ON THE LIVING CELL

A Theoretical Exploration of Biology

Baocheng Pan

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I think, therefore I am.

——*René Descartes*

PREFACE

Life is mysterious! We human beings have been searching for the mystery since the time of Aristotle and even now we are still striving for it. There are not any other scientific disciplines like biology attracting so many researchers and investigators since last decades. Since the 1980s, biology has made many achievements, especially in the field of molecular biology. More recently, the research findings in the field of stem cell biology provided a lot of new insights into the properties of the cell and improved our understanding of the essentials of the cell. Indeed, the experimental results in biology have been accumulated enormously. I am confident that it is high time for us to investigate these experimental results from the theoretical viewpoints and to explore theoretical framework of biology.

The living system and the non-living system are the two fundamentally different systems in the natural world. These two kinds of systems display essentially different features. While philosophy and methodology for the non-living systems are quite sophisticated, we are now still basically at the experimental stage of the study of the living system and most of the current research mainly concentrates on experimental investigation. Undoubtedly, experimental biology has been advancing by leaps and bounds in recent decades. Comparatively, however, theoretical biology has made little progress. Indeed, investigation of the living system still remains at the stage of experimentation, which is the preliminary stage of scientific research. Theoretical biology is a new land with hope and fruits and needs to be explored and cultivated. Even though it seems amazing and attractive, theoretical exploration of biology is very challenging and even risky. In this book I am willing to take such a risk.

The first and maybe the most difficult hurdle for theoretical study of biology comes from the traditional scientific concepts rooted in the philosophy of sciences, which may be more accurately termed philosophy of physical sciences. We have been so accustomed to these concepts which come directly from physical sciences that we take it for granted that they are also applicable to biological sciences and that furthermore they can explain all the phenomena and activities of biological systems. First of all, therefore, we need to investigate the basic concepts from the philosophical perspectives to determine whether or not they are actually valid for biological sciences.

Biology can be classified into two branches, functional biology and evolutionary biology. Functional biology studies structures, activities and interactions and uses experimentation as its research method. Evolutionary biology, on the other hand, investigates historical aspects and uses comparative method. Functional biology uses the similar concepts and methods as physical sciences but evolutionary biology introduces new concepts and uses new methods that are different from physical sciences. Functional biology studies "how" questions and evolutionary biology investigates "why" questions (Mayr, 1997; 2004). The research in this book falls in the category of functional biology, namely, investigation of the "how" questions in biology. Take teleonomy of the living system for an example. The book will not investigate the source from which the system has obtained this property, which is the work of evolutionary biology. The book only studies how this property affects the behaviors and characteristics of the system. Even so, I still want to emphasize that this property should not be classified into the category of vital force or any other supernatural forces. Instead, the property presumably results from the total interactions between all the components of the system, namely, the emergent property of the system when the parts form the whole.

The book mostly studies the basic unit of the living system, namely, the cell. The cell is a living system with many biological components and inorganic elements. It is not a simple machine made up of chemicals. It has its own power and its own intention. If it has to be regarded as a machine, then it must be a

machine with at least an engine because it has its own driving force to fulfill its tasks without any help, signals or directives from the environment.

The book presents one axiom and four basic hypotheses for theoretical biology on cellular level based on my understanding of current concepts and knowledge of biology, with an attempt to use them to describe the principles and mechanisms of biological processes in the living cell. It has six chapters. In Chapter One, the fundamental issues in theoretical biology are discussed, including the limitation of traditional philosophy of sciences, the autonomy of biology, the dual attributes of the living system, and the systems that are most suitable for theoretical study. In Chapter Two, the axiom of survival is proposed and discussion of purposefulness in biology is given mostly based on philosophical considerations. In Chapter Three, the hypothesis of orderliness of the cell is suggested and its application to senescence is discussed. In Chapter Four, the hypothesis of mitosis and cell growth and the hypothesis of meiosis and cellular genetic diversity are proposed and the related corollaries are given. Also the economic principle of cell division is discussed. In Chapter Five, the principle of cell differentiation is hypothesized and the transitions between different types of cells are discussed. In the last chapter, the similarity between the machine code of artificial intelligence and the genome of the cell is investigated. Based on such similarity, a conjecture is presented about the "Final Rules" in theoretical biology.

At present, theoretical biology is still in its preliminary stage. Generally speaking, most of the current works on theoretical biology, in my opinion, should be essentially classified as the works of computational biology. Basically, these researches started with some mathematical models obtained by simplifying some processes of biological systems, and performed calculations using analytical or computational methods of mathematics, and then compared and discussed these results with the experimental results obtained in related biological processes. More importantly, these works usually simplified the living system into physical or chemical system and ignored the fundamental differences between the living system and the non-living system. However, I think that the

main goal of theoretical biology is not just to do such model computation, but to start from the autonomy of biology, and explore the basic concepts and characteristic quantities unique to biology, and establish its own theoretical system.

Writing the book was indeed a tremendously difficult and risky work. There were so many philosophical and scientific hurdles to overcome and the direction and paths for the establishment of theoretical biology were still unclear. In the past seven years, I consulted a lot of literature, including some classical works by pioneers in the fields of biological sciences. There were myriad experimental results and philosophical discussions about the similar topics. Some of them were equivocal and even contradictory to each other. What was worse, there were so few theoretical analyses and concepts available for reference. Indeed, theoretical biology was a brand new field. There was nothing to follow. Therefore, exploration in this field needed not only wisdom but also courage because many years of hard work might end up with nothing.

What was the starting point for the exploration of theoretical biology? After deep consideration for a long time, I thought that philosophy of sciences might be the best candidate because it provided the most fundamental perspective of the nature and could free us of the restriction of the knowledge and concepts of specific disciplines. Once the starting point had been set, I had to keep working hard. The odyssey was full of ups and downs. Sometimes I felt the endeavor to explore the theory of biology as if looking for a needle in a haystack. The truth of biological world looked like a mirage on the Promised Land. It was so attractive but so mysterious at the same time. Sometimes the truth seemed so close to me that it was near my fingertips and sometimes it looked so far away from me that I did not know how to march forward. It was my belief in the simplicity of the Nature and the existence of the theory that kept me going on and on. I was sure that the more I did the closer I would be to the truth.

Based on consideration of the fundamental differences between the living system and the non-living system, the book is intended to explore the principles that govern the processes of living systems. These principles should be

independent of the physical sciences and peculiar to biological sciences. Obviously the theory in this book is preliminary and I do not expect all the statements and discussions in the book are correct. Instead, I would be fully satisfied if my work can serve as a starting point for the theoretical exploration of the principles in the biological world. Even though I know that the theory is immature I still want to share with you because exploration of theoretical biology is a gigantic endeavor and the establishment of theoretical biology relies on participation and cooperation of scientists from various disciplines and different fields. I am confident that when many people come together to investigate theoretical biology we can eventually unravel the mysteries of life. I hope that the immature but interesting concepts and ideas in the book can stimulate your interest in the fundamental issues of biology and philosophy and inspire your enthusiasm to search for the laws and principles of the biological world. I expect that the field of theoretical biology will be more and more promising in the near future.

I remember an interesting story. The main script is as follows: In a dark night, a passerby saw a person looking for something under streetlight and asked: "What are you looking for?" The person answered: "I was looking for a key." The passerby asked: "Where did you lose your key?" The person answered: "I did not know." The passerby asked further: "Why are you looking for it here?" The person answered: "Because there is light here and it is the only place that I can see." This simple story conveyed an important message that if we overemphasize the guidance of the existing concepts and theories, we may get trapped into the cage of the old concepts and theories.

In writing this book, I received a lot of support and help from Professor Tinghuai Wang at Xinhua College of Sun Yat-sen University. He provided me with a stable environment in the campus and gave me continuous encouragement in my work so that I could concentrate myself on the final stage of writing the book. Here, I show my greatest gratitude to him for his great support.

During the whole course of writing the book. I had a lot of discussions and consultations with my colleagues and friends: especially Yu Peng, Shiney

Zhang, Donna Lai, Xiangjun Chen, Li Feng, Yong Xiong, Dehua Pei and Xiaoyu Liu. They provided many constructive suggestions and opinions, which improved the book very much. Without their help and support, the book would not be finished. I hope that the book could serve as a thankful gift to all of them for their help and encouragement.

B. P.
Xinhua College
Sun Yat-sen University
Guangzhou, China
August 22, 2017

我思故我在。

—— 雷内·笛卡尔（*René Descartes*）

前 言

生命是神秘的！从亚里士多德时代起，我们人类就一直努力不懈地探索生命的奥秘，甚至到现在我们还在为之奋斗。近几十年来，没有任何一门科学学科像生物学那样吸引着无数研究人员。从20世纪80年代至今，生物学取得了长足的进步，分子生物学领域表现尤为突出。最近，干细胞生物学领域的研究进展为细胞的属性提供了不少新见解，加深了我们对细胞本质的理解。确实，生物学的实验结果已经累积得相当多了。我深信，现在是我们从理论的角度来研究这些实验结果、探讨生物学理论框架的时候了。

生命系统和非生命系统是自然界中两个根本不同的系统。这两类系统显示出截然不同的特性。虽然我们对非生命系统的研究在理念和方法上已经相当严谨、成熟，但对生命系统的研究我们基本上还处于实验阶段，目前大部分工作主要还集中在实验研究上。毫无疑问，实验生物学在近几十年来发展神速。相对而言，理论生物学研究进展不大。确实，对生命系统的研究仍然停留在实验这样一个科学研究的初级阶段。理论生物学是充满希望和成果的“新大陆”，有待我们去开发和耕耘。它虽然看上去似乎精彩迷人，但事实上生物学的理论探索极具挑战性，甚至是要冒险的。在这本书里我愿意冒这样的风险。

生物学理论研究的第一个障碍或许也是最难以克服的障碍来自于根植于科学哲学的传统的科学概念，而这种科学哲学更准确地说应该是物理科学的哲学。然而，我们已经太过习惯于这些来自物理科学的概念，以至于理所当然地认为它们同样适用于生物学，并且能够用来解释生物系统所有的现象和行为。因此，首先我们需要从哲学的角度来考查这些基本的科学概念，以确定它们是否对生物学依然有效。

生物学可分为功能生物学和进化生物学两大分支。功能生物学研究结构、活动和相互作用，并以实验为研究方法。而进化生物学研究历史特性

和使用比较方法。功能生物学使用与物理科学类似的概念和方法，但进化生物学引入新的概念，使用不同于物理科学的新方法。功能生物学研究“如何”的问题，而进化生物学研究“为什么”的问题（Mayr，1997，2004）。本书的研究属于功能生物学范畴，即生物学中“如何”问题的研究。以生命系统的目的性为例。这本书不会考查系统获得这个属性的来源，这是进化生物学的工作。这本书只研究这个属性如何影响系统的行为和特性。即便如此，我仍然想强调，这种属性不应归入生命力或任何其他超自然力量的范畴，相反，这种属性可能是由系统各组成部分之间的总的相互作用引起的，也就是说，当各部分组成整体时系统所出现的新质。

这本书主要研究生命系统的基本单元——细胞。细胞是一个具有多种生物成分和无机元素的生命系统。它不是一个由化学物质构成的简单机器。它有自己的动力和意图。如果它必须被视为一台机器，那么它至少是一台有发动机的机器，因为它有自己的驱动力去完成任务，而不需要任何帮助或者来自环境的信号或指令。

基于我对现有的生物学概念和知识的理解，本书在细胞水平上提出了理论生物学的一个公理和四个基本假设，试图用它们来描述活细胞中生物过程的原理和机制。全书共有六章。第一章讨论了理论生物学的基本问题，包括传统科学哲学的局限性、生物学的自主性、生命系统的属性二象性以及最适合理论研究的系统。第二章提出了生存公理，并且主要从哲学角度来讨论生物学的目的性。第三章提出细胞的有序性假设，并讨论其在衰老中的应用。第四章提出了有丝分裂和细胞生长假设以及减数分裂和细胞遗传多样性假设，并且给出了相关的推论。此外，还讨论了细胞分裂的经济原则。第五章提出了细胞分化原理假设，并讨论了不同类型细胞之间的转变。最后一章研究了人工智能机器代码与细胞基因组的相似性。基于这种相似性，我提出了关于理论生物学的“终极法则”猜想。

当前，理论生物学仍处于初级阶段。综观目前大部分理论生物学的研究工作，在我看来，本质上应该属于计算生物学的工作。这些研究基本上是以通过简化生物系统的某些过程而获取的一些数学模型为出发点，然后运用数学分析或计算机方法进行运算，再比较和讨论这些结果和相关生物过程的实验结果之间的关联。更重要的是，这些研究将生命系统简化成物理或化学系统来进行研究，而忽视了生命系统和非生命系统之间的本质区别。然而，我认为理论生物学的主要目的并不应该只是做这样一些模型计

算，而应该是从生物学的自主性出发，发掘生物学本身特有的基本概念和特征量，建立其自身的理论体系。

这本书的写作确实是一项极其困难和冒险的工作，要克服许多哲学上和科学上的障碍，而且建立理论生物学的方向和途径还不明确。在过去的7年中，我查阅了大量的文献，包括一些生物科学领域先驱者的经典著作。关于类似课题的实验结果和哲学讨论都有很多，其中有些是模棱两可的，有些甚至是互相矛盾的。更糟糕的是，很少有理论分析和概念可供参考。确实，理论生物学是一个崭新的领域，没有什么可跟随的。因此，在这一领域的探索不仅需要智慧，更需要勇气，因为多年的辛勤工作最终可能是一无所获。

探索理论生物学的出发点是什么？经过长时间的深入思考，我认为科学哲学可能是最好的选择，因为它提供了最基本的自然观，可以使我们摆脱特定学科知识和概念的限制。出发点一旦确定，我就要努力工作了。探索的征程充满了跌宕起伏，有时我觉得探索生物学理论就像大海捞针一样。生物世界的真理看起来就像是乐土上的海市蜃楼，它很吸引人，但同时又很神秘。有时真理似乎离我很近，它就在我的指尖，有时它离我很远，我不知道如何向前走。正是对自然简单性和理论存在性的笃信让我不断地前行。我深信做得越多，我就越接近真理。

考虑到生命系统和非生命系统的本质区别，本书旨在探索支配生命系统过程的原理。这些原理应该独立于物理科学，而且是生物科学所特有的。显然，这本书中的理论是初步的，我并不期望书中所有的陈述和讨论都是正确的。相反，如果我的工作能够作为对生物世界中基本原理的理论探索的起点，我将深感欣慰。虽然我知道理论还不成熟，但我还是想和大家分享，因为对理论生物学的探索是一个巨大工程，并且理论生物学的建立有赖于各个学科和领域的科学家的参与和合作。我相信，当许多人聚集在一起研究理论生物学时，我们最终可以揭示生命的奥秘。我希望书中那些不成熟但有趣的概念和想法能够引起您对生物学和哲学基本问题的兴趣，能激发您对探索生命世界的定律和原理的热情。我期待理论生物学领域在不久的将来会有越来越广阔的发展前景。

我记得一个有趣的故事。故事的大致情节如下：在一个漆黑的夜晚，一个过路人看到一个人在路灯下找东西，便问道："你在找什么？"那个人回答说："我在找钥匙。"过路人问："钥匙是在哪里丢的？"那个人回答：

“我不知道。”路人问：“那你为什么要在这里找呢?”那人回答说：“因为这里有灯光，这是我唯一能看到的地方。”这个简单的故事传递了一个很重要的启示，如果我们过分强调现有概念和理论的指导作用，我们有可能会被困在旧概念和旧理论的笼子里。

在这本书的写作过程中，我得到了中山大学新华学院王庭槐教授的大力支持和帮助。他给予我很多鼓励并在校园里为我提供了安定的工作环境，使我得以专注于这本书的后期写作。在此表示衷心的感谢。

在这本书的整个写作过程中，我与同事和朋友们进行了大量的讨论和磋商，特别是 Yu Peng, Shiney Zhang, Donna Lai, Xiangjun Chen, Li Feng, Yong Xiong, Dehua Pei 和 Xiaoyu Liu。他们提出了许多建设性的建议和意见，大大改进了这本书的内容。没有他们的帮助和支持，这本书就不会完成。我希望这本书能成为感谢他们的帮助和鼓励的礼物。

潘宝成

2017 年 8 月 22 日

于中国广州中山大学新华学院

CONTENTS

All the answers to biology are eventually sought in the cells because all organisms are or once were a cell.

——EB Wilson

Chapter One Fundamental Issues in Theoretical Study of Biology

1.1 Background

What is life? The answer to this seemingly simple question has been being searched for by many philosophers and scientists since the time of Aristotle but until now we still do not have a clear and satisfactory answer. Erwin Schrödinger asked this question in the 1940s and tried to answer it within the framework of physics. He considered the chromosome as an aperiodic solid in which every group of atoms plays an individual role and proposed some concepts such as negative entropy flow to sustain the living system (Schrödinger, 1944). Ernst Mayr studied the meaning of life from the philosophical prospective. He proposed that all biological processes are controlled not only by natural laws but also by genetic programs (Mayr, 1997; 2004). In other words, all living organisms obey two causalities. One is the natural laws that, together with chance, control completely everything that happens in the world of the exact sciences. The other causality consists of the genetic programs that characterize the living world uniquely. The dualism of modern biology is basically physicochemical, and it arises from the fact that organisms possess both a genotype and a phenotype (Mayr, 1997; 2004). Stuart Kauffman studied life from the viewpoint of holism and believed that life is the emergent phenomenon which arises when the molecular diversity increases beyond some threshold values of complexity (Kauffman, 1995). Therefore life is a collective property of systems of interacting molecules. Addy Pross investigated living systems from the basis of