

# Preface

Evolutionary Systems Biology is an emerging field and a scientific synthesis in the making. There is currently no single definition that captures all the facets of this fast-developing field (as discussed below, there may never be one). There is, however, one binding aim at the core of this synthesis to understand better the genotype–phenotype mapping at the cellular level and its evolution.

The abstract notions of genotype and phenotype were first proposed by geneticist Wilhelm Johannsen to describe broadly the low-level mechanisms and their higher level manifestations in biological systems. These abstract notions became highly useful to study the evolutionary process at different biological levels. For example, in the context of macromolecules such as RNA, primary sequence and secondary structure can be taken as the genotype and phenotype, while in a cellular context, one can define all the genes and their interactions in a given cell as the genotype and physiological behavior of the cell as the phenotype. Construction of such biologically meaningful genotype–phenotype definitions immediately leads to the natural formulation of several challenging questions: which phenotype a given genotype leads to and vice versa? What are the key features of the genotype–phenotype mapping, is it, for example, a one-to-one mapping or one-to-many? Which evolutionary processes have shaped the genotype–phenotype mapping and how? How does evolution steer in the genotype–phenotype map?

The answers to these questions hold the key to many more specific questions in the context of particular biological systems both at the cellular and higher levels. For example, a full understanding of the genotype–phenotype map in metabolic networks would allow us to predict which environments a cell can survive in, which new environments it can adapt to, and which perturbations would alter its metabolic state (i.e., how robust it is to perturbations). Similarly, understanding how evolution, under specific environmental conditions, shapes the genotype–phenotype map might allow us to infer genetic structures and physiological capabilities in microbes with different lifestyles. Thus, a detailed understanding of the genotype–phenotype map and how evolution steers in it and shapes it at the same time is directly linked to our ability to understand and manipulate biological systems.

Evolutionary Systems Biology, with its focus on better understanding the genotype–phenotype map, is thus bound to be an overarching field linking to several existing fields including systems biology, population and quantitative genetics, systems medicine, and synthetic biology. Research in Evolutionary Systems Biology either uses techniques, concepts, and data generated in these fields, or makes significant contributions to them by providing conceptual and system-specific insights. This is the reason Evolutionary Systems Biology has many facets, employs diverse research techniques, integrates different data sets, and eludes, so far, a compact self-description. The last feature might remain so, even when the field matures, as it might well be that a complete understanding of genotype–phenotype maps requires an umbrella field such as Evolutionary Systems Biology.

The opening chapter of this book aims to define the many facets of this umbrella from philosophical and historical perspectives. The insightful treatment therein also identifies the centrality of the genotype–phenotype map in Evolutionary Systems Biology. A significant part of the current research in the field, covered in the first part of the book, is aimed at understanding the shape of these maps. Chapters 2–7 present several different approaches for achieving this goal and their findings in the context of different genotype–phenotype maps. While a full description of these maps might be difficult to achieve, especially due to high dimensionality of the genotypic spaces considered, it might be possible to identify unique genotypic features that underlie specific phenotypes. Deciphering such potential features (which one might call “design principles”) is discussed in Chaps. 8 and 9. As with any biological property, such features and the overall shape of the genotype–phenotype maps are the result of evolution itself. Thus, a significant research effort is devoted to understanding how combinations of evolutionary processes (adaptive or neutral), environmental conditions (fluctuating environments, species interactions), and biophysical constraints/realities (e.g., noise, multilevel nature of biological systems) shape the genotypes and genotype–phenotype maps. The second part of the book, comprising Chaps. 10–16, gives a detailed summary of the findings of these efforts to date. As illustrated in these two parts, Evolutionary Systems Biology as a field already possesses a strong integrative nature, making use of diverse approaches including mechanistic models, experimental measurements at pathway and cell-scale, comparative analysis of genomic data, *in silico* evolution, experimental evolution, reverse engineering, and system dynamics analyses. Chapters 17 and 18 indicate that combining some of these approaches with quantitative and population genetics might present a highly significant and unique facet of Evolutionary Systems Biology. It is expected that this combination would allow novel findings that would not be possible by employing population genetics and systems biology in isolation. The combination of understanding the key features of genotype–phenotype maps, and the evolutionary forces resulting in these, is already making significant contributions to our understanding of biological systems and our ability to manipulate them. These contributions are exemplified in the context of synthetic biology in Chap. 19 and in the insightful discussion of robustness in Chap. 20.

This collection of chapters represents the first systematic attempt to demonstrate all the different facets of the emerging field of Evolutionary Systems Biology.

It brings together the many aspects of the field and demonstrates its current breadth and wealth. It is possible that some readers might find that certain areas are not represented as much as they should have been or that are all together omitted. I hope that such potential shortcomings are minimal and can be forgiven by the consideration that the primary purpose of this book is to excite and inform the reader about the emerging field of Evolutionary Systems Biology and facilitate its further development. Let us hope that many such volumes will follow this one as the field matures.

Evolutionary Systems Biology increasingly takes shape as a key research direction in our quest towards deciphering broad biological principles. For any researcher who shares this aim, this book will provide a highly interesting and, hopefully, thought-provoking read. Providing the reader with an understanding of the motivation behind Evolutionary Systems Biology, its key findings to date, and the wide range of approaches and data sets it draws on, this book would also serve as a basis for a graduate level course or undergraduate reading club.

I would like to give my sincere thanks to all contributing authors for their timely and hard work in putting this volume together and to Springer and the editorial team led by Melanie Wilichinsky Tucker for their commitment in making it a reality.

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