# 14


# Regulation of Bacterial Cellular Processes

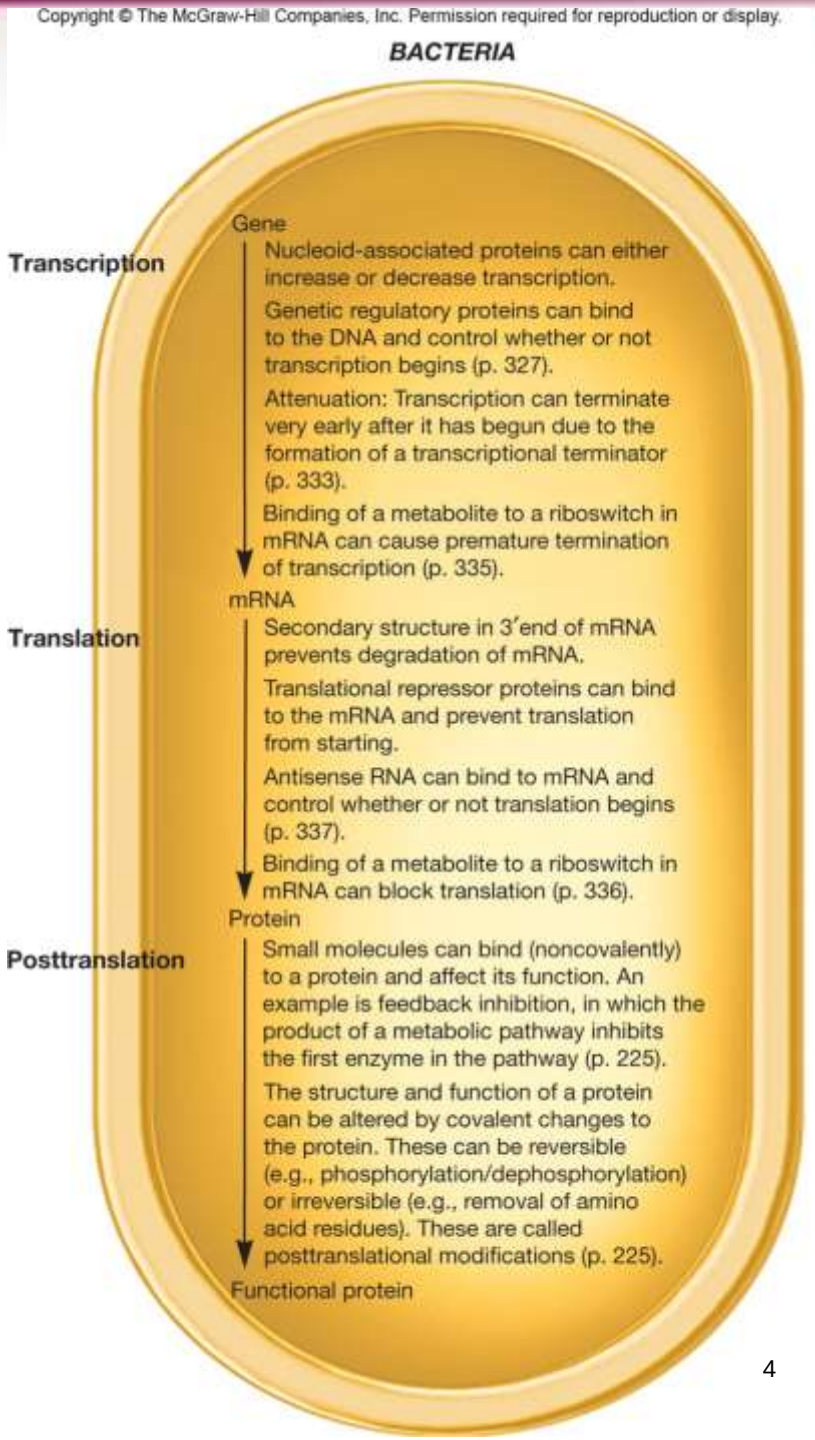
# 14.1 Levels of Regulation

1. List when, during the flow of genetic information, bacterial cells can regulate gene expression
2. Speculate why microbial geneticists for many years focused almost exclusively on the regulation of transcription initiation

# Two Approaches to Regulation

- Regulation of gene expression
  - transcription initiation
  - transcription elongation
  - translation
- Alter activity of enzymes and proteins
  - posttranslational
- Three domains of life differ in genome structure and regulatory mechanisms used

# Steps Leading from the Information Coded in DNA to a Functional Protein



# 14.2 Regulation of Transcription Initiation

1. Compare and contrast housekeeping, constitutive, inducible, and repressible genes
2. Describe the two common motifs in DNA-binding proteins
3. Summarize how negative transcriptional control and positive transcriptional control can be used to regulate both inducible and repressible genes
4. Outline the regulatory “decisions” made by cells

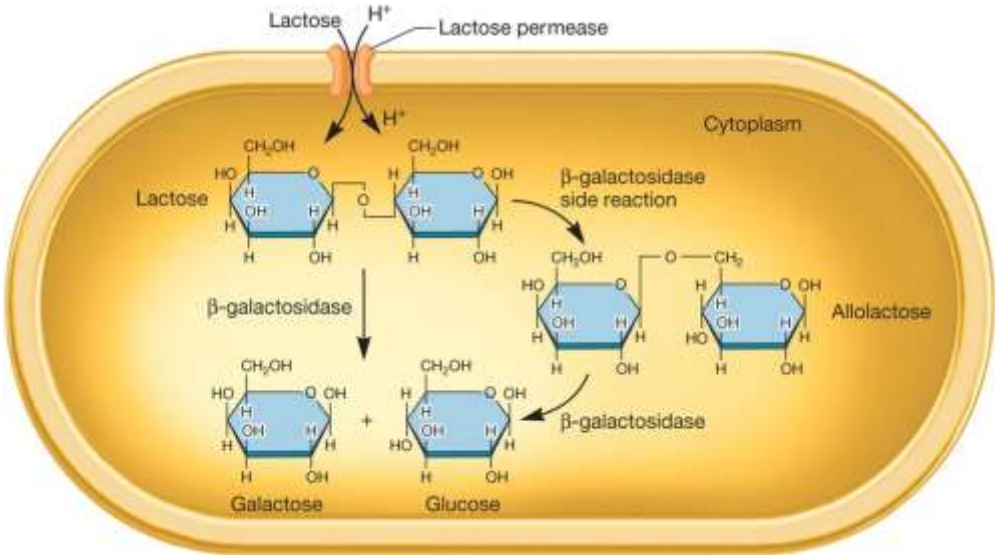
# Regulation of Transcription Initiation

- Replacement of degraded enzymes
  - constitutive genes
    - are housekeeping genes that are expressed continuously by the cell
  - inducible genes
    - are genes that code for inducible enzymes needed only in certain environments
      - such as β-Galactosidase

# Inducible Genes
# β-Galactosidase Enzyme

- Inducible enzyme functions in a catabolic pathway
- Inducible enzymes are present only when their substrate (inducer - effector molecule) is available
- β-galactosidase reaction catalyzed is lactose hydrolysis into galactose and glucose





# Repressible Genes

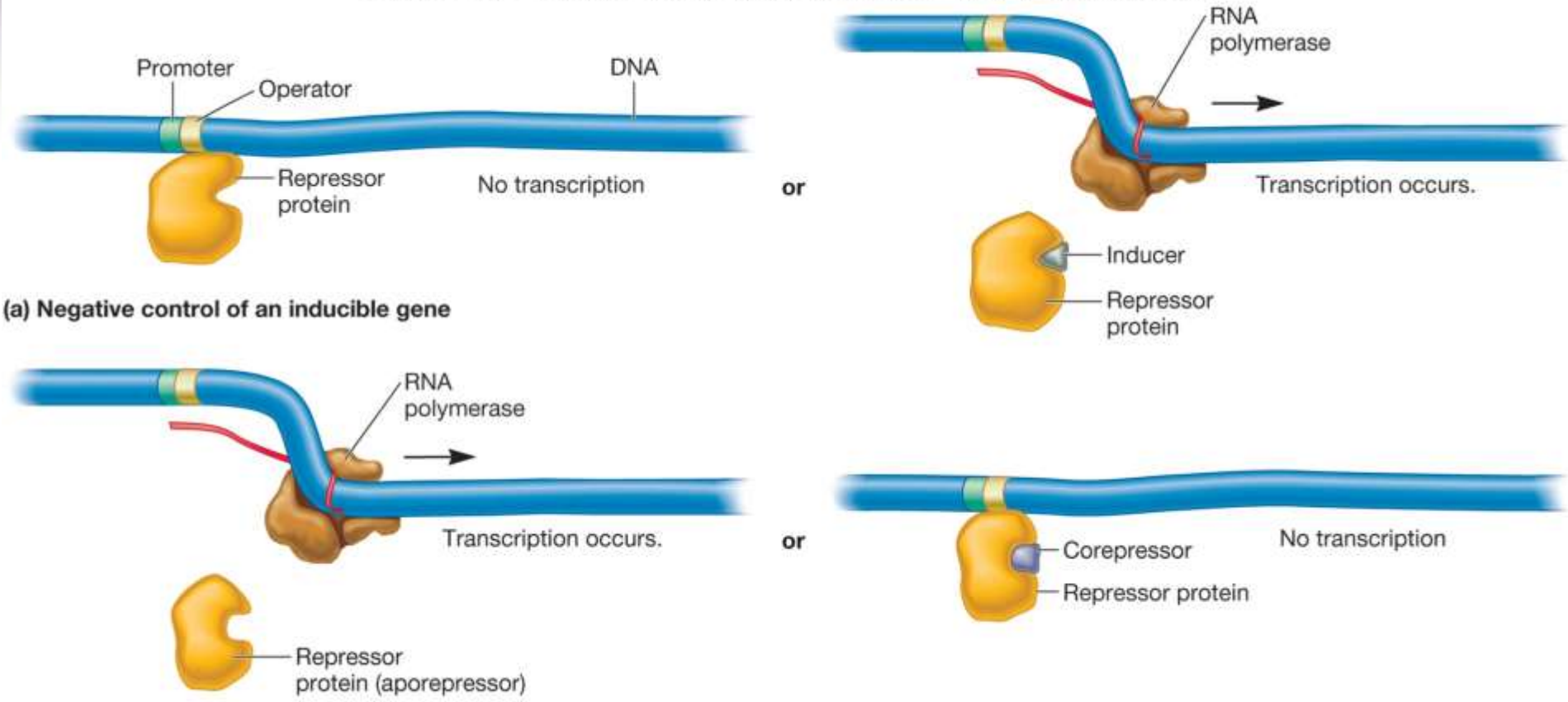
- Enzymes that function in biosynthetic pathways are products of repressible genes
- Generally these enzymes are always present unless the end product in the biosynthetic pathway is available

# Control of Transcription Initiation by Regulatory Proteins

- Induction and repression occur because of the activity of regulatory proteins and DNA binding domains
- These proteins either inhibit transcription (negative control) or promote transcription (positive control)

# Negative Transcriptional Control

- Binding of regulatory protein (repressor) at DNA regulatory site (operator) inhibits initiation of transcription
  - mRNA expression is reduced
- Repressor proteins
  - exist in active and inactive forms
  - inducers (substrates) and corepressors (enzymatic products) alter activity of repressor by binding

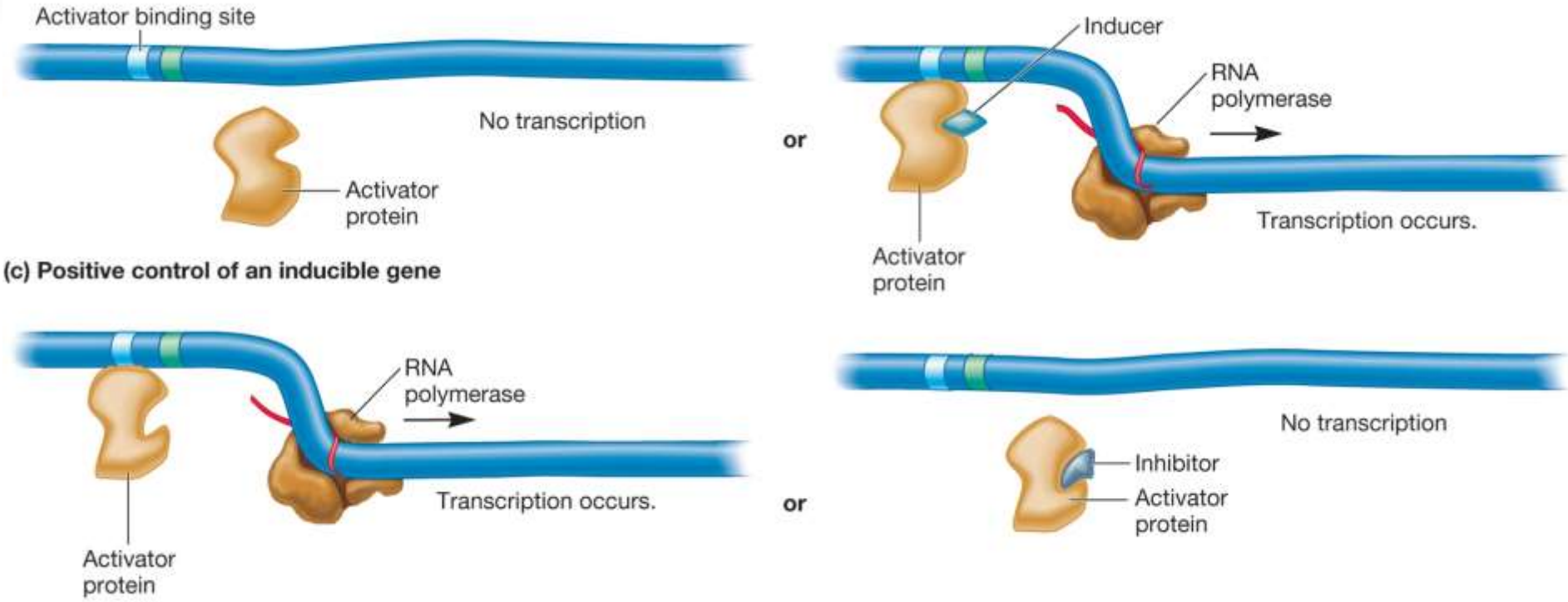



**(a) Negative control of an inducible gene**

**(b) Negative control of a repressible gene**

# Positive Control

- Binding of a regulatory protein (activator protein) at a regulatory region on DNA (activator binding sites) promotes transcription initiation
  - mRNA synthesis is increased
- Activation
  - inactive protein is activated by inducer (activator protein)
  - active protein is inactivated by inhibitor

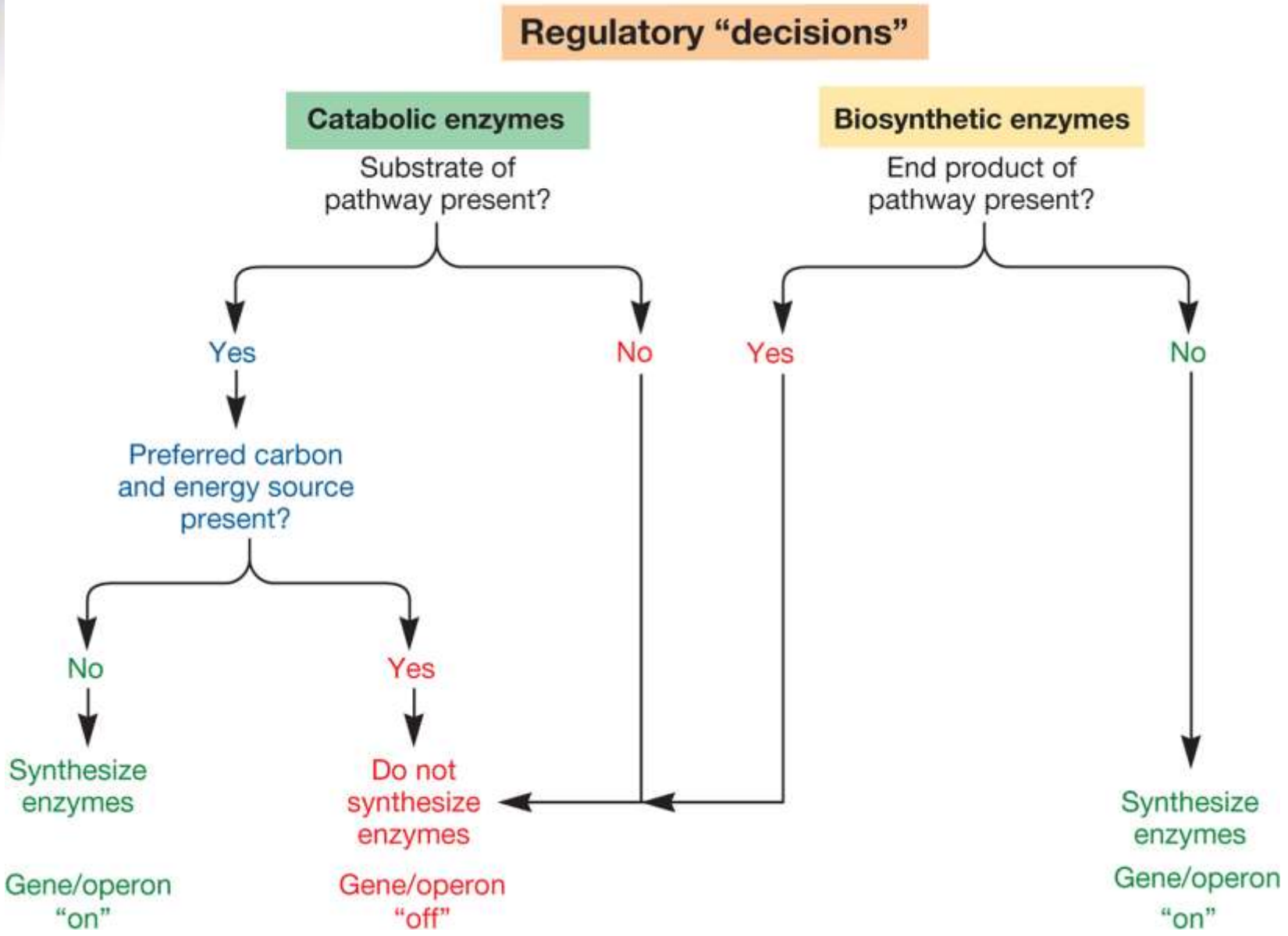



**(c) Positive control of an inducible gene**

**(d) Positive control of a repressible gene**

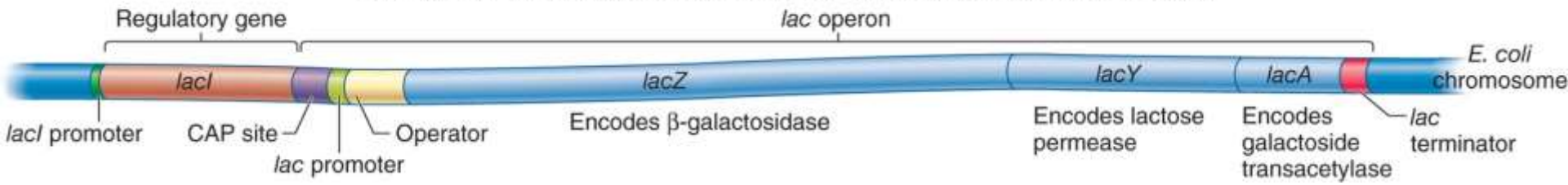
# “Decision” Process in Gene Expression

- Enzymes of a catabolite pathway are only needed (increased mRNA synthesis) when the preferred substrate is available
- Enzymes not synthesized when substrate absent
- Efficient use of energy and materials



# Negative Control of Lactose (*Lac*) Operon



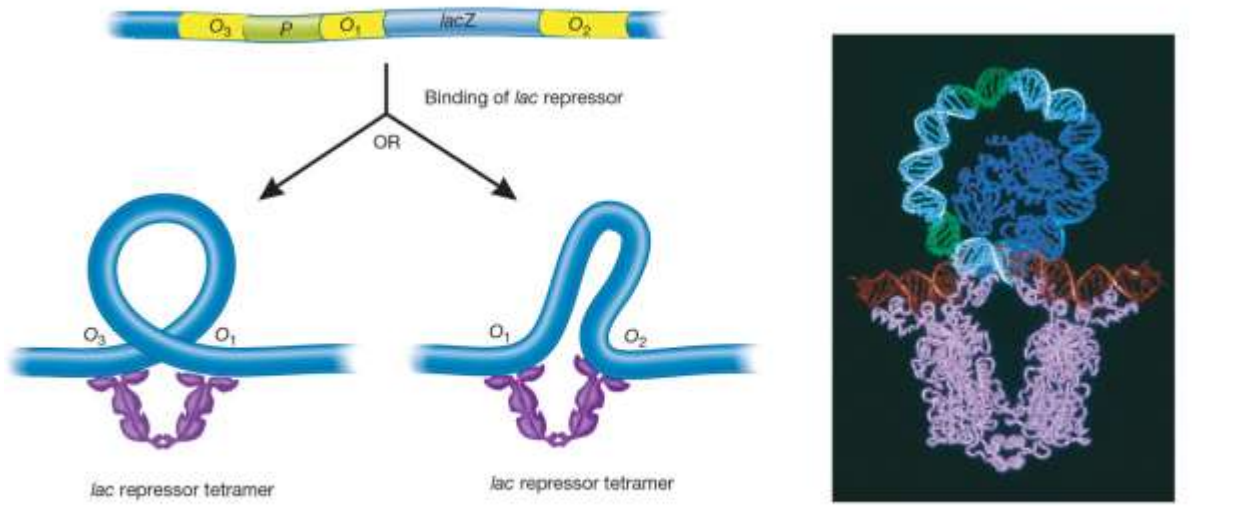



- Inducible genes
  - three structural genes coding for lactose uptake and metabolism
  - *lac* repressor (*lac*I) binds operator
    - inhibits transcription
- Enzymes normally not produced unless lactose present

# *lac* Repressor

- Tetramers of repressor form and bind to three operator sites ($O_1$, $O_2$, $O_3$)
- Bends DNA, prevents RNA polymerase from accessing promoter
- Presence of allolactose binds repressor – no longer binds operator



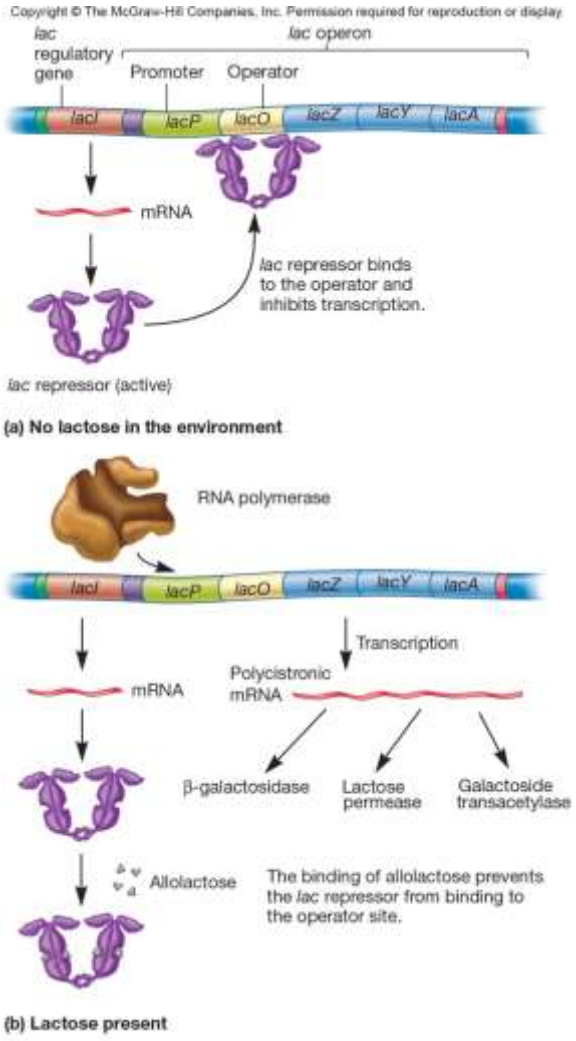



(a) Possible DNA loops caused by the binding of the lac repressor

(b) Proposed model of the *lac* repressor binding to $O_1$ and $O_3$ (red) based on crystallography studies

Lewis et al. Crystal Structure of the Lactose Operon Repressor and Its Complexes with DNA and Inducer. *Science*, 1996 Mar 1, Vol. 271 cover

# Regulation of the *lac* Operon by the *lac* Repressor



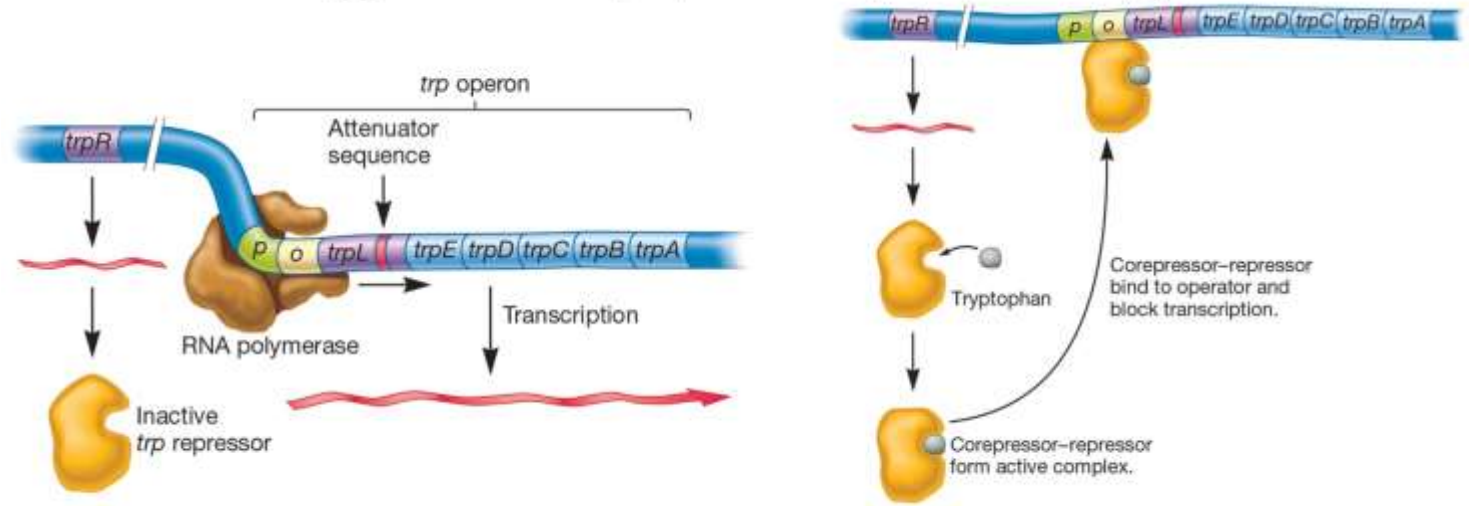
# Positive Control of the *lac* Operon

- Regulated by catabolite activator protein (CAP)
  - regulates in response to presence or absence of glucose
  - allows for preferential use of glucose

# The Tryptophan (*trp*) Operon

- Consists of 5 structural genes which code for enzymes needed to synthesize tryptophan
- Negative transcriptional control of repressible genes by *trp* repressor
- Operon only functions in the absence of tryptophan






(a) Low tryptophan levels, transcription of the entire *trp* operon occurs

(b) High tryptophan levels, repression occurs

# Quorum Sensing

- Cell-to-cell communication mediated by small signaling molecules such as N-acyl-homoserine lactone (AHL)
- Couples cells density and intercellular communication to transcription regulation

# Quorum Sensing in *V. fischeri*

- High concentrations of AHL produced by increased density of cells diffuse back into the cell, bind to the transcriptional regulator LuxR and activate transcription
- LuxR stimulates transcription of the genes for AHL synthase (luxl) and proteins needed for light production