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

SUMMARY OF KEY CONCEPTS

Section 2.1 Common Characteristics of Viruses

- Viruses are small. Most viruses are in the range of 20–200 nm, although some viruses can exceed 1000 nm in length. A typical bacterium is 2–3 µM in length; a typical eukaryotic cell is 10–30 µM in diameter.
- Viruses are obligate intracellular parasites and are completely dependent upon the cell for replication. Unlike cells that undergo mitosis and split in two, viruses completely disassemble within the cell and new virions (infectious particles) are assembled de novo from newly made components.
- While living things have dsDNA genomes, the genetic material of viruses can be composed of DNA or RNA, and single- or double-stranded. Most virus genomes fall within the range of 7–20 kb, but they range from 3 kb to over 2 mb.

Section 2.2 Structure of Viruses

- The simplest viruses are composed of a protein capsid that protects the viral nucleic acid from the harsh environment outside the cell.
- Virus capsids are predominantly one of two shapes, helical or icosahedral, although a few viruses have a complex architecture. In addition, some viruses also have a lipid membrane envelope, derived from the cell. All helical animal viruses are enveloped.
- Helical capsid proteins wind around the viral nucleic acid to form the nucleocapsid. A helix is mathematically defined by amplitude and pitch.
- An icosahedron is a geometric shape with 20 sides, each composed of an equilateral triangle. The sides are composed of viral protein subunits that create a structural unit, which is repeated to form a larger side and the other sides of the icosahedron. The triangulation number refers to the number of structural units per side.

Section 2.3 Virus Classification and Taxonomy

- The Baltimore classification system categorizes viruses based upon the type and replication strategy of the nucleic acid genome of the virus. There are seven classes.
- The ICTV was formed to assign viruses to a taxonomical hierarchy. The taxa used for classifying viruses are order, family, genus, and species. Because they are not alive, viruses are not categorized within the same taxonomical tree as living organisms.

FLASH CARD VOCABULARY

Virion	Triangulation number
Genome	Capsomere
Capsid	Bacteriophage
Nucleocapsid	Baltimore classification system
Enveloped virus	Positive-strand (positive-sense)
Naked (unenveloped) virus	Negative-strand (negative-sense)
Matrix proteins	Reverse transcribe
Virus attachment protein	Taxonomy
Helix	Nomenclature
Icosahedron: Face, edge, vertex	International Committee on Taxonomy of Viruses
Structural unit	Taxon

CHAPTER REVIEW QUESTIONS

1. Why are viruses considered obligate intracellular pathogens?
2. How does viral replication differ from cell replication?
3. What is the function of the capsid? Why must viruses repeat the same capsid protein subunits over and over again, rather than having hundreds of different capsid proteins?
4. Explain what 2–3–5 symmetry is, pertaining to an icosahedron.
5. What is a structural unit? In a $T=3$ virus that has three subunits per structural unit, how many total subunits form the capsid?
6. List the seven groups of the Baltimore classification system.
7. What taxa are used to classify viruses? How does this differ from the classification of a living organism?
8. What viral properties are used to classify viruses?

FURTHER READING

Bourne, C.R., Finn, M.G., Zlotnick, A., 2006. Global structural changes in hepatitis B virus capsids induced by the assembly effector HAP1. J. Virol. 80, 11055–11061.

Cáceres, A., Perdiguero, B., Gómez, C.E., et al., 2013. Involvement of the cellular phosphatase DUSP1 in vaccinia virus infection. PLoS Pathog. 9. http://dx.doi.org/10.1371/journal.ppat.1003719.

Clare, D.K., Orlova, E.V., 2010. 4.6A Cryo-EM reconstruction of tobacco mosaic virus from images recorded at 300 keV on a 4k × 4k CCD camera. J. Struct. Biol. 171, 303–308.

Dixon, L.K., Alonso, C., Escribano, J.M., et al., 2012. Virus taxonomy. In: Virus Taxonomy: Ninth Report of the International Committee on Taxonomy of Viruses, pp. 153–162.

Kaufmann, B., Simpson, A.A., Rossmann, M.G., 2004. The structure of human parvovirus B19. Proc. Natl. Acad. Sci. U. S. A. 101, 11628–11633.

Kuhn, R.J., Zhang, W., Rossmann, M.G., et al., 2002. Structure of dengue virus: implications for flavivirus organization, maturation, and fusion. Cell 108, 717–725.

Prasad, B.V., Hardy, M.E., Dokland, T., Bella, J., Rossmann, M.G., Estes, M.K., 1999. X-ray crystallographic structure of the Norwalk virus capsid. Science 286, 287–290.

Prasad, B.V.V., Schmid, M.F., 2012. Principles of virus structural organization. Adv. Exp. Med. Biol. 726, 17–47.

Tarini, M., Cignoni, P., Montani, C., 2006. Ambient occlusion and edge cueing to enhance real time molecular visualization. IEEE Trans. Vis. Comput. Graph 12, 1237–1244.

Van Regenmortel, M.H., 1990. Virus species, a much overlooked but essential concept in virus classification. Intervirology 31, 241–254.