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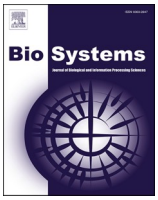

Editorial: The foundations of mathematics and theoretical biology

Since the early 1950s, marked by the revolutionary discovery of the double helix structure of DNA by Francis Crick and James Watson, biology has probably been the most intensively developing natural science. In spite of a remarkable progress made during the last century, theoretical foundations of biology remain in a nascent state, which can be compared with the state of theoretical physics before Newton. A variety of mathematical approaches of different degrees of effectiveness, generality and abstractness, which are currently used in biology, has not converged so far into a set of mathematical methods and principles that would form part of theoretical foundations of this science. Robert M. May, an Australian- British physicist and biologist, wrote in 2004:

> A paradigmatic account of the uses of mathematics in the natural sciences comes, in deliberately oversimplified fashion, from the classic sequence of Brahe, Kepler, Newton: observed facts, patterns that give coherence to the observations, fundamental laws that explain the patterns […]. Consider the role played by applications of mathematics in sequencing the human and other genomes […]. The sequence information, however, represents only the Tycho Brahe stage. Current work on various genomes uses pattern-seeking programs to sort out coding sequences corresponding to individual genes […]. Again, elegant and sometimes novel mathematics is involved in this Keplerian stage of the work in progress. We are only just beginning, if that, the Newtonian stage of addressing the deeper evolutionary questions posed by these patterns. (May 2004).

Foundations of Mathematics (FOM) is a field of study at the junction of mathematics, logic, and philosophy. In the 20th century, the mainstream FOM developed into a rather specialized research that combined the methods of mathematical logic with some philosophical reasoning about mathematics. The mainstream FOM revealed many unexpected properties of mathematical theories such as their incompleteness discovered by Kurt Gödel back in 1931. However, as many working mathematicians have stressed, FOM in this particular form appeared to be largely irrelevant to their works and concerns. In particular, the mainstream 20th century FOM remained wholly silent on what Eugene Wigner famously called the "unreasonable effectiveness" of mathematics in the natural sciences (Wigner, 1960). Some mathematicians reacted against this divide between mathematics and its foundations by making independent attempts to develop new "practical" foundations for their science.

Vladimir Voevodsky (1966–2017). By courtesy of Voevodsky Archives (https://www.math.ias.edu/Voevodsky/).

The most recent significant attempt of this sort is due to Vladimir Voevodsky who designed new perspective foundations for mathematics, which he called the Univalent Foundations (Grayson, 2018). The present Special Issue is dedicated to the memory of Vladimir Voevodsky (1966–2017) who invested his time and energy to renewing foundations of mathematics in view of prospective applications of mathematics in theoretical and applied sciences including biology.

Thus, the Foundations of Mathematics referred to in the title of this Special Issue are foundations in a *practical* sense that, by William Lawvere's word

> […] makes explicit the essential general features, ingredients, and operations of a science, […][and] provides a guide to [its] learning,

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use, and further development. (Lawvere and Rosebrugh, 2003), p.235]

So understood, FOM include the problems of applicability of mathematics in the natural sciences as their essential part. A study of FOM in the context of theoretical biology presents a double challenge and a double opportunity. First, it involves reconsidering and rebuilding the junction between mathematics and natural sciences on their fundamental level. Second, it involves a more specific problem of developing mathematical foundations for theoretical biology. As it has been explained above, there are strong reasons to believe that this latter task cannot be accomplished separately from the former.

In this Special Issue, we tried to find a balance between three focal points. Firstly, three articles (Shabat, 2021), (Rodin, 2021), (Fimmel, 2021) present the work of Vladimir Voevodsky in the field of foundations of mathematics and (theoretical) population dynamics with a special focus on his ideas about the role of mathematics in natural sciences. Secondly, the articles (Iurato and Igamberdiev, 2020), (Louie, 2020), (Maruyama, 2021), (Igamberdiev and Brenner, 2021), (Blanchard and Longo, 2021), (Borovik, 2021) which concentrate on scientific-philosophical and historical questions around the connection of the foundations of mathematics to theoretical biology. Finally, the third focus (Shelah and Strüngmann, 2021), (Basieva et al., 2020), (Dragovich et al., 2020), (Ignatov, 2021) presents some novel mathematical approaches to put theoretical biology on a stable foundation.

Let us now take a more detailed look at specific topics and articles in the Special Issue starting with the focus on Vladimir Voevodsky's contribution to mathematics and the understanding of its role in the natural sciences.

George Shabat (2021), the first mathematical instructor, a co-author and friend of Vladimir Voevodsky, provides a very personal description of some aspects of Vladimir's mathematical development and ideas, which is based on his memory and an experience of joint mathematical work.

Andrei Rodin (2021) reconstructs, on the basis of archival sources, Voevodsky's general ideas regarding the role of applied mathematics for the natural sciences and, conversely, of mathematical applications in natural sciences as a source of new ideas in mathematics itself. Rodin shows a conceptual link between these ideas and Voevodsky's work on the Univalent Foundations of mathematics, and proposes some ways of their further development.

Elena Fimmel (2021) provides a concise commentary on Voevodsky's unpublished manuscripts related to his attempt to develop a mathematical theory of population dynamics, which will be hopefully useful for anyone who may wish to further develop Voevodsky's unfinished projects in this area of research.

One of the first attempts to use mathematics for biological questions was the famous book by D'Arcy Thompson "On Growth and Form" written at the beginning of the 20th century, which is honoured in this Special Issue with the article by Giuseppe Iurato and Abir U. Igamberdiev (Iurato and Igamberdiev, 2020). The pioneering work by D'Arcy Thompson paved the way for new ideas in the field of structuring biological knowledge. The authors point to its role in the development of the Relational Biology by Nicholas Rashevsky and Robert Rosen as well as this in the development of the structuralist approach to evolutionary biology, especially the new view on epigenetic factors, complementary to the functionalist approach based on the Darwinian ideas.

Since then, only a few attempts to give biology as a whole a solid foundation are known to have found serious resonance. One of the best known of these attempts, which unfortunately did not have a significant impact on the overall course of biology as a science, was Relational Biology, developed mainly by N. Rashevsky and R. Rosen. In the Special Issue, the article written by a student and popularizer of Rosen's theory Aloisius H. Louie (2020) is devoted to the subject.

Yoshihiro Maruyama (2021) gives an example of the application of Category theory in the cognitive science. He presents a category-theoretical apparatus, which has been earlier successfully applied in Quantum Information, and then applies it for modelling human reasoning in the presence of what he calls cognitive biases. In this context Maruyama discusses related epistemological and ontological issues and develops a structuralist methodology for Cognitive Science. He argues that the structural similarity of certain quantum physical processes and cognitive processes revealed with Category theory shows that the mind is *structurally* quantum but not that the mind is quantum.

Abir U. Igamberdiev and Joseph E. Brenner (Igamberdiev and Brenner, 2021) provide an original realistic perspective on mathematics and its logical foundations, which differs drastically from the standard forms of Mathematical Platonism. They argue that mathematics in its human symbolic form is rooted in the constitution of living systems and their evolution. In this context Igamberdiev and Brenner consider some recent approaches in the foundations of mathematics including Category theory and Univalent Foundations as well as certain developments in the philosophical logic. More specifically the authors analyze the concept of computation and its emergence in the living systems. Finally, Igamberdiev and Brenner bring the notion of epistemic cut to the fore, and provide a naturalistic account of separation between the observer and the observed reality.

Enka Blanchard and Giuseppe Longo (Blanchard and Longo, 2021) explore an analogy between the formal axiomatic systems in mathematics and what the authors call the genocentric approach in molecular biology. According to this latter approach, the genotype of an individual organism comprises the full information about the molecular dynamics and even the phenotype of this organism. Referring to the classical metamathematical results and to some new biological evidence, the authors demonstrate the limits of the two approaches. On the positive side, the authors stress the importance of contextuality and historicity both in biology and in mathematics.

Alexander Borovik (2021) explores the apparent contrast between the effectiveness of mathematics in physics and the relatively low effectiveness of mathematical approaches in biology. Borovik's paper is motivated by the author's reflexions on his past collaboration with Israel M. Gelfand, who made significant contributions to the mathematical biology and shared with the author his ideas related to this subject. After a thorough analysis of various aspects of relationships between mathematics, physics and biology, Borovik comes to the conclusion according to which todays mathematical theories can hardly be successfully applied in biology beyond genomics and related areas. He describes a broad projects of developing new mathematical theories and approaches apt for biological applications, where stochastic methods and a new generation of Artificial Intelligence is supposed to play a major role.

Saharon Shelah and Lutz Strüngmann (Shelah and Strüngmann, 2021) present some aspects of infinite combinatorics with the aim of making it accessible to interested biologists without a systematic mathematical background. The main focus of their paper is on the theory of forcing, with the aid of which it was proven in the 1960s that the famous Continuum Hypothesis is undecidable and which was later developed considerably further by the first-named author of the article. The description of development of ideas in the field of the foundations of mathematics in the 20th century, starting with the Set theory by Georg Cantor, and ending in the theory of forcing, is embedded in a scientific-historical context, which is very helpful for understanding the topic. In the article, it is impressively shown how powerful the theory of forcing is. Using as an example the construction of circular genetic codes it is speculated that this theory, which is not a part of the standard toolkit for even the most professional mathematicians, can be used for biological applications.

Irina Basieva, Andrei Khrennikov and Masanao Osawa (Basieva et al., 2020) present a new approach to modelling the behaviour of biological systems, based on the formalism and methodology of quantum mechanics, but without addressing micro-level modelling of real quantum physical processes in biosystems such as cells. The authors call

this type of modelling quantum-like, emphasizing the importance of the development of the quantum information theory for that and even speak of the emergence of the quantum information biology. For a better understanding of the subject and for the convenience of the reader, the article explains briefly and non-specialist friendly the basics of quantum probability theory with special attention to its differences from classical probability, as well as the fundamentals of the theory of quantum instruments in general. The theoretical tools developed in this paper are then used for demonstration purposes, including modelling of combinations of cognitive effects and of gene regulation in glucose/lactose metabolism in *Escherichia coli* bacteria.

Branko Dragovich, Andrei Khrennikov, Sergei Kozyrev and Natasa Mišić (Dragovich et al., 2020) argue that due to its naturally existing hierarchical structure, *p*-adic mathematics is particularly well suited for modelling biological phenomena in which usual quantitative methods meet difficulties. After an overview of the basics of *p*-adic analysis written for non-mathematicians, some important examples of *p*-adic and in general ultrametric modelling in biology, especially the modelling of cognition, genetic code and proteins, are given.

An interesting hypothesis that *p*-adic arithmetic can be used to model the morphology of biological organisms is elaborated in detail by Victor V. Ignatov in the article (Ignatov, 2021) and substantiated with numerous computer calculations. Thus, the article is linked to both the classical work by D'Arcy Thompson "On Growth and Form" (see (Iurato and Igamberdiev, 2020)) and the article by Dragovich et al. (2020) from the current Special Issue.

We hope that the ideas and approaches presented in the Special Issue will be found interesting by the relevant research community and serve to further development of the interplay between mathematics and theoretical biology.

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