THE INNER WORKINGS OF LIFE

Living systems are dynamic and extremely complex and their behavior is often hard to predict by studying their individual parts. Systems biology promises to reveal and analyze these highly connected, regulated, and adaptable systems, using mathematical modeling and computational analysis. This new systems approach is already having a broad impact on biological research and has potentially far-reaching implications for our understanding of life. Written in an informal and non-technical style, this book provides an accessible introduction to systems biology. Self-contained vignettes each convey a key theme and are intended to enlighten, provoke, and interest readers of different academic disciplines, but also to offer new insight to those working in the field. With subtle wit and eloquence, Voit manages to convey complex ideas and give the reader a genuine sense of the excitement that systems biology brings with it, as well as the current challenges and opportunities.

Eberhard O. Voit is a pioneer and leader in systems biology, with a passion for education at all levels. He is Professor and David D. Flanagan Chair in Biological Systems, as well as a Georgia Research Alliance Eminent Scholar in the Wallace H. Coulter Department of Biomedical Engineering at the Georgia Institute of Technology and Emory University. He is the author of one of the leading textbooks in the field, wrote one of the first systems biology books published, and has written over 250 scientific articles. His research focuses on genomic, metabolic, and signaling systems, with applications reaching from microbial, ecological, and plant systems to human diseases.

THE INNER WORKINGS OF LIFE

VIGNETTES IN SYSTEMS BIOLOGY

Eberhard O. Voit
Georgia Institute of Technology, USA

CAMBRIDGE UNIVERSITY PRESS

CAMBRIDGE
UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org
Information on this title: www.cambridge.org/9781316604427

First published 2016

Printed in the United Kingdom by Clays, St Ives plc

A catalogue record for this publication is available from the British Library

Library of Congress Cataloguing in Publication data
Names: Voit, Eberhard O., author.
Title: The inner workings of life : vignettes in systems biology / Eberhard O. Voit.
Description: Cambridge; New York : Cambridge University Press, 2016. |
Includes bibliographical references and index.
Identifiers: LCCN 2016005715| ISBN 9781107149953 (hardback) |
Subjects: | MESH: Systems Biology
Classification: LCC QH324.2 | NLM QU 26.5 | DDC 570.1/13–dc23
LC record available at http://lccn.loc.gov/2016005715

ISBN 978-1-107-14995-3 Hardback
ISBN 978-1-316-60442-7 Paperback

Cambridge University Press
978-1-107-14995-3 - The Inner Workings of Life: Vignettes in Systems Biology
Eberhard O. Voit
Frontmatter
More information

Contents

Appetizer

Yes, I called this first section *Appetizer* because *Preface* or *Foreword* is just too boring. Many a preface consists of a laundry list of topics, which the author felt obliged to include, followed by acknowledgments in often cumbersome prose. And even if a preface actually contains true morsels of wisdom, readers don't expect as much and don't do what readers are supposed to do: read it. An appetizer, by contrast, is an artfully created tidbit to whet your appetite. Here it goes loosely with the theme of vignettes, that is, wine, vine leaves and stories that are short enough to fit on them. It is also more in line with the somewhat provocative chapter titles such as *I'd rather be fishin'*, but I will not launch into a laundry list. Mind you, esteemed reader, you are still with me, and I hope you will keep on reading until, as your mother might have said, you have earned the privilege to enjoy the *Dessert*. In the process, I hope to ease you into the fascinating field of systems biology as it attempts to decipher and understand the inner workings of life. As you will see, systems biology uses a lot of sophisticated techniques, all with their own jargon, so this is not exactly an easy topic to discuss. But there are so many exciting things going on in this young field, and in biology in general, that I am convinced you would be at a loss if you remained in the dark. You did not have the opportunity to experience the industrial revolution firsthand, and you may have missed the electronics revolution, so don't miss out on the biological revolution!

Allow me to back up a little and provide some context for the rise of systems biology. To some degree, we all have been systems biologists since our early days. We have marveled at ecological systems in our backyards and across the world, in deserts, on mountains, and in oceans, either with our own eyes and ears, or maybe through magazines and documentaries. We have watched with amazement how tiny ants carry heavy loads into their nests, apparently knowing that this is their assigned task in life and that other ants have their own roles and responsibilities for the greater good of the colony. Time and again we have been perplexed by the beauty of butterflies siphoning nectar from flowers, and the intricacies of complicated food webs that have evolved over eons and have sustained and renewed themselves from one year to the next, in spite of – or maybe due to – their reliance on dozens of plant and animal species.

When we literally dig deeper and analyze a tablespoon of soil, we find not only plant roots and worms and insects, but also hundreds if not thousands of microbial species. They form complex and constantly adapting systems of their own, and without them plants and animals simply could not thrive. Similarly, our gut, our skin, our oral cavity are all home to thousands of microbial species, most of which are beneficial and indeed necessary for our health. But the complexity does not stop there. Each microbe, each plant or animal cell contains myriad genes, proteins, sugars, lipids and uncounted other molecules that play their specific roles for the organism's inner workings and are collectively essential to the well-being of the community of life.

The more we learn about these molecular systems, the more even hard-core scientists are in awe of the enormous complexity with which the components in these systems interact as self-organizing and controlling machines, reacting to signals from the outside and collaborating to mount appropriate and well-coordinated responses. These sub-microscopic systems are so robust and tolerant to all kinds of disturbances that we often take the living world around us for granted. Only if something goes wrong, if our well-being is compromised, whether the problem is a headache, an infection, or the onset of neurodegenerative disease, do we realize how intricate and vulnerable these systems are, and how processes, often entirely unknown to us before, can derail our existence when they fail. Intriguingly, the molecular systems in our cells involve thousands of different molecules and processes, yet they work together so smoothly, and usually adapt so effectively to altered conditions, that we don't even notice their normal function or their compensatory activities and internal rearrangements unless something is out of order.

Systems biology has declared that its goal is to elucidate and understand the functioning and regulation of biological systems under normal and disturbed conditions. That is a tall order, but then again, the potential of reaching, or even just approaching, the goal promises essentially unlimited rewards. Just imagine how well we could address cancer in a personalized manner if we really understood what had gone wrong. Try to fathom the possibilities of reliably steering microorganisms or cells into making valuable medicines cheaply or into churning out lots of food products or energy without negative side effects.

The systems of life contain many different "moving parts," and it is therefore no surprise that their exploration requires a rich mix of diverse expertise. Clearly, one needs vast amounts of data, which immediately implies many types of biomedical investigation, but also the necessity of computer support for data handling and analysis. In addition, systems biology draws heavily from chemistry and physics. It needs sophisticated pure math to decode systems and formulate the laws that govern them, as well as applied math, on which all computer algorithms are based. Last but not least, the field could not possibly prosper without a constant stream of ingenious engineering feats that enable, automate, and miniaturize experimental explorations of ever finer biological details.

As a novel concoction of biology, chemistry, physics, math, computer science and engineering, systems biology is as yet a largely untested, but very promising, scientific endeavor. It has received quite a bit of buzz in recent years, to a point where it has become fashionable to sneak "systems biology" into the titles of articles or applications for research funding. Yet, outside the trenches, many laypeople and scientists alike only have a vague idea of how exactly systems biology intends to attack some of the biomedical grand challenges of our times, what one might realistically expect to be achievable, and what the current obstacles and limitations of systems biology are.

Several textbooks on systems biology have entered the market in recent years, but by the nature of the beast, these publications rely heavily on biological and mathematical jargon. This bridging between actual biological entities and the abstract language of mathematics is necessary to advance the field, and it can be very beautiful – to the expert. Unfortunately, it also triggers in some the all too familiar knot in the stomach that is often associated with everything mathematical. As a result, the curious and well-intended, yet unsuspecting, casual browser in a bookstore may be intrigued by the idea of trying to find out how life works but, opening any current systems biology book, finds so many unfamiliar or long-forgotten symbols and equations, and so much jargon of molecular biology, that the only way to save face seems to be a stroll to an aisle in the bookstore that offers something lighter, much lighter.

I started pondering the feasibility of a book on *Systems Biology without Equal … Signs* many years ago. At first, it was difficult to envision doing the new field of systems biology justice without discussing computing and math, but I convinced myself that there is a big difference between making music or movies and sitting in the audience listening or watching. In fact, deep knowledge of all that's behind a literary play or a piece of art sometimes diminishes the visceral enjoyment that non-experts experience. Most of us do not have the opportunity, or are simply not fit enough, to climb Mount Kilimanjaro, and we will never feel the exhilaration of having made it to the top. Yet, we can vicariously enjoy the views through travelogs on television or in an IMAX theater. Borrowing from these analogies, I hope that you, the reader, will somewhat vicariously enjoy witnessing how we systems biologists are beginning to explore and decipher and understand the inner workings of life.

This book is certainly not an 8:00 a.m., hard-core text that is to be studied for an advanced college class. It is much too casual and non-technical for that. Rather, it is a curling-up-in-a-hammock-with-milk-and-cookies-in-a-summer-breeze read or maybe a deep-thoughts-about-the-secrets-of-life-at-midnight-with-scotch-and-candlelight treatise. It consists of vignettes, each of which is only a few pages long. These vignettes are presented in a loosely logical order, but they are all self-contained. My hope is that each vignette conveys a key thought that enlightens, provokes, interests, is maybe even fun to read, and leads to lasting thoughts that could easily float beyond biology and enter the philosophical realm of life.

Acknowledgments

Notwithstanding the non-preface, I am truly thankful for the support, curiosity, and intellectual stimulation that I regularly receive from my family, students, and peers. Most of all, I really do want to thank Ann Voit and James Wade for reading the entire draft manuscript and giving me uncounted valuable suggestions for improvements. I also express my appreciation to Drs. Edward Harpham, Manu Platt, Rabin Tirouvanziam, and three reviewers, who gave me excellent feedback on some of the material, Vickie Okrzesik for the beautiful cover, as well as Roland Voit for his help figuring out how many notes are in a Beethoven symphony; yes, stay tuned! Finally, I express my gratitude to Katrina Halliday and Victoria Parrin at Cambridge for their most effective and supportive shepherding of the book through the process, from my initial inquiry all the way to its run off the printing press.