VIRAL REPLICATION

Course: Medical-Virology

Code: MA 423

Semester Summer

2024-2025

Outline

- Replication of viruses
- Types of Bacteriophage cycle
- Replication of RNA viruses
- Replication of DNA viruses

Viral replication and host cells

- **Viral replication is the mechanism through which viruses, small infectious agents, reproduce by generating copies of themselves inside the cells of a host organism.**
- Viruses **lack the cellular machinery** required for independent metabolism and **reproduction**.
- Viruses can replicate only inside the host cells with the help of host cell **protein-synthesizing Machinery.**
- The host cell must provide the **energy, synthetic machinery** and **the precursors for the synthesis of viral protein and nucleic acids.**

Why is the study of viral replication important?

Studying viral replication is of important for several reasons

1. Understanding disease mechanisms
2. Vaccine development
3. Antiviral drug development
4. Biotechnology and gene therapy

General steps of viral replication

1. **Attachment:** Viral proteins on the capsid or envelope interact with specific receptors on the host cellular surface.
2. **Entry: main ways are**

    1. Endocytosis for the naked viruses.
    2. Fusion (envelope fusion) for the enveloped viruses.

3. **Uncoating:** The viral capsid is removed and degraded by viral enzymes.

4. **Replication and Synthesis: The viral genetic material is used to produce messenger RNA (mRNA).**

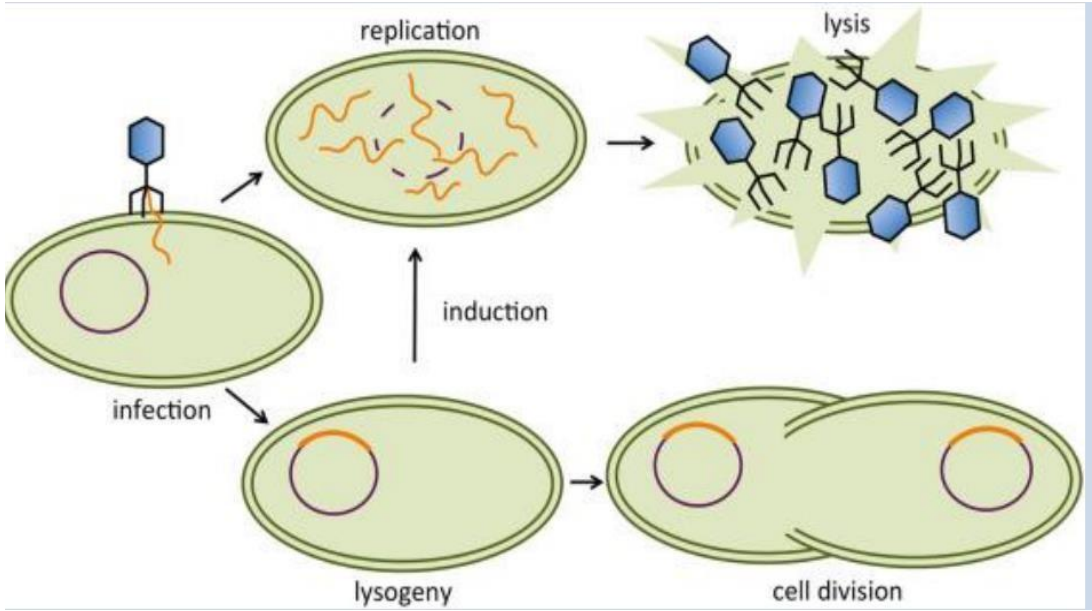
A- Translation: The mRNA is used to synthesize viral proteins (Capsid).
B- Genome Replication: The viral genetic material is copied to create many new copies of the viral genome.

5. Assembly: After synthesis of new viral genome and proteins, viral proteins (capsid) are packaged with newly replicated viral genome into new virions that are ready for release from the host cell.

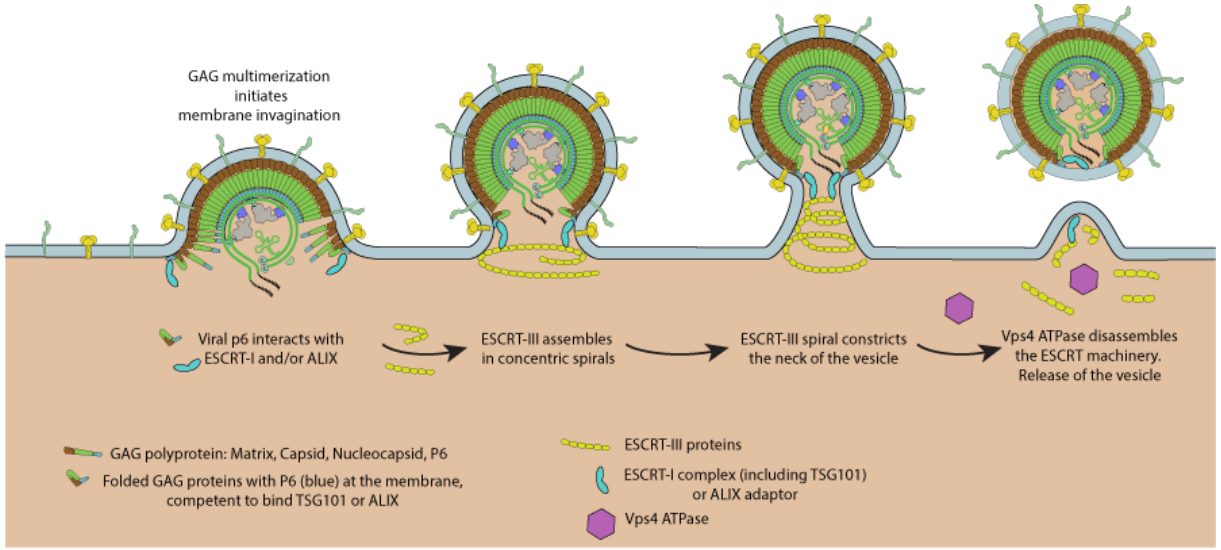
- **Virion release:** There are two methods of viral release: **lysis** or **budding**.

1- Lysis results in the death of an infected host cell, these types of viruses are referred to as **cytolytic**.
2- Budding:
Enveloped viruses, such as influenza A virus, are typically released from the host cell by budding.

It is this process that results in the acquisition of the viral phospholipid envelope. These types of virus do not usually kill the infected cell and are termed **cytopathic viruses**.



Viral release by cell lysis



Enveloped Viral Release

Examples Viral replication

Viruses employ various methods of replication, which are often categorized based on their genetic material (DNA or RNA) and the strategies they use. Here are the primary methods of viral replication

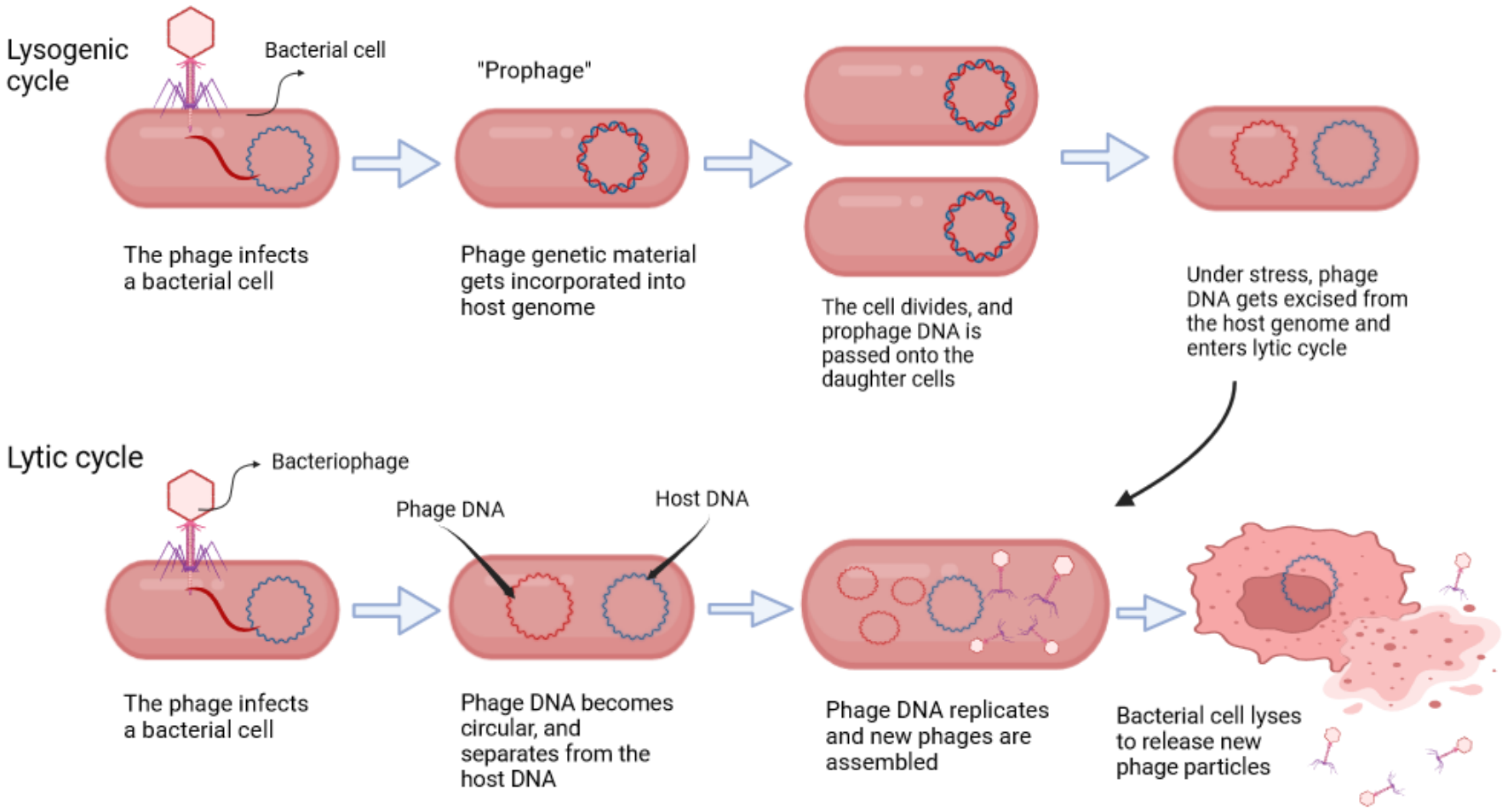
1. Bacteriophage Replication
2. Replication of RNA viruses
3. Replication of DNA viruses

Lytic Replication

Lytic replication includes the following steps

1. **Attachment:** The virus (**bacteriophage**) attaches to the surface of the host bacterial cell. This attachment is often mediated by specific **viral proteins on the phage's tail** that interact with **receptors** on the bacterial cell wall or membrane.
2. **Penetration (Entry):** genome (DNA or RNA according to the phage) enters host cell and **leaving capsid outside**.
3. **Replication:** viral components produced
4. **Assembly:** Newly synthesized viral components come together within the host cell to form complete viral particles (virions).
5. **Lysis (Release):** The host cell is eventually ruptured, or lysed, by the newly assembled virions. The released virions can then go on to infect other host cells and continue the cycle

Lytic Replication



Lysogeny: the silent virus infection

The process of lysogeny involves several key steps

1. **Attachment.** Bacteriophage attaches to bacterial cell.
2. **Entry.** Bacteriophage injects DNA into bacterial cell.
3. **Integration.**

- Once inside the host cell, the phage's DNA integrates into the host cell's DNA.
- This integration is catalyzed by specific enzymes, such as **integrase**, and results in the formation of a **prophage**.
- The prophage becomes part of the host cell's genetic material and is replicated along with the host genome during cell division.

4. **Replication**
5. **Assembly**
6. **Lysis (Release)**

- **Prophage** is the genetic material of a bacteriophage, incorporated into the genome of a bacterium and able to produce phages if specifically activated.

- **What is the difference between lytic and lysogenic cycle?**

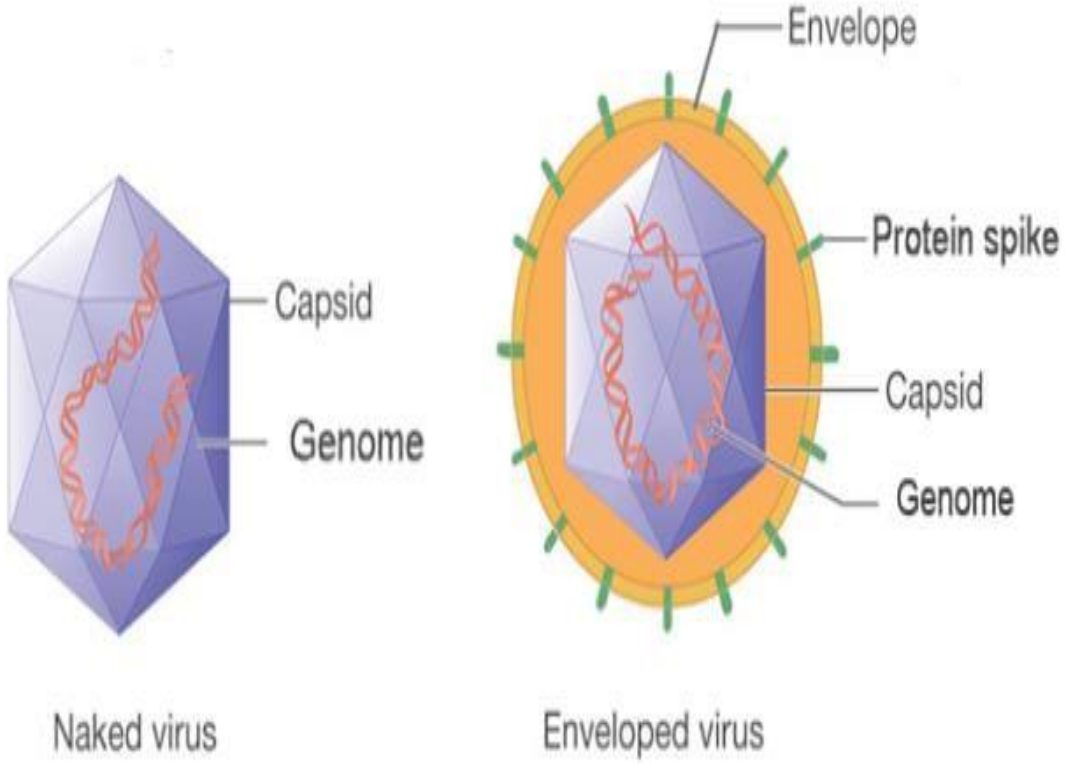
- The lytic cycle is a direct, destructive replication, whereas the lysogenic cycle is a more delayed, integrated form of replication that can switch to the lytic cycle.

Baltimore classification

According to the Baltimore classification, viruses are divided into seven groups (classes) based on the way of synthesizing their mRNAs:

1. dsDNA viruses "double strand DNA".
2. ssDNA viruses "single strand DNA".
3. dsRNA viruses "double strand RNA".
4. (+) sense ssRNA viruses (codes directly for protein).
5. (-) sense ssRNA viruses.
6. RNA reverse transcribing viruses.
7. DNA reverse transcribing viruses.

Overall, **DNA viruses** are in **groups I and II**, **RNA viruses** are in **groups III, IV, and V**, and **reverse transcribing viruses** are in groups **VI and VII**.



Replication of RNA viruses

General steps in the multiplication of RNA viruses:

1. **Attachment:** The virus attaches to specific receptors on the surface of the host cell.
2. **Entry:** Depending on the virus, it can enter the host cell through **endocytosis**, **direct membrane fusion**, or other mechanisms.
3. **Uncoating:** The viral genetic material is released from its protective protein coat (capsid) inside the host cell.

4. Translation:

- The viral RNA serves as a template for the synthesis of viral proteins, including **replicases** (enzymes responsible for replicating the viral RNA).
- Host ribosomes are used for translation

Replication of RNA viruses

6. Replication of viral genome:

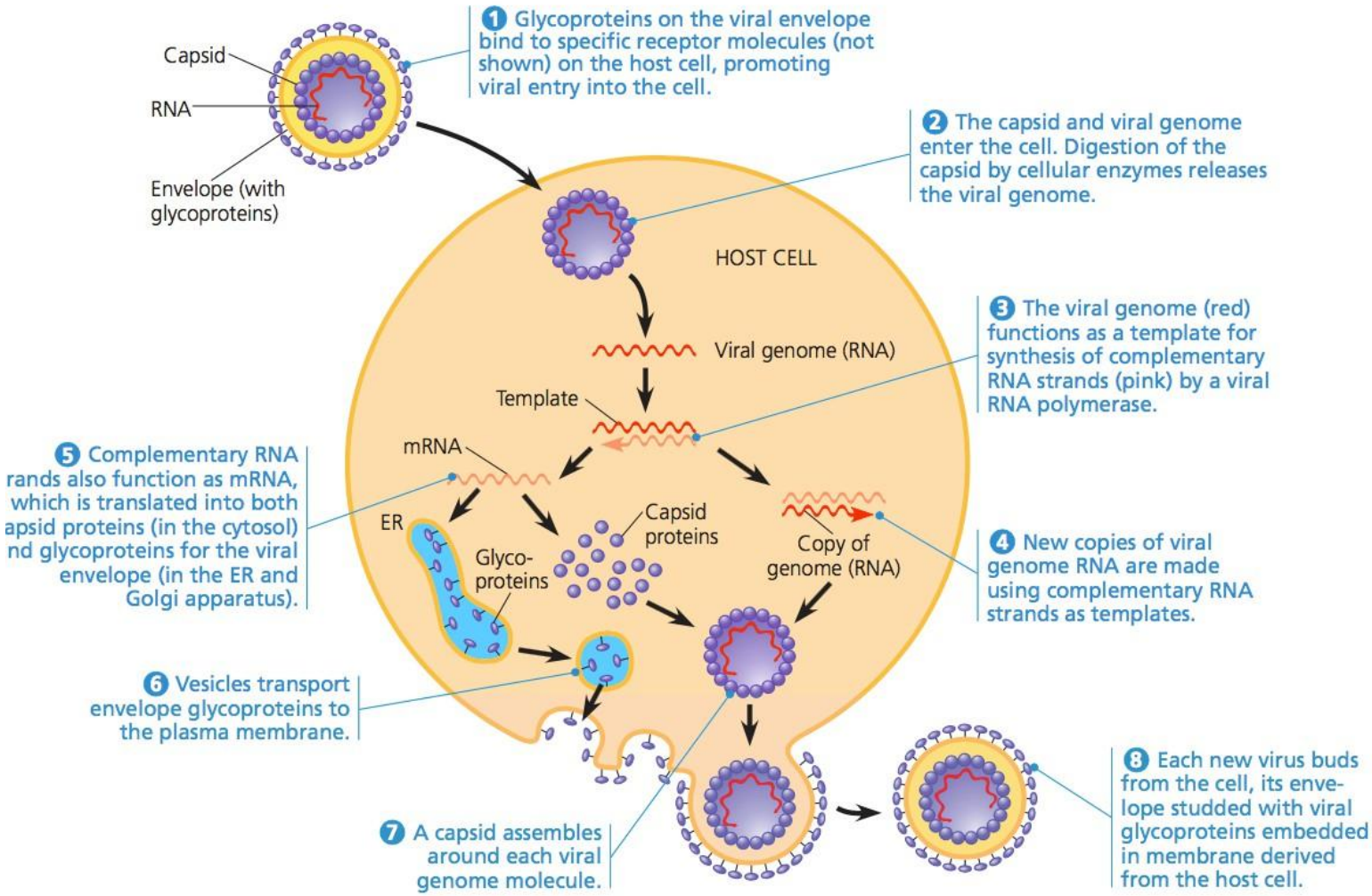
- The viral RNA is copied to produce more viral RNA molecules.
- The replicase proteins generated from the viral RNA catalyze the replication of the viral genome.

7. Assembly of new virions:

8. Budding and release: The newly formed virions are released from the host cell to infect other cells.

- Some RNA viruses, like **enveloped viruses**, exit the host cell via **budding**, where they acquire a lipid envelope from the host cell membrane.
- Others, like **non-enveloped RNA viruses,** can cause cell lysis (cell destruction) to release virions.

Replication of RNA viruses



Replication of DNA viruses

General steps in the multiplication of DNA viruses:

1. **Attachment:** The virus attaches to specific receptors on the surface of the host cell.
2. **Entry:** After attachment, the virus may enter the host cell through various mechanisms, such as
3. **Uncoating:** Once inside the host cell, the viral DNA is released from the protective protein coat (capsid) or envelope.
4. **Replication of DNA:**

- The viral DNA serves as a template for the replication of new DNA.
- The specific enzymes and mechanisms used for replication can vary among different viruses.
- In many cases, the virus encodes its own **DNA polymerase** or **helicase enzymes** for replication**.**

Replication of DNA viruses

General steps in the multiplication of DNA viruses:

6. Transcription: Viral genes are transcribed into messenger RNA (mRNA) using the host cell's transcription machinery. These viral mRNAs are then used for the translation of viral proteins

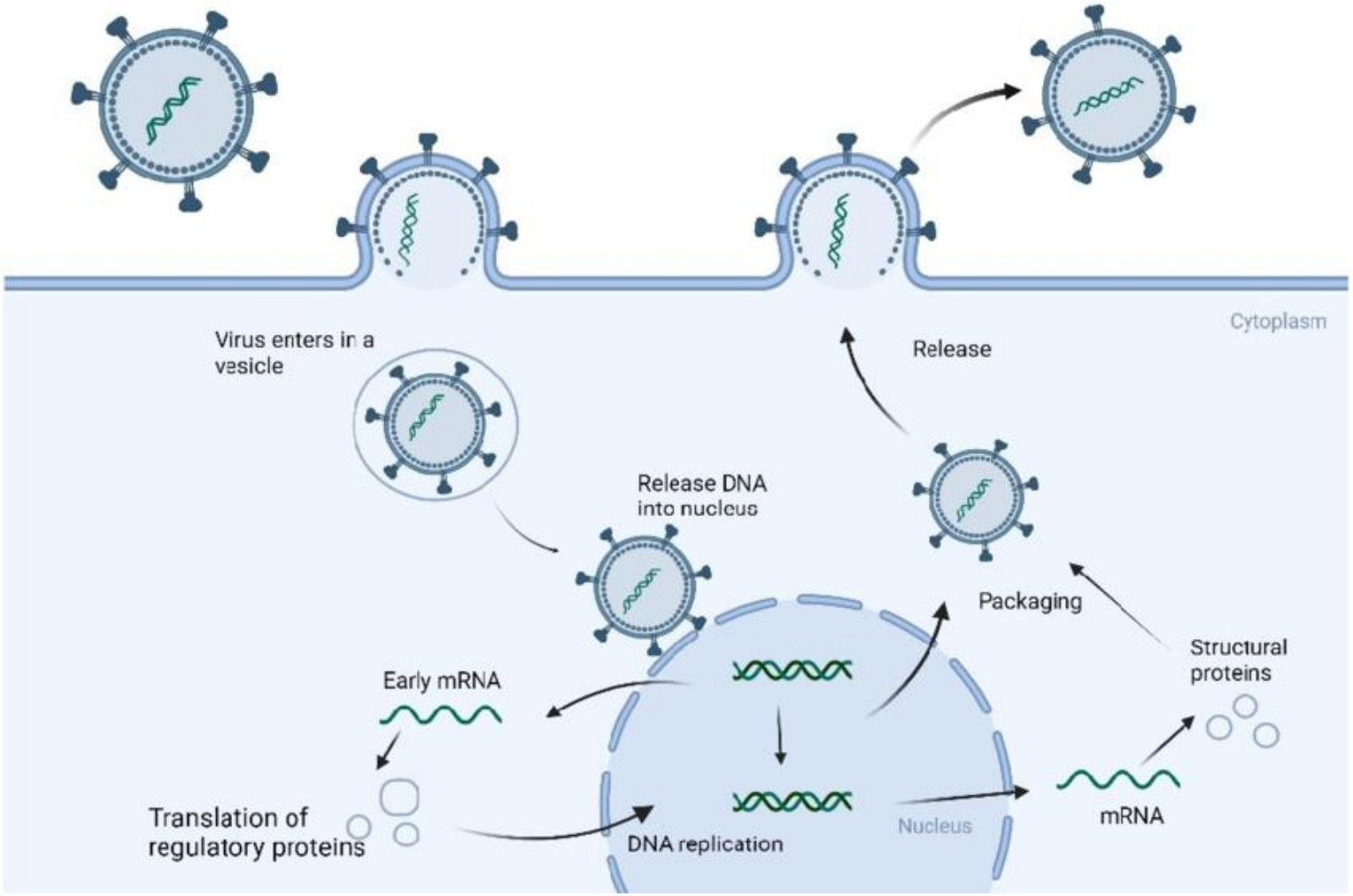
7. Translation:

- The viral proteins are synthesized using the host cell's ribosomes and translation machinery.
- These proteins include components necessary for DNA replication and the assembly of new viral particles.

8. DNA Packaging and Assembly: Newly replicated viral DNA, along with synthesized viral proteins and other components, are assembled to form new viral particles.

9. Release: The newly formed virions are released from the host cell to infect other cells. The mechanisms of release can vary, such as budding or cell lysis.

Replication of DNA viruses



What is the difference between DNA and RNA virus replication?

- DNA viruses must first transcribe viral DNA into mRNA to synthesize proteins, whereas some RNA viruses (positive-strand) can use their RNA directly as mRNA for protein synthesis, while others (negative-strand) must first be transcribed into mRNA

Replication of viruses

The replication cycle can be summarized into

1. **Cell infection step:** this step consists of attachment, penetration and uncoating.
2. **mRNA production step:** this step includes nucleic acid transcription to produce mRNA
3. **Viral protein synthesis step:** this step includes translation of mRNA to virus-specific proteins
4. **Genome replication step:** this step includes production of new viral nucleic acid (replication)
5. **Virus assembly and release** of new virions: in this step the new virus produces and releases

References (in APA style)

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