Virology

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THE IMPORTANCE OF STUDYING VIRUSES

- We study viruses and the diseases they cause for a variety of reasons.
- **First:** viruses are everywhere.

  Found in: the air, the ocean, the soil, and in rivers.
- They are present wherever life occurs, and it is thought that every living thing has a virus that infects it.

THE IMPORTANCE OF STUDYING VIRUSES

- There are around **3000** documented species of viruses that infect a range of living organisms, although there are thousands of different strains and isolates within these species.
- All living organisms have a relationship with viruses.
- Viruses have been around since the beginning of life on Earth.

Figure 1. Viruses have existed as long as humans have. The mummy of Ramses V, who died in 1157 BC, exhibits a rash on the lower face and neck that is characteristic of a smallpox rash.

THE IMPORTANCE OF STUDYING VIRUSES

- **Second:** Viruses cause **diseases**.

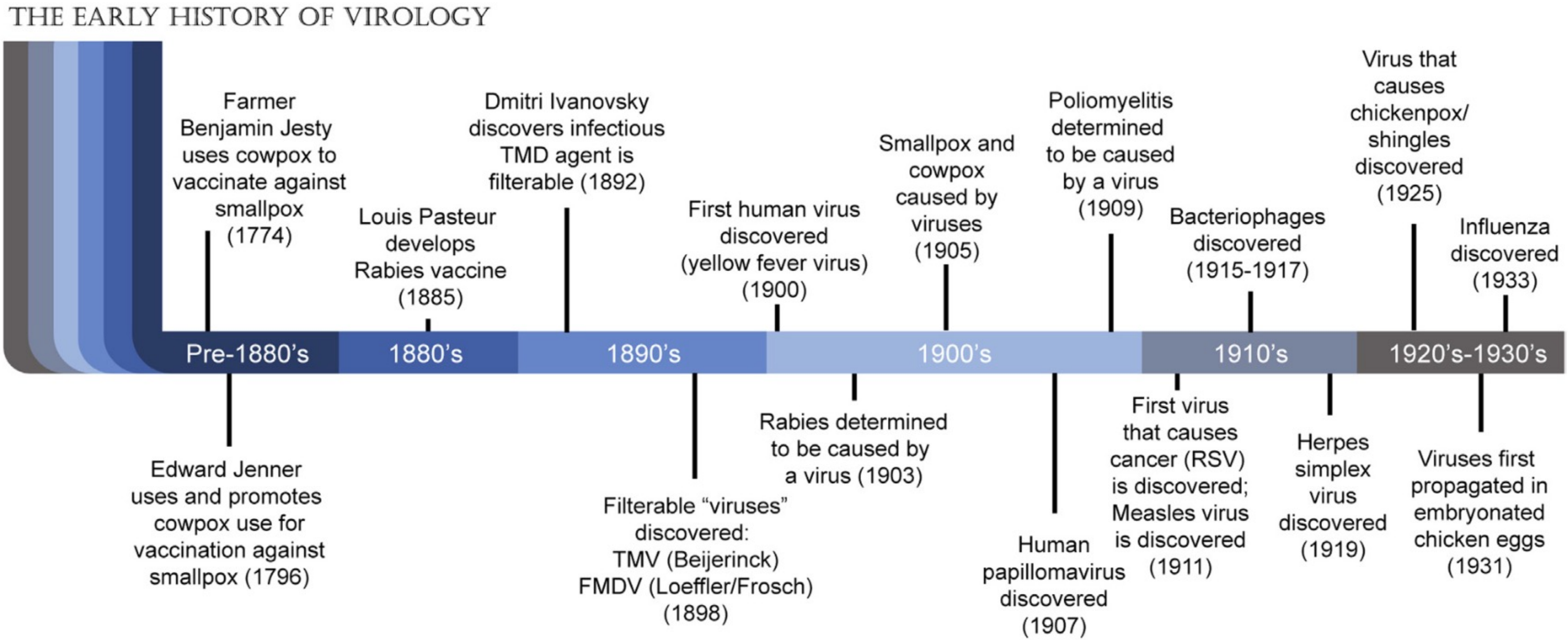
They cause conditions as simple as the **common cold** or as complex as **cancer**.

- **Epidemic**, an outbreak where the virus infects many more individuals than normal and spreads throughout an area.
- **Poliovirus:**
- One of the first major epidemics occurred in New York City in 1916 and resulted in over 9000 cases and 2343 deaths.
- In 1955, the **first polio vaccine** was introduced and cases dropped precipitously

- A **pandemic** when a virus spreads throughout a much larger area, such as several countries, a continent, or the entire world.
- In late 1918, a strain of **influenza** originating in the United States spread throughout the entire world, killing 20–50 million people.

Figure.2 An influenza ward in a U.S. Army camp hospital in France in 1918, during World War I

Figure.3 Timeline of important discoveries in the early history of virology.



- In the earlier half of the 20th century, scientists were uncertain as to whether **protein** (composed of amino acids) or **DNA** (composed of nucleotides) was the hereditary instructions for cell development and function.
- In 1944, Oswald Avery, Colin macleod, and Maclyn mccarty demonstrated that **DNA** is the molecule that encodes inheritable traits.

Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA)

- Are made of many **nucleotides** bonded together.
- **A nucleotide of DNA** (Fig. 4A) is composed of a sugar, called **deoxyribose**, but in RNA (**ribose)** with a **phosphate group** attached at one end of the sugar and a **base** attached at the other end.
- There are **four** different bases in a DNA nucleotide: **adenine, guanine, cytosine, and thymine.**

✓ **In RNA: Uracil** replaces the base **thymine**

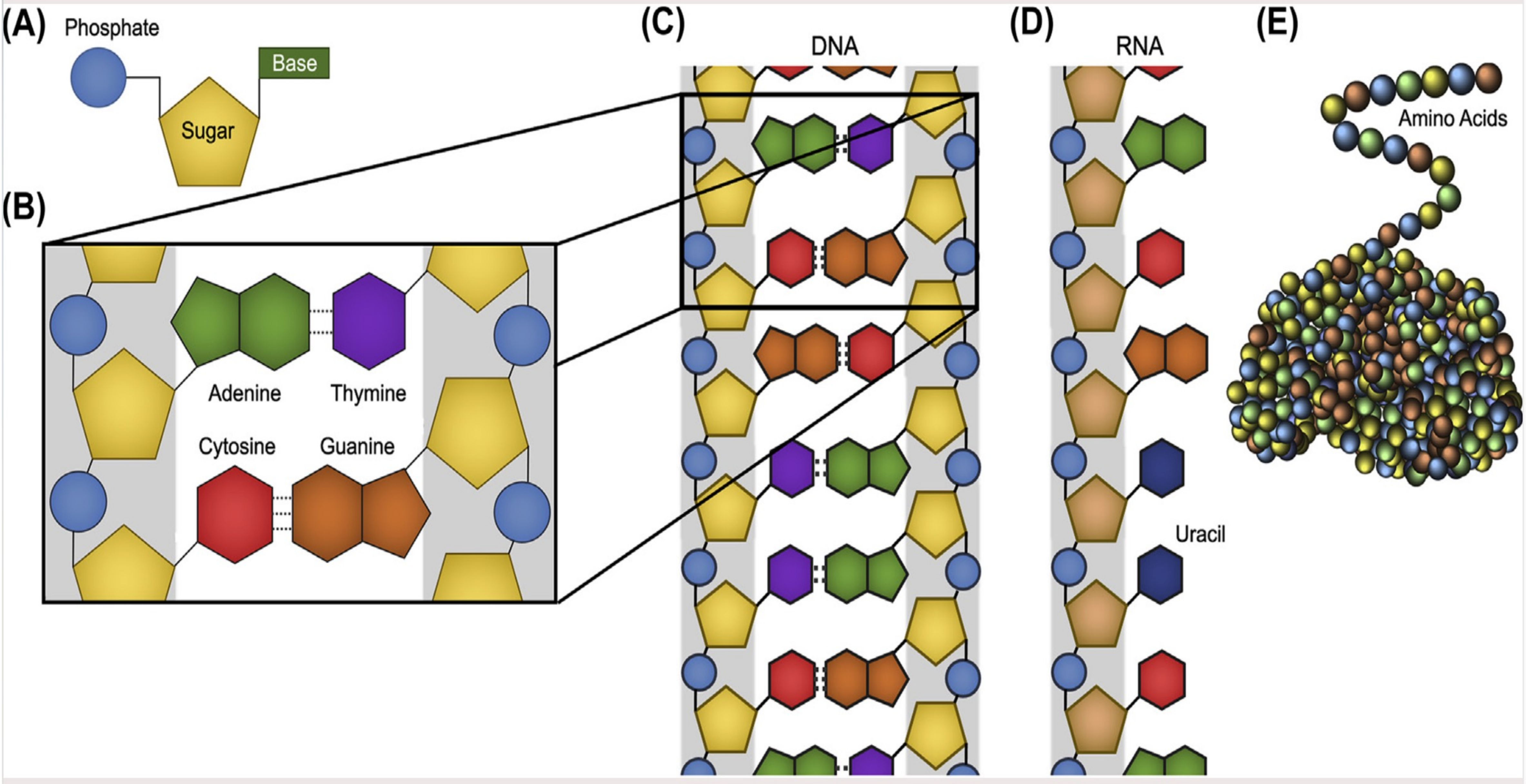
Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA)

- DNA is double-stranded in all living organisms, while RNA is single-stranded (Fig. 4D).
- The bases in one strand bond to the bases in the other strand (Fig. 4C). This is known as a **base pair**.
- In living things, DNA is used as a template for making RNA.
- DNA and RNA are **nucleic acids**.

Protein

- **Protein** is a different biological molecule that is made of **amino acids** bonded together (Fig. 4E).
- There are 20 slightly different amino acids, composed of **carbon**, **hydrogen**, **oxygen**, and **nitrogen**.
- Enzymes are a very important class of proteins.

Figure.4. Three important biological molecules: (A–C) DNA, (D) RNA, and (E) Protein.



VIRUSES ARE NOT ALIVE

- In order to understand why viruses are **not alive**

To be considered alive, an organism must satisfy several criteria:

1. It must have a genome, or genetic material.
2. It has to be able to engage in metabolic activities, meaning that it can obtain and use energy and raw materials from the environment.
3. It has to be able to reproduce and grow.
4. It must be able to compensate for changes in the external environment to maintain homeostasis.
5. Populations of living organisms are also able to adapt to their environments through evolution.

VIRUSES ARE NOT ALIVE

Viruses share some of these characteristics:

- Every virus has genetic material, or a **genome**, composed of DNA or RNA, depending upon the virus.
- Many viruses also have **high mutation rates** that lead to the evolution of the virus.

- Viruses, however, are unable to perform metabolic reactions while outside a cell, they are inert particles that **do not have the ability to generate their own energy.**
- They use the cell's energy and machinery to synthesize new virus particles.

- To reproduce, a cell makes a copy of its DNA, expands in size, and divides the DNA and cell in two. This is known as **binary fission** in prokaryotes and **mitosis** in eukaryotes.
- Viruses, however, do not reproduce in this way. When a virus particle enters the cell, it completely **disassembles.**
- The viral nucleic acid encodes the instructions, and the cell's machinery will be used to make new **infectious virus particles (virions)**

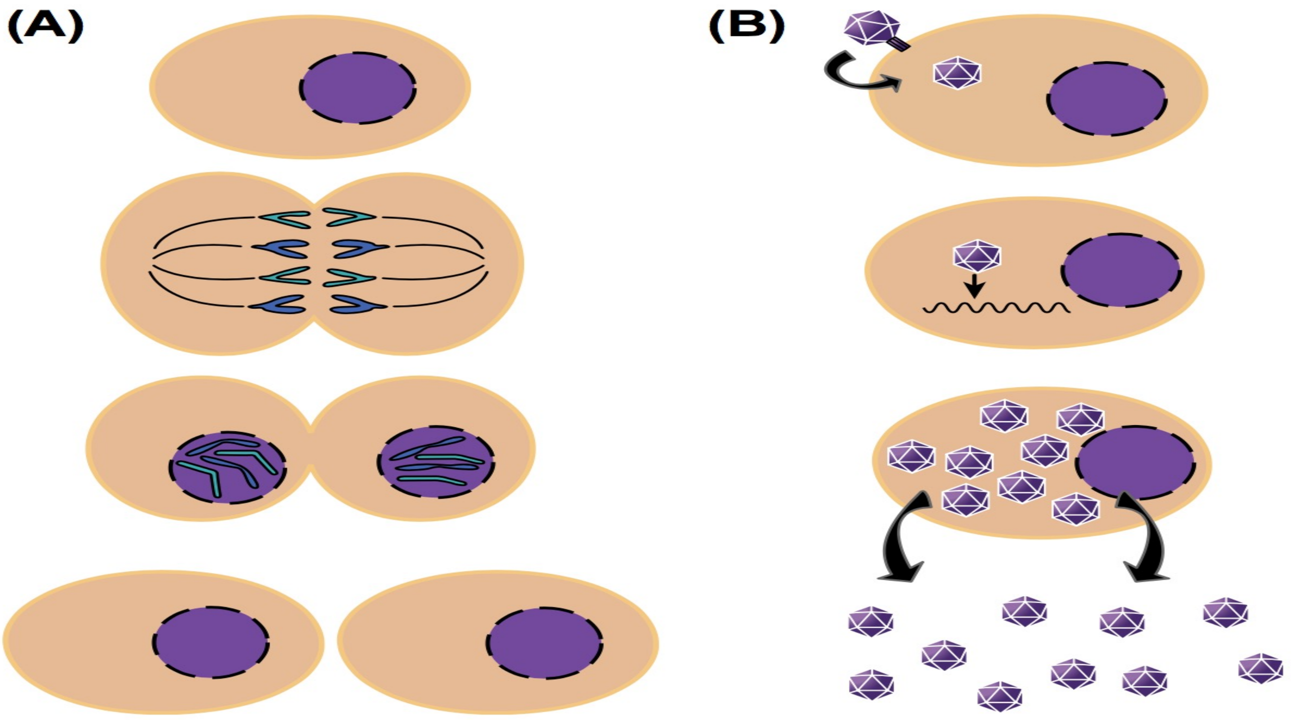


Figure.5. Cell division versus viral replication.

(A) Eukaryotic cells make a copy of their genetic information and divide into two cells through the process of mitosis. All cells arise from the growth and division of previously existing cells.

(B) Viruses, on the other hand, attach to cells and disassemble within the cell. New virions are assembled from newly made components and are released from the cell.

- Despite not being alive, viruses still **share many similarities** with living organisms.
- They are composed of the same biological substances, such as nucleic acids or amino acids,
- Their proteins are translated by ribosomes much in the same way as living organisms.

OTHER NONLIVING INFECTIOUS AGENTS

1- Viroids

- Viruses are not the only nonliving infectious entities:
- **1- Viroids** are very small circular pieces of RNA, generally only 200–400 nucleotides in size, that have been found only in **plants**.

1- Viroids

- Unlike viruses, viroids do not have a protective protein coat
- Their RNA does not encode information to make proteins. Instead, enzymes in the cell copy the viroid RNA, which is then transmitted to the next host plant in the process of infection.

1- Viroids

- The RNA of some viroids has enzymatic activity, RNA could function both as genetic material and as enzymes.
- Viroids are transmitted from plant to plant through close contact or by tools and machinery.
- Viroids have been discovered that infect tomato plants, citrus trees, apple trees, potato plants, coconut trees.

2- Prions

- Are another type of subviral infectious agent that causes *spongiform encephalopathy*, meaning a disease of the brain (encephalopathy) that looks sponge-like when examined under a microscope.

2- Prions

- Examples of Diseases caused by prions are scrapie in sheep, **bovine spongiform encephalopathy** (BSE, or “mad cow disease”) in cows, and **Creutzfeldt–Jakob Disease (CJD)** in humans.
- A prion is not a separate organism or entity and has no nucleic acid genome; it is simply a normal mammalian **protein** which accumulates in the brain and causes neurological damage and death.

The Difference Between "Virus" and "Virion"

- Many people use the word "**virus**" and "**virion**" interchangeably, but the two words have subtle but important differences.

1- The word "**virion**" is used to describe the infectious virus package that is assembled. It is the extracellular form of the virus, also referred to as a virus particle, that is released from one cell and binds to the surface of another cell.

The Difference Between "Virus" and "Virion"

- On the other hand, the word "**virus**" refers to the biological entity in all its stages and the general characteristics that differentiate it from another infectious entry.
- **Rhinovirus** and **Epstein–Barr virus** are two different entities with different properties.

Virus Structure and Classification

COMMON CHARACTERISTICS OF VIRUSES

1. Viruses are very small in size.

- The smallest of viruses are about 20nm in diameter
- Although influenza and the human immunodeficiency virus have a more typical size, about 100 nm in diameter.
- Average human cells are 10–30µm (microns) in diameter.

COMMON CHARACTERISTICS OF VIRUSES

- However, some viruses are significantly larger than 100 nm.
- Poxviruses, such as the variola virus that causes smallpox, can approach 400nm in length.

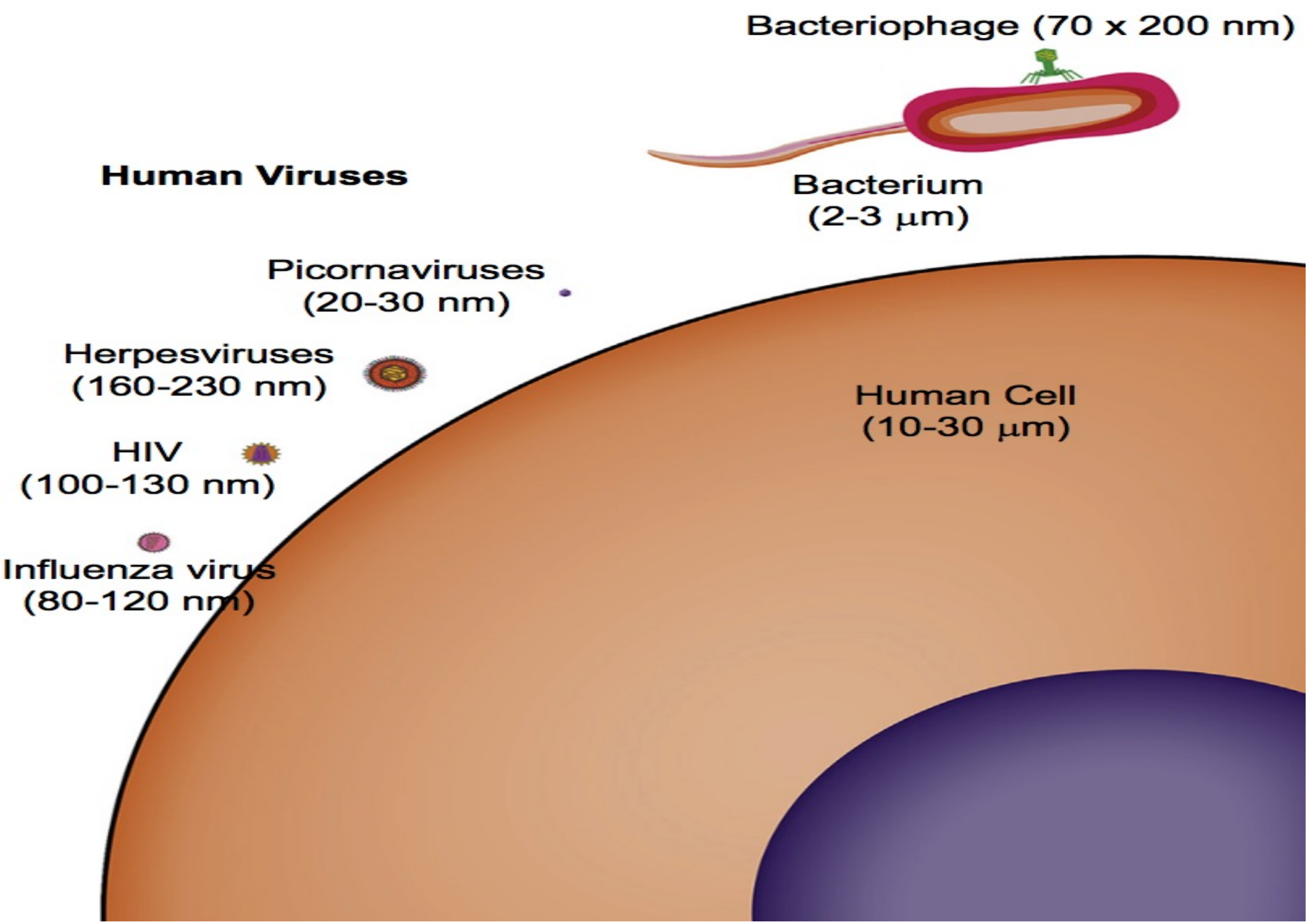


Figure 1 Virus and cell size comparison. Human viruses can vary in size but are generally in the range of 20–200nm in diameter.

COMMON CHARACTERISTICS OF VIRUSES

2. Viruses are obligate intracellular parasites, meaning that they are completely dependent upon the internal environment of the cell to create new infectious virus particles, or **virions**.

COMMON CHARACTERISTICS OF VIRUSES

3. The genetic material of viruses can be composed of DNA or RNA.

- All living cells, whether human, animal, plant, or bacterial, have double-stranded DNA (dsDNA) as their genetic material.
- Viruses, on the other hand, have **genomes**, or genetic material, that can be composed of **DNA** *or* **RNA** (but not both).

COMMON CHARACTERISTICS OF VIRUSES

- Genomes are not necessarily double-stranded
- Different virus types can also have single-stranded DNA (ssDNA) genomes
- And viruses with RNA genomes can be single-stranded or double-stranded.

- Similarly to how the size of the virus particle varies significantly, the genome size can also vary greatly from virus to virus.
- A typical virus genome falls in the range of 7000–20,000 base pairs (bp) (7–20 kilobase pairs (kb)).
- Smaller-sized virions will naturally be able to hold less nucleic acid than larger virions.

STRUCTURE OF VIRUSES

STRUCTURE OF VIRUSES

- The infectious virus particle must be released from the host cell to infect other cells and individuals.
- Whether dsDNA, ssDNA, dsRNA, or ssRNA, the nucleic acid genome of the virus must be protected in the process.

STRUCTURE OF VIRUSES

- In the extracellular environment, the virus will be exposed to:

  1-enzymes that could break down or degrade nucleic acid.

  2- Physical stresses, such as the flow of air or liquid, could also shear the nucleic acid strands into pieces.

  3- viral genomes are susceptible to damage by ultraviolet radiation or radioactivity, much in the same way that our DNA is.

- In order to protect the fragile nucleic acid from harsh environment, the virus surrounds its nucleic acid with a protein shell, called the **capsid**, from the Latin *capsa*, meaning "box."
- The capsid is composed of one or more different types of proteins.
- This repeating structure forms a strong but slightly flexible capsid.
- Together, the nucleic acid and the capsid form the **nucleocapsid** of the virion

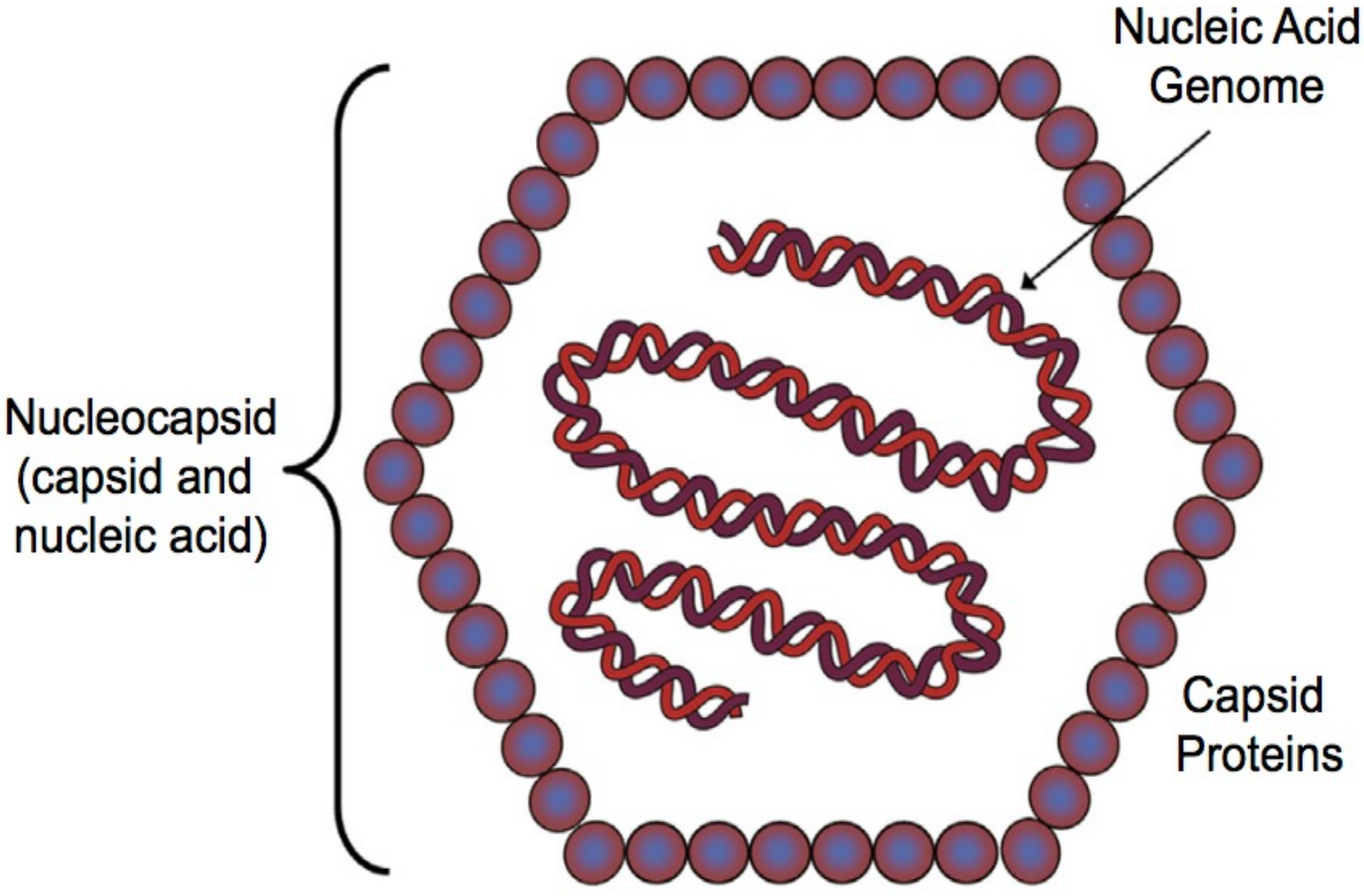


Figure 2 Basic virus architecture.

Viral capsid proteins protect the fragile genome. The capsid and nucleic acid together are known as the nucleocapsid.

- Most viruses also have an **envelope** surrounding the capsid.
- The envelope is a **lipid membrane** that is derived from one of the cell's membranes, most often the plasma membrane
- Although the envelope can also come from the cell's endoplasmic reticulum, Golgi complex, or even the nuclear membrane, depending upon the virus.
- These viruses often have proteins, called **matrix proteins**, that function to connect the envelope to the capsid inside.
- A virus that lacks an envelope is known as a **nonenveloped** or **naked virus** (Fig.3).

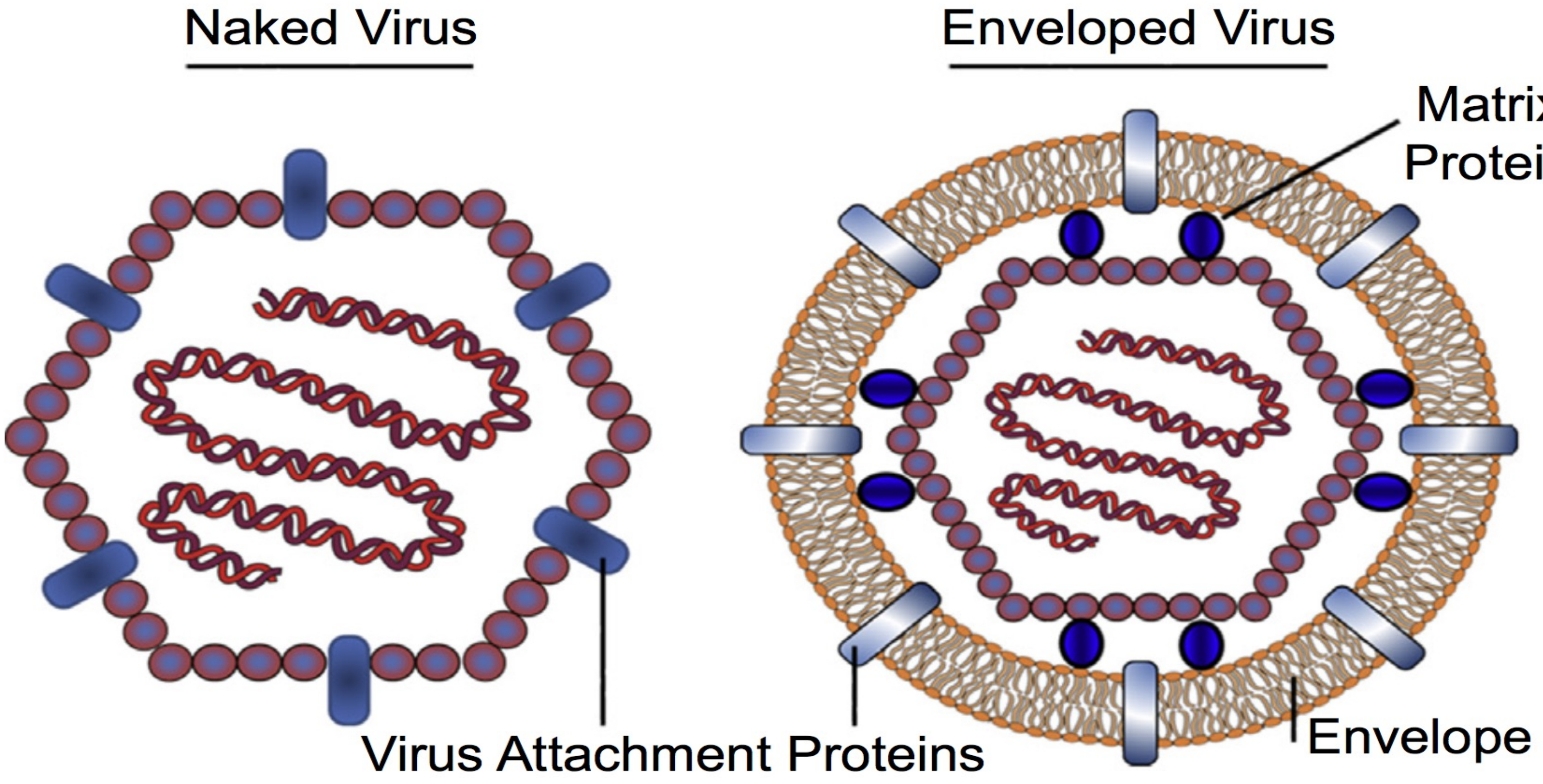


Figure 3 Comparison between a Naked and Enveloped Virion.
The capsid of an enveloped virion is wrapped with a lipid membrane derived from the cell. Virus attachment proteins located in the capsid or envelope facilitate binding of the virus to its host cell.

- Each virus also possesses a **virus attachment protein** embedded in its outer- most layer.
- This will be found in the **capsid**, in the case of a naked virus, or the **envelope**, in the case of an enveloped virus.
- The virus attachment protein is the viral protein that facilitates the docking of the virus to the plasma membrane of the host cell, the first step in gaining entry into a cell.

Virus capsids shapes

Helical

Icosahedral

1- Helical Capsid Structure

- The helix (plural: helices) is a spiral shape that curves cylindrically around an axis.
- In the case of a helical virus, the viral nucleic acid coils into a helical shape and the capsid proteins wind around the nucleic acid, forming a long tube or rod-like structure

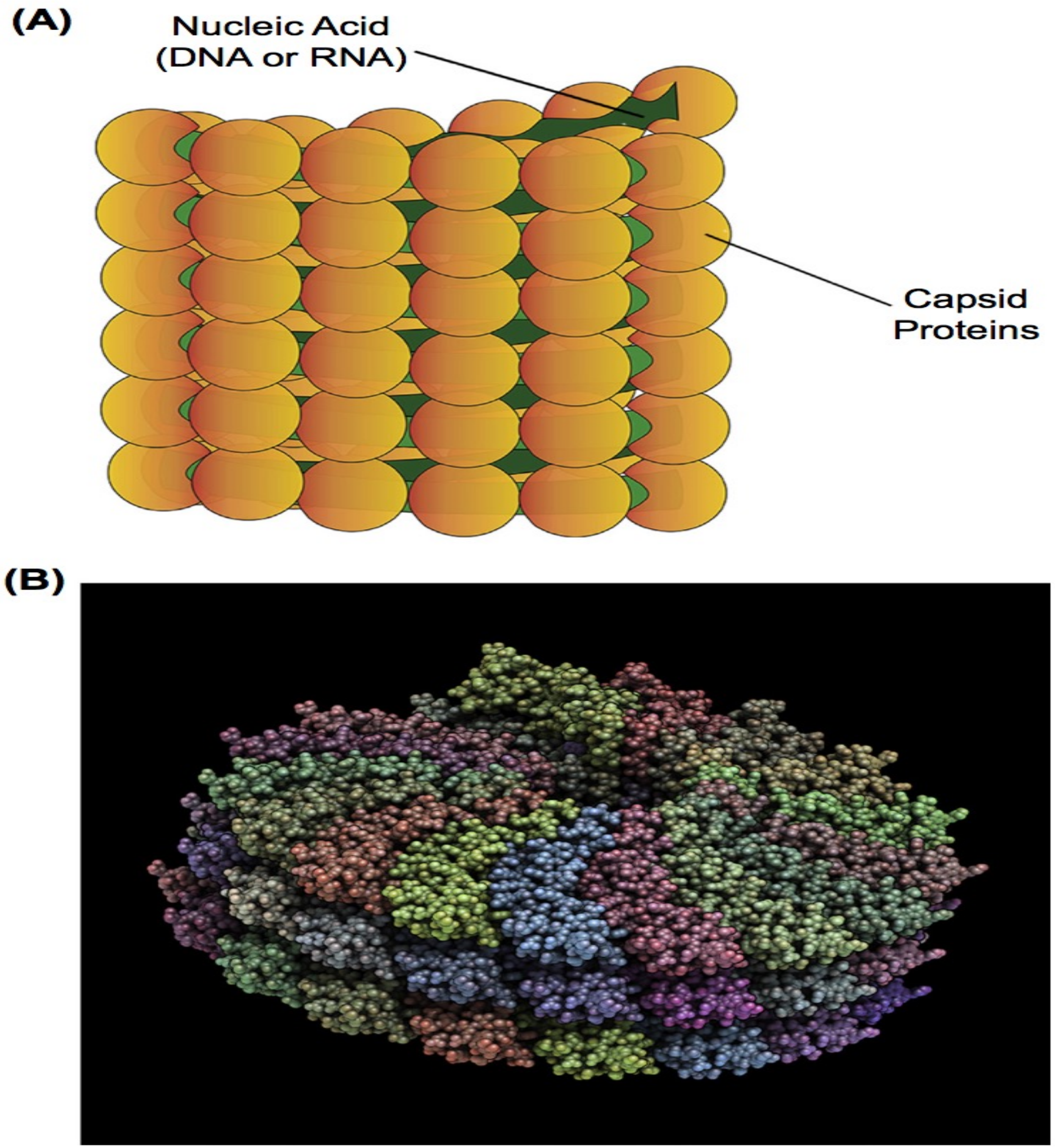


Figure 4 Helical capsid structure.

(A) Viral capsid proteins wind around the nucleic acid, forming a helical nucleocapsid.

(B) Helical structure of tobacco mosaic virus.

There are several perceived advantages to forming a helical capsid.

- First, only **one type of capsid protein** is required. This protein subunit is repeated over and over again to form the capsid.
- This structure is simple and requires **less free energy** to assemble than a capsid composed of multiple proteins.
- In addition, having only one nucleocapsid protein means that **only one gene** is required instead of several, thereby reducing the length of nucleic acid required.

- Helical viruses can be **enveloped** or **naked**.
- The first virus described, **tobacco mosaic virus**, is a **naked helical virus**.
- In fact, most plant viruses are helical, and it is very uncommon that a helical plant virus is enveloped.
- In contrast, all **helical animal** viruses are **enveloped**.
- These include well-known viruses such as **influenza virus**, **measles virus**, **mumps virus**, **rabies virus**, and **Ebola virus** (fig.5)

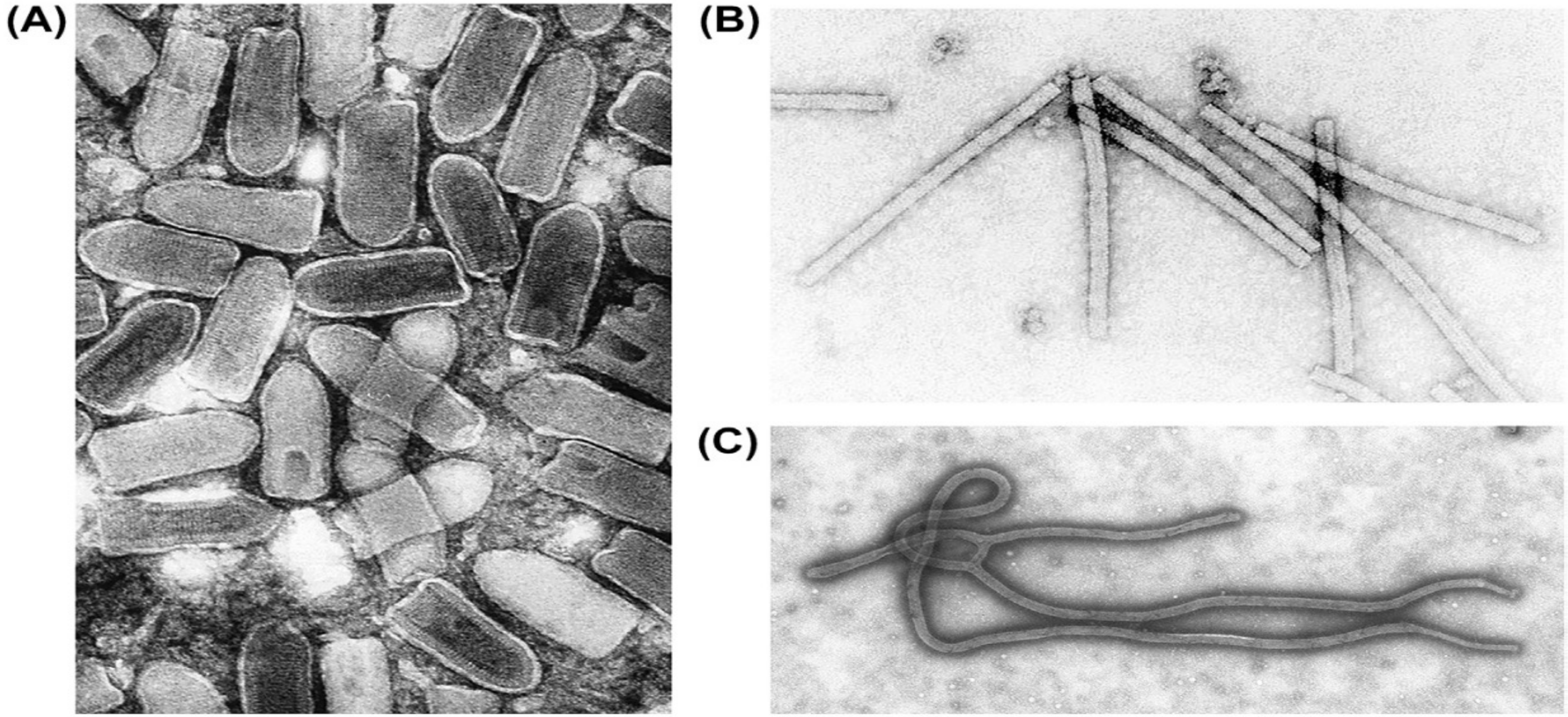


Figure 5 Electron micrographs of helical viruses. (A) Vesicular stomatitis virus forms bullet-shaped helical nucleocapsids. (B) Tobacco mosaic virus forms long helical tubes. (C) The helical Ebola virus forms long threads that can extend over 1000 nm in length.

2- Icosahedral Capsid Structure

- Of the two major capsid structures, the icosahedron is by far more prevalent than the helical architecture.
- In comparison to a helical virus where the capsid proteins wind around the nucleic acid, the genomes of icosahedral viruses are packaged completely within an icosahedral capsid that acts as a protein shell.
- An icosahedron is a geometric shape with 20sides (or **faces**), each composed of an equilateral triangle fig.6
- Ex. **Poliovirus**

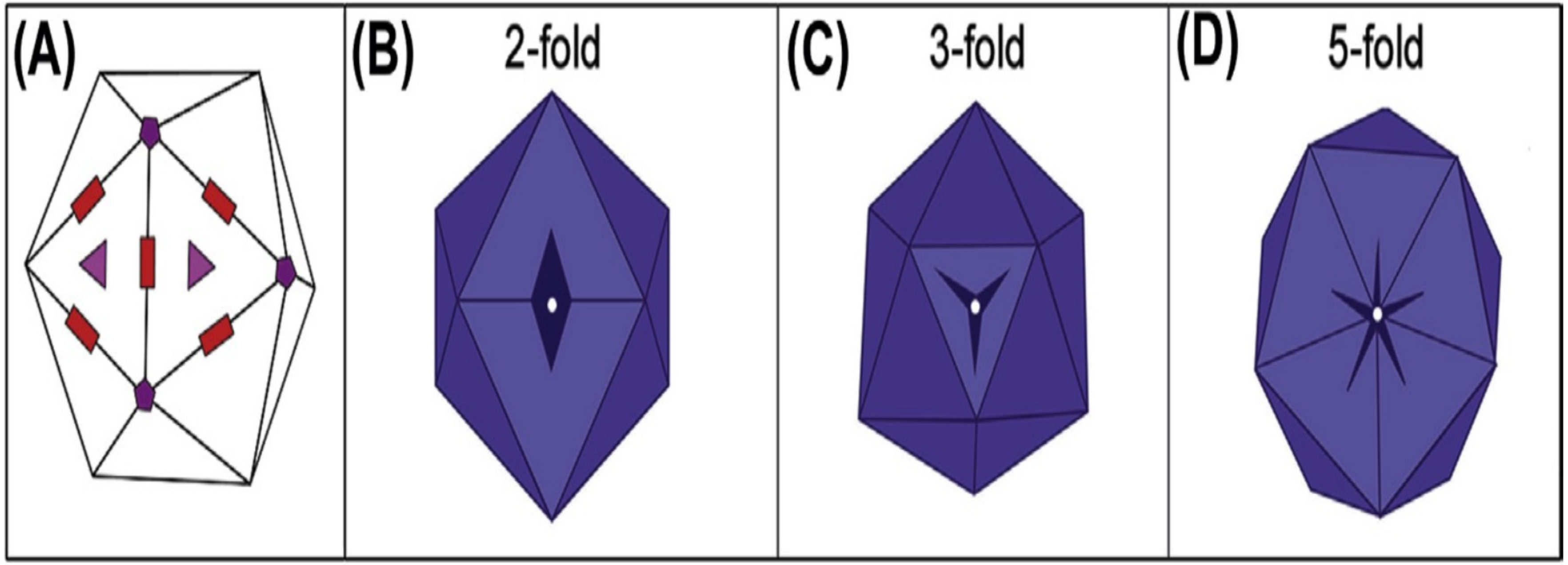


Figure 6 Icosahedron terminology and axes of symmetry.
(A) Icosahedron faces (fuchsia triangles), edges (red rectangles), and vertices (violet pentagons) are indicated on the white icosahedron. (B) The twofold axis of symmetry occurs when the axis is placed through the center of an edge. The threefold axis occurs when the axis is placed in the center of a face (C), and the fivefold axis passes through a vertex of the icosahedron (D).

3- Complex Viral Structures

- A few viruses, however, have a **complex** architecture that does not strictly conform to a simple helical or icosahedral shape.

  Poxviruses, and many **bacteriophages** are examples of viruses with complex structure.
- Poxviruses, including the viruses that cause smallpox or cowpox, are large oval or brick-shaped particles 200–400 nm long.

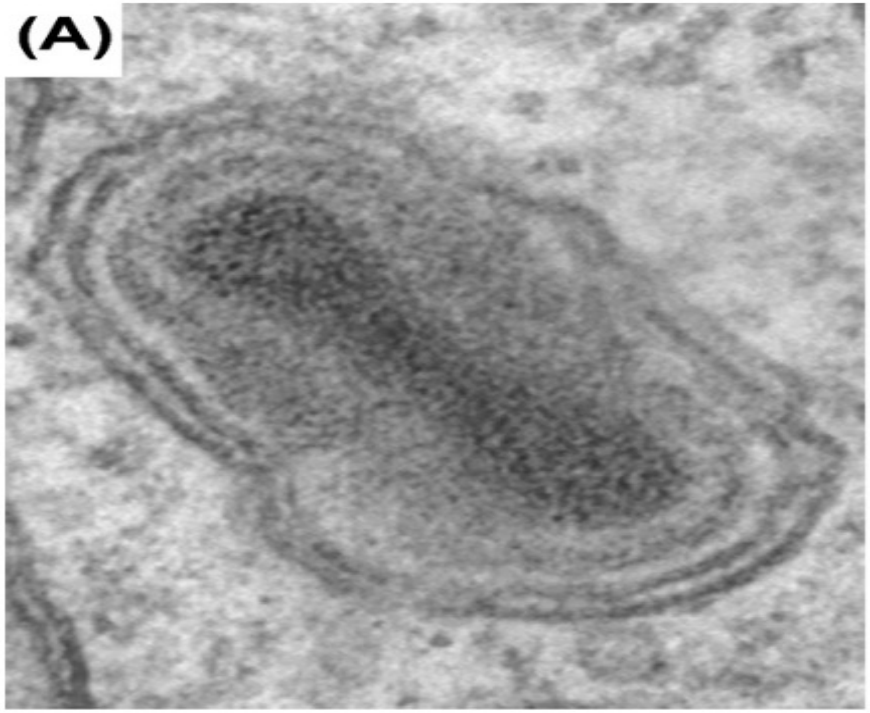


Figure 7 Electron micrograph of viruses with complex architecture.
Vaccinia virus (A), a virus belonging to the poxvirus family, has a complex capsid architecture with a dumbbell-shaped core