Available online at www.sciencedirect.com

ScienceDirect

Physics of Life Reviews 12 (2015) 44–64

PHYSICS of LIFE reviews

www.elsevier.com/locate/plrev

Review

On the interplay between mathematics and biology Hallmarks toward a new systems biology

Nicola Bellomo *, Ahmed Elaiw, Abdullah M. Althiabi, Mohammed Ali Alghamdi

Department of Mathematics, Faculty of Sciences, King Abdulaziz University, Jeddah, Saudi Arabia

Received 13 October 2014; received in revised form 3 December 2014; accepted 3 December 2014

Available online 5 December 2014

Communicated by J. Fontanari

Abstract

This paper proposes a critical analysis of the existing literature on mathematical tools developed toward systems biology approaches and, out of this overview, develops a new approach whose main features can be briefly summarized as follows: derivation of mathematical structures suitable to capture the complexity of biological, hence living, systems, modeling, by appropriate mathematical tools, Darwinian type dynamics, namely mutations followed by selection and evolution. Moreover, multiscale methods to move from genes to cells, and from cells to tissue are analyzed in view of a new systems biology approach.

Keywords: Kinetic theory; Stochastic differential games; Evolution; Mutations; Systems biology; Active particles

1. Motivations and plan of the paper

The main motivation for the contents of this paper is the expectation of the scientific community who looks forward to a mathematical formalization of phenomena in the life sciences similarly to what, in the past two centuries, was the development of mathematical methods in the physical sciences. Namely, it is expected that the heuristic experimental approach, which is the traditional investigative method in the biological sciences, will be systematically supported by rigorous methods offered by hard sciences and, in particular, by mathematics. One of the challenging objectives is the development of a *mathematical biology* with some analogy with the theories developed by mathematical physics.

Several hints can be recovered in the existing literature both in fields of biology and mathematics. Two of them are selected among others. The first one appears in the field of biology by Nobel Laureate Hartwell who, in a celebrated paper [1], stated the following:

* Corresponding author.
E-mail addresses: nicola.bellomo@polito.it (N. Bellomo), aelaiwksu.edu.sa@kau.edu.sa (A. Elaiw), aalroqi@kau.edu.sa (A.M. Althiabi), Proff-malghamdi@hotmail.com (M.A. Alghamdi).

http://dx.doi.org/10.1016/j.plrev.2014.12.002
1571-0645/

Biological systems are very different from the physical or chemical systems of the inanimate matter. In fact, although living systems obey the laws of physics and chemistry, the notion of function or purpose differentiate biology from other natural sciences. Indeed, cells are not molecules, but have a living dynamics induced by the lower scale of genes and is organized into organs.

Going through the literature in the field of mathematics, an additional important hint can be found in the essay by Gromov [2], Abel prize for mathematics, who, in the abstract, states the following:

Mathematics is about "interesting structures". What makes a structure interesting is an abundance of interesting problems; we study a structure by solving these problems. The worlds of science, as well as of mathematics itself, is abundant with gems (germs?) of simple beautiful ideas. When and how many such an idea direct you toward beautiful mathematics?

The first hint, which is the viewpoint of a biologist, motivates the search of new mathematical tools suitable to understand the complexity of biological systems. Therefore, mathematicians should go beyond traditional methods used for the inert matter, which definitely fails in the case of living entities. This means overcoming the pessimistic overview by Wiegner [3] by new ideas, namely new frontiers of applied mathematics. The second hint indicates how the quest for new methods should end up with the design of mathematical structures appropriate to constitute the background of any development of interest for the applications. Both sentences can be interpreted in the light of the same objective.

Gromov pursues the idea of looking for structures suitable to capture the main feature of biological systems as documented by his studied Mendelian dynamics [4]. It is a highly interesting contribution to be related to the multiscale essence of all biological phenomena. Moreover, it is worth observing that the author suggests more than what contained in the just quoted sentence. In fact, he states that a structure might even be richer than that needed by a well defined modeling project. Therefore, mathematicians are motivated to investigate all properties of the said structure looking at its complete predictive ability. This idea is shared by the authors of this paper, where the last section is devoted to this speculation.

As it is known, theoretical biologists hunt for a new systems biology approach as one of the conceivable great discovery of this century [5–7]. Bearing all above in mind, the following research fields will be examined in the critical analysis proposed in this paper in view of the aforesaid new ideas and developments:

– *Interplay between the theory of evolution* [8–12], *and mathematics* focusing on the recent mathematical approaches which aim at providing a general framework to model mutations and selections [13–15].
– *Biological theory of the immune competition* [16] related to learning [17,18] and evolutive dynamics of the immune system [19].
– *Mutations and selection in biology referred to specific pathology such as cancer dynamics* [20–25] as well as to the immune system and related mathematical models [26,27].
– *Mathematical tools of the kinetic theory for active particles* developed from [28] to [29] and [30], which includes migrations over networks.
– *Theoretical tools of evolutionary game theory*, among others [31–36], to model interactions at the different scales, which appear in biological systems. The dynamics of games can appear both in graphs [37], or on small networks [30].
– *Multi-scale links* between the molecular scale and that of cells as studied in various papers, e.g. [38–47], and between the cellular scale and that of tissues, among others [48–57].
– *Networks*, mathematical theory and applications, see, among others, [30,58–61].

A detailed and "critical" analysis of the pertinent literature guides the contents of this present paper, which is devoted to the quest for a systems biology approach based on mathematical tools specifically derived to model living systems. More in detail and anticipating contents of next sections, the hallmarks of such approach are the following:

(i) Understanding the complexity features of biological, hence living systems, and developing critical analysis of the existing literature in the field of mathematical sciences;