ANNAMALAI UNIVERSITY

FACULTY OF AGRICULTURE

DEPARTMENT OF GENETICS AND PLANT BREEDING

THEORY LECTURE NOTES

GPB 214 PRINCIPLES OF GENETICS AND CYTOGENETICS (2+1)

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JOHANN MENDEL

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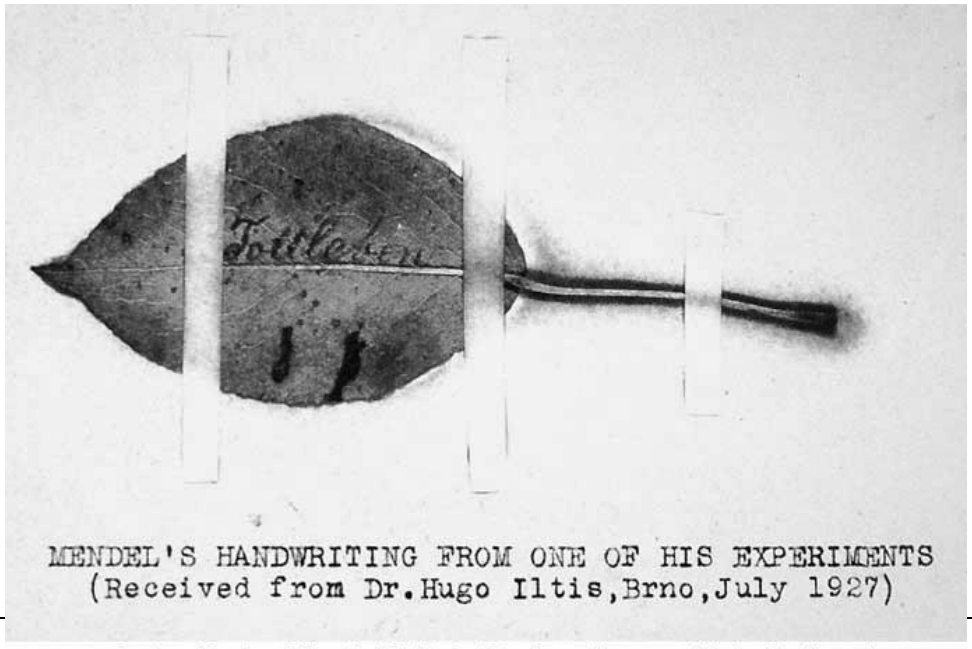
MENDEL'S GARDEN



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1. INRTODUCTION

The word genetics, coined by William Bateson (1906), is derived from the Latin word *genesis*, which means birth. Genetics is the study of heredity and variation. Heredity refers to the transmission of genetic information, more precisely genes, from parents to offspring. Variation refers to the difference among the individuals of a species for a character. It may be due to heredity or environment.

BRANCHES OF GENETICS

Modern genetics is traditionally classified into three branches as transmission genetics, molecular genetics and population genetics.

(1) Transmission genetics

Transmission genetics deals with the study of passage of characters from one generation to the next. It is studied mainly through breeding experiments in individual organism. It also encompasses the basic principles of genetics such as the relationship between chromosomes and heredity, the arrangement of genes on chromosomes, and gene mapping. It has important practical application in the development of new varieties in plants and animals. As Mendel pioneered this approach to genetics it is frequently called as Mendelian genetics or classical genetics.

(2) Molecular genetics

Molecular genetics involves the study of the chemical nature of the gene, its structure, organization, and function at molecular level. It includes the cellular processes of replication, transcription, and translation and also gene regulation which is the processes of control of expression of the genetic information. The developments in molecular genetics has lead to breakthroughs in cloning and genetic engineering.

(3) Population genetics

Population genetics is the study of the variation of genes between and within populations of a species and its changes over time and space. It is important in evolutionary studies, as evolution is just the change in the genetic makeup of population over time. However, these fields may overlap each other and each organism for example Drosophila or maize may be studied at the level of transmission, molecular and population genetics.

IMPORTANCE AND APPLICATIONS OF GENETICS

Although the science of genetics is relatively new, people have understood the hereditary nature of traits and have genetic principles for thousands of years. The growth of agriculture began with application of genetic principles to the domestication of plants and animals. Now, the major crops and animals used in agriculture have undergone extensive genetic alterations to for better yield and other desirable traits, such as disease resistance, pest resistance (eg. Bt cotton), special nutritional qualities (eg. Golden rice) and several other traits. The Green Revolution of 1960s relied chiefly on the application of genetics. Today, genetically engineered maize, soybeans, rapeseed and other crops constitute major proportion of the food produced worldwide.

An understanding of genetics is critical to the student of biology as it provides one of biology's unifying principles: all organisms use nucleic acids for their genetic material and encode genetic information in the same manner.

Development of better breed of animals has been made possible with due knowledge on their pedigree and genetics. In pharmaceutical industry, genetically modified fungi and bacteria are used for synthesizing numerous drugs and food additives. Growth hormone, insulin, and clotting factor are now commercially produced by genetically engineered bacteria.

The biotechnology industry employs molecular genetic techniques to develop and mass-produce compounds of commercial value. The molecular genetic techniques have also been used to develop highly efficient bacteria that remove minerals from ore, break down toxic chemicals, and obstruct frost formation on crop plants.

Genetics plays a vital role in the field of medicine as many diseases and disorders have a hereditary component. Diagnosis of several genetic disorders which may be expressed in later stages of growth can now be studied in new born babies. Examples are genetic disorders such as sickle-cell anemia, Huntington disease and common diseases such as asthma, diabetes, and hypertension.

Gene therapy, the direct alteration of genes to treat human diseases, has become a reality due to developments in the field of genetics.

The research findings in genetics have ethical and economical implications to society and individuals. Genetics also involves the study of developmental biology, taxonomy, biochemistry, ecology and evolution.

Genetic variation is the foundation of all evolutionary change and the ultimate basis of all life forms. Genetics, the study of genetic variation and its inheritance, is therefore crucial to understanding the past, present, and future of life.

2. EARLIER CONCEPTS OF HEREDITY

The general aspects of heredity were known to Assyrians and Babylonians centuries before the Christian era. The nature of heredity of traits has been understood and the genetic principles have been applied in the domestication of crops such as wheat, peas, lentil, barley and animals like dogs, goats and sheep. This had lead to the development of agriculture and fixed human settlements. As early as 700 B.C, Babylonians and Assyrians developed date-palm varieties that differed in fruit colour, size and ripening time. They noted that female palm trees produced fruits only when their flowers were dusted with pollen and that the pollen parent had a marked effect on the quality of fruits produced by female plants. This effect is knows as metaxenia. Around 4000 BC, the Chinese attempted to improve rice varieties.

Majority of biologists at the time of Mendel believed, in the *theory of spontaneous generation*, that primitive organisms originated from non-living matter e.g., decaying organic matter which was disproved by the experiments of Redi (1621 – 1697) and Spallanzani (1729 –1799)

Fig. 2.1. Sketch of homunculus inside sperm

1.Preformation theory of Swammerdam

According to preformation theory, the egg or sperm contains the miniature copy of adult called *homunculus*, which later enlarges during development. It implied that all traits would be inherited from only one parent. Although many observations suggested that offspring possess a mixture of traits from both parents, preformationism remained a popular concept throughout 17th and 18th centuries (Fig. 2.1).

2.Epigenesis concept of Wolff

Wolff (1738 –1794) proposed that during early stages of development the embryonic tissues are composed of cells similar in structure and function which later differentiate into adult tissues and organs. This concept is known as Epigenesis.

3.Inheritance of Acquired characters or Lamarckism

Lamarck (1744 –1829) proposed that characters acquired by individuals of one generation are transmitted to those in the next generation. According to this theory, if a person develop strong muscles by physical exercise, his children will inherit this character. The early idea of the inheritance of acquired characters was initially suggested by Hypocrates (400 B.C.).

4.Pangenesis theory of Charles Darwin

Charles Darwin proposed the concept of pangenesis according to which the particles called gemmules or pangenes carry information from various parts of the body to the reproductive organs which are transmitted through the gametes to its progeny and will produce a similar modification in the corresponding organ of the progeny. This concept though incorrect, persisted from the time of ancient Greeks till 18th century.

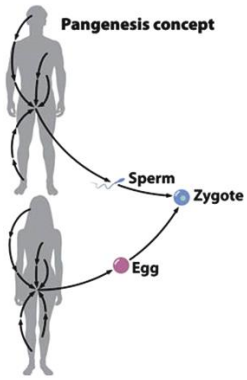


Fig.2. 2. Pangenesis

5.The Germplasm Theory or Weismannism

August Weismann proposed the germplasm theory and explained that the cells in the reproductive organs carry the complete set of genetic information that is passed to the gametes and hence the changes taking place in the germplasm are transmitted to the next generation.

Weismann disproved the theory of inheritance of acquired characters and pangenesis. He cut-off the tails of a group of mice for 22 successive generations and showed that the tail length remained same in all the descendents.

Castle and Philip transplanted the ovary of the black guinea pig into the albino guinea pig. They mated the ovary transplanted albino pig with albino pig, as male. All the progeneies had black fur. If the theories of inheritance of acquired character and pangenes were correct, all the progenesis of the above mating must be albino, but all were black coloured.

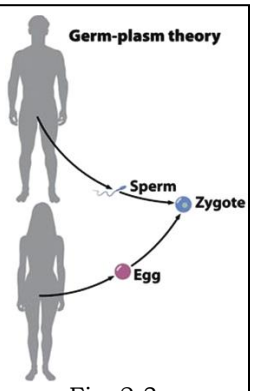


Fig. 2.3.
Germplasm theory

6.Blending Inheritance

Biologists before Mendel believed that the medium for inheritance is liquid, possibly blood and that the offspring are a blend of both the parents. This suggests that the genetic material itself blends and once blended the genetic differences could not be separated out in the future generation. The fact that the offspring possessed the characters of both the parents strengthened the blending type of inheritance. Later this theory was disproved by Mendel.

7.Hybridization in plants

Grew (1641-1712) reported that plants reproduce sexually by using pollen grains which induced many botanists to effect crossing in plants and create hybrids. Kolreuter (1733-1806), foremost among these early plant breeders, conducted extensive study on hybridization in tobacco. He noted uniformity and heterosis in F_1

generation and appearance of variation in F_2 generation. As he crossed plants that differed in many traits, Kolreuter was unable to discern any general pattern of inheritance.

Thomas Fairchild produced the first artificial hybrid in plants called 'Fairchild's mule' by crossing Carnation and Sweet William in the year 1717. John Knight (1759-1835) developed commercial varieties of apple, pear, apricot, and grapes through hybridization. Gaertner used a backcross programme to convert one species into another.

The work of Amici (1830) regarding the entry of pollen tubes into the ovary and Strausberger (1884) regarding the fusion of sperm and egg nuclei i.e., fertilization had clarified the role of male and female gametes in sexual reproduction. Other scientists like Naudin and Darwin also hybridized plants and studied the subsequent generations. However, they could not give an explanation for their results.

Developments in cytology in the 1800s had a strong influence on genetics. Robert Brown described the nucleus in 1833. Matthis Jacob Schleiden and Theodor Schwann proposed the concept of the cell theory in 1839, according to which, all life is composed of cells, cells arise only from preexisting cells, and the cell is the fundamental unit of structure and function in living organisms. Biologists began to examine cells to see how traits were transmitted in the course of cell division.

Darwin recognized that heredity was fundamental to evolution and he conducted extensive genetic crosses with pigeons and other organisms. In 1856, he put forth the theory of evolution through natural selection and published his ideas in "On the Origin of Species". However, his lack of understanding on the nature of inheritance became a major lapse in his theory of evolution.

The invention of the microtome, for cutting thin sections of tissue for microscopic examination, in the mid nineteenth century along with improvement in development of histological stains kindled research in cytology. In 1882, Walter Flemming observed the division of chromosomes and coined the word 'mitosis'. In 1885, Waldeyer coined the term 'chromosomes' and also it was generally recognized that the nucleus contained the hereditary information.

8.Particulate inheritance of Mendel

Gregor Johann Mendel began his experiments on garden peas in 1857 presuming that the hybrids will have blending of the parental traits. Instead, for all the seven traits studied, he observed that the hybrids showed only one of the two parental traits. Mendel's results clearly disproved the blending mechanism of inheritance and suggested a particulate theory of inheritance.

The science of genetics founded by Mendel reached the present status by the contribution of many scientists which are tabulated as follows.

YEAR	SCIENTISTS AND DISCOVERY
1869	Friedrich Miescher identified DNA
1901	Hugo de vries coined the term “mutation”
1902	Sutton & Boveri proposes Chromosomal theory of inheritance
1906	Bateson coined the term “genetics”
1909	-Johannsen coined the term “gene”. -Archibald Garrod published the book “Inborn errors of metabolism”
1910	T.H. Morgan studied linkage and crossing over in Drosophila and coined the term “ crossing over ” (Nobel prize, 1933).
1911	Sturtevant constructed the first linkage map in Drosophila.
1917 -1923	Bridges gave genic balance theory and non-disjunction theory. He described the different chromosomal abnormalities and aberrations.
1925	Bernestein proposed multiple allelic inheritance of ABO blood group
1927	H.J. Muller reported use of CIB technique to show X-rays are mutagenic (Nobel prize, 1946).
1928	Griffith discovered transformation in *Diplococcus pneumoniae*.
1930	R.A. Fisher, J.B.S. Haldane and Sewell Wright laid the foundation for population genetics.
1941	Beadle and Tatum proposed “one gene-one enzyme” in Neurospora (Nobel prize 1958).
1944	Avery, MacLeod and McCarty demonstrated the transforming principle as DNA, the genetic material
1950	Chargaff proved that in DNA, the amount of adenine is equal to amount of thymine; the amount of guanine is equal to amount of cytosine and the content of purine is equal to content of pyrimidine.
1952	Hershey (Nobel prize, 1969) and Chase revealed DNA as the genetic material of bacteriophage.
1953	J. D. Watson, F.H.C. Crick (Nobel prize, 1962) proposed double-helical structure model of DNA using X-ray diffraction data of Wilkins (Nobel prize, 1962) and base composition data of Chargaff.
1955	Benzer described fine structure of the phage T_4rII locus

1956	Tjio and Levan resolved the normal diploid chromosome number of humans as 46
1957	Frankel Conrat and Singer established RNA as the genetic material of tobacco mosaic virus
1958	Meselson and Stahl identified semi-conservative replication of DNA
1961	- Nirenberg and Mathaei cracked the genetic code present on mRNA - Jacob and Monod proposed the "Operon model" for gene regulation (Nobel prize, 1978)
1965	Harris Watkins produced hybrid cell fusing somatic cells of mouse and man.
1970	Nathan and Smith isolated first restriction endonucleases (Nobel prize, 1968).
1972	Berg produces first recombinant *in vitro* (Nobel prize, 1980).
1977	Maxim, Gilbert and Singer published DNA sequencing techniques (Nobel prize, 1980)
1983	-Kary Mullis and others developed the polymerase chain reaction (PCR) for quick amplification of DNA. -Nobel prize for Barbera McClintock for her jumping genes concept.
1986	Nirenberg and Har Govind Khorana established the complete genetic code.
1990	-Gene therapy used to treat human genetic diseases in U.S.A. - Human Genome Project was launched.
1995	DNA of the bacterium *Haemophilus influenzae* was fully sequenced.
1997	Ian Wilmut cloned a sheep "Dolly"
1998	Rough draft of human genome map showing more than 30,000 genes was released. Development of Terminator gene technology by Delta and Pine Co and Bollguard cotton by Monsanto
2001	Craig Venter and Francis Collins announced first complete draft of human genome.
2003	The Human Genome Project was successfully completed.

3. CYTOLOGY

The cell is the fundamental, structural and functional unit of living organisms. In 1665, Robert Hook observed the presence of cells in cork tissue. The scientific study of cell is called as cytology whereas, cytogenetics refers to the branch of biology which deals with the study of chromosomes in relation to genetics.

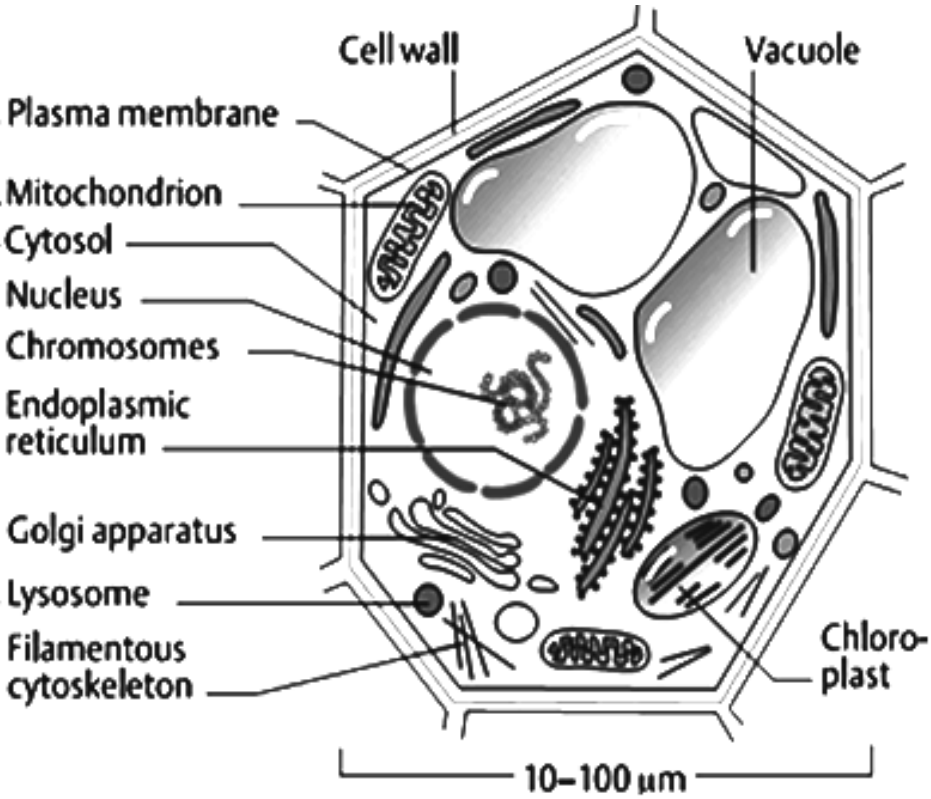
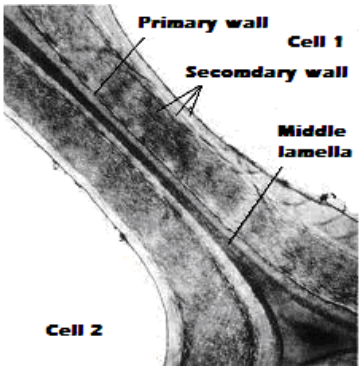
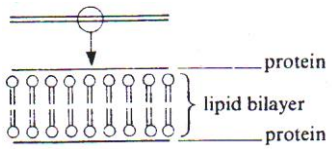
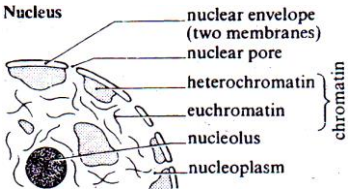
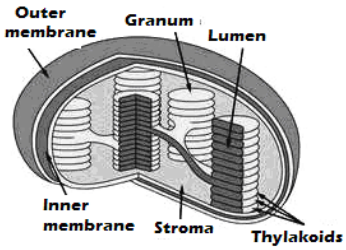
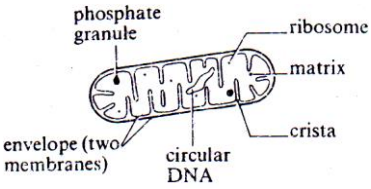


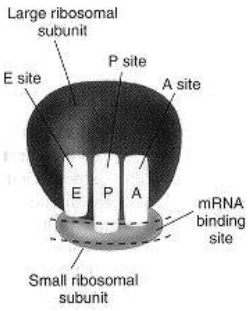
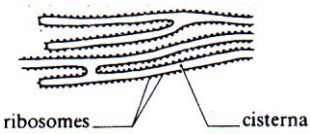
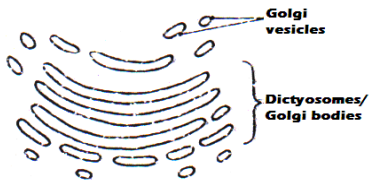
FIG. 3.1. ULTRASTRUCTURE OF PLANT CELL

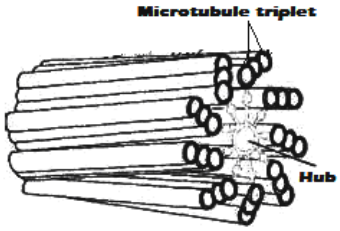
Shape, size and number of cells

Generally the shape of the cell correlates with its function. For example epithelial cells are flat while muscle cells are elongated. The cells may be spherical, cylindrical, tubular, hexagonal or irregular in shape. Mostly the cells are cylinders of 15-30 µ in diameter. The size of the cells ranges from 0.2-0.5 µ in bacteria to 75mm in case of Ostrich eggs. The number of cells in an organism varies from one (bacteria, protozoans) to trillions (human beings).

CELL STRUCTURES	COMPONENTS	FUNCTIONS
Cell wall  	It consists of three parts (i) *Middle lamella*: It is the outmost layer composed of Ca and Mg pectate. *(ii). Primary cell wall*: It lies between middle lamella and secondary cell wall. It is a thin, elastic layer made of cellulose, hemicellulose, and pectins. It is formed after middle lamella formation. *(iii). Secondary cell wall*: It is the inner most layer next to plasma membrane. It is primarily composed of cellulose microfibrils along with lignin and suberin. The cell wall has minute pores called *plasmodesmata*. The pore is lined with cell surface membrane and has a central tubular core often associated with ER.	• Middle lamella connects neighbouring cells together. • Cell wall provides mechanical support and protection. It allows pressure potential to develop in the cell and prevents bursting of the cell. It is a pathway for movement of water and mineral salts. It also has modification such as lignification, for specialized function. • Plasmodesmata enables a continuous system of cytoplasm, the **symplast**, to be formed between adjacent cells for transport of substances between cells.
Plasma membrane  	The membrane enclosing the cell is the plasmamembrane. It is composed of two lipid layers (bilayer) sandwiched between two protein layers. Its structure is best explained by fluid-mosaic model.	• It acts as a partially permeable layer controlling exchange of materials into and out of the cell. The passage of substances may require expenditure of energy (active transport) or may be passive (diffusion).
Nucleus  	It is the largest organelle containing the genetic material and is composed of (a) *Nuclear envelop,* a double membrane structure with numerous pores. (b) *Chromatin*, is the nucleoprotein component of chromosomes visible only at condensed condition. (c) *Nucleolus* are dense spherical bodies present in nucleus during interphase. It is rich in RNA and protein and is visible even under light microscope. (d)*Nucleoplasm,* the space around the chromosomes and the nucleolus.	• Nuclear envelop controls the movement of materials between nucleus and cytoplasm, contains pores that communicates with ER. • only the DNA component alone is hereditary. • Nucleolus are sites on chromatin where ribosomal RNA (rRNA) is synthesized; disappears form light microscope during cellular replication • Nucleoplasm is the non-nuleolar region of the nucleus containing materials for making DNA and mRNA.
Cytoplasm	The plasma membrane encloses cytoplasm. Cytoplasm encompasses cytoplasmic matrix and cytoplasmic structures. The portion of cytoplasm other than	• The space between the plasma membrane and the nucleus filled by translucent, colloidal liquid known as *cytoplasmic matrix*. • The *cytoplasmic structures* include

	cell organelles is known as *hyaloplasm*.	plastids, mitochondria, endoplasmic reticulum (ER), golgi complex, lysosomes, ribosomes, microtubules, microfilaments, centrosome etc and non-living inclusions such as ergastic substances, fats, oil droplets, starch granules, vacuole etc,
Chloroplast **(Genetic organelle)**  	Chloroplasts are biconvex structures surrounded by a lipoprotein double membrane (and contains a gel-like ***stroma***. It also consists of many membranous chlorophyll rich structures known as the ***grana***. Each granum is composed of 10-100 disc like membranous structures known as ***thylakoids***. The inner surface of the lamellar membrane contain small spherical structures called ***quantosomes*** within which photophosphorylation occurs. Grana are interconnected by network of membranous tubules called ***stroma lamella or Fret's channels***. Stroma also contains 70S ribosomes, circular DNA and lipid droplets.	• Chloroplasts are plastids that carry out the process of photosynthesis in plants where light energy is converted into chemical energy. They are present in palisade and spongy parenchyma tissue of leaves and cortical cells of young stems. Plants have 20 - 40 chloroplasts per cell. • The dark reaction of photosynthesis occurs in the stroma which contains the multienzyme complex for the dark reactions. • The light reaction of photosynthesis takes place in the grana. It may also store starch. • The chloroplast DNA is involved in cytoplasmic inheritance.
Mitochondria **(Singular: Mitochondrion)** **(Genetic organelle)**  	Mitochondrion is covered by an envelop of two membranes, the outer and inner membrane. The inner membrane folds into the lumen to form finger-like ***cristae or villi***. The space between the outer and inner mitochondrial membrane as well as the central space is filled up by a viscous ***mitochondrial matrix.*** There are a number of spherical bodies attached to the inner membrane by a stalk, called as ***oxysomes***. The matrix also contains a few ribosomes, a circular DNA and phosphate granules.	• Due to its capacity to convert potential energy from food into ATP, which can be used by the cell to carryout its various activities, mitochondria is aptly termed as the *power house of the cell*. • As oxidation of carbohydrates, lipids and proteins occurs in mitochondria it is the site of cellular respiration. • In aerobic respiration, cristae are the sites of oxidative phosphorylation and electron transport. Matrix is the site of Krebs cycle enzymes and fatty acid oxidation.
Ribosomes	Ribosomes are very small organelles associated with ER or free floating in cytoplasm. Prokaryotes have 70S and eukaryotes have 80S (Svedberg units) ribosomes. It consists of a larger and smaller subunit. The association of units depends upon Mg++ concentration.	Sites of protein synthesis. Made up of roughly equal parts of protein and RNA. They are often found in clusters called as polyribosomes or polysomes.

		
Endoplasmic reticulum (ER) 	It is a network of flattened, membrane bound *cisternae*, forming tubes and sheets through out the cell. ER with ribosomes over it are termed as Rough ER, without ribosomes it is called as smooth ER.	It gives mechanical support to cytoplasm; helps in storage of synthesized molecules and involved in intercellular exchange of materials; synthesis of new nuclear membrane during cell division and synthesis of lipids.
Golgi apparatus (Dictyosomes in plants) 	They are a stack of flattened membrane-bound sacks called *cistrenae*, continuously being formed at one end of the stack and budded off as vesicles at the other. The stacks may form discrete dictyosomes as in plant cells or an extensive network as in animal cells	Involved in cell-plate formation. A place where sugars, phosphates, sulphates or fatty acids are added to certain proteins. As membranes bud from Golgi system they are marked for transfer via transport vesicles to specific sites such as plasma membrane or lysosomes.
Lysosomes 	Lysosome is a single membrane bound sac of digestive enzymes present in all eukaryotic cells. They digest the food particles and release digested food particles into cytoplasm.	It helps in intracellular digestion of bacteria and other foreign bodies. It aids in autolysis, endocytosis and exocytosis.
Microbodies 	Microbodies are single membrane bound spherical organelle which are large in number. They are of several types such as spherosomes, peroxisomes, glyoxisomes and lomasomes.	All contain catalase, an enzyme that breaks down hydrogen peroxide. They are the sites of glyoxalate cycle in plants.
Vacuoles 	A sac bound by tonoplast containing the cell sap. Plant cells have a large central vacuole that makes cell turgid.	It is a storage deposit for water and metabolic products like sugars, aminoacids etc. It helps in osmotic property of the cell by creating turgor pressure, when filled with fluid.
Centrosome or centriole	A specialized portion of the cytoplasm present adjacent to the interphase nucleus, capable of being replicated after each cell division. It consists of structural protein, tubulin and lipid molecues.	Centrioles are involved in the organization of the mitotic spindle and in the completion of cytokinesis; rarely present in plants.

		
Cilia and flagella  a. Movement of Cilia	They are not universal but present in most plant and animal cells. Cilia is short and present in large numbers. Flagella are large but less numerous.	They help in locomotion of the cells.  b. Movement of flagellum
Cytoskeleton	It is composed of *microtubules* of the protein tubulin, *microfilaments* of actin and myosin (as in muscle cells) and *intermediate filaments* (each with a distinct protein as keratin).	It contributes to shape, division and motility of cells and its ability to arrange its components.
Ergastic substances	The portion of cytoplasm other than cell organelles is known as hyaloplasm or cytosol.	It contains water, minerals, ions, sugars, aminoacids and other nutrients for building macromolecular biopolymers (nucleic acids, proteins, lipids, starch, cellulose etc.)

CELL THEORY

The German microscopists, Matthias Schleiden and Theodor Schwann proposed the Cell theory in 1839, which states that all plants and animals are constructed from small fundamental units called cells, and that all cells arise from preexisting cells.

Table -3.1. Differences between prokaryotes and eukaryotes

CHARACTER	PROKARYOTES	EUKARYOTES
Cell size and shape	Small in size ; rod or spherical	Large in size; mostly spheroid
Cell division	By binary fission	Mitosis or meiosis occurs
Nucleus and Nuclear envelop	Absent.	Present.
Chromosomes	Absent. Circular DNA molecules lies in cytoplasm	Multiple chromosomes present inside the nucleus
DNA	Shorter & circular DNA. Histone proteins absent. DNA rejoins rapidly after denaturation	Long & linear DNA. Histone proteins present. DNA rejoins slowly after denaturation.
Mitochondria	Absent	Present
Chloroplast	Absent	Present
Cell wall	Made of polysaccharides	Made of cellulose, hemicellulose & pectins
Spindle fibers	Absent	Present
Pigments	Present throughout cytoplasm	Present in plastids
Endo–membrane	Absent	Present
DNA polymerase	Sensitive to ethinobromide	In-sensitive to ethinobromide
RNA polymerase	Sensitive to Vifamycin	In-sensitive to Vifamycin
Ribosomes	70S (50S + 30S)	80S (60S + 40S)
Ribosomal RNA (r RNA)	16S, 23S	18S, 28S
Transfer RNA (t RNA)	Formyl methionyl t RNA present	Absent
Protein-synthesis	Inhibited by chloramphenicol	Inhibited by cyclohexinoide
Cholesterol	Either absent or very low	Present
Locomotion	By flagella with a single fibril	By both cilia and flagella
Exocytosis & endocytosis	Absent	Present
Example	Bacteria, Blue green algae (BGA)	Plants, Fungus, animals, human beings

4. CHROMOSOME MORPHOLOGY

Strausberger in 1875 first observed thread like structures during cell division. Waldeyer first used the term chromosome (Chroma = colour; soma = body) in 1888. The study of structure and function of chromosomes is termed as *Cytogenetics.*

A chromosome is a rod shaped, self replicating, organized mass of DNA present in the nucleus of the eukaryotic cell, visible only during metaphase of cell division. Prokaryotes have naked circular DNA in their nucleus.

CHROMOSOME NUMBER

All organisms have a characteristic number of chromosomes in their body cells referred to as *somatic chromosome number* or *diploid* (or **2n**) number. The somatic cells normally will have two copies of the chromosome which are identical in gene content, arrangement and morphology and hence are called as *homologous chromosomes*. One member of each pair is acquired from the gamete of one of the two parents.

The gametes viz., pollen grains, sperms, egg cells, have only half of the somatic chromosome number termed as *gametic chromosome number* or *haploid* (**n**). The term 'ploidy' refers to the sets of chromosome in the cells. Somatic cells have two sets of chromosomes and are called *diploid* (2n). Gametes or sex cells contain only half the somatic chromosome number and are called as *haploid* (n). Fusion of the male and female gametes gives rise to diploid zygote and the offspring will get half the chromosome from the mother and half from the father.

Table 4.1. Organism & Chromosome Number

Plants	
Pea	- 14
Pearl millet	- 14
Rice	- 24
Bread wheat	- 42
Pepper	- 128
Animals	
Fruit fly	- 8
Dog, chicken	- 78
Rat	- 42
Rhesus monkey	- 48
Humans	- 46

A *genome* refers to a set of chromosomes corresponding to the haploid set of a species and is represented by X. The term *haplodiploid* refers to the presence of both haploid and diploid chromosome number in an organism. Eg. In bees and wasps, the females are diploid (2n) and males are haploid (n). The chromosome numbers of some organisms are given in Table 4.1.

CHROMOSOME SIZE

Chromosomes are generally measured during mitotic metaphase as they are very thick and spread well in the cell. It may be as short as 0.25 µm in fungi and birds, or as long as 30 µm in *Trillium*. The giant chromosomes in diptera are 300 µ in length and 10 µ in diameter and are visible even in interphase nucleus. In general, plants have longer chromosomes than animals. The organisms with less number of

chromosomes contain comparatively large-sized chromosomes than the chromosomes of the organisms having many chromosomes. Further, the chromosomes in a cell are never alike in size, some may be exceptionally large and others may be too small. Stretched end-to-end, the DNA in a single human diploid cell would extend over 2 meters.

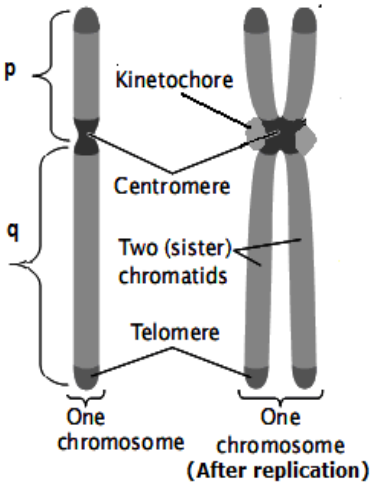


Fig. 4.1. Chromosome

CHROMOSOME MORPHOLOGY

A mitotic metaphase chromosome have the following components namely, chromatids, centromere, telomere, secondary constriction with satellite and chromomere. The short arm is called as 'p' arm while the long arm is 'q' arm. The regions and bands are numbered from the centromere out. to identify a band in the chromosome, a sequence of four items are used namely, chromosome number, arm, region and band number. For example, 9q34 refers to chromosome 9, the long arm, region 4 and band 4.

(1) Chromatid: The longitudinal sections of a metaphase chromosome are called as chromatid. The chromosome at interphase and telophase is represented by a single chromatid where each chromatid is composed of a single DNA double helix. A metaphase chromosome has two chromatids held together at centromere (Fig. 4.1).

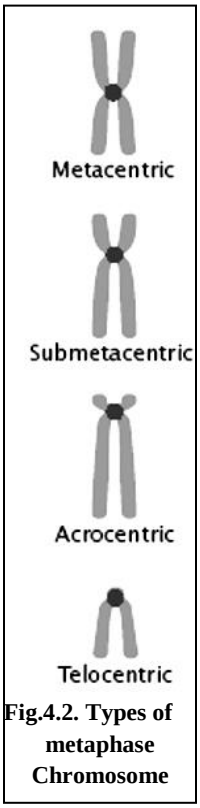


Fig.4.2. Types of metaphase Chromosome

Since the two chromatids of a chromosome are produced by replication of a single chromatid during S phase they are called as *sister chromatids*. The chromatids of a homologous chromosome are called as *non-sister chromatids*.

(2) Centromere: A centromere is the constricted region of chromosome which separates it into a short arm and a long arm (q). The short arm of the chromosome is denoted by ***p*** (in French, *petite* means *small*) while the long arm is denoted by **q** (Fig. 4.1). After DNA replication, the chromosome consists of two identical structures called *sister chromatids* which are held together by centromere.

The centromere, known as *primary constriction,* is the point of attachment for spindle microtubules. Before cell division, a protein complex called *kinetochore* assembles over centromere on each side of the chromosome to which the spindle microtubules later attach. As a result centromeres are the first part of chromosome to be pulled towards the poles during anaphase. Hence, chromosomes without centromere cannot be pulled into newly formed nuclei and are lost causing catastrophic damage to the cell.

Depending on the position of the centromeres, chromosomes can be grouped as: (i) ***Metacentric***: Centromere is located at the centre of the chromosome. Here, both arms are equal in size and appear as 'V' shape during anaphase. (ii) **Submetacentric**: The centromere is located on one side of the centre point such that one arm is longer than the other. These chromosomes appear as 'j' or 'V' shaped during anaphase. (iii) **Acrocentric**: Centromere is located close to one end of the chromosome forming a very short arm and a very long arm. They appear as 'j' or rod shaped during anaphase and (iv) **Telocentric**: Centromere is located at one end of the chromosome so that the chromosome has only one arm. These chromosomes always appear 'I' shaped or rod shaped during anaphase. Centromeres are the last segment to replicated during S phase. As the position of centromere remains fixed in a chromosome, except for structural chromosomal aberrations, they are used for identification of different chromosomes of a species.

(3) Telomere: The two ends of linear chromosomes are known as telomeres. They help in stabilizing the ends of chromosomes. If a chromosome breaks, producing new ends, these ends have a tendency to fuse together and the chromosome id degraded at the newly broken ends. Telomeres provide stability to chromosomes. They also participate in limiting cell division and plays an important role in ageing and cancer.

(4) Secondary constriction: The constricted or narrow region other than the centromere is called as secondary constriction Chromosome may have secondary constriction in one or both arms. Chromosomal end distal to the secondary constriction is known as satellite or *sat-chromosome*.

The production of nucleolus is associated with secondary constriction. Therefore, it is also called Nucleolus Organizer Region (NOR) and the satellite chromosomes are often referred to as Nucleolus Organizer Chromosomes (NOC).

(5) Chromomere: Chromosomes in pachytene stage of meiosis show small bead like structures called chromomeres. They are regions of tightly folded DNA which are invisible during mitotic metaphase. The distribution of chromomeres in chromosomes is highly characteristic and constant whereas, the pattern of distribution differs for different chromosomes. They are clearly visible as dark staining bands in the giant salivary gland chromosomes. Chromomeres may differ in size in a single chromosome of maize or they appear uniform in size as in rye.

HETEROCHROMATIN AND EUCHROMATIN

The chromosomes are composed of thread like structures called chromatin. Based on its affinity to basic dyes (acetocarmine or feulgen) during prophase the chromatin was classified into two groups namely *heterochromatin*, which are darkly stained regions and *euchromatin* whch are lightly stained regions.

In general heterochromatin is found in centromeric and telomeric regions which generally replicate later than the euchromatic regions of chromosomes. The genes within the heterochromatic regions are usually inactive. Most of the genome of an active cell is euchromatic and the genes within this euchromatic region are expressed. Heterochromatin is further classified into two groups:

a) Constitutive heterochromatin: They are genetically inactive present near centromere and telomere. They do not revert to euchromatic state and is present at identical positions on both homologous chromosomes of a pair.

b) Facultative heterochromatin: They are genetically active region present in the middle of the chromosome between centromere and telomere. They play a active role in transcription. A well known example of facultative heterochromatin is the Barr body, an inactivated X chromosome in somatic cells of mammalian female(XX).

KARYOTYPE AND IDEOGRAM

The complete set of chromosomes, in the cells of an organism, arranged and numbered by size, from largest to smallest. is its ***karyotype***. It is most often studied when the cell is at metaphase of mitosis and all the chromosomes are present as dyads.

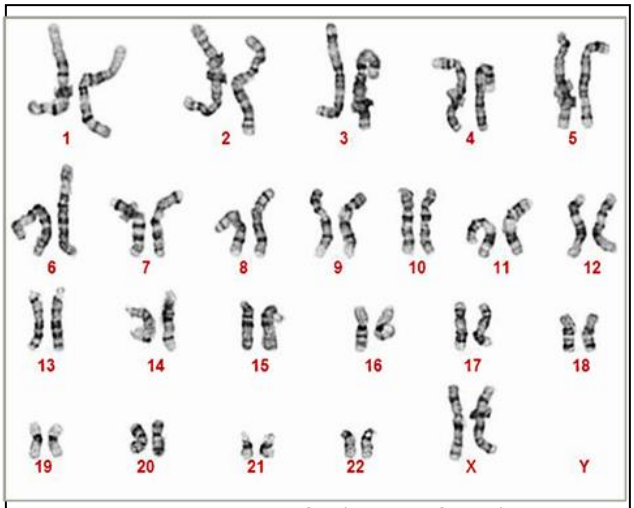


Fig. Karyotype of a human female

The general morphology, including size of chromosome, position of centromere, presence of secondary constriction and size of satellite bodies, of somatic chromosomal complement of an individual constitutes its karyotype.

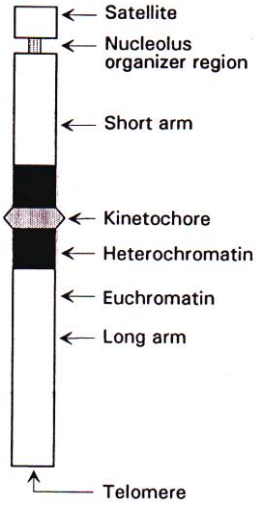


Fig 4.3. Ideogram

Eg. The karyotype of the human female contains 23 pairs of homologous chromosomes (22 pairs of autosomes and a pair of X chromosomes). While, the karyotype of the human male contains the same 22 pairs of autosomes, one X chromosome and one Y chromosome

Karyotypes are used identify chromosomal alterations that may result in a genetic disorder. It is also useful to confirm the presence of specific species and to study genetic diversity in species with a wide range.

The diagrammatic representation of the karyotype of a species showing all the morphological features of chromosomes is known as ***ideogram or ideotype***.

5. MOLECULAR STRUCTURE OF CHROMOSOME

Prokaryotic chromosomes consists of a single DNA molecule which is usually circular, with only small amount of associated proteins. Each prokaryotic chromosome has a single origin of DNA replication. Eukaryotes have several linear chromosomes and the DNA is tightly associated with large amount of proteins. Each eukaryoti chromosome has multiple origins of DNA replication.

FOLDED FIBER MODEL (Du Praw, 1965)

Du Praw proposed that the chromosomes are made up of chromatin fibers of about 230 – 300 Å diameter and that each chromatin fiber consists of a DNA double helix in coiled state. Thus the 300 Å chromatin fiber is produced by coiling of a single DNA double helix which replicates during interphase, producing two sister chromatin fibers (Fig. 5.1).

As the 0.3 % of DNA remains unreplicated during S phase, the two sister fibers remain joined in the centromeric region until its replication in zygotene phase.

The folding of the two sister chromatin fibers, reduces their length and increases their thickness and stainability, and gives rise to two sister chromatids. *DuPraw's model of DNA-histone association is now considered wrong by the discovery that DNA itself is looped around histone beads to form nucleosomes.*

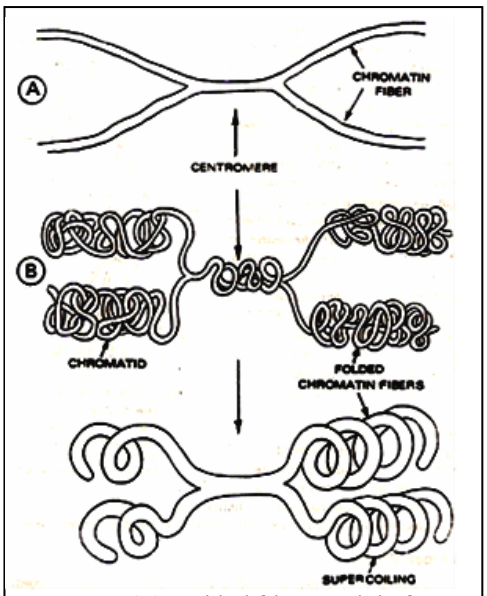


Fig. 5.1. Folded fiber model of chromosome organization

NUCLEOSOME-SOLENOID MODEL (Kornberg and Thomas, 1974)

Chromosomes are composed of *chromatin fibers.* The term chromatin refers to the mixture of DNA and proteins that composes the chromosomes. The proteins are of two types viz., histone (basic)proteins and non-histone (acidic) proteins.

Histones are proteins with a high proportion of positively charged aminoacids (lysine and arginine) which enable them to bind firmly to the negatively charged DNA double helix. The quantity of histones in chromatin is equivalent to the quantity of DNA in the chromatin, in dry weight basis. All the species and tissues have five types of histone proteins namely, H1, H2a,

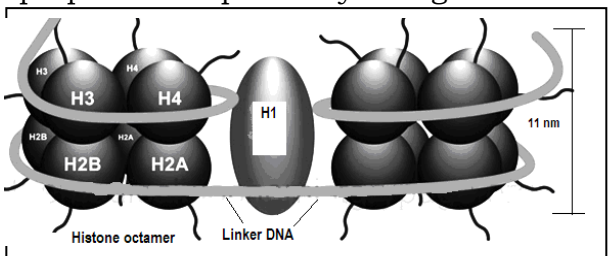


Fig. Structure of nucleosome

H2b, H3 and H5. The aminoacid sequence of the histones is highly conserved throughout evolution suggesting the importance of their role in the survival of eukaryotes. DNA coil around the histones to form nucleosome.

Nucleosome is a beadlike subunit of chromatin made up of *histone octamer* (two molecules each of H2a, H2b, H3 and H4). This bead like histone octamer is wound twice by 146 bp of DNA. A molecule of H1 histone seals the DNA with the octamer. The nucleosomes now resemble beads on a string. The section of DNA between the two nucleosomes is called as *linker DNA*. The length of the linker DNA varies with species and in humans, it is about 60bp long. This forms the first level of coiling of DNA.

The string of nucleosomes coils further to form 30 nm thick helical structure called ***solenoid***, which forms the second level of coiling. Solenoid fiber can be seen in electron micrographs of metaphase chromosome. The solenoid structure further supercoils to form 300 nm loop like structure. This is followed by formation of 700nm rosette structure (consisting of six connected loops), which then coil finally to form the metaphase chromosome with two chromatids. DNA packed into solenoids, unlike DNA in nucleosome form, is not transcriptionally active.

The organization of these structures involves the binding of chromatin fibers on to a chromosomal scaffolding by the non-histone protein, *topoisomerase II*. The non-histone proteins are also involved in regulation of gene expression.

Each eukaryotic chromosome is composed of a single DNA double helix. The various structures and their packing ratio are given in table.

STRUCTURE	DIAMETER	PACKING RATIO
DNA double helix	2 nm	-
Nucleosomes	11 nm	6
Solenoid	30 nm	40
Looping of solenoid	700 nm	1000
Metaphase chromosome	1400 nm	10000

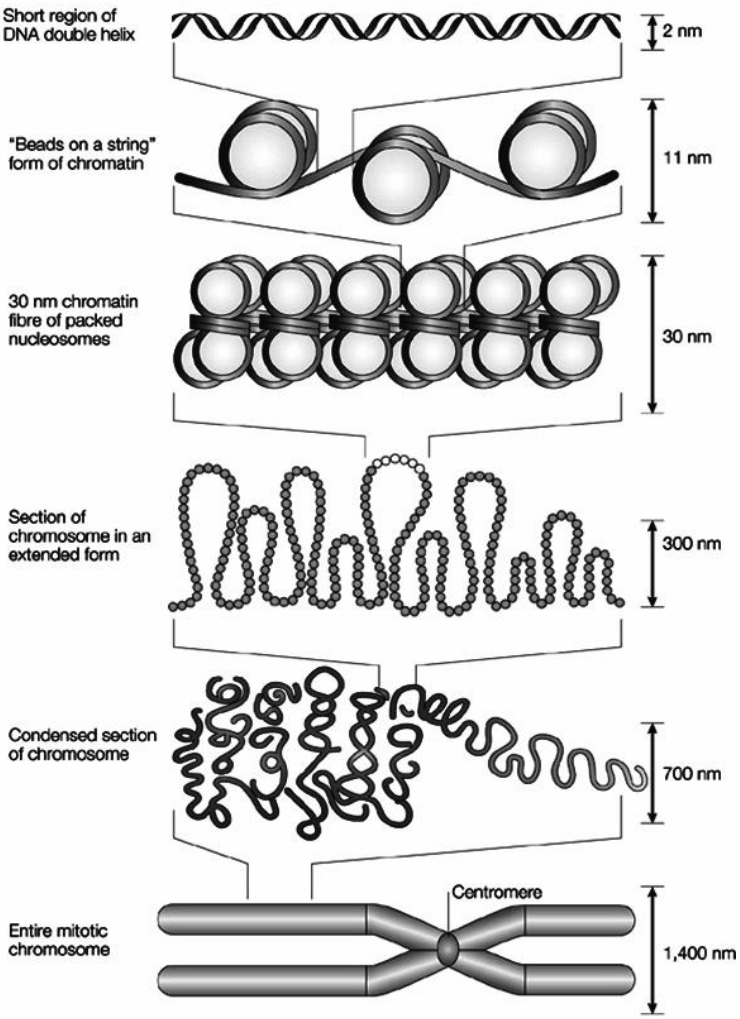


Fig. Molecular structure of chromosome

6. SPECIAL TYPES OF CHROMOSOMES

Tissues of some organisms have chromosomes which differ significantly from the normal chromosomes in morphology or function. Such chromosomes are referred to as special chromosomes. They include:

1. GIANT CHROMOSOMES OR POLYTENE CHROMOSOMES

To increase cell volume, some specialized cells undergo repeated rounds of DNA replication without cell division (*endoreduplication*). As a result each chromosome becomes a bundle of numerous chromatids all aligned lengthwise. Being thick and 200 times longer than somatic chromosomes they are called as *giant chromosomes* or *polytene chromosomes* and the condition is known as polyteny.

Fig 5.1. Giant chromosomes in salivary gland of *D. melanogaster*

Polytene chromosomes were originally observed in the larval salivary glands of *Chironomus* midges by Balbiani in 1881. They are known to occur in secretory tissues of other dipteran insects such as the Malpighian tubules of *Sciara* and also in protists, insects, plants and mammals, and hence are called as *salivary gland chromosomes*. The diffused uncoiled regions of the polytene chromosome, called as **chromosome puffs** , are sites of RNA transcription. A large chromosome puff is called as a **Balbiani ring**.

Uses

Polytene chromosomes have characteristic light and dark banding patterns. Dark banding frequently corresponds to inactive chromatin, whereas light banding is usually found at areas with higher transcriptional activity. Any change in chromosome structure is reflected on the banding pattern. Hence, genetic research involving deletion, inversion, duplication or translocation can be identified by observing changes in the banding pattern.

2. LAMP BRUSH CHROMOSOMES

They are a special form of giant chromosomes found in the growing oocytes (immature eggs) of most animals, except mammals, visible even in light microscope. They are first seen by Flemming in 1882. Chromosomes transform into the lampbrush form during the diplotene stage of meiotic prophase I due to an active transcription of many genes. They are highly extended meiotic half-bivalents, each consisting of 2 sister chromatids which are organized into a series of chromomeres. From each chromosome, pair of loops emerge in the opposite directions, vertical to the main chromosomal axis. These lateral loops give these chromosomes the appearance of a lampbrush, and hence are called as *Lampbrush chromosomes.*

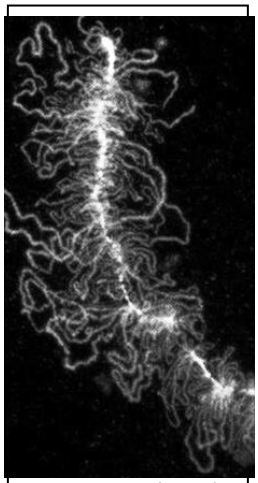


Fig 5. Lampbrush chromosome

Amphibian and avian lampbrush chromosomes can be microsurgically isolated from oocyte nucleus (germinal vesicle) with either forceps or needles. A given loop always contains the same DNA sequence, and it remains extended in the same manner as the oocytes grows. These chromosomes produce large amounts of RNA for the oocyte, and most of the genes present in the DNA loops are being actively expressed.

Uses

Giant chromosomes in the lampbrush form are useful model for studying chromosome organization, genome function and gene expression during meiotic prophase, since they allow the individual transcription units to be visualized. Moreover, lampbrush chromosomes are widely used for high-resolution mapping of DNA sequences and construction of detail cytological maps of individual chromosomes.

3. ACCESSORY/SUPERNUMERARY CHROMOSOMES

In many species, some extra chromosomes are found in addition to normal somatic chromosomes. These extra chromosomes are called *accessory chromosomes or B-chromosomes or supernumerary chromosomes.* They have some peculiar functional aspects. In some animal species, they may arise due to fragmentation of heterochromatic Y chromosome. These chromosomes are generally smaller in size than the normal somatic complement. They are believed to be generally inactive genetically. In many species they tend to be eliminated from somatic tissues due to lagging and non-disjunction and they frequently change their morphology through fragmentation. Eg. The presence of 25 – 30 such chromosomes often leads to reduction in vigour and fertility in Maize.

7. CELL DIVISION

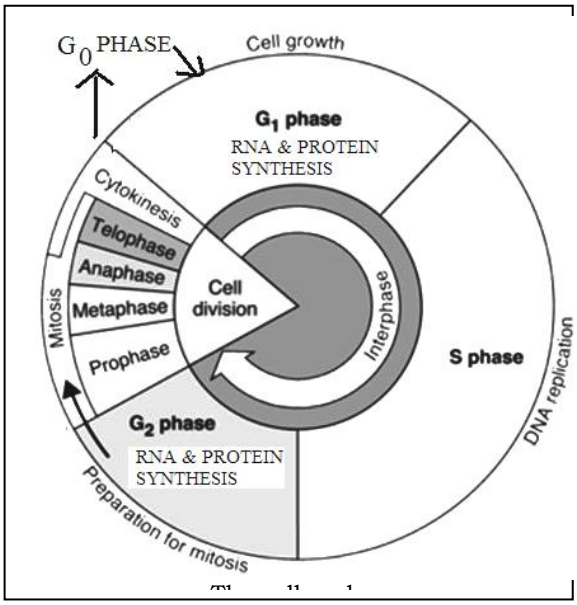
For any cell to reproduce successfully, three fundamental events must take place:(1) Its genetic information must be copied,(2) The copies of genetic information must be separated from one another and (3) The cell must divide. All cellular reproduction includes these three events, but the processes that lead to these events differ in prokaryotic and eukaryotic cells. The division of chromosomes and cytoplasm of a cell into two cells is known as *cell division*. The cell that undergoes division is known as *parent cell*, while the cell derived from the division of a parent cell are known as *daughter cells*.

In prokaryotes, the cell division occurs by an asexual division called as ***binary fission***.. In bacteria, the circular bacterial chromosome replicates, and the two new genomes move toward opposite ends of the cell. A new plasma membrane is formed between them and the the cytoplasm divides into two leading to cell division. The new daughter cells absorb nutrients for growth; replicate their bacterial chromosome, and divide again.

In eukaryotes, chromosomes are separated from the cytoplasm by the nuclear envelope. The cell reproduction requires the processes of DNA replication, copy separation, and division of the cytoplasm. However, the presence of multiple DNA molecules requires a more complex mechanism.

CELL CYCLE

The entire sequence of repeating events from one mitotic division to the next is referred to as the cell cycle. The cycle has two major phases, viz., (1) Interphase, the period between cell divisions and (2) M phase, which includes mitosis and cytokinesis. In plants, cell division occurs in meristems. In dormant meristems, the cell rest in Go phase. When conditions are correct, the cell enters into the cell cycle.



I. INTERPHASE mainly consists of three phases namely, G_1, S and G_2 phases. G_1 and G_2 are resting phase called gap 1 and 2 respectively, S phase is the period of DNA replication. A fourth interphase stage called Go phase occurs in plants during adverse growth conditions. The Go phase is a non-dividing stage during which cells usually maintain a constant size. The cells can remain in Go phase for a long period, even indefinitely, or they can reenter into G_1 phase again. Many cells never enter Go phase.

G_1 phase: The period between telophase and S phase is called as G1 phase where synthesis of proteins and RNA occurs. During this stage, the nucleus migrates to the centre of the cell and is surrounded by phragmosome. A critical point termed the *G_1/S checkpoint* occurs in G_1 phase after which the cell is committed to divide. Before reaching the G /S checkpoint, cells may exit and pass into Go, a non-dividing phase.

S (Synthetic) Phase: The phase between G1 and G2 where DNA synthesis and chromosome replication occurs is called as S phase. Before S phase, each chromosome is composed of one chromatid and after S phase, each chromosome is composed of two chromatids i.e. two copies of its genetic information.

G_2 Phase: The phase after DNA replication and beginning of prophase where synthesis of protein and RNA necessary for cell division take place is termed as G_2 phase. The important point called *G_2/M checkpoint* occurs in G_2 phase. Only after passing this checkpoint, the cell which is ready to divide can enter into M phase.

REGULATION OF CELL CYCLE

The plant hormones like auxin and cytokinins are known to initiate cell cycle. Auxin stimulates DNA replication while cytokinin initiates the mitotic cell division events.

During the cell cycle, the cell has check points to check for problems during DNA synthesis and chromosome segregation. The cell cycle is controlled by activity of proteins called as ***cyclins***, and ***cyclin-dependent protein kinases*** (CDPK) enzymes. A kinase is an enzyme which will phosphoryate another protein. One group of cyclins called the *G_1 cyclins*, are manufactured and activate CDPKs which stimulate DNA synthesis at the G /S check point. If sufficient G_1 cyclins are not formed, the cell will not progress to the S phase. After passing this point, the G_1 cyclins are degraded and a new class of cyclins called *M cyclins* are produced. These activate a second set of CDPKs which permit the cells to pass the G_2/M check point into mitosis.

After passing through G_2/M check point, the animal cells will divide whereas the cells plant cells will not divide. This means that the plant cells continue to replicate DNA without dividing. This phenomenon known as ***endoreduplication***, occurs in more than 80% of the plant cells. These mechanisms arrest the cell cycle and allow the cell to repair defects so that it is not transmitted to the next generation.

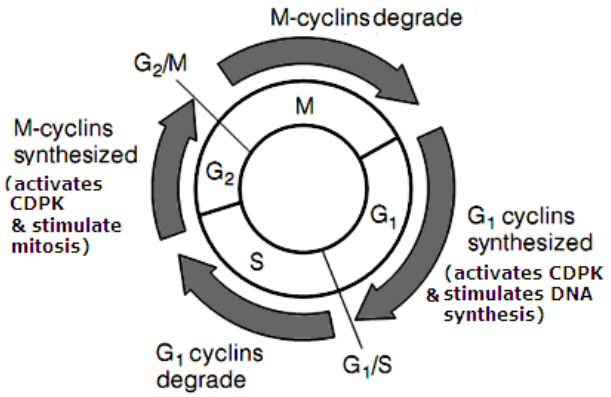


Fig. Regulation of cell cycle

DURATION OF CELL CYCLE

Although the length of interphase varies from cell type to cell type, a typical dividing mammalian cell spends about 10 hours in G_1, 9 hours in S, and 4 hours in G_2 phase. In *Vicia faba*, the duration is about 12 hours in G_1, 4 hours in S, and 12 hours in G_2 phase.

II. MITOSIS

Prophase

1. The chromosomes appear as thin thread like structure.
2. Each chromosome possesses two chromatids as the chromosome was duplicated in the preceding S phase.
3. In animal cells, the spindle grows out from a pair of centrosomes which migrate to opposite sides of the cell. Each centrosome has a centriole, which is also composed of microtubules. Higher plant cells do not have centrosomes or centrioles, but they do have mitotic spindles.
4. Chromosomes begin to condense, while nuclear envelop and nucleolus are present.

Prometaphase

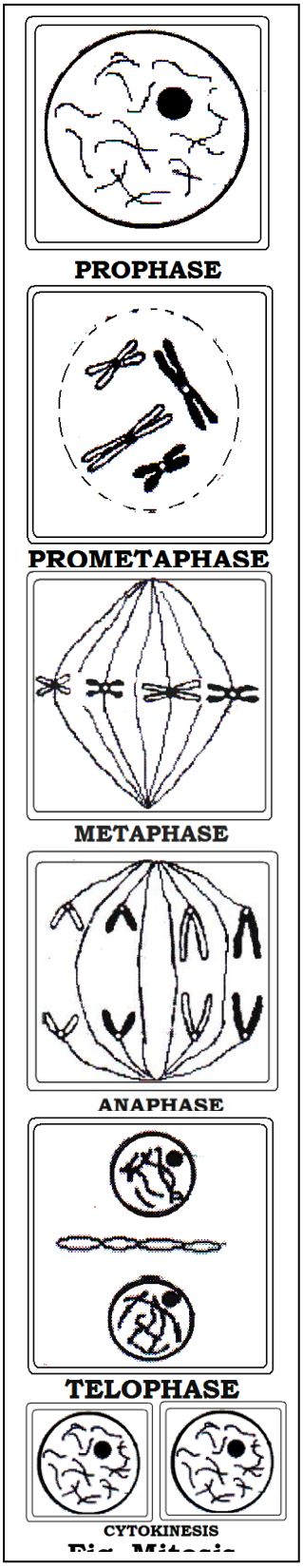
1. Nuclear envelop begins to disintegrate marking the beginning of prometaphase.
2. Spindle microtubules, which are outside the nucleus, enter the nuclear region and connect to the kinetochore of the sister chromatids.
3. Some microtubules do not attach to a chromosome and remain at the center of the cell.
4. The two chromatids of each chromosome further condense and become visible due to matrix coating and relational coiling.

Metaphase

1. During metaphase, the chromosomes arrange themselves in the metaphase plate, between the two centrosomes.
2. The movement of chromosome to the equatorial plate and their orientation is termed as *metakinesis*.
3. The chromosomes are shortest and thickest only during metaphase.
4. The chromatids are held together at the centromeres and relational coiling is absent during this stage.

Anaphase

1. Anaphase begins when the centromere of each chromosome divides longitudinally leading to separation of chromatids. After separation, each one is considered as a separate chromosome.
2. Centromere is the first portion of each of the chromosome to begin to move towards the poles.
3. Depending on the position of the centromeres viz., metacentric, acrocentric or



telocentric, the chromosomes resemble 'V', 'L' or 'I' shapes respectively.

4. The sister chromatids move towards the poles.

Telophase

1. Telophase begins with the arrival of chromosomes at the poles.
2. The chromosomes unwinds and lengthens to become a mass of chromatin fibers and the nucleus will be reorganized from the chromatin.
3. Nuclear envelop is formed around each set of chromosomes producing two separate nuclei within the cell. Nucleolus also reappears.

Cytokinesis

The division of cytoplasm into two halves is called as ***cytokinesis***. It usually occurs during late anaphase or occurs simultaneous with telophase. In plants, cytokinesis takes place through the formation of cell plate at the centre of the cell which gradually moves outwards towards the periphery dividing the cytoplasm into two daughter cells.

In animal cells, cytokinesis occurs by a process known as cleavage, forming a cleavage furrow. The two daughter cells produced by mitosis has the same number of chromosomes as the parent cell. Each daughter cell later enlarges in size till it becomes comparable to the parent cell.

The major features of the cell cycle are summarized below

STAGE	MAJOR FEATURES
Go phase	A stable nondividing period of variable length in plants
Interphase	
G_1 phase	Growth and development of cell, protein and RNA synthesis;G_1/S check point occurs
S phase	Synthesis of DNA; formation of chromosome with two chromatids
G_2 phase	Protein and RNA synthesis; preparation for cell division; G_2/M check point
M phase	
Prophase	Chromosomes condense; mitotic spindle formation begins
Prometaphase	Nuclear envelop disintegrates, spindle microtubules attach to kinetochores
Metaphase	Chromosomes arrange at equatorial plate
Anaphase	Sister chromatids separates and become individual chromosomes; moves towards poles
Telophase	Chromosomes arrive at poles; nuclear envelop and nucleolus reappears; chromosomes relax to become chromatid
Cytokinesis	Cyroplasm divides; cell wall forms in plant cells

Occurrence and importance of mitosis

In plants, mitosis is confined to the meristematic tissues of root and shoot tip, young leaves, flower buds and cambium. In adult animals mitosis is confined with the production of blood cell, outer skin and gut epithelium. Healing of wounds and replacement of damaged organs in both plant and animals is based on mitotic cell division.

7. 1. MEIOSIS

Meiosis occurs in reproductive tissues of plants during gamete formation. Meiosis reduces the chromosome number of a cell to one half so that each cell has only one set (haploid number) of chromososmes. The reduction in chromosome number of the daughter cells is mainly due to a single 'S' phase followed by two successive nuclear divisions. The full chromosome complement (diploid condition) is restored after fertilization. Meiotic division of one diploid (2n) cell gives rise to four haploid (n) daughter cells.

Stages of meiosis

Meiosis is divided into two stages as follows: Meiosis I, which includes prophase I (PI), metaphase I (MI), anaphase I (AI), telophase I (TI) and Meiosis II which includes prophase II, metaphase II, anaphase II and telophase II.

FIRST MEIOTIC DIVISION / MEIOSIS I
PROPHASE I

This stage is divided into five substages, namely
1. Leptotene, 2. Zygotene, 3. Pachytene, 4. Diplotene and 5. Diakinesis

Leplotene
1. Nuclear volume increases and chromosomes begins to condense.
2. In some species, chromomeres may be visible throughout the length at specific positions.
3. RNA synthesis and hence increase in nucleolus happens.
4. Proteins required for chromosome condensation are also synthesized.

Zygotene
1. ***Pairing*** between homologous chromosomes (from maternal and paternal cells) occurs and is called as ***synapsis***.
2. Replication of the remaining 0.3% DNA which does not replicate during the premeiotic interphase occurs. This DNA is referred to as Z-DNA.
3. Synthesis of a specific nuclear proteins and development of the synaptenemal complex occurs and
4. Progressive condensation of chromosomes takes place.

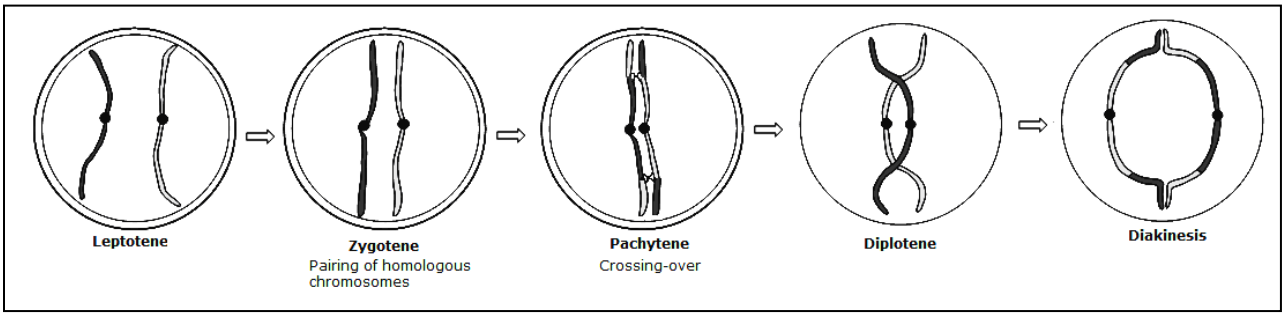
Pachytene
1. Condensation of chromosomes continues and the chromosome pairs become shorter and thicker.
2. Due to synapsis between homologous chromosomes, the number of observable chromosomes is only half of the somatic chromosome number. This haploid number of chromosome pair commonly referred to as ***bivalents.***
3. As the two chromosomes of a bivalent consists of two sister chromatids, each bivalent has four chromatids or strands; called as *tetrad*.
4. ***Crossing-over*** which is the exchange of chromosomal segments between nonsister chromatids of homologous chromosomes takes place during this stage.

Diplotene

1. The two homologues chromosomes of each bivalent appear to be attached with each other at one or more points, these attachments are known as ***chiasma***.
2. *Chiasma terminalization* i.e. movement of chiasma towards the end of homologous chromosomes occurs
3. Further condensation of chromosomes occurs.

Diakinesis

1. The end of chiasma terminalization marks the beginning of diakinesis and the the two homologous chromosomes are attached at the telomeres only.
2. Chromosomes become shorter and thicker due to further condensation.
3. Nucleolus and nuclear envelope disappear; the spindle apparatus is organized and the bivalent begins to migrate towards the equatorial plate of cells.



METAPHASE I

1. Bivalents are arranged at the metaphase plate.
2. The centromeres of the two homologous of each bivalent lie on the either side of the equatorial plate.
3. The part of the bivalents lying on the equatorial plate is the central part of each bivalent, which consists of the telomeres of the two homologous chromosomes attached almost end-to-end with each other.
4. The centromere of each chromosome is structurally divided into two, but these two parts functionally behave as a single centromere.

ANAPHASE I

1. The two *homologous chromosomes begins to separate* from each other and begins to move towards the poles.
2. The number of chromosomes at the poles are exactly half (n) of the somatic chromosome number (2n).
3. During this phase, the two sister chromatids of each chromosomes seem to repel each other but are attached with each other at the centromere. Anaphase ends when the homologous chromosomes reach the opposite pole.

TELOPHASE I

1. The chromosomes uncoil only partially.
2. Nuclear envelope becomes organized around the two groups of chromosomes. Nucleolus also reappears.

CYTOKINESIS AND INTERPHASE

In many plant species, the cytoplasm of each cell divides into two halves which do not separate but they stay together (e.g., maize). This two-celled structure is known as a ***Dyad***. It is important to note that *DNA synthesis does not occur* during this interphase.

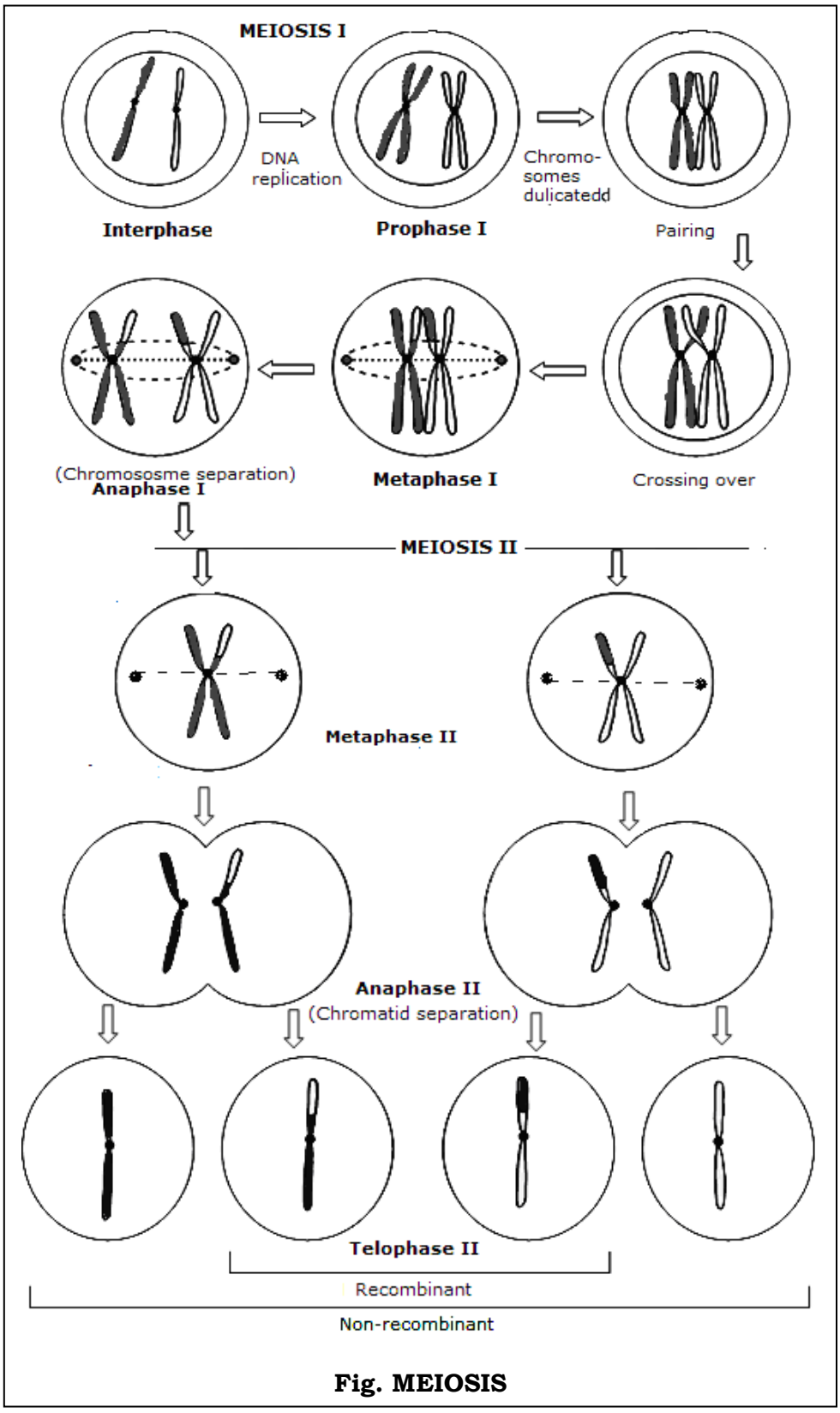

MEIOSIS I
DNA replication
Chromo-somes dulicatedd
Interphase
Prophase I
Pairing
(Chromososme separation)
Anaphase I
Metaphase I
Crossing over
MEIOSIS II
Metaphase II
Anaphase II
(Chromatid separation)
Telophase II
Recombinant
Non-recombinant

Fig. MEIOSIS

SECOND MEIOTIC DIVISION / MEIOSIS II

During the second division of meiosis, the two haploid nuclei of each dyad divide synchronously. The two sister chromatids of each chromosome separate and migrate to the opposite poles hence, the number of chromosomes in each of the haploid nuclei remains the same at the end of this division. Therefore, the second division of meiosis is often referred to as *equatorial division*. The second meiotic division is also divided into four stages viz., 1. Prophase-II, 2. Metaphase-II, 3. Anaphase – II and 4. Telophase – II.

PROPHASE II

There is no relational coiling between sister chromatids and the two sister chromatids of each chromosome are clearly visible. There is further condensation of chromosomes and the nucleolus and nuclear envelope disappears while the spindle apparatus is organized. Later, the chromosomes migrate towards the equatorial plate.

METAPHASE II

Nucleolus and nuclear envelope are absent and spindle apparatus is present. The centromeres of all the chromosomes are arranged in a single plane at the equatorial plate. The two sister chromatids of each chromosome remain attached at the centromere. Chromosomes are at their most condensed stage.

ANAPHASE II

In this stage centromeres divide longitudinally. The two *sister chromatids begin to separate* and move towards the poles.

TELOPHASE II

Telophase begins when sister chromatids reach the opposite poles. The chromatids uncoil to become a loose ball of thread. Nucleolus reappears and nuclear envelope is reorganized from the elements of endoplasmic reticulum.

CYTOKINESIS

By the end of telophase – II, four haploid daughter cells are produced from a single parent cell. The four daughter cells present together are known as *Tetrad*. Cytokinesis divides four daughter cells each of which contains a single haploid nucleus. In pollen formation, all the four cells survive and in ovule formation three cells normally abort leaving one to form the ovule.

SIGNIFICANCE OF MEIOSIS

Meiosis maintains the chromosome number of the species by reducing the chromosome number by one half (n) during gamete formation and restoring it again to diploid during fertilization.

FUNCTIONS OF MEIOSIS

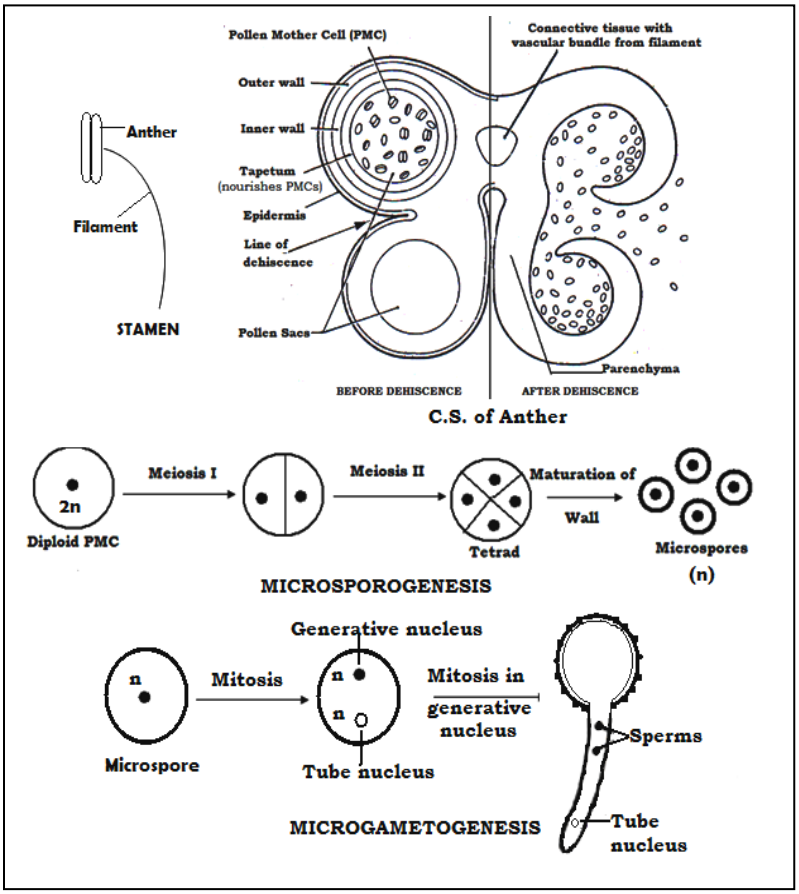
1. Production of gametes with haploid (n) chromosome number.
2. Segregation of the two alleles of a gene due to pairing and their separation at the first anaphase.
3. Independent segregation of the alleles of genes located in separate chromosome due to independent orientation of bivalents during first metaphase.
4. Recombination between genes by crossing over during pachytene stage and generation of genetic variation through segregation, independent assortment and recombination.

8. SEXUAL REPRODUCTION

Sexual reproduction in plants involves two processes: (i) *Meiosis*, which reduces the diploid cell to form haploid gametes and (ii) *Fertilization*, which involves the fusion of haploid (n) male and female gametes to form diploid (2n) zygote which develops into an embryo.

In most plants, these processes divide the life cycle of the plant into two distinct phases or generations, between which the plant alternates. This is as called *alternation of generations.* The first generation, called the *gametophytic generation*, begins with a haploid spore produced by meiosis and the multicellular gametophyte produces gametes by mitosis. During fertilization the haploid gametes unites to produce a diploid zygote which marks the beginning of the diploid *sporophytic generation.*

A biologist should be familiar with the flower structure, as the flower flower affects the kinds of tools and techniques that can be used for emasculation and crossing. A flower usually consists of four major parts namely, sepals, petals, stamens and pistil. A flower with both stamens and pistil is called as a *perfect or hermaphrodite flower.* A flower with stamens alone is known as *staminate flower* (pistil is absent). A flower with only pistil is known as a *pistillate flower* (stamens absent).



A plant with male and female flowers separately is called as a ***monoecious plant***. Eg. Maize, castor, coconut, colocasia etc. Sometimes a plant may either be staminate (male plant) or pistillate (female plant) and are called as ***dioecious plant***. Eg. Papaya, date palm, hemp, asparagus etc. In plants, the microspores and megaspores are produced by *meiotic division* of specific cells in

stamen and pistil, respectively. This is followed by *mitotic division* of the spore nuclei to produce gametes.

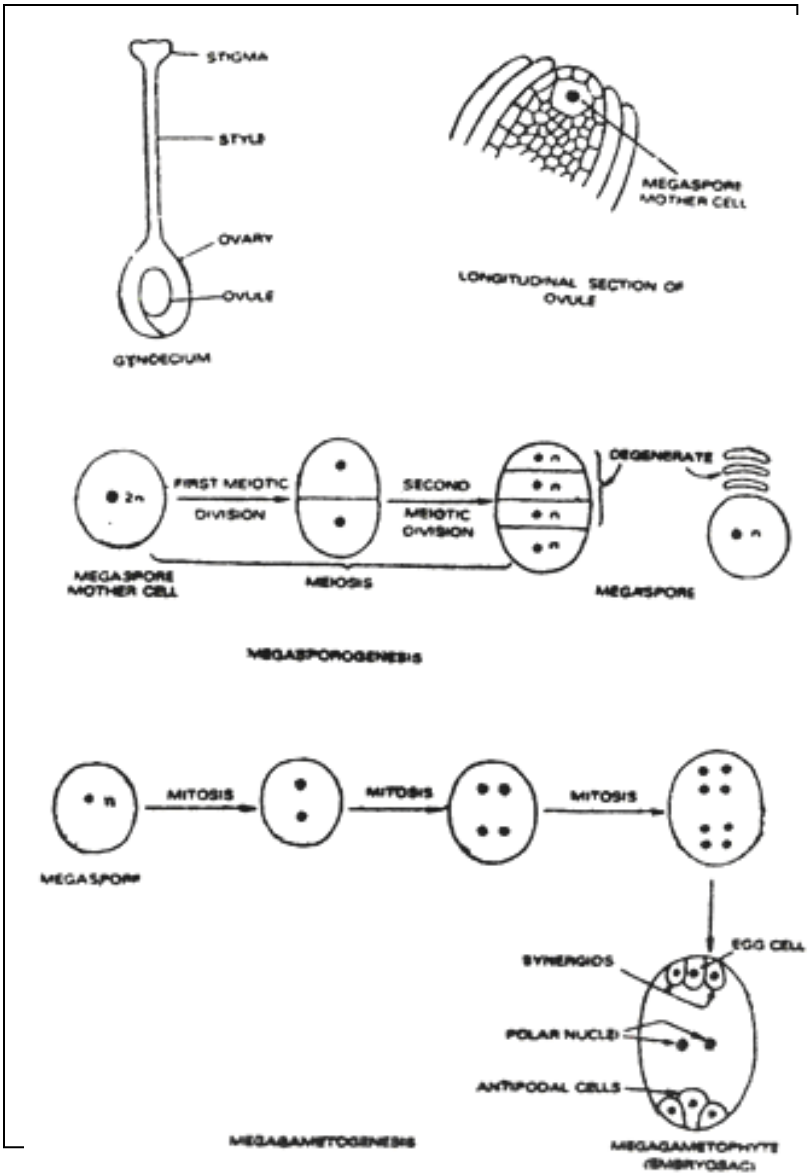
I. SPOROGENESIS refers to the production of microspores and megaspores. It is of two types:

i. Microsporogenesis refers to the production of microspores in anthers. An anther has four pollen sacs, which contain numerous pollen mother cells (PMCs). Each PMC undergoes *meiosis* to produce four haploid microspores. The microspores mature into pollen grains by thickening of their walls.

ii. Megasporogenesis refers to the production of megaspores in ovules. A single cell in each ovule differentiates into a megaspore mother cell (MMC). The MMC undergoes meiosis to produce four haploid megaspores. Three of the megaspores degenerate leaving one functional megaspore per ovule.

II. GAMETOGENESIS refers to the production of male and female gametes in the microspores and the megaspores, respectively. It is of two types:

i. Microgametogenesis refers to the production of male gametes or sperms. During the maturation of pollen grains, the microspore nucleus divides *mitotically* to produce a generative nucleus and tube (vegetative) nucleus. The pollen is generally released in this binucleate stage. The pollen on the stigmatic surface germinates and produces a pollen tube which enters the stigma and grows through the style. The generative nucleus now undergoes a mitotic division to produce two



male gametes (sperms). The pollen, along with the pollen tube, is known as *microgametophyte*. The pollen tube finally enters the ovule through a small pore called micropyle, and discharges the two sperms into the embryo sac.

ii. Megagametogenesis refers to the development of a megaspore into a mature *megagametophyte* or embryo sac. The nucleus of a megaspore undergoes three *mitotic divisions* to produce eight nuclei. Three of these nuclei move to one pole and produce a central egg cell with two synergids on its side. Another three nuclei move to the opposite pole to form antipodal cells. The two polar nuclei at the center fuse to form a secondary nucleus. The number and arrangement of the nuclei varies with species. The embryo sac generally contains a haploid egg cell, two haploid synergids, three haploid antipodal cells and one diploid secondary nucleus.

POLLINATION AND FERTILIZATION

Pollination refers to the transfer of pollen grains from the anther to the stigma of a flower. When compatible pollen falls on a receptive stigma, a pollen tube with two sperms or male gametes grows down the style. The tube penetrates the embryo sac through the micropyle and discharges the two sperm cells. One of the sperms unites with the egg cell (fertilization) to produce a diploid zygote. The other sperm cell unites with the two polar nuclei (called ***triple fusion***) to form a triploid primary endosperm nucleus. The simultaneous occurrence of two fusion events in the embryo sac is called ***double fertilization***. During seed development, the endosperm provides nutrition to the developing embryo.

SIGNIFICANCE OF SEXUAL REPRODUCTION

The sexual reproduction in plants makes it possible to combine genes, from the maternal parent (through the egg) and the paternal parent (through the pollen), to form a diploid zygote with two forms of each gene. This occurrence is called ***biparental inheritance*** and as a result in creating enormous genetic variation. Breeding of crop plants mainly depends on sexual reproduction for creation of variation.

9. MENDELIAN GENETICS

Gregor Johann Mendel was the first scientist to explain the mechanism of inheritance even before the discovery of existence of chromosomes and laid the foundation for the science of genetics. Hence, he is called as "Father of Genetics".

Johann Mendel was born on July 22, 1822 in the village of Heinzendorft, in the region of the Austria-Hungary Empire called Moravia. Today it is known as Hyncice and is in the Czech Republic. He came from a family of peasant farmers.

Mendel conducted his breeding experiments in garden pea, *Pisum sativum* for nearly nine years from 1856. His classical experiments and his explanations were reported in 1865 to the Bruno Society for the Study of Natural Science and published as "Experiments in Plant Hybridization", in The Annual Proceedings of the Natural History Society of Brunn in 1866. His contributions remained unnoticed. Mendel died at the age of 61 in 1884.

In 1900, three botanists, Karl Correns of Germany, Hugo de Vries of Netherlands and Erich von Tschermak of Austria independently rediscovered Mendel's work and laws. This marked the beginning of modern genetic research. Mendel's original paper was later republished in 1901 in the journal 'Flora' (Vol. 89 Page 364).

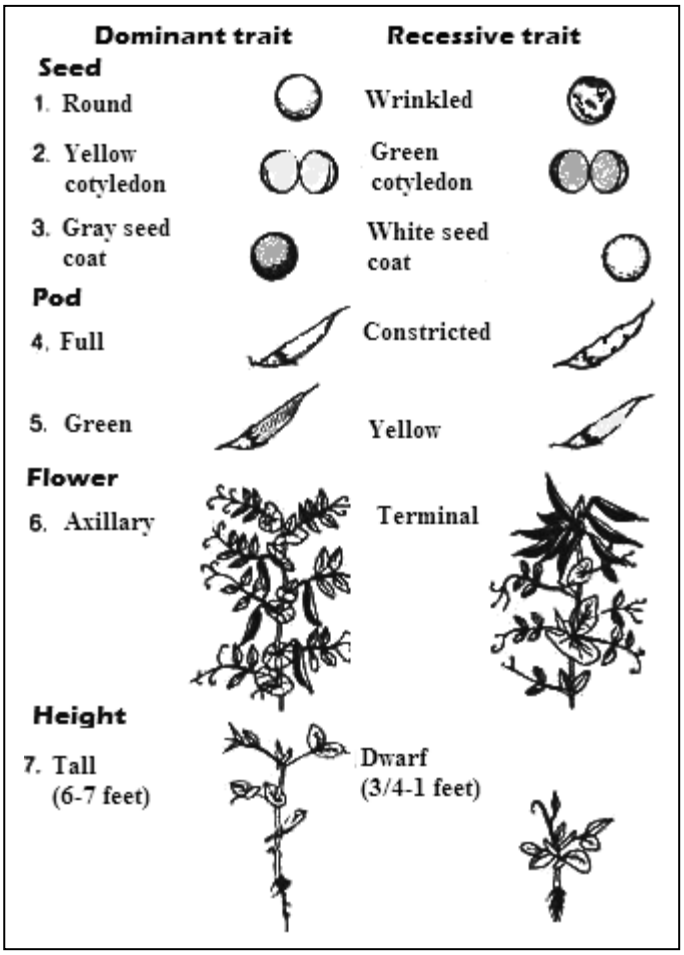
REASONS FOR SELECTION OF GARDEN PEA

The principles of inheritance explained by Mendel was based on his experiments with garden pea (*Pisum sativum*). He selected garden pea as (i) It has a short life cycle, which makes it possible to study several generations within a short period (ii) Its self pollinating, bisexual nature with the presence of contrasting characters makes it easy to get true breeding lines (iii) It is easy to produce hybrids by transferring pollen from one plant to another.

REASONS FOR MENDEL'S SUCCESS

The key reason for Mendel's success was that (i) He approached the problem of inheritance in a systematic and quantitative way (ii) He applied laws of probability to his results (iii) He chose true-breeding garden pea varieties with observable contrasting traits. (iv) He kept records of his experiments and subjected his results to simple mathematical analysis (v) He was lucky as the traits selected him showed complete dominance i.e. they were governed by a single gene and segregated independently in dihybrid crosses.

Mendel's methodology involved (i) Crossing true-breeding lines for only one pair of contrasting character at a time. (ii) Counting the seeds and grouping them quantitatively allowed him to classify all the F_2 progeny into two clear-cut groups. (iii) He draw generalizations on the basis of numerical relationships of his experiments and he proceeded to test these hypotheses experimentally to prove the correctness of his explanations.



Mendel selected seven visible characters, each with two contrasting traits which showed *qualitative inheritance.* He studied the inheritance of single pair of characters first and later took the inheritance of two or more characters.

Mendel's use of clear-cut variables and application of mathematics enabled him to demonstrate that the traits were passed from each parent to their offspring. When the pea plant with contrasting characters were crossed only one character alone appears in the first generation offspring (F_1). In the second generation (F_2) both the characters appeared.

BASIC CONCEPTS IN GENETICS

The morphological characteristics of an organism is termed as a *character* or *trait*. An organism which have been inbred or selfed for many generations in which a certain phenotype remains the same is called as *pure--breeding line*. The mating or crossing between two individuals that differ by one or more characters is called as *hybridization* eg. Tall plant x Dwarf plant. The offspring that result from such a mating is called as a *hybrid*.

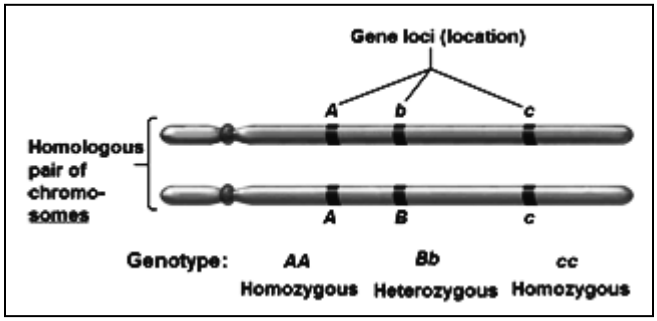
Genotype: The genetic constitution of an organism.
Phenotype: The external or outward appearance of an organism is called as phenotype.
Gene: Gene is the basic unit of heredity that is transferred from one generation to the next.

Allele (Allelomorph) : Alternative forms of a gene situated at the same locus in homologous chromosomes. More than two alternative forms of a gene are called multiple alleles.

Locus: The point of attachment of alleles on a chromosome.

Homozygous: An individual with two identical alleles at one or more loci is called as homozygous Eg. TT/tt.

Heterozygote: An individual with two different alleles for one or more genes is called as heterozygote Eg. Tt or RrYy.



Monohybrid cross: Hybridization between two individuals which differ for a single character. Eg. TT x tt.

Dihybrid cross: The progeny from a cross between two homozygous parents differing for two genes. Eg. RRYY x rryy.

Reciprocal cross: The two crosses in which the same two parents are involved, but the strain which serves as the male parent in one cross is used as the female parent in the other, and *vice-versa*.

Testcross: The cross of an F_1 hybrid with an individual having the recessive phenotype for the trait concerned. Eg. Tt x tt

F_1 or first filial generation: The progeny generation resulting from crossing two different parents is referred to as F_1 generation.

Dominant: The parental character expressed in heterozygous condition in the hybrid is called as dominant character.

Recessive: The parental character which is expressed in the homozygous condition in F_2 generation is called as recessive character.

MENDEL'S PRINCIPLES OF INHERITANCE

The consistent results from different monohybrid crosses led Mendel to propose postulates, which have been called as *Principles of inheritance*. Mendel's 'factors' were later recognized as genes. The postulates of Mendel were referred to as *Principles* of inheritance and not as *Laws* of Mendel as deviations were observed.

1. Principle of dominance

When two homozygous individuals with a contrasting character are crossed the character that appear in the F_1 hybrid is called as *dominant character* and the condition is termed as *dominance*. The parent is referred to as *dominant parent*. The character that does not appear in the F_1 but appear in the F_2 generation is called as *recessive character*, the condition is called as *recessive* and the parents as *recessive parents*.

2. Principle of Segregation or Purity of gametes

The principle of segregation states that allelic pairs in a heterozygote (F_1) do not contaminate each other but segregate or separate equally during gamete formation and are again paired by the random fusion of gametes during fertilization.

3. Principle of independent assortment

The principle of independent assortment states that if the inheritance of more than two or more pairs of genes is considered, the distribution of their alleles in the gametes and in the progeny of subsequent generation is independent of each other.

EXPLANATION TO PRINCIPLES OF MENDEL

1. THE PRINCIPLE OF DOMINANCE

Mendel observed that one of the parental form of a trait was always present in the F_1 while the other form was always absent in the hybrid, but reappeared unchanged in the F_2 generation. This observation of Mendel proved the *particulate nature of inheritance* and disproved blending type of inheritance. As alternate forms of a trait could retain their identity in the hybrid and reappear unchanged in the subsequent generations, Mendel concluded that the traits transmitted from parents to offspring are *discrete factors*.

The factor associated with the form expressed in F_1 was called as *dominant*. For example, the factor for yellow seed colour, tallness are dominant factors. The factor associated with the form which was not expressed, but hidden in F_1 but reappeared in the F_2 was *recessive*. For example, the green seed colour and dwarf stature are recessive factors. Mendel's factor is now recognized as the gene.

2. THE PRINCIPLE OF SEGREGATION

The principle of segregation states that allelic pairs in a heterozygote (F_1) do not contaminate each other but segregate or separate equally during gamete formation and are again paired by the random fusion of gametes during fertilization.

The principle of segregation or law of purity of gametes can be explained by considering the *monohybrid cross*. For example, In pea, round seed (WW) shape is dominant over wrinkled seed shape (ww). Crossing the round seeded parent with wrinkle seeded parent produced hybrid with round seeds.

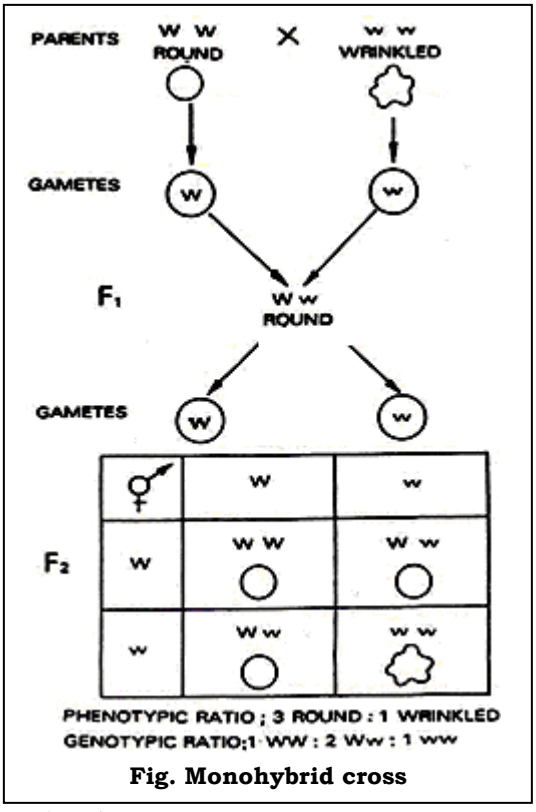


Fig. Monohybrid cross

Even though the hybrid was round seeded in the F_1, it produced both round and wrinkled seeded progeny in F_2 generation. Thus both the alleles for round shape (W) and wrinkled shape (w) remained together in the hybrid without contaminating each other and remained pure.

The separation of homologous chromosomes during anaphase I of meiosis may be regarded as the reason for segregation of the two alleles of a gene. This is because the alleles of a gene are located in an identical position in the two homologous chromosomes.

A random union of male and female gametes produces the typical *3:1 monohybrid ratio* as it is observed in the F_2 generation of crosses segregating for a single character or gene.

Back cross and Test Cross

Crossing of F1 with any one of the parent is known as backcross. Crossing the hybrid with the dominant parent will produce offspring with dominant characters. *A cross between F_1 hybrid and the homozygous recessive parent is known as test cross*. The test cross ratio is 1:1. The purpose of a test cross is to check the purity of parents. If the segregation of alleles of a single gene in the hybrid produces two types of gametes in equal frequencies (1:1) then the parents are pure.

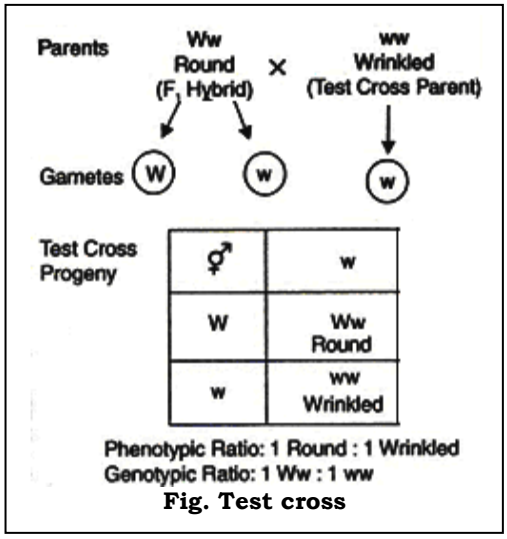


Fig. Test cross

F_1

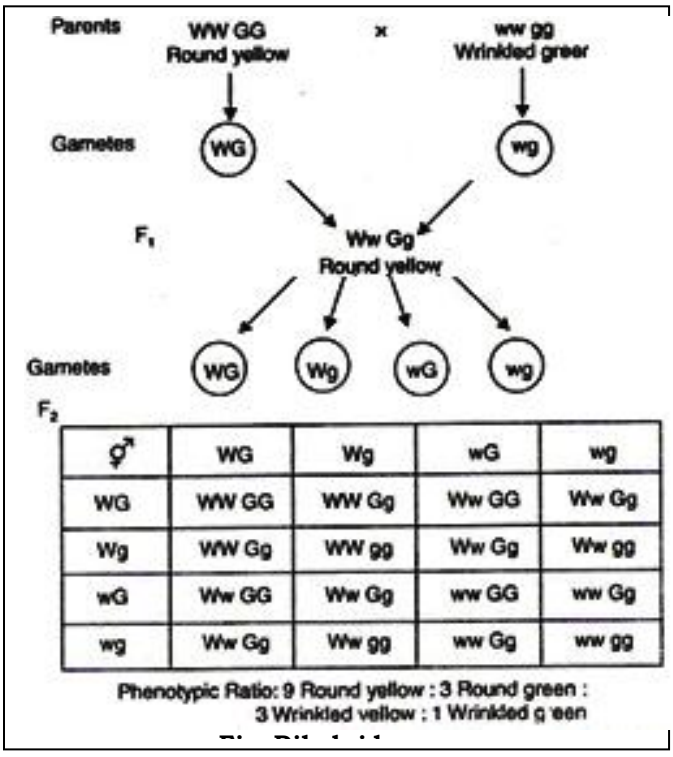
3. THE PRINCIPLE OF INDEPENDENT ASSORTMENT

The principle of independent assortment states that if the inheritance of more than two or more pairs of genes is considered, the distribution of their alleles in the gametes and in the progeny of subsequent generation is independent of each other.

The principle of independent assortment can be explained by considering *dihybrid cross*, in which the parents differed for two pairs of contrasting characters. For example Mendel crossed two varieties of garden pea namely, round yellow cotyledons (WWGG) with wrinkled green cotyledons (wwgg). The F_1 was round yellow type.

When Mendel self-fertilized the F_1 plants to produce F_2 generation, four different types of plants were observed. The male and female gametes can combine in 16 possible ways as shown in Punnet's square. namely, 9/16 round yellow, 3/16 wrinkled yellow, 3/16 round green and 1/16 wrinkled green. Thus the dihybrid phenotypic ratio is 9:3:3:1.

The principle of independent assortment explains that as each gene has two alleles, the allelic pair at each locus assort independent of the other during gamete formation i.e. (1)



R assort from Y while, r assort from y to produce RY and ry gametes (2) R separates from y and r separates from Y to produce Ry and rY gametes. These observations of Mendel are often referred to as the principle of independent assortment. When Mendel tried to confirm his results with hawk weed (*Hieraceum* sp.) he failed due to the presence of parthenogenesis in that species.

EXCEPTIONS TO MENDEL'S PRINCIPLES

1. Polyploidy and mutations are exceptions to the Mendel's principle of segregation.
2. Linkage is an exception to Mendel's principle of independent assortment.
3. Incomplete dominance is an exception to Mendel's principle of dominance.
4. Pleiotropism is an exception to the principle of unit characters.
5. Modification of F_2 ratios due to incomplete-dominance, co-dominance, lethal genes, gene interaction, epistatic factors are all exceptions to Mendel's principles.

10. GENE ACTION

Gene action refers to the way in which genes control the phenotypic expression of various characters in an organism. Alleles of a gene may interact with one another in a number of ways to produce variability in their phenotypic expression. The dominant and recessive relationship is fundamental and is constant with each pair of alleles.

TYPES OF GENE ACTION Gene action can be classified as follows:

1. Based on the dominance effect:
    a) Complete dominance
    b) Incomplete dominance
    c) Co-dominance
    d) Over dominance
    e) Pseudo-dominance
2. Based on lethal effects :
    a) Lethal genes
        (i) Dominant lethal
        (ii) Recessive lethal
        (iii)Conditional
        (iv) Balanced lethal
        (v) Gametic lethal
    b) Semi lethal gene
    c) Sub-vital gene
    d) Vital gene
    e) Super vital gene
    b) Recessive lethals
3. Based on epistatic gene action
    a) Epistatic factors
    b) Supplementary factors
    c) Duplicate factors
    d) Complementary factors
    e) Additive factors
    f) Inhibitory factors
4. Based on number of genes involved:
    a) Monogenic
    b) Digenic
    c) Oligogenic
    d) Polygenic
5. Based on pleiotropism / pleiotropic gene action

The different types of gene action are explained in detail as follows:

11. PRINCIPLES OF DOMINANCE

The phenomenon of a F_1 hybrid being identical to one of its parents for a particular character is termed as ***dominance***. The form of a character that appears in the F_1 hybrid is known as d***ominant character*** and the allele responsible is called as *dominant allele*. The form of trait which does not appear in F_1 but appears in F_2 is known as ***recessive character*** and the allele is called as *recessive allele*. In F_1, both the alleles of a gene are present together in heterozygous state. These two terms were first used by Mendel.

The phenomenon of dominance describes the relationship between two alleles of the same gene. The alleles of different genes may show different patterns of dominance relationships as indicated above.

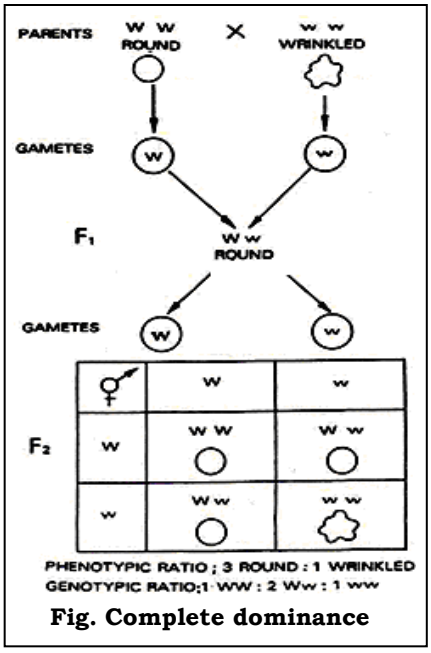


Fig. Complete dominance

a). Complete Dominance

The dominance described by Mendel is complete dominance. When the phenotype of the heterozygote (F_{1s}) is identical with the phenotype of by any one of the parent for the concerned dominant allele then the phenomenon is called as complete dominance.

Example: Inheritance of seed shape in peas. Round seed shape is produced by the dominant allele W, while wrinkled shape is determined by its recessive allele w. Seeds having the genotype Ww are round and indistinguishable from those having the genotype WW. As a result, character showing complete dominance yield the typical 3:1 monohybrid ratio in F_2.

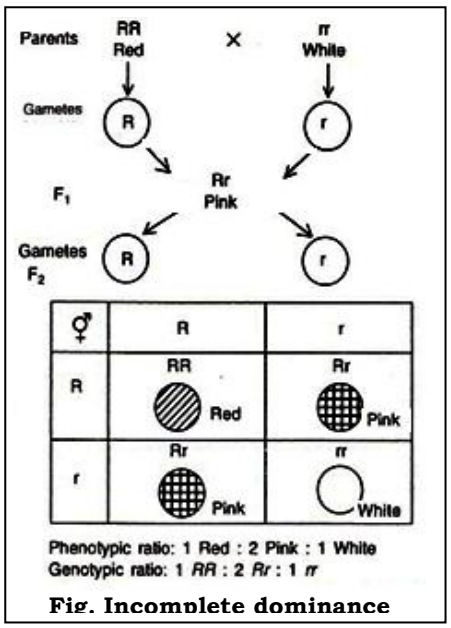


Fig. Incomplete dominance

b). Incomplete Dominance

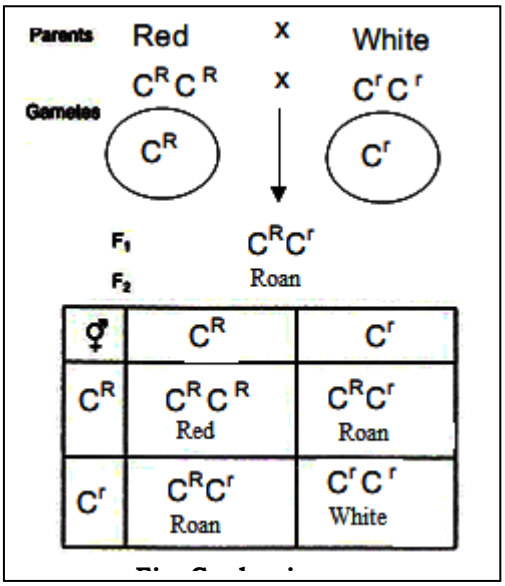
When the intensity of phenotype produced by the hybrid is intermediate to that of its parents then the phenomenon is termed as incomplete or partial dominance.

E.g. : In *Mirabilis jalapa*, a red-flowered variety when crossed with a white-flowered variety produced F_1 with pink flowers which in F_2 generation segregated in the ratio of 1 red : 2 pink : 1 white. As the intensity of the F_1 (pink) is lower than that of its parents (red, white) it is classified under incomplete or partial dominance.

c). Co-Dominance

When both the genes of the parents express

themselves equally in F_1 hybrids then the condition is referred to as co-dominance. It means that the F_1 will exhibit both the parental characters side by side.



E.g. Inheritance of coat colour in Cattle. The gene C^R stands for red coat colour, C^r stands for white colour. When red cattle was crossed with white cattle, the F_1 hybrids have roan coloured skin (Not intermediate). The roan colour is actually expressed by a mixture of red and white hairs, which develop side by side in the hybrid. In F_2 generation, red, roan and white appear in the ratio of 1:2:1.

d). Over Dominance

In case of some genes, the intensity of character governed by them is greater in heterozygotes than in the two homozygotes. This situation is known as over dominance. Over dominance is not the property of an allele and is the consequence of the heterozygous state of the concerned gene.

E.g. The white eye (W) gene of Drosophila exhibits over dominance for some of the eye pigments e.g. Sepiapteridine and himmelblaus.

Allele w produces white eye in the homozygous state (ww) while its completely dominant allele W give rise to the normal dull red eye colour both in homozygous and in heterozygous states (WW and Ww). Both the eye pigments are present in low concentrations in ww homozygotes while WW homozygous have relatively higher concentration of these pigments. However, flies heterozygous for this gene (Ww) have an appreciably higher concentrations of these two pigments than the two homozygotes (WW and ww).

The white eye gene of Drosophila is a sex-linked gene and as a result of this, it would not exhibit the typical ratio in F_2, but autosomal genes (genes not located in X-chromosome) showing over dominance would give rise to a 1:2:1 ratio in F_2 as long as the two homozygotes have distinctly different levels of expression of the character.

Transgressive segregation: The appearance of individuals in F_2 or subsequent generation which exceed the parental types with reference to one or more characters is known as transgressive segregation.

e). Pseudo dominance

Expression of the recessive allele in the hemizygous condition or due to loss of the dominant allele due to deletion or sex linkage is known as pseudo-dominance. Eg. Colour blindness in humans

12. LETHAL GENES

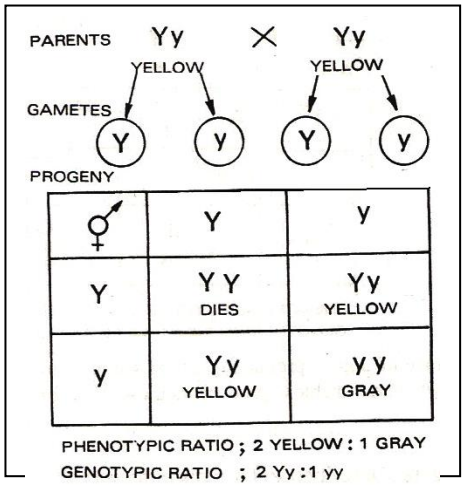
A. LETHAL GENES

One of the most important assumptions of inheritance of any trait is the equal survival of all gametes and zygotes produced as a result of segregation. Some genes affect the survival of those zygotes or individuals in which they are present in the appropriate genotype and are called as lethal genes. They may be grouped as: (i) lethal, (ii) semi lethal, (iii) sub vital,
(iv) vital and (v) super vital genes.

(i) A lethal gene causes death of all the individuals carrying this gene in the appropriate genotype before these individuals reach adulthood. The appropriate genotype for an allele would depend on its dominance relationship with its other allele(s). For an allele producing a recessive effect on survival, the appropriate genotype would be the homozygous state, while for an allele having a dominant effect on survival both homozygous and heterozygous states would be the appropriate genotype. Lethal genes may be grouped into the following five categories:
(a) Recessive lethals, (b) Dominant lethals, (c) Conditional lethals, (d) Balanced lethals and (e) Gametic lethals.

(a) Recessive Lethals

Most of the lethal genes are recessive lethals as their effect is expressed only when they are in the homozygous state. The survival of heterozygotes is unaffected.



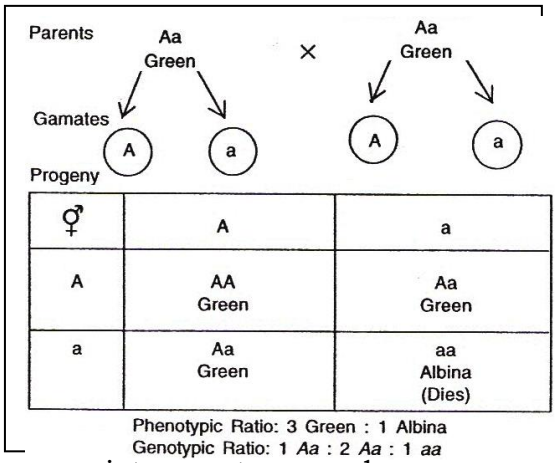
A recessive lethal affecting coat colour in mice was discovered by the French geneticist Cuenot in 1905. He found that yellow coat colour in mice is produced by a dominant gene Y, while its recessive allele y determines the normal grey coat colour. Further, all the mice with yellow coat colour were heterozygotes (Yy) and he was unable to find a mouse homozygous for the Y allele (YY).

Later in 1910, it was shown by Castle and Little that the dominant allele Y is a recessive lethal and that it causes death of homozygous YY embryos at an early stage of development. They showed that approximately 25 per cent of the embryos of yellow females mated to yellow males are inviable and fail to develop beyond a very early stage of embryonic development. The gene Y has now been redesignated as the dominant allele N in the agouti (A) series that affects fur colour in mice.

But many genes are recessive both in their phenotypic as well as lethal effects. In such cases, heterozygous individuals have normal phenotype as well as normal survival and they cannot be differentiated from normal homozygotes. An example of

such a gene are the genes producing albina seedlings in barley.

Albina character is governed by recessive alleles in barley. When anyone of these alleles is in homozygous state, the seedlings are near-white and totally devoid of chlorophyll. Albina seedlings survive only as long as the food stored in seeds is available since they are not able to carry out photosynthesis. The heterozygotes, however, are normal green and are identical with the normal homozygotes in their phenotype as well as survival. Segregation for such genes yields 3 green: 1 albina, if the seedlings are scored within a week from germination. However, if the plants are scored several weeks after germination or at maturity, there will be only green plants in the progeny.



♀	A	a
A	AA Green	Aa Green
a	Aa Green	aa Albina (Dies)

Phenotypic Ratio: 3 Green : 1 Albina
Genotypic Ratio: 1 *Aa* : 2 *Aa* : 1 *aa*

The lethal genes that reduce the survival of zygotes that carry them in the appropriate genotype are known as ***zygotic lethal.*** They constitute the vast majority of lethal genes.

The stage of development at which a lethal gene produces its lethal effect varies considerably from one gene to the other. Some genes cause the death of embryo very early in development, e.g., the Y gene in mice, while others allow survival and development close to the reproductive age, e.g., Epiloia in man.

(b) Dominant Lethals

When the lethal genes reduce viability of an organism in the heterozygous state also they are known as dominant lethals. An example of a dominant lethal is the epiloia gene in human beings. This gene causes abnormal skin growths, severe mental defects and multiple tumors in the heterozygotes so that they die before reaching adulthood. Dominant lethals, therefore, cannot be maintained in the population. They have to be produced in every generation through mutation.

(c) Conditional Lethals

Some lethal genes act only under specified condition which is necessary for their lethal effect and such lethal genes are termed as conditional lethals. Otherwise, they behave as the normal allele.

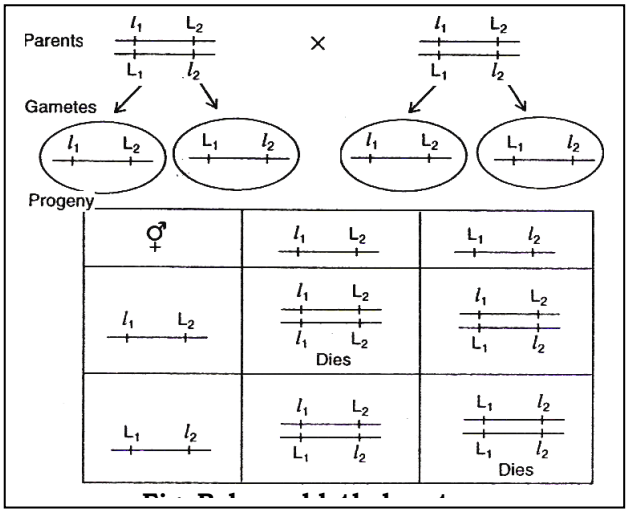
An example of a temperature sensitive lethal gene is the Kidney-eyed mutant of the wasp *Bracon hebetor.* This gene allows normal development and survival at lower temperatures, but is lethal at 30°C. Similarly, a chlorophyll mutant of barley permits normal chlorophyll development at a temperature of 19°C or above but produces albina seedlings at temperatures below 8°C. This conditional lethal in barley requires a lower temperature to exert its lethal effect.

(d) Balanced Lethals

In progeny from the matings between heterozygotes for a lethal gene, about 1/3 individuals are homozygous for the normal allele, while the remaining 2/3 are heterozygous for this gene. But in a balanced lethal system all the surviving progeny

are heterozygous for the lethal genes and the homozygotes for their normal alleles are not obtained. In such a system, two nonallelic recessive lethals are linked in the repulsion phase. In repulsion phase linkage, recessive allele of one gene and dominant allele of the other gene are present in the same chromosome.

In the example of a balanced lethal system shown, the recessive allele (l_1) of the first lethal gene and the normal allele (L_2) of the second lethal gene are present in one chromosome, while the homologous chromosome carries normal allele (L_1) of the first gene and recessive lethal allele (l_2) of the second gene.



Lethal genes arranged in this manner are known as balanced lethal and the arrangement itself is called as balanced lethal system. Heterozygotes for both the recessive lethal are viable. When crossed, 25% of the zygotes will be homozygous for the recessive lethal l_1 and will not survive. Another 75% will be homozygous for the other recessive lethal l_2 and will die. Only heterozygotes will survive.

Thus a balanced lethal system maintains the genes closely linked to the lethal genes in a perpetual heterozygous state.

(e) Gametic Lethals

Some genes lead to inviability of gametes, making them incapable of fertilization and such genes are termed as gametic lethals. Gametic lethals lead to a drastic departure from the typical ratios expected in segregating generations. This phenomenon is commonly known as ***segregation distortion or meiotic drive***.

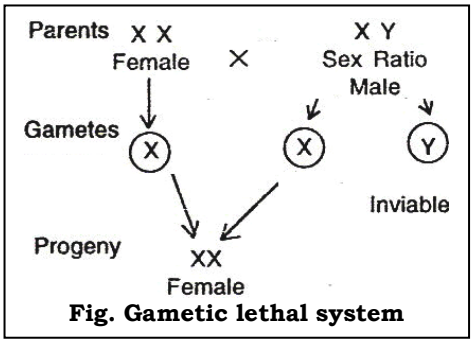


Fig. Gametic lethal system

B. SEMILETHAL GENES

Semilethal genes do not lead to death of all the individuals that carry them in appropriate genotype but *cause death of more than 90% of the individuals*. Example, xantha mutants of many plants are semilethal in the homozygous state.

C. SUBVITAL GENES

When the mutant genes reduce viability of the individuals and *kill less than 90% of the individuals* carrying them in appropriate genotype they are called as subvital genes. Most of the mutant genes are subvital in their effect. Example, miniature wings in Drosophila, Viridis mutants of barley etc.

D. VITAL GENES

Those genes, which *do not affect survival* of the individuals in which they are present are known as vital genes. The vital genes neither enhance nor reduce the viability of individuals carrying them in appropriate genotype. Wild type alleles of all the genes of an organism are regarded as vital genes. They serve as the reference point

in determining the effect of mutant alleles of these genes on survival.

E. SUPERVITAL GENES

Some mutant alleles *enhance the survival* of those individuals that carry them in appropriate genotype and such genes are known as supervital genes. Example, genes for disease resistance, genes conferring resistance/tolerance to the various abiotic stresses, e.g., salinity, alkalinity, high temperature, low temperature, drought etc., may be regarded as supervital genes as they enhance the fitness of plants in presence of the concerned stress.

13. EPISTASIS / GENE INTERACTION

The phenomenon of two or more non-allelic genes affecting the expression of each other in the development of a single character of an organism is known as gene interaction or epistasis. The gene which masks the expression of the other gene is referred to as epistatic gene. The gene which is being masked is known as hypostatic gene.

The various types of gene interaction include
1) Simple gene interaction or collaboratory gene action,
2) Recessive epistasis or supplementary gene action,
3) Dominant epistasis or masking gene action,
4) Dominant and recessive interaction,
5) Duplicate genes with cumulative effect,
6) Duplicate dominant genes and
7) Duplicate recessive genes.

SIMPLE GENE INTERACTION OR COLLABORATORY GENE INTERACTION (9:3:3:1)

In Mendelian digenic interaction two genes control two different characters, whereas in simple gene interaction two genes control a single character and interaction occurs without epistasis producing the typical dihybrid ratio of 9:3:3:1.

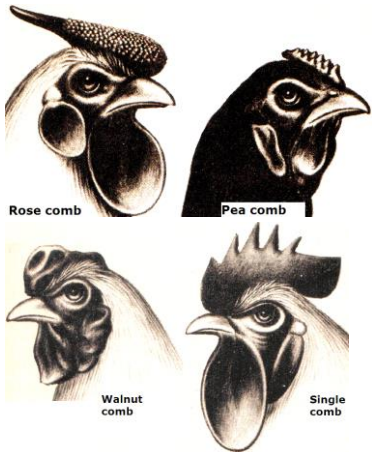
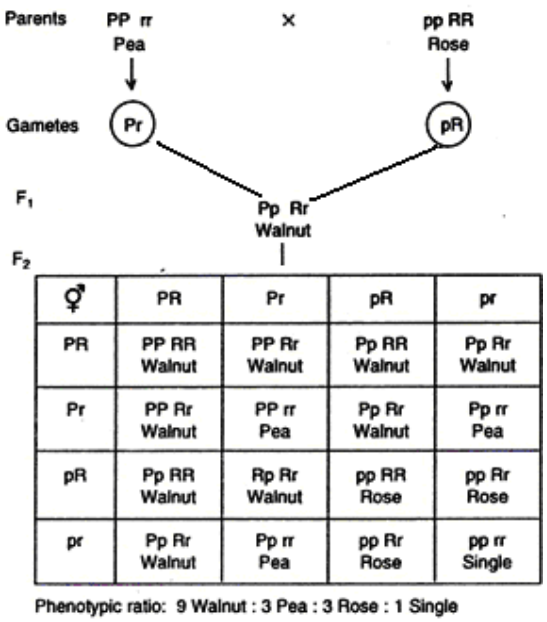


Fig. Comb shape in chicken



♀ / ♂	PR	Pr	pR	pr
PR	PP RR Walnut	PP Rr Walnut	Pp RR Walnut	Pp Rr Walnut
Pr	PP Rr Walnut	PP rr Pea	Pp Rr Walnut	Pp rr Pea
pR	Pp RR Walnut	Rp Rr Walnut	pp RR Rose	pp Rr Rose
pr	Pp Rr Walnut	Pp rr Pea	pp Rr Rose	pp rr Single

Phenotypic ratio: 9 Walnut : 3 Pea : 3 Rose : 1 Single

Fig. Simple / Collaboratory gene interaction

Two non-allelic genes influencing the same trait, produces a different form of character when alone but together they produce a distinct phenotype. At homozygous recessive state it gives rise to yet another phenotype.

For example, inheritance of comb shape in chickens follow simple interaction. The dominant allele of gene P produces pea comb while, R produces rose comb. But when both the dominant genes P and R are present together (PPRR) it produces walnut comb. The homozygous recessive condition (pprr) give rise to single comb.

When a pea comb (PP rr) and rose comb (pp RR) parents were crossed, the F_1 (PpRr) has walnut comb, as it has the dominant allele of both the genes P & R. Segregation in F_2 produces *nine walnut comb* types as they have at least one P and one R allele; *three pea comb* type, as they have one or two P alleles along with rr alleles; *three rose comb* types as they are homozygous for p along with one or two R alleles; single comb type at the homozygous recessive condition. Thus the interaction between two dominant genes controlling the development of a single trait generates 9:3:3:1 ratio in F_2 for a single character.

SUPPLEMENTARY GENE INTERACTION OR RECESSIVE EPISTASIS (9:3:4)

In recessive epistasis, the recessive genotype at one locus (eg., aa) suppresses the expression of the alleles at the 'B' locus, then the 'A' locus is said to exhibit recessive epistasis over 'B' locus. The hypostatic 'B' locus will express only when dominant allele is present at 'A' locus. Example, inheritance of aleurone or grain colour in maize is controlled by recessive epistasis.

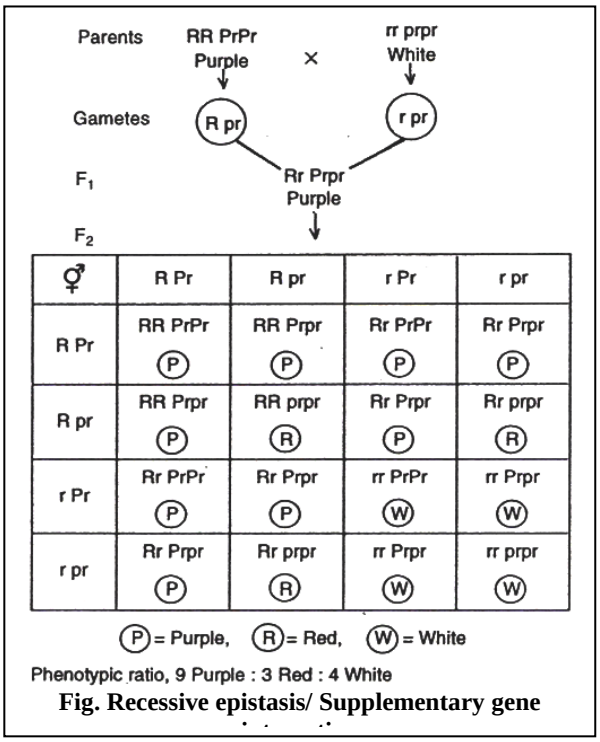


Fig. Recessive epistasis/ Supplementary gene

The development of aleurone is governed by two dominant genes R and Pr. The dominant allele *R* produces red colour grains while, the recessive allele *r* prevents the production of red colour. The gene Pr is unable to produce any colour but modifies the red colour produced by gene R to purple colour. The recessive allele *pr* has no effect on grain colour.

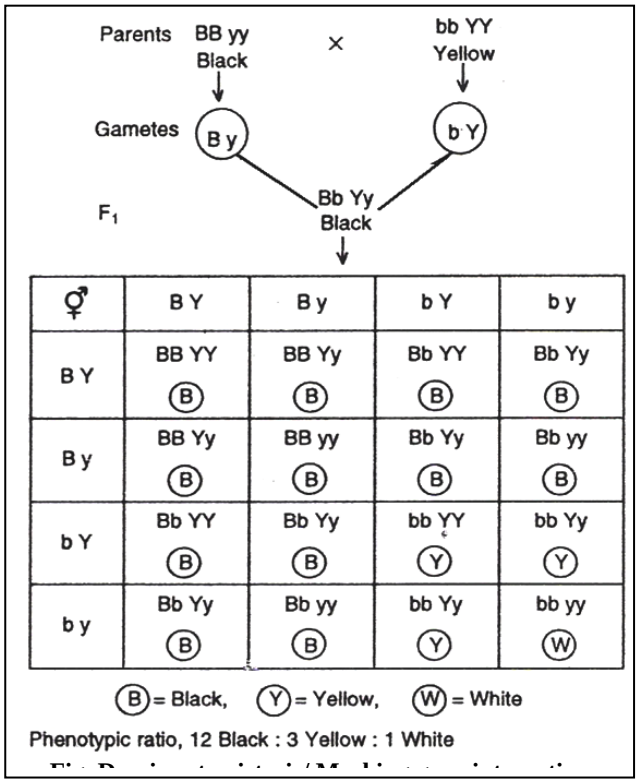
When purple aleurone coloured maize (RR PrPr) was crossed with white aleurone coloured maize (rr prpr), the F_1 hybrids had purple aleurone colour. The F_2 progenies segregated for 9 purple : 3 red and 4 white aleurone colored grains. A similar gene interaction occurs in the development of agouty (gray) coat colour in mice.

MASKING GENE INTERACTION OR DOMINANT – EPISTASIS (12:3:1)

In dominant epistasis, the two genes affecting the same character produce distinct phenotypes when they are alone. But when both the genes are present together, the expression of one gene masks the expression of the other. At homozygous recessive state, a different phenotype is produced.

Example is inheritance of seed colour in barley. When black seeded (BByy) variety was crossed with yellow seeded (bbYY) variety, the F_1 (BbYy) had black seed colour. In F_1, both the dominant alleles B and Y express themselves. But, the black colour masks the yellow colour produced by the Y gene. As the dominant gene is epistatic it is called as dominant epistasis. The F_2 showed 12 black : 3 yellow and 1 white seed colour.

In F_2, on an average 9 seeds will have one dominant allele of both the genes B and Y; 3 seeds will have B but will be homozygous for recessive allele y and will develop black seed coats since the presence of yellow colour in their seed coats cannot be detected. Another 3 seeds will have the allele b with Y and produce yellow seed coat. The remaining one combination (bbyy) is homozygous recessive for both the genes and will develop white seed coat color.



♂	B Y	B y	b Y	b y
B Y	BB YY (B)	BB Yy (B)	Bb YY (B)	Bb Yy (B)
B y	BB Yy (B)	BB yy (B)	Bb Yy (B)	Bb yy (B)
b Y	Bb YY (B)	Bb Yy (B)	bb YY (Y)	bb Yy (Y)
b y	Bb Yy (B)	Bb yy (B)	bb Yy (Y)	bb yy (W)

(B) = Black, (Y) = Yellow, (W) = White

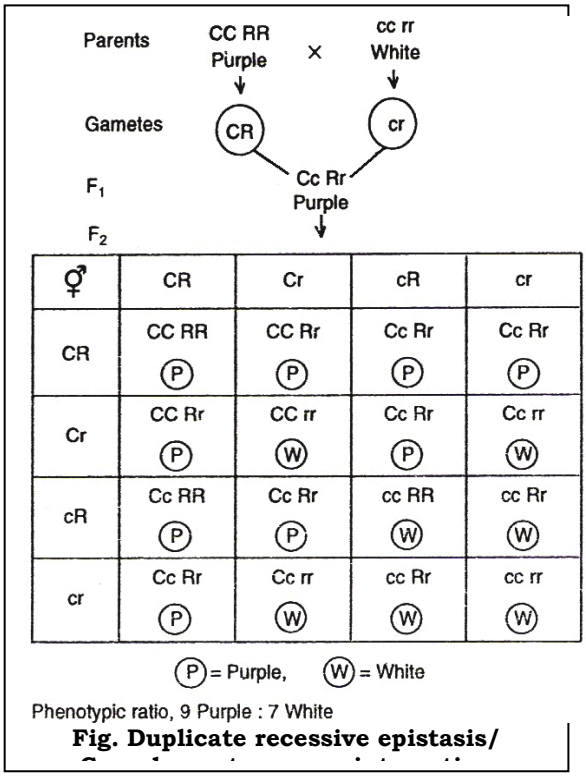
Phenotypic ratio, 12 Black : 3 Yellow : 1 White

COMPLEMENTARY GENE ACTION OR DUPLICATE RECESSIVE EPISTASIS (9:7)

In this interaction, both homozygous recessive genotypes viz., aaB-, and A-bb produce the same phenotype. The double recessive genotype also produce the above same phenotype. Both dominant alleles, when present together, complement each other and produce a different phenotype. Hence, this duplicate recessive epistasis is also called as complementary gene action.

Example is inheritance of flower colour in sweet pea. When a purple flowered variety of sweet pea (CCRR) is crossed with a white flowered variety (ccrr), the F_1 (CcRr) has purple flowers. The F_2 progenies segregated as 9 purple flowered and 7 white flowered plants.

The development of purple flowers



♂	CR	Cr	cR	cr
CR	CC RR (P)	CC Rr (P)	Cc Rr (P)	Cc Rr (P)
Cr	CC Rr (P)	CC rr (W)	Cc Rr (P)	Cc rr (W)
cR	Cc RR (P)	Cc Rr (P)	cc RR (W)	cc Rr (W)
cr	Cc Rr (P)	Cc rr (W)	cc Rr (W)	cc rr (W)

(P) = Purple, (W) = White

Phenotypic ratio, 9 Purple : 7 White

Fig. Duplicate recessive epistasis/

requires the presence of two dominant genes, C and R, When either C or R or both the genes are present in homozygous recessive condition, purple flower colour cannot be produced as a result of which white flowers are obtained. As both dominant genes complement each other and produces coloured flowers it is also called as complementary gene interaction.

POLYMERIC GENE ACTION OR DUPLICATE WITH CUMULATIVE EFFECT (9 : 6 : 1)

In polymeric gene action, the two genes controlling a character produce identical phenotypes when their dominant alleles are alone. But when dominant alleles of both the genes are present together, their phenotypic effect is enhanced as if the effects of the two genes were cumulative or additive

Example is inheritance of awn (needle like extension of lemma) character in barley is governed by duplicate genes with cumulative effect.

In barley, two dominant genes A and B affect the length of awns. Gene A or B alone (e.g., AAbb and aaBB), gives rise to awns of medium length. But when both the genes are present together, they produce long awns, indicating that the effects of A and B on awn length are added together. Individuals homozygous recessive for both these genes are awnless.

In barley, when long awned variety (AABB) was crossed with awnless variety (aabb), the F_1 progenies were long awned. The F_2 progenies segregated for 9 long awned; 6 medium awned and one awnless plants.

Thus polymeric gene interaction changes the typical 9 : 3 : 3 : 1 F_2 ratio into a 9 : 6 : 1 ratio. Some other examples of this interaction are also known, e.g., fruit shape in summer squash etc.

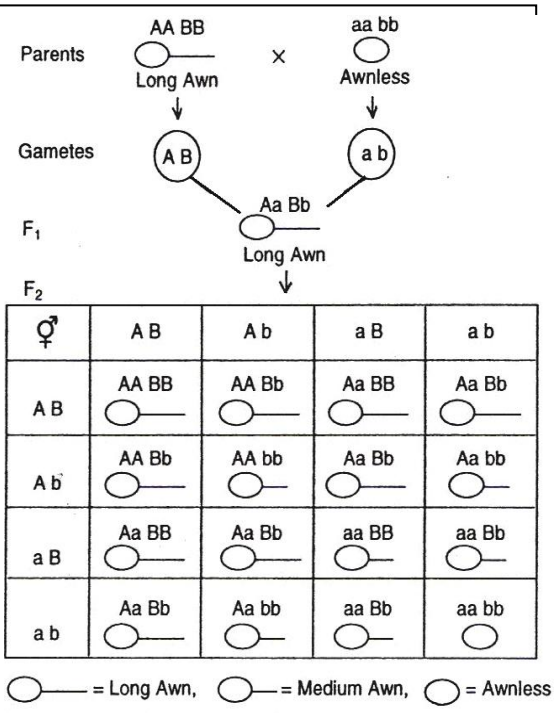


Fig . Duplicate with cumulative effect / Polymeric gene interaction

DUPLICATE GENE INTERACTION OR DUPLICATE DOMINANT EPISTASIS (15:1)

In case of duplicate gene interaction, a single dominant allele of any one of the two genes, governing the trait produce the dominant phenotyptic effect. The contrasting phenotypes is produced only when both the genes are in homozygous recessive state.

Example is inheritance of floating habit in rice. The non floating habit in rice is controlled by two dominant genes DW_1 and DW_2. Genes DW_1 and DW_2 alone or together produces the same phenotype, viz., non floating. The floating habit is obtained, only when both these genes are in the recessive state.

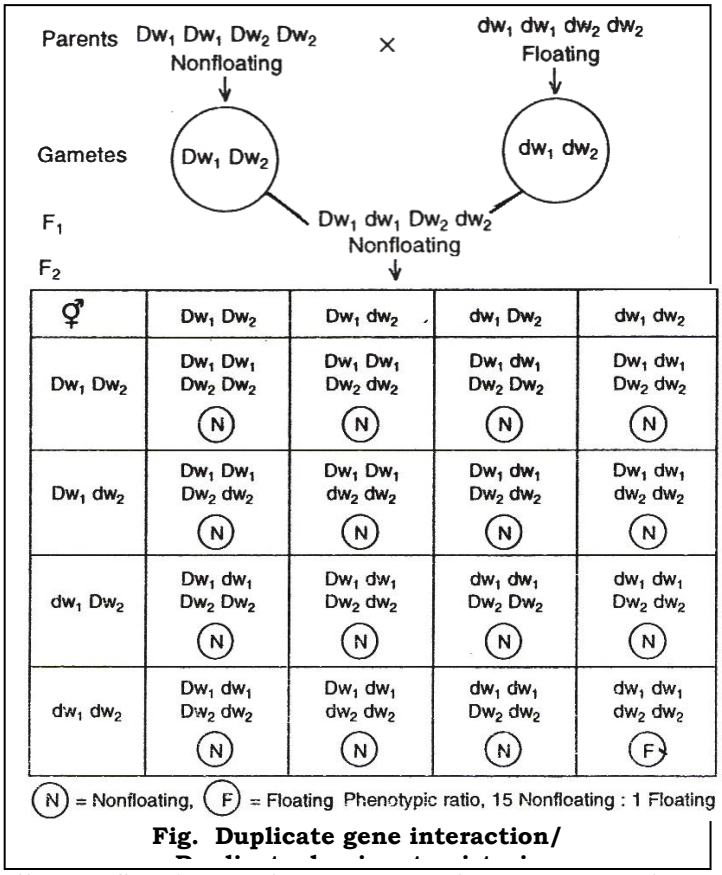


Fig. Duplicate gene interaction/

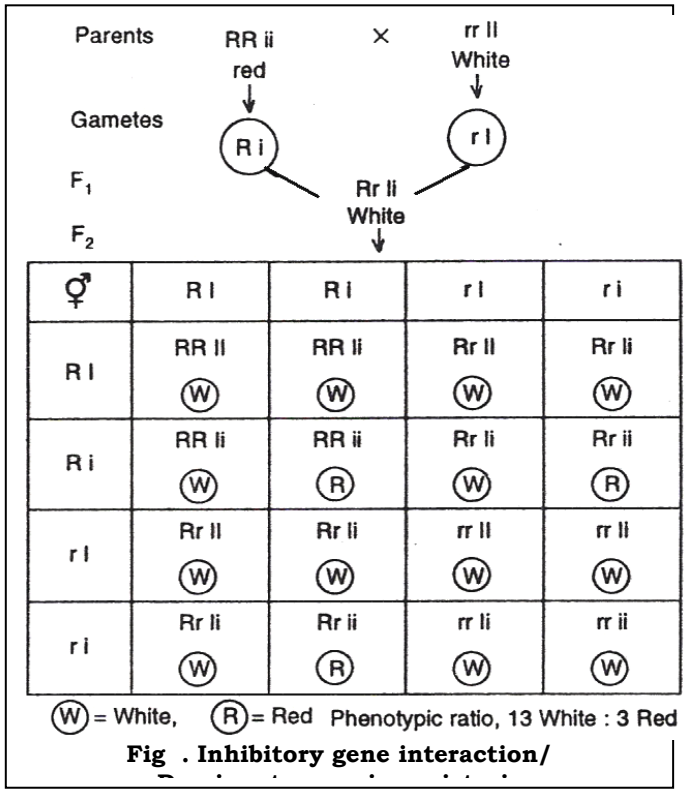
When non-floating rice variety ($DW_1DW_1DW_2DW_2$) was crossed with floating variety ($dw_1dw_1dw_2dw_2$), the F_1 progenies ($DW_1dw_1DW_2dw_2$) were all non-floating. The F_2 progenies segregated as 15 non-floating and one floating plant.

INHIBITORY GENE INTERACTION OR DOMINANT RECESSIVE EPISTASIS (13:3)

In inhibitory gene action, one dominant gene is capable of producing a character only if its expression is not inhibited by another dominant gene called inhibitory gene (I).

Inheritance of seed colour in maize is controlled by dominant and recessive epistasis. A dominant gene R produces red colour, while its recessive allele r produces no colour. Another dominant gene I does not produce any colour by itself but prevents the colour production by R. The recessive allele i, does not affect in any way, the colour production in maize aleurone.

Dominant recessive epistasis can be easily identified as more number of recessive phenotypes can be observed. When red seeded variety (RRii) was crossed with white seeded variety (rrII), the F_1 hybrids (RrIi) had white seed colour. The F_2 progenies segregated for 13 white seeded plants and 3 red seeded plants.



♂	R I	R i	r I	r i
R I	RR II (W)	RR Ii (W)	Rr II (W)	Rr Ii (W)
R i	RR Ii (W)	RR ii (R)	Rr Ii (W)	Rr ii (R)
r I	Rr II (W)	Rr Ii (W)	rr II (W)	rr Ii (W)
r i	Rr Ii (W)	Rr ii (R)	rr Ii (W)	rr ii (W)

(W) = White, (R) = Red Phenotypic ratio, 13 White : 3 Red

Fig . Inhibitory gene interaction/

MODIFYING GENES OR MODIFIERS

Modifying genes are a group of genes which enhance or reduce the phenotypic effect of a major gene.

Modifying genes have small but cumulative effect on the expression of major genes. As a result, modifying genes convert a qualitative character into a quantitative character and exhibit continuous variation. They can alter dominance relationship at a locus, and can suppress the mutant alleles of some genes.

PLEIOTROPISM

In general, one gene affects a single character. But some of the genes are known to affect or control more than one character. Such genes are called pleiotropic genes and the phenomenon is known as pleiotropism. *The manifold effect of a single gene i.e when a single gene controls more than unrelated characters it is called as pleiotropism.* The gene is called a *pleiotropic gene* and the condition is known as *pleiotropy*".

E.g., (1) In cotton, the Punjab hairy lintless gene, Iic produces seeds which are without lint. This gene also causes incomplete lacination of the leaf, reduction in the number and length of internodes and reduction in boll size and fertility.

(2) In plants a gene may produce a red pigment in several organs such as flowers, stem and leaves but it is not quite correct to say that the gene is pleirotropic because the gene has only one general effect, the production of pigment.

14. MULTIPLE ALLELES

ALLELES

Alternate forms of a gene is known as an allele. The point of attachment of an allele on the chromosome is known as locus. Alleles are of two types namely, dominant allele and recessive allele. They may be grouped as wild type (normal type) and mutant type alleles.

MULTIPLE ALLELES

Usually two alleles of a gene govern the contrasting form of a trait. For example, plant height has two alleles, T for tall and t for dwarf condition. In some cases, a trait may be governed by three or more number of alleles. *Many alleles of a single gene controlling different forms of a single character is known as multiple alleles*. Eg. Inheritance of coat colour in rabbit, inheritance of blood group in man and self incompatibility in plants.

1. Inheritance of Blood Group in Man

Karl Landsteiner (1900) classified blood group of human beings into four types based on the presence or absence of certain antigens. The ABO blood group system is believed to be controlled by a single gene, designated as I. The gene I has three alleles ; I^A, I^B and I°.

Allele I^A controls the production of antigen A, allele I^B determines antigen B, while allele i (I°) does not produce any active antigen. These alleles are ***codominant*** so that individuals having the genotype I^AI^B have both the antigens A and B on their RBC and hence have AB blood group.

Individuals with the genotype I^AI^A or I^Ai produce antigen A and are classified into the blood group A; those with the genotype I^BI^B or I^Bi produce antigen B and belong to the group B; persons with the genotype I^AI^B have both the antigen A and B and are placed into the group AB. Those individuals having the genotype ii ($I^\circ I^\circ$) produce neither A or B and are classified into the group 0.

Alleles	Blood group	Antigen found	Antibody present
I^A I^A or I^Ai	A	A	B
I^B I^B or I^Bi	B	B	A
I^A I^B	AB	AB	None
ii	O	None	AB

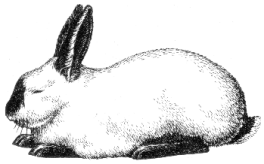
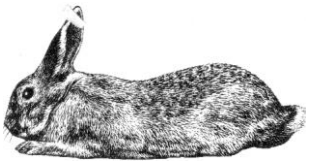
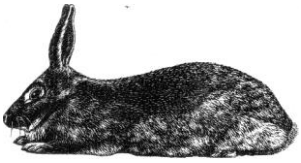
2. Inheritance of Fur Colour in Rabbits

The fur colour (colour of body hairs) in rabbits shows considerable variation. The fur colour is controlled by gene c, which has many alleles. The various types of fur colours produced are, agouti or full colour, chinchilla, Himalayan and albino.

The allele C for full colour is dominant over the alleles c^h (for himalayan); c^{ch} (for chinchilla) and c (for albino); allele c^{ch} is dominant over the alleles c^h and c, while allele c^h is dominant over allele c; thus allele c is recessive to the other three alleles. The allele c^h produces a temperature sensitive form of the enzyme tyrosinase, which is involved in the production of melanin (the skin and hair pigment) from the cyclic

amino acid tyrosine. This mutant form of the enzyme is active at low temperature but is inactive at higher temperatures.

Table Multiple alleles controlling fur colour in rabbits

Allele	Genotype	Phenotype	
c	cc	Albino (no pigment, white fur colour)	
c^h	c^hc^h,c^hc	Himalayan (white body/trunk; only tips of ears, feet, face and tail black)	
c^{ch}	$c^{ch}c^{ch}$, $c^{ch}c^h$, $c^{ch}c$	Chinchilla (fur has a mixture of coloured and white hairs over the whole body; intensity of colour less than that in full coloured)	
c^+ or C	c^+c^+, c^+c^{ch} c^+c^h, c^+c^h	Agouti or Full coloured (Entire body coloured black or grey).	
Dominance relationship = $c^+>c^{ch}>c^h>c$			

When Himalayan types were shaved off the hairs from a part of their body, and the shaven part was kept cool by placing ice on the shaven part or by keeping the animal in a cold place, it was observed that the new fur is coloured rather than white. If the rabbits were kept in a warm place, the new fur grown would be white. This explains the coloured fur at the extremities of the Himalayan type rabbits. As the extremities namely, ear, nose and tail tips becomes cooler than the rest of their body, the temperature sensitive tyrosinase is able to function normally and produce melanin in these areas.

3. Self Incompatibility (SIC) in plants

In a large number of plant species, self pollination may not lead to fertilization eventhough both the male and female gametes are functional. This condition is referred to as self incompatibility (SIC). It is of two types viz., Sporophytic self incompatibility and Gametophytic self incompatibility.

a. Sporophytic self incompatability

In the sporophytic system, the SIC reaction of pollen grain is determined by the genotype of the plant that produces it.

The sporophytic system exhibits dominance for the allele S. The dominance is determined by the pollen parent. Incompatible pollen may be inhibited on the stigma surface itself. For example, a plant with genotype S_1S_2 where S_1 is dominant to S_2, will produce pollen that will function like S_1. Furthermore, on selfing the S_1 pollen will be rejected by the S_1 style but received by an S_2 style. Hence, homozygotes of S alleles are possible. It occurs in species such as broccoli, radish, and kale.

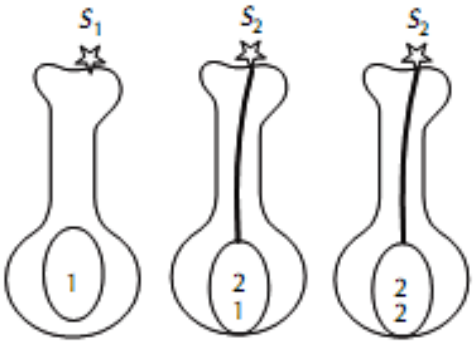


Fig. SPOROPHYTIC INCOMPATABILITY

b. Gametophytic self incompatability

In the gametophytic system, the incompatible reaction of the pollen is determined by the genotype of the individual pollen and not by the plant that produces it. This system is also called ***homomorphic SIC system*** because the flowering structures in both the female and male plants are similar.

The gametophytic SIC is controlled by a series of alleles at a single locus (S1, S2,... Sn) or alleles at two loci, in some species. The alleles of the incompatibility gene(s) act individually in the style. They exhibit no dominance. The incompatible pollen is inhibited in the style. The pistil is diploid and hence contains two incompatibility alleles (e.g., S_1S_3, S_3S_4). When both pollen and style have identical alleles then incompatible reaction occurs. Only heterozygotes for S alleles are produced in this system. Gametophytic incompatibility is more widespread than sporophytic incompatibility and occurs in species such as red clover, white clover, and yellow sweet clover.

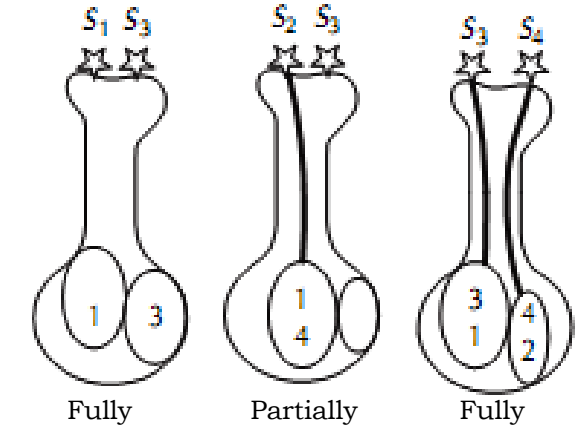


Fig. Gametophytic self incompatibility

15. QUALITATIVE AND QUANTITATIVE CHARACTERS

The character expressed by the phenotype of an individual can be classified into two types as 1) Qualitative character and 2) Quantitative character.

1. QUALITATIVE CHARACTERS

The characters that show discontinuous variation and which cannot be measured easily are known as qualitative characters. They are also known as Mendelian characters. Eg. Corolla colour (Red or white or pink), seed shape (Round or wrinkled) does not show continuous variation.

2. QUANTITATIVE CHARACTERS

The characters that show continuous variation and can be measured easily into discrete units are referred to as quantitative characters. These characters are also known as metric traits and the data obtained for such characters is known as quantitative data. The branch of science which deals with statistical analysis of this data is known as *quantitative genetics* or *biometrical genetics*. Eg : Yield, Plant height.

The major difference between the qualitative and quantitative characters are as follows.

Content	Quantitative character	Qualitative character
Example	Plant height, yield, seed weight etc.	Flower colour, seed shape etc.
Variation	Continuous variation	Discontinuous variation
No. of genes involved	Many genes (Polygenes)	One or few genes (mono or oligogenic system)
Effect of individual gene	Each gene has small effect	Large effect
Grouping into distinct classes	Not possible	Possible
Dominance effect	Absent	Present
Cumulative effect	Present	Absent
Environmental effect	High	Low
Stability of trait	Low	High
Statistical analysis	Based on mean, variance, standard deviation etc.	Based on frequencies and ratios.

BASED ON NUMBER OF GENES INVOLVED

When a character is controlled by one gene it is said to be *monogenic character*. When a trait is governed by two genes it is called as *digenic character.* When a trait is controlled by few genes it is called as *oligogenic character*. The trait controlled by many genes, each with small individual effect is referred to as *polygenic character*.

16. POLYGENIC INHERITANCE

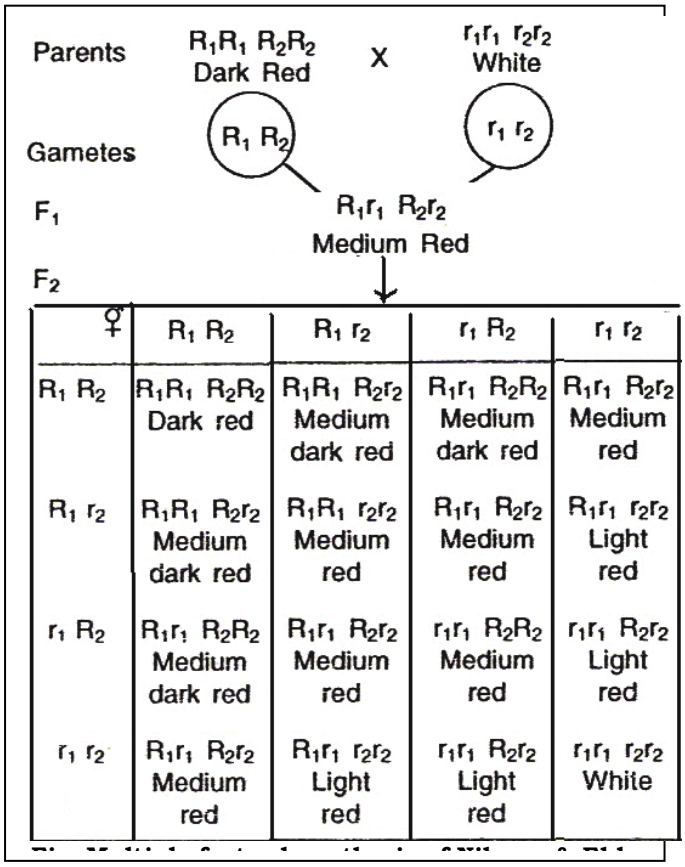
When the inheritance of a character is controlled by more than few non-allelic genes, it is referred to as *polygenic inheritance or multiple gene inheritance*. As the polygenic inheritance follow continuous variation (eg. Height, weight, and number.), it is also called as ***quantitative inheritance***. These variations are heritable. The genes controlling measurable traits are called as *polygenes* or *minor genes*. These genes exert a small effect on the expression of a character. The intensity of the character depends upon the total number of genes involved.

FEATURES OF POLYGENES

The main characteristics of polygenes are as follows: 1) The effect of each contributing gene are additive 2) Each and every allele has equal effect, 3) No dominance, epistasis and linkage is involved, 4) Effect of environment may be negligible.

MULTIPLE FACTOR HYPOTHESIS

Nilsson Ehle (1909) proposed the multiple factor hypothesis. He crossed a dark red kerneled variety ($R_1R_1R_2R_2$) of wheat with a white kerneled strain ($r_1r_1r_2r_2$). Since F_1 seeds have only two dominant alleles, they are intermediate and produced Medium red colour. The F_2 progenies segregated for 1/16 red: 6/16 medium red: 4/16 light red and 1/16 white kerneled plants. This experiment remains to be the first example for polygeneic inheritance. The inheritance of showed 1:4:6:4:1 ratio in F_2 generation.



♀	R_1 R_2	R_1 r_2	r_1 R_2	r_1 r_2
R_1 R_2	R_1R_1 R_2R_2 Dark red	R_1R_1 R_2r_2 Medium dark red	R_1r_1 R_2R_2 Medium dark red	R_1r_1 R_2r_2 Medium red
R_1 r_2	R_1R_1 R_2r_2 Medium dark red	R_1R_1 r_2r_2 Medium red	R_1r_1 R_2r_2 Medium red	R_1r_1 r_2r_2 Light red
r_1 R_2	R_1r_1 R_2R_2 Medium dark red	R_1r_1 R_2r_2 Medium red	r_1r_1 R_2R_2 Medium red	r_1r_1 R_2r_2 Light red
r_1 r_2	R_1r_1 R_2r_2 Medium red	R_1r_1 r_2r_2 Light red	r_1r_1 R_2r_2 Light red	r_1r_1 r_2r_2 White

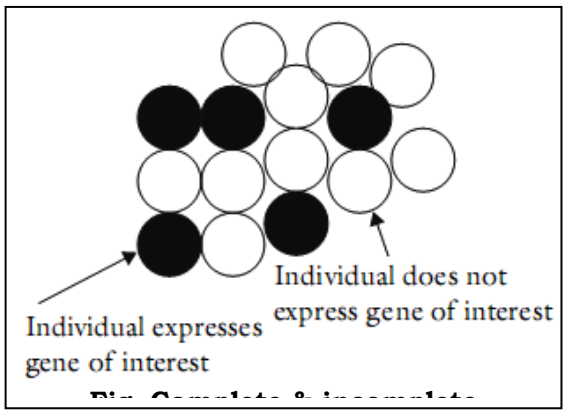
STUDIES ON *Nicotiana longiflora*

In 1916, East reported that inheritance of corolla length in *Nicotiania longiflora,* followed polygenic inheritance. He crossed two inbred lines with contrasting corolla lengths of 40 and 93 mm. The F_1 was intermediate with mean corolla length of 63 mm. In F_2, a much larger variation for corolla length than that present in the parents on the F_1 was observed, this variation was continuous as well.

PENETRANCE

The ability of gene to express itself in all the individuals which carry them is called *penetrance or* ***complete penetrance***. E.g., In peas, the red and white flower colour, tall and dwarf character, the seed colour and shape exhibit complete penetrance.

If a gene expresses only in a part the individual which carry it is called ***incomplete penetrance***. For example chlorophyll deficiency gene in lima bean has a penetrance of 10 per cent.



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EXPRESSIVITY

The degree of expression of a gene in an individual is referred to as expressivity. If the degree of expression of a gene is uniform in all the individuals carrying it, it is called as ***complete expressivity***. If the degree of expression of a gene in all the individual which carry it, is not uniform, it is called as ***incomplete expressivity***.

E.g. The gene producing chlorophyll deficiency in Lima bean *(Phaseolus lunatus)* exhibit variable expressivity in addition to incomplete penetrance. In some seedlings, the cotyledonary leaves lack chlorophyll; in some only the leaf tip lacks the chlorophyll, while in others the margins of the leaves have no chlorophyll.

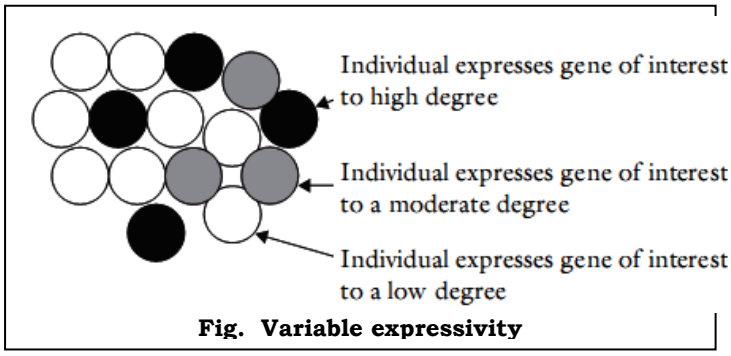
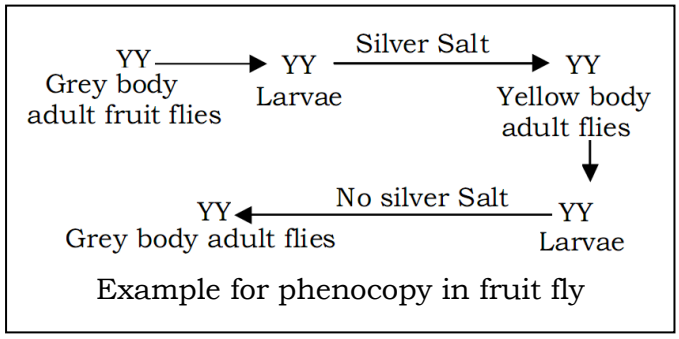


Fig. Variable expressivity

PHENOCOPY EFFECT

Different genotypes having same phenotype due to certain specific environmental change is referred to as *phenocopy effect*. The individuals possessing such altered phenotypes are called *phenocopies*. It represents an alteration in the phenotype due to a modification of the *expression* of the concerned gene and it does not represent a change in the gene itself. Hence, the change is not transmitted to the next generation.



Example for phenocopy in fruit fly

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17. LINKAGE

T. H. Morgan (1911) proposed the theory of linkage. Every species has a specific number of chromosomes. Each chromosome carries many genes. The genes located in the same chromosome very near to each other cannot assort independently and are inherited together.

The phenomenon of inheritance of genes together maintaining the parental combination is known as ***linkage*** or ***complete linkage***. When new recombinants, in addition to the parental characters are also present it is called as ***incomplete linkage.*** The genes are called ***linked genes*** and the characters controlled by them as ***linked characters***. The maximum number of genes linked as a group in an organism is equal to the number of chromosome pairs. Eg. Drosophila has 4 linkage groups while a human being has 23.

MAIN FEATURES OF LINKAGE

The main features of linkage and the linked genes are as follows:

(i) The linked genes are located in the same chromosome,

(ii) The linked genes are in linear order

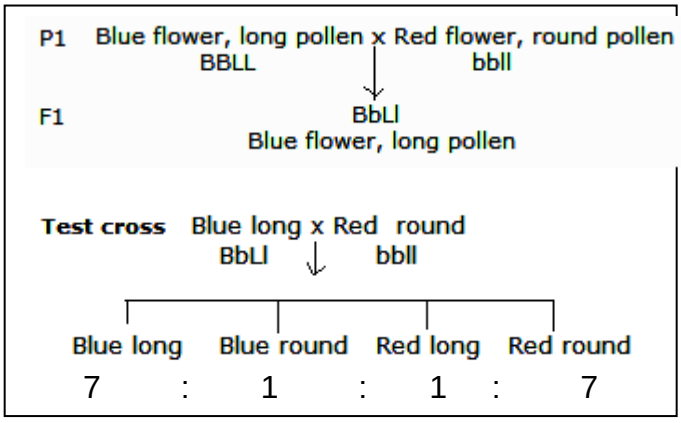
(iii) The linked genes retain their original parental combination during inheritance

(iv) The distance between the linked genes is inversely proportional to the length of the genes

(v) Linked genes do not show independent segregation hence the F_2 and test-cross ratios are altered.

COUPLING AND REPULSION PHASES OF LINKAGE

Bateson and Punnet in 1905 studied the inheritance of flower colour and pollen shape in sweetpea. They observed that the test cross result does not agree with the Mendelian ratio. The usual test cross ratio of 1:1:1:1 was modified to 7:1:1:7. The result of test cross indicate that the parental combinations are seven times more than the non-parental combinations.



Bateson and Punnet observed that, when the two dominant alleles on one chromosome and two recessive alleles on the other chromosome have an affinity for each other and tend to stay together during inheritance it is called as ***coupling phase linkage***.

On the other hand, when one dominant allele for first character and one recessive allele for the second character are located in the same chromosome and tend to stay together during inheritance, the condition is called as ***repulsion phase linkage***.

ARRANGEMENT OF LINKED GENES

1. **cis-arrangement** When both the dominant alleles are located in the same chromosome and their recessive alleles are located in the other member of the pair the condition is called as cis-arrangement (C Sh/c sh).

2. **trans-arrangement** When a dominant allele for first character and a recessive allele for second character are located in the same chromosome the condition is called as trans-arrangement (C sh/c Sh).

COUPLING PHASE LINKAGE IN MAIZE

In maize, a dominant gene 'C' produces coloured seeds, while its recessive allele, 'c' determines colourless seeds. Another dominant gene 'Sh' governs full seeds, whereas its recessive allele 'sh' gives rise to shrunken seeds.

When plants having coloured full seeds were crossed with the having colourless shrunken seeds, F_1 seeds were coloured full (Cc Shsh). Out of the 8,368 seeds obtained from the test cross, 4,032 (48.2%) were coloured full 4035 (48.3%) were colourless shrunken, 149 (1.7%) were coloured shrunken and 152 (1.8%) were colourless full. The expected ratio of 1:1:1:1 is modified. The phenotypic classes of the parental combinations are much higher than the expected. They are known as ***parental phenotypes*** (coloured full and colourless shrunken). The remaining two phenotypic classes, coloured shrunken and colourless full are far less frequent than expected (25%). These two character combinations are called ***recombinant phenotypes***, since they are

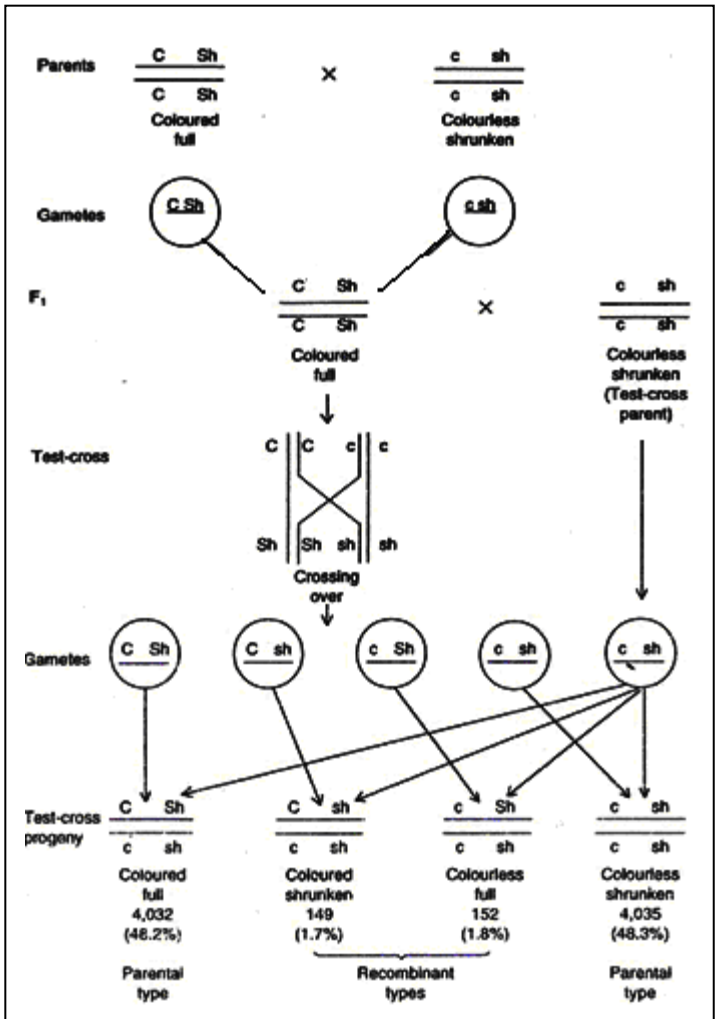


Fig. Coupling Phase Linkage in Maize

generated by reshuffling of the characters of the two parents of the F_1 used in the test cross.

In the above example, it appears as if the two dominant gene C and Sh have a strong affinity for each other so that the frequencies of coloured full and colourless shrunken phenotypes are greater than expected. This situation is referred to a ***coupling phase***, and is due to the presence of genes C and Sh in the same chromosome.

REPULSION PHASE LINKAGE IN MAIZE

Similarly, when plants having coloured shrunken seeds were crossed with those having colourless full seeds, the F_1 seeds were coloured full . But when F_1 plants were test-crossed (CcShsh) x (ccshsh), 47.9 % of the seeds were coloured shrunken, 49.1 % were colourless full, 1.4 % were coloured full and 1.5 % were colourless shrunken. In this case also, the parental types were more frequent while the recombinant types were less frequent than expected.

It appears as if the dominant genes C and Sh dislike each other so that the phenotypic classes coloured shrunken and colourless full are much more frequent than expected. This situation is referred to as repulsion phase. It is due to the presence of the dominant allele of one gene (C) with the recessive allele of the other gene (sh) in the same chromosome.

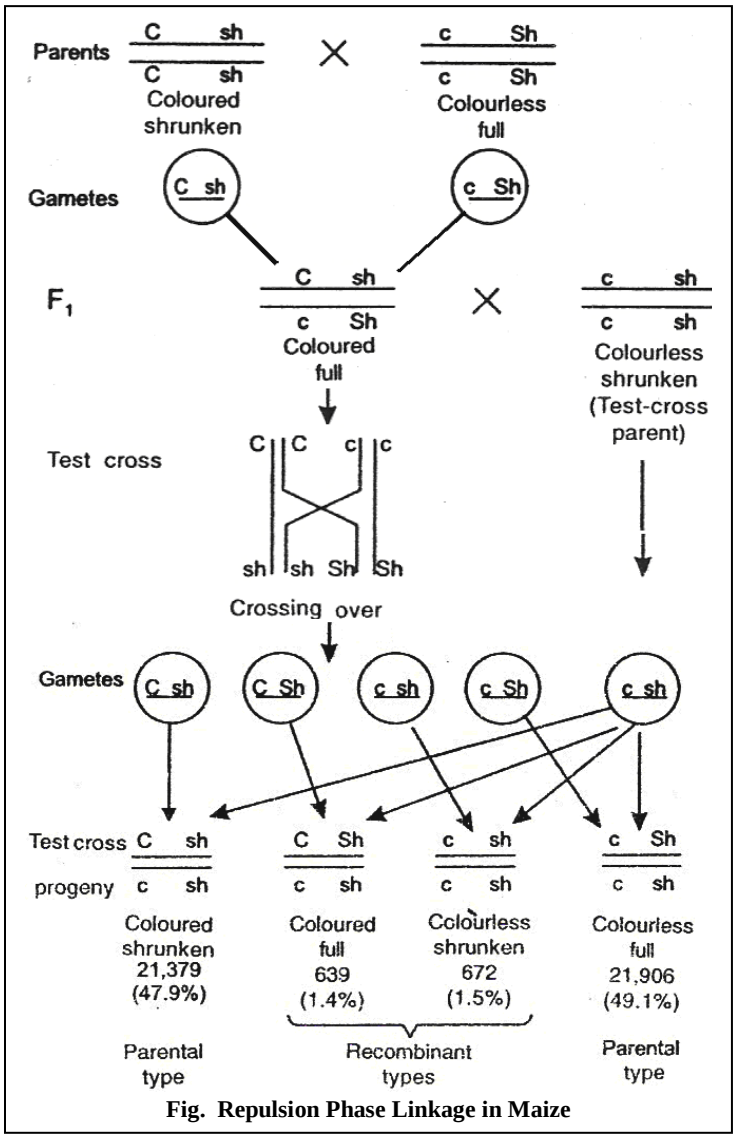


Fig. Repulsion Phase Linkage in Maize

INCOMPLETE LINKAGE

When only parental character combinations, are recovered in the test cross progeny, it is called complete linkage. Sometimes, their alleles recombine to produce recombinant gametes, e.g., Csh and cSh when such recombinant (due to crossing over) types are also recovered, in addition to the two parental types, in the test cross progeny, it is called incomplete linkage.

STRENGTH OF LINKAGE

Strength of gene linkage depends on distance between genes on chromatid. For example if two genes Aa and Bb are a distance of 10 units and other gene pair Cc and Dd are at a distance of 4 units. In this case, the linkage in Cc and Dd will be stronger than linkage in Aa and Bb. In other words the stronger linkage leads to lesser crossing over between the linked genes. Also, weaker linkage leads to possibility of more crossing over among them. Therefore it can be said that strength of linkage depends on possibilities of occurrence of crossing over.

18. CROSSING OVER

Morgan observed that, in addition to parental combinations, new recombinants called non-parental combinations also appear. He termed this phenomenon as crossing over. *The exchange of homologous segments between non-sister chromatids of homologous chromosomes is known as crossing over*. It is responsible for recombination between linked genes. Crossing over occurs during pachytene, stage of Prophase I of meiosis.

During pachytene, each chromosome of a bivalent (chromosome pair) has two chromatids so that each bivalent has four chromatids or strands (four stranded stage). Generally, one chromatid from each of the two homologous of a bivalent is involved in crossing over . The point of exchange of the homologous segment of the non-sister chromatids of homologous chromosome is known as ***chiasma***.

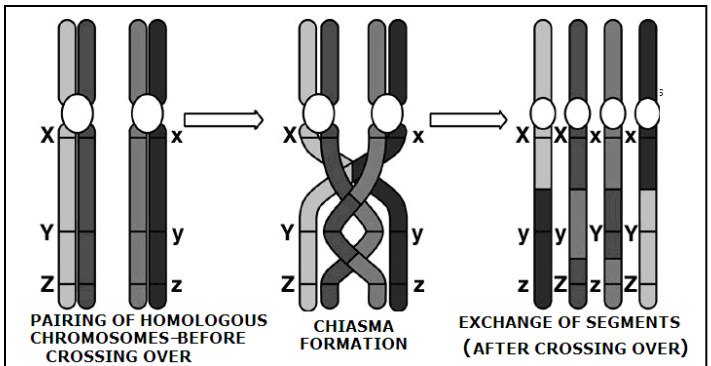


Fig. 14.3 Crossing Over Between Non-sister Chromatids

Obviously, each event of cross over produces two recombined chromatids, called ***crossover chromatids***, and two original chromatids referred to as ***non-crossover chromatids***. The frequency of crossing over between two genes can be estimated as the frequency of recombinant progeny from a test cross for these genes. It is expressed in percentage.

$$\text{Frequency of crossing over (\%)} = \frac{\text{Number of recombinant progenies from a test cross}}{\text{Total number of progenies}} \times 100$$

CROSSING OVER IN FOUR-STRAND STAGE (Experiments on *Neurospora*)

Earlier there were doubts regarding occurrence of crossing over during four-stranded stage. This question was answered through genetic studies in *Neurospora* (ascospores colour) and *Drosophila* (using attached X chromosome).

In *Neurospora*, each zygote undergoes meiosis to yield four haploid nuclei; these nuclei undergo mitosis to yield eight haploid (n) nuclei. They are arranged in a linear order; each nucleus gives rise to one ascospore (Fig).

The first meiotic division in the zygote Aa would produce two nuclei A and a; the four haploid nuclei obtained A, A, a and a ; and the eight nuclei generated after the mitotic division would lie in the order Al,Al,Al,Al, al,al,al,al. Thus the arrangement of ascospore in a mature ascus may be used to deduce the arrangements of the

concerned homologous chromosomes and their chromatids during the meiotic and mitotic division.

The dominant gene 'Al' of *Neurospora* produces black ascospores, while its recessive allele 'al' determines albino ascospores. The regular arrangement of ascospores makes it possible to predict the consequence of crossing over between this gene and its centromere on the spore arrangement.

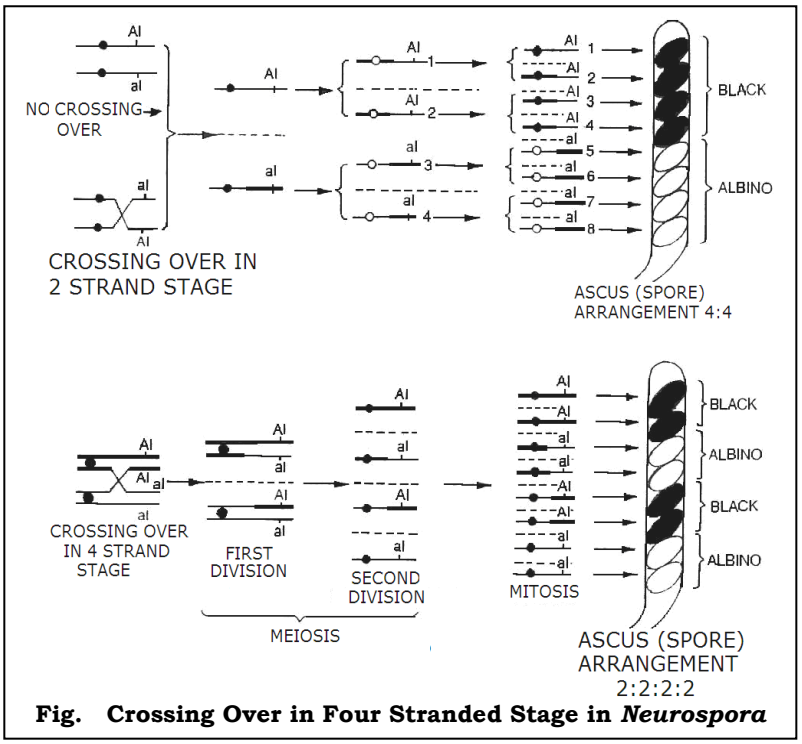


Fig. Crossing Over in Four Stranded Stage in *Neurospora*

If there is no crossing over between the gene and the centromere or if crossing over takes place between two-strand stage, the ascospores obtained from the heterozygous Alal, zygotes would show 4 black: 4 albino spore arrangement. However, if the crossing over occurred in four strand stage, the spores would show a 2 black : 2 albino : 2 black : 2 albino or 2 :4:2 arrangement.

The asci from Alal heterozygotes show 4 : 4, 2 : 4 : 2 as well as 2 : 2 : 2 : 2 spore arrangement. The 4 : 4 arrangement may be due to no crossing over or due to crossing over in two-strand stage. But 2 : 4 : 2 and 2 : 2 : 2 : 2 arrangement in some of the asci of Alal heterozygotes clearly show that crossing over takes place in four-strand stage.

CYTOLOGICAL PROOF OF CROSSING OVER

Curt Stern used female *Drosophila* with one 'X' chromosome shorter than the normal; this chromosome had the recessive gene *car* (carnation eye colour) and the dominant gene *B* (Bar eye shape). The other 'X' chromosome of this female was of normal length, but a segment of 'Y' chromosome was translocated into its short arm; this chromosome had the dominant gene *car*$^+$ (wild type allele of car, producing dull red eye colour) and the recessive gene *B*$^+$ (wild type allele of B, producing normal ovate eye shape). Stern, test crossed this female to a Car B$^+$ male. As expected, the following four types of flies were recovered in test-cross progeny; red normal (Car$^+$B$^+$), red bar (Car$^+$B); carnation normal (Car B$^+$); and carnation bar (Car B).

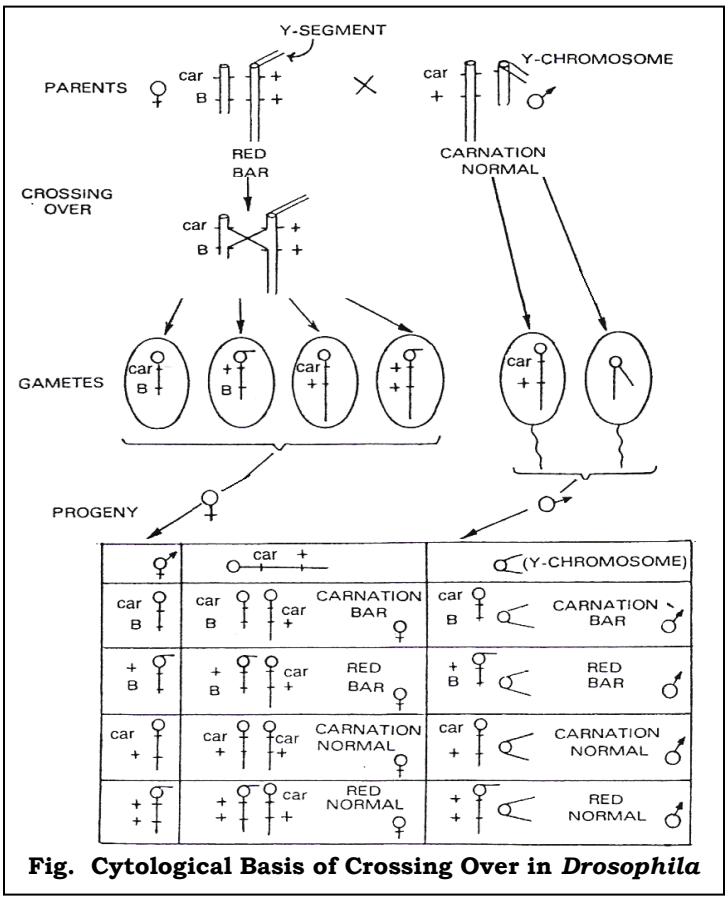


Fig. Cytological Basis of Crossing Over in *Drosophila*

Two of these four phenotypes, viz., red normal and carnation bar, are non-cross over types. Therefore the carnation bar individuals are expected to carry one short 'X', while the red normal over would have one long 'X' with a 'Y' segment. In contrast, the remaining two phenotypes, viz., red bar and carnation normal, are crossover or recombinant types.

If crossing over involves an exchange of homologous chromatid segments between homologous chromosomes, then one 'X' chromosome of these individuals would be the product of such an exchange .

Therefore carnation normal (Car B$^+$) flies are expected to have normal or long 'X' chromosome without the attached 'Y' segment, while red bar (Car$^+$B) individuals will have one short 'X' with the attached 'Y' segment. Stern concluded that (1) During meiosis, there is exchange of precisely homologous chromatid segments between homologous chromosome, (2) Crossing over is responsible between linked genes.

CROSSING OVER BETWEEN THREE LINKED GENES

A test cross for three linked genes eg., c, sh and wx in maize, yields eight types of gametes and phenotypes. Two of these types i.e., CWxSh and cwxsh are the most frequent and represent the parental or non-recombinant types, while two others i.e., CwxSh and cWxsh are the least frequent and are double cross overs. The remaining four types i.e., Cwxsh, cWxSh, cwxSh and CWxsh are produced by single cross overs between three linked genes, and the frequency is intermediate between the parental and double cross over types.

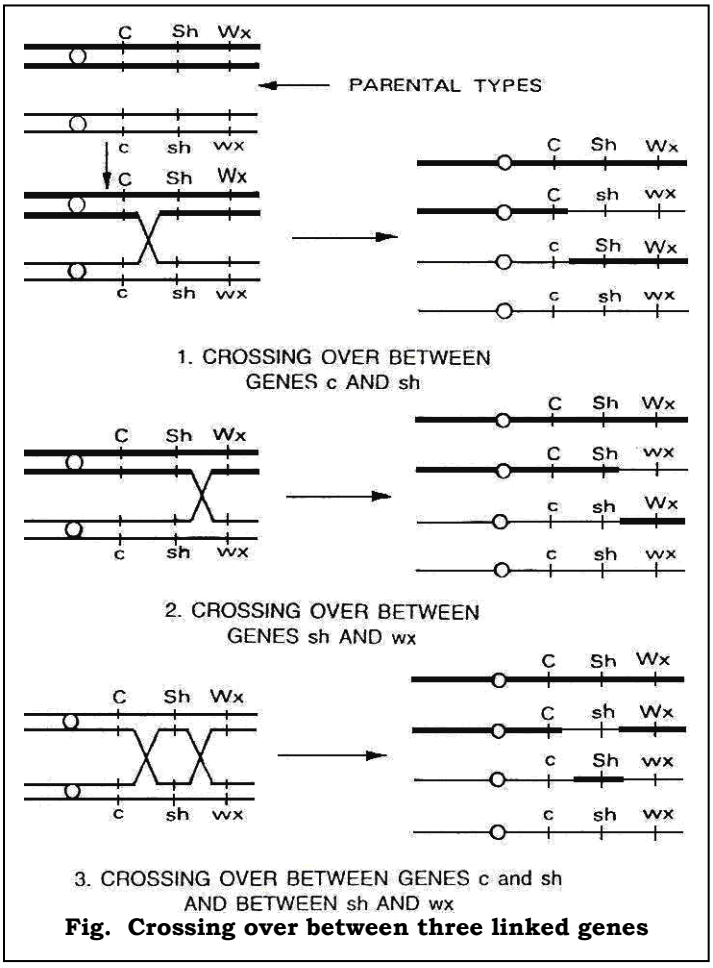


Fig. Crossing over between three linked genes

CHROMOSOMAL THEORY OF LINKAGE

This theory was proposed by Morgan and Castle. Genes located in the same chromosome are inherited together and are said to be linked. They are arranged in a linear fashion on the chromosome. The degrees of linkage is determined by the distance between genes, closely located genes show strong linkage while genes widely located show weak linkage.

19. GENETIC AND PHYSICAL MAP

Genetic map (or linkage map)refers to chromosome maps calculated by using recombination frequencies. Strurtvent constructed the first genetic map of Drosphila in 1913. Here, the distance between markers is determined by the frequency of recombination during meiosis, which is in turn determined by the relative distance between the loci. The genetic map provides the relative position of a gene according to the recombination frequency. It is expressed in centimorgans (cM).

CONSTRUCTION OF GENETIC MAP

The basic principles of constructing a genetic map is discussed in brief. Two individuals heterozygous for two or more genetic loci are crossed, and the frequency of recombination between loci is determined by examining the progeny. If the recombination frequency between two loci is 50%, then the loci are located on different chromosomes or are far apart on the same chromosome. If the recombination frequency is less than 50%, the loci are located close together on the same chromosome (they belong to the same linkage group).

For linked genes, the rate of recombination is proportional to the physical distance between the loci. Distances on genetic maps are measured in percent recombination (centimorgans, cM) or map units. Data from multiple two-point or three-point crosses can be integrated into linkage maps for whole chromosomes. It is necessary to know the number of genes inherited together or linked. As the number of genes in each linkage group is established, the relative distance between them has to be calculated.

The distance between two genes is calculated according to the percentage of crossing over as the crossover frequency is directly proportional to the distance between the two genes. If the percentage of crossing over between two linked genes is 1 %, it means that the map distance between them is one unit in map distance.

In a genetic map, the distance between two genes are measured in map units (m.u.). One map unit is equal to 1% recombination. Map units are also called as centimorgans (cM), in the honor of T. H. Morgan. Genetic distances measured with recombination rates are approximately additive.

TWO-POINT TEST CROSS

The percentage of crossing over between two linked genes is calculated by crossing dihybrid F_1 with a homozygous recessive parent. As this cross involves crossing over at two points it is also called as two-point test cross. For example, in coupling phase linkage in maize, the test cross produces parental type gametes (48.2% and 48.3%) and recombinant/ cross over gametes (1.7 % and 1.8%). Thus 3.5% of gametes were of crossover types and the distance between the loci C and Sh is estimated to be 3.5 centimorgans. For genes located farther away, three-point test cross is used.

THREE-POINT TEST CROSS

A three-point test cross involving three genes provides information regarding the relative distance between these genes and also shows the linear order in which these genes are located in the chromosome.

Example: Crossing over between three linked genes (ABC). First, the crossing over between A and B (Single Cross Over/ SCO I = 5 %) is calculated followed by calculating the distance between B and C (SCO II = 10%). Later, double crossing over (DCO) is calculated to find out the middle gene. If the distance from gene A to B is 5 m.u., the distance from gene B to C is 10 m.u., and the distance from gene A to C is 15 m.u., then gene B must be located between genes A and C. On the basis of the map distances given, a genetic map for genes A, B,and C, can be drawn.

INTERFERENCE AND COINCIDENCE

In higher organisms it has been observed that one chiasma formation interferes with another in the adjacent region of chromosome. This may be due to physical inability of the chromatids to bend back within a certain minimum distance. *The degree to which one crossover interferes with other crossovers in the same region is termed the interference.*

The percent of interference varies in different segments of the chromosome and is usually expressed in terms of coefficient of coincidence, which is the ratio of between the observed and expected double crossover.

The coefficient of coincidence is the ratio of observed double crossing over to expected double crossing over. If the coefficient of coefficient is 0.6, it means that actually only 60% of the double cross over, when compared to expected double cross over, is observed.

$$\textbf{Coefficient of coincidence} = \frac{\textbf{Number of observed double cross over}}{\textbf{Number of expected double cross over}}$$

In the double cross over, the occurrence of crossing over in one region of a chromosome interferes with its occurrence in the neighbouring segments. This is called ***interference***.

Coefficient of interference =1 – coefficient of coincidence

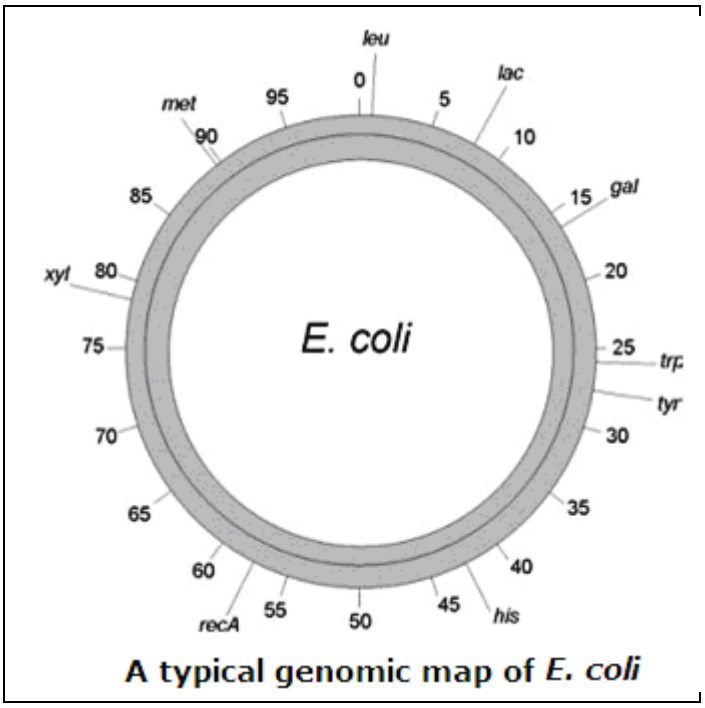
So, 1- 0.6 = 0.4. It means the interference is 40 % and that the 40 % of the expected DCO progeny will not be observed due to interference. When interference is complete, no double cross over progeny will be observed and the coefficient of coincidence is 0. Rarely, the observed number of double cross over may be more than the expected number, because the occurrence of a cross over increases the probability of occurrence of another cross over near it. In this case, the coefficient of coincidence will be greater than 1 and the interference will be negative.

PHYSICAL MAP

Physical map refers to chromosome maps based on direct analysis of DNA and the distance between the gene loci is expressed by numbers of base pairs (bp), kilobases or megabases. Physical maps generally have higher resolution and are more accurate than genetic maps.

Physical maps are created by *restriction mapping*, which determines the positions of restriction sites on DNA; *sequence-tagged site (STS) mapping*, which locates the positions of short unique sequences of DNA on a chromosome; fluorescent in situ hybridization (*FISH*), by which markers can be visually mapped to locations on chromosomes and DNA sequencing.

A genetic map is analogous to a highway map that shows the locations of major towns and cities whereas, a physical map is analogous to a neighborhood map that shows the location of every house along a street,



A typical genomic map of *E. coli*

20. SEX DETERMINATION

The various mechanisms of sex determination are:

1. Chromosomal mechanism sex determination
    a. XX-XY type
    b. ZW-ZZ type
    c. XX-XO type
2. Haplodiploidy mechanism
3. Genic balance system
4. Hormonal mechanism of sex
5. Sex determination due to environmental factors
6. Sex determination in human beings

1. CHROMOSOMAL MECHANISM OF SEX DETERMINATION

The chromosomal theory of sex determination of Wilson and Stevens (1902) states that genes are located on chromosomes. Chromosomes act as vehicles for segregation of genes during meiosis. In most of the organisms a pair or sex chromosomes are present and are termed as X and Y. Henking (1891) first identified X chromosome in an insect.

The X and Y chromosomes, in an organism, are called as sex chromosomes or allosomes and the remaining chromosomes are called as somatic chromosomes or autosomes.

a. XX-XY TYPE

In many species females heve two X chromosomes and males have one X and one Y chromosome. Eg. *Drosophila*, humans etc. The females produce only one type of eggs and are called as homogametic while, the males produce two types of sperms i.e. 50% X type and 50% Y type and are called heterogametic.

b. ZW-ZZ TYPE

In insects like moths, butterflies and fowls, the females are heterogametic and produce two types of eggs (X and Y) while males produce only one type of sperm (X). To avoid confusion it was labeled as Z and W. So females are ZW and males are ZZ

c. XX-XO TYPE

In Squash bug and grasshopper, the males have 21 chromosomes and females have 22 chromosomes. So, the two types of sperms are produced. 50% of sperms will have 11 chromosomes and 50% will have 10 chromosomes. Fertilization of an egg by a sperm with 11 chromosome produces a female and with a sperm having 10 chromosomes will produce a male bug.

2. HAPLODIPLOIDY MECHANISM

In some hymenopterans parthenogenesis occurs. In case of honeybees three types of individual are produced.

a. Queens (2n): They develop from fertilized eggs with 32 chromosomes and develop into fully functional females.

b. Workers (2n): They also develop from fertilized eggs with 32 chromosomes and develop into non-functional females.

c. Males or drones (n): They are developed by parthenogenesis from haploid eggs and become functional males with 16 chromosomes.

3. GENIC BALANCE SYSTEM

According to the genic balance theory, the ratio of X chromosome to autosomes determine the sex of an organism. Patterson discovered that in *Drosophila,* Y chromosome has no significant role in sex determination and that the ratio between X chromosome and autosomes determines the sex in *Drosphila* i.e.,

Sex index = Number of sex chromosomes/ Number of sets of autosomes

NO. OF X CHROMOSOMES & SETS OF AUTOSOMES	SEX INDEX	SEX
X & AA	0.5	Normal male
XXXX & AAAA	1.0	Normal female
XX & AA; XXX & AAAA	0.66	Intersex
XXX & AA	1.5	Super female
X & AAA	0.33	Super male

REASON FOR INTERSEX

Due to meiotic irregularities during gamete formation, both X chromosomes fail to separate and move towards the same pole instead of moving towards the opposite pole. This is called ***non-disjunction*** and it leads to formation of abnormal gametes and hence formation of intersex. Usually the intersexes are sterile.

GYNANDROMORPHS

In some *Drosophila*, a part of the body exhibits female characters and the other part exhibits male characters. They are called as gynandromorphs. The occurrence of gynandromorph is a evidence for genic balance theory of sex determination in *Drosophila*.

Male **Female**

Fig. Gynandromorph

4. HORMONAL DETERMINATION OF SEX

Many examples are available where the sex is modified due to hormones secreted from sex organs.

Eg 1. Sex reversal: Crew (1923) reported that in his farm, a hen which laid fertile eggs lost its ovary and stopped laying eggs. Later, it developed male comb, male

plumage and began crowing like a cock. It also fathered two chickens. It was explained that as the ovary is damaged and lost, the ovarian hormones stopped and the rudimentary gonads began to function as testis.

Eg 2. Freemartins: In cattles, when twin calves of opposite sex (one male and one female) are born, the male is normal while the female is sterile with many male traits. Such sterule females are called as freemartins. In foetal development, the twins share common blood circulation and the male hormones are produced slightly earlier than the female hormones. This male hormone when circulatated in the body of female twin results in sterile female with many male traits.

5. ENVIRONMENTAL FACTORS IN SEX ETERMINATION

In a number of organisms, sex is determined by environmental factors. For example, in *Bonellia viridis* a worm, the larvae are potentially hermaphroditic. But if a single worm is reared in isolation it develops into a female. But when the newly hatched worms are released in water containing mature females, young worms attached to the substratum develops into females, while those attach with the proboscis develops into males. In turtles, warm temperature produces females during certain times of the year, while cool temperature produces males. The reverse is true in case of alligators.

21. SEX DETERMINATION IN HUMANBEINGS

During the first month of embryo development, the gonads that develop are neither testes nor ovaries. Only at about six or seven weeks of development, the gonads become either testes or ovaries. The Y chromosome has a sex-determining region called SRY, which act as the testis-determining factor (TDF). Also, ovary-determining gene (*od* gene) was also identified. To determine sex, the first gene in the testis determining pathway must function before the *od* genes to allow XY individuals to develop as males. This leads to shut down of the other pathway.

DOSAGE COMPENSATION

In humans and mammals, the females and males have only one functional X chromosome per cell. This is accomplished by inactivating the remaining X chromosomes, a phenomenon called as dosage compensation. The X chromosome is inactivated at around 16th day of development and is seen as a dense mass of sex chromatin called as ***barr body***. The number of barr body is directly proportional to the extra X chromosomes. The XO females have no barr body while, XX females have one and XXXX females have three barr bodies.

SEX-LINKED INHERITANCE

The sex chromosomes (XX/XY) which determine the sex of an individual also carry genes for other body characters. The characters whose genes are located on the sex chromosomes and follow the sex during inheritance are called as sex-linked characters, the genes are called as ***sex-linked genes*** while the mode of inheritance is called as sex-linked inheritance. Eg. Inheritance of white eye in *Drosophila*, colour blindness, myopia, muscular dystrophy, juvenile glaucoma and haemophilia in humans. The genes in the Y chromosome are exclusively transmitted through the males and are called as *holandric traits*.

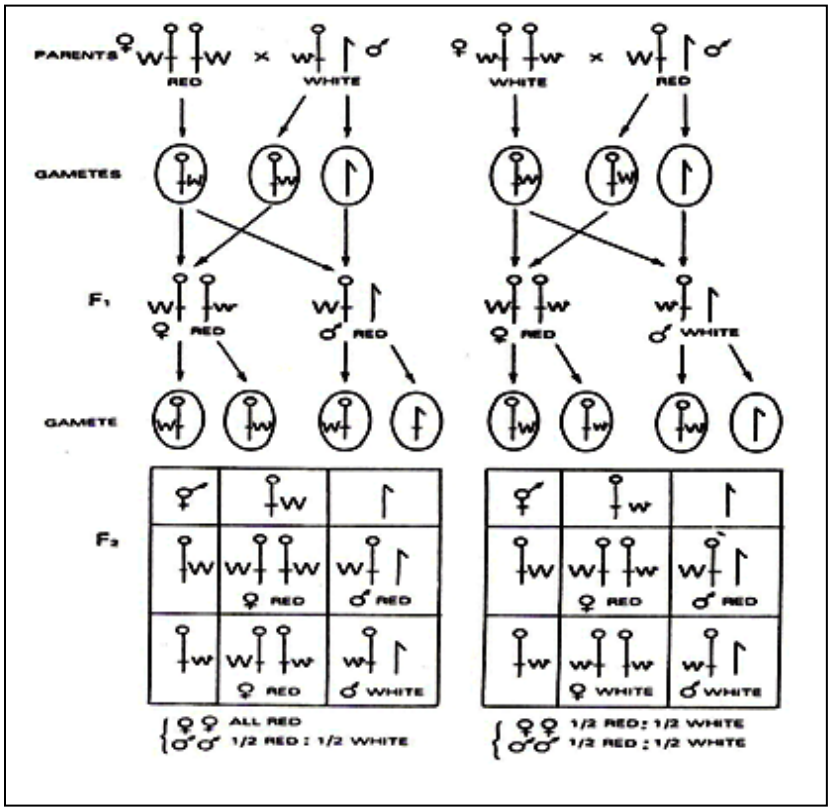
Eg. Inheritance of White Eye in *Drosophila*

Morgan reasoned that white eye gene was located in 'X' chromosome of *Drosophila* and the inheritance pattern of this gene is closely parallel to that of the X chromosome. It also assumed that the Y chromosome did not carry an allele for this gene.

Accordingly, female flies will have two copies of w gene, while male have only one copy. Thus the male *Drosophila* will be hemizygous (having only one copy of a gene) for w gene and therefore a single copy of the recessive allele w will express itself in the hemizygous males for a simple reason that Y chromosome does not contain an allele for this gene.

The genotypes of red-eyed females and white-eyed males may be written as X^WX^W and X^WY, respectively. The location of w gene in the X chromosome is indicated by writing it as superscript of X. A random union between male and female gametes will produce the following four zygotes viz., two red-eyed females, a red-eyed male and a white-eyed male.

In the reciprocal cross, a white-eyed female ($X^w X^w$) was mated with a red-eyed male (X^WY), the F_1, consisted of 50% red eyed and 50% white eyed flies. All the red-eyed flies were females and all males were white-eyed. When selfed, the F2 generation is composed of equal proportion of red and white eyed flies in both the sexes. In *Drosophila*, the sex-linked trait such as white eye colour follows a criss-cross inheritance. The male transmits the sex-linked traits to grandsons theough his daughters who are carriers.



SEX-LIMITED INHERITANCE

Sex-limited genes are present in the autosomes (body chromosomes) but their expression is determined by the presence or absence of one of the sex hormone. Hence, these genes express only in one sex. Examples include secondary sexual characters like beard development, genes for deep male voice, musculature, genes for feminine voice.

Eventhough both male and female have the genes for beard and mammary gland development, due to sex hormones the females lack beard while males lack developed breasts. Milk production in cattle is also sex-limited trait as both males and females have the gene but they express only in females.

Another example is Plumage or feathering pattern in birds. For instance, in domestic foul of leghorn breed, males have long, pointed, curved, fringed feathers on tail and neck, but feathers of female are shorter, rounded, straighter and without the fringe. Thus, males are cock feathered and females are hen feathered.

It has been shown that hen feathering result from a single gene 'H' and cock feathering from its allele, 'h' as follows.

Genotypes	Phenotypes	
	Males	Females
HH	Hen-feathering	Hen-feathering
Hh	Hen-feathering	Hen-feathering
hh	Cock feathering	Hen-feathering

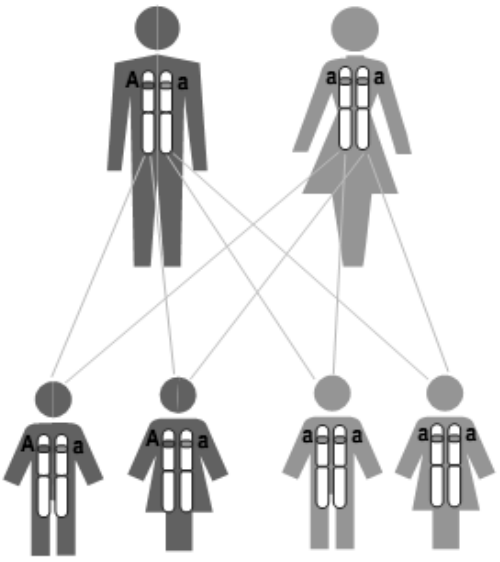
It has been found that the expression of gene H and h, depends upon the sex hormones, because where the ovaries or testes of chickens have been removed, all become cock feathered regardless of genotype. It shows that particular type of feathering depends upon specific combination of genotype and sex hormones and H gene produces hen feathering in the presence of either sex hormone; and cock feathering in the absence of any hormone. The "h' gene produces cock feathering if female hormone is absent and hen feathering if female hormone is present.

SEX-INFLUENCED INHERITANCE

Sex-influenced traits are determined by autosomal genes and they follow Mendel's principles of inheritance but are expressed differently in males and females.

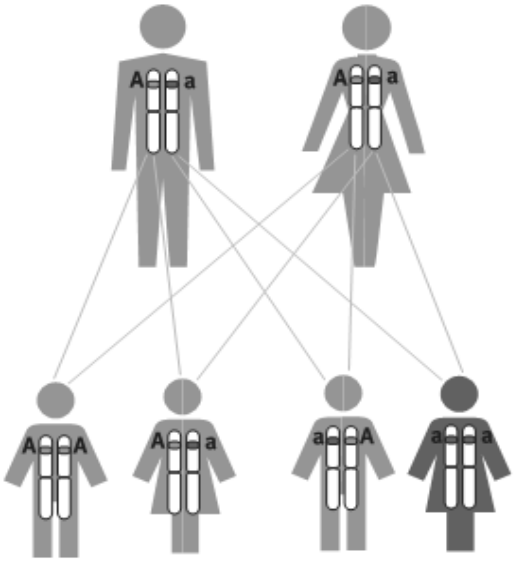
Eg. Inheritance of baldness in humans. The gene B for baldness is found to be dominant in males and recessive in females. In heterozygous conditions it expresses itself only in the presence of male androgenic hormone (in male sex).

Genotype	Phenotype	
	Man	Woman
BB	Bald	Bald
Bb	Bald	Non-Bald
bb	Non-bald	Non-bald



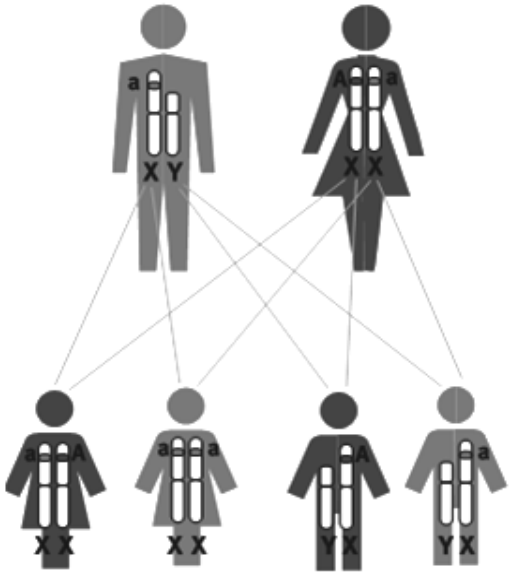
AUTOSOMAL DOMINANT

1. Individuals carrying one mutated copy of a gene in each cell will be affected by the disease
2. Each affected person usually has one affected parent
3. Tends to occur in every generation of an affected family.



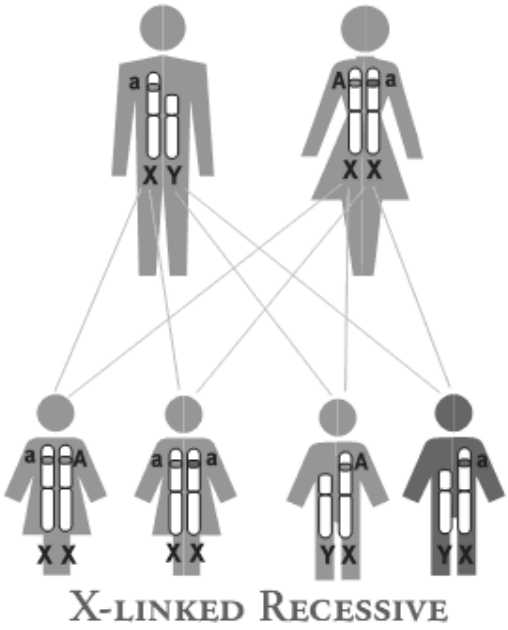
AUTOSOMAL RECESSIVE

1. Affected individuals must carry two mutated copies of a gene.
2. Parents of affected individual are usually unaffected and each carry a single copy of the mutated gene, known as carriers.
3. Not typically seen in every generation



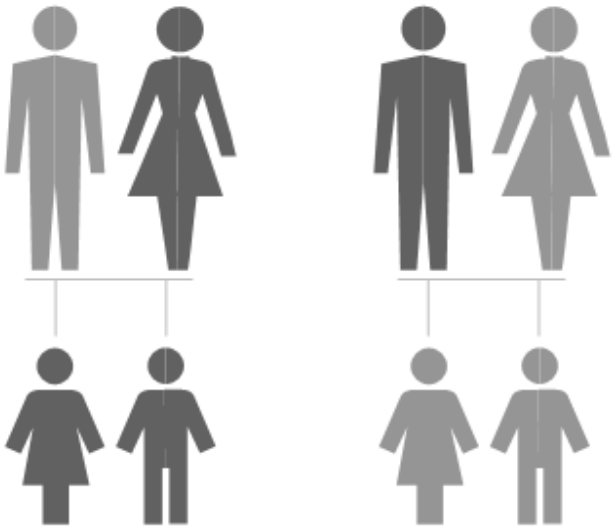
X-linked Dominant

1. Females are more frequently affected than males
2. Fathers cannot pass X-linked traits to their sons.



X-linked Recessive

1.Males are more frequently affected than females.
2.Both parents of an affected daughter must be carriers.
3. Only mother must be carrier of affected son.



Mitochondrial

1. Only females can pass on mitochondrial condition to their children (maternal inheritance).
2. Both males and females can be affected.
3. Can appear in every generation of a family

22. MUTATION

Though DNA is a highly stable molecule, changes occurs in DNA structure and during replication. *Mutation is defined as the sudden heritable phenotypic change in an organism*. The individuals showing these changes are known as *mutants*. The allele producing the changed phenotype is called *mutant allele*.

Even though mutation is source of new variation, most of the mutations are harmful. Hugo de Vries in 1900 coined the term mutation. Seth Wright in 1791 observed a short-legged breed of sheep which cannot jump over the fence. This breed was called as Ancon breed. Morgan in 1910 reported a white-eyed mutant in *Drosophila.* More the 500 mutations are observed in fruit flies so far. H.J. Muller (1927) won Nobel prize for his work in *Drosophila.*

FEATURES OF MUTATION

1. Mutant alleles are generally recessive.
2. Mutations are random.
3. Most mutations have harmful effect. The frequency of beneficial mutation is about 0.1 % .
4. Mutations are recurrent.
5. Mutations occur at very low frequencies in nature.

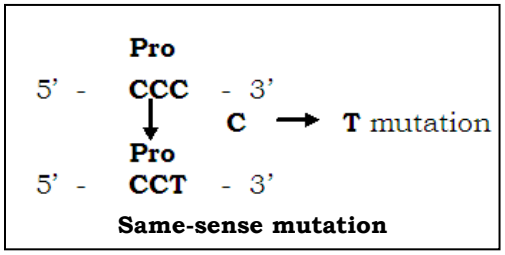
Mutations may occur at very low frequency and such mutations are called spontaneous mutations. The rate of spontaneous mutations vary between 10^{-7} and 10^{-4}. Some genes show exceptionally high rates of spontaneous mutations: they are known as *mutable genes*. Some genes increase the spontaneous mutation rates of other genes and such genes are called *mutator genes*. Some genes suppress the mutation of other genes of the genome and are termed as *antimutator genes*. Some sites within the genome have very high rate of mutation and are called as *hot spots*.

CLASSIFICATION OF MUTATION

I. BASED ON SIZE

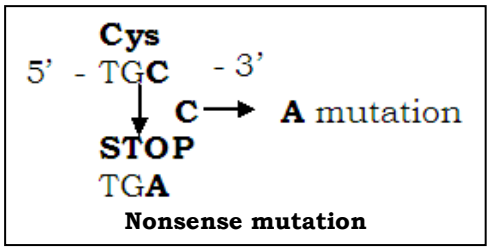
(A) Point Mutation A mutation which arise due to a change in the base sequence of a gene is called as *gene mutation or point mutation*. It usually involves a single nucleotide or nucleotide pair.

1. Same sense/ Silent mutation—change in a codon (usually at the third position) that fails to change the amino acid and hence no change in the protein. They contribute to variability in the DNA sequence of individuals of a species.

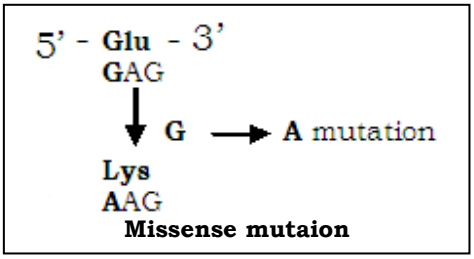


Same-sense mutation

2. Nonsense mutation— Nonsense mutation changes a codon for an aminoacid into a termination codon, resulting in a shortening of the protein product due to a chain-termination signal. It often produces a mutant phenotype



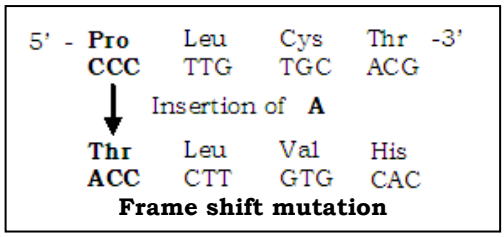
Nonsense mutation



Missense mutaion

3. Missense mutation— Missense mutation alters a single base and changes the amino acid sequence in the polypeptide chain. They have serious effect on the protein produced and leads to mutant phenotypes.

4. Frameshift mutation— It shifts the reading frame by insertion or deletion of a base. As the number of bases inserted or deleted is not a multiple of three the reading frame will be altered, creating numerous missense or nonsense codons through the remainder of the cistron.



Frame shift mutation

(B) Gross Mutation Changes involving more than one nucleotide pair, may involve the entire gene, the entire chromosome, or sets of chromosomes (polyploidy).

II. BASED ON CELL TYPE

(1) Somatic mutation: Occurs in non-reproductive cells of the body, often producing a mutant phenotype in only a sector of the organism (mosaic or chimera).

(2) Gametic mutation: Occurs in the sex cell, producing a heritable change.

III. BASED ON QUALITY

(A) Structural Mutation: Changes in the nucleotide content of the gene.

1. Substitution mutation – Substitution of one nucleotide for another.

a. *Transition mutation* substitute one purine for another or one pyrimidine for another.

b. *Transversion mutation* substitute a purine for a pyrimidine or vice versa.

2. Deletion mutation: It involves the loss of a portion of the DNA sequence. The amount lost varies greatly. Deletion mutation can be as small as a single base or much larger in some cases corresponding to the entire gene sequence.

3. Insertion mutation: Insertion or addition of extra bases, usually from another part of a chromosome causes insertion mutation. The amount inserted may be one or two bases or may be much larger.

(B) Rearrangement Mutation: Changing the location of a gene within the genome often leads to "position effects".

1. Within a gene – two mutations within the same functional gene can produce different effects, depending on whether they occur in the cis or trans position.

2. Number of genes per chromosome – different phenotype efforts can be produced if the number of gene replicas are nonequivalent on the homologues chromosomes.

3. Moving the gene locus may create new phenotypes, especially when the gene is relocated near heterochromatin.

a. Translocation – movement to a non-homologous chromosome.

b. Inversion – a portion of the DNA sequence is excised then reinserted at the same position but in the opposite orientation.

IV. BASED ON ORIGIN

(A) Spontaneous mutation: Occurs naturally and is of unknown origin. It is also known as background mutation. It occurs at a frequency of 10^{-6}

(B) Genetic control: The mutability of some genes is known to be influenced by other 'mutator genes'.

1. Specific mutator – It affects one locus.

2. Nonspecific mutator – It simultaneously affects many loci.

(C) Induced mutation: Mutations produced due to the treatment with either a chemical or a physical agent are called as induced mutation. The agents capable of inducing mutations are known as *mutagens*. Induced mutations are useful in genetic and biochemical studies and also in crop improvement. The process of inducing mutations through treatment with a mutagen is known as *mutagenesis*, while the exploitation of induced mutation for crop improvement is called *mutation breeding*.

V. BASED ON DIRECTION

(A) Forward mutation : Creates a change from wild type to abnormal phenotype.

(B) Reverse or back mutation: Produces a change from abnormal phenotype to wild type. Adenine $\xrightarrow{forward}$ Guanine $\xrightarrow{reverse}$ Adenine

i). Mutation suppressor – A gene change which occurs at a different site from the primary mutation, yet reverses its effect.

a. Extragenic (intergenic) suppressor – It occurs in a gene different from that of the mutant gene.

b. Intragenic suppressor – It occurs at a different nucleotide within the same gene. It shifts the reading frame back to original position.

VI. BASED ON MAGNITUDE OF PHENOTYPIC EFFECT

(A) Change in mutation rate: Some alleles can be distinguished only by the frequency with which they mutate.

(B) Isoalleles: Produce identical phenotypes in homozygous or heterozygous combinations with each other, but prove to be distinguishable when in combination with other alleles.

(C) Mutations affecting viability:

i) Subvitals – relative viability is greater than 10% but less than 100% compared to wild type.

ii) Semilethals – cause more than 90% but < 100% mortality.

iii) Lethals – kill all individuals before adult stage.

MUTAGENS

The agent that induces mutation is termed as mutagen. Mutagens include physical agents, chemical agents and radiations. The most commonly used mutagens are presented below.

1. ionizing radiation : Changes in chemical valence through the ejection of e-.
   a. Particulate radiation α–rays, β–rays, fast neutrons, thermal neutrons.
   b.Nonparticulate/electromagnetic radiation–X rays, γ-rays etc.

2. Non-ionising radiation: It raises the energy levels of atoms (excitation), rendering them less stable. eg. UV-rays and heat. UV produces thymine dimmers i.e., bonding between thymines on the same strand.

3. Chemical mutagens: These are chemical substances that increase the mutability of genes. They are as follows;

1. Alkylating agents – sulphur mustards, nitrogen mustards, epoxides, ethylene imine (EI), sulphate and sulphonates (eg. Ethyl Methane Sulphonate (EMS), Methyl Methane Sulphonate (MMS), diazoalkanes, nitroso compounds.
2. Acrdine dyes – acriflavine, proflavine, acridine orange, acridine yellow, ethidium bromide(EB).
3. Base analogues – 5- bromouracil, 5-chlorouracil.
4. Others – nitrous acid, hydroxyl amine, sodium azide.

DETECTION OF MUTATION

A large number of testing methodologies are now available to screen for mutagenicity.

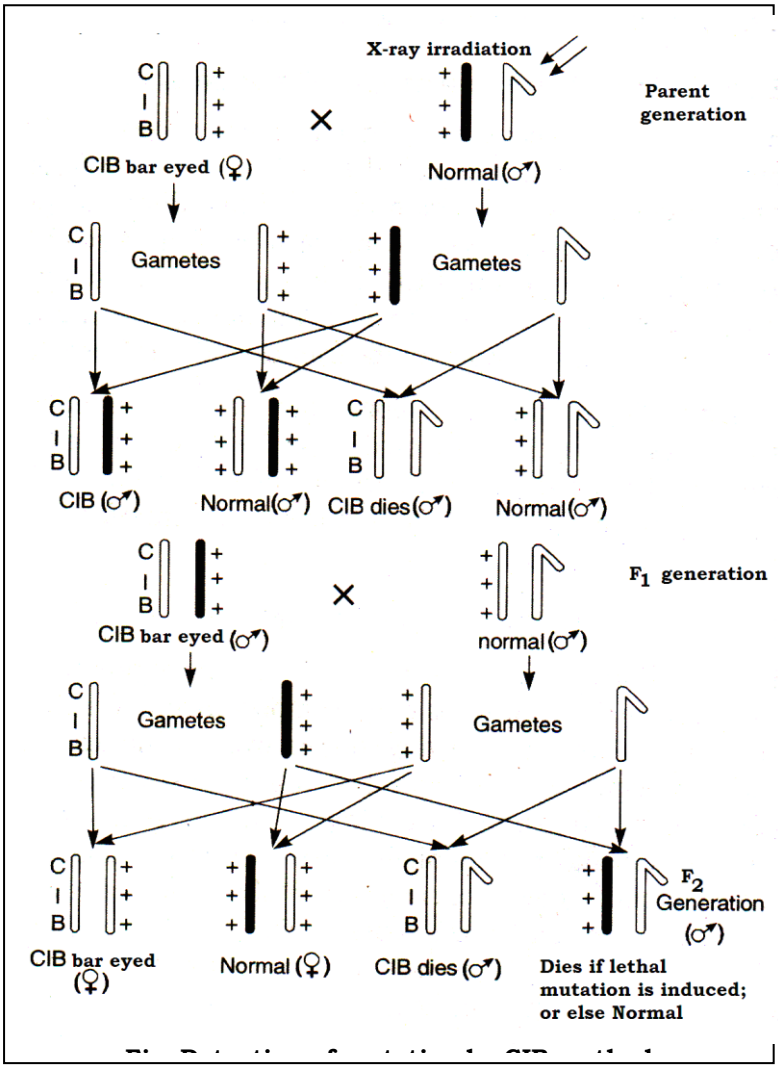
1. CIB Method

The CIB method was used by H.J. Muller for detecting X-linked (sex linked) mutations in male *Drosophila.* In CIB, B designates dominant mutation gene for bar-shaped eyes, which is used as a marker for flies. 'l' stands for recessive lethal gene present in the X chromosome. The l and B are always inherited together in the same chromosome. All the female *Drosophila* with bar-shaped eyes are heterozygous for this chromosome as homozygous females and males with CIB chromosome do not survive because of the lethal gene l.

The CIB technique was used for identification of sex-linked recessive lethal mutants in male *Drosophila* after treating them with X-rays. The male *Drosophila* were first exposed to X-rays and were called X_1 generation as X-rays were used as the

mutagen. They are then crossed with bar-eyed CIB females. The resulting X_2 generation consisted of a normal-eyed and bar-eyed CIB females alone and no males were recovered. As all the males with the CIB chromosome dies due to the lethal gene l.

The F_1 CIB female will have one CIB chromosome and one X chromosome from the irradiated male. When this F_1 CIB female is mated to a normal male, the half of the male progenies will receive one CIB chromosome and die due to the lethal gene l. The remaining half of the male progeny will receive the X chromosome from the irradiated grandfather. If a lethal mutation was induced by X-rays in the X chromosome then this male progenies will also die.



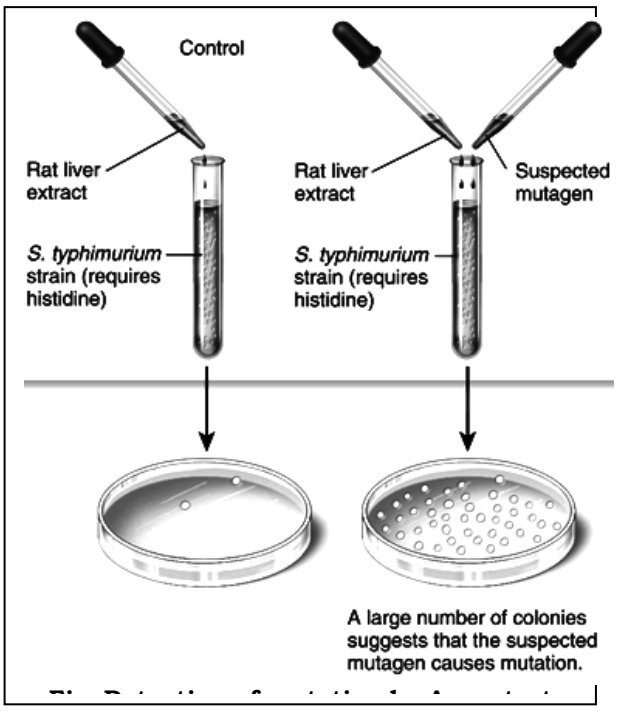
The detection of sex linked recessive lethal gene in this method is based solely on the presence or absence of male progenies in crosses between F1 CIB female and normal male. If the mutation induced is not lethal, then the X_2 will have 50% males. The frequency of the recessive lethal mutation in X chromosome is the ratio between the number of F1 CIB females producing no males to the total number of females tested.

AMES TEST

Ames in 1974 developed a simple test for evaluating the potential of chemicals to cause mutations. The Ames test is based on the principle that both cancer and mutations result from damage of DNA. The results have confirmed that 90 % of known carcinogens are also mutagens and the mutagenesis in bacteria could serve as an indicator of carcinogens in humans.

The Ames test uses four strains of Salmonella typhimurium that have defective coat protein. This coat normally protects the bacteria from chemicals in the

surrounding. Also, their DNA repair system has been inactivated to enhance their susceptibility to mutagens. One of the four strains detects base-pair substitution while the other three detect different types of frameshift mutations. The strains carry a mutation rendering them incapable of producing the aminoacid histidine (*his*$^-$). Only bacteria that have mutated (*his*$^+$) alone are able to synthesize histidine and grow on the medium.



Then the chemicals to be tested are added to the plates inoculated with the bacteria and the number of mutant colonies developed is compared with the control plates with no chemicals. Any chemical which increases the number of colonies is mutagenic and is also mostly carcinogenic in nature.

23. CHROMOSOMAL ABERRATIONS
I - STRUCTURAL VARIATIONS

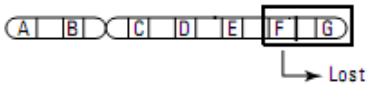
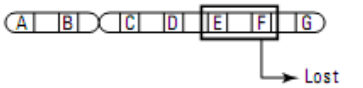
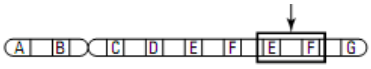
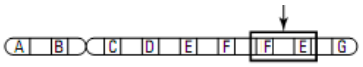
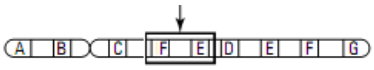
The occurrence of spontaneous variations in structure of number of chromosome is called chromosome aberration. The chromosome aberrations is of two types 1) Structural variations and (2) Numerical variations

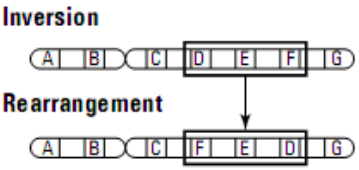
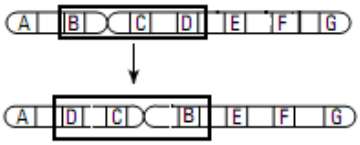
Structural aberrations refers to visible changes in the structure of chromosomes. They are also called as chromosomal aberrations. They are of four types: Changes involving the number of gene loci:

1. Deletion or deficiency
2. Duplication or addition

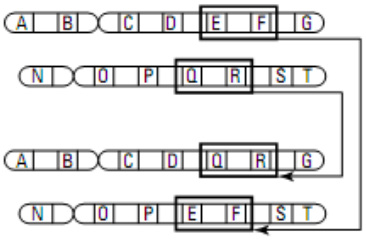
Changes involving the arrangement of gene loci:

3. Inversion
4. Translocation.

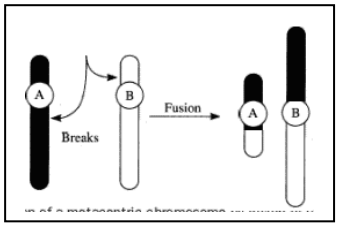
TYPE OF ABERRATION	REMARKS	EXAMPLE
1. Deletion	Loss of a segment of a chromosome.	Produces pseudodominance for recessive alleles located in the lost segment.
a. Terminal deletion	Lost segment includes telomere. A segment between telomere and centromere is lost.	
b. Interstitial deletion	A segment between telomere and centromere is lost	
Significance of deletion As deletion involves loss of genetic material, it has deleterious effect. It allows recessive mutations on the undeleted chromosome to be expressed and this is known as **pseudodominance.**		
2. Duplication	A chromosome segment present in more than two copies in the same nucleus.	Duplications are the source of all new genes
a. Tandem duplication	The additional chromosome segment located just after the normal segment, gene sequence being the same.	
b. Reverse duplication	Same as above but the gene sequence of the additional segment is inverted.	
c. Displaced duplication	The additional segment is located in the same chromosome but away from the normal segment.	
d.Translocation duplication	The additional segment located in a non homologous chromosome.	
Significance of duplication Duplications are more frequent and less deleterious. They produce abnormality in structure and function. As duplication increases the number of genes in the chromosome it plays a significant role in evolution		

3.Inversion	A chromosome segment contains genes in a sequence which is reverse of the normal gene sequence	Produces characteristics dicentric bridge.
a. Paracentric inversion	The inverted segment does not contain centromere.	
b. Pericentric inversion	The inverted segment contains centromereand change centromere location.	

Significance of inversion Inverstion helps in the origin of new species. Inversions reduces the cross over frequency and hence the recombination rate also is reduced.

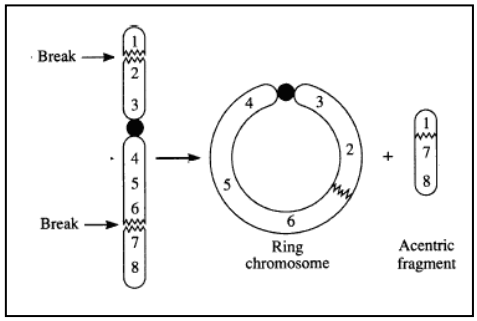
Translocation	Chromosome segment(s) integrated into non-homologous chromosome(s).	The main mechanism for changes in chromosome number and morphology in nature.
a. Simple translocation	A segment of a chromosome integrated into a nonhomologous chromosome.	May lead to translocation duplication.
b. Reciprocal translocation	A segment of chromosome integrated into a nonhomologous chromosome from which a segment is integrated into the first one.	

Significance of translocation Translocation introduces new genetic polymorphism and plays a key role in the formation of new species. Translocation also changes the morphology or appearance of chromosomes by centric fusion between two acrocentric chromosomes.



Robertsonian translocation: When the two acrocentric chromosomes break and join to a form a metacentric chromosome it is referred as Robertsonian translocation.

The X-xhaped structure during synapsis is formed due to pairing of translocated chromosomes. During pachytene stage of meiosis, the chromosomes pair to form a cross shaped structure due to reciprocal translocation heterozygote (two normal and two translocated) while normal chromosome forms a bivalent. The occurance of crossing over in each arm of the quadrivalent results in the formation of a ring or circle of four chromosomes at diakinesis and at metaphase of first meiotic division.



24. CHROMOSOMAL ABERRATIONS

II – NUMERICAL VARIATIONS

Diploid organism have two copies of the genome in their somatic chromosomes (2n = 2x) and their gametes have a single genome (n = x). Any change from the normal diploid condition of an organism is called as a numerical chromosome aberration, often is referred to as *heteroploidy* and the individuals are known as *heteroploid*s.

Numerical aberrations are of two types 1) Aneuploidy and 2) Euploidy. Aneuploidy involves change in chromosome number by addition or deletion of few number of chromosomes. Euploidy involves changes in whole sets of chromosomes. Most common euploid is a diploid which has two sets of the same chromosome.

Monoploidy refers to the presence of only one copy of the genome and is represented by x. Haploidy refers to the gametic chromosome number of a species of a normal diploid or a polyploid and is represented by n. Haploids derived from diploid species are known as monoploids, while those obtained from polyploid species are called polyhaploids.

ANEUPLOIDY

Aneuploidy is of many types. A dipoild cell (2n) with a missing chromosome (2n-1) is called monosomic; a monosomic person has 45 chromosomes. A cell which lacks both copies of a chromosome is called as nullisomic (2n-2); a nullisomic person has 44 chromosomes. Loss of a chromosome is lost from two different pairs in a cell is called as double monosomic (2n-1-1). Aneuploidy arises due to non-disjunction of chromosomes in meiosis during formation of gametes.

Considering addition of a chromosome, a diploid cell with an extra chromosome is called as trisomic (2n+1); a trisomic person has 47 chromosomes. If there are two additional chromosomes in a cell it is called as tetrasomic (2n+2).

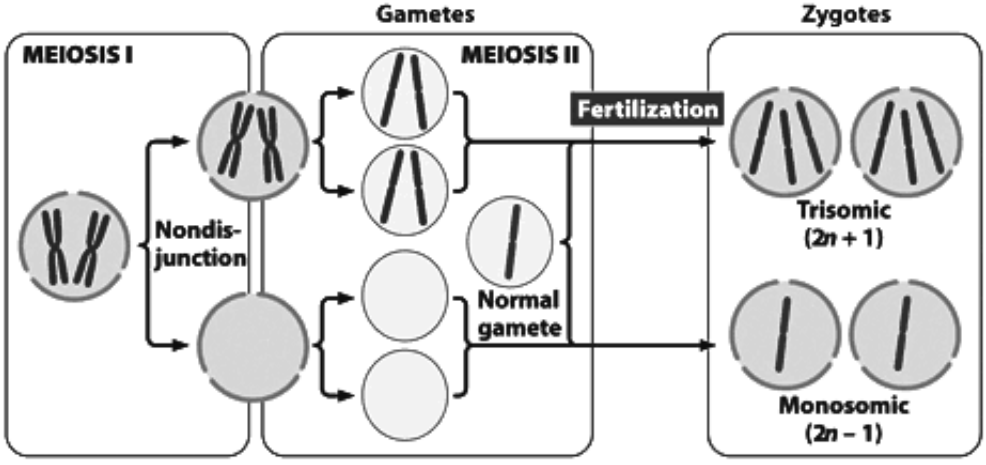


Fig. Formation of aneuploids due to non-disjunction

ANEUPLOIDY IN HUMANS

The common aneuploids in humans are *sex-chromosomal aneuploids* eg. Turner syndrome and Klienfelter syndrome. The common *autosomal aneuploid* is trisomy 21, also called Down syndrome.

Turner Syndrome (45, XO, females)

Persons with Turner syndrome are females who lacks one X chromosome (monosomy). This condition is produced when an egg with X chromosome is fertilized by a sperm without a sex chromosome resulting in a XO female. They do not undergo puberty and their female secondary sex characteristics remain immature: menstruation is usually absent, breast development is slight, pubic hair is sparse, deformed heart, horse shoe shaped kidney. This syndrome is seen in 1 of 3000 female births. Affected women are frequently short and have a low hairline, a relatively broad chest, and folds of skin on the neck. It is highly lethal in embryos and leads to abortion. 98 % of the Turner syndrome is lost during first three months of pregnancy. Most women who have Turner syndrome are sterile.

Klinefelter Syndrome (47, XXY, males)

The males has one extra X chromosome which inhibits the development of male characters. When an abnormal egg with XX chromosome fuses with normal sperm, a zygote with normal autosomes and XXY is formed, Persons with this condition has long legs, small testes, female like breast enlargement (gynecomastia), and no sperm production. They are infertile, most have normal intelligence while some are mentally retarded. Klinefelter syndrome occurs with a frequency of about 1 in 1000 male births.

This condition can be treated by surgical removal of breast. But sterility cannot be altered. Treatment with testosterone promotes development of sex organs, musculature, body hair and deeper male voice.

Down Syndrome (47, XX or XY)

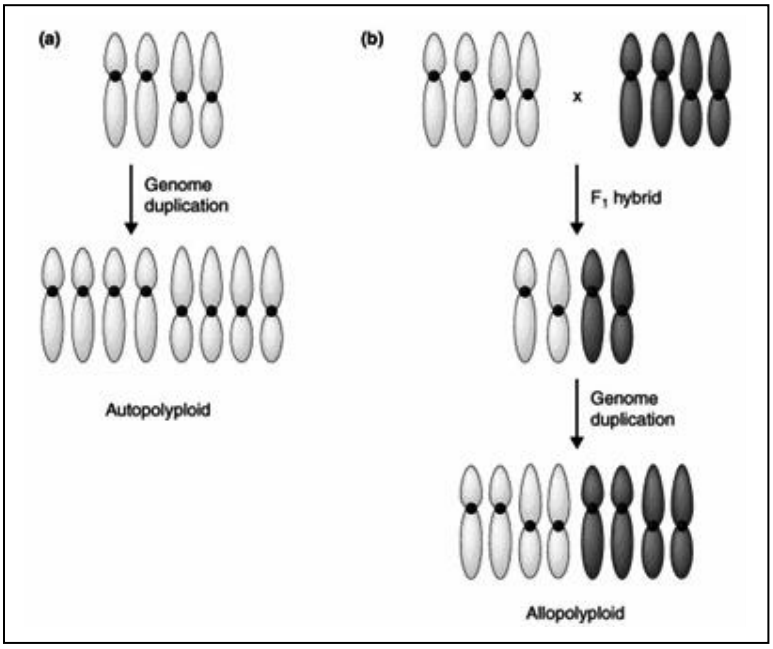
It was first reported by Langdon Down in 1866. The defect is caused by trisomy of 21st chromosome. Most of the Down's syndrome children are born to normal parents. The occurrence of Down syndrome increases with the age of the mother. The small extra chromosome is formed due to the non-disjunction of chromosomes during gamete formation where the 21st chromosomes fail to separate. Down syndrome also occurs due to translocation of chromosomes 21 and 14 or 15. This is called *familial Down syndrome.*

The features are moon face, open mouth, projecting lower lip, stubby hands and feet, slanting eyes, broad forehead, congenital malformation of heart, lower blood calcium level and susceptibility to respiratory disorders.

EUPLOIDY

An organism with varying number of complete haploid chromosome set is called as an euploid. The somatic cells with two sets of chromosomes are diploids (2n) while gametes with only one set of chromosome are haploids (n). Organisms with multiple copies of haploid chromosome sets, such as three sets (3n) are triploids, four sets (4n) are tetraploids, five sets (5n) are pentaploids. They are collectively called as polyploids.

Approximately 40% of flowering plants and 70% of grasses are polyploids. Some species like *Triticum* have many states polyploidy namely diploid, tetraploid and hexaploid. Oats, cotton, potato, sugarcane and frogs, lizards, fishes are examples for polyploids.



Polyploidy is of two types namely,

1. Autopolyploidy, in which all the chromosome sets are from a single species and
2. Allopolyploidy, in which the chromosome sets are from two or more species.

AUTOPOLYPLOIDY

Presence of more copies of chromosome sets from the same species is called as autopolyploidy. An organism with three sets of the same genome is called as an autotriploid (3x); four sets as autotetraploid (4x); five sets as autopentaploid (5x) etc.

Autopolyploidy occurs in many ways. For example, the fusion of an abnormal diploid gamete with a normal haploid gamete results in a triploid. Also, fertilization of a diploid gamete by another diploid gamete results in a tetraploid. A tetraploid can also be formed by chromosome doubling of somatic tissues by using colchicine.

Since all the chromosomes are form the same species, they are homologous and their segregation produces unbalanced gamets with various number of chromosomes resulting in sterility. The sterility due to autopolyploidy has commercial value. For example, the diploid bananas have 2n=22 and produce hard , inedible seeds while, triploid bananas with 3n=33 are sterile and lack seeds. Polyploidy has been used in agriculture to produce “seedless” and “jumbo” varieties of crops. For example, seedless triploid watermelons are produced by crossing a tetraploid and a diploid. Jumbo macintosh apples are tetraploids.

ALLOPOLYPLOIDY

Presence of multiple copies of chromosome sets from different species is called as allopolyploidy. This can be explained by the following example with a cross involving two species with same chromosome number 2n=6. The parents are AABBCC (species 1) and GGHHII (species 2). The fusion of their gametes ABC and GHI produces a hybrid with six chromosomes, ABCGHI. Since the chromosomes are different, they will not pair during meiosis and the segregation is not normal and hence they will be sterile. As each chromosome has it homologue, this is also referred to as *amphidiploid*.

Korpechenko in 1920s created polyploidy by crossing cabbage *Brassica oleracea* (2n=18) with radish *Raphanus sativus* (2n=18). The new plants possessed the roots of cabbage and leaves of radish and are sterile.

TYPE OF PLOIDY	SYMBOL	EXAMPLE
Heteroploid **A) Aneuploid**	2n ± few chromosome	
Nullisomic	2n – 2	AA BB --
Monosomic	2n - 1	AA BB C-
Double monosomic	2n - 1 - 1	AA B- C-
Trisomic	2n + 1	AA BB CCC
Double trisomic	2n + 1 + 1	AA BBB CCC
Tetrasomic	2n + 2	AA BB CCCC
B) Euploid		
Monoploid	x	A
Haploid	n	A
Diploid	2n	AA
1) Autopolyploid		
Autotriploid	3x	AAA
Autotetraploid	4x	AAAA
Autopentaploid	5x	AAAAA
Autohexaploid	6x	AAAAAA
Autooctaploid	8x	AAAAAAAA
2) Allopolyploid		Parent 1=AA, Parent2=BB
Allotetraploid	$(2X_1 + 2X_2)$	AA BB
Allohexaploid	$(2X_1 + 2X_2 + 2X_3)$	AA BB CC
Alloctaploid	$(2X_1 + 2X_2 + 2X_3 + 2X_4)$	AA BB CC DD

25. DNA AS CARRIER OF GENETIC MATERIAL

Even before nucleic acids were identified as the genetic material, biologists recognized that the genetic material must possess the following three important characteristics.

1. Genetic material must replicate faithfully

Every organism begins life as a single cell, undergoes billions of cell divisions to produce a complex, multicellular organism. At each cell division, the genetic material must be transmitted to the daughter cells with great accuracy. When organisms reproduce the coding instructions must be copied with fidelity.

2. Genetic material must store complex information

The genetic material must be capable of storing large amounts of information or instructions for all the traits and functions of an organism. At the same time it must be stable and it must allow errors in low frequency for the origin of new genetic variation through mutation.

3. Genetic material must encode phenotype

The genetic material i.e. the genotype must be able to express itself by exercising a control on the development of character it governs and must encode phenotype. The product of a gene is often a protein; so there must be a mechanism for genetic instructions to be translated into the amino acid sequence of a protein.

- Friedrich Miescher (1869) discovered DNA as as a phosphorus containing acidic substance made up of very large molecules called *nuclein*. Richard Altmann called it as *nucleic acid* in 1889.
- By 1900 the purine and pyrimidine bases were identified and in 1920s the two kinds of nucleic acids, DNA and RNA were distinguished.
- An incidental observation by Griffith in 1928 and relevant investigations by Avery, MacLeod and McCarty in 1944 indicated that DNA could be the carrier of genetic information.
- The experiments of Hershey and Chase in 1952 confirmed that the transforming principle is DNA. Surprisingly, the idea that genes are made of nucleic acids was not widely accepted until after 1950.

THE DISCOVERY OF BACTERIAL TRANSFORMING PRINCIPLE

Griffith (1928), an English microbiologist observed that there are two strains of pneumonia causing bacterium *D. pneumoniae*, one that forms smooth colonies (S strain) protected by a capsule and another that forms a irregular or rough colonies (R strain) without a capsule.

He found that the mice injected with S strain died while those injected with R strain were alive. When the heat inactivated lethal S strain was injected the animal

survived. Surprisingly, a mixture of non-lethal R strain and heat inactivated S strain had a lethal effect like the normal S strain. Griffith found the normal alive S strain of

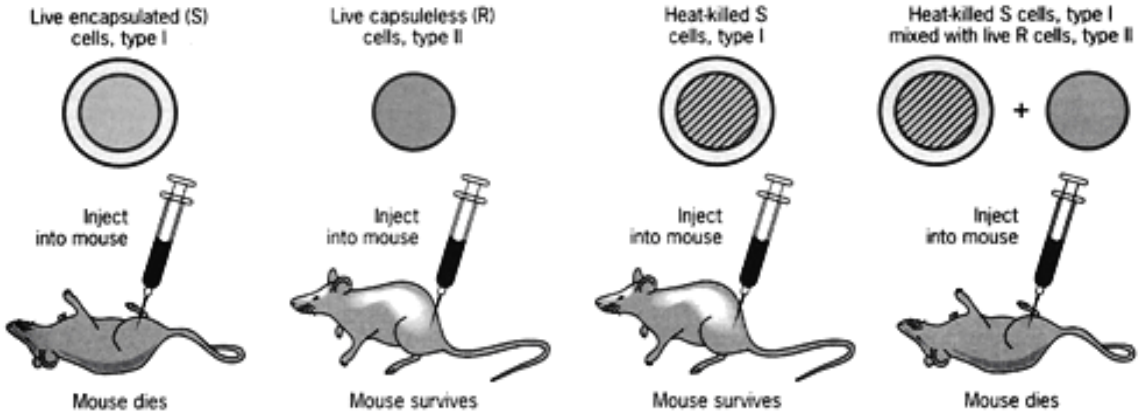


Fig.. Griffith's Experiment with *Streptococcus pneumoniae*

pneumococci in the animals blood. This showed that the cells of R strain were changed (transformed) into cells of S strain. *The phenomenon by which the DNA isolated from one type of cell, when introduced into another type, is able to bestow some of the properties of the former to the latter, is referred as transformation.* The experiments of Griffith thus demonstrated transformation but did not reveal the identity of the transforming principle.

THE TRANSFORMING PRINCIPLE IS DNA

In 1944, Avery, MacLeod and McCarty gave molecular explanation for the observations of Griffith. After ten years of research they succeeded in isolating and purifying the transforming principle. Avery, MacLeod and McCarty found out that the transforming principle was not affected by protease and RNase but by DNase alone.

They found that the transforming principle precipitated and also absorbed ultraviolet light at the same wavelength as that of DNA. Thus they showed that the chemical basis of the transforming principle is DNA. But many biologists refused to accept the idea and instead believed that protein as the genetic material.

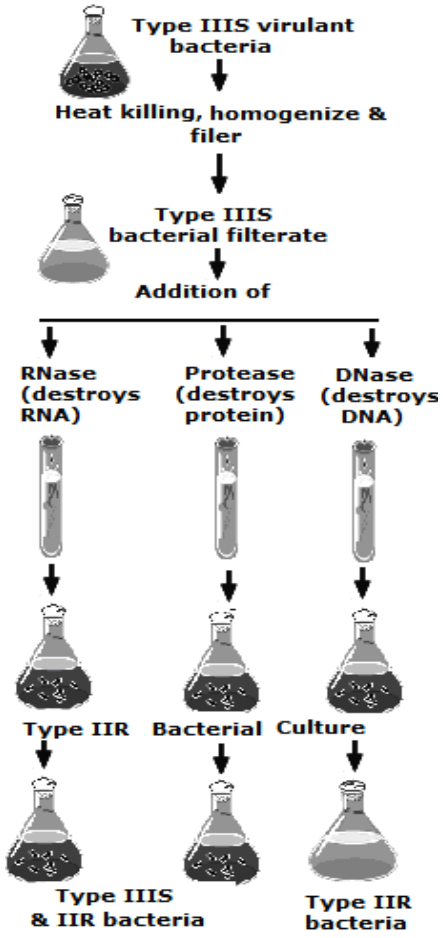


Fig. Experiments of Avery, MacCleod & McCarty (1944) showing transforming principle is DNA

GENETIC INFORMATION IS TRANSMITTED BY DNA ALONE

The final evidence that DNA alone transmits genetic information was provided by Hershey and Chase in 1952. In two set of experiments, Hershey and Chase labeled the capsular protein of the T_2 virus (a bacteriophage) with radioactive Sulphur (^{35}S) and the DNA with radioactive phosphorus (^{32}P) separately. When the *E. coli* bacteria were infected with the labeled bacteriophage, only ^{32}P (DNA) entered the cells, and not the ^{35}S (capsular protein). The newly formed new phage particles emitted radioactivity which proved that the DNA was the exclusive carrier of genetic information.

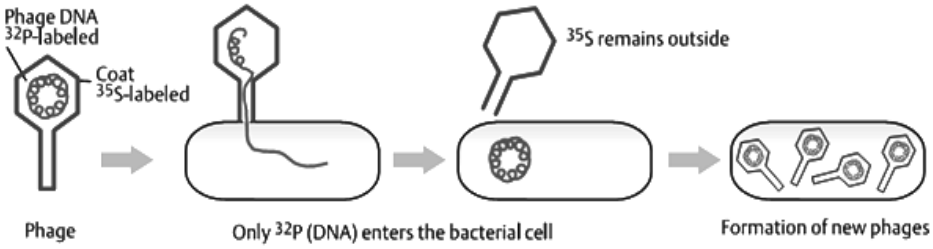


Fig.. Experiments of Hershey and Chase (1952) proving DNA as the genetic material

26. THE STRUCTURE OF DNA

Though the structure of DNA is relatively simple it performs a complex task unparalleled by other large molecules. The structure of DNA can be studied in three levels as primary, secondary and tertiary structure. The primary structure refers to the structure of nucleotide and how they are joined together. The secondary structure refers to the double helical structure proposed by Watson and Crick. The tertiary arrangement refers to the complex packing of the double stranded DNA in chromosomes.

I. PRIMARY STRUCTURE OF DNA

Nucleic acids (DNA and RNA) are polymers made up of repeating units of ***nucleotides***. A nucleotide consists of three basic components: 1. Pentose sugar, 2. Nitrogenous base, and 3. Phosphate group.

1. PENTOSE SUGAR

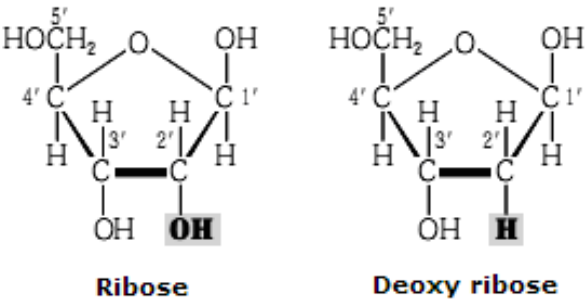


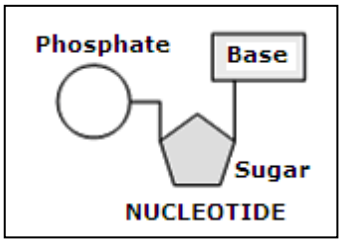
Fig. The chemical structure of sugars. RNA has ribose and DNA has deoxy ribose sugar.

The sugar is a cyclic five-carbon structure. It contains a hydroxyl group attached to 2'-carbon atom and called as ribose in RNA. In DNA, the sugar lacks oxygen atom and hence called deoxyribose. This minor chemical difference is recognized by all the cellular enzymes that interact with DNA or RNA, thus yielding specific functions for each nucleic acid. Further, the additional oxygen atom in the RNA nucleotide makes it more reactive and less chemically stable than DNA.

The carbon atoms are numbered as 1' (called one prime), 2', 3', 4' and 5' in order to differentiate them from the carbon atoms in the DNA and RNA bases. The 5' and 3' carbons of the pentoses forms the phosphodiester linkage, while the l' carbon is always occupied by an organic base.

2. NITROGENOUS BASES

There are two kinds of bases: ***purines*** and ***pyrimidines***. Each purine consists of a six-sided ring attached to a five-sided ring whereas, a pyrimidine consists of a six-sided ring only. There are two purines, adenine (A) and guanine (G),and three pyrimidines, cytosine (C), thymine (T), and uracil (U). Thymine occurs only in DNA, while uracil occurs only in RNA. The letters A, C, T, G, are usually referred to as the alphabets of life.



When a base is linked to a sugar, the product is called a ***nucleoside***. A nucleoside linked to a phosphate is called as a ***nucleotide*** (Nucleotide = Nucleoside + Phosphate) (Fig.). In a nucleotide, the nitrogenous base

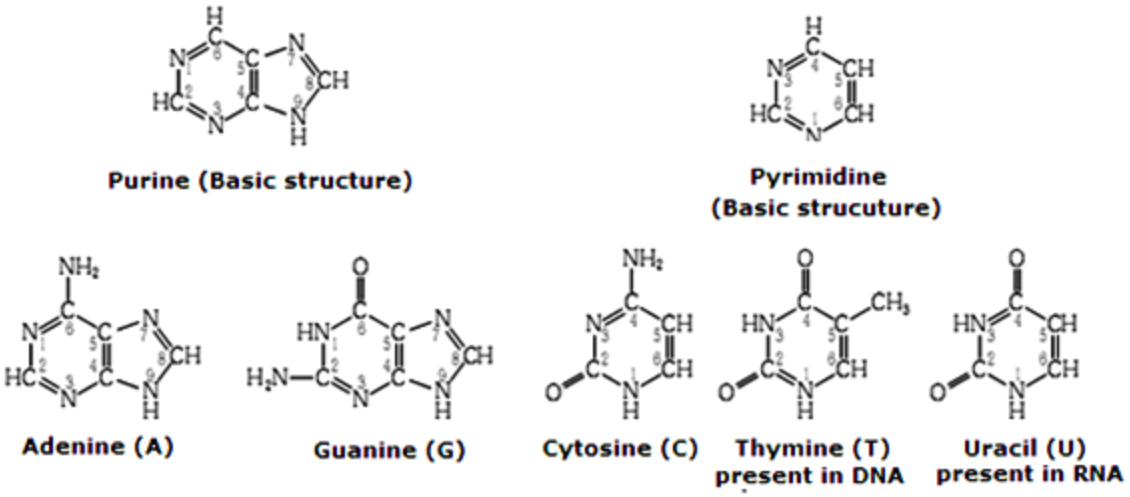


Fig. . Structure of purine and pyrimidines bases. The carbon atoms are assigned unprimed numbers

always forms a covalent bond with the 1'-carbon atom of the sugar.

3. PHOSPHATE GROUP

The third component of a nucleotide is the phosphate group, which consists of a phosphorus atom bonded to four oxygen atoms. Phosphate groups are found in every nucleotide and frequently carry a negative charge, which makes DNA acidic. The phosphate is always bonded to the 5-carbon atom of the sugar in a nucleotide.

The DNA nucleotides are properly known as ***deoxyribonucleotides*** or deoxyribonucleoside 5-monophosphates. Because there are four types ofbases,there are four different kinds of DNA nucleotides. The equivalent RNA nucleotides are termed ***ribonucleotides*** or ribonucleoside 5-monophosphates.

POLYNUCLEOTIDES

Two nucleotides are linked by a phosphodiester group i.e. the 5'-phosphate group of one nucleotide joins to the 3'-carbon atom of the next nucleotide. These

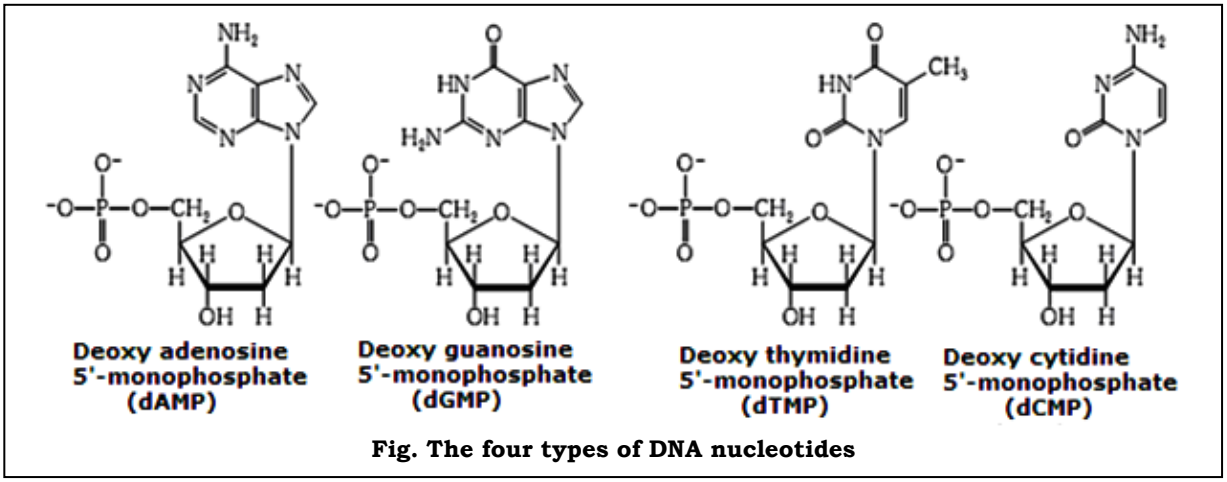


Fig. The four types of DNA nucleotides

bonds, called ***phosphodiester linkages***, are relatively strong covalent bonds. Shorter chains (consisting of less than 20 nucleotides) are called oligonucleotides while longer chains are called ***polynucleotides***. The backbone of the polynucleotide strand is composed of alternating sugars and phosphates; the bases project away from the long axis of the strand.

An important characteristic of the polynucleotide strand is its direction or polarity. At one end of the strand a phosphate group is attached only to the 5'-carbon atom of the sugar in the nucleotide. This end of the strand is therefore referred to as the **5' end**. The other end of the strand, referred to as the **3' end**, has an OH group attached to the 3-carbon atom of the sugar.

RNA nucleotides also are connected by phosphodiester linkages to form similar polynucleotide strands.

II. SECONDARY STRUCTURE OF DNA

The secondary structure refers to the ***double helical structure of DNA*** proposed by Watson and Crick at Cambridge. The double helix consists of two polynucleotide strands wound around each other. The sugar-phosphate linkages are on the outside of the helix, and the bases are stacked in the interior of the molecule (Fig.).

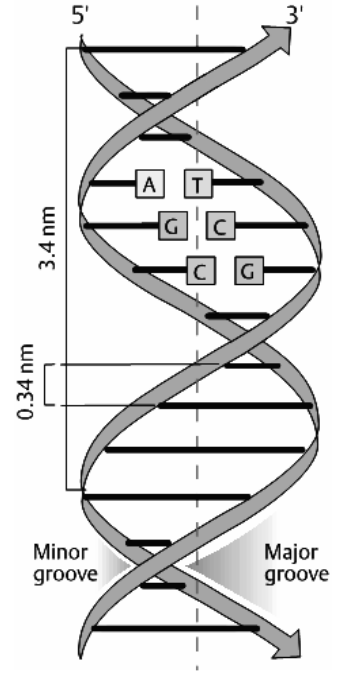


Fig. Watson & Crick's double helical structure of DNA

Using metal wires, Watson and Crick built molecular models based on the X-ray diffraction data of Rosalind Franklin and Maurice Wilkins. The X-ray analysis revealed that the DNA was a helix with a width of 2 nm. The purine and pyrimidines bases were stacked 0.34 nm apart in a ladder (Fig.). Since the width of the helix is 2 nm it can accommodate only two strands. Linus Pauling, who received Nobel prize for unraveling helical structure of proteins thought that DNA consists of three strands. Watson and Crick found that the best model for X-ray data was a double helix with the sugar-phosphate chain on the outside and nitrogenous bases on the inside. The two chains run in antiparallel direction with one chain having a 5'-3' orientation while the other has 3'-5' orientation. Thus the DNA double helix is like a rope ladder with rigid steps (rungs) twisted into a spiral shape. The two ropes constitute the sugar-phosphate backbone. Each step constitute a base pair, with each base attached to the

sugar–phosphate backbone. Erwin Chargaff found that A=T and G=C and that the number of purine bases (A + G) is equal to the number of pyrimidine bases (C + T). Watson and Crick, along with Maurice Wilkins, were awarded a Nobel Prize in 1962.

The key features about the double helical structure of DNA molecule are as follows:

1. The DNA double helix (DNAdh) consists of two polynucleotide chains coiled around a central axis in a spiral fashion.
2. The polynucleotide chains are antiparallel; one chain runs in the 5' to 3' orientation and the other in 3' to 5' direction. This anti-parallel orientation of the two strands is essential for the formation of hydrogen bonds between the pairs of DNA bases.
3. The two bases in each base pair lie in the same plane which is perpendicular to the axis of the helix. Neighbouring bases lie 3.4 A apart. There are 10 base pairs per helical turn i.e. the helix repeats itself at an interval of 34 A.
4. The helix has two kinds of alternating external grooves: a deep groove (called the major groove) and a shallow groove (called the minor groove).
5. The nitrogenous bases on one strand pair with those on the other strand in complementary fashion (A always pairs with T, while G pairs with C). The most common natural form of DNA is a right-handed ouble helix of diameter 2.0nm, called the B-DNA. DNA can also assume other forms like Z DNA, A DNA.

In addition to these features described above, certain implications deserve emphasis:

1. ***Complementary base pairing*** means that the replicate of each strand is given the base sequence of its complementary strand when DNA replicates.

2. Because the strands are ***antiparallel***, when two nucleotides are paired, the sugar portions of these molecules lie in opposite directions (one upward and the other downward along the chain) (Fig.).

3. Because the strands are antiparallel, the convention for writing the sequence of bases in a strand is to start from the 5' P terminus at the left (e.g., GAC refers to a trinucleotide 5' -P-GAC-3' -OH).

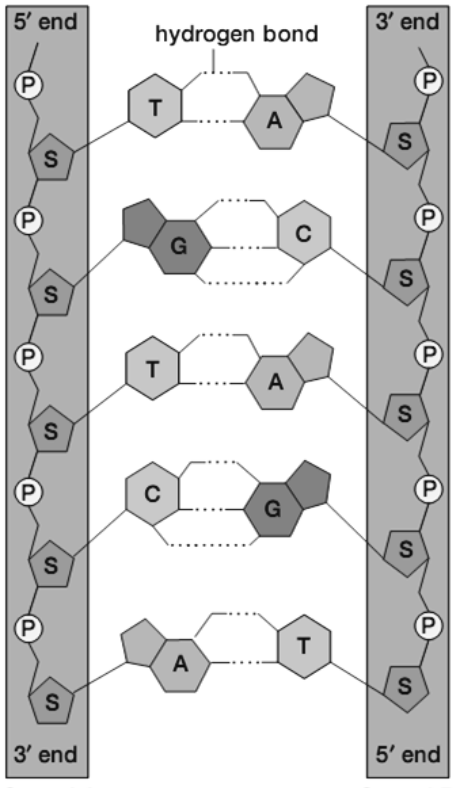


Fig. DNA consisting of two polynucleotide chains running antiparallel to each other & Composed of complementary strands. RNA has single nucleotide

4. The conventional way of expressing the base composition of an organism is by the percentage of [G] + [C]. This value is approximately 50% for most eukaryotes with only minor variations among species. In simpler organisms, there are significant variations (e.g., 27% for *Clostridium*, 50% for *Escherichia coli*, and 76% for *Sarcina*, all of these organisms being bacteria).

5 The chains of the double helix are held together by hydrogen bonds between base pairs in opposite strands. The bond between A and T is a double bond, while the bond between G and C is a triple hydrogen bond.

The DNA molecule satisfies the requirement of genetic material in the following ways:

1. It can replicate itself accurately during cell growth and division.
2. Its structure is sufficiently stable so that heritable charges i.e., mutations can occur only very rarely.
3. It has a potential to carry all kinds of necessary biological information.
4. It transmits all the biological information to the daughter cells.

Thus the essential functions of DNA are the storage and transmission of genetic information and the expression of this information in the form of synthesis of cellular proteins.

ALTERNATIVE DNA STRUCTURE

The double helix described by Watson and Crick has right handed helical coiling and is called ***B-DNA***. It is a biologically important and most stable form of DNA that is commonly and naturally found in most living systems. The B-form of DNA can change to another form depending upon the humidity and salt concentration of the sample. The alternate forms of DNA are ***A-form, C-form, D-form, Z-form*** etc.

The A-form is also a right-handed helix, but it has 11 base pairs per turn. The C-form of DNA has 9.3 base pairs per turn, while the D-form of DNA, which is rare form, has 8 base pairs per turn. The Z-form is a left-handed helix, in which the sugar and phosphate linkages follow a zigzag pattern and hence called ***Z-DNA***. A segment of B-DNA consisting of GC pairs can be converted into Z-DNA when the bases are rotated by 180^0. They are thermodynamically unstable and plays a role in the regulation of the gene activity.

CHARESTERISTIC FEATURES	A-DNA	B-DNA	Z-DNA
Conditions required to produce the structure	75 % H_2O	92% H_2O	Alternating purine & pyrimidines bases
Direction of helix	Right-handed	Right-handed	Left-handed
Average base pairs per turn	11	10	12
Rotation per base pair	32.7^0	36^O	-
Distance between adjacent bases	0.26 nm	0.34 nm	0.37 nm
Diameter	2.3 nm	1.9 nm	1.8 nm
Overall shape	Short and wide	Long and narrow	Elongated and narrow

Denaturation: The hydrogen bonds between the DNA strands break on heating the DNA to high temperature (nearly 100 ^oC). The process of separation of DNA strands is known as denaturation.

Renaturation: Reunion of the separated or denatured DNA strands on cooling is called renaturation or annealing. The optimum temperature for renaturation is 20 – 25 ^oC.

27. DNA REPLICATION

The process by which a DNA molecule makes identical copies of itself is called as DNA replication. Accurate DNA replication is fundamental to normal cell function and health. Also, it must take place at breakneck speed. For example, the single, circular chromosome of *E.coli* contains about 4.7million base pairs. At a rate of more than 1000 nucleotides per minute, replication of the entire chromosome would require almost 3 days. Yet, these bacteria are capable of dividing every 20 minutes. In *E.coli* the DNA replication occurs at a rate of 1000 nucleotides per second, with less than one in a billion errors.

THREE MODELS OF DNA REPLICATION

1. Dispersive: In dispersive mode of replication, the old DNA molecule would break into several pieces, each fragment would replicate and the old and new segments would recombine randomly to yield the progeny DNA molecule. Each progeny molecule would have both old and new segments along its length.

2. Conservative: According to conservative scheme, after replication the two newly synthesized strands would form a double helix, while the two old parental strands would form another double helix.

3. Semi conservative: In the semi conservative model of DNA replication, one of the two parental DNA strand serves as a template for the synthesis of new, complementary daughter strand. Each progeny DNA molecule would consist of one old and one newly synthesized strand. As one of the parental strand is conserved in the new daughter DNA molecule it is called as semi conservative model and is the universally accepted model.

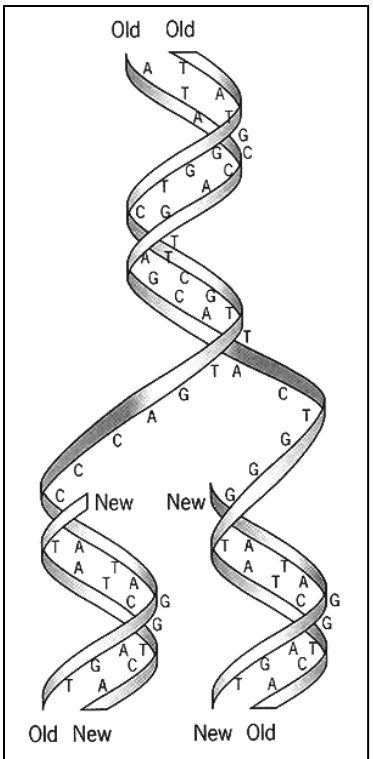


Fig. Semiconservative model of replication

EVIDENCE FOR SEMICONSERVATIVE REPLICATION

The experimental evidence for the semiconservative method of replication was provided by Meselson and Stahl (1958). They cultured *E.Coli* in a medium containing radioactive ^{15}N. and labeled its DNA with ^{15}N. This radioactively labelled *E.coli* was transferred to a medium containing normal nitrogen, ^{14}N, and allowed to divide.

The DNA of newly formed daughter cells contained one DNA strand labelled with ^{15}N and the other strand labelled with ^{14}N. This showed that each progeny DNA molecule would consist of one old and one newly synthesized strand.

MODES OF REPLICATION

1. ***In theta replication*** of DNA, the two nucleotide strands of a *circular* DNA molecule unwind, creating a replication bubble. Within each replication bubble, DNA is normally synthesized on both strands and at both replication forks, producing two circular DNA molecules.

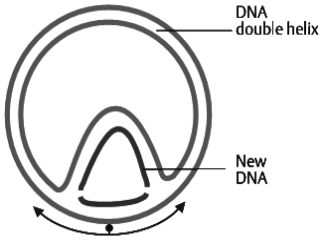


Fig. Circular replication in bacteria at one site

2. ***Rolling-circle replication*** is initiated by a nick in one strand of circular DNA, which produces a 3-OH group to which new nucleotides are added while the 5 end of the broken strand is displaced from the circle. Replication proceeds around the circle, producing a circular DNA molecule and a single-stranded linear molecule.

3. ***Linear eukaryotic DNA*** contains many origins of replication. At each origin, the DNA unwinds, producing two nucleotide strands that serve as templates. Unwinding and replication take place on both templates at both ends of the replication bubble until adjacent replicons meet, resulting in two linear DNA molecules.

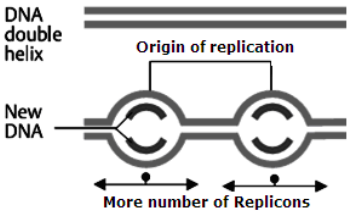


Fig. Replication in eukaryotes originates at many sites

REQUIREMENTS OF REPLICATION

Although the process of replication includes many components, they can be combined into three major groups:

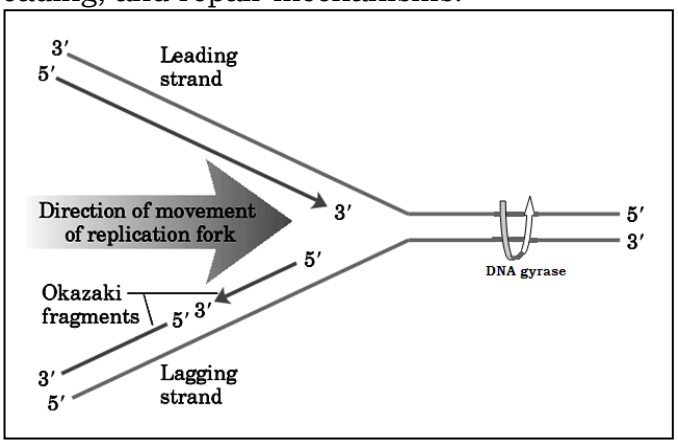
1. A template consisting of single-stranded DNA,
2. Substrates for new nucleotide strand, and
3. Enzymes and other proteins that *read* the template and assemble the substrates into a DNA molecule.

Table - Major components required for DNA replication in bacteria

Sl. No	COMPONENTS	FUNCTION
1.	Initiator protein	Initiates replication by binding to origin and unwinds DNA strands
2.	DNA helicase	Unwinds DNA at the replication fork
3.	Single-stranded binding proteins	Attach to single stranded DNA and prevent reannealing (re-joining)
4.	DNA gyrase	Moves before replication fork, cutting and resealing breaks in the DNA to release the torque developed in it due to unwinding of DNA
5.	DNA primase	Synthesizes short RNA primers
6.	DNA polymerase III	Elongates a new nucleotide strand
7.	DNA polymerase I	Replaces RNA primers with DNA
8.	DNA ligase	Joins Okazaki fragments by sealing sugar-PO_4 backbone

MAJOR STEPS IN DNA REPLICATION

1. Replication is always semi conservative. The DNA double helix separates and each strand serves as a template on which a new strand is synthesized.
2. A unit of replication that contains an origin of replication is called as a ***replicon***.
3. DNA synthesis is initiated by short segments of RNA called primers.
4. The elongation of DNA strands is always in the 5' to 3' direction.
5. New DNA is synthesized from dNTPs; in the polymerization of DNA, two phosphates are cleaved from a dNTP and the resulting nucleotide is added to the3-OH group of the growing nucleotide strand.
6. Replication is continuous on the leading strand and discontinuous on the lagging strand.
7. New nucleotide strands formed are complementary and antiparallel to their template strands.
8. Replication takes place at very high rates and is astonishingly accurate, due to precise nucleotide selection, proof reading, and repair mechanisms.



Replication begins when an initiator protein binds to a replication origin and unwinds a short stretch of DNA, to which DNA helicase attaches. *DNA helicase* unwinds the DNA at the replication fork and *single-strand-binding proteins* bind to single nucleotide strands to prevent them from reannealing. *DNA gyrase* (a

topoisomerase) removes the strain ahead of the replication fork that is generated by unwinding.

During replication, *primase* synthesizes short primers of RNA nucleotides, providing a 3'-OH group to which *DNA polymerase* can add DNA nucleotides. DNA polymerase adds new nucleotides to the 3' end of a growing polynucleotide strand. The leading strand is continuously synthesized in the direction taken by the replication fork. The other strand, the lagging strand, is synthesized discontinuously in short pieces (Okazaki fragments) in a direction opposite to that in which the replication fork moves. The Okazaki fragments are spliced together by DNA ligase. In bacteria, Okazaki fragments are ~1,000 to 2,000 nucleotides long. In eukaryotic cells, they are 150 to 200 nucleotides long.

Most cells have several DNA polymerases. E. coli has DNA polymerase III, which synthesizes new DNA on the leading and lagging strands and DNA polymerase I, which removes and replaces primers and is responsible for replication, recombination and repair.

DNA ligase seals nicks that remain in the sugar-phosphate backbones when the RNA primers are replaced by DNA nucleotides. The high accuracy of DNA replication is maintained by (1) base selection by the polymerase, (2) a 3' to 5' proofreading exonuclease activity that is part of most DNA polymerases, and (3) specific repair systems for mismatches left behind after replication.

EUKARYOTIC DNA REPLICATION

Although not as well understood, eukaryotic replication resembles bacterial replication in many respects. The most obvious differences are that eukaryotes have:(1) Multiple origins of replication in their chromosomes; (2) Different types of DNA polymerases, with different functions; and (3) Assembly of nucleosome immediately after DNA replication. Precise replication at multiple origins is ensured by a licensing factor that must attach to an origin before replication can begin. The licensing factor is removed after replication is initiated and renewed after cell division. Eukaryotic nucleosomes are quickly assembled on new molecules of DNA. The newly assembled nucleosomes consist of a random mixture of old and new histone proteins. The ends of linear eukaryotic DNA molecules are replicated by the enzyme *telomerase*.

28. RNA AS GENETIC MATERIAL

In most organisms, DNA carries the genetic information. However, in a few viruses RNA acts as the genetic material. This fact was demonstrated by Heinz Fraenkel-Conrat and Bea Singer in 1956. They worked with tobacco mosaic virus (TMV), a virus that infects and causes disease in tobacco plants. The tobacco mosaic virus possesses a single molecule of RNA surrounded by a helically arranged cylinder of protein molecules. Fraenkal-Conrat found that, after separating the RNA and protein of TMV, he could remix them and obtain intact, infectious viral particles.

Singer and Fraenkal-Conrat then created hybrid viruses by mixing RNA and protein from two different strains of TMV (Fig.). When these hybrid viruses infected tobacco leaves, new viral particles were produced. The new viral progeny were identical to the strain from which the RNA had been isolated and did not exhibit the characteristics of the strain that donated the protein.

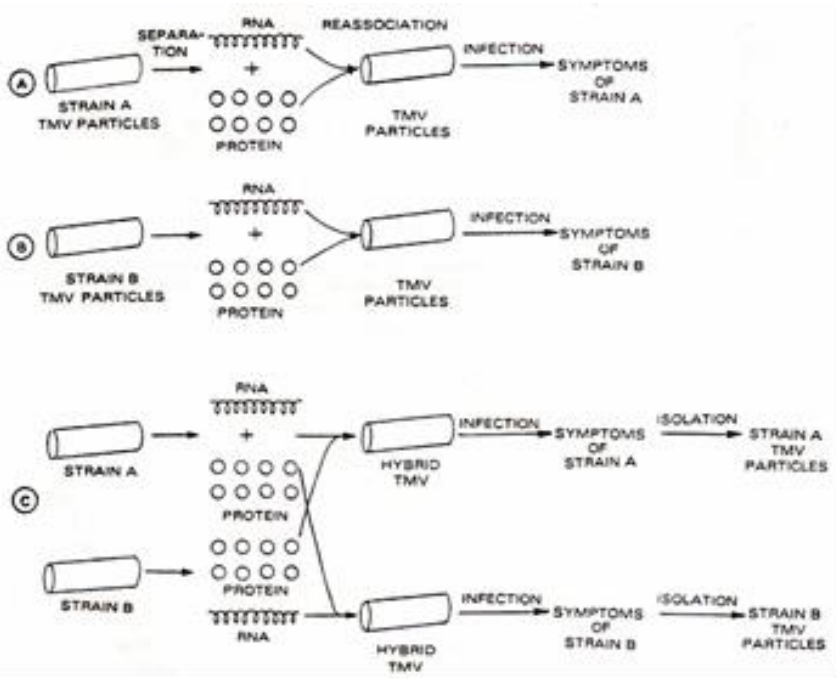


Fig. Fraenkal-Conrat and Singer's experiment showing RNA as genetic material in Tobacco Mosaic Virus

These results showed that RNA carries the genetic information in TMV. Also in 1956, Alfred Gierer and Gerhard Schramm demonstrated that RNA isolated from TMV is sufficient to infect tobacco plants and direct the production of new TMV particles, confirming that RNA carries genetic instructions. . It is now known that in many other viruses, e.g., animal viruses causing poliomyletis, influenza, encephalitis etc., most of the plant viruses, and some small bacteriophages (such as, F2, MS2, R17 etc.), RNA functions as the genetic material.

29. STRUCTURE OF RNA

RNA is similar in structure to DNA. However, there are significant differences, the key ones being:

Table. Differences between DNA and RNA

CHARACTERITICS	DNA	RNA
1. Strands	Double stranded	Single stranded
2.Secondary structure	Double helix	Many types
3. Sugar	Dexoy ribose	Ribose
4. Bases	A, T, G, C	A, U, G, C
5. Pairing	AT and GC	AU and GC
6. Replication	Self replicating	Formed from DNA, self replicating only in some viruses
7. Size	Up to 4.3 million nucleotides	Contains up to 12,000 nucleotides
8. Function	Genetic role	Protein synthesis and genetic role in some viruses (Eg. TMV, Plant Tumour virus)
9. Stability	Stable	Easily degraded

TYPES OF RNA: There are three types of RNA viz, mRNA, tRNA and rRNA. Their major functions and structure are as follows.

1. STRUCTURE OF MESSENGER RNA

Messenger RNA (mRNA) is the carrier of genetic information from the DNA to ribosomes, where this DNA transcript or template is translated into proteins. Because genes vary in size (number of nucleotides) the mRNA species are variable in length.

2. STRUCTURE OF TRANSFER RNA

The nucleotide sequence of the first tRNA (yeast alanyl tRNA) was determined by Robert Holley (1965), who proposed the clover leaf model of secondary structure of tRNA. The tRNA molecules are small, very stable and range from 75 to 90 nucleotides in size. They are single stranded molecules which are able to fold back onto itself and undergo complementary base pairing in short stretches to form double strands. This folding also creates four characteristic loops and a cloverleaf shaped 2D structure.

Each tRNA is specific for each aminoacid. tRNA molecule contains the sequence of CCA at the 3' end, called ***amino acid binding site.*** The terminal adenine residue is the point of attachment for an amino acid and hence is called ***the amino acid attachment (or binding) site***.

During protein synthesis, the amino acid corresponding to a particular mRNA codon that base pairs with the tRNA anticodon is attached to this terminal and transported to the appropriate segment of the mRNA. For example, a tRNA molecule specific for lysine cannot bind to the arginine. tRNA consists of three loops; ***(a) DHU-loop*** or D-loop aminoacyl recognition region, ***(b) The anticodon loop*** (or simply anticodon) contains a short sequence of bases, which permits temporary complementary pairing with the codons of mRNA. The stop codons do not have tRNA with anticodons for them. and ***(c) Thymine loop*** (ribosome attachment region).

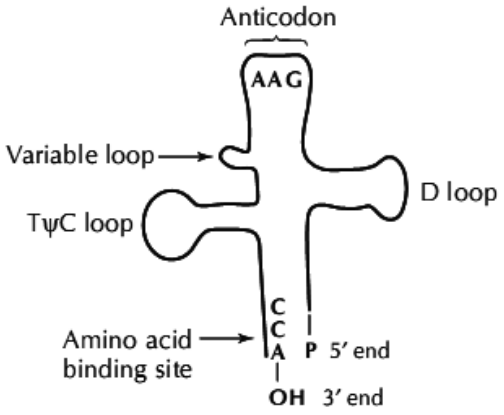


Figure 3.14 A tRNA molecule has a cloverleaf shape. The anticodon and the amino acid binding sites are critical in protein synthesis.

3. STRUCTURE OF RIBOSOMAL RNA

Ribosomes are the sites of protein synthesis. A ribosome consists of two subunits, which together form the monosome. The ribosomal particles are classified according to their sedimentation coefficient or rate (S). Monosomes of bacteria are 70S (70S ribosomes) whereas eukaryotic monosomes are about 80S.

Because sedimentation coefficients are not additive, a 70S monosome in actuality comprises two subunits that are 50S and 30S, while an 80S monosome consists of 60S and 40S subunits. A ribosome subunit consists of molecules of rRNA and proteins. For example, the 50S subunit contains one 55 rRNA molecule, one 235 rRNA molecule, and 32 different ribosomal proteins. A bacterial cell may contain about 1,000 ribosomes.

30. THE GENETIC CODE

It is clear from various experiments that a sequence of three nucleotides in mRNA, code for an amino acid. This triplet is referred to as ***codon.*** For example, the mRNA sequence AUG codes for the aminoacid methionine. The set of all the codons that specify the 20 amino acids is termed as ***the genetic code.*** The set of bases in tRNA which base pair with a codon of mRNA is known as ***anti-codon***. The sequence of bases in an anti-codon is exactly the opposite of that present in the codon. Since the codon and anticodon segments run anti-parallel to each other when they base pair, codons are written in 5' - 3' direction, and anticodons are written in 3' - 5' direction.

There are 20 amino acids involved in protein synthesis and there are only four bases (A,T,G,C) in the DNA coding for all the amino acids. Thus the 4 bases when arranged in the form of triplet code (4^3) can generate 64 codons. Of these, three codons, UAA, UAG and UGA do not code for any amino acid and serve as **stop codons** (*nonsense codons or termination codons*). One codon, AUG serves as ***initiation or start codon*** as it starts the synthesis of polypeptide chain. This codon also codes for amino acid methionine. In eukaryotes, the starting amino acid is methionine, while in prokaryotes it is N-formyl methionine.

It has become clear from various experiments that a sequence of three nucleotides in the mRNA codes for an amino acid (***a triplet code*** or codon), and that the code is ***non-overlapping*** and ***commaless*** (Fig. 23.2). A commaless code means that all the bases in a polynucleotide are parts of codons and that no base serves as a punctuation mark. The genetic code is said to be ***degenerate*** because nearly all amino acids are specified by at least two codons. Some (serine, arginine, leucine) are encoded by six different codons. Only tryptophan and methionine are encoded by single codons. Further, for a set of codons encoding the same amino acid, the first two letters in the figure are the same, with only the third being different (called the ***wobble hypothesis***).

First base	Second base: U	Second base: C	Second base: A	Second base: G	Third base
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Fig. The genetic code

31. CENTRAL DOGMA OF MOLECULAR BIOLOGY

The genetic information of the DNA is changed into biological material principally through proteins, according to the central dogma of molecular biology. The three major pathways of information flow in the cell include *replication*, wherein information passes from one DNA molecule to other DNA molecules; in *transcription*, information passes from DNA to RNA; and, in *translation*, information passes from RNA to protein. This concept of information flow was formalized by Francis Crick in a concept called the ***central dogma of molecular biology***.

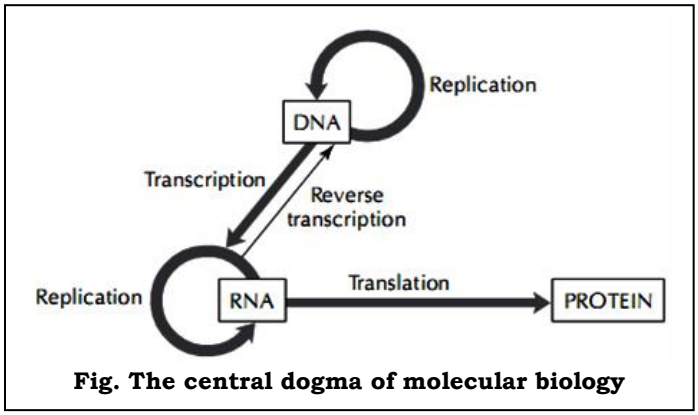


Fig. The central dogma of molecular biology

It was now realized that the central dogma is an over simplification. In addition to the three general information pathways of replication, transcription and translation, other transfers may take place in certain organisms or under special circumstances, including the transfer of information from RNA to DNA, (in *reverse transcription*) and the transfer of information from RNA to RNA (in *RNA replication*). Reverse transcription takes place in retroviruses and in some transposable elements while RNA replication takes place in some RNA viruses.

This flow of information can also be reversed *in vitro* (in the test tube) by scientists. Thus, once a protein is known, the nucleotide sequence in the prescribing DNA strand can be determined and synthesized (the product is called a complementary DNA or cDNA). Production of cDNA is a technique used in genetic engineering.

32. TRANSCRIPTION AND TRANSLATION

TRANSCRIPTION (mRNA SYNTHESIS)

The process of copying the genetic information of the DNA to mRNA (messenger RNA) is called as transcription. The DNA strand which is transcribed is called as the ***template strand or antisense strand*** and the other strand is called as *sense strand*. The mRNA thus produced is complementary to the template stand and identical to the sense strand.

(i) The process of transcription is carried out by enzymes called *RNA polymerases*. These polymerases begin by unwinding a portion of DNA near a special DNA sequence called *promoter* region.

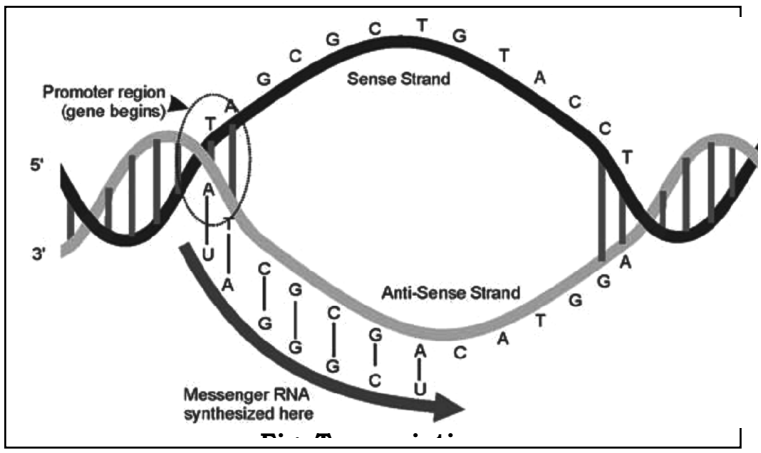
(ii) The transcription proceeds from 5' to 3' direction.

(iii) The beginning of the code for a specific polypeptide chain is always indicated by the start codon AUG. As it codes for the amino acid methionine, all proteins begin with methionine.

(iv) The end of the polypeptide sequence is indicated by the stop codons UAA, UAG, or UGA.

(v) The newly synthesized mRNA remaining inside the nucleus is called *hn-RNA (heterogeneous nuclear RNA)*.

(vi) This hnRNA is processed by capping it with methyl guanosine at the 5' end and by addition of a number of adenines (poly -A) at 3' end. This capping and addition of poly A-tail is to protect the mRNA from degradation by cytoplasmic enzymes.



(vii) This molecule undergoes severe alterations to remove *non-coding parts called introns*, leaving only the *coding parts or exons* to produce the mRNA. This mRNA is about 25% of the original length.

(viii) The mRNA is then transported from the nucleus to the ribosomes in the cytoplasm for protein synthesis.

As prokaryotes have only exons and no introns, the translation can begin even before transcription of the mRNA is complete. This is not possible in eukaryotes as the mRNA must be processed to remove the introns and the mRNA must leave the nucleus.

TRANSLATION (PROTEIN SYNTHESIS)

Translation is an unidirectional process by which the sequence of nucleotides present in the mRNA is translated into the sequence of aminoacids of a polypeptide chain. Usually, a small quantity of protein is synthesized in the nucleus, while the majority of the protein is synthesized in the cytoplasm. Ribosomes are the sites of protein synthesis. Translation requires mRNA, rRNA, ribosomes, 20 kinds of aminoacids and their specific tRNAs and many translation factors.

The process of translation (protein synthesis) consists of five major steps viz.,

(1) Activation of aminoacids
(2)Transfer of activated aminoacids to tRNA
(3) Chain initiation
(4) Chain elongation and
(5) Chain termination.

Each step is governed by specific enzymes and cofactors.

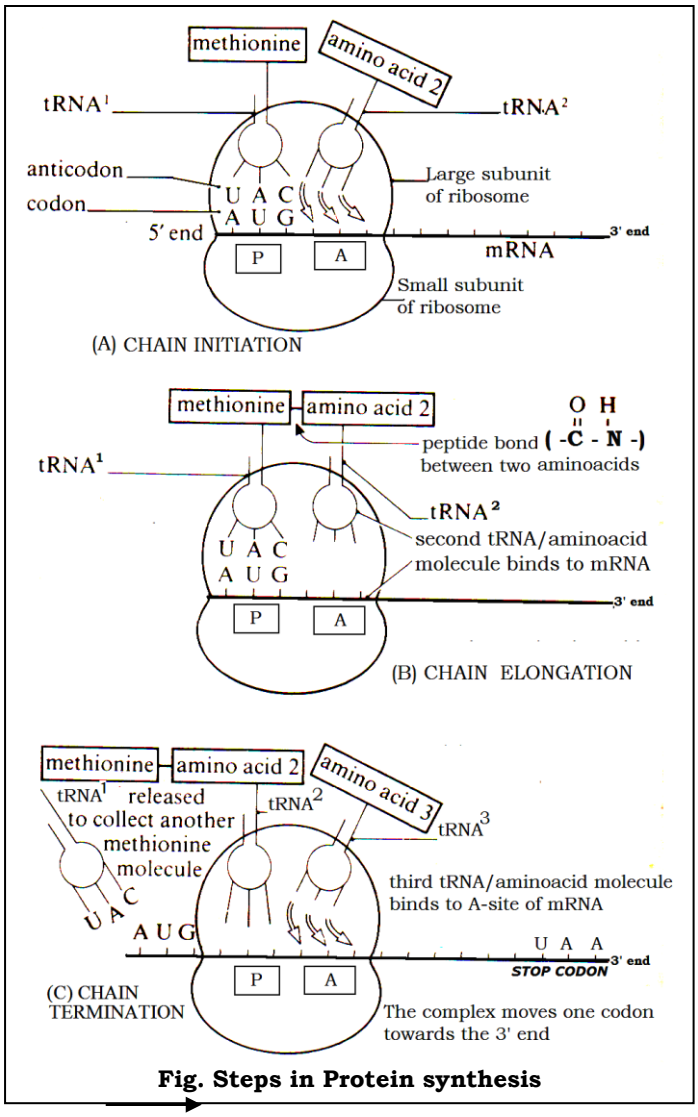


Fig. Steps in Protein synthesis

1. Activation of aminoacid

As the processed mRNA leaves nucleus, it binds to ribosome which serve as the site for protein synthesis. In the cytoplasm, the amino acids are activated in the presence of ATP. Then the enzyme amino acyl synthetase links with amino acid ~ AMP to form amino acyl adenylate enzyme complex. This complex is called *activated amino acid*.

Amino acid + ATP
⟶ AA~AMP + PP

AA~AMP + Amino acyl synthetase
⟶
AA~AMP - Enzyme

2. Transfer of activated aminoacid to tRNA

When an activated aminoacid collides with a specific tRNA, it binds with the A site (aminoacid attachment site) of tRNA, forming aminoacyl tRNA. The aminoacyl tRNA then moves towards the ribosome.

3. Chain initiation

Translation begins when an aminoacylated tRNA base pairs with the start codon AUG., present in the mRNA located in the smaller subunit of ribosome. The initiation codon and the small sub unit forms the *initiation complex* to which the larger subunit joins.

4. Chain elongation

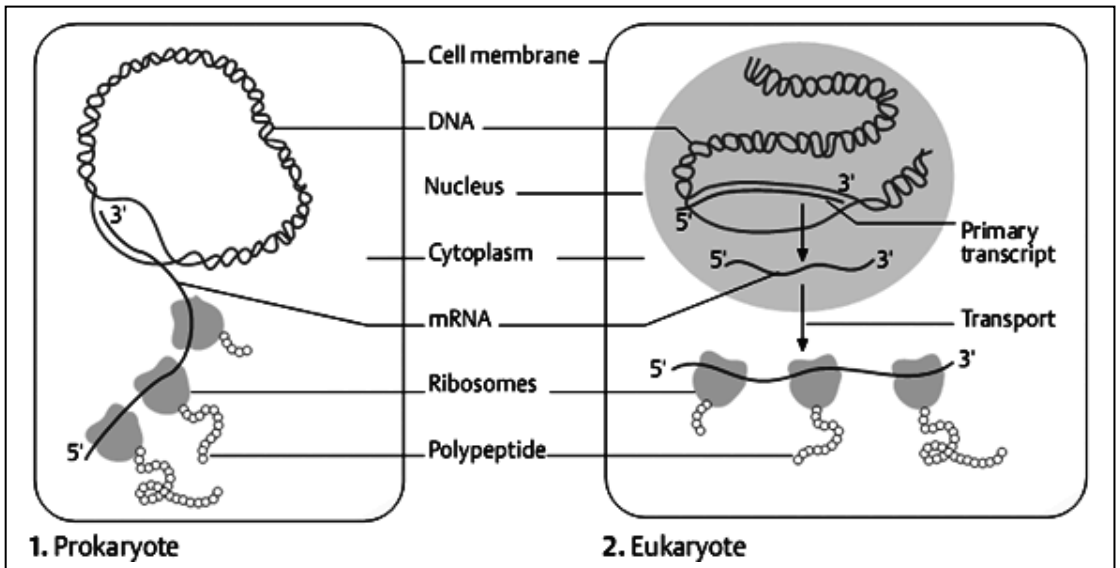
The ribosome has two distinct sites namely, A-site (acceptor or aminoacyl attachment site) and P-site (peptidyl site). Each new aminoacyl-tRNA enters the ribosome and attaches to A-site. The mRNA codon of A-site determines which charged tRNA with aminoacid will attach next. As soon as the next tRNA attaches at the A-site, a *peptide bond* is formed between the aminoacid (-COOH) on the A-site and the polypeptide (-NH2) on the P-site. The peptide bond formation is catalysed by the enzyme peptidyl transferase.

After the formation of peptide bond, the tRNA from P-site is released to the cytosol and the polypeptide chain is transferred to tRNA on A-site. Then, the tRNA on A-site is shifted to P-site, making A-site available for new tRNA. Then the ribosome complex moves one codon towards the 3' end on the mRNA, releasing the first tRNA from initiation point to pick another methionine. The free initiation point can now form a new initiation complex. During protein synthesis a number of ribosomes are attached to a single mRNA molecule, each forming a different polypeptide chain. The complex thus formed is known as ***polyribosome***. The process is repeated until the whole mRNA is translated, and adjacent amino acids are linked by peptide bonds.

5. Chain termination

The translation will proceed until a *releasing factor* binds to the *stop codon (UAA, UAG, UGA)* and terminates translation, as they does not code for any aminoacid. The interval between the start and stop codons is called the open reading frame (ORF).

The ribosome releases the polypeptide and mRNA and subsequently dissociates into two subunits. Further processing of polypeptide chain into proteins and enzymes is done in the cytoplasm itself depending on the bonding properties of the aminoacids in it. Most of the mRNA molecules are unstable and degraded after the release of polypeptide chain, but some mRNAs such as those coding for hemoglobin may be stable.



Transcription and translation in prokaryote and eukaryotes

Polyribosomes or polysomes: Many ribosomes read one strand of mRNA simultaneously, helping to synthesize the same protein at different spots on the mRNA.

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PROTEIN STRUCTURE

Polypeptides are precursors of proteins. Polypeptides fold to assume 3-dimensional forms, which are the functional stage of proteins. There are four basic levels of protein structure namely, primary, secondary, tertiary, and quaternary. The primary structure of proteins is the sequence of the amino acids. The secondary structure is an a-helix which is stabilized by hydrogen bonds. The tertiary structure is a 3D conformation of the entire chain in space. Proteins with more than one polypeptide chain may exhibit the quaternary protein structure through aggregations of the polypeptides.

33. DNA PROTECTION AND REPAIR SYSTEMS

The genetic material must retain its structure with a very high fidelity during replication and transcription and protects itself from damages. Bacteria and other organisms protect their genetic material from contamination by foreign DNA through the action of restriction enzymes, which disintegrates the DNA molecules possessing specific recognition sites. However, the restriction enzymes of an organism do not attack its own DNA due to ***methylation*** of the restriction site.

DNA METHYLATION

DNA methylation refers to the addition of methyl group ($-CH_3$) to the DNA bases namely, adenine and cytosine to yield
6-methyladenine and 5-methylcytosine, respectively. DNA methylation is mediated by enzymes called methylases. *E.coli* has three distinct methylation systems.

i) *The hsd system*: This system methylates adenine. Occur in many bacteria.

ii) *The dam system*: This system also methylates adenine and is involved in the control of DNA replication and in marking DNA strands for repair.

iii). *The dm system*: It methylates cytosine., Its function is still unknown.

ROLE OF DNA METHYLATION

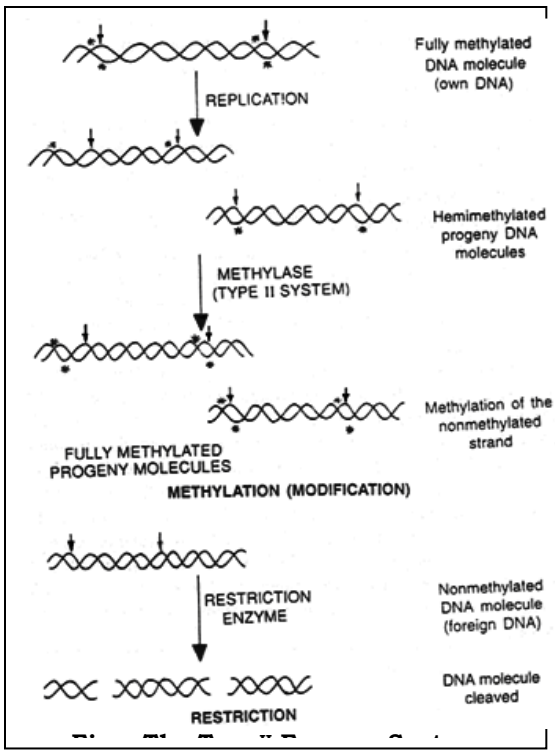
In prokaryotes, methylation is involved in the modification of restriction sites, DNA repair and control of replication. In Eukaryotes it is concerned with the regulation of gene action. DNA molecules having the same methylation pattern will be recognised as own DNA and those without methylation will be regarded as foreign DNA and is destroyed by restriction enzymes.

The restriction enzymes are enzymes, which produce cuts within DNA molecules. As a rule they recognize highly specific, short base sequences for binding to DNA molecules and may produce the cut either within the recognition site (Type II restriction enzymes) or awayd from this site (Type I and III restriction enzymes). Type II systems consist of separate enzymes for methylation and restriction activity while in type I and III systems the same enzyme carries out both the activities.

The Type^{II} Enzyme system

The type^{II} system is widespread in bacteria' about 1/3 of the bacterial strains have them. In this system a type^{II} restriction enzyme is responsible for clearing the DNA, while a separate enzyme methylates the same site which is recognized by the restriction enzyme. Eg : Eco R1 system in which the restriction enzyme is a dimer of identical polypeptides, while the methylase is a monomer (Fig.).

The recognition sites for type II enzymes are generally palindromes of 4-6 bp so that the bases to be methylated occur on both the strands. The replication of a fully methylated target site yields target sites that are hemimethylated. "The restriction enzymes do not recognize either fully methylated or hemimethylated generally recognize the hemimethylated DNA molecules and brings about the methylation of their non-methylated strands to make them fully methylated".



DNA DAMAGE

The various damages to DNA may be grouped into the following two types:

(i) Single Base Changes affecting a single base of a DNA molecule. It involves the conversion of one base into another. E.g., Deamination of 5 methylcytosine results in thyamine. (ii) Addition of a small group to a base affects its pairing behavior.

Single base changes do not produce structural disturbance and do not affect replication and transcription of the affected molecules.

(ii) **Structural Distortions** generally adversely affect the replication and transcription of the affected DNA molecule. They are represented by a single strand nick, removal of a base etc.

DNA REPAIR

One of the best understood repair mechanisms involves removal of pyrimidine dimers (usually covalently linked adjacent thymines in the same strand). Thymine dimers are easily induced in bacteria by ultraviolet (U V) light. These dimers are lethal if left unrepaired because they interfere with the normal replication of progeny DNA strands. There are at least three mechanisms known for repairing pyrimidine dimers.

A. EXCISION REPAIR / PHOTOREACTIVATION

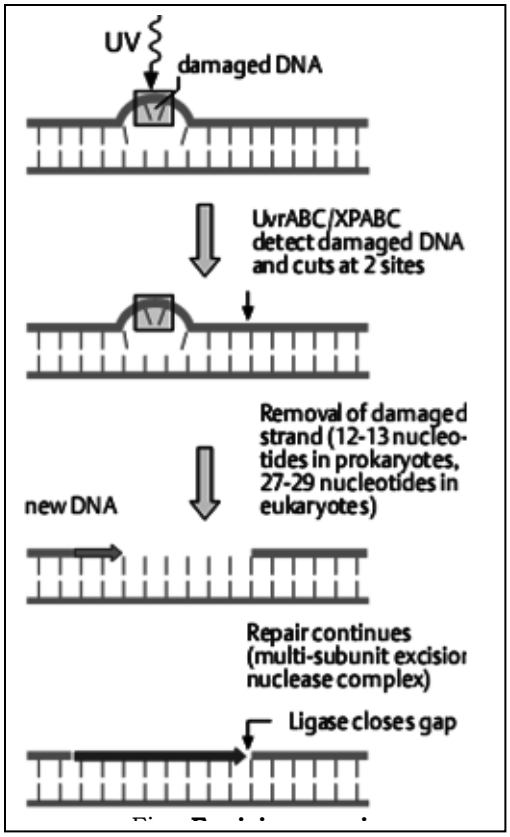
Some cells, such as the bacterium *E. coli*, contain a light-dependent enzyme that can remove or correct damaged DNA. Excision is a four-step process:

a. One strand is broken by an enzyme called UV endonuclease.
b. A DNA polymerase removes nucleotides near the cut, including the damaged area.

c. A DNA polymerase replaces the nucleotides with the correct ones, working from the uncut complementary strand.

d. An enzyme called polynucleotide ligase seals the break.

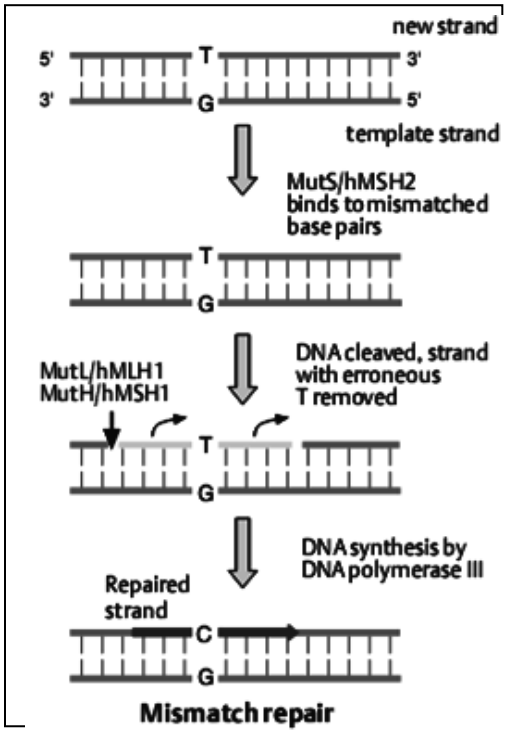
The damaged strand of DNA is distorted and can be recognized by a set of three proteins, the *UvrA, UvrB, and UvrC endonucleases* in prokaryotes and XPA, XPB, and XPC in human cells. This DNA strand is cleaved on both sides of the damage by an exonuclease protein complex, and a stretch of about 12 or 13 nucleotides in prokaryotes and 27 to 29 nucleotides in eukaryotes is removed. DNA repair synthesis restores the missing stretch and a DNA ligase closes the gap.



B. MISMATCH REPAIR

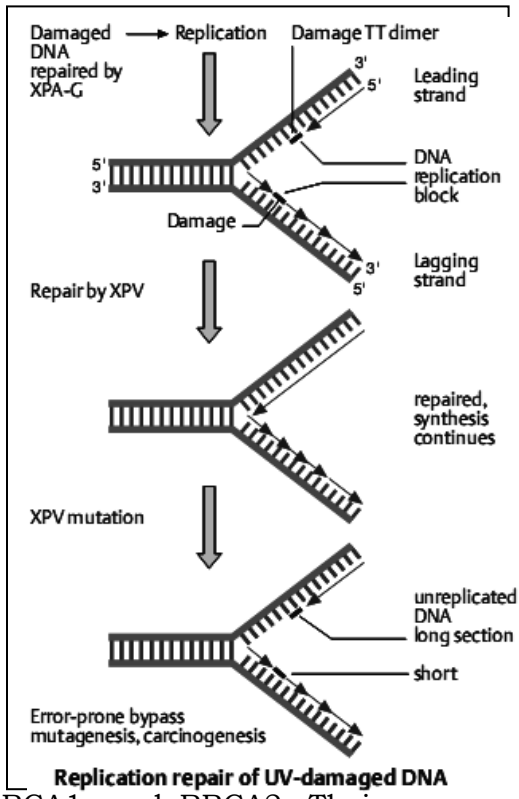
Mismatch repair corrects errors of replication in which the bases that are not paired with their proper counterparts can also be repaired using excision. However, the newly synthesized DNA strand containing the wrong base must be distinguished from the parent strand, and the site of a mismatch identified. The former is based on a difference in methylation in prokaryotes. The daughter strand is undermethylated at this stage.

E. coli has three mismatch repair systems: long patch, short patch, and very short patch. The long patch system can replace 1 kb DNA and more. It requires three repair proteins, MutH, MutL, and MutS, which have the human homologues hMSH1, hMLH1, and hMSH2. Mutations in their respective genes lead to cancer due to defective mismatch repair.



C. REPLICATION REPAIR OF UV-DAMAGED DNA

DNA damage interferes with replication, especially in the leading strand. Large stretches remain unreplicated beyond the damaged site (in the 3' direction of the new strand) unless swiftly repaired. The lagging strand is not affected as much because Okazaki fragments (about 100 nucleotides in length) of newly synthesized DNA are also formed beyond the damaged site. This leads to an asymmetric replication fork and single-stranded regions of the leading strand. Aside from repair by recombination, the damaged site can be bypassed.



Replication repair of UV-damaged DNA

D. DOUBLE-STRAND REPAIR BY HOMOLOGOUS RECOMBINATION

Double-strand damage is a common consequence of ! radiation. An important human pathway for mediating repair requires three proteins, encoded by the genes ATM, BRCA1, and BRCA2. Their names are derived from important diseases that result from mutations in these genes: ataxia telangiectasia and hereditary predisposition to breast cancer (BRCA1 and BRCA2, see p. 328. ATM, a member of a protein kinase family, is activated in response to DNA damage (1). Its active form phosphorylates BRCA1 at specific sites (2). Phosphorylated BRCA1 induces homologous recombination in cooperation with BRCA2 and mRAD5, the mammalian homologue of E. coli RecA repair protein (3). This is required for efficient DNA double-break repair. Phosphorylated BRCA1 may also be involved in transcriptionand transcription-coupled DNA repair (4).

E. SOS REPAIR

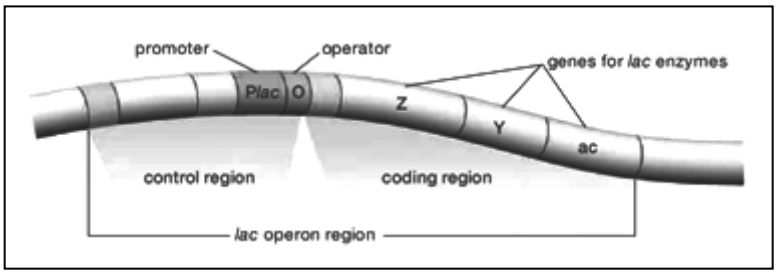
Breaks in a DNA strand can sometimes simply be sealed without any regard for the original sequence. This is seen in cases of extreme DNA damage. While this may allow the cell containing the damaged DNA to survive, it greatly increases the possibility that the cell will contain one or more mutations.

34. REGULATION OF GENE EXPRESSION
1. PROKARYOTES

Regulation of gene expression is important for proper growth and development as the gene should be expressed at the appropriate time and to the desired level. Regulation involves the turning on and turning off of genes. Gene expression may be controlled at any point along the molecular pathway from transcription, mRNA processing, RNA stability, translation, and posttranslational modification.

STRUCTURE OF OPERON

The significant difference in prokaryotic and eukaryotic gene regulation is the organization of functionally related genes. Many bacterial genes that have related functions are clustered and are under the control of a single promoter. These genes are often transcribed together into a single mRNA. In contrast, the eukaryotic genes are dispersed, and each gene is transcribed into a separate mRNA.



A group of bacterial structural genes that are transcribed together, along with their promoter and additional sequences that control transcription, is called an operon.

REGULATION OF OPERON

There are two basic categories of gene regulation: *negative* and *positive*. In negative regulation, an inhibitor that is bound to a DNA must be removed in order for transcription to occur. In positive regulation, gene transcription occurs when an activator binds to the DNA. Some operons are inducible, in which transcription is normally off and must be turned on. Other operons are repressible; transcription is normally on and must be turned off.

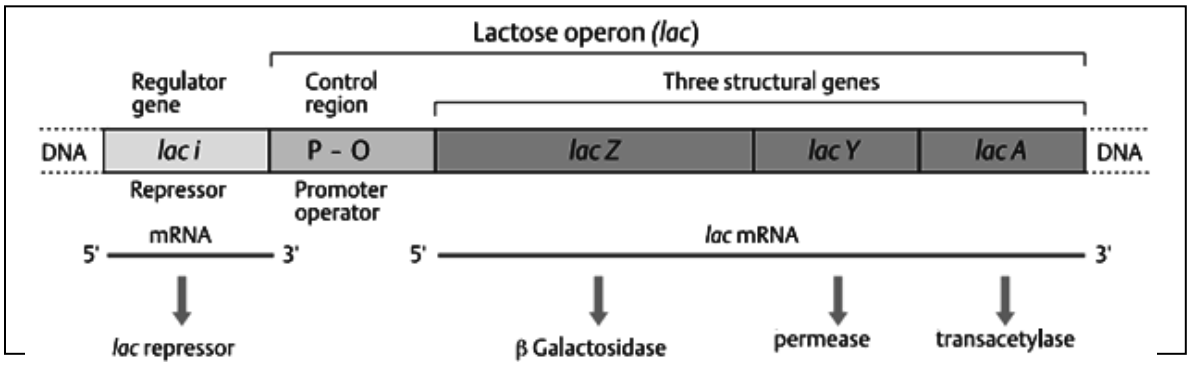
THE *LAC* OPERON OF *E. COLI*

The Operon concept was proposed by Jacob and Monod in 1961. An Operon is a group of structural genes whose transcription is regulated by the coordinated action of a regulator 'r', a promotor 'p' and an operator 'o' gene. The three structural genes of *E. coli* bacterium namely, *lac*Z, *lac*Y and *lac*A forms the lactose operon (*lac* operon).

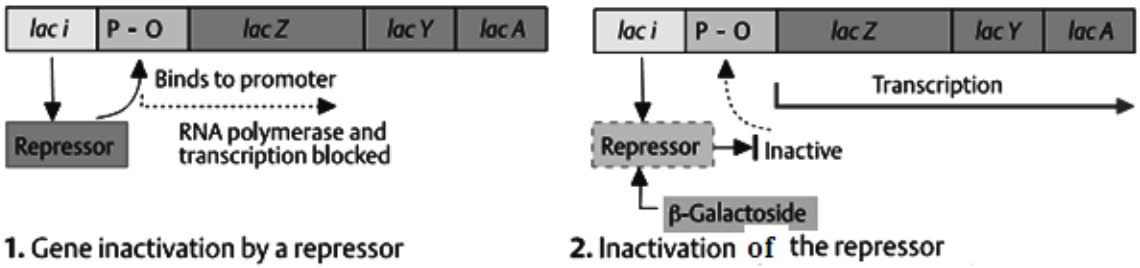
The *lac* operon of E. coli controls the transcription of three genes in lactose metabolism: the *lac*Z gene, which encodes β-galactosidase; the *lac*Y gene, which encodes permease; and the *lac*A gene, which encodes thiogalactoside transacetylase.

Mechanism of *lac* operon model

When *E. coli* is cultured in a medium devoid of lactose, the enzymes for lactose catabolism are not required. In such cases the lac-operon remains switched off or repressed. Under such conditions, the regulator gene produces a repressor protein. The repressor binds to the operator site, preventing the binding of RNA polymerase and inhibits transcription of structural genes.



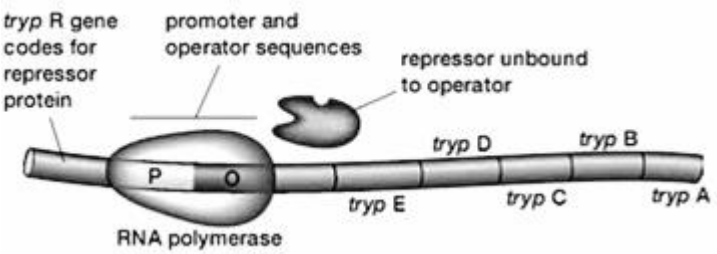
When lactose is present in the medium, some of it is converted into allolactose which binds to the regulatory protein (repressor), making it inactive. The binding of RNA polymerase is not blocked and hence, the transcription of *lac*Z, *lac*Y and *lac*A takes place and *lac* enzymes are produced for the catabolism of lactose.



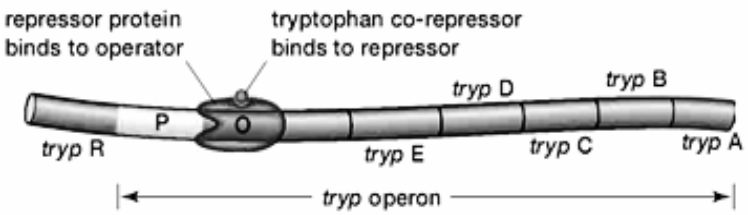
1. In the absence of lactose, the regulator protein (a repressor) binds to the operator and inhibits transcription. 2. When lactose is present, some of it is converted into allolactose which binds to the regulatory protein (repressor), making it inactive. Hence, structural genes are transcribed and translated.

THE trp OPERON

The trp operon is a repressible operon that controls the biosynthesis of tryptophan. In a repressible operon, transcription is normally turned on and must be repressed. Repression is accomplished through the binding of tryptophan to the repressor, which renders the repressor active. The active repressor binds to the operator and prevents RNA polymerase from transcribing the structural genes.



When tryptophan levels are low , the repressor protein is present but does not bind to the operator. The RNA polymerase is thus able to bind to the promoter and transcription occurs



When tryptophan level is high, tryptophan binds to the repressor protein. As a result, the repressor binds more readily to the operator, thereby preventing RNA polymerase from binding and prevents transcription

CISTRON : A sub division of gene which acts as a unit of function with a gene.
MUTON : A sub division of gene which is the site of mutation.
RECON : The smallest subunit of gene capable of undergoing recombination.

COMPLEMENTATION TEST

A complementation test is one in which individuals homozygous for different mutations are crossed and it can be used to determine if the mutations occur at the same locus or at different loci.

INTRON refers to the non-coding region of the eukaryotic genes that are transcribed into mRNA. They are removed by splicing of RNA.

EXON refers to the region of DNA that codes for a protein. In eukaryotes, the exons are separated by many introns.

35. REGULATION OF GENE EXPRESSION
2. EUKARYOTES

Many features of gene regulation are common to both bacterial and eukaryotic cells. For example, in both types of cells, DNA-binding proteins influence the ability of RNA polymerase to initiate transcription. However, there are also some differences.

First, eukaryotic genes are not organized into operons and are rarely transcribed together into a single mRNA molecule; instead, each structural gene typically has its own promoter and is transcribed separately.

Second, chromatin structure affects gene expression in eukaryotic cells; DNA must unwind from the histone proteins before transcription can take place.

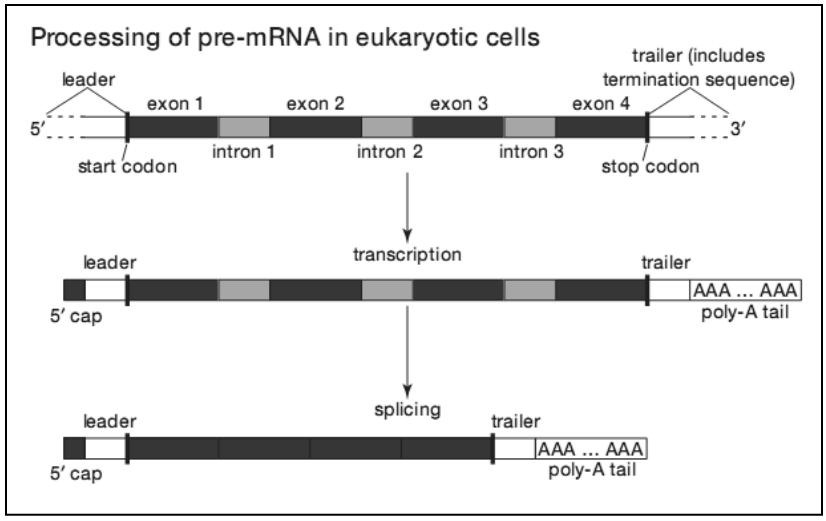
Third, although both repressors and activators function in eukaryotic and bacterial gene regulation, activators seem to be more common in eukaryotic cells.

Finally, the regulation of gene expression in eukaryotic cells is characterized by a greater diversity of mechanisms that act at different points in the transfer of information from DNA to protein.

There are three major methods by which eucaryotic cells are known to regulate translation: A) by altering the life of the mRNA, B) by controlling the initiation of translation, and C) by changing the overall rate of translation.

A typical eucaryotic mature mRNA consists of four major regions: A) a 5' noncoding region (leader), B) a coding region, C) a 3' noncoding region (trailer), and D) a poly-A tail. Each of the four segments may affect the half-life of mRNA molecules.

Eucaryotic genes contain introns (noncoding regions) interspersed among the coding regions (exons). Part of the process that converts primary transcripts to complete mRNA molecules involves removal of the introns and splicing the exons together. Variations in the excision and splicing jobs can lead to different mRNAs and, following translation, to different protein products.



Eukaryotic gene regulation is less well understood than bacterial regulation, partly owing to the larger genomes in eukaryotes, their greater sequence complexity, and the diffi- culty of isolating and manipulating mutations that can be used in the study of gene regulation. Nevertheless, great advances in our understanding of the regulation of eukaryotic genes have been made in recent years, and eukaryotic regulation continues to be one of the cutting-edge areas of research in genetics.

Gene and Enzyme sequences

In bacteria and viruses, genes governing enzymes of a metabolic pathway are, in many cases clustered together. Often the sequence of these genes closely corresponds the sequence of involvement of the enzymes produced by them in the metabolic pathway. For eg., in *Salmonella*, histidine biosynthesis involves nine clustered genes occurring in the order E-I-F-A-H-B-C-D-G. This is precisely the sequence in which the enzymes produced by them participate in histidine biosynthesis, except that the last gene, G controls the first enzyme pyrophosphorylase. However, in eukaryotes such a correlation is generally lacking. For eg., in *Neurospora* genes concerned with the biosynthesis of the same amino acid are located in different chromosomes. Thus the situation found in *salmonella*, *E.coli* etc. appears to be a primitive genetic organization.

One – Gene – One Enzyme Hypothesis

This was originally postulated by Beadle and Tatum in 1941. From their work on *Neurospora* biochemical mutants, they concluded that each gene controlled a single specific chemical reaction. Genes control chemical reactions by controlling the presence of specific enzymes catalysing these reactions. Thus one – gene – one enzyme hypothesis simply states that each gene controls a single specific enzyme. One of the first clear-cut proofs for this hypothesis came from arginine biosynthesis pathway in *E. coli*. The pathway consists of eight chemical reactions each cataylsed by a specific enzyme. The presence of each gene as specific enzymes are absent in mutants for specific genes.

One - Gene – One Polypeptide Hypothesis

Many enzymes (and protein molecules) are composed of a single polypeptide and are termed as monomers, while others are made up of two or more polypeptides and are known as dimers, tetramers etc., depending on the number of polypeptides in the moelcule. A polypeptide consists of several amino acids joined by peptide bonds and generally lacks full protein activity. It is now accepted that each polypeptide is controlled by a single specific gene. For eg., trptophan synthetase in *E.coli* consists of four polypeptide chains, two alfa and two beta chains, which are governed by two different genes located adjacent to each other. Similarly, a haemoglobin molecule has four polypeptide chains of two distinct types therefore two $\propto$ and two β polypeptides. Polypeptides $\propto$ and β are specified by two different genes located in two different chromosomes.

Thus the one – gene – one enzyme hypothesis is valid for only those enzymes that are composed of a single polypeptide. In addition, many genes specify non-enzyme protein molecules, eg., haemoglobin, myoglobin structural proteins etc. Therefore the one - gene – one polypeptide hypothesis proposed by Ingram is more appropriate and accounts for monomeric as well as dimeric etc., enzymes and for non-enzyme proteins.

"According to this hypothesis, a gene specifies a single polypeptide chain". However, many genes do not produce any polypeptides, eg., operator and promotor genes, and the genes specify tRNA (transfer RNA) and rRNA (ribosomal RNA). Therefore one – gene – one polypeptide hypothesis may be regarded as applicable to those genes which specify polypeptide sequences, that is structural and regulator genes.

Genetic control of protein (or) polypeptide structure

Proteins (or polypeptides) are composed of several smaller sub units, amino acids. There are 20 different amino acids that occur in most of the proteins. Each amino acid has an alpha carbon atom to which four groups are attached: a carboxyl group (-COOH) with a potential negative charge an amino group ($-NH_2$) with a potential positive charge ($NH3^+$), an H atom and a polar or non polar side chain (R). The side chain (R) may consists of a single H atom (alanine), several carbon atoms (lysine, arginine) or even a benzene ring (phenylalanine). The carboxyl group of one and the amino group of the other of two neighbouring amino acids react to produce a peptide linkage and one molecule of water is released. The peptide linkages, elucidate by Emil Fischer, link together sequence yielding a polypeptide chain. The polypeptide chain, therefore has a back bone of alpha carbon alternated with linkage i.e., repeats, with the side chains (denoted by R) dangling away from the alpha-carbon atoms; this may be represented as polypeptide structure.

36. FINE STRUCTURE OF GENES

MODERN CONCEPT OF GENE

The fine structure of a gene is the linkage map of its various mutant alleles. In this map, the sites of mutational changes in different alleles of the same gene are determined on the basis of the frequency of recombination among these alleles. Thus the fine structure map of a gene is essentially comparable to the linkage map of a chromosome [except for the number of genes involved (one in the case of gene fine structures and several in the case of chromosome maps)]. Understandably, the values of crossing over observed in the studies on fine structure of a gene are very low (e.g., 0.01 or even 0.0001%). Therefore extremely large progeny populations have to be effectively screened for efficient identification of the cross over products.

For this reason, fine genetic analysis is more convenient in prokaryotes than in eukaryotes.

THE FINE STRUCTURE OF A GENE IN A PROKARYOTE

The most extensive fine structure map of a locus constructed to date is that of the r II locus of T4 phage of *E.coli* due to Seymour Benzer. T4 is similar to T2 in morphology, is an obligate parasite like all viruses, and contains a chromosome of about 200,000 bp (base pairs) long, which is packed within its head. When a T4 phage particle infects a cell of *E. coli* the bacterial cell lyses in about 20 – 25 minutes liberating 200 - 300 progeny phage particles.

When *E. coli* cells are plated (in an agar medium in petriplates) in sufficiently large numbers they produce a uniform confluent growth or 'lawn'. If individual T_4 particles are placed on the surface of an agar medium seeded with a lawn of *E. coli* cells, each phage particle would initiate a chain of infection-lysis so that all the *E. coli* cells in the immediate vicinity of the phage particles will be lysed. This leads to the development of clear zones, called plaques, the lawn of bacterial cells. The plaques produced by the wild type T_4 particles are relatively small with fuzzy or turbid margins called halos. The halos are produced due to a phenomenon called lysis inhibition, which is a delay in the lysis of T_4-infected *E. coli* cells as a consequence of its subsequent infection by another T_4 particle.

The R^{II} LOCUS

Several mutants of T_4 do not exhibit lysis inhibition, and produce relatively large plaques with clear margins, these mutants are called rapid lysis mutants and are denoted by r. Most of the r mutants map in one of the three distinct loci called r^{I}, r^{II} and r^{III}. Mutants in the r^{II} locus are easily recognized due to their inability to multiply in *E. coli* strain K_{12} (λ), which has the chromosome of phage λ integrated, in its chromosome. However, r^{II} mutants grow rapidly in other strains of *E. coli* e.g., strain B and K_{12} (lacking the λ chromosome). Thus r^{II} mutants are conditional lethal as they are unable to grow in K_{12} (λ) ; this property was exploited by Benzer for a genetic analysis of r^{II} locus.

COMPLEMENTATION TEST

Benzer isolated over 3000 independent mutants of the rII locus and subject them to complementation test. For this purpose, cells of E. coli strain K12 (λ) were infected with a mixture of the two rII mutants to be tested. Free phage particles not involved in infection were removed from the suspension of bacterial cells through centrifugation. Many bacterial cells will be infected by particles of both the mutants. If there is complementation between the two rII mutants, the phages will multiply in such host cells and lyse them releasing progeny phage particles. However, if there was no complementation, they will fail to multiply and no progeny phage particles will be released.

A suspension of *E. coli* K_{12} (λ) cells infected in this manner is kept for about 90-120 minutes to permit phage multiplication and bacterial-cell lysis samples from the whole suspension or its supernatant are now placed on *E. coli* strain b lawn to detect the presence of phage particles. "If plaques develop on *E. coli* B lawn, it reveals complementation between the two r^{II} mutants used for co-infection; while the absence of plaques signifies a lack of complementation".

Benzer placed two r^{II} mutants which failed to complement each other in two arbitrary groups designated as A and B. Each of the r^{II} mutants showed complementation either with the mutant belonging to group A or with that belonging to group B, but never with both. Thus all r^{II} mutants could be classified into two clear cut groups (group A and B); mutants of one group showed complementation with the mutants of the other group, but mutants within a group failed to complement each other. Thus the r^{II} locus was divided into two cistrons, cistron A (r^{II} A, represented by the r^{II} mutant of group A) and cistron B (r^{II} B evidenced by the r^{II} mutants of group B) on the basis of complementation test.

THE ULTIMATE FINE STRUCTURE OF GENE

"The complementation test resolves a locus into distinct cistrons, while the recombination test maps different mutants within each of the cistrons". The recombination mapping, however, relates to only those regions of a gene that are involved in coding of amino acids of the concerned polypeptide (called exons for expressed sequences). But most eukaryotic genes have one or more intervening non-coding sequences (called introns) within their genes. Such features of the genetic fine structure are revealed only by partial or total determination of the nucleotide sequence of a gene, which constitutes the ultimate fine structure of a gene. Introns and exons are collectively known as split genes since their coding sequences are split into several parts due to the introns.

37. JUMPING GENES

Most genes reside at a specific locus or position on the chromosome. Some genes or closely linked sets of genes can mediate their own movement from one location to another location in a chromosome. These elements are called as "jumping genes," "mobile elements." "cassettes," "insertion sequences," and "transposons." The formal name for this family of mobile genes is transposable elements, and their movement is called *transposition*.

NATURE OF TRANSPOSONS

Transposable elements were first discovered in maize and later in phages, bacteria, fungi, insects, viruses and human beings. Barbara McClintock was awarded the Nobel Prize in 1983 for the discovery of transposons in maize. They make up at least 50% of human DNA. Most transposable elements are able to insert at different locations and cause mutations either by inserting into another gene or by promoting DNA rearrangements such as deletions, duplications and inversions.

The transposable elements of bacteria is grouped into

1. **Simple transposons** (Insertion sequences, or IS) carry only the genetic information necessary for their transposition and
2. **Complex transposons** contain additional genetic material unrelated to transposition.

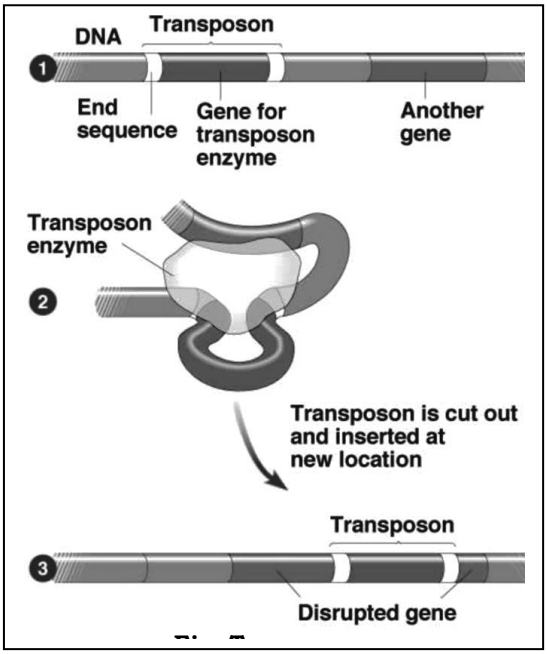
STRUCTURE OF A TRANSPOSON

Most transposons have *short direct repeats* of 3 to 12 base pairs on both sides. They are not a part of a transposable element and do not travel with it but are generated in the process of transposition, at the point of insertion. Also, they have the presence of identical, inverted terminal repeat sequences of 8-38 base pairs. The presence of flanking direct repeats indicates that staggered cuts are made in the target DNA when a transposable element inserts itself. The staggered cuts leave short, single-stranded pieces of DNA on either side of the transposable element. Replication of the single-stranded DNA then creates the flanking direct repeats.

At the ends of transposable elements are *terminal inverted repeats*, which are sequences from 9 to 40 bp in length that are inverted complements of one another. Each type of transposon has its own *unique inverted repeat*. The sequence into which a transposable element inserts is called the *target sequence*.

MECHANISM OF TRANSPOSITION

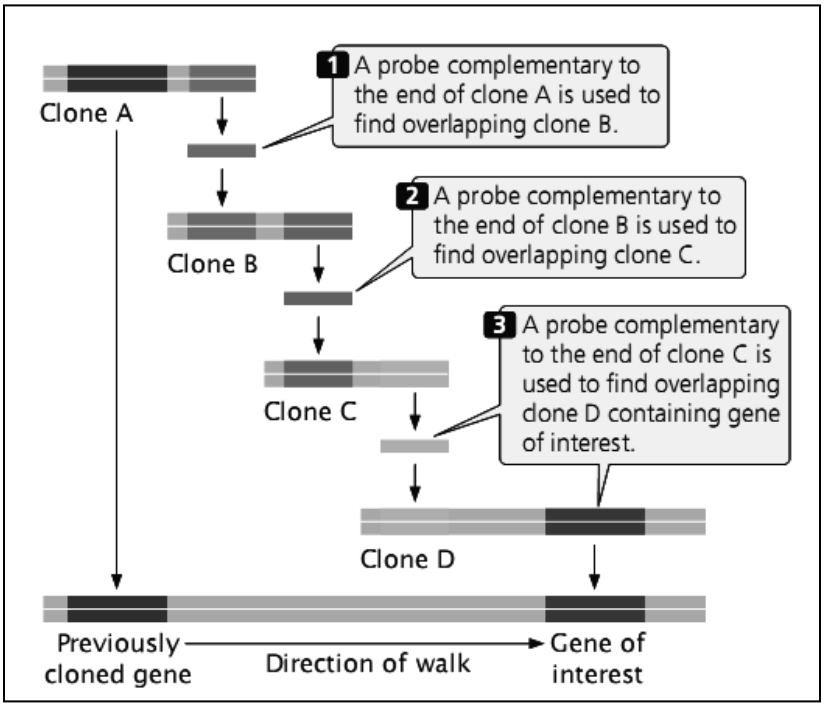
Transposition refers to the movement of a transposable element from one location to another. Two models of transposition in prokaryotes have been proposed, on the basis of the fate of the donor site.



1. *In non-replicative transposition,* the transposon might be excised from the donor site, leaving no copy of itself at the donor site. It is also called as conservative model.

2. *In replicative transposition,* the transposon might be replicated, allowing one copy to transpose to another site and leaving an identical copy at the donor site. The replicative mode could produce multiple copies at various sites in the genome. In bacteria, the number of copies of a transposon appears to be regulated, seldom exceeding 20 copies per genome. In eukaryotes, however, the copy number can be very high.

CHROMOSOME WALKING



In chromosome walking, a gene is first mapped in relation to a previously cloned gene. A probe made from one end of the cloned gene is used to find an overlapping clone, which is then used to find another overlapping clone. In this way, it is possible to walk down the chromosome to the gene of interest.

The basis of chromosome walking is the fact that a genomic library consists of a set of overlapping DNA fragments. We start with a cloned gene or DNA sequence that is close to the new gene of interest so that the "walk" will be as short as possible. One end of the clone of a neighboring gene (clone A in Figure) is used to make a complementary

probe. This probe is used to screen the genomic library to find a second clone (clone B) that overlaps with the first and extends in the direction of the gene of interest. This second clone is isolated and purified and a probe is prepared from its end. The second probe is used to screen the library for a third clone (clone C) that overlaps with the second. In this way, one can walk systematically toward the gene of interest, one clone at a time. A number of important human genes and genes of other organisms have been found in this way.

38. TWINS

Twins refers to a pair of offspring that go through the same gestation period at the same time in the same mother. Analysis of twins is an important technique for the study of human genetic characteristics. Twins are also common in many animal species, such as cats, sheep, ferrets, giant pandas, dogs and deer. Twins are of two types 1. Identical or monozygotic twins and 2. Non-identical or fraternal twins.

1. IDENTICAL TWINS

The identical twins are formed when a single egg fertilized by a single sperm splits into two during development forming two separate embryos. Hence, they are also called as ***monozygotic twins***. They are nearly 100% genetically similar and are called as identical twins. They are of same sex and always have a common placenta (monoplacental). They may share a common amniotic cavity (monoamniotic) or lie in two amniotic cavities (diamniotic).

Identical twins do not have the same fingerprints, as even in a small space inside the womb, the offspring have contact with different parts of the environment, which gives small variations and make them unique..

Conjoined twins (Siamese twins) are monozygotic twins whose bodies are joined together during pregnancy. This occurs where the single zygote of MZ twins fails to separate completely, and the zygote starts to split after day 12 following fertilization.

2. NON-IDENTICAL / FRATERNAL TWINS

Nonidentical twins or ***fraternal twins*** are formed by fertilization of two separate eggs by two different sperms. Hence, they are called as ***dizygotic twins***. They have 50% of the genes in common and may be of different sex. They always have a separate amniotic cavity and are diamniotic. They may either be monoplacental or diplacental.

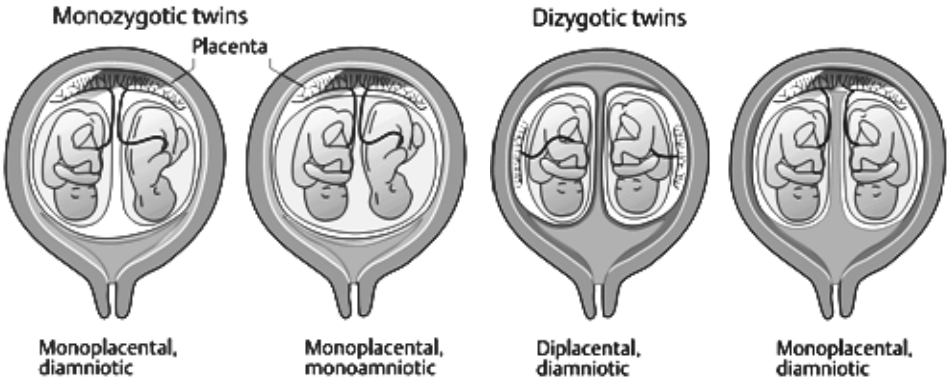


Fig. TWINS

CONCORDANCE AND DISCORDANCE

When both the twins show the same trait they are said to be concordant. When they differ for a trait, they are said to be discordant. Higher concordance rate in monozygotic twins than in dizygotic twins indicates a genetic influence on the trait. When the concordance is less than 100% monozygotic twins, it indicates environmental influence on the trait.

39. EUGENICS AND EUTHENICS

EUGENICS

Eugenics is a branch of genetics in which the laws of inheritance are used to improve human beings. Sir Francis Galton in 1883 coined the word eugenics which in Greek means *well born*. Sir Francis Galton stated that like other animals, human beings also undergo the process of evolution and it is possible to breed for genetically superior human beings by opting for selective mating. The improvement of the human germplasm can be done by two methods

1. Negative eugenics It aims to prevent the spread of undesirable germplasm. Negative eugenics controls and eliminates the defective genes from the society by regulation of child marriages, sexual union with defective individuals by sterilizing them, preventing consanguineous marriages (marriage between blood relatives) and also by restricting the immigration of persons with physical and mental defects.

2. Positive eugenics It aims to develop human beings with superior traits. It advocates that persons with better knowledge and heredity should be allowed to produce more progenies.

Positive eugenics can be excised by (a). Selective mating of individuals (b) Opting for consanguineous marriage between elite persons to bring together the good germplasm (c) Favouring early marriage to prevent loss of good germplasm and (d) Preservation of good germplasm (sperm and ova) from outstanding persons by keeping it under deep freeze for artificial insemination in the future (e) Preventing loss of good germplasm by avoiding wars.

EUTHENICS

It is a known fact that environment influences the genes and its expression. Hence, genetic improvement by eugenics alone is not sufficient to improve the germplasm. In this context, euthenics aims to improve the already existing human germplasm by providing better environment, education, nutrition, medicines, clothing and housing etc.

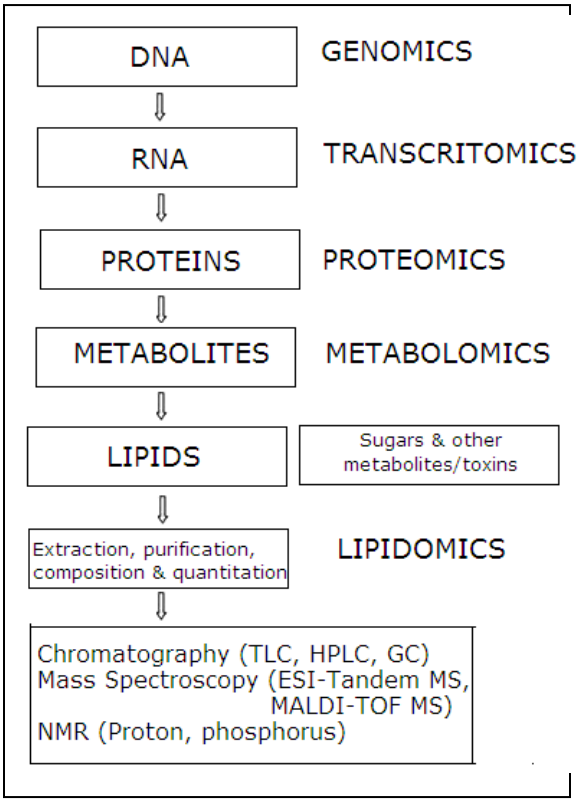
EUPHENICS

Euphenics deals with treatment of inherited diseases which are genetic errors. For example, phenylketonuria disease. Phenylketonuric individuals accumulate phenylalanine in their blood which causes mental retatdation and epilepsies. Human gene pool might be improved through gene cloning, genetic engineering, gene insertion and protoplast fusion.

40. GENOMICS AND METAGENOMICS

I. GENOMICS

Genomics is the field of genetics that refers to the study of the structure, organization, function, and evolution of genetic information contained in whole genomes. The term "Genomics" was coined by Thomas Roderick in 1986. Genomics consists of a) structural genomics b) functional genomics and c) Comparative genomics.



1. Structural genomics deals with the determination of the organization and sequence of the genetic information contained within a genome of an organism. The major steps in structural genomics include (i) Construction of high resolution genetic and physical maps, (ii) Sequencing of the entire genome, and (iii) Determination of complete set of proteins in an organism

2. Functional genomics is the study of function of the genes and sequences elucidated by structural genomics. It includes the analyses of transcriptome (a complete set of RNAs transcribed from a genome) and proteome (the complete set of proteins encoded by a genome).

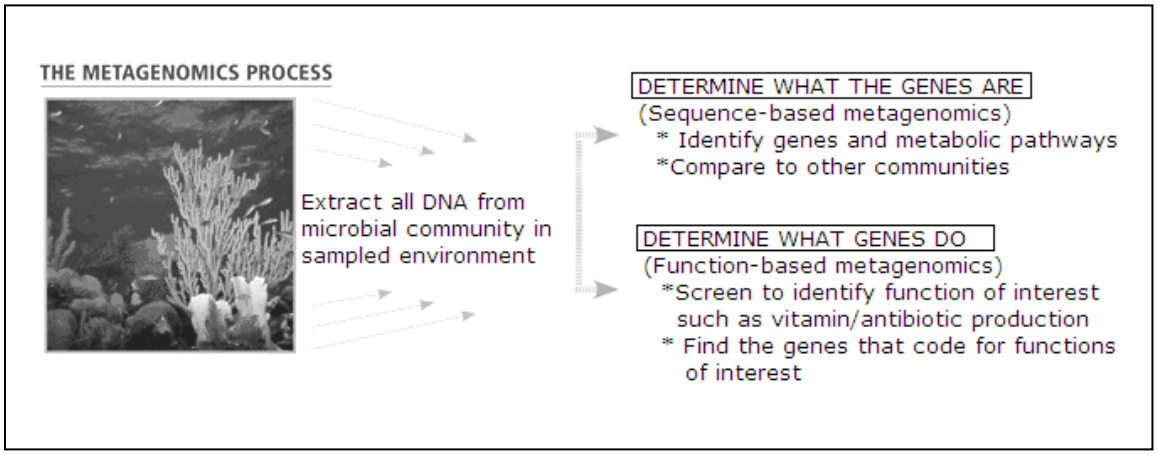
3. Comparative genomics compares the gene content, function, and organization of whole genomic sequences from different organisms. Prokaryotic genomes are small, usually ranging from 1 million to 3 million base pairs of DNA, with several thousand genes. Among multicellular eukaryotic organisms, there is no clear relation between organismal complexity and amount of DNA or gene number.

II. METAGENOMICS

Metagenomics is an emerging field in which the power of genomic analysis (the analysis of all the DNA in an organism) is applied to entire communities of microbes, bypassing the need to isolate and culture individual microbial species. It is also called as *community genomics* or *environmental genomics.*

THE METAGENOMICS PROCESS

Metagenomics includes a wide variety of novel techniques and approaches, and it is likely that other new methods will arise as the field progresses. Here are some of the basic steps:



- Researchers often start a metagenomics project by taking a sample of a particular environment (such as soil, seawater, or the human mouth) and extracting the DNA from all the microbes in the sample.
- This genetic information is then studied to reveal important characteristics of the microbial community.
- In sequence-based metagenomics, researchers study the entire genetic sequence-the pattern of the four different nucleotide bases (A, C, G, and T) in the DNA strands-found in a sample.
- In function-based metagenomics, researchers screen the extracted genes for various functions, such as vitamin or antibiotic production. New antibiotics have already been discovered using this approach.

NEED FOR METAGENOMICS

- The tools of classical genomics and microbiology largely rely on isolating individual microbial species in pure cultures—that is, cultures containing only microbes of a particular species.
- This means that the vast majority of the microbial world has been inaccessible to science because merely a miniscule fraction—most scientists estimate less than 1%—of the estimated millions of microbial species on Earth can be cultured.
- By allowing scientists to access a community's genome without relying on pure cultures, metagenomics transcends the limitations of classical genomics and microbiology.

- Metagenomics gives scientists access to millions of microbes that have not previously been studied.

III. TRANSCRIPTOMICS

A ***transcriptome*** is the set of all RNA molecules (mRNA, tRNA and rRNA) transcribed from a genome in one cell or a population of cells and the study of its constitution and function is referred to as ***transcriptomics***. Transcriptome also refers to the total set of transcripts present in a particular type of cell. As it includes the mRNA transcripts, the transcriptome reflects the active genes excluding mRNA degradation phenomena such as transcriptional attunation. It exmines the expression level of mRNAs in a given cell population using high-throughput techniques based on DNA microarray technology and RNA-sequsncing.

IV. PROTEOMICS

Proteins are responsible for an endless number of tasks within the cell. The complete set of proteins in a cell encoded by genes can be referred to as its ***proteome*** and the study of protein structure and function and what every protein in the cell is doing is known as ***proteomics***. The proteome is highly dynamic and it changes from time to time in response to different environmental stimuli.

By definition, proteomics aims to identify and characterize the expression pattern, cellular location, activity, regulation, post-translational modifications (PTMs), molecular interactions, three-dimensional (3D) structures and functions of each protein in a biological system.

Proteome analysis is applied on different levels: (i) to catalogue the proteins synthesized in an organism, tissue or organelle; (ii) to characterize changes occurring during a developmental process; (iii) to identify proteins differing between biological samples or (iv) to identify proteins on the basis of a functional property (e.g. ligand binding).

Separation of proteins in complex mixtures has been achieved by 2D-gel electrophoresis. However, gel-free techniques based solely on chromatographic separations and mass spectrometry are used increasingly frequently and have enabled the identification and characterization of low abundance, hydrophobic, basic or otherwise elusive proteins that are not amenable to 2D-gel analysis.

APPLICATION OF PROTEOMICS

An application of proteomics is known as protein "***expression profiling***" where proteins are identified at a certain time in an organism as a result of the expression to a stimulus. Proteomics can also be used to develop a protein-network map where interaction among proteins can be determined for a particular living system.

Proteomics can also be applied to map protein modification to determine the difference between a wild type and a genetically modified organism. It is also used to study protein-protein interactions involved in plant defense reactions.

For example, proteomics research at Iowa State University, USA includes:

- an examination of changes of protein in the corn proteome during low temperatures which is a major problem for young corn seedlings;
- analysis of the differences that occur in the genome expression in developing soybean stressed by high temperatures; and
- identifying the proteins expressed in response to diseases like soybean cyst nematode.

V. METABOLOMICS

Metabolomics is one of the newest 'omics' sciences. The metabolome refers to the complete set of low molecular weight compounds in a sample. These compounds are the substrates and by-products of enzymatic reactions and have a direct effect on the phenotype of the cell. Thus, metabolomics aims at determining a sample's profile of these compounds at a specified time under specific environmental conditions.

Metabolomics can be used to determine differences between the levels of thousands of molecules between a healthy and diseased plant. The technology can also be used to determine the nutritional difference between traditional and genetically modified crops, and in identifying plant defense metabolites.

In short, genomics provides an overview of the complete set of genetic instructions provided by the DNA, while transcriptomics looks into gene expression patterns. Proteomics studies dynamic protein products and their interactions, while metabolomics is also an intermediate step in understanding organism's entire metabolism.

STRUCTURE OF PLANT GENOME

The genome of *Arabidopsis thaliana*, a small mustardlike plant, consists of 167 million base pairs of DNA, encoding 25,706 predicted genes. Although *Arabidopsis* has many proteins in common with yeast, worm, fly, and humans, it has roughly 150 protein families not seen in other eukaryotes, including structural proteins, transcription factors, enzymes, and proteins of unknown function.

Gene duplication has played an important role in the evolution of Arabidopsis, with 60% of its genome consisting of duplicated segments. Seventeen percent of the genes exist in tandem arrays, which are multiple copies of the same gene positioned one after another. One of the processes that produce tandem arrays of duplicated genes is unequal crossing over. A number of large duplicated regions, encompassing hundreds of thousands or millions of base pairs of DNA also are present.

The large extent of duplication in the *Arabidopsis* genome suggests that this species had a tetraploid (4N) ancestor and that all genes were duplicated in the past, followed by extensive gene rearrangement and divergence. Thus, at least two different mechanisms seem to have led to the large number of duplications seen in the

Arabidopsis genome: 1) duplication of the whole genome through polyploidy; and (2) duplication of individual genes arrayed in tandem through unequal crossing over.

Transposable elements are common in the *Arabidopsis* genome and make up about 10% of the genome but are much less frequent than in the human genome and in some other plant genomes. Most of these transposable elements are not ranscribed, and many are concentrated in the regions surrounding the centromere. Although *Arabidopsis, C. elegans*, and *Drosophila* have similar numbers of proteins, the Arabidopsis genome has more genes. This difference can be explained by the large number of duplicated copies of genes found in the *Arabidopsis* genome.

siRNA and RNAi (RNA INTERFERENCE OR RNA SILENCING)

siRNA also called as small interfering RNAs are double stranded RNA molecules of 20-25 base pairs long and it plays a vital role in gene regulation by silencing the gene. The process through which the expression of some genes may be suppressed is known as RNA interference or RNA silencing.

The process appears to be widespread, existing in fungi, plants, and animals. It may also prove to be a powerful tool for artificially regulating gene expression in genetically engineered organisms.

RNA silencing is initiated by the presence of double-stranded RNA, which may arise in several ways: by the transcription of inverted repeats in DNA into a single RNA molecule that base pairs with itself; by the simultaneous transcription of two different RNA molecules that are complementary to one another and pair; or by the replication of double-stranded RNA viruses.

In *Drosophila*, an enzyme called Dicer cleaves and processes the double-stranded RNA to produce small pieces of single-stranded RNA that range in length from 21 to 25 nucleotides. These small interfering RNAs (siRNAs) then pair with complementary sequences in mRNA and attract an RNA–protein complex that cleaves the mRNA approximately in the middle of the bound siRNA. After cleavage, the mRNA is further degraded. In the nucleus, siRNAs serve as guides for the methylation of complementary sequences in DNA, which then affects transcription. Some related RNA molecules produced through the cleavage of double-stranded RNA bind to complementary sequences in the 3□ UTR of mRNA and inhibit their translation.

RNA silencing is thought to have evolved as a defense against RNA viruses and transposable elements that move through an RNA intermediate. The extent to which it contributes to normal gene regulation is uncertain, but dramatic phenotypic effects result from some mutations that occur in the enzymes that carry out RNA silencing. RNA silencing leads to the degradation of mRNA and the methylation of DNA.

DNA METHYLATION

Another change in chromatin structure associated with transcription is the methylation of cytosine bases, which yields 5-methylcytosine. Heavily methylated DNA is associated with the repression of transcription in vertebrates and plants, whereas transcriptionally active DNA is usually unmethylated in these organisms. DNA methylation is most common on cytosine bases adjacent to guanine nucleotides on the same strand (CpG); so two methylated cytosines sit diagonally across from each other on opposing strands. DNA methylation is required for normal embryonic development. Genomic imprinting, X chromosome inactivation, chromatinmodification, and silencing of endogenous retroviruses all depend on establishing and maintaining proper methylation patterns. DNA methylation is gene specific and occurs genome-wide. Two types of methyltransferase can be distinguished by their basic functions: maintenance methylation and de novo methylation.

GENOMIC IMPRINTING

Recent genetic studies revealed that the expressions of several mammalian genes are significantly affected by their parents. This phenomenon of differential expression of genetic material depending on whether it is inherited from the male or female parent is called *Genomic Imprinting*.

GENE THERAPY

Gene therapy is the direct transfer of genes into humans to treat disease. Gene therapy was first successfully implemented in 1990 and is now being used to treat genetic diseases, cancer, and infectious diseases. Gene therapy conducted to date has targeted only non-reproductive, somatic cells. Correcting a genetic defect in these cells (termed somatic gene therapy) may provide positive benefits to patients but will not affect the genes of future generations. Gene therapy that alters reproductive, or germ-line cells (termed germ-line gene therapy) is technically possible but raises a number of significant ethical issues, because it has the capacity to alter the gene pool of future generations

In 1990, gene therapy became reality. W. French Anderson and his colleagues at the U.S. National Institutes of Health (NIH) transferred a functional gene for adenosine deaminase to a young girl with severe combined immuno-deficiency disease, an autosomal recessive condition that produces impaired immune function.

CHROMOSOME BANDING

Chromosomes are visualized by the use of traditional dyes which stain them uniformly and provide uniform colouration to chromosomes. Caspersson et al in 1970, introduced newer staining procedures and used different dyes which produced dark and light cross bands of varying widths on chromosomes. Each chromosome in a haploid set has a unique banding pattern and can be distinguished from the other chromosomes of similar size and shape.

Generally there are four types of banding namely, Giemsa or G banding, centromeric or C banding, Quinacrine or Q banding and reverse or R banding.

G BANDING It involves Giemsa stain after trypsin treatment of metaphase chromosome to differentiate the chromosomal bands. When viewed through the microscope, the chromosomes show dark bands (G bands) and light bands (R bands). By this method approximately 400 dark and light bands could be resolved in a haploid set of chromosome. This is the most widely used procedure.

C BANDING It requires heating in an alkali solution and staining with Giemsa. C bands are of constitutive heterochromatin located adjacent ot the centromeres of all the chromosomes.

Q BANDING In Q banding, Quinacrine mustard is used to stain the chromosome. They are observed under fluorescent microscopy. The bright Q bands are equivalent to G bands.

R BANDING This is reverse banding and it uses Giemsa under elevated temperature to produce the reverse pattern to that seen in G banding.

CHROMOSOME PAINTING

In 1980s, a technique called FISH (Fluorescent *in situ* hybridization) was developed to prepare brilliantly coloured whole chromosomes. This technique requires complex mixtures of specially constructed DNA sequences called probes which are complementary to the different chromosomal regions, along with a set of fluorescent dyes. A special microscope with optical filters is also needed along with computer software to analyse the image and convert them into a dazzling multicoloured display. Chromosome painting is useful for quickly detecting cells with extra or less chromosomes or with other structural abnormalities, especially in cancer cells.

THE HUMAN GENOME PROJECT

The Human Genome Project (HGP) is an international effort to investigate the human genome in its entirety. The project began officially in 1990. Sequencing of human genome was carried out by the public-funded Human Genome Sequencing Consortium and the private company Celera genomics established by Craig Venter. Five major centers were involved, with four in United States and one in United Kingdom contributed 85% of the data. The United States National Human Genome Research Institute (NHGRI) functions as a central agency.

A nearly complete sequence of the human genome comprising 99 percent of the euchromatic DNA was released in October, 2004. The first draft of human genome sequence, which is over 3 billion nucleotide long, consists of 24 chapters, viz., 22 autosomes and X and Y sex chromosomes.

AIMS OF HGP

It aims to dentify all the genes in human DNA; to determine the sequences of the 3 billion chemical base pairs that make up human DNA; to store this information in public databases; to develop tools for data analysis; to transfer related technologies to the private sectors and to address the ethical, legal, and social issues (ELSIs) that may arise from the project.

SALIENT FEATURES OF THE HUMAN GENOME

The human genome contains over 3 billion nucleotide pairs. On an average there is one gene per 145 kb in the human genome. Human genome is estimated to have about 20,000 – 25,000 genes that encode protein products. Average gene consists of 3000 bases. But sizes of genes vary greatly, with the largest known human gene encoding dystrophin containing 2.5 million base pairs. Only about 1.1%of the genome encodes amino acid sequences of polypeptides The functions are unknown for over 50% of the discovered genes. The repetitive sequences makeup very large portion of human genome. Repetitive sequences have no direct coding function but they shed light on the chromosome structure, dynamics and evolution. Chromosome 1 has most genes (2968) and Y chromosome has the lowest (231). Almost all nucleotide bases are exactly the same in all people. Genome sequences of different individuals differ for less than 0.2% of base p airs. Most of these differences occur in the form of single base differences in the sequence. These single base differences are called single nucleotide polymorphisms (SNPs). One SNP occurs at every ~ 1,000 bp of human genome. About 85% of all differences in human DNAs are due to SNPs.

41. CYTOPLASMIC INHERITANCE

DNA in the nucleus is the universal genetic material. However, not all the genetic material of a cell is found in the nucleus. Some traits are governed by genes present in the cytopslasm. Those traits which are transmitted by DNA in cytoplasmic organelles are called as cytoplasmic inheritance.

They are also referred to as extra-nuclear inheritance, non-Mendelian inheritance and maternal inheritance. As the genes for cytoplasmic inheritance are located in the cytoplasm, they are referred to as plasmagenes, cytoplasmic genes, extra-nuclear genes or extra-chromosomal genes. Plasmagenes are located in the DNA present in mitochondria (mt –DNA) and chloroplasts (cp–DNA); together these DNA's are termed as organelle DNA.

Cytoplasmic inheritance was first reported by Carl Correns (1909) while studying the inheritance of leaf variegation in *Mirabilis jalapa*.

FEATURES OF CYTOPLASMIC INHERITANCE

1. In most organisms, the cytoplasm of the offspring is inherited from the mother. Hence, the cytoplasmically inherited characters are passed only from mother to offspring and never from the father.

2. As a result, reciprocal crosses (AxB; BxA) exhibit differences and deviate from Mendelian pattern.

3. Cytoplasmic genes are not uniformly distributed during cell division. Hence, there is an extensive phenotypic variation as the cells of an individual will contain cytoplasmic genes in various proportions. Usually the females has more influence on the trait as they carry more cytoplasm than the male.

4. Unlike nuclear genes which show linkage, the extra-nuclear genes fail to show linkage.

MITOCHONDRIA AND CYTOPLASMIC INHERITANCE

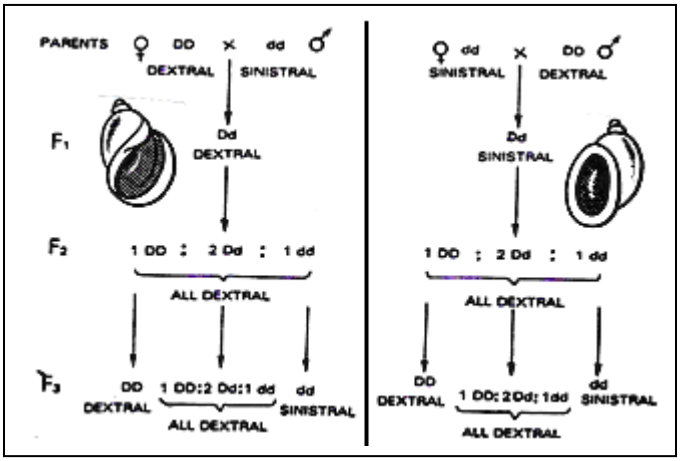
Organelles like mitochondria and chloroplasts contain DNA. Mitochondria are presently considered as living organisms. The mitochondrial DNA (mtDNA) is a circular molecule ranging from 16 kb to several hundred kilobase pairs. The mtDNAs of humans, mice and cattle exhibit the same basic organization. Each mtDNA has 2 rRNA genes, 22 tRNA genes and 13 structural genes. The entire mtDNA is equivalent to one operon in bacteria. The human mitochondrion contain about 15,000 nucleotides and enclodes 37 genes while the nuclear DNA contains 3 billion nucleotides and encodes 35,000 genes.

MATERNAL EFFECTS

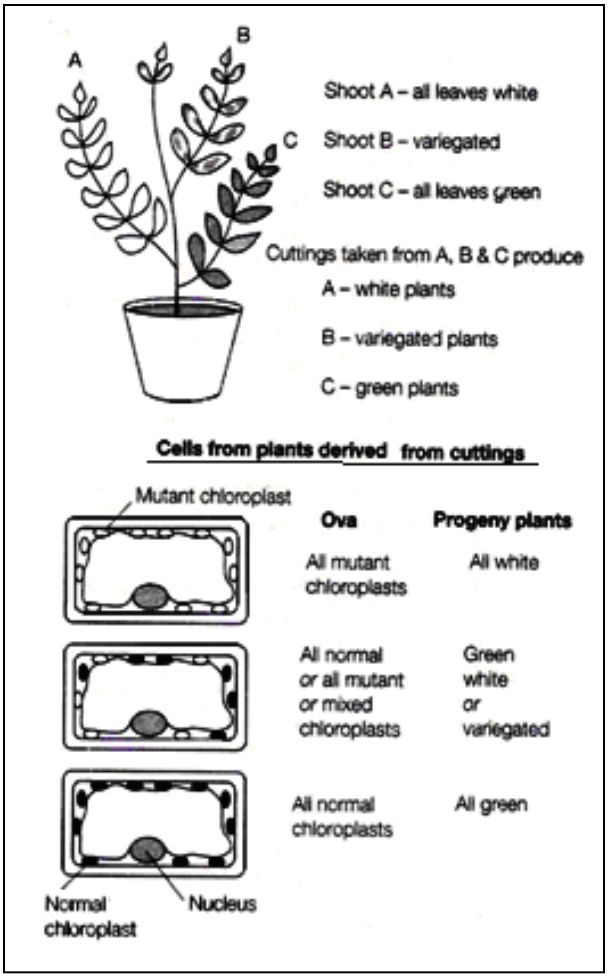
Maternal effect is a genetic phenomenon often confused with cytoplasmic inheritance. In maternal effect, the phenotype of the offspring is determined by the genotype of the mother. Eg. Shell coiling in Snail.

In *Limnaea* (a snail), the dominant allele D produces right-handed coiling, while the recessive allele d produces left-handed coiling. The direction of shell coiling in an individual is governed by the genotype of its female parent and not by its own

genotype. As a result, reciprocal crosses show difference in coiling in F_1 and there is no phenotypic segregation in F_2. The phenotypic effect of segregation is observable in F_3 crosses between female with left handed coil (dd) and males having right handed coil (DD) produce F_1 progeny (Dd) with left handed coil since the genotype of the female parent is dd. In F_2, segregation of Dd produces three genotypes in the ratio of 1:2:1. But snails with DD, Dd as well as dd genotype exhibit right handed coiling since their female parent has the genotype Dd producing right handed coiling in all it progeny (irrespective of the genotype of the progeny). The F_3 progeny from F_2 individuals with the genotype DD and Dd will show right handed coiling while those from dd F_2 individuals will exhibit left handed coiling of their shells this produces the typical 3:1 ratio (right handed : left handed) in F_3.



The reciprocal crosses (female right handed DD x male left handed dd) on the other hand, yields right handed coiling in F_1 (Dd) as well in the three genotypes, 1 DD :2Dd : 1dd, obtained in F_2. But in F_3 2/3 of the progenies show right handed coiling since they are derived from F_2 individuals with the genotypes DD and Dd. The remaining 1/3 of the F_3 progenies exhibit left handed coiling since the female parents had the genotype dd; this yields the typical 3:1 ratio in F_3.



PLASTID INHERITANCE

Inheritance of characters due to genes located in plastids is known as plastid inheritance. This was the first case of cytoplasmic inheritance to be discovered by Correns and Baur in 1908.

Leaves of *Mirabilis jalapa*, the four 0' clock plant, may be green, white or variegated. Correns made reciprocal crosses in all combinations among the flowers produced on these three types of branches. When flowers from a green branch are used as female, all the progeny are green irrespective of the phenotype (green, white or variegated)

of the male parent. Similarly, progeny from the crosses involving flowers from white branches as the female parent were all white irrespective of the male flowers being from green, white or variegated branches. But in the progeny from all the crosses involving flowers from variegated branches as the female parent, green, white and variegated plants were recovered in variable proportions.

The maternal transmission of plasmagenes in higher plants and animals is explained on the basis of unequal contribution by male and female gametes to the cytoplasm of the zygote. During fertilization, ordinarily only the nucleus enters the egg cell and its cytoplasm is left outside the egg cell. As a result, the mitochondria and proplastids present in the zygote are derived from the female parent only. Therefore, plasmagenes located in these organelles will also be derived from the female parent only.

NUCLEAR CYTOPLASMIC INTERACTION

An unusual case of interaction between nuclear and cytoplasmic genomes is reported in maize. A type of variegation, called iojap, is produced by a recessive gene ij; plants homozygous (ij ij) for this gene develop the typical iojap variegation. But once this variegation is produced by the nuclear gene ij, it shows a typical cytoplasmic inheritance. Clearly, the nuclear genotype ij ij has a mutagenic effect on the plastid genome. Once, this mutation is induced in some cp-DNA molecules the variegation is inherited cytoplasmically.

A cross between normal (Ij Ij) plants as female and iojap (ij ij) plants as males produces all green plants in F_1 with the nuclear genotype Ij ij. In F_2 generation of this cross ¼ progeny are ij ij and develop the iojap variegation, ¾ of the progeny are normal green. When the iojap F_2 plants are mated with normal green plants, a marked-reciprocal difference is observed in the progeny. When iojap plants are used as males and green plants as females, all the progeny are normal green. But in the reciprocal cross green, white and iojap progeny are recovered, the ratio between the three types of progeny is quite variable.

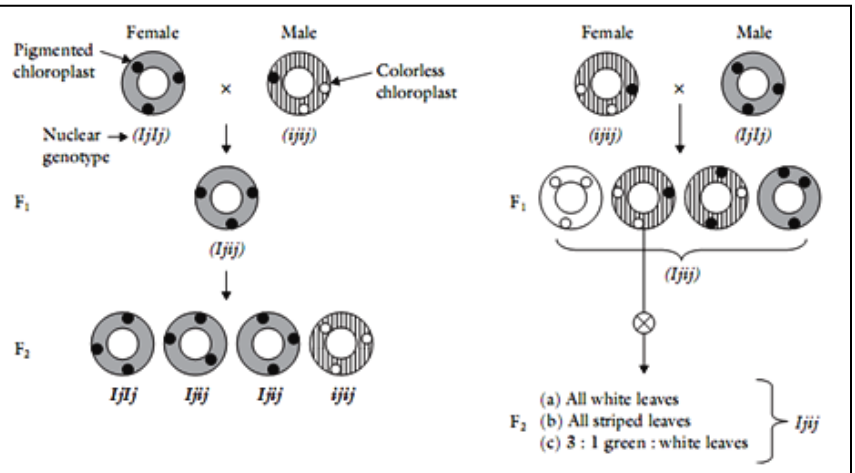


Fig. Maternal inheritance of iojap gene (ij) in maize. The wild type gene is Ij. The appearance of leaf colour is solely determined by the phenotype of the female parent i.e. maternally inherited

GLOSSARY

Aberration (Chromosomal aberration): Structural/ numerical changes in chromosomes; chromosome mutation.

Accessory chromosome : Supernumerary heterochromatic chromosomes found in some plant and animal species, in addition to normal or A chromosomes ; they are designated as B chromosomes.

Acentric : Chromosome or chromosome fragment without a centromere.

Acentric chromosome: A chromosome fragment without centromere.

Acrocentric : A chromosome or chromatid where the centromere is very close to one end.

Acrocentric chromosome: A chromosome with its centromere near one end.

Additive gene effect: In case of polygenes; the effects of different genes having cumulative and equal effect

Adenine: A purine base designated as "A", found in nucleic acids.

Adenosine: Adenine attached to ribose.

Allele (Allelomorph) : One of a pair or more alternative forms of a gene situated at the same locus in homologous chromosomes. More than two alternative forms of a gene are called multiple alleles.

Allopolyploid: A polyploid having two or more distinct genomes; usually produced by chromosome doubling of interspecific hybrids (F_1s).

Allotetraploid: An allopolyploid having four genomes; usually two copies each of two genomes; may be four different genomes.

Amphidiploid: An allopolyploid having two copies each of two or more distinct genomes; natural amphidiploids behave as diploids during meiosis, *i.e.,* they show normal bivalent formation, *e.g.,* wheat, tobacco, oats, cotton etc.

Anaphase: The stage in which sister chromatids of each chromosome (in mitosis and AII of meiosis) or the homologous chromosomes (at AI of meiosis) separate by their movement toward opposite poles of the spindle.

Aneuploid: An organism or a cell having one or few chromosomes more or less than the normal disomic number of the species; the chromosome number is not a multiple of the basic number *(x).*

Antibody: A protein molecule that interacts specifically with an antigen molecule; usually produced by an animal in response to the antigen in question.

Anticodon: A sequence of three bases (triplets) in tRNA, complementary to the three bases of mRNA coding for an amino acid.

Antigen: A substance, usually a protein, which induces specific antibody production when introduced into a living system, usually an animal, in which it does not occur naturally.

Apomixis: The development of an embryo (and seed) without fertilization.

Apospory: Formation of a diploid embryo sac directly from a cell of the nucellus or integument.

Asexual reproduction: The progeny are produced through a process which does not involve the fusion between male and female gametes.

Asynapsis: Failure of pairing (synapsis) of homologous chromosomes during meiosis (zygotene of prophase I).

ATP: Adenosine triphosphate; consists of adenine, ribose (5-carbon sugar) and three phosphate

groups ; it is a major carrier of energy and phosphate in biological system.

Autoallopolyploid : Cell or individual whose chromosome complement shows the characteristic of auto-and allo-polyploidy. If A and B represent different genomes, the autoallopolyploid may be AAAABB, AABBBB or AAAABBBB.

Autogamy: Self-fertilization; union between male and female gametes produced by the same individual; in *Paramecium*, sexual reproduction within a single animal without conjugation.

Autopolyploid: An individual having more than two copies of a single genome.

Autosome: Chromosomes other than sex chromosomes; their kind and number is the same in males and females of a species.

Autotetraploid: A cell or individual possessing 4 sets of the basic chromosome number.

Balanced lethals: Lethal genes linked in repulsion phase; they are maintained in this phase either due to tight linkage or crossover suppression; only their heterozygotes survive.

Base pair (bp) : Two nitrogenous bases (one purine and one pyrimidine) which pair in double-stranded DNA or RNA molecules. Adenine pairs with thymine

Base pair ratio : The ratio A + T / G + C.

Basic number: The haploid or gametic chromosome number of a diploid species *(genomic number);* in polyploid species, haploid number of the parental diploid species; represented by *x.*

Bisexual : In plants, the flower having both androecium and gynaecium ; in animals, the individual having both testes and ovaries.

Bivalent: The structure formed by pairing of two homologous chromosomes during meiosis; seen during pachytene onward till the beginning of anaphase I.

C value: Total amount of DNA in a haploid genome.

Cell: The smallest membrane-bound structural; the functional unit of all living matter, capable of independent reproduction.

Cell cycle: The life cycle of the individual cell, the period from one division to the next. In somatic cells, it consists of interphase (G-phase,
S-phase)

Cell differentiation: The process by which the descendants of a single cell achieve and maintain specialization of structure and function during the development of the individual.

Central dogma: The functional relationship among DNA, RNA and protein regarding the direction of information flow. DNA serves as a template for its own replication and for RNA synthesis (transcription) and RNA is template for protein synthesis (translation), thus the information flows as : DNA- RNA-Protein. However, in certain RNA viruses, DNA is synthesized on RNA template.

Centromere: In a chromosome, the specialized region to which the spindle fibre is attached during cell division; it is involved in chromosome movement at anaphase.

Character: Derived from characteristic; a morphological, anatomical, physiological or behavioural feature of an organism; usually, the end-product of development; a result of the genotype, environment and genotype x environment interaction effects.

Chiasma: The cross-shaped points of contact between nonsister chromatids of homologous chromosomes during diplotene-MI, formed as a result of crossing over.

Chimera (chimaera) : A plant (rarely an animal) composed of tissues of two or more genotypes or ideotypes ; as a consequence of mutation, fusion of different zygotes or grafting.

Chi-Square (χ^2) Test: A statistical test for determining whether observed data agree with an expected ratio.

Chloroplast: A highly differentiated plastid with typical granna; contains all the chlorophyll in higher plants; has DNA and participates in cytoplasmic inheritance.

Chromatid: Of a metaphase chromosome, one of the two identical longitudinal strands produced by replication of the single chromatid of a telophase chromosome; the two chromatids of a

chromosome are called *sister chromatids.*

Chromatin: A complex between DNA, histones and other proteins, and chromosomal RNA, making up the chromosomes; in form of 300 A^0 *chromatin fibers* (derived from, chromaticity = property of taking up stain).

Chromocentre: In salivary gland chromosomes of certain Diptera; the body produced by a fusion of the heterochromatic regions of the autosomes and X chromosome, and the entire *Y* chromosome.

Chromomeres: Bead-like condensed chromosome segments linearly arranged in prophase of mitosis and meiosis; they are called bands in polytene chromosomes.

Chromosomal aberration: A change in chromosome number from the diploid state, or a change in chromosome structure from the normal chromosome complement.

Chromosome: Nucleoprotein bodies composed of 300 A chromatin fibers; clearly observable during cell division; dark-staining with basic dyes; bearers of the genetic material and the genes.

Chromosome banding: The staining of chromosomes following specific procedures which produce many dark and light zones along their lengths; the pattern of banding is highly specific, and all the 23 human chromosomes can be identified.

Chromosome theory: The chromosome theory of inheritance states that the chromosomes are the carriers of genes.

Cistron: Functional unit of gene; a section of DNA or RNA which codes for a specific gene product.

Clone: Group of cells or organisms which are genetically identical and are derived from a single cell or common ancestor by mitosis. Also, the molecules identical with a single ancestral molecule.

Codominance: Both the alleles of a gene express themselves in the heterozygotes.

Codon: A group of three adjacent nucleotides of mRNA which code for one amino acid; *nonsense codons* specify no amino acid and function in polypeptide chain termination.

Colchicine: An alkaloid derived from autumn crocus; it prevents the organisation of spindle apparatus and, thereby, induces chromosome doubling.

Colour blindness: Inability of an individual to distinguish between two colours, e.g., red-green colour blindness; usually, sex-linked.

Complementary genes: Two (or more) dominant genes capable of producing a character only when both (or all) of them are present together in the dominant state.

Continuous variation: Variation not separable into distinct classes; governed by polygenes; markedly affected by the environment; in quantitative traits; analysis based on measurement data.

Coupling phase: In linkage; the dominant alleles of two or more genes present in the same chromosome and, hence, linked together; contributed by the same parent

Crossing over: The exchange of segments between nonsister chromatids of homologous chromosomes leading to recombination.

Crossover unit: The distance between two linked genes which permits 1 % recombination between them (Syn., map unit, Morgan).

Cytogenetics: A branch of biology devoted to the study of chromosomes and their implications in genetics.

Cytokinesis: The process of the division of cytoplasm of a cell into two or more parts ; usually it occurs after nuclear division (karyokinesis).

Cytology: A study of the structural and functional organisation of the cell.

Cytoplasm: The entire content of a cell other than the nucleus; includes ER, plastids, mitochondria, microtubules etc., and the hyaloplasm.

Cytoplasmic inheritance: Inheritance due to the genes located in the cytoplasm (Plasmagenes), *e.g.,* mitochondria and plastids; typical uniparental transmission and the lack of

segregation; in higher plants and animals, transmission through the female parent. (Syn., extranuclear, extrachromosomal and maternal inheritance).

Cytoskeleton: The networks of fibres in the eukaryotic cytoplasm.

Deoxyribonucleic acid (DNA) : The genetic material of all cells; a polymer of deoxyribonucleotides which are joined by phosphodiester bonds.

Deficiency: The loss of a segment from a chormosome; deficiency heterozygotes are hemizygous for the genes located in the deleted segment; many deficiencies produce genetic effects similar to gene mutations (Syn., deletion).

Denaturation: The loss of natural or native configuration of a macromolecule; generally, accompanied with a loss in the biological activity of the molecule; a separation of the two strands of DNA double-helix producing single-stranded DNA molecules.

Diakinesis: A substage of prophase I of meiosis; the chiasma terminalization is complete; the bivalents are short and thick, and well-spread in the cell.

Dicentric chromosome: A chromosome having two centromeres.

Differentiation: The modification of identical cells derived from a zygote into the different cell types; usually associated with organ formation, and characterised by differences in the kinds of genes being transcribed.

Dihybrid: The progeny from a cross between two homozygous parents differing for two genes; A cross involving two gene pairs (character pairs).

Diploid: A cell, organism or species having two copies of a single genome; specified by 2x (not 2n).

Diplospory: A type of apomixis in which the embryo sac (gametophyte) is formed after mitotic divisions of the archesporial cell ; meiosis either does not occur or does not result in reduction of chromosome number.

Diplotene: The state after pachytene and before diakinesis during prophase I of meiosis; characterised by the movement of homologous chromosomes, paired to form bivalents, away from each other and the appearance of chiasmata.

Discontinuous variation: Variation which can be divided into distinct classes; in case of qualitative characters; usually little affected by the environment; yields typical F_2 ratios.

Disomic: Cell or individual having two homologous sets of chromosomes (2n), i.e., each chromosome is represented by a pair of homologues.

DNAase: An enzyme that specifically digests or hydrolyses DNA.

Dominance: In the heterozygote, one allele expresses itself at the expense of the other.

Duplex: The condition where two dominant alleles of a given locus are present in an autopolyploid, e.g., AAa in triploid, AAaa in autotetraploid.

Duplicate genes: Two dominant genes produce the same phenotypic effect whether they are alone or together, the alternative phenotype being produced only when both are in the recessive state.

Duplication: The occurrence of a chromosome segment more than once in the same chromosome

Dyad : A pair of daughter cells produced from the first meiotic division.

Egg (**Ovum**) **:** The gamete produced by a female organism.

Embryo sac: In plants; the structure derived from a megaspore through mitosis; generally, contains one egg cell, two synergids, three antipodal cells and two polar nuclei.

Embryo: The early stages of development of an organism from the zygote.

Endomitosis: Replication of chromosomes without cell or nuclear divisions, leading to polyploidy.

Endonuclease: An enzyme which induces internal cuts or cleavages in a DNA molecule.

Endoplasmic reticulum: A network of membranes in the cytoplasm; consists of tubules, vesicles and cisterns; provides the attachment site for ribosomes; may be rough or smooth.

Endosperm: The nutritive tissue of developing seeds derived from repeated mitotic divisions of the

fusion product of the two polar nuclei of all embryo sac with a sperm; usually it is 3n, but in some cases
it is 5n.

Enzyme: A protein which catalyses or speeds up a specific chemical reaction; usually in a living system.

Epistasis: The expression of a gene is modified by another gene; in quantitative genetics, nonallelic interaction or simply interaction.

Equational division: The second division of meiosis when the sister chromatids separate; when crossing over occurs between a gene and its centromere, segregation for the gene takes place during this division.

Equatorial plate: It is the arbitrary plane at which the chromosomes are arranged during metaphase.

Euchromatin: The chromosome or chromosome regions which show the normal coiling-decoiling cycle and normal staining properties.

Eukaryote: An organism whose cells have true nuclei, *i.e.,* nuclei enclosed by typical nuclear envelope.

Euploid: A cell or an organism in which the chromosome number is an exact multiple of the basic number *(x)* for the concerned species.

Evolution: The development of new varieties, races, species, genera etc. through the origin of variation and natural selection.

Exon: The part of an eukaryotic gene which is represented in the mature mRNA and in the polypeptide specified by the gene.

Exonuclease: An enzyme which degrades DNA or RNA from the end of the strand. Exonuclease may be specific for either the 5' end or 3' end of the polynucleotide chain.

Expected ratio: In chi-square test; the ratio in which the data are expected to occur in a given experiment; based on known facts and theoretical considerations.

Expressivity: The degree of phenotypic expression of a gene in the different individuals; it may be uniform or variable.

Extranuclear gene: Genes residing outside· the nucleus, in organelles such as mitochondria and chloroplasts.

F_1 : The progeny obtained by crossing or mating two strains or individuals; first filial generation.

F_2 : The second filial generation; obtained by self-fertilization of or intermating among the individuals of F_1 generation.

Fertilization: The fusion of male and female gametes to produce a zygote.

Frameshift mutation (reading frame mutation) : Mutations that arise by insertion or deletion of base pairs which are not a multiple of 3. They change the reading frame due to displacing the starting point of transcription, thus the mRNA is misread.

G1 (gap-l period) : In eukaryotic cell cycle, the first gap period of
interphase ; the period (stage) between the end of mitosis and beginning of DNA synthesis.

G2 (gap-2 period): In eukaryotic cell cycle, the second gap period of interphase; the periof between the end of DNA synthesis and start of next mitosis.

Gamete: A specialized haploid (usually) cell which participates in sexual reproduction; one male and one female gametes fuse to produce a zygote.

Gametic chromosome number: The chromosome number normally present in the gametes of a species; ordinarily, it is the haploid number (n).

Gametogenesis: The production of male and female gametes.

Gene (cistron): Segment of DNA (or RNA in certain viruses) which represent a functional unit of inheritance, defined by the cis-trans test or a particular sequence of nuc1eotides along DNA molecule (or RNA in certain viruses) involved in producing a polypeptide chain.

Gene mutation: A change in the base sequence of a gene, usually producing a mutant phenotype.

Gene pool: The sum total of all the alleles present in the breeding or reproductive members of a random mating population.

Gene symbol: A letter or a group of letters used to denote a gene; usually derived from the name of the mutant phenotype; the first letter of the symbol for the dominant allele is capital, while all the letters in the symbols for recessive alleles are in lower case.

Gene: A segment of DNA which specifies a single polypeptide (structural gene); also, a segment of DNA which codes for an RNA molecule (e.g., rRNA and tRNA genes), or may serve as a binding site for regulatory proteins (e.g., operator and promoter genes).

Genetic code: In DNA and RNA, the base triplets that carry genetic information for protein synthesis.

Genetic map: The linear arrangement of mutational sites belonging to the gene concerned (cistron) in a chromosome plotted graphically to correspond with their relative distances from one another, as deduced from recombination experiments.

Genetics: The branch of biology concerned with the study of heredity and variation.

Genome: A complete set of chromosomes of a diploid species; all the members of a genome are distinct from each other in gene content and, often, in morphology; members of a genome do not pair.

Genotype: The genetic constitution of an organism.

Germ cell: A cell 'destined to produce gametes for sexual reproduction.

Germplasm: The sum total of hereditary material or genes present in a species.

Haploid: The cell or individual with gametic chromosome number, symbolised by "n".

Heredity: The transmission of traits (more precisely, genes) from parents to offspring.

Heritability: The ratio of genotypic variance (broad sense heritability) or additive genetic variance (narrow sense heritability) to the total phenotypic variance.

Heterochromatin: The parts of chromosomes (or chromatin) which take up dark stain during interphase; genetically inactive; usually, contains repetitive DNA sequences which are rarely transcribed; may be constitutive or facultative.

Heteromorphic chromosomes: Homologous chromosomes differing in morphology.

Heterosis (Hybrid vigour): Superiority of the heterozygote over the corresponding homozygotes with respect to one or more characters (or superiority of the F_1 over both the parents.).

Heterosis: The superiority of a heterozygote over both the concerned homozygotes in respect of one or more characters; in practice, the superiority of an F_1 over both its parents.

Heterozygote: An individual having two different alleles for one or more genes.

Hexaploid: An individual having six genomes of one (auto hexaploid) or more (allohexaploid) kind.

Histones: The conserved basic proteins complexed with DNA in eukaryotes, forming nucleosome.

Holandric gene: A gene carried in the *Y* chromosome and, thereby, showing only male-to-male transmission; confined to the male sex only (in mammals).

Homoeologous chromosomes: Partially homologous chromosomes; they are derived from ancestral chromosomes which were homologous.

Homogametic sex: The sex which produces only one type of gametes with regard to the sex chromosome.

Homologous chromosomes: The chromosomes which pair regularly and freely with each other during meiosis; they are identical in gene content and, usually, in morphology.

Homozygote: A cell or individual having identical alleles at one or more loci.

Hormone: A compound produced by the cell of one part of the body which acts in the other parts of the organism.

Hybrid: The progeny obtained by crossing or mating two individuals or strains having different

genotypes.

Hybridization: The process of obtaining progeny through the union between male gametes of one strain with the female gametes of another strain. (Syn., crossing, mating).

Idiogram (Karyogram) : A diagrammatic representation of the chromosome morphology (karyotype) of an organism.

Idiotype: Refers to the sum total of hereditary determinants of an organism, comprising its chromosomal genes (genotype) and extrachromosomal genes (plasmotype). in translation.

***In vitro* :** When biological processes are made to occur outside the organism in a vessel or test tube.

***In vivo*:** Within the living organism.

Inbreeding: Mating between two individuals related by descent, i.e., having a common ancestor.

Incomplete dominance: The phenotypic expression of heterozygotes for a gene being intermediate between those of the two concerned homozygotes.

Independent assortment: The segregation of one pair of alleles being independent of that of another pair of alleles, that is, an allele of one gene passes with either one of the two alleles of the other gene with equal frequency.

Inhibitory gene: A dominant gene which prevents the expression of another dominant gene; generally, denoted by I.

Interference: Effect of one crossing over event on the occurrence of a second crossing over (double crossing over) in its vicinity (adjacent region). It may be positive or negative interference (see, chromatid interference chiasma interference).

Interphase: The stage in cell cycle when the nucleus of a cell is not undergoing division; a period of active protein (G1 and G2 phases) and DNA (S phase) synthesis.

Intron: The part of an eukaryotic gene which are not represented in the mature mRNA molecules; derived from 'intervening sequences'.

Inversion: Rotation of a segment of a chromosome by 180^0 so the genes in this segment are present in the reverse order; characteristic inversion loops are produced during meiosis in the inversion heterozygotes.

Iojap : In maize, a mutant nuclear gene changing the chloroplast characters; the mutant chloroplasts behave autonomously after it.

Isochromosome: A chromosome whose arms are equal and genetically identical homologous.

Isogenic lines: Lines having identical genotype, except for one gene at which they differ e.g. A and B lines is male sterility.

Karyokinesis: The division of a nucleus into two daughter nuclei; through mitosis or meiosis.

Karyotype: Chromosome complement of an individual defined by the number and morphology of the chromosomes usually at mitotic metaphase. It is often used for photomicrographs of metaphase chromosomes, arranged in a standard sequence.

Lagging chromosome (s) (laggards) : At anaphase of mitosis or meiosis, the chromosomes which either do not move or move much slowly towards poles are called laggards and so they are not included in the daughter nuclei.

Lagging strand (of DNA): The DNA strand synthesized discontinuously in the form of short fragments (5' to 3' direction) which are later connected covalently by the enzyme ligase, thus the overall growth being in 3' to 5' direction.

Lampbrush chromosome: In diplotene stage of vertebrate oocytes, particularly, in amphibia; the two chromosomes of each bivalent have numerous paired loop like lateral extensions; loops are the sites of active transcription.

Leading strand (of DNA) : The DNA strand synthesized continuously in the 5' to 3' direction.

Lethal gene: An allele of a gene which causes the death of all those individuals which carry it in the appropriate genotype; death occurs any time before the individuals reach adulthood.

Ligase: An enzyme which seals the nicks or the cuts in a DNA strand.

Linkage map: A linear map of the genes showing linkage with each other; it depicts the sequences in which genes are located in the chromosome as well as the frequency of recombination between the adjacent genes.

Linkage: The tendency of genes to stay together during inheritance; due to the genes being located relatively close to each other in the same chromosome.

Locus: The fixed position in a chromosome occupied by a gene; often used as a synonym of gene since, ordinarily, genes occupy a fixed position in the concerned chromosome.

Malesterility: The male gametes produced by an individual being nonfunctional.

Maternal effect: The phenotypes of progeny being affected by the genotypes of their mothers.

Maternal inheritance: The transmission to progeny of a character from the female parent only.

Megaspore: Haploid spores produced by meiosis in megasporocytes in angiosperms. One of the haploid megaspores divides to produce the embryo sac (female gametophyte).

Megasporogenesis: The production of female spore through meiosis in the ovules of plants.

Meiosis: The eukaryotic cell division that produces haploid spores. It completes in two successive cell divisions following one replication of chromosomes (DNA replication). In the I division, homologous chromosomes pair and separate and are reduced to half in number *(n)* ; in the II division chromatid separation occurs to produce four haploid daughter cells - the spores (plants) or gametes (animals).

Merozygote: In bacteria, a partially diploid cell (zygote) containing complete genome of the recipient and a chromosome fragment (merogenote) derived from the donor cell.

Messenger RNA (mRNA) : The RNA molecules formed by transcription of DNA and carrying information for amino acid sequences of specific polypeptides and serve as template for protein synthesis ..

Messenger RNA *(*mRNA*):* The RNA molecules which carry the information for amino acid sequences of specific proteins which is deciphered with the help of ribosomes and specific tRNAs.

Metacentric chromosome: A chromosome with the centromere in its centre or close to the centre; the two arms of such a chromosome are nearly equal.

Metaphase: The stage during cell division after prophase and before anaphase; the chromosomes are short, thick distinct from each other and arranged on the equatorial plate.

Microsporogenesis: The production of haploid male spores (pollen grains) through meiosis in the anthers of plants.

Mitochondria: Cytoplasmic organelles enclosed by two concentric membranes, the inner membrane having characteristic infolds called cristae; concerned with oxidative phosphorylation and production of ATP; contains DNA and participates in cytoplasmic inheritance.

Mitosis: The cell division in which each nuclear division is preceded by DNA replication; the daughter cells are identical in chromosome number and genetic content to one another and to the parent cell.

Mitotic apparatus: The organelle consisting of asters which surround the centriole, mitotic spindle which connect the centromeres of the chromosomes to centrosome and the matrix in which the spindle fibres are embedded,

Mitotic crossing over: (somatic crossing over): Crossing over during mitosis of somatic cells resulting in the segregation of heterozygous alleles.

Modifying gene: A gene that increases the phenotypic expression of a major gene; usually, several modifying genes act in an additive manner and generate a continuous variation in an otherwise qualitative trait.

Monogenic: Governed by or involving a single gene.

Monohybrid cross: Hybridization between two individuals or strains which differ for a single character, or which are taken to differ for a single character.

Monohybrid: The progeny derived by mating or crossing two individuals or strains which differ for one gene (in practice, one character).

Monoploid: A cell or individual having the basic chromosome number (x) ; hapoid from a diploid (2x) species.

Monosomic: An individual having one chromosome less than the normal somatic complment of the species.

Mosaic: An individual or tissue having cells of two or more different genotypes.

Multiple alleles: More than two alleles of a single gene (more precisely, of a single cistron).

Mutable gene: A gene having an unusually high spontaneous mutation rate.

Mutagen: A chemical or physical agent which induces mutation.

Mutant: An organism or cell showing a mutant phenotype due to the mutant allele of a gene.

Mutation: A sudden and heritable change in the character of an organism which is not due to segregation or recombination.

Mutator gene: A gene which causes another gene or genes to undergo spontaneous mutation.

Muton: The unit of mutation; the smallest unit of a gene capable of undergoing mutation; represented by one nucleotide.

Natural Selection: Differential rate of reprodution of different genotypes of an organism in response to the environmental factors; the basis of organic evolution.

Nondisjunction: The failure of a chromosome pair (during A I of meiosis) or of sister chromatids of a chromosome (during A II of meiosis and anaphase of mitosis) to separate during anaphase; as a result, they pass to the same pole leading to the production of n + 1 and n - 1 gametes (meiosis) or 2n + 1 and 2n - 1 daughter cells (mitosis).

Nonsense codon: The codons that do not specify an amino acid, and used for protein chain termination; they are UAA (called ochre), UAG (called amber) and UGA.

Nuclear envelope: The double-membraned structure surrounding the nucleus (in eukaryotes).

Nuclear lamina: A proteinaceous layer consisting of 3 lamin proteins on the inside of the nuclear envelope.

Nuclear pores: Pores in the nuclear envelope, used for transport of macromolecules.

Nucleic acid: The macromolecules composed of phosphate, pentose and organic bases, viz., DNA and RNA.

Nucleoid: In bacterial cell, the DNA containing region which is functionally equivalent to the nucleus of eukaryotes.

Nucleolus Organizer Region (NOR): The segment of a chromosome containing the genes concerned with the synthesis of ribosomes; usually, seen as a constriction in metaphase chromosomes and associated with the nucleolus during the prophase I of meiosis.

Nucleolus: A relatively dense, spherical structure rich in RNA and protein, and associated with the NOR; the site of ribosome assembly and synthesis of ribosomal components.

Nucleoside: A nitrogenous base (purine or pyrimidine) attached to ribose or deoxyribose.

Nucleosome: The bead like structure of chromatin fibers; each composed of a histone octamer and 146 base pairs of DNA.

Nucleotide: The unit of DNA and RNA organisation; each nucleotide has one molecule each of phosphate, pentose (ribose in RNA, deoxyribose in DNA) and one of the five organic bases [A, G, C, T in DNA) and U (in the place of T in RNA)].

Nucleus: In eukaryotes; the organelle containing chromosomes and nucleolus, and surrounded by a typical nuclear envelope composed of two concentric membranes.

Nullisomic: An individual having one chromosome pair less than the normal somatic complement of the species.

Octaploid: A cell or an organism having eight identical (autooctaploid) or different (allooctaploid) genomes.

Okazaki fragments: Short segments of DNA (about 1000 to 2000 bases) synthesized during discontinuous replication; they are later joined by ligase into a covalently intact strand.

Oligogene: A gene producing a marked effect on the expression of a character so that the individuals can be easily grouped into separate classes on the basis of this trait; its expression is relatively little affected by the environment.

Operator gene: In operons; the gene to which the repressor molecule binds; it is the gene adjacent to the first structural gene of an operon.

Operon: A group of structural genes whose transcription is regulated by act of regulator, promoter and operator genes, which are often located next to (upstream or onto the left of) the structural genes.

Organelle: A specialized structure located in the eukaryotic cytoplasm surrounded by a membrane and performing specialized functions.

Ovary: The gonad of a female animal; in plants, the basal part of pistil containing ovules.

Ovule: In plants, the megasporangium which develops into seed (embryo).

Pachytene (pachynema): A substage of meiotic prophase I, between zygotene and diplotene , the homologous chromosomes have paired to become bivalents, each bivalent contains 4 strands (tetrad) made up of 2 chromatids of each chromosome. Crossing over occurs at this stage.

Parthenogenesis: The development of an individual from an unfertilized egg.

Penetrance: The ability of a gene to express itself in all the individuals which carry it in the appropriate genotype (complete penetrance); many genes fail to do so (incomplete penetrance).

Phenotype: The observable characteristics (of appearance, anatomy etc.) of an organism.

Pleiotropy: A single gene affecting more than one character.

Polygenes: Genes having individually small but cumulative effect on a character; they govern quantitative characters.

Polymorphism: Two or (usually) more phenotypes maintained in a random mating population; due to the effects of environment.

Polynucleotide: A macromolecule in which several nucleotides are joined by the phosphodiester linkage, e.g., DNA and RNA.

Polypeptide: A macromolecule in which several amino acids are joined by the peptide bond.

Polyploid: A cell or an organism having more than two genomes; they may be copies of a single genome (autopolyploidy) or of different genomes (allopolyploidy).

Polysome (polyribosome): A series of ribosomes bound to an mRNA.

Polytene chromosome: A giant chromosome consisting of several fibrils.

Prokaryote (procaryote): The organism lacking a true nucleus and meiosis, i.e., chromosomes are not enclosed by a nuclear envelope, e.g., bacteria and viruses.

Promoter gene: The gene or DNA segment of an operon to which RNA polymerase binds before it initiates the transcription of an operon.

Proof reading: Correction of errors in nucleic acid or protein at the time of their synthesis.

Prophase: The first stage of cell division after interphase and before metaphase; the chromosomes become shorter and thicker, and are visibly double-stranded toward the end (mitosis, prophase II of meiosis); chromosomes pair to form typical bivalents (prophase I of meiosis).

Puff: Expansion of a band of a polytene chromosome involved in RNA synthesis (RNA puff). A DNA

puff synthesizes excessive amounts of DNA.

Recessive: An allele which is incapable of expressing itself phenotypically in the heterozygous state.

Reciprocal Crosses: The two crosses in which the same two parents are involved, but the strain which serves as the male parent in one cross is used as the female parent in the other, and *vice-versa.*

Recombination: Usually, in the case of linked genes or characters; the production of new combinations of genes or characters not present in the parents of a cross or generation; involves crossing over.

Recon: The unit of recombination; is represented by one nucleotide; the part of gene within which recombination cannot take place.

Repetitive (repetitious) DNA: Repeated nucleotide sequences, a type of DNA making up significant fraction of the total DNA of most eukaryotes. Replication and transcription; may be unique or repetitive.

Replication fork: The point where strands of double-stranded DNA are separated so that replication can proceed.

Replication: The process of production of new copies of a macromolecule by exactly copying the preexisting macromolecule.

Replicon: A segment of DNA capable of undergoing replication; it has a unique 'origin' site at which the replication begins.

Repulsion Phase: A linkage between the dominant allele(s) of one (or more) gene(s) and the recessive allele(s) of another (several other) gene(s); in such a case one parent involved in a cross contributes the dominant allele of one (or more) gene(s), while the second parent provides the dominant allele(s) of the other gene(s). Respect to a single specialized pair of allelic genes.

Restriction endonuclease: An enzyme which cleaves a DNA molecule either within or close to a site having specific sequence of nucleotides.

Retrovirus: An RNA virus which propagates via reverse transcription into duplex DNA.

Reverse mutation: The mutation of a mutant allele back to the wild type allele.

Reverse transcriptase: RNA dependent DNA polymerase enzyme that synthesizes DNA on a template of RNA.

Ribonucleic acid: It is polynucleotide having ribose as the pentose sugar and ordinarily uracil in place of thymine; genetic material in many viruses and may undergo replication; generally, single-stranded; is of five types: mRNA, tRNA, rRNA, chromosomal RNA, and genetic RNA ; produced by the transcription of DNA.

Ring chromosome: Circular chromosomes. In prokaryotes, they are normally found in *E.coli* and some viruses. In eukaryotes, they arise as a result of chromosome structural change.

SAT-chromosome: A chromosome containing a satellite.

Satellite: A distal segment of a chromosome separated from the rest of the chromosome by a secondary constriction.

Segregation: Separation of the two alleles of a gene during gamete formation and their passage into different gametes; usually due to the separation of homologous chromosomes during AI; each gamete contains only a single copy of only one allele, and leads to the typical 3 : 1 or 1 : 2 : 1 ratios in the F_2 generations of monohybrid crosses.

Self-fertilization: The union between male gametes of an individual with the female gametes produced by the same individual; usually in plants, self-pollination.

Self-incompatibility: The inability of fully functional pollen grains to effect fertilization and seed set on self-pollination; usually, due to multiple alleles of a single gene S; gametophytic or sporophytic in nature.

Semiconservative replication: The mode of DNA replication in which the DNA molecule separates into two strands, each strand is conserved and acts as a template for synthesis of a new strand.

Sex chromosome: A chromosome which differs in number or kind between the male and female individuals of the same species, and is involved in sex determination (Syn., allosome.)

Sex-influenced trait: Alleles of the gene governing such a trait show opposite dominance relationship in the males and females of the species.

Sex-limited character: A character which is expressed in one of the two sexes only.

Sex-linkage: The association between a character and the sex during inheritance; the concerned gene is located in the X chromosome; in human beings several genetic diseases are sex-linked.

Sexual reproduction: The production of new individuals through the fusion of male and female gametes.

Somatic cell: A cell making up the body of an organism, excluding the germ cell; such cells have the full somatic complement of the species.

Somatic chromosome number: The chromosome number normally found in the somatic cells, more specifically in the meristematic cells, of a species; represented by 2n.

S-phase: The part of interphase of eukaryotic cell cycle during which DNA synthesis occurs.

Spindle: A bipolar collection of fibres (called spindle fibres) observed during cell division in eukaryotes.

Spontaneous mutation: A mutation that arises naturally without the application of any mutagen (by man); the cause of such mutations is not definitely known.

Sporogenesis: The production of haploid micro- and megaspores from the diploid microspore and megaspore mother cells, respectively, through meiosis; in plants.

Staggered cut: In double-stranded DNA cut made at different points near each other in the two strands.

Sterility: Inability to produce progeny usually due to nonfunctional gametes; male and female sterility.

Sticky ends: Complementary single strands of DNA at opposite ends of a double-stranded DNA or at ends of different duplex molecules.

Sub vital: A gene which kills some of the individuals which carry it in the appropriate genotype.

Sublethal gene: A gene which causes the death of most, but not all, of the individuals that carry it in the appropriate genotype.

Synapsis: During prophase I of meiosis; close, longitudinal, point-to-point precise association between homolgous chromosomes. (Syn., Chromosome pairing.)

Synaptenemal complex: A proteinaceous structure about 1000 A^0 wide formed between homologous chromosomes during synapsis; considered to facilitate recombination or crossing over.

Transcription: RNA synthesis on a DNA template.

Telocentric: A chromosome having centromere at one end (in the place of telomere).

Telomere: The natural unipolar chromosome ends in eukaryotes; the DNA sequence consists of a short repeating unit with a protruding single stranded end.

Telophase: The last stage of cell division following anaphase preceding interphase; the chromosomes gather at the opposite poles and begin to uncoil to finally form loosely packed masses of chromatin fibers.

Template: A mould; a substance used to create identical copies as specified by itself; DNA molecules serve as templates during replication and transcription.

Terminal deletion: Loss of segment at the end of a chromosome.

Testcross: The cross of an F_1 hybrid with an individual or strain having the recessive phenotype for the concerned trait.

Tetrad: The group of four daughter cells produced by meiotic division of a single cell; also, the four-stranded structure (i.e., bivalent) produced due to the synapsis of two homologous chromosomes, each having two chromatids.

Tetraploid: A cell or an organism having four genomes; the genomes may be copies of a single genome (autotetraploid) or of different genomes (allotetraploid).

Tetrasomic: A cell or an organism having one chromosome pair in addition to the normal somatic complement of the species; one chromosome of the genome has four copies or homologoues.

Transcription: The production of an RNA molecule complementary to a DNA molecule which serves as the template for RNA polymerase, the enzyme that catalyzes transcription.

Transduction: Transfer of a bacterial gene from one bacterium to the other by a phage particle.

Transduction: Genetic recombination in bacteria following the transfer by a virus of a segment of the bacterial chromosome from one bacterial cell into another.

Transfer RNA (tRNA): RNA molecules that transport specific amino acids to the ribosome; each tRNA species has a specific anticodon which base-pairs with the appropriate mRNA codon.

Transformation: The genetic modification of a cell induced by the incorporation of DNA purified from cells or viruses.

Transgenic: Individual created by introduction of new DNA sequences into the germ line via addition to the egg.

Transition: The substitution, in a DNA or an RNA molecule, of purine by another purine or of a pyrimidine by another pyrimidine; leads to gene mutation.

Translation: The process of protein synthesis ; genetic information present in an mRNA molecule directs the order of the specific amino acids to produce the polypeptide.

Translocation: Integration of a segment of one chromosome into a nonhomologous chromosome; this integration may be reciprocal, i.e., the two nonhomologous chromosomes involved in the translocation may exchange segments.

Transposable element (transposon): A sequence of DNA that has the ability to insert itself at a new location in the genome.

Transposase: Enzyme involved in insertion of a transposable element at a new site.

Transversion: In DNA or RNA; substitution of a purine by a pyrimidine and *vice versa*.

Triplet code: A code consisting of a set of 3 nucleotides to specify an amino acid.

Trisomic: A cell or an organism having one chromosome in excess of the normal somatic complement of the species; one chromosome has three homologous in place of the normal two; denoted by 2n + 1.

Unidirectional replication: Movement of a single replication fork from a given origin.

Variation: The occurrence of differences among the individuals belonging to a single species for one or more traits.

Watson - Crick model: A model of DNA structure given by Watson and Crick in 1953. According to this model DNA forms double helix which is held together by hydrogen bonds between specific pairs of bases.

W - Chromosome: The sex chromosome limited to the female sex in case of female heterogamety (ZW = female; ZZ = male).

Wild type: Refers to a strain, organism or gene commonly found in nature or arbitrarily designated as "normal".

X - Chromosome: The sex chromosome which occurs in both male and female individuals but in different numbers, e.g., human male has one X chromosome, while females have two; in most animals and many plants, it has the genes for femaleness.

Y - Chromosome: The sex chromosome which occurs either in the males (man, rodents, *Drosophila* etc.) or females (birds, reptiles) of a species, but never in both the sexes; usually the major portion of Y is genetically inactive; may or may not determine maleness depending on the species.

Z - Chromosome: The sex chromosome present in both sexes where female is heterogametic sex (ZZ = male; ZW or ZO = male).

Zygote: The cell derived through fusion of one male and one female gamete; it has 2n chromosome complement as opposed to the n for the gametes; it develops into a new individual through mitosis (higher plants and animals) or may undergo meiosis to yield the haploid phase.