BP 6: Bacterial Biophysics I

Time: Monday 15:00–18:00 Location: H 1028

Invited Talk BP 6.1 Mon 15:00 H 1028

Proton:ion antiporters generate membrane potential, and thus proton motive force in E.coli — •Teuta Pilizota — Centre for Engineering Biology, University of Edinburgh, Edinburgh, UK

To stay outside of thermodynamic equilibrium, all living cells need energy. Arguably the main energy source of life is the electrochemical potential of a given ion, so-called ion motive force, with the ATP molecule being the other. Because bacteria are unicellular the energy production is tightly linked with all the other processes in the cell. For example, the electrochemical potential of a given ion is composed of two parts. The electrical potential across the membrane, which is generated by the charge accumulated at the membrane, and 'drives' all ions. But also the specific chemical concentration differences of a given ion, where the exact concentration of ions in the cell matters, particularly that of protons. Lastly, bacteria maintain significant osmotic pressures, which depend on the difference between the extracellular and intracellular concentrations of all solutes, including ions. The result is a non-trivially intertwined set of physiological variables, yet, the bacterial cell does it; it achieves the necessary homeostasis of them all. How?

To begin answering the question here I'll focus on the bacterium Escherichia coli and show how it achieves a sufficient electrical potential, and in turn the electrochemical gradient of protons. The results champion a shift of perspective in the fundamental principle driving pH regulation.

BP 6.2 Mon 15:30 H 1028

Understanding the mechanisms of novel and existing antibiotics at the single-cell level — •Lars Renner[1], Felix Wong[2], James Collins[2], Jens Friedrichs[1], and Ralf Helbig[1] — [1]Leibniz-Institute of Polymer Research, Max Bergmann Center of Biomaterials, Dresden, Germany — [2]Massachusetts Institute of Technology, Cambridge, MA, USA

Many existing antibiotics are becoming increasingly ineffective causing antibiotic resistance in bacteria. Antibiotics have different molecular targets, however, even after decades of medical use, many effects of antibiotics on bacteria are still unknown. We investigate the mechanistic mode of action of antibiotics, particularly at the single cell level. Using various techniques, we are corroborating the cellular physiology and biochemical regulation as well as the different molecular mechanism downstream caused by the application of antibiotics, specifically for aminoglycoside, beta-lactams and quinolones. We have observed that cell death is preceded by cytoplasmic condensation for aminoglycosides and quinolones. When beta-lactams are used, cell wall synthesis is significantly disrupted, resulting in cellular lysis, which we are studying both in bulk and at the single cell level. By elucidating the molecular effects, we hope to address the problem of antibiotic misuse and the associated potential antibiotic resistance. In addition, we are using machine-learning approaches to determine structure-function relationships which in turn are used to identify and discover novel, underutilized or untouched structural classes of antibiotics with explainable deep learning to fight the antibiotic resistance crisis.

BP 6.3 Mon 15:45 H 1028

Genealogical organization in growing bacterial colonies — Garima Rani[1] and •Anupam Sengupta[1,2] — [1]Physics of Living Matter Group, Department of Physics and Materials Science, University of Luxembourg — [2]Institute for Advanced Studies, University of Luxembourg

Spatio-temporal organization of individuals within growing bacterial colonies is a key determinant of intraspecific interactions and colony-scale heterogeneities. The evolving cellular distribution, in relation to the genealogical lineage, is thus central to our understanding of bacterial fate across scales. Yet, how bacteria self-organize genealogically as a colony expands has remained unknown. In this work we report recent results obtained using a custom-built label-free algorithm to track bacterial genealogy in growing colonies. Our results reveal emergence of distinct self-similar genealogical enclaves, whose dynamics are governed by biological activity. The enclaves boundaries are populated by topological defects, which tune finger-like morphologies of the active interfaces. Estimation of the Shannon entropy of cell arrangements show a reduction over time; with faster dividing cells possessing higher spatial affinity to genealogical relatives, at the cost of a well-mixed, entropically favorable state. We complement the experimental results with a coarse-grained lattice model, demonstrating that the genealogical enclaves emerge due to an interplay of division-mediated dispersal, stochasticity of division events, and cell-cell interactions. Our study reports so-far hidden emergent self-organizing features which modulate genealogical distances within growing bacterial colonies.

BP 6.4 Mon 16:00 H 1028

Exploiting Spatial Dynamics to Optimize Evolution-Based Therapy Strategies in Dense Cellular Populations — Nico Appold[1,2], Serhii Aif[1,2], and •Kayser Jona[1,2] — [1]Max Planck Institute for the Science of Light, Erlangen, Germany — [2]Max Planck Zentrum für Physik und Medizin, Erlangen, Germany

The ubiquitous emergence of resistant mutants in pathogenic cellular populations is one of the primary challenges for modern antibiotic or anti-cancer therapies. Despite advances in evolution-based adaptive therapies and mathematical or computational models, a gap remains in translating these findings to clinical application. Empirical investigations are particularly challenging for densely packed cellular communities, such as microbial biofilms or solid tumors, as a result of their inherently complex spatio-temporal dynamics. Addressing this, we introduce a yeast-based model system tailored for the systematic study of resistant mutant emergence and therapy failure dynamics in dense populations. This model combines the precise tracking of de novo mutant clones with an accurate control over temporally varying fitness landscapes. Applying concepts from active granular matter physics and collective growth dynamics, our research uncovers a previously unidentified mode of competitive release. We then integrate our results with a tailored reinforcement learning approach to optimize the balance between immediate efficacy and long-term control of population size. Our findings underscores the importance of integrating physical principles of population dynamics into the design of evolution-based treatment strategies.

BP 6.5 Mon 16:15 H 1028

Beta-lactamase induced social dynamics of E. Coli — •Rotem Gross[1], Muhittin Mungan[1], Suman G. Das[2], Tobias Bollenbach[1], Joachim Krug[1], and J. Arjan G. M. de Visser[3] — [1]Institute for Biological Physics, University of Cologne, Köln, Germany — [2]Institute of Ecology and Evolution, University of Bern, Bern, Switzerland — [3]Labaratory of Genetics, Wageningen University & Research, Wageningen, The Netherlands

Treating Escherichia coli with the antibiotic cefotaxime at sub-lethal concentration leads to a complex response: cells are filamenting, a known mechanism related to delayed lysis and enhanced antibiotic tolerance. Moreover, near lethal concentrations, the population displays complex dynamics, with a crossover from filamented to normal-sized cells after about 14 hours of exposure. Our experiments show that the filamentation causes an active break-down of the antibiotic by a chromosomally encoded enzyme. In fact, freshly introduced bacteria grow in this spent medium and survive at antibiotic concentrations higher than twice the lethal dose. Combining experimental results with theoretical modeling, we explore the biological and chemical pathway through which the bacterial colony inactivates the antibiotic. We argue that this pathway is ancient and common across a wide range of bacteria and constitutes a first line of defense which is triggered even when it is not necessarily effective against the cause of stress.

BP 6.6 Mon 16:30 H 1028

Evaluation of nanoparticle influence on living microorganisms — •Stefanie Schuba, Rico Illing, Xinne Zhao, Jürgen Fassbender, Larysa Baraban, and Denys Makarov — Helmholtz-Zentrum Dresden-Rossendorf

The discovery of antibiotics against bacterial infections has led to a higher life expectancy and quality of life for people worldwide. However, a major issue with using antibiotics is they also cause an increase resistance in bacterial pathogen resistance. The search for alternatives to classical active substances is pushing nanoparticles (NP) into the focus of scientific research. Particular attention is being paid to Nano-Silver (Ag-NP) due to its biocide and antibacterial effect, which is used in many medical products and consumer goods. But how reliable is

Ag-Np? Conventional methods are used to analyze NPs, but these are limited in terms of labor, material costs, and statistical power. To tackle these limitations, we have developed a droplet-based millifluidic analysis platform as a tool to elucidate the effects of NPs on microorganisms (MO) with high statistical evaluation and detection power, enabling the separation of MO into individual droplets as bioreactors. In this work, we focus on the screening of the metabolism of gram-negative bacteria in the presence of NP under different stress factors. With the influence of Ag-NP, an inhibited bacterial activity was observed, which indicates the antibacterial effect of NP could be confirmed in our analysis platform. Further experiments are needed to clarify the stability of this effect.

15 min. break

BP 6.7 Mon 17:00 H 1028

Ultrasensitive dependence of fitness costs on membrane protein overexpression — •Janina Müller, Andreas Angermayr, Gerrit Ansmann, and Tobias Bollenbach — Institute for Biological Physics, University of Cologne

Perturbing expression levels of genes is a key technique for studying their function. In E. coli, strong overexpression of gratuitous proteins leads to fitness costs that are partially predictable from bacterial growth laws and sector models of proteome allocation. Here, we systematically quantified the precise dependence of fitness costs on the level of overexpression using a genome-wide library. Our results confirm that the fitness cost for membrane proteins is extremely high compared to cytosolic proteins, and reveal that this cost is ultrasensitive to the expression level. To elucidate the mechanisms underlying this ultrasensitive response to membrane protein overexpression, we characterized the role of membrane translocation by examining the fitness costs of mutants of a model membrane protein with different translocation requirements, resulting in a reduction in translocation success. Single-cell experiments to detect membrane localization using protein-GFP fusions further demonstrated that overexpression of membrane proteins leads to displacement of other membrane proteins. This displacement closely coincides with the abrupt collapse of the growth rate. A minimal physical model can explain these observations and suggests that the abrupt growth collapse is caused by zero-order ultrasensitivity in the translocation pathway.

BP 6.8 Mon 17:15 H 1028

Using simulations to investigate the mechanical properties of peptidoglycan — •Marco Mauri[1], Abimbola F. Adedeji Olulana[2], Jamie K Hobbs[2], Sheila Hoshyaripour[1], and Rosalind J Allen[1] — [1]FSU Jena - Balance of the Microverse — [2]University of Sheffield

In bacteria, the peptidoglycan (PG) cell wall consists of a mesh of glycan strands crosslinked by short peptides. PG counteracts the internal turgor pressure and its integrity is necessary to prevent cell lysis; indeed, many antibiotics target PG synthesis. The mechanical properties of the PG mesh are important for understanding the biophysics of cell growth, cell shape and antibiotic action: yet these properties are hard to measure experimentally.

Here, we present a coarse-grained molecular simulation model for the PG mesh in Gram negative bacteria such as *E. coli*. Inspired by previous works, we model PG as a network of beads and springs governed by a system of overdamped Langevin equations. However, our model incorporates real PG configurations, informed by AFM and biochemical measurements.

We use dynamical simulations to study how a patch of PG responds to biochemical perturbations. We predict the mechanical effects of antibiotic action via uncontrolled hydrolase enzymes, and explore the role of biophysical properties of the mesh, such as connectivity, on mechanical stability. Our work provides a connection between the molecular-scale PG configuration and the macro-scale mechanical properties of the cell wall.

BP 6.9 Mon 17:30 H 1028

Heterogeneity in Bacterial Contact Formation — •Johannes Mischo[1], Samer Alokaidi[1], Cao Nguyen Duong[2], Markus Bischoff[3], and Karin Jacobs[1] — [1]Experimental Physics, Center for Biophysics, Saarland University, 66123 Saarbrücken, Germany — [2]INM Leibniz Institute for New Materials, Campus D2 2, 66123 Saarbrücken, Germany — [3]Institute of Medical Microbiology and Hygiene, Saarland University, 66421 Homburg (Saar), Germany

Bacteria adhere to virtually every surface and promote the formation of sometimes desirable but often unwanted biofilms. As the adhesion of a single bacterial cell is the critical initial step in biofilm formation, we analyse the adhesion properties using single cell force spectroscopy. The contact formation is mainly attributed to bacterial cell wall macromolecules: Their nature and their distribution on the cell wall are a highly individual property of the bacterial cells and define the contact formation properties of the respective cell. We showed that Staphylococcus aureus cells have several distinct spots of high adhesion capability causing heterogeneous distributions of adhesive strength on the cell wall [1]. During cell division, bacteria synthesise about 33 - 50 % fresh cell wall structures, leading to further heterogeneity within individual cells [2]. We combine Atomic Force Microscopy of single S. aureus cells with high resolution fluorescence microscopy to investigate the influence of cell wall age on the adhesion capability of individual cells. [1] Spengler, C. et.al., DOI: 10.1039/d3sm01045g [2] Monteiro, J. M. et.al NatCom. 2015., DOI: 10.1038/ncomms9055.

BP 6.10 Mon 17:45 H 1028

Bacteria in shear flow — •Pierre Martin[1], Tapan Chandra Adhyapak[2], and Holger Stark[1] — [1]Institute of Theoretical Physics, Technische Universität Berlin, Hardenbergstr. 36, 10623 Berlin, Germany — [2]Indian Institute of Science Education and Research (IISER), Tirupati, India

This study aims to investigate the behavior of flagellated bacteria under shear flow conditions, focusing on the specific case of E. coli bacteria. E. coli employs a rotating bundle of helical flagella for self-propulsion, and its ability to alter direction is facilitated by the reversal of flagellar rotation, a process known as tumbling.

In the presence of shear flow, helical objects, experience a chirality-induced drift force propelling them in the direction of vorticity. Additionally, objects in shear flow exhibit the well-known Jeffery orbit causing them to rotate. However, due to the helical bundle driving a non-chiral head, E. coli experiences a rheotactic torque and aligns along the vorticity axis. A phenomena known as rheotaxis.

To gain insights into these phenomena, we conducted a detailed analysis using a realistic model of E. coli coupled with fluid flow at low Reynolds numbers. The fluid flow was simulated using the method of multi-particle collision dynamics and Lees-Edwards boundary conditions were implemented to reproduce a planar shear flow in bulk.

Our research contributes to a deeper understanding of the complex interplay between flagellated bacteria and shear flow, shedding light on the responses of E. coli in such environments.