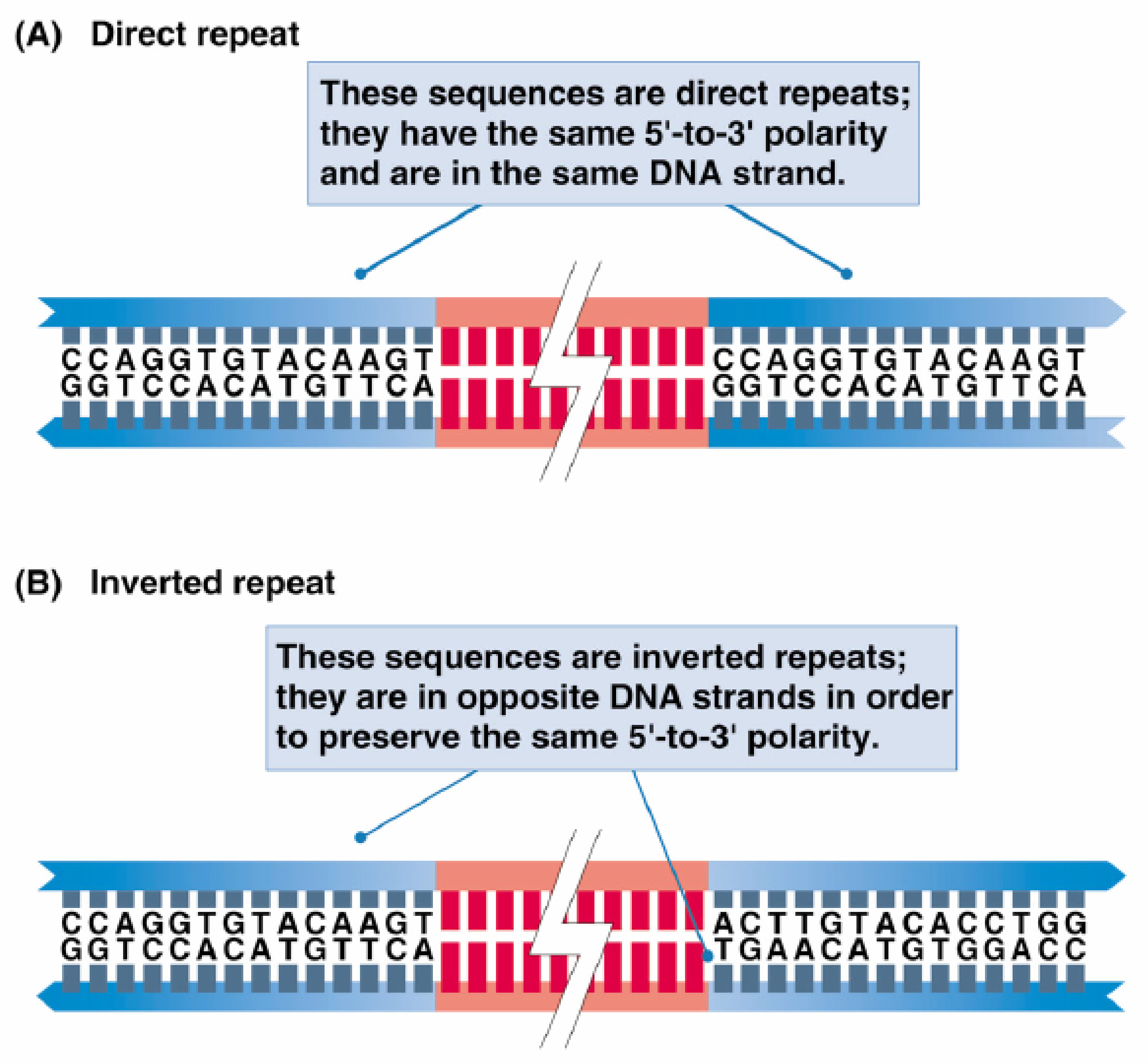
Nature of transposable elements

DNA móvel

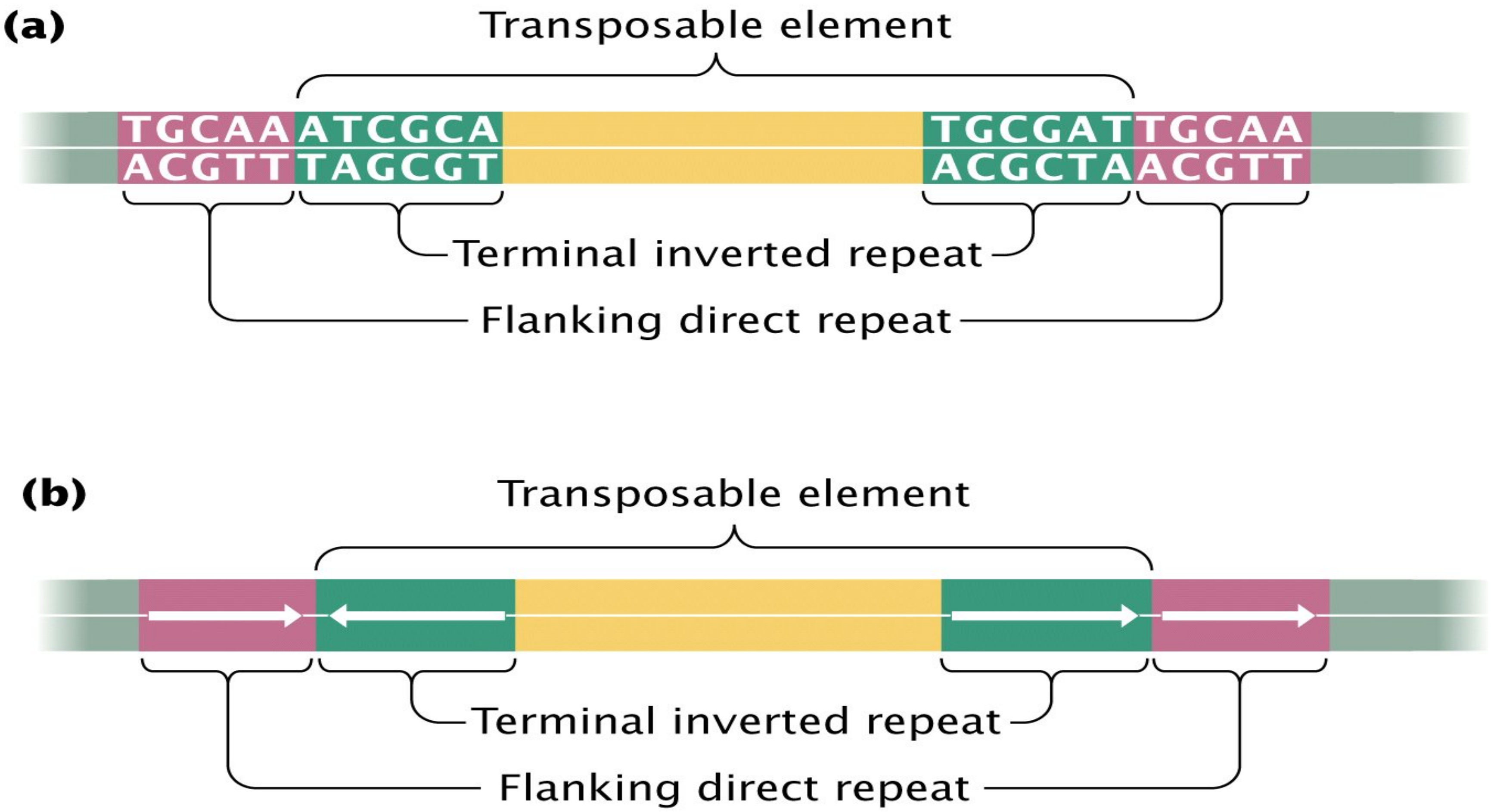
Elementos transponíveis

Direct and inverted repeats



Hartl

Common characteristics of transposable elements



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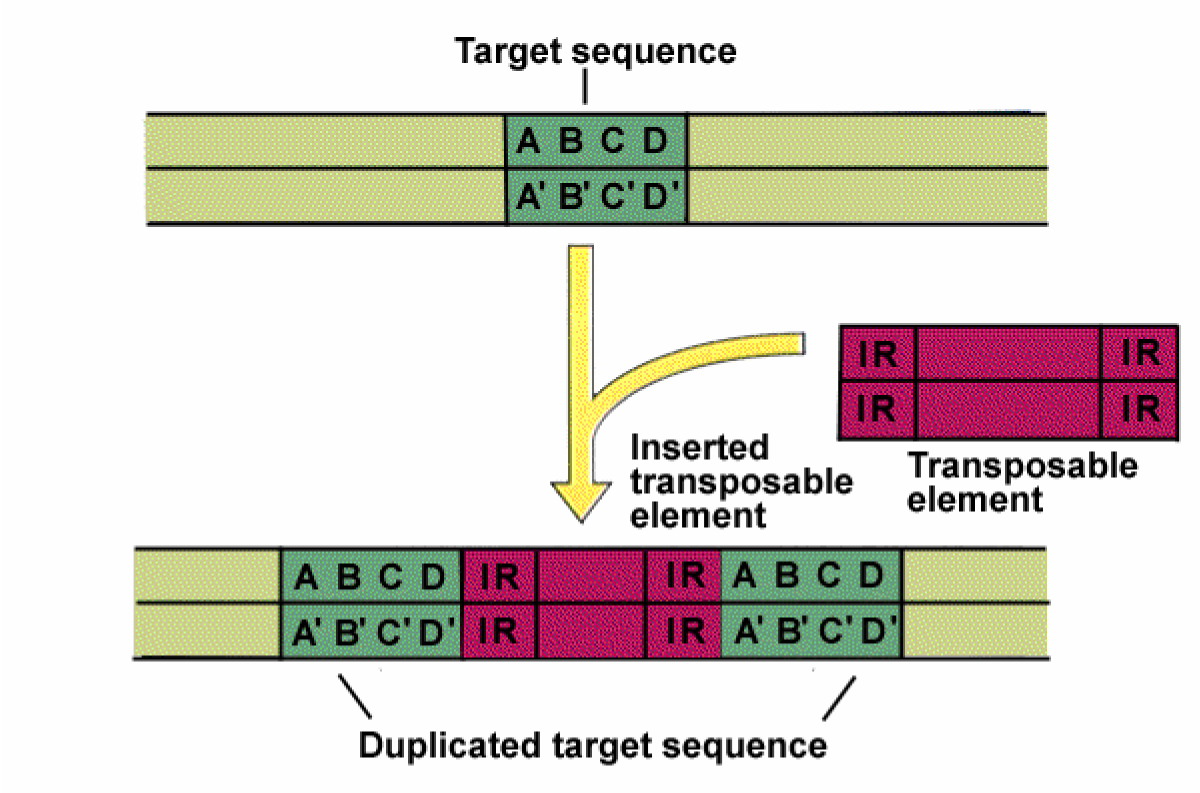
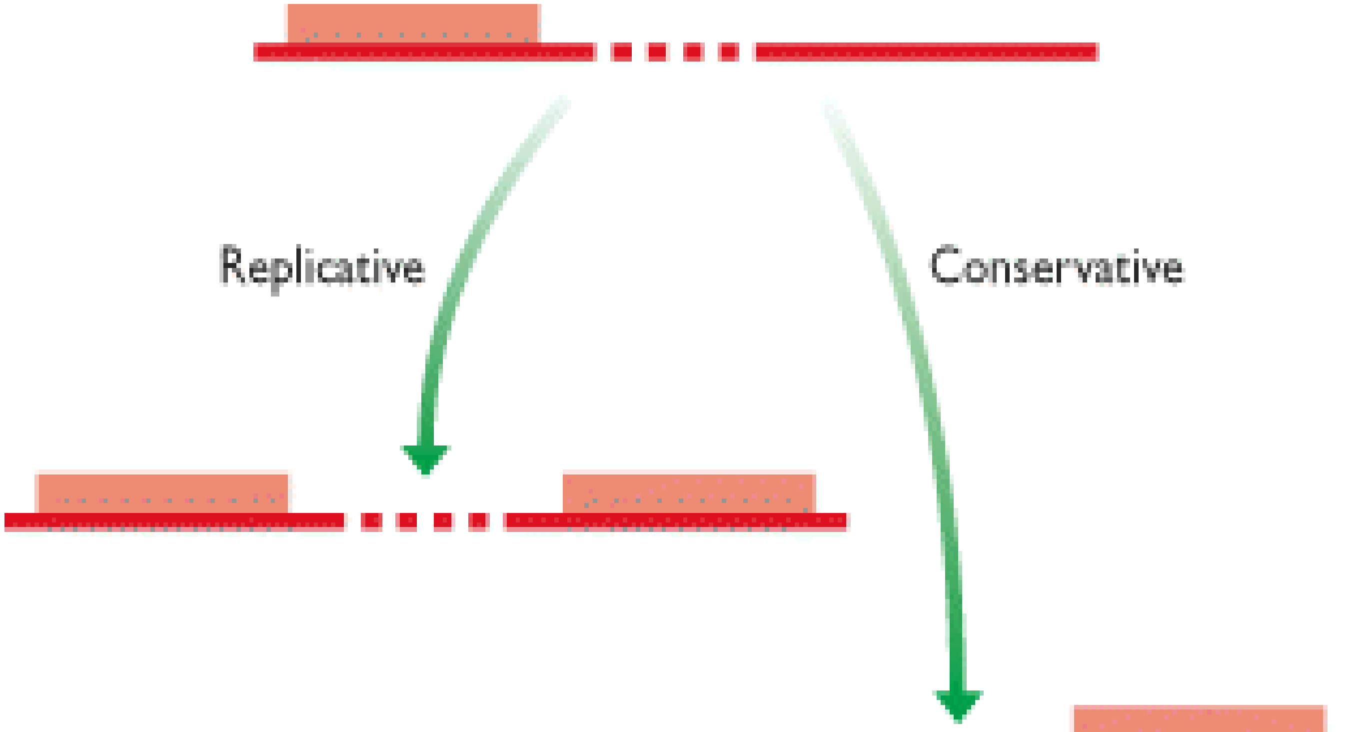
IR belongs to the transposable element



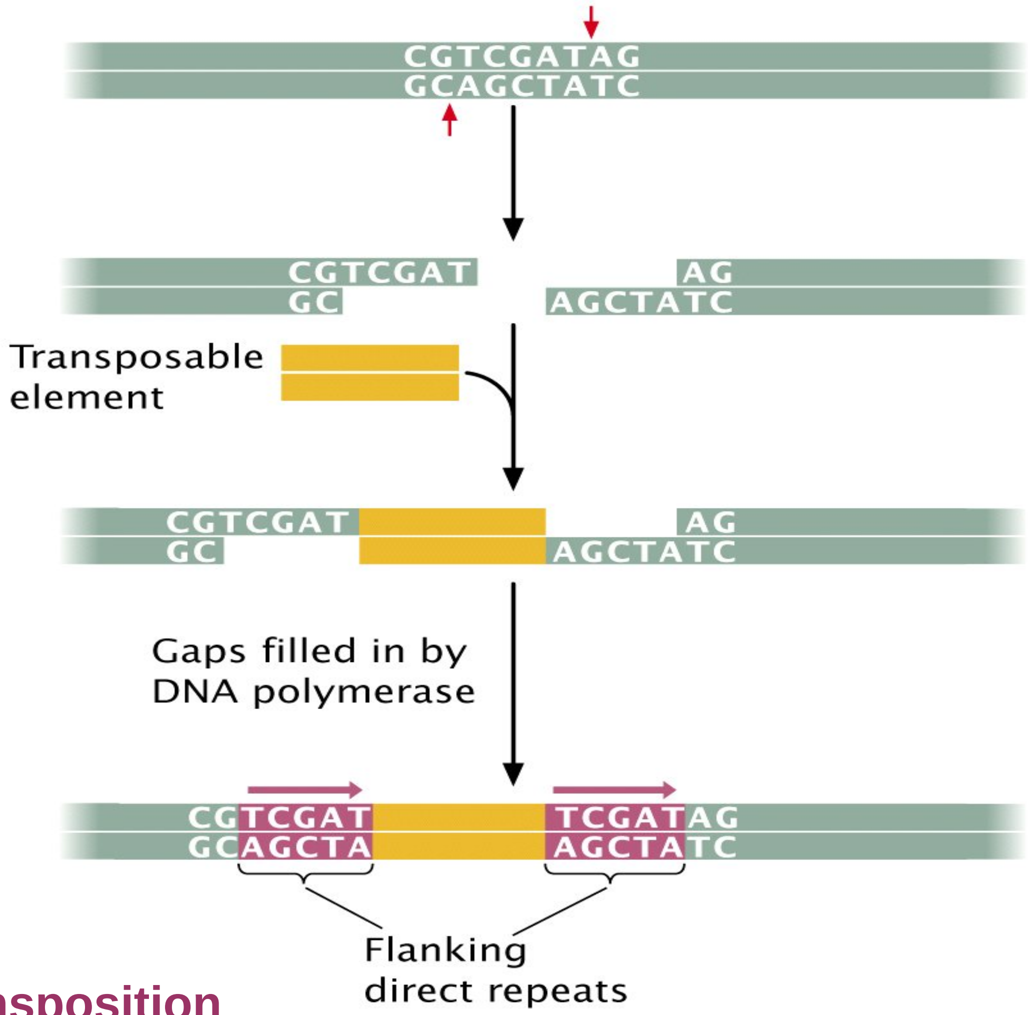
Mechanisms of transposition

Replicative transposition
(copy-paste)
Conservative transposition
(cut-paste)

Replicative and Conservative transposition



Flanking direct repeats are generated when a transposable element inserts into DNA



Conservative transposition

Ex. Tn10

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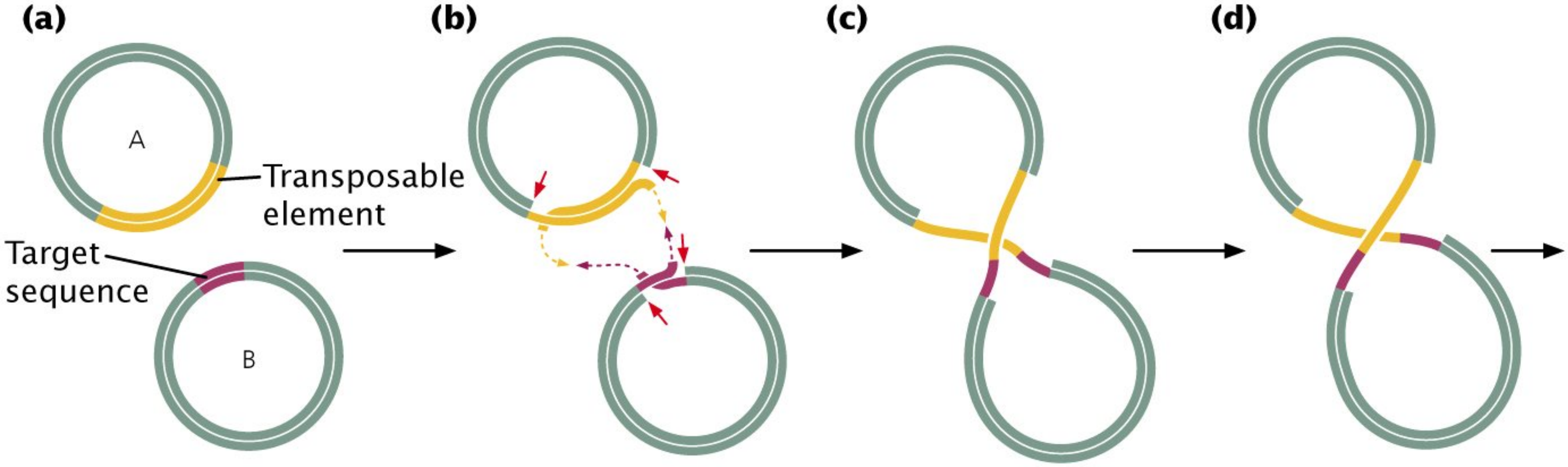
Replicative transposition

A transposase makes a single-Strand breaks at each end of the transposable element

Replication takes place on the single-stranded templates, begining at the 3'-OH ends of single strands



The free ends of the transposable Element attach to the free ends of the target sequence

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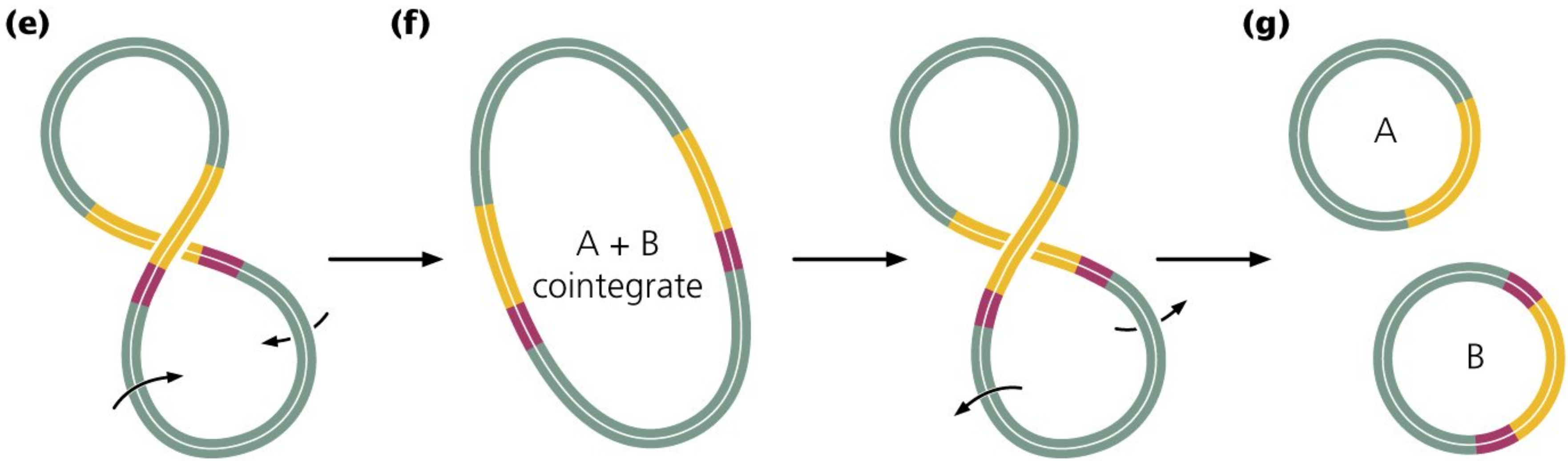
Replication proceeds through the transposable element and the target sequences

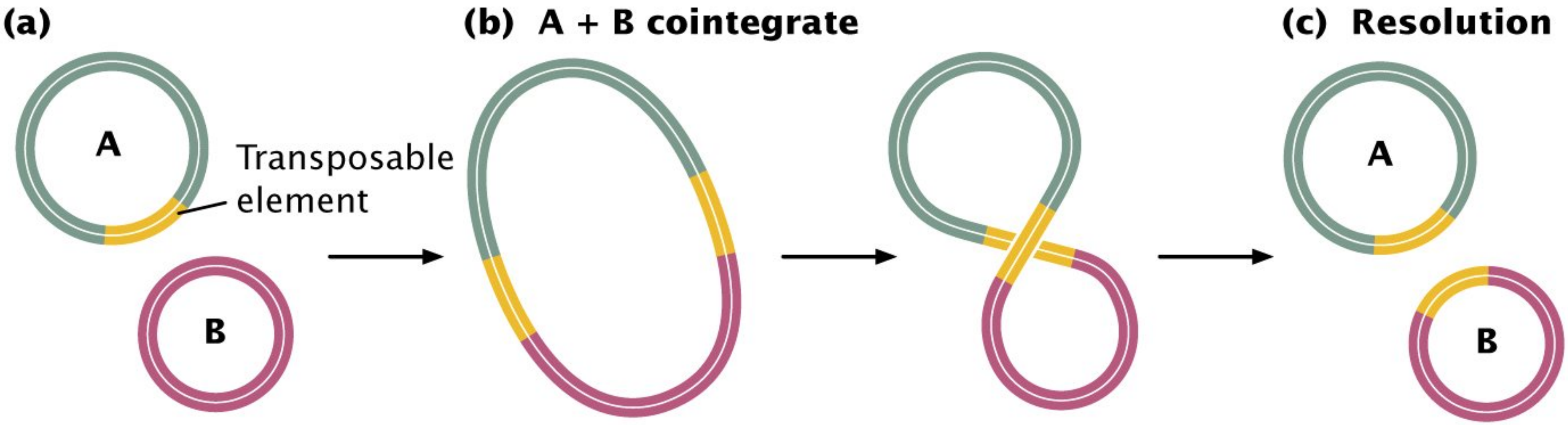
Cointegrate resolution crossing over between sites within the transposable element



Cointegrate formation with two copies of the transposable element and two copies of the target sequence

Two separate copies of the transposable element. The new copy is flanked by direct repeats of the target sequence.

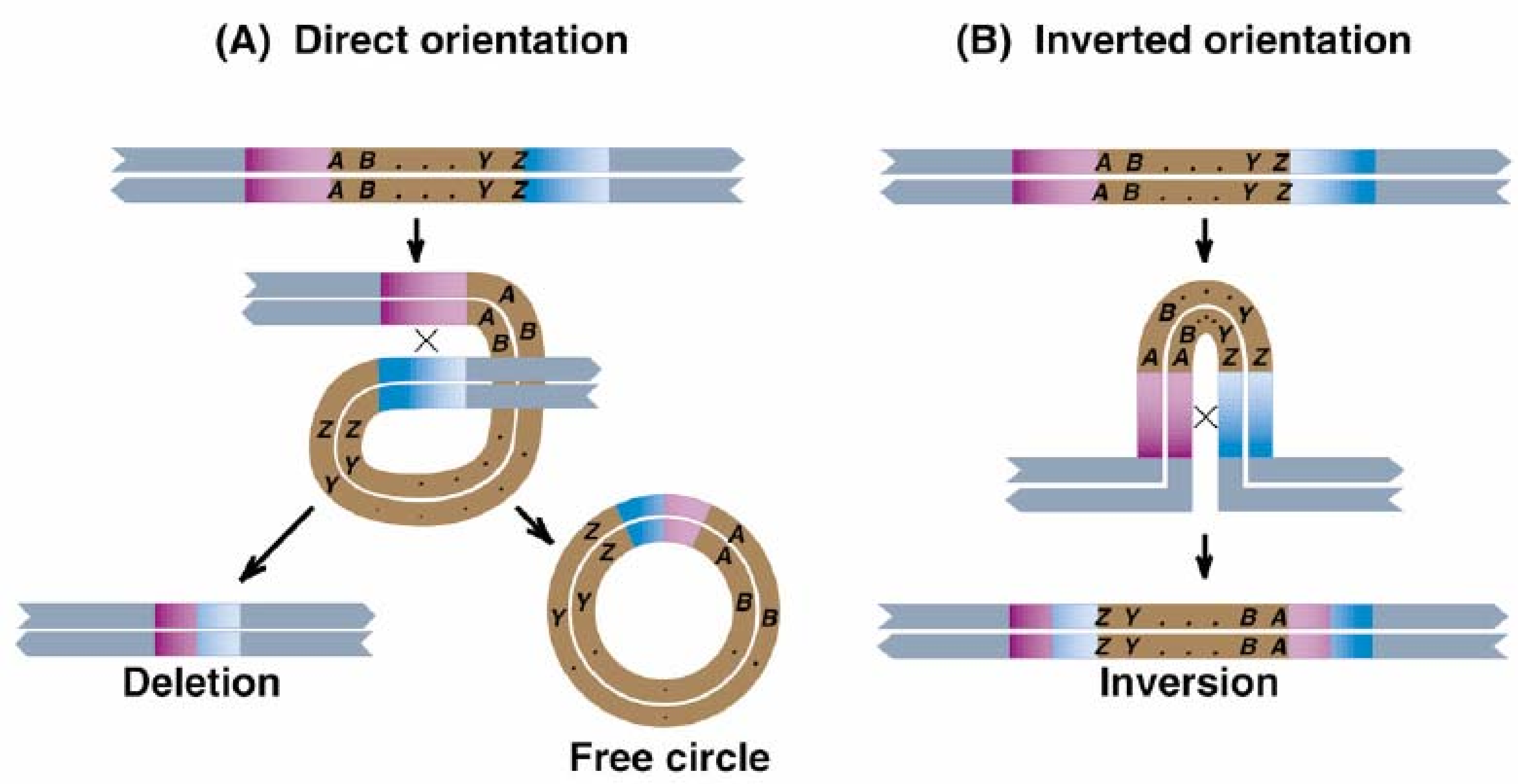
Replicative transposition requires single-strand breaks, replication and resolution



Tn3 has na internal resolution site

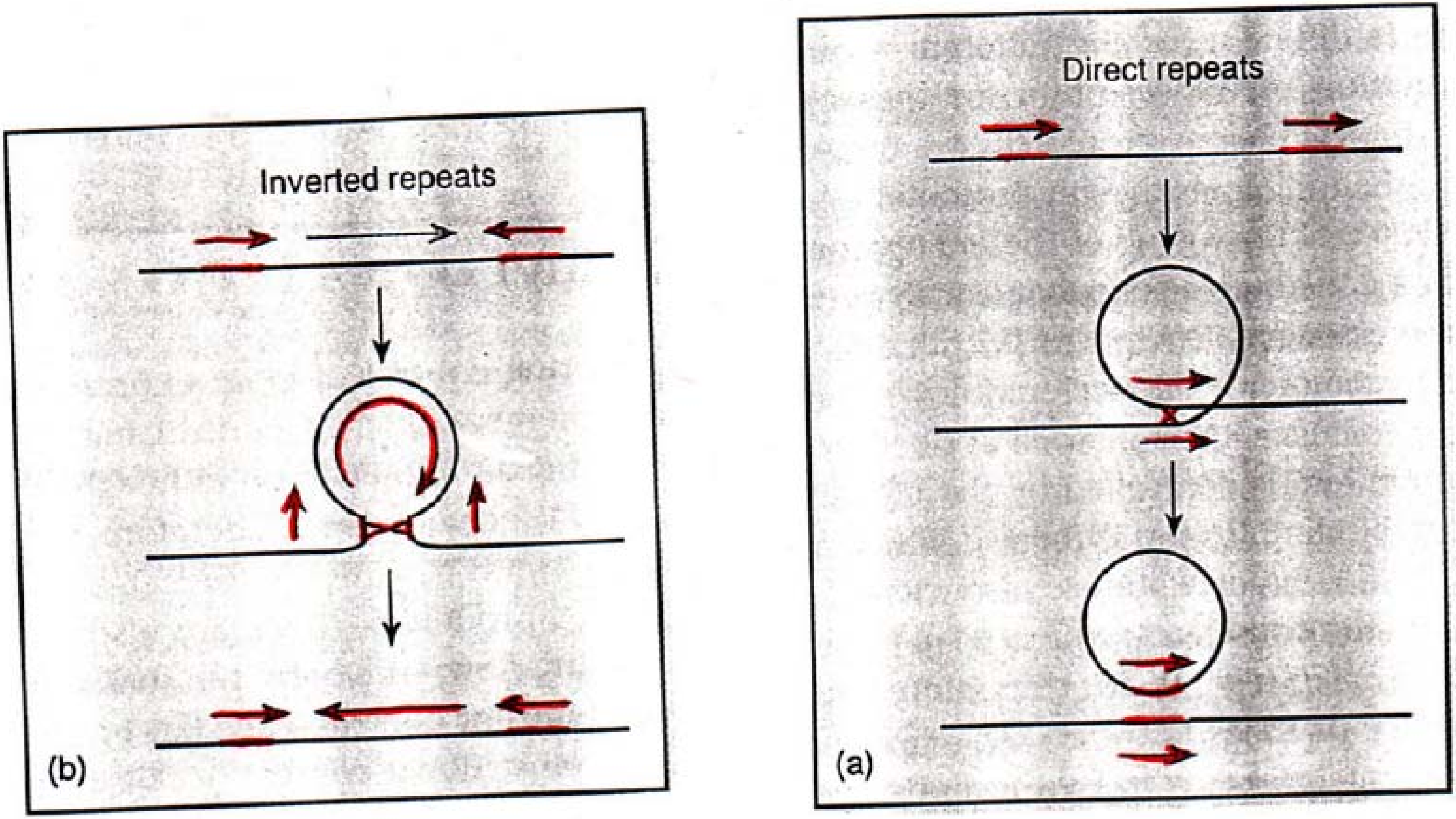
Consequences of transposition and of recombination between transposable elements

Recombination between transposable elements (or other repeated sequences) in the same chromosome

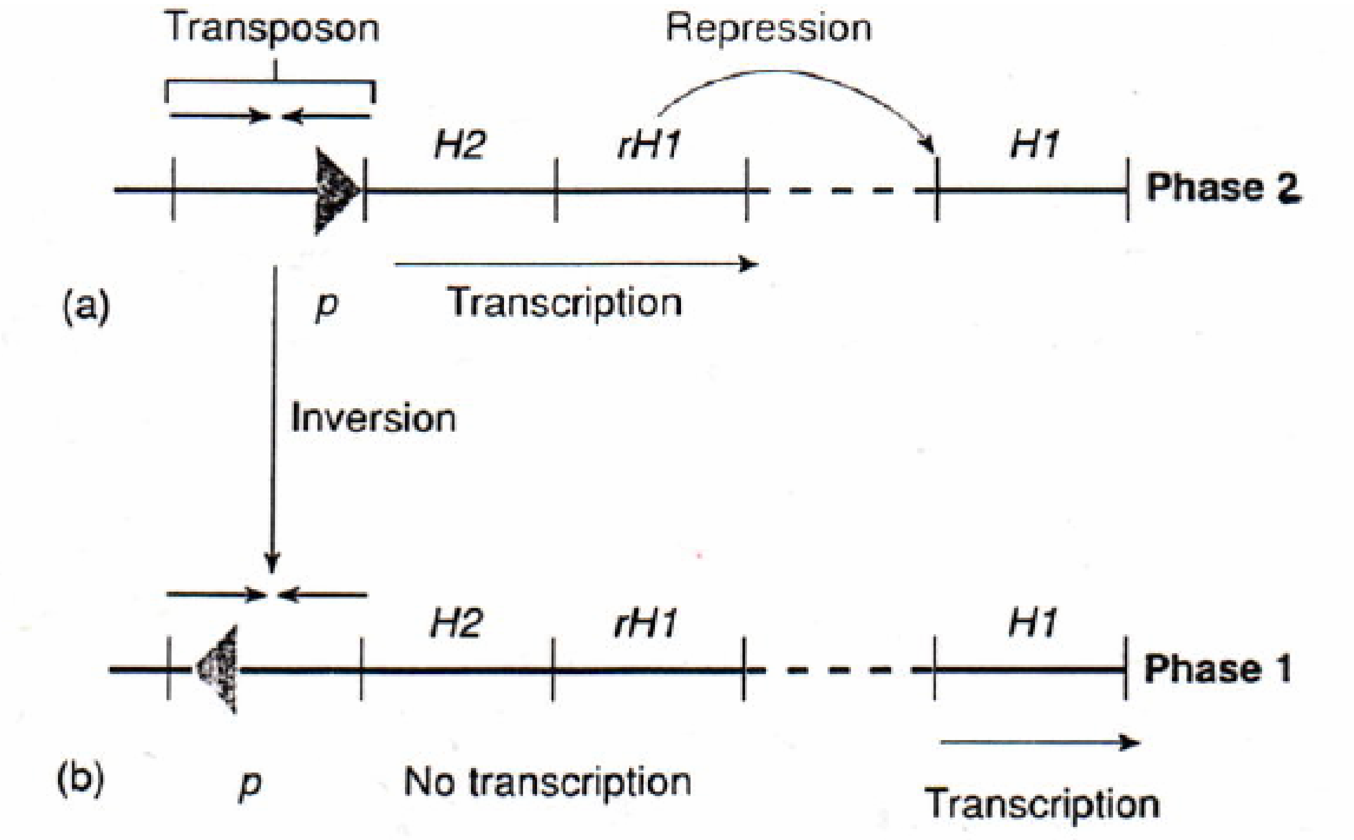


Two copies of tansposable elements can act in concert to transpose the DNA segments in between them

Consequências da transposição
(exemplo)

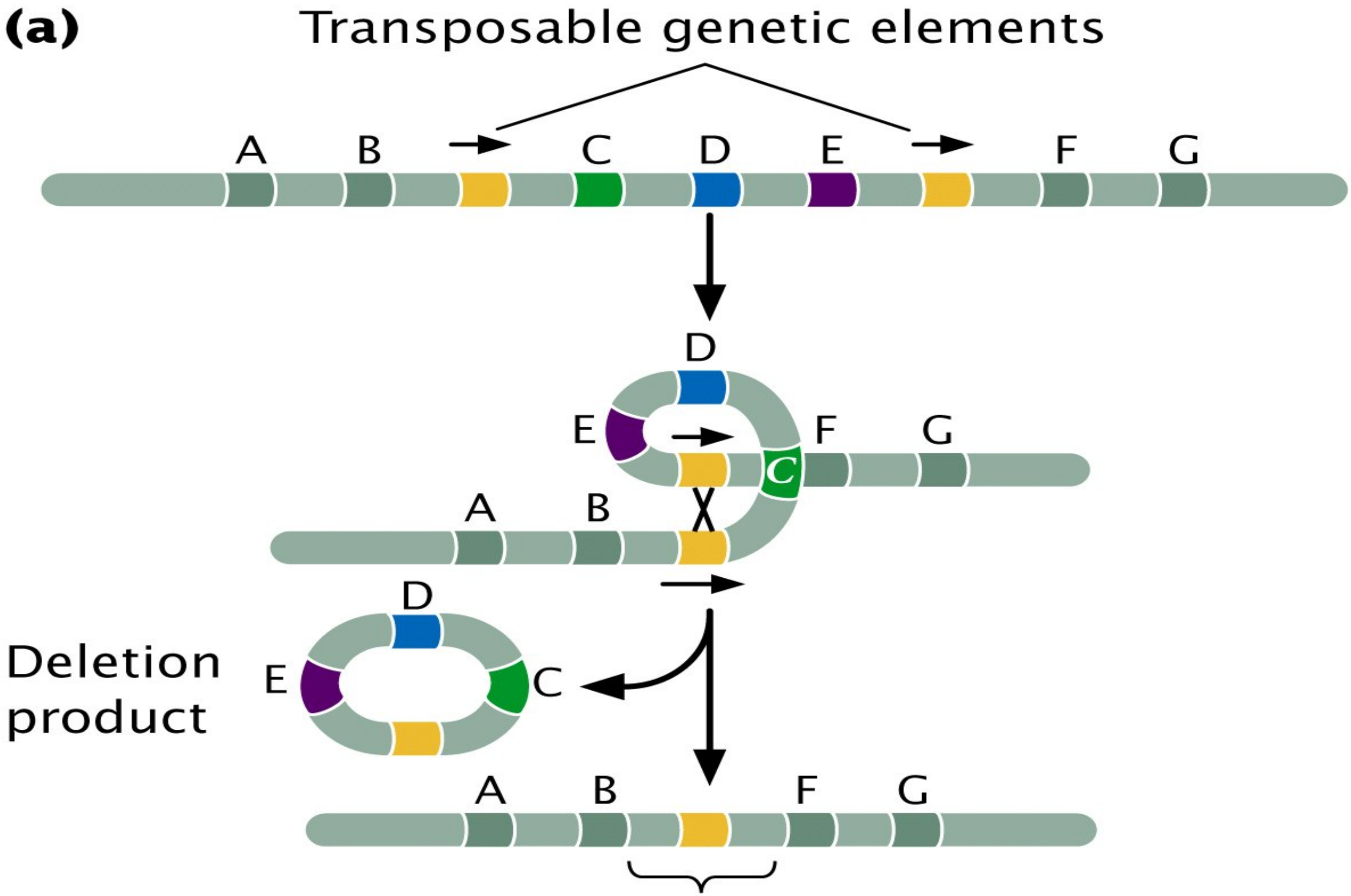


Arrangement of flagellin genes on the *Salmonella* chromosome



The promoter (P) is within a transposon. In one direction (a), the *H2* operon is transcribed, which results in H2 flagellin and rH1 protein, the repressor of the *H1* gene. In the the second orientation (b), the *H2* operon is not transcribed, resulting in uninhibited transcription of the *H1* gene

Chromosome rearrangements are often generated by transposition



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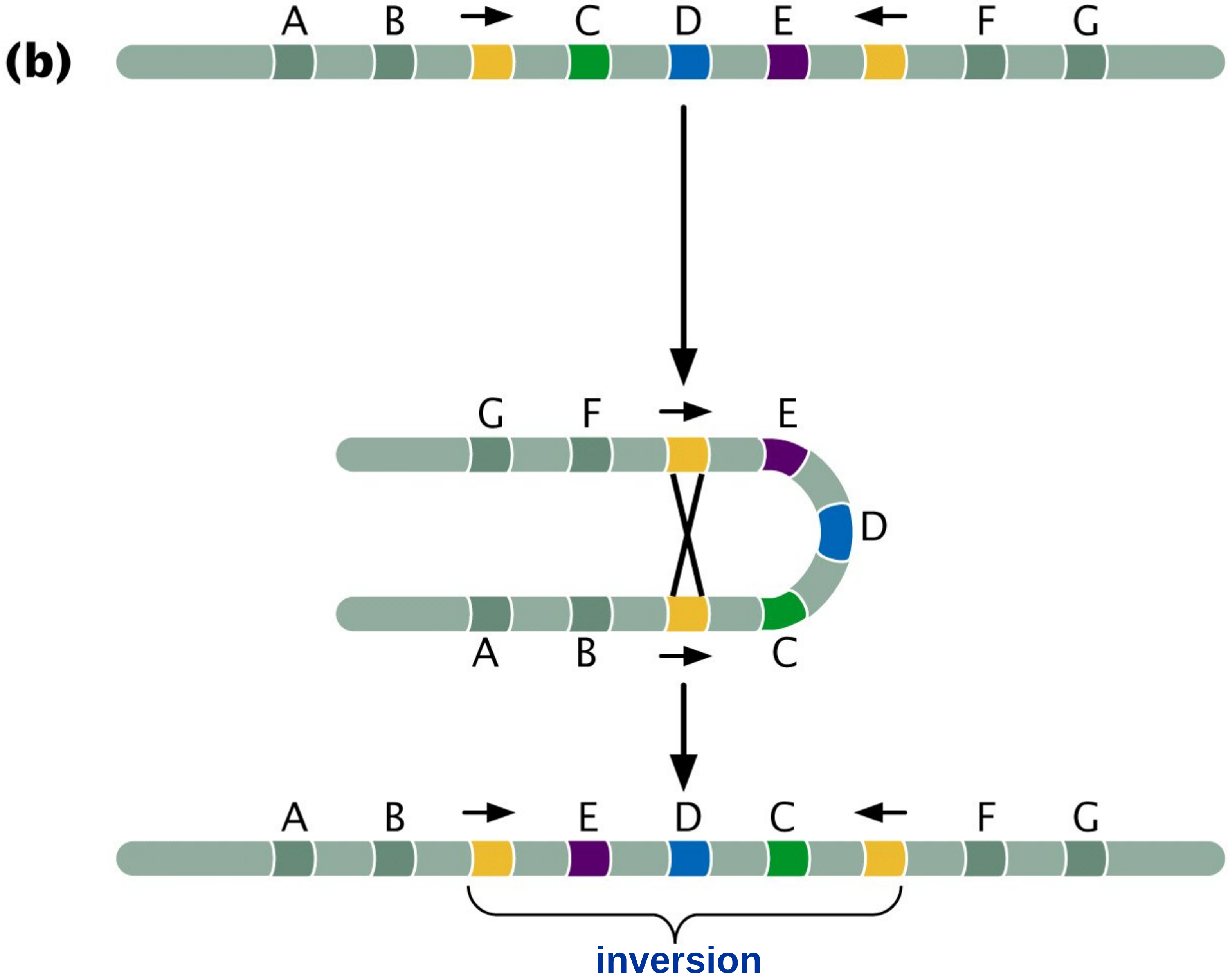

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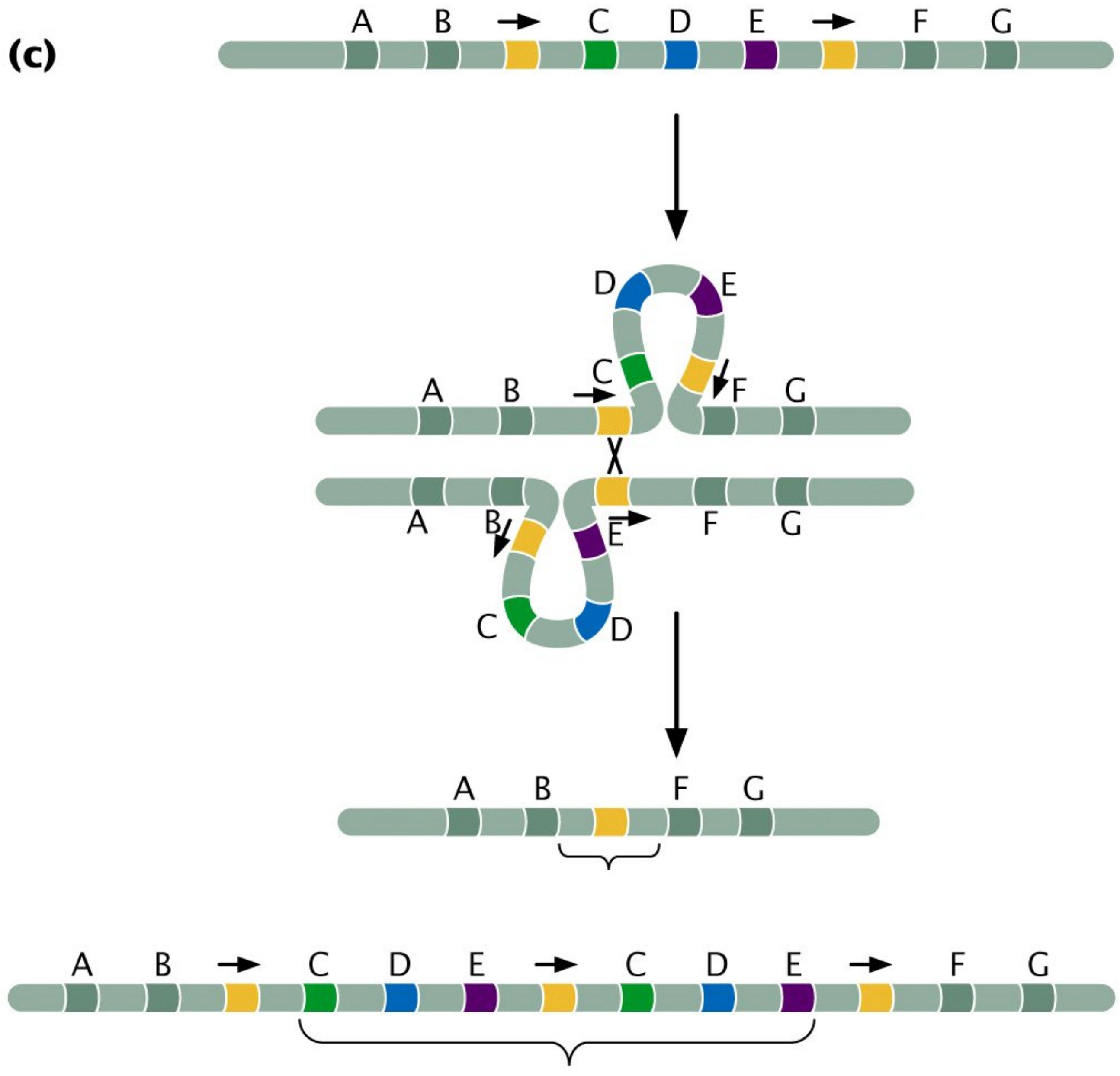
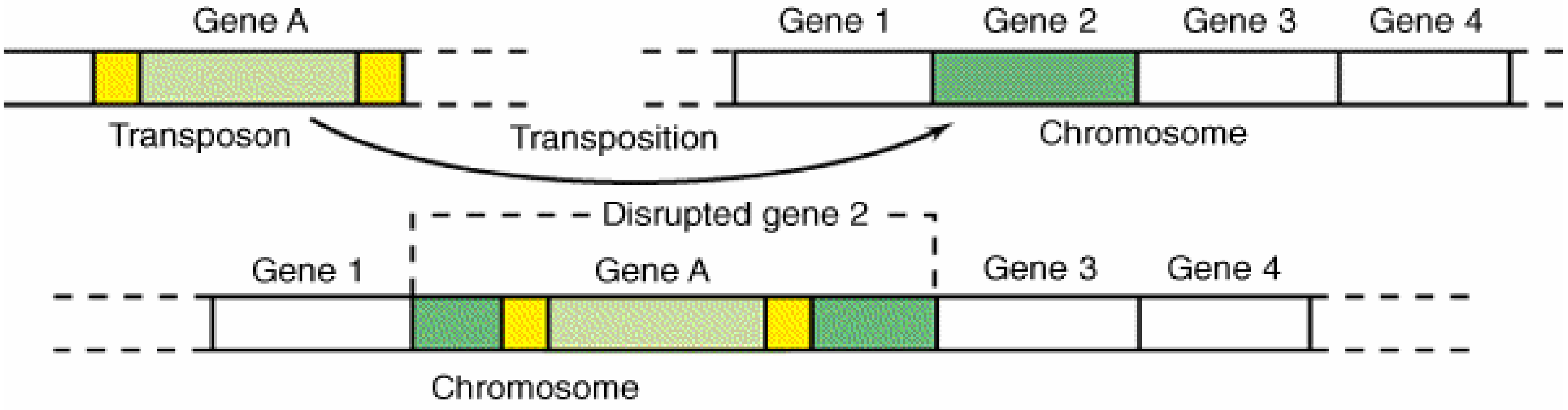
(c)



Transposon mutagenesis



Brock

Consequências da transposição

- Causa deleções e inversões
- Melhoram *fitness* da bacteria
- Mutagénese (interrompe expressão génica)
- Aquisição de novos genes pelas células (dissiminação de resistência a antibióticos)
- Evolução do genoma
- Rearranjos na expressão génica
- Podem servir de substracto para recombinação homóloga, que conduz a translocações e inversões

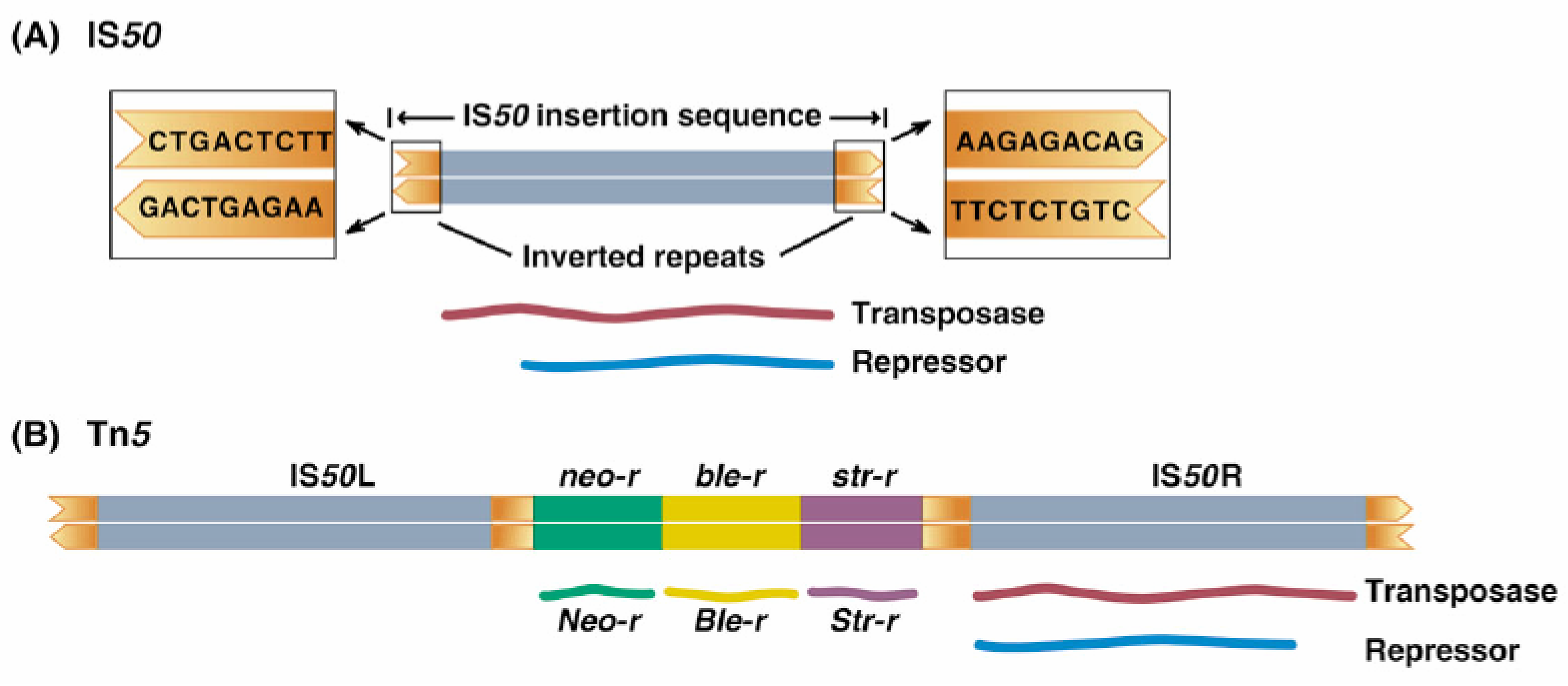
Regulação da transposição

- **Ao nível da <u>transcrição</u> da transposase**

- **Ao nível da <u>tradução</u> do mRNA da transposase**

- **Inibição do mecanismo de transposição**
  - **Ex RIP (repeat-induced point mutation)- mecanismo de defesa em que as sequências repetitivas sofrem mutações**

Repressor of transposition in transposable elements in bacteria



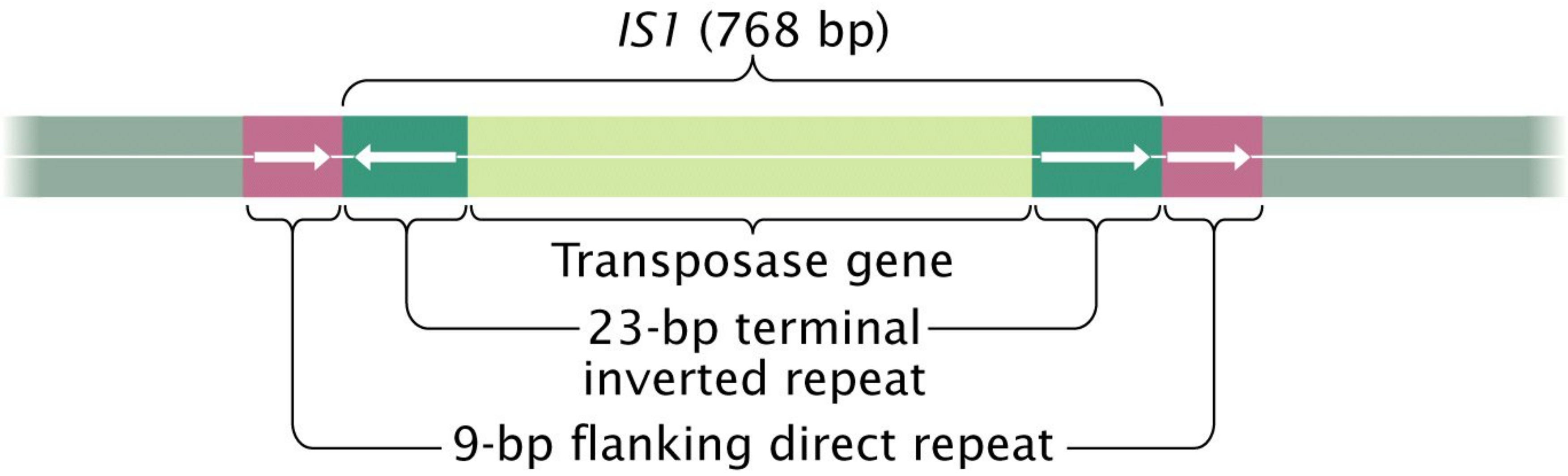
Hartl 10.4

Structure of transposable elements

Transposable elements in bacteria

Transposable elements in eukaryotes

Typical Insertion Sequence (IS)



Insertion sequences are simple transposable elements found in bacteria

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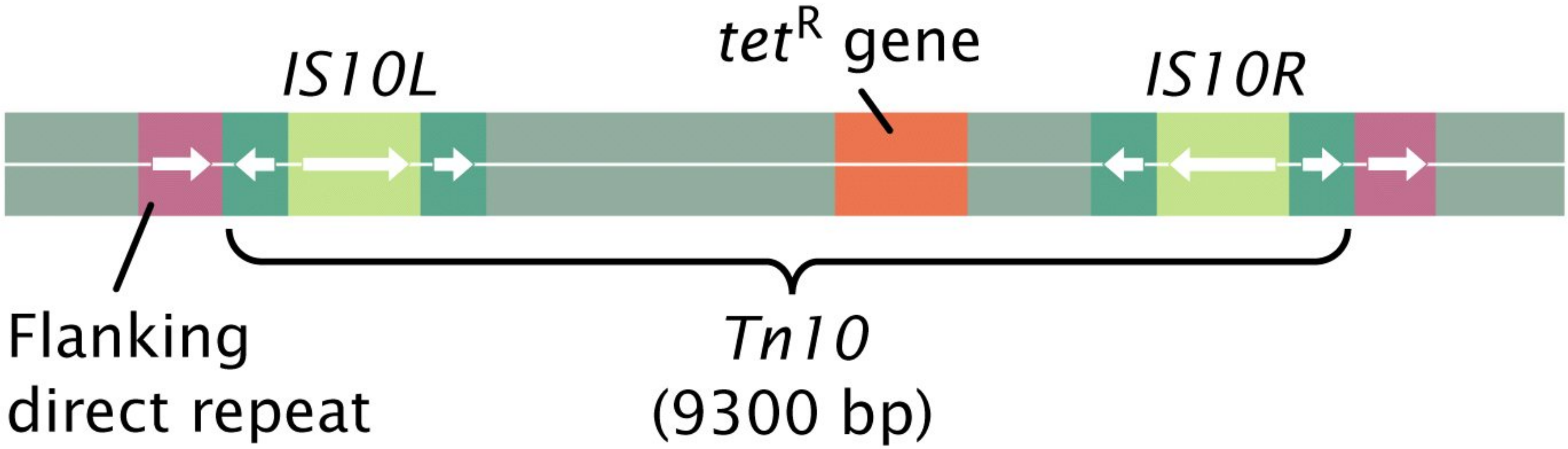
Stuctures of common insertion sequences

Table 11.4 Structures of some common insertion sequences

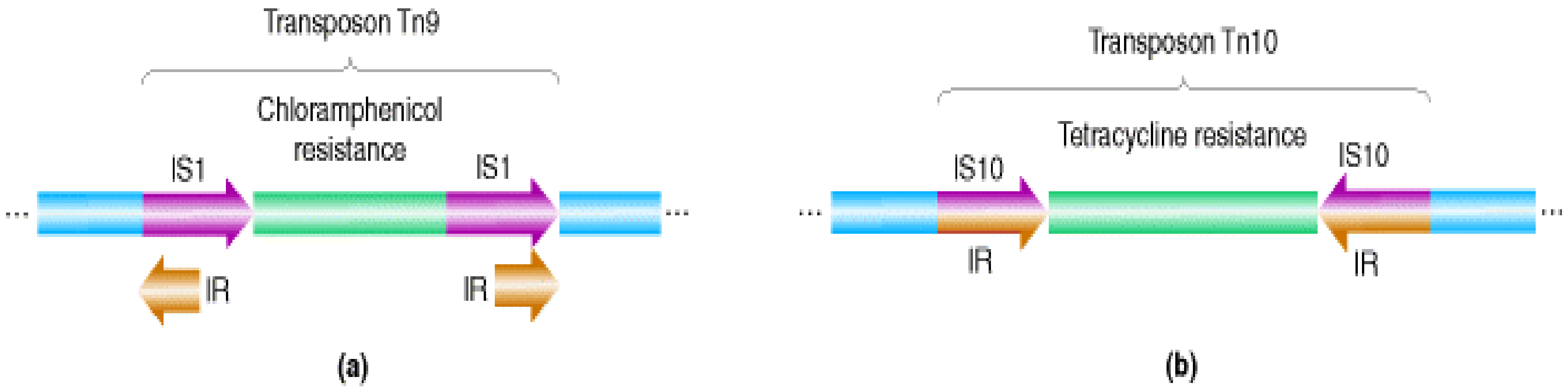
		Length of	
Insertion Sequence	**Total Length (bp)**	**Inverted Repeats (bp)**	**Flanking Direct Repeats (bp)**
IS1	768	23	9
IS2	1327	41	5
IS4	1428	18	11 or 12
IS5	1195	16	4

Source: B. Lewin, *Genes*, 3d ed. (New York: Wiley, 1987), p. 591.

Tn10 ia a composite transposon in bacteria



A composite transposon has a central region carrying markers (such as drug resistance) flanked by IS modules. The modules have short inverted terminal repeats. The modules themselves might be in inverted orientation (as drawn) or have the same orientation.



Two different transposons having different IR regions and carrying different drug-resistance genes.

a) Tn9 has a short IR region, because the two IS1 elements are in the same orientation and each element has a short inverted repeat

b) Tn10 has a large IR region because the two IS10 components have opposite directions and the entire IS10 sequence constitutes the inverted repeat

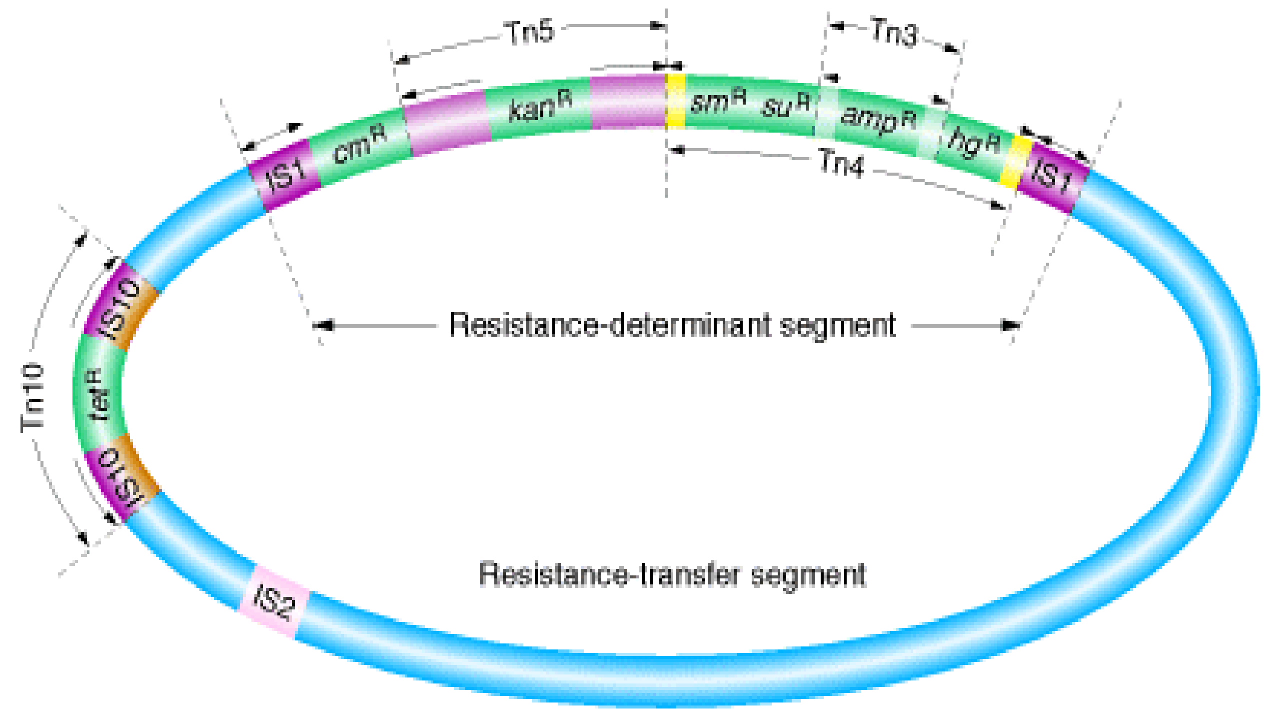
Suzuki 20-15

Table 11.5 Characteristics of several composite transposons

Composite Transposon	Total Length (bp)	Associated IS Elements	Other Genes Within the Transposon
Tn9	2500	*IS1*	Chloramphen-icol resistance
Tn10	9300	*IS10*	Tetracycline resistance
Tn5	5700	*IS50*	Kanamycin resistance
Tn903	3100	*IS903*	Kanamycin resistance

Transposon	Left end	Markers	Right end
Tn903	IS903	kan^R	both IS ends functional
Tn10	IS10L nonfunctional	tet^R	IS10R fuctional
Tn5	IS50L nonfunctional	kan^R	IS50R functional
Tn9	IS1	cam^R	IS modules identical both functional

Role of transposable elements in the evolution of antibiotic resistance plasmids carrying many resistance genes



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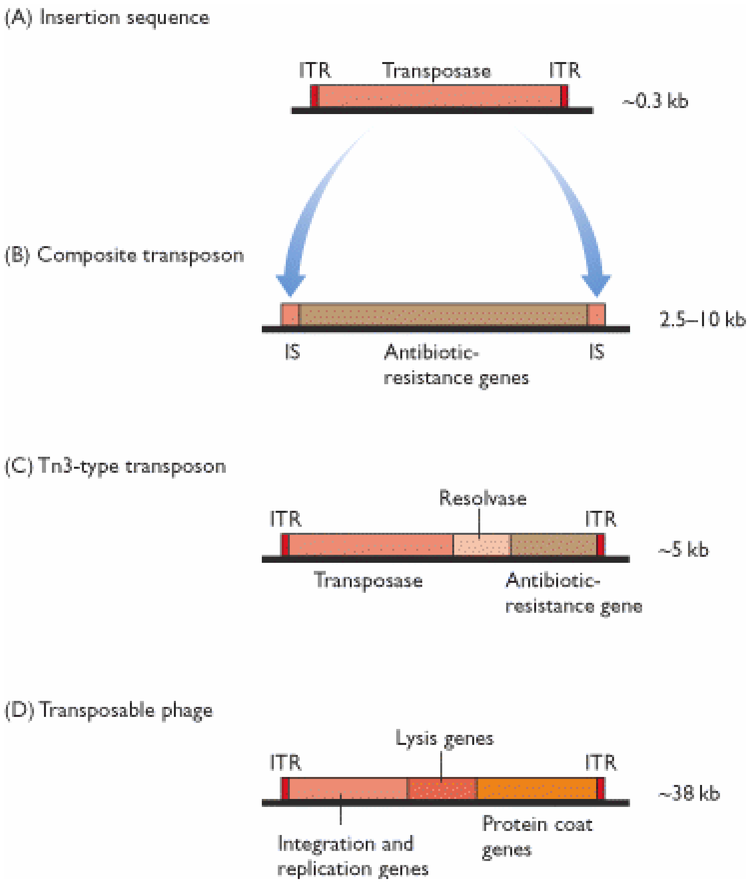
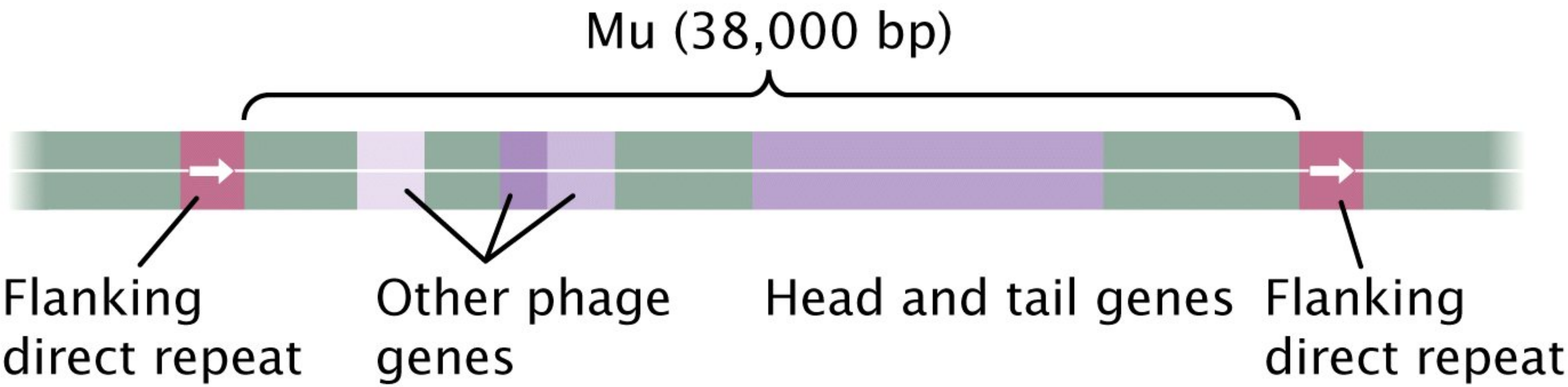
Other transposable elements in **bacteria**

Transposable phage



Noncomposite transposon lack insertion sequences

Mu is a transposing bacteriophage



Integration
Replication
Lysis
etc

. Does not posses IR
. Inserts randomly into DNA
. Replicative transposition

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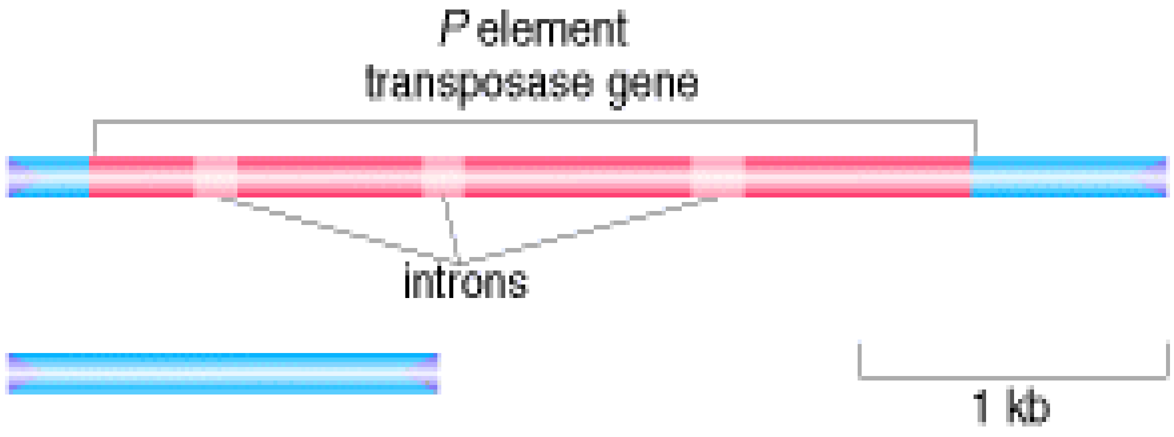
Transposable elements in eukaryotes

DNA transposable elements

Retrotransposons

P element structure
DNA transposable element of *Drosophila*

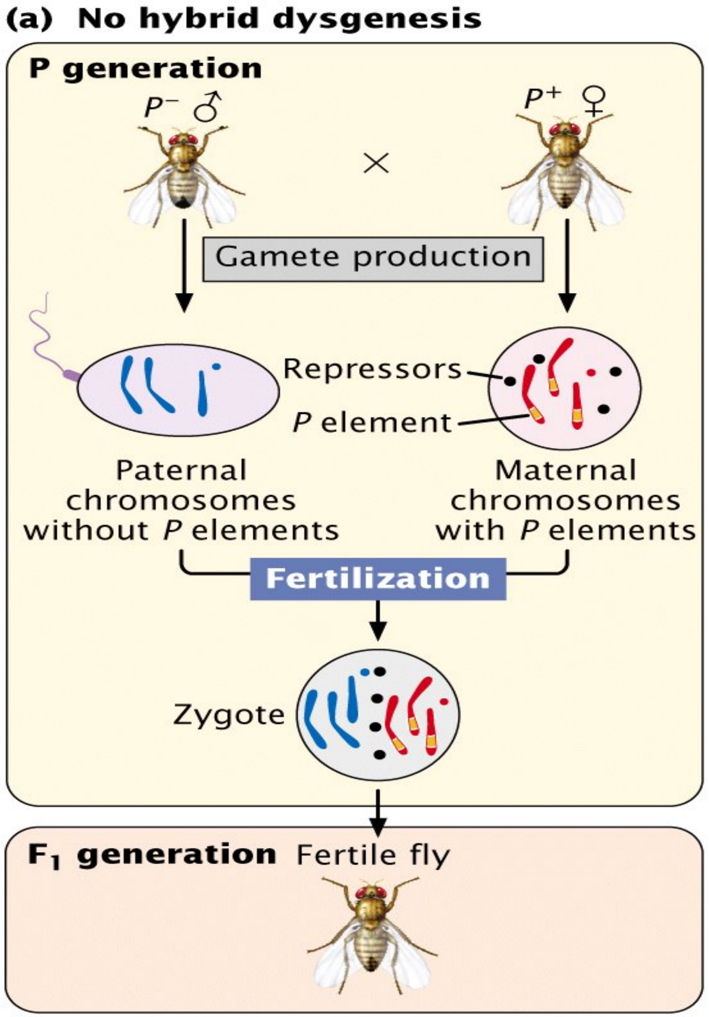


. 2907 bp long
. There is a perfect 31 bp IR at each terminus
. Transposition is controlled by repressors encoded by the element

Hybrid dygenesis in *Drosophila* is caused by the transposition of *P* elements

Hybrid dygenesis is the sudden appearance of numerous mutations, chromosome aberrations and sterility in the offspring of a cross between:
P^+male fly x P^- female fly.

The reciprocal cross produces normal offspring.



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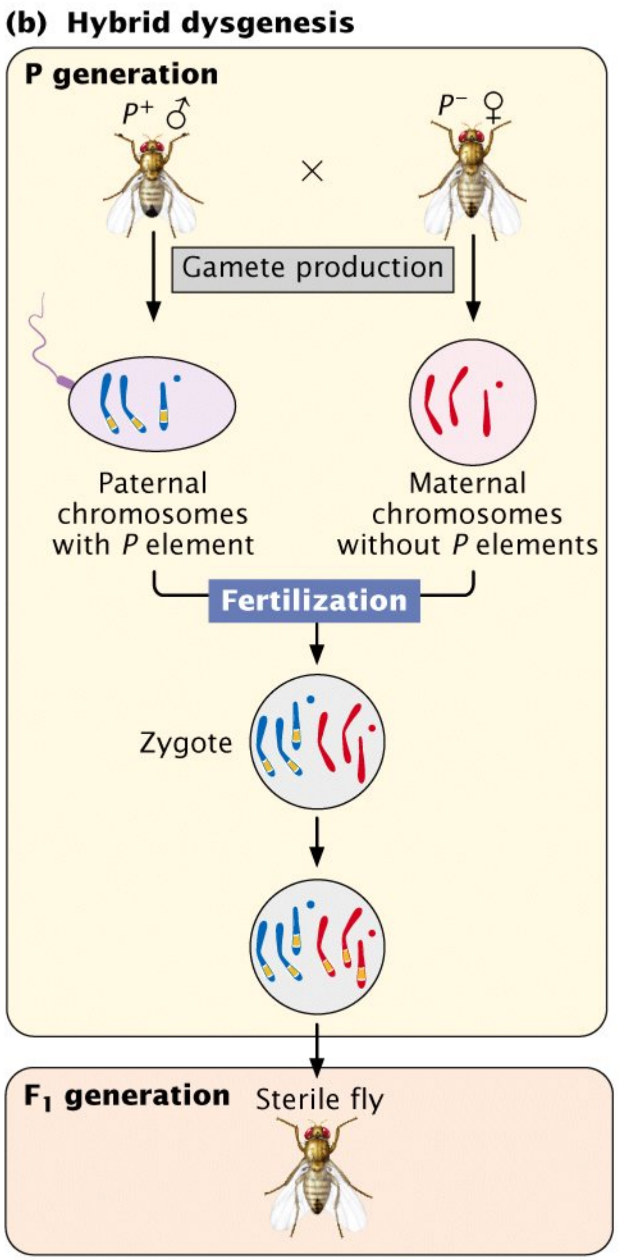
(b) Hybrid dysgenesis
P generation
P^+ ♂
P^- ♀
×
Gamete production
Paternal chromosomes with *P* element
Maternal chromosomes without *P* elements
Fertilization
Zygote
F_1 generation
Sterile fly

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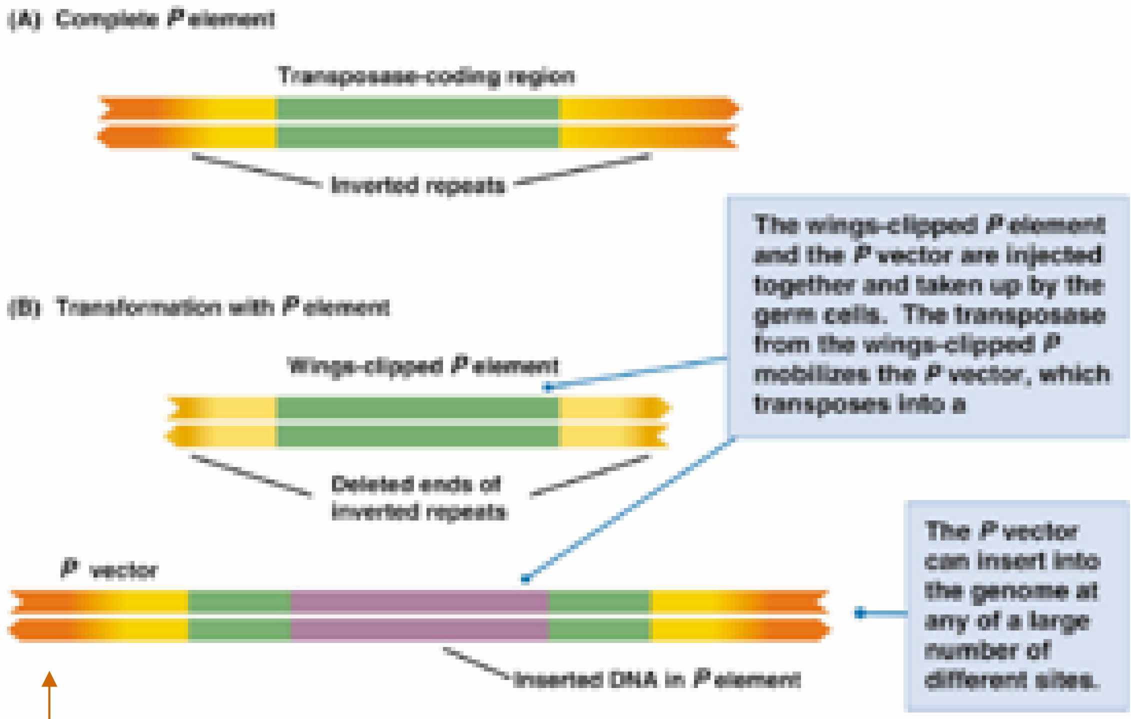
Some transposable elements can be used as tools for cloning and gene manipulation



Recognition sequences needed for transposition

Two component transformation system

- The wings-clipped P element is a modified P element that codes for a transposase but cannot transpose itself because critical recognition sequences are deleted

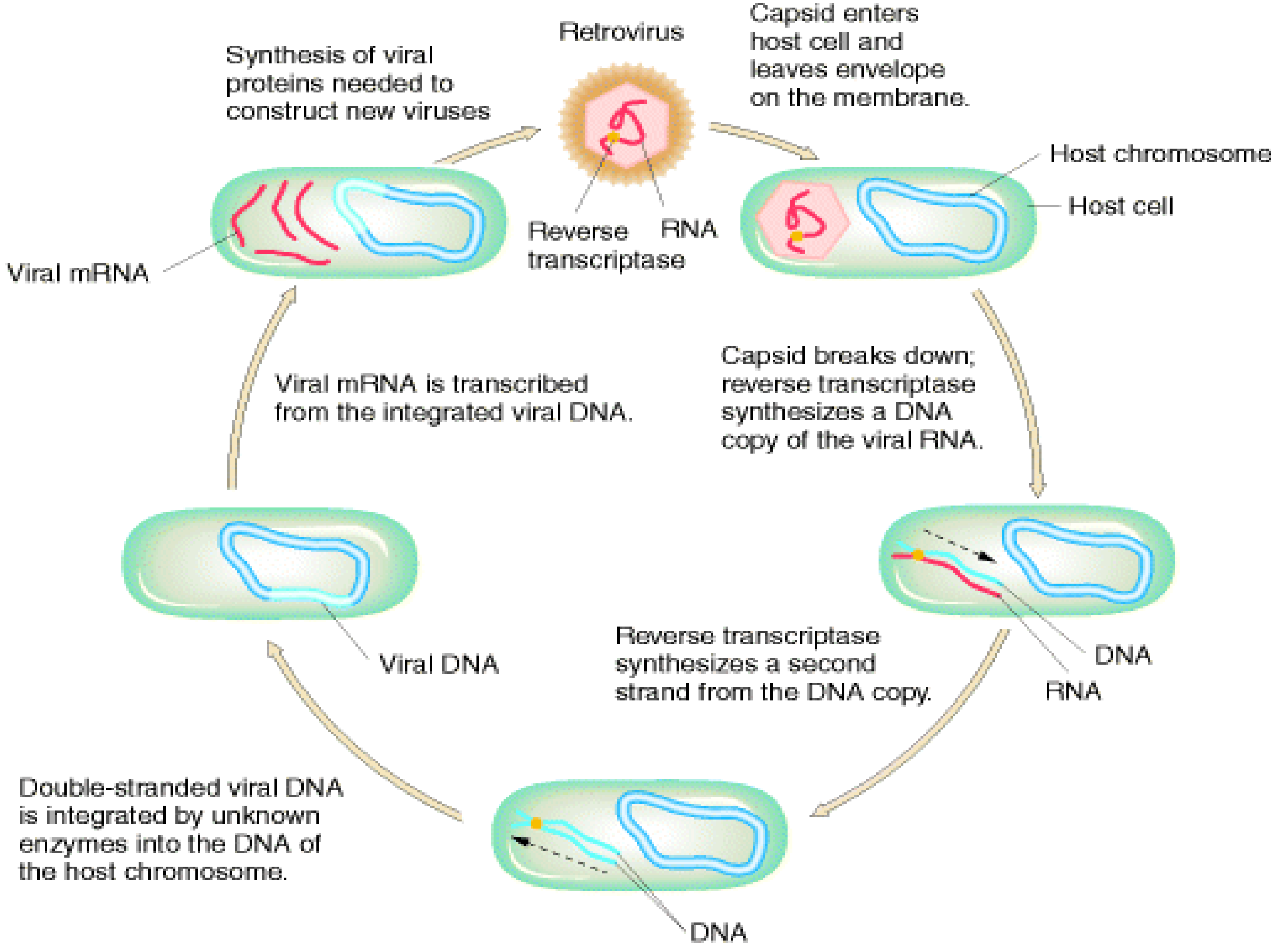
- Random location
- Transformats are detected among the progeny of the injected flies because of the eye color or other genetic marker included in the P vector

Retrotransposons

Retroviral-like retrotransposons

Nonretroviral retrotransposons

Life cycle of a retrovirus



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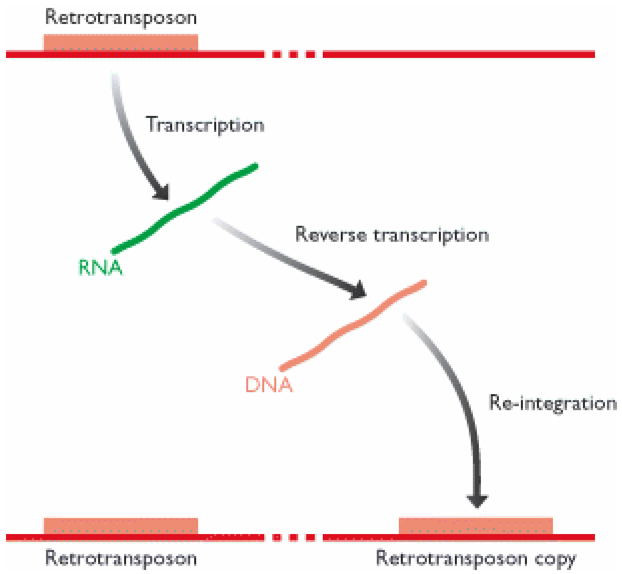
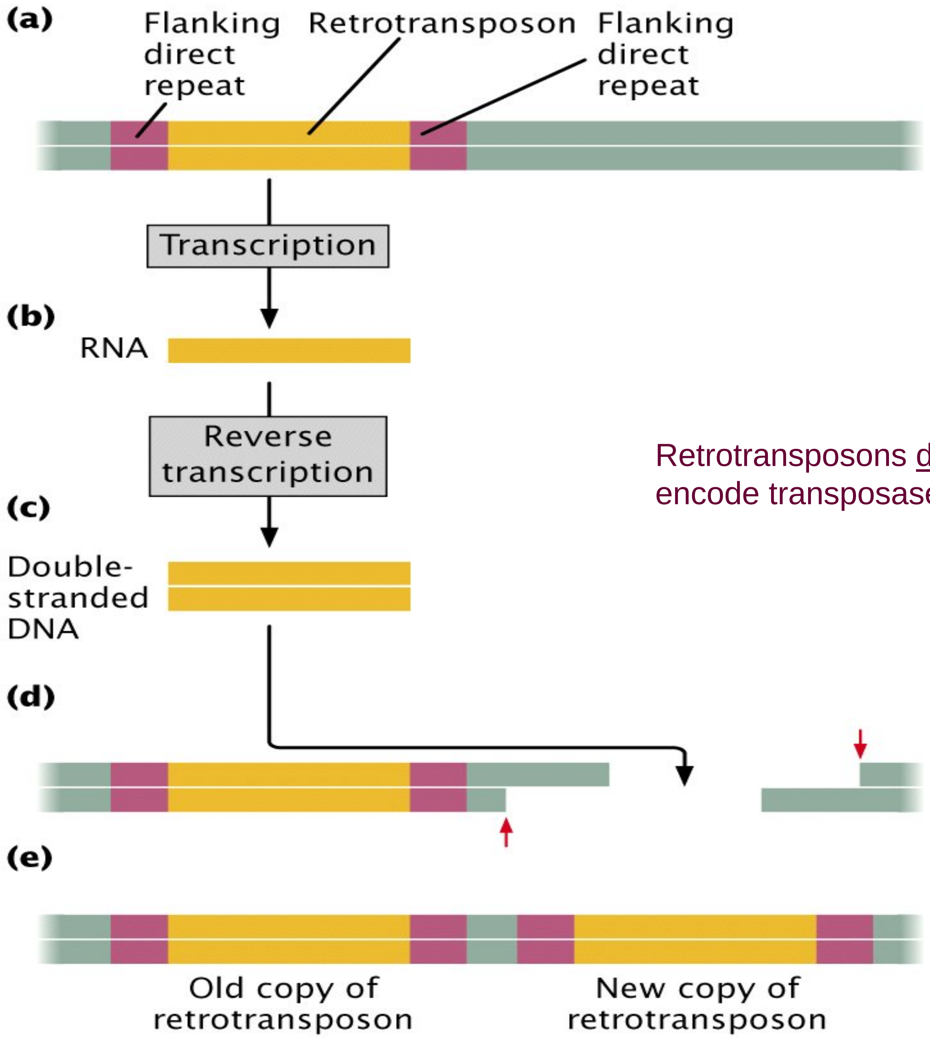
Retrotransposition



Eukaryotic transposable elements that transpose through RNA intermediates are called **retrotransposons**

Retrotransposons transpose through RNA intermediates



Retrotransposons <u>do not</u> encode transposase

Retrotransposons also generate <u>flanking direct repeats</u> at their points of insertion in DNA

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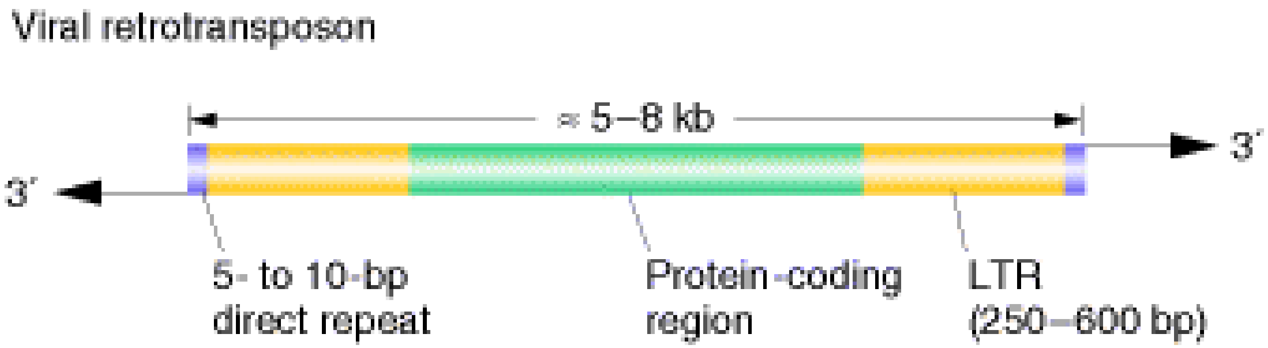
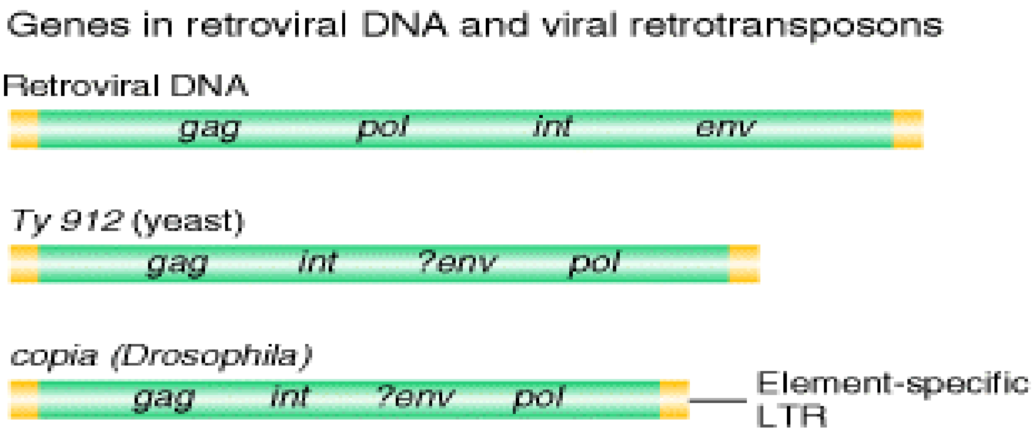
Retrotransposons
(ex.)

- Retroviral retrotransposons have properties similar to those of retrovirus
  - *Ty* elements in yeast
  - *Drosophila copia* elements



Schematic representation of a viral transposon

Comparision of the genes of integrated retrovirus DNA and the yeast Ty element and *Drosophila copia* elements



gag- capsid core proteins
pol- reverse transcriptase
int- integrase and protease
env- envelope antigens

The four functions encoded by the retroviral DNA have counterparts in the yeast and *Drosophila* elements

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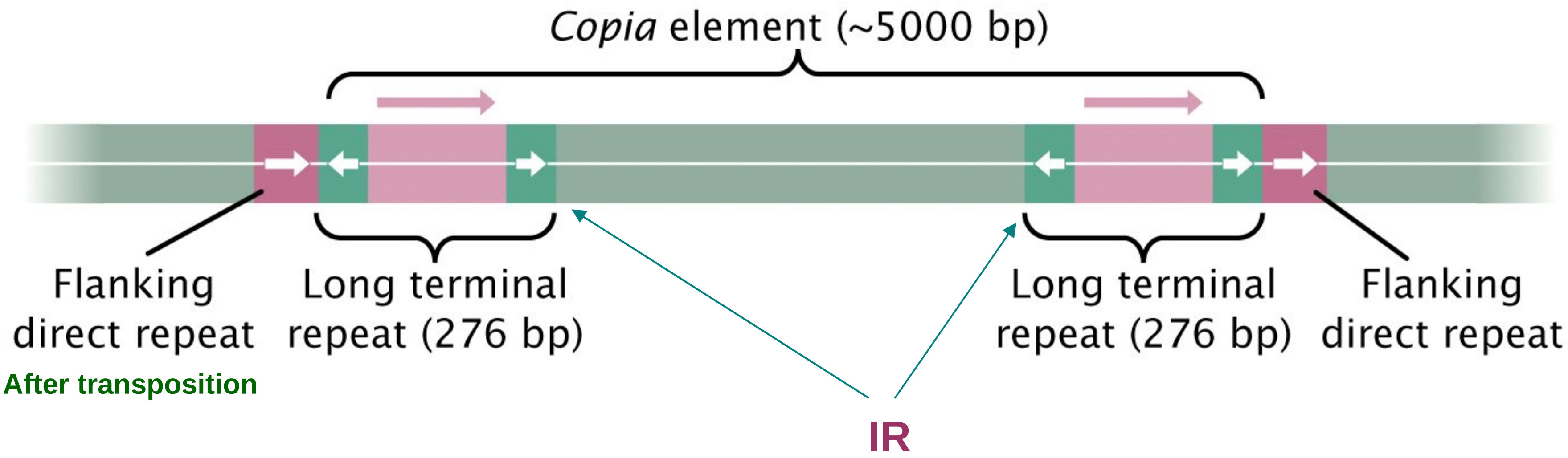
Copia is a retrotransposable element of *Drosophila*



Seven families
5 kb to 8.5 kb
10-100 positions in *Drosophila*

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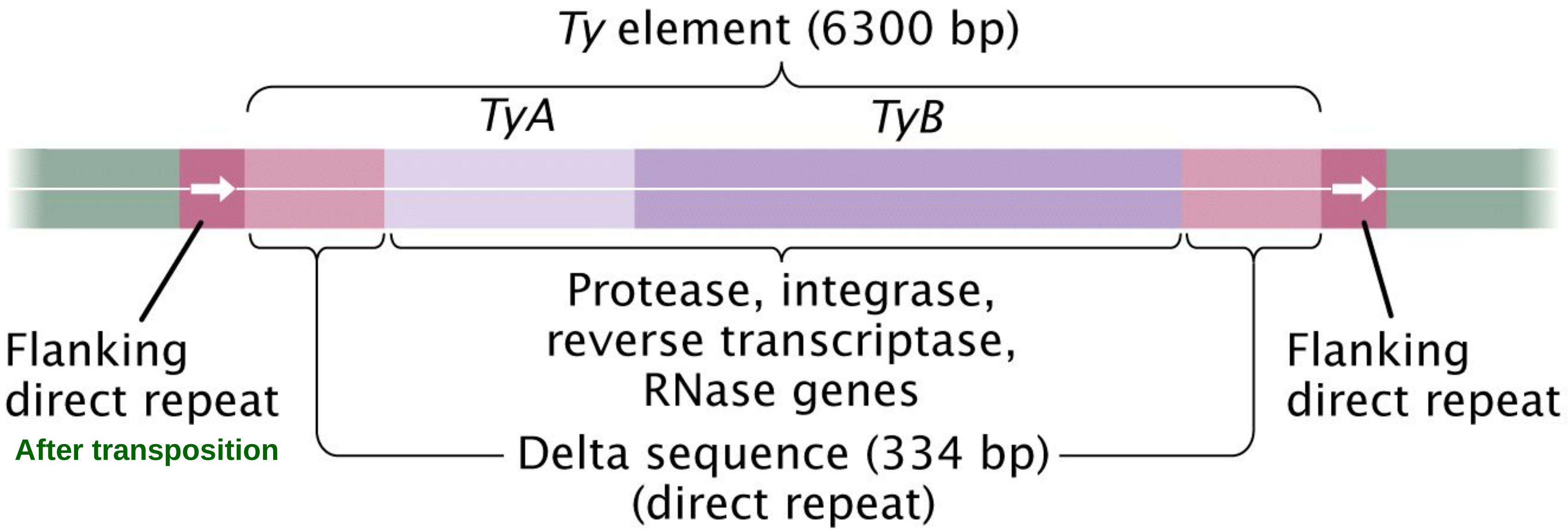
Ty is a transposable element of yeast



Ex: Ty1 sequence appears approximately 35 times in the yeast genome

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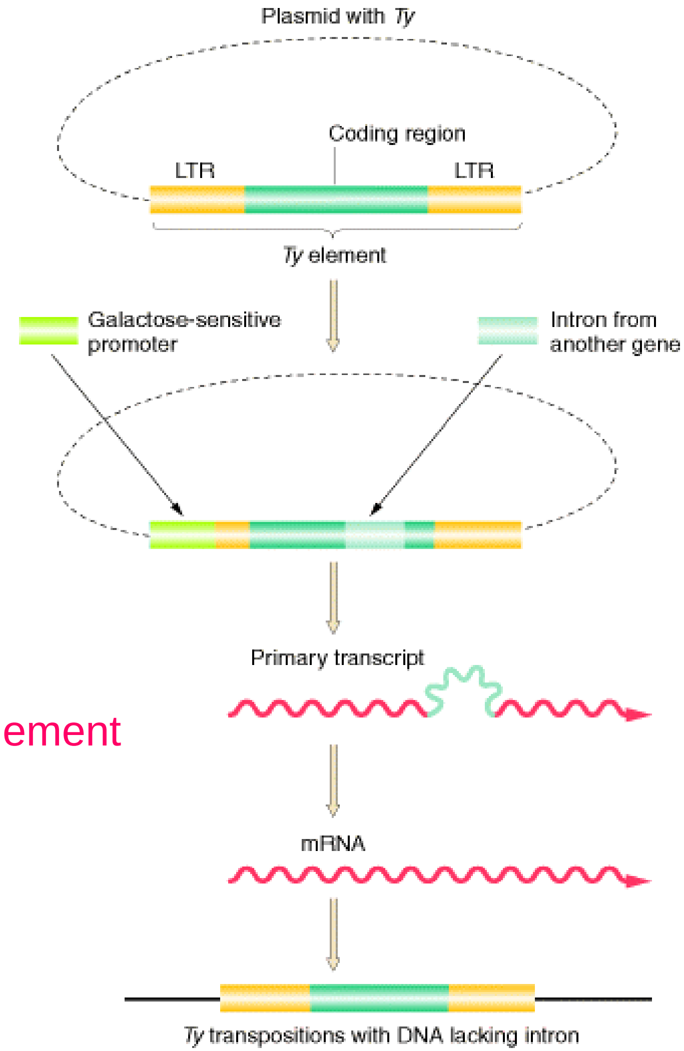
Demonstration of transposition through an RNA intermediate

Galactose induced promoter

Increased expression of Ty element



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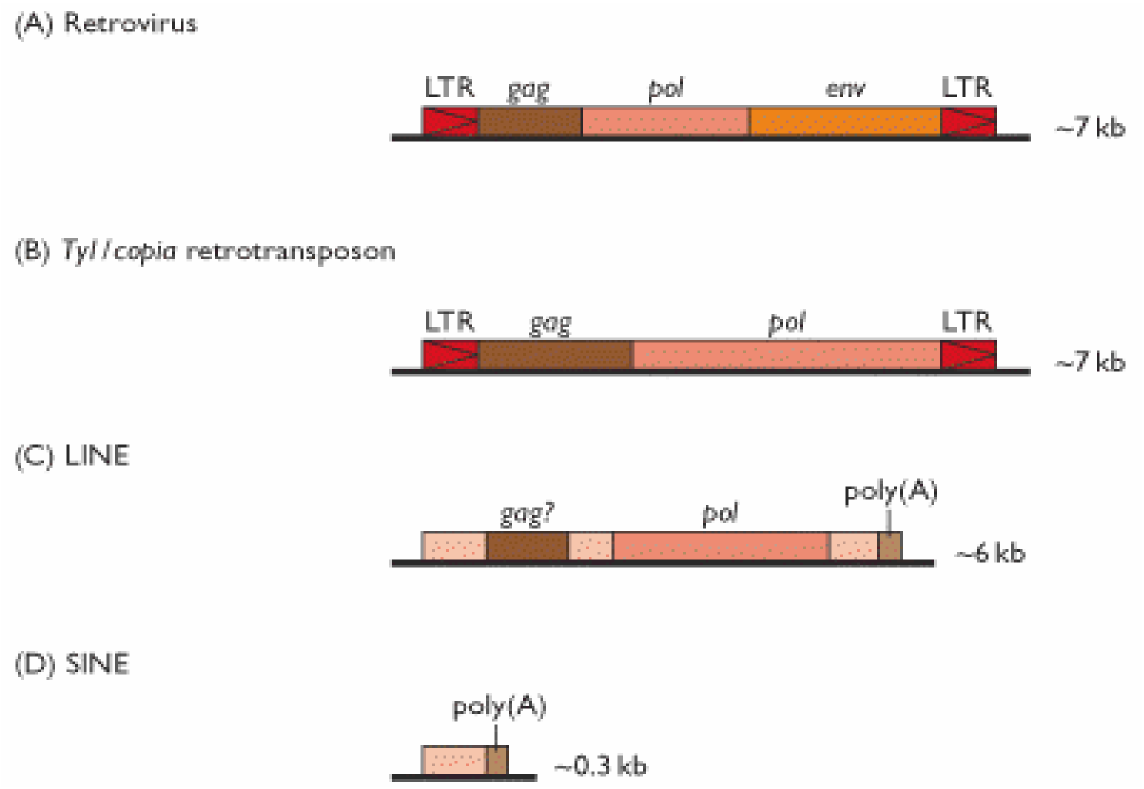
Retrovirus and retroviral *vs* nonretroviral retrotransposons



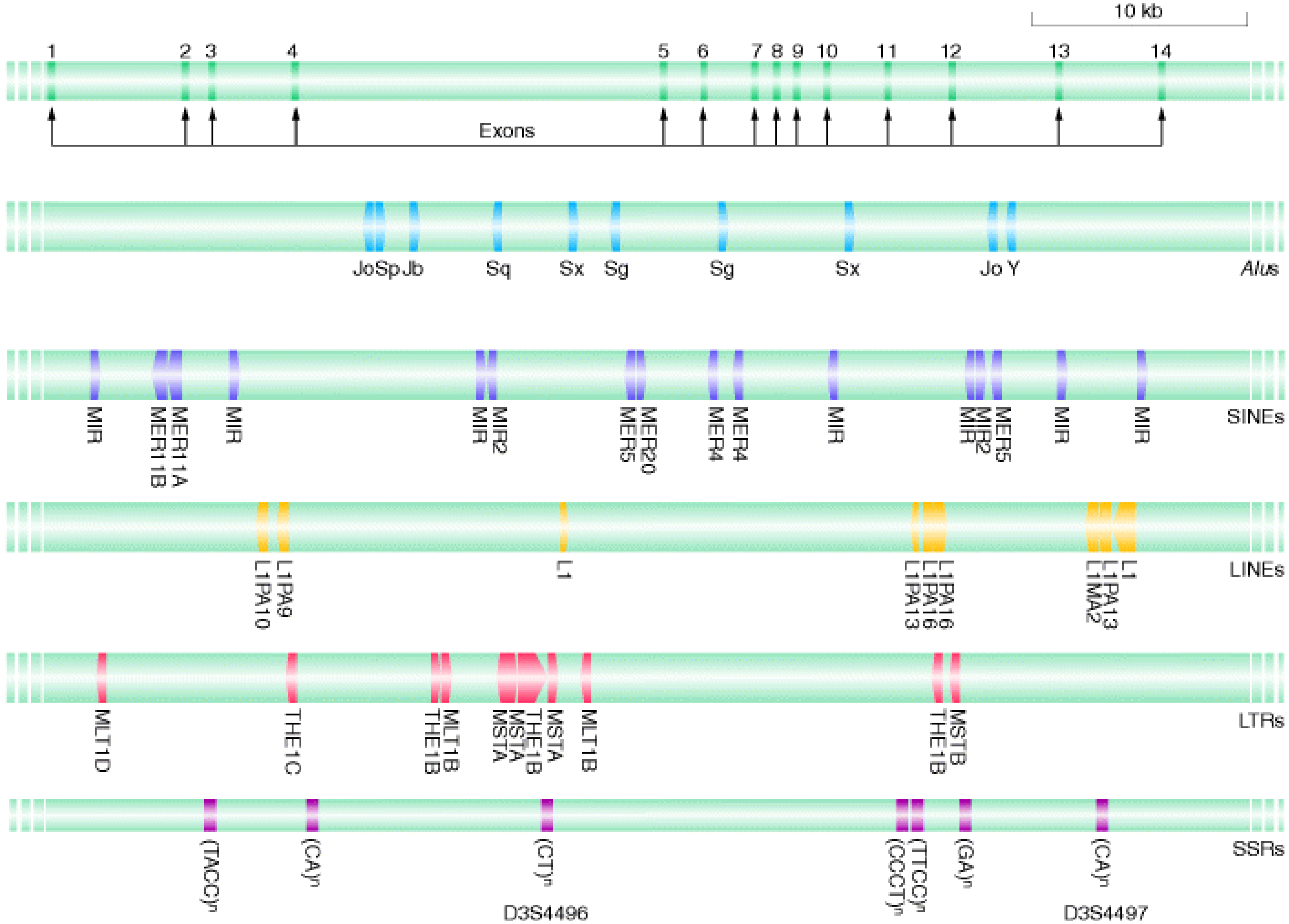
Encodes reverse transcriptase and moves via a RNA intermediate produced by promoter in LTR
Ex in humans- THE-1

Encodes reverse transcriptase and moves via a RNA intermediate produced from a neighboring promoter
(more frequent in mammals)

LINE- long interspersed nuclear element
SINE- short interspersed nuclear element ex: Alu

Repetitive elements found in the human gene *HGO*

(homogentisate 1,2-dioxygenase)



Alu- blue; SINEs- purple; LINEs- orange; LTRs (retrotransposons derived sequences)- red; SSRs (short-sequence repeats)- maroon

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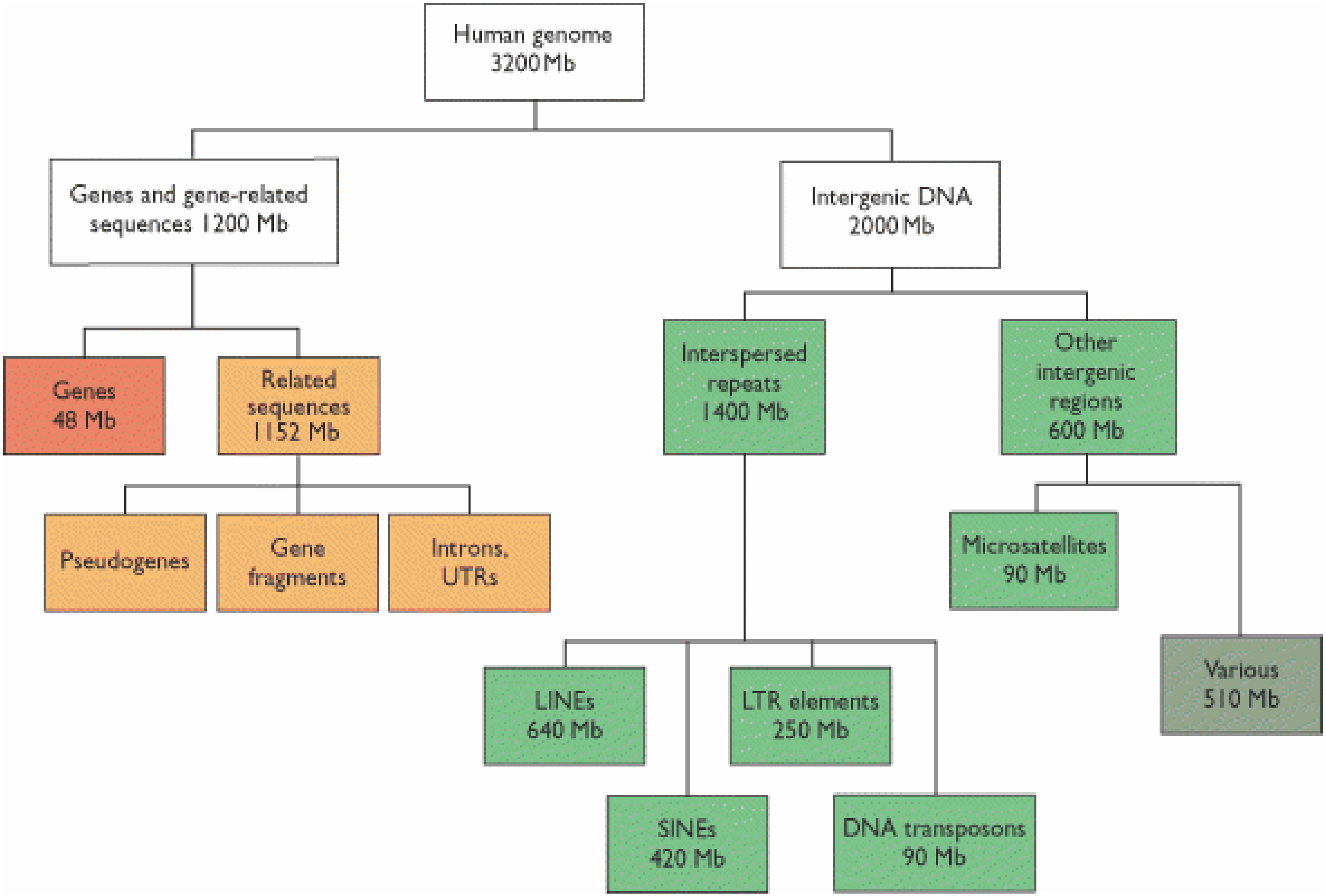
Table 19.4 Percentage of genome consisting of interspersed repeats derived from transposable elements

Organism	Percentage of Genome
Plant (*Arabidopsis thaliana*)	10.5
Worm (*Caenorhabditis elegans*)	6.5
Fly (*Drosophila melanogaster*)	3.1
Human (*Homo sapiens*)	44.4

A proporção e o tipo de sequências repetitivas presentes no genoma dos eucariotas difere muito


Human genome
3200 Mb
Genes and gene-related sequences 1200 Mb
Intergenic DNA
2000 Mb
Genes
48 Mb
Related sequences
1152 Mb
Pseudogenes
Gene fragments
Introns, UTRs
Interspersed repeats
1400 Mb
Other intergenic regions
600 Mb
Microsatellites
90 Mb
Various
510 Mb
LINEs
640 Mb
LTR elements
250 Mb
SINEs
420 Mb
DNA transposons
90 Mb