
**Stochastic Dynamics: Fundamentals and Applications**

# Nonequilibrium Nanoscale Fluctuations: Single Molecules, Chemical Reactions, and Microfluidics

ESF workshop in Schloss Goldrain, June 25 to 30, 2006

http://www.fhi-berlin.mpg.de/complsys/nano2006/

**Organizers:**

R. Kapral (Toronto)
A. S. Mikhailov (Berlin)
M. Rauscher (Stuttgart)
R. Rigler (Stockholm/Lausanne)

# Scientific Report

## 1. Summary

The workshop brought together theoreticians and experimentalists working on fluctuations in nanoscale nonequilibrium systems. Central topics of contributions were fluctuations in biological networks, chemical reactions, small volumes of simple and complex fluids, e.g., in nano-fluidic systems.

The particular combination of experimentalists and theorists with backgrounds in statistical physics, computer simulation, bio-physics, chemical physics, and physical chemistry created a lively and productive atmosphere. The workshop was particularly successful in bridging boundaries between different communities and initiating new collaborations between scientists in different European countries.

The workshop was attended (apart from the four organizers) by 20 participants from nine countries (17 with affiliations in the EU), of which seven were experimentalists and 13 theoreticians. 15 invited and 7 contributed talks were given and sufficient time for intensive informal discussions between the participants has been provided.

## 2. Scientific content and discussions

The aim of this small workshop was to intensify scientific contacts between several groups of scientists, working on single macromolecules and molecular machines, chemical reactions, nonequilibrium processes in soft matter systems and hydrodynamics on very small spatial scales. In all these systems, nonequilibrium nanoscale fluctuations play an important role, but their effects and methods of their description are different. The functioning of a biological cell involves all these systems and processes and, therefore, contacts and collaborations between the respective groups of scientists are important. Moreover, similar problems are encountered in studies of microfluidic chemical reactors, which are being now constructed.

Soft objects, e.g., actin filaments, DNA molecules, and lipid membranes, immersed in a flowing and fluctuating medium are ubiquitous not only in biological systems. Theoretical (theory and simulation) as well as experimental approaches to polymers and membranes in flow were presented and the influence on their conformation and migration properties were discussed. Objects in bulk fluids as well as in confined geometries down to nano-channels were considered experimentally and theoretically. Techniques to monitor the interaction of objects with membranes were presented.

Physical properties of single macromolecules and molecular machines have been discussed in the talks by R. Rigler, A.S. Mikhailov, K. Hassler, H.-Ph. Lerch and P. Gaspard. Molecular machines, including enzymes, are the key building blocks in any biological cell. Discussed were the role of molecular machines and their inherent time scales and noise in intracellular signal processing cascades, design principles, and their non-equilibrium statistical dynamics. Experimental techniques which allow to analyze the fluctuation dominated properties of single molecular machines and reaction networks and their working in living cells (e.g., in chemotaxis), as well as the theoretical models, were presented. Chemical reactions and processes, involving small numbers of molecules, have been considered in the talks by T. Shibata, P. Gaspard, M. Malek-Mansour, G. Wurpel, P. Rein ten Wolde, Y. Togashi, T. Sakaue, and C. Beta.

Hydrodynamical effects are important, when properties of individual macromolecules in aqueous solutions and interactions between such molecules are considered. In the talks by R. Kapral, J. Yeomans, A. Archer and W. Zimmermann, such effects were considered in the framework of different theoretical approaches. Experiments, using microfluidic setups, have been reported in the talks by Th. Pfohl, H. Evans and C. Beta.

Nonequilibrium nanoscale systems with combustion were considered by F. Baras. In the talk by G. Rückner, chemically powered nanomotors were theoretically analyzed. A detailed analysis of nanoscale hydrodynamic fluctuations has been performed in the talk by M. Rauscher.

# 3. Results and impact

This workshop has provided an opportunity to review progress in theoretical and experimental studies of nonequilibrium nanoscale systems at the European level. The speakers represented the major European research centers, such as the Oxford University, the Free University of Brussels, the Dutch FOM Institute for Atomic and Molecular Physics, the Swiss Federal Institute of Technology (Lausanne), the Karolinska Institute in Sweden, three leading Max Planck Institutes from Germany, and the universities of Dijon (France) and Bayreuth (Germany). Active participation of Japanese scientists, representing universities of Kyoto and Hiroshima, should also be noted.

The scientific fields of soft matter studies, nonequilibrium chemical kinetics and hydrodynamics have been so far developing independently and only little interaction between them has been present. It is a success of this workshop that the groups working in such diverse fields were brought together and have actively participated in the discussions involving all these topics. Combining the efforts of different scientists, a coherent and clear picture of nonequilbrium nanoscale processes can be reached.

The presence of strong fluctuations is an intrinsic property of nonequilibrium processes that take place on nanoscales and, therefore, inclusion of this workshop in the ESF programme on applications of stochastic dynamics was fully justified.

The meeting represented a good combination of experienced scientists, giving invited talks, and young researchers. Almost all young researches could give contributed oral presentations and have actively participated. The workshop has therefore contributed substantially to the training of young European scientists.

An evidence of the success of this workshop is that its organizers have received a special invitation from the World Scientific Publishing Company (Singapore), expressing strong interest in the publication of its proceedings. The participants has agreed to continue scientific contacts and to consider organization of similar meetings in the future.

The Cultural and Educational Center of the Vinschgau region of Italy, located in the castle of Goldrain and hosting the workshop, has provided an efficient organizational support to this meeting. Both the conference facilities and the accommodation were excellent. We can recommend this conference center as a location of further ESF meetings.

# 4. Final program

See the attached book of abstracts as it is published on the website and as it was handed out to the participants.

Prof. R. Blossey had to cancel his attendance because of an illness of a family member. Prof. M. Bonn, who also could not attend, was replaced by his coworker Dr. George W.H. Wurpel from Amsterdam.


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# Conference Program and Abstracts

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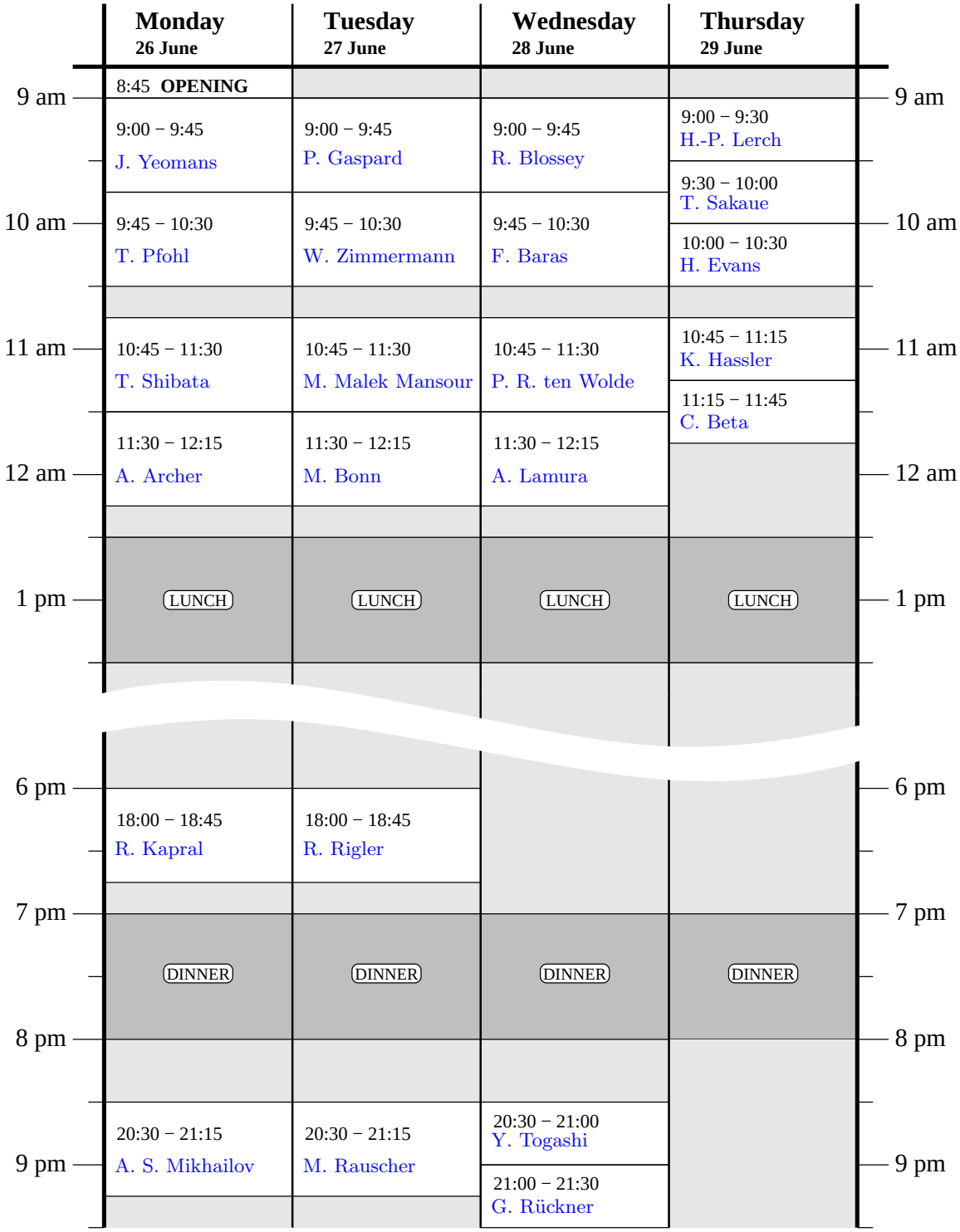
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# 2 Abstracts

## 2.1 Monday, June 26

### 2.1.1 Morning session

9:00—9:45 J. Yeomans

### Mesoscale Modelling of Biophysical Systems

Julia Yeomans

The Rudolf Peierls Centre for Theoretical Physics, 1 Keble Road, Oxford, OX1 3NP, England

We discuss ways in which mesoscale modelling approaches, such as the lattice Boltzmann algorithm, stochastic rotation dynamics, or using the Oseen tensor, can be applied to biophysical problems where hydrodynamics is relevant.

We first consider the dynamics of polymers moving in confined geometries. In particular we discuss how biopolymers pack into and eject from viral capsids, demonstrating that both equilibrium and non-equilibrium effects are important.

We also model low Reynolds number swimmers, investigating the applicability of the different numerical approaches, and present recent results on how the hydrodynamic interactions between swimmers affects their motion.

9:45—10:30 T. Pfohl

### Actin in Microfluidic Environment: From Single Filaments to Bundles and Networks

Thomas Pfohl

Max-Planck-Institut für Dynamik und Selbstorganisation, Bunsenstraße 10, D-37073 Göttingen, Germany

The protein actin is one of the most abundant building blocks of the cytoskeleton. Deeper fundamental insights into the structural and functional properties of this fibrous protein are essential for a further understanding of cellular mechanics and processes. As a principle tool for the manipulation and analysis of single biomacromolecules, we use microfluidics to take advantage of the small-scale controllability and the possibility to mimic physical as well as chemical conditions of physiological

systems in a discriminating manner. This technique proves to be well suited for investigations of single actin filaments as well as for in situ studies of the self-assembly of actin filaments into bundles and networks.

We are able to mimic the natural environment of actin filaments that, in a cell, are embedded in a tight network of fibrous cytoskeletal proteins. Analyzing the fluctuations of single actin filaments under the influence of confinement in terms of tangent correlation functions, radial distribution functions, and segment distributions yields a thorough characterization of the properties and mechanics of the system. The behavior of single filaments depends strongly on their contour length as well as on the degree of confinement, which is determined by the dimensions and the geometry of the microfluidic environment.

The fluctuations and extension of single actin filaments in elogational flow can be observed using a microfluidic hydrodynamic focusing device. Moreover, a concurrent addition of intra-chain linker molecules allows for the study of non-equilibrium dynamics of actin bundling and network formation on the level of individual macromolecules. A detailed analysis of the fluctuations of the formed bundles and networks provides insights into their stiffness and mechanical properties depending on the number of interlinked actin filaments.

10:45—11:30 T. Shibata

## Stochastic signal processing in living cells

Tatsuo Shibata

Department of Mathematical and Life Sciences, Hiroshima University, 1-3-1, Kagamiyama, Higashi-Hiroshima, 739-8526, Japan

Living cells can sense and respond to environmental signals through the dynamic processes of molecular machines such as molecular sensors, signal transducer, and molecular motors. Recent progress in single-molecule analysis has been revealing the stochastic nature of the molecular machines in eukaryotic cells. Thus, living cells is considered as stochastically-operating bimolecular computation systems. The chemotactic cell Dyctostelium can detect chemoattractant gradients that differ by as little as 2% between the front and the back of the cell. Stochastic fluctuations involving in the signaling process may have strong influence on the chemotaxis. Here, we study a stochastic model of chemotactic signaling in order to discuss quantitatively the propagation of signal and noise along transmembrane signaling processes. Our theoretical result on the accuracy of chemotaxis shows good agreement with experimental results.

11:30—12:15 A. Archer

## Dynamical density functional theory for colloidal fluids

Andrew Archer

H.H. Wills Physics Laboratory, University of Bristol, Bristol, BS8 1TL, UK

The dynamical density functional theory (DDFT) of Marconi and Tarazona [*J. Chem. Phys.*, **110**, 8032 (1999)] has been applied by a number of authors in the last few years to various colloid dynamical phenomena such as sedimentation and phase separation in confinement. Where comparison with Brownian dynamics simulation results has been made, the theory seems to be remarkably accurate. In my talk, I will outline the basis of the DDFT and the realm of its applicability. I will also show results for when the DDFT is applied to a number of model colloidal systems. I will also discuss recent efforts to construct a DDFT for atomic liquids.

### 2.1.2 Evening session

18:00—10:45 R. Kapral

## Reaction-Diffusion Dynamics in Crowded Geometries

Raymond Kapral and Kay Tucci*

Chemical Physics Theory Group, Department of Chemistry, University of Toronto, Toronto, ON M5S 3H6 Canada

Reaction dynamics often occurs in media with obstacles or complex geometries. Examples include reactions in porous media and in the cell. For biochemical reactions in the cell one has the additional feature that the relevant space scales are mesoscopic and fluctuations can play an important role. The talk will describe how mesoscopic models for simple examples of reaction-diffusion dynamics can be constructed to study the effects of crowding on the reaction kinetics. The mesoscopic modelling is based on an extension of multi-particle collision dynamics to reacting systems. The modifications of the chemical reaction rate and diffusion constants arising from crowding will be discussed. An extension of the model, which combines multi-particle collision dynamics with a birth-death description of reactions and allows one to study more complex reacting systems, will also be described.

* SUMA-CeSiMo, Universidad de Los Andes, Merida 5101, Venezuela

20:30—21:15 A. Mikhailov

## Relaxation phenomena in complex elastic networks and design principles of molecular machines

Alexander S. Mikhailov

Fritz-Haber-Institute, Abteilung Physikalische Chemie, Faradayweg 4–6, D-14195 Berlin, Germany

Molecular machines play a fundamental role in biology and construction of similar artificial nanodevices is a major challenge. Slow conformational motions in proteins, essential for their functions, can be described by models of elastic networks. We show that random elastic networks lack properties needed for machine operation. However, special complex elastic networks with soft modes can be constructed by evolutionary optimization. In contrast to random networks, relaxation proceeds there along a unique attractive path in the conformational space approached from various initial conditions. Such networks may undergo large-scale motions without strong internal strains and behave as consisting of rigid blocks connected by flexible joints. They respond by well-defined internal motions to energetic perturbations and can be viewed as prototypes of molecular machines. An example of a constructed elastic network, operating as a stochastic cyclic machine with robust hinge motions powered by binding a ligand, is presented.

## 2.2 Tuesday, June 27

### 2.2.1 Morning session

9:00—9:45 P. Gaspard

### Nonequilibrium Nanosystems

Pierre Gaspard

Université Libre de Bruxelles, Interdisciplinary Center for Nonlinear Phenomena and Complex Systems & Service de Physique Non-Linéaire and Méchanique Statistique, Brussels, Belgium

Many nanosystems are important because they are driven out of equilibrium. Because of their small sizes, their thermodynamic properties are affected by the molecular fluctuations. Several examples of nonequilibrium nanosystems are presented:

(1) Sliding carbon nanotubes where friction already manifests itself;

(2) F1-ATPase molecular rotary motor;

(3) Nonequilibrium chemical clocks.

Finally, it is shown how a fluctuation theorem for currents can be applied to nonequilibrium nanosystems.

**References:**

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J. Servantie and P. Gaspard, Methods of calculation of a friction coefficient: Application to the nanotubes, Physical Review Letters 91 (2003) 185503 (4 pages)

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D. Andrieux and P. Gaspard, Fluctuation theorem and Onsager reciprocity relations, Journal of Chemical Physics 121 (2004) 6167-6174.

D. Andrieux and P. Gaspard, Fluctuation theorem for transport in mesoscopic systems, Journal of Statistical Mechanics: Theory and Experiment (2006) P01011 (23 pages).

D. Andrieux and P. Gaspard, Fluctuation theorems and the nonequilibrium thermodynamics of molecular motors, Physical Review E (2006).

9:45—10:30 W. Zimmermann

## Cross-streamline migration and oscillation of bead spring models in simple flows

W. Zimmermann

Universität Bayreuth, LS Theoretische Physik Ia, Bayreuth, Germany

It is discussed that deformable objects like bead spring models or vesicles may migrate perpendicular to the parallel flow lines in the case of nonlinear shear gradients as in Poiseuille flow. It is also shown, that small spheres, which are held by linear springs in a low Reynolds number shear flow at neighboring locactions may oscillate due to the hydrodynamics interaction between the beads.

10:45—11:30 M. Malek Mansour

## Hydrodynamic description of the adiabatic piston

M. Malek Mansour* and F. Baras**

* Centre for Nonlinear Phenomena and Complex Systems Université Libre de Bruxelles, Campus Plaine, C.P. 231, 1050 Brussels, Belgium

** Laboratoire de Recherches sur la Réactivité des Solides, UMR 5613 CNRS-Université de Bourgogne - BP 47870, 21078 Dijon Cedex, France

Consider an isolated cylinder with two compartments, separated by a piston. The piston is free to move without friction along the axis of the cylinder and it has a zero heat conductivity, hence its designation as the *adiabatic piston*. This construction,

first introduced by Callen in late fifties, became widely known after Feynman discussed it in his famous lecture series. Until recently it was generally believed that the adiabatic piston problem was beyond the realm of macroscopic physics and could only be addressed through microscopic approaches, such as the kinetic theory. In this talk we will show that standard hydrodynamics described perfectly well the first stage of the evolution of the piston. Molecular dynamic simulations are used as a guideline to build a simple macroscopic theory with progressively increasing levels of sophistication, leading finally to a closed piston equation of motion. We will then show that this equation describes very accurately the motion of a heavy piston from an arbitrary initial state up to the final mechanical equilibrium state.

11:30—12:15 M. Bonn

## DNA interactions with lipid surfaces

George W.H. Wurpel, Mischa Bonn

FOM Institute for Atomic and Molecular Physics [AMOLF], Kruislaan 407
Amsterdam, The Netherlands

We demonstrate a novel method for extremely sensitive detection of DNA using nonlinear spectroscopic techniques. The technique relies on changes in the water structure at the air/water interface due to binding of the DNA onto interfacial cationic lipids. Cationic lipids (CL) are widely used as in vitro DNA transfection vectors and show promise as nonviral carriers for in vivo gene therapy. Understanding and ultimately controlling the electrostatic interactions between these lipids and DNA is therefore essential to optimize these genetic carriers.

Here, we show how non-linear vibrational surface spectroscopy can be used to sensitively detect the binding of DNA to a monolayer of cationic lipids. This spectroscopic technique provides surface specific, molecular information. Simultaneously, it provides direct information on the surface charge. These measurements reveal that complete shielding of the electric charges of a monolayer of CL occurs in the presence of sub-picomolar concentrations of DNA. We discuss possible applications for DNA sensing and implications for DNA transfection.

### 2.2.2 Evening session

18:00—18:45 H. Rigler

## Non equilibrium single molecule enzyme catalysis

R. Rigler

Karolinska Institute and Swiss Federal Institute of Technology Lausanne

20:30—21:15 M. Rauscher

## Thin film dynamics influenced by thermal fluctuations

Markus Rauscher

Max-Planck-Institut für Metallforschung, Heisenbergstr. 3, 70569 Stuttgart, Germany and

Institut für Theoretische und Angewandte Physik, Universität Stuttgart, Germany

Thermal noise becomes more and more important the smaller a system is. Recent studies of thin film evolution indicate that thermal noise might influence characteristic time-scales of film dewetting. Up to now, thin film flow was only studied with deterministic equations.

We develop a stochastic version of the thin film equation. In the thin film approximation, the stochastic incompressible hydrodynamic equations [Landau and Lifshitz, Vol. IV] reduce to the deterministic thin film equation plus a conserved noise term. We show that the noise term is consistent with the thermodynamical equilibrium distribution of the film thickness.

With numerical solutions of the stochastic thin film equation we show, that thermal fluctuations significantly influence the time scales of dewetting. We also find clear indications for thermal fluctuations in the early linear regime of spinodal dewetting.

## 2.3 Wednesday, June 28

### 2.3.1 Morning session

9:00—9:45 R. Blossey

### A Compositional Approach to the Stochastic Dynamics of Gene Networks

Ralf Blossey[1], Luca Cardelli[2], and Andrew Phillips[2]

[1] Interdisciplinary Research Institute, Villeneuve d'Ascq, France

[2] Microsoft Research, Cambridge, United Kingdom

We propose a compositional approach to the dynamics of gene regulatory networks based on the stochastic À-calculus, and develop a representation of gene network elements which can be used to build complex circuits in a transparent and efficient way. To demonstrate the power of the approach we apply it to several artificial networks, such as the repressilator and combinatorial gene circuits first studied in Combinatorial Synthesis of Genetic Networks. For two examples of the latter systems, we point out how the topology of the circuits and the interplay of the stochastic gate interactions influence the circuit behavior. Our approach may be useful for the testing of biological mechanisms proposed to explain the experimentally observed circuit dynamics.

9:45—10:30 F. Baras

### Fluctuations in Combustion Synthesis

F. Baras* and M. Malek Mansour**

* Laboratoire de Recherches sur la Réactivité des Solides UMR 5613 CNRS-Université de Bourgogne - BP 47870 21078 Dijon Cedex, France

** Centre for Nonlinear Phenomena and Complex Systems Université Libre de Bruxelles, Campus Plaine, C.P. 231 1050 Brussels, Belgium

In this talk we illustrate the dominant role played by fluctuations in the synthesis of intermetallic products. The reactive material is a solid powder formed by particles (grains) of different size, ranging from $1\,\mu m$ to $500\,\mu m$. The grains are made of pure metallic nano-crystallites. The solid powder is densified to form a compact sample of about 2 $cm$ long which is subsequently used in the experiment.

The reactive process is highly exothermic and involves two metals $A$ and $B$. The final product is an intermetallic nano-structured solid $AB$. The reaction is initiated by heating one edge of the sample which then leads to a self-propagating reaction front throughout the system. Using a digital high-speed microscopic video recording device, it is possible to follow the progress of the reaction front and to analyze the instantaneous structure of the associated heat wave quite accurately, the time and space resolutions being of about $10^{-3}\,s$ and $1.7\,\mu m$, respectively. This visualization technique allows to detect new phenomena such as *scintillating waves* which have no analog in the macroscopic description. We will show that the complexity observed experimentally arises from the coupling between the propagation of the exothermic reaction front and physico-chemical processes directly related to the micro-metric character of the reactive particles.

For this kind of micro-heterogeneous material, the width of the reaction front covers only a few grain diameters. As a consequence, the characteristic time of heat transfer between grains may becomes larger than the intrinsic time scale of the reaction, so that the system behaves basically as a lattice of weakly coupled micro-reactors. The reaction front thus propagates with a *relay-rice mode of combustion*. We have developed a mesoscopic description of this particular mode of combustion which allows to study the role of the various system parameters on the evolution of the reaction front. In particular, we will show that thermal fluctuations give rise to spontaneous random ignitions and that the variability of the initial composition of the particles leads to a strong deformation of the front shape.

To analyze the properties of the final intermetallic product, we study the behavior of an individual grain when it experiences a temperature rise due to the propagation of the heat front. Using a "mean-field" approach, we investigate the effect of various parameters such as the initial grain size and the heat of the reaction on the development of the global reactive process. This modeling proves to be quite helpful for interpreting the experimental observations and for understanding the micro-structural properties of the final material.

10:45—11:30 P. R. ten Wolde

## Noise propagation in biochemical networks

Pieter Rein ten Wolde

FOM-Institute AMOLF, Kruislaan 407, 1098 SJ Amsterdam, The Netherlands

Biochemical networks are the analog computers of life. They allow the cell to perform a large number of computational tasks in a manner analogous to electronic

circuits. However, their design principles are markedly different. In particular, biochemical networks process information in a stochastic manner. We use a combination of database analyses, computer simulations and theory in order to elucidate the design principles that allow biochemical networks to process information reliably in the presence of biochemical noise.

11:30—12:15 A. Lamura

## Hydrodynamic Effects on Closed Membranes in Shear Flow

A. Lamura[a] and G. Gompper [b]

[a] Istituto Applicazioni Calcolo, CNR, Sezione di Bari, Via Amendola 122/D, 70126 Bari, Italy

[b] Institut fuer Festkoerperforschung, Forschungszentrum Juelich, 52425 Juelich, Germany

Understanding dynamical properties of membranes and vesicles in shear flow is important for both basic research and biological applications. In this presentation we will show some preliminary results for the study of shear flow effects on two-dimensional vesicles. We consider a single vesicle whose dynamics is described by Molecular Simulation. It is embedded in a solvent which is modeled at a mesoscopic level through multi-particle collision dynamics which conserves mass, momentum, and energy. Solvent particles undergo bounce-back collisions with the vesicle. Thermal fluctuations of the solvent and of the membrane are consistently taken into account. We will focus our attention on two aspects: The deformation and alignment of the vesicle in flow as a function of the shear rate and the hydrodynamic effects on the spectrum of fluctuations of the membrane.

### 2.3.2 Evening session

20:30—21:00 Y. Togashi

## Synchronization and spatiotemporal patterns enhanced by fluctuations in an array of allosteric enzymes

Yuichi Togashi, Vanessa Casagrande, Alexander S. Mikhailov

Fritz-Haber-Institute, Abteilung Physikalische Chemie, Faradayweg 4–6, D-14195 Berlin, Germany

We study spatiotemporal pattern formation in a reaction-diffusion system with allosteric enzymes. Each enzyme is modeled as a cyclic machine, releasing a diffusible product at a certain point; the product promotes initiation of the cycle [1]. In the continuum limit, the system is described by reaction-diffusion equations with delay terms.

To investigate effects of fluctuations, we adopt stochastic simulations. There are two major sources of fluctuation: the conformation of each enzyme fluctuates individually and thus disperses the cycle time (intramolecular fluctuation); stochastic attachment and detachment of a low density of molecules varies the waiting time (intermolecular fluctuation).

We observe spatiotemporal patterns such as traveling waves or spirals as well as uniform oscillations, both in the continuum limit and stochastic simulations. Within some parameter regions, however, effects of fluctuations are significant. Intermolecular fluctuations may even reinforce synchronization of the enzymes and induce patterns not seen with the corresponding reaction-diffusion equations, while intramolecular fluctuations just disturb synchronization.

[1] P. Stange, A. S. Mikhailov, and B. Hess, J. Phys. Chem. B 102, 6273 (1998).

21:00—21:30 G. Rückner

## Chemically Powered Nanomotors

Gunnar Rückner and Raymond Kapral

Chemical Physics Theory Group, Department of Chemistry, University of Toronto, Toronto, ON M5S 3H6 Canada

Molecular motors play important roles in transport in biological systems. These molecular machines operate in the regime of low Reynolds number hydrodynamics. Recently a class of simple inorganic molecular motors has been constructed and studied experimentally [1,2]. These motors are bimetallic rods, one end of which is chemically active. The talk will describe simple mesoscopic models for the motion of such nanomotors. Our model motor consists of two linked spheres, one of which catalyzes the conversion between two chemical species. These species interact differently with the other sphere in the linked pair. The nanomotor is solvated by a mesoscopic solvent whose evolution is governed by multi-particle collision dynamics. The system conserves mass, momentum and energy so that coupling between the nanomotor and the hydrodynamic modes of the solvent is treated correctly. The simulations allow one to explore the mechanisms of the chemically powered motion and the effects of fluctuations on the motor dynamics.

[1] W. F. Paxton, K. C. Kistler, C. C. Olmeda, A. Sen, S. K. St. Angelo, Y. Cao, T. E. Mallouk, P. E. Lammert, and V. H. Crespi, "Catalytic Nanomotors: Autonomous Movement of Striped Nanorods", J. Am. Chem. Soc. (JACS), 126 (41), 13424 (2004).

[2] S. Fournier-Bidoz, A. C. Arsenault, I. Manners and G. A. Ozin, "Synthetic Self-Propelled Nanorotors", Chem. Commun., (4), 441 (2005).

## 2.4 Thursday, June 29

### 2.4.1 Morning session

9:00—9:30 Lerch

### Functional conformational motions in single-enzyme kinetics

Hans-Philipp Lerch, Rudolf Rigler, and Alexander S. Mikhailov

Fritz-Haber-Institute, Abteilung Physikalische Chemie, Faradayweg 4–6, D-14195 Berlin, Germany

The classical biochemical description of enzymatic reactions, the Michaelis-Menten law, is based on the picture of transitions between discrete states. Michaelis-Menten kinetics has been used to describe experiments averaging over large ensembles of molecules and in time. Application to single molecules leads to the description of the transitions between the discrete chemical states as probability rates.

Recent progress in experimental techniques, involving measurements of the activity of single enzyme molecules, and time-resolved experiments employing x-ray diffraction or NMR techniques lead to a new way of theoretical understanding the functioning of enzymes, including the intramolecular dynamics of proteins. We will consider here two models based on the concept of conformational relaxation for horseradish peroxidase. In the simplest model, only one path leading to the release of product is present. In contrast to this, two different catalytic paths are possible in the second considered model. If a cycle is started from an active state, immediately after the previous product release, it follows a different conformational route and is much shorter. Our numerical investigations show that both models generate non-Markovian molecular statistics in contrast to the standardMichaelis-Menten mechanism. However, their memory landscapes and distributions of cycle times are significantly different. The memory landscape of the double-path model bears strong similarity to the recent experimental data for horseradish peroxidase.

Reexamining single-molecule microscopy experimental data of cholesterol oxidase, we find that the existing Michaelis-Menten models with dynamical disorder cannot explain strong correlations between subsequent turnover cycles revealed in the diagonal feature in the joint statistical distribution of adjacent on-times of this enzyme. We suggest that functional conformational motions representing ordered sequences of transitions between a set of conformational substates are involved, along with equilibrium conformational fluctuations in the turnover cycle of cholesterol oxidase. A two-channel model of single-enzyme dynamics, including a slow functional conformational motion in one of the channels, is proposed that allows us to reproduce such strong correlations.

Finally, statistical tools will be considered to identify the fingerprint of functional conformational motions in the time series of single-enzyme microscopy experiments. Besides the memory landscaspe, which expresses the deviation from the Markov assumption, the difference distribution of on-times, which gives the non-Markovian part of the joint probability distribution of adjacent on-times, can also be used for this purpose.

9:30—10:00 T. Sakaue

## DNA electrophoresis in designed nano-channels

Takahiro Sakaue

Yukawa Institute for Theoretical Physics, Kyoto University, Kyoto, Japan

We present a simple description on the electrophoretic dynamics of polyelectrolytes going through designed channels with narrow constrictions of slit geometry. By analyzing rheological behaviours of the stuck chain, which is coupled to the effect of solvent flow, three critical electric fields (permeation field $E^{(per)} \sim N^{-1}$, deformation field $E^{(def)} \sim N^{-3/5}$ and injection field $E^{(inj)} \simeq N^0$, with $N$ polymerization index) are clarified. Between $E^{(per)}$ and $E^{(inj)}$, the chain migration is dictated by the driven activation process. In particular, at $E > E^{(def)}$, the stuck chain at the slit entrance is strongly deformed, which enhances the rate of the permeation. From these observations, electrophoretic mobility at a given electric field is deduced, which shows non-monotonic dependence on $N$. For long enough chains, mobility increases with $N$, in good agreement with experiments. An abrupt change in the electrophoretic flow at a threshold electric field is formally regarded as a nonequilibrium phase transition.

As a related topic, we also make some remarks on the fundamental nature of confined polymers.

10:00—10:30 H. Evans

## Fundamental Investigations of the Blood Clotting Protein Fibrin in Microfluidic Channels

Heather Evans, Sarah Köster, Thomas Pfohl

Max-Planck-Institut für Dynamik und Selbstorganisation, Bunsenstraße 10, D-37073 Göttingen, Germany

Fibrin is a prominent protein in the complex process of hemostasis, or blood clotting. This protein and its constituents have also been implicated in a variety of illnesses such as artherosclerosis, cancer, and multiple sclerosis. Despite major advances in molecular models of fibrin (i.e. high resolution x-ray diffraction), leading experts in the field confess that much remains to be understood regarding various properties of fibrin bundles, in particular mechanical properties as they relate to fibrin's physiological functions. Fibrin is formed via a complex biochemical pathway, but fortunately the system can be simplified to two major components, namely the monomeric protein fibrinogen and the enzyme thrombin, which selectively cleaves fibrinogen in order to induce bundling and subsequent three-dimensional biomolecular network formation.

Our studies aim to elucidate mechanisms of fibrin assembly while utilizing the spatiotemporal resolution and confinement induced by microfluidic structures, not to mention the ability to conduct in situ studies in ambient and physiologically relevant conditions. In our experimental system, formation of fibrin can be carefully controlled by adjusting parameters such as monomer and enzyme concentrations, flow rate, and channel geometry. We chiefly use hydrodynamic focusing within the microfluidic channels. This creates a diffusion-controlled gradient of reactants, and enables non-equilibrium investigations of fibrin. In analogy to our previous studies on the fibrous extracellular protein collagen, we use microscopy to investigate formation of fibrin within microfluidic channels. Owing to our recent development of x-ray compatible microflow foils, we also conduct real-time small angle x-ray microdiffraction studies of fibrin. This technique is especially useful, since it yields information about the supramolecular assembly of fibrin on the nanometer length scale and provides snapshots of the dynamic evolution of fibrin formation.

Network densities and fibrin bundle sizes of structures formed within microchannel devices will be discussed in light of these experimental techniques. A particularly new development toward artificial blood vessels formed within microfluidic channels will also be addressed, which has arisen from the insight that fibrin as well as collagen (two ubiquitous extracellular proteins of which blood vessels consist, along with cells) can easily be introduced within, and used to coat, microchannel structures.

10:45—11:15 K. Hassler

## Investigation of single molecule kinetics on surfaces with total internal reflection fluorescence correlation spectroscopy

Kai Hassler, Jerker Widengren

Laboratoire d'Optique Biomedicale, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

The high signal to background ratio featured by objective-type total internal reflection fluorescence correlation spectroscopy allows for sensitive investigation of the kinetics of single, immobilized molecules. A particularly interesting application of this technique is the investigation of receptor molecules with fluorescently labeled ligands. The signaling processes of cells are mediated by the interaction of receptors with ligands on the cell membrane or within the cell. In order to better understand the different factors influencing the efficiency of cellular signaling it is important to be able to accurately measure the association and dissociation rates for receptor - ligand interactions. The measurement technique as well as the derivation of the autocorrelation function for reversible receptor - ligand interaction will be presented and discussed during this talk.

11:15—11:45 C. Beta

## Chemotaxis at low concentrations limits of chemoreception

Carsten Beta

Max-Planck-Institut für Dynamik und Selbstorganisation, Bunsenstraße 10, D-37073 Göttingen, Germany

The chemotactic response of *Dictyostelium discoideum* cells to stationary, linear gradients of cyclic adenosine 3',5'-monophosphate (cAMP) is studied using microfluidic devices. We observe a threshold for the chemotacitc response at gradients of around $10^{-3}$ nM/$\mu$m. For steeper gradients motility and chemotactic speed increase with increasing steepness of the concentration profile. For shallower gradients, on the other hand, the chemotactic response is lost and cells perform a random type of motion. The observed threshold of chemotactic sensing is discussed in the light of earlier theoretical estimates for the limits of chemoreception.

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