Chapter 19

Viruses
Overview: A Borrowed Life

- Viruses called bacteriophages can infect and set in motion a genetic takeover of bacteria, such as *Escherichia coli*
- Viruses lead “a kind of borrowed life” between life-forms and chemicals
- The origins of molecular biology lie in early studies of viruses that infect bacteria
Concept 19.1: A virus consists of a nucleic acid surrounded by a protein coat

- Viruses were detected indirectly long before they were actually seen
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 a particle smaller than bacteria caused the disease
• In 1935, Wendell Stanley confirmed this hypothesis by crystallizing the infectious particle, now known as tobacco mosaic virus (TMV)
RESULTS

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
Viral Genomes

- Viral genomes may consist of either
  - Double- or single-stranded DNA, or
  - Double- or single-stranded RNA
- Depending on its type of nucleic acid, a virus is called a DNA virus or an RNA virus
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 various structures
Figure 19.3

(a) Tobacco mosaic virus
(b) Adenoviruses
(c) Influenza viruses
(d) Bacteriophage T4

Capsomere of capsid
Glycoprotein
RNA
DNA
Membranous envelope
Capsid
Head
DNA
Tail sheath
Tail fiber

18 × 250 nm
70–90 nm (diameter)
80–200 nm (diameter)
80 × 225 nm

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• Some viruses have membranous envelopes that help them infect hosts
• These **viral envelopes** surround the capsids of influenza viruses and many other viruses found in animals
• Viral envelopes, which are derived from the host cell’s membrane, contain a combination of viral and host cell molecules
• **Bacteriophages**, also called **phages**, are viruses that infect bacteria
• They have the most complex capsids found among viruses
• Phages 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 cells that it can infect
General Features of Viral Replicative Cycles

- 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
2. Replication
3. Transcription and manufacture of capsid proteins
4. Self-assembly of new virus particles and their exit from the cell

VIRUS
DNA
Capsid
VIRUS
DNA
HOST CELL
Viral DNA
mRNA
Viral DNA
Capsid proteins

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Replicative Cycles of Phages

• Phages are the best understood of all viruses
• Phages have two 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**.
- Bacteria have defenses against phages, including **restriction enzymes** that recognize and cut up certain phage DNA.
Figure 19.5-5

1. **Attachment**

2. **Entry of phage DNA and degradation of host DNA**

3. **Synthesis of viral genomes and proteins**

4. **Assembly**

5. **Release**

Phage assembly

- Head
- Tail
- Tail fibers
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
• This 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
• Phages that use both the lytic and lysogenic cycles are called **temperate phages**
New phage DNA and proteins are synthesized and assembled into phages.

The cell lyses, releasing phages.

Phage DNA injects its DNA.

Bacterial chromosome circularizes.

Phage DNA circularizes.

Occasionally, a prophage exits the bacterial chromosome, initiating a lytic cycle.

Cell divisions produce a population of bacteria infected with the prophage.

Lytic cycle

Lysogenic cycle

Certain factors determine whether lysogenic cycle is entered or lytic cycle is induced.

Prophage

Daughter cell with prophage

The bacterium reproduces, copying the prophage and transmitting it to daughter cells.

Phage DNA integrates into the bacterial chromosome, becoming a prophage.
New phage DNA and proteins are synthesized and assembled into phages.

The phage injects its DNA.

Phage DNA circularizes.

Bacterial chromosome

Lytic cycle

The cell lyses, releasing phages.

Certain factors determine whether lytic cycle is induced or lysogenic cycle is entered.

Figure 19.6a
Certain factors determine whether lysogenic cycle is entered or lytic cycle is induced. Phage DNA integrates into the bacterial chromosome, becoming a prophage. Occasionally, a prophage exits the bacterial chromosome, initiating a lytic cycle. The bacterium reproduces, copying the prophage and transmitting it to daughter cells. Cell divisions produce a population of bacteria infected with the prophage. Daughter cell with prophage.
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
There are two key variables used to classify viruses that infect animals:

- DNA or RNA?
- Single-stranded or double-stranded?
### Table 19.1 Classes of Animal Viruses

<table>
<thead>
<tr>
<th>Class/Family</th>
<th>Envelope</th>
<th>Examples That Cause Human Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Double-Stranded DNA (dsDNA)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>No</td>
<td>Respiratory viruses; tumor-causing viruses</td>
</tr>
<tr>
<td>Papovavirus</td>
<td>No</td>
<td>Papillomavirus (warts, cervical cancer); polyomavirus (tumors)</td>
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<tr>
<td>Herpesvirus</td>
<td>Yes</td>
<td>Herpes simplex I and II (cold sores, genital sores); varicella zoster (shingles, chicken pox); Epstein-Barr virus (mononucleosis, Burkitt’s lymphoma)</td>
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<tr>
<td>Poxvirus</td>
<td>Yes</td>
<td>Smallpox virus; cowpox virus</td>
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<tr>
<td><strong>II. Single-Stranded DNA (ssDNA)</strong></td>
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<td></td>
</tr>
<tr>
<td>Parvovirus</td>
<td>No</td>
<td>B19 parvovirus (mild rash)</td>
</tr>
<tr>
<td><strong>III. Double-Stranded RNA (dsRNA)</strong></td>
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<td></td>
</tr>
<tr>
<td>Reovirus</td>
<td>No</td>
<td>Rotavirus (diarrhea); Colorado tick fever virus</td>
</tr>
<tr>
<td>Class/Family</td>
<td>Envelope</td>
<td>Examples That Cause Human Diseases</td>
</tr>
<tr>
<td>----------------------</td>
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<td>------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>IV. Single-Stranded RNA (ssRNA); Serves as mRNA</td>
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<td></td>
</tr>
<tr>
<td>Picornavirus</td>
<td>No</td>
<td>Rhinovirus (common cold); poliovirus; hepatitis A virus; other enteric (intestinal) viruses</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>Yes</td>
<td>Severe acute respiratory syndrome (SARS)</td>
</tr>
<tr>
<td>Flavivirus</td>
<td>Yes</td>
<td>Yellow fever virus; West Nile virus; hepatitis C virus</td>
</tr>
<tr>
<td>Togavirus</td>
<td>Yes</td>
<td>Rubella virus; equine encephalitis viruses</td>
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<tr>
<td>V. ssRNA; Template for mRNA Synthesis</td>
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<td></td>
</tr>
<tr>
<td>Filovirus</td>
<td>Yes</td>
<td>Ebola virus (hemorrhagic fever)</td>
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<tr>
<td>Orthomyxovirus</td>
<td>Yes</td>
<td>Influenza virus</td>
</tr>
<tr>
<td>(see Figures 19.3c</td>
<td></td>
<td></td>
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<tr>
<td>and 19.9a)</td>
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<tr>
<td>Paramyxovirus</td>
<td>Yes</td>
<td>Measles virus; mumps virus</td>
</tr>
<tr>
<td>Rhabdovirus</td>
<td>Yes</td>
<td>Rabies virus</td>
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<tr>
<td>VI. ssRNA; Template for DNA Synthesis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrovirus</td>
<td>Yes</td>
<td>Human immunodeficiency virus (HIV/AIDS); RNA tumor viruses (leukemia)</td>
</tr>
</tbody>
</table>
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
• Some viral envelopes are formed from the host cell’s plasma membrane as the viral capsids exit
• Other viral membranes form from the host’s nuclear envelope and are then replaced by an envelope made from Golgi apparatus membrane.
Figure 19.7

Capsid and viral genome enter the cell

HOST CELL

Viral genome (RNA)

Template

mRNA

Capsid proteins

Copy of genome (RNA)

New virus

Capsid

RNA

Envelope (with glycoproteins)

Glycoproteins

ER

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RNA as 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)**.
Glycoprotein

Viral envelope

Capsid

RNA (two identical strands)

Reverse transcriptase

HIV

Viral RNA

Reverse transcriptase

RNA-DNA hybrid

DNA

HOST CELL

NUCLEUS

Chromosomal DNA

RNA genome for the next viral generation

mRNA

New virus

New HIV leaving a cell

Figure 19.8

Membrane of white blood cell

HIV entering a cell

HIV leaving a cell

0.25 μm
Figure 19.8a

Glycoprotein

Reverse transcriptase

Viral envelope

Capsid

RNA (two identical strands)

HIV

HOST CELL

Viral RNA

Reverse transcriptase

RNA-DNA hybrid

DNA

NUCLEUS

Chromosomal DNA

Proivirus

RNA genome for the next viral generation

mRNA

New virus

RNA genome for the next viral generation
Figure 19.8b

Membrane of white blood cell

HIV entering a cell

New HIV leaving a cell

0.25 μm
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.
The host’s 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.
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 are plasmids, circular DNA in bacteria and yeasts, and transposons, small mobile DNA segments
- Plasmids, transposons, and viruses are all mobile genetic elements
• Mimivirus, a double-stranded DNA virus, the largest virus yet discovered, is the size of a small bacterium

• There is controversy about whether this virus evolved before or after cells
Concept 19.3: Viruses, viroids, 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 viroids and prions also cause disease in plants and animals, respectively
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.
• **Vaccines** are harmless derivatives of pathogenic microbes that stimulate the immune system to mount defenses against the harmful pathogen
• Vaccines can prevent certain viral illnesses
• Viral infections cannot be treated by antibiotics
• Antiviral drugs can help to treat, though not cure, viral infections
Emerging Viruses

- Emerging viruses are those that suddenly become apparent.
- Recently, a general outbreak (epidemic) of a flu-like illness appeared in Mexico and the United States, caused by an influenza virus named H1N1.
- Flu epidemics are caused by new strains of influenza virus to which people have little immunity.
• Viral diseases in a small isolated population can emerge and become global
• New viral diseases can emerge when viruses spread from animals to humans
• Viral strains that jump species can exchange genetic information with other viruses to which humans have no immunity
• These strains can cause **pandemics**, global epidemics
• The 2009 flu pandemic was likely passed to humans from pigs; for this reason it was originally called the “swine flu”
Figure 19.9

(a) 2009 pandemic H1N1 influenza A virus

(b) 2009 pandemic screening

(c) 1918 flu pandemic
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 plant viruses have an RNA genome
• Plant viruses spread disease in two major modes
  – Horizontal transmission, entering through damaged cell walls
  – Vertical transmission, inheriting the virus from a parent
Viroids and Prions: The Simplest Infectious Agents

- **Viroids** are small circular RNA molecules that infect plants and disrupt their growth
- **Prions** are slow-acting, virtually indestructible infectious proteins that cause brain diseases in mammals
- Prions propagate by converting normal proteins into the prion version
- Scrapie in sheep, mad cow disease, and Creutzfeldt-Jakob disease in humans are all caused by prions
Figure 19.11

- Prion
- Normal protein
- Original prion
- New prion
- Aggregates of prions