River Valley High School
2025 JC1 H2 Biology

Lecture Topic 14: Organisation of Genomes – Viruses

Name: _____ ( ) Class: 25J__ Date: _____

References

Title	Author
Biology (8th edition)	Campbell and Reece
Biological Science 1: Organisms, Energy & Environment (3rd edition)	Taylor, Green and Stout
Brock Biology of Microorganisms (12th edition)	Madigan, Martinko, Dunlap and Clark
Foundations in Microbiology (7th edition)	Talaro
Microbiology (4th edition)	Baker, Griffiths, Nicklin

H2 Biology Syllabus 9477 (2025)

Candidates should be able to use the knowledge gained in the following section(s) in new situations or to solve related problems.

Related Topics	Content
Organisation of Genomes - Prokaryotes	Role of bacteriophage in bacterial transduction
Infectious Diseases	How viruses cause disease in humans

Learning Outcomes

1A. Organelles and Cellular Structures

e. Describe the structural components of viruses, including enveloped viruses and bacteriophages, and interpret drawings and photographs of them.

f. Discuss how viruses challenge the cell theory and concepts of what is considered living.

2B. Organelles and Cellular Structures

a. Describe the structure and organisation of viral genomes, (including DNA/RNA, single-/double-stranded, number of nucleotides, packing of DNA, linearity/circularity and presence/absence of introns).

b. Describe how the genomes of viruses are inherited through outlining the reproductive cycles of:
   i. bacteriophages that reproduce via lytic and lysogenic cycles, e.g. lambda phage;
   ii. enveloped viruses, e.g. influenza; and
   iii. retroviruses, e.g. HIV.

c. Describe how variation in viral genomes arises, including antigenic shift and antigenic drift.

Extension Topic A: Infectious Diseases

g. Explain how viruses, including influenza and HIV, cause diseases in humans through the disruption of host tissue and functions (e.g. HIV and T helper cells, influenza and epithelial cells of the respiratory tract).

Lecture Outline

I. Characteristics of Viruses
- A. Are viruses alive?
- B. Viruses are obligate intracellular parasites
- C. Viruses exhibit host specificity

II. Viral Structure

III. Reproductive Cycles of Viruses
- A. General features of viral reproductive cycles
- B. Reproductive cycles of naked virus- Bacteriophage
  - B1. Lytic and Lysogenic cycle of lambda phage
- C. Reproductive cycle of enveloped virus – Influenza
- D. Reproductive cycle of retrovirus – Human Immunodeficiency Virus
- E. Comparison of reproductive cycles of viruses

IV. Variation in Viral Genomes
- A. Antigenic Drift
- B. Antigenic Shift

V. Viral Infections
- A. How viral infections cause diseases
- B. Impact of Influenza infection
- C. Impact of HIV infection

Websites

URL	Description
http://bio-alive.com/animations/virology.htm	List of virology animations
https://highered.mheducation.com/sites/9834092339/student_view0/chapter23/how_the_hiv_infection_cycle_works.html	Animations on reproductive cycles of HIV *Note: you would need to use a laptop/desktop and download a chrome extension (e.g. “Flash Player for Chrome”) to view the tutorial.
http://viralzone.expasy.org/all_by_species/254.html	Baltimore classification of viruses
https://www.researchgate.net/publication/8131916_Are_Viruses_Alive	Insights from Scientific American: Are Viruses Alive?

I. CHARACTERISTICS OF VIRUSES

Are viruses alive?

Viruses are considered to exist at the border between chemistry and life, because they possess both living and non-living characteristics.

Living characteristics:

1. Viruses can reproduce at a fast rate, but only upon infecting living host cells.
2. They possess a genome, and are capable of transmitting their genetic characteristics from one viral generation to the next. Viral genomes are also capable of evolving by natural selection.

Non-living characteristics:

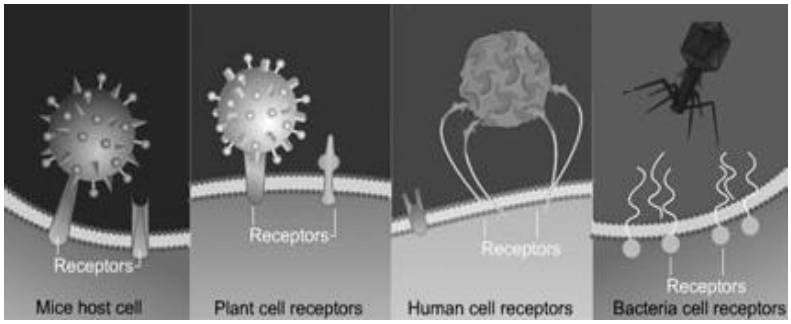
1. Viruses are **acellular**, since they lack key cellular components such as cytoplasm and cellular organelles. In their simplest forms, they comprise only genomic nucleic acid (DNA or RNA) surrounded by a protein coat.
2. They do not carry out metabolic processes outside a host cell, since they lack essential cellular machinery, and are thus unable to grow and divide on their own.
3. While all cells contain double-stranded DNA genomes, viruses have either DNA or RNA genomes, which can in turn be single or double-stranded.
4. They are not capable of movement, because they lack the means to physically propel themselves

B. Viruses are obligate intracellular parasites

- A virus is a sub-microscopic infectious agent that cannot replicate independently of a host cell, the cell which is infected by the virus.
- Viruses are therefore **obligate intracellular parasites** that must rely on entering a suitable living cell, i.e. **infecting** a host cell, to carry out their replication cycle and thus multiply.
- Upon infecting a host cell, the virus hijack host cell machinery and exploits the energy resources, raw materials and metabolic machinery of the host cell.
    - The virus redirects host metabolic functions to support its own replication cycle via the assembly of new viral particles. Eventually, the new viral particles are released, and the process can repeat itself as the infection spreads.
- Although viruses can only replicate after infecting a host cell, they have an extracellular form, known as the **viral particle** or **virion**[1] that enables them to exist outside the host for long periods, and that facilitates their transmission from one host cell to another.
    - Viral particles can be passed from host to host either through direct contact (e.g. body fluids) or through a **vector** or **carrier** (e.g. dengue is transmitted by *Aedes* mosquito)

[1] Virion is a term used for viral particle that is outside the host cell.

C. Viruses exhibit host specificity



Host specificity of viruses due to complementary binding between viral surface proteins and host cell surface receptors

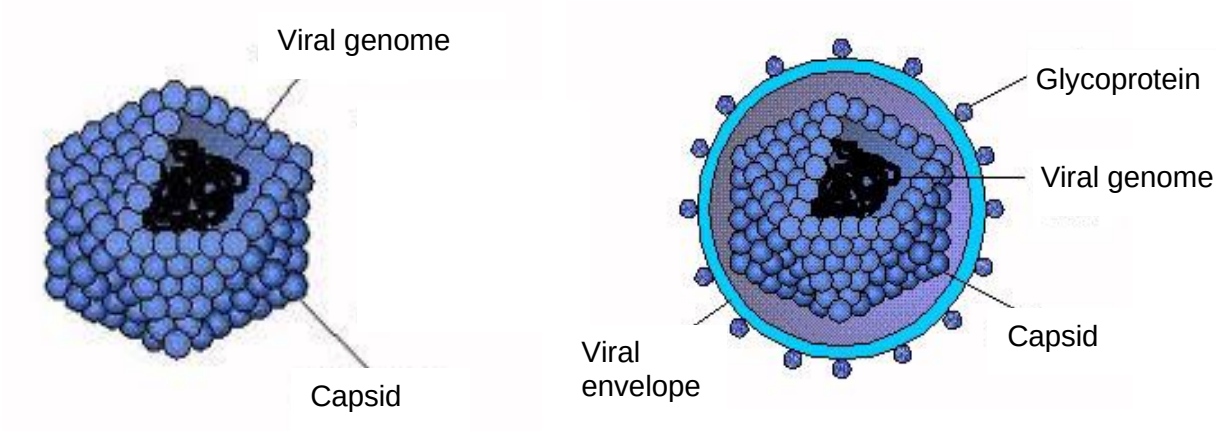
While viruses infect all types of organisms, from animals and plants to bacteria and archaea[2], each type of virus infects only a limited variety of hosts. Thus viruses exhibit **host specificity**. Virus infects specific host cell by a 'lock-and-key' fit between viral surface proteins and specific receptor molecules on the host cell surface.

Checkpoint 1:

Tobacco Mosaic Virus (TMV) has been isolated from virtually all commercial tobacco products. Why is TMV infection **not** an additional hazard for smokers?

[2] Archaea is one of the two prokaryotic domains, the other being Bacteria. The domain comprises unicellular organisms that are genetically distinct from bacteria and eukaryotes, and often found inhabiting in extreme environmental conditions.

II. VIRAL STRUCTURE



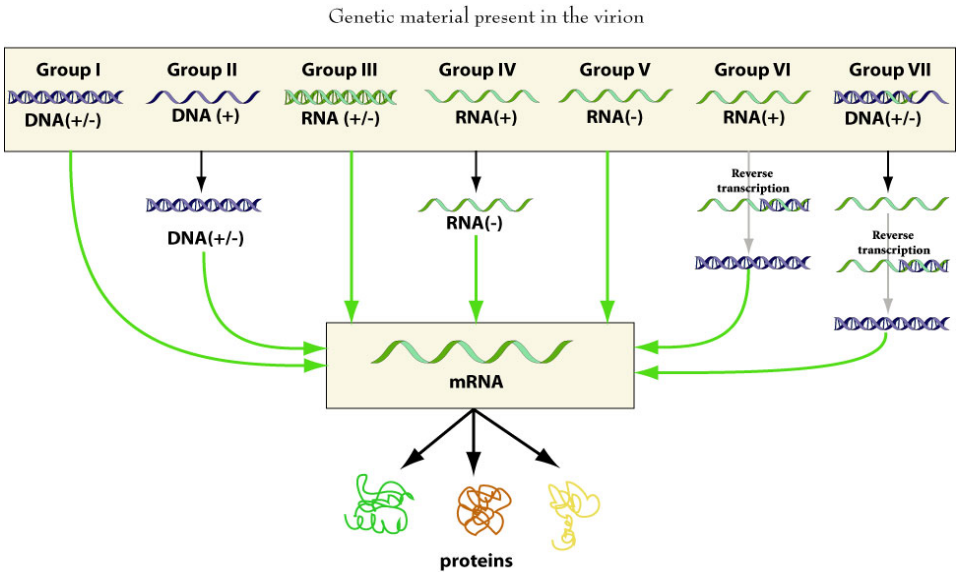
Representation of structure of a naked virus (left) and an enveloped virus (right)

- Most viruses are smaller than prokaryotic cells, ranging in size from 0.01 – 0.3 µm. They are visible only under the electron microscope.
- Their structures are diverse, varying widely in size, shape and chemical composition.
- Nonetheless, all viruses contain a **genome** and **capsid**

1. Viral genome

Viral genome can be:

- Made of DNA or RNA
- Linear or circular
- Organised as a single molecule of DNA/RNA, or as multiple molecules
- Single-stranded (ss) or double-stranded (ds)
    - ssDNA and ssRNA genomes can be of **positive (+)** or **negative (-) configuration**
    - By convention, mRNA is defined as (+) configuration. The strand with the complementary sequence will have (-) configuration.
    - E.g. A virus with ssRNA genome that is identical to its mRNA is called a **ssRNA (+)** virus.
    - E.g. A virus with ssRNA genome that is complementary to its mRNA is called a **ssRNA (-)** virus.



The Baltimore classification system groups viruses according to their type of genome and replication strategy

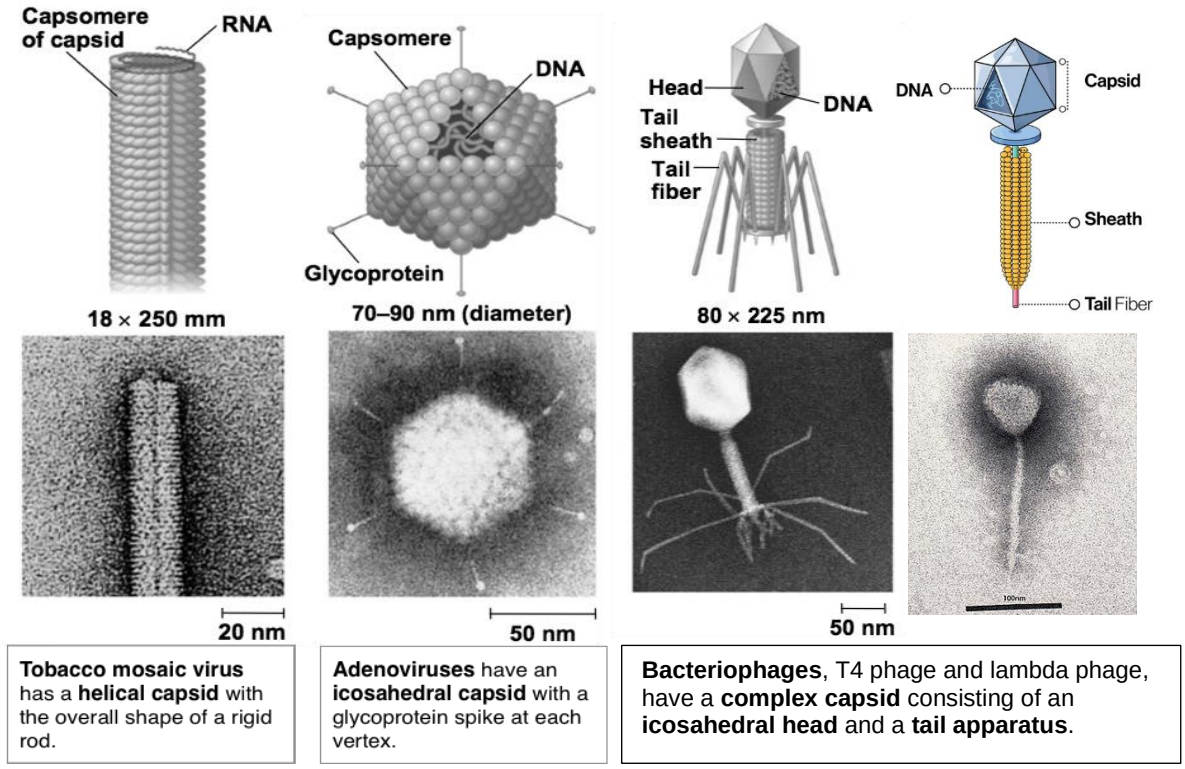
		Examples	
Class	***Description of genome and replication strategy***	***Bacterial viruses***	***Animal viruses***
I	Double-stranded DNA genome	Lambda, T4	Herpesvirus, pox virus
II	Single-stranded DNA genome	ϕX174	Chicken anemia virus
III	Double-stranded RNA genome	ϕ6	Reoviruses
IV	Single-stranded RNA genome of plus sense	MS2	Poliovirus
V	Single-stranded RNA genome of minus sense		Influenza virus, rabies virus
VI	Single-stranded RNA genome that replicates with DNA intermediate		Retroviruses
VII	Double-stranded DNA genome that replicates with RNA intermediate		Hepatitis B virus

Examples of virus in various classes under the Baltimore classification system

- The viral genome usually contains 4-100 genes, depending on the type of virus.
- The genome contains genes coding for viral proteins that function as:
  1. viral structural components (e.g. capsid, glycoproteins)
  2. viral enzymes for production of new viral particles (e.g. RNA-dependent RNA polymerase, reverse transcriptase)

2. Capsid

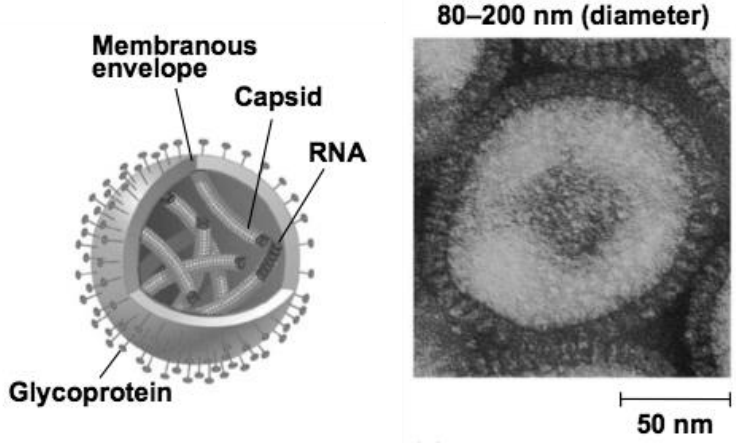
- Capsid is a protein coat enclosing the viral genome.
- It comprises a large number of protein molecules called **capsomeres**. These protein molecules are arranged in a precise, highly repetitive and highly symmetrical pattern around the nucleic acid.
- This results in a variety of capsid shapes, e.g. **helical** (rod-shaped), **icosahedral** (20-sided polyhedron), or **more complex shapes**.



Three examples of naked viruses exemplifying three types of capsids – helical, icosahedral and complex

- The complete complex of nucleic acid and capsid is known as the virus **nucleocapsid**. Some viruses comprise only the nucleocapsid and are called **naked viruses**.
- The capsid serves to
  1. protect the viral genome from digestion by restriction enzymes
  2. enable the viral particle to inject its genome into a potential host cell
  3. Some viruses may contain their own enzymes within their capsids.
     - These enzymes play various important roles that allow the production of new viral particles, they may facilitate infection, replicate the viral genome, transcribe virus-specific RNA, or facilitate the release of new viral particles from the host cells.

3. Viral envelope



Influenza viruses have an **outer envelope** studded with **glycoprotein spikes**. The genome comprises 8 different RNA molecules, each wrapped in a helical capsid.

Example of an enveloped virus – influenza virus

- **Enveloped viruses** possess an additional membrane around the nucleocapsid called a **viral envelope**.
- Enveloped viruses are usually animal viruses (e.g. influenza virus, HIV), although a few enveloped bacterial and plant viruses are also known.
- The envelope comprises a phospholipid bilayer with embedded proteins, usually glycoproteins.
  - The phospholipids of the envelope are derived from the membranes of the host cell via budding.
  - The glycoproteins of the envelope are encoded by viral genes. Some might also be derived from the host.
  - These virus-specific glycoproteins are critical for
    1. attachment of the virus to specific surface receptor molecules on the host cell for infection
    2. release of new viral particles from the host cell after replication

Checkpoint 2:

Compare and contrast naked virus and enveloped virus.

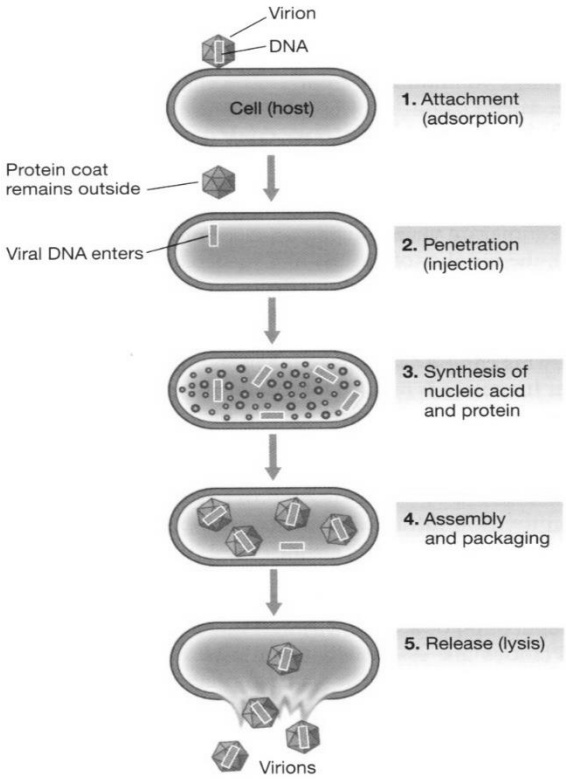
III. REPRODUCTIVE CYCLES OF VIRUSES

A. General features of viral reproductive cycles

For a virus to replicate, it must induce a living host cell to synthesise all the essential components needed to make more viral particles. These components must then be assembled into new viral particles that escape from the cell.

The phases of viral replication can be divided into five general steps:

1. **Attachment** of the viral particle to a specific host cell.
2. **Penetration** of the viral particle or its nucleic acid into the cell.
3. **Synthesis of viral nucleic acid and protein** by host cell machinery as directed by the virus. The virus uses host cell's nucleotides, enzymes, ribosomes, tRNAs, amino acids, ATP and other components for such synthesis.
4. **Maturation** involves **assembly** of capsids and **packaging** of viral genomes into new viral particles.
5. **Release** of mature viral particles from the cell.



A general viral reproductive cycle of a naked virus

B. Reproductive cycles of naked virus- Bacteriophage

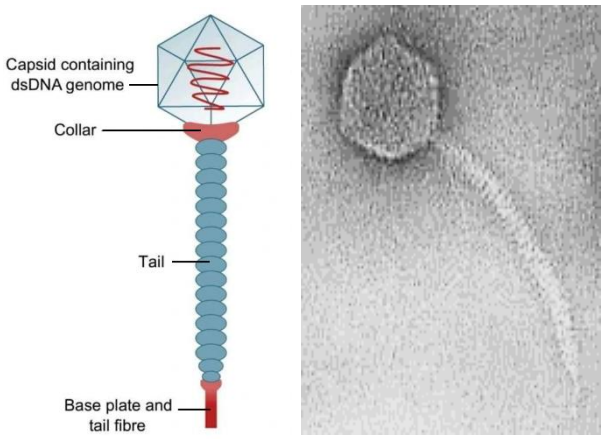
Bacteriophages, or "phages", are viruses that infect bacteria.

They can reproduce by two alternative mechanisms: the **lytic cycle** and the **lysogenic cycle**.

- The **lytic cycle** culminates in lysis (breaking open) and thus death of the host cell. Upon lysis, new viral particles that were produced in the original host cell are released to infect new host cells.
- The **lysogenic cycle** allows replication of the phage genome without destroying host cells.
    - The phage genome is incorporated into the bacterial chromosome, but it exists in a **repressed state**, known as a **prophage**, in which most of the phage genes are not transcribed.
    - Each time the host cell divides, it passes copies of the mostly silent phage genome to daughter cells.
    - This easily gives rise to many generations of bacteria carrying the virus in prophage form, with no apparent harm to the bacterial hosts.
    - However, the prophage can eventually be induced to exit the bacterial chromosome and initiate a lytic cycle, thus generating active phages that lyse the host cell.
- A phage that reproduces only by a lytic cycle is known as a **lytic / virulent phage**.
- A phage that can reproduce by either the lytic or lysogenic cycle is known as a **lysogenic/ temperate phage.**

B1. Lytic and Lysogenic cycle of lambda (λ) phage

Virus	**Lambda bacteriophage**, a temperate phage (i.e. undergoes lytic cycle or lysogenic cycle)
Host	***Escherichia coli*** bacteria
Capsid	Complex capsid with an elongated icosahedral head
Genome	Linear dsDNA genome
Structure	Resembles the T4 phage, but its tail contains only one short tail fibre



Left: Model of Lambda bacteriophage. Right: Electron micrograph of Lambda bacteriophage.

- As a temperate phage, it can replicate via the lytic or lysogenic cycle.
- Upon entering the bacterial cell, the lambda DNA genome can either:
  a. Integrate into the bacterial chromosome as a prophage (i.e. undergo the lysogenic cycle)
  b. Immediately initiate the production of a large number of progeny phages (i.e. undergo the lytic cycle)

Stages of the λ phage Lytic Cycle

1. **Attachment**

- The phage tail fibres bind to specific receptor on host bacterium outer cell surface membrane.

2. **Penetration**

- The tail sheath contracts, driving a hollow tube through the bacterial cell wall and cell membrane.
- The λ phage dsDNA genome is injected into the bacterial cytoplasm.

3. **Synthesis of viral genome and proteins**

- The λ phage enzymes hydrolyse the cell's DNA.
- The λ phage DNA directs the metabolic machinery (e.g. ribosomes, DNA polymerase, RNA polymerase) and raw materials (e.g. amino acids, ATP, nucleotides) of the host cell towards:
  a. Synthesising phage proteins
  b. Making new copies of the phage genome

4. **Maturation**

- Three separate sets of proteins self-assemble to form new phage heads, tail sheaths and tail fibres.
- The phage genome is packaged inside the capsid as the head forms.

5. **Release**

- The phage directs the synthesis of lysozyme – an enzyme that breaks down the bacterial peptidoglycan[3] cell wall.
- With the cell wall damaged, entry of water into the cell by osmosis causes the cell to swell and burst. Phage particles are released upon cell lysis.

[3] Petidoglycan is a polymer consisting of sugars and amino acids that forms cell wall of bacteria.

Stages of the λ phage Lysogenic Cycle

1. Attachment

- The phage tail fibre binds to specific receptor on host bacterium outer cell surface membrane.

2. Penetration

- The tail sheath contracts, driving a hollow tube through the host cell wall and cell membrane.
- The λ phage dsDNA genome is injected into the host cell's cytoplasm.

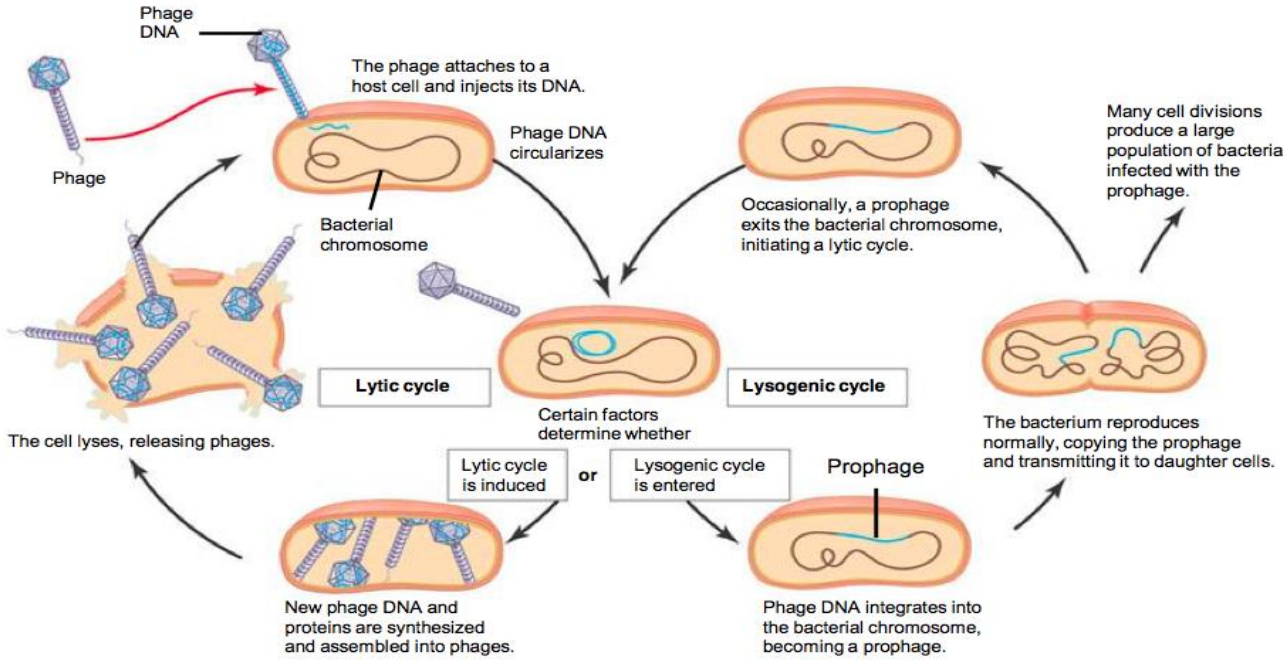
3. Synthesis of lambda repressor protein and viral genome

- λ DNA genome circularizes and is incorporated into a specific site on the bacterial chromosome. At this stage the phage genome is known as a prophage.
- A particular **prophage gene** coding for a **repressor protein** called the **lambda repressor** is expressed, resulting in synthesis of the lambda repressor.
- The lambda repressor blocks transcription of most other prophage genes, as a result, the rest of the prophage remains "silent".

  (Note: Host cell machinery and resources are thus not hijacked, and host DNA is not hydrolysed.)
- Each time the host cell divides, it replicates λ DNA along with its own, and passes copies to daughter cells.
- The phage continues to propagate without killing the host bacterial cells.

4. Prophage induction

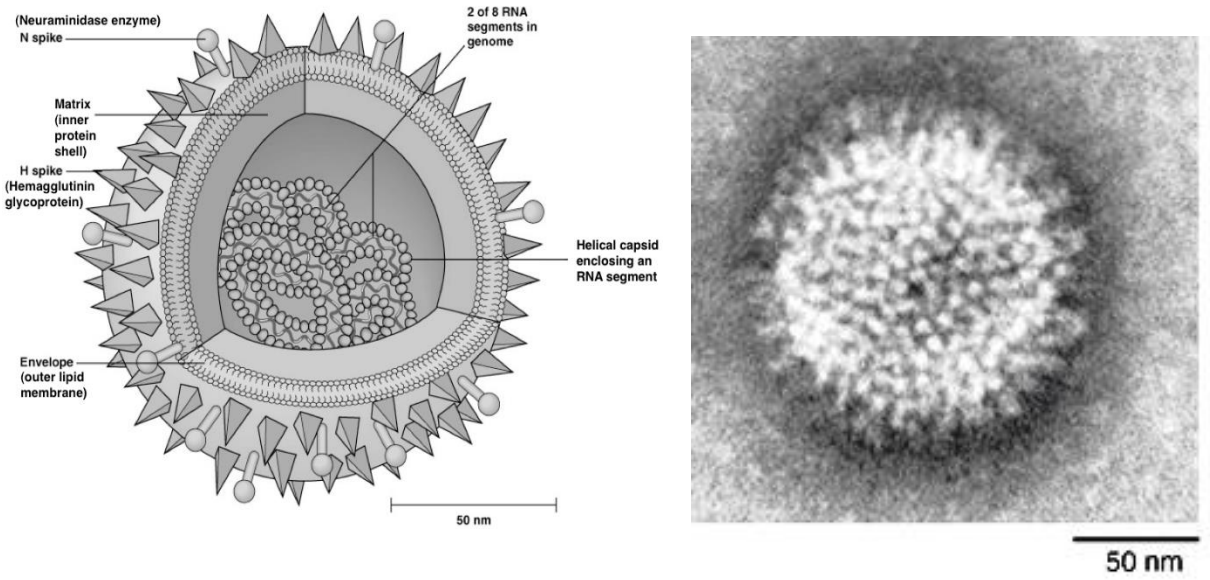
- Upon detection of host cell damage or stress (due to factors such as starvation, radiation, and presence of poisons such as antibiotics), lambda repressor protein may be broken down. This results in expression of the phage genes.
- The λ DNA genome of activated phage is excised from the bacterial chromosome and enters the lytic cycle.
- The host cell metabolic machinery is hijacked, generating active phages that eventually lyse their host cells.



The lytic and lysogenic cycles of λ phage, a temperate phage.

C. Reproductive cycle of an enveloped virus - Influenza

Virus	**Influenza virus**, an <u>enveloped</u> animal virus
Host	Birds, pigs and mammals- epithelial cells lining mucous membranes of respiratory tract
Capsid	Helical capsid
Genome	♦ 8 distinct linear segments of ssRNA (-), each wrapped in a helical capsid ♦ ssRNA genome is <u>negative configuration</u> (i.e. complementary to the viral mRNA)
Enzyme in capsid	♦ **Viral RNA-dependent RNA polymerase** found in the viral particle uses the <u>ssRNA (-)</u> genome as a <u>template</u> for <u>mRNA production</u> (*Note: The host cell's RNA polymerases cannot be used to synthesise mRNA from the viral RNA genome since they use a DNA template)*
Viral envelope	♦ Viral envelope is <u>derived from the host cell surface membrane</u> ♦ Two different types of <u>protein spikes</u> are <u>embedded</u> in the envelope[4]: a. **Haemagglutinin** (80%) – a <u>glycoprotein</u> that facilitates <u>attachment of viral particle to host cell surface membrane</u> by <u>binding to specific receptors</u> on a variety of cells, e.g. lung/throat epithelial cells. b. **Neuraminidase** (20%) – an <u>enzyme</u> that facilitates the <u>release of newly formed viral particles</u> from the infected host cell.



Left: Model of influenza virus. Right: Electron micrograph of influenza virus.

[4] Haemagglutinin (H) and neuraminidase (N) are the proteins that determine the type of influenza virus (A, B, or C) and the subtype (e.g. A/H1N1). H and N are important in the immune response against the virus; antibodies against these spikes may protect against infection. The N protein, for instance, is the target of the antiviral drugs Relenza and Tamiflu.

Stages of the Influenza Virus Reproductive Cycle

1. Attachment

- Haemagglutinin on the viral envelope binds to specific glycoprotein receptors / sialic acid receptors on the cell surface membrane of a suitable host cell.

2. Penetration and uncoating

- The viral particle is taken into the host cell by receptor-mediated endocytosis as the host cell surface membrane invaginates and pinches off, enclosing the viral particle in a coated vesicle / endosome (*Recall: Transport Across Membranes)*
- The drop in pH in the endosome triggers the viral envelope to fuse with the membrane of the endosome. The capsids are degraded by cellular enzymes, releasing the ssRNA (-) genome segments and viral RNA-dependent RNA polymerase into the cytoplasm.
- The viral RNA polymerase and ssRNA (-) are transported into the nucleus.

3. Synthesis of viral genome and proteins

- In the nucleus, the viral RNA-dependent RNA polymerase uses the ssRNA (-) as a template to transcribe complementary ssRNA (+).
- These complementary ssRNA (+) strands serve as:
  a. mRNAs for eventual translation into viral proteins in the cytoplasm; or
  b. Templates for making new copies of the ssRNA (-) genome in the nucleus.
- Viral mRNA is exported from the nucleus to be translated into viral proteins

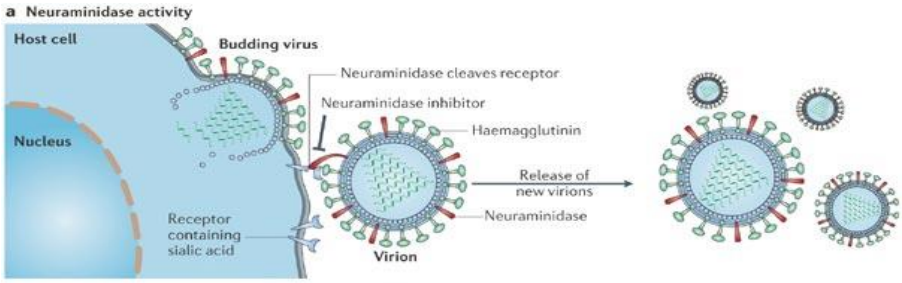
  i.e. viral RNA-dependent RNA polymerase, capsid proteins, haemagglutinin, neuraminidase
- Newly synthesised viral proteins are:
  a. Transported back into the nucleus (i.e. capsid proteins and RNA-dependent RNA polymerase)
  b. Incorporated into the cell surface membrane (i.e. neuraminidase and haemagglutinin).

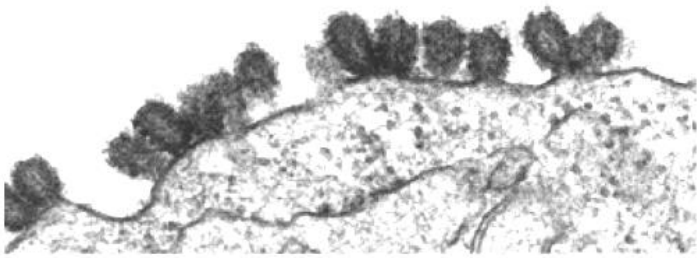
4. Maturation

- In the nucleus, capsid proteins assemble and the ssRNA (-) strands and RNA-dependent RNA polymerase are packaged to form new viral particles.
- 10,000 – 50,000 viral particles can be produced from a single infected host cell.

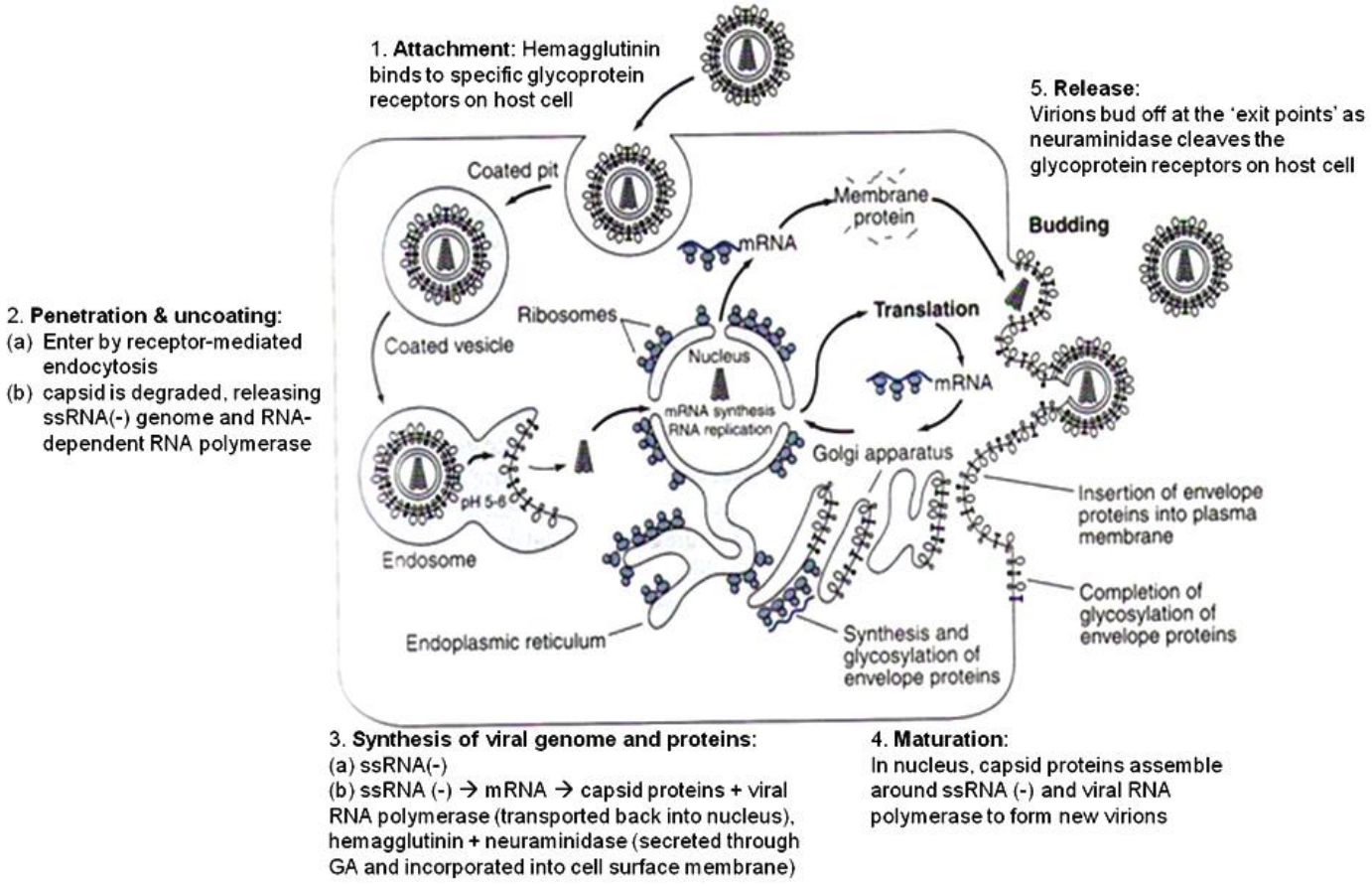
5. Release

- The new viral particles leave the nucleus and move towards cell surface membrane where neuraminidase and haemagglutinin have clustered.
- The viral particles are released from the host cell by **budding off** at these 'exit points', acquiring their envelope from portions of the host cell surface membrane with haemagglutinin and neuraminidase embedded.
- Mature viral particles detach from the host once their neuraminidase cleaves the glycoprotein receptors on the host cell.
- Released viral particles are ready to infect other cells.

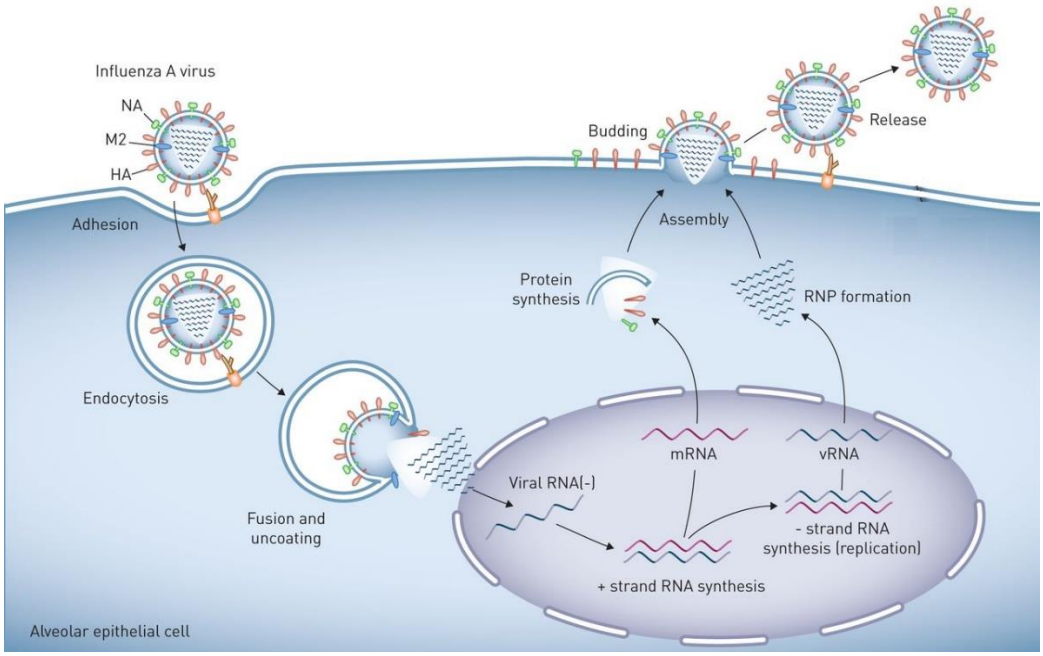




Electron micrograph of influenza viral particles budding off from the cell surface membrane of an infected mouse cell.

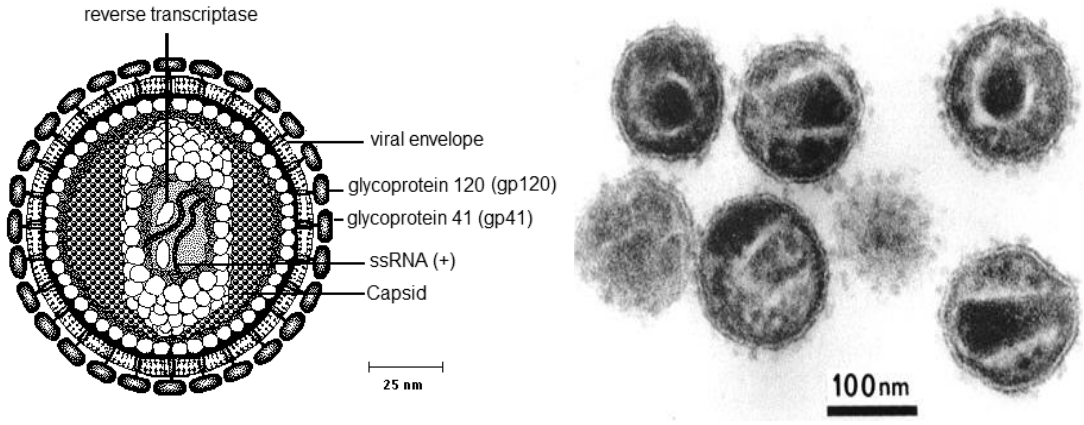


Reproductive cycle of influenza virus with simplified summary notes of the process.



D. Reproductive cycle of a retrovirus – Human Immunodeficiency Virus (HIV)

Virus	**Human immunodeficiency virus** (HIV), a **retrovirus** that is enveloped.
Host	Human immune cells that express the **CD4 cell surface protein**, especially **T helper cells**, a type of lymphocyte
Capsid	Conical capsid
Genome	The HIV-1 genome comprises 2 identical copies of ssRNA (+) enclosed in a conical capsid
Enzymes in capsid	The capsid also encloses various key enzymes necessary for viral replication: a. **Reverse transcriptase** is a **RNA-dependent DNA polymerase** that reverse transcribes viral RNA into cDNA. This process, known as **reverse transcription**, is unique to retroviruses b. **Integrase** incorporates the resulting double-stranded viral DNA into the host cell's DNA as a provirus c. **HIV protease** cleaves immature viral polyproteins synthesised by the host cell into individual and functional viral proteins during the maturation phase of the reproductive cycle
Viral envelope	♦ Viral envelope derived from the host cell surface membrane ♦ On the surface of the viral envelope of HIV-1 are many copies of a complex **glycoprotein** that comprises two types of subunits that together mediate penetration of the host cell: a. **Glycoprotein 120** (**gp120**) is a docking glycoprotein that binds to a specific receptor (CD4) on the host cell surface for viral attachment. b. **Glycoprotein 41** (**gp41**) brings about subsequent fusion of the viral envelope and host cell surface membrane. It is the transmembrane portion of the complex that anchors the complex into the viral envelope.

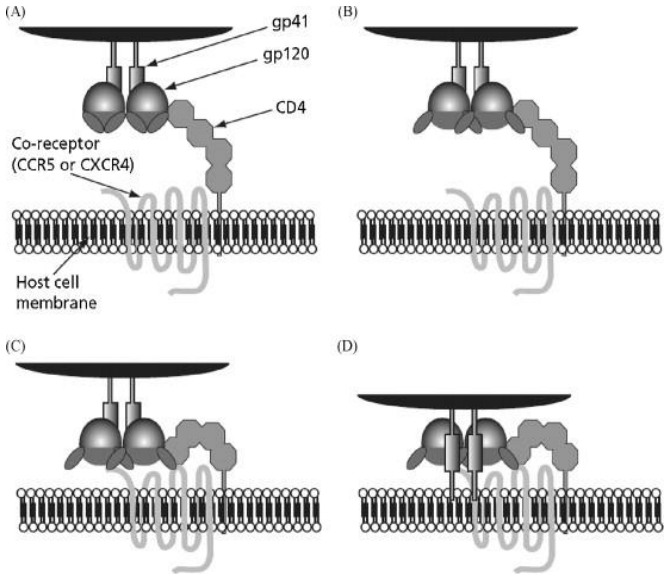


Left: Model of Human immunodeficiency virus (HIV). Right: Electron micrograph of HIV.

Stages of the HIV Reproductive Cycle

1. Attachment

- Glycoprotein 120 (gp120) on HIV envelope binds specifically to both a CD4 receptor and co-receptor on the cell surface membrane of T helper cells in the following sequence of events:
  - gp120 binds first to a CD4 receptor on the host cell surface membrane.
  - The interaction between gp120 and CD4 receptor induces a conformational change in gp120, enabling binding of gp120 to host cell's co-receptor [5] (i.e. CXCR4 on T helper cell or CCR5 on macrophage).
  - The interaction between gp120 and the co-receptor brings about a conformational change in gp41 on the HIV viral particle, which leads to fusion of the HIV envelope to the host cell surface membrane.



Interactions between HIV glycoproteins (gp120 and gp 41) and receptors on host cell surface membrane.

(A) gp 120 first on HIV envelope binds to CD4 receptor on host cell surface membrane.

(B) This induces conformational changes in gp120 and exposes its co-receptor binding site.

(C) Binding of gp120 to co-receptor.

(D)Interaction between gp120 and co-receptor induces a conformational change in gp 41, which leads to the insertion of a fusion peptide into the host cell surface membrane, causing it to fuse with the viral envelope.

2. Penetration and uncoating

- Fusion of the HIV envelope with the host cell surface membrane releases the capsid into the cytoplasm of the host cell.
- The capsid is subsequently degraded by cellular enzymes, thus releasing the viral genome and enzymes (reverse transcriptase, integrase, HIV protease) into the host cell. This process is known as uncoating.

3. Synthesis of viral genome and proteins

- Reverse transcriptase uses viral RNA as a template for **reverse transcription**

  i.e. to synthesize a complementary DNA (cDNA) strand. After the synthesis, viral RNA is degraded. Reverse transcriptase then synthesizes a second DNA strand complementary to the first strand.
- Integrase incorporates the resulting double-stranded viral DNA into the host cell's DNA as a **provirus**.
- Provirus may then lie dormant in the latent stage of HIV infection.
- During viral replication, provirus genes are transcribed into viral ssRNA (+) molecules by the host cell's RNA polymerase. These viral ssRNA (+) molecules serve as:
  a. New ssRNA (+) genomes for new viral particles
  b. mRNA for translation into HIV proteins

[5] Co-receptors, also known as chemokine receptors are G protein-coupled receptors containing 7 transmembrane domains that are found predominantly on the surface of leukocytes. They are responsible for signal transduction within a cell.

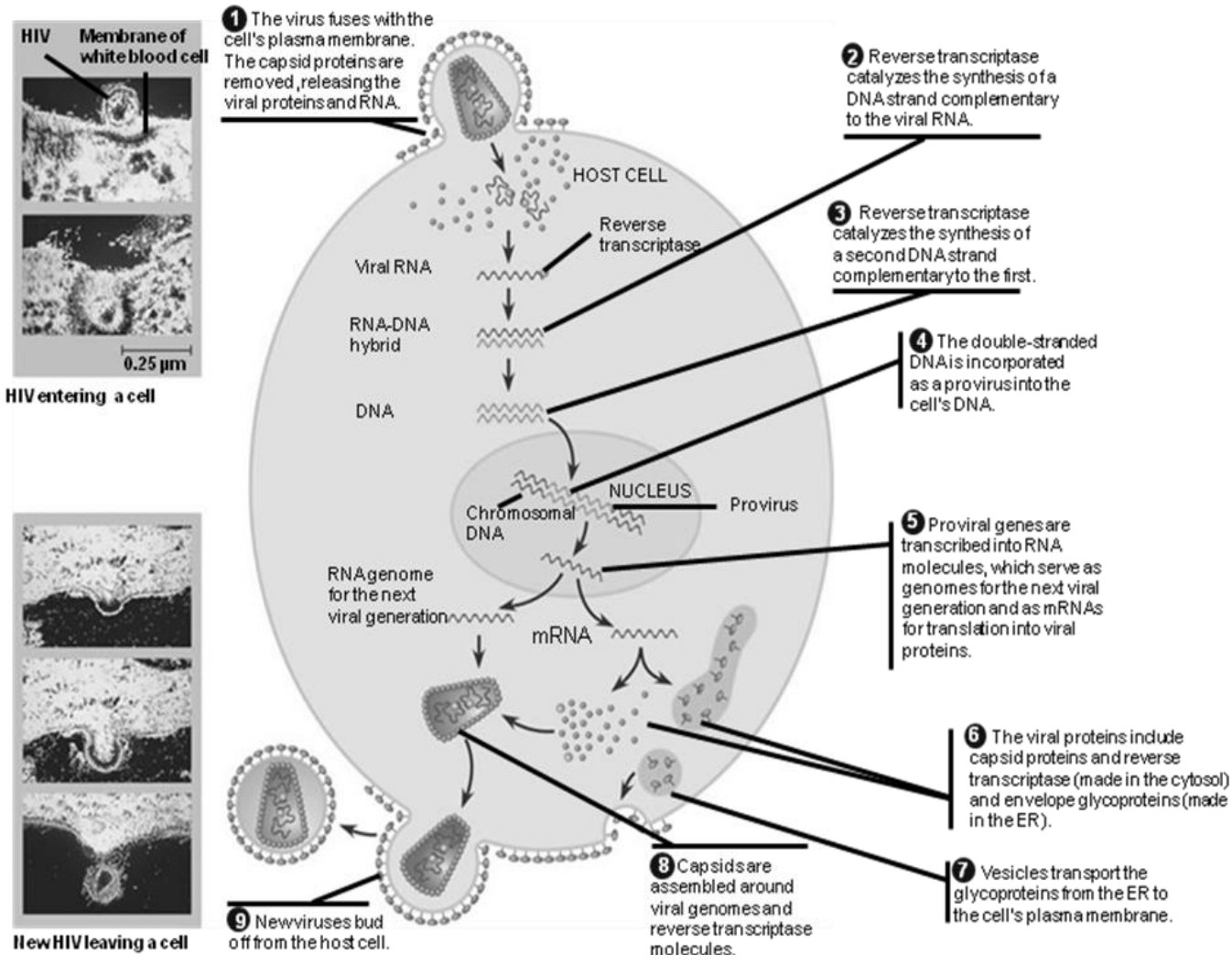
- Translation of mRNA leads to the synthesis of gp120, gp 41 and immature viral polyproteins.
- gp120 and gp41 are incorporated into the cell surface membrane to form 'exit points' for new viral particles.
- Immature viral polyproteins are transported to these 'exit points'.

4. Release

- Viral particles **bud off** from the host cell's membrane at these 'exit points' and acquire viral envelopes with gp120 and gp41.
- The immature viral particles are released in large numbers outside the host cell. However, they are not infectious until particle maturation

5. Maturation

- Maturation of viral particles occurs in the forming bud, or after immature viral particles bud off from the host cell.
- During maturation, HIV protease cleaves the immature polyproteins into individual functional HIV proteins, giving rise to functional capsid proteins, reverse transcriptase and integrase.
- The various structural components are then assembled within the viral envelope to form mature HIV viral particles which can then infect other host cells.



Reproductive cycle of HIV. Electron micrographs on the left show HIV entering and leaving a human white blood cell.

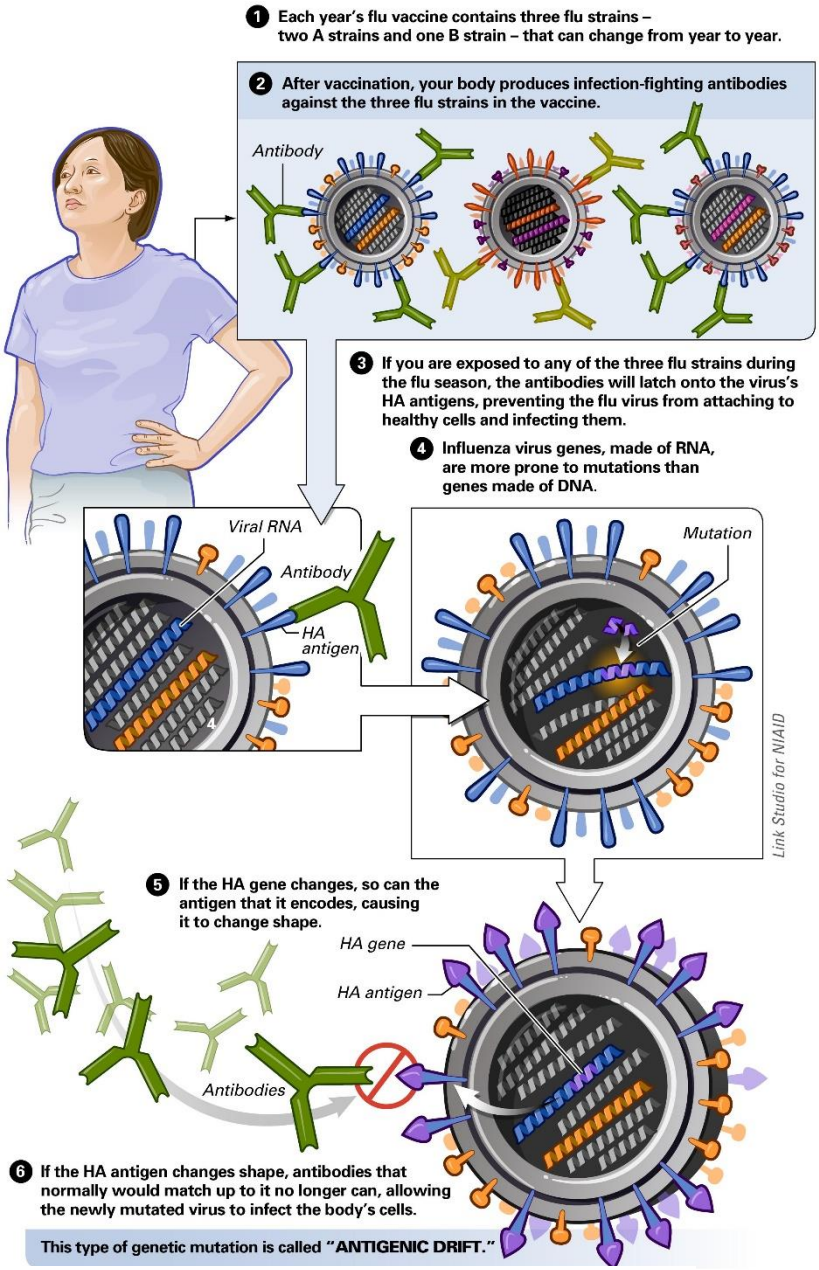
E. Comparison of reproductive cycles of viruses

Features	**T4 phage** *(Virulent phage)*	**λ phage** *(Temperate phage)*	**Influenza**	**HIV**
Type of host	*Escherichia coli* bacteria	*Escherichia coli* bacteria	Birds, pigs and mammals – epithelial cells lining mucous membranes of respiratory tract	Human immune cells expressing the CD4 cell surface receptor, e.g. T helper cells
Viral Envelope	Absent	Absent	Spherical / ovoid; derived from host cell surface membrane	Spherical / ovoid; derived from host cell surface membrane
Type of proteins attached to viral envelope	-	-	Haemagglutinin and neuraminidase	Envelope protein comprising glycoprotein 120 (gp120) and glycoprotein 41 (gp41)
Capsid	Complex; comprising icosahedral head, tail sheath with baseplate and tail fibres	Complex; comprising icosahedral head, tail sheath with 1 short tail fibre	Helical	Conical
Viral Genome	Single linear dsDNA	Single linear dsDNA	8 distinct linear segments of ssRNA (-)	2 identical linear copies of ssRNA (+)
Enzymes enclosed in capsid	-	-	RNA-dependent RNA polymerase	Reverse transcriptase, integrase, HIV protease
Key features of reproductive cycle	Lytic, i.e. results in osmotic lysis of host cell; dsDNA transcribed to give mRNA for viral protein synthesis	Lytic, i.e. results in osmotic lysis of host cell; dsDNA transcribed to give mRNA for viral protein synthesis or Lysogenic, i.e. genome incorporated into bacterial chromosome as prophage Most prophage genes repressed by λ repressor and not transcribed	Viral RNA-dependent RNA polymerase uses ssRNA (-) as template to synthesise ssRNA (+), which serves as mRNA and templates for viral genome replication	Viral reverse transcriptase uses ssRNA (+) as template to synthesise viral dsDNA via reverse transcription Viral integrase incorporates viral dsDNA into host cell's chromosome as provirus Host cell machinery transcribes provirus transcribed into viral mRNA and new copies of viral genome Viral HIV protease cleaves immature polyproteins into individual functional capsid proteins, integrase and reverse transcriptase

IV. VARIATION IN VIRAL GENOMES

A. Antigenic Drift

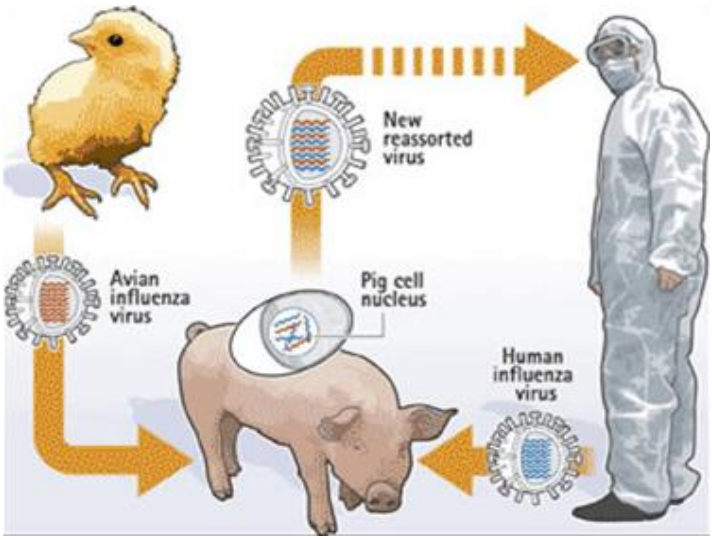
- Antigenic drift results when genes coding for the antigens of viruses undergo numerous **mutations**, leading to a change in the antigenic properties of the virus.
- A newly mutated virus antigen can evolve, which the body's immune system fails to recognise. As a result, the body cannot effectively deal with the infection.
- As a result of antigenic drift, the components of flu vaccines are reviewed on a yearly basis in order to keep up with the evolving viruses.



Source:
http://www.niaid.nih.gov/SiteCollectionImages/topics/flu/AntigenicDrift_HiRes.jpg

B. Antigenic Shift

- Antigenic shift results when there is a sudden and abrupt change in the antigenic properties of a virus, as a result of **genetic recombination** of viral genomes from different strains. These strains may originally infect different species altogether.



- Influenza virus strains, for example, can have many types of haemagglutinin and neuraminidase glycoproteins. They are thus classified by the types of these glycoproteins present (e.g. H5N1, H7N9).
- When a single cell in an animal is infected with more than one strain of influenza virus, the different strains can undergo **genetic recombination** if the RNA molecules making up their genomes reassort during viral assembly.
- This leads to an emergence of a novel strain with an unusual combination of antigens that is capable of infecting humans.
- Not having been exposed to the novel strain before, humans will lack immunity towards it, and the recombinant virus has the potential to be highly pathogenic.
- The 2009 H1N1 Swine Flu pandemic was a result of genetic recombination of influenza strains of swine, avian and human origins.

V. VIRAL INFECTIONS

A. How viral infections cause diseases

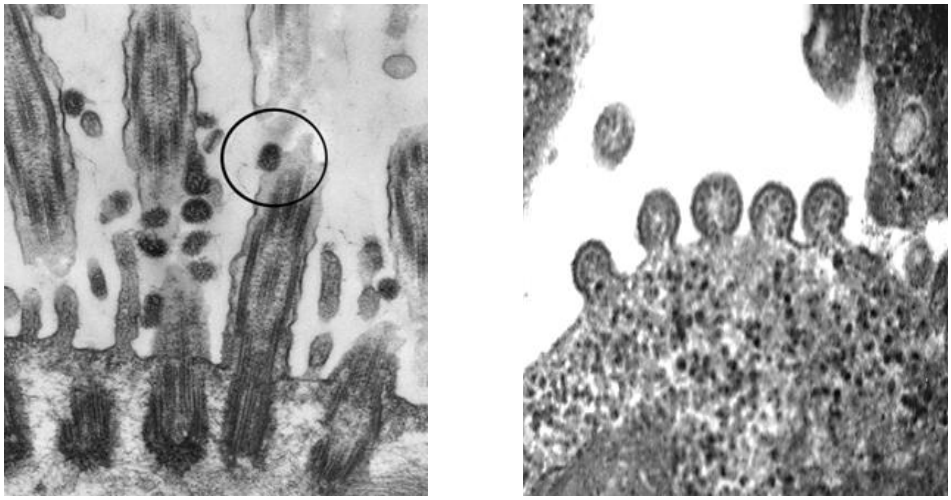
Viruses produce disease in their hosts via different mechanisms:

1. Viruses can cause cell lysis and thus cell death as they replicate in the host. In multicellular organisms, when enough cells and tissues are destroyed, the entire organism suffers larger scale effects from failure of various physiological functions.
2. Viruses can inhibit normal host cell processes, e.g. DNA, RNA and protein synthesis, resulting in structural and/or functional defects. These defects may lead to grossly altered cell functions, which trigger programmed cell death, also known as **apoptosis**.
3. Viruses deplete essential cellular materials, e.g. energy resources, amino acids, nucleotides, that are necessary for normal functioning of host cells.
4. Viruses can cause chromosomal damage in host cells by causing chromosomal gaps or nicks.
5. Viruses can disrupt the normal functioning of host genes by integrating their genetic material into the host chromosome.
6. Viruses can lead to oncogenesis, i.e. development of cancer. Integration of viral genetic material into host cells may donate an oncogene to the cell, disrupt a tumour-suppressor gene, or convert a proto-

oncogene to an oncogene. Some viruses also produce proteins that inactivate tumour-suppressor proteins, making the cell more prone to being cancerous.

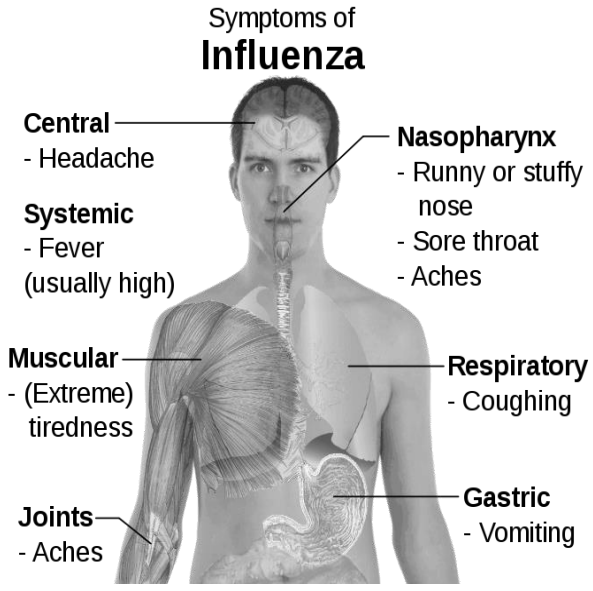
7. Viruses can alter the host cell surface membrane by inserting viral proteins, resulting in the host cell being recognised as foreign and getting destroyed by the immune system.
8. Viruses can induce infected host cells to produce toxins that lead to disease symptoms.

B. Impact of influenza infection



Left: Several viral particles (one is circled) attached to an infected ciliated epithelial cell. Right: Five viral particles budding from an infected cell.

- The influenza virus specifically targets epithelial cells making up the mucous membranes of the respiratory tract resulting in the disease known as influenza.
- In the young, elderly or individuals with weak immune systems, influenza can invade the lungs, causing the more severe condition known as pneumonia. More virulent strains, e.g. H5N1, may bind more readily to receptors found deep in the lungs, and thus infect lung epithelial cells.
- Once epithelial cells are infected, viral reproduction occurs and viral particles are released to infect other nearby cells.
- Hijacking of cellular machinery and resources towards producing new viral particles disrupts normal activities needed for cell survival, eventually causing cell death. Budding of a large amount of viral particles from the cell surface might also disrupt the cell surface membrane sufficiently for host cell to die.
- Damage of epithelial tissue reduces the efficiency of ciliary clearance, leading to impaired sweeping of mucus to the pharynx.
    - Mucus thus accumulates in the respiratory tract, causing symptoms like nasal congestion, cough and breathing difficulties.
    - This also reduces the efficiency of removing infectious agents from the tract.



- At the same time, huge amounts of pro-inflammatory cytokines and chemokine[6] are produced from influenza-infected cells, causing symptoms such as fever, headaches and fatigue.

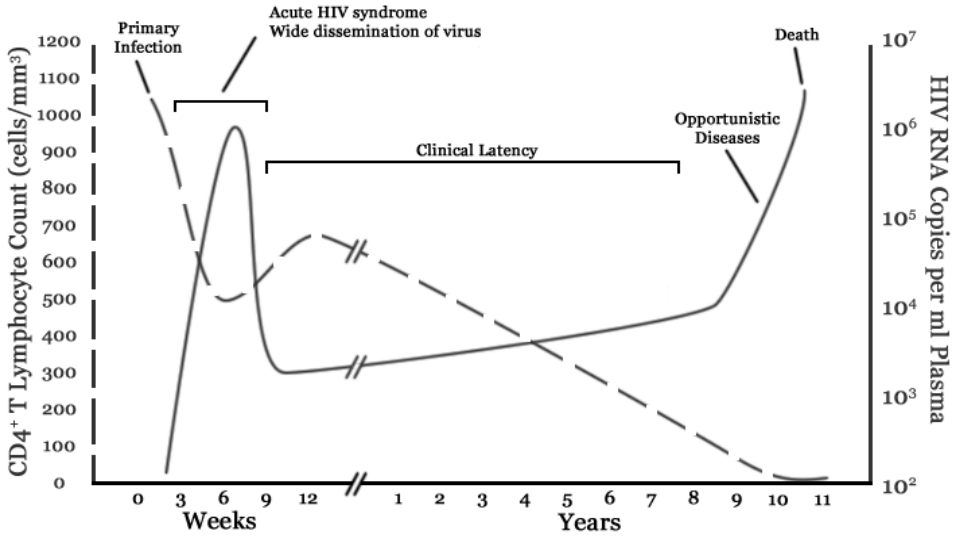
Symptoms of influenza

Checkpoint 3:

Why swine-origin influenza (H1N1) is capable of infecting humans even though viruses are said to be host-specific?

C. Impact of HIV infection

- HIV specifically infects human immune cells that contain the CD4 cell surface protein – especially **lymphocytes** (white blood cells) called **T helper cells**.
  - T helper cells are involved in recognising pathogens that invade the body, and subsequently activating and directing other immune cells to bring about an immune response to combat these pathogens.
- Eventually, HIV infection causes destruction of T helper cells by the following mechanisms:
  - T helper cells infected by HIV may be killed when a large amount of viral particles are produced by a cell. Hijacking of cellular machinery and resources towards producing new viral particles disrupts normal activities needed for cell survival.
  - Budding of a large amount of viral particles from the cell surface might disrupt the cell surface membrane sufficiently for the cell to die.
  - Grossly altered cell functions in infected T helper cells may trigger the cells to die via programmed cell death, i.e. apoptosis.



Levels of T lymphocyte count and viral RNA copies following HIV infection

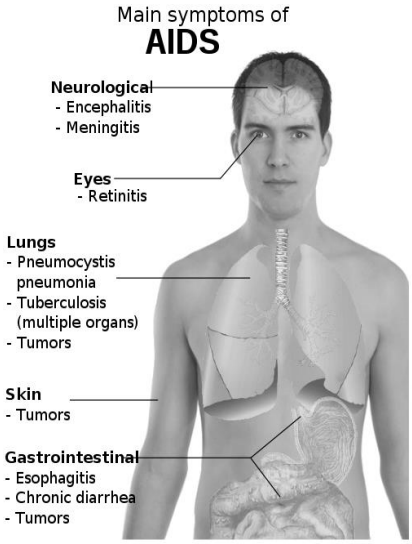
[6] Inflammatory chemokines and cytokines function mainly as chemoattractants recruiting various leukocytes from the blood to sites of infection or tissue damage.

- As HIV continues to replicate in the individual, <u>functional T helper cell levels decline to a critical point</u> where the T cell population is too small to effectively recognise various pathogens and trigger an efficient immune response against them. The immune system is thus said to be **compromised**. This leads to the core symptoms of **Acquired Immunodeficiency Syndrome (AIDS).** AIDS is diagnosed if T cell count falls below 200 cells/ mm^3 (Healthy range: 500-1500 cells/ mm^3).
- AIDS is characterised by:
  - <u>Opportunistic infections</u> by pathogens that bypass the immune system, causing diseases that would not normally occur in individuals with normal immune systems.

    E.g. *Pneumocytis* pneumonia is an opportunistic infection by *Pneumocytis* fungus.
  - Increased risk of developing various <u>cancers</u> due to inability of the immune system to remove cancer cells, or to ward off infections by oncogenic viruses.

    E.g. Kaposi's sarcoma is a cancer that develops from cells lining lymph or blood vessels. It is caused by a herpes virus.

    E.g. Cervical cancer, caused by the human papillomavirus (HPV), is common among women with AIDS.
  - <u>Systemic symptoms</u> of infection and malignancies, e.g. fevers, night sweats, chills, swollen glands, exhaustion and weight loss.



Symptoms of AIDS

Checkpoint 4:
Why is HIV a deadly virus with no cure for it currently?