Chapter 2

Virus Structure and Classification

2.1 COMMON CHARACTERISTICS OF VIRUSES

As described in Chapter 1, "The World of Viruses" viruses were initially characterized as filterable agents capable of causing disease. Since that time, advances in microscopy and scientific techniques have led to a better classification of viruses and their properties. Electron microscopy has allowed us to visualize viruses in great detail, while molecular and cellular assays have broadened our understanding of how viruses function and are related to one another. Taken together, we have learned that although they can be quite diverse, viruses share several common characteristics:

1. Viruses are Small in Size.
   The smallest of viruses are about 20 nm in diameter, although influenza and the human immunodeficiency virus have a more typical size, about 100 nm in diameter. Average human cells are 10–30 µm (microns) in diameter, which means that they are generally 100 to 1000 times larger than the viruses that are infecting them.
   However, some viruses are significantly larger than 100 nm. Poxviruses, such as the variola virus that causes smallpox, can approach 400 nm in length, and filoviruses, such as the dangerous Ebola virus and Marburg virus, are only 80 nm in diameter but extend into long threads that can reach lengths of over 1000 nm. Several very large viruses that infect amoebas have recently been discovered: megavirus is 400 nm in diameter, and pandoraviruses have an elliptical or ovoid structure approaching 1000 nm in length. It is a common mistake to think that all viruses are smaller than bacteria; most bacteria are typically 2000–3000 nm in size, but certain strains of bacteria called *Mycobacteria* can be 10 times smaller than this, putting them in the range of these large viruses. So although a characteristic of viruses is that they are all small in size, this ranges from only a few nanometers to larger than some bacteria (Fig. 2.1).
2. Viruses are **obligate intracellular parasites**, meaning that they are completely dependent upon the internal environment of the cell to create new infectious virus particles, or **virions**.
   All viruses make contact with and bind the surface of a cell to gain entry into the cell. The virus disassembles and its genetic material (made of nucleic acid) encodes the instructions for the proteins that will spontaneously assemble into the new virions. This is known as de novo replication, from the Latin for "from new." In contrast to cells, which grow in size and divide equally in two to replicate, viruses use the cell's energy and machinery to create and assemble new virions piece by piece, completely from scratch.
3. The genetic material of viruses can be composed of DNA or RNA.
   All living cells, whether human, animal, plant, or bacterial, have double-stranded DNA (dsDNA) as their genetic material. Viruses, on the other hand, have **genomes**, or genetic material, that can be composed of DNA *or* RNA (but not both). Genomes are not necessarily double-stranded, either; different virus types can also have single-stranded DNA (ssDNA) genomes, and viruses with RNA genomes can be single-stranded or double-stranded. Any particular virus will only have one type of nucleic acid genome, however, and so viruses are not encountered that have both ssDNA and ssRNA genomes, for example.
   Similarly to how the size of the virus particle varies significantly, the genome size can also vary greatly from virus to virus. A typical virus genome falls in the range of 7000–20,000 base pairs (bp) (7–20 kilobase pairs (kb)). Smaller-sized virions will naturally be able to hold less nucleic acid than larger virions, but large viruses do not necessarily have large genomes. While most viruses do not contain much nucleic acid, some dsDNA viruses have very large genomes: herpesviruses

Refresher: Orders of Magnitude and Scientific Notation

Virion size: Getting Smaller

1000 millimeters (mm) in a meter (m)	1 mm = 10^{-3} m
1000 micrometers (µm, or microns) in a millimeter	1 µm = 10^{-6} m
1000 nanometers (nm) in a micrometer	1 nm = 10^{-9} m

Virus genome size: Getting Bigger

1000 base pairs (nucleotide pairs, bp) in a kilobase pair (kb)	1 kb = 10^3 bp
1000 kb in a megabase pair (mb)	1 mb = 10^6 bp
1000 mb in a gigabase pair (gb)	1 gb = 10^9 bp

Essential Human Virology. http://dx.doi.org/10.1016/B978-0-12-800947-5.00002-8

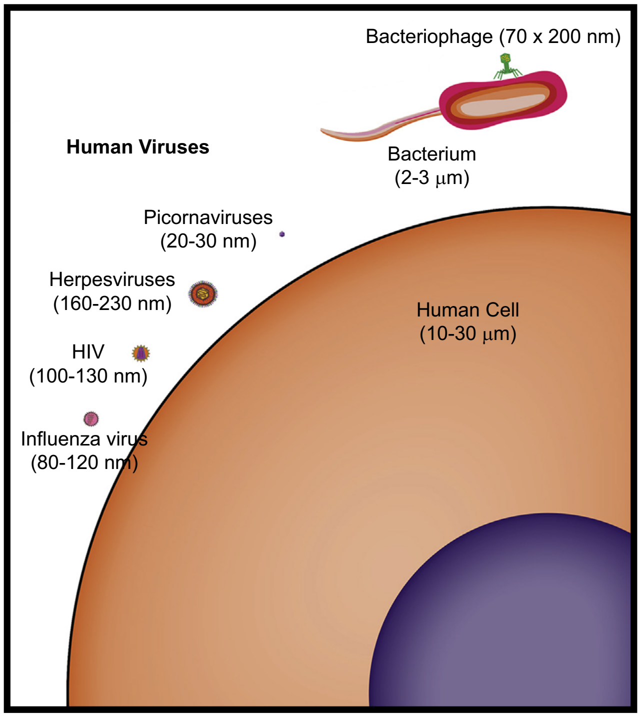

FIGURE 2.1 Virus and cell size comparison. Human viruses can vary in size but are generally in the range of 20–200 nm in diameter. In comparison, bacteria are generally 2–3 μM in length, and an average human cell is 10–30 μM.

have genomes that are 120–200 kb in total, and the very large pandoraviruses mentioned previously have the largest genomes: up to 2.5 million bases, rivaling the genome size of many bacteria! In comparison, eukaryotic cells have much larger genomes: a red alga has the smallest known eukaryotic genome, at 8 million base pairs; a human cell contains over 3 billion nucleotides in its hereditary material; the largest genome yet sequenced, at over 22 billion base pairs, is that of the loblolly pine tree.

Study Break
Describe the common characteristics of viruses.

2.2 STRUCTURE OF VIRUSES

The infectious virus particle must be released from the host cell to infect other cells and individuals. Whether dsDNA, ssDNA, dsRNA, or ssRNA, the nucleic acid genome of the virus must be protected in the process. In the extracellular environment, the virus will be exposed to enzymes that could break down or degrade nucleic acid. Physical stresses, such as the flow of air or liquid, could also shear the nucleic acid strands into pieces. In addition, viral genomes are susceptible to damage by ultraviolet radiation or radioactivity, much in the same way that our DNA is. If the nucleic acid

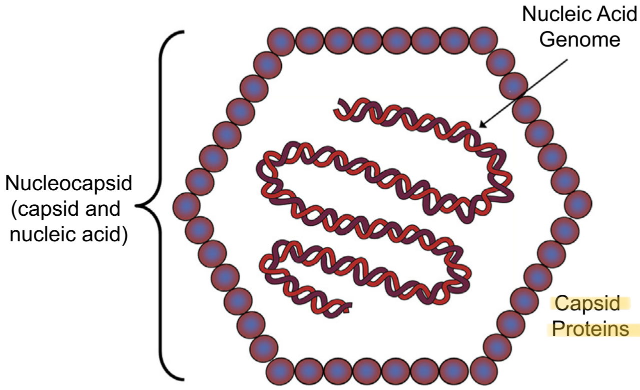

FIGURE 2.2 Basic virus architecture. Viral capsid proteins protect the fragile genome, composed of nucleic acid, from the harsh environment. The capsid and nucleic acid together are known as the nucleocapsid.

genome of the virus is damaged, then it will be unable to produce progeny virions.

In order to protect the fragile nucleic acid from this harsh environment, the virus surrounds its nucleic acid with a protein shell, called the **capsid**, from the Latin *capsa*, meaning "box." The capsid is composed of one or more different types of proteins that repeat over and over again to create the entire capsid, in the same way that many bricks fit together to form a wall. This repeating structure forms a strong but slightly flexible capsid. Combined with its small size, the capsid is physically very difficult to break open and sufficiently protects the nucleic acid inside of it. Together, the nucleic acid and the capsid form the **nucleocapsid** of the virion (Fig. 2.2).

Remember that the genomes of most viruses are very small. Genes encode the instructions to make proteins, so small genomes cannot encode many proteins. It is for this reason that the capsid of the virion is composed of one or only a few proteins that repeat over and over again to form the structure. The nucleic acid of the virus would be physically too large to fit inside the capsid if it were composed of more than just a few proteins.

In the same way that a roll of magnets will spontaneously assemble together, capsid proteins also exhibit self-assembly. The first to show this were H. Fraenkel-Conrat and Robley Williams in 1955. They separated the RNA genome from the protein subunits of tobacco mosaic virus, and when they put them back together in a test tube, infectious virions formed automatically. This indicated that no additional information is necessary to assemble a virus: the physical components will assemble spontaneously, primarily held together by electrostatic and hydrophobic forces.

Most viruses also have an **envelope** surrounding the capsid. The envelope is a lipid membrane that is derived from one of the cell's membranes, most often the plasma membrane, although the envelope can also come from the cell's endoplasmic reticulum, Golgi complex, or even the nuclear membrane,