk1.

Few of the membrane bound organelles of the cytoplasm remain relatively intact through mitosis; these include mitochondria, lysosomes, and peroxisomes, as well as the chloroplasts of a plant cell.

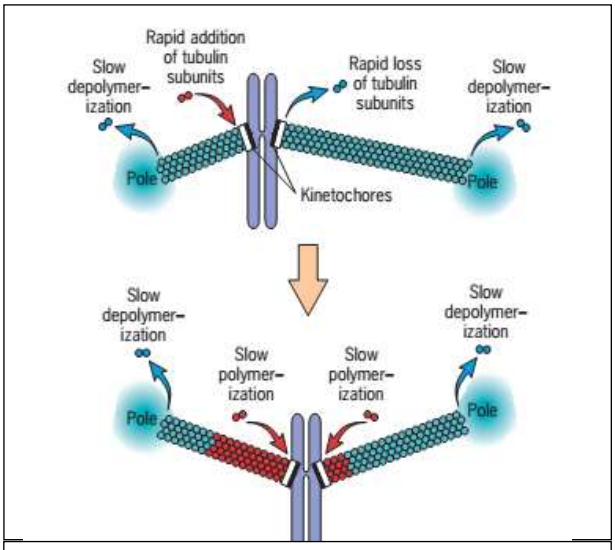
Recent studies on living, cultured mammalian cells suggest that the ER network remains relatively intact during mitosis. This study has challanged the earlier studies performed largely on eggs and embryos that proposed that ER undergoes extensive fragmentation during prophase.

5.2 PROMETAPHASE (Refer Fig: 5.5)

http://course1.winona.edu/kbates/bio241/images/figure-09-08-3-photo.jpg

5.5 - Microscopic View of Cell in Prometaphase Stage of Cell Cycle

Dissolution of the nuclear envelope marks the start of the next phase of



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5.6 - Microtubule behavior during formation of the metaphase plate. Initially, the chromosome is connected to microtubules from opposite poles that may be very different in length. As prometaphase continues, this imbalance is corrected as the result of the shortening of microtubules from one pole, due to the rapid loss of tubulin subunits at the kinetochore, and the lengthening of microtubules from the opposite

mitosis, prometaphase.

During this stage assembly of mitotic spindle is completed inside a dividing cell and the chromosomes are directed towards the equitorial region of the cell.

As the microtubules of the spindle penetrate into the central region of the cell, the free (plus) ends of the microtubules are seen to grow and shrink in a very dynamic fashion, as if they were “probing” for a chromosome.

Microtubule that makes contact with kinetochore are “captured” and stabilized.

A kinetochore usually makes initial contact with the side wall of a microtubule rather than its end.

The kinetochore has a tendency to become stably associated with the plus end of one or more spindle microtubules arising from one of the spindle poles.

The two sister chromatids of each mitotic chromosome finally get connected by their kinetochores to microtubules that extend from opposite poles of a dividing cell.

Congression is a process of movement of chromosomes of a prometaphase cell toward the center of the mitotic spindle, midway between the poles.

Forces essential for chromosome movements during prometaphase are generated by motor proteins which are associated with both the kinetochores and arms of the chromosomes.

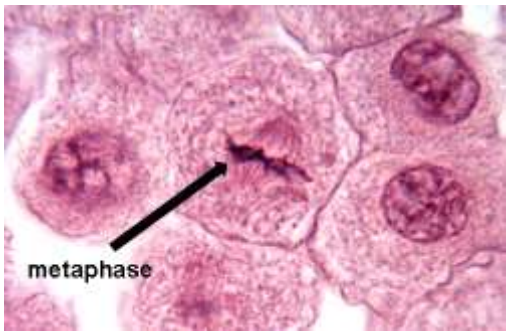
Chromosomes connected to microtubule from opposite poles may differ in length so this imbalance is corrected by longer microtubules attached to one kinetochore are shortened, while the shorter microtubules attached to the sister kinetochore are elongated. (Refer Fig: 5.6)

The length of microtubule is changed by the process governing differences in pulling force (tension) on the two sister kinetochores.

The dynamic activiy of shortening and elongation of microtubules occur primarily by loss or gain of tubulin subunits at the plus end of the microtubule, while the plus end of microtubules remain attached to a kinetochore

5.3 METAPHASE:

Chromosomes become aligned at the spindle equator. One chromatid of each chromosome establish connection to microtubule from one pole by its kinetochore and its sister chromatid get connected by its kinetochore microtubules from the opposite pole. This marks that the cell has reached the stage of metaphase. (Refer Fig: 5.7)



http://facstaff.gpc.edu/~sfinazzo/mitosis/metaphase Whitefish.gif

5.7 – Microscopic View of Cell in Metaphase

What is metaphase plate??

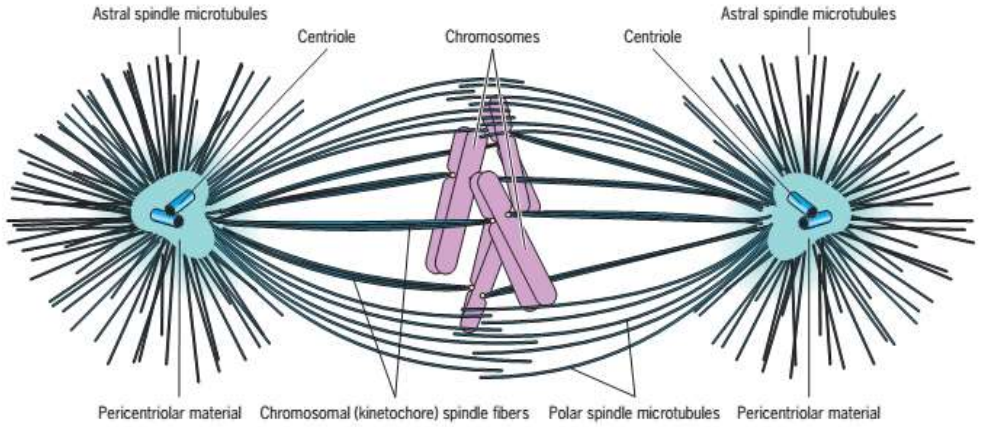
The plane of alignment of the chromosomes at metaphase is referred to as the metaphase plate.

Three groups of microtubules of the metaphase spindle of an animal cell: (Refer Fig: 5.8)

Astral microtubule: It radiate outward from the centrosome towards the region outside the body of the spindle. They help in the positioning of the spindle apparatus in the cell. It may even help to determine the plane of cytokinesis.

Chromosomal (or kinetochore) microtubules: It extend between the region of the centrosome and the kinetochores of the chromosomes. The chromosomal microtubules exert a pulling force on the kinetochores. As a result of which it maintains chromosome in the equitorial plane, by a “tug-of-war” between balanced pulling forces (exerted by chromosomal spindle fibers from opposite poles). During anaphase, chromosomal microtubules are responsible for the movement of the chromosomes toward their respective poles.

Polar (or interpolar) microtubules: It extends from the centrosome past the chromosomes. It is responsible for maintaining the mechanical integrity of the spindle. There is an overlap of polar microtubules arising from one centrosome with their counterparts from the opposite centrosome.



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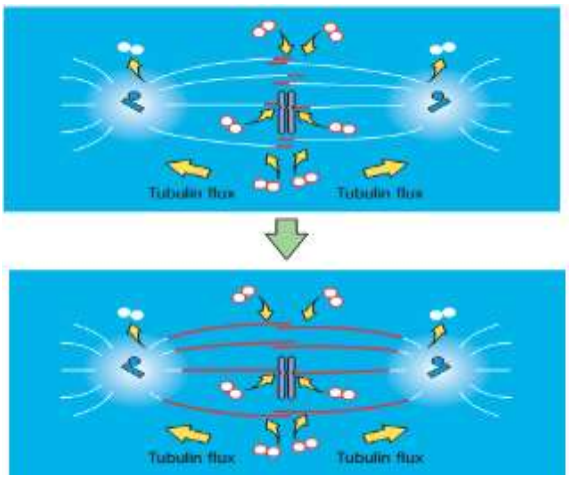
5.8 - The mitotic spindle of an animal cell. Each spindle pole contains a pair of centrioles surrounded by amorphous pericentriolar material at which the microtubules are nucleated. Three types of microtubule discussed above are shown.

Microtubule Flux in the Metaphase Spindle:

5.9 - Tubulin flux through the microtubules of the mitotic spindle at metaphase. Even though the microtubules appear stationary at this stage, injection of fluorescently labeled tubulin subunits indicates that the components of the spindle are in a dynamic state of flux. Subunits are incorporated preferentially at the kinetochores of the chromosomal microtubules and the equatorial ends of the polar microtubules, and they are lost preferentially from the minus ends of the microtubules in the region of the poles. Tubulin subunits move through the microtubules of a metaphase spindle at a rate of about 1 µm/min.



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The microtubules in mitotic spindle exist in a highly dynamic state.

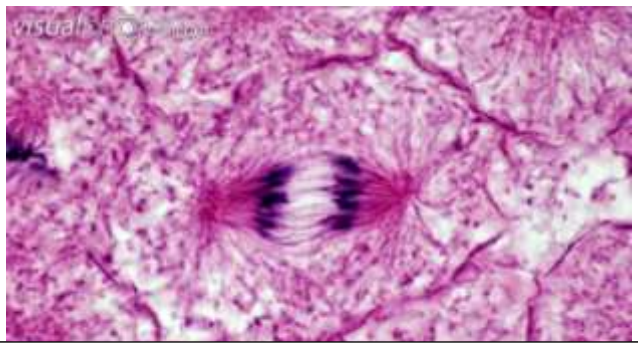
Microtubule flux involves rapid loss and gain of the tubulin subunit at the plus end of the of the chromosomal microtubules, even though ends of microtubules are attached to the kinetochore (Appear stationary).

Kinetochore is not like a cap at the end of the microtubule, (blocking the entry or exit of terminal subunits). Kinetochore is the site of dynamic activity.

How subunits move along the chromosomal microtubules from the kinetochore toward the pole??

More subunits are added to the plus end than are lost (net addition of subunits at the kinetochore region). In the intervening time, there is net loss of the tubulin subunits at the minus end minus ends. Protein of kinesin-13 family (promotes depolarization) aid in the loss of tubulin subunit at the poles. (Refer Fig: 5.9)

5.4 ANAPHASE: (Refer Fig: 5.10)



http://www.visualphotos.com/image/1x3744268/a_cell_in_anaphase_of_mitosis_a_whitefish_cell_in

5.10 – Microscopic View of Cell in Anaphase Stage of Cell Cycle

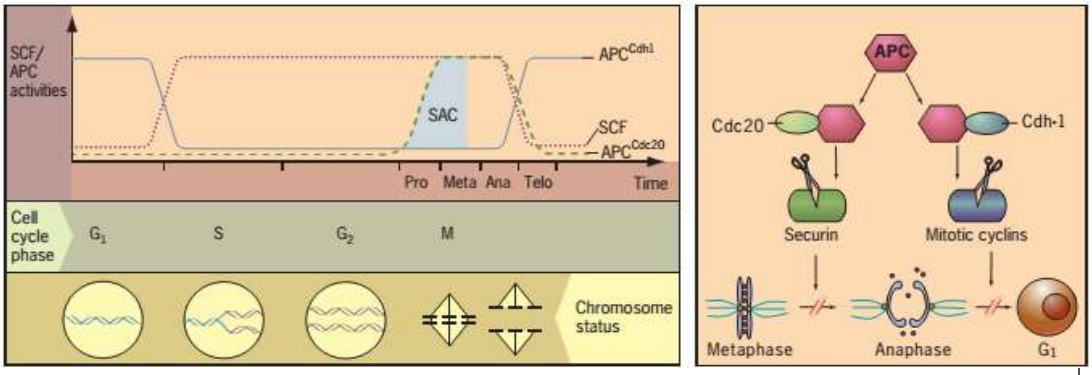
It is a phase that begins with the splitting of the sister chromatids of each chromosomes and their movement towards opposite poles.

SCF and APC (multi subunit complexes) that ubiquitinate substrates, ultimately their destruction by proteasomes.

SCF (active majorly in interphase), whereas **APC** (anaphase promoting complex) is primarily active during mitosis and G1. APC have two versions. These versions of APCs differ in the type of adapter, containing either Cdc20 or a Cdh1 adaptor protein. These adapters can alter the substrates recognition by the APC complex. **APC Cdc20** is active earlier in mitosis than its other version **APC Cdh1**.

SAC (spindle assembly checkpoint) inhibits APC Cdc20 from eliciting anaphase until all the replicated chromosomes become properly aligned at Metaphase plate region.

APC Cdc20 version of APC complex is responsible for destroying proteins, such as securing (It inhibits anaphase). Destruction of securin (APC cdc20 substrates) promotes the **metaphase–anaphase transition**. (Refer Fig: 5.11)



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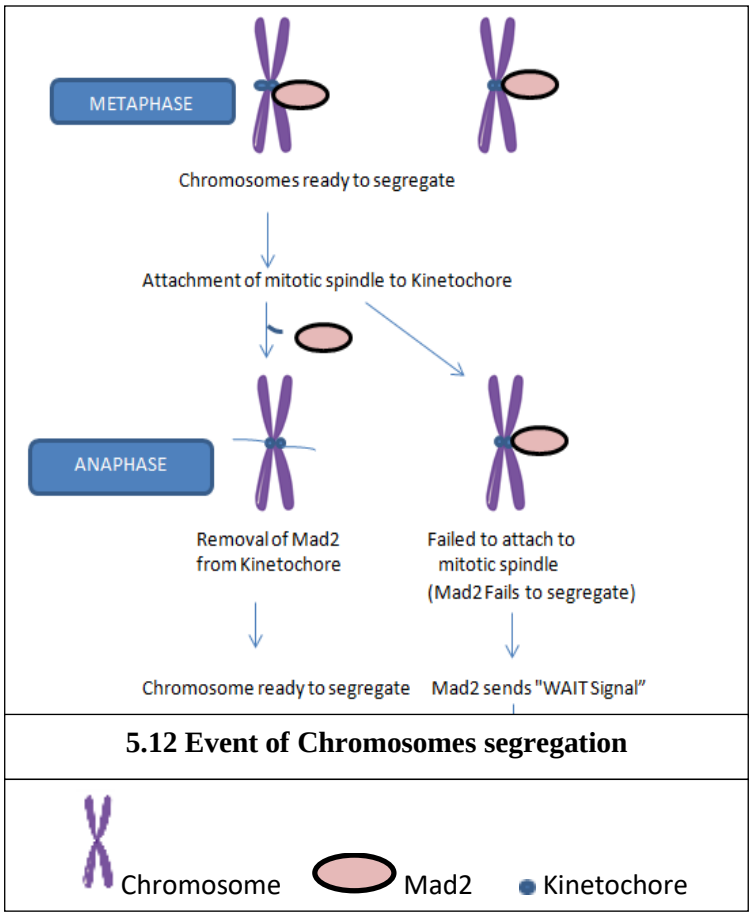
5.11 - SCF and APC (multisubunit complexes) that ubiquitinate substrates, leading to their destruction by proteasomes.

APC Cdh1 version of APC complex for ubiquitinating proteins, like mitotic cyclins, (It inhibit exit of the cell from mitosis). Destruction of these mitotic cyclin (APC Cdh1 substrates) promotes the mitosis–G1transition. APC Cdh1 activity during early G1 helps maintain the low cyclin–Cdk activity required to assemble pre-replication complexes at the origins of replication.

How cell determine whether or not all of the chromosomes are properly aligned at the metaphase plate?



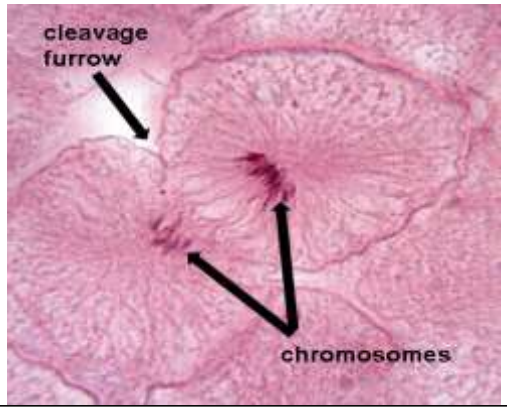
5.12 Event of Chromosomes segregation

Kinetochore which is not attached to microtubule contains a complex of proteins**, Mad2** (best studied). It is a main controller of the spindle assembly checkpoint. The presence of Mad2 proteins at an unattached kinetochore sends a "wait" signal to the cell cycle machinery that can prevents the cell from continuing further into anaphase. (Refer Fig: 5.12)

Colchicine is a mitotic inhibitor drug that can inhibit mitosis by disrupting microtubules formation (It helps in chromosomal segregation). It is also used in Cancer treatment.

5.5 <u>TELOPHASE</u>: (Refer Fig: 5.13)

As the chromosomes have reached their respective poles, they are likely to collect in a mass (chromatin). It is marking the commencement of the final stage of mitosis, or telophase. During this phase, cells start returning to the interphase condition of the cell.



http://www.biology.lifeeasy.org/2517/what-are-two-important-events-of-telophase

5.13 - Microscopic View of Cell in Telophase State

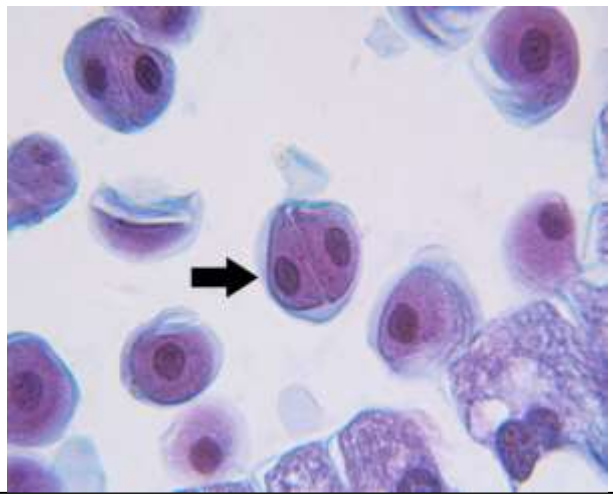
Following Changes occur:

The mitotic spindle disassembles

The nuclear envelope starts its reformation

The chromosomes start dispersing until they disappear from view under the microscope.

5.6 <u>CYTOKINESIS</u>: (Refer Fig: 5.14)



http://www.tooloop.com/pictures-of-cytokinesis/pictures-of-cytokinesis/

5.14 - Microscopic View of Cell in Cytokinesis Stage

Mitosis involves the equal segregation of duplicated chromosomes of parent cell into daughter nuclei. Cytokinesis is the final stage of mitosis.

The cytokinesis in most of the animal start during anaphase by the appearance of a furrow in the plasma membrane, which gradually deepens and finally joins in the centre dividing the cell cytoplasm into two. The plane of the furrow lies in the same plane earlier occupied by the chromosomes of the metaphase plate. Finally the two sets of chromosomes are ultimately equally partitioned into two daughter cells.

In a plant cell, cell wall formation starts in the centre and grows towards the lateral walls and finally joins. Unlike animal cell, plane of cell plate formation is perpendicular to the plane occupied by mitotic spindle.

What would happen if karyokinesis is not followed by cytokinesis??

5.7 SIGNIFICANCE OF MITOSIS:

Chromosome number remains constant and genetic stability is maintained.

It play major role in growth and development of the zygote.
It helps in the formation of new cell to repair wounds.
It plays important role in asexual mode of reproduction, budding, fragmentation etc.

6. Meiosis

It is a type of cell division (Reductional cell division) involving single chromososme duplication, but cell divides twice. Parent cell divides to form four daughter cells each with only half the number of chromosome and DNA content compared to parent cell. It occurs in germ cells of sex organs (eg: spermatogenesis, oogenesis). Meiosis was demonstrated by **Van Benden** (1883 A.D.). Term“meiosis” was given by **Farmer and Moore** from a greek word meioum = to reduce. Meiosis consist of two major events

Karyokinesis – Nuclear division.

Cytokinesis – Cytoplasmic division

6.1 PHASES OF MEIOSIS

6.1.1 MEIOSIS – I

A. Karyokinesis – I
   a. Prophase –I
      i. Leptotene
      ii. Zygotene
      iii. Pachytene
      iv. Diplotene
      v. Diakinesis
   b. Metaphase – I
   c. Anaphase – I
   d. Telophase – I
B. Cytokinesis - I

INTERKINESIS

6.1.2 MEIOSIS – II

A. Karyokinesis – II
   a. Prophase –II
   b. Metaphase – II
   c. Anaphase – II
   d. Telophase – II
B. Cytokinesis - II

6.2 MEIOSIS – I

KARYOKINESIS – I: It involves division of nucleus. (Refer Fig: 6.1)

PROPHASE –I: It has longest duration, even longer than mitosis. It is further divided into five subphase:

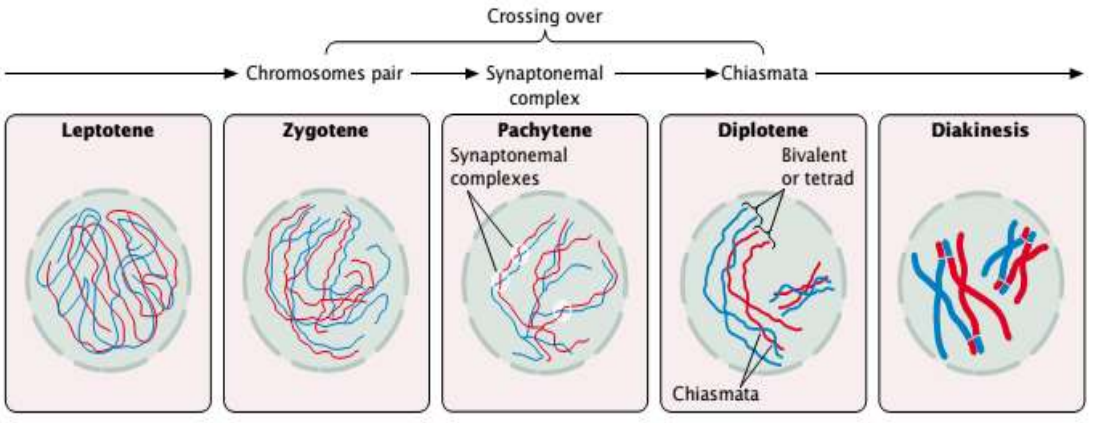
Leptotene - Chromosomes are in the form of thin thread, aster formation starts, nuclear DNA starts condensing.

Zygotene – Pairing (Synapsis) of homologous chromosomes starts (form bivalent) because of the attraction between the alleles on homologous chromosomes, synaptonemal complex formation starts (A filamentous ladder – like nucleoprotein complex, creating a structural base for pairing and synapsis for meiotic chromosomes)

Pachytene – Chromosomes are still in thread like phase, chromosomes still condenses, tetra (each bivalent has two dyads – two sister chromatids joined at centromere for a dyad) visible under microscope, exchange of genetic material starts (crossing over) between two non sister chromatids. Crossing over is an enzmatically regulated process controlled by recombinase enzyme. (Refer Fig: 6.2).

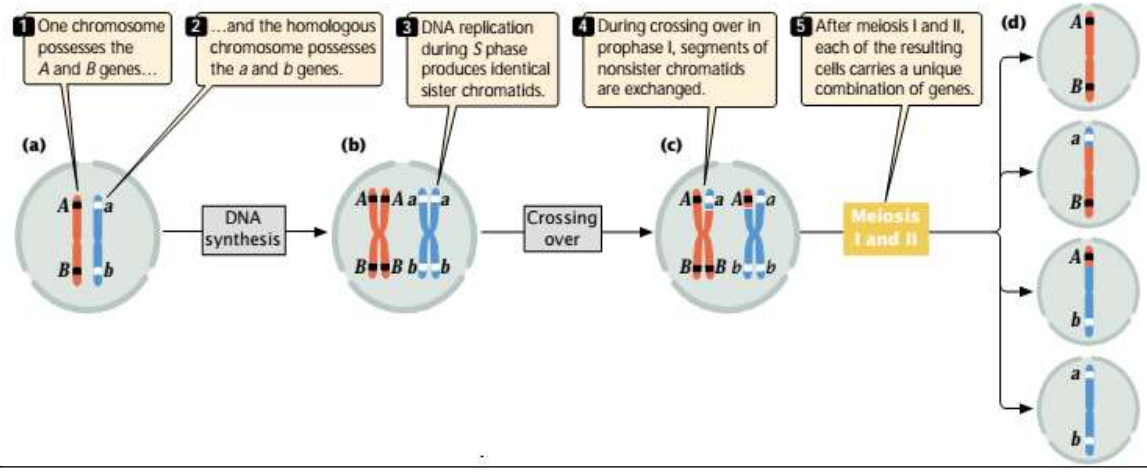
Diplotene (double thread stage) – During this stage nuclear envelop & nuleoli starts separating, synaptonemal complex starts dissolves leading to separation of homologous chromosomes. Separation of chromosomes is not complete, homologous chromosomes remain attach at chiasmata (point of chromosomal exchange), chiasmata movement starts towards the ends of chromosomes (terminalisation).

Diakinesis – Process of terminalisation is completed, non sister chromatids of homologous chromosomes only remain attach near telomeric region, bivalent structure appear like ring, nuclear membrane and nucleoli completely dissappear, spindle formation starts .



http://www.amazon.com/Genetics-Conceptual-Approach-Benjamin-Pierce/dp/1429251697

6.1 - Stages of Meiosis - I: Prophase - I Crossing over



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6.2 - Production of Genetic Variation by Crossing Over

METAPHASE–I : (Refer Fig: 6.3)

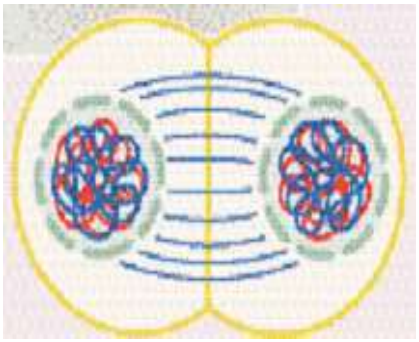
Bivalents arrange in two parallel equatorial planes. Centromeres of all homologous chromosomes are equidistant from equator lie towards the poles. Two kinetochores of each homologous chromosome are attached to spindle fibers of same side.

6.3 – Metaphase - I

6.4 - Anaphase - I

ANAPHASE–I: (Refer Fig: 6.4)

In this phase homologous chromosomes separates and start moving towards opposite poles, dividing each tetrad into two dyads leading to reduction in chromosome number (called disjunction).



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6.5 - Telophase - I

TELOPHASE–I: (Refer Fig: 6.5)

Nuclear membrane and nucleolus is formed, astral ray and spindle fibres disappear and chromosomes decondense to form long thread like structure.

CYTOKINESIS– I: It involves division of cytoplasm. This takes place by cell furrow formation in an animal cell and by cell plate formation in plant cells.

INTERKINESIS: (Period between Telophase-I of Meiosis-I and Prophase–II of Meiosis-II): During this phase only protein synthesis takes place, no DNA synthesis during this phase, only centrioles get duplicated.

6.3 MEIOSIS– II

It is also known as "Equational division" (number of chromosomes remains the same in daughter cells compared to parent cell. Meiosis – II is of short duration compared to meiosis – I.

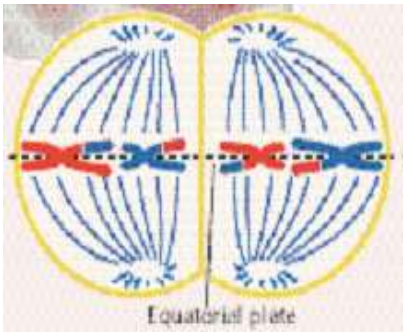
It is divided into:

Karyokinesis – II
Cytokinesis – II

KARYOKINESIS – II: In this phase two chromatids of each chromosomes get separated to separate cell. It is further divided into:

Prophase- II: This phase involves formation of aster from centriole, nuclear membrane and nucleolus disappear, chromatin fibres condense to thick chromosomes, spindle formed in Prophase-II is perpendicular to that formed in Prophase-I (Refer Fig: 6.6)

Metaphase-II: Chromosomes arrange in one equatorial plane, each centromere is joined by mitotic spindle arising from opposite poles at the kinetochore region. (Refer Fig: 6.7).



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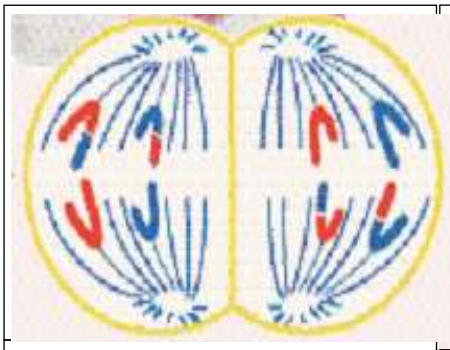
6.7 - Metaphase - II

http://biologyjunction.com/meiosis_labeling.htm

6.6 - Prophase - II

Anaphase–II: Centromere of each chromosome get split leading to the formation of two daughter chromosomes, after splitting daughter chromosomes move to opposite poles. (Refer Fig: 6.8).

Telophase-II: Changes during the Telophase is always opposite to that of Prophase, nuclear membrane and nucleolus of daughter cells reappear, astral rays disappear. (Refer Fig: 6.9).



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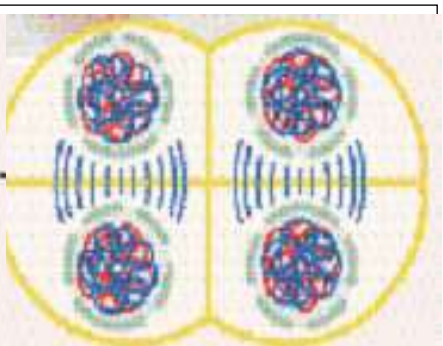
6.8 - Anaphase - II



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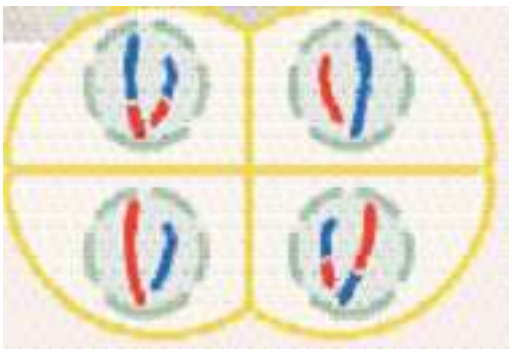
6.9 - Telophase - II

CYTOKINESIS – II: Cytoplasm is always divided by cell furrow in an animal cell, by cell plate in plant cell. (Refer Fig: 6.10).



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6.10 - Product of Meiosis

6.4 SIGNIFICANCE OF MEIOSIS:

Haploid gametes or spores are formed by this process by gametogenesis or sporognesis.

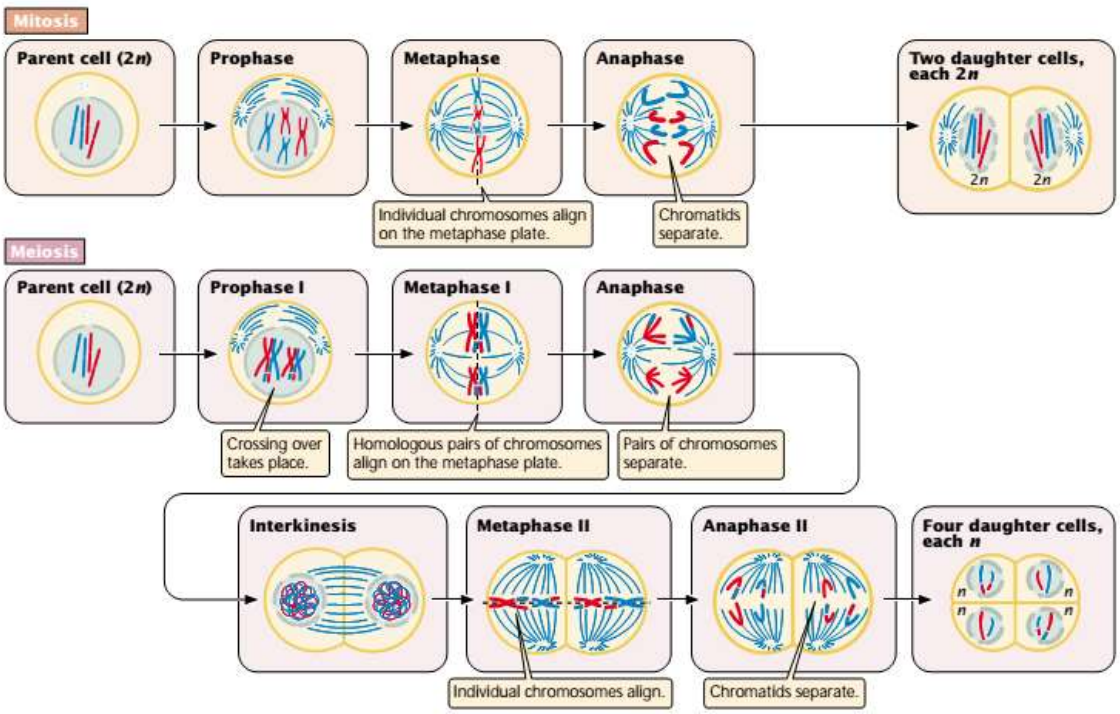
Meiosis & fertilization play a very important role in maintaining constant chromosome number from one generation to another.

Meiosis plays a very vital role in sexual reproduction by generating variations (play important role in evolution).

7. Comparison between Mitosis and Meiosis

CHARACTERS	MITOSIS	MEIOSIS
Occurence	Occur in somatic cells and in germ cells during multiplicative phase of gametogenesis.	In the germ cells of gonads.
Period of occurence	Throughout life	During sexual phase
Nature of cells	Either haploid or diploid	Always diploid
Number of division	Parent cell divide once	Parent cell divides twice
Number of daughter cells	Two	Four

Nature of daughter cells	Daughter cells are genetically similar to parent cell, chromosome number identical to parents.	Genetically different to parent cell, chromosome number is half compared to parent cell.



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7.1 - Comparison of Mitosis and Meiosis

8. Summary

According to Third tenet of cell cycle proposed by Rudolf Ludwig Karl Virchow "New cells arise from pre-existing cells". It is achieved by the process of cell division in which a parent cell divides into two newly formed daughter cells.

A prokaryotic cell having a single chromosome replicates, and attaches each copy of its DNA to the plasma membrane. Later on it is followed by cell division - involving separation of daughter cells by the growth of plasma membrane.

In a eukaryotic cells process of cell reproduction is more complex and highly regulated compared to a prokaryotic cell. It involves both mitosis and meiosis to ensure equal segregation of genetic information to new cells.

All sexually reproducing eukaryotic organisms starts their life from a single-celled zygote. The process of cell division doesn't ceases at maturity, it continues throughout the life cycle.

It consists of various stages through which a eukaryotic cell passes between cell division.

Basically cell cycle is divided into two major phases:

Interphase- It is a period during which cell prepares itself for next cell division. Interphase is further divided into G1, S and G2. During gap phases G1 and G2 cell mainly undergo growth and carries normal metabolism. S - phase involves DNA replication.

M-phase- It is a period of actual cell division. It is further divided into Prophase, Metaphase, Anaphase and Telophase.

During prophase DNA condenses to form chromosomes that become visible under microscope. This phase also involves assembly of mitotic spindle. By the end of prophase nucleolus and nuclear membrane disappear.

Metaphase involves alignment of chromosomes near the equatorial plane.

During Anaphase centromeres splits leading to the separation of chromatids towards the opposite poles.

Telophase-Once chromosomal segregations is over, cells returns to interphase condition by DNA decondensation, reappearance of nuclear membrane and nucleolus. This phase is known as Telophase.

Karyokinesis is followed by cytokinesis that involves division of cytoplasmic material. Cytoplasm is always divided by cell furrow in an animal cell, by cell plate in plant cell.

By the end of mitosis two genetically identical daughter cells are formed having same number of chromosomes as that of parent cell.

In comparison to mitosis, meiosis takes place in germ cells destined to form gametes. It takes place in two different phases Meiosis–I and Meiosis-II.

Meiosis-I is reductional division and Meiosis-II is equational division. Meiosis & fertilization plays a very important role in maintaining constant chromosome from one generation to another.

First meiotic phase has long prophase involving pairing of homologous chromosomes to form bivalents that undergo crossing over.

It is divided into leptotene, zygotene, pachytene, diplotene and diakinesis. It is followed by next phase which is metaphase-I. It is marked by the arrangement of bivalents on the equatorial plate.

Metaphase-I is followed by anaphase I in which homologous chromosomes separate and move towards the opposite poles with both their chromatids.

Nuclear membrane and nucleolus which got disappeared at the end of Prophase-I again reappear during the telophase-I.

Meiosis-I finally divides the chromosomes of parent cell into half leading to reductional division. There is a short gap between Meiosis-I and Meiosis-II known as Interkinesis.

Meiosis II is almost similar to mitosis. The anaphase II of meiosis-II involves separation of sister chromatids ultimately leading to the formation of four daughter cells that are genetically variable.

Genetic variation produced during the meiosis by crossing over as well as by the random distribution of maternal and paternal chromosomes which serve a very crucial role in evolution.

Cyclins and cyclin-dependent kinases interact throughout the cell cycle and plays major role in controlling cell cycle progress.