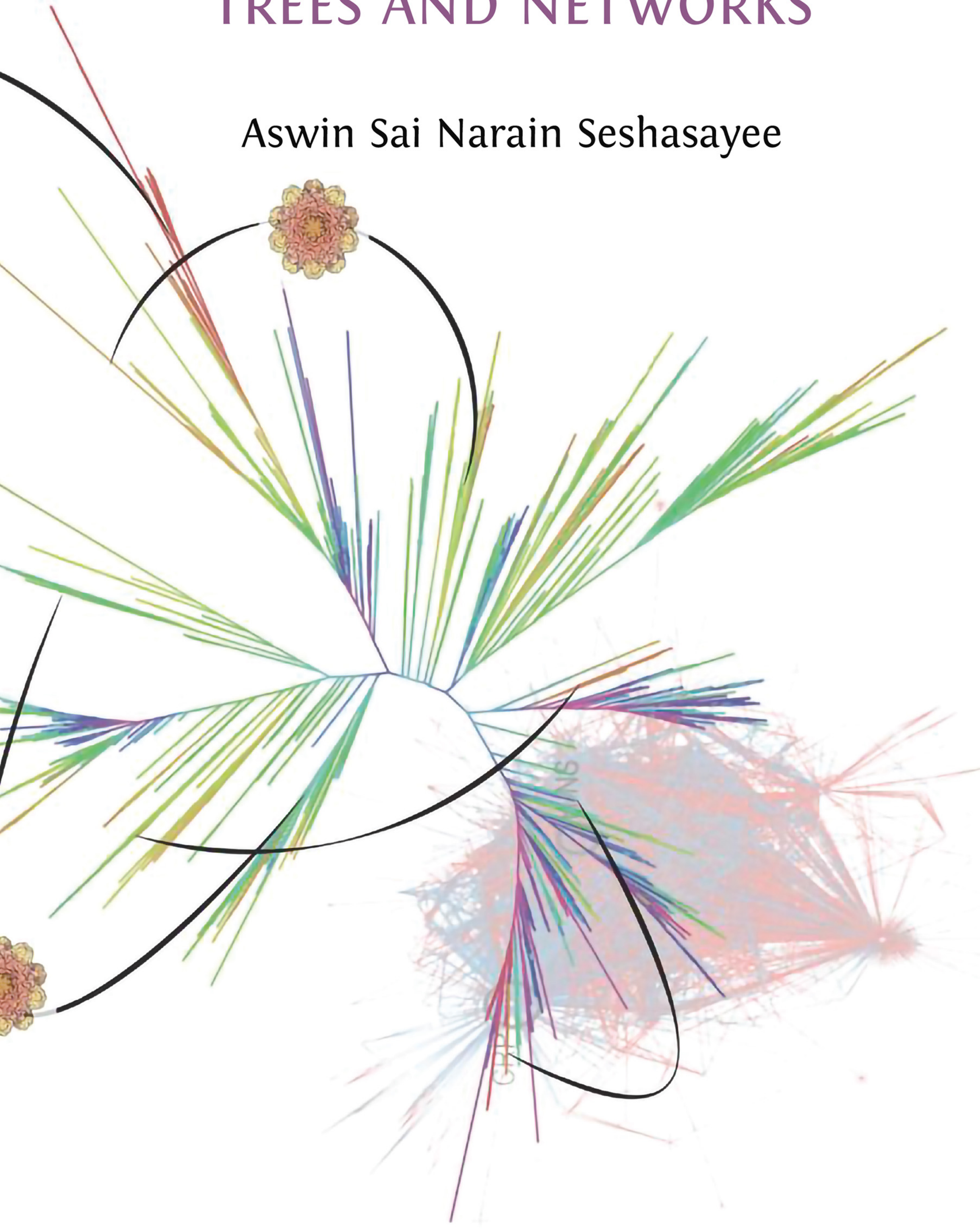
BACTERIAL GENOMES

TREES AND NETWORKS

Aswin Sai Narain Seshasayee



https://www.openbookpublishers.com
©2025 Aswin Sai Narain Seshasayee

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0). This license allows you to share, copy, distribute and transmit the text; to adapt the text for non-commercial purposes of the text providing attribution is made to the author (but not in any way that suggests that they endorse you or your use of the work). Attribution should include the following information:

Aswin Sai Narain Seshasayee, *Bacterial Genomes: Trees and Networks*. Cambridge, UK: Open Book Publishers, 2025, https://doi.org/10.11647/OBP.0446

Copyright and permissions for the reuse of many of the images included in this publication differ from the above. This information is provided in the captions and in the list of illustrations. Every effort has been made to identify and contact copyright holders and any omission or error will be corrected if notification is made to the publisher.

Further details about CC BY-NC licenses are available at https://creativecommons.org/licenses/by-nc/4.0/

All external links were active at the time of publication unless otherwise stated and have been archived via the Internet Archive Wayback Machine at https://archive.org/web

Any digital material and resources associated with this volume will be available at https://doi.org/10.11647/OBP.0446#resources

ISBN Paperback: 978-1-80511-495-6
ISBN Hardback: 978-1-80511-496-3
ISBN Digital (PDF): 978-1-80511-497-0
ISBN Digital ebook (EPUB): 978-1-80511-498-7
ISBN HTML: 978-1-80511-499-4
DOI: 10.11647/OBP.0446

Cover images by Prerana Sudarshan and David Goodsell, assembled by Ashitha Arun, Inder Raj Singh and Madhumitha K. Cover design: Jeevanjot Kaur Nagpal.

Preface

Bacteria are the most dominant form of cellular life on Earth. Not just in terms of numbers, but also in terms of their capabilities that allowed other life forms to emerge a few billion years ago, and continue to help sustain life to this day. To fear them as pedlars of disease would be to do great disservice to their incomparable contribution to making life on Earth habitable; after all it is only a minuscule minority of bacteria that are pathogenic.

Bacteria are hardy. They are everywhere. In the human body, they contribute to processes that we take for granted and we are often ignorant of their role (a quick Google search for human microbiomes[1] is instructive). They are present in extreme environments—from hydrothermal vents on the one hand to arctic permafrost on the other. Of course, they are also present in large numbers in the soil and in fresh and salt water. One would not be too far off the mark to claim that any catastrophe that drives most life forms to extinction would leave these organisms relatively unscathed. The only exception would be events that create conditions that are inimical to the very foundations of life.

Central to the bacterial dominance of our planet is their insatiable ability to adapt. Imagine the first bacterial cell living in a very ancient world of water, devoid of oxygen, and lacking even the most common source of energy necessary to modern-day life forms—i.e., sugars—spreading outwards and eventually colonising every conceivable habitat on Earth, and along the way oxygenating it and sowing the seeds for many other life forms to emerge and evolve. We are justifiably in awe (and at times in despair when concerned about the environment) of the great journey of *Homo sapiens* out of Africa some 50,000–100,000 years ago, culminating in our habitation of all continents including Antarctica. This was enabled by our outsize brains, which provided us with the wherewithal to invent new tools, create societies, cities, civilisations, religions, all the way through to rockets and artificial intelligence. Bacteria are not so endowed. They are single cells and what they have achieved is a product of their chemical capabilities. Underlying this is their genetic material or their genome, its ability to change and stabilise in a manner best suited to their circumstances. This is what we call genetic evolution, which has, over several billion years, caused the emergence of a whole diversity of simple and complex bacterial individuals and species starting from a presumably primitive ancestor.

1 A small piece of advice: it might be best to give AI summaries produced by Google a pass for the time being.

©2025 Aswin Sai Narain Seshasayee, CC BY-NC 4.0 https://doi.org/10.11647/OBP.0446.00

Talking about evolution over such epochs creates a striking narrative. Yet, this is merely an accumulation of more humble changes that happen every day to permit bacteria to adapt from one day's circumstance to the next. These circumstances might be the external environment, or they can themselves be genetic. One genetic change can require that subsequent genetic changes must occur, and this also constitutes adaptation. The genome merely specifies a recipe that needs to be acted upon for anything to happen. How this recipe is interpreted by the cellular machinery and how this reading is regulated is yet another contributor to adaptation, one that can effect physiological switches in a matter of minutes, in contrast to genetic changes which take generations to establish.

This book is about bacterial genetic diversity, the processes that establish such diversity, and how this is driven by the need for bacteria to adapt to circumstances. Here we use a very broad definition of adaptation (from the Cambridge Dictionary): "the process of changing to suit different conditions," and not merely evolutionary adaptation that necessarily requires genetic change for adaptation; according to our use of this word, even physiological changes can be adaptive. Thus, tightly regulated cellular processes that read the information contained in the genome to produce life-sustaining molecules such as proteins are also central to adaptation, but mostly over a timescale different from that over which genetic changes operate. However, the genome and its reading are intertwined. Regulation of the processes that read the genome are also evolvable and in a manner that helps bacteria adapt. More than that, one drives the other. The way the genome is organised helps facilitate its seamless reading by the cellular machinery, and this organisation might have evolved in response to the need to ensure that the genome is read efficiently.

Finally, from a human standpoint, what bacteria are capable of doing is one thing, and what we know of it is another. Human knowledge of bacteria is nearly 350 years old and, like technological progress, has accelerated over time, reaching a crescendo over the last few decades.

The book is about bacterial adaptation. It begins by presenting a selection of people and ideas that have helped us understand bacteria. Much of this work, especially in the 20th century, was driven by the medical need to combat infectious diseases. Additionally, the ease with which some bacteria could be grown and manipulated in the laboratory allowed them to serve as models for studies of the fundamental processes that drive life. A whole body of research was facilitated by the plasticity and adaptability of bacteria, and in turn helped us understand bacterial adaptation. After nearly 300 years of scratching our heads, we finally developed an understanding of the place of bacteria in the universal tree of life only in the final quarter of the 20th century, before establishing how we can know what the genome encodes.

The book then takes a more technical turn and discusses how bacterial genomes span two orders of magnitude in size, but remain compact and rich in information. We will also see how natural selection, or 'survival of the fittest' as espoused by Charles Darwin, underlies the evolution of the bacterial genetic material, and how the bacterial genome differs from much of the mammalian genome in this respect. We explore how the genome changes, how it expands and how it contracts, and how all these facilitate adaptation. We will then attempt to understand the processes the cell uses to interpret its own genetic material and produce molecules that determine its traits, how these processes are regulated, how such regulation has played a role in shaping the genome, and how various contemporary researchers have addressed these questions.

Chapter 1 discusses the history of our study of bacteria, starting from their first microscopic observation in the 17th century. It then discusses how we learnt, mostly in the 19th century, about the vast array of functions they perform, from causing disease to running biogeochemical cycles. Medical microbiology came into its own with the discovery of antibiotics in the first half of the 20th century, simultaneously highlighting the role of microbial competition in the environment. The first indication of bacterial resistance to antimicrobial agents as early as in the 1920s also brought to light their metabolic flexibility and adaptability.

Chapter 2 first discusses the fascinating story of the discovery of viruses that prey on bacteria and how research (once again) demonstrating the flexibility of bacterial traits led to the stunning revelation that DNA and not protein was the genetic material of cellular life. This led to a cascade of discoveries that created the field of molecular biology, which not only helped us to understand our phylogenetic relationships with bacteria, but also culminated in the complete sequencing of the first cellular genomes towards the end of the 20th century.

In Chapter 3, we introduce the bacterial genome. We discuss how they span two orders of magnitude in size and at the smaller end of the spectrum can approximate the theoretical minimal genetic requirement for cellular life to exist. Even the largest bacterial genome is compact and information-rich, in contrast to ‘junk’-filled genomes of the so-called higher eukaryotes like ourselves. We see how this is a reflection of the degree to which Darwinian natural selection operates on the genomes of various organisms.

In Chapter 4, we ask what the forces are that determine the range of bacterial genome sizes. Gene loss underlies parasitic lifestyles, whereas genome growth is driven by the remarkable phenomenon of horizontal gene transfer by which DNA is transferred, not vertically from parent to progeny, but from one organism to another unrelated one. We ask how the prevalence of these processes compare with the humbler mutation that changes one, or just a few, monomeric units of the DNA polymer at a time, and how these processes reflect the need for bacteria to adapt to their circumstances.

Finally in Chapter 5, we introduce the process of transcription by which the genetic material is read to eventually produce proteins that do the cell‘s work. We talk about how this process is regulated and how this enables rapid adaptation to changing situations. Genetic evolution by mutation or DNA loss or horizontal transfer meets physiological adaptation when genetic changes act on regulators of transcription. We ask how this plays out, especially in the face of collateral damage that any mutation affecting regulators of many processes can suffer. Then we conclude by asking how transcription and replication are factors in determining how the very organisation of the bacterial genome is determined.

Bacterial adaptation is an extraordinarily vast field. A search of the Pubmed database of scholarly biomedical literature with the key "(gene OR genetics OR genome) AND bacteria AND adaptation" returns nearly 60,000 journal articles! This will include influential papers, run-of-the mill works that are the bread and butter of scientists like me, as well as hidden gems that have unfortunately not received as much recognition as they deserve. It is impossible for anyone to read, absorb and write about the entirety of this vast literature. It would be extremely challenging to even represent all the many dimensions of bacterial adaptation that these papers encompass. I have taken a decision of my own volition, reflecting my interest in this field, to limit the ambit of this book to the principles underlying the organisation of the genome, the way it is read by the cell, how these two talk to each other and how all these things together result in bacterial adaptation.

I thank Ganesh Muthu for helping to compile and organise the figures for this book. Nitish Malhotra and Meghna Nandy also suggested figures for some sections. I thank Sunil Laxman for reading most of this manuscript and providing detailed comments and suggestions while also taking the liberty of correcting any minor typos he might have found, making life that much easier for me! I thank Anjali Vinodh, a young high school student at the time, for her comments on the first two chapters of this book. I thank the editorial team at OBP, Alessandra Tosi and Annie Hine in particular, for helping get the book in the shape it is in now. Thanks to Jeevanjot Singh for creating a lovely design for the book cover working with visual material created by Prerana Sudarshan, Ashitha Arun, Inder Raj Singh and Madhumitha Krishnaswamy in my lab. Many thanks to all the scientists and illustrators who made their work available under an open access licence, allowing me to embellish the contents of this book with their work. Working on a book does make demands, not only of the author, but also of his or her family, who may not be invested in his or her research interests. Many thanks to my father, Gayathri, my better half, and Harini and Hamsini for putting up with me.

Most of the first draft of the book (except the sections that almost wrote themselves) were written by hand with fountain pens, especially Indian handmade pens. A shout out to Gama Pens and to Mr. Pandurangan and Mr. Kandan at Ranga Pens for crafting these gorgeous pens!

Finally, I dedicate this book to the memory of Mrs Nagalakshmi, my mother and a teacher to many hundreds more!