A Guide to Virology for Engineers and Applied Scientists

Epidemiology, Emergency Management, and Optimization

Megan M. Reynolds
Louis Theodore

WILEY

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TO
My father, Dr. Joseph P. Reynolds (MMR)

AND

My friends and colleagues working in the field of virology (LT)

“When an epidemic of physical disease starts to spread, the community approves and joins in a quarantine of the patients in order to protect the health of the community against the spread of the disease…”

Franklin Delano Roosevelt (1882–1945)

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Preface

As its title implies, this book offers a guide to virology which provides information on viruses from an engineer's and applied scientist's perspective. Concise and easy to use, this guide brings together a wealth of general information on viruses in one compact book. It additionally offers practical and technical information plus calculation details.

The guide has been written not only for students but also for those in technical roles, such as engineers and applied scientists who work in public health, pharmaceuticals, or other health-related fields. It is a tool that may be used whenever and wherever information about viruses is likely to be sought.

In the wake of the COVID-19 pandemic, it has become evident that knowledge of virology is no longer critical only to doctors or epidemiologists; there is an urgent need for cooperation among varied disciplines to address the current pandemic and prepare for the next one. The authors feel that no one source currently covers all of the information on viruses in the manner presented in this book. It is hoped that this book will serve to fill the growing need for concise and digestible information – both academically and professionally – in these fields.

The guide is divided into three parts. Part I provides an overview of the science of viruses, including what they are, how they work, and how illnesses can be prevented and treated. Parts II and III provide information on practical/technical considerations and on calculation details, respectively. In addition, a number of illustrative examples are included for each chapter.

Reasonable care has been taken to ensure the accuracy of the information contained in this book. However, the authors and the publisher cannot be held responsible for erroneous omissions in the information presented or for any consequences arising from the use of the information published in the book. Accordingly, reference to original sources is encouraged. Reporting of any errors or omissions is solicited in order to ensure that appropriate changes may be made in future editions.

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Finally, the authors also wish to acknowledge the contributing authors: Sarah Forster (Overview of Molecular Biology), Emma Parente (Safety Protocols and Personal Protection Equipment), Vishal Bhatty (Engineering Principles and Fundamentals), Paul DiGaetano, Jr. (Ethical Considerations in Virology), and Julian Theodore (Introduction to Mathematical Methods).

August 2022

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About the Authors

Megan M. Reynolds, BS, MS, MBA, is a freelance medical writer and editor with a particular focus on infectious diseases. With degrees in chemical engineering, international business, and medicine, she worked in the pharmaceutical field in various capacities for more than a dozen years in both the United States and Europe. Her experience encompasses manufacturing, sales, and marketing from managing production scale-up for the launch of new drug manufacturing lines to spearheading an education initiative for healthcare providers at a large New York public hospital aimed at increasing vaccine utilization. She also studied methods for minimizing bacterial resistance due to the overuse of antibiotics. Previous publications include textbook chapter contributions, a case report on the successful treatment of a patient with a rare, highly resistant infection, as well as a medical narrative on treating patients in severe pain. Her recent research interests have focused on addressing the high rate of hospital-acquired infections leading to sepsis and on reducing vaccine hesitancy towards measles, mumps, and rubella vaccine (MMR). Raised in New York City, Ms. Reynolds is multilingual and has lived and worked in several countries, including Italy, Spain, and Germany, and has studied in the United States, Mexico, and Grenada. She is currently based in northern Italy and enjoys living in the Alps while pursuing her passions in rock climbing, yoga, and skiing.

Born and raised in Hell's Kitchen, Louis Theodore received the degrees of MChE and EngScD from the New York University and a BChE from the Cooper Union. For over 50 years, Dr. Theodore was a chemical engineering professor, as well as graduate program director, researcher, professional innovator, and communicator in the engineering field. He has authored numerous texts and reference books, nearly 200 technical papers, and is section editor to the last four editions of Perry's Chemical Engineers' Handbook. He has served as a consultant to the US EPA, DOE and DOJ, and Theodore Tutorials. Dr. Theodore is a member of Phi Lambda Upsilon, Sigma Xi, Tau Beta Pi, American Chemical Society, American Society of Engineering Education, Royal Hellenic Society, and a fellow of the International

Air & Waste Management Association (AWMA). In addition to providing invited testimony to a Presidential (Ford) Crime Commission Hearing, Dr. Theodore was honored at Madison Square Garden in 2008 for his contributions to basketball and the youth of America. His current technical interests include risk management, desalination, and pandemic modeling.

Part I

Introduction to Viruses

Merriam-Webster defines *Introduction* as "something that introduces, such as,

- a part of a book or treatise preliminary to the main portion,
- a preliminary treatise or course of study" (Merriam-Webster 2022)

Indeed, that is exactly what this Part I of the book is all about. The chapters contain material that one might view as a prerequisite for the technical considerations and engineering calculations that are addressed in Parts II and III, respectively.

It is no secret that viruses are responsible for a host of diseases that can include something as simple as the so-called "common" cold to those that are more serious and fatal, i.e., COVID-19, West Nile, AIDS, Ebola, etc. The technical community began to realize that viruses, in general, were responsible for a range of diseases at the turn of the 20th century. The variation in disease severity occurs because various viruses attack different tissues and organs. In addition, one of the problems with virus detection has been the extremely small size of many of viruses, i.e., both the SARS-CoV-2 and polio viruses are in the 0.01-0.1-micron size range.

There are six chapters covering these issues in Part I. The chapter numbers and accompanying titles are listed below:

Chapter 1: Overview of Molecular Biology
Chapter 2: Basics of Virology
Chapter 3: Pandemics, Epidemics, and Outbreaks
Chapter 4: Virus Prevention, Diagnosis, and Treatment
Chapter 5: Safety Protocols and Personal Protection Equipment
Chapter 6: Epidemiology and Virus Transmission

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1

Overview of Molecular Biology

Contributing Author: Sarah Forster

CHAPTER MENU

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After much deliberation, the authors have decided to include a preliminary chapter concerned with molecular biology and the immune system. This decision was based on the fact that the book was written for engineers and applied scientists who may not have a background in biology. Why the inclusion? The authors felt that these topics, for those interested, could provide the readers with a better understanding of how cells function under normal circumstances, and thus better comprehend how viruses take over and use these mechanisms against the body.

Biology, as the science of life, involves the general study of living forms. *Molecular* biology, which includes *biophysics* and *biochemistry*, has made fundamental contributions to modern biology. Thus, more information is now available about the structure and function of nucleic acids – the base of DNA and proteins, and the key molecules of all living matter. *Cellular* biology is closely related to molecular biology (the title of this chapter). It primarily deals with the functions of the cell – the basic structural unit of life – which studies its components and their

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interactions. The life functions of multicellular organisms are governed by the activities and interactions of their cellular components. The study of organisms includes not only their growth and development but also how they function.

When a virus infects a host, it utilizes the genetic code of the invaded cell to hijack the normal replication process in order to replicate numerous copies of itself. Thus, it is helpful to have some understanding as to how genetic coding works under normal circumstances, in order to fully comprehend the complex mechanism with which the virus commandeers a cell for its own purposes. While viruses are not themselves cellular, they do contain the same basic genetic materials as cells, either DNA or RNA.

This chapter attempts to provide the reader with some of the key terms that have become integral to the study of molecular biology. The chapter also endeavors to offer a framework of normal cell functions critical to the understanding of virology. Chapter 2: Basics of Virology, the next chapter, utilizes this framework to depict how viruses invade and hijack standard cell function. Hopefully, the importance of the definitions and explanations in this earlier section will become clear. In the same vein, those already familiar with molecular biology may wish to skip this chapter in favor of Chapter 2.

1.1 CELL BASICS

This section describes the basic concepts of *eukaryotic* cells, which compose all multicellular organisms, such as humans, animals, and plants. Alternatively, single-celled microorganisms such as bacteria are referred to as *prokaryotes*. Different viruses infect different types of cells. As discussed above, Chapter 2 further examines how viruses invade and infect human cells.

Within each eukaryotic cell is a highly complex system of *organelles* – the tiny cellular structures that perform specific functions within the cell. These structures keep the cell running, much like organs do in the human body. Several key organelles are shown below in Figure 1.1.

(Louten 2016)

The following subsections below highlight a few organelles that play a crucial role during virus invasion leading to infection. These include the cytoplasm, ribosomes, and nucleus.

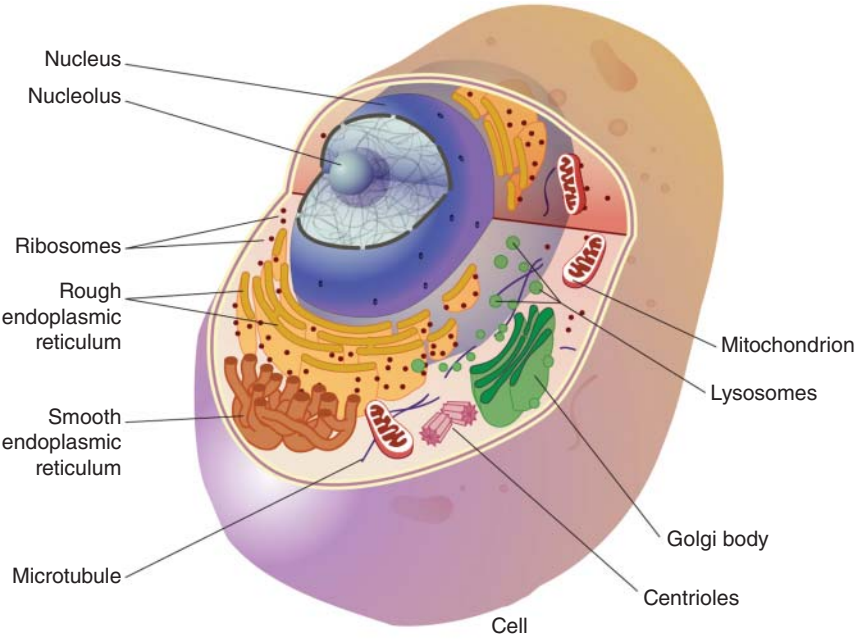

Figure 1.1 Illustration of organelles within a cell. *Source*: National Cancer Institute/U.S. Department of Health and Human Services/Public Domain.

1.1.1 Cytoplasm

The cytoplasm is one of the most important organelles within the cell membrane since it holds the other organelles together in its gel-like composition and allows for numerous processes to occur within the cell through the suspension of organelles and cellular molecules. Cytoplasm also allows for the occurrence of biochemical reactions within the cell, such as the replication of RNA viruses and protein synthesis (Denison 2008). The replication of RNA viruses occurs here in the cytoplasm as a majority of the enzymes used to replicate RNA are virally encoded.

1.1.2 Ribosomes

Ribosomes found in the cytosol play an important role in the manufacture of proteins within the cell. These ribosomes are located not only attached to the *rough*

endoplasmic reticulum (rER), but also floating within the cytosol. The ribosomes attached to the endoplasmic reticulum have the ability to create proteins. Once transferred to the lumen, proteins are modified to be utilized by the remaining organelles throughout the cell. This is all possible due to the binding of the ribosomes to the messenger RNA (mRNA) prior to the production of proteins (Louten 2016). Viruses have the ability to overtake the production of these proteins by the ribosomes for their own use.

1.1.3 Nucleus

The nucleus within eukaryotic cells contains organelles necessary for the regulation of cellular activities as well as the structures that contain the cell's DNA and other hereditary information. These structures inside the nucleus are comprised of chromosomes, the nuclear matrix, nucleoli, the nucleoplasm, the outer and inner nuclear membranes as well as the nuclear pores (Louten 2016).

The nucleus also allows for the replication of DNA which is then transcribed into messenger RNA to be used throughout the cell. Because of this, viruses must be able to have access to the cell's nucleus in order to replicate their DNA and attack other cells (Geer and Messersmith 2002).

1.2 CELL REPLICATION

Cell replication is a detailed process involving the copying of DNA to make new cells. DNA contains the genetic code that is present in every cell in the human body. DNA and RNA are both made up of nucleic acids, which are described below. They are critical to the process of replication and survival, not only for the cell but also for the invading virus (Denison 2008).

1.2.1 Nucleic Acids

This subsection will review the structure and function of DNA and RNA, which, as previously mentioned, are both made up of various nucleotides. Nucleotides are the basic building blocks for all living organisms, and are a crucial component in all cells. Nucleotides are comprised of three basic components:

- A five-carbon sugar molecule (deoxyribose for DNA or ribose for RNA)
- A phosphate group containing phosphorus and oxygen
- A *nitrogenous base*, a ringed molecule of nitrogen, oxygen, and hydrogen

There are four variations of nitrogenous bases, and together they form the basic building blocks for all living organisms: adenine (A), guanine (G), cytosine (C), and thymine (T). (Note: Uracil (U) replaces thymine in RNA) Together, these four different nucleotides combine to form polynucleotide base pairs. In DNA, adenine

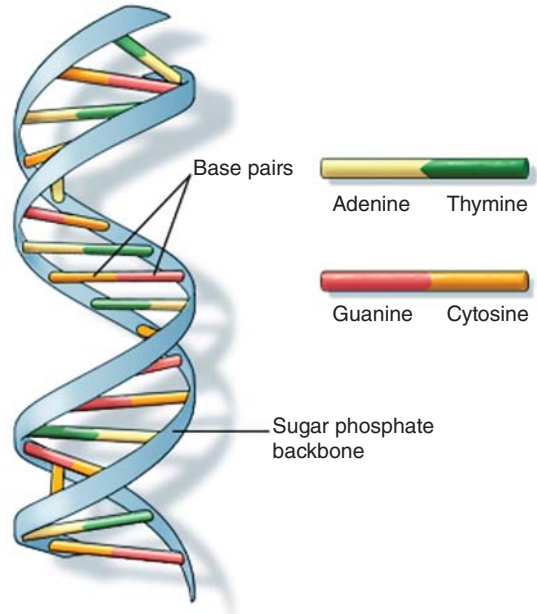

Figure 1.2 DNA polynucleotide base pairs with sugar--phosphate backbone https://medlineplus.gov/genetics/understanding/basics/dna/

always pairs with thymine, while cytosine pairs with guanine. The pairs are bound together by hydrogen bonds. These base pairs form the coding sequences within the DNA double helix, as shown in Figure 1.2. (Seladi-Schulman 2019; NIH 2010).

The double helix of DNA is structured as two complementary polynucleotide strands, with the leading strand running from the 5′ to 3′ carbon and the lagging strand running from the 3′ to 5′ carbon, as shown in the middle of Figure 1.3, below. The base pairs are located within the resulting double helix. The code, which is the order of nucleotides, determines which amino acids will be produced, and therefore, which proteins. Each amino acid is encoded by the order of three nucleotides (Geer and Messersmith 2002).

1.2.2 DNA Replication

The cell cycle consists of four stages including gap 1(G_1), synthesis (S Phase), gap 2(G_2), and mitosis. Within these four stages, each cell has the ability to grow and divide while also replicating its DNA. The process of DNA replication occurs when the cell creates a direct copy of its chromosomes either during synthesis or during the s-phase of the cell cycle.

As depicted in Figure 1.3, the DNA molecule is untwined during replication, and the two DNA strands are separated from one another through the presence of *cellular enzymes* within the cell. *DNA polymerase* is one of the main

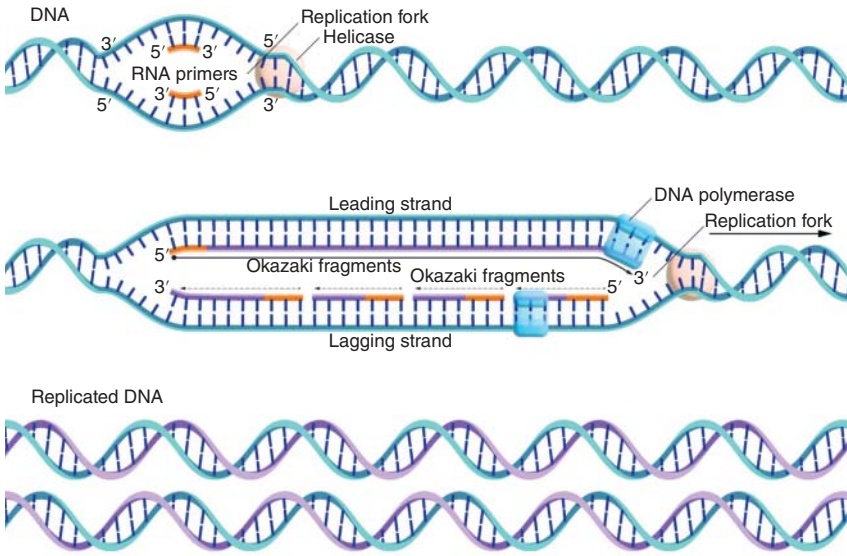

Figure 1.3 DNA Replication https://www.genome.gov/genetics-glossary/DNA-Replication

enzymes utilized in DNA replication due to its ability to place the complementary nucleotides of the new DNA strand in the 5′ to 3′ direction. DNA polymerase also adds in nucleotides based upon the complementary base pair rules as discussed in the previous section and is highly accurate, so there is a very low rate of misplaced nucleotides. This is shown in Figure 1.3. (Geer and Messersmith 2002).

Working alongside DNA polymerase is an enzyme known as *RNA polymerase* that synthesizes RNA. Similar to DNA polymerase, this enzyme uses a DNA template to produce a section of RNA that adds nucleotides in a 5′ to 3′ direction while also using the complementary base pair rule. RNA polymerase is known to have a lower rate of fidelity as compared to DNA polymerase (Louten 2016). This fact is highly relevant to virus replication, since an RNA virus tends to have more replicating errors—and as a result, more mutations than a DNA virus, as will be discussed in Chapter 2.

Another enzyme involved with DNA replication is known as *primase*, which is an enzyme that allows DNA polymerase to bind to a formerly single strand of DNA. Primase has the ability to form a double-stranded segment that allows for the binding of DNA polymerase through laying a complementary fragment of RNA on top of the single strand of DNA. (Geer and Messersmith 2002).

Because DNA replication is performed in the cell's nucleus, viruses must gain entry before taking advantage of DNA polymerase and other enzymes to replicate their own genomes and divide further (Louten 2016).