The Sackler Biophysics Symposium 2017

Mesoscopic Physics of Cellular Phenomena

1

Yasmine Meroz

Tel Aviv University

Uncovering organismal memory phenomena: from cellular chemotaxis to plant tropisms

Statistical physics relates macroscopic dynamics of a system to the underlying microscopic physics through a probabilistic examination - we adopt this approach in the investigation of organismal memory phenomena. We study motor responses of biological organisms to external stimuli, with the aim of uncovering dominant physical mechanisms at the microscopic level. In this talk we will give two examples of memory phenomena in very different systems.

We will first discuss the phenomenon of directional memory in cellular chemotaxis, the orientation of a biological cell in the direction of a chemical gradient. The cell seems to remember the direction it was sensing before, making it robust to fluctuations of the signal in time. We show that a probabilistic minimal model of cellular response dynamics, where the inherent stochasticity of underlying signaling processes is taken into account, gives an understanding of the underlying principles of directional memory. A second example concerns the ability of plants to integrate over a history of stimuli over time. Our approach allows to compare these two very different systems, unveiling common principles across scale and complexity.

2

Shlomi Reuveni

Tel Aviv University

Sculpted by self-replication

Many fine-scale features of ribosomes have been explained in terms of function, revealing a molecular machine that is optimized for error-correction, speed and control. In this talk, I will demonstrate mathematically that much less understood, larger-scale features of ribosomes—such as why RNA dominates the ribosome mass and why the ribosomal protein content is divided into 55–80 small and similarly sized segments—could all be explained by optimization for self-replication.

3

Yoav Lahini

Tel Aviv University

Fast, label free nanoscopy: towards optical measurements of virus self-assembly

Viruses, some of nature's most effective parasites, can also be surprisingly simple: some viruses consist only of a single molecule of genomic information (DNA or RNA) surrounded by a protective shell made of many copies of a single protein. While the structure of some viruses is known down to atomic resolution, much less is known about the mechanism by which they spontaneously and perfectly assemble themselves from a randomly fluctuating soup of components. Measurements of viral self-assembly are particularly challenging due to the combination of length and time scales involved: viruses are only few tens of nanometers in size, and the self-assembly process spans many time-scales, from milliseconds to minutes.

I will describe the realization of a new, ultra-sensitive and ultra-fast measurement technique, that relies on elastic scattering of light in a nano-fluidic optical fiber. With this method we have been able to detect and track single, unlabeled viruses as small as 26 nanometers in diameter, freely diffusing in solution, at rates that are faster than the expected self-assembly times and over many seconds. I will describe some of the preliminary results and outline a possible route towards resolving the assembly process. Finally, I will discuss other uses of this technology for bio-detection and for resolving fast bio-physical and physical processes at the nano-scale.

4

Natalie Elia

Ben Gurion University of the Negev, Beer Sheva

Resolution, resolution, resolution: new mechanistic insights on ESCRT- mediated membrane fission obtained from high-resolution imaging

The ESCRT (endosomal sorting complexes required for transport) machinery mediates membrane fission in a verity of processes in cells. According to the proposed mechanism, ESCRT-III proteins drive membrane fission by assembling into helical filaments on membranes. Yet, ESCRT-III filaments have never been directly visualized in a cellular process that utilizes this machinery for its function. Here we used 3D STORM imaging of endogenous ESCRT-III component IST1, to describe the structural organization of ESCRT-III during the last step of mammalian cell division, cytokinetic abscission. Using this approach, ESCRT-III ring and spiral assemblies were resolved at the intercellular tube of cells at different stages of abscission. Characterization of these structures reveals the structural remodeling that ESCRT-III filaments undergo during abscission. Structural analysis of ESCRT-III polymers in cells depleted of different ESCRT components highlights the contribution of these components to ESCRT-III spiral formation and remodeling. This work provides the first evidence that ESCRT-III proteins assemble into helical filaments in physiological context, indicating that the ESCRT-III machine indeed derives its contractile activity through spiral assemblies. Moreover, it provides new structural information on ESCRT-III filaments, which raise new mechanistic scenarios for ESCRT-driven membrane constriction.

4

Yoram Burak

The Hebrew University of Jerusalem

Encoding of an animal's trajectory by grid cells in the entorhinal cortex

The neural representation, in the brain, of an animal's location within its environment has been studied in detail since the discovery in 1971 of 'place cells' in the hippocampus, which are selectively active when an animal visits a particular location. The main cortical input to the hippocampus, the entorhinal cortex, has been found in 2005 to contain neurons that are active in multiple locations within the animal's environment. Remarkably, these locations are arranged on the vertices of a two dimensional hexagonal lattice that tiles the plane. Both discoveries, of place cells and grid cells, were recognized by the 2014 Nobel Prize in Physiology or Medicine, awarded to John O'Keefe (UCL, London), May-Britt Moser, and Edvard Moser (NTNU, Trondheim). The periodic response of grid cells, as a function of the animal's position, raises many questions – both about the mechanisms responsible for this periodicity, and about the properties of grid cell activity as a neural coding scheme for position. I will briefly survey these questions, and will then discuss how principles borrowed from physics and information theory have been applied to address them. In particular, I will focus on our recent proposal, that the grid cell coding scheme is optimized to efficiently represent a dynamic trajectory of the animal, rather than a static position.

5

Tuomas P.J. Knowles

University of Cambridge

Biophysics of protein self-assembly and aggregation

The self-assembly of protein molecules into functional structures underlies core aspects of biological activity in living systems. When this process doesn't occur correctly, however, misfolded and misassembled species are formed, which can have deleterious activity, including compromising the viability of neurons and thus leading to neurodegeneration in the context of Alzheimer's and Parkinson's diseases. This talk outlines our efforts to develop and apply new biophysical approaches to probe and understand protein self-assembly and misassembly, and their roles in biological function and malfunction. A particular focus will be on elucidating molecular mechanisms of protein aggregation. Furthermore, I will outline our efforts to probe protein behaviour using microfluidic tools, and I will discuss a number of cases where experiments in ultra-small volumes allow key aspects of protein behaviour to be quantified that remain challenging to obtain from conventional bulk experiments.