IOP Institute of Physics
Biological Physics Group

NEWSLETTER

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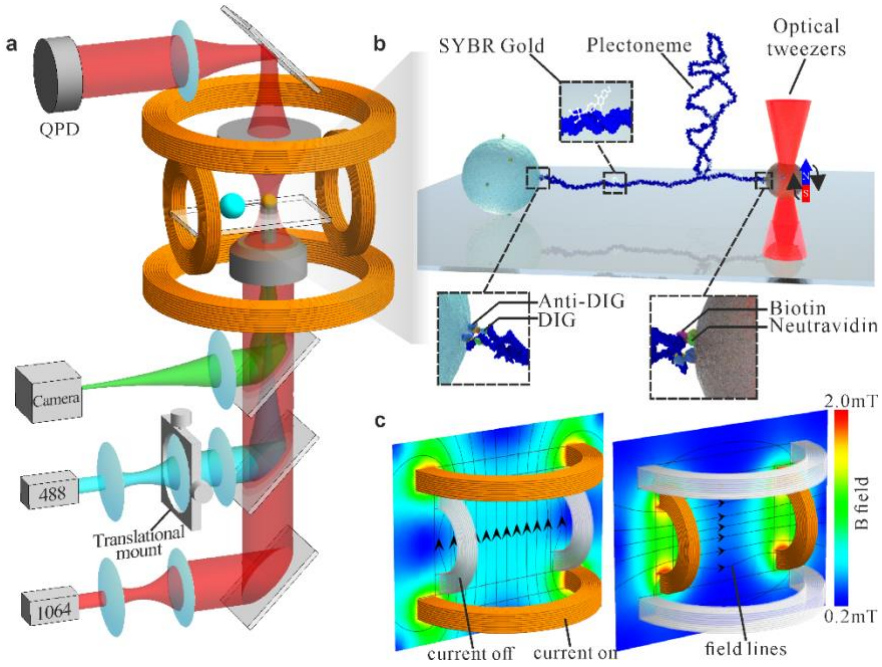


Cover Image

Development of a new biomolecular microscopy technology 'COMBI-TWEEZ', which simulatouesly combines optical and magnetic tweezers with single-molecule fluorescence imaging to study symmetry breaking and structural emergence in single chiral biomolecules, such as DNA.

More details available at https://www.nature.com/articles/s41467-024-47126-6
Image credit: Shepherd, Guilbaud, Zhou & Howard et al. Correlating fluorescence microscopy, optical and magnetic tweezers to study single chiral biopolymers such as DNA. *Nature Communications* (2024).

Contents

Websites
www.iop.org/physics-community/special-interest-groups/biological-physics-group#gref
sites.google.com/view/biologicalphysicsgroupuk/home

The Chair's commentary

Dear Biological Physics Group,

2023 saw the BPG sponsor either jointly or in full eight major events, including the fabulous inaugural Physics of Life 2023 meeting in Harrogate which attracted over 500 participants spanning the full range of stakeholders involved in biological physics research in the UK, and included unique support from multiple bodies in addition to the BPG from the Physics of Living Matter and Physics meet Biology consortia, the British Biophysical Society, and the Physics of Life Network PoLNET. In addition, we sponsored a very well-received lecture tour of the winner of the Tom Duke lecture prize 2023, Prof Pietro Cicuta from the University of Cambridge. The BPG has had a really successful year, helping to stimulate wide new interest in a range of diverse areas of biological physics research in the UK. At a personal level as Chair, it is has been a real privilege to work with such talented and enthusiastic committee members, who give their time for free just for the sheer passion of wanting to help our biological physics community.

Sadly though, the community lost one of its true pioneers in Prof Tom McLeish FRS from the University of York, who passed away on Monday 27 February 2023 following at short illness. Tom, friend and colleague to many in the BPG, in addition to being an exceptional researcher in the theory of biopolymer physics, was a passionate polymath who had a unique talent to shine a blazing spotlight focused upon the beauties of interdisciplinarity in research, which in particular had substantive impacts about the recent growth of biological physics research and research culture within the UK. Notably, Tom's passion included a huge depth of support for early career researchers and for helping to develop creative ideas for how to improve the opportunities for those early in their education career trajectories, as seen through his roles in chairing the Royal Society' Education Committee and PoLNET. Tom's passing represents an enormous loss, but his legacy lives on unbounded, with such promising and productive engagement of previously disparate researchers from across the physical-life sciences interface. Thank you, Tom; it's such a privilege to have known and worked with you. We miss you, but will not your flame diminish.

Mark Leake, University of York, Chair of the Biological Physics Committee

Tom McLeish being, as ever, dynamic! Picture courtesy of Prof Giles Gasper, University of Durham.

The current committee

Professor Mark Leake (Chair)
University of York
Develops new biophysical instrumentation to apply to open biological questions

Professor Mark Wallace
(*Treasurer)*
KCL
Mark's group builds artificial mimics of cell membranes

Professor Michelle Peckham
(Secretary)
University of Leeds.
Interested in the cytoskeleton, molecular motors, super-resolution imaging.

Dr Marco Mazza
University of Loughborough
Uses theory and computer simulations across scales to identify the driving mechanisms of complex matter organization

Dr Chiu Fan Lee (Website).
Imperial College London:
Works on universal behaviour in biology, protein amyloid self-assembly and pathogenesis, phase separation in the cell cytoplasm, and active matter

Dr Diana Fusco (Newsletter Editor*)*
University of Cambridge
Physics of microbial ecology and evolution

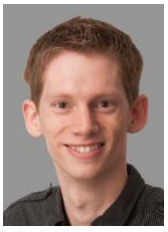
Dr Isabella Guido
University of Surrey
Interested in self-organisation and mechanical instability of active systems made of biopolymers and motor proteins

Dr Margarita Staykova,
University of Durham
Interested in understanding the functional principles of biological membranes and capture them in artificially designed smart interfaces

Dr Bartlomiej Waclaw,
(Website Editor)
University of Edinburgh,
Interested in applications of statistical and soft matter physics to biological evolution

Dr Nirvana Caballero,
University of Geneva,
Theoretical Physicists, specialises in statistical and computational physics

Dr Timothy Saunders,
University of Warwick,
Quantitative Developmental Biologist



Dr Peter Adams,
University of Leeds,
Nanoscale Physics

Dr Massimo Vassali,
University of Glasgow,
Mechanobiology

Dr Matteo Degiacomi
Durham University
Uses molecular simulation and machine learning to study protein structure, dynamics, and assembly.

The 2022 Tom Duke Lecturer: Prof. Pietro Cicuta

I was very grateful to be appointed by the IOP Biological Physics group committee as "Tom Duke lecturer" in 2022. Being appointed makes you think the committee believes you can do it, which is clearly an honor... but what is the task? My understanding is that this lectureship is intended to empower the holder to travel to three or four places, give a talk, and make some splash and noise to promote biological physics, whilst stimulating as much as possible local interactions. The IOP group has been appointing Tom Duke lecturers on a two-year cycle, and I believe I have now been the 5th, following in the big steps of Martin Howard, Andrew Turberfield, Rob Endres and Rosalind Allen.

Tom Duke (1964-2012) was a pioneer of what I think of as the "modern wave" of biological physics. He was a theoretical physicist, talented in soft matter, dynamical systems, statistical physics, always working closely with experimentalists, and with amazing ability to home in on great questions. Reflecting on his contributions, which among others spanned from early work on DNA in flow treated with polymer physics models, to understanding stereocilia in the ear as non-linear amplifiers of sound, up to his latest contributions on tumor transitions to metastasis, I found myself also thinking back at how the connections between physics and biology seem to have come in waves.

I dared start my talks with a slide on this history of engagement across disciplines. There is of course a history of technologies, which is partly entwined with what people could do, but I tried to follow a thread of what people were trying to discover. The immediate post-war set foundations of quantitative microbiology (e.g. cell growth laws) and physiology (e.g. membrane potentials, waves in axons). Many techniques, model organisms, classical questions all date back to that period, and so much of that work is still fresh and appealing across all disciplines today. The language of that time, be it size distributions or voltages, is very "physicsy", and scientists 100 years ago had no fear of maths and physical models! DNA structure and the central dogma in the 50s clearly shifted the emphasis of biology as whole for decades thereafter and, after the inital roles of several well-known physicsts, perhaps the partner science to the genetics side of this endeavour was primarily chemistry. The power of crystallography in its various sorts underpinned a huge growth of structural biology that continues to date, and my sense is that this tied well with a body of work we label as "biophysics", exploring for example ion channels, molecular motors, lipid bilayer membranes, and cytoskeleton. This flavour of biophysics started in the 70s and grew over 30 years, with strong overlaps to the soft matter physics community establishing at the same time. What perhaps distinguishes our contemporary period, these last 20 years, of which Tom as mentioned was a pioneer, is the attempt to go beyond the "pieces" and address a whole question and a process within life. We now embrace challenges that can be complex, and involve all kinds of elements from gene regulation to solid and fluid mechanics. Often riding on new technology and new protocols, new classes of experiments have also become possible exploiting microfluidics, unprecedented live imaging, micromanipulation and labelling approaches, up to creating and controlling cell differentiation, organoids and complex organ on chip. Even communities of species can be explored in the lab, as models of new classes of biological systems to test questions in evolution and ecology. There is need of expertise from all directions. I would say that in all of this the role of physicists remains the ability to perform measurement (in all its forms from bespoke instrumentation to robust data analysis of complex data) and to rationalise results in terms of minimal physical models, which encompass a clear mechanism and allow some form of prediction and extrapolation. This was the essence of my short introduction, and I hope Tom would have recognised the spirit of his work here.

My research talk was on waves in motile cilia. Motile cilia are active filaments present on the surface of various human organs (e.g. the lung and brain epithelia), where they perform crucial functions by driving surface flows. Structurally, they are conserved across the eukaryotes. Cilia can affect each other, for example leading to phase locking of their beating, by the forces they exert on each other through the fluid and in some cases through the cell cytoskeleton. Some beautiful physics has been developed by various teams in the last decade to understand how the details of beating on each cilium can lead to specific phase locking, and to the emergence of collective waves. I talked about our recent work exploring the role of external flows, both oscillatory and constant, and their role in development and in health/disease. I chose this topic because I was hoping to appeal also to non-bio physicists, since analogies can be drawn between these flows and the effect of external magnetic fields in magnetic systems. I presented experimental results but also numerical explorations of a simple class of ”rower” models of motile cilia, again trying to reach out to the large community who work with numerical techniques and could be attracted to biological questions.

By tradition the first lecture of the series is held at UCL, which was Tom Duke's last place of work. I then headed West and avoiding institutions visited by previous holders of the lectureship I visited Bath and Cardiff in September 2023. There were great audiences at all three places, and the experience was certainly useful to me in seeing up close what people do in their labs! Post-pandemic the frequency of in-person events is not as high as before, and perhaps we have particularly lost occasions for more established people to meet early career researchers. I was therefore very grateful that Charlotte Dodson in Bath managed to bring together an afternoon of short talks by ECRs from various departments - great research, and it felt like my visit had catalysed something good. UCL and Cardiff were also great: I spoke non-stop for hours and met so many old and new friends! Thanks particularly to Bart Hoogenboom, Paola Borri and Bo Hou for hosting and organising.

A final reflection if I may, as these thoughts also came up in many conversations. Our community of biological physics has grown and there are signs of optimism, from the successful March 2023 meeting in Harrogate (to be repeated in 2025) to the two UKRI-funded Physics of Life funding rounds in recent years. But we are still quite thin compared to USA and many EU countries, and still at risk of fragmentation possibly entrenched by the still fragmented research funding structure. Indeed quite worryingly we do not have a solid funding horizon ahead (despite the need, demonstrated by the large number of applications, no other rounds of Physics of Life UKRI funding are planned as far as I know) nor are we seeing an increase of PhD studentships or CDT centers in our area. The Tom Duke lecturer is tasked with advocating for all of this, but of course has very little actual impact. It is up to everyone, in the right places, with the right people, with the right language and examples, to make the case for what this community has to offer.

Pietro Cicuta, University of Cambridge

Physicist of the Month: Rosalind Franklin

We are introducing a new segment of this newsletter: every issue will now feature a short paragraph on a renown physicist who has made significant contributions at the intersection of physics and biology, topics we've explored in our 'Major Contributions of Physics to Biology'." (link to the site https://sites.google.com/view/biologicalphysicsgroupuk/major-achievements).

We begin, perhaps unsurprisingly, with Rosalind Franklin. She is mostly associated with her research that helped to develop the model of DNA, but her contributions to biological physics were much wider and involved studying other organic molecules with the help of X ray crystallography.

Rosalind Franklin was born in 1920 into a prominent British Jewish family, and showed exceptional abilities already in her childhood. She excelled at school (with the exception of music!), and won a scholarship to attend Cambridge, where she focused on chemistry. She then worked in Paris under the supervision of Jacques Mering, where she learned X ray crystallography. She later moved to King's College London, where she worked on the structure of the DNA, and finally to Birkbeck College where she became a senior scientist supervising her own research group.

While in France, she published papers on the physics and chemistry of coal and graphite. After returning to the UK, she focused on the structure of the DNA, but later moved on to work on the structure of the tobacco mosaic virus and the Polio virus.

Regarding her most famous contributions, she was the first to state that phosphate groups resided on the exterior of the DNA molecule. This aspect was initially overlooked by Watson, leading him to devise the incorrect three-helical model. Franklin then provided her seminal "photo 51" of the DNA X-ray diffraction image (acquired by her student Raymond Gosling) which, upon presentation to Watson, prompted him to recognize the pattern as indicative of a helix. This was possible because Francis Crick, Watson's collaborator, had previously predicted the diffraction pattern expected from a helix. This insight aided Watson and Crick in developing their model, incorporating data from various sources, culminating in the publication of a Nature paper in 1953, alongside another paper authored by Gosling and Franklin.

Franklin was never nominated for a Nobel Prize. She died of cancer in 1958 before the structure of the DNA was considered to be fully proven. It has been speculated that her exposure to X-rays was a contributing factor to her untimely death.

Bartek Waclaw, University of Edinburgh

Meeting reports

Super-resolution workshop, July 2023, Leeds

Organizers: Michelle Peckham (Leeds) and Izzy Jayazinge (Sheffield))

The aim of this workshop was to talk about advanced imaging, and specifically to address the challenges and problems that are commonly encountered. This highly popular workshop was attended by approximately 70 people, including the 6 invited speakers, and company representatives, some of whom gave short technobyte talks. The first talk was from Joerg Bewersdorf (Yale, USA), who gave an overview of his new DNA Exchange Paint related approach to super-resolution imaging (Schueder et al., preprint available on BioXriv) doi: https://doi.org/10.1101/2023.05.17.541061) called 'FLASH PAINT'. He pointed out that the problem with exchange PAINT is that it requires multiple imaging DNA strands, which are expensive to make, that the sample requires extensive washing to remove each one, before adding the next, and is best used in total internal reflection fluorescence microscopy (TIRFM). In this new, faster approach, TIRFM is not required, and only a single imager probe is required in this multiplex imaging approach, removing the need for extensive washing and making the cost of this approach much cheaper. Lothar Schermelleh (Oxford), an expert in structured illumination microscopy (SIM), talked about using this approach to image chromatin in nuclei, and how well his results matched those of EM. He explained how it was important to check if SIM was working correctly and not introducing any artefacts. Hari Shroff (Janelia) provided a great and clear introduction to image restoration via deep learning approaches, something he has used effectively in iSIM to enable long term imaging at low light (and low signal to noise) intensities. He explained how we need better predictors of when these methods fail, how to be aware of failures, what was sensible to try and what should be avoided. Sandrine Leveque-Fort (Paris) how she is adapting her single molecule microscopy approaches to image thicker specimens such as spheroids., using an approach called 'Modloc' (time-modulated excitation for enhanced single-molecule localisation microscopy) to increase resolution x2.4 in one direction, showing beautiful images that demonstrated this new approach. Juliette Griffié (Stockholm) explained inputs, encoders and decoders in AI and how she could use AI to assign fluorescent images of bacteria sequentially to specific points in the cell division cycle, if the data is presented in the right way (backed up with simulations), together with all the pitfalls to look out for. Finally, Christian Eggeling introduced his work on diffusion at the plasma membrane: picket fences or not? He gave a great overview of all of the different imaging methods he has used to try to understand this process, and the advantages and disadvantages of each, and how potential errors in the measurements might arise. In addition to the main speakers, we had 7 short talks from early career researchers on a range of topics related to the main meeting, from expansion microscopy to using nanodiamonds in microscopy.
Michelle Peckham

Advancing Radiation Biology, October 2023, London

Organizers: Colin Whyte (Strathclyde), Ken Long (Oxford), Mark Leake (York), Richard Amos (UCL), Tim Greenshaw (Liverpool)

The Biological Physics, Medical Physics, High Energy Particle Physics, and Particle and Beams Groups of the Institute of Physics came together to discuss the novel techniques required to elucidate the mechanisms that determine the impact of ionising radiation on tissue (https://indico.stfc.ac.uk/event/915/). Such techniques have the potential to significantly impact clinical practice in particle beam therapy, synergising interdisciplinary integration in the Physics of Life and wider collaborations in the U.K. such as through PoLNET to build bridges between physical and life scientists and biomedicine.

The meeting served to discuss the recent UKRI seed-corn funding for the development of LhARA, the Laser-hybrid Accelerator for Radiobiological Applications, to serve the Ion Therapy Research Facility (ITRF). The LhARA collaboration's long-term vision is to transform the clinical practice of proton- and ion-beam therapy (IBT) by creating a fully automated, highly flexible system to harness the unique properties of laser-driven ion beams. The meeting was opened with an outline of LhARA, and how it will be a uniquely flexible proton/ion-beam facility dedicated to the systematic study of radiation biology - the laser-driven source will allow protons and ions to be delivered in FLASH and mini/micro beams with a flexible time structure up to a maximum repetition rate of 10 Hz. The exploitation of the LhARA beams requires the development of novel techniques capable of interrogating chemical and biological processes on short, < 0.1 s, timescales. Full exploitation of the facility requires a range of developments from automated sample handling to fast feedback from the experimental end stations to the accelerator. This requires that advances in a variety of branches of physics be harnessed.

The morning session involved talks focusing on radiation biology and biophysics, and novel accelerator systems, with afternoon themes of novel instrumentation & computing, and biomedical and clinical impact. The day was tailed off with a productive discussion focused around challenges in the field, with a conclusion to build the community in this area and have a further meeting in this fast moving field in the near future, in particular aimed at the development of transformational biomedical capabilities.

Mark Leake

Interfacing Biophysics and Physical Science Microscopy, December 2023, London

Organizers: Mark Leake (York)

This one-day meeting (https://iop.eventsair.com/biophys2023/programme) aimed to promote synergy and engagement across the biological and physical sciences, through co-badging support from the Biological Physics Group (BPG) and the Electron Microscopy and Analysis Group (EMAG). This meeting focused on advances in microscopy research emerging at the frontiers between physics and biology, covering the progress and challenges in imaging biological materials and opportunities for low-dose imaging in cryogenic and liquid conditions enabled

by new instrumentation in the physical sciences. Recent developments associated with atomistic modelling of molecular systems and data analysis of large volumes were presented. The meeting provide opportunities for established researchers and early career researchers to present their work, networking and fuel future collaboration in this fertile and exciting multidisciplinary field across the interface between the biological and physical disciplines. The day ended with a discussion session focused on the challenges of research in this field, with interesting and open points made focused on the need for larger cross-disciplinary challenge-led research funding calls, the benefits of centralisation of instrumentation and technical support into dedicated centralised facilities, the value of combining computational and simulation approaches with advanced experimentation, and the need to dedicate time to establishing cross-disciplinary collaborations to understand questions across the disciplinary interfaces and reframe associated challenges. There was enthusiasm to engage in further EMAG/BPG community building meetings with a steer towards greater engagement from end users with key biological and biomedical questions.
Mark Leake

Super-resolution in the North, December 2023, York
Organizers: Mark Leake (York), Alex Payne-Dwer (York) and Jamie Howard (York)

The BPG supported a further incarnation of what has grown to be an increasingly popular regional meeting, co-badged with the Royal Microscopical Society, focused, loosely, in the North of the UK around themes relating to super-resolution optical microscopy (https://www.rms.org.uk/rms-event-calendar/2023-events/super-resolution-in-the-north/programme.html). This meeting, primarily co-organised by early career researcher Dr Alex Payne-Dwyer (pictured below) from the University of York, assisted by Dr Jamie Howard and myself, attracted approximately 40 participants from a broad range of career levels from PhD student through to full professor, with attendees coming from up to ~150 miles away, with talks focused around several aspects of bespoke optical microscopy development and image analysis tools focused around super-resolution light microscopy approaches to address biological questions.

Several of the talks came from early career researchers, and there was a good balance between speakers who identified as being female and male. The focused size of the meeting facilitated and constructive informal environment for discussion throughout, also including contributions from industry sponsors of Cairn Research and Nikon. This series of meetings is clearly going from strength to strength, and the fantastic increase in its popularity may require a future more fluid definition of what constitutes being in the "North"!
Mark Leake

Physics of Life Winter School, December 2023, Durham
Organizers: Mark Leake (York) and Alice Pyne (Sheffield)

It was a real treat to pitch in with the Physics of Life network PoLNET with its Winter School just before Christmas 2023, based at the University of Durham - https://www.physicsoflife.org.uk/winter-school-challenges-and-opportunities-in-physics-of-life.html. After I set the scene with fellow co-organizer Alice Pyne from the University of Sheffield we had three super days packed with exciting science and testimonials of career development at the physical-life sciences interface from Maddy Parsons (KCL) Tannie Liverpool (Bristol), Kislon Voitchovsky (Durham), Daniele Faccio (Glasgow), Alice Pyne (Sheffield), Stuart Higgins (York), Tim Saunders (Warwick), and Hannah Smithson (Oxford). I also chaired a super discussion session framed around the perspectives of early career researchers in regards to the future "roadmap" for the Physics of Life in the UK. These ca. 40 early career researcher participants came from diverse backgrounds across the country split between PhD students and postdocs and really made the meeting such a huge success with their fantastic interactive engagement, especially through the grant writing sessions led by gurus Dan Allwood (Peak Writing) and Elaine Massung (Academic Shortcuts). These PoLNET framed summer and winter schools grow from success to success with their scope not just to teach aspects of exciting science methods and approaches, but also in their crucial role in provide mentorship and career development for our talented next generation of interdisciplinary science researchers, it is so clear that they are hugely valuable to the early career researcher community and something the BPG should continue to support!
Mark Leake

Upcoming meetings

Elasticity Imaging: *10 April 2024, Nottingham*

Innovations in biomedical detector/clinical diagnosis technologies: June 2024

Tom Mcleish Celebration: 2-4 September 2024, Durham

Active Soft Matter: Early September 2024, London

AI in Biophysics: 9-11 September 2024, London

Joint BPG/BBS meeting: 11-13 September 2024, Swansea

Super-resolution in the North: December 2024, Leeds

Physics of Life 2025: March 2025, Harrogate

IoP – Biological Physics Prizes

We are pleased to announce a series of new prizes celebrating the achievements of biological physicists in the UK. Nominations for these prizes will be open from early summer, watch this space.

- The **Tom McLeish Biological Physics Communication Prize** will be awarded for work to bring awareness of the nature and impact of Biological Physics to the wider public. The prize will be made annually.
- The **Tom Duke Biological Physics Prize** recognises outstanding work in service to the Biological Physics community. The prize will be made annually.
- The **Biological Physics Early Career Prize** will promote and recognise the contributions of new group leaders in the field of Biological Physics. The BPG will award an annual prize for outstanding work in the field of Biophysics whose recent work has been carried out in the UK. It will be presented at a major BPG-supported conference each year.
- The **Biological Physics Thesis Prize** will encourage new researchers by recognising outstanding work at the postgraduate level in the field of Biological Physics. The BPG will award an annual thesis prize for the best PhD thesis in the field of biological physics.

These prizes will be in addition to the IoP Rosalind Franklin Medal and Prize awarded annual for distinguished contributions to physics applied to the life sciences including biological physics.