MODULE-1: INTRODUCTION

Learning objectives

After completing this module, the learner should be able to:

- understand the basic principles of inheritance.
- test and deepen their mastery of genetics by applying this knowledge in a variety of problem-solving situations.

GENETICS

- Genetics is the scientific study of the mechanism of heredity and variation. Hereditary characteristics are determined by elementary units transmitted between generations in uniform predictable fashion. Each unit called a gene must satisfy at least two essential requirements:

    1. that it is inherited in such fashion that each descendant has a physical copy of the material and
    2. that it provides information to its carriers in respect to structure, function and other biological attributes.

- William Bateson introduced the term "genetics" (from the Greek word genno: to give birth) to describe the study of inheritance and the science of variation in a personal letter to Alan Sedgwick, dated April 18, 1905. The term "genetics" first used publicly by Bateson at the Third International Conference on Plant Hybridization in London in 1906.
- The terms gene, phenotype and genotype were coined by the Danish botanist Wilhelm Johannsen and first used from 1909.
- Biological inheritance is the process by which a living organism produces a new organism with many of the same traits as itself.
- Variation in inheritance is a fundamental concept in Darwin's theory of evolution.
- *Drosophila melanogaster* is the convenient model for the study of genetic principles.

GENETICS APPLICATIONS

Some of the broad uses of knowledge of genetics are following:

- Genetics and eugenics: Genetics has suggested suitable possibilities for the betterment of human race through certain fundamental laws of heredity.
- Genetics and agriculture: A significant advance in agricultural and animal genetics and breeding improved the food production. The so called "green revolution" and "white revolution" of to-day's India are the principal outcomes of application of knowledge of genetics to the agriculture and animal breeding.
- Genetics and medical science: Genetics has significant applications in the various human heritable diseases diagnosis and treatment.
- Genetics and legality: Genetics is helpful in solving various legal problems with ease.
- Genetics in removing false concepts about heredity: Genetics has removed various faulty beliefs and misunderstandings concerning the heredity which commonly prevailed among the, different human societies.

MODULE-2: HISTORY OF GENETICS

Learning objectives

After completing this module, the learner should be able to:

- aware of the history and significant discoveries that can enrich the understanding of the genetics present.

HISTORY OF GENETICS

- The history of genetics is generally held to have started with the work of the Augustinian monk, Gregor Johann Mendel who is called the "Father of Genetics" for his study on the inheritance of traits in pea plants.
- The significance of Mendel's work was not recognized until their rediscovery by the three scientists: Hugo de Vries (Holland), Carl Correns (Germany) and Erich von Tschermak (Austria).
- The following outline is provided as an overview of and as topical guide to the history of genetics:
    - Pre - Mendelian Ideas on Heredity
    - Mendel
    - Post - Mendel

PRE - MENDELIAN IDEAS ON HEREDITY

- As early as the sixth century B.C., Greek philosophers had begun to search for explanations of how and why the world and human beings came to be formed and organized as they were.
- The work of Socrates (470-399 B.C.), Plato (429-347 B.C.), and Aristotle (384-322 B.C.) established the foundations of *Western philosophy*.
- Pythagoras (570-495 B.C.) proposed the theory that animals are born from one another by seeds and that seed is a drop from the brain which contains in itself a warm vapour; and that when this is applied to the womb, it transmits virtue, and moisture, and blood from the brain, from which flesh, and sinews, and bones, and hair, and the whole body are produced. And from the vapour is produced the soul, and also sensation.
    - Pythagoras was one of the first to elaborate a theory of generation, the biological production of offspring.
- According to Aristotle, the female parent contributed only unorganized matter to the new individual while the male provided the form.
- Jan Swammerdam made observations using microscopes in the late 17th century, and interpreted their findings to develop the *preformation theory*, supposing that an egg contained all the future generations of its kind as preformed miniatures.
- William Harvey (1578-1657), in his publication the generation of animals (1651) argue that all living beings arose from eggs.
- Dutch microscopist Antonie van Leeuwenhoek (1932-1723) was one of the first to observe spermatozoa.He reasoned that the movement of spermatozoa was evidence of animal life, which presumed a complex structure and, for human sperm, a soul.
- In 1694, Nicolas Hartsoeker produced an image of tiny men inside the sperm, which he called **" *animalcule" or "homunculus* ".**
- Carl Linnaeus (1707-1778) Swedish naturalist and explorer was the first to frame principles for defining natural *genera* and *species* of organisms and to create a uniform system for naming them (binomial nomenclature).
- Lamarck (1744–1829) pioneer French biologist who is best known for his idea that *acquired characters* are inheritable, an idea also known as ***Lamarckism*,** and which is controverted by modern genetics and evolutionary theory.

- Lamarckism or Lamarckian evolution refers to the once widely accepted idea that an organism can pass on characteristics that it acquired during its lifetime to its offspring (also known as based on heritability of acquired characteristics or "soft inheritance"). Lamarck stressed two main themes in his biological work.
    - The first was that the environment gives rise to changes in animals.
    - The second principle was that life was structured in an orderly manner and that many different parts of all bodies make it possible for the organic movements of animals. It proposed that individual efforts during the lifetime of the organisms were the main mechanism driving species to adaptation, as they supposedly would acquire adaptive changes and pass them on to offspring.
- Charles Robert Darwin (1809-1882) English naturalist and founder of modern evolutionary theory proposed and provided scientific evidence that all species of life have evolved over time from common ancestors through the process which he called Natural Selection**.**
    - Darwin found that those organisms more suited to their environment were more likely to survive. This resulted in the well known phrase *survival of the fittest*.
    - Pangenesis was Charles Darwin's hypothetical mechanism for heredity. *Gemmules*, also called *plastitudes or pangenes*, were assumed to be shed by the organs of the body and carried in the bloodstream to the reproductive organs where they accumulated in the germ cells or gametes.
    - They thus provided a possible mechanism for the inheritance of acquired characteristics, as proposed by Jean-Baptiste Lamarck.
- Regnier De Graaf is famous for having discovered the ovarian follicle (which is named Graafian follicle in his honour).
- A new way of thinking about heredity, fertilization, and development was made possible by the establishment of the Cell Theory in the 1830s.
- The establishment of *cell theory* is generally attributed to Matthias Jacob Schleiden (1804-1881) and Theodor Schwann (1810-1882), who recognized the importance of Robert Brown's (1773-1858) discover of the cell nucleus.
- Further investigations during the last quarter of the nineteenth century provided many insights into the role played by the nucleus during cell division, and the recognition of fundamental cytological phenomena such as mitosis, maturation, and fertilization and important cellular organelles, such as mitochondria, chloroplasts, and the Golgi apparatus.
- Cytological studies led to the discoveries that linked cytology to inheritance and development.
- Based on these studies, Friedrich Leopold August Weismann (1834-1914) proposed the theory of the continuity of the germplasm and predicted the reduction division of the chromosomes during the formation of the germ cells. He advocated the germ plasm theory, according to which (in a multicellular organism) inheritance only takes place by means of the germ cells -the gametes such as egg cells and sperm cells. -
- In *Cell-Formation and Cell-Division* (1875) Eduard Strasburger (1844-1912) described the division of plant cells.
- Walter Flemming's (1843-1905) *Cell Substance, Nucleus, and Cell Division* (1882) established a basic framework for the stages of cell division. Flemming used the term chromatin for the nuclear substance and coined the term mitosis.
- Heinrich W.G. Waldeyer (1836-1921) introduced the term chromosome in 1888.

MENDEL

- Joseph Gottlieb Koelreuter (1733-1806) was one of the first botanists to systematically make and test hybrids.
- Koelreuter's work was extended by Carl Friedrich von Gaertner (1772-1850). In the 1860s, Gregor Mendel carried out a remarkable series of hybridization experiments and systematically analyzed the results of his tests.

- Gregor Johann Mendel (1822–1884) Austrian botanist, teacher, Augustinian monk and is often called the father of genetics for his study of the inheritance of traits in pea plants, the first to lay the mathematical foundation of the science of genetics, in what came to be called Mendelism.
  - The significance of Mendel's work was not recognized until the turn of the 20th century.
  - Its rediscovery prompted the foundation of the discipline of genetics.
- Between 1856 and 1863 Mendel cultivated and tested some 29,000 pea plants (i.e. Pisum sativum).
  - Mendel read his paper, "Experiments on Plant Hybridization", at two meetings of the Natural History Society of Brunn in Moravia in 1865.
  - When Mendel's paper was published in 1866 in Proceedings of the Natural History Society of Brunn, it had little impact and was cited about three times over the next thirty-five years.

POST - MENDEL

- It was not until the early 20th century that of Mendel's work were recognized.
- In 1900, his work was rediscovered by Dutch botanist Hugo de Vries (1848-1935), German botanist Carl Correns (1864-1933) and Austrian agronomist Erich von Tschermak (1871-1962). His results were quickly replicated, and genetic linkage studies quickly worked out.
- William Bateson (1861–1926) was the chief populariser of the ideas of Gregor Mendel following their rediscovery in 1900.
- Ronald Fisher in 1918 used Mendelian genetics as the basis of the start of the modern synthesis in evolutionary biology.
- In 1909 Wilhelm L. Johannsen introduced the term gene to replace older terms like factor, trait, and character. He coined the terms phenotype and genotype, which are now used to indicate the appearance of the individual and its actual genetic makeup, respectively.
- Wilhelm Weinberg (1862—1937) and Godfrey Harold Hardy (1877 –1947) in 1908 independently formulated the Hardy-Weinberg principle of population genetics.
- Thomas Hunt Morgan (1866 – 1945), American zoologist and geneticist, famous for his experimental research with the fruit fly (Drosophila) by which he established the chromosome theory of heredity and also discovers the first sex-linked lethal gene.
- Hermann Joseph Muller (1890–1967) demonstrates that X-rays are mutagenic in Drosophila.
- In 1941 George Wells Beadle and Edward Lawrie Tatum proposes the one gene - one enzyme (polypeptide) concept.
- In 1944 Oswald Theodore Avery et al describe the DNA as the hereditary material.

- Francis Crick, James D. Watson and Maurice Wilkins were awarded the 1962 Nobel Prize for Physiology or Medicine, "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material."
- Har Gobind Khorana is an Indian-American molecular biologist. He was awarded the Nobel Prize (shared with Robert W. Holley and Marshall Warren Nirenberg) in 1968 for his work on the interpretation of the genetic code and its function in protein synthesis.
- The Human Genome Project (HGP) was a 13-year project coordinated by the U.S. Department of Energy and the National Institutes of Health.
    - In 1988 Project began with the goal of determining the entire sequence of DNA composing human chromosomes.
    - The project began in 1990 initially headed by James D. Watson at the U.S. National Institutes of Health.
    - A working draft of the genome was released in 2000 and a complete one in 2003.

MODULE-3: CHROMOSOME

Learning objectives

After completing this module, the learner should be able to:

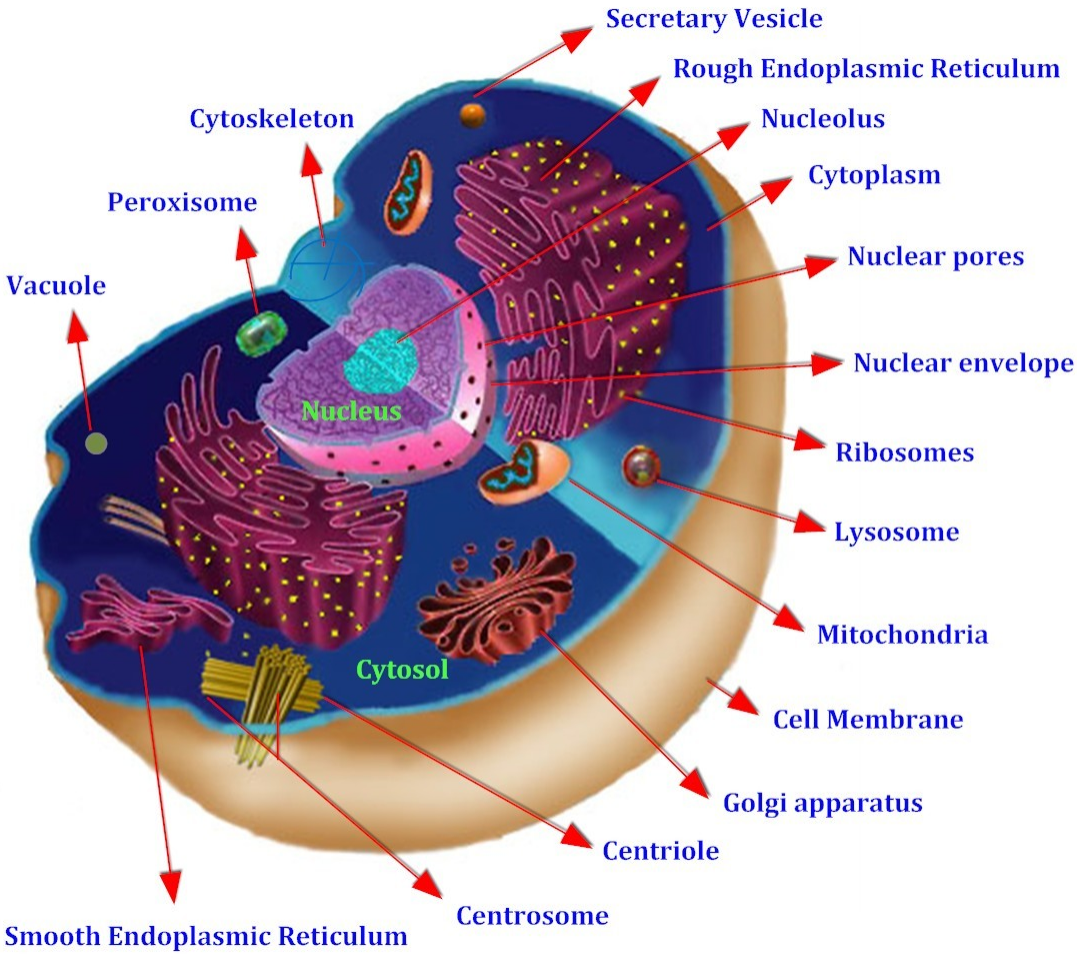
- understand the structures and purposes of basic components of eukaryotic cell, especially macromolecules, membranes, and organelles
- understand the terms used to describe chromosome morphology
- become familiar with diploid chromosome number in livestock and poultry

CELL

- Cell is the basic unit of life.
- Animal cells are typical of the eukaryotic cell, enclosed by a plasma membrane and present in different shapes and containing a membrane-bound nucleus and cell organelles.
- Cell contents are called the protoplasm.
- Genes reside in cell nucleus.
- It is necessary, therefore, to study a cell and its role in transmitting genes from generation to generation.
- Most cells, both animals and plants, range in size between 1 and 100 micrometers and are thus visible only with the aid of a microscope.
- Discovery of living cells would have been difficult, if not impossible, before the compound microscope was invented by Zacharias Jansen of Holland in 1590.
- In 1665, Robert Hooke of England discovered “Cell” and applied the term “Cell” to the cavities he saw in sections of cork.
- In 1675, Marcello Malpighi published an "Anatomy of Plants", the first systematic study of cell structure.
- In 1839 Theodor Schwann, an animal anatomist, formulated the Cell Theory which set forth the concept that “the elementary parts of all tissues are formed of cells through much diversified in manner”.

- Animal cell is distinct from other eukaryotes especially plant cells by lack of cell walls and chloroplasts, and have smaller vacuoles.
- The lack of a rigid cell wall allowed animals to develop a greater diversity of cell types, tissues, and organs.
- Most animal tissues are bound together in an extracellular matrix by a triple helix of protein known as collagen.
- Plant and fungal cells are bound together by molecules like pectin.
- In animals, there are many different cell types and have a variety of internal membranes and structures.
- An organelle is a specialized sub-unit within a cell that has a specific function, and is separately enclosed within its own lipid membrane.

To view "Animal Cell Animation"



Cell Membrane

- The [redacted] (also called the [redacted]) is a [redacted] It physically separates the intracellular components from the extra cellular environment and serves as a protection layer for the interior of the cell.
- The cell membrane is selectively permeable, allowing some substances to pass into the cell and blocking others.

Cytoplasm

- This is a [redacted] les suspended within the cytosol.
- The cytoplasm has three major elements as follows,
  - The cytosol
  - Organelles and
  - Inclusions

Cytosol

- The [redacted] anelles reside. It is the internal fluid of the cell.
- In cytosol, a portion of cell metabolism occurs. [redacted] including signal transduction pathways, glycolysis, intracellular receptors and transcription factors.

Centrosome/Microtubule Organizing Center (MTOC)

- [redacted])C)".
- It is a small body located near the nucleus where microtubules are produced. It is a regulator of cell-cycle progression. [redacted] one is perpendicular to the other) called centrioles but the plant cell centrosome is simpler and does not have centrioles.
- The centrosome is duplicated during cell division resulting in two centrosomes, each with its own pair of centrioles.
- [redacted] eus of the dividing cell and from each [redacted] which is responsible for separating replicated chromosomes into two daughter cells. Thus each daughter cell inherits one centrosome.

Centriole

- Centrioles are barrel shaped self-replicating organelles found in most animal eukaryotic cells, though absent in higher plants and fungi.
- [redacted] icrotubules and [redacted] f [redacted] s ([redacted]
- [redacted] he completion of [redacted] s.

Golgi Apparatus

- [redacted]
- It is an o [redacted]
- [redacted] molecules su [redacted] - bound vesicles for cell secretion (exocytosis) or for use within the cell.

Smooth Endoplasmic Reticulum

- Endoplasmic reticulum (ER) is a vast system of interconnected, membranous, infolded and convoluted tubes that are located in the cell's cytoplasm.
- The [redacted] and provides a pipeline between the [redacted]. The space within the ER is called the ER lumen which acts as a transport system for the cell.
- The functions of the Endoplasmic Reticulum vary greatly depending on the exact type of endoplasmic reticulum and the type of cell in which it resides.
- The smooth endoplasmic reticulum is so named because it appears smooth by electron microscopy. [redacted]
- [redacted]

Rough Endoplasmic Reticulum

- The surface of the rough endoplasmic reticulum is studded with [redacted].
- Proteins synthesized on these ribosomes are collected in the endoplasmic reticulum for transport throughout the cell.
- The [redacted] of the rough endoplasmic reticulum is to synthesize and [redacted]

Ribosomes

- [redacted] protein that [redacted].
- Ribosomes are classified as being either "free" (anywhere in the cytoplasm) or "*membrane-bound*" (endoplasmic reticulum).

Mitochondria

- Mitochondria also called as "*cellular power plants*".
- Are spherical to rod-shaped organelles with a double membrane.
- The inner membrane is infolded many times, forming a series of projections called as cristae.
- The space bounded by the inner membrane is called matrix.
- The most prominent role of the mitochondrion is production of energy stored in glucose by conversion into ATP (adenosine triphosphate) - the primary energy source for the cell.

Lysosome

- Lysosome is nicknamed as "*cell vesicles*" or "*suicide-bags*" or "*suicide - sacs*".
- Lysosomes are organelles that contain digestive enzymes necessary for intracellular digestion.
- They are common in animal cells, but rare in plant cells.
- They digest excess or worn-out organelles, food particles, and engulfed viruses or bacteria, which are transferred to the cytoplasm as new cell-building materials.

Peroxisome

- Peroxisomes sometimes called microbodies are membrane-bound packets of oxidative enzymes.
- Peroxisomes break down organic molecules by the process of oxidation to produce hydrogen peroxide and then quickly into water and oxygen.
- They are called peroxisomes because they all produce hydrogen peroxide.
- A major function of the peroxisome is the breakdown of fatty acid molecules.

Secretary vesicle

- It is a membrane bounded vesicle derived from the golgi apparatus and containing cell secretions - e.g. hormones, neurotransmitters that are to be released from the cell.
- The contents may be densely packed, and then transported to the cell surface. The vesicle fuses with the cell membrane at a structure called the Porosome, in a process called Exocytosis, dump its contents out of the cell's environment.

Vacuoles

- Vacuoles are found in the cytoplasm of most plant cells and some animal cells.
- It is a fluid-filled, membrane-surrounded cavity inside a cell.
- The vacuole fills with food being digested and waste material that is on its way out of the cell.

Cytoskeleton (CSK)

- Cytoskeleton is a network of protein filaments and motor proteins in the cytoplasm that give shape to a cell, hold and move organelles, and typically involved in cell movement.
- The cytoskeleton maintains the cell shape.
- The cytoskeleton consists of three types of proteins,
    - Microtubules,
    - Intermediate filaments, and
    - Microfilaments

Nucleus

- The nucleus is the largest cellular organelle that includes the nucleolus.It is enclosed by a nuclear envelope, a double membrane and communicates with the surrounding cytosol via numerous nuclear pores.
- Besides the nucleolus, the nucleus contains a number of other non-membrane delineated bodies like Cajal bodies, Gemini of coiled bodies, polymorphic interphase karyosomal association (PIKA), promyelocytic leukaemia (PML) bodies, paraspeckles and splicing speckles.
- The viscous liquid within the nucleus is called nucleoplasm.
- Nucleus contains most of the cell's genetic material, double helix DNA molecules held in complex with a large variety of proteins, such as histones, to form chromosomes.
- Similar DNA is present in every cell of the body, but depending on the specific cell type, some genes within chromosomes may be turned on or off - that's why a fat cell is different from a liver cell.
- The main function of the nucleus is the coordination of the cell's activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

Nuclear Membrane

- Nuclear envelope known as the perinuclear envelope, nuclear membrane, nucleolemma or karyotheca.
- It is a double membrane surrounds the nucleus and separates the contents of the nucleus (DNA in particular) from the cytosol (cytoplasm).
- The outer membrane is continuous with the rough endoplasmic reticulum.
- The space between the two membranes that make up the nuclear envelope is called the perinuclear space (also called the perinuclear cisterna).

Nuclear Pores

- They are formed at sites where the inner and outer membranes of the nuclear envelope are joined.

Nucleolus

- The nucleolus is a membrane less organelle found in the nucleus, and is sometimes called a sub organelle.
- The main function of the nucleolus is the biogenesis and assembly of ribosome components.
- Some cells have more than one nucleolus, but some cell types do not have any.

CHROMOSOMES

Chromosome (chroma - colour; some - body)

- A chromosome is a thread-like self-replicating genetic structure containing organized DNA molecule package found in the nucleus of the cell.
- Clear and detaile decriptions of mitotic chromosomes in plants and animals were published by Strasburger in 1875 and by the German scientist Walter Flemming in 1879-1882.
- Heinrich Wilhelm Gottfried Waldeyer coined the term chromosome in 1888.
- Normally Chromosomes are of two types
    - Autosomes - Control characters other than sex characters or carry genes for somatic characters.
    - Sex chromosomes *(Synonym: Gonosomes)* - Chromosomes involved in sex determination.
        - Humans and most other mammals have two sex chromosomes X & Y, also called heterosome, odd chromosome, or idiosome.
        - Females have two X chromosomes in diploid cells; males have an X and a Y chromosome.
        - In birds the female (ZW) is hetero-gametic and male (ZZ) is homo-gametic.

CHROMOSOME NUMBER

Haploid, Diploid

- Diploid cells (2N where N- chromosome number) have two homologous copies of each chromosome.
- The body cells of animals are diploid.
- Haploid cells (N) have only one copy of each chromosome.
- In animals, gametes (sperm and eggs) are haploid.

Homologous Chromosomes

- Diploid organisms have two copies of each chromosome (except the sex chromosomes). Both the copies are ordinarily identical in morphology, gene content and gene order and hence known as homologous chromosomes.
- Each pair of chromosomes made up of two homologs.
- Homologous chromosome is inherited from separate parents; one homolog comes from the mother and the other comes from the father.

Chromosome Number

- The number of chromosomes in a given species is generally constant.

- Chromosomes come in pairs.
- Different organisms have different numbers of chromosomes. Normally all individual of a species have the same chromosome number.
    - Diploid Chromosome number in Livestock
    - Diploid Chromosome number in Wild & Laboratory Animals
    - Diploid Chromosome number in different species of Birds

DIPLOID CHROMOSOME NUMBER IN LIVESTOCK

Sl. No.	Common Name	Genus and Species	Diploid Chromosome Number
1	Cat	*Felis catus*	38
2	Cattle	*Bos taurus, Bos indicus*	60
3	Dog	*Canis familiaris*	78
4	Donkey	*Equus asinus*	62
5	Goat	*Capra hircus*	60
6	Horse	*Equus caballus*	64
7	Human	*Homo sapiens*	46
8	Pig	*Sus scrofa*	38
9	Rabbit	*Oryctolagus cuniculus*	44
10	River buffalo	*Bubalus bubalis* (riverine type)	50
11	Swamp buffalo	*Bubalus bubalis* (swamp type)	48
12	Sheep	*Ovis aries*	54
13	Llama	*Lama glama*	74
14	Mule	(Hinny, hybrids of horse and ass)	63
15	African buffalo or Cape buffalo	*Syncerus caffer*	52

DIPLOID CHROMOSOME NUMBER IN WILD AND LABORATORY ANIMALS

Sl. No.	Common Name	Genus and Species	Diploid Chromosome Number
1	Alligator	*Alligator mississipiensis*	32
2	Bison	*Bison bison*	60
3	Camel	*Camilus bactrianus* (Bactrian-two humped) and *Camilus dromedaries* (Dromedari-single humped)	74
4	Chimpanzee	*Pan troglodytes*	48
5	Deer	*Cervus elaphus*	68

6	Elephant	*Elephas maximus* (Asian) and *Loxodonta Africana* (African)	56
7	Golden hamster	*Mesocricetus auratus*	44
8	Gorilla	*Gorilla gorilla*	48
9	Guinea pig	*Cavia cobaya*	64
10	Hare	*Lepus nigricollis*	48
11	Lion	*Panthera leo*	38
12	Mouse	*Mus musculus*	40
13	Musk ox	*Ovibus moschatus*	48
14	Rat	*Rattus norvegicus*	42
15	Reindeer	*Rangifer tarandus*	70
16	Syrian hamster	*Mesocricetus auratus*	44
17	Tiger	*Panthera tigris*	38
18	Honey bee	*Apis mellifera*	32, 16
19	House fly	*Musca domestica*	12
20	Common fruit fly	*Drosophila melanogaster*	8

DIPLOID CHROMOSOME NUMBER IN DIFFERENT SPECIES OF BIRDS

<b**Sl. No.</b**	Common Name	Genus and Species	Diploid Chromosome Number
1	Chicken	*Gallus domesticus*	78
2	Domestic duck	*Anas platyrhyncha*	80
3	Emu	*Dromaius novaehollandiae*	80
4	Goose	*Anser anser*	80
5	Guinea fowl	*Numida meleagris*	74
6	Japanese quail	*Coturnix japonica*	78
7	Muscovy duck	*Cairina moschata*	80
8	Ostrich	*Struthio camelus*	80
9	Pigeon	*Columbia livia*	80

10	Ring-necked pheasant	*Phasianus colchicus*	82
11	Turkey	*Meleagris gallopavo*	80

STRUCTURE OF CHROMOSOME

Chromosome Morphology

- The chromosome morphology changes during cell division and mitotic metaphase is the most suitable stage for studies on chromosome morphology.
- The DNA of eukaryotic cells is tightly bound to small basic proteins (histones) that package the DNA in an orderly way in the cell nucleus.
- The complexes between eukaryotic DNA and proteins are called chromatin, which typically contains about twice as much protein as DNA.
- The major proteins of chromatin are the histones - H1, H2A, H2B, H3, and H4 which are very similar among different species of eukaryotes.
- The shape of the eukaryotic chromosomes is changeable from phase to phase in the continuous process of the cell growth and cell division.
- Chromosomes are thin, coiled, elastic, thread-like structures during the interphase.
- As cells enter mitosis, their chromosomes become highly condensed so that they can be distributed to daughter cells.
- In mitotic metaphase chromosomes, the following structural features can be seen under the light microscope.

Chromatid

- Each metaphase chromosome appears to be longitudinally divided into two identical parts each of which is called chromatid. Both the chromatids of a chromosome appear to be joined together at a point known as centromere. The two chromatids of chromosome separate from each other during mitotic anaphase (and during anaphase II of meiosis) and move towards opposite poles.
- Since the two chromatids making up a chromosome are produced through replication of a single chromatid during synthesis (S) phase of interphase, they are referred to as sister chromatids. In contrast, the chromatids of homologous chromosomes are known as non-sister chromatids.

Centromere (Primary constriction)

- Each chromosome has a constriction point called the centromere (Synonym: Kinetochore), which divides the chromosome into two sections or arms.
- The short arm of the chromosome is labeled the "p" arm. The long arm of the chromosome is labeled the "q" arm.

Telomere

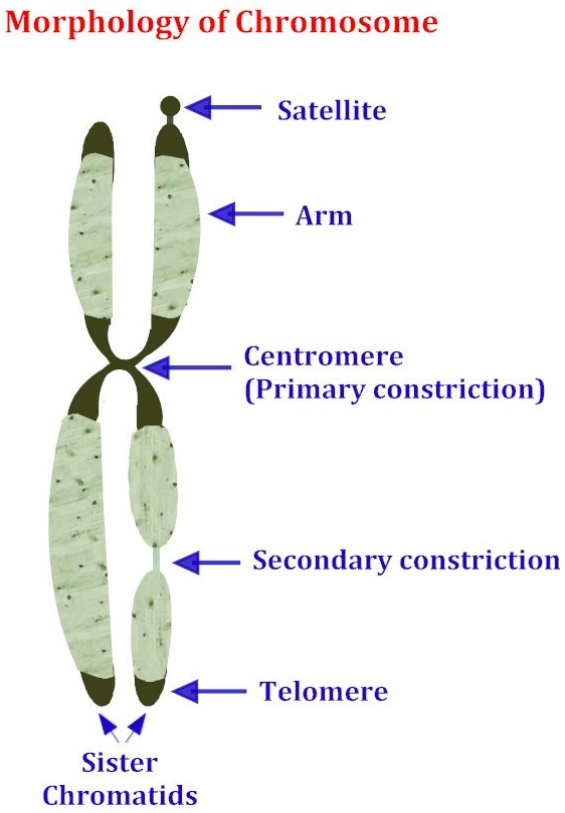
- The sequences at the ends of eukaryotic chromosomes, called telomeres, play critical roles in chromosome replication and maintenance.

Secondary constriction

- In addition to centromere / primary constriction, one or more constrictions in the chromosome are present termed secondary constrictions.

Satellite

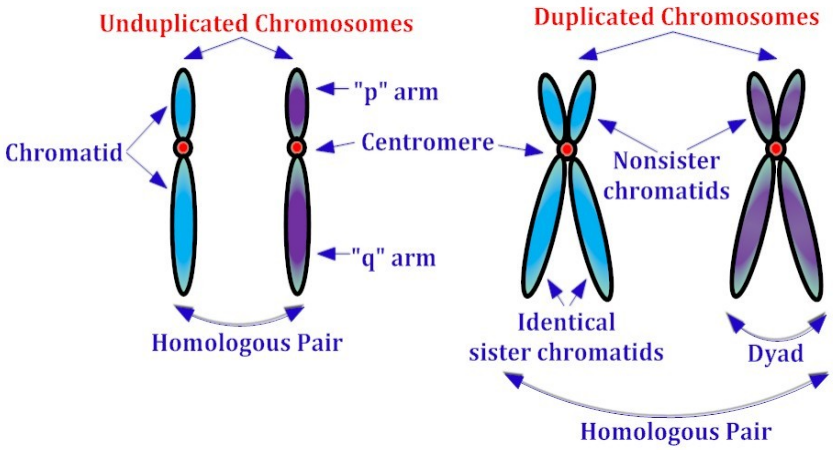
- A small chromosomal segment separated from the main body of the chromosome by a secondary constriction is called Satellite.



CENTROMERE POSITIONS

Size of the chromosome

- The size of the chromosome shows a remarkable variation depending upon the stage of cell division. The chromosomes are the longest and thinnest during interphase (resting stage) and hence not visible under light microscope. Chromosomes are the smallest and thickest during mitotic metaphase.
- Chromosome size is not proportional to the number of genes present on the chromosome.
- The location of the centromere on each chromosome gives the chromosome its characteristic shape.



Centromere position

- Chromosomes are classified according to the centromere position is at one end (acrocentric), closer to one end than the other (submetacentric) or in the middle (metacentric).
- Each chromosome has two arms, labeled p (the shorter of the two) and q (the longer).
- The p arm is named for "petite" meaning 'small'; the q arm is named q simply because it follows p in the alphabet. (According to the NCBI, "q" refers to the French word "queue")

To view "Centromere Position Animation"

Metacentric

- The centromere is localized approximately midway between each end and thereby two arms are roughly equal in length.
- Metacentric chromosome takes V shape during anaphase.

Submetacentric

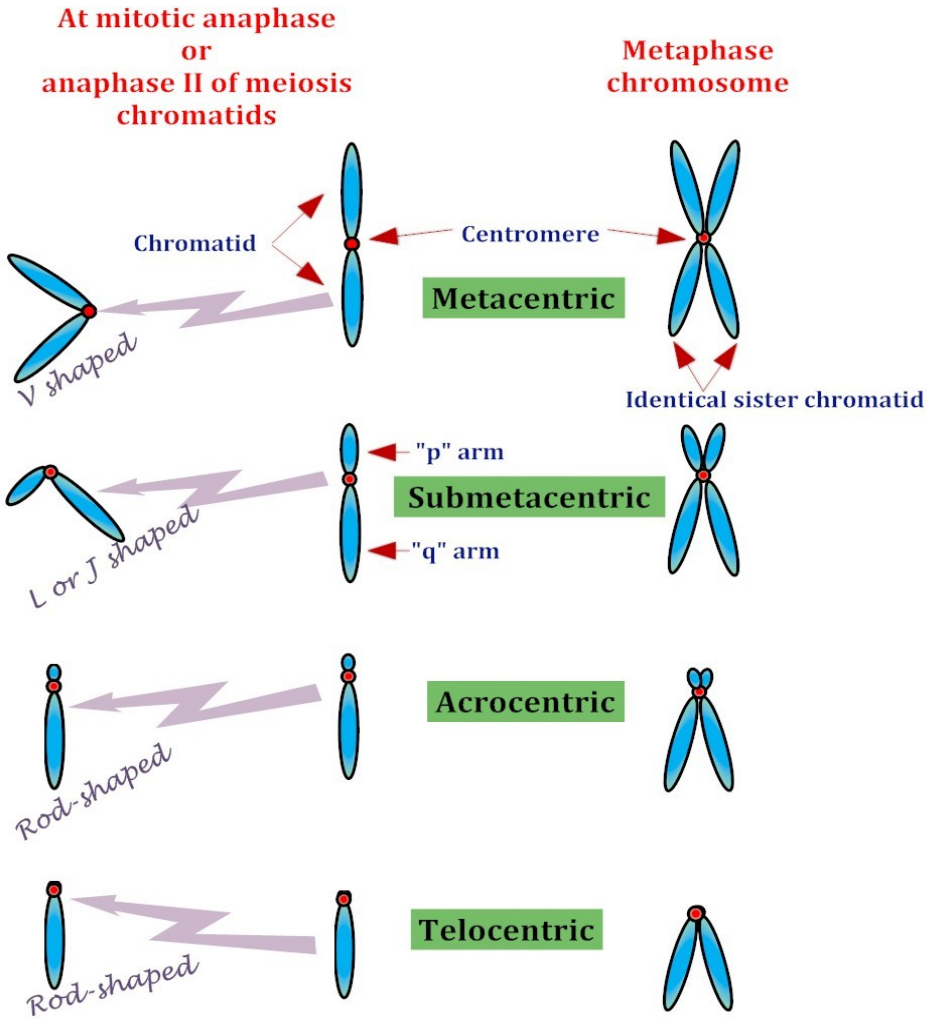
- Centromere is submedian, giving one longer and one shorter arm.
- Submetacentric chromosome may be J or L shaped during anaphase.

Acrocentric

- The centromere is more terminally placed and forms very unequal arm length (The "acro-" in acrocentric refers to the Greek word for "peak").
- The p (short) arm is so short that is hard to observe, but still present.
- Acrocentric chromosome may be rod shaped during anaphase.

Telocentric

- Centromere lies at one end.
- Telocentic chromosome may be rod shaped during anaphase.



- According to the number of the centromere the eukaryotic chromosomes may be acentric (without any centromere), mono centric (with one centromere), dicentric (with two centromeres) or polycentric (with more than two centromeres).

KARYOTYPE AND IDEOGRAM

Karyotype

- The general morphology (size of chromosomes, position of centromere, presence of secondary constriction and size of satellite bodies) of somatic chromosomal complement of an individual constitutes its karyotype.
- In a karyotype, chromosomes are arranged and numbered by size, from largest to smallest.
- The karyotype of a normal somatic cell of a normal individual represents the karyotype of the concerned species.
- This arrangement helps scientists quickly identify chromosomal alterations that may result in a genetic disorder.
- To make a karyotype, picture of someone's chromosomes taken, cut them out and match them up using size, banding pattern and centromere position as guides.

- Avian karyotype is different from mammalian karyotype because of presence of very small autosomes called *microchromosomes*.

Ideogram

- The karyotype of a species can be represented diagrammatically showing all the morphological features of chromosomes. Such a diagram is known as ideogram or ideotype.

SPECIAL TYPES OF CHROMOSOMES

Polytene chromosomes

- Polytene chromosomes are giant chromosomes common to many dipteran (two-winged) flies.
- These were first discovered by E. G. Balbiani in 1882 in Dipteran salivary glands and hence commonly called salivary gland chromosomes.
- They begin as normal chromosomes, but through repeated rounds of DNA replication without any cell division (called endoreplication), they become large, banded chromosomes (see figure).
- For unknown reasons, the centromeric regions of the chromosomes do not endoreplicate very well.
- As a result, the centromeres of all the chromosomes bundle together in a mass called the chromocenter.
- Polytene chromosomes are usually found in the larvae, where it is believed these many-replicated chromosomes allow for much faster larval growth than if the cells remained diploid.
- Simply because each cell now has many copies of each gene, it can transcribe at a much higher rate than with only two copies in diploid cells.
- The polytene chromosomes at the right are from the salivary glands of the fruit fly Drosophila melanogaster.
- The bands on each chromosome are like a road map, unique to each chromosome and well defined enough to allow high resolution mapping of each chromosome.
- The Drosophila Genome Project uses polytene chromosomes as a framework for the map.

Lampbrush chromosomes

- It was first observed by W. Flemming in 1882 and was described in detail in oocytes of sharks by Rukert in 1892.
- It consists of an axis from which paired loops extend in opposite directions, giving the appearance of a lamp brush. Hence the name Lamp Brush Chromosomes.
- It is found in the Oocytes of amphibians and in some insects.
- They are formed during the active synthesis of mRNA molecules for the future use by the egg during cleavage when no synthesis of mRNA molecules is possible due to active involvement of chromosomes in the mitotic cell division.
- It is larger in size. Hence it is called a giant chromosome.

B-chromosomes

- B-Chromosomes (also called supernumerary chromosomes, accessory chromosomes, accessory fragments, etc.) are without obvious genetic function and usually have a normal structure, are somewhat smaller than the autosomes.

Holokinetic chromosomes

- The chromosomes with a non-localized centromere are called as either holocentric or holokinetic chromosomes.

MODULE-4: CELL DIVISION

Learning objectives

After completing this module, the learner should be able to:

- understand the key roles of mitosis and meiosis during the life cycle
- understand the stages of mitosis and meiosis; focus on behavior of chromosomes

CELL DIVISION

- The *cell cycle, or cell-division cycle,* is an ordered series of events that take place in a cell leading to cell growth and its division and duplication (replication into two daughter cells).
- *Cytokinesis* is the physical division of the cytoplasm whereby the nuclei, cytoplasm, organelles and cell membrane of a single eukaryotic cell is divided into two daughter cells containing roughly equal shares.

Types of Cell Division

Mitosis

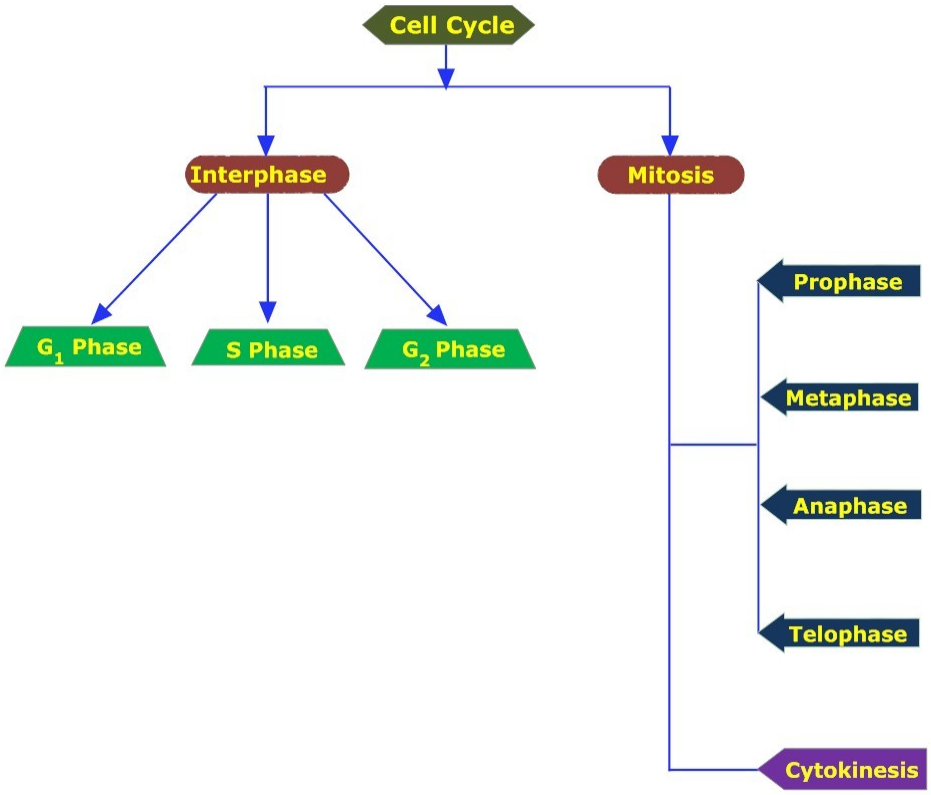
- Mitosis produces two daughter cells that are identical to the parent cell.
- This type of cell division allows multicellular organisms to grow and repair damaged tissue.

Meiosis

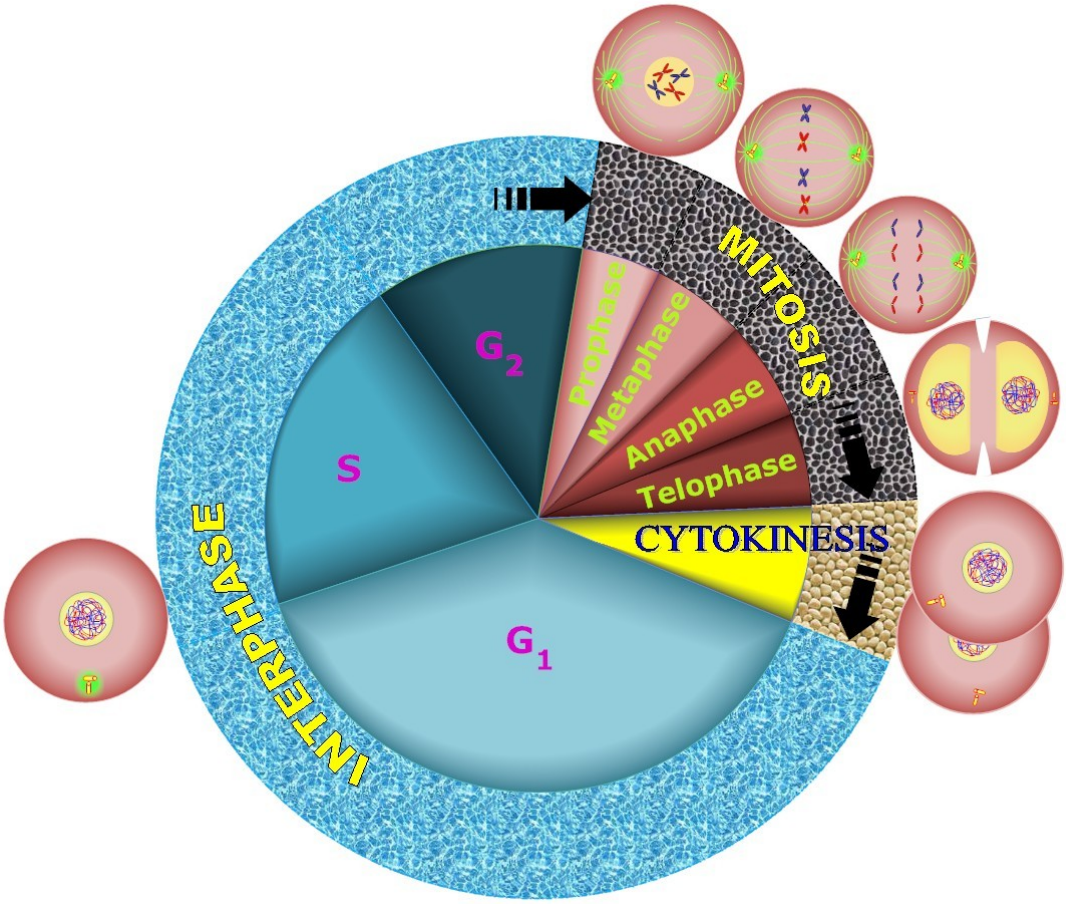
- Meiosis (double cell division) produces daughter cells that have one half the numbers of chromosomes as the parent cell.
- Meiosis is necessary in sexually-reproducing organisms because the fusion of two gametes (fertilization) doubles the number of chromosomes.

MITOSIS

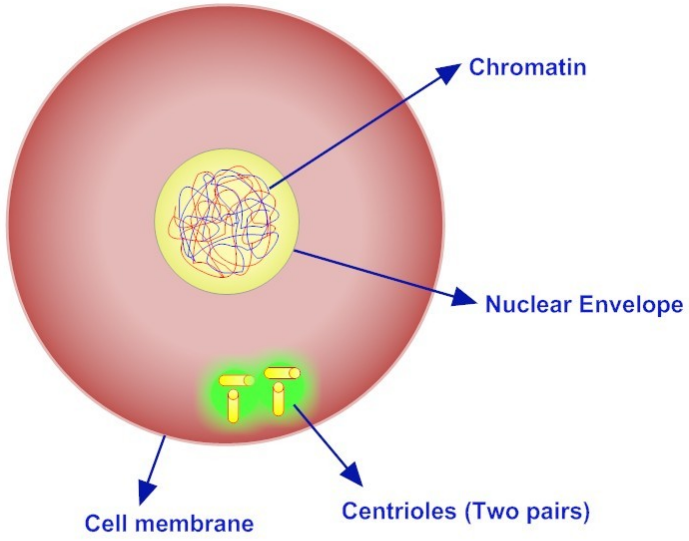
- Mitosis is a process of nuclear and cytoplasmic division (Karyokinesis and cytokinesis respectively) in which two daughter cells are produced that has chromosomal numbers identical to the parental cell.



- *Mitosis* (designated M Phase) is part of the total cell cycle for cells undergoing division.
- The initial event in the cell cycle is the growth phase, called *Interphase*.


INTERPHASE
MITOSIS
CYTOKINESIS
G1
S
G2
Prophase
Metaphase
Anaphase
Telophase

INTERPHASE



INTERPHASE

- The mitotic phase is a relatively short period of the cell cycle.
- It alternates with the much longer *interphase*, where the cell prepares itself for cell division.
- Interphase is often included in discussions of mitosis, but interphase is technically not part of mitosis.
- Interphase is divided into three phases, **G_1** (first gap), **S** (synthesis), and **G_2** (second gap).
- During all three phases of Interphase, the cell *grows by producing proteins* and engaged in high metabolic activity and performing its prepare for mitosis.

G1 PHASE

- In this phase, the cell increases in mass and prepares for DNA replication.
- The metabolic rate of the cell will be high.
- It takes about 10 hr for a cell requiring 24 hrs for its cell cycle.

S PHASE

- DNA is replicated.
- The centrosome is also duplicated.
- Cells will take between 5 and 6 hours to complete S phase.

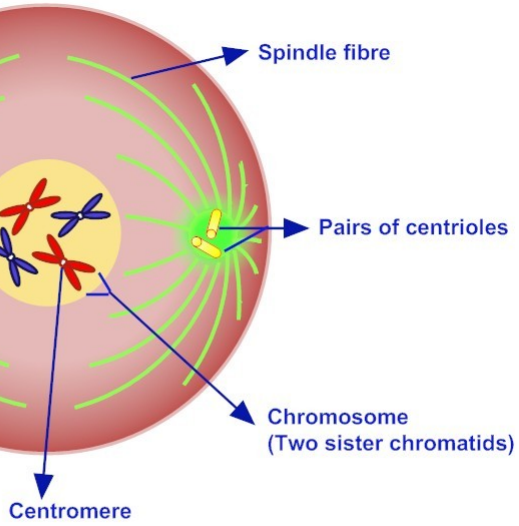
G2 PHASE

- The cell undergoes a period of rapid growth to prepare for mitosis.
- G_2 is third, final, shortest subphase, lasting only 3 to 4 hours.
- G_2 period is after DNA synthesis has occurred but is prior to the start of prophase.

STAGES OF MITOSIS

- Mitosis is divided into,
  - Prophase
  - Metaphase
  - Anaphase and
  - Telophase

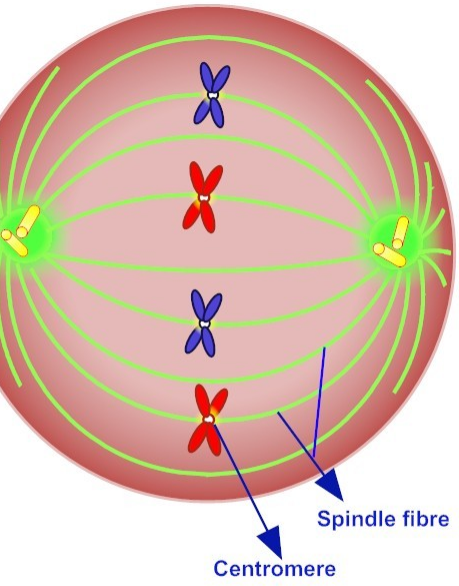
PROPHASE



ROPHASE

- The first phase of mitosis within M phase is called prophase.
- The nucleolus fades and chromatin (replicated DNA and associated pr condenses into chromosomes and each chromosome has two chromat a centromere.
- The mitotic spindle initially appears as structures called asters which s each centriole pair.
- The two pair of centrioles (formed from the replication of one pair in I move away from one another toward opposite ends of the cell due to th lengthening of the microtubules that form between them.
- The nuclear envelope breaks up.
- Polar fibers, which are microtubules that make up the spindle fibers, r each cell pole to the cell's equator.
- The kinetochore (protein bundles at the centromere region on the chro where sister chromatids are joined) fibers "interact" with the spindle p connecting the kinetochores to the polar fibers.
- The chromosomes begin to migrate toward the cell center.

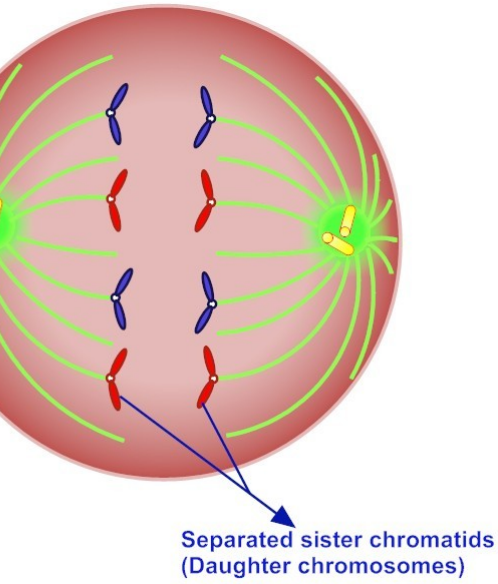
METAPHASE



METAPHASE

- The nuclear membrane disappears completely.
- Chromosomes align at the metaphase plate at right angles to the s
- Tension applied by the spindle fibers aligns all chromosomes in o the center of the cell.

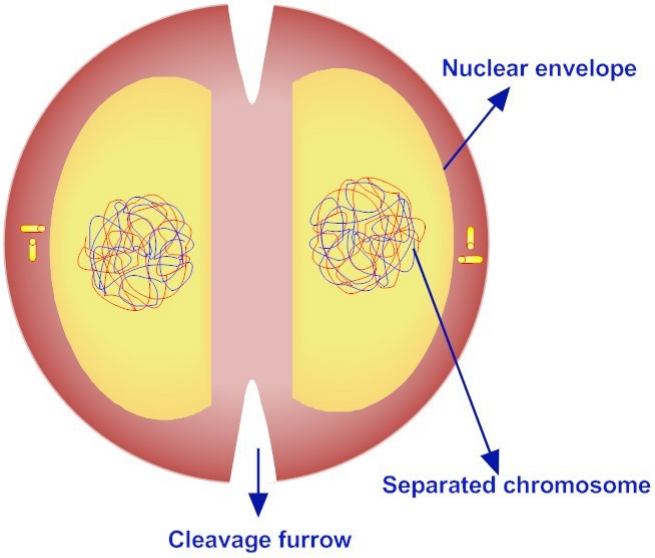
ANAPHASE



ANAPHASE

- Spindle fibers shorten; the kinetochores separate and the paired c in each distinct chromosome begin to move apart to the cell poles
- Once the paired sister chromatids separate from one another, eac considered a "full" chromosome. They are referred to as daughter chromosomes.
- Through the spindle apparatus, the daughter chromosomes move at opposite ends of the cell.
- At the end of anaphase, each pole contains a complete compilatio chromosomes.

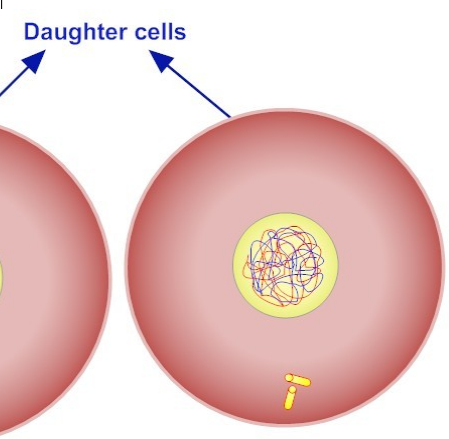
TELOPHASE



TELOPHASE

- Telophase is technically the final stag
- Its name derives from the Latin word 'end'.
- The daughter chromosomes arrive at nuclei (plural form of nucleus) begin poles.
- The nuclear envelopes of these nuclei
- Nucleoli (plural form of nucleolus) al
- Chromatin fibers of chromosomes un
- The spindle fibers that have pulled th
- The chromosomes begin to deconden more diffuse.

CYTOKINESIS

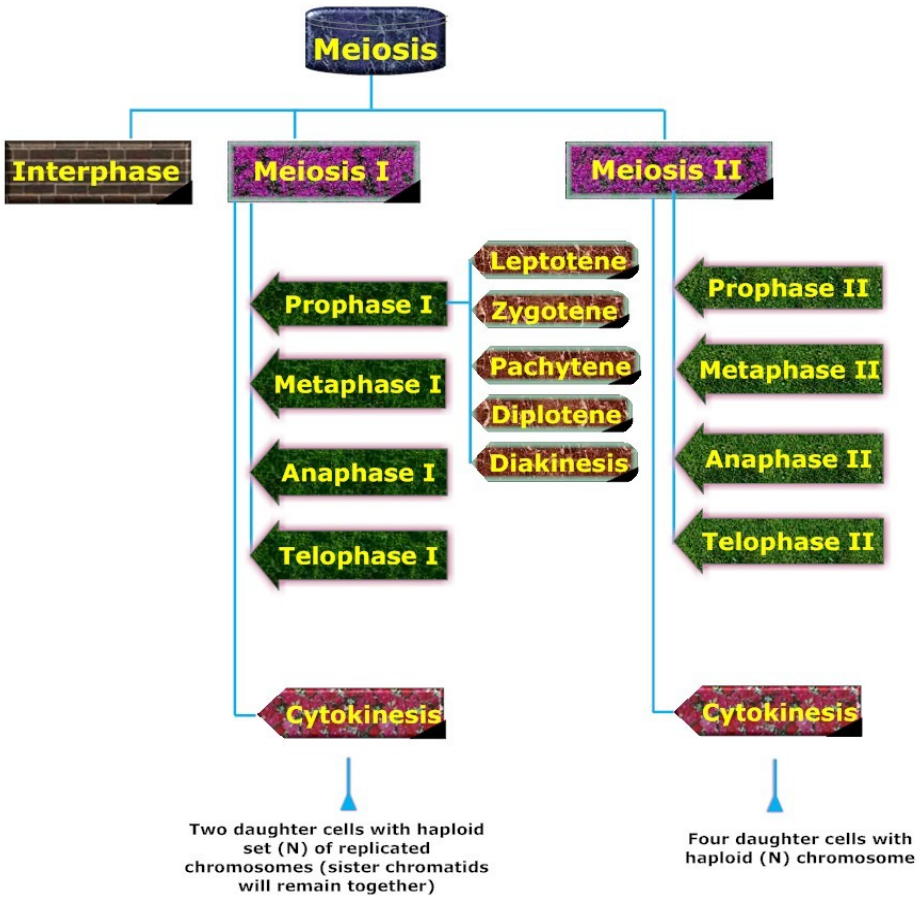


CYTOKINESIS

- Cytokinesis is the division of the cell's cytoplasm and organelles.
- With the two nuclei already at opposite poles of the cell, the cell cytoplas separates, and the cell pinches in the middle, ultimately leading to cleav
- At the end of cytokinesis, there are genetically identical two daughter cel
- Leland H. (Lee) Hartwell, Tim Hunt and Sir Paul M. Nurse were awarde Nobel Prize in Physiology or Medicine 2001 for their discoveries of key regulators of the cell cycle.

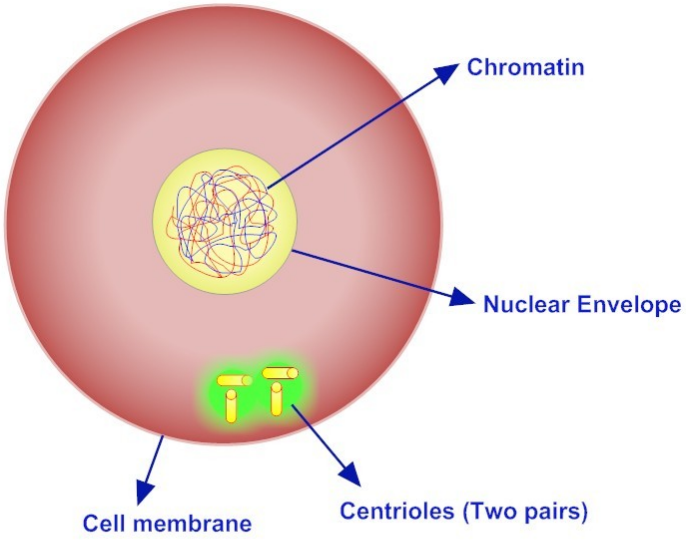
MEIOSIS

- Meiosis occurs in eukaryotic life cycles involving sexual reproduction.
- During meiosis, the genome of a diploid germ cell undergoes two rounds of division, resulting in four haploid daughter cells.
- Each of the resulting daughter cells has one half of the number of chromosomes as the parent cell.
- This reduction is accomplished by two successive nuclear divisions, as opposed to the one division found in mitosis.
- The two stages of meiosis are *Meiosis I and Meiosis II* called Reductional Division and Equational Division respectively. (Click here to view the picture)
- Before a dividing cell enters meiosis, it undergoes a period of growth called *Interphase.*
- In animals, meiosis used to produces the *gametes*: sperms and eggs.



INTERPHASE

- The preparatory steps that lead up to meiosis occurs in the same fashion as it does during mitotic interphase of the mitotic cell cycle.



INTERPHASE

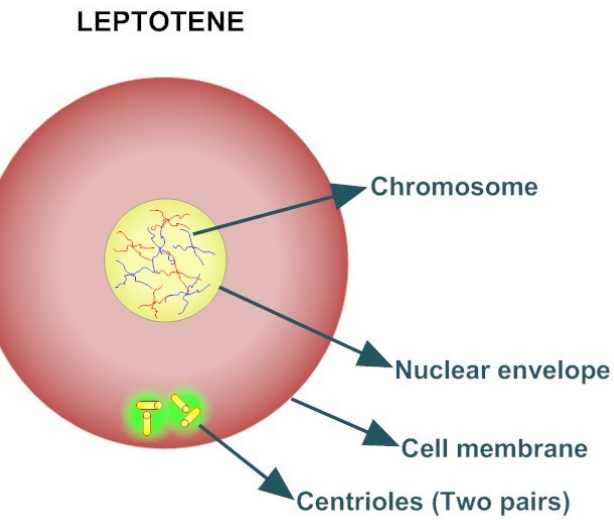
MEIOSIS I

- Meiosis I consist of four stages,
  - Prophase I
  - Metaphase I
  - Anaphase I and
  - Telophase I.
- Meiosis I separate homologous chromosomes producing two haploid cells (N), and therefore referred as Reductional Division.
- However, after Meiosis I, although the cell contains 2N chromatids it is only considered as being N, because later in anaphase I the sister chromatids will remain together as the spindle pulls the pair towards the pole of the new cell.

PROPHASE I

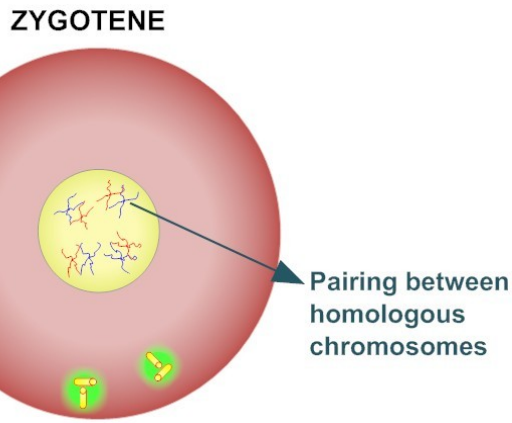
- Prophase I is usually longer in duration when compared to Prophase in mitosis, accounts for 85 - 95 percent of the total time for meiosis and is usually much more complex.
- The lengthy and complex events of Prophase I can be broken down into 5 stages.
  - Leptotene
  - Zygotene
  - Pachytene
  - Diplotene and
  - Diakinesis

LEPTOTENE STAGE



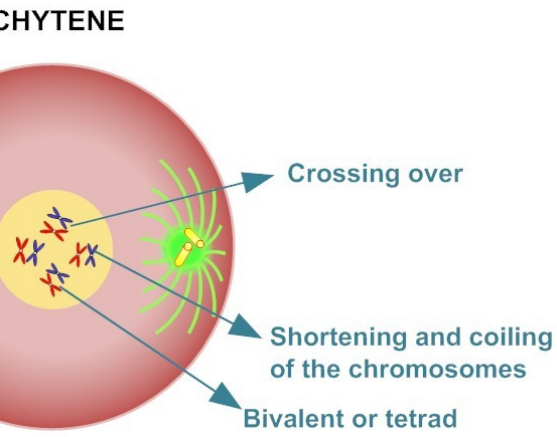
- The first stage is called Leptotene also known as *lep*
- All the chromosomes begin to condense.
- A process called 'homology search' which precedes essential to the initial pairing of homologs, begins d leptonema.

ZYGOTENE STAGE



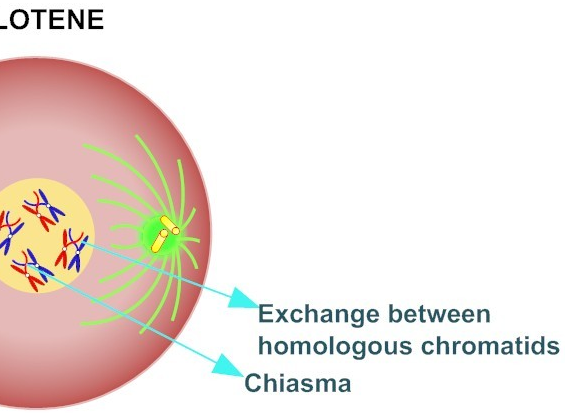
- The *zygotene* stage, also known as *zygonema*.
- Homologous dyads (pairs of sister chromatids) find each other an themselves from end to end. This pairing process is called Synaps
- At the completion of zygonema, the paired homologs take the forn bivalents.
- The number of bivalents in each species is equal to the haploid nu

PACHYTENE STAGE



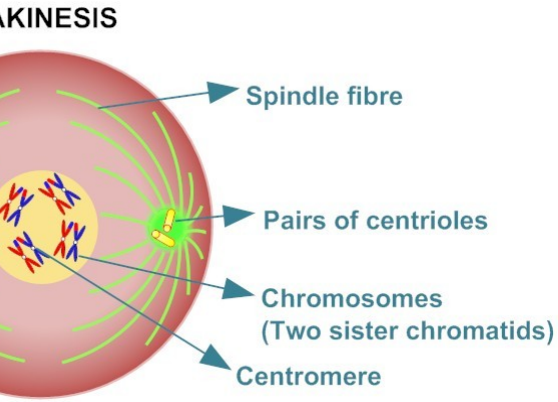
- The pachytene stage, also known as pachynema.
- Synapsis is now complete.
- Recombination nodules (chiasmata) appear.
- Homologous chromosomes randomly exchange segments of gene information over regions of homology.
- Crossing over is a precise breakage, swapping reunion between tw chromatids.
- Crossovers make new gene combinations and are an important so genetic variations in populations.

DIPLOTENE STAGE



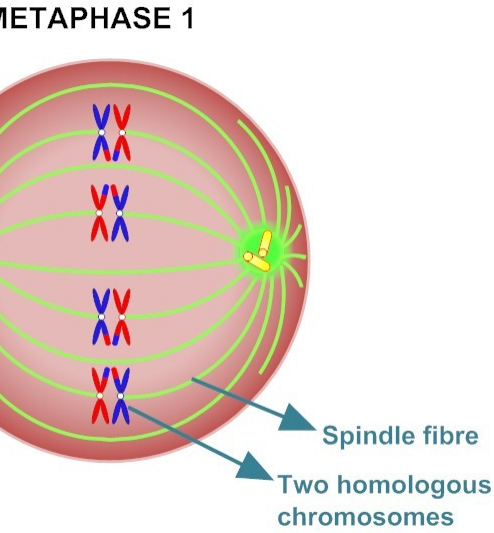
- The diplotene stage, also known as diplonema.
- DNA recombination is complete.
- In this phase, the chromatids continue to shorten and thicken and sister chromatids in a group is called a tetrad.
- The synaptonemal complex begins to break down.
- The paired chromatids begin to pull apart, causing the strands to longitudinally in some areas to from loops.
- The chiasmata tend to slip toward the ends of the tetrads and ther terminalised as the meiotic prophase continues.

DIAKINESIS



- Shortening of each tetrad continues through diakinesis, resulting units.
- Similar to mitosis, the centrioles migrate away from one another a nuclear envelope and nucleoli break down.

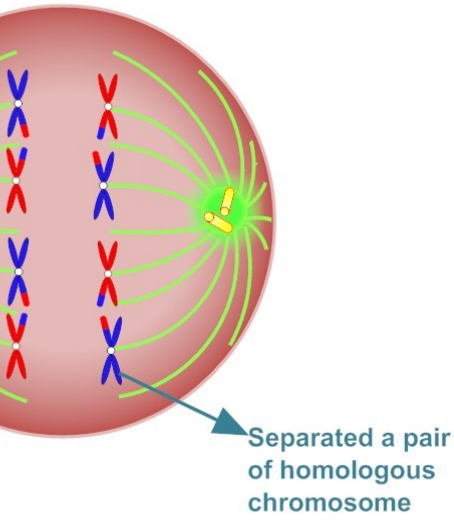
METAPHASE I



- Tetrads align at the metaphase plate.
- One homologue is pulled above the metaphase plate, the other be
- The centromeres of homologous chromosomes are oriented towar opposite cell poles.
- The centrioles are at opposite poles of the cell.
- Spindle fibers from one pole of the cell attach to one chromosome (seen as sister chromatids), and spindle fibers from the opposite p the homologous chromosome (again, seen as sister chromatids).

ANAPHASE I

APHASE 1

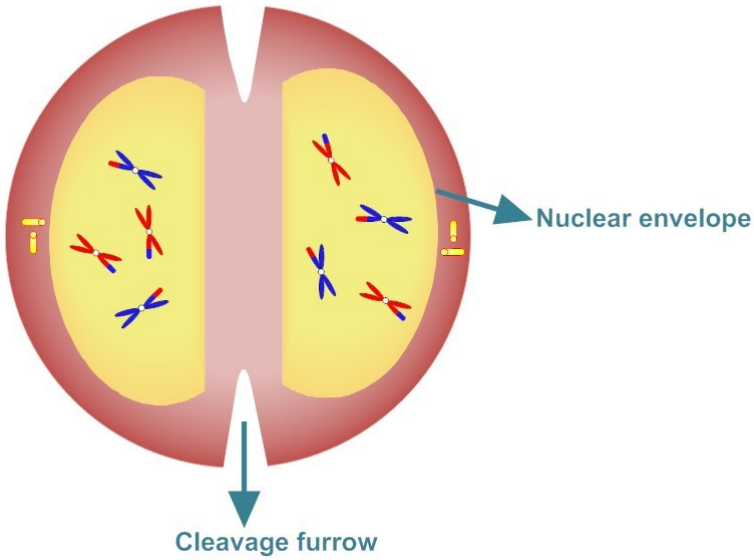


- Chromosomes move to the opposite cell poles.
- Similar to mitosis, the microtubules and the kinetochore fibers interact t movement.
- A key difference between mitosis and meiosis is that sister chromatids re after metaphase in meiosis I, whereas in mitosis they separate.
- During this stage, the original maternal and paternal chromosomes sepa reducing the number of chromosomes from 2N to N number, yet the siste chromatids remain together.

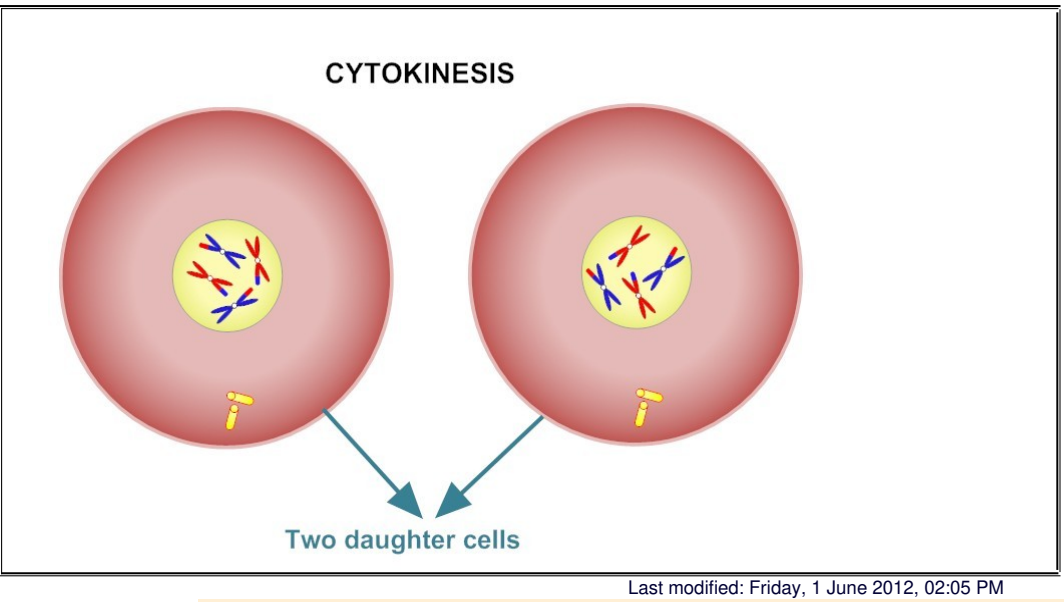
TELOPHASE I

mologous chromosome pairs complete their migration to the two poles as t of the action of the spindle.

TELOPHASE 1



nesis involves the formation of a cleavage furrow, resulting in the pinching ell into two cells.
end of Telophase I and Cytokinesis, two daughter cells are produced, each ne half of the number of chromosomes (haploid set of replicated osomes) of the original parent cell.



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INTERKINESIS

- Interkinesis (Interphase II) is similar to interphase except DNA replication does not occur during this stage.

MEIOSIS II

- Meiosis II is the second part of the meiotic process.
- The Meiosis II consists of
    - Prophase II
        - Each dyad is composed of a pair of sister chromatids attached by a common centromere.
    - Metaphase II
        - Centromeres are positioned at the equatorial plane.
    - Anaphase II and
        - Centromeres divide and the sister chromatids of each dyad are pulled to opposite poles
    - Telophase II
        - Reveals one member of each pair of homologous chromosome present in each pole. Each chromosome is referred as monad (a combination of maternal and paternal genetic information). Nuclei reform around chromosomes at the poles. Following cytokinesis in telophase II, four haploid gametes result from a single meiotic event.

Functions of Meiosis

1. It helps in maintaining a definite and constant number of chromosomes in a species.
2. Meiosis results in production of gametes with haploid (half) chromosome number. Union of male and female gametes leads to formation of zygote which receives half chromosome number from male gamete and half from the female gamete and thus the original somatic chromosome number is restored.
3. Meiosis facilitates segregation and independent assortment of chromosomes and genes.

4. It provides an opportunity for the exchange of genes through the process of crossing over. Recombination of genes results in generation of variability in a biological population which is important from evolution points of view.
5. In sexually reproducing species, meiosis is essential for the continuity of generation. Because meiosis results in the formation of male and female gametes and union of such gametes leads to the development of zygotes and thereby new individual.

DIFFERENCES BETWEEN MITOSIS AND MEIOSIS

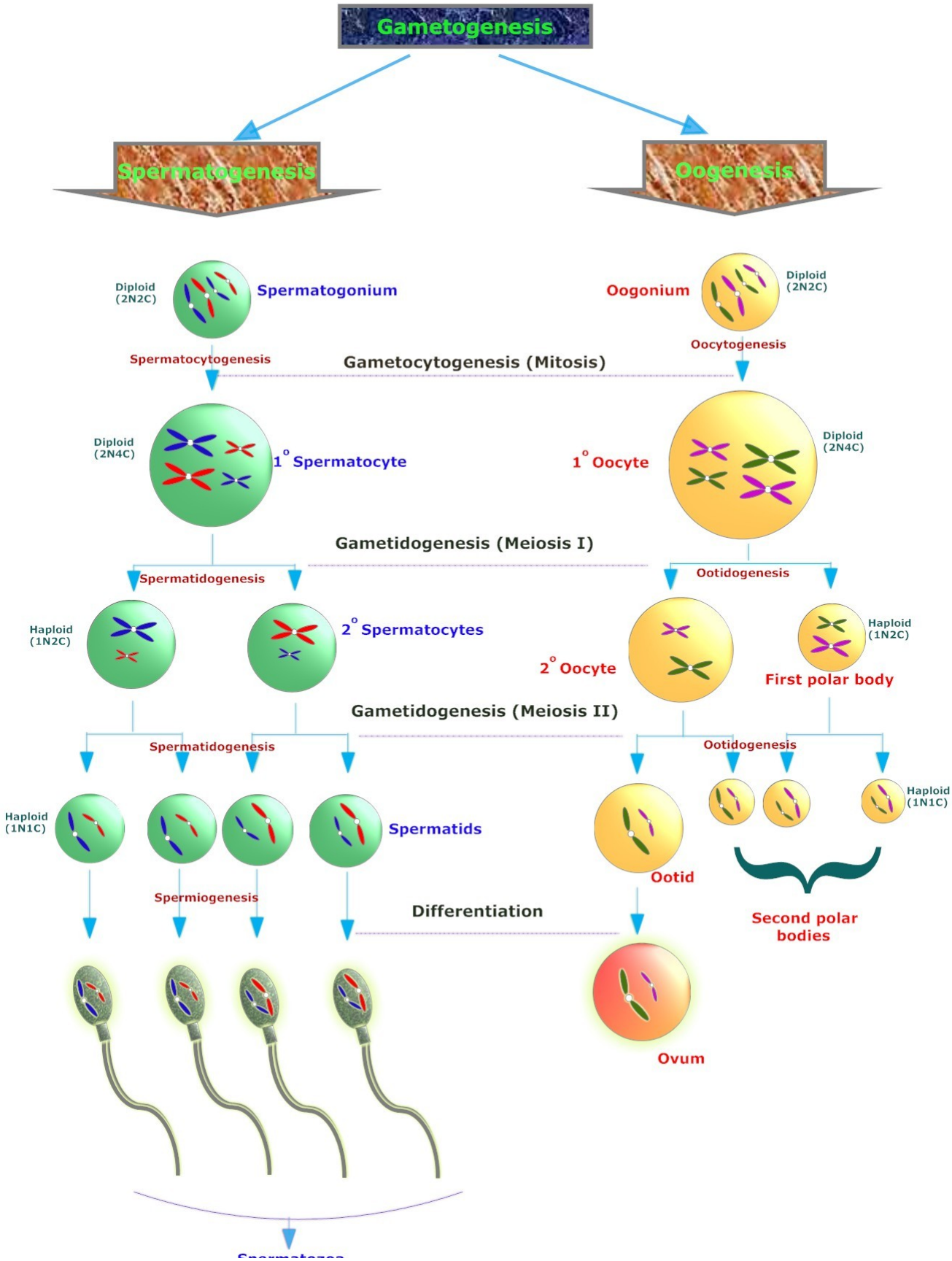
Sl.No.	Mitosis	Meiosis
1.	An equation division separating sister chromatids.	A reduction division. The first stage is a reduction division which separates homologous chromosomes at first anaphase. Sister chromatids separate in an equational division at II anaphase.
2.	Only one division per cycle i.e. one cytoplasmic division (cytokinesis) per equational division.	Two divisions per cycle i.e. two cytoplasmic divisions, one following the reduction division and one following equation division.
3.	Chromosomes fail to synapse. No chiasmata formation.	Chromosomes synapse and form chiasmata.
4.	Genetic exchange between homologous chromosomes does not occur.	Genetic exchange through chiasmata occurs between homologous chromosomes.
5.	Two daughter cells are produced.	Four daughter cells are produced.
6.	Genetic contents of daughter cells are identical.	Genetic contents of daughter cells are different. Centromere may be replica of either paternal or maternal centromeres in varying combinations.
7.	Chromosome number of daughter cells is the same as that of mother cell.	Chromosome number of daughter cells is half of that of mother cells.
8.	Daughter cells are capable of undergoing additional mitotic divisions.	Daughter cells are not capable of undergoing another meiotic division although they may undergo mitotic division.
9.	Normally occurs in all somatic cells.	Occurs only in specialized germ cells.
10.	Begins at the zygote stage and continues through the life of the organism.	Occurs only after puberty, in higher organisms, but occurs in the zygote of algae and fungi.

GAMETOGENESIS

- Gametogenesis is the production of haploid sex cells.
- Gametes carry only one-half the genetic material from the germ cell line of each parent and fusion of spermatozoa and ova during fertilization results in a zygote with diploid genome.
- The production of spermatozoa is called Spermatogenesis and the production of ovum is termed Oogenesis.
- Mature haploid sex cells, either male or female, are called gametes (in human and animal, ovum and spermatozoa).

		Ploidy (or) Chromosomes / Chromatids	Process		
Male	Female		Common term	Male	Female

Spermatogonium	Oogonium	Diploid / 2N2C	Gametocytogenesis (Mitosis)	Spermatocytogenesis	Oocytogenesis
Primary Spermatocyte	Primary Oocyte	Diploid / 2N4C	Gametidogenesis (Meiosis I)	Spermatidogenesis	Ootidogenesis (Folliculogenesis)
Secondary Spermatocytes	Secondary Oocyte	Haploid / 1N2C	Gametidogenesis (Meiosis II)	Spermatidogenesis	Ootidogenesis
Spermatazoa	Ovum	Haploid / 1N1C		Spermiogenesis	


Gametogenesis
Spermatogenesis
Oogenesis
Diploid (2N2C)
Spermatogonium
Oogonium
Diploid (2N2C)
Spermatocytogenesis
Gametocytogenesis (Mitosis)
Oocytogenesis
Diploid (2N4C)
1° Spermatocyte
1° Oocyte
Diploid (2N4C)
Gametidogenesis (Meiosis I)
Spermatidogenesis
Ootidogenesis
Haploid (1N2C)
2° Spermatocytes
2° Oocyte
Haploid (1N2C)
First polar body
Gametidogenesis (Meiosis II)
Spermatidogenesis
Ootidogenesis
Haploid (1N1C)
Spermatids
Haploid (1N1C)
Ootid
Second polar bodies
Spermiogenesis
Differentiation
Ovum

SPERMATOGENESIS

- Spermatogenesis is the process of producing sperm cell in the male reproductive organs or testes, through a sequence of mitotic and meiotic divisions (spermatocytogenesis) and a metamorphic change (spermiogenesis) to produce spermatozoa.

SPERMIOGENESIS

- The differentiation of the spermatids into sperm cells is called spermiogenesis.
    - Through a progressive sequence of changes, each of the comparatively large, spherical, non-motile spermatid is metamorphosed in to a small, elongated, motile sperm composed typically of three parts- head, middle piece and tail.

Nuclear condensation

- The nucleus moves to one edge of the cell;
- Thickening and reduction of the nuclear size;
- Condensation of the nuclear contents into the smallest space
    - Cytoplasma reduction
        - Sloughening and elimination of all unnecessary cytoplasm
    - Acrosome formation
        - Golgi apparatus produces the acrosome containing enzymes and it takes its place around the anterior end of the sperm head.
        - It plays an important role in the penetration through the pellucid zone of the oocyte.
    - Flagellum formation
        - Form the sperm cell tail

OOGENESIS

- Oogenesis is the process of meiosis in female organisms from an oogonium to a primary oocyte, to a secondary oocyte, and then to an ovum.
- The gamete formed by oogenesis contains all the materials needed to initiate and maintain metabolism and development of the embryo outside the mothers body.
- Therefore, in addition to forming a haploid nucleus, oogenesis also builds up a store of cytoplasmic enzymes, mRNAs, organelles, and metabolic substrates.
- During the first division of Oogenic meiosis, unequal cytokinesis take place and result in one of the two daughter cells containing hardly any cytoplasm, whereas the other cell has nearly the entire volume of cellular constituents.
- The smaller cell is called the first polar body, and the larger cell is called as the secondary oocyte.
- During the second division of meiosis, a similar unequal cytokinesis takes place in secondary oocyte and result in o ne large cell (ovum), and a small cell (second polar body) .
- The polar bodies receive the same chromosome complement as the secondary oocyte and ovum, but are not functional sex cells.
- Because of accumulation of nutrient materials, an egg is usually much larger than a sperm of the same species.

MODULE-5: MENDEL'S EXPERIMENTS

Learning objectives

After completing this module, the learner should be able to:

- know who Gregor Mendel was and why his work was important?
- define some of the terms in the module
- define punnet square and know how to use one?

MENDEL'S EXPERIMENTAL ORGANISM

- Gregor Johann Mendel (1822-1884), a monk and scientist in the Augustian Abbey in Brno (now in the Czech Republic).
- He developed the principles of heredity while studying seven pairs of inherited characteristics in pea plants.
- Although the significance of his work went unrecognized until 1900 , his laws of heredity are the basis for the present-day field of genetics.

Mendel's selection of the experimental plant,

- Mendel picked common garden pea plants (*Pisum sativum*) as his experimental organism for the following reasons
    - It is annual plant and could be grown easily in large numbers
    - Has well-defined characteristics
    - Has perfect flowers that have both male and female reproductive organs.
        - The male gamete, equivalent to the sperm, is the pollen grain.
        - The female gamete, equivalent to the egg, is the ovule.
    - Controlled mating: Normally natural self-fertilization and cross-pollination is rare without human intervention.
    - Presence of variation: Peas were available from seed merchants in a wide array of distinct shapes and colours that could be easily identified and analyzed.
    - Cheap and easy to obtain.
    - Take up little space.
    - Short life cycle.
    - Produce large number of fertile off-springs.

MENDEL'S TRAITS

- The seven pairs of contrasting traits chosen by Mendel were:

Seven characteristics in Peas observed by Mendel

Character	Dominant trait	Recessive trait
Stem length	Tall 	Dwarf 
Flower colour	Purple 	White 
Flower position	Axial 	Terminal 
Seed colour	Yellow 	Green 
Seed shape	Smooth 	Wrinkled 
Pod colour	Green 	Yellow 

MENDEL'S PROCEDURE

- Mendel first developed pure parental (P) lines for each contrasted seven pairs of characters of pea by self-fertilizing.
- The two pure lines (e.g. TALL x DWARF) for a pair of contrasted characters was crossed.
- The offspring were the F_1 (first filial) generation.
- Mendel found that all the F_1 hybrids always showed only one of the parent trait and never the other.
- F_1 plants were self-pollinated to get the F_2 (second filial) generation.
- Original contrasting characters of the parental generation reappeared in the F_2 generation.
-

MENDEL'S EXPLANATIONS AND PREDICTIONS

- Mendel made some important conclusions based on his experimental results.
    - Mendel called the determining agent responsible for each character or trait as "units" or "factors" that are passed on to offspring unchanged (these units are now called genes).
    - An individual inherits one such unit from each parent for each trait. Factors thus occur in pairs (*Diploid*) in an individual.
    - Each parent passed only one factor of a pair to their offspring.
    - A trait may not show up in an individual but can still be passed on to the next generation and reappear.
    - Further, he predicted that each factor retained its individuality from generation to generation and it was not modified in the hybrid.
- Mendel's conclusive theoretical and statistical explanations for his hybridization experiments can be summarized in two principles,
    - The Principle of Segregation
    - The Principle of Independent Assortment

TERMINOLOGY

- Mendel used letters of the alphabet as symbols for factors (genes).
- The character that expresses itself in all the offspring of a monohybrid cross is termed *dominant* and the trait that fails to express is termed *recessive*.
- A capital letter signified a dominant and a lowercase letter a recessive member of a pair of alleles.
- The female parent is written first in genetic crosses.
- A female and a male gamete combine in fertilization to produce a zygote.
- Zygotes or individual organisms carrying two units of one allele (Example DD or dd) are *homozygous* and those with two alleles (Example: Dd) are *heterozygous*.
- A gene can have many different versions, called *alleles*.
- Phenotype : observable physical characteristics or visible expression of a trait .
- Genotype: actual gene constitution .
- Hybrids: The F1 progeny produced by two pure line parental generations are called *hybrids*.
- Monohybrid cross: A cross involving contrasting expression of one trait is called *Monohybrid cross*.
- *Dihybrid:* have two pairs of different characters.
- *Polyhybrid:* have more than two pairs of different characters.

METHODS FOR DETERMINING THE THEORETICAL OUTCOME OF ANY CROSS

- When mating two parents whose genotypes are known, offspring phenotypes, genotypes, and ratios can easily be found.
- There are three methods for determination of genetic ratios or probabilities:
    1. Punnett-Square (Checker Board) and
    2. Forked-line or branch diagram method
    3. Probability Rules

PUNNETT SQUARE

- The genotypes and phenotypes resulting from various combinations of gametes can be easily determenined by Punnett squares, devised by Reginald C. Punnett(1875-1967). Here each of the possible gamete is placed in an individual column or row, with vertical column representing the female and horizontal row the male parent.
- The gametes are arranged in all possible combinations and the resulting genotypes are in the boxes along with the phenotypes.
- It is a convenient method if small numbers of unlinked genes are present.
- Example for a dihybrid crosses:
    - In garden pea plants, Round (RR) and Yellow seeds (YY) are dominant over the Wrinkled (rr) and Green seeds (yy) respectively.
    - When plants of garden pea with round yellow seeds (RRYY) were crossed with plants having wrinkled green seeds (rryy), round yellow seed plants (RrYy) were obtained in F_1. Thus round seed shape over wrinkled seed shape and yellow colour of seed exhibited dominance over green independently.
    - In F_1 plants (RrYy), the possible combinations of alleles in the gametes are RY, Ry, rY, and ry.
    - Below is the Punnett-square which will give all the possible combinations in the F_2 after selfing of the F_1.

		Female gametes			
		RY	Ry	rY	ry
Male gametes	RY	RRYY	RRYy	RrYY	RrYy
	Ry	RRYy	RRyy	RrYy	Rryy
	rY	RrYY	RrYy	rrYY	rrYy
	ry	RrYy	Rryy	rrYy	rryy

FORKED LINE METHOD

- The other method for determining the outcome of a cross is the forked line or branch diagram method which is based on phenotypic rather than genotypic distributions.
- The forked line method is especially useful when three or more characteristics are crossed simultaneously.
- Each branch point represents the expected distribution of phenotypes at a particular locus.
- To determine the overall probability of a particular phenotype, all of the probabilities along a particular line are multiplied.
- Example for a dihybrid crosses:
    - Round and Yellow (RRYY) are dominant over Wrinkled and Green (rryy) respectively.
    - Selfing of the F_1.

PROBABILITY RULES

By Probability Rules

1. Sum Rule
2. Product Rule

MODULE-6: MONOHYBRID AND DIHYBRID INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- understand Mendel's laws of classical genetics.
- aware of experiments proving the principles of Mendel.
- understand the concept of alleles, dominant genes and recessive genes.

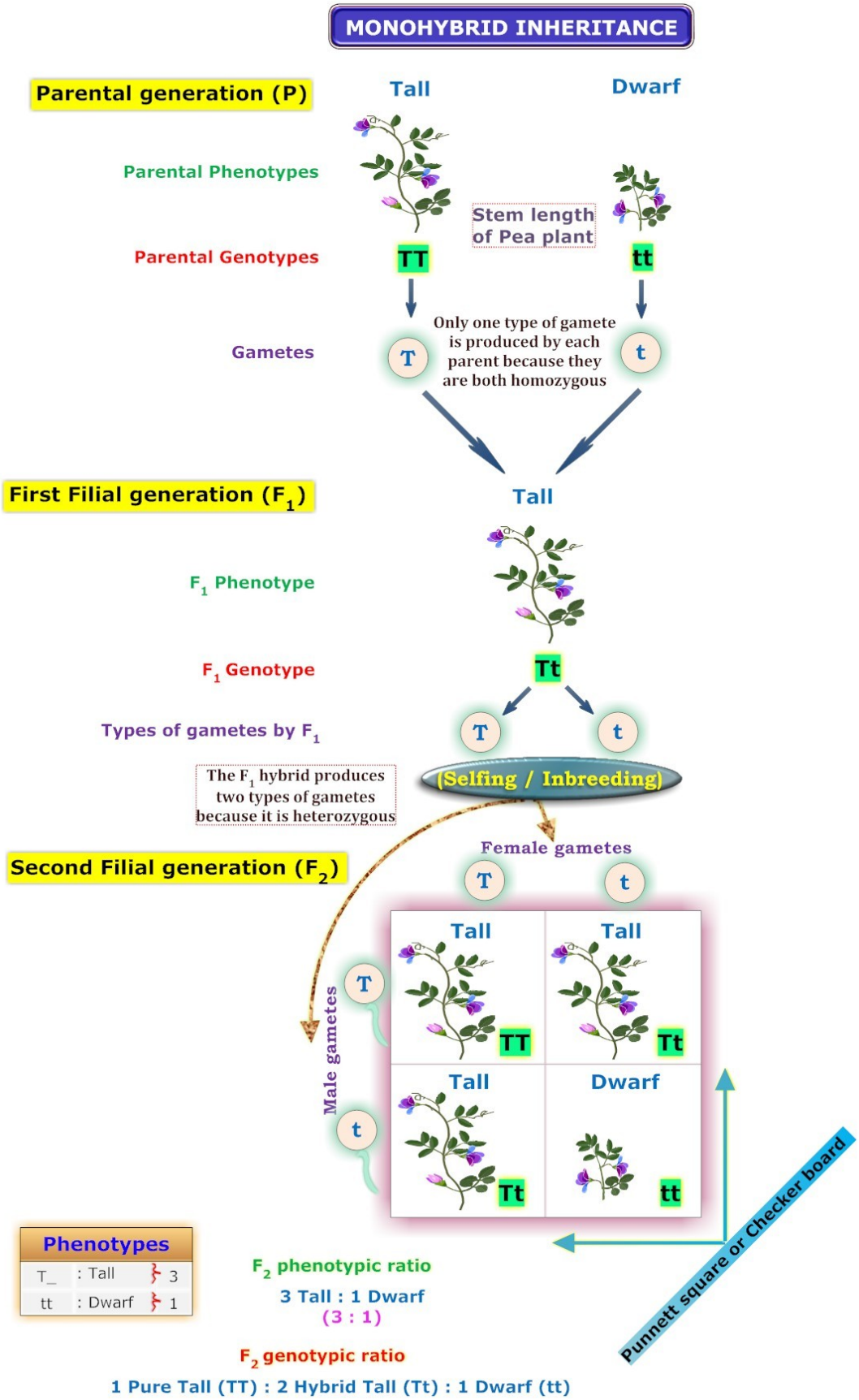
MONOHYBRID INHERITANCE

- Mendel studied the behavior of a single character alone first; he then studied two traits together.

To view "Monohybrid Cross Animation"

- Some pea plants have long stem length (Tall) and others have short stem length (Dwarf).
- *Pure-breeding* plants were produced by self fertilization. A pure-breeding Tall plant for example would only produce Tall offspring.
- He cross pollinated a pure-breeding *Tall* plant with a pure-breeding *Dwarf* plant.
- All F_1 generation were *Tall*.
- Next he self-fertilized all the F_1 Tall plants.
- He noticed that 3/4 of the F_2 plants had long stem and about 1/4 had short stem (3:1).
- 3:1 is called Monohybrid Ratio.

- The Dwarf plants reappeared in the F_2 generation.


MONOHYBRID INHERITANCE
Parental generation (P)
Tall
Dwarf
Parental Phenotypes
Stem length of Pea plant
Parental Genotypes
TT
tt
Gametes
T
t
Only one type of gamete is produced by each parent because they are both homozygous
First Filial generation (F1)
Tall
F1 Phenotype
F1 Genotype
Tt
Types of gametes by F1
T
t
The F1 hybrid produces two types of gametes because it is heterozygous
(Selfing / Inbreeding)
Second Filial generation (F2)
Female gametes
T
t
Male gametes
T
t
Tall
TT
Tall
Tt
Tall
Tt
Dwarf
tt
Phenotypes
T_ : Tall 3
tt : Dwarf 1
F2 phenotypic ratio
3 Tall : 1 Dwarf
(3 : 1)
F2 genotypic ratio
1 Pure Tall (TT) : 2 Hybrid Tall (Tt) : 1 Dwarf (tt)
Punnett square or Checker board

LAW OF SEGREGATION

- Results of Mendel's' First Experiment on Seven pairs of characteristics in the Garden Pea.

Characteristics	F_2 Results		Ratio
Form of seed	5474 round	1850 wrinkled	2.96: 1
Colour albumen	6022 yellow	2001 green	3.01: 1
Colour of seed-coats	705 grey-brown	224 white	3.15: 1
Form of pods	882 inflated	299 constricted	2.95: 1
Colour of pods	428 green	152 yellow	2.82: 1
Position of flowers	651 axial	207 terminal	3.14: 1
Length of stem	787 tall	277 dwarf	2.84: 1
All characteristics combined	14,889 dominant	5010 recessive	2.98: 1

How are traits passed from parents to offspring?

- After a careful study of his experimental results Mendel formulated what is now known as *Mendel's law of segregation*.
- There must be two hereditary units in the body cells of a mature organism (he called them as factors, we now call them genes or alleles), which were responsible for the transmission of characteristics.
- The pair of alleles of each parent separated into gametes during reproduction. Equal numbers of gametes were produced that contained each allele.
- Both parents contributed equally to the factors of heredity in the offspring.
- Gametes randomly unite at fertilization.
- When the two alleles of a pair are different (hybrid), one is dominant and the other is recessive.
- Due to non-mixing of alleles in the hybrid, the masked recessive trait reappears in the next generation.
- Mendel's first principle, the law of segregation, referring to the non-mixing of alleles in the hybrid and their subsequent segregation or separation in the gametes in equal frequencies, may be considered as the most important contribution of Mendel to heredity, since there no contrary experimental evidence as to the prevalence of any mixing of alleles in the hybrids.
- So Mendel's first law is universally applicable.

The law of segregation or the law of purity of gametes

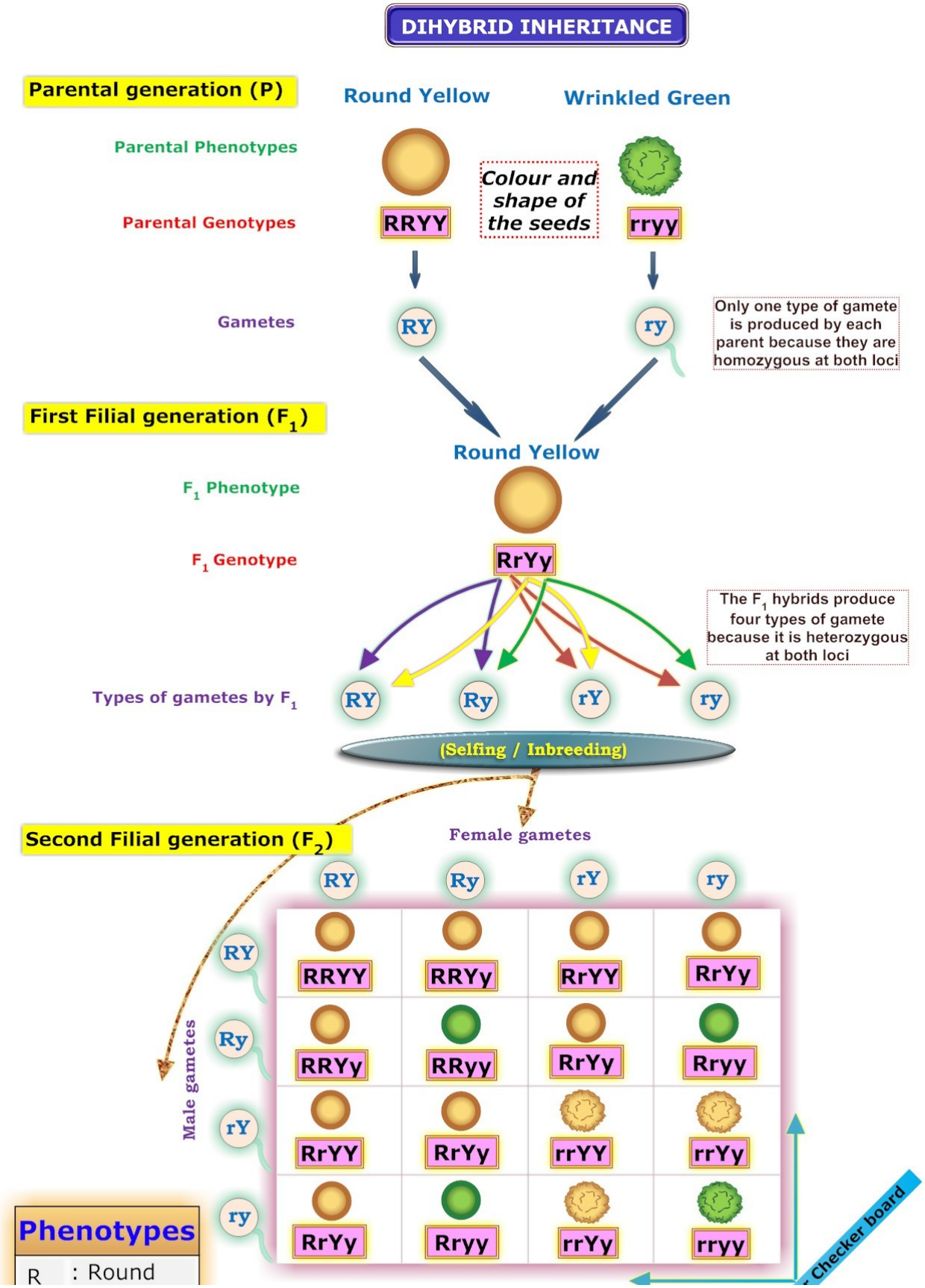
It states that when a pair of factors / allelomorphs (alleles) is brought together in a hybrid (F_1) they remain together without contaminating each other and they separate or segregate from each other into a gamete in a complete and pure form during the formation of gametes.

DIHYBRID INHERITANCE

- Mendel crossed two varieties of pea plants which were differing in two pairs of contrasting characters.

To view "Dihybrid Cross Animation"

- *Trait 1 :* Seed shape – *Round* and *Wrinkled.*
- *Trait 2 :* Seed colour – *Yellow* and *Green.*
- *Round* and *Yellow* (RRYY) are dominant over *Wrinkled* and *Green* (rryy) *respectively*.
- Mendel developed plants that were pure breeding for the two traits.
- When cross-pollinated, the offspring of such a cross were hybrids for two factors or genes, so they were called *dihybrids.*
- F1 generation was all heterozygous for round shape and yellow colour seeds (RrYy).
- When the F1 hybrids were allowed to self-pollinate, they produced four types of seeds in the ratio of 9: 3: 3:1 (9 round yellow: 3 round green: 3 wrinkled yellow : 1 wrinkled green).
- In F_2 generation new combinations of genes were present - round green and wrinkled yellow. Neither parents had this trait combination.


DIHYBRID INHERITANCE
Parental generation (P)
Round Yellow
Wrinkled Green
Parental Phenotypes
Parental Genotypes
RRYY
Colour and shape of the seeds
rryy
Gametes
RY
ry
Only one type of gamete is produced by each parent because they are homozygous at both loci
First Filial generation (F1)
Round Yellow
F1 Phenotype
F1 Genotype
RrYy
The F1 hybrids produce four types of gamete because it is heterozygous at both loci
Types of gametes by F1
RY
Ry
rY
ry
(Selfing / Inbreeding)
Second Filial generation (F2)
Female gametes
Male gametes
RRYY
RRYy
RrYY
RrYy
RRYy
RRyy
RrYy
Rryy
RrYY
RrYy
rrYY
rrYy
RrYy
Rryy
rrYy
rryy
Checker board
Phenotypes
R : Round

LAW OF INDEPENDENT ASSORTMENT

- According to the *Principle of Independent Assortment*, different pairs of alleles are passed to offspring independently of each other.
- The members of the different pairs of factors (genes) segregate quite independently of each other during gamete formation and result in new combination of genes.
- 9:3:3:1 is a typical dihybrid ratio.
- Today, we know this is due to the genes for traits that are located on different chromosomes.

LAW OF INDEPENDENT ASSORTMENT
The factors in an allelomorphic pair separates independently to the separation of factors in the other allelomorphic pair

MODULE-7: POLYHYBRID CROSSES

Learning objectives

After completing this module, the learner should be able to:

- understand the polyhybrid cross and the concept of back cross and test cross
- list several features of Mendel' s methods that contributed to his success.

POLY HYBRIDS

- The parents differing in more than three independently inheritable characters are crossed, then the cross between them is called *polyhybrid or multihybrid* cross and, their progeny are called *polyhybrids or multihybrids*.

Calculation of F_2 Phenotypes and Genotypes if dominance is complete

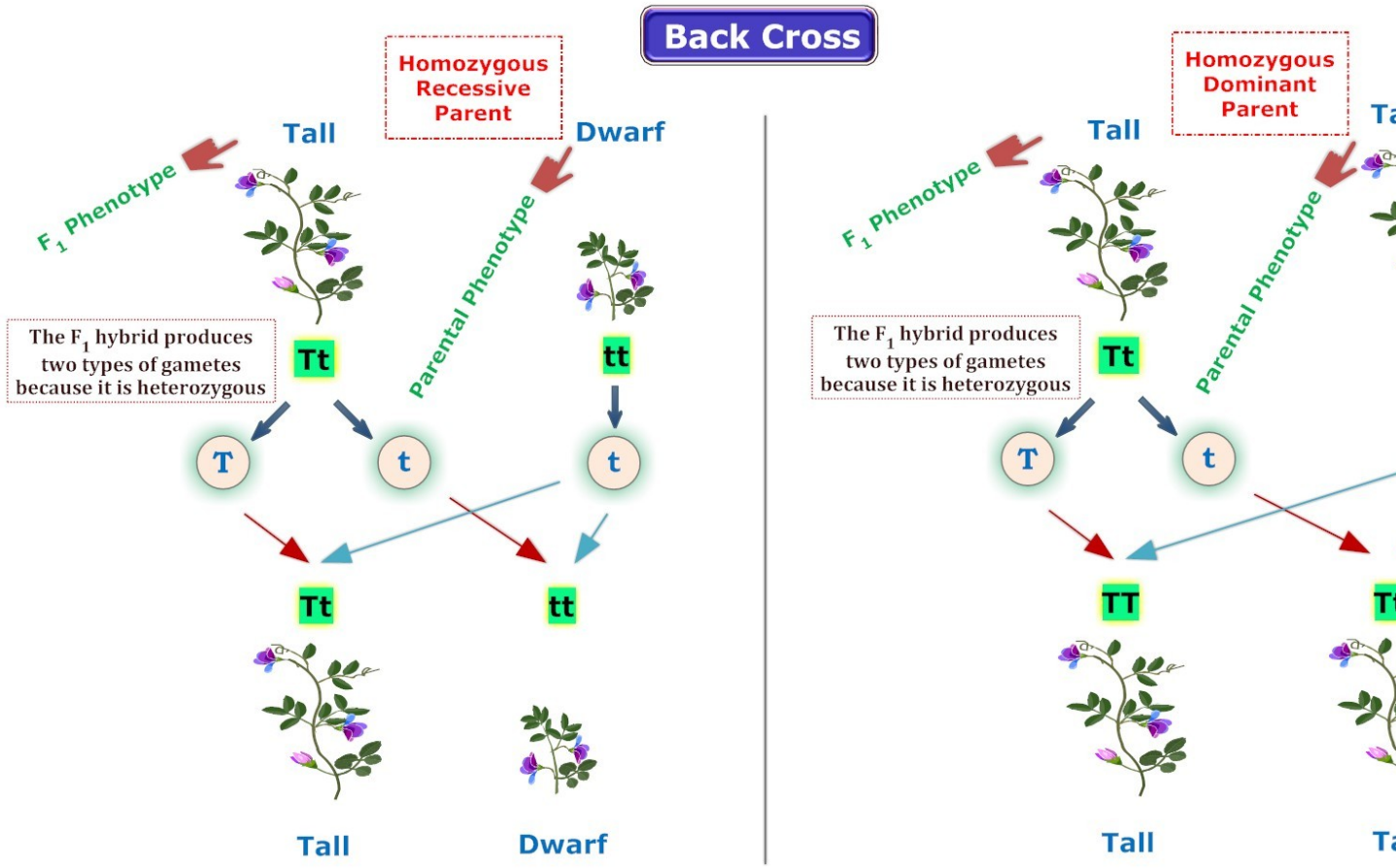
of genes volved in he cross gregating he pairs)	No. of phenotypes	No. of genotypes	No. of gametes by F_1 hybrids	No. of Gametic combination	Genotypic ratio
n	2^n	3^n	2^n	4^n	$(2:1:1)^n$
1 nohybrid)	2	3	2	4	$(2:1:1)^1 = 2:1:1$
2 ihybrid)	4	9	4	16	$(2:1:1)^2 = 4:2:2.2:2:1:1:1:1$
3 rihybrid)	8	27	8	64	$(2:1:1)^3 =$ 8:4:4:4:4:4:4:2:2:2:2:2:2:2:2:2:2:2:2:1:1:1:1:1:1:

BACK CROSS AND TEST CROSS

Back cross

- *Back cross* is a cross between F 1 hybrid and one of its homozygous parents .

Example



Test Cross

- Test cross is crossing of an incompletely known genotype to a genotype which is homozygous, recessive at all the loci under consideration.
- Test cross help to differentiate whether the individual is homozygous dominant or heterozygous.
- If the tested individual is heterozygous and the pairs of factors are segregating and assorting independently then the following phenotypic ratio will be obtained.
    - Mono hybrid test cross – 1 : 1
    - Di-hybrid test cross - 1 : 1 : 1 : 1
    - Tri-hybrid test cross - 1 : 1 : 1 : 1 : 1 : 1 : 1 : 1

PHENOCOPY

- Not all the changes in phenotype are the result of genetic causes. The environment for example temperature may influence the development of an embryo. The result of an environmental influence, which mimics the effect of a specific allele, is referred to as **phenocopy**.

- A phenocopy is a one-time event affecting the phenotype but not causing any transmissible change in the genotype. This is not transmitted to offspring in the way like that of the genetic abnormality.
- Example: Harelip condition in mice due to injection cortisone, low oxygen concentration and removal of amniotic fluid around embryo.

VALIDITY OF MENDEL'S FIRST AND SECOND PRINCIPLES

- Mendel's first principle, the law of segregation, referring to the non-mixing of alleles in the hybrid and their subsequent segregation or separation in the gametes in equal frequencies, may be considered as the most important contribution of Mendel to heredity, since there no contrary experimental evidence as to the prevalence of any mixing of alleles in the hybrids.
    - So Mendel's first law is universally applicable.
- Mendel's second principle, the law of independent assortment referring to the separation of two pairs of alleles independently has only limited application, and hence cannot be considered as a universal law.
    - The second principle is valid only when two or more pairs of genes or alleles are situated in different chromosomes, enabling their independent assortment during the formation of gemetes.
    - This law has only limited applications when the genes are situated in the same chromosome.

REASONS FOR THE SUCCESS OF MENDEL

- Mendel chose peas plant as his study organism which was most ideal for controlled breeding.
- He chose only clear contrasting characters.
- He was lucky in choosing those traits, which showed complete independent assortment.
- He used an experimental approach.
- Maintained an accurate record of all the observations.
- Applied mathematics to the study of natural phenomena.

REASONS FOR THE NON - RECOGNITION OF MENDEL'S WORK

- Mendel was not a botanist and was neither a member of any university nor held any high post.
- The journal *"Proceedings of Brunn Natural History Society"* was not so popular.
- Scientific world at that time was busy with the implications of Darwin 's conclusion of origin of species.
- Statistical calculations carried out by Mendel were beyond the comprehension of common biologists.

POST MENDEL ERA

- Until the early 20th century, the importance of Mendel's ideas was not realized.
- Three botanists - Hugo de Vries, Carl Correns and Erich von Tschermak - Seysenegg independently rediscovered Mendel's laws in 1900.

EXCEPTIONS TO MENDEL'S LAW

- Mutations and polyploidy are exceptions to the law of segregation or law of purity of gametes.
- Linkage is an exception to Mendel's second law i.e. law of independent assortment.
- Incomplete dominance is an exception to the principle of dominance.
- Pleiotropism is an exception to the principle of unit characters.
- Modification of F_2 ratios due to incomplete dominance, codominance, lethal factors, interaction of factors, epistatic factors are all exceptions.

MODULE-8: MODIFIED MENDELIAN INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- reason for extension of Mendelian Genetics
- understand the Gene Interactions and Modified Mendelian Ratios

MODIFICATIONS OF MENDELIAN 3:1 PHENOTYPIC RATIO

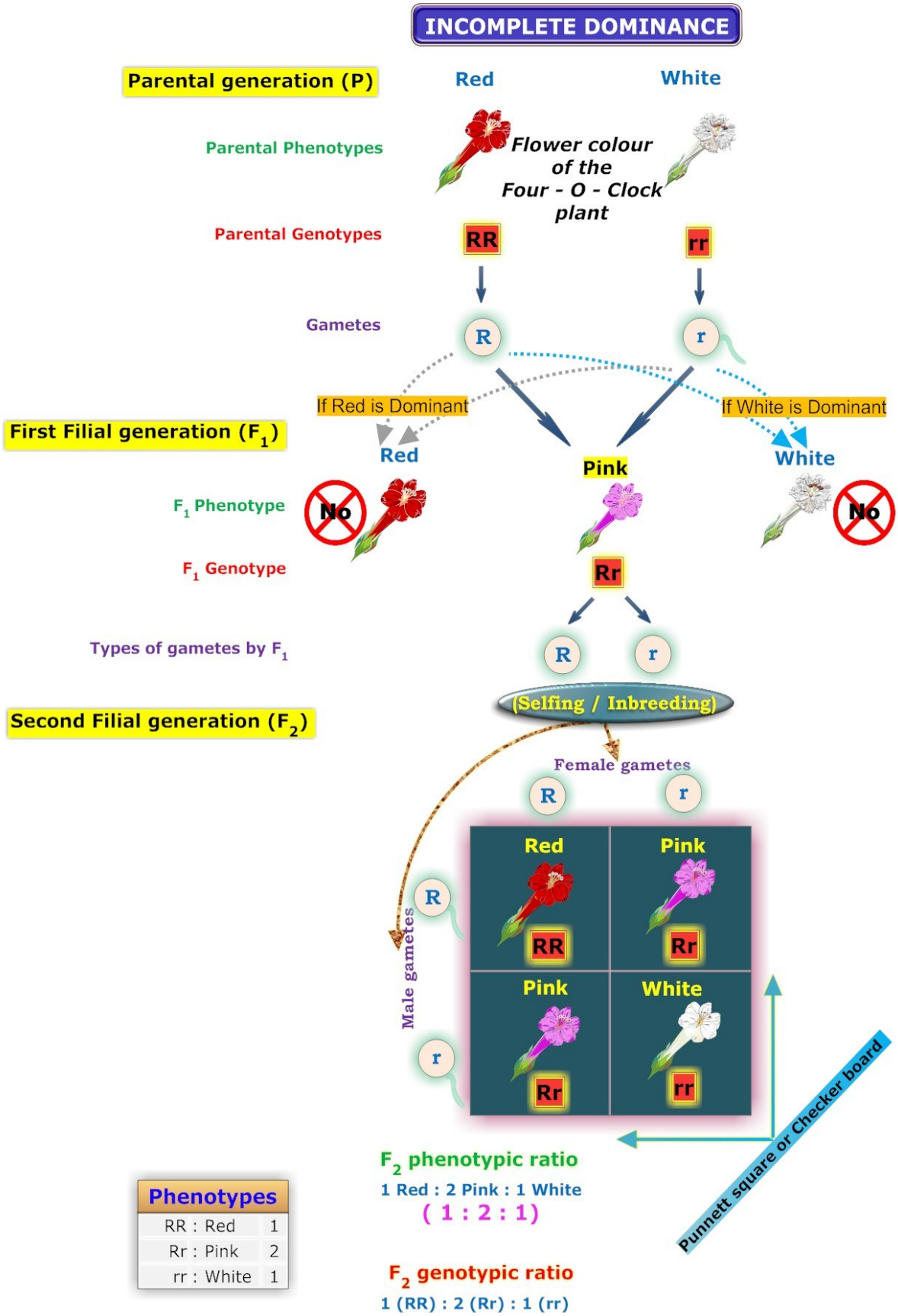
- The phenotypic ratio of 3:1 in monohybrid crosses is obtained when there is complete dominance.
- The ratio is modified in conditions like incomplete dominance, codominance and lethality.

INCOMPLETE DOMINANCE

- In all Mendel's crosses, one allele was dominant over the other.
- The rule of dominance and recessive holds in many cases but not in all.
- Alleles which modify the expression of the other alleles are called *incomplete* or *intermediate* or *semidominant* alleles.
- Each allele is capable of expressing itself to some degree when it is in heterozygous condition.
- The absence of complete dominance by one allele thus makes each genotype individually distinguishable.
- So it is not necessary to do a test cross to identify the heterozygotes.

INCOMPLETE DOMINANCE / SEMIDOMINANCE EXAMPLE

- In the heterozygous condition, the total product is intermediate between that of the dominant and recessive alleles.
- *For example*
    - In four- O'- clock plants (Mirabilis Jalapa) and Snapdragon (Antirrhinum majus), when red-flowered plants are crossed with white - flowered plants, the heterozygotes F_1produce pink flowers. The phenotypic ratio for the monohybrid cross becomes 1:2:1 instead of 3:1.


INCOMPLETE DOMINANCE
Parental generation (P)
Red
White
Parental Phenotypes
Flower colour of the Four - O - Clock plant
Parental Genotypes
RR
rr
Gametes
R
r
If Red is Dominant
If White is Dominant
First Filial generation (F1)
Red
Pink
White
F1 Phenotype
No
No
F1 Genotype
Rr
Types of gametes by F1
R
r
(Selfing / Inbreeding)
Second Filial generation (F2)
Female gametes
R
r
Male gametes
R
r
Red
RR
Pink
Rr
Pink
Rr
White
rr
Punnett square or Checker board
F2 phenotypic ratio
1 Red : 2 Pink : 1 White
(1 : 2 : 1)
F2 genotypic ratio
1 (RR) : 2 (Rr) : 1 (rr)
Phenotypes
RR : Red 1
Rr : Pink 2
rr : White 1

To view "Incomplete Dominance Animation"

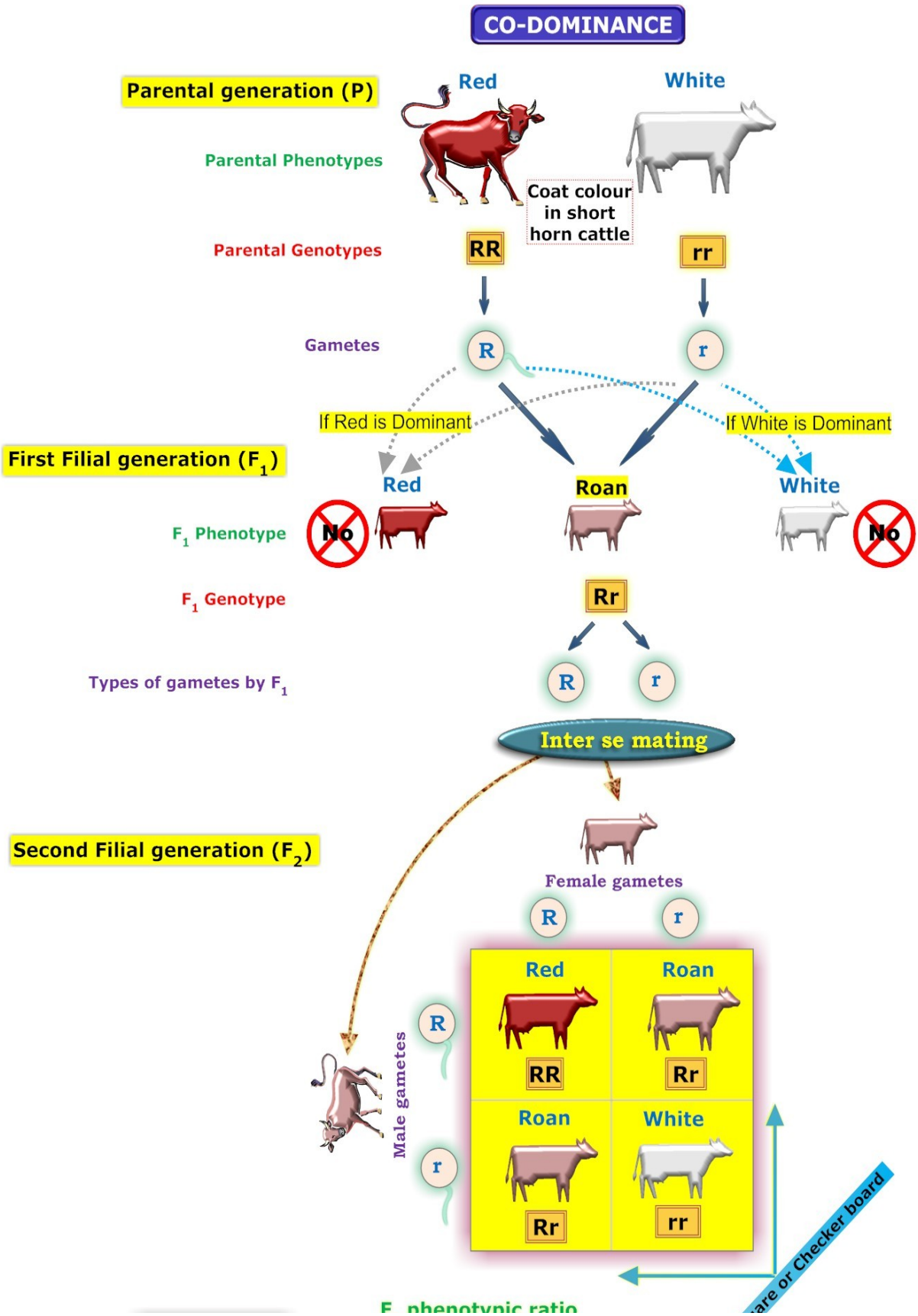
- Another interesting example is the Blue Andalusian chickens.
- These breeds were developed by crossing black chicken of a certain strain with a white splashed white chicken (White with black splashes).
- The offspring are blue. When crossed together, these blue chicken produce black, blue and white in the ratio of 1:2:1.

CODOMINANCE

- If the heterozygote exhibits a mixture of the phenotypic characters of both homozygotes, instead of a single intermediate expression, then both alleles are called *co-dominant* alleles.
- The phenotypic ratio is 1: 2: 1, identical as that of incomplete or intermediate dominance.

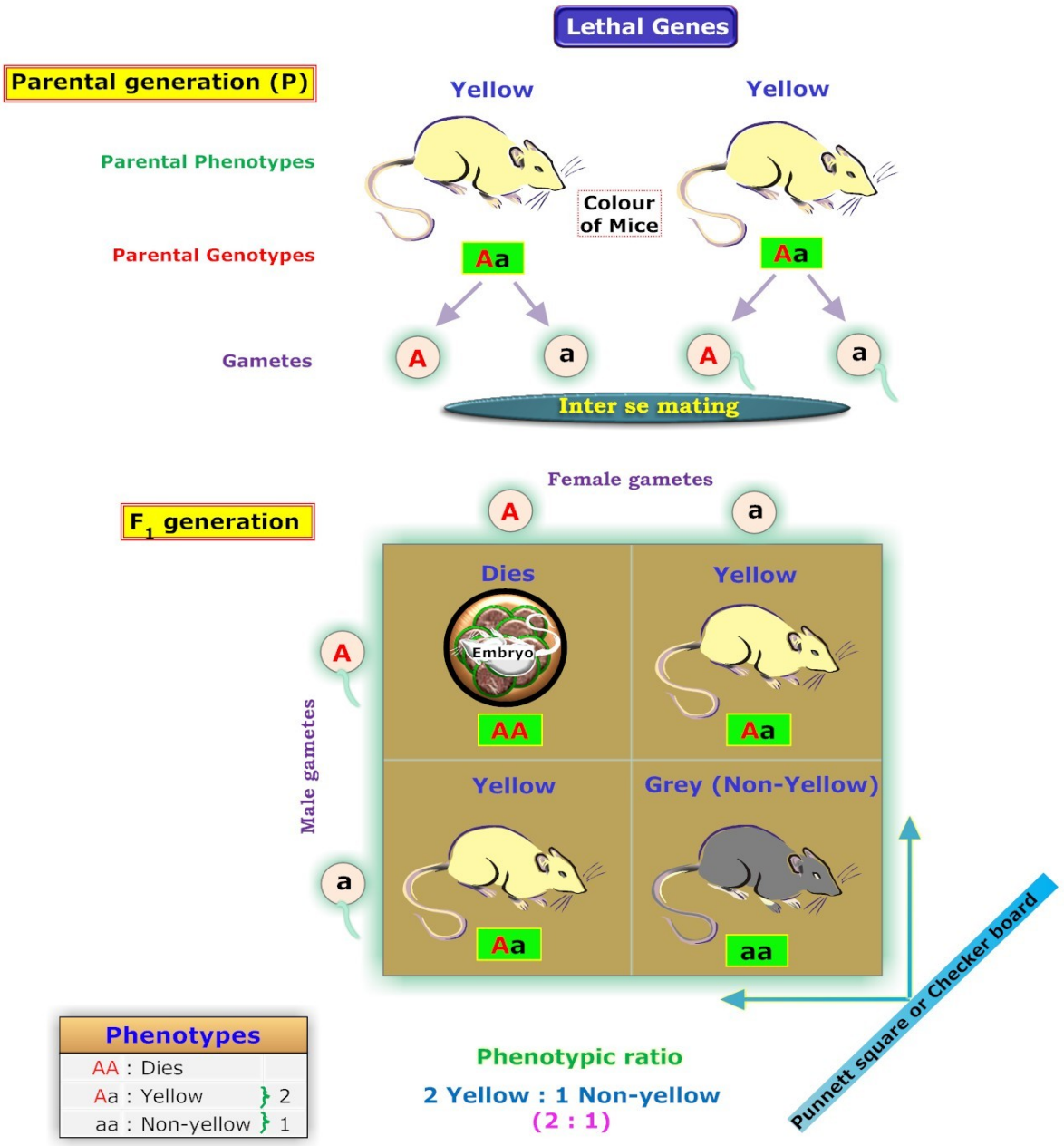
Example

- MN blood group antigens in human : Allele L^M for M-type blood is codominant with allele L^N for N-type blood. The heterozygotes L^ML^N will have both M and N antigens on the red blood cells.
- Hair colour in Short-horn cattle: If we cross a red bull with a white cow, the offspring are reddish gray or roan (mixture of red hairs and white hairs).


CO-DOMINANCE
Parental generation (P)
Red
White
Parental Phenotypes
Coat colour in short horn cattle
Parental Genotypes
RR
rr
Gametes
R
r
If Red is Dominant
If White is Dominant
First Filial generation (F1)
Red
Roan
White
F1 Phenotype
No
No
F1 Genotype
Rr
Types of gametes by F1
R
r
Inter se mating
Second Filial generation (F2)
Female gametes
R
r
Male gametes
R
r
Red
RR
Roan
Rr
Roan
Rr
White
rr
Punnett square or Checker board
F2 phenotypic ratio

LETHALS

- Genes which affect the viability as well as the visible traits of an organism are called *lethal genes* and the phenomenon is called *lethality*.
- Lethal genes can be recessive , dominant , conditional, semilethal / sublethal, or synthetic, depending on the gene or genes involved.
- If the lethal effect is dominant and immediate in expression, all individuals carrying the gene will die and the gene will be lost.
- Dominant lethal genes are expressed in both homozygotes and heterozygotes. All individuals carrying the genes will die and the genes will be lost in populations.
- Recessive lethal allele carried in the heterozygous condition has no effect but they cause death when an organism carries two copies of the lethal allele.
- Recessive lethal may come to expression when mating between carriers occurs.



GENE INTERACTION

- The phenomenon of two or more genes governing the development of a single character in such a way that they affect the expressions of each other in various ways is known as *Gene Interaction* .
- Gene interactions can be classified as,
    1. Allelic gene interaction
    2. Non-allelic gene interaction.

Non-allelic gene interaction

- Expression of character is produced by interaction between two or more genes.
  a) Inter-allelic

i. Without modification of normal F2 ratio.
ii. With modification of normal F2 ratio.
Such kinds of interactions modify the normal F2 ratio (9:3:3:1). Various types of such interactions are as below.

1. Complementary Gene Interaction
2. Supplementary Gene Interaction
3. Epistasis
4. Duplicate Factor
5. Inhibitory Factor
6. Polymerism or Additive Factor

b) Intra-allelic

i. Lethal Gene

Allelic gene interaction

- Expression of character is produced by interaction between alleles of a single gene.

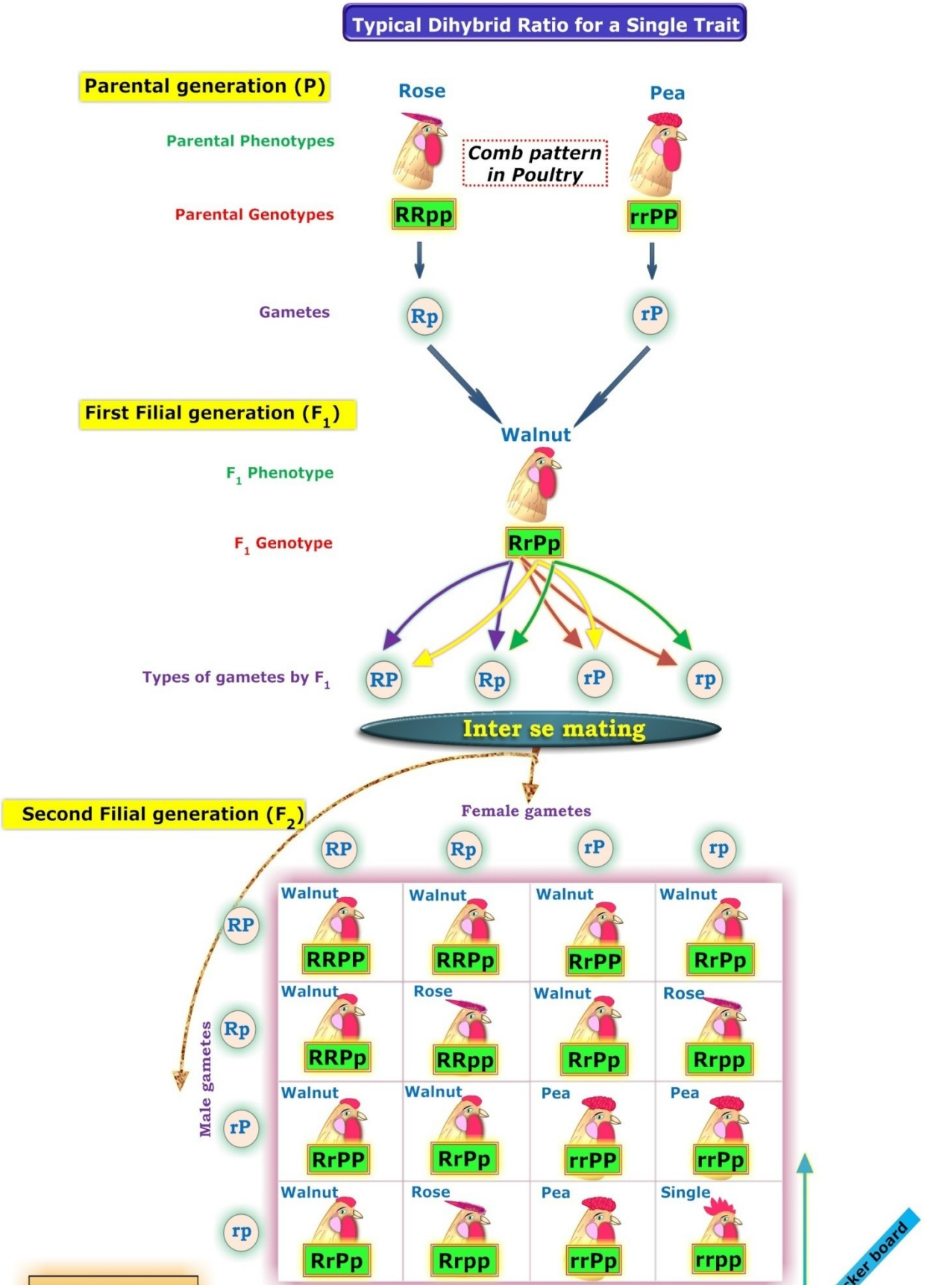
1. Complete dominance
2. Incomplete dominance
3. Co-dominance
4. Over Dominance

INTER - ALLELIC INTERACTION

A classical example of two genes influencing the same character,

- Each variety of poultry possesses a characteristic comb type.
  - Wyandotte – Rose comb
  - Brahmas – Pea comb
  - Leghorns – Single comb
- Each of these varieties breed true.
- Crosses between Rose combed and single combed variety showed that Rose was dominant over single and a 3:1 ratio appeared in the F2.
- Crosses between Pea combed and single combed variety showed that Pea was dominant over single and a 3:1 ratio appeared in the F2.
- When Rose was crossed with Pea, all the offspring showed a new comb form known as “Walnut”
- When the F1 Walnut combed birds were inbred, in the F2 generation Walnut, Rose, Pea and Single combed ones also appeared.
- Because the four comb shapes appeared in a 9:3:3:1 ratio (i.e., nine Walnut chickens per every three Rose chickens per every three Pea chickens per every one Single-comb chicken), it seemed that two different genes must play a role in comb shape.
- This ratio is expected in F2 from a cross of parents differing in two genes.
- Differences from normal dihybrid inheritance are
  - The F1 resembles neither the parent (Walnut comb)
  - Apparently novel characters appear in F2 (Single comb)

    - Walnut character results from an interaction between two independently inherited dominant Rose and Pea genes.
- Single comb results from interaction of their two recessive alleles.


Typical Dihybrid Ratio for a Single Trait
Parental generation (P)
Rose
Pea
Parental Phenotypes
Comb pattern in Poultry
Parental Genotypes
RRpp
rrPP
Gametes
Rp
rP
First Filial generation (F1)
Walnut
F1 Phenotype
F1 Genotype
RrPp
Types of gametes by F1
RP
Rp
rP
rp
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
Walnut RRPP
Walnut RRPp
Walnut RrPP
Walnut RrPp
Walnut RRPp
Rose RRpp
Walnut RrPp
Rose Rrpp
Walnut RrPP
Walnut RrPp
Pea rrPP
Pea rrPp
Walnut RrPp
Rose Rrpp
Pea rrPp
Single rrpp

EPISTASIS

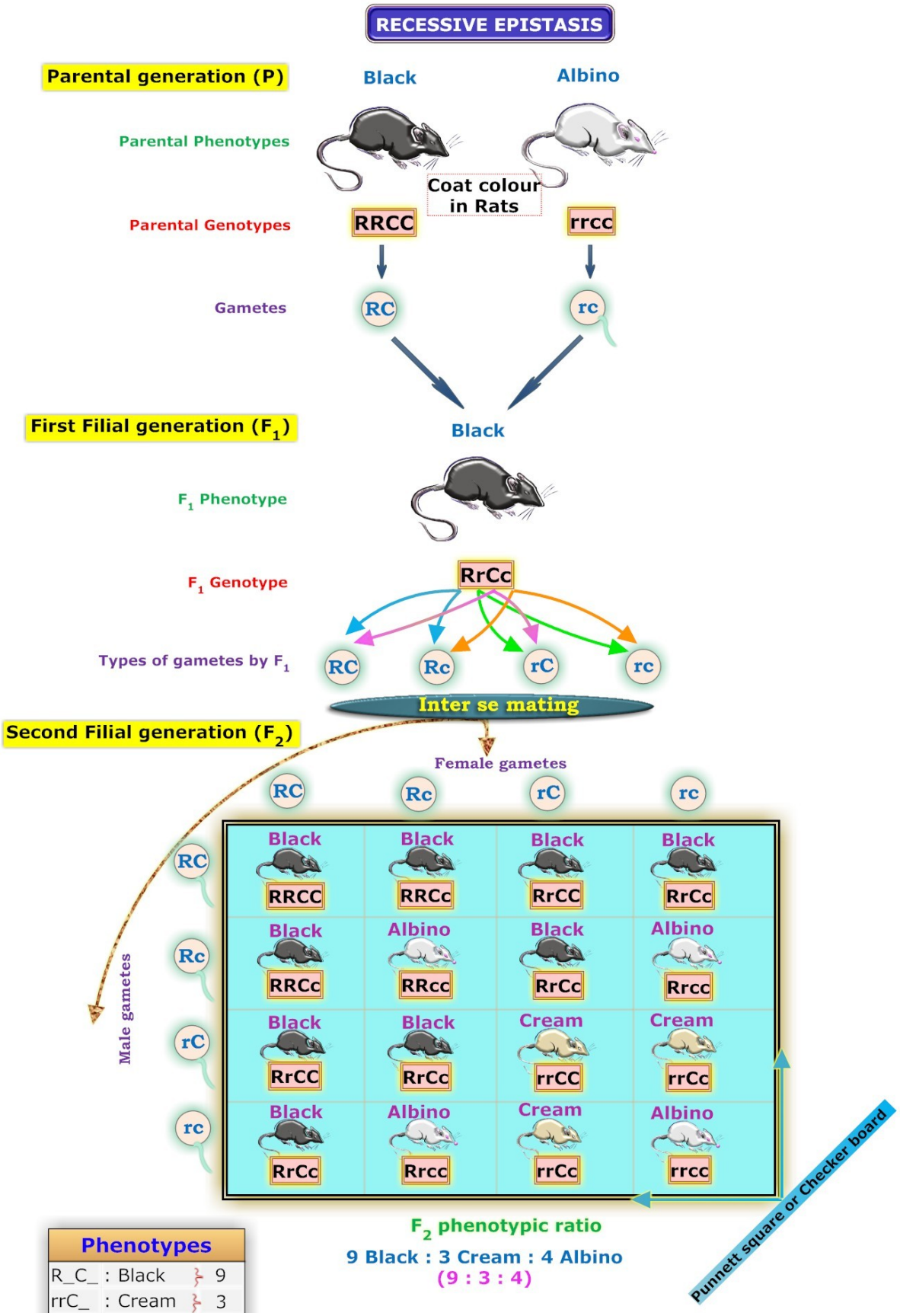
- When an allele of one gene masks expression of alleles of another gene and expresses its own phenotype instead, it is known as *Epistasis*.
- This is a Greek word meaning standing upon.
- The gene responsible for the suppression is called Epistatic and the genes, which are being suppressed, are called *Hypostatic*.

Types of Genetic Interaction in Dihybrid Ratio

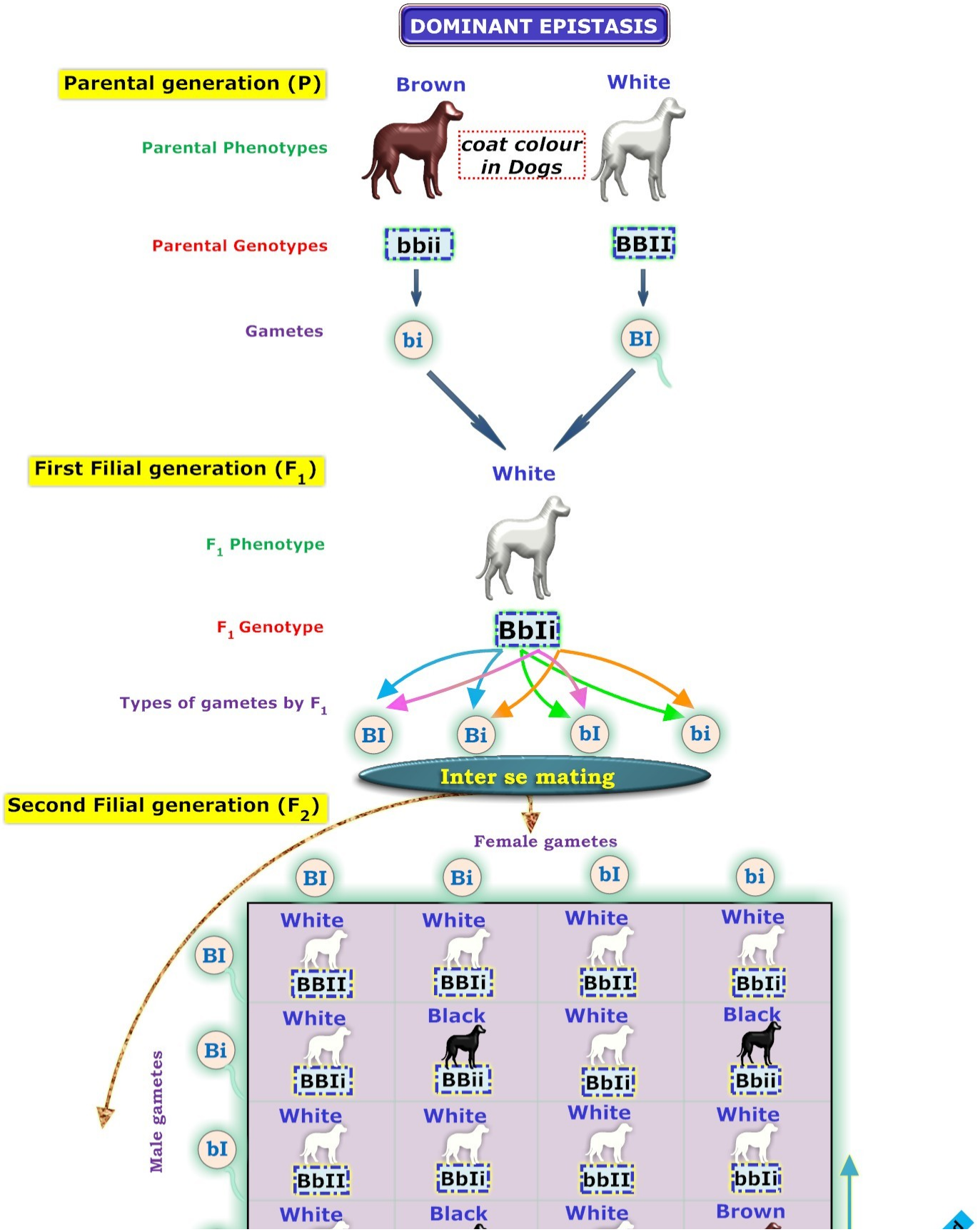
GENETIC EXPLANATION	F_2 PHENOTYPIC RATIO								
	AABB	AABb	AaBB	AaBb	AAbb	Aabb	aaBB	aaBb	aabb
Classical Dihybrid Ratio	9				3		3		1
Complete dominance at one locus and Incomplete dominance at another locus (co-dominance)	3		6		1	2	3		1
Complete dominance lacking at either locus (co-dominance at both locus)	1	2	2	4	1	2	1	2	1
Complete dominance at one locus and Homozygous dominant lethal at another locus		6			3			2	1
Incomplete dominance at one locus (co-dominance) and Homozygous dominant lethal at another locus		2		4	1	2		2	1
Homozygous recesive lethal at either locus	1	2	2	4					
Recessive Epistasis When one gene is homozygous recessive, it hides the phenotype of the other gene. (aa epistatic to B and b)	9				3		4		
Dominant Epistasis When one gene is dominant, it hides the phenotype of the other gene. (A epistatic to B and b)	12						3		1
Dominant and Recessive Epistasis When either gene is dominant, it hides the effects of the other gene. (A epistatic to B and b, bb epistatic to A and a, A and bb produce identical phenotypes)	13						3		
Duplicate Recessive Epistasis When either gene is homozygous recessive, it hides the effect of the other gene. (aa epistatic to Bb, bb epistatic to A and a)	9				7				
Duplicate Dominant Epistasis When either gene is dominant, it hides the effects of the other gene.	15								1

(A epistatic to B and b, B eptistatic to A and a)			
Duplicate Interaction When either gene is dominant, it hides the effects of the other gene. (A and B interact)	**9**	**6**	**1**

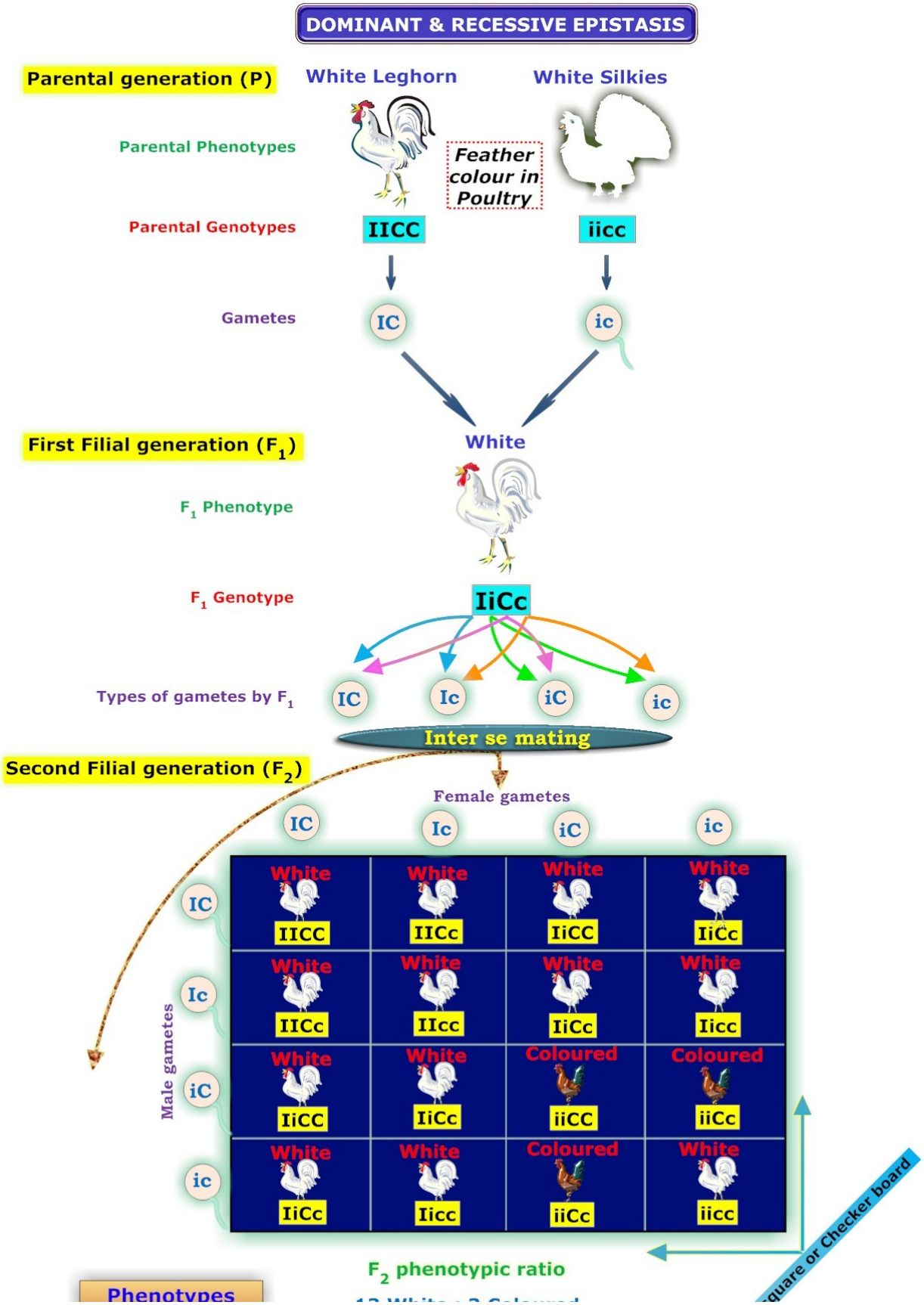
RECESSIVE EPISTASIS


RECESSIVE EPISTASIS
Parental generation (P)
Black
Albino
Parental Phenotypes
Coat colour in Rats
Parental Genotypes
RRCC
rrcc
Gametes
RC
rc
First Filial generation (F1)
Black
F1 Phenotype
F1 Genotype
RrCc
Types of gametes by F1
RC
Rc
rC
rc
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
Black RRCC
Black RRCc
Black RrCC
Black RrCc
Black RRCc
Albino RRcc
Black RrCc
Albino Rrcc
Black RrCC
Black RrCc
Cream rrCC
Cream rrCc
Black RrCc
Albino Rrcc
Cream rrCc
Albino rrcc
Phenotypes
R_C_ : Black 9
rrC_ : Cream 3
F2 phenotypic ratio
9 Black : 3 Cream : 4 Albino
(9 : 3 : 4)
Punnett square or Checker board

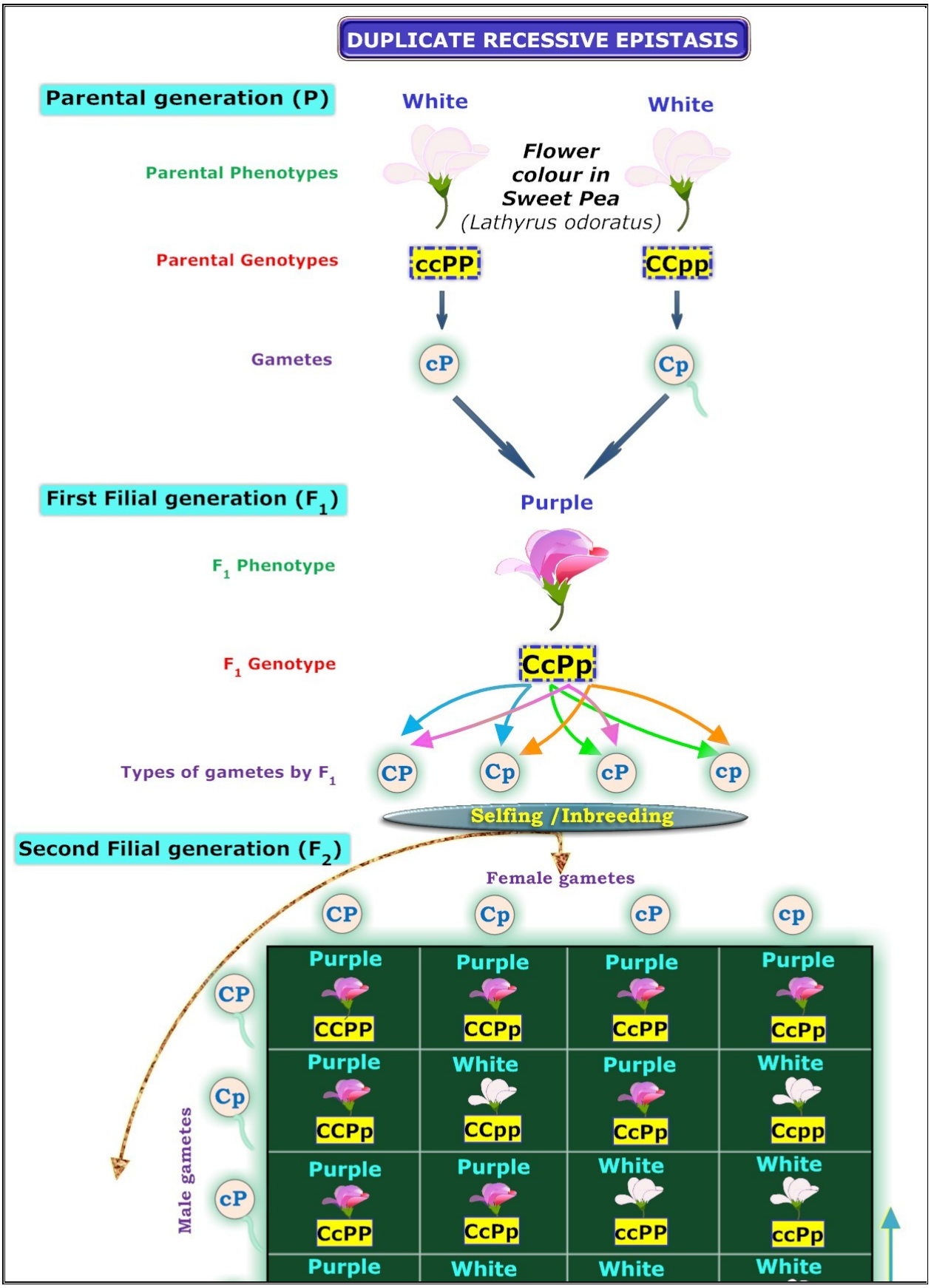
DOMINANT EPISTASIS


DOMINANT EPISTASIS
Parental generation (P)
Brown
White
Parental Phenotypes
coat colour in Dogs
Parental Genotypes
bbii
BBII
Gametes
bi
BI
First Filial generation (F1)
White
F1 Phenotype
F1 Genotype
BbIi
Types of gametes by F1
BI
Bi
bI
bi
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
White BBII
White BBIi
White BbII
White BbIi
White BBIi
Black BBii
White BbIi
Black Bbii
White BbII
White BbIi
White bbII
White bbIi
White
Black
White
Brown

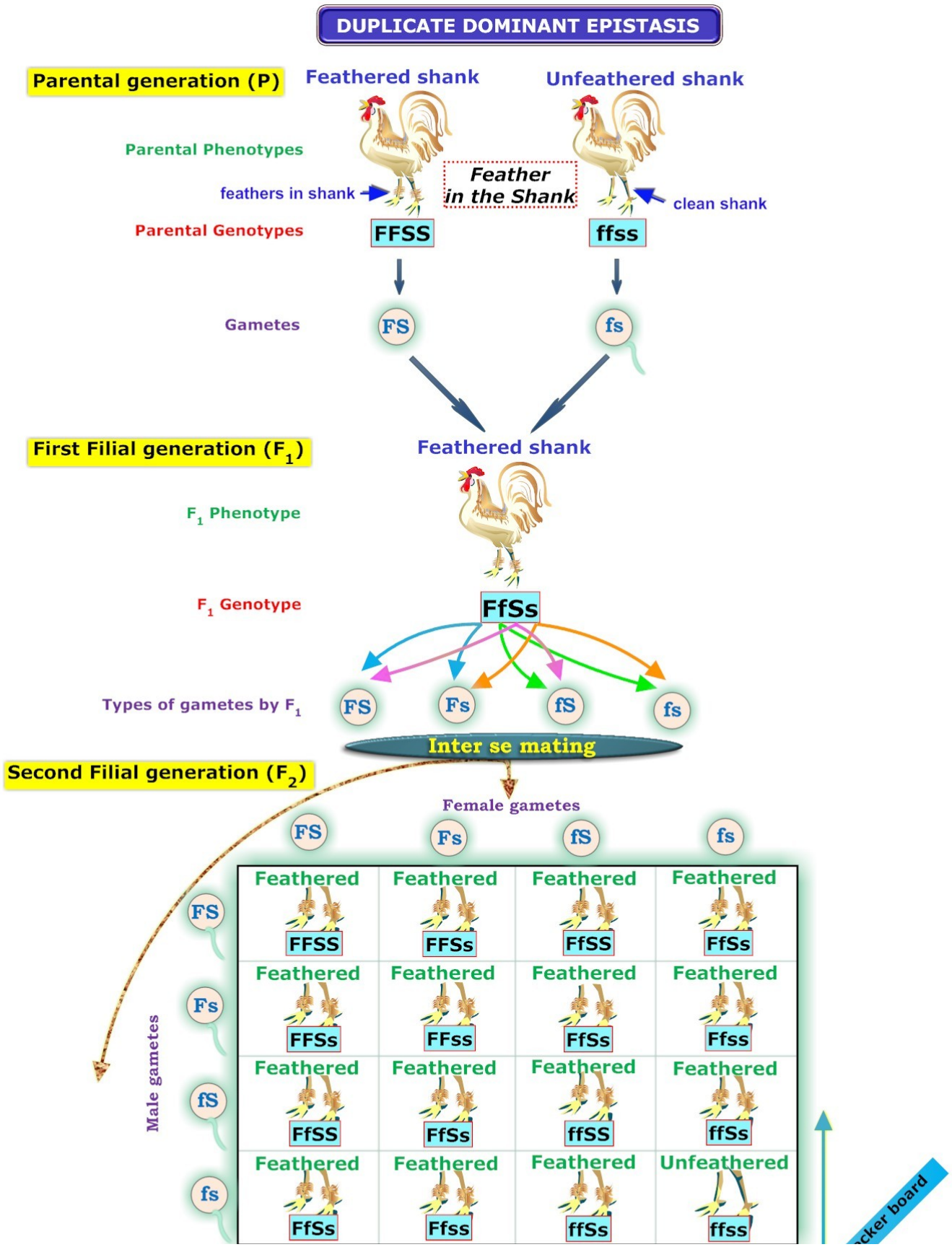
DOMINANT AND RECESSIVE EPISTASIS


DOMINANT & RECESSIVE EPISTASIS
Parental generation (P)
White Leghorn
White Silkies
Parental Phenotypes
Feather colour in Poultry
Parental Genotypes
IICC
iicc
Gametes
IC
ic
First Filial generation (F1)
White
F1 Phenotype
F1 Genotype
IiCc
Types of gametes by F1
IC
Ic
iC
ic
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
White IICC
White IICc
White IiCC
White IiCc
White IICc
White IIcc
White IiCc
White Iicc
White IiCC
White IiCc
Coloured iiCC
Coloured iiCc
White IiCc
White Iicc
Coloured iiCc
White iicc
F2 phenotypic ratio
Phenotypes
quare or Checker board

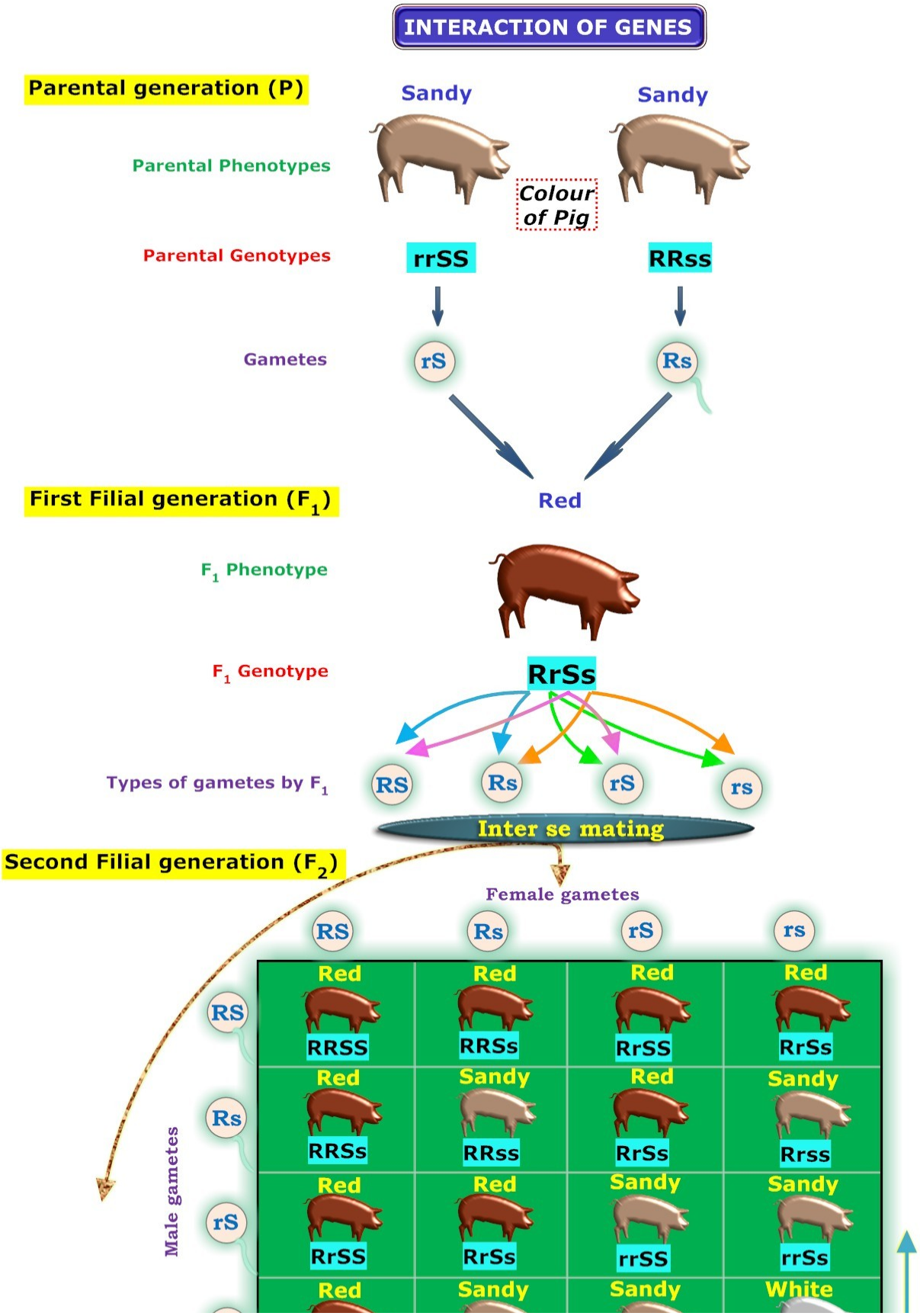
DUPLICATE RECESSIVE EPISTASIS


DUPLICATE RECESSIVE EPISTASIS
Parental generation (P)
White
White
Parental Phenotypes
Flower colour in Sweet Pea (Lathyrus odoratus)
Parental Genotypes
ccPP
CCpp
Gametes
cP
Cp
First Filial generation (F1)
Purple
F1 Phenotype
F1 Genotype
CcPp
Types of gametes by F1
CP
Cp
cP
cp
Selfing /Inbreeding
Second Filial generation (F2)
Female gametes
Male gametes
Purple CCPP
Purple CCPp
Purple CcPP
Purple CcPp
Purple CCPp
White CCpp
Purple CcPp
White Ccpp
Purple CcPP
Purple CcPp
White ccPP
White ccPp
Purple
White
White
White

DUPLICATE DOMINANT EPISTASIS


DUPLICATE DOMINANT EPISTASIS
Parental generation (P)
Feathered shank
Unfeathered shank
Parental Phenotypes
feathers in shank
Feather in the Shank
clean shank
Parental Genotypes
FFSS
ffss
Gametes
FS
fs
First Filial generation (F1)
Feathered shank
F1 Phenotype
F1 Genotype
FfSs
Types of gametes by F1
FS
Fs
fS
fs
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
Feathered FFSS
Feathered FFSs
Feathered FfSS
Feathered FfSs
Feathered FFSs
Feathered FFss
Feathered FfSs
Feathered Ffss
Feathered FfSS
Feathered FfSs
Feathered ffSS
Feathered ffSs
Feathered FfSs
Feathered Ffss
Feathered ffSs
Unfeathered ffss
cker board

DUPLICATE GENES WITH INTERACTION


INTERACTION OF GENES
Parental generation (P)
Sandy
Sandy
Parental Phenotypes
Colour of Pig
Parental Genotypes
rrSS
RRss
Gametes
rS
Rs
First Filial generation (F1)
Red
F1 Phenotype
F1 Genotype
RrSs
Types of gametes by F1
RS
Rs
rS
rs
Inter se mating
Second Filial generation (F2)
Female gametes
Male gametes
RS
Rs
rS
rs
Red RRSS
Red RRSs
Red RrSS
Red RrSs
Red RRSs
Sandy RRss
Red RrSs
Sandy Rrss
Red RrSS
Red RrSs
Sandy rrSS
Sandy rrSs
Red
Sandy
Sandy
White

MODULE-9: MULTIPLE ALLELES

Learning objectives

After completing this module, the learner should be able to understand the term multiple alleles.

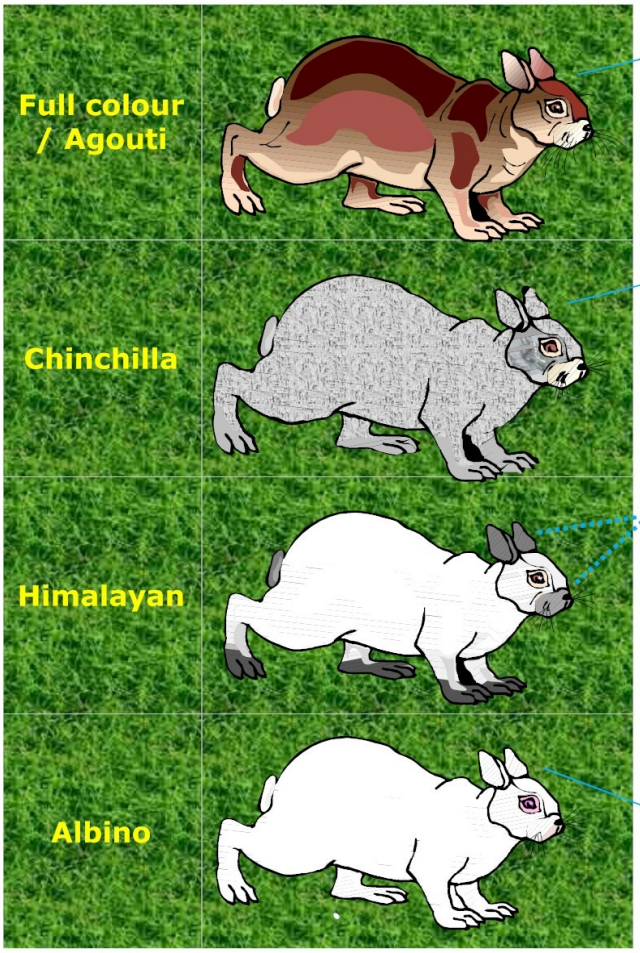
MULTIPLE ALLELES

- In all diploid organisms, in each somatic cell there are two homologous chromosomes.
- Each one of these homologous chromosomes carries one allele of a gene at a particular locus. So there are two alleles in a locus of each cell of an individual.
- When more than two alternative alleles are present for a gene, they are called *multiple alleles*.
- In these cases two or more different mutations must have taken place at the same locus but in different individuals or at different times.
- A capital letter symbol is used to designate allele which is dominant to all other alleles for that specific gene.
- Corresponding small letter is used to designate allele which is recessive to all other alleles for that specific gene.
- Other intermediate alleles are designated with same letter with some suitable subscript based on their degree of dominance between the two extreme alleles.

1. COAT COLOUR IN RABBITS

- The most famous example of multiple alleles was discovered in the coat colour of rabbits.
- The rabbits may have the following colour.
    - Full colour/Agouti (brownish grey)
    - Chinchilla (silvery grey)
    - Himalayan – white with black extremities
    - Albino - complete white

Rabbit Coat Colour



Brownish grey - wild type

Mutant type - Black and grey hairs, have the appearance of silvery grey.

Mutant type - The extremities such as ears, nose, tips of limbs are black coloured, while the rest of the body is white.

The condition in which black pigmentation is confined to the ears, muzzle, feet and tail, is called acromelanism. Eyes are pigmented

Mutant type - totally lacks in pigmentation and the eyes of a albino remain pink due to lack of pigment in iris of eye.

Possible Genotypes of Rabbits with Different Coat Colour

Crosses	F1	F2	Order of Dominance	Allele	Possible Genotype
Agouti X Chinchilla			Agouti	C	CC
Agouti X Himalayan					$C^{ch}C^{h}$
Agouti X Albino					Cc
Chinchilla X Himalayan			Chinchilla	C^{ch}	$C^{ch}C^{ch}$
Chinchilla X Albino					$C^{ch}C^{h}$ $C^{ch}C^{ch}$
Himalayan X Albino			Himalayan	C^{h}	$C^{h}C^{h}$ $C^{h}C^{h}$
Albino X Albino			Albino	c	cc

- In addition to the four alleles discussed above, two more alleles have been found to affect the degree of expression of the chinchilla pattern. The six alleles n order of dominance from left to right are $C > c^{d} > c^{ch} > c^{l} > c^{h} > c$ (alleles c^{d} - dark chinchilla and c^{l} light chinchilla)

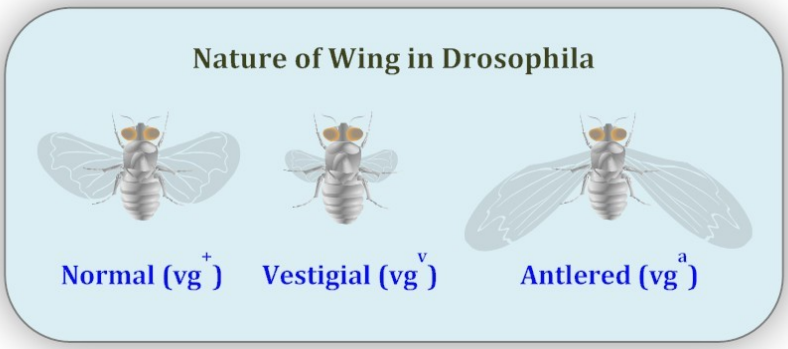
To view "Multiple Alleles - Coat Colour in Rabbits Animation"

- As the number of genes in a series of multiple alleles increases the number of genotypes possible increases rapidly. The numer of genotypes possible in a diploid organism with 'n' different alleles is given by the formula [n(n+1)]/2.

Alleles in a series	Genotypes
2	3
3	6
4	10
5	15
n	n (n+1)/ 2

2. NATURE OF WING IN DROSOPHILA

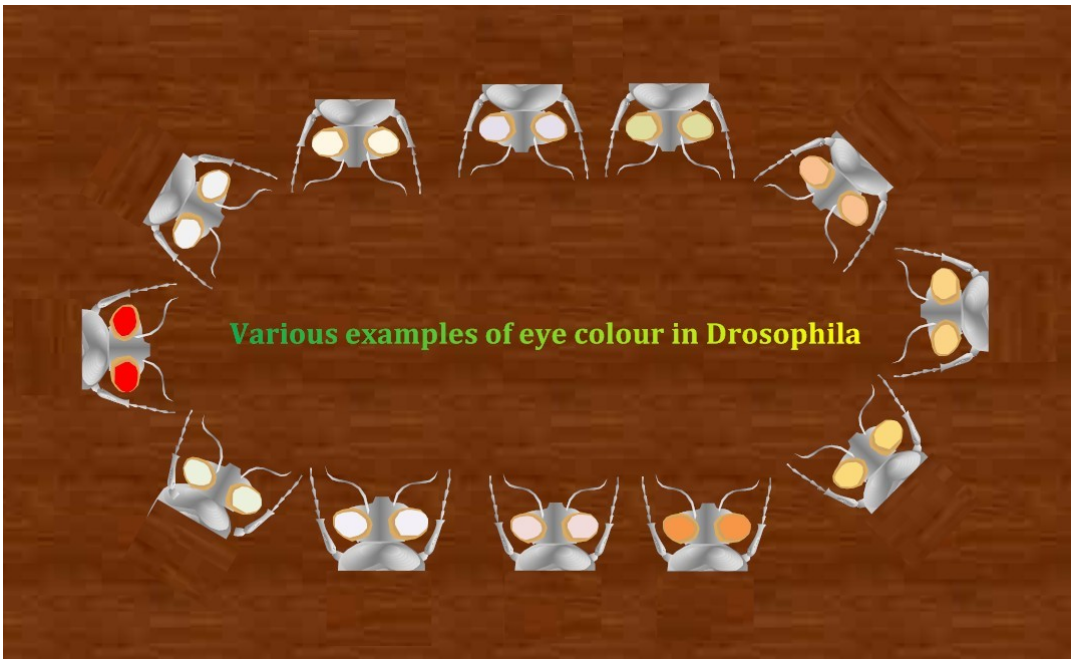
- In the wild strain of Drosophila, the wings are normally long (vg^{+}).
- The two mutant alleles in this locus are vg^{v} (vestigial) and vg^{a} (antlered).



- The mutant alleles are recessive to the normal gene.
- But when the vestigial wing and antlered flies are crossed the F1 hybrids are intermediate in appearance and this phenotype is often called vestigial-antlered.
- This suggest that vg^{v} and vg^{a} are neither dominant nor recessive to each other but only intermediate in effect.
- In addition to these alleles the vestigial locus carries other mutants such as strap (vg^{st}), nicked (vg^{ni}) and notched (vg^{no}) etc.

3. EYE COLOUR IN DROSOPHILA

- Another example of multiple alleles in *Drosophila* is eye colur.
- Wild type *Drosophila* have red eyes; but a vast variety of eye-colour mutants have been studied extensively.
- More than a dozen mutant alleles of one gene (white, symbolized w) results in flies with eye colour ranging from pure white through a series of intermediate colours up to nearly the wild-type red when present in the homozygous condition.
- The recessive mutant white was discovered by T.H. Morgan and C. Bridges in 1912.
- The other mutants alleles of this gene are w^{a} (white apricot), w^{e} (white eosin), w^{ch} (white cherry), w^{co} (white coral), w^{col} (white coloured), w^{w} (white wine), w^{bl} (white blood), w^{crr} (white carrot) w^{cf}(white coffee) etc.,
- Generally a cross between any two mutants results in the appearance of intermediate phenotype in the F1 progeny.
- The genotype appearing as wild type are w^{+S}/ w^{+S} - Stellen bush strain, w^{+C}/w^{+C} - Canton S strain and w^{+G}/w^{+G} - Graff-Reinet strain.
- The various wild type genotypes that appear as red can be quantitatively seperated.
- Such types of alleles, which act within the phenotypic range of each other, are called *isoalleles*.
- Many such isoalleles have been discovered at a later period.



4. ABO BLOOD GROUP SYSTEM IN HUMAN

- The first case of multiple alleles demonstrated in man was the ABO blood group system by Karl Landsteiner(University of Vienna) in 1900.
- In 1930, he belatedly received the Nobel Prize for this discovery.
- The ABO locus has three common alleles of a single gene I^A, I^B, I^O (located on chromosome 9) forming four different phenotypes viz.,

Phenotype	Genotype	Antigen
A	I^AI^A, $I^A I^O$	A
B	I^BI^B, $I^B I^O$	B
AB	I^AI^B	AB
O	$I^O I^O$	Neither

I^A and I^B,are co-dominant and I^O is recessive to both I^A and I^B

- The ABO locus controls the type of glycolipids found on the surface of erythrocytes, apparently by specifying the glycosyl-transferases (enzymes catalysing the synthesis of polysaccharides) synthesized in the red blood cells.
- The specific types of glycolipids on the red blood cell surface in turn provide the antigenic determinants that react with specific antibodies in blood serum.
- The cell surface antigens and the serum antibodies present in the four ABO blood types are summarised as follows.

Blood Group	Antigens on RBCs	Serum antibody	Transfusions accepted	Red cells agglutinated

A	A	Anti-B	A or O	B, AB
B	B	Anti-A	B or O	A, AB
AB	A and B	None	A, B, AB and O	None
O	none	Anti –A and Anti-B	O	A, B and AB

- The AB blood group individuals can receive blood from all the group and hence they are called *Universal recipients*.
- O individuals can donate blood to all the groups and hence they are called *Universal donors*.
- The A and B antigens are found not only on red blood cells but often in the body fluids as well.
- Individuals who possess such antigens are called Secretors and can be shown to be either homozygous (SeSe) or heterozygous (Sese) for the dominant allele.
- The secretors are controlled by a different pair other than ABO blood group genes.

Rh - FACTOR ALLELES IN HUMANS

- The Rh-factor was discovered by K Landsteiner in 1940 along with A.S. Weiner.
- They immunized rabbits with blood of a monkey (*Macaca rhesus*).
- The rabbits developed antibodies that could agglutinate not only rhesus blood, but also the blood of human beings.
- The antigens of both monkeys and humans were called Rhesus (Rh-antigen).
- Individuals carrying the Rh-antigens are called Rh-positives and those who do not carry Rh-antigen are called Rh-negatives.
- Most people - about 85% - are Rh-positive.
- But if a woman who is Rh-negative and a man who is Rh-positive conceive a baby, there is the potential for a baby to have a health problem.
- The baby growing inside the Rh-negative mother may have Rh-positive blood, inherited from the father.
- Rh-incompatibility usually isn't a problem if it's the mother's first pregnancy because, unless there's some sort of abnormality, the fetus's blood does not normally enter the mother's circulatory system during the course of the pregnancy.
- However, during delivery, the mother's and baby's blood can intermingle.
    - If this happens, the mother's body recognizes the Rh-protein as a foreign substance and can begin producing antibodies (protein molecules in the immune system that recognize, and later work to destroy, foreign substances) against the Rh-proteins introduced into her blood.
    - Rh antibodies are harmless until the mother's second or later pregnancies.
    - If she is ever carrying another Rh-positive child, her Rh-antibodies will recognize the Rh-proteins on the surface of the baby's blood cells as foreign, and pass into the baby's bloodstream and attack those cells.
    - This can lead to haemolysis of the normal blood cells.
    - A baby's blood count can get dangerously low when this condition, known as *haemolytic disease of the newborn, "Erythroblastosis foetalis"* occurs.
- Other ways Rh-negative pregnant women can be exposed to the Rh- protein that might cause antibody production include blood transfusions with Rh-positive blood, miscarriage, and ectopic pregnancy.
- At first, the genetic control of the Rh-system seemed to be simple. A simple pair of R and r was postulated to account for the difference between Rh-positive and negative individuals.

- However, based on molecular studies of other genes, it seems likely that multiple alleles exist at the locus or loci encoding the Rh-antigens(s).

OTHER EXAMPLES

- Restricted Mallard > Mallard > dusky mallard in ducks
- Yellow > Agouti with light belly > Agouti > Black and tan > Black in mice
- Hereford spotting = Pinzgauer spotting > solid colour > Holstein spotting in cattle (SH = SP > S+ > s)
- Normal > Retarded > Tardy feathering in poultry
- Horned > Knob > Small scurs > Hornless in certain breeds of sheep

MODULE-10: LETHAL GENES

Learning objectives

After completing this module, the learner should be able to:

- understand the term lethal genes
- explain why lethal dominant genes are much rarer than lethal recessive genes
- describe the procedure for elimination of lethal genes from the population

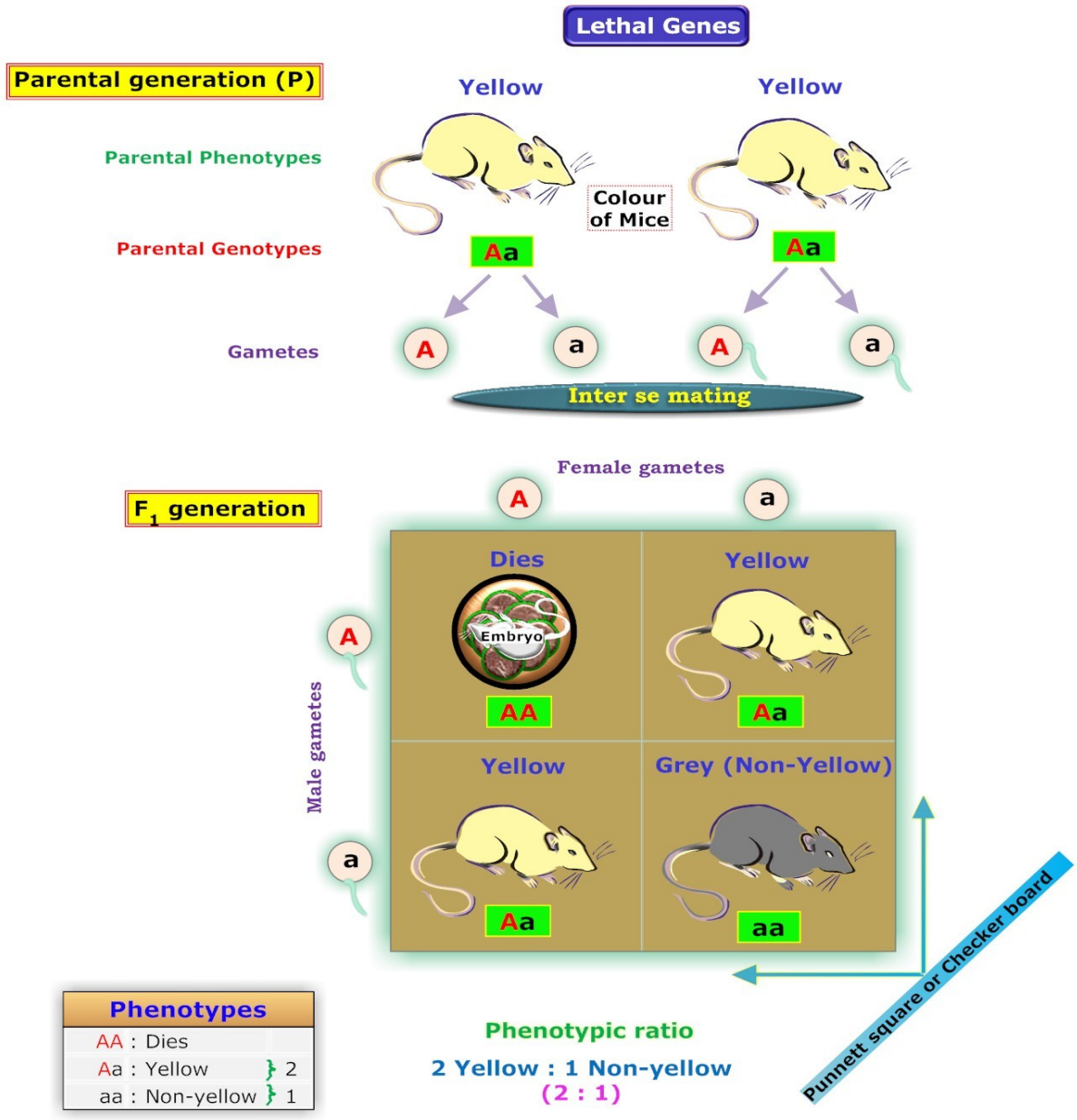
LETHAL GENES

- Genes which result in the premature death of the organism are called **Lethal Genes**.
- Phenomenon of action of lethal genes is called **lethality**.
- Lethal genes can be recessive, dominant, conditional, semilethal, or synthetic, depending on the gene or genes involved.

YELLOW FUR IN MICE

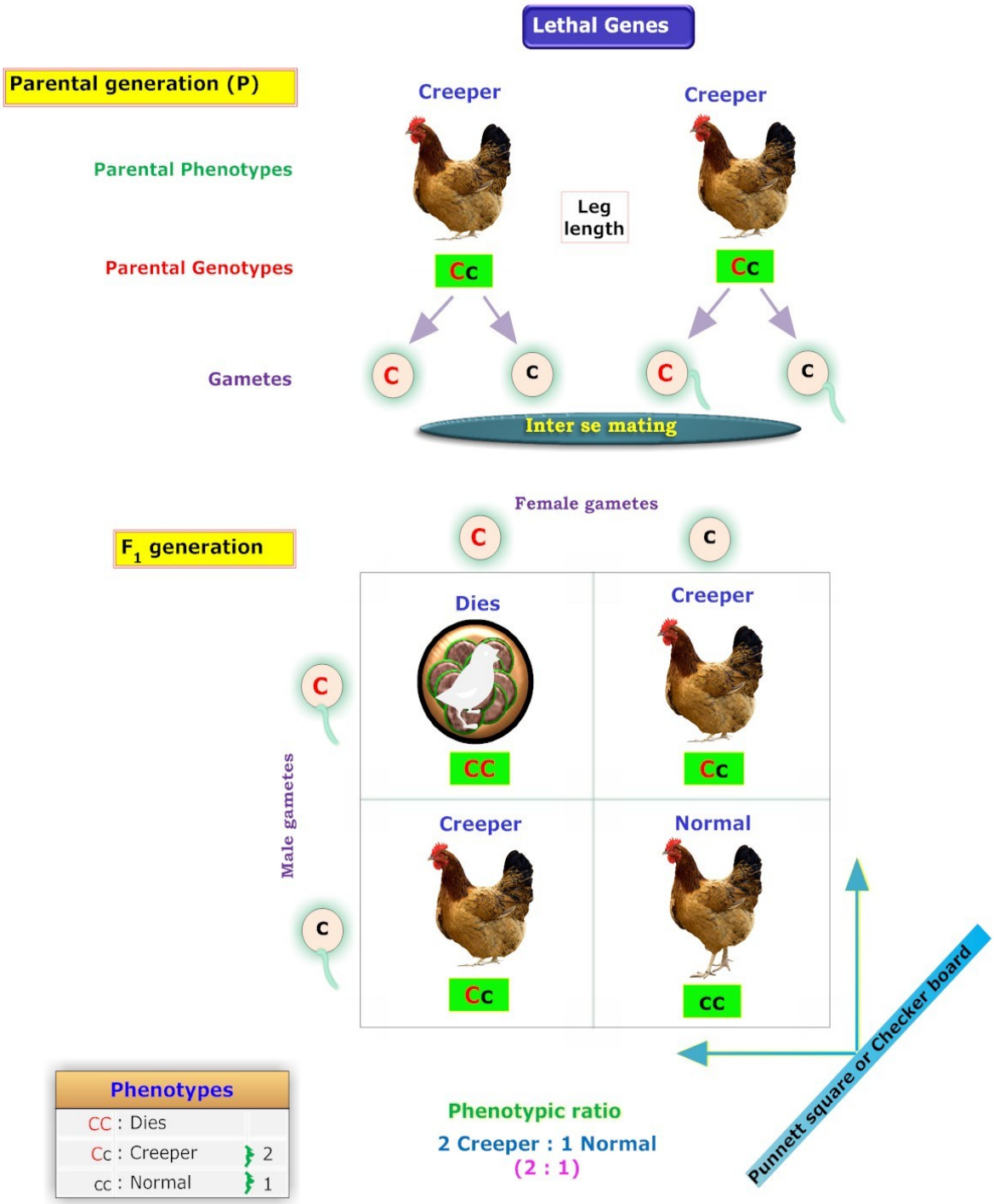
Semi dominant lethal : (Incompletely dominant lethal, intermediate lethal)

- In 1905, Cuenot, a French zoologist found that when yellow mice were mated inter se, they never bred true to type and yielded “yellow” and “non-yellow” progeny in the ratio of 2:1.
- Backcross of yellow into non-yellow yielded a ratio of 1:1.
- After more experimentation, it was eventually realized that all yellow mice were heterozygote and those zygotes homozygous for yellow died at an early stage of gestation.
- Thus the yellow mice provided the first demonstration where genes could be lethal in the homozygous state.



CREEPER CONDITION IN DOMESTIC FOWL

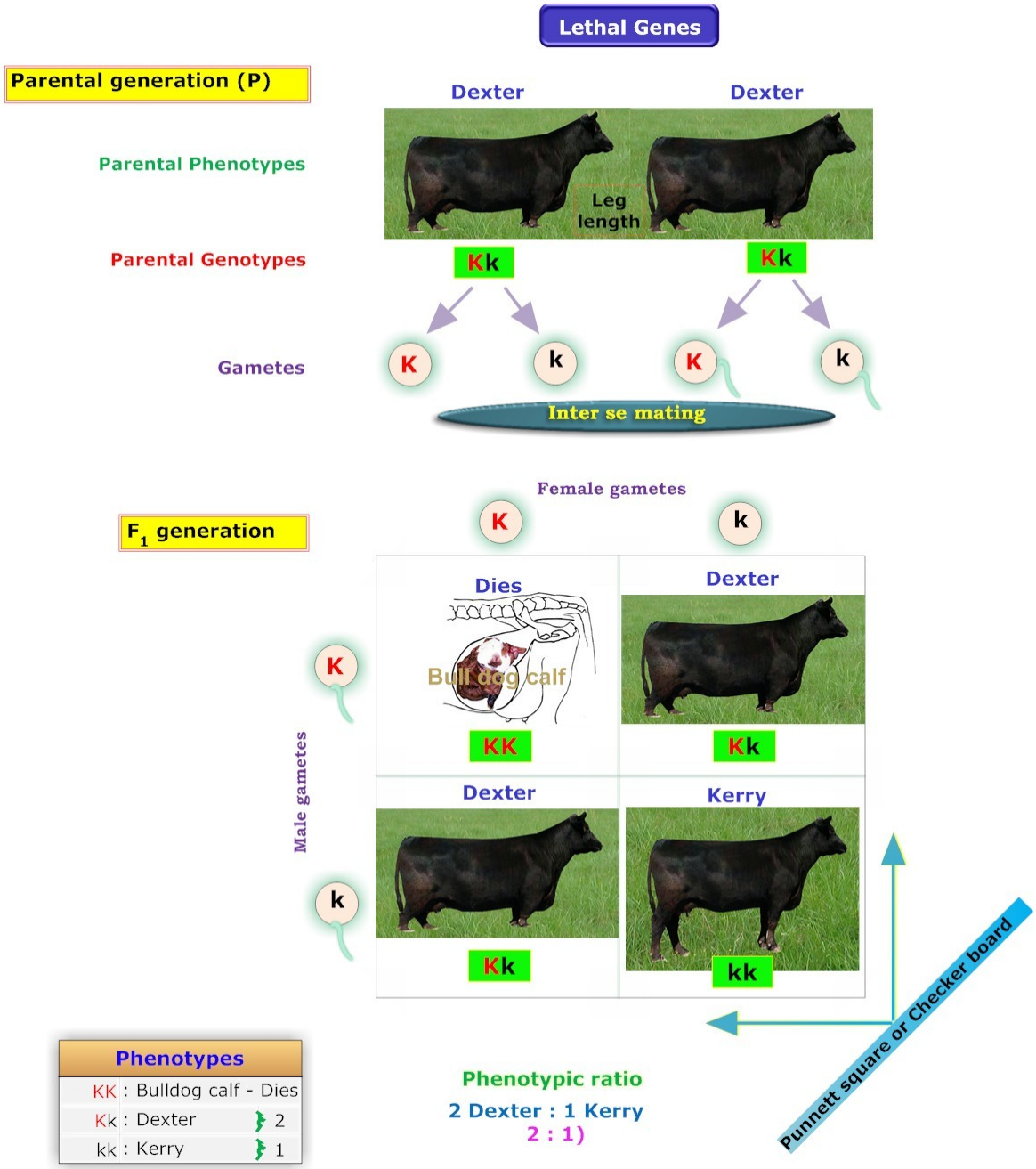
- Semi dominant lethal: (Incompletely dominant lethal, intermediate lethal)
- In domestic fowl, an intermediate lethal gene when heterozygous gives rise to a peculiar condition called creeper.
- The creeper chicken have short and crooked legs: they are unable to move normally and creep about without lifting their bodies off the ground.
- The same lethal gene when homozygous causes death during the embryonic stages.
- When two creeper chickens are crossed they yield a peculiar ratio of 2:1.



- An explanation for the altered ratio can be found if we consider all the eggs which were incubated. One fourth of these failed to hatch which had dead embryos (at about 4th day of incubation).
- Hence it is evident that creeper condition in chicken is a heterozygous expression of a gene which is lethal when homozygous.

ACHONDROPLASIA IN CATTLE

- Semi dominant lethal: (Incompletely dominant lethal, intermediate lethal)
- Dexter and Kerry are beef breeds of cattle of England. Dexter (has short limbs) is a better beef producer than the Kerry. But it is impossible to establish a pure breeding herd of Dexters because these desirable characteristics of the breed result in association with heterozygous expression of lethal gene.
- When two Dexters are crossed the offspring are produced in the ratio of 1 Kerry : 2 Dexter : 1 bull dog calf. The bull dog calf usually dies.



AMPUTATED: A RECESSIVE LETHAL IN CATTLE

- In Swedish Holstein Friesian cattle, there is a recessive gene producing condition described as “amputated” which when homozygous results in calves without legs and parrot jaws.

EFFECTS OF LETHAL GENES

- Some lethal genes induce gross abnormalities, some interfere with physiological processes and others kill or are not yet been identified. They produce lethal effect in homozygous state.
- Lethal action may be due to single gene or at times more than a single gene.
- Expressed lethal effect is due to environment, incomplete penetrance and variable expressivity and epistasis.
- In majority of cases, it is difficult to determine the type of gene action.

DETECTION AND ELIMINATION OF LETHAL GENES

- Elimination of lethal genes from the population could be carried out by identifying the carriers (heterozygotes) and preventing them from further breeding.
- ***Intermediate lethal genes*** are much easier to detect because all the individuals will exhibit some phenotypic expression of the gene.
- ***Dominant lethals*** kill the individual either in homozygous or heterozygous conditions and therefore is eliminated from the population in the same generation in which it arises.
- ***Recessive lethals*** kill only when in homzygous stage. They are very difficult to eliminate from the population. Heterozygous carrier parents that produce a lethal effect could be used as testers to identify others in the population.

MODULE-11: SEX-LINKED INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- understand the term sex chromosomes and sex linked inheritance
- aware of some example of sex linked characters

SEX LINKAGE

- There are two types of chromosomes,
  - Autosomes and
  - Sex chromosomes
- *Autosome* refers to those chromosomes that are not involved in sex determination.
- Sex chromosomes determine the sex of an organism. A human somatic cell has two sex chromosomes: XY in male (hetero-gametic) and XX in female (homo-gametic).
- In birds the female (ZW) is hetero-gametic and male (ZZ) is homo-gametic.

Sex linkage

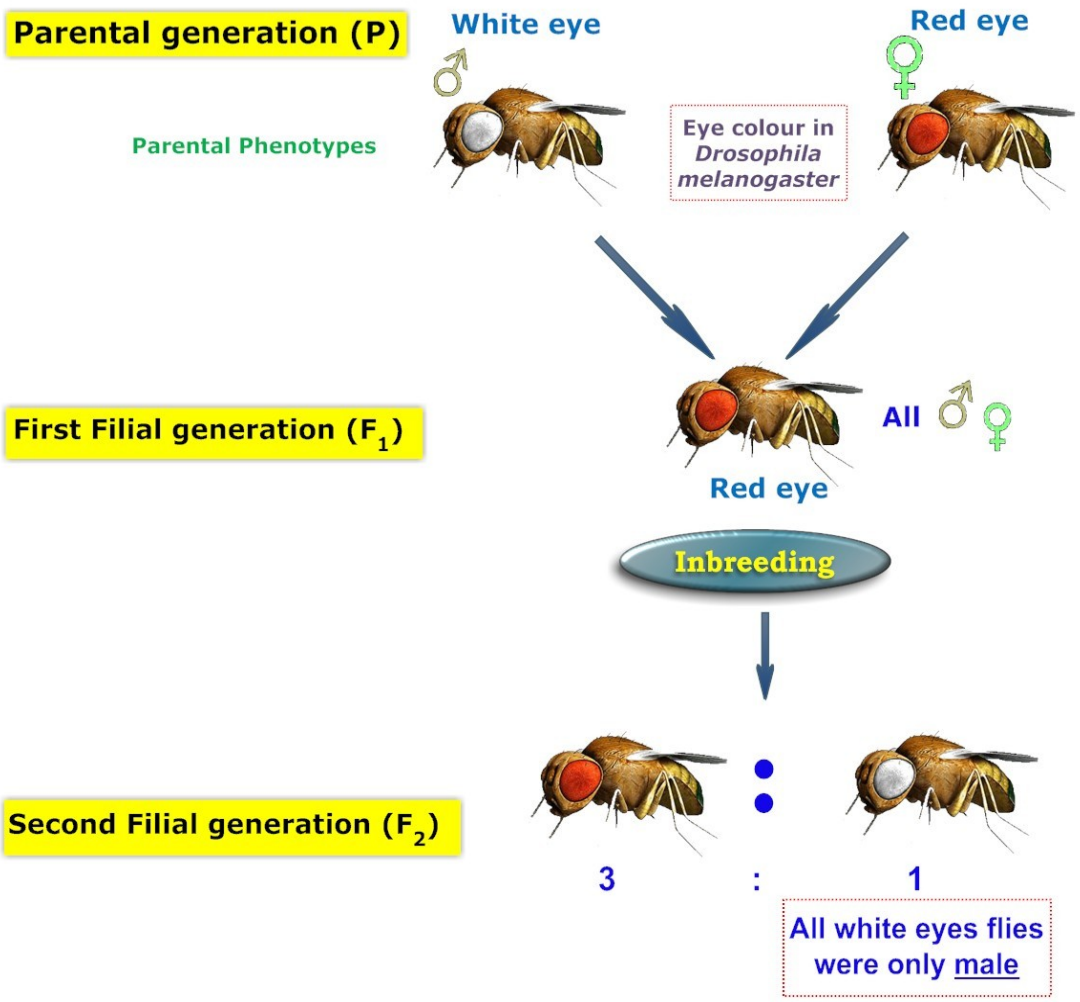
- Sex chromosome contains genes not only for sex but also for other traits.
- Sex linkage refers to the association or linkage of a hereditary trait with sex chromosomes.
- Most traits carried are present only on the X-chromosome.
- The Y-chromosome is smaller, and so, very few genes are located on this chromosome.
- Because of their location in the sex chromosomes, they are said to be *“sex linked traits”*.

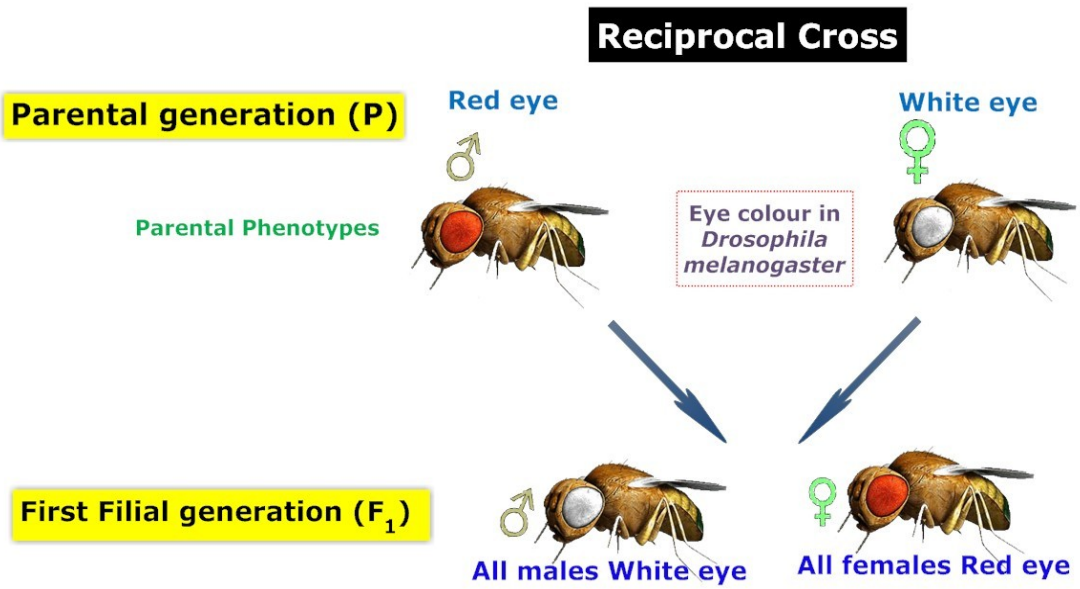
X LINKED INHERITANCE

- Certain sex linked genes are located only on X chromosomes and their alleles are absent from Y chromosome.
- These genes are called *X linked genes;* the characters controlled by these genes are called *X linked characters* and their mode of inheritance is called *X linked inheritance*.
- X-linked inherited diseases occur far more frequently in males because they only have one X chromosome.
- X linked inheritance may be X - linked dominant, X-linked recessive or X - linked co dominant.

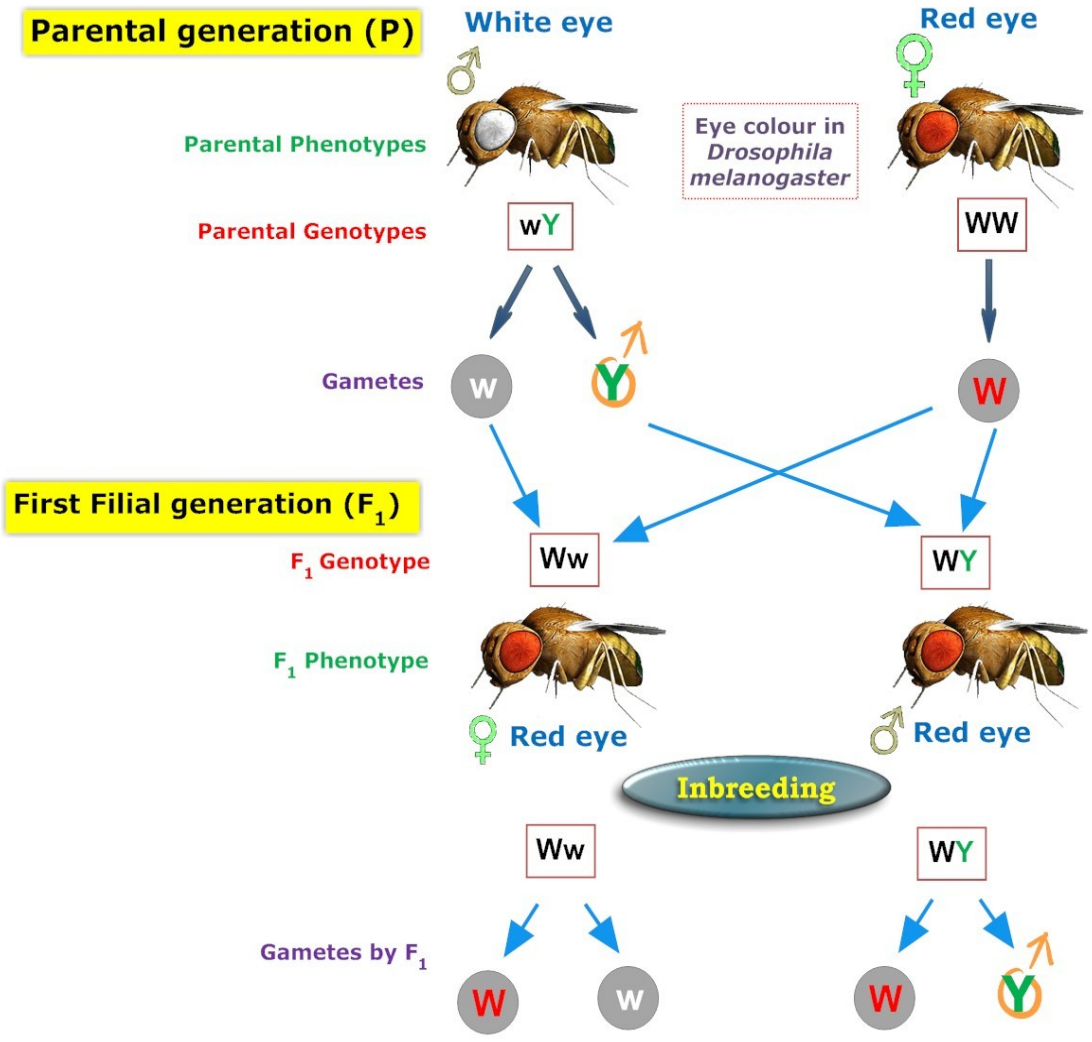
X-LINKED DOMINANT

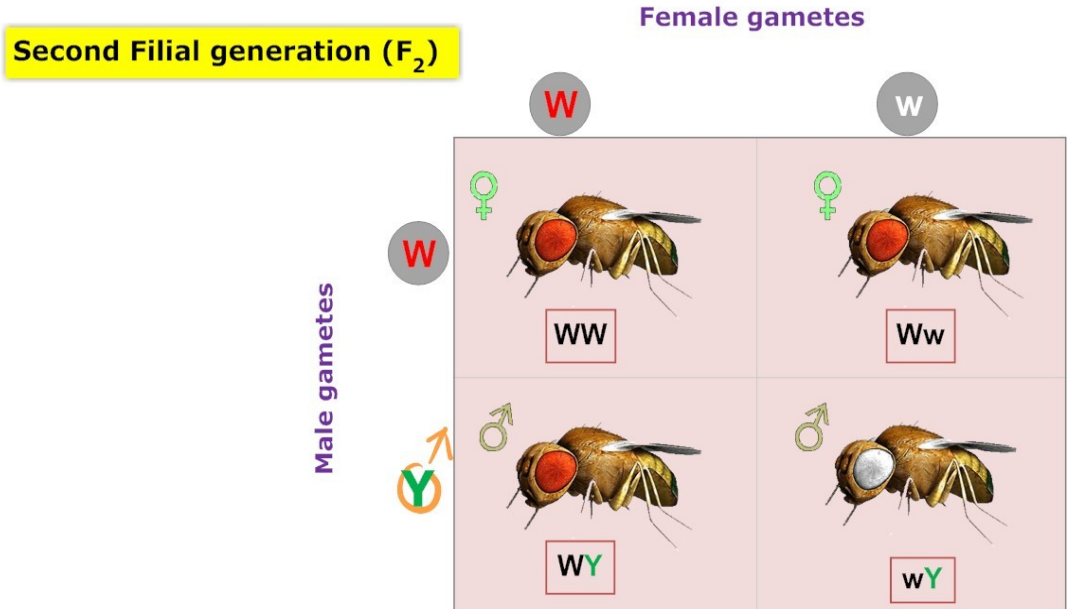
- In X-linked dominance, both males and females can display the trait or disorder by having only one copy of the allele.
    - *Example* : Incontinentia Pigmenti (IP), X-linked hypophosphatemia, Fragile X syndrome, Aicardi syndrome, Congenital hemidysplasia with ichthyosiform erythroderma and limb defects (also known as "CHILD syndrome"), Lujan–Fryns syndrome (LFS) also referred to as X-linked mental retardation with Marfanoid habitus and Lujan syndrome.
- In 1910 Thomas Hunt Morgan observed a male *Drosophila melanogaster* which was white eyed. He mated this fly with a red eyed female and got the following result.


Parental generation (P)
White eye
Red eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
First Filial generation (F_1)
All
Red eye
Inbreeding
Second Filial generation (F_2)
3 : 1
All white eyes flies were only male
No white eyed female flies were noticed


Reciprocal Cross
Parental generation (P)
Red eye
White eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
First Filial generation (F_1)
All males White eye
All females Red eye

- Morgan interpreted the above results assuming that the genes for eye colour must be located on the sex chromosome. He postulated that females must be homogametic carrying two X chromosomes (XX) and males with one X chromosome and one Y chromosome (XY) therefore heterogametic.

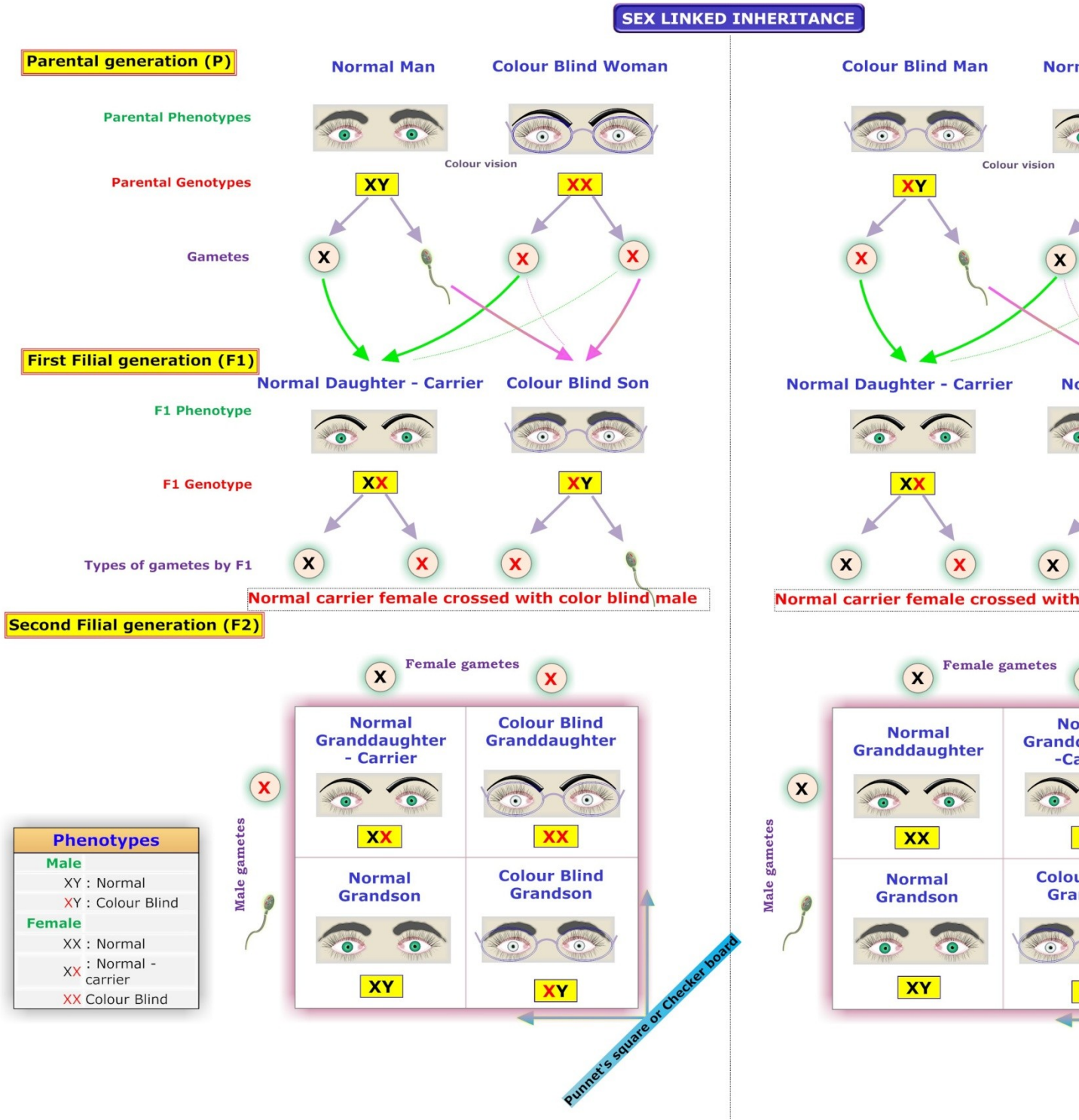

Parental generation (P)
White eye
Red eye
Parental Phenotypes
Eye colour in Drosophila melanogaster
Parental Genotypes
wY
WW
Gametes
w
Y
W
First Filial generation (F1)
F1 Genotype
Ww
WY
F1 Phenotype
Red eye
Red eye
Inbreeding
Ww
WY
Gametes by F1
W
w
W
Y


Second Filial generation (F2)
Female gametes
W
w
Male gametes
W
Y
WW
Ww
WY
wY

- In F2, equal number of red and white eyed individuals with normal sex ratio appeared.
- This is a significant deviation from normal autosomal gene inheritance wherein, when crosses are made between two pure breeding varieties which differ with reference to one or two characters there is no difference between reciprocal crosses.
- Thus this peculiar pattern of genetic behaviour shown by the white-eye colour indicates that its gene is carried on the X-chromosome.

X - LINKED RECESSIVE

- In male, Y chromosome does not carry many of the same genes as the X chromosome.
- Since males have only one X chromosome, a single recessive allele on that X chromosome will cause the disease.
- Females have two X chromosome, so two copies of the recessive allele are required for the disease to express in females.
- Affected males never pass the disease to their sons because there is no male-to-male transmission of the X chromosome.
- Affected males pass the defective X chromosome to all of their daughters, who are described as obligate carriers.
- Transmission of the sex linked disease from affected males to male grandchildren through carrier daughters is described as a "Nasse's Law".
- Female carriers pass the defective X chromosome to half their sons.
- Sex linked traits in one parent passes to the opposite sex of the next generation. This is known as “Criss Cross Inheritance”.
    - *Example* : Haemophilia, Color Blindness, etc.

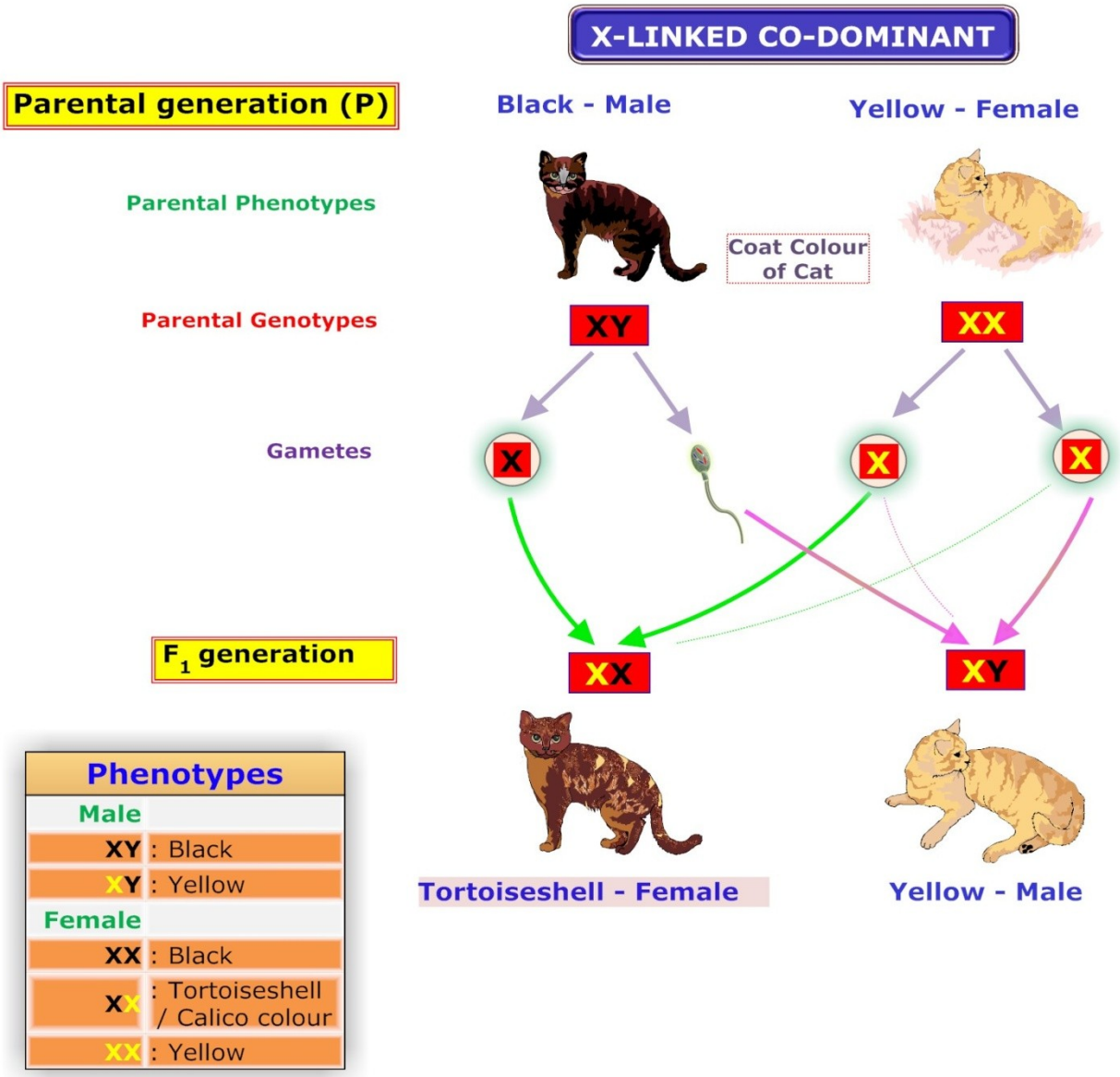


X - LINKED CO-DOMINANT

X-linked co-dominant

- In female cells, one or the other X chromosome must be inactivated. This occurs more or less at random.

- Female mammal has patches of cells with one X chromosome inactivated, and patches with the other X chromosome inactivated.
- If the gene is expressed directly within the cell, the mosaic nature of the female may become obvious.
    - *Example* : Tortoiseshell cat



Y - LINKED GENES OR HOLANDRIC GENES

- Y chromosome carries a few genes with visible effects, called holandric genes.
- Such Y-linked genes would be transmitted directly from father to son and never appears in female.
- Pedigree analysis for transmission from father to son provides the only evidence for holandric genes.

Example

- A histocompatability gene (H-Y) present on the short arm of human Y - chromosome.
- Various failures in the SRY (Sex-determining Region Y) genes.
- The hairy pinna of the ear in man has been interpreted as holandric.

XY LINKED INHERITANCE

- Certain sex linked genes are located in homologous sections of both X and Y chromosomes.
- They are called *XY linked genes* and their mode of inheritance is called *XY linked inheritance*.
    - Example : In Drosophila melanogaster - bobbed bristles, Xeroderma pigmentosum, Nephritis, Retinitis pigmentosa, etc

CHARACTERISTICS OF SEX-LINKED INHERITANCE

Features of sex-linked recessive diseases

- The frequency is higher in heterogametic than homogametic sex.
- It is transmitted from affected man through normal daughter to half of the grandsons.
- Does not occur in a woman unless her father has it.
- All the sons of the woman having this trait are affected.

Features of sex-linked dominant diseases

- More common in females.
- All female offspring of affected male will be affected
- If mother is normal sons will not be affected with the diseases.

SEX-LINKED INHERITANCE AND AUTOSEXING IN CHICKEN

- In birds, moths, butterflies, silkworm and in some fishes, different kinds of sex linkages occur where males are homogametic and females are heterogametic.
- In poultry sex chromosomes are described as “ZZ” in males and “ZW” in females.
- The general principle for autosexing in fowls is that homogametic sex (*male*) should have the recessive character in homozygous condition and heterogametic sex (*female*) should have the dominant character.

> ***Autosexing*** *is when pure bred day old chicks can be sexed by their different appearances when they have hatched.*

- The 'barring' pattern is sex-linked. That is the males have two chromosomes for barring and the females only one, resulting in day old chicks have a light coloured patch on the top of the head.
- When the barring is combined with brown colouring, the light spot on the head of the females is small and well defined and in addition, there is a very clearly defined stripe down the body.
- The male chicks on the other-hand have a light patch covering most of the head and there is only a very blurred, indistinct body stripe. The down of the male chick is much paler.
- The first autosexing breed was developed and described by Punnett and Pease (1930).
- Some autosexing traits in poultry:
    - Barring and non-barring in Plymouth Rock

- Silver plumage in Sussex x Golden plumage in Rhode Island Red and New Hampshire
- Rapid feathering x Late feathering

MODULE-12: SEX INFLUENCED AND SEX LIMITED INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- explain the difference between sex influenced and sex limited genetic traits.

SEX INFLUENCED INHERITANCE

- A trait which is influenced by th sex of the individual is called sex-influenced trait.
- Sex-influenced traits are those that are dominant in one sex but recessive in the other. This is due to the different cellular environments in males and females provided by sex hormones.
- Different hormonal environments affect expression of heterozygote of a trait. However, both homozygotes are unaffected and express the trait irrelevant of the hormones produced .
  - *Example*
    - Baldness in man 
    - Mahogany and Red colour in Ayrshire Cattle 
    - Horns in Sheep 

Certain features of sex-influenced traits

- The genes governing sex influenced traits are carried on autosomes and not on sex chromosomes.
- No difference between reciprocal crosses in F_1 and F_2.
- Dominance in the heterozygous condition depends on the sex of the individual or the dominance of the allele may differ in the heterozygote of the two sexes.

Example: Horned condition in sheep

- Dorset horn – both males and females horned
- Suffolk – both males and females hornless (polled)

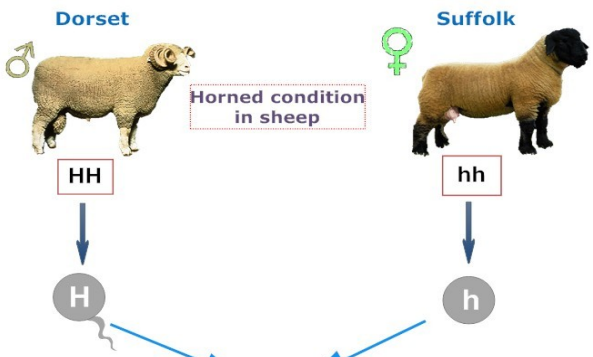
Reciprocal Cr

Parental generation (P)

Parental Phenotypes

Parental Genotypes

Gametes

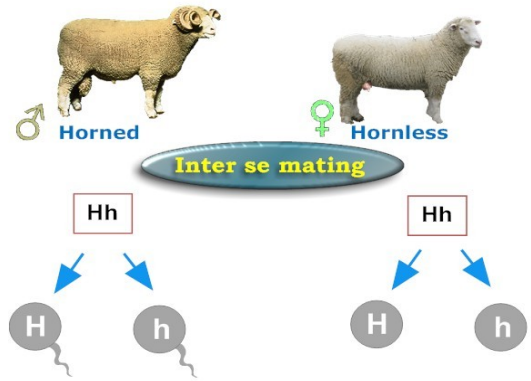


First Filial generation (F_1)

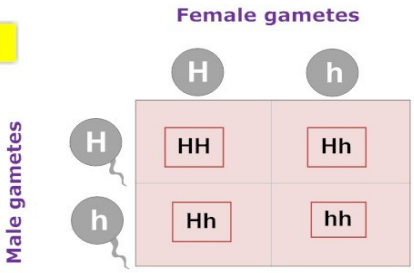
F_1 Genotype

F_1 Phenotype

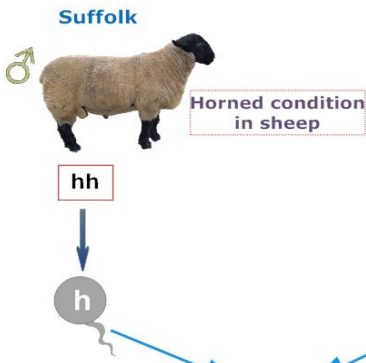
Gametes by F_1

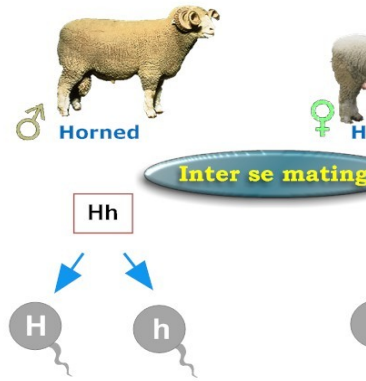


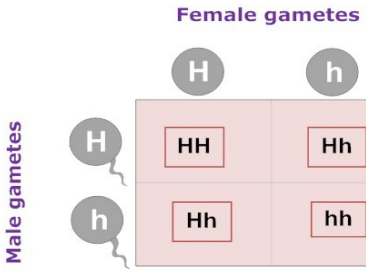
Second Filial generation (F_2)

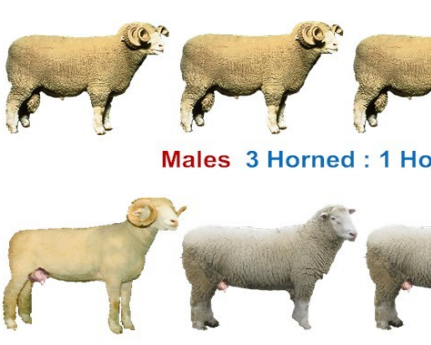


F_2 phenotypic ratio









- So F1 and F2 ratios must be read for males and females separately. The gene for horns is dominant in males and recessive in females while its recessive allele for hornless condition is dominant in females and recessive in males.

SEX LIMITED INHERITANCE

Sex Limited Genes

- Some autosomal genes express characters in only one sex (either male or female) .
- These are autosomal genes but can be expressed only in particular sex. As teir expression islimite to only one sex, they are called sex-limited trats.
- The sex limited traits expression is governed by the internal hormonal environment or the anatomical dissimilarities.

Example

- Milk production in mammals
- Egg production in chicken
- Genes responsible for secondary sexual characteristics as well as primary sexual characters.
    - In man - Development of beard
    - In women - Development of mammary glands
    - Both man and woman have genes for beard and mammary gland development but due to sex hormones the female lacks in heavy beard and male lacks in developed mammar glands.
    - When the penetrance of a gene in one sex i zero, thetrait is a limited one.
- Another example is cock-feathring trait in bird. Hen- feathering resultfrom a single gene "H" and cock-feathering result from its allele, "h".

SEX LIMITED INHERITANCE

Plumage pattern in Poultry

Genotype	Phenotype	
	Cock	Hen
HH	 Hen feathered	 Hen feathered
Hh	 Hen feathered	 Hen feathered
hh	 Cock feathered	 Hen feathered

- Particular type of feathering depends upon specific combination of genotype and sex hormones.
- The expression of gene “H” and “h” depends upon the sex hormones.
- The “h” gene produces hen feathering if female hormone is present, cock-feathering if female hormone is absent.
- This was proved by removing the ovaries in female or testes in hen feathered male birds, results in production of cock feathering even though “H” allele present.

MODULE-13: LINKAGE AND CROSSING OVER

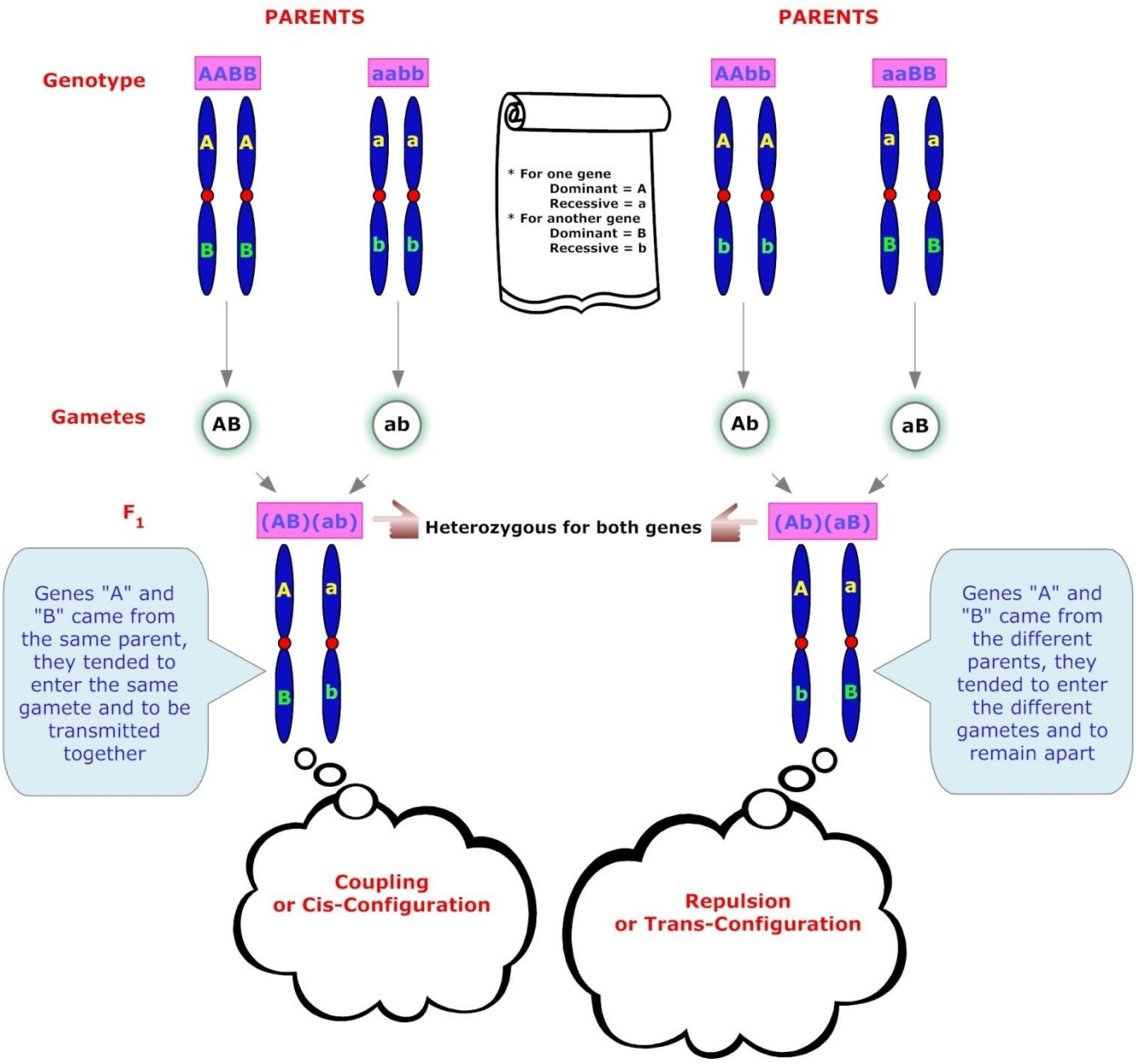
Learning objectives

After completing this module, the learner should be able to:

- understand the meaning of the terms linkage and crossing-over
- explain the effect of linkage and crossing-over on the phenotypic ratios from dihybrid crosses.

LINKAGE

- Each of the chromosomes is distributed independently to the gametes at meiosis.
- Because of this reason, the genes carried in different chromosome undergo independent assortment which was explained so successfully by Mendel's Principle.
- An organism may have numerous genes for its various phenotypic traits, but contain limited number of chromosomes.
- Each chromosome must contain many genes.
- Thus genes in the same chromosome will not be assorted independently.
- Mendel's second principle, the law of independent assortment referring to the separation of two pairs of alleles independently has only limited application, and hence cannot be considered as a universal law.
    - The second principle is valid only when two or more pairs of genes or alleles are situated in different chromosomes, enabling their independent assortment during the formation of gemetes.
    - This law has only limited applications when the genes are situated in the same chromosome.
- Sturtevant first showed that genes are arranged in a linear fashion on the chromosome.
- In 1906 Bateson and Punnett found two pairs of alleles in sweet Peas did not assort independently named this behaviour as coupling and repulsion phase.



To view "Linkage Animation"

- Bateson and Punnett could not explain the exact reasons of coupling and repulsion.
- T.H. Morgan who while performing experiments with Drosophila, in 1911 proposed the new concept of "linkage".
- He proposed that each chromosome contains a collection of small units called genes and are arranged on the chromosome in a linear fashion.
- Each gene must reside on a particular chromosome and tend to be inherited together.

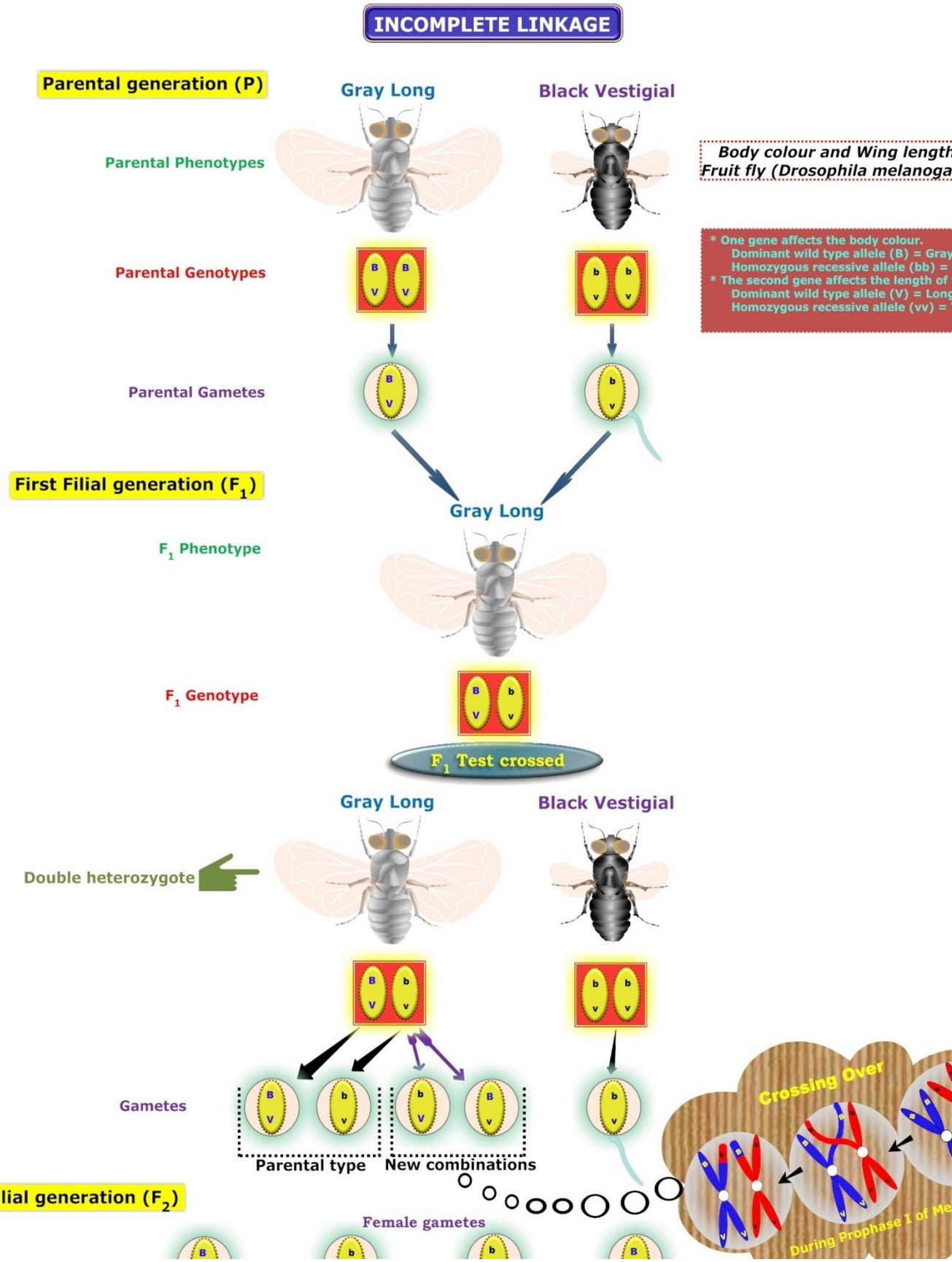
- All the genes on a chromosome are said to be linked to one another and belong to the same linkage group. The phenomenon of inheritance of linked genes in same linkage group is called linkage.
- He also suggested that the strength of linkage between genes depended on the distance between them on the chromosome.

TYPES OF LINKAGE

- All the genes, which are linked with another, form a linkage group.
- Since linked genes are present in the same chromosome, the number of linkage group in an animal or plant is equal to the haploid number of chromosomes present in one cell.
- Linkage is an exception to Random Assortment.

Kinds of Linkage

- The phenomenon of linkage is of following two kinds
- Complete linkage
    - A phenomenon in which two or more genes of characteristics inherited together for a number of generations.
    - In these genes are closely situated in the chromosome and there occurs no breakage in between them.
    - Only combinations of parental characteristics are recovered in test cross progeny.
    - Complete linkage is seen only in male Drosophila.
- Incomplete Linkage
    - In in-complete linkage the linked genes do not always stay together because homologus non-sister chromatids may exchange segments of varying length (which bearing many linked genes) with one another during meiotic prophase, by the process of crossing over and lead to recombinants.
    - Here the recombinant types are also recovered along with parental types in the test cross progeny.
    - *Examples* : seen in female Drosophila, Pea, Zea mays (maize), Tomato, Mice, Poultry and Man. Here, the examples of linkage have been considered only for Drosophila


INCOMPLETE LINKAGE
Parental generation (P)
Gray Long
Black Vestigial
Parental Phenotypes
Body colour and Wing length
Fruit fly (Drosophila melanoga
Parental Genotypes
* One gene affects the body colour.
Dominant wild type allele (B) = Gray
Homozygous recessive allele (bb) =
* The second gene affects the length of
Dominant wild type allele (V) = Long
Homozygous recessive allele (vv) =
Parental Gametes
First Filial generation (F1)
Gray Long
F1 Phenotype
F1 Genotype
F1 Test crossed
Gray Long
Black Vestigial
Double heterozygote
Gametes
Parental type
New combinations
Crossing Over
Second Filial generation (F2)
Female gametes
During Prophase I of Me

STRENGTH OF LINKAGE

- The strength of linkage between any two genes on a chromosome depends up on the distance between them.
- Closely located genes show strong linkage.

Chromosome theory of Linkage (Morgan & Castle)

- Genes located on the same chromosome are inherited together and are said to be linked.
- The linked genes are arranged in a linear fashion of the chromosome.
- The degree of linkage is determined by the distance between genes.
- Coupling and repulsion are two phases of the aspect of linkage.

Factors affecting linkage

- *Distance:* Genes widely located show weak linkage.
- *Age:* With increasing age, the strength of linkage decreases.
- *Temperature:* Increasing temperature decreases the strength of linkage.
- *Radioactive rays:* such as X-rays reduce the strength of linkage.

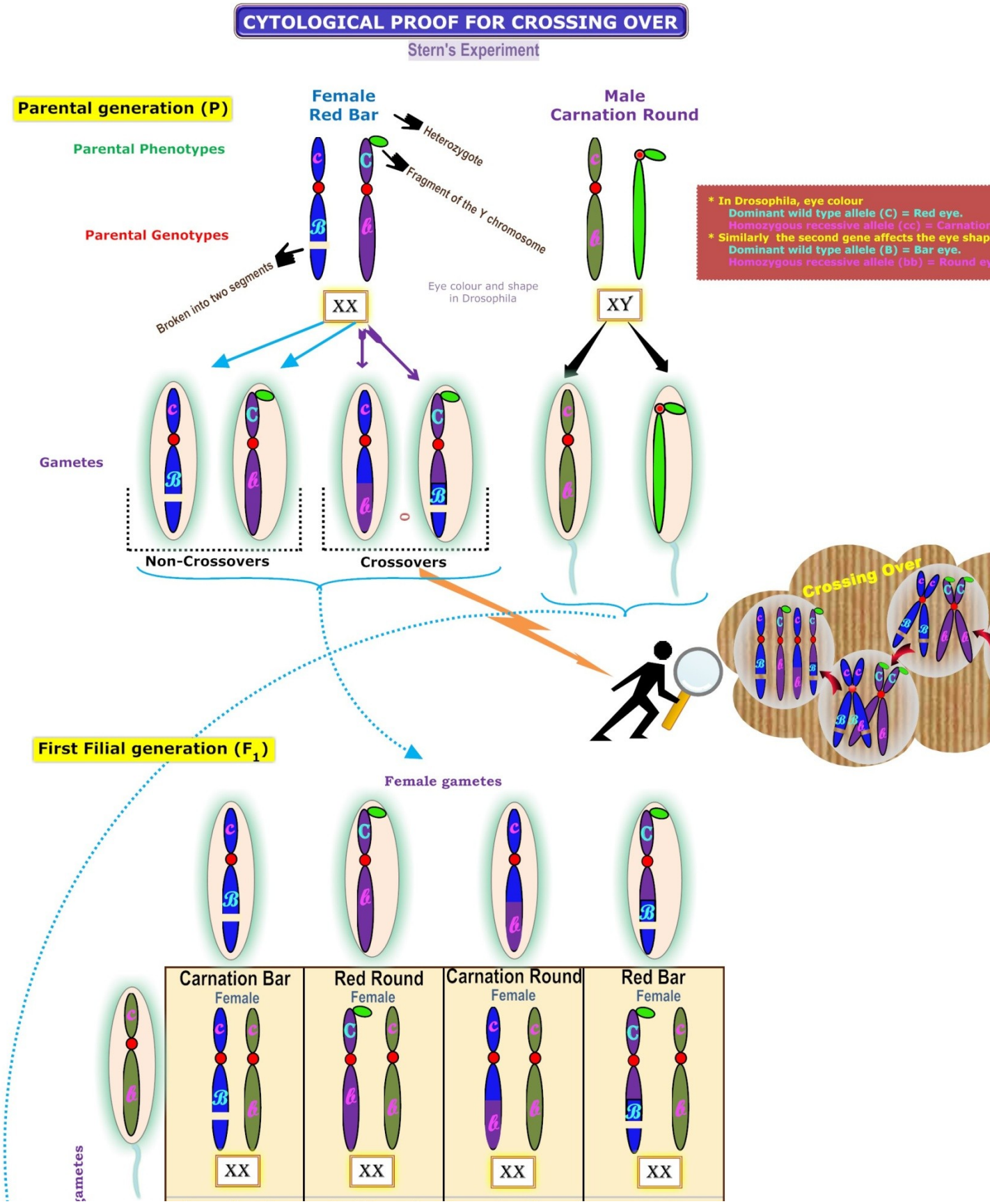
CROSSING OVER

- Complete linkage between genes on the same chromosome is rare.
- The location of a gene on a chromosome is called a *locus (plural loci)*. The loci of the genes on a chromosome are arranged in a linear sequence.
- *Crossing over* is the exchange of genetic material between homologous segments of non sister chromatids of homologous chromosomes that occurs during meiosis and contributes to genetic variability.
- *The important features of the concept of crossing over are as follows,*
    - The two alleles of a gene in a heterozygote occupy corresponding positions in the homologous chromosomes.
    - Crossing over involves the breakage of each of the two homologous chromosomes and the exchange of parts.
    - Crossing over occurs in the post replication tetrad stage of prophase-1 of meiosis during which 4 chromatids are present for each pair of homologous chromosomes.
    - Chromosomes with recombinant combinations of linked genes are formed by the occurrence of crossing over in the region between the two loci.
    - The probability that crossing over will occur between two loci increases with increasing distance between the two loci on the chromosome.
- Crossing over is an exception to Linkage.
- Crossing over and independent assortments are two important mechanisms for the generation of new combinations of genes.
- The first cytological demonstration of genetic crossing over has been given by Stern (working with Drosophila) and H. B. Creighton and B. McClintock (working with maize) in 1931.

STERN'S CLASSICAL EXPIRIMENT

- C. Stern in 1931 by direct cytological evidence, demonstrated that crossing over involves the interchange of parts of homologous chromosomes.
- The female Drosophila carries XX chromosome and the male Drosophila carries one X chromosome and one Y chromosome.

- He made the two X chromosomes of the female are different from each other X chromosomes by treating such flies with X-rays.
- One X chromosome had a part of a Y chromosome attached to one end.
- The other X chromosome has been broken into two unequal segments.
- Thus, both aberrant X chromosomes were cytologically detectable.
- The broken X chromosome contains a recessive gene (c) for carnation eye colour and a dominant gene (B) for bar eye shape (one fragment having both of the genes).
- While its homologue X chromosome contains the dominant gene (C) for red colour and the recessive gene (b) for round eye shape.
- Female flies heterozygous for these two morphologically distinguishable X-chromosomes were produced by crossing. These heterozygous females with trans-configuration were crossed to males with carnation eye colour (c) and round eye shape (b).


CYTOLOGICAL PROOF FOR CROSSING OVER
Stern's Experiment
Parental generation (P)
Female
Red Bar
Male
Carnation Round
Parental Phenotypes
Parental Genotypes
Heterozygote
Fragment of the Y chromosome
Broken into two segments
Eye colour and shape in Drosophila
XX
XY
* In Drosophila, eye colour
Dominant wild type allele (C) = Red eye.
Homozygous recessive allele (cc) = Carnation
* Similarly the second gene affects the eye shap
Dominant wild type allele (B) = Bar eye.
Homozygous recessive allele (bb) = Round ey
Gametes
Non-Crossovers
Crossovers
Crossing Over
First Filial generation (F1)
Female gametes
Carnation Bar
Female
Red Round
Female
Carnation Round
Female
Red Bar
Female
XX
XX
XX
XX

To view "Stern's Classical Experiment Animation"

- Fertilization produced following four kinds of female offspring,
  - Carnation Bar
  - Red Round
  - Carnation Round &
  - Red Bar.
  - The crossing over was indicated phenotypically showed microscopic evidence of exchanges between homologous chromosomes.
  - The physical or cytological basis of crossing over was thus established

CREIGHTON AND McCLINTOCK'S - LINKAGE IN MAIZE

- Creighton and McClintock worked with a strain of maize and developed a strain with a knob on one end and extra (translocated) piece of chromosome at the other end of the 9thchromosome .
- This knobbed chromosome was thus clearly different from its normal homologue.
- This knobbed chromosome had one dominant gene for coloured kernel (C) allele and the another gene for recessive waxy texture endosperm (wx) allele.
- This strain was crossed with a plant having normal chromosome with colourless (c) and starchy (Wx) phenotype.
- When the off spring examined, they found crossing over occurrence by visible cytological observations causing the knob to become associated with an otherwise normal chromosome and the extra piece of chromosome to be associated with a knobless chromosome.

EVENTS OF CROSSING OVER

- Crossing over occurs during Meiosis of Gametogenesis.
  - During Zygotene stage of Prophase - I of Meiosis, the homologous chromosomes (genetically identical chromosomes) move towards each other. This phenomenon of pairing of homologous chromosomes is called *Synapsis*.
  - Each homologous chromosome of a bivalent split longitudinally and form two identical sister chromatids and results in four chromosomes. This stage is called *tetrad stage*.
  - Crossing over involves the breakage and exchange of parts between two non-sister chromatids of a homologous pair of chromosomes. This produces an X-like structure at the point of exchange of the chromatid segments. This structure is called *Chiasma* (plural chaismata).
  - After the completion of crossing over, the non-sister chromatids start to repel each other. They separate from each other from the centromere towards chiasma and to the end of tetrad. The separation is called *Terminilisation*. Due to this terminilisation the homologous chromosomes are separated.
  - Each event of crossing over produces two recombinant chromatids called as *crossover chromatids* and two *non crossover chromatids* (original chromosomes).

KINDS OF CROSSING OVER

Single crossing over

- Only one chiasma is formed at one point of the chromosome pair.
- It produces two non-crossover chromatids and two cross over chromatids .

Double crossing over

- Crossing over occurs at two points between any two given points in the same chromosome pair.
- Two chiasmata are formed.
- The chiasmata may be formed between the same chromatids or between different chromatids.
    - Two-strand double crossover occurs when both crossovers involve the same two chromatids.
    - Three-strand double crossovers are those in which the second cross over involves one of the same two chromatids as the first crossover plus one different chromatids
    - Four-strand double crossovers occur when the second crossover involves the two chromatids not involved in the first crossover.

Multiple crossing over

Crossing over occurs at three, four, or more points between any two given points in the same chromosome pair, they are called as triple, quadruple or multiple crossing over.

FREQUENCY OR PERCENTAGE OF CROSSING OVER

- The percentage of crossing over between two genes depends upon the number of crossovers between them.
- The maximum frequency of recombination that can result from crossing-over between linked genes is 50 per cent.

FACTORS AFFECTING CROSSING OVER

- High temperature and exposure to radiation rays such as x-rays increase the frequency of crossing over.
- As the age advances the frequency of crossing over decreases.
- Some mutation decreases the frequency.
- Crossing over is less frequent near centromeres and the tips of the chromosomes.
- Inversion of chromosome segments suppresses the crossing over.
    - A rearrangement of linear array of genes on chromosome in such a way that their order in the chromosome is reversed is called Inversion.
- Crossing over at point reduces the chances of another crossing over in adjacent regions. In other words chiasma formation at one point prevents the chiasma formation in the vicinity. This phenomenon is called *Interference* .
- Certain chemicals and radiomimetic substances have been found to increase somatic crossing over.
    - E.g. Ethylmethane-sulphonate
- Some chemicals have been found to decrease crossing over.
    - E.g. Colchicine, Selenium in its excess amount.

SIGNIFICANCE OF CROSSING OVER

- Crossing over produces new combination of genes often leading to genetic variation, which is the raw material for evolution.
- Crossing over clearly provides direct evidence for linear arrangement of linked genes in chromosomes .
- The frequency of crossing over is the basis for constructing chromosome (linkage) maps.

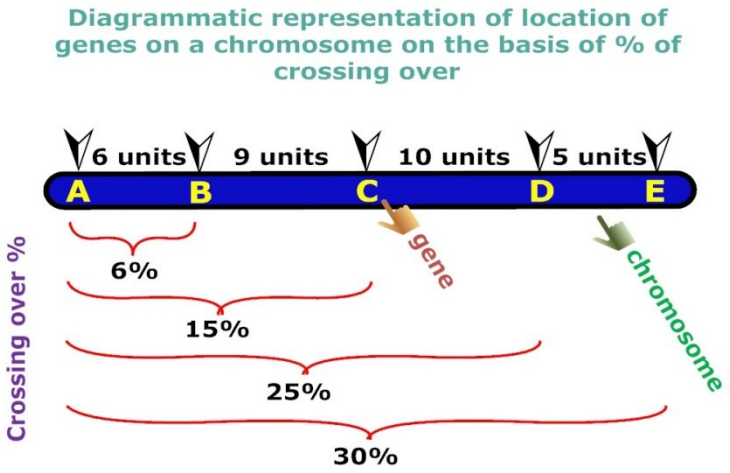
CHROMOSOME MAPPING

- "Gene mapping" refers to the mapping of genes to specific locations on chromosomes.
- There are two types of gene mapping:
    1. Genetic / Linkage Mapping - using linkage analysis to determine the relative position between two genes on a chromosome.
    2. Physical / Cytological Mapping - using all available molecular biology techniques to examine DNA molecules directly to determine the absolute position of a gene on a chromosome.
- The first chromosome maps were made in 1913 by A.H. Sturtevant.
- Drosophila is the earliest material used by the scientists, for constructing maps.

GENETIC MAP / LINKAGE MAP

- Each gene has definite order and location in a linkage group or chromosome.
- The percentage or frequency of crossing over appears to be directly proportional to physical distance between two given genes. So the genetic maps are also referred to as cross over map .
- Linkage map is a diagrammatic graphical representation of relative distances between linked genes in a chromosome.
- The percentage of crossing over is calculated by test crosses.
- If the percentage of crossing over between two linked genes is 1 per cent (yields 1 per cent recombinant chromosome or gametes), the map distance between these genes is one unit of map distance, which is known *Map unit, Morgan unit or Centimorgan (cM).*
    - *Examples*
        - If a F_1 hybrid having the genotype (Ab)(aB) produces 8% of “AB” and 8% of “ab” cross over gametes, then the distance between “A” and “B” is estimated to be 16 Map units or Morgan unit or Centimorgan.
        - If the map distance between the gene loci “C” and “D” is 10 centimorgan, then 10% of gametes of genotype (CD)(cd) should be cross over types, i.e., 5% “Cd” and 5% “cD”.
- After determining the relative distances between the genes of a linkage group, it becomes easy to place genes in their proper linear order.
- *For example,* five genes A, B, C, D and E are to be plotted on a chromosome. All the gene combination crossing over percentages are to be found. The two genes which have highest percentage of crossing over should be placed on each end.

    - In this example, genes A and E have the highest percentage of 30% of crossing over; it means that these should be placed at the maximum distance.
    - The gene A can be taken as a starting point in the chromosome and can be represented by 0.
    - The gene A and B exhibit 6% crossing over, the gene B can be plotted on the chromosome at a distance of 6 units.
    - The gene C shows 15% crossing over with gene A and 9% crossing over with gene B, it can be plotted on the chromosome at a distance of 9 units from gene B.
    - The gene D shows 25% crossing over with gene A and 10% crossing over with gene C, it can be plotted on the chromosome at a distance of 10 units from gene C.
    - The gene E shows 30% crossing over with gene A and 5% crossing over with gene D, it can be plotted on the chromosome at a distance of 5 units from gene D.



FACTORS AFFECTING THE MAPPING

- Genetic map can be constructed only with the help of crossing over percentage. The crossing over percentage is highly modified by Interference and Coincidence.

Interference

- One chiasma formation reduces the probability of another chiasma formation at other points immediately adjacent to the part of the chromosome . This is called Interference.
- The interference is inversely proportional to the crossing over percentage.

Coincidence

- The coincidence is an inverse measure of interference.
- It is a ratio between actual number of double cross overs and the expected number of double cross overs
- If the actual number of double cross overs is zero, then coincidence is zero and interference is complete.
- If the actual number of double cross over is the same as the expected number, coincidence is one and interference is nil .
- When, interference decreases, coincidence increases.
- Coincidence + Interference = 1.0
- So coincidence ranges from 0 to 1.

MODULE-14: CHANGE IN STRUCTURE OF GENETICS MATERIAL

Learning objectives

After completing this module, the learner should be able to:

- understand the term mutation and different causes for mutation

- state the types of mutation and the advantages and disadvantages of mutation
- explain the different DNA repair mechanisms

MUTATION

- Mutations are sudden heritable changes in a gene or chromosome, involving qualitative or quantitative alterations in the genetic material itself.
- It produces an alteration in the character under its control.
- The term mutation refers both to the changes in the genetic material and to the processes by which the change occurs.
- The earliest record of point mutations dates back to 1791, when Seth Wright noticed a lamb with exceptionally short legs in his flock of sheep.
- Visualizing the economic significance of this short-legged sheep, he produced a flock of sheep, each of which having short legs, by employing artificial breeding techniques.
- The short legged breed of sheep was known as Ancon breed.
- Hugo de Vries introduced the term "mutation" to describe the heritable phenotypic changes of the evening primrose, *Oenothera lamarckiana*.
- The first scientific study of mutation was started in 1910, when Morgan started his work on fruitfly, *Drosophila melanogaster* and reported white eyed male individuals among red eyed male individuals.
- The discovery of white eyed mutants in Drosophila is followed by an extensive search of other mutants of Drosophila by Morgan and his co-workers and other geneticists.
- Consequently about 500 mutants of Drosophila have been reported by geneticists all over the world.
- Later on, several cases of mutations have been reported in a variety of micro-organisms, plants and animals.

Mutant

- The rate of mutation is increased either by using physical or chemical agents and this process is called as *Mutagenesis* .
- An agent that has the ability to produce mutation is called the *Mutagen* .
- The mutability of some genes is influenced by other genes called *Mutator genes* .

Mutation classification

- Mutations have been classified variously by different geneticsts, each of which adopted different criteria. (Click here to view several ways of classifcation of mutation)
- There are two kinds of change in structure of Genetic material, *Chromosomal and Gene / Point Mutations*. (Click here for detailed Change in structure of Genetic Material)

Beneficial Mutations

- Most mutations make the organism less efficient and are thus disadvantageous.
- But mutations are invaluable for the process of evolution.
- Plant breeders have reported that induced mutation can be used for improving grains and vegetables.
- Barley mutant, for example have been obtained that provide increased yield.

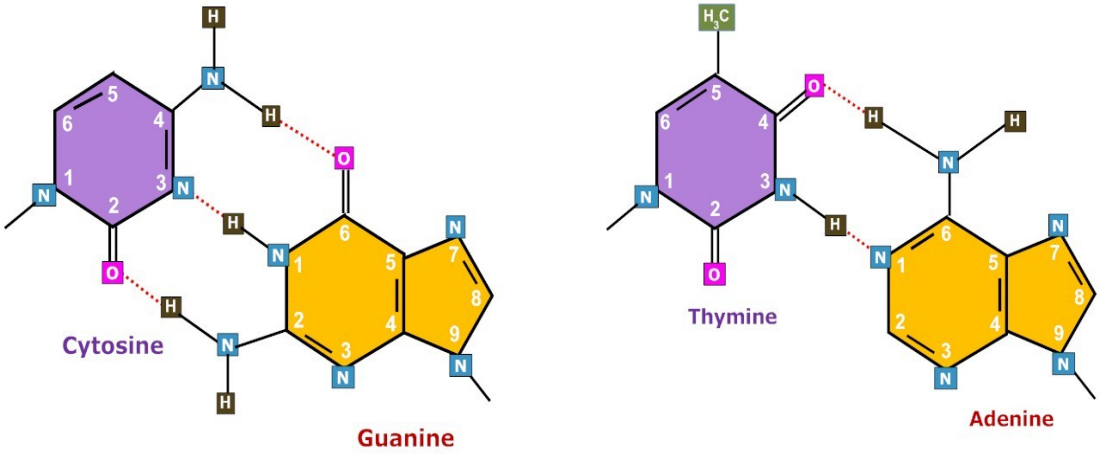
MUTATION FREQUENCY

- Although mutation is necessary to provide the genetic variability required for the evolutionary adaptability of species to environmental changes, most mutations are deleterious.
- Each gene probability has its own characteristic mutational behaviour.
- Some genes undergo mutations more frequently than others in the same organism.
- A wide range of mutation rates exists among genes that are considered stable.
- The mutation rate per gene in bacteria is on the order of 1 in 100,000 to 1 in 10 million per cell generation.
- For fruit flies the average mutation rate in a particular gene is 1 in 100,000 gametes.
- Genes associated with human traits such as intestinal polyposis and muscular dystrophy have been estimated to mutate once in 10^4 to 10^5 people.

GENETIC MATERIAL

DNA

- DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms.
- The information in DNA is stored as a code made up of four chemical bases: **A**denine (A), **G**uanine (G), **C**ytosine (C), and **T**hymine (T).
- DNA bases pair up with each other, A with T and C with G, to form units called base pairs.
- DNA is organized into long structures called chromosomes.



FORWARD MUTATION

- The mutation of a “wild type” gene to a form that results in mutant phenotype is usually referred to a “ Forward mutation ”.

BACKWARD MUTATION

The mutation from a mutant phenotype back to the original wild type phenotype is referred to as *Back mutation, Reverse mutation or Reversion.*

Genetic Suppression

- The effect of a mutation on the phenotype can be reversed, so that the original wild type phenotype is brought back. This reversal may be due to *True Reversion or Suppression*.
- Reversion may occur in two different ways.
- Restoration of the original phenotype may occur by
    - True Reversion
        - The mutation from a mutant phenotype back to the original wild type phenotype is referred as Back Mutation, Reverse Mutation or Reversion.
        - In a true reversion there is a reversal of the original genetic change.
    - Suppression
        - In suppression a change at a different site brings about phenotypic correction of the mutation.
        - In Suppression mutation, the occurrence of a second mutation at a different location in the genome, brings about phenotypic correction or compensation for the first mutation.
        - Suppressor mutations may occur at distinct sites in the same gene as the original mutation or in different genes or even in different chromosomes.
        - Suppression mutations are of two types,
            - Intragenic suppression and
            - Extragenic or Intergenic suppression.
        - In intragenic suppression a mutation in a gene is suppressed by another mutation in the same gene.
        - In intragenic suppression a mutation in a gene is suppressed by another mutation in the in different gene of the same chromosome or even in another chromosomes gene.

Suppressor genes

- Genes which suppress the activity of other mutated genes are called *suppressor genes*.

TISSUE OF ORIGIN

- On the basis of the type of cells in which mutations occur, there are two types of mutations

Somatic Mutation

- Mutations may occur in any cell and at any stage in the cell cycle.
- The immediate effect of the mutation and its ability to produce a phenotypic change are determined by its dominance, the type of the cell in which it occurs and when it happens relative to the life cycle of the organism.

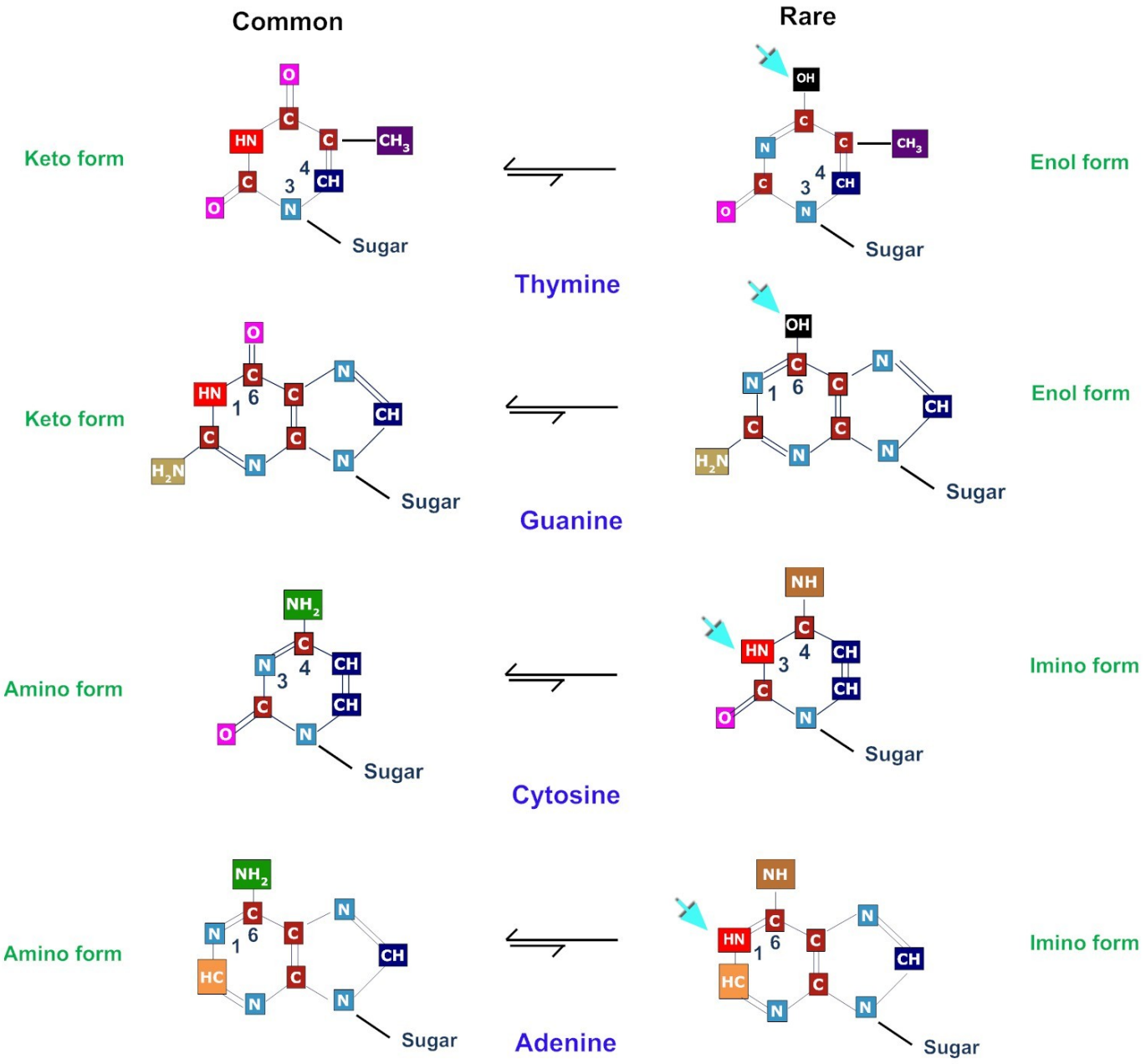
- If the mutation occurs in a somatic cell, the mutant gene will be perpetuated only in somatic cells that descend from the original cell in which the mutation occurred.
- Examples: Delicious apple and the novel orange.
- Through vegetative propagation, they were later propagated as a mutant variety.

Germinal Mutation

- If dominant mutations occur in germ cells, their effects may be expressed immediately in progeny.
- If mutations are recessive, their effects are often obscured in diploids.
- If the mutation arises in a gamete, only a single member of the progeny is likely to have mutant gene.
- If mutations occur in germinal cells, several gametes may receive the mutant gene and thus enhance its potential for perpetuation.

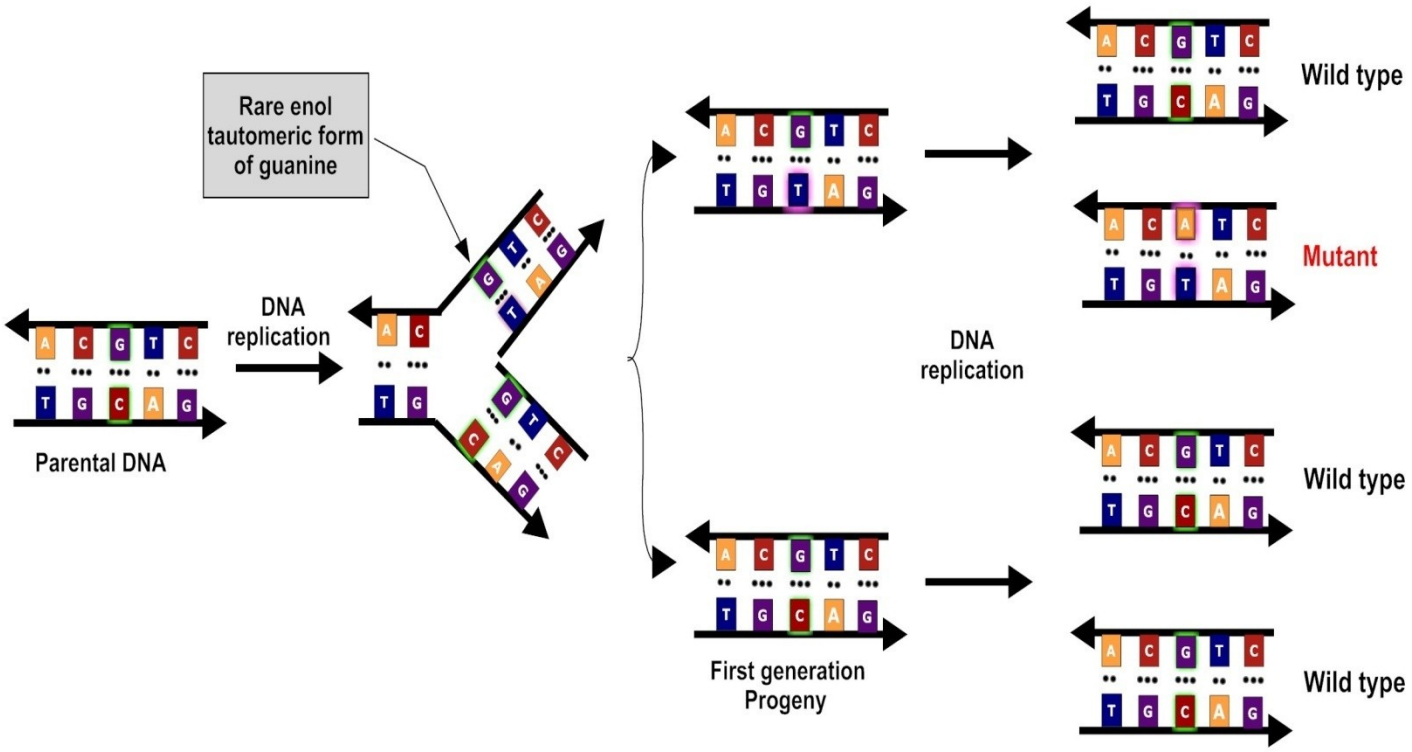
MOLECULAR BASIS OF MUTATION

- The bases in DNA are not static.
- Hydrogen atoms can move from one position in a purine or pyrimidine to another position, for example from an amino group to ring nitrogen.
- Such chemical fluctuation are called *tautomeric shifts*.
- The ability of a molecule to exist in more than one chemical form is called *tautomerism*.
- The common keto forms of *thymine* and *guanine* will always pair with *adenine* and *cytosine*, respectively.
- The common amino forms of *cytosine* and *adenine* will always pair with *guanine* and *thymine*, respectively.
- The more stable keto forms of thymine and guanine and amino forms of adenine and cytosine may infrequently undergo tautomeric shifts to less stable enol and imino forms respectively.
- When the bases are present in their rare enol and imino forms, they can form adenine — cytosine and guanine — thymine base pairs.



TAUTOMERIC SHIFTS

- This will ultimately leads an AT to GC or a GC to AT base pair substitution.



TYPE OF AMINO ACID REPLACEMENT

- Missense Mutation
- Nonsense mutation
- Frameshift mutation
- Silent mutation

MIS - SENSE MUTATION

- Mutations occurring at the first or second nucleotide position of a codon which results in the replacement of one amino acid in a polypeptide chain by another.
    - For example: one of the codons for phenylalanine is UUU.
    - A second base substitution (U --> G) changes it to UGU, the codon for cysteine
- This may results in a change of the activity of the protein.
- This change may be harmful or beneficial.

NONSENSE MUTATION

- Any mutation that changes a codon into a codon that codes for a STOP signal (termination codon) is called a *Nonsense mutation*.
- The three termination codons are UAA, UAG, and UGA.
- *For example* : if the codon UAC (for tyrosine) undergoes a one base substitution (C --> G) it becomes UAG, a termination condon.
  As a result is a premature termination of translation and the protein / polypeptide is shorter than usual and does not contain all the amino acids.
- Such protein / polypeptide are likely to be biologically inactive or nonfunctional.

SILENT MUTATION

- Any gene mutation which does not result in phenotypic expression is called a *Silent Mutation*.
- Silent mutations are of several types.
    - The genetic code is degenerate, (most amino acids are coded for by several alternative codons)
        - Mutation may occur in the third location of the codon, the resulting new codon may still code for the same amino acid.
        - For example both AAG and AAA specify lysine. If the codon AAG undergoes a mutation to AAA the latter codon will still specify lysine. When a mutated triplet codes for the same amino acid, results in no effect on the amino acid sequence of the gene product.
    - The codon change may result in an amino acid substitution, but this amino acid change may not modify the activity of the protein.
    - The mutation may occur in a gene that is no longer functional or whose protein is not essential at the particular stage of testing.
    - Simultaneous presence of suppressor mutations may cause a mutation to become silent. In genetic suppression a second mutation at a different site neutralizes the effects of the first mutation.

CAUSES OF MUTATION

- Based on the agency involved, there are two types of mutations
    - Spontaneous
    - Induced
- Mutagenesis is a process by which the genetic information of an organism is changed in a stable manner, either in nature or experimentally by the use of chemicals or radiation.

SPONTANEOUS MUTATION

- Mutations which occur as a result of natural processes in cells are called spontaneous mutations.

INDUCED MUTATION

- A mutagen is a natural or man-made agent (physical or chemical) which can alter the structure or sequence of DNA.
- Induced mutations increase the mutation rate over the spontaneous rate.

MUTAGENS

- Mutagens can be classified into two groups
    - Physical and
    - Chemical

PHYSICAL MUTAGENS

Radiation induced mutation

- That portion of the electromagnetic spectrum containing wavelengths that are shorter and of higher energy than visible light (wavelengths below about 100 nm) can be subdivided into
    - Ionizing radiations (X-rays, protons, neutrons, and alpha, beta and gamma rays) and

- Non-ionizing radiations (UV light).

Ionizing radiation

- Ionizing radiations induce point mutations as well as various kinds of gross changes in chromosome structure such as deletions, duplications, inversions and translocations.
- The ionizing radiations such as X-rays (about 0.1 to 1 nm) are of high energy and can penetrate living tissues.
- In the process of penetrating matter, these high energy rays collide with atoms and cause release of electrons, leaving positively charged ions or radicals.
- These ions, in turn, collide with other molecules, causing the release of further electrons.
- The net result is that a "core" of ions is formed along the track of each high energy ray as it passes through matter or living tissues.
- This process of ionization is produced by X-rays, protons, neutrons, and alpha, beta and gamma rays released by radio active isotopes of the elements such as ^{32}P, ^{35}S or Cobalt-90 etc.

Non - ionizing radiation

- Ultra violet rays, having lower energy, penetrate only the surface layer of cells in higher animals and do not induce ionization.
- UV lights dissipate their energy to atoms that they encounter, raising the electrons in the outer orbital to higher energy levels, a state referred to as *excitation*.
- Molecules containing atoms in either ionic forms or excited states are chemically more reactive than those containing atoms in their normal stable states.
- The increased reactivity of atoms present in DNA molecules is the basis of mutagenic effects of UV and ionizing radiations.
- Ultra violet rays are readily absorbed by purines and pyrimidines in DNA, which then enter a more *reactive or excited state*.
- The maximum absorption of UV by DNA is at wavelength of 260 nm.
- Maximum mutagenicity also occurs at 260 nm, suggesting that the UV induced mutation process is mediated directly by the absorption of UV by purines and pyrimidines.
- UV absorption by pyrimidines results in pyrimidine hydrates (example : Cytosine hydrate) and pyrimidine dimers (example: thymine dimer) which cause mispairing of bases and blockage of DNA replication, respectively.

CHEMICAL MUTAGENS

- The first chemical mutagen discovered was mustard gas (sulfur mustard).
- Chemical mutagens can be divided in to five main classes
  - Those that are mutagenic only to replicating DNA such as acridine dyes (which bind to DNA and increase the probability of mistakes during DNA replication) and base analogs (which are incorporated into DNA instead of normal bases).
  - Those that are mutagenic to both replicating and non-replicating DNA, such as alkylating agents (that transfer alkyl groups such as CH_3-, CH_3CH_2- etc to DNA) and deaminating agents (nitrous acid).

Base analogs

- The mutagenic base analogs have similar structure to normal bases and are thus metabolized and incorporated in to DNA during replication.
- Example:

5 Bromo Uracil (5 - BU)

- The pyrimidine 5-bromo uracil is a thymine analog.
- The base 2-aminopurine is a purine analog.
- In the more stable keto form, 5 bromo uracil mimics the pairing behavior of the thymine that it replaces, pairing with adenine.
- After a tautomeric shift to its enol form, rare ionized form of 5 bromo uracil pairs with guanine.
- It can thus cause GC to AT transition and AT to GC transition.

2 Amino-P(2 - AP)

- Another analog widely used in research is 2-amino-purine (2-AP), which is an analog of adenine that can pair with thymine.
- But in its protonated state it can pair with cytosine

Acridine Dyes

- Dyes such as proflavin, acridine orange and a series of compounds called ICR170, ICR191 etc are powerful mutagens that induce frameshift mutations.
- The positively charged acridines intercalate or sandwich themselves between the stalked base pairs in DNA and increase the rigidity and cause slight “kinks” in the DNA double helix.
- When such DNA replicate, additions or deletions of base pairs occur causing frameshift mutations.

Alkylating agents

- They cause transfer of methyl or ethyl groups to bases changing their base pairing potential, causing transitions. They also induce transversions, frameshifts and chromosomal aberrations.
- Example nitrogen and sulfur mustards, methyl and ethyl methane sulfonate (MMS and EMS), nitrosoguanidine (NTG) have several effects on DNA.

Deaminating agents

Nitrous acid (HNO_2)

- Causes mutation by the oxidative deamination of adenine, guanine and cytosine which contain amino groups.
- Adenine is deaminated to hypoxanthine, which base pairs with cytosine rather than thymine.
- This results in AT to GC transition.
- Deamination of guanine produces xanthine which pairs with cytosine just like guanine. So it is not directly mutagenic.
- Deamination of cytosine results in uracil which pairs with adenine and thus causes GC to AT transition.
- Therefore nitrous acid can cause both GC to AT and AT to GC transitions.

Miscellaneous

Hydroxylating agents

- Example : Hydroxylamine (NH_2OH). It induces only GC to AT transition.

- It hydroxylates amino group of cytosine to from hydroxylamine cytosine which can base pair with adenine causing GC to AT transition.

CIB TECHNIQUE - DROSOPHILA

Attached X chromosome method detecting sex-linked visible mutation

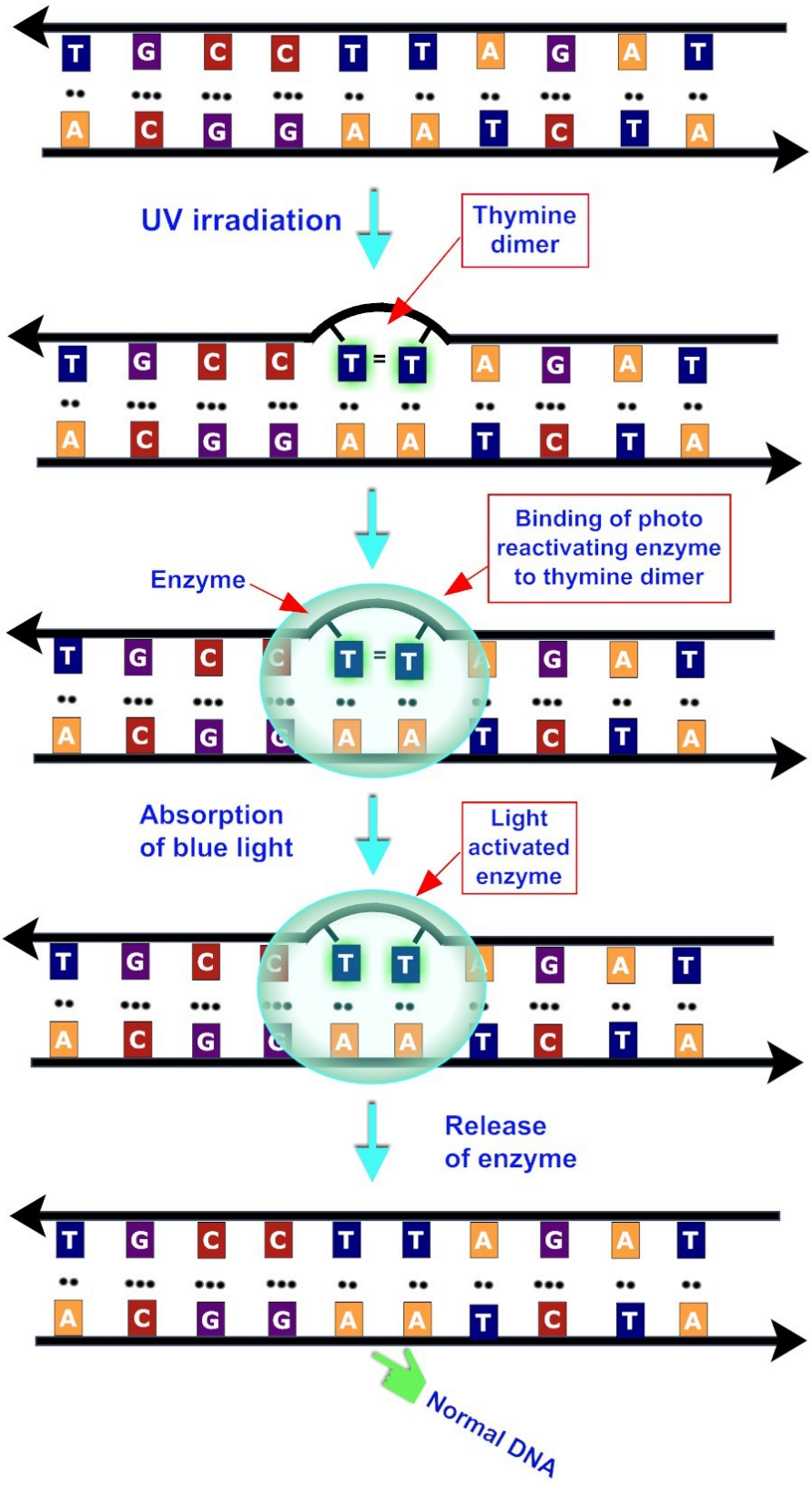
- In this method females with attached X-chromosomes are used.
- Attached X - chromosomes undergo compulsory non-disjunction (failure of homologous chromosome to separate during anaphase) since the two X - chromosomes are joined to a single centromere.
- The mutagen treated males are crossed with XXY females.
- In this case if any mutation with visible effect has occurred, that will be expressed in all the viable the male progeny.
- In such attached-X mating, the male progeny receive their X chromosome from their male parent rather than from their female parent as in a normal mating.
- If the male parent is treated with a mutagenic agent such as X - rays, the increased frequency of recessive visible mutations can be easily assessed by screening the male progeny of attached-X mating.
- X rays and most other forms of ionising radiation are quantified in roentgen units (r units), which are measured in terms of the number of ionizations per unit volume under a standard set of conditions.
- More specifically one r unit is the quantity of ionising radiations that produces one electrostatic unit of charge in a 1 - cm^3 volume.
- The same dosage of irradiation may be obtained by a low intensity of irradiation over a long period of time or high intensity of irradiation for a short period of time.
- This is important because in most studies the frequency of induced point mutations is directly proportional to the dosage of irradiation.

DNA REPAIR MECHANISMS

- Mechanisms for the repair of damaged DNA are probably universal.
- For example: *E. coli* possesses at least three different mechanisms for the repair of DNA containing thymine dimers.
    - Photoreactivation
    - Excision repair
    - Post replication recombination repair

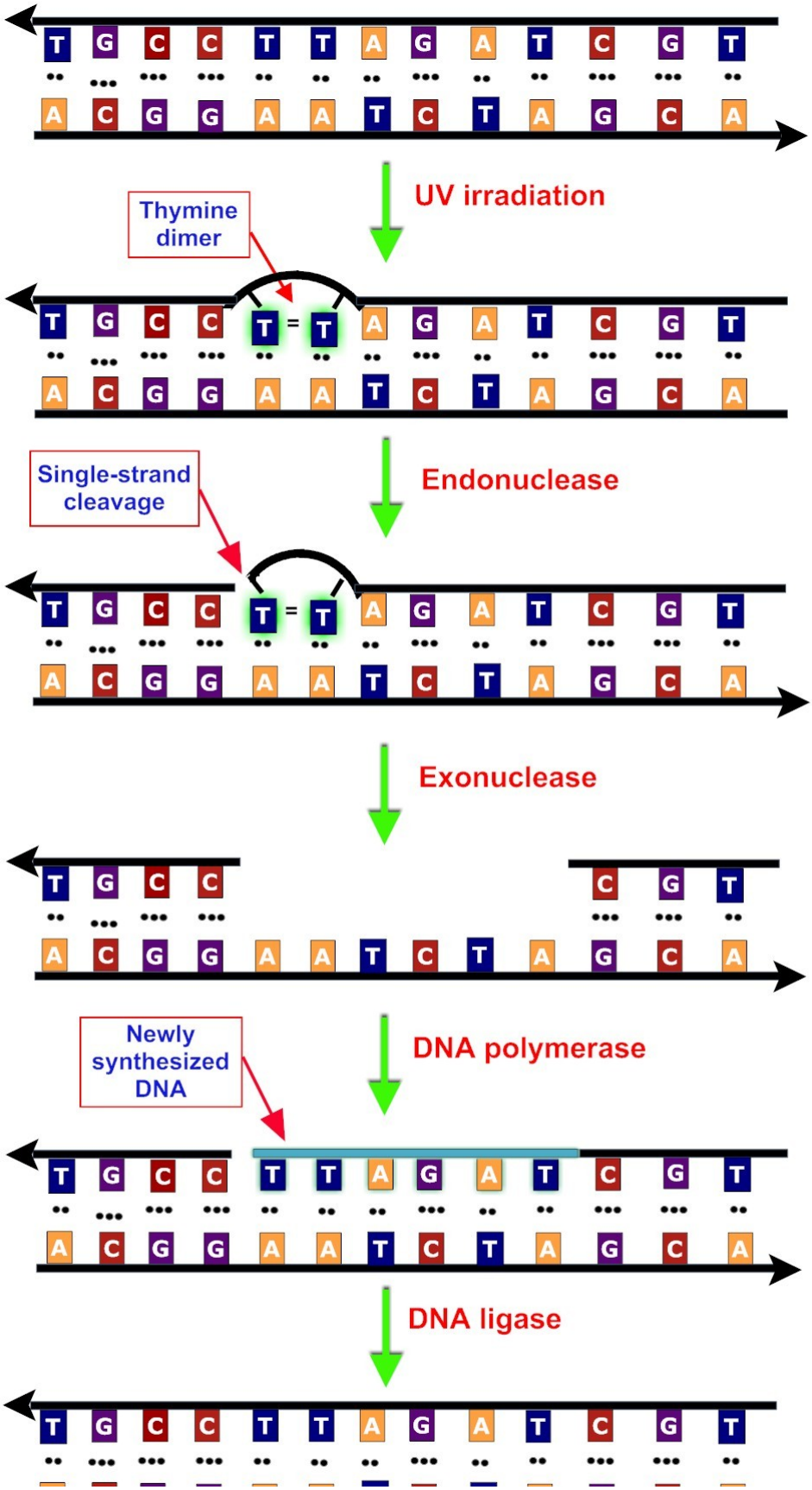
PHOTOREACTIVATION

- It involves an enzyme that splits thymine dimers directly without the removal of any nucleotides.
- This enzyme will bind to thymine dimers in DNA in the dark, but it cannot catalyse the cleavage of the bonds joining the thymine molecules without energy derived from visible light specifically light within the blue region of the spectrum.
- The enzyme is also active on cytosine dimmers and cytosine-thymine dimmers.
- Thus UV light is used as an experimental mutagen, the treatment is usually carried out in the dark to maximise the mutation frequency.


UV irradiation
Thymine dimer
Binding of photo reactivating enzyme to thymine dimer
Enzyme
Absorption of blue light
Light activated enzyme
Release of enzyme
Normal DNA

EXCISION REPAIR (DARK REPAIR)

- Involves sequence of enzyme catalysed steps in which the thymine dimers are removed from the DNA molecule and a new segment of DNA is synthesized.
- Excision repair occurs both in darkness and in the presence of blue light.
- First, an endonuclease recognizes the thymine dimer and cleaves the phosphodiester bond near the site of damage.
- Then an exonuclease, probably the 5’ 3 exonuclease activity of DNA polymerase-I removes a segment of the strand adjacent to the endonuclease cut, including the dimer.
- DNA polymerase-I then fills the gap using the complementary strand as the template.
- DNA ligase then catalyses the formation of phosphodiester linkage between adjacent nucleotides.

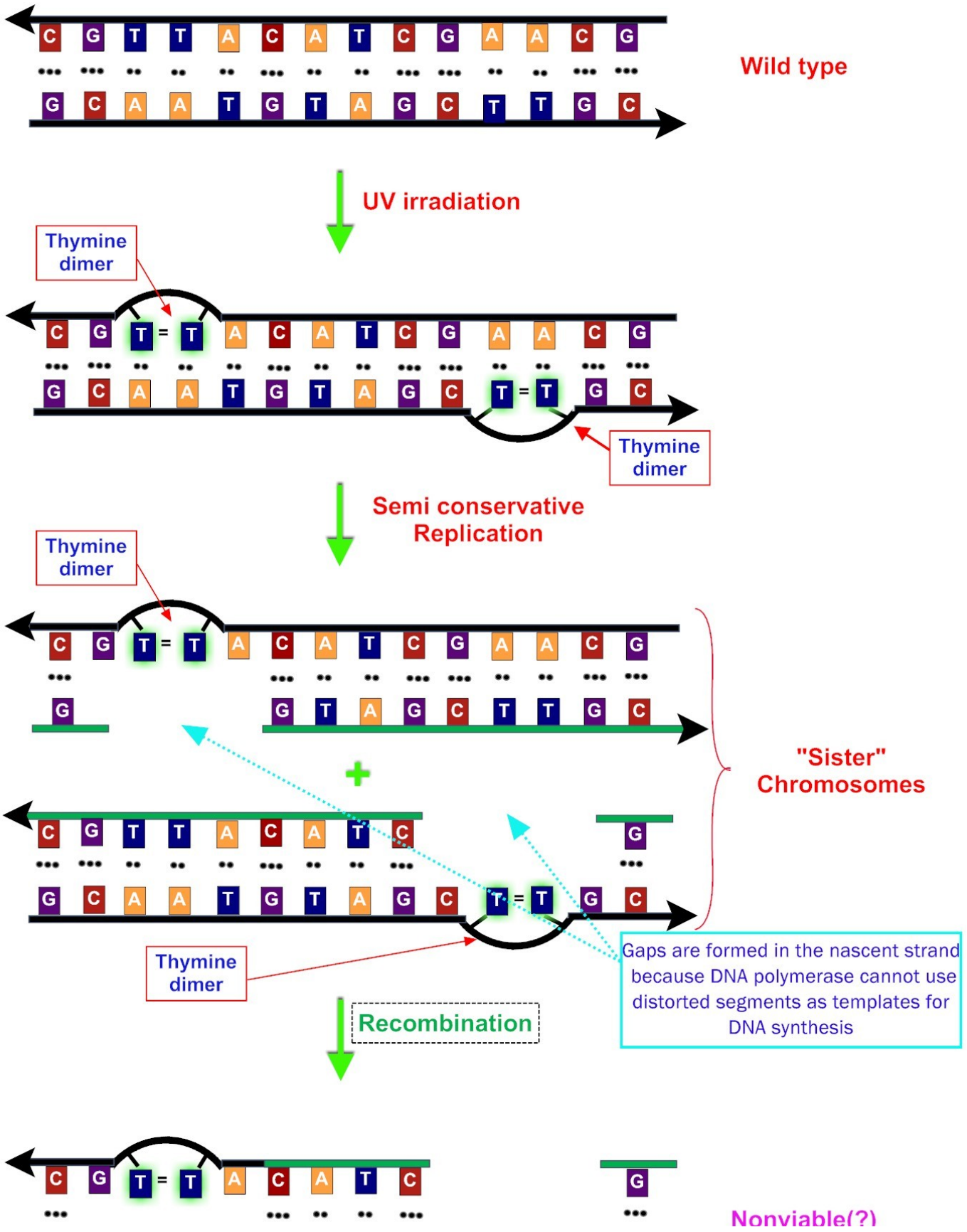

UV irradiation
Thymine dimer
Endonuclease
Single-strand cleavage
Exonuclease
DNA polymerase
Newly synthesized DNA
DNA ligase

Repair by Uracil DNA glycosylase

- Uracil is produced in the DNA by deamination of cytosine (by nitrous acid).
- The enzyme uracil-DNA glycosylase removes uracil from DNA creating an AP site (apyrimidinic / apurinic site).
- Such AP sites undergo excision repair mechanism described earlier.

POST REPLICATION RECOMBINATION REPAIR

- This type of dark repair involves both replication and recombination.
- When DNA molecules containing thymine dimers are replicated, gaps are formed in the nascent strand because DNA polymerase cannot use distorted segments as templates for DNA synthesis.
- This results in progeny double helices with thymine dimers in one strand and gaps in the complementary strand.
- If these two sister chromosomes recombine, dimers and gaps end up in one chromosome and the intact, undamaged segments end up in the other chromosome, the later will be functional and produce a viable cell.


Wild type
UV irradiation
Thymine dimer
Thymine dimer
Semi conservative Replication
Thymine dimer
"Sister" Chromosomes
Thymine dimer
Gaps are formed in the nascent strand because DNA polymerase cannot use distorted segments as templates for DNA synthesis
Recombination
Nonviable(?)

CORRELATION BETWEEN MUTAGENICITY AND CARCINOGENICITY

- For many years it has been recognised that most of the strongly mutagenic agents, such as ionizing radiations, UV light and chemicals like those discussed earlier are carcinogenic.
- Somatic mutations can cause cancer.
- Mutation in a gene involved in the control of cell division can cause loss of normal control of cell division.

BENEFICIAL MUTATIONS

- Most mutations make the organism less efficient and are thus disadvantageous.
- But mutations are invaluable for the process of evolution.
- Plant breeders have reported that induced mutation can be used for improving grains and vegetables.
- Barley mutant, for example have been obtained that provide increased yield.

MODULE-15: GENE OR POINT MUTATION

Learning objectives

After completing this module, the learner should be able to:

- understand the term point mutations
- distinguish between base-pair substitutions and base-pair insertions

POINT / GENE MUTATON

- A *gene or point mutation* is defined as any permanent change in a DNA sequence that makes up a gene.
- Gene mutations occur in two ways,
  - Inherited from a parent or
  - Acquired during its lifetime.
- Mutation can result in several different types of change in DNA sequences; these can either have
  - no effect,
  - alter the product of a gene,
  - prevent the gene from functioning, or
  - cause lethal.

KINDS OF GENE MUTATION

Base pair (nucleotide pair) substitutions

Transitions

- Mutations resulting from tautomeric shifts in the bases of DNA involve the replacement of a purine in one strand of DNA with the other purine (A <—> G) and the replacement of a pyrimidine in the complementary strand with the other pyrimidine (C <—> T). Such base pair substitutions are called *transitions*.

- Example: Four different transitions are possible

A•T —> G•C

G•C —> A•T

T•A —> C•G

C•G —> T•A

Transversions

- Purine replaced by a pyrimidine, or pyrimidine replaced by a purine are called *transversions*.
- Example: Eight different transversions are possible.

A•T —> C•G

A•T —> T•A

G•C —> T•A

G•C —> C•G

C•G —> A•T

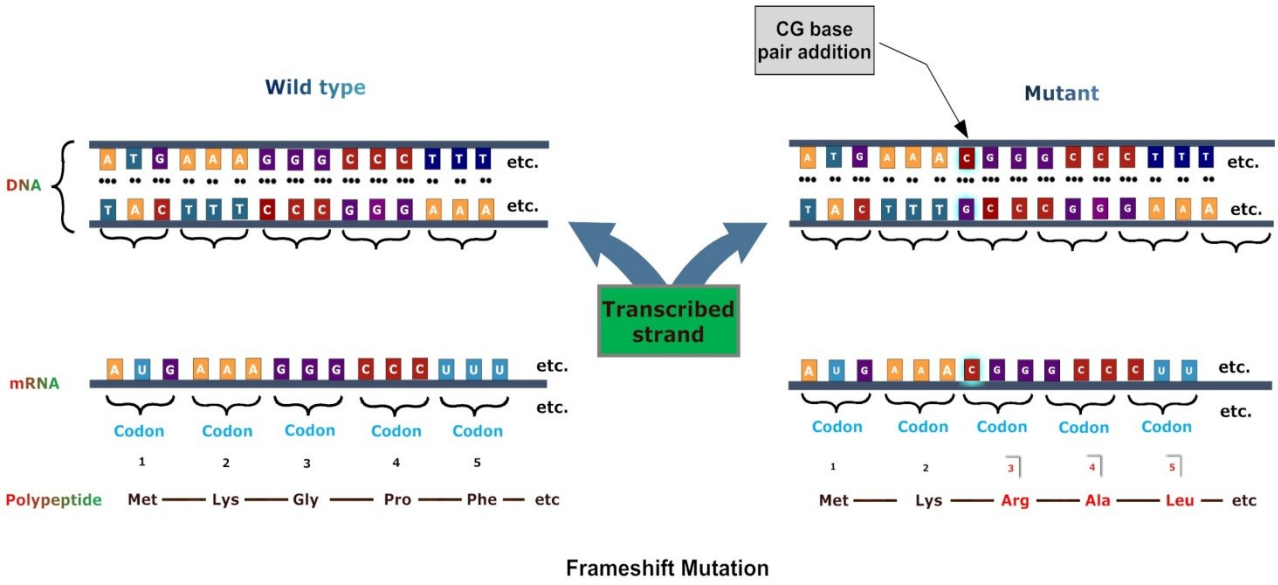
C•G —> G•C

T•A —> G•C

T•A —> A•T

Frameshift mutations

- In this type of mutation, one or a few base pairs are inserted or deleted.
- Base-pair additions and deletions are collectively referred to as *frame-shift mutations,* because they alter the reading frame of all base pair triplets in the gene distal to the mutation.



Frameshift Mutation

MODULE-16: CHROMOSOMAL ABERRATIONS - NUMBER

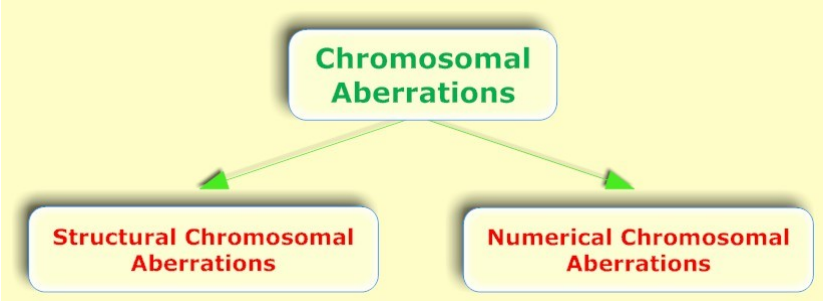
Learning objectives

After completing this module, the learner should be able to:

- describe the type of chromosomal number alterations
- understand the mechanisms that give rise to numerical chromosomal aberration

CHROMOSOMAL ABERRATIONS

- Different cells of the same body and different individuals of the same species have, as a rule, specific number of chromosomes in pairs (2n).
- But in rare instances, variations in the chromosome number, structure, size or gene arrangement of chromosome called ' *chromosomal aberrations* ' can occur during cell division.
- Such variations may produce phenotypic changes, changes in the expected genetic ratios or changes in the linkage relationships of certain genes.



VARIATIONS IN THE CHROMOSOME NUMBER

- Change in the number of chromosomes is called Ploidy.

- It can be broadly classified into two,
  - Euploidy (changes in *whole* chromosome sets)
  - Aneuploidy (changes in *parts* of chromosome sets)

EUPLOIDY

- Changes in the number of chromosomes involving entire set of chromosomes; n= basic number.
- Euploidy are three types viz;
  - Monoploidy or haploidy
  - Diploidy (normal number of chromosome sets in most of the animals and plants)
  - Polyploidy

MONOPLOIDY / HAPLOIDY

- Individual having one chromosome set (*n*) of genome per nucleus is called monoploidy.
- In most cases the gametes will be monoploid with *n* number of chromosomes.
- During fertilization the parental chromosomes unite together by the fusion of gametes forming diploid number (2n) of chromosomes.
- In diploid taxa, an individual organism with only one chromosome set(*n*) is called a monoploid whereas species in which all individual with normally only one chromosome set are haploid (also *n*).
- Male bees, wasps, and ants are monoploid.

POLYPLOIDY

- Polyploidy is a general name for the condition where more than two sets of chromosomes are present.
  - *Example :* Triploidy (3n); Tetraploidy (4n); Pentaploidy (5n); Hexaploidy (6n) etc., in somatic cells.
- Polyploidy is classified into the following types,
  - Autopolyploidy
  - Allopolyploidy

AUTOPOLYPLOIDY

- Autopolyploidy refers to polyploids arising from duplication of the chromosomes sets of a single species.
- Generation of Autopolyploids
  - Union of two diploid (unreduced) gametes - Tetraploid
  - Somatic doubling (tetraploid)
  - Union of a haploid and a diploid gamete (triploid)
  - A cross between a tetraploid and a diploid parent (triploid)
  - Fertilization of an egg by two sperms (triploid)
  - Autoploy ploidy can also be induced artificilly with colchicine or similar drugs.
- All autopolyploids with odd number of sets of chromosomes (3n, 5n, 7n) are sterile due to abnormal meiosis.

- Organisms with even numbered sets of abnormalities (4n, 6n etc) can have equal distribution of chromosomes during meiosis and may form some normal gametes.
- There are a few examples of polyploidy in animals. It is rare probably because it interferes with sex-determination.
- Examples are found in flatworms, leeches, and brine shrimps. In these animals, reproduction is by parthenogenesis.
- Polyploidy is much more common in plants.
    - Examples are wheat (6x), alfalfa (4x), coffee (4x), peanuts (4x), strawberries (8x), and cotton (4x). Ornamentals such as roses, chrysanthemums, and tulips are also polyploid.
    - Some of the examples of autotriploids are seedless watermelon, blue berries, grapes, banana etc.
    - Potato is a natural auto tetrapolyploid (4n).
- Polyploid plants are often larger and have larger component parts than their diploid relatives.

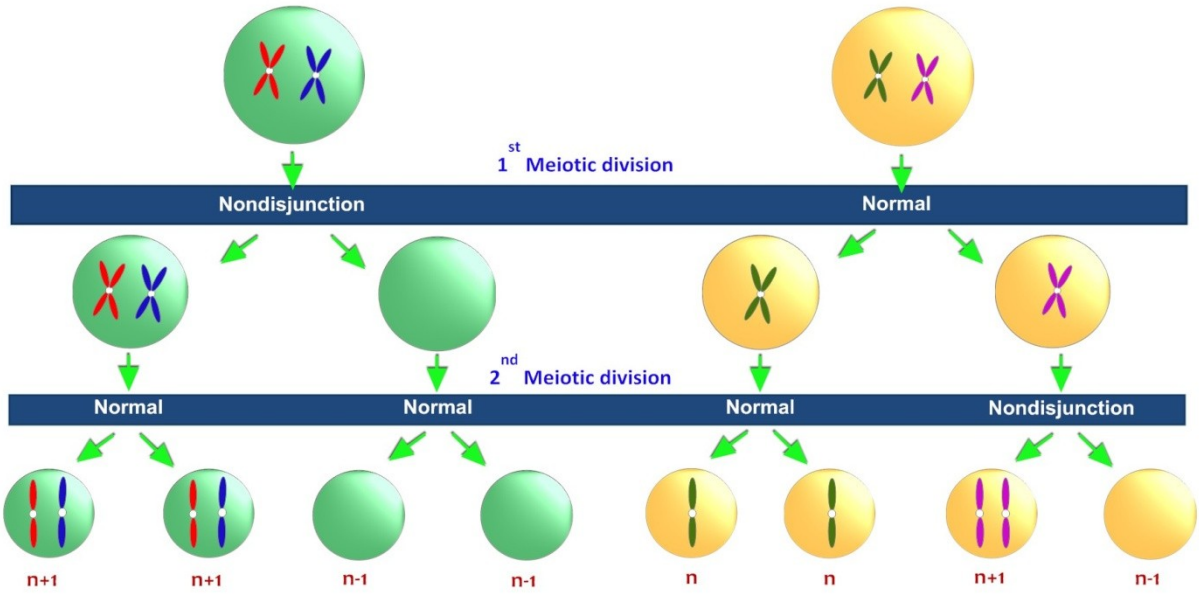
ALLOPOLYPLOIDY

- Allopolyploids are polyploids resulted from the multiplication of chromosome sets of closely related species; however, the different chromosome sets are only partly homologous (homeologous), not fully homologous, as they are in autopolyploids.
- The allopolyploidy does not occur naturally in the nature.
- However, some cytologists have produce allopolyploidy in certain plants by selective breeding methods.
- The Russian cytologist, G. D. Karpechenko (1928) first synthesized an allotetraploid genus called Rhaphanobrassica from the artificial crosses between vegetables belonging to different genera, the radish (Raphanus satirum, 20 = 18) and the cabbage (Brassica oleracea, 2n= 18) in an attempt to produce a hybrid plant with edible portions of the root and the shoot of cabbage.
- However, this hybrid was functionally sterile because the 9 chromosomes from the cabbage parent were different from the radish chromosomes such that pairs did not synapse and segregate normally.
- Fertile amphidiploid arose from spontaneous doubling in the 2n=18 sterile hybrid.
- This kind of allopolyploid is sometimes called an amphidiploid , which means doubled diploid.
- Allopolyploids can be used in plant breeding to combine the useful features of parental species into one type.

ANEUPLOIDY

- Aneuploidy is a numerical departure from normal diploid complement of chromosomes with a gain or loss of one or more of whole chromosomes.
- Aneuploidy results due to a phenomenon called non - disjunction of chromosomes at meiosis.

The origin of Aneuploid gametes by Nondisjunction at the first or second meiotic division



- The homologous chromosomes may fail to synapse at zygotene stage and the unpaired univalents pass randomly to one pole or the other resulting in gametes with n+1 or n-1 chromosome number.
- If the n+1 gamete fertilize with a normal gamete (n), it will result in a 2n +1 zygote and if an n-1 gamete fuses with a normal gamete it will result in a 2n-1 zygote, both being aneuploids.

MONOSOMY

- It is a chromosomal aberration where one chromosome is lost from a pair.
- The monosomic individual has one chromosome less than the normal number of chromosomes.
- Monosomic will result when an n-1 gamete fuses with a normal gamete.
- *Examples*
  - Turners' syndrome in females (45, XO)
    - Individual will be having only a single X chromosome (XO).
    - About 1 in 5000 female births show Turner syndrome.
    - Affected people have a characteristic phenotype: they are sterile females, short in stature, and often have a web of skin extending between the neck and shoulders.
    - Turner syndrome is named after Dr. Henry Turner, who in 1938 published a report describing the disorder.
  - One example of partial monosomy is found in cri-du-chat syndrome, which result from loss of part of the short arm of chromosome 5. Individuals with this syndrome suffer severe mental and physical impairment, and have a distinctive cry like that of a cat (which gives the syndrome its name).

TRISOMY (2n+1)

- The diploid organisms which have one extra chromosome are called trisomies.
- They have the chromosomal formula 2n+1.
- This results when n+1 and a normal gamete undergo fertilization.
- There are two types of trisomy, namely
  - Trisomy of autosomes
  - Trisomy of sex chromosomes

TRISOMY OF AUTOSOMES

- Trisomy of autosome is due to the addition of one chromosome to any one homologous pair of autosome.
- There are several examples of viable human autosomal trisomics .
    - Down syndrome (47, +21)
    - Trisomy 13 (Patau's syndrome) (47, +13)
    - Trisomy 18 (Edward's syndrome) (47, +18)

DOWN'S SYNDROME

- Down syndrome is set of mental and physical symptoms that result from having an extra copy of Chromosome 21.
- It is named after John Langdon Down, the British doctor who described the syndrome in 1866.
- The disorder was identified as a chromosome 21 trisomy by Jerome Lejeune in 1959.
- The chromosome nomenclature is 47, +21 for Down Syndrome
- Other names people use for Down syndrome
    - Down's Syndrome
    - Trisomy 21
    - 47,XX,+21
    - 47,XY,+21
- How do people get Down syndrome?
    - If a pair of number 21 chromosomes fails to separate during the formation of an egg (or sperm), that egg (or sperm) unites with a normal sperm (or egg) to form an embryo, that embryo ends up with three copies of chromosome 21 instead of the normal two.
    - In rare cases Down syndrome is caused by a Robertsonian translocation, which occurs when the long arm of chromosome 21 breaks off and attaches to another chromosome at the centromere.
    - The carrier of such a translocation will not have Down syndrome, but can produce children with Down syndrome.
- What are the symptoms of Down syndrome?
    - People with Down syndrome have very distinct facial features: a flat face, a small broad nose, abnormally shaped ears, a large tongue, and upward slanting eyes with small folds of skin in the corners.
    - Health concerns for individuals with Down syndrome include a higher risk for : respiratory infections, gastrointestinal tract obstruction (blocked digestive tract), leukemia, heart defects, hearing loss, hypothyroidism, and various eye abnormalities.
    - Individuals with Downs' syndrome are mentally retarded and are also called Mongoloid idiots because their facial features resemble those of Mongoloid race.
    - They also exhibit moderate to severe mental retardation; children with Down syndrome usually develop more slowly than their peers, and have trouble learning to walk, talk, and take care of themselves.
    - Because of these medical problems most people with Down syndrome have a decreased life expectancy. About half live to be 50 years of age.

TRISOMY 13 OR PATAU'S SYNDROME

- Trisomy 13 results from having three copies of chromosome 13 in each cell in the body instead of the usual two copies.
- Trisomy - 13 or Patau's syndrome was described by K. Patau in 1960.
- It is rare and frequency is about 1 in 20,000 in new born.

- The chromosome nomenclature is 47, +13 Patau Syndrome
- Other names people use for trisomy 13,
  - Bartholin-Patau syndrome
  - Complete trisomy 13 syndrome
  - Patau's syndrome
  - Patau syndrome
  - Trisomy 13 syndrome
- Main phenotypic characteristics,
  - Heart defects,
  - Brain or spinal cord abnormalities,
  - Very small or poorly developed eyes (microphthalmia),
  - Extra fingers and/or toes,
  - An opening in the lip (a cleft lip) with or without an opening in the roof of the mouth (a cleft palate), and
  - Weak muscle tone (hypotonia).

TRISOMY 18 OR EDWARD'S SYNDROME

- Trisomy 18 results from having three copies of chromosome 18 in each cell in the body instead of the usual two copies.
- This was first described by J.H. Edwards and his colleagues in 1960.
- Frequency occurance is 1 in 8000.
- Trisomy 18 (Edwards syndrome) is the most common autosomal abnormality among live births after Down syndrome (trisomy 21).
- The chromosome nomenclature is 47, +18 Edward Syndrome
- Other names people use for trisomy 18
  - Complete trisomy 18 syndrome
  - Edwards Syndrome
  - Trisomy 18 syndrome
- Main phenotypic characteristics:
  - Central nervous system disorders (holoprosencephaly, meningomyelocele),
  - Eye malformations (hypo/hypertolerism, monophthalmia),
  - Nose malformations (cebocephaly),
  - Cleft lip and/or palate,
  - Abnormal ears,
  - Malformed extremities (polydactyly, rocker-bottom feet), and
  - Defects of the heart, genitals, and midline.

TRISOMY OF SEX CHROMOSOMES

- Trisomy of sex chromosome is due to the addition of one sex chromosome (X or Y) to pair of sex chromosome.
- People typically have two sex chromosomes in each cell:
  - Females have two X chromosomes (46,XX), and
  - Males have one X and one Y chromosome (46,XY).
- There are several examples of viable human sex chromosomal trisomics .
  - Triple X syndrome
  - 47,XYY syndrome
  - Klinefelter syndrome

TRIPLE X SYNDROME

- Triple X syndrome, also called trisomy X or 47,XXX, is characterized by the presence of an additional X chromosome in each of a female's cells.
- This condition occurs in about 1 in 1,000 newborn girls.
- Other names people use for triple X syndrome
  - Triplo X syndrome
  - Trisomy X
  - 47,XXX
  - XXX syndrome
- Main phenotypic characteristics
  - Triple X syndrome cases are phenotypically normal and fertile females.
  - Triple X syndrome cases typically have tall stature by adolescence and normal sexual development and puberty.

47,XYY SYNDROME

- 47,XYY syndrome is characterized by an extra copy of the Y chromosome in each of a male's cells.
- This condition occurs in about 1 in 1,000 newborn boys.
- Other names people use for 47,XYY syndrome
  - Jacob's syndrome
  - XYY Karyotype
  - XYY syndrome
  - YY syndrome
- Main phenotypic characteristics
  - Although males with this condition may be taller than average, this chromosomal change typically causes no unusual physical features.
  - Most males with 47,XYY syndrome have normal sexual development and are able to father children.

KLINEFELTER SYNDROME

- Named after Dr. Harry Klinefelter, an endocrinologist at Massachusetts General Hospital , who first described it in 1942.
- Extra copies of genes on the X chromosome interfere with male sexual development, preventing the testes from functioning normally and reducing the levels of testosterone.
- Klinefelter syndrome affects 1 in 500 to 1,000 males.
- Other names people use for Klinefelter syndrome
  - Klinefelter's Syndrome
  - 47,XXY
  - XXY syndrome
  - XXY trisomy
- Affected males have one extra copy of the X-chromosome in each of a male's cells (47,XXY).

Main phenotypic characteristics

- Learning disabilities and difficulty with speech and language development.
- Quiet, sensitive, and unassertive, but personality characteristics vary among males with this condition.
- A shortage of testosterone during puberty can lead to breast enlargement (gynecomastia), reduced facial and body hair, and an inability to father children (infertility).

NULLISOMIC (2n - 2)

- These are reported implants only and the genome lacks a full set of a homologous pair, so that its somatic chromosome number is 2n-2.
- Nullisomic individual usually fail to survive.

MODULE-17: CHROMOSOMAL ABERRATIONS - STRUCTURE

Learning objectives

After completing this module, the learner should be able to:

- understand the classification of structural chromosome aberrations
- understand the mechanisms that give rise to structural chromosomal aberration

STRUCTURAL CHANGES IN CHROMOSOMES

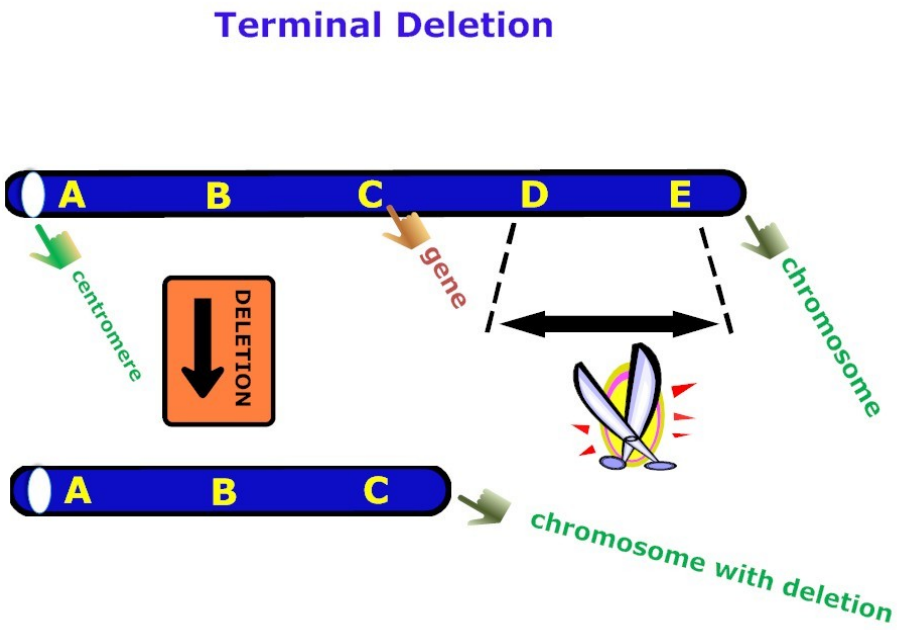
- The chromosome structural abnormalities may confine to a single chromosome or may extend to both of the member of the homologous pair.
- It may be of following types,
    - Intrachromosomal Aberrations
        - Deletion
        - Inversion
        - Duplication
    - Interchromosomal Aberrations
        - Translocation

DELETION

- Deletion is a chromosomal aberration where a segment or a portion of the chromosome is lost.
- Deletions lead to decrease in gene number.
- Deletion was first discovered by Bridges in 1917.
- Deletions are classified into two types based upon the position where deletion occurs.
    - Terminal Deletion
    - Intercalary / Interstitial Deletion.
- One example: Cri-du-chat syndrome, which result from loss of part of the short arm of chromosome 5. Individuals with this syndrome suffer severe mental and physical impairment, and have a distinctive cry like that of a cat (which gives the syndrome its name).

TERMINAL DELETION

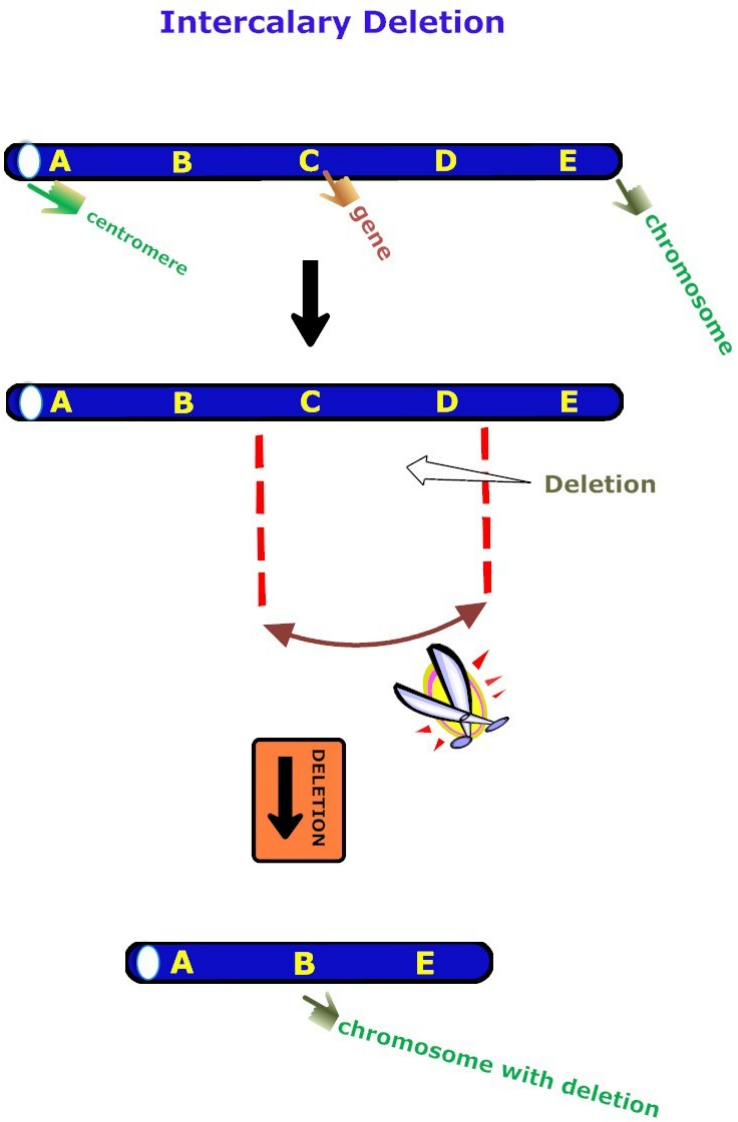
- Terminal deletion / deficiency **:** in which a segment is lost from the end of a chromosome.
- Example: The notch deficiency in Drosophila occurring due to the loss of a part of the X chromosome near the end.



INTERCALARY / INTERSTITIAL DELETION

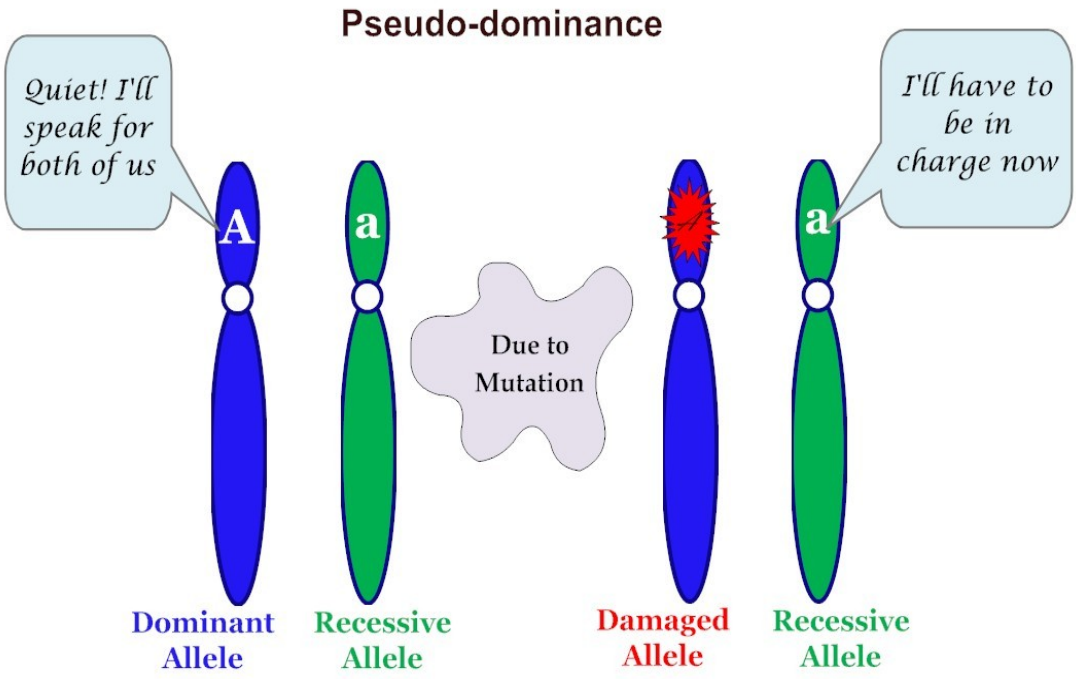
Intercalary deletion / deficiency

- An intermediate segment of the chromosome is lost, leaving the ends of the chromosome intact.
- This is the result of two breaks in the chromosome followed by the union of the two ends.



EFFECTS OF DEFICIENCY OR DELETION

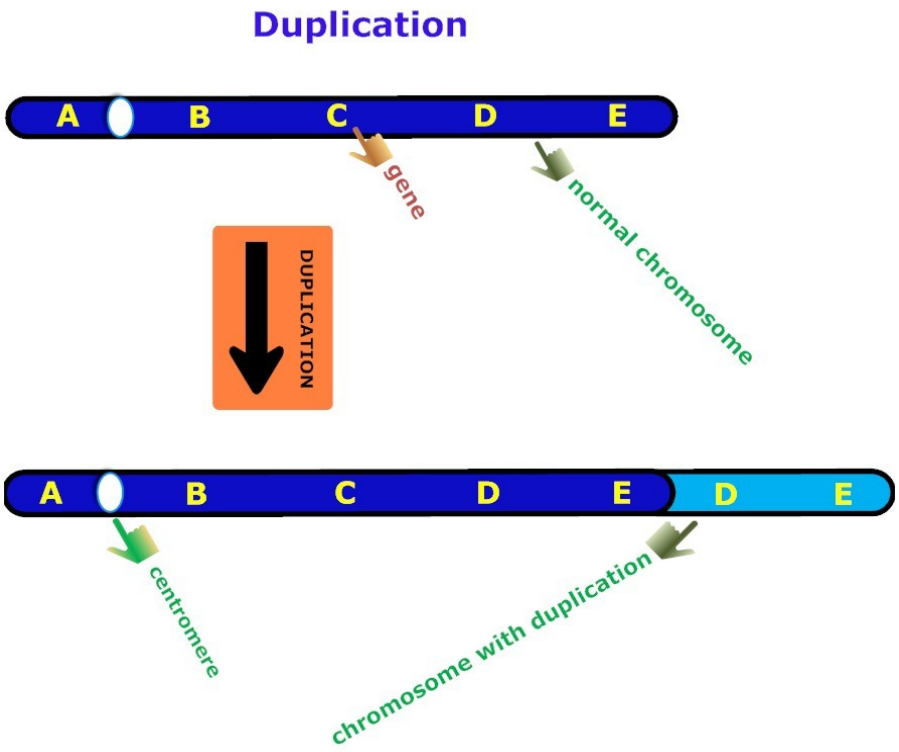
- Chromosomes with a deletion cannot be reverted back to wild type conditions.
  - If the deleted portion is without a centromere, the individual will not survive.
  - When deletion chromosomal gamete unites with another normal gamete a zygote is produced that carries a particular group of genes in a single dose.
  - Expression of single recessive trait with a single dose of recessive gene in the absence of a deficiency/deletion is called pseudo-dominance.



- Deficiencies have deleterious effects in the organisms.
    - For example, a deletion of a portion of long arm of chromosome 21 leads to chronic myeloid leukemia in human beings.
    - Similarly, a loss of the short arm of chromosome 5 results in Cri-Du-Chat syndrome (cry of cat syndrome).

DUPLICATION

- In a diploid organism, the presence of an additional chromosome segment per nucleus is known as duplication.
- The extra piece either exists as a free fragment chromosome or is attached to one of the chromosomes in the complement.



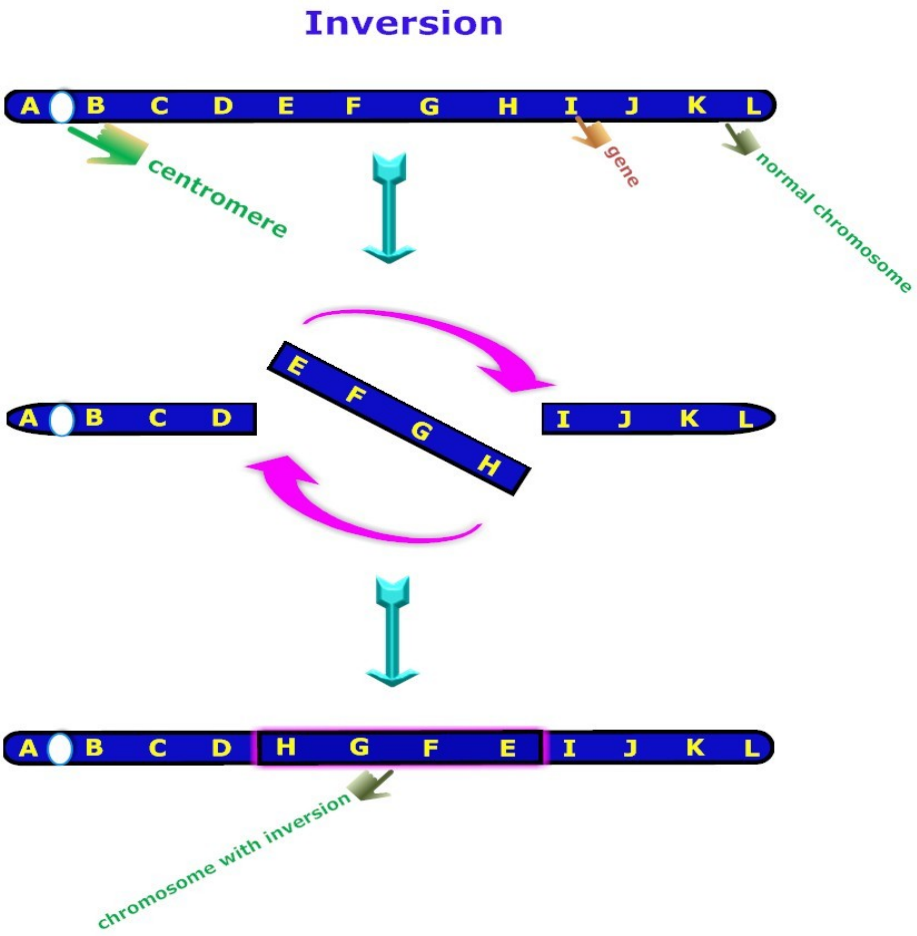
To view "Duplication Mutation Animation"

- The duplications are less deleterious for an individual than the deletions, although individuals carrying duplications show abnormalities in bodily characters.
- Duplication provides additional genetic material potentially capable of giving rise to new genes during the process of evolution.
- An altered phenotypic effect produced by change in position of a gene or a group of genes is called *position effect*.
- Position effect: When a chromosome rearrangement involves no change in the amount of genetic material but only in the order of genes, the term position effect is used to describe any associated phenotypic alterations that occur along with mutation. Position effect represents a source of genetic variation.
- Position effects on gene expression fall into two classes:
    1. Stable: Eg. Bar eye in Drosophila
    2. Variegated/unstable: Eg. Drosophila w[m4] translocation.
- C.B. Bridges (1936) provided concrete evidence to prove that phenotypic expression of bar eye in Drosophila is due to the duplication of five-banded segment in the X chromosome.

INVERSION

- An Inversion is a reversal in the order of a segment of a chromosome within the chromosome, or a gene.
- It arises by breakage of the chromosome followed by the joining of pieces in the reverse order.

- Change in the linear order of genes or a series of nucleotides in the gene by rotation of a section of a chromosome through 180 degrees.



CLICK HERE! To view "Inversion Mutation Animation"

- If the centromere lies within the inverted region, the inversions are known as pericentric inversions.
- If centromere lies outside the inverted segment, the inversion is called paracentric inversion.
- Inversion effectively suppresses crossing over.

TRANSLOCATION

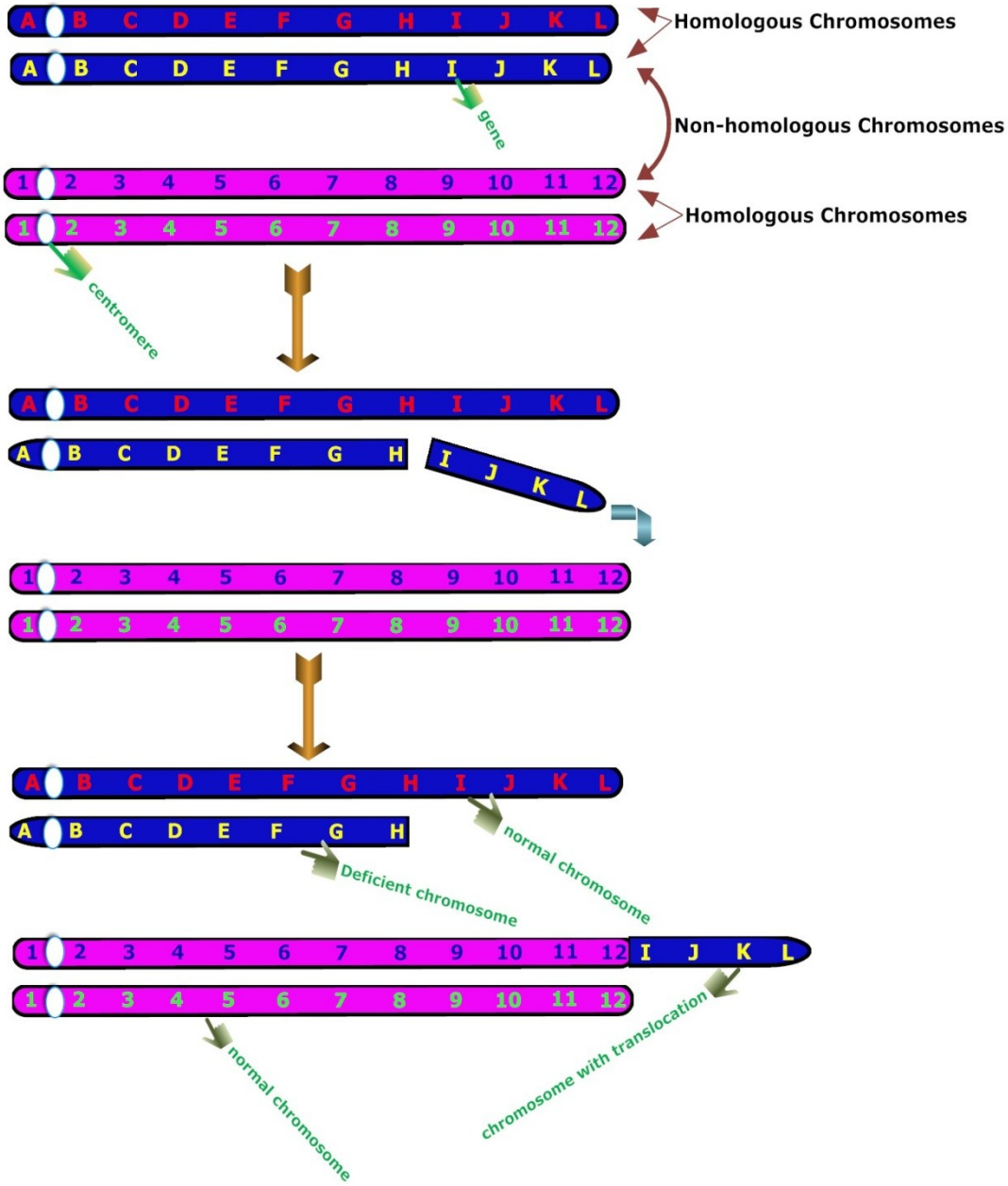
- Segment from one of two homologous chromosomes breaks and binds to the other non-homologous chromosomes.
- Translocation of genes has resulted in some genes from one of the chromosomes attaching to the other non-homologous chromosomes.

- Non-reciprocal Chromosome Translocation - a part of chromosome is translocated to another non-homologous chromosome so that one chromosome becomes deficient and the other gains certain segments of chromosome.
- Reciprocal Chromosome Translocation - two non homologous chromosomes exchange segments.

NON - RECIPROCAL TRANSLOCATIONS

- Non-reciprocal translocations are of two types
- Simple translocations
    - Involving a single break in the chromosome.
    - The broken piece is then directly added on to the end of another non-homologous chromosome.
    - The ends of the chromosomes (telomeres) are nonsticky in nature and the pieces of other chromosomes cannot be attached to them.
    - Therefore, this type of translocations is rarely produced.

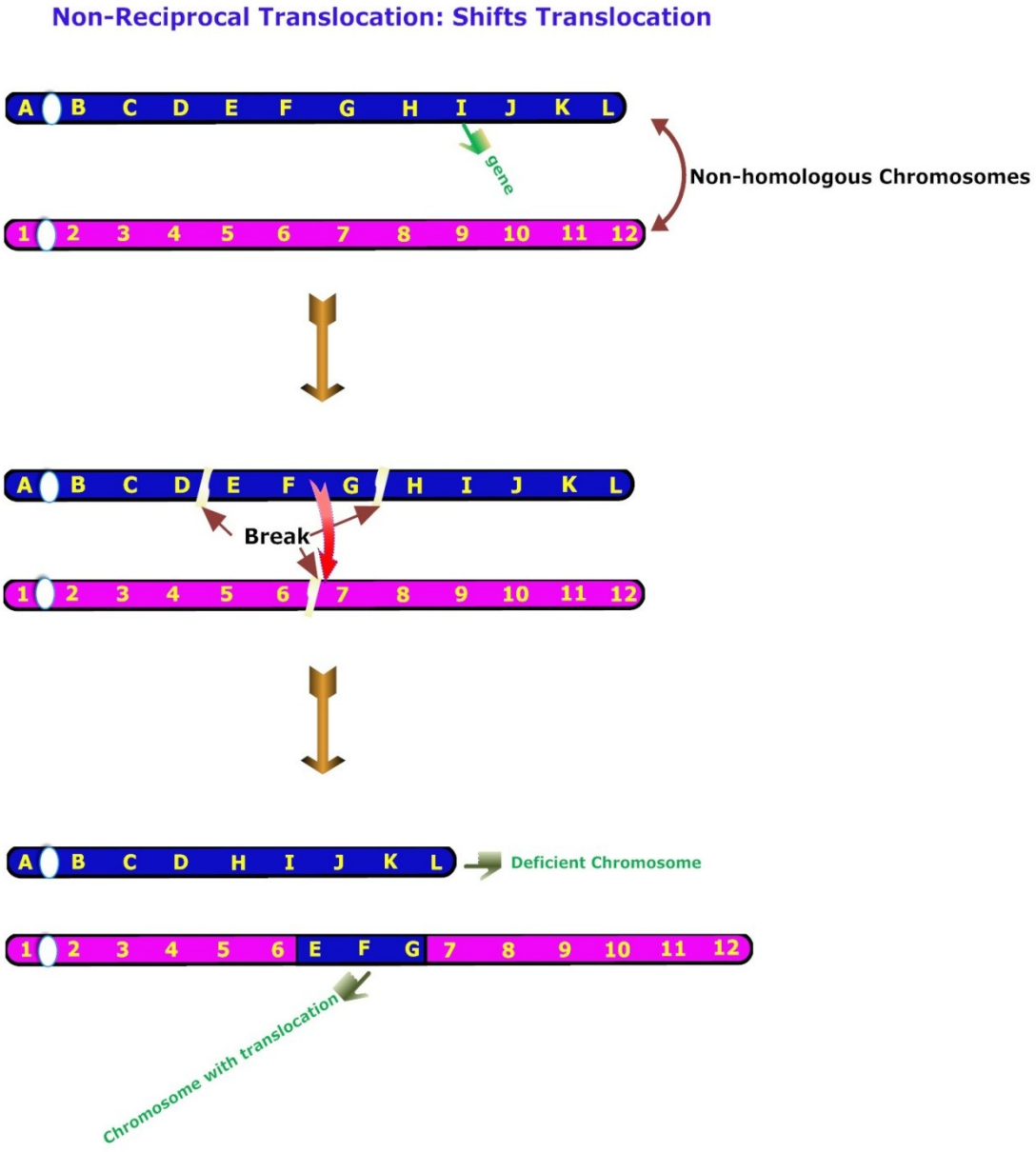
Non-Reciprocal Translocation: Simple Translocation



To view "Simple translocations Mutation Animation"

- Intercalary Chromosome Translocation / Shifts involving three breaks

- An interstitial segment of a chromosome is detached from it with the help of two breaks and is inserted within the break produced in another non-homologous chromosome.



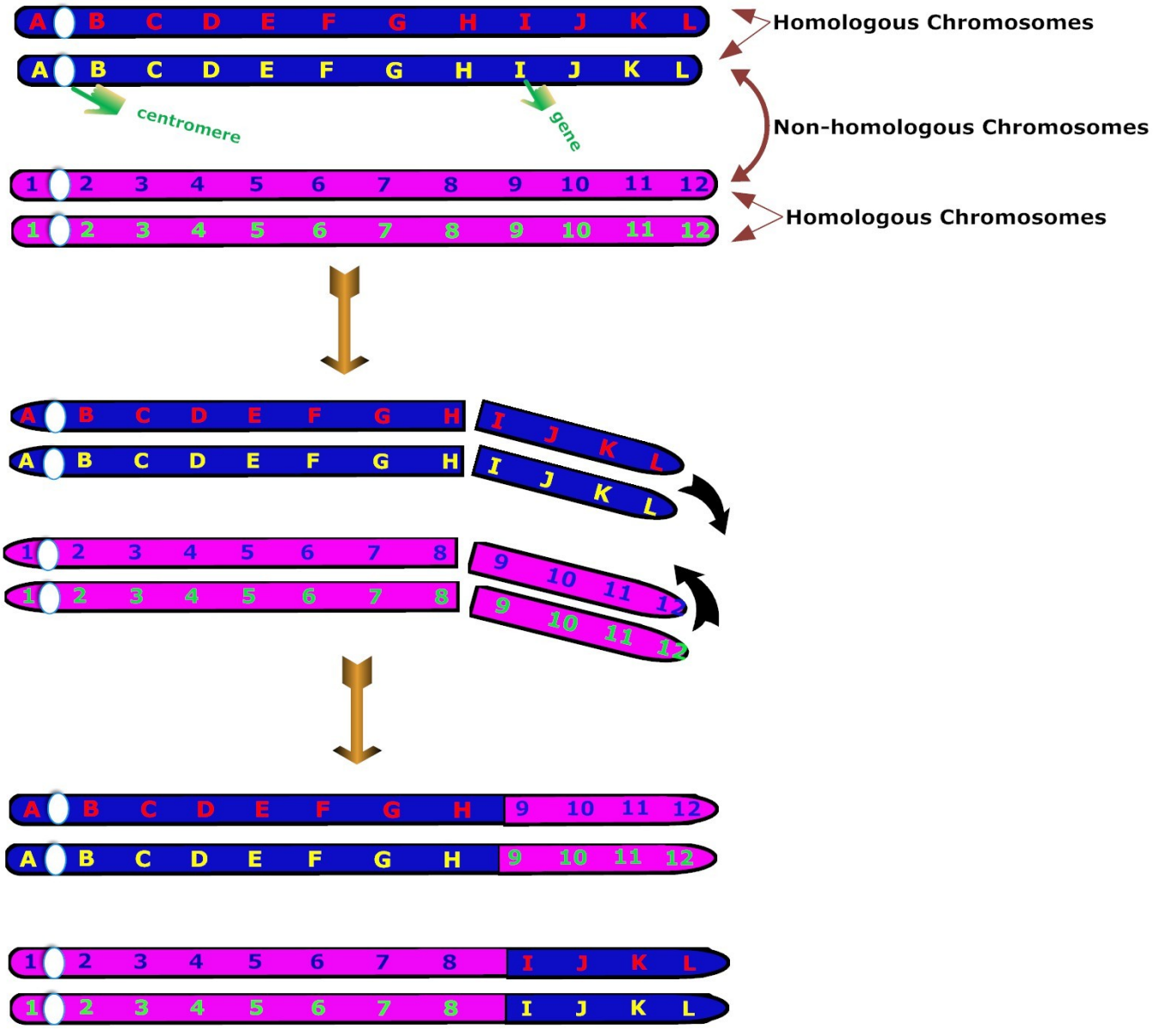
RECIPROCAL TRANSLOCATIONS

- Reciprocal translocations are of two types,
  - Homozygous translocations
  - Heterozygous translocations

Homozygous translocations

- In which both the homologous chromosomes exchange parts with the two homologues of another pair.
- These are difficult to detect cytologically, since they have normal meiosis.
- Generally they can influence the phenotype, if the translocated genes have position effects, since after translocation they form linkage groups different from what they had before.

Homozygous Reciprocal Translocation



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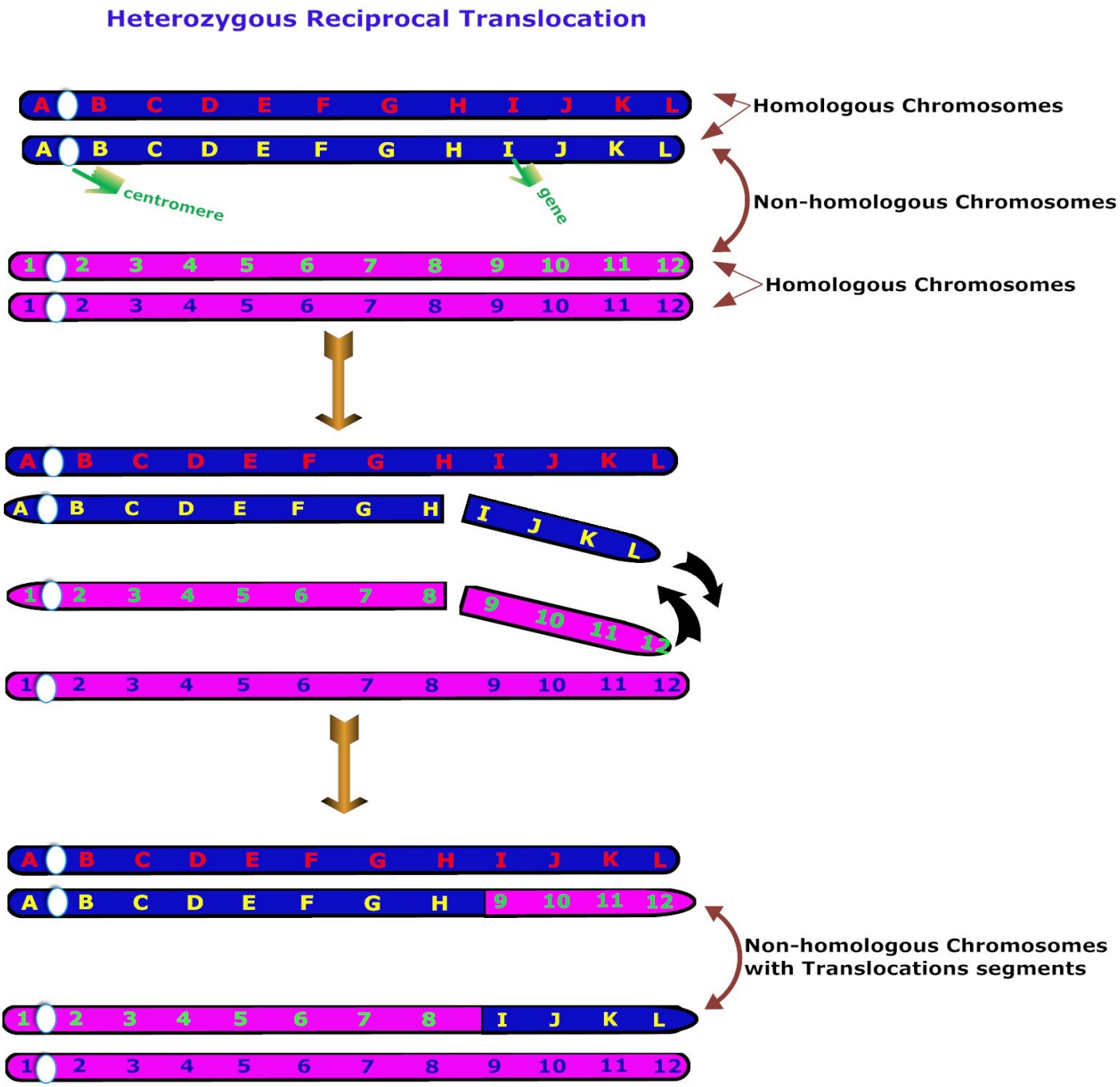
Heterozygous translocations

- Are those involving only one member of each of the two homologous pairs.
- These are detected cytologically by characteristic configurations they make at synopsis.



MODULE-18: CYTOGENETICS

Learning objectives

After completing this module, the learner should be able to:

- identify features of normal chromosome
- understand the basic nomenclature used
- understand the advantages of different banding techniques
- describe several cytogenetic polymorphisms

CYTOGENETICS

- Cytogenetics is the study of chromosomes and their abnormalities.
- Cytogenetics includes the study of normal and abnormal chromosomes, and investigation of the causes of chromosomal abnormalities.
- Chromosome abnormalities are responsible for a significant portion of genetic disease.

Two kinds of Cytogenetic Examination

- Basic Chromosomal Analysis
  - Staining methods (solid staining, G-banding etc.)
  - Based on analysis of metaphase chromosomes
- Molecular Cytogenetic Analysis
  - Identification of chromosomal abnormalities using molecular biological methods

Example

- Hybridization
  - *in situ* hybridization and its modifications (Comparative Genomic Hybridization (CGH), M-FISH)
  - Gene chips, High-resolution array CGH, DNA microarray etc.
- Polymerase Chain Reaction (PCR)
  - Primed in situ labeling (PRINS), PCR *in situ*
  - Quantitative fluorescent PCR, real time PCR
  - Methods based on amplification of probe attached to target sequence (MLPA, MAPH)

CHROMOSOME BANDING

- The chromosomes need to be stained in order to see them under a microscope.
- Several chromosome-banding techniques are used to enable the chromosome segments to be identify the chromosome.
  - **Example:** Quinacrine banding (Q-banding), Giemsa banding (G-banding), Reverse banding (R-banding), C-banding and Nucleolar Organizing Region stains (NOR stains).
- Most methods can distinguish between 300 and 450 bands in condensed chromosome.
- High resolution methods can distinguish up to 800 bands that can allow identification of small interstitial deletions.

KARYOTYPE

- A karyotype is an organized profile of an organism's chromosomes.
- In a karyotype, chromosomes are arranged and numbered by size, from largest to smallest.
- This arrangement helps in quick identification of chromosomal alterations that may result in a genetic disorder.

- To make a karyotype, picture of someone's metaphase chromosomes will be taken and is cut out and matched up using size, banding pattern and centromere position as guides.

Karyotyping

- Karyotyping is a test to examine chromosomes in a sample of cells, which can help identify genetic problems as the cause of a disorder or disease. This test can:
  - Count the number of chromosomes
  - Look for structural changes in chromosomes

KARYOTYPE NOMENCLATURE

Karyotype	Description
6,XY	Normal male
7, XX,+21	Female with trisomy 21, Down Syndrome.
7, XY,+21 / 46, XY	Male mosaic for trisomy 21 and normal cells
6, XY, del(4)(p14)	Male with distal deletion of the short arm of chromosome 4 band designated 14.
6,XX, dup (5p)	Female with a duplication of short arm of chromosome 5.
5, XY, -13, -14, (13q;14q)	Male with a balanced Robertsonian translocation of chromosome 13 and 14, with a norma 13 and normal 14 missing.
6, XX, t(11;22)(q23;q22)	Male with a balanced reciprocal translocation
6,XX, inv(3)(p21;q13)	Female with an inversion on chromosome 3 from p21 to q13; because it includes the centromere this is a pericentric inversion.
6, X.r(X)	A female with one normal X and one ring X chromosome.
6, X, i(Xq)	Female with one normal X chromosome and and isochromsome of the long arm of the X.

FLUORESCENCE IN SITU AND COMPARATIVE GENOMIC HYBRIDIZATION

- New technique that uses chromosome specific DNA as a probe to hybridize to metaphase, prophase and interphase chromosomes. Can be used to identify deletions, as well as inversions and translocations.

SKY TECHNIQUE

- Spectral karyotyping (SKY) is a laboratory technique that allows to visualize all pairs of chromosomes in an organism at one time, with each pair of chromosomes painted in a different fluorescent colour.

Uses

- For example, chromosomes in cancerous cells frequently exhibit aberrations called translocations, where a piece of one chromosome breaks off and attaches to the end of another chromosome.

- Identifying such chromosome abnormalities and determining their role in disease is an important step in developing new methods for diagnosing many genetic disorders

MODULE-19: EXTRA-CHROMOSOMAL INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- understand the role of extra-nuclear inheritance
- explain the reasons why extra nuclear genes are not inherited in a Mendelian fashion

CYTOPLASMIC INHERITANCE

Cytoplasmic inheritance

- There are many exceptions to the rule in genetics.
- One of them is that not all inherited characters are determined by genes located in the nucleus.
- Some self replicating genes (DNA) are present in the cytoplasm (mitochondrial DNA and chloroplast DNA) also. These are called *plasmagenes* or *cytogenes* or *plasmids* or *plasmons* etc. The inheritance of characters by plasmagenes is called *Non-mendelian* or *Extra-chromosomal* or *Cytoplasmic* or *Extra-nuclear inheritance*.
- Since they are *extrachromosomal* (i.e. outside the chromosomes), such genes are not subject to the normal rules of Mendelian heredity.
- In most organisms, the organelles pass through the egg and not the sperm, giving a strict *maternal pattern of inheritance* for any mutations that may be present in the organelle DNA.
- In cytoplasmic inheritance, the results of reciprocal crosses are not the same.

Maternal inheritance

- The determination of the phenotype of offspring by the genotype of female parent is called *maternal inheritance* or *uniparental inheritance or maternal effect*.
- Example: Pattern of shell coiling in snail.
    - Here the shell coiling is determined by the genotype of the mother and not by the individual's own genotype.

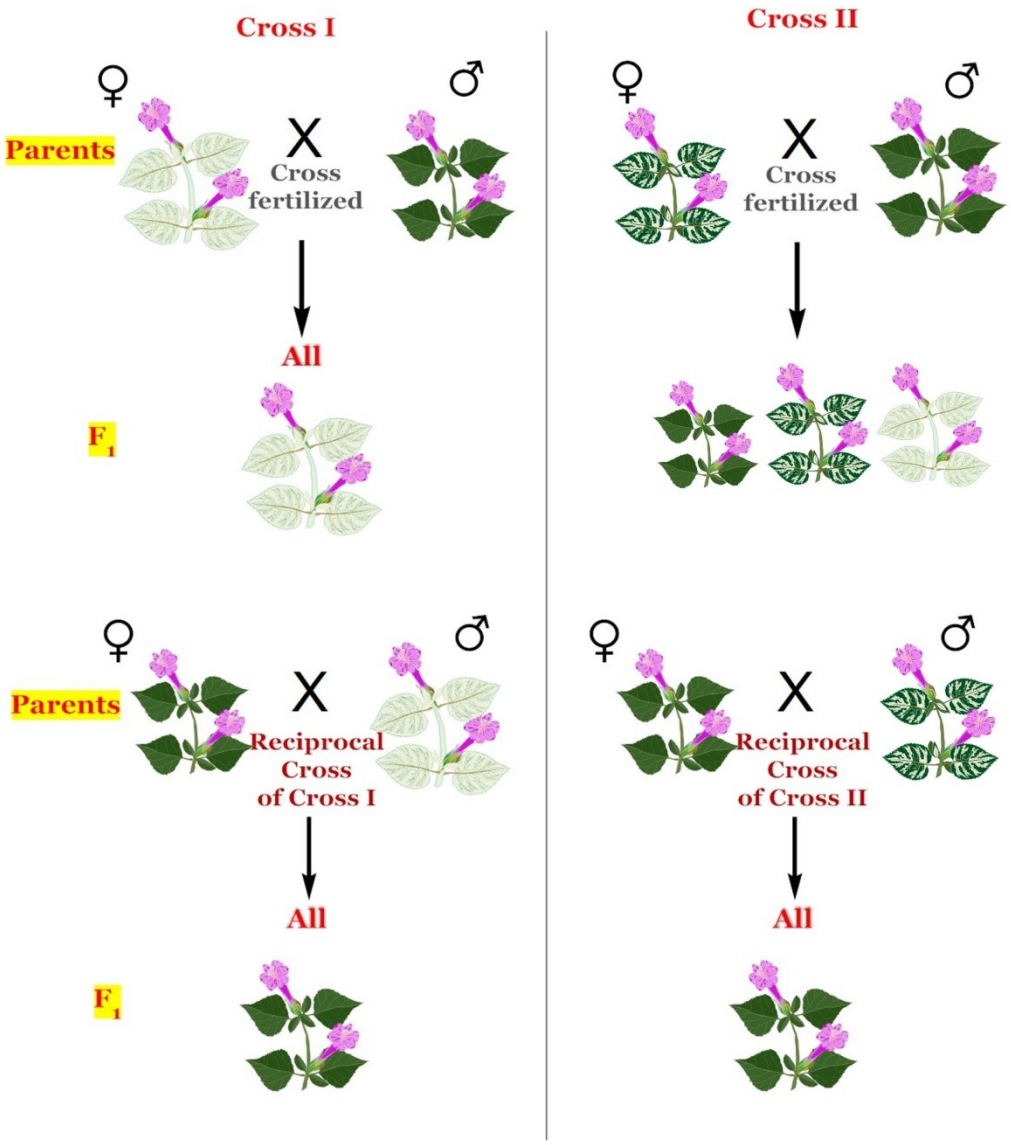
Examples for cytoplasmic inheritance

- Plastid inheritance in Mirabilis
- Shell-coiling in snail
- Kappa particles in Paramecium
- Cytoplasmic male sterility in maize
- Sigma virus in *Drosophila melanogaster*
- Milk factor in mice

LEAF VARIEGATION IN PLANTS

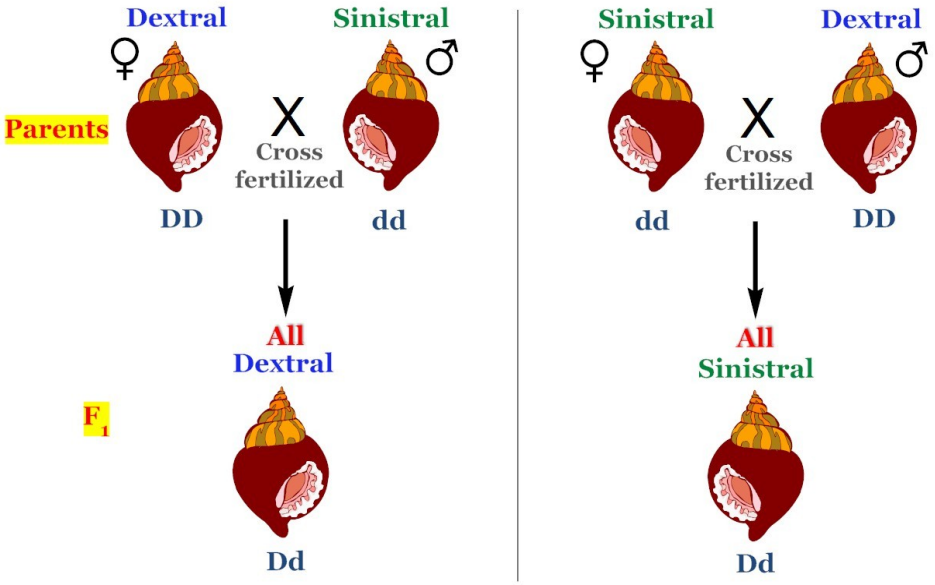
- The first example of cytoplasmic inheritance was reported by Correns (1909) in a variegated variety of the four-o'clock plant *Mirabilis jalapa*.

- Variegated plants have some branches which carry normal green leaves, some branches with variegated leaves (mosaic of green and white patches) and some branches which have all white leaves.
- Flowers on wholly green branches produce seeds that grow into normal plants.
- Flowers on variegated branches yield offspring of three kinds- green, white and variegated in variable proportions.
- Flowers from branches wholly white produce seeds that grow into white plants that is without chlorophyll.
- But in every case the source of pollen has no influence on the offspring.
- In other words, the phenotype of the progeny always resembled the female parent and the male made no contribution at all to the character. So cytoplasm of the egg influences the type of leaf in Mirabilis.
- The explanation for this unusual pattern of inheritance is that the genes concerned are located in the *plastids* within the cytoplasm, not in the nucleus and are therefore transmitted only through the female parent.
- Plastids are of two types, namely green *chloroplasts* and colourless *leucoplasts*.
- *Green* branches contain Green plastids in their leaves , Variegated branches contain Green plastids and Colourless plastids and Colourless branches are due to the presence of Colourless plastids.



SNAIL SHELL COILING

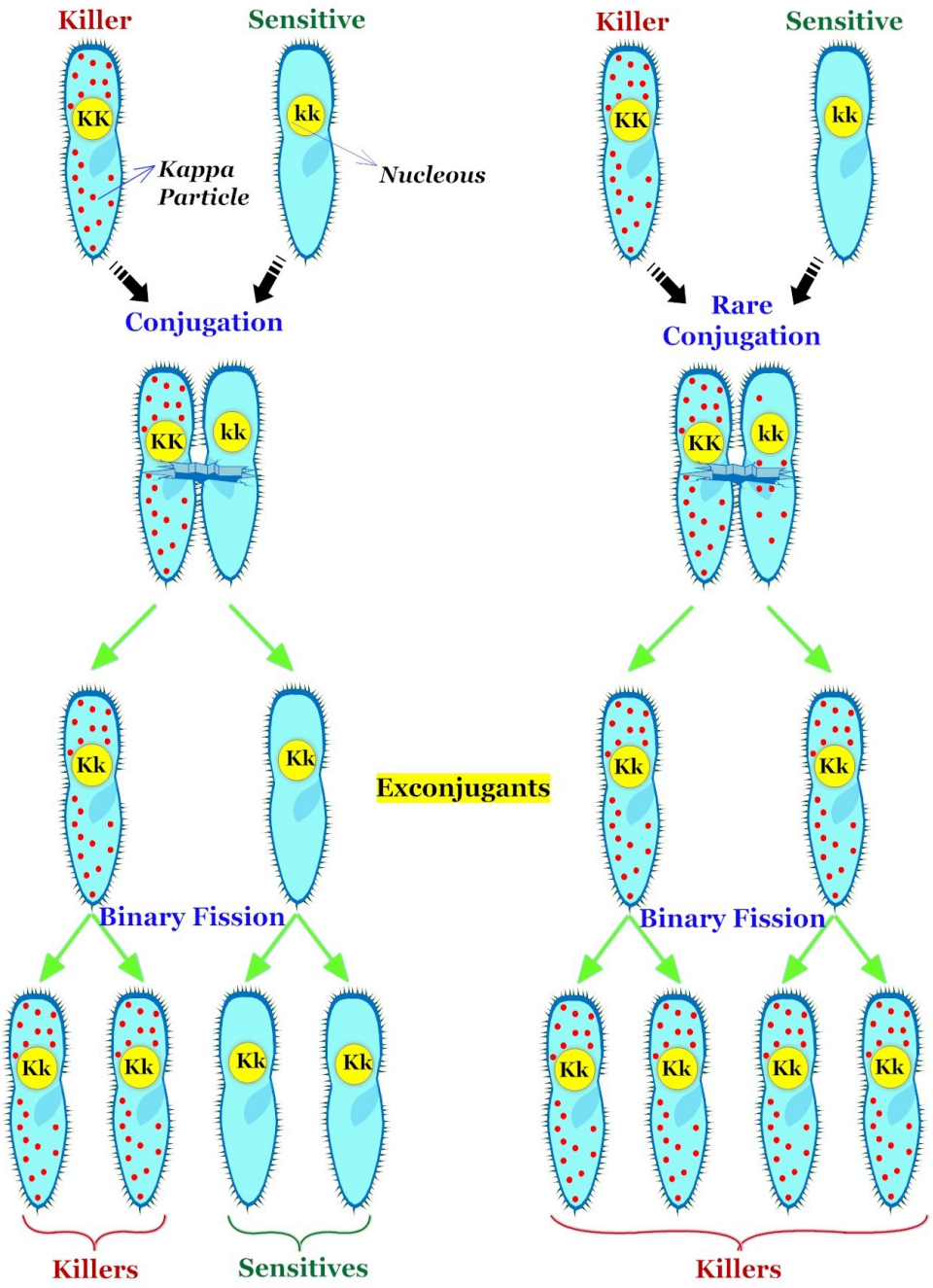
- The classic phenotype which exhibits maternal effects is coiling direction of snail shells.
- Shell coiling in *Limnaea peregra*, a fresh water snail , is of two types, Dextral (clockwise) and Sinistral (anticlockwise).
- The dextral shell is dominant and is controlled by dominant gene D.
- The sinistral shell is recessive and is controlled by recessive gene d.
- The following crosses were made between pure line snails.
- When dextral female (DD) was crossed with sinistral male (dd), all the offsprings of F_1 generation (Dd) have dextral coiling.
- If sinistral female (dd) is crossed with dextral male (DD), the offspring have Dd genotype but coiling is sinistral.
- In the above two crosses, the F_1 snails have the same genotypes.
- The F1 phenotype is not the same for both crosses.



- The coiling phenotype that is seen in the offspring is controlled by the genotype of the mother.
- In the first cross, the offspring has dextral shell because the mother's genotype is DD.
- In the second cross, the offspring has sinistral shell because the mother's genotype is dd.
- Since, zygote receives whole of its cytoplasm from the egg, the direction of shell coiling in the offspring is governed by cytoplasm of the mother.

KAPPA PARTICLES IN PARAMECIUM

- T. M. Sonneborn described the inheritance of some cytoplasmic particles known as kappa and their relation to nuclear gene in the common cillate protozoan, *Paramecium aurelia*.
- There are two strains of Paramecium. They are killer and sensitive.
- Killer strain produces a toxic substance called paramecin that is lethal to other individuals called "sensitives" .
- The production of paramecin in killer type is controlled by certain cytoplasmic particles known as kappa particles. The sensitive strains lack these particles.
- The kappa particles are transmitted through the cytoplasm.
- The existence, production and maintenance of kappa particles are controlled by a dominant gene 'K' present in the nucleus. However, 'K' cannot initiate the production of kappa in the total absence of kappa in the cytoplasm.
- When a Paramecium of killer strain is having the genotype "KK" or (K+) conjugates with the Paramecium of non-killer strain having the genotype "kk", the exconjugants are all heterozygous for "Kk" genes.
- The development of a particular type depends upon the duration of cytoplasmic exchange
    - If conjugation is normal, i.e., lasts only for a short time, and no exchange of cytoplasm takes place between the two, both killers and non-killers (sensitive) are produced.
    - However in rare or prolonged conjugation (i.e., lasting for long time) the cytoplasmic bridge between the two conjugants is larger. In such cases, in addition to the nuclear material, the cytoplasmic materials are also exchanged.
    - During this cytoplasmic exchange, the kappa particles present in the cytoplasm of the killer type enter the non-killer type and convert it into a killer type. So all the offspring produced by the exconjugants are killer type.



- This shows that a Paramecium becomes a killer when it receives kappa particles and it becomes a sensitive when it does not receive kappa particles.

MODULE-20: GENE CONCEPT

- Learning objective
- After completing this module, the learner should be able to understand the concept of gene expression.

GENE CONCEPT

- “Gene” is a theoretical term. Like all theoretical terms, its meaning has dramatically changed over and over in time, and it has been defined in so many different operational ways.
- Firstly it shows that the theoretical concepts of classical genetics cannot be correlated unambiguously with the theoretical concepts of molecular genetics.
- It was only in the nineteenth century that heredity became a major problem to be dealt with in biology.
- In the second half of the nineteenth century, Carl Naegeli and August Weismann distinguished the body substance, the “trophoplasm” or “soma”, from a specific hereditary substance, the “idioplasm” or “germ plasm”, which was assumed to be responsible for intergenerational hereditary continuity.
- Charles Darwin called the presumed hereditary particles as “gemmules”; Hugo de Vries, “pangenes”.

CLASSICAL CONCEPT

- Gregor Johan Mendel (1865) found that individual traits are determined by discrete “factors” and these factors or elements undergo segregation and independent assortment. These factors are then passed on unchanged (except in arrangement) to offspring thus yielding a very large, but finite number of possible variations.
- Three botanists, Hugo de Vries, Carl Correns, and Erich Tschermak, observed that the elements responsible for pairs of alternative traits “allelomorphs” in the later terminology of William Bateson (1902), which soon came into general use under the abbreviation of “alleles” segregated randomly in the second filial generation (Mendel's law of segregation), and that these elements were transmitted independently from each other (Mendel's law of independent assortment).
- Bateson had coined the term *genetics* for the emerging new field of transmission studies in 1906.
- Wilhelm Johannsen coined the terms phenotype and genotype, which are now used to indicate the appearance of the individual and its actual genetic makeup, respectively
- He proposed the notion of *gene* to replace older terms like factor, trait, and character .
- Thomas Hunt Morgan and his research group used mutants of the fruit fly *Drosophila melanogaster* and constructed a map of the fruit fly genotype in which genes, and alleles thereof, figured as genetic markers occupying a particular locus on one of the four homologous chromosome pairs of the fly. He established the chromosome theory of heredity.
- These basic assumptions allowed that genes were located in a linear order along the different chromosomes, and that the frequency of recombination events between homologous chromosomes, that is, the frequency of crossovers during reduction division, gave a measure of the distance between the genes, at the same time defining them as units of recombination
- Meanwhile, cytological work had also added credence to the materiality of genes-on-chromosomes.
- In 1933 Jean Brachet was able to show that DNA is found in chromosomes and that RNA is present in the cytoplasm of all cells.
- In 1941 Edward Lawrie Tatum and George Wells Beadle show that genes code for proteins.
- "Gene" is a theoretical term. Like all theoretical terms, its meaning has dramatically changed over and over in time, and it has been defined in so many different operational ways.

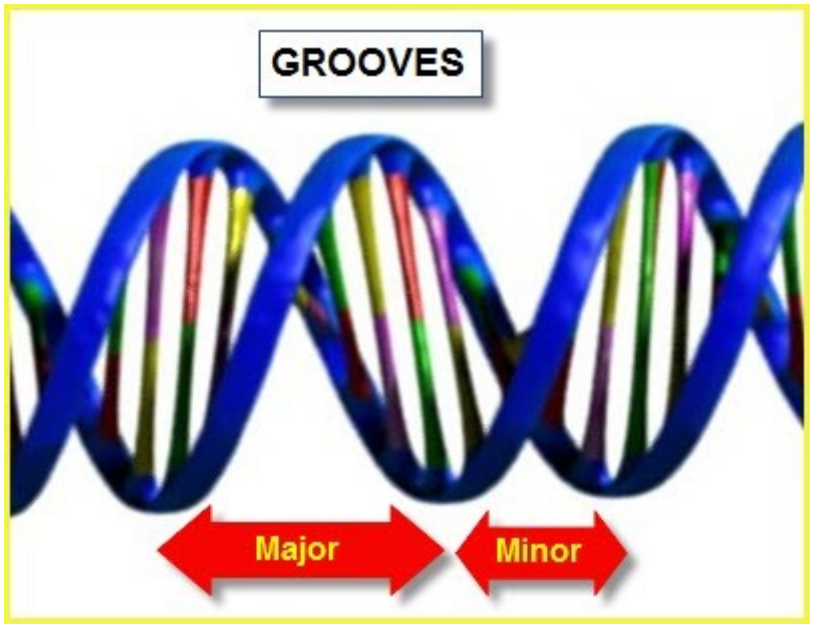
MODERN CONCEPT

- The classical concept of the gene started to break down as soon as it had been completely formulated.
- The nature of the genetic material became more accurate when Avery, Macleod and McCarty (1944) demonstrated that the substance causing transformation in bacteria was DNA.
- Support for the DNA theory of inheritance was gained when Alfred D. Hershey and Martha Chase demonstrated that DNA alone was responsible for the multiplication of bacteriophages.
- James D.Watson and Francis H. C. Crick (1953) demonstrated that deoxyribonucleic acid (DNA) is a double-stranded helix of nucleotides.
- Alexander Dounce and George Gamow independently presented the so-called colinearity hypothesis, according to which the linear structure of DNA determines the linear primary structure of a polypeptide.
- The concept of "one gene-one enzyme" hypothesis was proposed by George Beadle and Edward Tatum.
- Advances in biochemical genetics made the one gene-one enzyme hypothesis seem very unlikely and leading to a "one gene-one polypeptide" hypothesis instead.
- Proteins or enzymes are generally aggregates of more than one kind of polypeptides. This hypothesis is correct to a very great extent and applies to all organisms.
- However, it is now known that certain genes also direct the formation of ribosomal and t-RNA molecules and not the formation of proteins.

Structure of DNA

- DNA is a ncleic acid and nucleotides are the building blocks of all nucleic acid molecules. The structural unit consists of
    - Pentose sugar (2' deoxy ribose)
    - phosphoric acid and
    - four nitrogenous bases: two of these nitrogenous bases are
        - Purines- a double ring structure
            - Adenine (A)
            - Guanine (G)
        - Pyrimidines- a single ring
            - Thymine (T)
            - Cytosine (C)
- In DNA, each base is chemically linked to a deoxyribose sugar, forming a nucleoside. A phosphate group is also attached to the sugar of each nucleoside yielding a nucleotide (a nucleotide is a nucleoside phosphate). It is common to name nucleotides as monophosphates i.e. deoxyadenosine 5' –monophosphate and abbreviated as dAMP for a adenine containing nucleotides others are named as dGMP, dCMP, and dTMP. The double helix measures 20A^{o} (2.0 nm) in diameter.
- Two polynucleotide chains twisted around one another forming a rigt handed double-stranded helix in which Adenine pairs only with thymine (complementary base pairing) and Guanine with Cytosine. (The content of purine always equals the contents of pyrimidine, furthermore the amount of adenine and thymine are always equal and so are the amounts of guanine and cytosine-Chargaff's rule). In the double helix, one polynucleotide strand is in 5'-> 3' direction and the other is in 3' -> 5' direction and hence are said to be anti parallel.
- The nucleotides are joined together to form a polynucleotide chain in which 5' carbon of one sugar is linked by its phosphate group to the 3' carbon of the next sugar. (The chemical bonds by which the sugar components of the adjacent nucleotides are linked through the phosphate groups are called phosphor diester bonds). This 5'-> 3'-> 5'->3' orientation of these linkages continues throughout the chain. In each polynucleotide chain there are a 5' phosphonyl group (5'-p) at one end and 3'-hydroxyl group (3'-OH) at the other.
- Each chain makes one complete turn every 34 A^{o}. The bases are spaced at 3.4 A^{o} such that there are ten base pairs per helical turn.
- Each base is paired to a base in other strand by hydrogen bonds. An AT pair has two hydrogen bonds and a GC pair has three hydrogen bonds.

- The double helix structure of DNA are closer together on one side of the helix than on the other. The major groove occurs where the backbones are far apart, the minor groove occurs where they are close together.



Gene

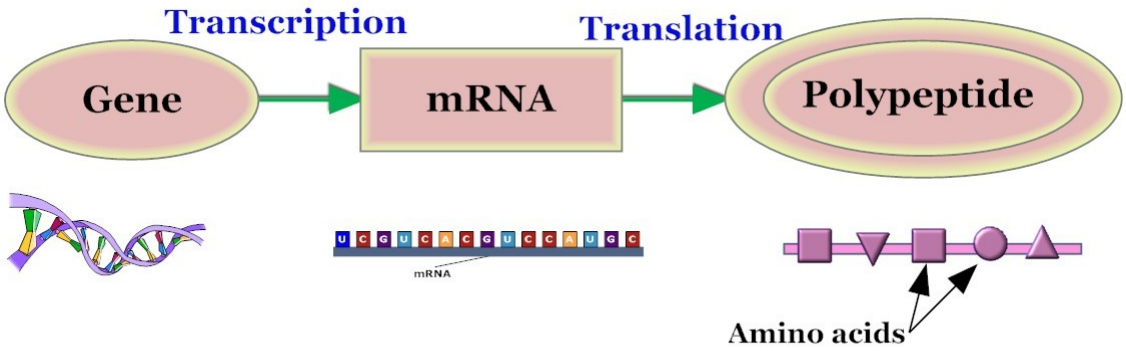
- A gene is a unit of information and corresponds to a discrete segment of DNA that encodes the amino acid sequence of a polypeptide.
- In higher organisms, the coding sequence of a gene is split into a series of segments called **exons** which are separated by non coding sequences called **introns**, which do not contain useful information.
- Introns are removed from RNA transcripts by a process called splicing during protein synthesis.
- Genes vary greatly in size from less than 100 bp to several million bp.

Central Dogma Concept

- The central dogma of genetics describes the two-step process, transcription and translation, by which the information in genes flows into proteins: DNA -> RNA -> protein.
- This flow of information is unidirectional and irreversible.

Gene Expression

- Gene expression refers to the mechanism by which a gene expresses a phenotype.
- A gene contains the code or plan for a polypeptide chain in the form of a specific sequence of nucleotide bases.
- It transfers its codes to mRNA. It is called transcription.
- The code present in the mRNA is translated in the ribosome with the help to tRNA.
- The tRNA picks up the required amino acids and are linked in specific sequence as per the sequence of nucleotides present in the mRNA.
- The amino acids form a polypeptide chain. It functions as a structural protein or as an enzyme.
- In other words, the polypeptide contributes to the morphological or functional trait of the cell.



Gene Expression

- The specificity of base pairing is such that each base along one polynucleotide strand of the DNA determines the base in opposite position on the other strand. Hence the sequence of bases along the two strands is complementary in nature.

DIFFERENCES BETWEEN DNA AND RNA

DNA (Deoxy ribonucleic acid)	RNA (Ribo nucleic acid)
Majority of DNA is present in nucleus	Majority of RNA is present in cytoplasm and as well as in nucleus
Double stranded	Single stranded
The usual genetic material	Genetic material for some viruses-plays important role in protein synthesis
Contains deoxyribo sugar	Contains ribose sugar
Common nitrogenous bases are A, G, C	Instead of thymine, uracil is present A, G, C & U
Base pairing A with T and G with C	Base pairing A with U and G with C

MODULE-21: POPULATION GENETICS

Learning objectives

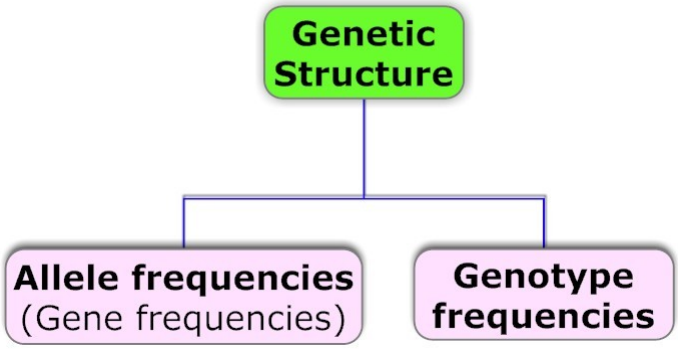
After completing this module, the learner should be able to:

- understand the assumption of basic population genetics
- understand the causes of genetic diversity among and within populations

POPULATION GENETICS

- A population is a set of organisms in which any pair of members can breed together. I t may be a local population such as the cattle in a farm or it could be as large as an entire species.
- Population genetics is concerned with the genetic constitution (allele and genotype frequencies) of populations, their relationship and how this constitution changes with time.
- Population genetics describes how genetic transmission happens between a population of parents and a population of offspring.
- Traditionally, the study of population genetics involved the identification of different alleles through observation of the expressed traits, broadly called the phenotype.
- Alleles are different versions of the same gene that are expressed as different phenotypes.
- Every diploid individual has two copies (two alleles) of each gene, one inherited from each parent.
    - If an individual has two different versions of a particular gene, the individual is said to be heterozygous for that gene.
    - If the two alleles are the same, the individual is homozygous for that gene.
- In the transmission, the genotypes of the parents are broken down and a new set of genotypes is constituted in the progeny, from the genes transmitted in the gametes.
- The genes carried by the population thus have continuity from generation to generation, but the genotypes in which they appear do not.
- *Gene pool* is defined as the sum total of genes present in a Mendelian population. It includes all the genes of all the individuals of a population.
- The transfer of genes from one gene pool to another is called *gene flow*.
- The classical Mendelian traits which are qualitative in nature can be classified into distinct phenotypic classes/categories.
- These traits are controlled by only one or a very few genes with almost no environmental effect to modify the gene effects.
- Population genetics was first used as the basis for genetic improvement of livestock by J.L.Lush

GENETIC STRUCTURE OF POPULATIONS



GENE FREQUENCY

- Standard usage in population genetics uses the term gene frequency for what is actually allele frequency.
- Gene or allele frequency is the proportion of one allele relative to all alleles at the locus in the population.

$$f(allele) = \frac{No.of\ copies\ of\ the\ allele\ in\ a\ population}{Sum\ of\ all\ alleles}$$

- Gene frequency is usually expressed as a proportion or a percentage.
- The frequency of a phenotype in a population depends on the frequency of the allele controlling it.
- Frequently used over genotypic frequencies in calculations because
  - Genotypes break down to alleles when gametes are formed
  - Alleles (not genotypes) are passed on to progeny
- If *f(AA)*, *f(Aa)*, and *f(aa)* are the frequencies of the three genotypes at a locus with two alleles "*A*" and "*a*"

The frequency of the *A*-allele

- $f(A) = p$

The frequency of the *a*-allele

- $f(a) = q$

$f(A) + f(a) = p + q = 1$

- Calculation from observed number of individuals with each genotype

$$f(A) = p = f(AA) + \frac{1}{2} f(Aa)$$

$$f(a) = q = f(aa) + \frac{1}{2} f(Aa)$$

$$p + q = f(AA) + f(Aa) + f(aa) = 1$$

from this we get

$$q = 1 - p \quad and \quad p = 1 - q$$

GENOTYPE FREQUENCY

- Genotype frequency is the proportion of a population that has one genotype relative to all genotypes at a specific locus.
- For example: Two alleles are possible - *A* or *a*, that can combine to give the following genotypes *AA* (homozygous dominant), *Aa* (heterozygous), *aa* (homozygous recessive).

Genotype	No. of individuals	Genotype frequency
AA	60	f(AA) = 60/200 = 0.3 or 30%
Aa	100	f(Aa) = 100/200 = 0.5 or 50%
aa	40	f(aa) = 40/200 = 0.2 or 20%
Total	**200**	=1.0 or 100%

GENETIC VARIATION

- Some of the causes for genetic variation being present within a population are

- Polymorphism
- Crossing over
- Independent assortment of the homologous pairs of chromatids
- Mutation - gene and chromosome
- Random fertilisation

FACTORS AFFECTING GENETIC CONSTITUTION

Factors affecting genetic constitution of a population

- Selection
  - Variation in fitness and heritability favors a single phenotype and therefore allele frequency continuously shifts in one direction
- Mutation
  - Change in DNA of genes and thereby introduce new allele are introduced into the gene pool
- Migration
  - Migration means movement of individuals
  - This movement introduces new alleles into the population (gene flow).
  - The gene frequencies in the population may be changed by immigration of individuals from another population or emigration of individuals from the population.
  - Dispersal of animals, pollen on the wind etc.
- Recombination
  - Exchange of gene segments shuffle the genes into new combinations which can result in organisms exhibiting different traits.
- Mating system
  - Mating system two types: Random mating (Panmixia) and Non-random mating.
  - Individuals those are more closely (inbreeding) or less closely related mate more often rather than by chance.
  - Resulting in c hange of genetic constitution of a population.
- Random Genetic Drift
  - If populations are small enough, by chance, sampling will result in a different allele frequency from one generation to the next.
- Differences in fertility and viability
  - The individuals in a population (different genotypes) differ in fertility and contribute unequally to the next generation thus changing the gene frequency in the subsequent generation.

MODULE-22: HARDY WEINBERG LAW

Learning objectives

After completing this module, the learner should be able to:

- understand the concept of Hardy - Weinberg Law
- understand the five conditions that hold for Hardy-Weinberg Equilibrium
- predict genotype frequencies in a population given allele frequencies and assuming random mating using Hardy - Weinberg Proportions

HARDY- WEINBERG LAW

- Hardy-Weinberg law was proposed independently in 1908 by Wilhelm Weinberg, a German physician, and Godfrey Harold Hardy, a British mathematician.

Both gene and genotype frequencies in a population remain constant generation after generation when the population is large; mating is at random and in the absence of selection, mutation and migration.

- When the gene frequency remains constant generations after generations, the population is in genetic equilibrium or Hardy-Weinberg equilibrium non-evolutionary model.
- When the population is in genetic equilibrium, the rate of evolution is zero. That is, when a population obeys, hardy-Weinberg law the population will not undergo evolution. So evolution occurs only when Hardy-Weinberg equilibrium is altered.
- The Hardy-Weinberg law is represented by a simple formula.
    - For 2 alleles (A_1 and A_2) of one gene

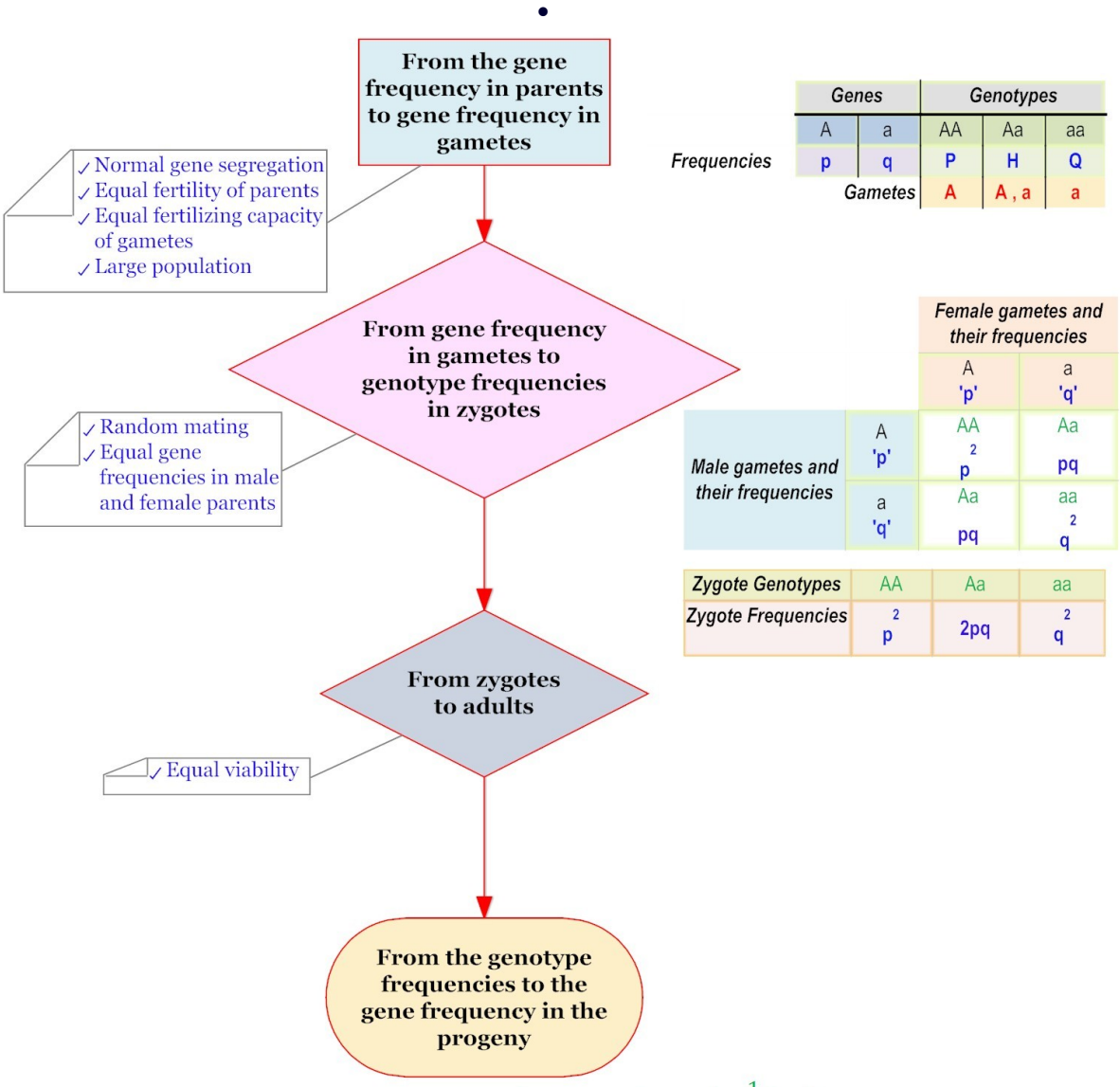
      p = f(A) Frequency of 'A_1' gene
      q = f(a) Frequency of 'A_2' gene

    - Then the next generation will have:
        - The frequency of homozygotes is equal to the gene frequency squared
            - The frequency of the A_1A_1 genotype = p^2
            - The frequency of the A_2A_2 genotype = q^2
        - The frequency of heterozygotes is equal to twice the product of the two gene frequencies
            - The frequency of the A_1A_2 genotype = 2pq
    - For a dimorphic gene the Hardy-Weinberg equation is based on the binomial distribution:
        - $p^2 + 2pq + q^2 = 1$
    - This formula is used to find out the frequency of dominant gene and recessive gene in a population.

p = Frequency of dominant gene
q = Frequency of recessive gene
p^2 = Frequency of dominant homozygote
2pq = Frequency of heterozygote
q^2 = Frequency of recessive homozygote

        - Hardy-Weinberg law lays the foundation for the study of population genetics.
- It gives a mathematical approach for genetics and evolution.
- The relationship between gene (allele) frequencies and genotype frequencies expressed by the H-W equation only holds if these 5 conditions are met
    - no new mutations
    - no migration in or out of the population
    - no selection (all genotypes have equal fitness)
    - random mating
    - very large population

PROOF OF HARDY-WEINBERG LAW



	Genes		Genotypes		
	A	a	AA	Aa	aa
Frequencies	p	q	P	H	Q
Gametes			A	A , a	a

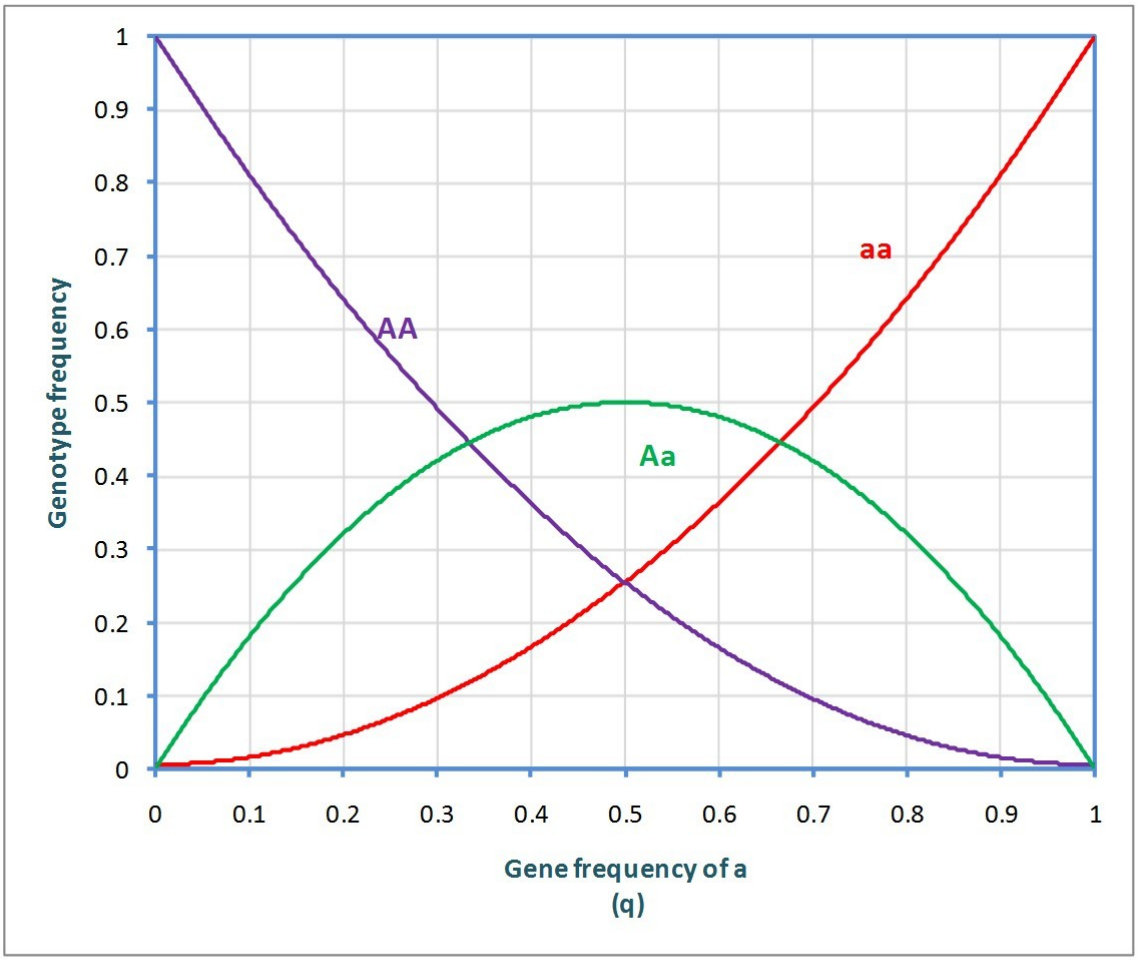
		Female gametes and their frequencies	
		A 'p'	a 'q'
Male gametes and their frequencies	A 'p'	AA p^2	Aa pq
	a 'q'	Aa pq	aa q^2

Zygote Genotypes	AA	Aa	aa
Zygote Frequencies	p^2	2pq	q^2

$$Gene\ frequency\ of\ A = p^2 + \frac{1}{2}(2pq)$$
$$= p(p+q) \ \ since\ p+q=1$$
$$= p\ [which\ is\ same\ as\ the\ parent\ generation]$$

$$Gene\ frequency\ of\ a = q^2 + \frac{1}{2}(2pq)$$
$$= q(p+q) \ \ since\ p+q=1$$
$$= q\ [which\ is\ same\ as\ the\ parent\ generation]$$

RELATIONSHIP BETWEEN GENOTYPE AND GENE FREQUENCIES



Relationship between genotype frequencies and gene frequency for two alleles in a population in Hardy-Weinberg equilibrium

- The properties of the population with respect to a single autosomal locus expressed in the Hardy-Weinberg law are:
  - A large random mating population in the absence of migration, mutation and selection is stable with respect to both gene and genotype frequencies.
  - The genotype frequencies in the progeny produced by random mating among the parents are determined solely by the gene frequency among parents.
  - The frequency of homozygotes equals the square of the relevant gene frequency.
  - The frequency of heterozygote equals twice the product of the relevant gene frequencies. Since the frequencies of the genotypes of the homozygotes correspond to the squares of gametic frequencies.
  - Such populations is said to be genetic equilibrium. For a single autosomal locus, the Hardy-Weinberg genotype frequencies are established by one generation of random mating irrespective of the genotype frequencies among parents.
  - For a single locus with two alleles: the maximum frequency of heterozygote will be 0.5. Then p=q=0.5

APPLICATIONS OF HARDY-WEINBERG LAW

Hardy-Weinberg law has the following applications:

- Calculation of frequencies of recessive and dominant genes in a population
- Calculation of frequency of carriers or heterozygotes in a population
- To test for agreement with a population in Hardy -Weinberg equilibrium

Calculation of frequencies of recessive and dominant genes in a population

- Gene frequencies can be determined from their genotype frequencies, but for this it is necessary to know the frequencies of all three genotypes.
- When there is complete dominance at a locus the expression q = Q + ½ H cannot be used as the classification of genotypes is not possible.
- The heterozygote genotype frequency cannot be estimated, as it cannot be phenotypically distinguished from dominant homozygote.
    - e.g.: Stem length in garden pea plant
        - Tall - dominant (TT, Tt)
        - Dwarf - recessive (tt)
- However, if all the genotypes are in Hardy – Weinberg equilibrium, we need not know the frequencies of all genotypes.
    - Let T - be a dominant gene with a frequency of p and t - be a recessive gene with a frequency of q ; then the frequency of tt homozygote is q^2 and therefore the frequency of recessive allele will be square root of the homozygote frequency.
- For this estimation to be valid there should not be selective elimination of recessive homozygotes.
- Since $p + q = 1$
- p (frequency of dominant allele) = $1 - q$

(TOP)

Calculation of frequency of carriers or heterozygotes in a population

- It is often of interest to know the frequency of heterozygotes or carriers of recessive genes or recessive abnormalities. This can be calculated if the gene frequency is known.
- If Hardy-Weinberg equilibrium is assumed the frequency of heterozygotes among all individuals in the population can be estimated from the formula $2pq = 2q\ (1-q)$.
    - Example: if q^2 is 0.04 then the gene frequency is q = $(0.04)^{1/2}$ = 0.2
    - The frequency of heterozygote is $2q\ (1-q)$ = 2 × 0.2 × (1-0.2) = 2× 0.2× 0.8 = 0.32
    - 0.32 or 32% is of carriers or hererozygotes.

(TOP)

To test for agreement with a population in Hardy -Weinberg equilibrium

- If data are available for a locus where all the genotypes are recognizable then the observed genotype frequencies are used to test for Hardy-Weinberg equilibrium.
- According to the Hardy-Weinberg law, the genotype frequencies of progenies are determined from the gene frequencies of their parents.
- If the population is in H-W equilibrium, frequency is same in progenies as in parents.
- From the gene frequency expected genotype frequencies are calculated. From them the expected numbers are arrived. The agreement between the expected and observed numbers is tested using Chi-square test.

- Example:
  - In a given population of randomly mating gerbils, 500 homozygote brown (BB), 400 heterozygote brown (Bb) and 100 homozygote black (bb) gerbils were observed.
  - Test whether this population is in Hardy-Weinberg equilibrium.
  - NOTE: the black allele (b) is recessive to the wild type brown (agouti) allele (B).

	Genotype				Gene frequency	
	BB	Bb	bb	Total	p	
ıber erved	500	400	100	1000	{500+(400x0.5)}/1000 =0.7	1-(
ıber ected	$(0.7)^2$x1000 = 490	(2x0.7x0.3)x1000 = 420	$(0.3)^2$x1000 = 90	1000		
erence (O –	10	-20	10			
)² / E	0.204	0.952	1.111			

- Chi-square value = 2.267
- P value = 0.32
- The discrepancy is not significant and could easily have arisen by chance in the sampling.
- We conclude that the genotype frequencies in this population are not significantly different than what would be expected if the population is in Hardy-Weinberg equilibrium

(TOP)

HARDY-WEINBERG LAW-MULTIPLE ALLELES

- If dominance is lacking, calculation of gene frequency is simple in multiple allelic systems.
- The best gene frequency estimate comes from simple gene counting.
- For example, in European cattle breeds, three transferrin alleles A, D and E occur.
- No dominance exists and so six genotypes can be distinguished, i.e., AA, AD, AE, DD, DE and EE.
- If we let these symbols denote the numbers of each genotype and N denotes the total number, we may calculate the gene frequencies as follows:

$$f(A) = p = \frac{2AA + AD + AE}{2N}$$

$$f(D) = q = \frac{2DD + DA + DE}{2N}$$

$$f(E) = r = \frac{2EE + EA + ED}{2N}$$

- For a three allele system, the equilibrium genotype frequencies can be expressed algebraically as p + q + r = 1

$$(p + q + r)^2 = p^2 + q^2 + r^2 + 2pq + 2pr + 2qr = 1$$

- The ABO blood groups in man are determined by a series of three multiple allelic genes: A, B and O alleles.
- If there is dominance, then the estimation is slightly complicated, and approximate methods have to be used.

HARDY-WEINBERG LAW: SEX-LINKED GENES

- In mammals, the female is the homozygous sex, with two X chromosomes (XX), while the male is heterozygous, with one X and one Y chromosome (XY).
- Genes on the X or Y chromosome are called sex linked genes.
- The relationship between gene frequency and genotype frequency in the homogametic sex is the same as with an autosomal gene; but the heterogametic sex has only two genotypes and carries only one gene instead of two.
- So , two-thirds of the sex-linked genes in the population are carried by the homogametic sex and one-third by the heterogametic sex.
- Consider two alleles A and a with frequency *p* and *q*

	Female			**Male**	
Genotype	AA	Aa	aa	A	a
Genotype Frequency	*P*	*H*	*Q*	*R*	*S*

- The frequency of A among the females is

$$p_f = P + \frac{1}{2}H$$

- The frequency of A among the male is

$$p_m = R$$

- The frequency of A in the whole populations is

$$\overline{p} = \frac{2}{3}p_f + \frac{1}{3}p_m$$

$$\overline{p} = \frac{1}{3}(2\,p_f + p_m)$$

$$\overline{p} = \frac{1}{3}(2P + H + R)$$

- Hence, if gene frequencies among males and among females are different, the population will not be in equilibrium.
- The gene frequency in the population as a whole does not change; but its distribution between the two sexes oscillates as the population approaches equilibrium.
- This oscillation is because of getting sex linked genes in males only from their mother.

$$p'_m = p_f$$

- Females get their sex linked genes equally from both parents

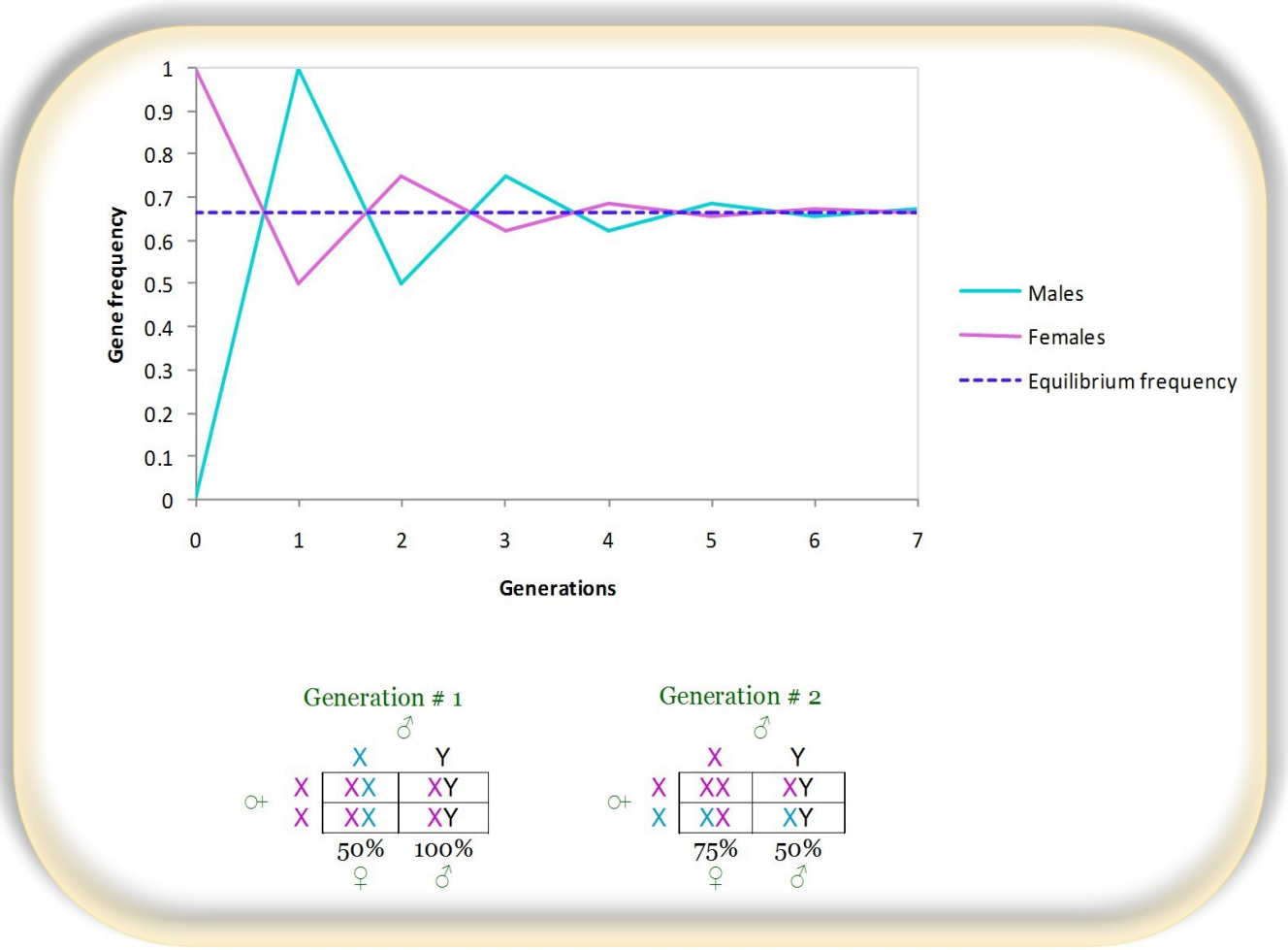
$$p'_f = \frac{1}{2}(p_f + p_m)$$

- The difference between the frequencies in the two sexes is

$$p'_f - p'_m = \frac{1}{2}(p_f + p_m) - p_f$$

$$p'_f - p'_m = -\frac{1}{2}(p_f - p_m)$$

- It is half the difference in the previous generation. Therefore, if the gene frequencies are different in males and females then one generation of random mating is not sufficient to achieve Hardy-Weinberg equilibrium.
- It may take several generations and the number of generations will depend on the magnitude of difference between the sexes in gene frequency.
- The difference in gene frequency between the sexes will be halved as compared to the previous generation and the sign will be opposite.



- The most important implication is that sex-linked characters are expected to occur with different frequencies in males and females.
- This is relevant to the sex-linked recessive traits for which the frequency of the condition in males (q) is expected to be much higher than the frequency of the conditions in females (q^2).

MORE THAN ONE LOCUS

- The attainment of equilibrium in genotype frequencies after one generation of random mating is true of all autosomal loci considered individually.
- But it is not true of the genotypes considered jointly .
- Consider a population made up of equal numbers of AABB and aabb individuals of both sexes. The gene frequency at both loci is 0.5.
- If the individuals are mated at random the possible genotypes are:

AABB	**AaBB**	**aaBB**
AABb	**AaBb**	**aaBb**
AAbb	**Aabb**	**aabb**

- Only three out of nine genotypes would appear in the progeny in the next generation i.e. the two original homozygotes (AABB and aabb) and the double heterozygote (AaBb).
- The genotype AAbb would be absent though its frequency in equilibrium population would be 1/16.
- The missing genotypes appear in subsequent generations but not immediately at their equilibrium frequency.
- Therefore when two loci are considered together the genotype frequencies will reach equilibrium after several generations of random mating.
- If three loci are considered together, then the number of generations required to reach equilibrium genotype frequencies will be more than that required for two loci considered jointly.

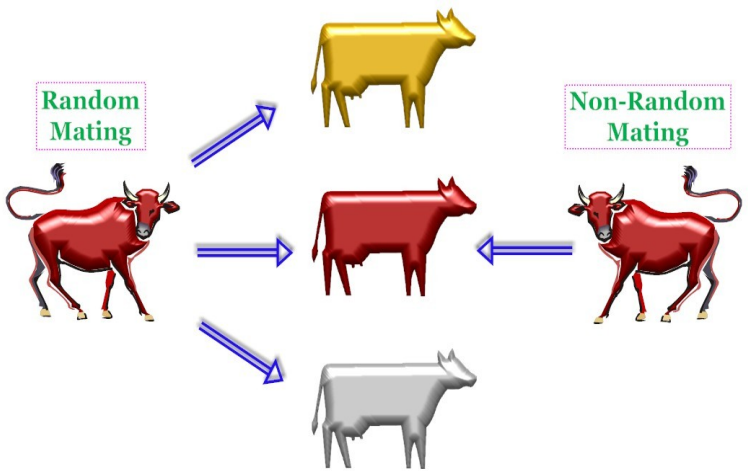
Linked loci

- Under random mating, loci that are linked approach equilibrium more slowly than do loci segregating independently.
- Further more closely the linkage the slower the approach to equilibrium. When equilibrium is reached coupling and repulsion phases are equally frequent:
    - Coupling heterozygotes:
    - AB / ab Repulsion heterozygotes: Ab / aB

FACTORS UPSETING HARDY - WEINBERG EQUILIBRIUM

- This deviation of the equilibrium is brought about by the following evolutionary forces,
    - Mutation.
    - Natural selection.
    - Non-random mating.
    - Genetic drift and
    - Migration and gene flow.

NON-RANDOM MATING



- Nonrandom mating occurs when the probability that two individuals in a population will mate is not the same for all possible pairs of individuals.
- There are two types of non-random mating

Assortative mating

- If mated pairs are of the same phenotype more than would occur by chance this is called assortative mating.
- Mates are genetically similar Example: inbreeding – mating between close relatives includes self-pollination.

Disassortative mating

- Disassortative mating is mating of individuals of different phenotypes.
- Mates are genetically different.

MODULE-23: CHANGE OF GENE AND GENOTYPIC FREQUENCIES

- Learning objective
- After completing this module, the learner should be able to understand the agents that change and affect the genetic makeup of populations.

FORCES OR AGENCIES CHANGING GENE AND GENOTYPE FREQUENCIES

- A large random mating population is stable with respect to gene frequencies and genotype frequencies in the absence of agencies tending to change its genetic properties.
- The shifts or changes in frequencies can be produced by two sorts of process.

Systematic processes

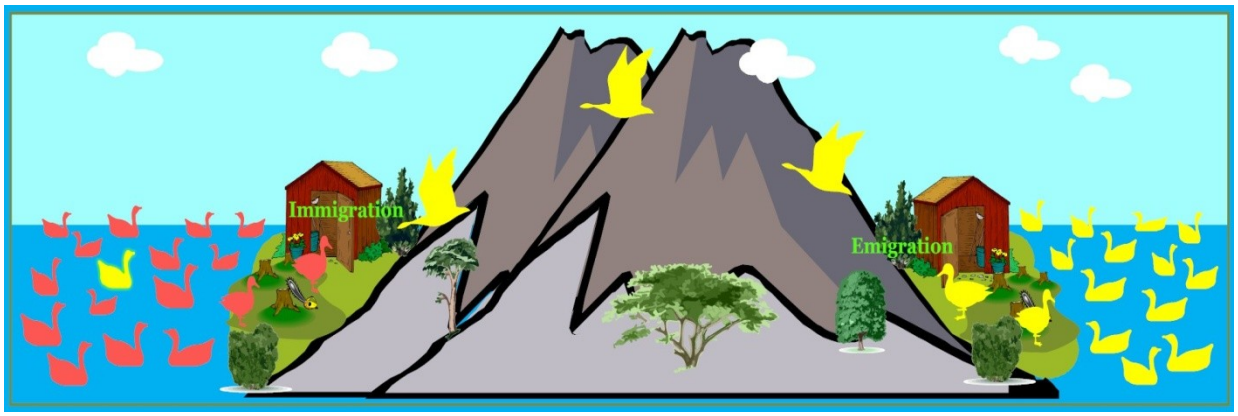
- These tend to change the gene frequency in a manner predictable both in amount and in direction.
- These act both in large and small population.
    - There are three systematic processes :
        - Migration
        - Mutation and
        - Selection.

Dispersive process

- This arises in small populations from the effects of sampling and predictable in amount but not in direction.
- These act only in small population from the effect of sampling.

MIGRATION

- Migration is the movement of individuals from one breeding population to another.
  - *Immigration* is the inward migration of individuals into a population from other populations.
  - *Emigration* is the outward migration of individuals from a population. This brings about the reduction in the size of the gene pool.
- The migration of breeding animals to or from a population can cause changes in gene frequency.



- Let us suppose that a large population consists of a proportion of "*m*" of new immigrants in one generation then the remainder (*1-m*) being natives.
  - Number of natives = n_1
  - Number of immigrants = n_2

$$m = \frac{n_2}{n_1 + n_2}$$

$$1 - m = \frac{n_1}{n_1 + n_2}$$

- Let the frequency of a certain allele (A) be q_m among the immigrants and q_o among the natives.

- Then the frequency of the allele in the mixed population q_1 will be

$q_1 = m\, q_m + (1 - m)\, q_o$

$q_1 = m\, q_m + q_o - m\, q_o$

$q_1 = m\, q_m - m\, q_o + q_o$

$q_1 = m\, (q_m - q_o) + q_o$

- The gene frequency in mixed population will depend on the original gene frequency of the population and the difference in gene frequency between the immigrants and native ($q_m - q_o$) and the proportion of immigrants.
- The change of gene frequency Δq brought about by one generation of immigration is the difference between the frequency before immigration and the frequency after immigration.

$\Delta\, q = q_1 - q_o$

$\Delta\, q = m\, (q_m - q_o) + q_o - q_o$

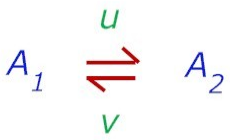
$\Delta\, q = m\, (q_m - q_o)$

- Thus the rate of change of gene frequency in a population subject to immigration depends on the immigration rate and the difference in gene frequency between the immigrants and the natives.

MUTATION

- Mutations could lead to occurrence of new alleles and thereby it changes the gene pool of the population.
- It may be favourable or deleterious to the individual's ability to survive.
- If changes are advantageous, then the new alleles will tend to prevail by being selected in the population.

- If a wild allele A_1 mutates to A_2 with a frequency of u per generation.
- u is the proportion of all A_1 alleles that mutate to A_2 between one generation and the next.
- If the frequency of A_1 in one generation is p_o
- Then
  - The frequency of newly mutated gene A_2 in the next generation = $u\, p_o$
  - The new gene frequency of A_1 in the mutated population = $p_o - u\, p_o$
  - Therefore the change of gene frequency = $-\, u\, p_o$
- Suppose the gene mutates in both directions and the initial allele (gene) frequencies are p (A_1), q (A_2)



- Then the change of gene frequency in one generation
  - $\Delta q = up - vq$
- This situation leads to equilibrium in gene frequency at which no further change takes place. The point of equilibrium can be found by equating the change of frequency Δ q to zero.
  - $pu - qv = 0$
  - $qv = pu$
  - $qv = (1-q)u$
  - $qv = u - qu$
  - $qv + qu = u$
  - $q(v+u)=u$
  - $q = u / (u + v)$
  - Similary $p = v / (v + u)$
- If the mutational rates of A_1 to A_2 (u) and A_2 to A_1 (v) are known at equilibrium then the frequency of A_1 allele and A_2 allele can be calculated directly without using conventional method of estimating gene frequency

SELECTION

- Selection is differential reproduction. It occurs whenever the various kinds of individuals reproduce at different rates.
- Individuals differ in viability and fertility and contribute different number of progeny to the next generation.
- The contribution of offspring to the next generation is called fitness (W) of the individual or adaptive value or selective value.
- Selection favoring certain genotypes should cause alleles to increase in frequency and vice versa.
- The strength of selection is expressed as the *coefficient of selection* "s" which is the proportionate reduction in the gametic contribution of a particular genotype compared with the standard genotype, the usually most favoured one.
- If the fitness of the standard genotype is taken as 1, then the fitness of the genotype selected against is 1 – s.
  - W = 1 - s

Complete selection against dominant gene

- The coefficient of selection is *1* or fitness is *0*
- One generation of selection is sufficient to eliminate all the dominant genes provided there is complete penetrance.
- In the next generation, all the individuals will be of recessive homozygotes and the frequency of recessive allele (q) will be one.

Selection against recessive homozygote (partial selection against recessive)

	Genotypes			
	$A_1 A_1$	$A_1 A_2$	$A_2 A_2$	Total

Initial frequency	p_o^2	$2p_oq_o$	q_o^2	1
Coefficient of selection	0	0	s	
Fitness	1	1	1-s	
Gametic contribution	p_o^2	$2p_oq_o$	$q_o^2(1-s)$	$1-s\ q_o^2$

$$q_1 = \frac{q_0 - sq_0^2}{1 - sq_0^2}$$

- The change in gene frequency of a recessive allele as a result of selection

$$\Delta q = q_1 - q_0 = -\frac{sq_0^2(1 - q_0)}{1 - sq_0^2}$$

- Complete selection against recessive: It will not be possible because we can eliminate only those recessive alleles which are present in recessive homozygote, leaving the heterozygote undetected.
- Number of generations required
  - The number of generations required to change the gene frequency from q_o to q_t is

$$t = \frac{1}{q_t} - \frac{1}{q_0}$$

where t = number of generations

q_t is the frequency after t generations of complete elimination of recessives

q_o is the initial (recessive) gene frequency

Selection favouring heterozygote (Overdominance)

- If the fitness of the heterozygote is superior to the respective homozygote then selection will favour heterozygote

	Genotypes			
	A_1A_1	A_1A_2	A_2A_2	Total
Initial frequency	p_o^2	$2p_oq_o$	q_o^2	1
Coefficient of selection	s_1	0	s_2	
Fitness	$1-s_1$	1	$1-s_2$	

Gametic contribution	$p_o^2(1-s_1)$	$2p_oq_o$	$q_o^2(1-s_2)$	$1-s_1p_o^2-s_2q_o^2$

$$\Delta q = \frac{p_0 q_0 (s_1 p_0 - s_2 q_0)}{1 - s_1 p_0^2 - s_2 q_0^2}$$

- When selection favours the heterozygote, the gene frequency of the two alleles A_1 and A_2 tend towards equilibrium at an intermediate value, both alleles remaining in the population.
- The condition for equilibrium is that $\Delta q = 0$ and is fulfilled in generation when $s_1 p = s_2 q$

$$q = \frac{s_1}{s_1 + s_2} \text{ and similary } p = \frac{s_2}{s_1 + s_2}$$

DISPERSIVE PROCESS

- Dispersive process differs from systematic processes in being random in direction and predictable only in amount.
- If systematic factors were present, as in very large population, gene frequencies would reach equilibrium and remain there until external conditions change.
- This property of stability does not hold in small populations and the gene frequencies are subject to random fluctuations arising from sampling of gametes.
- The gametes that transmit genes to the next generation carry a sample of the genes in the parent generation.
- If the sample is not large, the gene frequencies are liable to change from one generation to the next.

Causes

- Small population size
- Founder effects – occurs when a population is initially established by small number of breeding individuals
- Bottleneck effect – occurs when a population is dramatically reduced in size

Effects

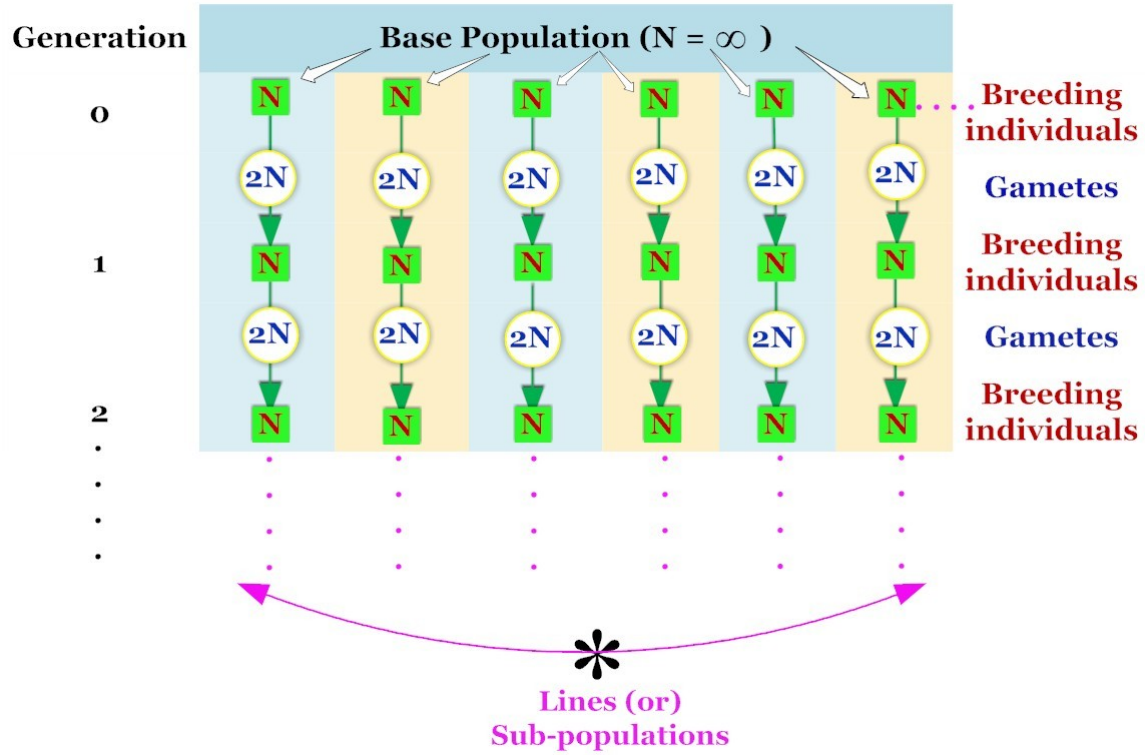
- Random drift
- Differentiation between sub-populations
- Uniformity within sub-populations
- Increased homozygosity

THE IDEALIZED POPULATION

- The Idealized Population In order to deduce the dispersive process to its simplest form we imagine an idealized population as follows:
    - Suppose there is one large population in which mating is random, and this population becomes sub divided into a number of sub-populations.

- The initial random mating populations will be referred as the base population and the sub-populations will be referred to as lines.
- Each line is considered as a small population in which gene frequencies are subject to the dispersive process.

- Conditions for the idealized population are as follows:
  - The generations are distinct and do not overlap.
  - Mating is restricted to members of the same line or in other words migration is excluded.
  - The number of breeding individuals is equal for all lines and in all generations.
  - Mating is random within each line.
  - Selection is absent.
  - Mutation is disregarded.



- The conditions specified for the idealized population may not hold in real population.

VARIANCE OF GENE FREQUENCY

- The change of gene frequency Δq resulting from sampling in one generation can be stated in terms of its variance
  - This variance of Δq expresses the magnitude of the change of gene frequency resulting from dispersive process.
  - In the next generation, the sampling process is repeated starting from the gene frequency in the previous generation.
  - The effect of continued sampling through successive generations is that each line fluctuates irregularly in gene frequency and the lines spread apart progressively, thus becoming differentiated.
  - Sooner or later each line must reach the limits of *0* or *1*.
  - When a particular allele frequency has reached *1* it is said to be fixed in that line and if it reaches *0* it is lost.

- When a particular allele is fixed in all individuals in a line; all are identical for that genotype and become genetically identical.
- This is the basis of the genetic uniformity of highly inbred strains.

$$\sigma^2_{\Delta q} = \frac{pq}{2N}$$

where N - subpopulation or line size (sample)

INBREEDING

Inbreeding means the mating together of individuals that are related to each other by ancestry

- Pairs mating at random are more closely related to each other in a small population than in a large one.
- Hence, the properties of small population can be treated as the consequence of inbreeding.
- So the degree of relationship between the individuals in a population depends on the size of the population.
- Genes may be similar or identical due to two different reasons
- Homozygotes – *Identical by descent*
  - Two genes are identical by descent (autozygous) if they are biochemical replicates produced without mutation from a common ancestral gene.
- Homozygotes - *Alike in state (independent/ allozygous)*
  - Two genes are regarded as alike because of their nucleotide sequence and similar function.

Inbreeding coefficient

- Inbreeding coefficient is probability that the two genes at any locus in an individual are identical by descent.
- The symbol for coefficient inbreeding is *F*.

Panmictic index is the probability that genes at any single locus are independent by descent P = (1 – F)

- The inbreeding coefficient of subsequent generations expresses the amount of dispersive process that has taken place since the formation of the base population.
- The amount of dispersive process expressed in terms of increment of inbreeding or rate of inbreeding is $\Delta F = 1/2N$
  - Where ΔF is the increment in inbreeding in each generation and N is the number of breeding individuals in the population.
- Therefore, the increment of inbreeding can be used instead of the population size to estimate the variance of change of gene frequency

$$\sigma^2_{\Delta q} = \frac{pq}{2N} = pq\Delta F$$

EFFECTIVE POPULATION SIZE

- In domestic animals, the sexes are often unequally represented among breeding individuals and, in general, fewer males than females are used.

Genetically Effective Population Size: "The number of breeding individuals in an idealized population that would show the same amount of dispersion of allele frequencies under random genetic drift or the same amount of inbreeding as the population under consideration"

- The effective population size is based on the number of genes in the population that can be passed on to the next generation. The symbol is N_e (N-effective)
- N_e the harmonic mean of the two sexes

$$\frac{4}{N_e} = \frac{1}{N_{males}} + \frac{1}{N_{females}}$$

$$N_e = \frac{4N_m N_f}{N_m + N_f}$$

Then the rate of inbreeding is

$$\Delta F = \frac{1}{8N_m} + \frac{1}{8N_f}$$

- Rate of inbreeding is inversely proportional to the effective population size.
- That is, the smaller the effective population size, the greater the increase in inbreeding per generation.
- Thus increase in the number of homozygote in the smaller population.

MODULE-24: QUANTITATIVE INHERITANCE

Learning objectives

After completing this module, the learner should be able to:

- distinguish between qualitative and quantitative traits
- understand the quantitative traits values and means of population

QUANTITATIVE TRAITS

- Continuously varying characters are called quantitative characters or metric characters (Example: economically important traits such as height, weight, milk yield, wool yield, egg production etc.) and variation in them is called quantitative variation or continuous variations.

Quantitative genetics is the study of continuous traits and their underlying mechanisms.

- Quantitative traits are controlled by multiple genes, each segregating according to Mendel's laws.
- The inheritance of quantitative traits or poly genes is called Quantitative inheritance, Multiple factor inheritance, Multiple gene inheritance or Polygenic inheritance.

PHENOTYPIC TRAITS	
Qualitative Traits	**Quantitative Traits**
Traits of kind	Traits of degree
Discrete phenotypic classes ↓ Discontinuous variations	A spectrum of phenotypic classes ↓ Continuous variations
Each trait is governed by two or many alleles of a single gene	Each trait is governed by many non-allelic genes or poly genes.
Single gene effects can be detected	Due to poly genetic control effects single gene effects can be detected too slightly
The phenotypic expression of a gene is not influenced by environment.	The phenotypic expression is affected by environmental conditions to varying degrees
Analysis is made by counts and ratios.	Analysis is made by statistical methods.

VALUES AND MEANS

- Genetic properties of a population are expressed in terms of gene frequencies and genotype frequencies.
- To understand the connection between gene frequencies and the quantitative differences exhibited in a quantitative/metric character, the concept of value is introduced.
- A given quantitative trait is characterized by a mean value and a standard deviation expressed in metric units by which the character is measured.

Phenotypic value (*P*)

- The phenotypic value of a given quantitative trait is the yield of the individual with respect to the trait.
- The phenotypic value symbol is *P*.
- The phenotypic value can be measured and is evaluated in relation to the population mean value.
- The phenotypic value (*P*) of an individual is determined by the combined effect of the genotypic value (*G*) and the environmental deviation (*E*)

$P = G + E$

Genotypic value (*G*)

- Genotype is the sum total of genes possessed by an individual in pairs and environment is all the non-genetic circumstances that influence the phenotypic value.
- For any individual the genotypic value (G) is determined by the combined effect of all genes in all the loci which influence the trait.
- The genotypic value symbol is *G*.

Environmental deviation (E)

- The environmental deviation represents the combined effect of all non-genetic factors that have influenced the phenotypic values.
- The environmental deviation symbol is *E*.
- The genotype will confer certain value on the individual whereas the environment causes a deviation from this in one direction or the other.
- For a single locus, the mean environmental deviation in the whole population is taken to be zero. So the mean phenotypic value is equal to the mean genotypic value.

GENOTYPIC VALUE

- Genotypic value may be calculated by taking a mean of a large population with same genotype raised under similar conditions.
- Here mean environmental deviation in the whole population is taken as zero.
- The genotypic value is partitioned into additive gene action, dominance and epistatis.
    - $G = A + D + I$

where

- G - Genotypic value
- A - Additive value
- D - Dominance deviation and
- I - Interaction or epistatic value

- Considering a single locus with two alleles, A_1 and A_2.
    - The genotypic value of
        - A_1A_1 homozygote = $+a$
        - A_2A_2 homozygote = $-a$ and
        - A_1A_2 heterozygote = d
    - The value of d of the heterozygote depends on the degree of dominance.
    - The degree of dominance may be expressed as d/a .

POPULATION MEAN

- Consider the following assumption:
    - Diploid organism
    - Diallelic autosomal locus

- Random mating population
- The mean phenotype is obtained by summing the frequency weighted genotypic values (assuming that the environmental deviation is zero for each genotype).
- Let the gene frequency of A_1 and A_2 be p and q

Genotype	Frequency	Genotypic value	Frequency-weighted genotypic value
$A_1 A_1$	p^2	$+a$	p^2a
$A_1 A_2$	$2pq$	d	$2pqd$
$A_2 A_2$	q^2	$-a$	$-q^2a$
Total			$\boldsymbol{a(p-q)+2pqd}$

- The contribution of any locus to the population mean has two terms: $a\,(p\text{-}q)$ attributable to the homozygote and $2pqd$ attributable to heterozygote.
- With additive combinations the population mean value resulting from the joint effects of several loci is the sum of the contributions of each locus.
  - $Population\ mean\ (M) = \Sigma\, a\,(p - q) + 2\,\Sigma\, pqd$
- Population Mean Genotypic Value is a function allele frequency. This Population Mean Genotypic Value is identical to the population mean phenotypic value if the mean environmental deviation is zero.

MODULE-25: AVERAGE EFFECT AND BREEDING VALUE

Learning objectives

After completing this module, the learner should be able to:

- understand the concept of average effect and breeding value and its properties

AVERAGE EFFECT

- Parents pass on their genes and not their genotypes to the next generation.
- Thus genotypic value cannot be transmitted from parents to offspring.
- A new measure of value is therefore needed which will refer to genes.
- The new measure is the *average effect* **.**

The average effect of a gene is the mean deviation from the population mean of individuals which received that allele from one parent, with the other allele received from the other parent having come at random from the population

- The average effect of a gene depends on the gene frequency. The average effect is therefore a property of the population as well as of the gene.
- Consider a locus with two alleles A_1 and A_2 at frequencies p and q respectively.
  - Let us first take the average effect of the gene A_1 , for which we shall use the symbol $\propto_1$.
  - If A_1 gametes unite at random with gametes from the population

        - $A_1 A_1$ genotype produced frequency = p of and
        - $A_1 A_2$ genotype produced frequency = q
        - The genotypic value of $A_1 A_1 = +a$ and that of $A_1 A_2 = d$
        - The mean of these = pa + qd (taking of the proportions in which they occur)
    - Average effect of the A_1 gene $(\propto_1) = pa + qd - M$
        - $\propto_1 = pa + qd - \{ a (p - q) + 2pqd \}$
        - $\propto_1 = q [a + d (q - p)]$
    - Similary for the A_2 gene
        - $\propto_2 = -p [a + d (q - p)]$
    - Now consider the average effect of the gene substitution. This is the difference which would be caused by changing one allele in an average individual into the other allele, so that $\propto = p (a - d) + q (d + a) = a + d (q - p)$
        - The relation of $\propto$ to $\propto_1$ and $\propto_2$ can be seen as
            - $\propto_1 - \propto_2 = a + d (q - p) = \propto$
    - Therefore $\propto_1 = q \propto ; \propto_2 = -p \propto$

BREEDING VALUE (BV)

- The value of an individual, as measured by the average value of its progeny is called the breeding value of the individual .
- This is also the sum of the average effects alleles (α - *alpha*) of the individual.

If an individual is mated to a number of individuals at random, from the population then its breeding value is twice the mean deviation of the progeny from the population mean (since the individual only contributes half of the alleles to its offspring) .

    - Breeding value = the value of genes to progeny
    - Genetic value = the value of genes to self
- It includes non-additive effects (such as dominance) which cannot be passed on to progeny

Genotype	Breeding value
$A_1 A_1$	$2 \alpha_1 = 2q \alpha$
$A_1 A_2$	$\alpha_1 + \alpha_2 = (q - p) \alpha$
$A_1 A_2$	$2 \alpha_2 = -2p \alpha$

- The mean breeding value = $2p^2q \alpha + 2pq (q-p) \alpha - q^2p \alpha = 2pq \alpha (p + q - p - q) = 0$.
    - With random mating, the mean breeding value is zero.
- *A* (additive genetic effect) is also sometimes referred to as breeding value.

DOMINANCE DEVIATION

- When a single locus only is under consideration, the difference between the genotypic value (G) and the breeding value (A) of particular genotype is known as dominance deviation. (Deviations of the genotypic value from the breeding value are dominance deviations).

- The genetic effects (*G*) can be further partitioned, ignoring interactions among loci,

$G = A + D$

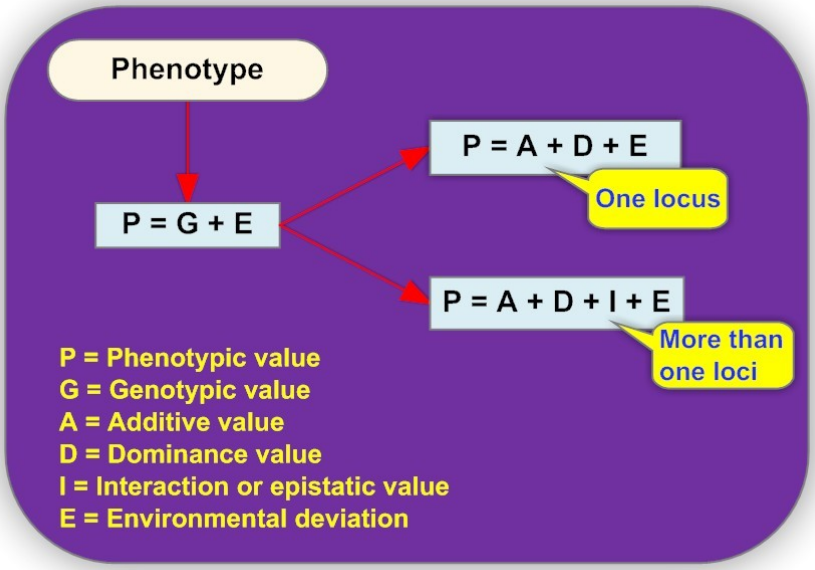
Where

- *A* - Additive effects *(* sum of the breeding values) and
- *D* - Dominance deviations

- The dominance deviation arises from the property of dominance between alleles at the same locus .

INTERACTION DEVIATION

- When only a single locus is under consideration, the genotypic value is made up of breeding value and dominance deviation only.
  - $G = A + D$
- Metric traits are polygenic in inheritance and the genotype refers to more than one locus, the genotypic value may contain an additional deviation due to non-additive combination.
  - $G = A + D + I$
  - The deviation *I* is called the interaction deviation or epistatic deviation.
- We know that
  - $P = G + E$
- So now the phenotypic value can be partitioned as
  - $P = A + D + I + E$



MODULE-26: COMPONENTS OF VARIANCE

Learning objectives

After completing this module, the learner should be able to:

- understand the concept of genetic variance
- understand the different components of the phenotypic variance; the components of values and corresponding variance
- understand the properties of genotypic variance and environmental variance

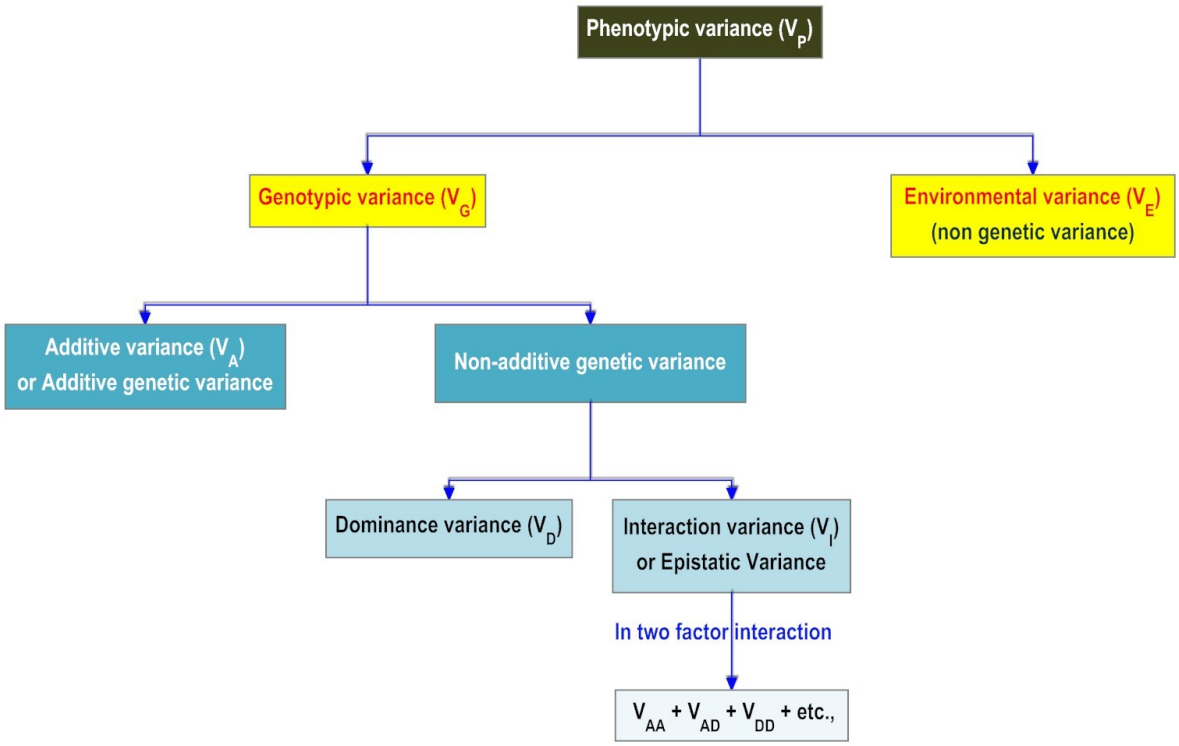
VARIANCE

- The differences in phenotypic values of quantitative traits among individuals of a population are referred to as variation.
- The amount of variation is measured and expressed as variance. Variance measures the variability from an average or mean.
- The basic idea in the study of variance is its partitioning into components attributable to different causes.
- If there is no genetic variation then there is no scope for improvement.
- The components into which the phenotypic variance is partitioned are the same as the components of phenotypic value described earlier.

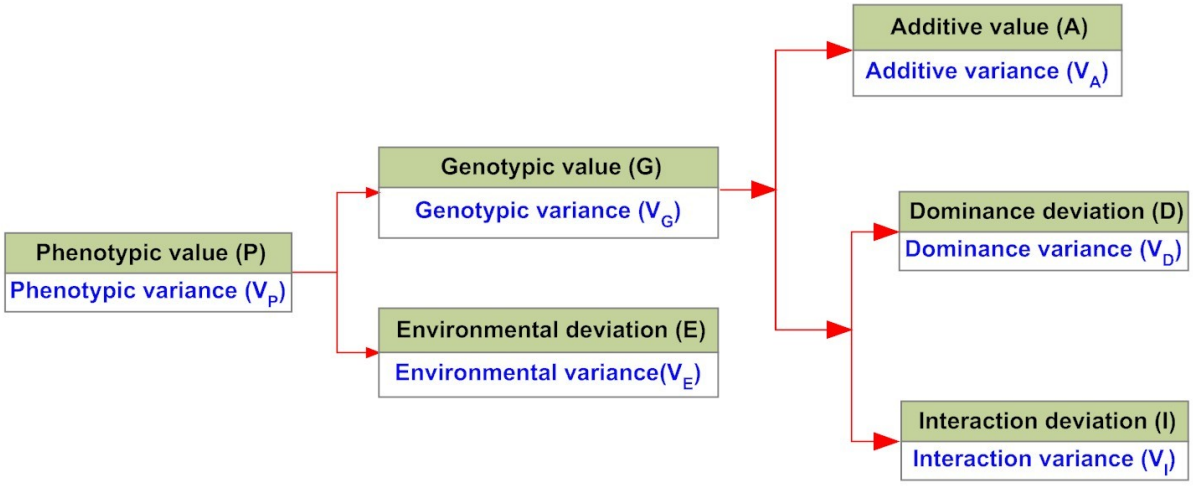
- The relative magnitude of variance components is determined by the degree of resemblance between relatives.

COMPONENTS OF VARIANCE

- The different components of variance are the same as the components of the phenotypic value.



- The components of values and corresponding variance



- The important difference between components of value and variance is that in case of phenotypic value, each component can have positive or negative values on the other hand phenotypic variance are always positive.
- There is usually a substantial amount of non genetic variation whose cause is unknown and which cannot be eliminated by experimental design. This is referred to as "*intangible variation*".

GENOTYPE VARIANCE

- The variances are obtained by squaring the values multiplying by the frequency of the genotypes concerned and summing over the all genotypes.
- Genotypic variance is due to additive effects of genes and non-additive effects of genes.
- Additive effects are connected with breeding values of the individual because parents pass their genes to their offspring not their genotype.

Additive and Dominace variance

- Variance is obtained by squaring the values then multiplying by the frequency of the genotype concerned, and summing the three genotypes.

Genotype	**$A_1 A_1$**	**$A_1 A_2$**	**$A_2 A_2$**
Frequencies	p^2	2pq	q^2
Assigned values	a	d	-a
Breeding values	2q a	(q-p) a	-2p a
Dominance deviation	$-2q^2$ d	2pqd	$-2p^2$ d

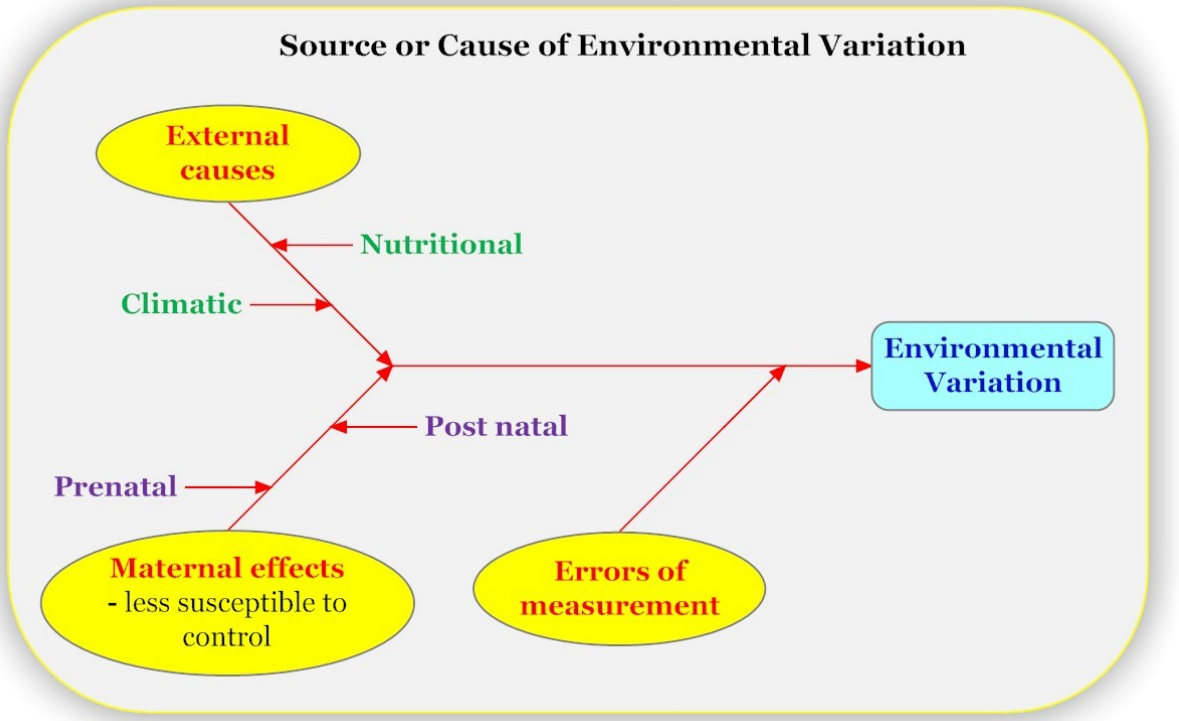
- The additive variance which is the variance of breeding value is obtained as follows
  - $V_A = (2q\ a)^2p^2 + [(q-p)\ a]^2 2pq + (-2p\ a)q^2$
  - $V_A = 4p^2q^2\ a^2 + (q^2-2pq+p^2)\ a^2 2pq + 4p^2q^2\ a^2$
  - $V_A = 2pq\ a^2(2pq + q^2 - 2pq + p^2 + 2pq)$
  - $V_A = 2pq\ a^2(1)$
  - $V_A = 2pq\ [a + d\ (q-p)]^2$
- The variance of dominance deviation is
  - $V_D = (-2q^2d)^2 + (2pqd)^2 + (-2p^2d)^2$
  - $V_D = (2pqd)^2$
- Total genetic variance
  - $V_G = V_A + V_D$
  - $V_G = 2pq\ [a + d\ (q-p)]^2 + (2pqd)^2$
  - $V_G = 2pq\ a^2 + (2pqd)^2$
- In general the genes contribute much more variance when at intermediate frequencies than when at high or low frequencies, recessives at low frequency, in particular, contribute very little variance.

Interaction variance

- When more than one locus is under consideration then the interaction deviations give rise to the interaction variance.
- It is the variation of the interaction deviations brought about by the epistatic interactions at different loci.
- Two factor interactions arise from interaction of two loci three factor from three loci etc.
- In two factor interaction
  - $V_I = V_{AA} + V_{AD} + V_{DD}$ + etc

ENVIRONMENTAL VARIANCE

- It includes all variations of non genetic origin environmental variance is a source of error that reduces precision in genetic studies.



- Environmental variance may partitioned into
  - Special environmental variance (V_{Es}) - within individual variance
  - General environmental variance (V_{Eg})

MODULE-27: GENOTYPE ENVIRONMENT CORRELATION AND INTERACTION

Learning objectives

After completing this module, the learner should be able to:

- define and provide examples of genotype-environment correlation and interaction
- understand the properties and importance of genotype-environment correlation and interaction

GENOTYPE ENVIRONMENT CORRELATION AND INTERACTION

- So far we have assumed that phenotype is determined by Genotype and Environment. But besides $G + E$, the phenotype can also be influenced by two complications viz.
  - Genotype – Environment Correlation (G x E correlation)
  - Genotype – Environment Interaction (G x E interaction)

GENOTYPE – ENVIRONMENT CORRELATION

- The correlation between genotype and environment arises when better genotypes are given better environment or vice versa.
    - Example: Milk yield in dairy cattle.
        - The normal practice of dairy husbandry is to feed cows according to their milk yield, the better genotypes being given more feed. This introduces correlation between phenotypic value and environmental deviation.
    - Since genotypic and phenotypic values are correlated there is a correlation between genotypic value and environmental deviation.
    - When *G* x *E* correlation is present, the phenotypic variance is increased by twice the covariance of genotypic values and environmental deviations and equation becomes $\boldsymbol{V_P = V_G + V_E + 2\ cov_{GE}}$
    - If V_G and V_E are estimated, the *G* x *E* correlation component $2\ cov_{GE}$ can be estimated as $\boldsymbol{2\ cov_{GE} = V_P - (V_G + V_E)}$.
    - The genotype environmental correlation is best regarded as part of the genetic variance (V_G).
    - The correlation between genotype and environment is seldom an important complication and normally neglected in experimental populations, where randomization is one of the main objectives of experimental design.

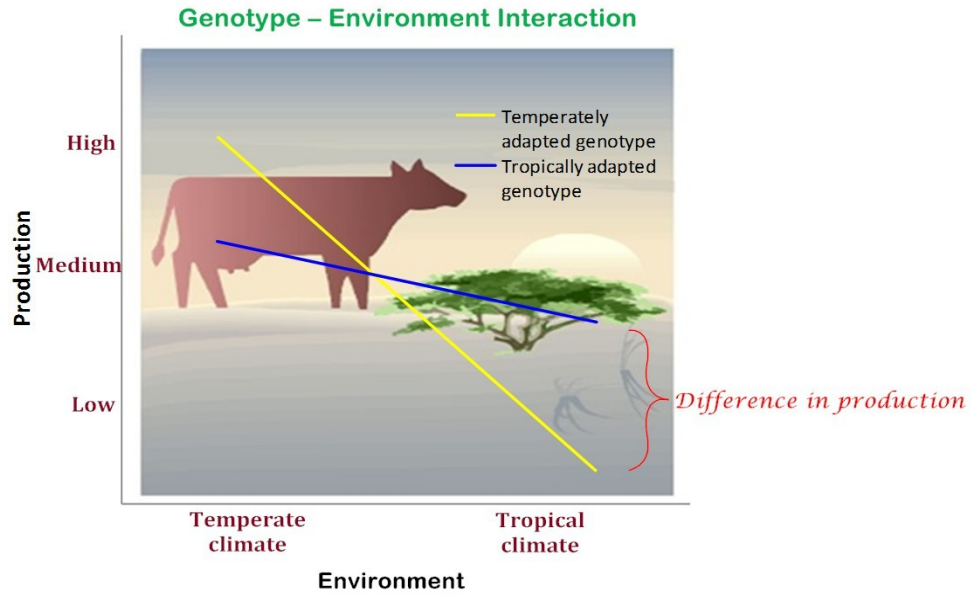
GENOTYPE – ENVIRONMENT INTERACTION

- Under certain combination of genotype and environment, the phenotype may not be equal to the sum of these two variables but rather be smaller or larger.
    - $P < or > (G + E)$
- When interaction is absent the phenotype equals the sum of genotype and environment.
    - $P = (G + E)$
- If the ranking order of two (or more) genotypes varies from environment to environment in which they are conducted then there is $G \times E$ interaction.
- The best genotype in one environment is not th e best in another environment.
- The $G \times E$ interaction is defined as the relative change in the performance of two or more genotypes in two or more environments. That is the phenomenon of genotype – environment interaction is reflected by the differential expression of different genotypes over environments (The genotype can be breeds, strains or lines. The environments can be nutrition, climate, housing and management etc.).
- For example the genotype *A* may be superior to genotype *B* in the environment - I, but inferior in environment – II, when $G \times E$ interaction is present.

Genotype	Environment - I	Environment - I
A	Superior	Inferior
B	Inferior	Superior

- Therefore each genotype has its specific *adaptability* for which the $G \times E$ interaction is responsible.
- When there is no interaction the best genotype in one environment will be the best in all.
- When the interaction between genotype and environment is present, the phenotypic value becomes $\boldsymbol{P = G + E + I_{GE}}$.
- The interaction component also makes changes in the sources of variation for the phenotypic variance and result in $\boldsymbol{V_p = V_G + V_E + V_{GE}}$.
- Since the variance occurring in genetically uniform groups is entirely due to environmental differences among the individual, the variance due to interaction is included with environment variance.

- In practical breeding, an important concept concerning $G \times E$ interaction is adaptability. In temperate climate, Zebu cattle (*Bos indicus*) are inferior to the various European breeds of cattle (*Bos taurus*). In tropical climate, Zebus are superior. The ranking of European breeds and Zebus depend upon the climate in which they are tested. For example the ranking of bulls may vary according to the country in which the performance of their daughters is measured.



Importance of *G*×*E* interaction

- Genotype – Environmental ($G \times E$) Interaction are very important if individuals of a population are reared under different conditions, where environment cannot be controlled.
- Experimental evidences shows that the best dairy breed sires in the temperate countries were not the best in the tropical countries.
- The importance of I_{GE} was also found between countries with a high level of concentrate feeding versus pasture feeding base.
- The best sires in low environment level were not the best in the high environment level.
- Therefore the $G \times E$ interaction requires additional efforts in selection of breeding stock with a general adaptability to more than one environment condition or specifically suitable for desired environmental condition.

MODULE-28: RESEMBLANCE BETWEEN RELATIVES

Learning objectives

After completing this module, the learner should be able to:

- understand the uses of resemblance between relatives
- understand how to estimate resemblance between relatives
- understand to estimate the intra class correlation coefficient and regression of offspring on parents

USES OF RESEMBLANCE BETWEEN RELATIVES

- The resemblance between relatives is one of the basic genetic phenomena displayed be metric characters.
- The degree of resemblance is a property of the character and can be determined by simple measurements made on the population and it provides the means of estimating the amount of additive genetic variance.
- It is the proportionate amount of additive genetic variance (i.e. the heritability) that chiefly determines the best breeding method to be used for improvement.
- The principle is that the relatives resemble each other due to the effects of common genes they have.
- So its degree provides the means to estimate the additive genetic variance which is heritable and is a fixed component of genotypic variance.
- Hence the knowledge on the causes of resemblance between relatives and the method of estimating the additive genetic variance from the observed degree of resemblance between relatives is useful in the study of metric characters.

ESTIMATION OF RESEMBLANCE BETWEEN RELATIVES

- The partitioning of phenotypic variance into components attributable to different causes (V_A, V_D, V_I) are called as *causal components* of variance denoted by V.
- The measurement of the degree of resemblance between relatives rests on the partitioning of the phenotypic variance into components corresponding to the grouping of the individuals into families (full sibs, half sibs).
- These components can be estimated directly from the observed phenotypic values and are known as *observational components* of phenotypic variance denoted by σ^2.
- For estimation of resemblance between relatives (full sibs, half sibs) the total observed variance is partitioned into two components namely between group components (σ^2_B) and within group components (σ^2_W).
- The greater the similarity within the groups, the greater in proportion will be the difference between the groups.
- The resemblance between relatives can be either similarity of individuals in the same group or the difference between individuals in different groups.

INTRA CLASS CORRELATION COEFFICIENT

- The degree of resemblance can therefore be expressed as the proportion of between group component to the total variance. This is known as intra class correlation (t) coefficient and is given
by

$$t = \frac{\sigma_B^2}{\sigma_B^2 + \sigma_W^2}$$

Where σ_B^2 is the between group component and σ_W^2 the within group component

- The between group component expresses the amount of variation that is common to members of the same group and it can be equally well referred to as the covariance of members of the groups.

DEGREE OF RESEMBLANCE BETWEEN OFFSPRING AND PARENTS

- For the estimation of degree of resemblance between offspring and parents, the grouping of the individuals into pairs rather than families is required.
- One parent or mean of the parents is paired with one offspring or mean of several offsprings.
- The degree of resemblance is therefore expressed as the regression (b_{OP}) of offspring on parents and is given by

$$b_{OP} = \frac{cov_{OP}}{\sigma_P^2}$$

Where cov_{OP} is the covariance of offspring and parents and σ_P^2 is variance of parents

MODULE-29: HERITABILITY

Learning objectives

After completing this module, the learner should be able to:

- understand the various definition, importance, features and uses of heritability
- understand the approximate heritability value of some important economical traits of livestock
- understand the relationship between breeding value and progeny difference

DEFINITION

Narrow sense

- Breeding value is of prime importance in selection programme since breeding values are passed on from parent to offspring and not the genotype. Therefore we are interested in the proportion of phenotypic variance attributable to breeding values. This is represented by the fraction of V_A/V_P, which is called the heritability in the narrow sense (h^2).
- Heritability is defined as the ratio of additive genetic variance to phenotypic variance.

Heritability in narrow sense is used to refer per cent or proportion of the phenotypic variation between individuals for a particular trait that is due to differences in the additive genetic effects of the trait.

$$h^2 = V_A/V_P$$

- The ratio V_A/V_P expresses the extent to which phenotypes are determined by the genes transmitted from parents. It represents the percentage of genetic progress made in the next generation when superior individuals are selected as parents.

Broad sense

- The ratio V_G/V_P is called the heritability in the broad sense or the degree of genetic determination.
- It expresses the extent to which individual's phenotypes are determined by the genotypes. Heritability in broad sense includes variation due to additive gene action (V_A), dominance (V_D) and epistasis (V_I).

- In the selection programme it is the heritability in the narrow sense or simply heritability, which is very important. Unless otherwise specified, heritability means heritability in the narrow sense (h^2).

Symbol

- The customary symbol h^2 stands for the heritability itself and not for its square.
- The symbol derives from Wright's (1921) terminology where "h" stands for the corresponding ratio of standard deviations.

Mathematically heritability

- Mathematically heritability is the regression of breeding value on phenotypic value. $h^2 = b_{AP}$. Therefore h^2 can be taken as the change in breeding value expected per unit change in phenotypic value.

IMPORTANCE AND FEATURES OF HERITABILITY

Importance of heritability

- If the breeder chooses individuals to be parents according to their phenotypic values, his success in changing the characteristics of the population can be predicted only from knowledge of the degree of relationship between phenotypic values and breeding values. This degree of correspondence is measured by the heritability.
- Heritability in narrow sense is a measure of the strength of the relationship between phenotypic values and breeding values for a trait in a population.
- Heritability in the broad sense is a measure of the strength of the relationship between phenotypic values and genotypic values.

Features of Heritability

- Heritability is a population measure, not a value to be associated with an individual animal.
- Heritability is a property of the character and also of the population and the environment in which it is measured.
- The value of the heritability depends on the magnitude of all the components of variance ($V_P = V_A+V_D+V_I+V_E$), so change in any one of these will affect it.
- All the genetic components are influenced by gene frequencies and may therefore differ from one population to another. More variable environment reduces the heritability and more uniform condition increases. Therefore heritability of a trait is not fixed. It varies from population to population and from environment to environment.
- Heritability ranges from 0 to 1.
- If heritability is high, selection tends to be effective and vice versa.

HERITABILITY OF SOME IMPORTANT TRAITS

- Approximate heritability value of various traits in various animal species

Species	Trait	h^2
Cattle (dairy)	Calving interval	0.10

	Milk yield	0.25
	Fat %	0.55
	Protein %	0.50
Cattle (beef)	Calving interval	0.05
	Birth weight	0.40
	Weaning weight	0.30
	Yearling weight	0.40
	Mature weight	0.65
	Feed conversion	0.40
Pigs	Litter size (number born alive)	0.05
	Little size (number weaned)	0.10
	Weaning weight	0.10
	Feed conversion	0.50
	Loin eye area	0.50
	Back fat thickness	0.70
Sheep	Litter size	0.15
	Birth weight	0.30
	Weaning weight (60-day)	0.20
	Yearling weight	0.40
	Grease fleece weight	0.40
	Staple length	0.50
Horses	Wither height	0.40
	Cannon bone circumference	0.45
	Temperament	0.25
	Walking speed	0.40
	Time to trot one mile	0.45
	Time to run one mile	0.35
	Pulling power	0.25
Poultry	Egg production (to 72 wks)	0.10
	Egg size	0.45
	Egg weight (at 32 wks)	0.50
	Hatchability	0.10
	Viability	0.10
	Body weight (at 32 wks)	0.55

- On the whole, the characters with the lowest heritability are those most closely connected with reproductive fitness.
- Characters with the highest heritability are those that have least importance with regard to natural fitness.
- Heritability can be expressed as percentage from 0 to 100 or in decimal ranging from 0 to 1.
- According to Turner and Young (1969) the estimates of h^2 values was grouped as
    - 0.3 or more - high
    - 0.3 - 0.1 - intermediate / medium
    - below 0.1 - low

- When we say heritability of a trait is 0.25, it mean that 25 per cent of the differences in performance for the trait in the population are heritable.
    - For example the heritability of milk yield in cattle is 25 % and average of the herd is 2000 kg. This does not mean that 500 kg (25%) is due to heredity and the remaining 1500 kg to environment. It means that of the difference between individual in the herd in milk yield approximately 25 % is due to heredity and 75 % is due to environment.

USES

Uses of heritability estimates

- To understand the relative contribution of heredity and environment in a trait in the population.
- To predict the breeding values and genetic gain of a trait under selection programme.
- To formulate suitable breeding plans for genetic improvement.

BREEDING VALUE AND PROGENY DIFFERENCE

Breeding value

The value of an individual judged by the mean value of its progeny is called breeding value of the individual.

- All of genotypic value is not heritable. Breeding value is the part of an individual's genotypic value that is due to independent gene effects that can be transmitted from parents to offspring.
- If an individual is mated to a number of individuals taken at random from the population, then its breeding value is twice the mean deviation of the progeny from the population mean.

Estimated breeding value (EBV)

- Prediction of breeding value using performance data is known as estimated breeding value or EBV.

Progeny Difference (PD) or Transmitting ability (TA)

- A parent passes on a sample half of its genes and therefore a sample half of the independent effects of those genes to its offspring. Because breeding value is the sum of the independent effects of all of an individual's genes affecting a trait, a parent passes on, *on average*, half its breeding value to its offspring. Half the parent's breeding value for a trait is our expectation of what is inherited from the parent and is called *progeny difference or transmitting ability*.

PD = ½ BV

- Like breeding values, progeny differences are not directly measurable, but can be predicted from performance data. Such predictions are called *expected progeny difference (EPDs), predicted difference (PDs), or estimated transmitting abilities (ETAs)* and are commonly used to make genetic comparisons among animals during selection.

MODULE-30: ESTIMATION OF HERITABILITY

Learning objectives

After completing this module, the learner should be able to:

- understand the different methods of estimating heritability and advantages of each method

INTRODUCTION

Causal components of variance

- All heritability estimates are based on how much more relatives resemble each other for certain traits than non-relatives.
- Relatives resemble each other more than non-relatives because they have more genes in common.
- The degree of resemblance provides the means of estimating the amount of additive genetic variance (V_A) and other components of variance.
- The V_P can be partitioned into components attributable to different causes as $V_P = V_A+V_D+V_I+V_E$. These components are called *causal components* of variance. These components cannot be estimated directly.

Observational components of variance

- The measurement of degree of resemblance between relatives rests on the partitioning of the phenotypic variance in a different way, into components corresponding to the grouping of the individual into families like half sib, full sib.
- After grouping we can measure the phenotypic values between and within groups.
- Hence these components are estimated directly from phenotypic values. We shall call them as *observational components* of phenotypic variance and denote them by symbol σ^2.

HERITABILITY ESTIMATION METHODS

- The degree of resemblance between offspring and parent is measured by **regression coefficient** and that between full or half sib is measured by **correlation**.
- Coefficients of the casual component (variance components) in the Covariance (COV) with two factor interactions of relatives

Relatives	Variance components and their contribution				
	V_A	V_D	V_{AA}	V_{AD}	V_{DD}
Offspring – parent : cov_{op}	1/2	-	1/4	-	-
Half sibs : $cov_{(HS)}$	1/4	-	1/16	-	-
Full sibs : $cov_{(FS)}$	1/2	1/4	1/4	1/8	1/16

- In case of full sib the COV includes V_{Ec} (common environmental circumstances that cause differences between unrelated individual are not a cause of differences between members of the same family).

- Therefore, by observing the phenotypic covariance of different sorts of relationship the amount V_A obtained is

Relatives	Amount of V_A provided by COV
Offspring and one parent	½ V_A
Offspring and mid-parent	½ V_A
Half sib	¼ V_A
Full sib	½V_A+ ¼ V_D + V_{Ec}

Heritability estimation methods

- Regression method Regression of offspring on one parent
  - Regression of offspring on mid parent
  - Intra sire regression of offspring on dam
- Correlation method:
  - Half sib correlation
  - Full sib correlation
- Using twin data in human [Dizygotic (fraternal) and Monozygotic (identical) twins]
  - The genetic covariance of twins is very simple. In case of Dizygotic twins the genetic COV are related as full sibs. The monozygotic twins have identical genotypes, so there is no genetic variance within pairs and the whole of the genetic variance appears in the between pair component. The genetic COV is therefore $COV_{(MZ)}$: V_G
- Heritability can also be estimated from selection experiment data

i.e. $R = h^2S$

$h^2 = R/S$

Where R = Response to selection and S = Selection differential

The heritability estimated by this way is called Realized heritability.

ESTIMATION OF HERITABILITY BY REGRESSION METHOD

- In this method the resemblance between offspring and parents, the grouping of the observations is into pairs rather than groups. That is one parent (or) mean of two parents – paired with their one offspring (or) mean of several offsprings.
- The degree of resemblance is expressed as the regression of offspring on parents (Here correlation is often inappropriate).
- The regression is given by

$$b_{OP} = \frac{cov_{OP}}{\sigma_P^2}$$

Where cov_{OP} is the *cov* of offspring and parents

σ_P^2 is the variance of parents

- In general, for regression method the data of both parent and offspring are required.

REGRESSION OF OFFSPRING ON ONE PARENT

- The *cov* between parent and offspring is $1/2V_A + 1/4\ V_{AA}$.
- Ignoring $1/4V_{AA}$ which is negligible, then the regression is

$$b_{OP} = \frac{1/_2 V_A}{V_P}$$

$$b_{OP} = \frac{1/_2 V_A}{V_P}$$

$$b = \frac{1}{2} h^2$$

$$\therefore h^2 = 2b$$

REGRESSION OF OFFSPRING ON MID-PARENT

- The covariance of offspring with mean of both parents is the same as the *cov* with a single parent i.e ½ V_A.
- But the total variance is ½ V_P because in general, the variance of the mean of ' n ' individuals is one n^{th} of the variance of single individual.

$$b_{OP} = \frac{1/_2 V_A}{1/_2 V_P} = \frac{V_A}{V_P} = h^2$$

INTRA SIRE REGRESSION OF OFFSPRING ON DAM

- In farm animals a male is mated to several females and therefore the regression of offspring on mid parent is inappropriate.
- Since there are usually a few male parents and the mating is not random the simple regression on one or other parents are both unsuitable.
- The h^2 can however be satisfactorily estimated from the average regression of offspring on dams calculated within sire groups. That is to say, the regression of offspring on dam is calculated separately for each set of dams mated to one sire and the regression in each set is pooled in a weighted average.

- The ISD estimates half the h^2 as

$$b_{OP(ISD)} = \frac{{}^1/_2 V_A}{V_P} = {}^1/_2\ h^2\ ;\ \therefore h^2 = 2b$$

- This method eliminates the environmental *cov* that arises if sire groups have been in different environment / herds. This method also helps to overcome the differences among herds / breeds / sires.

ESTIMATION OF HERITABILITY BY CORRELATION

- This method is used when data of progeny but not of parents are averaged.
- Here the individuals are grouped as half sib or full sib families.
- By analysis of variance the total observed variance can be partitioned into between groups and within groups.
- The ratio of between group component to total variance is called the **intraclass correlation coefficient** and is given by

$$t = \frac{\sigma_B^2}{\sigma_B^2 + \sigma_W^2}$$

$$Where\ \sigma_B^2 = \text{is the between group component}$$
$$\sigma_W^2 = \text{is the within} - \text{group component}$$
$$t = \text{symbol for intraclass correlation}$$

- The between group component expresses the amount of variation that is common to members of the same group and it can be referred as *cov* of members of the groups.
- The intra class correlation (t) among half sib or full sib is used to estimate h^2.

HALF SIB CORRELATION

- Half sibs are relatives, which have one parent common.
- The coefficient of relationship between half sib is 0.25.
- The *cov* between half sib is due to ¼ V_A+ 1/16 V_{AA}.
- Ignoring 1/16 V_{AA}, which is negligible, the h^2 estimate in half sib correlation is

$$t = \frac{{}^1/_4 V_A}{V_P}$$

$$t_{(HS)} = {}^1/_4\ h^2\ ;\ \therefore h^2 = 4t_{(HS)}$$

- The intraclass correlation (t) between half sibs is multiplied by 4 to get heritability.

FULL SIB CORRELATION

- Full sibs are relatives who have both parents in common.
- The coefficient of relationship between full sibs is 0.50.
- The *cov* between full sibs is due to ½ V_A + ¼ V_D + V_{Ec}.

$$t = \frac{{}^1/_2 V_A + {}^1/_4 V_D + {}^1/_4 V_{Ec}}{V_P}$$

$$t_{(FS)} = {}^1/_2\ h^2\ ;\ \therefore h^2 = 2t_{(FS)}$$

- The heritability based upon full sib correlation is therefore often over estimated since it includes ¼ V_D+V_{Ec}.
- Therefore, the intraclass correlation among full sibs can therefore be used to estimate heritability of those character in which the effects of V_{Ec} and V_D are negligible.

CHOICE OF METHOD FOR DETERMINING HERITABILITY AND PRECISION OF HERITABILITY ESTIMATE

- The choice of what sort of relatives to be used for estimation of heritability depends on the circumstances and for sorts of relationship the data available.
- There are two points to consider in estimation of heritability
    - Bias
    - Precision

Bias

- It is introduced by environmental source of *cov* and non-additive genetic causes.
- Absence of non-additive genetic causes of resemblance in relationship (i.e. V_D and V_I) and maternal environmental variance (V_{Ec}) are the most important criteria in choosing method.
    - Example, in full sib, *cov* includes the ¼ V_D+V_{Ec} and in regression of offspring on dam, it includes V_{Ec}.
- Therefore, the estimate of heritability from full sib or regression of offspring-dam is valid or reliable only in the absence of V_D and V_{Ec}.
- Generally the half sib correlation and regression of offspring on sire are the most reliable from this point of view.

Precision

- The precision of an estimate of heritability is indicated by its standard error (S.E.). Generally standard error of heritability are uncomfortably large unless the regression (*b*) is based on large number of pairs and the correlation is based on more number of sire groups and large number of progenies per sire group. But there are many limitations to achieve these objectives. They are space, labour, cost and etc. Normally the estimate of heritability is valid or reliable only when it has very low standard error.
- In general, the closer the relationship the more precise is the estimate. The reason for this is that the observed *b* or *t* must be multiplied by a larger factor (*1/r*) in distant relatives compared to closer relationship. That is in case of half sib, '*t*' is multiplied by 4 and in case regression of offspring on one parent or intrasire regression of offspring on dam, the ' *b* ' is multiplied by 2. In this point of view, regression of offspring on mid parent gives better precision than the other methods.

In general low heritability are more efficiently estimated by the half-sib correlation and heritability higher than about 0.25 are more efficiently estimated by offspring-parent regressions. However the difficulty in the latter method is that we need data of both parent and offspring.

MODULE-31: REPEATABILITY

Learning objectives

After completing this module, the learner should be able to:

- understand the concept of repeatability
- understand methods of estimation of repeatability
- understand the uses of repeatability
- understand the repeatability value of some important economic traits

REPEATABILITY

Repeatability is defined as the correlation between measurements on the same animal for traits, which are measured more than once.

- It is represented by the symbol '*r*'.
- It ranges from *0* to *1* or *0* to *100* per cent.
- Example: Lactation milk yield, Fleece weight in sheep, and Litter size in swine.

Repeatability Vs Heritability

- The meaning of repeatability becomes clearer when it is compared with heritability.
- Repeatability is an indicator of the extent to which an animal's superiority in one measurement will be seen in subsequent measurements of the same animal.
- But heritability indicates the extent to which the superiority of parents will be seen in their offspring.

Repeatability Vs Environmental Variance

- To understand repeatability and to calculate it, a different division of environmental variance is required.
- Some environmental effects are permanent and therefore influence permanently in all periods and affect all measurements.
- Other environmental effects are temporary and vary from one period to the next. Since the temporary effects are independent from period to period, they are likely to be positive and negative and tend to be zero over several periods.
- *Permanent environmental factors*
    - Repeatability is concerned with the extent to which differences between individuals are permanent. i.e remain throughout their lives. Those permanent differences must be due to factors that remain permanent throughout the individuals' lifetime. These include the individuals genotype (G=A+D+I) and a deviation due to any permanent environmental factors E_p. i.e. a deviation due to environmental factors that exert the same effect on all measure of performances throughout the individuals life time.
        - Example: permanent defects like udder damage in cows.
    - E_P is also referred to as general environmental effect.

- *Temporary environmental factors*
  - This is due to temporary environmental factors E_t, which affect one measurement but not the rest and vary from one period to next.
    - Example, quality / quantity of feed, climate etc.
  - E_t is also referred to as special environmental effect.
  - Using the distinction between E_p and E_t we can say that permanent differences between the performances of individuals are due to differences in $G + E_p$.
- *Environmental variances*
  - The respective environmental variances are referred as V_{Ep} or V_{Eg} and V_{Et} or V_{Es}.
    - Where
      - V_{Ep} or V_{Eg} refers to permanent or general environmental variance contributing to the between-individual component and
      - V_{Et} or V_{Es} refers to temporary or special environment variance arising from temporary or special circumstances within individual.
  - Heritability indicates the relative contribution of V_A to V_P.
  - In a similar manner, repeatability indicates the relative contribution of $V_G + V_{Ep}$ to V_P.
  - In terms of causal components of variance, repeatability is expressed as

$$Repeatability\ (r) = \frac{V_G + V_{Ep}}{V_P}$$

  - Because of this, we can conclude that for repeatable character, heritability is never greater than repeatability.

ESTIMATION OF REPEATABILITY

- Repeatability can be estimated by Intraclass correlation method.
- The ratio of the between individual component to the total phenotypic variance is the intraclass correlation (r).
- When more than one measurement of the character can be made on each individual the phenotypic variance can be partitioned into:
  - Variance within animals, which is equal to V_{Et}
  - Variance between animals, which is equal to $V_G + V_{Ep}$

$$r = \frac{\text{Between animal variance}}{\text{Between animal variance } + \text{ Within animal variance}} = \frac{V_G + V_{Ep}}{V_P}$$

- It is the correlation between repeated measurements on the same individual and is known as the repeatability of the character. By analysis of variance the variance components are estimated and repeatability is estimated.
- Like heritability, repeatability is a population measure and is not a value associated with an individual animal. Like heritability, repeatability is not fixed, and varies from population to population and from environment to environment.

USES OF REPEATABILITY

- Repeatability estimate sets upper limits to heritability in broad sense. Since repeatability is easier to estimate than heritability we can reasonably guess the probable value of heritability from the estimate of repeatability.

- Repeatability estimates are used to predict future performance from past records. When the repeatability for a trait is high, selection for the trait on the basis of the first record itself would be effective in improving the over-all performance of the herd in the next year.
- Repeatability indicates gain in accuracy expected from multiple measurements. If repeatability is high multiple measurements are not going to improve the accuracy of selection. If repeatability is low then two or more measurements will improve the accuracy of selection because increase in number of measurements reduces V_{Et} or V_{Es} that appears in the phenotype variance (V_P), and thus the reduction of V_P represents the gain in accuracy.
- Used to estimate the future performance of animals or **Most probable Producing Ability (MPPA).** *Lush* suggested the formula for estimating MPPA using repeatability estimate to adjust the records of cows with varying number of records / observations to uniform basis for comparison during selection programme.

$$MPPA = Herd\ average + \frac{nr}{1+(n-1)r}(Individual\ average - Herd\ average)$$

Where n = number of records and
r = repeatability of the trait

- Repeatability estimate also throw light on the nature of environmental variance affecting the trait.

REPEATABILITY ESTIMATES OF IMPORTANT ECONOMIC TRAITS IN LIVESTOCK AND POULTRY

Species	Trait	Repeatability
Cattle (dairy)	Services per conception	0.15
	Calving interval	0.15
	Milk yield	0.50
	Fat %	0.60
Cattle (beef)	Birth weight	0.20
	Weaning weight	0.40
	Body measurements	0.80
Sheep	Birth weight	0.35
	Weaning weight (60-day)	0.25
	Grease fleece weight	0.40
Swine	Litter size (number born alive)	0.15
	Litter size (number weaned)	0.10
	Birth weight	0.30
	Weaning weight	0.15
Horses	1-mile time (flat races)	0.57
	1-mile time (trotters)	0.39

	1-mile time (pacers)	0.45
	Cutting score	0.22
Poultry	Egg weight	0.90
	Egg shape	0.95
	Shell thickness	0.65

- The estimates of repeatability values are grouped as:
  - 0.0 - 0.3 : Low
  - 0.3 - 0.6 : Medium
  - 0.6 and above : High

MODULE-32: GENETIC AND PHENOTYPIC CORRELATIONS

Learning objectives

After completing this module, the learner should be able to:

- understand the concept, classification and uses of correlations
- predict the phenotypic, genetic and environmental correlation between important economic traits in farm animals

CORRELATIONS

- The correlation or correlation coefficient is a measure of the strength of the relationship between two variables or two metric characters.
- The notation for the correlation between characters X and Y is r_{XY}.
- Correlations are used to describe the relationship between two traits in a population
  - Example: correlation between daily weight gain and feed conversion efficiency in swine.
- The values for a correlation coefficient range from –1 to +1.
- The correlation can either be positive or negative.

Types of correlation

- There are three types of correlation:
  - Phenotypic correlation (r_P)
  - Genetic correlation (r_G) or (r_A)
  - Environmental correlation (r_E)

PHENOTYPIC CORRELATION

- The association between two characters that can be directly observed is the correlation of phenotypic values or phenotypic correlation (r_P).
- It measures the strength of the relationship between phenotypic value in one trait and phenotypic value in another trait.
- In genetic studies the phenotypic correlation is partitioned into genetic (r_A) and environmental (r_E) correlations.

- The phenotypic correlation is determined from measurements of the two characters in a number of individuals from the population.
- A correlation, whatever its nature is the ratio of the appropriate covariance to the product of the two standard deviations.
- Therefore the phenotypic correlation between two traits X and Y is

$$Phenotypic\ correlation\ (r_P) = \frac{\mathrm{COV_{P(XY)}}}{\sqrt{\mathrm{VAR_{P(X)}VAR_{P(Y)}}}} = \frac{\mathrm{COV_{P(XY)}}}{\sigma_{P(X)}\sigma_{P(Y)}}$$

Where

- $COV_{P(XY)}$ is the phenotypic covariance between X and Y traits,
- $\sigma_{P(X)}$ and $\sigma_{P(Y)}$ are the phenotypic standard deviations of X and Y traits.
- Here the phenotypic COV is the sum of the genetic and environmental covariance .i.e. $COV_P = COV_A + COV_E$

GENETIC CORRELATIONS

- The genetic correlation (r_A) is the correlation of breeding values between two characters.
- It is caused by the association between the breeding values of the two traits. The reason why genetic correlations are so important is that if two traits are genetically correlated, selection for one will cause genetic change in the other.
- The genetic correlations are mostly caused by genes with pleiotropic action. **Pleiotropy** is the property of a gene whereby it affects two or more characters, so that if the gene is segregating it cause simultaneous variation in the character it affects.
    - For example, genes that increase growth rate also increase both stature (height) and weight, so that they cause correlation between these two characters.
- **Linkage** is another cause of correlation and may persist for a few generations until linkage is broken down due to recombination.

$$Genetic\ correlation\ (r_A) = \frac{\mathrm{COV_{A(XY)}}}{\sqrt{\mathrm{VAR_{A(X)}VAR_{A(Y)}}}} = \frac{\mathrm{COV_{A(XY)}}}{\sigma_{A(X)}\sigma_{A(Y)}}$$

Where

- $COV_{A(XY)}$ is the genetic covariance of the additive deviations between X and Y traits and
- $\sigma_{A(X)}$ and $\sigma_{A(Y)}$ are the standard deviations of the additive genetic value of the traits X and Y.

USES / APPLICATIONS

- From the animal breeder's point of view, genetic correlation is important, because of the change brought by selection. It is important to know how the improvement of one character will cause simultaneous changes in other character. This is called **correlated response** brought in the character not selected for (may be positive or negative). Selection for a character affects favourably or adversely the other characters if they are genetically correlated.
- Example:
    - Milk yield and butter fat % are genetically negatively correlated
    - Egg production and egg size are genetically negatively correlated

- Here selection for milk yield in dairy cattle reduces the fat percentage. Likewise selection for egg yield in poultry reduces egg size. Therefore the reductions in other economically important traits through genetic antagonism need to be taken note in designing selection programmes.

- Uses of genetic correlation are
  - To predict the direction and magnitude of response of correlated character during selection. The knowledge of genetic correlation is useful to forecast reduction in the correlated traits in single trait selection if they are negatively correlated.
  - **Indirect selection:** Sometimes certain traits are difficult and costly to measure. So these traits can be improved by selecting easily measurable trait by correlated response.
  - The r_P and r_A are used in the construction of selection indices .

METHODS OF ESTIMATING GENETIC CORRELATION

- The genetic correlation can be estimated by
  - Parent - offspring analysis and
  - Sib-analysis

PARENT-OFFSPRING ANALYSIS

- The parent-offspring relationship can be used for estimating the genetic correlation.
- To estimate heritability of one character from the resemblance between offspring and parents, we compute the COV of offspring and parent for the one character by taking the product of the parent or mid parent value and mean value of the offspring.
- To estimate the genetic correlation between two characters we compute what might be called the **cross-covariance** obtained from the product of the value of trait X in parents and value of trait Y in offspring or vice versa.
- This cross covariance is half the genetic covariance of the two characters that is ½ $COV_{A(XY)}$.
- In addition, the covariance of offspring and parents for each of the trait are also needed separately for the estimation of genetic correlation and the genetic correlation is given by

$$Genetic\ correlation\ (r_A) = \frac{{}^1/_2\ \mathrm{COV_{A(XY)}}}{\sqrt{{}^1/_2\ \mathrm{COV_{A(XX)}}\ {}^1/_2\ \mathrm{COV_{A(YY)}}}} = \frac{\mathrm{COV_{A(XY)}}}{\sigma_{A(XX)}\sigma_{A(YY)}}$$

SIB-ANALYSIS

- **Half-sib analysis**: The casual components of covariance are exactly similar to those of components of variance. Thus analysis of half-sib families the components of COV between sires estimates ¼ $COV_{A(XY)}$ i.e. one-quarter of the COV of breeding values of two characters.
- For the estimation of correlation the components of variance of each character are also needed.
- Thus the between sire components of variance, $\sigma^2_{S(X)}$ and $\sigma^2_{S(Y)}$ estimate ¼ $VAR_{A(X)}$ and ¼ VARA(Y) respectively for the trait-X and trait-Y. Therefore the rA is obtained as **¼** $VAR_{A(Y)}$ respectively for the trait-X and trait-Y. Therefore the r_A is obtained as

$$Genetic\ correlation\ (r_A) = \frac{{}^1/_4\,\mathrm{COV_{A(XY)}}}{\sqrt{{}^1/_4\,\mathrm{COV_{A(X)}}\ {}^1/_4\,\mathrm{COV_{A(Y)}}}} = \frac{\mathrm{COV_{A(XY)}}}{\sigma_{A(X)}\sigma_{A(Y)}}$$

ENVIRONMENTAL CORRELATION

- The Environmental correlation is the correlation of environmental deviations together with non-additive genetic deviations between two characters.

$$Environmental\ correlation\ (r_E) = \frac{\mathrm{COV_{E(XY)}}}{\sqrt{\mathrm{VAR_{E(X)}VAR_{E(Y)}}}} = \frac{\mathrm{COV_{E(XY)}}}{\sigma_{E(X)}\sigma_{E(Y)}}$$

Where

- $COV_{E(XY)}$ is the environmental covariance between X and Y traits and
- $\sigma_{E(X)}$ and $\sigma_{E(Y)}$ are the standard deviations of the environmental values of the traits X and Y.
- In practice, the environmental covariance and variance are obtained by subtracting additive genetic covariance and variance from the phenotypic covariance and variance. For example, the phenotypic correlation is

$$Phenotypic\ correlation\ (r_P) = \frac{\mathrm{COV_{P(XY)}}}{\sigma_{P(X)}\sigma_{P(Y)}}$$

and the phenotypic covariance can be written as

$$Phenotypic\ correlation\ (r_P) = \frac{\mathrm{COV_{P(XY)}}}{\sigma_{P(X)}\sigma_{P(Y)}}$$

- The phenotypic covariance is the sum of the genetic and environmental covariances i.e., $COV_P = COV_A + COV_E$
- Writing these covariances in terms of the correlations and standard deviations as above gives:

$r_P\ \sigma_{P(X)}\ \sigma_{P(Y)} = r_A\ \sigma_{A(X)}\ \sigma_{A(Y)} + r_E\ \sigma_{E(X)}\ \sigma_{E(Y)}$

Substituting $\sigma_A = h\ \sigma_P$ and $\sigma_E = e\ \sigma_P$

$r_P\ \sigma_{P(X)}\ \sigma_{P(Y)} = r_A\ h_X\ \sigma_{P(X)}\ h_Y\ \sigma_{P(Y)} + r_E\ e_X\ \sigma_{P(X)}\ e_Y\ \sigma_{P(Y)}$

Dividing through by $\sigma_{P(X)}\ \sigma_{P(Y)}$ on both sides leads to

$r_P = r_A\ h_X\ h_Y + r_E\ e_X\ e_Y$

- The above equation reveals how genetic and environmental causes of correlations combine together to give phenotypic correlation.
- If both characters have low heritability, the phenotypic correlation is chiefly determined by environmental correlation.
- If they have high heritability, then the r_P is almost entirely genetic.

PHENOTYPIC (r_P), GENETIC (r_A) AND ENVIRONMENTAL

CORRELATION (r_E) BETWEEN IMPORTANT ECONOMIC TRAITS IN FARM ANIMALS

Traits	r_P	r_A	r_E
Cattle			
Milk yield: Butter fat yield	0.93	0.85	0.96
Milk yield: Butter fat per cent	- 0.26	- 0.38	- 0.18
Pigs			
Weight gain: Back fat thickness	0.0	0.13	- 0.18
Growth rate: Feed efficiency	- 0.84	- 0.96	- 0.50
Weight gain: Feed efficiency	0.66	0.69	0.64
Sheep			
Fleece weight: Staple length	0.35	0.35	0.40
Fleece weight: Crimps per inch	- 0.21	- 0.56	0.10
Fleece weight: Body weight	0.36	0.11	-
Poultry			
Body weight: Egg production	0.01	- 0.17	0.08
Body weight: Egg weight	0.33	0.42	0.23
Egg weight : Egg production	-0.05	-0.31	0.02

- The r_A and r_E are different in magnitude, or even in sign. A difference in sign between the two correlations indicates that the genetic and environmental sources affect the characters through different physiological mechanism.

Correlations	Negative	Positive
Low	- 0.2 to - 0.4	0.2 to 0.4
Medium	- 0.4 to - 0.6	0.4 to 0.6
High	- 0.6 and above	0.6 and above