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Learning Physics of Living Systems from Dictyostelium

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Abstract

Unlike a new generation of scientists that are being trained directly to work on the physics of living systems, most of us more senior members of the community had to find our way from other research areas. We all have our own stories as to how we made this transition. Here, I describe how a chance encounter with the eukaryotic microorganism *Dictyostelium discoideum* led to a decades-long research project and taught me valuable lessons about how physics and biology can be mutually supportive disciplines.

Keywords

Dictyostelium; biophysics; biological physics; interdisciplinary

It was a dark and stormy night one June in the mid-80s, following the condensed-matter physics Gordon conference. The field I was then working in, the non-equilibrium physics of spatial pattern formation, was celebrating hard-fought victories over longstanding problems dealing with patterns formed via crystal growth, multiphase fluid flow and electrochemical deposition [1, 2, 3]. Although it would take another decade to fill in all the details and generalize the findings to other processes, the basic framework being presented in numerous talks at that meeting has proven its resilience ever since.

That night, I rode back from New Hampshire to Connecticut (where I was then employed) in the company of Eshel Ben-Jacob, now at Tel-Aviv University. We discussed at length the exciting notion that the real challenge of non-equilibrium physics was to make sense of living matter. No serious scientist believes in vitalism (the notion that there is some intrinsic difference between living and non-living systems), but yet the coordinated set of complex processes that must come together to allow for the amazing variety of life seems at times magical. To begin that task, however, we needed to find a model problem. This model problem would serve as a scalable pass across the barrier separating the abiotic from the biotic, i.e. would teach us how to combine physics with biology to address the way living systems are organized and function. We resolved to spend some time searching for such a problem, as we continued to pursue our normal scientific agendas.

After several false leads, I found my pass about five years later, by which time I had moved to UCSD. I happened upon an article in Physica D [4] on the nonlinear waves that are used by the eukaryotic microorganism *Dictyostelium discoideum* to aggregate upon starvation. These waves were quite analogous to those seen in other so-called excitable media, most notably the Belusov-Zhabotinskii chemical dynamics system on which I was coincidentally doing some research [5]. The major difference that I noted was that the wave dynamics in the Dicty system were coupled to cell density, the latter changing due to directed cell motion in response to the chemical gradients carried by the waves. With an adventurous graduate student, I studied the coupled systems and found a pattern-forming instability that helped explain experimental observations regarding azimuthal density collapse during aggregation. The results were published in Physical Review Letters [6].

Then came the real breakthrough. My student (William Reynolds) decided that we needed to learn more about the underlying biology of our now favorite organism. He went to the library (a long-lost art) and came back with a monograph on the subject [7]. When we opened the book, we discovered that the author, William Loomis, was also at UCSD and in fact was in the building right next door to the Physics department. We made an appointment to see him and discovered that he actually felt that theoretical physics could help (an opinion much less common then than now). Bill graciously offered to help us learn about Dicty biology. By playing around in his lab, attending group meetings and mostly just by talking with Bill, I came to appreciate the complementary approaches taken by biologists when faced with a complex living system. Bill and I have been collaborating now for almost two decades. We have jointly explored many aspects of this organism's behavior, ranging from single cell issues such as the signal transduction networks underlying directed cell motion [8] and their relationship to cell motility mechanics [9], to multicellular processes involving the coupling of the aforementioned waves with genetic degrees of freedom of the participating cells [10], as well as the collective motions akin to bird flocking that can be seen in the nascent aggregate [11]. My hope of finding a pass had indeed become reality. Dicty had provided a tractable model system in which we could learn how to combine non-equilibrium physics with modern biology, to the benefit of both.

As perhaps expected from the biblical pronouncement “Seek and ye shall find”, others seeking their own route to the living world have also been successful at finding their own model systems. My long-time colleague Eshel started working on bacterial colonies, where combining nutrient limitations with suppressed cell motility leads to a variety of self-organized structures [12]. Some of these are similar to what is seen in analogous chemical and physical systems and some are wholly new. This research eventually helped usher in the entire field of active condensed-matter, via the recognition that the collective dynamics of this type of living multi-particle system is radically different than that expected based on free energy considerations. Ultimately this is due to the bacteria having their own source of free energy which can be traded in for functional behavior.

What in the end has Dicty taught me, as I go forward to study more complex mammalian cells, the tissues they form, and the diseases that alter their normal functioning? The first lesson is that even relatively simple cells can exhibit extremely sophisticated behavior, especially when challenged by harsh environments. Whenever I come across work on neural systems that automatically assumes that neurons are behaving simply and that the complexity is all in the network, I become rather suspicious. Similarly, I am skeptical of treatment approaches that rely on considering cancer cells to be malfunctioning agents operating in a blind, uncoordinated manner. On the other hand, simplified models can be useful for specific phenomena in which many degrees of freedom are not dynamically active. For example, aggregation in Dicty can be partly understood without fully understanding the cell, just as highway traffic can be partly understood without a full theory of human cognition. The trick here is to focus on possible mechanisms and on their characteristic signatures and not insist on a completely quantitative agreement between data and model. The latter is necessarily incomplete and hence should not be expected to precisely match experiment.

Finally, I learned that most physicists, myself definitely included, cannot go it alone. Living systems really are different and demand of investigators years and years of experience to know when data is reproducible, when controls are sufficient, and when phenomena are meaningful. Having first-rate biologists at your side is a necessity, not a luxury. For me, the physics of living systems could not exist without the biology of living systems. The field is inherently multidisciplinary and that is part of its continuing attraction.

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References

1. Kessler DA, Koplik J, Levine H. Adv. Phys. 1988; 37:255.
2. Langer J. Science. 1989; 243:1150. [PubMed: 17799896]
3. Ben-Jacob E, Garik P. Nature. 1990; 33:523.
4. Tyson JJ, Alexander KA, Manoranjan V S, Murray D. Physica D. 1989; 34(1):193.
5. Kessler DA, Levine H. Physica D. 1989; 39:1.
6. Levine H, Reynolds WN. Phys. Rev. Lett. 1991; 66:2400. [PubMed: 10043475]
7. Loomis, WF. The Development of Dictyostelium discoideum. Academic Press; New York: 1982.
8. Fuller D, Chen W, Adler M, Groisman A, Levine H, Rappel WJ, Loomis WF. Proc Nat Acad Sci. 2010; 107:9656. [PubMed: 20457897]
9. Hecht I, Skoge M, Charest P, Ben-Jacob E, Firtel R, Loomis W F, Levine H, Rappel WJ. PLOS Comp. Bio. 2011; 7:e1002044.
10. Levine H, Aronson I, Tsimring L, Truong T. Proc Nat Acad Sci. 1996; 93:1151. [PubMed: 8577731]
11. Rappel WJ, Nicol A, Sarkissian A, Levine H, Loomis WF. Phys. Rev. Lett. 1999; 83:1247.
12. Ben-Jacob E, Cohen I, Levine H. Adv. Phys. 49 395. 2000