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Physical Principles in Biology In the Faculty of Natural Sciences

Biological cells, although alive, exist in a physical world and follow its laws. Keeping this in mind can help answer questions such as how cells work and why they implement solutions to problems the way they do. At Imperial College, researchers are taking this approach to solve challenging problems at the interface between biology and the physical sciences.

Importance of quantitative modelling in biology

Mathematical modelling is successfully applied in climate research, finance, market research, crime solving, as well as in biological research.

While mathematical models are quickly written down and may or may not be difficult to solve, the challenge in biology lies in deciding what details to include in the model and which ones to neglect, as well as what features to focus on in the biological data. Biological processes are highly complex and nonlinear, and hence their mathematical formulation can depend on many parameters, which may or may not be important to include in the model to describe the observations. The difficulty with the data arises in part since biological experiments are less controlled than their counterparts in physics or engineering. As a result, data is sometimes noisy and even variable across different laboratories. Consequently, setting up a model of a biological problem requires a great deal of intuition and is highly nontrivial. Once this is achieved, solving the model is often relatively easy.

The goal of any such modelling is to inform the biology community and to be quantitative enough to make useful predictions for new experiments. Such new data can in return be fed into the model for further exploration. This close connectedness between theory and experiment is the general approach of Systems Biology, allowing groups of multidisciplinary scientists to work on the "big problems" in life sciences.



Schematic of bacterial cell with chemoreceptors and flagellated motors.

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Current members of the Biological Physics group with Dr. Endres on the right

The Biological Physics group

The Biological Physics group was founded by Dr Robert Endres in 2007. The group's research interests are the quantitative understanding of sensing and signalling in biological cells based on physical principles.

While chemical sensing by cell-surface receptors and their intracellular pathways are often well characterized, the physical limitations of sensing and the affect of constraints from the physical environment on the design of sensory systems and pathways are rather unexplored. In addition to chemicals, cells sense mechanical stimuli, including shear from fluid flow, forces from cell-cell and cell-substrate adhesion, as well as physical properties of bulky objects. These stimuli are important for embryonic development, tissue formation and repair, as well as our immune response. In general, very little is known about how these types of stimuli are sensed and encoded in the biochemical signalling pathways.

To answer these challenging questions, the group uses mathematical and computational tools from statistical physics, in combination with explicit biological data from experimental collaborators. The group's multidisciplinary work is further integrated in the Division of Molecular Biosciences and the Centre for Integrated Systems Biology at Imperial College (CISBIC).

Collaborators include: HEIDELBERG UNIVERSITY



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Reverse engineering of sensory systems

Sensory systems have evolved to respond to input stimuli of certain statistical properties. and to reliably transmit this information through biochemical pathways. Hence, once a sensory system is experimentally well characterised, e.g. by measurement of dose-response curves, one is able to extract valuable information about the statistics of the stimuli by reverse engineering. Based on dose-response curves from in vivo fluorescence resonance energy transfer (FRET) experiments of bacterial chemotaxis, the aim is to predict the chemical gradients chemotactic cells typically encounter. The results will allow the researchers to characterise the complex micro-environments, such as the human intestine, in which cellular communities live. This type of information is extremely difficult to obtain from experiments alone.

How accurately can cells sense?

The accuracy of sensing chemicals has many limitations due to extra-cellular and intra-cellular noise. However, the fundamental limit of sensing chemicals is due to the external noise from the random arrival of ligand molecules at the cell-surface receptors by diffusion. It is unknown how receptor distribution and dynamics on the cell membrane affect the accuracy of sensing. The researchers use tools from statistical physics to study the effects of receptor clustering, internalization by endocytosis, and diffusion on the accuracy of sensing chemicals. These results will have a large impact in biology by providing quantitative answers to why some receptors exhibit unusual fast diffusion and internalization rates, e.g. in neural synapses, or why ligand-degrading enzymes are located on cell surfaces.



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Chemotactic response and adaptation of Escherichia coli bacteria from in vivo FRET experiments. Data provided by the Sourjik lab at the University of Heidelberg.

Mechanosensing of particles in phagocytosis

Phagocytosis allows specialized cells of our immune system to bind, engulf and destroy bacteria and inert particles. Engulfment is also an essential step in bacterial sporulation, during which the mother cell engulfs the forespore. To understand the observed mechanosensitivity during engulfment, in particular the dependence on particle size, shape, and elasticity, the group develops finite-element simulations of cells based on simplified, intuitive model ingredients, which can readily be analysed. The results will allow the researchers to understand why bacteria, such as the spiral-shaped Helicobacter and Campylobacter species, may not be easily taken up and destroyed by our immune cells, as well as help improving drug delivery into cells.



Phagocytic engulfment of a particle from simulations and imaging experiments.

References

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