جامعة الملك سعود
King Saud University

Lecture 6:

Virus Replication & Infectious Cycle

By

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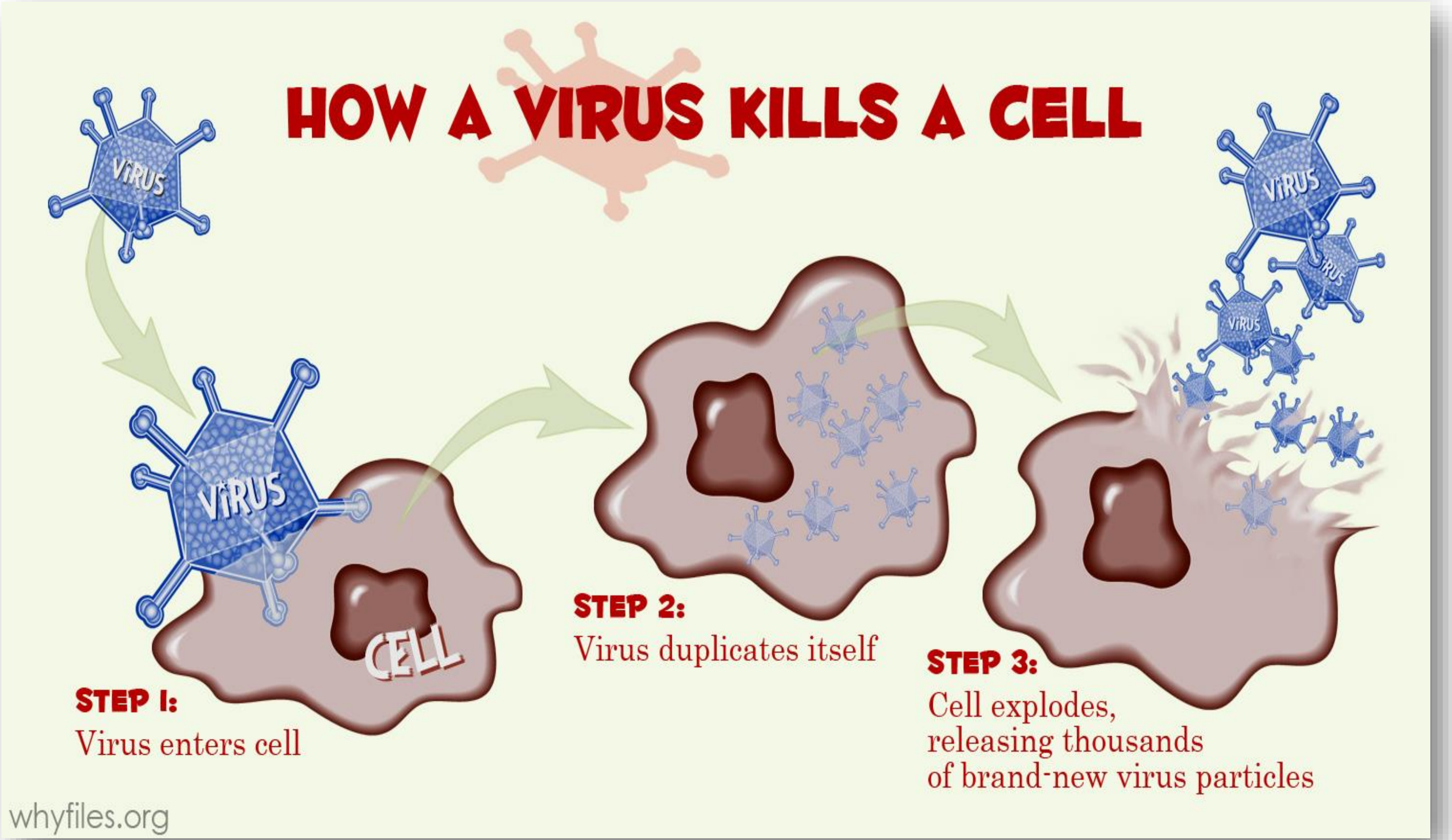
Learning Objectives

- ✓ Describe the replication (infectious) process of human and animal viruses.
- ✓ Describe unique replication characteristics of different viruses.
- ✓ Discuss human viruses and their virus-host cell interactions.

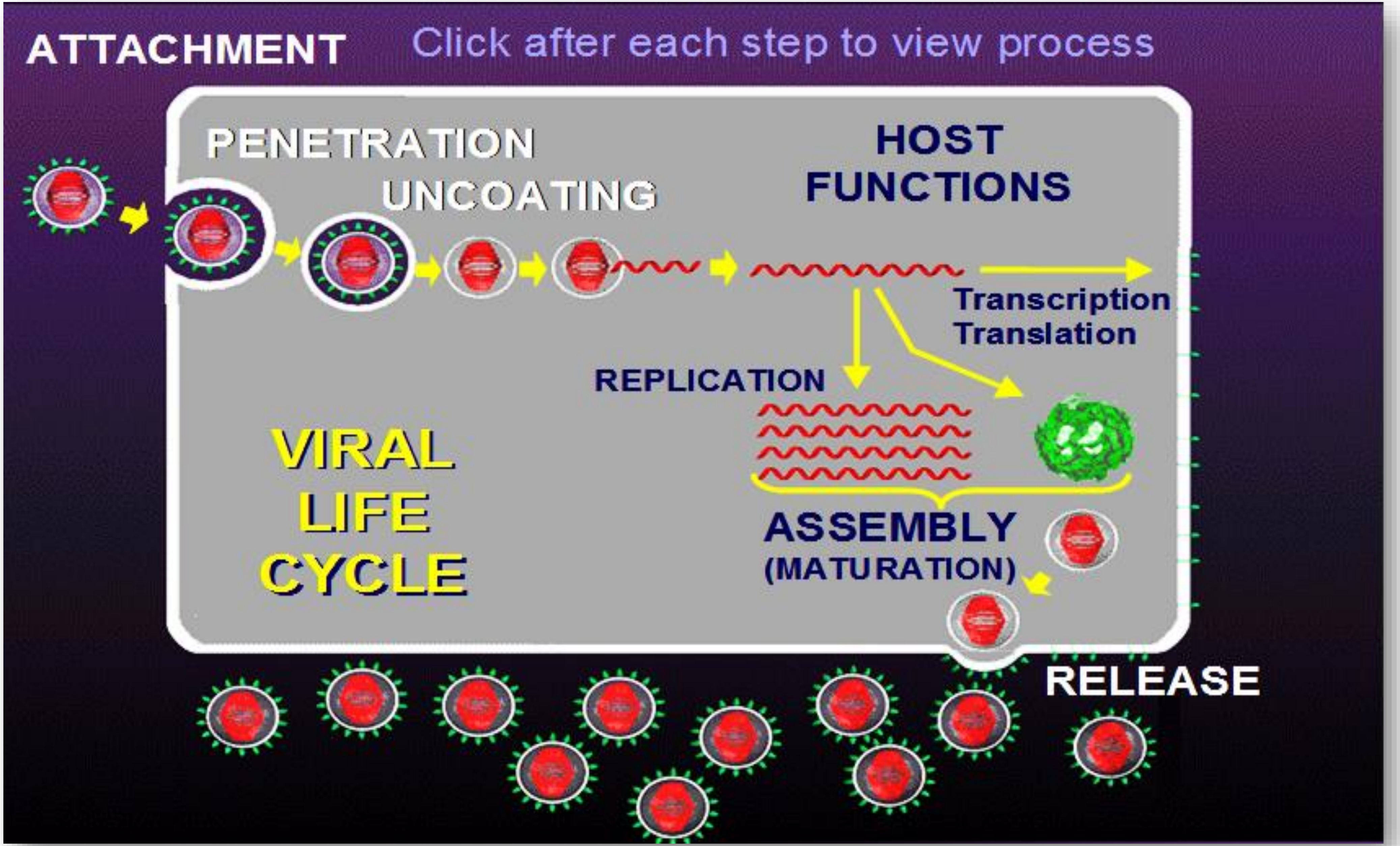
Steps of Virus Replication Cycle

1. Attachment to target cell.
2. Penetration (entry) from cell membrane.
3. Uncoating.
4. Expression (transcription and translation) of viral proteins.
5. Replication of the viral nucleic acid.
6. Virus assembly.
7. Maturation.
8. Release from infected cell.

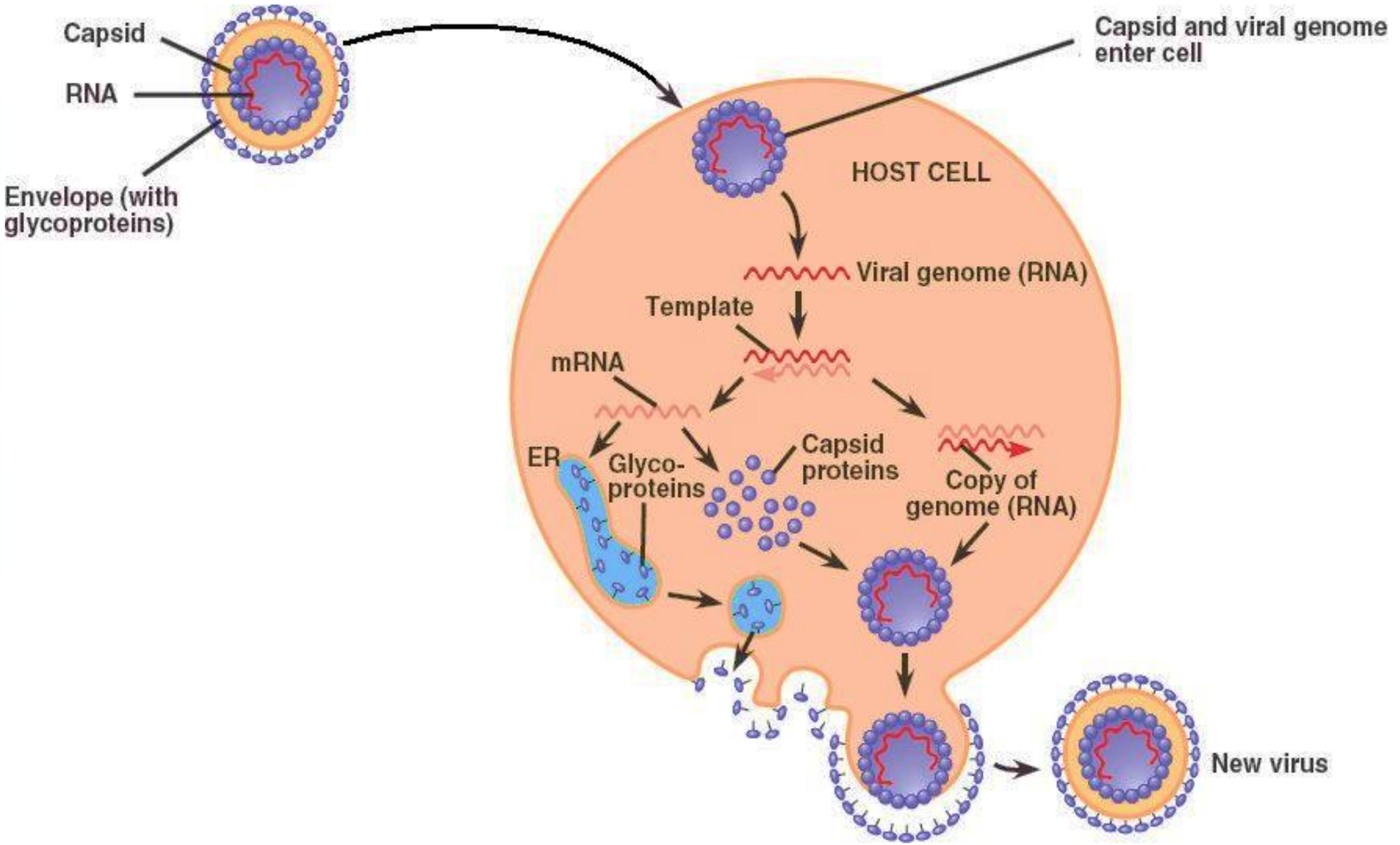
Virus-Cell Interaction



Steps of Virus Replication Cycle



Steps of Virus Replication Cycle



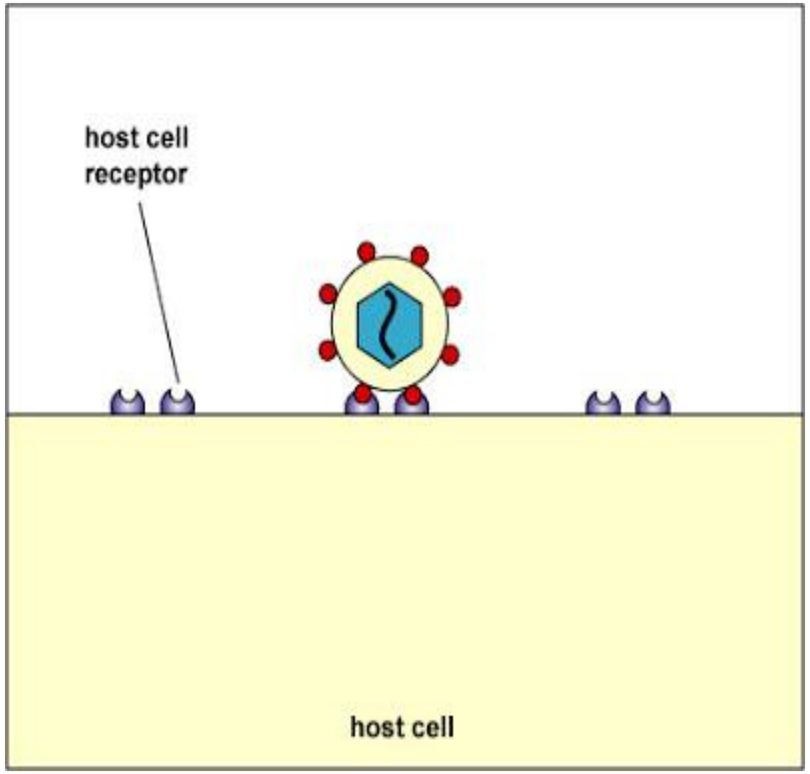
1 ➤ Attachment

To initiate replication (infection) the virus must be able to bind to target cell.

Binding occurs between:

- Ligands on the virus surface (viral attachment proteins)

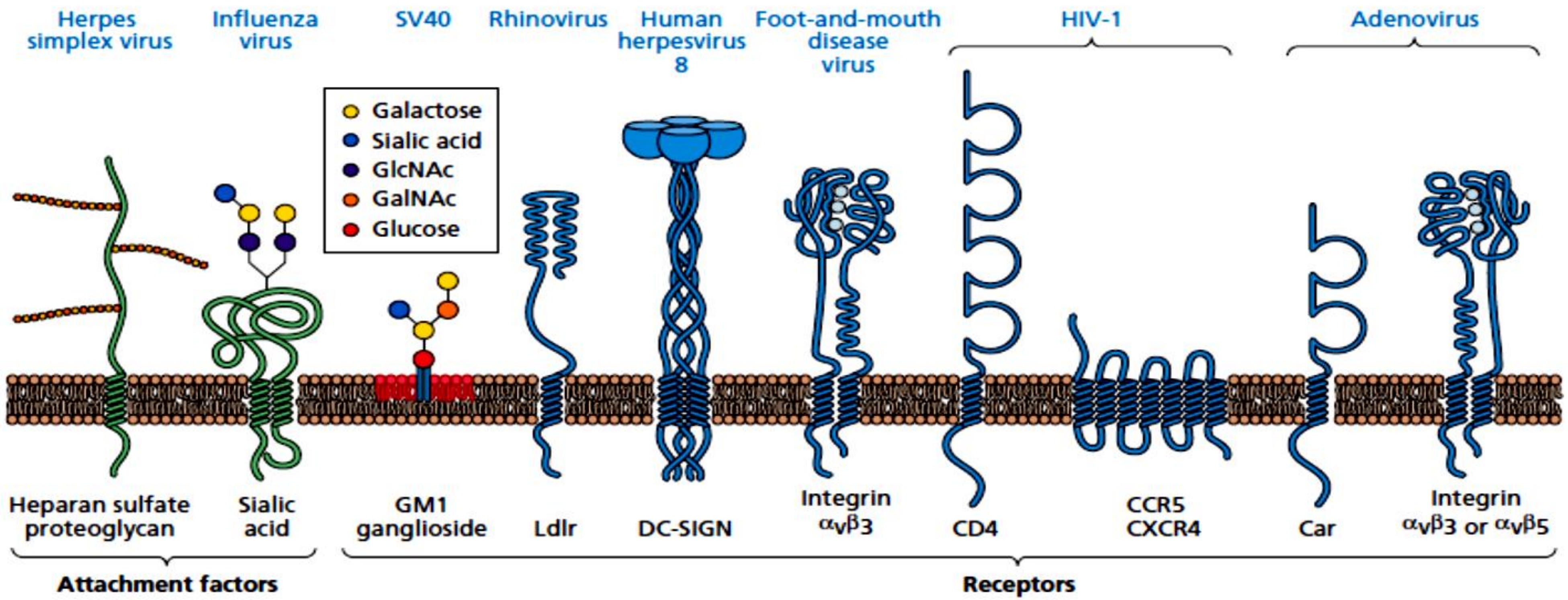
- Receptors on cell membrane



1 ➢ Attachment

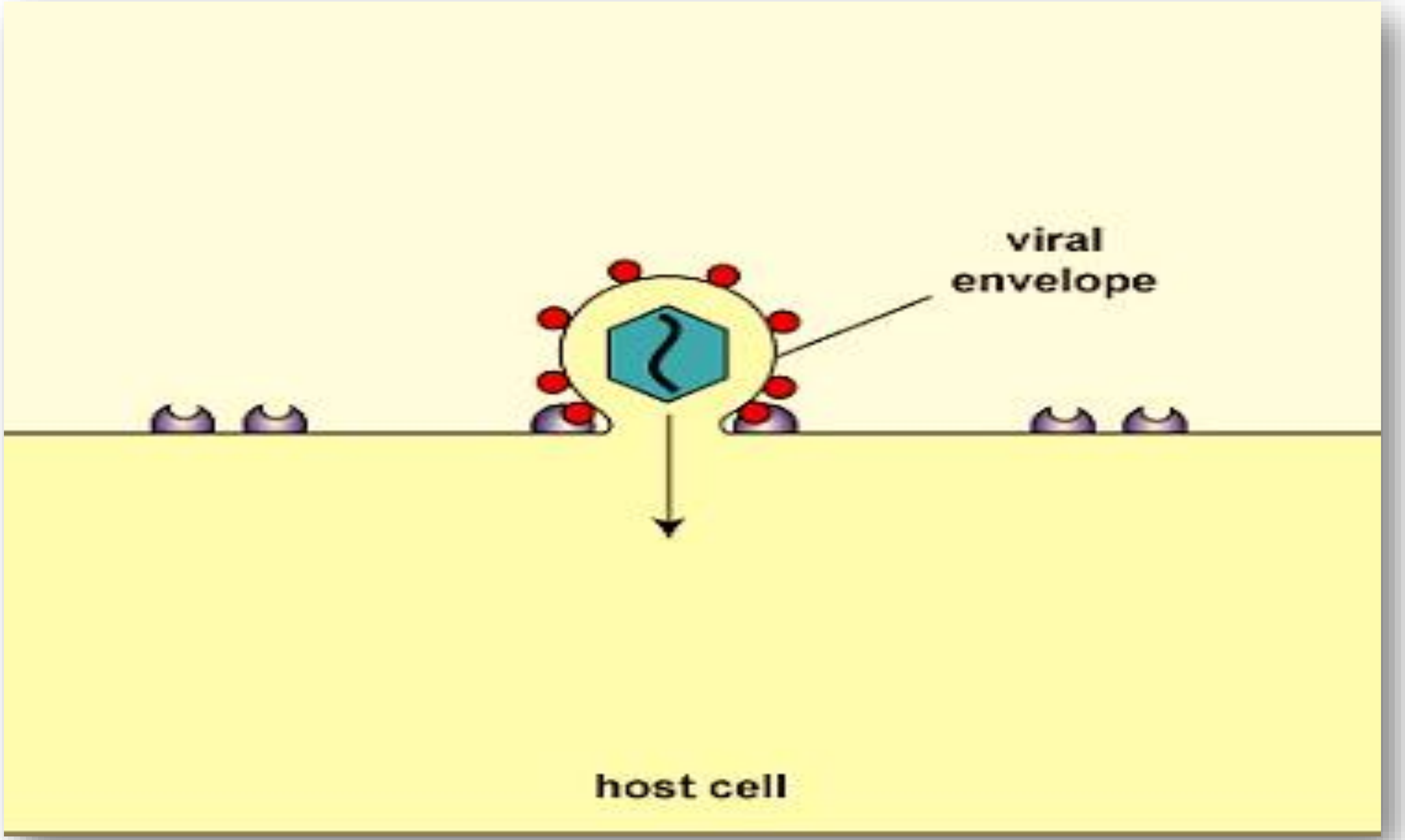
To initiate infection, the virus must be able to bind to target cell.

Binding is highly specific. So, each virus can infect only special types of cells.



2 ➢ Penetration

Following attachment, the virus should enters its genetic material into the target cell.

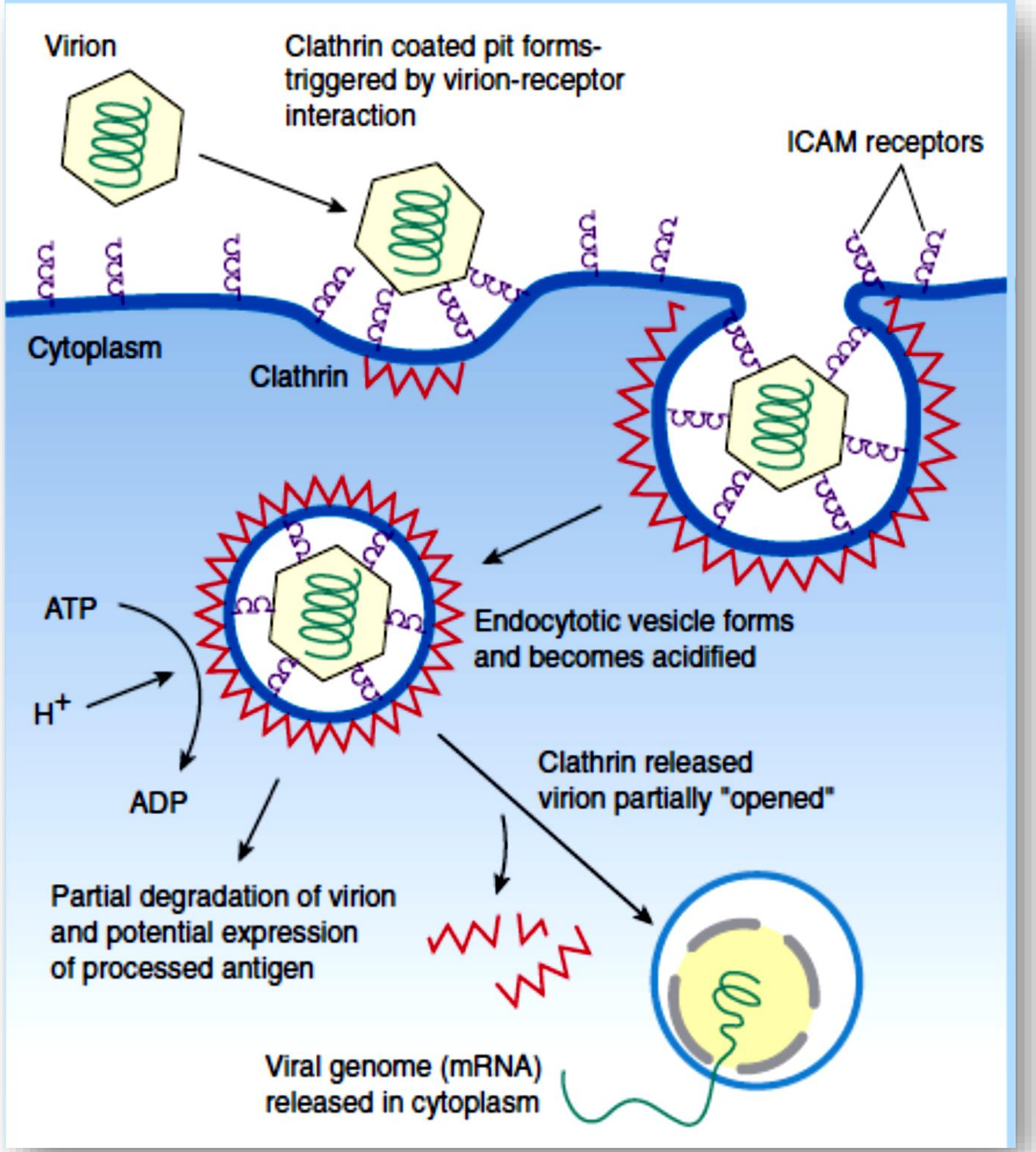


2 ➤ Penetration

A- Endocytosis:

Enveloped and naked viruses

- Receptor mediated endocytosis is a normal cell mechanism for the uptake of macromolecules.
- Many enveloped and nonenveloped viruses use this essential cell function to initiate infection.



Steps of Endocytosis:

1- Virion attachment to receptors, which cluster at clathrin-coated pits.

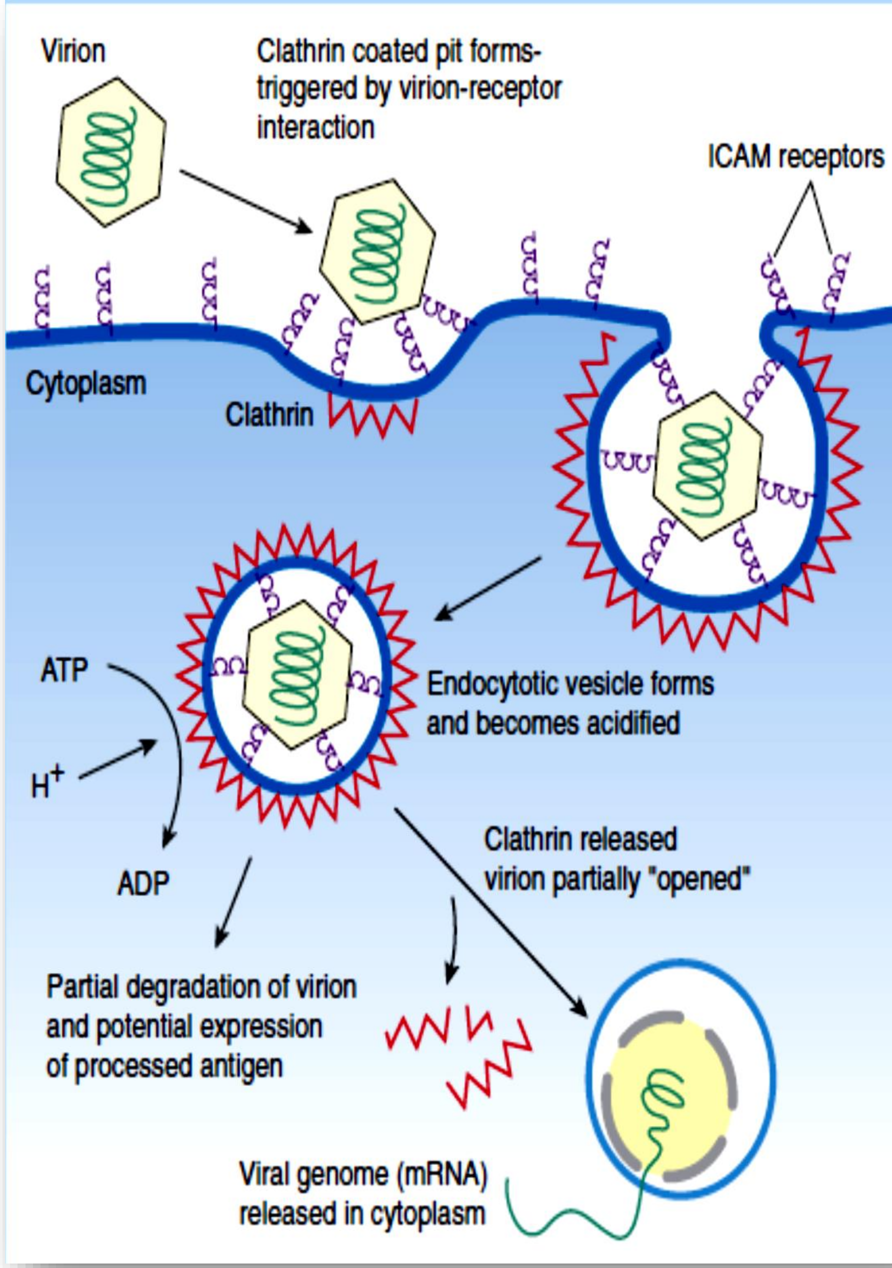
2- Endocytosis into clathrin-coated vesicles.

3- Vesicles enter the cytoplasm

4- After removal of the clathrin coat, vesicle fused with the endosome (acidic prelysosomal vacuoles).

5- Acidification within the vesicle triggers changes in virion proteins and surface structures.

6- These changes lead to the release of virus in the cytoplasm (e.g. fusion with the endonsomal membrane in influenza).

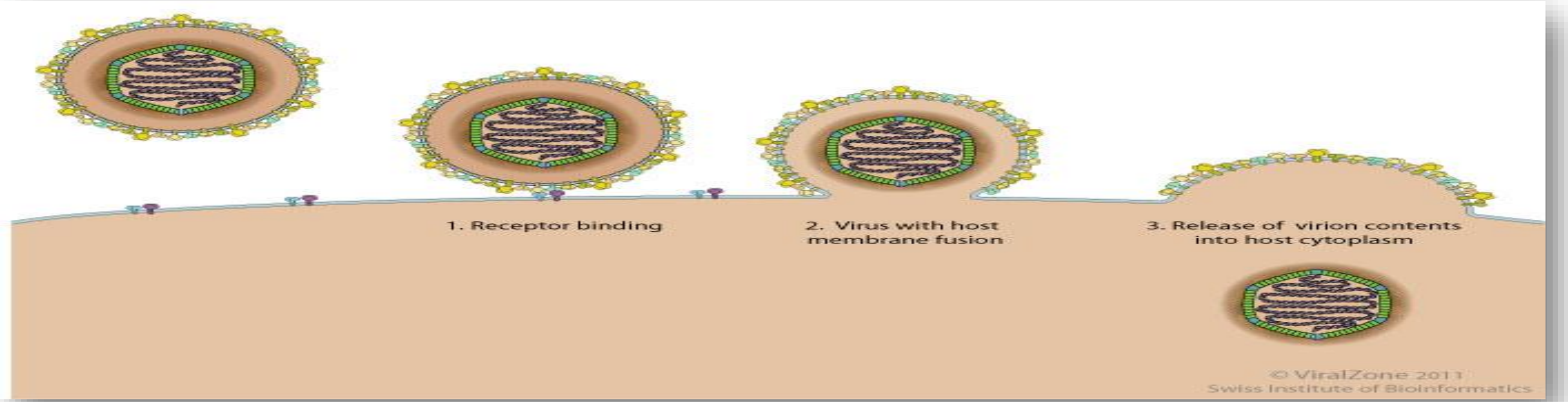


2 ➢ Penetration

Enveloped viruses

B- Fusion:

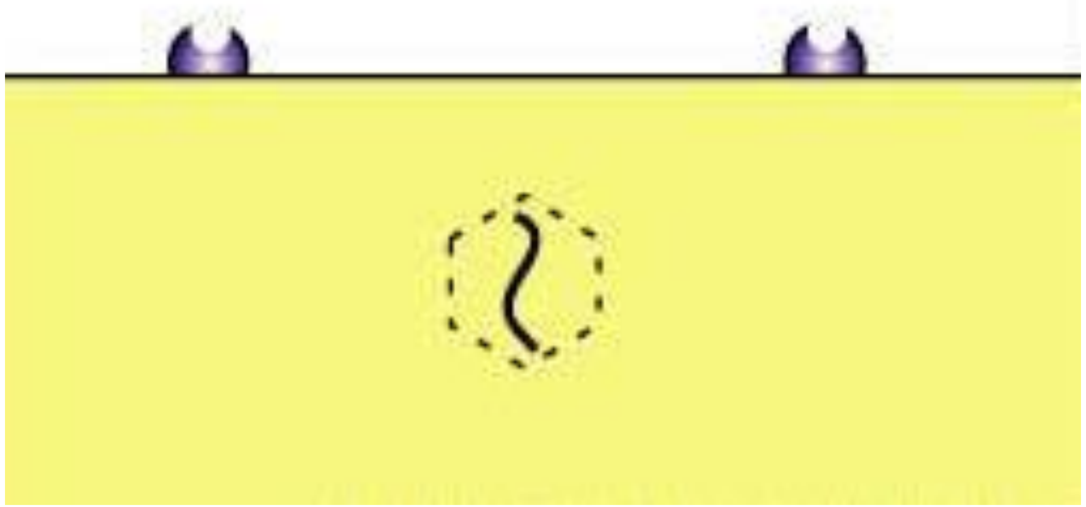
- **F (fusion) glycoprotein present in some viruses causes the envelope of these viruses to fuse directly with the plasma membrane of the cell.**
- **This allows the nucleocapsid to be released directly into the cytoplasm.e.g. Paramyxoviruses and some other enveloped viruses**

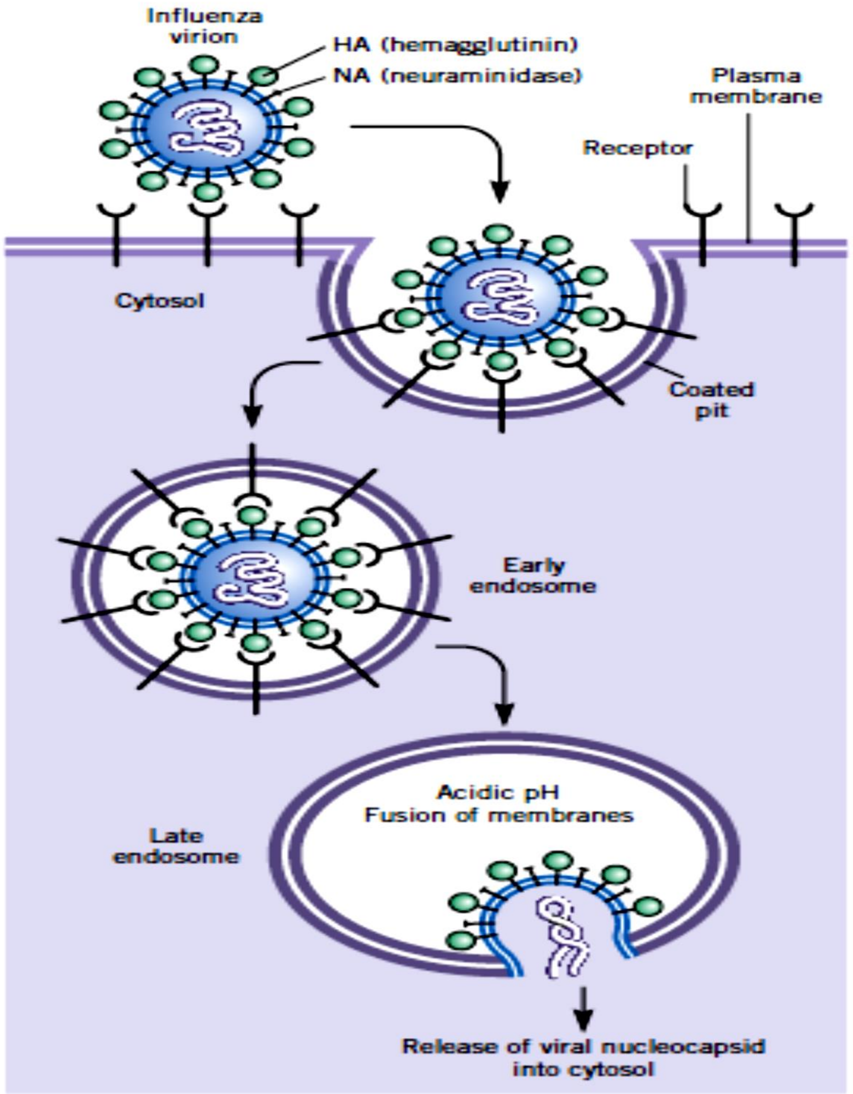


3 ➢ Uncoating

The virus coat is removed to expose viral genes for transcription and replication.

Partial





3 ➤ Uncoating

Aim:

To expose viral genes for transcription and replication

1- Complete uncoating:

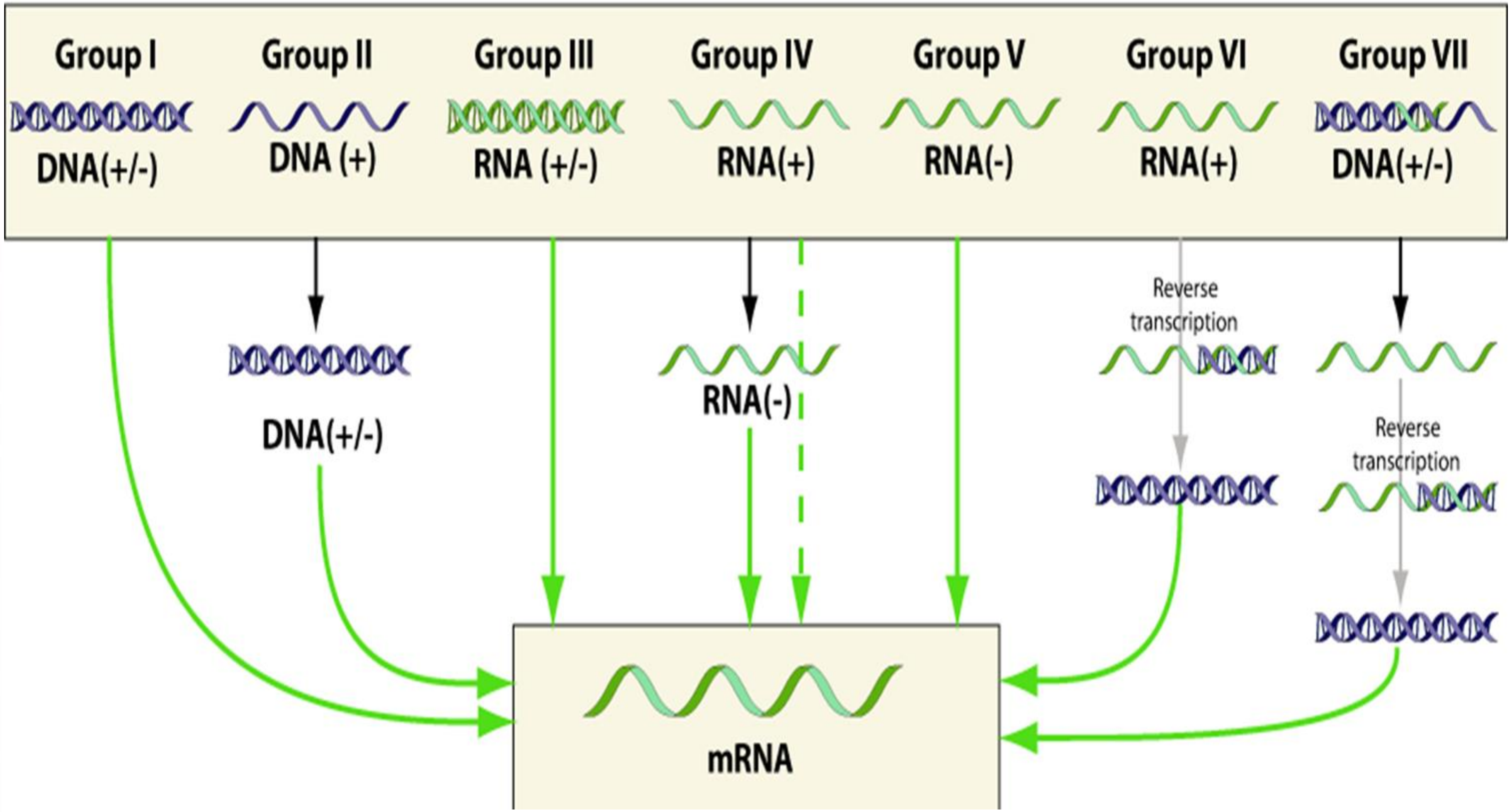
- Occurs in enveloped viruses that enter the cell by fusion with plasma or endosomal membrane.
- The nucleocapsid is discharged directly into the cytoplasm and transcription occurs directly.

2- Partial uncoating:

- Occurs with some naked viruses (e.g. reovirus).
- Only certain capsid proteins are removed and the viral genome expresses all its functions without ever being released from the virion core.

4 5 ➢ Replication Strategy

Genetic material present in the virion



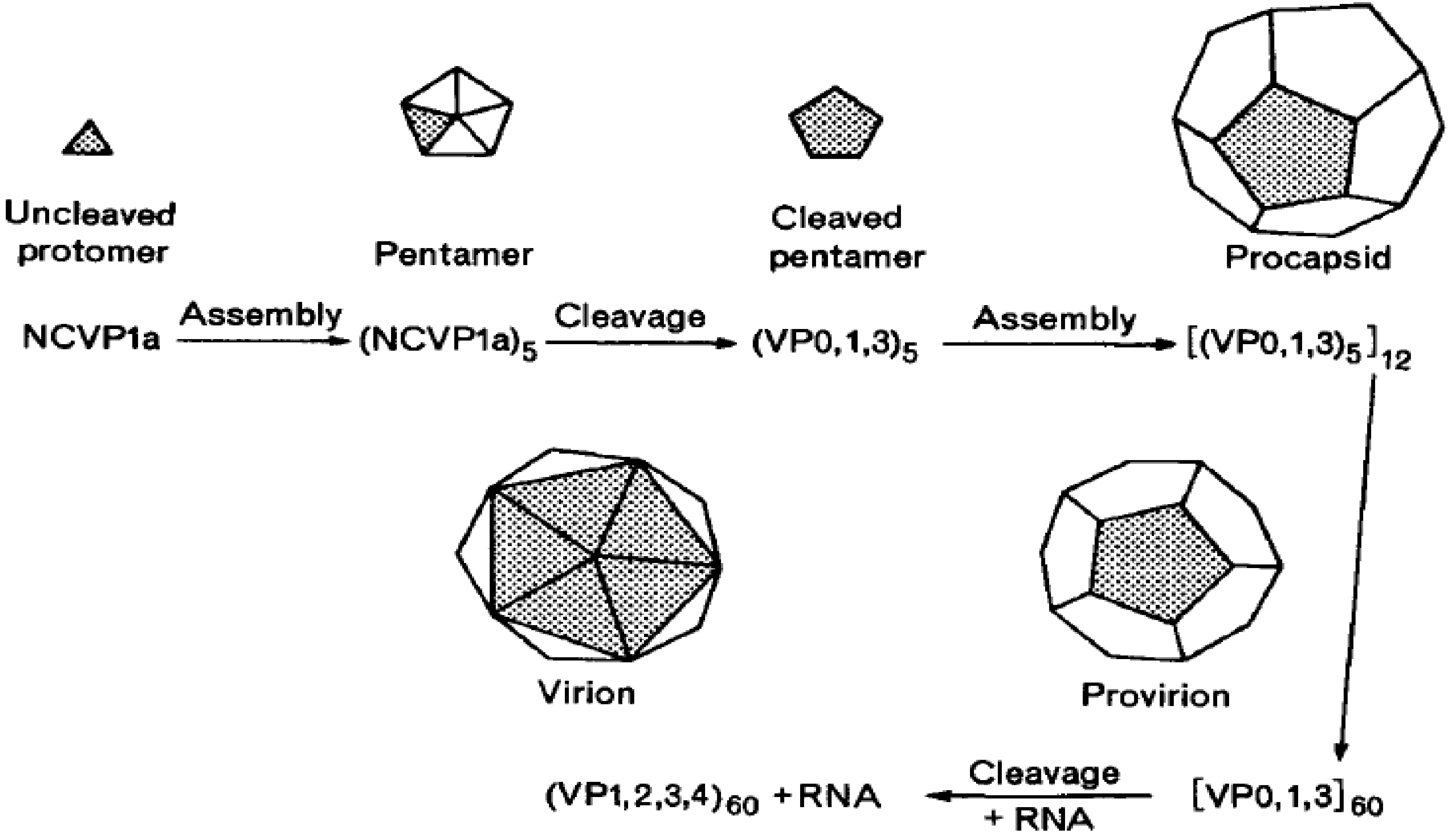
6 ➢ Virus Assembly

The viral components are organized to form complete new virus particles

1. Non-enveloped Viruses:

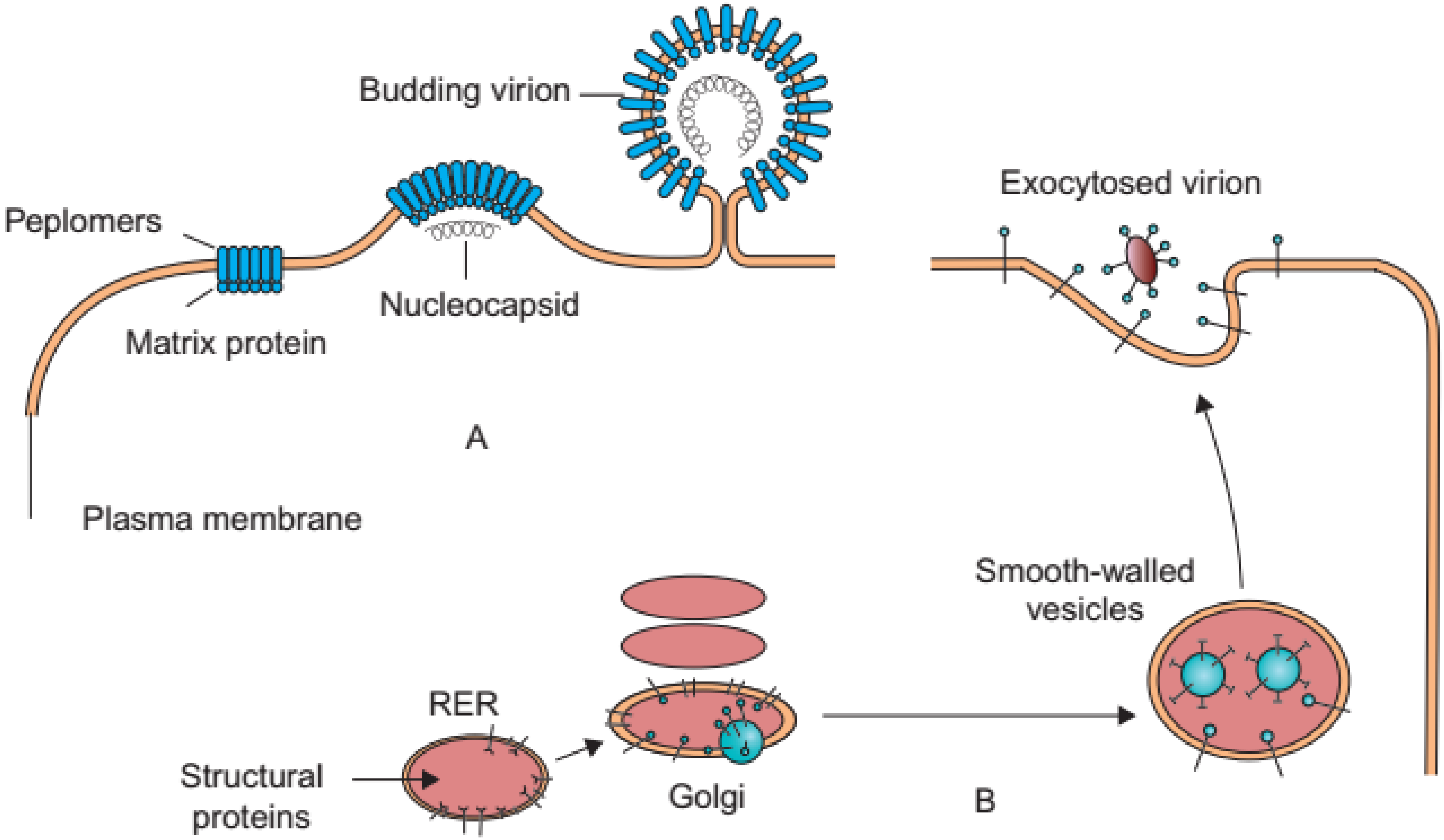
- All of them have icosahedral capsids.
- The structural components (protomers) associate spontaneously to form capsomers, which self assemble to form capsid, into which viral NA is packaged.
- Packaging of NA occurs through binding of a particular protein to a nucleotide sequence at the end of viral NA (packaging sequence); which enables the NA to enter the procapsid bound to basic core proteins.

6 ➢ Virus Assembly



6 ➢ Virus Assembly

2- Enveloped Viruses: helical or icosahedral.



7 ➢ Maturation

Changes that occur in the virus components before release from the infected cell:

- Glycosylation: Addition of carbohydrate side changes to the viral protein (e.g. most peplomeres are glycoproteins).
- Phosphorylation: Addition of phosphate group to the viral protein (e.g. phosphoprotein (P) of paramyxoviruses).
- Oligomerization: Gathering of two or more units of the viral protein (e.g. hemagglutinin of influenza virus).
- Cleavage: Splitting of a viral protein into two active fractions (e.g. fusion protein of parainfluenza viruses).

8 ➢ Virus Release

Exit of newly formed mature virus particles (virions) from infected cells.

1	2	3
Cell lysis	Budding	Exocytosis

1-Cell lysis

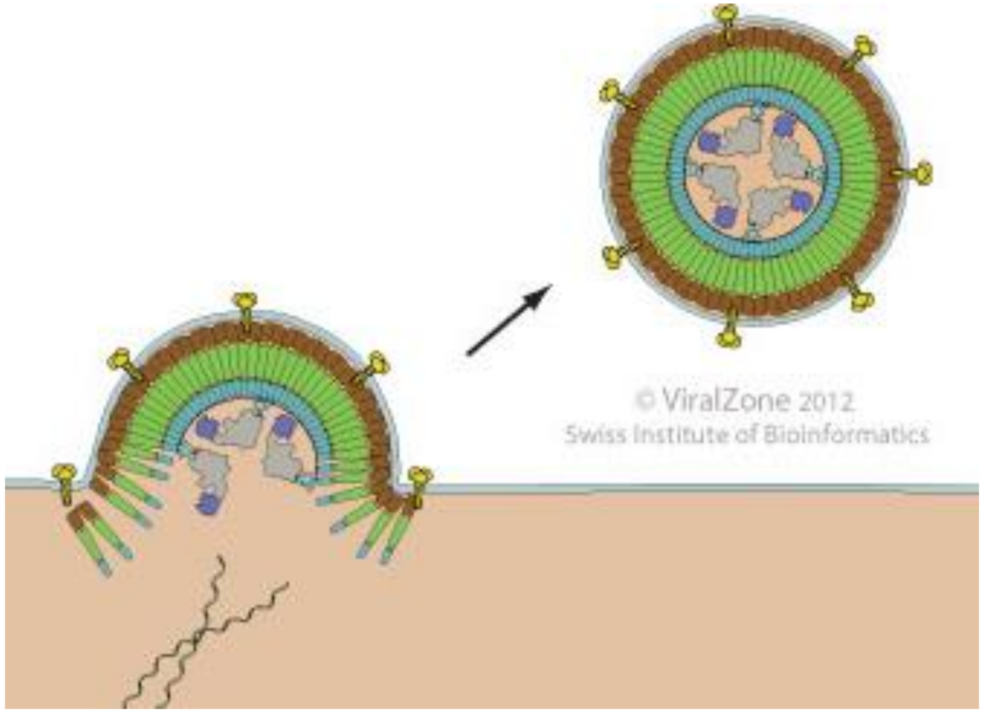
Naked viruses

8 ➢ Virus Release

Exit of newly formed mature virus particles (virions) from infected cells.

2- Budding

Occurs mostly by enveloped viruses that acquire the outer envelop from cell plasma membrane



Enveloped viruses

8 ➢ Virus Release

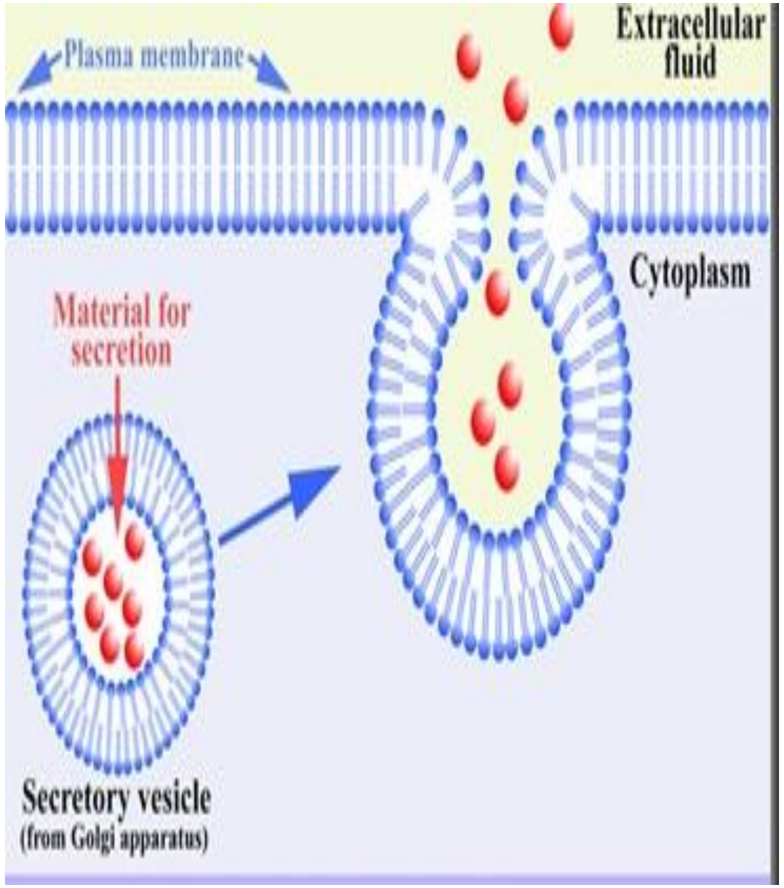
3- Exocytosis

Budding that occurs from the membranes of internal organelles such as:

1- Nuclear membrane (viruses replicate in nucleus like herpes viruses).

2- Golgi apparatus (viruses replicate in cytoplasm near Golgi membranes like (RVF).

3- Endoplasmic reticulum (many viruses like hepatitis B).



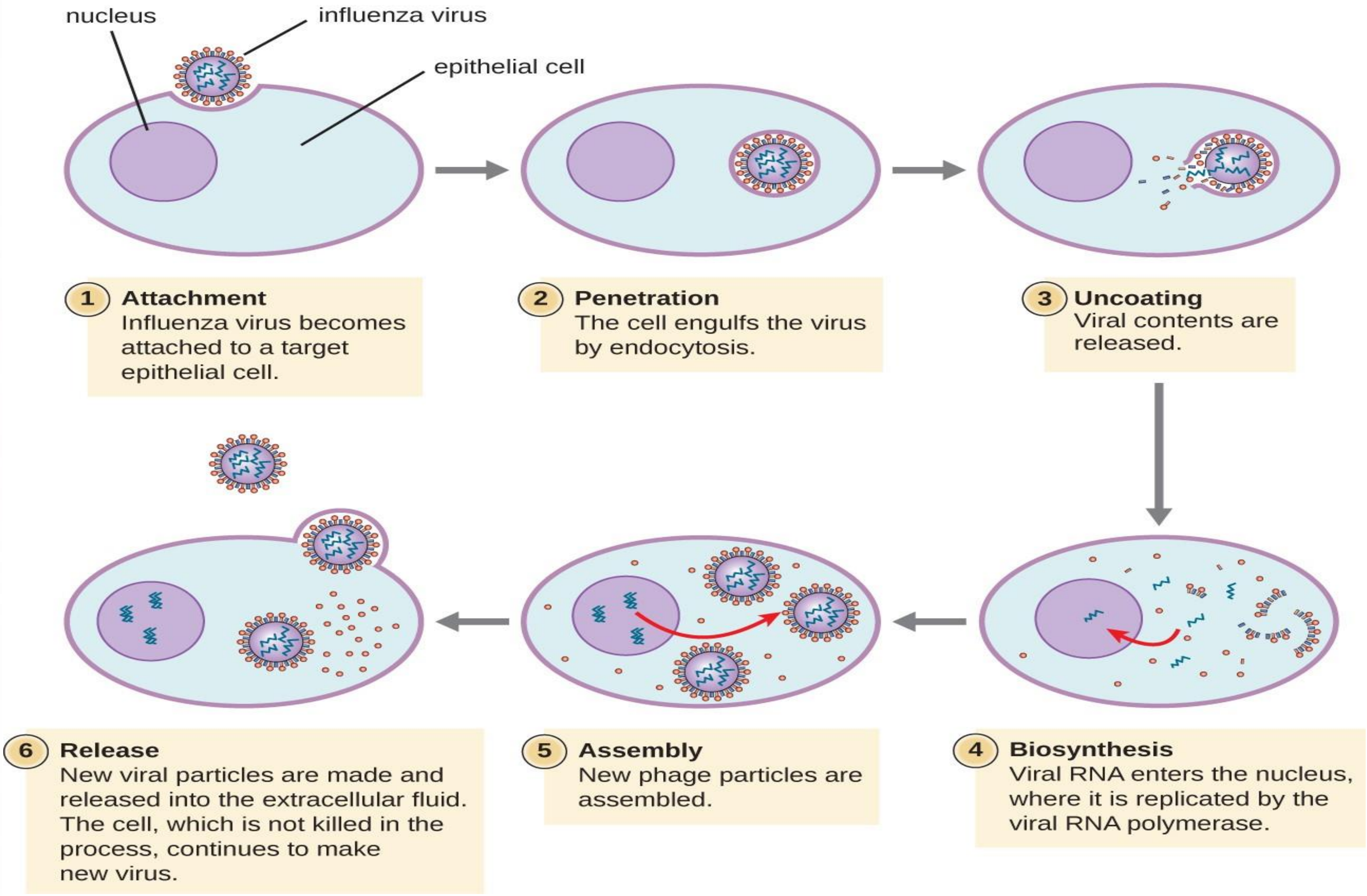
Some Enveloped viruses

8 ➢ Virus Release

3- Exocytosis

Family	Virus	Replication site	Budding location
Arteriviridae	Equine arteritis virus	ER DMV	ERGIC
Bunyaviridae	Bunyamwera virus	Golgi tubes	Golgi
Coronaviridae	Human SARS coronavirus	ER DMV	ERGIC
Flaviviridae	Dengue virus	ER spherules	ER
Hepadnaviridae	Hepatitis B virus	Cytoplasm	ER
Herpesviridae	Herpes simplex virus	Nucleus	Golgi
Poxviridae	Vaccinia virus	Viroplasm	Trans-Golgi network, or early endosome
Reoviridae	Rotavirus	Viroplasm	ER

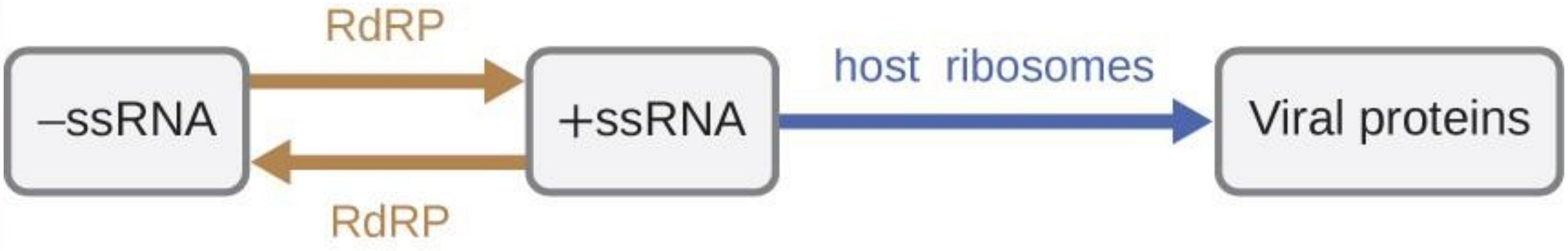
ER-Golgi intermediate compartment (ERGIC)


nucleus
influenza virus
epithelial cell
1 Attachment
Influenza virus becomes attached to a target epithelial cell.
2 Penetration
The cell engulfs the virus by endocytosis.
3 Uncoating
Viral contents are released.
4 Biosynthesis
Viral RNA enters the nucleus, where it is replicated by the viral RNA polymerase.
5 Assembly
New phage particles are assembled.
6 Release
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.

Viral replication site

- All RNA virus replication takes place within the cytoplasm <u>EXCEPT</u> the influenza virus.

- The type of the viral genome determines how the viral genome is replicated and expressed as viral proteins.



RdRP = viral RNA-dependent RNA polymerase

+ssRNA = positive (+) single strand

–ssRNA = negative (–) single-strand RNA

RNA viruses can contain +ssRNA that can be directly read by the ribosomes to synthesize viral proteins. Viruses containing–ssRNA must first use the –ssRNA as a template for the synthesis of +ssRNA before viral proteins can be synthesized.

Questions

1. What occurs after a virus attaches to a host cell in the viral replication process?
2. In the host cell, replication of RNA virus took place in--------.
3. For many viruses to penetrate the cell membrane and complete their replication inside the cell, the virus must attach to their host cells. Describe how a virus attaches to a host cell.
4. What happens in the viral replication cycle during the budding process?
5. What happens in the viral replication cycle during the maturation process?
6. What happens during the release step in the viral replication cycle?
7. What factor determines how the viral genome replicate and express as viral proteins?
8. A virus obtains its envelope during which of the following phases?
9. A positive-strand RNA virus must first be converted to ______before it can be translated.
10. Viruses containing–ssRNA must first use the –ssRNA as a template for the synthesis of_ before viral proteins can be synthesized.
11. The Viral replication (infectious) process consists of 6 main steps. Motion and provide the definition of each step.
12. What are the steps of viral endocytosis?

Today is better than yesterday


Thank
You