Topological defects in biological matter

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Topological defects play an important role in biology, as shown by a growing body of evidence. Aleksandra Ardaševa and Amin Doostmohammadi survey the new research directions that are opening.

Nature relies on the subtle balance between order and disorder. In condensed-matter systems and in high-energy physics, breakdown of order can lead to the formation of topological defects — singular regions where the order parameter collapses. Because of their topological nature, these defects are protected against structural deformations and their removal requires energy: no smooth rearrangement of the order parameter can eliminate the topological defects. As such, in many circumstances topological defects carry a physical function. A striking example is the vortex and antivortex pairs in superconductors, which lead to the emergence of finite resistance[1]. Remarkably, in addition to classical applications in condensed-matter and high-energy physics, there is now a growing line of evidence that suggests the crucial role of topological defects in biology.

Living topological defects

Orientational order is pivotal in a range of biological systems at different scales. It can be seen simply by looking at the alignment of individual cells or subcellular elongated filaments inside the cells. Because the orientational order drives complex multiscale phenomena, such as cell migration or transmission of mechanical and biochemical signals, any disruption in the order may carry a biological response. Indeed, such a breakdown of order and the formation of topological defects has long been identified in biological systems spanning length scales from subcellular filaments and motor protein mixtures to cellular tissues and bacterial collectives[2,3].

What distinguishes these topological defects in biological matter from their inanimate counterparts in condensed-matter and high-energy physics is the activity of the biological matter: the energy is injected at the level of each individual particle (be it a cell, bacteria or motor protein), driving the entire system continuously far away from equilibrium. Such activity can then endow topological defects with new physics, making them self-propelled, allowing them to bind and unbind with activity, and even leading to non-reciprocal interactions and large-scale self-organization of the topological defects[3,4].

In addition to identifying topological defects in various biological systems, evidence from recent years points to remarkable functionalities for topological defects in fundamental biological processes. Making analogies with the physics of liquid crystals, experiments and modelling[5] show that comet-shaped half-vortices — that is, +1/2-charged topological defects (FIG. 1) — govern cell death and extrusion from the monolayer. These processes occur due to a build-up of compressive mechanical stresses at the head of a comet-like defect, which activates signalling pathways for cell death and is accompanied by the expulsion of the cell from the layer.

The types of defect found in biological systems crucially depend on the topology of the system; in realistic in vivo scenarios, systems are usually 3D and confined. Experiments on *Hydra*, a regenerating freshwater animal, have found that where the head and the base of the foot of the animal form depends on the locations of two full-integer +1 defects that emerge on the spherical surface. In other words, the defects set the body axis and can work as organizational centres for morphogenesis[6].

Topological defects occur not only in tissues, but also in bacterial colonies, where in many cases bacteria of different types coexist and compete together. In *Pseudomonas aeruginosa* — a highly infectious strain of bacteria — moving on a surface, the faster, more active bacteria are able to initiate a merger of several +1/2 comet-like defects. The merged defects eventually form a +1 aster-like defect[7]. Within such a full-integer defect, the faster cells escape out-of-plane and become trapped inside the defect, whereas slower-moving bacteria dominate the invasion front (FIG. 1). In other words, topology can put a constraint on how fast cells move, and fast-moving mutants can get trapped in the topological defects of their own creation.

All the examples above, together with other biological phenomena, such as wound healing, cell sorting and cell accumulation and depletion[8], demonstrate that topological defects are not only present in biological systems, but also can govern important processes.

Future directions

Despite the booming interest and increasing knowledge in understanding and studying topological defects in biological matter, much remains to be uncovered. On the practical side, one of the most exciting questions is whether one can use this knowledge and apply topological defects towards the design of state-of-the-art biomaterials and tools to guide biological processes.

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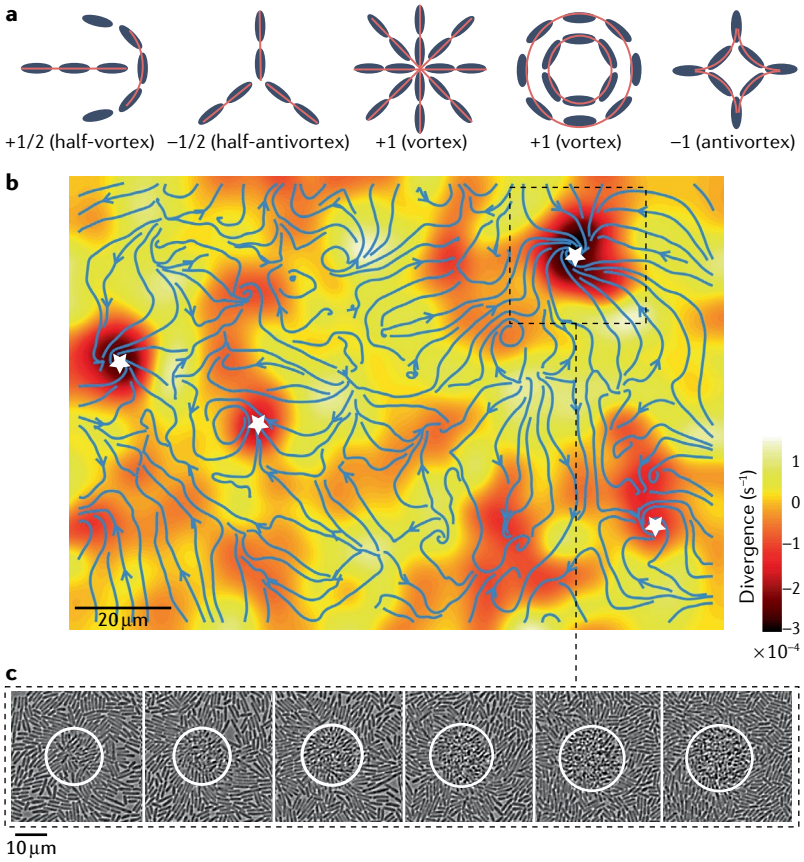

Fig. 1 | **Moving bacteria can be trapped by topological defects of their own making.** **a** | Half-integer (half-vortex and half-antivortex) and integer (vortex and antivortex) defects. The topological defects are identified by their charge: how much the phase of the order parameter changes around the singularity. **b** | The divergence and averaged velocity field of bacterial cells demonstrating formation of integer defects (denoted by stars), where cells accumulate. **c** | A time-series of images around the +1 defect showing the escape of the bacteria to the third dimension. Credit: panels **b** and **c** adapted from REF.[6], Springer Nature Ltd.

Such an application has an immense potential in the area of tissue regeneration, among others. First steps in this direction have already been taken by constructing pre-patterned surfaces using liquid crystal elastomers[9] to synthetically induce formation of topological defects, which allow for controlling cell positions and density, and, remarkably, even giving control over cell signalling and consequent activation and deactivation of mechanotransduction, a process through which cells read and react to mechanical stimuli[10]. Moreover, 3D topological defect structures in active matter present an exciting potential for actively shaping metamaterials and could stimulate design of new materials that are capable of self-organization and self-healing.

From the fundamental physics point of view, outstanding questions remain about active topological defects. There is a compelling need for generic frameworks for describing defect dynamics in an active material in the presence of hydrodynamic interactions, geometrical constraints, and fluctuations. Analogies with nematic liquid crystals and superfluids have proven successful in capturing some aspects of the complexity of defect dynamics in active matter and understanding their behaviour as active quasi-particles presents an exciting frontier in soft condensed-matter physics.

Existing theoretical models and experimental setups rely on a suite of simplifying assumptions, making the analysis tractable, yet lacking incorporation of important biological details. Most of the current understanding relies on considering active matter as being homogeneous in its properties but, realistically, cells and bacteria deviate from this assumption. They differ in their activity strengths and other physical properties, demonstrating a high degree of heterogeneity even within one pool of cells. Adding to this complexity, in many real biological scenarios, cells of different types often coexist and actively interact with each other. The contribution of topological defects in shaping interfaces between distinct active phases is intriguing, and further experimental and theoretical work is needed to shed light on the physical attributes of the competition between different cell types.

Furthermore, the effect of growth and its connection with the activity of biological matter remains poorly understood. Cell proliferation itself provides a source of active stress generation in living materials and markedly impacts the topology and morphology of growing cell colonies; conversely, the occurrence and direction of cell proliferation events can be affected by the mechanical stresses within the cell collectives. More generally, an interesting challenge is to understand how the physics of topological active matter is coupled to biochemical signalling. Not only does biochemical signalling direct the physics of active stress generation and cell–cell interactions, but also the mechanical stresses impact the biochemical signalling within the cells, creating a vital mechanochemical feedback loop.

Additionally, living materials are constantly being driven out of equilibrium and are prone to various types of fluctuations. Fluctuations in the cell shape and forces have been documented experimentally, likely having consequences on the behaviour of active systems. A prominent challenge is to disentangle impact of various forms of fluctuations from activity, to construct a full phase space of topological transitions in active materials. Moreover, there is an ongoing effort to characterize the dominant symmetries in biological systems: cells and bacteria are typically endowed with polarity and chirality, but they can exhibit polar, apolar, and even chiral interactions. To what extent these different symmetries in self-propulsion and cell–cell interactions compete to shape the collective behaviour of active matter is an outstanding question. Whether it can lead to new phases of coexistence between different types of topological defects presents an intriguing challenge at the interface between topology, biology and physics.

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Competing interests
The authors declare no competing interests.