Lecture Outline: Chromosomes, Linkage, and Large-Scale Mutation

I. **The Chromosomal Basis of Inheritance**

A. **Genes and Chromosomes**

1. Genes are like "passengers on a large boat" where the large boat is the **chromosome**.
2. It is **chromosomes** that independently assort during meiosis, not individual genes.
3. A **locus** (plural: loci) is the specific position a gene occupies on a chromosome.

B. **Revisiting the Dihybrid Cross**

1. Involves tracking **two different characteristics** (e.g., seed color and texture) simultaneously.
2. Original parental crosses (e.g., yellow round seed x green wrinkled seed) show differing traits for each characteristic.
3. The F1 generation is typically doubly heterozygous and expresses the **dominant phenotypes** for both characteristics.

C. **Mendel's Laws Explained by Chromosome Behavior**

1. **Law of Segregation**: The two alleles for each gene separate during gamete formation.
    a. The physical basis for segregation is the separation of **homologous chromosomes** (which carry the alleles).
    b. This process primarily occurs during **Anaphase I of meiosis**.
2. **Law of Independent Assortment**: Alleles of genes on non-homologous chromosomes assort independently during gamete formation.
    a. This applies when genes are on **different chromosomes** ("different boats"), allowing them to go to different cells randomly.

b. The independent assortment of chromosomes occurs during their alignment in **Metaphase I of meiosis**.

c. This law leads to the possibility of all four different kinds of gametes being produced and explains the typical **9:3:3:1 phenotypic ratio** observed in the F2 generation of a dihybrid cross.

3. **Recombinants (Nonparentals)**: Offspring with combinations of traits that are different from those found in either of the original parents.

II. **Sex-Linked Inheritance and Chromosomal Variations**

A. **Autosomes vs. Sex Chromosomes**

1. **Autosomes** are most chromosomes in an organism; they are considered **truly homologous**, meaning they have the same number and type of genes and are similar in size.
2. **Sex chromosomes** are responsible for determining sex (e.g., X and Y in humans and fruit flies) and are **not truly homologous**.
   a. The **X chromosome** is significantly larger than the Y chromosome.
   b. Genes located on sex chromosomes are referred to as **sex-linked genes** (or X-linked if specifically on the X chromosome).

B. **Sex Determination Systems**

1. **XY System** (e.g., Mammals, Drosophila):
   a. **XX individuals** are female; **XY individuals** are male.
   b. Males are **hemizygous** for X-linked genes, meaning they only possess one allele for these genes.
   c. In this system, the **father determines the sex** of the offspring.
2. **X0 System** (e.g., Grasshoppers):
   a. **XX individuals** are female; **X0 individuals** (having only one X chromosome) are male.
   b. Males in this system have one fewer chromosome than females.
3. **ZW System** (e.g., Birds):
   a. **ZW individuals** are female; **ZZ individuals** are male.
   b. In contrast to the XY system, the **female determines the sex** of the offspring.

4. **Haplo-diploid System** (e.g., Bees and other social insects):
    a. **Diploid individuals** are female; **haploid individuals** are male.
    b. Males develop from **unfertilized eggs** (a process called parthenogenesis).
    c. A unique aspect is that males in this system have no biological father but can have a grandfather and can have grandsons (though not sons directly).

C. **Dosage Compensation: X-Chromosome Inactivation**

1. The challenge of **dosage difference** arises because males have effectively half the "dose" of X-linked genes compared to females.
2. In mammals, **X-chromosome inactivation** is the mechanism for dosage compensation: one of the two X chromosomes in a female is randomly inactivated (becomes supercoiled and untranscribable) during early embryonic development.
3. This inactivation leads to heterozygous females being **genetic mosaics**, where different patches of their bodies express different alleles (e.g., distinct fur colors in calico cats, patches of sweating ability in humans).

III. **Gene Linkage and Chromosomal Mutations**

A. **Linked Genes and Recombination**

1. **Linked genes** are two different genes that are located on the **same chromosome**.
2. If genes are perfectly linked, they would ideally always be inherited together, leading to only parental types.
3. The role of **Crossing Over**:
    a. Crossing over is the exchange of genetic material between homologous chromosomes during meiosis.
    b. It allows for the formation of **recombinant types** even when genes are linked, provided that a crossover event occurs specifically between the loci of the two linked genes.
    c. This explains why observed offspring ratios for linked genes show a significantly higher proportion of parental types compared to

recombinants, rather than a complete absence of recombinants.

4. **Recombination Frequency**:
    a. Calculated as: (Number of recombinant offspring / Total number of offspring) x 100%.
    b. There is an inverse relationship between recombination frequency and gene distance: a **lower frequency** indicates genes are **closer together** on the chromosome, while a **higher frequency** indicates they are **farther apart**.
    c. Recombination frequencies are used as the basis for **gene mapping**, allowing scientists to determine the relative positions of linked genes on a chromosome without directly observing the DNA sequence.

B. **Chromosomal Mutations (Large-Scale Changes)**

1. Unlike **point mutations** which involve changes at a single nucleotide pair, chromosomal mutations involve large-scale alterations to chromosome structure.
2. These mutations typically have **huge effects** because they can impact many genes and disrupt their normal regulation.
3. **Types of Chromosomal Mutations**:
    a. **Deletion**: The loss of a segment of a chromosome, and thus all the genes within that segment.
    b. **Duplication**: The repetition of a chromosomal segment.
        (1) This can be beneficial from an evolutionary perspective, as it provides extra copies of genes that can then undergo mutation and lead to the development of new gene functions.
    d. **Inversion**: A segment of a chromosome is reversed end-to-end.
        (1) Even without loss or gain of genetic material, inversions can disrupt gene regulation, potentially turning a normally regulated gene into a **constitutive gene** (one that is always "on").
    f. **Reciprocal Translocation**: An exchange of segments between **non-homologous chromosomes**.

(1) This is generally the most complex and least likely type of chromosomal mutation to occur.

(2) It can disrupt gene regulation and potentially break genes at the points of exchange. An example is the **Philadelphia chromosome** in humans.

IV. **Epigenetics: Genetic Imprinting**

A. **Epigenetics** refers to heritable changes in gene expression that do **not involve alterations to the underlying DNA sequence** itself.

B. **Genetic Imprinting Mechanism**:

1. It involves differential gene expression based on the **parental origin** of an allele.
2. The primary mechanism is **methylation**, the addition of methyl (CH_3) groups to DNA, which effectively silences gene transcription by making the gene unreadable.
3. Imprinting leads to one parent's allele being permanently silenced for the lifetime of the offspring (e.g., in some cases, the paternal allele is expressed while the maternal allele is methylated).
4. This can result in unexpected phenotypes (e.g., a dwarf mouse from a heterozygous parent if the normal allele received from one parent is silenced by imprinting).
5. Genetic imprinting differs from X-chromosome inactivation because it targets **specific genes** (often on autosomes) rather than an entire chromosome.