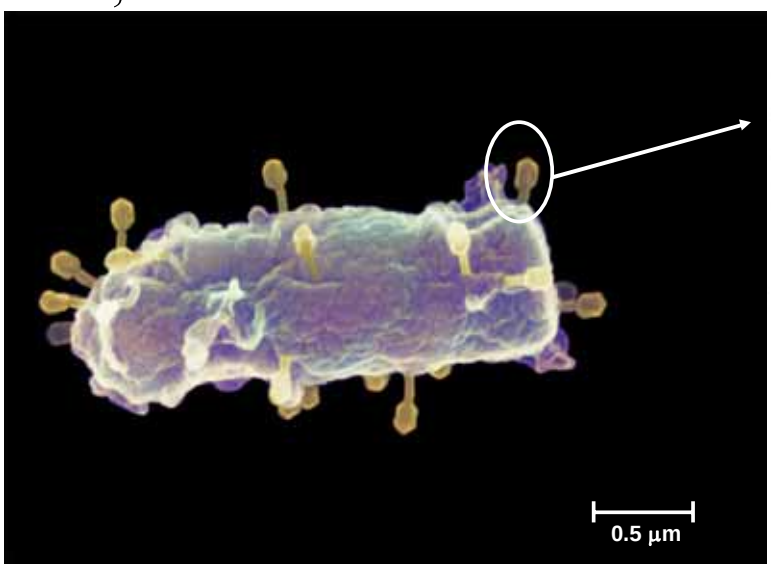
The Genetics of Viruses and Bacteria

Molecular biology was born in the laboratories of microbiologists studying viruses and bacteria

Neil Campbell and Jane Reece ***Biology, Seventh Edition***

- **Overview: Microbial Model Systems**
- Bacteriophages (a kind of virus)
  - Can infect and set in motion a genetic takeover of bacteria, such as *Escherichia coli*



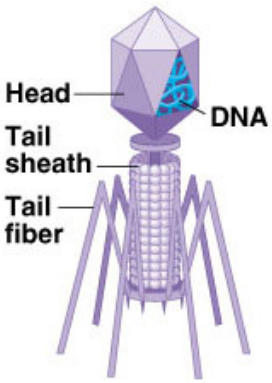


Figure 18.1

Comparing the size of a virus, a bacterium, and an animal cell.

- The diameter of animal cells is about ten times greater than the length of E. coli.
- Viruses are smaller and simpler still. Lacking the structures and metabolic machinery found in cells
- A virus has a genome but can reproduce only within a host cell

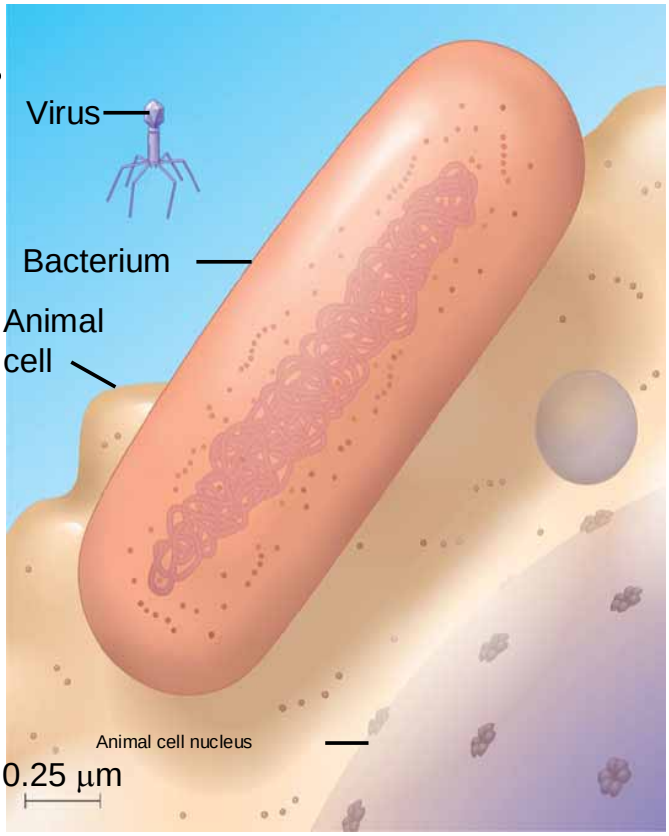


Figure 18.2

The Discovery of Viruses

- **Tobacco mosaic disease (菸草鑲嵌病)**

1883 Adolf Mayer (German)
The disease could be transmitted from plant to plant by rubbing sap

1890s Dimitri Ivanowsky (Russian)
The disease van pass through a filter designed to remove bacteria

1890s Martinus Beijerinck (Dutch botanist)
The infectious agent in the filtered sap could reproduce

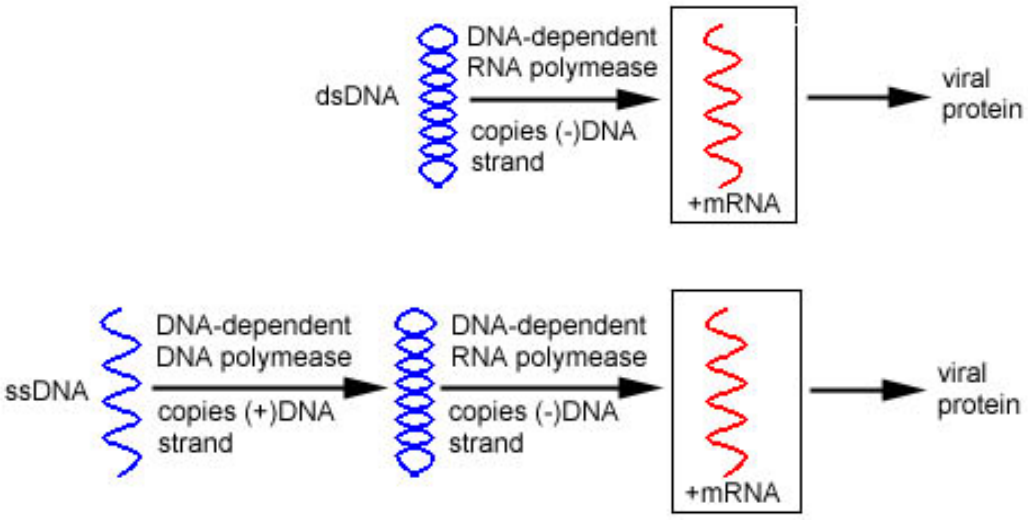
1935 Wendell Stanley (American)
Crystallized tobacco mosaic virus (TMV)

Figure 18.3

Structure of Viruses (genome; Capsid; Envelope)

Genome

- Double- or single-stranded DNA
- Double- or single-stranded RNA



http://www.cat.cc.md.us/courses/bio141/lecguide/unit4/genetics/virus/virus.html

Structure of Viruses (genome; Capsid; Envelope)

Genome

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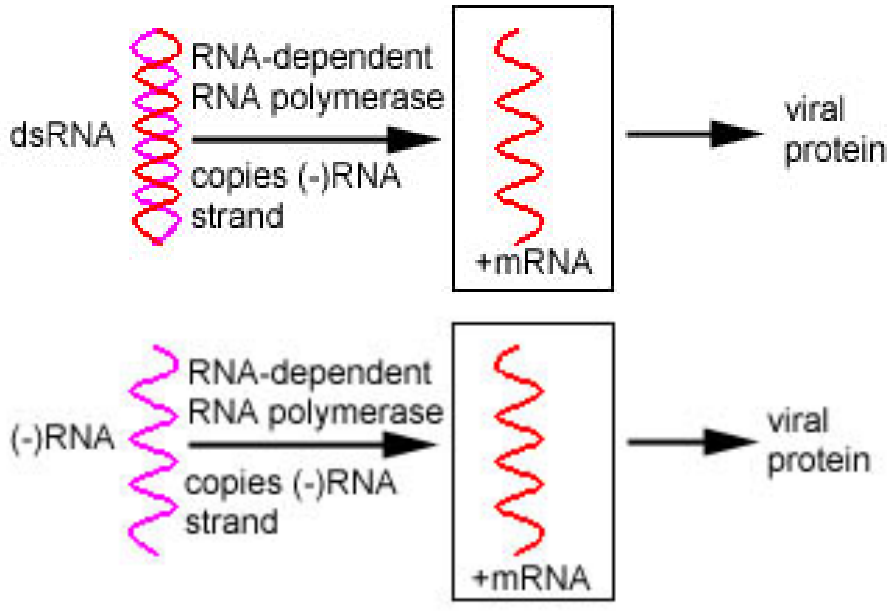
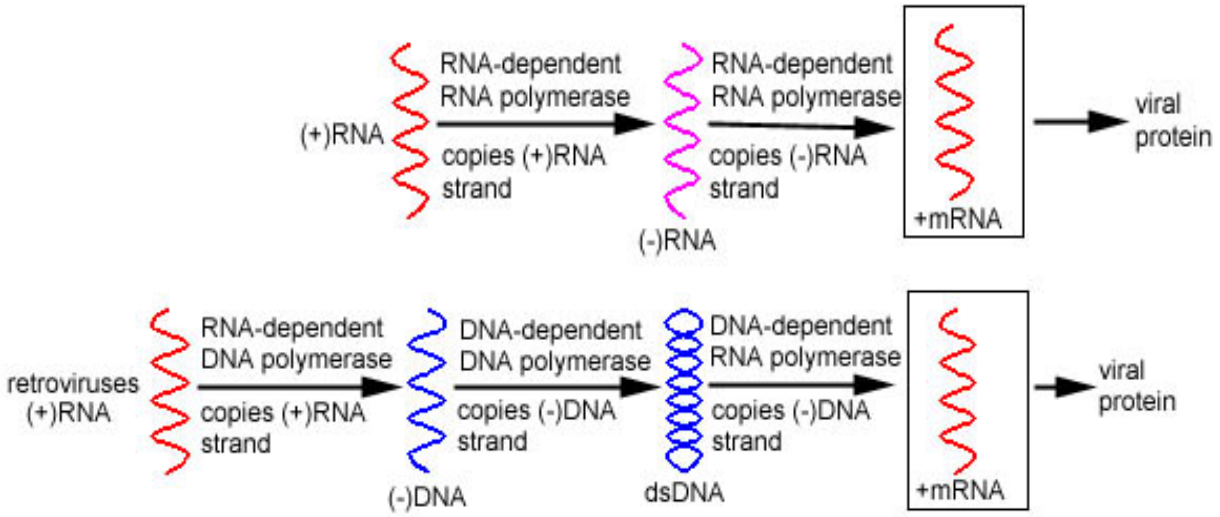


Structure of Viruses (genome; Capsid; Envelope)

Genome

Double- or single-stranded DNA

Double- or single-stranded RNA



Structure of Viruses (genome; Capsid; Envelope)

Capsid

- The various protein shell enclosing the viral genome
  - —capsomere: individual protein subunits of viral capsid

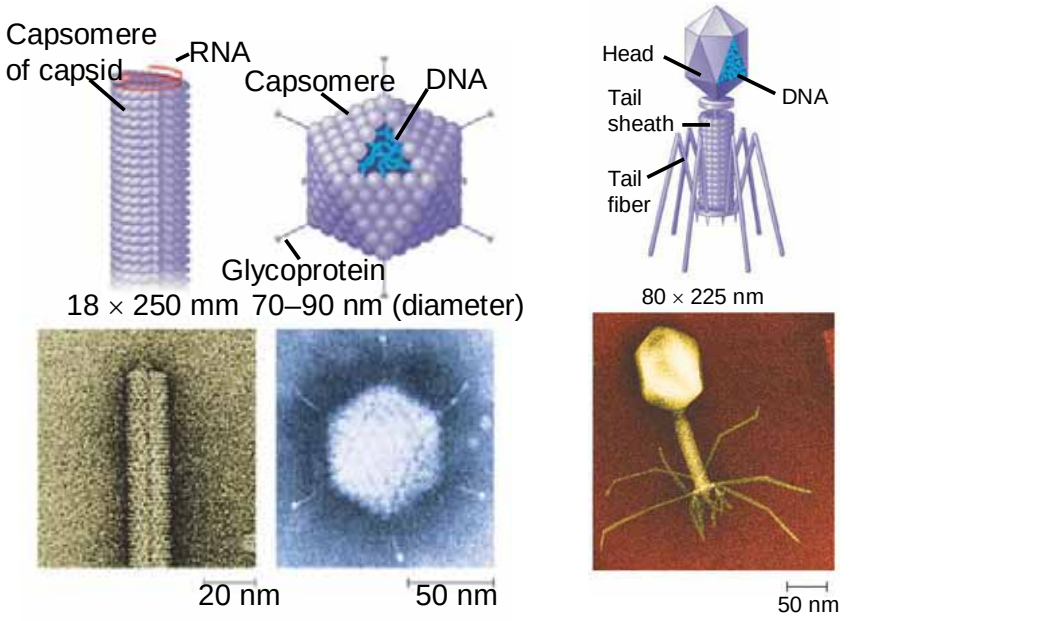


Figure 18.4a, b, d (a) Tobacco mosaic virus (b) Adenoviruses (d) Bacteriophage T4

Structure of Viruses (genome; Capsid; Envelope)

Envelope

- Derived from host membrane that enclose capsid of some viruses.
- Could help virus infect their hosts.

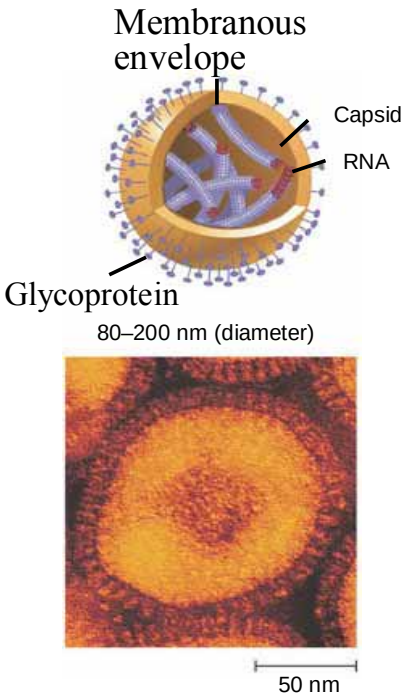


Figure 18.4c (c) Influenza viruses

General Features of Viral Reproductive Cycles

- **Viruses can reproduce only within a host cell**
  - —lack the enzymes for metabolism or ribosomes for protein synthesis.
- Each type of virus can infect and parasitize only a limited range of host cells, called its **host range**.
  - —Some viruses (like equine encephalitis 脑炎 virus) have a broad host range, while others infect only a single species.
- Most viruses of eukaryotes attack specific tissues.
  - — Cold viruses → respiratory tract.
  - — AIDS virus →T helper cells.

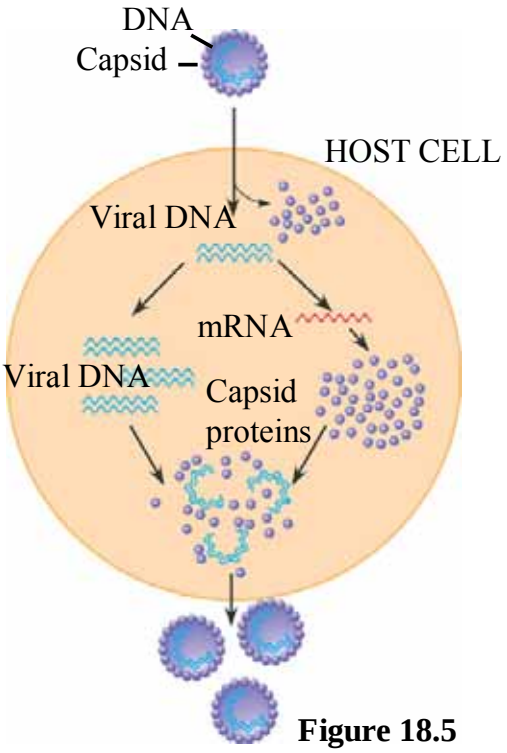


Figure 18.5

Reproductive Cycles of Phages

–the best understood of all viruses

–Go through two alternative reproductive mechanisms:

- **The lytic cycle**

  A phage reproductive cycle that culminates in the death of the host

  ➔ **Virulent phage**

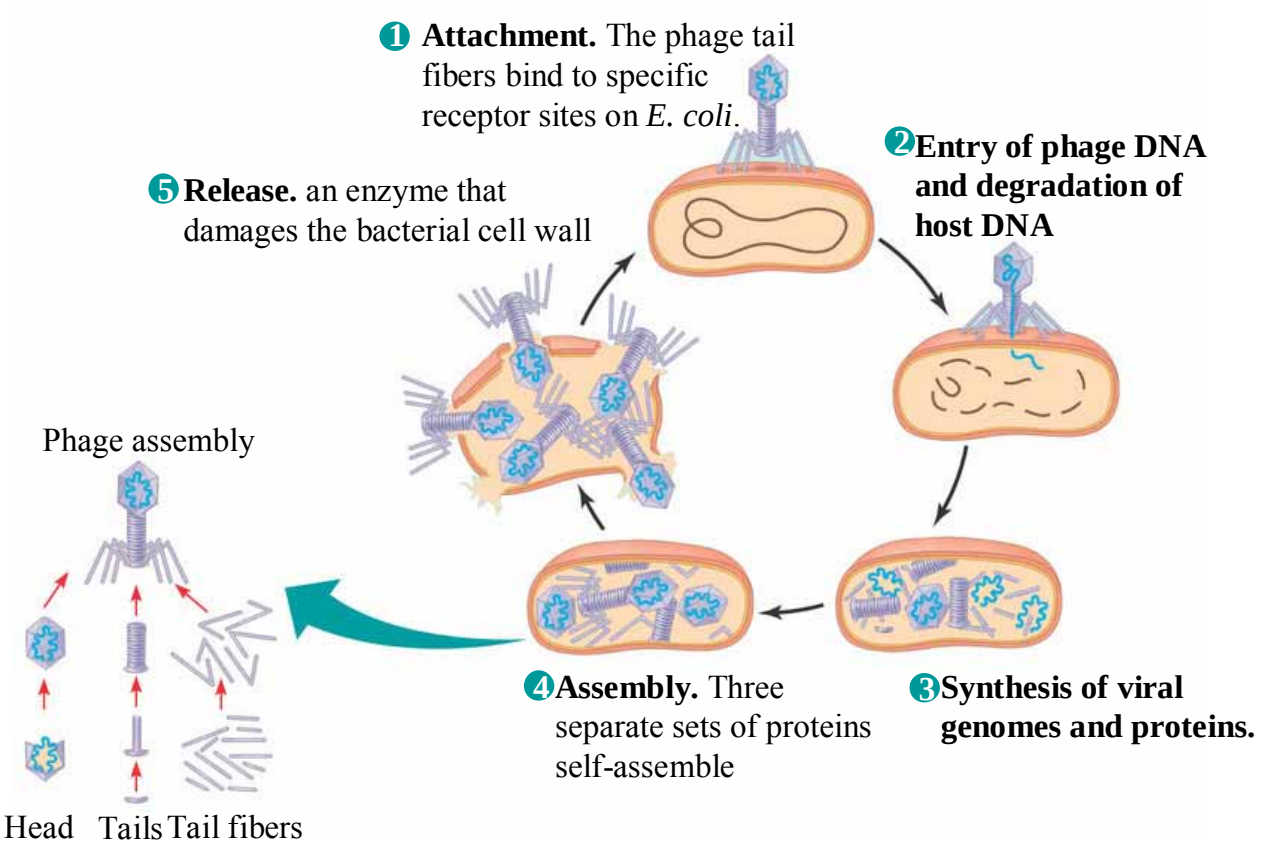
- **The lysogenic cycle**

  Replicates the genome without destroying the host

  ➔ **Temperate phages**

  Are capable of using **both the lytic and lysogenic cycles** of reproduction

The lytic cycle of phage T4, a virulent phage



Temperate phage (phage λ)
— Use both the lytic and lysogenic cycles

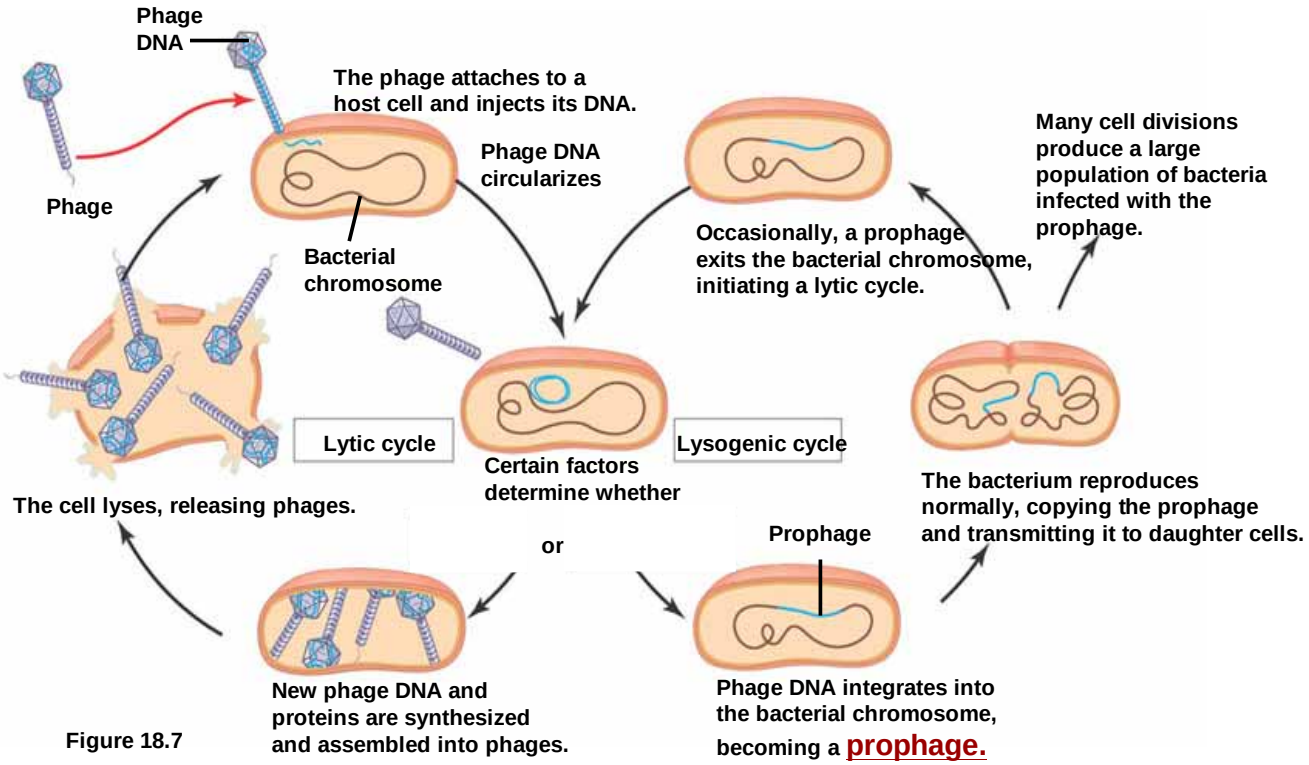


Figure 18.7

Why phages haven't exterminated all bacteria?
– Natural balance

- The lytic cycle takes only 20 – 30 minutes at 37°C.
  - Natural selection favors **bacterial mutants with receptors sites** that are no longer recognized by a particular type of phage.
  - Bacteria produce **restriction nucleases** that recognize and cut up foreign DNA, including certain phage DNA.
    - Modifications to the bacteria's own DNA prevent its destruction by restriction nucleases.
  - But, natural selection favors phage mutants that are resistant to these enzymes.

Classes of animal viruses

Animal viruses are diverse in their modes of infection and replication

1

Double- or single-stranded DNA?
Double- or single-stranded RNA?

2

Presence or absence of a membranous envelope derived from host cell membrane.

DNA

RNA

Table 18.1 Classes of Animal Viruses

Class/ Family	Envelope	Examples/ Disease
I. Double-stranded DNA (dsDNA)		
Adenovirus (see Figure 18.4b)	No	Respiratory diseases; animal tumors
Papovavirus	No	Papillomavirus (warts, cervical cancer); polyomavirus (animal tumors)
Herpesvirus	Yes	Herpes simplex I and II (cold sores, genital sores); varicella zoster (shingles, chicken pox); Epstein-Barr virus (mononucleosis, Burkitt's lymphoma)
Poxvirus	Yes	Smallpox virus; cowpox virus
II. Single-stranded DNA (ssDNA)		
Parvovirus	No	B19 parvovirus (mild rash)
III. Double-stranded RNA (dsRNA)		
Reovirus	No	Rotavirus (diarrhea); Colorado tick fever virus
IV. Single-stranded RNA (ssRNA); serves as mRNA		
Picornavirus	No	Rhinovirus (common cold); poliovirus, hepatitis A virus, and other enteric (intestinal) viruses
Coronavirus (see Figure 18.11b)	Yes	Severe acute respiratory syndrome (SARS)
Flavivirus	Yes	Yellow fever virus; West Nile virus; hepatitis C virus
Togavirus	Yes	Rubella virus; equine encephalitis viruses
V. ssRNA; template for mRNA synthesis		
Filovirus	Yes	Ebola virus (hemorrhagic fever)
Orthomyxovirus (see Figure 18.4c)	Yes	Influenza virus
Paramyxovirus	Yes	Measles virus; mumps virus
Rhabdovirus	Yes	Rabies virus
VI. ssRNA; template for DNA synthesis		
Retrovirus (see Figure 18.9)	Yes	HIV, human immunodeficiency virus (AIDS); RNA tumor viruses (leukemia)

Table 18.1

The reproductive cycle of an enveloped RNA virus

Some enveloped viruses enter the host cell by fusion of the envelope with the cell's plasma membrane; others enter by endocytosis.

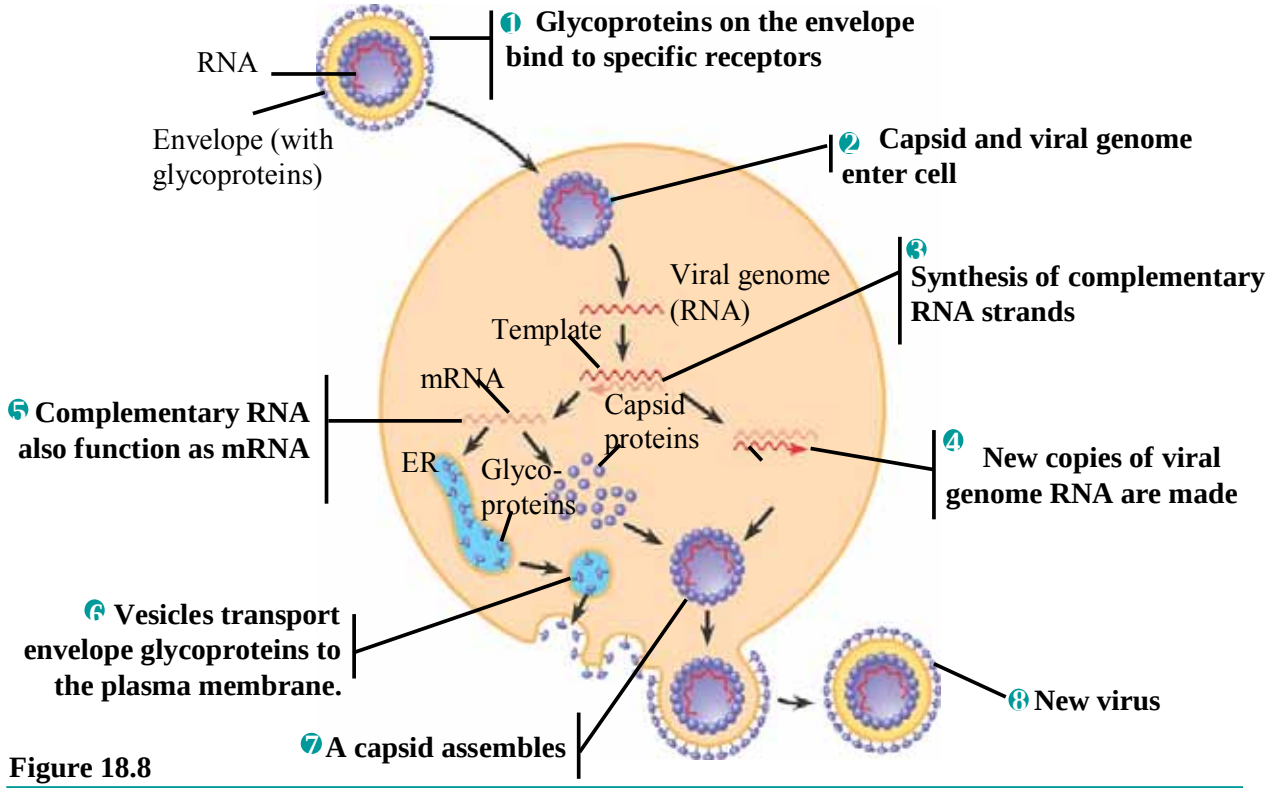


Figure 18.8

Retroviruses (class VI; eg. HIV)

- Contains two identical strands
- Virus carries an enzyme, **reverse transcriptase**, which transcribes DNA from an RNA template.
- The newly made DNA is inserted as a provirus into a chromosome in the animal cell.

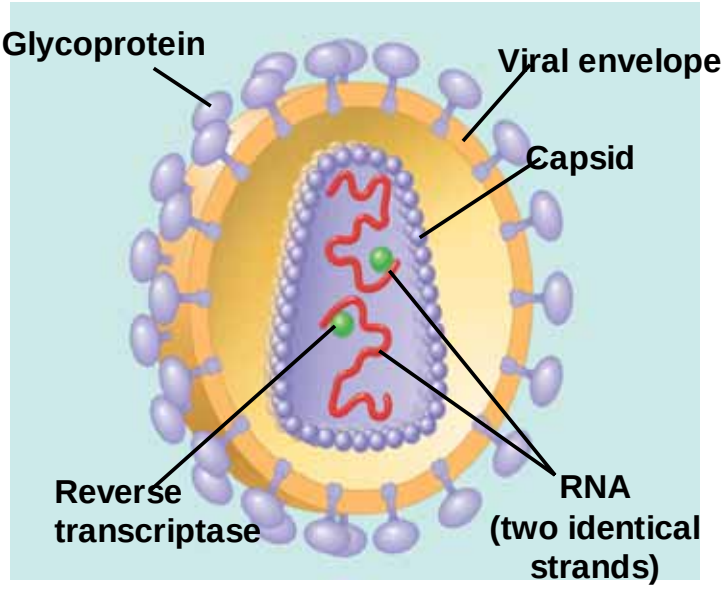
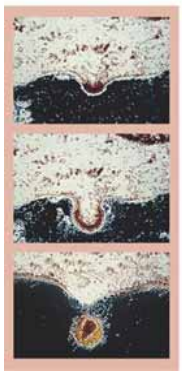


Figure 18.9

The reproductive cycle of HIV, a retrovirus

HIV entering a cell



Leaving a cell

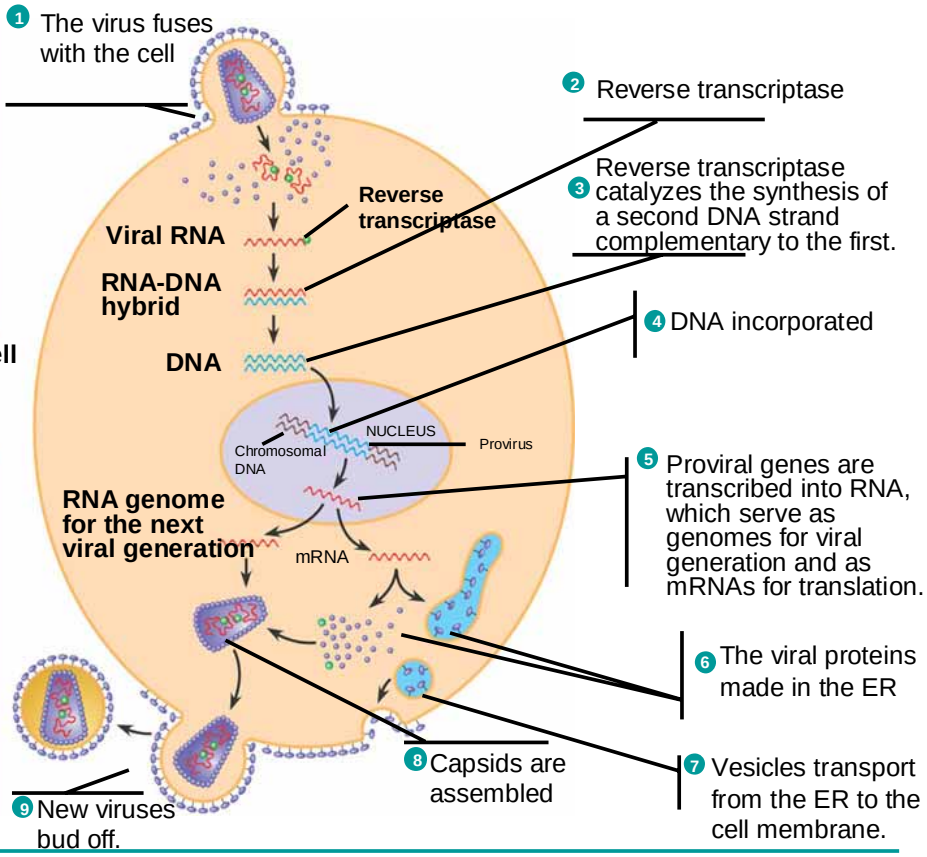


Figure 18.10

Evolution of Viruses —How did viruses originate?

The most complex or simplest forms of life???

- Viruses most likely are not the original forms of life
- A viral genome usually has more in common with the genome of its host than with the genomes of viruses infecting other hosts

Hypothesis

- Viruses may originate from fragments of cellular nucleic acids that could move from one cell to another via injured cell surfaces. The evolution of capsid proteins may have facilitated the infection of undamaged cells.

Candidates for the original sources of viral genomes

➔ plasmids and transposons

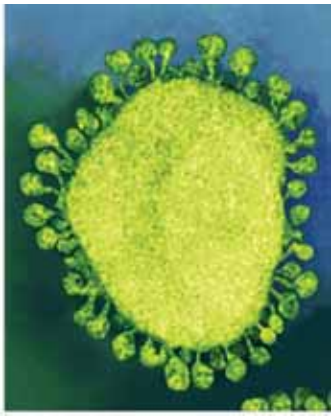
Emerging Viruses

Viruses that appear suddenly or that suddenly come to the attention of medical scientists

Examples:

- HIV: appeared in San Francisco in the early 1980s
- Ebola virus: recognized initially in central Africa in 1976
- SARS: first appeared in southern China in November 2002

(a)



(b) The SARS-causing agent is a coronavirus,so named for the “corona” of glycoprotein spikes protruding from the envelope.

Figure 18.11 A, B

From where and how do such viruses burst on the human scene (Outbreaks)?

1. The mutation of existing viruses

   RNA viruses tend to have the highest rate of mutation.
   eg. Flu virus

2. Spread of existing viruses from one host species to another

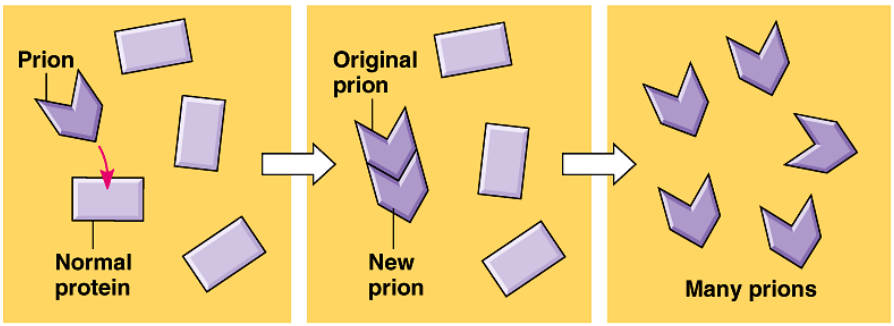
   ~3/4 of new human diseases originate in other animals.
   eg. Hantavirus; SARS

3. The dissemination from a small and isolated population through technological and social factors

   eg. HIV (AIDS)

Viroids (類病毒) and prions (朊毒體) are infectious agents even simpler than viruses

- **Viroids:** circular RNA molecules (only 200-400 nucleotides long) that infect plants.
- **Prions** are infectious *proteins* that spread diseases.
  - Hypothesis: a prion is a **misfolded form** of a normal brain protein.



  - cause several degenerative brain diseases including scrapie in sheep, “mad cow disease”, and Creutzfeldt-Jacob disease in humans.

Section: The Genetics of Bacteria

— "the laboratory rat of molecular biology."

- The bacterial genome is one **double-stranded, circular DNA** molecule.
  - For *E. coli*, the chromosomal DNA consists of about 4.6 million nucleotide pairs with about **4,400 genes**.
  - This is 100 times more DNA than in a typical virus and 1,000 times less than in a typical eukaryote cell.
  - Tight coiling of the DNA results in a dense region of DNA, called the **nucleoid,** not bounded by a membrane.
- In addition, many bacteria have **plasmids**, much smaller circles of DNA that can **replicate independently**.
  - Each plasmid has only a small number of genes, from just a few to several dozen.

•Replication of the bacterial chromosome is from a single origin of replication.

•Enzymes that cut and reseal the double helix prevent the DNA from tangling.

•E. coli growing under optimal conditions can divide every 20 minutes.

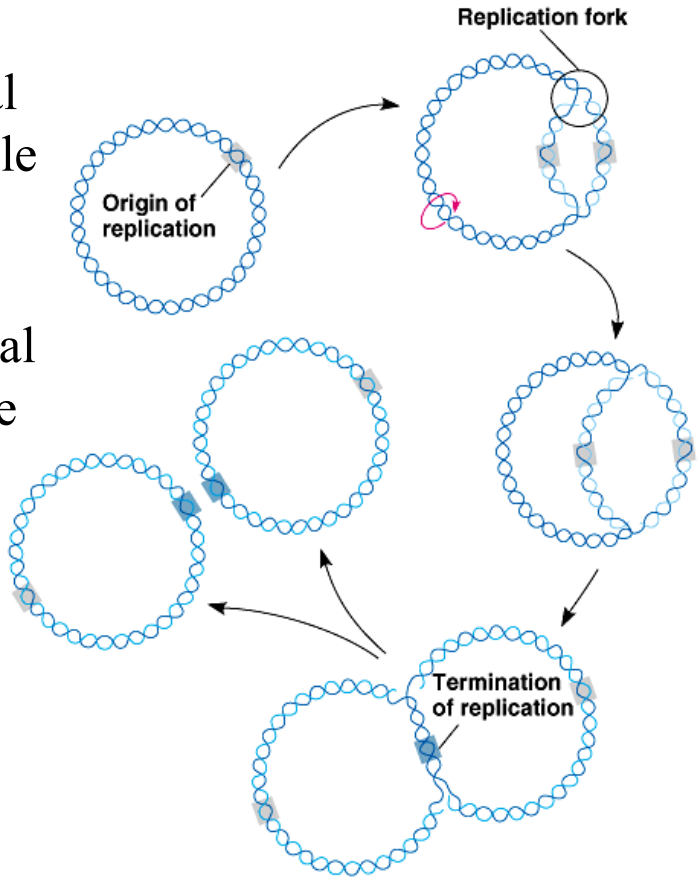
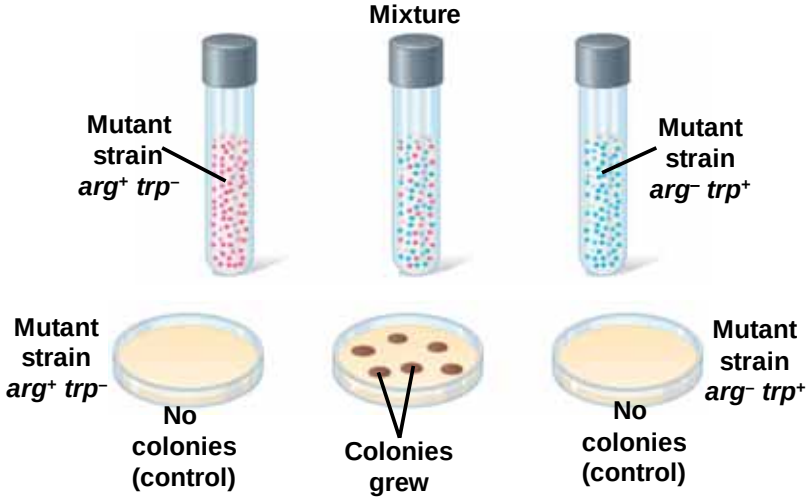


Fig. 18.14

Mutation and genetic recombination produces new bacterial strains

- Spontaneous mutation rate in E. coli gene:
  ➔ ~1 x 10^{-7} per cell division

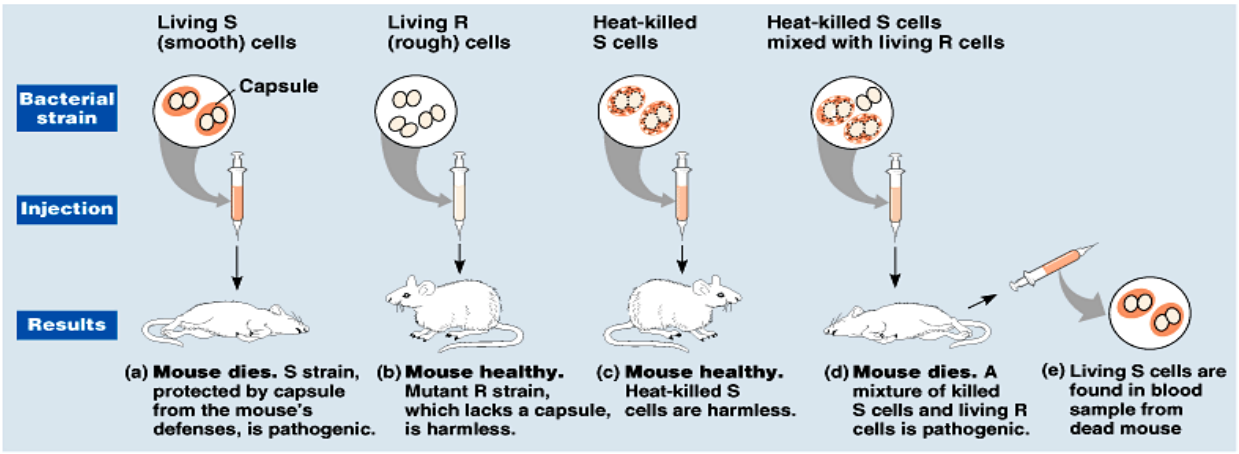
- Genetic recombination



The genetic recombination in bacteria includes three processes :

1. Transformation

The alteration of a bacterial cell ´ s genotype and phenotype by the uptake of naked, foreign DNA from the surrounding environment.



The genetic recombination in bacteria includes three processes :

2. Transduction

- Case 1:

Phages (the bacterial viruses) carry bacterial genes from one host cell to another as a result of aberrations in the phage reproductive cycle.

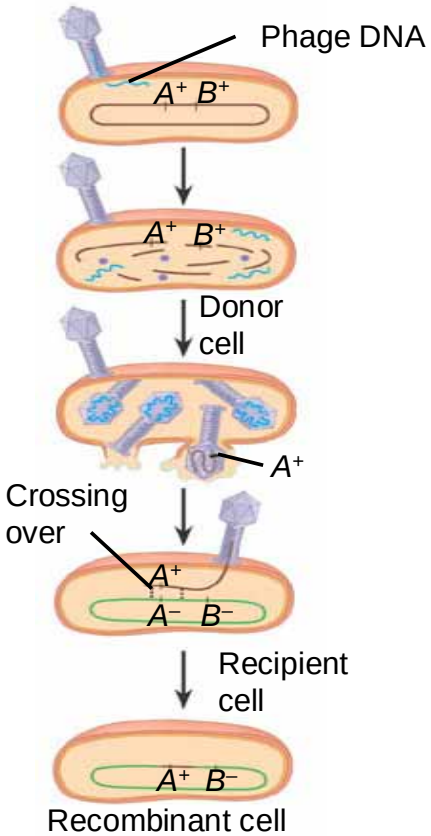


Figure 18.16

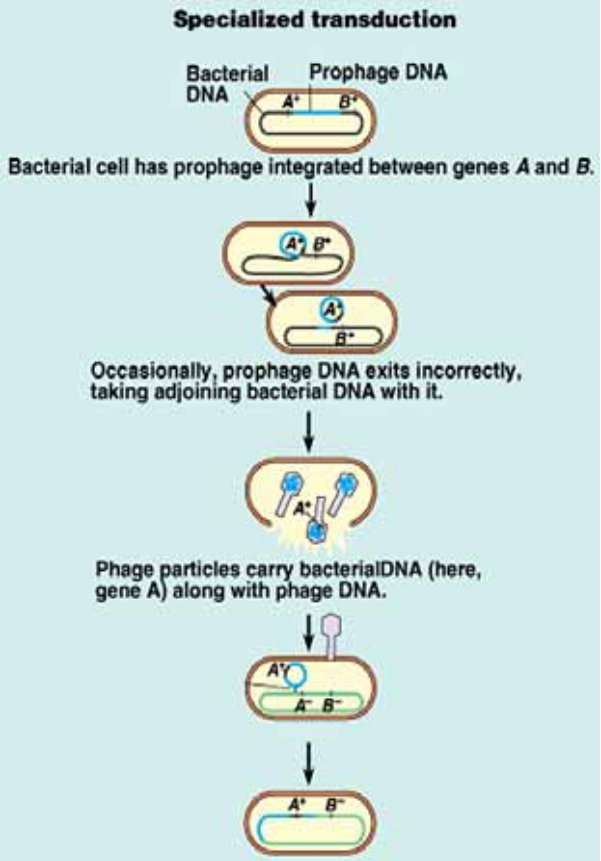
The genetic recombination in bacteria includes three processes :

2. Transduction

- Case 2:

Temperate phage (eg. phage λ)

Prophage picks up adjacent bacterial genes and transfers them to a new host cell



The genetic recombination in bacteria includes three processes :

3. Conjugation — bacterial "sex,"

- The direct transfer of genetic material between two bacterial cells that are temporarily joined
- The DNA transfer is one–way:
  ➔ From the donor (form sex pili) to the recipient
- A temporary cytoplasmic mating bridge then forms between the two cells

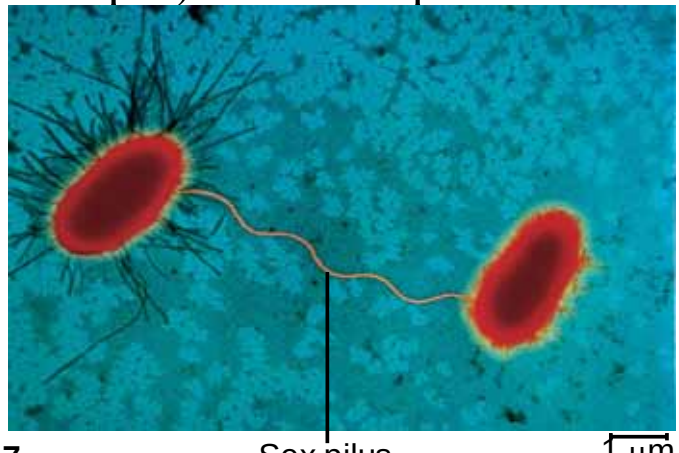


Figure 18.17

F factor (F for fertility):

- A special piece of DNA that allows the bacteria to form sex pili and donate DNA during conjugation.
- Can exist either as a segment of DNA within the bacterial chromosome, as a plasmid or as a **episome**.
  - **Episome**
    A genetic element that can replicate either as part of the bacterial chromosome or independently of it.
- **F Plasmid**
  - The plasmid contains the F factor
- **Hfr cell (for High frequency of recombination)**
  - A cell with the F factor built into its chromosome

Conjugation and transfer of an **F plasmid** from an F^+ donor to an F^- recipient

Rolling circle replication ("toilet paper" model)

- DNA replication is initiated at a specific point on the F factor DNA; from that point, a single strand of the F factor DNA rolls into the F− partner

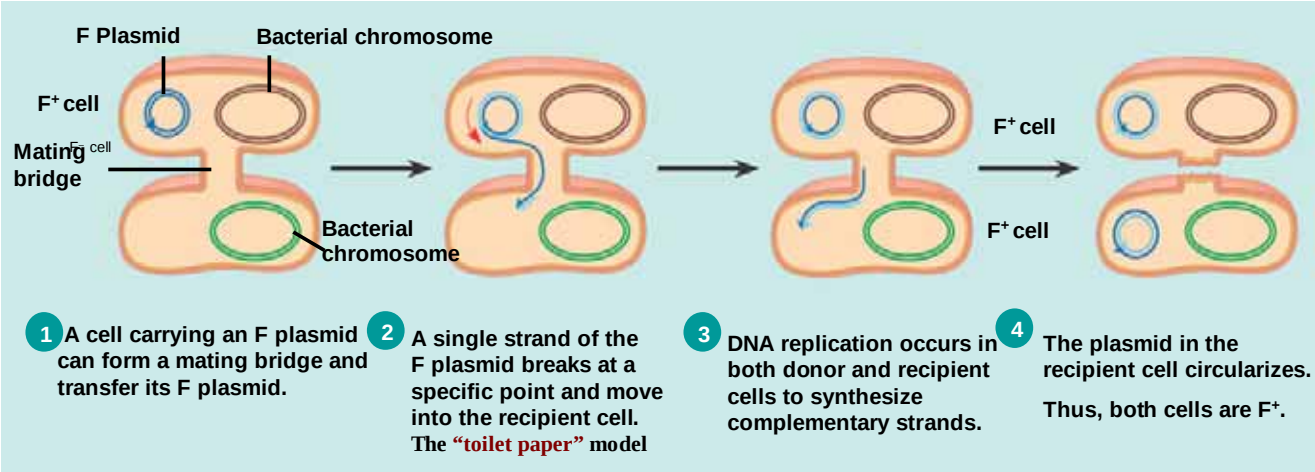


Figure 18.18a. Conjugation and transfer of an F plasmid from an F+ donor to an F– recipient

Conjugation and transfer of part of the bacterial chromosome from an Hfr donor to an F⁻ recipient, resulting in recombination

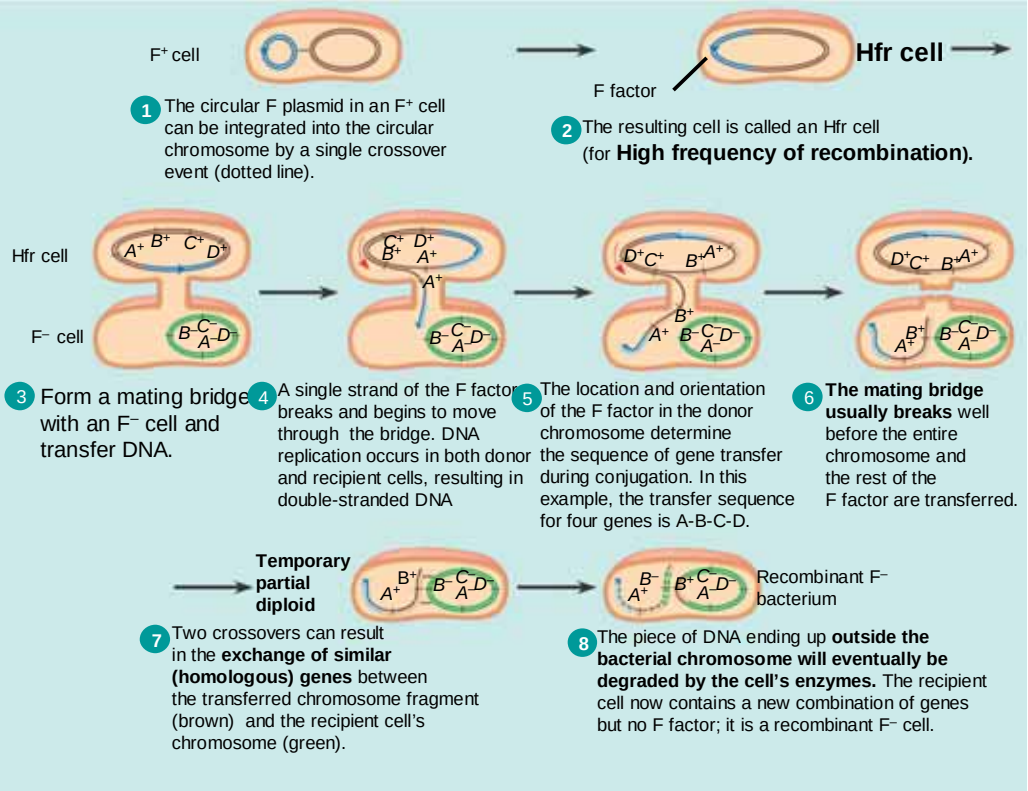


Figure 18.18(b)

R plasmids and Antibiotic Resistance

- **R plasmids (R for resistance)**
  Plasmids that contain genes conferring resistance to various antibiotics
  - Reduce the pathogen´s ability to **transport** a particular antibiotic into the cell.
  - **Alter the intracellular target protein** for an antibiotic molecule, reducing its inhibitory effect.
  - **Code for enzymes** that specifically destroy certain antibiotics, such as tetracycline or ampicillin.

Transposition of Genetic Elements

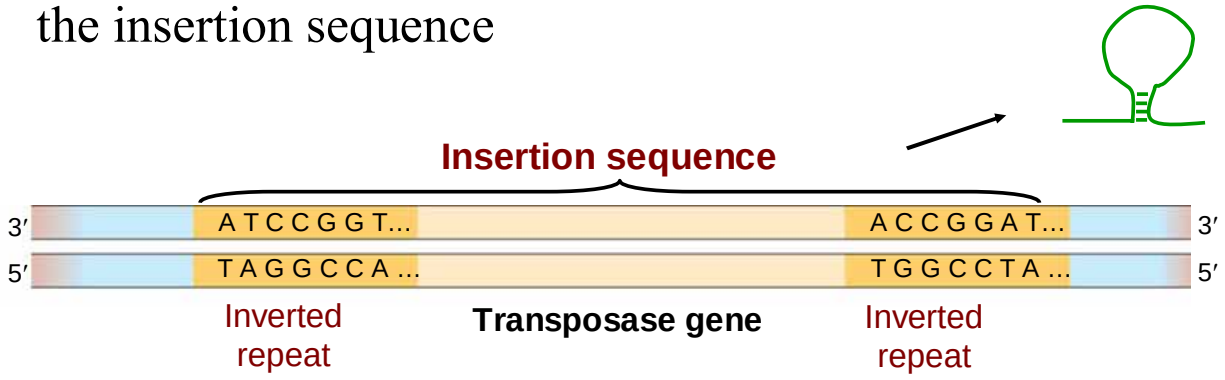
- **Transposable elements**
  - —The DNA fragment of a single cell can undergo **recombination** to move from one site in a cell´s DNA to another site
- **The misleading of "jumping genes"**
  - — Unlike a plasmid or prophage, transposable elements **never exist independently** but are always part of chromosomal or plasmid DNA.
  - —The original and new DNA sites are brought together by DNA folding.

    By "cut–and–paste" mechanism or
    "copy–and–paste" mechanism

2 types of transposable elements

Insertion sequences

- The simplest transposable elements **exist only in bacteria**
- Contains only one single gene, which codes for **transposase**, an enzyme that catalyzes movement of the insertion sequence



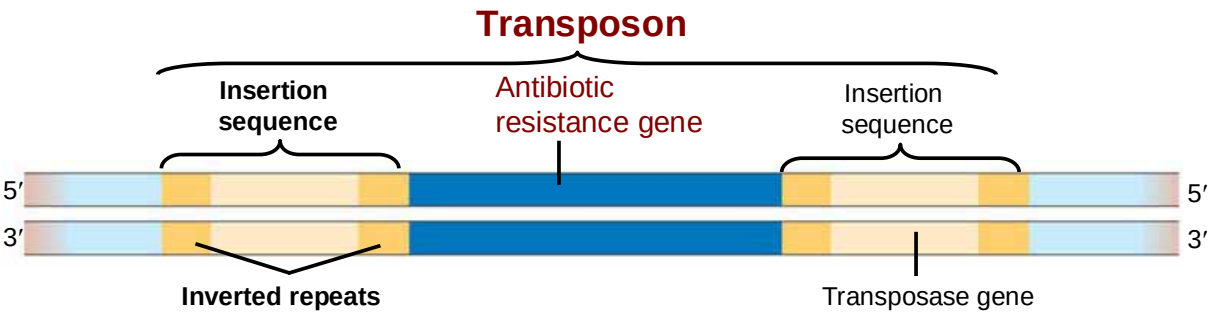
(a) The inverted repeats are backward, upside-down versions of each other; only a portion is shown. The inverted repeat sequence varies from one type of insertion sequence to another.

Figure 18.19a

2 types of transposable elements

Transposons

- Transposable elements longer and more complex than insertion sequences
- Include extra genes such as genes for antibiotic resistance



(b) Transposons contain one or more genes in addition to the transposase gene located between twin insertion sequences.

Figure 18.19

Barbara McClintock (1902-1992)
1983 Nobel Laureate in Medicine

Bacteria respond to environmental change by regulating their gene expression

– Metabolic control occurs on two levels

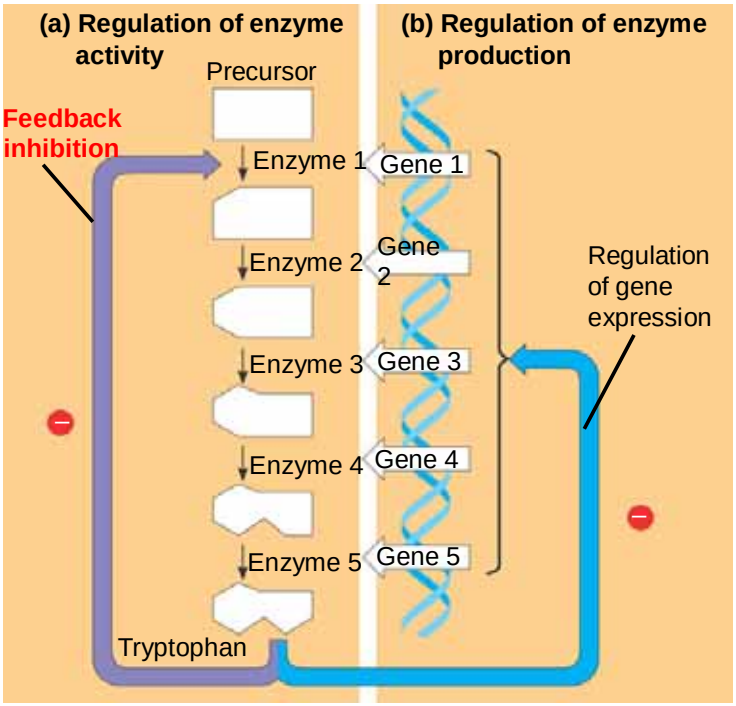


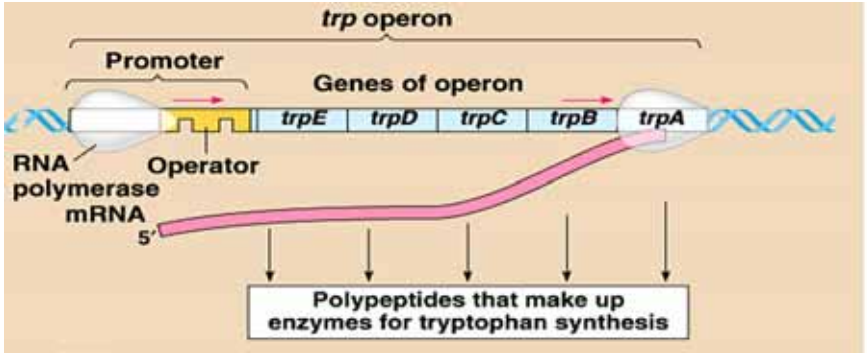
Figure 18.20a, b

Operator and operon

- **Operator**

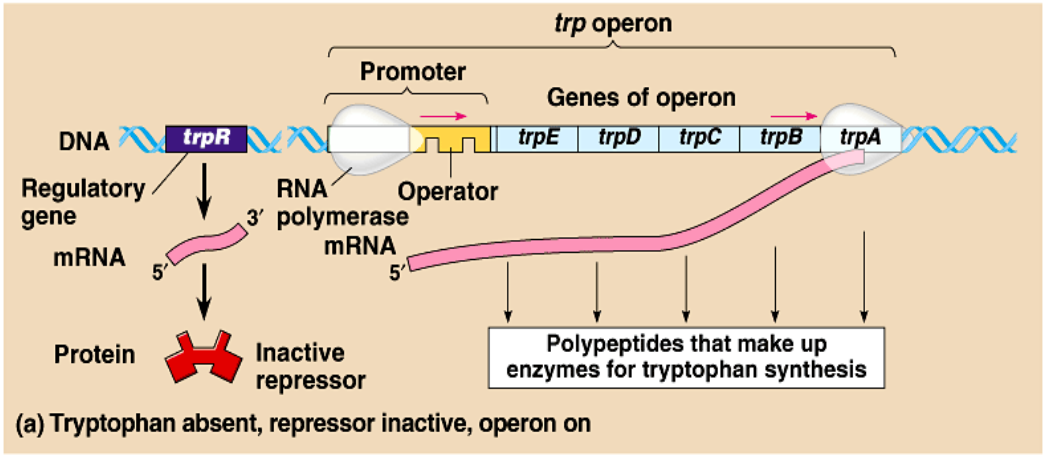
  A segment of DNA (an on–off "switch") can control the whole cluster of functionally related genes.

  Positioned within the promoter or between the promoter and the enzyme–coding genes



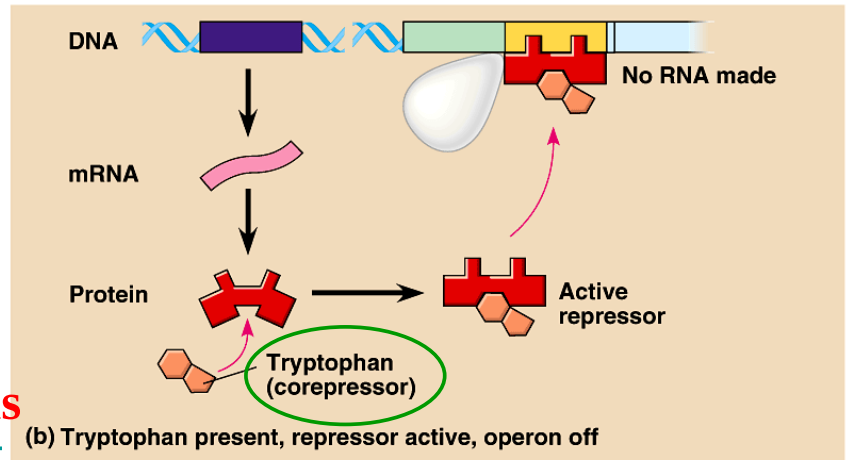
- **Operon**

  A cluster of that contains operator, the promoter, and the genes they control



The *trp* operon can be switched off by a protein called the **repressor, the product of a regulatory gene**

- **Repressible operons**



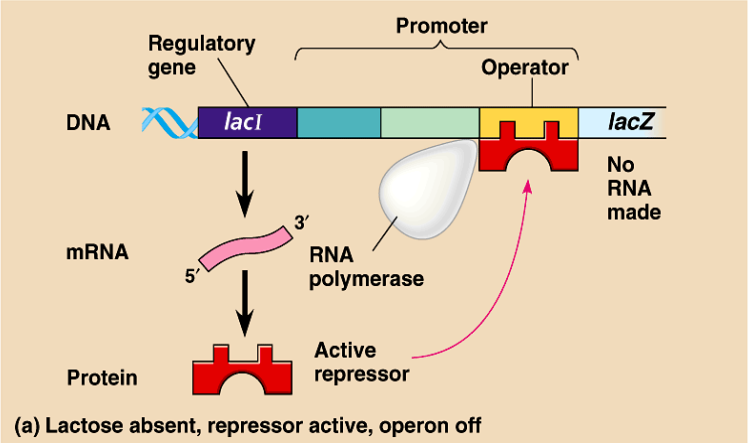
Repressible and Inducible Operons: Two Types of Negative Gene Regulation

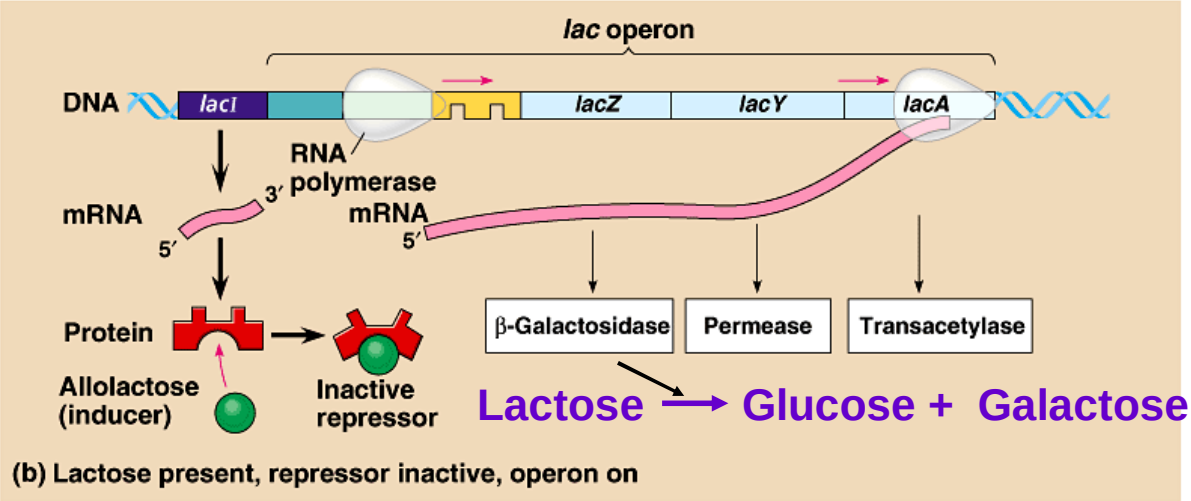
- **In a repressible operon**
  Binding of a specific repressor protein to the operator **shuts off** transcription
  - eg. The *trp* operon

- **In an inducible operon**
  Binding of an inducer to an innately inactive repressor inactivates the repressor and **turns on** transcription
  - eg. the *lac* operon (lactose (milk sugar) **)**

Inducible operon

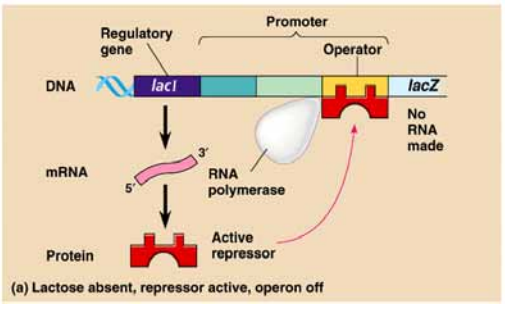
Inducer: **allolactose**, an isomer of lactose formed in small amounts from lactose





Negative Gene Regulation

- eg. Regulation of both the *trp* and *lac* operons
  - — because the operons are switched off by the active form of the repressor protein



Positive Gene Regulation

- eg. *lac* operons controlled by catabolite activator protein **(CAP)**
  - — CAP is an activator of transcription.

Lactose ⟶ Glucose + Galactose

- In *E. coli*, when glucose, a preferred food source, is scarce
  - ➔ cyclic AMP (cAMP) which accumulates
    - ➔ cAMP binds to CAP and assumes its active shape
      - ➔ Activated CAP binds to a specific site at the upstream end of the lac promoter

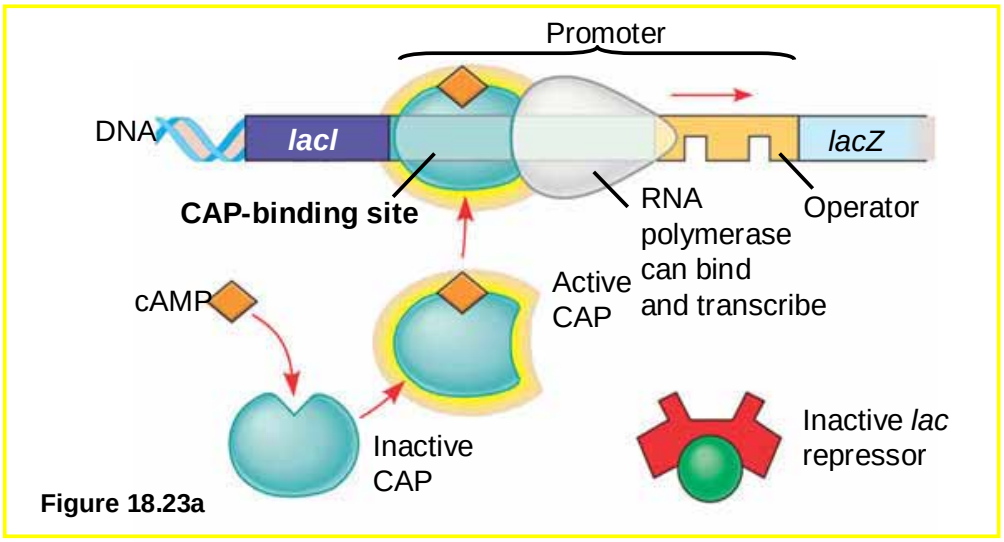


Figure 18.23a

- **When glucose is present**
  - ➔ cAMP is scarce
    - ➔ CAP is unable to stimulate transcription.

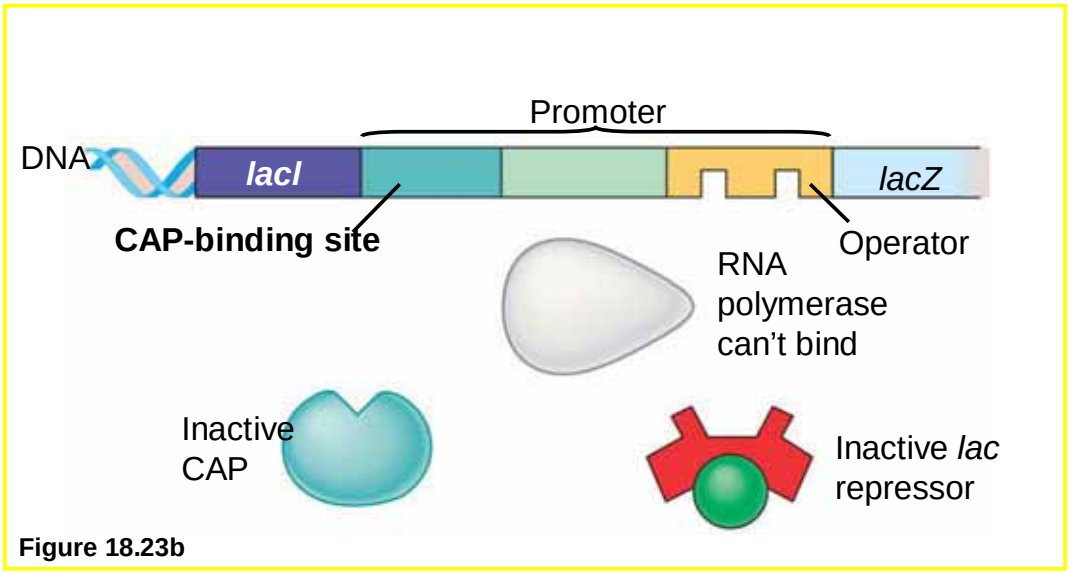


Figure 18.23b