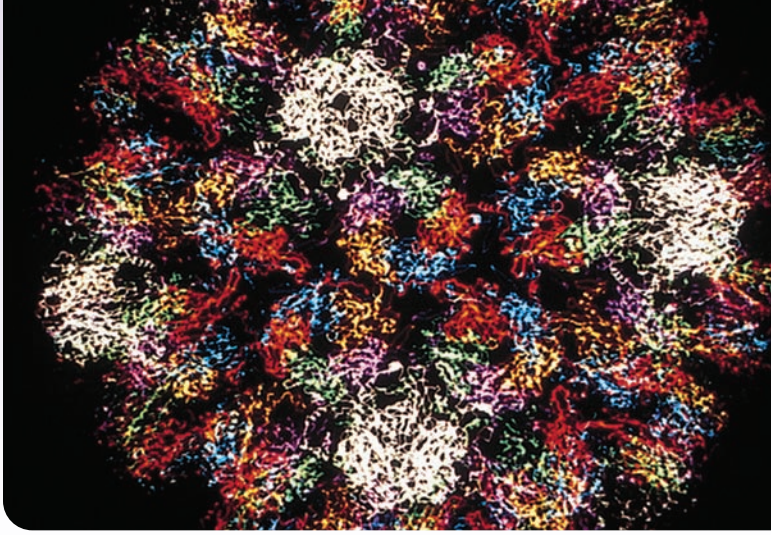
16 The Viruses: Introduction and General Characteristics



The simian virus 40 (SV-40) capsid shown here differs from most icosahedral capsids in containing only pentameric capsomers. SV-40 is a small double-stranded DNA polyomavirus with 72 capsomers. It may cause a central nervous system disease in rhesus monkeys and can produce tumors in hamsters. SV-40 was first discovered in cultures of monkey kidney cells during preparation of the poliovirus vaccine.

Preview

- Viruses are simple, acellular entities. They can reproduce only within living cells because they are obligate intracellular parasites.
- All viruses have a nucleocapsid composed of a nucleic acid genome surrounded by a protein capsid. Some viruses have a membranous envelope that lies outside the nucleocapsid. The nucleic acid of the virus can be RNA or DNA, single-stranded or double-stranded, linear or circular.
- Capsids may have helical, icosahedral, or complex symmetry. They are constructed of protomers that self-assemble through noncovalent bonds.
- Although each virus has unique aspects to its life cycle, a general pattern of replication is observable. The typical virus life cycle consists of five steps: attachment to the host cell, entry into the host cell, synthesis of viral nucleic acid and proteins within the host cell, self-assembly of virions within the host cell, and release of virions from the host cell.
- Viruses are cultured by inoculating living hosts or cell cultures with a virion preparation. Purification depends mainly on their large size relative to cell components, high protein content, and great stability. The virus concentration may be determined from the virion count or from the number of infectious units.
- Viruses are classified primarily on the basis of their nucleic acid's characteristics, reproductive strategy, capsid symmetry, and the presence or absence of an envelope.

In chapters 16, 17, and 18 we turn our attention to the viruses. These are infectious agents with fairly simple, acellular organization. Most possess only one type of nucleic acid, either DNA or RNA, and they only reproduce within living cells. Clearly viruses are quite different from procaryotic and eucaryotic microorganisms; they are studied by **virologists.**

Despite their simplicity, viruses are extremely important and deserve close attention. Many human viral diseases are known and more are discovered every year, as demonstrated by the appearance of SARS and avian influenza viruses. The study of viruses has contributed significantly to the discipline of molecular biology. In fact, the field of genetic engineering is based in large part upon discoveries in virology. Thus **virology** (the study of viruses) is a significant part of microbiology.

In this chapter we focus on the broader aspects of virology: its development as a scientific discipline, the general properties and structure of viruses, the ways in which viruses are cultured and studied, and viral taxonomy. In chapter 17 our concern is with viruses of the *Bacteria* and *Archaea*, and in chapter 18 we consider viruses of eucaryotes.

Viruses have had enormous impact on humans and other organisms, yet very little was known about their nature until fairly recently. A brief history of their discovery and recognition as uniquely different infectious agents can help clarify their nature.

16.1 Early Development of Virology

Although the ancients did not understand the nature of their illnesses, they were acquainted with diseases, such as rabies, that are now known to be viral in origin. In fact, there is some evidence that the great epidemics of A.D. 165 to 180 and A.D. 251 to 266, which severely weakened the Roman Empire and aided its decline, may have been caused by measles and smallpox viruses. Smallpox had an equally profound impact on the New World.

Great fleas have little fleas upon their backs to bite 'em
And little fleas have lesser fleas, and so on ad infinitum.

—Augustus De Morgan

Hernán Cortés's conquest of the Aztec Empire in Mexico was made possible by an epidemic that ravaged Mexico City. The virus was probably brought to Mexico in 1520 by the relief expedition sent to join Cortés. Before the smallpox epidemic subsided, it had killed the Aztec King Cuitlahuac (the nephew and son-in-law of the slain emperor, Montezuma II) and possibly 1/3 of the population. Since the Spaniards were not similarly afflicted, it appeared that God's wrath was reserved for Native Americans, and this disaster was viewed as divine support for the Spanish conquest (**Historical Highlights 16.1**).

Progress in preventing viral diseases began years before the discovery of viruses. Early in the eighteenth century, Lady Wortley Montagu, wife of the English ambassador to Turkey, observed that Turkish women inoculated their children against smallpox. The children came down with a mild case but subsequently were immune. Lady Montagu tried to educate the English public about the procedure but without great success. Later in the century an English country doctor, Edward Jenner, stimulated by a girl's claim that she could not catch smallpox because she had had cowpox, began inoculating humans with material from cowpox lesions. He published the results of 23 successful vaccinations in 1798. Although Jenner did not understand the nature of smallpox, he did manage to successfully protect his patients from the dreaded disease through exposure to the cowpox virus.

Until well into the nineteenth century, harmful agents were often grouped together and sometimes called viruses [Latin *virus*, poison or venom]. Even Louis Pasteur used the term virus for any living infectious disease agent. The development in 1884 of the porcelain bacterial filter by Charles Chamberland, one of Pasteur's collaborators and inventor of the autoclave, made possible the discovery of what are now called viruses. Tobacco mosaic disease was the first to be studied with Chamberland's filter. In 1892 Dimitri Ivanowski published studies showing that leaf extracts from infected plants would induce tobacco mosaic disease even after filtration removed all bacteria. However, he attributed this to the presence of a toxin. Martinus Beijerinck, working independently of Ivanowski, published the results of extensive studies on tobacco mosaic disease in 1898 and 1900. Because the filtered sap of diseased plants was still infectious, he proposed that the disease was caused by an entity different from bacteria, what he called a filterable virus. He observed that the virus would multiply only in living plant cells, but could survive for long periods in a dried state. At the same time Friedrich Loeffler and Paul Frosch in Germany found that the hoof-and-mouth disease of cattle was also caused by a virus rather than by a toxin. In 1900 Walter Reed began his study of the yellow fever disease whose incidence had been increasing in Cuba. Reed showed that this human disease was due to a virus that was transmitted by mosquitoes. Mosquito control soon reduced the severity of the yellow fever problem. Thus by the beginning of the 20th century, it had been established that viruses were different from bacteria and could cause diseases in plants, livestock, and humans.

Shortly after the turn of the century, Vilhelm Ellermann and Oluf Bang in Copenhagen reported that leukemia could be transmitted between chickens by cell-free filtrates and was probably caused by a virus. Three years later in 1911, Peyton Rous from the Rockefeller Institute in New York City reported that a virus,

Historical Highlights

16.1 Disease and the Early Colonization of America

There is considerable evidence that disease, and particularly smallpox, played a major role in reducing Indian resistance to the European colonization of North America. It has been estimated that Indian populations in Mexico declined about 90% within 100 years of initial contact with the Spanish. Smallpox and other diseases were a major factor in this decline, and there is no reason to suppose that North America was any different. As many as 10 to 12 million Indians may have lived north of the Rio Grande before contact with Europeans. In New England alone, there may have been over 72,000 in 1600; yet only around 8,600 remained in New England by 1674, and the decline continued in subsequent years.

Such an incredible catastrophe can be accounted for by consideration of the situation at the time of European contact with the Native Americans. The Europeans, having already suffered major epidemics in the preceding centuries, were relatively immune to the diseases they carried. On the other hand, the Native Americans had never been exposed to diseases like smallpox and were decimated by epidemics. In the sixteenth century, before any permanent English colonies had been established, many contacts were made by missionaries and explorers who undoubtedly brought disease with them and infected native populations. Indeed, the English noted at the end of the century that Indian populations had declined greatly but attributed it to armed conflict rather than to disease.

Establishment of colonies simply provided further opportunities for infection and outbreak of epidemics. For example, the Huron Indians decreased from a minimum of 32,000 people to 10,000 in 10 years. Between the time of initial English colonization and 1674, the Narraganset Indians declined from around 5,000 warriors to 1,000, and the Massachusetts Indians, from 3,000 to 300. Similar stories can be seen in other parts of the colonies. Some colonists interpreted these plagues as a sign of God's punishment of Indian resistance: the "Lord put an end to this quarrel by smiting them with smallpox. . . . Thus did the Lord allay their quarrelsome spirit and make room for the following part of his army."

It seems clear that epidemics of European diseases like smallpox decimated Native American populations and prepared the way for colonization of the North American continent. Many American cities—for example, Boston, Philadelphia, and Plymouth—grew upon sites of previous Indian villages.

now known as the Rous sarcoma virus, was responsible for a malignant muscle tumor in chickens. These studies established that at least some malignancies are caused by viruses. The Rous sarcoma virus is still extensively used in cancer research.

In 1915 Frederick Twort reported that bacteria also could be attacked by viruses. Twort isolated bacterial viruses that could attack and destroy micrococci and intestinal bacilli. Although he speculated that his preparations might contain viruses, Twort did not follow up on these observations. It remained for Felix d'Herelle to establish decisively the existence of bacterial viruses. d'Herelle isolated bacterial viruses from patients with dysentery, probably caused by *Shigella dysenteriae*. He noted that when a virus suspension was spread on a layer of bacteria growing on agar, clear circular areas containing viruses and lysed cells developed. A count of these clear zones allowed d'Herelle to estimate the number of viruses present. This procedure for enumerating viruses is now called a plaque assay; it is described in section 16.6. d'Herelle demonstrated that bacterial viruses could reproduce only in live bacteria; therefore he named them **bacteriophages** (or just **phages**) because they could eat holes in bacterial "lawns."

The chemical nature of viruses was established when Wendell Stanley announced in 1935 that he had crystallized the tobacco mosaic virus (TMV) and found it to be largely or completely protein. A short time later Frederick Bawden and Norman Pirie managed to separate the TMV virus particles into protein and nucleic acid. Thus by the late 1930s it was becoming clear that viruses are complexes of nucleic acids and proteins able to reproduce only in living cells.

16.2 General Properties of Viruses

Viruses are a unique group of infectious agents whose distinctiveness resides in their simple, acellular organization and pattern of reproduction. A complete virus particle or **virion** consists of one or more molecules of DNA or RNA enclosed in a coat of protein. Some viruses have additional layers that can be very complex and contain carbohydrates, lipids, and additional proteins (**figure 16.1**). Viruses can exist in two phases: extracellular and intracellular. Virions, the extracellular phase, possess few if any enzymes and cannot reproduce independent of living cells. In the intracellular phase, viruses exist primarily as replicating nucleic acids that induce host metabolism to synthesize virion components; eventually complete virus particles or virions are released.

In summary, viruses differ from living cells in at least three ways: (1) their simple, acellular organization; (2) the presence of either DNA or RNA, but not both, in almost all virions; and (3) their inability to reproduce independent of cells and carry out cell division as procaryotes and eucaryotes do.

1. Describe the major technical advances and important discoveries in the early development of virology. Why might virology have developed much more slowly without the use of Chamberland's filter?
2. Which scientists made important contributions to the development of virology? What were their contributions?
3. How are viruses similar to cellular organisms? How do they differ?

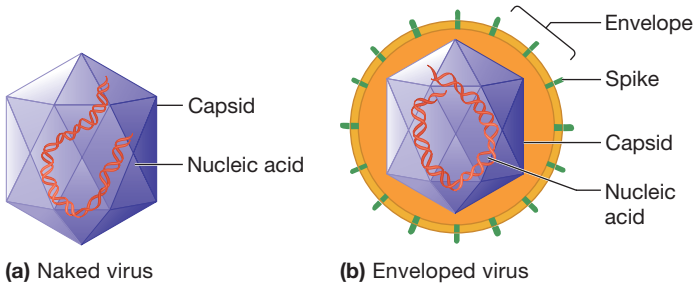


Figure 16.1 Generalized Structure of Viruses. **(a)** The simplest virus is a naked virus (nucleocapsid) consisting of a geometric capsid assembled around a nucleic acid strand. **(b)** An enveloped virus is composed of a nucleocapsid surrounded by a flexible membrane called an envelope. The envelope usually has viral proteins called spikes inserted into it.

16.3 The Structure of Viruses

Virus morphology has been intensely studied over the past decades because of the importance of viruses and the realization that virus structure was simple enough to be understood. Progress has come from the use of several different techniques: electron microscopy, X-ray diffraction, biochemical analysis, and immunology. Although our knowledge is incomplete due to the large number of different viruses, the general nature of virus structure is becoming clear.

Virion Size

Virions range in size from about 10 to 400 nm in diameter (**figure 16.2**). The smallest viruses are a little larger than ribosomes, whereas the poxviruses, which include vaccinia, are about the same size as the smallest bacteria and can be seen in the light microscope. Most viruses, however, are too small to be visible in the light microscope and must be viewed with scanning and transmission electron microscopes. Electron microscopy (section 2.4)

General Structural Properties

All virions, even if they possess other constituents, are constructed around a **nucleocapsid** core (indeed, some viruses consist only of a nucleocapsid). The nucleocapsid is composed of a nucleic acid, usually either DNA or RNA, held within a protein coat called the **capsid,** which protects viral genetic material and aids in its transfer between host cells.

Capsids are large macromolecular structures that self-assemble from many copies of one or a few types of proteins. The proteins used to build the capsid are called **protomers.** Probably the most important advantage of this design strategy is that the information stored in viral genetic material is used with maximum efficiency. For example, the tobacco mosaic virus (TMV) capsid is constructed using a single type of protomer that is 158 amino acids in length (**figure 16.3**). Therefore, of the 6,000 nucleotides in the TMV genome, only about 474 nucleotides are required to code

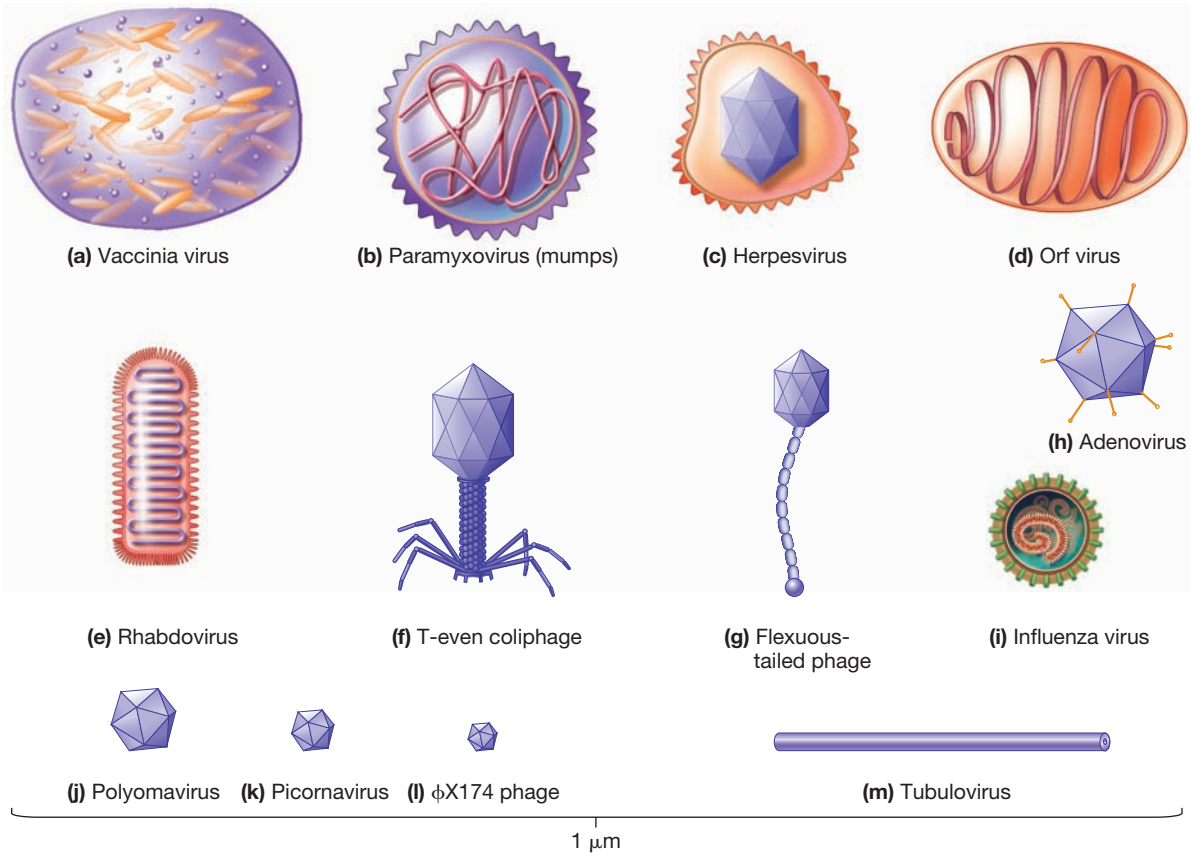


Figure 16.2 The Size and Morphology of Selected Viruses. The viruses are drawn to scale. A 1 μm line is provided at the bottom of the figure.

for the coat protein. Suppose, however, that the TMV capsid was composed of six different protomers all about 150 amino acids in length. If this were the case, about 2,900 of the 6,000 nucleotides in the TMV genome would be required just for capsid construction, and much less genetic material would be available for other purposes.

The various morphological types of viruses primarily result from the combination of a particular type of capsid symmetry with the presence or absence of an envelope, which is a lipid layer external to the nucleocapsid. There are three types of capsid symmetry: helical, icosahedral, and complex. Those virions having an envelope are called **enveloped viruses;** whereas those lacking an envelope are called **naked viruses** (figure 16.1).

Helical Capsids

Helical capsids are shaped like hollow tubes with protein walls. The tobacco mosaic virus provides a well-studied example of helical capsid structure (figure 16.3). In this virus, the self-assembly of protomers in a helical or spiral arrangement produces a long, rigid tube, 15 to 18 nm in diameter by 300 nm long. The capsid encloses an RNA genome, which is wound in a spiral and lies within a groove formed by the protein subunits. Not all helical capsids are as rigid as the TMV capsid. The influenza virus genome is enclosed in thin, flexible helical capsids that are folded within an envelope (**figure 16.4**).

The size of a helical capsid is influenced by both its protomers and the nucleic acid enclosed within the capsid. The diameter of the capsid is a function of the size, shape, and interactions of the protomers. The nucleic acid appears to determine helical capsid length because the capsid does not extend much beyond the end of the DNA or RNA.

Icosahedral Capsids

The icosahedron is a regular polyhedron with 20 equilateral triangular faces and 12 vertices (figure 16.2*h, j–l*). It is one of nature's favorite shapes. The **icosahedral capsid** is the most efficient way to enclose a space. A few genes, sometimes only one, can code for proteins that self-assemble to form the capsid. In this way a small number of genes can specify a large three-dimensional structure.

When icosahedral viruses are negatively stained and viewed in the transmission electron microscope, a complex structure is revealed (**figure 16.5**). The capsids are constructed from ring- or knob-shaped units called **capsomers,** each usually made of five

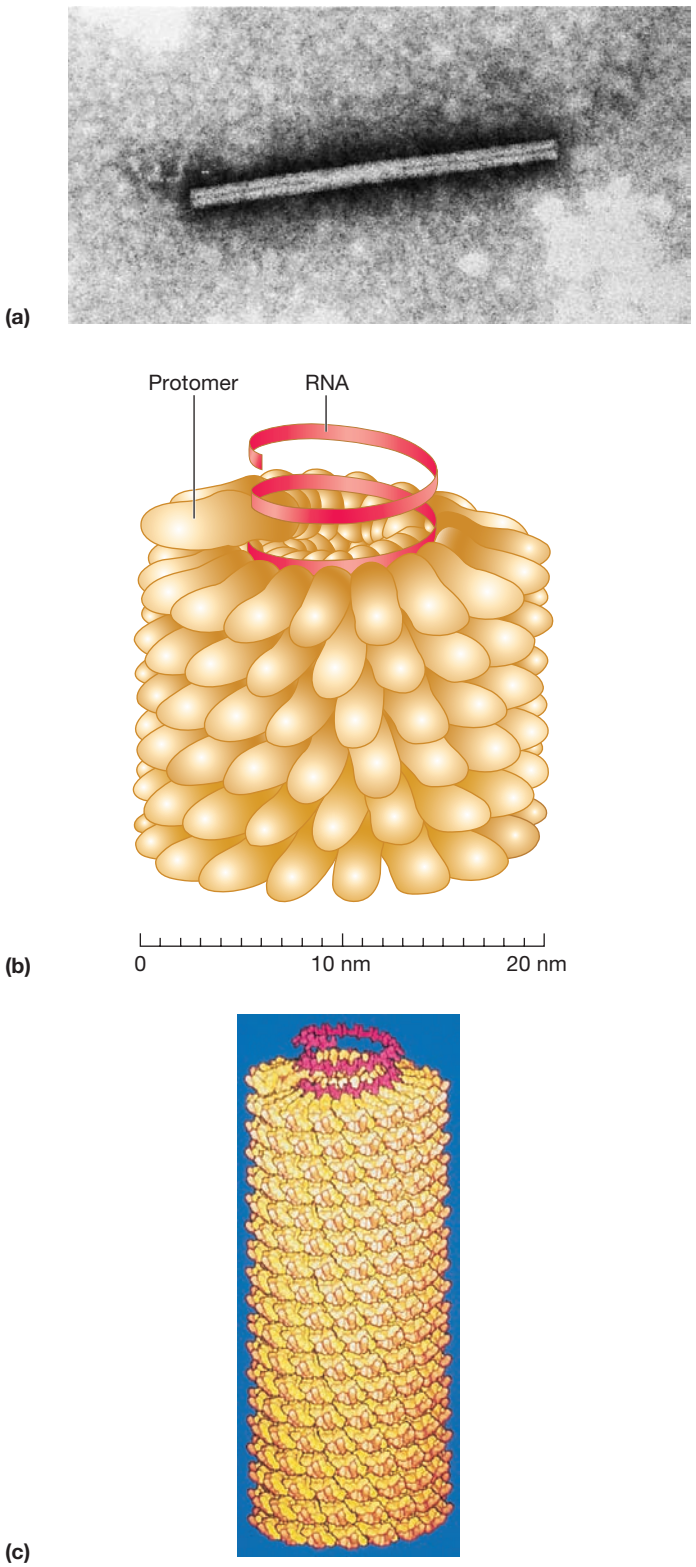


Figure 16.3 Tobacco Mosaic Virus Structure. **(a)** An electron micrograph of the negatively stained helical capsid (×400,000). **(b)** Illustration of TMV structure. Note that the nucleocapsid is composed of a helical array of protomers with the RNA spiraling on the inside. **(c)** A model of TMV.

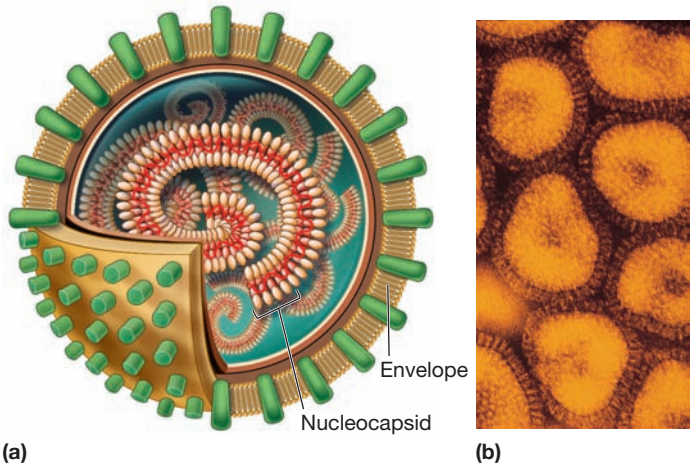


Figure 16.4 Influenza Virus. Influenza virus is an enveloped virus with a helical nucleocapsid. **(a)** Schematic view. Influenza viruses have segmented genomes consisting of 7 to 8 different RNA molecules. Each is coated by capsid proteins. **(b)** Because there are 7 to 8 flexible nucleocapsids enclosed by an envelope, the virions are pleomorphic. Electron micrograph (×350,000).

or six protomers. **Pentamers (pentons)** have five subunits; **hexamers (hexons)** possess six. Pentamers are usually at the vertices of the icosahedron, whereas hexamers generally form its edges and triangular faces (**figure 16.6**). The icosahedron in figure 16.6 is constructed of 42 capsomers; larger icosahedra are made if more hexamers are used to form the edges and faces (e.g., adenoviruses have a capsid with 252 capsomers as shown in figure 16.5*c*,*d*). In some RNA viruses, both the pentamers and hexamers of a capsid are constructed with only one type of subunit. In other viruses, pentamers are composed of different proteins than are the hexamers.

The self-assembly of capsids is a remarkable process that is not fully understood. Enzymatic activity is not required to link protomers together. However, noncapsid proteins may be involved. They usually provide a scaffolding upon which the protomers are assembled.

Although most icosahedral capsids appear to contain both pentamers and hexamers, simian virus 40 (SV-40), a small, double-stranded DNA virus, has only pentamers (**figure 16.7*a***). The virus is constructed of 72 cylindrical pentamers with hollow centers. Five flexible arms extend from the edge of each pentamer toward neighboring pentamers (figure 16.7*b*,*c*). The arms of adjacent pentamers twist around each other and act as ropes that tie the pentamers together.

Viruses with Capsids of Complex Symmetry

Although most viruses have either icosahedral or helical capsids, many viruses do not fit into either category. The poxviruses and large bacteriophages are two important examples.

The poxviruses are the largest of the animal viruses (about 400 × 240 × 200 nm in size) and can even be seen with a phase-contrast microscope or in stained preparations. They possess an

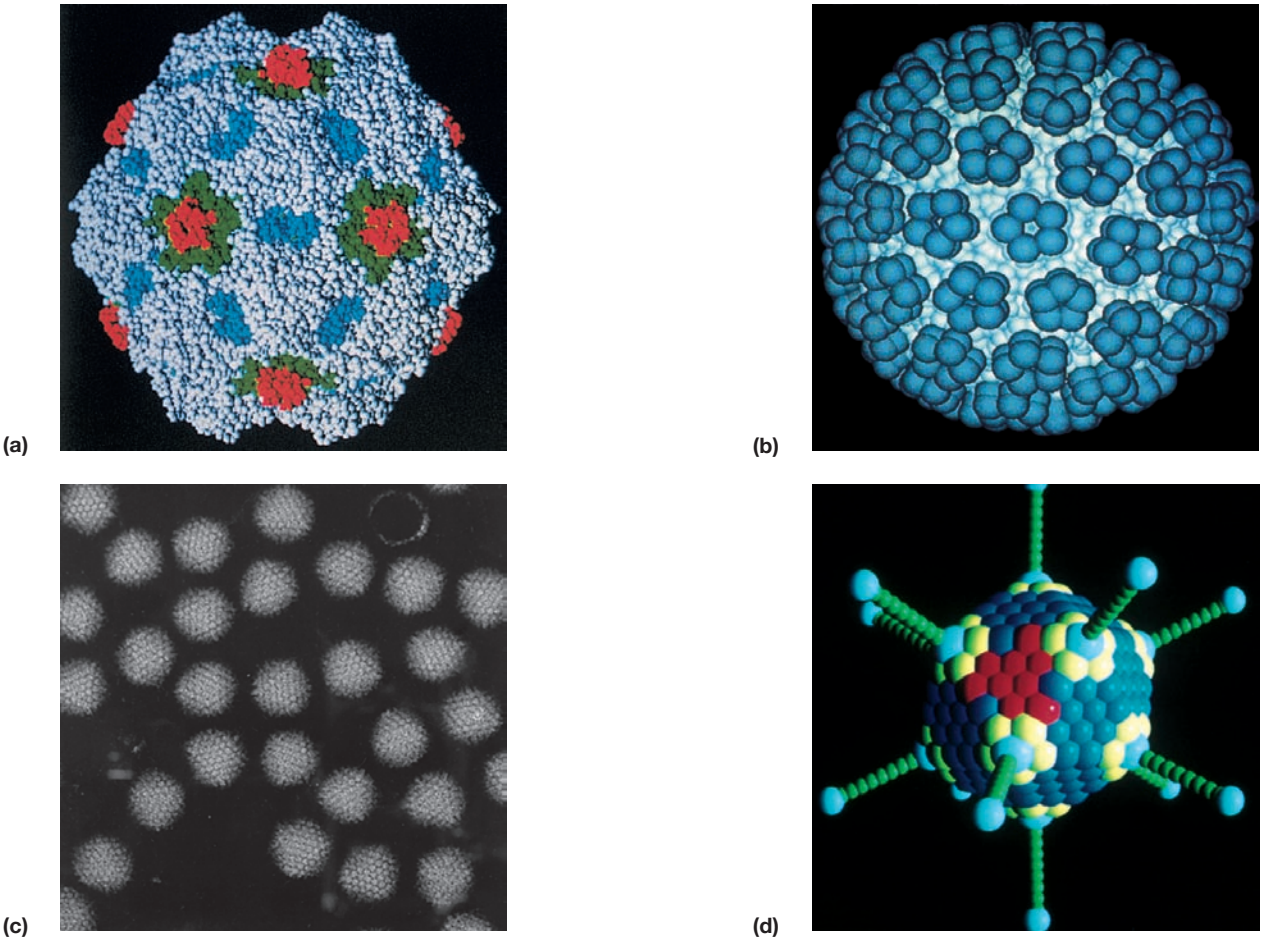


Figure 16.5 Examples of Icosahedral Capsids. **(a)** Canine parvovirus model, 12 capsomers. **(b)** Computer-simulated image of the polyomavirus (72 capsomers) that causes a rare demyelinating disease of the central nervous system. **(c)** Adenovirus, 252 capsomers (×171,000). **(d)** Computer-simulated model of adenovirus.

exceptionally complex internal structure with an ovoid- to brick-shaped exterior. **Figure 16.8** shows the morphology of vaccinia virus, a poxvirus. The double-stranded DNA is associated with proteins and contained in the nucleoid, a central structure shaped like a biconcave disk and surrounded by a membrane. Two elliptical or lateral bodies lie between the nucleoid and its outer envelope, a membrane and a thick layer covered by an array of tubules or fibers.

Some large bacteriophages are even more elaborate than the poxviruses. The T2, T4, and T6 phages (T-even phages) that infect *Escherichia coli* are said to have **binal symmetry** because they have a head that resembles an icosahedron and a tail that is helical. The icosahedral head is elongated by one or two rows of hexamers in the middle and contains the DNA genome (**figure 16.9**). The tail is composed of a collar joining it to the head, a central hollow tube, a sheath surrounding the tube, and a complex baseplate. The sheath is made of 144 copies of the gp18 protein arranged in 24 rings, each containing six copies. In T-even phages, the baseplate is hexagonal and has a pin and a jointed tail fiber at each corner.

There is considerable variation in structure among the large bacteriophages, even those infecting a single host. In contrast with the T-even phages, many other coliphages (phages that infect *E. coli*) have true icosahedral heads. T1, T5, and lambda phages have sheathless tails that lack a baseplate and terminate in rudimentary tail fibers. Coliphages T3 and T7 have short, noncontractile tails without tail fibers. Bacteriophages are discussed in more detail in chapter 17.

Viral Envelopes and Enzymes

Many animal viruses, some plant viruses, and at least one bacterial virus are bounded by an outer membranous layer called an **envelope** (**figure 16.10**). Animal virus envelopes usually arise from host cell nuclear or plasma membranes; their lipids and carbohydrates are normal host constituents. In contrast, envelope proteins are coded for by virus genes and may even project from the envelope surface as **spikes,** which are also called **peplomers.** In many cases, these spikes are involved in virus attachment to the host cell surface. Because they differ among viruses, they also

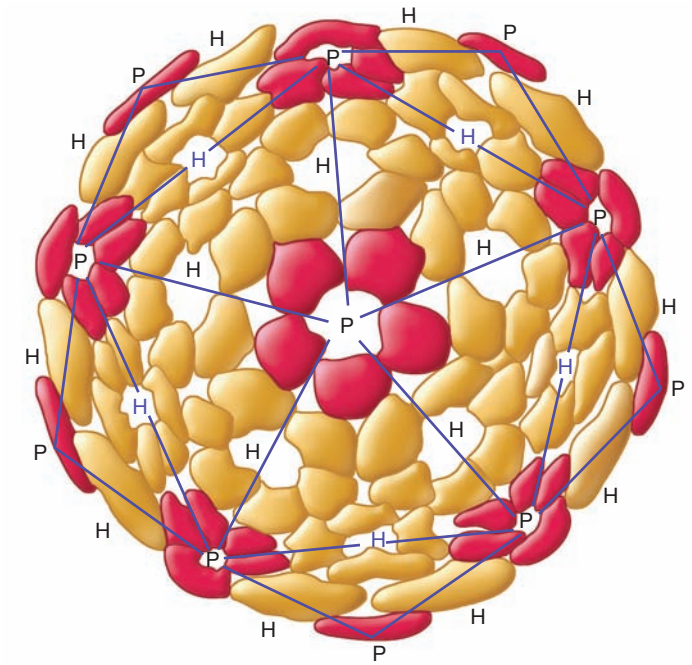


Figure 16.6 The Structure of an Icosahedral Capsid Formed from a Single Type of Protomer. The protomers associate to form either pentons (P), shown in red, or hexons (H), shown in gold. The blue lines define the triangular faces of the icosahedron. Notice that pentons are located at the vertices and that the hexons form the edges and faces of the icosahedron. This capsid contains 42 capsomers.

can be used to identify some viruses. The envelope is a flexible, membranous structure, so enveloped viruses frequently have a somewhat variable shape and are called pleomorphic. However, the envelopes of viruses like the bullet-shaped rabies virus are firmly attached to the underlying nucleocapsid and endow the virion with a constant, characteristic shape (figure 16.10*b*). In some viruses the envelope is disrupted by solvents like ether to such an extent that lipid-mediated activities are blocked or envelope proteins are denatured and rendered inactive. The virus is then said to be "ether sensitive."

Influenza virus (figure 16.10*a*) is a well-studied example of an enveloped virus. Spikes project about 10 nm from the surface at 7 to 8 nm intervals. Some spikes possess the enzyme neuraminidase, which functions in the release of mature virions from the host cell. Other spikes have hemagglutinin proteins, so named because they can bind the virions to red blood cell membranes and cause the red blood cells to clump together (agglutinate). This is called hemagglutination (*see figure 35.11*). Hemagglutinins participate in virion attachment to host cells. Proteins, like the spike proteins that are exposed on the outer envelope surface, are generally glycoproteins—that is, the proteins have carbohydrate attached to them. A nonglycosylated protein, the M or matrix protein, is found on the inner surface of the envelope and helps stabilize it.

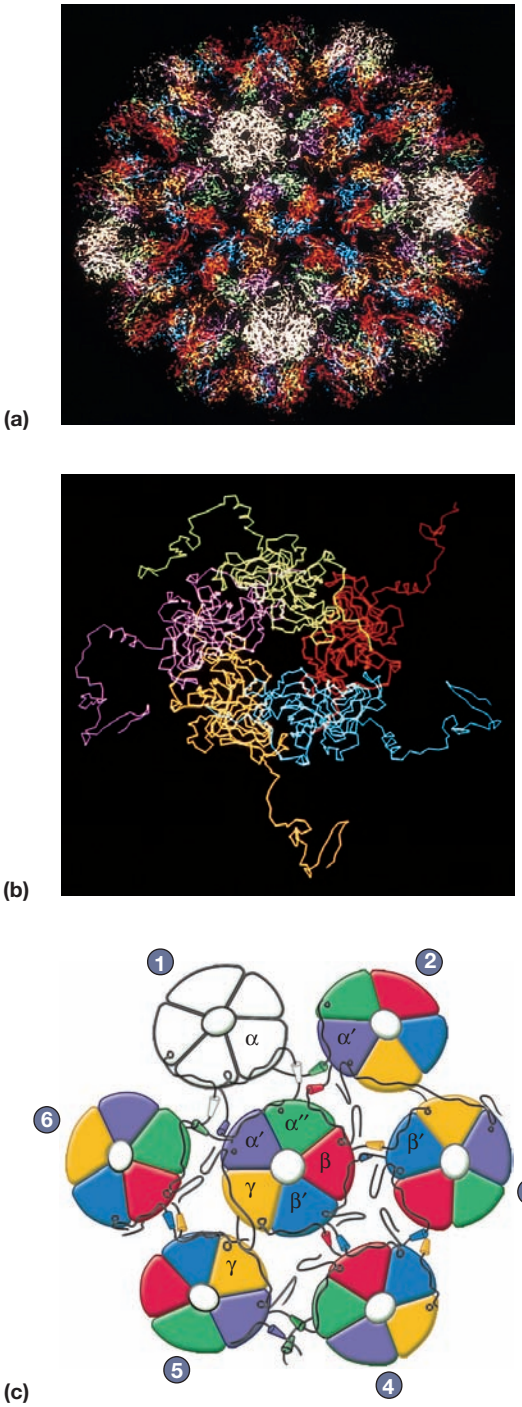


Figure 16.7 An Icosahedral Capsid Constructed of Pentamers. **(a)** The simian virus 40 capsid. The 12 pentamers at the icosahedron vertices are in white. The nonvertex pentamers are shown with each polypeptide chain in a different color. **(b)** A pentamer with extended arms. **(c)** A schematic diagram of the surface structure depicted in part a. The body of each pentamer is represented by a five-petaled flower design. Each arm is shown as a line or a line and cylinder (α-helix) with the same color as the rest of its protomer. The outer protomers are numbered clockwise beginning with the one at the vertex.

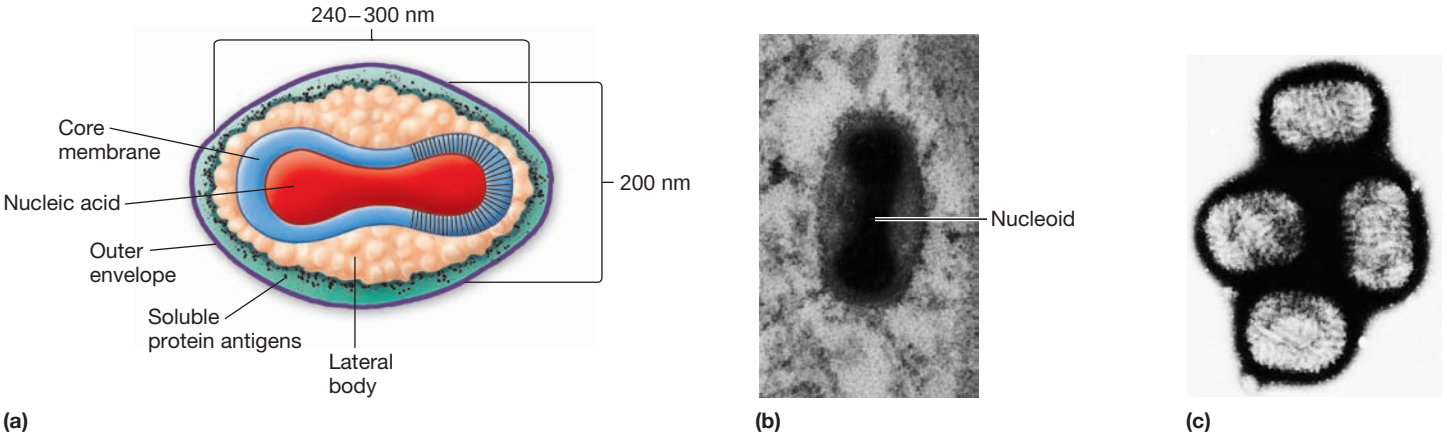


Figure 16.8 Vaccinia Virus Morphology. **(a)** Diagram of vaccinia structure. **(b)** Micrograph of the virion clearly showing the nucleoid (×200,000). **(c)** Vaccinia surface structure. An electron micrograph of four virions showing the thick array of surface fibers (×150,000).

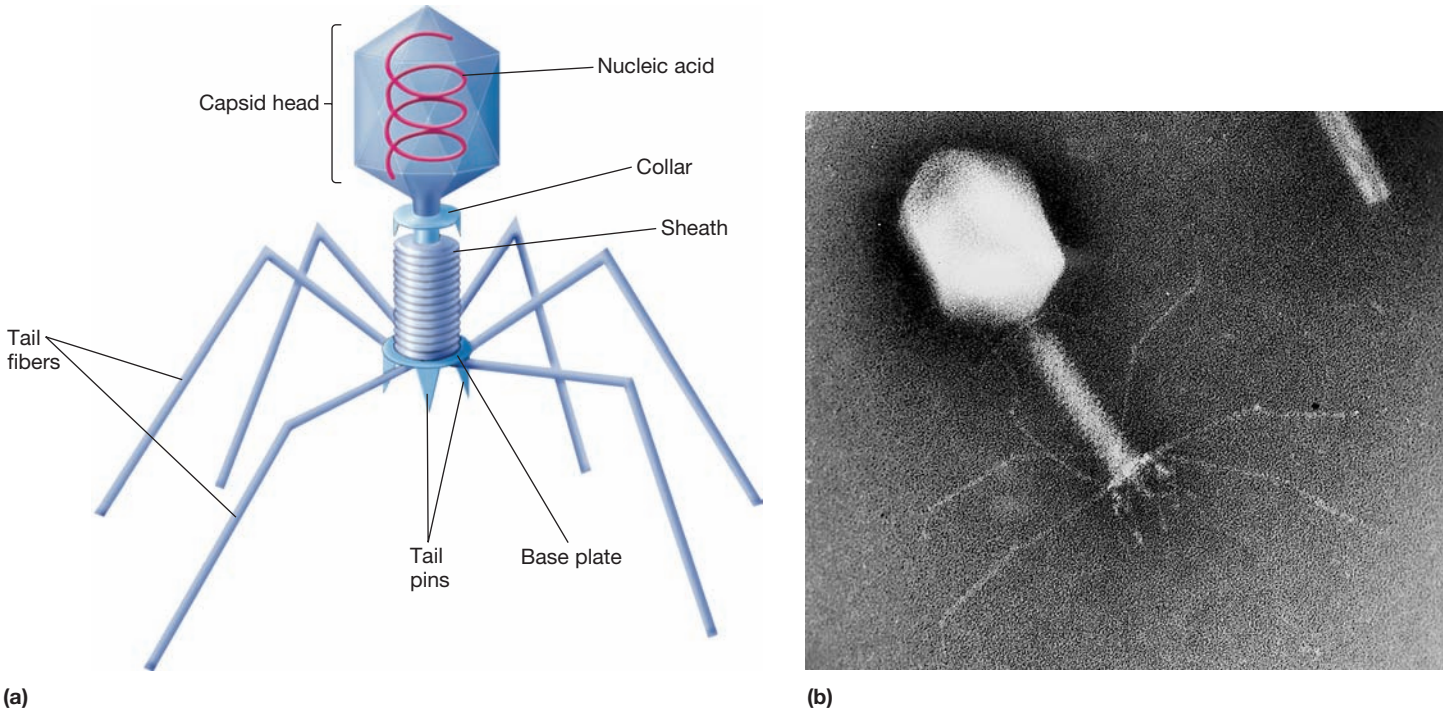
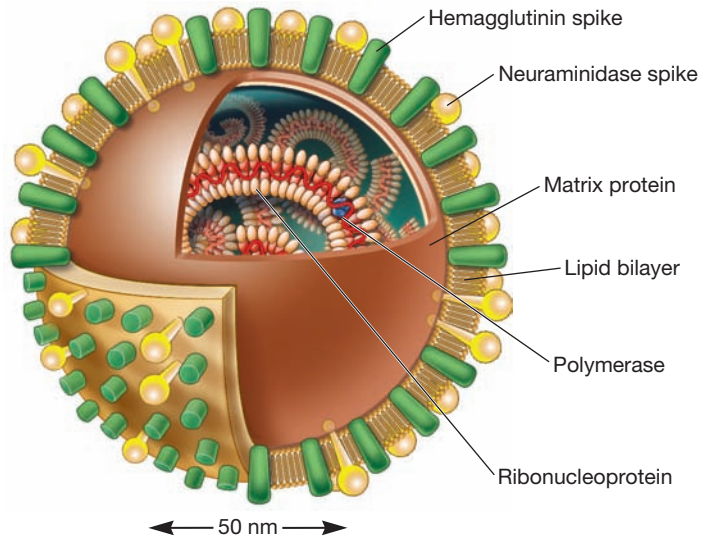


Figure 16.9 T-Even Coliphages. **(a)** The structure of the T4 bacteriophage. **(b)** The micrograph shows the phage before injection of its DNA.

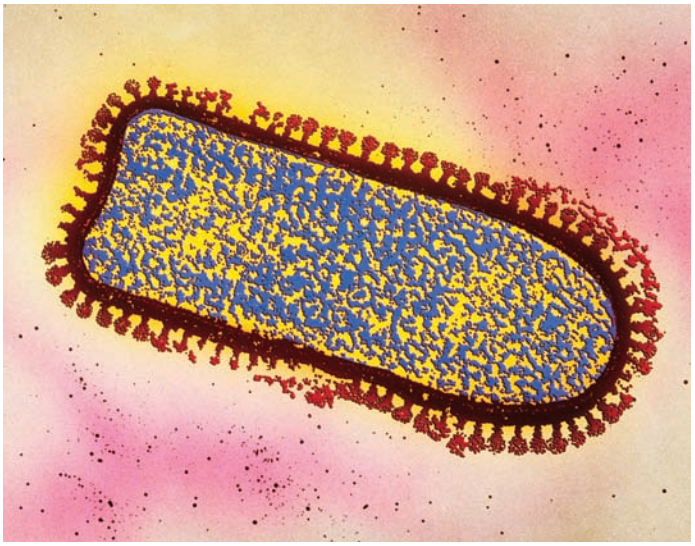
It was originally thought that all virions lacked enzymes. However, as just illustrated in the discussion of influenza virus, this is not the case. In some instances, enzymes are associated with the envelope or capsid (e.g., influenza neuraminidase), but most viral enzymes are located within the capsid. Many of these are involved in nucleic acid replication. For example, the influenza virus uses RNA as its genetic material and carries an enzyme that synthesizes RNA using an RNA template. Such enzymes are called RNA-dependent RNA polymerases. Thus although viruses lack true metabolism and cannot reproduce independently of living cells, they may carry one or more enzymes essential to the completion of their life cycles.

Viral Genomes

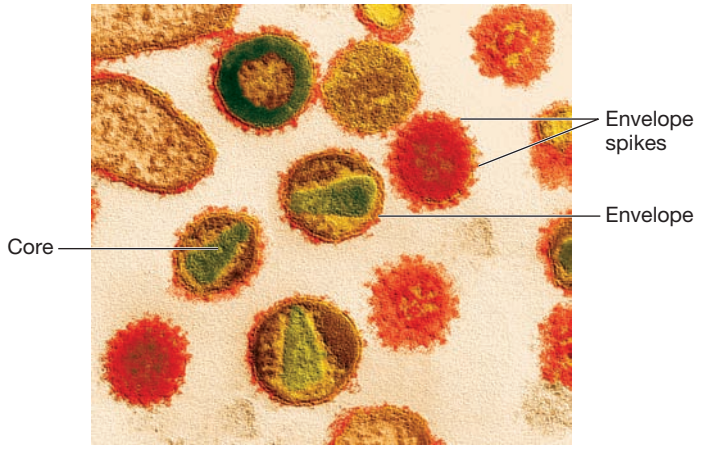
Viruses are exceptionally flexible with respect to the nature of their genomes. They employ all four possible nucleic acid types: single-stranded DNA, double-stranded DNA, single-stranded



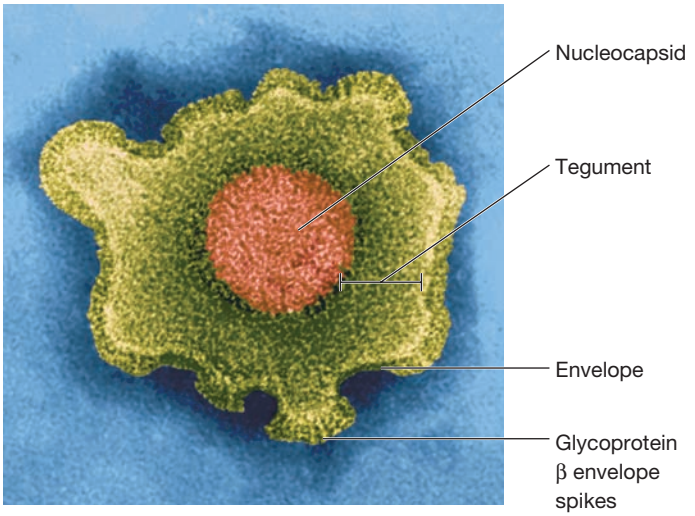
(a) Influenza virus



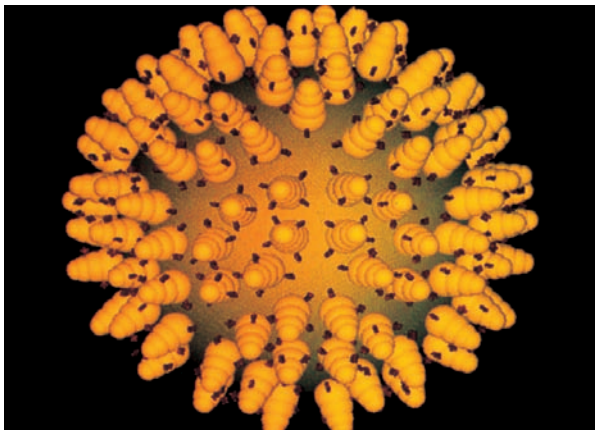
(b) Rabies virus



(c) HIV



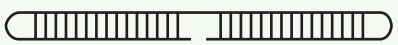
(d) Herpesvirus



(e) Semliki Forest virus

Figure 16.10 Examples of Enveloped Viruses. **(a)** Diagram of the influenza virion. **(b)** Negatively stained rabies virus. **(c)** Human immunodeficiency viruses. **(d)** Herpesviruses. **(e)** Computer image of the Semliki Forest virus, a virus that occasionally causes encephalitis in humans. Images (b), (c), and (d) are artificially colorized.

Table 16.1 Types of Viral Nucleic Acids

Nucleic Acid Type	Nucleic Acid Structure	Virus Examples
DNA		
Single Stranded	Linear, single-stranded DNA	Parvoviruses
	Circular, single-stranded DNA	ϕX174, M13, fd phages
Double Stranded	Linear, double-stranded DNA	Herpesviruses (herpes simplex viruses, cytomegalovirus, Epstein-Barr virus), adenoviruses, T coliphages, lambda phage, and other bacteriophages
	Linear, double-stranded DNA with single chain breaks 	T5 coliphage
	Double-stranded DNA with cross-linked ends 	Vaccinia, smallpox viruses
	Closed, circular, double-stranded DNA	Polyomaviruses (SV-40), papillomaviruses, PM2 phage, cauliflower mosaic virus
RNA		
Single-Stranded	Linear, single-stranded, positive-strand RNA	Picornaviruses (polio, rhinoviruses), togaviruses, RNA bacteriophages, TMV, and most plant viruses
	Linear, single-stranded, negative-strand RNA	Rhabdoviruses (rabies), paramyxoviruses (mumps, measles)
	Linear, single-stranded, segmented, positive-strand RNA	Brome mosaic virus (individual segments in separate virions)
	Linear, single-stranded, diploid (two identical single strands), positive-strand RNA	Retroviruses (Rous sarcoma virus, human immunodeficiency virus)
	Linear, single-stranded, segmented, negative-strand RNA	Paramyxoviruses, orthomyxoviruses (influenza)
Double-Stranded	Linear, double-stranded, segmented RNA	Reoviruses, wound-tumor virus of plants, cytoplasmic polyhedrosis virus of insects, phage ϕ6, many mycoviruses

Modified from S. E. Luria, et al., *General Virology*, 3d edition, 1983. John Wiley & Sons, Inc., New York, NY.

RNA, and double-stranded RNA. All four types are found in animal viruses. Most plant viruses have single-stranded RNA genomes, and most bacterial viruses contain double-stranded DNA. **Table 16.1** summarizes many variations seen in viral nucleic acids. The size of viral genetic material also varies greatly. The smallest genomes (those of the MS2 and Qβ viruses) are around 4,000 nucleotides, just large enough to code for three or four proteins. MS2, Qβ, and some other viruses even save space by using overlapping genes. At the other extreme, T-even bacteriophages, herpesvirus, and vaccinia virus have genomes of 1.0 to 2.0×10^5 nucleotides and may be able to direct the synthesis of over 100 proteins. In the following paragraphs the nature of each nucleic acid type is briefly summarized. Gene structure (section 11.5)

Most DNA viruses use double-stranded DNA (dsDNA) as their genetic material. However, some have single-stranded DNA (ssDNA) genomes. In both cases, the genomes can be either linear or circular (**figure 16.11**). Some DNA genomes can switch from one form to the other. For instance, the *E. coli* phage lambda has a genome that is linear in the capsid, but is converted into a circular form once the genome enters the host cell. Another important characteristic of DNA viruses is that their genomes often contain unusual nitrogenous bases. For example, the T-even phages of *E. coli* have 5-hydroxymethylcytosine (*see figure 17.9*) instead of cytosine, and the hydroxymethyl group is often modified by attachment of a glucose moiety.

RNA viruses also can be either double-stranded (dsRNA) or single-stranded (ssRNA). Although relatively few RNA viruses have dsRNA genomes, dsRNA viruses are known to infect animals, plants, fungi, and at least one bacterial species. More common are the viruses with ssRNA genomes. Some ssRNA genomes have a base sequence that is identical to that of viral mRNA, in which case the genomic RNA strand is called the **plus strand** or **positive strand.** In fact, plus strand RNAs can direct protein synthesis immediately after entering the cell. However, other viral RNA genomes are complementary rather than identical to viral mRNA, and are called **minus** or **negative strands.** Polio, tobacco mosaic, brome mosaic, and Rous sarcoma viruses are all positive strand RNA viruses; rabies, mumps, measles, and influenza

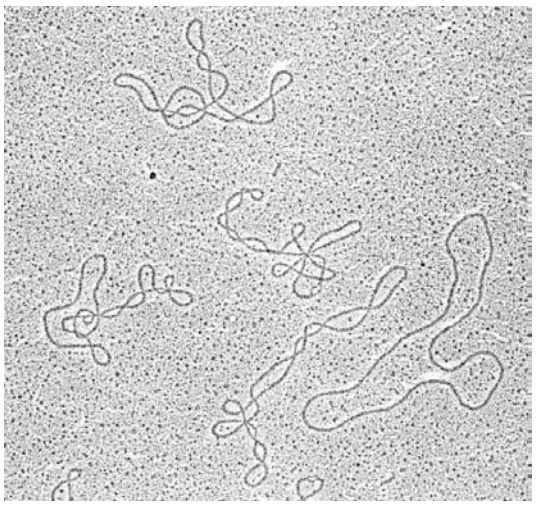


Figure 16.11 Circular Phage DNA. The closed circular DNA of the phage PM2 (×93,000). Note both the relaxed and highly twisted or supercoiled forms.

viruses are examples of negative strand RNA viruses. Many RNA viruses have **segmented genomes**—that is, the genome consists of more than one RNA strand or segment. In many cases, each segment codes for one protein. Usually all segments are enclosed in the same capsid even though some virus genomes may be composed of as many as 10 to 12 segments. However, it is not necessary that all segments be located in the same virion for successful reproduction. The genome of brome mosaic virus, a virus that infects certain grass species, is composed of four segments distributed among three different virus particles. All three of the largest segments are required for infectivity. Despite this complex and seemingly inefficient arrangement, the different brome mosaic virions manage to successfully infect the same host.

Plus strand viral RNA often resembles mRNA in more than the equivalence of its nucleotide sequence. Just as eucaryotic mRNA usually has a 5′ cap of 7-methylguanosine, many plant and animal viral RNA genomes are capped. In addition, most plus strand RNA animal viruses also have a poly-A sequence at the 3′ end of their genome, and thus closely resemble eucaryotic mRNA with respect to the structure of both ends. Strangely enough, a number of single-stranded plant viral RNAs have 3′ ends that resemble eucaryotic transfer RNA. Indeed, the genome of tobacco mosaic virus actually accepts amino acids. Transcription (section 11.6); Translation (section 11.8)

1. Define the following terms: nucleocapsid, capsid, icosahedral capsid, helical capsid, complex virus, binal symmetry, protomer, capsomer, pentamer or penton, and hexamer or hexon. How do pentamers and hexamers associate to form a complete icosahedron; what determines helical capsid length and diameter?
2. What is an envelope? What are spikes (peplomers)? Why are some enveloped viruses pleomorphic? Give two functions spikes might serve in the virus life cycle, and the proteins that the influenza virus uses in these processes.
3. All four nucleic acid forms can serve as virus genomes. Describe each, the types of virion possessing it, and any distinctive physical characteristics the nucleic acid can have. What are the following: plus strand, minus strand, and segmented genome?
4. What advantage would an RNA virus gain by having its genome resemble eucaryotic mRNA?

16.4 Virus Reproduction[1]

The differences in virus structure and viral genomes have important implications for the mechanism a virus uses to reproduce within its host cell. Indeed, even among viruses with similar structures and genomes, each can exhibit unique life cycles. However, despite these differences a general pattern of virus reproduction can be discerned. Because viruses need a host cell in which to reproduce, the first step in the life cycle of a virus is attachment to a host (**figure 16.12**). This is followed by entry of either the nucleocapsid or the viral nucleic acid into the host. If the nucleocapsid enters, uncoating of the genome usually occurs before further steps can occur. Once free in the cytoplasm, genes encoded by the viral genome are expressed. That is, the viral genes are transcribed and translated. This allows the virus to take control of the host cell's biosynthetic machinery so that new virions can be made. The viral genome is then replicated and viral proteins are synthesized. New virions are constructed by self-assembly of coat proteins with the nucleic acids, and finally the mature virions are released from the host. As discussed in chapters 17 and 18, the details of virus reproduction can vary dramatically. For instance, some viruses are released by lysing their hosts, whereas others bud from the host without lysis.

16.5 The Cultivation of Viruses

Because they are unable to reproduce independent of living cells, viruses cannot be cultured in the same way as procaryotic and eucaryotic microorganisms. For many years researchers have cultivated animal viruses by inoculating suitable host animals or embryonated eggs—fertilized chicken eggs incubated about 6 to 8 days after laying (**figure 16.13**). To prepare the egg for cultivation of viruses, the shell surface is first disinfected with iodine and penetrated with a small sterile drill. After inoculation, the drill hole is sealed with gelatin and the egg incubated. Some viruses reproduce only in certain parts of the embryo; consequently they must be injected into the proper region. For example, the myxoma virus grows well on the chorioallantoic membrane, whereas the mumps

[1]Virologists usually refer to the production of new virus particles within a host cell as virus replication. Indeed, many virologists state that viruses do not reproduce, they replicate. However, to avoid confusion about the meaning of the term replication, we will use the term reproduction when discussing the production of new virions, and use the term replication when discussing the synthesis of new copies of viral genomes.

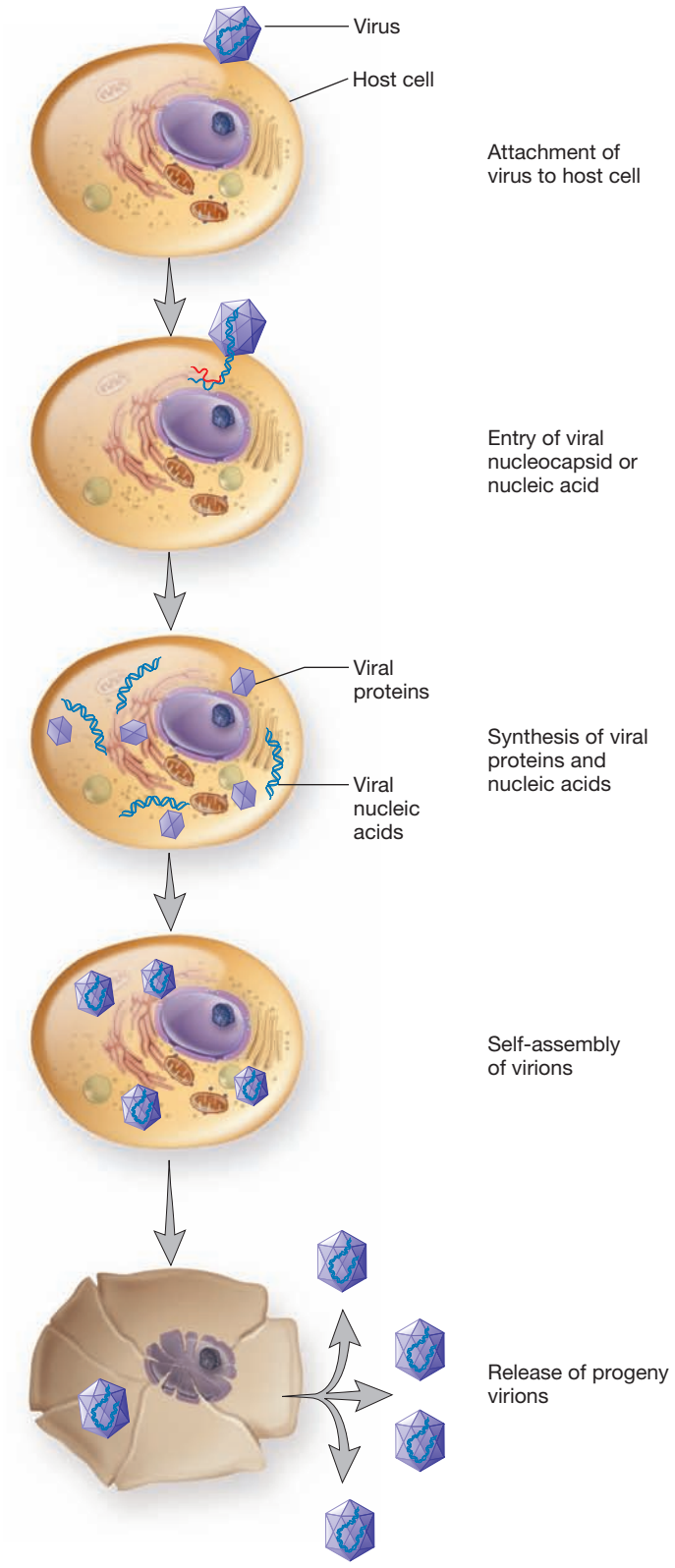


Figure 16.12 Generalized Illustration of Virus Reproduction. There is great variation in the details of virus reproduction for individual virus species.

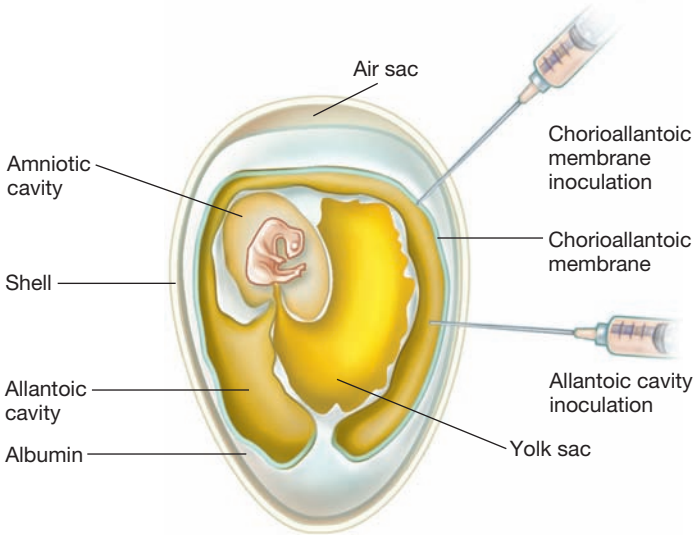


Figure 16.13 Cultivation of Viruses in an Embryonated Egg. Two sites that are often used to grow animal viruses are the chorioallantoic membrane and the allantoic cavity. The diagram shows a 9-day chicken embryo.

virus grows best in the allantoic cavity. The infection may produce a local tissue lesion known as a pock, whose appearance often is characteristic of the virus.

More recently animal viruses have been grown in tissue (cell) culture on monolayers of animal cells. This technique is made possible by the development of growth media for animal cells and by the use of antimicrobial agents that prevent bacterial and fungal contamination. Viruses are added to a layer of animal cells in a specially prepared petri dish and allowed time to attach to the cells. The cells are then covered with a thin layer of agar to limit virion spread so that only adjacent cells are infected by newly produced virions. As a result, localized areas of cellular destruction and lysis called **plaques** often are formed (**figure 16.14**) and may be detected if stained with dyes, such as neutral red or trypan blue, that can distinguish living from dead cells. Viral growth does not always result in the lysis of cells to form a plaque. Animal viruses, in particular, can cause microscopic or macroscopic degenerative changes or abnormalities in host cells and in tissues. These are called **cytopathic effects** (**figure 16.15**). Cytopathic effects may be lethal, but plaque formation from cell lysis does not always occur.

Bacterial and archaeal viruses are cultivated in either broth or agar cultures of young, actively growing cells. In some infected cultures, so many host cells are destroyed that turbid cultures clear rapidly because of cell lysis. Agar cultures are prepared by mixing viruses with cool, liquid agar and a suitable culture of host cells. The mixture is quickly poured into a petri dish containing a bottom layer of sterile agar. After hardening, cells in the layer of top agar grow and reproduce, forming a continuous, opaque layer or "lawn." Wherever a virion comes to rest in the top agar, the virus infects an adjacent cell and reproduces. Eventually, lysis of

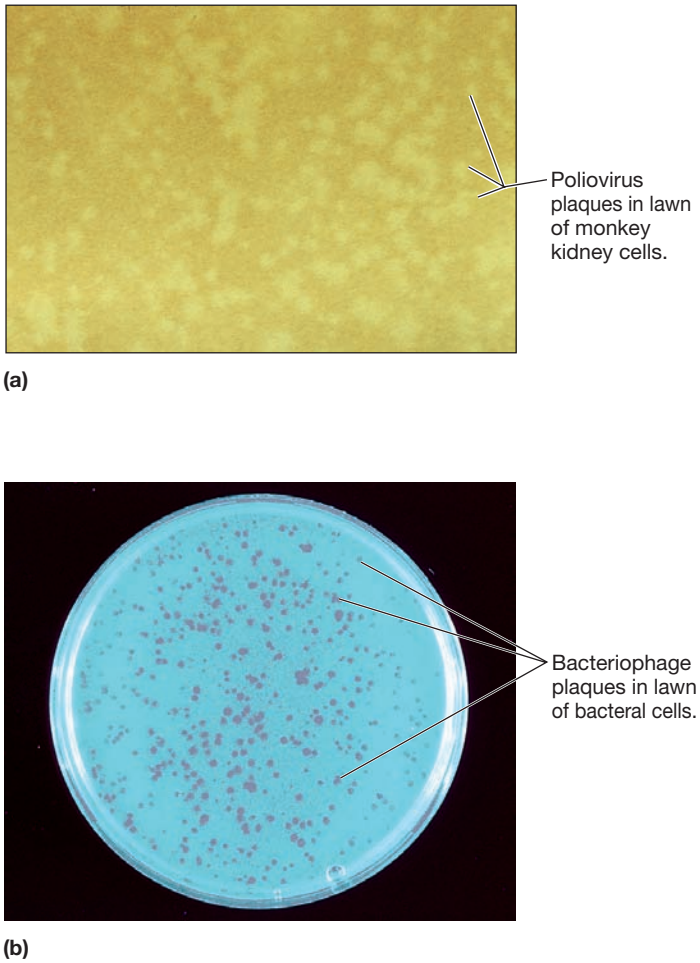


Figure 16.14 Virus Plaques. **(a)** Poliovirus plaques in a monkey kidney cell culture. **(b)** Plaques formed by bacteriophages growing on a lawn of bacterial cells.

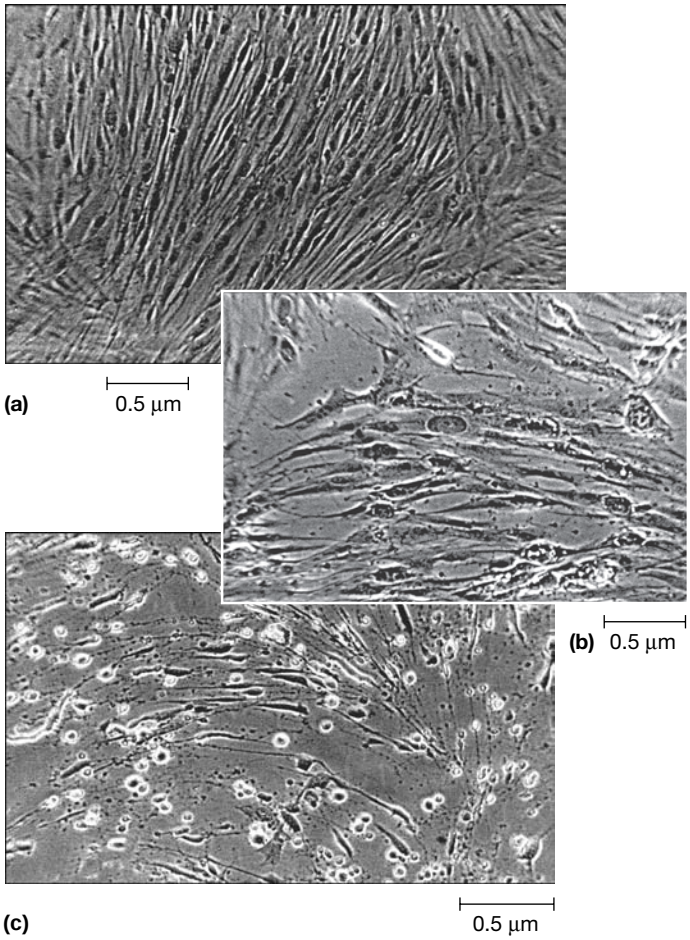


Figure 16.15 Cytopathic Effects of Viruses. **(a)** A monolayer of normal fibroblast cells from fetal tonsils. **(b)** Cytopathic effects caused by infection of fetal tonsil fibroblasts with adenovirus. **(c)** Cytopathic effects caused by infection of fetal tonsil fibroblasts with herpes simplex virus.

the cells generates a plaque or clearing in the lawn (figure 16.14*b* and **figure 16.16**). As shown in figure 16.16, plaque appearance often is characteristic of the virus being cultivated.

Plant viruses are cultivated in a variety of ways. Plant tissue cultures, cultures of separated cells, or cultures of protoplasts (cells lacking cell walls) may be used. Viruses also can be grown in whole plants. Leaves are mechanically inoculated when rubbed with a mixture of viruses and an abrasive. When the cell walls are broken by the abrasive, the viruses directly contact the plasma membrane and infect the exposed host cells. (In nature, the role of the abrasive is frequently filled by insects that suck or crush plant leaves and thus transmit viruses.) A localized **necrotic lesion** often develops due to the rapid death of cells in the infected area (**figure 16.17**). Even when lesions do not occur, the infected plant may show symptoms such as changes in pigmentation or leaf shape. Some plant viruses can be transmitted only if a diseased part is grafted onto a healthy plant.

16.6 Virus Purification and Assays

Virologists must be able to purify viruses and accurately determine their concentrations in order to study virus structure, reproduction, and other aspects of their biology. These methods are so important that the growth of virology as a modern discipline depended on their development.

Virus Purification

Purification makes use of several virus properties. Virions are very large relative to proteins, are often more stable than normal cell components, and have surface proteins. Because of these characteristics, many techniques useful for the isolation of proteins and organelles can be employed to isolate viruses. Four of the most widely used approaches are (1) differential and density gradient centrifugation, (2) precipitation of viruses,

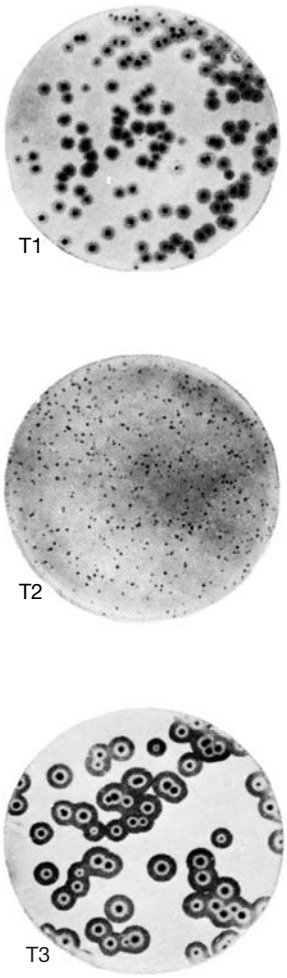


Figure 16.16 Phage Plaques. Plaques produced on a lawn of *E. coli* by some of the T coliphages (T1, T2, and T3 phages). Note the large differences in plaque appearance. The photographs are about 1/3 full size.

(a)

(b)

Figure 16.17 Necrotic Lesions on Plant Leaves. **(a)** Tobacco mosaic virus on *Nicotiana glutinosa.* **(b)** Tobacco mosaic virus infection of an orchid showing leaf color changes.

(3) denaturation of contaminants, and (4) enzymatic digestion of host cell constituents.

Differential and density gradient centrifugation often are used in the initial purification steps to separate virus particles from host cells. The process begins with host cells in later stages of infection because they contain mature virions. Infected cells are first disrupted in a buffer to produce an aqueous suspension or homogenate consisting of cell components and viruses. Viruses can then be isolated by **differential centrifugation,** the centrifugation of a suspension at various speeds to separate particles of different sizes (**figure 16.18**). Usually the homogenate is first centrifuged at high speed to sediment viruses and other large cellular particles. The supernatant, which contains the homogenate's soluble molecules, is discarded. The pellet is next resuspended and centrifuged at a low speed to remove substances heavier than viruses. Finally, higher speed centrifugation sediments the viruses. This process may be repeated to purify the virus particles further.

Additional purification of a virus preparation can be achieved by **gradient centrifugation** (**figure 16.19**). A sucrose solution is poured into a centrifuge tube so that its concentration smoothly and linearly increases from the top to the bottom of the tube. The virus preparation, often produced by differential centrifugation, is layered on top of the gradient and centrifuged. As shown in figure 16.19*a*, the particles settle under centrifugal force until they come to rest at the level where the virus and sucrose densities are equal (isopycnic gradient centrifugation). Viruses can be separated from other particles based on very small differences in density. Gradients also can separate viruses based on differences in their sedimentation rate (rate zonal gradient centrifugation). When this is done, particles are separated on the basis of both size and density; usually the largest virus will move most rapidly down the gradient. Figure 16.19*b* shows that viruses differ from one another and cell components with respect to either density (grams per milliliter) or sedimentation coefficient(s). Thus these

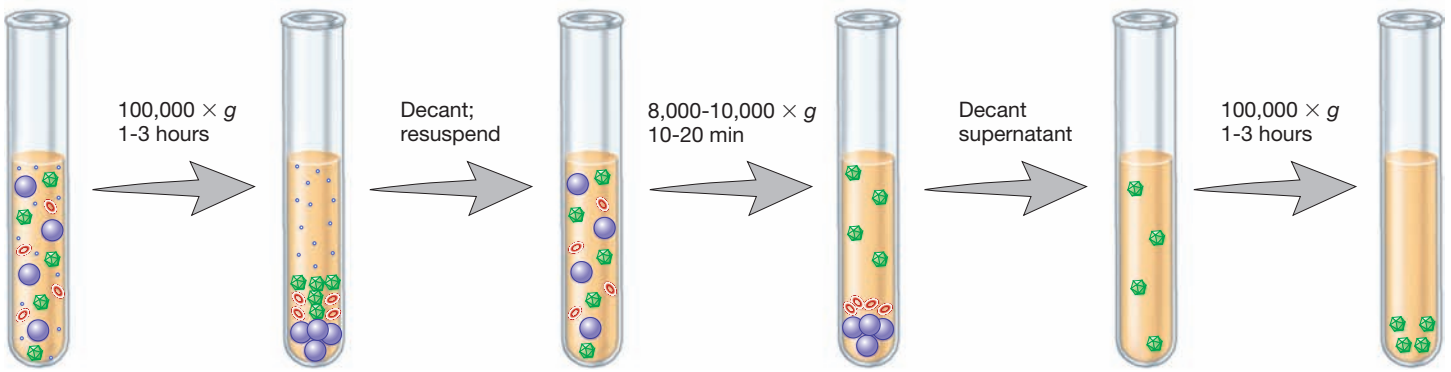
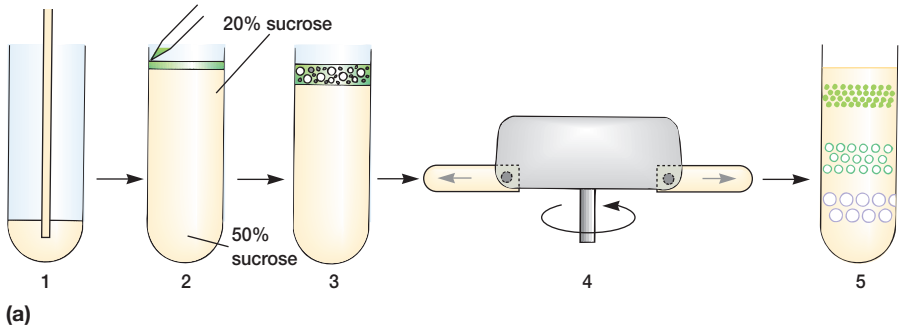


Figure 16.18 The Use of Differential Centrifugation to Purify a Virus. At the beginning the centrifuge tube contains homogenate and icosahedral viruses (in green). First, the viruses and heavier cell organelles are removed from smaller molecules. After resuspension, the mixture is centrifuged just fast enough to sediment cell organelles while leaving the smaller virus particles in suspension; the purified viruses are then collected. This process can be repeated several times to further purify the virions.



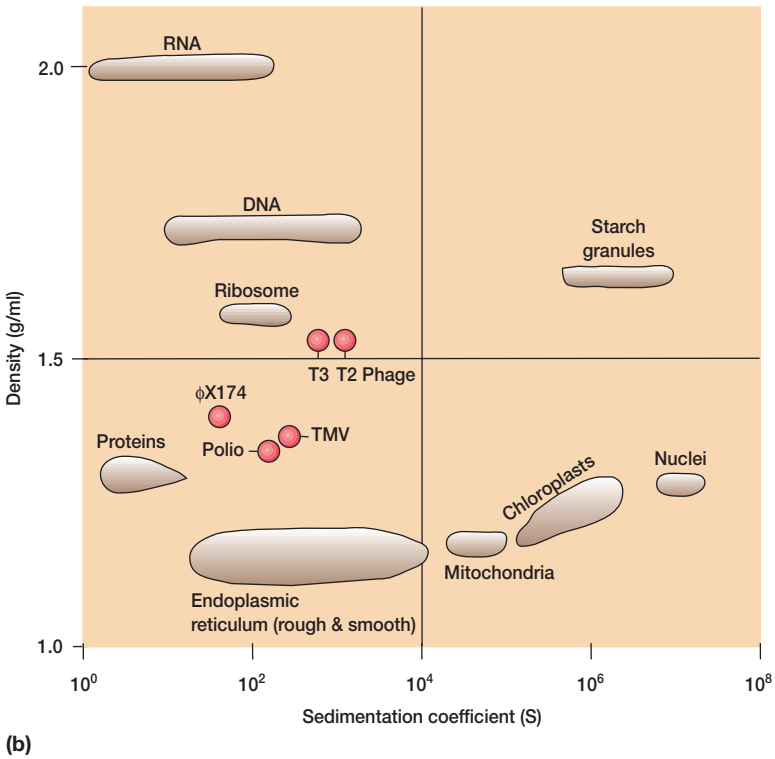


Figure 16.19 Gradient Centrifugation.
(a) A linear sucrose gradient is prepared, *1*, and the particle mixture is layered on top, *2* and *3*. Centrifugation, *4*, separates the particles on the basis of their density and sedimentation coefficient, (the arrows in the centrifuge tubes indicate the direction of centrifugal force). *5*. In isopycnic gradient centrifugation, the bottom of the gradient is denser than any particle, and each particle comes to rest at a point in the gradient equal to its density. Rate zonal centrifugation separates particles based on their sedimentation coefficient, a function of both size and density, because the bottom of the gradient is less dense than the densest particles and centrifugation is carried out for a shorter time so that particles do not come to rest. The largest, most dense particles travel fastest. **(b)** The densities and sedimentation coefficients of representative viruses (shown in color) and other biological substances.

two types of gradient centrifugation are very effective in virus purification.

Although centrifugation procedures remove much cellular material, some cell components can remain in the virus preparation. Viruses can be separated from any remaining cellular contaminants by precipitation, denaturing, or enzymatic degradation of the contaminants. Many precipitation procedures use ammonium sulfate to precipitate the cellular contaminants. Initially, ammonium sulfate is added to a concentration just below that needed to precipitate the virus particles. Thus many cell components precipitate while the virus remains in solution. After any precipitated contaminants are removed, more ammonium sulfate is added and the precipitated viruses are collected by centrifugation. Viruses sensitive to ammonium sulfate often are purified by precipitation with polyethylene glycol.

Because viruses frequently are less sensitive to denaturing conditions than many cell components, exposure of a virus preparation to heat or a change in pH can be used in the final steps of virus purification. Furthermore, some viruses also tolerate treatment with organic solvents like butanol and chloroform. Thus solvent treatment can be used to both denature protein contaminants and extract any lipids in the preparation. The solvent is thoroughly mixed with the virus preparation, then allowed to stand and separate into organic and aqueous layers. The unaltered virus remains suspended in the aqueous phase while lipids dissolve in the organic phase. Substances denatured by organic solvents collect at the interface between the aqueous and organic phases.

One of the last steps used to purify viruses is enzymatic degradation of contaminants. This often is used to remove any remaining cellular proteins and nucleic acids in the virus preparation. Although viruses are composed of a protein coat surrounding a nucleic acid, they usually are more resistant to attack by nucleases and proteases than are free nucleic acids and proteins. For example, ribonuclease and trypsin often degrade cellular ribonucleic acids and proteins while leaving virions unaltered.

Virus Assays

The quantity of viruses in a sample can be determined either directly by counting particle numbers or indirectly by measurement of an observable effect of the virus. The values obtained by the two approaches often do not correlate closely; however, both are of value.

Virions can be counted directly with the electron microscope. In one procedure the virus-containing sample is mixed with a known concentration of small latex beads and sprayed on a coated specimen grid. The beads and virions are counted; the virus concentration is calculated from these counts and from the bead concentration (**figure 16.20**). This technique often works well with concentrated preparations of viruses of known morphology. Viruses can be concentrated by centrifugation before counting if the preparation is too dilute. However, if the beads and viruses are not evenly distributed (as sometimes happens), the final count will be inaccurate.

An indirect method of counting virus particles is the **hemagglutination assay.** Many viruses can bind to the surface of red blood cells (*see figure 35.11*). If the ratio of viruses to cells is large enough, virus particles join the red blood cells together—that is, they agglutinate, forming a network that settles out of suspension. In practice, red blood cells are mixed with a series of virus dilutions and each mixture is examined. The hemagglutination titer is the highest dilution of virus (or the reciprocal of the dilution) that still causes hemagglutination. This assay is an accurate, rapid method for determining the relative quantity of viruses such as the influenza virus. If the actual number of viruses needed to cause hemagglutination is determined by another technique, the assay can be used to ascertain the number of virions present in a sample.

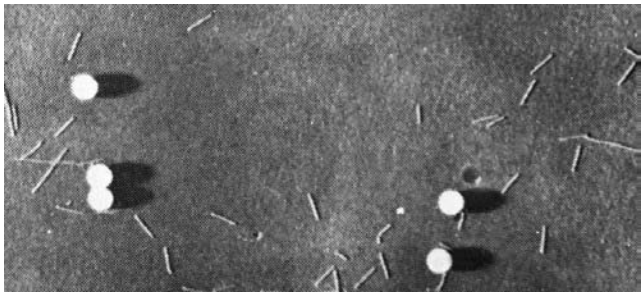


Figure 16.20 Tobacco Mosaic Virus. A tobacco mosaic virus preparation viewed in the transmission electron microscope. Latex beads 264 nm in diameter (white spheres) have been added.

A variety of indirect assays determine virus numbers in terms of infectivity, and many of these are based on the same techniques used for virus cultivation. For example, in the **plaque assay** several dilutions of viruses are plated out with appropriate host cells. When the number of viruses plated are much lower than the number of host cells available for infection and when the viruses are distributed evenly, each plaque in a layer of host cells is assumed to have arisen from the reproduction of a single virion. Therefore a count of the plaques produced at a particular dilution will give the number of infectious virions, called **plaque-forming units (PFU),** and the concentration of infectious units in the original sample can be easily calculated. For instance, suppose that 0.10 ml of a 10^{-6} dilution of the virus preparation yields 75 plaques. The original concentration of plaque-forming units is

$$\text{PFU/ml} = (75\ \text{PFU}/0.10\ \text{ml})(10^6) = 7.5 \times 10^8.$$

Viruses producing different plaque morphology types on the same plate may be counted separately. Although the number of PFU does not equal the number of virions, their ratios are proportional: a preparation with twice as many viruses will have twice the plaque-forming units.

The same approach employed in the plaque assay may be used with embryos and plants. Chicken embryos can be inoculated with a diluted preparation or plant leaves rubbed with a mixture of diluted virus and abrasive. The number of pocks on embryonic membranes or necrotic lesions on leaves is multiplied by the dilution factor and divided by the inoculum volume to obtain the concentration of infectious units.

When biological effects are not readily quantified in these ways, the amount of virus required to cause disease or death can be determined by the endpoint method. Organisms or cell cultures are inoculated with serial dilutions of a virus suspension. The results are used to find the endpoint dilution at which 50% of the host cells or organisms are killed (**figure 16.21**). The **lethal dose (LD_{50})** is the dilution that contains a dose large enough to destroy 50% of the host cells or organisms. In a similar sense, the **infectious dose (ID_{50})** is the dose that, when given to a number of hosts, causes an infection of 50% of the hosts under the conditions employed.

1. Discuss the ways that viruses can be cultivated. Define the terms pock, plaque, cytopathic effect, and necrotic lesion.
2. Give the four major approaches by which viruses may be purified, and describe how each works. Distinguish between differential and density gradient centrifugation in terms of how they are carried out.
3. How can one find the virus concentration, both directly and indirectly, by particle counts and measurement of infectious unit concentration? Define plaque-forming units, lethal dose, and infectious dose.

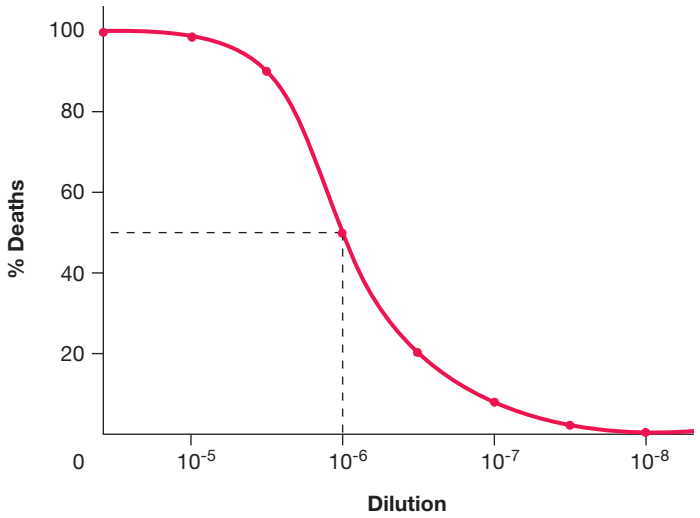


Figure 16.21 A Hypothetical Dose-Response Curve. The LD_{50} is indicated by the dashed line.

16.7 Principles of Virus Taxonomy

The classification of viruses is in a much less satisfactory state than that of cellular microorganisms. In part, this is due to a lack of knowledge of their origin and evolutionary history (**Microbial Tidbits 16.2**). In 1971, the International Committee for Taxonomy of Viruses (ICTV) developed a uniform classification system. Since then the number of viruses and taxonomic categories has continued to expand. In its eighth report, the ICTV described almost 2000 virus species and placed them in 3 orders, 73 families, 9 subfamilies, and 287 genera (**table 16.2**). The committee places greatest weight on specific properties to define families: nucleic acid type, nucleic acid strandedness, the sense (positive or negative) of ssRNA genomes, presence or absence of an envelope, symmetry of the capsid, and dimensions of the virion and capsid. Virus order

Microbial Tidbits

16.2 The Origin of Viruses

The origin and subsequent evolution of viruses are shrouded in mystery, in part because of the lack of a fossil record. However, recent advances in the understanding of virus structure and reproduction have made possible more informed speculation on virus origins. At present there are two major hypotheses entertained by virologists. It has been proposed that at least some of the more complex enveloped viruses, such as the poxviruses and herpesviruses, arose from small cells, probably procaryotic, that parasitized larger, more complex cells. These parasitic cells became ever simpler and more dependent on their hosts, much like multicellular parasites have done, in a process known as retrograde evolution. There are several problems with this hypothesis. Viruses are radically different from procaryotes, and it is difficult to envision the mechanisms by which such a transformation might have occurred or the selective pressures leading to it. In addition, one would expect to find some forms intermediate between procaryotes and at least the more complex enveloped viruses, but such forms have not been detected.

The second hypothesis is that viruses represent cellular nucleic acids that have become partially independent of the cell. Possibly a few mutations could convert nucleic acids, which are only synthesized at specific times, into infectious nucleic acids whose replication could not be controlled. This conjecture is supported by the observation that the nucleic acids of retroviruses (*see section 18.2*) and a number of other virions contain sequences quite similar to those of normal cells, plasmids, and transposons (*see chapter 13*). The small, infectious RNAs called viroids (*see section 18.9*) have base sequences complementary to transposons (*see section 13.5*), the regions around the boundary of mRNA introns, and portions of host DNA. This has led to speculation that they have arisen from introns or transposons. It has been proposed that cellular proteins spontaneously assembled into icosahedra around infectious nucleic acids to produce primitive virions.

It is possible that viruses have arisen by way of both mechanisms. Because viruses differ so greatly from one another, it seems likely that they have originated independently many times during the course of evolution. Many viruses have evolved from other viruses just as cellular organisms have arisen from specific predecessors. The question of virus origins is complex and quite speculative; future progress in understanding virus structure and reproduction may clarify this question.

names end in *virales;* virus family names in *viridae;* subfamily names, in *virinae;* and genus (and species) names, in *virus.* An example of this nomenclature scheme is shown in **figure 16.22.**

Although the ICTV committee reports are the official authority on viral taxonomy, many virologists find it useful to use an alternative classification scheme devised by Nobel laureate David Baltimore. The Baltimore system complements the ICTV system but focuses on the genome of the virus and the process used to synthesize viral mRNA. Baltimore's original system recognized six groups of viruses. Since then the system has been expanded to include seven groups. This was done in part by considering genome replication as well as mRNA synthesis in the classification scheme (**table 16.3**). As discussed in chapters 17 and 18, such a system helps virologists (and microbiology students) simplify the vast array of viral life cycles into a relatively small number of basic types.

Table 16.2 Some Common Virus Groups and Their Characteristics

ICTV Taxon (Baltimore System Group)[a]	Genome Size (kbp or kb)	Nucleic Acid	Strandedness	Capsid Symmetry[b]	Number of Capsomers	Presence of Envelope	Size of Capsid (nm)[c]	Host Range[d]
Picornaviridae (IV)	7–8	RNA	Single	I	32	−	22–30	A
Togaviridae (IV)	10–12		Single	I	32	+	40–70(e)	A
Retroviridae (VI)	7–12		Single	I?		+	100(e)	A
Orthomyxoviridae (V)	10–15		Single	H		+	9(h), 80–120(e)	A
Paramyxoviridae (V)	15		Single	H		+	18(h), 125–250(e)	A
Coronaviridae (IV)	27–31		Single	H		+	14–16(h), 80–160(e)	A
Rhabdoviridae (V)	11–15		Single	H		+	18(h), 70–80 × 130–240 (bullet shaped)	A
Bromoviridae (IV)	8–9		Single	I,B		−	26–35; 18–26 × 30–85	P
Tobamovirus (IV)	7		Single	H		−	18 × 300	P
Leviviridae [Qβ] *(IV)*	3–4		Single	I	32	−	26–27	B
Reoviridae (III)	19–32	RNA	Double	I	92	−	70–80	A,P
Cystoviridae (III)	13		Double	I		+	100(e)	B
Parvoviridae (II)	4–6	DNA	Single	I	12	−	20–25	A
Geminiviridae (II)	3–6		Single	I		−	18 × 30 (paired particles)	P
Microviridae (II)	4–6		Single	I		−	25–35	B
Inoviridae (II)	7–9		Single	H		−	6 × 900–1,900	B
Polyomaviridae (I)	5	DNA	Double	I	72	−	40	A
Papillomaviridae (I)	7–8		Double	I	72	−	55	A
Adenoviridae (I)	28–45		Double	I	252	−	60–90	A
Iridoviridae (I)	140–383		Double	I		−	130–180	A
Herpesviridae (I)	125–240		Double	I	162	+	100, 180–200(e)	A
Poxviridae (I)	130–375		Double	C		+	200–260 × 250–290(e)	A
Baculoviridae (I)	80–180		Double	H		+	40 × 300(e)	A
Hepadnaviridae (VII)	3		Double	C	42	+	28 (core), 42(e)	A
Caulimoviridae (I)	8		Double	I,B		−	50; 30 × 60–900	P
Corticoviridae (I)	9		Double	I		−	60	B
Myoviridae (I)	39–169		Double	Bi		−	80 × 110, 110[e]	B, Arch
Lipothrixviridae (I)	16		Double	H		+	38 × 410	Arch

[a]ICTV = International Committee on Virus Taxonomy. The ICTV and Baltimore Clarification Systems are discussed in section 16.7.

[b]Types of symmetry: I, icosahedral; H, helical; C, complex; Bi, binal; B, bacilliform.

[c]Diameter of helical capsid (h); diameter of enveloped virion (e).

[d]Host range: A, animal; P, plant; B, bacterium; Arch, archaeon.

[e]The first number is the head diameter; the second number, the tail length.

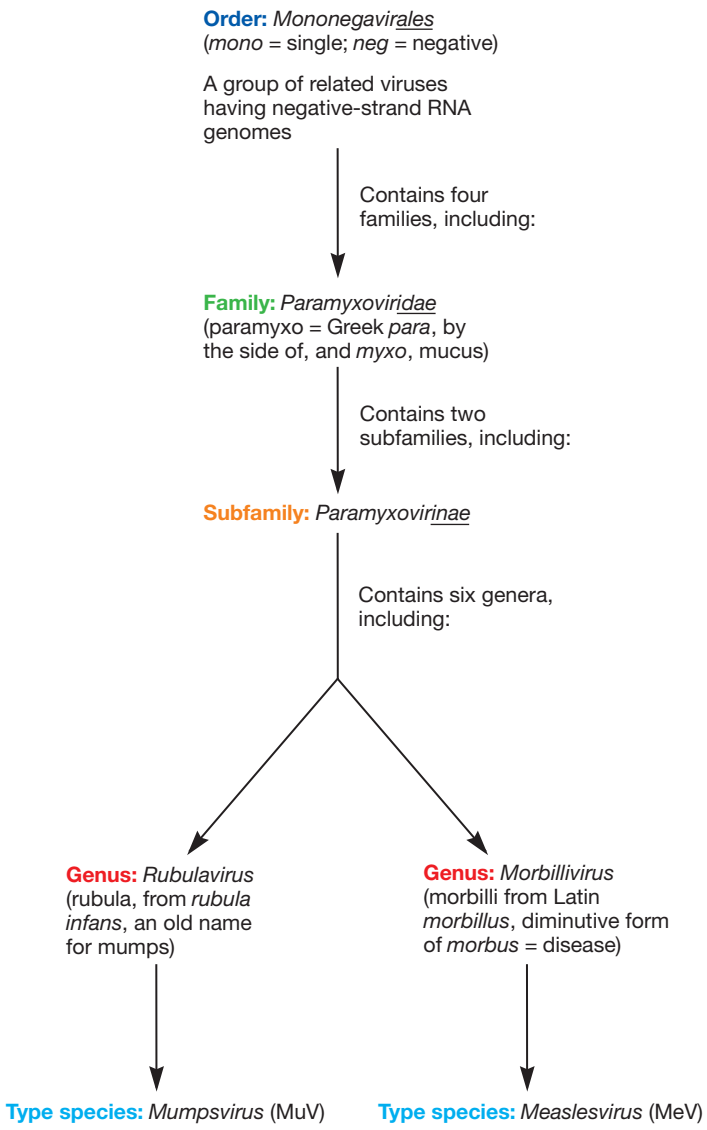


Figure 16.22 The Naming of Viruses. Because of the difficulty in establishing evolutionary relationships, most virus families have not been placed into an order. Virus names are derived from various aspects of their biology and history, including the features of their structure, diseases they cause, and locations where they were first identified or recognized.

Table 16.3 The Baltimore System of Virus Classification

Group	Description
I	Double-stranded DNA genome *genome replication: dsDNA → dsDNA* *mRNA synthesis: dsDNA → mRNA*
II	Single-stranded DNA genome *genome replication: ssDNA → dsDNA → ssDNA* *mRNA synthesis: ssDNA → dsDNA → mRNA*
III	Double-stranded RNA genome *replication: dsRNA → ssRNA → dsRNA* *mRNA synthesis: dsRNA → mRNA*
IV	Plus-strand RNA genome *replication: +RNA → −RNA → +RNA* *mRNA synthesis: +RNA = mRNA*
V	Negative-strand RNA genome *replication: −RNA → +RNA → −RNA* *mRNA synthesis: −RNA → mRNA*
VI	Single-stranded RNA genome *replication: ssRNA → dsDNA → ssRNA* *mRNA synthesis: ssRNA → dsDNA → mRNA*
VII	Double-stranded gapped DNA genome *replication: gapped dsDNA → dsDNA → +RNA → −DNA → gapped dsDNA* *mRNA synthesis: gapped dsDNA → dsDNA → mRNA*

As is the case with the taxonomy of cellular life forms, the taxonomy of viruses is rapidly changing as more and more viral genomes are sequenced. They have been useful in establishing evolutionary relationships among viruses, and have led to the creation of new virus families and genera.

1. List some characteristics used in classifying viruses. Which seem to be the most important?
2. What are the endings for the names of virus families, subfamilies, and genera or species?

Summary

16.1 Early Development of Virology

a. Europeans were first protected from a viral disease when Edward Jenner developed a smallpox vaccine in 1798.

b. Chamberland's invention of a porcelain filter that could remove bacteria from virus samples enabled microbiologists to show that viruses were different from bacteria.

c. In the late 1930s Stanley, Bawden, and Pirie crystallized the tobacco mosaic virus and demonstrated that it was composed only of protein and nucleic acid.

16.2 General Properties of Viruses

a. A virion is composed of either DNA or RNA enclosed in a coat of protein (and sometimes other substances as well). It cannot reproduce independently of living cells.

16.3 The Structure of Viruses

a. All virions have a nucleocapsid composed of a nucleic acid, usually either DNA or RNA, held within a protein capsid made of one or more types of protein subunits called protomers (**figure 16.1**).

b. There are four types of viral morphology: naked icosahedral, naked helical, enveloped icosahedral and helical, and complex.

c. Helical capsids resemble long hollow protein tubes and may be either rigid or quite flexible. The nucleic acid is coiled in a spiral on the inside of the cylinder (**figure 16.3*b***).

d. Icosahedral capsids are usually constructed from two types of capsomers: pentamers (pentons) at the vertices and hexamers (hexons) on the edges and faces of the icosahedron (**figure 16.6**).