IUPAP Commission on Biological Physics (C6)

Report on Activities from 2017 to 2021

Ramin Golestanian, C6 Chair Jeff Gore, C6 Vice Chair Masaki Sasai, C6 Secretary

1. Joint EBSA-IUPAP ICBP2019 in Madrid, Spain

The 10th IUPAP International Conference on Biological Physics (ICBP2019) was held jointly with the European Biophysical Societies Association (EBSA) during 20-24th July 2019 in Madrid, Spain. More than 1000 participants from all over the world and working a diverse range of topics related to biophysics attended the meeting. Professor Juan Manuel Rodríguez Parrondo from Universidad Complutense in Madrid, who is member of C6, was co-chair of the ICBP2019 conference together with the EBSA Vice President Prof. Jesus Perez-Gil. There were three satellite meetings organized in Ljubljana, Madrid, and Lausanne. Senior members of both communities put together 14 symposia that were very well attended. This ensured a good synergy between the two organizations. This was a very exciting development as it was the first time that two historically separated communities that represent different parts of the spectrum of this interdisciplinary field joined up forces to have an active participation in bridging the barriers amongst them. The conference was balanced well in terms of invited speakers, symposia chairs, and members of the scientific advisory board.

2. IUPAP C6 Young Scientist Prize in Biological Physics 2018, 2019, 2020, 2021

Two winners were selected for the prizes of 2018 and 2019, which was collectively presented at the 10th international conference in biological physics (ICBP), held in Madrid, Spain, during July 20 - 24, 2019. Two winners were selected for the prizes of 2020 and 2021, to be presented in a virtual ceremony.

2021: Dr. Amin Doostmohammadi, Niels Bohr Institute, Copenhagen, Denmark "For his groundbreaking contributions applying the concepts of active matter physics and topological defects in biological contexts."

2020: Dr. Anne-Florence Bitbol, EPFL, Laussane, Switzerland

"For her significant contributions to predicting protein-protein interactions from sequence data and to modeling the evolution of microbial populations with complex spatial structures or time-varying environments, employing methods inspired by statistical physics."

2019: Dr. Knut Drescher, Max Planck Institute for Terrestrial Microbiology, Germany "For his significant contributions to imaging and understanding the spatiotemporal development and function of bacterial multicellular behaviors, ranging from collective motion to bacterial biofilm communities." Knut Drescher is currently both a professor of biophysics at the Philipps-Universitaet Marburg and a Max Planck Research Group Leader at the Max Planck Institute for Terrestrial Microbiology in Marburg, Germany. Knut received his undergraduate education in physics at the University of Oxford from 2003-2007, before completing a PhD in biophysics at the University of Cambridge in 2011, where he pioneered measurements of flow fields around microorganisms and their hydrodynamic interactions. He became interested in bacterial multicellular behaviors and molecular biology during his postdoctoral fellowship at Princeton University, in the Department of Molecular Biology from 2011-2014. In 2014, Knut Drescher moved to Marburg, Germany, to take up his current positions. Knut's work focuses on understanding the morphogenesis of bacterial communities, and the evolutionary fitness consequences of life within bacterial communities. His work combines genetics, biochemistry, and biophysical techniques to explore molecular, physical, and evolutionary mechanisms underlying bacterial behaviors

within communities. Most recently, he has developed live-cell imaging techniques for biofilms and swarms that simultaneously capture the single-cell dynamics and community dynamics, thereby facilitating major new insights into bacterial collective behaviors.

2018: Dr. Nikta Fakhri, MIT, USA

"For her significant contributions to applying fundamental principles of thermodynamics to experimental nonequilibrium biological systems, and advancing our understanding of how molecular-scale non-equilibrium processes are manifest in the system dynamics at larger scales." Nikta Fakhri is Thomas D. and Virginia W. Cabot Career Development Assistant Professor of Physics at MIT (Cambridge, MA, USA). She completed her undergraduate degree at Sharif University of Technology, Tehran, Iran and her PhD at Rice University (Houston, TX, USA) in 2011. She was a Human Frontier Science Program postdoctoral fellow at Georg-August-Universistät in Göttingen, Germany where she pioneered the use and development of fluorescent single-walled carbon nanotubes as probes in soft matter and biophysics. At MIT, her lab focuses on identifying underlying principles of collective dynamics and complex spatiotemporal patterns in far from equilibrium biological systems.

3. ICBP2023

We have decided to hold the next ICBP conference at the Seoul National University, Seoul during the week of July 10 (Mon) to 14 (Fri), 2023.

4. Proposal for a C6 Senior Award

We have decided to establish a senior award for C6. This will help the process of community building for those who work at the interface between physics and biology with a strong emphasis on answering physical questions about biological systems and life in general. We have named the prize as the *Schrödinger Medal in Biological Physics* from C6 IUPAP. The details of the process including membership of the award committee and the decision-making guidelines will be determined by the next C6 commission.

All the questions about biophysics

Ramin Golestanian, Chair of IUPAP Commission on Biological Physics (C6)

What is biophysics? Who is a biophysicist? How can I evaluate a biophysicist colleague? What type of research agenda should be considered as high-quality biophysics work? What does it mean to have an impact in biophysics? There are many questions like these that many of us are grappling with. We could be very early career aspiring researchers and trying to plan our future, early career researchers and trying to steer our plans through the rugged academic landscapes, or established researchers in the field and struggling to explain ourselves to others. Or we could be senior researchers serving on evaluation panels for grants and promotions, advisory boards for conferences, and search committees for academic hires, editors of high-profile journals and trying to decide what type of work should be considered sufficiently important for consideration, or even decision-makers in national science funding agencies and needing to decide how to allocate funds for interdisciplinary research. We all face these questions.

The interface between physics and biology offers one of the most exciting research opportunities for the 21st century; it covers questions ranging from the origin of life to understanding why living systems are hierarchically structured and how they can achieve homeostasis under non-equilibrium conditions. These challenges will keep physicists busy for many years to come. Therefore, it is important to find a way to answer the above questions. We cannot afford to get these questions wrong.

The first step towards answering the questions is to acknowledge that the interface between physics and biology offers a wide spectrum of possibilities, and it will be naturally wrong of us to assume that there is only one type of biophysics or biophysicist. I have found over the years that a good way to break down this wide spectrum is to use the following four indices for researchers in biophysics: the background training they have had, the tools and techniques that they use, the systems they are studying, and the sort of questions they are trying to answer. A combinatorial construction with these indices is shown in the Table below. Viewed in this way, it is evident that there are many different flavours of biophysics that cannot be directly compared with one another. They can have very powerful synergistic relationships.

There are many physicists who choose Class 8 for their career and immigrate to biology, or choose Class 4 and take powerful tools with them in addition to their training. Due to the nature of this path, the right way to evaluate the research outcome of such physicists is to gauge the impact they have had in biology by asking the opinion of biologists. For those who choose Class 3, on the other hand, the impact should be gauged by probing the contribution they make towards developing new physical insights into the complex behaviour of non-equilibrium living matter. Evidently, it would be a travesty to evaluate Class 3 based on the appropriate criteria for Class 8 or Class 4, and vice versa. Other cases can also be considered to explore the different styles of biophysical research that are possible. Interestingly, there are some combinations that offer new challenges, and can be considered for future expansions of the research agenda at this interface.

These indices play an important role in building research communities. Similar training provides common language that is essential for community cohesion, and tool development is a major part of the work for most researchers and they find it helpful to share tips and technical expertise. The use of common systems allows researchers to compile practical knowledge about calibration, sample preparation, and so on, whereas common questions give focus to shared research programmes.

The interdisciplinarity of the field allows people to complement each other, which means that many research teams are defined based on the last two indices, i.e. systems and questions, and contain members that cover complementary realizations of the first two induces, i.e. training and tools. Moreover, in recent years a number of interdisciplinary training programmes have been established to develop background that can cover physics and biology both in terms of academic training and techniques. While

such plans to integrate interdisciplinarity at the early stages of training will help blur some of the divisions arising from the classification shown in the Table, I believe awareness of the existence of such differences is important when we try to define what biophysics is, and find answers to the all the other questions about biophysics.

	training	tools	systems	questions	comment
1	phys	phys	phys	phys	physics
2	phys	phys	phys	bio	synthetic living systems; origin of life
3	phys	phys	bio	phys	biological systems as living matter
4	phys	phys	bio	bio	bio-oriented biophysics; instrumentation
5	phys	bio	phys	phys	a new challenge?
6	phys	bio	phys	bio	a new challenge?
7	phys	bio	bio	phys	a new challenge?
8	phys	bio	bio	bio	(immigration to) biology
9	bio	phys	phys	phys	(immigration to) physics
10	bio	phys	phys	bio	synthetic living systems; origin of life
11	bio	phys	bio	phys	biological systems as living matter
12	bio	phys	bio	bio	bio-oriented biophysics; biology
13	bio	bio	phys	phys	a new challenge?
14	bio	bio	phys	bio	a new challenge?
15	bio	bio	bio	phys	a new challenge?
16	bio	bio	bio	bio	biology

Table: Multiple variants of research style at the interface between physics (phys) and biology (bio).

Joint 12th EBSA 10th ICBP-IUPAP BIOPHYS-ICS CONGRESS

MADRID, Palacio Municipal IFEMA. July 20-24, 2019.

Jesús Pérez Gil, Chair. Universidad Complutense de Madrid. Juan MR Parrondo, Co-Chair. Universidad Complutense de Madrid.

The 10th International Conference on Biological Physics (ICBP), organized by the C6 IUPAP Commission, took place last July in Madrid. In this occasion, ICBP merged with one of the most important events for the biophysics community in Europe, the biannual congress of the European Biophysical Societies' Association (EBSA), which embraces more than thirty national societies.

The joint effort of IUPAP and EBSA has made possible the participation of almost one thousand researchers from all over the world, the organization of 32 symposia, and the presence of eight outstanding plenary speakers, including two Nobel Laureated, Gregory P. Winter and Stefan W. Hell.

But, more importantly, the combination of the topics covered by the two organizations brought forth a unique conference that has explored the role of physics in almost every aspect of life, from molecular and cell biology to tissues, ecosystems, bacterial colonies, and evolution; as well as how physics is revolutionizing the instrumentation to study biological phenomena, from microscopy and fluorescence to single molecule manipulation and bio-informatics.

This multidisciplinary and exhaustive character of the conference in Madrid is illustrated by the variety of topics covered by the plenary speakers and the symposia.



Gregoy P. Winter in his plenary lecture on Saturday 20th.

The congress started on Saturday, July 20th, with a plenary lecture by **Gregory Paul Winter** (University of Cambridge, Nobel Laureated, 2018) on the development of antibodies enhanced through evolution of a massive number of combined modules exposed by bacteriophages. We learn not only the basic features of this "phage display" technique, but also its therapeutic and economic relevance as a source of new drugs based on antibodies.

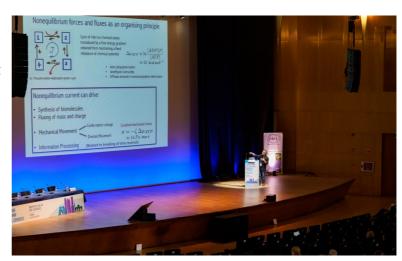
There were a number of contributions dealing with the detailed characterization of biological systems at the molecular scale. **Eva Nogales** (UC Berkeley) showed in her plenary lecture how the most recent Cryo-EM techniques can reveal the structure of protein complexes without the need of crystallization. Nogales presented a detailed description of the structure and function of transcription factors in the complex machinery of polymerases. In another plenary lecture **Julio M. Fernández** (U. Columbia) explained the physics of titin, a large polymer that, in combination with myosin, is able to store elastic energy in muscles.

Mechanochemistry was also present in a number of symposia. There was a symposium on **mechanobiology** and one on **molecular motors**, that covered a rather coherent overview of different studies on classical motor systems. Talks dealt with different biophysical approaches to muscle contraction, operation of DNA polymerases during replication, and actin cytoskeleton pushing forces as collective molecular motors. Mechanical properties were also addressed in the symposium **biophysics of the cytoskeleton**, where we had talks on neural intermediate filaments that serve as shock absorbers under mechanical compression, the mechanical and assembly properties of microtubules on the reconstitution of mitotic spindles, and the spindle dynamics in cell

division and polarization. The mechanics of the cytoskeleton in reconstituted systems was also present at **Patricia Bassereau**'s (Curie Institute, CNRS) plenary lecture, connected with membrane curvature and its effect on lipid and protein sorting.

Several symposia focused on different aspects of regulation, signaling, and the physics of DNA. The session on **DNA architecture and gene regulation** discussed multiscale structural and dynamical issues of DNA, nucleosomes and chromatin up to genome-wide scales. The observation of DNA asymmetrical unwrapping and the relationship between transcription and the dynamics of nucleosomes were some of the topics within this symposium.

A session on trafficking and signaling focused on the mechanisms of information transmission through the cell membrane and intracellularly. The variety of subjects falling within this definition generated a diverse session that triggered lively discussions. The invited speakers presented results based on novel imaging techniques: a detailed dynamic reconstruction of the yeast endocytic machinery based on super-resolution microscopy, the formation of signaling platforms on the cell membrane through visualization at the single molecule level, and cryo-EM structural information on talin autoinhibition state and its effect on cell migration and signaling. Madan Rao's plenary lecture also addressed signaling from a more general perspective, explaining how the clustering of



Madan Rao's plenary talk.

receptors allows for a reduction of noise and a more accurate estimation of the environment.

The symposium on **gene network dynamics and signaling** explored the signaling problem at a larger scale and including the comparison between experimental data and mathematical models. The talks presented a wide spectrum of the challenges we face in this area, such as our characterization and understanding of spatial and/or temporally coordinated phenomena, the wiring of gene circuits and protein networks, stochastic dynamics and heterogeneous responses. These aspects were addressed across different talks of the symposium, which covered a wide range of organisms and processes: a differentiation process in cyanobacteria that involves communication between cells, time differences in the oscillatory dynamics of notch signaling components between different animal species, or the analysis of the dormant state of yeast spores.

Physics is the main tool to analyze how matter is organized. The different forms of matter organization in living systems were one of the main subjects of the conference, both passive, like lipid membranes and ionic liquids, and active, like actin-myosin gels, swarming bacteria, and biofilms.

Two symposia, one on **liquid-liquid phase separation in biological systems** and another one on **ionic liquids and biomolecules** focused on the effect of organic ionic liquids on proteins, DNA and biomembranes. Different talks presented molecular dynamic simulations and experimental data from novel electron microscopy methods that are able to unveil nanoscale processes in ionic liquids. A symposium on **lipid and lipidome** was concerned with factors that affect the mechanical properties of lipid bilayers. The invited lectures focused on membrane remodeling by amyloidogenic peptides, partitioning of a glycolipid in a phase-separated bilayer upon Shiga toxin binding, and understanding the effect of compositional asymmetry on the bilayer bending rigidity.

In the symposium membrane structure and dynamics, one major topic was the mode of action of antimicrobial peptides on membranes. For a detailed biophysical study, model membranes such as vesicles are frequently used. In this context, speakers reported on the development of methods to produce large unilamellar vesicles with asymmetric lipid distributions as well as techniques to handle, manipulate, and analyse giant unilamellar. We also learned that modern fluorescence imaging techniques as well as surface sensitive techniques are

becoming invaluable tools to investigate protein-lipid (IQGAP1 - phosphoinositides) as well as virus-glycocalyx (herpes simplex virus - cell surface glycosaminglycans) interactions.

Other symposia on the biochemistry and biophysics of membranes comprised biophysics of membrane oxidation, cell membrane biophysics, and mechanisms of membrane proteins.

Active matter was the topic of a symposium with talks that covered a wide range of computational studies on collective behavior of biological active matter, including swarming bacteria and sperms as well as large scale models of cytoskeletal dynamics. There were also talks on experiments of active gels which mix microtubules and motors. A similar topic was addressed by Nikta Fakhir, recipient of the IUPAP Young Scientist Prize in Biological Physics 2019, who talked in a plenary session about irreversibility and thermodynamics of active

matter. The session was also closely related to the symposium non-equilibrium physics in biology, which highlighted the role of concepts from nonequilibrium physics for various problems in biophysics. Two of the invited talks focused on how active processes in membranes and cells affect their morphology and fluctuations and which quantitative signatures of non-equilibrium can be extracted from such data. The third invited talk highlighted the subtle role of virus geometry for the dynamics of their uptake at the cell membrane and how fluctuations modify a simple deterministic scenario.



Ramin Golestanian (Chair of C6) and Jeff Gore (Secretary of C6) with Nikta Fakhri, IUPAP Young Scientist Prize 2019.

The symposium on cellular prolifera-

tion was mainly devoted to biofilms and bacterial colonies. The IUPAP Young Prize awardee, **Knut Drescher**, presented —in this symposium and in a plenary session— extensive simulations of biofilms, showing that relatively simple interaction potentials can reproduce most of the morphology and phenomenology of these bacterial ensembles. Other talks also pointed out the similarities between biofilms and liquids, and there was also some evidence that the behavior of bacterial colonies can help to understand the dynamics of tumor growth.

At a larger scale, physics is relevant to explore more complex biological systems like morphogenesis and tissue organization, the immune system and evolution. Three symposia addressed these topics. A session on **tissue biophysics and morphogenesis** brought together biophysicists of cancer and embryonic development (organoids, tumor growth, measurement of forces generated in epithelia by biomimetic emulsions, etc.) and theoreticians using the approach of statistical physics and fluid mechanics to model the behavior of cells, tissues, cancer morphogenesis and active droplets of bacteria. The symposium on the **biophysics of the immune response** focused on the immunological synapse (for T cells) and showed how current developments in real-time imaging and molecular manipulation are changing our view of the field. In particular, physical mechanisms as protein or lipid diffusion or mechanosensing are main actors in the activation of T cells, shifting traditional kinetic measurements as secondary. On the side of activation via the innate system, the talks provided innovative information regarding the structural aspects of the cellular signaling. This new information opens the way to the rational design of new activators and inhibitors of the cellular immune response.

The symposium on evolutionary dynamics had three invited contributions covering different areas that nicely

relate empirical observations and theoretical developments: experiments that analyzed the accumulation and prevalence of different mutations during colonization of the mouse gut; the use of advanced techniques (cell imaging and laser ablation) to question nature with the final aim of discarding or accepting dynamical models of cell division; and the monitorization of bacterial evolutionary dynamics using microfluidic cell traps.

Finally, there were a number of plenary lectures and symposia dedicated to the last developments in instrumentation, bio-informatics, big data, and biomolecular simulation.



Posters and company stands

The two sessions on biomolecular simulation and computational biophysics covered a variety of topics related to timely biophysical research questions, such as lipid-modulated protein activation, the development of coarse-grained models for large-scale studies of biomolecular systems, including a cell membrane hosting more than 1000 membrane proteins, and the development of novel means to use machine learning and deep learning for the analysis of research data. There was also a symposium on big data in biophysics.

Gregory A. Voth (U. Chicago) gave an excellent plenary talk on multiscale simulation of biomolecular systems where we learned that the thermodynamics of the formation of viral capsids can be crucial for drug design.

In the session on **live imaging and optical microscopy** a recurring discussion topic was to raise awareness for the bias we experience when looking at microscopy images followed by the request to move beyond "seeing is believing". This requires a critical review of sample preparation and the selection of imaging techniques and proper analysis, especially of localization microscopy data, as well as the integration of as much information and parameters as possible with the help of complementary approaches (multimodal imaging). A symposium on **macromolecular complexes** also presented novel techniques for structural biophysics.

The symposium on **new frontiers in bioimaging** covered the applications of optical nanoscopy MoNaLISA for brain cell imaging, MESOLENS for 3D optical imaging of large biological specimens with sub-cellular resolution, and BRILLOUIN IMAGING to explore biomechanics in cells and tissues. Two outstanding plenary talks showed the relevance and the possibilities of new fluorescence and imaging techniques. **Jennifer Lippincott-Schwartz** (Howard Hughes Medical Institute) showed spectacular movies obtained by multispectral imaging that enable her to track single molecules with a time resolution of 50 microseconds. The Nobel Laureated, **Stefan W. Hell**, presented his revolutionary microscopy method that uses the bistability of fluorescence molecules to increase the image resolution far beyond the optical limitation given by the wavelength. He convinced the audience that this super-resolution microscopy will be soon present in every competitive laboratory.

The sessions on instrumentation where completed by two symposia. The first one was organized by the ARBRE-MOBIEU COST Action and entitled **emerging breakthrough molecular-scale biophysics methodologies**. Several novel approaches and technology developments were presented: mass spectrometry approaches to investigate protein conformational changes and dynamics; novel chemical biology strategies for atomic resolution structural information; AFM single molecule approach allowing to combine information on interactions forces, energy landscapes and kinetic rate constants; μ -Raman and μ -Brillouin spectroscopy with sub-nanometric resolution for biological material characterization; newly developed mass photometry approaches based on interferometric scattering microscopy for protein dynamics and interactions studies; and development of two micro- and nano-structured surface architectures for label-free spectroscopic and microscopic protein studies.

The second one was organized by INSTRUCT-ERIC (www.instruct-eric.eu) with the topic: **integrating access to biophysics and structural biology in Europe**. In this session, four scientific talks provided excellent examples of the integrated use of Cryo-EM, Cryo-ET, in-cell NMR, X-ray crystallography, AFM and molecular dynamics simulations, in situations as diverse as Perforin-2 structure and function, cellular signaling, bacterio-phage structures and alpha synuclein deposition.

The conference also benefited from the presence of a number of companies that presented their new products and a delegate of the European Research Council who conducted an informative session on the ERC Grants.

In summary, we think that the Madrid EBSA-IUPAP Congress offered an unprecedent exhaustive panorama of the interplay between physics and biology, and that this has been possible thanks to the collaboration of the two institutions. As reported by the chairs of the symposia, the talks had a very high quality and triggered lively and interesting discussions.

We would also like to take this opportunity to thank the plenary speakers, the chairs of the symposia, who have done an excellent work designing and leading the sessions, the spectacular work of the local committee and the volunteers, and all the participants. In the closing session EBSA and IUPAP, respectively, announced the locations of the next conferences: the 13th EBSA conference will take place in Vienna (Austria) in 2021, and the 11th ICBP organized by IUPAP-C6 will take place in Seoul (South Korea) in 2023.

Thanks again to all participants, congratulations for the high quality of the talks, and see you soon in Vienna and Seoul!