frontiers | Frontiers in Physics

TYPE Editorial
PUBLISHED 20 February 2023
DOI 10.3389/fphy.2023.1161890

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Biophysics, a section of the journal Frontiers in Physics

RECEIVED 08 February 2023
ACCEPTED 10 February 2023
PUBLISHED 20 February 2023

CITATION
Formosa-Jordan P, Holloway DM and Diambra L (2023), Editorial: Pattern formation in biology.
Front. Phys. 11:1161890.
doi: 10.3389/fphy.2023.1161890

Editorial: Pattern formation in biology

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KEYWORDS

patterning, Turing patterns, biological patterns, morphodynamics, segmentation, morphogenesis, modelling, nonlinear dynamics

Editorial on the Research Topic
Pattern formation in biology

Cells can self-organize in time and space forming biological patterns [1]. Examples of pattern formation in biology are very diverse and can be found in a wide variety of tissues and organisms. For instance, the segmentation process along the longitudinal axes of vertebrates and invertebrates [2, 3], the fine-grained mixtures of different cell types appearing in both plant and animal tissues [4], the regular arrangement of organs along the plant shoot [5], and the cell polarity patterns appearing in multiple cell types [6], among many others. Pattern formation arises from the coordination and interplay of several mechanisms and processes across molecular, cellular and tissue scales. At the cellular level, growth, cell fate specification, migration and cell–cell interactions can be important and influence each other during the formation of a tissue. All these processes are finely orchestrated in space and time by gene expression, which in turn can also be affected by these processes. Over the past two decades, the study of pattern formation in biology has attracted the attention of many scientists from diverse fields, ranging from developmental biology, cell biology and synthetic biology, to physics, mathematics and computer science. Quantitative and interdisciplinary approaches have become essential for understanding these challenging phenomena [7, 8].

This Research Topic contains a collection of articles and reviews that use quantitative and interdisciplinary perspectives to understand the underlying mechanisms driving biological pattern formation. Modeling morphogenetic processes, gene regulatory network dynamics and morphogen gradients link the articles of this Research Topic, with a focus on three research areas: 1) underlying mechanisms of patterning processes; 2) cross-talk of morphogenetic and pattern formation processes, and 3) mathematical methods for modeling and quantifying biological patterning and morphogenesis. Below, each of the present Research Topic papers is briefly discussed.

One of the most celebrated mechanisms to explain self-organizing spatial structures is known as the Turing instability [9–13]. Lacalli's review provides a history of the application of Turing's ideas in developmental biology, which he has been a part of since the 1970's. In particular, Lacalli emphasizes the progress that can be made by investigating and understanding the role of such physicochemical systems that can make patterns *de novo* within the context of evolved biochemical or gene regulatory networks and that confer some degree of "programmatic assembly" on developmental phenomena. Lacalli details ways in which the relative contribution of *de novo* and programmatic elements may manifest in the generation of robust body and brain structures, including consciousness.

Certainly, although today there are no doubts about the Turing instability as a source of symmetry breaking in biological patterning, the molecular mechanisms behind Turing

remain difficult to validate experimentally, as many of the kinetic parameters cannot be reliably assessed in biological tissues.

Experiments and modeling have continued to reveal new extensions or alternatives to Turing for periodic pattern formation. The spatial patterns driven by Turing instabilities are stable structures historically associated with stable fixed points of the system [9–12]. However, exploring a known morphogenetic model [14], Guisoni and Diambra find that Turing patterns can also exist associated to unstable fixed points, enabling in this case the emergence of transient and also metastable spatial patterns.

In line with Turing ideas, Casanova-Ferrer et al. describe former and more recent quantitative modeling studies of heterocyst patterning in filamentous cyanobacteria in an in-depth review. In this case, in addition to an activator-inhibitor system, a particular type of Turing system, there exists another inhibitor gen, hetN, whose production is restricted to the heterocysts. This cell–cell scale inhibition provides an additional dynamics in the pattern formation, extending the diffusion-based Turing mechanism.

Iber and Mederacke offer a detailed state-of-the-art report on tracheal ring formation, reviewing recently elucidated molecular regulatory interactions. Despite these advances, the mechanism forming periodic rings in the trachea remains poorly understood. In this regard, the authors describe several putative mechanisms that could be better explored, such as chemotaxis, differential adhesion, and differential growth of two adjacent tissue layers, in addition to Turing instabilities.

A classic example of patterning is the periodic structure formed during somitogenesis resulting from the interplay of oscillatory gene expression and a maturation wavefront [2]. Carraco et al. provide an extensive bibliography on the embryonic clock of vertebrates over the last 25 years, with special emphasis on the understanding of species-specific oscillation periods, where similar gene architectures produce different periods in different contexts. Fernández Arancibia et al. propose a modified reaction wavefront model [15] which sequentially produces segments in the zebrafish notochord in a periodic manner, even in the presence of noise. In particular, the new model adds a reaction wavefront that sequentially activates the chemical reactions of the FitzHugh–Nagumo model [12].

Besides mechanisms based on biochemical interactions, there is a great deal of interest in how mechanical cues also drive biological patterning [16, 17]. Song et al. study the formation of the gastrovascular canal network in jellyfish through a combination of anatomical studies and mechanical modeling. The authors propose that mechanical stress acts as a trigger of differential growth of the canal network. Contraction during swimming is different for different parts of the tissue, and depends on the stiffness of the canal network itself. In this way, differential stiffness influences the growth direction of the canals and biases the connectivity of the canal network, affecting morphogenesis.

In addition, Moreno and Alonso address the interaction between pattern formation and locomotion at the cellular level. They performed a numerical analysis of a model of amoeboid cell morphology dynamics proposed in [18] and found that polarization, based on bistability, is sensitive to changes in parameter values. The authors introduce mass conservation constraints to increase the robustness of the model.

How cells are geometrically organized and packed in space is crucial in the formation of tissues and organs. Iber and Vetter review and discuss the physical principles driving 3D cellular organization and packing in tissues, focusing on the case of pseudostratified epithelia, a type of epithelia found in animal tissues where nuclei are positioned along the apical–basal axis. The authors propose a new geometrical shape, which they term "punakoid", whose irregular shape is reminiscent of the rocks at the beach of Punakaiki in New Zealand.

Finally, adequate mathematical tools and methodologies are critical for ensuring robust and reliable predictions from biological patterning models. From a more methodological and theoretical perspective, Mjolsness presents a fundamental study about dynamical graph grammars. In this work, the author extends the framework introduced in [19] and proposes a general expression that reduces products of rewrite rule operators to sums of such operators, resulting in two theorems that comprise a general modeling framework. Mjolsness presents an application of this multiscale mathematical method for modeling microtubule dynamics of the cytoskeleton in plant cells.

The spatial patterns of Min proteins on bacterial cells have been extensively studied with respect to pattern-formation mechanisms [20]. However, the transient and irregular nature of these patterns makes image processing and extraction of pattern quantities, such as wavelength, challenging. Meindlhumer et al. introduce a new analysis pipeline that quantifies temporal and spatial information from data images, which could provide a more reliable support for model development.

Pattern formation has been classically modeled and simulated in systems that are continuous in space [9, 10]. Yet, it has been increasingly important to have computational frameworks that can simulate biological pattern formation taking into account the underlying cellular spatial structure [7, 21] a feature that is limited in continuous models. In the last few years, several agent-based modeling frameworks have emerged, in which cells are treated as individual agents whose dynamics are governed by rules. Pleyer and Fleck discuss the use of agent-based modeling on cellular systems and multicellular pattern formation, and review different available computational frameworks of interest.

We hope this Research Topic will stimulate further studies from mathematical biologists and theoreticians interested in modeling biological patterning.

Author contributions

LD, PF-J, and DH conceived and wrote the editorial.

Acknowledgments

We would like to thank all the authors in the articles of this Research Topic for their contributions, all the reviewers for their constructive comments and Jizeng Wang for participating as guest Editor. PF-J acknowledges for being funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy—EXC-2048/1—project ID 390686111 and by the Max Planck Society (Germany), DH acknowledges the support of BCIT and NSERC Canada, and LD acknowledges the support by CONICET (Argentina).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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