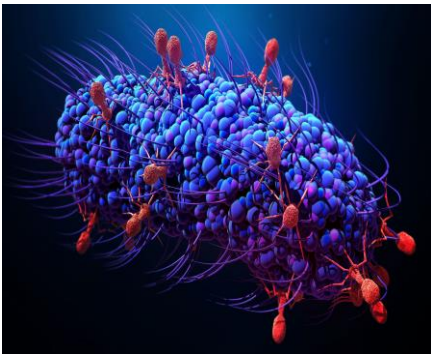




MLS 602

L2 ANIMAL VIRUSES & BACTERIOPHAGES



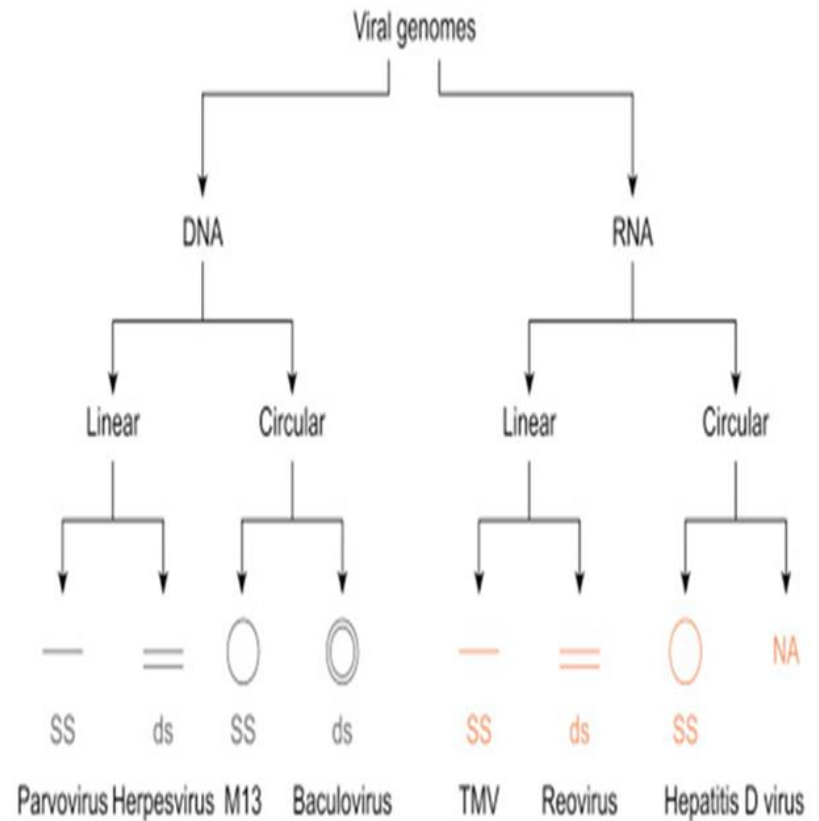
TAINA NAIVALU

At the end of this lecture you should be able to:

- Differentiate between RNA and DNA viruses
- Understand the life-cycle of viruses

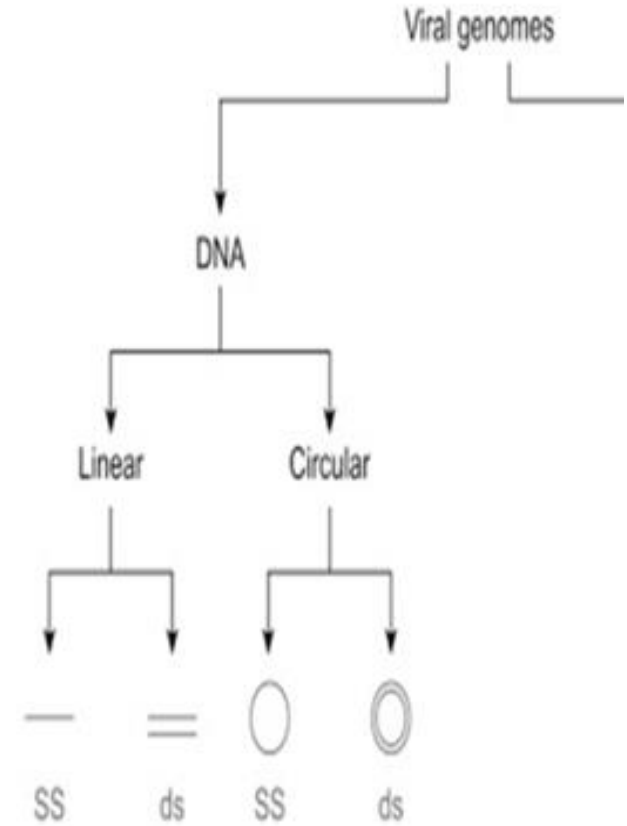
Viral Genome

- Either DNA or RNA and never both
- DNA viruses have DNA in their genome obviously 😁 and the same goes for RNA viruses



DNA VIRUSES





- Larger than RNA viruses
- Can have
 - i) Small genome
 - Use host factors (DNA polymerase in host) for replication
 - ii) Large genome
 - Encode a DNA polymerase
 - More genes encode proteins
- Most Replicate in the nucleus to use the host cell DNA-dependent polymerase to synthesize their mRNA (poxvirus replicates in the cytoplasm as it has its own polymerase)



Examples of DNA Viruses

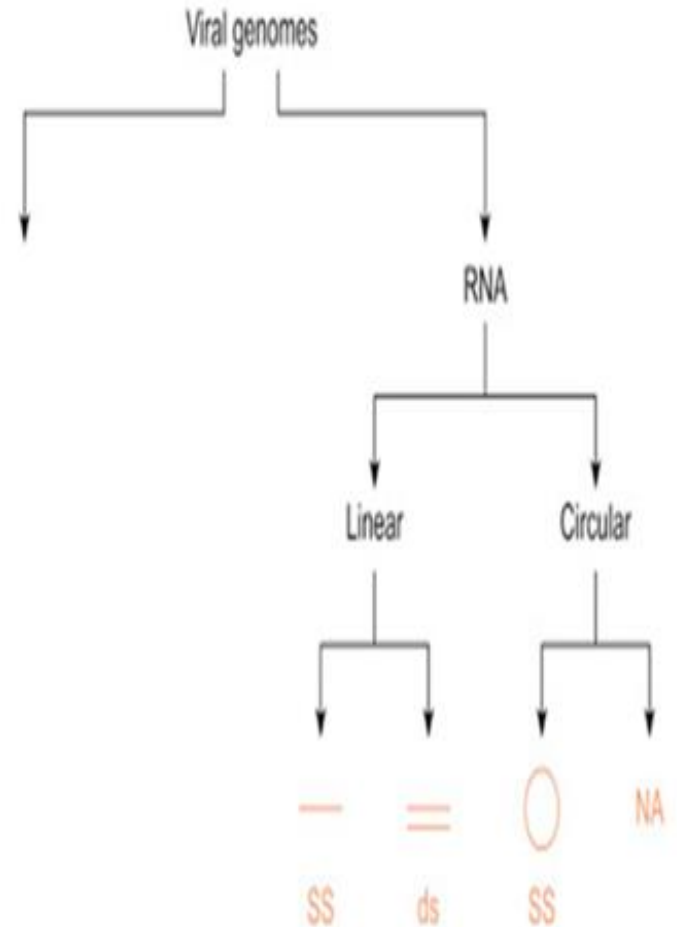
TABLE 13.2

Families of Viruses That Affect Humans







Characteristics/ Dimensions	Viral Family	Important Genera	Clinical or Special Features
40–57 nm	Papovaviridae 	<i>Papillomavirus</i> (human wart virus) <i>Polyomavirus</i>	Small viruses that induce tumors; the human wart virus (papilloma) and certain viruses that produce cancer in animals (polyoma and simian) belong to this family. Refer to Chapters 21 and 26.
Double-stranded DNA enveloped 200–350 nm	Poxviridae 	<i>Orthopoxvirus</i> (vaccinia and smallpox viruses) <i>Molluscipoxvirus</i>	Very large, complex, brick-shaped viruses that cause diseases such as smallpox (variola), molluscum contagiosum (wartlike skin lesion), and cowpox. Refer to Chapter 21.
150–200 nm	Herpesviridae 	<i>Simplexvirus</i> (HHV-1 and 2) <i>Varicellovirus</i> (HHV-3) <i>Lymphocryptovirus</i> (HHV-4) <i>Cytomegalovirus</i> (HHV-5) <i>Roseolovirus</i> (HHV-6) HHV-7 Kaposi's sarcoma (HHV-8)	Medium-sized viruses that cause various human diseases, such as fever blisters, chickenpox, shingles, and infectious mononucleosis; implicated in a type of human cancer called Burkitt's lymphoma. Refer to Chapters 21, 23, and 26.
42 nm	Hepadnaviridae 	<i>Hepadnavirus</i> (hepatitis B virus)	After protein synthesis, hepatitis B virus uses reverse transcriptase to produce its DNA from mRNA; causes hepatitis B and liver tumors. Refer to Chapter 25.

RNA Víruses

- Minimal genome size
- Encode a limited number of proteins
- Often encodes a RNA-dependent RNA polymerase (RdRp)
 - Essential for replication
- Most RNA viruses undergo their entire replication in cytoplasm (except for Retroviruses and Influenza viruses as both have an important replication step in the nucleus)
- All RNA viruses are ss except for Reovirus which has ds RNA



Examples of RNA Viruses

TABLE 13.2		Families of Viruses That Affect Humans	
Characteristics/ Dimensions	Viral Family	Important Genera	Clinical or Special Features
Single-stranded RNA, + strand nonenveloped 28–30 nm	Picornaviridae 	<i>Enterovirus</i> <i>Rhinovirus</i> (common cold virus) <i>Hepatitis A virus</i>	At least 70 human enteroviruses are known, including the polio-, coxsackie-, and echoviruses; more than 100 rhinoviruses exist and are the most common cause of colds. Refer to Chapters 22, 23, 24, and 25.
40–50 nm	Flaviviridae 	<i>Flavivirus</i> <i>Pestivirus</i> <i>Hepatitis C virus</i>	Can replicate in arthropods that transmit them; diseases include yellow fever, dengue, St. Louis encephalitis, and West Nile virus. Refer to Chapters 22 and 23.
Nidovirales 80–160 nm	Coronaviridae 	<i>Coronavirus</i>	Associated with upper respiratory tract infections and the common cold. Refer to Chapter 24.
80–14,000 nm	Filoviridae 	<i>Filovirus</i>	Enveloped, helical viruses; Ebola and Marburg viruses are filoviruses. Refer to Chapter 23.
–strand, multiple strands of RNA 80–200 nm	Orthomyxoviridae 	<i>Influenzavirus</i> (influenza viruses A and B) <i>Influenza C virus</i>	Envelope spikes can agglutinate red blood cells. Refer to Chapter 24.
Produce DNA 100–120 nm	Retroviridae 	Oncoviruses <i>Lentivirus</i> (HIV)	Includes all RNA tumor viruses and double-stranded RNA viruses. Oncoviruses can cause leukemia and tumors in animals; the <i>Lentivirus</i> HIV causes AIDS. Refer to Chapter 19.

VIRUS REPLICATION STRATEGIES

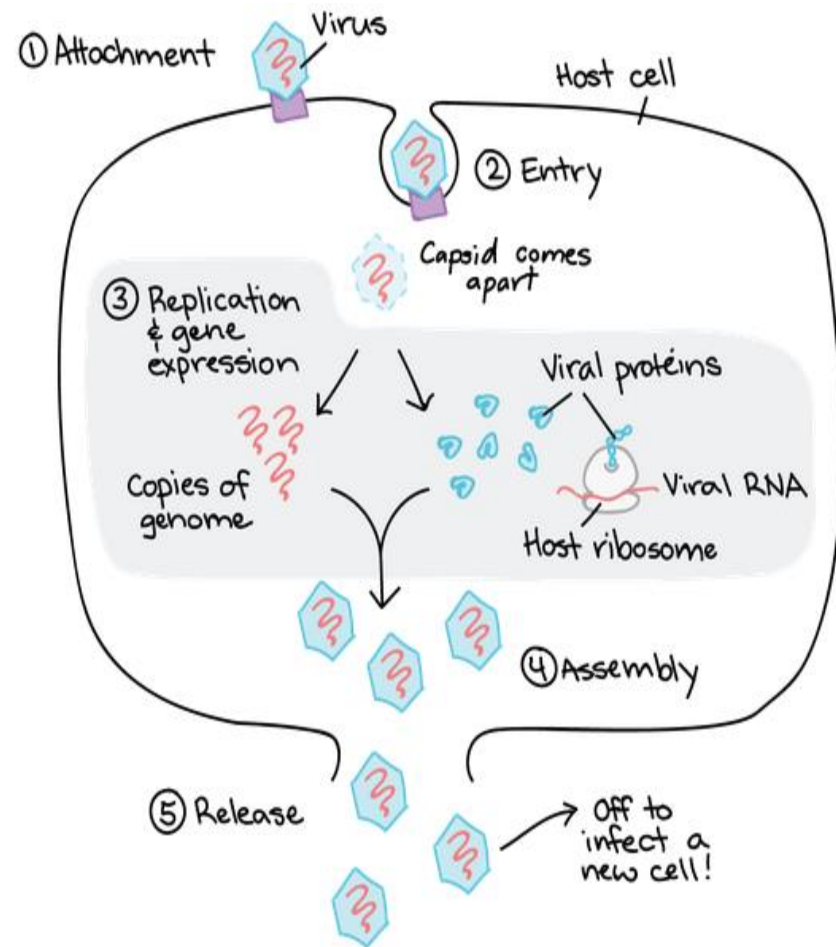
- All virus replication occurs within the host cell
- Host cell provides:
 - Nucleotide substrates
 - Energy
 - Enzymes
 - Other proteins
- All virus genomes must produce mRNA which can be translated by host ribosomes

VIRUS LIFECYCLE

- Viruses need to:
 - Get their genome into the host cell
 - Produce mRNA; leads to viral protein synthesis
 - Synthesis of viral mRNA
 - Synthesis of viral proteins
 - Synthesis of viral nucleic acid
 - Replicate their own genome
 - Assemble new virions and leave the cell
 - Continue infection

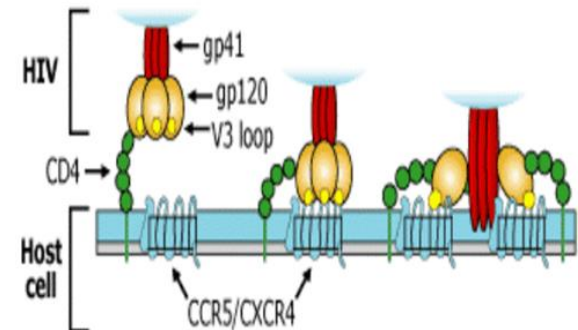
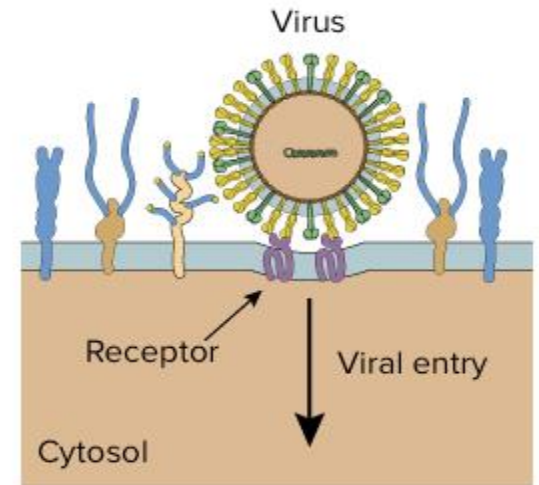
The Lifecycle

- **Attachment.** The virus recognizes and binds to a host cell via a receptor molecule on the cell surface.
- **Entry.** The virus or its genetic material enters the cell.
- **Uncoating** – exposing the genetic material
- **Genome replication and gene expression or biosynthesis.** The viral genome is copied and its genes are expressed to make viral proteins.
- **Assembly.** New viral particles are assembled (the genome copies and viral proteins)
- **Release.** Completed viral particles exit the cell and can infect other cells.



Attachment

- In attachment, a specific protein on the capsid of the virus physically "sticks/binds" to a specific molecule on the membrane of the host cell.
- This molecule, called a receptor, is usually a protein. A virus recognizes its host cells based on the receptors they carry, and a cell without receptors for a virus can't be infected by that virus.
- One virus may use more than one cellular receptors
 - Co-receptors can be involved e.g. HIV uses CD4 as a primary receptor and CCR5 or CXCR4 as co-receptors
- A cellular receptor may be shared by multiple viruses

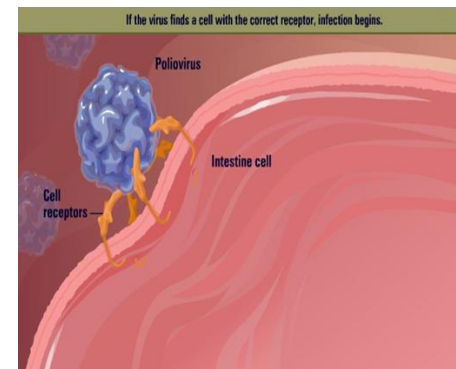
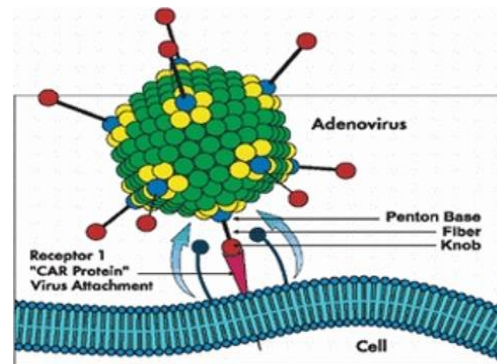


Attachment of enveloped viruses

- glycoproteins are present in the viral envelope that interact with cellular receptors to attach

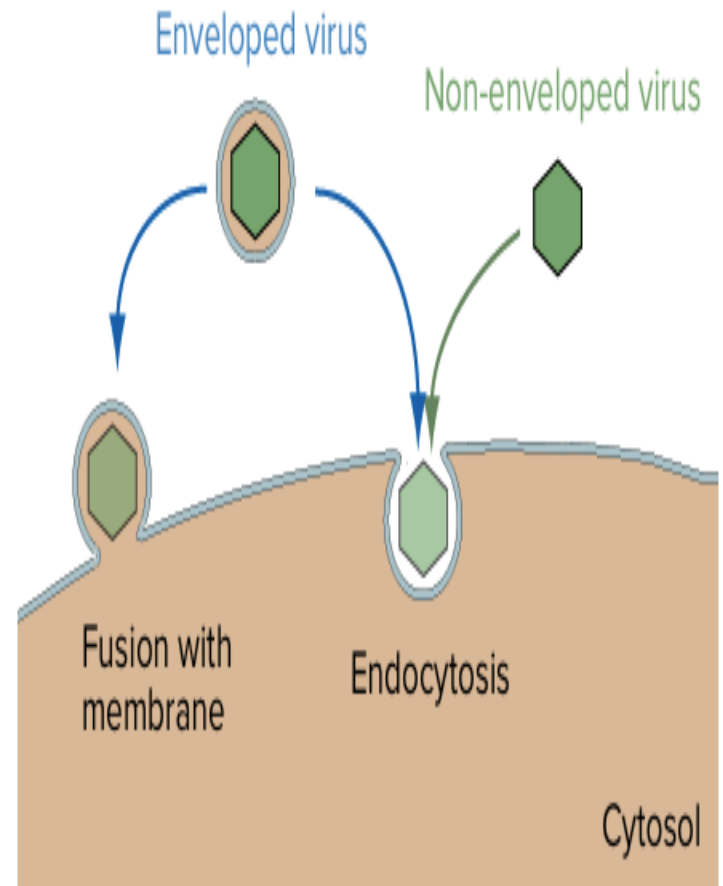
Attachment of non-enveloped viruses

- viral surface protein(s) may play a role in causing some localized membrane disruption that allows entry to occur OR
- via a depression, or "canyon", in the structure is the region that provides the specific binding site for attachment to cells.

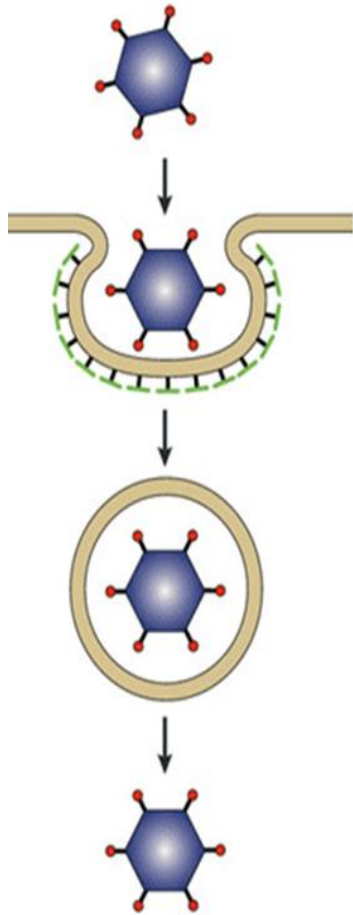


Entry into cells

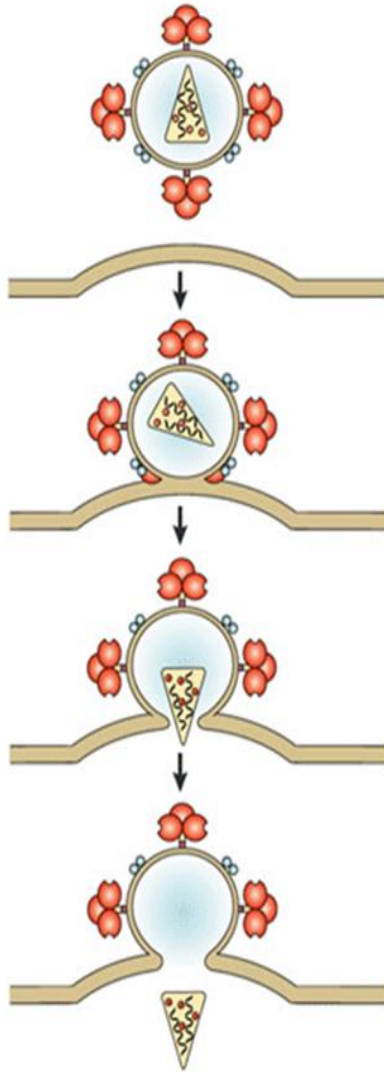
- One typical route for viral entry is fusion with the membrane, which is most common in viruses with envelopes.
- Viruses may also trick the cell into taking them in by a bulk transport process called endocytosis.
- Some even inject their DNA into the cell!
(Bacteriophages)



a Endocytic route:
clathrin-mediated
endocytosis and
penetration



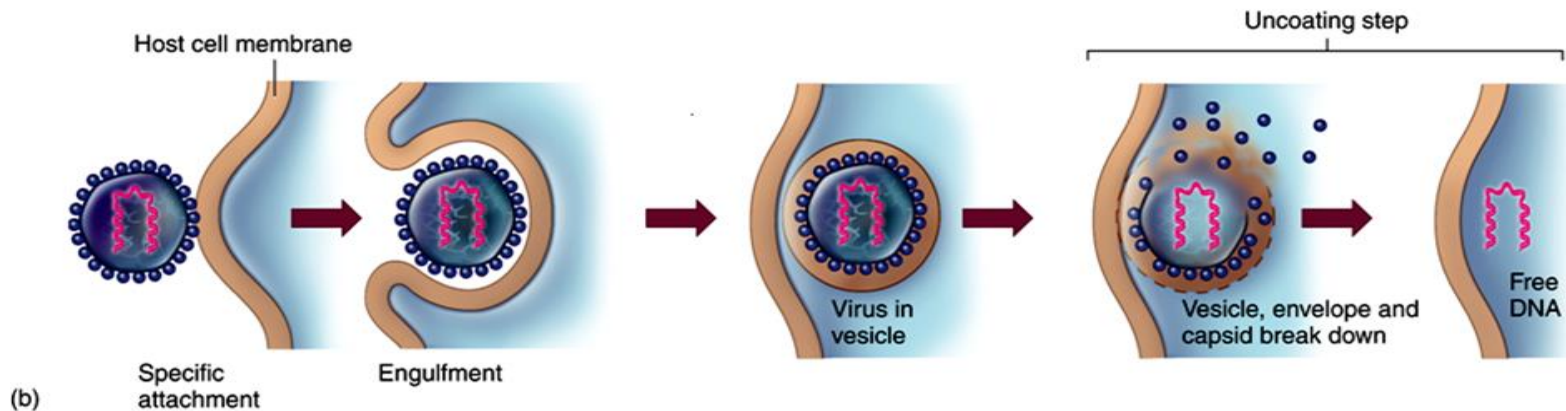
b Non-endocytic route:
fusion at the cell surface



- Entry by **fusing** with the plasma membrane.
 - Some enveloped viruses fuse directly with the plasma membrane.
 - Then, the internal components of the virion are immediately delivered to the cytoplasm of the cell
- Some enveloped viruses require an acid pH for fusion to occur and are unable to fuse directly with the plasma membrane.
 - These viruses are taken up by invagination of the membrane into endosomes.
 - As the endosomes become acidified, the latent fusion activity of the virus proteins becomes activated by the fall in pH and the virion membrane fuses with the endosome membrane.
 - This results in delivery of the internal components of the virus to the cytoplasm of the cell
- Non-enveloped viruses may be taken up into endosomes.
 - They then cross (or destroy) the endosomal membrane.

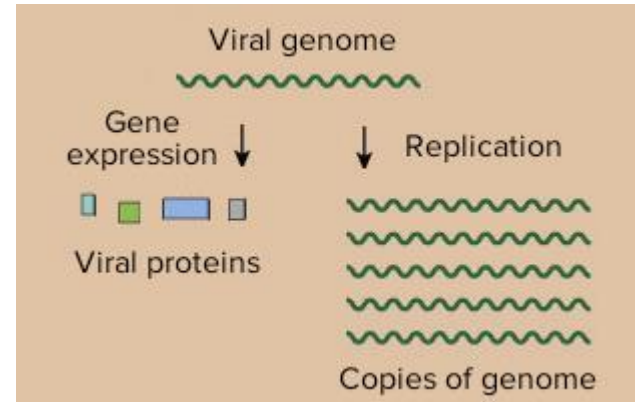
UNCOATING

- A poorly understood process where the genome is released from the capsid
- Nucleic acid has to be sufficiently uncoated that virus replication can begin at this stage
- Uncoating can occur at:
 - The plasma membrane
 - Within endosomes
 - The nuclear membrane



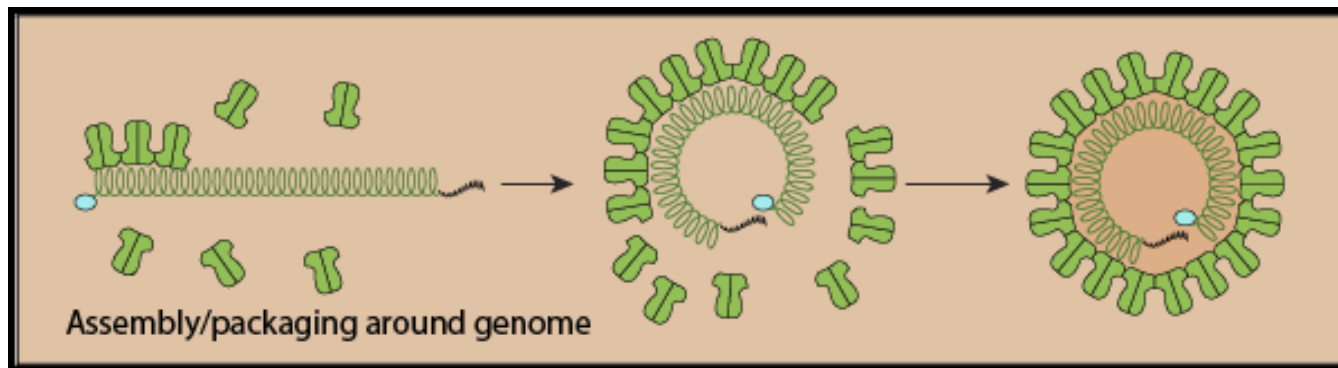
Genome replication and gene expression or biosynthesis.

- This step involves copying the viral genome and making more viral proteins, so that new virus particles can be assembled.
- The materials for these processes (such as nucleotides to make new DNA or RNA) come from the host cell, not the virus.
- Most of the "machinery" for replication and gene expression is also provided by the host cell.
 - For instance, the messenger RNAs (mRNAs) encoding viral genes are translated into viral proteins using the host cell's ribosomes.
- However, certain steps, such as the copying of an RNA virus's genome, cannot be performed by host cell enzymes. In such cases, the viruses must encode their own enzymes.
- All viruses must encode capsid proteins, and enveloped viruses typically also encode envelope proteins
- Viruses may also encode proteins that manipulate the host genome (e.g., by blocking host defenses or driving expression of genes to benefit the virus), help with viral genome replication, or play a role in other parts of the viral lifecycle.



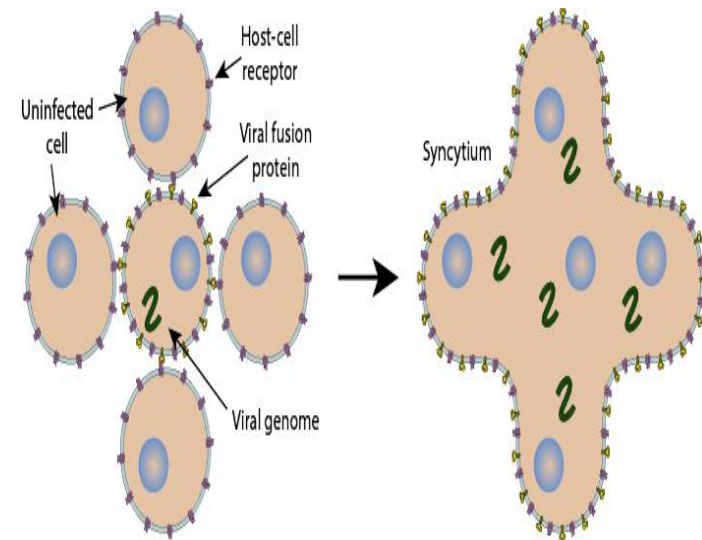
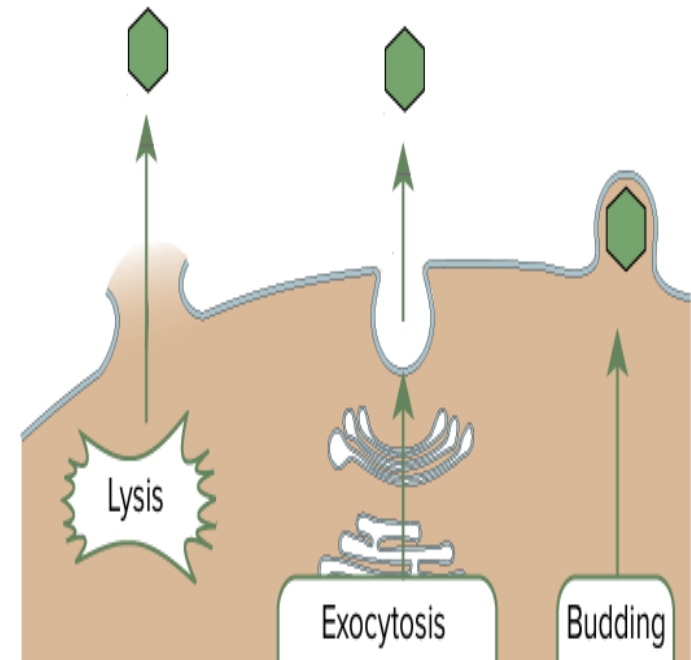
Assembly

- Virus assembly occurs spontaneously within the infected cell and is a highly ordered process
- During assembly, newly synthesized capsid proteins come together to form capsomers, which interact with other capsomers to form the full-sized capsid.
- Some viruses, first assemble an “empty” capsid and then stuff the viral genome inside. Other viruses build the capsid around the viral genome, as shown below.



Release

- The last step in the virus lifecycle is the release of newly made viruses from the host cell.
- Different types of viruses exit the cell by different routes: some make the host cell burst (a process called **lysis**), while others exit through the cell's own export pathways (**exocytosis**), and others yet **bud** from the plasma membrane, taking a patch of it with them as they go.
- In some cases, the release of the new viruses kills the host cell. (For instance, a host cell that bursts will not survive.)
- In other cases, the exiting viruses leave the host cell intact so it can continue cranking out more virus particles.
- **Direct cell to cell transmission** - Some viruses spread directly from one cell to another and may cause fusion of infected cells (syncytia)

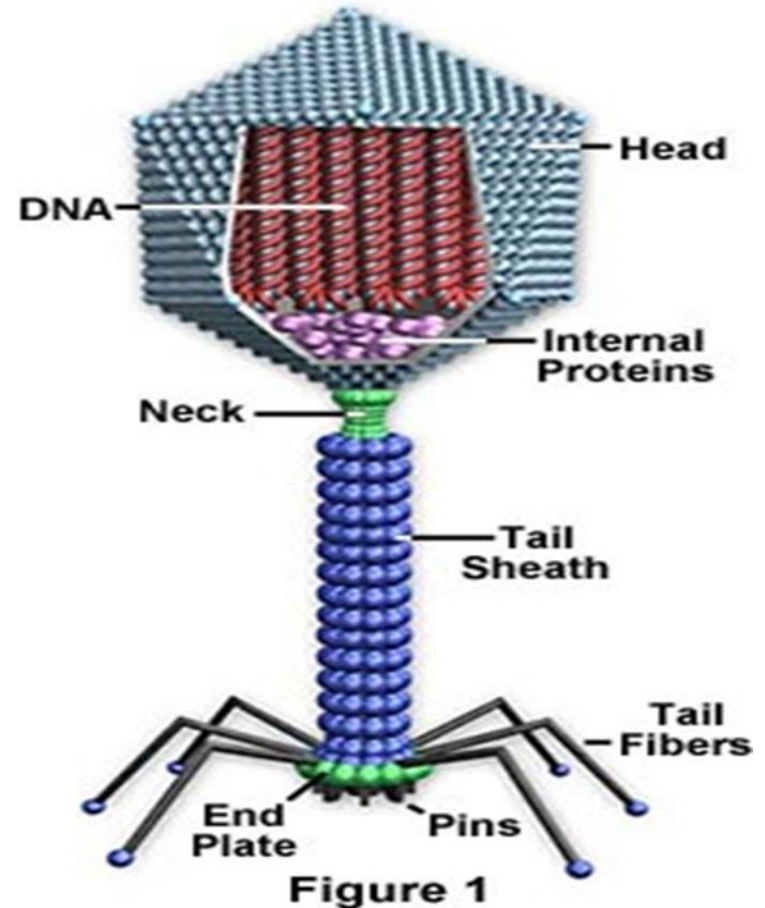


Outcome of Viral Infections

- Virus-host cell interaction may result in:
 - Cell death (lytic) - due to cytopathic effect of virus
 - Cell transformation - cell converted to malignant or cancerous cell
 - Latent infection (occult) - persistent infection in dormant state which may reactive anytime to produce disease; continuous or intermittent shedding
 - Cell fusion to form multinucleated cells

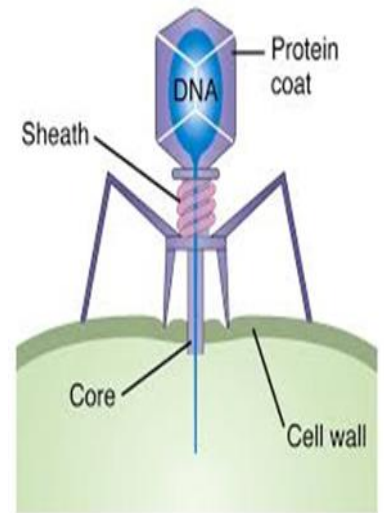
Bacteriophages or phages

- Bacteria-infecting viruses
- They are ubiquitous in the environment
- Phage genomes can consist of either DNA or RNA
- just like other viruses, must infect a host cell (bacteria) in order to reproduce
- come in different sizes and shapes but most of them have the same basic features:
 - a head or capsid and a tail.



Structure of Bacteriophage

- head structure, regardless of its size or shape, is made up of one or more proteins which protectively coats the nucleic acid
- some phages that don't have a tail, most of them do have one attached to its head structure. It is a hollow tube through which the nucleic acid passes through when the bacteriophage infects a host cell.
- Some of the more complex phages such as T4 have a tail with a base plate as well as one or more tail fibers that aid the phage in attaching itself to a bacterial cell
- One of the characteristics of bacteriophages is their temperateness. Temperateness refers to the ability of some bacteriophages, particularly lambda phage, to choose between **two cycles: lysogenic or lytic.**



Lifecycle of Bacteriophage

- **Lytic**

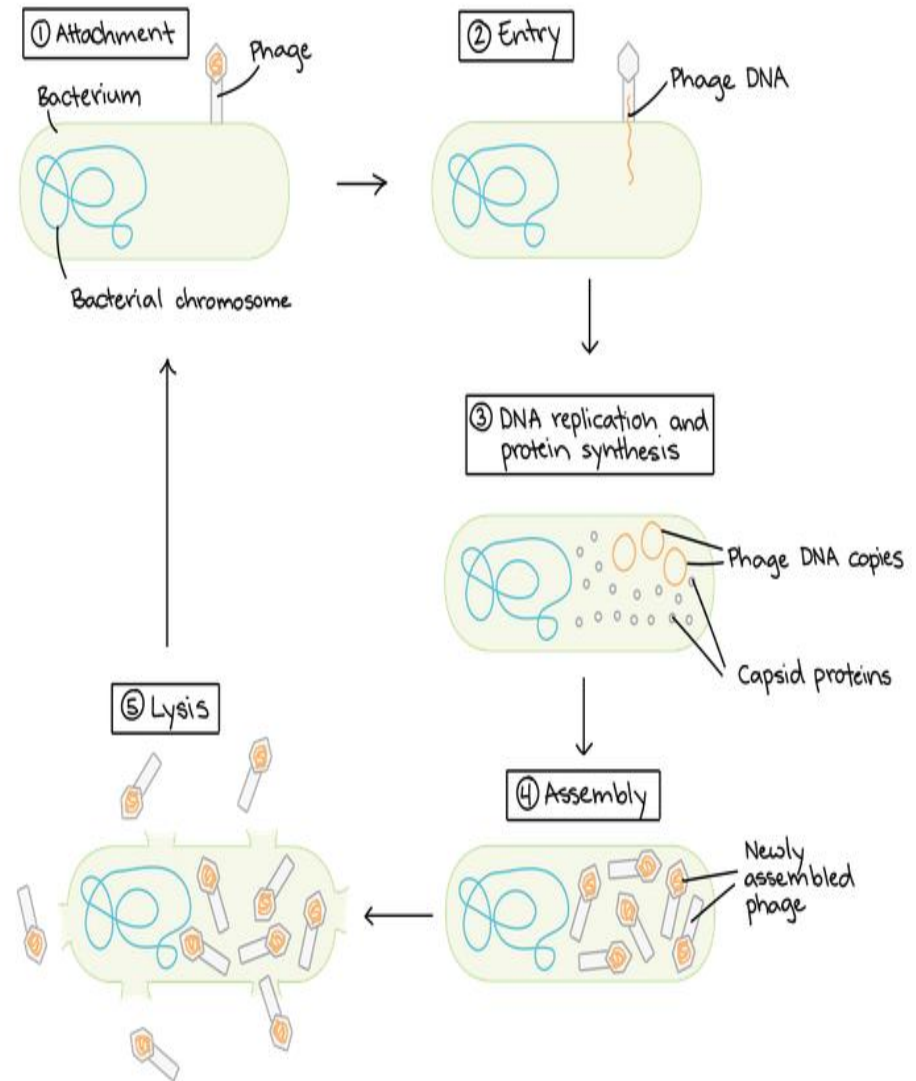
- Attach and entry
- Synthesis
- Assembly
- Lysis

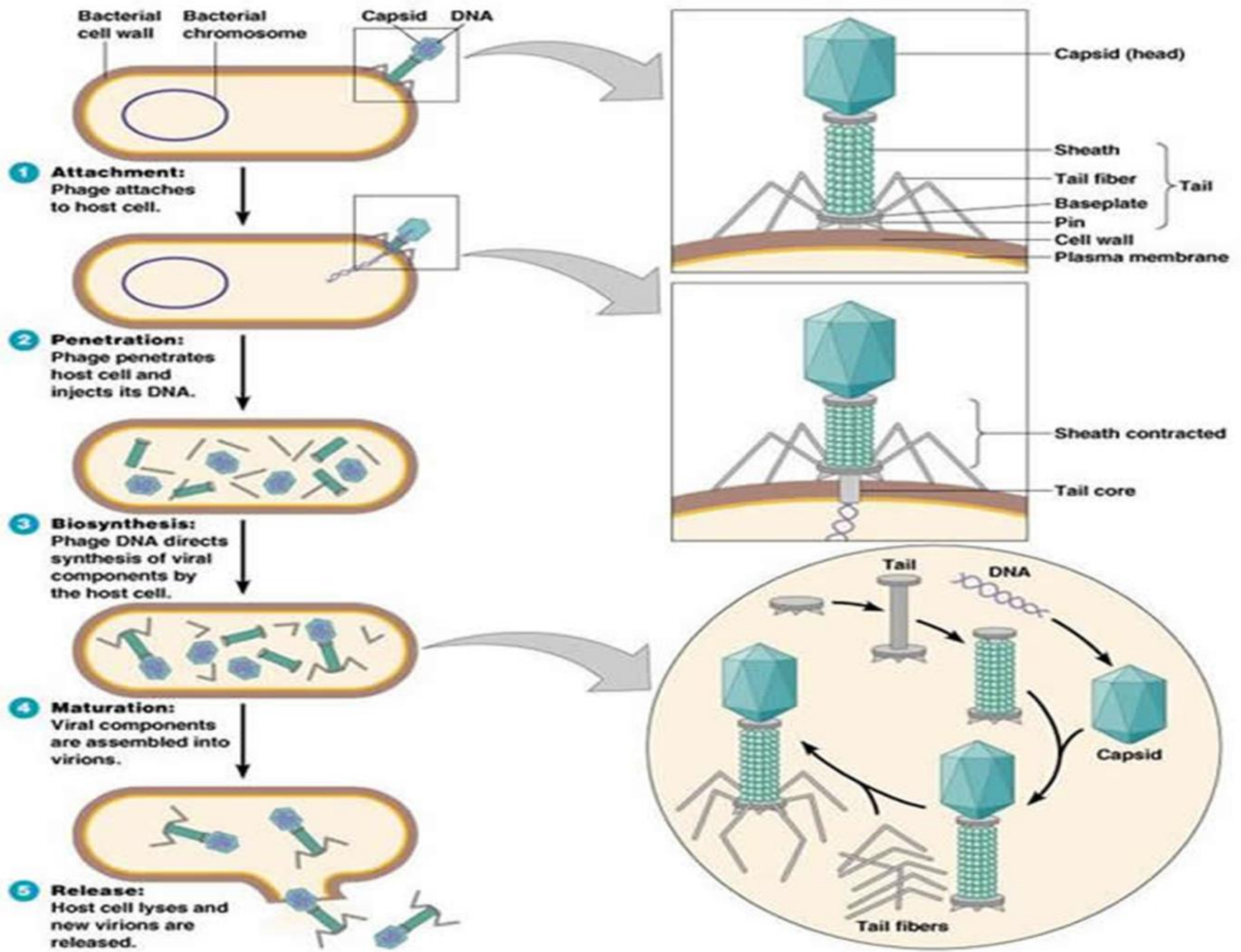
- **Lysogenic**

- Attach and entry
- NA in chromosome
- Bacterial divides by Binary fission
- Re-enters Lytic phase
- Synthesis
- Assembly
- Lysis

Lytic cycle

- In the lytic cycle, a phage acts like a typical virus: it hijacks its host cell and uses the cell's resources to make lots of new phages, causing the cell to lyse (burst) and die in the process.





1 Attachment:
Phage attaches to host cell.

2 Penetration:
Phage penetrates host cell and injects its DNA.

3 Biosynthesis:
Phage DNA directs synthesis of viral components by the host cell.

4 Maturation:
Viral components are assembled into virions.

5 Release:
Host cell lyses and new virions are released.

Capsid (head)

Sheath

Tail fiber

Baseplate

Pin

Cell wall

Plasma membrane

Tail

Sheath contracted

Tail core

Tail

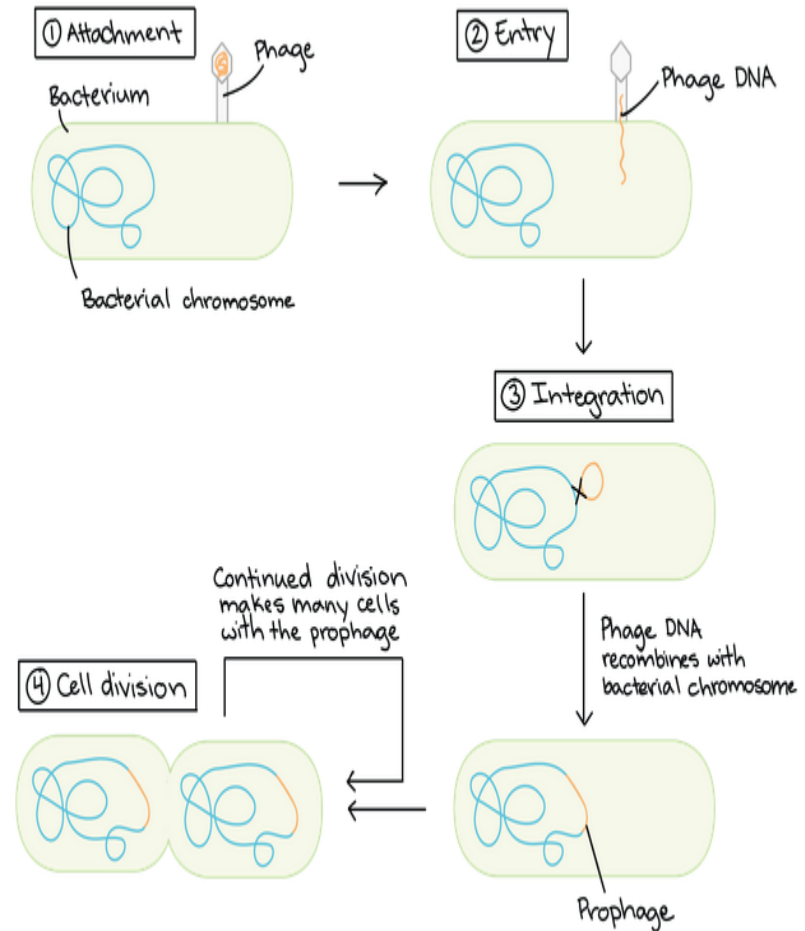
DNA

Capsid

Tail fibers

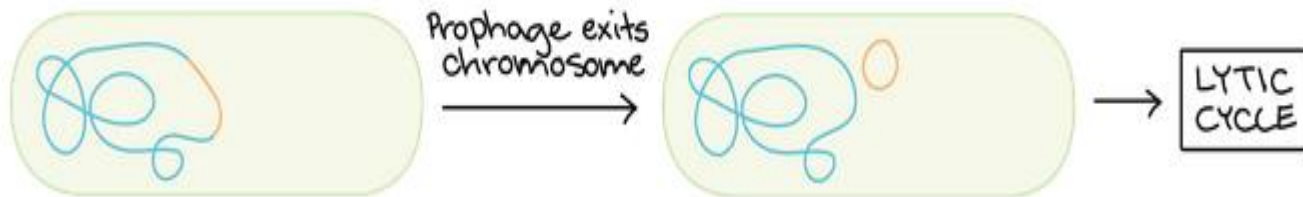
Lysogenic cycle

- The lysogenic cycle allows a phage to reproduce without killing its host. Some phages can only use the lytic cycle, but the phage we are following, lambda (λ), can switch between the two cycles.
- In the lysogenic cycle, the first two steps (attachment and DNA injection) occur just as they do for the lytic cycle. However, once the phage DNA is inside the cell, it is not immediately copied or expressed to make proteins. Instead, it recombines with a particular region of the bacterial chromosome. This causes the phage DNA to be integrated into the chromosome.
- The integrated phage DNA, called a prophage, is not active: its genes aren't expressed, and it doesn't drive production of new phages.
- However, each time a host cell divides, the prophage is copied along with the host DNA, getting a free ride.

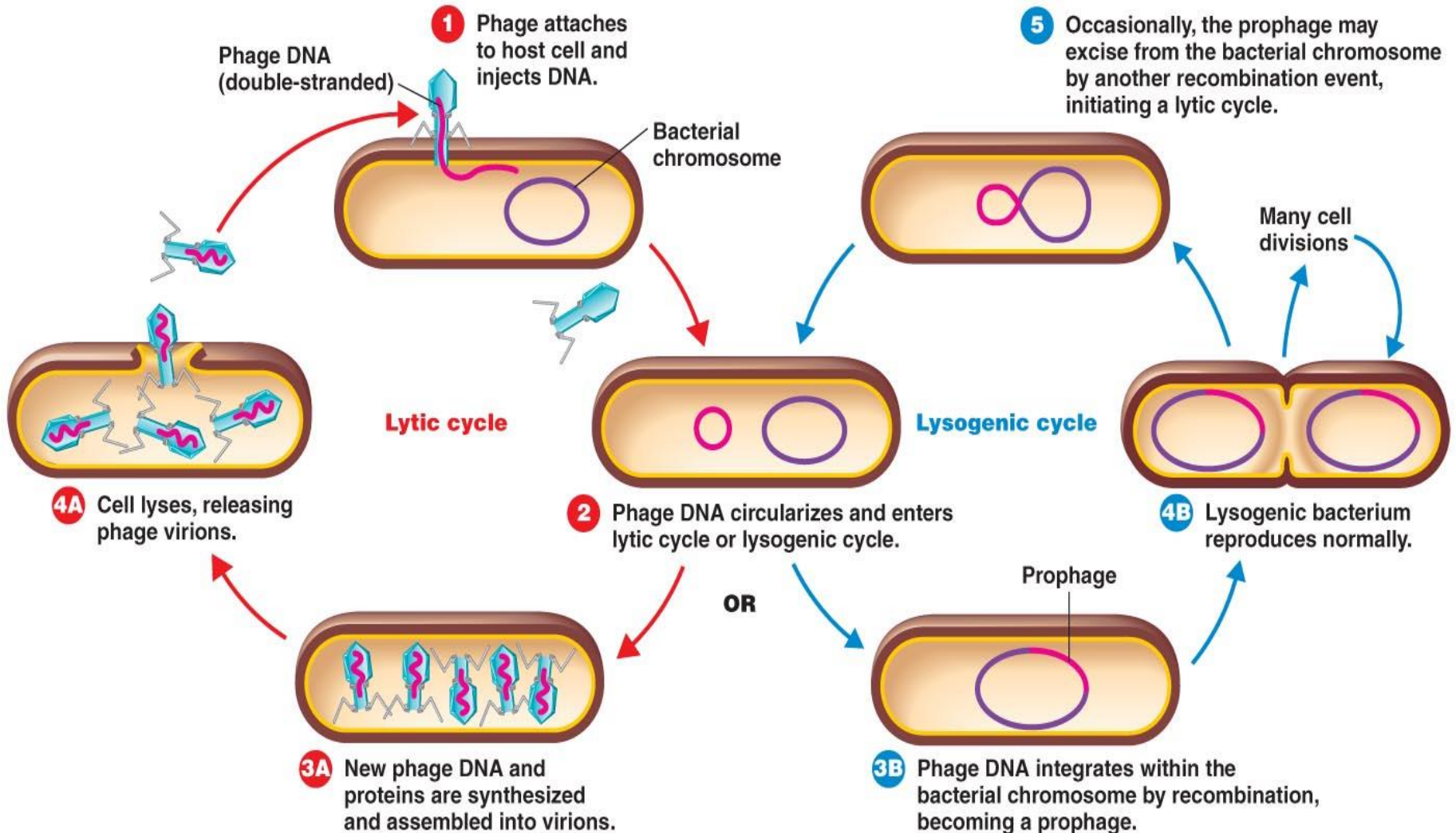


To Lyse or not to Lyse?

- Under the right conditions, the prophage can become active and come back out of the bacterial chromosome, triggering the remaining steps of the lytic cycle (DNA copying and protein synthesis, phage assembly, and lysis).
- However, a small fraction of the prophages in a population spontaneously "go lytic" even without these external cues



Lytic and Lysogenic Cycles



Videos

- Virus lifecycle

<https://www.youtube.com/watch?v=ulutoovWCEg>

- HIV Lifecycle

<https://www.youtube.com/watch?v=8sipX86Jfuw>

- Bacteriophage infecting a bacteria

<https://www.youtube.com/watch?v=-w4C74cu6dk>

Tutorial questions

1. Differentiate between DNA and RNA viruses?
2. i) Draw and label the basic structure of a bacteriophage.
ii) Describe the consequences of an animal viral infection on cells.
3. Describe in detail the lifecycle of animal viruses.
4. Describe in detail the lifecycle of a bacteriophages.
5. Differentiate between the lifecycle of an animal virus and a bacteriophage.
6. Differentiate the differences between how enveloped and non-envelope viruses attach, enter and exit host cells.

**I NEED ANTIBIOTICS
FOR MY COLD-**

IT'S A VIRUS!

