

Chapter 16

The Viruses: Introduction and General Characteristics

Viruses

- acellular infectious agents
- virologists
 - scientists that study viruses
- virology
 - study of viruses

Early Development of Virology

- Many epidemics of viral diseases occurred before anyone understood the nature of their causative agents.

Early attempts to prevent viral disease

- Lady Wortley Montagu (early 1700s)
 - proponent of inoculation of children with material from smallpox lesions
 - observed this practice among Turkish women
- Edward Jenner (1798)
 - published case reports of successful attempts to prevent smallpox by exposure to cowpox

Discovery of viruses

- Charles Chamberland (1884)
 - developed porcelain bacterial filters used later in discovery of viruses
- Dimitri Ivanowski (1892)
 - demonstrated that causative agent of tobacco mosaic disease passed through bacterial filters
 - thought agent was toxin

Discovery of viruses...

- Martinus Beijerinck (1898-1900)
 - showed that causative agent of tobacco mosaic disease was still infectious after filtration
 - referred to agent as filterable virus
- Loeffler and Frosch (1898-1900)
 - showed that hoof-and-mouth disease in cattle was caused by filterable virus

Discovery of viruses...

- Walter Reed (1900)
 - showed that yellow fever in humans was caused by filterable virus transmitted by mosquitoes
- Ellerman and Bang (1908)
 - showed that leukemia in chickens was caused by a virus
- Peyton Rous (1911)
 - showed that muscle tumors in chickens were caused by a virus

Discovery of bacterial viruses

- Frederick Twort (1915)
 - first to isolate viruses that infect bacteria (bacteriophages)
- Felix d'Herelle (1917)
 - firmly established the existence of bacteriophages
 - devised method for enumerating them
 - demonstrated that bacteriophages only reproduce in live bacteria

Discovery of chemical nature of viruses

- W. M. Stanley (1935)
 - crystallized tobacco mosaic virus (TMV)
 - showed that TMV was composed mostly of protein
- F. C. Bawden and N. W. Pirie (1935)
 - separated TMV particles into protein and nucleic acid components

General Properties of Viruses

- virion
 - complete virus particle
 - consists of ≥ 1 molecule of DNA or RNA enclosed in coat of protein
 - may have additional layers

Viruses versus cellular organisms

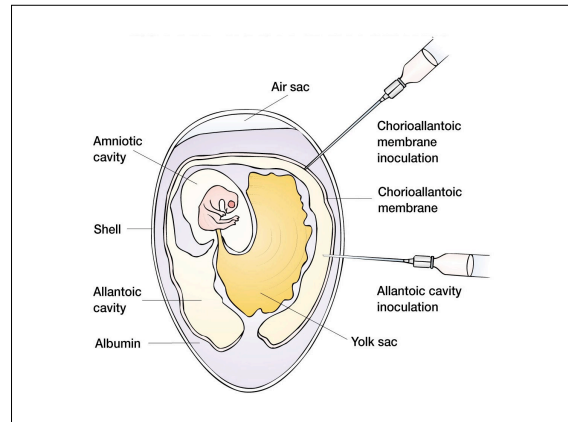
- | Viruses | Cellular Organisms |
|--|---|
| <ul style="list-style-type: none">• simple organization• DNA or RNA but not both (one exception)• unable to reproduce outside of living cells• obligate intracellular parasites | <ul style="list-style-type: none">• complex organization• both DNA and RNA• carry out cell division• some are obligate intracellular parasites |

The Cultivation of Viruses

- requires appropriate living host

Hosts for animal viruses

- suitable animals
- embryonated eggs
 - monolayers of animal cells
 - plaques
 - localized area of cellular destruction and lysis
- cytopathic effects
 - microscopic or macroscopic degenerative changes or abnormalities in host cells and tissues



Hosts for bacteriophages

- usually cultivated in **broth** or **agar** cultures of suitable, young, actively growing bacteria
 - broth cultures lose turbidity as viruses reproduce
 - plaques observed on agar cultures

Hosts for plant viruses

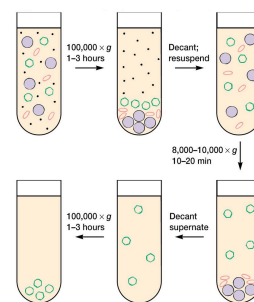
- plant tissue cultures
- plant protoplast cultures
- suitable whole plants
 - may cause localized necrotic lesions or generalized symptoms of infection

Virus Purification

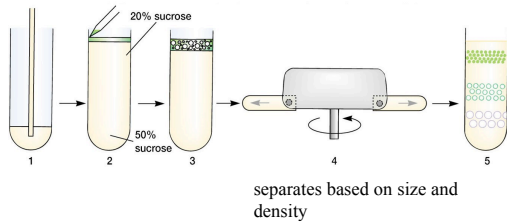
- four commonly used methods
 - differential centrifugation and density gradient centrifugation
 - precipitation of viruses
 - denaturation of contaminants
 - enzymatic digestion of cell constituents

Differential centrifugation

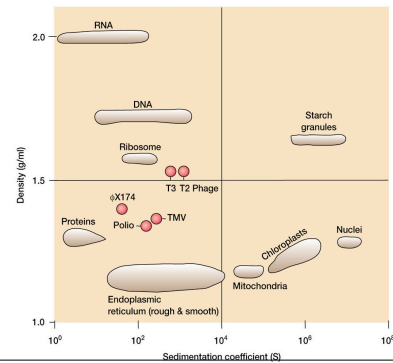
- separates based on size



Density gradient centrifugation



Gradient Centrifugation



Differential precipitation

- commonly uses ammonium sulfate or polyethylene glycol
- separates viruses from other components in a virus preparation mixture

Denaturation and precipitation of contaminants

- can be achieved with heat, pH, and organic solvents

Enzymatic degradation of cellular constituents

- proteases and nucleases used to remove cellular proteins and nucleic acids

Virus Assays

- used to determine quantity of viruses in a sample
- two types of approaches
 - count particles
 - measure concentration of infectious units

Particle counts

- direct counts
 - made with an electron microscope

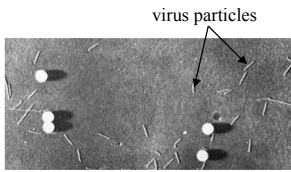


Figure 16.8

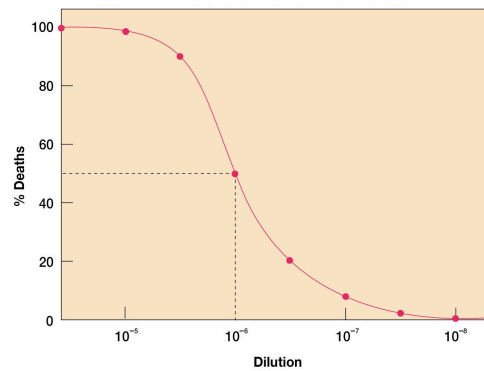
- indirect counts
 - e.g., hemagglutination assay
 - determines highest dilution of virus that causes red blood cells to clump together

Measuring concentration of infectious units

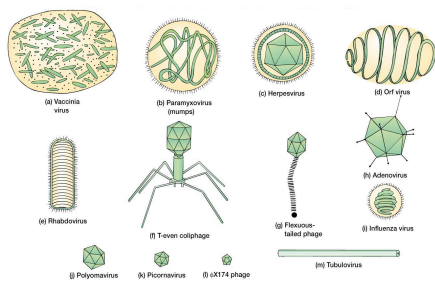
- plaque assays
 - dilutions of virus preparation made and plated on lawn of host cells
 - number of plaques counted
 - results expressed as plaque-forming units (PFU)

Measuring concentration of infectious units...

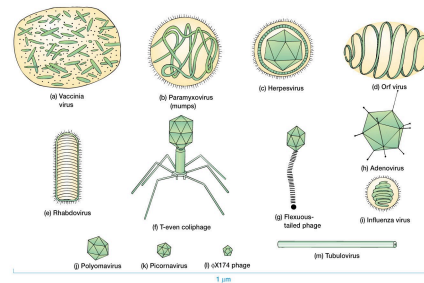
- infectious dose and lethal dose assays
 - determine smallest amount of virus needed to cause infection or death of 50% of exposed host cells or organisms
 - results expressed as ID_{50} or LD_{50}



The Structure of Viruses



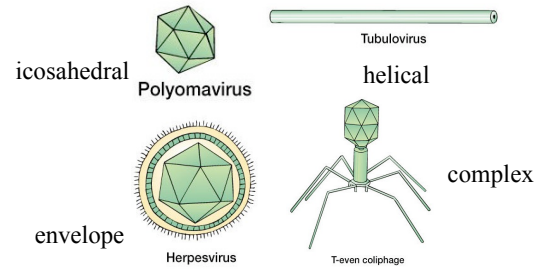
Virion Size



General Structural Properties

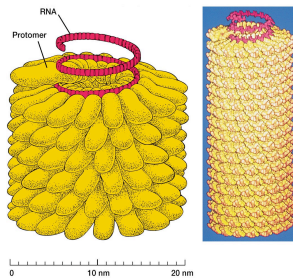
- nucleocapsid
 - nucleic acid held within protein coat
- capsid
 - protein coat that surrounds viral genome
 - protects genome and aids in transfer between host cells
- protomer
 - protein subunits that make up capsid

Morphological types



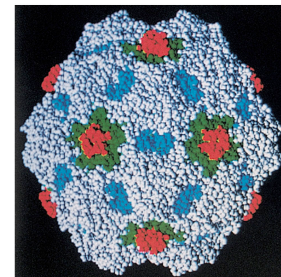
Helical Capsids

- shaped like hollow tubes with protein walls

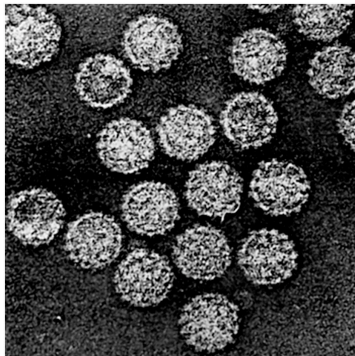


Icosahedral Capsids

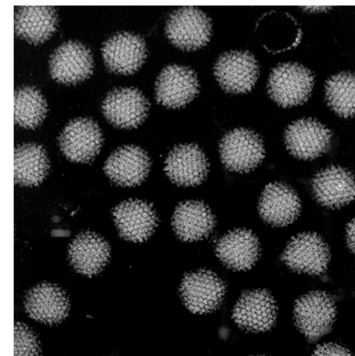
- regular polyhedron with 20 equilateral triangular faces and 12 vertices



simian virus

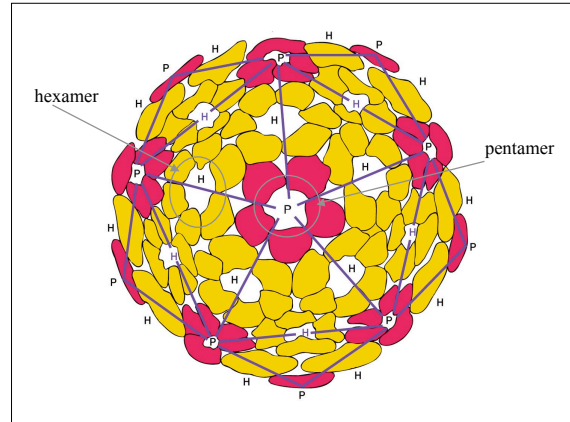


adenovirus

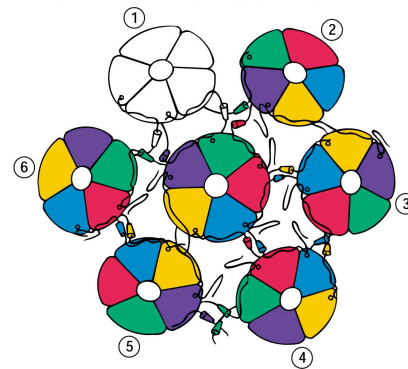
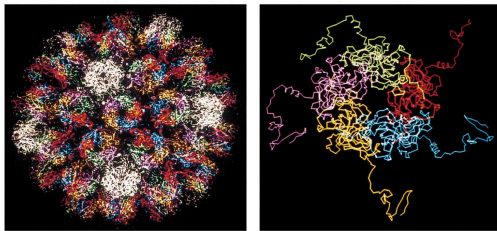


Icosahedral capsid structure

- capsomers
 - ring- or knob-shaped units made of five or six protomers
 - pentamers (pentons) – five subunit capsomers
 - hexamers (hexons) – six subunit capsomers

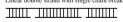

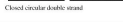


some viruses composed only of pentamers (e.g., SV40)



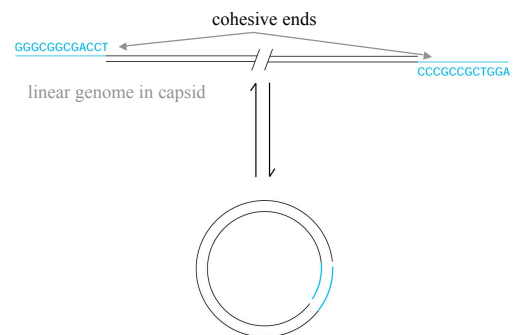
Nucleic Acids

Table 16.1 Types of Viral Nucleic Acids

Nucleic Acid Type	Nucleic Acid Structure	Virus Examples
DNA		
Single-Stranded	Linear single strand Circular single strand	Parvoviruses φX174, φ1, φ phages
Double-Stranded	Linear double strand Linear double strand with single-chain breaks  Double strand with cross-linked ends  Closed circular double strand 	Herpesviruses (herpes simplex viruses, cytomegalovirus, Epstein-Barr virus), adenoviruses, T. coliphages, lambda phage, and other bacteriophages T4 phage Vaccinia, smallpox Polyomaviruses (SV-40), papillomaviruses, P22 phage, cauliflower mosaic
RNA		
Single-Stranded	Linear, single stranded, positive strand Linear, single stranded, negative strand Linear, single stranded, segmented, positive strand Linear, single stranded, segmented, diploid (two identical single strands), positive strand Linear, single stranded, segmented, negative strand	Picornaviruses (polio, rhinoviruses), togaviruses, RNA bacteriophages, TMV, and most plant viruses Rhabdoviruses (rabies), paramyxoviruses (mumps, measles) Borna disease virus (isolated segments in separate viruses) Borna disease virus, hepatitis virus, human immunodeficiency virus Paramyxoviruses, orthomyxoviruses (influenza)
Double-Stranded	Linear, double stranded, segmented	Reoviruses, wood-nymph virus of plants, cytomegalus polyhedrus virus of insects, phage φ6, many myoviruses

Madigan & S. L. Malik, et al., *General Virology*, 3rd Edition, 1997, John Wiley & Sons, Inc., New York, NY.

Lambda DNA



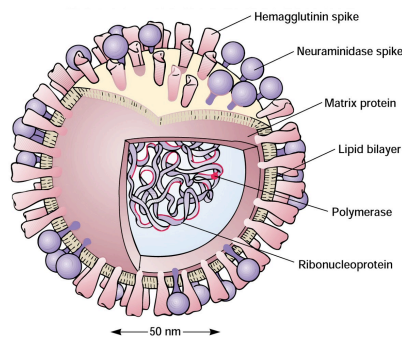
Types of ssRNA viruses

- plus (positive) strand RNA viruses
 - sequence of nucleotides in genomic RNA = sequence of nucleotides in viral mRNA
- minus (negative) strand RNA viruses
 - sequence of nucleotides in genomic RNA is complementary to viral mRNA
- segmented genomes
 - virion contains >1 unique RNA

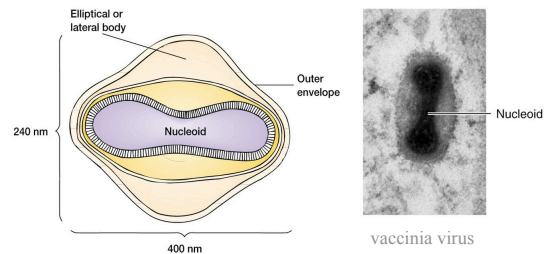
Viral Envelopes and Enzymes

- viral envelopes
 - membrane structures surrounding some viruses
 - lipids and carbohydrates in envelope – usually derived from host membranes
 - peplomers (spikes)
 - proteins in envelope – virus specific
- viral enzymes
 - observed in some viruses
 - associated with or are within capsid

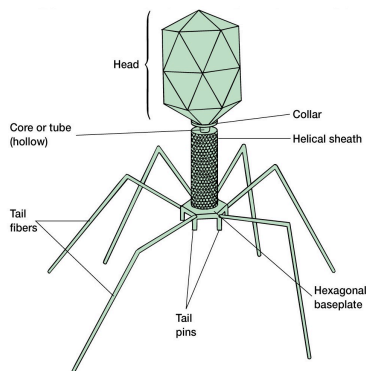
Influenza virus



Viruses with Capsids of Complex Symmetry



binal symmetry – having both icosahedral and helical symmetry



Principals of Virus Taxonomy

- classified based on numerous characteristics
 - most important – nature of genome

Table 16.2 Some Common Virus Groups and Their Characteristics

Nucleic Acid	Strandedness	Capid Symmetry ^a	Presence of Envelope	Size of Capid (nm) ^b	Number of Capioneres	Virus Group	Host Range ^c
RNA	Single	I	-	22-30	32	Picornaviridae	A
		I	+	40-70(e)	32	Togaviridae	A
		I ²	+	100(e)		Reoviridae	A
		H	+	90x, 80-120(e)		Orthomyxoviridae	A
		H	+	180x, 125-250(e)		Paramyxoviridae	A
		H	+	14-16(h), 80-100(e)		Coronaviridae	A
		H	+	180x, 70-80 x 110-130		Rhabdoviridae	A
		LI	-	(bullet shaped)		Bunyaviridae	P
		H	-	20-35, 18-25 x 30-45		Tobamovirus	P
		I	-	18 x 300	32	Leviviridae (Qβ)	B
RNA	Double	I	-	70-80	92	Reoviridae	A, P
		I	+	100(e)		Cytoviridae	B
DNA	Single	I	-	20-25	12	Parsviridae	A
		I	-	18 x 30 (paired particles)		Geminiviridae	P
		I	-	25-35		Moviridae	B
		H	-	6 x 90x-1,900		Iridoviridae	B
DNA	Double	I	-	40	72	Polyomaviridae	A
		I	-	55	72	Papillomaviridae	A
		I	-	60-60	252	Adenoviridae	A
		I	+	130-180		Iridoviridae	A
		I	+	100, 180-200(e)		Herpesviridae	A
		C	+	200-260 x 250-290(e)	162	Poiviridae	A
		H	+	40 x 300(e)		Budoviridae	A
		C	+	28 (core), 42(e)	42	Hepadnaviridae	A
		LI	-	50, 30 x 60-900		Caulimoviridae	P
		I	-	60		Circoviridae	B
Hi	-	80 x 110, 110 ²		Mesoviridae	B		

^aType of symmetry: I, icosahedral; H, helical; C, complex; Hi, head; B, bacilloform.

^bPresence of helical capid (by diameter of uncoiled core, nm).

^cHost range: A, animal; P, plant; B, bacterium.

^dHost free number in the head fraction; the second number, the tail length.