Chapter 25.3 Part I:
Homologous Recombination

1. Homologous recombination in bacteria
    - Major role at stalled replication forks
    - Machinery: central role of RecA
    - Replication restart

2. Homologous recombination in eukaryotes
    - Role in meiosis

Homologous Recombination

Genetic exchanges between molecules that share sequence similarity

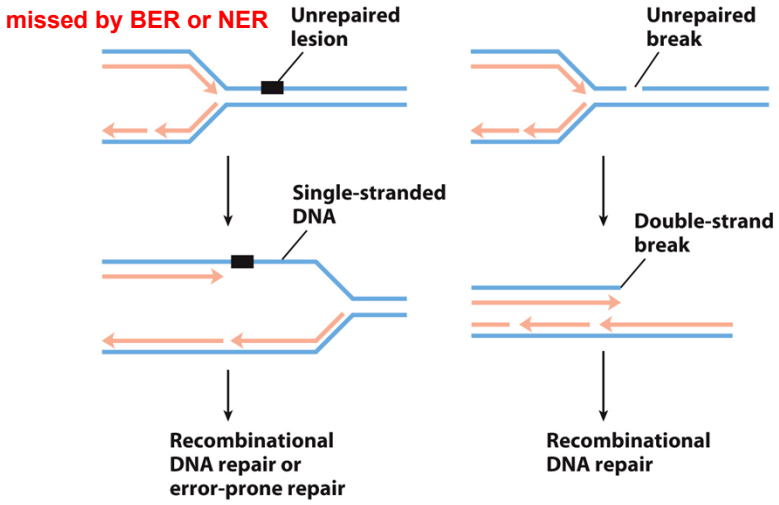
- In principle, can occur at any sequence

- Bacteria: primarily repair function, can also occur during conjugation

- Eukaryotes: repair and meiosis

Homologous recombination in bacteria

Primary function: repair of stalled replication forks



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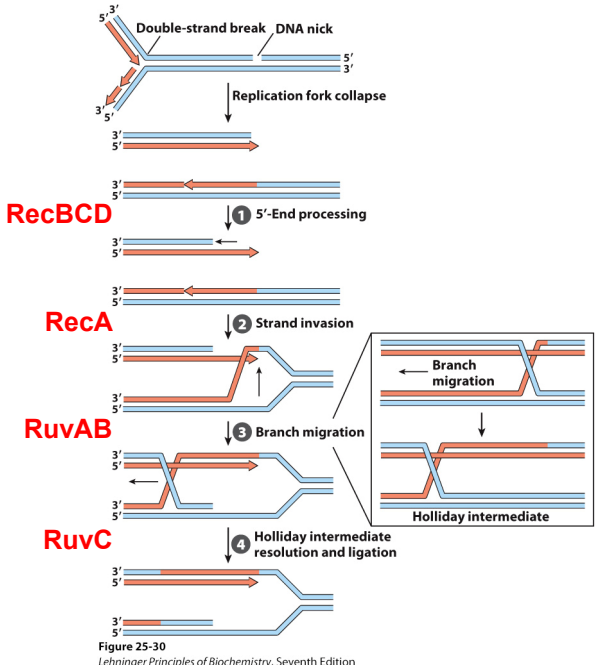
Homologous recombination in bacteria



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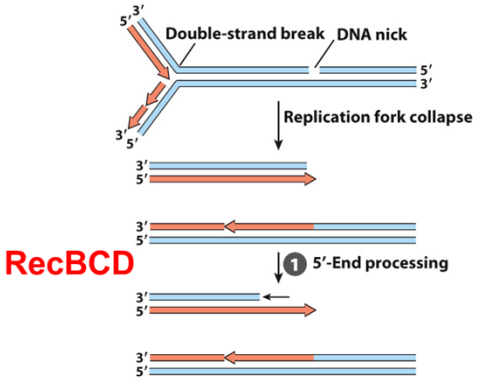
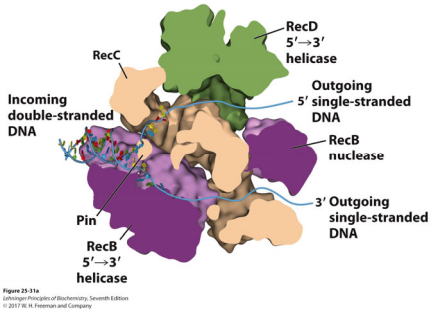
Homologous recombination in bacteria

Step 1:



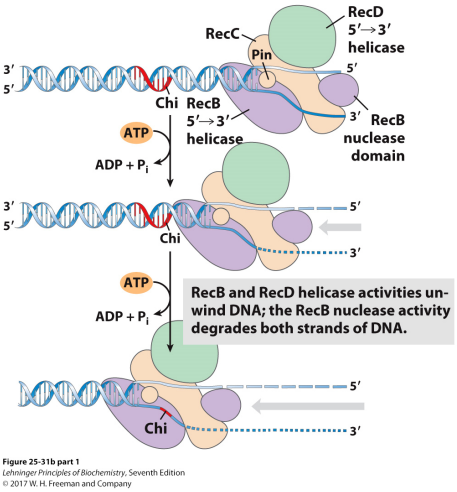


RecB and RecD: ATP-dependent helicase

RecB: nuclease activity

RecC: binds to chi

RecBCD creates 3'-overhang



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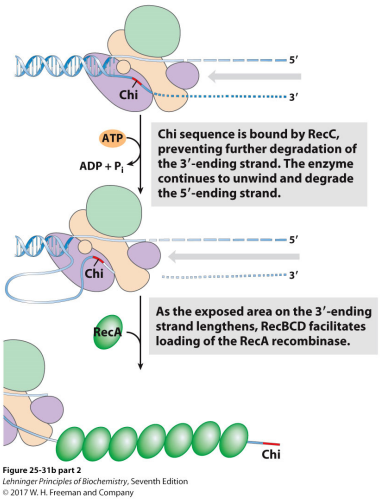

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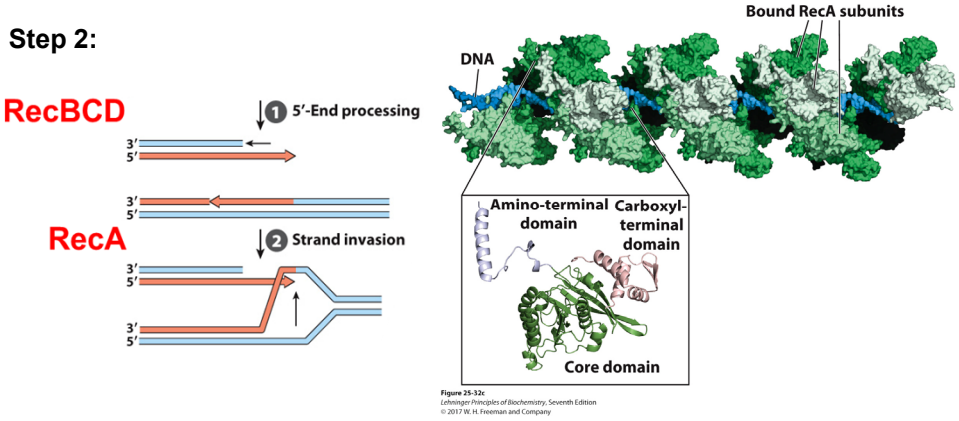
Chi- 1009 sequences spread around *E. coli* genome

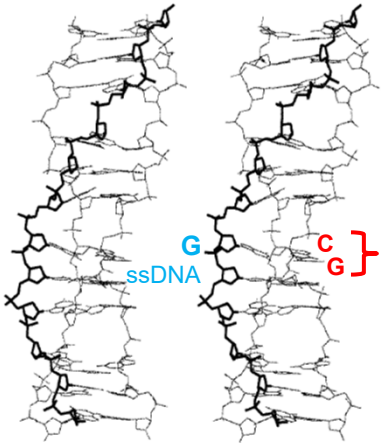
Homologous recombination in bacteria

Step 2:



RecA:
- filament on ssDNA
- when interacts with homologous duplex, starts to catalyze strand exchange
- sometimes called "bacterial recombinase"

RecA catalyzes strand exchange

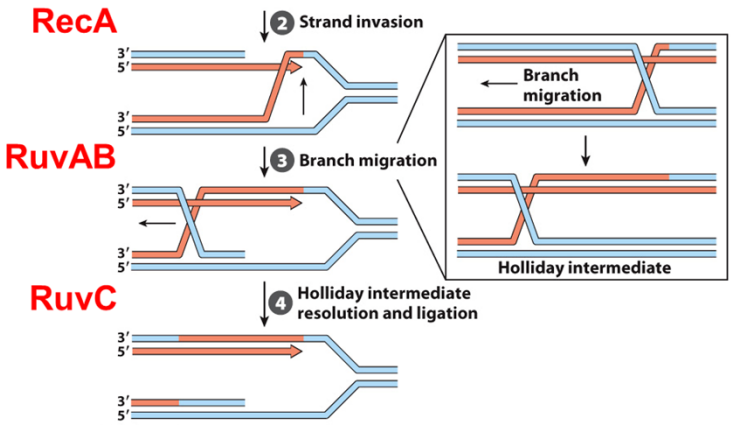


<u>Triple helical structure:</u>
ssDNA (dark strand) running along the minor groove of the double helix to be invaded

Bertucat et al., Biophys J., 1999 (77:1562-75)

Homologous recombination in bacteria

Steps 3 and 4:



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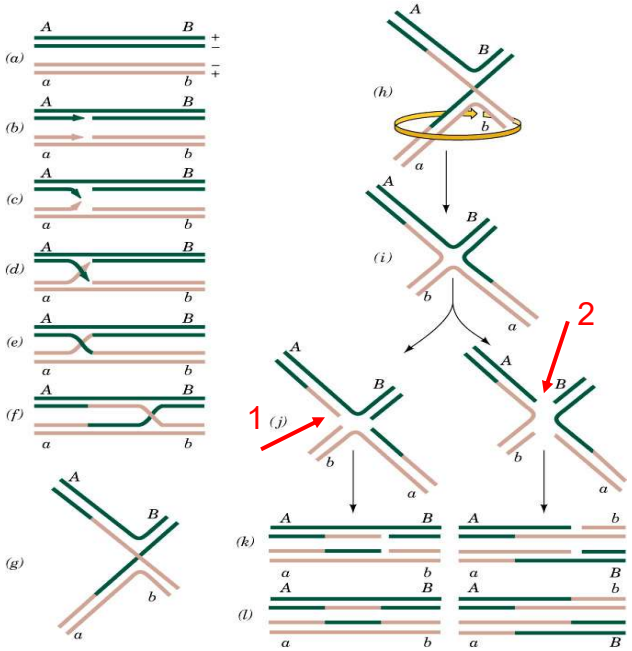
Holliday intermediates can be resolved in two different ways



Stalled replication fork repair- finish the job

Once the fork is reformed- need to restart DNA synthesis

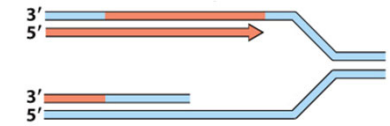


Figure 25-30

Origin-independent- replication restart primosome
- Requires 7 proteins
  DnaB and helicase loading complex (DnaC)
  Primase (DnaG)
  specialized helicases (PriABC, DnaT)

Also requires: Topoisomerases, other nucleases, polymerases, DNA ligase

Chapter 25.3 Part I: Homologous Recombination

1. Homologous recombination in bacteria
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2. Homologous recombination in eukaryotes
   - Role in meiosis

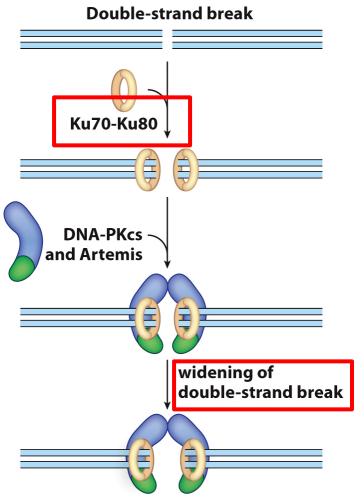
Double strand breaks in eukaryotes

1) Non homologous end joining (NHEJ)
   - major pathway in somatic cells

   requires protein heterodimer (Ku)
   Ku70 and Ku80

2) Homologous recombination repair
   - when homologous chromosome is nearby: a programmed role in meiosis

NHEJ in somatic cells



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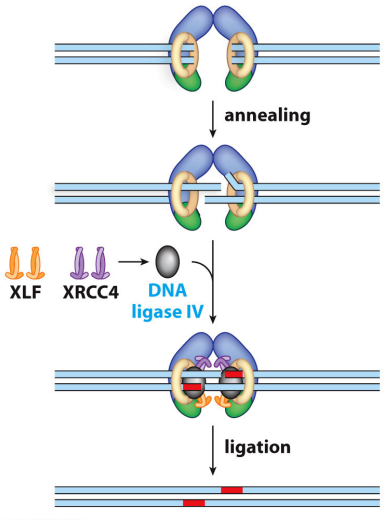

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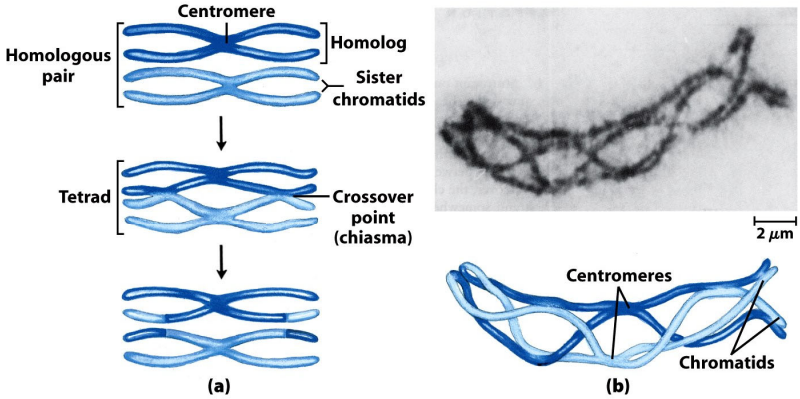
Homologous recombination during meiosis

"crossing over" reactions at chiasma



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although there are "hot spots"- can happen with relatively equal probability along chromosomes- thus could use for gene mapping experiments