Homologous Recombination at the Molecular Level
Recombination is the exchange of genetic information between DNA molecules; when the exchange is between homologous DNA molecules, it is called **homologous recombination**.

Recombination is an extremely important genetic process because it increases genetic variation.
Homologous recombination is a remarkable process: a nucleotide strand of one chromosome aligns precisely with a nucleotide strand of the other homologous chromosome, breaks arise in corresponding regions of different DNA molecules, parts of the molecules precisely change place, and then the pieces are correctly joined. In this complicated series of events, no genetic information is lost or gained.
Models for Homologous Recombination (two models)

The Holliday Model

The Double-Strand-Break Model

Homologous Recombination Protein Machines (RecBCD pathway)**
The Holliday Model

1. Two double-stranded DNA molecules from homologous chromosomes align.

2. Single-strand breaks occur in the same position on both DNA molecules.

3. The free end of each broken strand migrates to the other DNA molecule.
4 Each invading strand joins to the broken end of the other DNA molecule, creating a Holliday junction, and begins to displace the original complementary strand.

5 Branch migration takes place as the two nucleotide strands exchange positions, creating the two duplex molecules.
We can view of this structure with the ends of the two interconnected duplexes pulled away from one another.

Rotation of the bottom half of the structure...
8. Produces this structure.

9. Cleavage in the horizontal plane...

10. ...and rejoicing of the nucleotide strands...

11. ...produces non-crossover recombinants consisting of two heteroduplex molecules.

12. Cleavage in the vertical plane...

13. ...and rejoicing of the nucleotide strands...

14. ...produces crossover recombinants consisting of two heteroduplex molecules.

(g) Horizontal plane

(h) (i) Non-crossover recombinants

(j) (k) Crossover recombinants
Double-strand-break model

1. Two double-stranded DNA molecules from homologous chromosomes align.

2. A double-strand break occurs in one of the molecules.

3. Nucleotides are enzymatically removed on one of the strands, producing some single-stranded DNA on each side.

4. A free 3’ end invades and displaces a strand of the unbroken DNA molecule.
5. The 3′ end then elongates, further displacing the original strand.

6. The displaced strand forms a loop that base pairs with the broken DNA molecule.

7. DNA synthesis is initiated at the 3′ end of the bottom strand, the displaced loop being used as a template.

8. Strand attachment produces two Holliday junctions, which can each be separated by cleavage and reunion.
The proteins that promote the recombination in E.coli via a major DSB repair way, known as the **RecBCD pathway**

**The steps of the RecBCD pathway**

1. This strand usually has a DSB in one DNA molecule.

2. Unwinding of dsDNA, preferential degradation of 3’-terminal strand
3. The RecB moves more slowly than RecD, so the DNA molecules accumulate a single strand loop on the top strand during the unwinding.


Chi sites
• Chi sites are recombination hot spots in the genomes of *E.coli* bacteria.
  • *Chi is the DNA sequence 5‘ GCTGGTGGG 3’.*
  • *When RecBCD encounters a Chi sequence, its function changes from an exonuclease to a helicase, producing a single strand of DNA that can invade homologous double-stranded DNA mediated by RecA*
The RecA protein

Pairing homologous DNAs and strand invasion
The structure of the RecA
RuvAB complexes catalyzes the branch migration
RuvC complexes catalyze the Holliday junction resolution
Homologous Recombination in Eukaryotes

Homologous Recombination in Eukaryotes is required for Chromosome Segregation during Meiosis

Programmed Generation of the DSBs during Meiosis