# Viral replication

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Dr. Sulaiman Mahmoud Bani Abdel-Rahman

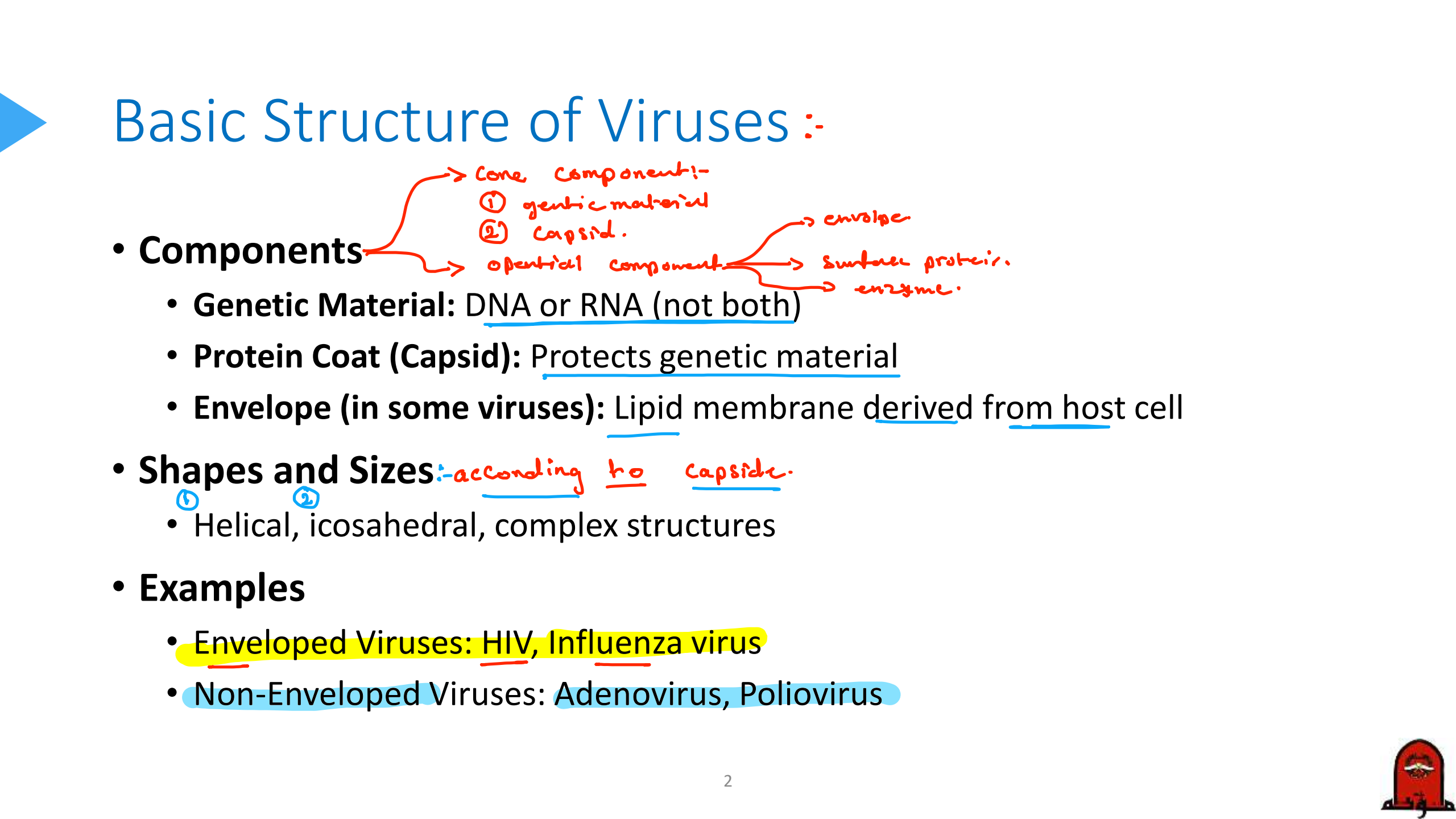
Bachelor degree in Medicine and Surgery - Mutah university

MSC Medical Microbiology – University of Manchester

PhD Medical Virology - University of Manchester

# Basic Structure of Viruses :-

- **Components**
  - **Genetic Material:** DNA or RNA (not both)
  - **Protein Coat (Capsid):** Protects genetic material
  - **Envelope (in some viruses):** Lipid membrane derived from host cell
- **Shapes and Sizes**
  - Helical, icosahedral, complex structures
- **Examples**
  - Enveloped Viruses: HIV, Influenza virus
  - Non-Enveloped Viruses: Adenovirus, Poliovirus



# Viral Classification = classified into 7 Groups.

- **Based on Genetic Material**
  - DNA Viruses
  - RNA Viruses
- **Based on Replication Strategy**
  - Baltimore Classification (detailed later)

1- what're the genral steps of replication ?

2- what does the viruse action site depend on ?

⇒ The site of viruse action depend on :-
a- The protein -> viruse.
b- The receptor on host cell surface.

# Overview of Viral Replication Steps

-> most viruses share these steps.

- **General Steps:**
  1. Attachment (Adsorption)
  2. Penetration (Entry) ⇒ it depened if it b- enrolped / non- enrolped vinues.
  3. Uncoating
  4. Synthesis (Replication and Protein Production) ⇒ need to synthize protein + genic material. (a- protein, b- genic material)
  5. Assembly (Maturation) ⇒ assembly togather.
  6. Release (Egress) ⇒ Release.

-> and releasing of genic material.

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  5. Assembly (Maturation)
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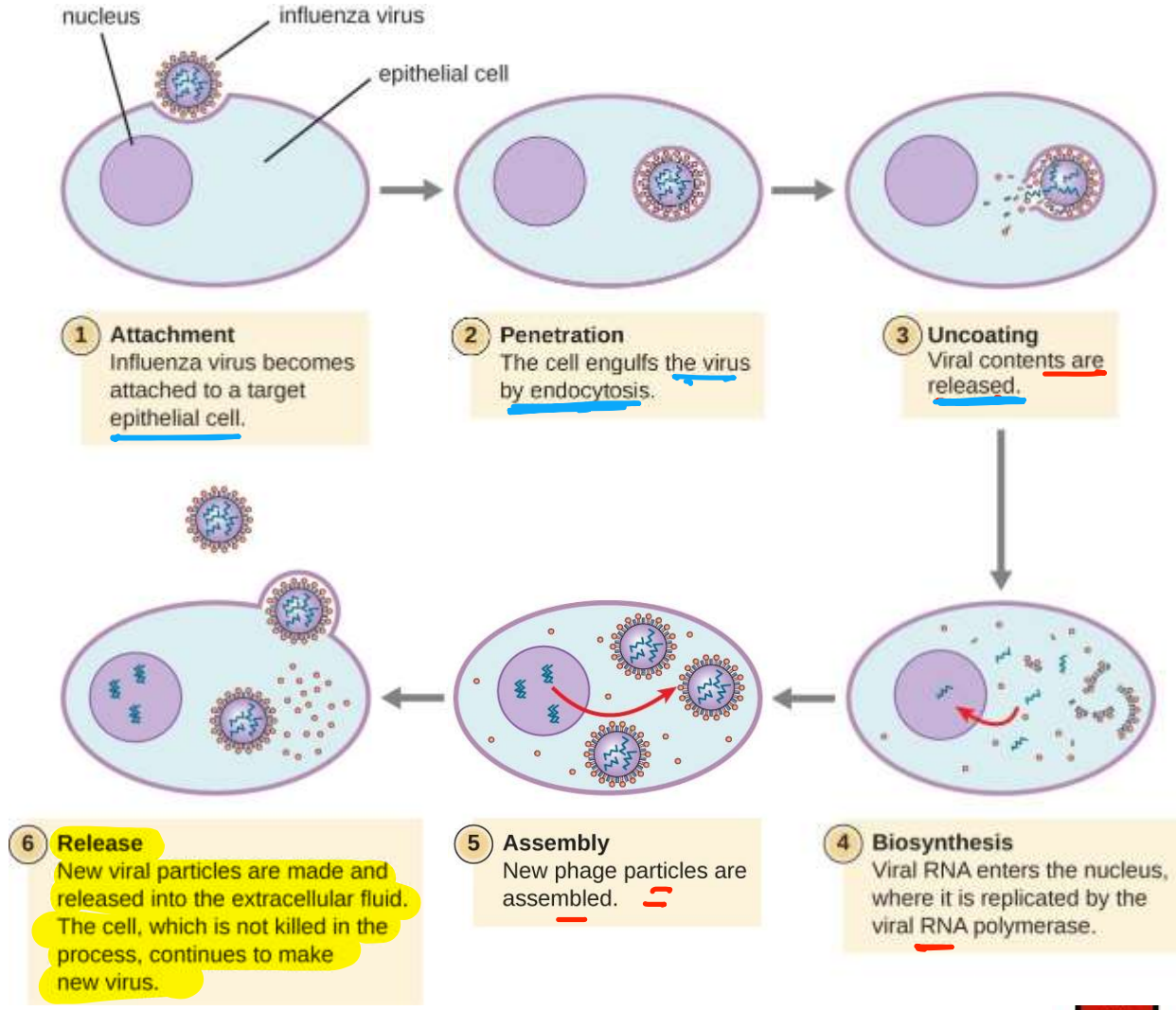


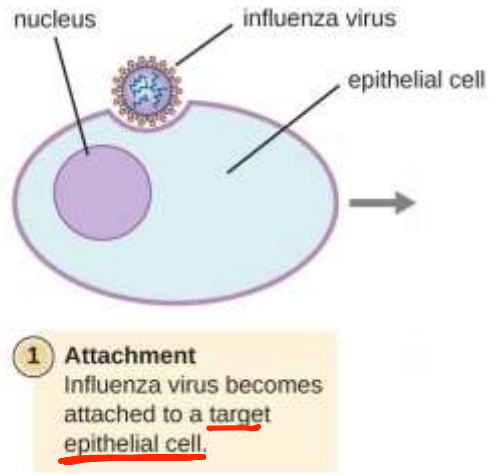
1-what's the machanizm ? 2-what're the type of receptor host cell ? 3- Give an example ?

# Viral Replication Steps

## Step 1 - Attachment (Adsorption)

- **Mechanism:**
  - Viral surface proteins (ligands) bind to specific receptors on the host cell membrane. ex, influnze → hemoglotamin.
  - The receptors on cells are protein or carbohydrate or lipid components of the cell surface.
- **Specificity:**
  - Determines host range and tissue tropism. [Receptor on host cell]
  - Cells without the appropriate receptors are not susceptible to the virus.
- **Examples:**
  - **HIV:** gp120 binds to CD4 receptors on T-helper cells. [occur with immune suppresion].
  - **Influenza Virus:** Hemagglutinin binds to sialic acid residues on respiratory epithelial cells.

→ bind to receptor on epi cell on respiratory.

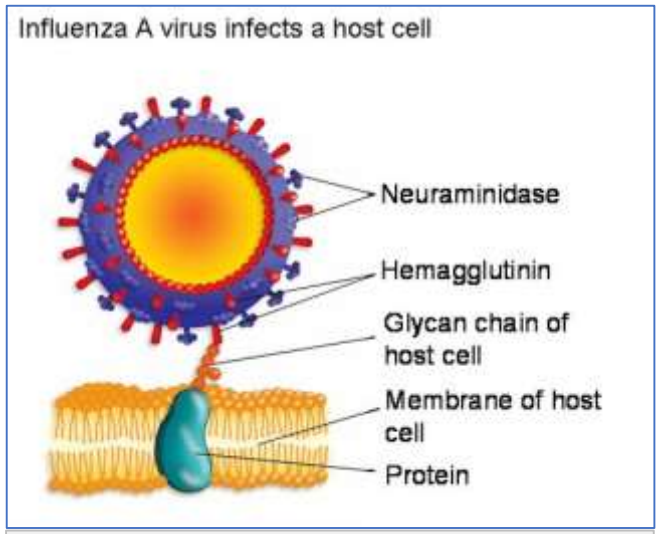


# Viral Replication Steps

## Step 1 - Attachment (Adsorption) - Examples

immune suppressed

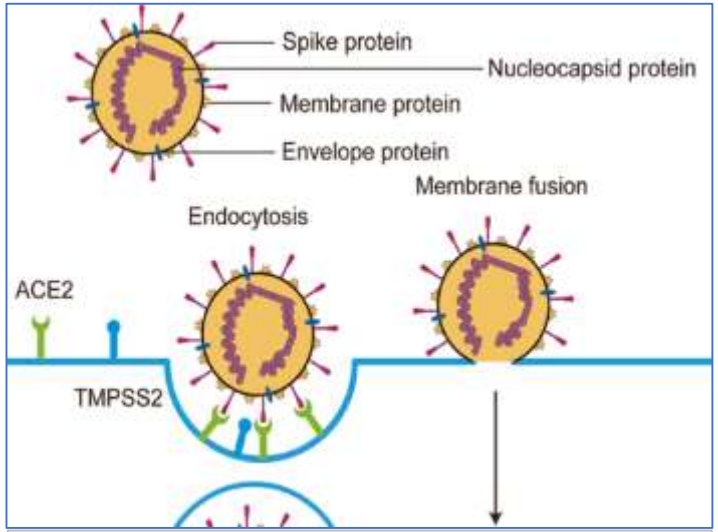
### Influenza virus




**Hemagglutinin (HA):** attaches to sialic acid-containing receptors on respiratory epithelial cells

**Neuraminidase (NA):** cleaves newly formed virions off the sialic acid-containing receptor, allowing the virus to exit cells

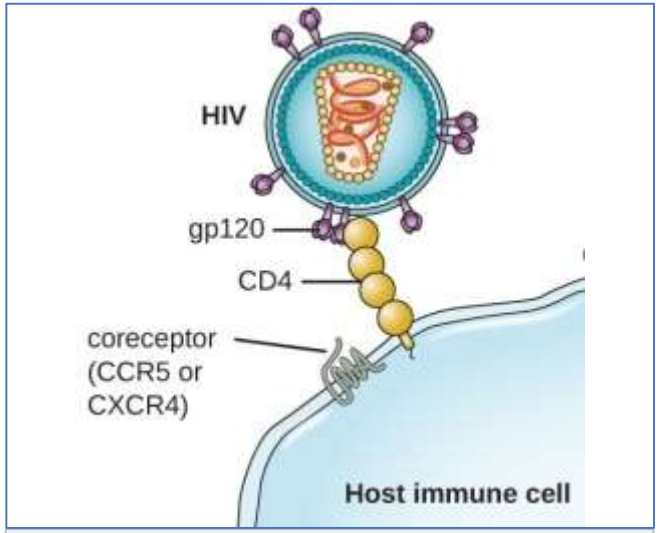
### COVID-19




The spike protein binds to the membrane protein angiotensin-converting enzyme 2 (ACE2). → Angiotencin converting enzyme.

Transmembrane protease serine 2 (TMPRSS2) activates the spike protein. Membrane fusion and uncoating of the viral RNA occur.

### HIV




The joining ligand of HIV is **gp120** which binds to the most common cellular receptors glycoproteins (CD4).

↳ and destroy the CD4 ($TH_2$)

1- what're the type of penetration according to type of virus.

2- describe the direct fusion & what's the result from it?

3- describe the endocytosis & give an example?

# Viral Replication Steps

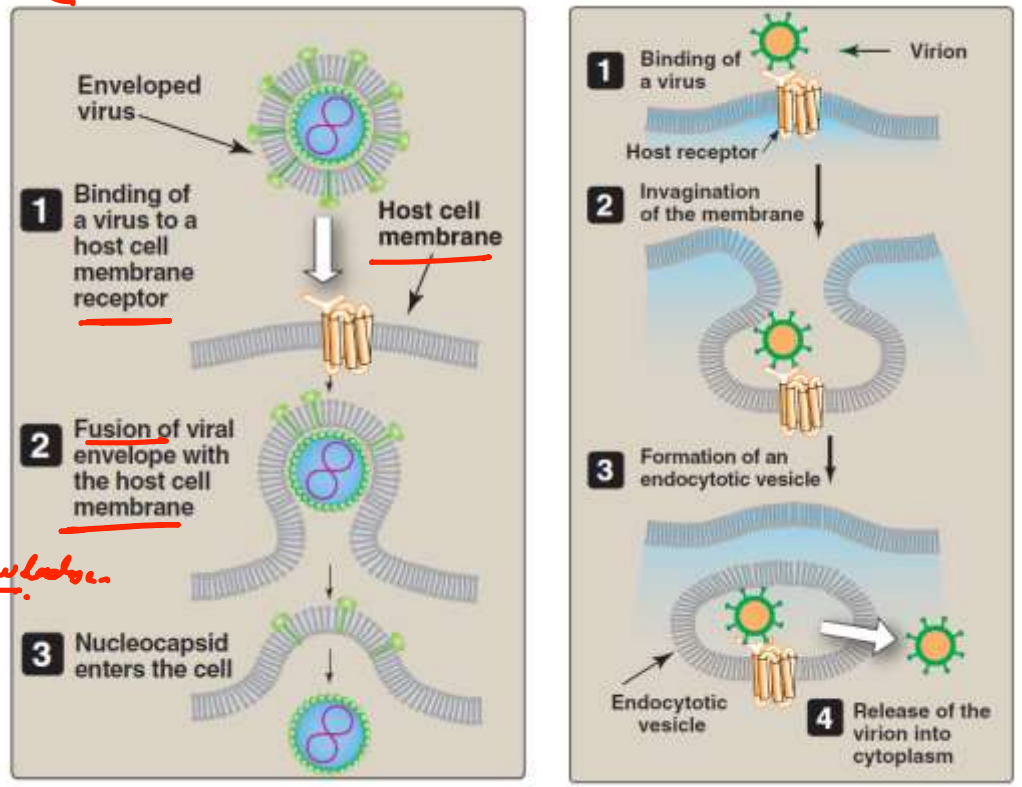
## Step 2 - Penetration (Entry)

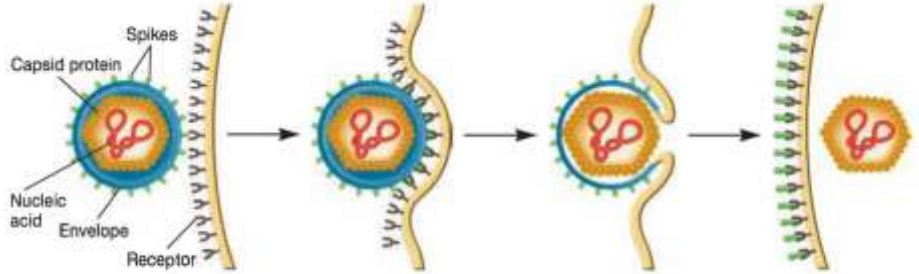
→ leave the envelope coat with host cell and enter inside it

**Mechanisms:**

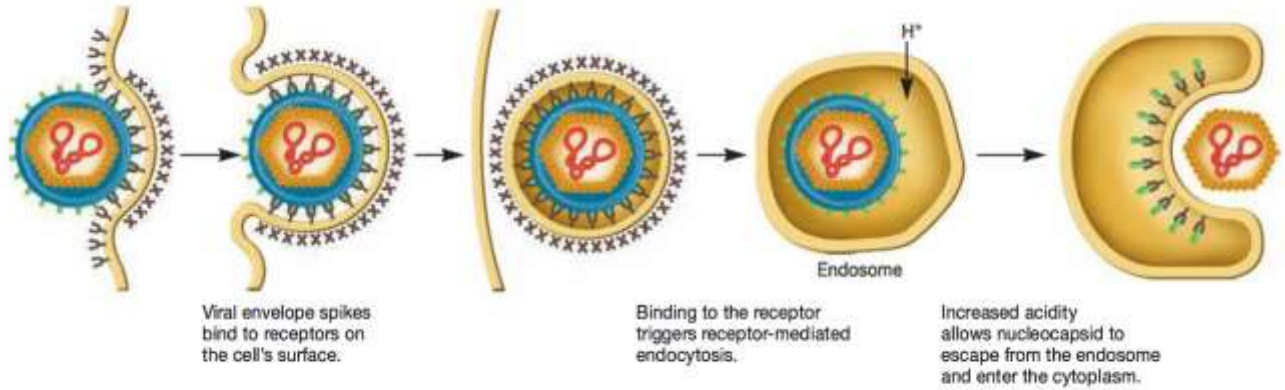
- **Direct Fusion (Enveloped Viruses):**
  - Viral envelope fuses with the plasma membrane of the cell.
  - The end result of this process is that the nucleocapsid is free in the cytoplasm, whereas the viral membrane remains associated with the plasma membrane of the host cell.
  - Example: HIV entering T-cells.
- **Receptor-mediated endocytosis (Enveloped and Non-Enveloped Viruses):**
  - The cell membrane invaginates, enclosing the virion in an endocytotic vesicle (endosome).
  - Clathrin-mediated endocytosis:e.g. Adenoviridae/ Caveolin mediated endocytosis: e.g. Papillomaviridae / Macropinocytosis: e.g Picornaviridae / Non-clathrin, non-caveolin mediated endocytosis
  - Example: Adenovirus (Clathrin-mediated endocytosis).

for your knowledge

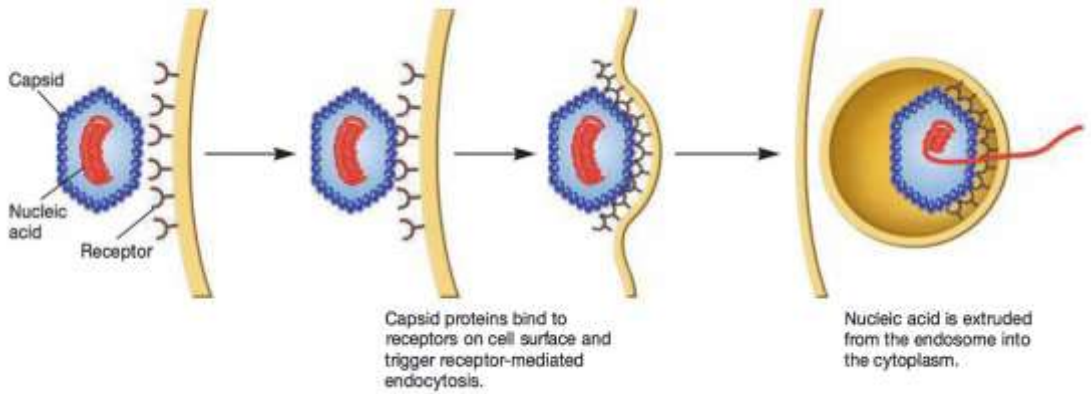





(a) Entry of enveloped virus by fusing with plasma membrane



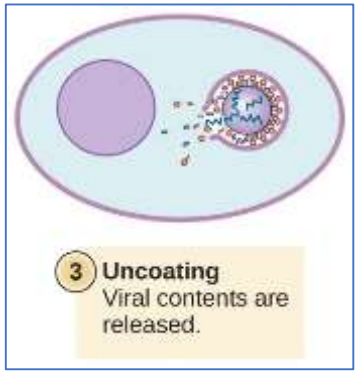

(b) Entry of enveloped virus by endocytosis




(c) Entry of nonenveloped virus by endocytosis

# Viral Replication Steps
## Step 3 - Uncoating

- **Definition:**
  - Refers to the separation of the capsid from the viral genome. It results in the loss of virion infectivity.
- **Mechanisms:**
  - Lysosomal Enzymes: degrade the proteins of the viral capsid.
  - Conformational Changes: Triggered by pH shifts.
- **Examples:**
  - Influenza Virus: Uncoating facilitated by M2 ion channel in acidic endosome.



1- what's special about Nucliz acid production site?

2- where does nucleic acid take place?

DNA dependent DNA.

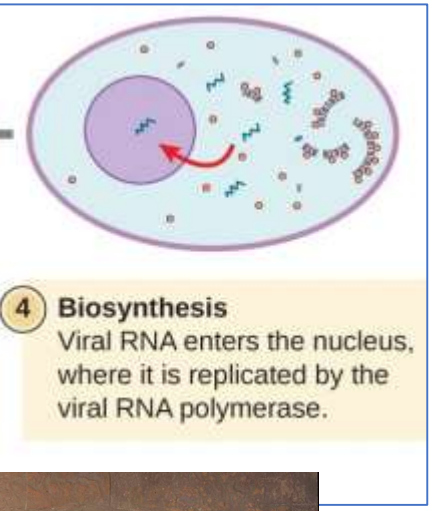
# Viral Replication Steps

## Step 4 –Synthesis: Replication and Protein Production

- Once uncoating has taken place, synthesis of viral nucleic acid starts.
- The site of production of nucleic acid also varies between viruses.
  - Most of the DNA viruses except Pox and Herpes replicate in nucleus.
  - All RNA viruses replicate in cytoplasm except Orthomyxoviruses and Retroviruses, which for certain stages of replication get into the nucleus of the cell
- How different viruses with different genome replicate? **Baltimore Classification**

Harry potter

which contain influenza.

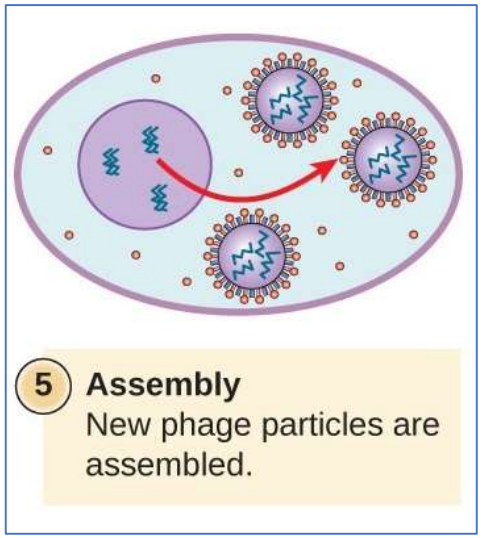



1- explain the mechanism?
2- where does it take place?

# Viral Replication Steps

## Step 5 – Assembly (Maturation)

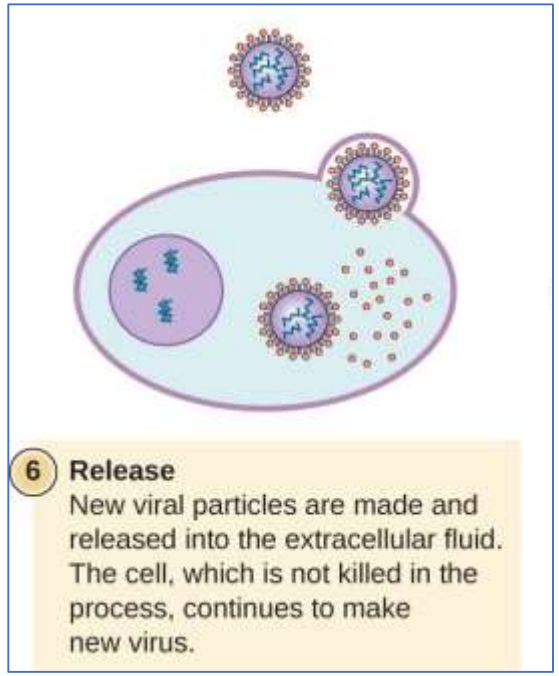
- **Process:**
  - Assembly of viral genome and proteins into new virions.
- **Locations:**
  - Assembly of nucleocapsids generally takes place in the host cell compartment where the viral nucleic acid replication occurs (that is, in the cytoplasm for most RNA viruses and in the nucleus for most DNA viruses).
    - For DNA viruses, this requires that capsid proteins be transported from their site of synthesis (cytoplasm) to the nucleus.



# Viral Replication Steps

## Step 6 –Release

- Release is a simple process – the cell breaks and releases the virus.
- Enveloped viruses acquire the lipid membrane as the virus buds out through the cell membrane.



1- which strand use to produce mRNA ? why ؟

# Negative vs. Positive Sense Strand of DNA and RNA

DNA


**Negative-sense**

**Positive-sense**

anti-sense.

why we use it ؟

- Negative DNA strand was used to make mRNA (+ssRNA)

⇒ To produce ⊕ ssRNA

- mRNA can then be translated to make proteins

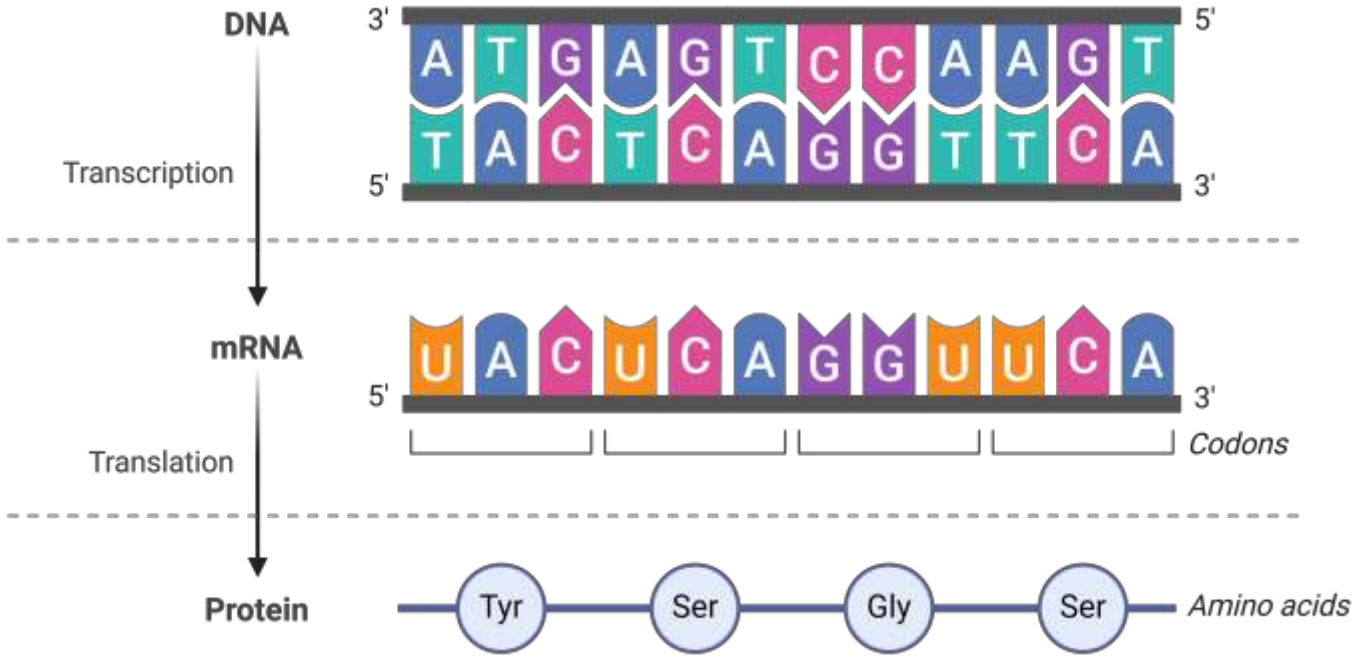
→ To have ⊕ mRNA.

dsDNA → Transcription → mRNA

Negative sense.

All viruses reach to this step, then either they use mRNA to produce protein. or genetic material.

# Negative vs. Positive Sense Strand of DNA and RNA



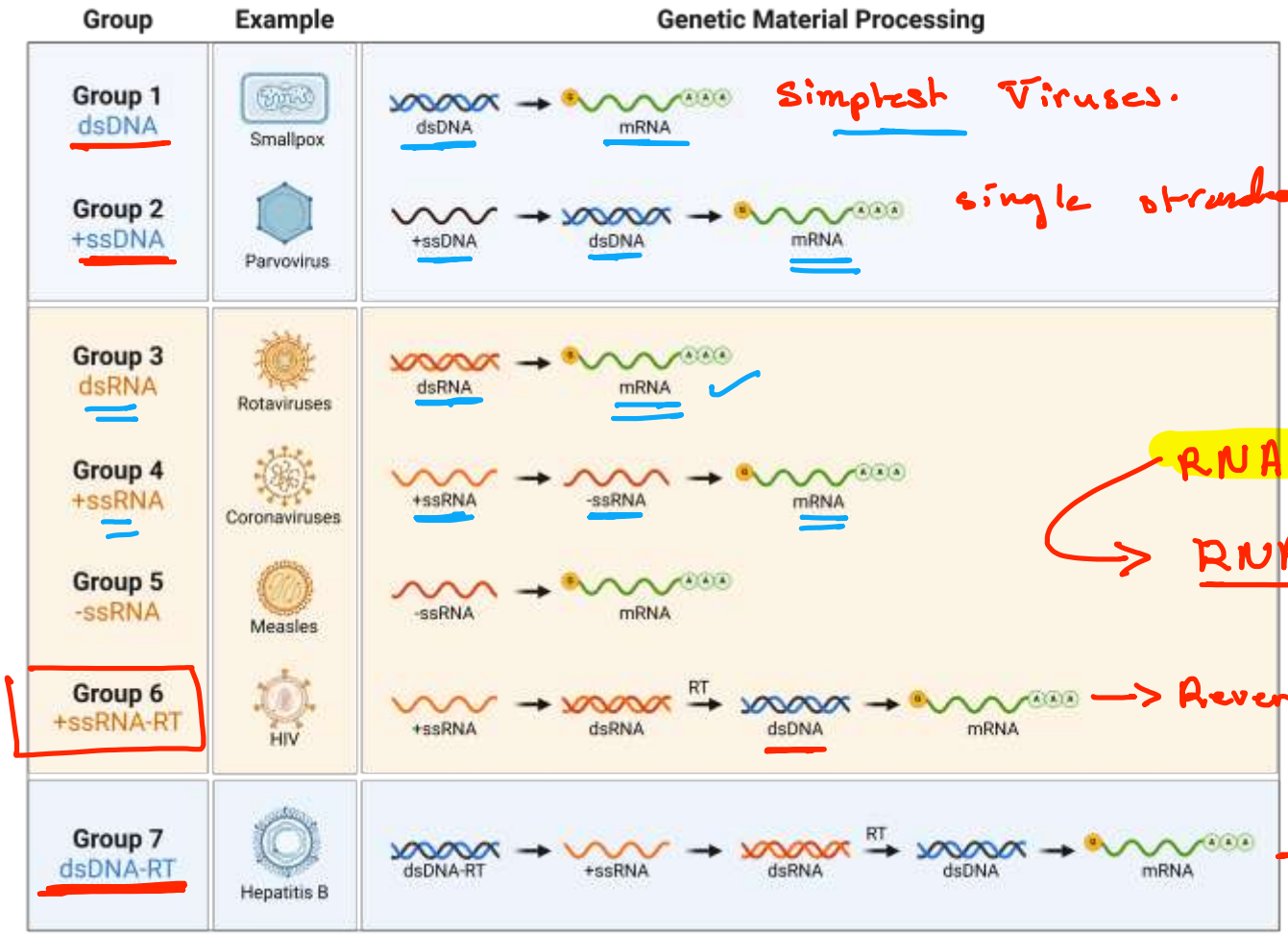

Viral replication = Protein synthesis + copying genetic material

BUT

It's not as simple—or as romantic—as it might seem. Viruses have their own complex dance with life!

# Baltimore Classification

DNA
- Group ① dsDNA
- Group ② ssDNA
- Group ⑦ dsDNA-RT




Simplest Viruses.

single stranded DNA

RNA dependent DNA polymerase.

RNA → DNA

→ Reverse transcriptase

→ double stranded DNA

→ gapped genome.

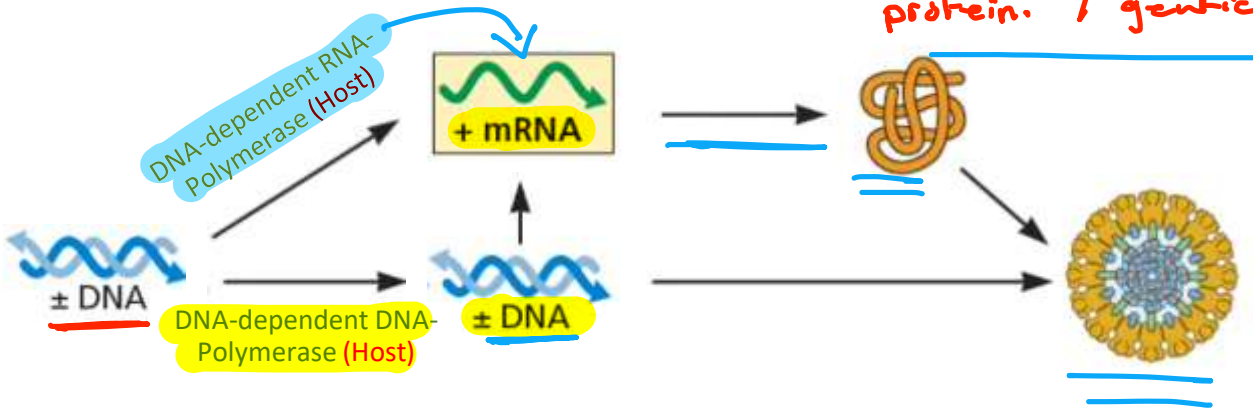
1- what's special about this replication?

2- explain the machanism of it?

3- Give an example about Viruses undergo this type of replication?

# Group 1: Replication of dsDNA Virus

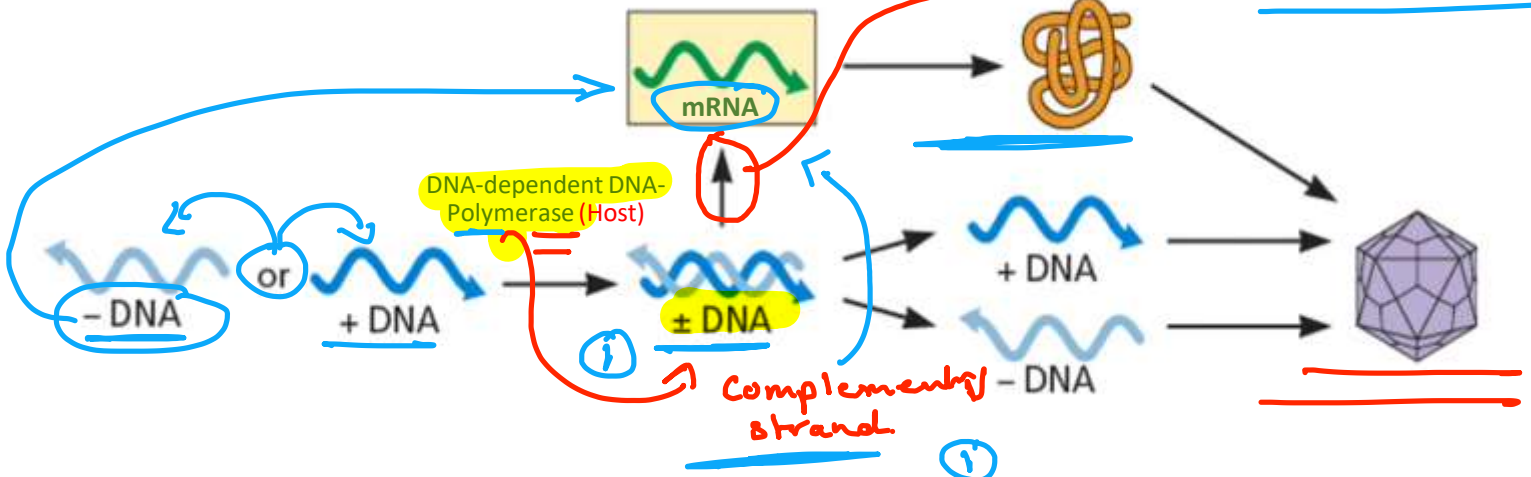
→ Viruses don't bring any enzyme with it.




protein / genetic material.

- The replication of dsDNA viruses is a straight-forward.
- They use the cell's replication machinery to transcribe their genome into mRNA immediately.
- Host enzymes for mRNA synthesis and DNA replication are available in nucleus hence, it needs to enter the nucleus.
- **Example:** papillomaviruses, polyomaviruses, adenoviruses and herpesviruses.

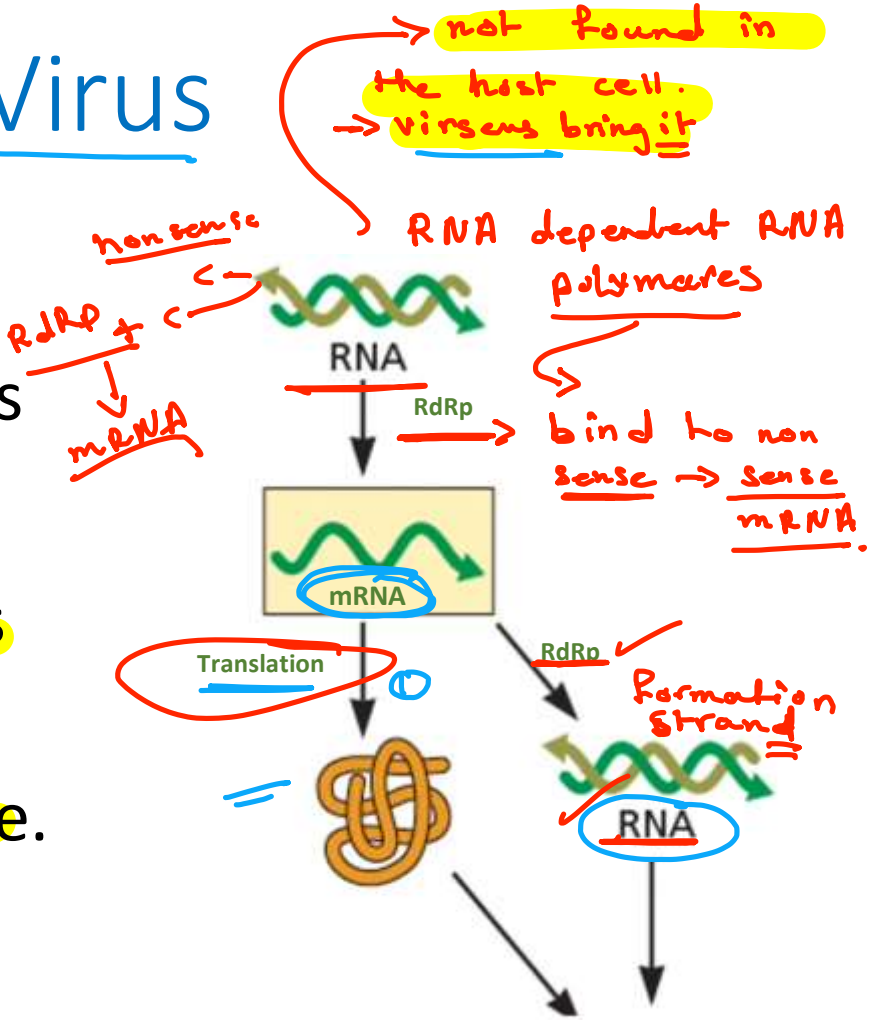
# Group 2: Replication of ssDNA Virus




- This can be used to both manufacture viral proteins and as a template for viral genome copies.
- For the minus-strand DNA viruses, the genome can be used directly to produce mRNA but a complementary copy will still need to be made, to serve as a template for viral genome copies.

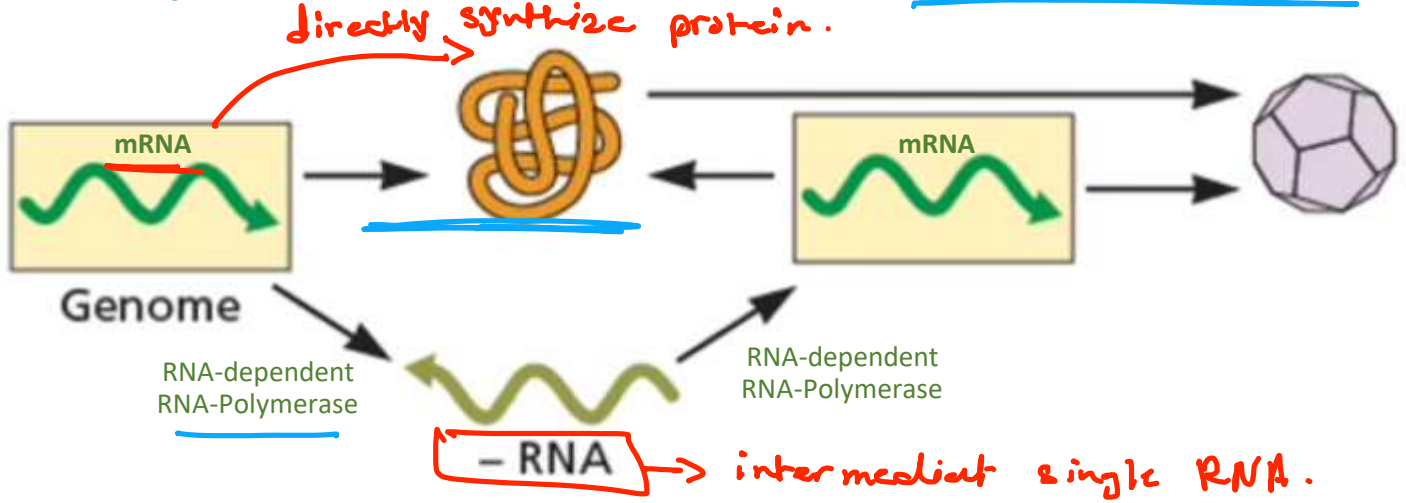
# Group 3: Replication of dsRNA Virus

- Double-stranded RNA viruses infect bacteria, fungi, plants, and animals, such as the rotavirus that causes diarrheal illness in humans.
- The viral RNA-dependent RNA polymerase acts as both a **transcriptase** to transcribe mRNA, as well as a **replicase** to replicate the RNA genome.
- Prokaryotic and eukaryotic cells do not carry **RdRp**.



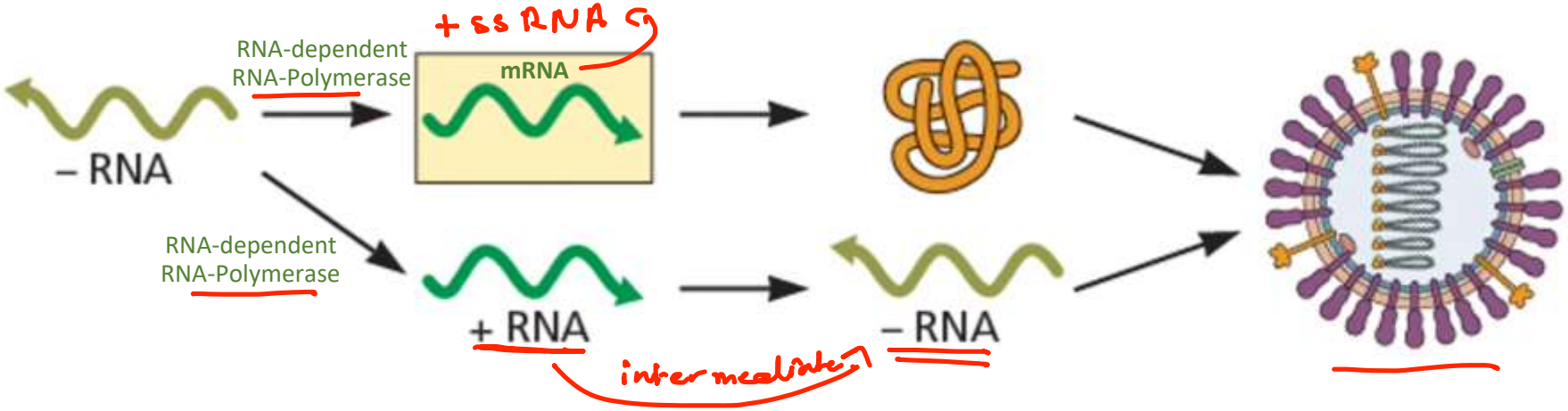

After entering the host body, the viral RNA-dependent RNA polymerase (RdRp) transcribed the dsRNA genome into mRNA, later this transcribed mRNA is used for the translation or replication.

# Group 4: Replication of (+) ssRNA Virus




- Viruses with plus-strand RNA, such as poliovirus, can use their genome directly as mRNA with translation by the host ribosome occurring as soon as the viral genome gains entry into the cell.
- One of the viral genes expressed yields an RNA-dependent RNA-polymerase (or RNA replicase), which creates minus-strand RNA from the plus-strand genome.
- The minus-strand RNA can be used as a template for more plus-strand RNA, which can be used as mRNA or as genomes for the newly forming viruses.

# Group 5: Replication of (-) ssRNA Virus




- Minus-strand RNA viruses include many members notable for humans, such as influenza virus, rabies virus, and Ebola virus.
- Since the genome of minus-strand RNA viruses cannot be used directly as mRNA, the virus must carry an RNA-dependent RNA-polymerase within its capsid.
- Upon entrance into the host cell, the plus-strand RNAs generated by the polymerase are used as mRNA for protein production.
- When viral genomes are needed the plus-strand RNAs are used as templates to make minus-strand RNA.

# **Group 6:** Replication of (+) ssRNA-RT Virus (dsDNA intermediate)

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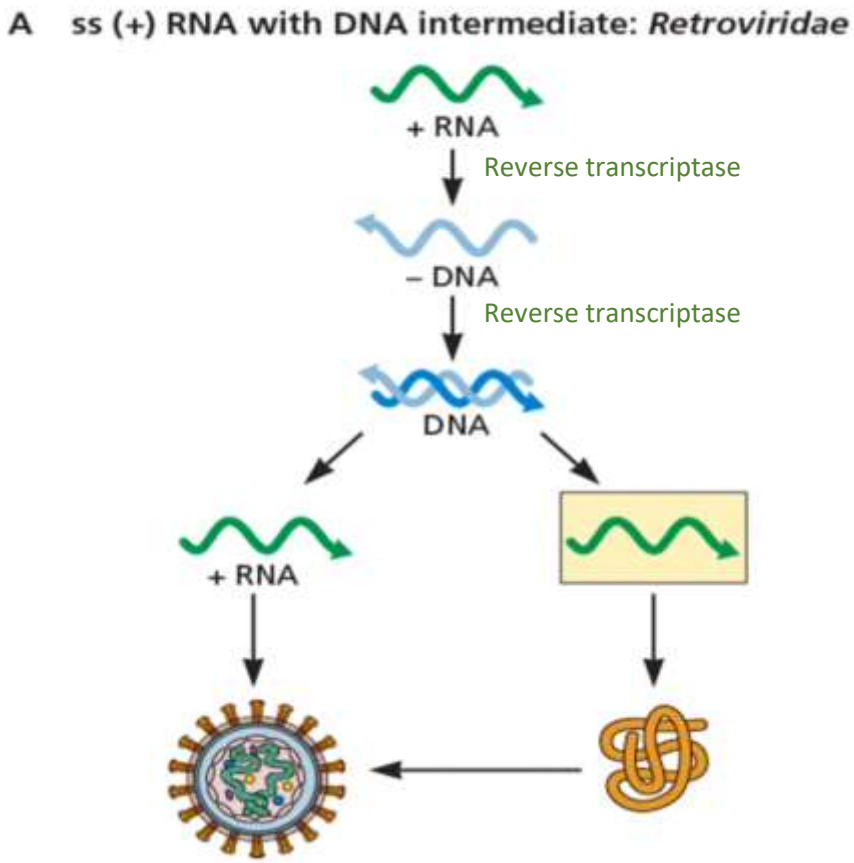
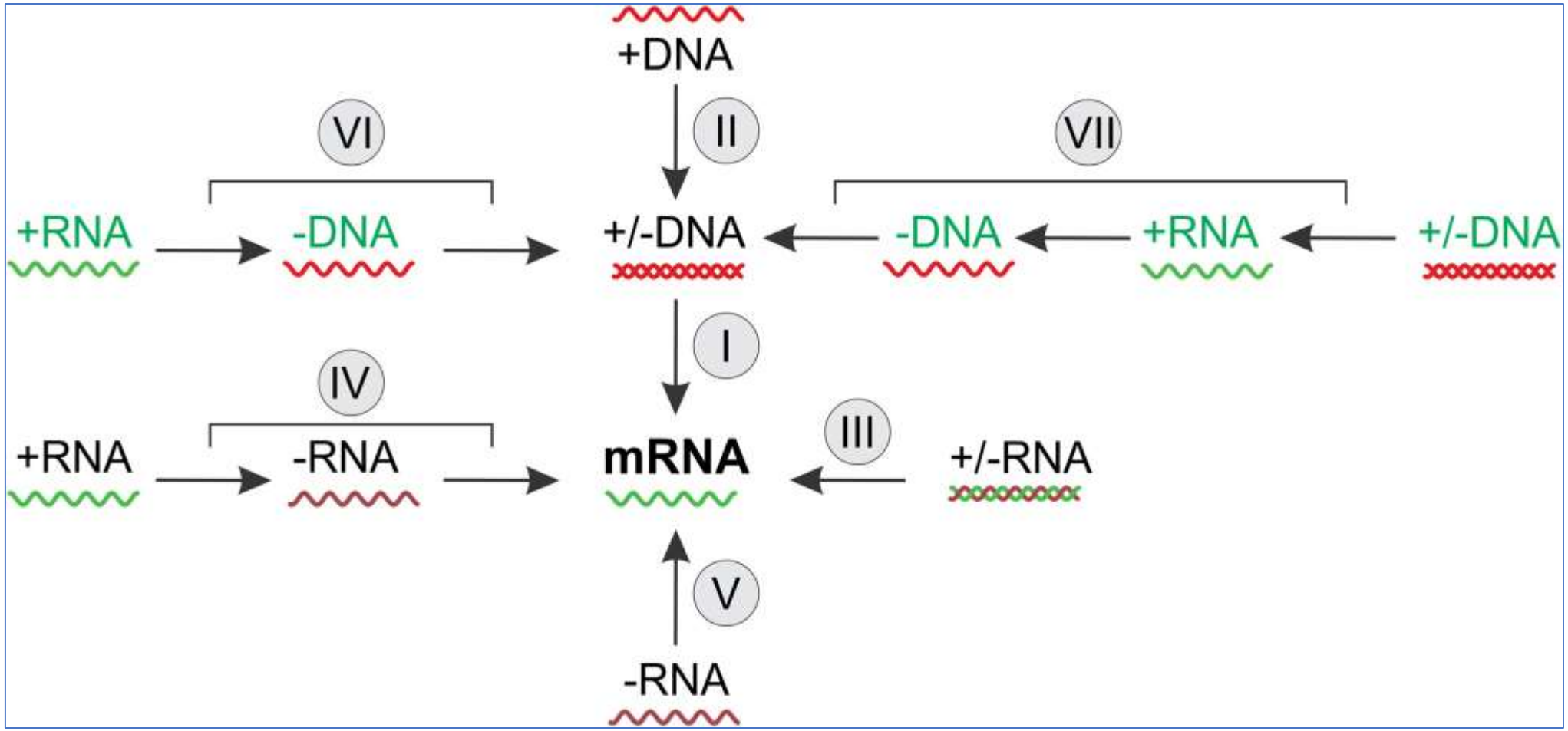
- Despite the fact that the retroviral genome is composed of +ssRNA, it is not used as mRNA. Instead, the virus uses its reverse transcriptase to synthesize a piece of ssDNA complementary to the viral genome. The reverse transcriptase also possesses **ribonuclease** activity, which is used to degrade the RNA strand of the RNA-DNA hybrid. Lastly, the reverse transcriptase is used as a DNA polymerase to make a complimentary copy to the ssDNA, yielding a dsDNA molecule.
- **Example:** Human immunodeficiency virus (HIV)




+DNA
VI
II
VII
+RNA
-DNA
+/-DNA
-DNA
+RNA
+/-DNA
I
IV
III
+RNA
-RNA
mRNA
+/-RNA
V
-RNA