Viral size and organization

• Size
  – 20-250nm
  – 0.000000002m-0.000000025m

• Virion structure
  – Capsid
  – Core

• Acellular obligatory intracellular parasites
  – Lack organelles, metabolic activities, and reproduction
  – Replicated by live host cells
Size comparison

- Red blood cell (10,000 nm in diameter)
- E. coli (bacterium) (1000 nm x 3000 nm)
- Poliovirus (30 nm)
- Bacterial ribosomes (25 nm)
- Bacteriophage T4 (50 nm x 225 nm)
- Tobacco mosaic virus (15 nm x 300 nm)

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# Viral sizes table

<table>
<thead>
<tr>
<th>RELATIVE SIZES OF SELECTED CELLS, VIRUSES, AND MOLECULES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cells</strong></td>
</tr>
<tr>
<td>Herpes simplex</td>
</tr>
<tr>
<td>Rabies</td>
</tr>
<tr>
<td>Influenza</td>
</tr>
<tr>
<td>Adenovirus</td>
</tr>
<tr>
<td>T2 bacteriophage</td>
</tr>
<tr>
<td>Poliomyelitis</td>
</tr>
<tr>
<td>Yellow fever</td>
</tr>
<tr>
<td>Foot-and-mouth</td>
</tr>
<tr>
<td>Tobacco mosaic</td>
</tr>
</tbody>
</table>

**Molecules**

| Hemoglobin molecule | 15 |
| Egg albumin molecule | 10 |
Host specificity

- Type of host organism is specific
  - Specific host required for infection

- Examples of host specificity
  - Animal, plant, bacteria
  - Mammalian, Human

- Host Tropism
  - Highly Specific relationship between tissue or cell type and virus ligand
    - HIV - leukocytes, CD4 receptor
    - Rabies – neurons, Acetylcholine receptor
    - Herpes viruses – Nerve growth factor receptor
Viral external structures

- **Envelope**
  - Host membrane – outside of the capsid
  - Identity and immune proteins

- **Capsid**
  - Repeated protein coat
  - Naked – without envelope

- **Spike**
  - **Ligand**
    - Protein attachment structures for host receptors
    - Host membrane receptors, proteins, or glycocalyx are attachment sites
  - **Enzyme ligand**
    - Metabolizes external host barriers
Viral structure image

(a) Naked virus

(b) Enveloped virus
Animal viral spikes

- RNA
- Envelope
- Spike
- Nucleocapsid
- Reverse transcriptase
- Entry into host cell

Bacterial viral spikes

- E. coli outer membrane
- Viral DNA
- Host plasma membrane with receptors
- Loss of envelope; nucleocapsid in host

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Viral Core

• Everything interior to the capsid
• Single RNA or DNA chromosome
  – Ranges from 4 to 200 genes
  – RNA viruses subject to rapid mutation changes
• Core enzymes – RNA viruses
  – Nucleic acid polymerase enzymes
    • attached to the chromosome to initiate replication of new chromosomes
Viral core enzymes

Hemagglutinin spike
Neuraminidase spike
Matrix protein
Lipid bilayer
Polymerase
Ribonucleoprotein

Influenza

GP-120
GP-41
RNA strands
Reverse transcriptase

HIV
Viral classification or naming

• Historical
  – Pox, influenza, measles, herpes

• Mode or source of transmission
  – Arbo = forest > insect transmitted
    • West Nile Virus
    • Dengue Fever Virus

• Clinical properties
  – HIV, SARS, encephalitis, hepatitis

• Anatomical or Physical properties
  – Chromosome type - DNA or RNA
  – Size and appearance
    • picorna (polio), corona (SARS)
Arbovirus Transmission mode
<table>
<thead>
<tr>
<th>Disease</th>
<th>Vector</th>
<th>Natural Host(s)</th>
<th>Distribution</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Togaviridae</strong> (enveloped, +ssRNA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern equine encephalitis (EEE)</td>
<td>Aedes and Culiseta mosquitoes</td>
<td>Birds</td>
<td>Americas</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>Western equine encephalitis (WEE)</td>
<td>Culex and culiseta mosquitoes</td>
<td>Birds</td>
<td>Americas</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>Venezuelan equine encephalitis (VEE)</td>
<td>Aedes and Culex mosquitoes</td>
<td>Rodents, horses</td>
<td>Americas</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td><strong>Flaviviridae</strong> (enveloped, +ssRNA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Culex mosquitoes</td>
<td>Birds, pigs</td>
<td>Asia</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>West Nile encephalitis</td>
<td>Culex mosquitoes</td>
<td>Birds</td>
<td>Africa, Europe, Asia, North America</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>St. Louis encephalitis</td>
<td>Culex mosquitoes</td>
<td>Birds</td>
<td>North America</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>Russian spring-summer encephalitis</td>
<td>Ixodes and Dermacentor ticks</td>
<td>Birds</td>
<td>Russia</td>
<td>Flu-like symptoms and encephalitis</td>
</tr>
<tr>
<td>Dengue and dengue hemorrhagic fever</td>
<td>Aedes mosquitoes</td>
<td>Monkeys, humans</td>
<td>Worldwide, especially tropics</td>
<td>Severe pain, hemorrhaging, hepatitis, shock</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Aedes mosquitoes</td>
<td>Monkeys, humans</td>
<td>Africa, South America</td>
<td>Hepatitis, hemorrhagic fever, shock</td>
</tr>
</tbody>
</table>
Medically important DNA viruses

• Pox
  – Small pox (variola)
  – Cowpox (vaccinia)
  – Monkeypox

• Herpes
  – Cytomegalovirus (CMV)
  – Epstein-Barr
  – Varicella (chickenpox)
  – HSV1,2

• See DNA virus Table
Medically important DNA viruses

**Enveloped**

*Poxviridae*: Smallpox, Molluscum contagiosum
- Complex structure, lack capsid
- Lateral body
- Envelope
- Nucleosome
- Core membrane

*Herpesviridae*: Cold sores, Mononucleosis
- Bud off nucleus, tend to become latent

*Hepadnaviridae*: Hepatitis B
- Unusual genome containing both double- and single-stranded DNA

**Nonenveloped**

*Adenoviridae*: Common cold, Keratoconjunctivitis

*Papovaviridae*: Common and genital warts, Leucoencephalopathy

*Parvoviridae*: Erythema contagiosum
- Unusual single-stranded DNA genome

Legend
- Genome strandedness
- Double (DS) DNA
- Single (SS) DNA
Hepatitis B particles

Filamentous form (22 nm diameter)
Dane particle (42 nm diameter)
Spherical particle (22 ± 2 nm diameter)

HepB Pathology

Healthy

Cirrhosis

Courtesy of Fred P. Williams, Jr., U.S. Environmental Protection Agency
Herpes Simplex 1 virus

HSV1 lesion
Medically important RNA viruses

- Picorna – Polio, HepA, Rhino
- Paramyxvo – Rubeola, Mumps, RSV
- Toga - Rubella - Adult or German measles
- Flavi – Hep C
- Retro – HIV, HTLV
- Rhabdo
- See RNA viruses Table 1 and 2
Medically important RNA viruses table 1

<table>
<thead>
<tr>
<th>Enveloped</th>
<th>Nonenveloped</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmented, Single-Stranded, Negative-Sense Genome*</td>
<td>Nonsegmented, Single-Stranded, Positive-Sense Genome</td>
</tr>
<tr>
<td>Orthomyxoviridae: Influenza</td>
<td>Picornaviridae: Polio virus</td>
</tr>
<tr>
<td>Bunyaviridae: California encephalitis virus</td>
<td>Hepatitis A virus</td>
</tr>
<tr>
<td>Hantavirus hemorrhagic fever</td>
<td>Rhinoviruses</td>
</tr>
<tr>
<td>Arenaviridae: Hemorrhagic fevers</td>
<td>Caliciviridae: Norwalk agent</td>
</tr>
<tr>
<td>Lassa fever virus</td>
<td></td>
</tr>
<tr>
<td>Argentine hemorrhagic fever virus</td>
<td></td>
</tr>
<tr>
<td>Nonsegmented, Single-Stranded, Negative Sense</td>
<td></td>
</tr>
<tr>
<td>Paramyxoviridae: Mumps virus</td>
<td></td>
</tr>
<tr>
<td>Measles virus</td>
<td></td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td></td>
</tr>
<tr>
<td>Rhabdoviridae: Rabies virus</td>
<td></td>
</tr>
<tr>
<td>Vesicular stomatitis virus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Child with Polio paralysis photo
1930-40’s Polio epidemic
Medically important RNA viruses 2

Filoviridae: Ebola fever virus  
Marburg virus

Nonsegmented, Single-Stranded,  
Positive Sense
Togaviridae: Rubella virus  
Western and Eastern equine  
encephalitis
Flaviviridae: Dengue fever virus  
Yellow fever virus

Coronaviridae: Common  
cold virus

Single-Stranded, Positive Sense,  
Reverse Transcriptase
Retroviridae: AIDS (HIV)  
T-cell leukemia virus  
Hairy cell leukemia virus
Viral replication events overview

• Attachment and Entry
  – Uncoating of capsid from enveloped viruses

• Replication
  – Chromosome
  – Capsid

• Assembly and Release
  – Inside host cell
  – On membrane
Viral replication model image

1. Replication
   - Viral DNA
   - Capsid proteins

2. Transcription
   - mRNA
   - Translation
   - Capsid proteins

3. Self-assembly of new virus particles and their exit from cell
Viral Attachment and Entry

• Three modes

• Adsorption – naked viruses
  – Capsid or spike proteins attach to host membrane
  – Viral plasmid admitted into cell
  – Capsid remains external

• Fusion - enveloped
  – Envelope spikes attach to receptors and fuses with host membrane
  – Capsid admitted into cell

• Receptor-mediated endocytosis - enveloped
  – Envelope spikes attach to host membrane receptors
  – Endocytosis response
  – Entire enveloped virus admitted into cell
Viral Entry modes image

(a) Direct penetration by naked viruses
Capsid → Nucleic acid → Receptor → Animal Virus Entry

(b) Enveloped virus fusing with plasma membrane
Capsid protein → Spikes → Envelope → Nucleic acid → Capsid

(c) Entry of enveloped virus by endocytosis
Naked virus Entry

1. Receptors on cytoplasmic membrane
2. Capsid
3. Viral genome

1. Cut edge of host cytoplasmic membrane
Enveloped virus Entry

1. Cytoplasmic membrane
2. Viral glycoproteins
3. Envelope
4. Viral glycoproteins remain in cytoplasmic membrane
5. Viral genome
6. Uncoating capsid

Fusion

Endocytosis
HIV receptor attachment image
Endocytosis entry into host photo

- Enveloped virus
- Host cell
Influenza spikes

- Two step entry
- Neuraminidase
  - Enzyme ligand
  - digests host glycocalyx
- Hemagglutinin
  - Attachment ligand
  - Growth hormone receptors
Hemagglutination
Used to ID viruses with hemagglutinin

Patient fluid sample mixed with RBC’s
Viral Plasmid Replication

- Plasmid is uncoated from capsid
- Viral plasmid copies are made
  - Viral core enzymes initiates replication (RNA)
  OR
  - Host cell enzymes initiate replication (DNA)
- Replication occurs in the cytoplasm or nucleus
DNA viral chromosome

- Viral DNA chromosome is used as a template to synthesize new viral DNA chromosomes
- Viral DNA → DNA synthesis → New viral DNA chromosomes
RNA viral chromosome

- Viral RNA chromosome is used as a template to synthesize new viral DNA chromosomes
  - Reverse Transcriptase (RT)
- Viral DNA is then a template for new viral RNA chromosome synthesis
  - Viral DNA may be a transposon in host DNA
- Viral RNA > RT > Viral DNA chromosome > Viral RNA chromosome
Lysogeny

• Genetic transformation of host
  – Viral chromosome is a permanent resident of the host cell
  – Viral DNA chromosome integrated into host chromosome
    • Bacterial = Transposon
    • Eukaryotic = Provirus
    • Retroviruses
  – Viral DNA chromosome stored in cytoplasm
    • Plasmid
    • Herpes viruses
Cell and viral chromosomes image

Eucaryote (composite)

Cells
- Chromosomes
- Nucleus
- Mitochondrion
- Extrachromosomal DNA
- Plasmid
- Chloroplast

Procaryote
- Chromosome
- Plasmids

Viruses
- DNA
- RNA
Viral Protein Synthesis

• Viral transcription
  – Viral chromosome transcribed to mRNA

• Viral translation
  – Viral mRNA translated to a large polypeptide

• Viral protein processing
  – Viral polypeptide cleaved into separate proteins
    • Capsid
    • Spikes
    • Nucleic acid polymerases
  – Viral proteins folded and assembled together
Viral protein synthesis image

Integrated DNA (provirus) \(\rightarrow\) Integration of DNA copy into host chromosome

Host DNA \(\rightarrow\) Transcription of viral genes

Many RNA copies, each coding for many proteins \(\rightarrow\) Translation of viral RNA into polyprotein

Polyprotein \(\rightarrow\) Protease cleaves polyprotein into individual proteins

Capsid protein \(\rightarrow\) Assembly of many new virus particles each containing reverse transcriptase.

Envelope protein (spikes)
Viral assembly and release

• Viral assembly
  – Spikes, Capsids and Chromosomes
    • at the host outer membrane
    • in the host cytoplasm

• Viral release modes
  – Lytic (lysis = splitting or bursting)
    • Acute
  – Budding = exocytosis or secretion
    • Leads to cell death
    • Persistent, Chronic or Recurrent
Enveloped viral release

1. **Protein spikes**
2. **Capsid protein**
3. **Nucleic acid**
4. **Host plasma membrane**

Viral proteins that are to become spikes of virus attach to host plasma membrane.

5. **Viral matrix protein**

Viral matrix protein coats inside of plasma membrane.

6. **Matrix protein**

Nucleocapsid becomes enclosed by viral envelope which is composed of the host’s plasma membrane (shown in green).

7. **Budding**

Budding is completed.

8. **Enveloped virus**

Intact host membrane
Enveloped virus budding

1. Viral glycoproteins
2. Cross section of host cytoplasmic membrane
3. Budding of enveloped virus
4. Enveloped virion
SARS viral particles in human lung cell photo
Viral release modes image

Virus inside host cell

Integration of viral DNA

Integration

Plasmid

Normal cells are transformed into tumor cells

Latent infection

Normal cells are transformed into tumor cells

Acute infection

Cell dies and virus is released when cells lyse.

Virus is released by budding and cell usually survives.

Viral DNA present in cell as a plasmid without adverse effects; virus replicates as a plasmid.

Latent infection
Bacterial viruses

• Bacterial viruses are called PHAGES
  – Specific for certain bacteria species
  – Responsible for transferring antibiotic resistance between bacteria

• Phage replication
  – Adsorption is the method of attachment to host receptors
  – Entry of viral chromosome (plasmid) only
Phage attachment and entry image

1. **Attachment:** Phage attaches to host cell.
2. **Penetration:** Phage penetrates host cell and injects its DNA.

- Capsid (head)
- Sheath
- Tail fiber
- Baseplate
- Pin
- Cell wall
- Plasma membrane
- Sheath contracted
- Tail core

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Phage replication

• Lytic
  – Viral assembly and release cause lysis of host cell

• Lysogenic
  – Viral chromosome or plasmid is replicated and then passed on to dividing bacteria
  – Lysis may occur in any generation
Phage replication and release image

3. Biosynthesis:
   Phage DNA directs synthesis of viral components by the host cell.

4. Maturation:
   Viral components are assembled into virions.

5. Release:
   Host cell lyses and new virions are released.

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Phage lysis and lysogeny image

Phage λ attaches to bacteria

Injected phage DNA may either integrate or replicate

Linear phage DNA circularizes

(a) Replication Pathway (lytic cycle)

(b) Integration Pathway (lysogenic cycle)

(d) Replication of phage DNA

New virions are formed (assembly)

Prophage is integrated into bacterial chromosome

(c) Excision of phage DNA

Cell lyses with release of phage λ
Phage gene recombination image

1. Prophage exists in galactose-using host (containing the *gal* gene).
2. Phage genome excises, carrying with it the adjacent *gal* gene from the host.
3. Phage matures and cell lyses, releasing phage carrying *gal* gene.
4. Phage infects a cell that cannot utilize galactose (lacking *gal* gene).
5. Along with the prophage, the bacterial *gal* gene becomes integrated into the new host's DNA.
6. Lysogenic cell can now metabolize galactose.