VIVEKANANDA COLLEGE
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NAAC ACCREDITED ‘A’ GRADE

TOPIC	: **RECOMBINATION AND HOLLIDAY MODEL**
COURSE TITLE	: **GENETICS AND EVOLUTIONARY BIOLOGY**
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UNIT	: **UNIT.2**
SEMESTER	: **4TH SEMESTER [GENERAL]**
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RECOMBINATION

A.Types of Recombination

1. **Homologous** - occurs between sequences that are nearly identical (e.g., during meiosis)
2. **Site-Specific** - occurs between sequences with a limited stretch of similarity; involves specific sites
3. **Transposition** – DNA element moves from one site to another, usually little sequence similarity involved

B. Biological Roles for Recombination

1. Generating new gene/allele combinations (crossing over during meiosis)
2. Generating new genes (e.g.,Immunoglobulin rearrangement)
3. Integration of a specific DNA element (or virus)
4. DNA repair

C. Practical Uses of Recombination

1. Used to map genes on chromosomes
   - recombination frequency proportional to distance between genes
2. Making transgenic cells and organisms

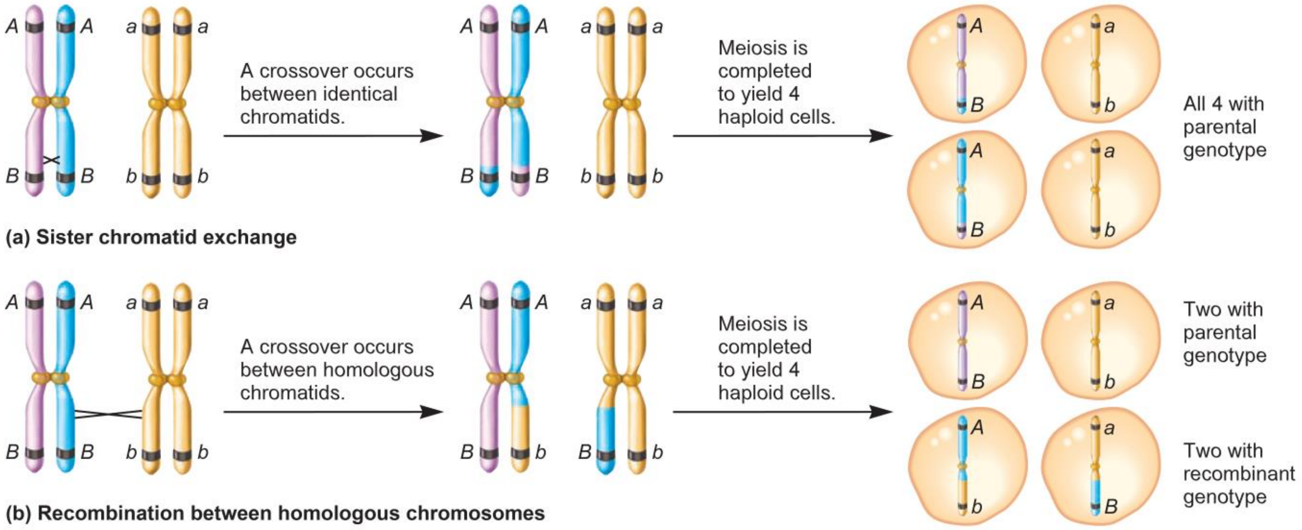
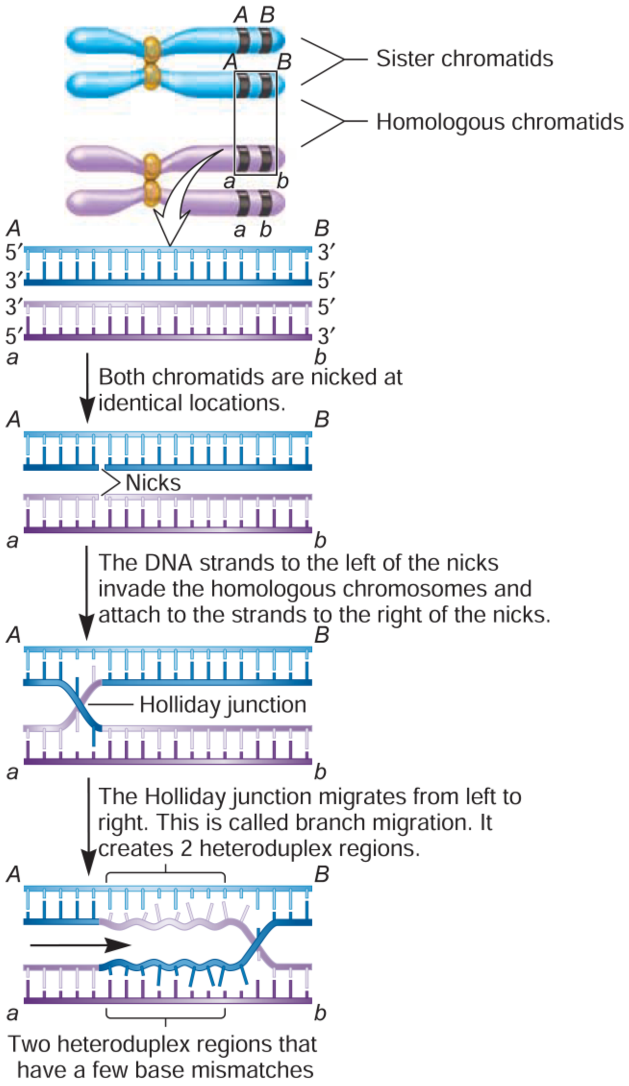


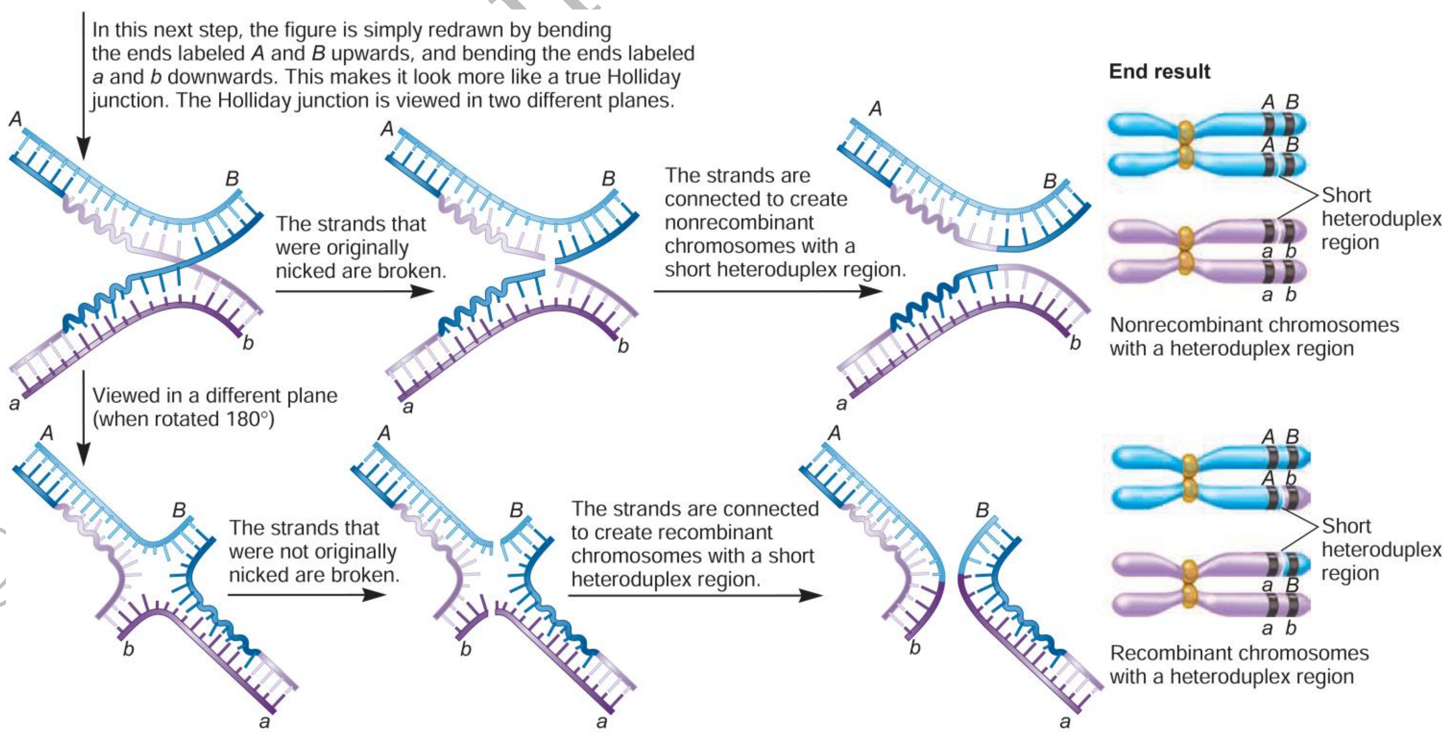
FIGURE 17.1 Crossing over between eukaryotic chromosomes. (**a**) Sister chromatid exchange occurs when genetically identical chromatids cross over. (**b**) Homologous recombination can also occur when homologous chromosomes cross over. This form of homologous recombination may lead to a new combination of alleles, which is called a recombinant (or nonparental) genotype.

Genes→Traits Homologous recombination is particularly important when we consider the relationships between multiple genes and multiple traits. For example, if the X chromosome in a female fruit fly carried alleles for red eyes and gray body and its homologue carried alleles for white eyes and yellow body, homologous recombination could produce recombinant chromosomes that carry alleles for red eyes and yellow body, or alleles for white eyes and gray body. Therefore, new combinations of two or more alleles can arise when homologous recombination takes place.

D. HOLLIDAY JUNCTION



1. At the beginning of the process, two homologous chromatids are aligned with each other.
2. According to the model, a break or nick occurs at identical sites in one strand of each of the two homologous chromatids. The strands then invade the opposite helices and base pair with the complementary strands. This event is followed by a covalent linkage to create a **Holliday junction.**
3. The cross in the Holliday junction can migrate in a lateral direction. As it does so, a DNA strand in one helix is swapped for a DNA strand in the other helix. This process is called **branch migration** because the branch connecting the two double helices migrates laterally.
4. Because the DNA sequences in the homologous chromosomes are similar but not identical, the swapping of the DNA strands during branch migration may produce a **heteroduplex,** a region in the double-stranded DNA that contains base mismatches.
5. In other words, because the DNA strands in this region are from homologous chromosomes, their sequences are not perfectly complementary, yielding mismatches.
6. The final two steps in the recombination process are collectively called **resolution** because they involve the breakage and rejoining of two DNA strands to create two separate chromosomes.
7. In other words, the entangled DNA strands become resolved into two separate structures.

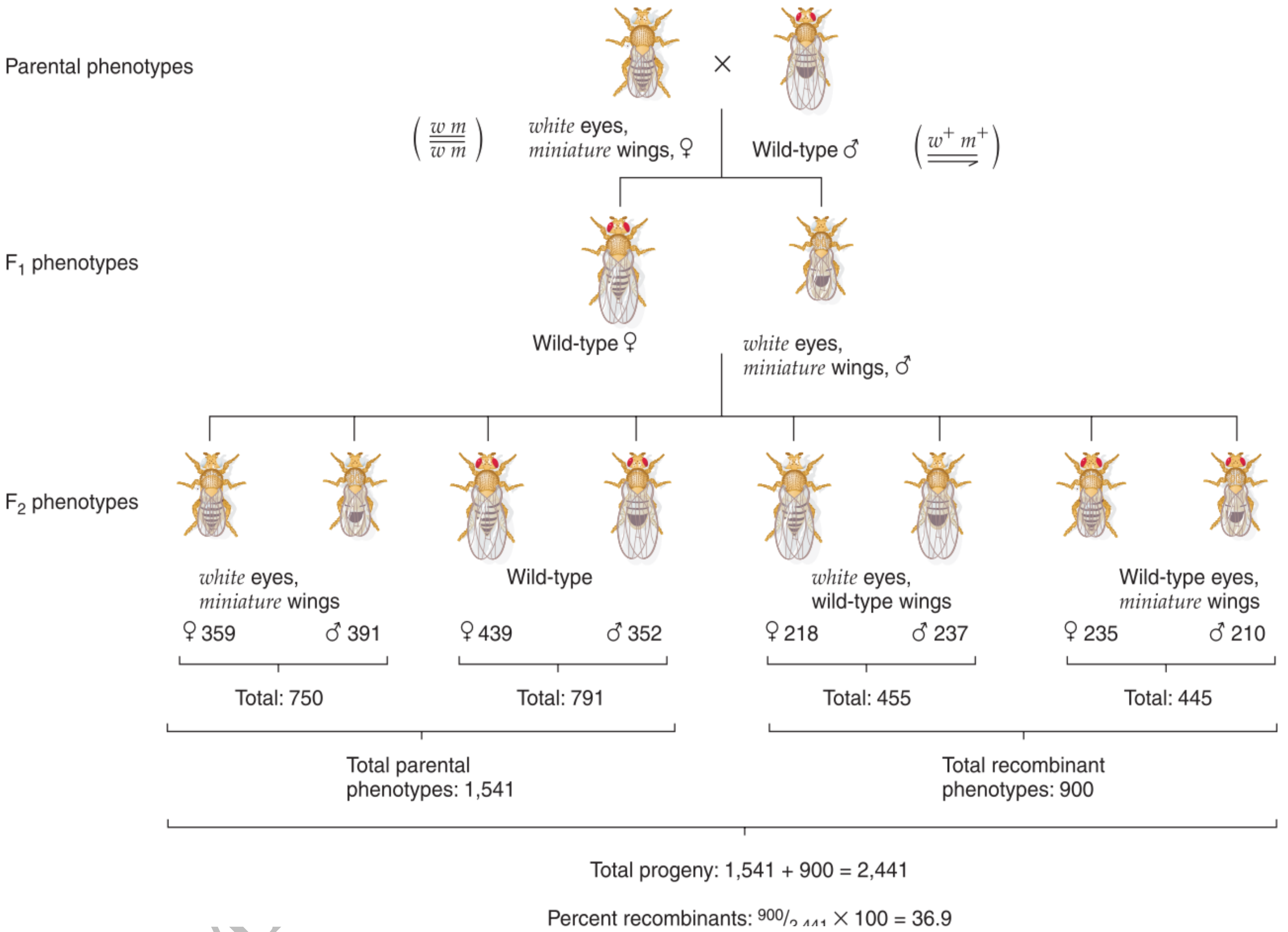


(a) The Holliday model for homologous recombination

8. If breakage occurs in the same two DNA strands that were originally nicked at the beginning of this process, the subsequent joining of strands produces nonrecombinant chromosomes with a heteroduplex region.
9. Alternatively, if breakage occurs in the strands that were not originally nicked, the rejoining process results in recombinant chromosomes, also with a heteroduplex region.

E. RECOMBINATION AS A MEASURE OF LINKAGE INTENSITY

Morgan's experimental crosses of white eye and miniature wing variants of *Drosophila melanogaster*, showing evidence of linkage and recombination in the X chromosome. (Figure from *Genetics*, 2/e by Ursala W. Goodenough, copyright © 1978 Brooks/Cole, a part of Cengage Learning, Inc. Reproduced by permission.)



1. Morgan observed that ***900 of the 2441 F_2 flies, or 36.9%, had nonparental phenotypic*** combinations of white eyes plus normal wings, and red eyes plus miniature wings. ***Nonparental combinations of linked alleles are called recombinants***.
2. A ***total of 50% recombinant phenotypes is expected in the case of independent assortment***; thus, the lower percentage observed is evidence of linkage of the two genes. To explain the recombinants, Morgan proposed that, in meiosis, of genes had occurred between the two X chromosomes of the F_1 females.
3. Morgan's group analyzed a large number of other crosses of this type. *In each case, the parental phenotypic classes were the most frequent, and the recombinant classes occurred less frequently*. Approximately equal numbers of each of the two parental classes, and approximately equal numbers of each of the two recombinant classes, were obtained.
4. Morgan's general conclusion was that, *during meiosis, alleles of some genes assort together because they lie near each other on the same chromosome*. To turn this statement around, ***the closer two genes are on the chromosome, the more likely they are to remain together during meiosis; hence, they will not assort independently. The reason is that the recombinants are produced as a result of crossing-over between***

homologous chromosomes during meiosis, and the closer two genes are together, the less likely there will be a recombination event between them.

5. The genes on a chromosome, then, can be represented by a one-dimensional genetic map that shows, in linear order, the genes belonging to the chromosome. Crossover and recombination frequencies give the linear order of the genes on a chromosome and provide information about the genetic distance between any two genes. The farther apart two genes are, the greater is the *crossover frequency*.

$$\frac{\text{number of recombinants}}{\text{total number of testcross progeny}} \times 100 = \text{recombination frequency} = \text{map units}$$

F. SOLVED EXAMPLE

Given that the two genes are linked, the crosses can be diagrammed to reflect their linkage as follows:

P: $\frac{C\ S}{C\ S} \times \frac{c\ s}{c\ s}$

↓

F_1: $\frac{C\ S}{c\ s}$

Testcross: $\frac{C\ S}{c\ s} \times \frac{c\ s}{c\ s}$

To calculate the map distance between the two genes, we need to compute the frequency of crossovers in that region of the chromosome during meiosis. We cannot do that directly, but we can compute the percentage of recombinant progeny:

Parental types:	colored, full	4,032
	colorless, shrunken	4,035
		8,067
Recombinant types:	colored, shrunken	149
	colorless, full	152
		301

This calculation gives about 3.6% recombinant types (301/8,368 × 100) and about 96.4% parental types (8,067/8,368 × 100). Since the recombination frequency can be used directly as an indication of map distance, especially when the distance is small, we can conclude that the distance between the two genes is 3.6 mu (3.6 cM).