Modeling and computer simulations of microswimming and bacterial motility

September 17-19, 2007, TU Munich, Garching, Germany.

1) Summary

The workshop addressed various aspects of biological fluid dynamics on a microscale with a focus on mechanisms of swimming at low Reynolds numbers and bacterial motility. It essentially became the first organized event for a new cross-disciplinary research community working on physics of bacterial motility. Many of major theoretical and experimental contributors as well as founders of the field were represented. The workshop confirmed the growing interest to mechanics of bacterial and cellular propulsion over the last years. This interest has been stimulated, in particular, by recent successes in making biomimetic micromachines and advances in computational techniques, which seem to be capable to replace the traditional methods of computational fluid dynamics in studying the motion of active objects at low Reynolds numbers. The new community stated the need for coordinated effort in the theory of microhydrodynamics of active systems and for continuation of series of meetings along these lines.

The workshop took part at the Mechanical Engineering Department of the Technical University of Munich (Garching campus), Germany on September 17-19, 2007. The program of the meeting consisted of 19 invited (45 minutes) and 5 contributed (30 min) talks. The total number of registered participants amounted to 40 including 3 organizers. The participants represented Germany (22 participants), USA (4), France (4), Israel (3), UK (3) as well as Spain, Japan, and Hungary. Several research groups and institutions in Germany were represented at the meeting and took active part in the discussions. In addition to the funding provided by the ESF, which was used for supporting EU participants, the workshop was supported by the CompInt program (Materials Science of Complex Interfaces) of the Excellence Network of Bavaria, which mainly funded the attendance of the US and Israeli scientists.

The discussion topics of the workshop can be grouped into the following main directions:

1) mechanisms of bacterial and cellular propulsion: functioning of flagella, cilia, and lamellipodia, mechanics of body reshaping, hydrodynamic coupling of the moving parts

2) theoretical aspects of biological fluid dynamics: interplay of elasticity and hydrodynamics, motion in viscoelastic media, simulation techniques for microhydrodynamics

3) statistical mechanics of active objects: Langevin theory and simulation of active objects, their dynamic self-organisation, pattern formation and swarming in bacterial colonies, anomalous diffusion of active objects

4) new trends in design of biomimetic micromachines: artificial field-driven flagellar and ciliated swimmers, artificial chemotactic and thermosensitive ratchet systems

5) general theory of swimming at low Reynolds numbers: geometrical and physical foundations of microswimming, performance analysis and optimization of simple microswimmers

2) Description of the scientific content of and discussion at the event

The workshop was dedicated to physics of bacterial motility, which is a cross-disciplinary field by definition. In the program, we tried to cover all the major trends in studying bacterial and cellular motility and design of biomimetic micromachines. The content, therefore, was very diverse. Nevertheless, it is possible to group the presentations along the few main directions. Below, we will describe the content of the five sessions.

The Monday morning session chaired by Dr. V. Lobaskin addressed the *collective phenomena in ensembles of active objects*. The opening talk by Prof. Raymond Goldstein (Cambridge University) gave an overview of collective dynamics of colonies of volvocean green algae, which assemble into a spheroidal shell and use flagellar beating to propel the body and improve food transport by local flows. Although it is established that activity of different cells must follow certain temporal-spatial (phase shift) pattern to produce the maximum effect, little is known about existence of any intercellular interaction. The current model of the organized behaviour assumes the “hardware”-implemented organization, namely the predefined growth of cells with their flagella oriented according to their position on the spheroid so that the flagella of neighbouring cells could take the proper direction and phase shift of the beating cycle. The talk by Prof. Mitsugu Matsushita (Chuo University, Tokyo) overviewed experimental observation of self-organized dynamics and pattern formation in bacterial colonies made by his group. The preliminary explanation of fascinating spatial patterns can be obtained on the basis of reaction-diffusion schemes, where the growth rate in the colony is defined by the balance between the propagation velocity of the colony boundary and the supply rate of nutrients. The talk by Prof. Tamas Vicsek (Budapest University) addressed various observations of collective dynamics and swarming phenomena in groups of animals. One of the main issues addressed in his analysis was the existence and nature of a phase transition between the stochastic motion regime and organized swarms on varying the noise level and concentration of species. The multimedia support of the presentation was impressive as it featured 3D animations of swarming behaviour. The talk by Dr. Udo Erdmann (Helmholtz Association) was dedicated to phenomenological coarse-grained description of active motion using the model of active Brownian particle. This latter model was developed in the late nineties by the statistical physics group at Humboldt University in Berlin lead by Prof. Ebeling with a significant contribution by Dr. Erdmann. Dr. Erdmann has demonstrated in his presentation that the transition between the dynamic regimes of a single active particle can be predicted in terms of the energy balance equation, where the transition from a dissipative to a driven regime occurs on increasing the energy influx rate as compared to the thermal energy, and can be predicted using the information about the concentration of nutrients and the rate of its transformation into mechanical energy of motion. Thus, the main discussions within the session concerned the types of interactions between different active species and their role in reaching the needed collective motion pattern. The consensus was that in most cases no specific interaction were detected and, moreover, no specific interaction was needed to achieve the efficient collective operation. Still, the drive produced by the energy influx always remains the essential property. It was stressed, in particular, that the minimal model of swarming has to include an orienting interaction of hydrodynamic type. For example, the Vicsek model of active motion with orienting local collision kernel resembles the multiparticle collision dynamics (stochastic rotation dynamics) technique developed by Malevanets and Kapral, which is now widely used for modeling hydrodynamic interactions. In such a model, the only interaction between different species comes not via a pair potential but rather via a collision operator that possesses a “shear viscosity”, i.e. suppresses the motions differing from the local average flow direction.

The Monday afternoon session was chaired by Prof. R. Goldstein and included two invited contributions as well as four contributed short talks by younger researchers. The talk by Prof. Ignacio Paganobarraga (University of Barcelona) continued the discussion of collective dynamics of active objects and discussed the modeling opportunities opened with an application of a Lattice-Boltzmann/Langevin dynamics hybrid simulation scheme. In the next invited presentation Prof. Ralf Metzler overviewed the theoretical advances in the statistical analysis of trajectories of active objects and role of anomalous diffusion in various biological functions. He has shown, in particular, that the modern studies deliver us the evidence of both, superdiffusive motion of live objects (the Levy flights) and subdiffusive motion. Depending on the geometry and distribution of the targets (usually food) the optimal search strategies may vary from following a low-dimensional fractal trajectories with Levy flights on fields with the sparse target distribution or exercising long waiting or switching times to permform a more efficient one-dimensional search. The first short talk of the meeting was given by Pawel Romanczuk (HU Berlin) and concerned the numerical modeling of swarming in ensembles of chemotactic bacteria. The two-dimensional simulations were performed using the active Brownian particle model. Various dynamic scenarios including spontaneous transition to circular trajectories and Ostwald ripening scenario were predicted depending on the system parameters. The talk by Dr. Benjamin Friedrich (MPIKS Dresden) addressed the mechanics of flagellar beat and sperm propulsion. A simple model based on the linear elasticity theory was suggested for a beating curved flagellum and for possible mechanisms of switching between different motion patterns by changing the local curvature (stiffness) of the flagellum. The presentation by Dr. Markus Roper (Harvard University) was dedicated to asymptotic methods of studying self-propulsion and justification of underlying physics assumptions. The final talk by Oren Raz (Technion Haifa) dealt with the general solution of the Purcell's three-link swimmer and a derivation of its optimal motion cycle using the geometrical principles. We note here that all of the younger speakers demonstrated their ability for thoughtful and inspired research and bright lecturing style.

The Tuesday morning session chaired by Prof. L. Bocquet featured several contributions on *polymer-based propulsion* as well as presentation of a new synthetic chemotactic system. The first talk by Prof. Jean-Francois Joanny (Institute Curie, Paris) presented a theoretical study of the organized action of cilia. The model discussed the parameters conditioning formation of a metachronal wave in ciliar arrays. It was shown for a one-dimensional array that the phase shift of the beating between the neighbouring cilia, corresponding to their own relaxation times leads to a metachronal wave resulting from an interplay of bending elasticity and the drag produced by the local flow. It was noted, however, that for complete understanding of the ciliar propulsion, a solution of a complete model including hydrodynamic interaction between the cilia is needed. The contribution by Dr. Martin Falcke addressed the propulsion based on polymerization-depolymerization kinetics of actins constituting the lamellipodia of skin cells and lysteria bacterium. The talk by Prof. Frank Jülicher (MPIKS Dresden) addressed the machinery of flagellar beating. One of the central findings reported was the simple model of bending of a multifilament flagellum by molecular motors. It was shown that the flagellum architecture and the ratchet dynamics of the motors provide the inherent symmetry breaking of the flagellum bending and thus a consistency in the direction of swimming. The last talk of the morning session was presented by Prof. Ramin Golestanian (University of Sheffield). He reported about the theory and experiments on asymmetric particles, whose surface on one side is treated with a chemical catalyst. These particles, if placed in a multicomponent medium, would promote a reaction close to the treated part of their surface. If the reaction product corresponds to increasing number of molecules, the treated part of the surface would experience a higher local pressure of the solution. Thus, the particle becomes active as it converts the concentration inhomogeneities into translational motion. It was shown that the motion of these active particles is diffusive at long times but corresponds to a much higher diffusion coefficient as compared to the Stokes-Einstein value. To summarize, the main questions in this session were related to energy transformation and rectification into the mechanical energy of directed motion. A number of new ideas and possibilities of preparing active surfaces were suggested during the discussion, including the use of electrowetting effect, thermophoresis, and diffusiophoresis for propulsion.

The Tuesday afternoon session was chaired by Prof. J.-F. Joanny and dealt with the ways of *computational modeling of self-propelling micromachines*. In the first talk, Prof. Ubbo Felderhof, one of the founders of the field of physics of microswimming, described the theoretical framework and constitutive equations for analysis of animalcules using the point forces. In this framework, the microswimmers are presented by a set of stokeslets so that the solution of the Stokes equation can be replaced by a solution of a linear system relating the forces acting on the stokeslets with their velocities via the mobility (Oseen) tensor. These ideas proved successful in computer simulations and have been used for modeling self-propulsion by a number of researchers including H. Stark, who presented the last contribution of this session, R. Netz and H. Wada, the organizer and author of the final talk of the meeting. The second talk of the session opened a new topic of modeling microscopic fluid dynamics with the explicit solvent models. The lecture was presented by Prof. Dennis Rapaport (Bar-Ilan University), a specialist in molecular dynamics simulation. He demonstrated a few spectacular examples of using molecular dynamics with Lennard-Jones solvent for various problems of fluid dynamics. His demonstration included a Rayleigh-Bernard instability in fluids and a zoo of animalcules propelling themselves with traveling surface waves, jets, or flagellar beat an convinced the audience in usefulness of the direct solvent simulation for microhydrodynamics. The next presentation was delivered by Prof. Eric Lauga (University of California at San Diego), who studied the bacterial motion close to soft surfaces and in viscoelastic media and discussed the new physics originating from these conditions. His talk addressed at once two directions, in which the microhydrodynamics tends to expand. He stressed the importance of both, viscoelasticity and softness of interfaces, for biological fluid dynamics as the blood and cell membranes (endothelium) are far from an ideal Newtonian fluid and smooth no-slip interface. At the same time, he stressed that the adequate theoretical framework for dealing with these conditions is still missing. Examples of creation of artificial biomimetic swimmers and fluid pumping with active magnetic filaments were presented by Dr. Marc Fermigier (ESPCI Paris), who has succeeded recently in producing a flagellar swimmer driven by oscillating magnetic field. The lecturer discussed the possibilities and problems in making microactuators, the limitations of their power and operational frequency. Finally, the last speaker of the day, Prof. Holger Stark (TU Berlin) presented a point-force based computational analysis of propelling efficiency of the artificial flagellated swimmer made by M. Fermigier and coworkers and a study of interplay between hydrodynamic coupling and elasticity of two rotating helical flagella. He stated, in particular, that rigidity of the helices hampers their coupled motion and stresses the importance of accurate treatment of the elasticity of flagella. As a whole, much attention in this session and the discussions was paid to comparative analysis of various computational methods applied to microhydrodynamics. Whereas the stokeslet analysis showed its usefulness for small systems moving in homogeneous incompressible fluids, an explicit molecular dynamics would be more efficient in modeling complex boundary conditions and complex fluids. On the largest scale, simplified solvent models should be used. The ways of microswimmer design and efficiency optimization were also discussed.

The Wednesday morning session was chaired by Prof. R. Netz. The opening talk by Prof Yosi Avron (Technion Haifa) overviewed the geometrical principles of self-propulsion. It was demonstrated that various swimmer properties, such as energy dissipation rate, translation length per motion cycle, the generated thrust force, etc., are optimized using different swimmer parameters and, therefore, these differences have to be taken into account in the design of micromachines. In particular, optimal values of the spiral attack angle for a helical flagellum ranging from 35° to 45° were obtained for all these properties. Besides, an example of an efficient animalcule, dubbed “push-me-pull-you”, consisting of just two spheres with a possibility of volume exchange between them was presented. It was shown, that such a swimmer reaches an optimal performance of all animalcules having the same relative length variation during the motion cycle. The second talk of the day presented by Dr. Igor Kulic (Harvard University) was dedicated to a construction of active systems based on the ratchet principle, such as ring motor made of a supercoiled DNA molecule. The motor is using an inherent asymmetry of elasticity of two DNA strands to rectify the energy of local temperature variation into twirling motion and propulsion. A problem of coupled swimming of two animalcules (the three-point swimmers by Najafi and Golestanian) was considered in the short contributed talk by Dr. Gareth Alexander (Oxford University). Although the study was based on the ready solution of two interacting hydrodynamic dipoles, it represented the first attempt to understand the phenomenology of hydrodynamic coupling of microswimmers and the effect of coupling on their motion. Different regimes of coupled propulsion were predicted, including the attractive head-to-tail motion, parallel, and oscillating motion. Yet another new principle of propulsion based on an interplay of elasticity and hydrodynamics was discussed in the last two lectures. Prof. Joshua Shaevitz (Princeton University) reported on experiments with propulsion of spiroplasma, one of the smallest and simplest bacteria, that propels itself without any cilia or flagella by a mere by body reshaping. An anomalous variation of the propulsion speed of the bacterium was found: at certain conditions the velocity grows with the viscosity of the medium. The theory and modeling by Dr. Hirofumi Wada (TU Munich), who presented the last talk of the day, allowed one to understand the principle of its propulsion, which is based on the propagation of the domain wall that divides the bacterium body into two parts of different helicity. The discussions after the talks indicated that the theoretically predicted optimal value of the angle of attack of the spiroplasma helical body is about 35°, in agreement with the general result by Prof. Avron and with experimental observations. Moreover, a simple model of bulk viscosity was suggested to explain the observations for anomalous dynamics of spiroplasma. This main topics of this session were propulsion using elastic helices, the interaction and motion pattern of coupled swimmers, and reiteration of the problem of treatment of viscoelasticity and optimization of swimming in viscoeleastic media.

3) Assessment of the results and impact of the event on the future direction of the field

As it was stressed by most participants, the workshop became the first international event dedicated to microswimming and theoretical aspects of bacterial motility. It for the first time brought together theorists and experimentalists working on various aspects of bacterial and cellular motility and provided a unique arena for cross-disciplinary discussions. The workshop allowed the new-born community to outline the range of its present interest and competence, to extend the concepts of a biomimetic active system from purely mechanical to chemically active and thermosensitive systems, formulate the priority directions in the microscopic biological fluid dynamics and in studying the principles of self-propulsion. The definitive recommendation of the participants was to continue the meetings on microswimming, motility and active systems in the future.

In more detail, the main outcome of the workshop consists of

- Formulation of theoretical framework for studying propulsion mechanics, efficiency, and design of self-propelling machines on a microscale basing on the point-force hydrodynamics and methods of differential geometry
- Comparative analysis of computational methods used in biological fluid dynamics, presentation of new opportunities and recommendations for numerical research using molecular mechanics with explicit solvent, Langevin dynamics and lattice-Boltzmann methods
- Recognition of importance and formulation of the theoretical approaches needed for treating dynamics of active systems in viscoelastic media within the point force analysis and using explicit solvent models
- Indication of new directions in the design and preparation of self-propelling micromachines using active surfaces: chemically active, driven by electric and magnetic field, as well as temperature and pressure waves
- Establishing contacts and collaborations between experimental and theoretical groups working in the field

Since the works by Purcell in the late seventies, the next major breakthrough in the theory of bacterial motility and propulsion was made in the early nineties. The seminal works by Shapere and Wilczek, who considered the geometrical foundations of microswimming, stimulated a significant theoretical effort, which later resulted in broadening the initial idea and in first attempts to formulate the problem in terms of hydrodynamics. Here one can name the contributions by Felderhof and Jones, Stone and Samuel, who, like Shapere and Wilczek, explored compact objects (spheroids) with surface waves.

A new wave in the study of microswimming was initiated in 2003-04. This wave opened several new directions. On one hand, some progress was reached in understanding of the classical models, such as the Purcell's three-link swimmer. Another direction was related to reformulation of the hydrodynamic problem in terms of point forces instead of surface and volume integrals. The stokeslet/rotlet approximation, such that the swimmers, or animalcules, were represented by a set of stokeslets or rotlets, allows one to use the ready solutions of the Navier-Stokes equation at low Reynolds numbers for small point-like objects. The swimming principles can be studied on a small set of particles, which makes the problem treatable analytically or with a modest numerical effort. The simplest swimmer suggested by Najafi and Golestanian in 2004 consists of just three stokeslets. On a larger scale, the use of stokeslets and rotlets allowed one to attack more compex problems like flagellar and ciliar beating, the dynamic stability and performance of rotating helical flagella, etc. Moreover, the point methods became the basis of more efficient computer-based modeling of microscopic flows, such as in colloidal dynamics. The computer implementation of these ideas includes the treatment of hydrodynamic interactions between the stokeslets via the Rotne-Prager tensors. The *theoretical framework* of solving the problem of animalcule motion has been developed by U. B. Felderhof and others. The audience suggested also the further development of the method by introduction of Green functions for interaction of stokeslets with no-slip walls and Green functions for compressible fluids. In addition to his talk, the power of this method as demonstrated at the workshop by several researchers and thus confirmed its central role for the microcopic fluid dynamics. It was stated that a wide scope of problems can be attacked with this method in the nearest future:

- the hydrodynamic coupling of microswimmers and efficiency of their coupled propulsion
- the dynamic modes of ciliar arrays
- the motion in viscoelastic media

At the same time, while the stokeslet approximation remains the main method for studying small systems of up to few hundred particles and dynamics of a single animalcule, it is unsuitable for modeling collective dynamics of active systems due to unfavourable size scaling of the computational effort. A variety of *simulation methods* was suggested, starting from explicit solvent models to hybrid schemes using lattice-Boltzmann methods for modeling the solvent, which scale linearly with the number of solute particles (animalcules) and therefore, overcome the stokeslet-based methods for large systems. The discussions have shown that the solvent-based methods possess another important advantage: the possibility of inclusion of complex boundary conditions and the solvent viscoeleasticity. In the MD method the slip boundary conditions, soft, surfaces, and *viscoelasticity* (for example, with the Oldroyd-B model) can be easily implemented.

Finally, we stress that the workshop promoted cross-disciplinary contacts between biologists, experimental and theoretical physicists, engineers, and applied mathematicians, which is otherwise difficult in their respective communities. A number of talented young scientists have got the opportunity to present their research, attend the lectures and meet the established scientists in the field. It should be also stressed that the workshop brought together the leading specialists in microhydrodynamics and bacterial motility from several EU countries, USA, Israel, and Japan and thus built a basement for future international collaboration in this field.

4) Final Program

Monday, September 17, 2007
8:50 Welcome
Morning session: Chair V. Lobaskin
9:00 **Ray Goldstein** (Cambridge University)
"Motility, Mixing, and Multicellularity"
9:45 **Mitsugu Matsushita** (Chuo University, Tokyo)
"Colony Formation in Bacteria - Experiments and modeling"
11:00 **Tamás Vicsek** (Budapest University)
"Transition to ordered motion in experiments and models of collective motion"
11:45 **Udo Erdmann** (Helmholz Association)
"Aspects of Swarming Theory with Applications to Bacterial Motion"

Afternoon session: Chair R. Goldstein
14:00 **Ignacio Paganobarraga** (University of Barcelona)
"Dynamic regimes of self propelled particles"
14:45 **Ralf Metzler** (TU München)
"Levy flights and weak ergodicity breaking in stochastic search processes"
16:00 **Pawel Romanczuk** (Humboldt University, Berlin)
"Pattern Formation and Moving Structures in Bacterial Colonies"
16:30 **Benjamin Friedrich** (MPI Physics of Complex Systems, Dresden)
"Sperm swimming and sperm chemotaxis"
17:00 **Marcus Roper** (Harvard University)
"Can asymptotic studies teach us anything about microswimming?"
17:30 **Oren Raz** (Technion Haifa)
"Optimal strokes for Purcell's three-link swimmer"

Tuesday, September 18, 2007
Morning session: Chair L. Bocquet
9:00 **Jean-François Joanny** (Institute Curie, Paris)
"Macroscopic flow and metachronal waves in ana array of cilia"
9:45 **Martin Falcke** (TU Berlin)
"Actin-based motility"
11:00 **Frank Jülicher** (MPI Physics of Complex Systems, Dresden)
"How molecular motors shape the flagellar beat"
11:45 **Ramin Golestanian** (Sheffield University)
"Designing swimmers powered by chemical reactions"

Afternoon session: Chair J.-F. Joanny
14:00 **Ubbo Felderhof** (RWTH Aachen)
"The swimming of animalcules"
14:45 **Dennis Rapaport** (Bar-Ilan University)
"Swimming at the microscale: A molecular dynamics approach"
16:00 **Eric Lauga** (University of California San Diego)
"Low-Re swimming in complex fluids and geometries"

16:45 **Marc Fermigier** (ESPCI Paris)
"Physical models of flagellar and ciliary propulsion: magnetic colloids and elastic filaments."

17:30 **Holger Stark** (TU Berlin)
"Microswimming and fluid transport using artificial flagella"

Wednesday, September 19, 2007

Morning session: Chair R. Netz

9:00 **Yosi Avron** (Technion Haifa)
"Swimming and pumping at low Reynolds numbers"

9:45 **Igor Kulic** (Harvard University)
"Hydrodynamics and mechanics of twirling rings"

11:00 **Gareth Alexander** (Oxford University)
"Two swimmer interactions at low Reynolds number"

11:45 **Joshua Shaevitz** (Princeton University)
"Self-propulsion using whole body undulations: how Spiroplasma move their entire bodies to achieve motility"

12:30 **Hirofumi Wada** (TU München)
"Domain-Wall Motion Model for Bacterial Motility"