Medical Virology

Introduction to Basics

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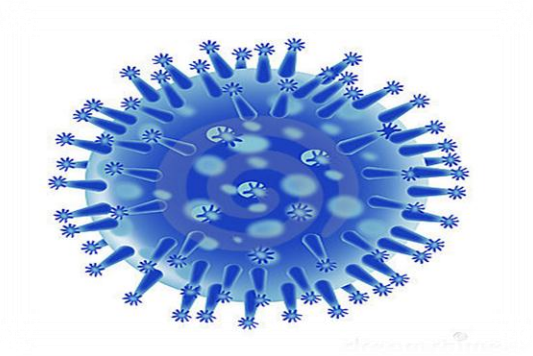
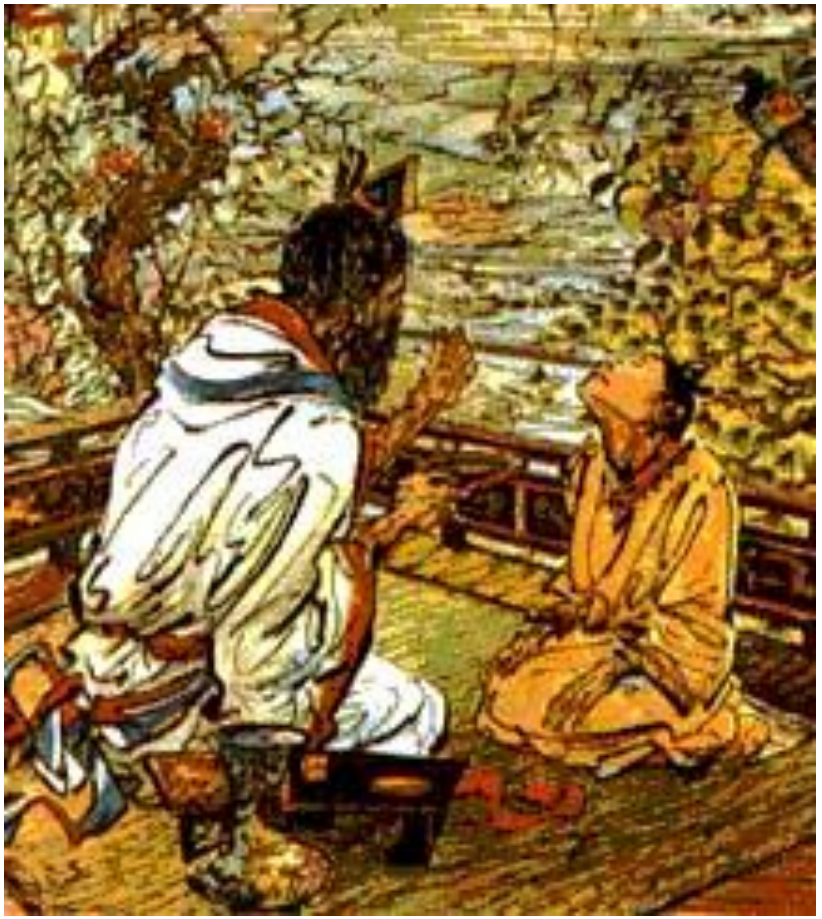
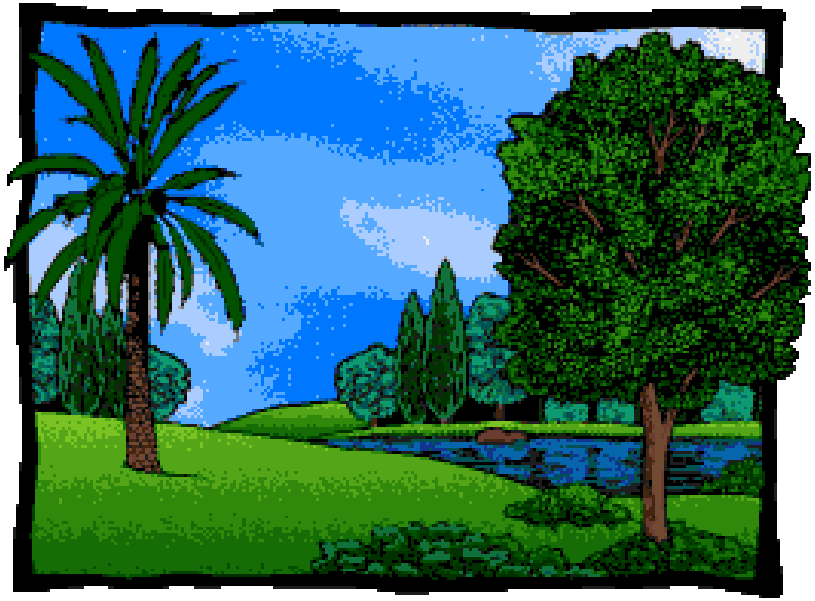


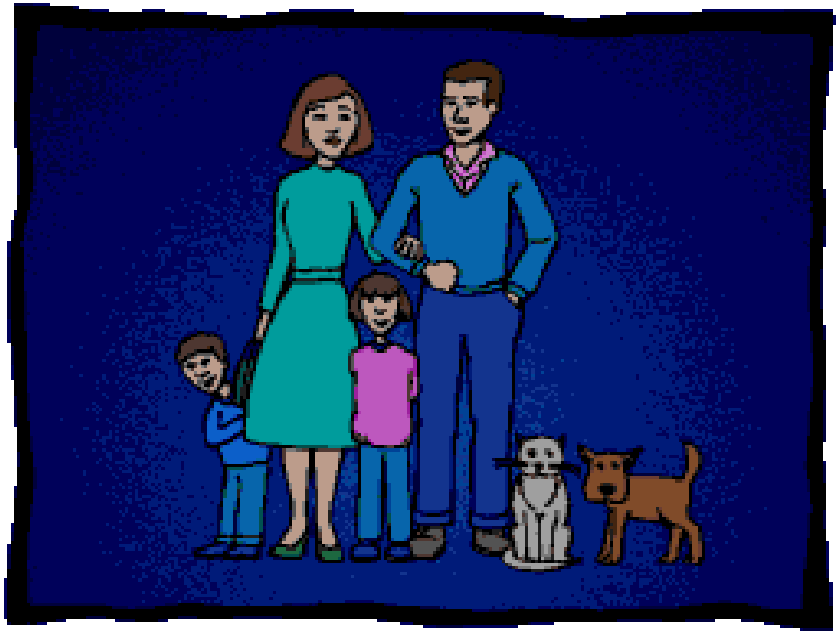
History Virology

- Smallpox was endemic in China in the past . In response, the practice of **variolation** was developed. Recognizing that survivors of smallpox outbreaks were protected from subsequent infection, variolation involved inhalation of the dried crusts from smallpox lesions like snuff, or in later modifications, inoculation of the pus from a lesion into a scratch on the forearm of a child.



Virus infections are Universal …….





Introduction to Virology

- A virus is an obligate intracellular parasite containing genetic material surrounded by protein
- Virus particles can only be observed by an **electron microscope**

General Properties of Viruses

General Properties

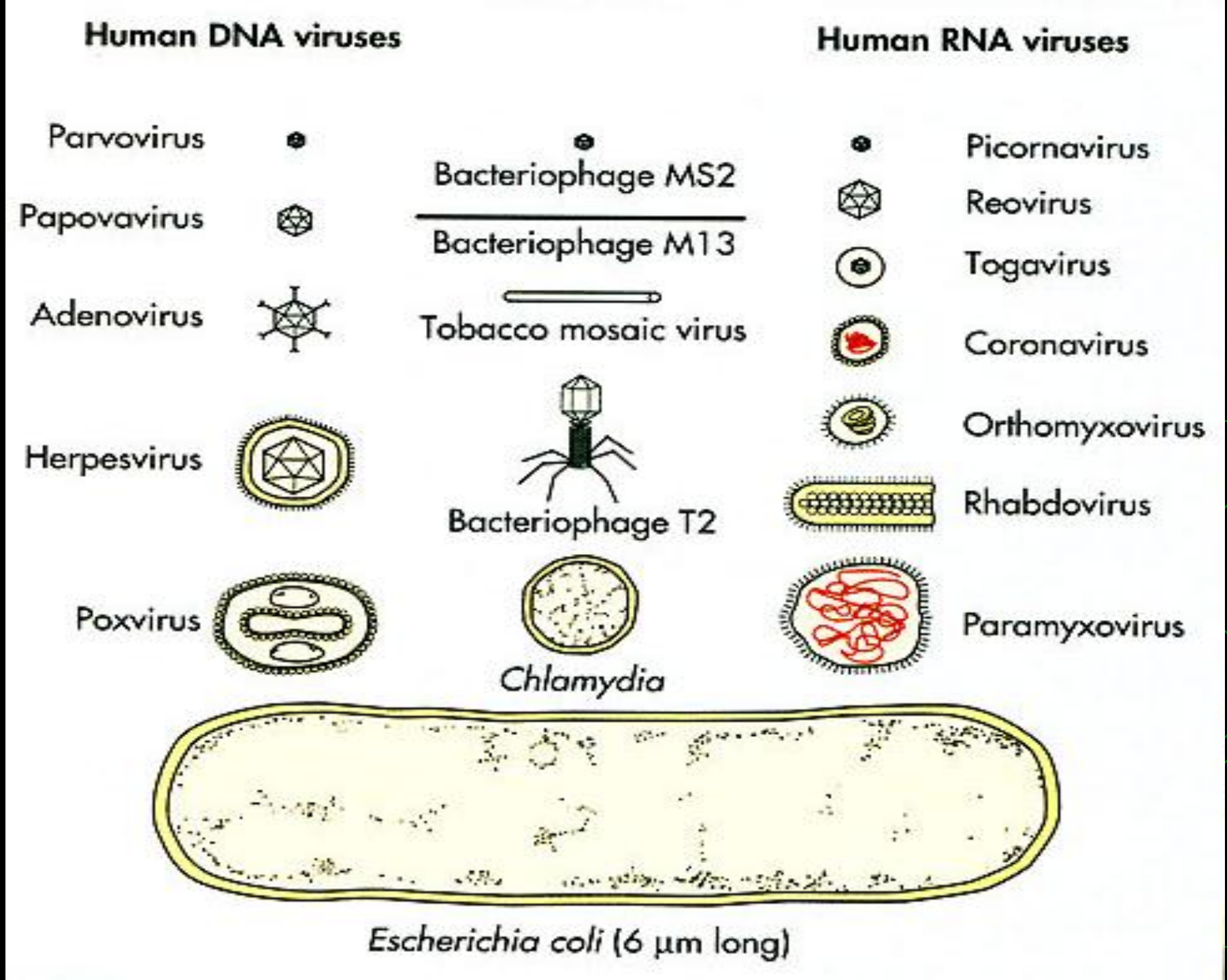
- Obligate intracellular parasites
- Contain only one type of nucleic acid, either DNA or RNA
- Do not possess cellular organization
- Lacks enzymes necessary for protein & NA synthesis
- Depends on host cell machinery for replication
- Causes a large no. of human diseases ranging from minor ailments like common cold to terrifying diseases such as rabies, HIV etc.

General Properties

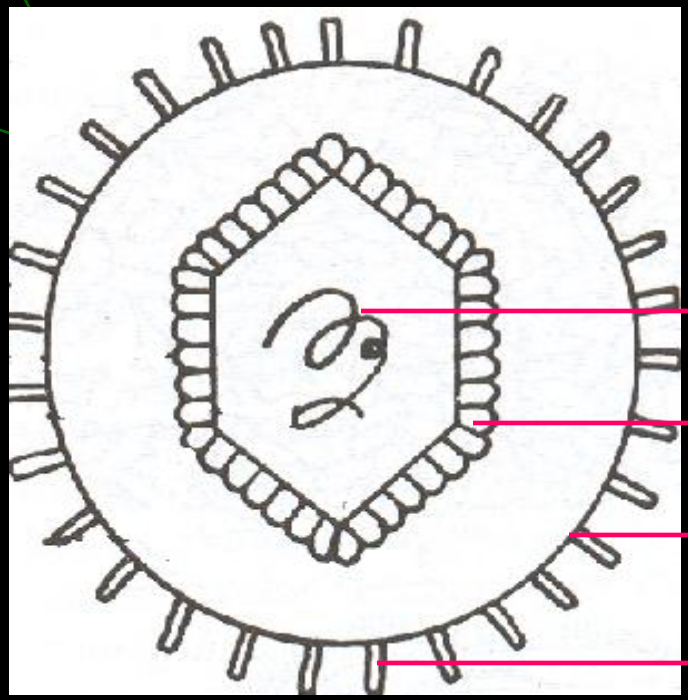
- Morphology – size, structure, shape, chemical properties, resistance
- Replication
- Hemagglutination
- Cultivation
- Viral assay
- Viral infections: virus-host interactions

Morphology - Size

- Much smaller than bacteria
- "Filterable agents" – can pass through filters that can hold back bacteria
- Vary widely in size:
  - Largest – poxvirus (300nm)
  - Smallest – parvovirus (20nm)
- Virion – extracellular infectious virus particle


Human DNA viruses
Human RNA viruses
Parvovirus
Papovavirus
Adenovirus
Herpesvirus
Poxvirus
Bacteriophage MS2
Bacteriophage M13
Tobacco mosaic virus
Bacteriophage T2
Chlamydia
Picornavirus
Reovirus
Togavirus
Coronavirus
Orthomyxovirus
Rhabdovirus
Paramyxovirus
Escherichia coli (6 µm long)

Morphology - Structure of Virus



- Nucleic acid
- Capsid
- Envelope
- Peplomer

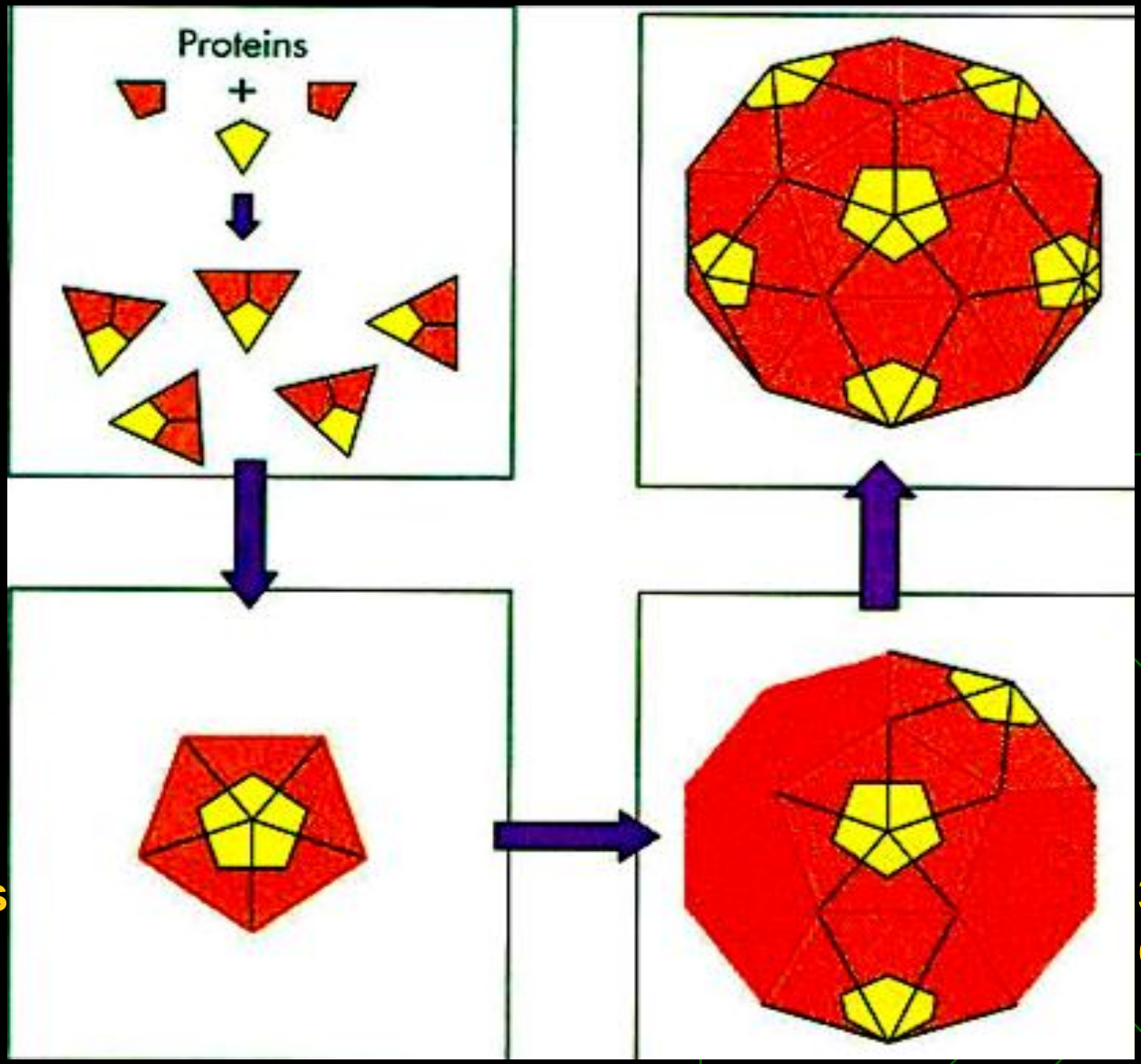
Size in nanometers

ELECTRON MICROSCOPE

Morphology – Structure & Shape of a virus

- Nucleic acid & capsid with or without envelope.
- Capsid – the protein coat surrounding the nucleic acid core. It
  - protects nucleic acid from inactivation
  - helps to introduce viral genome into host cell
- Capsomers - the repeating protein subunits that make up the capsid
- Protomers – the polypeptide chains which make up the capsomers

1. Protomers



4. Mature Capsid

2. Capsomers

3. Pro-Capsid

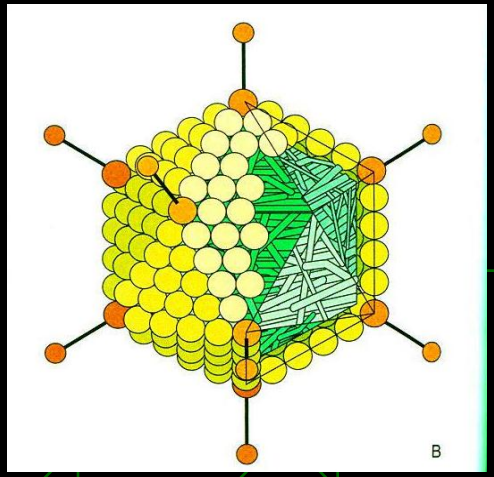
Morphology – Structure & Shape of a virus: Capsid

- Capsomers – symmetrically arranged to form an impenetrable shell (capsid) around the nucleic acid core.

- This symmetry is of two types:
  - Icosahedral (cubical)
  - Helical

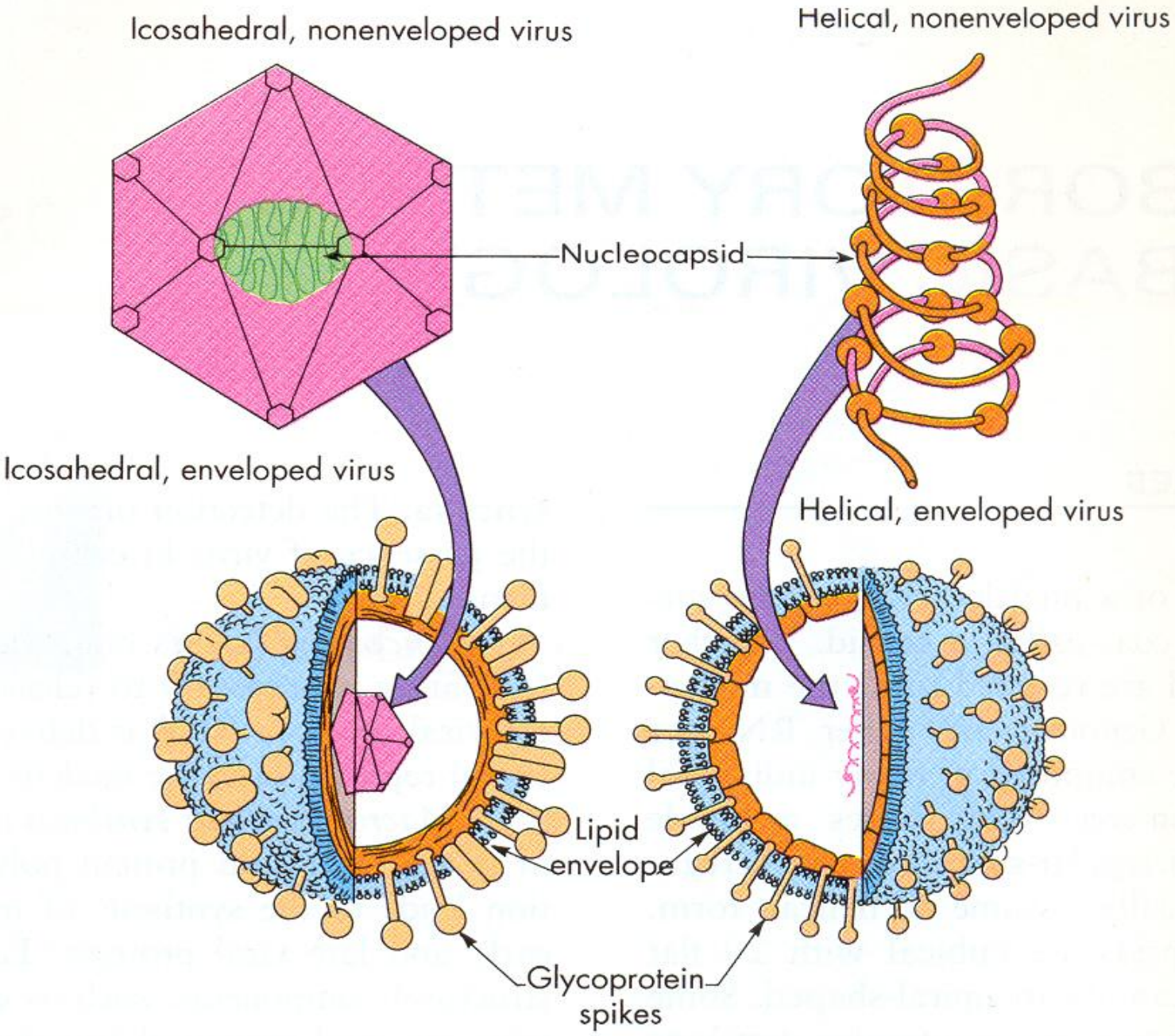
Morphology – Structure & Shape of a virus: Capsid

- Icosahedron – a polygon with 12 corners (vertices) & 20 sides (facets)
  - Side – equilateral triangle
  - Two types of capsomers form the capsid
  - Pentagonal capsomers form the vertices
  - Hexagonal capsomers form the sides.



- Helical – the capsomers & nucleic acid are wound together to form a helical or spiral tube.

- The overall shape of virus is quite variable, but mostly they are spherical.


Icosahedral, nonenveloped virus
Helical, nonenveloped virus
Nucleocapsid
Icosahedral, enveloped virus
Helical, enveloped virus
Lipid envelope
Glycoprotein spikes

Morphology – Structure & Shape of a virus: Envelope

- May or may not be present
- Derived from the host cell membrane
- Lipoprotein in nature – lipid is of host cell origin while protein is from virus.
- Protein subunits seen as projecting spikes on the surface of envelope – called Peplomer.
- A virus may have more than one type of peplomer e.g. influenza virus.
- Confers chemical, antigenic & biological properties.
- Susceptible to lipid solvents

Comparison of naked and enveloped virus, two basic types of virus particles.

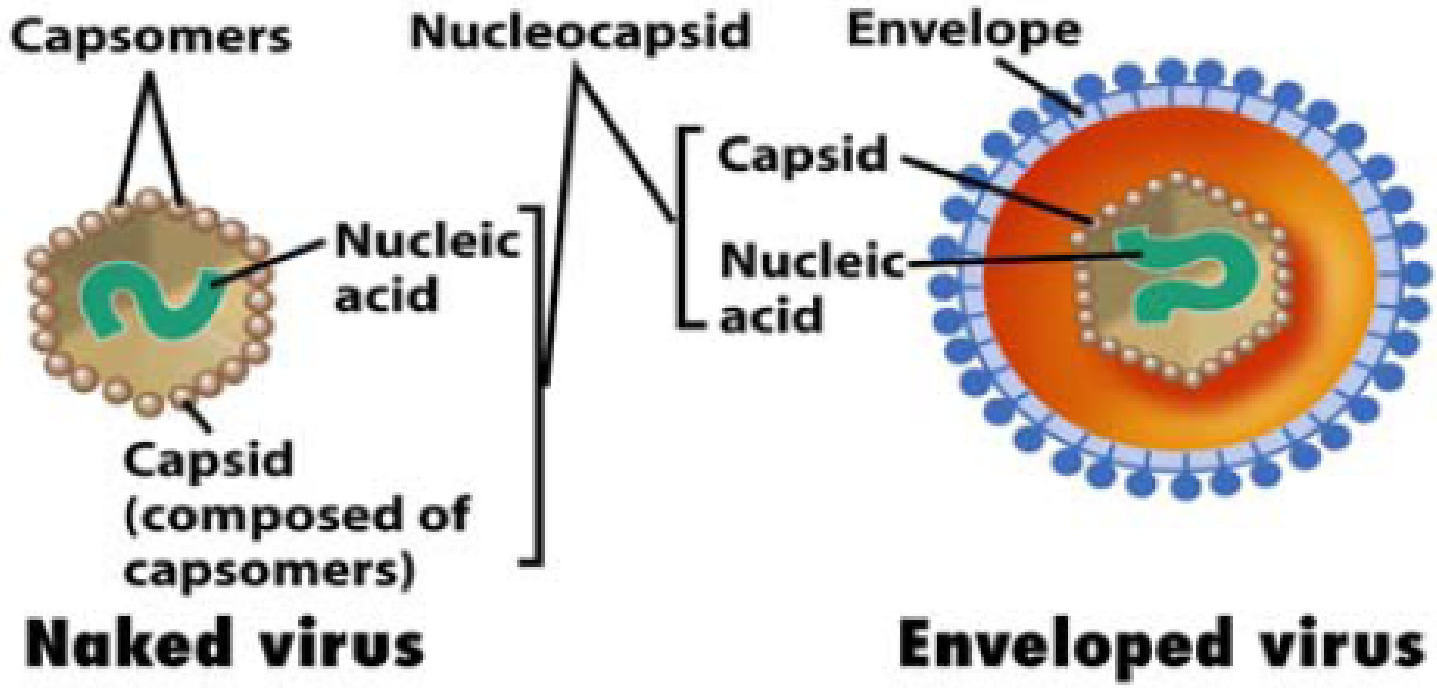


Figure 9-3 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.

Caption: Many enveloped viruses are so because they become covered with host cytoplasmic membrane as they are released from the cell.

Resistance

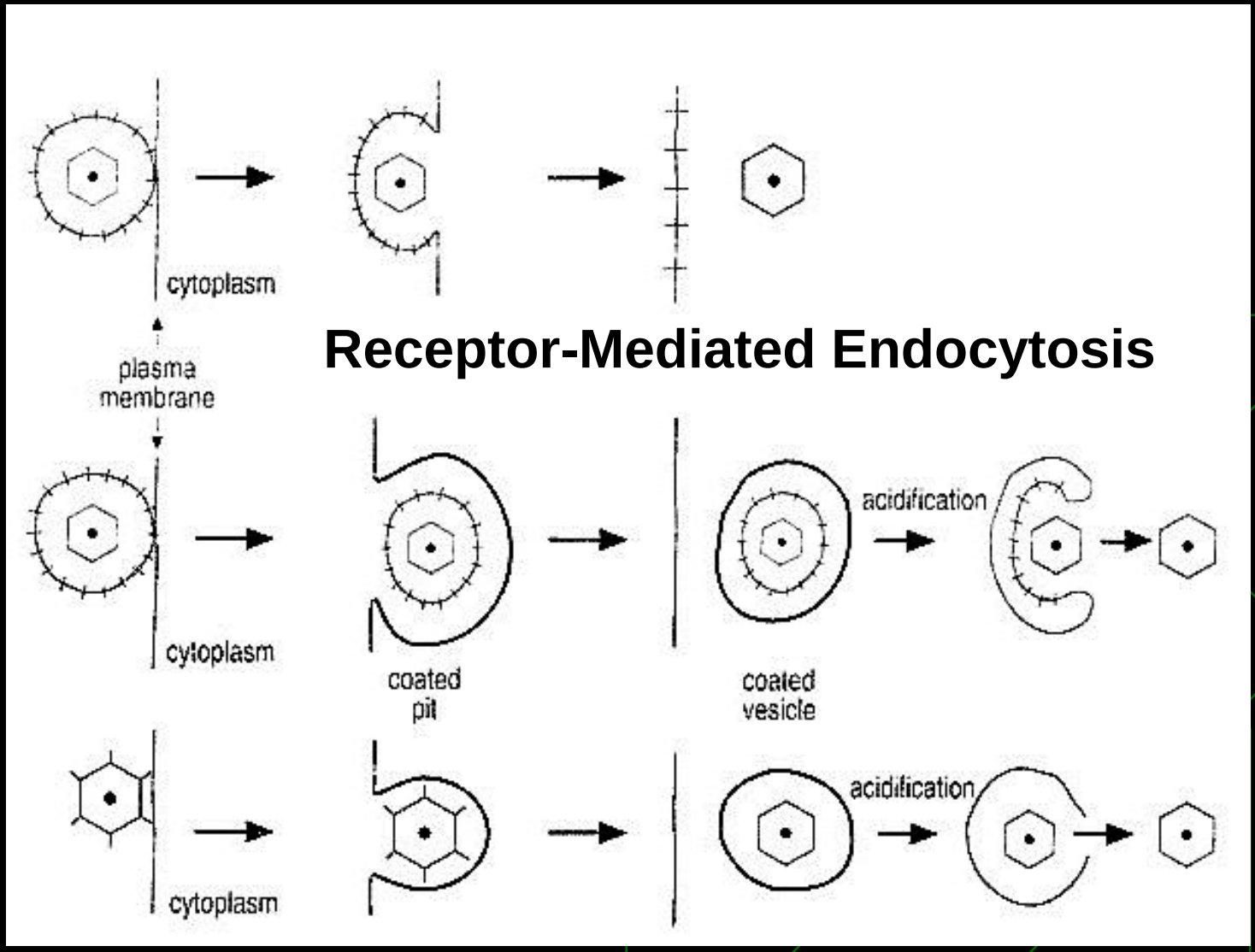
- Very heat labile but stable at low temperatures
  - Inactivated within seconds at 56°C.
  - Can be kept frozen at -70°C for long term storage.
- Inactivated by sunlight, UV rays & ionising radiations.
- More resistant than bacteria to chemical disinfectants.
- Most active antiviral agents (virucidal) – oxidising agents like hydrogen peroxide, potassium permangnate, hypochlorites

Pathways for Viral Entry into Host Cell

Surface Fusion

Fusion in Endosome

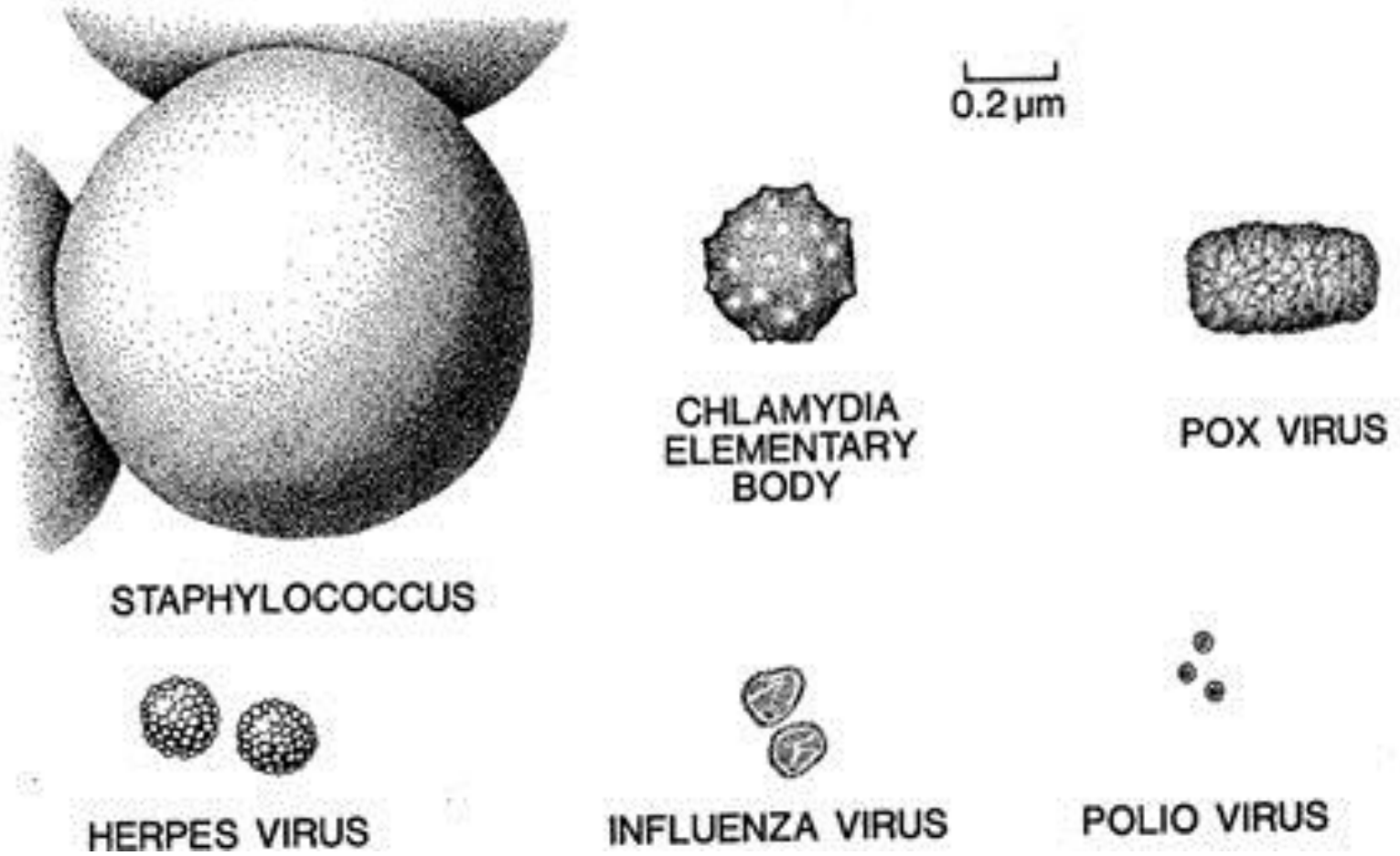
Lysis of Endosome



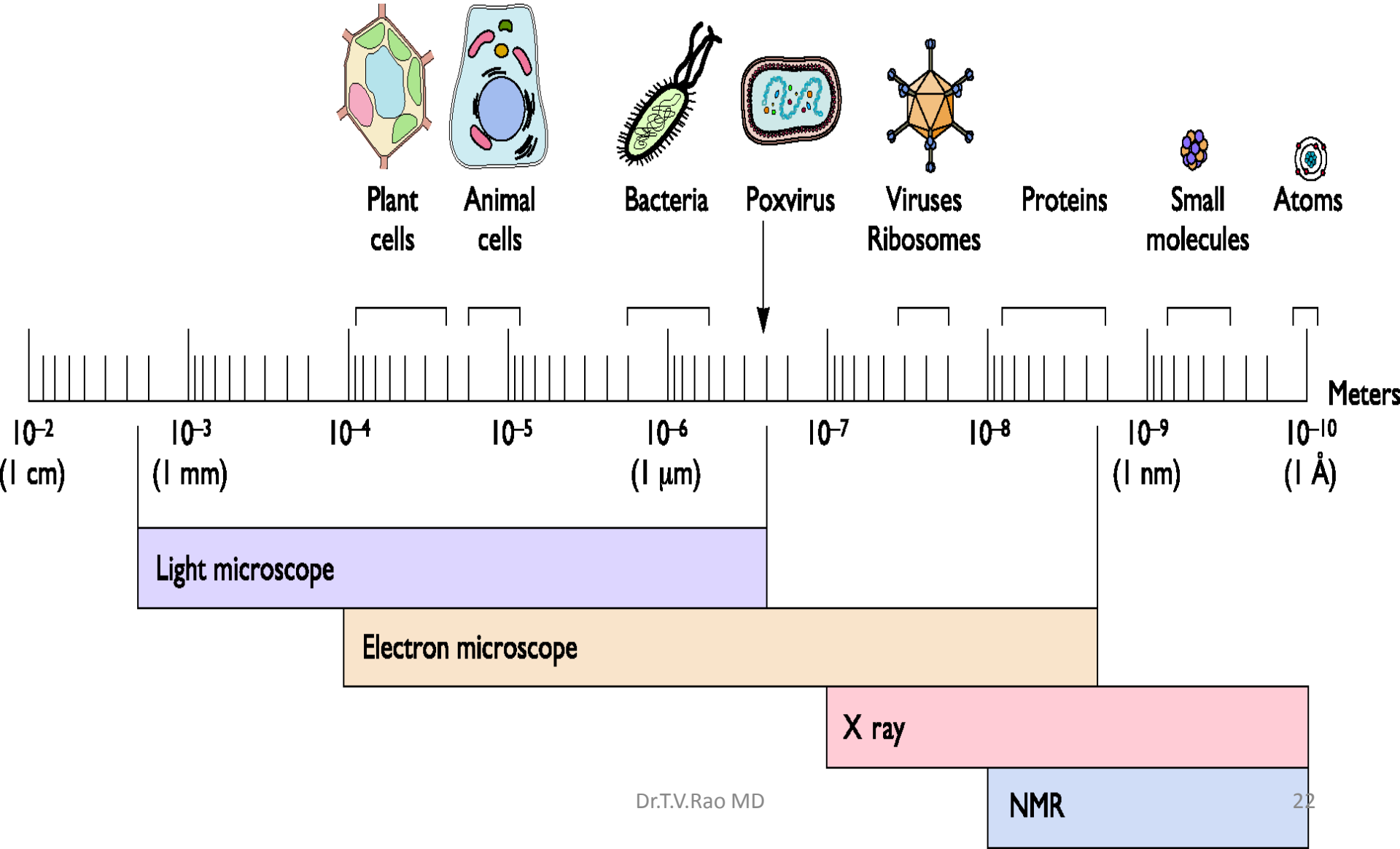
Viral Properties

- **Viruses are inert (nucleoprotein) filterable Agents**
- **Viruses are obligate intracellular parasites**
- **Viruses cannot make energy or proteins independent of a host cell**
- **Viral genome are RNA or DNA but not both.**
- **Viruses have a naked capsid or envelope with attached proteins**
- **Viruses do not have the genetic capability to multiply by division.**
- **Viruses are non-living entities**

Viruses are Ultramicroscopic



The size of viruses



VIRAL STRUCTURE – SOME TERMINOLOGY

- virus particle = virion
- protein which coats the genome = capsid
- capsid usually symmetrical
- capsid + genome = nucleocapsid
- may have an envelope

5 Characteristics of Life

- 1. Cells
- 2. Grow and maintain their structure by taking up chemicals and energy from the environment
- 3. Respond to their external environment
- 4. Reproduce and pass on their organization to their offspring
- 5. Evolve and Adapt to their environment

Viruses are:

- 1. Acellular
- 2. Obligate intracellular parasites
- 3. No ATP generating system
- 4. No Ribosomes or means of Protein Synthesis

Typical Virus 2 Parts

- 1. Nucleic Acid
  - DNA or RNA (But never both)
- 2. Capsid (Coat Protein)

- Some Viruses:
  - A. Envelope
  - B. Enzymes

Host range

- Spectrum of host cells that a virus can infect

- Some viruses only infect:
  - plants
  - invertebrates
  - protists
  - fungi
  - bacteria (Bacteriophages)

Host range

- Most viruses have a narrow host range

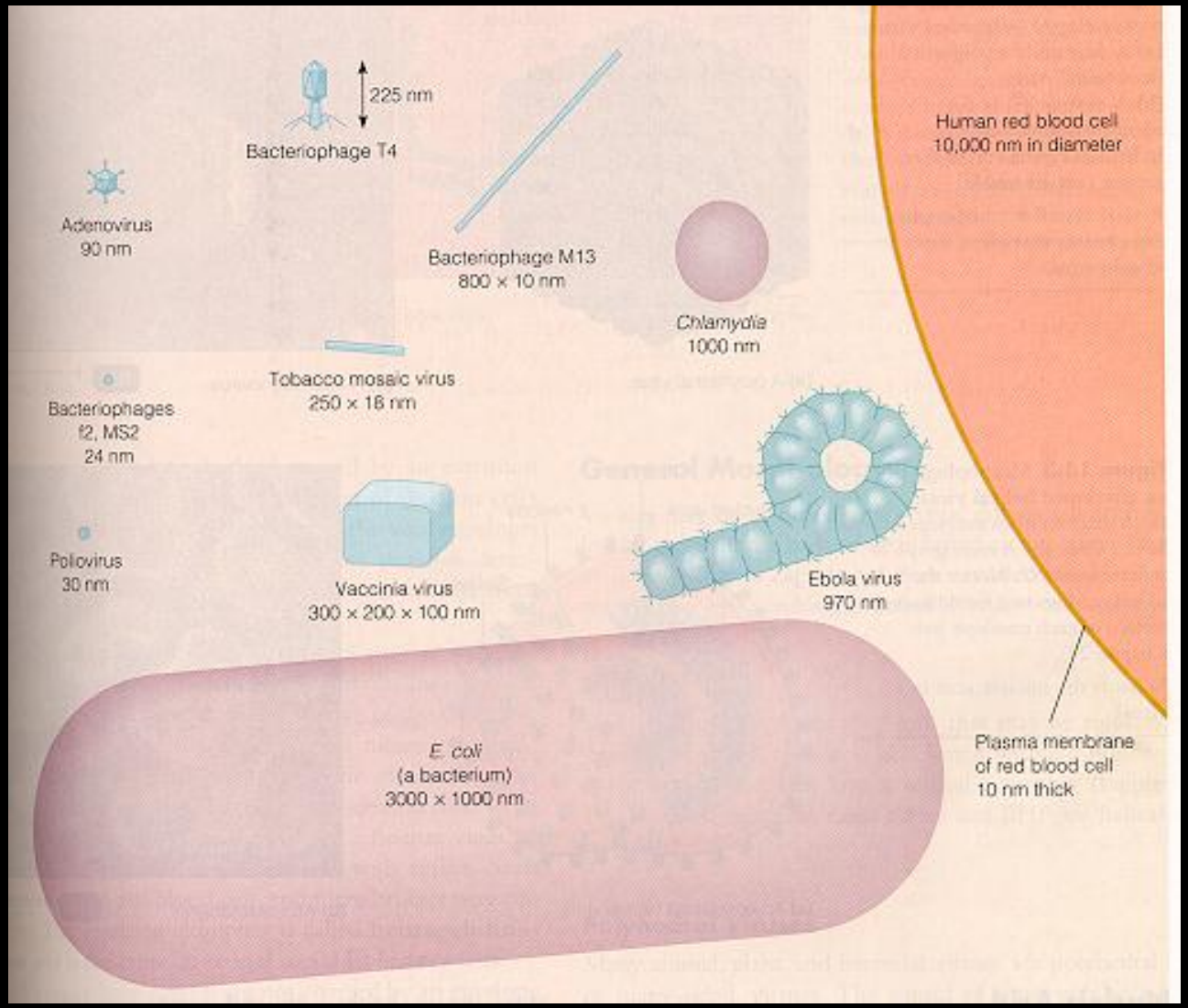
- Polio virus - nerve cells
- Adenovirus - cells in upper Respiratory Tract

Host range is determined by Viruses ability to interact with its host cell

- Binding Sites match Receptor Sites

- Binding Sites - on viral capsid or envelope
- Receptor Sites - on host cell membrane

Viral Size



20 nm to 1,000 nm

.02 u to 1 u

Viral Structure

- 1. Nucleic Acid
- 2. Capsid (Coat Protein)

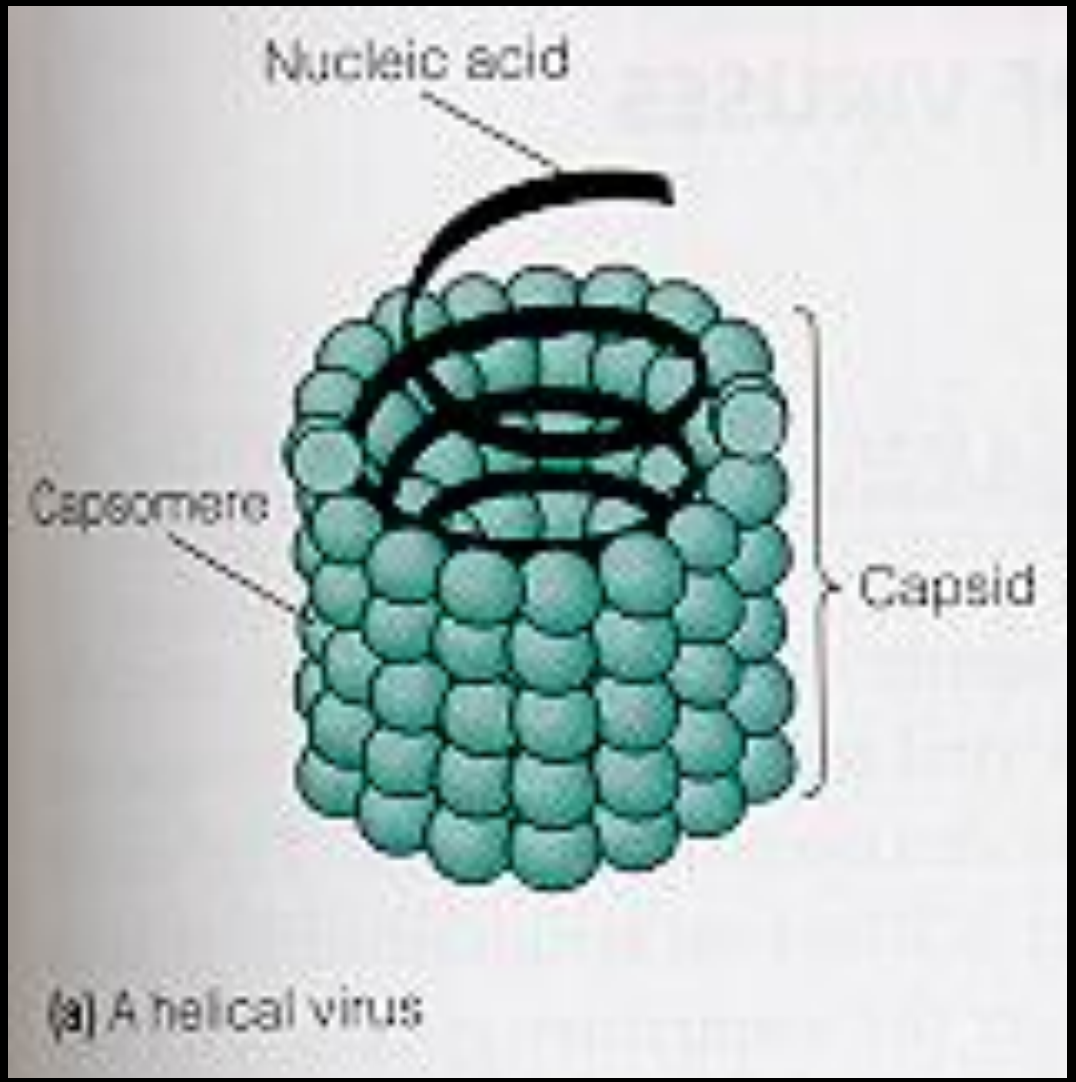
- Nucleic Acid
  - DNA or RNA (But never both)
    - ssDNA
    - ds DNA
    - ss RNA
    - ds RNA

Viral Structure

- Capsid (Coat Protein)
  - protects viral genome from host endonucleases
  - capsomeres
  - Binding Sites
- Envelope
  - derived from the host cell
  - Binding Sites

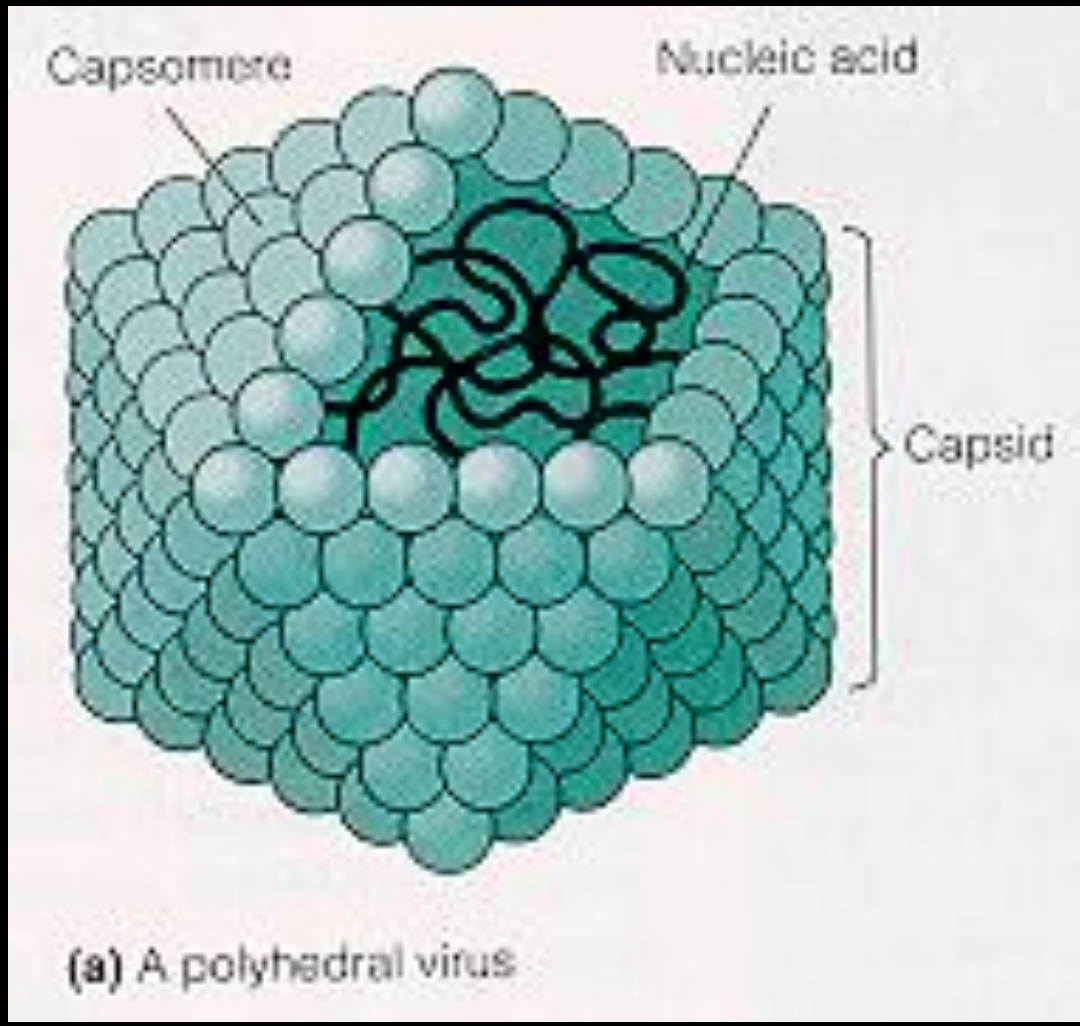
Viral Morphology

1. Helical



Viral Morphology

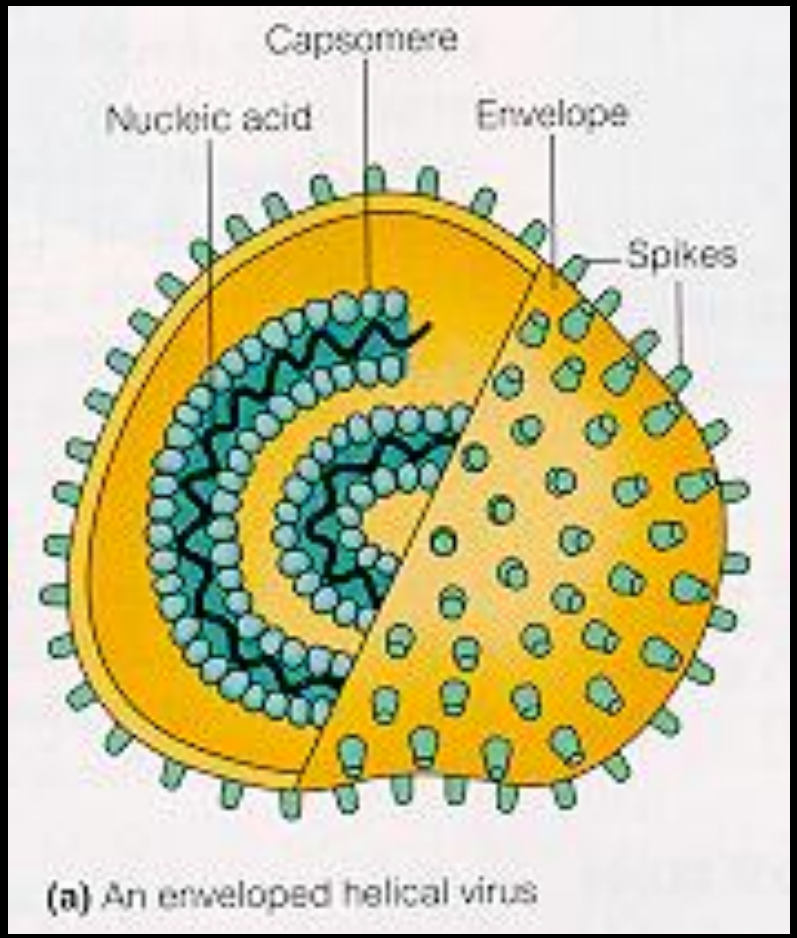
2. Polyhedral



icosahedral

Viral Morphology

3. Enveloped

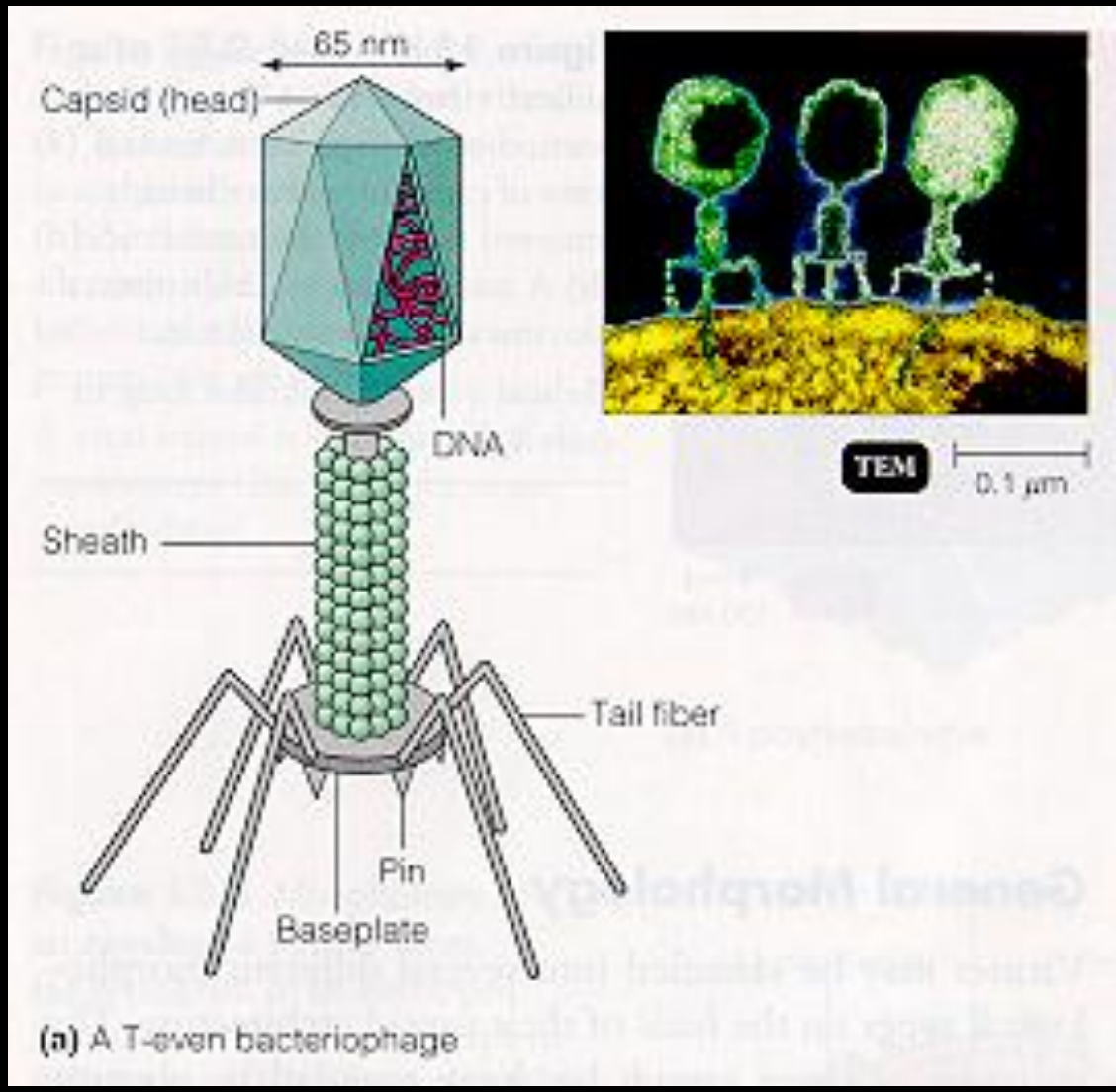


A. Enveloped Helical

B. Enveloped Polyhedral

Viral Morphology

4. Complex

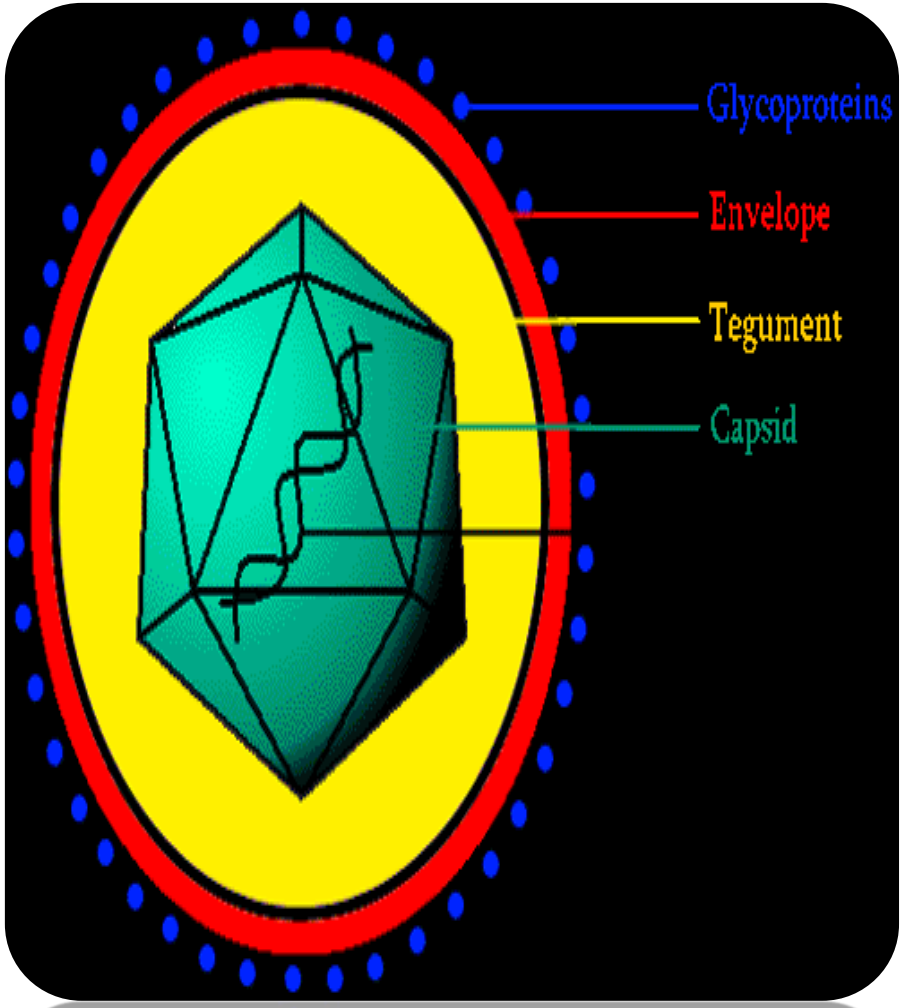


Viral Classification

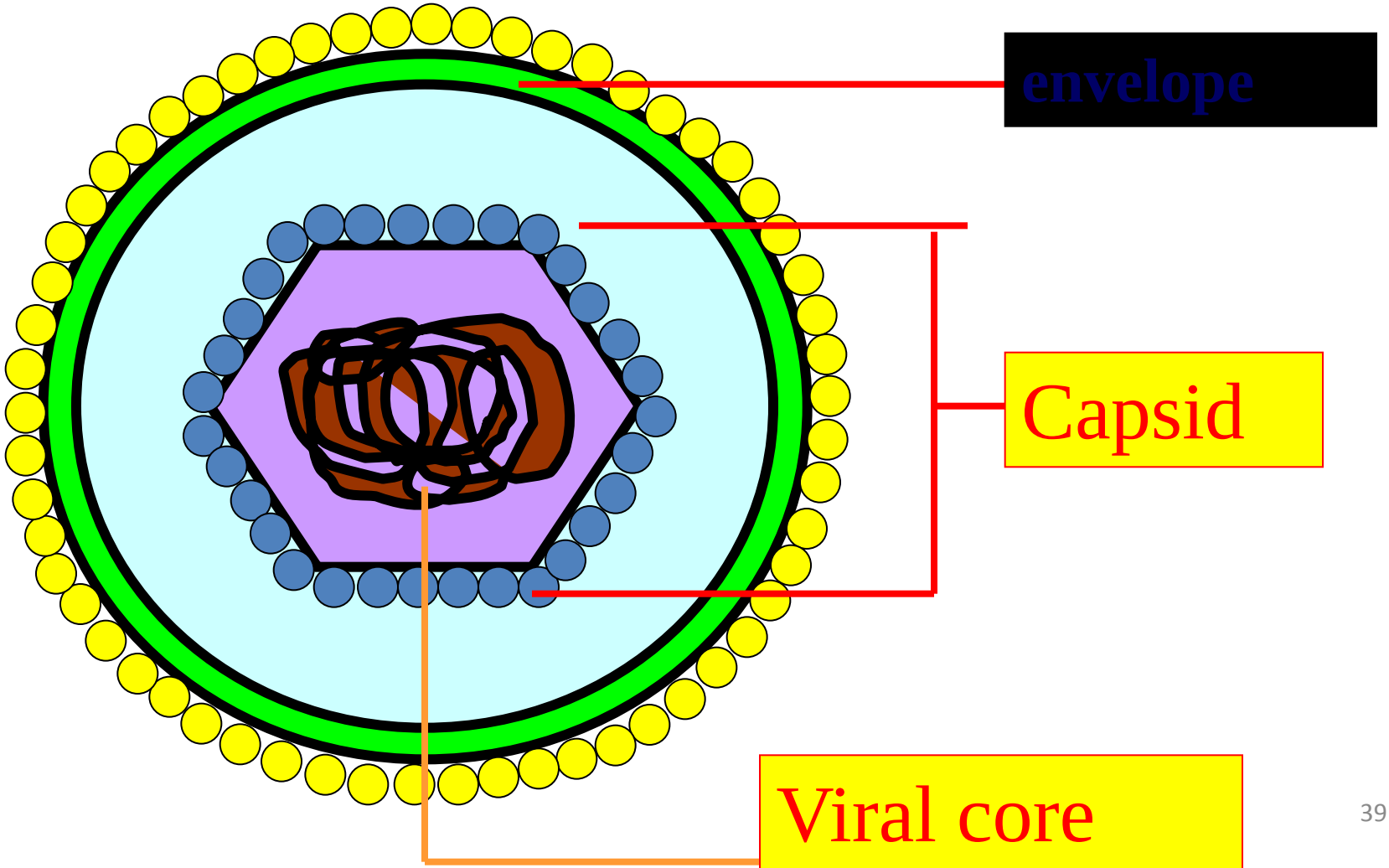
- 1. Nucleic Acid
- 2. Morphology
- 3. Strategy for replication

Virion

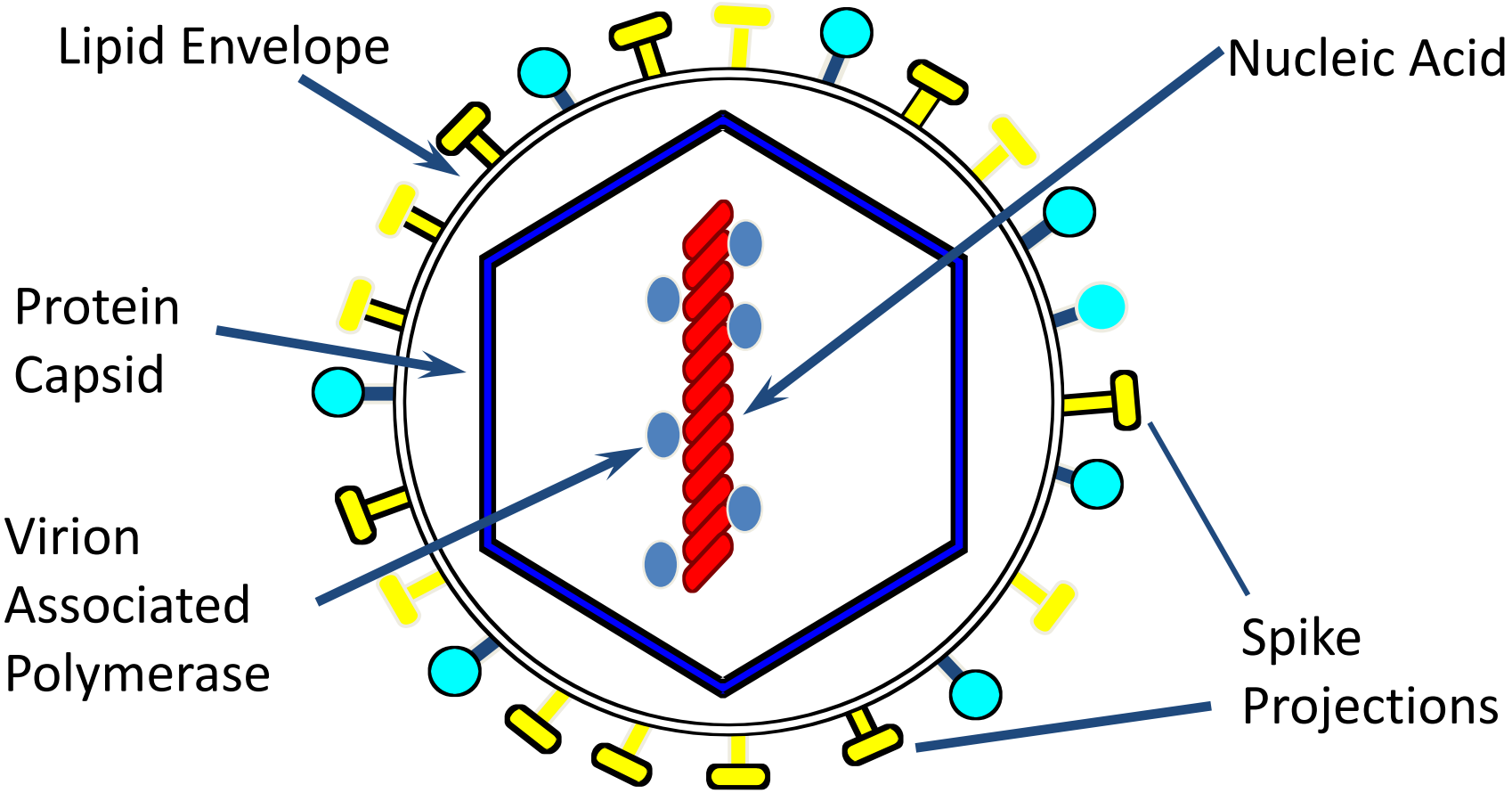
- **The complete infectious unit of virus particle**
- **Structurally mature, extracellular virus particles.**



Virion



Virion Structure



Distinguishing characteristics of viruses

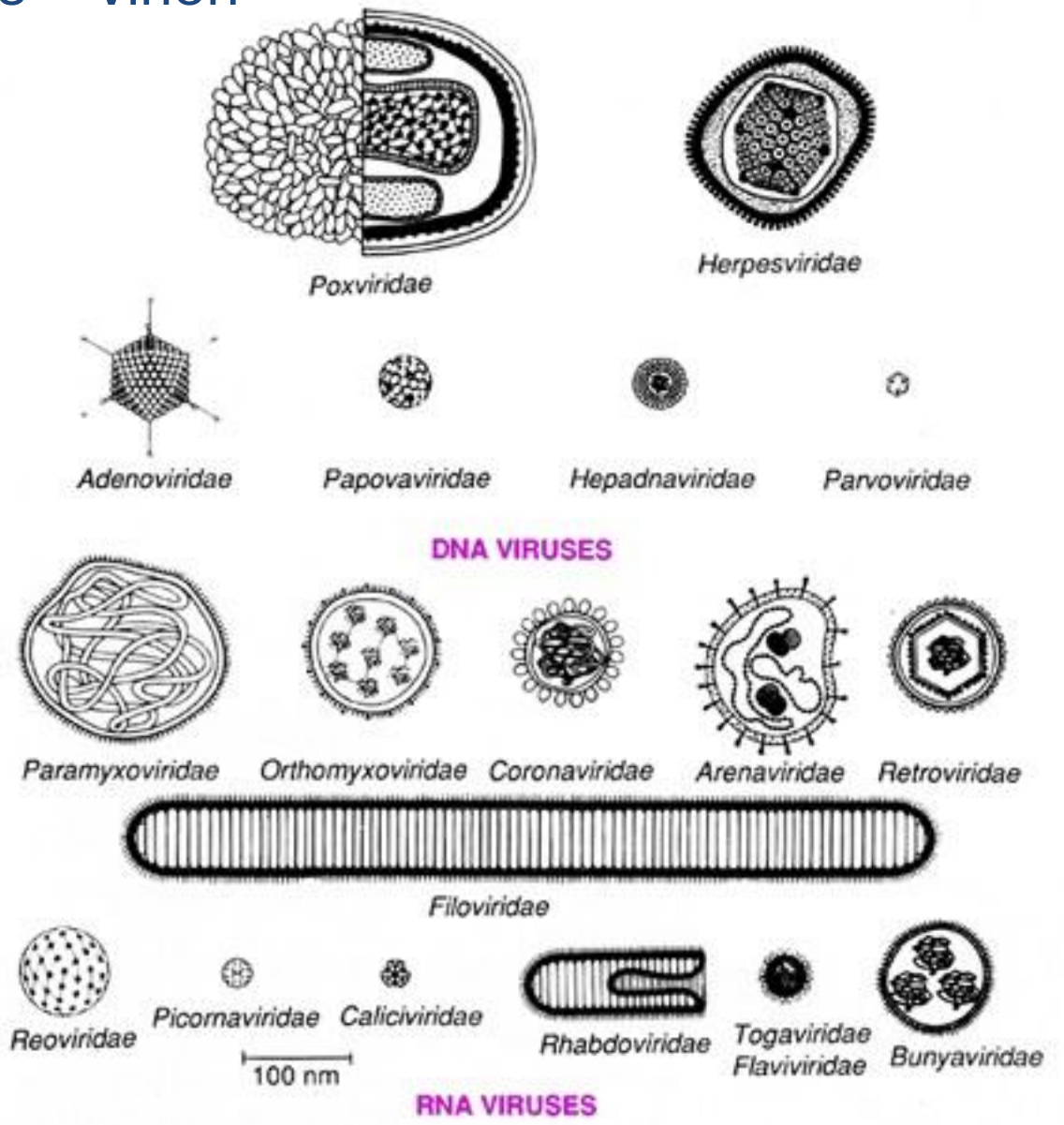
- Obligate intracellular parasites
- Extreme genetic simplicity
- Contain DNA or RNA
- Replication involves disassembly and reassembly
- Replicate by "one-step growth”

How are viruses named?

- Based on:
  - the disease they cause
    poliovirus, rabies virus
  - the type of disease
    murine leukemia virus
  - geographic locations
    Sendai virus, Coxsackie virus
  - their discovers
    Epstein-Barr virus
  - how they were originally thought to be contracted
    dengue virus (“evil spirit”), influenza virus (the “influence” of bad air)
  - combinations of the above
    Rous Sarcoma virus

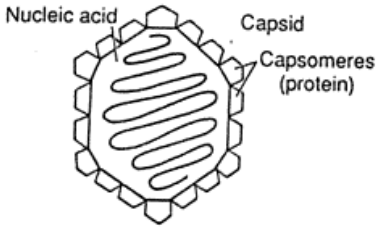
Virus particle = virion

White, DO and Fenner, FJ.
al Virology, 4th Ed. 1994

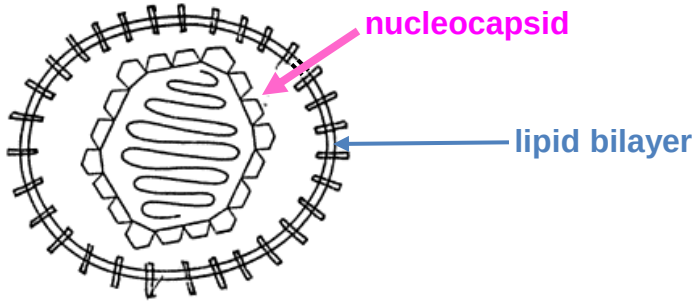


5 BASIC TYPES OF VIRAL STRUCTURE

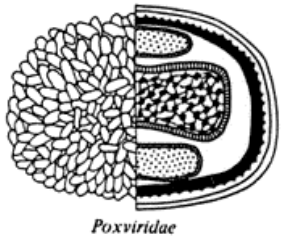
icosahedral nucleocapsid



ICOSAHEDRAL

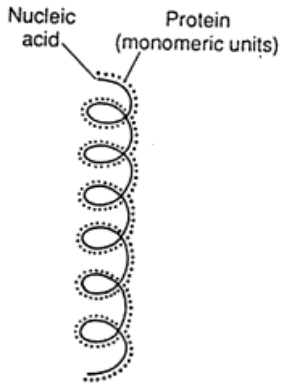


ENVELOPED ICOSAHEDRAL

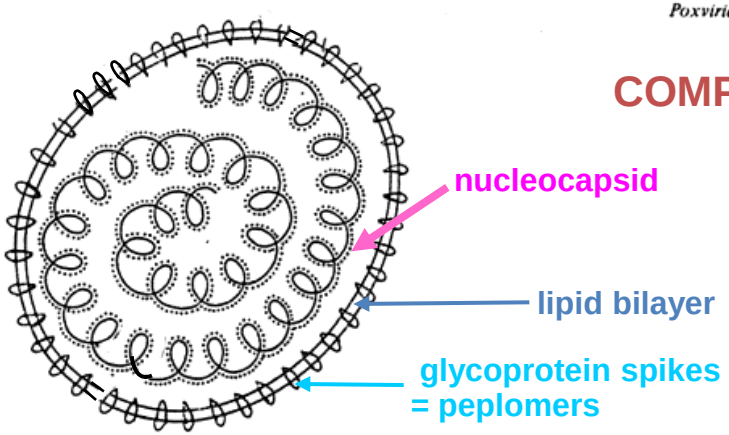


COMPLEX

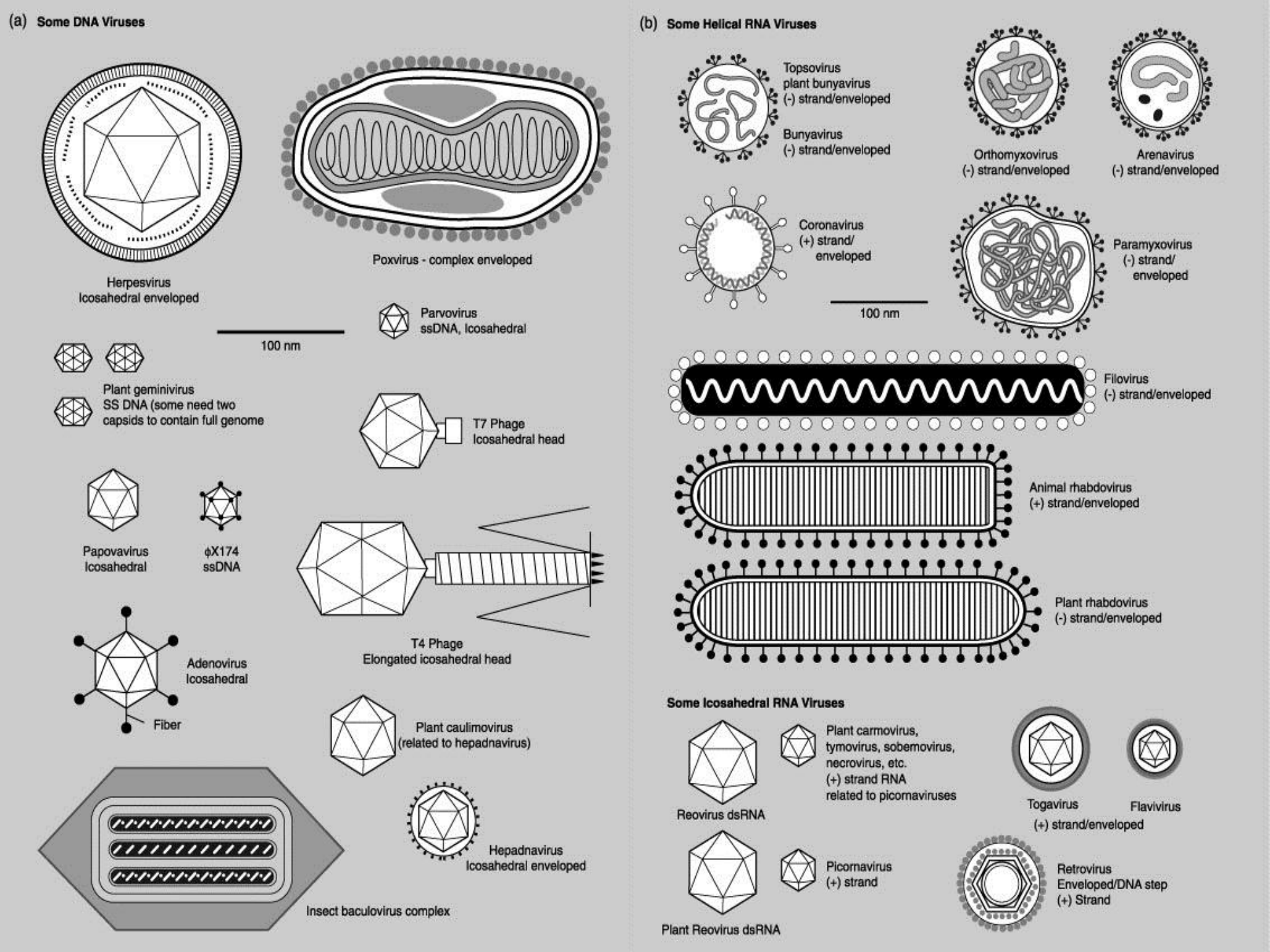
helical nucleocapsid

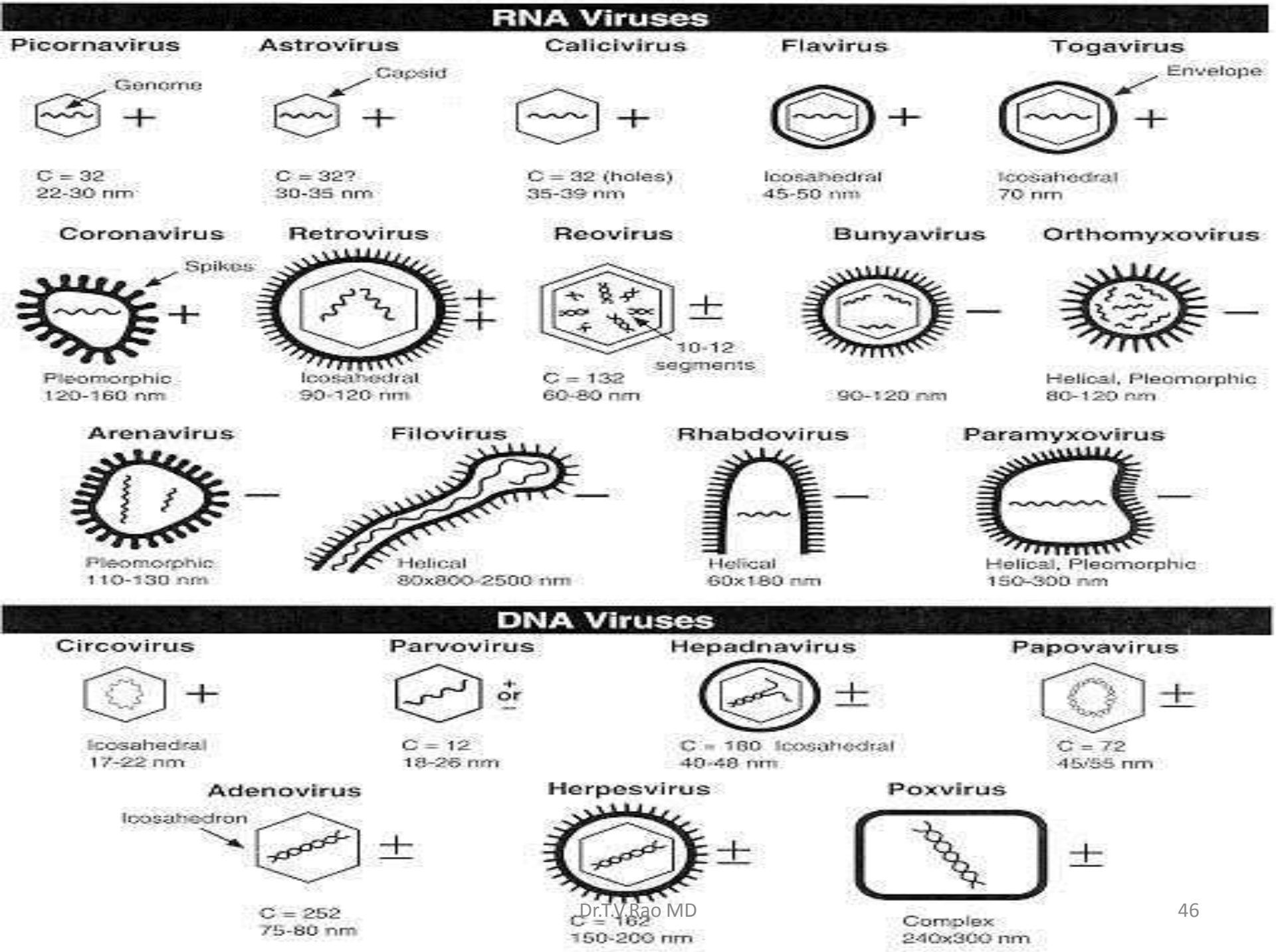


HELICAL



ENVELOPED HELICAL


(a) Some DNA Viruses
Herpesvirus
Icosahedral enveloped
Poxvirus - complex enveloped
Parvovirus
ssDNA, Icosahedral
100 nm
Plant geminivirus
SS DNA (some need two
capsids to contain full genome
T7 Phage
Icosahedral head
Papovavirus
Icosahedral
ϕX174
ssDNA
T4 Phage
Elongated icosahedral head
Adenovirus
Icosahedral
Fiber
Plant caulimovirus
(related to hepadnavirus)
Hepadnavirus
Icosahedral enveloped
Insect baculovirus complex
(b) Some Helical RNA Viruses
Topsovirus
plant bunyavirus
(-) strand/enveloped
Bunyavirus
(-) strand/enveloped
Orthomyxovirus
(-) strand/enveloped
Arenavirus
(-) strand/enveloped
Coronavirus
(+) strand/
enveloped
100 nm
Paramyxovirus
(-) strand/
enveloped
Filovirus
(-) strand/enveloped
Animal rhabdovirus
(+) strand/enveloped
Plant rhabdovirus
(-) strand/enveloped
Some Icosahedral RNA Viruses
Reovirus dsRNA
Plant carmovirus,
tymovirus, sobemovirus,
necrovirus, etc.
(+) strand RNA
related to picornaviruses
Togavirus
Flavivirus
(+) strand/enveloped
Picornavirus
(+) strand
Retrovirus
Enveloped/DNA step
(+) Strand
Plant Reovirus dsRNA


RNA Viruses
Picornavirus
Genome
C = 32
22-30 nm
Astrovirus
Capsid
C = 32?
30-35 nm
Calicivirus
C = 32 (holes)
35-39 nm
Flavirus
Icosahedral
45-50 nm
Togavirus
Envelope
Icosahedral
70 nm
Coronavirus
Spikes
Pleomorphic
120-160 nm
Retrovirus
Icosahedral
90-120 nm
Reovirus
10-12 segments
C = 132
60-80 nm
Bunyavirus
90-120 nm
Orthomyxovirus
Helical, Pleomorphic
80-120 nm
Arenavirus
Pleomorphic
110-130 nm
Filovirus
Helical
80x800-2500 nm
Rhabdovirus
Helical
60x180 nm
Paramyxovirus
Helical, Pleomorphic
150-300 nm
DNA Viruses
Circovirus
Icosahedral
17-22 nm
Parvovirus
or
C = 12
18-26 nm
Hepadnavirus
C = 180 Icosahedral
40-48 nm
Papovavirus
C = 72
45/55 nm
Adenovirus
Icosahedron
C = 252
75-80 nm
Herpesvirus
C = 162
150-200 nm
Poxvirus
Complex
240x300 nm

Icosahedral

- Adeno-associated Virus (AAV)
  Adenovirus
  B19
  Coxsackievirus - A
  Coxsackievirus - B
  Cytomegalovirus (CMV)
  Eastern Equine Encephalitis Virus (EEEV)
  Echovirus
  Epstein-Barr Virus (EBV)
  Hepatitis A Virus (HAV)
  Hepatitis B Virus (HBV)
  Hepatitis C Virus (HCV)
  Hepatitis Delta Virus (HDV)
  Hepatitis E Virus (HEV)
- Herpes Simplex Virus 1 (HHV1)
  Herpes Simplex Virus 2 (HHV2)
  Human Immunodeficiency Virus (HIV)
  Human T-lymphotrophic Virus (HTLV)
  Norwalk Virus
  Papilloma Virus (HPV)
  Polio virus
  Rhinovirus
  Rubella Virus
  Saint Louis Encephalitis Virus
  Varicella-Zoster Virus (HHV3)
  Western Equine Encephalitis Virus (WEEV)
  Yellow Fever Virus

Viral Replication

Stages in virus replication begin when virions infect cells

Attachment/ Adsorption

↓

Penetration

↓

Uncoating

↓

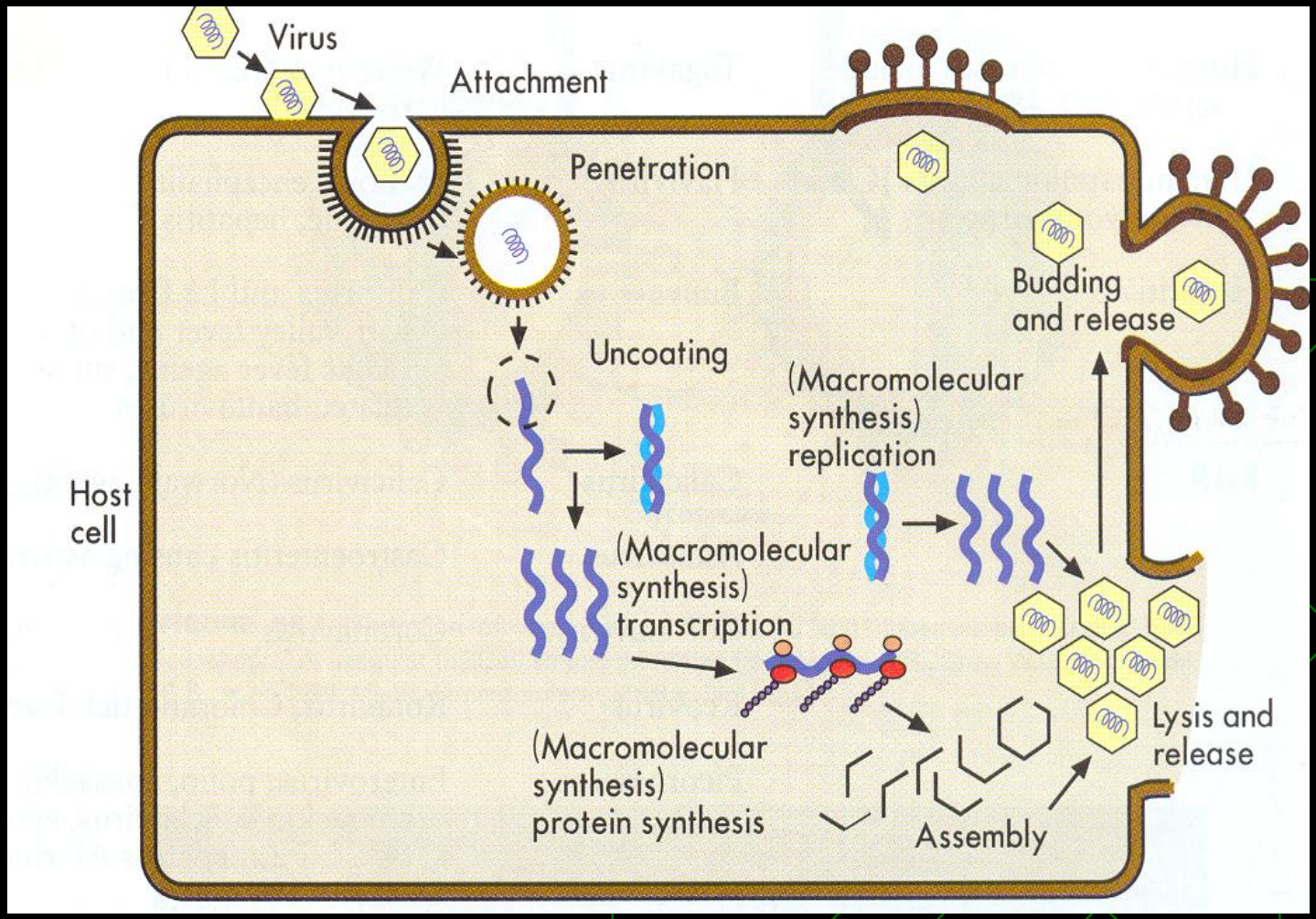
Biosynthesis

↓

Maturation & Assembly

↓

Release



Viral Replication

- Eclipse phase – from the stage of penetration till the appearance of mature daughter virions, the virions cannot be detected inside the host cell.

http://www.liquidjigsaw.com/animation/anim5.htm#