8.1: Types and Examples of Recombination

At least four types of naturally occurring recombination have been identified in living organisms (Figure 8.1).

1. **General or homologous recombination** occurs between DNA molecules of very similar sequence, such as homologous chromosomes in diploid organisms. General recombination can occur throughout the genome of diploid organisms, using one or a small number of common enzymatic pathways. This chapter will be concerned almost entirely with general recombination.

2. **Illegitimate or nonhomologous** recombination occurs in regions where no large-scale sequence similarity is apparent, e.g. translocations between different chromosomes or deletions that remove several genes along a chromosome. However, when the DNA sequence at the breakpoints for these events is analyzed, short regions of sequence similarity are found in some cases. For instance, recombination between two similar genes that are several million bp apart can lead to deletion of the intervening genes in somatic cells.

3. **Site-specific recombination** occurs between particular short sequences (about 12 to 24 bp) present on otherwise dissimilar parental molecules. Site-specific recombination requires a special enzymatic machinery, basically one enzyme or enzyme system for each particular site. Good examples are the systems for integration of some bacteriophage, such as λ, into a bacterial chromosome and the rearrangement of immunoglobulin genes in vertebrate animals.

4. The third type is **replicative recombination**, which generates a new copy of a segment of DNA. Many transposable elements use a process of replicative recombination to generate a new copy of the transposable element at a new location.
Figure 8.1. Types of natural recombination. Each line represents a chromosome or segment of a chromosome; thus a single line represents both strands of duplex DNA. For homologous or general recombination, each homologous chromosome is shown as a different shade of blue and a distinctive thickness, with different alleles for each of the three genes on each. Recombination between genes A and B leads to a reciprocal exchange of genetic information, changing the arrangement of alleles on the chromosomes. For nonhomologous (or illegitimate) recombination, two different chromosomes (denoted by the different colors and different genes) recombine, moving, e.g. gene C so that it is now on the same chromosome as genes D and E. Although the sequences of the two chromosomes differ for most of their lengths, the segments at the sites of recombination may be related, denoted by the yellow and orange rectangles. Site-specific recombination leads to the combination of two different DNA molecules, illustrated here for a bacteriophage λ integrating into the E. coli chromosome. This reaction is catalyzed by a specific enzyme that recognizes a short sequence present in both the phage DNA and the target site in the bacterial chromosome, called att. Replicative recombination is seen for some transposable elements, shown as red rectangles, again using a specific enzyme, in this case encoded by the transposable element.

Recombinant DNA technology uses two other types of recombination. The directed cutting and rejoicing of different DNA molecules in vitro using restriction endonucleases and DNA ligases is well-known, as covered in Chapter 2. Once made, these recombinant DNA molecules are then introduced into a host organism, often a bacterium. If the recombinant DNA is a plasmid, phage or other molecule capable of replicating in the host, it will stay extrachromosomal. However, one can introduce the recombinant DNA molecule into a host in which it cannot replicate, such as a plant, an animal cell in culture, or a fertilized mouse egg. In order for the host to be stably transformed, the introduced DNA has to be taken up into a host chromosome. In bacteria and yeast, this can occur by homologous recombination at a reasonably high frequency. However, this does not occur in plant or animal cells. In contrast, at a low frequency, some of these introduced DNA molecules are incorporated into random locations in the chromosomes of the host cell. Thus random recombination into chromosomes can make stably transfected cells and transgenic plants and animals. The mechanism of this recombination during transformation or transfection is not well understood, although it is commonly used in the laboratory.

General recombination is an integral part of the complex process of meiosis in sexually reproducing organisms. It results in a crossing over between pairs of genes along a chromosome, which are revealed in appropriate matings (Chapter 1). The chiasmata that link homologous chromosomes during meiosis are the likely sites of the crossovers that result in recombination. General recombination also occurs in nonsexual organisms when two copies of a chromosome or chromosomal segment are present. We have encountered this as recombination during F-factor...
mediated conjugal transfer of parts of chromosomes in *E. coli* (Chapter 1). Recombination between two phage during a mixed infection of bacteria is another example. Also, the retrieval system for post-replicative repair (Chapter 7) involves general recombination.

The mechanism of recombination has been intensively studied in bacteria and fungi, and some of the enzymes involved have been well characterized. However, a full picture of the mechanism, or mechanisms, of recombination has yet to be achieved. We will discuss the general properties of recombination, cover two models of recombination, and discuss some of the properties of key enzymes in the pathways of recombination.

### Reciprocal and Nonreciprocal Recombination

General recombination can appear to result in either an equal or an unequal exchange of genetic information. Equal exchange is referred to as **reciprocal recombination**, as illustrated in Figure 8.1. In this example, two homologous chromosomes are distinguished by having wild type alleles on one chromosome (A+, B+ and C+) and mutant alleles on the other (A-, B- and C-). Homologous recombination between genes A and B exchanges the segment of one chromosome containing the wild type alleles of genes B and C (B+ and C+) for the segment containing the mutant alleles (B- and C-) on the homologous chromosome. This could be explained by breaking and rejoining of the two homologous chromosomes during meiosis; however, we will see later that the enzymatic mechanism is more complex than simple cutting and ligation. The DNA that is removed from the top (thin dark blue) chromosome is joined with the bottom (thick light blue) chromosome, and the DNA removed from the bottom chromosome is added to the top chromosome. This process resulting in new DNA molecules that carry genetic information derived from both parental DNA molecules is called **reciprocal recombination**. The number of alleles for each gene remains the same in the products of this recombination, only their arrangement has changed.

General recombination can also result in a one-way transfer of genetic information, resulting in an allele of a gene on one chromosome being changed to the allele on the homologous chromosome. This is called **gene conversion**. As illustrated in Figure 8.2, recombination between two homologous chromosomes A+B+C+ and A-B-C- can result in a new arrangement, A-B+C-, without a change in the parental A+B+C+. In this case, the allele of gene B on the bottom chromosome has changed from B- to B+ without a reciprocal change on the other chromosome. Thus, in contrast to reciprocal recombination, the number of types of alleles for gene B has changed in the products of this recombination; now there is only one (B+). This is an example of interchromosomal gene conversion, i.e. between homologous chromosomes. Similar copies of genes can be on the same chromosome, and these can undergo gene conversion as well. Cases of intrachromosomal gene conversion have been documented for the gamma-globin genes of humans. The occurrence of gene conversion during general recombination is one indication that the enzymatic mechanism is not a simple cutting and pasting.

![Figure 8.2: Gene conversion changing allele B- on the bottom (thick, light blue) chromosome to B+. Note that the arrangement of alleles on the top (thin, dark blue) chromosome has not changed.](https://bio.libretexts.org/Bookshelves/Genetics/Book%3A_Working_with_Molecular_Genetics_(Hardison)/Unit_II%3A_Replica…)
Exercise 8.1

Why would you not interpret the A-B+C- chromosome as resulting from two reciprocal crossovers, one on each side of gene B?

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