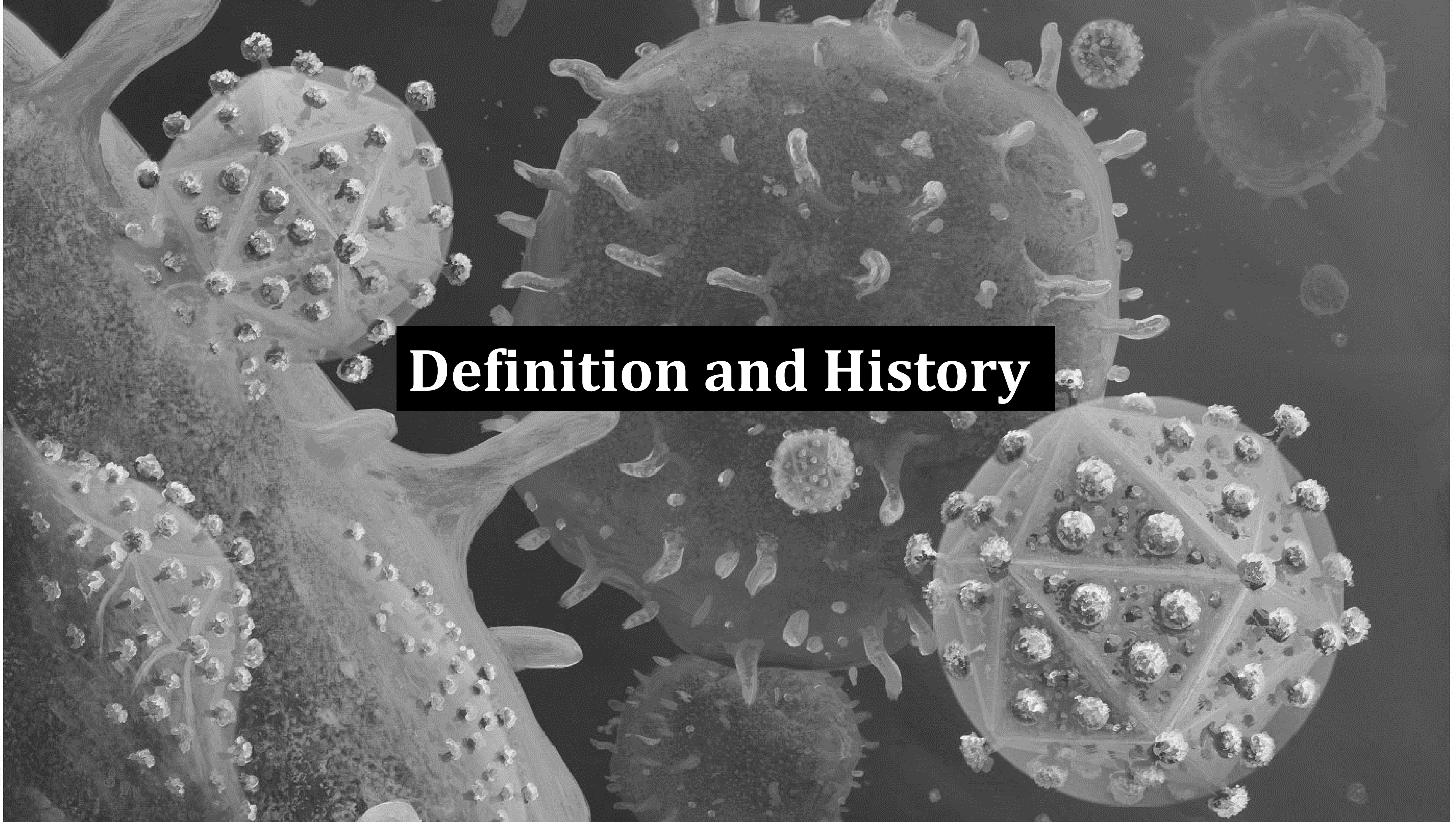
An introduction to viruses

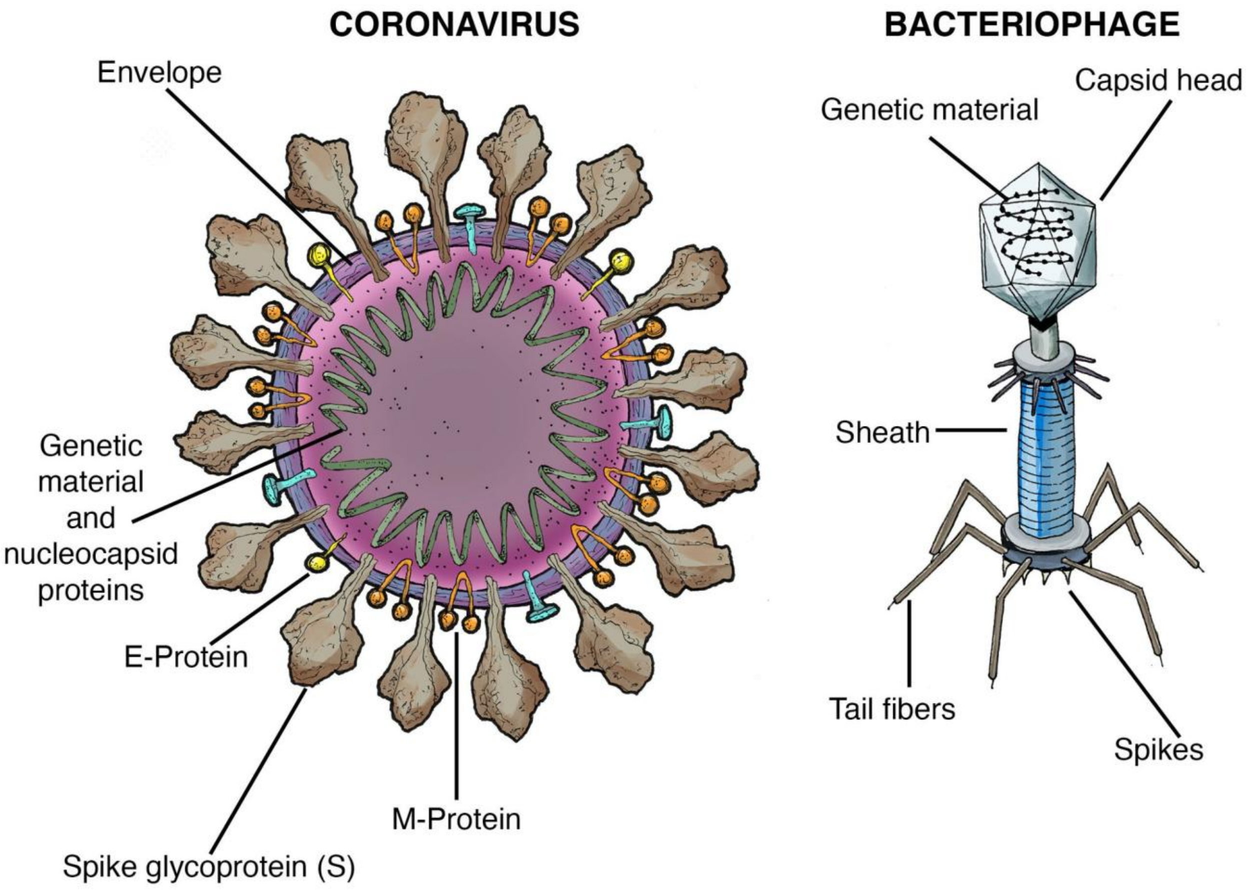
What are we going to learn today?

- Definition and history of viruses
- Viral structures
- Viral replication and host mechanisms against viruses
- Viral evolution and antiviral molecules
- Emerging viruses
- Bonus: Prions


Definition and History

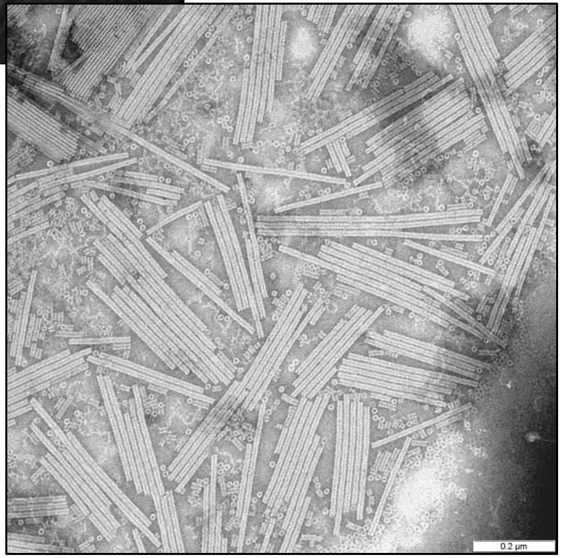
Viruses: A Borrowed Life

- 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 **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"



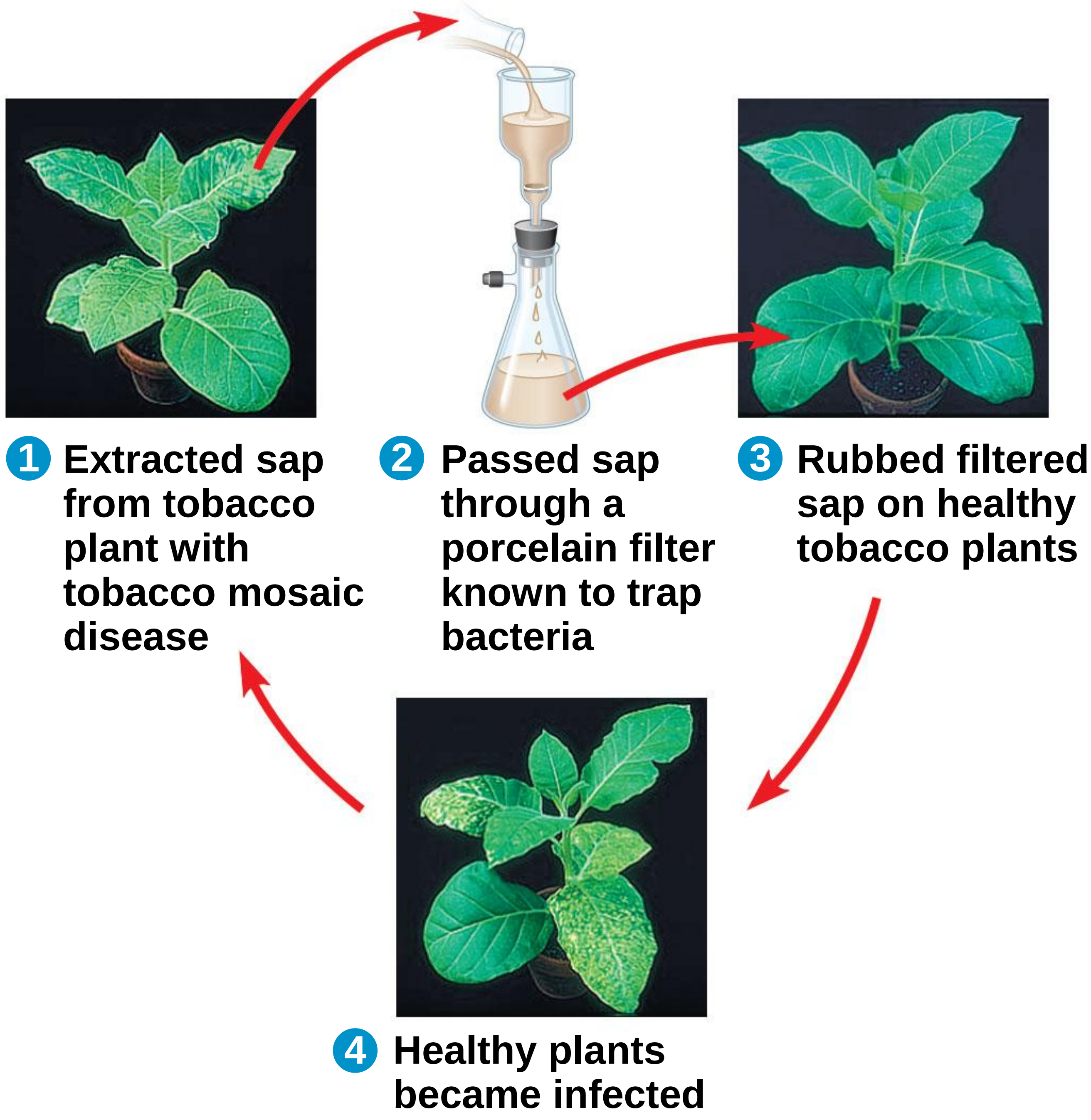
The Discovery of Viruses

- **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)**

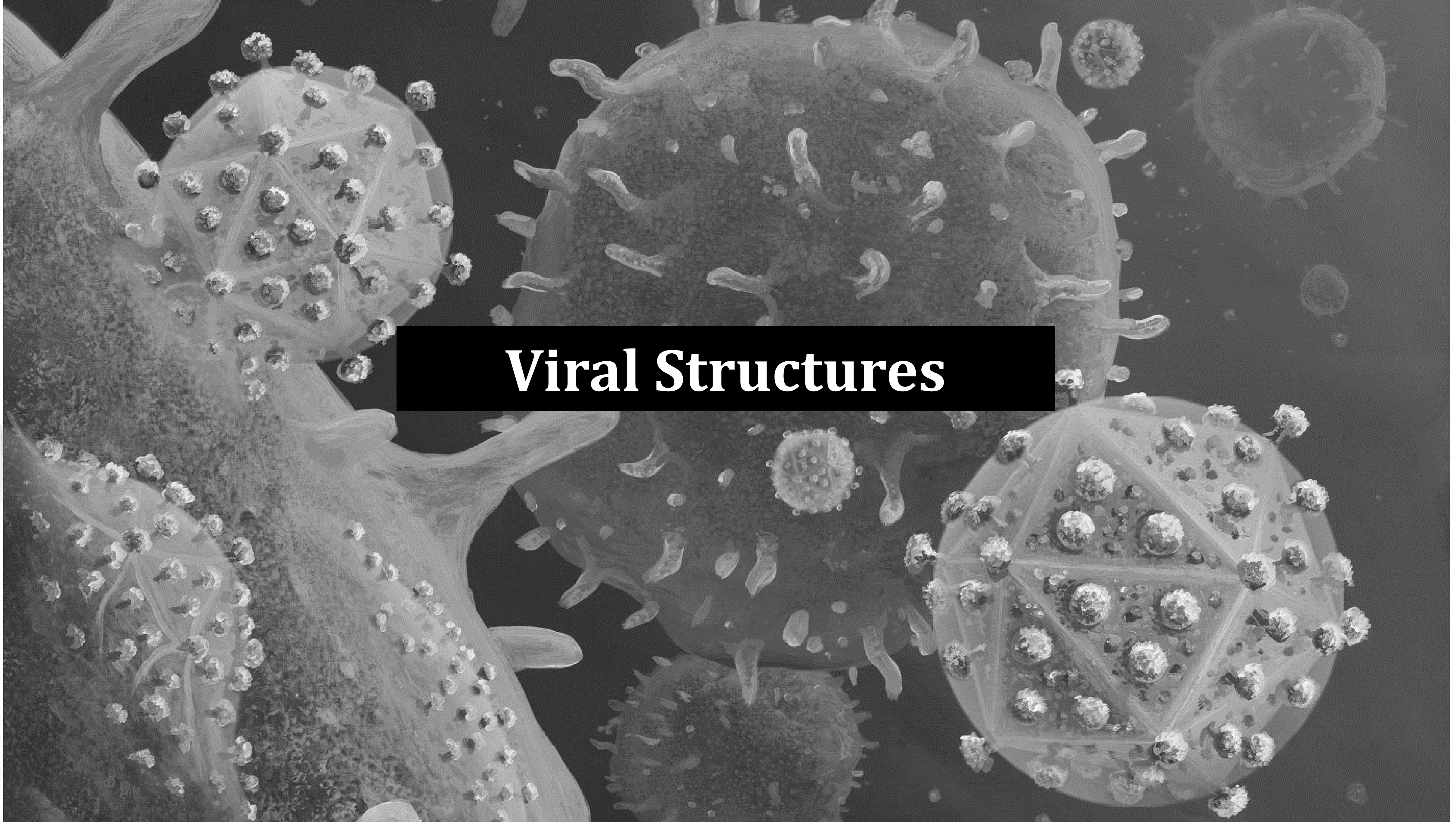


What causes tobacco mosaic disease?

Experiments Dmitri Ivanovsky, 1892
Martinus Beijerinck, 1898

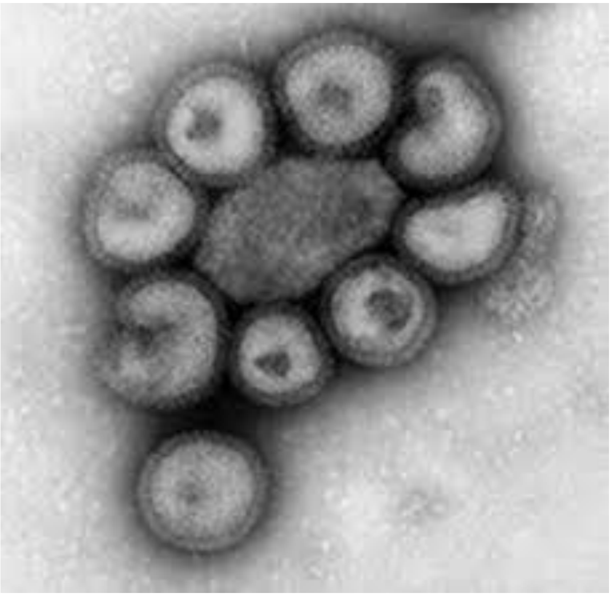


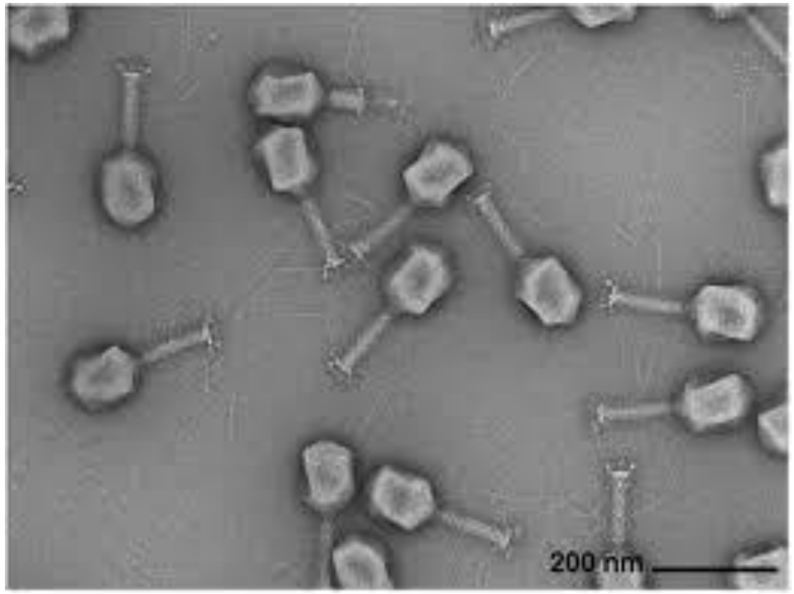
Viral Structures

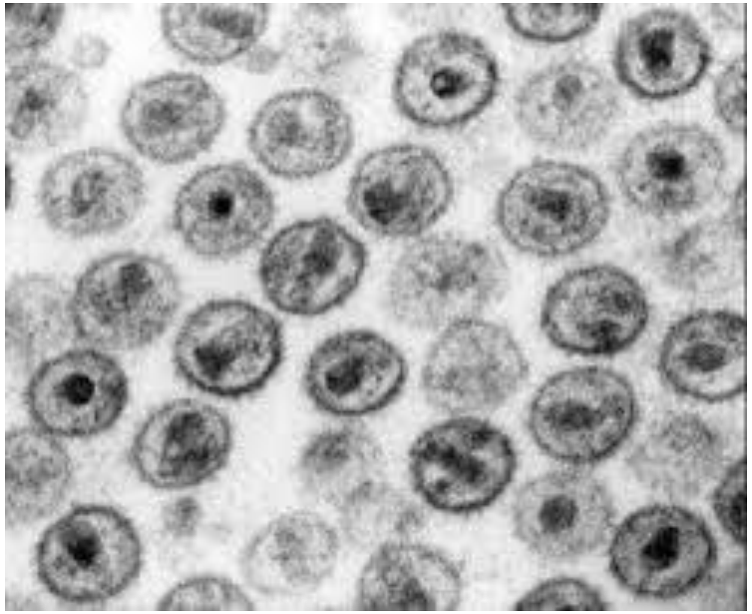


Structure of Viruses

- 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

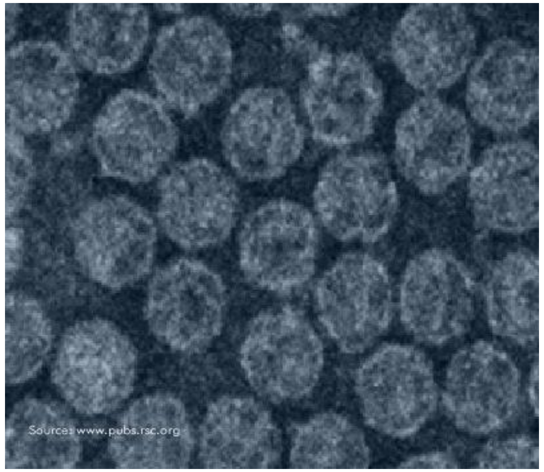




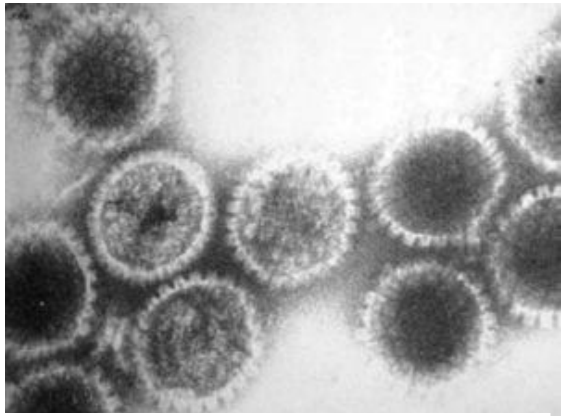


Viral Genomes

- Viral genomes may consist of either
  - double- or single-stranded **DNA** or
  - double- or single-stranded **RNA**
- 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



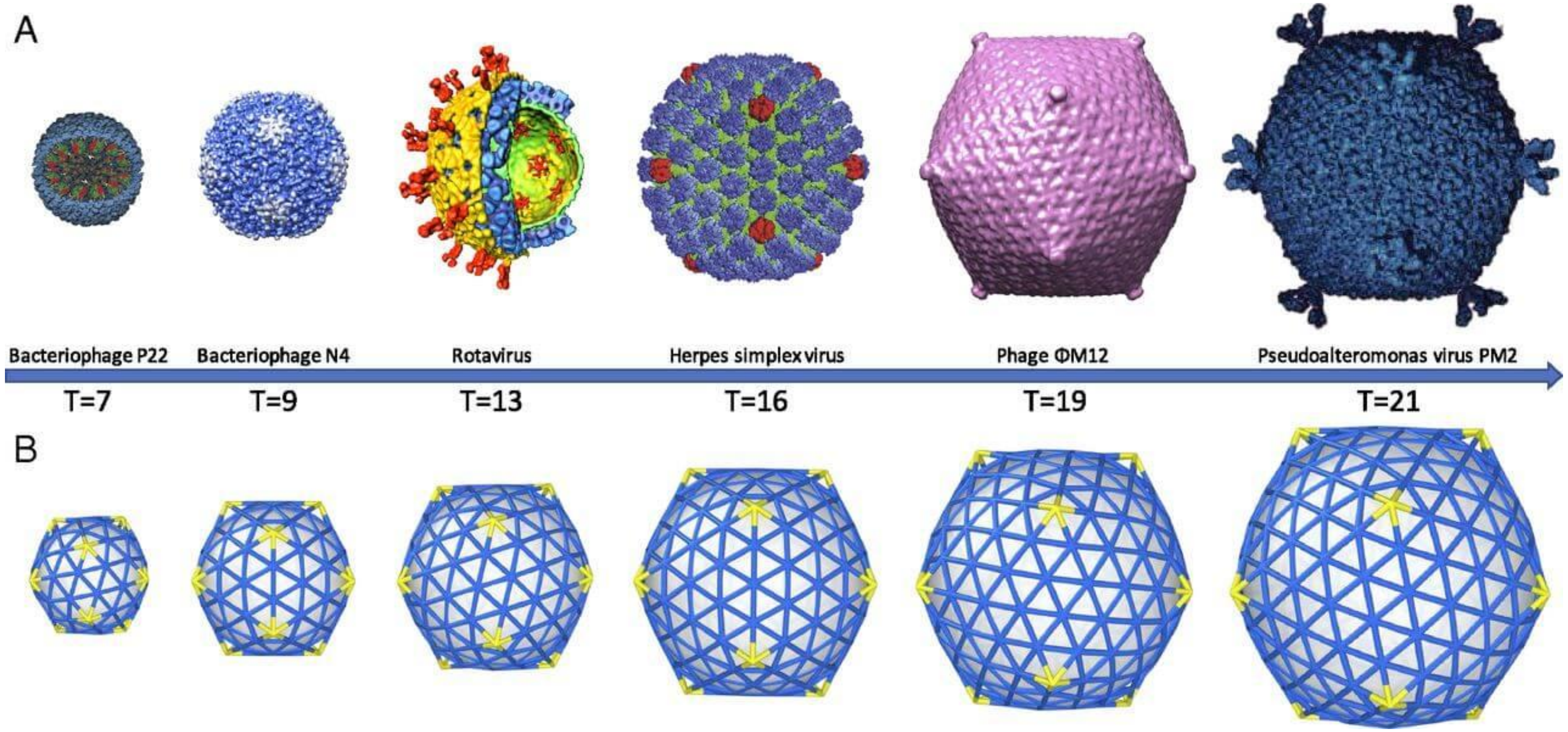
MS2 phage, 3569 nucleotides, 4 proteins

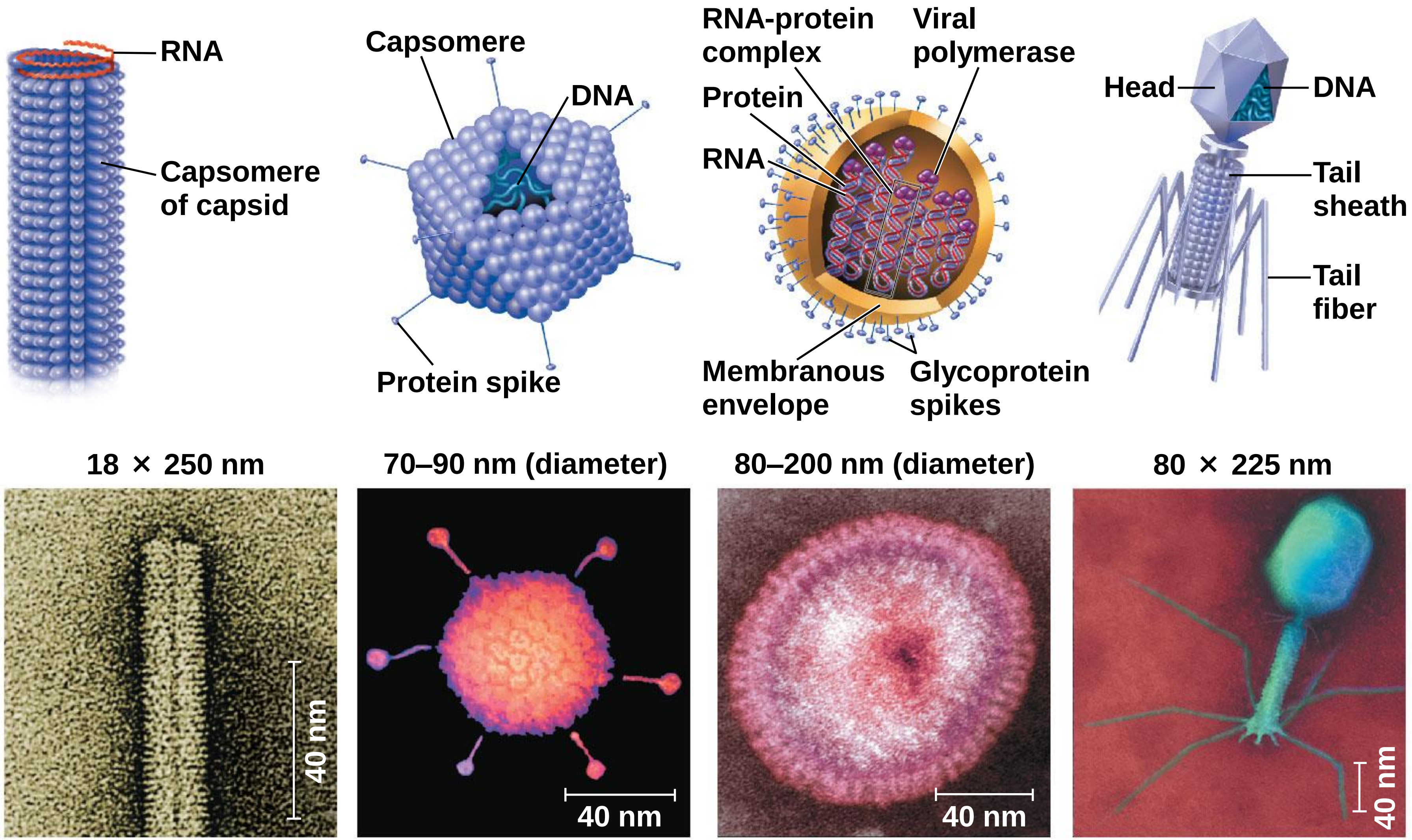


Herpes simplex virus (HSV), 152000 nucleotides, 80 proteins

Viral capsids

- 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

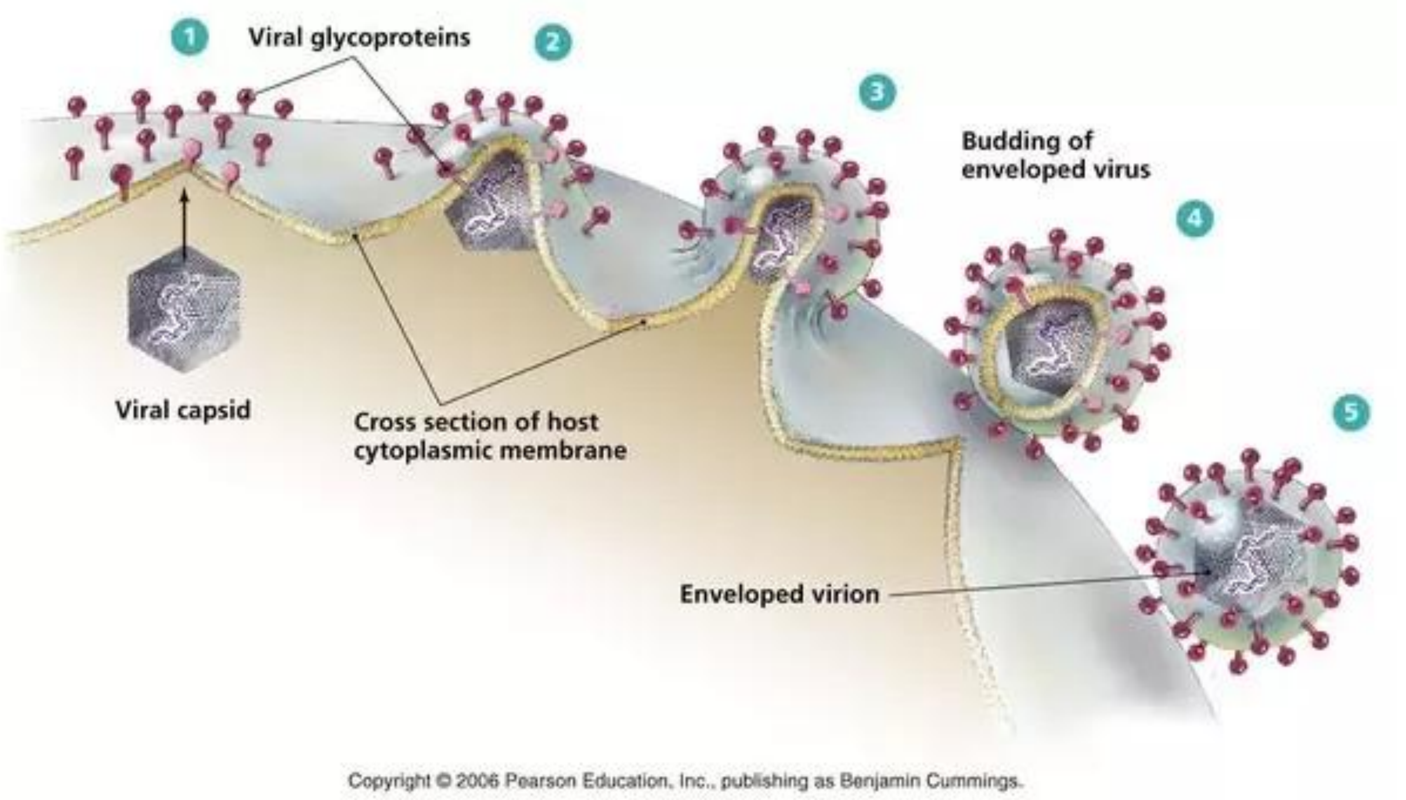




(a) Tobacco mosaic virus (b) Adenoviruses (c) Influenza viruses (d) Bacteriophage T4

Viral envelops

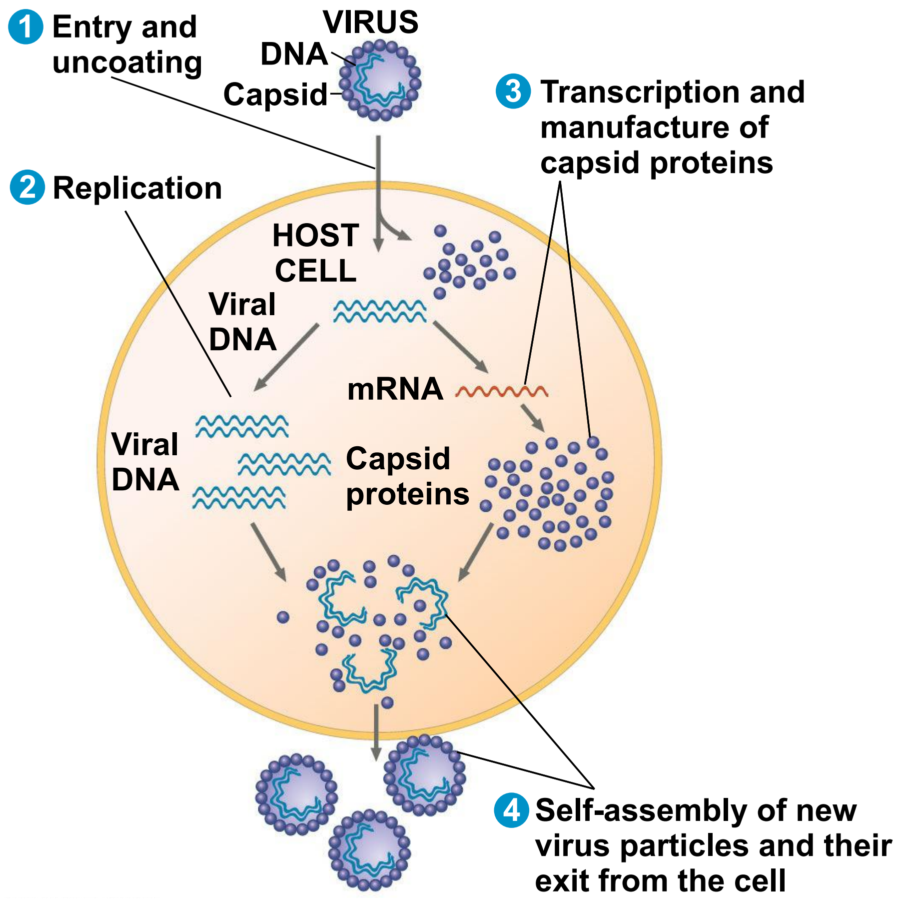
- Some viruses have accessory structures that help them infect hosts
- Viral envelopes (**derived from membranes of host cells**) surround the capsids of influenza viruses and many other viruses found in animals
- Viral envelopes contain a combination of viral and host cell molecules



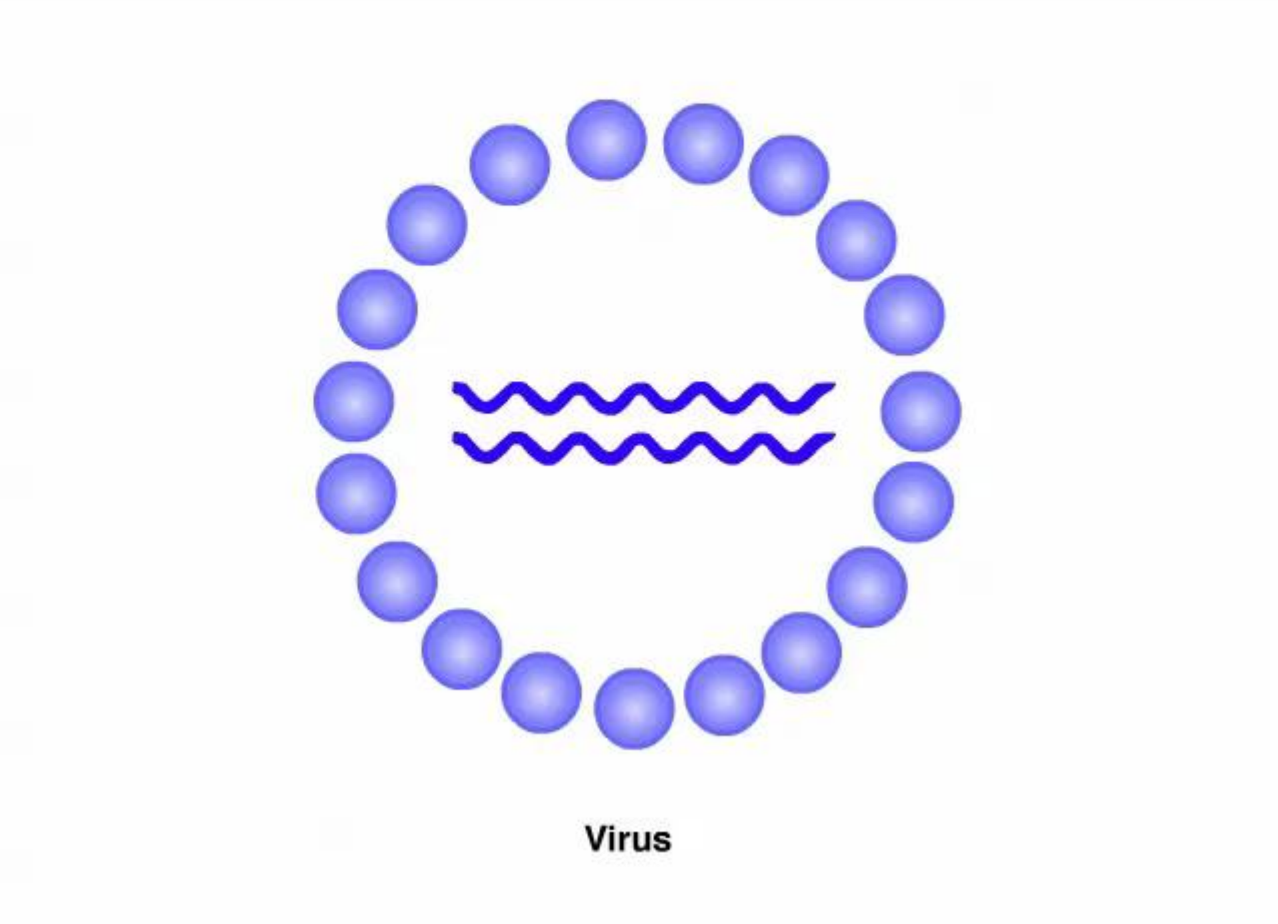
Viral replication

General Features of Viral Replication Cycles

Viruses are **obligate intracellular parasites**, which means they can replicate only within a host cell

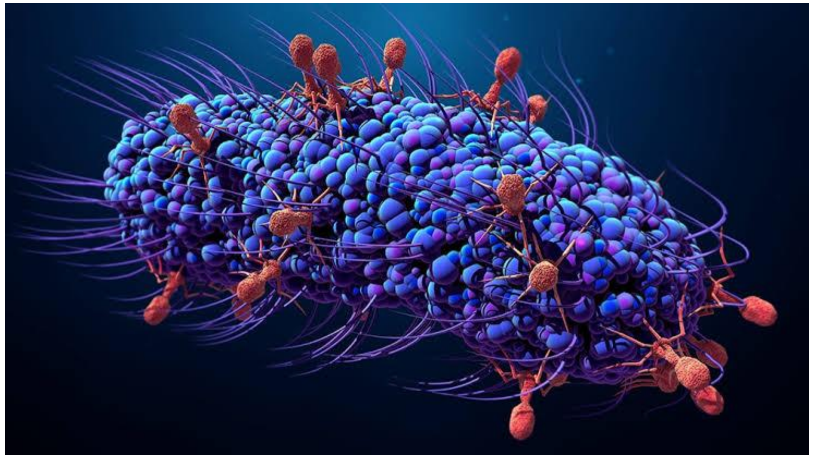
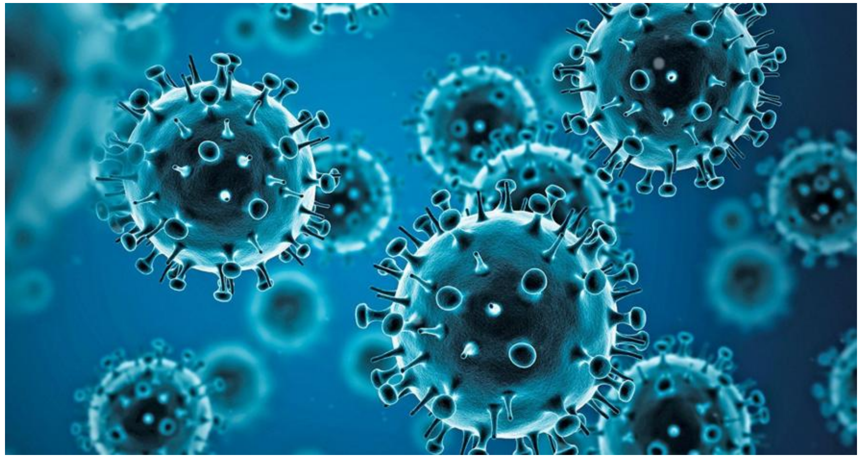


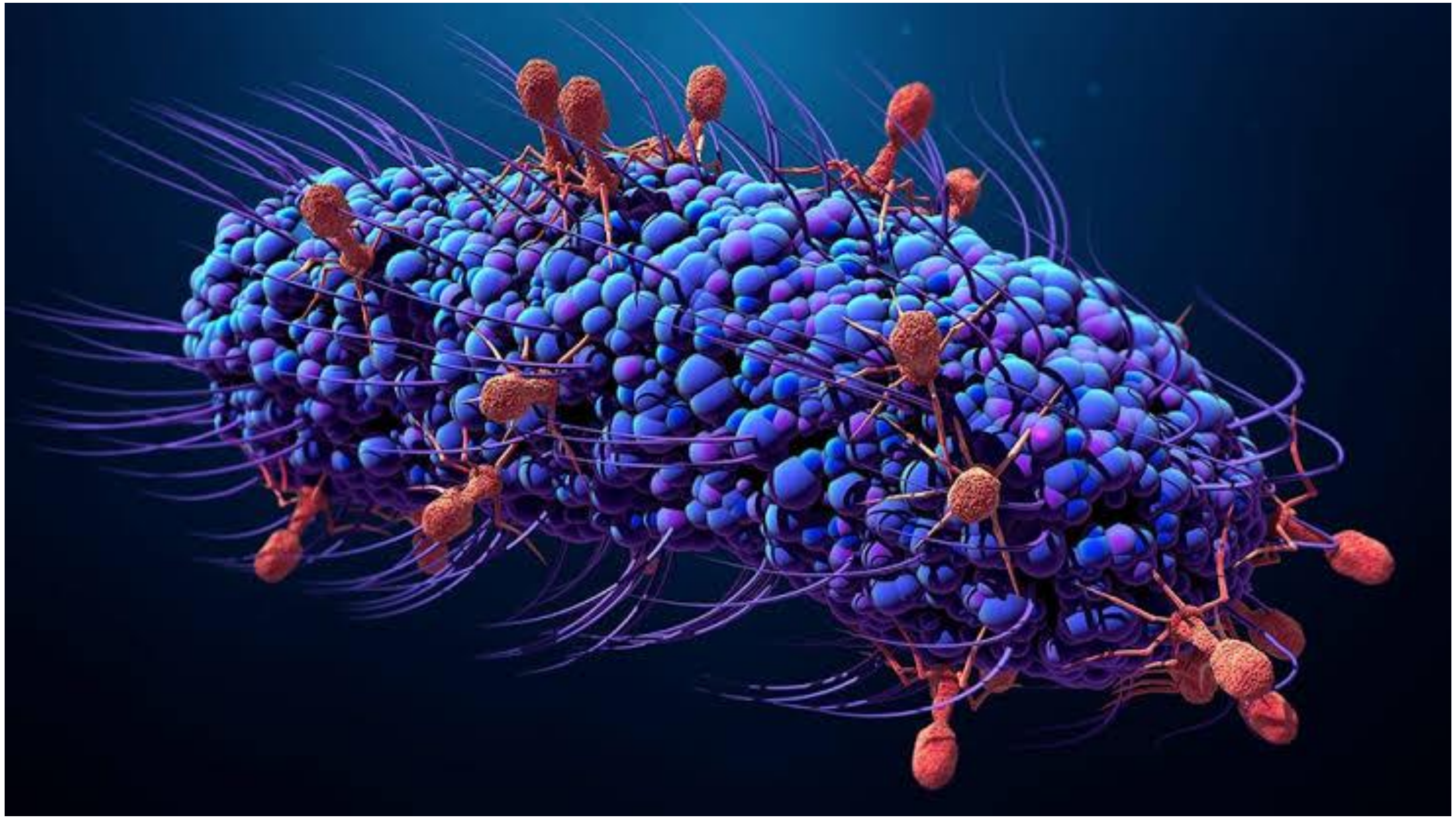
Animation: Simplified Viral Replication Cycle



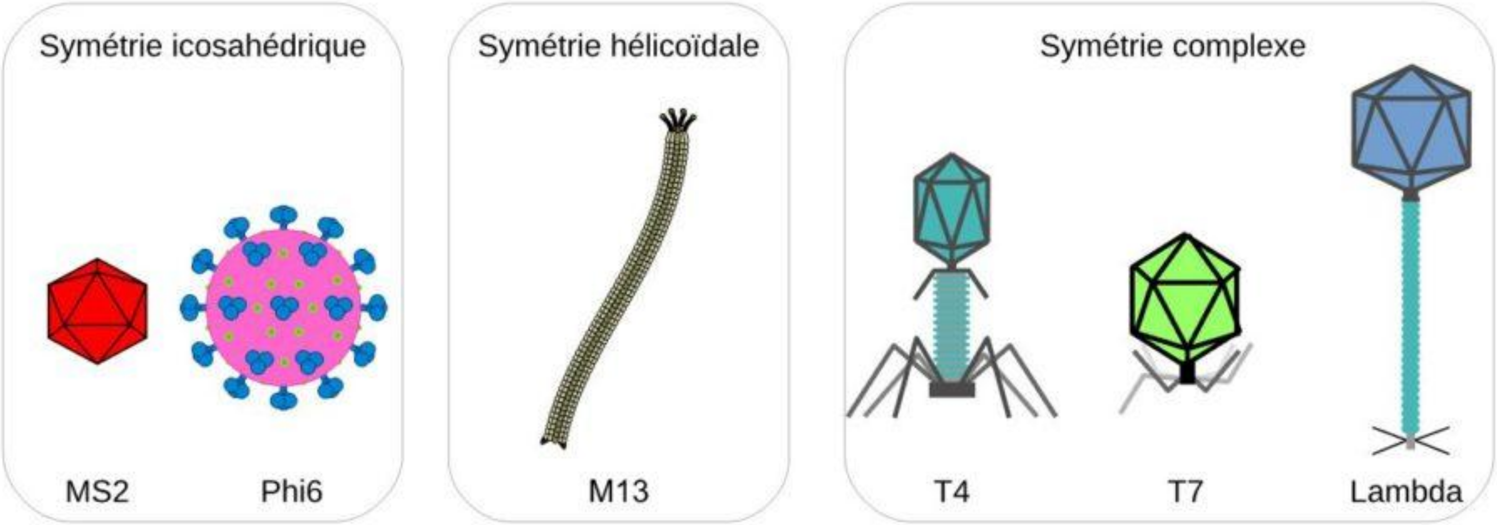
*Viruses have **narrow host ranges***

Viruses have very specific host range but there is viruses infecting all sorts of living organisms including bacteria



Bacterio**phages** = Viruses that infect bacteria



- **Bacteriophages**, also called **phages**, are viruses that infect bacteria
- They are the best characterized of all viruses
- 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

Replication Cycles of Phages

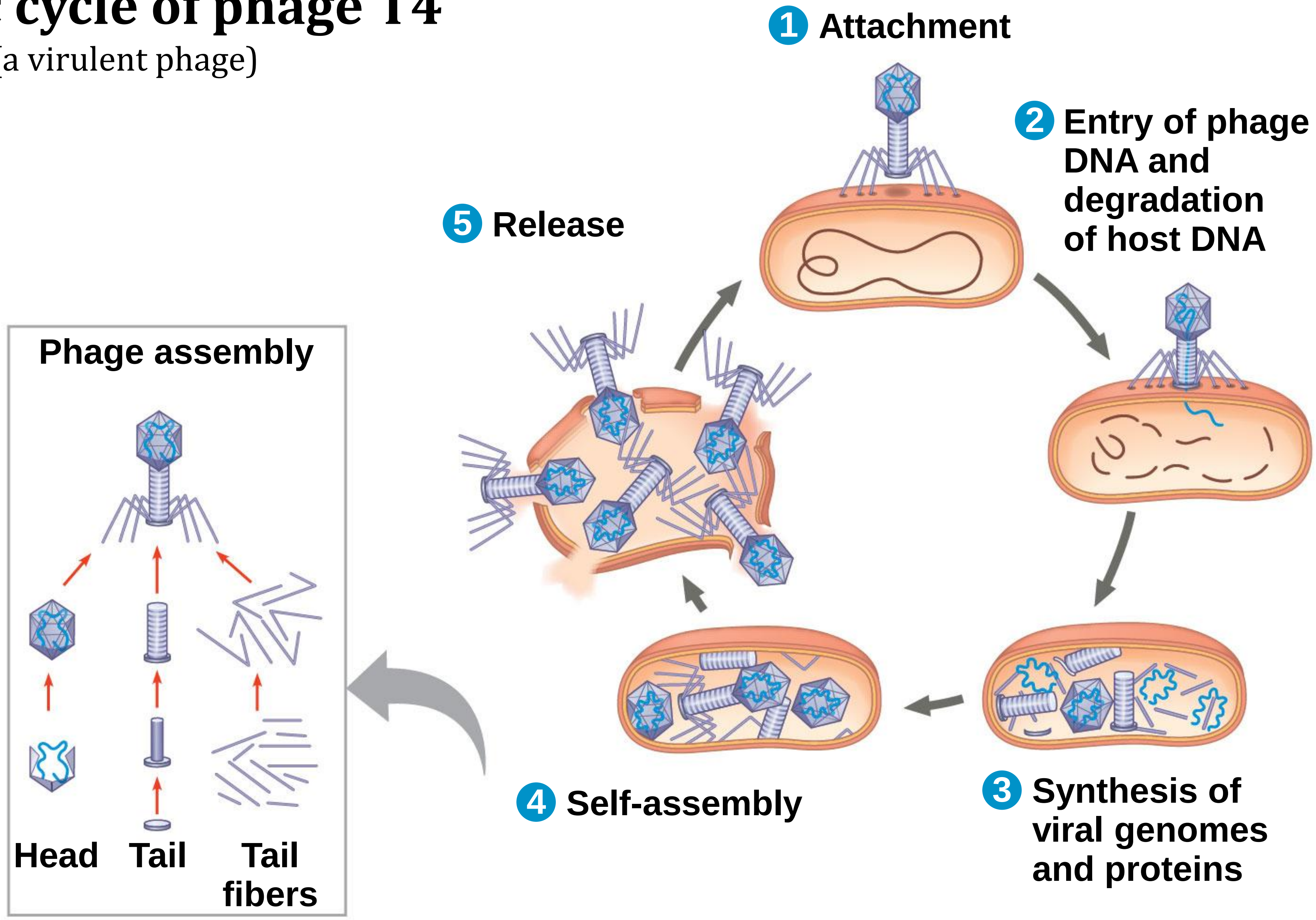
Phages have two alternative replication mechanisms: the **lytic cycle** and the **lysogenic cycle**

The Lytic Cycle

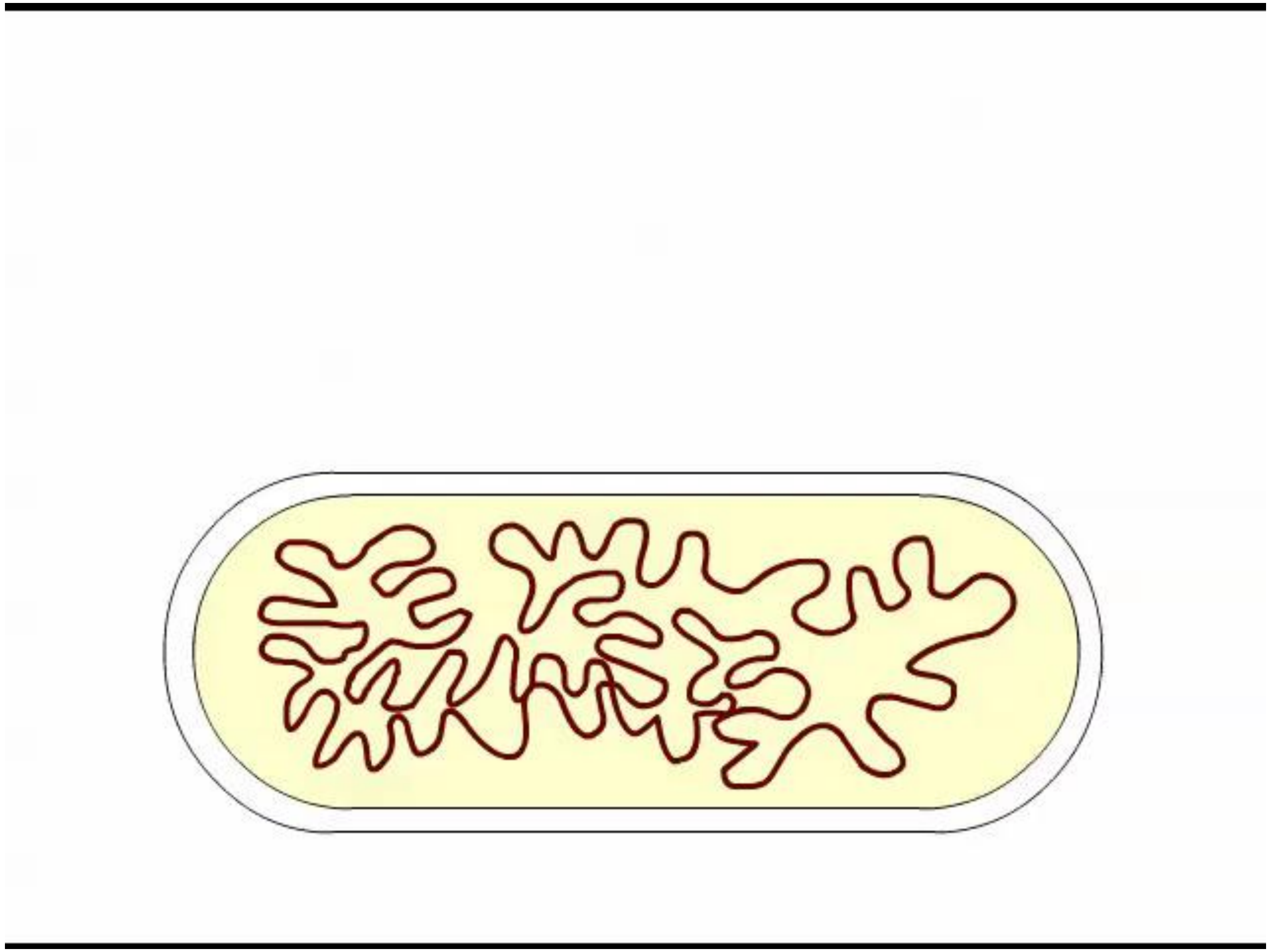
- The lytic cycle is a phage replicative cycle that culminates in the **death of the host cell**
- The lytic cycle produces new phages and lyses (breaks open) the host’s cell wall, releasing the progeny viruses
- A phage that reproduces only by the lytic cycle is called a **virulent phage**

The lytic cycle of phage T4

(a virulent phage)



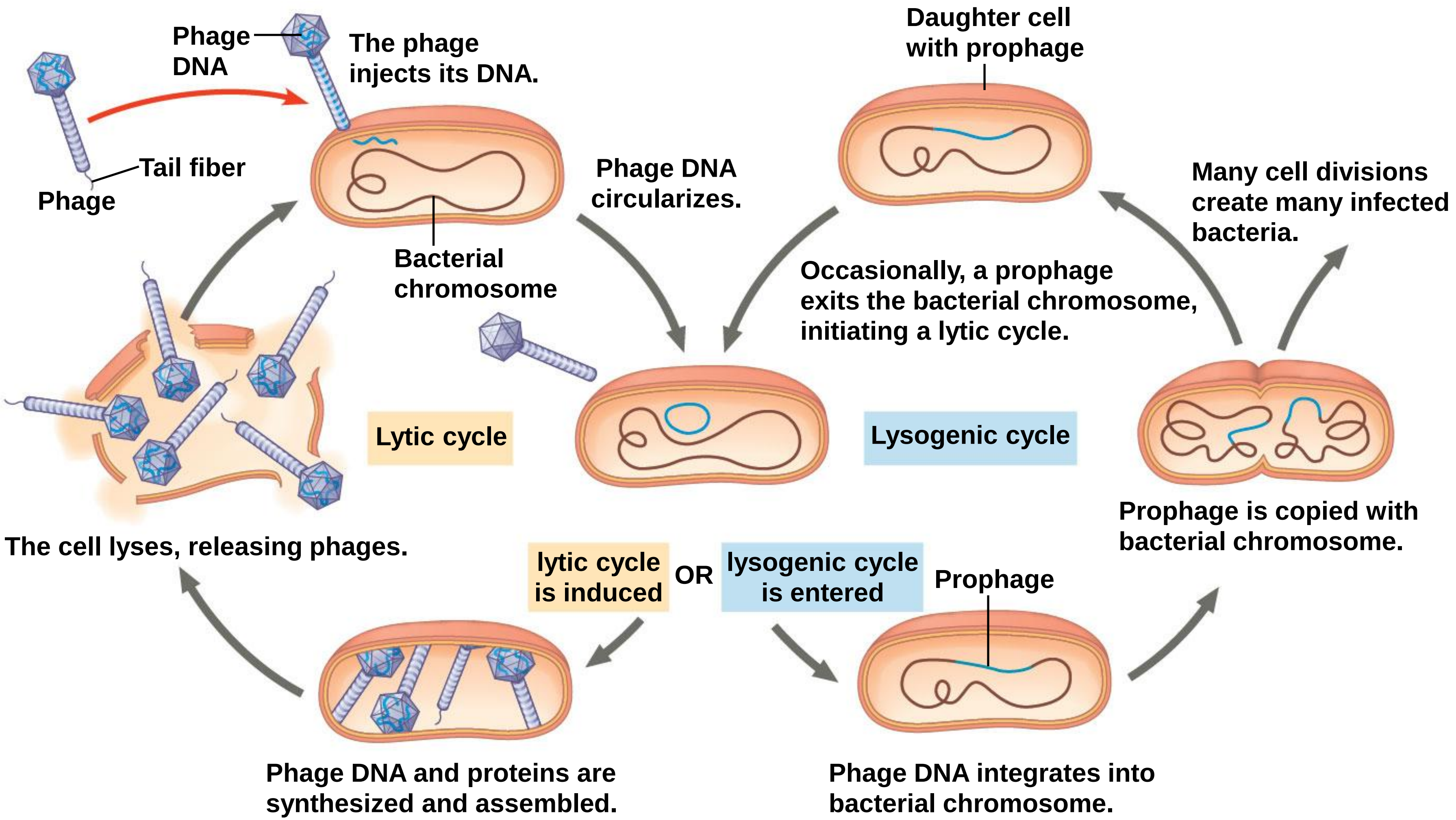
Animation: Phage T4 Lytic Cycle

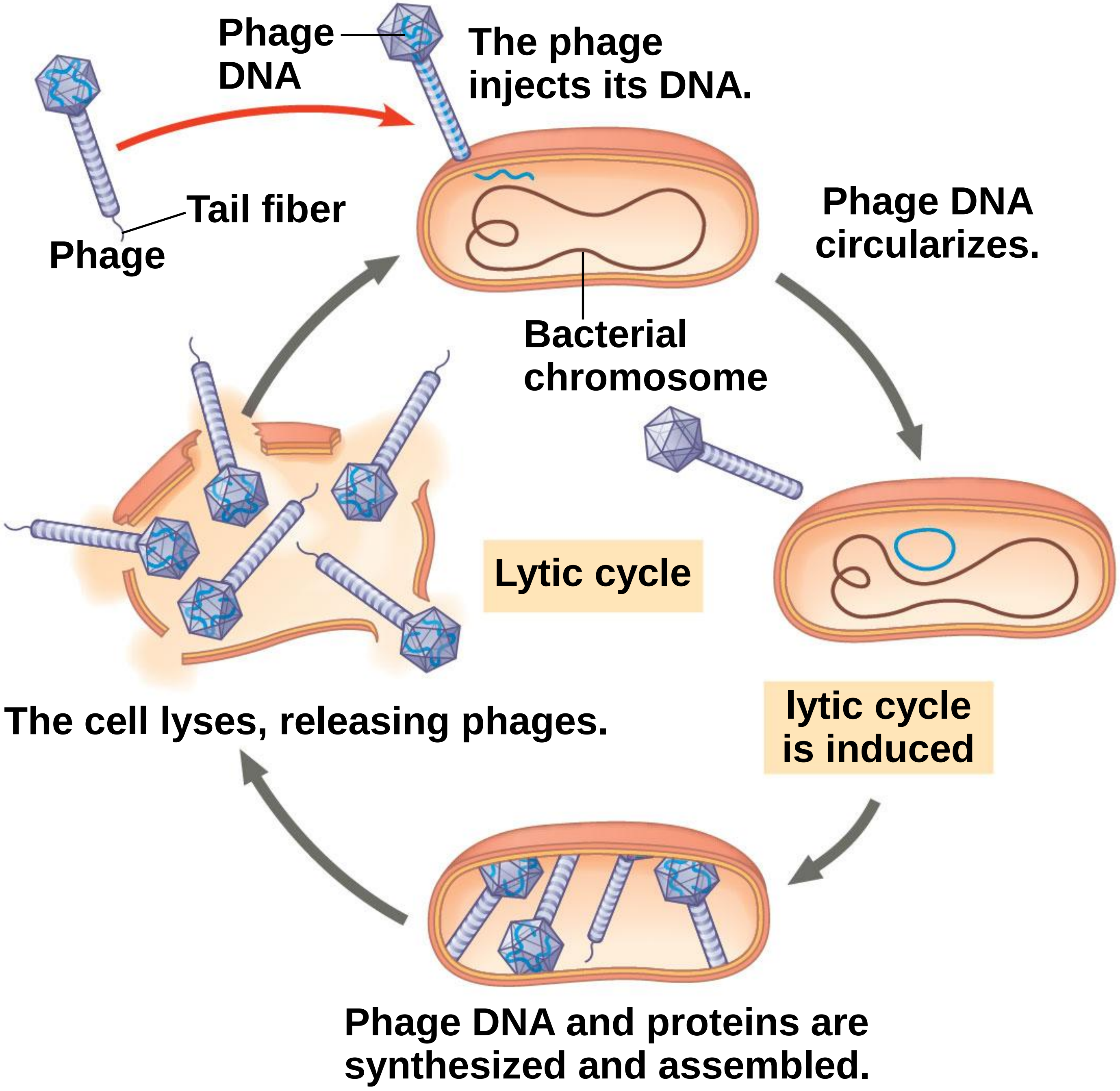


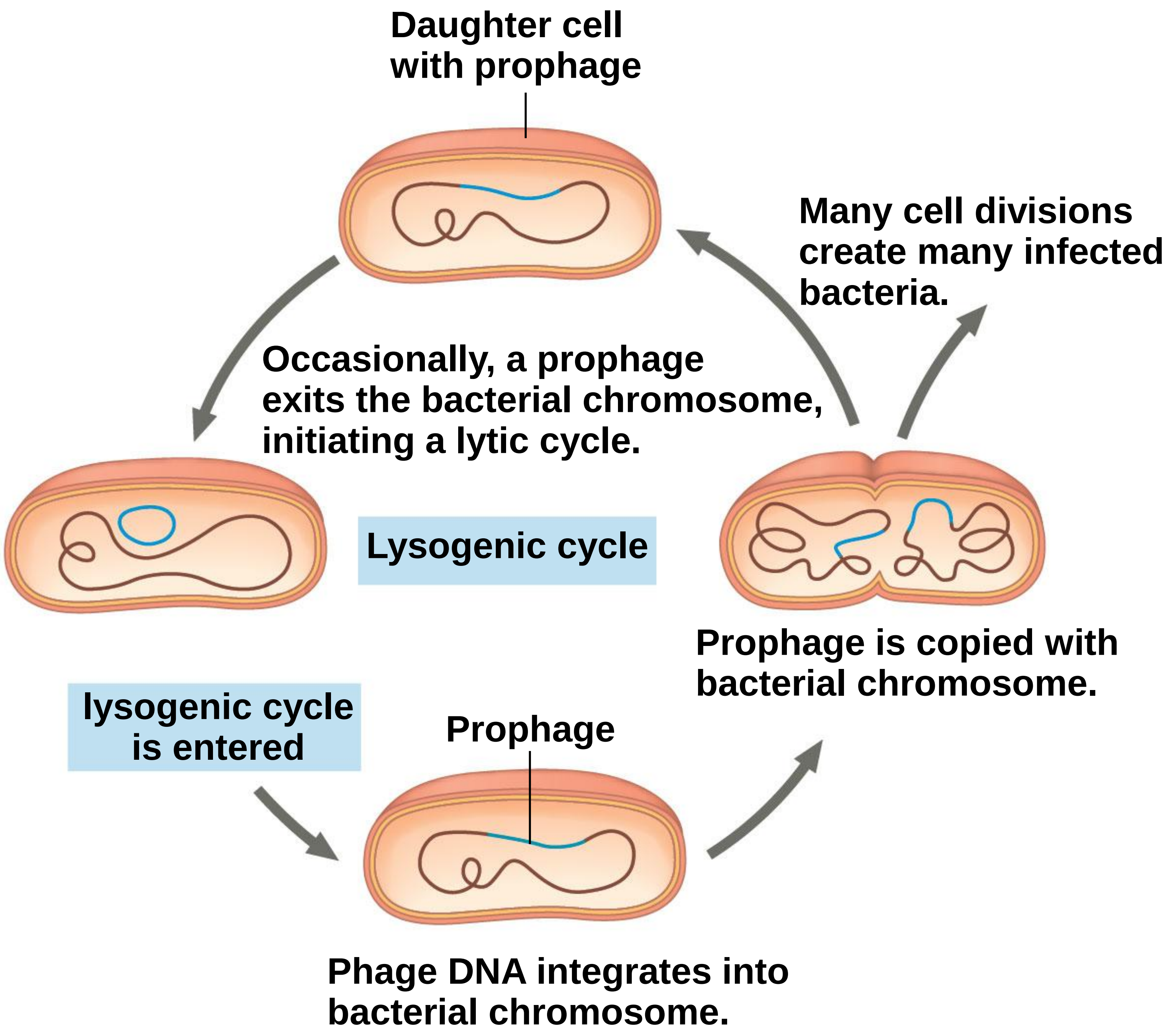
The Lysogenic Cycle

- 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**
- 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

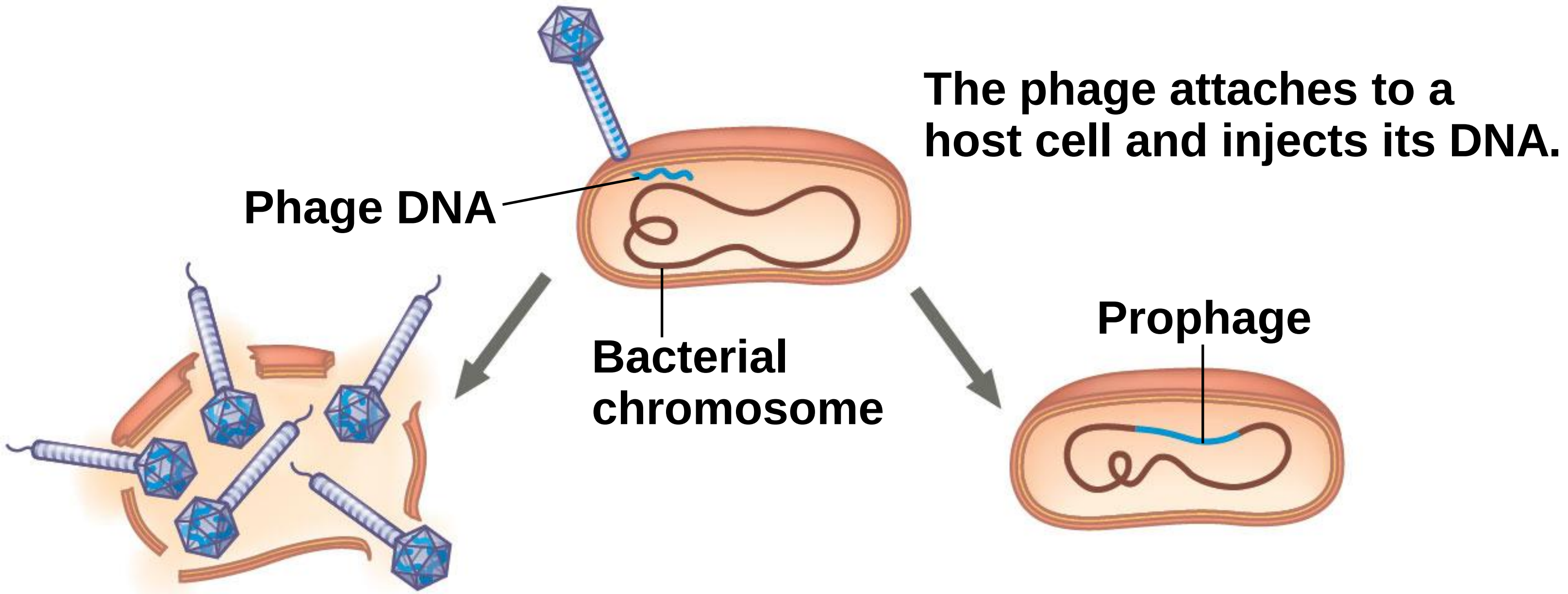
The lytic and lysogenic cycles of phage λ
(a temperate phage)




Phage DNA
The phage injects its DNA.
Tail fiber
Phage
Phage DNA circularizes.
Bacterial chromosome
Lytic cycle
lytic cycle is induced
The cell lyses, releasing phages.
Phage DNA and proteins are synthesized and assembled.


Daughter cell
with prophage
Many cell divisions
create many infected
bacteria.
Occasionally, a prophage
exits the bacterial chromosome,
initiating a lytic cycle.
Lysogenic cycle
Prophage is copied with
bacterial chromosome.
lysogenic cycle
is entered
Prophage
Phage DNA integrates into
bacterial chromosome.

Summary of key concepts: lytic and lysogenic cycles



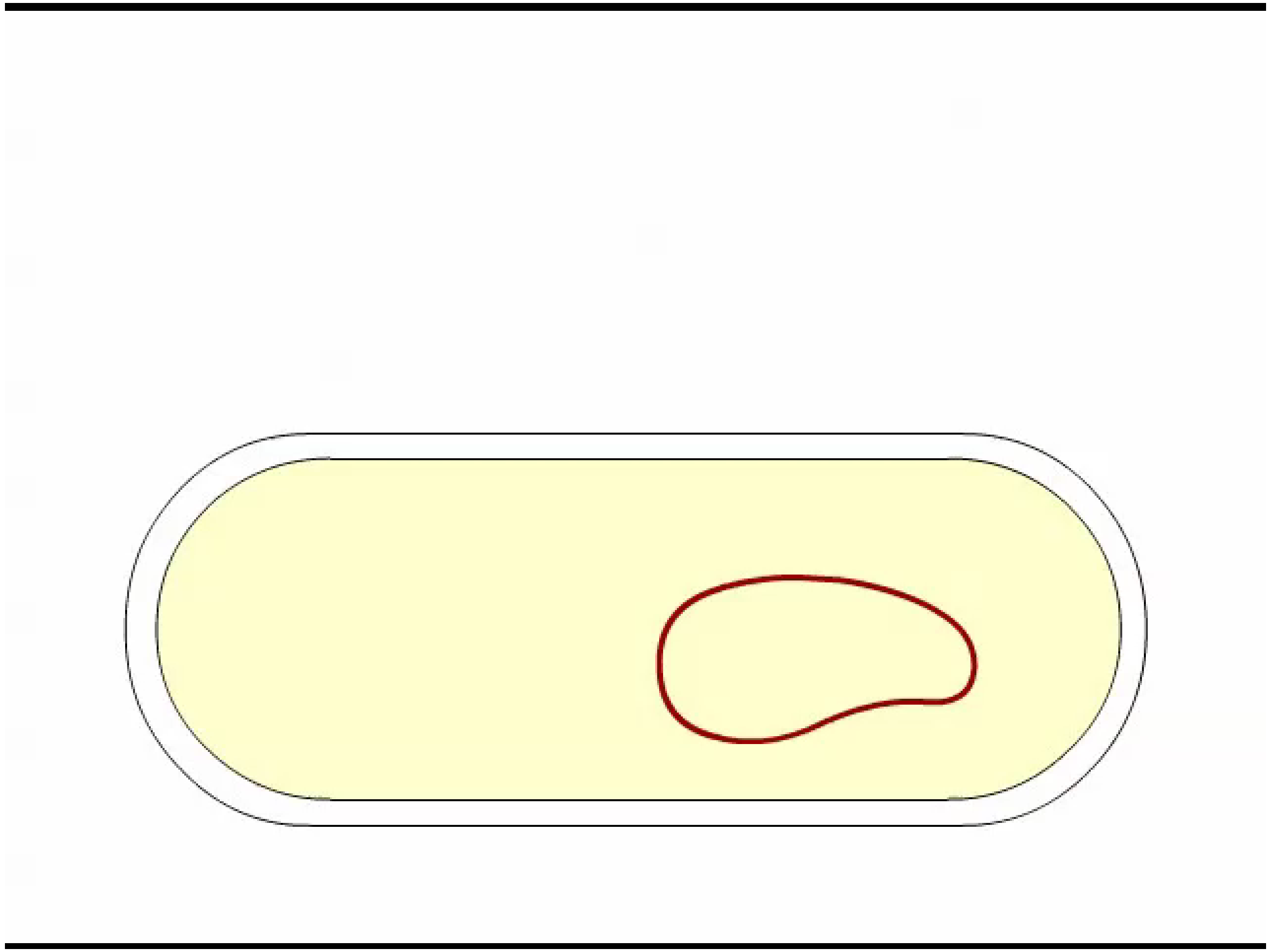
Lytic cycle

- 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

Animation: Phage Lysogenic and Lytic Cycles

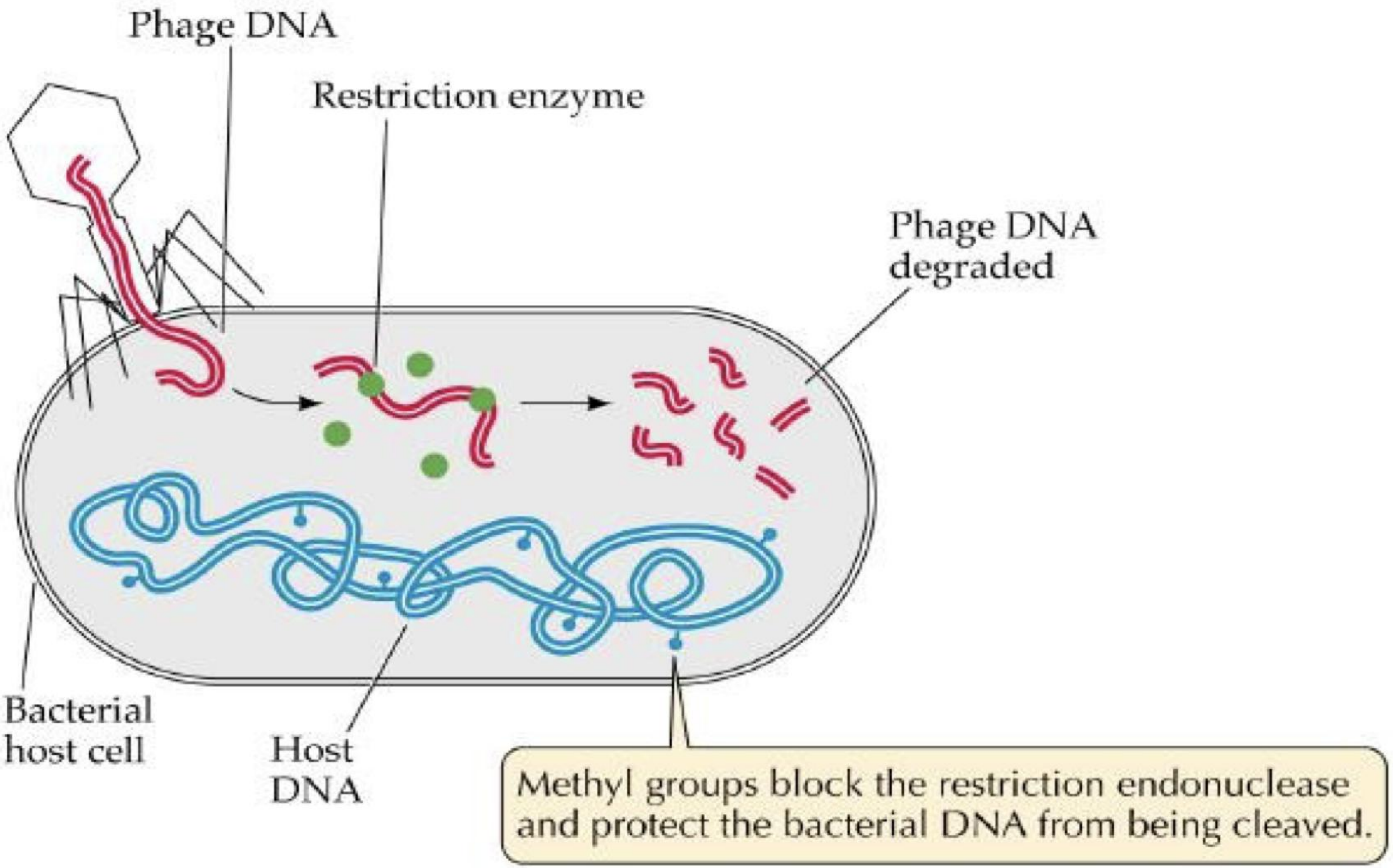


Bacterial Defenses Against Phages

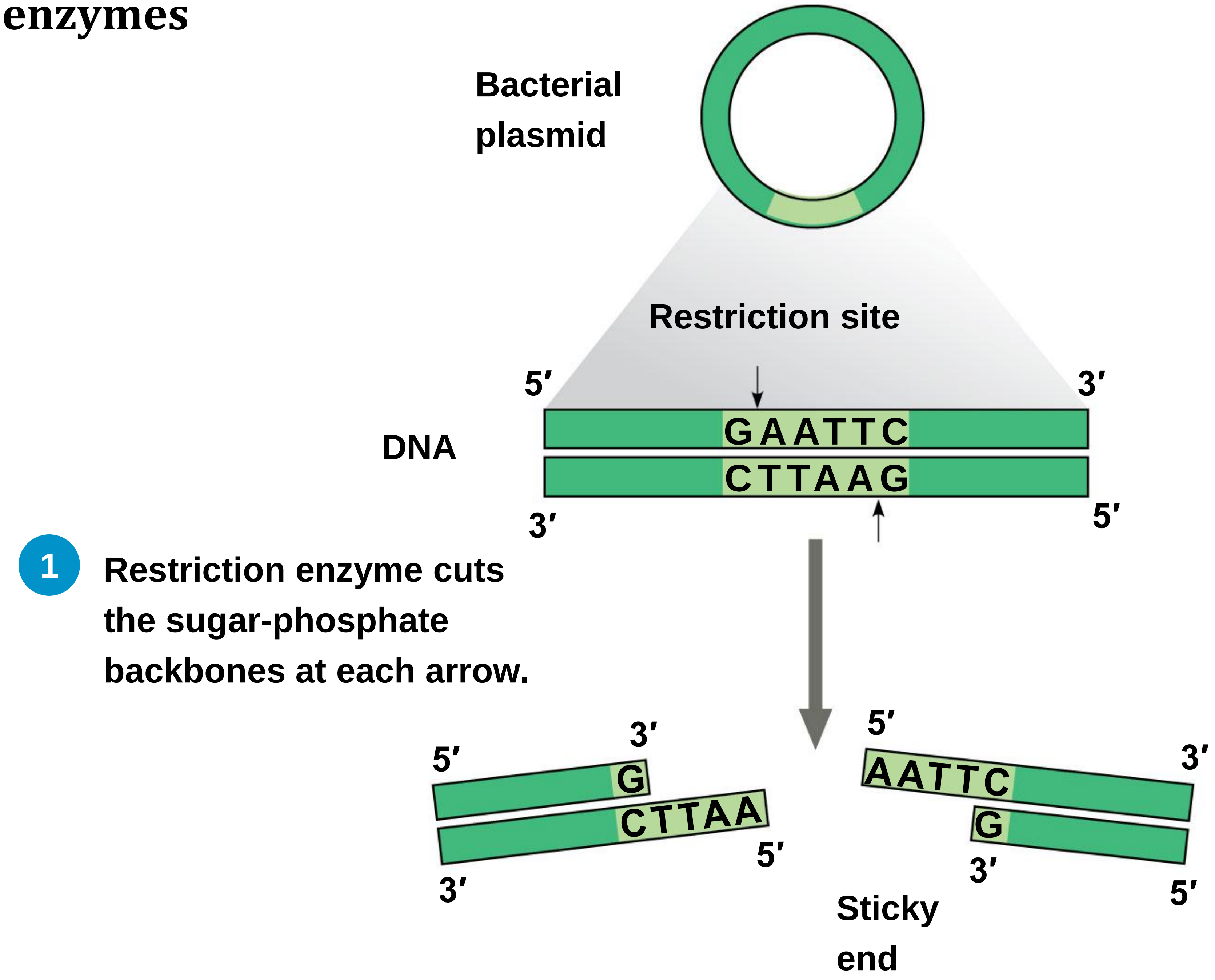
Restriction enzymes

- 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

Restriction enzymes



Restriction enzymes

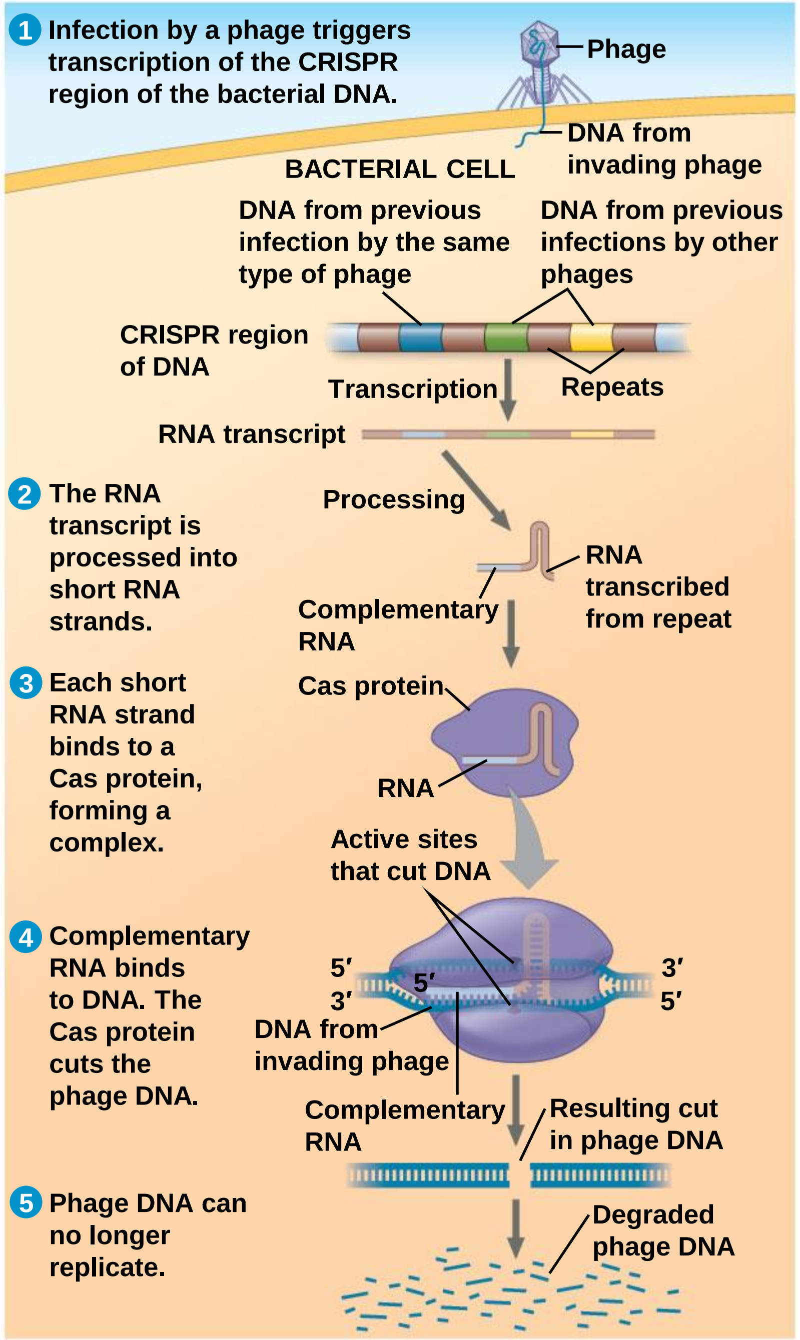


Bacterial Defenses Against Phages

CRISPR-Cas system

- Both bacteria and archaea can protect themselves from viral infection with the CRISPR-Cas system (**family of DNA sequences**)
- 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

The CRISPR-Cas system: a type of bacterial immune system



- 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

- 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**

Viruses that infect animals

Replication 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

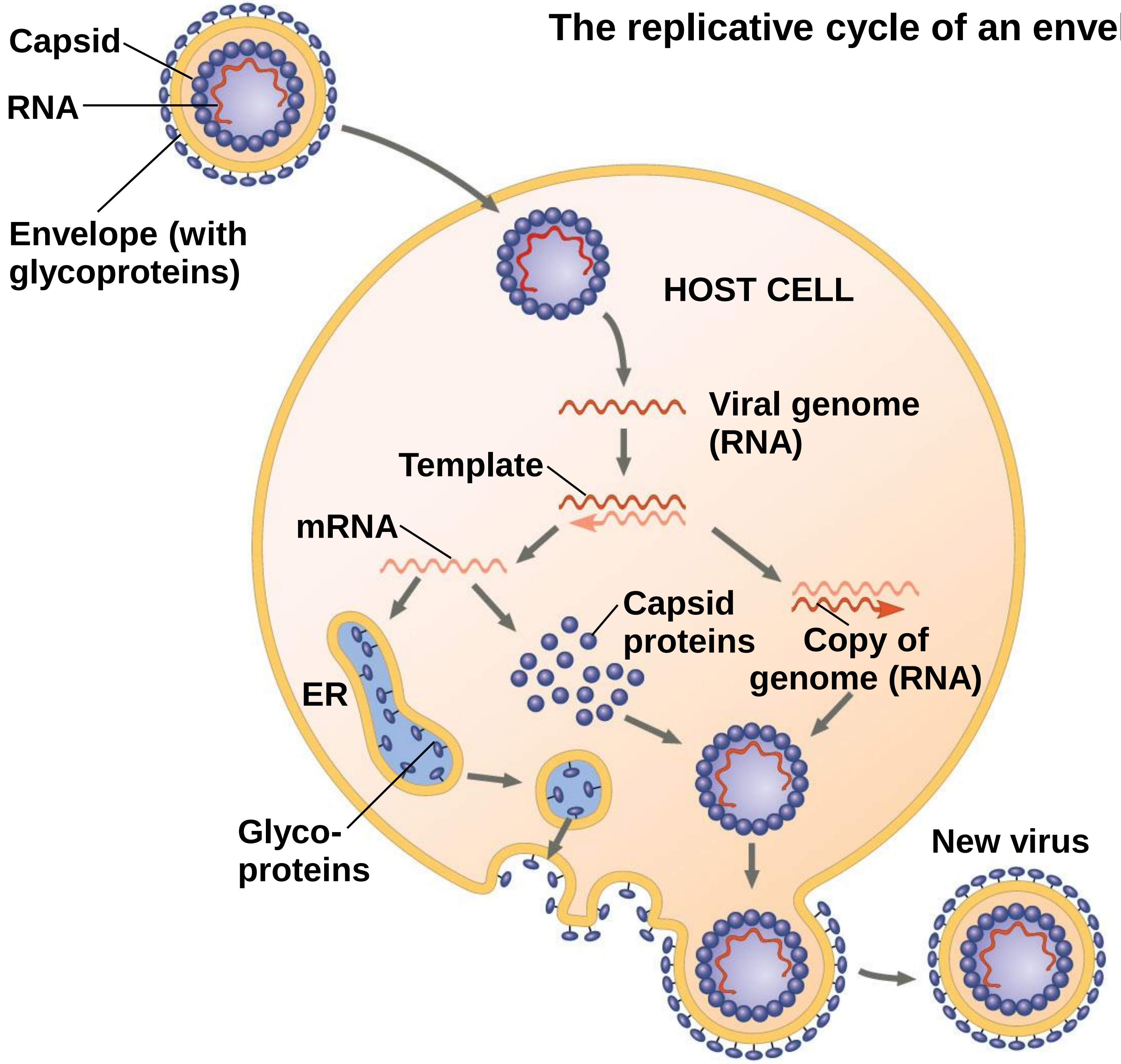
Table 26.1 Classes of Animal Viruses

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

Table 26.1 Classes of Animal Viruses

Class/Family	Envelope?	Examples That Cause Human Diseases
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); RNA tumor viruses (leukemia)

The replicative cycle of an enveloped RNA virus

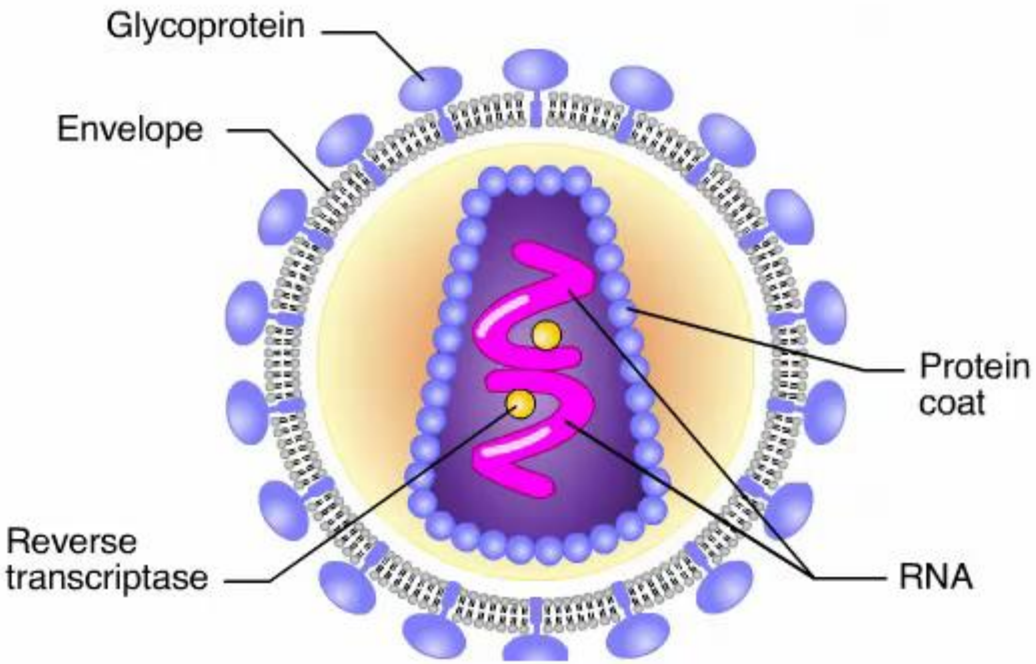


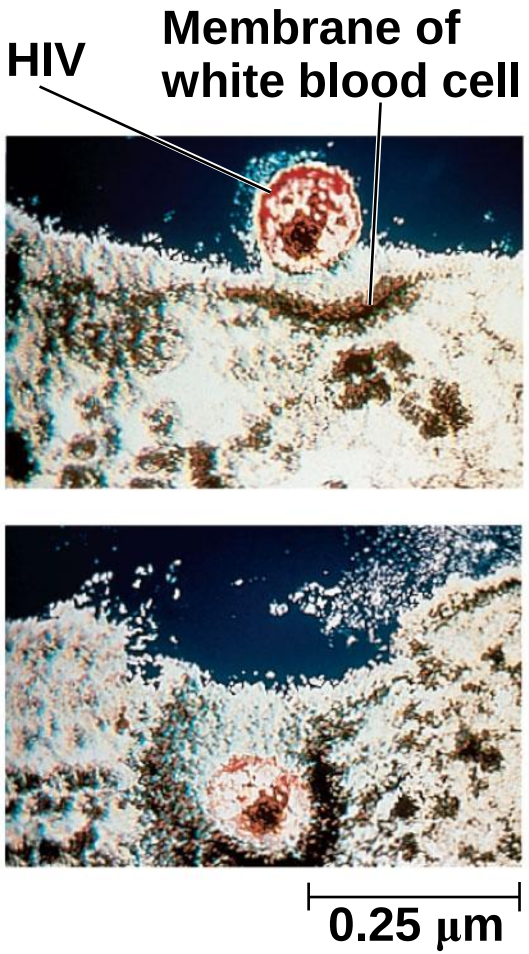
Viral Genetic Material

- 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)**

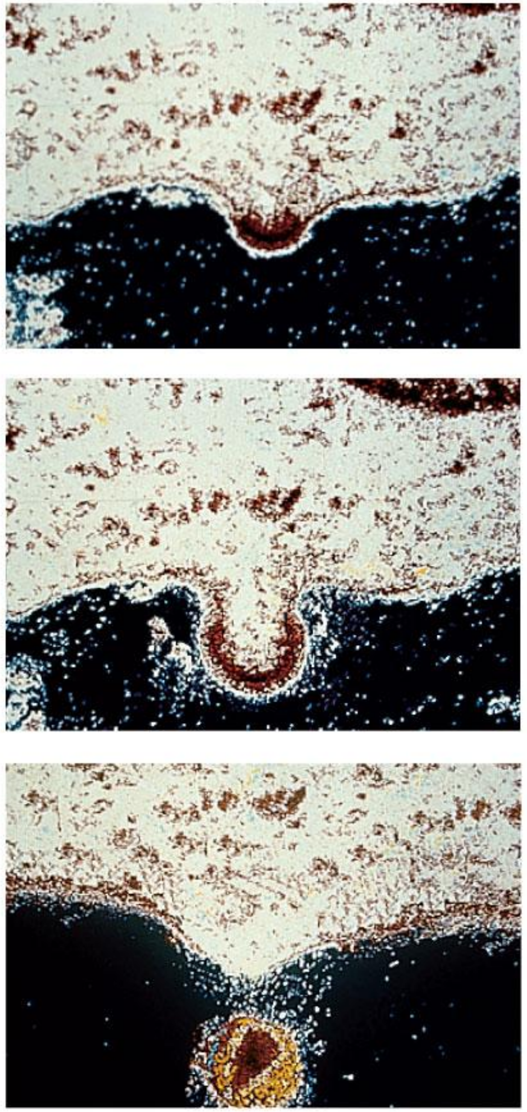
- The viral DNA that is integrated into the host genome is called a **provirus**
- Unlike a prophage, a provirus remains a permanent resident of the host cell
- RNA polymerase transcribes the proviral DNA into RNA molecules
- The RNA molecules function both as mRNA for synthesis of viral proteins and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

Animation: HIV Replication Cycle





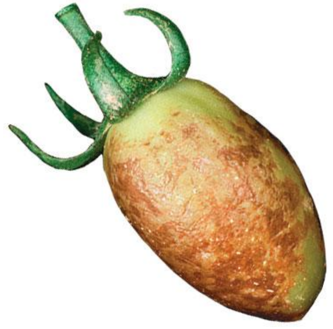
HIV entering a cell



New HIV leaving a cell

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
- Many have a helical capsid, while others have an icosahedral capsid
- Plant viruses spread disease by two major routes:
  - Horizontal transmission, **entering** through damaged cell walls
  - Vertical transmission, **inheriting** the virus from a parent



Immature tomato infected by a virus

Viral evolution and antiviral molecules

Evolution of Viruses

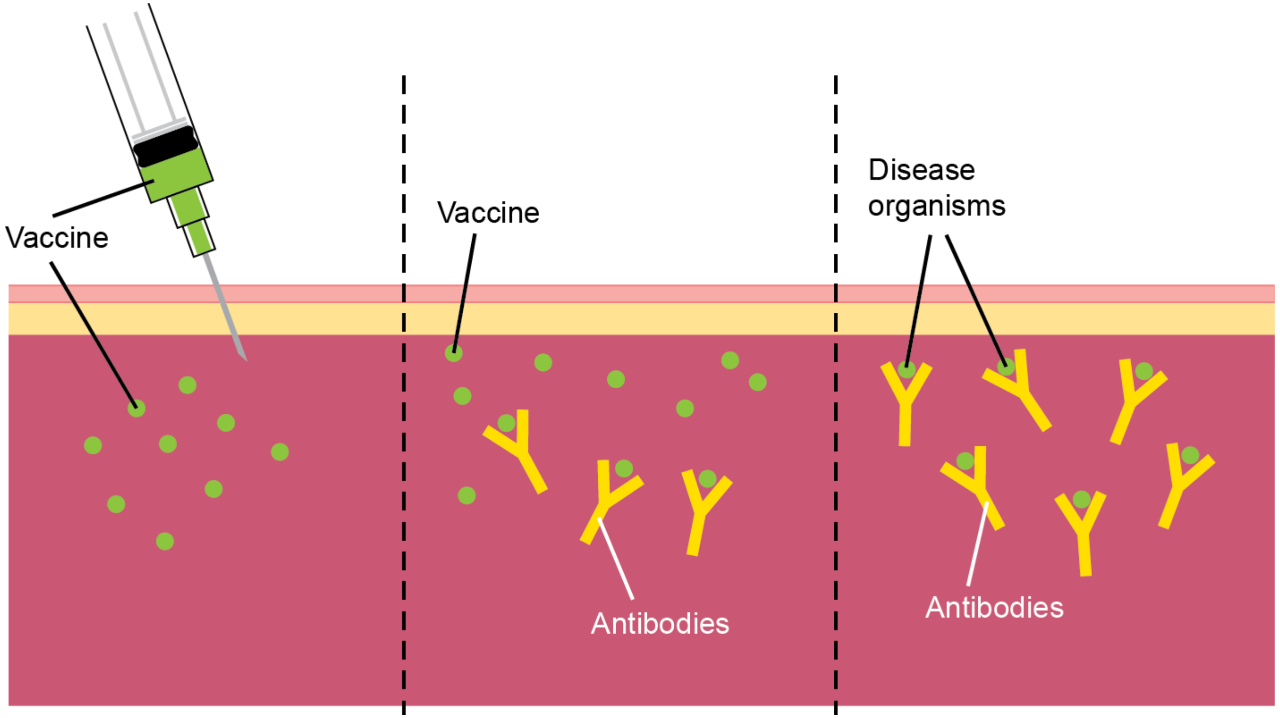
- Viruses do not fit our definition of living organisms
- Since viruses can replicate only within cells, they probably evolved as bits of cellular nucleic acid
- Candidates for the source of viral genomes include plasmids and transposons
- Plasmids, transposons, and viruses are all **mobile genetic elements**

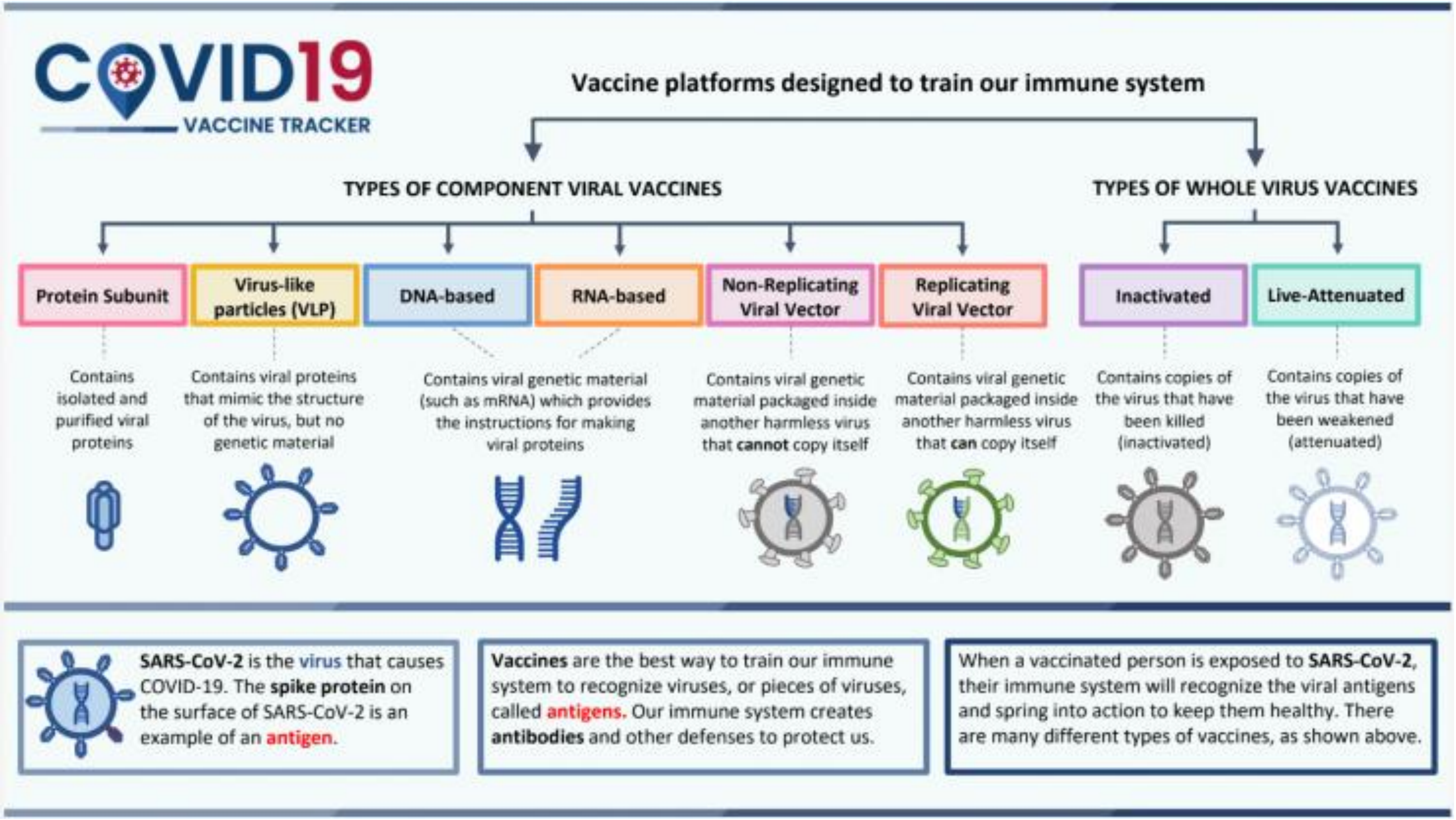
Viruses and prions are **formidable pathogens** in animals and plants

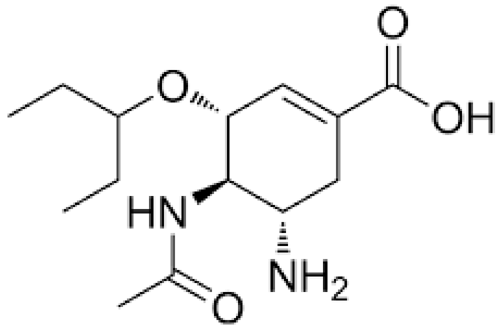
- Diseases caused by viral infections **affect humans, agricultural crops, and livestock worldwide**
- Smaller, less complex entities called prions also cause disease in plants and animals, respectively
- Viruses may **damage or kill cells** by causing the release of hydrolytic enzymes from lysosomes
- Some viruses cause infected cells to **produce toxins** that lead to disease symptoms
- Others have molecular components such as **envelope proteins that are toxic**

Viruses: vaccines and antiviral drugs

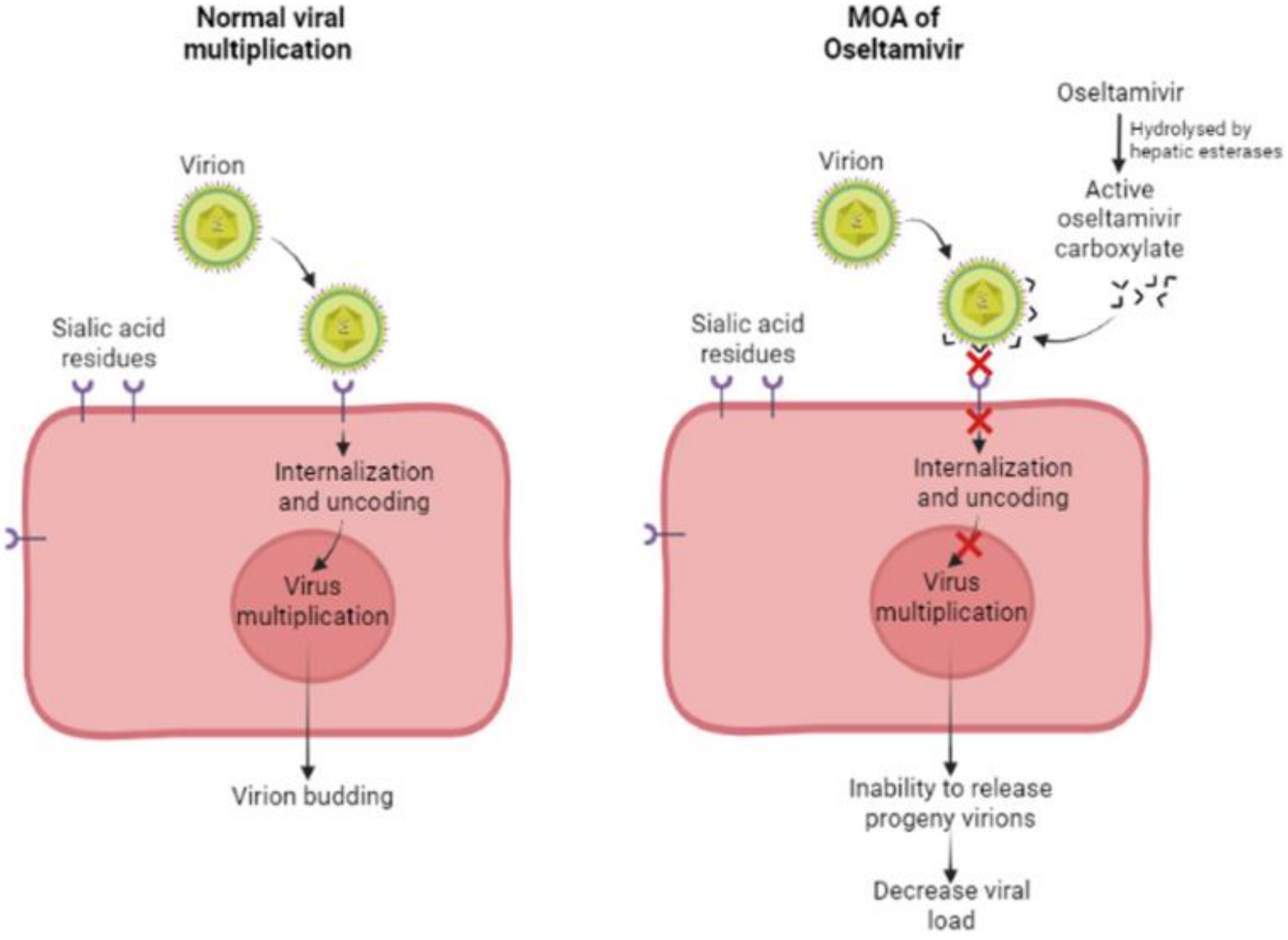
- A vaccine is a harmless derivatives of pathogenic microbes that **stimulate the immune system** to mount defenses against the harmful pathogen
- Vaccines can **prevent** certain viral illnesses
- Viral infections **cannot be treated by antibiotics**
- Antiviral drugs can help to treat, not cure, viral infections by inhibiting synthesis of viral DNA and by interfering with viral assembly

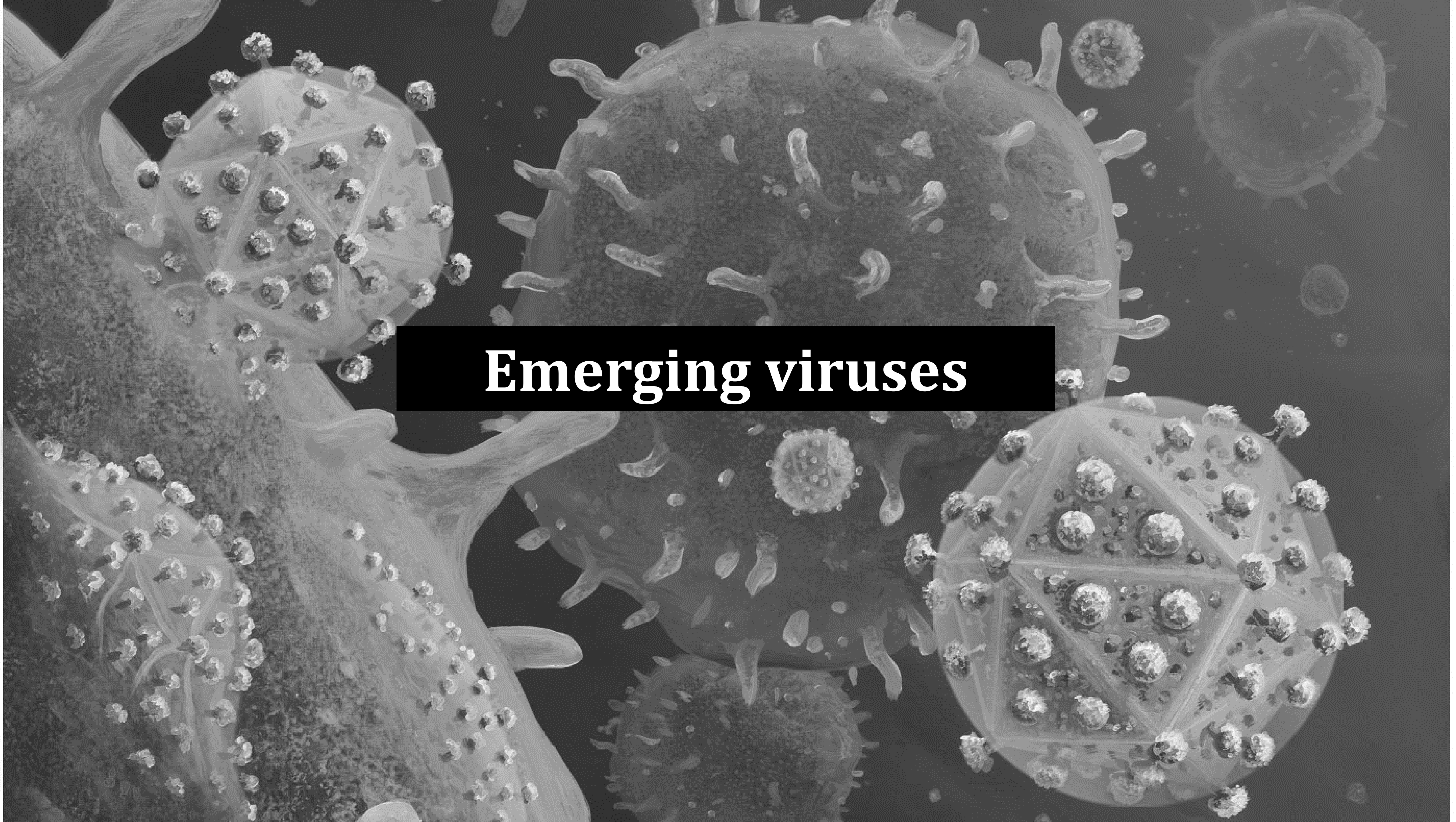



COVID19
VACCINE TRACKER
Vaccine platforms designed to train our immune system
TYPES OF COMPONENT VIRAL VACCINES
TYPES OF WHOLE VIRUS VACCINES
Protein Subunit
Virus-like particles (VLP)
DNA-based
RNA-based
Non-Replicating Viral Vector
Replicating Viral Vector
Inactivated
Live-Attenuated
Contains isolated and purified viral proteins
Contains viral proteins that mimic the structure of the virus, but no genetic material
Contains viral genetic material (such as mRNA) which provides the instructions for making viral proteins
Contains viral genetic material packaged inside another harmless virus that cannot copy itself
Contains viral genetic material packaged inside another harmless virus that can copy itself
Contains copies of the virus that have been killed (inactivated)
Contains copies of the virus that have been weakened (attenuated)
SARS-CoV-2 is the virus that causes COVID-19. The spike protein on the surface of SARS-CoV-2 is an example of an antigen.
Vaccines are the best way to train our immune system to recognize viruses, or pieces of viruses, called antigens. Our immune system creates antibodies and other defenses to protect us.
When a vaccinated person is exposed to SARS-CoV-2, their immune system will recognize the viral antigens and spring into action to keep them healthy. There are many different types of vaccines, as shown above.



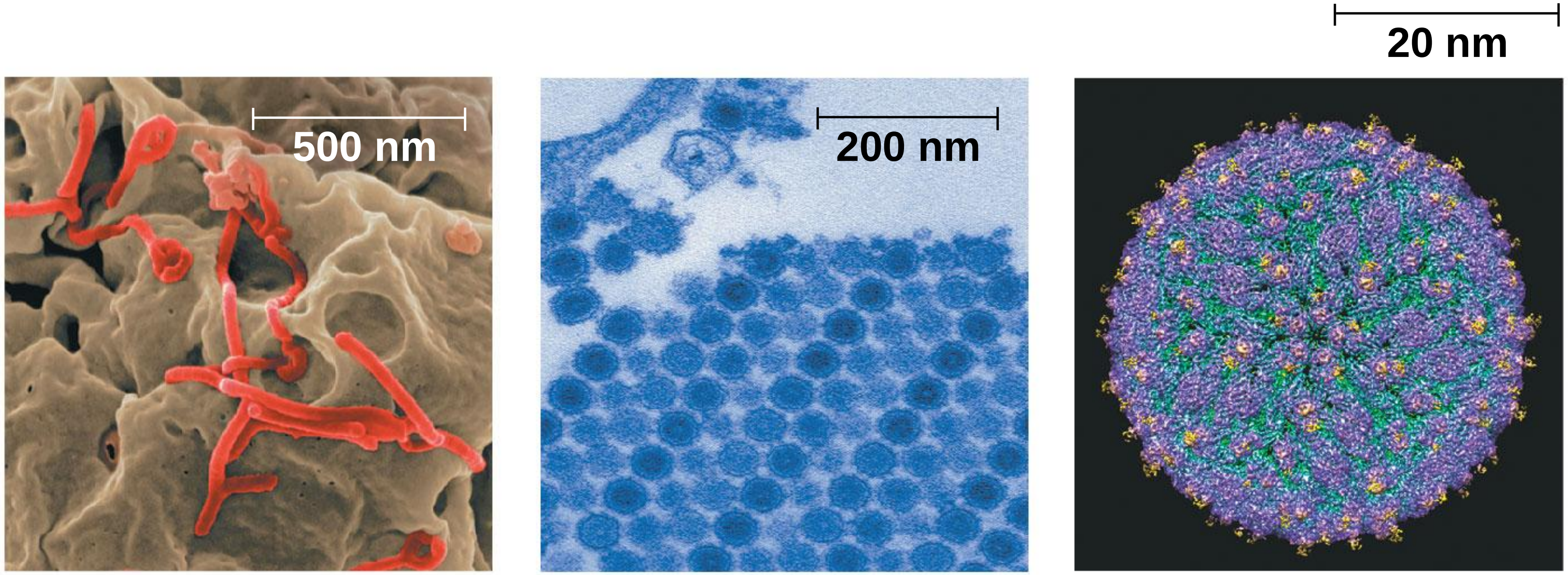
Mode of action **Oseltamivir, antiviral** used against Influenza




Emerging viruses

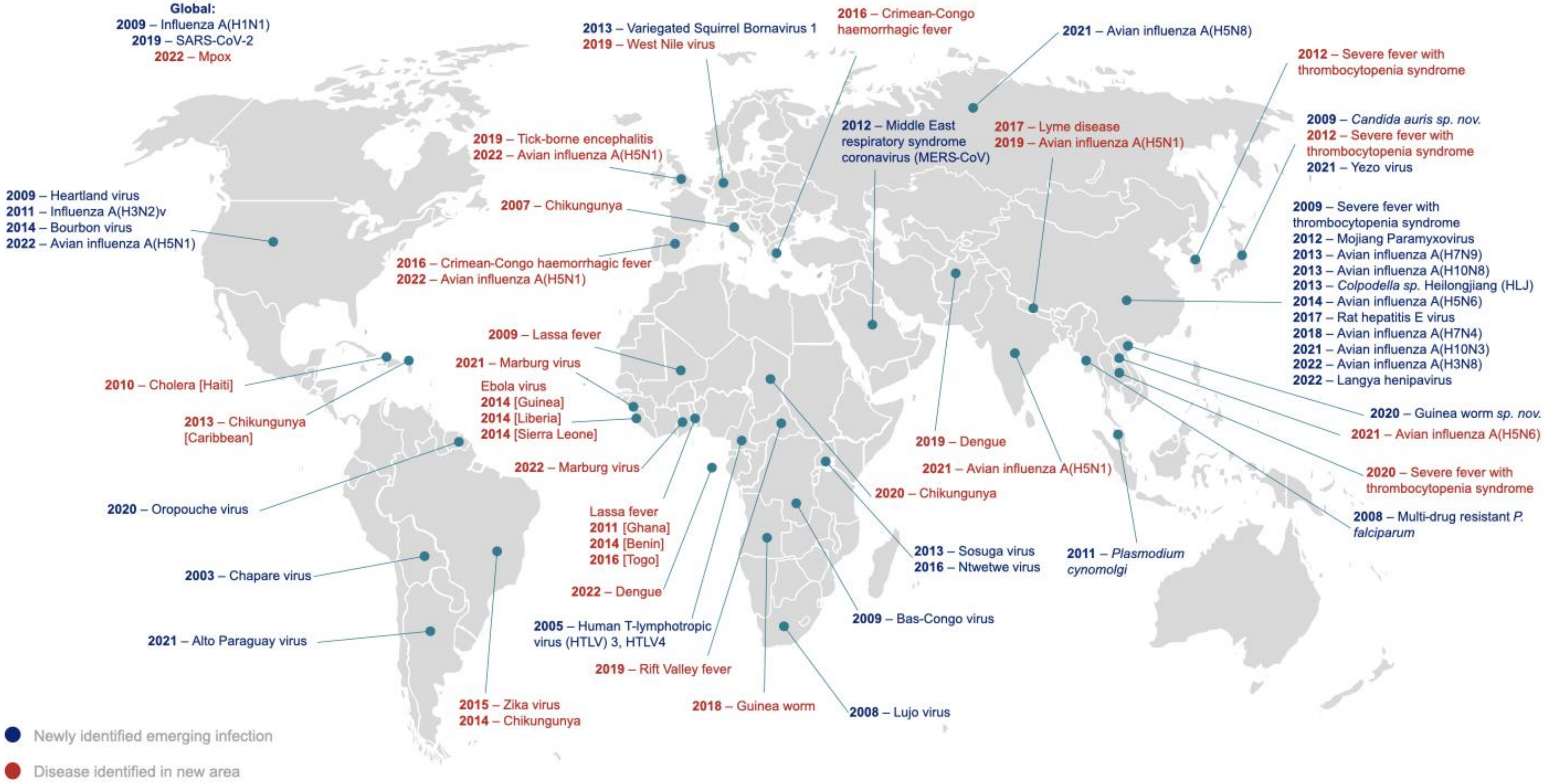
Emerging Viruses

- Emerging viruses are those that **suddenly become apparent**
- The Ebola virus is one of several emerging viruses that cause hemorrhagic fever, an often fatal illness
- Other examples include the chikungunya virus and the recently emerging Zika virus (2015)



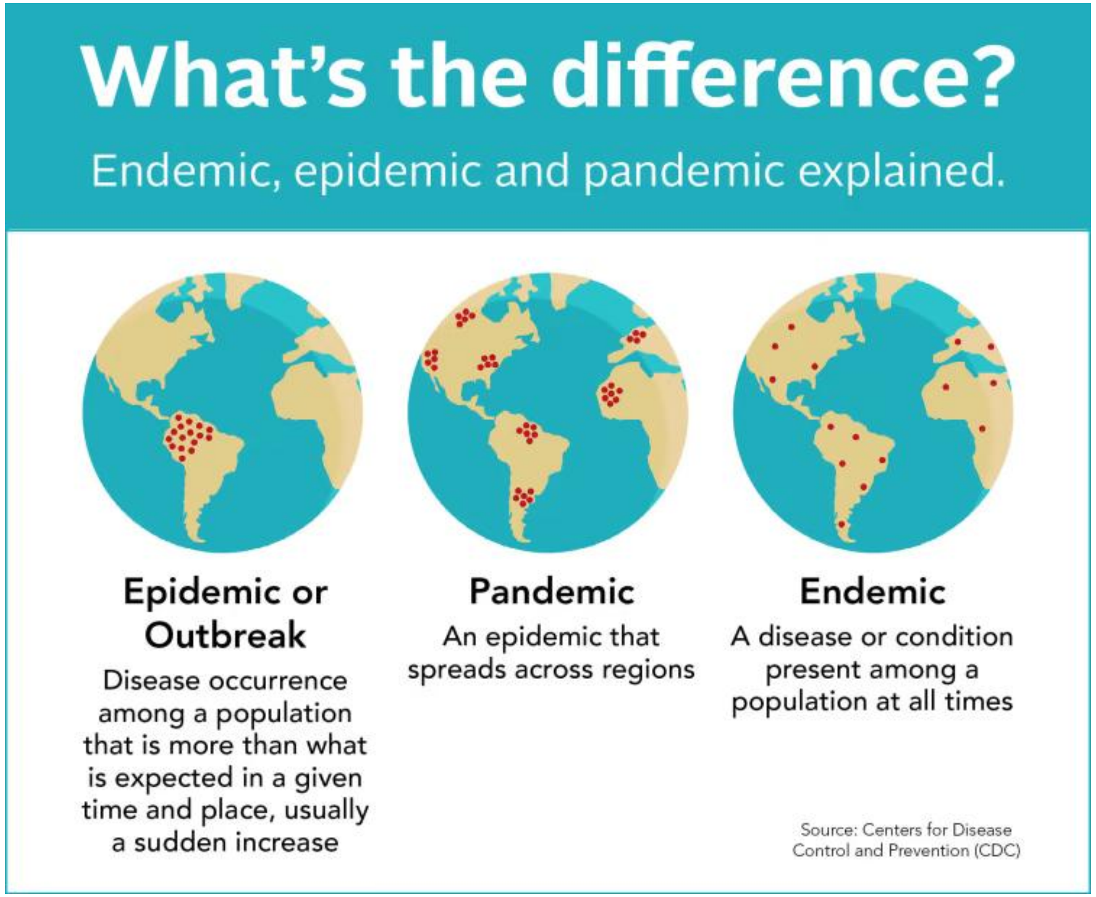
(a) Ebola viruses (b) Chikungunya viruses (c) Zika virus

Global map of emerging infections since 2003

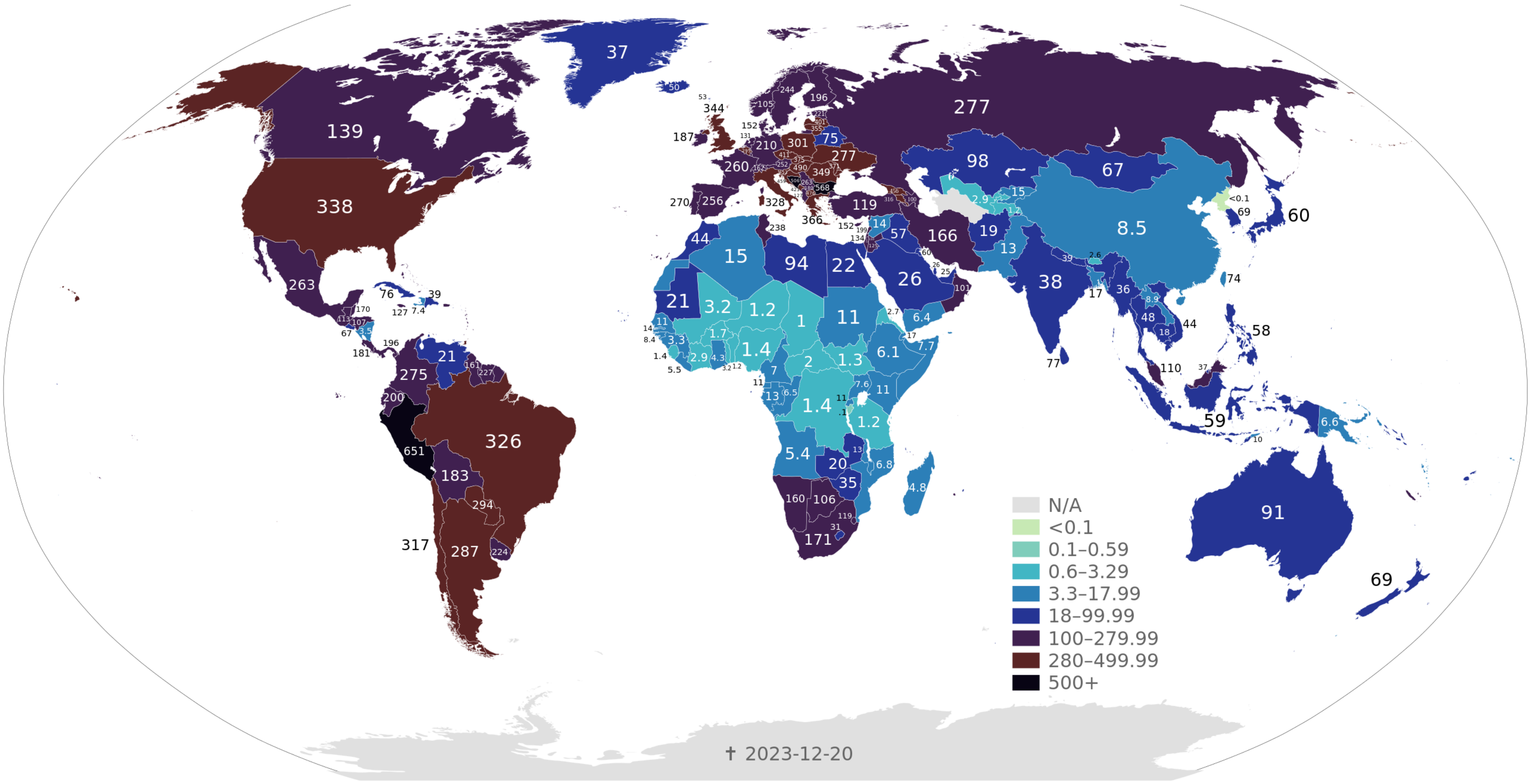


Epidemic vs. pandemic

- In 2009, a general outbreak (**epidemic**) of a flu-like illness appeared in Mexico and the United States, caused by an influenza virus named H1N1
- A global epidemic is called a **pandemic**

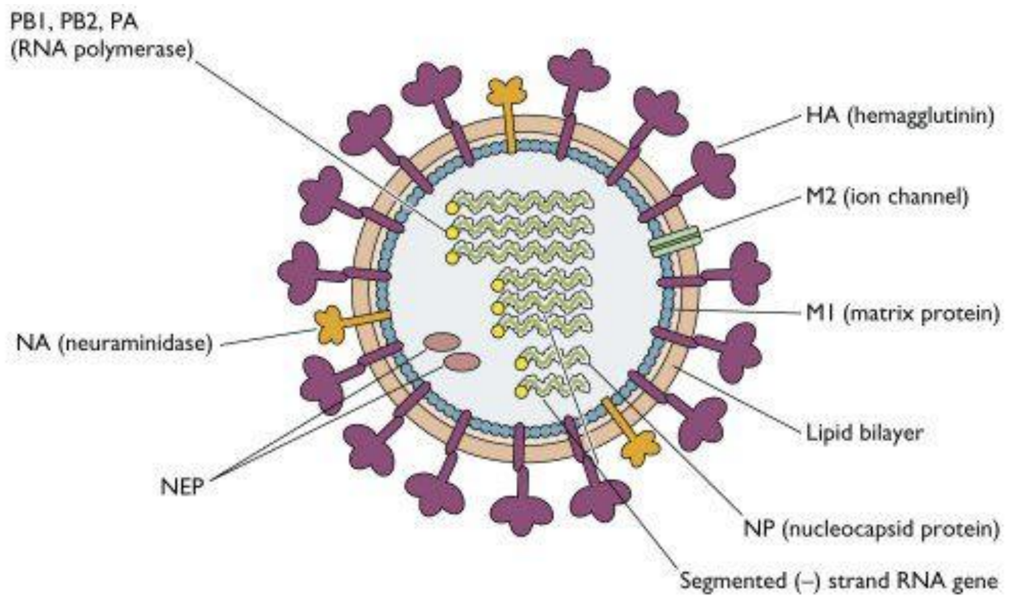


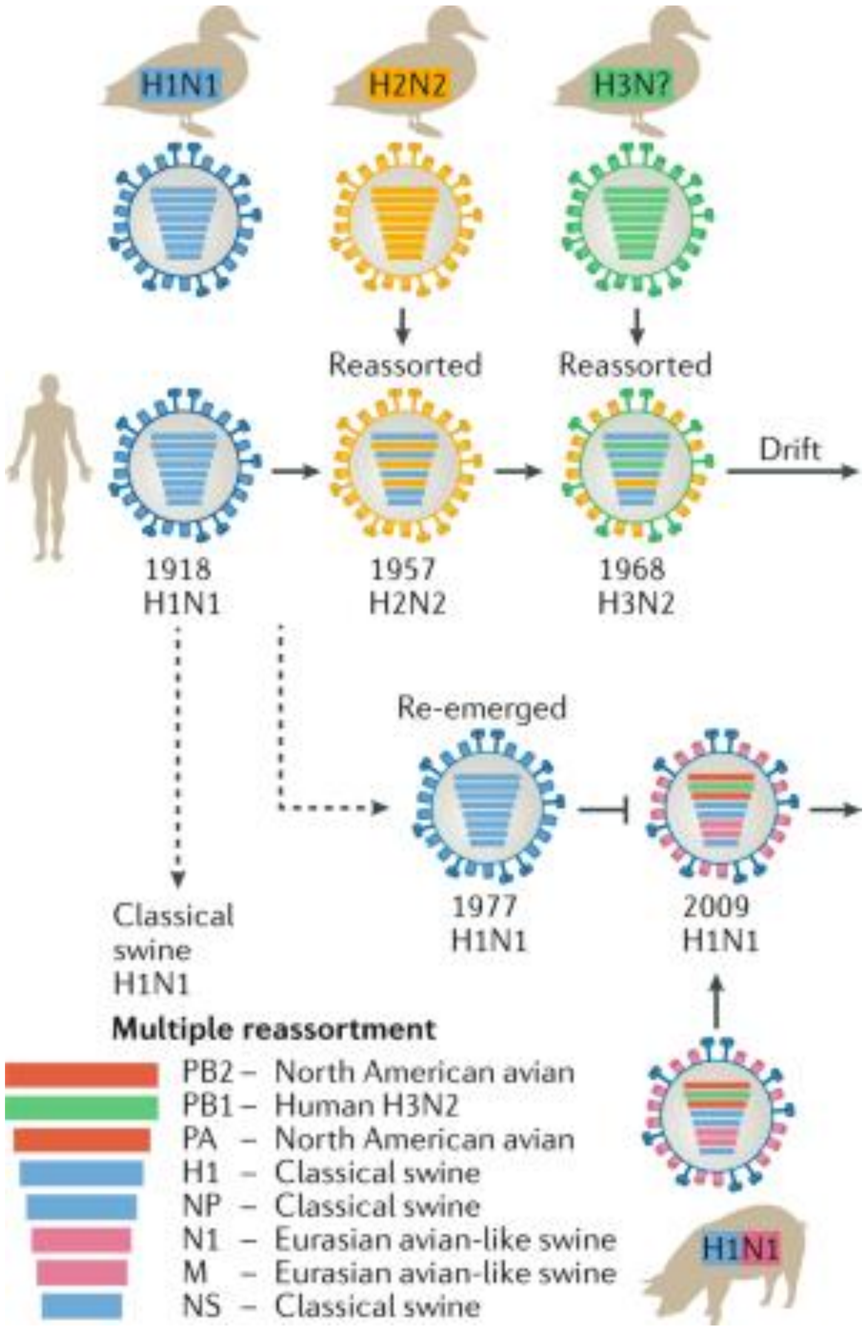
COVID-19 Outbreak World Map Total Reported Deaths per Capita



Flu epidemics

- 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)
- H1N1 is the strain that caused the 2009 flu pandemic




H1N1
H2N2
H3N?
Reassorted
Reassorted
Drift
1918
H1N1
1957
H2N2
1968
H3N2
Re-emerged
1977
H1N1
2009
H1N1
Classical
swine
H1N1
Multiple reassortment
PB2 – North American avian
PB1 – Human H3N2
PA – North American avian
H1 – Classical swine
NP – Classical swine
N1 – Eurasian avian-like swine
M – Eurasian avian-like swine
NS – Classical swine
H1N1

Factors influencing virus emergence

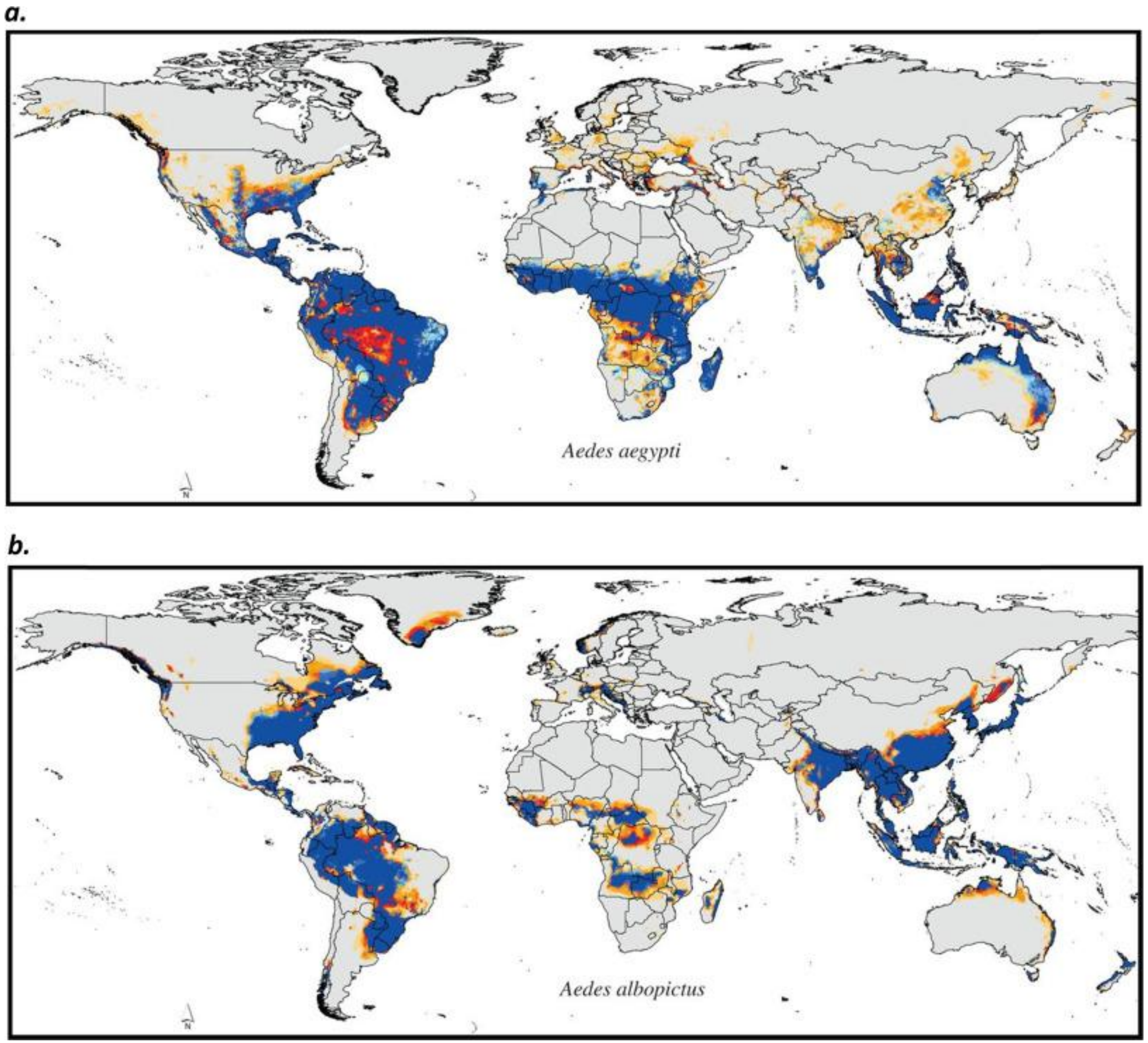
Three processes contribute to the emergence of new viral diseases:

1. RNA viruses have an unusually high rate of mutation
2. The disease can be disseminated from a small, isolated human population and can eventually spread around the world
3. About three-quarters of new human diseases originate by spreading to humans from animals

Factors influencing virus emergence

- 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

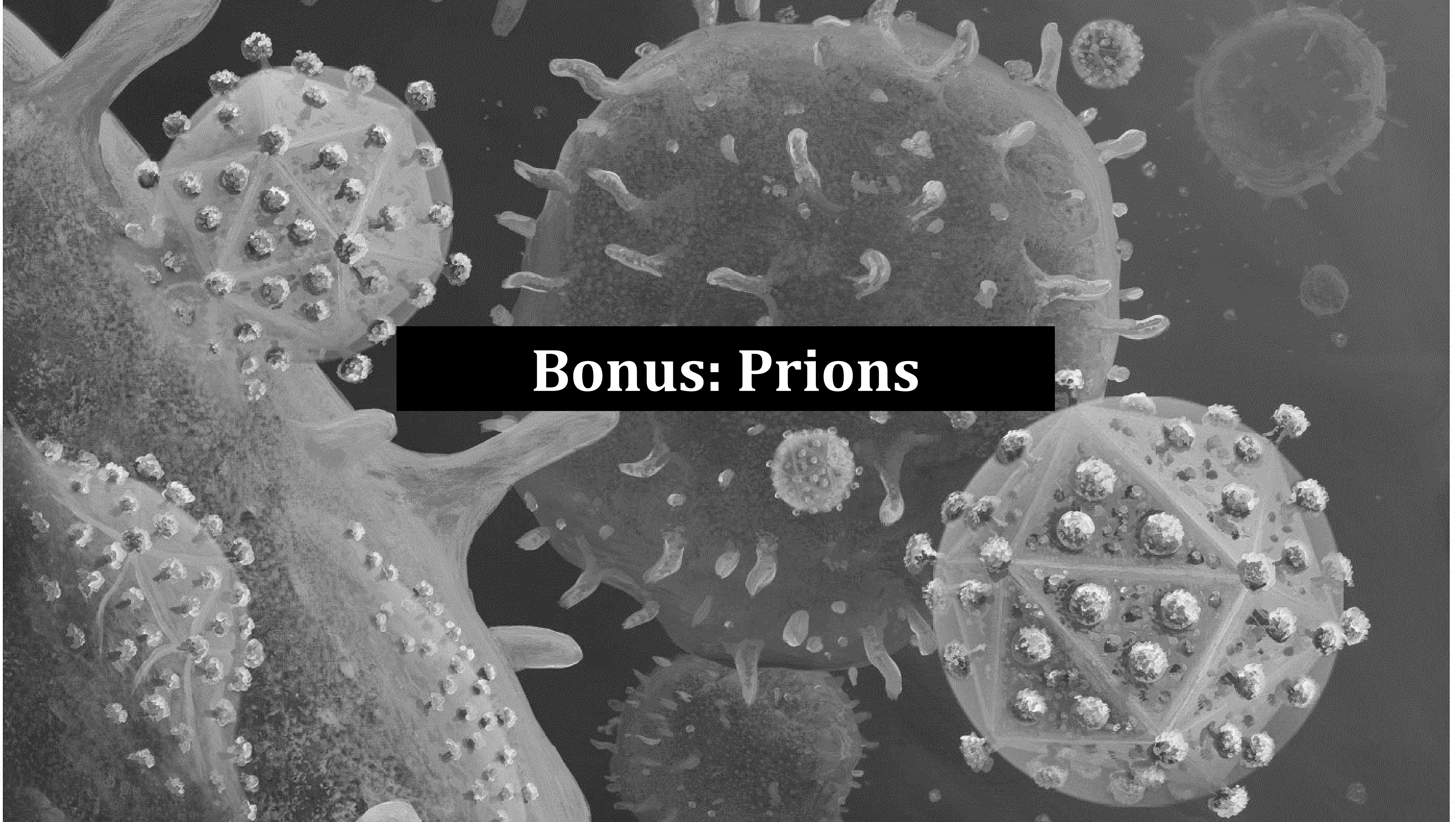
Mosquitoes as vectors for diseases



Examples:

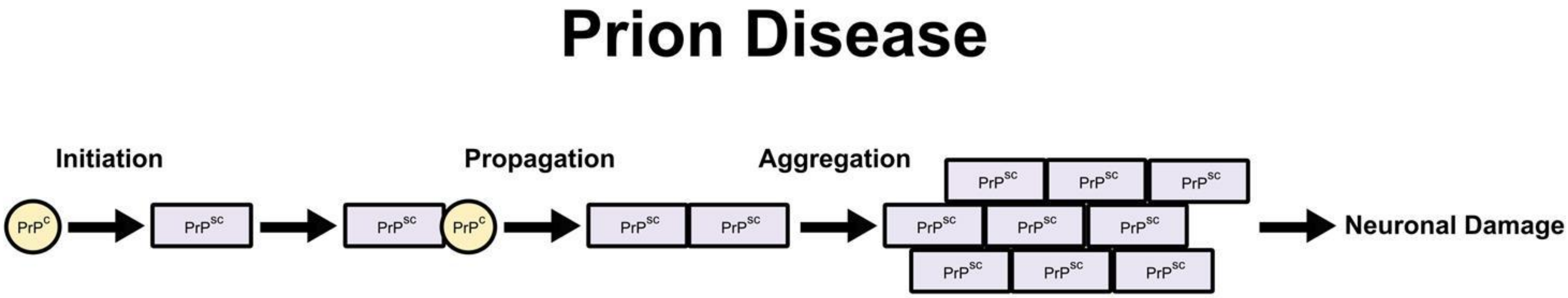
Dengue fever
Chikungunya virus
Yellow fever
Zika virus
Malaria (*Anopheles* mosquitoes)

Bonus: Prions



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: Proteins as Infectious Agents

- Prions are somehow able to convert a normal form of the protein into the **misfolded version**
- Then several prions aggregate into a complex that can convert more proteins to prions
- Prions might also be involved in diseases such as Alzheimer's and Parkinson's disease

Questions?