DNA Recombination

DNA recombination refers to the process that a DNA segment moves from one DNA molecule to another:

1) Homologous / general recombination/ DNA cross over:

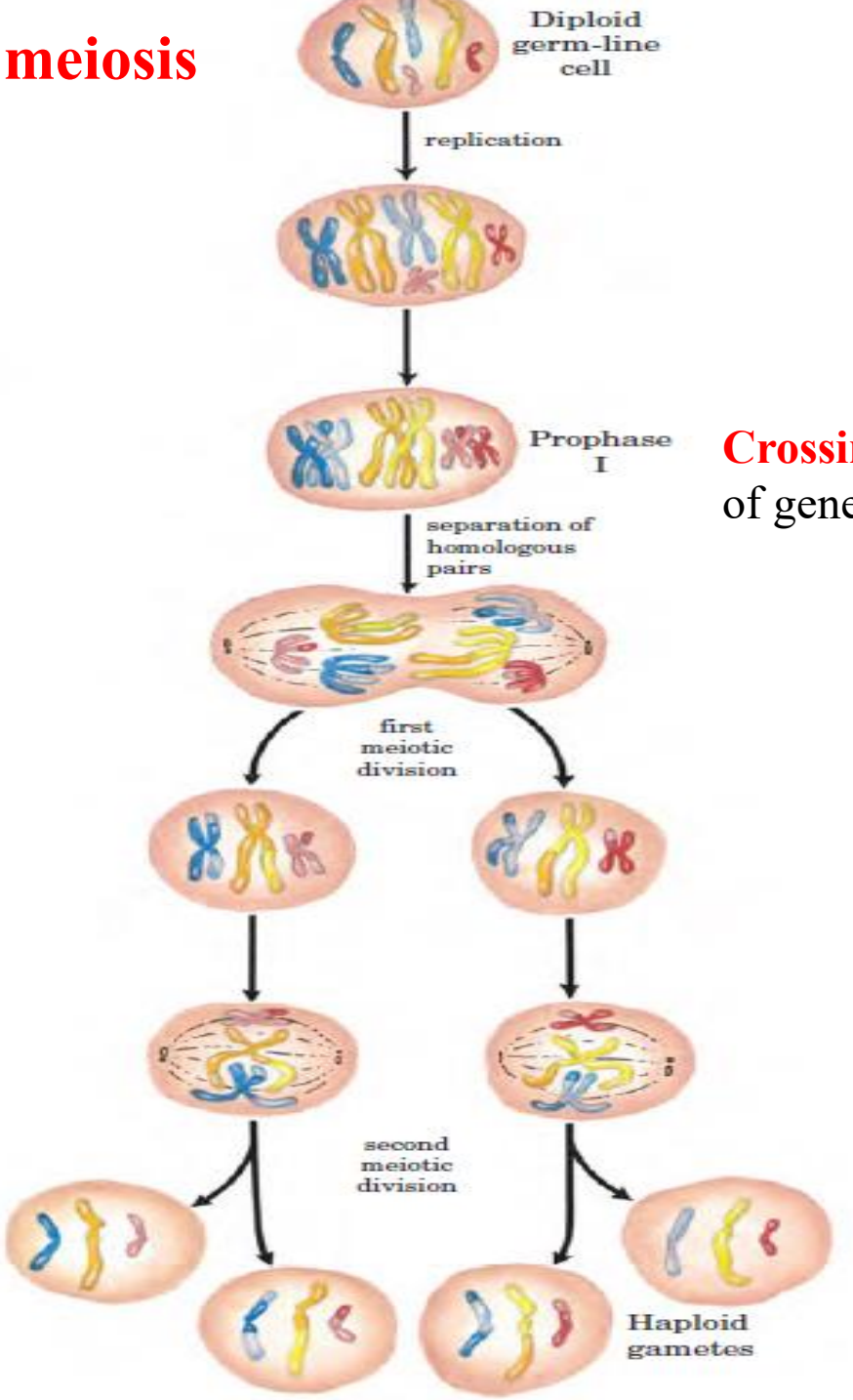
2) Site-specific recombination:

3) Transpositional recombination:

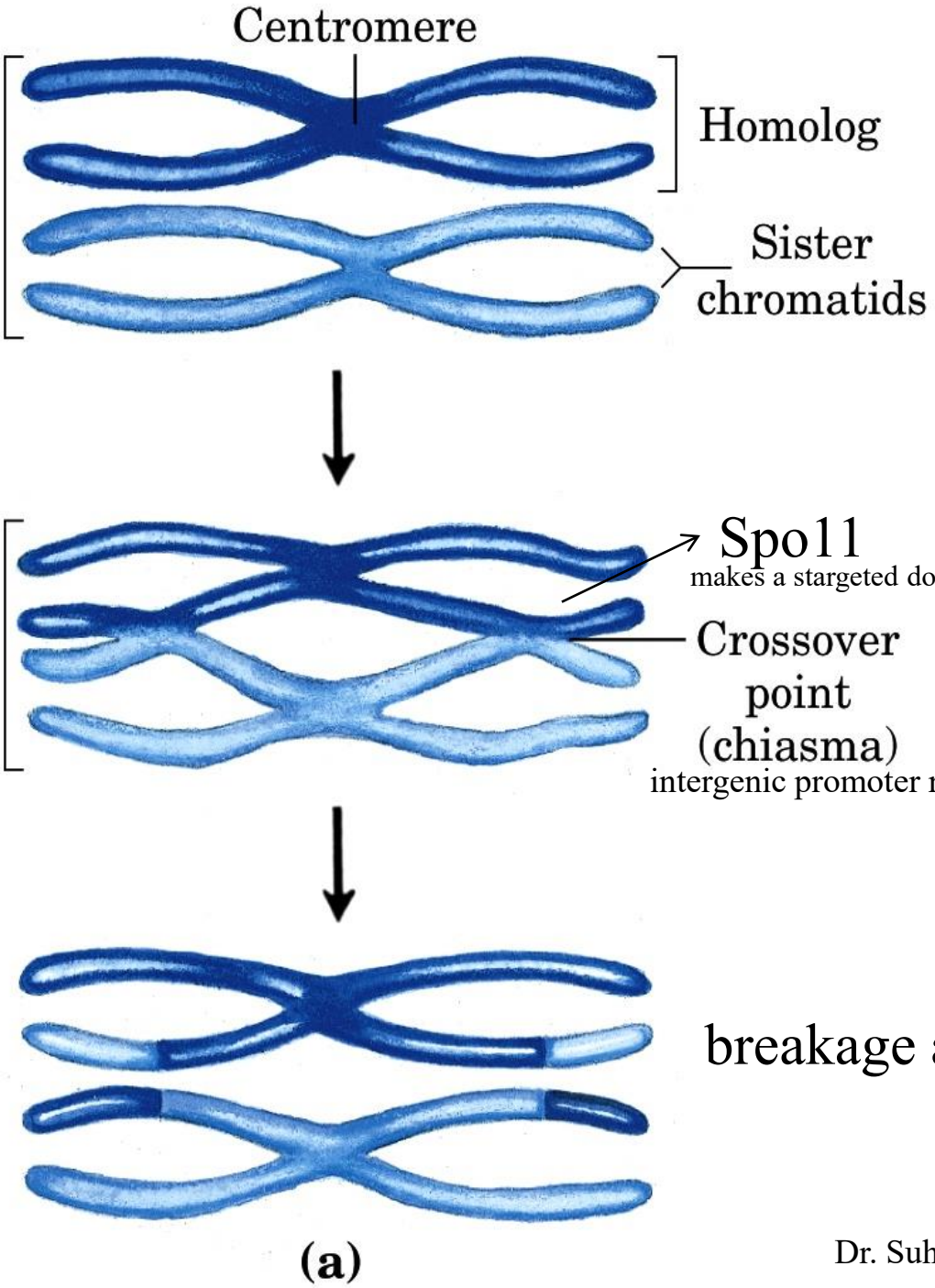
functions of genetic recombination systems

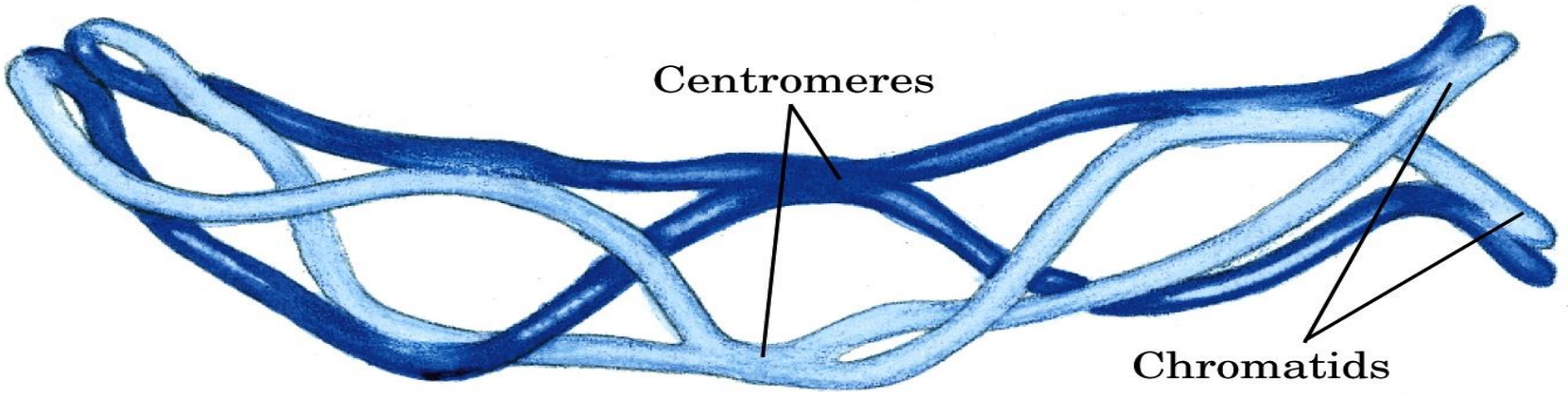
1-specialized DNA repair systems
2- maintenance of genetic diversity
3-implementation of programmed genetic rearrangements during embryonic development.
4-regulation of expression of certain genes

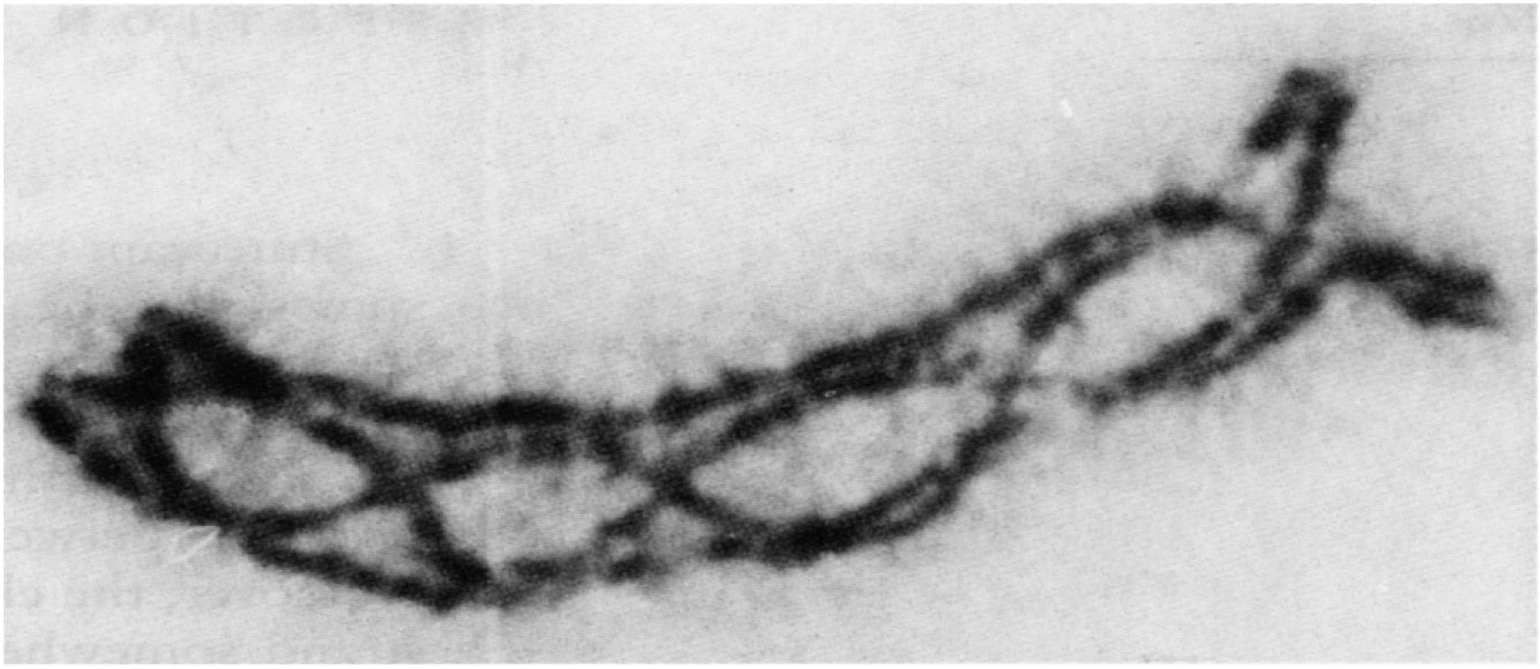
Recombination during meiosis



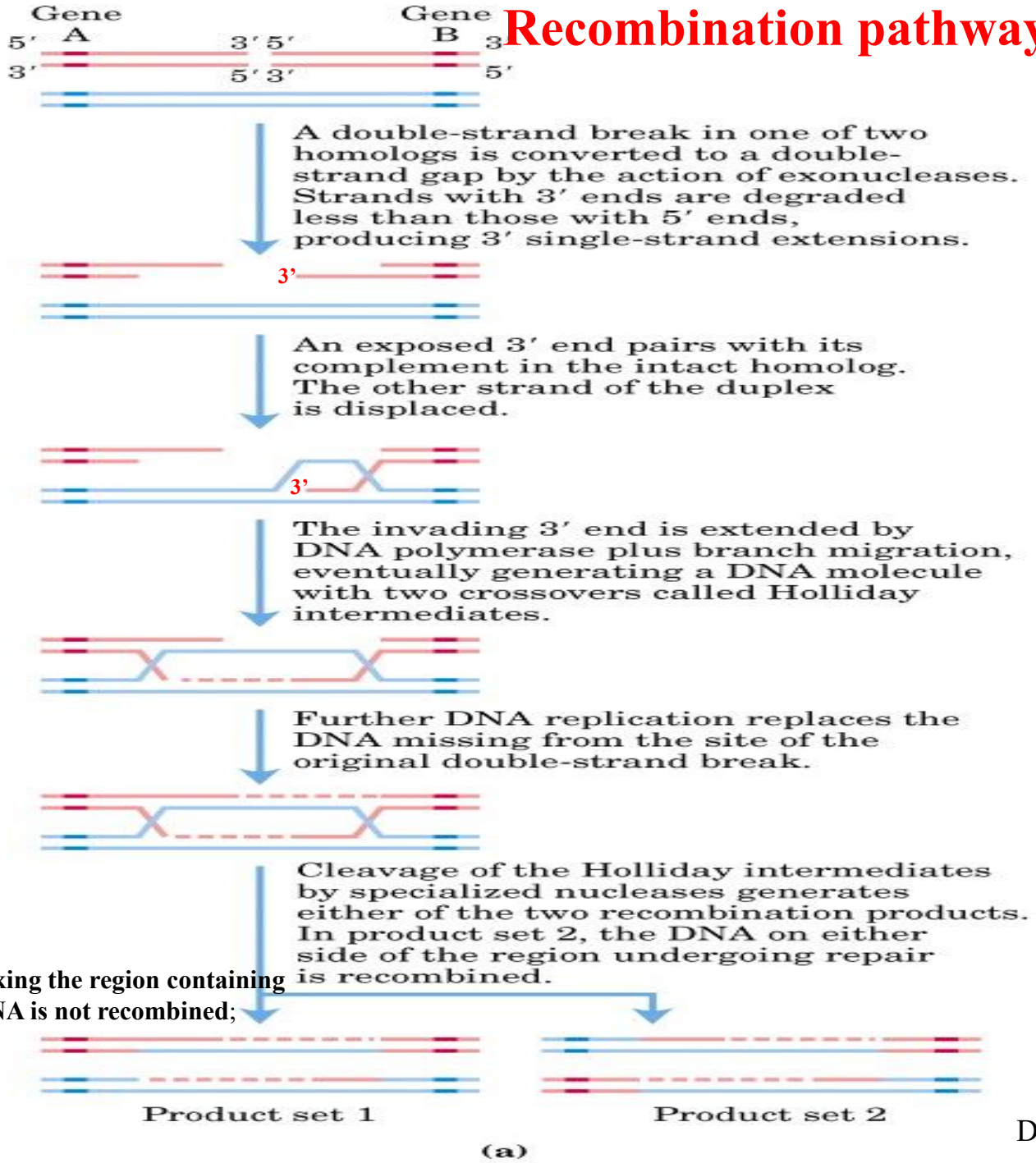
Crossing over : exchange of genetic info.


Centromere
Homologous pair
Homolog
Sister chromatids
Tetrad
like a group of four
Spo11
makes a stargeted double-strand break in DNA
Crossover point (chiasma)
intergenic promoter regions
breakage and rejoining
(a)


Centromeres
Chromatids


2 μm

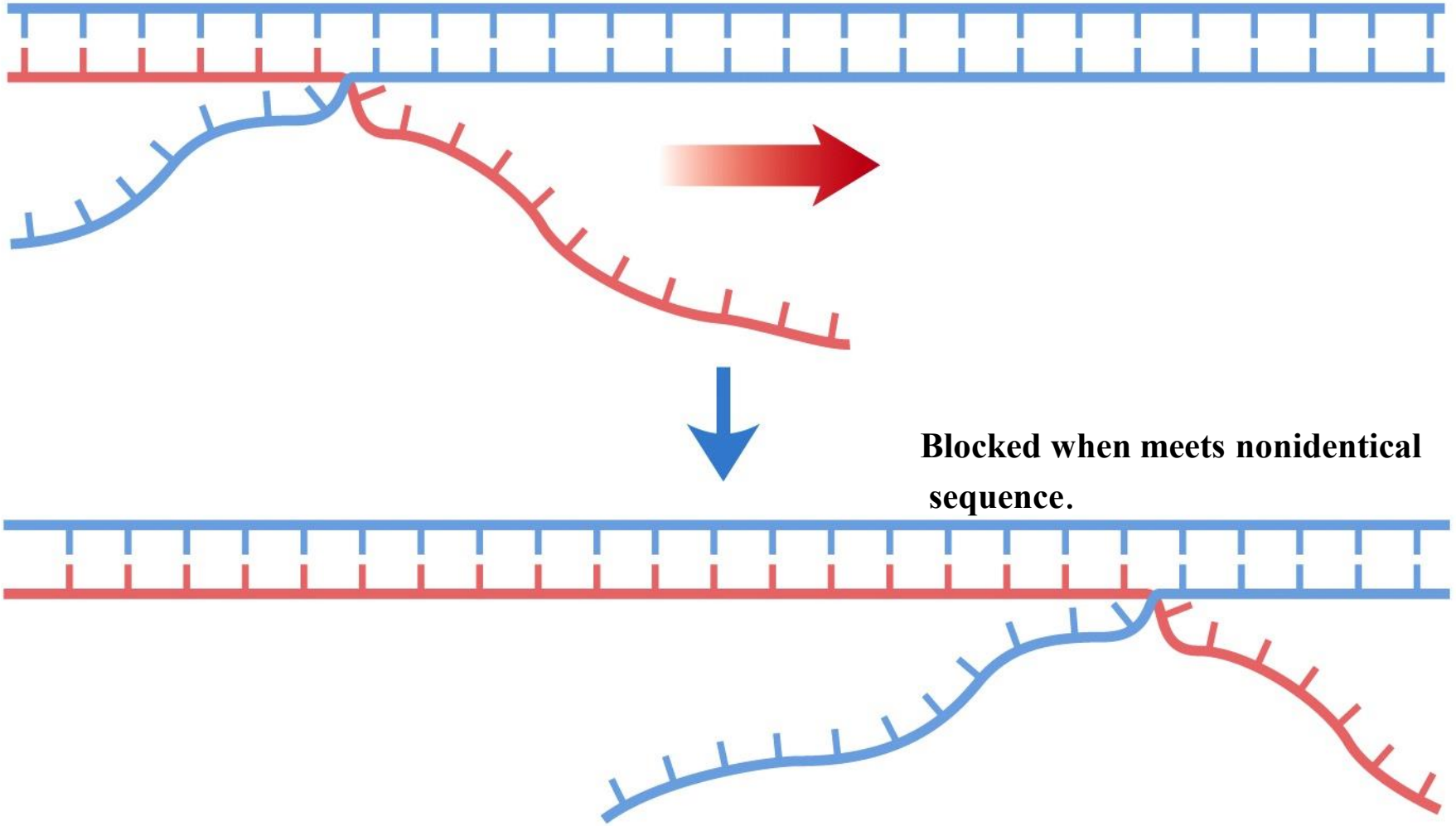
Recombination pathway during meiosis.



(a)

the DNA flanking the region containing the hybrid DNA is not recombined;

Branch migration



the ability of a DNA strand partially paired with its complement in a duplex to extend its pairing by displacing the resident strand with which it is homologous.

Homologous Recombination: double-strand break repair model

The model has four key features:

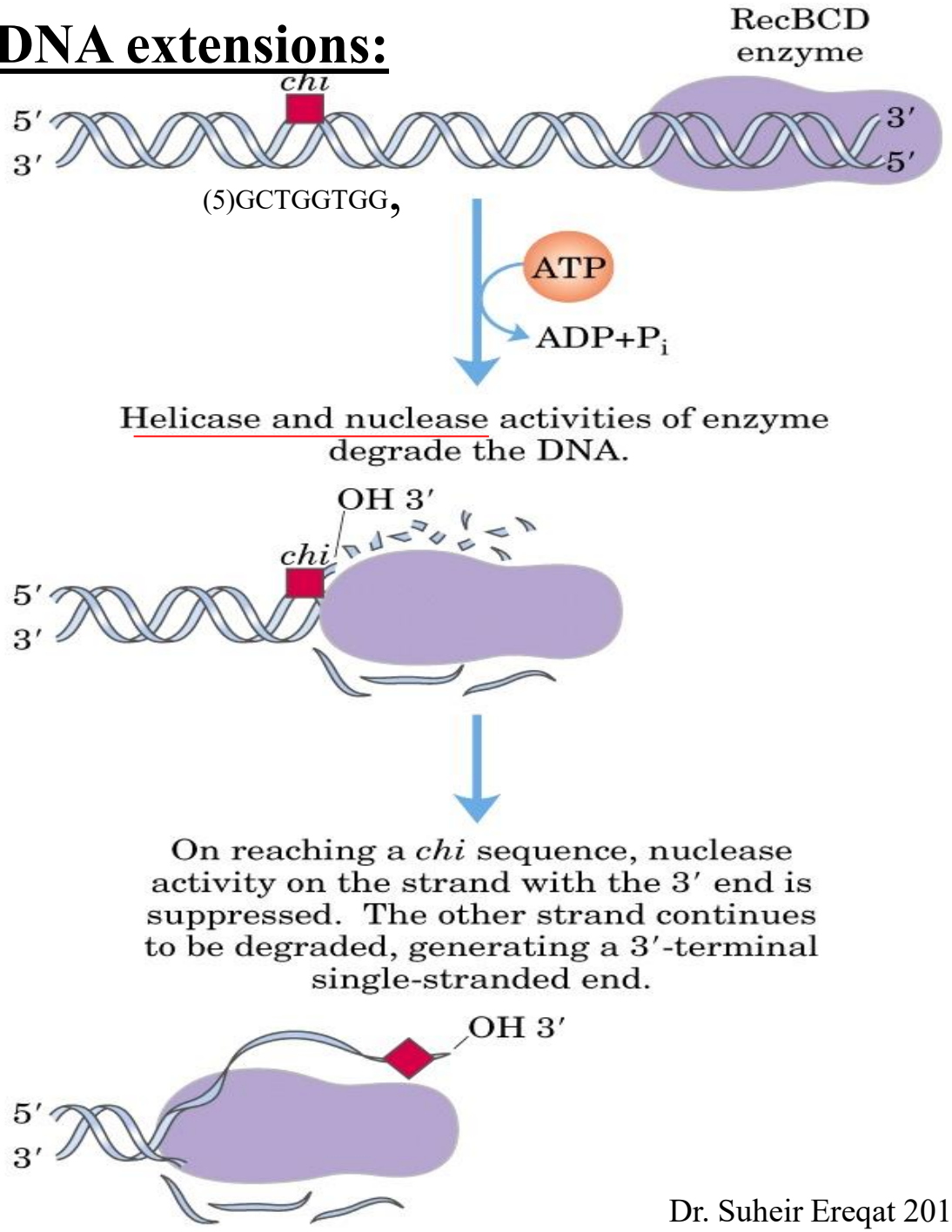
1- homologous chromosomes are aligned.

2-a double-strand break in a DNA molecule is enlarged by an exonuclease, leaving a single strand extension with a free 3-OH group at the broken end

3-the exposed 3' ends invade the intact duplex DNA of the homolog, and this is followed by **branch migration and/or by** replication to create a pair of crossover structures, called Holliday intermediates (4-stranded DNA)

4-cleavage of the two crossovers by resolvase enzymes creates either of two pairs of complete recombinant products

Formation of 3'ssDNA extensions:



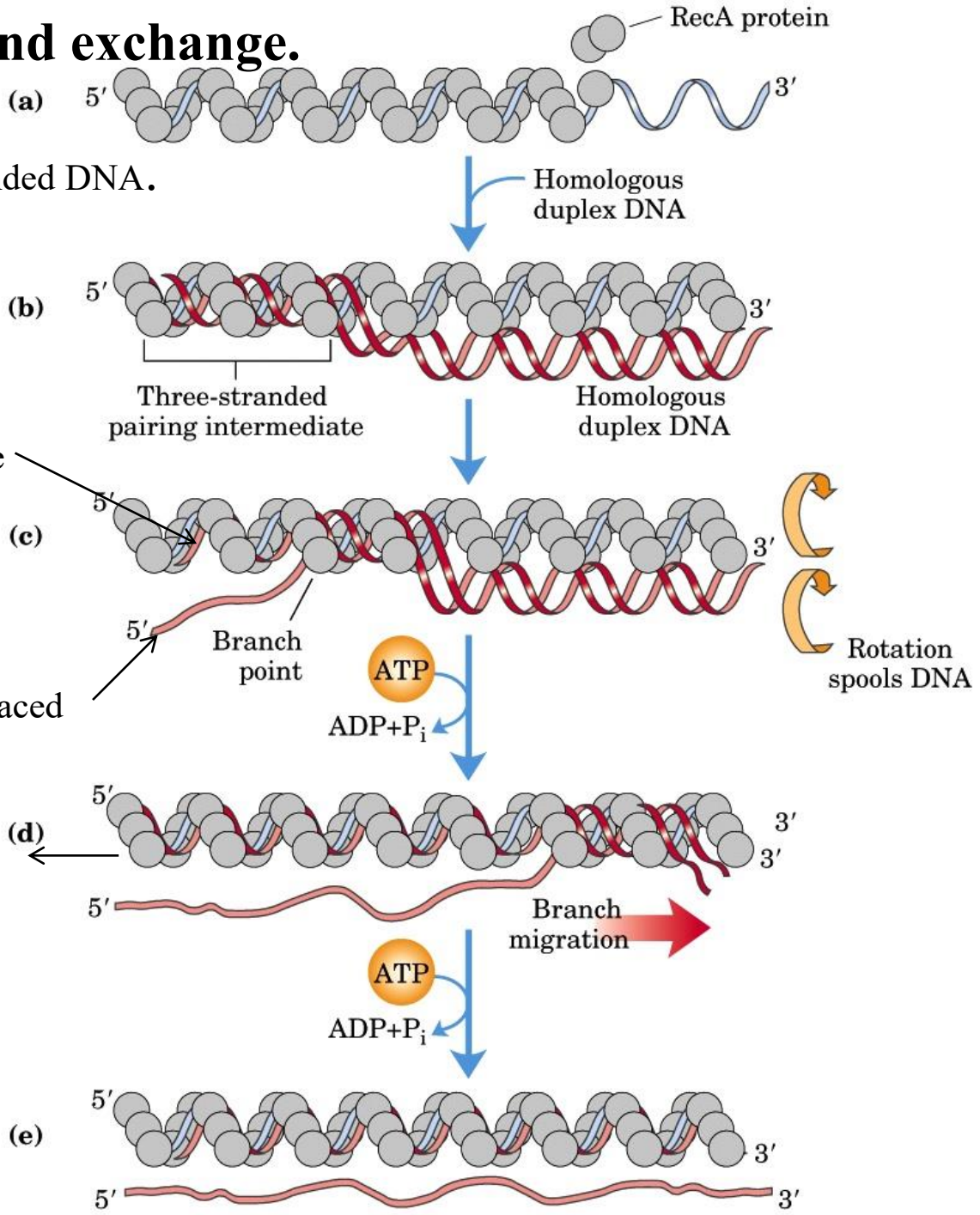
RecA-mediated DNA strand exchange.

RecA forms a filament on the single-stranded DNA.

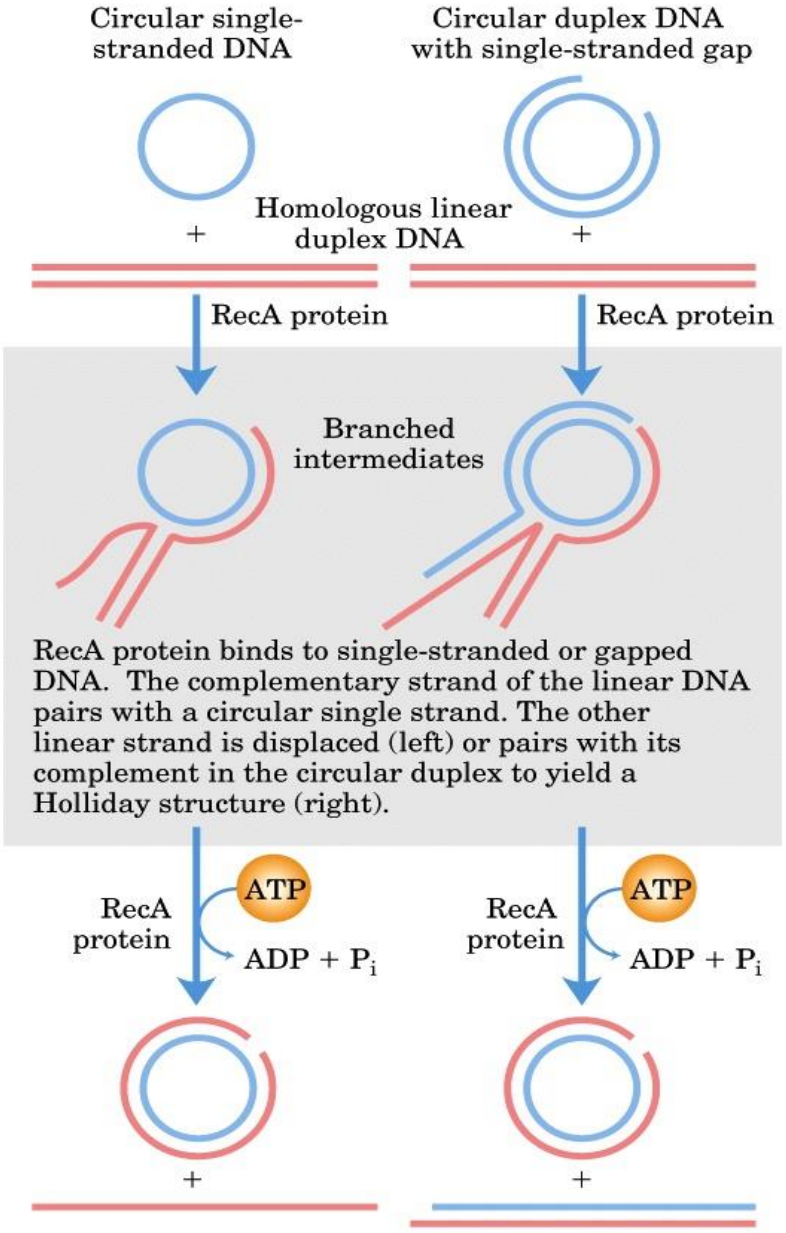
One strand is transferred to the Rec bound single strand.

The other strand is displaced

a new duplex forms within the filament.



RecA-promoted DNA strand exchange in vitro



Continued branch migration yields a circular duplex with a nick and (left) a displaced linear strand or (right) a partially single-stranded linear duplex.

Keep in mind!

- the two homologous chromosomes that undergo recombination are **NOT** necessarily identical. The linear array of genes may be the same, but the base sequences in some of the genes may differ slightly (in different alleles).
- One chromosome contains the allele of hemoglobin A (normal) the other hemoglobin S (**sickle cell anemia**).

  The difference one bp among millions!!.

(A to T)= glutamic acid being substituted by valine

- Most DNA damage repaired by BER/NER but replication fork - in its journey from origin to terminus - encounters DNA ds breaks / lesions.

- DNA pol III can't continue → **Recombinational DNA repair**
  Origin-independent restart of replication:
  Complex of 7 proteins:(priA, C, DnaB, C, G, T) and **DNA pol II**.

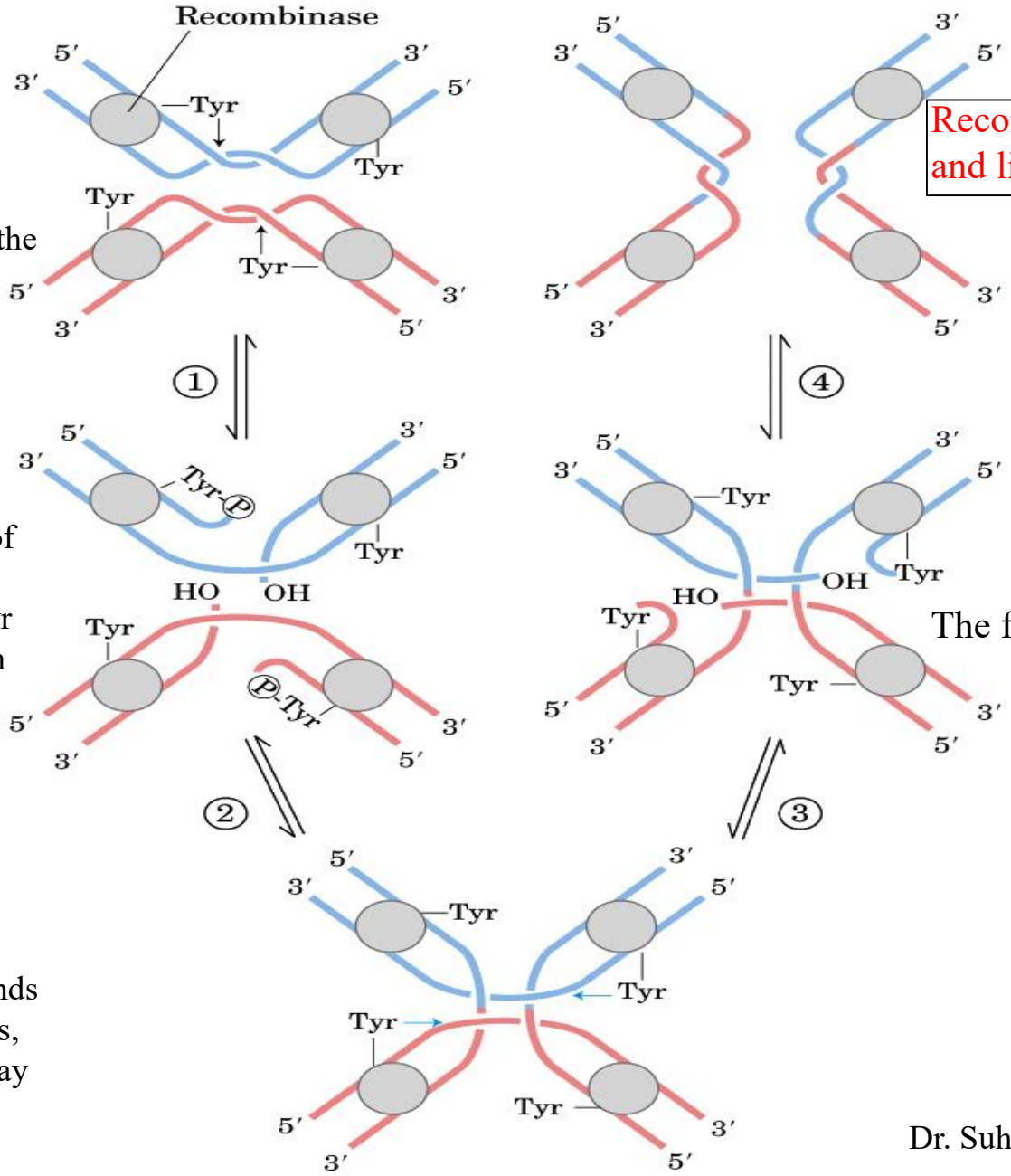
- Repair of stalled/ blocked replication fork :Transition from replication→ recombinational repair → replication.

Site specific recombination: is limited to specific sequences.

1-Recombinase subunits bind to a specific sequence, the recombination site

2-The nucleophile is the —OH group of an active-site Tyr residue=phospho Tyr link between protein and DNA.

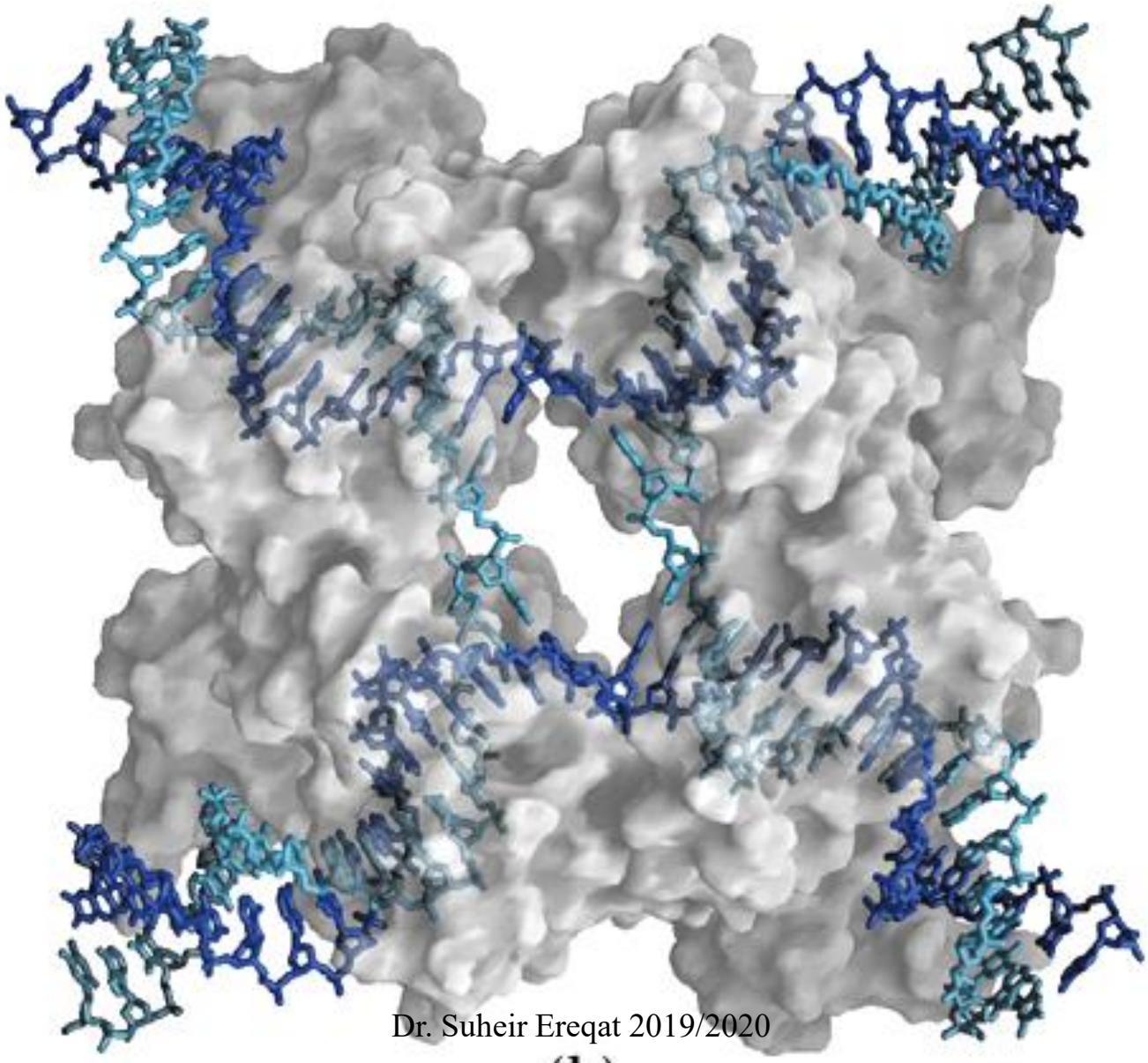
3-The cleaved strands join to new partners, producing a Holliday intermediate



Recombinase: endonuclease and ligase in one package!!

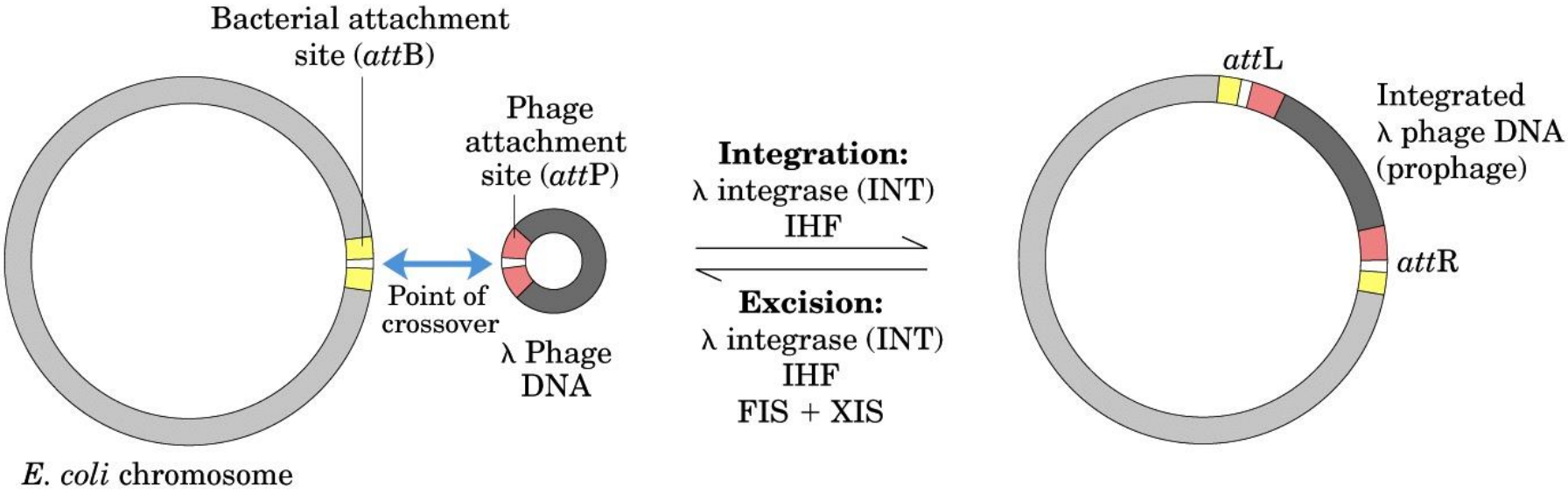
The first two steps are repeated

Holliday intermediate:



(b)

Example: Integration and excision of bacteriophage DNA at the chromosomal target site



Transpositional recombination

Transpositinal recombination : allows the movement of transposable elements (**transposons)** from one place on a chromosome (**the donor site**) to another on the same or a different chromosome **(the target site**)

Transposable Genetic Elements:

Simple transposons:

contains only the sequence required for transposition. The genes for transposase.

Complex transposons:

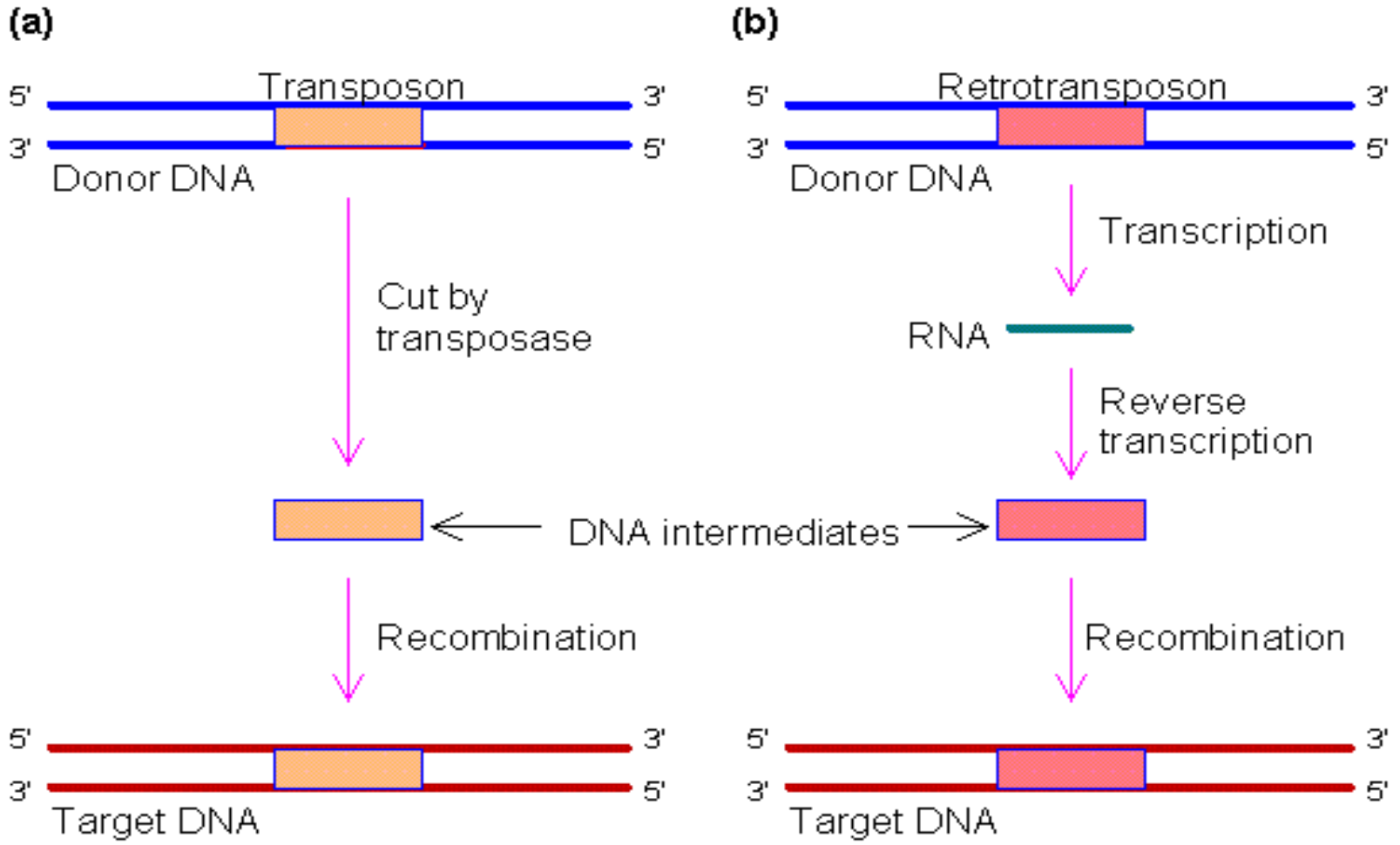
contains one/ more genes in addition to those needed for transposition.

e.g. confer resistance to antibiotics.

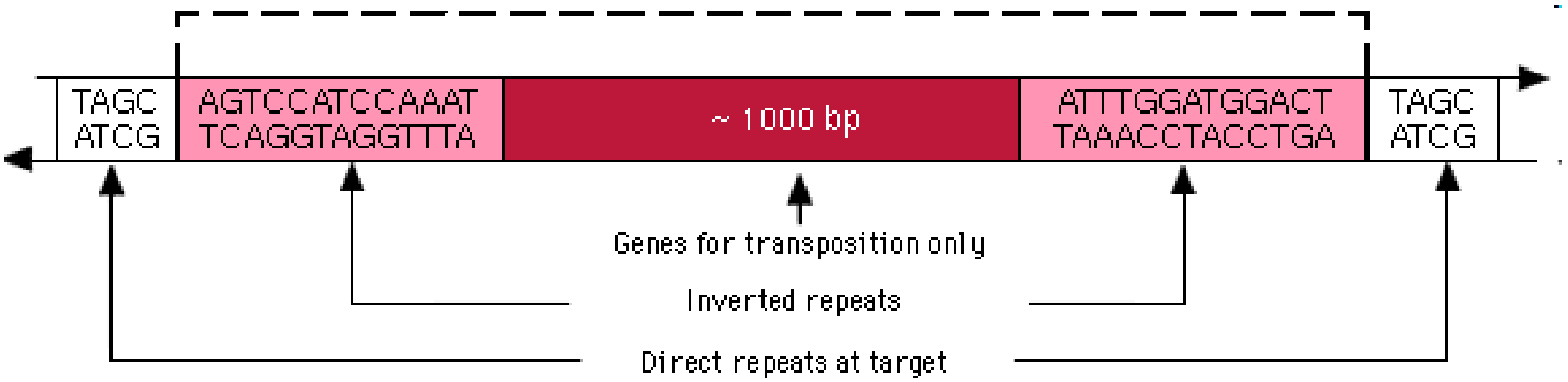
- **Classes of transpositional recombination**

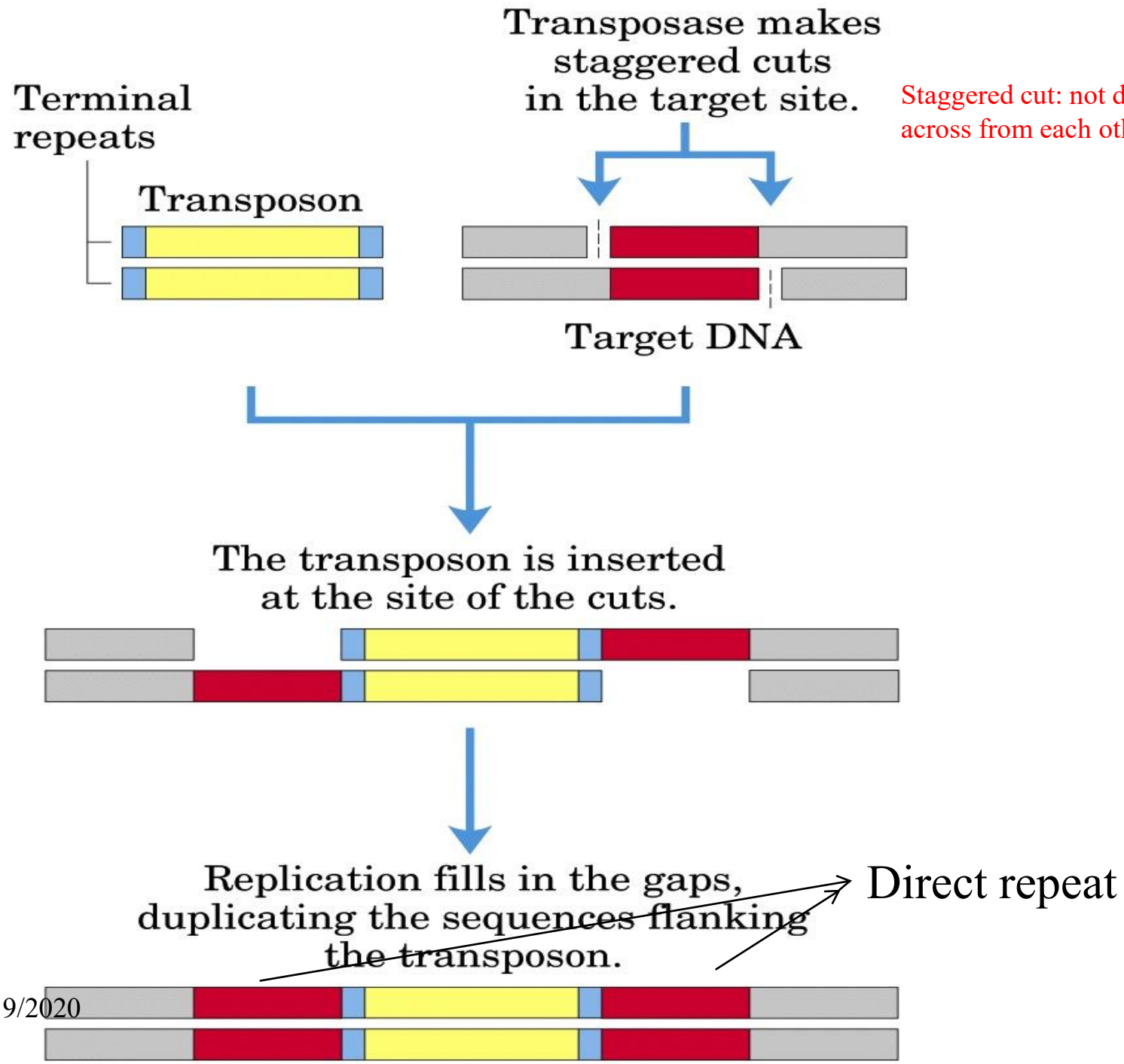
a) Class I: retrotransposons

b) Class II: DNA-transposons.



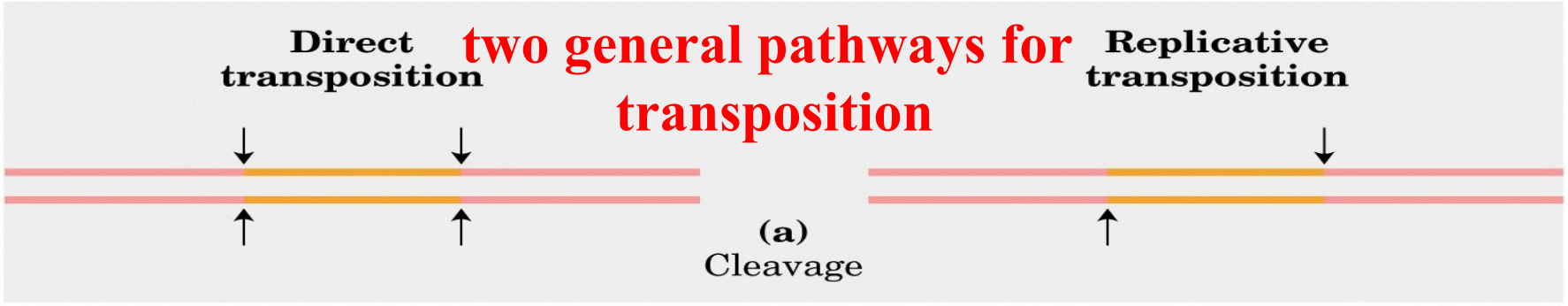
transposons class II

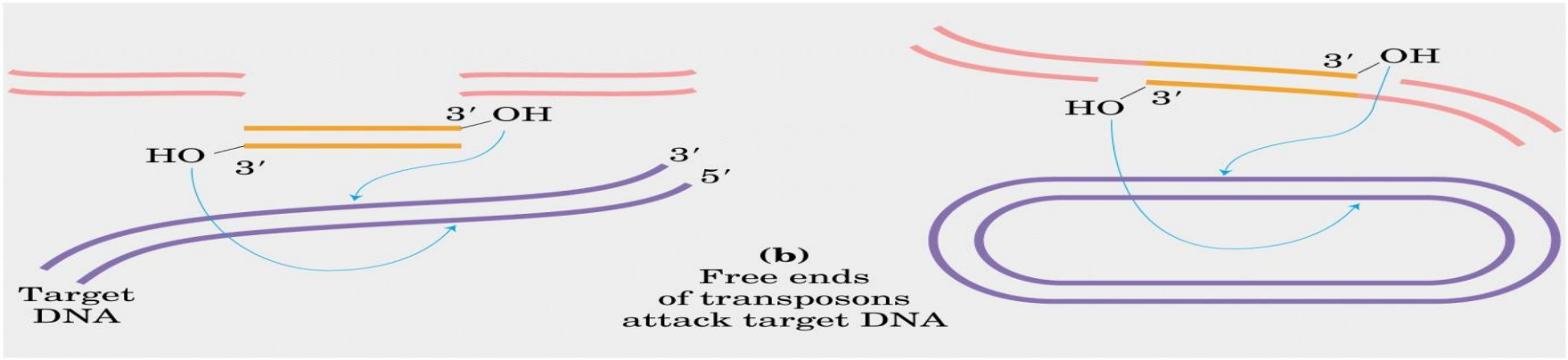


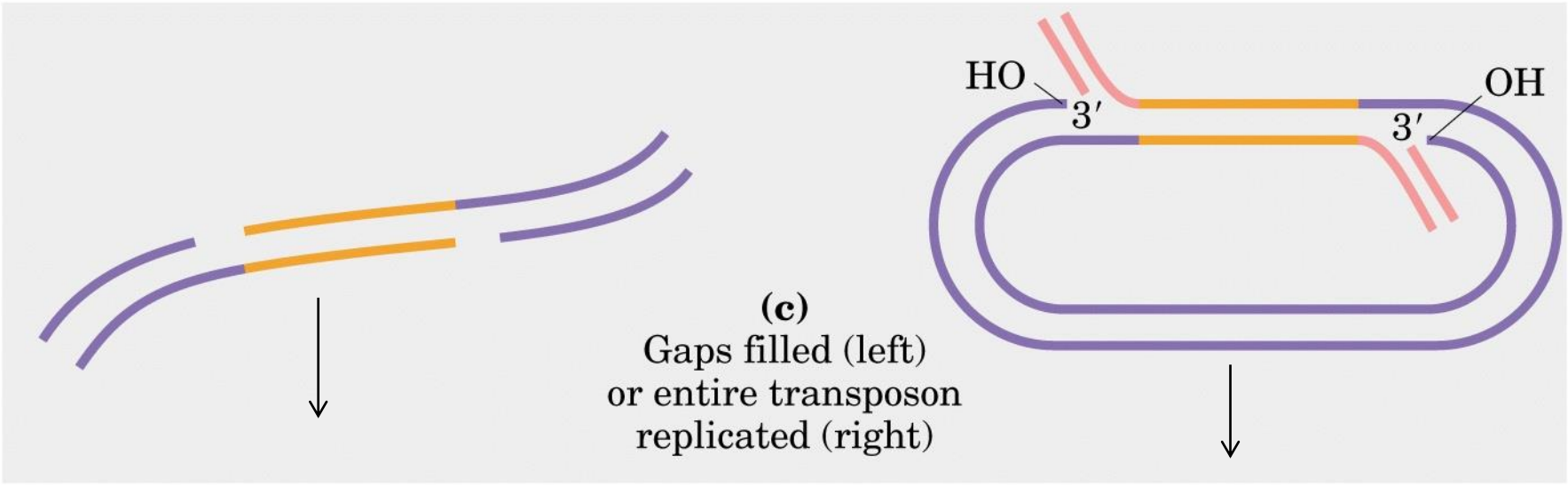


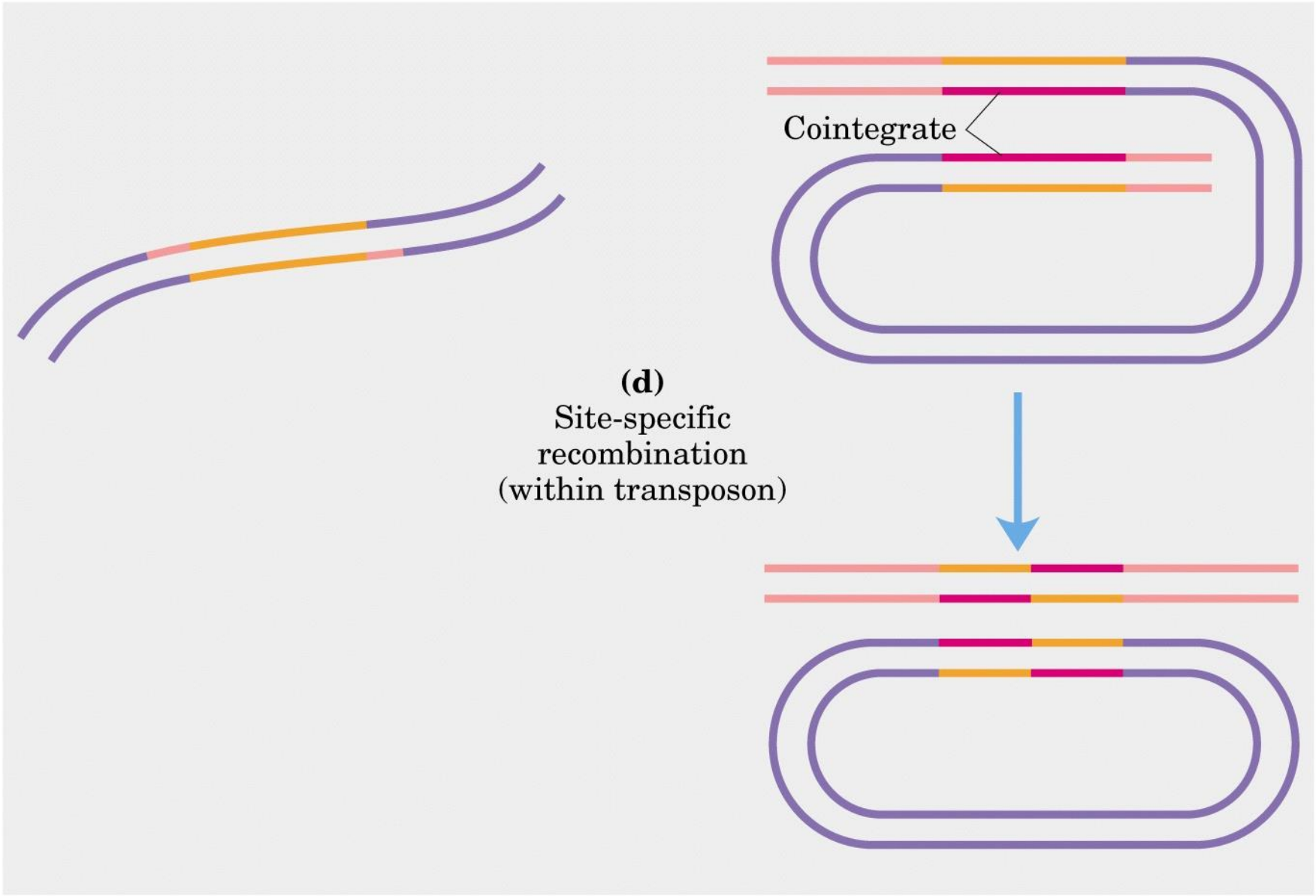
Staggered cut: not directly across from each other

two general pathways for transposition








Cointegrate
(d)
Site-specific
recombination
(within transposon)