Academy Report Affirms Emergence of Biological Physics

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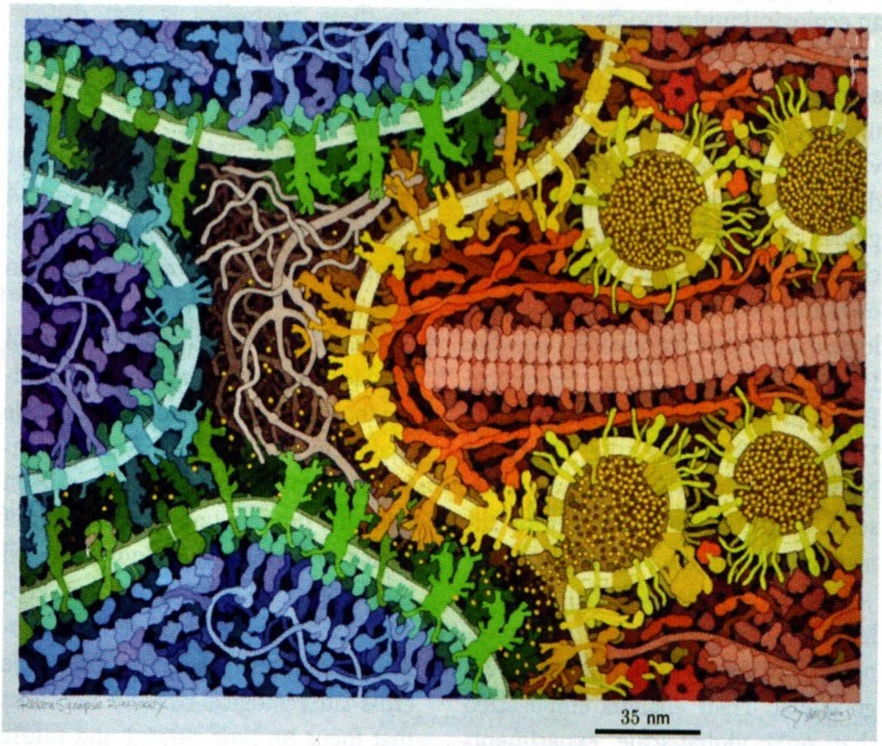
Scientists look to the promise of the physics of living systems.

On 15 March 2022, William Bialek gave a talk to some 200 people at a business meeting of the American Physical Society's (APS) Division of Biological Physics. His address updated them about a report from the National Academies of Sciences, Engineering, and Medicine (NASEM) that would be published the following week. It was the first-ever decadal survey of biological physics.

One of the first slides presented by Bialek, a physics professor at Princeton University and chair of the NASEM report committee, noted that physics decadal surveys had been ongoing since 1966, focused on other fields of physics. Then Bialek drew attention to the last line on the slide, which stated, "In the 2020 [decadal survey] cycle, for the first time, biological physics stands alongside other fields of physics, with its own survey volume."

"That was the point at which I was interrupted by applause. I was totally surprised since, of course, it wasn't news," Bialek says. The emergence of biological physics has been a decades-long process, with roots going back much further. In addition, the fruits of biological physics already have had an enormous impact, including research that has been key to the global response to the COVID-19 pandemic. That audience applause "was just the community reacting that, yes, okay, now we are a branch of physics, and that's not ambiguous anymore," he says. "There was a sense that we had arrived as a field of physics."



Artist's depiction of a ribbon synapse between a photoreceptor cell (right, red/orange) and the next neuron in the human retina (left, blue/purple). The image is based on crystallographic structure as seen in electron microscopy. Vesicles filled with neurotransmitter appear on the right (transmitting) side; one vesicle has fused and is releasing its contents. Image: Art by David Goodsell, from "From Photon to Neuron" by Philip Nelson (Princeton Univ. Press, 2017). Reprinted with permission.

The primary conclusion of the report, *Physics of Life* (https://doi.org/10.17226/26403), released on 23 March, is that "a new field has emerged." It now stands alongside more traditional fields of astrophysics and cosmology, atomic, molecular and optical physics, condensed matter physics, nuclear physics, particle physics, and plasma physics.

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Emergence

The new field that has emerged, biological physics, "brings the physicist's style of inquiry to bear on the beautiful phenomena of life," the report states. "The enormous range of phenomena encountered in living systems—phenomena that often have no analog or precedent in the inanimate world—means that the intellectual agenda of biological physics is exceptionally broad, even by the ambitious standards of physics."

By definition, biological physics connects with biology, and its links also reach further: to chemistry, engineering, medicine, and technology, "ultimately having deep implications for society," according to the report. The document notes that phenomena in nature do not come labeled as belonging to a particular discipline and that the behavior of electrons in solids, for instance, may be of interest to chemists, engineers, and materials scientists while also being a core topic in condensed matter physics. "Similarly, the phenomena of life have attracted the attention of biologists, chemists, engineers, and psychologists, as well as the growing community of physicists" whose work the report explores.

Physics is not about studying any particular thing but rather about reaching an understanding of the world, summarizable in mathematical terms and allowing for quantitative predictions, explains Bialek. "Biological physics is the effort to bring that point of view to bear on the beautiful and complicated phenomena of life, so we can reach an understanding which is summarizable in mathematics, which is predictive, and which is unified."

Margaret Cheung, chair of the American Physical Society's Division of Biological Physics, further boils down the definition. Biological physics is "knowing how life works," says Cheung, a scientist in the Environmental Molecular Sciences Laboratory at the US Department of Energy's Pacific Northwest National Laboratory.

Cheung and many others, including Gail Robertson, president of the Biophysical Society, welcomed the report and its recommendations to help federal agencies, policymakers, and academic leadership understand the importance of biological physics research and make informed decisions about funding, workforce, and research directions.

"The clearly defined recommendations of this report resonate with our mission and will serve to broaden the community of biophysicists working in basic and translational science in the [United States] and with our collaborators worldwide," says Robertson, a professor in the Department of Neuroscience at the University of Wisconsin–Madison. The Biophysical Society, established in 1958, serves a membership that applies physical principles to important biological questions. The Biophysical Society and the APS Division of Biological Physics held town meetings to gather science community input for the report.

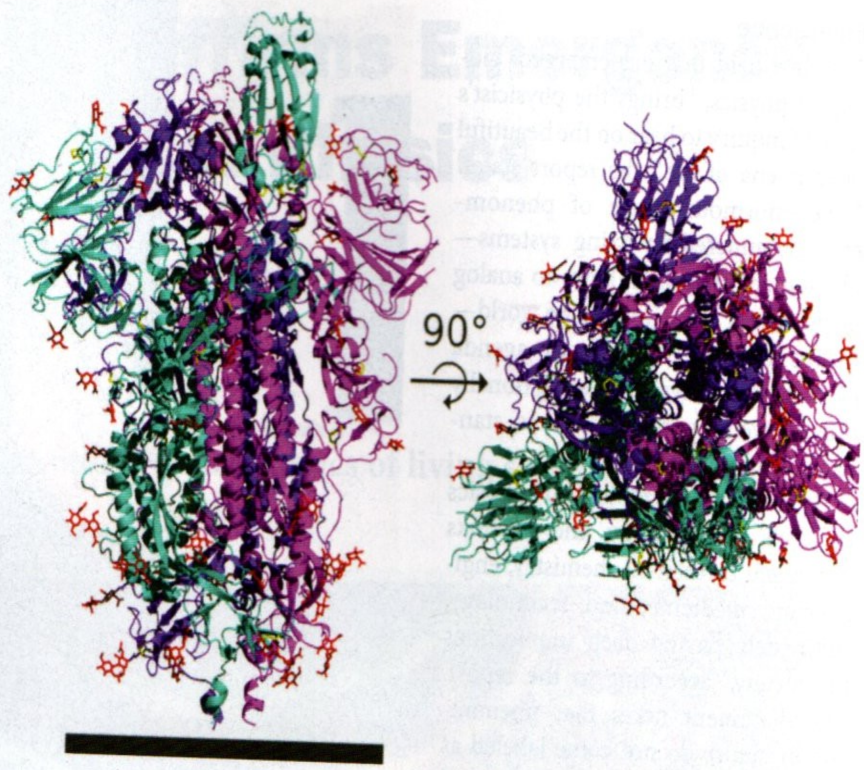
Margaret Cheung, chair of the American Physical Society's Division of Biological Physics. Photograph: Andrea Starr, Pacific Northwest National Laboratory.

Assessment and recommendations

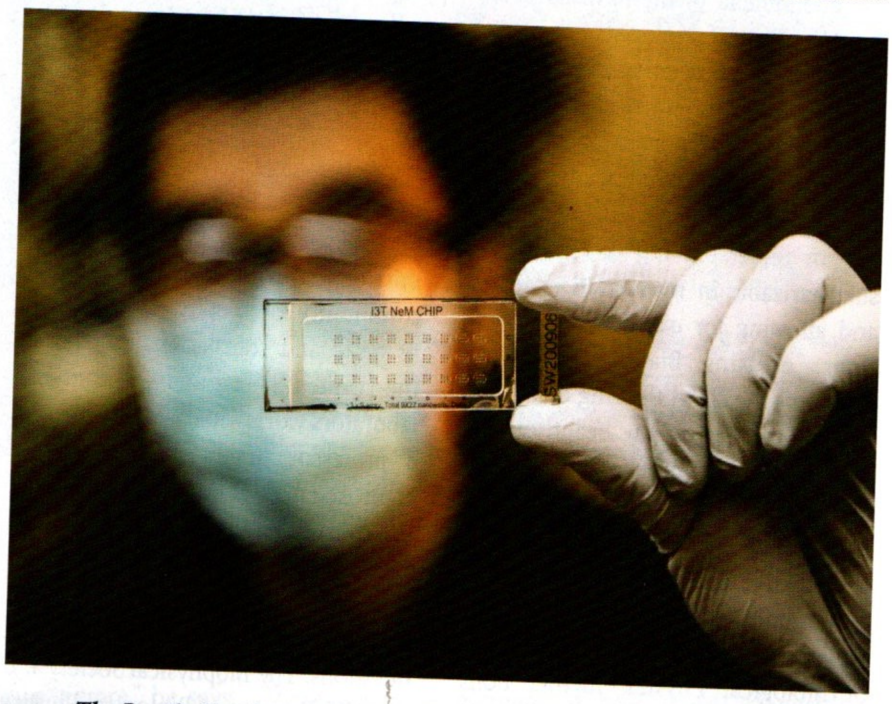
The decadal survey, designed to regularly assess the state of physics research and education in the United States, now takes an expansive view of biological physics as an effort to understand the phenomena of life in ways that parallel the physicists' understanding of the inanimate world. The report recognizes the connections between biological physics and other branches of physics plus engineering, chemistry, biology, medicine, and other fields of science.

The report highlights productive examples of the interaction between physics and biology, such as research about the double-helical structure of DNA and magnetic resonance images of human brains in action. The results of the collaboration between physics and biology "are central to the modern view of life," but some of these successes "were codified as parts of biology, not physics," according to the report, which also notes that biophysics and quantitative biology have a continuing overlap with biological physics.

The report states that conceptual conundrums for biological physics include the physics problems organisms need to solve, how living systems represent and process information, how macroscopic functions emerge



Spike glycoprotein from SARS-CoV-2 illustrated from side and top angles. The top angle image is rotated by 90 degrees. The top of the protein (left) binds with human ACE2 receptors through which SARS-CoV-2 binds to cells and infects them. Image: Author 5-HT2AR Creative Commons CC0 1.0 Universal Public Domain Dedication.



The Pacific Northwest National Laboratory has designed and fabricated a new microcell chip for a technology that enables high throughput single-cell proteomics (analysis of the full complement of proteins in a system or organism). Photograph: Andrea Starr, Pacific Northwest National Laboratory.

from interactions among many microscopic constituents, and how living systems navigate parameter space. The intellectual agenda of biological physics touches on phenomena "on scales ranging from molecules to ecosystems." More specific inquiries might include research into such things as the folding of single protein molecules or birds flocking. In the process of investigation, the biological physics community has provided new tools for scientific discoveries, new instruments for medical diagnosis, new ideas for systems biology, new methods and theories for exploring the brain, and new algorithms for artificial intelligence, according to the report.

A current example of biological physics in action regards the scientific community's response to COVID-19. Once the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus was isolated, the scientific community rapidly determined the structures of crucial molecular components, including the spike protein that enables viral entry into cells. Work in biological physics "has been critical to our understanding of the SARS-CoV-2 spike protein structure, its interactions with host receptors, with neutralizing antibodies, and with potential drugs," the report states.

Specifically, it was fundamental research in structural biology, supported by decades of developments in X-ray crystallography and cryogenic electron microscopy methods, that "provided a running start to the development of vaccines for COVID-19," notes the report. Many of the novel vaccine strategies used to deliver vaccines in record time were informed "by very detailed knowledge of the structure and dynamics of the spike protein."

Realizing the promise of biological physics "requires recognition that it is distinct from but synergistic with related fields, both in physics and in biology," according to the report. Important in that recognition is improving the funding stream for biological physics. Support for the field typically follows a model of biophysics as the application of physics to biology. That perspective, suggests the report, constrains what funding agencies perceive as relevant, reinforcing an organization of the field around classical subdivisions of biological sciences. The report argues that now is the time for the funding environment to respond more fully to the community.

Funding agencies, including the US National Science Foundation (NSF), the National Institutes of Health, the Department of Energy, and the Department of Defense, as well as private foundations, should develop and expand programs "that match the breadth of biological physics as a coherent field," the report recommends.

Researcher Geremy Clair prepares a cell suspension from simulated lung tissue samples by performing tissue dissociation followed by filtration. The samples can then be further processed to extract metabolites, proteins, and lipids for further analysis. Photograph: Andrea Starr, Pacific Northwest National Laboratory.

A multigenerational project

The report also recognizes that building a new scientific field is "a multigenerational project" and considers it crucial to educate the next generation about biological physics. The report recommends that universities and colleges integrate biological physics into all levels of the mainstream physics curriculum. "In colleges and universities, it should have a home in physics departments, even as its intellectual agenda connects profoundly to efforts in many other departments across schools of science, engineering, and medicine."

"For a long time now, physicists have made amazing contributions to the life sciences. But you wouldn't know it from our undergraduate physics major curricula," says Catherine Crouch, department chair and professor of physics at Swarthmore College, in Pennsylvania. She says that incorporating examples from the field throughout the undergraduate curriculum would allow students to learn more about it earlier in their academic careers.

Crouch, a reviewer of the report, says the undergraduate physics curriculum is very well established, with legitimate recognition of basic material every physicist needs to know. However, the curriculum "has been pretty static for a while," she says, with few areas of current physics research well-represented in the undergraduate curriculum.

Crouch also agrees with the report's concluding statement: "The biological physics community has a special opportunity to reach broader audiences, leveraging human fascination with the living world to create entrance points to physics for a more diverse population of students and for the general public."

Biological physics is an exciting area that can draw people in if they know about it, says Crouch. The prospect of better understanding living systems, especially with the acknowledgement that physicists could contribute more to human health and well-being, "is a real draw," she says. "When physics is perceived as being exclusively about very abstract things that are disconnected from human reality—and also very disconnected from practical needs—that makes physics much less appealing to a broad base." Crouch says that biological physics is not the only way to draw a more diverse population into physics, but it is a promising opportunity.

"Right now, you can go to any university and get a degree in physics and still not hear anything at all about biological physics unless you choose to take an elective course on that subject," says Philip Nelson, professor of physics at the University of Pennsylvania, Philadelphia. He suggests that if every undergraduate learns the basics of astrophysics or condensed matter physics, it would also be valuable to learn the basics of biological physics.

Nelson, the author of *Physical Models of Living Systems*, points to the scientific efforts focused on COVID-19 as one of the most recent examples of what biological physics can offer society. If you want more people in the future who are poised to make important discoveries like the efforts related to COVID-19, there should be a discipline called biological physics for them to get that training and for there to be a pipeline of students entering the field, he says. "You can't have the discoveries without the people who are ready to make discoveries. So, I would like to see more of those people on the planet."

In trying to persuade students to get involved in biological physics, Nelson tells them, "If you thought that physics was all balls rolling down inclined planes, if you thought that physics was all black holes, then you are missing an important aspect of physics that is relevant to improving people's lives and sustainability." A biological physics viewpoint, he notes, provides a fundamental understanding of topics not previously considered within the domain of physics.

While the report points to growth in the number of doctoral students working in biological physics, it also finds biological physics poorly represented in the core undergraduate curriculum. At the moment, few students have opportunities to take specialized courses that convey the full breadth and depth of the field.

Cheung adds that physics is a "gateway course." Without that foundation, it is difficult for students to major in fields such as engineering or medicine. She notes that in some institutions where students may not have taken physics, teaching introductory physics through the lens of biological physics can be an effective opportunity to reach out to them. The report also recommends that federal agencies make new resources available to support core undergraduate physics education for underrepresented and historically excluded groups.

A flock of birds (auklets) in flight. Biological physics provides new ways of examining the behaviors of animals in motion. Photograph: D. Dibenski, USFWS National Digital Library.

Convergence of scientific fields

The NSF sponsored the decadal survey, which charged the NASEM committee to take a broad look at biological physics, its connections to other fields, and the challenges the community faces in realizing the potential of the newly emerged field. The foundation launched an initiative nearly 20 years ago to support biological physics within its physics division. That has evolved into the Physics of Living Systems program.

Denise Caldwell, director of the NSF's Division of Physics, says of the decadal survey that opening up the living world as a recognized part of physics and what physicists do "sends a message to undergraduates and all the way through university programs that this is something you should think about." Biological physics, she adds, offers an opportunity to provide undergraduate programs that simultaneously train them in what they need to know from biology and physics.

The NSF, Caldwell notes, supports initiatives that help train the future workforce, and biological physics fits in with that effort. Caldwell says that if you consider the critical questions today—including health, climate change, our environment, and resources—"at some point, the living world has a key role to play." She says that understanding the living world with whatever tools are available is vital for future generations, and biological physics is one of those tools. "Through this, we're saying to students and young people, 'It's going to be your world. Our goal is to help you figure out ways to frame that world and address the problems.'"

The NSF's partnership between its Division of Physics and the Directorate of Biological Sciences has been essential to advancing the field and bringing different perspectives to the fore so that scientists could learn from each other, she says. "I think we're seeing the fruits of that."

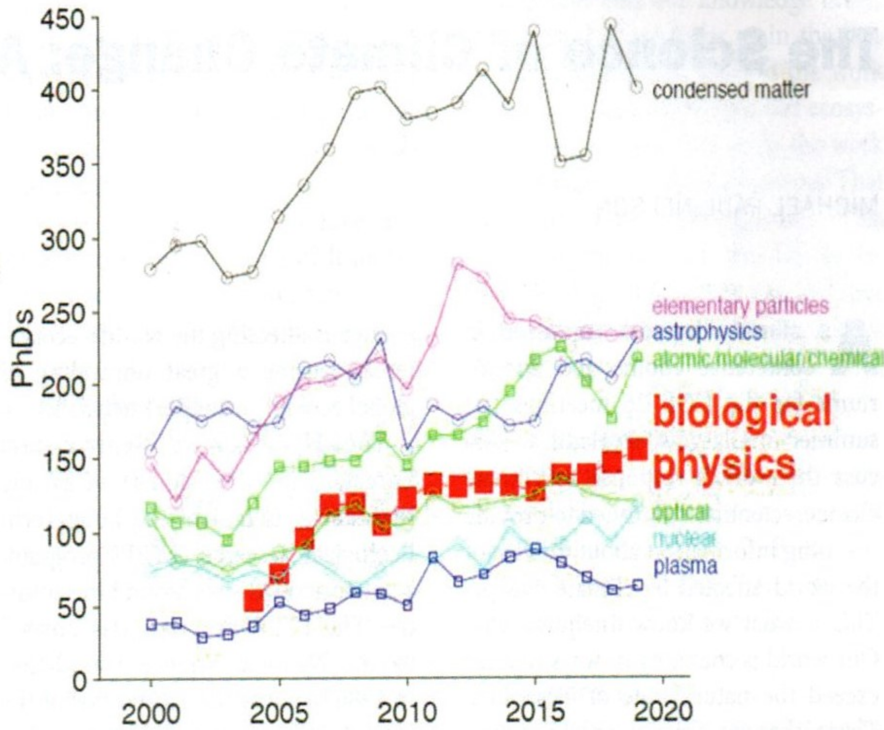
Others at the NSF echo this sentiment. Edda Thiels, a program director in the NSF's Neural Systems Cluster, supporting mechanistic studies in neuroscience, says we are in an era of integrative convergent thinking about science and bringing different disciplines together. Physics and biology "are not exempt from this interdisciplinary thinking," she says. Recognizing the field of biological physics also sets the stage to provide training and establishes biological physics "as something that is not ephemeral," she adds.

"In molecular and cellular biosciences, we believe that if you're going to advance biology, you need to bring in expertise from other fields. Physics is one of the fields we think is important in terms of growing our understanding of biology," says Theresa Good, director of the NSF's Division of Molecular and Cellular Biosciences, which has played a significant role in shaping biological physics through its scientific and financial support. "I think that the fields have converged. That is the beauty of the way that science advances," says Good.

Krastan Blagoev, program director of Physics of Living Systems in the NSF's Division of Physics, says the NSF decided to fund the NASEM survey to see whether there is actually a "new" field, which scientists had been working in for at least several decades. "We were very happy to find that there is a substantial effort in the world in that field and that it has become a new physics discipline."

Blagoev and others expressed excitement about the "new" field. From a scientific perspective, he is excited about biological physics looking into the living world and what that might mean for physics. From a societal perspective, Blagoev thinks biological physics can help advance many areas. He notes that during the past 15 years, biological physics has grown into a much wider field. Termed *the physics of living systems* in the United States and *the physics of life* in Europe, it includes areas like robotic physics; the physics of behavior, such as quantifying the complexity of animal motion; and the physics of cities and sustainability.

Looking to the future, he suggests that current artificial intelligence, for instance, "will look like a child compared to what is possible if we understand how the brain works." He noted that biological systems are impressively efficient compared to current computational capabilities requiring enormous energy. "We need to understand why biological systems are so efficient. This [understanding] is extremely important for the Earth and for sustainability."



Monitoring the growth of biological physics as a subfield of physics in the twenty-first century. Doctoral degrees awarded in biological physics, compared with other subfields of physics. Data for 2010–2019. Image: National Science Foundation, 2020,* Doctorate Recipients from U.S. Universities: 2019, *NSF 21-308, Alexandria, VA, https://www.nsf.gov/statistics/doctorates/no. tabs-1.

This is our moment

Biological physics has great societal relevance, says Cheung, whose interests include the bioeconomy—a term that links biology and economic activity—and how microbes can better reduce waste material.

Cheung believes biological physics could aid many potential advances in sustainability. It is a field that she says could also help transform the economy. Cheung says a biological physics focus on matters such as curing human disease is very important. For her, a biological physics focus on environmental issues is critically important too. Cheung, who works in an environmental molecular science laboratory, would also like to see better use of microbes in the future, potentially helping reduce the demand for hydrocarbons. "Thinking about the Manhattan Project of a couple of decades ago," Cheung says, "I think we are on another Manhattan Project in a sense, as physicists, to transform how we live with microbes."

In addition to its usefulness, biological physics promotes a sense of adventure in exploring living systems, notes Bialek. "If you are the kind of person who wants to think about the world in this way that we call physics, and you are also fascinated by life, there's no longer a barrier," he says. "That's marvelous. It is liberating of the human spirit and of our intellectual creativity as scientists."

Biological physics, notes Cheung, uses a physics approach to understand our environment, probe how it works, ensure we do no harm, and aim for sustainable solutions for humanity to work in harmony with the environment. For biological physics, she says, "This is our moment."

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