WILHELM UND ELSE HERAEUS-STIFTUNG

DPG Physics School 2012

Forces and Flow in Biological Systems

23 – 28 September 2012
Physikzentrum Bad Honnef, Germany

We thank the Wilhelm und Else Heraeus-Stiftung for its generous support for this DPG physics school. The Wilhelm und Else Heraeus-Stiftung is a private foundation which supports research and education in science, especially in physics. A major activity is the organisation of seminars. To German physicists the foundation is recognized as the most important private funding institution in their fields. Some activities of the foundation are carried out in cooperation with the German Physical Society (Deutsche Physikalische Gesellschaft).

Aims and Scope of the DPG Physics School 2012 on Forces and Flow in Biological Systems

Force and movement are central elements of life. In contrast to traditional man-made material, however, biomaterials have unusual elastic and viscous properties and therefore deform and flow differently. In order to understand the physics related to forces and flow in biological systems, one has to extend traditional approaches like continuum mechanics to address the fact that they are complex, hierarchical, thermally fluctuating, and active. Recent advances in the physics of soft condensed matter and non-equilibrium physics provide rewarding avenues for meeting this challenge. Moreover large and complex systems can be approached today with computer simulations to much more quantitative detail than formerly possible.

This school will bring together some of the leading physicists working with analytical and computational approaches to study forces and flow in cellular systems. Important biological systems addressed in the course will be the mechanics of red blood cells, deformation and transport of cells in the blood flow, active swimming of microorganisms (e.g. sperm, bacteria and algae), mechanics, traction and shape of adherent cells, flow inside migrating cells, hydrodynamic and mechanical interactions of cells, and the large-scale mechanics of tissue.

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Registration:

Sunday 4-6 pm and Monday 8-9 am
at the Physikzentrum

Door Code:

XXXXX For entering the Physikzentrum during the whole school

Schedule

Schedule DPG physics school *Forces and flow in biological systems*
Physikzentrum Bad Honnef, September 23-28 2012

	Sun	Mon	Tue	Wed	Thu	Fri
08:00-09:00		Breakfast	Breakfast	Breakfast	Breakfast	Breakfast
09:00-10:30	Arrival	**Tom Powers** Intro Hydro	**Gerhard Gompper** Intro Comp	**Erwin Frey**	**Frank Jülicher**	**Ray Goldstein**
10:30-11:00		Coffee	Coffee	Coffee	Coffee	Coffee
11:00-12:30		**Holger Stark**	**Dmitry Fedosov**	**Andreas Bausch**	**Dirk Drasdo**	**Nir Gov**
12:30-14:00		Lunch break	Lunch break	Lunch break	Lunch break	Lunch break
14:00-15:30		**Ulrich Schwarz** Intro Elast	**Ramin Golestanian**	Hiking	**Fred MacKintosh**	Departure
15:30-16:00		Coffee	Coffee		Coffee	
16:00-17:30		**Stephan Grill**	**Tom Powers**		**Carina Edwards**	
18:00 19:00	Dinner	Dinner	Dinner	Dinner	Conference dinner	
19:30-21:00	Get together	Poster session I	Poster session II			

Program

Sunday, 23 September 2012

16:00 – 18:00	Arrival and registration at the Physikzentrum Bad Honnef
18:00	DINNER
19:30 – 21:00	Get together

Monday, 24 September 2012

08:00	BREAKFAST
09:00 – 10:30	*Introduction to low-Reynolds-number hydrodynamics* Tom Powers (U Brown)
10:30 – 11:00	COFFEE
11:00 – 12:30	*Hydrodynamic interactions in soft matter and active particle systems* Holger Stark (TU Berlin)
12:30	LUNCH
14:00 – 15:30	*Basics and limitations of continuum elasticity theory* Ulrich Schwarz (U Heidelberg)
15:30 – 16:00	COFFEE
16:00 – 17:30	*Cellular polarization by coupling an active fluid to a pattern forming system* Stephan Grill (MPI Dresden)

18:00 DINNER

19:30 – 21:00 *Poster Session I*

Tuesday, 25 September 2012

08:00 BREAKFAST

09:00 – 10:30 *Mesoscale hydrodynamic simulations*
Gerhard Gompper (FZ Jülich)

10:30 – 11:00 COFFEE

11:00 – 12:30 *Modeling blood flow on the cell scale*
Dmitry Fedosov (FZ Jülich)

12:30 LUNCH

14:00 – 15:30 *Active hydrodynamics at small scales: self-propulsion and coordination*
Ramin Golestanian (U Oxford)

15:30 – 16:00 COFFEE

16:00 – 17:30 *Swimming in viscoelastic media*
Tom Powers (U Brown)

18:00 DINNER

19:30 – 21:00 *Poster Session II*

Wednesday, 26 September 2012

08:00	BREAKFAST
09:00 – 10:30	*Collective phenomena in active cytoskeletal systems* Erwin Frey (LMU Munich)
10:30 – 11:00	COFFEE
11:00 – 12:30	*Cytoskeletal pattern formation: Self-organization of driven filaments* Andreas Bausch (TU Munich)
12:30	LUNCH
14:00	CONFERENCE TRIP Hiking (Ölberg in Siebengebirge)
19:00	DINNER

Thursday, 27 September 2012

08:00	BREAKFAST
09:00 – 10:30	*Dynamic organization of developing tissues* Frank Jülicher (MPI Dresden)
10:30 - 11:00	COFFEE
11:00 – 12:30	*Towards predictive quantitative modeling of tissue organization on histological scales: imaging, image analysis and modeling of liver regeneration and tumorigenesis* Dirk Drasdo (INRIA Paris)

12:30	LUNCH
14:00 – 15:30	*Cytoskeletal networks: mechanics and non-equilibrium effects* Fred MacKintosh (Vrije Universiteit Amsterdam)
15:30 – 16:00	COFFEE
16:00 – 17:30	*Continuum modelling of tissue contraction, growth and morphogenesis* Carina Edwards (University of Surrey)
18:00	CONFERENCE DINNER

Friday, 28 September 2012

08:00	BREAKFAST
09:00 – 10:30	*Green algae as model organisms for biological fluid dynamics* Ray Goldstein (U Cambridge)
10:30 – 11:00	COFFEE
11:00 – 12:30	*Modeling active particles, membranes and gels* Nir Gov (Weizmann Institute Israel)
12:30	LUNCH

END OF SUMMER SCHOOL AND DEPARTURE

Abstracts Speakers

Introduction to low-Reynolds-number hydrodynamics /
Swimming in viscoelastic media

Thomas Powers
U Brown

Introduction to low-Reynolds-number hydrodynamics

This lecture will introduce the basic concepts of fluid mechanics at the small scale, where inertia is unimportant. The main applications will be swimming microorganisms, although the framework we develop is useful for studying colloids, polymers, and microfluidics. Topics discussed will include Stokes flow, singular solutions to Stokes equations, hydrodynamic interactions, and slender-body theory. The fundamentals will be illustrated with examples from the literature on swimming microorganisms.

Swimming in viscoelastic media

Swimming microorganisms commonly encounter fluids that are laden with polymers. The polymers give the fluid an elastic nature, and we study how microorganisms swim in elastic fluids. Using a combination of theory, simulation, and table-top model experiments, we explore the fundamental principles of swimming in a viscoelastic medium.

Hydrodynamic interactions in soft matter and active particle systems

Holger Stark
TU Berlin

Micron-sized colloidal particles moving in a viscous solvent create long-range flow fields that influence the motion of neighboring particles. These so-called hydrodynamic interactions are of immense importance in colloidal as well as biological systems including swimming microorganisms or, more generally, active particle systems.

The method of mobilities treats the viscous environment implicitly by introducing cross mobilities that describe hydrodynamic interactions between two objects, mostly spherical particles. In the first part, I will explain this method starting from the Green function of the Stokes equation and also comment how hydrodynamic interactions with bounding walls are taken into account. Illustrative examples are presented.

In the second part, I will demonstrate the importance of hydrodynamic interactions in various systems of current interest ranging from soft matter to biology, with special emphasis on self-propelled particles. Possible topics include: synchronization via hydrodynamic interactions, a semiflexible polymer under Poiseuille flow in a microchannel, and self-propelled particles in a gravitational field. Finally, the dynamics of a single microswimmer moving in a narrow channel under Poiseuille flow can be mapped onto a Hamiltonian system where hydrodynamic interactions with bounding walls introduce dissipation.

Basics and limitations of continuum elasticity theory

Ulrich Schwarz
U Heidelberg

In the first part of this lecture, I will give an introduction to the central concepts and equations of continuum elasticity theory, on the level of standard textbooks in theoretical physics [1] and biomechanics [2]. We will start with one-dimensional (scalar) elasticity and introduce the concepts of linear viscoelasticity (creep function, relaxation function, complex modulus) and the standard linear model. We then turn to three-dimensional materials, which require a tensorial theory. We will introduce the stress and strain tensors, and discuss the difference between a Lagrangian and an Eulerian description, in particular the corres-ponding geometrical non-linearity. We then discuss materials laws (constitutive equations) relating stress and strain, including the possibility of a physical non-linearity. Finally we discuss the central equations for linear isotropic elasticity, for which both the geometrical and physical relations are linearized, and the meaning of its two elastic constants (bulk and shear modulus).

One important feature of cells and tissue, which is not present in traditional man-made material, is active contractility. In the second part of the lecture, I will discuss how this important feature can be incorporated in elasticity theory. By using an analogy to thermal cooling, active contractility can be implemented with software for the finite element method (FEM) typically developed in applied math and mechanical engineering. During recent years, such models have been increasingly used to predict traction patterns and shapes of actively contracting cells and tissue, compare e.g. [3,4,5]. Finally we introduce the model of active cable networks (ACN), which goes beyond traditional elasticity theory and combines the concepts of cable elasticity and tension in a relatively simple computational framework [6,7].

[1] LD Landau and EM Lifshitz, Theory of Elasticity, Vol. 7 of the Course of Theoretical Physics, Pergamon 1981
[2] C Oomens, M Brekelmans, F Baaijens, Biomechanics, Cambridge University Press 2009
[3] VS Deshpande, RM McMeeking and AG Evans, PNAS 103: 14015, 2006.
[4] CM Edwards and US Schwarz. *Phys. Rev. Lett.,* 107:128101, 2011.
[5] AF Mertz et al., Phys. Rev. Lett. 108: 198101, 2012.
[6] IB Bischofs et al*., Biophys. J.,* 95:3488-3496, 2008.
[7] P Guthardt Torres, IB Bischofs and US Schwarz*. Phys. Rev. E*, 85:011913, 2012.

Cellular polarization by coupling an active fluid to a pattern forming system

Stephan Grill
MPI Dresden

I will present recent advances in our understanding of the coupling of mechanical and biochemical processes for the purpose of forming intracellular patterns. I will discuss in general terms the mechanism of pattern formation in active fluids in which active stress is regulated by diffusing molecular components. I will then present a particular biological example, the polarization of the *C. elegans* zygote, a classic example for mechanochemical coupling. I illustrate how passive advection by actively generated fluid flow is sufficient to drive asymmetry in PAR proteins and thereby acts as a trigger for pattern formation. Our work suggests that passive advective transport in a regulated active material is a general mechanism by which patterns are established in developmental biology.

Mesoscale Hydrodynamics Simulations of Swimmers and Flow

Gerhard Gompper
FZ Jülich

Mesoscale hydrodynamics simulation techniques are an important tool to bridge the length- and time-scale gap between the small molecules of a solvent and the mesocopic scale of macromolecules, colloids, vesicles, cells, and microswimmers. The main idea in these approaches is to drastically simplify the dynamics on the microscale, but to satisfy the conservations laws for mass and momentum, so that hydrodynamic behavior emerges naturally on larger length scales. The techniques can be divided into particle-based off-lattice methods such as Dissipative Particle Dynamics (DPD) [1] and Multi-Particle Collision Dynamics (MPC) [2,3] and lattice-based velocity-distribution approaches such as
the Lattice-Boltzmann Method (LBM) [4].

After an overview and a comparison of these simulation techniques, the MPC-approach will be discussed in some detail. This method consists of alternating streaming and collision steps in an ensemble of point particles. The implementation of boundary conditions, the flow generation, and the coupling of the fluid to embedded particles will be explained on the basis of this approach [2,3].

In the second part, applications of the mesoscale simulations to fluid vesicles [5], red-blood-cell deformations and correlations [6,7], and white-blood-cell margination [8] in shear and microchannel flows, and to microswimmers like sperm [9,10] and bacteria [11] will be discussed. The results show that the dynamical properties of these soft or active objects are determined by an intricate
interplay of confinement, deformation, orientation, hydrodynamic interactions, thermal fluctuations, and active motion.

[1] I. V. Pivkin, B. Caswell, and G. E. Karniadakis, Rev. Comp. Chem. 27, 85 (2010).
[2] R. Kapral, Adv. Chem. Phys. 140 , 89 (2008).
[3] G. Gompper, T. Ihle, D.M. Kroll, and R.G. Winkler, Adv. Polymer Sci. 221, 1 (2009).
[4] B. Dünweg and A.J.C. Ladd, Adv. Polymer Sci. 221, 89 (2009).
[5] H. Noguchi and G. Gompper, Phys. Rev. Lett. 93, 258102 (2004).
[6] H. Noguchi and G. Gompper, Proc. Natl. Acad. Sci. USA 102, 14159 (2005).
[7] J.L. McWhirter, H. Noguchi, and G. Gompper, Proc. Natl. Acad. Sci. USA 106, 6039 (2009).
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[9] Y. Yang, J. Elgeti, and G. Gompper, Phys. Rev. E 78, 061903 (2008).
[10] J. Elgeti, U.B. Kaupp, and G. Gompper, Biophys. J. 99, 1018 (2010).
[11] S.Y. Reigh, R.G. Winkler, and G. Gompper, Soft Matter 8, 4363 (2012).

Modeling blood flow on the cell scale

Dmitry Fedosov
FZ Jülich

Blood flow plays an important role in many physiological processes and pathologies in the organism including transport of the necessary elements and cells to and away from the body tissues, organism defense through immune and inflammatory response, hemodynamic resistance, haemostasis, and blood-related diseases. To understand these processes, detailed investigation of blood flow is required under realistic conditions including cell deformability, hydrodynamic interactions, and complex geometries. Blood consists of red blood cells (RBCs), white blood cells (WBCs), platelets, and plasma containing various molecules and ions. RBCs constitute approximately 45% of the total blood volume, WBCs around 0.7%, and the rest is taken up by blood plasma and its substances. Due to a high volume fraction of RBCs, the rheological properties of blood are mainly determined by the RBC properties.

Blood can be modeled as a suspension of deformable cells whose membranes are represented by a viscoelastic spring-network which incorporates appropriate mechanical and rheological cell-membrane properties. In this lecture, we will review modeling of single cells and their suspension (blood) as well as the flow behavior of blood. Blood rheology as well as blood flow in idealized micro-channel geometries will be presented. In particular, the relation between blood rheology and RBC dynamics and structure, and the physical mechanisms, which govern WBC margination towards the walls in micro-vessels, will be discussed.

Active hydrodynamics at small scales: self-propulsion and coordination

Ramin Golestanian
U Oxford

The directed propulsion of small scale objects in water is problematic because of the combination of low Reynolds number and strong thermal fluctuations at these length scales. One possibility for designing propulsion is to devise non-reciprocal deformation strategies that are simple enough to be realizable. For molecular-scale swimmers, directed propulsion could not come from pre-specified deterministic periodic deformations because of thermal fluctuations, and there will be need to develop strategies to extract a net directed motion from a series of random transitions in the conformation space of the swimmer.

Microorganisms and the mechanical components of the cell motility machinery such as cilia and flagella operate in low Reynolds number conditions where hydrodynamics is dominated by viscous forces. The medium thus induces a long-ranged hydrodynamic interaction between these active objects, which could lead to coordination and other emergent many-body behaviors.

The force-free nature of phoretic transport mechanisms allow us to design self-propelled particles by equipping them with a mechanism that could create the appropriate gradient that could lead to directed motion, e.g. by using asymmetric particles with built-in sources.

The stochastic motion of such active colloids is anomalous due the memory effect of the concentration profile of the solute molecules and density fluctuations. A dilute solution of such active particles will exhibit interesting collective behaviors, including depletion and instabilities, depending on the parameters.

Collective phenomena in active cytoskeletal systems

Erwin Frey
LMU München

Active systems are many-body systems where the constituent particles are either self-propelled or externally driven. Examples include flocks of animals and cohorts of cells in tissue, intracellular transport and cytoskeletal networks, and fluctuating granular matter. These systems exhibit a rich spectrum of steady states and emergent phenomena. Traffic jams of molecular motors along microtubules regulate the length of these cytoskeletal filaments. Assemblies of biopolymers and molecular motors self-organize into coherent swarms and density waves and thereby drive cytoskeletal organization. Vibrated granular matter may either form strongly fluctuating states with short-lived structures that are continually created and destroyed, or long-lived patterns and jammed states. In this talk we give an overview of these active systems and review recent progress in applying principles of non-equilibrium statistical mechanics and kinetic theory to understand some of the mechanisms underlying the observed collective phenomena.

Cytoskeletal pattern formation: Self-organization of driven filaments

Andreas Bausch
Lehrstuhl für Biophysik (E27), TU München
James-Franck-Strasse D-85747
Garching, Germany

Living cells rely on the self organization mechanisms of cytoskeleton to adapt to their requirements. Especially in processes such as cell division, intracellular transport or cellular motility the controlled self assembly to well defined structures, which still allow a dynamic reorganization on different time scales are of outstanding importance. Thereby, the intricate interplay of cytoskeletal filaments, crosslinking proteins and molecular motors a central role. One important and promising strategy to identify the underlying governing principles is to quantify the physical process in model systems mimicking the functional units of living cells. Here I will present in vitro minimal model systems consisting of actin filaments, crosslinking molecules and myosin-II filaments exhibiting collective long range order and dynamics. I will discuss how a balance of local force exertion, alignment interactions, crosslinking and hydrodynamics affect the evolving dynamic structures.

Dynamic organization of developing tissues

Frank Jülicher
MPI Dresden

During the development of an organism, dividing cells form growing tissues. Spatial patterns of gene products are set up to control the formation of morphologies in these dynamic tissues. Tissue dynamics and morphogenesis result from the interplay of active mechanical processes and signaling systems. An important model system to study the dynamics of developing tissues is the formation of the wing of the fly Drosophila. The wing imaginal disk, the wind precursor, is a two-dimensional epithelium. It grows from about 50 cells to 50000 cells and undergoes important morphological changes. It is divided in two compartments of anterior and posterior cell populations which are separated by a compartment boundary. The biophysics and dynamics of cell packings in developing epithelium can be described theoretically by vertex models. In such models, the network geometry of adhesive junctions between cells is determined by force balances. The remodeling of the tissue during growth can be accounted for by introducing repeated cell divisions. Cell division leads to local network rearrangements and to topological changes of the network.
The interplay of cell mechanics and cell division also governs the morphology of compartment boundaries in the tissue. These compartment boundaries serve as important organizers for growth and patterning of the tissue. These boundaries define localized sources of morphogens. These are signaling molecules that spread in the tissue and form graded concentration profiles that stimulate cells far from the source.
We discuss the interplay of tissue growth and morphogen patterns and present a general mechanism by which 2-d tissues can self-organize their growth using dynamic morphogen concentration profiles.

Towards predictive quantitative modeling of tissue organization on histological scales: imaging, image analysis and modeling of liver regeneration and tumorigenesis

Dirk Drasdo
Paris

A major challenge is to extend quantitative modeling towards the tissue scale. This is fundamental to understand how cells coordinately behave to establish functional tissue structure. Research in this field suffers from a lack of techniques that permits quantification of tissue architecture and its development. To bridge this gap we have established a procedure based on confocal laser scans, image processing and three-dimensional tissue reconstruction, as well as on quantitative mathematical modeling (Hoehme et. al., 2007; 2010). We illustrate our method by regeneration after toxic liver damage and partial hepatectomy, and by tumor nodule formation in liver. The example of the liver has been chosen, because liver function depends on the complex micro-architecture formed by hepatocytes (the main type of cells in liver) and micro-vessels (sinusoids) that ensures optimal exchange of metabolites between blood and hepatocytes. Our model of regeneration after toxic damage captures hepatocytes and sinusoids of a liver lobule during the regeneration process. Hepatocytes are modeled as individual agents parameterized by measurable biophysical and cell-biological quantities (Drasdo et. al., 2007). Cell migration is mimicked by an equation of motion for each cell subject to cell-cell-, cell-extra-cellular matrix-, and cell-sinusoid-forces, as well as the cell micro-motility. We demonstrate how by iterative application of the above procedure of experiments, image processing and modeling a final model emerged that unambiguously predicted a so far unrecognized order mechanism essential for liver regeneration. A three-dimensional image analysis clearly confirmed the model prediction. We then consider regeneration after partial removal (hepatectomy) of the liver. We show how our model is firstly calibrated with static and dynamic mouse data, and in a second step re-calibrated with only static pig data providing a valid prediction for liver regeneration in pig. This may serve as a first proof-of-concept step to use models of tissue organization to extrapolate from an animal model to patients. In our last example we study how the model may be used to classify the phenotypes of liver tumor nodules by variation of the model parameters.

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[3] Hoehme, S., Hengstler J.G., Brulport M., Schäfer M., Bauer A., Gebhardt R. and Drasdo D. (2007) *Mathematical modelling of liver regeneration after intoxication with CCl4.* Chemico-Biological Interaction, 168, 74-93.

Cytoskeletal networks: mechanics and non-equilibrium effects

Fred MacKintosh
Amsterdam

Much like the bones in our bodies, the cytoskeleton consisting of filamentous proteins largely determines the mechanical response and stability of cells. We review the fundamentals of biopolymer network mechanics and discuss recent advances, both in theoretical modeling of such networks, as well as experiments on reconstituted in vitro acto-myosin networks and on living cells. Unlike passive materials, living cells are kept far out of equilibrium by metabolic processes and energy-consuming molecular motors that generate forces to drive the machinery behind various cellular processes. We describe how such internal force generation by motors can lead to dramatic non-equilibrium effects. We also review the fundamentals of thermal Brownian motion and we contrast this with active fluctuations, as have been reported in recent experiments on living cells.

Continuum modeling of tissue contraction, growth and morphogenesis

Carina Edwards
London

Tissues grow and develop through the coordinated actions of their cells. These actions include growing, contracting and moving, each of which exerts a force on the tissue and contributes to generating the complex structures observed in nature. It is also clear that tissue growth can be directed and altered by externally applied forces, with for example cancers observed to restrict their size in less mechanically permissive environments.

Fundamental to understanding tissue development is finding out how the requisite forces are actively generated or withstood. There is thus a need to integrate mechanical models into our understanding of cell and tissue behaviour. Many approaches are presently being adopted drawing on physical concepts from e.g. fluid dynamics, elasticity theory and plasticity, and ranging in modelling length scale from descriptions of individual cells to whole tissue models. A crucial aspect of this research is developing methodologies for correctly accounting for tissue growth.

This talk will discuss current approaches from a continuum mechanics perspective. I will first introduce models for tissue growth and cellular contractility based on an analogy with thermoelasticity [1]. The talk will then proceed to discuss alternative methodologies for describing mechanically active growing tissues, including a popular methodology based on a decomposition of the deformation gradient tensor [2]. We will additionally address the important concept of residual stress. Finally, we will consider how tissue shapes such as the folded structures observed in the brain [3] and gut [4] can be explained from a perspective of mechanical instability leading to a physical understanding of tissue morphogenesis.

[1] Edwards, C.M. and Schwarz, U.S. (2011) Phys. Rev. Lett., 107(12) 128101.
[2] Lubarda, V.A. and Hoger, A. (2002) Int. J. Solids Struct. 39, 4627-64.
[3] Holfeld, E. and Mahadevan, L. (2011) Phys. Rev. Lett., 106(10) 105702.
[4] Edwards, C.M. and Chapman, S.J. (2007) Bull. Math. Biol. 69, 1927-42.

Green algea as model organisms for biological fluid dynamics

Ray Goldstein
U Cambridge

In the past 6 years the Volvocine green algae, spanning from the unicellular Chlamydomonas to multicellular Volvox, has emerged as a class of model organisms for a number of problems in biological fluid dynamics. These include general issues of propulsion by the action of beating flagella, nutrient uptake by swimming organisms, hydrodynamic interactions mediated by walls, velocity fluctuations and tracer particle statistics in suspensions of swimming organisms, the fluid dynamics and biology of phototaxis, and the incredibly rich and fascinating stochastic dynamics of flagellar synchronization. The utility of this class of organisms derives from the range of sizes they span (from 10 microns to several millimetres), their geometric regularity, the ease with which they can be cultured and the availability of many mutants whose existence allows for connections to be made between molecular details and organism-level behaviour. This talk will provide an overview of these recent developments and highlight promising future directions in the study of biological fluid dynamics and evolutionary biology which can take advantage of these remarkable organisms.

Modeling active particles, membranes and gels

Nir Gov
Weizmann Instiute, Israel

Biologically driven nonequilibrium fluctuations are often characterized by their non-Gaussianity or by an “effective temperature”, which is frequency dependent and higher than the ambient temperature. We address these two measures theoretically by examining a randomly kicked particle, with a variable number of kicking motors, and show how these two indicators of nonequilibrium behavior can contradict. We compare our results with new experiments on shape fluctuations of red-blood cell membranes, and demonstrate how the physical nature of the motors in this system can be revealed using these global measures of nonequilibrium. Furthermore, the concept of the effective temperature is extended to active particles trapped in a potential well. We calculated the average escape time and find that Kramers’ reaction-rate theory holds in this system, under certain condition, but with another “effective temperature”. We calculate the escape time distribution dependence on the distribution of trapping potentials, and can make predictions regarding the random-walk of the tracer particle in the active gel.

Abstracts Posters

Particle based simulation of dense cellular flow in microvessels

Davod Alizadehrad[1,3], Yohsuke Imai[2], Takuji Ishikawa[2], Holger Stark[3] and Takami Yamaguchi[1]

[1]*Department of Biomedical Engineering, Tohoku University, Japan*

[2]*Department of Bioengineering and Robotics, Tohoku University, Japan*

[3]*Institut für Theoretische Physik, Technische Universität Berlin, Germany*

In microvessels, the motion and deformation of RBC play a dominant role in the mechanics of blood flow and mass transport of chemical substances. Red blood cells (RBCs) dynamics and deformation at physiologically relevant hematocrits are more complex and differ from that in a dilute suspension. Experimental techniques still encounter difficulties in tracking RBC in high hematocrit (Hct) conditions owing to opaque images; it is also difficult to create complex networks of circular channels mimicking the in vivo microvasculature. To overcome these problems, we have developed a large-scale parallel simulation of dense cellular flow in microvessels. We employed a particle method, where all blood components were modeled using a finite number of particles. The deformation of RBCs was modeled by a spring network of membrane particles. A domain decomposition method was developed for parallel implementation on distributed memory systems. The accuracy of the developed model was quantitatively investigated. The present method can be used to investigate large scale complex hemodynamics includes the study of blood disease and the design of microfluidic devices for blood diagnosis.

Clustering of vesicles in a parabolic flow

O. Aouane (1,2,4) , H. Selmi (3) , C. Misbah (2) and C. Wagner (1)

1 Dynamics of Fluids, Saarland University, Germany

2 Laboratoire Interdisciplinaire de Physique (LIPhy), Grenoble University, France

3 Laboratoire d'Ingénierie Mathématique (LIM), Ecole Polytechnique de Tunisie (EPT), Tunisia

4 Laboratoire de Magnétisme et Physique des Hautes Energies (LMPHE), Faculté des Sciences de Rabat, Morocco

Blood performs multiple functions in the body, like oxygen, carbon dioxyde and nutrients transfer or body temperature control by heat transfer. The flow properties of blood are complex, in opposite to simple fluids such as water or air. This complexity arises from its inhomogeneous composition: blood is a suspension of different types of blood cells suspended in an aqueous fluid (called plasma). The most common type of blood cells are erythrocytes or red blood cells (RBCs). RBCs tendency to aggregate, also called rouleaux formation, is a normal occurring phenomenon caused by the presence of fibrinogen (a cross-linking protein) in plasma. Our objective is to study the tendency of RBCs to form clusters under a parabolic flow in an unbounded and bounded geometry and under different polymer concentrations. To achieve this, we assumed that the membrane is deformable and incompressible, and we consider the small Reynolds number limit, so that inertial effects may be neglected. The numerical procedure used to solve Stokes equations is based on the boundary integral formulation (BIM) combined with RBC-RBC interaction mechanisms. We proposed a Lennard-Jones potential to reproduce the depletion model introduced by Neu and Meiselman. Furthermore, the fast multipole method (FMM) is used to increase

sensibly the speed up of the calculation by reducing the cost of computing from O(N^2) to O(N).

Mechanics of integrin bonds and integrin-bound cytoskeleton and membrane structures

K. Berghoff[1,2,3], Y. Nakano[3,4], P. Y. W. Dankers[3,4], L.J. van IJzendoorn[2], E.W. Meijer[3,4]and H. Kress[1,2,3]

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Transmembrane proteins like integrins are essential building blocks for fundamental cell processes such as adhesion and signal transduction. Understanding the mechanics of integrin bonds and integrin-bound cytoskeleton and membrane structures will help to understand how integrins fulfill their role as anchors and messengers. We investigate the mechanics of extracellular and intracellular integrin bonds as well as the mechanics of integrin-bound cytoskeleton and membrane structures. We use optical traps to bind functionalized RGD-coated microparticles to fibroblasts and to measure rupture forces of intracellular and extracellular integrin-bonds. By using a combination of high-speed image acquisition and a temporal modulation of the trapping laser, we investigate the viscoelastic properties of the integrin-bound actin network and the integrin-bound cell membrane. Our work provides an experimental basis for testing and improving recent models of cell membrane and cytoskeletal mechanics and will help to improve our understanding of the mechanics of integrins and associated structures.

Circular Ruffle Dynamics on Fibroblast Cells

Erik Bernitt, Julia Strübig, Malte Ohmstede, Pritpal Singh, Cheng-Gee Koh & Hans-Günther Döbereiner

Circular Dorsal Ruffles (CDRs) are ring-like actin-based structures that, in contrast to peripheral ruffles, form at the dorsal side of cells. The biological function of CDRs is still under discussion. CDRs might play a role in endocytotic uptake and cytoskeletal rearrangements. CDRs are a phenomenon that is known to occur, e.g., on fibroblast cells upon growth factor stimulation. Even though this has been known for decades, the underlying mechanisms leading to formation and propagation of these coherent solitary waves are not well understood and it is only recently that models have been published describing CDRs as being based on diffusion reaction processes in the cytosol and at the membrane.

We present data of actin waves on NIH 3T3 fibroblast cells showing that these actin waves lead to different types of ruffle morphology, ranging from flat soliton waves of high wavelengths to barrel-like structures composed of lamellipodia-like walls. The later typically collapses after a few minutes under formation of one ore more endocytotic vesicles. We analyze and discuss the dynamics of these waves with regard to the proposed models for explanation of CDRs.

Understanding temporal and spatial features of polarity establishment

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Cell polarity is crucial for proper development and homeostasis of metazoan organisms. The PAR proteins were discovered in *C. elegans* and subsequently found to be important for cell polarity throughout metazoan evolution. Even though polarity has been studied qualitatively in *C. elegans* embryo using notably forward genetic and RNAi-based functional genomics, how polarity components interact in space and time remains incompletely understood. In order to address this question, we take advantage of the great spatial and temporal resolution offered by the one-cell stage *C. elegans* embryo, acquiring multi-channel time-lapse recordings of this asymmetric division.

To circumventing the inherent drawbacks of manual quantification, we developed an automated image-based quantification algorithm, termed ASSET, that permits the fast and coherent processing of a large number of recordings. Using ASSET, we measure precisely the fluorescence intensities of the posterior GFP-PAR-2 fusion protein to calibrate the rate constants of a reaction-diffusion-advection mathematical model [Goehring et al., Science, 2011] using an evolution strategy. Of particular interest, we infer the mutual inhibition rates of the anterior and posterior polarity complexes, which cannot be determined experimentally.

Ultimately, we aim at applying a systems biology approach to calibrate, challenge and improve our model using quantitative data. We expect this model to correctly predict known mutant behaviors, to provide a framework for further analysis and to uncover general principles of cell polarization.

Dynamics of spheroid formation

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Cellular spheroids – ball-shaped three-dimensional cell clusters with organotypic characteristics - are model systems for tissue growth and tumour formation. They are physiologically more relevant than two-dimensional monolayers and have, therefore,

become an important tool in toxicological studies and drug development (Pampaloni et al., 2007, Nat. Rev. Mol. Cell Biol. 8, 839-45). Spheroids usually form within 24 h, once a sufficient number of cells has been placed at the bottom of a convex non-adhesive well.

The current understanding is that once a spheroid has formed, its size increases through cell divisions occurring in a cell layer at its periphery (Lin and Chang, 2008, Biotech. J. 3, 1172-84). The details of the cellular dynamics during the first 24h that lead to the formation of the spheroid are still studied.

In this presentation, we focus on the formation of spheroids and investigate the process with a combination of live-cell imaging and a mathematical *ab initio* model. Some assumptions of the model are: a) the cells move randomly, b) whenever two cells meet they form a bond with a certain probability, c) cell clusters continue to move randomly, and d) if two cells connected by a bond move apart, the bond breaks with a probability depending on the distance between the cells.

We are able to calculate the formation of spheroids. For certain parameter values we obtain results that match the experimental data, which enables us to draw conclusions about the binding and unbinding properties of the breast cancer cells.

Flagellar synchronization independent of hydrodynamic interactions

*Benjamin M Friedrich, Frank Jülicher

Inspired by the coordinated beating of the flagellar pair of the green algae Chlamydomonas, we study theoretically a simple, mirror-symmetric swimmer, which propels itself at low Reynolds number by a revolving motion of a pair of spheres. We show that perfect synchronization between these two driven spheres can occur due to the motion of the swimmer and local hydrodynamic friction forces.
Hydrodynamic interactions, though crucial for net propulsion, contribute little to synchronization for this free moving swimmer.

*BM Friedrich, F Jülicher, accepted for publication in Phys. Rev. Lett.

Elastic Birod Mechanics applied to DNA Molecules Configurations

Alexandre Grandchamp

We propose to describe DNA mechanics at the base level through an explicit double stranded elastic model: two elastic rods endowed with an interaction potential. This is the Elastic Birod Model. In the same spirit of the continuum Worm-Like-Chain Model, and its discrete versions for single stranded polymers, we investigate the geometrical and mechanical issues of this finer elastic model for DNA molecules configurations. Birod stiffness matrices and shape parameters are delivered from Molecular dynamic simulations, and constant solutions are shown to be helices in the physical space in the homogeneous approximation.

Self-assembly of simple, coarse-grained chiral polymers studied with Langevin dynamics

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Malfunction or disfunction of certain mechanisms along the protein folding pathway may lead to the protein aggregation. The aggregates - some of them called amyloids - are known to accompany several diseases such as Alzheimer disease, Parkinson disease, Hutchinson disease or type II diabetes.
The structure of the amyloid forming protein fibrils is highly ordered and repetitive, typically emerging in the form of twisted ribbons. In this work we propose a simple, coarse-grained numerical model of a chiral polymer and study the morphology and stability of 1 to 3 element clusters obtained in Langevin dynamics simulations depending on the temperature of aggregation or initial twist of the constituting polymers.

Three-dimensional elastic force sensors for live cell investigations

Sören Björn Gutekunst, Christine Selhuber-Unkel

Phagocytosis is of key importance for the functioning of biological systems and tissues. There are still many open questions regarding the forces during the uptake of target cells and particles, such as force distribution, force direction and force magnitude. Furthermore, pathogenic amoebae such as *Acanthamoebae* presumably exert large forces when killing target cells. In order to elucidate the complexity of force generation in different cellular systems and to gain further insight into the underlying processes, we study the forces exerted during the uptake of elastic polyacrylamide beads (EPABs). For measuring forces that are exerted by cells to two-dimensional surface, traction force microscopy is a well-established tool. We now transfer this concept into the third dimension and synthesize fluorescent EPABs by means of inversed emulsion polymerisation. The elasticity of these particles can be changed by varying the amounts of crosslinker between 0.01 % and 10 %. Our goal is to relate changes in particle shape to the forces exerted by cells in a bead deformation assay (BDA). We will in particular use this method to investigate the processes, by which *Acanthamoebae* can kill their target cells. In addition to the BDA, we will also use 2D traction force microscopy to investigate *Acanthamoeba* surface forces during cell movement and target cell killing.

Model and numerical simulations of micro-swimmer suspensions

Levan Jibuti (Universität Bayreuth, Germany)
Philippe Peyla and Salima Rafaï (Liphy – Université Joseph Fourier-Grenoble1, France)

We investigate numerically the rheological and dynamical behavior of a Chlamydomonas micro-swimmer suspension where we experimentally have shown the increase of the effective viscosity of sheared suspensions of live unicellular motile micro-algae compared to the effective viscosity of suspensions containing the same volume fraction of dead cells and a shear thinning behavior [1]. Using our model that reproduces such a dynamics, our numerical simulations show that micro algae, despite their spherical shape contribute significantly to the shear stress and provides a good agreement with the experimental results. The model is also expendable for pusher type micro swimmer suspensions where the opposite effect, the decrease of the effective viscosity of active bacterial suspensions was observed experimentally [2].

[1] S. Rafaï et al, Phys. Rev. Lett. 104, 098102 (2010)
[2] A. Sokolov and I. S. Aranson Phys. Rev. Lett. 103, 148101 (2009)

Different regimes of MDCK tissue growth on soft and hard substrates

S. Kaliman, C. Jayachandran, F. Rehfeldt, A.-S. Smith

Morphogenesis is a process that determines the spatial distribution of cells within a growing tissue. It is key to embryonic development, tissue regeneration and tumor growth. We study the aging effects of tissues by observing their development from single cells to confluent layers.
Thereby, we grow MDCK cell lines on polyacrylamide gels (Youngs modulus ≥ 1 kPa) and glass substrates, all coated with collagen I. Cells were fixed after 6, 12 and 24 hours, as well as every 2 days up to the day 12. Samples were stained for nuclei and actin. Very different regimes of growth are observed as a function of substrate stiffness. On soft substrates, the tissue develops with constant very high density from the onset, whereas on hard substrates, the tissue grows by increasing density in the center of the cluster until a steady state is observed. After several days, significant rearrangement of actin filaments and the deformations of cell nuclei could be quantified.

The interplay between shear and planar cell polarity in the Drosophila wing

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Epithelia are two-dimensional sheets of cells, which often exhibit large-scale patterns of planar cell polarity (PCP) in the tissue plane. Within a single cell, PCP is reflected in an anisotropic distribution of a class of proteins, called PCP proteins. We study PCP in the Drosophila wing epithelium. During development of the fly, two processes are observed: PCP reorients on large scales and a complex flow field reshapes the wing. This flow field includes a stereotypical pattern of tissue shear. We study the influence of tissue shear on PCP on different length scales using different models. On the tissue scale, we characterize PCP reorientation in wild type and mutant wings, which we describe with a simple hydrodynamic model for polar liquids. Our model includes a coupling of PCP to local tissue rotation and local tissue shear as well as local PCP interactions. We find that we can fit stationary states of the hydrodynamic description to adult polarity patterns. These fits suggest that the sign of the coupling of PCP to tissue shear depends on the local expression of PCP proteins. We underpin our findings by numerical solutions of the dynamical equations. On the sub-cellular scale, we develop a vertex model in which cells are polygons and the local organization of PCP proteins is described by variables on all bonds. Within this model, we study the effect of shear on the reorientation of PCP depending on local rules. Using simple shear simulations, we aim to create a hydrodynamic description of vertex model tissue.

Intercellular adhesion orchestrates epithelial mechanical cooperativity

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E-cadherin-based cell–cell adhesions are essential for skin-tissue integrity and function by mediating interactions between cells and modulating adhesion to extracellular-matrix (ECM) molecules. We recently showed that cohesive groups of

differentiated keratinocytes are mechanically coupled and that the force exerted by cell colonies on the ECM is proportional to the colony's geometrical size, not to the number of adhesions formed in the colony. Here, we explore the requirement of E-cadherin-mediated adhesions for the development and formation of collective mechanics in differentiated primary keratinocytes. By measuring traction forces of colonies of live differentiating keratinocytes, we demonstrate that the formation of E-cadherin-based adhesions corresponds to the transition of cell–ECM force from a disorganized arrangement to an organized concentration of force at the colony's periphery. Through genetic or antibody-mediated loss of cadherin expression or function, we show that cadherin-based adhesions are essential for cooperative mechanics. Mechanical coordination between cells is recapitulated in migrating keratinocytes in *ex vivo* epidermal explants and is dependent on myosin-II activity. Finally, a minimal model of elastic, contracting two-dimensional shapes linked to each by springs of different stiffness and coupled to an elastic substrate reproduces the spatial distributions of traction stress observed in our experiments. This work defines the importance of cadherin-based cell–cell adhesions in the mechanical coordination of skin cells and suggests that mechanical regulation is essential for coordinated cell movements during wound healing or stratification in the skin.

Modelling platelet margination in blood flow

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As a response to an injury of a vessel wall platelets bind to the damaged site and build clots to close the opening, and thus stop the bleeding (hemostasis). The platelets must be located near the vessel wall to start the process promptly. For instance, a decrease of hematocrit (volume density of red blood cells) leads to a reduced concentration of platelets near the wall, which may considerably increase the bleeding times [1]. Numerical simulations of blood flow help us to understand this complex process.
Blood flow simulations are performed in two and three dimensions in idealised geometries using the dissipative particle dynamics method. The blood is modelled as a fluid with suspended red blood cells (rbcs) and platelets. The cells are represented by a viscoelastic spring network model [2]. The platelet distribution in flow is investigated depending on the hematocrit, shear rate, shape and deformability of the platelets in order to identify the conditions for their efficient margination as well as wall contact. Furthermore, different mechanisms which are mainly responsible for the platelet margination are characterised.

[1] A. J. Reininger, Haemophilia **14** (Suppl. 5), 11-26, (2008)
[2] D. A. Fedosov, B. Caswell, and G. E. Karniadakis, Biophys. J. **98**, 2215-2225, (2010)

Modelling active transport and spatial-temporal organization of motor proteins along the cytoskeleton

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We present a minimalistic statistical physics approach to the modelling of active transport along the cytoskeleton. Motor proteins move actively through the consumption of chemical energy along a scaffolding of filaments. A process which is important for the internal organization of cells. We use two main ingredients to model this transport process: we model the various complex topologies of the cytoskeleton using concepts from random-graph theory while the active transport of motor proteins is modelled using excluded-volume processes. We present an efficient, flexible and simple mean-field algorithm which allows to study the transport on various scales. This approach is validated using long run simulations on the random graphs. Using this mean field method we can determine the density profile in each segment along the graph which allows to make an indepth study of the stationary transport characteristics on mesoscopic scales using microscopic modelling. With this method we show that motor protein transport along the cytoskeleton contains three different qualitative regimes. At high processivities, irregular graphs develop strong heterogeneities on a network scale and a microscopic description taking into consideration the complex network topology is necessary. When decreasing the processivity or making the graph more regular, these strong heterogeneities disappear. In this regime phase separation can still appear within single filaments. At very low processivities, motor proteins detach so fast and the proteins distribute themselves completely homogeneous along the network.

Swimming contest amongst ellipsoidal three-body swimmers

Jayant Pande, Ana-Suncana Smith

We study a three-body, two-spring model of a micro-swimmer, based on the three-sphere swimmer introduced by Najafi and Golestanian (A. Najafi and R. Golestanian, Physical Review E 69, 062901, 2004). We focus our study on the effect of a change of shape of the bodies on the velocity of the swimmer. Swimmers consisting of spheres, cylindrical capsules and ellipsoids are considered. For constant swimmer volumes and driving forces, we find that the three-sphere swimmer is generally not the fastest one. Depending on the spring stiffness and the fluid viscosity, an optimum ratio of the ellipsoid's axes can be found that maximises the swimmer's speed. The theoretical results are presented in conjunction with numerical simulations based on a combined rigid body and Lattice-Boltzmann framework.

Simulation of Microscopic Swimmers

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We present a 3D simulation of self-driven microorganisms (swimmers) in a fluid in low Reynolds number regimes. The motion of these swimmers is incorporated by consistently coupling our existing lattice Boltzmann based fluid dynamics framework waLBerla (widely applicable Lattice Boltzmann solver from Erlangen) with our rigid body simulation tool *pe*. We model the swimmer by three bodies connected with two damped harmonic springs. Using capsules and spheres we are able to simulate symmetric and asymmetric designs. In order to gain a net movement of the selfdriven microorganism in the highly viscous fluid we apply external sinusoidal driving forces that follow a non-time reversible cycling strategy. In simulations of three-sphere swimmers the resulting propulsion velocity agrees well with theoretical predictions. If some or all spheres are replaced by capsules, we explored that the asymmetry of the design strongly affects the propelling efficiency. Moreover, first simulation runs with two or three swimmers open up the opportunity to investigate hydrodynamic interactions within swarms.

Collective behavior of self-propelled rods: from low to high densities

Masoud Pourmoosa, Thorsten Auth, Kristian Marx, Gerhard Gompper

Collective behavior can be seen in the macroscopic world---for example bird flocks and fish schools---and in microscopic systems such as sperm cells and motility assays. On the microscopic scale, these systems can be simulated using self-propelled rods and Brownian dynamics [1]. The simplicity of the rod model allows to identify universal features in collective behavior also for high rod densities that are computationally more demanding.

We simulate self-propelled rods in two dimensions that consist of beads. The beads interact either by a Lennard-Jones potential or by a Yukawa potential. For very low rod densities and high environmental noise, we find polar and motile clusters using either potential. If we increase the density and decrease the noise, we obtain giant immobile clusters for the Lennard-Jones potential, but motile clusters for the Yukawa potential. As we further increase the density, nematic and smectic phases appear. The system can be characterized by cluster size distribution functions for low densities and by correlation functions for nematic and polar orientation of the rods for high densities. We present simulations at different densities and discuss both approaches to characterize the systems.

[1] Y. Yang, V. Marceau, G. Gompper, Phys. Rev. E 82, 031904 (2010)

Simple and faithful nonlinear field equations for aligning self-propelled rods

Anton Peshkov, Igor S. Aranson, Eric Bertin, Hugues Chate and Francesco Ginelli

We derive a set of minimal and well-behaved nonlinear field equations describing the collective properties of self-propelled rods from a simple microscopic starting point, the Vicsek model with nematic alignment. Analysis of their linear and nonlinear dynamics shows good agreement with the original microscopic model. In particular, we derive an explicit expression for the fronts forming density-segregated, banded solutions, allowing us to develop a more complete analytic picture of the problem at the nonlinear level.

Studying the nanomechanical properties of living cells with the scanning ion conductance microscope

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Living cells are complex mechanical systems and the underlying processes and mechanisms are by far not completely understood yet. Studying the mechanical properties of living cells with nanoscale spatial resolution is therefore of high relevance for the understanding of cell function. However, current imaging techniques for mapping the nanomechanical properties of live cells all have the limitation that they require direct mechanical contact between the probe and the cell, involving the inherent risk of cell damage or probe contamination. Therefore, we developed a method for fast, quantitative, and noncontact mechanical investigation of living cells with sub-micrometer lateral resolution. We applied a hydrostatic pressure to the nanopipette in a scanning ion conductance microscope (SICM) to induce a microfluidic flow in the pipette tip. This flow exerts a localized force and thereby indents the sample. We then quantified the local mechanical properties of the sample using a finite element model. The new method was employed to address a current question in cell mechanics: The role of actin-polymerization and osmotic cell swelling in cell migration. It was found that in migrating fibroblasts both mechanisms are present with a highly variable ratio.

A Mesoscale model for Coarse-grained Protein Dynamics Simulations

Robin Richardson, Oliver Harlen, Daniel Read, Sarah Harris, Robin Oliver

Modeling the dynamics of proteins is a very computationally expensive task. A wide variety of simulation techniques exist, a popular example being Molecular Dynamics. However, these models typically involve detailed simulation of the protein's structure at or near to the atomic level, and as such are unsuitable for modeling many biological entities, in particular molecular motors composed of large protein domains (e.g. Dynein), or systems in which many very large proteins are interacting. This project takes a coarse-graining approach, in which such proteins can be approximated by

finite element meshes parameterized only by their bulk, continuum properties. In this way the evolution of large systems over large time scales can be simulated.

Phase transition and lateral organization of lipid membranes

Sina Sadeghi and Richard Vink

Domain formation in plasma membranes is believed as an important component in many cellular processes and have attracted a lot of experimental and theoretical attention. In the present work, we first consider the main transition in a single-component membrane using computer simulations on the Pink model. We have shown that in the presence of static obstacle the macroscopic phase separation no longer exists and instead we observe a stable multi-domain structure of gel and fluid domains. In the second part, we study the effect of curvature on the lipid compositions in a binary mixture membrane. We find that membrane height fluctuations have a profound effect on the lateral heterogeneity in the membrane.

Laser Ablation on Actomyosin Network

Arnab Saha, Guillaume Salbreux, Frank Julicher, S. W. Grill

The cell cortex is a thin layer beneath the membrane that largely consists of cross-linked actin filaments, non-muscle myosin motor protein and a plethora of actin binding proteins (ABPs). Collective dynamics of myosin on actin meshwork (assembled by ABPs), that converts chemical energy to mechanical work by ATP hydrolysis, generates active contractility at large cellular length scale. Contractility can build up mechanical stress in the actomyosin network of the cortex. Sudden up-or-down regulation of myosin induces spatial inhomogeneity in the stress profile of the actomyosin mesh which finally leads to cortical flow. In order to understand the flow pattern we need to know the stress profile within the mesh as well as the velocity profile of the flow. Here we describe the actomyosin mesh at a coarse grained level as a viscoelastic, active and contractile gel. We develop a two dimensional hydrodynamic model, valid at long length scale and short-to-long time scales, using basic symmetry principle and conservation laws. We then utilize our description to investigate the spatio-temporal dynamics observed after the laser ablation on actomyosin cable during zebrafish epiboly by close comparison between theory and experiment.

Scanning ion conductance microscopy on living cells

Jan Seifert and Tilman E. Schäffer

The scanning ion conductance microscope (SICM) provides a technique to image and study samples in an aqueous, electrolytic environment with high resolution without any mechanical contact between the probe and the sample. This makes this technique perfectly suited for investigations of living cells. We have developed a SICM dedicated specifically to the imaging of living cells, featuring a large scan range and a fast scan speed. A specially designed sample heat stage with closed-loop temperature control allows long-term imaging of living cells with nearly no influence on the imaging process.

Cell division is an important area in current biological and medical research. With the SICM, we were able to image the changing morphology of fibroblasts during cell division with high spatial and temporal resolution. The cell volume, which is an important parameter in cell division, could be determined as a function of time.

Nematic Growth of Microtubules that Changed into Giant Spiral Structure Through Dynamic Ordering

Kazuhiro Shikinaka, Kiyotaka Shigehara, Hiroki Kudoh, Saori Mori, Yoshiki Tamura, Akira Kakugo, Ryuzo Kawamura, Hidemitsu Furukawa, Jian Ping Gong, Hiroyasu Masunaga, Tomomi Masui, Satoshi Koizumi

In a long capillary cell with temperature gradient, tubulin dimers of alpha and beta subunits polymerized according to the preferential polarity, i.e., the anisotropic spiral addition of the dimers to the beta-terminated “plus end” dominated the formation of microtubules. As the result, the helical hollow cylinders generated the oriented nematic liquid crystalline structure with centimeter-length. In the next stage, where microtubules were under the partial polymerization/ depolymerization equilibrium due to the concentration fluctuation, the dynamic rearrangement of microtubules such as their shortening (depolymerization) and subsequent tilting of orientation axis caused the structural change from the oriented nematic liquid crystalline structure to some giant spiral structure which was subjected by the ordered dipole and the helical chirality of microtubules.

Two-Way Diffusion Problems in Stochastic Swimming

Kajetan Sikorski, Peter Kramer, Patrick Underhill

A key observation derived from mean field theories for micro-swimmers is the stability of the uniform isotropic state for pullers vs. its instability for pushers. In experiments and simulations of suspensions of swimmers, orientational correlations are apparent for pushers over much larger spatial scales than for pullers. We study this phenomenon in a simplified system consisting of two hydrodynamically interacting 2D swimmers. A Fokker-Planck equation for the distance and relative angles of these swimmers is derived; it can be classified as a two-way diffusion equation. A Two-way

diffusion problem looks like a heat equation for which the time direction reverses within the domain. These equations have many interesting mathematical properties. An analytical method for obtaining an approximate solution to our problem is described.

Dynamics of active bottom-heavy particles in external fields

Katrin Wolff, Holger Stark

Active particles in external fields have been shown to display alignment and increased sedimentation lengths [1,2]. Here, we investigate self-propelled particles which additionally are bottom-heavy, that is they feel a torque aligning them to swim against the gravitational field. We study their dynamics in an external gravitational field analytically and numerically using Brownian dynamics simulations. For bottom-heavy particles the gravitational field has the two opposite effects of i) sedimentation and ii) upward alignment of the particles' swimming direction. Depending on the gravitational Peclet number \alpha, the active Peclet number Pe and the particle excentricity r_0, we observe either effective sedimentation with increased sedimentation length (compared with the passive case but also the active case without bottom-heaviness) or inversion where particles concentrate at the top of the box. We identify analytically the set of parameters for which these effects compensate such that the steady state density profile is constant in the bulk and for fixed particle properties Pe and r_0 we find the value of \alpha resulting in maximum density inversion.

[1] J. Palacci et al., Phys. Rev. Lett. 105, 088304 (2010)
[2] M. Enculescu and H. Stark, Phys. Rev. Lett. 107, 058301 (2011)

Computer Simulation of Charged Colloids under Alternating Electric Fields

Jiajia Zhou and Friederike Schmid
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We study the dielectric response of spherical charged colloids under alternating electric fields (AC-fields) by mesoscopic simulation methods, accounting in full for hydrodynamic and electrostatic interactions. Specifically, we systematically investigate the effect of frequency and amplitude of the AC-fields, the ionic strength of the solution, and the bare charge of the colloids. A coarse-grained molecular dynamics approach is taken to model the fluids, in which the solvent particles are simulated using Dissipative Particle Dynamics (DPD). The electrostatic interaction between all charges are calculated explicitly using Particle-Particle-Particle Mesh (P3M) method.

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