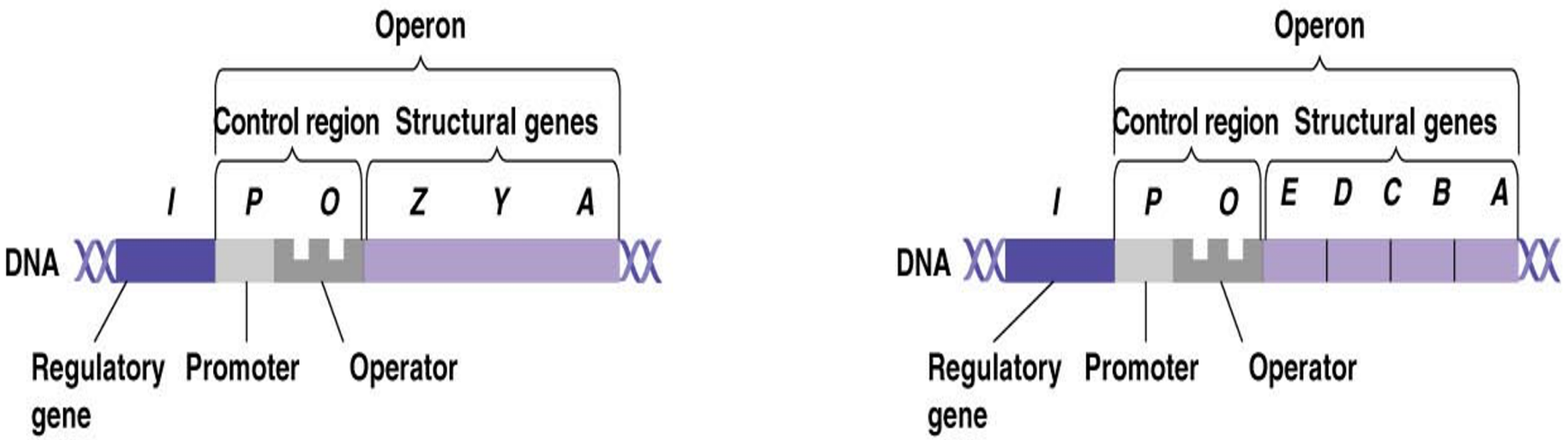
Genetics 2.

Regulation of bacterial gene expression

Mutations

Regulation of bacterial gene expression → Repression and Induction → The operon model



1 Structure of the operon. The operon consists of the promoter (*P*) and operator (*O*) sites and structural genes that code for the protein. The operon is regulated by the product of the regulatory gene (*I*).

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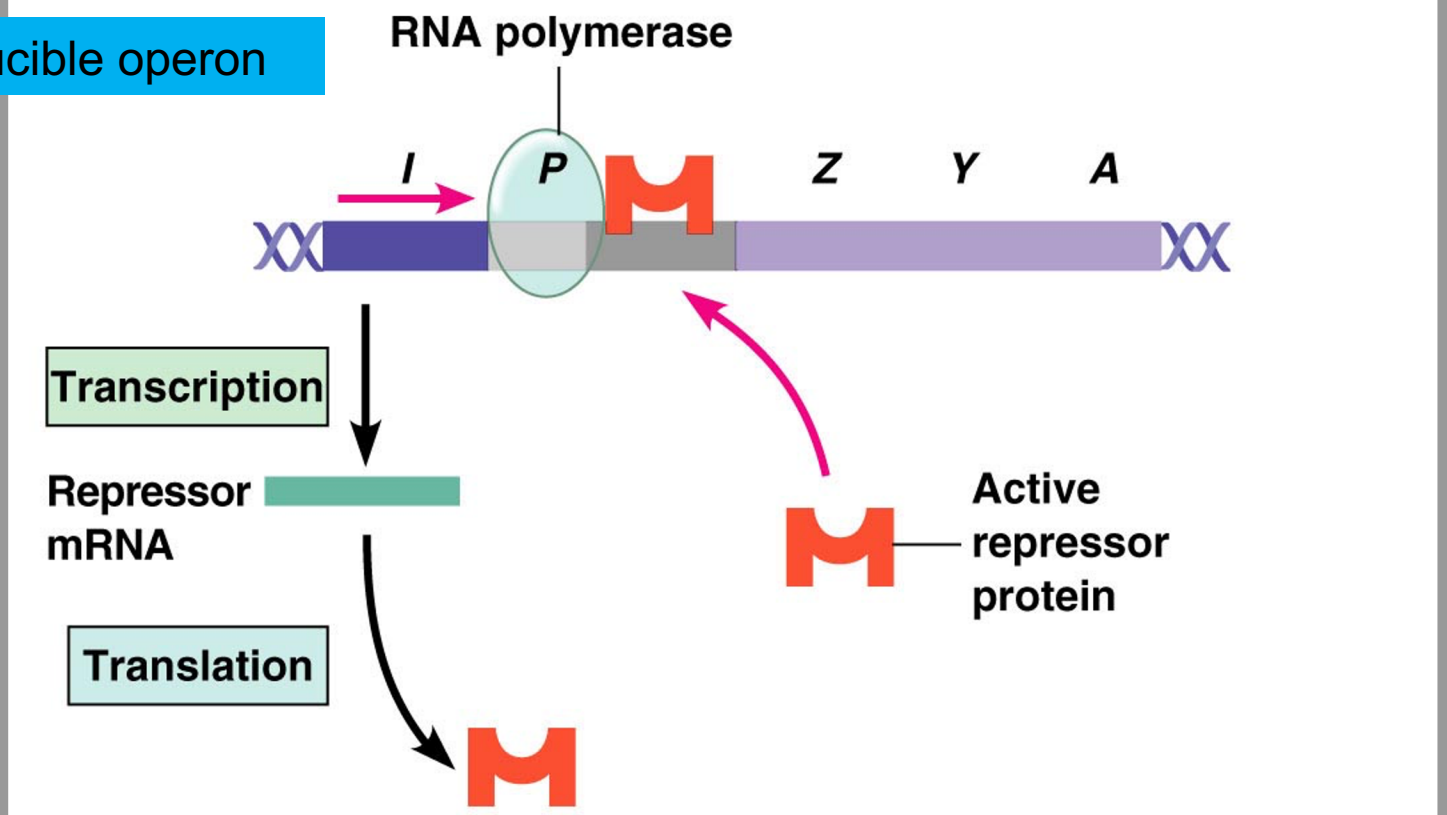
An inducible operon



2 **Repressor active, operon off.** The repressor protein binds with the operator, preventing transcription from the operon.

(a) An inducible operon

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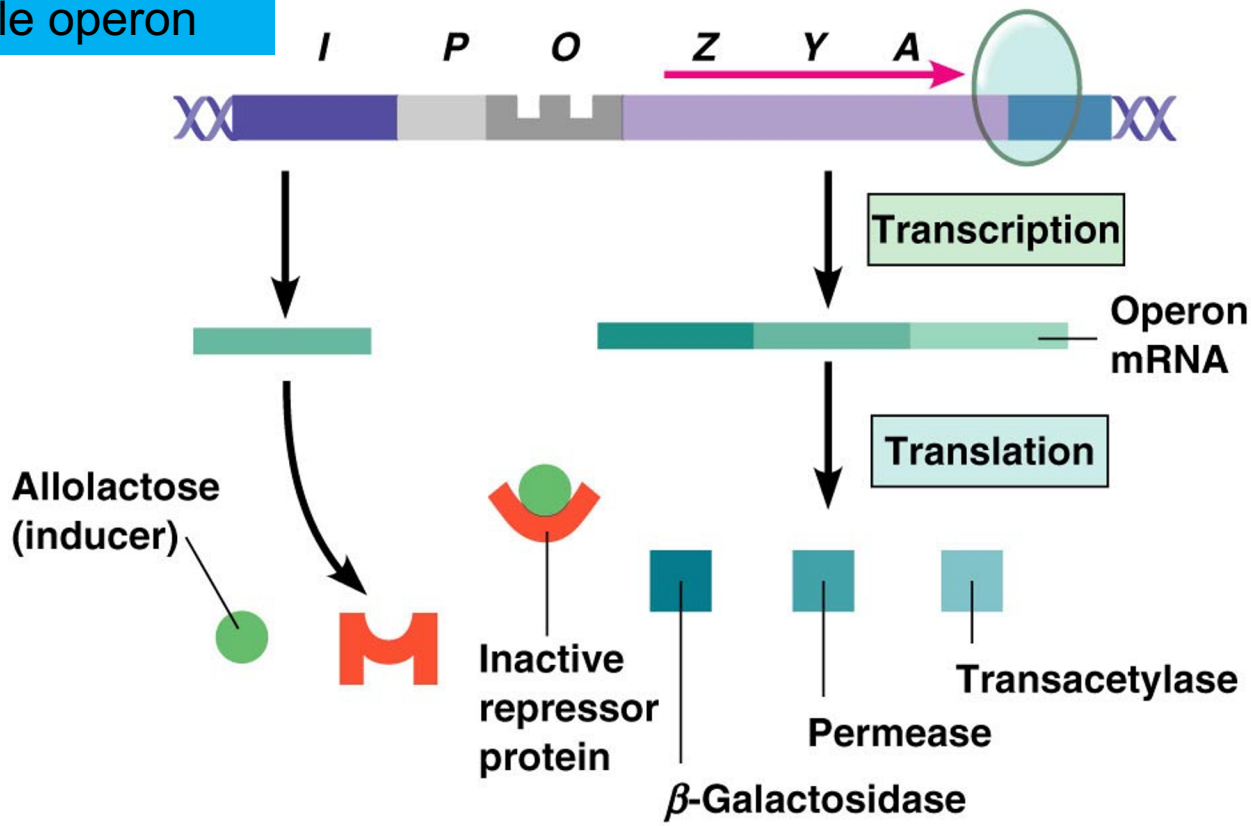
Figure 8.12a, step 2

An inducible operon



3 **Repressor inactive, operon on.** When the inducer allolactose binds to the repressor protein, the inactivated repressor can no longer block transcription. The structural genes are transcribed, ultimately resulting in the production of the enzymes needed for lactose catabolism.

(a) An inducible operon

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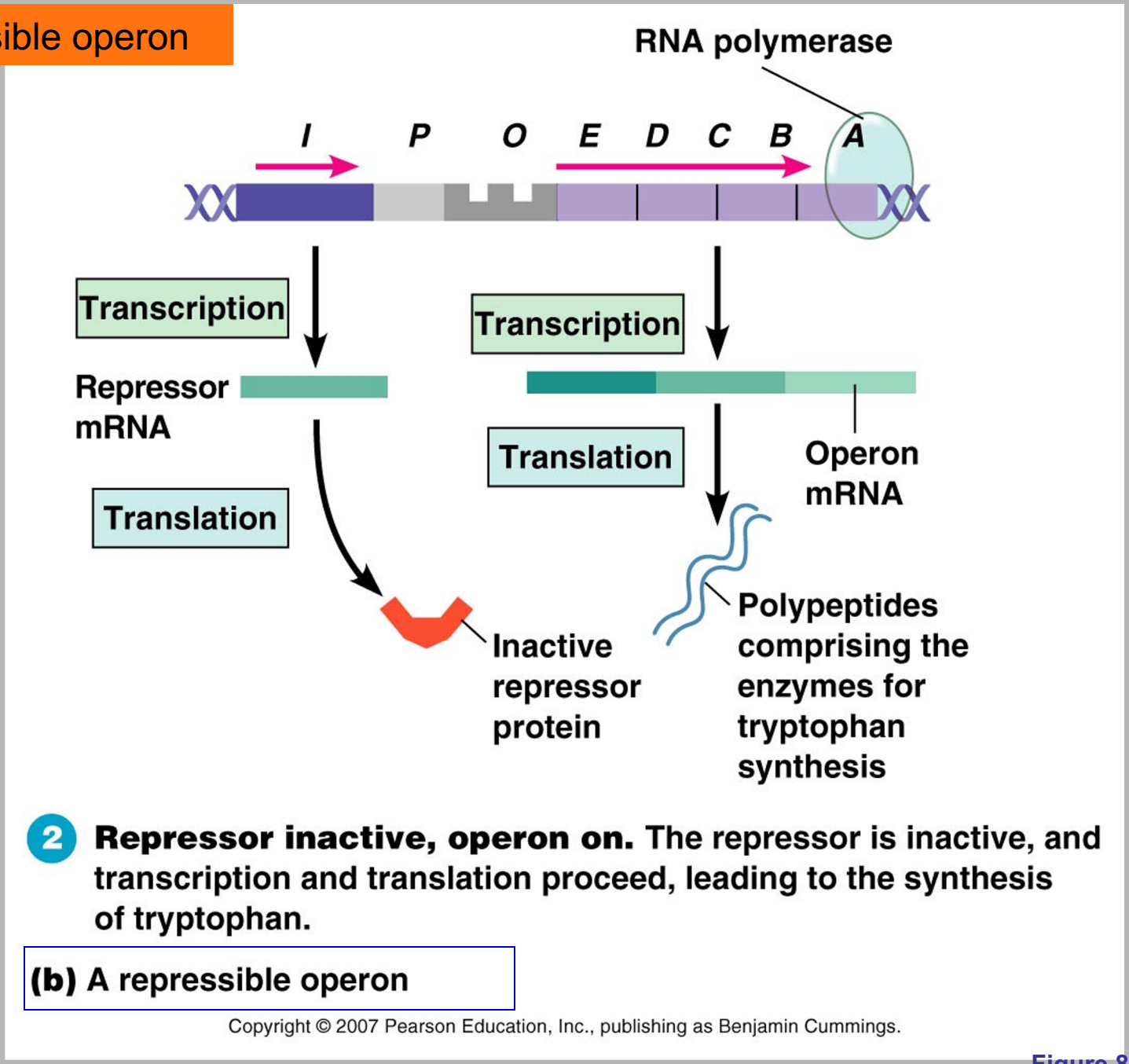
Figure 8.12a, step 3

A repressible operon



2 **Repressor inactive, operon on.** The repressor is inactive, and transcription and translation proceed, leading to the synthesis of tryptophan.

(b) A repressible operon

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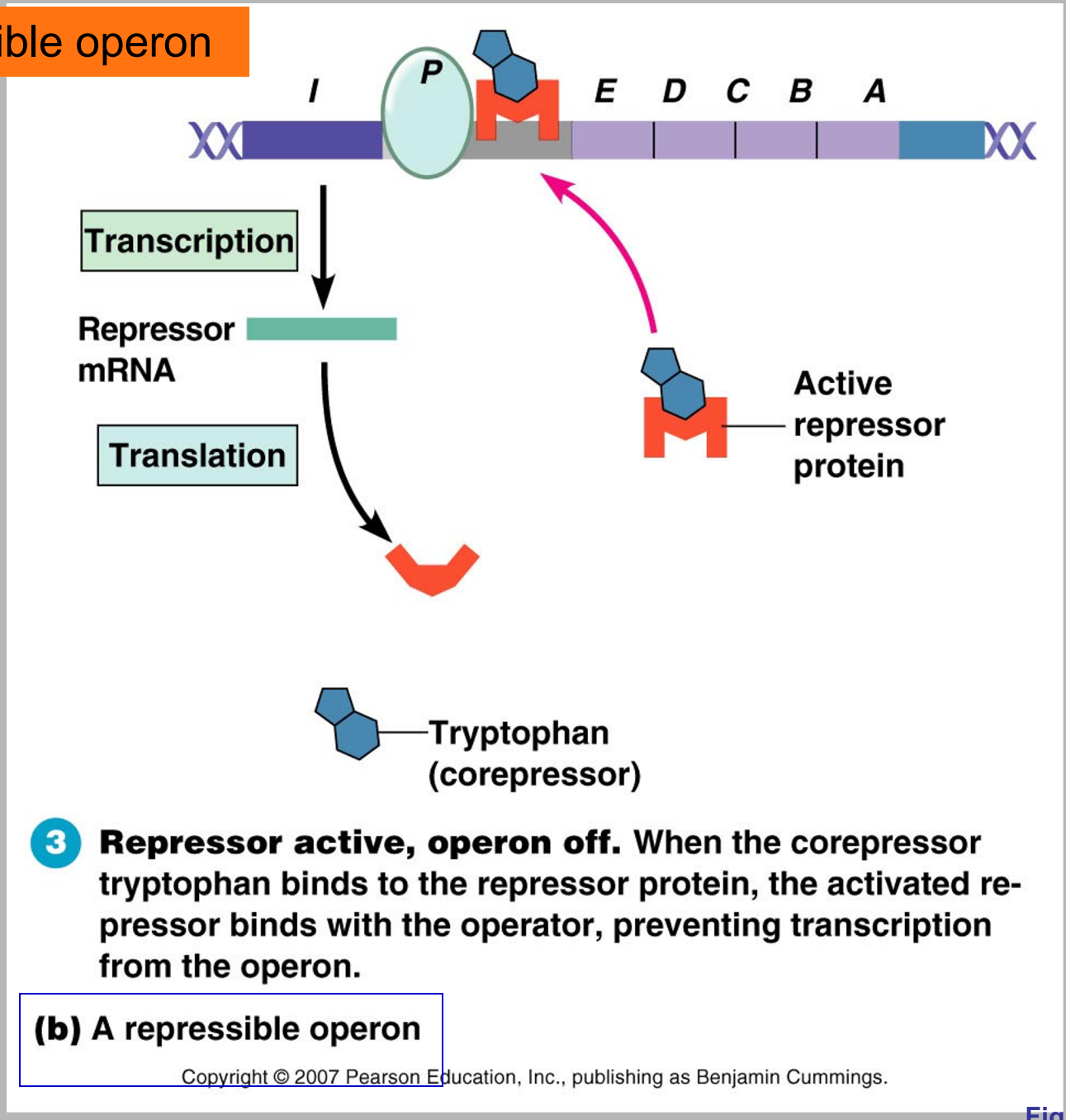
Figure 8.12b, step 2

A repressible operon



3 **Repressor active, operon off.** When the corepressor tryptophan binds to the repressor protein, the activated repressor binds with the operator, preventing transcription from the operon.

(b) A repressible operon

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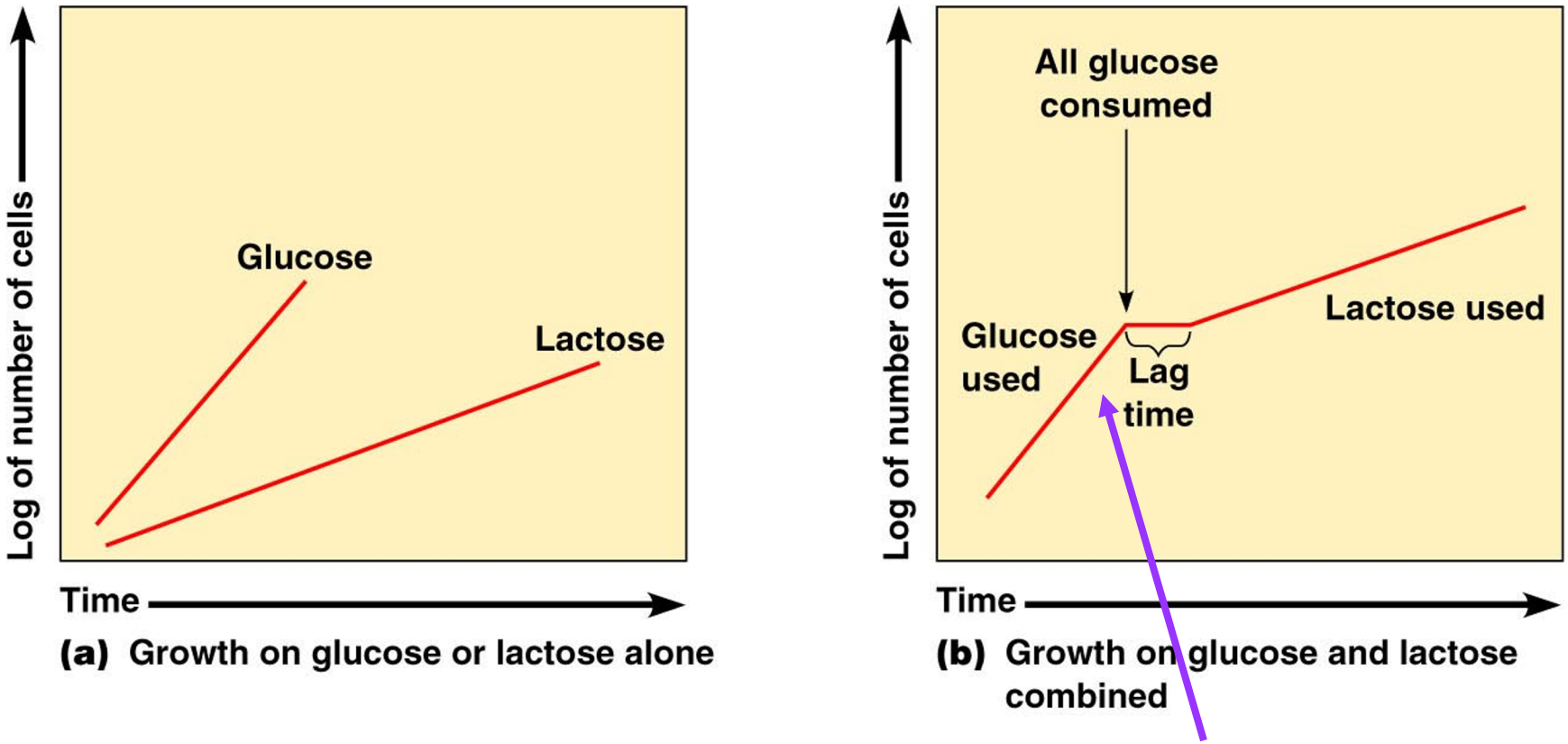
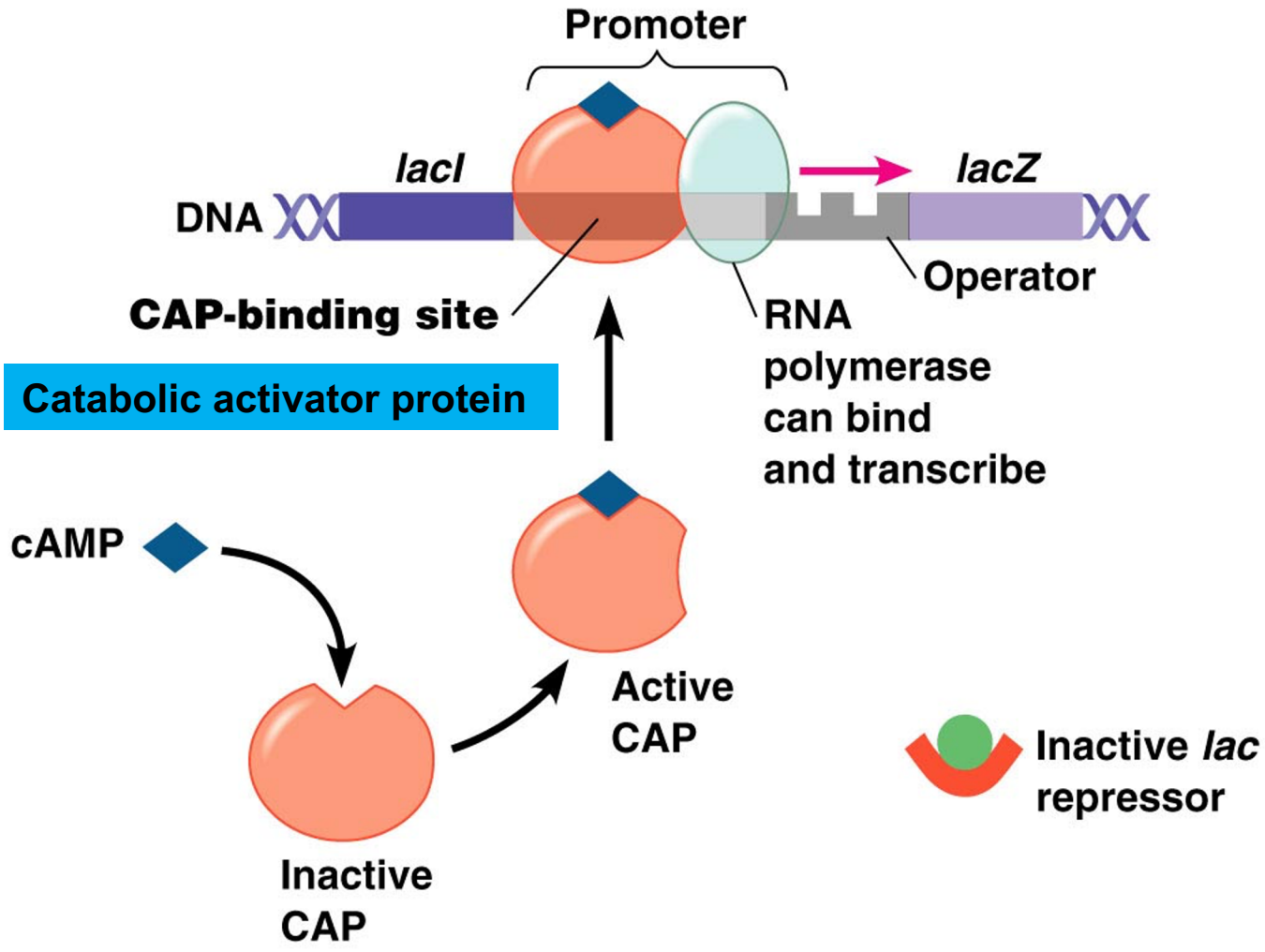
Figure 8.12b, step 3

Positive Regulation



cAMP acummulation (alarmone), binding to allosteric site CAP (catabolic activator protein), followed by binding to *lac* promoter

Figure 8.13 - Overview



(a) Lactose present, glucose scarce (cAMP level high) If glucose is scarce, the high level of cAMP activates CAP, and the *lac* operon produces large amounts of mRNA for lactose digestion.

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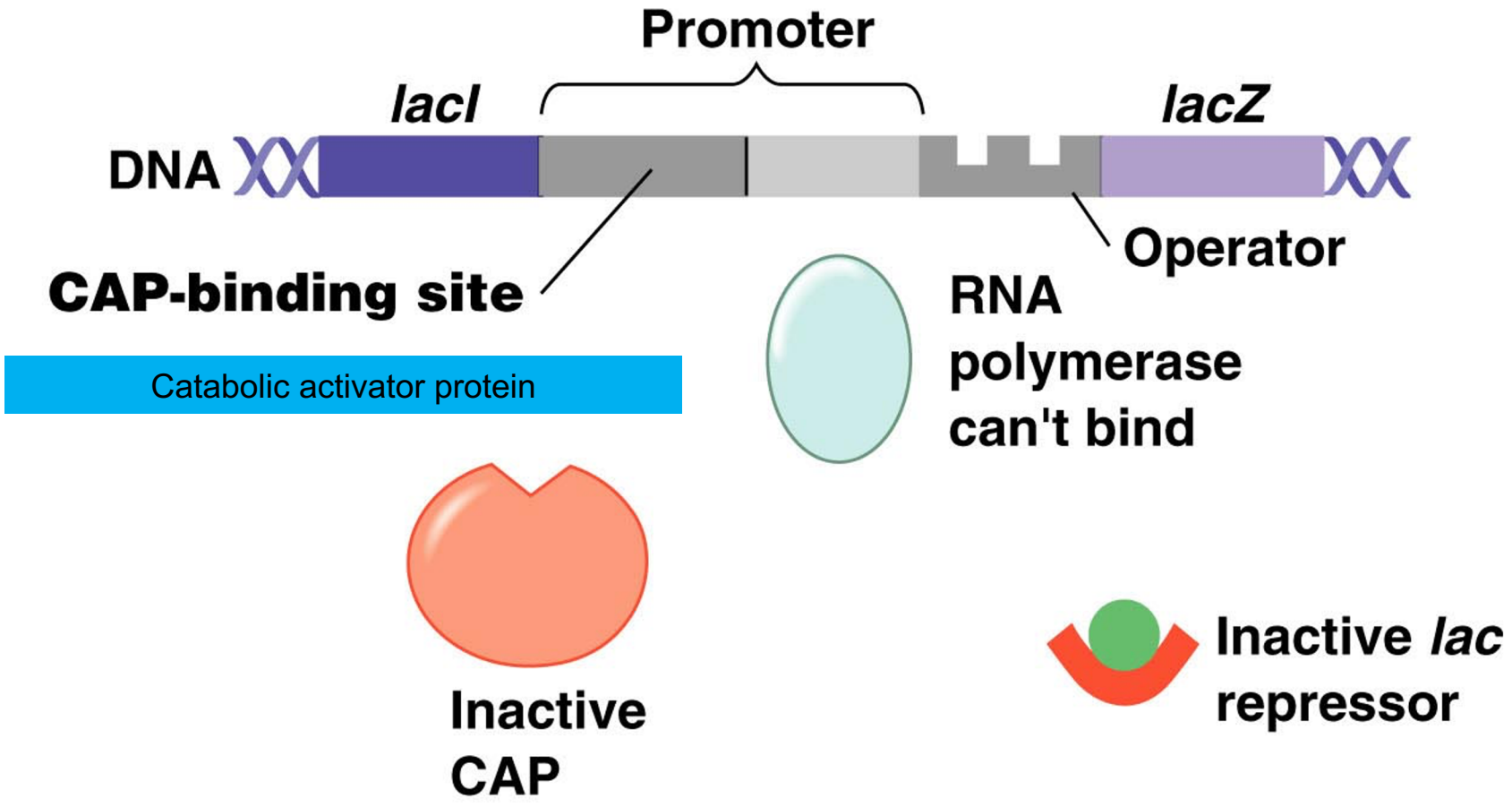
Figure 8.14a



(b) Lactose present, glucose scarce (cAMP level low)
When glucose is present, cAMP is scarce, and CAP is unable to stimulate transcription.

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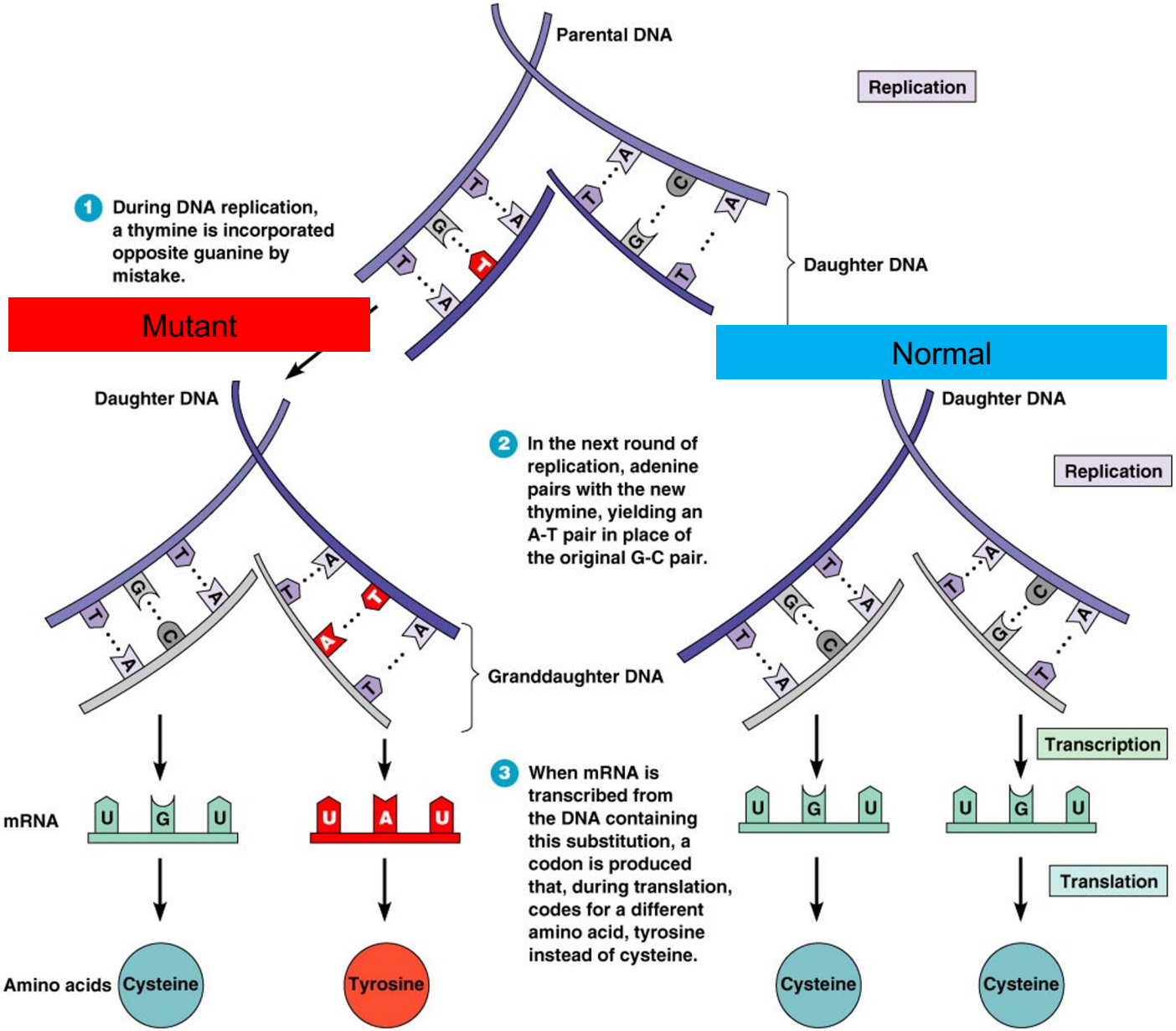
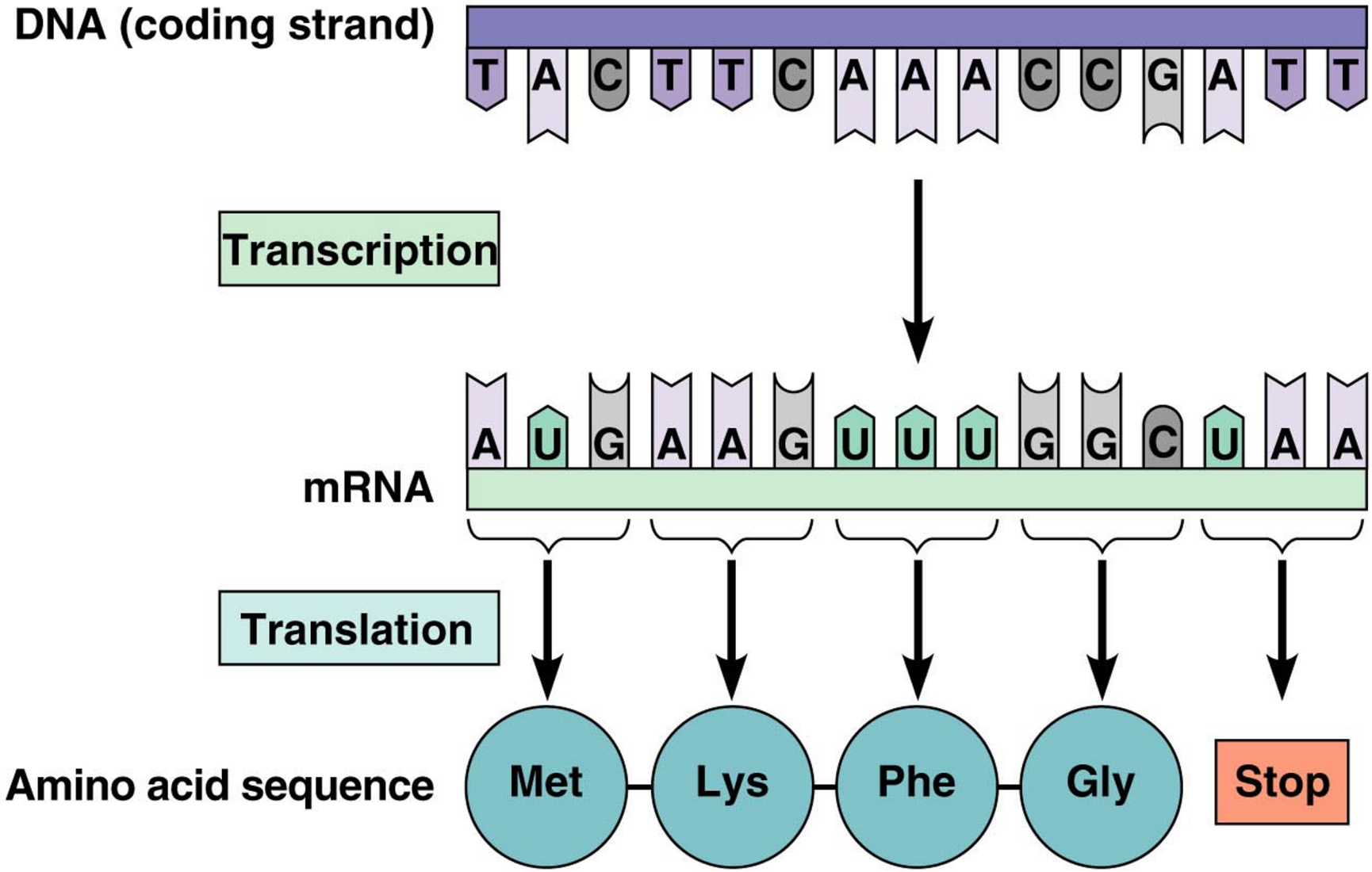
Figure 8.14b


Mutations



Base substitution



(a) Normal DNA molecule

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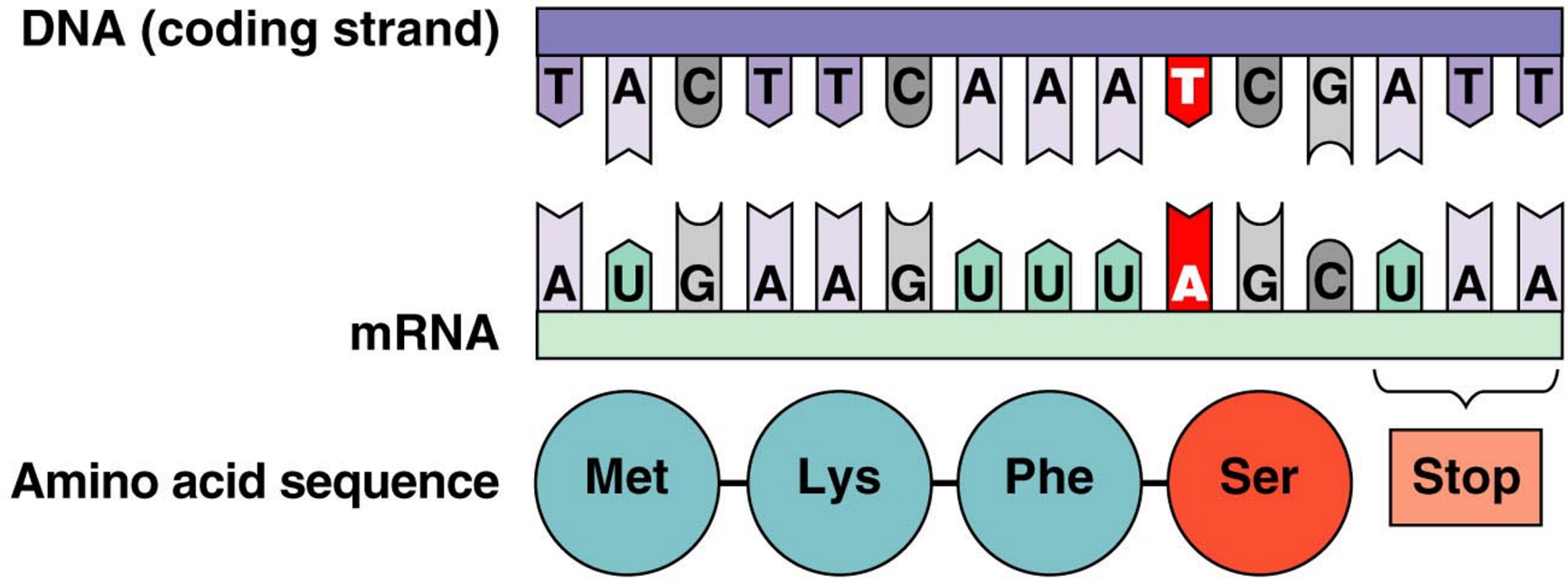

(b) Missense mutation

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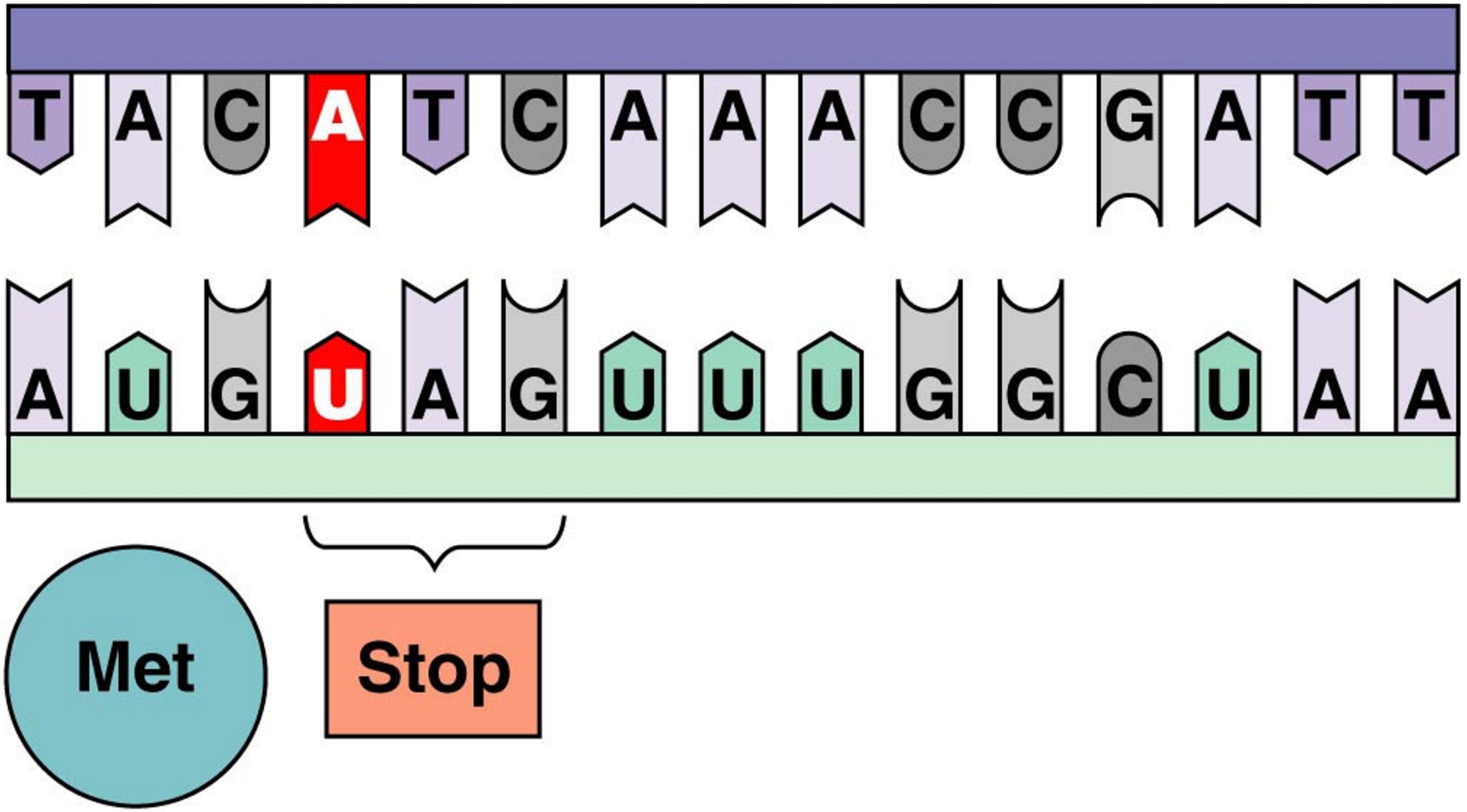

(c) Nonsense mutation

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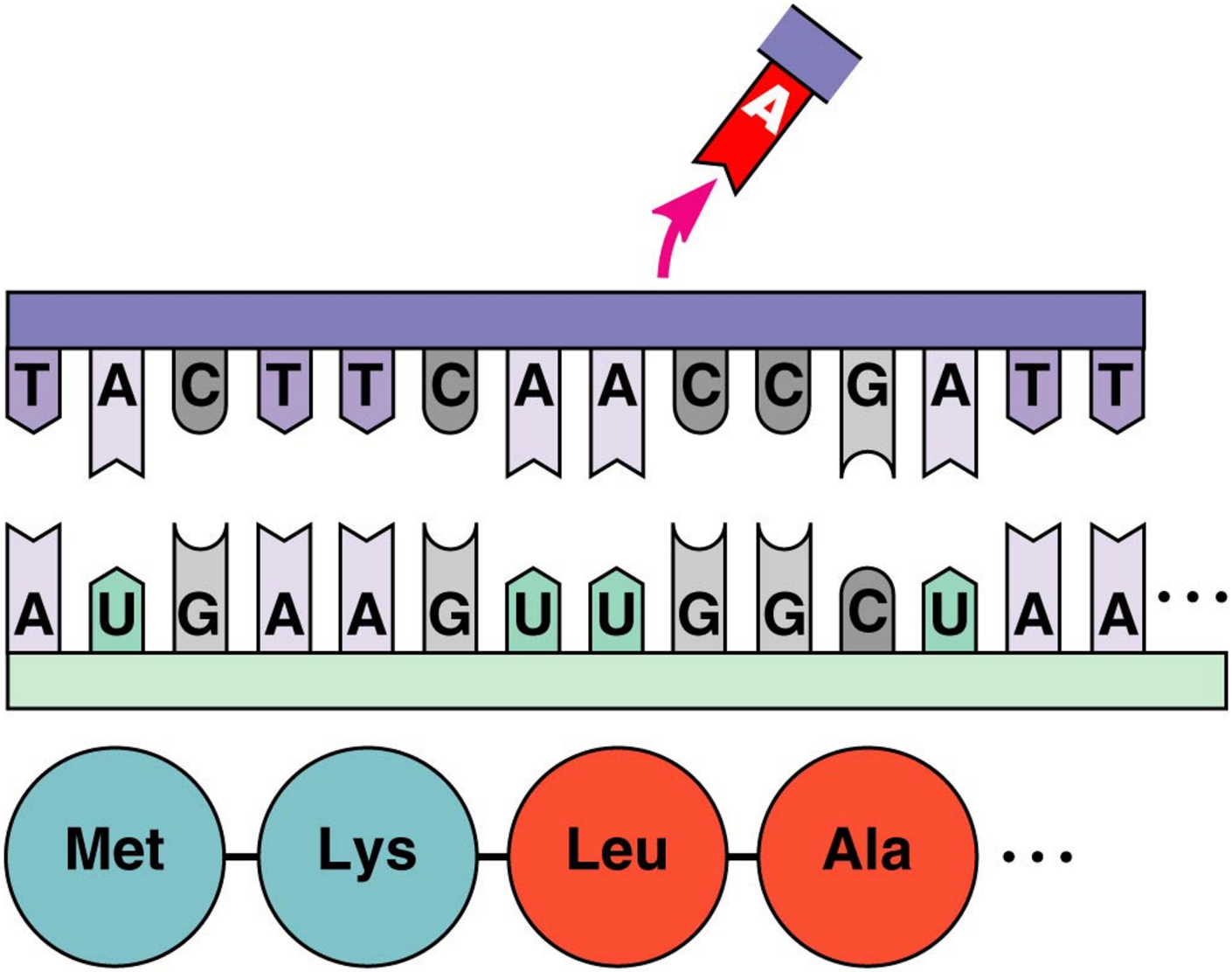

(d) Frameshift mutation

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Figure 8.16d

Mutagens are chemical, physical, or **biological** agents that increase the mutation rate.

- Mutagens can alter DNA in many different ways. However, alterations in DNA are not mutations unless they can be inherited.

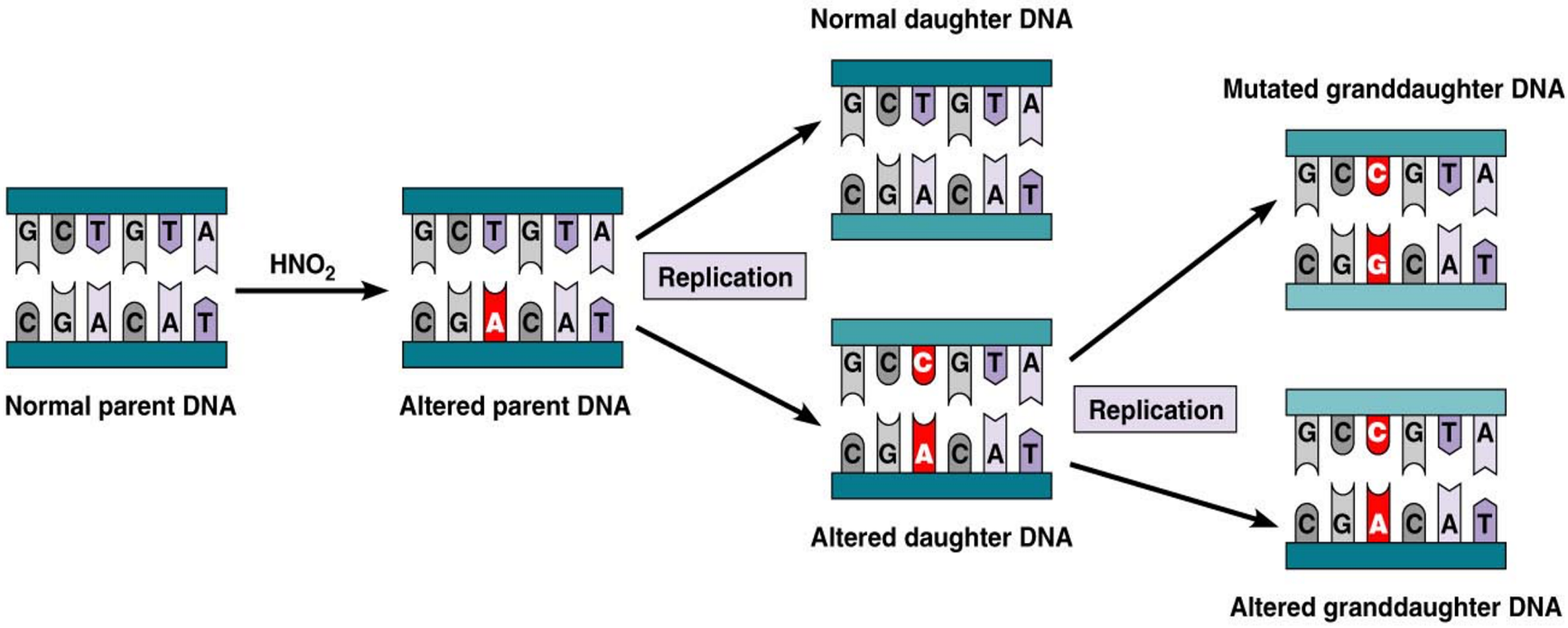
- Some DNA damage can lead to cell death if not repaired, and both error-prone as well as high-fidelity DNA repair systems exist.

Table 10.3 Types of mutant strains

Designation	Phenotype
Auxotroph	Requires an exogenous growth factor, e.g., an amino acid or vitamin
Carbon source	Unable to use a particular compound as a source of carbon
Nitrogen source	Unable to use a particular compound as a source of nitrogen
Phosphorus source	Unable to use a particular compound as a source of phosphorus
Sulfur source	Unable to use a particular compound as a source of sulfur
Temperature sensitive	Loses a particular function at a high or low temperature
Heat sensitive	Loses a particular function at a high temperature
Cold sensitive	Loses a particular function at a low temperature
Osmotic sensitive	Loses a particular function at high or low osmolarity
Conditional lethal	Unable to grow in a particular environment (e.g., high temperature) in any medium

Table 10.7 Some physical and chemical mutagens

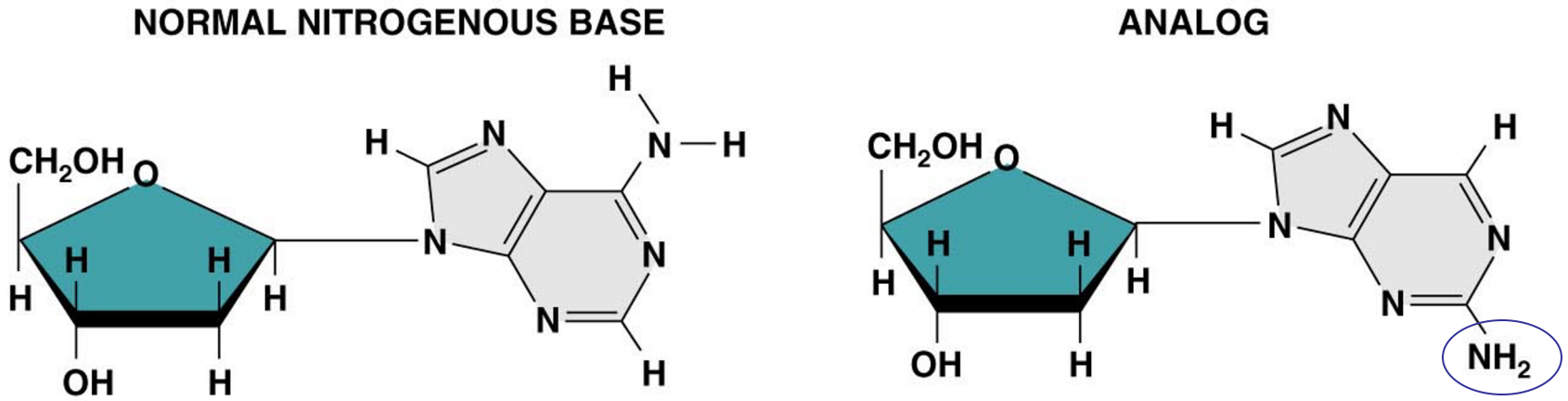
Agent	Mutagenic action
Physical agents	
X rays	Cause double-strand breaks in DNA, the repair of which leads to macrolesions
UV light	Cause adjacent pyrimidines in DNA to join at positions 4 and 5, forming dimers, which in the process of their repair result mostly in transversions, but also in frameshifts and transitions
Chemical agents	
Base analogs	Become incorporated in DNA and then, owing to their ambiguous pairing on subsequent replication, cause transitions
2-Aminopurine	Can pair with either thymine or cytosine
5-Bromouracil	Can pair with either adenine or guanine
DNA modifiers	
Nitrous acid	Deaminates bases; deamination of cytosine produces uracil and then a CG-to-TA transition
Hydroxylamine	Hydroxylates 6 amino group of cytosine, causing CG-to-TA transition
Alkylating agents (e.g., nitrosoguanidine and ethyl methane sulfonate)	Alkylate DNA bases, distorting DNA structure and resulting in a variety of types of mutations
Intercalating agents (e.g., acridine orange and ethidium bromide)	Intercalate between stacked bases in DNA; replication results in frameshift mutations



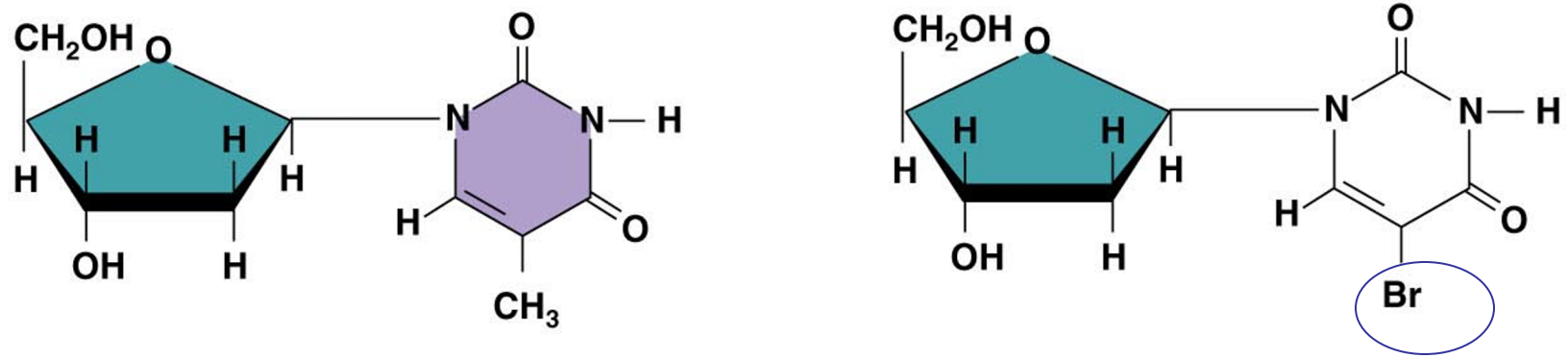
Nitrous acid (HNO_2) mutation

Figure 8.17 - Overview (1 of 3)

Nucleoside analogs



(a) The 2-aminopurine is incorporated into DNA in place of adenine but can pair with cytosine, so an AT pair becomes a CG pair.



(b) 5-bromouracil is used as an anticancer drug because it is mistaken for thymine by cellular enzymes but pairs with cytosine. In the next DNA replication, an AT pair becomes a GC pair.

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Figure 8.18 - Overview

Thymine dimers

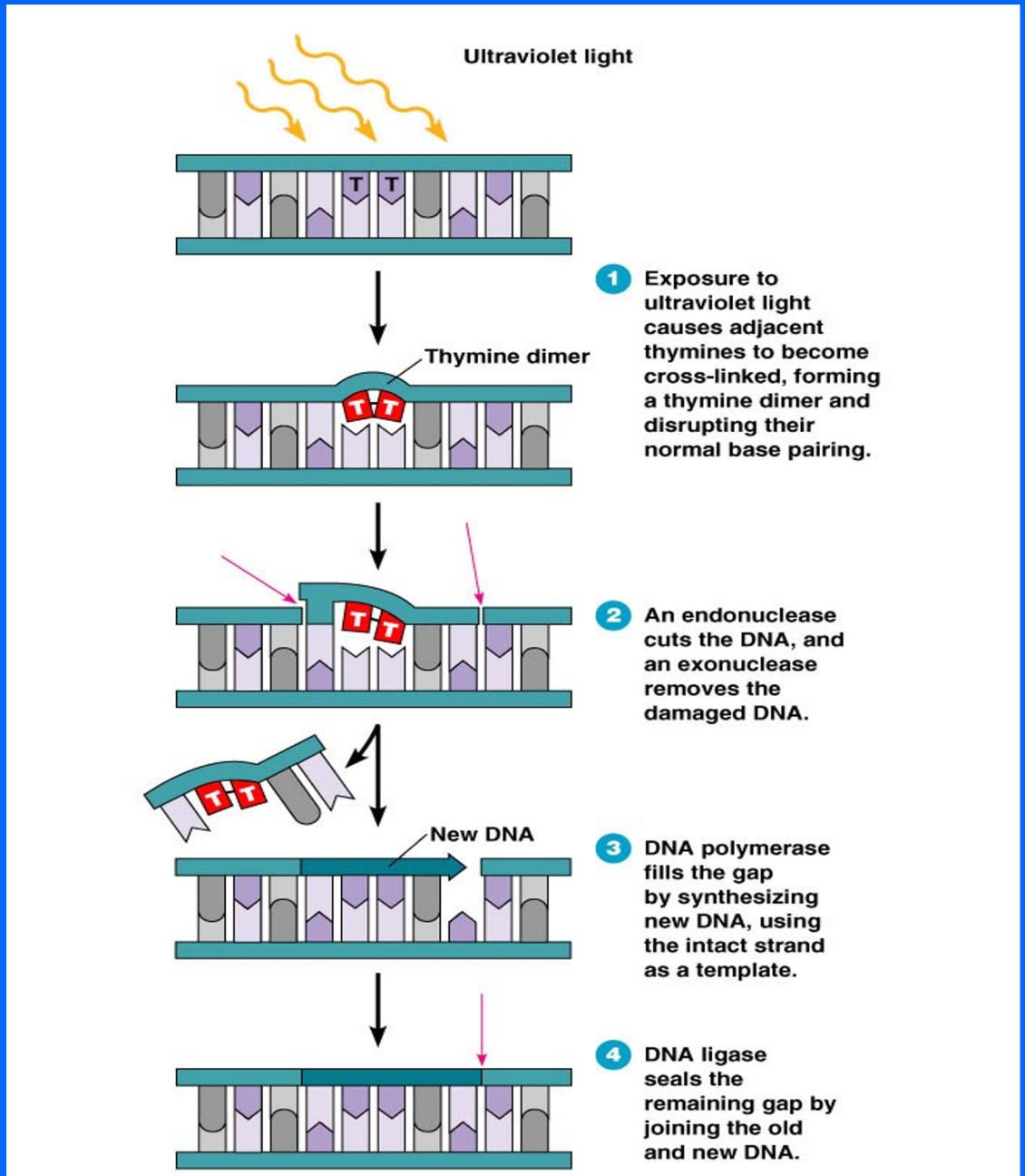

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Figure 8.19 - Overview

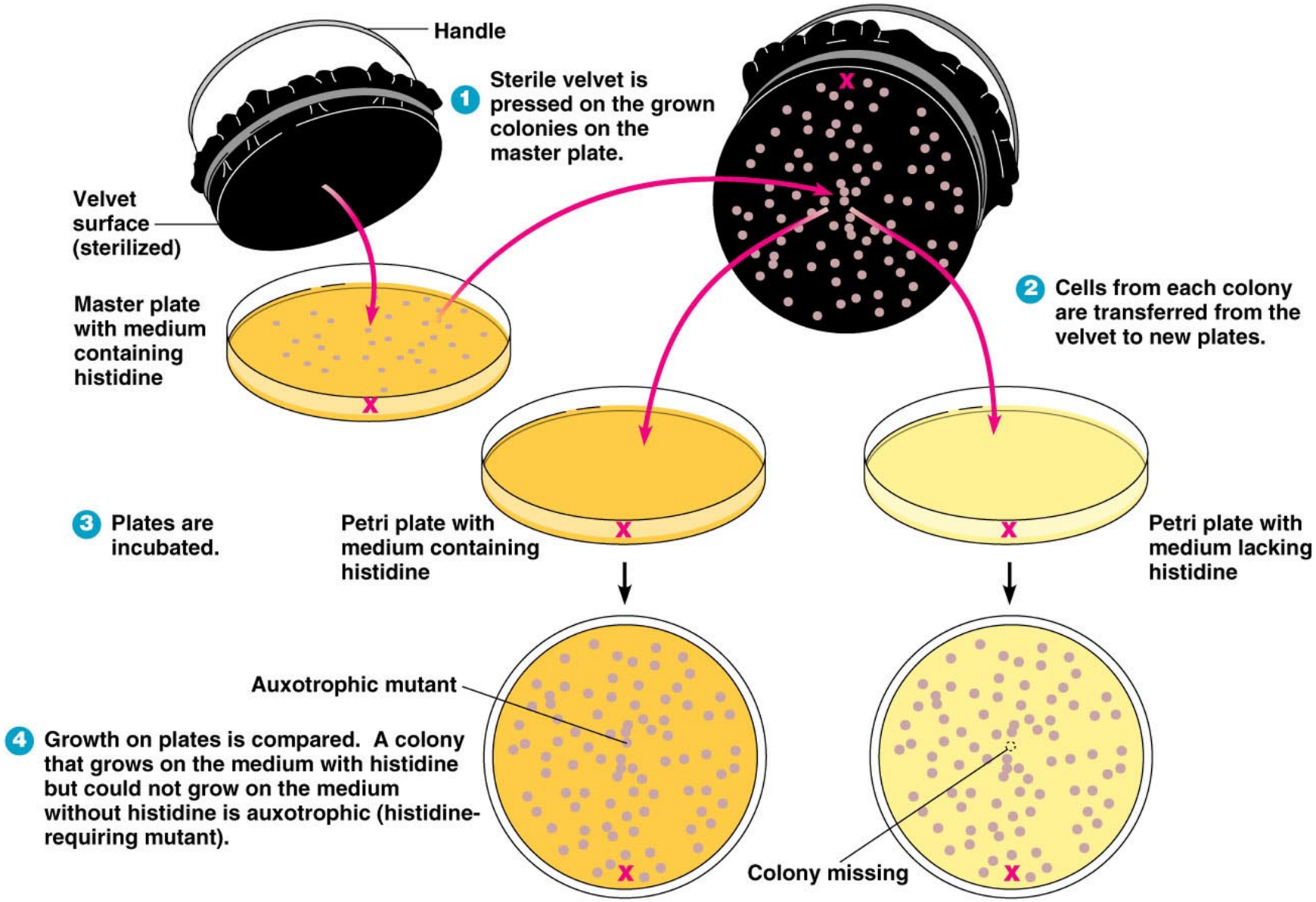

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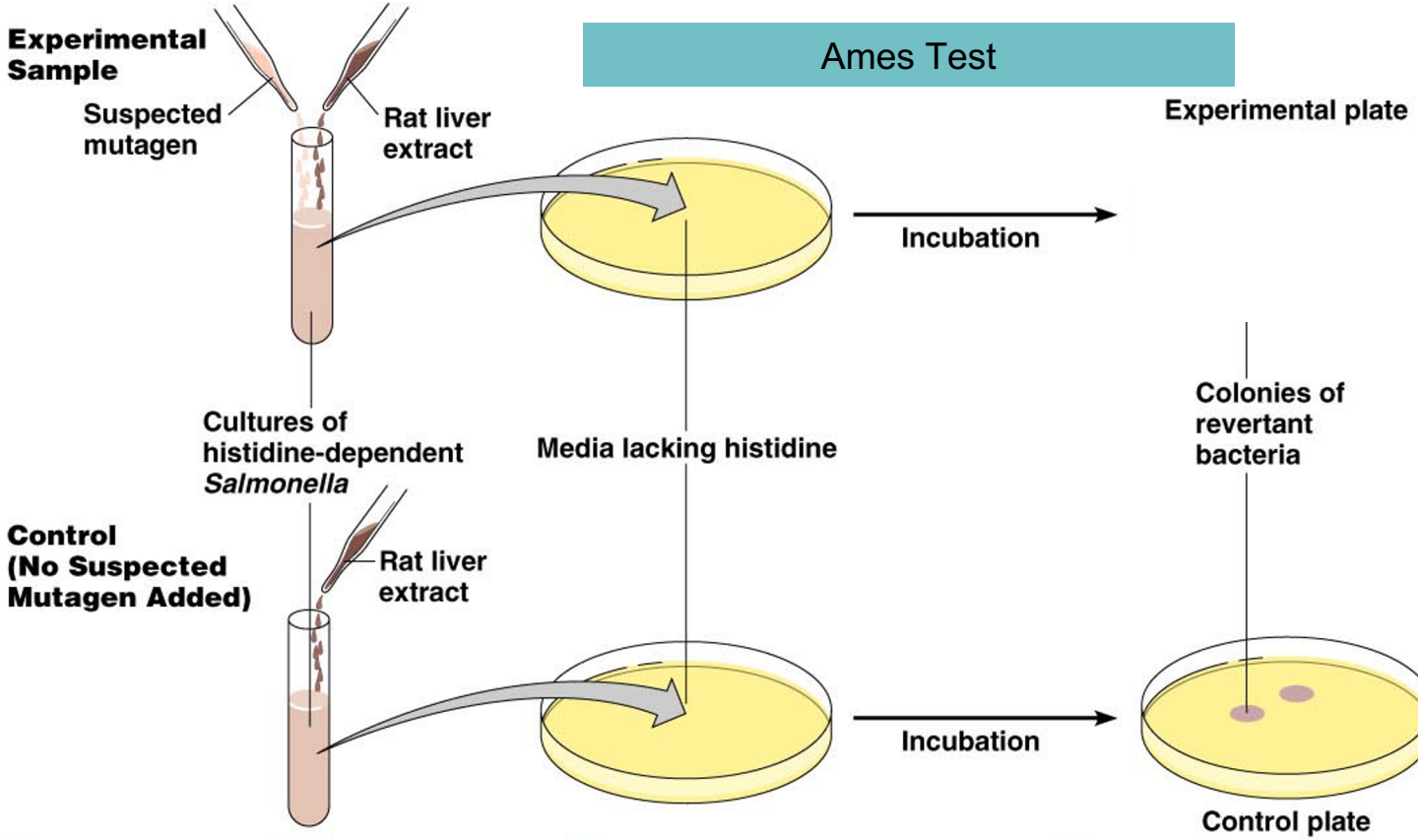
Figure 8.20 - Overview

Ames Test



1. Two cultures are prepared of *Salmonella* bacteria that have lost the ability to synthesize histidine (histidine-dependent).
2. The suspected mutagen is added to the experimental sample only; rat liver extract (an activator) is added to both samples.
3. Each sample is poured onto a plate of medium lacking histidine. The plates are then incubated at 37°C for two days. Only bacteria whose histidine-dependent phenotype has mutated back (reverted) to histidine-synthesizing will grow into colonies.
4. The numbers of colonies on the experimental and control plates are compared. The control plate may show a few spontaneous histidine-synthesizing revertants. The test plates will show an increase in the number of histidine-synthesizing revertants if the test chemical is indeed a mutagen and potential carcinogen. The higher the concentration of mutagen used, the more revertant colonies will result.

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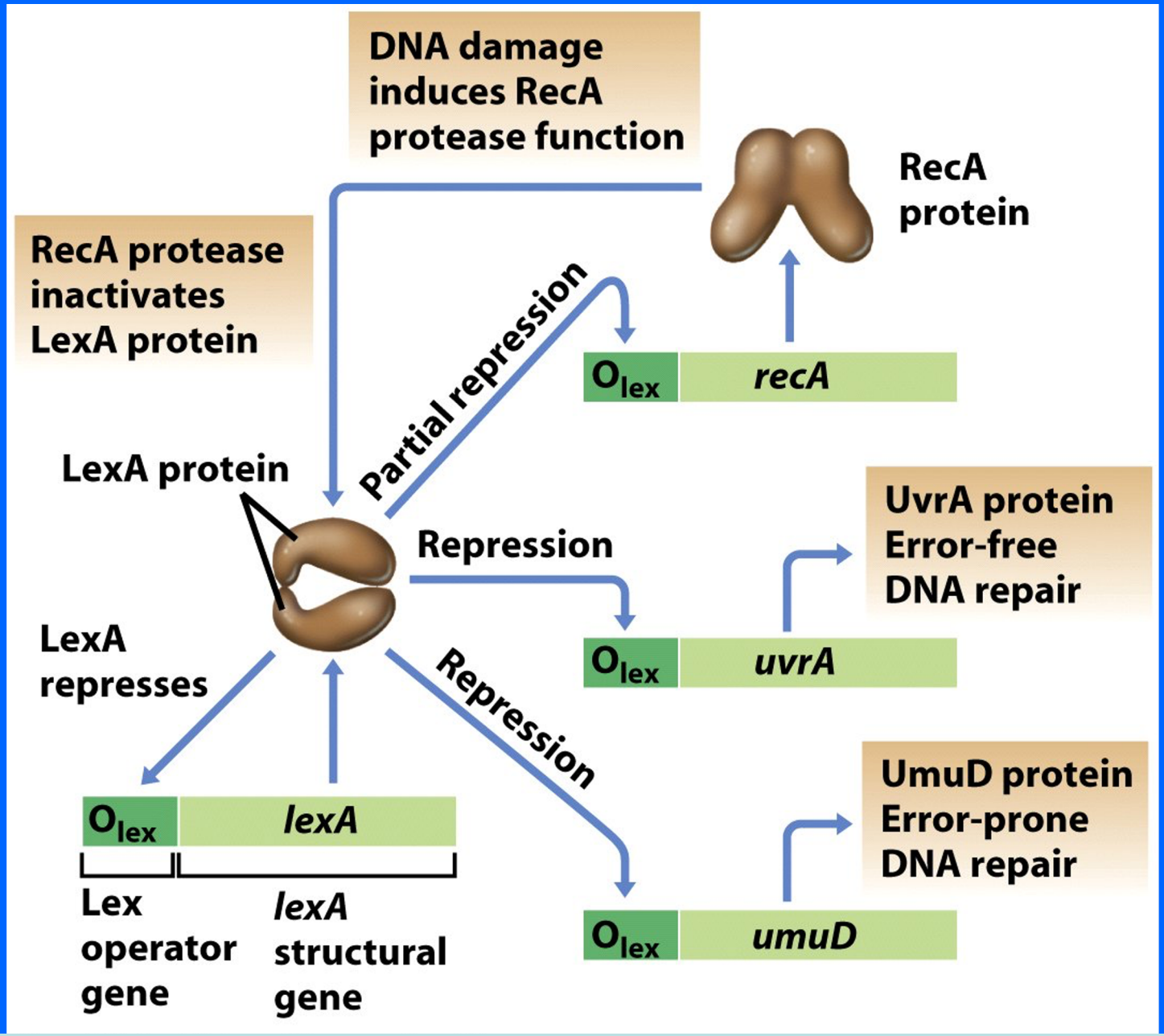

The SOS system

Molecular Events in Homologous Recombination

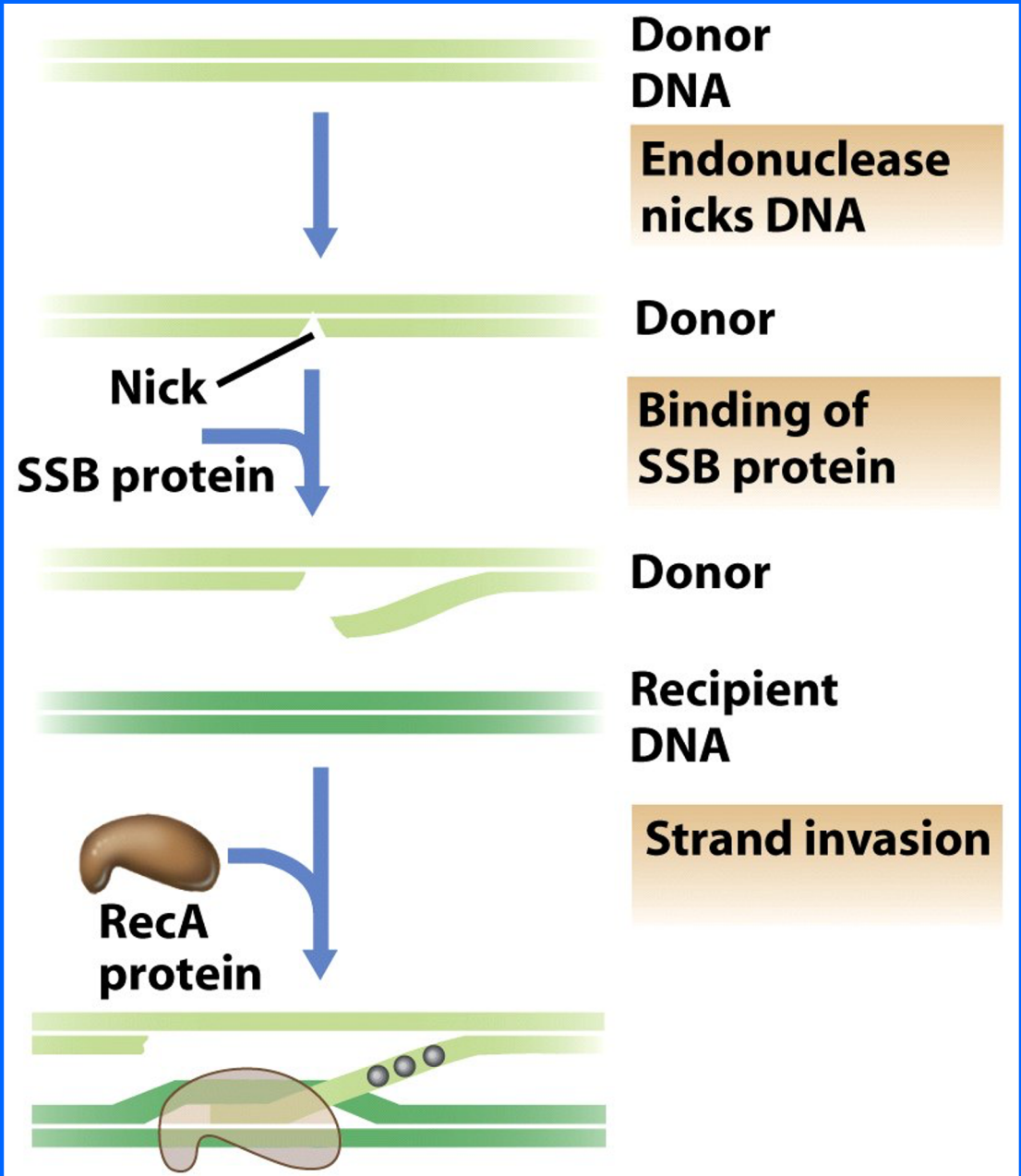

Figure 10-9 part 1 Brock Biology of Microorganisms 11/e

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Molecular Events in Homologous Recombination