Course Content

- Definition of Virus/ History
- Classification of viruses
- Properties of viruses
- Viral replication
- Bacteriophage
- HIV

VIRORLOGY

Definition

Virology is the study of virus and other virus-like substances (viroids and prions).

What is a virus?

- Virus is Greek word **venom** which means **poison**. It is an infectious obligate intracellular parasite comprising genetic material (DNA or RNA) surrounded by a protein coat and/or a membrane.
- The main purpose of a virus is to deliver its genome into the host cell to allow its expression (transcription and translation) by the host cell.

Viroids

- Viroids are a group of virus-like pathogens much smaller and distinctly different from viruses, consists solely of small single-stranded circular RNA molecule and have no protein coat.

Prions

- Prions are infectious agents composed primarily of protein, lacking nucleic acid (DNA or RNA) They cause a variety of neurodegenerative diseases in humans and animals. E.g. Scrapie prion in sheep.

Virus and the virion

- A virus is an organism with two phases, virion (infectious particle) and infected cells

- **Virion** are a fully assembled infectious virus. It is complete virus particle .

- The main function of the virion is to deliver its DNA or RNA genome into the host cell
- so that the genome can be expressed (transcribed and translated) by the host cell.

Collectively virus can contain these type of nucleic acid

- RNA -------- ssRNA

  ------- dsRNA

  DNA ------- ssDNA

  ------- dsDNA

- dsDNA/ssRNA hybrid

History

- **Iwanoski** first discovered virus while Louis Pasteur coined the term virus.

- **Tward**; amd **Hexelle** discovered Bactriophage

- **LA Montaignoc** discovered HIV and there are 10^{16} Hiv genome on the planet today.

- **Stanley** first crystallized the first mosaic virus (FMV)

- **Francis Rous** discovered Rous Sarcoma virus.

- **Bawden** and **Pierie** proposed nucleo protein nature of virus by studying chemical nature of TMV

History contd

- TMV was the first to be discovered and crystallized.

- **Martinus Beijerinck** (1851–1931), stated virus as ’’ contagium vivum fluidum’’ means they are contagious nature fluid.

Viruses are ubiquitous

- Virus infects every living thing:

  a) eukaryotes (vertebrate & invertebrate animals, plants, fungi)

  b) prokaryotes (bacteria and archaea)

- present within their hosts and are also found in soil, air and water.
- The viruses that infect prokaryotes are often referred to as bacteriophages, or phages

Classification of Viruses

- Classification scheme helps to understand the features shared among different groups of viruses.
- Scientist’s method of classification could not work here because viruses are not known to evolve from a common ancestor.
- Biologists have used several classification systems in the past, based on the morphology and genetics
- Baltimore classification scheme is mostly used now and is based on how messenger RNA (mRNA) is generated in each particular type of virus.

Baltimore Classification

- most modern and commonly used system of virus classification

- was developed by Nobel Prize-winning biologist David Baltimore in 1970s

- groups viruses according to how the mRNA is produced during the replicative cycle of the virus.

- Grouped virus into 7 groups

Group I viruses contain double-stranded DNA (dsDNA) as their genome

- Their mRNA is produced by transcription in much the same way as with cellular DNA

- **Group II** viruses have single-stranded DNA (ssDNA) as their genome.

- They convert their single-stranded genomes into a dsDNA intermediate before transcription to mRNA can occur

Group III viruses use dsRNA as their genome.

- The strands separate, and one of them is used as a template for the generation of mRNA using the RNA-dependent RNA polymerase encoded by the virus
- **Group IV** viruses have ssRNA as their genome with a positive polarity
- **Positive polarity** means that the genomic RNA can serve directly as mRNA.
- Intermediates of dsRNA, called **replicative intermediates**, are made in the process of copying the genomic RNA

- Multiple, full-length RNA strands of negative polarity (complimentary to the positive-stranded genomic RNA) are formed from these intermediates, which may then serve as templates for the production of RNA with positive polarity, including both full-length genomic RNA and shorter viral mRNAs.
- **Group V** viruses contain ssRNA genomes with a **negative polarity**, meaning that their sequence is complementary to the mRNA.
- As with Group IV viruses, dsRNA intermediates are used to make copies of the genome and produce mRNAs

- In this case, the negative-stranded genome can be converted directly to mRNA.

- Additionally, full-length positive RNA strands are made to serve as templates for the production of the negative-stranded genome

- **Group VI** viruses have diploid (two copies) ssRNA genomes that must be converted, using the enzyme **reverse transcriptase**, to dsDNA;

- the dsDNA is then transported to the nucleus of the host cell and inserted into the host genome

- Then, mRNA can be produced by transcription of the viral DNA that was integrated into the host genome

- **Group VII** viruses have partial dsDNA genomes

- make ssRNA intermediates that act as mRNA,

- but are also converted back into dsDNA genomes by reverse transcriptase, necessary for genome replication

Baltimore Classification

Group	Characteristics	Mode of mRNA Production	Example
I	Double-stranded DNA	mRNA is transcribed directly from the DNA template	Herpes simplex (herpesvirus)
II	Single-stranded DNA	DNA is converted to double-stranded form before RNA is transcribed	Canine parvovirus (parvovirus)
III	Double-stranded RNA	mRNA is transcribed from the RNA genome	Childhood gastroenteritis (rotavirus)
IV	Single stranded RNA (+)	Genome functions as mRNA	Common cold (pircornavirus)
V	Single stranded RNA (-)	mRNA is transcribed from the RNA genome	Rabies (rhabdovirus)
VI	Single stranded RNA viruses with reverse transcriptase	Reverse transcriptase makes DNA from the RNA genome; DNA is then incorporated in the host genome; mRNA is transcribed from the incorporated DNA	Human immunodeficiency virus (HIV)
VII	Double stranded DNA viruses with reverse transcriptase	The viral genome is double-stranded DNA, but viral DNA is replicated through an RNA intermediate; the RNA may serve directly as mRNA or as a template to make mRNA	Hepatitis B virus (hepadnavirus)

General characteristic of viruses

1. Smallest known infectious agents. Built up of **nucleic acid** and **protein coat(s)** and may in addition have an outer lipoprotein **envelope**.

2. Connecting link between living and non living.

living nature - Nucleic acid & reproduction.

non living ,, - Non cellular & crystal outside living host cell

3. Virus is obligate parasite of cells, and are dependent on their hosts for most of their requirements, including

- building-blocks such as amino acids and nucleosides;
- protein-synthesizing machinery (ribosomes);
- energy, in the form of adenosine triphosphate

4. Made up of nucleic acid core surrounded by protein coat. Size ----- approx 20 – 400nm.

5. Passive agent. completely inanimate. They do not think.

6. Replicate in cells -- lead to cell damage and cause disease.

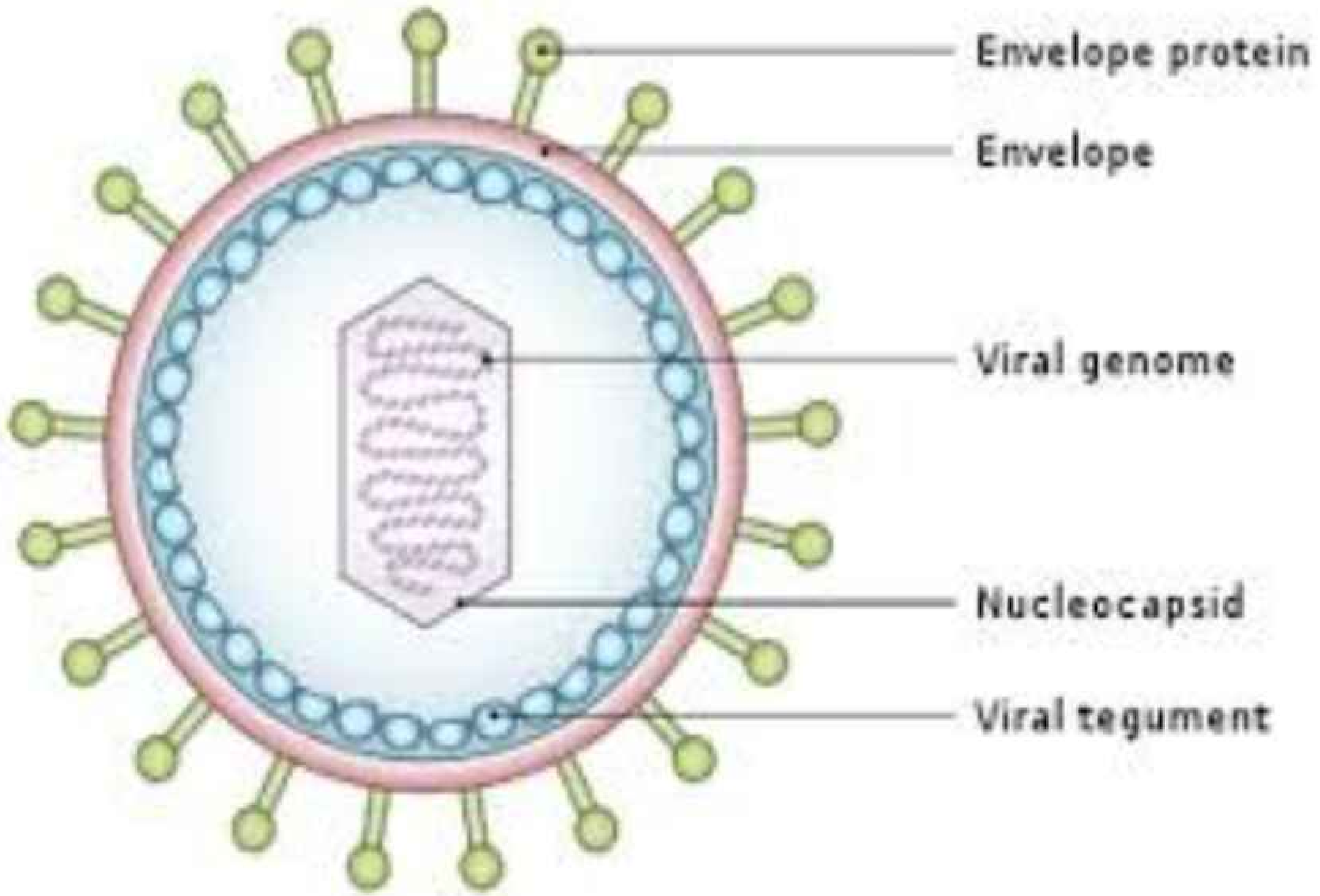
Host defenses -- lead to cell damage as they clear virus- infected cells.

Structure of Viruses

- Any virus has: -- a **nucleic acid** (DNA or RNA)

Capsid -- formed in 3 shapes or symmetry Helical, Icosahedral and Complex.

Structure of Virus



envelope -- (most advance virus eg influenza virus and herpes).

- nucleic acid and capsid (nucleo capsid), can be naked as seen in Papilloma viruses and adeno viruses.

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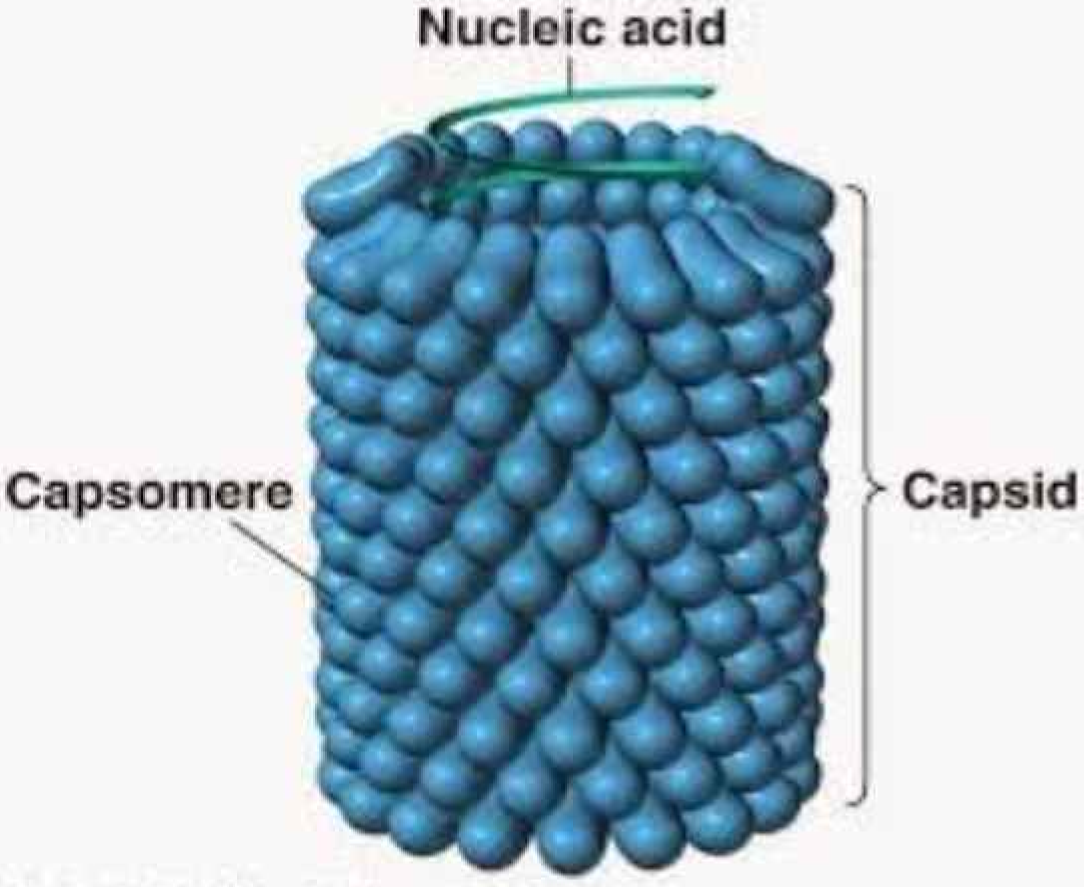
Viral Nucleic acid

- can be either RNA or DNA
- Outside host cells, viruses survive as virus particles (virions)
- Virion ---- contains the viral genome -- functions to protect the genome help it to enter a host cell ---gene delivery system

Viral Capsid

- protein coat or shell that surrounds the nucleic acid.
- made up of many small protein particles called **capsomeres**
- formed in three general shapes or symmetry called Helical, Icosahedral and Complex



(a) A helical virus

- Protect the nucleic acid and aids in its transmission between host cells

- Recognizes and attaches to a host cell in which the virus can be replicated.

- Stable enough to survive in the extracellular environment

- Ability to alter its conformation so that, it can release its genome into the host cell.

Helical Symmetry of a Capsid

- RNA is coiled in the form of a helix
- Many copies of the same protein specie`s are arranged around the coil.
- capsids of many ssRNA viruses have helical symmetry eg measles and influenza viruses.
- Some plant viruses have helical symmetry e.g tobacco mosaic virus.

Icosahedral Symmetry of a Capsid

- consist of a shell built from protein molecules.
- appears to have been arranged on scaffolding in the form of an icosahedron.

- An icosahedron is an object with:
  - 20 faces, each an equilateral triangle.

- 12 vertices, each formed where the vertices of five triangles meet;

- 30 edges, at each of which the sides of two triangles meet. Eg. Satellite tobacco mosaic virus

Complex Symmetry of a Capsid

- phages are constructed in the form of a tail attached to a head, which contains the virus genome.
- have dsDNA genomes, head has icosahedral symmetry

Envelope (in most advance virus)

- third structure that surrounds the capsid.
- composed of -- a **bi-lipid layer** like the membrane on a cell

  -- **glycoproteins** which are protein and carbohydrate comp.
- disguises the virus to look like the real cell protecting them from being seen as a foreign substance to the immune system of the host.

Viral Replication

- **Overview of Virus Replication**
- 1. Attachment
- 2. Entry
- 3. Transcription
- 4. Translation
- 5. Genome replication
- 6. Assembly
- 7. Exit
- The first letter from each step gives the acronym
- **AETTGAE**, which may provide a memory aid.

- Aim of a virus is to replicate itself.

- To achieve this, the virus need;
  - to enter a host cell,
  - make copies of itself and
  - release the new copies out of the cell to infect neighboring cells.

. Viruses differ from cells in the way in which they multiply.
. A new cell is always formed directly from a pre-existing cell, but a new virion is never formed directly from a pre-existing virion.

- New virions are formed by a process of replication, which takes place inside a host cell

- It involves the synthesis of components followed by their assembly into virions.

- A virus modifies the intracellular environment of its host in order to enhance the efficiency of the replication process.

- Modifications might include production of new membranous structures, reduced expression of cell genes or enhancement of a cell process.

- Some large phages encode proteins that boost photosynthesis in the cells of their photosynthetic bacterial hosts, thereby probably boosting the yields of virus from the cells.

1. **Attachment**-
A virion attaches via one or more of its surface proteins to specific molecules on the surface of a host cell.

- These cellular molecules are known as receptors and the recognition of a receptor by a virion is highly specific, like a key fitting in its lock.

- It has been found that some viruses need to bind to a second type of cell surface molecule (a co-receptor) in order to infect a cell

- Many of the cell surface molecules used by viruses as receptors are in regions of the plasma membrane

2. **Entry-** In entry or penetration, the virus particle is uncoated, i.e releases its genetic material from the capsid to inside of the host cell.

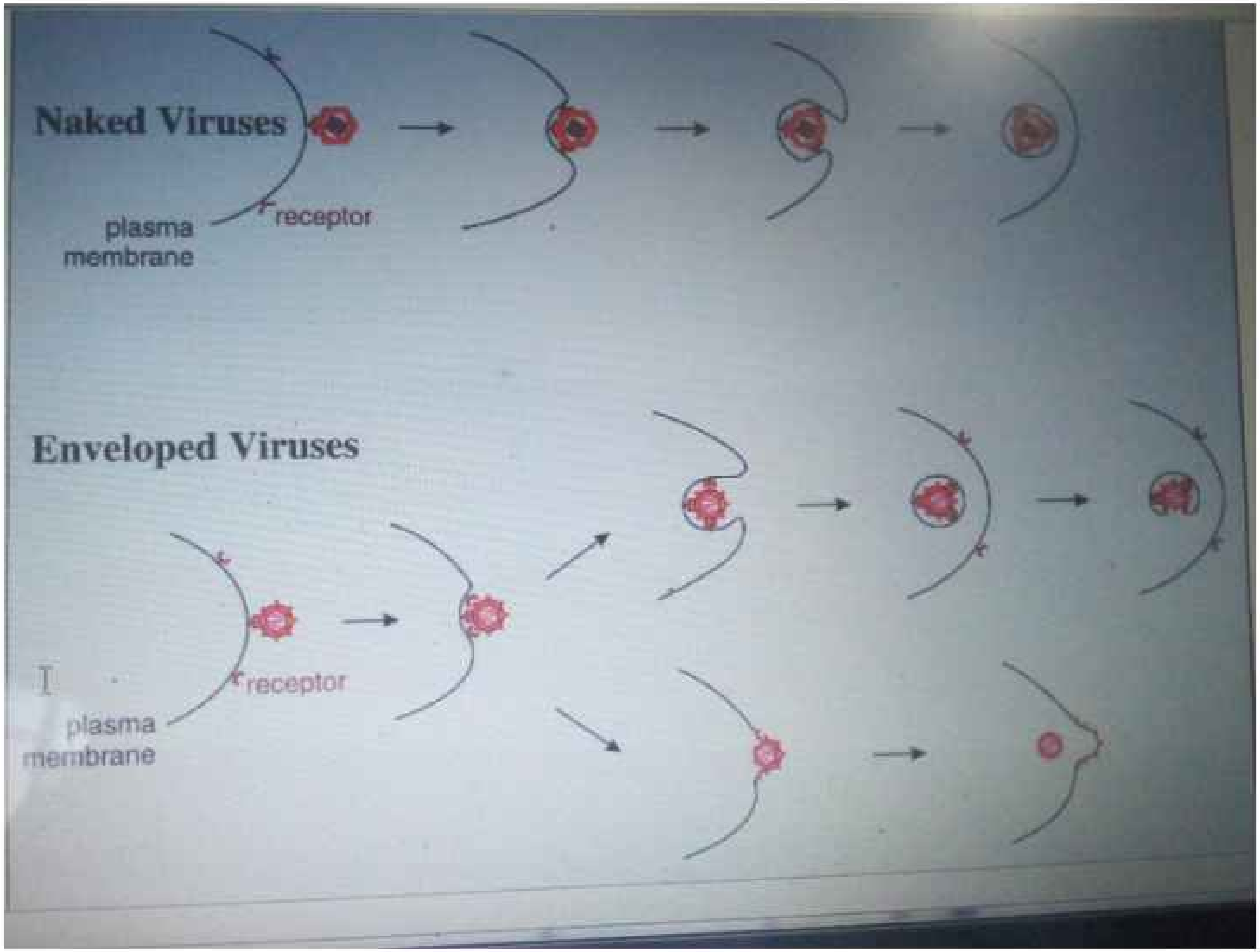
Attachment and entry of a naked virion.

- As more receptors bind to the virion its attachment becomes irreversible. The virion is taken into an endosome, the membrane of which is formed by pinching off from the plasma membrane.

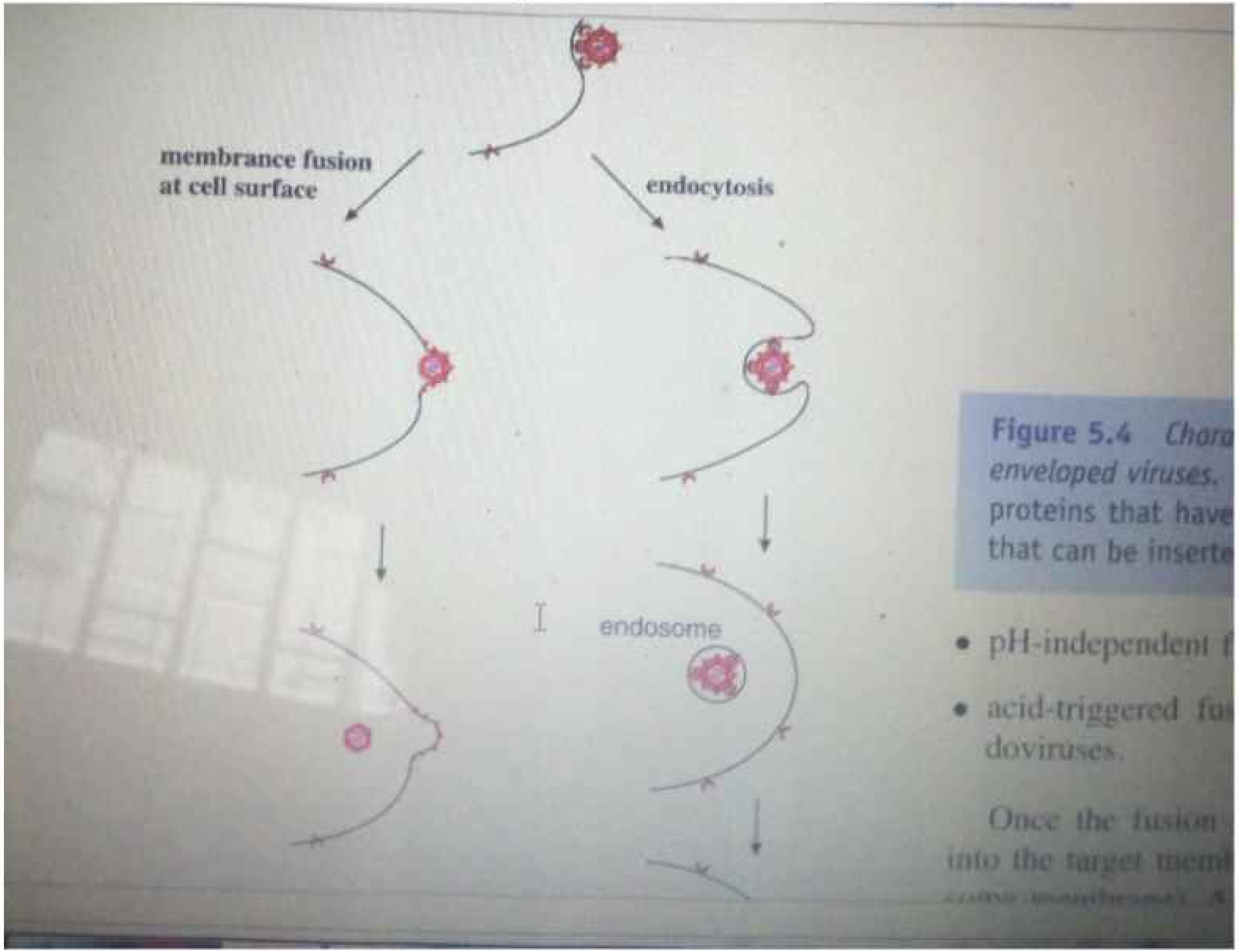
Attachment and entry of an enveloped virion.

- Some enveloped viruses can enter a host cell both by membrane fusion at the cell surface and by endocytosis.
- Others can enter only by endocytosis

Attachment and entry of a naked and Enveloped virion



Attachment and entry of a naked and Enveloped virion



3. **Transcription** (**Synthesis**)- During this step, the virus directs the host machinery for the synthesis of nucleic acid and protein.

- **Transcription= writing across**
- **Translation = bearing across**
- **Transport = carrying across.**

- Transcription refers to the writing across of genetic information from a sequence of bases in a nucleic acid to the complementary sequence in messenger RNA (mRNA)

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4**. Translation** (**Assembly** and Maturation)- The synthesized capsids and genomes are channeled to different location in the cell (nucleus or cytoplasm) for assembly and release. It bears across the written genetic information (aminoacid) which later form the protein.

5. **Genome Replication**

- The synthesized genome are replicated or multiplied in the cytoplasm.

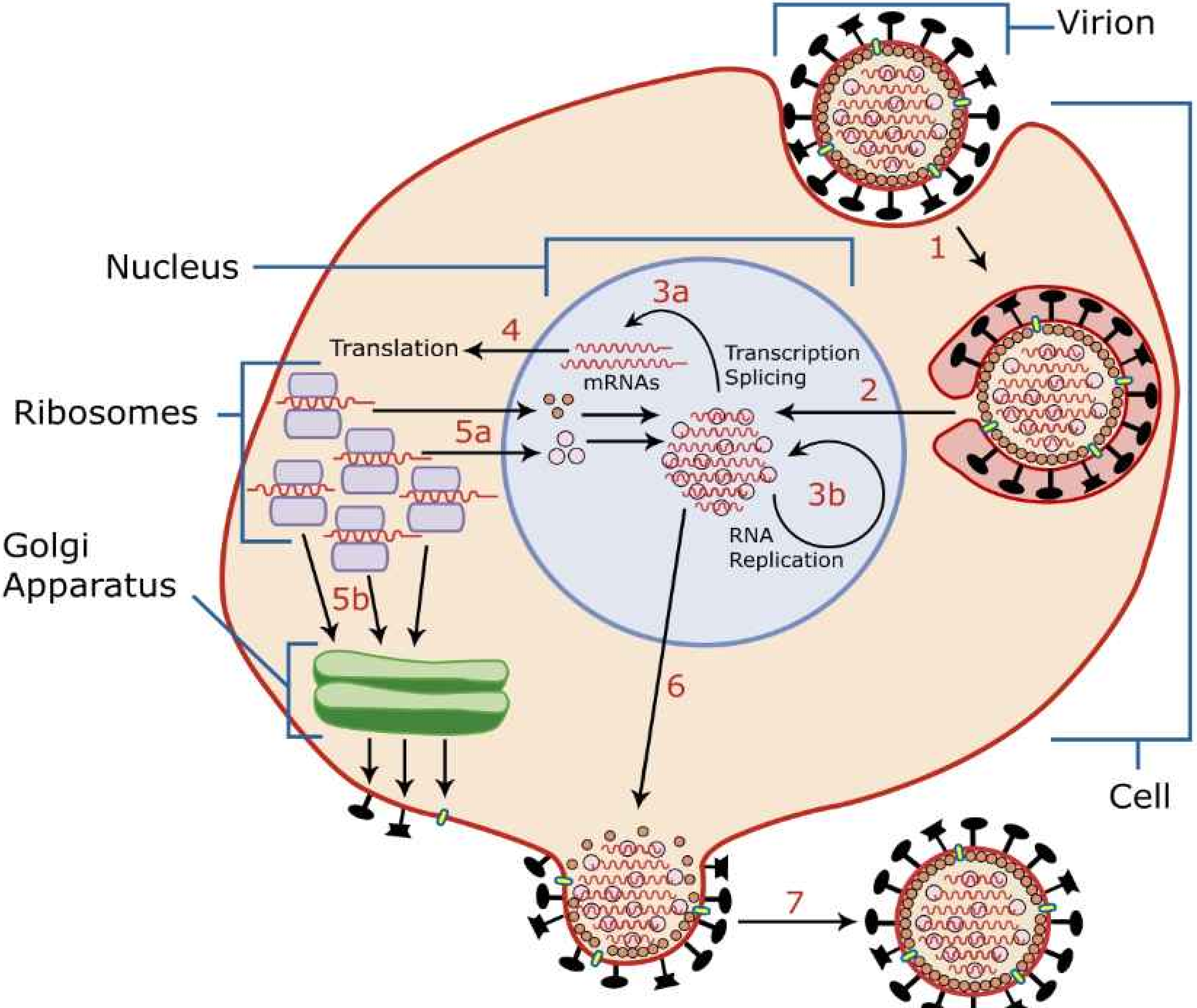
6. **Assembly** and Maturation

- They are assembled, parkaged and made ready to leave the cell

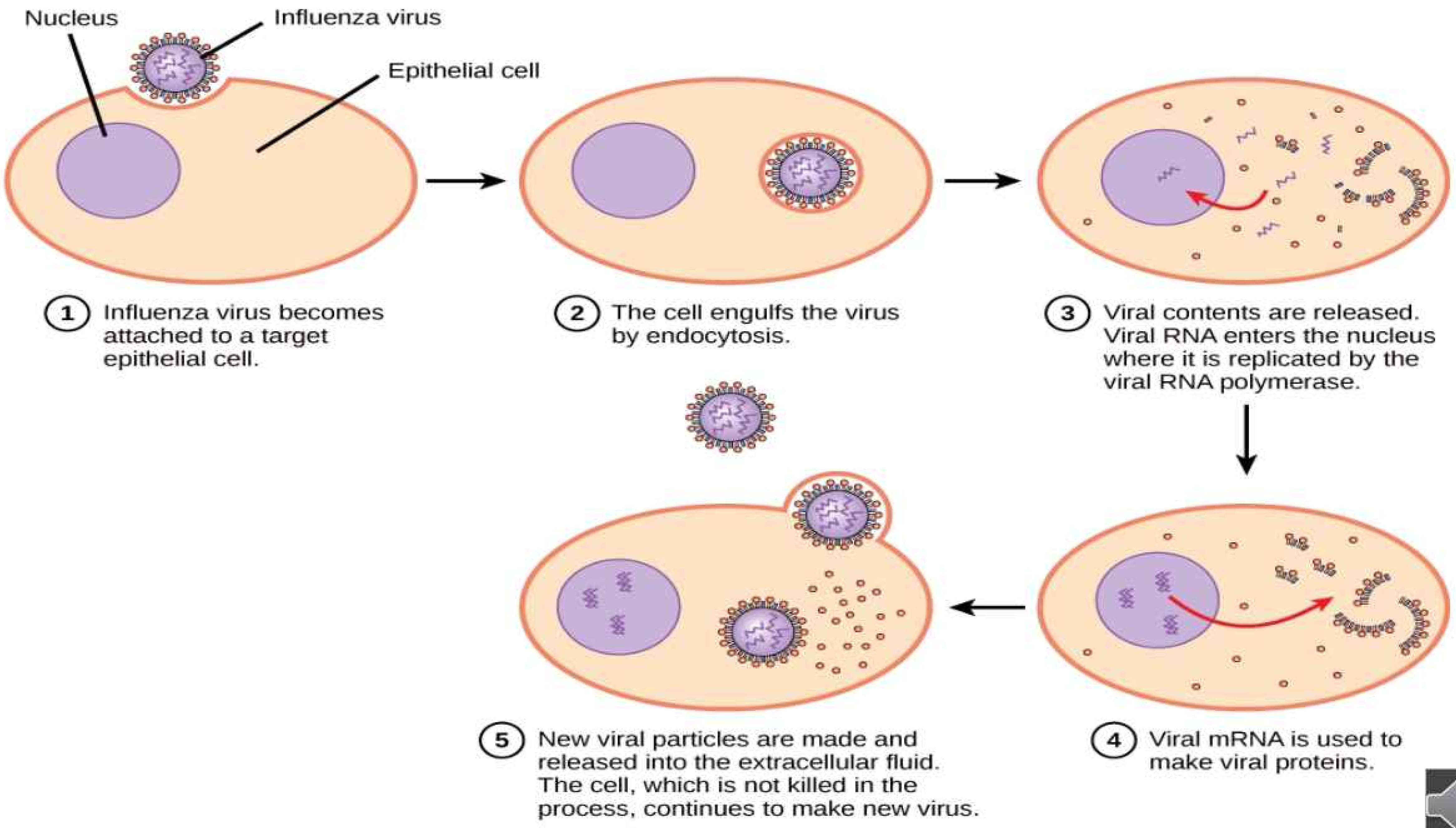
7. Exit or Release-

- The assembled particles first bud out in an envelope form from the nuclear compartment and fuse with the outer cell membrane.

- The release may occur by budding through the cell membrane or by cell-lysis releasing the progeny viruses.



Virion
Nucleus
1
3a
4
Translation
mRNAs
Transcription
Splicing
2
Ribosomes
5a
3b
RNA
Replication
Golgi
Apparatus
5b
6
Cell
7



Nucleus
Influenza virus
Epithelial cell
1 Influenza virus becomes attached to a target epithelial cell.
2 The cell engulfs the virus by endocytosis.
3 Viral contents are released. Viral RNA enters the nucleus where it is replicated by the viral RNA polymerase.
4 Viral mRNA is used to make viral proteins.
5 New viral particles are made and released into the extracellular fluid. The cell, which is not killed in the process, continues to make new virus.

- Bacteriophage (phage) are obligate intracellular viruses that specifically infect bacteria
- 2 researchers, 1. Frederick William Twort in 1915 discovered it

2. Félix d'Herelle in 1917 confirmed and coined the term bacteriophage

- Phage must first enter the host cell to reproduce

- bind to specific receptors with their tail fibers (adsorption) and create a hole

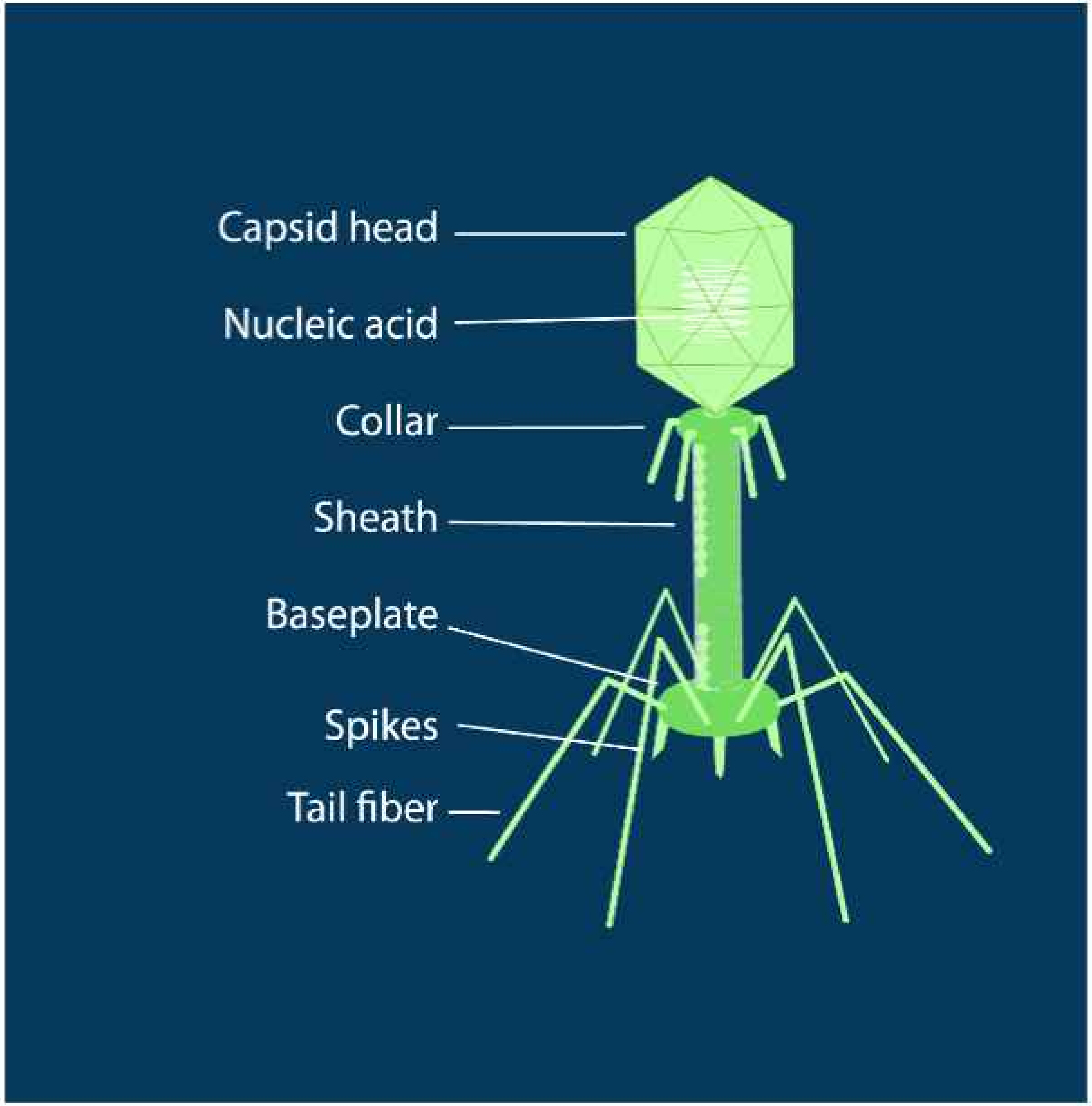
- Base plate coordinates it along with attachment

- A rigid tube is propelled out of the sheath, puncturing a hole in the bacterial cell membrane and inject their genetic material

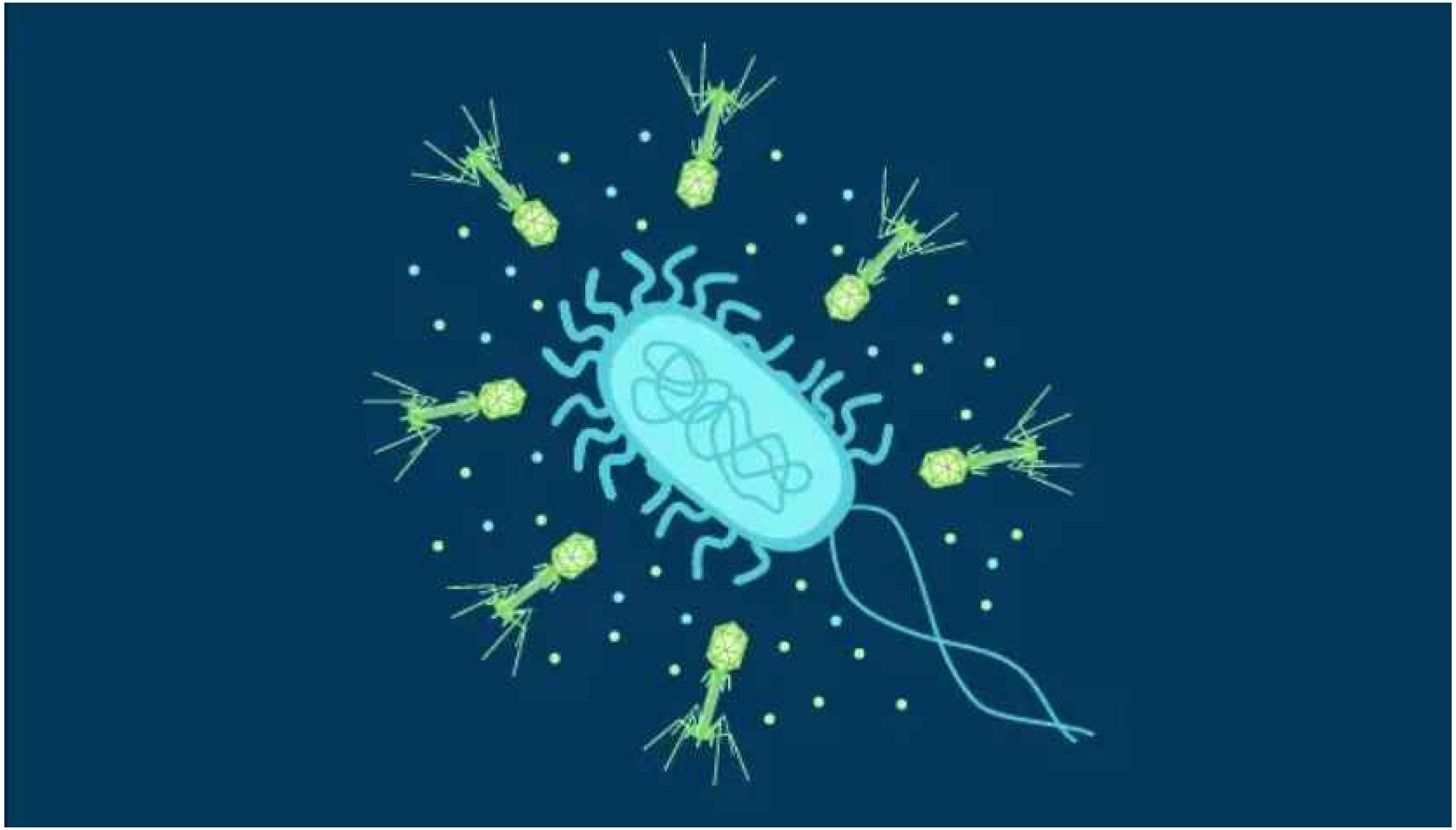
- hijack the host cell’s cellular machinery for their own replication

- Do this using a process called **lytic** and **lysogenic cycle**

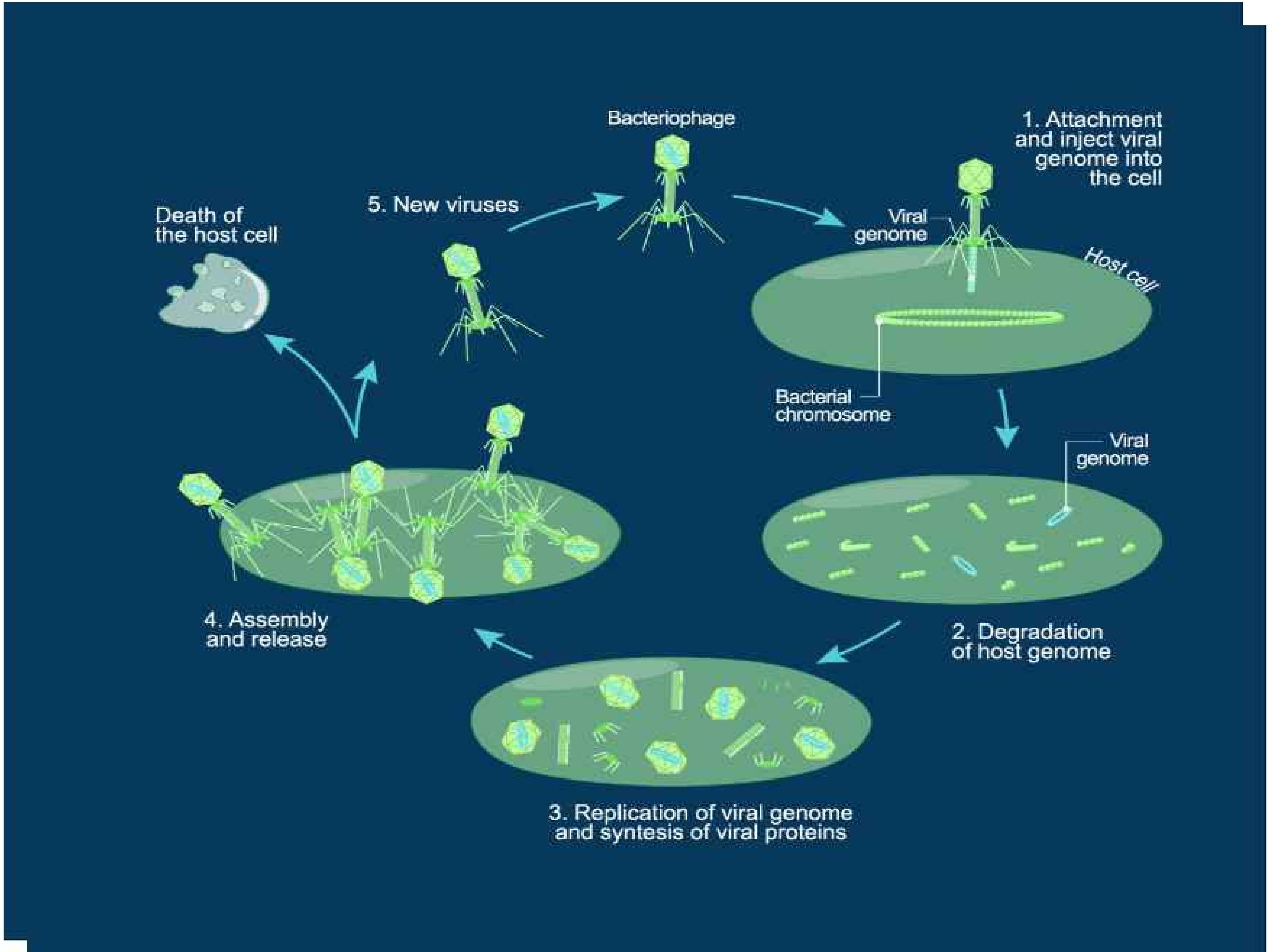
STRUCTURE OF A BACTERIOPHAGE

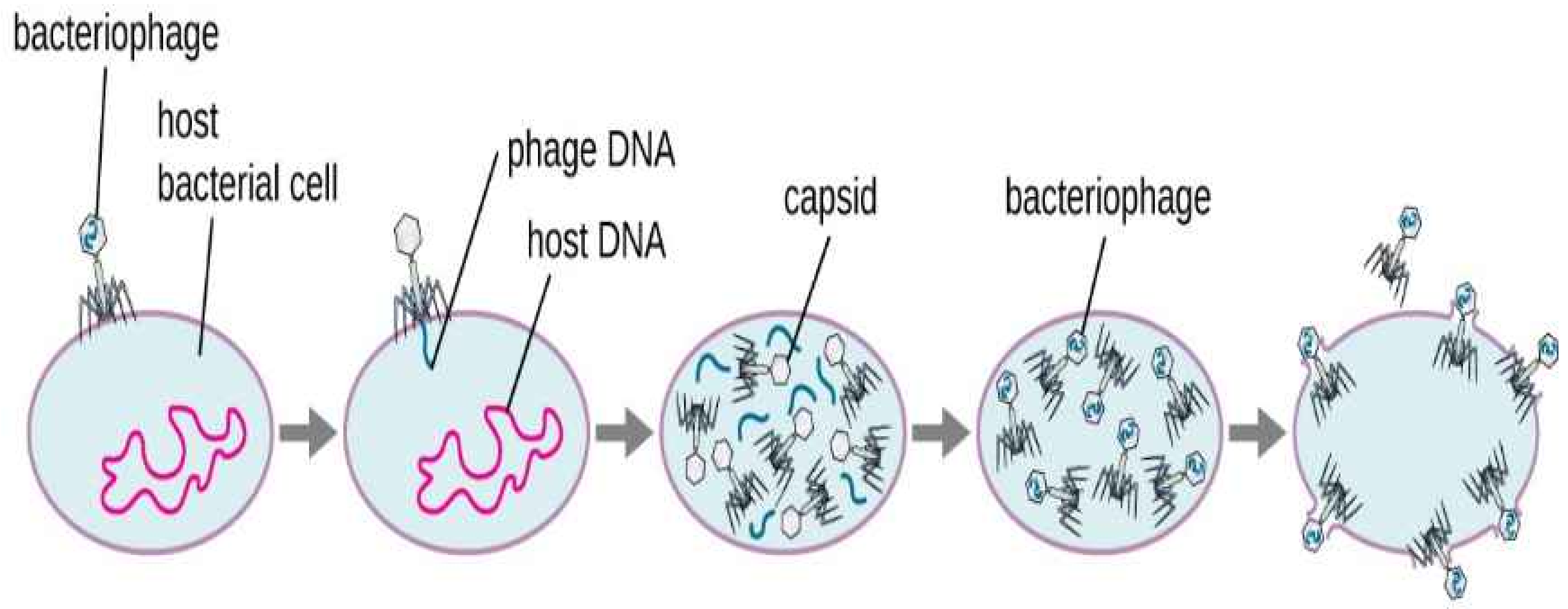


Picture of a phage trying to infect a bacteria



Lytic cycle


Bacteriophage
1. Attachment and inject viral genome into the cell
Viral genome
Host cell
Bacterial chromosome
Viral genome
2. Degradation of host genome
3. Replication of viral genome and syntesis of viral proteins
4. Assembly and release
Death of the host cell
5. New viruses



1 **Attachment**
The phage attaches to the surface of the host.

2 **Penetration**
The viral DNA enters the host cell.

3 **Biosynthesis**
Phage DNA replicates and phage proteins are made.

4 **Maturation**
New phage particles are assembled.

5 **Lysis**
The cell lyses, releasing the newly made phages.

1. the infecting phage ultimately kill the host cell to produce many of their own progeny.

- On injection into the host cell, the phage genome synthesizes early proteins that break down the host DNA and takes control of the cellular machinery
- uses the host cell to synthesize proteins required to build new phage particles.

- Heads and sheaths assembled, new genetic material packed into head, new daughter phage particles constructed

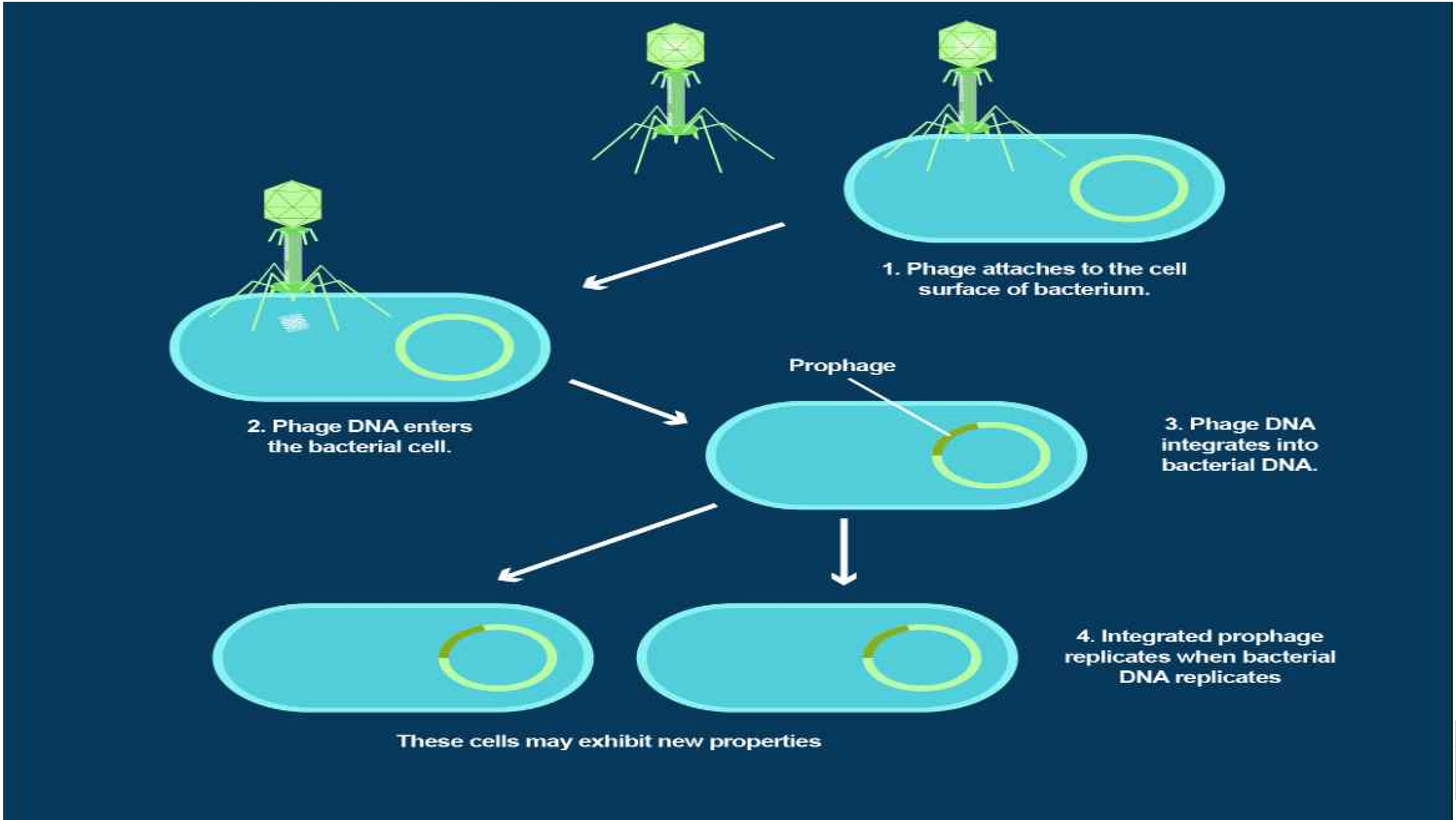
- host cells gradually become weakened by phage enzymes and eventually burst, releasing on average 100-200 new phage progeny into the environment.
- Referred to as virulent infection, or infecting phage

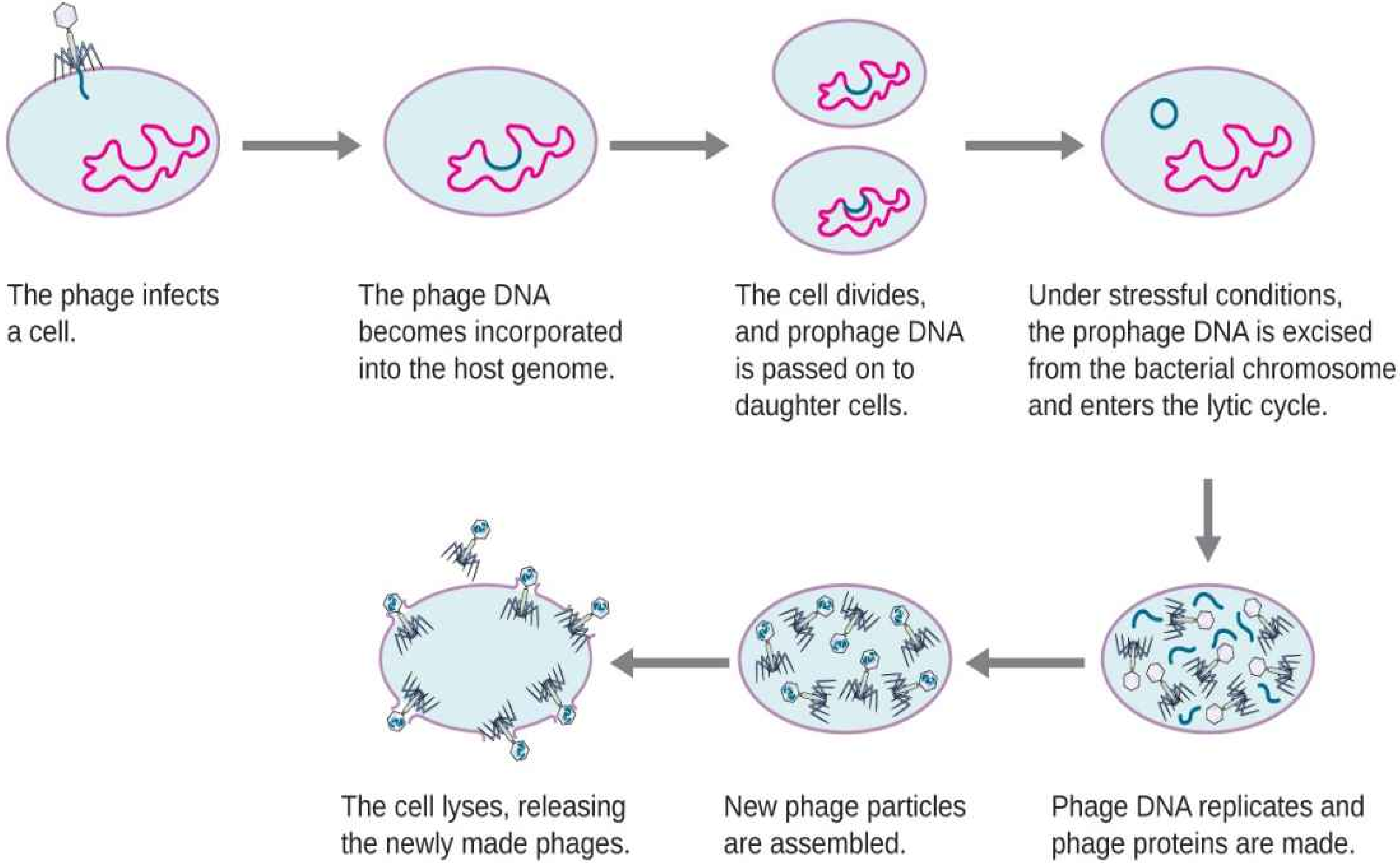
Lysogenic cycle

- Refered to as temperate or non-virulent infection
- Does not kill the host cell, but uses it as refuges where it exists in a dormant state
- After Injection of the phage DNA into the host cell, it integrates itself into the host genome, termed as **prophage**

- Prophage genome is then replicated passively along with the host genome as the host cell divides
- Phage genome is small, so the bacterial hosts are unharmed by this process.

Lysogenic cycle




The phage infects a cell.
The phage DNA becomes incorporated into the host genome.
The cell divides, and prophage DNA is passed on to daughter cells.
Under stressful conditions, the prophage DNA is excised from the bacterial chromosome and enters the lytic cycle.
Phage DNA replicates and phage proteins are made.
New phage particles are assembled.
The cell lyses, releasing the newly made phages.

If a bacterium with prophage is exposed to UV light, low nutrient conditions, or chemicals like mitomycin C, prophage may spontaneously extract themselves from the host genome and enter the lytic cycle in a process called **induction.**

Uses of phage therapy

- a vehicle to move genetic material between many organisms
- method for treating bacterial infections.
- phage are able to infect and destroy bacteria and have been successfully used to treat life-threatening infection

- packaging occasionally makes a mistake. Instead of packaging viral DNA, it takes a random piece of host DNA and inserts it into the capsid. Once released, this virion will then inject the former host’s DNA into a newly infected host. Resistance gene can be transferred in such manner.

HIV

- **HIV (human immunodeficiency virus)** is a virus that attacks the body's immun**e** system called CD4 cells. These are types of T cell (white blood cells). The virus destroys these cells and uses them to make copies of itself.

- It targets and alters the immune system
- HIV is a sexually transmitted infection (STI). It can also be spread by contact with infected blood or from mother to child during pregnancy, childbirth or breast-feeding. Without medication, it may take years before HIV weakens your immune system to the point that you have AIDS.
- There's no cure for HIV/AIDS, but medications can dramatically slow the progression of the disease. These drugs have

- AIDS is the late stage of HIV infection that occurs when the body's immune system is badly damaged because of the virus.
- In the U.S., most people with HIV do not develop AIDS because taking HIV medicine every day as prescribed stops the progression of the disease.

Symptoms

Primary infection (Acute HIV)

- Includes flu-like illness within two to four weeks after the virus enters the body. This stage may last for a few weeks

Possible signs and symptoms includes:

- Fever, Headache
- Muscle aches and joint pain
- Rash
- Sore throat and painful mouth sores
- Swollen lymph glands, mainly on the neck
- Diarrhea
- Weight loss
- Cough
- Night sweats

- About 38 million people are living with HIV around the world today with 1.8 million being newly infected in 2018, and over two-thirds of them live in Africa.
- In 2018, 770 000 people died from HIV-related causes globally according to the World Health Organisation with 1.7 million new infections
- HIV is commonest in the following groups:
- Sex workers and their clients;
- Men who have sex with men;
- People who inject drugs;
- People in prisons;
- Transgender_people.

- **Symptoms of AIDS can include:**
- blurred vision
- a dry cough
- night sweats
- white spots on the tongue or mouth
- shortness of breath, or dyspnea
- swollen glands lasting for weeks
- diarrhea, which is usually persistent or chronic
- a fever of over 100°F (37°C) that lasts for weeks
- continuous fatigue
- unintentional weight loss

Stages of HIV Infection

- **Stage 1: Acute HIV Infection (**large amount HIV in their blood. very contagious)
- **Stage 2: Chronic HIV Infection (**asymptomatic)
- **Stage 3: Acquired Immunodeficiency Syndrome (AIDS)**
- When a person with HIV takes effective treatment, the infection may never progress to stage 3

HISTORY

- HIV infection in humans came from a type of chimpanzee in Central Africa.
- The chimpanzee version of the virus (called simian immunodeficiency virus, or SIV) was probably passed to humans when humans hunted these chimpanzees for meat and came in contact with their infected blood.

- Studies show that HIV may have jumped from chimpanzees to humans as far back as the late 1800s.
- Over decades, HIV slowly spread across Africa and later into other parts of the world. We know that the virus has existed in the United States since at least the mid to late 1970s.

Treatment

- Strict adherence to antiretroviral regimens(ARV’s) to prevent secondary infections and complications.
- Use of Inhibitors
- No cure, no vaccine

Causes of HIV

- To become infected with HIV , **infected blood, semen or vaginal secretions must enter your body**.
- This can happen in several ways: By having sex. You may become infected if you have vaginal, anal or oral sex with an infected partner whose blood, semen or vaginal secretions enter your body
- when body fluids containing the virus come into contact with a permeable barrier in the body or small breaks in moist tissues of areas such as the genitals.

- **Specifically, HIV can transmit via:**
- blood
- semen
- pre-seminal fluid
- vaginal fluids
- rectal fluids
- breast milk
- The virus cannot transmit through saliva, so a person cannot contract HIV through open-mouthed kissing, for example.
- One of the main_causes of HIV transmission in the U.S. is anal or vaginal intercourse
- Another main cause of HIV transmission in the country is sharing equipment for injecting drugs

- Less commonly, HIV transmits to babies during pregnancy, childbirth, or breastfeeding.
- Also, there is a chance of transmission in blood transfusions, though the risk is extremely low when blood donations are effectively screened.
- 1 in 7 people with HIV in the U.S. do not know that they have it.

How does HIV become AIDS?

- HIV destroys CD4 T cells — white blood cells that play a large role in helping your body fight disease. As the virus destroys these cells, they use them to make copies of itself.
- The fewer CD4 T cells you have, the weaker your immune system becomes.
- AIDS is diagnosed when the CD4 T cell count falls below 200 or you have an AIDS-defining complication, such as a serious