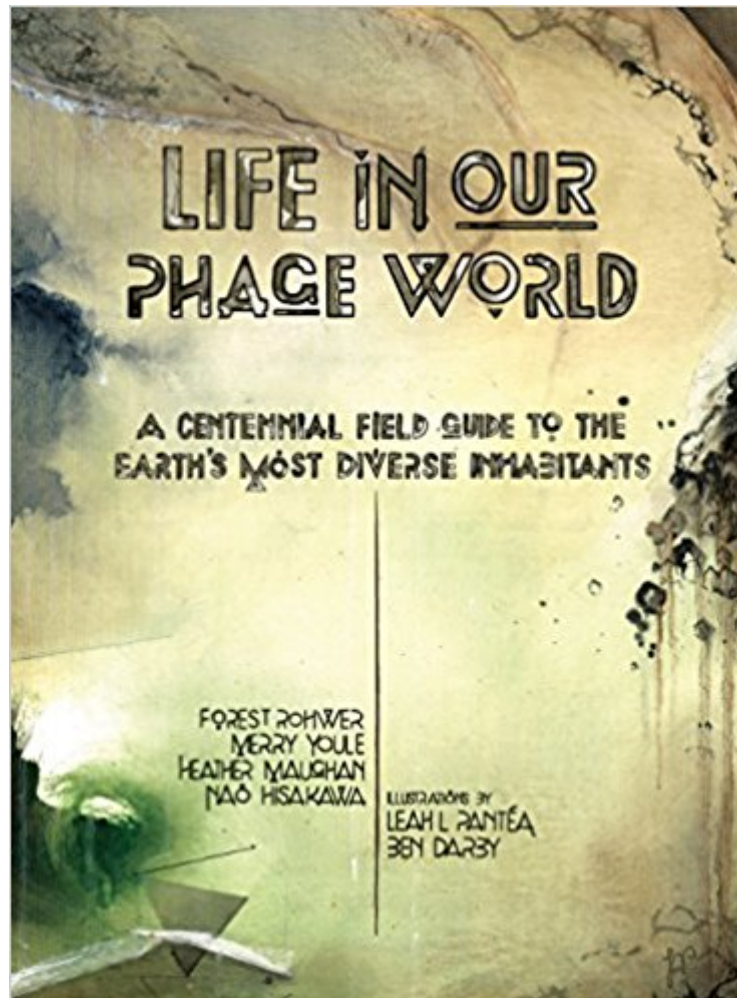




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# Life In Our Phage World



## Synopsis

We share the Earth with more than 10,000,000,000,000,000,000,000,000,000 phages.

Everywhere they thrive, from well-fed guts to near-boiling acidic springs, from cryoconite holes to endolithic fissures. They travel from one microbial host to the next as virions, their genetic weapons packaged inside a protective protein shell. If you could lay all of these nanoscopic phage virions side-by-side, the line-up would stretch over 42 million light years. Through their daily shenanigans they kill or collaborate with their microbial hosts to spur microbial evolution and maintain ecosystem functioning. We have learned much about them since their discovery by Frederick Twort a century ago. They also taught us that DNA, not protein, is the hereditary material, unraveled the triplet genetic code, and offered their enzymes as indispensable tools for the molecular biology revolution. More contributions will be forthcoming since the vast majority of phages await discovery. Phage genomes harbor the world's largest cache of unexplored genetic diversity, and we now have the equipment needed to go prospecting. Although there are field guides to birds, insects, wild flowers, even Bacteria, there was no such handbook to guide the phage explorer. Forest Rohwer decided to correct this oversight, for novice and expert alike, and thus was born *Life in Our Phage World*. A diverse collection of 30 phages are featured. Each phage is characterized by its distinctive traits, including details about its genome, habitat, lifestyle, global range, and close relatives. The beauty of its intricate virion is captured in a pen-and-ink portrait by artist Benjamin Darby. Each phage also stars in a carefully researched action story relating how that phage encounters, exploits, kills, or otherwise manipulates its host. These behaviors are imaginatively illustrated by fine artist Leah L. Pantano. Eight researchers that work closely with phages also relate their experiences as inhabitants of the phage world. Rohwer has years of first-hand experience with the phage multitudes in ecosystems ranging from coral reefs to the human lung to arctic waters. He pioneered the key metagenomic methods now widely used to catalog and characterize Earth's microbial and viral life. Despite research advances, most people, many scientists included, remain unaware of the ongoing drama in our phage world. In anticipation of 2015, the centennial of phage discovery, Forest assembled a cadre of writers, artists, scientists, and a cartographer and set them to work. The result? This alluring field guide-a feast for the imagination and a celebration of phage diversity. Please see Forest Rohwer's website for additional information about this book.

## Book Information

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## Customer Reviews

"...spectacular, unique, trailblazing...I have never seen such a display of scholarship and artistry. You have freed scientific writing from its conventional shackles." -Moselio Schaechter, Distinguished Professor, emeritus, Tufts University, and author of *Microbe and In the Company of Mushrooms*"...an excellent piece of written and visual art for newcomers to phage research and seasoned phage biologists alike. If you think phage are not relevant to your life or research, reading this is sure to change your mind!" -Mya Breitbart, Associate Professor, University of South Florida"Beautiful art, fascinating book and a wonderful historical perspective on the field." -Lita M. Proctor, Project Coordinator, NIH Human Microbiome Project"The illustrations, the stories, and the vignettes are just delightful. It is very difficult to create such a perfect combination of science, art, and human warmth, but the authors have managed this superbly."-- Eugene Koonin, Senior Investigator, National Center for Biotechnology Information"the 21st-century hitchhiker's guide to the (phage) universe...a welcome refresher on phage complexity and diversity that would serve as an amazing resource for biology instructors...even accessible enough for the casual science aficionado to browse..."-review in *Science* magazine by Michael Koeris, Founder and VPO of Sample6.

Forest Rohwer is an internationally known microbial ecologist with an intense interest in phage and their impact on all life on Earth. His studies of ecosystems ranging from coral reefs to the human body have led to more than 150 peer-reviewed research articles. He is a Fellow of the American Academy for Advancement of Science (AAAS), American Academy of Microbiology (AAM) and Canadian Institute for Advanced Research (CIFAR). In 2008 he was awarded the International Society of Microbial Ecology Young Investigators Award and in 2014 was listed as one of the World's Most Influential Scientific Minds (Thomson Reuters). This is his second book with

microbiology writer Merry Youle. Their first book, *Coral Reefs in the Microbial Seas*, was published in 2010.

I have to tell you: I adore this book, and for a number of important reasons. First, it is an accessible introduction and reminder of how central viruses are to the biosphere, with a unique and engaging perspective. With all the talk about the "microbiome" in the news, the more numerous and just as important "virobiome" does not get as much attention or PR. We tend to reflexively think of viruses as "bad," when in fact viruses help keep ecological systems in balance (and that may very well include issues of human health). Bacteriophages, bacterial viruses, are not only fascinating as a model system, genetic tool, and driver of ecological balance....but beautiful to behold. This brings me to something special about this fine book, by authors possessing expertise, writing chops, and enthusiasm (as well as quirky humor): the artwork. I am used to "scientific publications" being somewhat dry and technical. Not so with this publication. This is a beautiful as well as informative tome. If you have any interest in the intersection of art and biology, this book is simply a "must have." Let me say something really important to finish up this review: the system states that this book is "temporarily out of stock," and implies it will take some time to receive. I ordered my copy early January, and received it in less than a week. I have no explanation for the verbiage. If you order this lovely book, you will get it quickly. It's a great book, and sits with pride on my office bookshelf.

Wonderful book, a master piece!

This book stimulated me to start learning about contemporary biology. The last time I had a biology class was in 1961! The drawings really made it fun to read. I also got the book within a week of ordering it.

I absolutely love this book - it's the perfect combination between accurate scientific knowledge, fun personal stories, and a rarely-seen artistic interpretation! I highly recommend this book for anyone with an interest in viruses!

what an impressive summation and perspective(s) of the virus world; thought provoking!

The year 2015 celebrates the centenary of the first documentation of phages by Frederick W. Twort.

Since then, however, phages (the viruses that infect bacteria) have often been ignored, discounted and underestimated. Forest Rohwer and his distinguished co-authors now address this glaring omission. A centennial field guide to the most abundant biological entities in the world has been missing until today. In the tradition of other field guides the authors include a global map showing the known geographic range of each featured phage as well as its habitats. Additionally, phage genomes are represented by two versions. First, an artist-created overview of the variety of genome structures of phages when travelling between virion and host (e.g., linear or circular, single-stranded or double-stranded, sticky ends, direct or inverted terminal repeat nucleotide syntax). Second, a detailed genome map allows the reader to follow each gene, finding information about its function, its homology with other phage genes and the localisation of its protein product. With this field guide a second century of phage study has begun.

**Bacteriophages** A bacteriophage is a virus that infects and replicates within a bacterium only. There are  $10^{31}$  phage virions on earth. This is ten times more than all cells that constitute cellular organisms. Every second,  $10^{24}$  phage infections occur on this planet, whereas lytic infection by a single phage yields 20 to 400 progeny per infectious cycle. In the human gut we can find  $10^{16}$  phage virions. Together there are 4 million families of viral proteins on earth. If all  $10^{31}$  phage virions were placed side by side they would stretch to 42 million light years! The book heralds a second century on phage research, but under very different circumstances. In the first century phages have been viewed as curious prokaryote parasites now they are part of the pre-dominant global virosphere. All chapters start with a description of genome structure, followed by encapsidation methods, the commonly shared host organism and its habitat and a note on its lifestyle, a global map where the samples on this planet have been taken and, interestingly, a detailed map of genome architecture, each segment linked by colours to the various lifestyles typical of phages.

**Main Behavioural Motifs of Phages** In chapter 1 an overview on the phage lifecycle answers the questions of why there are so many genes in such simple organisms and why it is beneficial to have a temperate lifestyle. Additionally, a coherent phage classification for the twenty-first century is presented by Daniel Nelson. This is biosemiotically important because phages code their information into all available nucleic acid sequences from single-stranded RNA to double-stranded RNA to single-stranded DNA and double-stranded DNA. In this same context Forest Rohwer adopts a pioneering role in that he and Rob Edwards put forward the phage proteomic tree, a proteome-based classification system that groups phages relative to their near neighbours as well as in the context of other phages. In chapter 2 an overview of how to test the water for phages is given and, very important, how  $\hat{GOD}^{\text{TM}}$  (Generation of Diversity) is the driving force in phage evolution and survival; this means the generation of variety that paves the

way for biological selection. The brief history of environmental phage ecology from marine to human ecosystems, which means phages use every environment, is also of considerable interest. Mathew Sullivan describes the metagenomic approach in which phages modulate microbial population structures to determine microbe identities. In chapter 3 the entry strategy of phages into their host organisms is investigated. There are several distinct strategies. Virion proteins are discarded and only the genome enters the host cell. However, recent research has demonstrated that nearly all phages package essential proteins inside their virions before placing themselves within host genomes. Some proteins serve as start-up replication tools, others as bodyguards to detect host defences and yet others assist during genome delivery, forming protective tubes for genome passage or escorting the genome into host cell. In chapter 4 the takeover of host replication systems is discussed. When a phage enters a host cell, an abundance of metabolic regulations are organised and regulated for efficient survival and reproduction. The interesting thing is that the phage does not immediately kill its host cell but instead converts the cell into a virocell, a finely tuned virion factory within a complete virion order. This is a complete turnabout and a manipulation of the former cell, but a new dominant genetic content order. In another publication exactly this process rises the question whether virocells represent a really new cellular identity. If this machinery functions to produce a number of virions the cellular organism is executed. However, in this interplay the phages and the targeted host cells continuously develop counter-defence and entry tools and strategies, immune defence and counter-defence both striving constantly for evolutionary novelty in order to reach their goals. Chapter 5 focuses on phage replication and the mosaic construction of phage genomes. The general strategy seems to be to minimise intergenic regions and encode efficient proteins. Additionally, some phages such as Lambda invest in a complex genetic switch to govern lysis or in contrary lysogeny, depending on a decision process. Some phages exchange genes and non-coding regions extensively, which means they are highly dynamic and volatile, as the phage world continuously exchanges information within its own natural genetic language. Chapter 6 investigates how viruses are chromosomally creative. They constantly change or invent their genomic content in order to adapt to emerging new host identities. Phage evolution therefore occurs rapidly. Some replicate within their original approach; others are assisted by helper phages. Importantly, some reuse defective parts which in other content arrangements are reinstated features previously lost or deleted. In difference to decade lasting assumptions that defective viral genetic parts are degraded or at best resource for nucleotide recycling processes it is now obvious that they may play essential roles in new genetic content order. Additionally it must be mentioned that in capsid innovation phages are ingenious

thieves. In chapter 7 escape strategies out of the host are presented. Every bacteriophage with a double stranded genome, whether RNA or DNA, shares a holin-endolysin technique for host lysis. Holins are responsible for lethal lesions in the cell membrane. Interestingly, all known phage holins share similar functions but do not have a common origin. This means that lytic competence does not evolve from a common ancestor but from several roots to generate lysins, a commonly shared tool/technique of escape. Additionally holins indicate the evolutionary origin of nuclear pores of eukaryotic nuclei, a pre-condition for the signaling pathways that regulate replication, transcription and translation in every eukaryote.

### Behavioural Motifs Represented in Gene Word Order

The detailed list after each described phage species and how the gene word order in these phages is structured are especially relevant to biosemiotics. Here we find the interactional motifs in phage life which are not solely about replication but the phage-centred goals that are not the same in cellular hosts and look rather different. Additionally, the stored information that is essential to phage life is clustered. This means the conserved genetic contents that resemble single behavioural motifs are not in a coherent line-up, but are split up into several information tools throughout the genome. The most prevalent motifs in phage gene word order that are commonly shared are: *on the prowl* (for cellular host) *entry* *takeover* (of host replication behaviour), then the two different behavioral motifs: a *lytic replication cycle* or conversely a *lysogenic replication cycle*, followed by the *(re)assembly*, the *escape*. For regulation properties this is followed by *transfer RNAs* and the important regulatory tools hidden in *non-coding RNAs*. Additionally, we know some genetically conserved regions of *multiple functions coded within these sequence structures* and also the *unknown functions of sequences that are relevant in future research*. At the end of the book two Appendices offer special background information such as technical notes (the sources for the field guide data), the strategy for drawing phage *portraits*<sup>TM</sup>, the phage proteomic tree, global maps. If one wants to probe the meaning of biosemiotics one has to look at the context in which a competent agent uses the sign, i.e., the concrete behaviour within its habitat. To biosemioticians the lexicon of phage behaviours in Appendix B is of considerable interest.

### Relevance to Biology

This book provides the ideal accompaniment to the abundance of research results in virology of the last decade. Although it focuses on bacteriophages it constitutes the missing link in the rich world of the virosphere outlined by some of the recent publications. It demonstrates that cellularly built organisms are like islands in a virospheric ocean, and it gives the most coherent overview available of the most abundant biological entities on the planet. Especially in the chapters about adaptive immunity in bacteria, which is the result of highly adaptive and dynamic CRIPR/Cas (clustered regularly interspaced short

palindromic repeats and CRISPR-associated proteins), the authors convincingly demonstrate that the gene word order represented in the genetic code is not the result of selection of mutation (replication errors), or computable and formalisable procedures of self-organisation of matter, or the result of physics and chemistry behaving according to thermodynamic laws. In contrast to these dominant narratives of the evolution of the genetic code for the last six decades it is now evident that viruses and virus-like agents edit the genetic code, determine the gene word order of host organisms, drive evolutionary novelty and remain as adaptational tools in the genomic content most relevant for the survival of their host organisms. This is a major paradigmatic shift not only in biology which means life is not the result of interactions of signs but of interactions of agents that are competent to use signs.

**Conclusion** The book is written by several leading researchers in their field and contains seven chapters with rich appendices of additional information on the phage world. Although the book meets all the criteria of scientific research and investigation it can be read by novices in the field, encouraging each reader to integrate this excellent database into an up-to-date understanding of life in general. Additionally, which is most important, the excellent and unique artwork of Benjamin Darby which illustrates the phage morphology as well as the variety of behavioural patterns is convincingly the best way to drive imagination regarding the fascinating world of biology. Although phages are essentially different from cells of prokaryotes they represent the main habitat for phages. Together with their host they continuously drive the evolution of both and therefore are crucial for microbial ecology. To denote phages as molecular assemblies which function mechanistically as selfish entities really misses the point of these agents.

I have seen the proof copy and highly compliment all who made this book so beautiful to behold. No one will need to struggle with readability. Illustrations are fantastic. All those hours of collaboration have paid off. Congratulations!

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