Viruses: Dead or alive?

Structure of a virus

Viruses are microscopic unistructural organisms that can infect host cells.

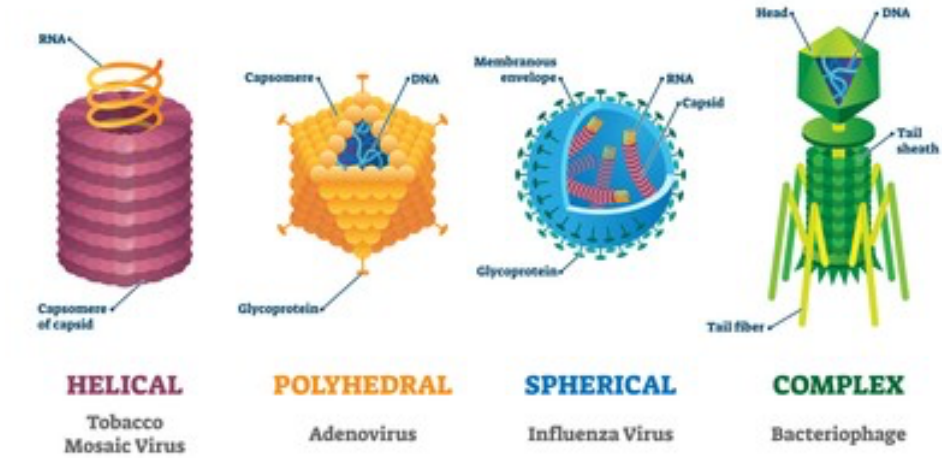
Whatever their type, they all have the following features:

- Genetic information, in form of DNA or RNA. A virus infects a host cell to be able to replicate this genetic information.

Note: The (D/R)NA molecules of a virus can be either single-stranded or double-stranded, and their length is highly variable (from app. 2500 nucleotides for the Geminivirus tobacco yellow dwarf virus, to almost 3 million pairs of bases for the pandoravirus).

- A capsid, which is a protein coat (capsomeres) surrounding the viral genome.
  It protects the genetic information, by shielding it from the host immune system, and also plays an essential role in the infection of the host cell.

Note: The capsid can exist in an important diversity of shapes, classified in 4 types.



The capacity for a virus to infect a specific host-cell depends on its shape.

- A series of enzymes, involved in several processes during the "life-cycle" of the virus:
  - Immune evasion:
    - *RNA-capping enzymes, found in Rhabdoviruses, modify viral RNA to avoid host immune detection*
    - *UL41, found in Herpesviruses, degrade host mRNA, thus weakening the host's immune system*
  - Genome replication and production of new virus organisms:
    - *Reverse Transcriptase (RT), found in retroviruses like HIV, convert RNA into DNA, which can then enter the host genome thanks to another enzyme, Integrase, allowing long-term infection.*
    - *Proteases, found in HIV- or polyoviruses cleave large polyproteins into functional individual proteins*
  - Entry and exit of the host cell:
    - *Hemagglutinin (HA), found in Influenza viruses, help the virus bind to the host cell and enter*
    - *Neuraminidase (NA), also found in Influenza viruses, help the new virus detach from the host cell*

Note: Some viruses (e.g. Coronaviruses like SARS-Cov-2, responsible for COVID-19) also have an envelope, made of a lipid bilayer, like the cell-membrane.
This envelope protects the viral genom, helps the virus to avoid immune detection and to bind and fuse with host cells (thanks to membrane fluidity), and allows the virus leave the host via budding. However, it makes the viruses vulnerable to detergents and drying.

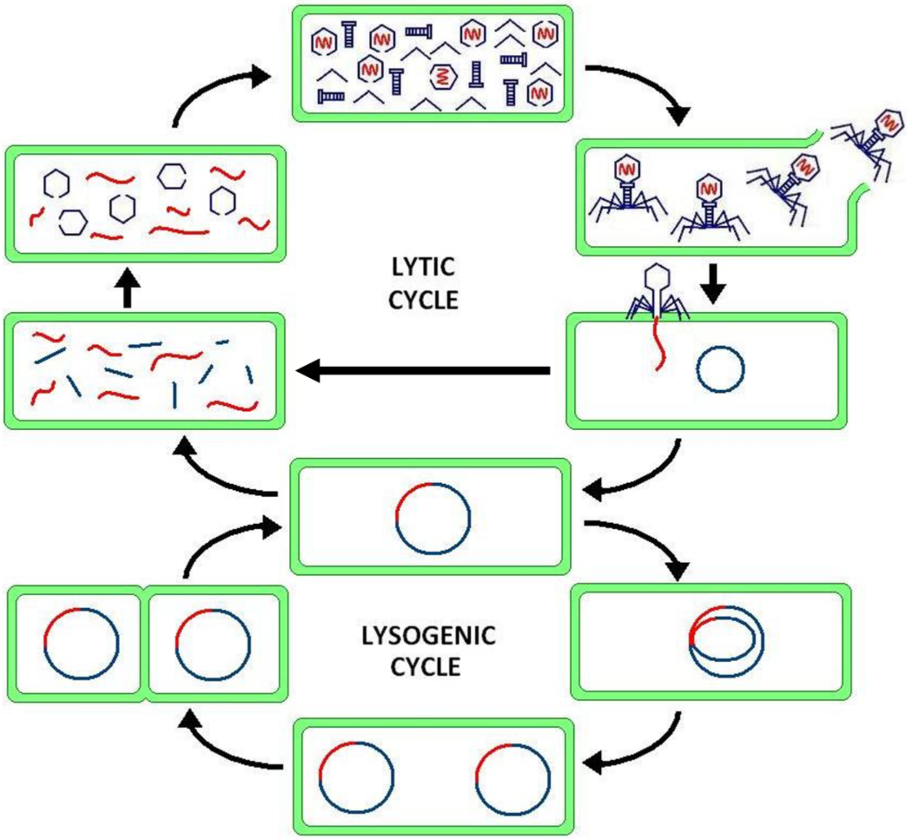
A reproduction process involving a host cell

A virus doesn't have the enzymes needed to replicate its genetic information and to produce the material needed for new individuals (capsid, envelope, …). Therefore, it infects a host cell to use its machinery. It is called the **lytic cycle** of the virus:

- The virus attaches to the host cell, and injects its genetic material
- The host cell replicates the viruses genome, and produces the proteins needed to form the capsid and eventually the lipids needed for the envelope.
- New individuals of the virus are assembled.
- The cell bursts (lysis), releasing these new individuals.

In some cases, the genetic material of the virus integrates the host's DNA (prophage). It is then dormant (inactive for days, weeks, years or even a lifetime). The host cell replicates normally, passing the viral DNA to its daughter cells. This is called the **lysogenic cycle**.

The virus is later activated by external triggers (hormonal changes, UV, immune suppression, …) and enters the last steps of the lytic cycle, making new viruses and destroying the host cell.



Dead or alive?

At the brisk between alive and not, a virus cannot reproduce without host cell. Therefore, it is considered as not alive regarding the actual definition of life.

Note: *often, a stable equilibrium is to be found b the virus between lethality and contagiousness:*

- *Too lethal => no host available anymore*
- *Symptoms too visible => isolation of infected individual => no host available anymore*
- *Infectivity rate too low => reproduction rate too low*

Therefore, often, the natural evolution of viruses leads to a decrease in death rate and an increase in infection rate.

Impact of viruses on life

Even if not alive, viruses have an important impact on their environment, both negative and positive:

- Some viruses lead to diseases or cancer.

Ex: The banana bunchy top disease is due to a virus transmitted by aphids. Once infected, a plant rarely produce fruit. In the 1920s, it almost completely destroyed the banana growing industry in Australia.
Almost all cervical cancer are due to a persistent Human PapillomaVirus infection. Studies on the vaccination against HPV shows a significant decrease in the appearance of these cancers.

- Some viruses cause a weakening of the immune system, making these organisms vulnerable to other infections.

Ex: HIV can lead to AIDS (Acquired ImmunoDeficiency Syndrom). The host's immune system is not able anymore to fight Opportunistic Infections, leading to a drastic decrease of life expectancy.

- The high spreading rate can lead to an important disruption of societies (e.g. Spanish Flu in the early 20th century).

Ex: The 1918-1920 flu pandemic was caused by the H1N1 subtype of the influenza A virus. Nearly a third of the world population (around 500 million people) had been infected, with an estimates of 17 to 50 million death (some estimations giving even a possibility of 100 million dead), making it one of the deadliest pandemics in human history.

- Through the insertion of their DNA into host genomes during the lysogenic cycle, viruses drive genetic diversity.

Ex: About 8% of the human genome consists of Endogenous retrovirus (ERV) sequence, that have been trapped in our DNA millions of years ago. These genes have lost their original viral function to be expressed differently. One ERV turned up in a gene known as Suppressyn (SUPYN), which encodes a protein produced in the placenta and in early mammal embryos. This ERV probably had an essential role in the appearance of mammals.

- Bacteriophages (viruses infecting bacteria) regulate microbial ecosystems, keeping harmful bacteria under control.

Ex: T4 bacteriophage target E. coli bacteria (consequences from abdominal cramps or severe diarrhea to kidney failure and death), thus regulating their population in natural environments.

- Viruses are more and more used as vectors in medicine.

Ex: Adenovirus-based vaccines for Ebola use viruses as vectors to enter the host's cells and produce Spike proteins specific to the Ebolavirus. These Spike proteins are recognized by the immune system, which produces antibodies capable of neutralizing the ebolavirus.
Gene therapy is used in some cases of relapsing leukemia. Retroviruses are used to integrate genetic material into the patient's T-cells, thus allowing them to recognize and kill cancerous cells.