Viruses and their importance

At a glance

Viruses infect:

- **Humans**
  - Smallpox
  - Foot and mouth disease

- **Other vertebrates**
  - Leatherjackets infected with *Tipula* iridescent virus

- **Invertebrates**
  - Mushroom virus
  - Escherichia coli cell with phage T4 attached

- **Plants**
  - Delayed emergence of potato caused by tobacco rattle virus infection

- **Fungi**
  - Damaged potato (spraing) caused by tobacco rattle virus infection

- **Bacteria**
  - *Escherichia coli* cell with phage T4 attached

At a glance (continued)

**Some viruses are useful:**
- Phage typing of bacteria
- Sources of enzymes
- Pesticides
- Anti-bacterial agents
- Anti-cancer agents
- Gene vectors

Viruses are parasites; they depend on cells for molecular building blocks, machinery and energy.

Virus particles are small; dimensions range from approx. 20–400 nm.

**A virus genome is composed of one of the following:**

- double-stranded DNA
- single-stranded DNA
- double-stranded RNA
- single-stranded RNA

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1. World Health Organisation.
2. Animal Sciences Group, Wageningen UR.
4. Warwick HRI.
1.1 Viruses are ubiquitous on Earth

Viruses infect all cellular life forms: eukaryotes (vertebrate animals, invertebrate animals, plants, fungi) and prokaryotes (bacteria and archaea). The viruses that infect prokaryotes are often referred to as bacteriophages, or phages for short.

The presence of viruses is obvious in host organisms showing signs of disease. Many healthy organisms, however, are hosts of non-pathogenic virus infections, some of which are active, while some are quiescent. Furthermore, the genomes of many organisms contain remnants of ancient virus genomes that integrated into their host genomes long ago. As well being present within their hosts, viruses are also found in soil, air and water. Many aqueous environments contain very high concentrations of viruses that infect the organisms that live in those environments.

There is a strong correlation between how intensively a species is studied and the number of viruses found in that species. Our own species is the subject of most attention as we have a vested interest in learning about agents and processes that affect our health. It is not surprising that there are more viruses known that infect mankind than any other species, and new human viruses continue to be found. The intestinal bacterium *Escherichia coli* has also been the subject of much study and many viruses have been found in this species. If other species received the same amount of attention it is likely that many would be found to be hosts to similar numbers of viruses.

It is undoubtedly the case that the viruses that have been discovered represent only a tiny fraction of the viruses on the Earth. Most of the known plants, animals, fungi, bacteria and archaea have yet to be investigated for the presence of viruses, and new potential hosts for viruses continue to be discovered. Furthermore, the analysis of DNA from natural environments points to the existence of many bacterial species that have not yet been isolated in the laboratory; it is likely that these ‘non-cultivable bacteria’ are also hosts to viruses.

1.2 Reasons for studying viruses

1.2.1 Some viruses cause disease

Viruses are important agents of many human diseases, ranging from the trivial (e.g. common colds) to the lethal (e.g. rabies), and viruses also play roles in the development of several types of cancer. As well as causing individuals to suffer, virus diseases can also affect the well-being of societies. Smallpox had a great impact in the past and AIDS is having a great impact today.

There is therefore a requirement to understand the nature of viruses, how they replicate and how they cause disease. This knowledge permits the development of effective means for prevention, diagnosis and treatment of virus diseases through the production of vaccines, diagnostic reagents and techniques, and antiviral drugs. These medical applications therefore constitute major aspects of the science of virology.

Veterinary virology and plant virology are also important because of the economic impact of the many viruses that cause disease in domestic animals and crop plants: foot and mouth disease virus and rice yellow mottle virus are just two examples. Another area where viruses can cause economic damage is in the dairy industry, where phages can infect the lactic acid bacteria that are responsible for the fermentations that produce cheese, yogurt and other milk products.

1.2.2 Some viruses are useful

Some viruses are studied because they have useful current or potential applications.

- **Phage typing of bacteria.** Some groups of bacteria, such as some *Salmonella* species, are classified into strains on the basis of the spectrum of phages to which they are susceptible. Identification of the phage types of bacterial isolates can provide useful epidemiological information during outbreaks of disease caused by these bacteria.

- **Sources of enzymes.** A number of enzymes used in molecular biology are virus enzymes. Examples include reverse transcriptases from retroviruses and RNA polymerases from phages.

- **Pesticides.** Some insect pests are controlled with baculoviruses and myxoma virus has been used to control rabbits.

- **Anti-bacterial agents.** In the mid-20th century phages were used to treat some bacterial infections of humans. Interest waned with the discovery of
antibiotics, but has been renewed with the emergence of antibiotic-resistant strains of bacteria.

- **Anti-cancer agents.** Genetically modified strains of viruses, such as herpes simplex virus and vaccinia virus, are being investigated for treatment of cancers. These strains have been modified so that they are able to infect and destroy specific tumour cells, but are unable to infect normal cells.

- **Gene vectors for protein production.** Viruses such as certain baculoviruses and adenoviruses are used as vectors to take genes into animal cells growing in culture. This technology can be used to insert into cells genes encoding useful proteins, such as vaccine components, and the cells can then be used for mass production of the proteins.

- **Gene vectors for treatment of genetic diseases.** Children with severe combined immunodeficiency (baby in the bubble syndrome) have been successfully treated using retroviruses as vectors to introduce into their stem cells a non-mutated copy of the mutated gene responsible for the disease (Section 16.5).

### 1.3 The nature of viruses

#### 1.3.1 Viruses are small particles

Evidence for the existence of very small infectious agents was first provided in the late 19th century by two scientists working independently: Martinus Beijerinck in Holland and Dimitri Ivanovski in Russia. They made extracts from diseased plants, which we now know were infected with tobacco mosaic virus, and passed the extracts through fine filters. The filtrates contained an agent that was able to infect new plants, but no bacteria could be cultured from the filtrates. The agent remained infective through several transfers to new plants, eliminating the possibility of a toxin. Beijerinck called the agent a ‘virus’ and the term has been in use ever since.

At around the same time, Freidrich Löffler and Paul Frosch transmitted foot and mouth disease from animal to animal in inoculum that had been highly diluted. A few years later Walter Reed and James Carroll demonstrated that the causative agent of yellow fever is a filterable agent.
Figure 1.2 Transmission electron microscope. This is a microscope in which the image is formed by electrons transmitted through the specimen. Photograph courtesy of Kathryn Newton.

Figure 1.3 Virions of mimivirus, one of the largest viruses, and a parvovirus (arrowed), one of the smallest viruses. Electron micrograph of mimivirus courtesy of Prof. D. Raoult, Unité des Rickettsies, Marseille, France. Electron micrograph of parvovirus from Walters et al. (2004) Journal of Virology, 78, 3361. Reproduced by permission of the American Society for Microbiology.

1.3.2 Viruses have genes

The virion contains the genome of the virus. Whereas the genomes of cells are composed of double-stranded DNA, there are four possibilities for a virus genome:

- double-stranded DNA
- single-stranded DNA
- double-stranded RNA
- single-stranded RNA.

The genome is enclosed in a protein coat known as a capsid. The genome plus the capsid, plus other components in many cases, constitute the virion. The functions of the virion are to protect the genome and to deliver it into a cell in which it can replicate.

Generally, virus genomes are much smaller than cell genomes and the question arises as to how viruses encode all their requirements in a small genome. Viruses achieve this in a number of ways.
• **Viruses use host cell proteins.** The genomes of large viruses duplicate some of the functions of the host cell, but the small viruses rely very heavily on functions of the host cell. There is, however, one function that an RNA virus must encode, no matter how small its genome. That function is an RNA polymerase, because cells do not encode enzymes that can replicate virus RNA. A significant proportion of the genome of an RNA virus is taken up with the gene for an RNA polymerase.

• **Viruses code efficiently.** There may be overlapping genes and genes encoded within genes. The small genome of hepatitis B virus is a good example (see Section 18.6).

• **Many virus proteins are multifunctional.** A virus protein may have several enzyme activities.

### 1.3.3 Viruses are parasites

Viruses differ from cells in the way in which they multiply. A new cell is always formed directly from a pre-existing cell, but a new virion is never formed directly from a pre-existing virion. New virions are formed by a process of replication, which takes place inside a host cell and involves the synthesis of components followed by their assembly into virions.

Viruses are therefore parasites of cells, and are dependent on their hosts for most of their requirements, including

- building-blocks such as amino acids and nucleosides;
- protein-synthesizing machinery (ribosomes);
- energy, in the form of adenosine triphosphate.

A virus modifies the intracellular environment of its host in order to enhance the efficiency of the replication process. Modifications might include production of new membranous structures, reduced expression of cell genes or enhancement of a cell process. Some large phages encode proteins that boost photosynthesis in the cells of their photosynthetic bacterial hosts, thereby probably boosting the yields of virus from the cells.

A point has now been reached where the nature of viruses can be summarized in a concise definition (see the box).

### Virus definition

A virus is a very small, non-cellular parasite of cells. Its genome, which is composed of either DNA or RNA, is enclosed in a protein coat.

### 1.3.4 Are viruses living or nonliving?

‘Viruses belong to biology because they possess genes, replicate, evolve, and are adapted to particular hosts, biotic habitats, and ecological niches. However, …they are nonliving infectious entities that can be said, at best, to lead a kind of borrowed life.’

Marc van Regenmortel and Brian Mahy (2004)

‘It’s life, Jim, but not as we know it!’

Dr. McCoy speaking to Captain Kirk of the Starship Enterprise, *Star Trek*

There is an ongoing debate as to whether viruses are living or nonliving; the view taken depends on how life is defined. Viruses have genes and when they infect cells these genes are replicated, so in this sense viruses are living. They are, however, very different to cellular life forms, so Dr. McCoy’s stock phrase (see the box) on finding new life forms in the galaxy could be applied to viruses. When viruses are outside their host cells they exist as virus particles (virions), which are inert, and could be described as nonliving, but viable bacterial spores are inert and are not considered to be nonliving. You might form your own view as to whether viruses are living or nonliving as you progress through this book.

When Beijerinck selected the word ‘virus’ he chose the Latin word for poison. This term has now been in use for over a century and virology has developed into a huge subject. More recently, the term virus has acquired further meanings. Computers
are threatened by infection with viruses that can be found in the wild once they have been released by their authors. These viruses are specific for certain file types. Infected files may be put on several web sites and a virus epidemic may ensue. Another use of the term virus is exemplified in John Humphrys’ book ‘Lost For Words’, in which he talks about the deadly virus of management-speak infecting language. All the italicized terms in this paragraph are also used in the context of the viruses that are the subject of this book.

1.4 The remainder of the book

Having outlined the nature of viruses and why they are important, the remainder of the book will examine many aspects of fundamental and applied virology. The early chapters cover principles, such as the structure of virions, virus replication and the classification of viruses. There are then nine chapters devoted to reviews of particular groups of viruses, where both principles and applications of virology are covered. Towards the end of the book we consider specific applications of virology, including viral vaccines and anti-viral drugs. The final chapter is devoted to prions, which are not viruses!

It is important to point out that much of virology is concerned with characteristics of the proteins and nucleic acids of viruses, and with interactions between these molecules and the proteins and nucleic acids of cells (Figure 1.4). Most of these interactions rely on specific binding between the molecules. We shall also be discussing cellular structures, and processes such as transcription, translation and DNA replication. A good background in molecular biology and cell biology is therefore essential; some useful sources of information for plugging any gaps can be found under Sources of further information.

Learning outcomes

By the end of this chapter you should be able to

- discuss reasons for studying viruses;
- explain how viruses differ from other organisms;
- define the term ‘virus’.

Sources of further information

Cell biology and molecular biology books


Historical paper

Recent papers

Breitbart M. and Rohwer F. (2005) Here a virus, there a virus, everywhere the same virus? Trends In Microbiology, 13, 278–284


van Regenmortel M. H. V. and Mahy B. W. J. (2004) Emerging issues in virus taxonomy Emerging Infectious Diseases, 10(1) http://www.cdc.gov/ncidod/eid/vol10no1/03-0279.htm

Young L. S. et al. (2006) Viral gene therapy strategies: from basic science to clinical application Journal of Pathology, 208, 299–318