Time to go viral!

Understanding viruses and infectious diseases

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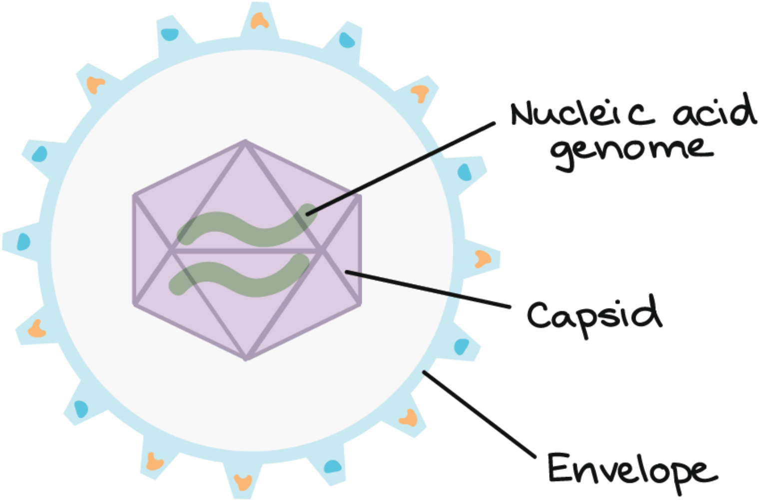
What are viruses?

Viruses are infectious agents that are smaller (20 – 300 nanometers) and simpler than cells.
They lack the cellular structure found in bacteria, fungi, plants, and animals.
Despite their simplicity, viruses are highly efficient at infecting and hijacking the cellular machinery of living organisms to replicate. They commandeer the host cell and use its resources to make more viruses, basically reprogramming it to become a virus factory. Viruses are not considered living.

The structure of a virus

Viruses vary a lot in their size, shape and life cycles but they have key features in common.

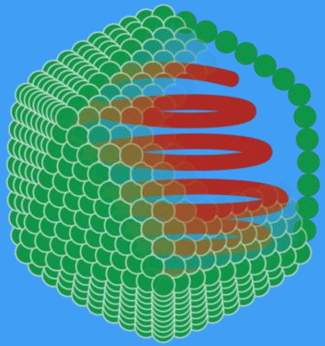
- A protective protein shell, or **capsid**
- A nucleic acid genome made of DNA or RNA, tucked inside of the capsid
- A layer of membrane called the **envelope** (some but not all viruses)



Virus capsid

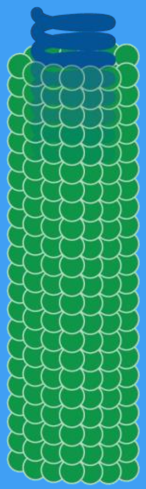
Proteins join to make capsomers, which make up the capsid.

Capsid proteins are encoded by the virus genome.



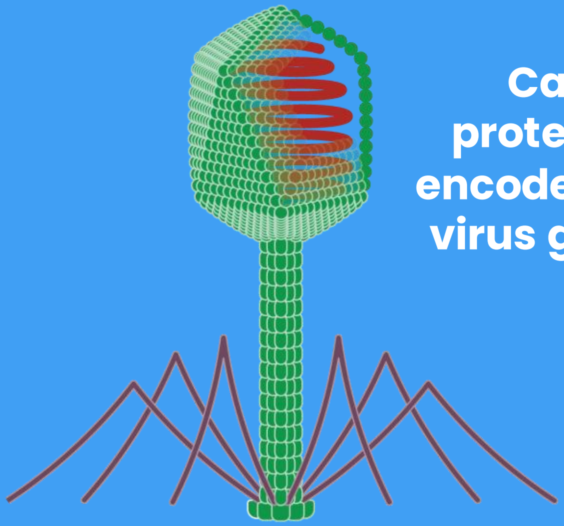
Icosahedral

20 faces.
Named after the twenty-sided shape called an icosahedron.



Filamentous

Named after their linear, thin, thread-like appearance.
Also called rod-shaped or helical

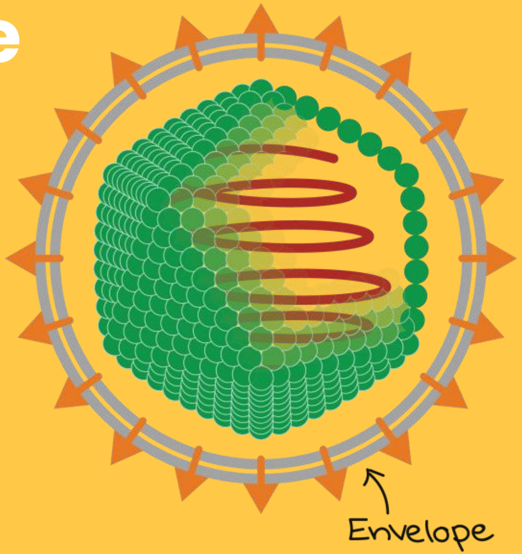


Head-tail

A hybrid between the filamentous (tail) and icosahedral (head) shapes.

Virus envelope

Some viruses also have an external lipid membrane surrounding the capsid.



This is not a universal feature.

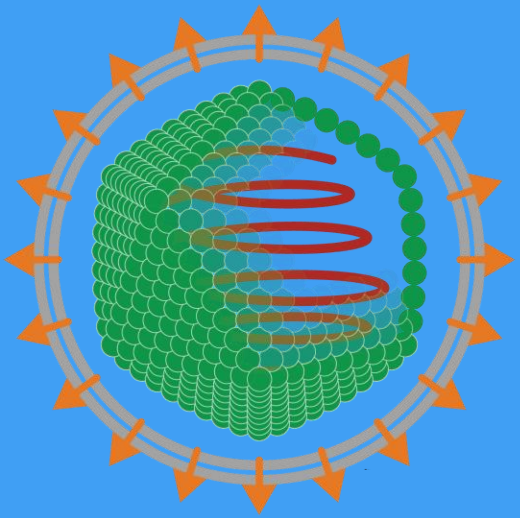
Instructions for the envelope lipids are not provided by the virus

Viruses "borrow" a patch from the host membranes on their way out of the cell

Envelopes do contain protein specified by the virus that help in binding

Virus genome

All viruses have genetic material (a genome) made of nucleic acid (DNA or RNA).



Capsid proteins are encoded by the virus genome.

Viruses can have all possible combos of strandedness and nucleic acid type.

Viral genomes also come in various shapes, sizes, and varieties.

DNA and RNA viruses always use the same genetic code.

What is a viral infection?

In everyday life, we tend to think of a viral infection as the collection of symptoms we get.

At a microscopic level, viral infection means that many viruses are using your cells to make more copies.

A virus recognizes and enters a host cell, "reprograms" the host with instructions (viral DNA or RNA), and uses the host's resources to make more virus particles.

1

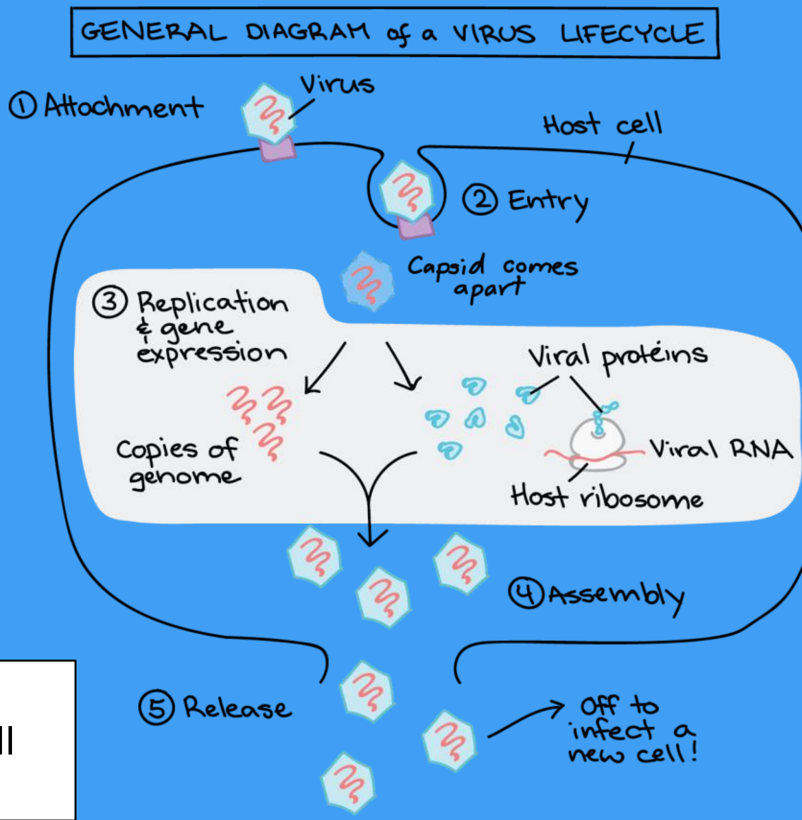
The virus recognizes and binds to a host cell via a receptor molecule on the cell surface.

3

The RNA genome is copied and translated into viral proteins .

5

Completed viral particles exit the cell and can infect.

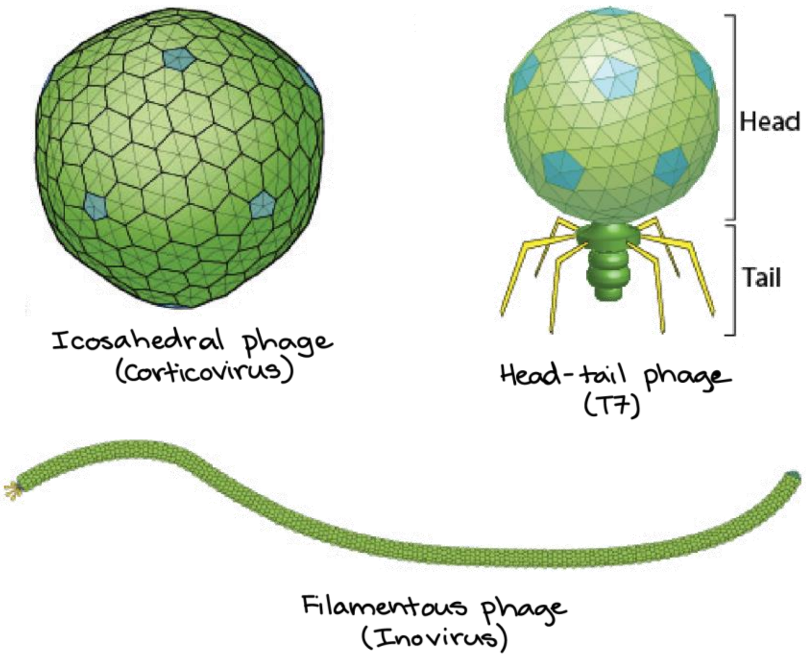


2

The virus or its genetic material enters the cell.

4

New viral particles are assembled from the genome copies and viral proteins.



Bacteriophages

Even bacteria can get a virus! The viruses that infect bacteria are called bacteriophages.

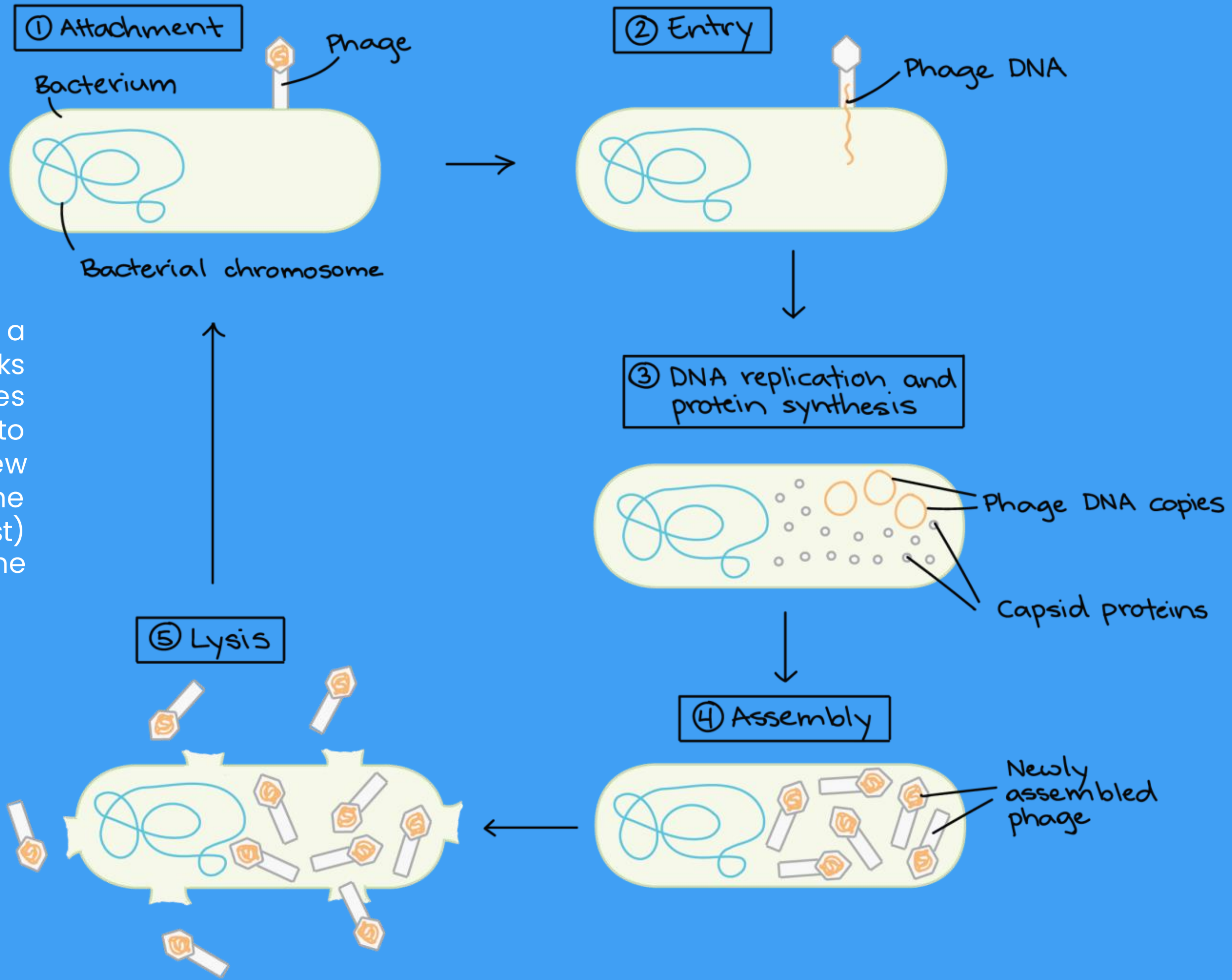
Phage genomes can consist of either DNA or RNA, and can contain as few as four genes or as many as several hundred.

The capsid of a bacteriophage can be icosahedral, filamentous, or head-tail in shape.

The steps that make up the infection process are collectively called the **lifecycle** of the phage.

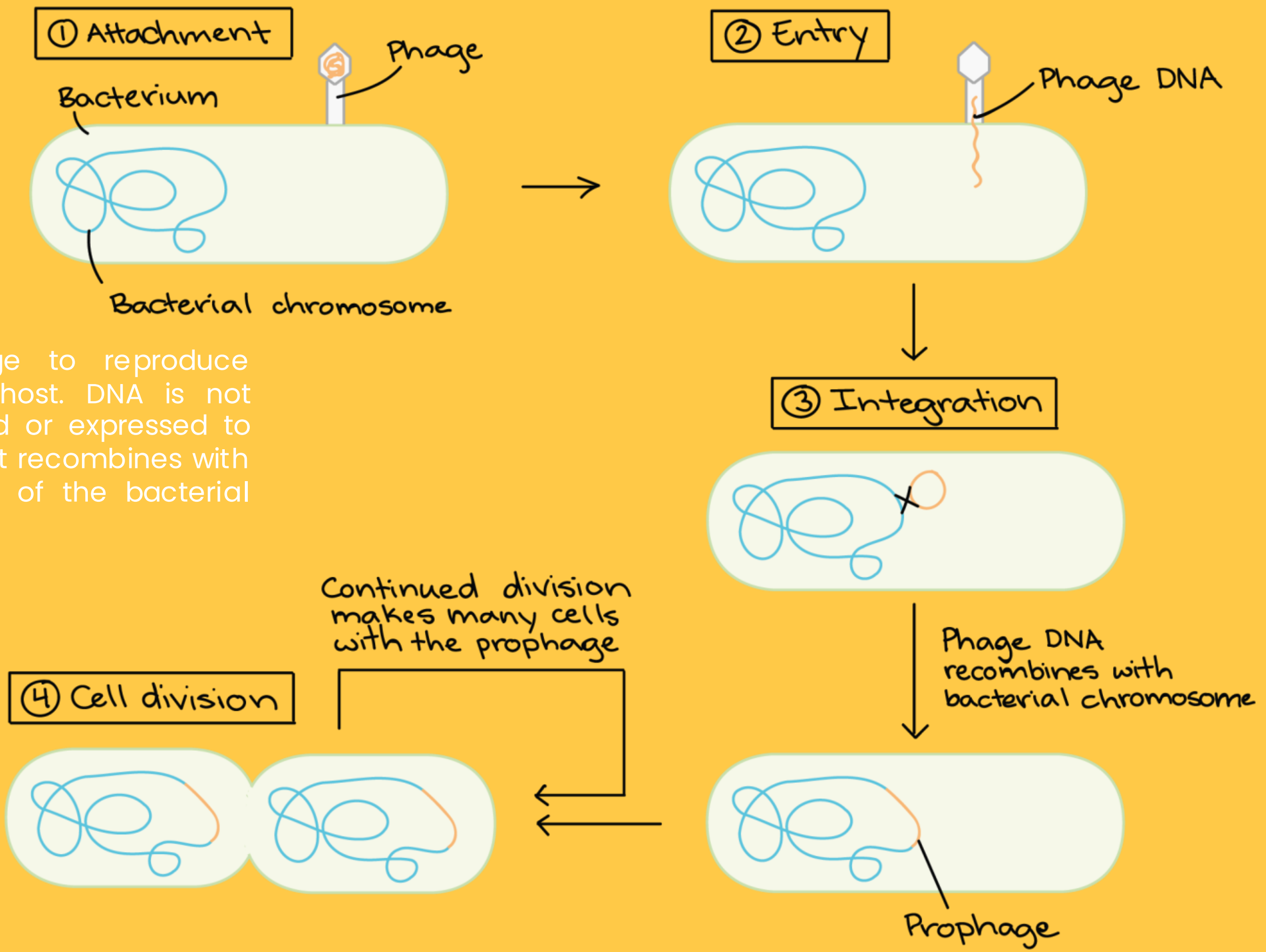
Bacteriophages may use two different cycles to infect their bacterial hosts:

the LYTIC CYCLE



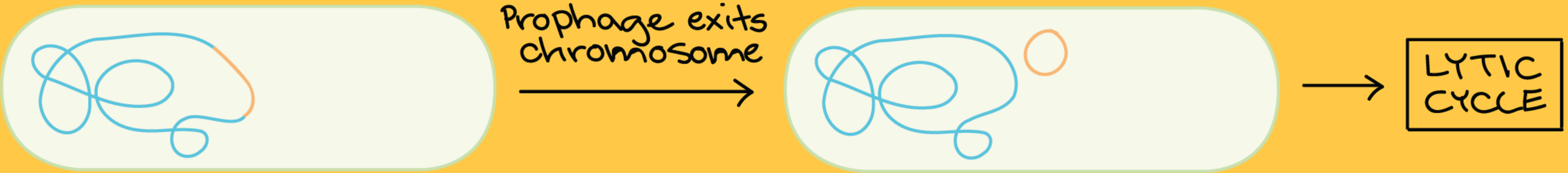
A phage acts like a typical virus: it hijacks its host cell and uses the cell's resources to make lots of new phages, causing the cell to lyse (burst) and die in the process.

the LYSOGENIC CYCLE



It allows a phage to reproduce without killing its host. DNA is not immediately copied or expressed to make proteins but it recombines with a particular region of the bacterial chromosome.

The prophage is not active: its genes aren't expressed, and it doesn't drive production of new phages. However, each time a host cell divides, the prophage is copied along with the host DNA, getting a free ride.



Under the right conditions, the prophage can become active and come back out of the bacterial chromosome, triggering the remaining steps of the lytic cycle (DNA copying and protein synthesis, phage assembly, and lysis).

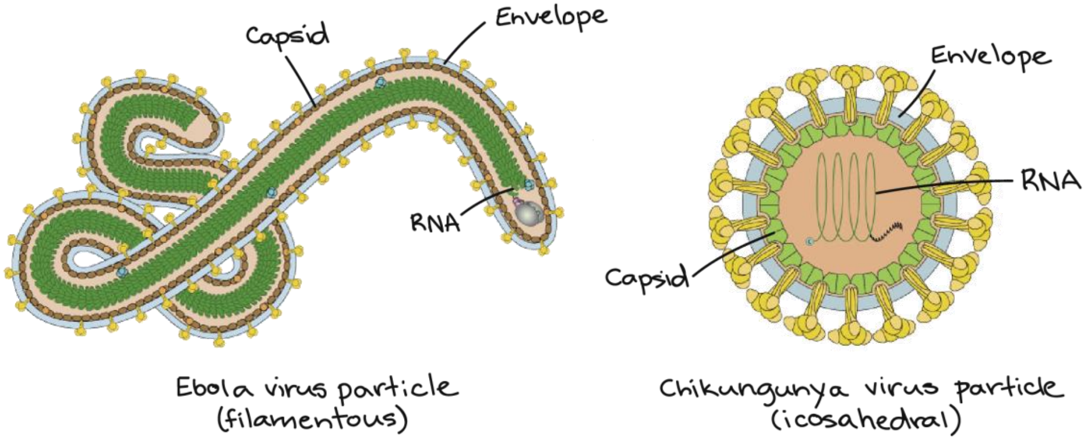
Animal and human viruses

There are many different kinds of viruses that infect humans and other animals, some causing serious illness and others not.

Viruses can be classified according to the Baltimore system, and human-infecting viruses fall into all of its seven categories.

The human immunodeficiency virus (HIV), which causes acquired immune deficiency syndrome (AIDS), is a retrovirus.

What does an animal virus look like?



Animal virus capsids come in many shapes. Ebola virus has a long, thread-like structure that loops back on itself. Chikungunya looks like a sphere, but is actually a 20-sided icosahedron.

How do animal viruses infect cells?

Recognition

An animal virus has special surface molecules that let it bind to receptors on the host cell membrane.

Enter

Endocytosis, where the membrane folds in; by **making channels** in the host membrane or, for enveloped viruses, by **fusing** with the membrane and releasing the capsid inside of the cell.

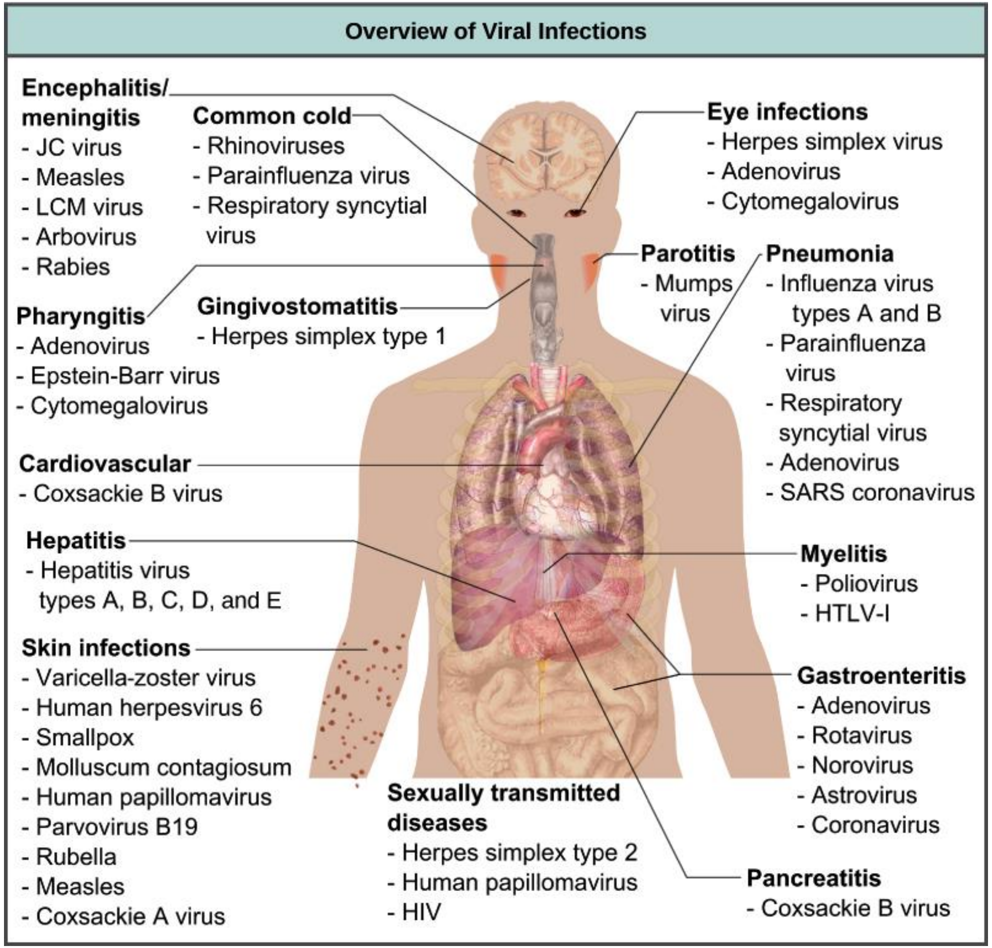
Assemble and exit

Enveloped ones

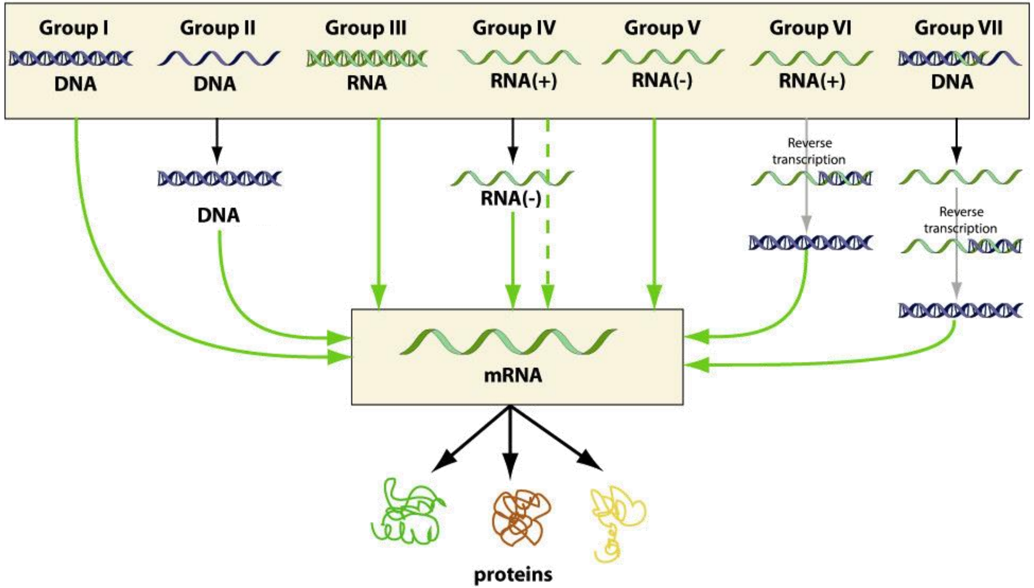
bud from the cell membrane as they form, taking a piece of the plasma membrane or internal membranes in the process.

Non-enveloped ones

typically build up in infected cells until the cell bursts and/or dies and the particles are released.


Overview of Viral Infections
Encephalitis/meningitis
- JC virus
- Measles
- LCM virus
- Arbovirus
- Rabies
Common cold
- Rhinoviruses
- Parainfluenza virus
- Respiratory syncytial virus
Eye infections
- Herpes simplex virus
- Adenovirus
- Cytomegalovirus
Pharyngitis
- Adenovirus
- Epstein-Barr virus
- Cytomegalovirus
Gingivostomatitis
- Herpes simplex type 1
Parotitis
- Mumps virus
Pneumonia
- Influenza virus types A and B
- Parainfluenza virus
- Respiratory syncytial virus
- Adenovirus
- SARS coronavirus
Cardiovascular
- Coxsackie B virus
Hepatitis
- Hepatitis virus types A, B, C, D, and E
Myelitis
- Poliovirus
- HTLV-I
Skin infections
- Varicella-zoster virus
- Human herpesvirus 6
- Smallpox
- Molluscum contagiosum
- Human papillomavirus
- Parvovirus B19
- Rubella
- Measles
- Coxsackie A virus
Gastroenteritis
- Adenovirus
- Rotavirus
- Norovirus
- Astrovirus
- Coronavirus
Sexually transmitted diseases
- Herpes simplex type 2
- Human papillomavirus
- HIV
Pancreatitis
- Coxsackie B virus

Classifying animal viruses



Green arrow = synthesis of an mRNA; dotted green arrow = direct use of the viral genome as an mRNA. Image modified from "The Baltimore classification clusters viruses into families depending on their type of genome, by ViralZone/Swiss Institute of Bioinformatics, CC BY-NC 4.0.

The **Baltimore system** groups viruses according to:

- The molecule it uses as genetic material (DNA or RNA)
- Whether the genetic material is single- or double-stranded
- The steps the virus uses to make an mRNA, key intermediate in the production of viral proteins and the assembly of new viruses.

Retroviruses

HIV, the virus that causes AIDS, is a retrovirus.

A retrovirus genome is single-stranded RNA and comes in two copies per viral particle. The RNA must be converted into double-stranded DNA by an enzyme called **reverse transcriptase**, reversing the normal flow of information from DNA to RNA to protein in cells.

The double-stranded DNA enters the nucleus of the host cell and is inserted into the host genome by an enzyme called **integrase**.

mRNA can then be made by transcription of the viral DNA, which, as a permanent part of the host cell's genome, is called a **provirus**.

The mRNA is read to produce viral proteins and may also serve as a genome for new viral particles that assemble and bud from the cell.

Anti-HIV drugs inhibit viral replication at many different phases of the HIV cycle.

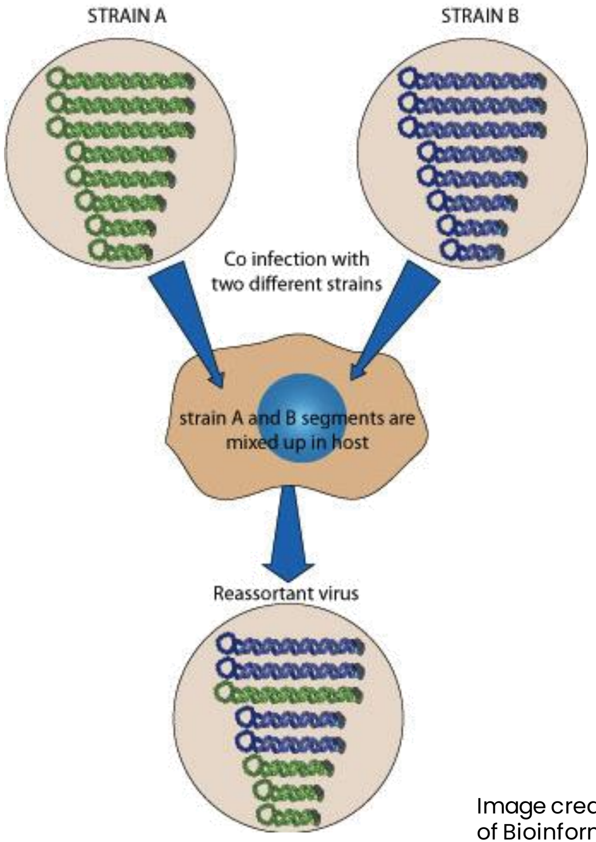
The "gene pool" of a virus population can change over time. In some cases, the viruses in a population may evolve by natural selection. Heritable traits that help a virus reproduce will tend to get more and more common in the virus population over time.

Evolution of viruses

Natural selection can only happen when it has the right starting material: genetic variation.
Recombination: viruses swap chunks of genetic material.
Random mutation: a change occurs in the genomic sequence of a virus

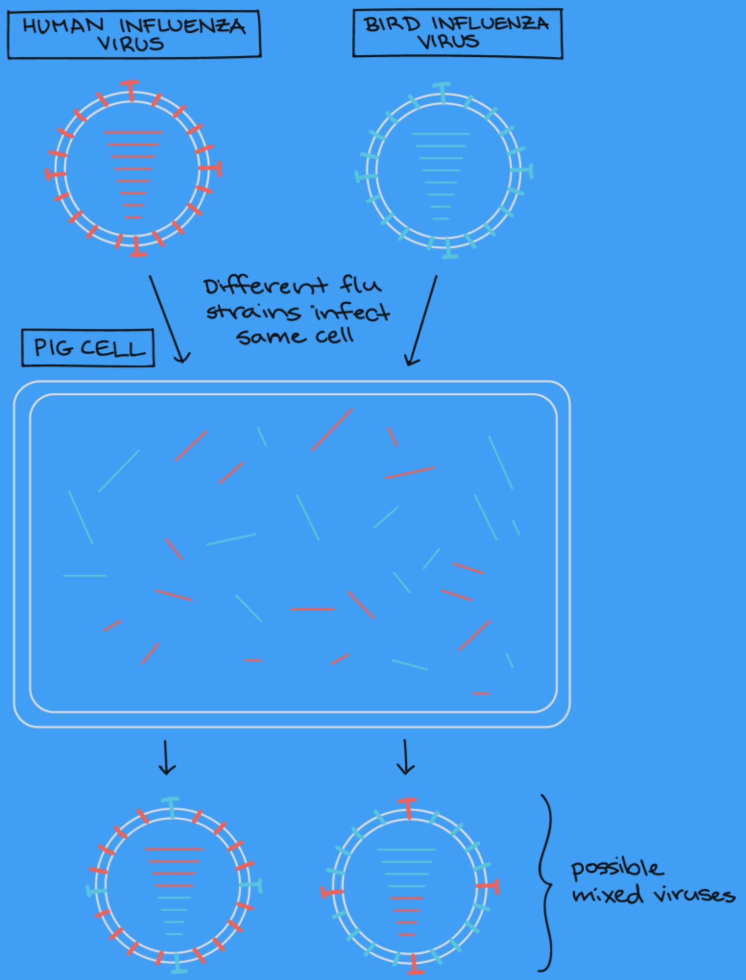
Mixing it up: Recombination

Happens when two viruses have infected the same cell at the same time.



Both viruses are using the cell to crank out more virus particles

There will be lots of virus parts floating around in the cell at once.



Influenza viruses are masters of reassortment

They have eight RNA segments, each carrying one or a few genes. When two influenza viruses infect the same cell at the same time, some of the new viruses made inside of the cell may have a mix of segments.

Pigs are "mixing vessels"

If a cell in the pig is infected with two types of influenza virus at the same time, it may release new viruses that contain a mixture of genetic material from the human and bird viruses.

H1N1 influenza strain ("swine flu")

H1N1 had RNA segment from human and bird viruses, as well as pig viruses from both North America and Asia.

Viral mutations

It's a permanent change in the genetic material of a virus.

A mutation can happen if there is a mistake during copying of the DNA or RNA of the virus.

RNA viruses tend to have high mutation rates, DNA viruses tend to have low mutation rates.

Most DNA viruses copy their genetic material using enzymes from the host cell (DNA polymerases), which proofread. RNA viruses use RNA polymerases, which don't proofread.

The key difference is in the copying machinery.

Viral mutations

Point mutations: involve changes in a single nucleotide base in the viral genome.

Nonsense: one nucleotide is substituted and this leads to the formation of a stop codon;
Missense: a different codon is formed;
Silent: the same amino acid is produced.

Insertions and Deletions: the addition or removal of nucleotide bases in the viral genome.

They can lead to frameshift mutations, impacting the reading frame of the genetic code.

Why do viruses evolve so fast?

Higher mutation rate

Large population size

Rapid life cycle

Solutions: prevent trasmission, identify new drugs, vaccines

Infectious diseases

Infectious diseases are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; the diseases can be spread, directly or indirectly, from one person to another. They can be classified into:

1

Diseases which cause high levels of mortality

2

Diseases which place on populations heavy burdens of disability

3

Diseases which owing to the rapid and unexpected nature of their spread can have serious global repercussions

Source: World Health Organization

Pathogenic Pathways

Most common in the US

- Sexually Transmitted (Chlamydia, Gonorrhea, Syphilis)
- Fecal-Oral Route (Campylobacter, Salmonella, E.coli)
- Vector-Borne aka "Bug transmitted" (Lyme, Spotted Fever)
- Blood-Borne (HIV, Hepatitis C)
- Air-Borne (Measles, Influenza, SARS-CoV-2)

Least common In the US

Source: Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System, 2018 Annual Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance, 2019

Air-borne infectious diseases

Mode of transmission

Droplets, aerosol

Route of infection

Inhalation of infectious particles

Virus stability in air

Viability in Airborne particles

Indoor vs outdoor

Poor ventilation, crowded places

Preventive measures

Respiratory protective equipment, ventilation systems, isolation measures

Examples

Influenza (flu), Tuberculosis (TB), SARS-CoV-2 (COVID-19), Measles virus

Air-borne infectious diseases

Public health implications

Pandemic potential, public health response is needed

Environmental factors

Temperature and humidity

Global spread

International cooperation is needed

Classification of Danger

Worldwide, the number of potential pathogens is very large. A WHO tool distinguishes which diseases pose the greatest public health risk due to their epidemic potential and/or whether there is no or insufficient countermeasures.

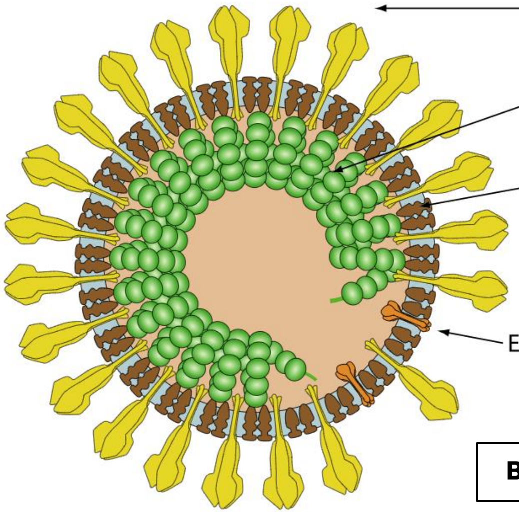
- **COVID-19**
- **Crimean-Congo haemorrhagic fever**
- **Ebola virus disease and Marburg virus disease**
- **Lassa fever**
- **Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)**
- **Nipah and henipaviral diseases**
- **Rift Valley fever**
- **Zika**
- **"Disease X"***

Source: World Health Organization

COVID-19

Virion

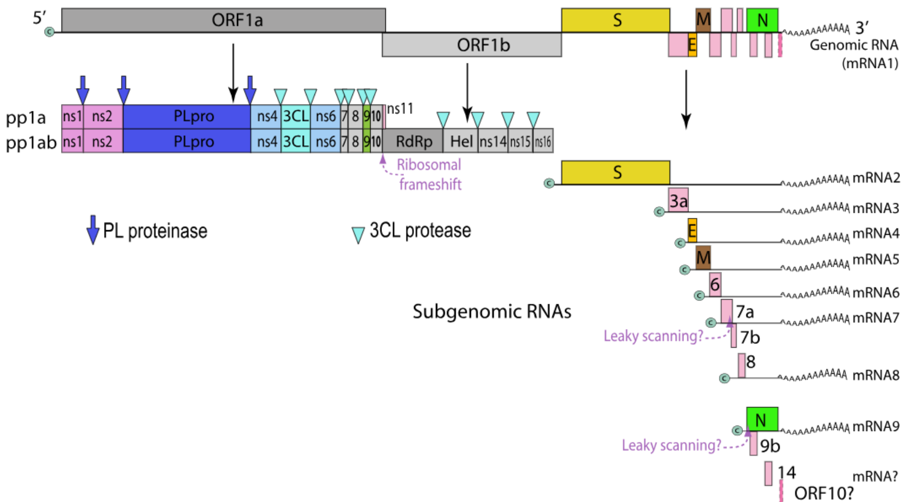
Enveloped, spherical, about 120 nm in diameter. The RNA genome is associated with the N protein to form the nucleocapsid. Monopartite, linear ssRNA(+) genome of 27-32kb in size (the largest of all RNA virus genomes). Capped, and polyadenylated. The leader RNA (65-89 bp) at the 5' end of the genome is also present at the end of each subgenomic RNAs.



Betacoronavirus

Image credit: ViralZone/Swiss Institute of Bioinformatics

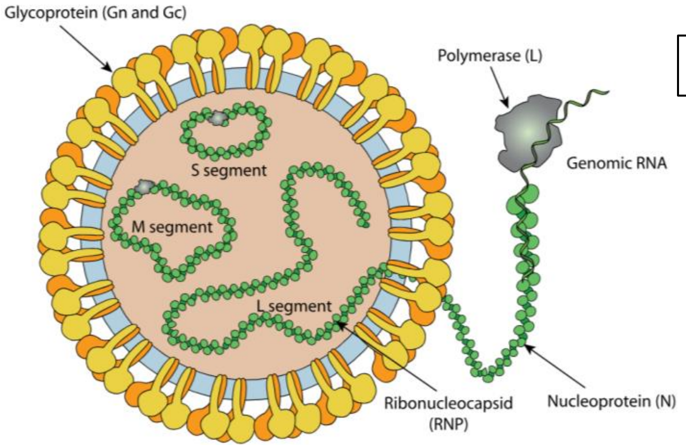
Genome



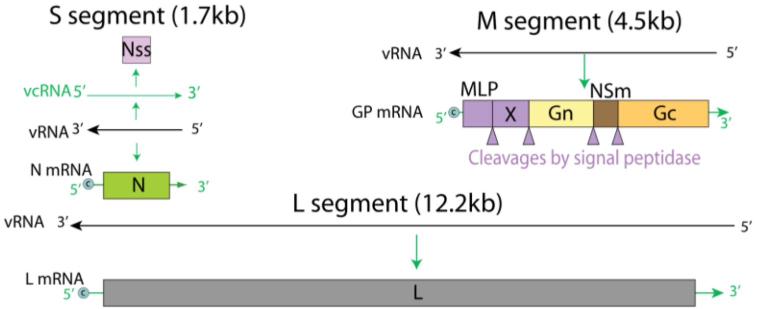
Gene Expression: The virion RNA is infectious and serves as both the genome and viral messenger RNA. Genomic RNA encodes ORF1a, as for ORF1b, it is translated by ribosomal frameshifting. Resulting polyproteins pp1a and pp1ab are processed into the viral polymerase (RdRp) and other non-structural proteins involved in RNA synthesis. Structural proteins are expressed as subgenomic RNAs.

Crimean-Congo haemorrhagic fever

Viron



Genome

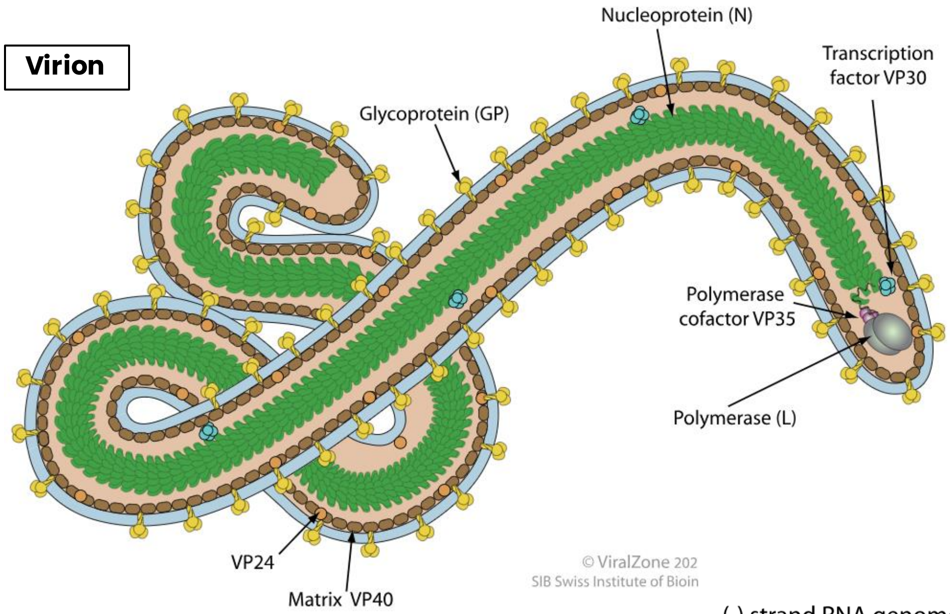


Viral diseases spread by tick bites or contact with infected animals. **Orthonairovirus** is a genus of ssRNA- viruses in the Nairoviridae family that infect vertebrates and are transmitted by arthropods (arbovirus). Enveloped, spherical. Diameter from 80 to 120nm. **Symptoms**: fever, muscle pains, headache, vomiting, diarrhea, and bleeding into the skin.

Segmented Negative-stranded RNA linear genome, L segment is between 6.8 and 12 kb, M segment between 3.2 and 4.9 kb and S segment between 1 and 3 kb. Encodes for four to six proteins.

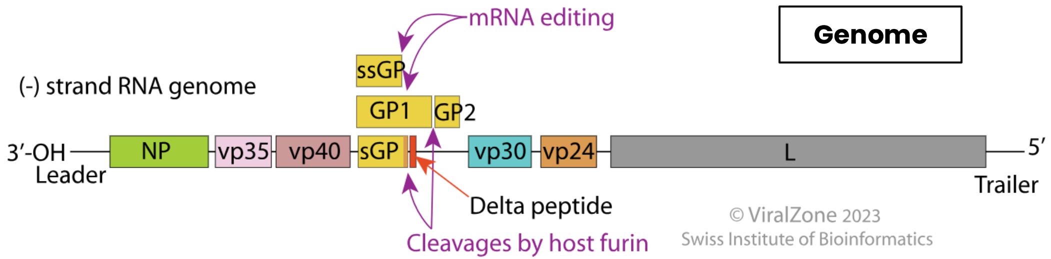
Ebola virus disease and Marburg virus disease

Virion



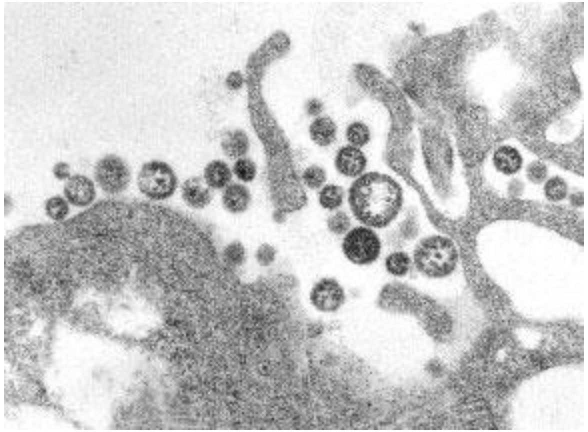
Ebolavirus is a genus of ssRNA- viruses in the family Filoviridae that infect mammals. Ebolavirus infection in humans leads to fatal hemorrhagic fever. Filamentous 970 nm long for Ebolavirus. Diameter is about 80nm.

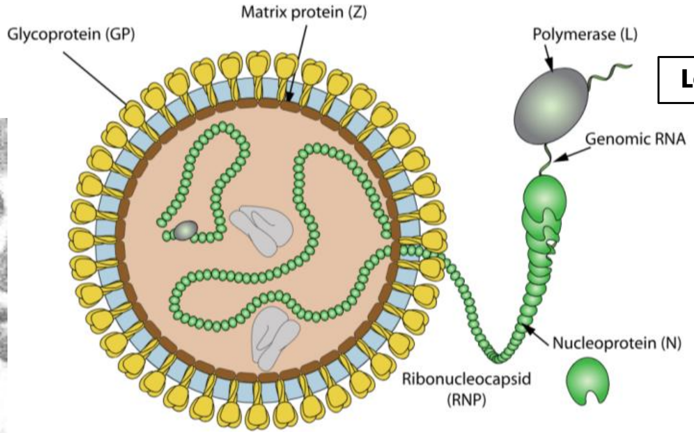
Genome



Negative-stranded RNA linear genome, about 18-19 kb in size. Encodes for seven proteins.

Lassa fever

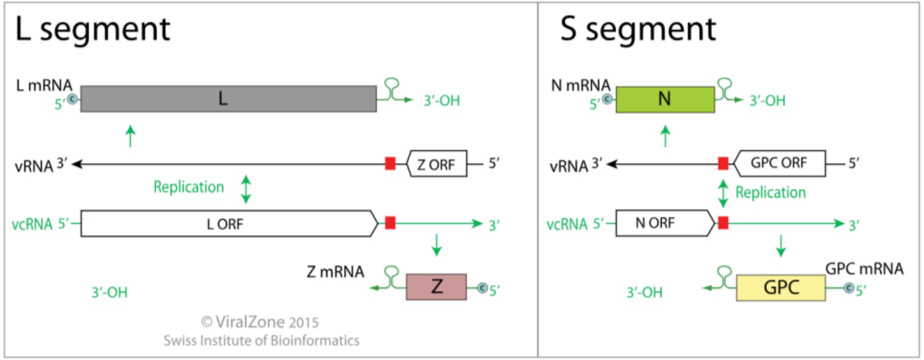




Lassa mammarenavirus

Enveloped, spherical. Diameter from 60 to 300 nm.

Genome



Lassa fever is an animal-borne, or zoonotic, acute viral illness spread by the common African rat.

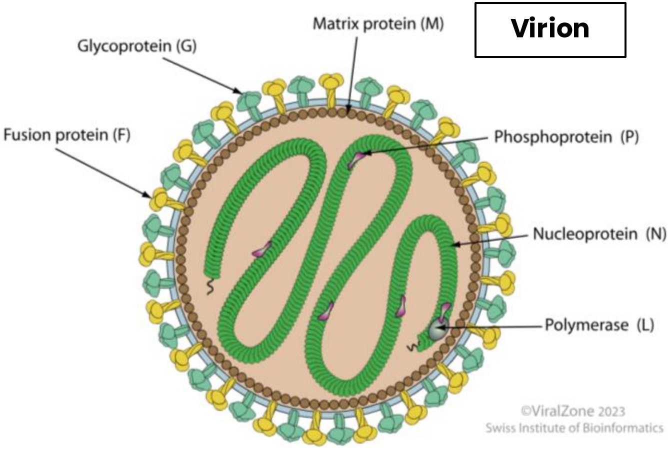
Segmented Negative-stranded RNA linear genome, L segment is about 7,5 kb and S segment 3,5 kb. Encodes for four proteins.

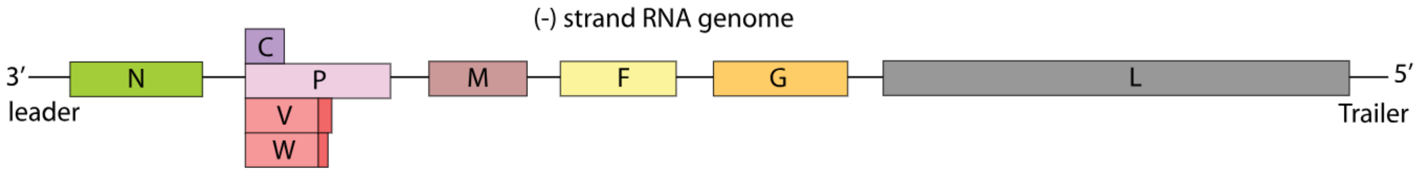
Nipah and henipaviral diseases

Henipavirus is a genus of ssRNA- viruses in the PAramyxoviridae family that infect bats and occasionally other mammals. In humans, these viruses can cause encephalitis or respiratory disease.

Enveloped, spherical. Diameter from about 150nm.

Virion

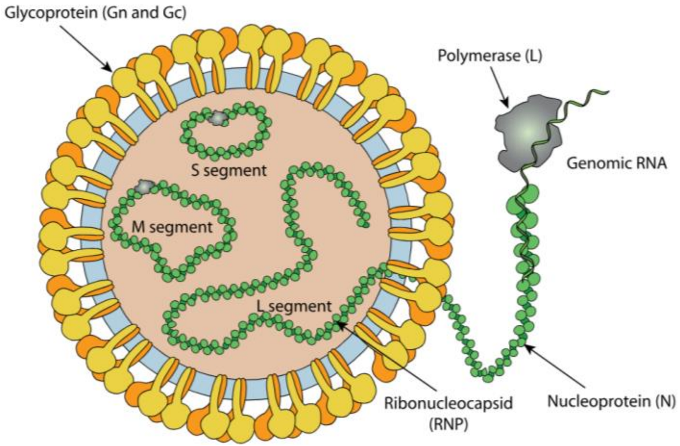




Genome

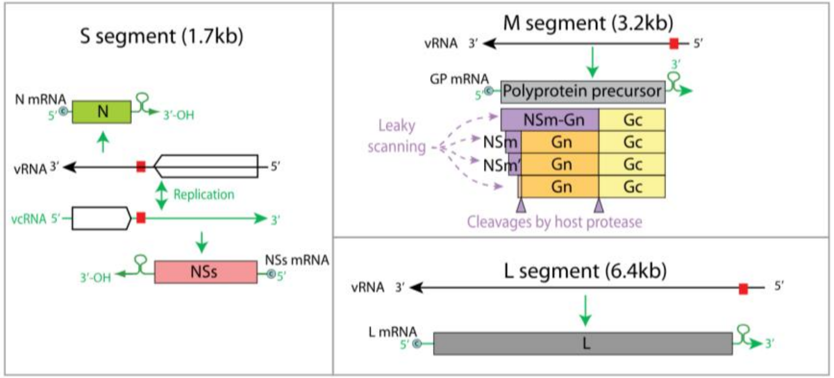
Negative-stranded RNA linear genome, about 18 kb in size.
Encodes for nine proteins.

Rift Valley fever



Phlebovirus

Enveloped, spherical. Diameter from 80 to 120nm. Glycoproteins at the surface of the envelope are arranged on an icosahedral lattice, with T=12 symmetry.



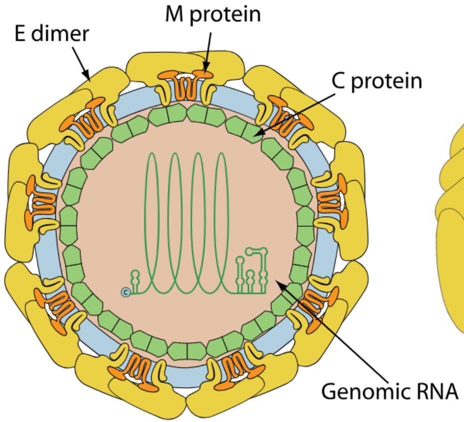
Genome

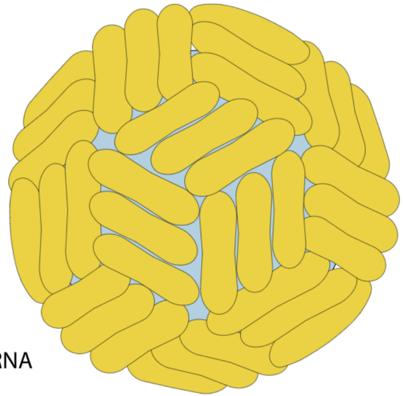
Segmented Negative-stranded RNA linear genome, L segment is about 6.4kb, M segment about 3.2kb and S segment about 1.7kb. Encodes for six proteins.

Zika fever

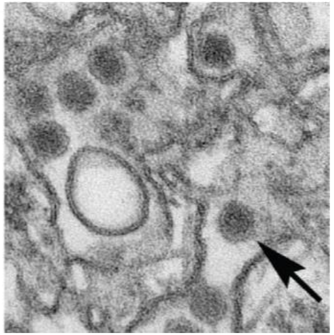
Flavivirus is a genus of ssRNA+ viruses in the Flaviviridae family that infect vertebrates and are transmitted by arthropods (arbovirus). In humans, these viruses can cause fevers with variable symptoms.

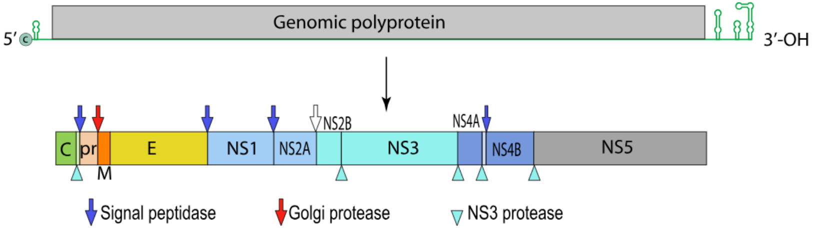
Enveloped, spherical, about 50 nm in diameter. The surface proteins are arranged in an icosahedral-like symmetry. Mature virions contain two virus-encoded membrane proteins (M and E), while immature virions contain a membrane protein precursor.



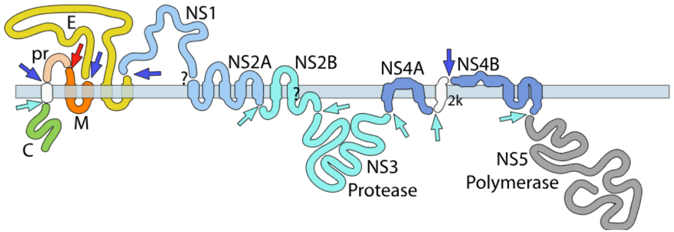


T=3-like organization of surface dimers





Genome



Overview of the greatest public health risks

Disease	Pathogen	Transmission	Synthoms	Severity	Outbreaks
COVID-19	SARS-CoV-2, a novel coronavirus	Primarily through respiratory droplets, airborne transmission, and contact with contaminated surfaces	Range from mild respiratory symptoms to severe pneumonia and acute respiratory distress syndrome (ARDS)	Varied, with severe cases more common in older adults and those with underlying health conditions	Declared a pandemic by the WHO, causing significant morbidity, mortality, and societal disruptions worldwide
Crimean-Congo Hemorrhagic Fever (CCHF)	Crimean-Congo Hemorrhagic Fever Virus	Primarily through ticks and direct contact with blood or tissues from infected animals or humans	Sudden onset of fever, muscle aches, and bleeding tendencies	Can progress to severe hemorrhagic fever with a high case fatality rate	Found in Africa, the Middle East, Europe, and Asia
Ebola Virus Disease and Marburg Virus Disease	Ebola virus and Marburg virus	Contact with blood or body fluids of infected animals or humans	Fever, severe headache, muscle pain, fatigue, and hemorrhagic manifestations	High case fatality rates, particularly during outbreaks	Occur in Central and West Africa, causing sporadic but severe outbreak
Lassa Fever	Lassa virus	Primarily through contact with urine or feces of infected rodents (mainly Mastomys rats)	Fever, headache, muscle aches, and, in severe cases, hemorrhagic fever	Fever, headache, muscle aches, and, in severe cases, hemorrhagic fever	Endemic in parts of West Africa

Overview of the greatest public health risks

Disease	Pathogen	Transmission	Synthoms	Severity	Outbreaks
Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS):	MERS-CoV and SARS-CoV, both coronaviruses	Human-to-human transmission, often in healthcare settings	Severe respiratory illness, including fever, cough, and difficulty breathing	Both MERS and SARS can cause severe respiratory distress, with varying case fatality rates	SARS emerged in 2002-2003, and MERS emerged in 2012; sporadic cases continue
Nipah and Henipaviral Diseases	Nipah virus and other henipaviruses	Often from fruit bats to humans, with subsequent human-to-human transmission	Respiratory and neurological symptoms, including encephalitis	Can cause severe respiratory and neurological disease, with a high case fatality rate	Sporadic outbreaks in South and Southeast Asia
Rift Valley Fever	Rift Valley Fever Virus	Primarily through mosquitoes, with potential for direct or indirect contact with infected animals	Fever, weakness, and in severe cases, hemorrhagic fever or encephalitis	Range from mild to severe; outbreaks can have significant economic impacts on livestock	Found in Africa and the Arabian Peninsula
Zika Fever	Zika virus	Primarily through the bite of infected Aedes mosquitoes; can also be transmitted sexually	Mild, with fever, rash, joint pain, and conjunctivitis	Associated with congenital anomalies, including microcephaly in infants born to infected mothers	Originally in Africa and Asia; recent outbreaks in the Americas

Conclusions

The recent pandemic illustrates the profound consequences of a new infectious agent in our globally interconnected society

Importance of sequencing genomes for monitoring and understanding variants

Adopting a "One Health" approach that recognizes the interconnectedness of human, animal, and environmental health

Increase knowledge, enhance readiness, and improve response capabilities for greater resilience against epidemics and pandemics

Thank you for the attention!