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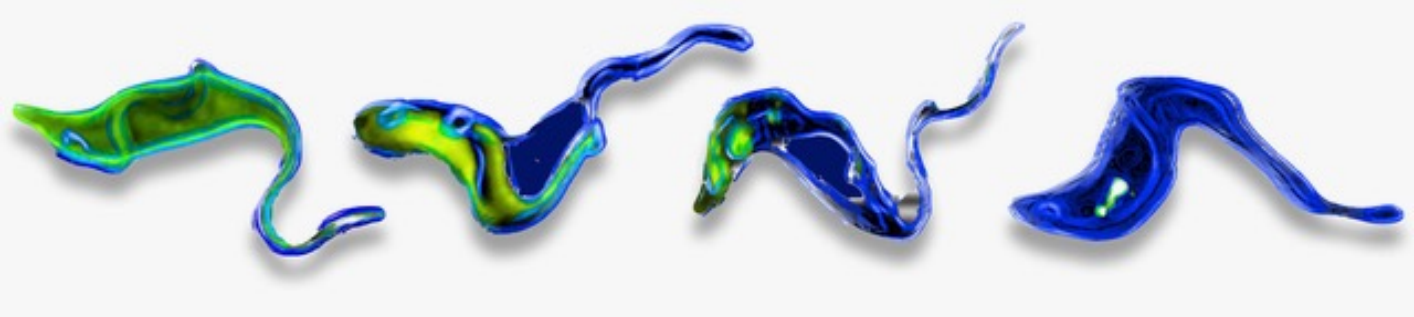
PHYMOT
Physics of Microbial Motility

JÜLICH
FORSCHUNGSZENTRUM

International Workshop

PHYSICS OF MICROBIAL MOTILITY

October 4-6, 2023, University of Würzburg, Germany



This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 955910.

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About

PHYMOT

PHYMOT is a European Consortium of Universities, Research institutes and industrial Partners located in Denmark, France, Germany, Israel, Italy, Spain, Switzerland and the United Kingdom.

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PHYMOT's broad scientific objective is to understand the physics of cell motility, from single cells to collective behavior. Research on cell motility is flourishing, driven by new experimental, theoretical, and numerical tools from mathematics, engineering, and physics. Within PHYMOT, young researchers will be trained at the interface between physics, biology, and engineering to face core challenges of a modern society such as food production, disease treatment strategies, sustainable and ecological development.

The workshop "Physics of Microbial Motility" aims to bring together theoretical and experimental researchers working on biological active matter at the microscale. The main topics of the workshop are a) Motility and Sensing, b) Collective Motion and c) Geometry and Motility

Timetable

IS: Invited Speaker, CT: Contributed Talk

Wednesday Oct. 4

11:00–13:45	**Registration**		
13:50–14:00	**Welcome remarks Engstler & Gompper**		
14:00–14:30	IS	**Remi Colin** MPI for Terrestrial Microbiology, Marburg	Active density patterns formation in bacterial binary mixtures
14:30–14:50	CT	**Francois Detcheverry** University Claude Bernard Lyon 1	Optimal run-and-tumble in confinement
14:50–15:10	CT	**Priyanka Sharan** TU Dresden, Dresden	Microfluidics to emulate the behavior of biological microswimmers using artificial alternatives
15:10–15:30	CT	**Riccardo Foffi** ETH Zürich	microArgos: a new tool for bacterial movement ecology
15:30–16:00	**Coffee**		
16:00–16:30	IS	**Raymond Goldstein** DAMTP, University of Cambridge	Elastic Bistability and the Geometry of Cellular Neighbourhoods in Choanoflagellates and Green Algae
16:30–16:50	CT	**Martin Maliet** Sorbonne University, Paris	Bacterial glass transition in Pseudomonas aeruginosa
16:50–17:10	CT	**Silvio Bianchi** Sapienza University of Rome	Effects of flagellar elasticity and cell body constraints on E.coli motility
17:10–17:30	CT	**Knut Drescher** University of Basel	Simultaneous spatiotemporal transcriptomics and microscopy of Bacillus subtilis swarm development reveal cooperation across generations
18:00–19:30	**Poster session with fingerfood & drinks**		

Thursday Oct. 5

09:00-09:30	IS	**Tâm Mignot** Lab. de chimie bactérienne, Marseille	Multicellular transitions in collective bacterial movements
09:30-09:50	CT	**Nils-Ole Walliser** Laboratoire Charles Coulomb, Université de Montpellier	Signature of (anti)cooperativity in the stochastic fluctuations of small systems: application to the mechano-sensitive assembly of the bacterial flagellar motor
09.50-10:10	CT	**Benjamin Perez Estay** PMMH-ESPCI, Paris	Control of bacteria turbulence through surfaces
10.10-10:30	CT	**Vyacheslav Misko** Vrije Universiteit Brussel	Microfluidics Approaches for Selection and Enhancement of Sperm Motility for Improved Fertilization
10:30-11:00	**Coffee**		
11:00-11:30	IS	**Christina Kurzthaler** MPI for the Physics of Complex Systems	The physics of bacterial transport in dilute and porous environments
11:30-11:50	CT	**Patryk Nienałtowski** Lyncée Tec SA	HoloV3C: unveiling eukaryotic flagella in 3D with holographic microscopy
11:50-12:10	CT	**Alexandros Fragkopoulos** MPI for Dynamics and Self-Organization	Swimming vs gliding: Exploring the first steps of biofilm formation of motile microbes
12:10-12:30	CT	**G. Gompper** IBI-5 Forschungszentrum Jülich	Sperm Navigation in Viscosity Gradients
12:30-14:00	**Lunch**		
14:00-14:30	IS	**Romain Briandet** INRAE, MICALIS, Jouy-en-Josas	Bacterial Torpedoes Assaulting Biofilms
14:30-14:50	CT	**Stefan Karpitschka** Universität Konstanz	Quantifying gliding forces of filamentous cyanobacteria
14:50-15:10	CT	**Tom Beneke** ZEB, Würzburg University	Inadequate migration of Leishmania-infected macrophages – the driver of parasite dissemination?
15:10-15:30	CT	**Narges Jamshidi** ZEB, Würzburg University	Evolution of micro-swimmer designs in distinct microenvironments
15:30–16:00	**Coffee**		
16:00-16:30	IS	**Rachel Bearon** Dept. of Math. Sciences, University of Liverpool	The impact of elongation on transport in shear flow
16:30–16.50	CT	**Federica Miano** Technical University Denmark	Functional morphologies and fluid dynamics of foraging in 'typical excavates'
16:50-17:10	CT	**Winfried Schmidt** Universität Bayreuth	Controlling bacterial swimming in wavy channels
17:10-17:30	CT	**Nicola Pellicciotta** University of Rome La Sapienza	Colloidal transport by light-induced gradients of active pressure
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11:50–12:10	CT	**Eric Clément** ESPCI, Paris	Dispersion of motile bacteria in confined and geometrically complex channels
12:10–12:30	CT	**Avishek Das** AMOLF Amsterdam	Utility of information in chemotaxis
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14:00–14:30	IS	**Benedikt Sabass** Ludwig-Maximilians-Universität München	SHOULD I STAY OR SHOULD I GO? THE ADHESION-MIGRATION TRADE-OFF OF PSEUDOMONAS AERUGINOSA
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14:50–15:10	CT	**Julien Bouvard** LadHyX, Institut Polytechnique de Paris	Transport of passive beads by random and directed motion of swimming micro- organisms Testing
15:10–15:30	CT	**Dmitry Fedosov** IBI-5, Forschungszentrum Jülich	Bacteria Propulsion and Interactions in Thin Biofilms
15:30–15:45	**Closing remarks Engstler & Gompper**		
15:45	**End of workshop & departure**		

List of Abstracts – Talks

Wednesday Oct. 4

Active density patterns formation in bacterial binary mixtures

R. Colin[1], **S. Espada Burriel**[1], **G. DiDio**[1]

Max Planck Institute for Terrestrial Microbiology, Marburg, Germany

In wild environments, phenotypically diverse microorganisms interact both physically and chemically to give rise to complex community organization [1]. We are interested in the role of physical interactions arising from flagellar motility, a major bacterial trait, in the structuration of such complex communities. This aspect, contrary to biochemical interactions, remains less studied in experiments, despite out-of-equilibrium mechanisms such as motility-induced phase separation (MIPS) offering potential routes for structure emergence [2]. We focused on a minimal system for complex microorganism communities, a binary mixture of motile and non-motile Escherichia coli bacteria. We report a novel non-equilibrium phenomenon by which strong large-scale density heterogeneity patterns of the non-motile bacteria emerge when mixed with motile ones, in a wide physiologically relevant range of concentrations. Experimental results together with quantitative modeling and numerical simulations show that circular swimming of motile cells at surfaces generate recirculation flows that advect the non-motile cells through hydrodynamic interactions, and that sedimentation, by breaking the vertical symmetry of the system, is essential for local non-motile cell accumulation and the emergence of the large-scale density fluctuations. This behavior represents a new type of non-equilibrium self-organization in active bacterial populations, distinct from MIPS-like phenomena, which appears crucial for complex microbial community structuration [3]. We also find that similar physical constraints govern non-motile segregation to the left-hand side when the binary mixture is under flow.

Optimal run-and-tumble in confinement

F. Detcheverry[1], **C. Cottin-Bizonne**[1], **T. Pietrangeli**[1], **C. Ybert**[1]

University Claude Bernard Lyon 1

Run-and-tumble is a basic model of persistent motion and a widespread moving strategy in micro-organisms and individuals cells. In many natural settings, motion occurs in the presence of surfaces and confinement [1]. While accumulation at the wall has been extensively studied [2,3], the transport along the surfaces has received less attention. We consider a run-and-tumble particle confined in a slit, and which may move, or not, at the wall. We first propose a four-direction model that is fully tractable and obtain analytically the long-time diffusion coefficient along the slit. Second, we show using numerical simulations of more realistic motions that our prediction is to a large extent valid more generally. Third, we find that lateral transport might be maximized by an optimal mean run time and identify the conditions for the existence of an optimum. Our results should help to assess the advantages of micro-organisms moving strategies in confined environments.

Microfluidics to emulate the behavior of biological microswimmers using artificial alternatives

P. Sharan[1], **J. Simmchen**[1,2]

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[2] Pure and applied chemistry, University of Strathclyde, UK

A key feature of biological microswimmers is their ability to navigate away from or toward a certain stimuli, and this skill is termed as 'taxis'. Tactic behavior can be induced by physicochemical changes in the environment such as light (phototaxis), chemical (chemotaxis), temperature (thermotaxis) and fluid flow (rheotaxis). In the last few years, a lot of research has been done for mimicking the behavior of the biological organisms in a fully synthetic way. Hence, artificial microswimmers were developed which have the same basic trait i.e. they are able to autonomously move at microscale. While these artificial devices lack any sensing and signaling capabilities, it is worth investigating if they can also mimic the taxis character of the biological organisms. In order to mimic the taxis behavior, one of the most crucial challenge is creating changes in the environment in a controlled manner. Here, microfluidics offers great solutions due to its excellent fluid manipulation abilities at the microscale [1]. Using microfluidics, we were able to create an otherwise technically challenging chemical gradients and fluid flow and study the chemotaxis [2] and rheotaxis [3] response of catalytically active Janus spheres. We also studied the phototaxis response of artificial microswimmers which did not require microfluidic setup and could be built using simple platform [4]. Here, I describe rheotaxis behavior in artificial microswimmers in detail: many motile microorganisms respond to the presence of the water currents by either migrating up or down the flow and this behavior is termed as rheotaxis. Similar to their biological counterparts, artificial microswimmers have also been shown to respond to fluid flows [5]. To deepen the understanding of how different microswimmers behave in an externally imposed flow, it is crucial to understand the influence played by their swimming patterns. Experimentally, pusher-type Pt@SiO2 Janus microswimmers have been shown to exhibit cross-stream migration in flow conditions. Whereas, theoretical studies have predicted an upstream response for puller-type microswimmers. In this work, we introduce Cu@SiO2 Janus spheres that swim towards their catalytic cap, quite differently from Pt@SiO2 which move towards SiO2. Using theoretical flow field calculations, we hypothesize that they behave as a puller-type system. Indeed, when placed in an externally imposed flow, these swimmers show a steady upstream response, which supports our hypothesis. Using a simple squirmer model for puller-type system, we reproduce all the experimental observations. To conclude, our study highlights the relevance of the flow field pattern around the microswimmers to comprehend the rheotactic behavior in motile systems.

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microArgos: a new tool for bacterial movement ecology

R. Foffi[1], **R. Henshaw**[1], **R. Stocker**[1], **F. Peaudecerf**[2]

[1] ETZ Zürich
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For a bacterium, the ocean is mostly a nutrient wasteland interspersed with ephemeral resource patches. Bacterial life is thus one torn between timescales: from the fast reaction to nutrient pulses (minutes) to the long waiting times between successive nutrient encounters (hours to days) [1]. In studying such systems, experimentalists are often forced to face a choice between long-term studies on single cells [2], or population studies where each individual is only observed for brief intervals [3]. However, to best understand the movement ecology of bacteria, long-term observations of individual cells need to be coupled with population statistics. To overcome this barrier, we present microArgos: a microfluidic platform designed to track dozens of individual cells simultaneously over multiple hours. Dilute populations of fluorescently-labelled bacteria are confined into a centimeter-scale arena and imaged at low resolution through a raster-scanning mechanism, and their trajectories are then reconstructed via particle tracking. This procedure sacrifices the fine-scale details of bacterial motion in favor of access to large spatio-temporal volumes and population statistics. Producing data on previously inaccessible scales, microArgos provides a fresh perspective into the role of motility and decision-making in aquatic environments. Currently able to follow individual cells from tens of minutes to hours in homogeneous environments, and planning to incorporate the production of controlled heterogeneous landscapes [4], we seek to elucidate questions such as how the nutrient encounter history of a bacterium can dictate its future behavior, and if temporal variations in motile behavior could be linked to different energy investment strategies.

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Elastic Bistability and the Geometry of Cellular Neighbourhoods in Choanoflagellates and Green Algae

R. Goldstein[1]

DAMTP, University of Cambridge, Cambridge, United Kingdom

This talk will describe two recent advances in understanding the physics of cellular organization in simple multicellular organisms. The first part concerns the fluid dynamical and elastic properties of the recently discovered [1] multicellular choanoflagellate C. flexa, which dynamically interconverts between two hemispherical forms of opposite curvature. The swimming and filter-feeding properties are described [2] within a simple model of a raft of spheres with associated stokeslets to represent the action of the flagella. An elastic model based on linear elasticity of the microvilli of adjacent cells that adhere to each other is shown to support bistability at the organism level as a consequence of the presence of numerous pentagonal neighbourhoods in the raft. In the second part I will first review the recent findings [3] that the cellular neighbourhood volumes in both lab-evolved and extant multicellular species, obtained by Voronoi tessellations based on the cell locations, are accurately described by gamma distributions, suggesting a hitherto unrecognized "universal" aspect of noise in cellular packing. Here we propose an explanation [4] of those observations by considering the very simplest models for stochastic ECM generation by somatic cells and show that they define Poisson point processes whose Voronoi tesselations are demonstrably governed by gamma distributions. I summarize by proposing a link between the two parts of the talk.

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Bacterial glass transition in Pseudomonas aeruginosa

M. Maliet[1], **M. Deforet**[1]

Sorbonne University

Motile bacteria self-organize in numerous collective phases, such as orientationally ordered phase or swarming state. These collective phases result from properties and activities at the single cell scale, such as growth rate, swimming speed and cell-cell interactions. Understanding how individual properties can trigger emergence of long range order is a crucial aspect of biological and physical studies on bacteria, and can lead to better understanding of the mechanisms of colonies and biofilms formation. Here we study the properties of the 2D swarming state of an elongated motile bacteria, Pseudomonas aeruginosa, in growing colonies. We are able to obtain large and dense bacterial monolayers at the edge of 3D colonies expanding on agar gels. We perform the detection of bacterial trajectories from high-speed movies through the use of an innovative deep learning technique that compute segmentation and tracking altogether, taking advantage of temporal information. As density increases in bacterial monolayers, P. aeruginosa undergoes kinetic arrest, and collectively transitions from a liquidlike state to a glassy state. We show that this transition does not only affect the scales of the system's relaxation times, but also the very nature of the dynamics at play. We reproduce the analysis to several P. aeruginosa mutants of different shapes and single-cell motion properties, and show that all flagellated mutants exhibit a similar glass transition. The critical surface density to trigger the transition does not depend on single-cell motion properties, and seems to only depend on the aspect ratio of cells.

Effects of flagellar elasticity and cell body constraints on E.coli motility

S. Bianchi[1]

NANOTEC-CNR, Institute of Nanotechnology, Soft and Living Matter Laboratory, Rome, and Sapienza" University of Rome, Department of Physics, Rome

Many motile bacteria, such as Escherichia coli, swim by rotating multiple flagella. These semiflexible helical filaments are independently actuated by flagellar motors randomly distributed on the surface of the cell body. When all the motors rotate in the same direction, within a fraction of a second, this complex elastohydrodynamic system transforms into a straight swimmer in which all the flagella form a tight bundle propelling the cell forward. Underlying this bundling phenomenon there are several physical factors, most of which have been analysed in isolation using theoretical or macroscopic models.
Here we report a direct study of bundling dynamics in bacterial cells whose flagellar motors can be switched on and off by light, while fluorescently labelled flagella are observed. Using optical tweezers and microfabrication to constrain cell body kinematics, we found that although translations are not essential for bundling, wobbling plays an important role in achieving a stable configuration of the bundle and body complex. We find that the curved shape of the hook, a flexible joint that transmits motor torque to flagella, strongly affects the vectorial nature of the exchanged torques and must be taken into account to correctly reproduce experimental observations.

Simultaneous spatiotemporal transcriptomics and microscopy of Bacillus subtilis swarm development reveal cooperation across generations

K. Drescher[1]

University of Basel

Development of microbial communities is a complex multi-scale phenomenon with wide-ranging biomedical and ecological implications. How biological and physical processes determine emergent spatial structures in microbial communities remains poorly understood due to a lack of simultaneous measurements of gene expression and cellular behaviour in space and time. Here, we combined live-cell microscopy with a robotic arm for spatiotemporal sampling, which enabled us to simultaneously acquire phenotypic imaging data and spatiotemporal transcriptomes during Bacillus subtilis swarm development. Quantitative characterization of the spatiotemporal gene expression patterns revealed correlations with cellular and collective properties, and phenotypic subpopulations. By integrating these data with spatiotemporal metabolome measurements, we discovered a spatiotemporal cross-feeding mechanism fueling swarm development: during their migration, earlier generations deposit metabolites which are consumed by later generations that swarm across the same location. These results highlight the importance of spatiotemporal effects during the emergence of phenotypic subpopulations and their interactions in bacterial communities.

Thursday Oct. 5

Multicellular transitions in collective bacterial movements

T. Mignot[1]

LABORATOIRE DE CHIMIE BACTÉRIENNE, Marseille, France

Bacteria exhibit the ability to move collectively as groups, displaying social behaviors that lead to the formation of massive colonies comprising billions of cells. However, the mechanisms underlying the coordination and expansion of such colonies remain poorly understood. In this study, we employ a combination of experiments, image analysis, and simulations to investigate Myxococcus xanthus, focusing on the formation of rippling and swarming patterns as well as their coexistence. We demonstrate that changes in alignment rules alone are sufficient to account for the formation of rippling and swarming patterns, as well as the reversal dynamics observed in each phenomenon. Our comprehensive analysis further reveals that the coexistence of rippling and swarming is achievable across various density levels and remains stable for extended durations, often lasting several hours.

Signature of (anti)cooperativity in the stochastic fluctuations of small systems: application to the

N.O. Walliser[1], **M.J. Franco-Oñate**[1], **J. Palmeri**[1]

Laboratoire Charles Coulomb (L2C), Université de Montpellier

The cooperative binding of molecular agents onto a substrate is pervasive in living systems, particularly stochastic processes inside cells. When the number of binding sites is small enough, we can rely on a fluctuation analysis of the number of substrate-bound units, an experimentally accessible quantity, to study whether a system shows cooperativity. First, we present a general-purpose grand canonical Hamiltonian description of a small one-dimensional (1D) lattice gas with either nearest-neighbor or long-range interactions as prototypical examples of cooperativity-influenced adsorption processes. We propose 1) a criterion to determine whether a given adsorption system exhibits cooperative or anti-cooperative behavior and 2) a method to quantify the amplitude of the ligand-ligand interaction potential. Second, we compare the theoretical predictions of our model to bead assay measurements of the bacterial flagellar motors (BFM) of E. coli. In this way, we find evidence that cooperativity controls the mechano-sensitive dynamical assembly of the torque-generating units, the so-called stator units, onto the BFM. Finally, we estimate the stator-stator interaction potential and attempt to quantify the adaptability of the BFM.

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Control of bacteria turbulence through surfaces

B. Pérez Estay[1,2], **E. Clément**[1,3], **A. Lindner**[1,2]

[1] PMMH
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Hydrodynamic instabilities appear in E. coli suspensions at high enough concentrations. Controlling such instabilities could allow extracting energies at the microscales. We achieved control of the collective motion size in a sample confined between two parallel solid surfaces at a distance of H. By measuring the velocity correlation function in the center of the sample, we determined that the decay length scales increase linearly with the value of H up to 800m. We also tracked passive beads inside the bacteria turbulence and determined the impact of this scaling in the mixing properties of the bath. These results show that controlling the size of the collective motion is possible even at larger scales, revealing the importance of surface effects in the properties of the active suspension.

Microfluidics Approaches for Selection and Enhancement of Sperm Motility for Improved Fertilization

V. Misko[1], **L. Baraban**[2], **D. Makarov**[2], **W. de Malsche**[1]

[1] Vrije Universiteit Brussel
[2] HZDR

Motility of sperm refers to its ability to swim in a forward direction to reach the oocyte and fertilize it. Normal sperm motility plays a crucial role in couple's reproductive health. Low motility of sperm cells could lead to issues with fertilization. Medical assisted reproduction (MAR) technologies are used to improve fertilization in this case. These imply selecting sperm with the highest motility using various techniques. However, it can occur that the selected sperm does not have the capacity of successful fertilization, due to reduced motility. In this case, it would be desirable to enhance their motility. Thus, it was shown that adding species of higher motility to other species of lower motility could result in an effect called "motility transfer" [1]. The motility transfer was demonstrated in a binary system of artificial microswimmers, i.e., synthetic Janus particles whose motility is caused by the catalytic chemical reactions at the surface of asymmetric microspheres (e.g., recently synthesized high-motility Ag/AgCl Janus particles active in bio-compatible environments [2, 3]). The proposed technique of motility control [1] can be implemented in various biological and medical systems, where one wishes to enhance the motility of insufficiently active nano- or micro-particles. In case of weakly motile sperm cells, this technique has advantages over other similar proposals (e.g., using self-propelled metallic rotors trapping sperm cells), whereby it is substantially less damaging to living sperms and much easier to implement, as it does not require the fast guest swimmers to localize and trap individual sperms one by one. We will also discuss our recent experimental advances in motility sperm selection techniques (with human sperm) using an acoustic microfluidic setup [4].

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The physics of bacterial transport in dilute and porous environments

C. Kurzthaler[1]

Max Planck Institute for the Physics of Complex Systems

Unraveling the motion of microorganisms in dilute and porous media is important for our understanding of both the molecular basis of their swim gait and their survival strategies in microbial habitats. First, I will show that by using renewal processes to analyze experimental measurements of wild-type E. Coli, we can provide a quantitative spatiotemporal characterization of their run-and-tumble dynamics in bulk [1,2]. We further demonstrate quantitatively how the persistence length of an engineered strain can be controlled by a chemical inducer and characterize a transition from perpetual tumbling to smooth swimming. Second, I will address how this run-and-tumble gait evolves towards a hop-and-trap motility pattern of agents moving in a porous environment [3]. Using computer simulations, we discover a geometric criterion for their optimal spreading, which emerges when their persistence lengths are comparable to the longest straight path available in the porous medium. Our criterion provides a fundamental principle for optimal transport in densely-packed environments, which could be tested experimentally by using engineered cells and may provide insights into microbial adaption mechanisms.

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HoloV3C: unveiling eukaryotic flagella in 3D with holographic microscopy

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The flagellum is pivotal in the survival mechanisms of eukaryotic cells and measuring its three-dimensional shape is essential to understanding these key mechanisms. However, accurately assessing the intricate structure of flagella has been challenging due to the lack of a reliable method for determining the 3D position of individual points. Our digital holographic microscopy (DHM) method overcomes this hurdle, enabling dynamic 3D tracking of eukaryotic cell flagella shape and motility. We harness holographic microscopy benefits, including high-speed imaging of large sample volumes, for 4D tracking (X, Y, Z, and time) of microorganisms and their flagella. This technique offers precise 3D localization of nanometer-sized, unlabeled structures and is robust against changes in reconstruction parameters. We reconstructed for the first time the shape of a 200 nm diameter Chrysochromulina simplex flagellum and measured mouse sperm flagella over time, capturing approximately 800 points along a single flagellum. Our proposed method unleashes the full potential of digital holography, enabling high-speed and precise 3D tracking of microorganisms and their flagella at the nanoscale across depths that are beyond the reach of other existing techniques. This opens new avenues for studying flagella's roles in cellular functions and survival strategies.

Swimming vs gliding: Exploring the first steps of biofilm formation of motile microbes

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Cilia and flagella are cellular appendages that enable microorganisms to propel themselves and interact with surfaces. Particularly, the unicellular microalga Chlamydomonas reinhardtii swims by actuating its two flagella, but it can also use them to attach to surfaces and perform gliding motility. Its flagellar adhesiveness can be switched on and off by blue and red light, respectively [1]. This makes C. reinhardtii ideal to study surface colonization and aggregation of photoactive microorganisms; the first steps towards biofilm formation. We employ single-cell micropipette force spectroscopy [2] on model substrates and find that flagellar adhesion is of around 1-2 nN in blue light, surface-unspecific, and mediated by electrostatic interactions [3]. We also use brightfield microscopy and a Langmuir-type model to quantify the adsorption and desorption kinetics of a confined suspension of motile C. reinhardtii cells under controlled light conditions [4]. Finally, we discovered that populations of surface-associated cells transition from local clusters to interconnected networks with increasing surface coverage by means of their gliding motility in conjunction with flagella mechanosensing [5].

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Sperm Navigation in Viscosity Gradients

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The motion of microswimmers can be strongly affected by variations of the physical properties of their environment [1]. Well-known examples are rheotaxis (the upstream swimming in microchannel flows), gravitaxis (swimming against the gravitational field), and durotaxis (directed motion on a substrate with a gradient of elasticity). Of course, unidirectional external signals can also induce biochemical processes in biological microswimmers, which result in steering and directional motion, such as photo- or chemotaxis. We focus here on the direct physical mechanisms.
We are interested in the motion of sperm in fluids with a viscosity gradient. Such a situation is often encountered by sperm on their way to the female egg. Here, the unique propulsion mechanism of sperm, with its sinusoidally beating flagellum, distinguishes its behavior from those of other microswimmers, such as those modelled by squirmers [2]. Our combined simulation and theoretical modelling study is based on a flagellum, which is described as a semiflexible filament on which we impose a travelling bending wave [3]. The simulations show that the behavior strongly depends on the magnitude of the gradient, and the average (spontaneous) curvature and the flexibility of the flagellum. In general we find positive viscotaxis (motion toward regions of higher viscosity), but there are also cases where sperm swims in drifting circles perpendicular to the gradient direction. Our results can be useful for controlling sperm motion in microfluidic devices [4].

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Bacterial Torpedoes Assaulting Biofilms

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Are the microorganisms constituting biofilms always immobilized within their organic matrix? Not so sure... We have demonstrated that certain biofilms spontaneously contain a subpopulation of motile bacteria capable of traversing the matrix in three dimensions. These continuous movements create a network of transient pores that enhance material transfers within the biofilm, allowing irrigation of the deeper layers. This phenomenon has also been observed when mobile bacilli were added to the surface of established biofilms consisting of other species. This vascularization of the biofilm matrix by mobile bacteria can facilitate the penetration of toxic substances into the deeper layers. We have shown the sensitizing effect of pre-exposing unwanted biofilms to a mixture of swimming bacteria regarding the effectiveness of a disinfectant used in industrial hygiene. This study has also demonstrated the possibility of using swimming bacteria that produce antimicrobial compounds to infiltrate the matrix of unwanted biofilms, inactivate the established pathogens, and occupy the newly freed space on the surface.

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DOI: 10.7554/eLife.76513
DOI: 10.1016/j.bioflm.2023.100109
DOI: 10.1073/pnas.1200791109
DOI: 10.1101/2023.01.06.522868

Quantifying gliding forces of filamentous cyanobacteria

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Filamentous cyanobacteria are one of the oldest and today still most abundant lifeforms on earth, with manifold implications in ecology and economics. Their flexible filaments, often several hundred cells long, exhibit gliding motility in contact with solid surfaces. The underlying force generating mechanism is not yet understood. Here, we demonstrate that propulsion forces and friction coefficients are strongly coupled in the gliding motility of filamentous cyanobacteria. We directly measure their bending moduli using micropipette force sensors, and quantify propulsion and friction forces by analyzing their self-buckling behavior, complemented with analytical theory and simulations. The results indicate that slime extrusion unlikely generates the gliding forces, but support adhesion-based hypotheses, similar to the better-studied single-celled myxobacteria. The critical self-buckling lengths align well with the peaks of natural length distributions, indicating the importance of self-buckling for the organization of their collective in natural and artificial settings.

Inadequate migration of Leishmania-infected macrophages – the driver of parasite dissemination?

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Leishmania is a protozoan parasite that predominantly resides intracellular in macrophages. They are transmitted by the bite of a sand fly and once inside their mammalian host can remain local (cutaneous leishmaniasis [CL]) or spread throughout the tissue and body (visceral leishmaniasis [VL]). This is the difference between a mild illness (CL) and a deadly disease (VL). We propose that the different clinical manifestations observed for leishmaniasis are driven by parasite-hijacked host cell migration and that macrophage migration is manipulated in a species-dependent manner by Leishmania parasites.

To test this hypothesis, we have developed assays to measure the motility of Leishmania and Leishmania-infected macrophages in both 2D and 3D environments. Our 2D tracking analysis shows that VL causing Leishmania species increase the migration speed of infected THP-1-derived macrophages compared to CL causing species. In addition, we demonstrate that Leishmania species do not exhibit sufficient movement in collagen type 1 matrices in order to contribute meaningful to parasite dissemination, while THP-1-derived macrophages migrate in these 3D environments.

To gain a better understanding of the host migration modes exploited by Leishmania parasites, we now have developed assays to track infected macrophages in 3D collagen type 1 matrices. In addition, we want to identify relevant molecular regulators and have therefore implemented a lentiviral-delivered CRISPR/Cas12a gene editing system in THP-1 cells suitable for multiplexed CRISPR screens.

We hope that our findings will give new insights into the mechanisms of Leishmania dissemination, thereby facilitating future designs of therapeutics aimed at controlling inadequate migration of infected macrophages.

Evolution of micro-swimmer designs in distinct microenvironments

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Trypanosoma brucei, a eukaryotic parasite with a single flagellum, is transmitted by tsetse flies and thrives across a broad range of vertebrate species. These parasites cause several diseases in their hosts, exemplified by sleeping sickness in humans. Throughout their life cycle, these cells encounter diverse microenvironments with different physical attributes, such as viscosity. These cells have demonstrated a notable capacity to adapt within these microenvironments. Cell morphology and propulsion are highly dependent on flagellar motion. The cell movement initiates with a planar bending wave on the flagellum in the anterior end of the cell, followed by a longitudinal rotation due to the helical attachment of the flagellum to the cell body. However, the details of the motion behavior and morphological cell changes remain insufficiently quantified. In this study, we acquired live cells at high temporal resolution. This allowed us to elucidate the single-cell movement of Trypanosoma brucei, particularly within different viscosities. This investigation involves quantitatively comparing cell behavior in different viscosities, revealing interesting correlations of rotational cell translocation, and frequency of flagellar beating. Further, the characterization of the environment's rheological properties is underway in order to determine how the environmental properties affect cell behavior. These prompted us to carry out experiments aimed at quantifying the mechanical properties of the cells, explaining the underlying morphological basis for changes in motility patterns.

The impact of elongation on transport in shear flow

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The motion of small spheroidal particles in a simple shear was first described by Jeffery in 1922 and remains a cornerstone of modern fluid dynamics. In addition to describing the motion of passive particles, this theory has also been used to understand how flow affects the distribution and transport of micro-swimmers. While fluid shear generally acts to reorient the motility of swimmers away from their intended direction of travel, the dynamics of this interaction crucially depends on the organism's morphology. I shall present two pieces of work investigating how shape effects the transport of micro-swimmers in shear. Firstly we will consider the 3D transport of elongated active particles under the action of an aligning force (e.g. gyrotactic swimmers) in some simple flow fields; and will see how shape can influence the vertical distribution, for example changing the structure of thin layers [1]; secondly we shall consider elongated bacteria swimming in a bounded channel and consider the interplay between the bulk flow boundaries [2].

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Functional morphologies and fluid dynamics of foraging in 'typical excavates'

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Excavates are phagotrophic flagellates characterized by a ventral groove and two flagella. The anterior flagellum is naked, and its beating creates a feeding current directed towards the groove, while the posterior flagellum is equipped with a vane and beats within the groove. We combined flow visualization and observations of prey capture in three clades of excavates with computational fluid dynamic modelling to understand the functional significance of this arrangement. We estimated clearance rate magnitudes from flow visualization and CFD modelling. We found that a vaned flagellum beating in a confined groove produces a very efficient feeding current at low energy costs, irrespective of the beat plane and the orientation of the vane and of all other morphological variations.

Controlling bacterial swimming in wavy channels

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The navigation of swimming microorganisms, such as bacteria, is guided by rheotaxis, their reorientation with respect to flow gradients. While recent investigations focused on the control of passive particles, such as red blood cells, in spatially modulated and time-dependent flows [1–3], less is known about the behavior of swimming agents in such flows. We show that bacteria modeled by deformable microswimmers can accumulate in flows through straight microchannels either in their center or on previously unknown attractors near the channel walls. In flows through wavy microchannels, a wavy-induced swinging motion is revealed which can become resonant. As a consequence swimmers are distributed across the channel instead of accumulating at its center. We show that wavy-induced tumbling exhibits a much larger amplitude compared to tumbling in planar flows and is characterized by rapid, oscillatory patterns of motion along the lateral direction. Our results suggest new strategies for controlling the behavior of live and synthetic swimmers in microchannels. For example, the wavy channel provides a means for the separation of bacteria according to their properties, such as size or swimming speed, potentially aiding their selective elimination [4].

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Colloidal transport by light-induced gradients of active pressure

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Active fluids, like all other fluids, exert mechanical pressure on confining walls. Unlike equilibrium, this pressure is generally not a function of the fluid state in the bulk and displays some peculiar properties. For example, when activity is not uniform, fluid regions with different activity may exert different pressures on the container walls but they can coexist side by side in mechanical equilibrium. Here we show that by spatially modulating bacterial motility with light, we can generate active pressure gradients capable of transporting passive probe particles in controlled directions. Although bacteria swim faster in the brighter side, we find that bacteria in the dark side apply a stronger pressure resulting in a net drift motion that points away from the low activity region. Using a combination of experiments and numerical simulations, we show that this drift originates mainly from an interaction pressure term that builds up due to the compression exerted by a layer of polarized cells surrounding the slow region. In addition to providing new insights into the generalization of pressure for interacting systems with non-uniform activity, our results demonstrate the possibility of exploiting active pressure for the controlled transport of microscopic objects.

Friday Oct. 6

Spectra of active turbulence

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Recent years witnessed a significant interest in physical, biological and engineering properties of self-propelled particles, such as bacteria or synthetic microswimmers. One of the most striking features of interacting microswimmers is the appearance of collective motion: at densities high enough, the system is characterised by jets and vortices comprising many individual swimmers. This 'active turbulence' is often quantified in terms of spectra of various observables (velocity, vorticity, etc.) in an attempt to draw parallels with high-Reynolds number hydrodynamic turbulence.
In this talk, I will discuss the current theoretical underpinning for spectra of active turbulence. I will argue that such spectra require a very different interpretation than their high-Reynolds number counterparts and demonstrate the emergence of an intrinsic lengthscale of active turbulence.

Multipad Agarose Plate (MAP): A Rapid and High-Throughput Approach for Antibiotic Susceptibility Testing

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Antibiotic resistance is a growing issue in healthcare worldwide and is currently responsible for over one million deaths annually. We seek to develop a new method for antibiotic susceptibility testing (AST) using single-cell microscopy. The assay is based on a multi-pad agarose plate (MAP), where one or more bacteria samples are placed on 96 small agarose pads. Each pad provides a growth environment where media, nutrients, and toxins can be added independently. The bacteria are confined to a single imaging plane using a glass coverslip and imaged for two hours with single-cell microscopy. We then analyse the image sets with a fully automated segmentation pipeline that outputs statistics for colony growth and single-cell characteristics. We demonstrate how, by adding concentration gradients of antibiotics to the pads, the minimum inhibitory concentration (MIC) can be consistently determined. Additional experiments were also conducted to demonstrate that the pads on the MAP are not affected by their neighbours and that the method is not sensitive to agarose concentration and seeding density.

Hydrodynamic near field effects give rise to fast synchronisation in finite groups of cilia

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When many cilia are located on the surface of a microorganism, their beating can synchronise such that their phases form metachronal waves. To understand the process of synchronisation, we study a model where each cilium is represented as a spherical particle, moving along a tilted trajectory with a position-dependent active driving force and a position-dependent internal drag coefficient. The model thus takes into account all the essential broken symmetries of the ciliary beat. We show that taking into account the near-field hydrodynamic interactions, the effective coupling between cilia can become nonreciprocal: the phase of a cilium is more strongly affected by an adjacent cilium on one side than by a cilium at the same distance in the opposite direction. As a result, synchronisation starts from a seed at the edge of a group of cilia and propagates rapidly across the system, leading to a synchronisation time that scales proportionally to the linear dimension of the system. A ciliated surface is thus characterised by three different velocities: the velocity of fluid transport, the phase velocity of metachronal waves and the group velocity of order propagation. Unlike in systems with reciprocal coupling, boundary effects are not detrimental for synchronisation, but rather help to initiate the wave.

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Mechanical coupling is sufficient to synchronize C. Reinhardtii flagella

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Physical laws apply differently at the microscale than at the macroscale, therefore constraining microorganisms' biological functions. A key instance of this is that microbes perceive their surrounding medium as extremely viscous, constraining them to adopt non-symmetric motion to be able to propel forward. Some bacteria (E. coli) and unicellular algae (C. reinhardtii) have evolved different asymmetric motions in order to propel. C. reinhardtii has two flagella, mechanically connected from inside the cell, that beat synchronously in a "breaststroke" pattern. Flagellar synchronization is necessary to propel forward but is not fully understood. More generally, many microorganisms, including human epithelial cells or multiciliate microbes display flagellar synchronization. Experiments on isolated pairs of flagella from multicellular alga Volvox have shown that hydrodynamic coupling alone is sufficient for metachronal synchronization. But C. reinhardtii also display internal mechanical coupling that has been shown to be necessary to synchronize its flagella in a breast stroke movement. So what are the respective roles of hydrodynamic and mechanical coupling in flagellar synchronization of these unicellular alga? To find out, we separate their two flagella by a cantilever to prevent interflagellar hydrodynamic interactions, while holding the cell with a micropipette. We then observe if flagella stay synchronized without hydrodynamic interactions, including when subject to stresses. Is mechanical coupling sufficient to synchronize flagella? If so, then what role does hydrodynamics play in motility?

Swimming and Rheology of Active Suspensions in Viscoelastic Fluids

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The natural habitat of microorganisms are non-Newtonian fluids, which besides shear viscosity also have an elastic response. Using a second-order model fluid, we present an analysis, how weak viscoelasticity affects the rheology of a dilute suspension of microswimmers [1]. Starting with modifications of the well-known Jeffery orbits and the orientational distribution due to tumbling and rotational diffusion, we show how the effective shear viscosity is influenced. In particular, for pushers such as E.coli bacteria, the shear viscosity is further reduced due to elastic stresses. In the end, we also comment on swimming in a viscoelastic fluid with a reciprocal stroke pattern [2].

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Droplet and waving instabilities of an active fluid jet

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Micro-algae in relatively dense suspensions modify their environment by absorbing light, consuming and releasing chemical compounds or generating flows. Instabilities that appear in those systems can in turn give biological insight regarding the way this critically important class of micro-organisms navigate their environment. Here we harness phototaxis to precisely control millions of swimming Chlamydomonas reinhardtii cells and experimentally test theoretical predictions regarding the behavior of dense suspensions, in which they interact via their self-generated flows [1,2,3,4,5]. Starting from a straight cell jet, we show for the first time the two kind of instabilities that were predicted : its breaking into drops and its buckling into waves, depending on the cells preferential orientation. The instabilities wavelength and growth rate can be controlled notably by light intensity.

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Dispersion of motile bacteria in confined and geometrically complex channels

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In the laboratory, we built via soft lithography , geometrically controlled micro-fluidic environments of various complexity. We monitor trajectories of motile wild-type E.coli to characterize the mean transport and dispersion processes under flow. We show that the swimming activity of motile species and in particular their specific trajectories in a flow, their interaction with the walls and well as the internal statistical features driving the run-and-tumble process, lead to emerging transport phenomena different from the classical Taylor-Aris dispersion processes for molecular and colloidal species

Utility of information in chemotaxis

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Living cells improve their fitness by sensing noisy environmental signals and tuning their behavior in response in a seemingly modular fashion. Yet these two processes often occur simultaneously, and behavioral response affects future signal values. Whether a cell is aware of and able to efficiently use the information it itself generates, is an open question. A complete understanding of the design of sensing and response motifs, in terms of the usability of sensed information, has so far been limited to perturbative regimes without accounting for the information feedback from the cell to the environment (Mattingly et al., 2021). We address this gap by studying the dynamics of chemotaxis of Escherichia coli in a steady chemoattractor gradient, with a coarse-grained model (Long et al., 2017) for sensory receptors and run-and-tumble motion in the seconds timescale. For computing the mutual information between signal and response trajectories, we extend a recently developed numerical algorithm, Path Weight Sampling (PWS) (Reinhardt et al., 2022), to achieve exact computation of mutual information rate in the presence of nonlinear coupling and feedback. We find that there exist distinct optima in terms of cell's behavioral parameters for maximum performance, measured by the chemotactic drift speed, and maximum mutual information rate. Further, irrespective of the cellular environment, sensed information and its usability independently constrain chemotactic performance. With analytical theory, we rationalize our findings in terms of the design and interdependence of the sensing and response motifs in E. coli and the bimodal nature of a run-and-tumble response.

SHOULD I STAY OR SHOULD I GO? THE ADHESION-MIGRATION TRADE-OFF OF PSEUDOMONAS AERUGINOSA

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The bacterial colonization of surfaces is a ubiquitous process that shapes nature and profoundly aects human health. While much is known about the biology of this process, the pivotal interplay between physical environment and active bacterial micromechanics remains poorly understood. In fact, strong adhesion and high motility, both of which are essential for surface colonization, are two apparently contradictory goals, as they mutually obstruct each other. We study this process here for the human pathogen Pseudomonas aeruginosa, both experimentally and numerically. We elucidate how P. aeruginosa optimizes its behavior for colonization of surfaces under ow. From the analysis of the dynamics of labelled type IV pili, we construct a theoretical model that quantitatively connects individual motor dynamics with whole-cell motility and migration. We demonstrate that cells upregulate the number of active motors on surface contact although individual pili do not display a measurable sensory response to surfaces. When applying shear ow, we unexpectedly find that robust sticking to a surface requires passive surface adhesion rather than pili attachment. Instead, pilus activity actually promotes cell detachment while enabling migration. Using pilus mutants, we demonstrate that wild-type cells achieve an optimum trade-o between adhesion and migration by limiting the number of pili. Simulations reveal a generic underlying trait space, where, depending on the interplay of active and passive forces, adhesion and migration are either compatible or a trade-o is required for ecient bacterial surface colonization. Our results on a common optimization problem at the core of pathogen colonization is paradigmatic for a broad class of piliated bacteria and may also have implications for other cells.

Motile cilia induce Periciliary transport

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The ciliated epithelium of the human respiratory tract is lined by a thin stratified fluid. The airway surface liquid (ASL) serves as a protective barrier and is essential for maintaining normal respiratory mechanics. However, our understanding on how it is propelled by cilia and how flow is coupled between the two ASL compartments is still fragmentary. Mucus transport can be measured experimentally via various techniques, but the complex and impenetrable structure of the Periciliary Layer (PCL), occupied by cilia-tethered mucins which create a brush with nanometric mesh size, is more challenging as for example it interferes with the conventional use of tracer beads. Earlier studies have measured the average displacement of fluorescent dyes localised in the PCL, but have not managed to extract a clear velocity profile in this layer. In the last decades, great effort has also been put in understanding cilia-driven flows from a theoretical perspective. However, given the complexity of the system, many studies simulated the problem by introducing one or several approximations, commonly producing contrasting results. We tackled the constrains posed by the PCL structure with the use of caged-fluorescent compound and high-speed imaging of airway epithelium from a side view. Briefly, we photoactivated the dye in a micrometric region within the PCL and followed its translation over time along lines parallel to the epithelium. The compound is activated at different distances from the cell apical surface to measure the transport as a function of the position within the PCL. Our findings show that the dye displacement is generally segmented, suggesting that the compound is transported with two prominent speeds for short (< 1 s) and long-times. The two speeds appear almost constant along the cilium length, with the first one being almost four time bigger than the second one. Moreover, we found that decreasing the temperature from 37°C to room temperature reduces PCL transport and has its major effects on the short-time speed.

Transport of passive beads by random and directed motion of swimming micro-organisms

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Passive particles immersed in an active bath of micro-swimmers, either artificial swimmers or living microorganisms, may be displaced due to the activity of the suspension [1]. This enhanced motion can lead to rich phenomena such as aggregation or phase separation. In this experimental work, we study how passive beads are moved by randomly swimming bacteria and directionally swimming micro-algae. First, in a uniform environment, we highlight the aggregation dynamics of the beads in a bacterial bath of Burkholderia contaminans [2]. Unexpectedly, the passive beads display a dynamic clustering similar to Ostwald ripening: clusters are slowly growing in time as a $t^{1/3}$ power-law, dynamically as beads are constantly getting exchanged from one cluster to another. Second, we bring our experiment closer to a natural environment by adding biases to the swimming motion of the microorganisms. This time, we use micro-algae Chlamydomonas reinhardtii considering their quick reaction to light [3]. As their local concentration grows, the algae push away the passive beads in a steric fashion. By varying the incoming light direction, we manage to create complex patterns of passive particles, and even direct them towards precise locations. Such directed motion of micro-particles opens up exciting perspectives, for instance in medicine.

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Bacteria Propulsion and Interactions in Thin Biofilms

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Bacteria are able to migrate collectively over wet surfaces and form stable and highly motile aggregates, which are often referred to as biofilms. Collective locomotion of bacteria within aggregates is called swarming [1], and is affected by interactions between bacteria, their shape and the strength of propulsion, and the density of bacteria packing within a biofilm [2,3]. To better understand the collective behavior of bacteria, numerical simulations of a large number of swimmers are performed. The swimmers are represented by the so-called squirmer model, in which bacteria propulsion is imposed by a prescribed slip velocity field at the surface of the swimmer [4]. This model allows the simulation of swimmers with different propulsion properties, including various motility types (e.g., pusher, puller) and propulsion strengths. We find that local interactions between swimmers mediated by the fluid environment determine their swarming behavior and the formation of clusters. In particular, swarming generally takes place at moderate volume fractions of swimmers, while at high swimmer densities, large non-motile clusters prevail. These results advance our understanding of bacterial film formation and the connection between the collective swarming behavior and the internal properties of individual swimmers.

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List of Posters

Viscotaxis for Symmetric and Asymmetric Flagellar beat patterns

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How do sperm steer? How do they change their swimming direction? How is directional motion achieved in complex environments? These are important issues to be clarified in order to understand how sperm can navigate their tortuous journey towards the egg [1,2,3]. The sperm flagellum besides propelling the cell also acts as a sensory antenna, detects environmental cues, enabling steering adjustments and beat pattern modifications for egg localization during fertilization [4,5]. Microswimmers in general often reside in gradients of temperature, chemicals, gravitation field and light [6], and can reorient and navigate along the gradients by a mechanism known as taxis. A well-known example is chemotaxis, where concentration gradients of a chemo-attractant are sensed and guide the sperm cell towards the egg cell. We investigate here another potentially relevant mechanism, viscotaxis, in which sperm reacts to gradients of fluid viscosity [6,7]. In previous research, different kinds of microswimmers have been found to respond to the viscosity gradients depending on their shape or hydrodynamic multipole strengths [6,7]. We use numerical simulations to investigate viscosity gradient effects on flagellum motion. Representing sperm cells through a bead-spring model experiencing anisotropic, space-dependent drag, our simulations reveal positive viscotaxis, where sperm cells reorient towards areas of higher viscosity. We quantify this behaviour in form of the rotational velocity and its dependencies on various factors. Furthermore, we explore the effects of asymmetric flagella waveforms and flagella elasticity.

Inadequate migration of Leishmania-infected macrophages – the driver of parasite dissemination?

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Leishmania is a protozoan parasite that predominantly resides intracellular in macrophages. They are transmitted by the bite of a sand fly and once inside their mammalian host can remain local (cutaneous leishmaniasis [CL]) or spread throughout the tissue and body (visceral leishmaniasis [VL]). This is the difference between a mild illness (CL) and a deadly disease (VL). We propose that the different clinical manifestations observed for leishmaniasis are driven by parasite-hijacked host cell migration and that macrophage migration is manipulated in a species-dependent manner by Leishmania parasites.

To test this hypothesis, we have developed assays to measure the motility of Leishmania and Leishmania-infected macrophages in both 2D and 3D environments. Our 2D tracking analysis shows that VL causing Leishmania species increase the migration speed of infected THP-1-derived macrophages compared to CL causing species. In addition, we demonstrate that Leishmania species do not exhibit sufficient movement in collagen type 1 matrices in order to contribute meaningful to parasite dissemination, while THP-1-derived macrophages migrate in these 3D environments.

To gain a better understanding of the host migration modes exploited by Leishmania parasites, we now have developed assays to track infected macrophages in 3D collagen type 1 matrices. In addition, we want to identify relevant molecular regulators and have therefore implemented a lentiviral-delivered CRISPR/Cas12a gene editing system in THP-1 cells suitable for multiplexed CRISPR screens.

We hope that our findings will give new insights into the mechanisms of Leishmania dissemination, thereby facilitating future designs of therapeutics aimed at controlling inadequate migration of infected macrophages.

Bacterial motility differs on slippery and non-slipper surfaces

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Many microorganisms form sessile communities, called biofilms, in self-secreted extracellular polymeric substances (EPS), which often attach to solid surfaces. Biofilm-associated infections have dramatic economic and societal impacts. Recently, slippery surfaces based on liquid infused surfaces have been developed to prevent biofilm formation [1]. However, their antibiofilm performance can decay in hydrodynamic conditions due to shear induced oil depletion [2]. Therefore, another slippery surfaces (i.e. liquid-like solid surfaces) have been proposed as an alternative antibiofilm strategy [2]. For both liquid infused surfaces and liquid-like solid surfaces, they can significantly inhibit initial bacterial attachment and biofilm formation which is possibly due low contact angle hysteresis. It has been reported that various surface parameters such as surface roughness, surface wettability and surface charge could affect bacterial attachment and motility [3]. We hypothesized that these slippery surfaces can significantly affect how bacteria sense the surfaces and the subsequent bacterial motility. In this work, we have designed flow cells, co-registered to microscope with high-speed camera, to enable the in-situ capture of bacterial movement. We have demonstrated that P. aeruginosa PAO1 and its mutant (e.g. type B Flagellin mutant, fliC) are much more motile on those slippery surfaces compared to non-slippery surfaces such as glass and Polydimethylsiloxane (PDMS). Furthermore, bacterial motility patterns have also significantly differed between slippery and non-slippery surfaces. This may advance our understanding about how bacteria sense the surfaces for better biofilm control.

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A metabolic switch controls bioconvection in a microbial suspension

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Photosynthesis is an essential process for life that converts light into energy for higher-level plants and also phototrophic microbes. Even in the absence of light, these microbes can produce energy through other metabolic processes, such as aerobic and anaerobic respiration. In the case of the unicellular microalga Chlamydomonas reinhardtii, the cell's swimming motility is affected by a number of parameters, e.g. the geometry of the confinement [1,2], but also by the cell's metabolic state. Under unfavourable light conditions for photosynthesis, the deprivation of oxygen severely reduces the cell's swimming velocity. In 2D compartments, the switch from photosynthesis to oxygen respiration causes the emergence of self-generated oxygen gradients and, ultimately, the formation of microbial aggregates [3]. In 3D, density patterns in Chlamydomonas suspensions may also form through bioconvection, a phenomenon that rises due to a natural tendency of bottom-heavy cells to move against gravity [4]. Here, we show that the formation of bioconvection patterns can be reversibly triggered by a metabolic switch of the cells. The intensity of light is employed to control the metabolic pathways. We quantify the bioconvection using top- and side-view experiments that allow to access a plethora of characteristic quantities, such as the wavelength, flow-field, and relative cell density. Finally, we directly link the single cell motility at different metabolic states to the spatio-temporal characteristics of the instability.

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Chemotaxis quantification methods with a three channel microfluidic chip

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Bacteria and plants communicate via chemical signals to establish symbiotic interaction. The chemosensory system of the bacteria receives chemical inputs that biases the random motility of the bacteria. Microfluidic technologies now make it possible to produce chips in which the chemical environment can be controlled. The model I use is a chip with three parallel channels on an agarose layer. Fluids containing known concentrations of the chemical species are placed in the outer channels. This generates a gradient of the chemical species across the agar layer. After a few minutes, we inject a suspension of bacteria into the central channel. The cell is placed under a microscope, allowing us to film the bacterial population regularly. The first series of studies we carried out aimed to characterize the method's limitations for determining the chemotactic response of bacteria. In particular, we looked at the influence of channel surfaces on the measurement. To this end, we used fluorescent E. coli bacteria and placed them in Casaminoacid gradients. By taking measurements at different heights over the 80-micron height of the channel, we have shown that the chemotactic response is not the same on the surfaces and in the middle of the channel. We will propose a model including this effect. We also want to characterize the influence of viscosity on chemotaxis by adding PVP to our suspension. We will conclude by applying this method to Sinorhizobia meliloti.

Light control of active turbulence

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The motility of bacteria E. coli represents one of the most studied examples yet to be investigated. When the density of these bacteria reaches a critical value, a collective dynamic occurs that is known as active turbulence [1,2]. In this state, the bacteria's motion appears chaotic, similar to that of a fluid in classical turbulence, with the presence of vortices of finite dimensions. It has been shown experimentally that this motion can be rectified through geometric confinements [3]. In this poster, I show how to control such dynamics through light. With photokinetic bacteria and a suitable experimental setup, it is possible to modulate activity with great spatio-temporal control. By activating a circular region, a coherent collective dynamic of limited duration is created, with a single vortex within it. I study the characteristics of this phenomenon as a function of the size of the light confinement and certain properties such as its mean lifetime and propose possible explanations.

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Screening for genetic determinants of Vibrio cholerae biofilm architecture

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Most of the bacterial biomass on Earth is found in three-dimensional communities, termed biofilms, which confer protection against many forms of physical, chemical, and biological stress. In this work we overcome previous limitations by developing a novel microfluidic high-throughput biofilm cultivation approach, as well as an automatized adaptive fluorescence microscopy screening procedure, to obtain single-cell resolution, three-dimensional biofilm images of a V. cholerae genome-wide transposon mutant library. Extraction of high-dimensional architectural data with the image analysis pipeline BiofilmQ and examination of the overall biofilm formation capabilities of each strain enabled us to establish the biofilm lifestyle in V. cholerae as a highly regulated one in which half of the V. cholerae genome plays an important role, most of its genes affecting either the temporal development of biofilm formation or the three-dimensional structure of the biofilm. Interestingly, we found that genes encoding motility- and chemotaxis-related proteins have an impact on biofilm structure, their absence leading to an exacerbated biofilm seeding density, biofilm size and cell packing in some cases, but also to a complete incapability to form three-dimensional biofilm structures.

AUTHOR

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Microbial communities are defined as multi-species assemblages, in which microbes strongly interact in a micro environment forming a local community [1]. This arrangement allows to analyse how biological systems are structured, which are their functional interactions and how community changes in space and time. In this spirit, we study a two-species system consisting of the bacteria Escherichia. coli (E.coli) and the algae Chlamydomonas reinhardtii (C.r.). The algae C.r. is a photosynthetic well-known model microorganism. It possesses the ability to generate oxygen through the photosynthesis, with the rate of oxygen production being conditional upon both the intensity and wavelength of the light source[2]. On the other hand, E.coli has several elaborate sensing mechanisms to monitor and response to availability of oxygen. E.coli has evolved an intrinsic navigational mechanism to efficiently navigate itself towards regions of high oxygen concentration. This strategy which is called aerotaxis was reported for the first time by Engelmann in 1881 [3]. We described a microbial community consisting of C.r. as an oxygen source in a shared environment with E.coli. We have employed the combination of molecular biology, microscopy, and digital light technologies to systematically explore the analytical aspects of this active systems in a controlled laboratory setting. We find that algae creates a bubble of oxygen around itself which restore bacteria motility in the defined radius. We investigated how bacterial concentration influences the distribution of activated E. coli cells around an algae and observed a significant impact on the shape of the density profile. What is more unexpected, however, is the existence of a region with an approximate radius of 60 m in- side which no appreciable variations in RCD (rate of change of direction) are observed between cells moving inwards and those moving outwards.

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Trypanosoma brucei collectives as active fluids

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We have studied the motility of unicellular, flagellate parasites in dense collectives on hydrogel surfaces. The microswimmers exhibit a highly motile swimming behaviour in tightly packed swarms. The collective migration of these swarms on the semi-solid surfaces produces striking patterns reminiscent of viscous fingering or swarming instabilities of bacteria.
The analyses of single cell motility in relationship to collective migration, showed it to be unlikely that trypanosome motility alone is responsible for the specific higher-order swarm behaviour. Rather, we observe physiochemical parameters to have a major influence on the collective behaviour. Hydrophobic interactions caused by the lipid composition of the environment, for example, need to be considered when analysing swarm migration in social motility assays.
The concentrated suspension of cells spreading on the hydrogel surface can thus be treated as a drop of active fluid, that is driven by the general, energy consuming, persistently motile nature of the trypanosomes, but directed by environmental factors that dominate the collective motion. We control different states of cell order (e. g. nematic) in the fluid by changing the gel surface and thus the fluid characteristics in the swarm.
Social motility assays are regarded as a proxy for parasitic success in the host, i. e. infectiousness, therefore a better understanding of the physical nature of these biologically active fluids is fundamental; a crucial goal at the interface of physics and biology for active matter scientists.

Changes in the phototactic behavior of Chlamydomonas reinhardtii resulting from the integration of past

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Organisms such as Chlamydomonas reinhardtii use phototaxis to explore their environment and find the best conditions for photosynthesis. In our work, we study the phototactic behavior of suspensions of C. reinhardtii confined within shallow cylindrical wells, and exposed to directional light stimuli of various intensities. We recover known results: at low light intensities, the algae exhibit positive phototaxis, at high light intensities, negative phototaxis and at intermediate light intensities, we find that the behavior depends on past phototactic stimuli, in a way that is the opposite of an adaptive behavior [1], [2] and [3]. It is known that cells adapt to previous stimuli, and that stimulating C. reinhardtii multiple times with an identical high light intensity leads to different responses; the first stimulus leads to negative phototaxis, while after several stimuli, the algae exhibit positive phototaxis, as if they sensed a lower stimulus [4] and [5]. In our experiments at intermediate light intensities, we highlight a behavior that is the opposite of adaptation: cells integrate the signal over time. Applying the same stimulus twice at a couple minutes interval leads to a change in phototactic response, from positive phototaxis to negative phototaxis, such that the response to the second stimulus is the same as if the light was of higher intensity. Waiting a couple hours between the experiments allows to recover the original positive phototactic behavior. A simplified model of phototaxis is introduced, where the time-integration of light stimuli results from the interplay between the underlying biological time scales and the time scales of the light stimuli. The outcome of the model captures qualitatively our experimental results.

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Influence of motility and hydrodynamics on phage-bacteria encounters

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Bacteriophages - or "phages" for short - are viruses that can infect and kill bacteria. They are small particles that rely on thermal diffusion to find target cells, but are also advected in the flow-field generated by motile bacteria. We use coupled lattice-Boltzmann and coarse-grained molecular dynamics simulations to investigate the encounter between phages and bacteria. We find that while motility increases the encounter rate, the effect is much smaller than what would be predicted if hydrodynamic interactions were neglected. This has important implications for our understanding of the evolutionary cost that bacteria have to pay for their motility.

Chemotactic swimming of two chiral squirmers

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In this work, we investigate the synchronous swimming of a pair of self-propelled low Reynolds number swimmers in a chemical field [1]. We observe that the hydrodynamic interaction between the swimmers helps them to reach the chemical target quicker than a single swimmer [1, 2]. We have used the chiral squirmer model [2, 4] to understand the dynamics of the swimmers. The former model swimmer possesses a translational V and an angular velocity . Chiral squirmers exhibit synchronized bounded motion apart from the regular monotonic attraction and repulsion depending on its nature, i.e., puller or pusher type. In bounded motion, they synchronize, approach each other, and separate from each other in a periodic manner [2, 4]. We observe that in a chemical landscape the former synchronized swimming mechanism helps them to reach the chemical target faster. This study is helpful in understanding the collective dynamics of swimmers in a complex environment.

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Bacterial chemotaxis considering memory effects

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The ability of motile microorganisms to sense and migrate along due to a chemical or ligand gradient is known as Chemotaxis. This process is a key ingredient in some biological performances, like the acting of immune systems or tumoral migration in metastasis. This mechanism is used also for bacteria to find places to proliferate. The first relevant theoretical model to describe this phenomenon at a macroscopic scale came at the hands of the Keller and Segel article [1]. They introduce a macroscopic equation that couples a diffusion-drift equation for bacterial density with a reaction-diffusion equation for the chemoattractant concentration. Over the years, chemotaxis has been increasingly understood. For example, a bacterium like E. coli, orients itself through run-and-tumble movements, altering its tumble rate when moving in the direction of the ligand gradient. The variation of this magnitude depends on fluctuations in the concentration of phosphorylated CheY protein (CheY-P) [2]. Tracking E. coli bacteria,it was found that these fluctuations have large amplitude and present long memory times (tens of seconds) [3]. These new performances are not taken into account in the Keller-Segel model and fails to predict some experimental results. The objective of this work is to obtain new macroscopic equations that can perform the phenomena precisely. Considering a stochastic differential model for CheY-P concentration with memory effects [4], we use a kinetic equation that presents the memory relaxation time and changes in tumble rate [5]. By identifying different scales of memory time, we derive a Keller–Segel type chemotaxis model by applying the Chapman-Enskog method in each case. For short memory times, we can only consider the bacteria's density as a conserved field. We deduce the equation, which allows us to obtain the diffusion coefficient and mobility. The results are in agreement with Keller-Segel's predictions for the memoryless time limit. When we consider long memory times, the density of CheY-P protein is a quasi-conserved field. In this case, macroscopic equations of bacteria's density and CheY-P density are derived, together with the associated transport coefficients. In this case, macroscopic equations of bacteria's density and CheY-P density are derived, together with the associated transport coefficients. An Onsager's relation is obtained for the transport coefficients. We validate these equations by analyzing the stationary regime and linear response to a spatiotemporal signal and compare them with simulations.

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Flow structures around a microswimmer at fluid-fluid interface

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Living organisms such as bacteria and algae often form biofilms at air-liquid and/or liquid-liquid interfaces. Therefore, it is important to understand the hydrodynamic interaction between the fluid-fluid interface and microorganisms. In this study, the flow field structures around a symmetrically trapped spherical microswimmer at an interface separating two fluids with different viscosities are investigated using lattice Boltzmann (LB) simulations. In these simulations, Reynolds (Re) and Capillary (Ca) numbers are very small, and hence the contribution of inertia and interface deformations are neglected. Simulations of different types of microswimmers (pusher, puller, and neutral) are achieved by varying the squirmer parameter (). It is observed that the flow structure and vorticity distribution around the microswimmers are strongly influenced by the squirmer parameter () and viscosity contrast (). Furthermore, the interplay between force-dipole and source-dipole along with viscosity contrast leads to a range of flow structures such as symmetric four-lobe, and asymmetric quadrupolar flow fields. Flow structure asymmetry is quantified for swimmer with different steady state orientations. Finally, the hydrodynamic interaction between microswimmer and passive tracer particles are presented in terms of trajectories.

Geometry and Motility: Ratcheting, Autonomous Pumping, Guidance and Filtering

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The interplay of motility and geometry can lead to a variety of striking effects such as rectification of motion of motile particles and autonomous pumping of passive particles in a ratchet channel [1], trapping and release of motile and immotile particles assisted by motile species [2], guidance and transient rectification of motion of motile particles due to the directional locking in presence of immotile species [3], and guidance of motion of motile particles by soft "boundaries" on a topographically flat surface of distinct chemical patterns allowing reflection, crossing and filtering of motile particles [4]. The mechanism of rectification of motion of motile particles in an asymmetric channel is different from that for the Brownian motion. It essentially involves the memory effect related to motility and the finite persistence length [1]. The direction locking leads to the increase of the persistence length and occurs due to the transient "embedding" of motile particles in clusters of immotile species [3]. An electrokinetic motile Janus particle can sense boundaries between distinct chemical patterns with different Zeta-potentials, via the feedback modification of the electroosmotic flows generated by the motile particle by these soft boundaries, resulting in gentle guidance of motile particles on topographically flat surfaces [4].

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ThirdPeak – a software to process, visualize and analyze tracks in two and three dimensions

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Life, as we know it, is sustained but also constrained by Brownian motion and the diffusion of vital nutrients and proteins required for cell growth and survival. The advent of super-resolution microscopy techniques has revolutionized our ability to observe molecular dynamics within cells with improved temporal and spatial resolution. Although tools exist for localizing [1] and connecting tracks [2] in two and three dimensions, visualization and analysis software often only cater to two-dimensional data [3]. To simplify the exploration and analysis of three-dimensional track data, we developed ThirdPeak— a MATLAB-based software with a user-friendly graphical interface. This software offers flexibility by supporting various data formats, accommodating track or localization data from diverse sources and length scales. During preprocessing, users can apply quality filters and correct for drift. Once the results are validated, in-depth analysis becomes possible. ThirdPeak enables users to select individual tracks, focus on tracks within specific regions of interest, or analyze multiple files concurrently. We have successfully utilized this software to uncover the dynamics within the endosomal system of Trypanosoma brucei. We believe that ThirdPeak can serve as a valuable addition to the workflow of researchers studying similar systems or conducting three-dimensional track analysis.

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Simulating Trypanosome Motility

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We investigate motility of the protozoan Trypanosoma, using numerical simulations. We have established a trypanosome model (see Fig. 1), which is motivated by experimental observations [1, 2] and builds upon the previously proposed model [3, 4]. The cell body is represented by a set of vertices which are distributed homogeneously on a pre-defined elongated surface and form a triangulated elastic network of springs. The network model also incorporates bending rigidity, and area and volume conservation constraints. For parasite propulsion, a flagellum is attached to the cell body. The flagellum is constructed from four parallely placed filaments, two of which are embedded into the body, and the other two are used for the generation of a propagating bending wave [5]. Flagellum beating leads to a deformation of the body and generates propulsion. We study the behavior of this model for different body stiffnesses, beating frequencies,wavelengths, and amplitudes. The simulations achieve values for the swimming velocity and the body rotation around its swimming axis, which are at the same order of magnitude as experimental measurements. The trypanosome model is flexible enough and can be adapted to reproduce the behavior of different trypanosome species. This model will be used to investigatetrypanosome locomotion in blood stream.

Characterising the motility of the novel SS-5 strain of Magnetotactic bacteria

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Magnetotactic bacteria (MTB) have garnered significant interest due to their unique ability to align with magnetic fields and respond to environmental stimuli. Currently, the well-studied species of MTBs exhibit complex cell morphologies and propulsion mechanisms, making them poorly suitable for physics modelling. In this project, we study the aerotaxis and magnetic alignment of the novel SS-5 strain of MTB, which features a simple rod shape similar to E.coli and performs run-reverse motion using a single flagellum. To achieve this, we have developed a custom experimental setup enabling precise tuning of both oxygen concentration and magnetic field within a microfluidic device. Our initial results provide an insightful understanding of the magnetic response of the SS-5 bacteria, indicating a strong ability to align with magnetic fields. Ongoing research focuses on how the SS-5 strain reacts to oxygen gradients, with preliminary results showing a significant aerotactic response to very low oxygen concentrations. These results lead towards a comprehensive modelling of MTB motion, with potential applications in employing their motility responses as navigation tools through complex and confined environments.

Without title

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Information theory of chemotaxis

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Biological cells and small organisms navigate in concentration fields of signaling molecules using two fundamental gradient-sensing strategies: spatial comparison of concentrations measured at different positions on their surface, or temporal comparison of concentrations measured at different locations visited along their motion path. It is believed that size and speed dictate which gradient-sensing strategy cells choose, yet this has never been formally proven. Using information theory, we investigate the optimal gradient sensing mechanism from the perspective of an ideal chemotactic agent that combines spatial and temporal comparison. We account for physical limits of chemosensation: molecule counting noise at physiological concentrations, and motility noise inevitable at the micro-scale. Our simulation data collapses onto an empirical power-law that predicts an optimal weighting of information as function of motility and sensing noise, demonstrating how spatial comparison becomes more beneficial for agents that are large, slow and less persistent. This refines and quantifies the previous heuristic notion. Our idealized model provides a base-line for biological chemotaxis and may inspire the design of robots guided by scalar fields.

Local curvature steers the self-organization of active particles in confinement

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The impact of confinement on the self-organization of active particles has gained much attention1,2,3. Previous investigations have primarily focused on circular or square/rectangular geometric constraint. However, to explore more realistic scenarios, like particles enclosed in a membrane, confinement in curved geometry is essential 4. A suitable and simple geometry for such a case happens to be the ellipse. Consequently, we present simulations (in Julia5) of active Brownian particles in hard elliptical confinement. The particles interact via hard sphere correction and experience reflection upon reaching the boundary. We found curvature-dependent organization of the particles, wherein more particles tend accumulate at high curvature (equators) of the ellipse. Moreover, the extent of curvature induced collection depends on various factors, including on the eccentricity of the ellipse, packing fraction, particle size, and velocity. Furthermore, we are actively looking for experimental evidence of this collective dynamics based on active Janus particles (Pt/silica) confined inside elliptical micro wells. To have the necessary confining structure, we successfully implemented a novel yet simple drop cast method allowing formation of a few microns sized elliptical wells in a PDMS film. These wells were able to confine the Janus particles, aiding observation. We anticipate our results might be applicable to the design of active particles-based microrobots, where environment-induced curvature of the membrane boundary could guide encapsulated active particles.

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P. sineare in confinement: breaking free through narrow escapes

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The microbial ecosystem is full of narrow constrictions that microorganisms need to learn to navigate in order to survive. Here, we study a Nature example of a "microorganism billiard": a system composed of a population of microorganisms packed in a closed space, with only a few narrow apertures to escape from. This situation occurs when the marine parasite Parvilucifera sinerae infects and replicates inside a dinoflagellate host, and the newly born parasites find themselves in the closed and extremely packed space represented by the dead host body (the "sporangium"). In order to start a new successful infection cycle, the parasite's zoospores must find their way out of this closed structure. Which strategies are deployed by the parasites to manage a successful escape? A particular interaction with the boundaries might help them navigate this structure, and collective behaviours between individual parasites might be key in finding the way out. Here, we present the preliminary results of an experiment aimed at reconstructing the 3D orientation of the zoospores inside the sporangium during the emptying process, to investigate the possible emergence of an ordered phase.

Run and Tumble Behavior of E. Coli

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E. coli is a multi-flagellated bacterium with a prolate spheroidally-shaped body and several left-handed helical flagella (typically between 2 and 5). The helical flagella are rotated by a motor, enabling the bacterium to propel forward. E. coli generally has two modes of swimming: (i) 'run' with a straight swimming direction, and (ii) 'tumble' during which the bacterium can change its swimming direction [1-3]. During the run stage, all flagella rotate anticlockwise, such that they bundle into a single propeller. During the tumble stage, one or more flagella switch to the clockwise rotation, so that they leave the bundle and facilitate E. coli to change its swimming direction. In our work, we investigate how different E. coli properties, including body and flagella geometry, flagella stiffness and the strength of actuation, govern the run-and-tumble behavior of these bacteria. We establish a realistic E. coli model (see Fig. 1) and validate it using available experimental observations [1-3]. The model properly captures the running speed of E. coli, rotational frequency of the head and flagella, tumbling time and angle in comparison to experimental measurements [1-5]. Furthermore, our simulations show that the stiffness of a hook (the short part of a flagellum which connects it directly to the motor) plays an important role in the run-and-tumble behavior, which has also been suggested in experimental studies [6-7]. This detailed model of E. coli helps us better understand its swimming behavior, and allows the exploration of E. coli locomotion in more complex realistic environments such as with walls [8].

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Anomalous bacterial transport in confined geometries

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Motile bacteria are known to interact with flows exhibiting in the bulk active Betherton-Jeffery trajectories or rheotactic drift due to the helical flagella shapes. In the vicinity of bounding surfaces, one also observes specific trajectories including persistent upstream swimming, an effect enhanced by the presence of edges. Statistically, the combination of hydrodynamic interactions and flow-induced orientation, leads to a strong density increase in the surface vicinity, inducing a boundary layer of around 10 in extension. In disordered and complex environments, the presence of surface and flow make large-scale dispersion properties of active bacteria a challenging issue. Based on the previous study, here we developed experimental model systems suited to observe individual trajectories and to assess the emerging dispersion processes in funnel-shape microfluidic device(figure(a)) varying the flow velocity using motile bacteria. We found: (1) a sharp density increases downstream close to surfaces at the same shear rate as in previous work(figure(a)); (2) the concentration difference indicator (1) increase with time and then reach a steady state. This work will help to understand the role of flow on the transport of motile bacteria, in the presence of geometrically complex surfaces and surface.

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Useful Information

In preparation

Venue

The workshop will take place at the Biozentrum of the University of Würzburg, Am Hubland

Talks will be held at room **A101** of the Biozentrum. It is situated at the University Campus "Am Hubland Süd" (please see map)

The **poster session** will be held on Wednesday night from 18.00 on at the Biozentrum near to the seminar room A101.

The **conference dinner** will be held on Thursday night from 19.00 on, at the Bürgerspital Weinstuben Theaterstraße 19, 97070 Würzburg. The Bürgerspital Weinstuben is located in the city centre (near Theatre) and can be reached by busses starting at Hubland (lines 29, 14, 114). Bus tickets can be obtained in the bus (single tickets) or online (see also https://www.wvv.de/mobil-b2c/preise/ [in German], a 6er ticket for 12.00 euros would cover all your needs for the three days.)

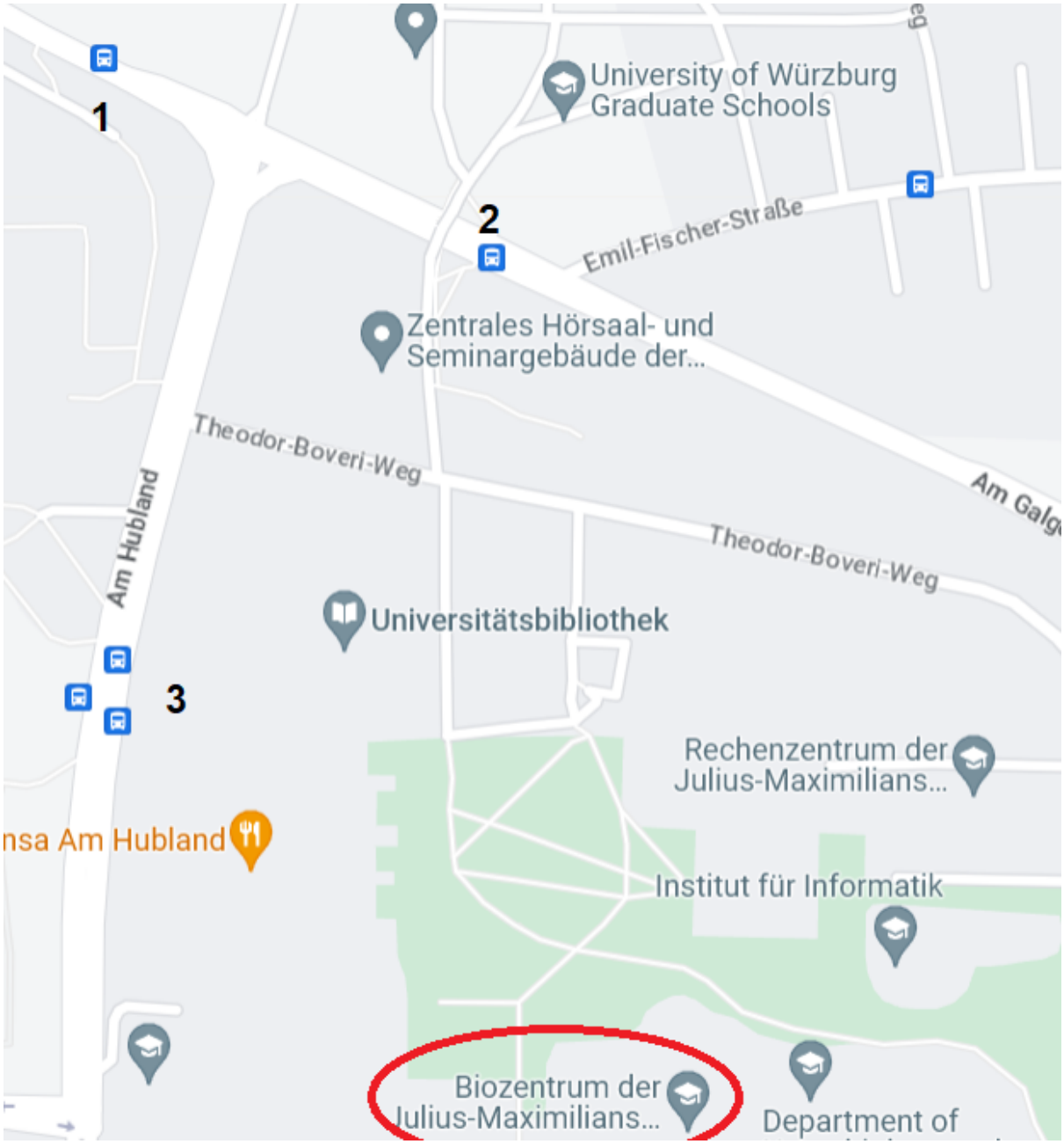
How to get to the Biozentrum?

The Biozentrum is located at am Hubland and can be reached by:

- **Bus** 1 = Line 29 “stop = Philosophisches Institut”
- **Bus** 2 = Line 14 “stop = Am Hubland”
- **Bus** 3 = Line 114 "stop = Hubland Mensa"

All busses start at the central station. The way from the busstops to the Biozentrum will be indicated by signs.

For the location see also the map at the next page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Theodor-Boveri-Weg
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Theodor-Boveri-Weg
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nsa Am Hubland
Institut für Informatik
Biozentrum der
Julius-Maximilians...
Department of