Physics of Life

Decadal Survey of Biological Physics/Physics of Living Systems

https://nap.nationalacademies.org/resource/26403/interactive/

DOE: BERAC | **nap.edu/physicsoflife** | **April 21, 2022**

The National Academies of
SCIENCES · ENGINEERING · MEDICINE

NASEM Staff

Christopher Jones
Senior Program Officer

Steven Moss
Program Officer

Amisha Jinandra
Associate Program Officer

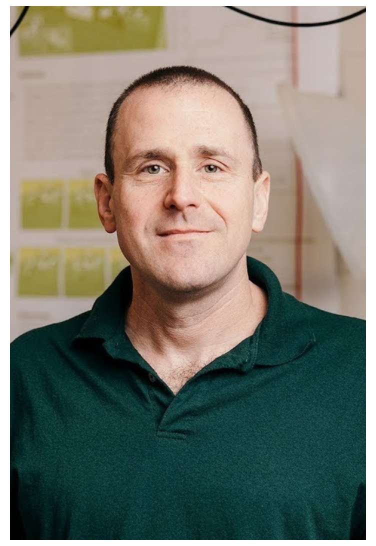
Neeraj Gorkhaly
Associate Program Officer

Linda Walker
Program Coordinator

Colleen N. Hartman
Director, Board on Physics and Astronomy

Kavita Berger
Director, Board on Life Sciences

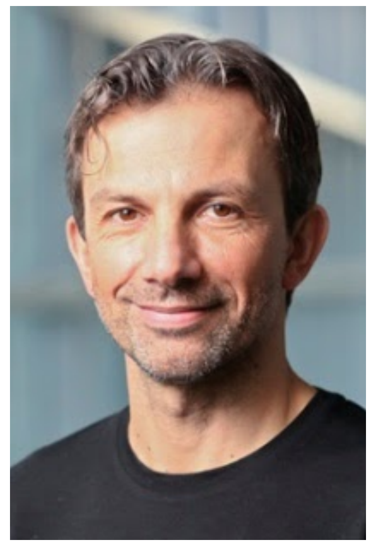
Bridget Carragher
Columbia University



Daniel I. Goldman
Georgia Institute of Technology

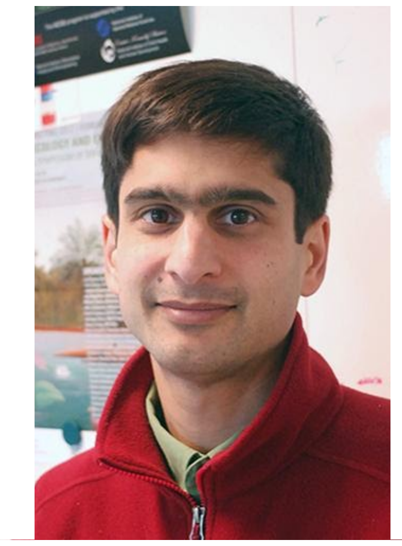
Mary E. Maxon
LBNL and Schmidt Futures

Ibrahim I. Cissé
MPI Freiburg



Jane Kondev
Brandeis University

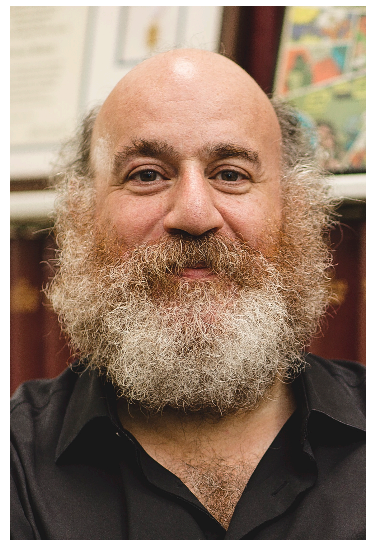
José N. Onuchic
Rice University



Michael M. Desai
Harvard University

Peter B. Littlewood
The University of Chicago

Mark J. Schnitzer
Stanford University



William Bialek, chair
Princeton University

Olga K. Dudko
University of California at San Diego

Andrea J. Liu
University of Pennsylvania

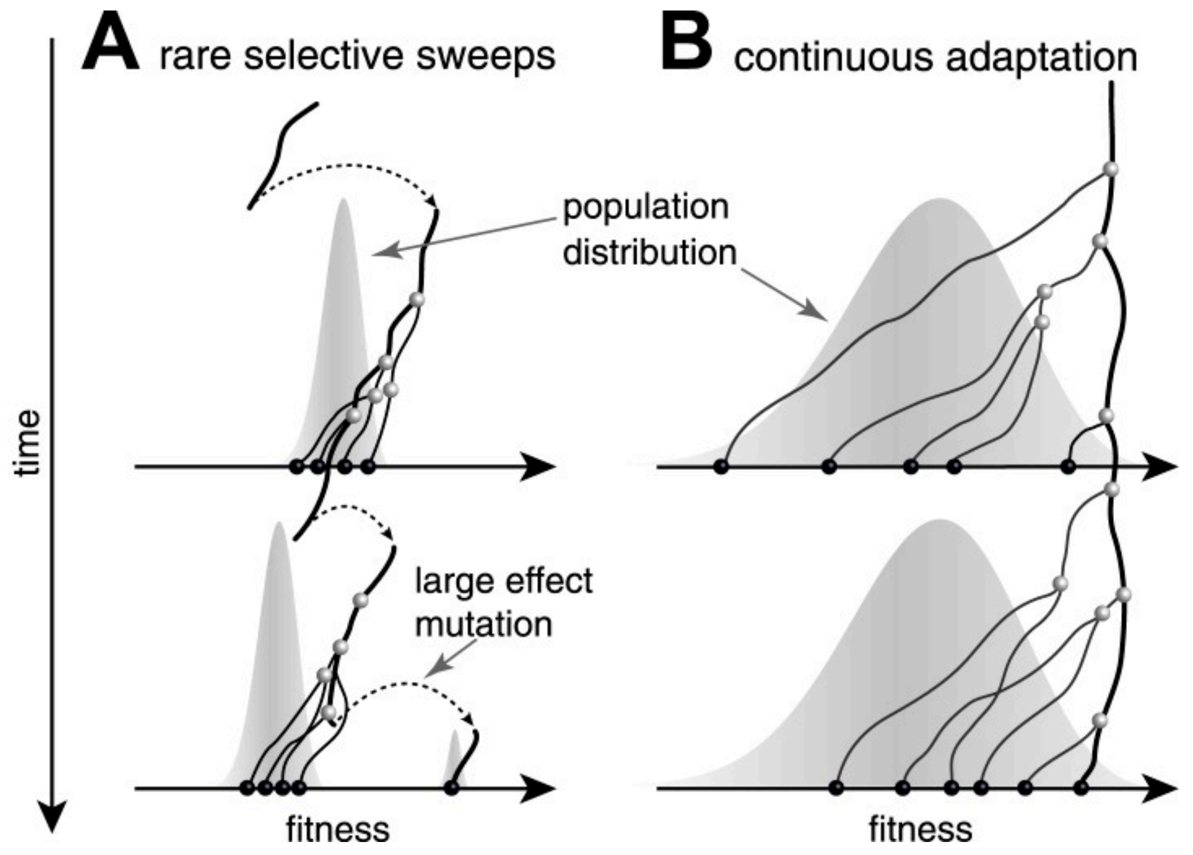
Clare Waterman
National Institutes of Health

We ask "physicist's questions" about the phenomena of life

How do living systems navigate parameter space?

Adaptation
Learning
Evolution

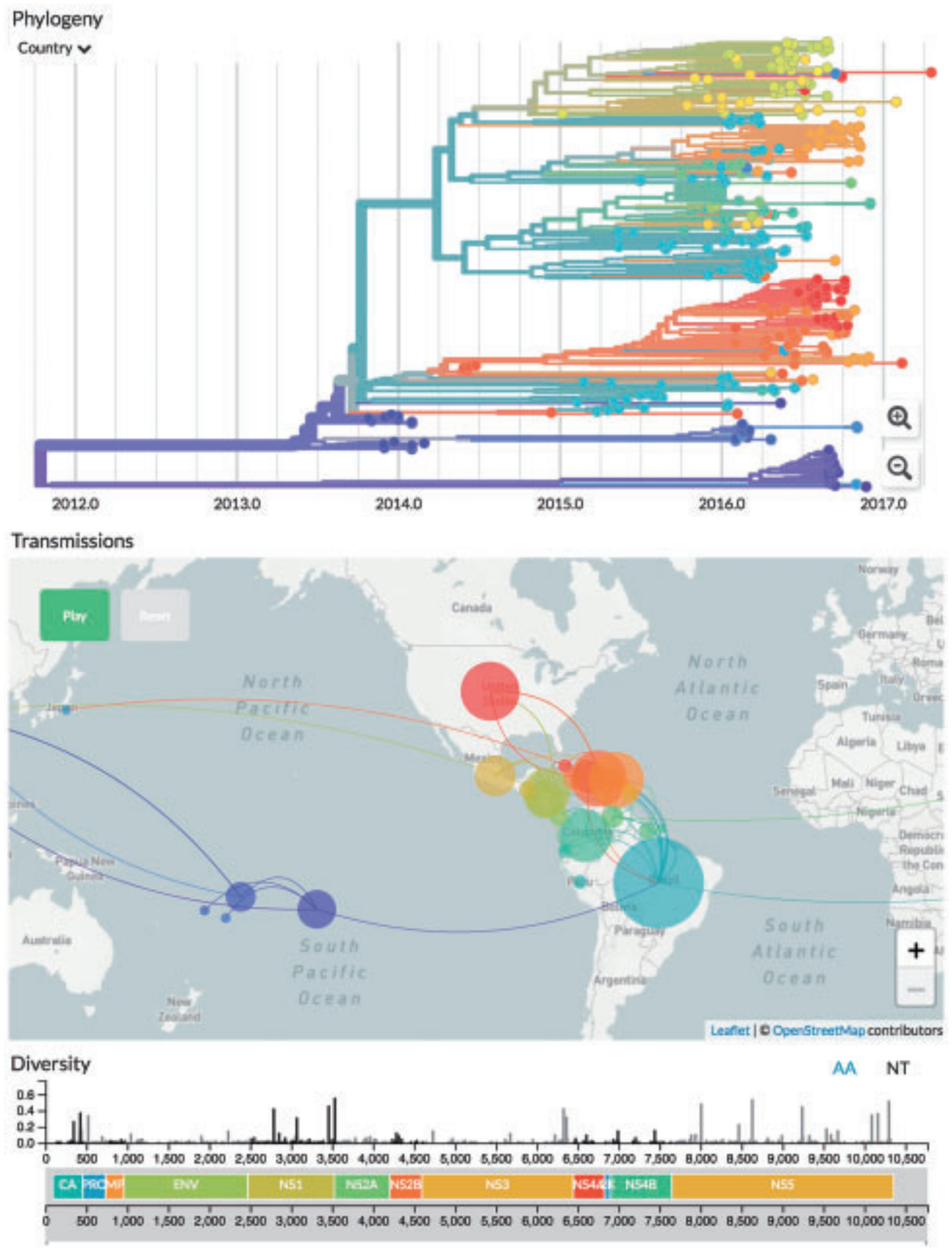
Theory uncovers hidden regularities: regimes in which evolution is predictable.



RA Neher et al, *eLife* **3,** e03568 (2014).

Develop new experimental tools for rapid, efficient DNA sequencing …

Theory and experiment come together in analyzing the evolution of viruses, including those that infect human populations.



Predicting evolution: Nextstrain tracks viral evolution and transmission (including covid); theory uses these data for prediction.

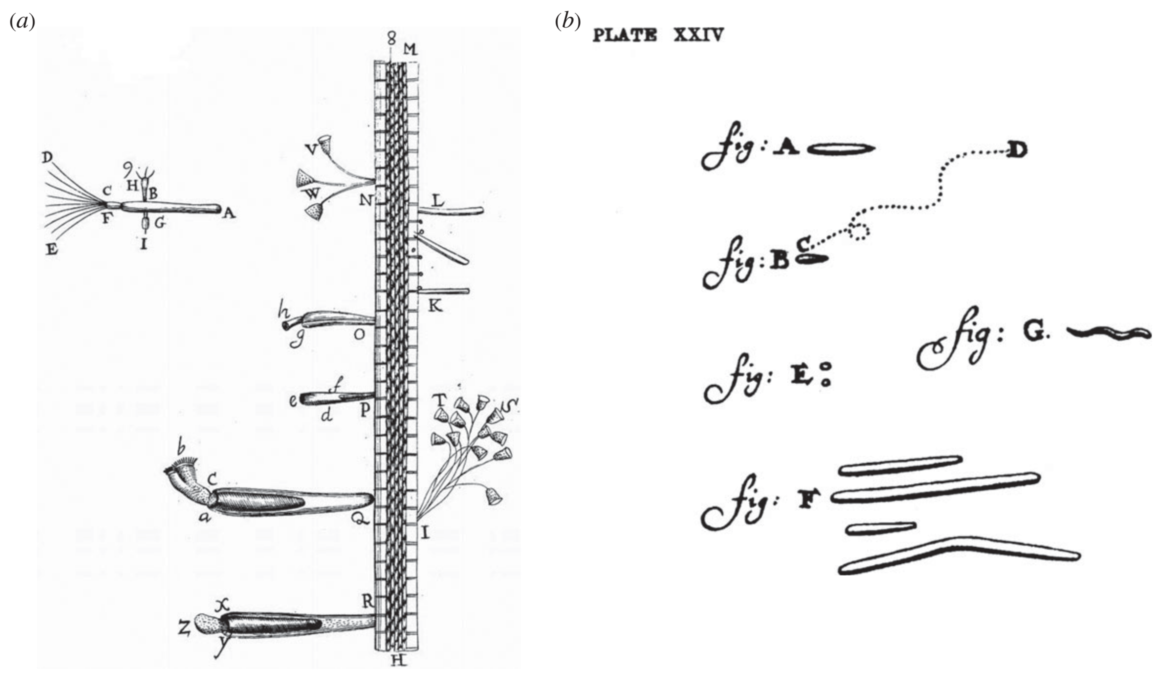
J Hadfield et al, *Bioinformatics* **34,** 4124 (2018).

Practical consequences: input to the WHO decision about next seasons' flu vaccine.

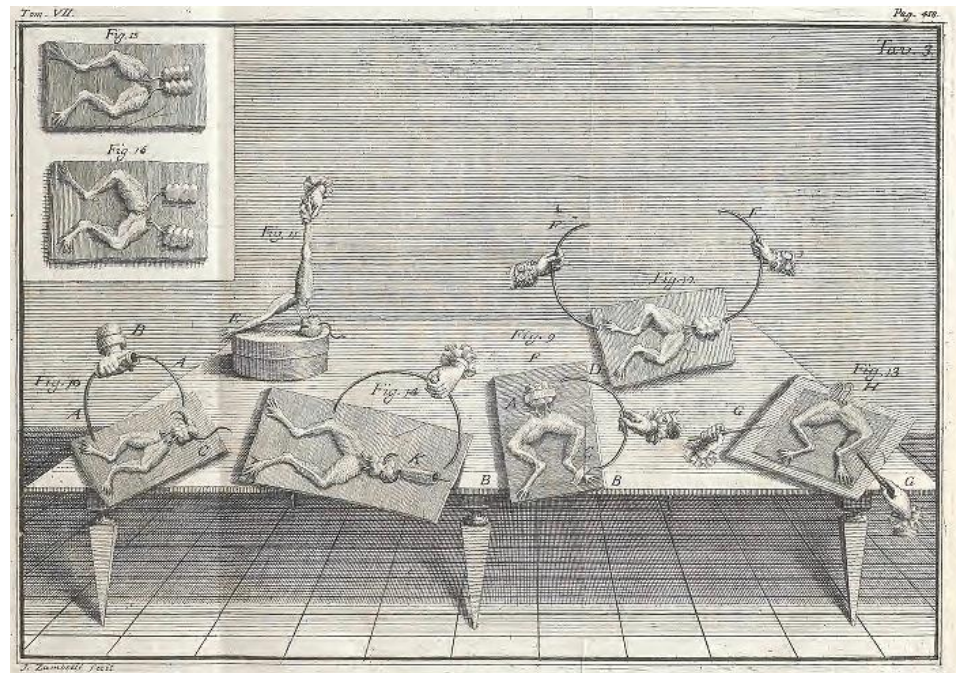
All these tools were ready when covid-19 hit, and quickly became a crucial part of the global response.

A longer view: the phenomena of life have long provided challenges to our understanding of the physical world

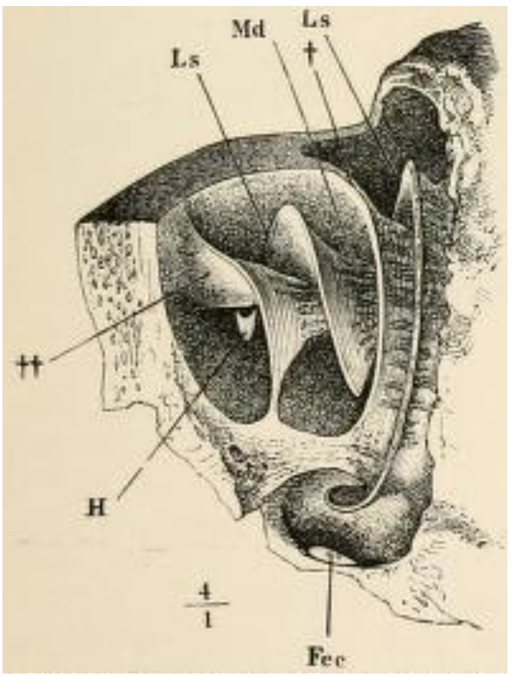
17th century



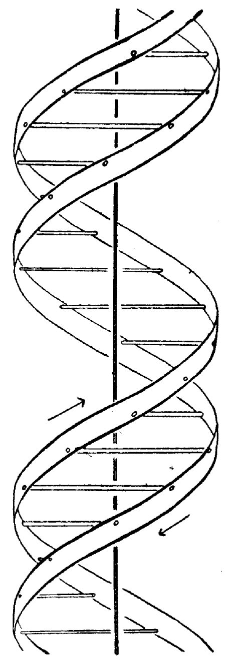
18th century

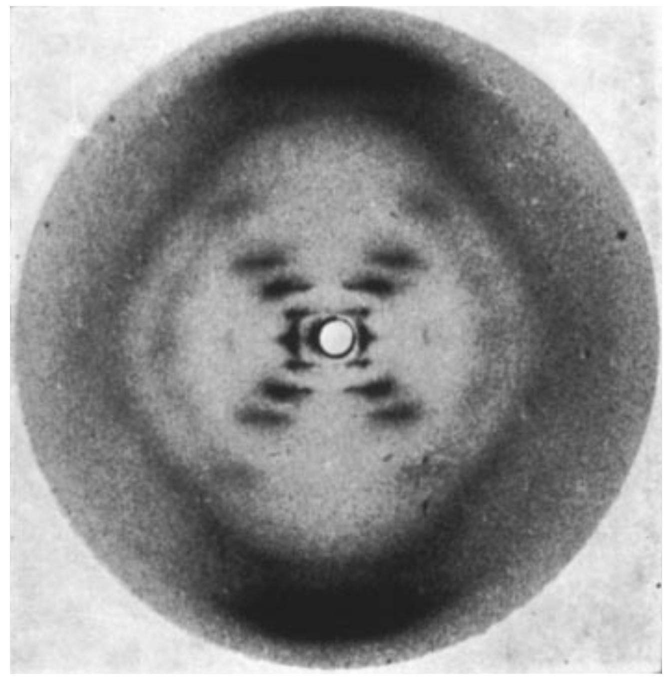


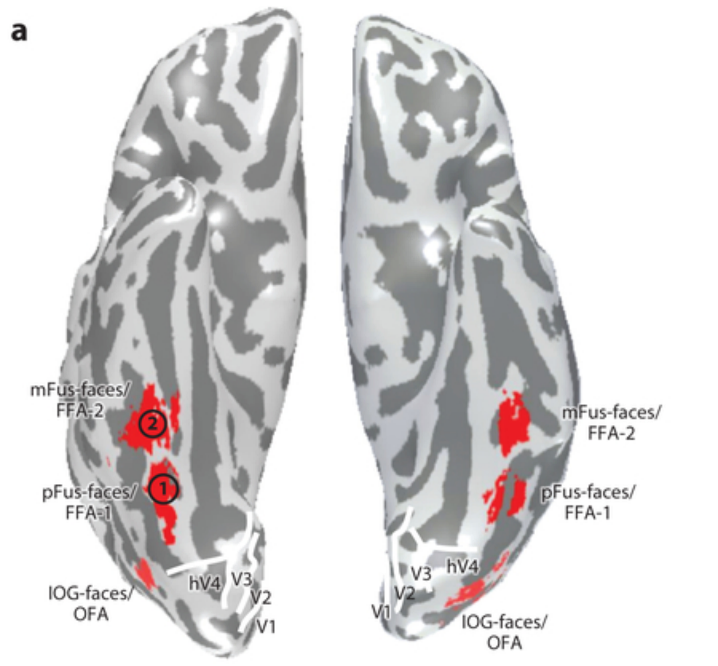
19th century



20th century







BUT, these successful example of physics/biology interaction are codified as progress in biology.

2000 ± 10: Growing appreciation that there is "real physics" in the physics of life.
No longer just the application of known physics to problems outside the field.

What changed? No single eureka moment.
Where are we now? How do we move forward?

More history and context in Introduction and Overview.

The Physics decadal survey

First effort in 1966 (!)

consensus reports
responding to task
community input
10 reviewers

e.g., the 2010 cycle:

- Astronomy and astrophysics
- Atomic, molecular, and optical physics
- Condensed matter physics
- Elementary particle physics
- Nuclear physics
- Plasma physics

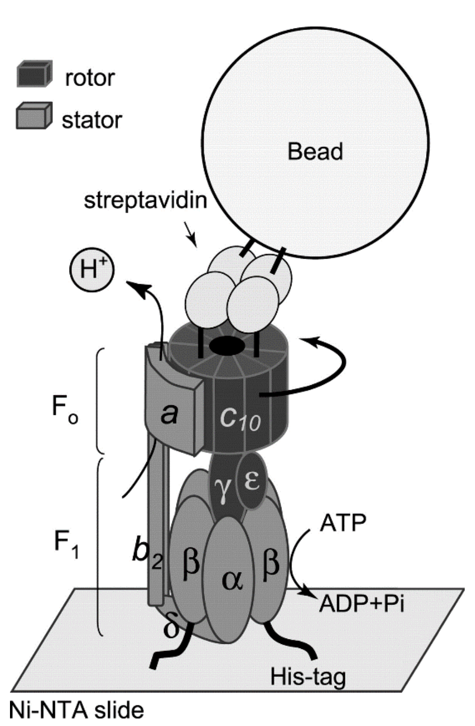
Different fields use the survey differently

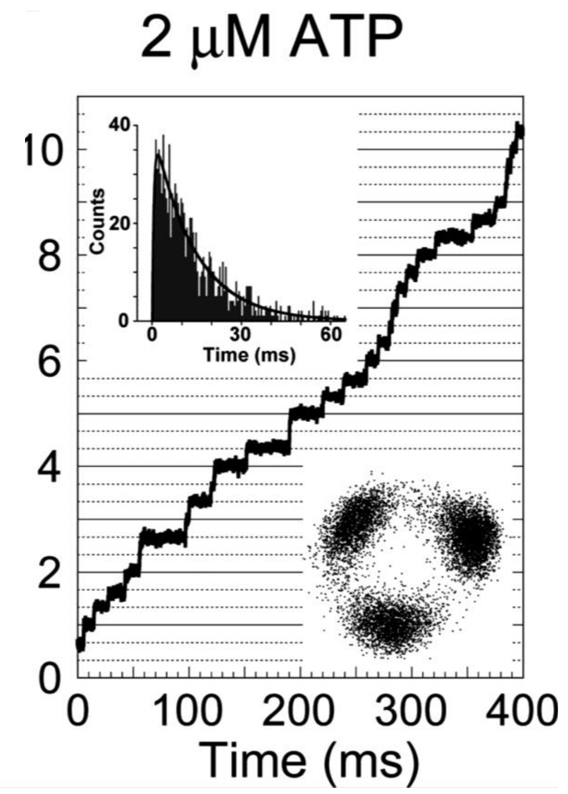
In the 2020 cycle, for the first time, biological physics stands alongside other fields of physics, with its own survey volume.

Exploring big questions

What physics problems do organisms need to solve?

Energy conversion
Mechanics, movement,
and the physics of behavior
Sensing the environment
Structures in space and time



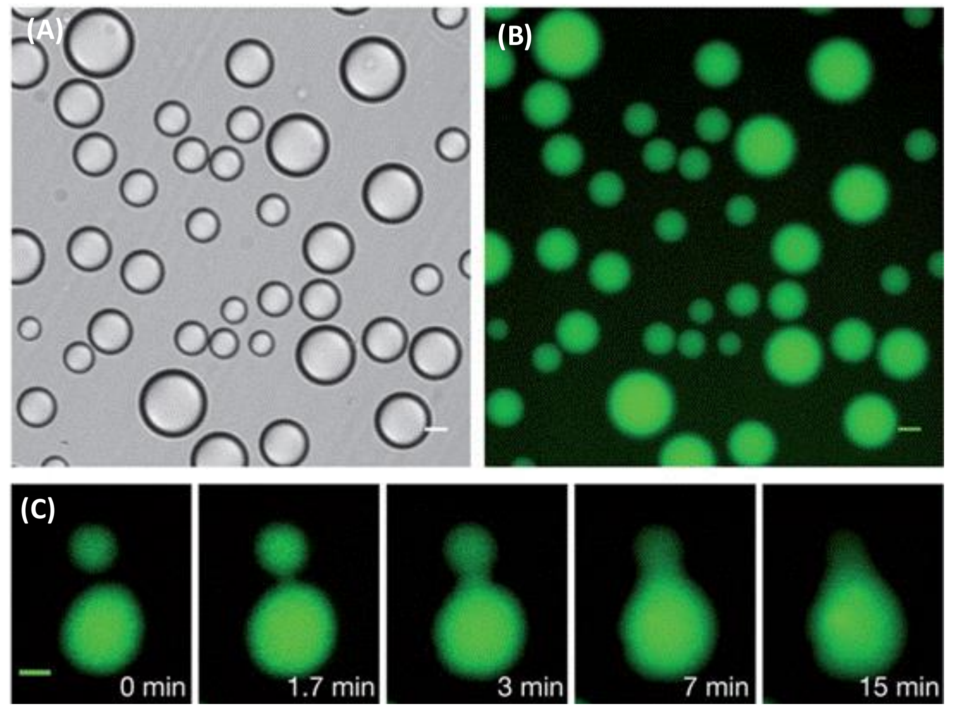


H Ueno et al, *Proc Natl Acad Sci (USA)* **102,** 1333 (2005).

Fuel for most of life produced by nano-scale rotary engine. New experimental tools to observe rotation directly, new theory for thermodynamics of small systems.

How do macroscopic functions of life emerge from interactions among microscopic constituents?

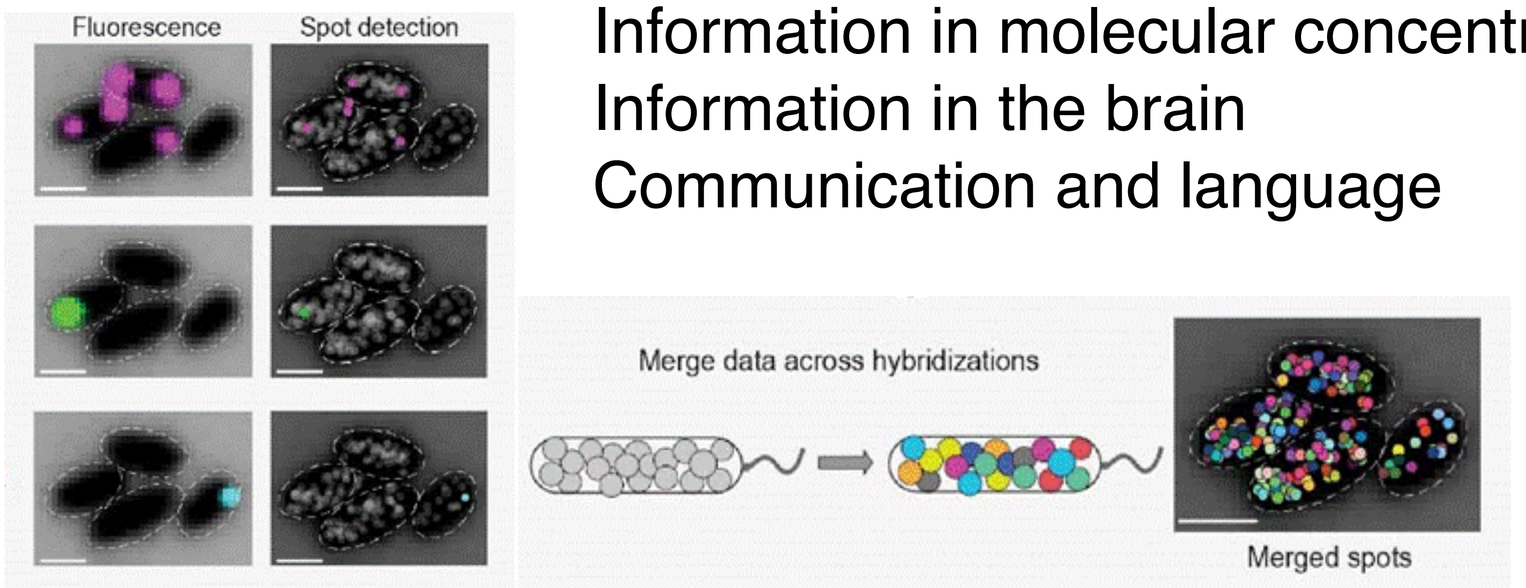
Protein folding, structure, and function
Chromosome architecture and dynamics
Phases and phase separation
Cellular mechanics and active matter
Networks of neurons
Collective behavior



Phase separation of proteins in cells: experiments in vivo and (here) in vitro; theory for condensation, function.

P Li et al, *Nature* **483,** 336 (2012).

How do living systems represent and process information?



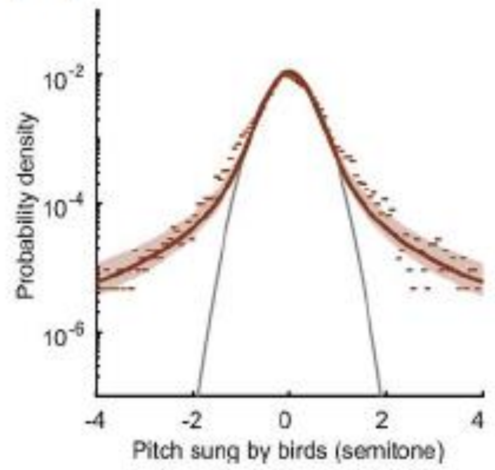
Information encoded in DNA sequence
Information in molecular concentrations
Information in the brain
Communication and language

Develop new physics-based measurements: localization microscopy to identify and count every single mRNA molecule in a cell

D Dar et al, *bioRxiv* 432792 (2021).

How do living systems navigate parameter space?

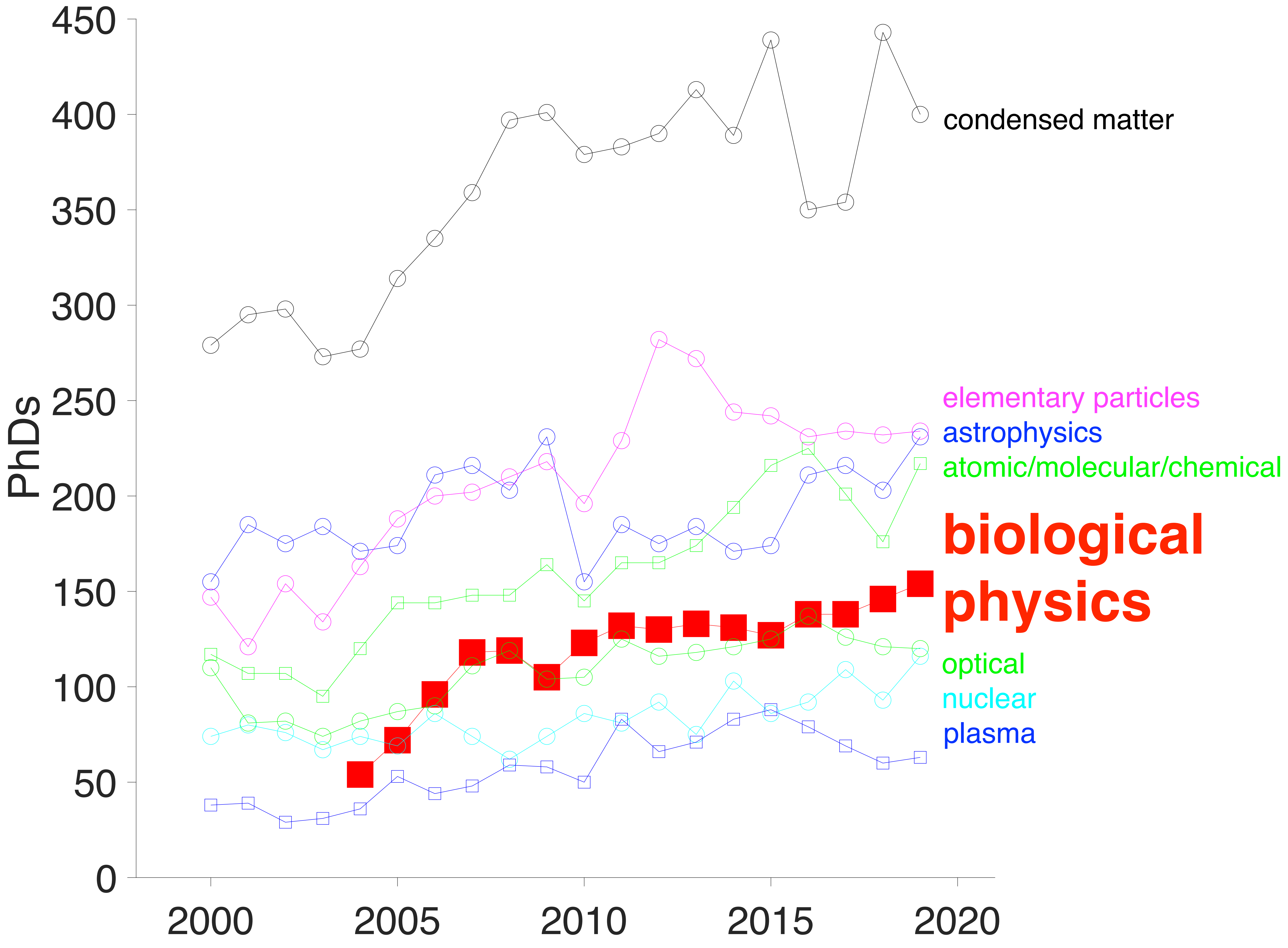
Adaptation
Learning
Evolution



Connecting theory and experiment: physical principles relate learning in songbirds to statistics of variations in the song itself.

B Zhou et al, *Proc Natl Acad Sci (USA)* **115,** E8538 (2018).

Scale of the field: Physics PhDs with thesis in biological physics



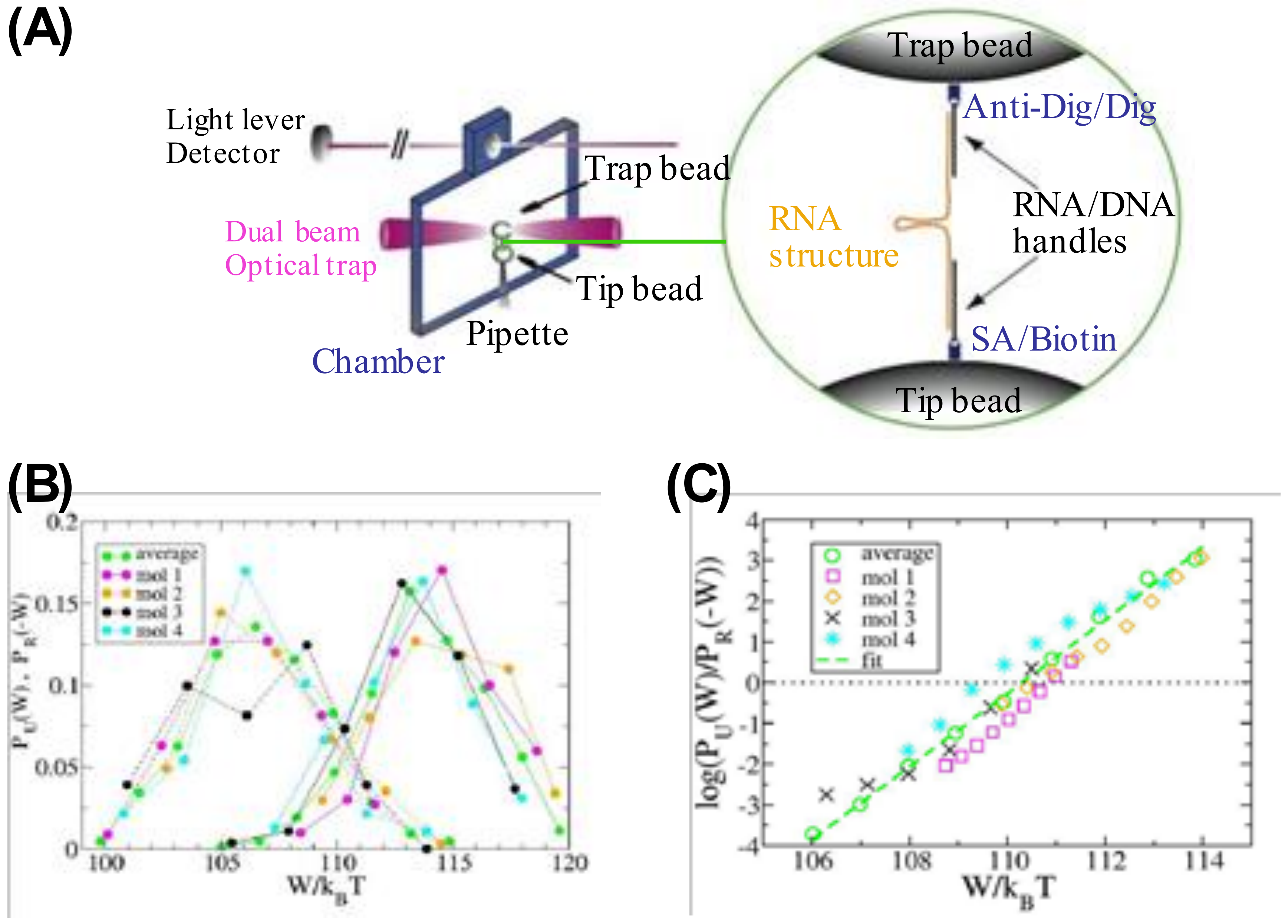
- **Biological physics today comparable to astrophysics or elementary particle physics in early 2000s.**
- **Growth of biological physics <u>as part of physics</u> in less than one generation**
- **Similar number of students in biophysics as part of biology.**

Source: *Doctorate Recipients from US Universities: 2019.* NSF 21-308 (National Science Foundation, Alexandria VA, 2020)

Conclusion: Biological physics, or the physics of living systems, now has emerged fully as a field of physics, alongside more traditional fields of astrophysics and cosmology; atomic, molecular, and optical physics; condensed matter physics; nuclear physics; particle physics; and plasma physics.

General Recommendation: Realizing the promise of biological physics requires recognition that is distinct from, but synergistic with, related fields, both in physics and in biology. 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.

Ideas, methods, and results flow between biological physics and other parts of physics – both ways.

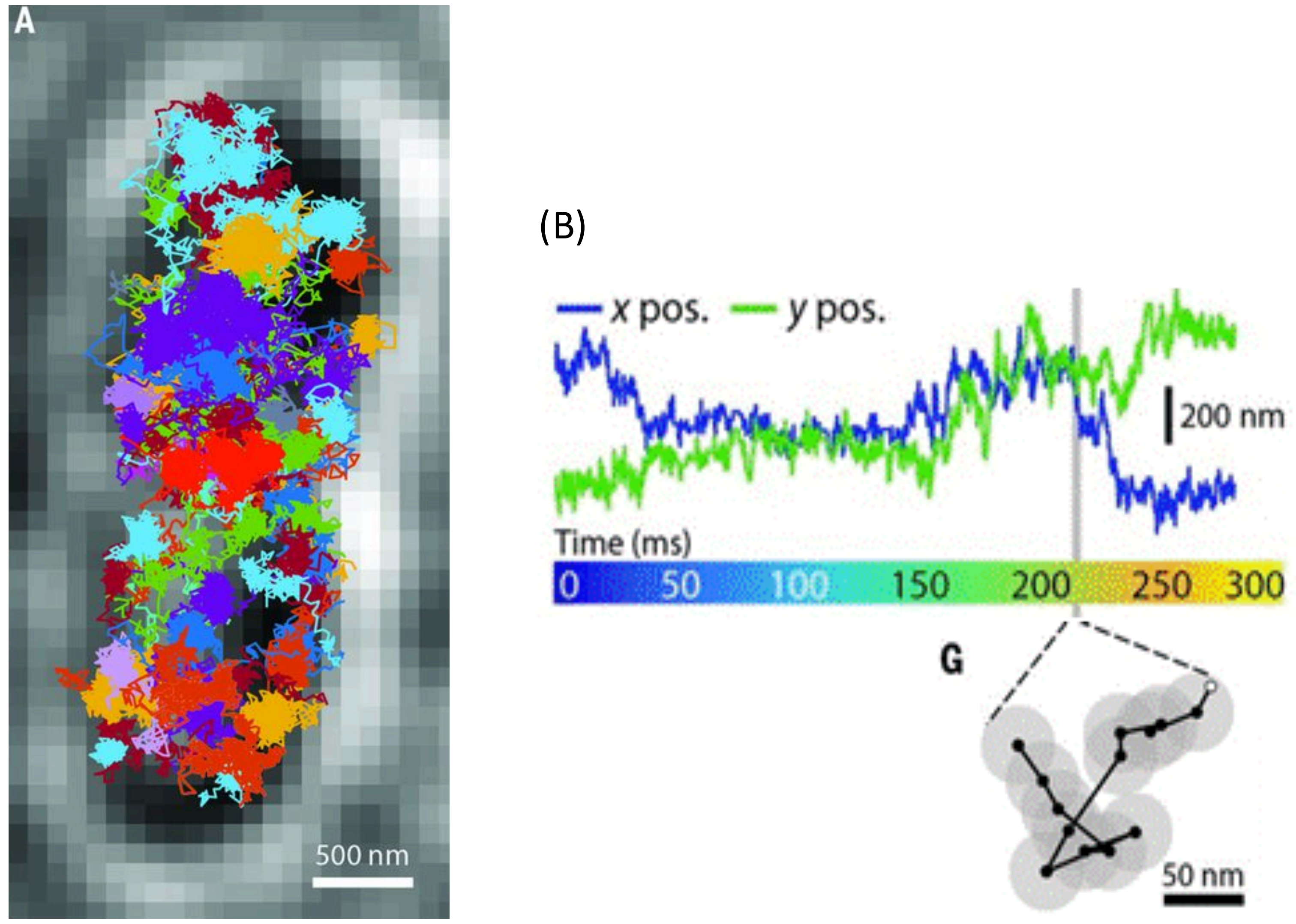


Best experimental tests of ideas in modern non-equilibrium statistical mechanics.

D Collin et al, *Nature* **437,** 231 (2005).

Biological physics connects with many areas of biology, drawing inspiration and driving progress

Breaking the diffraction limit: Tracking individual ribosomes in living cells with near-nanometer resolution.



F Balzarotti et al, *Science* **355,** 606 (2017).

This discussion only scratches the surface of the deep connections between biological physics and other areas of science, technology, and society

Tools for discovery
New microscopes, probes, …
Molecular and structural biology
Cryogenic electron microscopy
Genes, genomes, and evolution
Physics-based tools at the heart of the sequencing revolution
Cell and developmental biology
Condensates
From neuroscience to psychology
Functional magnetic resonance imaging

Imaging, diagnostics, and treatment
No more X-ray film (!)
Molecular design
New proteins for new functions
Synthetic biology
Network principles to practice
Predicting and controlling evolution
Next year's flu vaccine
Biomechanics and robotics
Gauge theories to robophysics
Neural networks and AI
Deep roots of deep learning

These connections are detailed in Part II: Chapters 5, 6, and 7.

To realize the promise of the field, strengthen the core of education and its integration with research

Physics students, even at well resourced institutions, can emerge with a degree and not know that biological physics exists as a field.

This matters not just for our field, but for the students' view of how physics connects to the world.

Within physics departments, this is entangled with other ways in which our curricula lag behind our modern understanding.

Meanwhile, substantial resources are being devoted to educating more quantitative biologists, bioengineers, etc.

General agreement that engagement in research is good for students, but this is disconnected from the core curriculum.

This was the biggest topic in community input!

Emergence of a new field is a chance to rethink how we teach, more generally.

Some problems can be solved by physics departments alone

General Recommendation: All universities and colleges should integrate biological physics into the mainstream physics curriculum, at all levels.

This is unpacked with specific recommendations in Chapter 8.

Some problems need university-wide attention

General Recommendation: University and college administrators should allocate resources to physics departments as part of their growing educational and research initiatives in quantitative biology and biological engineering, acknowledging the central role of biological physics in these fields.

And sometimes we need more help

Specific Recommendation: Federal funding agencies should establish grant program(s) for the direct, institutional support of graduate education in biological physics.

To maintain leadership in biological physics, and in other areas of science, the US must recover its privileged position on the world stage

Finding: Science in the United States has long benefited from the influx of talented students and scientists from elsewhere in the world.

Finding: Applications to U.S. physics graduate programs from international students have decreased since 2016.

Finding: Discussions of U.S. policy toward international students and scientists are being driven by concerns about national and economic security.

General Recommendation: All branches of the U.S. government should support the open exchange of people and ideas. The scientific community should support this openness by maintaining the highest ethical standards.

Specific Recommendation: Federal agencies and private foundations should establish programs for the support of international students in US PhD programs, in biological physics and more generally.

How do we support a field that is defined by its intellectual style rather the objects of study?

Conclusion: Biological physics is supported by multiple agencies and foundations, but this support is fragmented, obscuring the breadth and coherence of the field. It is dangerously close to the minimum needed for the health of the field.

General Recommendation: Funding agencies, including NIH, NSF, DOE, and DoD, as well as private foundations, should develop and expand programs that match the breadth of biological physics as a coherent field.

This is unpacked with specific recommendations in Chapter 9.

Finding: The United States has had a longstanding role as a leader in the area of biological physics at the molecular scale. Crucial support for this effort comes from Department of Energy (DOE) investment in programs and user facilities.

Finding: DOE has become a major sponsor of research in biological physics, especially through facilities, without acknowledging the field's supporting contribution to the DOE mission.

Specific Recommendation: Congress should expand the Department of Energy mission to partner with the National Institutes of Health and the National Science Foundation to construct and manage user facilities and infrastructure in order to advance the field of biological physics more broadly.

To build an inclusive community, resources should be targeted to core activities in underserved groups.

Finding: Physics education is layered, with one layer building strongly on the one below. Inequality of access or resources is compounded.

General Recommendation: Federal agencies should make new resources available to support core undergraduate physics education for under-represented and historically excluded groups, and the integration of research into their education.

Specific Recommendation: Recognizing the historical impact of HBCUs, MSIs, and TCUs, faculty from these institutions should play a central role in shaping and implementing new federal programs aimed at recruiting and retaining students from under-represented and historically excluded groups.

Chapter 10 provides details on building an inclusive community, along many dimensions.

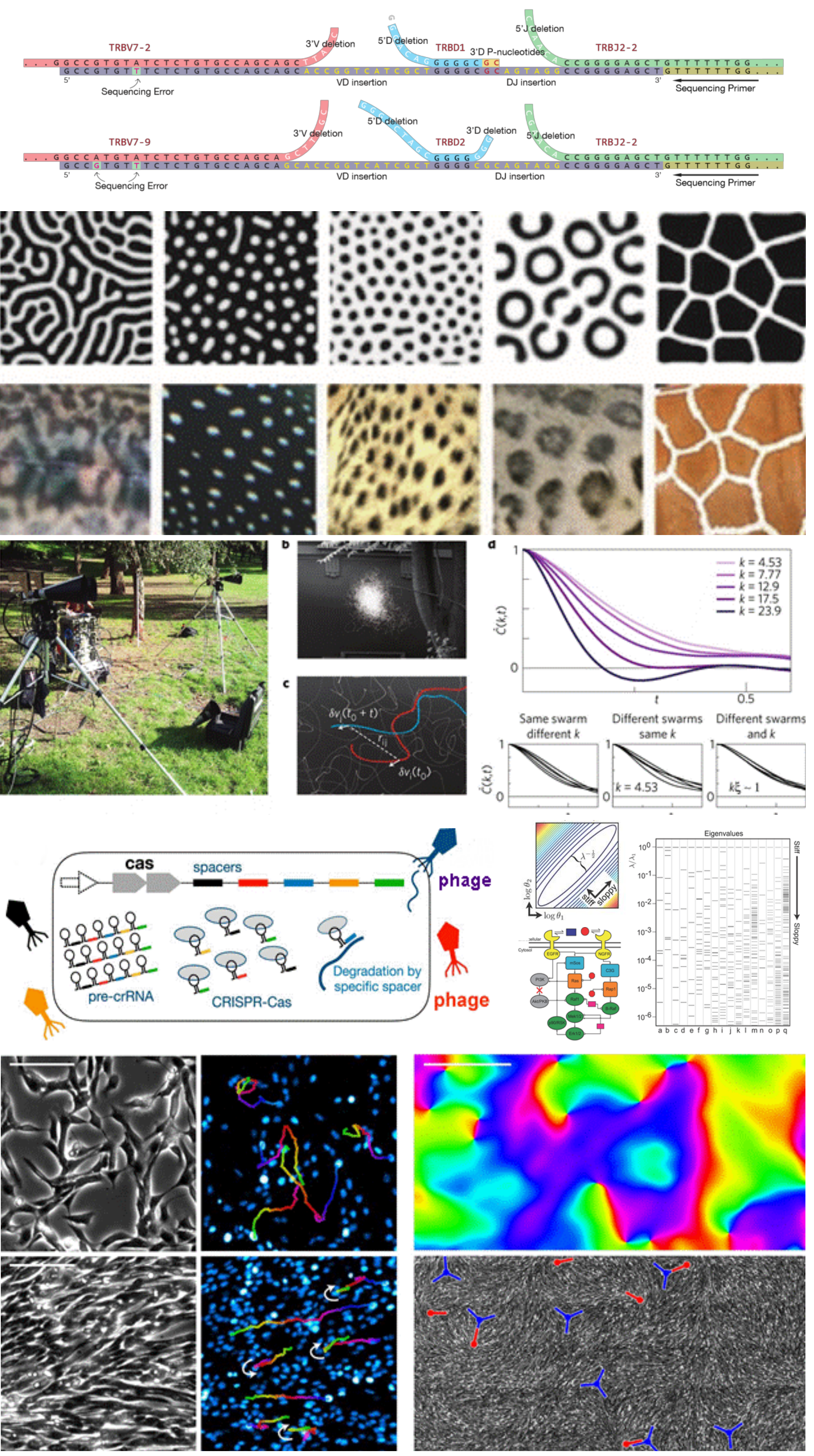
Women continue to be dramatically under-represented in the physics community.

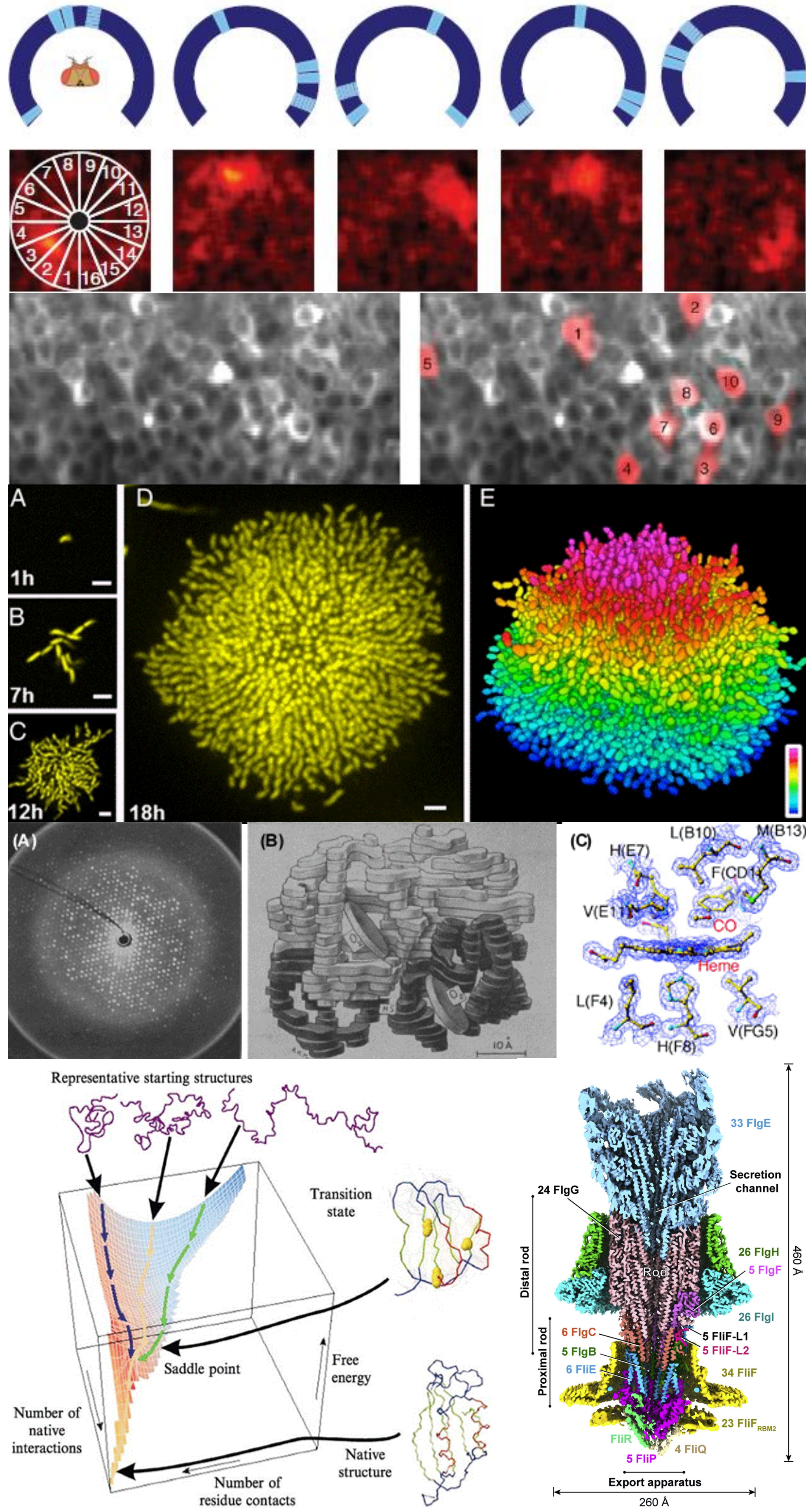
Finding: The fraction of women who take a high school physics course is almost equal to the fraction of men, but women comprise only ~ 25% of students in the most advanced high school courses.

Finding: After steady growth for a generation, the fraction of bachelor's degrees in Physics earned by women plateaued in 2007 at ~20%. The fraction of PhDs in Physics earned by women has continued to grow, now matching the fraction of bachelor's degrees.

Specific Recommendation: In implementing this report's recommendations on introductory undergraduate education and its integration with research, special attention should be paid to the experience of women students.

Perhaps the field has a special role to play: female physics students twice as likely to do thesis research in astrophysics or biological physics.





For the biological physics community, this is a moment to celebrate.

More broadly, it is exciting to reclaim as part of physics the beautiful phenomena of life, rekindling the dreams of our intellectual ancestors.

nap.edu/physicsoflife

The National Academies of
SCIENCES · ENGINEERING · MEDICINE