Journal of Physics D: Applied Physics

EDITORIAL • OPEN ACCESS

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To cite this article: Christina Oettmeier *et al* 2020 *J. Phys. D: Appl. Phys.* **53** 310201

OPEN ACCESS
IOP Publishing

Journal of Physics D: Applied Physics

J. Phys. D: Appl. Phys. 53 (2020) 310201 (6pp)

https://doi.org/10.1088/1361-6463/ab866c

Editorial

Slime mold on the rise: the physics of *Physarum polycephalum*

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The slime mold *Physarum polycephalum* has long been used as a model system for the study of motility, cell cycle, differentiation, and other cell biological topics. However, due to progress in animal cell culture and molecular techniques, research on *P. polycephalum* suffered from a dry spell in the 1990s. Driven by the variety and scope of the slime mold's complex behavior, it has regained momentum in recent years. One of the first experiments featuring seemingly 'intelligent' behavior was performed by Toshiyuki Nakagaki and coworkers, showing that *P. polycephalum* is able to find the shortest route through a maze (Nakagaki 2000). A plethora of further studies have revealed that *P. polycephalum* optimizes transport networks, makes decisions, anticipates periodic events, and even exhibits habituation.

These traits can be subsumed into the notion of cellular intelligence and, increasingly, cognition (Levin 2019). Capacities traditionally considered exclusive to animals with nervous systems have been identified and are now being actively studied in non-neural organisms, including plants, ciliates and bacteria. The emerging field of basal cognition (soon to be the focus of a special issue) is based on the hypothesis that functional analogues to many of the capacities instantiated by nervous systems exist in all organisms, albeit not at the same level of sophistication, which depends on the requirements for survival (Lyon 2019). In addition, the non-metaphorical deployment of cognitive terminology—the 'cognitive lens'—has recently been proposed for analysing information processing in multicellular development and regeneration precisely because of the presence of such capacities in single cells (Manicka and Levin 2019). In view of these developments, *P. polycephalum* continues to contribute to sciences outside of its traditional scope.

The papers presented in the present special issue give an account of the state of the art in research on the numerous phenomena associated with cell motility and signaling, network dynamics and oscillation, thereby laying the foundations for the investigation of basal cognition in *Physarum*. Formulating sensorimotor coupling within the framework of basal cognition connects the phenomena studied conceptually to human level cognition. It has even been proposed that cells already possess a (primitive) form of consciousness (Baluska and Reber 2019).

Several recent papers on *Physarum*, see Oettmeier (2017) for a historical review, have triggered a surge of activity in numerous fields including physics, cell biology, genetics, behavioral ecology, computer science, natural computation, and cognition among others, as well as philosophy of science, and finally philosophy of mind. In some areas, like molecular biology, research still needs to catch up in order to begin to tackle the underlying mechanisms of the observed complex behavior. For example, receptors on the organism's surface, which are of great relevance for the study of chemotaxis, still need to be identified.

Figure 1. World map locating those *Physarum* research hot spots where contributing authors work.

Research on *P. polycephalum* is a prime example for a recent transition in science: a transformation is underway from the traditional distributed, hierarchical scientific work methods to a new approach, which overcomes boundaries between disciplines. In particular, physics has become increasingly inter- and transdisciplinary. We have, for example, seen biological physics thrive by identifying genuinely new physics of living matter in biology. Stochastic thermodynamics is well on its way to provide a quantitative characterization of learning based on a thermodynamically consistent description of neural networks (Goldt 2017). More generally, complex systems and network theory have been applied to identify and analyze common elements and patterns that can be observed across diverse natural, technological and social complex systems.

This special issue is written by scientists from different disciplines working together to arrive at new insights, to tackle problems from different sides, and to apply the virtues of multiple disciplines to successfully enhance our knowledge of the fascinating complex system that is *P. polycephalum*. Most of the fields listed above, including physics, have so far described and analyzed *P. polycephalum* in a coarse grained and abstract fashion. However, in order to gain a complete picture and to unravel not only the detailed mechanisms of information processing and cognition, but also behavior and network dynamics, contributions in this issue discuss tasks achieved across all levels. The following section is meant as a signpost to help navigate the multitude of articles, and to introduce five diverse research categories: (i) growth, foraging and decisions, (ii) locomotion, (iii) oscillation and mechanics, (iv) methodology and (v) genetics. See the world map (figure 1) for the locations of all authors who contributed to this special issue.

1. History and state of the art

In total, 30 papers including this editorial were collected in our special issue, which starts off with a review introducing *P. polycephalum* as a model system (Oettmeier *et al* 2017). The other articles in this special issue can be attributed to the five overarching topics which we will address now in turn. **Growth, foraging and decisions** subsumes research on the overall shape and structure of the macroplasmodial networks. Vogel *et al* (2016) showed how multiple plasmodia interact and forage, and how the resulting networks are optimized depending on environmental conditions and initial growth pattern (isotropic or digitated). Akita *et al* (2017) examined plasmodia, which moved out of a confined area through a narrow exit, and found that they were able to form hydrodynamically optimized vein networks to achieve this task. Remaining with optimization, Takamatsu *et al* (2017) investigated the relationship between morphology and energy efficiency, leading to the conclusion that a low-dimensional network in terms of fractal dimension reduced energy consumption. The manifold morphology of plasmodial networks was also explored by Dirnberger and Mehlhorn (2017), who analyzed a total of 1998 graphs to establish a broad collection of motifs. Bäuerle *et al* (2017) examined the reorganization of *P. polycephalum*'s network after severe wounding, and Westendorf *et al* (2018) compared the growth, network development and chemotaxis of *P. polycephalum* to two other plasmodial slime mold species, *Badhamia utricularis* and *Fuligo septica*. The papers in this category illustrate the diversity and complexity of the slime mold networks, which are a hot topic with implications beyond myxomycete research. A huge part of the slime mold's life is devoted to the search for nourishment. Ntinas *et al* (2017) used a memristor-based model (a hypothetical electrical component) to assess foraging. Schenz *et al* (2017) constructed a fluid-flow model to explain their experimental results of a slime mold exploring. Lee *et al* (2018) described a novel search pattern, where the slime mold does not produce networks, but instead forms autonomous subunits to increase its chances of finding food. Foraging requires movement, and *P. polycephalum* is a highly motile amoeba. Another set of contributions deals with emergent phenomena in the slime mold. Kunita *et al* (2017) investigated the plasticity in behavior which is observed when the slime mold's path is blocked by a repellant. Moving or not moving across this barrier seems to depend on small intracellular fluctuations, which the authors also model with a canard solution. The slime mold's ability to find its way through different mazes was studied by Smith-Ferguson *et al* (2017), highlighting the importance of slime secretion as extracellular memory. The work of Masui *et al* (2018) investigates allorecognition, i.e. what happens when two different plasmodia come into contact with each other. A different slime mold, *P. rigidum*, was used in this study.

The next category, **Locomotion**, comprises three papers which explicitly deal with the particular way in which *P. polycephalum* moves. Zhang *et al* (2017) and Zhang *et al* (2019) and take a closer look at the intracellular flow, traction stresses generated on the substratum, and intracellular calcium. They conclude that spatio-temporal patterns of calcium concentration and its convective transport underlie the contractile patterns. The work of Lewis and Guy (2017) focuses on models of peristaltic pumping, which is supposed to drive locomotion. **Oscillations and mechanics** is the next category, which, together with **Growth, foraging and decisions**, has the most contributions. This category incorporates research on the rhythmic oscillations, which are a characteristic trait of *P. polycephalum*, and several contributions which examine the finer morphology, focusing mostly on the cytoskeleton. Iima *et al* (2017) use two- and one-dimensional coupled oscillator models to relate observed oscillations to amoeboid movement. The subject of Teplov (2017) is also amoeboid locomotion, but the focus lies on a rheological model to explain the mechanochemical autowave activity of the migrating plasmodium. Avsievich *et al* (2017) were looking at the underlying primary oscillator, a set of biochemical reactions causing the contraction-relaxation pattern which has so far escaped discovery. They showed that respiratory pathways are correlated with contractile activity. Umedachi *et al* (2017) investigated how the oscillations of *P. polycephalum* react to external stretching stimuli, and Alonso *et al* (2017) examined mechanochemical patterns, especially wave phenomena, by using two models for viscoelastic fluids and viscoelastic solids, respectively. Finally, self-organized motion is modelled by Kulawiak *et al* (2018) with a poroelastic two-phase model. Fessel *et al* (2017) investigated the biomechanical properties of slime mold microplasmodia, such as Young's modulus and Poisson's ratio. The actin filaments are the subject of Schumann (2017), especially their role in perceiving external stimuli, integrating them and reacting to them. Oettmeier *et al* (2018) investigated the ultrastructure of different morphotypes, by using electron microscopy and fluorescence microscopy.

Although methods are an important part of many aforementioned contributions, the category **Methodology** contains two papers which focus on the automated extraction of network structures from images (Fricker *et al* 2017), and an open repository for experimental data for making experimental data freely accessible (Dirnberger *et al* 2017); see http://smgr.mpi-inf.mpg.de. The last category is **Genetics**. Since the genome of *P. polycephalum* has been completely sequenced, advances have been made in this area. Stange *et al* (2017) provide insight into the positioning of nuclei and the microtubule cytoskeleton of *Dictyostelium discoideum*. Werthmann and Marwan (2017) introduce a Petri-net based approach to the analysis of cellular responses. They model the developmental switch to sporulation as a Waddington quasi-potential landscape, emphasizing the importance of epigenetics for the multitude and plasticity of *P. polycephalum*'s reactions to the environment.

2. Future challenges and opportunities

All of the five categories defined above present challenges for further research. For example, many molecular as well as macroscopic mechanisms interact to give rise to amoeboid locomotion and signaling. These processes need to be better understood. As mentioned above, *P. polycephalum* is now also under scrutiny for the investigation of cellular intelligence and the origins of cognition. This challenge will be no small feat, but the groundwork is being laid by research which is highlighted in this special issue. Apart from this project, more practical applications are also being evaluated. Soft robots, algorithms which mimic and emulate *Physarum*'s networking and maze-solving skills, are being developed. Moreover the improvement of methods, for instance finding techniques to genetically manipulate *Physarum*, present opportunities for future research. Like *Physarum* itself, the network is ever expanding to all sides, finding new exciting topics, creating new links and connecting researchers and disciplines.

Acknowledgments

Hans-Günther Döbereiner and Christina Oettmeier thank Wolfgang Marwan for his insights and enjoyable discussions, which have shaped our views, and Pamela Lyon for significantly improving our manuscript. This work was supported by Deutsche Forschungsgemeinschaft (DFG) with grant DO699/6-1.

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