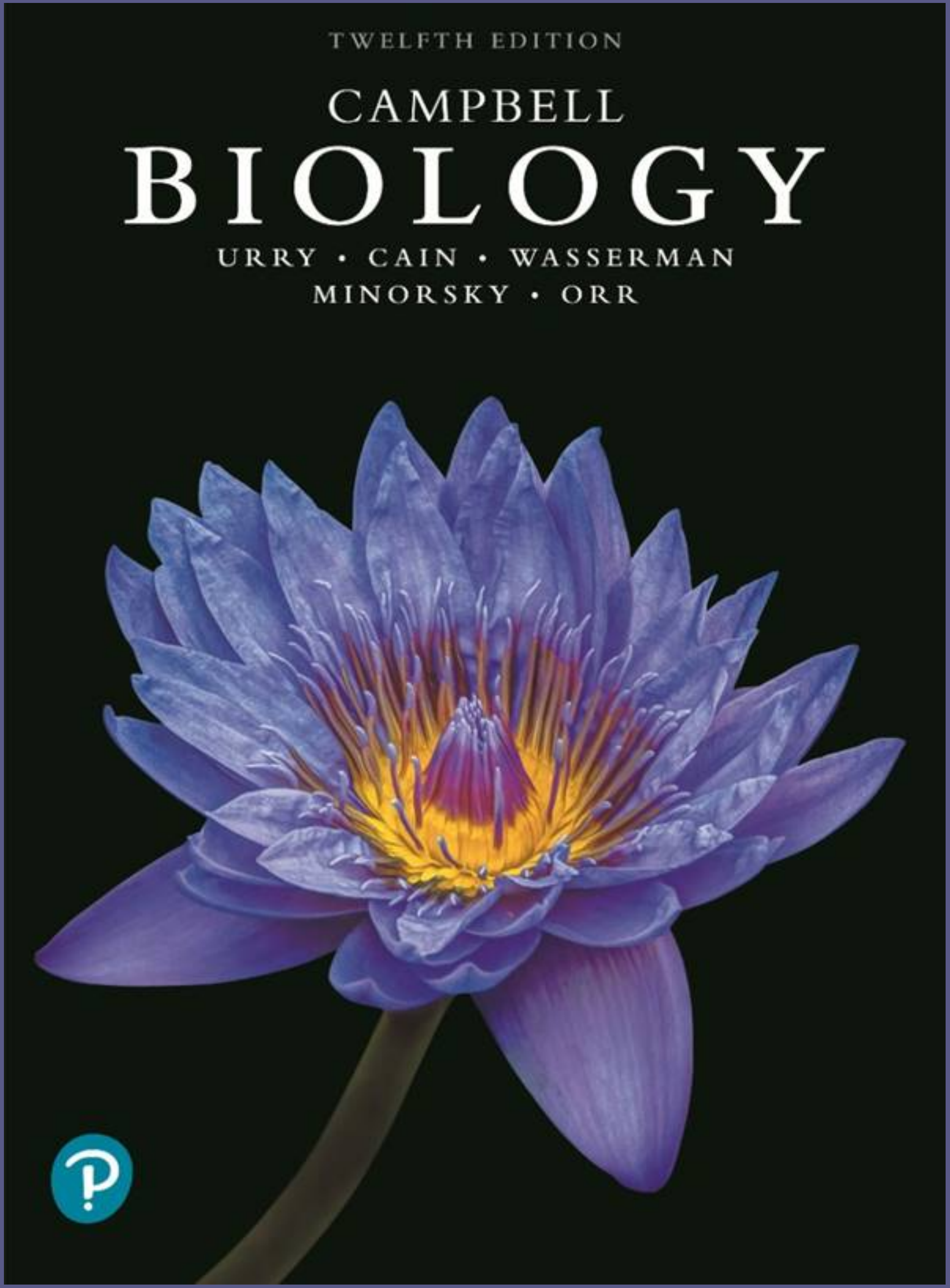


Chapter 19

Viruses

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

Figure 19.1a

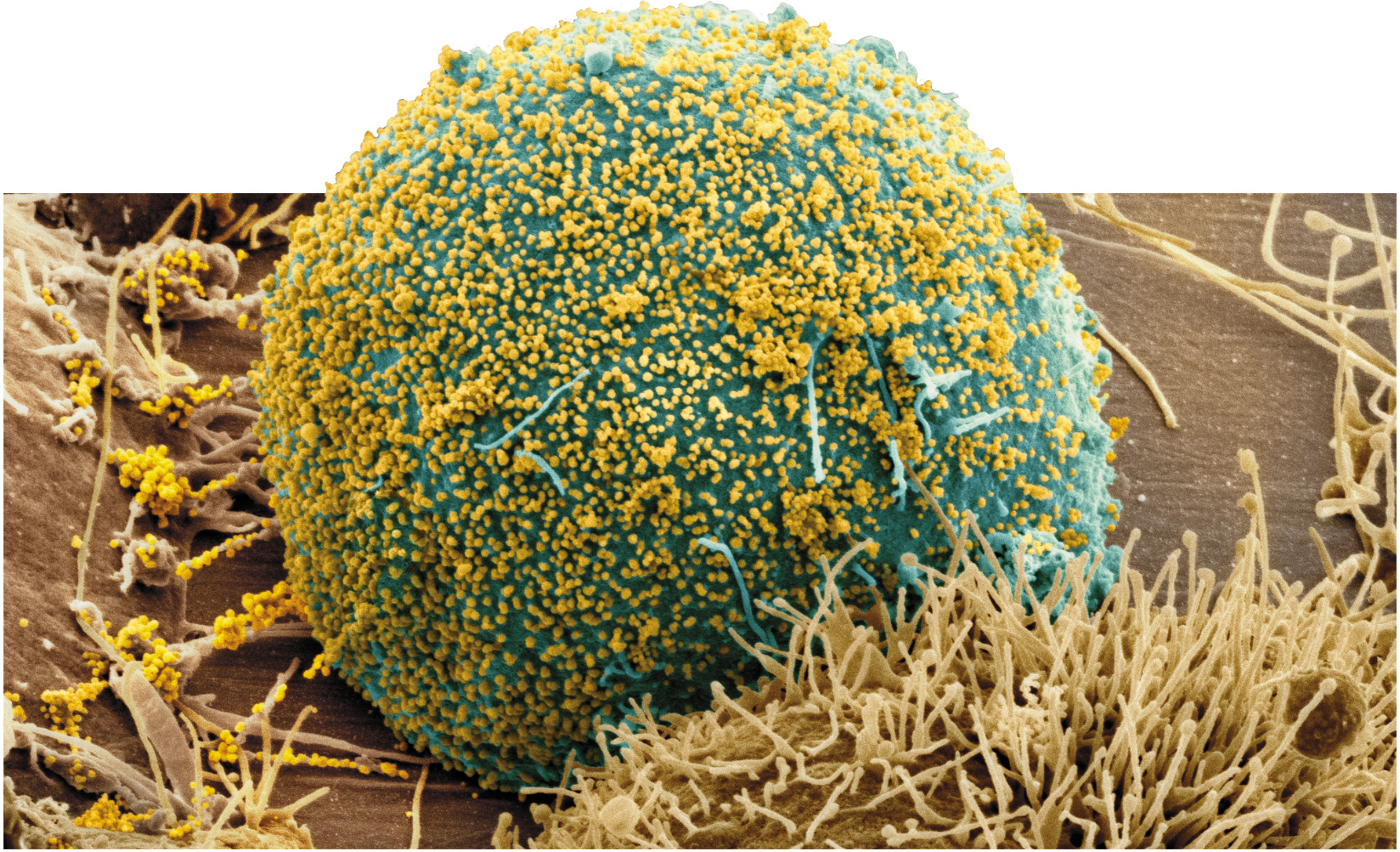
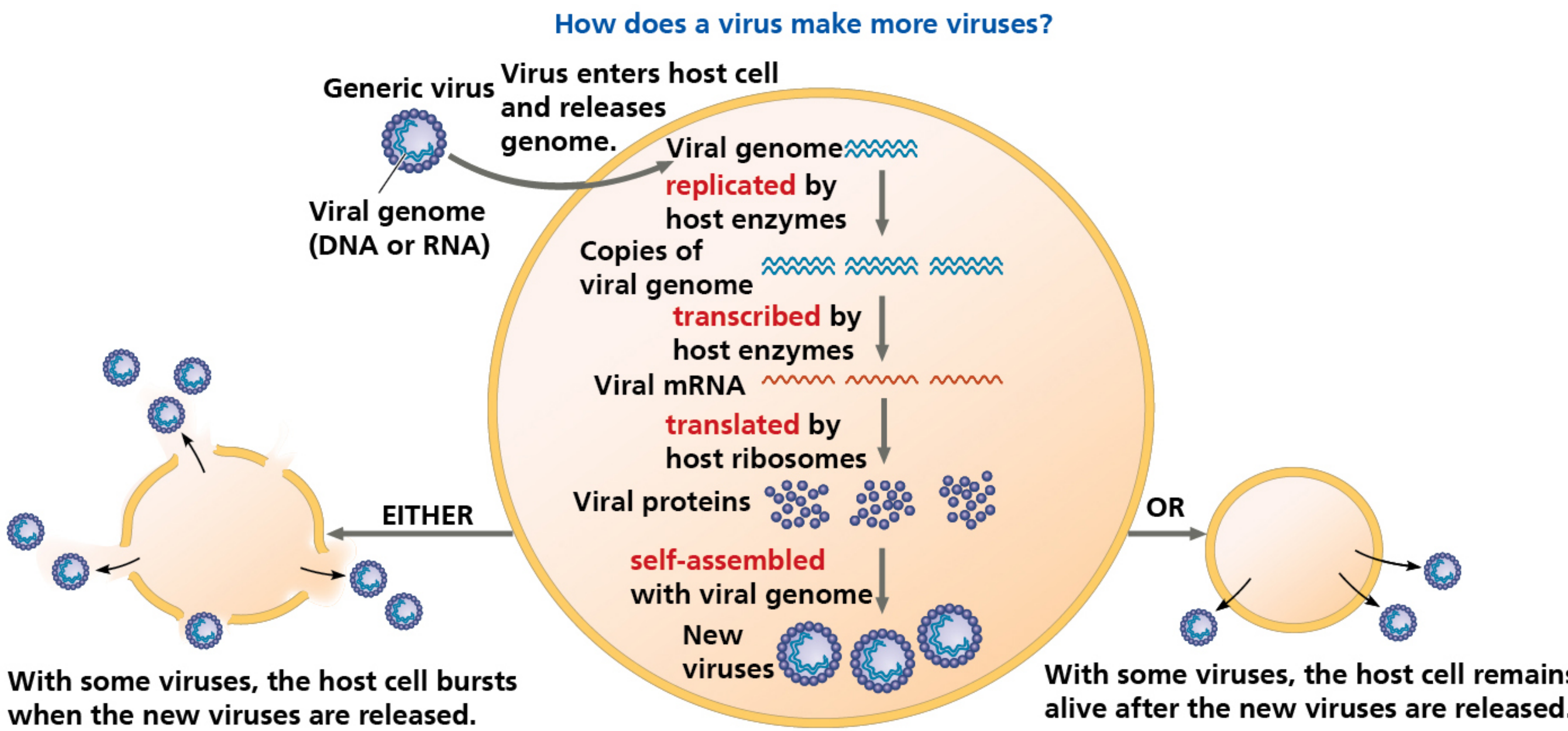


Figure 19.1b



How does a virus make more viruses?
Generic virus
Virus enters host cell and releases genome.
Viral genome (DNA or RNA)
Viral genome
replicated by host enzymes
Copies of viral genome
transcribed by host enzymes
Viral mRNA
translated by host ribosomes
Viral proteins
self-assembled with viral genome
New viruses
EITHER
OR
With some viruses, the host cell bursts when the new viruses are released.
With some viruses, the host cell remains alive after the new viruses are released.

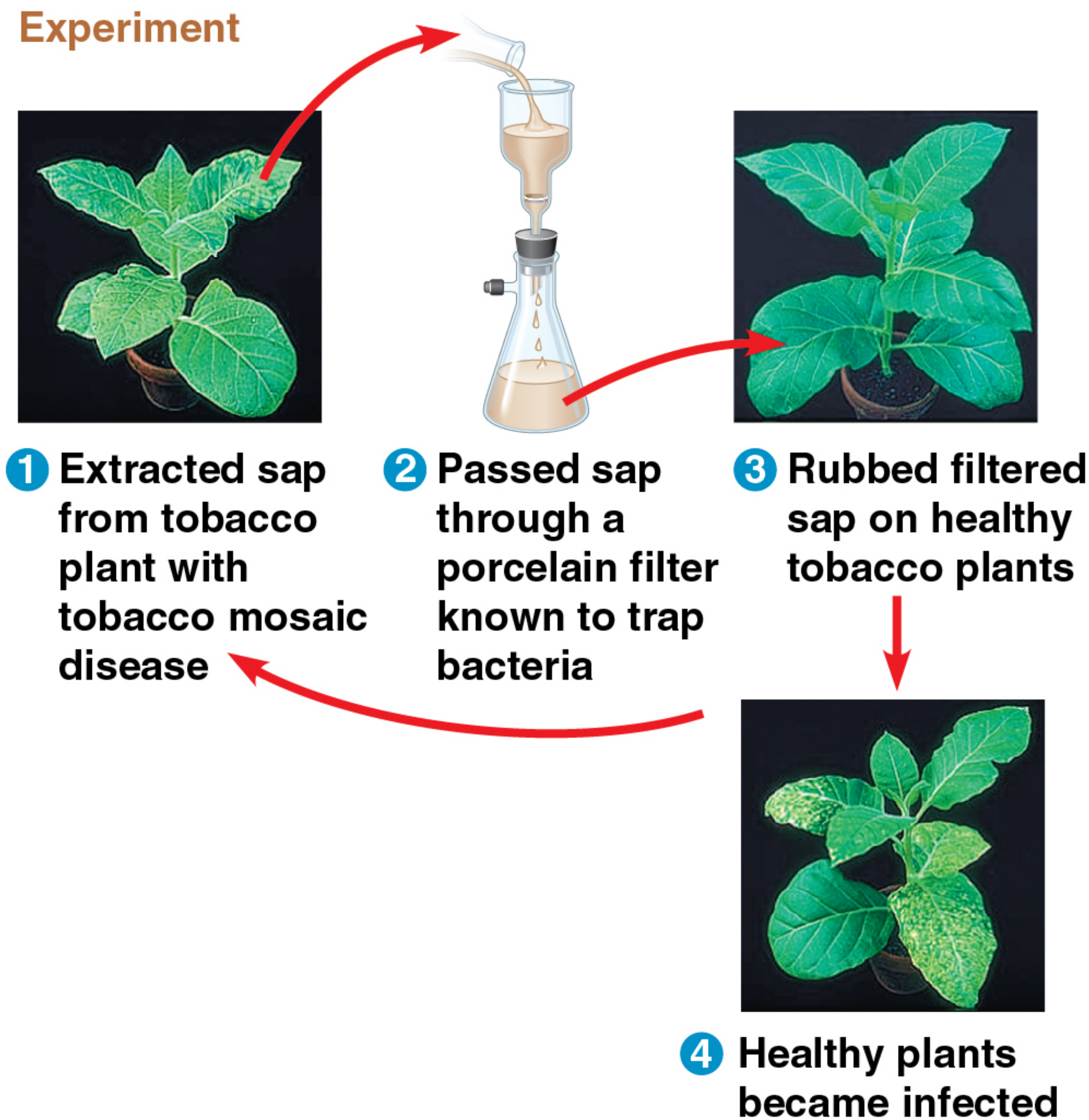
CONCEPT 19.1: A virus consists of a nucleic acid surrounded by a protein coat

- A **virus** is an infectious particle consisting of genes packaged in a protein coat
- Viruses are much simpler in structure than even prokaryotic cells
- Viruses can cause a wide variety of diseases
- They cannot reproduce or carry out metabolism outside of a host cell
- Viruses exist in a shady area between life-forms and chemicals, leading a kind of "borrowed life"

The Discovery of Viruses: *Scientific Inquiry*

- Tobacco mosaic disease stunts growth of tobacco plants and gives their leaves a mosaic coloration
- In the late 1800s, researchers hypothesized that unusually small bacteria might be responsible
- Later work suggested that the infectious agent did not share features with bacteria (such as the ability to grow on nutrient media)
- In 1935, Wendell Stanley confirmed this latter hypothesis by crystallizing the infectious particle, now known as tobacco mosaic virus (TMV)

Figure 19.2


Experiment
1 Extracted sap from tobacco plant with tobacco mosaic disease
2 Passed sap through a porcelain filter known to trap bacteria
3 Rubbed filtered sap on healthy tobacco plants
4 Healthy plants became infected

Structure of Viruses

- Viruses are not cells
- A virus is a very small infectious particle consisting of nucleic acid enclosed in a protein coat and, in some cases, a membranous envelope
- The simple structure of viruses make them a useful biological system

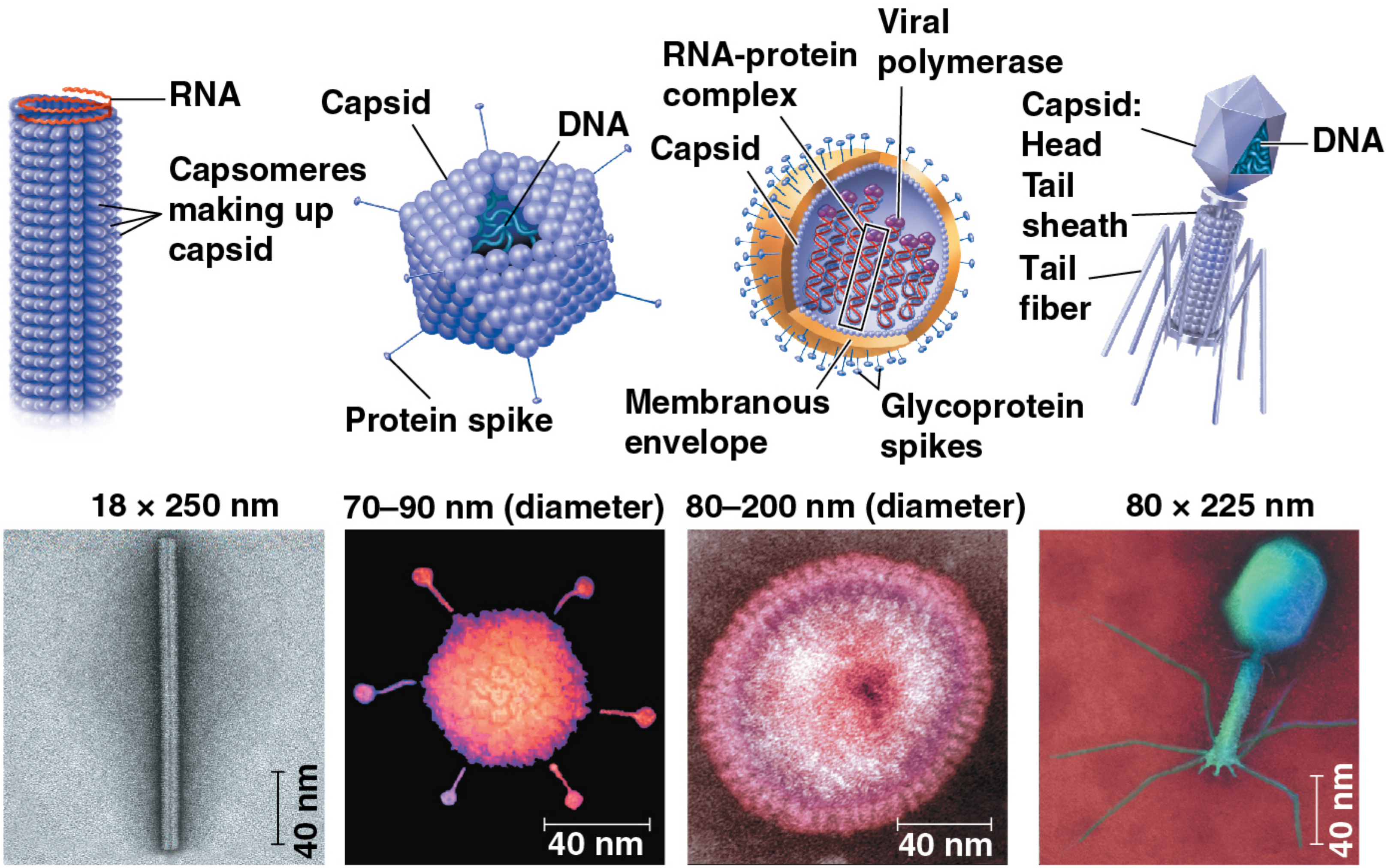
Viral Genomes

- Viral genomes may consist of either
  - double- or single-stranded DNA or
  - double- or single-stranded RNA
- Viruses are classified as DNA viruses or RNA viruses
- The genome is either a single linear or circular molecule of the nucleic acid
- Viruses have between 3 and 2,000 genes in their genome

Capsids and Envelopes

- A **capsid** is the protein shell that encloses the viral genome
- Capsids are built from protein subunits called *capsomeres*
- A capsid can have a variety of structures; associated viruses may be referred to as helical or icosahedral viruses

Figure 19.3



(a) Tobacco mosaic virus

(b) Adenovirus

(c) Influenza virus

(d) Bacteriophage T4

- Some viruses have accessory structures that help them infect hosts
- **Viral envelopes** (derived from membranes of host cells) surround the capsids of influenza viruses and many other viruses found in animals
- Viral envelopes contain a combination of viral and host cell molecules

- **Bacteriophages**, also called **phages**, are viruses that infect bacteria
- They have an elongated capsid head that encloses their DNA
- A protein tail piece attaches the phage to the host and injects the phage DNA inside

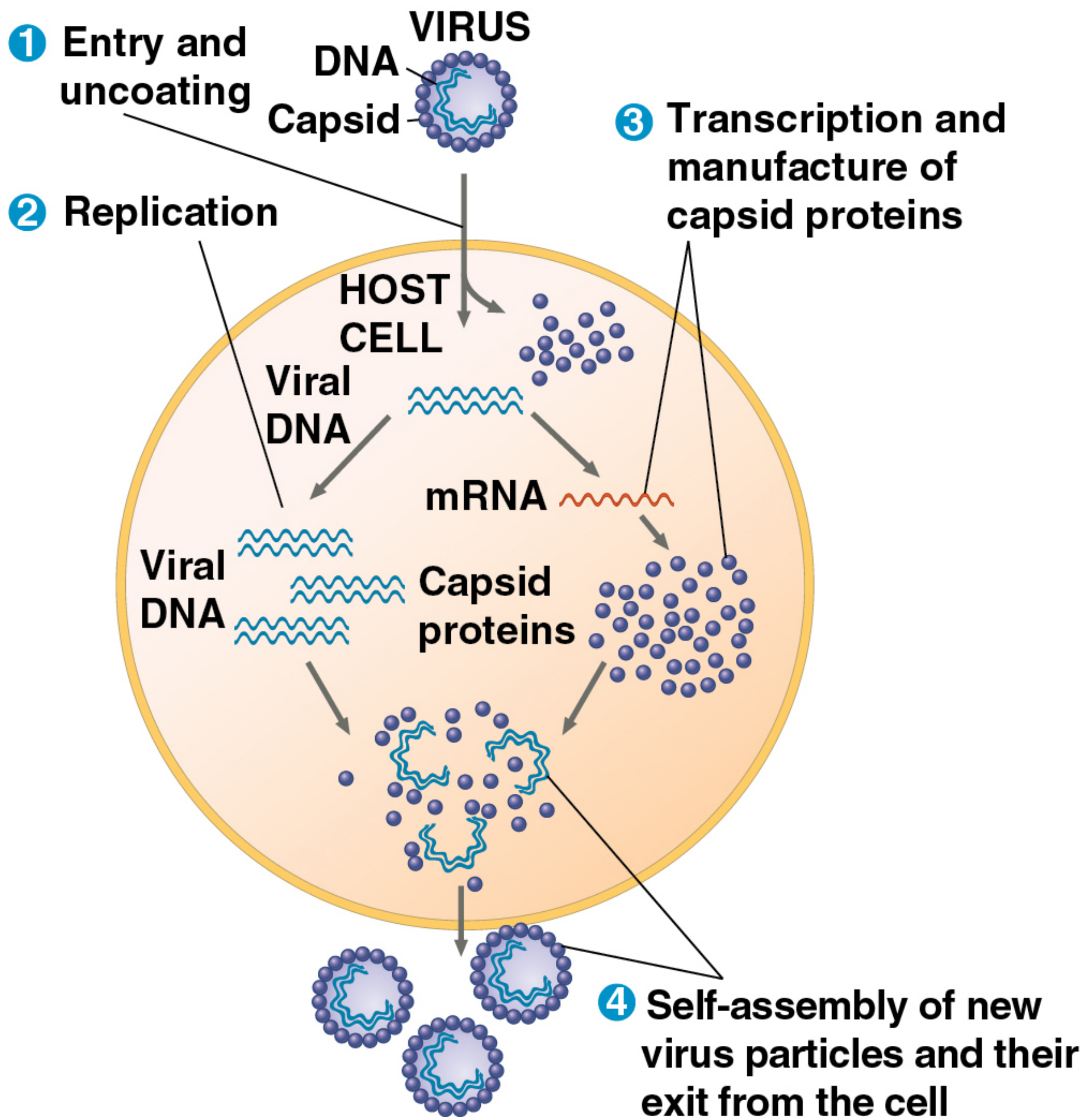
CONCEPT 19.2: Viruses replicate only in host cells

- Viruses are obligate intracellular parasites, which means they can replicate only within a host cell
- Each virus has a **host range**, a limited number of host species that it can infect
- Some viruses have broad host ranges, while others are able to infect only one species
- For example, measles virus only infects humans

General Features of Viral Replicative Cycles

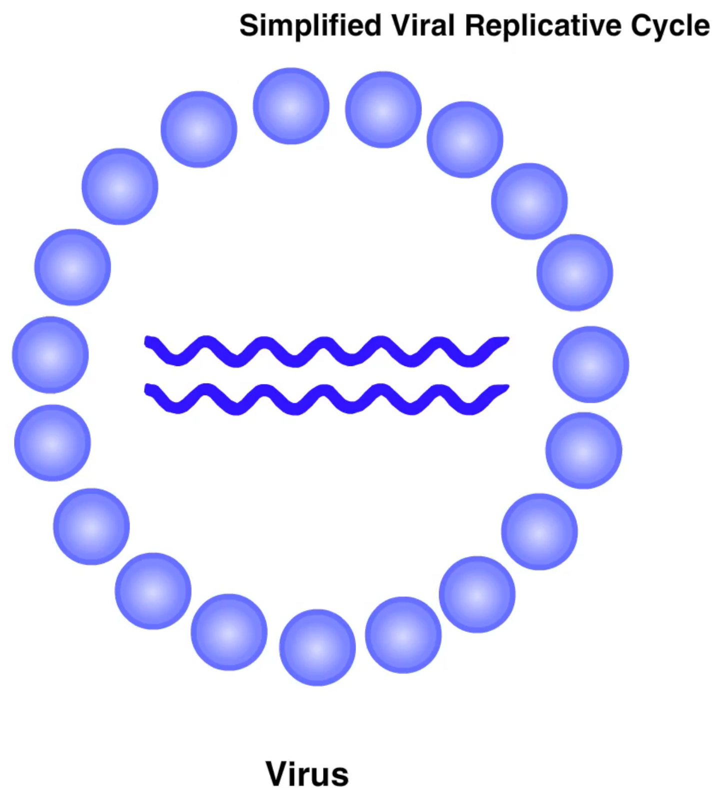
- The viral genome enters the host cell in a variety of ways
- Once a viral genome has entered a cell, the cell begins to manufacture viral proteins
- The virus makes use of host enzymes, ribosomes, tRNAs, amino acids, ATP, and other molecules
- Viral nucleic acid molecules and capsomeres spontaneously self-assemble into new viruses

Figure 19.4



1 Entry and uncoating
VIRUS
DNA
Capsid
2 Replication
3 Transcription and manufacture of capsid proteins
HOST CELL
Viral DNA
mRNA
Viral DNA
Capsid proteins
4 Self-assembly of new virus particles and their exit from the cell

Animation: Simplified Viral Replicative Cycle



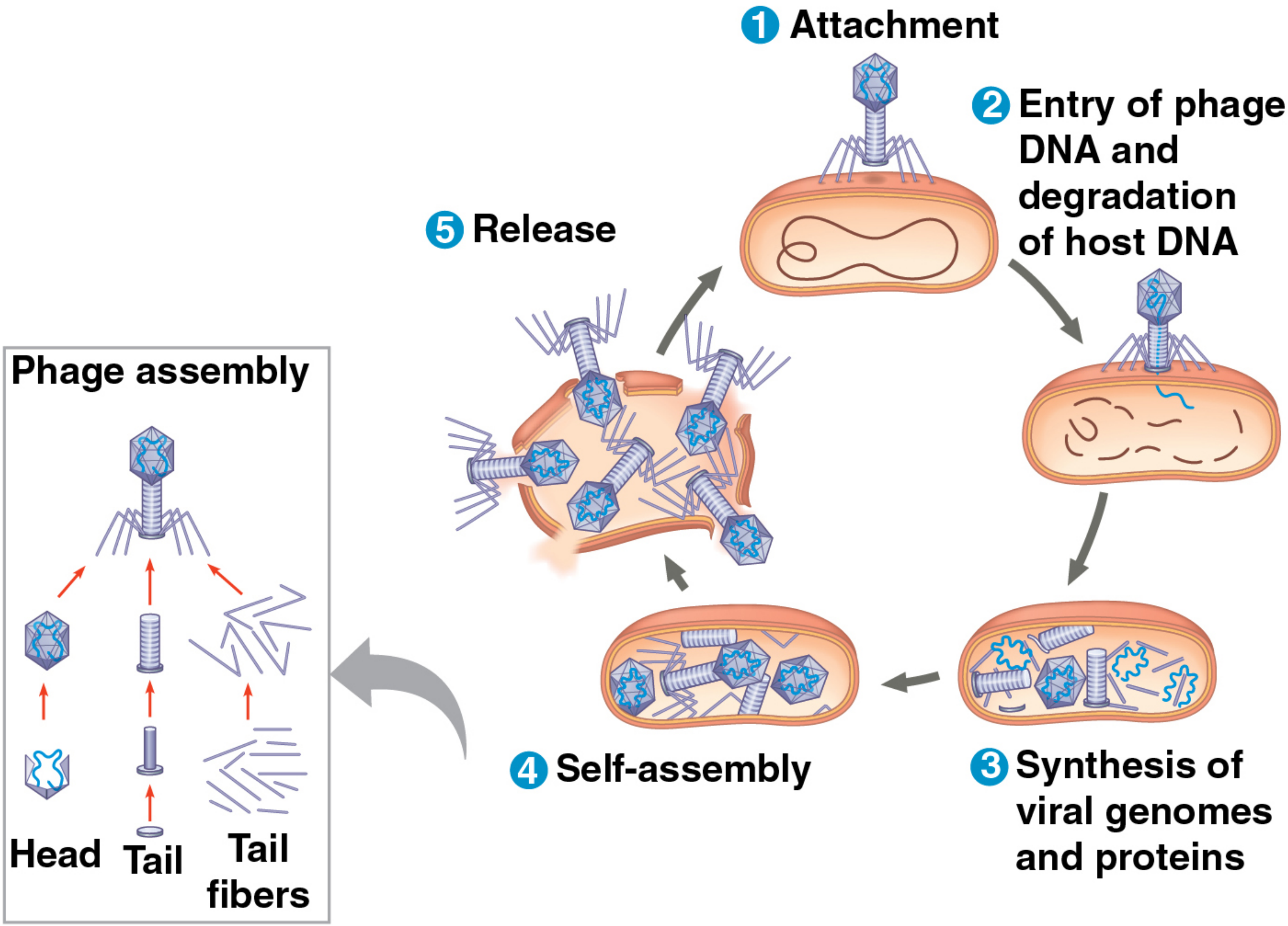
Replicative Cycles of Phages

- Phages are the best understood of all viruses
- Phages have two alternative reproductive mechanisms: the lytic cycle and the lysogenic cycle

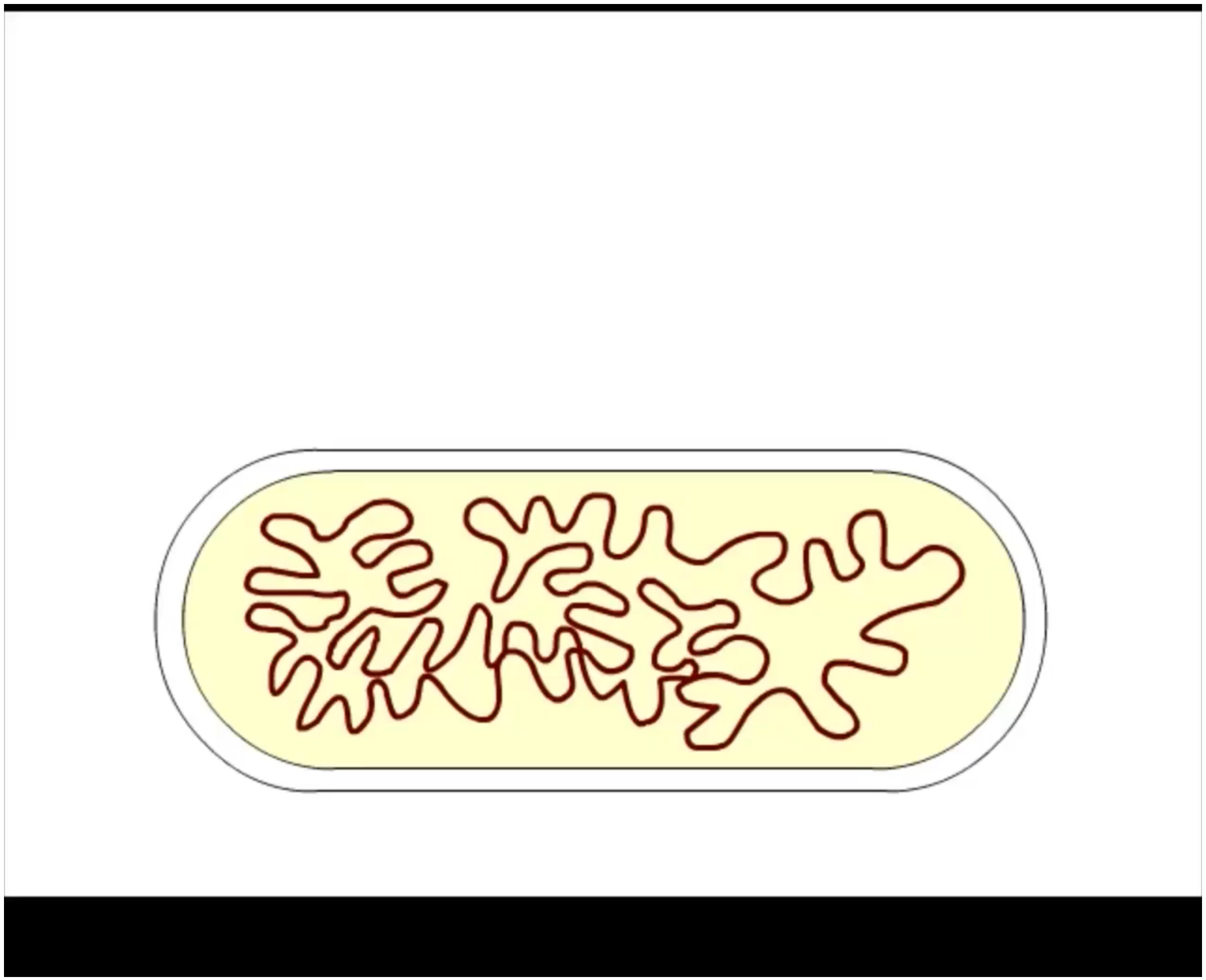
The Lytic Cycle

- The **lytic cycle** is a phage replicative cycle that culminates in the death of the host cell
- The lytic cycle produces new phages and lyses (breaks open) the host’s cell wall, releasing the progeny viruses
- A phage that reproduces only by the lytic cycle is called a **virulent phage**

Figure 19.5


1 Attachment
2 Entry of phage DNA and degradation of host DNA
3 Synthesis of viral genomes and proteins
4 Self-assembly
5 Release
Phage assembly
Head
Tail
Tail fibers

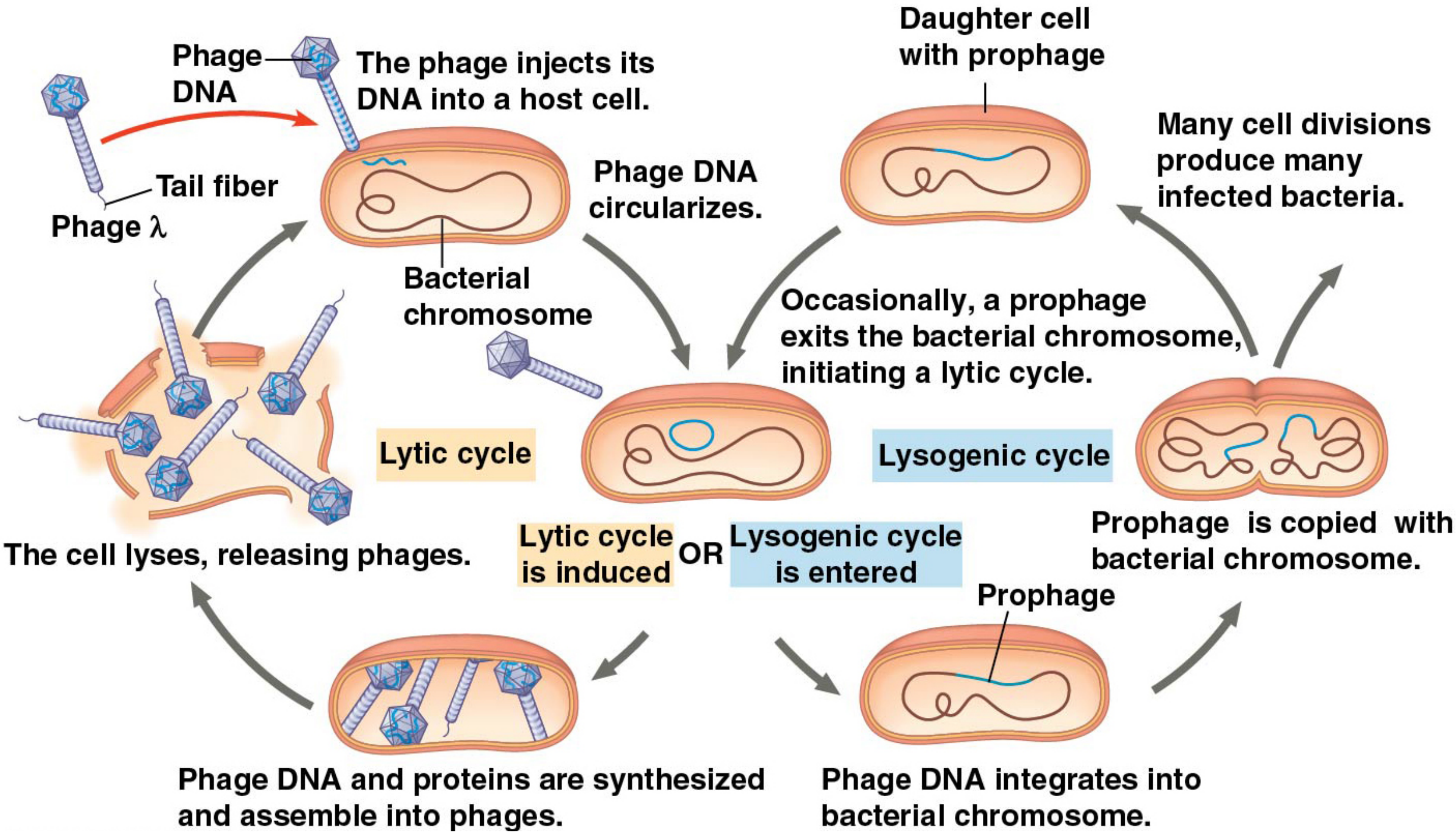
Animation: Phage Lytic Cycle



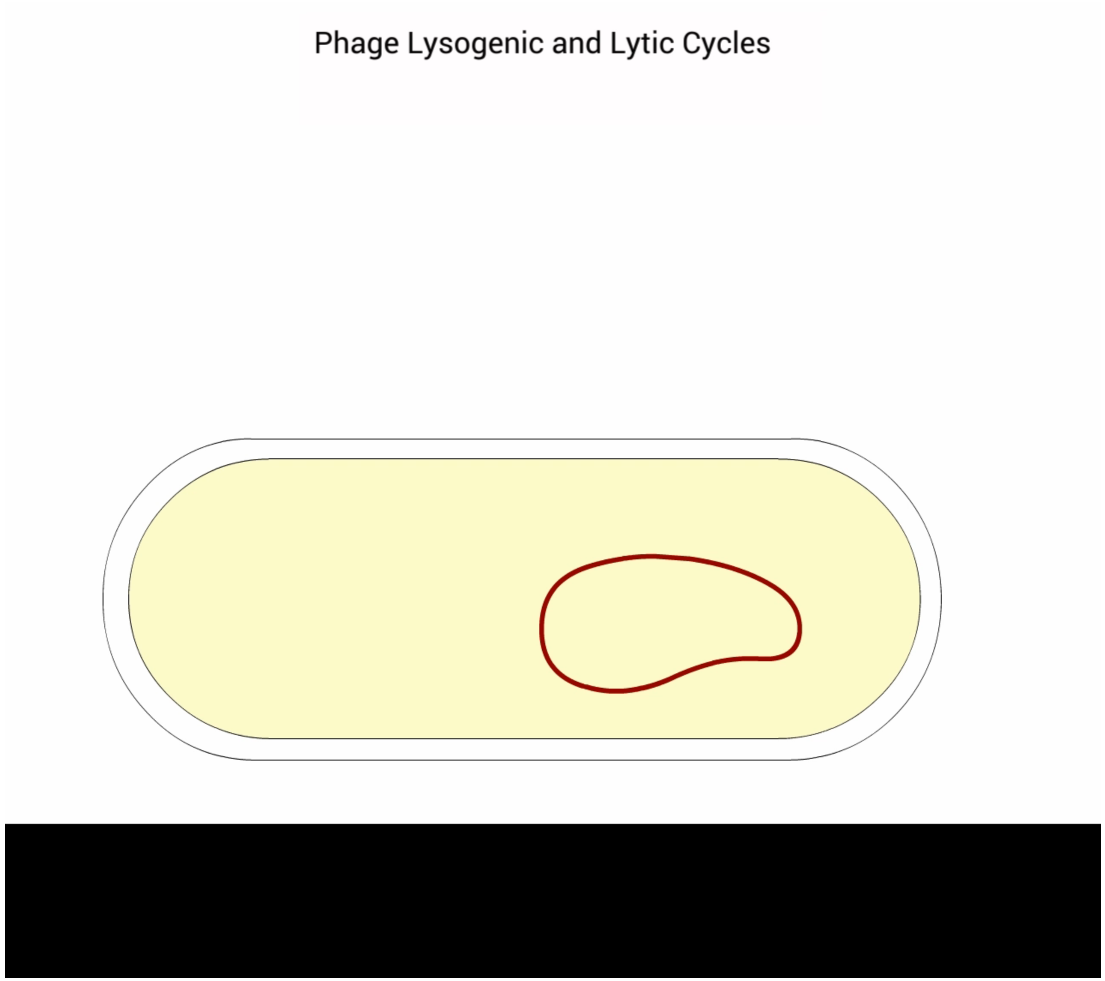
The Lysogenic Cycle

- The **lysogenic cycle** replicates the phage genome without destroying the host
- The viral DNA molecule is incorporated into the host cell's chromosome
- Phages that use both the lytic and lysogenic cycles are called **temperate phages**
- A temperate phage called lambda (λ) is widely used in biological research

Figure 19.6


Phage DNA
The phage injects its DNA into a host cell.
Tail fiber
Phage λ
Phage DNA circularizes.
Bacterial chromosome
Daughter cell with prophage
Many cell divisions produce many infected bacteria.
Occasionally, a prophage exits the bacterial chromosome, initiating a lytic cycle.
Lytic cycle
Lysogenic cycle
The cell lyses, releasing phages.
Lytic cycle is induced
OR
Lysogenic cycle is entered
Prophage is copied with bacterial chromosome.
Prophage
Phage DNA and proteins are synthesized and assemble into phages.
Phage DNA integrates into bacterial chromosome.

Animation: Phage Lysogenic and Lytic Cycles



- The integrated viral DNA is known as a **prophage**
- Every time the host divides, it copies the phage DNA and passes the copies to daughter cells
- An environmental signal can trigger the virus genome to exit the bacterial chromosome and switch to the lytic mode
- Some prophages are expressed during lysogeny, and some cause the host bacteria to secrete toxins that are harmful to humans

Bacterial Defenses Against Phages

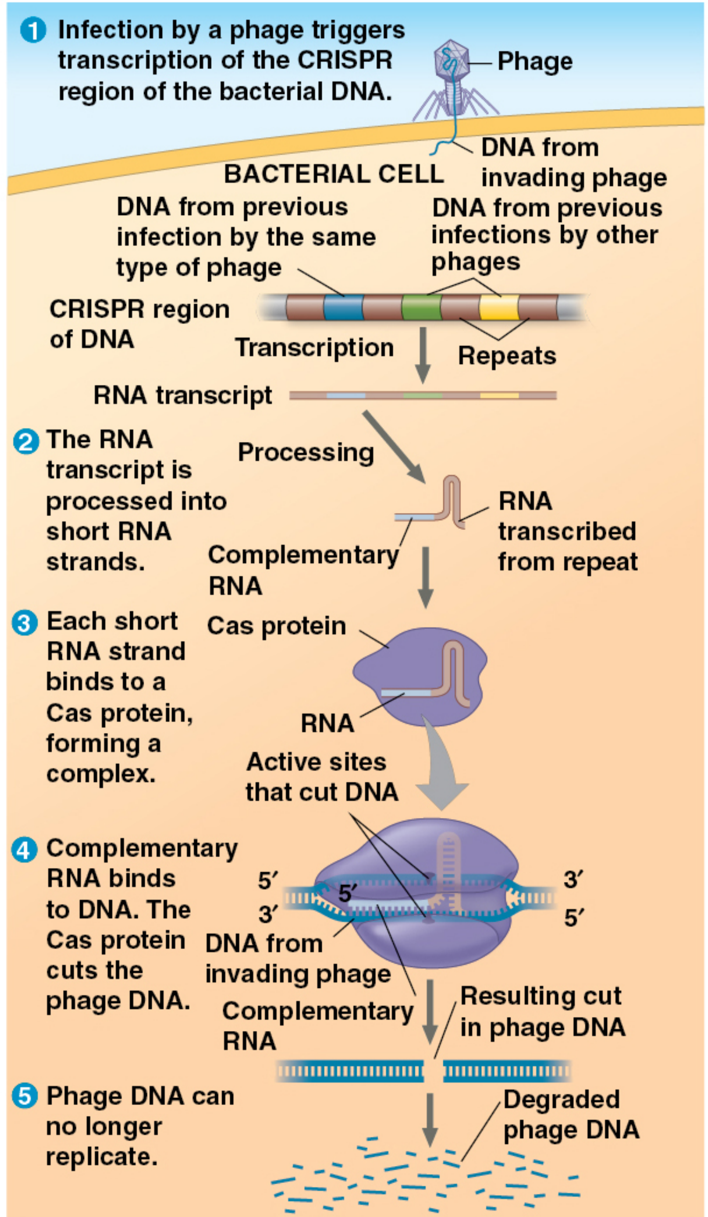
- Bacteria have their own defenses against phages
- Natural selection favors bacterial mutants with surface proteins that cannot be recognized as receptors by a particular type of phage
- Foreign DNA can be identified as such and cut up by cellular enzymes called **restriction enzymes**
- The bacterium’s own DNA is protected from the restriction enzymes by being methylated

- Both bacteria and archaea can protect themselves from viral infection with the CRISPR-Cas system
- It is based on sequences called clustered regularly interspaced short palindromic repeats (CRISPRs)
- Each “spacer” sequence between the repeats corresponds to DNA from a phage that had infected the cell
- Particular nuclease proteins interact with the CRISPR region; these are called CRISPR-associated (Cas) proteins

- When a phage infects a bacterial cell that has the CRISPR-Cas system, the phage DNA is integrated between two repeat sequences
- If the cell survives the infection, it can block any attempt of the same type of phage to reinfect it
- The attempt of the phage to infect the cell triggers transcription of the CRISPR region
- The resulting RNAs are cut into pieces and bound by Cas proteins

- The Cas proteins use the phage-related RNA to target the invading phage DNA
- The phage DNA is cut and destroyed
- Natural selection favors phage mutants that can bind to altered cell surface receptors or that are resistant to enzymes
- The relationship between phage and bacteria is in constant evolutionary flux

Figure 19.7



1 Infection by a phage triggers transcription of the CRISPR region of the bacterial DNA.
Phage
DNA from invading phage
BACTERIAL CELL
DNA from previous infection by the same type of phage
DNA from previous infections by other phages
CRISPR region of DNA
Transcription
Repeats
RNA transcript
2 The RNA transcript is processed into short RNA strands.
Processing
RNA transcribed from repeat
Complementary RNA
3 Each short RNA strand binds to a Cas protein, forming a complex.
Cas protein
RNA
Active sites that cut DNA
4 Complementary RNA binds to DNA. The Cas protein cuts the phage DNA.
5′
3′
5′
3′
5′
DNA from invading phage
Complementary RNA
Resulting cut in phage DNA
5 Phage DNA can no longer replicate.
Degraded phage DNA

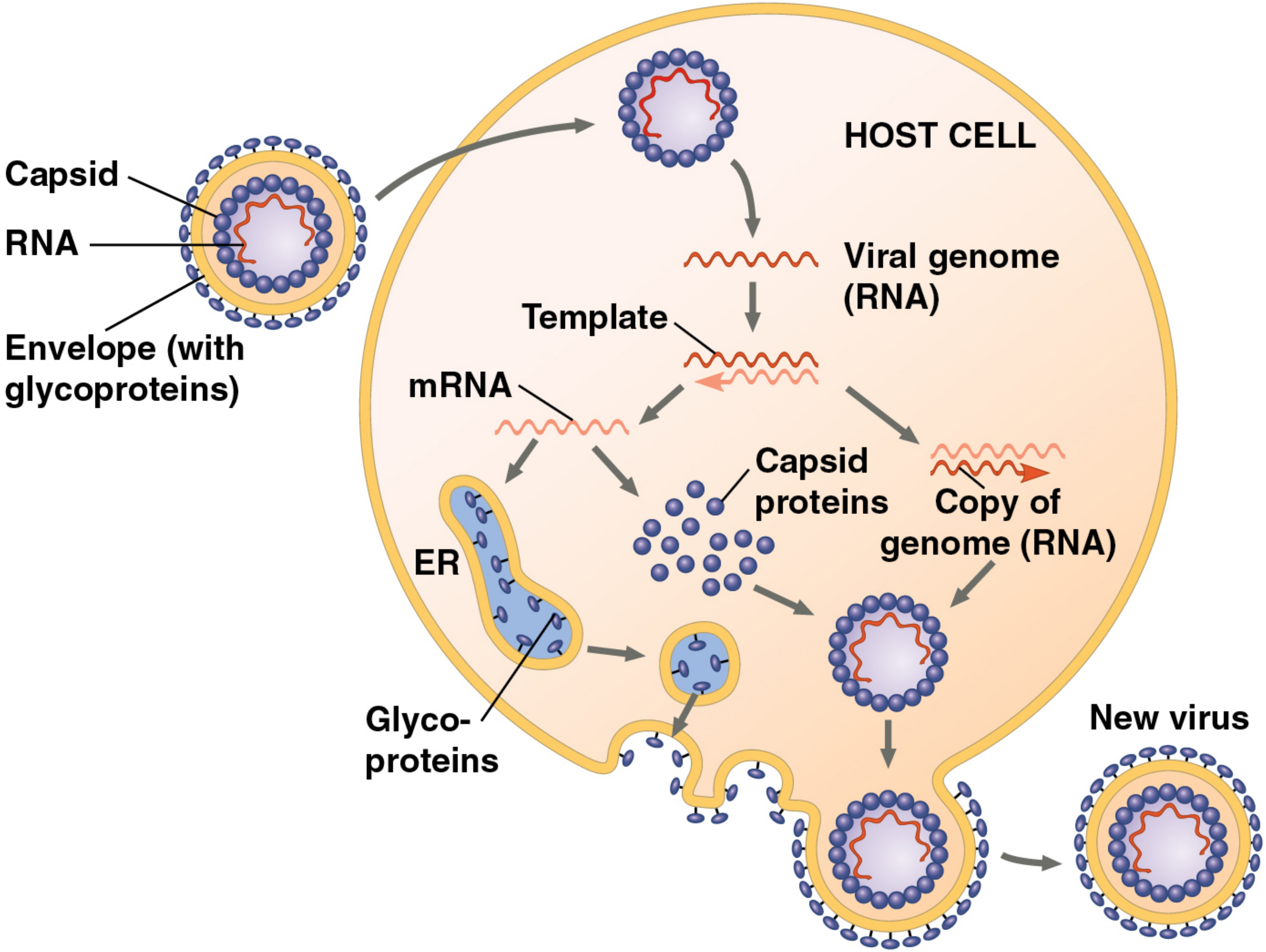
Replicative Cycles of Animal Viruses

- There are two key variables used to classify viruses that infect animals:
  - An RNA or DNA genome, either single-stranded or double-stranded
  - The presence or absence of a membranous envelope
- Whereas few bacteriophages have an envelope or an RNA genome, many animal viruses have both

Viral Envelopes

- Many viruses that infect animals have a membranous envelope
- Viral glycoproteins on the envelope bind to specific receptor molecules on the surface of a host cell
- The viral envelope is usually derived from the host cell's plasma membrane as the viral capsids exit

Figure 19.8



Capsid
RNA
Envelope (with glycoproteins)
HOST CELL
Viral genome (RNA)
Template
mRNA
Capsid proteins
Copy of genome (RNA)
ER
Glyco-proteins
New virus

- Other viral membranes form from the host's nuclear envelope and are then replaced by an envelope made from Golgi apparatus membrane
- The herpesvirus is an example of this

Viral Genetic Material

- The broadest variety of RNA genomes is found in viruses that infect animals
- **Retroviruses** use **reverse transcriptase** to copy their RNA genome into DNA
- **HIV (human immunodeficiency virus)** is the retrovirus that causes **AIDS (acquired immunodeficiency syndrome)**

- The viral DNA that is integrated into the host genome is called a **provirus**
- Unlike a prophage, a provirus remains a permanent resident of the host cell
- RNA polymerase transcribes the proviral DNA into RNA molecules
- The RNA molecules function both as mRNA for synthesis of viral proteins and as genomes for new virus particles released from the cell

Table 19.1

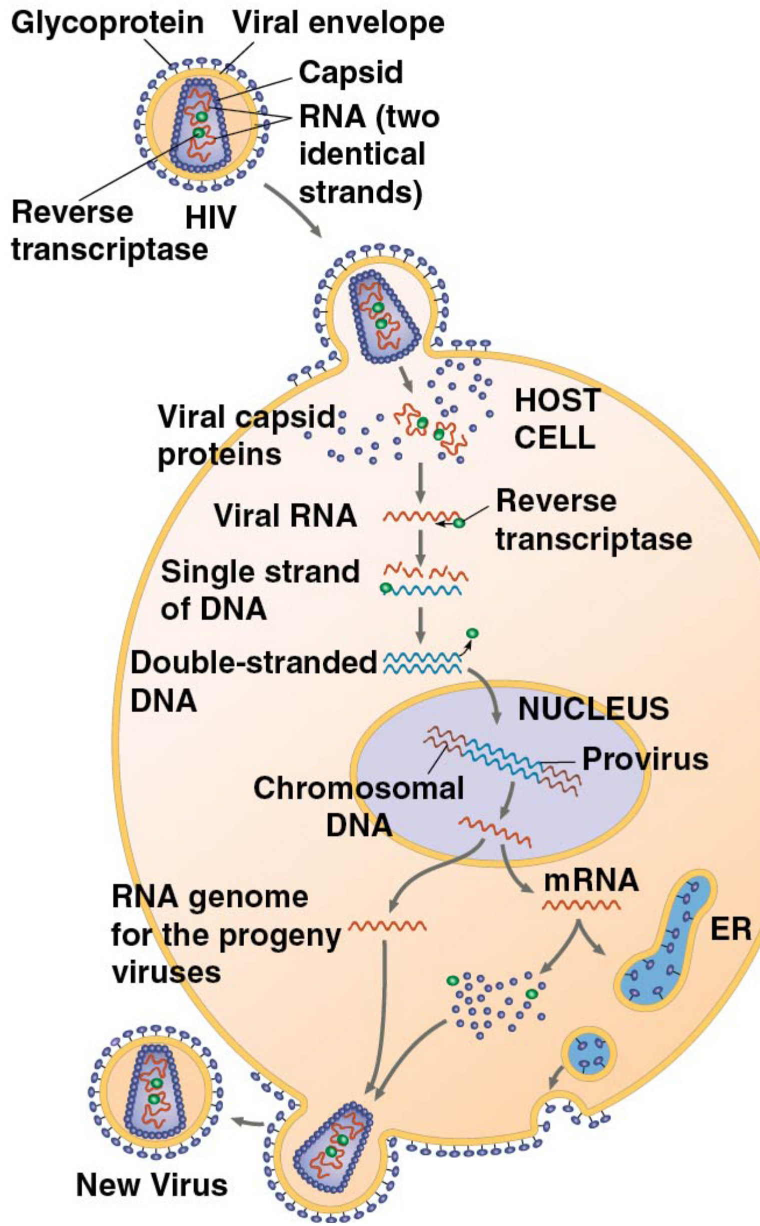
Table 19.1 Classes of Animal Viruses

Class/Family	Envelope?	Examples That Cause Human Diseases
I. Double-Stranded DNA (dsDNA)		
Adenovirus (see Figure 19.3b)	No	Respiratory viruses
Papillomavirus	No	Warts, cervical cancer
Polyomavirus	No	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; other intestinal viruses
Coronavirus	Yes	Severe acute respiratory syndrome (SARS); Middle East respiratory syndrome (MERS)
Flavivirus	Yes	Zika virus (see Figure 19.10c); yellow fever virus; dengue virus; West Nile virus; hepatitis C virus
Togavirus	Yes	Chikungunya virus (see Figure 19.10b); rubella virus; equine encephalitis viruses
V. ssRNA; Serves as Template for mRNA Synthesis		
Filovirus	Yes	Ebola virus (hemorrhagic fever; see Figure 19.10a)
Orthomyxovirus	Yes	Influenza virus (see Figure 19.3c)
Paramyxovirus	Yes	Measles virus; mumps virus
Rhabdovirus	Yes	Rabies virus
VI. ssRNA; Serves as Template for DNA Synthesis		
Retrovirus	Yes	Human immunodeficiency virus (HIV/AIDS; see Figure 19.9); human T-lymphotropic virus type 1 (HTLV-1) (leukemia)

Animation: HIV Replicative Cycle Animation: Retrovirus (HIV) Replicative Cycle

[redacted]

Figure 19.9


Glycoprotein
Viral envelope
Capsid
RNA (two identical strands)
Reverse transcriptase
HIV
HOST CELL
Viral capsid proteins
Viral RNA
Reverse transcriptase
Single strand of DNA
Double-stranded DNA
NUCLEUS
Provirus
Chromosomal DNA
mRNA
RNA genome for the progeny viruses
ER
New Virus

Evolution of Viruses

- Viruses do not fit our definition of living organisms
- Since viruses can replicate only within cells, they probably evolved as bits of cellular nucleic acid
- Candidates for the source of viral genomes include plasmids and transposons
- Plasmids, transposons, and viruses are all mobile genetic elements

- The largest virus identified about 20 years ago is the size of a small bacterium
- Its genome encodes proteins involved in translation, DNA repair, protein folding, and polysaccharide synthesis
- There is controversy about whether this virus evolved before or after cells
- In the past decade several even larger viruses have been identified; how these evolved is an unresolved question

CONCEPT 19.3: Viruses and prions are formidable pathogens in animals and plants

- Diseases caused by viral infections affect humans, agricultural crops, and livestock worldwide
- Smaller, less complex entities called prions also cause disease and animals

Viral Diseases in Animals

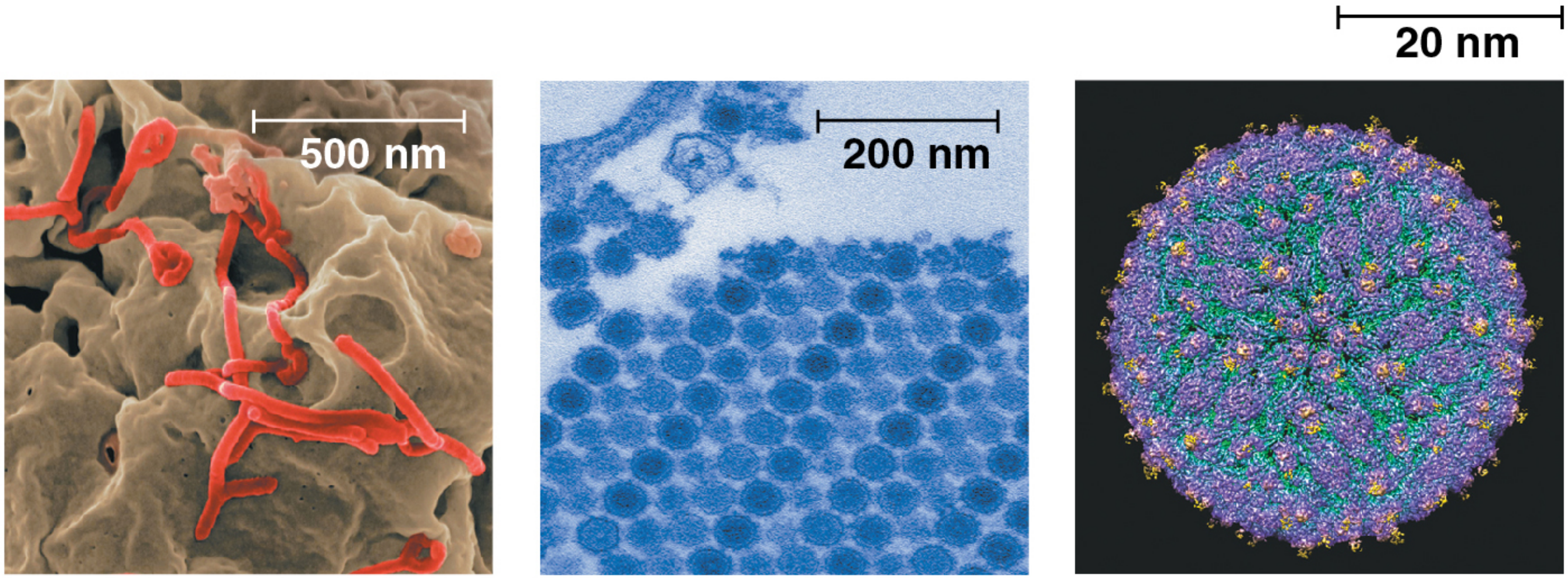
- Viruses may damage or kill cells by causing the release of hydrolytic enzymes from lysosomes
- Some viruses cause infected cells to produce toxins that lead to disease symptoms
- Others have molecular components such as envelope proteins that are toxic

- A **vaccine** is a harmless derivative of a pathogen that stimulates the immune system to mount defenses against the harmful pathogen
- Vaccines can prevent certain viral illnesses, such as smallpox, rubella, mumps, and others
- Viral infections cannot be treated by antibiotics
- Antiviral drugs can help to treat, not cure, viral infections by inhibiting synthesis of viral DNA and by interfering with viral assembly

Emerging Viral Diseases

- Emerging viruses are those that suddenly become apparent
- HIV, the AIDS virus, is a classic example

- The Ebola virus is one of several emerging viruses that cause hemorrhagic fever, an often fatal illness
- In 2014, a widespread outbreak (**epidemic**) of Ebola virus occurred
- In 2017, 2018, and 2019, smaller outbreaks occurred in the Democratic Republic of the Congo
- Other examples of emerging viruses include the chikungunya virus and the recently emerging Zika virus (2015)



(a) Ebola viruses (b) Chikungunya viruses (c) Zika virus

- One cause of rapidly emerging viral disease in humans is mutation of existing viruses into new ones that can spread more easily
- A second cause is the spread of a viral disease from a small, isolated human population
- A third cause is the spread of existing viruses from other animals
  - It is estimated that about three-quarters of new human diseases originate in this way

- Flu epidemics are caused by type A influenza viruses; these infect a wide variety of animals including birds, pigs, horses, and humans
- Strains of influenza A are given standardized names based on the viral surface proteins hemagglutinin (HA) and neuraminidase (NA)
- As of 2017 18 types of HA, and 11 types of neuraminidase, have been identified

- The H5N1 strain is quite deadly, because it is very different from influenza strains circulating among people for a long time
- It is thus difficult for people to mount an effective immune response to this strain
- However, it has not caused an epidemic because it is not transmitted from person-to-person

- A deadly strain of H1N1, originally called the swine flu, was not actually transmitted to humans from pigs
- Instead, the story was more complex, H1N1 was a unique combination of swine, avian, and human influenza genes
- An epidemic of H1N1 occurred in 2009, reaching 207 countries, infecting over 600,000 people and killing almost 8,000
- A global epidemic like this is called a **pandemic**

- Influenza viruses have nine RNA segments in their genome, leading to many new genetic combinations
- They also have a high rate of mutation
- Normal seasonal flu viruses are not considered emerging viruses because variants of these viruses have been circulating among humans for a long time
- However, these viruses still undergo mutation and reassortment
- Variations thought to be most likely to occur each year are selected to generate vaccines

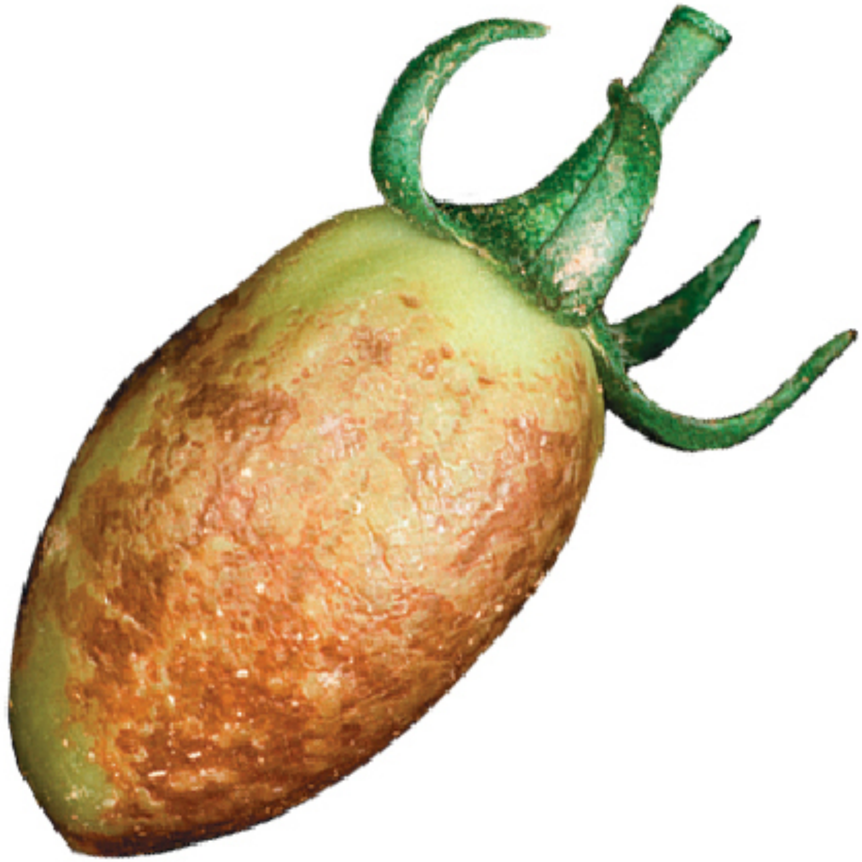
- Changes in host behavior or the environment can increase the spread of viruses responsible for emerging diseases
- New roads into a remote area may increase spread of viral diseases
- The use of insecticides and mosquito nets may help prevent the spread
- It is possible that global climate change may allow mosquitoes that carry viruses to expand their range

Figure 19.11

Viral Diseases in Plants

- More than 2,000 types of viral diseases of plants are known and cause spots on leaves and fruits, stunted growth, and damaged flowers or roots
- Most known plant viruses have an RNA genome
- Many have a helical capsid, while others have an icosahedral capsid

Figure 19.12



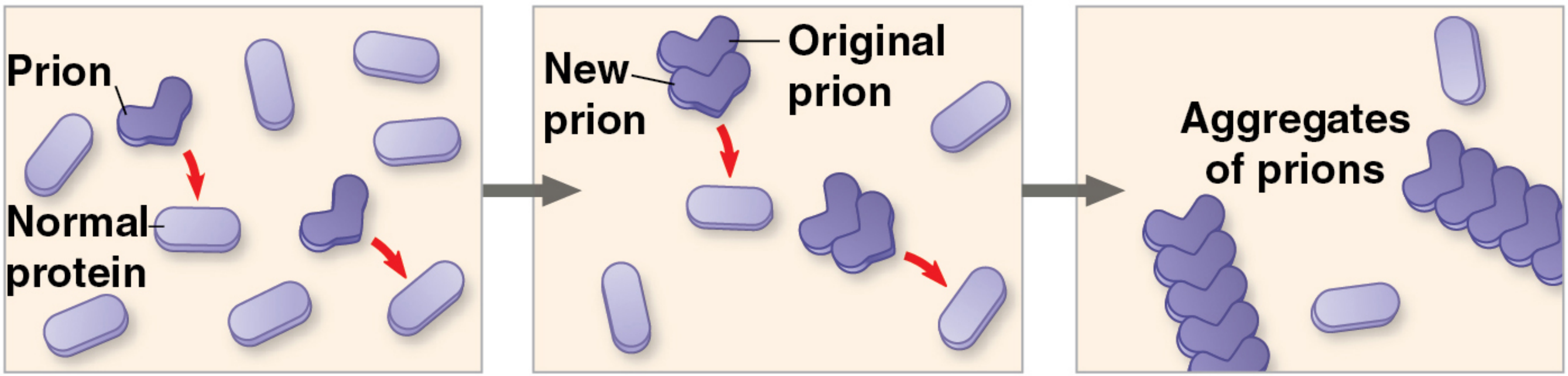
- Plant viruses spread disease by two major routes:
  - Horizontal transmission, entering through damaged cell walls
  - Vertical transmission, inheriting the virus from a parent

Prions: Proteins as Infectious Agents

- **Prions** are infectious proteins that appear to cause degenerative brain diseases in animals
- Scrapie in sheep, mad cow disease, and Creutzfeldt-Jakob disease in humans are all caused by prions
- Prions are incorrectly folded proteins, can be transmitted in food, act slowly, and are virtually indestructible

- Prions are somehow able to convert a normal form of a protein into the misfolded version
- Then several prions aggregate into a complex that can convert more proteins to prions, which join the chain
- Prions might also be involved in diseases such as Alzheimer’s and Parkinson’s disease
- There are many outstanding questions about these small infectious agents

Figure 19.13



Prion
Normal protein
New prion
Original prion
Aggregates of prions

Figure 19.UN01

Figure 19.UN02

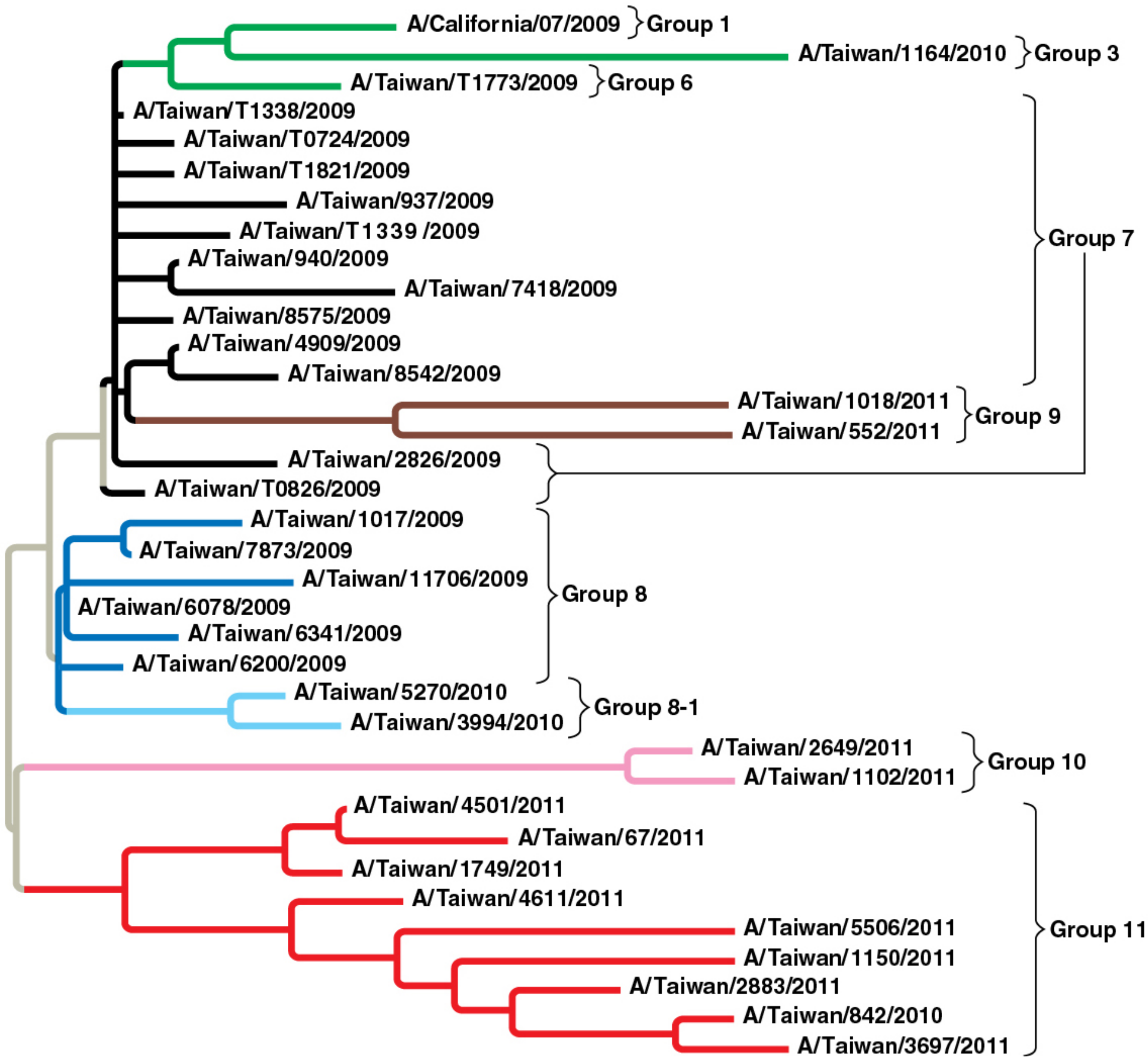


Figure 19.UN03

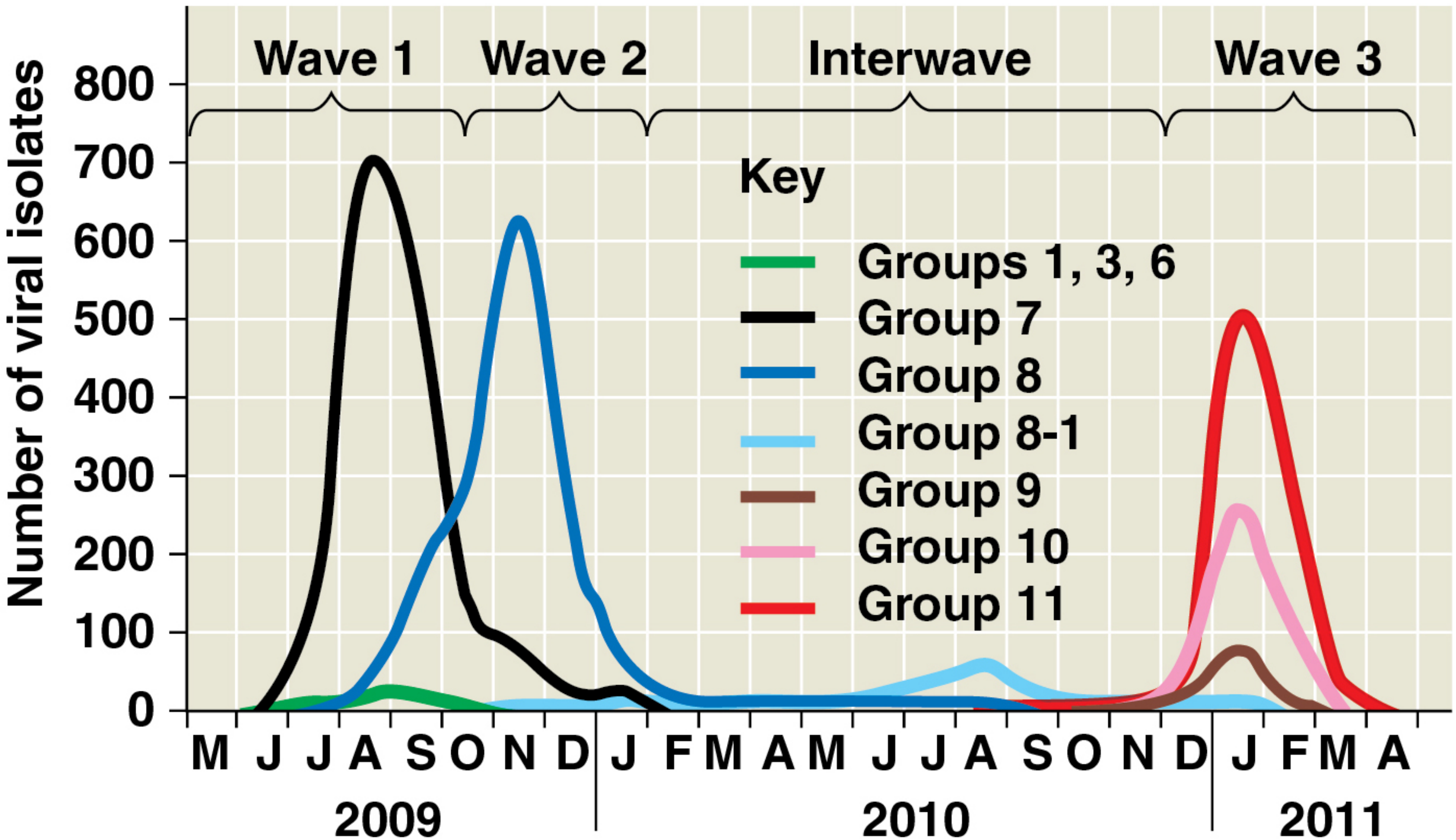
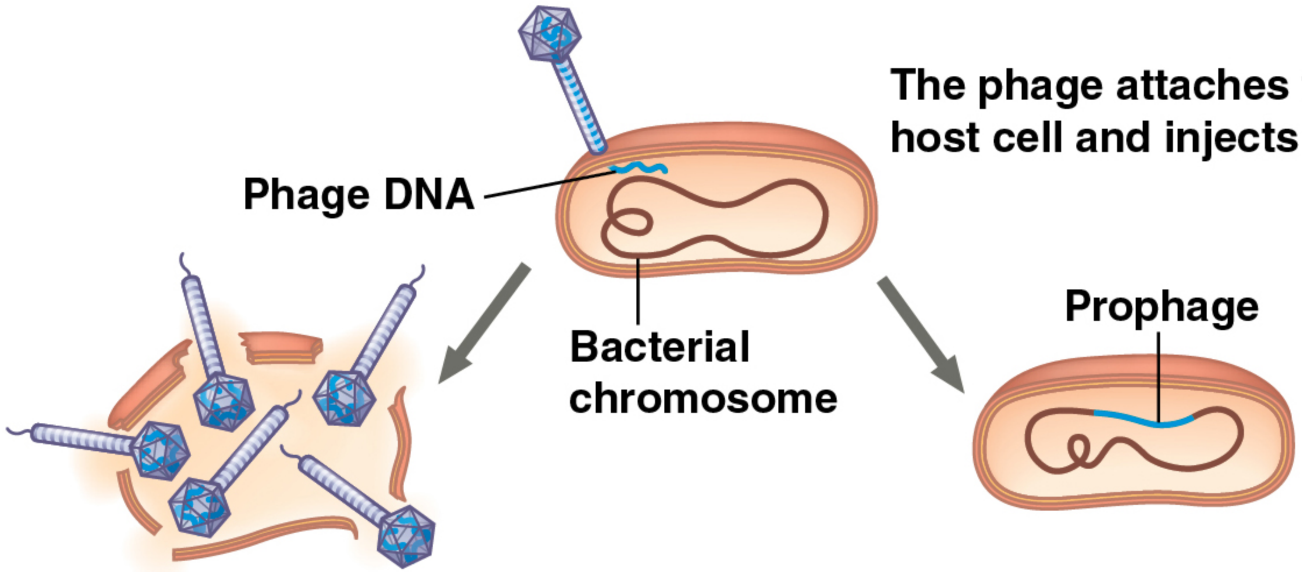


Figure 19.UN04



The phage attaches to a host cell and injects its DNA.

Lytic cycle
- **Virulent or temperate phage**
- **Destruction of host DNA**
- **Production of new phages**
- **Lysis of host cell causes release of progeny phages**

Lysogenic cycle
- **Temperate phage only**
- **Genome integrates into bacterial chromosome as prophage, which (1) is replicated and passed on to daughter cells and (2) can be induced to leave the chromosome and initiate a lytic cycle**

Figure 19.UN05

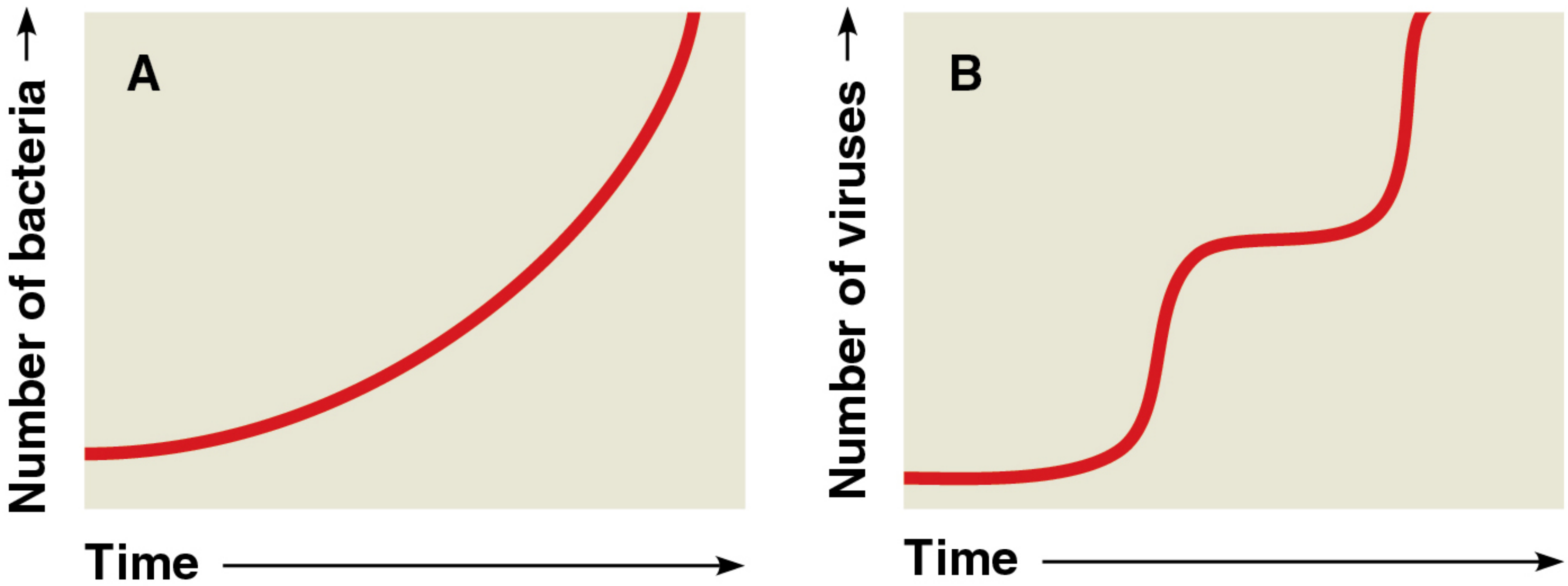


Figure 19.UN06