

## Understanding Coronavirus

Since the identification of the first cases of the coronavirus in December 2019, there has been a significant amount of confusion regarding the origin and spread of the so-called “coronavirus”, SARS-CoV-2, and the cause of the disease COVID-19.

Conflicting messages from the media and officials across different countries and organizations, the abundance of disparate sources of information, unfounded conspiracy theories on the origins of the virus, unproven therapies, and inconsistent public health measures, have all served to increase anxiety in the population.

Where did the virus come from? How is it transmitted? How does it cause disease? Is it like flu? What is a pandemic? In this concise and accessible introduction, a leading expert provides answers to these commonly asked questions.

This revised and updated edition now also covers how the virus mutates, how important these mutations are, how vaccines work, and what we can expect in the near and long-term future.

**Raul Rabadan** is the Gerald and Janet Carrus Professor in the Departments of Systems Biology and Biomedical Informatics, and the Director of the Program for Mathematical Genomics, at Columbia University. From 2001 to 2003, Dr. Rabadan was a fellow at the Theoretical Physics Division at CERN, the European Organization for Nuclear Research, in Geneva, Switzerland. In 2003 he joined the School of Natural Sciences at the Institute for Advanced Study in Princeton, New Jersey. He has been named one of *Popular Science's* Brilliant 10 (2010), a Stewart Trust Fellow (2013), and has received the Harold and Golden Lampton (2014), Diz Pintado (2018) and Phillip Sharp (2018) awards. Dr. Rabadan's current interest focuses on uncovering patterns of evolution in biological systems – in particular, RNA viruses and cancer. Dr. Rabadan is the founder of Genotwin, a data-driven genomic company.

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The *Understanding Life Series* is for anyone wanting an engaging and concise way into a key biological topic. Offering a multi-disciplinary perspective, these accessible guides address common misconceptions and misunderstandings in a thoughtful way to help stimulate debate and encourage a more indepth understanding. Written by leading thinkers in each field, these books are for anyone wanting an expert overview that will enable a deeper understanding of each topic.

Series Editor: Kostas Kampourakis <http://kampourakis.com>

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Revised and Updated Edition

RAUL RABADAN  
Columbia University, New York



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“An extremely concise and important book that everyone should read to understand the dynamics of the COVID-19 pandemic.”

Siddhartha Mukherjee, *Columbia University and author of The Gene and The Emperor of All Maladies, awarded the Pulitzer Prize in 2011*

“With all the technology and medical knowledge of the twenty-first century, a pandemic virus has defeated us. This book tells us why and how that could happen and what we can do about it. All this wrapped up in a clear, understandable, and interesting way. We learn what is happening to us now and how to better prepare for the future.”

Arnold J. Levine, *Institute for Advanced Study, New Jersey*

“... an essential book for the first pandemic of the twenty-first century, COVID-19 caused by SARS-CoV-2 ... a wonderfully concise and accessible explanation of everything you want to know about the virus, the disease, and the outbreak. I highly recommend this book.”

Vincent Racaniello, *Columbia University*

“A clear scientific guide to COVID-19 ... [it] illuminates coronavirus science not only with clear writing but also with good graphics and illustrations.”

Clive Cookson, *Financial Times*

“This small book could be required reading for many politicians and journalists ...”

Tilli Tansey, *Nature*

“What *Understanding Coronavirus* does very well is clarify virology and epidemiology basics. Asking how quickly the virus spreads means explaining the basic reproduction number  $R_0$  and concepts such as ‘flattening the curve’ and herd immunity. It explains the symptoms, the typical course of the disease, how deadly it is ... *Understanding Coronavirus* provides a lot of relevant information in a very readable and concise format.”

Leon Vlieger, *Natural History Book Service*

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This book is dedicated to my parents, Fernando and Felicitas,  
and to the healthcare workers who are fighting for all of us.

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## Foreword

*Understanding Coronavirus*, by Raul Rabadan, is not only a timely book given the current pandemic and the concerns about this virus worldwide; it is also a very useful book that explains the current situation and provides a solid understanding of SARS-CoV-2 in particular, and of viruses and pandemics more broadly. It covers the epidemiology and the biology of this virus, as well as relates it to the SARS and influenza viruses and outbreaks of the past. The book begins with the broader picture about how viruses spread, and then zooms in on what coronaviruses are and how they compare to other viruses, providing the necessary context for understanding the COVID-19 pandemic. The author is a well-known expert, who has been closely monitoring all developments since the pandemic began, and here provides the interested reader with a well-written, engaging, and concise book. This revised and updated edition covers all the developments since June 2020, and considers the ongoing challenges related to the new virus variants and the concerns about the effectiveness (and safety) of the widely used vaccines. I hope that this new edition will be at least as widely read and discussed as the initial one.

**Kostas Kampourakis, Series Editor**

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## Preface to the Revised and Updated Edition

The world has changed. It was not long ago that the idea of a world shaken by a global pandemic was far from our daily thoughts. By now, we have become painfully familiar with personal loss, lockdowns, travel bans, routine tests, telecommuting, and kids at home. By now, we have all known someone who has passed away from the disease, someone who has suffered from long-term effects of the infection, someone who has lost a job, a business, or their savings. We have become aware of how vulnerable our world is, and how different and how similar we are. We have realized how fragile our healthcare systems and our economy can be.

On the other hand, we have also realized that we can be much better prepared next time. In the history of humanity, we have never learned so much about a disease in so little time. We have learned how the virus enters the body and its cells, how it interacts with the immune system, how it is recognized by different immune cells, and how it causes disease and death. In an uncoordinated, somewhat chaotic worldwide effort, the whole scientific community has set aside previous priorities to put its technical expertise into the common enterprise of vanquishing the virus. From the surveillance point of view, it has been surprising how molecular technologies have become routine in our lives. PCR and antigen and antibody tests have become part of our daily lexicon. Virus genomes are now sequenced to an unprecedented scale all around the world. These efforts are making it possible to track the spread, identify new mutations and variants of interest, to evaluate how they contribute to the spread of the virus, the severity of the disease, and its potential resistance to vaccines. From the public health point of view, we now have evidence of the effectiveness of many measures implemented,

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including the role of masks, the quantification of the spread of viruses in schools and nursing homes, and the effectiveness of lockdowns and their economic costs.

But, undoubtedly, the most gratifying surprise is the celerity of the design, production, and delivery of vaccines. Novel RNA vaccines have been tested, produced, and distributed with a rapidity and an efficacy unmatched as vaccines go. As the virus evolves, it will not be surprising if we need to get updated vaccines, new boosters that incorporate new variants. But now we have the technology, the means, and the minds to be prepared for these challenges. If, in the future, as expected, novel viruses emerge, we will be more prepared as a society with faster test development and implementation, with effective mobilization of the healthcare system, with the social will to follow public health measures and with the capacity to quickly develop, test, produce, and distribute vaccines.

We have realized that infectious diseases are not the problem of a single country, specific groups, or political pettiness. The virus does not “understand” or “care” about these very human distinctions. Neither do the vaccines. The universal language of science provides the framework within which to understand and to fight these common problems. Only by building upon the common scientific experience will we be better prepared for future challenges.

This revised and updated edition of *Understanding Coronavirus* was written in spring 2021, a year after the first edition. It is interesting to compare our knowledge then and now, what we have learned and what remains to be discovered. Comparing editions and notes taken when writing the book, it has been astonishing how our understanding of the disease has evolved. There have been myriad developments that are impossible to cover in an introductory book. Although lacking in technical depth, the conciseness of this book presents a broader perspective and common narrative harder to perceive in more extensive work. I have focused on the many aspects that, in my opinion, are more relevant to understanding the events that have engulfed our lives, that allow a dispassionate assessment of our society and an evaluation of the short- and long-term challenges that face us. Most sections have been updated. There are new sections addressing the emergence of variants, and the last chapter discusses the vaccines. I have incorporated new data, figures, comments, and reflections with a larger historical perspective.

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I would like to thank my home institution, Columbia University, and the Spanish National Cancer Research Center in Madrid, Spain, for hosting me while writing this new edition of the book. In this second edition I would like to specially thank Suzanne Christen and Karen Gomez for their comments, suggestions, and careful editing of the book.

**New York, June 2021**

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## Preface to the First Edition

On a Friday evening in March 2020 I received a phone call from an old friend of mine, Luca. Luca lives in Treviso, a beautiful old town in the north of Italy, close to Venice. He was worried about my family, knowing that the number of coronavirus cases and deaths in New York was increasing at an alarming rate. I could sense that his voice was weak, with a mixture of exhaustion and anxiety. “I feel better now, but it has been a terrible month here,” he told me. “For me,” he paused, “it all started with a very high fever and a terrible cough a few days later. The cough felt like something was burning inside my lungs.” Luca was feeling better at this point, but the description of the situation was not encouraging. “Streets are completely deserted in Treviso and in Venice. You never would have thought about that.” That was some time ago, and Luca’s account is now just one of many, including from family and friends. By April 2020, New York, the city where I live, was a desert of empty streets, closed restaurants and schools, and few pedestrians. People in their homes followed the development of events with obsessive persistence, tracking the terrifying figures and official announcements. We were all learning and trying to adjust to the “new normal”: social distancing, quarantines, telecommuting, home schooling, to name a few.

The identification of the first cases of the coronavirus began in December 2019 in Wuhan, in the Chinese province of Hubei. Since then, there has been a significant amount of confusion regarding the origin and the spread of the coronavirus, officially named SARS-CoV-2, and the severity of the disease, named COVID-19. This confusion has been amplified by conflicting messages from the media, disparate communications from officials across different countries and organizations, and by the radically different measures taken

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in different parts of the world, ranging from locking down entire regions to a mild denial of the situation. Making things even more disconcerting, various media sources equated this epidemic to mild seasonal flu, the 1918 “Spanish flu” pandemic, or the 2003 SARS outbreak. Each of those outbreaks was caused by a separate virus in very disparate historical moments with very different outcomes. The lack of a clear message, the profusion of conflicting sources and comparisons, the unfounded conspiracy theories on the origins of the newly emerging virus, and the dissonant public health measures across different countries increased the levels of anxiety in the population.

The idea for this book was born through conversations with Cambridge University Press commissioning editor Katrina Halliday and her series editor, Kostas Kampourakis, regarding the current need for simple explanations clarifying some of the confusion generated since the beginning of the pandemic. It aims to provide a concise introduction to the COVID-19 coronavirus through a set of basic questions about the virus and the disease. The book is designed to inform a general reader, someone with an interest in learning more about the coronavirus without having to go to the scientific literature. Topics include the basic molecular biology and epidemiology of the virus, a bit of genomics, a description of the origin and evolution of the virus, and a comparison to other respiratory viruses. I also provide some conceptual tools to help frame the questions and answers addressed in the book.

This book was not planned in advance. I was supposed to enjoy a sabbatical year traveling and meeting colleagues around the world. That did not happen. With conferences cancelled and travel bans in place, it became evident that I was going to enjoy some quiet time, at home with my family. Worried by the rapid evolution of circumstances, I was drawn into research on the virus and the disease, together with colleagues at Columbia University. The sabbatical and frustrated travel plans allowed me to undertake the challenge of writing this book.

I would like to thank my home institution, Columbia University, as well as the Institute for Advanced Study in Princeton, and the Center for Theoretical Physics at Columbia University in New York City for hosting me during the writing of this book. I would like to thank Paula Ralph-Birkett, Andrew Chen, and Suzanne Christen for the initial editing of the book, and Zixuan Wang for the figures. Thanks also to Jean-Michel Bertoli, Katrina Halliday, Kostas

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Kampourakis, Matthew Kleban, and Cristina Rabadan, who provided constant feedback on content, structure, and ideas for the book. Arnold Levine carefully read the book and gave insightful comments and ideas. I would like to mention, in particular, Ioan Filip and Juan Patino Galindo for interesting collaborations on coronavirus genomics. I have discussed many aspects of the new coronavirus with members of my laboratory at Columbia University, including Luis Aparicio, Francesco Brundu, Mathieu Carriere, Oliver Elliott, Karen Gomez, Zhaoqi Liu, Tomin Perea-Chamblee, Wesley Tansey, Anqi Wang, and Junfei Zhao. I would like also to acknowledge friends and colleagues for useful feedback and comments, including Gyan Bhanot, Julian Bruat, Reuben Danzing, Bernard Dayrit, Lam Hui, Martin Hyatt, Hossein Khiabani, Luca Magri, Carmen McConnell, Do-Hyun Nam, Massimo Porri, Leonardo Rastelli, Jeffrey Shaman, Andrea Severin, and Jiguang Wang.

Most of all, I would like to thank my family, Jean-Michel, Emma and Alex, for their constant patience and support while I was writing this book.

**New York, May 2020**

## Abbreviations

ACE2	angiotensin-converting enzyme 2
AIDS	Acquired immunodeficiency syndrome
CCoV	canine coronavirus
COVID-19	Coronavirus disease 19
FCoV	feline coronavirus
HIV	human immunodeficiency virus
ICTV	International Committee on Taxonomy of Viruses
ICU	intensive care unit
ILI	influenza-like illnesses
MERS-CoV	Middle East respiratory syndrome
PCR	polymerase chain reaction
RBD	receptor binding domain
$R_0$	basic reproductive number
SARS	Severe acute respiratory syndrome
WHO	World Health Organization