Antibióticos

1. Histórico
2. Mecanismos de ação
3. Mecanismos de Resistência

Antibiotics

What are antibiotics?
Who are the main producers?
Biological functions?
Resistance
New developments

First antimicrobial drugs

Louis Pasteur (1822-1895):

"pasteurization"

Fermentation: wine contamination

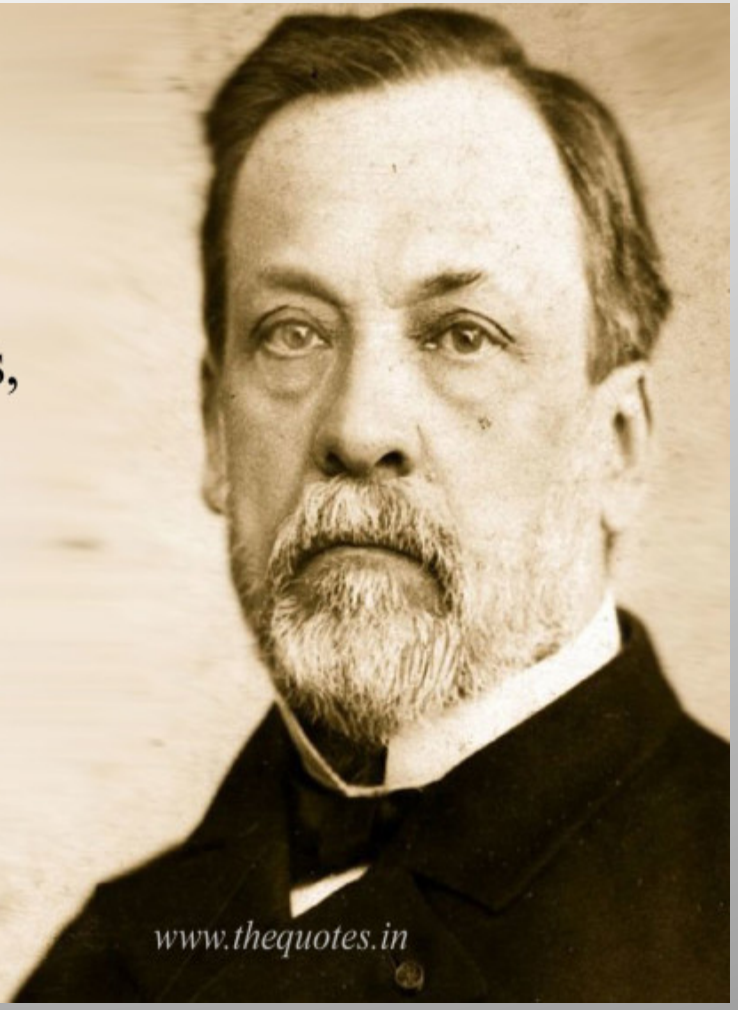
Germ theory: silkworn disease

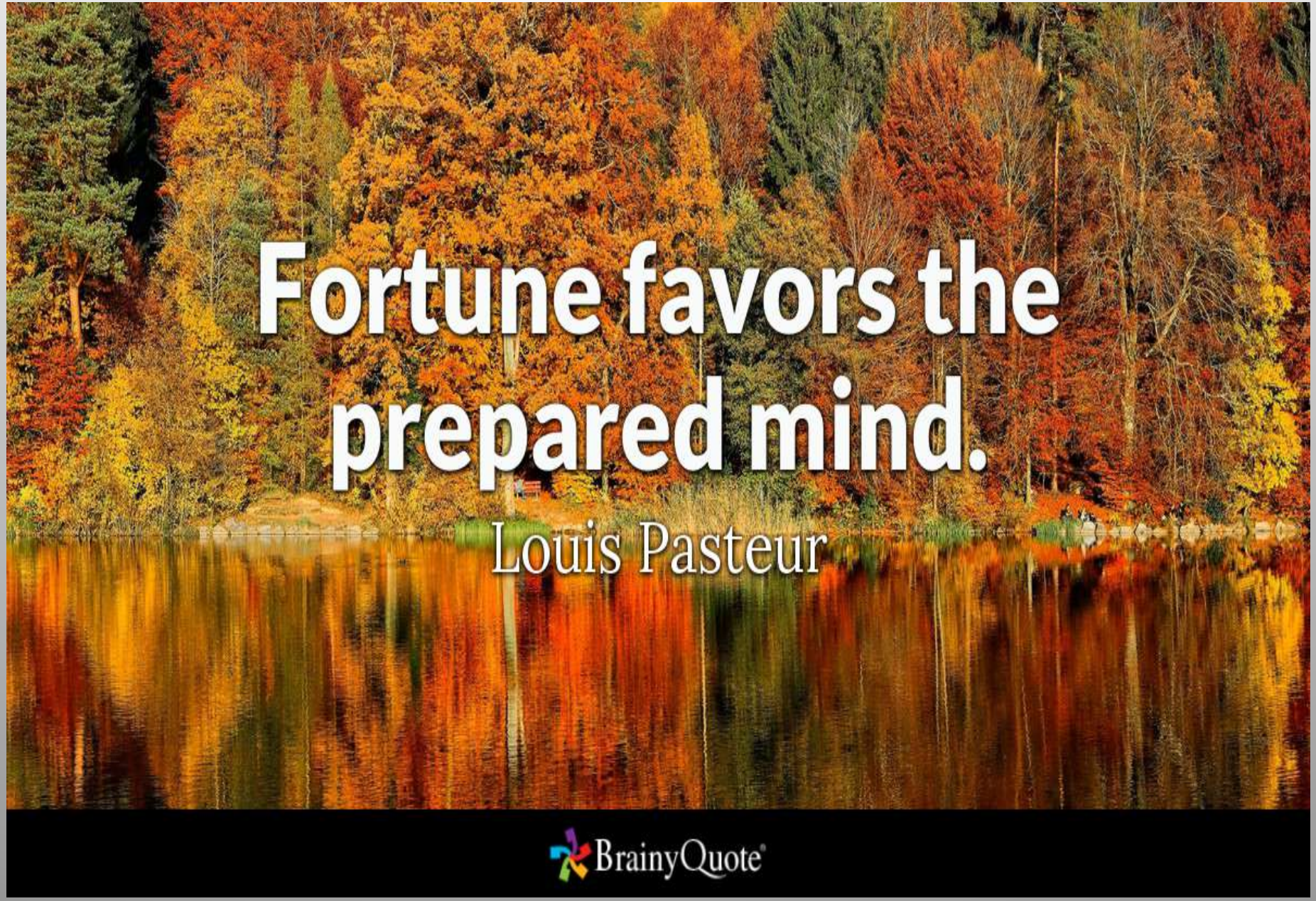
Vaccine: anthrax, fowl cholera

Rabies

There are no such things as applied sciences,
only applications of science.

Louis Pasteur




Fortune favors the prepared mind.
Louis Pasteur
BrainyQuote

First antimicrobial drugs

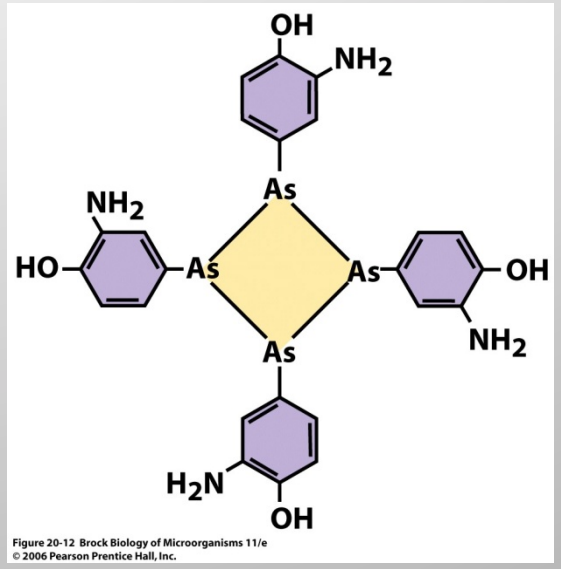
Paul Ehrilch (1854-1915):

- Methylene blue: malaria

-Toxin and antitoxin

-Salvarsan: magic bullet against syphilis, *Treponema pallidum*

First antimicrobial drugs



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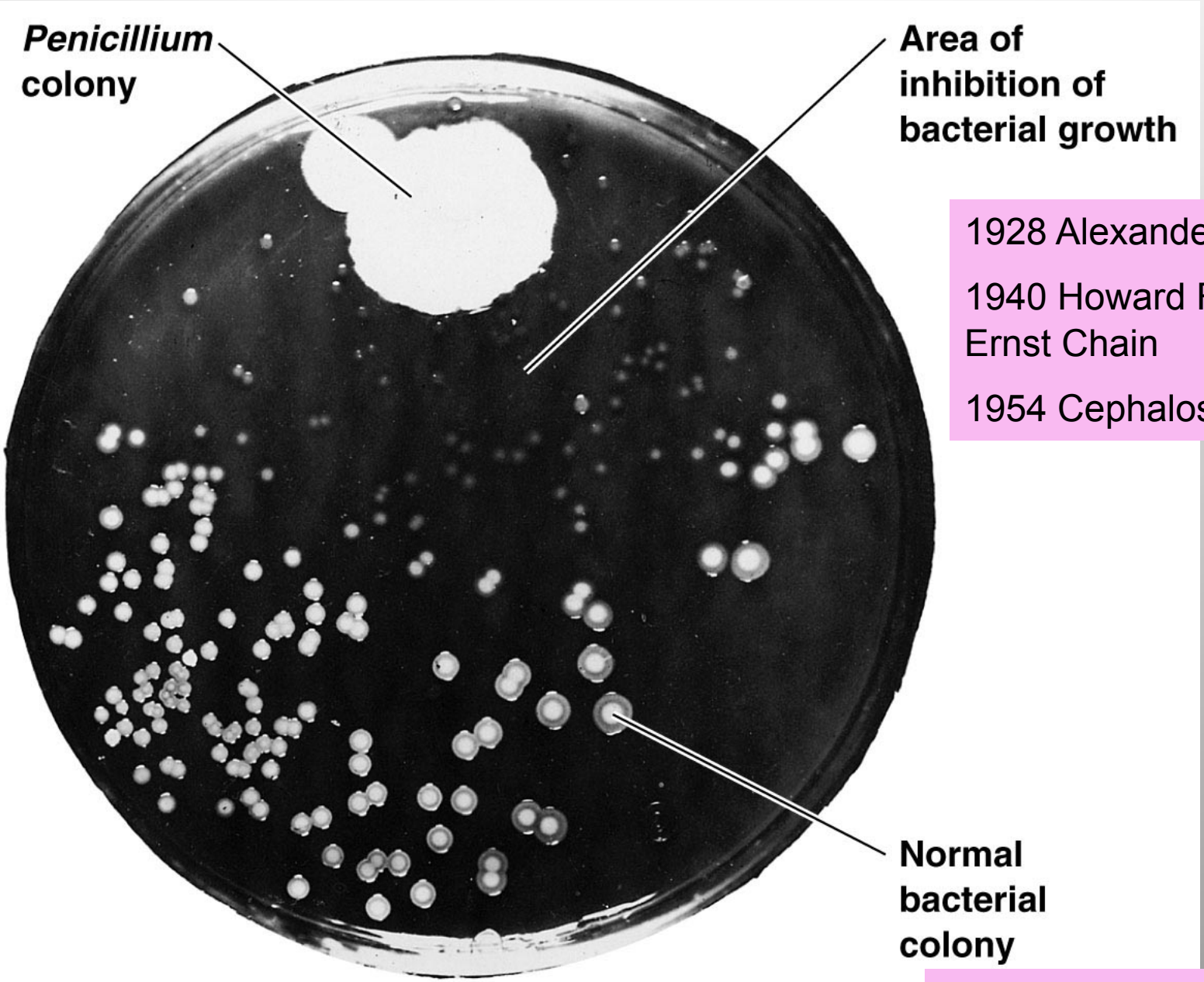
- Gerhard Domagk (Nobel Prize 1939)
  - Sulfa drugs
  - Prontosil
  - Sulfanilamide, analog of p-aminobenzoic acid
  - (part of folic acid, precursor of nucleic acids)
  - Development of antituberculosis compounds thiosemiccarbasone and isoniazid



1928 Alexander Fleming

1940 Howard Florey
Ernst Chain

1954 Cephalosporin C

Staphylococcus aureus

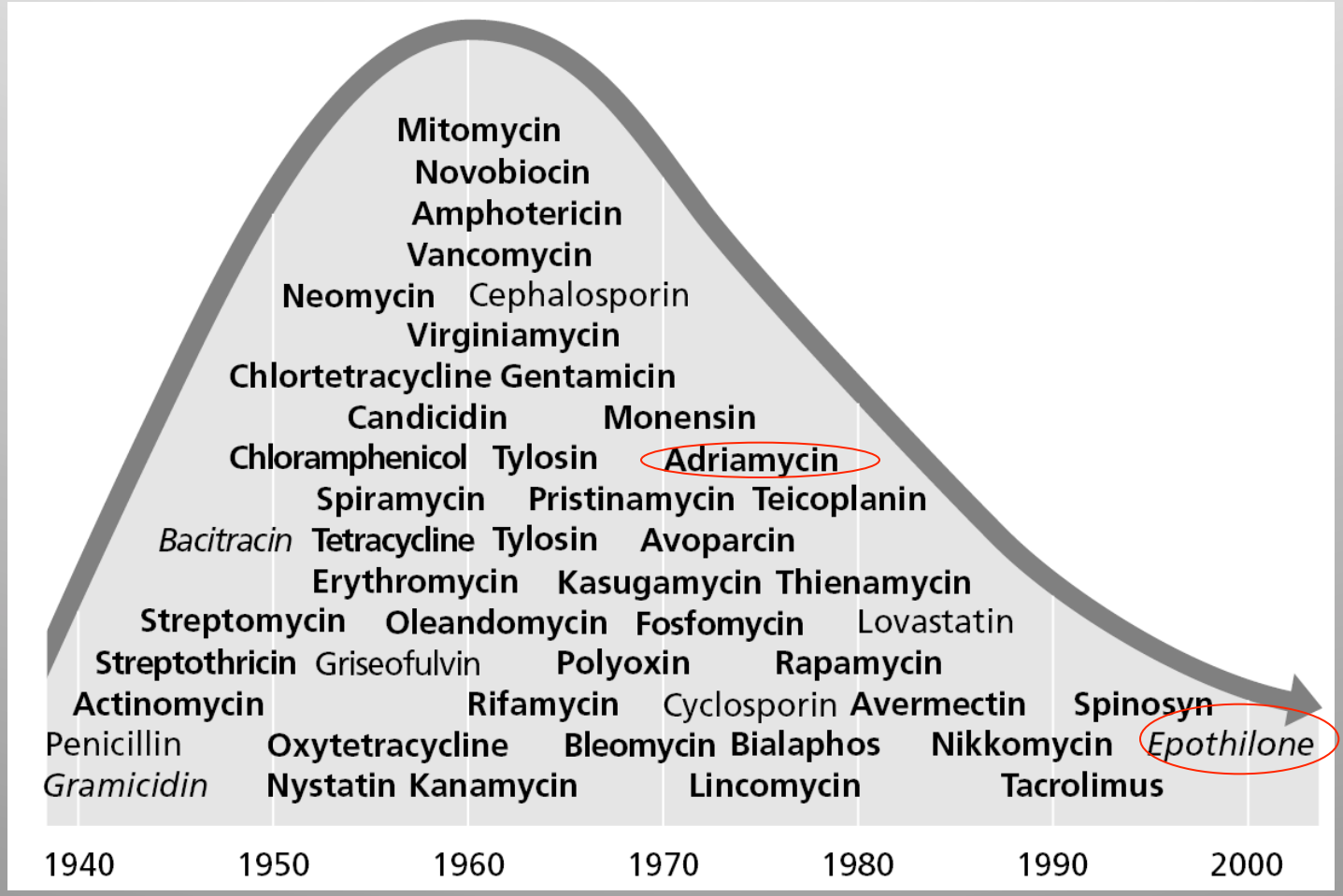
Figure 20.1

Salman Waksman, Albert Schatz

1943. Actinomycin

Streptomycin

Diminishing returns in finding natural products: Genetics to the rescue?



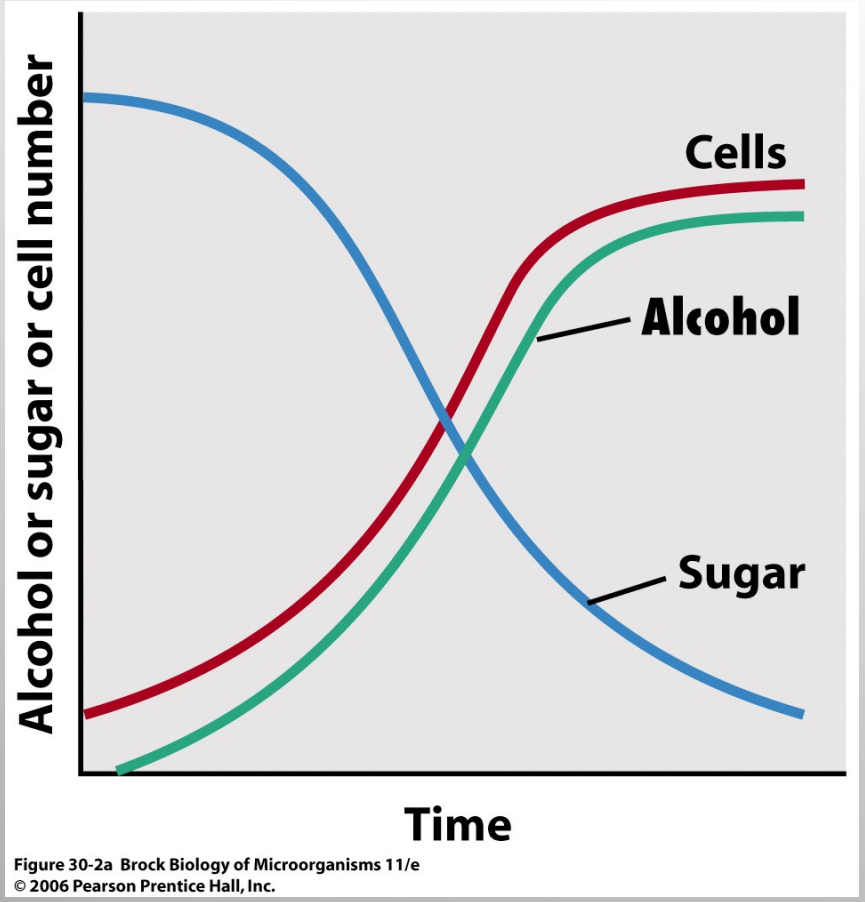
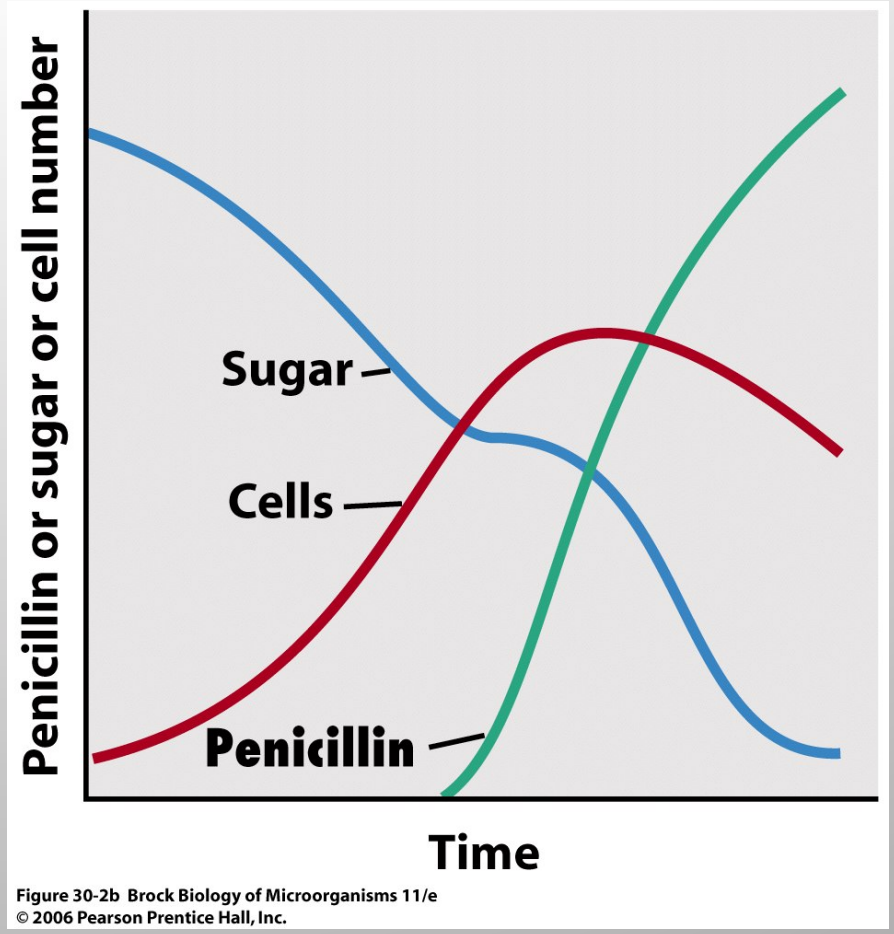


Figure 30-2a Brock Biology of Microorganisms 11/e



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Primary and secondary metabolism

What are antibiotics?

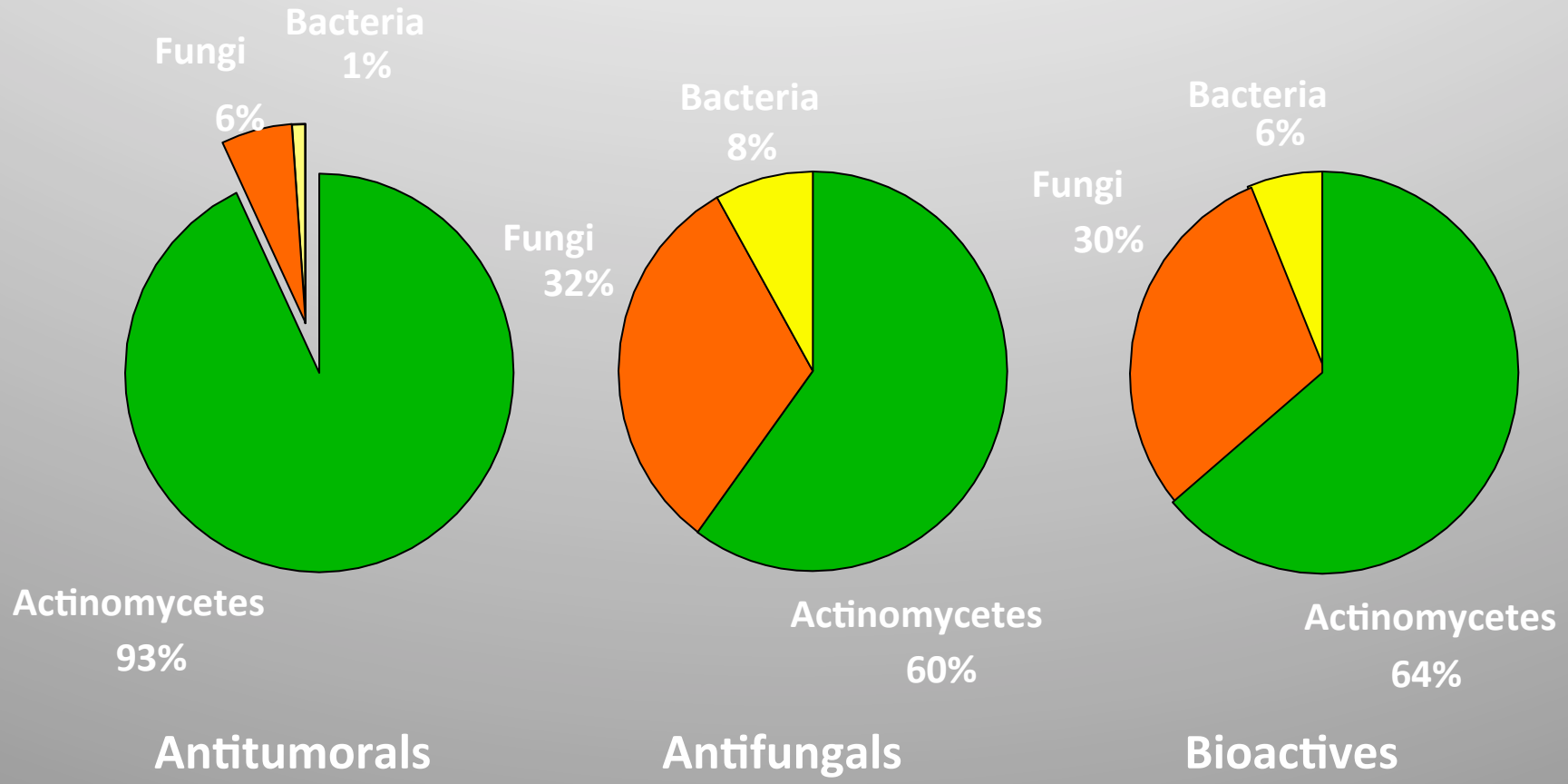
- Secondary metabolites synthesized by some microorganisms
- Any compound able to cause a damaged in a target cell

Who are the main producers

- Bacteria

  Gram positive *Streptomyces*
- Fungi
- Other bacteria

MICROORGANISMS and BIOACTIVE COMPOUNDS



BIOACTIVE COMPOUNDS SYNTHESIZED BY ACTINOMYCETES

ANTIBACTERIALS

Erythromycin
Tetracycline
Gentamicin

ANTIFUNGALS

Amphotericin B
Nystatin

ANTIPARASITICS

Avermectins

ANTITUMORALS

Doxorubicin
Mitramycin
Bleomycin

IMUNOSUPRESSANTS

Rapamycin
FK506

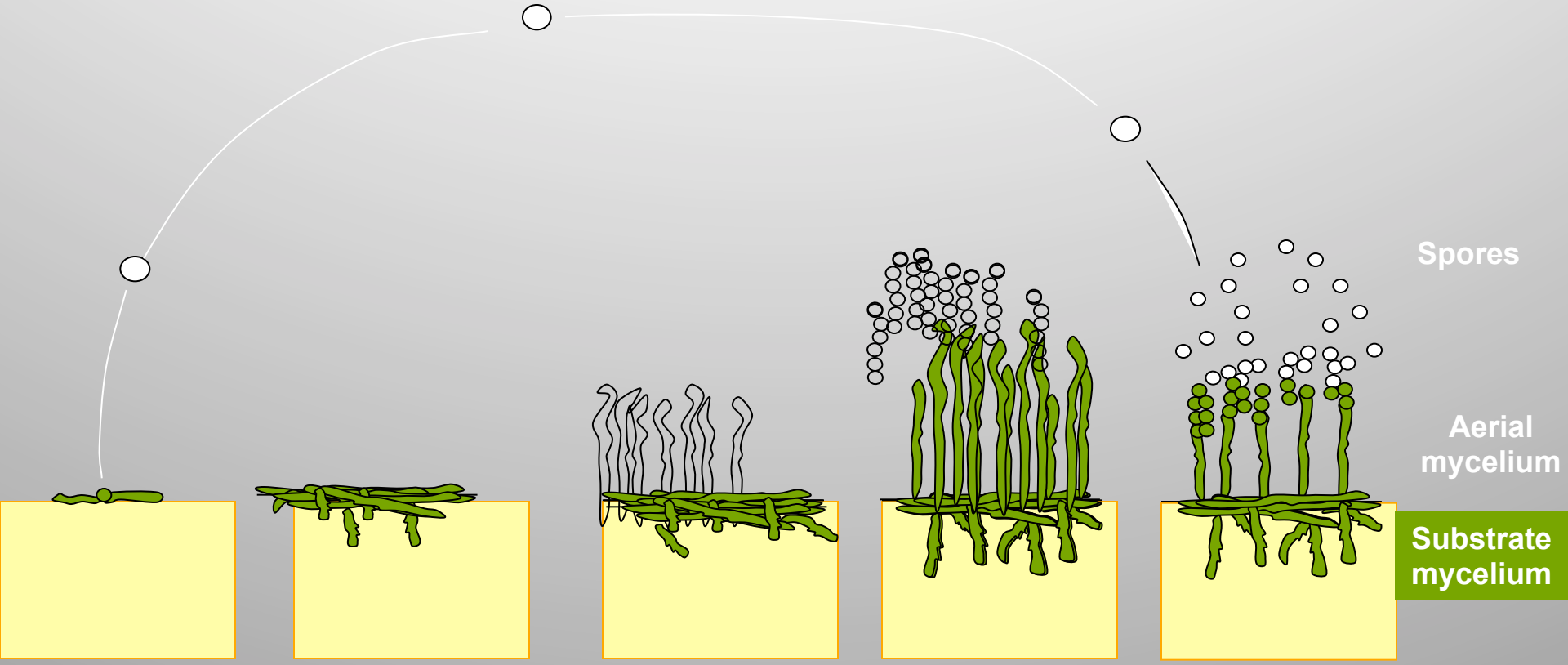
INSETICIDES

Espinosin

HERBICIDES

Bialaphos

LIFE CYCLE OF *Streptomyces*



Production of secondary metabolites

(antibiotics, fungicides, antitumorals,..)

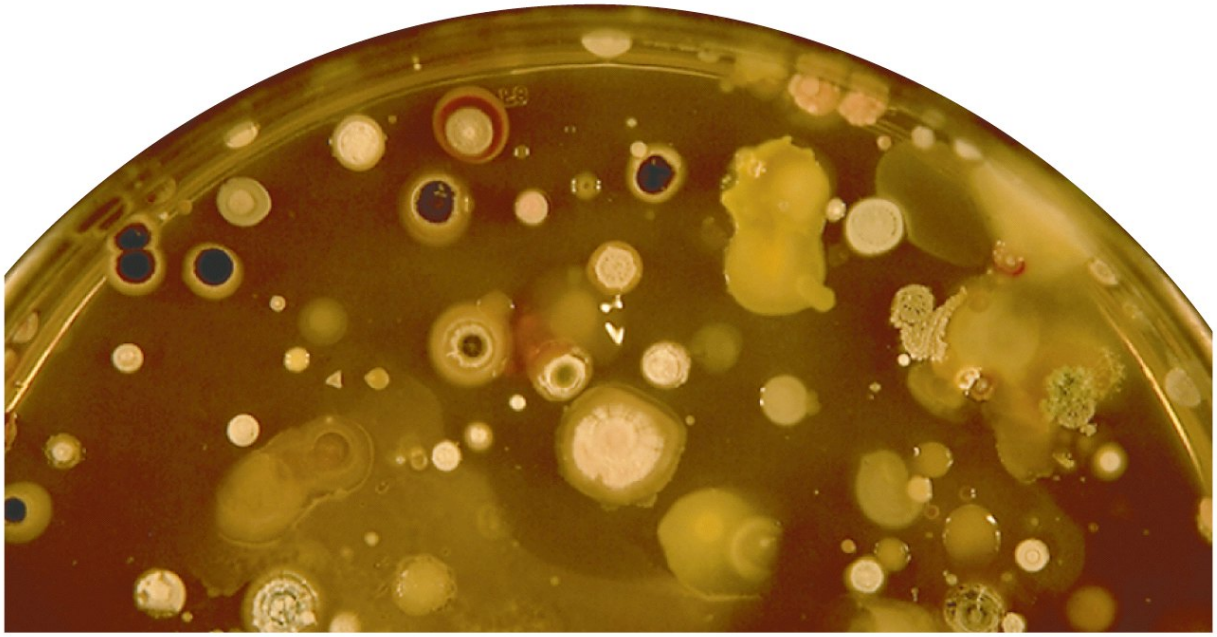


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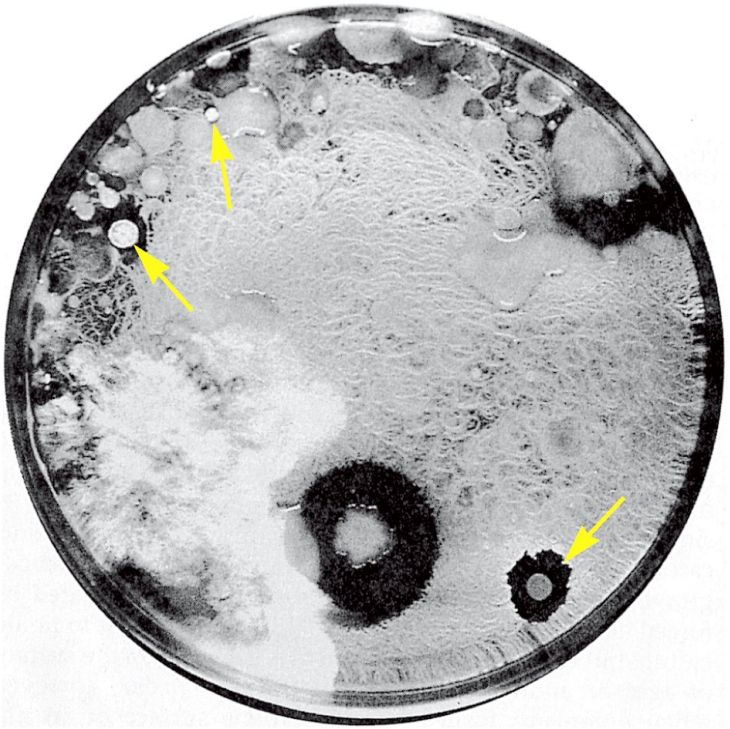
Figure 12-76b Brock Biology of Microorganisms 11/e



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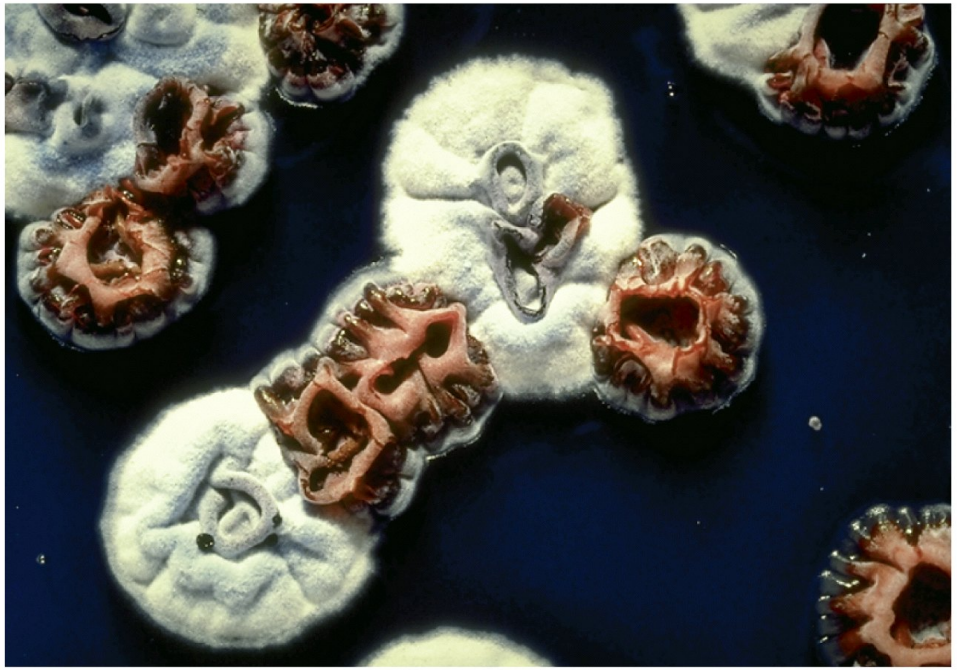

David A. Hopwood

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Biological functions of antibiotics?

- In the producer:

  Activators of morphological differentiation, UV protector, communication

- In the target microorganism:

  Toxicity

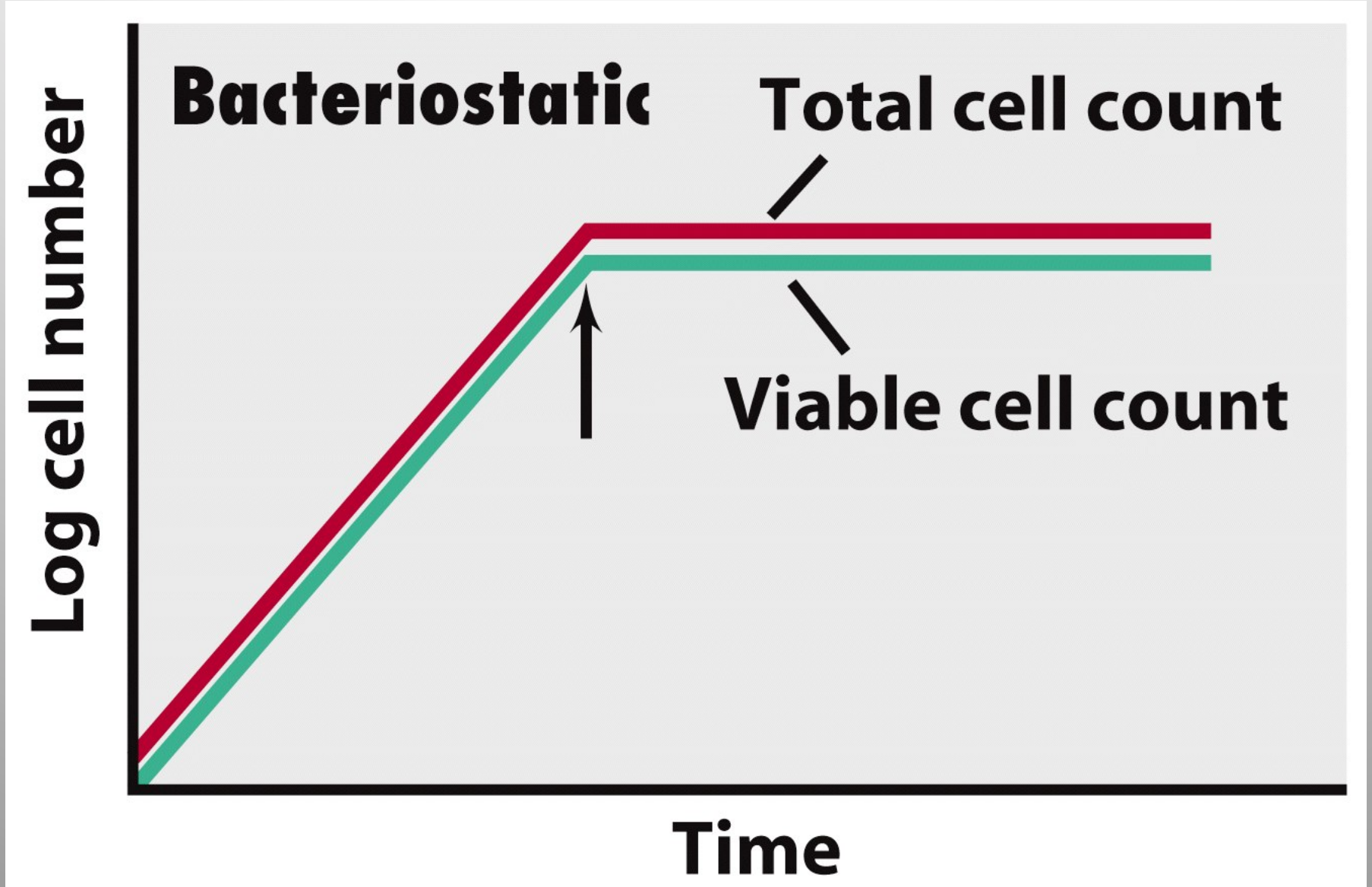


Figure 20-9a Brock Biology of Microorganisms 11/e

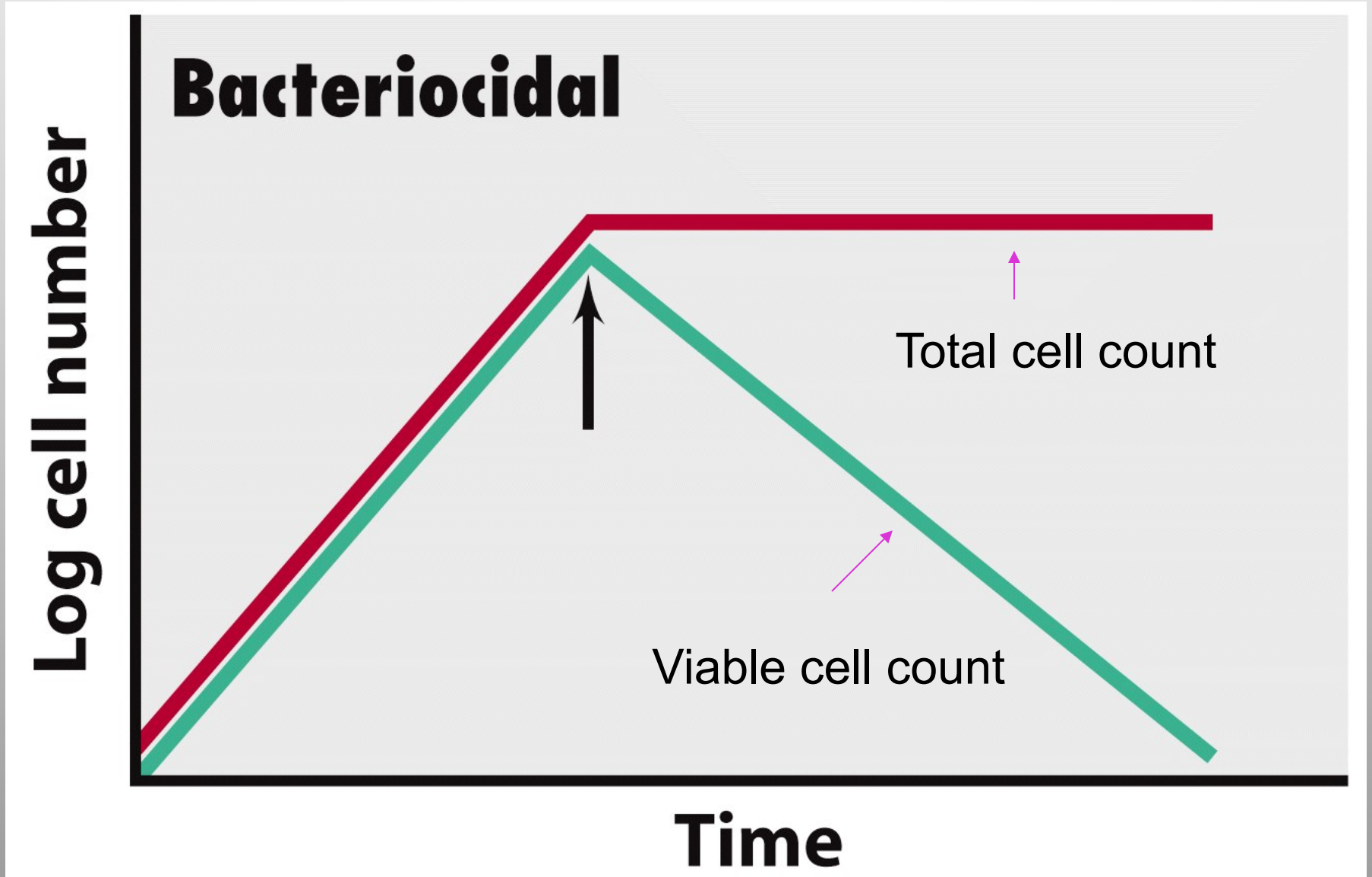


Figure 20-9b Brock Biology of Microorganisms 11/e

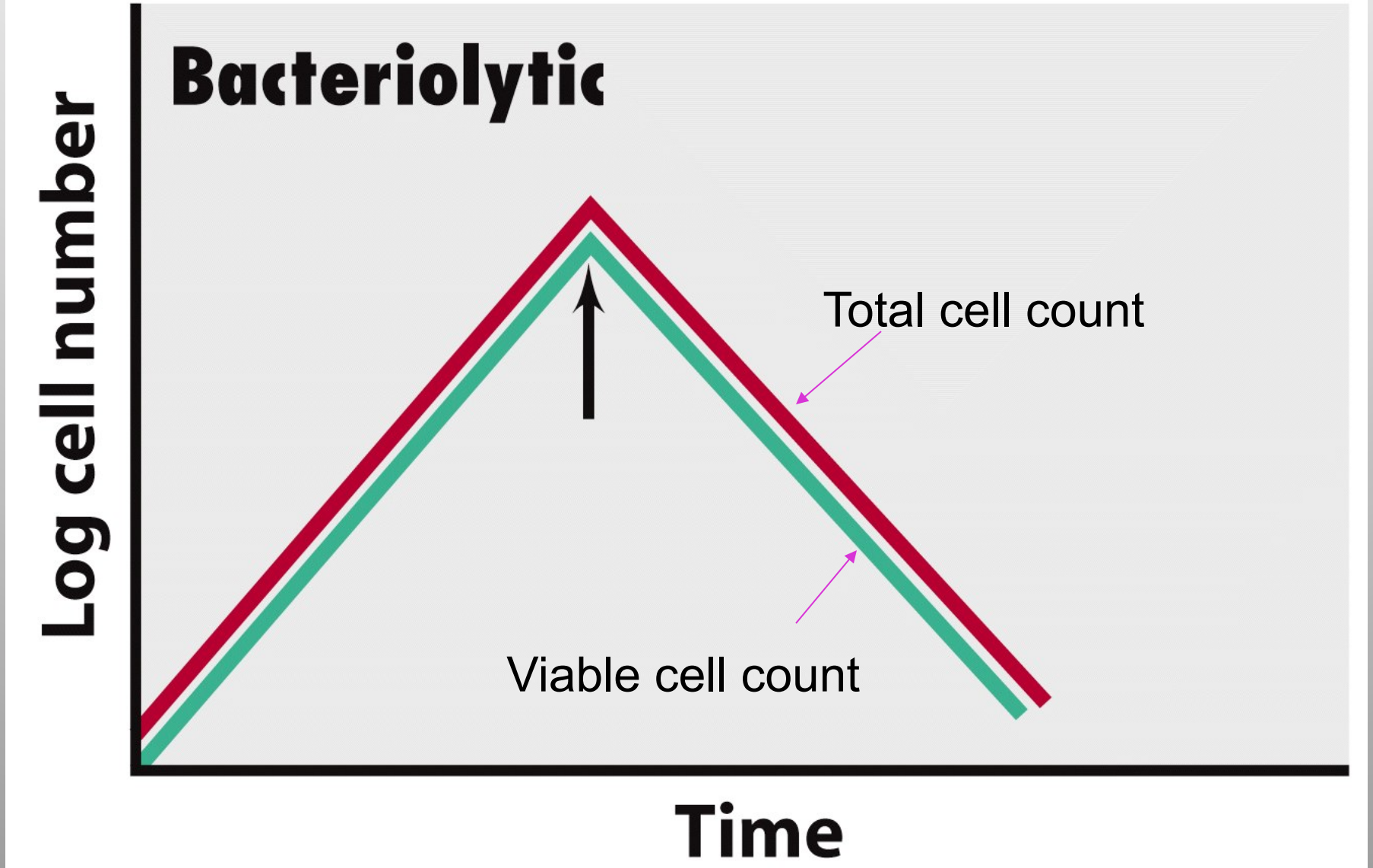


Figure 20-9c Brock Biology of Microorganisms 11/e

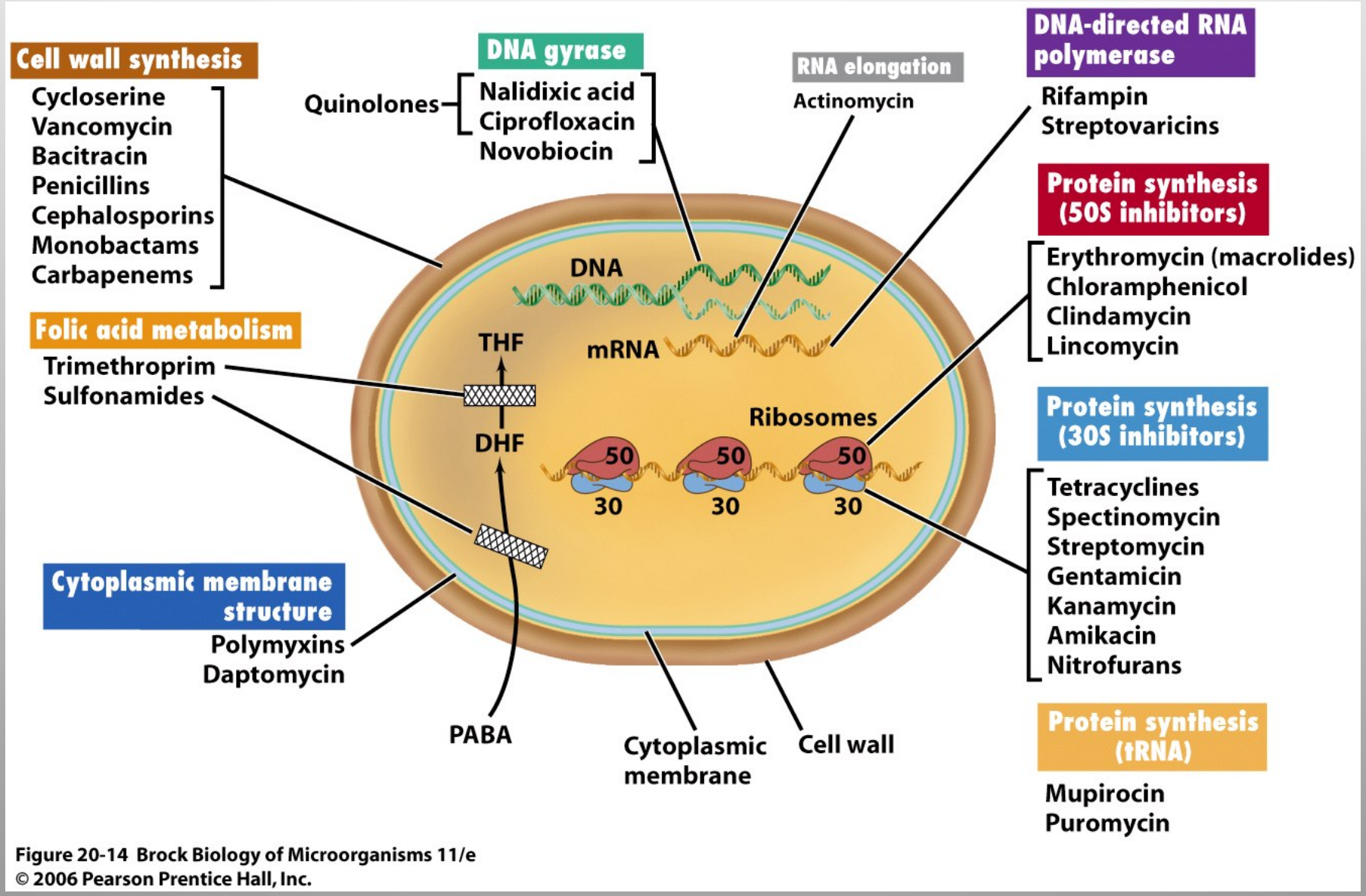


Figure 20-14 Brock Biology of Microorganisms 11/e

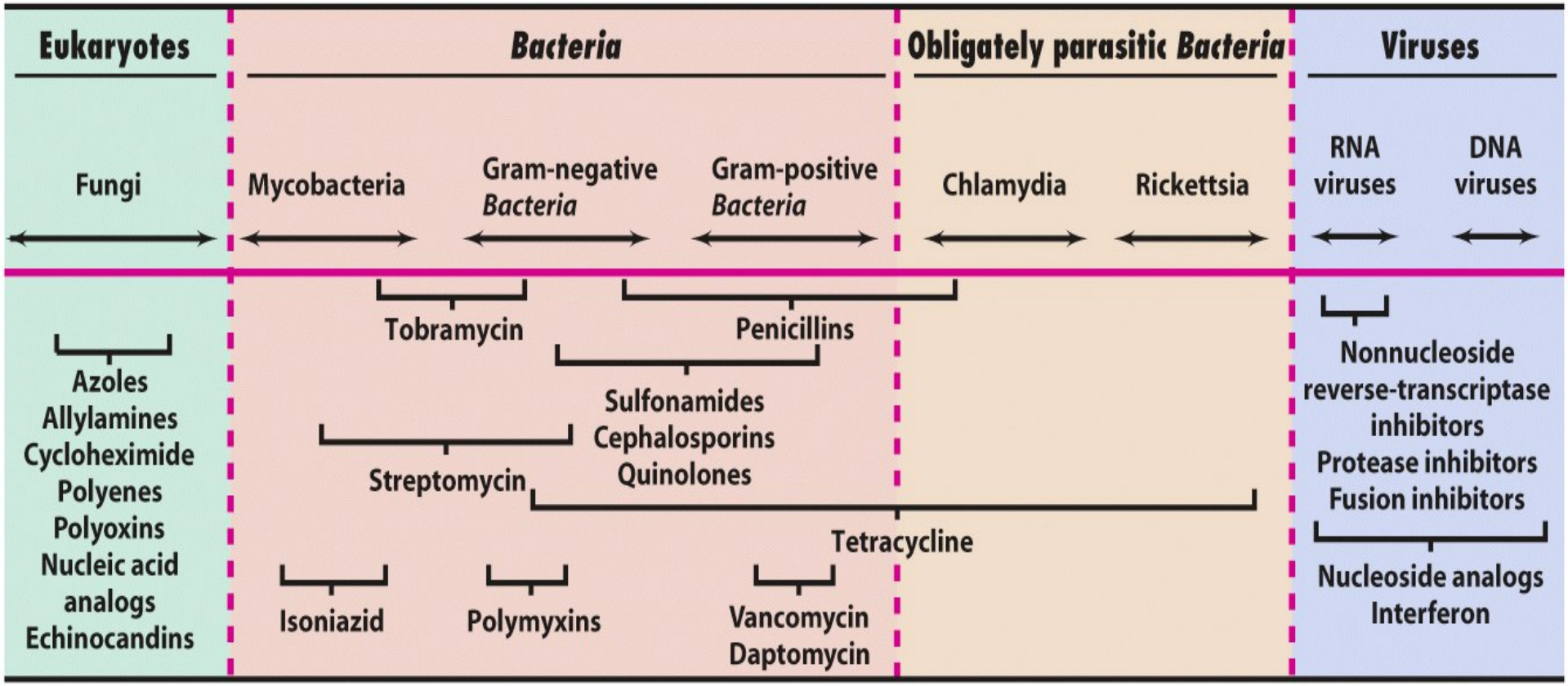


Figure 20-15 Brock Biology of Microorganisms 11/e

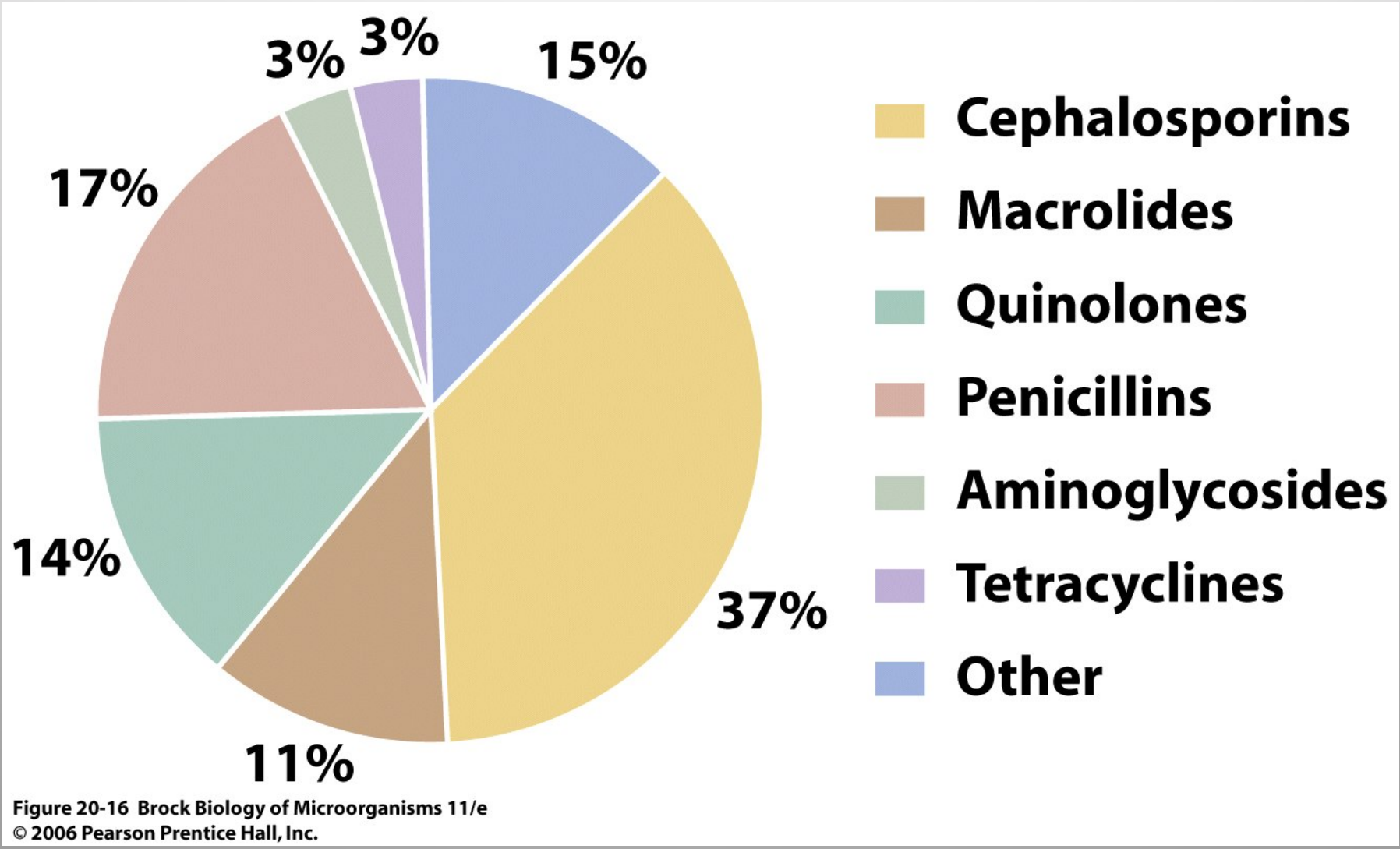


Figure 20-16 Brock Biology of Microorganisms 11/e

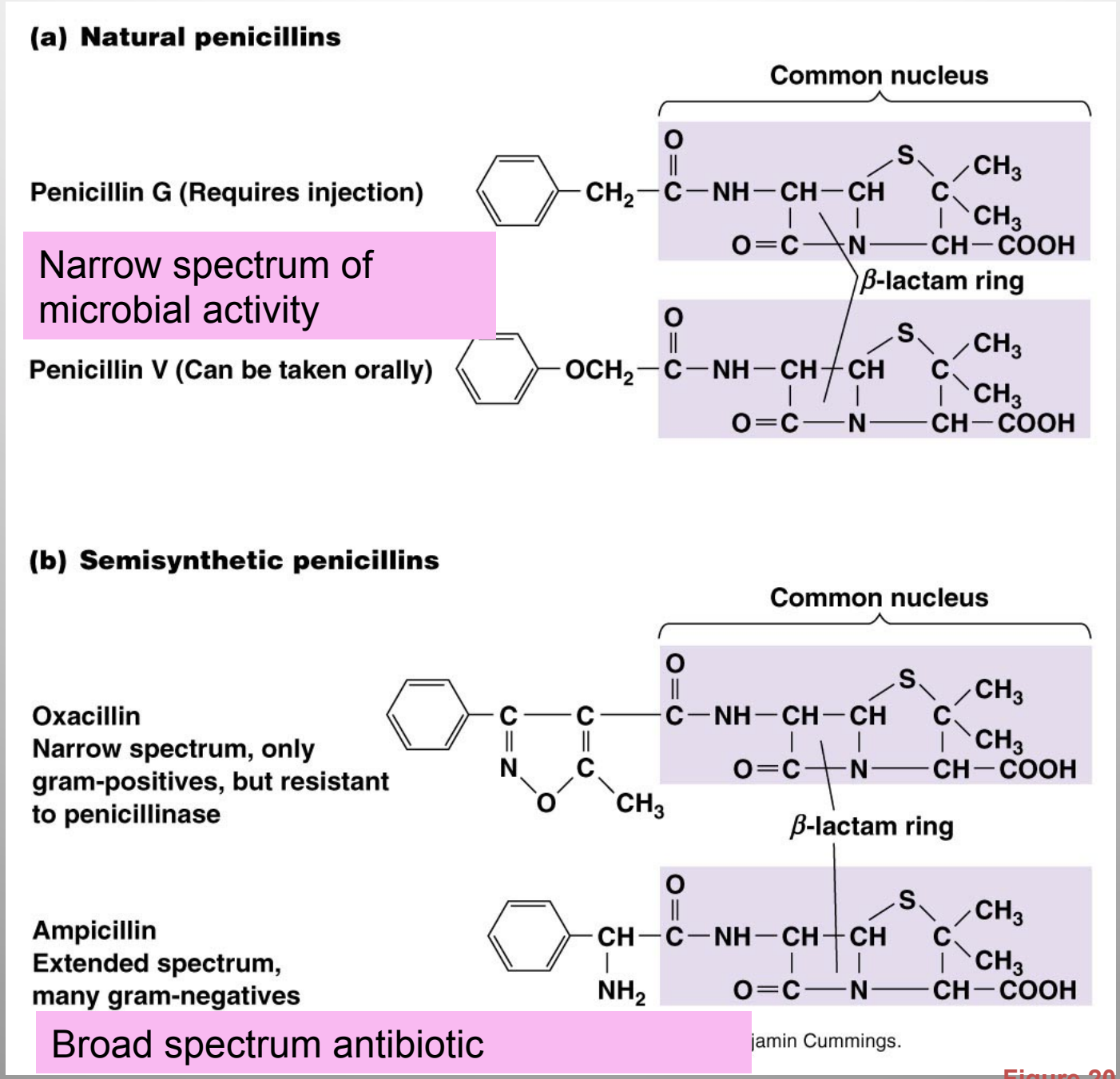


Figure 20.6 - Overview

Structure of peptidoglycan

glycan tetrapeptide

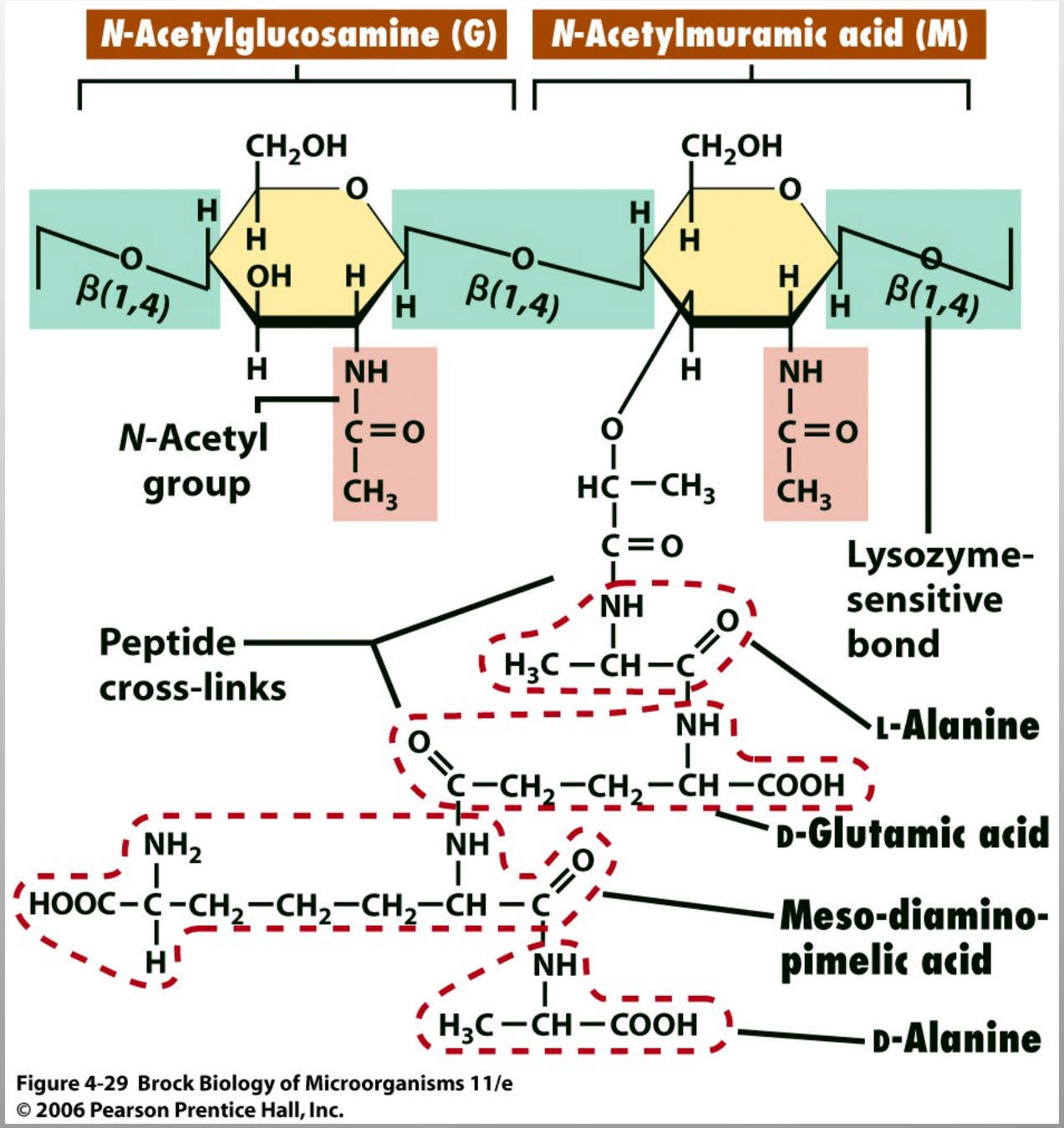


Figure 4-29 Brock Biology of Microorganisms 11/e

Peptidoglycan sheet in *Escherichia coli* and *Staphylococcus aureus*

Glycine interbridge in *S. aureus*

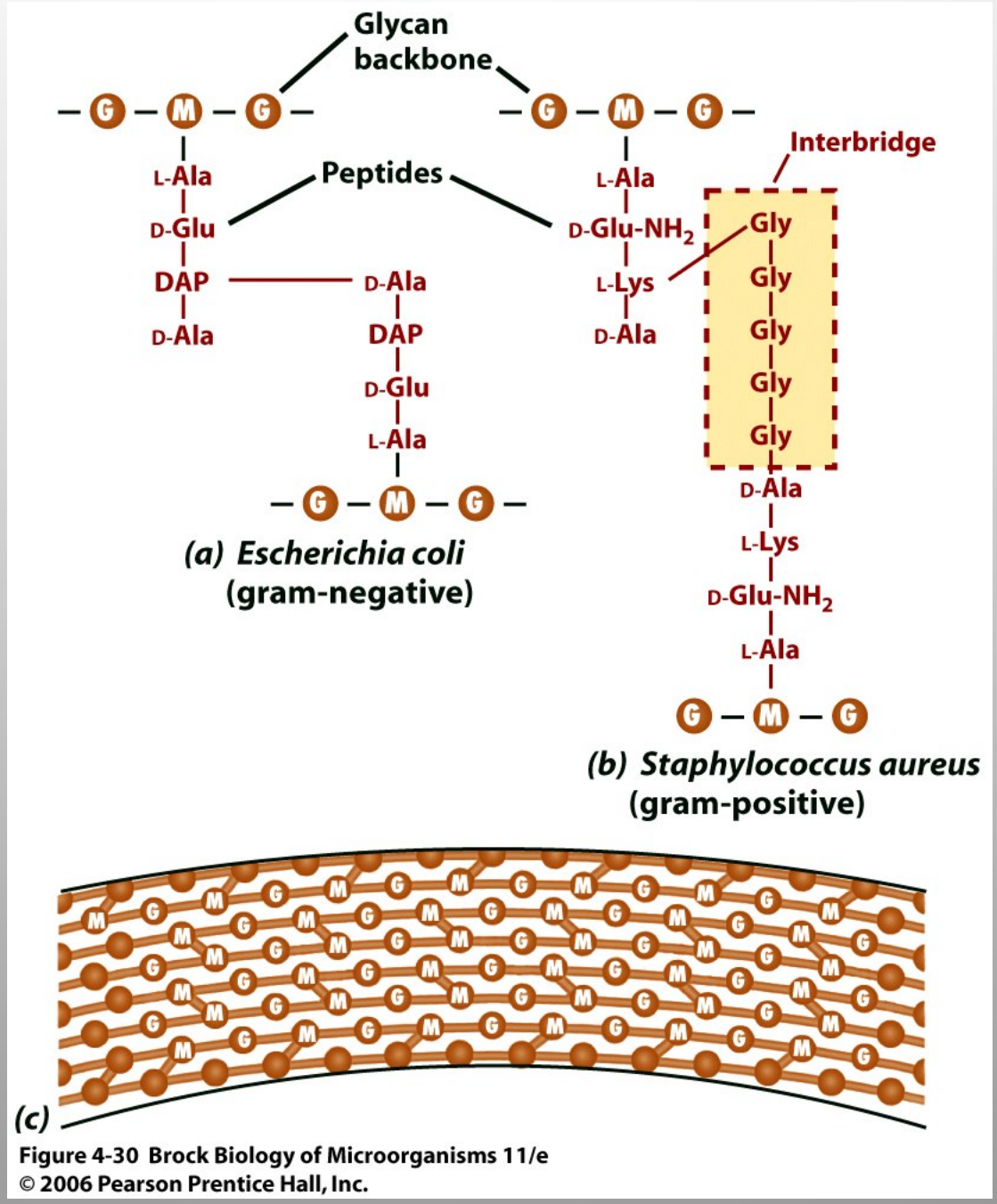
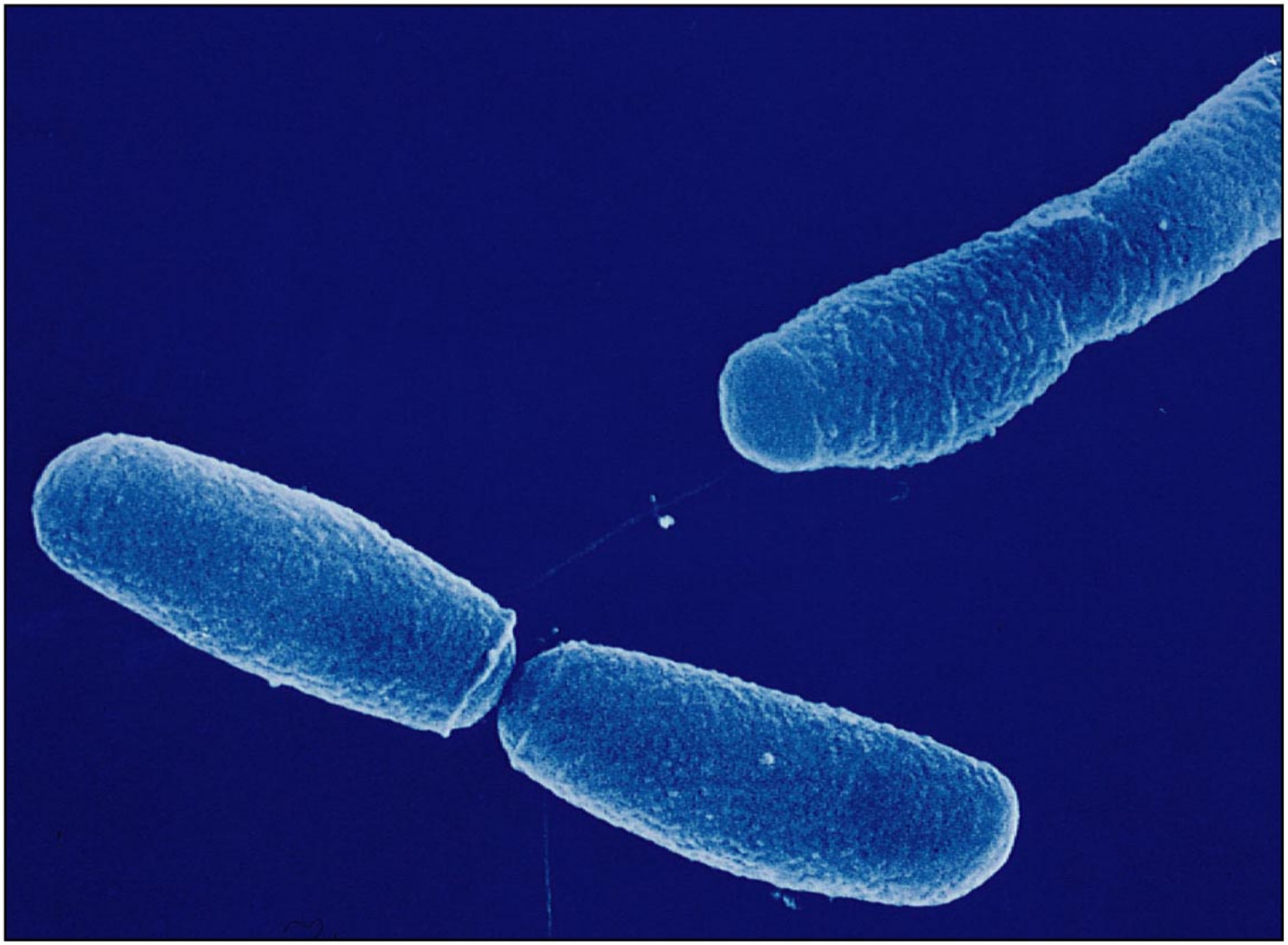
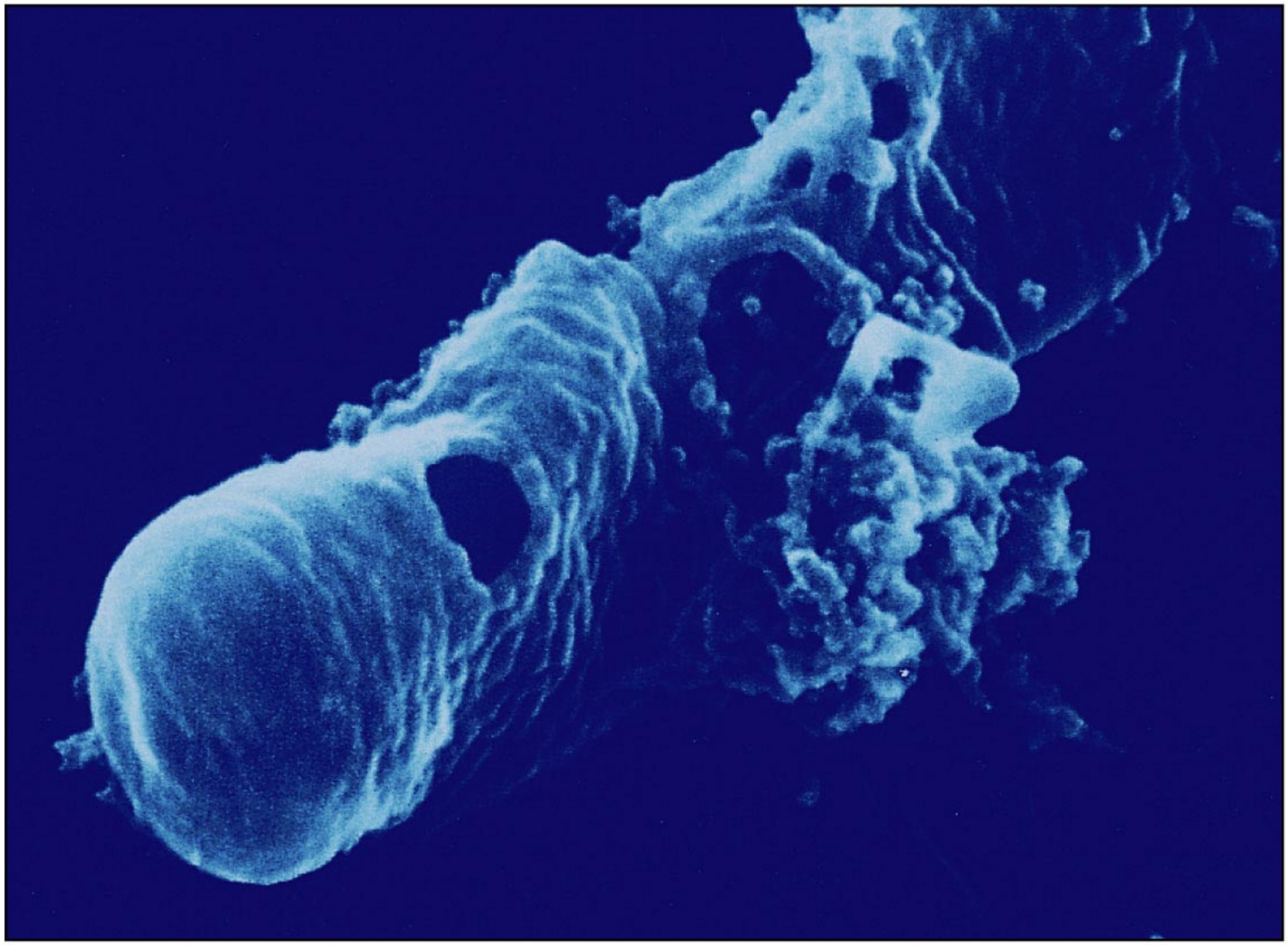


Figure 4-30 Brock Biology of Microorganisms 11/e



(a) Rod-shaped bacterium before penicillin. SEM 1 μm

Figure 20.3a



(b) The bacterial cell is lysing as penicillin weakens the cell wall.

SEM

1 μm

Figure 20.3b

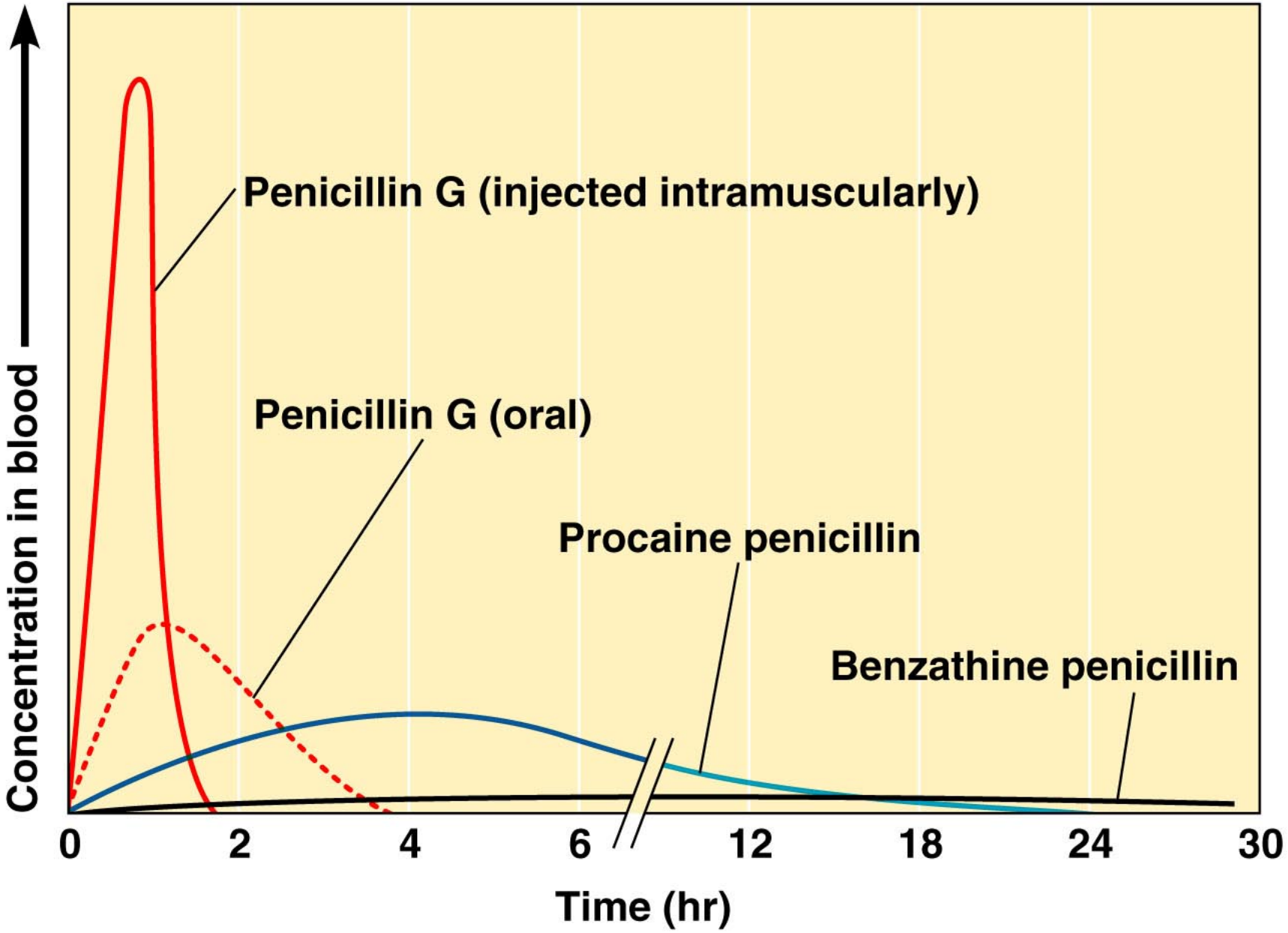
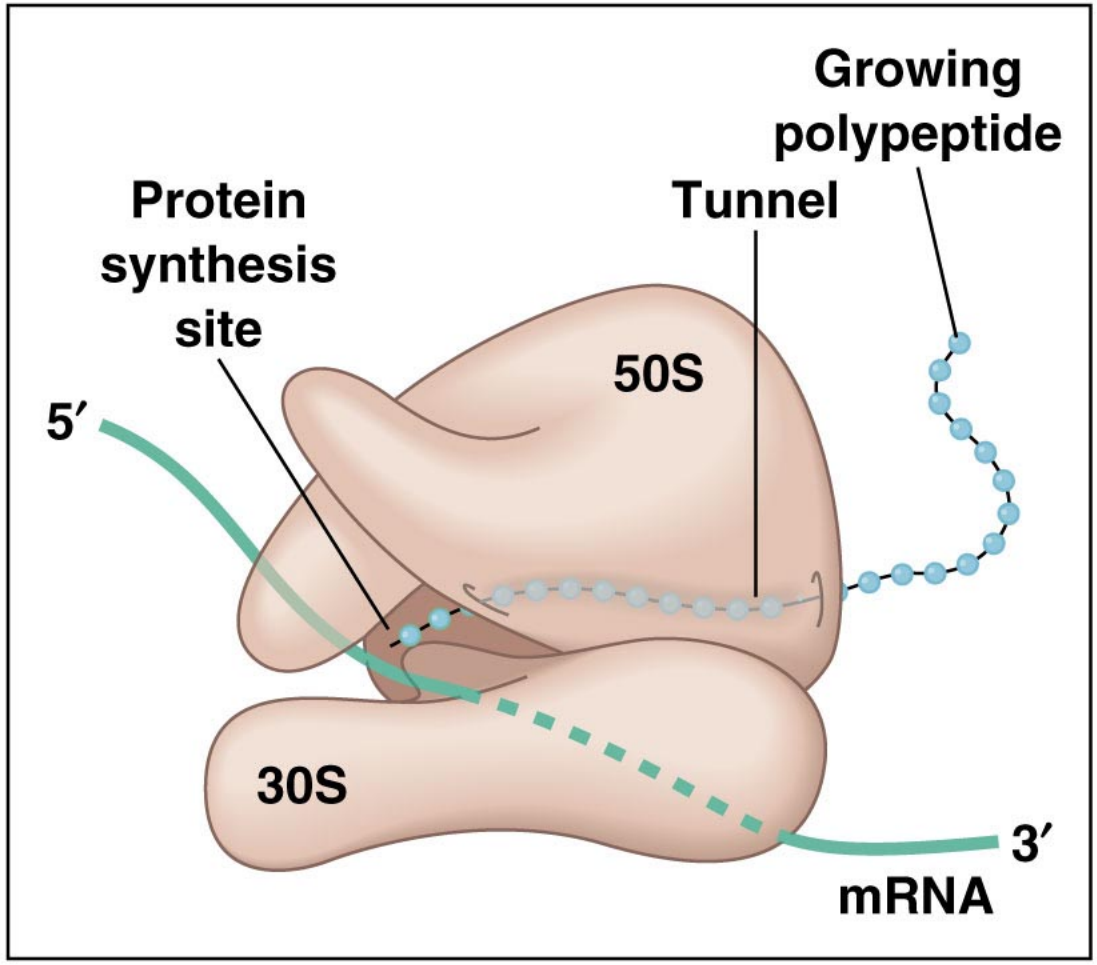
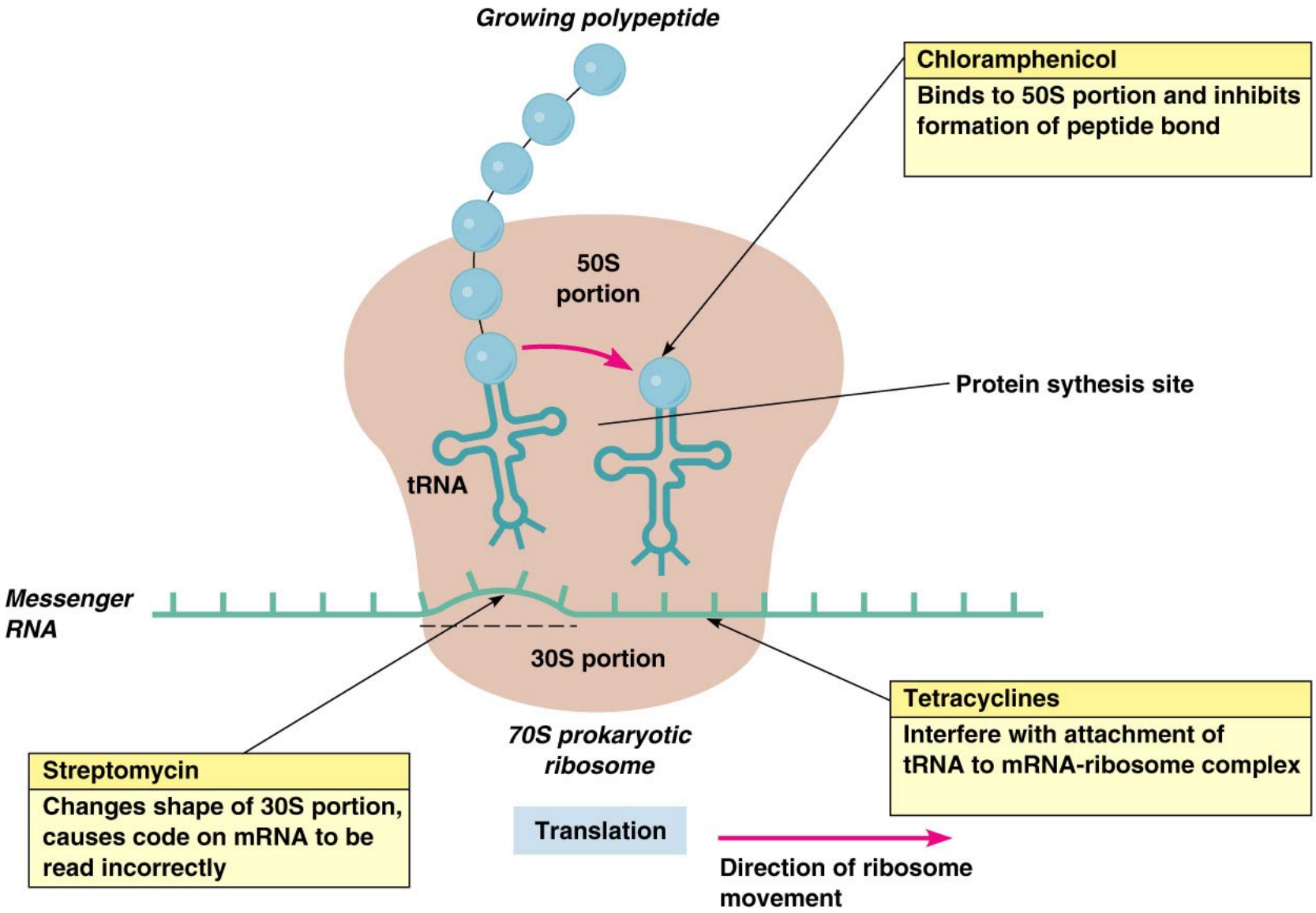


Figure 20.7



(a) Three-dimensional detail of the protein synthesis site showing the 30S and 50S subunit portions of the 70S prokaryotic ribosome.

Figure 20.4a



(b) In the diagram the black arrows indicate the different points at which chloramphenicol, the tetracyclines, and streptomycin exert their activities.

Figure 20.4b

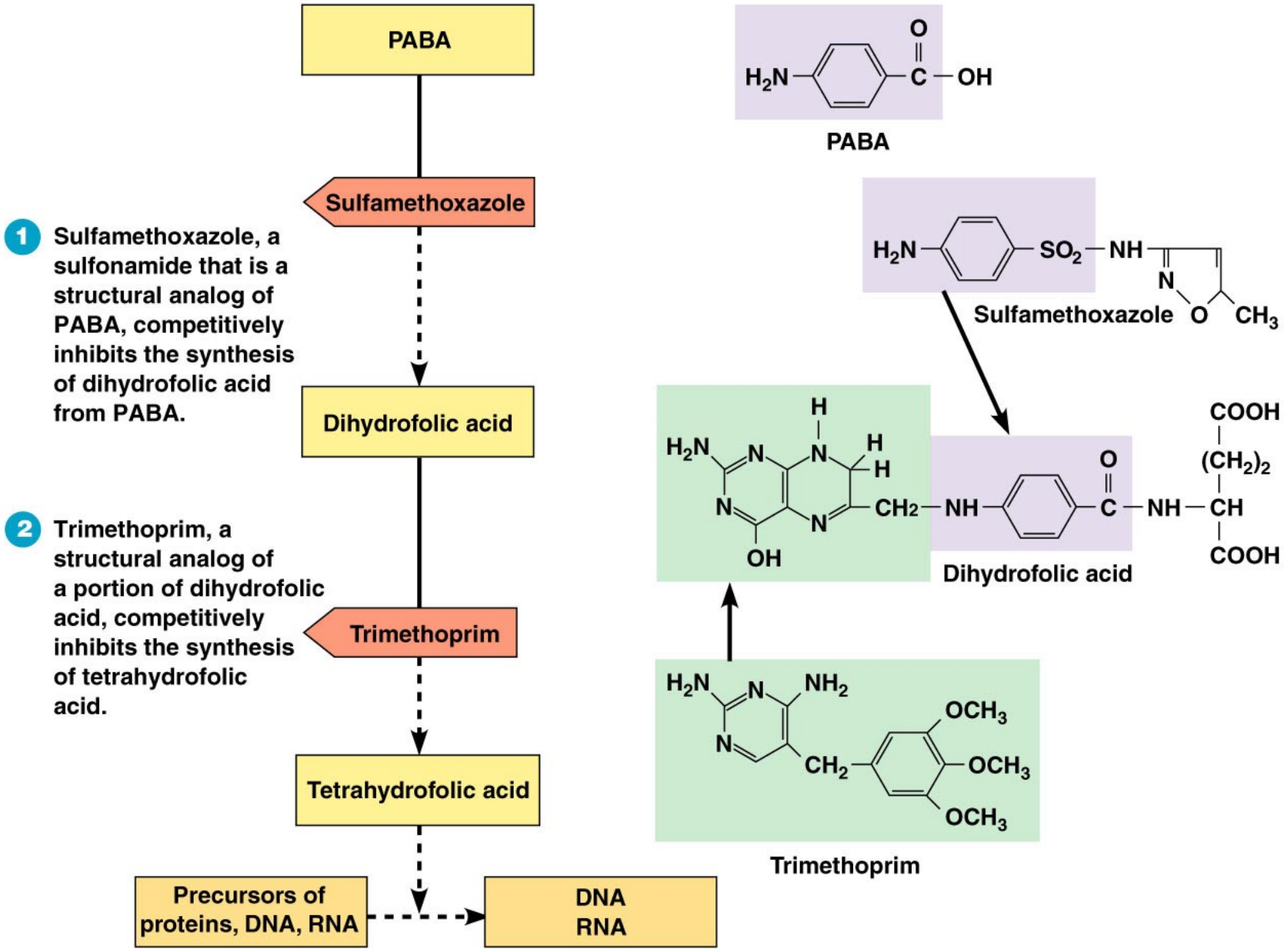


Figure 20.13 - Overview

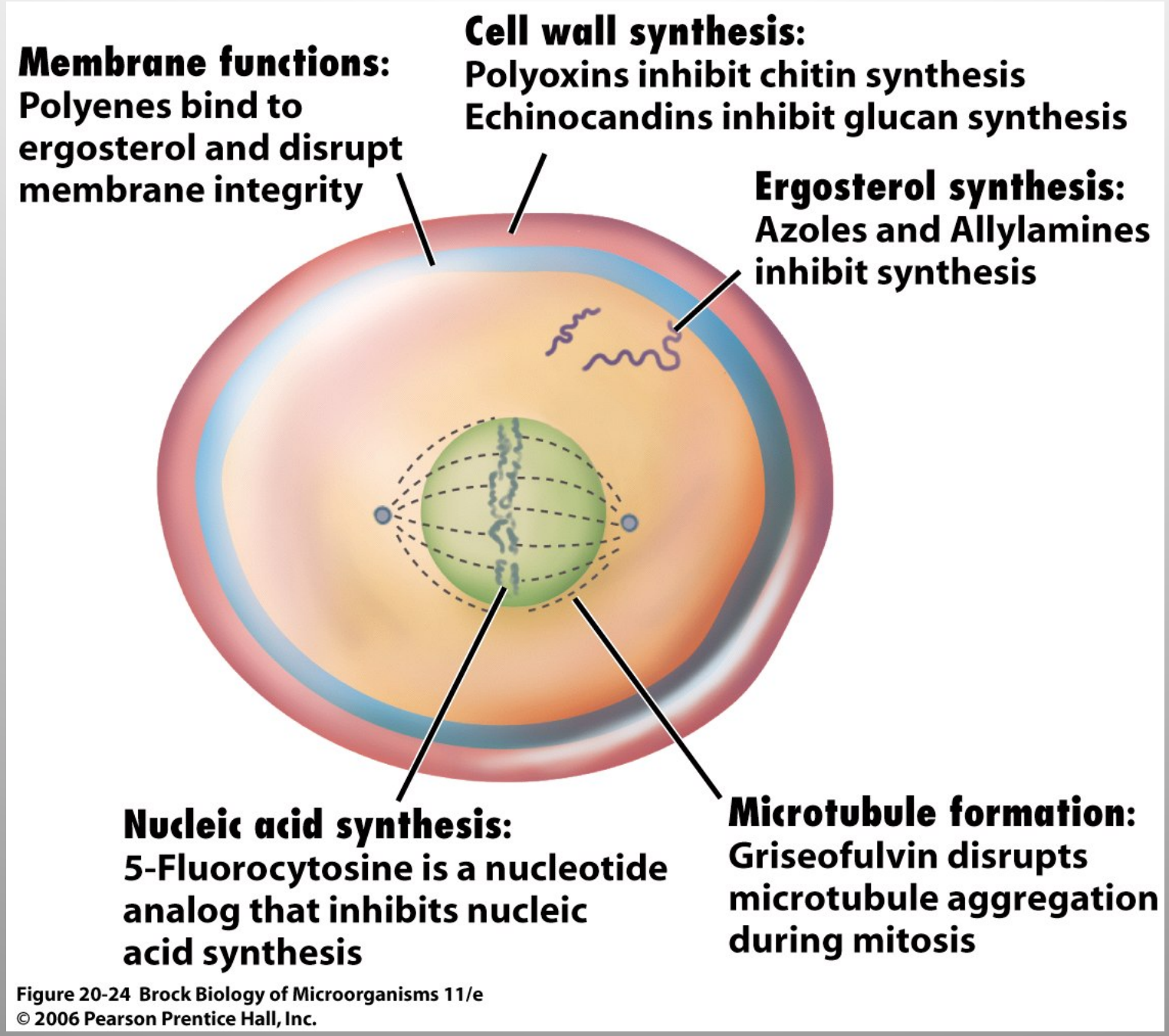
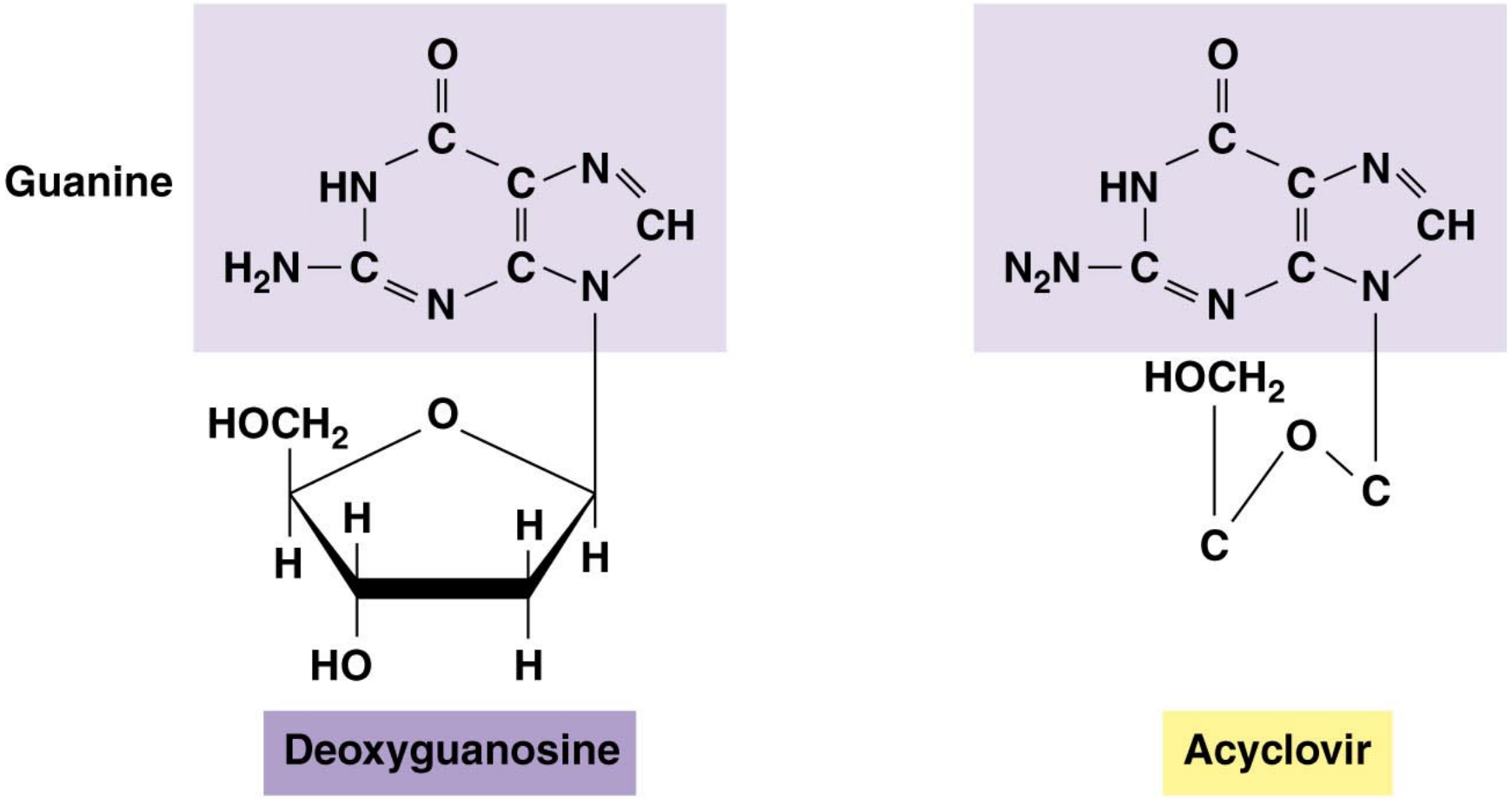


Figure 20-24 Brock Biology of Microorganisms 11/e

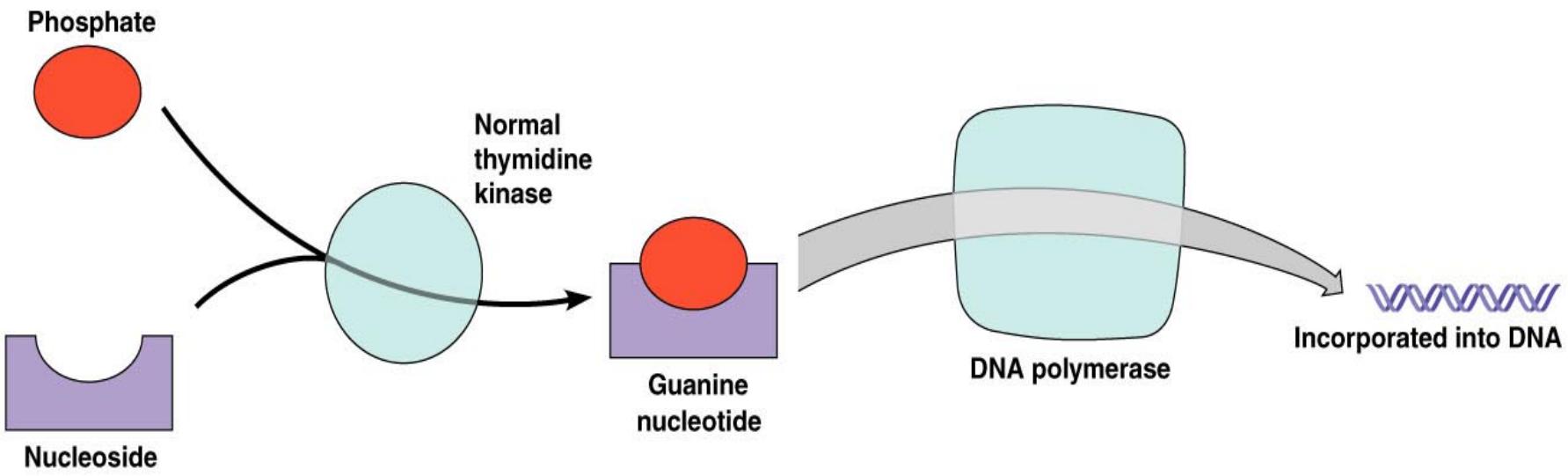
Injury of plasma membrane of a yeast caused by antifungal drug

Figure 20.5



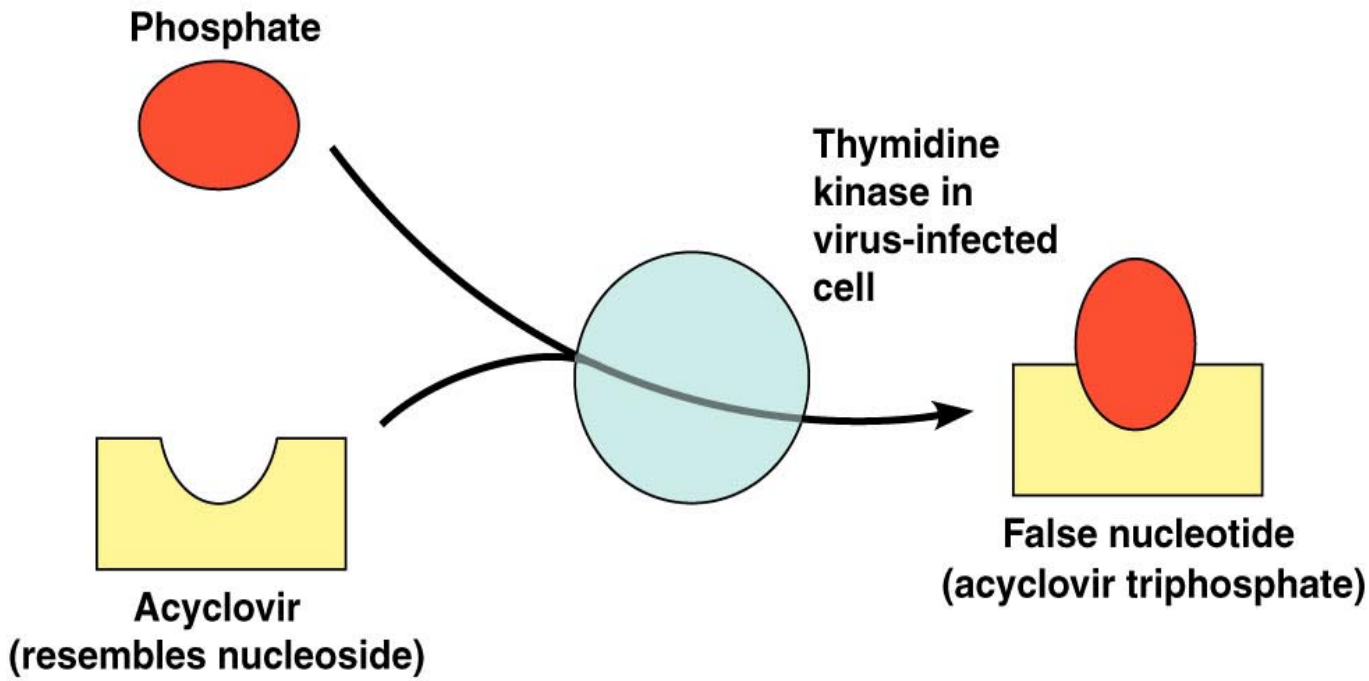
(a) Acyclovir structurally resembles the nucleoside deoxyguanosine.

Figure 20.16a



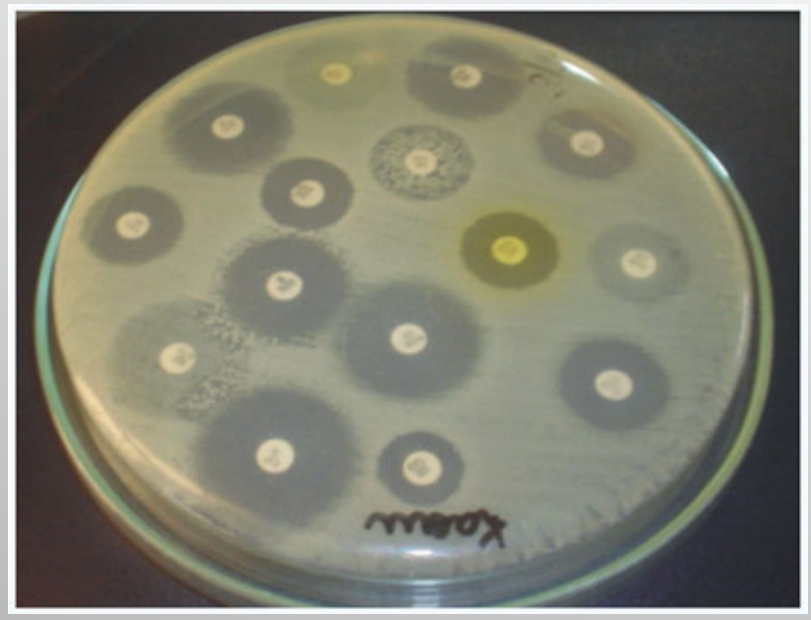
(b) The enzyme thymidine kinase combines phosphates with nucleosides to form nucleotides, which are then incorporated into DNA.

Figure 20.16b



(c) Acyclovir has no effect on a cell not infected by a virus, that is, with normal thymidine kinase. In a virally infected cell, the thymidine kinase is altered and converts the acyclovir (which resembles the nucleoside deoxyguanosine) into a false nucleotide—which blocks DNA synthesis by DNA polymerase.

Figure 20.16c



DEFINICIÓN

- Prueba in vitro que determina la sensibilidad de un microorganismo frente a diferentes antibióticos.

SENSIBLE

RESISTENTE