

Preface

As soon as the right method was found, discoveries came as easily as ripe apples from a tree.

—Robert Koch

We are in the midst of a paradigm change in biology. Animals and plants can no longer be considered individuals, but rather, all are holobionts consisting of the host and diverse symbiotic microorganisms. During the last two decades, numerous studies have demonstrated that these symbionts play a critical role in the physiology of all holobionts including metabolism, behavior, development, adaptation, and evolution. In 2007 and 2008, we presented the hologenome concept as a framework for describing and understanding the complex properties of holobionts (Rosenberg et al. 2007; Zilber-Rosenberg and Rosenberg 2008).

We would like to mention briefly how we came upon the hologenome concept. In 1996, we discovered bacterial bleaching of corals (Kushmaro et al. 1996, 1997). After 6 years of studying the mechanisms of infection (reviewed in Rosenberg and Falkovitz 2004), we observed that the coral had become resistant to infection and bleaching by the specific pathogen, *Vibrio shiloi*. Because corals possess a restricted adaptive immune system and do not produce antibodies, we presented the coral probiotic hypothesis (Reshef et al. 2006) to explain the coral development of resistance to infection by *V. shiloi*. The hypothesis posits that the corals acquired stochastically from the marine environment “beneficial” bacteria that prevent infection by the pathogen. If it is possible to have epidemics of pathogens, why is it not possible (even more likely) to have epidemics of beneficial bacteria? They simply generally go unnoticed. Recently, we have published data that support the coral probiotic hypothesis (Mills et al. 2013). A dynamic relationship exists between symbiotic microorganisms and corals under different environmental conditions that select for the most advantageous coral holobiont in the context of the prevailing conditions.

Although the hologenome concept was inspired by our coral probiotic hypothesis, the concept has been developed by consideration of the vast amount of data published by others on the microbiota of plants and animals, including humans. We especially acknowledge Lynn Margulis (1938–2011), who saw before anyone else the importance of bacteria in the evolution of higher organisms (Margulis 1970, 1992).

Let us mention but a few of the pioneers who used culturing and noncultured molecular techniques to examine microbial communities: in animals, David Relman (Kroes et al. 1999), Jeffrey Gordon (Hooper et al. 2001), Forest Rohwer (Rohwer et al. 2001), Margret McFall-Ngai (McFall-Ngai 2002), Harry Flint (Hold et al. 2003), Martin Blaser (Pei et al. 2004), Rob Knight (Lozupone and Knight 2005), and Ruth Ley (Ley et al. 2005); and in plants, Linda Thomashow (Weller et al. 2002), Steven Lindow (Lindow and Brand 2003), Erik Triplett (Tyler and Triplett 2008), Kiwamu Minamisawa (Ikeda et al. 2010), and Davidi Bulgarelli (Bulgarelli et al. 2012), with apologies to the many other important early contributors to this field.

In this book, we will present and discuss a large number of theoretical and experimental studies that have contributed to the paradigm change in biology, placing them within the broad concept of the hologenome. The first step in many ecological studies is determining the numbers of the different species in the study site. Using DNA sequencing techniques, it is now a routine procedure to determine the relative number of bacterial species in any ecological niche. During the last 15 years, these techniques have constantly been improved and applied to analyze microbial and viral communities associated with various plants and animals, including humans. The data demonstrate that all animals and plants contain abundant and diverse microbiota (summarized in [Chap. 3](#) for bacteria and for viruses in [Chap. 7](#)). Furthermore, it also has been shown that microbiotas are transferred from parent to offspring by a variety of mechanisms ensuring the continuation of each unique hologenome (summarized in [Chap. 4](#)). The biological and biomedical literature contains many reports on correlations between microbial populations and the health and disease of the host. In several cases, the specific contribution of the microbiota to the fitness of the host has been elucidated (summarized in [Chap. 5](#)). We will show that putting together these vast data clearly demonstrates that each holobiont (host + microbiota), with its hologenome (host genes + microbiome), is a unique biological entity, with the sum of the dynamic interactions within the holobiont giving rise to the genotype and phenotype of the organism, as we know it. The hologenome concept posits that the holobiont (host + all associated microorganisms, including viruses), being a unique biological entity, acts also as a level of selection in evolution. Accordingly, changes in either the host genome or the microbiome can lead to genetic variation—the raw material for selection and evolution. [Chapter 6](#) introduces several previously underappreciated modes of variation that became apparent when we considered the holobiont as a level of selection. One of the important sources of variation in holobionts is viruses, which are discussed in [Chap. 7](#). How these variations and others can lead to evolution of animals and plants is discussed in [Chap. 8](#).

Microbial pathogens are a special class of symbionts, which depending upon the particular strain and circumstance, can be harmful or beneficial to the holobiont ([Chap. 9](#)). Practical applications of the hologenome concept, in the form of probiotics, prebiotics, synbiotics, and phage therapy, show promise in promoting health (discussed in [Chap. 10](#)). We argue that understanding the complex

interactions of microbiotas with their hosts to generate holobionts, as unique biological entities, will lead to a greater understanding of many aspects of biology (Chap. 11).

One of the problems we faced in completing this book was each time we completed a draft, important new publications appeared, which caused us to rewrite many of the chapters. This was not surprising because of the fast-moving nature of this subject. Our literature search was completed in November 2013. We thank Ed Kosower, Gil Sharon, Carolyn Elya, and David Gutnick for providing useful references and interesting discussions. It was a pleasure to work with Ursula Gramm and the other editors of Springer-Verlag in bringing the manuscript to publication.

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