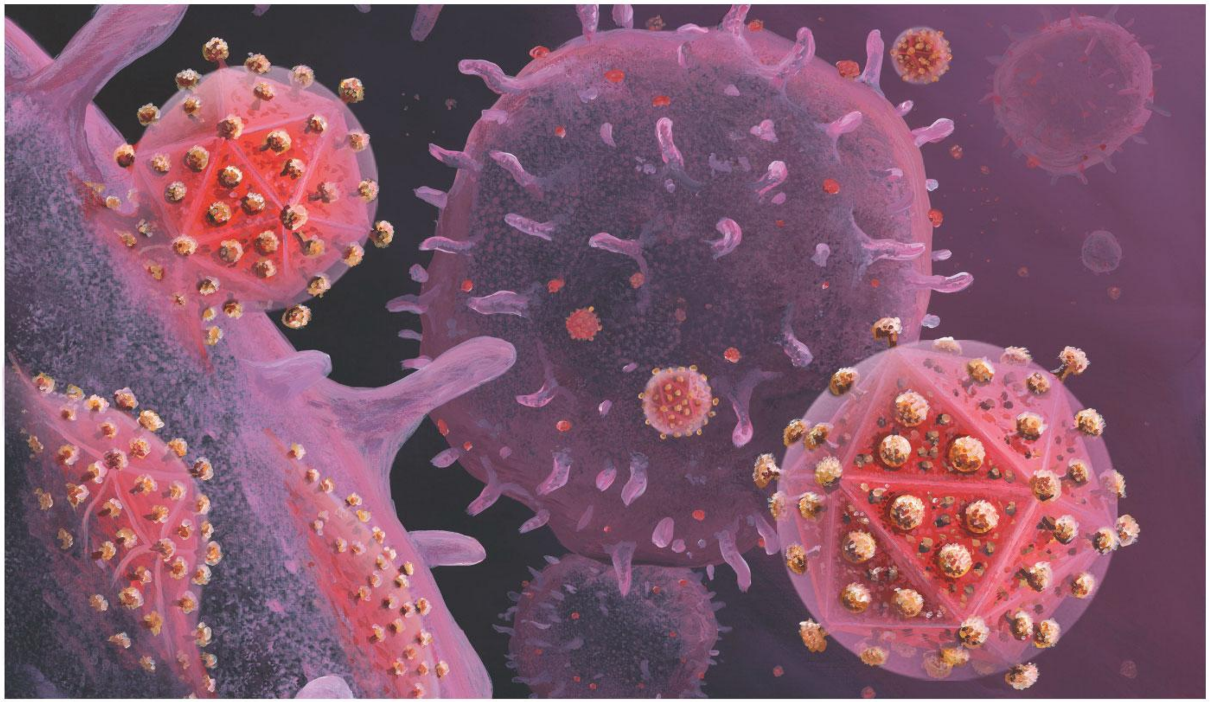
BIOL 1202
General Biology II Lecture



CHAPTER 19
Viruses
Dr. Adam Hrincevich

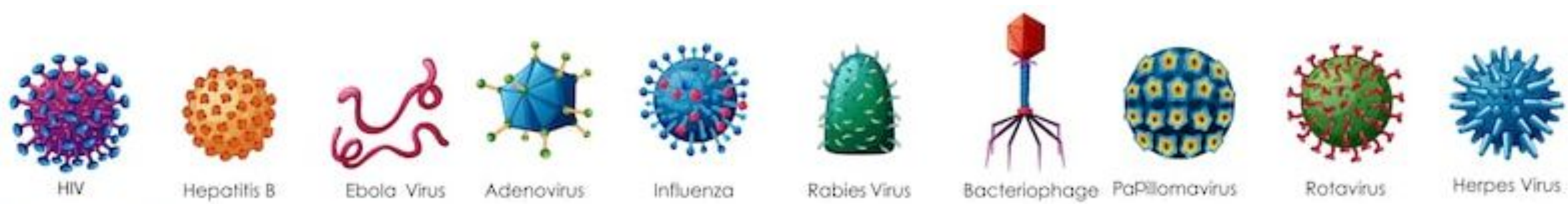
CH 19 Learning Objectives

1. Describe a virus.
2. Explain how viruses replicate and evolve.
3. Use examples to illustrate the effects of animal and plant viruses, as well as prions, on their hosts.
4. **Complete practice exercise "QUESTION SET #1 on restriction digests and agarose gel setup" posted to MOODLE**

I would suggest completing the crossword puzzle to help you understand the terminology and correlate how the terms relate to topics covered in this chapter.

A Borrowed Life

- A **virus** is an infectious particle consisting of genes packaged in a protein coat
- Viruses are much simpler in structure than 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”



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
- Tobacco mosaic disease (TMV) stunts growth of tobacco plants, 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 (i.e. inability 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)

Structure of Viruses

- Viruses are not cells and not technically "alive"
- 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 may consist of two types
  1. double- or single-stranded DNA
  2. double- or single-stranded RNA
- Viruses are classified as DNA viruses or RNA viruses
- Genome is either a single linear or circular molecule of the nucleic acid
- Viruses have between 3 genes to 2,000 genes in their genome

Capsids and Envelopes

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

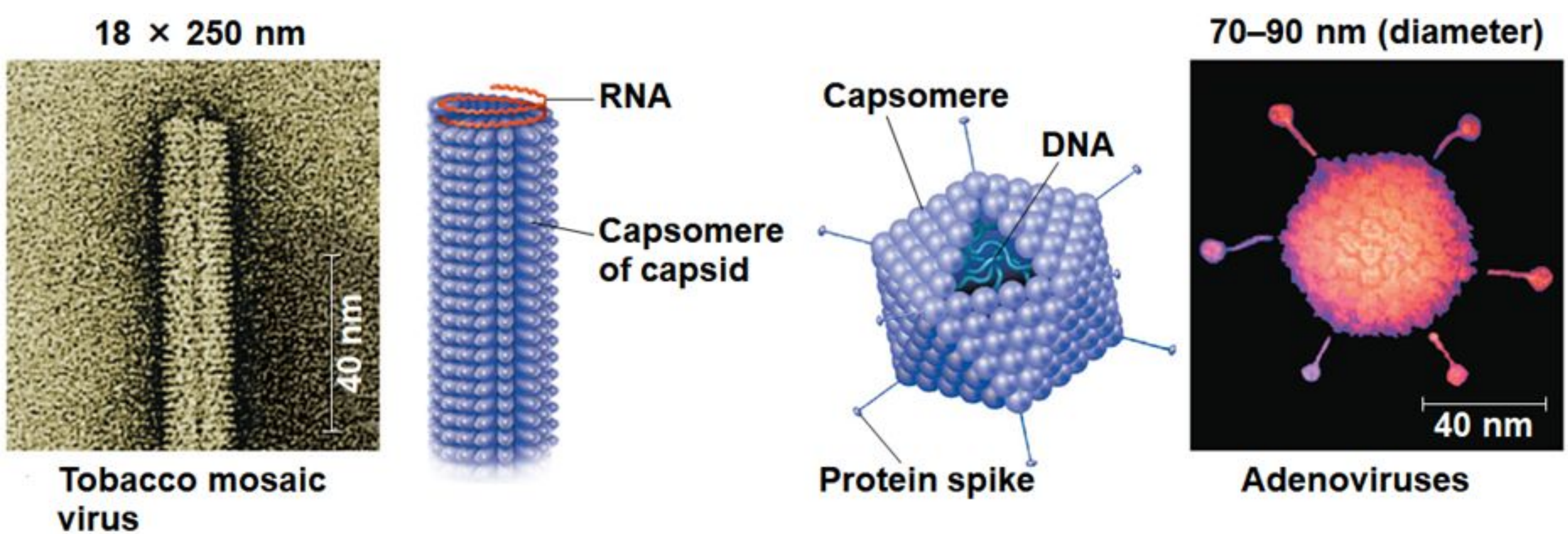
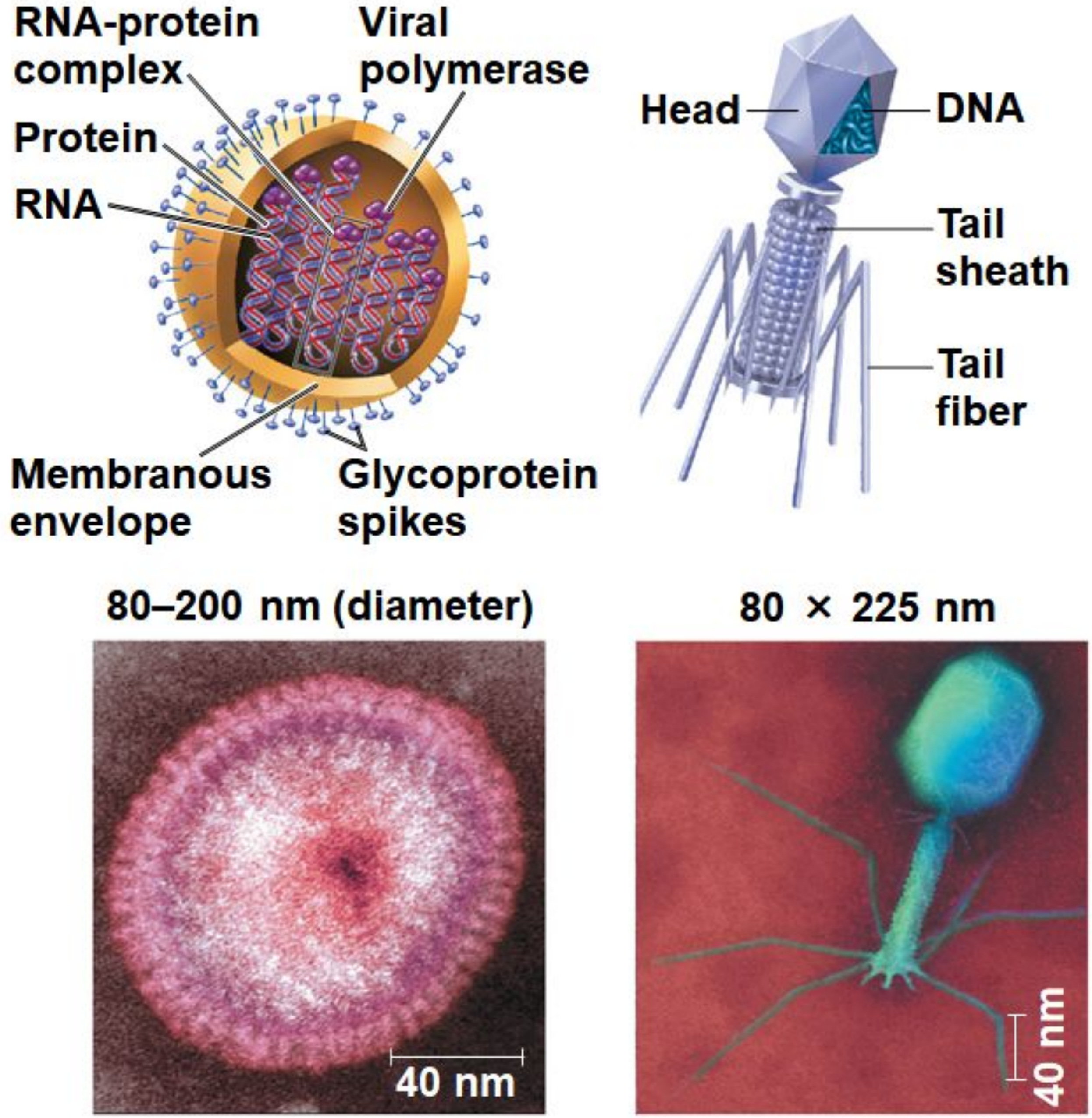


Figure 19.3b



(c) Influenza viruses

(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

Bacteriophages infecting bacteria

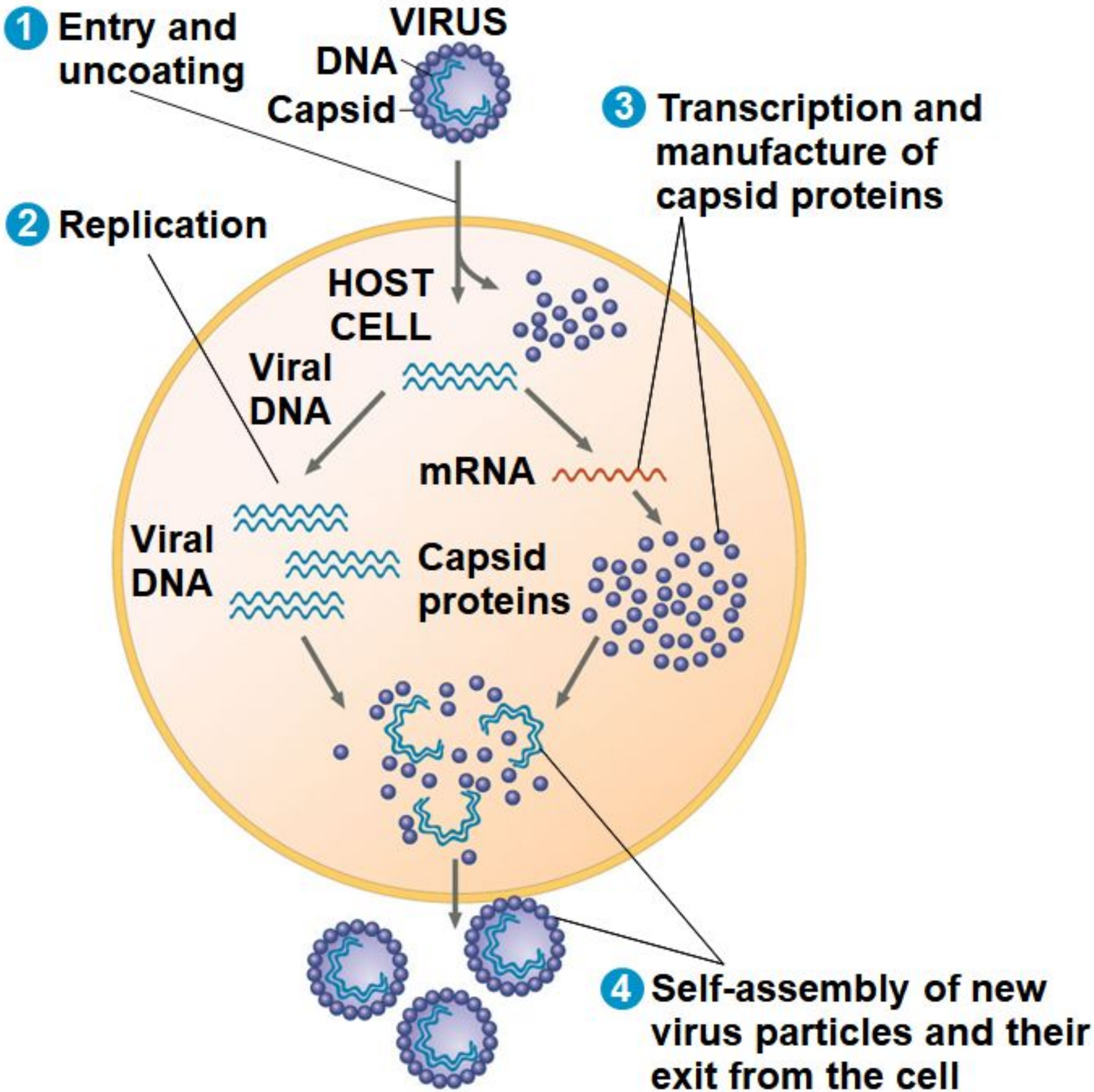
Injecting genetic material

"Ghost"
(empty bacteriophage)

Concept 19.2: Viruses replicate 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
- Cross-species transmission (CST) or spillover is ***rare***
- The viral genome enters the host cell many 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

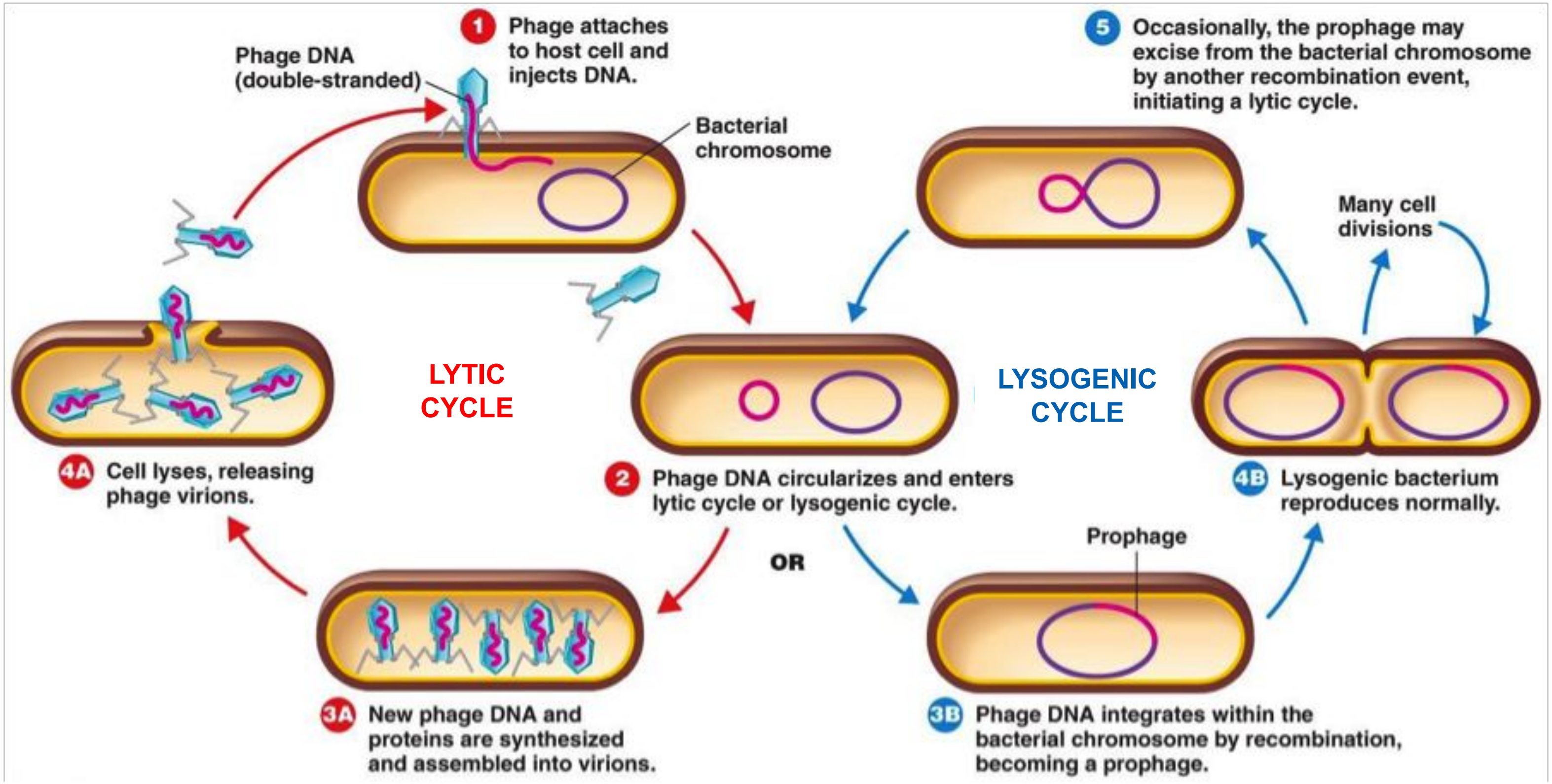


1 Entry and uncoating
VIRUS
DNA
Capsid
3 Transcription and manufacture of capsid proteins
2 Replication
HOST CELL
Viral DNA
mRNA
Viral DNA
Capsid proteins
4 Self-assembly of new virus particles and their exit from the cell

Replicative Cycles of Phages

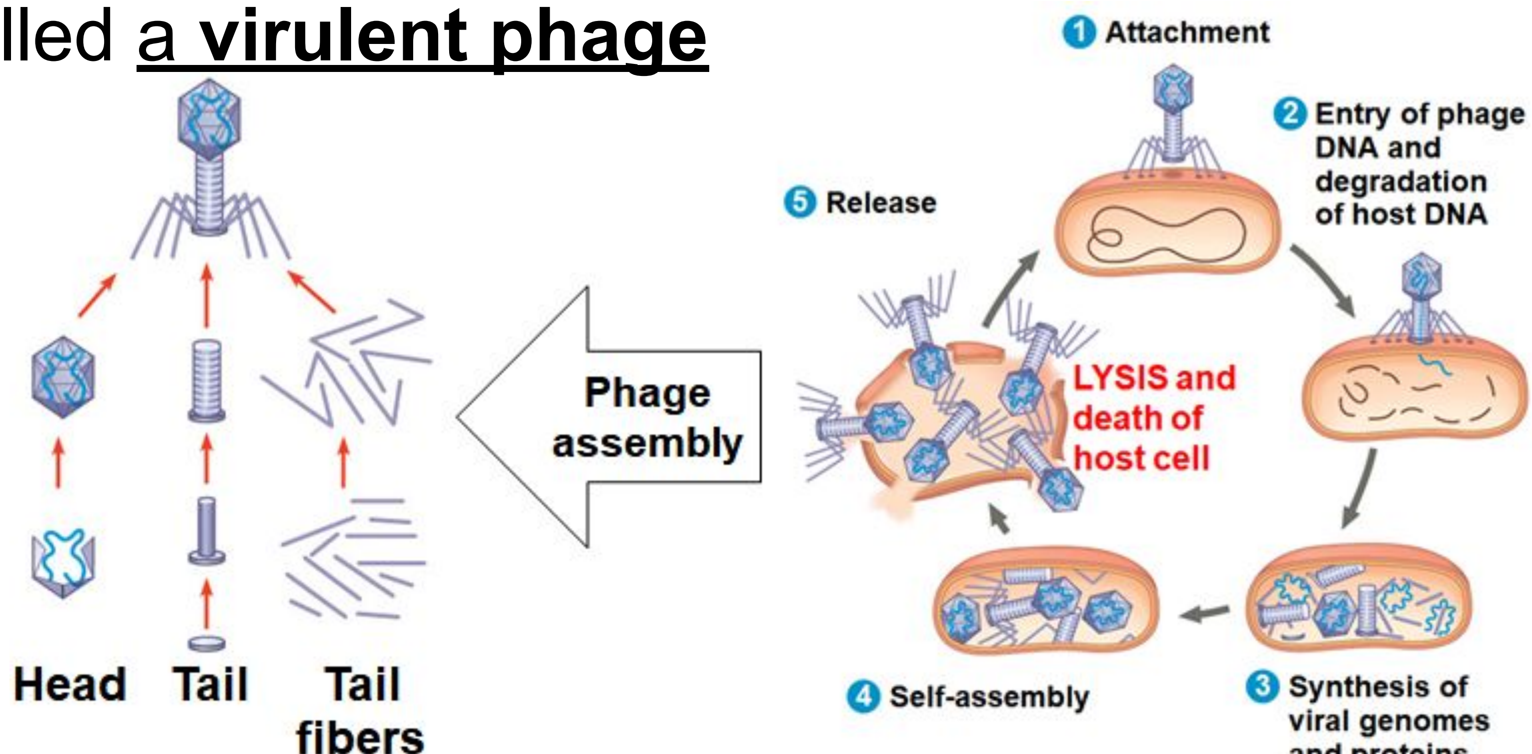
- Phages are <u>the best understood of all viruses</u>
- Phages have <u>2 alternative reproductive mechanisms</u>

1. **Lytic** cycle
2. **Lysogenic** cycle



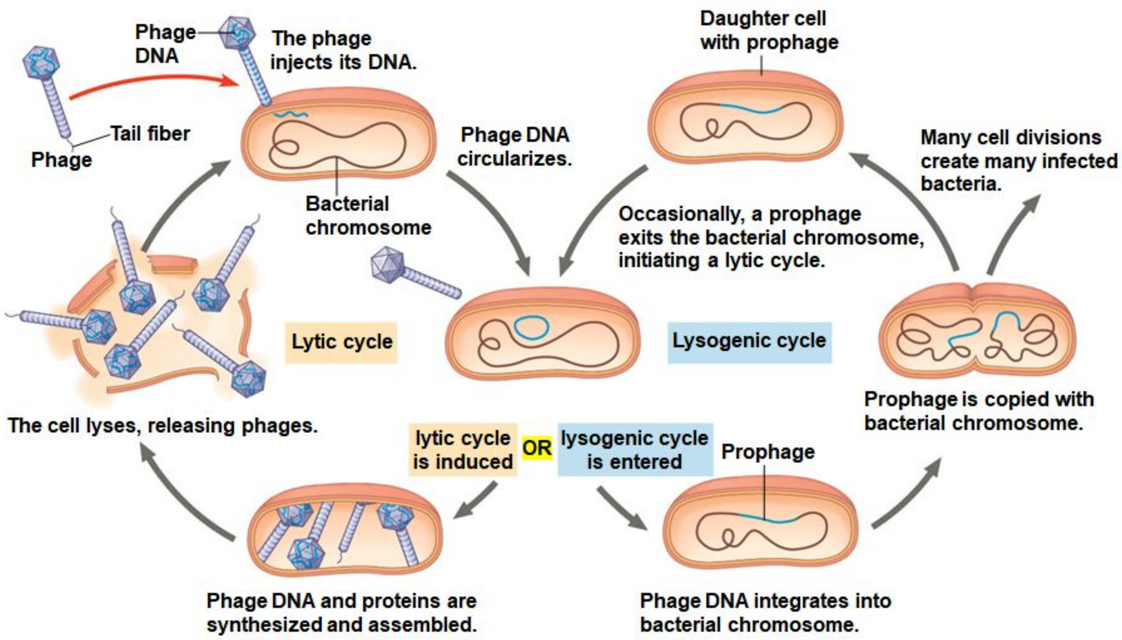
The Lytic Cycle

- 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 the host's cell wall, releasing the progeny viruses
- A phage that reproduces only by the lytic cycle is called a **virulent phage**

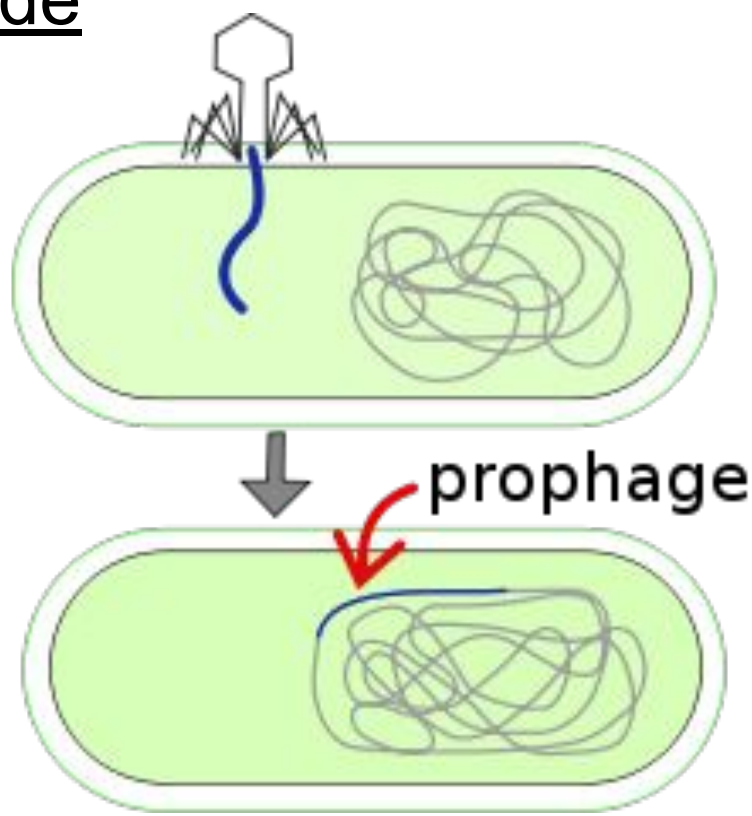


The Lysogenic Cycle

- 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 <u>is known as a prophage</u>
- Every time the host divides, it copies the phage DNA and <u>passes the copies to daughter cells</u>
- An environmental signal can trigger the virus genome to exit the <u>bacterial chromosome and switch to the lytic mode</u>



Bacterial Defenses Against Phages

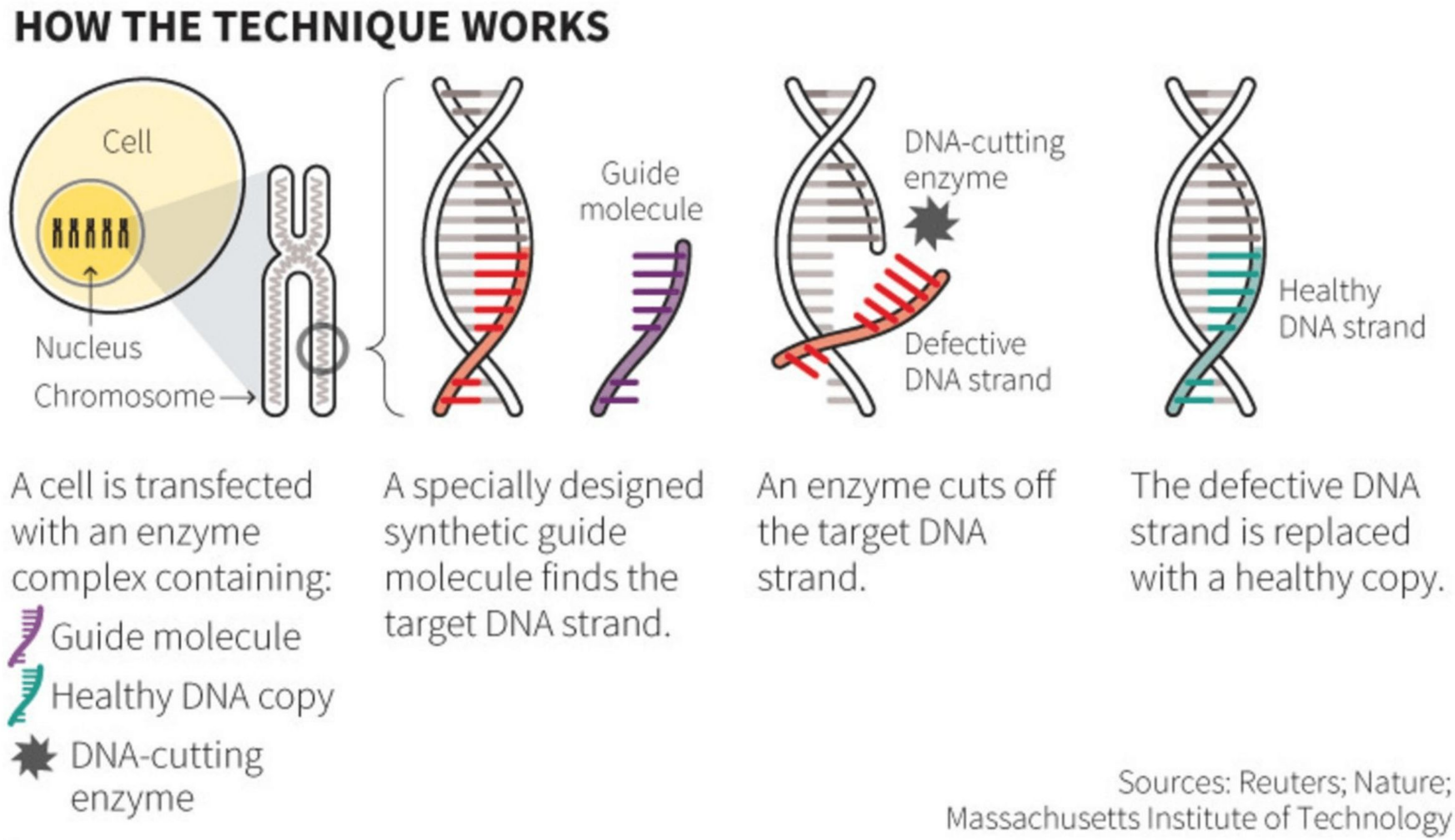
- Bacteria have their <u>own defenses against phages</u>
- Natural selection favors bacterial mutants with surface proteins that cannot be recognized as <u>receptors by a particular type of phage</u>
- Foreign DNA can be identified as such and cut up by cellular enzymes <u>called **restriction enzymes (RE)**</u>
- **RE** cleave DNA molecules at <u>specific base sequences</u>
- EX: Restriction enzyme AhaIII cuts 5’-TTT▼AAA-3’ (the “▼” symbol is where the <u>DNA sequence is cut)</u>
- The bacterium’s own DNA is protected from the <u>restriction enzymes by being methylated, preventing cuts</u>

- Restriction enzymes are nucleases that cut ***double stranded*** DNA at ***specific*** nucleotide sequences
- Restriction enzymes act <u>as "molecular scissors"</u>
- Number of cuts made in DNA will depend on number of times the <u>"target" sequence occurs</u>
- For example: 5'–ATT▼AAT–3' *Eco*RI
- The "▼" symbol indicates <u>where the cut is made</u>
- Recognize <u>"palindromic" sequences</u>
- "Madam, I'm Adam" ►same forward & backward◄
- **Question**: Aren't ALL DNA sequences palindromic?
- See **QUESTION SET #1** posted to MOODLE

- 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 re-infect 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 enzyme resistant
- The relationship between phage and bacteria is in constant evolutionary flux

CRISPR-Cas system: a type of bacterial immune system



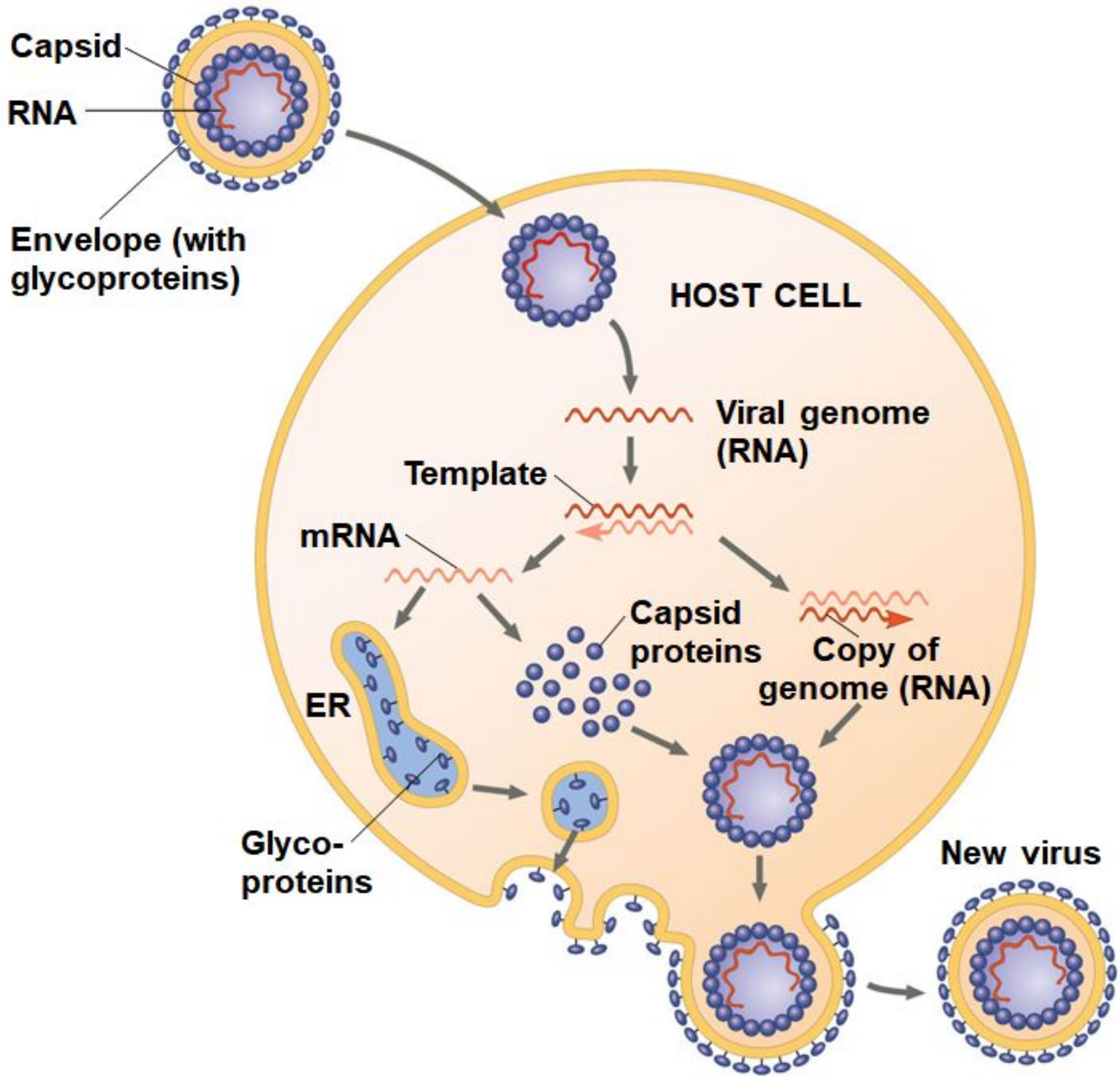
Replicative Cycles of Animal Viruses

- There are two key variables used to classify viruses that infect animals:
  1. An RNA or DNA genome, either single-stranded or double-stranded
  2. 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
- Other viral membranes form from the host's nuclear envelope and are then replaced by an envelope made from Golgi apparatus membrane

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

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 to RNA

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

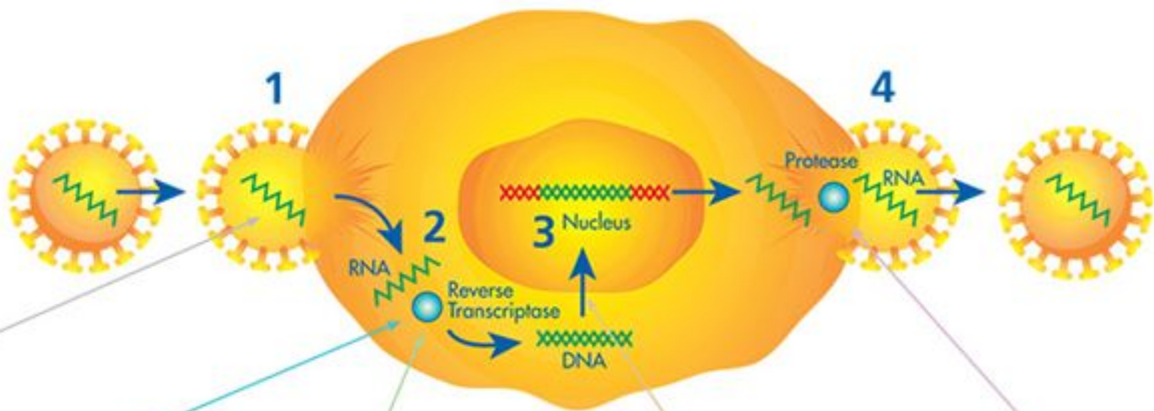
Class/Family	Envelope?	Examples That Cause Human Diseases
IV. Single-Stranded RNA (ssRNA); Serves as mRNA		
Picornavirus	No	Rhinovirus (common cold); poliovirus; hepatitis A virus; other intestinal viruses
Coronavirus	Yes	Severe acute respiratory syndrome (SARS); Middle East respiratory syndrome (MERS)
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

Antiretroviral Agents for HIV

Stages of HIV replication

1. HIV enters a CD4 cell.
2. HIV is a retrovirus, meaning that its genetic information is stored on single-stranded RNA instead of the double-stranded DNA found in most organisms.
3. HIV DNA enters the nucleus of the CD4 cell and inserts itself into the cell's DNA. HIV DNA then instructs the cell to make many copies of the original virus.
4. New virus particles are assembled and leave the cell, ready to infect other CD4 cells.

Targeting HIV Replication



Fusion and Entry inhibitors	Non-nucleoside reverse transcriptase inhibitors	Nucleoside/Nucleotide analogues	Integrase inhibitors	Protease inhibitors
Entry inhibitors work outside the cell. They prevent HIV from entering the CD4 cell by blocking binding or fusion of HIV with the CD4 cell membrane. If HIV cannot enter the CD4 cell it is unable to replicate.	Non-nucleoside reverse transcriptase inhibitors bind to reverse transcriptase and inhibit the enzyme, stopping HIV replication by preventing formation of HIV DNA. These drugs act in a completely different way to nucleoside/nucleotide analogues.	Nucleoside/nucleotide analogues act as false substrates for reverse transcriptase, causing chain termination. The resulting DNA is incomplete and prevents HIV replication.	Integrase inhibitors block the integration of HIV and cell DNA. This process prevents HIV replication.	Protease inhibitors work at the last stage of the HIV replication cycle. They prevent HIV from being successfully assembled and released from the infected CD4 cell.
Prevent HIV entry	**Prevent RT replication**	**Prevent HIV replication**	**Prevent HIV integration**	**Prevent HIV assembly**

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 discovered to date is the size of a small bacterium (*Megavirus chilensis*, 1.3 MB dsDNA genome, capsid 440 nm)
- There is controversy about whether viruses evolved before or after cells

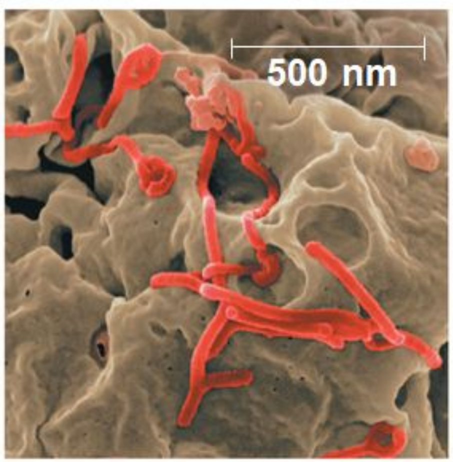
Concept 19.3: Viruses and prions are formidable pathogens in animals and plants

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

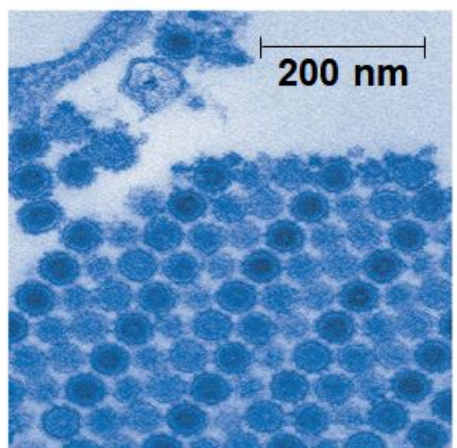
- A **vaccine** is a harmless derivative of pathogenic microbes that stimulate the immune system to mount defenses against the harmful pathogen
- **MISNOMER**: You can **NOT** get the flu from getting the yearly flu shot
- Is the flu vaccine 100% effective? Why so/not so?
- MOODLE SURVEY: Do you get a yearly flu shot?
- 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
- Vaccines and autism? There is no scientific link.

Emerging Viruses

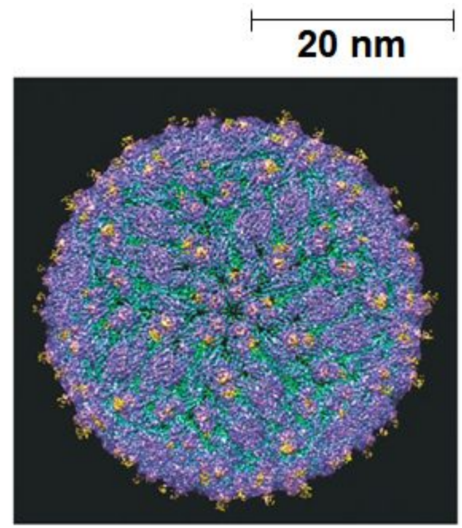
- Emerging viruses are those that suddenly become apparent
- The Ebola virus is one of several emerging viruses that cause hemorrhagic fever, an often fatal illness
- Other examples include the chikungunya virus and the recently emerging Zika virus (2015)



(a) Ebola viruses



(b) Chikungunya viruses



(c) Zika virus

Infectious Disease Transmission terminology

- A **epidemic** is a widespread occurrence of an infectious disease in a community at a particular time
  - EX: flu-like illness caused by the influenza virus H1N1 that appeared in Mexico and the United States in 2009
- A global epidemic is called a **pandemic**
  - EX: Black Death, 1918 Spanish flu, and HIV/AIDS
- A disease that exists permanently in a particular region or population is endemic
  - EX: malaria in Africa and chicken pox the United States
- Diseases that are seen only occasionally, and usually without geographic concentration, are called **sporadic**
  - EX: tetanus, rabies, and typhoid fever in United States

ENDEMIC OCCURRENCE
(Valley Fever)

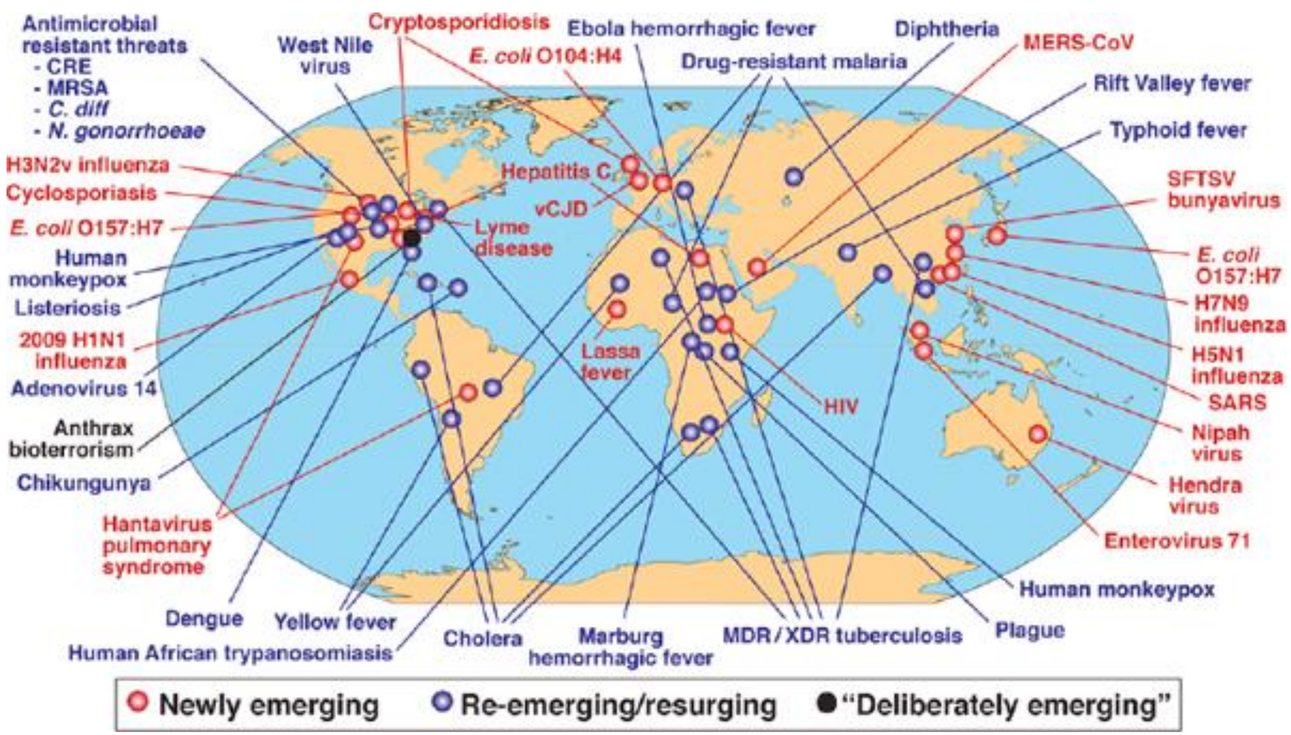
EPIDEMIC OCCURRENCE
(Syphilis)

= New case of disease

SPORADIC OCCURRENCE
(Measles)

PANDEMIC OCCURRENCE
(AIDS)

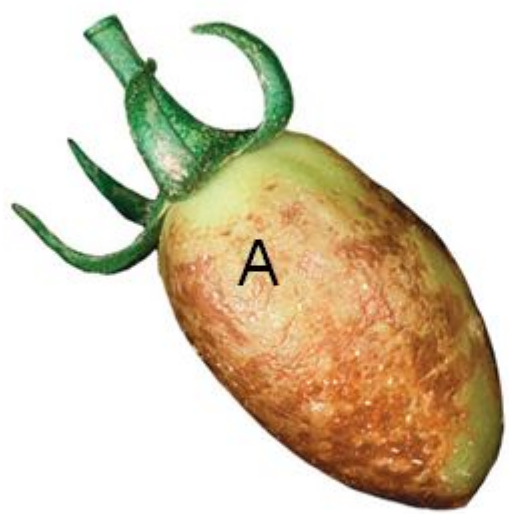
- Three processes contribute to the emergence of new viral diseases:
  1. RNA viruses have an unusually high rate of mutation
  2. The disease can be disseminated from a small, isolated human population and spread worldwide
  3. About three-quarters of new human diseases originate by spreading to humans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



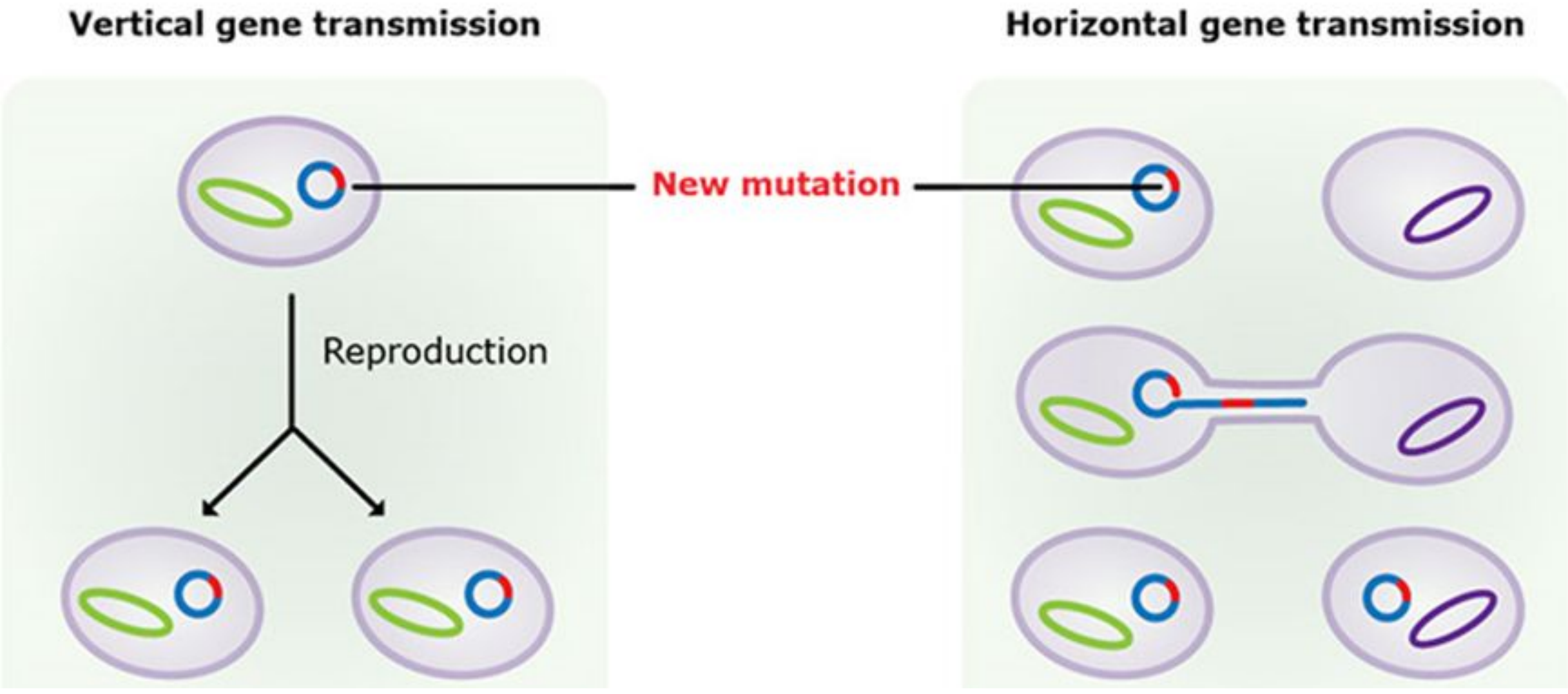
- Flu epidemics are caused by type A influenza viruses; infect birds, pigs, horses, and humans
- Strains of influenza A are given standardized names based on the viral surface proteins hemagglutinin (HA) and neuraminidase (NA)
- H1N1 is the strain that caused the 2009 flu pandemic
- Changes in host behavior 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 insectides may help prevent the spread
- It is possible that global climate change may allow mosquitoes that carry viruses to expand their range

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 <u>damaged flowers or roots</u>
- Most plant viruses <u>have an RNA genome</u>
- Many have a helical capsid, while others have <u>an icosahedral capsid</u>
- Immature tomato infected by a <u>virus (A)</u>
- <u>Tobacco mosaic virus (B)</u>

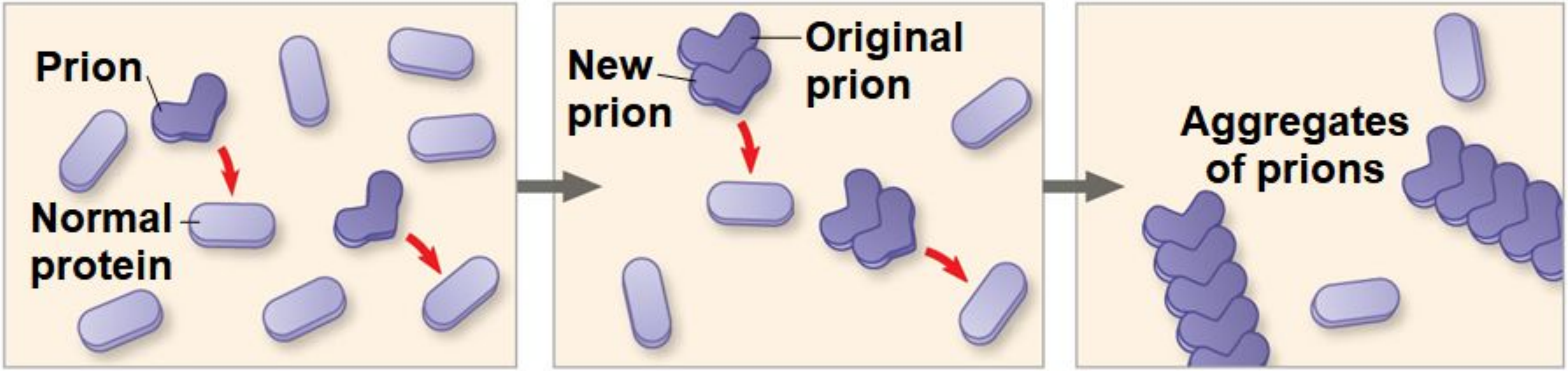


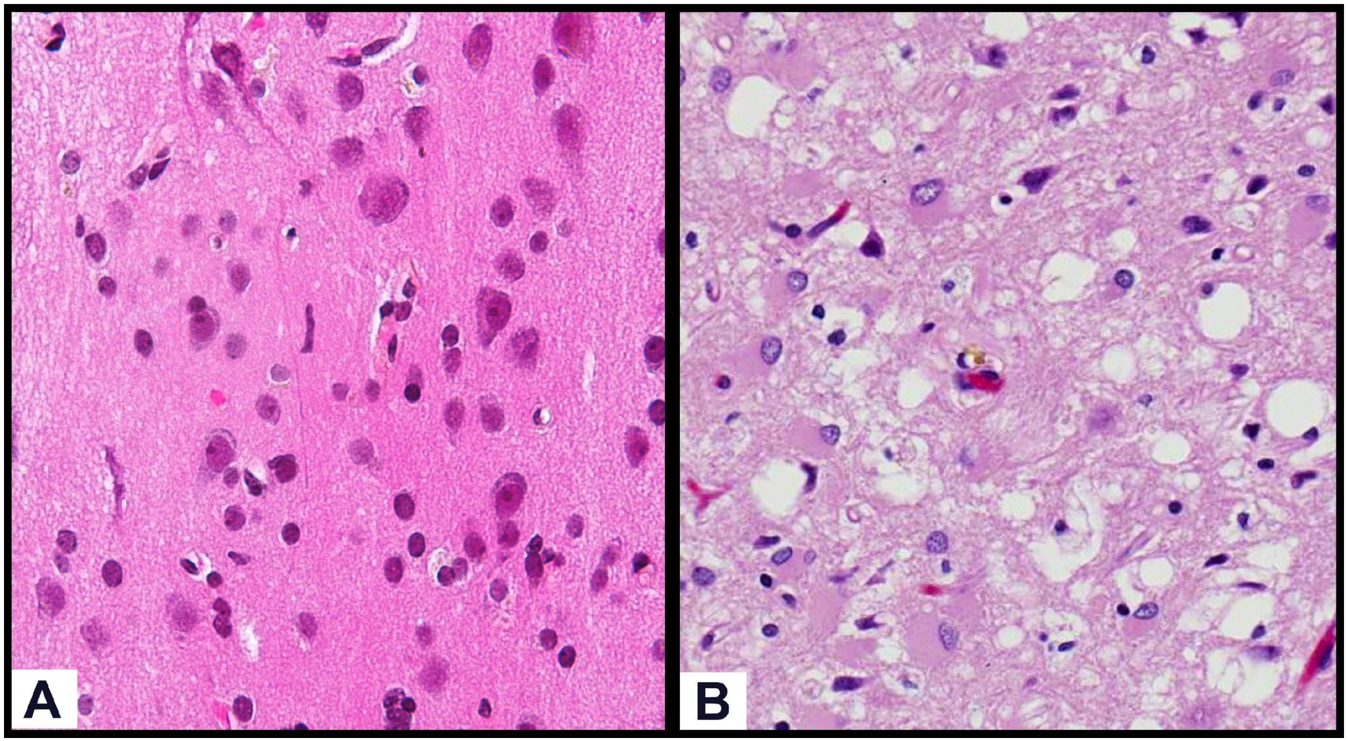
- Plant viruses spread disease by two major routes:
  1. ***Vertical*** transmission, <u>inheriting the virus from a parent</u>
  2. ***Horizontal*** transmission, <u>entering through damaged cell walls</u>



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 mis-folded proteins, can be transmitted in food, act slowly, and are virtually indestructible
- 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





(A) Normal healthy brain tissue. (B) Brain tissue from the temporal lobe of a patient with Creutzfeldt-Jakob's disease. Note the large spaces in the tissue where the prion proteins have caused damage.