General Virology I

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Lecture Outline

- Introduction
- History
- Definition of A virus
- Properties of unicellular microorganisms and viruses
- Viral structure
- Host range

Introduction

- Virology is the study of viruses, complexes of nucleic acids and proteins that have the capacity for replication in animal, plant and bacterial cells.
- To replicate themselves, viruses use up functions of the host cells on which they are parasites.
- The viral parasite causes changes in the cell, particularly its antigenicity; moreover, directing the host cell's metabolism to the production of new virus particles may cause cellular death.
- Virally-induced cell death, changes in antigenicity and the response of the host to the presence of the virus leads to the manifestations of viral disease.

Viruses come in two basic types, those that have a genome of DNA and those that have a genome of RNA.

1798

Jenner

“development of smallpox vaccine”

1798 — Jenner

1890 — Iwanowski, Beijerinck, Loeffler & Frosch

1798 — Jenner

1890 — Iwanowski, Beijerinck, Loeffler & Frosch

Virus

Latin Word Meaning “Poison”

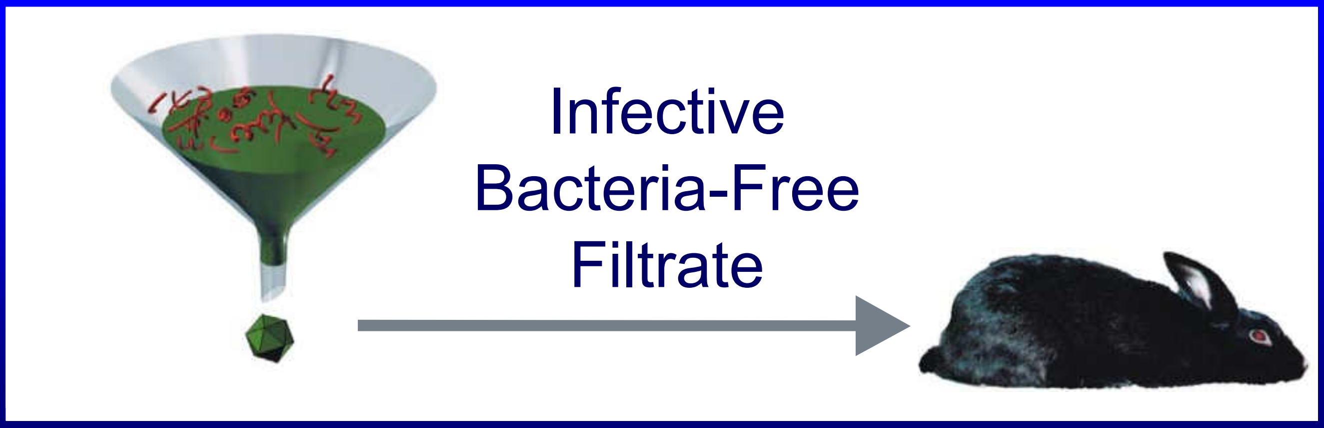
1798 — Jenner

1890 — Iwanowski, Beijerinck, Loeffler & Frosch

1911 — Rous

Transmission of Rous Sarcoma virus in Chicken

1798	1890	1911	1933
Jenner	Iwanowski, Beijerinck, Loeffler & Frosch	Rous	Shope



1798 — Jenner

1890 — Iwanowski, Beijerinck, Loeffler & Frosch

1911 — Rous

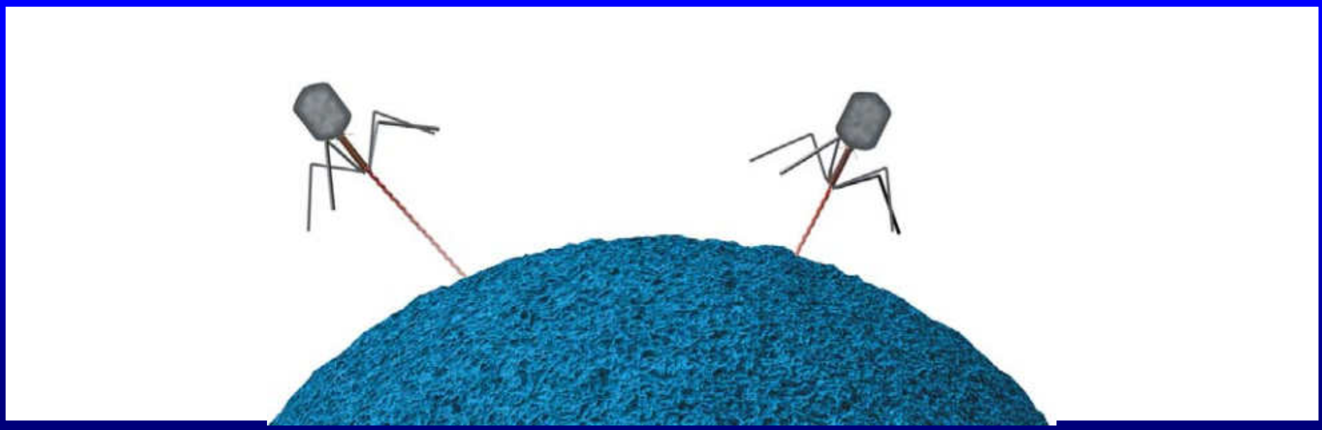
1933 — Shope

1935 — Stanley

Tobacco Mosaic Virus

Composed of Nucleic Acid & Protein

1798 — Jenner
1890 — Iwanowski, Beijerinck, Loeffler & Frosch
1911 — Rous
1933 — Shope
1935 — Stanley
1952 — Hershey, Chase



1798 — Jenner

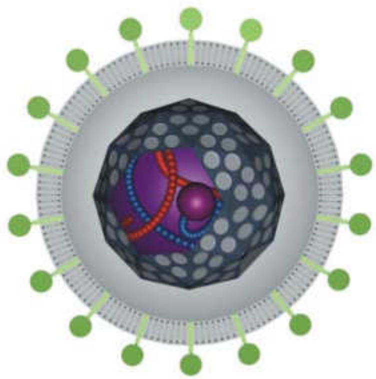
1890 — Iwanowski, Beijerinck, Loeffler & Frosch

1911 — Rous

1933 — Shope

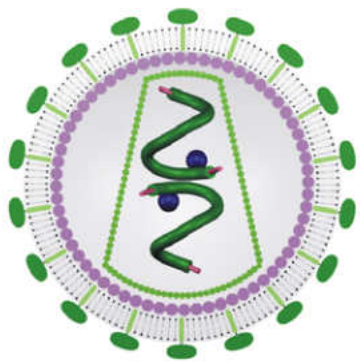
1935 — Stanley

1976 — Fiers, Temin, Erickson



RNA Tumor Virus

1798 Jenner
1890 Iwanowski, Beijerinck, Loeffler & Frosch
1911 Rous
1933 Shope
1935 Stanley
1976 Fiers, Temin, Erickson
1984 Gallo, Montagnier
1995



1984: Isolation of AIDS virus
1995: Multiple drug treatment (protease inhibitors + reverse transcriptase inhibitors)

Definition of A Virus

- **Viruses are organized associations of macromolecules:-**
  nucleic acid **(which carries the blueprint for the replication of progeny virions) contained within a protective** ***shell of protein units*****.**

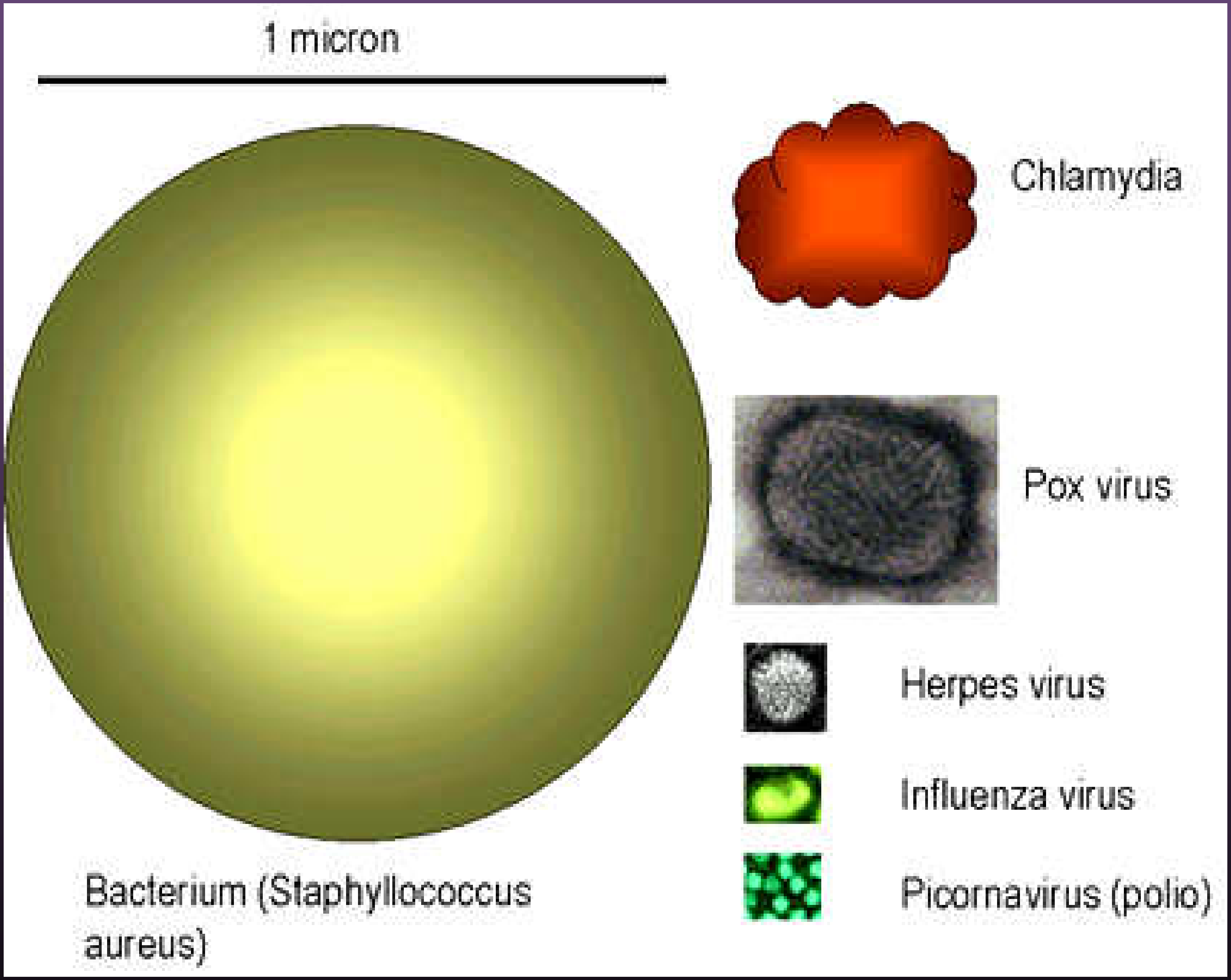
  - On its own, a virus may be considered as an inert biochemical complex since it cannot replicate outside of a living cell. Once it has invaded a cell it is able to direct the host cell machinery to synthesize new intact infectious virus particles (*virions*).

  - Because viruses are non-motile, they are entirely dependent on external physical factors for chance movement and spread to infect other susceptible cells.

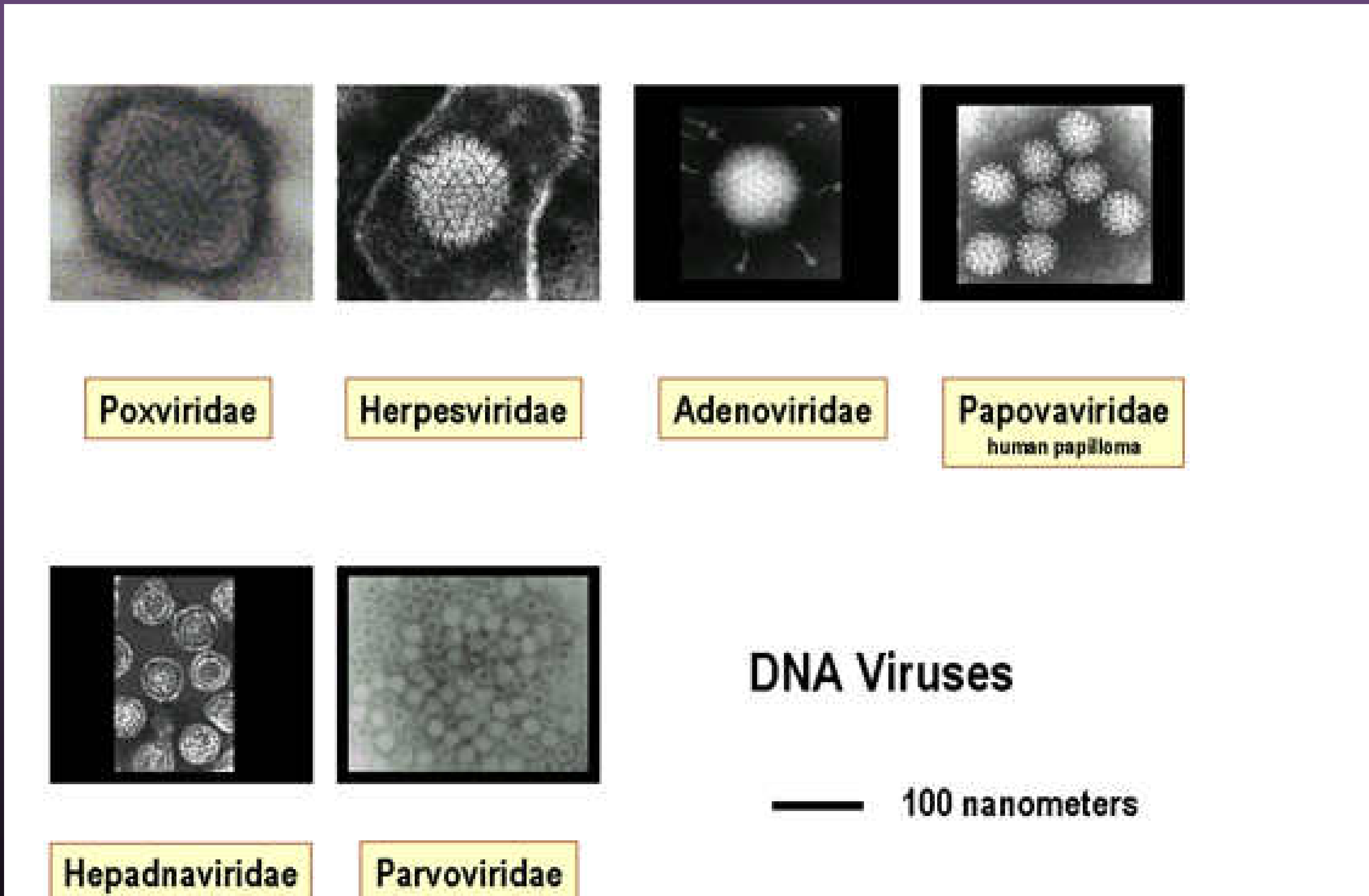
Properties of Unicellular Microorganisms and Viruses

Property	Bacteria	Rickettsiae	Chlamydiae	Virus
diameter(nm)	1000	500	300	250~25
Type of nucleic acid	DNA and RNA	DNA and RNA	DNA and RNA	DNA or RNA
Binary fission	+	+	+	-
Synthesis of proteins	+	+	+	-
Machinery of energy production	+	+	-	-
Growth out of cellular hosts	+	-	-	-

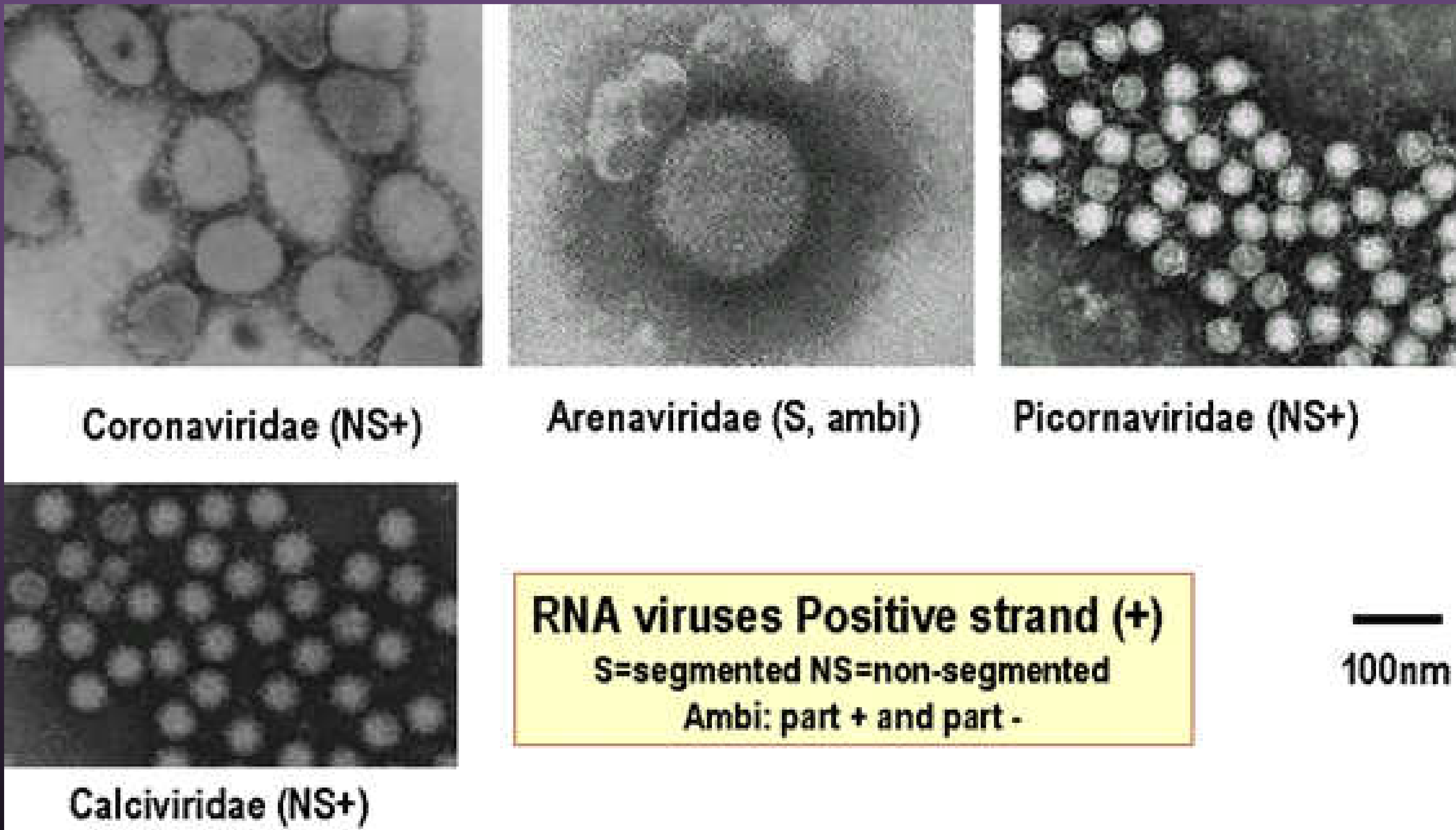
Relative Size of Viruses and Bacteria



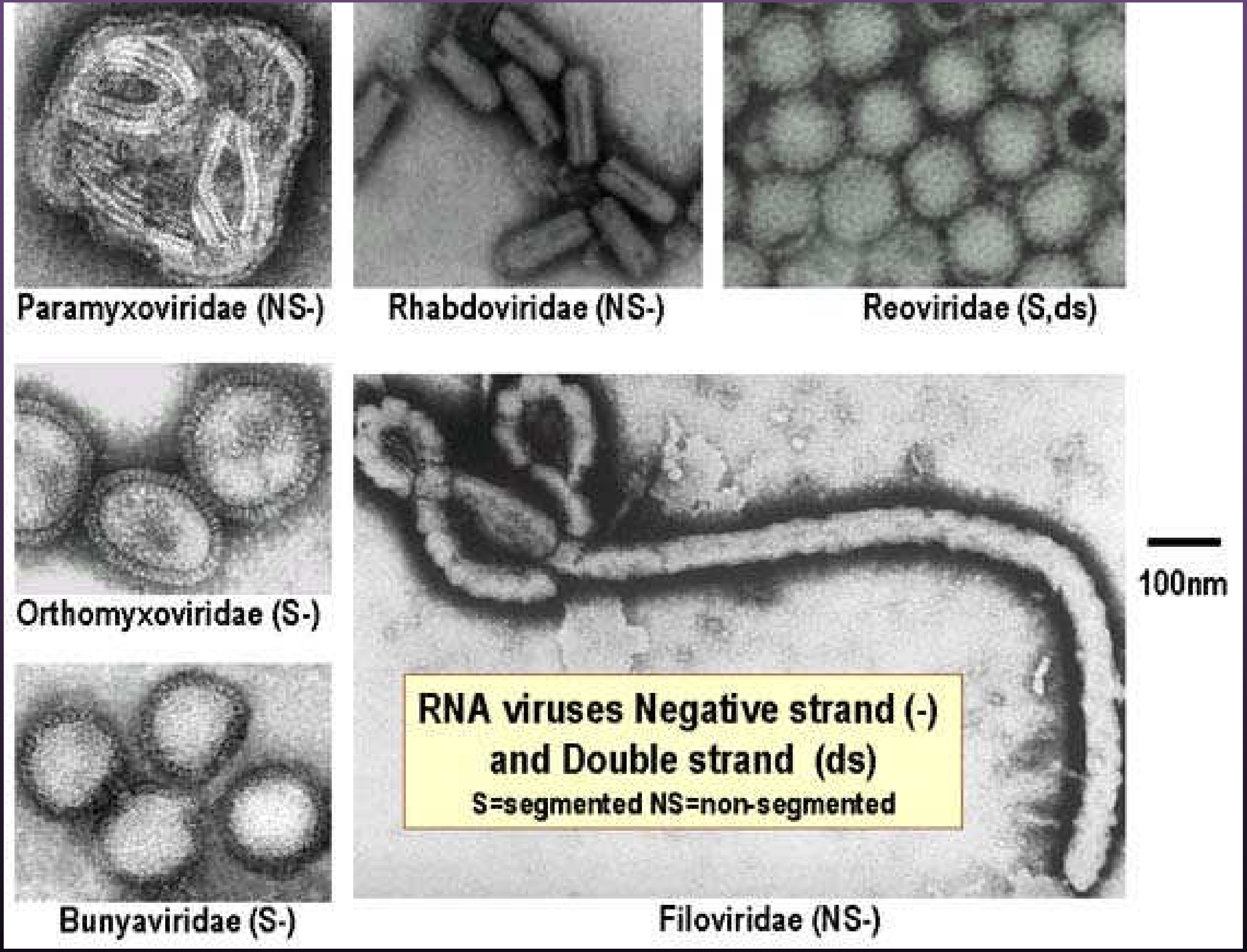
Relative Size of DNA Viruses



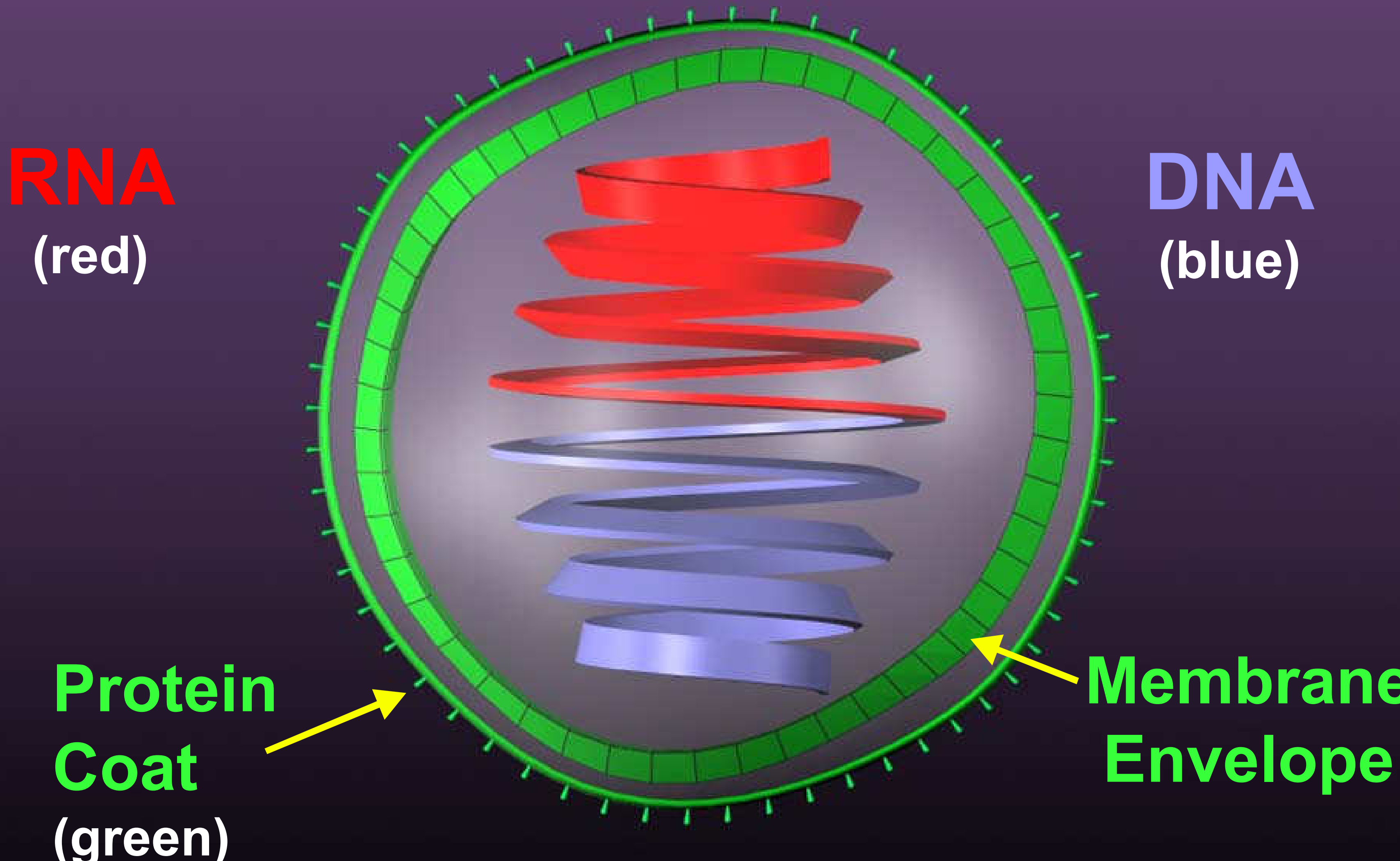
Relative Size of Positive Strand RNA Viruses



Relative Size of Negative Strand RNA Viruses



VIRUS



Virus Structure

- Viral components - general

  Viruses contain:

  - a nucleic acid genome (RNA or DNA)
  - a protective protein coat (called the capsid)

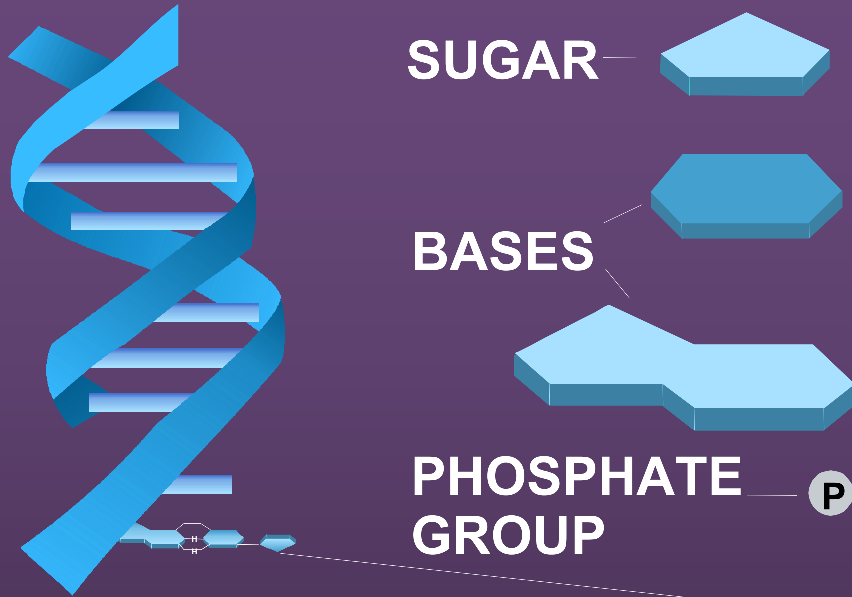
The nucleic acid genome plus the protective protein coat = nucleocapsid

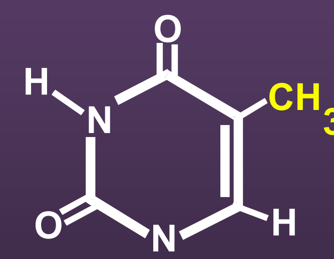
The nucleocapsid may have icosahedral or helical symmetry

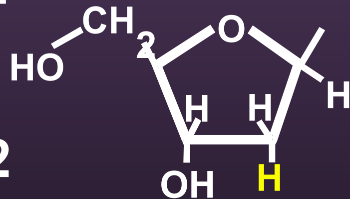
Viruses may or may not have an envelope made of lipid derived from the host cell

DNA

1. Double Stranded
2. Contains Deoxyribose
3. Contains Thymidine

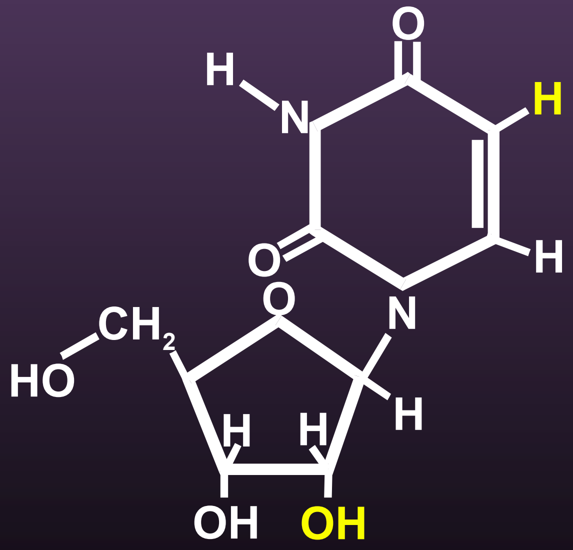


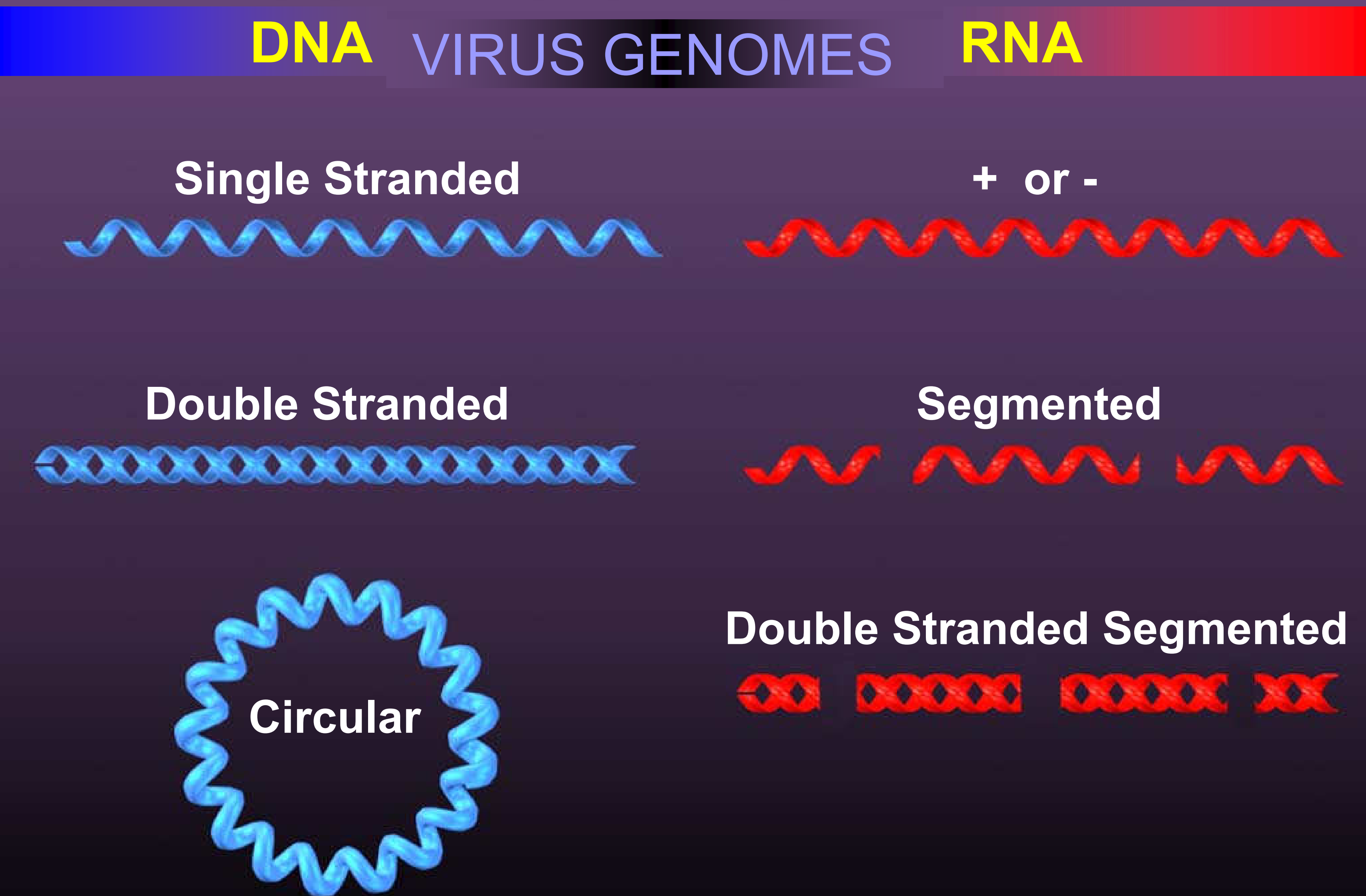




RNA

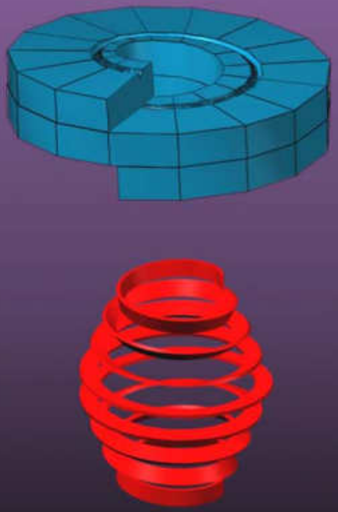
1. Usually Single Stranded
2. Contains Ribose
3. Contains Uridine




DNA
VIRUS GENOMES
RNA
Single Stranded
+ or -
Double Stranded
Segmented
Circular
Double Stranded Segmented

CAPSID FUNCTIONS

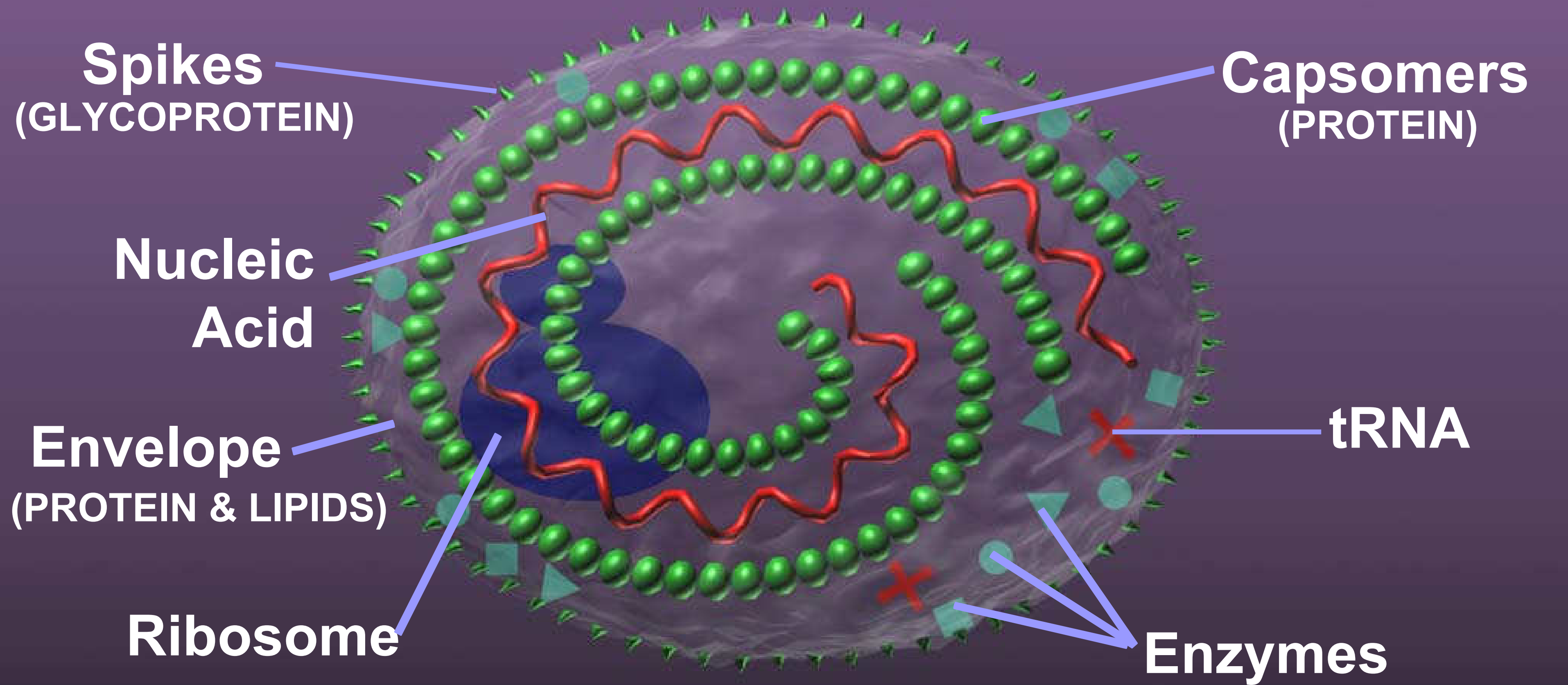
- Protection of Nucleic Acid
- Transport Nucleic Acid From Cell to Cell
- Provides Specificity for Attachment



Viral Envelope

- Enveloped viruses obtain their envelope by budding through a host cell membrane. In some cases, the virus buds through the plasma membrane but in other cases the envelope may be derived from other membranes such as those of the Golgi body or the nucleus.
- The envelope consists of a lipid bilayer and proteins and always includes at least one virally coded protein involved in attachment.
- Enveloped viruses do not necessarily have to kill cell in order to be released, since they can bud out of the cell - a process which is not necessarily lethal to the cell - hence some budding viruses can set up persistent infections.

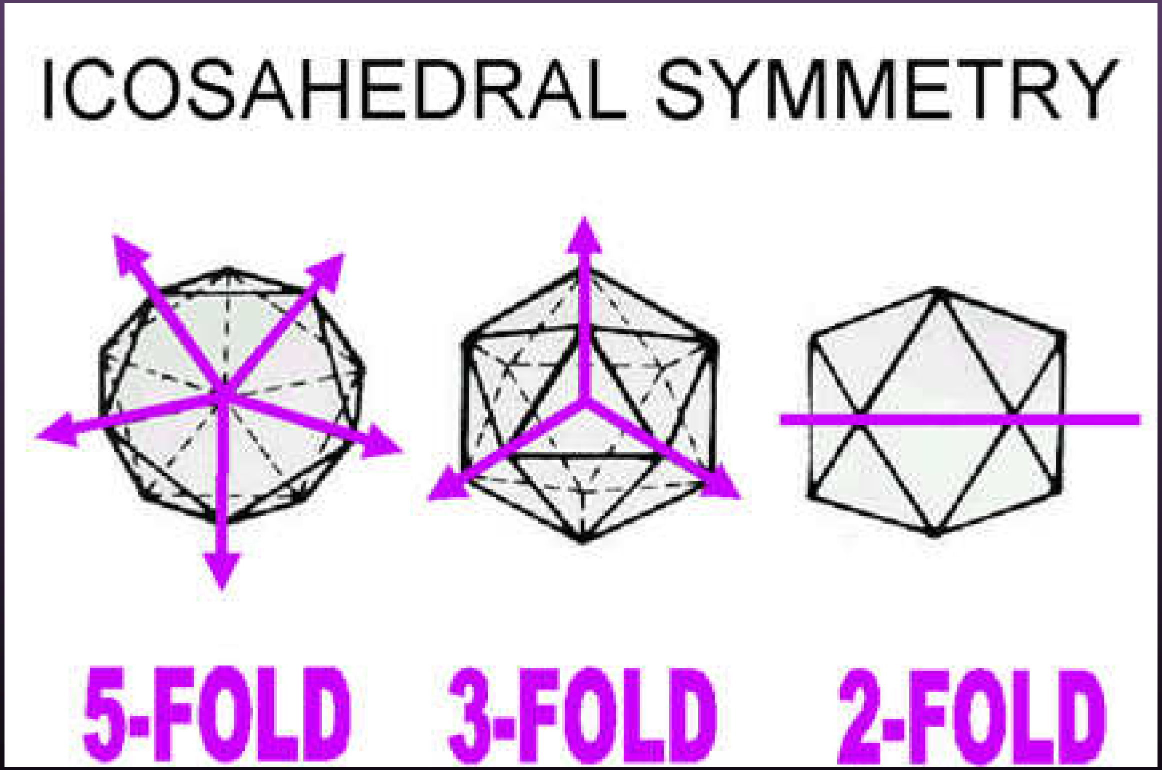
ENVELOPED HELICAL Nucleocapsid



Virion Nucleocapsid Structures (1)

A) ICOSAHEDRAL

- Icosahedron: solid figure, 20 faces, 5:3:2 rotational symmetry
- 12 corners or vertices, 5-fold symmetry around vertices



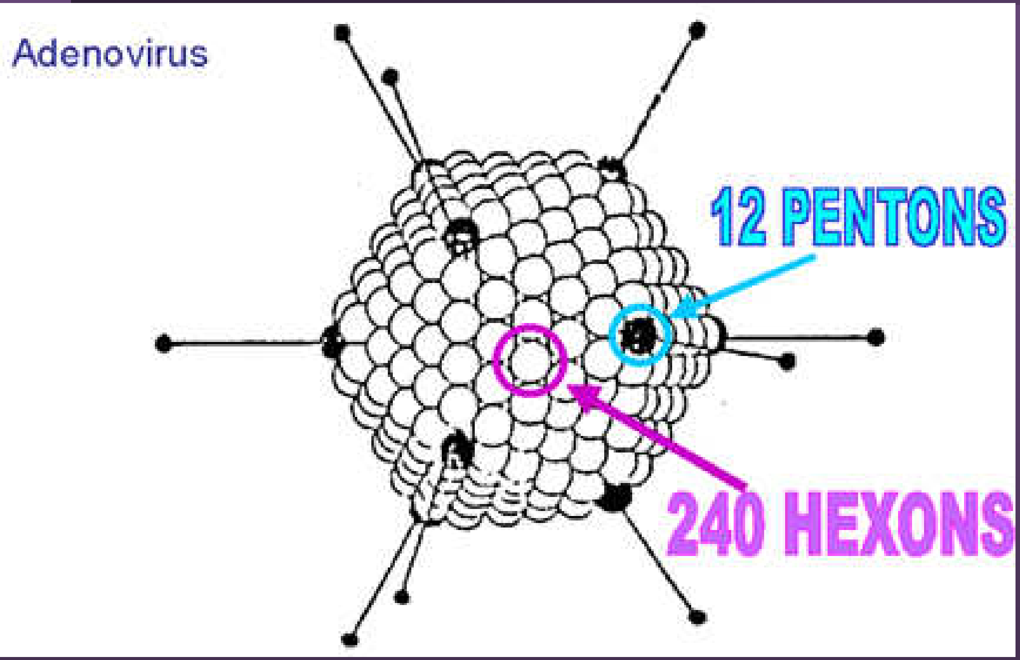
Icosahedral symmetry in viruses

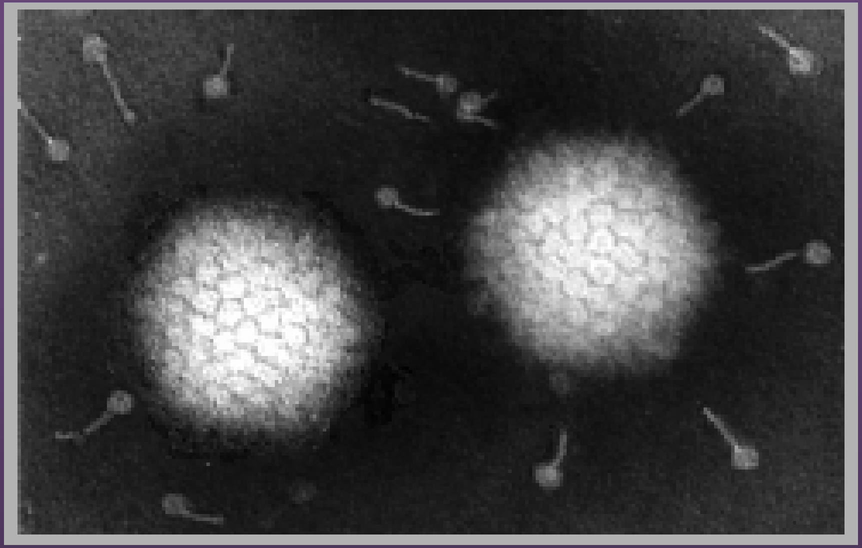
Virion Nucleocapsid Structures (2)

A) ICOSAHEDRAL (cont.)

- The capsid shell is made of repeating subunits of viral protein (may be one kind of subunit or several, according to the virus).
- All faces of the icosahedron are identical.
- The nucleic acid is packaged inside the capsid shell and protected from the environment by the capsid.
- Proteins associate into structural units (this is what one sees in the electron microscope or when start to disassociate a capsid), the structural units are known as capsomers - capsomers may contain one or several kinds of polypeptide chain.
- Capsids with icosahedral symmetry have 12 vertices, capsomers at the 12 corners have a 5-fold symmetry and interact with 5 neighboring capsomers, and are thus known as pentons (or pentamers).

Adenovirus Symmetry





Human adenovirus seen by negative staining

Larger viruses contain more capsomers, extra capsomers are arranged in a regular array on the faces of the icosahedrons, these often have six neighbors and are called hexons (or hexamers).

The size of such an icosahedron depends on the size and number of capsomers, there will always be 12 pentons, but the number of hexons may increase.

Virion Nucleocapsid Structures (3)

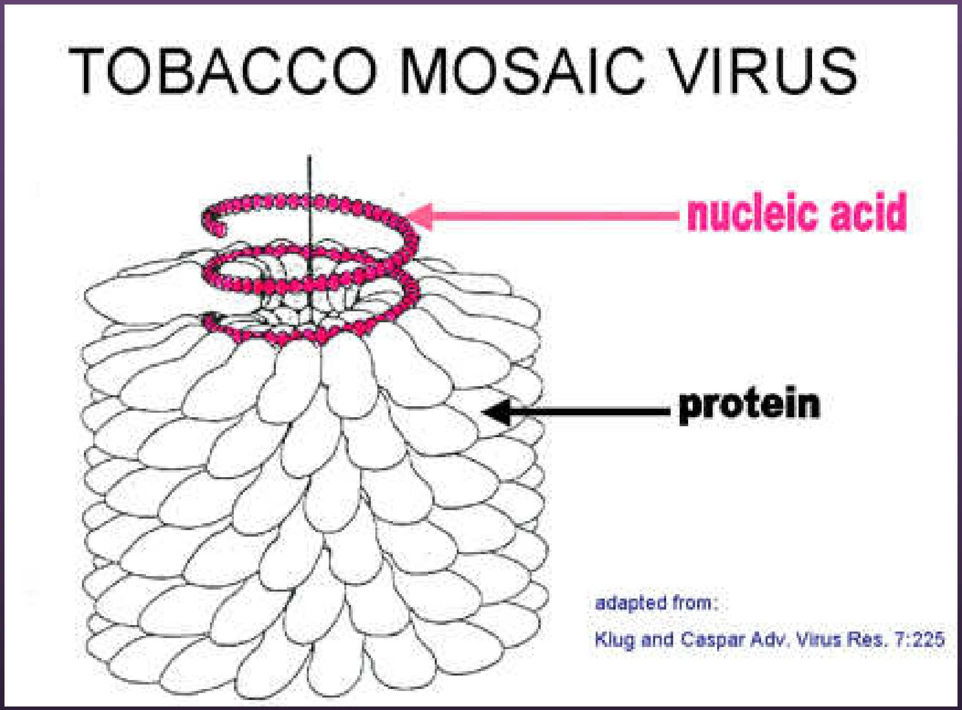
B) HELICAL

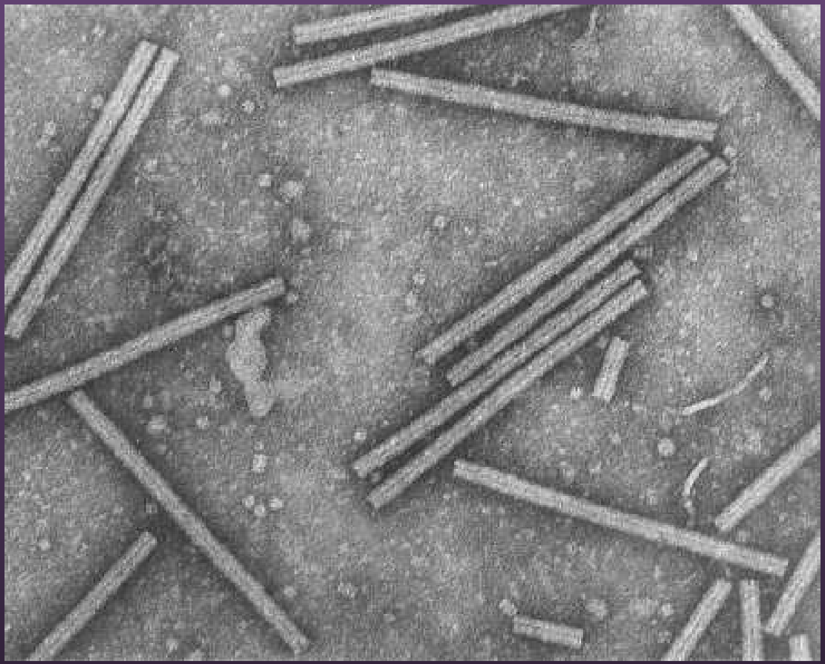
Protein subunits interact with each other and with the nucleic acid to form a coiled, ribbon like structure:

e. g. tobacco mosaic virus, influenza virus, rabies virus.

Helix may be very rod-like and inflexible (tobacco mosaic virus) or very flexible (Paramyxoviruses).

Tobacco Mosaic Virus Structure Showing a Helical Capsid Structure





Tobacco Mosaic Virus

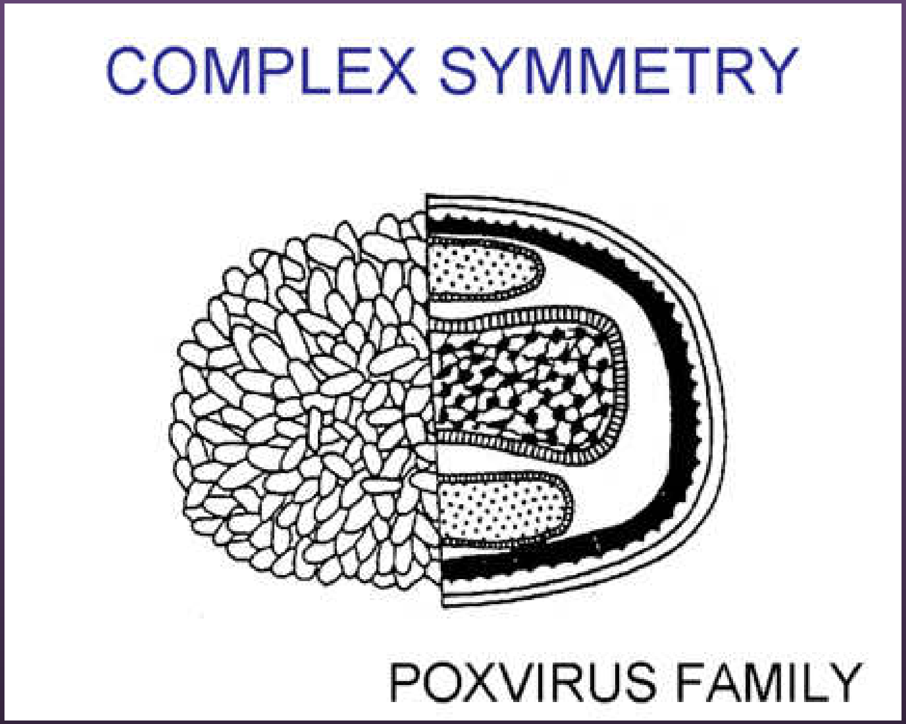
Virion Nucleocapsid Structures (4)

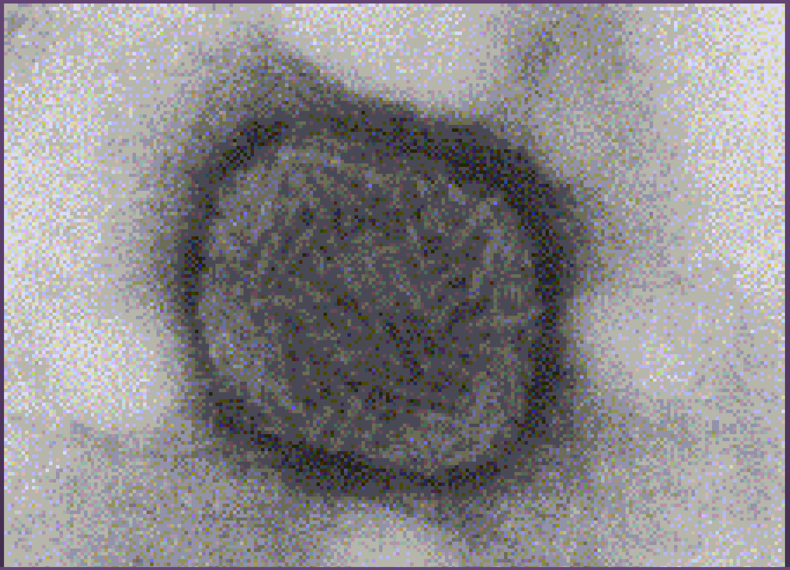
C) COMPLEX

Regular structures, but nature of symmetry not fully understood.

Example: Poxviruses

Complex Symmetry Found in Poxviruses



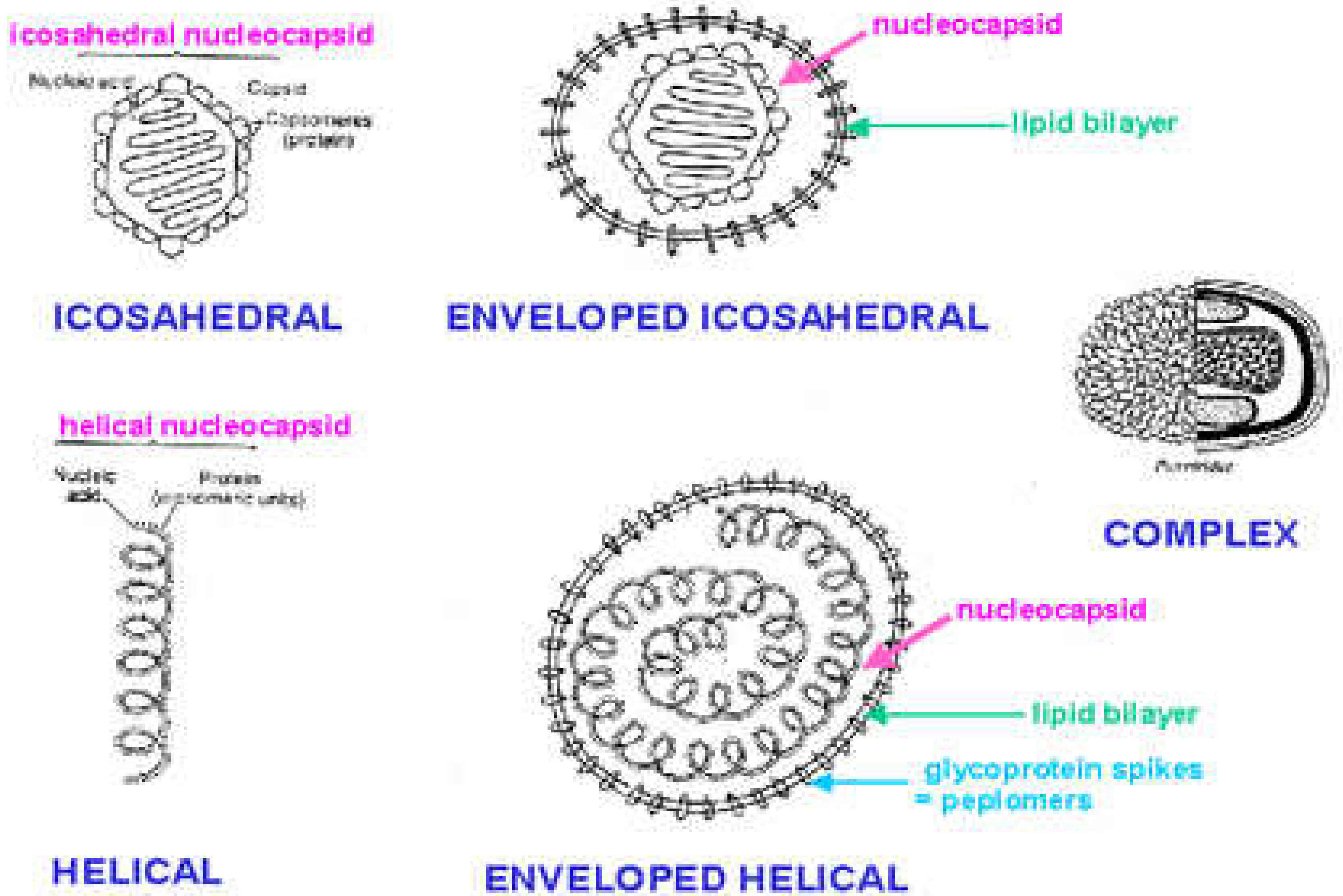


Pox virus seen by negative staining

Basic Structural Forms Of Viruses In Nature

1. **Naked icosahedral** e.g. Poliovirus, Adenovirus, Hepatitis A virus
2. **Naked helical** e.g. Tobacco mosaic virus, so far no human viruses with this structure known
3. **Enveloped icosahedral** e.g. Herpes virus, Yellow fever virus, Rubella virus
4. **Enveloped helical** e.g. Rabies virus, Influenza virus, Parainfluenza virus, Mumps, Measles
5. **Complex** e.g. Poxvirus

5 BASIC TYPES OF VIRAL SYMMETRY



Adapted from Schaeter et al., Mechanisms of Microbial Disease

Unconventional Agents

- **There are also the 'unconventional agents' sometimes known as 'unconventional viruses' or 'atypical viruses' - the main kinds which have been studied so far are:**

1- **VIROIDS**

2- **PRIONS**

Viroids (1)

- Viroids contain RNA only. Small (less than 400 nucleotides), single stranded, circular RNAs, these are not packaged, do not appear to code for any proteins, and so far have only been shown to be associated with plant disease. However, there are some suggestions that somewhat similar agents may possibly be involved in some human disease.

Viroids (2)

- So far the only known human disease agent to resemble viroids is hepatitis delta agent.

  - This agent has a small RNA genome, although somewhat larger than the true viroids, but features of the nucleic acid sequence and structure are somewhat similar to viroids.

  - Hepatitis delta agent (also known as hepatitis delta virus) does not code for its own attachment protein, but unlike the viroids, it is packaged - it acts as a parasite on hepatitis B virus, and uses hepatitis B virus envelopes with the hepatitis B attachment protein.

  - Hepatitis delta agent differs from viroids in that it does code for a few proteins. In some ways hepatitis delta agent appears to be intermediate between 'classical viruses' and viroids.

Prions

Prions contain protein only (although this is somewhat controversial). They are small, proteinaceous particles and there is controversy as to whether they contain any nucleic acid, but if there is any, there is very little, and almost certainly not enough to code for protein:

e.g. Scrapie, Kuru, Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome

Host Range

- **Viruses infect all major groups of organisms: vertebrates, invertebrates, plants, fungi, bacteria.**
- **Some viruses have a broader host range than others, but none can cross the eukaryotic/prokaryotic boundary.**

Factors which affect host range include;

i) whether the virus can get into the host cell

ii) if the virus can enter the cell, is the appropriate cellular machinery available for the virus to replicate?

iii) if the virus can replicate, can infectious virus get out of the cell and spread the infection?