

Introduction to Virology

Historical Background

Modern virology originated in the late 1880s with the pioneering work of Adolf Mayer, Dmitri Ivanovsky, and Martinus Beijerinck, who independently investigated tobacco mosaic disease and identified the agent later known as tobacco mosaic virus (TMV). Their findings revealed the existence of filterable infectious agents—too small to be seen by light microscopy and unable to grow on conventional bacteriological media—that could cause disease only by infecting living cells. The first animal virus, foot-and-mouth disease virus, was described by Friedrich Loeffler and Paul Frosch in 1898. Shortly afterwards, in 1901, Walter Reed identified yellow fever virus, the first human virus to be discovered.

The term *virus*, derived from the Latin word meaning “poison” or “viscous fluid,” gradually replaced the earlier expression “filterable agent.” In 1939, TMV became the first virus to be visualized by electron microscopy; in 1941, X-ray crystallography revealed its highly ordered, repetitive structure. In 1915, Frederick Twort discovered filterable agents capable of lysing bacteria; Félix d’Hérelle independently made similar observations and introduced the term *bacteriophage*. D’Hérelle also described key aspects of the phage life cycle, including viral adsorption to host cells, cell lysis, and the release of infectious progeny particles.

Research on bacteriophages during the following decades provided major insights into viral replication, the regulation of host-cell metabolism, and the mechanisms by which viruses redirect cellular biosynthesis. These studies contributed substantially to the emergence and development of molecular biology.

II. Definition

The word *virus* is derived from Latin and means “poison.” Viruses are associated with all forms of life, infecting bacteria, archaea, and eukaryotes.

A virus is an obligate intracellular parasite and infectious agent whose genome consists of either DNA or RNA. This viral genome directs its own replication and the synthesis of other viral components by exploiting the biosynthetic machinery of a suitable host cell. The newly synthesized components assemble within the infected cell to form viral particles, known as virions. The virion serves as the vehicle for transmitting the viral genome to a new host cell or organism; upon entry, its disassembly initiates a new infectious cycle.

A minimal virus consists of:

- A genome containing an origin of replication.
- A protein shell, called the capsid, which protects the viral genome.

In enveloped viruses, the capsid is surrounded by a lipid bilayer derived from the host-cell membrane and studded with viral glycoproteins. These glycoproteins often mediate attachment to host-cell receptors and entry into susceptible cells.

Finally, viruses are entirely dependent on host cells for the biosynthesis of proteins and other macromolecules required to complete their life cycle. Because they lack the metabolic and translational machinery necessary

for independent replication, they must hijack host-cell systems to produce viral proteins, replicate their genomes, and assemble progeny virions.

III. Origins of viruses

Viruses are thought to have emerged through several mechanisms during the history of life.

- The RNA-world hypothesis proposes that self-replicating RNA molecules existed before the evolution of cellular organisms. Parasitic genetic elements likely coexisted during this period. Among present-day genetic parasites, viroids appear to be the closest relatives of these primitive agents.
- Some viruses may have originated from intracellular DNA elements, such as transposons, that acquired the ability to exist outside the cell and spread between cells.
- Other viruses, including poxviruses, may have evolved through reductive evolution from more complex microorganisms, progressively losing genes and becoming dependent on host cells.

IV. Composition of viruses and viral components

A complete, infectious viral particle is called a virion. Its essential role is to protect the viral genome in the extracellular environment and to deliver it into a susceptible host cell, where viral replication can begin. A virion contains either DNA or RNA—never both—and its structural organization may be simple or highly complex.

IV.1. The viral genome

The viral genome is the genetic material of the virus. It may be composed of either:

- DNA, which may be single-stranded or double-stranded, linear or circular.
- RNA, which may be single-stranded or double-stranded, and, in the case of single-stranded RNA, positive-sense, negative-sense, or ambisense.

The genome carries the genetic information required for viral replication, synthesis of viral proteins, and assembly of progeny virions. It also contains regulatory sequences, including origins of replication, promoters, and signals for transcription, translation, and genome packaging. Viral genomes vary greatly in size and may consist of one or several nucleic-acid molecules.

IV.2. The capsid

The capsid is the protein shell that surrounds and protects the viral genome. It is composed of protein subunits called protomers, which associate to form larger structural units known as capsomeres. The capsid protects the genome from physical, chemical, and enzymatic damage, particularly from nucleases.

The capsid also participates in several stages of the viral life cycle:

- It contributes to the stability of the virion outside the host cell.
- In non-enveloped viruses, it often mediates attachment to specific receptors on the host-cell surface.
- It facilitates the entry or release of the viral genome into the host cell.
- It provides the structural framework for genome packaging during virion assembly.

The association between the viral genome and the capsid, sometimes together with associated viral proteins, forms the nucleocapsid.

The capsid may take one of three principal forms:

- **Helical capsids**, in which capsomeres are arranged in a helical pattern around the viral genome, forming a rod-shaped or filamentous nucleocapsid. This organization is observed, for example, in tobacco mosaic virus (TMV) and in many negative-sense RNA viruses such as influenza and rabies viruses.
- **Icosahedral capsids**, in which the protein subunits are arranged with icosahedral symmetry, producing an approximately spherical structure with 20 triangular faces and 12 vertices. This is the most common capsid organization among animal viruses and is found, for example, in adenoviruses, poliovirus, and herpesviruses.
- **Complex capsids**, which do not display simple helical or icosahedral symmetry. They possess more elaborate structures combining several components, such as the head-and-tail organization of many bacteriophages or the complex, multilayered architecture of poxviruses.

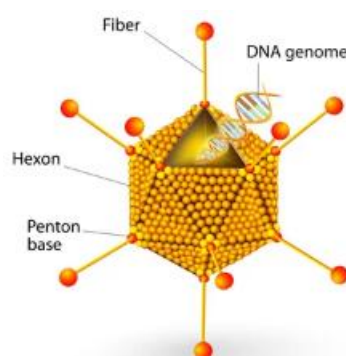
Thus, the capsid not only protects the viral genome but also determines the overall morphology of the virion. Its structure is closely related to the mode of genome packaging, host-cell recognition, and viral stability in the extracellular environment.

IV.3. Viral enzymes and internal proteins

Some virions contain enzymes or proteins that are essential for the initiation of infection. These components are incorporated into the particle during assembly and are released or activated after entry into the host cell.

Examples include:

- Reverse transcriptase in retroviruses, which converts viral RNA into DNA.
- Integrase in retroviruses, which inserts the viral DNA into the host-cell genome.
- RNA-dependent RNA polymerase in many negative-sense RNA viruses, which is required because host cells cannot replicate RNA from an RNA template.
- Proteases, which cleave viral polyproteins into functional proteins.
- Nucleoproteins, which bind viral nucleic acid and participate in genome protection, transcription, replication, and packaging.



This illustration shows the structure of an adenovirus, a non-enveloped virus with an icosahedral capsid. Its genome consists of double-stranded DNA (dsDNA), protected by a capsid composed mainly of hexons and pentons. The pentons are located at the vertices of the icosahedron and bear long projecting fibers, which enable the virus to recognize cellular receptors and attach to the host cell.

IV.4. The viral envelope

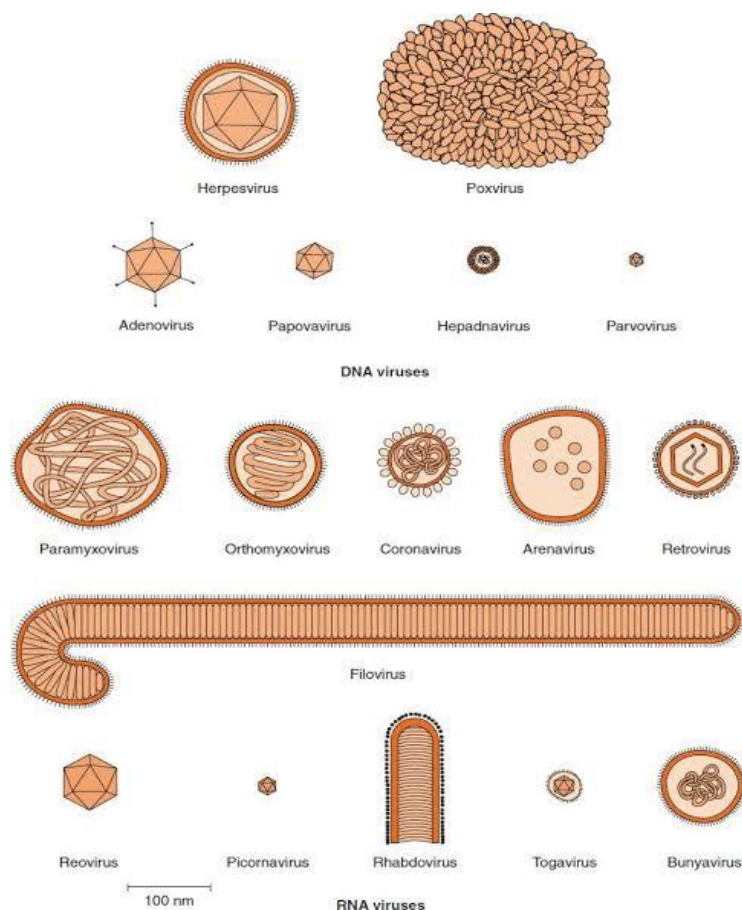
Some viruses, called enveloped viruses, possess an outer lipid bilayer surrounding the nucleocapsid. This envelope is generally derived from a host-cell membrane such as the plasma membrane, endoplasmic reticulum, Golgi apparatus, or nuclear membrane during the process of viral budding or maturation.

The envelope contains:

- Lipids, mainly phospholipids and cholesterol, derived from the host cell.
- Viral membrane proteins, inserted into the lipid bilayer by the virus.
- Viral glycoproteins, often exposed at the virion surface as projections called spikes or peplomers.

Viral glycoproteins are essential for many stages of infection. They mediate recognition of and attachment to specific host-cell receptors, membrane fusion or penetration, immune recognition, and, in some cases, release of newly formed virions.

Note: Non-enveloped viruses are generally more resistant to environmental conditions (desiccation, pH variations, and detergents), whereas enveloped viruses are more sensitive to these factors due to the fragility of their lipid envelope.



Shapes and sizes of some viruses