CHAPTER 18 LECTURE SLIDES

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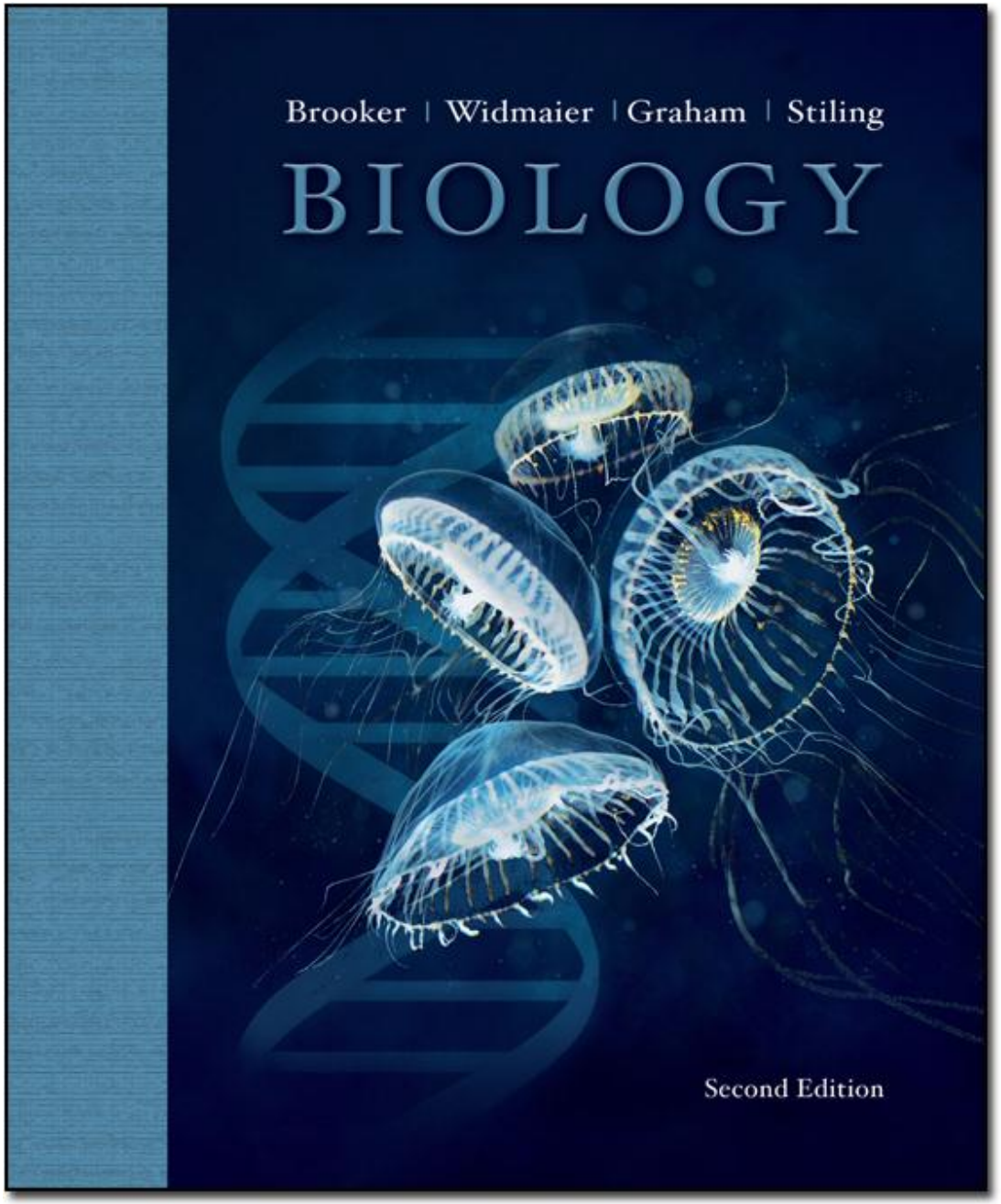

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Learning Objectives

18.1 Genetic Properties of Viruses

- Describe the different structures found in viruses.
- Understand the basic mechanism of viral replication.
- Compare and contrast a lytic viral reproductive cycle with a lysogenic viral reproductive cycle.
- Describe how viruses can contribute DNA to their hosts.
- Explain how the HIV virus compromises the immune system.
- Describe the disease AIDS.
- Describe potential sources of drug activity against HIV, and explain why common drug treatments lose their efficiency over time.

Learning Objectives

18.3 Genetic Properties of Bacteria

- Outline the key features of bacterial chromosome.
- Describe bacterial plasmids and list their functions.

Learning Objectives

18.4 Gene transfer Between Bacteria

- Distinguish the various methods of genetic transfer in bacteria.
- Describe how gene transfer contributes to the spread of antibiotic resistance.

Viral genetics

- Viruses and viroids are nonliving particles with nucleic acid genomes that require the assistance of living cells to reproduce
- Tobacco Mosaic Virus (TMV) first virus discovered

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Viruses

- Small infectious particle that consists of nucleic acid enclosed in a protein coat
- Over 4,000 different types
- Vary greatly in their characteristics, including their host range, structure, and genome composition

Differences

- Host range
  - Number of species and cell types that can be infected
- Structural
  - All viruses have a capsid (protein coat) but it varies in shape and complexity
  - Some have viral envelope derived from host cell plasma membrane
- Genome
  - DNA vs. RNA, Single stranded (ss) vs. Double stranded (ds), linear vs. circular

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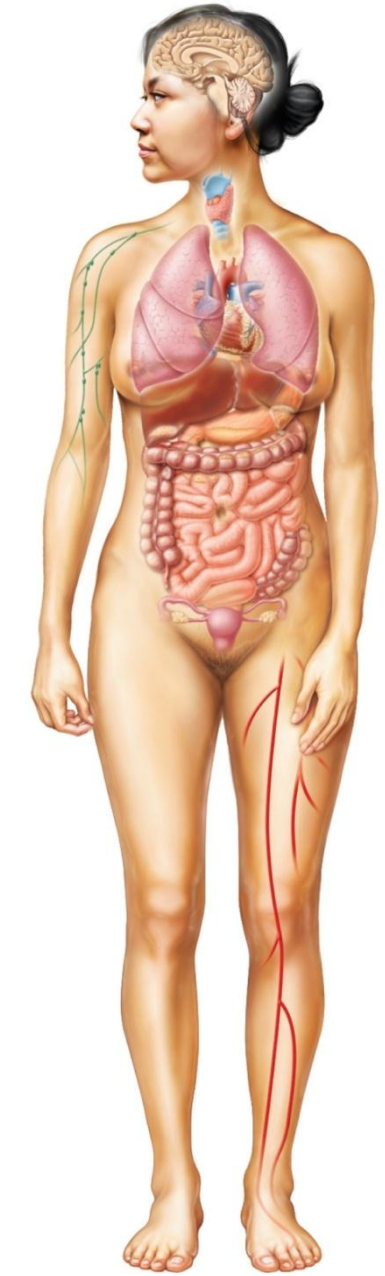

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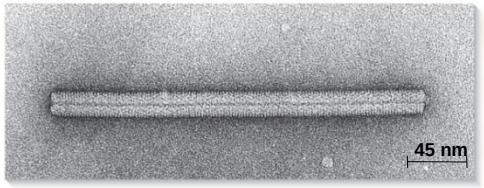
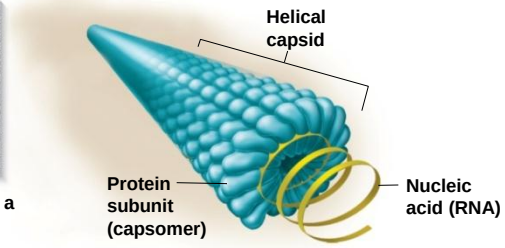
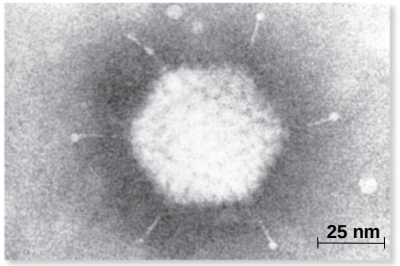
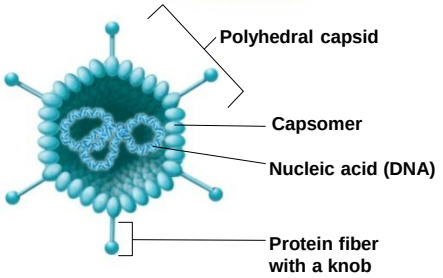


(a) Tobacco mosaic virus, a nonenveloped virus with a helical capsid

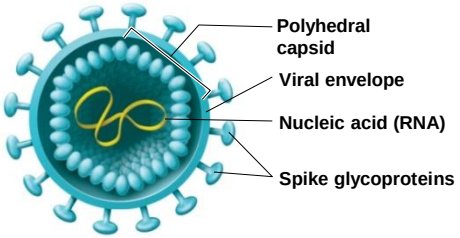




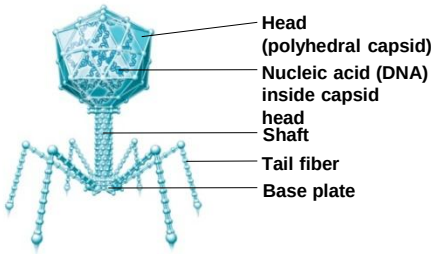
(b) Adenovirus, a nonenveloped virus with a polyhedral capsid and protein fibers with a knob



(c) Influenza virus, an enveloped virus with spikes



(d) T4, a bacteriophage



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- Viruses are not alive
  - Not cells or composed of cells
  - Cannot carry out metabolism on their own
- Viral reproductive cycle can be quite different among types of viruses and one virus may have alternative cycles

Basic steps

1. Attachment
2. Entry
3. Integration
4. Synthesis of viral components
5. Viral assembly
6. Release

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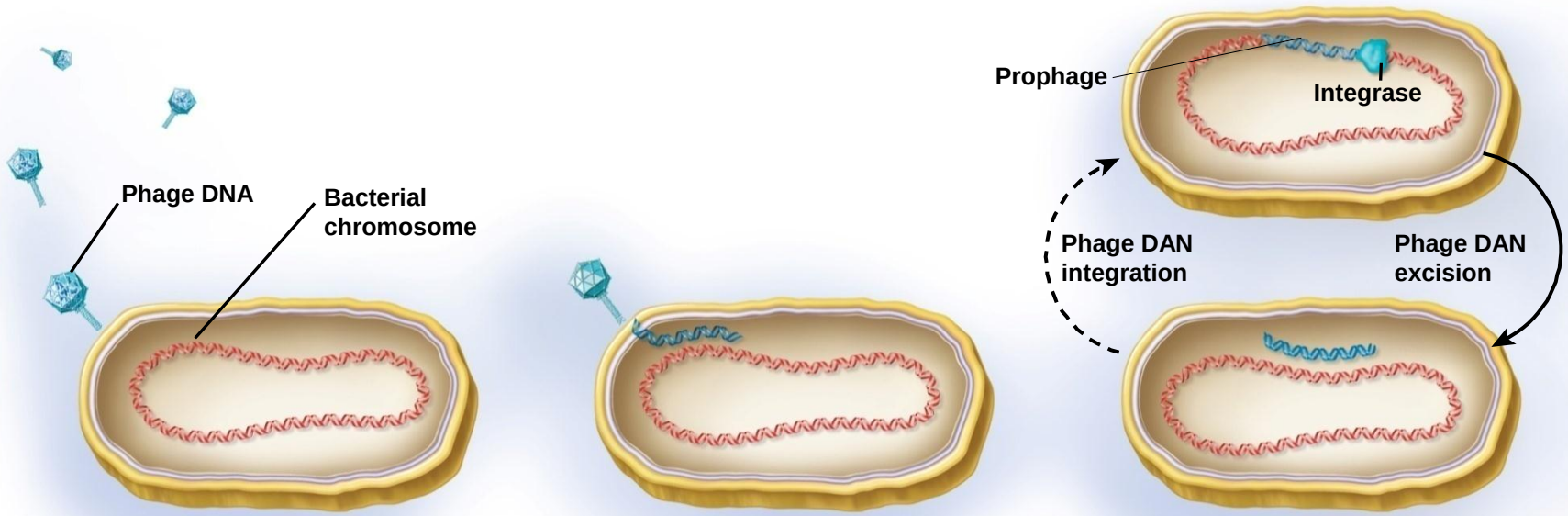

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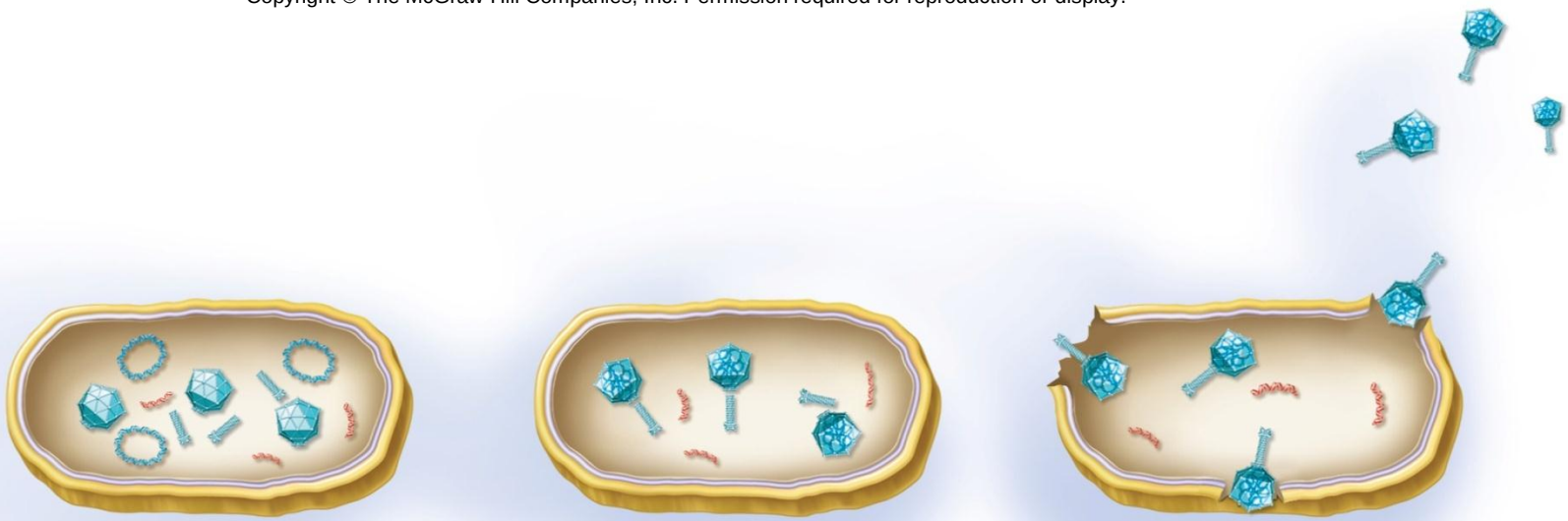

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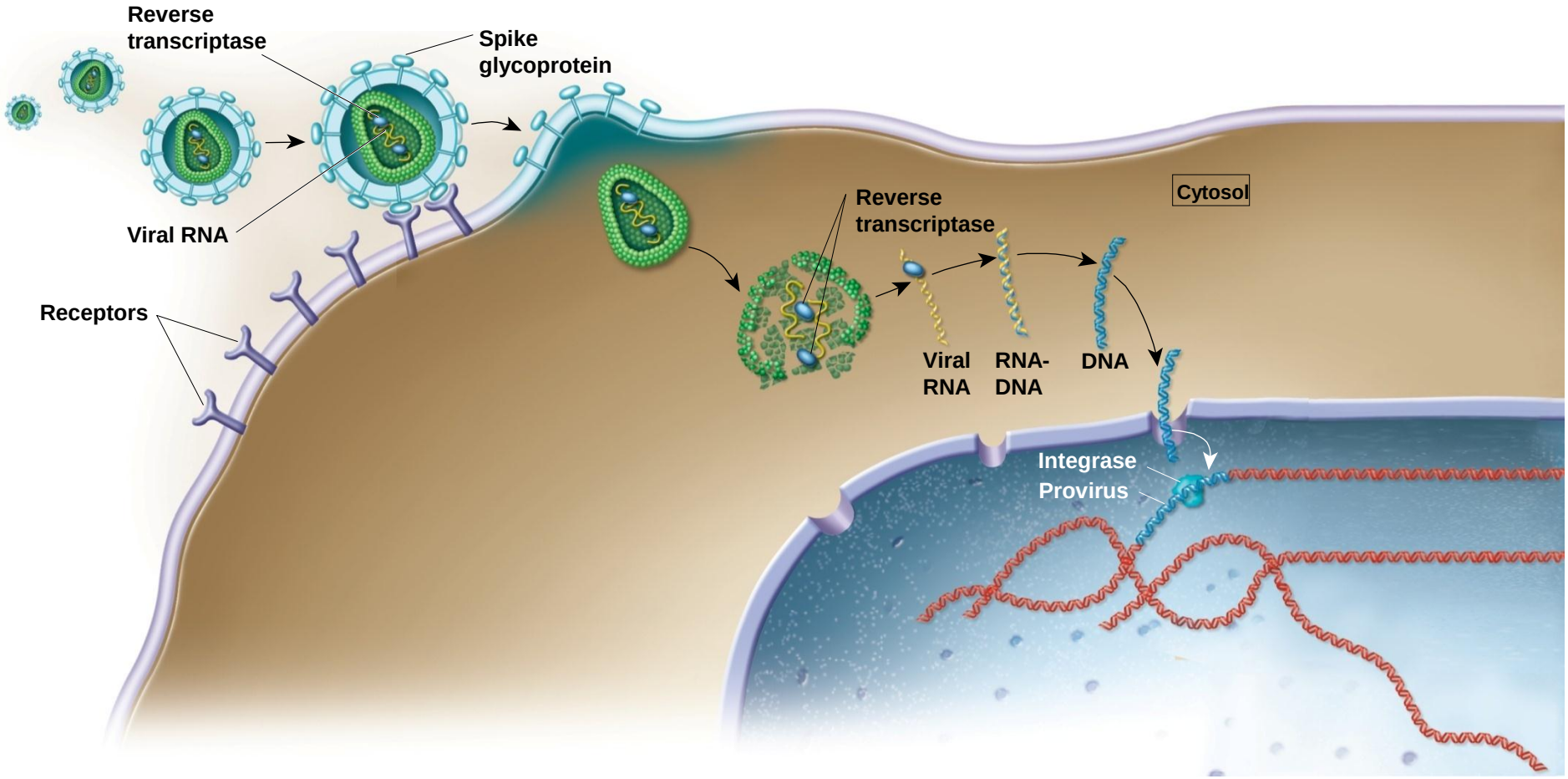

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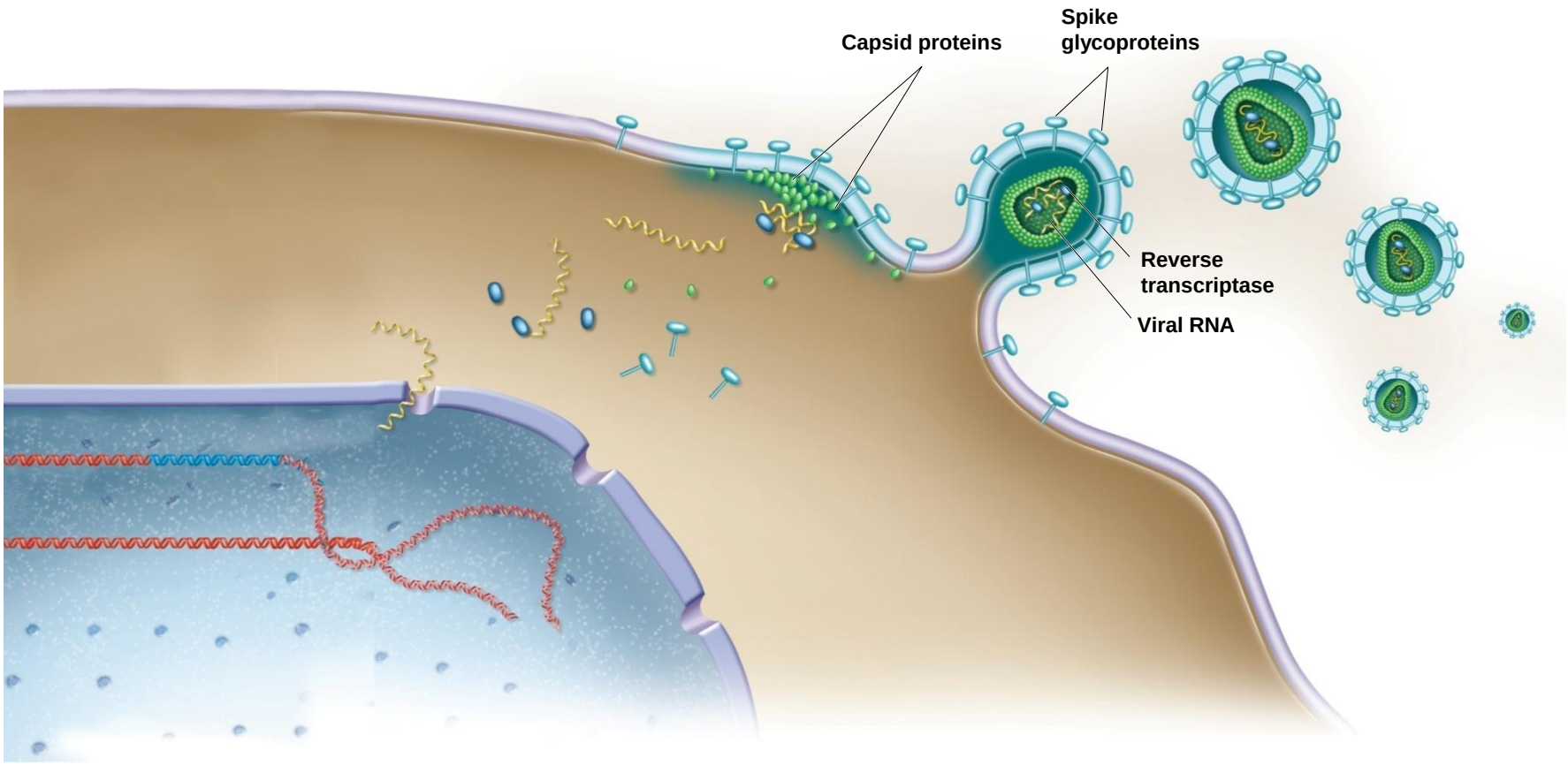

Attachment and Entry

- Attachment
  - Usually specific for one kind of cell due to binding to specific molecules on cell surface
- Entry
  - Bacteriophages or phage, injects only DNA into bacteria
  - HIV fuses with host membrane and the entire virus enters
  - One or several viral genes are expressed immediately
  - Virus may proceed to synthesis of viral components OR integrate into host chromosome

Integration

- Viral gene for integrase
- Integrase cuts host chromosomal DNA and inserts viral genome
- Phage in bacterial DNA called prophage
  - May excise later and proceed to synthesis
- HIV is an RNA virus
  - Uses viral reverse transcriptase to make complementary DNA strand that will be template for double stranded viral DNA
  - Integrates as a provirus

Synthesis of viral components

- Host cell enzymes such as DNA polymerase make many copies of the phage DNA and transcribe the genes within these copies into mRNA
- In the case of HIV, the DNA provirus is not excised from the host chromosome. Instead, it is transcribed in the nucleus to produce many copies of viral RNA
  - Translated to make viral proteins
  - Serve as genome for new viral particles

Viral assembly

- Some viruses self-assemble
- Other are too complicated to self-assemble
- Proteins modify capsid proteins or serve as scaffolding

Release

- Phages must lyse their host cell to escape
- Enveloped viruses bud from the host cell

Latency in bacteriophages

- Some viruses can integrate their genomes into a host chromosome
- Prophage or provirus is inactive or latent
- Most viral genes silenced

- Lysogeny – latency in bacteriophages
  - When host cell replicates, also copies prophage
  - Lysogenic cycle – integration, replication, and excision
  - Lytic cycle – synthesis, assembly, and release
- Temperate phages have a lysogenic cycle
  - Environmental conditions influence integration and length of latency
- Virulent phages do not

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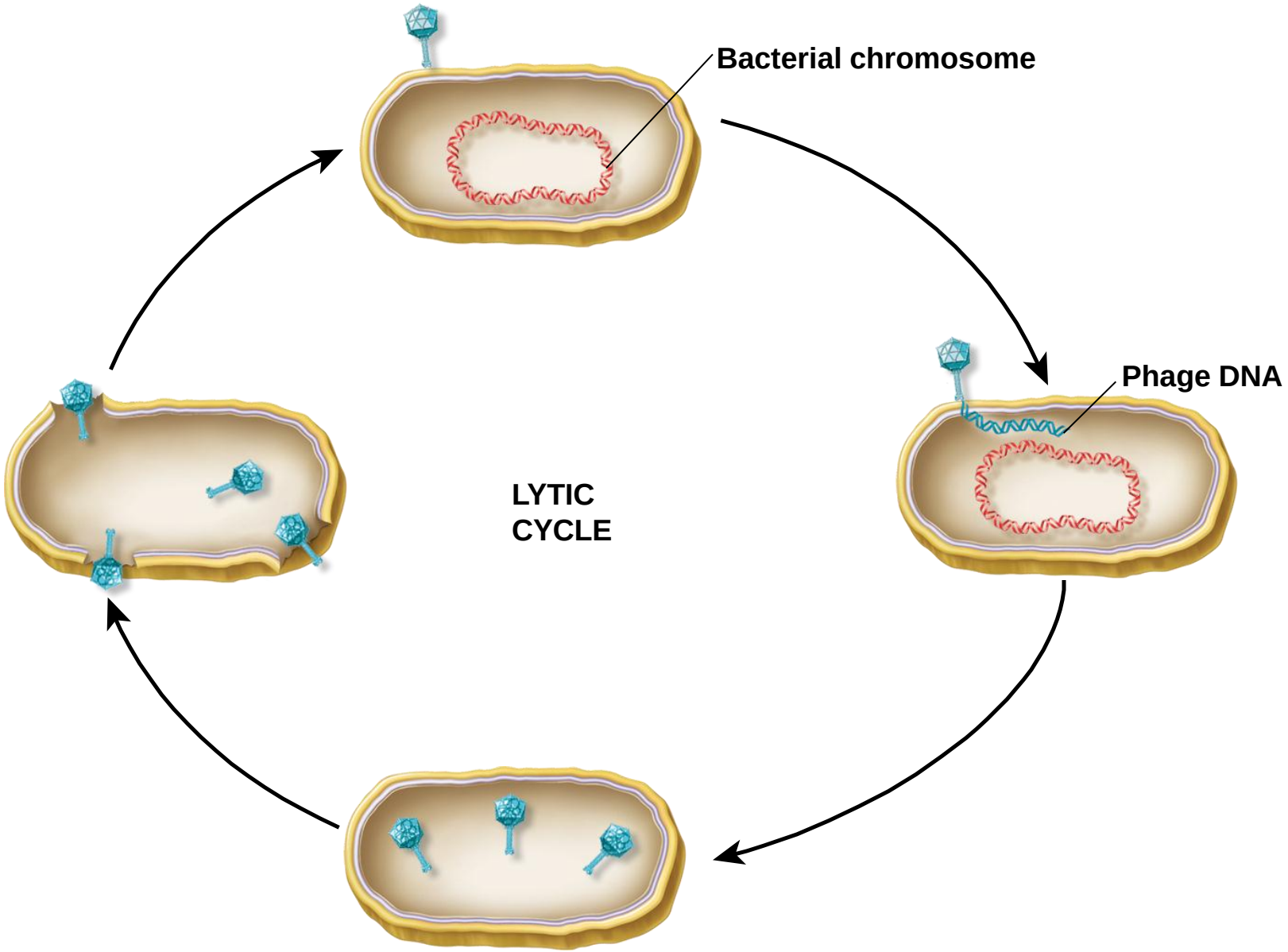

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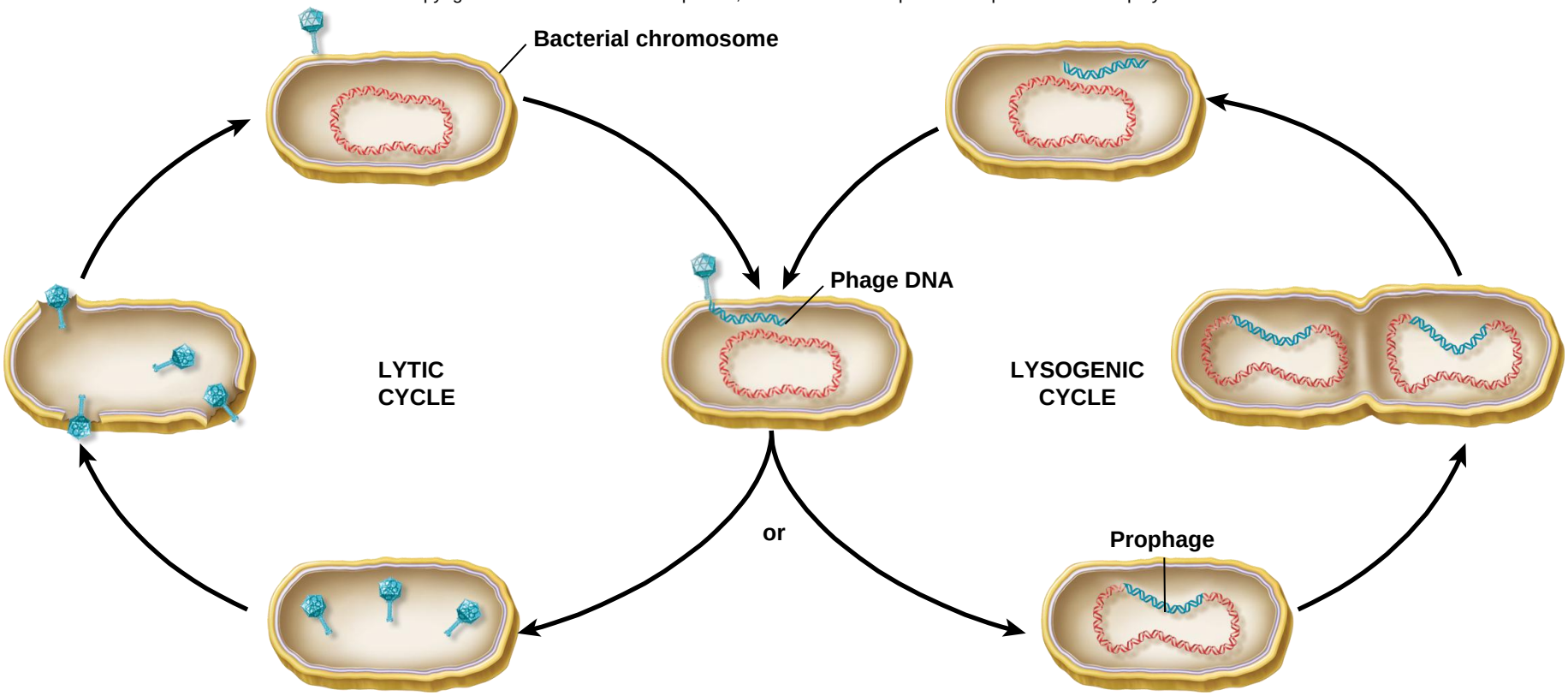

Latency in human viruses

- 2 different ways

1. HIV integrates into host genome and may remain dormant for long periods of time
2. Other viruses can exist as episomes – genetic element that can replicate independently of chromosomal DNA but occasionally integrates into chromosomal DNA
   - Herpes simplex type I and II, varicella zoster

AIDS and HIV

- Human immunodeficiency virus (HIV) is the causative agent of acquired immune deficiency syndrome (AIDS)
- AIDS is primarily spread by sexual contact between infected and uninfected individuals
- Can also be spread by the transfusion of HIV-infected blood, by the sharing of needles among drug users, and from infected mother to unborn child
- Total number of AIDS deaths between 1981 and the end of 2006 was over 25 million; more than 0.5 million of these deaths occurred in the U.S.
- During 2008, around 3 million adults and children became infected with HIV. Worldwide, nearly 1 in every 100 adults between 15 and 49 is infected
- In the U.S. about 55,000 new HIV infections occur each year
- 70% of these new infections are in men and 30% in women

- Devastating effects of AIDS result from viral destruction of a type of white blood cell termed a helper T cell, which plays an essential role in the immune system of mammals
- When large numbers of T cells are destroyed by HIV, the function of the immune system is seriously compromised and the individual becomes highly susceptible to opportunistic infections
  - Would not normally occur in a healthy person

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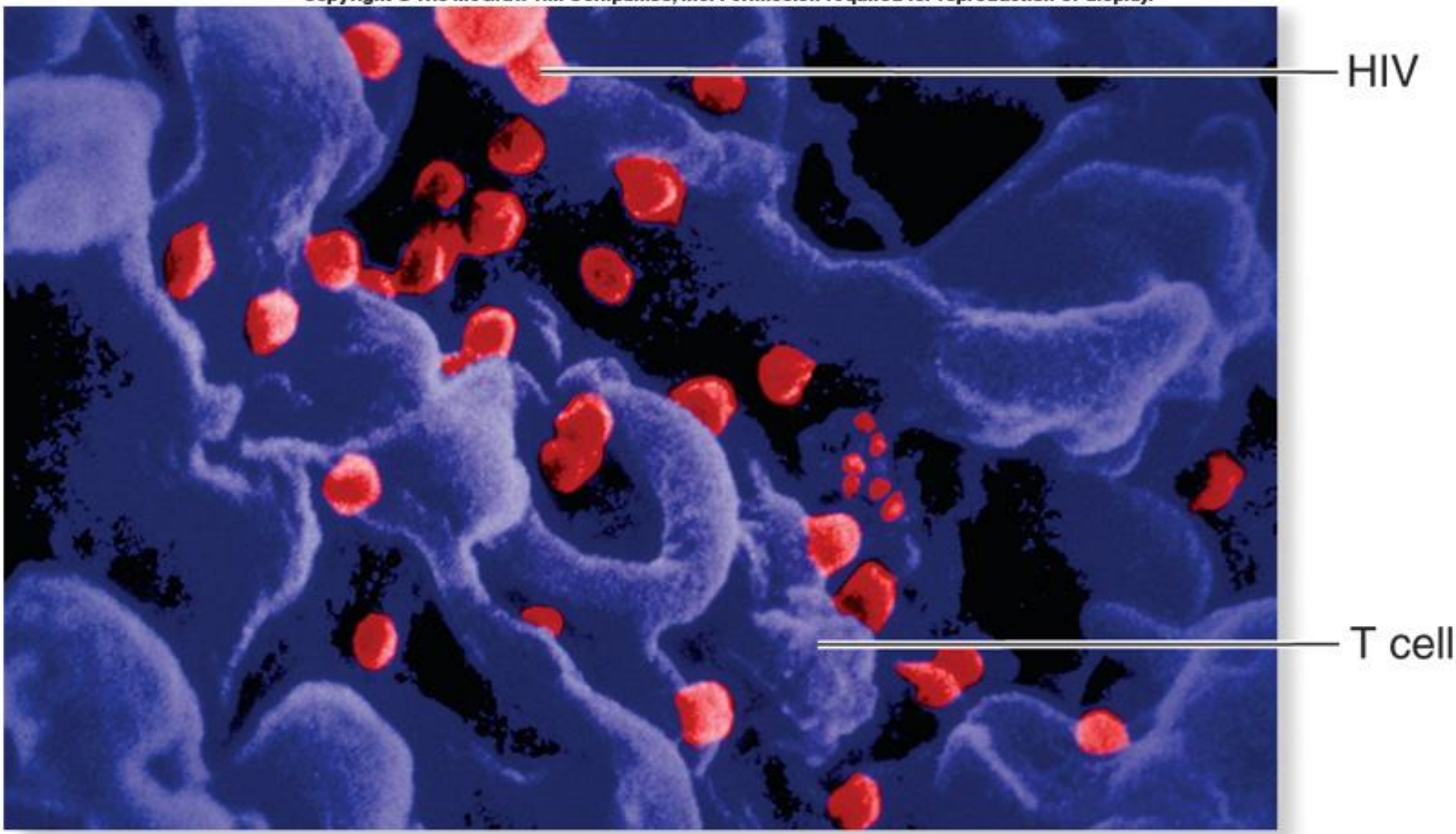

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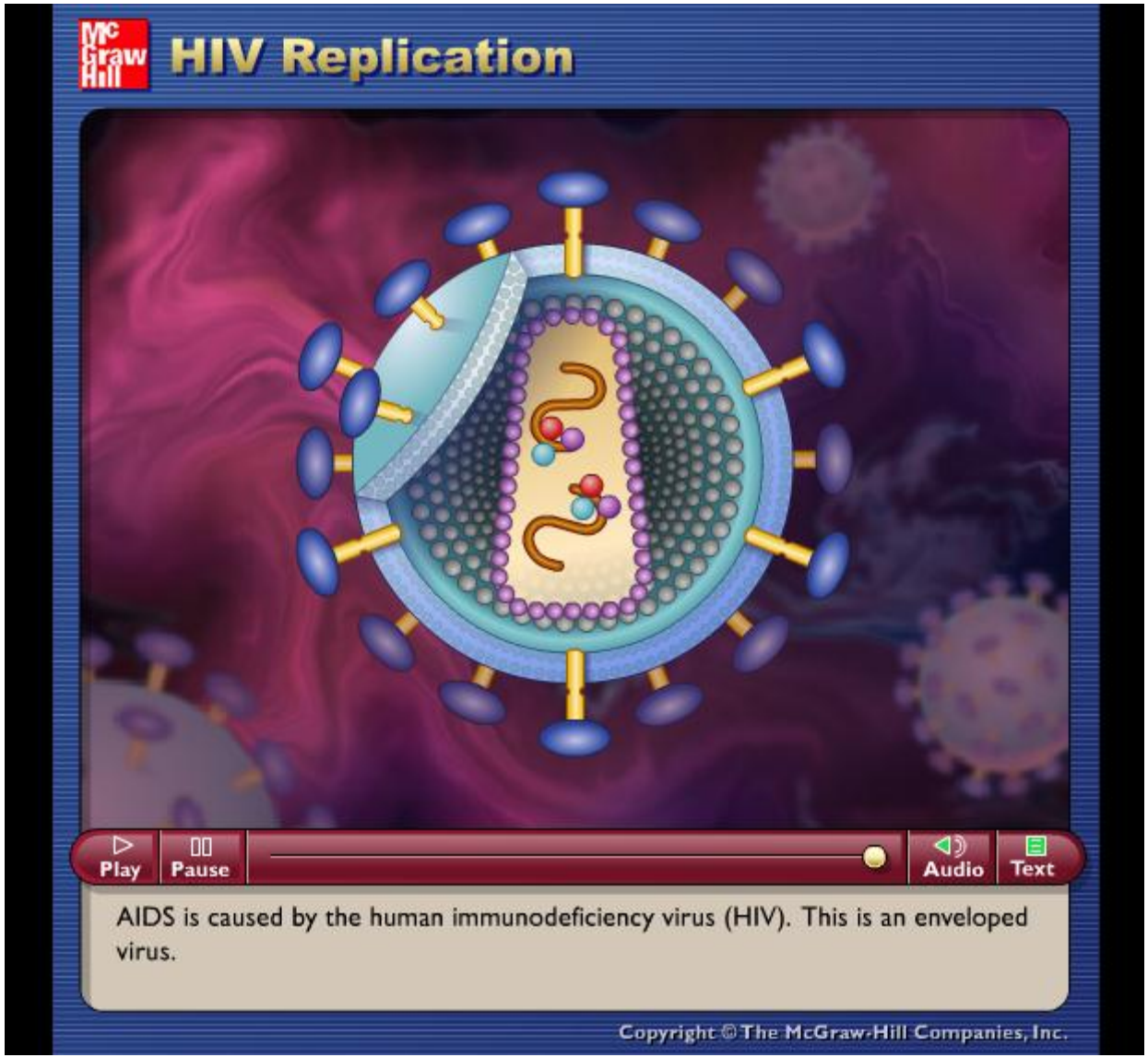
HIV

- Reverse transcriptase lacks a proofreading function
  - Makes more errors and tends to create mutant strains of HIV
  - Makes it difficult to create vaccine
- In U.S., estimated annual number of AIDS-related deaths fell 14% from 1998 to 2002 due in part to the use of new antiviral drugs


HIV Replication
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AIDS is caused by the human immunodeficiency virus (HIV). This is an enveloped virus.
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Origin of viruses

- Many biologists argue that cells evolved before viruses
  - Viruses evolved from macromolecules inside living cells (maybe plasmids)
- Others argue for regressive evolution
- Another theory is that viruses did not evolve from cells but evolved in parallel with cellular organisms

Genetic properties of bacteria

- Genes of bacteria are found in bacterial chromosomes
- Usually a single type of chromosome
- May have more than one copy of that chromosome
- Number of copies depends on the bacterial species and on growth conditions
- Typically 1-4 identical chromosomes
- Nucleoid – region where tightly packed bacterial chromosome found

- Molecules of double-stranded DNA
- Usually circular
- Tend to be shorter
- Contains a few thousand unique genes
- Mostly structural genes
- Single origin of replication

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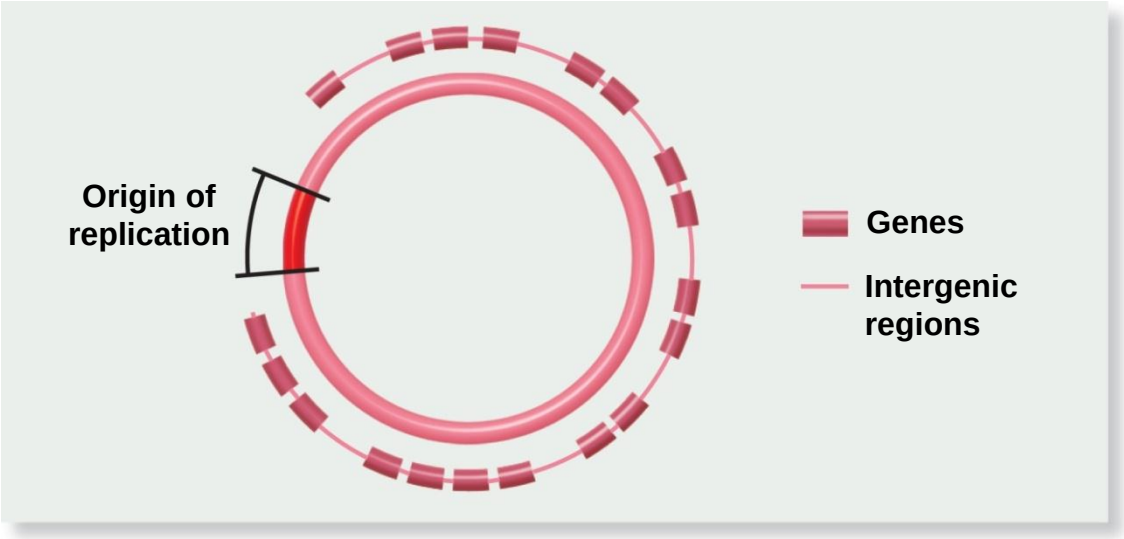

Key features

- Most, but not all, bacterial species contain circular chromosomal DNA.
- A typical chromosome is a few million base pairs in length.
- Most bacterial species contain a single type of chromosome, but it may be present in multiple copies.
- Several thousand different genes are interspersed throughout the chromosome.
- One origin of replication is required to initiate DN A replication.

Compaction

- Typical bacterial chromosome must be compacted about 1,000-fold
- Bacterial DNA is not wound around histone proteins to form nucleosomes
- Proteins important in forming loop domains
  - Compacts DNA about 10-fold
- DNA supercoiling
  - Topoisomerases twist the DNA and control degree of supercoiling

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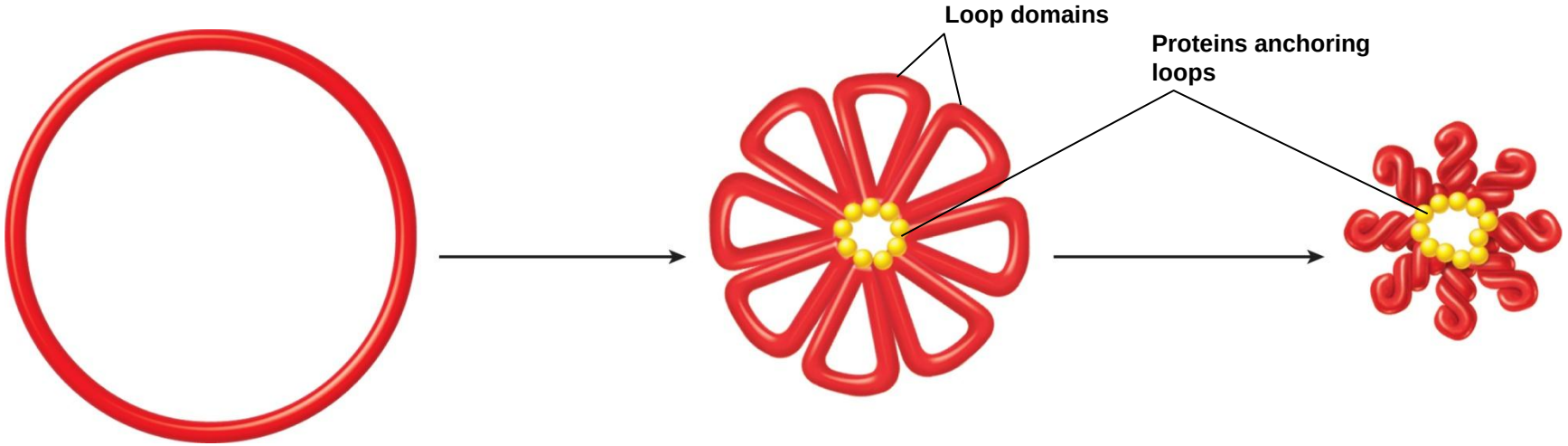

Plasmids

- Small, circular pieces of DNA that exist independently of the bacterial chromosome
- Occur naturally in many strains of bacteria and in a few types of eukaryotic cells, such as yeast
- Own origin of replication that allows it to be replicated independently of the bacterial chromosome
- Not usually necessary for survival but can provide growth advantages
- Episome – plasmid that can integrate into bacterial chromosome

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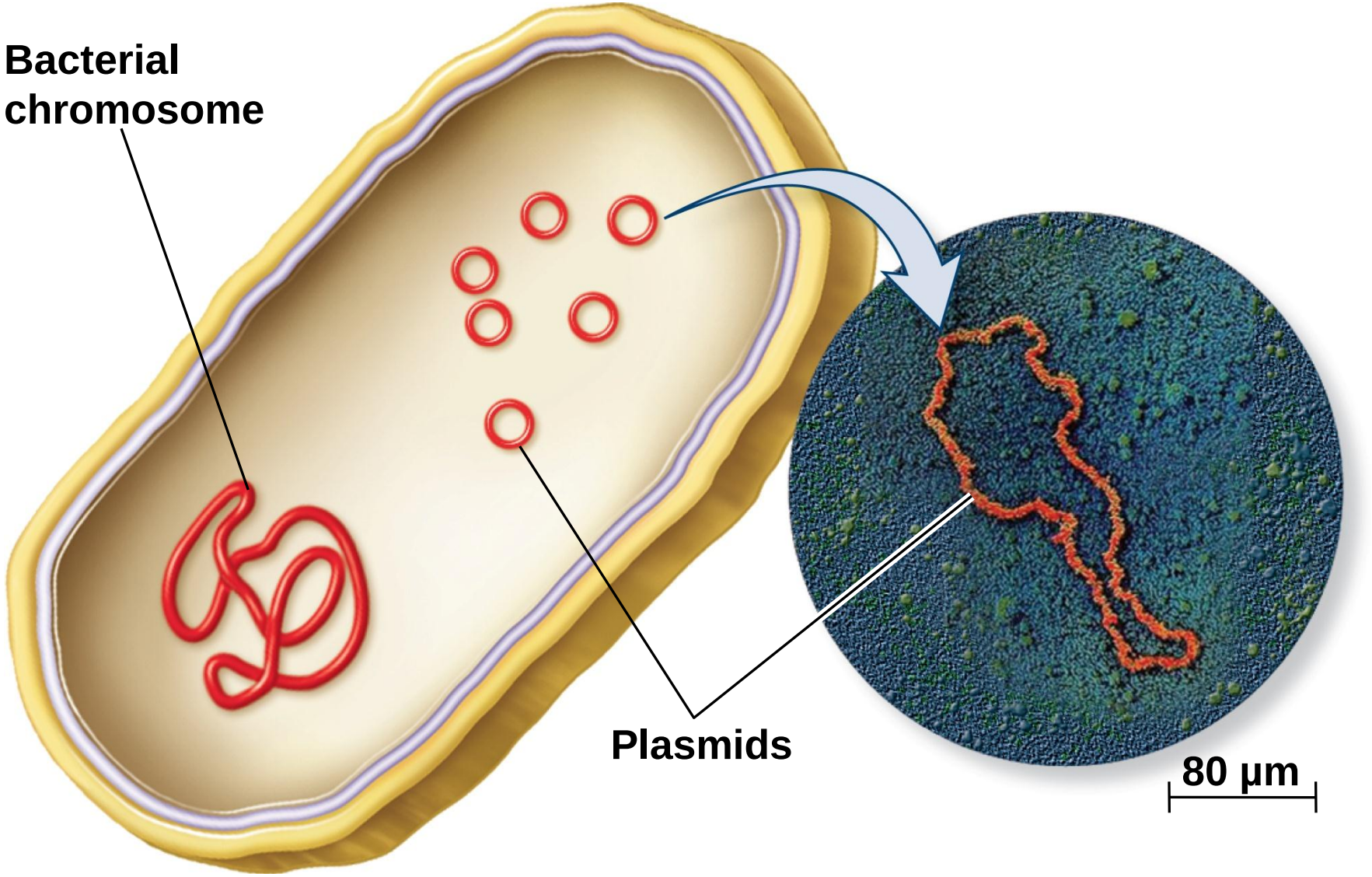

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5 types of plasmids

- Resistance plasmids (R factors)
  - Contain genes that confer resistance against antibiotics and other types of toxins
- Degradative plasmids
  - Carry genes that enable the bacterium to digest and utilize an unusual substance
- Col-plasmids
  - Contain genes that encode colicines, which are proteins that kill other bacteria
- Virulence plasmids
  - carry genes that turn a bacterium into a pathogenic strain
- Fertility plasmids (F factors)
  - Allow bacteria to mate with each other

Reproduction

- Cells of some species, such as *E. coli*, can divide every 20–30 minutes
- Single cell can form a bacterial colony in less than a day
- Reproduce by binary fission – NOT mitosis
- Except when a mutation occurs, each daughter cell contains an identical copy of the mother cell's genetic material
- Does not involve genetic contributions from two different parents
- Plasmids may replicate independently of the bacterial chromosome

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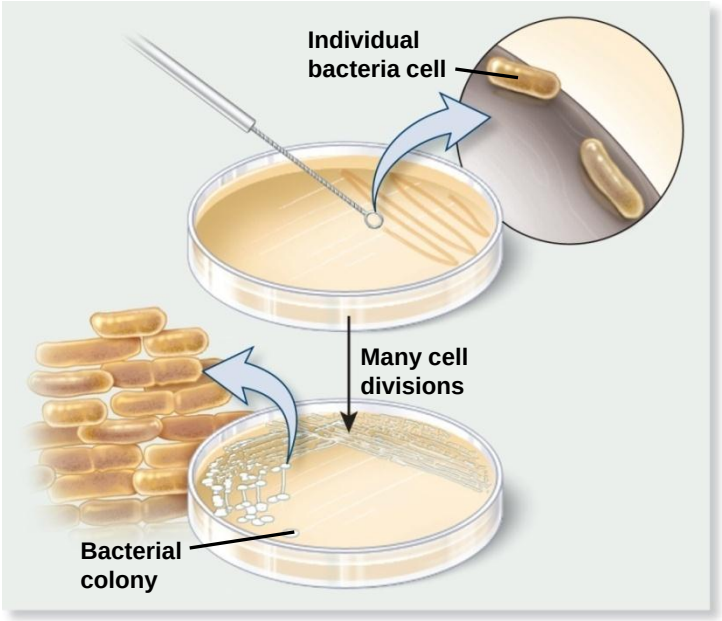

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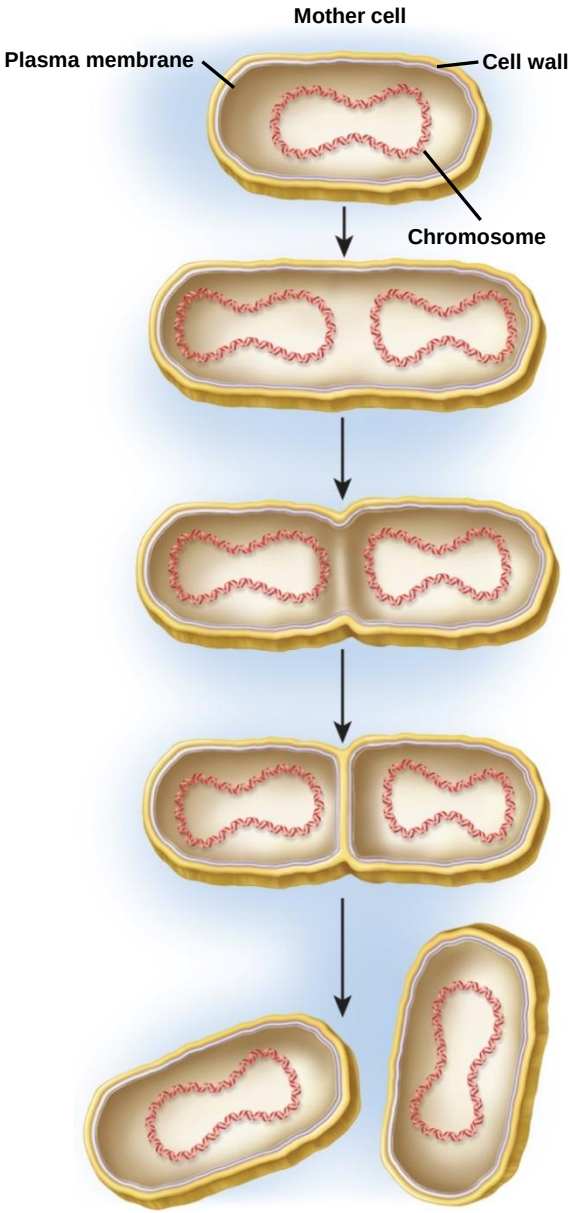

Genetic diversity in bacteria

- 2 sources
  1. Mutations can occur that alter the bacterial genome and affect the traits of bacterial cells
  2. Genetic transfer – genetic material is transferred from one bacterial cell to another

Genetic transfer

1. Conjugation
   - Direct physical interaction transfers genetic material from donor to recipient cell
2. Transformation
   - DNA released from a dead bacterium into the environment is taken up by another bacteria
3. Transduction
   - A virus transfers genetic information from one bacterium to another

Lederberg and Tatum's Work with *E. coli* Demonstrated Genetic Transfer Between Bacteria and Led to the Discovery of Conjugation

- Studying strains of *E. coli* that had different nutritional requirements for growth
- Differences in nutritional requirements correspond to allelic differences between the strains
- When 2 strains were mixed, found new genotypes
  - Not mutation
- Hypothesized that some genetic material was transferred between the two strains when they were mixed
- Either genetic material was released from one strain and taken up by the other, or cells of the two different strains made contact with each other and directly transferred genetic material
- U-tube allows pieces of DNA to transfer but not cells to touch
- Without physical contact, genetic material could not be transferred

Feature Investigation

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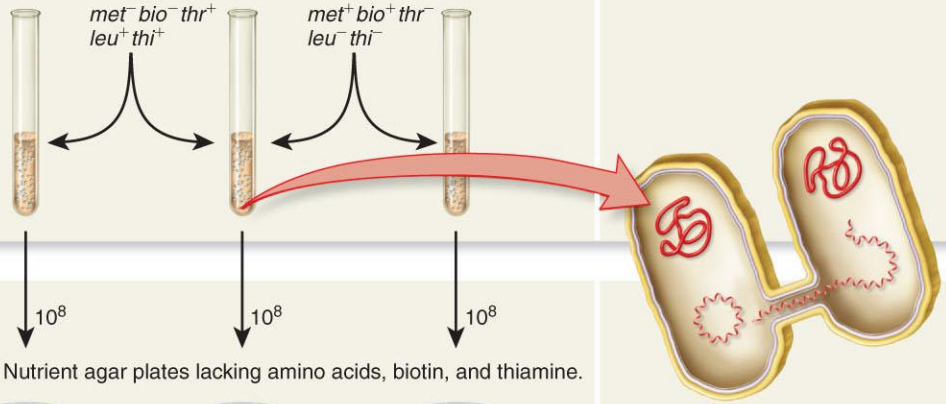
HYPOTHESIS Genetic material can be transferred from one bacterial strain to another.

STARTING MATERIALS Two bacterial strains, one that was *met*$^-$ *bio*$^-$ *thr*$^+$ *leu*$^+$ *thi*$^+$ and the other that was *met*$^+$ *bio*$^+$ *thr*$^-$ *leu*$^-$ *thi*$^-$.

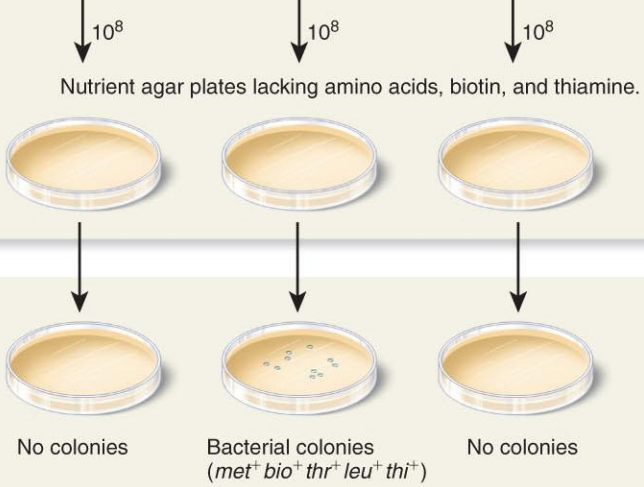
Experimental level **Conceptual level**

1 In 3 separate tubes, add either the *met*$^-$ *bio*$^-$ *thr*$^+$ *leu*$^+$ *thi*$^+$ strain, the *met*$^+$ *bio*$^+$ *thr*$^-$ *leu*$^-$ *thi*$^-$ strain, or a mixture of both strains.

Incubate several hours.



2 Remove 10^8 cells from each tube and spread onto plates that lack methionine, biotin, threonine, leucine, and thiamine.



3 Incubate overnight to allow growth of bacterial colonies.

4 **THE DATA**

Strain	Number of colonies after overnight growth
met$^-$ *bio*$^-$ *thr*$^+$ *leu*$^+$ *thi*$^+$	0
met$^+$ *bio*$^+$ *thr*$^-$ *leu*$^-$ *thi*$^-$	0
Both strains together	~10

Conjugation

- Only about 5% of *E. coli* strains found in nature can act as donor strains
- Donor strains contain a fertility factor (F factor) that can be transferred to recipient strains
  - Some donor strains are Hfr (for *H*igh *fr*equency of recombination)

F factors

- Carry several genes that are required for conjugation and also may carry genes that confer a growth advantage for the bacterium
- F^+ has an F factor, F^- does not
- Sex pili are made by F^+ cells that bind specifically to F^- cells
- Once contact is made, the pili shorten, drawing the donor and recipient cells closer together
- One strand of F factor is transferred, other strand stays in donor
- Both replicate so that donor and recipient now have complete double stranded F factor

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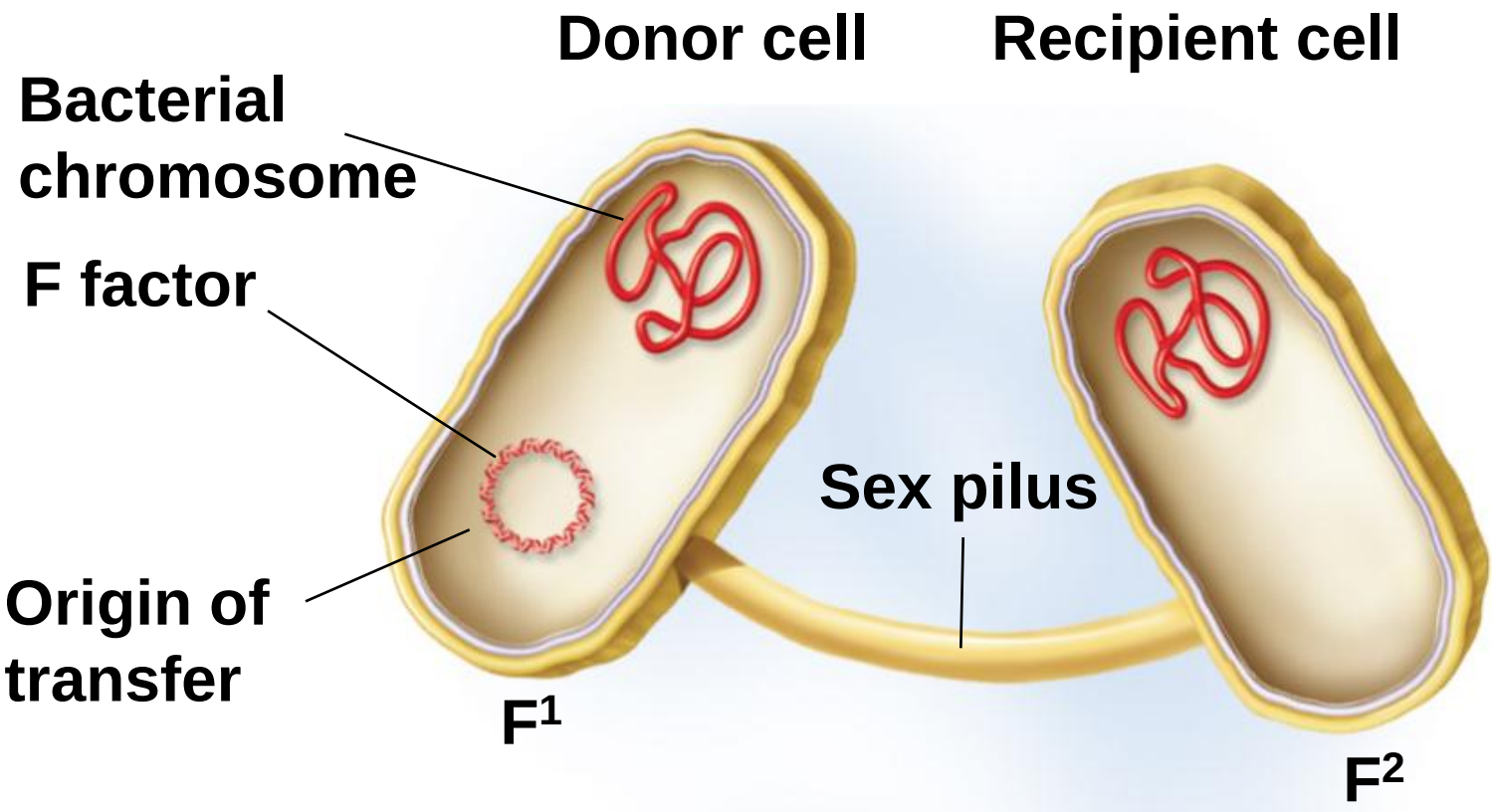

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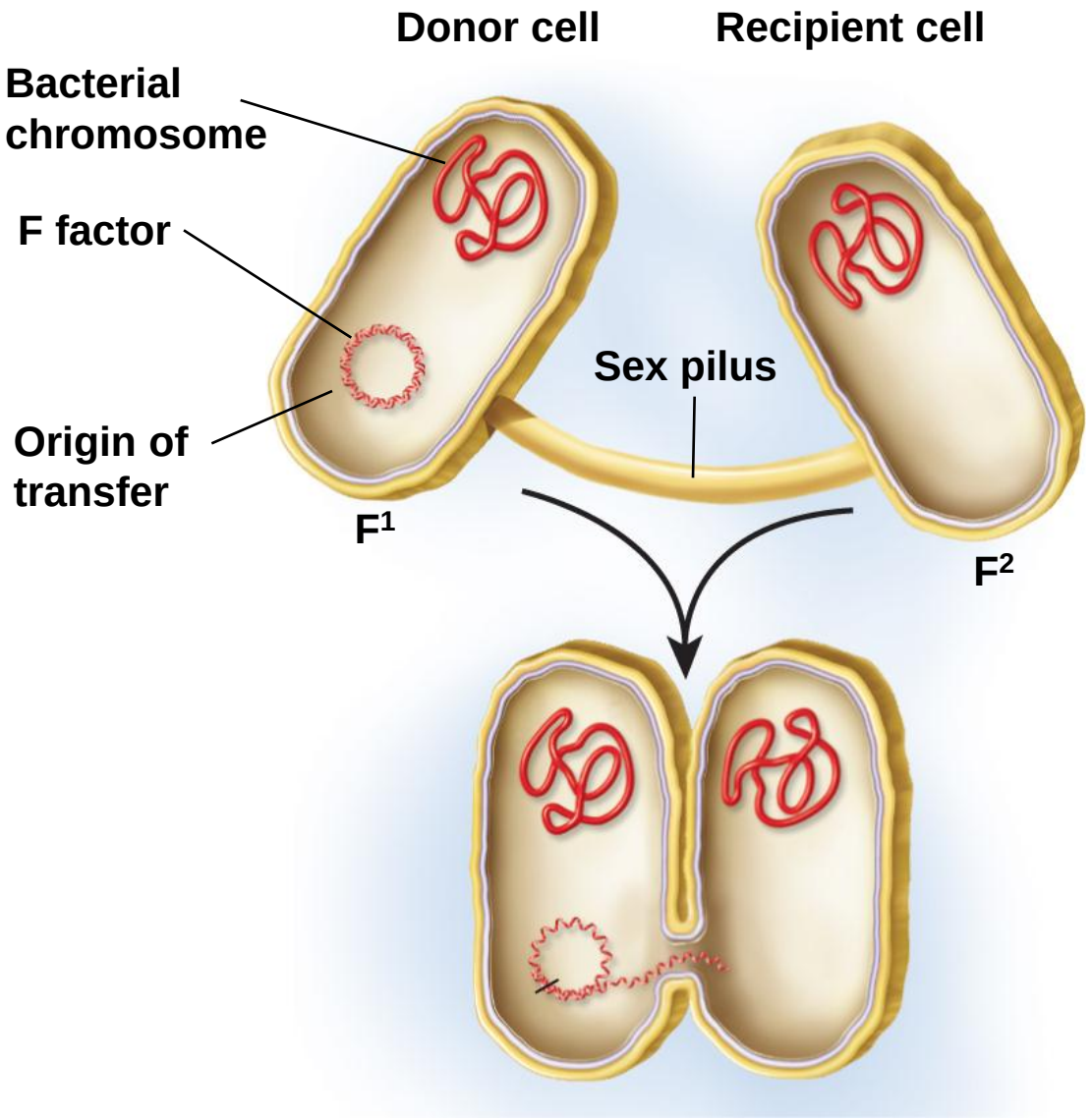

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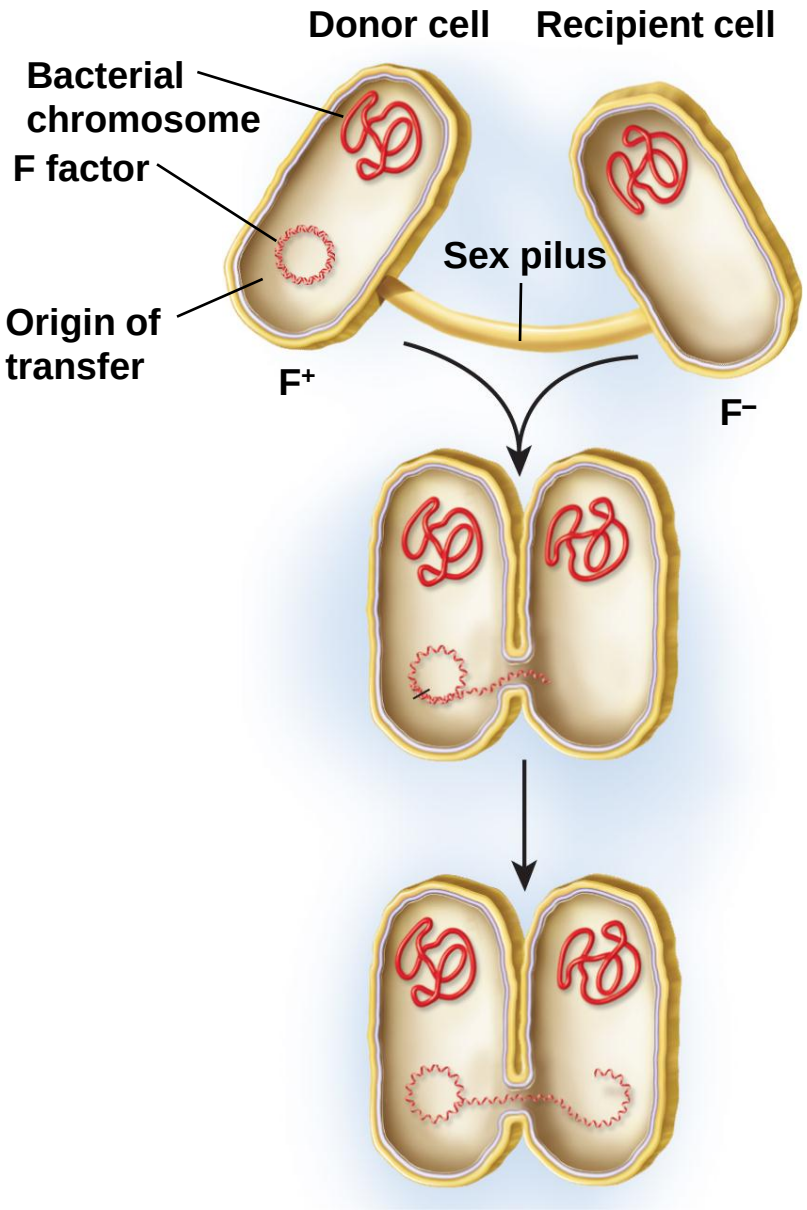

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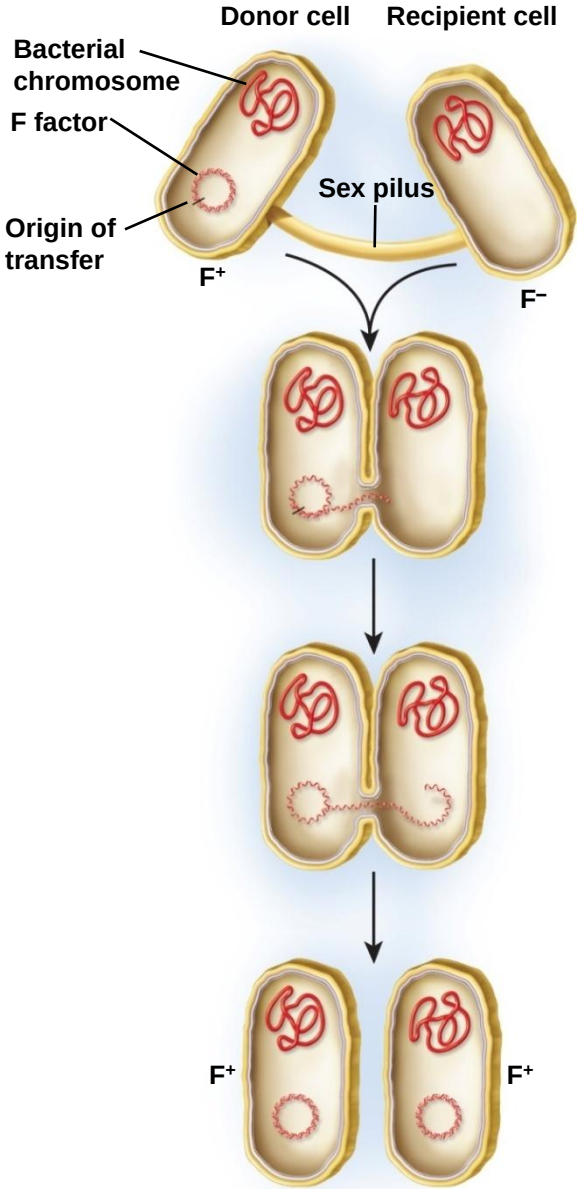
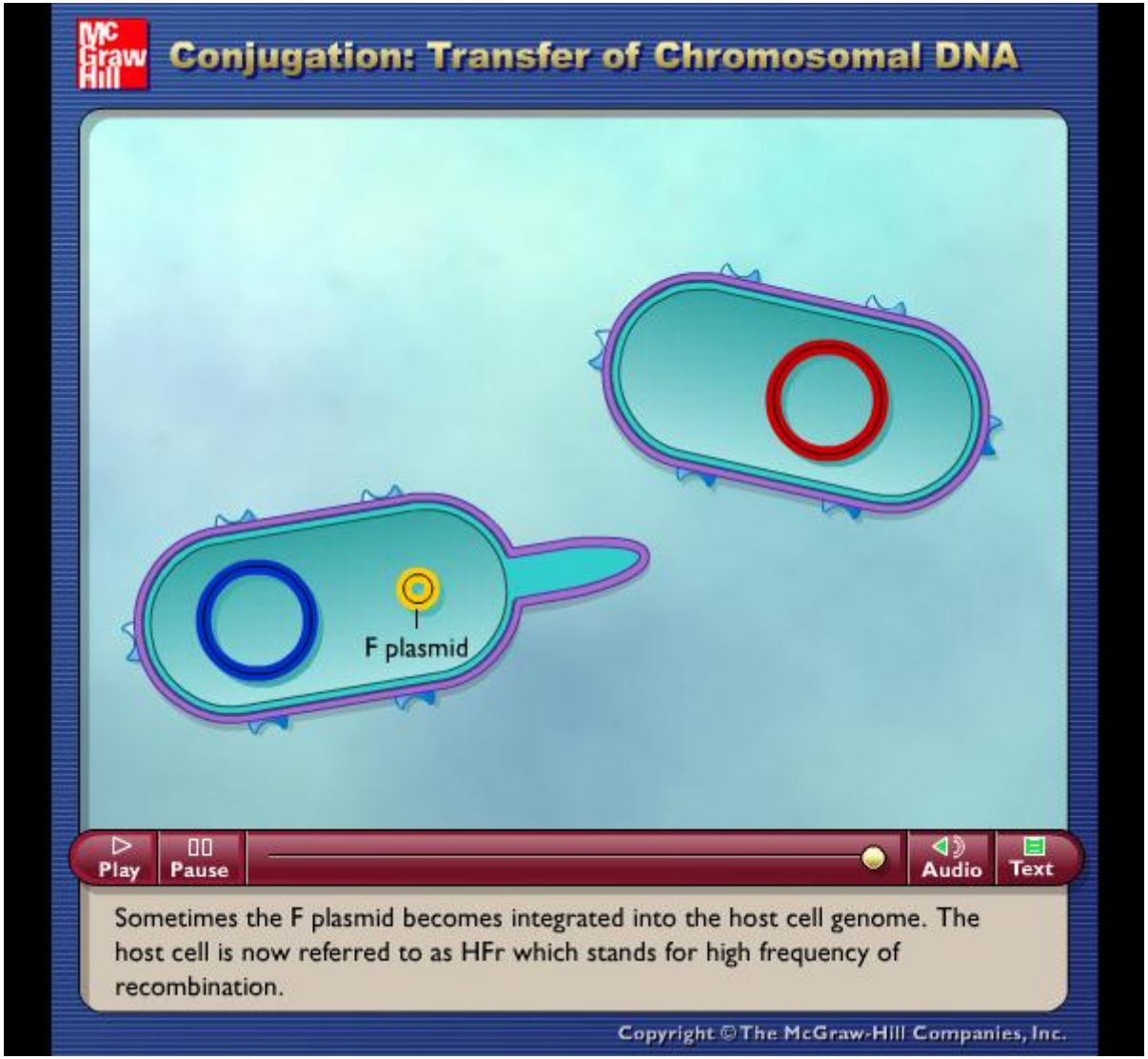


(b) Transfer of an F factor


Conjugation: Transfer of Chromosomal DNA
F plasmid
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Sometimes the F plasmid becomes integrated into the host cell genome. The host cell is now referred to as HFr which stands for high frequency of recombination.
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Transformation

- Does not require direct contact between bacterial cells
- Living bacterial cell imports a strand of DNA that another bacterium released into the environment when it died
- Only competent cells with competence factors can do this
- Facilitate the binding of DNA fragments to the bacterial cell surface, the uptake of DNA into the cytoplasm, and the incorporation of the imported DNA into the bacterial chromosome

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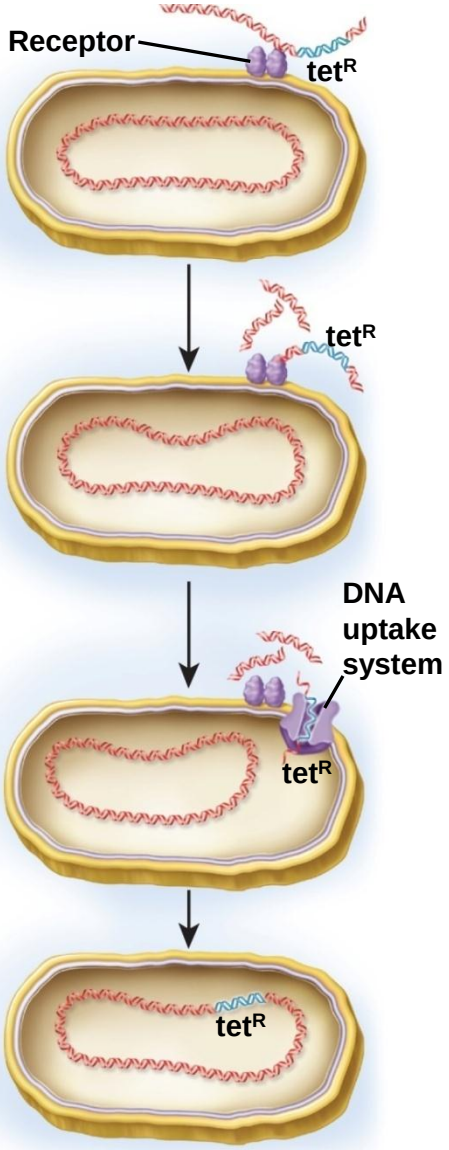

Transformed cell that is resistant to the antibiotic tetracycline

Transduction

- Viruses that infect bacteria transfer bacterial genes from one bacterium to another
- Usually an error in a phage lytic cycle
- Newly assembled phages incorporate piece of host DNA instead

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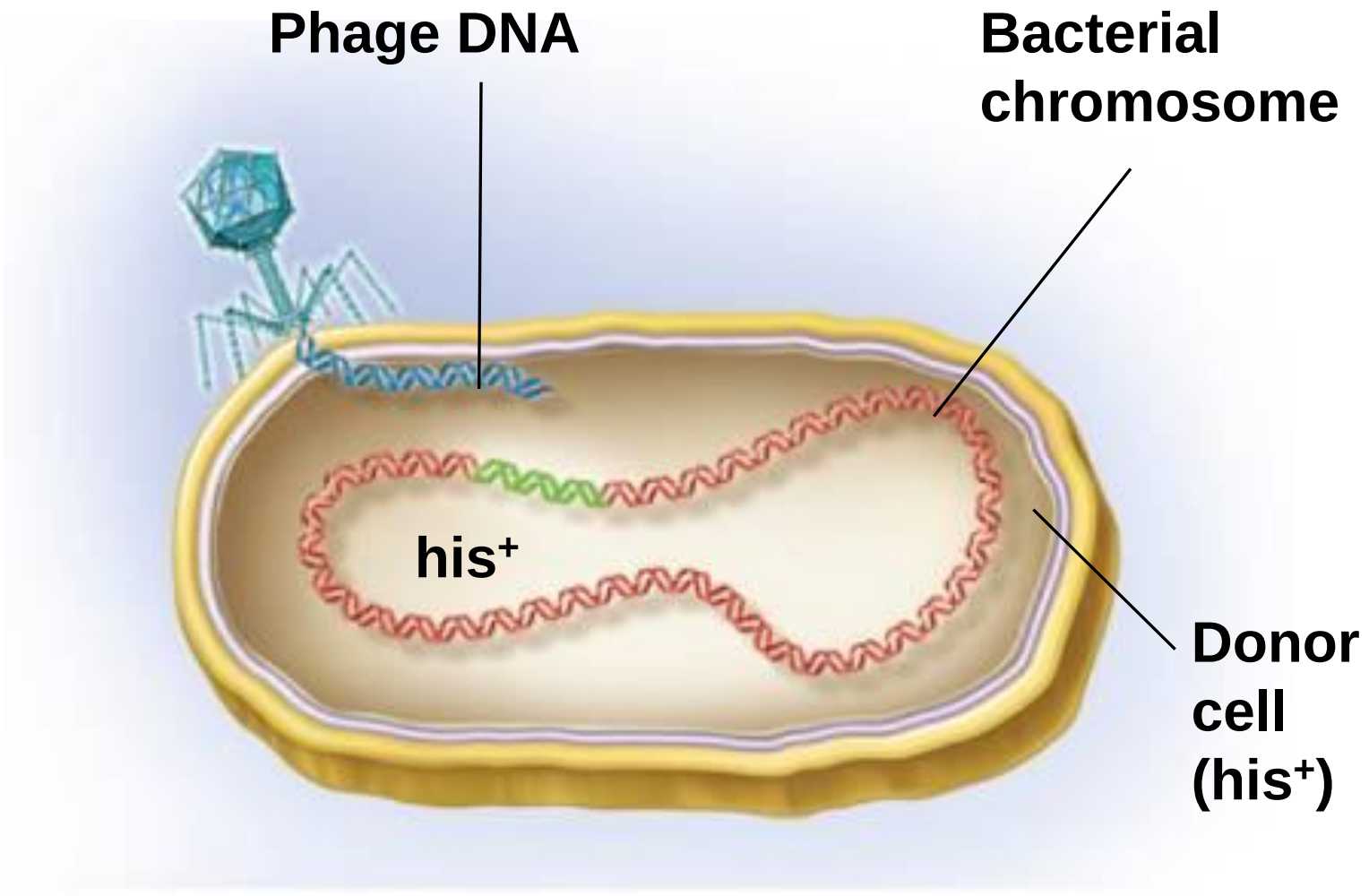

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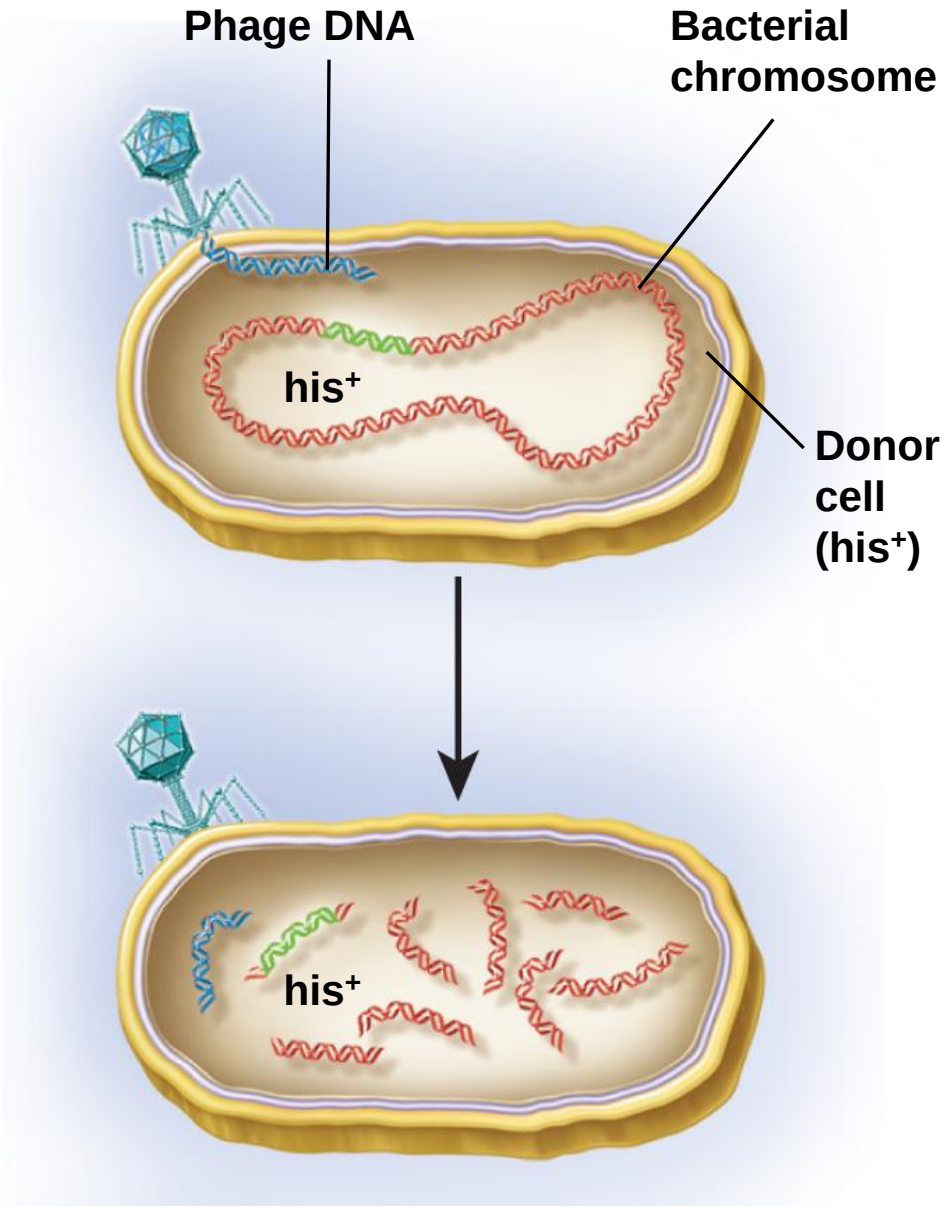

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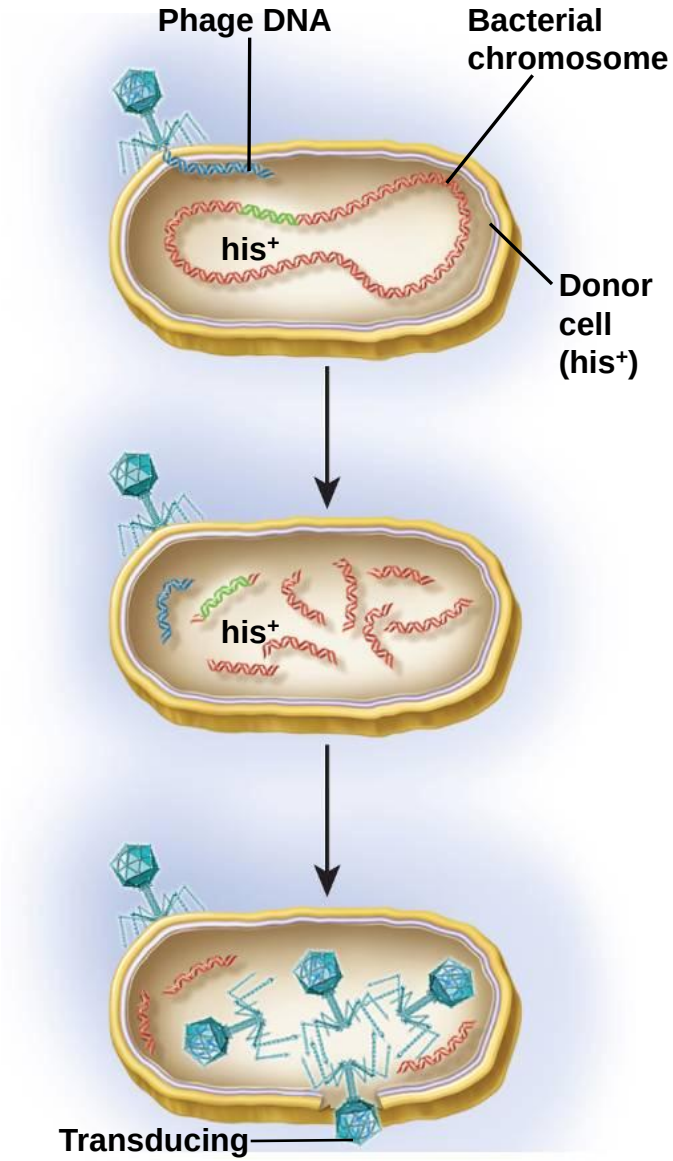

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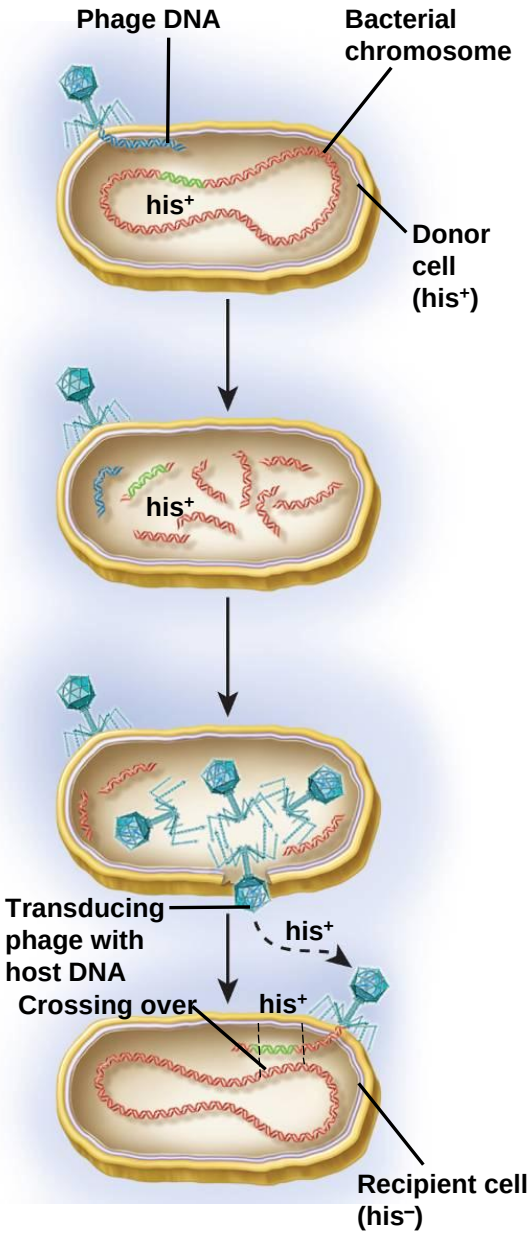

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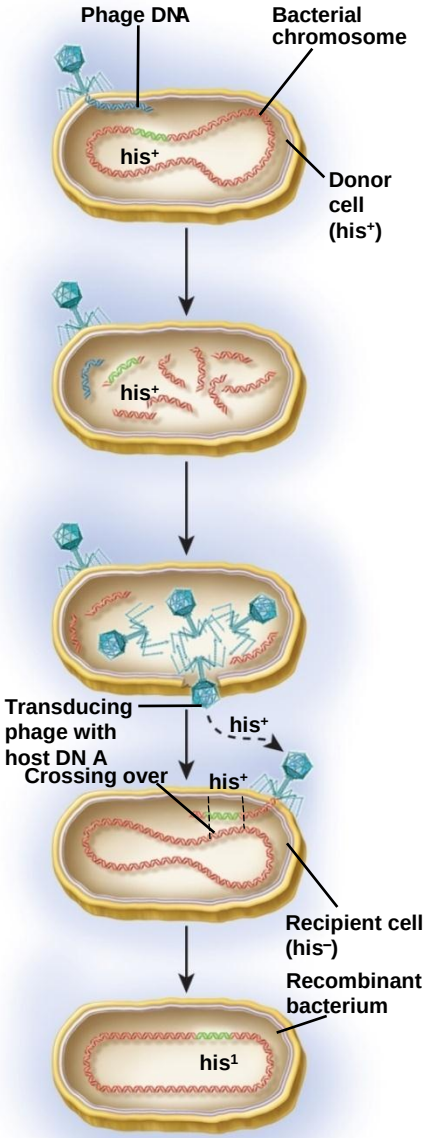

The recombinant bacterium has a genotype (his^+) that is different from the original recipient bacterial cell (his^-).

Horizontal Gene Transfer Is the Transfer of Genes Between Different Species

- Vertical gene transfer that occurs when genes are passed from one generation to the next among individuals of the same species
- Roughly 17% of the genes of *E. coli* and of *Salmonella typhimurium* have been acquired by horizontal transfer during the past 100 million years
- Medical relevance of horizontal gene transfer is profound – acquired antibiotic resistance