B.A./B.Sc SemIV paper 7 unit 1&2

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Mitosis And Meiosis

Meiosis from Greek, meiosis, meaning is a special type of cell division in sexually-reproducing organisms used to produce the gametes, such as sperm or egg cells. It involves two rounds of division that ultimately result in four cells with only one copy of each chromosome (haploid). Additionally, prior to the division, genetic material from the paternal and maternal copies of each chromosome is crossed over, creating new combinations of code on each chromosome. Later on, during fertilisation, the haploid cells produced by meiosis from a male and female will fuse to create a cell with two copies of each chromosome again, the zygote.

Errors in meiosis resulting in aneuploidy (an abnormal number of chromosomes) are the leading known cause of miscarriage and the most frequent genetic cause of developmental disabilities

In meiosis, DNA replication is followed by two rounds of cell division to produce four daughter cells, each with half the number of chromosomes as the original parent cell The two meiotic divisions are known as meiosis I and meiosis II. Before meiosis begins, during S phase of the cell cycle, the DNA of each chromosome is replicated so that it consists of two identical sister chromatids, which remain held together through sister chromatid cohesion. This S-phase can be referred to as "premeiotic S-phase" or "meiotic S-phase". Immediately following DNA replication, meiotic cells enter a prolonged G_2-like stage known as meiotic prophase. During this time, homologous chromosomes pair with each other and undergo genetic recombination, a programmed process in which DNA may be cut and then repaired, which allows them to exchange some of their genetic information. A subset of recombination events results in crossovers, which create physical links known as chiasmata (singular: chiasma, for the Greek letter Chi (X)) between the homologous chromosomes. In most organisms, these links can help direct each pair of homologous chromosomes to segregate away from each other during Meiosis I, resulting in two haploid cells that have half the number of chromosomes as the parent cell.

During meiosis II, the cohesion between sister chromatids is released and they segregate from one another, as during mitosis. In some cases, all four of the meiotic products form gametes such as sperm, spores or pollen. In female animals, three of the four meiotic products are typically eliminated by extrusion into polar bodies, and only one cell develops to produce an ovum. Because the number of chromosomes is halved during meiosis, gametes can fuse (i.e. fertilization) to form a diploid zygote that contains two copies of each chromosome, one from each parent. Thus, alternating cycles of meiosis and fertilization enable sexual reproduction, with successive generations maintaining the same number of chromosomes. For example, diploid human cells contain 23 pairs of chromosomes including 1 pair of sex

chromosomes (46 total), half of maternal origin and half of paternal origin. Meiosis produces haploid gametes (ova or sperm) that contain one set of 23 chromosomes. When two gametes (an egg and a sperm) fuse, the resulting zygote is once again diploid, with the mother and father each contributing 23 chromosomes. This same pattern, but not the same number of chromosomes, occurs in all organisms that utilize meiosis.

Meiosis occurs in all sexually-reproducing single-celled and multicellular organisms (which are all eukaryotes), including animals, plants and fungi. It is an essential process for oogenesis and spermatogenesis.

Although the process of meiosis is related to the more general cell division process of mitosis, it differs in two important respects:

Meiosis begins with a diploid cell, which contains two copies of each chromosome, termed homologs. First, the cell undergoes DNA replication, so each homolog now consists of two identical sister chromatids. Then each set of homologs pair with each other and exchange genetic information by homologous recombination often leading to physical connections (crossovers) between the homologs. In the first meiotic division, the homologs are segregated to separate daughter cells by the spindle apparatus. The cells then proceed to a second division without an intervening round of DNA replication. The sister chromatids are segregated to separate daughter cells to produce a total of four haploid cells. Female animals employ a slight variation on this pattern and produce one large ovum and two small polar bodies. Because of recombination, an individual chromatid can consist of a new combination of maternal and paternal genetic information, resulting in offspring that are genetically distinct from either parent. Furthermore, an individual gamete can include an assortment of maternal, paternal, and recombinant chromatids. This genetic diversity resulting from sexual reproduction contributes to the variation in traits upon which natural selection can act.

Meiosis uses many of the same mechanisms as mitosis, the type of cell division used by eukaryotes to divide one cell into two identical daughter cells. In some plants, fungi, and protists meiosis results in the formation of spores: haploid cells that can divide vegetatively without undergoing fertilization. Some eukaryotes, like bdelloid rotifers, do not have the ability to carry out meiosis and have acquired the ability to reproduce by parthenogenesis.

Meiosis does not occur in archaea or bacteria, which generally reproduce asexually via binary fission. However, a "sexual" process known as horizontal gene transfer involves the transfer of DNA from one bacterium or archaeon to another and recombination of these DNA molecules of different parental origin.

Meiosis was discovered and described for the first time in sea urchin eggs in 1876 by the German biologist Oscar Hertwig. It was described again in 1883, at the level of chromosomes, by the Belgian zoologist Edouard Van Beneden, in Ascaris roundworm eggs. The significance of meiosis for reproduction and inheritance, however, was described only in 1890 by German biologist August

Weismann, who noted that two cell divisions were necessary to transform one diploid cell into four haploid cells if the number of chromosomes had to be maintained. In 1911, the American geneticist Thomas Hunt Morgan detected crossovers in meiosis in the fruit fly Drosophila melanogaster, which helped to establish that genetic traits are transmitted on chromosomes.

The term "meiosis" (originally spelled "maiosis") is derived from the Greek word μείωσις, meaning 'lessening'. It was introduced to biology by J.B. Farmer and J.E.S. Moore in 1905:

We propose to apply the terms Maiosis or Maiotic phase to cover the whole series of nuclear changes included in the two divisions that were designated as Heterotype and Homotype by Flemming.

The term was linguistically corrected to "meiosis" by Koernicke (1905) and by Pantel and De Sinety (1906)

Stages

Meiosis is divided into meiosis I and meiosis II which are further divided into Karyokinesis I and Cytokinesis I and Karyokinesis II and Cytokinesis II respectively. The preparatory steps that lead up to meiosis are identical in pattern and name to interphase of the mitotic cell cycle.[8] Interphase is divided into three phases:

Growth 1 (G_1) phase: In this very active phase, the cell synthesizes its vast array of proteins, including the enzymes and structural proteins it will need for growth. In G_1, each of the chromosomes consists of a single linear molecule of DNA.

Synthesis (S) phase: The genetic material is replicated; each of the cell's chromosomes duplicates to become two identical sister chromatids attached at a centromere. This replication does not change the ploidy of the cell since the centromere number remains the same. The identical sister chromatids have not yet condensed into the densely packaged chromosomes visible with the light microscope. This will take place during prophase I in meiosis.

Growth 2 (G_2) phase: G_2 phase as seen before mitosis is not present in meiosis. Meiotic prophase corresponds most closely to the G_2 phase of the mitotic cell cycle.

Interphase is followed by meiosis I and then meiosis II. Meiosis I separates replicated homologous chromosomes, each still made up of two sister chromatids, into two daughter cells, thus reducing the chromosome number by half. During meiosis II, sister chromatids decouple and the resultant daughter chromosomes are segregated into four daughter cells. For diploid organisms, the daughter cells resulting from meiosis are haploid and contain only one copy of each chromosome. In some species, cells enter a resting phase known as interkinesis between meiosis I and meiosis II.

Meiosis I and II are each divided into prophase, metaphase, anaphase, and telophase stages, similar in purpose to their analogous subphases in the mitotic cell cycle. Therefore, meiosis includes the stages of

meiosis I (prophase I, metaphase I, anaphase I, telophase I) and meiosis II (prophase II, metaphase II, anaphase II, telophase II).

Meiosis generates gamete genetic diversity in two ways: (1) Law of Independent Assortment. The independent orientation of homologous chromosome pairs along the metaphase plate during metaphase I and orientation of sister chromatids in metaphase II, this is the subsequent separation of homologs and sister chromatids during anaphase I and II, it allows a random and independent distribution of chromosomes to each daughter cell (and ultimately to gametes);[9] and (2) Crossing Over. The physical exchange of homologous chromosomal regions by homologous recombination during prophase I results in new combinations of genetic information within chromosomes

During meiosis, specific genes are more highly transcribed. In addition to strong meiotic stage-specific expression of mRNA, there are also pervasive translational controls (e.g. selective usage of preformed mRNA), regulating the ultimate meiotic stage-specific protein expression of genes during meiosis. Thus, both transcriptional and translational controls determine the broad restructuring of meiotic cells needed to carry out meiosis.

Meiosis I

Meiosis I segregates homologous chromosomes, which are joined as tetrads (2n, 4c), producing two haploid cells (n chromosomes, 23 in humans) which each contain chromatid pairs (1n, 2c). Because the ploidy is reduced from diploid to haploid, meiosis I is referred to as a reductional division. Meiosis II is an equational division analogous to mitosis, in which the sister chromatids are segregated, creating four haploid daughter cells

Prophase I

Prophase I is typically the longest phase of meiosis. During prophase I, homologous chromosomes pair and exchange genetic information (homologous recombination). This often results in chromosomal crossover. This process facilitates pairing between homologous chromosomes and hence accurate segregation of the chromosomes at the first meiosis division. The new combinations of DNA created during crossover are a significant source of genetic variation, and result in new combinations of alleles, which may be beneficial. The paired and replicated chromosomes are called bivalents or tetrads, which have two chromosomes and four chromatids, with one chromosome coming from each parent. The process of pairing the homologous chromosomes is called synapsis. At this stage, non-sister chromatids may cross-over at points called chiasmata (plural; singular chiasma). Prophase I has historically been divided into a series of substages which are named according to the appearance of chromosomes.

Leptotene

The first stage of prophase I is the leptotene stage, also known as leptonema, from Greek words meaning "thin threads".[7] In this stage of prophase I, individual chromosomes—each consisting of two sister chromatids—become "individualized" to form visible strands within the nucleus. The two sister chromatids closely associate and are visually indistinguishable from one another. During leptotene,

lateral elements of the synaptonemal complex assemble. Leptotene is of very short duration and progressive condensation and coiling of chromosome fibers takes place.

Zygotene

The zygotene stage, also known as zygonema, from Greek words meaning "paired threads",[15]:27 occurs as the chromosomes approximately line up with each other into homologous chromosome pairs. In some organisms, this is called the bouquet stage because of the way the telomeres cluster at one end of the nucleus. At this stage, the synapsis (pairing/coming together) of homologous chromosomes takes place, facilitated by assembly of central element of the synaptonemal complex. Pairing is brought about in a zipper-like fashion and may start at the centromere (procentric), at the chromosome ends (proterminal), or at any other portion (intermediate). Individuals of a pair are equal in length and in position of the centromere. Thus pairing is highly specific and exact. The paired chromosomes are called bivalent or tetrad chromosomes.

Pachytene

The pachytene stage also known as pachynema, from Greek words meaning "thick threads".At this point a tetrad of the chromosomes has formed known as a bivalent. This is the stage when homologous recombination, including chromosomal crossover (crossing over), occurs. Nonsister chromatids of homologous chromosomes may exchange genetic information over regions of homology. DNA damage induced by gamma radiation during the leptotene to early pachytene stages induces an homologous recombinational repair (HRR) pathway that employs the key proteins DMC1 and RAD51. This HRR pathway is replaced at mid-pachytene by the less accurate repair pathway of non-homologous end joining and an HRR pathway that does not depend on DMC1. Sex chromosomes, however, are not wholly identical, and only exchange information over a small region of homology. At the sites where exchange happens, chiasmata form. The exchange of information between the non-sister chromatids results in a recombination of information; each chromosome has the complete set of information it had before, and there are no gaps formed as a result of the process. Because the chromosomes cannot be distinguished in the synaptonemal complex, the actual act of crossing over is not perceivable through the microscope, and chiasmata are not visible until the next stage.

Diplotene

During the diplotene stage, also known as diplonema, from Greek words meaning "two threads",[15]:30 the synaptonemal complex degrades and homologous chromosomes separate from one another a little. The chromosomes themselves uncoil a bit, allowing some transcription of DNA. However, the homologous chromosomes of each bivalent remain tightly bound at chiasmata, the regions where crossing-over occurred. The chiasmata remain on the chromosomes until they are severed at the transition to anaphase I.

In human fetal oogenesis, all developing oocytes develop to this stage and are arrested in prophase I before birth. This suspended state is referred to as the dictyotene stage or dictyate. It lasts until meiosis is resumed to prepare the oocyte for ovulation, which happens at puberty or even later.

Diakinesis[

Chromosomes condense further during the diakinesis stage, from Greek words meaning "moving through"This is the first point in meiosis where the four parts of the tetrads are actually visible. Sites of crossing over entangle together, effectively overlapping, making chiasmata clearly visible. Other than this observation, the rest of the stage closely resembles prometaphase of mitosis; the nucleoli disappear, the nuclear membrane disintegrates into vesicles, and the meiotic spindle begins to form.

Synchronous processes

During these stages, two centrosomes, containing a pair of centrioles in animal cells, migrate to the two poles of the cell. These centrosomes, which were duplicated during S-phase, function as microtubule organizing centers nucleating microtubules, which are essentially cellular ropes and poles. The microtubules invade the nuclear region after the nuclear envelope disintegrates, attaching to the chromosomes at the kinetochore. The kinetochore functions as a motor, pulling the chromosome along the attached microtubule toward the originating centrosome, like a train on a track. There are four kinetochores on each tetrad, but the pair of kinetochores on each sister chromatid fuses and functions as a unit during meiosis I

Microtubules that attach to the kinetochores are known as kinetochore microtubules. Other microtubules will interact with microtubules from the opposite centrosome: these are called nonkinetochore microtubules or polar microtubules. A third type of microtubules, the aster microtubules, radiates from the centrosome into the cytoplasm or contacts components of the membrane skeleton.

Metaphase I

Homologous pairs move together along the metaphase plate: As kinetochore microtubules from both centrosomes attach to their respective kinetochores, the paired homologous chromosomes align along an equatorial plane that bisects the spindle, due to continuous counterbalancing forces exerted on the bivalents by the microtubules emanating from the two kinetochores of homologous chromosomes. This attachment is referred to as a bipolar attachment. The physical basis of the independent assortment of chromosomes is the random orientation of each bivalent along the metaphase plate, with respect to the orientation of the other bivalents along the same equatorial line. The protein complex cohesin holds sister chromatids together from the time of their replication until anaphase. In mitosis, the force of kinetochore microtubules pulling in opposite directions creates tension. The cell senses this tension and does not progress with anaphase until all the chromosomes are properly bi-oriented. In meiosis, establishing tension ordinarily requires at least one crossover per chromosome pair in addition to cohesin between sister chromatid

Anaphase I

Kinetochore microtubules shorten, pulling homologous chromosomes (which each consist of a pair of sister chromatids) to opposite poles. Nonkinetochore microtubules lengthen, pushing the centrosomes farther apart. The cell elongates in preparation for division down the center. Unlike in mitosis, only the cohesin from the chromosome arms is degraded while the cohesin surrounding the centromere remains protected by a protein named Shugoshin (Japanese for "guardian spirit"), what prevents the sister chromatids from separating. This allows the sister chromatids to remain together while homologs are segregated.

Telophase I

The first meiotic division effectively ends when the chromosomes arrive at the poles. Each daughter cell now has half the number of chromosomes but each chromosome consists of a pair of chromatids. The microtubules that make up the spindle network disappear, and a new nuclear membrane surrounds each haploid set. The chromosomes uncoil back into chromatin. Cytokinesis, the pinching of the cell membrane in animal cells or the formation of the cell wall in plant cells, occurs, completing the creation of two daughter cells. Sister chromatids remain attached during telophase I.

Cells may enter a period of rest known as interkinesis or interphase II. No DNA replication occurs during this stage.

Meiosis II

Meiosis II is the second meiotic division, and usually involves equational segregation, or separation of sister chromatids. Mechanically, the process is similar to mitosis, though its genetic results are fundamentally different. The end result is production of four haploid cells (n chromosomes, 23 in humans) from the two haploid cells (with n chromosomes, each consisting of two sister chromatids) produced in meiosis I. The four main steps of meiosis II are: prophase II, metaphase II, anaphase II, and telophase II.

In prophase II, we see the disappearance of the nucleoli and the nuclear envelope again as well as the shortening and thickening of the chromatids. Centrosomes move to the polar regions and arrange spindle fibers for the second meiotic division.

In metaphase II, the centromeres contain two kinetochores that attach to spindle fibers from the centrosomes at opposite poles. The new equatorial metaphase plate is rotated by 90 degrees when compared to meiosis I, perpendicular to the previous plate.[22]

This is followed by anaphase II, in which the remaining centromeric cohesin, not protected by Shugoshin anymore, is cleaved, allowing the sister chromatids to segregate. The sister chromatids by convention are now called sister chromosomes as they move toward opposing poles.

The process ends with telophase II, which is similar to telophase I, and is marked by decondensation and lengthening of the chromosomes and the disassembly of the spindle. Nuclear envelopes re-form and

cleavage or cell plate formation eventually produces a total of four daughter cells, each with a haploid set of chromosomes.

Meiosis is now complete and ends up with four new daughter cells.

The origin and function of meiosis are currently not well understood scientifically, and would provide fundamental insight into the evolution of sexual reproduction in eukaryotes. There is no current consensus among biologists on the questions of how sex in eukaryotes arose in evolution, what basic function sexual reproduction serves, and why it is maintained, given the basic two-fold cost of sex. It is clear that it evolved over 1.2 billion years ago, and that almost all species which are descendants of the original sexually reproducing species are still sexual reproducers, including plants, fungi, and animals.

Meiosis is a key event of the sexual cycle in eukaryotes. It is the stage of the life cycle when a cell gives rise to two haploid cells (gametes) each having half as many chromosomes. Two such haploid gametes, arising from different individual organisms, fuse by the process of fertilization, thus completing the sexual cycle.

Meiosis is ubiquitous among eukaryotes. It occurs in single-celled organisms such as yeast, as well as in multicellular organisms, such as humans. Eukaryotes arose from prokaryotes more than 2.2 billion years ago and the earliest eukaryotes were likely single-celled organisms. To understand sex in eukaryotes, it is necessary to understand (1) how meiosis arose in single celled eukaryotes, and (2) the function of meiosis.

Meiosis occurs in eukaryotic life cycles involving sexual reproduction, consisting of the constant cyclical process of meiosis and fertilization. This takes place alongside normal mitotic cell division. In multicellular organisms, there is an intermediary step between the diploid and haploid transition where the organism grows. At certain stages of the life cycle, germ cells produce gametes. Somatic cells make up the body of the organism and are not involved in gamete production.

Cycling meiosis and fertilization events produces a series of transitions back and forth between alternating haploid and diploid states. The organism phase of the life cycle can occur either during the diploid state (diplontic life cycle), during the haploid state (haplontic life cycle), or both (haplodiplontic life cycle, in which there are two distinct organism phases, one during the haploid state and the other during the diploid state). In this sense there are three types of life cycles that utilize sexual reproduction, differentiated by the location of the organism phase(s).[

In the diplontic life cycle (with pre-gametic meiosis), of which humans are a part, the organism is diploid, grown from a diploid cell called the zygote. The organism's diploid germ-line stem cells undergo meiosis to create haploid gametes (the spermatozoa for males and ova for females), which fertilize to form the zygote. The diploid zygote undergoes repeated cellular division by mitosis to grow into the organism.

In the haplontic life cycle (with post-zygotic meiosis), the organism is haploid instead, spawned by the proliferation and differentiation of a single haploid cell called the gamete. Two organisms of opposing sex contribute their haploid gametes to form a diploid zygote. The zygote undergoes meiosis immediately, creating four haploid cells. These cells undergo mitosis to create the organism. Many fungi and many protozoa utilize the haplontic life cycle.[

Finally, in the haplodiplontic life cycle (with sporic or intermediate meiosis), the living organism alternates between haploid and diploid states. Consequently, this cycle is also known as the alternation of generations. The diploid organism's germ-line cells undergo meiosis to produce spores. The spores proliferate by mitosis, growing into a haploid organism. The haploid organism's gamete then combines with another haploid organism's gamete, creating the zygote. The zygote undergoes repeated mitosis and differentiation to become a diploid organism again. The haplodiplontic life cycle can be considered a fusion of the diplontic and haplontic life cycles.

Meiosis occurs in all animals and plants. The end result, the production of gametes with half the number of chromosomes as the parent cell, is the same, but the detailed process is different. In animals, meiosis produces gametes directly. In land plants and some algae, there is an alternation of generations such that meiosis in the diploid sporophyte generation produces haploid spores. These spores multiply by mitosis, developing into the haploid gametophyte generation, which then gives rise to gametes directly (i.e. without further meiosis). In both animals and plants, the final stage is for the gametes to fuse, restoring the original number of chromosomes.]

In mammals

In females, meiosis occurs in cells known as oocytes (singular: oocyte). Each primary oocyte divides twice in meiosis, unequally in each case. The first division produces a daughter cell, and a much smaller polar body which may or may not undergo a second division. In meiosis II, division of the daughter cell produces a second polar body, and a single haploid cell, which enlarges to become an ovum. Therefore, in females each primary oocyte that undergoes meiosis results in one mature ovum and one or two polar bodies.

Note that there are pauses during meiosis in females. Maturing oocytes are arrested in prophase I of meiosis I and lie dormant within a protective shell of somatic cells called the follicle. At the beginning of each menstrual cycle, FSH secretion from the anterior pituitary stimulates a few follicles to mature in a process known as folliculogenesis. During this process, the maturing oocytes resume meiosis and continue until metaphase II of meiosis II, where they are again arrested just before ovulation. If these oocytes are fertilized by sperm, they will resume and complete meiosis. During folliculogenesis in humans, usually one follicle becomes dominant while the others undergo atresia. The process of meiosis in females occurs during oogenesis, and differs from the typical meiosis in that it features a long period of meiotic arrest known as the dictyate stage and lacks the assistance of centrosomes.

In males, meiosis occurs during spermatogenesis in the seminiferous tubules of the testicles. Meiosis during spermatogenesis is specific to a type of cell called spermatocytes, which will later mature to

become spermatozoa. Meiosis of primordial germ cells happens at the time of puberty, much later than in females. Tissues of the male testis suppress meiosis by degrading retinoic acid, proposed to be a stimulator of meiosis. This is overcome at puberty when cells within seminiferous tubules called Sertoli cells start making their own retinoic acid. Sensitivity to retinoic acid is also adjusted by proteins called nanos and DAZL. Genetic loss-of-function studies on retinoic acid-generating enzymes have shown that retinoic acid is required postnatally to stimulate spermatogonia differentiation which results several days later in spermatocytes undergoing meiosis, however retinoic acid is not required during the time when meiosis initiates.

In female mammals, meiosis begins immediately after primordial germ cells migrate to the ovary in the embryo. Some studies suggest that retinoic acid derived from the primitive kidney (mesonephros) stimulates meiosis in embryonic ovarian oogonia and that tissues of the embryonic male testis suppress meiosis by degrading retinoic acid.[31] However, genetic loss-of-function studies on retinoic acid-generating enzymes have shown that retinoic acid is not required for initiation of either female meiosis which occurs during embryogenesisor male meiosis which initiates postnatally