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ORIGINAL ARTICLE

Systems biology, emergence and antireductionism

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Abstract This study explores the conceptual history of systems biology and its impact on philosophical and scientific conceptions of reductionism, antireductionism and emergence. Development of systems biology at the beginning of 21st century transformed biological science. Systems biology is a new holistic approach or strategy how to research biological organisms, developed through three phases. The first phase was completed when molecular biology transformed into systems molecular biology. Prior to the second phase, convergence between applied general systems theory and nonlinear dynamics took place, hence allowing the formation of systems mathematical biology. The second phase happened when systems molecular biology and systems mathematical biology, together, were applied for analysis of biological data. Finally, after successful application in science, medicine and biotechnology, the process of the formation of modern systems biology was completed.

Systems and molecular reductionist views on organisms were completely opposed to each other. Implications of systems and molecular biology on reductionist–antireductionist debate were quite different. The analysis of reductionism, antireductionism and emergence issues, in the era of systems biology, revealed the hierarchy between methodological, epistemological and ontological antireductionism. Primarily, methodological antireductionism followed from the systems biology. Only after, epistemological and ontological antireductionism could be supported.
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1. Introduction

Systems biology is a strategy or a way of thinking how to investigate biological organism. Systems biology studies the organisms as integrated systems composed of dynamic and interrelated genetic, protein, metabolic and cellular components with the help of biology, mathematics, technology and computer science (Auffray et al., 2003; Friboulet and Thomas, 2005; Bruggeman and Westerhoff, 2006). O'Malley and Dupré (2005) classified systems biology on pragmatic systems biology, whose emphasis is on the analysis of molecular interactions at the general level and system–theoretical biology which considers the systemic principles. Both parts of systems biology insist on mathematical modeling (O'Malley and Dupré, 2005).

When and how does systems biology emerged? According to Westerhoff and Palsson (2004) systems biology has two historical roots. The first and the most frequently mentioned root,

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relates to the discovery of the structure and function of the genetic material, as well as on the methods of gene manipulation. Second root is related to the thermodynamic aspects of living organisms introduced in biology during the 40s of the 20th century.

This article discusses three phases of systems biology development. First phase included the transformation of molecular biology into systems molecular biology. This phase referred to the discovery of the structure and function of genes and genetic engineering (Westerhoff and Palsson, 2004). Since 1953, molecular biologists discovered the structure and function of genes and finally, at the beginning of 21st century, deciphered human genome. In postgenomic era, the goal of molecular biology has changed. The search for explanation how complex molecular pathways and networks supported biological structure and function has become a central issue of molecular biology. Shifting from single molecule to molecular network approach definitely marked the emergence of systems molecular biology. The second phase, the development of systems-mathematical biology, referred to the general systems theory (GSS) and nonlinear dynamics of living organisms. Third phase, followed after the convergence of molecular systems biology and systems mathematical biology, relates to the development of systems based medicine, biotechnology and drug discovery.

Systems biology influenced the longstanding reductionism–antireductionism debate. Systems biology view on biology, as being holistic and integrative, was quite opposed to molecular reductionist position (Strange, 2005; Ahn et al., 2006). Reductionists claimed that every biological phenomenon could be explained in terms of molecular biology and ultimately physics. The physics is supposed to be only fundamental science of natural world. Hence, theories and laws of other natural sciences should be explainable by fundamental theories and laws of physics. All sciences should be a part of one unified science. In the 20th century, supporters of the unity of science used theory reduction for the unification project (Bechtel and Hamilton, 2007). Systems biology changed the way we think about the concept of emergence. As being the most important concept discussed in reductionism–antireductionism debate, it deserves necessary reexamination in the light of modern systems biology.

This article deals with conceptual history of systems biology and its impact on important scientific and philosophical issues. First I will argue that systems mathematical biology has two historical roots, general systems theory and nonlinear dynamics. Their convergence leads to modern systems mathematical biology. Afterward, I argued that contemporary systems biology rested on the convergence between systems of molecular biology and systems mathematical biology. The above mentioned convergence enabled application of systems approach to science, medicine, and biotechnology. Only after the completion of all historical steps, the modern systems biology was born. Then, it will be examined the impact of systems biology on longstanding philosophical and scientific conceptions of reductionism, antireductionism and emergence.

2. The birth of systems biology: molecular biology, general systems theory, and nonlinear dynamics

What are the differences between molecular biologist and systems biologist view on biological systems? Ahn and colleagues have made some of the crucial distinction between reductionist and system-oriented view on the biology (Ahn et al., 2006). When it comes to the underlying principles, the two approaches differ in understanding how biological systems behave. In reductionist view, the behavior of biological systems can be explained by the properties of components. The system oriented approach insisted that biological systems have emergent properties that only can have a system as a whole and not its constituent parts. The metaphors used by these two approaches are quite different: machine/magic bullet versus network. Considering the approach, reductionism gives explanatory significance only to one factor, while the system biology considers a number of factors in order to describe the behavior of dynamic system. In reductionist approach the critical factors are directly determining while in the system view it depends on time, space and context. According to reductionist approach, the characteristics of models that explain the behavior of the system are linearity, predictability and determinism. Contrastingly, the systems approach insists on nonlinearity, sensitivity to initial conditions, stochasticity (probabilism) and chaotic behavior. Systems-oriented overview of the concept of health in medicine implies robustness, adaptability/plasticity and homeodynamic (dynamic understood homeostasis). The reductionist approach emphasized the normalcy, reducing exposure to risk and static homeostasis. Obviously reductionist and systems view on biology are quite different. When and how does this Copernican revolution in biology happen?

From the early days, molecular biology treated the components of a cell as static and isolated, neglecting the dynamical interaction between them. But, the methodological aspect of reductionist approaches had a good side. After all, this approach influenced the development of so many diverse molecular techniques. Without them scientists would not be able to identify genes, molecules and processes, and surely human genome project would have never happened. Hence, the systems molecular biology would not exist. The negative side of reductionist molecular approach referred to lack of holistic and integrative knowledge of biological processes. As molecular biologists acquire vast number of facts about DNA, RNA and proteins, it becomes more difficult to give explanation of what organism is. Thus, how to connect molecular processes with higher level biological phenomena becomes the issue. Therefore, instead of concentrating on the physiochemical and biological properties of single or limited number of molecules, the priority has become to find out how the molecular networks assembled and function. Finally, the completion of human genome project directed molecular biology toward systems molecular biology. By developing the systems molecular biology, molecular biologist made the first step toward contemporary systems biology.

During the second half of 20th century systems mathematical biology existed in parallel with molecular biology. The term systems biology was introduced by Mihajlo Mesarovic in 1968 (Mesarovic, 1968; Mesarovic et al., 2004), but there are opinions that the term may be introduced in the 1920s by Ludwig von Bertalanffy, the father of general systems theory (Drack, 2007). However, Mesarovic applied general systems theory in order to discover how biological objects relate, rather than what they are composed of (Mesarovic, 1968; Mesarovic et al., 2004). Before the pioneering work of Mihajlo Mesarovic, general systems theory was developed by

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