Delft University of Technology
Friday, 26 May 2023

Focus session ‘Biophysics’

Speakers:
- Timon Idema (TU Delft): Nanobiology
- Dimphna Meijer (TU Delft): How neurons form networks
- Xin Shi (TU Delft): Nanopore-powered DNA turbines: towards bio-inspired nanorobotics
- Hylkje Geertsema (TU Delft): My story on exploring and teaching curiosity-driven research at the molecular scale

Session leader: Martin Depken (TU Delft)

Summary of the session

Biophysics is an interdisciplinary science that applies concepts and principles from physics and mathematics to study biological systems, ranging from molecules and cells to organisms and ecosystems. In biophysics, we move beyond causation and think of evolved purposes: the motion of a molecular motor might be directly caused by a chemical reaction, but it was also evolved for the purpose of transporting cargo in the cell. The appearance of evolved purpose adds complexity and a unique flavour to this fascinating and rapidly advancing field of physics.

Through the skilful use of lasers, magnets, electron beams, quantum mechanics, statistical mechanics, and other physics, we can now directly observe biological molecules at work. We can visualize how molecules replicate genetic information, form synapses in our brains, and convert chemical energy into mechanical work. With these new capabilities come exciting opportunities to understand and manipulate biology to meet pressing societal needs, from sustainability to theraputics. To make good on these promises, we need both interdisciplinary education and fundamental science. In this session we explore both science and education in the borderland of physics and biology.

Abstracts:

<u>Timon Idema (TU Delft): Nanobiology</u>

The aim of the Nanobiology programme is to teach students to use the language of math and the principles of physics to understand the complexity of biology. To achieve this goal, the programme is a joint degree between TU Delft and the Erasmus MC, combining the strengths of a technical university and a university medical center. In this talk, I’ll show how we work with students to get them to the cutting edge of current knowledge, and how they contribute on pushing that edge outwards. I’ll

illustrate with three examples: regulation and differentiation of stem cells, the organization of genetic information in DNA, and the close interaction between math, physics and biology in biological membranes.

<u>Dimphna Meijer (TU Delft): How neurons form networks</u>

In my research lab at TU Delft, we study how neurons form networks at the molecular and cellular scale. In this talk, I will give an introduction to the basic principles of molecular recognition mechanisms at the neuronal synapse. I will emphasize the current outstanding questions in our field, and explain how we can tackle these questions with a combination of structural biology and cell biological assays. Specifically, I will present a set of protein structures of synaptic cell adhesion molecules (CAMs) that are essential for important brain functions including vision, smell, and memory. We have identified multiple conformations that demonstrate the dynamic nature of this set of proteins. Also, we have identified three conserved calcium binding sites that control compactness and stability of synaptic CAMs. We then use in vivo cellular assays to demonstrate how these CAMs could function as molecular scaffolds to establish functional neuronal circuits. Throughout my talk, I will also discuss how interactions with our artists in residence stimulate us to reflect upon our work, create novel insights and foster new collaborations.

<u>Xin Shi (TU Delft): Nanopore-powered DNA turbines: towards bio-inspired nanorobotics</u>

Our societies have flourished because of macroscale machinery powered by engines and motors. And we are not alone in our reliance on active machines: life itself depends on energy-consuming nanoscale machines, as work at the nanoscale is being done by millions of sophisticated molecular motors. However, until today, designing and building active energy-consuming machines at the nanoscale has remained challenging.

In this talk, I will present our latest results on designing and building nanoscale DNA turbines: DNA nanostructures on nanopores that can autonomously convert transmembrane electrochemical potentials into rotary motion, similar to natural rotary motor proteins such as F_oF_1-ATP synthase and bacterial flagella motors. We have successfully designed and built two generations of such nanoturbines: a self-organised DNA active rotor (1), and a bottom-up designed chiral-shaped DNA turbine (2). We observed sustained unidirectional rotary motion of these nanoturbines at the single-molecule level as we applied a voltage or salt gradient across the nanopore. These exciting results lay the groundwork, both theoretically and experimentally, for further studies and the development of autonomous nanomachines that leverage autonomous, unidirectional rotational motion.

1. **<u>Xin Shi,</u>** A-K Pumm, J. Isensee, W. Zhao, D. Verschueren, A. Martin-Gonzalez, R. Golestanian, H. Dietz, C. Dekker, Sustained unidirectional rotation of a self-organized DNA rotor on a nanopore. **Nature Physics**. 18: 1105 *arXiv:2206.06613*. (2022)
2. **<u>Xin Shi,</u>** A-K Pumm, C M Maffeo, W Zhao, D. Verschueren, A. Aksimentiev, H. Dietz, C. Dekker. A nanopore-powered DNA nanoturbine. ***arXiv:2206.06612***. (2022)

Hylkje Geertsema (TU Delft): My story on exploring and teaching curiosity-driven research at the molecular scale

How do molecular processes regulate cellular function in our cells? And what causes the dysregulation of molecular processes and thereby cause disease? These are questions that I am curious about and want to answer in my research endeavors. To do so, I am using advanced single-molecule microscopy techniques to zoom in on the dynamic behavior and interplay of proteins in live and fixed cells. This allows me to unravel how protein distributions change during the cell's live cycle and dysregulate in diseased cells. Thereby, we can obtain a better understanding of the causes of disease at the molecular scale.

My research is fully curiosity-driven, and I aim to teach my students in their first-year practical course an open and curious mind-set towards research by using reflective educational activities. During this course, students explore different biophysical techniques, leading to a final open experiment where students design and perform an experiment based on their own curiosity and interest. By reflecting on what students have learned and where improvements can be made, students overcome their fear of making mistakes and start to see the course as a learning trajectory.

In this talk, I would like to tell you about the insights I have obtained regarding protein function in healthy and diseased cells and to elaborate on student-driven research experiments and reflective activities in my course.