

Course Title – Virology

Course Code – L.Sc. – 307

Marks: 75

S. No.	Topic
1.	Origins of virology, viruses as a living system etc
2.	Classification of viruses
3.	Organization of viruses Protein structure and assembly, nucleic acid packaging, geometrical aspects, icosahedral and helical symmetry
4.	Virus attachment and entry in to host cells
5.	Cellular and molecular biology of Host virus interaction
6.	Genome replication and mRNA production by RNA viruses
7.	Reverse transcription and integration in to the host genome (retroviruses)
8.	DNA virus replication strategies
9.	Unique features of viral gene expression
10.	Translational control of viral gene expression
11.	Viral pathogenesis and cell transformation by viruses
12.	Viral Genetics, Viral vaccines, Antiviral chemotherapy, Persistence of viruses
13.	Hepadnaviruses, HIV, Polyomaviruses (SV40), Baculovirus, Topsoviruses, Potyviruses
14.	Virus evolution
15.	Viral vectors and gene therapy

Virus

“Virus is a small, Ultramicroscopic particle composed of two types of substances protein and nucleic acid.”

- Virus means “poison”
- They are seen only with the help of electron microscope.
- They cause a wide range of diseases in plants and animals
- The study of Viruses is called **“Virology”** and Father of Virology **“M.Beijerinck”**

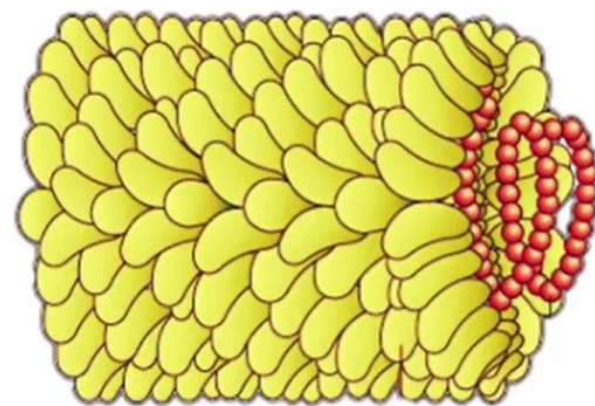


History of Virus

- In 1886, “A.Mayer” described Tobacco Mosaic disease but he could not find any causal agent.
- Credit for the discovery of viruses goes to the Russian botanist Iwanowsky (1892), who found the cause of mosaic disease of tobacco. He reported that the sap of infected plant filtered through bacteria proof filters and concluded that the cause of disease was not Bacterium but some other smaller particles known as **Virus**
- In 1935 W.M. Stanley crystallized TMV and show that crystals retained their infectivity even when stored for a indefinite period in a bottle.
- Bawden and Pirie (1937) studied the chemical nature of TMV particles and reported that they are nucleoproteins.

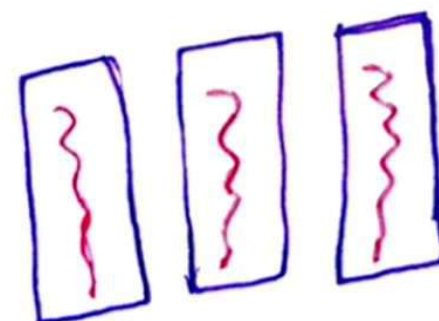
History of Virus Cont.

- Bacteriophages were discovered By **twort** 1915 and **D'herelle** 1917.
- **Shafferman** and **Moris** (1963) discovered Cyanophages that cause infection in blue green algae.
- **June Almeida** 1964, the woman who discovered first Coronavirus.



Characteristics of Virus

1. Viruses are ultramicroscopic infectious particles ranging from 20nm to 400nm in diameter
2. They are **nucleoproteins**
3. They contain **DNA** or **RNA** but not both which is either single stranded or double stranded
4. The DNA or RNA is surrounded by a **protein coat** that may be attached to more complicated structures



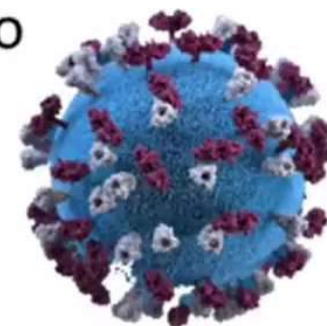
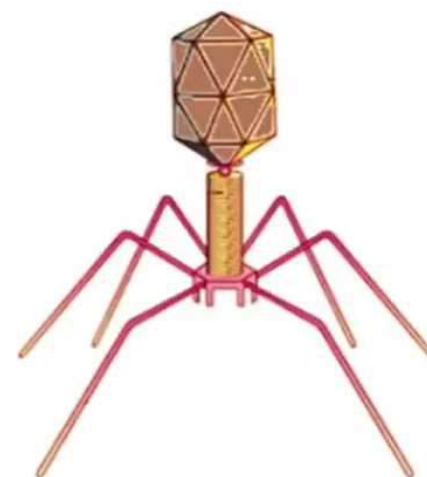
Characteristics of Virus

5. They are highly pathogenic cause disease in plants animals and bacteria
6. They are without protoplasm
7. They grow multiply only within living host cells
8. They cause infection in host by nucleic acids.
9. They are easily transmitted from one organism to another.



Characteristics of Virus

10. They are not affected by antibiotics.
11. They can be crystallized.
12. They are perfect obligate parasite i.e. they depend upon specific host for their reproduction and development. The cells of animals plants and bacteria can serve as host to virus
13. They have characters of both living and nonliving



THREE HYPOTHESIS FOR THE ORIGIN OF VIRUSES

The background of the slide is a dark blue, textured image featuring several virus particles. The most prominent virus in the center is a spherical particle with a dense, textured surface and numerous long, thin, rod-like protrusions extending from it. Other smaller, similar virus particles are visible in the background, some appearing as bright, glowing spheres.

They are said to have evolved 1.5 billion years ago.

1. Regressive Evolution Hypothesis
2. Escaped Host gene Hypothesis
3. Pre Cellular origin Hypothesis

Discovery Of Virus

Virus:

Viruses are simplest living entities/particles composed of small no of macromolecules i.e. DNA or RNA & proteins
Some time glycoprotein & lipoproteins also present

→ Viruses are obligate parasites

↓
Totally Depends on its host

→ They can infect and parasitize all form of life including bacteria.

Viruses living or Non-living:

→ They lie on border line b/w living & non-living.

Living characters:

- They possess DNA or RNA.
- They have ability of reproduction.
- They can cause infection.
- They can undergo mutation & genetic recombination.

Non-living characters:

- They are subcellular (non-cellular)
- They do not respire or excrete.
- They can be crystallized.

Discovery: Tobacco mosaic disease
→ It stunts the growth of plants & give their leaves a mottled or mosaic coloration.

→ 1838 Adolf Mayer → German scientist

→ Discovered that he could transmit the disease from plant to plant by rubbing sap extracted from diseased leaves
→ Caused by unusual Bacteria (invisible under microscope)

→ Ivanowsky → Russian Biologist.

→ Concluded → Bacteria were small enough to pass filter.
OR → Bacteria produce toxin which make infection.

→ Martinus Beijerinck → Dutch Botanist

Discover that infectious agent in filtrate can replicate.
→ it replicate only within the host.

→ Unlike Bacteria shows no growth on nutrient media. → Hence He coined the concept of virus.

→ In 1935 Stainely

→ Crystallize the TMV & find out they are simplest creature made of just Protein & DNA.

After that invention of Electron Microscope occurs & viruses were seen under EM.



1 Extracted sap from tobacco plant with tobacco mosaic disease



2 Passed sap through a porcelain filter known to trap bacteria



3 Rubbed filtered sap on healthy tobacco plants

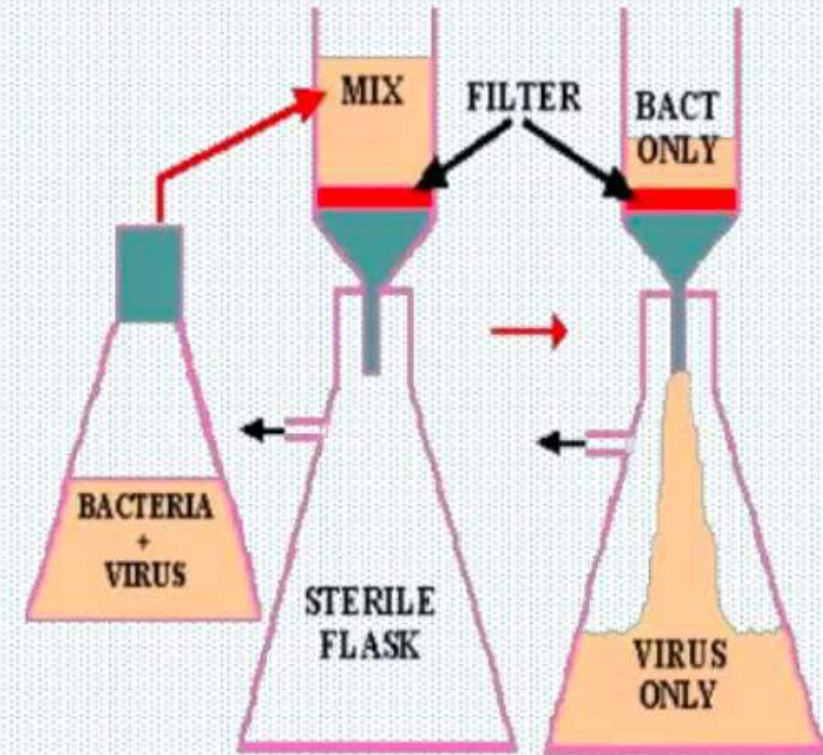


4 Healthy plants became infected

Discovery of viruses

In 1884 **C. Chamber land**, in Pasteur's lab, discovered that if you passed a liquid containing bacteria through an unglazed PORCELAIN tube, the bacteria were COMPLETELY RETAINED and the solution that passed through (the FILTRATE) was sterile.

In 1892 **D. IWANOWSKI** applied this test to a filtrate of plants suffering from TOBACCO MOSAIC DISEASE with shocking results; the filtrate was FULLY CAPABLE of producing the ORIGINAL DISEASE in new hosts.

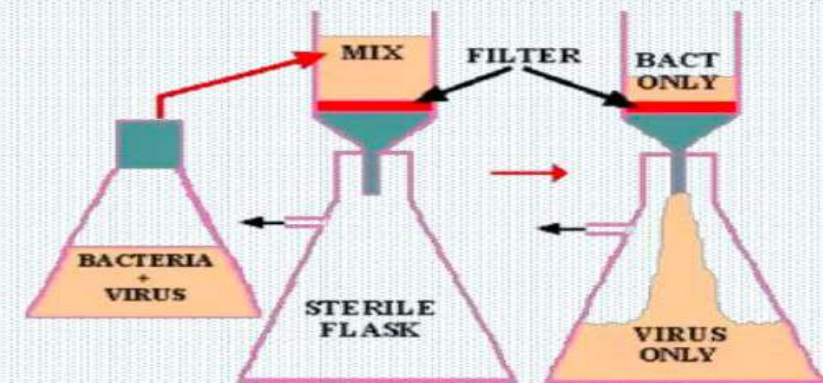


Filtration of a mixture of bacteria and viruses. If a mixture of viruses and bacteria are filtered through a bacterial-proof filter (red), the viruses will pass through into the filtrate in the flask. Filtered beer is produced by a similar process.

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Dr. Farzin Asghari Sana

What are Viruses? **Definition-**

Viruses are noncellular particles made up of genetic material and protein that can invade living cells.

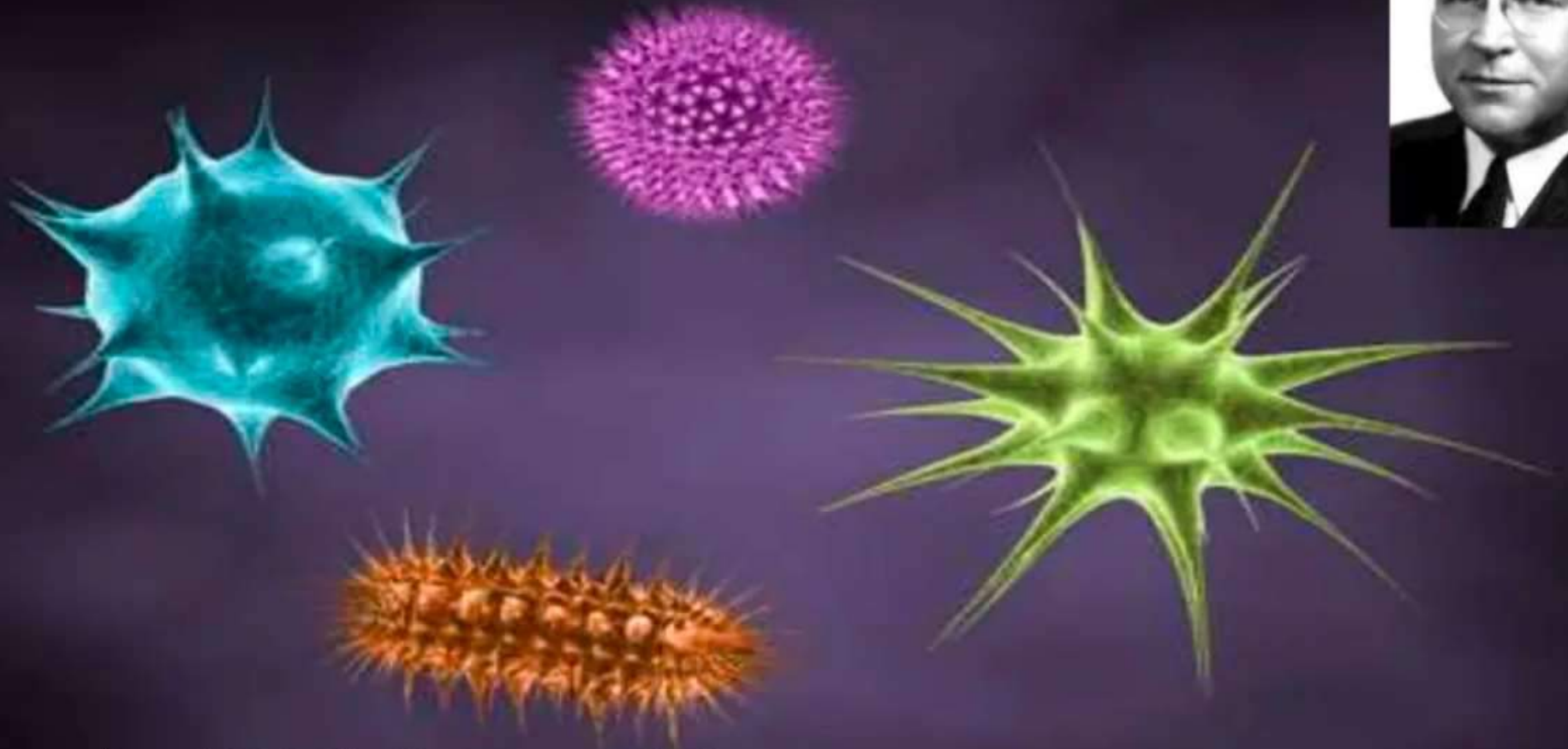
Discovery of Viruses

Martinus Willem Beijerinck (1897) coined the Latin name "virus" meaning poison



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Tobacco Mosaic Virus



Wendell Stanley (1935) discovered viruses were made of nucleic acid and protein

Viruses

Discovery / History

- Latin word meaning poisonous fluid and was 1st term coined by **Louis Pasteur**.
- First virus was discovered by **Ivanowsky** in **1892** from infected leaves of tobacco plant called as **Tobacco Mosaic Virus (TMV)**.
- M. W. **Beijerinck (1898)** demonstrated that viruses differ from other cellular organism by passing via agar gel and called the fluid as **Contagium Vivum Fluidum**.
- **Towrt and Herelle (1915)** reported that viruses have a tendency to even infect bacteria and they called such virus as **Bacteriophage**.
- **W. M Stanley** reported the presence of nucleic acid not only protein in Virus and was awarded **noble prize in 1946**.

Definition

Viruses are obligate parasite or holoparasite, ultra microscopic, self replicating highly infectious agents that multiply only inside living host cells without involving growth and division and essentially composed of a protein covering surrounding a nucleic acid molecule (RNA or DNA).

Fundamentally differ from cellular organism in that they contain only one type of nucleic acid which may be either DNA or RNA.

Deoxyviruses (which contain DNA)

Riboviruses (which contain RNA)

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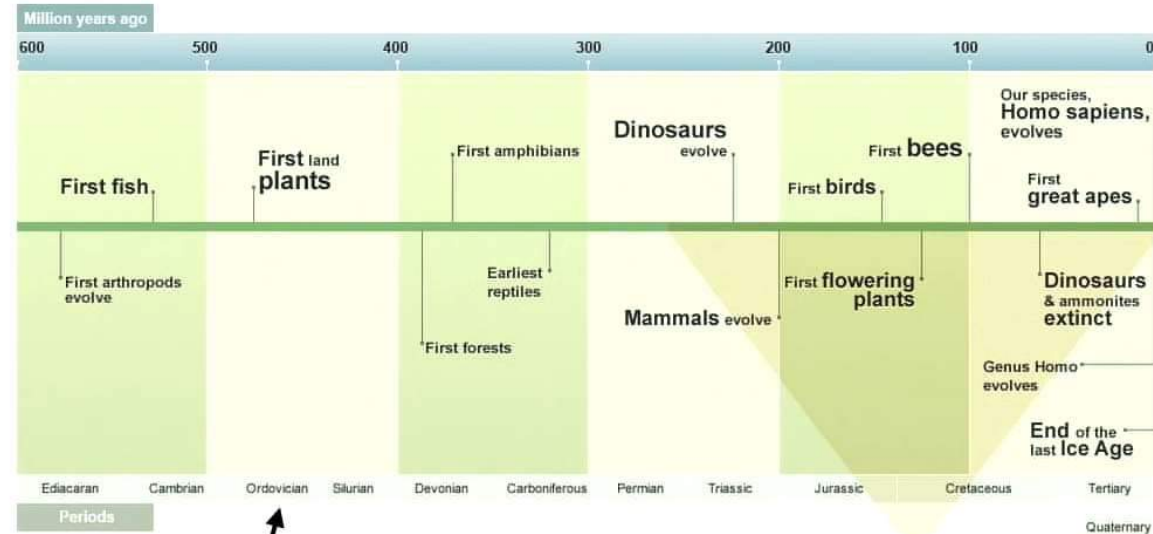
Deoxyviruses (which contain DNA)

Riboviruses (which contain RNA)

How old are viruses?

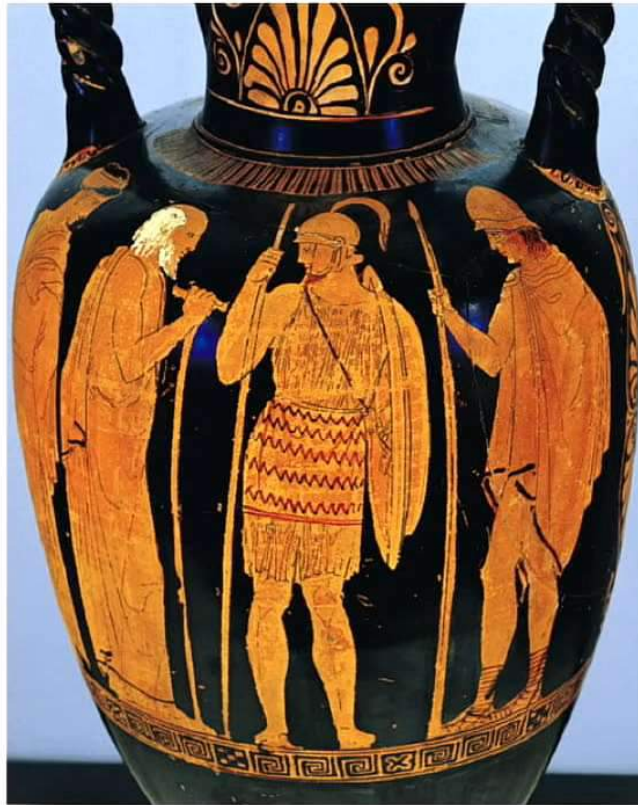


Nobu Tamura (<http://spinops.blogspot.com>)



- Estimates of molecular evolution suggest marine origin of some retroviruses >450 Ma, Ordovician period
- Likely originated billions of years ago - before cells?

Ancient references to viral diseases



Here this firebrand, rabid Hector, leads the charge.
Homer, *The Iliad*,
translated by Robert Fagels
(Viking Penguin)

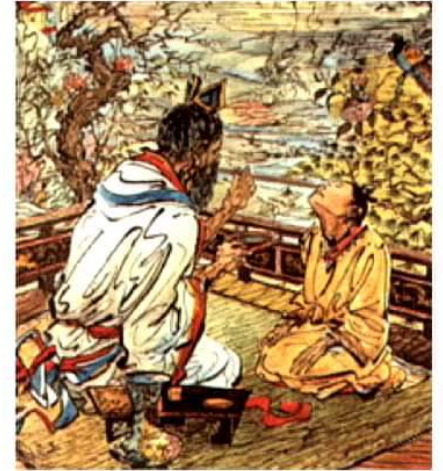
700 B.C.



1580-1350 B.C.

Vaccination to prevent viral disease

- Variolation - China (11th century), Lady Montagu (1700s)
- No knowledge of agent
- Survivors of smallpox protected against disease
- 1790s - experiments by Edward Jenner in England establish vaccination



1939 - Viruses are not liquids!

- Helmut Ruska built first electron microscope 1933
- First EM of bacteriophage, 1939



Virus classification

- Nature and sequence of nucleic acid in virus particle
- Symmetry of protein shell (capsid)
- Presence or absence of lipid membrane (envelope)
- Dimensions of virus particle

Virus classification

<http://ictvonline.org/>

Classical hierarchical system:

Kingdom

Phylum

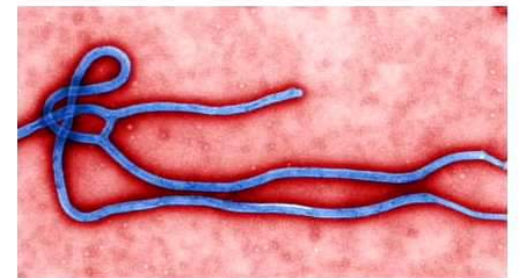
Class

Order (-*virales*)

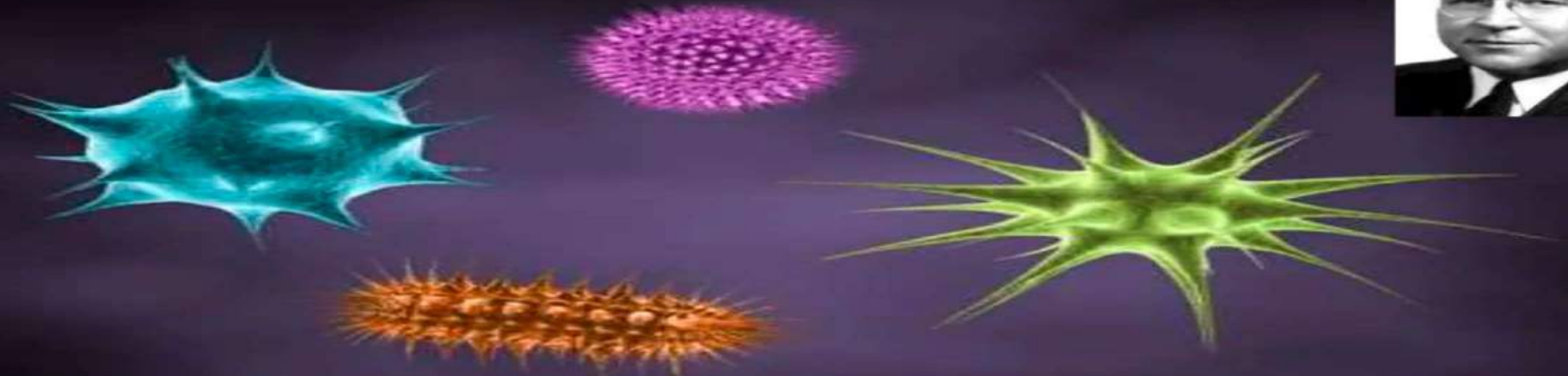
Family (-*viridae*) *Filoviridae* (filovirus family)

Genus (-*virus*) *Ebolavirus*

Species* *Zaire ebolavirus*



Tobacco Mosaic Virus



Wendell Stanley (1935) discovered viruses were made of nucleic acid and protein

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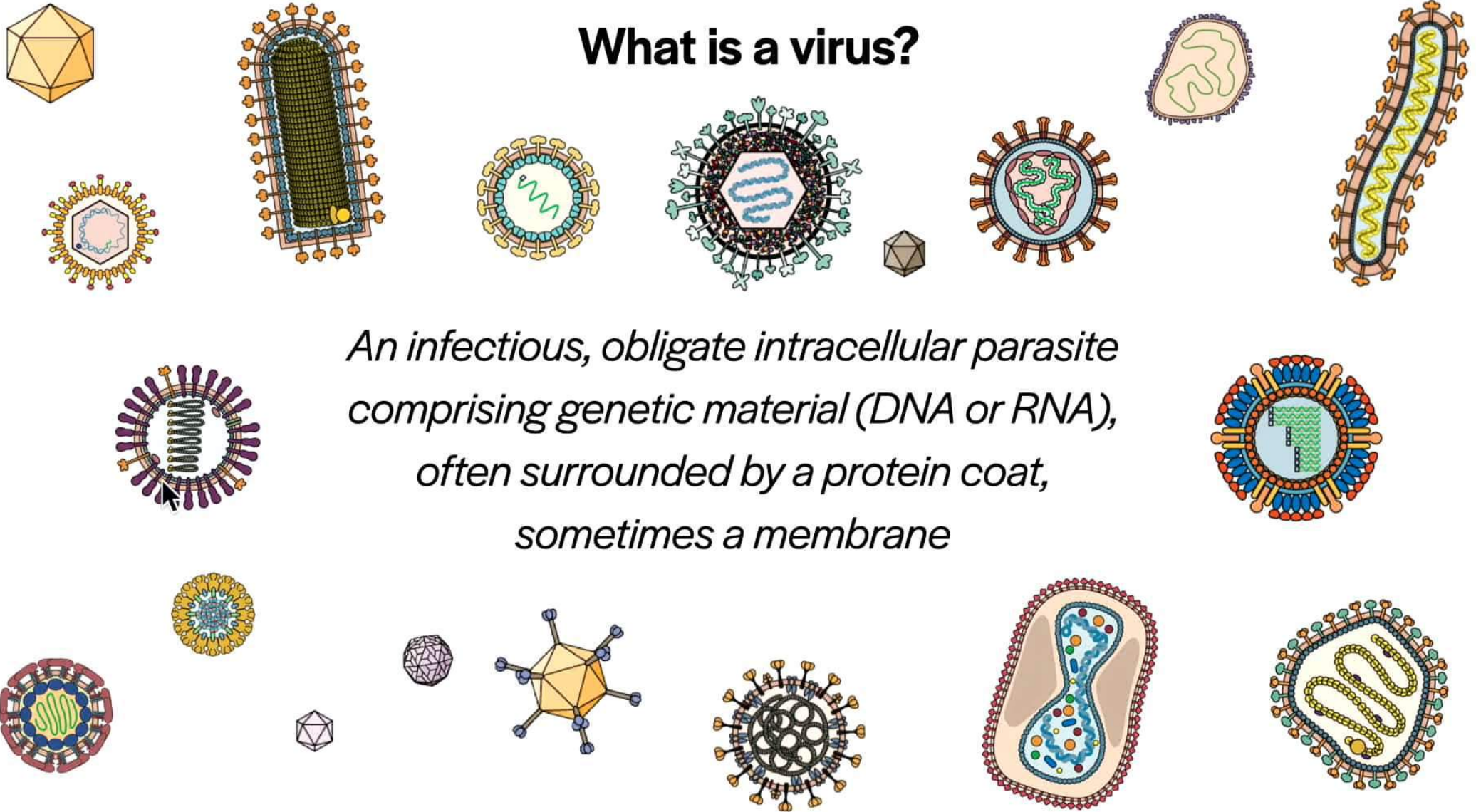
General characteristics of viruses

- Viruses are smaller than bacteria, they range in size between **20-300** nanometer (nm)
- Viruses contain only one type of nucleic acid, either **DNA** or **RNA**, but never both.
- Viruses consist of nucleic acid surrounded by a protein **coat**. Some viruses have additional lipoprotein **envelope**.
- Viruses **lack** cellular organelles, such as mitochondria and ribosomes.

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What is a virus?

An infectious, obligate intracellular parasite comprising genetic material (DNA or RNA), often surrounded by a protein coat, sometimes a membrane

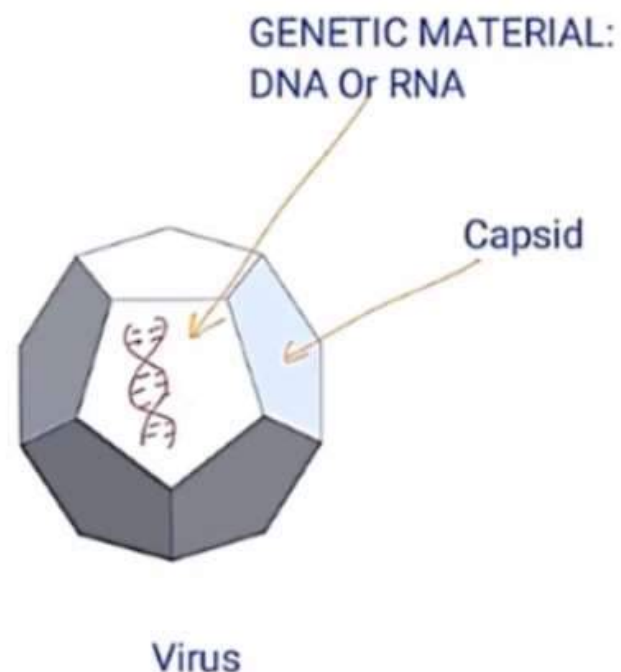


General characteristics of viruses

- ✚ Viruses are obligate cellular **parasites**. They replicate only inside living cells.
- ✚ Viruses **replicate** through replication of their nucleic acid and synthesis of the viral protein.
- ✚ Viruses do not multiply in chemically defined **media**.
- ✚ Viruses **do not** undergo binary fission.

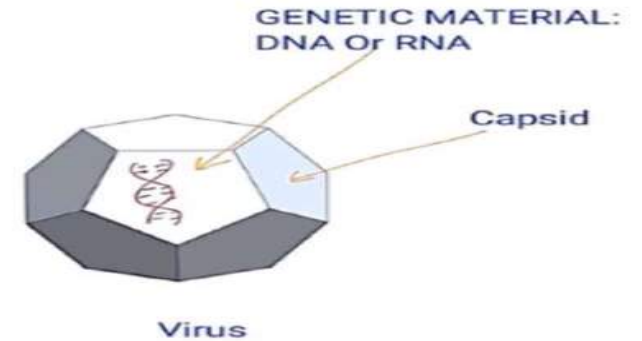
Virus

- Virus is a small entity consist of either DNA or RNA as genetic material.
- Genetic material is enclosed by protein coat called capsid.
- Virus may or may not surrounded by outer lipid membrane called envelope.
- Virus infect all types of organisms.



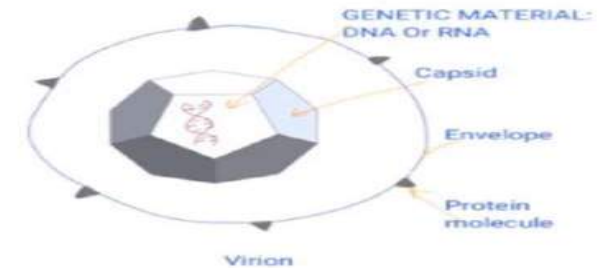
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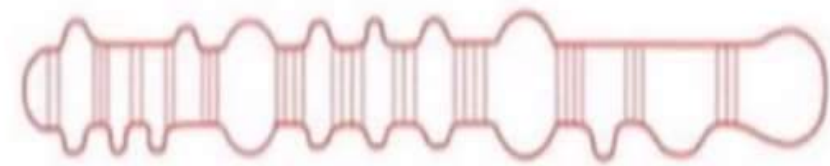
Virion

- A virion is a complete functional virus that has the capacity to infect living tissue.
- It includes the genetic material either RNA or DNA, capsid, envelope and membrane proteins.
- Membrane proteins allow the virus to bind to its host and enter it.



Viroids

- Viroid is smaller than virus.
- Viroid is single stranded covalently closed infectious RNA molecule without capsid.
- They replicate by RNA-RNA transcription and lack protein coding.
- Viroids only infect plants.

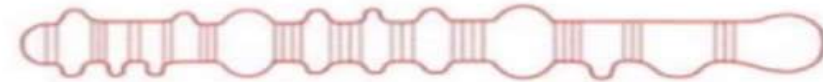


Structure of a viroid – circular single-stranded RNA with some pairing between complementary bases and loops where no such pairing occurs



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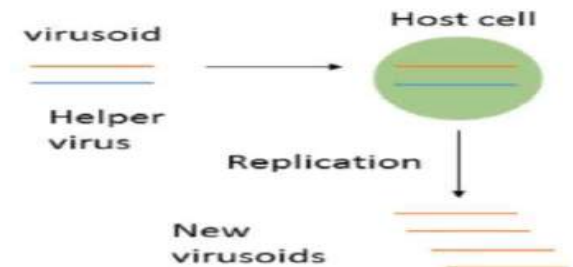


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Virusoids

- Virusoids possess linear or circular RNA as genetic material.
- Virusoids can not replicate autonomously they require the cells infected with a virus that function as a helper for replication.



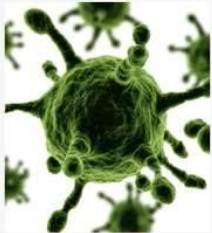
1. REGRESSIVE HYPOTHESIS

VIRUSES AROSE FROM CELLULAR ORGANISMS MOST LIKELY A BACTERIUM. THE CELLULAR ORGANISMS FORMED VIRUSES BY ENQUIRING THE ABILITY TO GRADUALLY DISCARD THEIR GENES UNTIL THEY BECAME SIMPLER ORGANISMS WHICH ARE THE VIRUSES WE SEE TODAY.

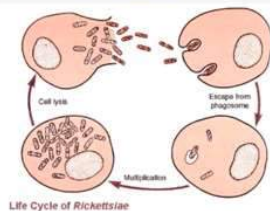
Evidence of this is shown from Virus like Bacterium's:



1. *Buchnera*: Bacteria that infects aphids. They have discarded more than 70% of their genome.

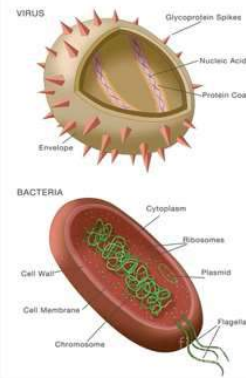


2. *Chlamydiae*: This is a bacteria but is unable to reproduce on its own.



3. *Rickettsia*: replication cycle is very similar to that of a retro viruses. As it affects a healthy cell and replaces its genome with the host and then moves onto the next cell.

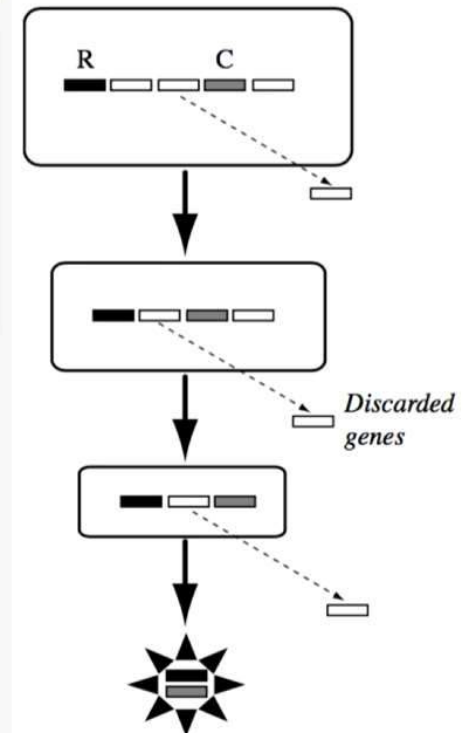
However:



The regressive theory predicts that viruses and bacteria share ancestors. However they are both very structurally and genetically different.

The genome size of a viruses is smaller than that of a bacterium as it is limited by fitness costs so is unclear how they could have previously existed with larger genomes.

(a) Regressive evolution



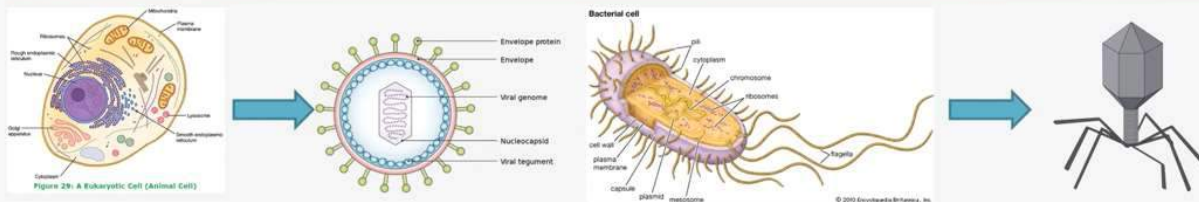
2. ESCAPED HOST GENES HYPOTHESIS

GENETIC MATERIAL OF A HOST CELL HAS ESCAPED OVER TIME AS THE GENETIC MATERIAL WAS NO LONGER NEEDED. THROUGH HORIZONTAL GENE TRANSFER THE GENETIC MATERIAL WAS EVOLVED TO BECOME VIRUSES.

In the host genome it was most likely mRNA molecules that acquired both the ability to self-replicate and the protective protein coats that allowed them to exist independently of cells.

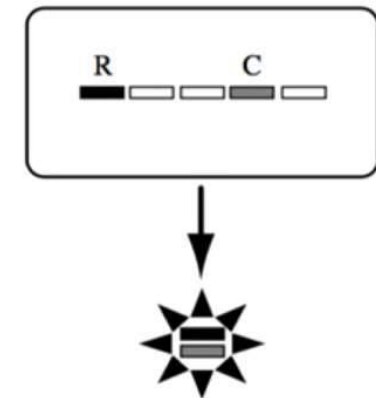
It proposes that both RNA and DNA viruses existed *after* the first cellular organisms, so that this may be considered a '**post-cellular**' theory of viruses.

Eukaryotic viruses originated in eukaryotic genomes while bacteria formed the bacteriophage.



However, this method does not explain how the formation of complex capsids and other particles were present in viruses but not in host cells.

(b) Escaped host gene



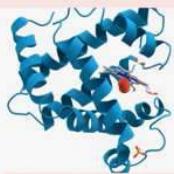
3. PRE-CELLULAR ORIGIN HYPOTHESIS

RNA VIRUSES ARE THE DESCENDANTS OF PRE CELLULAR RNA LIFE FORMS/PROTEINS THAT DATE BACK BILLIONS OF YEARS TO THE BEGINNING OF TIME. THROUGH EVOLUTIONARY TIME THEY HAVE ADOPTED A PARASITIC LIFESTYLE.

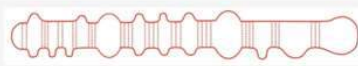
Evidence for this theory is because viruses with similar viral machinery are present in the three groups of life; Bacteria, Archaea and Eukaryotes.

DNA viruses are remnants of the first DNA replicators, while the retroviruses could be descendants of the first molecules that were able to make the transition between RNA and DNA.

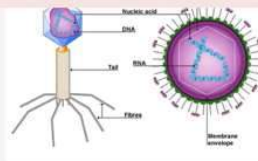
How did Viruses Form?



Proteins



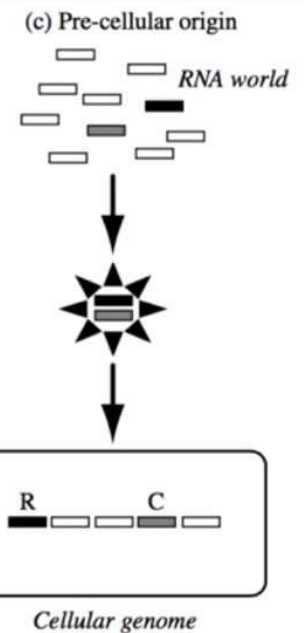
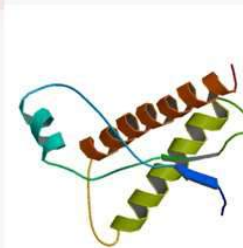
Viroid's

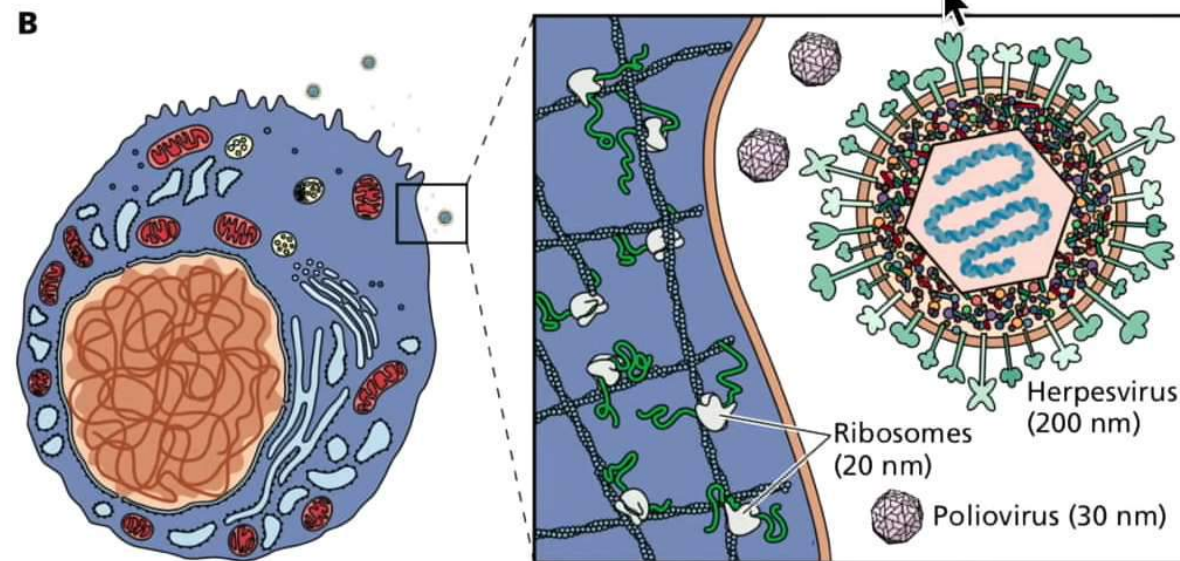
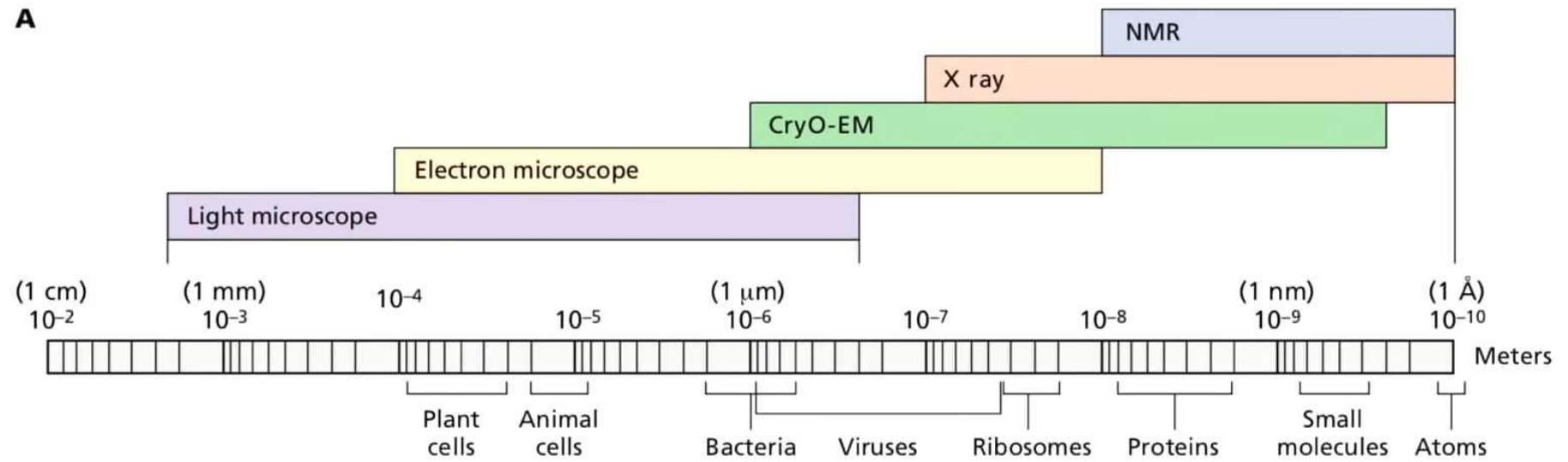


Viruses

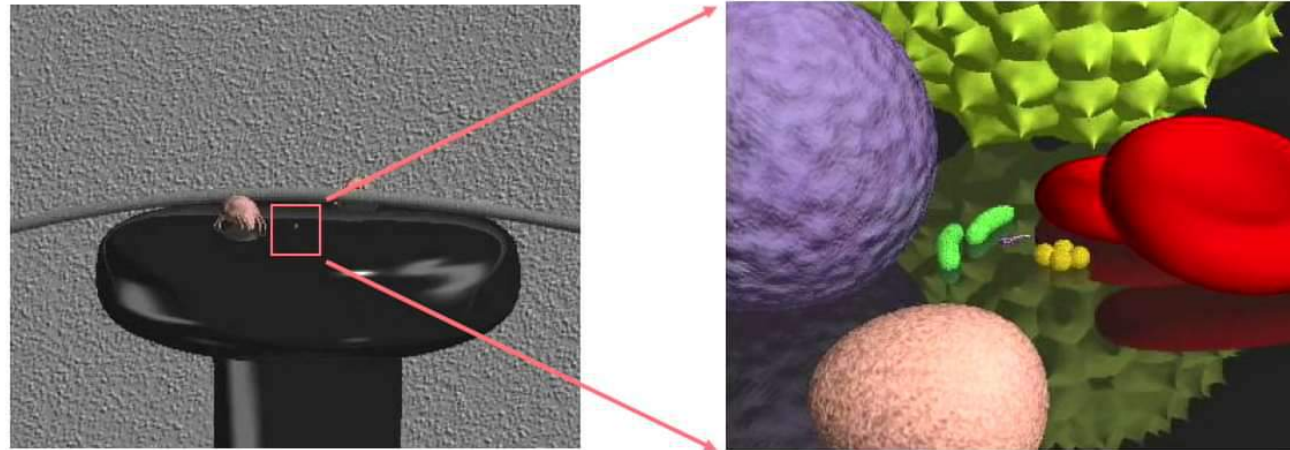
Evidence to suggest this model is correct:

Prions are infectious protein molecules that do not contain DNA or RNA. Although prions are fundamentally different from viruses and viroid's, their discovery gives credence to the theory that viruses could have evolved from self-replicating molecules.





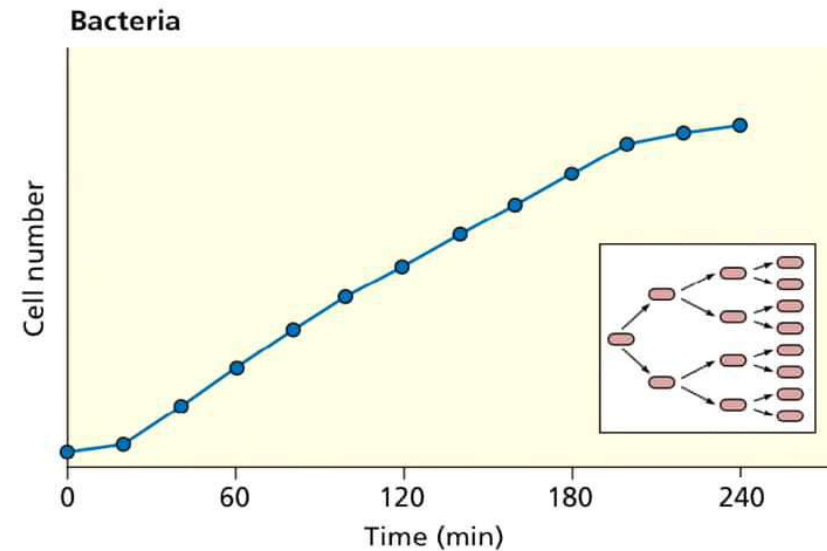
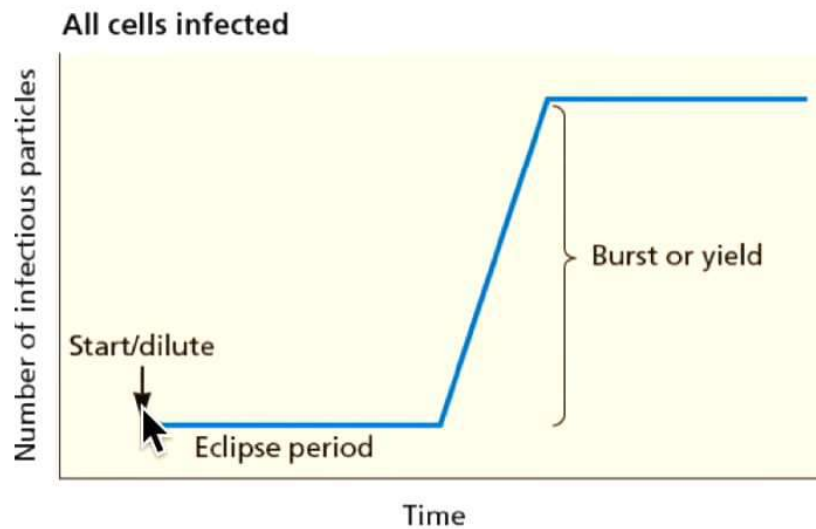
How many viruses can fit on the head of a pin?



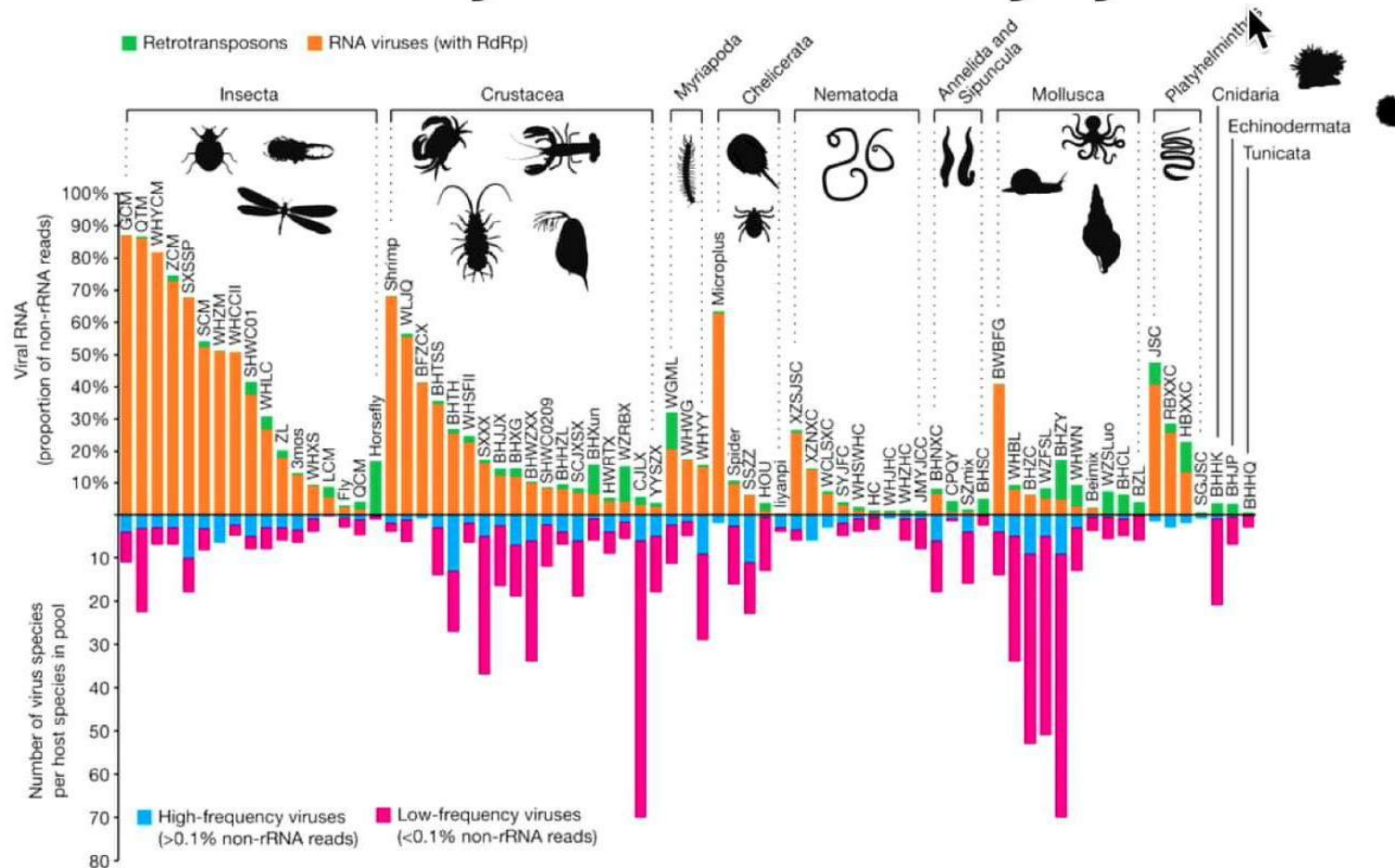
2 mm = 2000 microns

- 500 million rhinoviruses
- When you sneeze, you fire an aerosol that contains enough viruses to infect thousands

Key 1939 experiment proved that viruses were not simply small bacteria



Virus discovery - Once driven only by disease



Analyzed RNA from 220 invertebrate species, found 1,445 new viruses