GENERAL CHARACTERISTICS AND STRUCTURE OF VIRUSES

Lecture Objectives:

By the end of this instructional period, the students will be able to:

- Explain why viruses are classified as acellular, obligate intracellular parasites.
- Describe and label the essential components of a virus.
- Describe the key differences between virulent and temperate bacteriophages.
- Outline and describe the stages of the lytic and lysogenic cycle of bacteriophage replication.

What is a virus?

Viruses are the **smallest infectious agents** whose genomes consist of **deoxyribonucleic acid (DNA) or ribonucleic acid (RNA)** and that are absolutely **dependent** on living cells for their replication.

Are viruses living or non-living?

Why Viruses Are Considered "Non-Living"

1. **No Cell Structure:** They lack cellular structure. They consist solely of genetic material (DNA or RNA) encased in a protective protein shell (capsid), sometimes with a lipid envelope.
2. **Metabolic Deficiency**: They are incapable of generating their energy (ATP) or synthesizing proteins due to the absence of cellular organelles such as ribosomes and mitochondria.
3. **Lack of Autonomous Reproduction:** Viruses are incapable of dividing or proliferating independently. They are "obligate intracellular parasites," which means that to create new virus particles, they must take over and alter a living host cell.
4. **Inert Outside a Host**: When located outside a live host (for instance, on a surface), viruses exhibit no responsiveness to stimuli, do not proliferate, and fail to sustain internal equilibrium (homeostasis). Many viruses can be crystallized, a property typically associated with non-living matter such as minerals.

Why Viruses Are Considered "Living"

1. **Genetic Material:** Viruses possess nucleic acids (DNA or RNA), a trait common to all living species.
2. **Replication:** Viruses may reproduce and proliferate; however, they must commandeer a host cell to achieve this.
3. **Evolution and Adaptation:** Viruses undergo mutations and develop throughout time, adjusting to their habitats to circumvent immune systems (e.g., influenza).
4. **Complex Structure:** They have a protein covering (capsid) and occasionally a lipid envelope, functioning as organized living entities rather than mere chemical compounds.

General characteristics and properties of viruses:

Size: Viruses are measured in nanometres (1 nanometre = 10^{-9} meters). Their size ranges from 20 nm to 300 nm. They pass through filters that retain the smallest bacteria and cannot be seen with a light microscope; they require an electron microscope.

Lack of Organelles: Viruses lack cellular organization. They lack a cytoplasm, a cell wall, or any cellular organelles.

Genetic Material: Viruses contain either DNA or RNA, but a single species of virus will never contain both. Their genome size is relatively small, ranging from 2 kbp to 200 kbp (kilobase pairs).

Obligate Intracellular Parasites: Viruses cannot replicate or carry out metabolic processes outside of a host cell. They rely entirely on the host's machinery (ribosomes, ATP, enzymes).

Replication Method: Viruses do not multiply by binary fission (cell division, as in bacteria). Instead, they reproduce through a complex process of directed protein synthesis and nucleic acid production within a host.

Host Specificity: Viruses are highly selective. They usually infect only specific host organisms or specific cell types within that host. For example, some plant viruses infect only tobacco leaves; bacteriophages infect only bacteria. The interaction between viral surface molecules and host cell receptors determines this specificity.

Host Range: Viruses infect all life forms, from animals and plants to microorganisms, including bacteria and archaea. Viruses that infect only bacteria are called **bacteriophages**, and those that infect only fungi are termed **mycophages**.

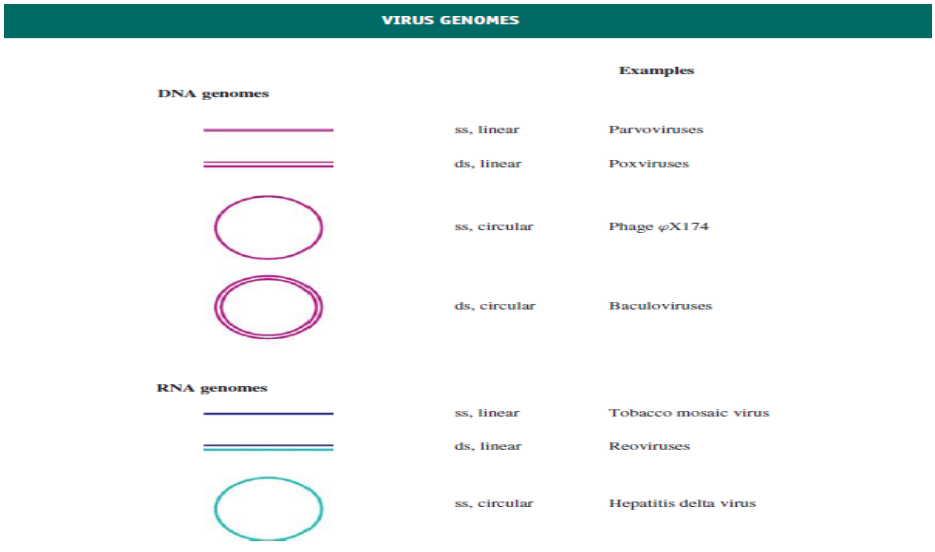
Structure of Viruses:

- A virus particle, or virion, consists of **nucleic acid (DNA or RNA)** enclosed by a protein coat called a **capsid.** The nucleocapsid can either be naked or enclosed by a membrane termed **an envelope.**

Viral Genome:

Viral nucleic acid contains the genes necessary to direct infected cells to synthesize viral components and replication enzymes.

- The viral nucleic acid (genome) consists of four possible nucleic acid types: single-stranded (ss) DNA, double-stranded (ds) DNA, single-stranded RNA, and double-stranded RNA.
- Single-stranded viral RNA genomes are further divided into "positive polarity" (messenger RNA sense, which can serve as a template for protein synthesis) and "negative polarity," or antisense (complementary to messenger RNA sense, which cannot be directly used as a template for protein synthesis).
- Viral nucleic acid may be linear or circular.

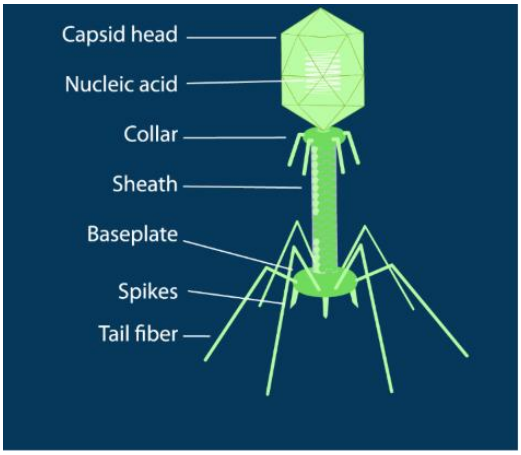


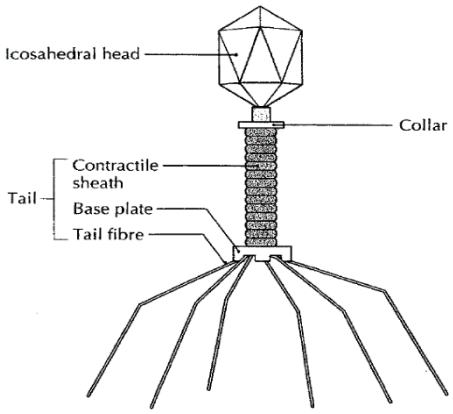
3.1 *Linear and circular viral genomes.*
ss: single-stranded
ds: double-stranded
There are no viruses known with circular dsRNA genomes

Capsid:

- The **capsid** is a protective outer shell that surrounds the viral nucleic acid, and is made up of several subunits called **capsomeres,** which are further composed of a **protomere.**
- The structure of the nucleic acid genome and the capsid proteins is called the **nucleocapsid.**
- The nucleocapsid can either be naked or enclosed by a membrane called an envelope.
- A capsid consists of one or more proteins unique to the virus that determine its shape.
- The capsid serves to:
    - protect the viral genome from harmful environmental factors, including UV light and desiccation, as well as from the acids and degradative enzymes encountered in the host's gastrointestinal tract.
    - mediates attachment to specific receptors on the host cell surface. This interaction between viral proteins and the cellular receptor is the primary determinant of species- and organ-specificity.
    - stimulates the production of neutralizing antibodies and activates cytotoxic T cells that kill virus-infected cells.
- **Capsid symmetry:**
    - Capsomers are arranged symmetrically into capsid shapes: icosahedral and helical.
- **Helical capsid**:
    - A helical capsid is composed of a single type of capsomer stacked around a central axis to form a helical structure, which may have a central cavity or hollow tube.
    - Most of the helical viruses are enveloped, and all are RNA viruses.
    - The typical virus with helical symmetry is tobacco mosaic virus (TMV), which is an RNA virus with 2130 identical capsomeres arranged in a helix.
- **Icosahedral capsid**:
    - An icosahedral capsid is a regular three-dimensional shape with 20 triangular faces and 12 points or corners. The capsomeres of each face form an equilateral triangle.
    - The icosahedral capsid is the most stable and is found in human-pathogenic viruses, e.g., Adenovirus, picornavirus, Papovavirus, Herpes virus, etc.

- **Complex viruses**
    - Some viruses are more complex, composed of several parts, each with distinct shapes and symmetries.
    - Examples of the most structurally complex viruses are found among bacterial viruses (bacteriophages), which have icosahedral heads and helical tails, and the poxvirus.



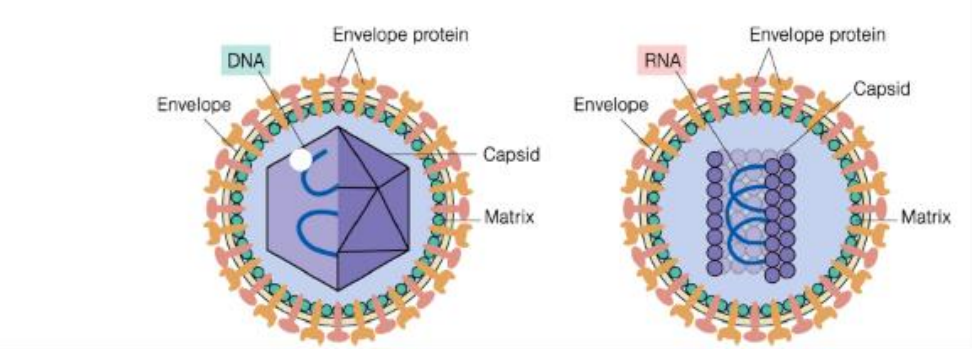


Envelope:

- An envelope is a lipid bilayer membrane that some viruses have outside their capsids.
- • The lipid bilayer is derived from host cell membranes during viral release, but virus-specific proteins replace the proteins.
- In enveloped viruses, capsomeres come together to form structures called "spikes" or "peplomers" that stick out from the lipid bilayer of the envelope.
- A virus that is not enveloped is called a **non-enveloped** virus, **nucleocapsid,** or **naked** virus.
- A naked virus exhibits greater resistance to environmental changes and is less susceptible to conditions that can damage the enveloped viruses. This is because it lacks

a fragile outer lipid membrane; instead, its genetic material is protected solely by a capsid.

- Environmental factors that can damage the envelope include elevated temperatures, freezing temperatures, pH below 6 or above 8, lipid solvents, and certain chemical disinfectants, including chlorine, hydrogen peroxide, and phenol.



Replication of Viruses:

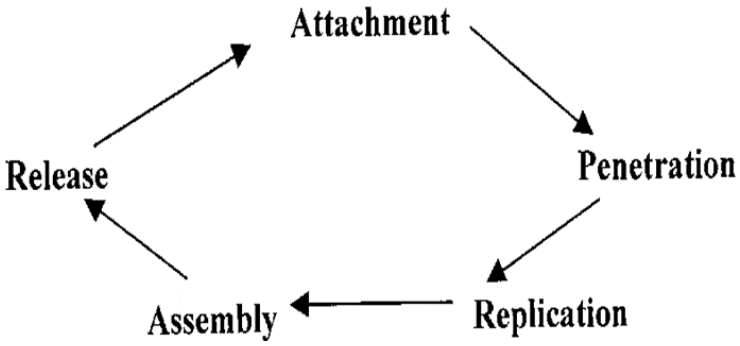
- Viral replication cycles follow the same general sequence of events with some differences from one type to another, determined by viral structure and the nature of the host cell.
- The life cycle of bacteriophages serves as an excellent model for understanding viral replication.
- The most studied bacteriophage is the T-even bacteriophage, a class of bacteriophages that infects *E. coli*.
- Bacteriophages can replicate through either a lytic or a lysogenic cycle and are categorised by their replication strategy as either virulent or temperate phages.

- **Virulent phages** adopt the lytic cycle, leading to the death of the host cell through cell lysis. On the contrary, t**emperate phages** can choose between the lytic and lysogenic cycles after infecting a host.
- The host cell dies at the end of the lytic cycle. In contrast, in the lysogenic cycle, phages integrate their genome into the host chromosome, where it remains dormant until induced to produce newly assembled viruses (progeny viruses).

Lytic Replication of Bacteriophage:

- The T-even bacteriophages are composed of a head-and-tail structure and contain double-stranded DNA genomes.

- During the lytic cycle, a virulent bacteriophage takes over the host cell, drives the synthesis of new phage components, assembles new phages, and ultimately destroys the host cell to release its progeny.
- The lytic cycle can be broken down into five distinct stages:



Attachment (Adsorption):

- Adsorption is the initial stage; the phage interacts with specific bacterial surface receptors, such as lipopolysaccharides or particular outer membrane proteins, with its tail fibres.
- The interaction between viral receptor-binding proteins and their corresponding receptors on the host cell contributes to host specificity.

Penetration (Entry):

- After attachment, bacteriophages use an enzyme called lysozyme in their tails to break down the bacterial cell wall, then use their tails like hypodermic needles to inject their DNA (nucleic acid) into the bacterium.
- The phage head (capsid) and other remaining components typically stay outside the bacterium.

Replication (Biosynthesis):

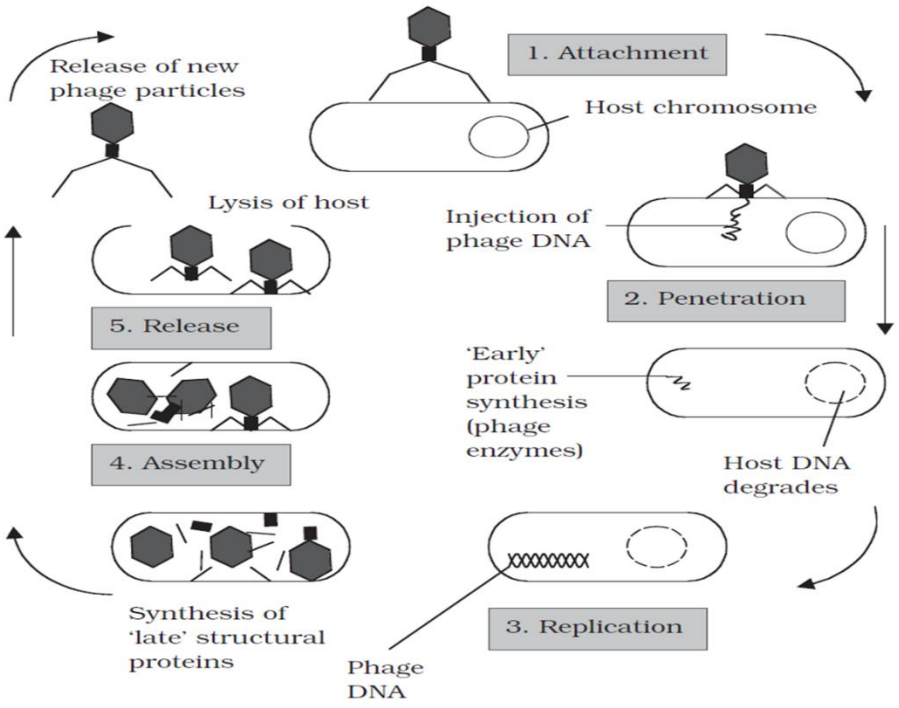
- Immediately the viral DNA has entered the host cell, it produces endonucleases (enzymes) that degrade the host bacterium's chromosome, leaving the viral genome as the primary template for the cell's machinery.
- The phage then hijacks the host cell's machinery for the synthesis of phage DNA and proteins.

Assembly (Maturation):

- During this phase, the newly synthesised viral components (genomes and proteins) self-assemble into complete new viral particles, or virions.
- Non-enveloped viruses are subsequently present in the host cell as fully developed virions, while enveloped viruses acquire their envelope from the plasma membrane during release

Release (Lysis):

- This is the final stage, when the newly assembled mature viruses burst out of the host cell.
- Phage-encoded proteins disrupt the bacterial cell wall, releasing progeny viruses into the environment, ready to infect new susceptible host cells and repeat the cycle.
- This process, called lysis, results in the death of the host cell.



Lysogenic Replication of Bacteriophage:

- In a lysogenic cycle, the phage genome also enters the cell through attachment and penetration, as in the lytic cycle. However, rather than immediately hijacking the cell for rapid replication and causing lysis, the phage genome integrates into the host genome.

- The presence of a prophage in the host cell can alter the phenotype (observable characteristics) of the host bacterium because the prophage can carry additional genes.
- This change in the host's phenotype due to the prophage is called **lysogenic conversion** or **phage conversion**.
- *Vibrio cholerae*, the causative agent of cholera, and *Clostridium botulinum*, responsible for botulism, show reduced virulence when their respective prophages are absent.
- These phages carry toxin genes in their genomes; for example, phage-encoded toxins in *V. cholerae* induce severe diarrhoea, whereas those in *C. botulinum* cause paralysis
- The lambda (λ) phage is a classic example of a temperate phage capable of lysogeny.

Attachment and Penetration:

- These initial steps are similar to the lytic cycle, where the phage attaches to the host cell and injects its DNA.

Integration (Prophage Formation):

- The temperate phage's DNA **integrates** into the bacterial chromosome at a specific site.
- The integrated phage genome is now called a **prophage**, while the host cell that harbours a prophage is known as a **lysogen**.

Replication with Host (Cellular Propagation):

- The prophage is typically **latent** or inactive within the host cell in terms of producing new virions.
- As a lysogenic bacterium replicates its own chromosome (e.g., during binary fission), the prophage genome is then passively replicated along with the host genome and passed on to all new daughter cells during cell division.

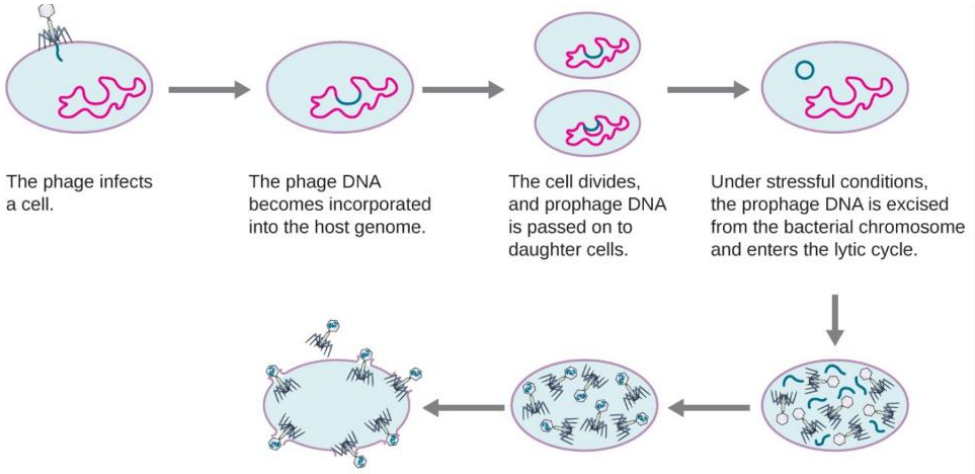
Induction:

- The prophage can persist within the host chromosome for many generations. However, under certain conditions, often triggered by environmental stressors (e.g., starvation, exposure to UV radiation, or toxic chemicals), the prophage can be induced.
- Induction results in the excision (cutting out) of the viral genome from the host chromosome to become an independent, circular molecule again.

Switch to the Lytic Cycle:

- After induction and excision, the temperate phage can then enter a lytic cycle.

- The now-active viral DNA directs the biosynthesis of new viral components, assembles new virions, and ultimately causes lysis of the host cell, releasing the newly formed phages.
- These released phages can then infect new host cells, where they may again enter either the lytic or lysogenic cycle, depending on the conditions.



Difference between the Lytic and Lysogenic Cycles

Feature	**Lytic Cycle**	**Lysogenic Cycle**
Viral Activity	Active and immediate (virulent).	Dormant (lysogency)
Host Cell Fate	**Destroyed**. The cell bursts (lyses) to release virions.	**Survives**. The cell continues to divide and function normally.
Viral DNA	Remains separate from the host's DNA	Integrated directly into the host genome as a prophage.
Reproduction Speed	Rapidly hijacks host machinery to mass-produce viruses immediately	Slow; viral DNA is quietly copied every time the host cell divides
Replication	Viral particles are synthesized and assembled independently of host DNA.	The viral DNA is copied automatically every time the host cell divides.
Transition Triggers	It is immediately active.	Stress or environmental changes can cause the virus to exit lysogeny and enter the lytic cycle.

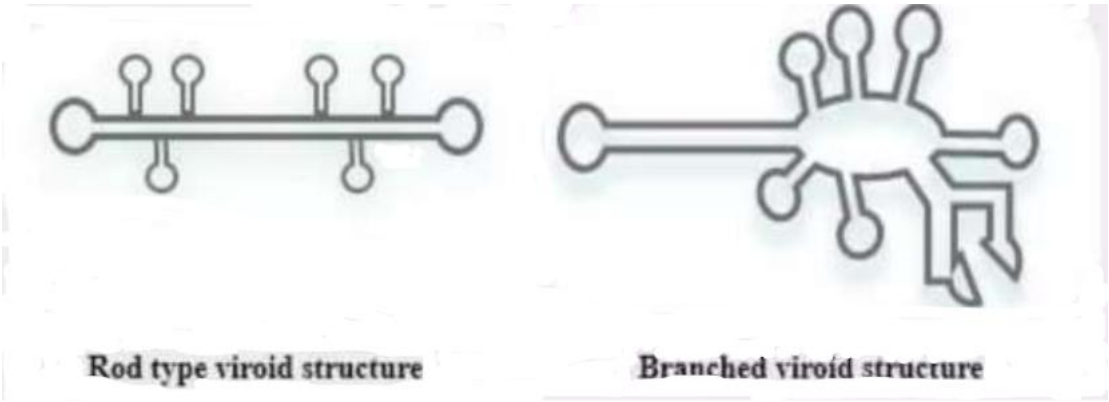
Atypical Virus-Like Particles

Viroids:

Viroids are small, infectious, circular, single-stranded RNA particles that cause disease in plants. Viroids consist of a single circular, single-stranded RNA molecule without a protein coat or envelope. They replicate and cause several diseases in plants, but not in humans.

In 1971, Theodor Diener, a pathologist at the Agriculture Research Service, discovered an acellular particle that he named a viroid, meaning "virus-like." The first viroid discovered causes potato spindle tuber disease, which leads to delayed sprouting and various deformities in potato plants. Viroids have two distinct structural types: rod-like and multibranched

Like a virus, a viroid invades a cell and hijacks its reproductive machinery to replicate its RNA. Unlike a virus, a viroid is the smallest known pathogen (2 nm wide and 40–130 nm long), composed solely of closed, circular ssRNA, lacking a protein coat (capsid), and infecting only plants.

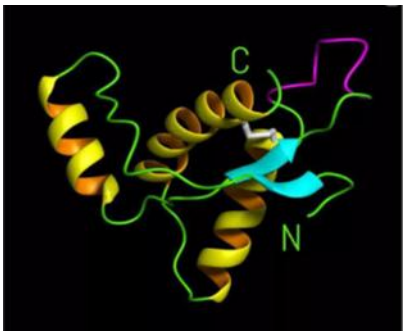


Prions:

Prions are infectious proteins whose extracellular forms contain no nucleic acid and no envelope. In 1982, Stanley Prusiner, a medical doctor, discovered prions (received the Nobel Prize in Physiology or Medicine in 1997). Normal prions contain 200 – 250 amino acids twisted into three helical coils, known as helices, with tails of more amino acids

Prions cause various forms of transmissible spongiform encephalopathy (TSE) in human and animals. TSE affects the brain and nervous system. It causes the brain tissue to become sponge-like, kills brain cells, forms holes in the tissue, leads to brain damage, loss of motor

coordination, and dementia. Infected individuals are mentally impaired and become unable to move or speak. There is no cure, and the disease progresses rapidly, eventual lead to death. TSEs can be transmitted between animals and from animals to humans by eating contaminated meat or animal.



Pseudoviruses:

A pseudovirus is an artificially engineered viral particle that mimics the structure and entry mechanism of a real virus but lacks the pathogenic genetic material required to replicate. Pseudoviruses contain host DNA instead of viral DNA; they infect the host cell but don't replicate. Pseudoviruses are widely employed in the mechanistic investigation of viral infection.

Defective viruses

Defective viruses contain viral nucleic acid and proteins but cannot replicate without a helper virus**.** Satellite viruses are defective viruses for which no intact version exists; they rely on helper viruses for replication. An example is the Delta agent, which is expressed only in the presence of the hepatitis B virus.