

CeNS/SFB1032 Workshop 2014

# Walk and Talk at the Nanoscale

September 22 - 26, 2014

Venice International University (VIU), San Servolo, Italy



## CONTENT

- Invited Talks **3**
- Poster Abstracts - Session I **18**
- Poster Abstracts - Session II **19**
- Presenting Authors **46**
- List of Participants **48**
- Accommodation, Lunch,  
Welcome Reception, Internet  
& Timetables **50**
- Map of Venice **51**
- Schedule **52**

## PROGRAM COMMITTEE

Prof. Achim Hartschuh (LMU Munich)  
Prof. Joachim Rädler (LMU Munich)  
Prof. Petra Schwille (MPI for Biochemistry)  
Prof. Jan von Delft (LMU Munich)  
Prof. Ernst Wagner (LMU Munich)

## ORGANIZERS

Dr. Susanne Hennig, Marilena Pinto & Anna Kager  
Center for NanoScience (CeNS)  
Ludwig-Maximilians Universität (LMU) Munich  
Geschwister-Scholl-Platz 1  
D-807539 Munich, Germany  
Homepage: [www.cens.de](http://www.cens.de)  
Email: [hennig@cens.de](mailto:hennig@cens.de)



## VENUE

Venice International University (VIU)  
Isola di San Servolo  
Venezia, Italy  
Phone: +39-041-2719511  
Fax: +39-041-2719510  
Homepage: <http://www.univiu.org/>  
Email: [viu@univiu.org](mailto:viu@univiu.org)



## PARTNERS



# INVITED TALKS

Force Scaling in Stress Fibers MANUEL THÉRY . . . . .	4	0.7-Anomaly in Quantum Point Contacts: Correlations in 1D STEFAN LUDWIG . . . . .	11
Approaching the Limit: Multiplexed Super-Resolution Microscopy with DNA-PAINT and Exchange-PAINT R. JUNGSMANN . . . . .	4	Electron Interactions in Quantum Point Contacts HERMANN SELLIER . . . . .	11
Can Thermal Traps drive Darwinian Evolution? CHRISTOF B. MAST . . . . .	5	Surface Plasmons and Phonon Polaritons in Atomically Thin Van der Waals Crystals DIMITRI N. BASOV . . . . .	12
Graphene Plasmons: Properties and Applications PHAEDON AVOURIS . . . . .	5	Nucleic Acid Delivery – From Academic Discovery to Drug Development CHRISTIAN PLANK . . . . .	12
Chemical Strategies for Delivery of RNAi Drugs MUTHIAH MANOHARAN . . . . .	6	Complement Sensing at Nanoscale S. MOEIN MOGHIMI . . . . .	13
Precision Positioning and Sensing for Nano-Manipulation Applications KHALED KARRAI . . . . .	6	Nanoscale Imaging and Single-Molecule Detection at Ultra-High Concentrations Using Photonic Antenna Devices MARIA F. GARCIA-PARAJO . . . . .	13
Plasmonic Metal Oxide Nanocrystals and their Near Infrared Electrochromism DELIA J. MILLIRON . . . . .	7	How Yeast Adapts to a Strong Genetic Perturbation: One Function at the Time LIEDEWIJ LAAN . . . . .	14
On the Use and Abuse of THERMODYNAMIC Entropy PETER HÄNGGI . . . . .	7	Strong Spin-Orbit Coupling of Spin-3/2 Holes in Gallium-Arsenide Semiconductor Nanostructures ALEX HAMILTON . . . . .	14
Molecular computing meets synthetic biology YAAKOV BENENSON . . . . .	8	Microfluidic Droplets for Quantitative Biological Studies CHARLES N. BAROUD . . . . .	15
Studying Cellular Structure and Function with 3D Structured Illumination Microscopy (3D-SIM) and Fluorescent Nanobodies HEINRICH LEONHARDT . . . . .	8	Non-Inertial Lift and its Application to Label-Free Microfluidic Cell Separation and Sorting THOMAS M. GEISLINGER . . . . .	15
Quantum Emulation with Microcavity Polaritons ALBERTO AMO . . . . .	8	Single-Molecule Fluorescence on DNA Origami PHILIP TINNEFELD . . . . .	16
Single-Molecule Studies of Genome Processing NYNKE DEKKER . . . . .	9	Photo-Induced Charge Carrier Generation in Covalent Organic Frameworks FLORIAN AURAS . . . . .	17
Targeted Nanocomplex Formulations for Gene and siRNA Therapy STEPHEN HART . . . . .	9	Imaging Electron Transport in Semiconductor Nanostructures on the Scale of the Electron Wavelength THOMAS IHN . . . . .	18
Phase Coexistence and Charge Traps in Organic Semiconductors – Enlighten the Disorder at the Nanoscale – CHRISTIAN WESTERMEIER . . . . .	10		
Cooling and Amplification of a Vacuum-Trapped Nanoparticle LUKAS NOVOTNY . . . . .	10		

**Force Scaling in Stress Fibers**

Timothée Vignaud, Laetitia Kurzawa, Ben Fogelson, Fabrice Senger, Jonathan Arnaud, Jean-Louis Martiel, Alex Mogilner, Laurent Blanchoin, **Manuel Théry**

Hopital Saint Louis, Unité de thérapie cellulaire, 1 Avenue Claude Vellefaux, Paris, 75010, FRANCE

Cells have the remarkable ability to sense geometrical and physical cues from their environment and adapt their architecture accordingly. This process requires a tight regulation of the permanent remodeling of the acto-myosin network, that can both transmit and generate intra-cellular forces. Despite numerous works on the molecular composition of stress fibers, little is known about the mechanism determining the magnitude of force production in these structures. Here we studied the scaling of contractile force magnitude in stress fibers and investigated the role of actin network dynamics and architecture in this process. We used micropatterned substrates to control the length and spatial organization of stress fibers in adherent cells and measured the traction forces they produced on deformable substrates.

Thereby, we demonstrated that forces scaling exhibit a biphasic behavior. Force magnitude first increased with the length of the stress fibers and then dropped above a critical length. Strikingly, very long cells appeared capable to produce only weak forces. Monitoring stress fiber relaxation upon laser nano-surgery, we showed that stress fibers were connected to the surrounding actin meshwork all along their length. A theoretical model accounting for the biphasic behavior of force scaling established friction between actin stress fibers and their surrounding cytoskeleton as being a key parameter in the regulation of force production by the cells.

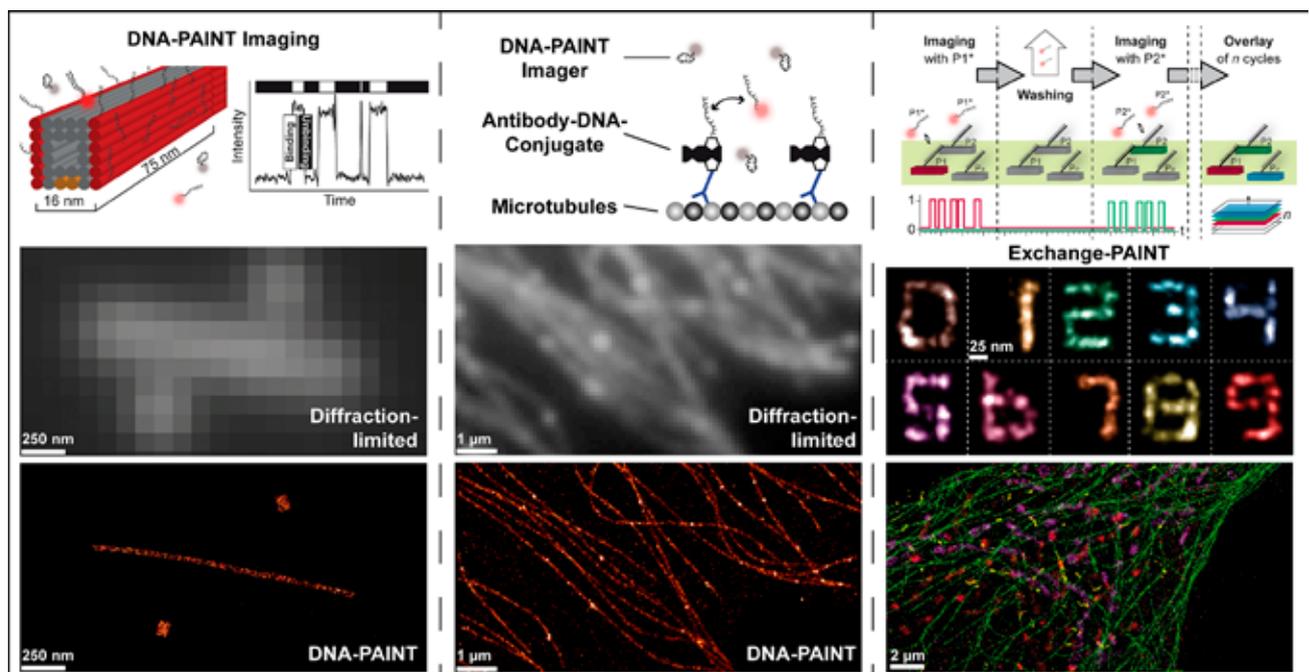
**Approaching the limit: Multiplexed Super-Resolution Microscopy with DNA-PAINT and Exchange-PAINT**

R. Jungmann<sup>1,2,3,4</sup>, M.S. Avendaño<sup>1,4</sup>, J.B. Woehrstein<sup>1</sup>, M. Dai<sup>1</sup>, W.M. Shih<sup>1,2,3</sup>, P. Yin<sup>1,4</sup>

1 Wyss Institute for Biologically Inspired Engineering, Harvard Medical School, 2 Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, 3 Department of Cancer Biology, Dana-Farber Cancer Institute, 4 Department of Systems Biology, Harvard Medical School

Super-resolution fluorescence microscopy is a powerful tool for biological research, but obtaining multiplexed images for a large number of distinct target species remains challenging. Here we use the transient binding of short fluorescently labeled oligonucleotides (DNA-PAINT, a variation of point accumulation for imaging in nanoscale topography) for simple and easy-to-implement multiplexed super-resolution imaging that achieves

sub-10-nm spatial resolution *in vitro* on synthetic DNA structures. We report a multiplexing approach (Exchange-PAINT) that allows sequential imaging of multiple targets using only a single dye and a single laser source. We experimentally demonstrate ten-color super-resolution imaging *in vitro* on synthetic DNA structures as well as four-color two-dimensional imaging and three-color 3D imaging of proteins in fixed cells.



## Can thermal traps drive Darwinian evolution?

**Christof B. Mast<sup>1</sup>, Matthias Morasch<sup>1</sup>, Severin Schink<sup>2</sup>, Ulrich Gerland<sup>2</sup> and Dieter Braun<sup>1</sup>**

*Ludwig-Maximilians-Universität München, 80799 Munich, Germany: 1 Systems Biophysics, Physics Department; 2 Technische Universität München, 85748 Garching, Germany, Theory of Complex Biosystems*

Long and complex biopolymers like RNA, DNA and proteins are essential for life on earth. Their emergence and replication are the prerequisites for early molecular Darwinian evolution. However, the origin of the first RNAzymes remains unclear because hydrolytic dissociation limits the maximal length of prebiotic polymers in aqueous, even millimolar concentrated nucleotide solutions to ~20 bases. While effective polymerization of RNA is possible in dry conditions<sup>[1]</sup>, we demonstrate how a simple thermal gradient across an elongated, water-filled pore enhances a hybridization-based, worst-case polymerization process<sup>[2]</sup>: The thermal gradient drives a fluid convection and an orthogonal movement of biomolecules, also known as thermophoresis. Both effects lead to a massive accumulation of biomolecules at the pore bottom. This thermal molecule trap concentrates longer polymers more effectively than short monomers while polymerization works the better, the higher the total monomer concentration is. In combination, both processes are mutually self-enhancing and lead to an escalation of polymerization. We developed a theory for trapped polymerization and experimentally validated it using the hybridization based polymerization of dsDNA in a laser driven thermal trap. Extrapolation of the theory toward the RNA-world shows that a pore height of 5 cm and a temperature difference of 10 K are sufficient to form RNA polymers longer than the shortest RNA based replicator. In the experiments, we found that the escalation of polymerization also leads to a sequence selective phase transition of diluted oligomers into a gel-like DNA complex. Only polymerizing monomers with matching sequence are gelled while non-polymerizing monomers remain in the diluted state. The millimeter-sized, highly concentrated complexes remain stable

even without active trapping and could have enhanced prebiotic, RNAzyme-catalyzed reactions. At the same time, the oligomer gel could have protected its selected constituents against diffusion without the help of lipids or fatty acids. We show that thermal traps can also drive the exponential replication of genetic information which is essential for Darwinian evolution<sup>[3]</sup>. The convective fluid flow thermally circulates oligomers and replicators, while replication products are accumulated and protected against outward diffusion into the diluted reservoir. In a proxy replication reaction, DNA replicating polymerase is able to double the amount of a 143mer product each 50 s, while the time constant for accumulation is 92 s. Thermal traps could therefore represent a possible non-equilibrium environment for the formation, selection and replication of the first biopolymers.

*[1] Dry polymerization of 3',5'-cyclic GMP to long strands of RNA. Matthias Morasch, Christof Mast, Johannes Langer, Pierre Schilcher and Dieter Braun (2014) ChemBioChem 15,6:879-883*

*[2] Escalation of polymerization in a thermal gradient. Mast CB, Schink S, Gerland U, Braun D (2013) Proceedings of the National Academy of Sciences 110:8030-8035.*

*[3] Thermal Trap for DNA Replication. Mast CB, Braun D (2010) Physical Review Letters 104:188102*

## Graphene Plasmons: Properties and Applications

**Phaedon Avouris**

*IBM, T.J. Watson Research Center, Yorktown Heights, NY 10598, USA*

I will begin with a short introduction to the electronic structure and the single particle excitations of graphene. The focus will then be on the collective excitations (plasmons) of this material. Next will be discussed the properties of graphene plasmons, comparing them with those of the surface plasmons of conventional metals. I will mostly concentrate on localized graphene plasmons in lithographically patterned nano- and micro-structures (quantum dots and ribbons). I will discuss their optical

behavior in the infrared and THz regions of the spectrum, size effects, doping effects, effects of external magnetic fields, and the hybridization of the graphene plasmons with substrate and adsorbed overlayer optical phonons and their damping mechanisms. Applications of graphene plasmons in passive THz optical elements, the enhancement of photocurrents in graphene infrared photodetectors, and the enhancement of infrared absorption spectra of molecules will be discussed.

## Chemical Strategies for Delivery of RNAi Drugs

Muthiah Manoharan

Department of Drug Discovery, Alnylam Pharmaceuticals, 300 Third Street, Cambridge, MA 02142 USA

Chemically engineered synthetic small interfering RNA siRNAs act as therapeutic agents through the RNA interference (RNAi) pathway and are specific and potent inhibitors of gene expression. These agents may be designed to target disease pathways previously considered “undruggable”. Numerous proof-of-concept studies both in animal models of human disease and in clinical trials demonstrate the broad potential and therapeutic value of RNAi therapeutics. The major challenge for the successful development of systemically delivered RNAi therapeutics had been the efficient delivery into organs or tissues and cells of interest to elicit RNAi mediated knockdown of faulty genes and effective translation of these approaches into clinic. Efficient delivery approaches have been developed over the years and clinical trials are advancing with RNAi therapeutic candidates formulated in lipid nanoparticles (LNPs) for intravenous administration.

We also have developed multiple conjugation strategies with the goal of robust *in vivo* delivery of siRNAs for therapeutic use. Covalent conjugation of small molecules to siRNA may avoid side effects resulting from the use of non-viral vectors, particles, or excipient-based delivery systems. Chemical modifications, mode of administration, and the nature of the conjugated ligand play significant roles in systemic delivery of siRNAs. In our early work with cholesterol and other lipophile-conjugated siRNAs, we demonstrated that covalent conjugation of small molecules can enhance bioavailability of siRNAs to multiple tissues including liver. Uptake of siRNA-lipophile conjugates is facilitated

by lipoprotein particles and associated receptors and by other transmembrane proteins that are ubiquitously expressed. Systemic and local applications of cholesterol-siRNA conjugates for various therapeutic targets have also been broadly documented.

More recently, systemic delivery of therapeutic siRNAs to liver hepatocytes by subcutaneous administration has been achieved by conjugating chemically modified siRNAs with multivalent N-acetylgalactosamine (GalNAc) residues that are recognized by the asialoglycoprotein receptor (ASGPR). ASGPR is a C-type lectin receptor expressed on the cell surfaces of mammalian hepatocytes at 0.5 to 1 million copies per cell and is highly conserved across species. ASGPR recognizes an exposed terminal galactose (Gal) and enables clearing of serum glycoproteins via clathrin-mediated endocytosis. Recognition by the ASGPR requires multi-valency with appropriate spatial orientation of the Gal or the high affinity sugar analog N-acetylgalactosamine (GalNAc). Binding affinities of these ligands vary from mM to low nM and depend on the number of sugar residues present. siRNA-GalNAc conjugates efficiently target and silence disease-causing genes produced in liver hepatocytes. Using this conjugation platform, Alnylam is advancing several RNAi agents specific for liver targets through pre-clinical and clinical development to address genetically defined diseases with highly unmet medical need. Our progress with the chemistry of siRNA-GalNAc conjugates and applications in several therapeutic areas will be presented.

## Precision Positioning and Sensing for Nano-Manipulation Applications

Khaled Karrai

attocube systems AG, Königinstrasse 11a, 80539 München, Germany

Precision positioning and precision position sensing in space constrained is particularly challenging. It becomes even more challenging to address applications demanding specific manipulation in environmental constraints, such as cryogenic temperatures, or ultrahigh vacuum. Here I review and discuss by way of example few of such applications. One of them concerns the fabrication of quantum dot based quantum devices. Pioneering novel techniques in semiconductor device fabrication have recently greatly benefitted from the possibility optical lithography to make novel quantum optical devices out of randomly distributed quantum optical light emitter<sup>[1-3]</sup>. For instance by exposing an appropriate photoresist while optically localizing the position of light emitting single quantum dots allowed high-yield fabrication of novel quantum optical devices. Here, as an example, once the single quantum dot light emitters are spatially individually localized and their emission color identified, appropriate optical devices are subsequently lithographically defined to imbed each quantum emitter individually to insure the device

full functionality. This so called deterministic lithography approach allows coping with the typical randomness of the spatial and spectral distribution of single semiconductor quantum dots demonstrating a rare case of confluence between bottom-up and top-down approaches in nano-device technology. The emission wavelength and intensity of single semiconductor quantum dots happens to be strongly temperature dependent and it is crucial that such deterministic optical lithography takes place at cryogenic temperatures ranging between 4K and 100K. In this work we show how the development of piezo displacement stages and accurate position readout allowed for building a cryogenic optical lithographer.

[1] A. Dousse et al., *Phys.Rev.Lett.* 101, 267404 (2008)

[2] A. Dousse et al., *App.Phys.Lett.* 94, 121102 (2009)

[3] A. K. Novak et. Al. *Nature Communication* (Feb. 2014)

## Plasmonic metal oxide nanocrystals and their near infrared electrochromism

Delia J. Milliron

McKetta Department of Chemical Engineering, The University of Texas at Austin, Austin, Texas, USA

Degenerately doped metal oxide semiconductors exhibit plasmonic resonance at wavelengths tunable by varying their composition. We have recently developed robust chemical strategies for incorporating high levels of dopants during colloidal nanocrystal synthesis and thereby fabricated a wide range of dispersible, processible nanocrystals with infrared plasmon absorption features.<sup>[1]</sup> For example, aluminum-doped zinc oxide nanocrystals exhibit broad absorption peaks in the mid-infrared that change intensity and position systematically with doping level, while plasmon absorption peaks of tin-doped indium oxide (ITO) nanocrystals can be tuned across the near infrared. These plasmonic metal oxide nanocrystals are chemically robust, which has enabled us to study their optical response to electrochemical charging and discharging. Over a few volts of applied bias, the carrier concentration and plasma frequency in a conductive network of ITO nanocrystals were reversibly modulated by nearly 3- and 2-fold, respectively.<sup>[2]</sup> The result is a strong and selective modulation of near infrared transmittance in visibly transparent films. This effect shows promise for energy-saving smart windows, a potential application which is even

more compelling when considering the electrochromic properties of inorganic composites containing these nanocrystals. ITO-in-amorphous niobium oxide composites exhibit sequential switching of near infrared and visible transmittance whose dynamic range is enhanced 5-fold by synergistic reorganization at the ITO-glass interface.<sup>[3]</sup> Our recent prototype “smart glass” devices demonstrate the opportunity to dynamically control solar heat gain and daylighting in buildings in response to changing environmental conditions. I will conclude by highlighting outstanding fundamental questions about plasmons in metal oxide nanocrystals<sup>[4]</sup> and their broad range of possible applications.

[1] R. Buonsati and D. J. Milliron, *Chem. Mater.*, 2013, 25, 1305

[2] G. Garcia et al., *Nano Lett.*, 2011, 11, 4415

[3] A. Llordes et al., *Nature*, 2013, 500, 323

[4] S. D. Lounis et al., *J. Phys. Chem. Lett.*, 2014, 5, 1564

## On the use and abuse of THERMODYNAMIC entropy

Peter Hänggi

Department of Physics, University of Augsburg, Germany

Let us elaborate on the notion of *thermodynamic* entropy  $S$  (Clausius 1865) and its consequences. Gibbs put forward two notions of entropy for isolated systems that I commonly will refer to as ‘volume entropy’ (involving the integrated density of states in modern language) and as the ‘surface entropy’, being proportional to the density of states, commonly also known (incorrectly) as the Boltzmann entropy. The absolute temperature,  $\partial S / \partial U$ , is then related to thermodynamic entropy; -- but which one to use? -- The consistency for thermodynamics, i.e. the validity for the celebrated 0-th, 1-st and 2-nd thermodynamic Law singles out the Gibbs-entropy<sup>[1]</sup>.

I shall address shortcomings that relate to the thermodynamics of small systems when sticking to the (Boltzmann)-surface entropy<sup>[2,3]</sup>. Most of all, the uncritical use of Boltzmann entropy for microcanonical systems may formally yield negative values of absolute temperatures. This is not only physically incorrect for the concept of an *absolute* temperature, but also would violate thermodynamic stability if the system is brought into (weak) contact with an omnipresent sort of environment of radiation source or otherwise with no upper bound in energy. This criticism applies to the concept of absolute negative (spin) temperature and, as well, to the interpretation of recent experiments with isolated ultra-cold atomic gases<sup>[4]</sup>.

Next, we address canonical entropy when describing quantum systems that interact (not strongly) with an environment. Then, the canonical specific heat can assume negative values away from absolute zero temperature<sup>[5,6]</sup>. Likewise, the thermodynamic entropy for a strongly coupled system, assuming a form which mimics a conditional entropy (but not quite) can be negative away from absolute  $S=0$ .

[1] S. Hilbert, P. Hänggi, and J. Dunkel, *Thermodynamic Laws in Isolated Systems*, arXiv:1408.5382 (2014).

[2] M. Campisi, *Microcanonical phase transitions in small systems*, arXiv 0709:1082; *ibid*, *On the mechanical foundations of thermodynamics: The generalized Helmholtz theorem. Studies in History and Philosophy of Modern Physics* 36, 275 (2005)

[3] J. Dunkel and S. Hilbert, *Phase transitions in small systems: microcanonical vs. canonical ensembles*, *Physica A* 370, 390 (2006).

[4] S. Braun, et al., *Negative absolute temperatures for motional degrees of freedom*, *Science* 339, 52 (2013); J. Dunkel and S. Hilbert, *Consistent Thermostatistics forbids Negative Absolute Temperatures*, *Nature Physics*, 10: 67-72 (2014).

[5] P. Hänggi, G.L. Ingold, and P. Talkner, *Finite quantum dissipation: the challenge of obtaining specific heat*, *New J. Phys.* 10, 115008 (2008); *ibid*, *Specific heat anomalies of open quantum systems*, *Phys. Rev. E* 79, 061105 (2009).

[6] M. Campisi, P. Talkner, and P. Hänggi, *Thermodynamics and fluctuation theorems for a strongly coupled open quantum system: an exactly solvable case*, *J. Phys. A: Math. Theor. (Fast Track)* 42, 392002 (2009).

See also the two links:

(1) “(Quantum)-Fluctuation Theorems”

<http://www.physik.uni-augsburg.de/theo1/hanggi/Fluctuation.html>

(2) “What is Temperature”

<http://www.physik.uni-augsburg.de/theo1/hanggi/Temperature.html>

## Molecular computing meets synthetic biology<sup>[1]</sup>

Yaakov Benenson, ETH Zurich, Switzerland

One of the motivations behind computing with molecules is to "computerize" living systems, for example to prevent disease or control artificial tissues. Biology, however, is already very good at computing - the human brain being one example. Even on a single cell level information is constantly being processed, and the development of a functional organism from a single fertilized cells is controlled by an ingenious if only partially understood program encoded in DNA. Does this mean that the efforts to "write" new molecular programs are redundant? Not at all - natural programs have taken three billion years to evolve and, despite their beauty, are very difficult to alter in any way.

In my view the optimal approach is to balance the engineering principles inspired by computer science and engineering such

as universal models, reprogrammability, modularity, etc., with the harsh reality of cell and organismal biology. The simple fact is that we do not know yet, even at the theory level, whether it is possible to perform reliable information processing in actual living cells as opposed to idealized "well-mixed reactors". Despite these limitations, the field of molecular computing in cells, or biological computing, has made significant steps forward with new design principles, new architectures, and new exciting experimental results. These developments also inform basic biological research.

[1] *Unconventional Computation and Natural Computation. 13th International Conference. Proceedings: LNCS 8553. Publisher: Springer, Cham, Switzerland*

## Studying cellular structure and function with 3D structured illumination microscopy (3D-SIM) and fluorescent nanobodies

Heinrich Leonhardt

Ludwig Maximilians University Munich, 82152 Planegg-Martinsried, Germany

Fluorescence light microscopy allows multicolor visualization of cellular components with high specificity, but its utility has until recently been constrained by the intrinsic limit of spatial resolution. We applied three-dimensional structured illumination microscopy (3D-SIM) to circumvent this limit and to study the mammalian nucleus (*Science*, 320, 1332-6). By simultaneously imaging chromatin, nuclear lamina, and the nuclear pore complex (NPC), we observed several features that escape detection by conventional microscopy. We are now studying the topological organization of nuclear functions at super-resolution. Multicolor 3D-SIM opens new possibilities to analyze subcellular structures beyond the diffraction limit of the emitted light.

We have recently generated fluorescent, antigen-binding proteins, termed chromobodies, combining epitope-recognizing fragments with fluorescent proteins (*Nature Methods*, 3, 887-9). Unlike conventional antibodies these chromobodies can be expressed in living cells and used to target or trace epitopes in subcellular compartments. As chromobodies are soluble and active in the intracellular environment, they provide an optical readout for novel high content analyses and enable functional studies in vivo (*Nature Struct. Mol. Biol.*, 17, 133-139). These antigen-binding fragments can also be produced in *E. coli*, chemically functionalized and used for super-resolution microscopy (*Science*, 331, 1616-20).

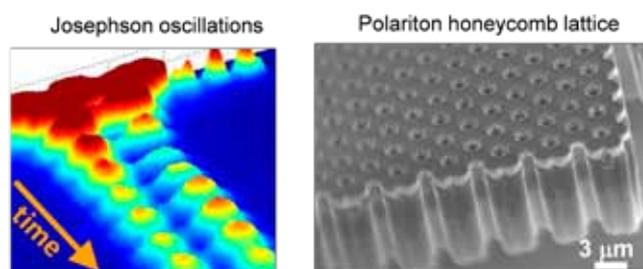
## Quantum emulation with microcavity polaritons

Alberto Amo

CNRS-Laboratoire de Photonique et Nanostructures, Marcoussis, France

Semiconductor microcavities are an excellent platform to study non-linear optical phenomena and the quantum fluid properties of Bose-Einstein condensates. The eigenstates of this system are polaritons, half-light/half matter quasiparticles arising from the strong coupling between excitons and photons confined in an optical cavity of micrometric size. Thanks to their very light mass ( $10^{-4}$  times the electron mass) these photonic bosons can form Bose-Einstein condensates at temperatures much higher than in atomic gases (10K for polaritons vs 100nK for atoms). By engineering the shape of the microcavities we can use polaritons to emulate various Hamiltonians in a photonic system directly accessible using standard optical techniques. Taking advantage of these properties we have experimentally studied

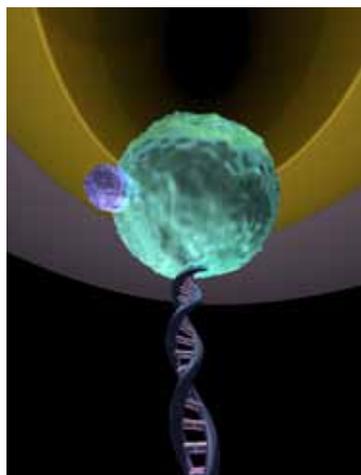
Josephson oscillations and photonic self-trapping in a microcavity, and fabricated a honeycomb lattice in which photons behave like electrons do in graphene.



## Single-molecule studies of genome processing

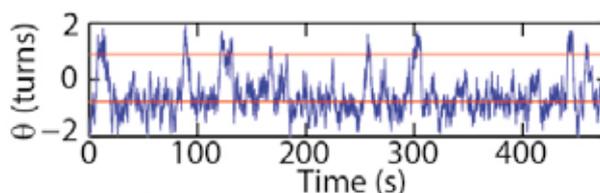
Nynke Dekker

Delft University of Technology, Delft, The Netherlands



Over the past few decades, there has been steady progress in both our ability to produce biological material and in our ability to manipulate matter at small length scales. These two developments merge in a fascinating area of confluence called single-molecule biophysics in which an understanding of biological matter from physical principles becomes possible. I will

illustrate how several newly-developed single-molecule force and torque spectroscopy techniques allow us to shed light on genomic processes such as transcription, replication, and DNA compaction. Lastly, as the true environment of biological molecules is the living cell, I will demonstrate our ability to track replication inside bacterial cells, and discuss implications for the future.



## TUESDAY, SEPTEMBER 23 (AFTERNOON SESSION)

### Targeted nanocomplex formulations for gene and siRNA therapy

Stephen Hart

Wolfson Centre for Gene Therapy of Childhood Disease, UCL In, 30 Guilford Str, London WC1N 1EH, UK

Synthetic, non-viral vectors such as cationic liposomal and polymeric formulations offer advantages over viral vectors for *in vivo* gene therapy in that they are less immunogenic, have fewer packaging constraints and are safe. However their transfection efficiencies *in vivo* are usually insufficient. Multifunctional synthetic formulations are being developed that emulate the properties and functionalities of viral capsids and higher transfection efficiencies. We are developing a formulation that we term a Receptor Targeted Nanocomplex (RTN), which is a mixture of cationic, receptor-targeting peptides and liposomes with nucleic acids, plasmid DNA (pDNA) or short interfering RNA (siRNA). The peptide mediates DNA packaging and receptor targeting while the lipid fuses with the endosomal membrane leading to improved cytoplasmic release of the DNA or siRNA. RTNs display a synergistic enhancement of transfection due to the combined functionality of these components, both for siRNA and plasmid delivery.

Diseases affecting different tissues are likely to need specifically designed formulations optimised for the target tissue and the route of delivery. RTN formulations have been developed with anionic or cationic charges, and with stealth properties resulting from PEGylation. The modularity of the RTN design enables development of formulations optimised for specific therapeutic strategies including lung disease in cystic fibrosis with delivery by nebulisation, neuroblastoma cancers by systemic administration, and brain delivery for neurodegenerative diseases by direct injection.

## Phase coexistence and charge traps in organic semiconductors – enlighten the disorder at the nanoscale –

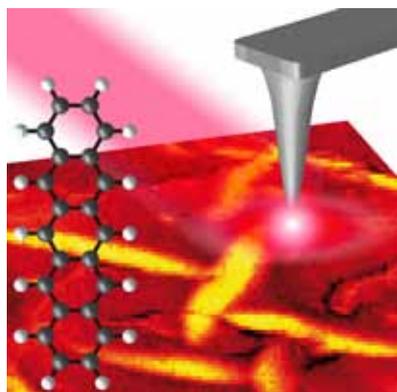
**Christian Westermeier<sup>1,2</sup>, Adrian Cernescu<sup>3</sup>, Sergiu Amarie<sup>3</sup>, Clemens Liewald<sup>1</sup>, Fritz Keilmann<sup>1</sup>, Bert Nickel<sup>1,2</sup>**

<sup>1</sup> Fakultät für Physik & CeNS, Ludwig-Maximilians-Universität München, D-80539, Germany

<sup>2</sup> Nanosystems Initiative Munich, Schellingstrasse 4, D-80799 Munich, Germany

<sup>3</sup> Neaspec GmbH, Bunsenstrasse 5, D-82152 Martinsried, Germany

The control of nanocrystallinity and disorder in organic thin films such as pentacene is crucial for the improvement of electronic applications. The distribution of crystalline phases and trap states at the emerging interfaces is, however, difficult to access experimentally. We have successfully developed a new imaging technique for trap densities in pentacene thin films by using essentially a pulsed laser scanning microscope to scan across the channel of an organic field-effect transistor during operation.<sup>[1]</sup> Here, filling of the trap states can be adjusted via the gate voltage,



subsequently the trapped charges are locally released by exciton-mediated trap clearing upon illumination and the released charge is detected as light-induced change of the transistor current. As this photoresponse is sensitive to the amount of trapped charges within the

The grain boundaries between two coexisting phases in organic semiconductor pentacene are expected to obstruct charge transport in its thin-film devices. We use infrared-spectroscopic nano-imaging to show an interlocking morphology, which is uncorrelated with its grain structures.

illuminated area, the recorded map mirrors the distribution of traps throughout the pentacene film and hotspots can be identified. While the laser focus of our trap imaging technique is diffraction limited, we also utilize s-SNOM imaging that allows for local excitation of an organic film with a resolution down to 20 nm due to near-field enhancement via a metalized tip. This resolution, being independent of the wavelength, also holds for mid-infrared light that excites molecular vibrations. We benefit from the sharp IR resonances of highly-ordered organic systems, which turn out to be sensitive even to the crystalline packing of molecules. Thus, IR-SNOM allows to image different crystalline phases of the same material in thin films for organic electronics. For the case of pentacene, we find that grains of a few microns size, which appear to be in the so called thin film phase, are indeed subject to massive nucleation of bulk phase pentacene.<sup>[2]</sup> This may explain contradicting reports on the correlation of grain size and carrier mobility in pentacene films.

[1] C. Westermeier, M. Fiebig, B. Nickel, Mapping of Trap Densities and Hotspots in Pentacene Thin-Film Transistors by Frequency-Resolved Scanning Photoresponse Microscopy, *Adv. Mater.* 25(40): 5719–5724 (2013).

[2] C. Westermeier, A. Cernescu, S. Amarie, C. Liewald, F. Keilmann, B. Nickel, Sub-micron phase coexistence in small-molecule organic thin films revealed by infrared nano-imaging, *Nat. Commun.* 5: 4101 (2014).

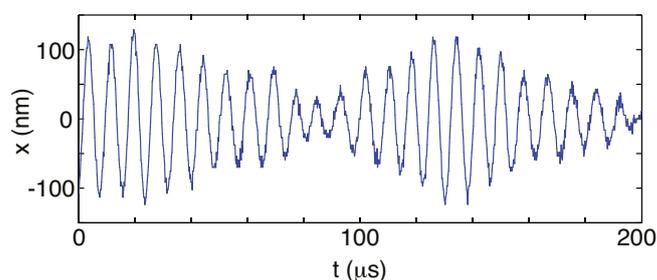
## Cooling and Amplification of a Vacuum-Trapped Nanoparticle

**Lukas Novotny<sup>a</sup>, Romain Quidant<sup>b</sup> and Jan Gieseler<sup>a</sup>**

<sup>a</sup> ETH Zurich, Photonics Laboratory, 8093 Zurich, Switzerland

<sup>b</sup> ICFO, Mediterranean Technology Park, 08860 Castelldefels, Spain

We optically trap a single nanoparticle in high vacuum and cool its three spatial degrees of freedom by means of active parametric feedback. The small size and mass of the nanoparticle yield high resonance frequencies and high Q-factors along with low recoil heating, which are essential conditions for ground state cooling and for low decoherence. The vacuum-trapped nanoparticle forms an ideal model system for studying non-equilibrium processes, nonlinear interactions, and ultras-small forces.



**Figure 1:** (top) Photograph of light scattered from a trapped 85 nm fused silica particle (arrow). The object to the right is the outline of the objective lens. (bottom) Time trace of the particles x coordinate (transverse to optical axis) at 2mbar pressure. Trapping times of several days have been achieved.

## 0.7-Anomaly in Quantum Point Contacts: Correlations in 1D

Florian Bauer,<sup>1,2</sup> Jan Heyder,<sup>1,2</sup> David Borowsky,<sup>1</sup> Enrico Schubert,<sup>1</sup> Daniela Taubert,<sup>1</sup> Dieter Schuh,<sup>3</sup> Benedikt Bruognolo,<sup>1,2</sup> Werner Wegscheider,<sup>4</sup> Jan von Delft,<sup>1,2</sup> and Stefan Ludwig<sup>1</sup>

<sup>1</sup> Center for NanoScience & Fakultät für Physik, Ludwig-Maximilians-Universität München, Germany

<sup>2</sup> Arnold Sommerfeld Center for Theoretical Physics, Ludwig-Maximilians-Universität München, Germany

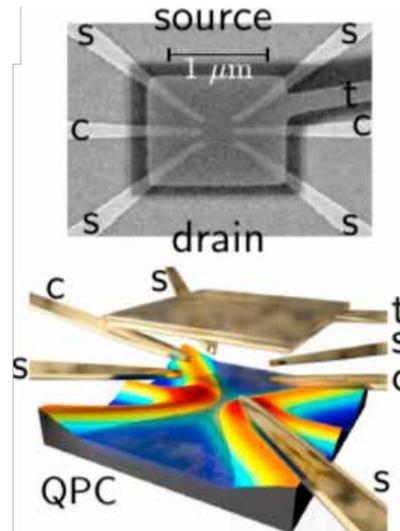
<sup>3</sup> Institut für Angewandte Physik, Universität Regensburg, Germany

<sup>4</sup> Laboratory for Solid State Physics, ETH Zürich, Switzerland

Quantum point contacts (QPCs), the ultimate building blocks of quantum electronic circuits, are 1D constrictions in a 2D electron system (2DES). When a QPC is pinched off, its conductance famously decreases in integer steps of the conductance quantum,  $G_0 = 2e^2/h$ . The source of an unexpected feature with an intriguing dependence on temperature, magnetic field and source-drain voltage has been debated for the last two decades<sup>[1]</sup>. Often entailing a kink of the pinch-off curve near  $0.7G_0$  it is called the 0.7-anomaly. In this talk I will explain how the 0.7-anomaly naturally arises from strong correlations fostered by the enhanced density of states in 1D at low energies. The correlations cause an anomalous increase of the spin susceptibility and the back-scattering rate. Our microscopic model is built on a combination of systematic measurements of a highly tunable QPC and detailed numeric calculations<sup>[2]</sup>. Compared to previous models we utilize no assumptions, such as a local moment or a broken time-reversal symmetry, in addition to experimental evidences.

[1] A. Micolich, *J. Phys. Cond. Matt.* 23, 443201 (2011)

[2] F. Bauer, et al., *Nature* 501, 73 (2013)



Scanning electron micrograph of our QPC sample (top) and animated potential view (bottom). A 2D electron system (2DES) resides 85nm beneath the surface of a GaAs/AlGaAs heterostructure. Two central gold gates (c), four side gates (s) and an electrically isolated global top gate (t) are used to shape by the electric field effect a 1D constriction in the 2DES. Electrons move through the QPC between source to drain contacts (dark blue areas) while they are repelled by high potential regions (yellow, red). [animation produced by Christoph Hohmann.]

## Electron Interactions in Quantum Point Contacts

Hermann Sellier

Institut Néel, CNRS et UJF, 25 rue des Martyrs, F-38042 Grenoble, France

Quantum point contacts (QPCs) are well known for their waveguide properties, but they also show a rich physics of electron interactions. Applying a negative voltage on split-gates patterned on a two-dimensional electron gas (2DEG) creates a quasi one-dimensional electron channel connecting two large reservoirs<sup>[1]</sup>. Each wave-guide mode carrying one conductance quantum  $2e^2/h$ , the conductance curve versus gate voltage shows a series of quantized plateaus which are well reproduced by a simple saddle potential model<sup>[2]</sup>. However, a shoulder-like feature is commonly observed at a conductance around  $0.7 \times 2e^2/h$  which cannot be explained by single-particle theory<sup>[3]</sup>. With lowering temperature, this "0.7 anomaly" shades off and a "zero-bias anomaly" emerges<sup>[4]</sup>. Although the link between these structures remains an open question, both are thought to arise from strong Coulomb interactions in the small 2DEG region forming the QPC where the electron density is low. Different theoretical models have been proposed to explain these anomalies, but no consensus could be reached so far on their interpretation<sup>[5]</sup>.

After a brief review of experimental observations and theoretical models, I will present recent experiments<sup>[6,7]</sup> that indicate the presence of self-consistently localized charges in QPCs. In particular, I will focus on our experimental approach<sup>[7]</sup> using a Scanning Gate Microscope (SGM)<sup>[8-10]</sup> to change in-situ the shape of the QPC potential. The SGM tip is used as a movable gate in a more flexible and less invasive way than what could be achieved with several fixed surface gates. Approaching the tip towards the QPC produces an oscillatory splitting of the zero-bias anomaly, correlated with simultaneous appearances of the 0.7 anomaly, thereby revealing that both features share a common origin. These repetitive changes are interpreted in terms of a many-body localized state, induced by the strong Coulomb repulsion in this low density region, and forming a small one-dimensional Wigner crystal<sup>[11-13]</sup>. The number of charges in this crystal is controlled by the tip position and produces different Kondo screenings from the leads depending on charge parity, with a conductance peak either at zero, or at finite bias<sup>[14,15]</sup>.

- [1] B. J. van Wees, et al., *Phys. Rev. Lett.* 60, 848 (1988).
- [2] M. Büttiker, *Phys. Rev. B* 41, 7906 (1990).
- [3] K. J. Thomas, et al., *Phys. Rev. Lett.* 77, 1 (1996).
- [4] S. M. Cronenwett, et al., *Phys. Rev. Lett.* 88, 22 (2002).
- [5] A. P. Micolich, *J. Phys.: Condens. Matter* 23, 443201 (2011).
- [6] M. J. Iqbal, et al., *Nature* 501, 79 (2013).
- [7] B. Brun, et al., *Nat. Commun.* 5, 4290 (2014).
- [8] M. A. Topinka, et al., *Nature* 410, 183 (2001).
- [9] R. Crook, et al., *Science* 312, 1359 (2006).
- [10] B. Hackens, et al., *Nat. Commun.* 1, 39 (2010).
- [11] Y. Meir, et al., *Phys. Rev. Lett.* 89, 196802 (2002).
- [12] K. A. Matveev, *Phys. Rev. Lett.* 92, 106801 (2004).
- [13] A. D. Guçlu, et al., *Phys. Rev. B* 80, 201302(R) (2009).
- [14] A. Georges and Y. Meir, *Phys. Rev. Lett.* 82, 17 (1999).
- [15] R. Aguado and D. C. Langreth, *Phys. Rev. Lett.* 85, 1946 (2000).

## Surface plasmons and phonon polaritons in atomically thin van der Waals crystals

**Dimitri N. Basov**

*University of California San Diego; dbasov@ucsd.edu; <http://infrared.ucsd.edu/>*

Layered van der Waals (vdW) crystals consist of individual atomic planes weakly coupled by vdW interaction, similar to graphene monolayers in bulk graphite. These materials can harbor superconductivity and ferromagnetism with high transition temperatures, emit light and exhibit topologically protected surface states. An ambitious practical goal is to exploit atomic planes of vdW crystals as building blocks of more complex artificially stacked structures where each such block will deliver layer-specific attributes for the purpose of their combined functionality. Infrared (IR) nano-spectroscopy and nano-imaging experiments on hexagonal boron nitride (hBN) have uncovered rich optical effects associated with phonon polaritons in this prototypical van der Waals crystal. We launched, detected and imaged the

polaritonic waves in real space and altered their wavelength by varying the number of crystal layers in our specimens [*Dai et al. Science, 343, 1125, (2014)*]. Unlike surface plasmons in graphene that we have imaged using a similar nano-IR toolset [*Fei et al. Nature 487, 82 (2012)*], highly confined phonon polaritons are immune to electronic losses and therefore can travel over distances exceeding 10-s of microns. I will also discuss an ability to control plasmonic response of graphene at femto second time scales that we have demonstrated using a unique pump-probe nano-IR apparatus [*Wagner et al. Nano Letters 14, 894 (2014)*].

## Nucleic Acid Delivery – From Academic Discovery to Drug Development

**Christian Plank**

*Ethris GmbH, Lochhamer Str. 11, 82152 Martinsried*

*Technical University of Munich, University Hospital Rechts der Isar, Institute of Experimental Oncology, München*

Nucleic acids carry the building plans of living systems and fulfil numerous further functions in living cells. In theory, any cellular function may be influenced in a purposeful manner if an appropriate nucleic acid can be shuttled into a target cell in a precise enough manner. In nucleic acid therapy, nucleic acids are used to complement or repair damaged genes or to interfere with endogenous gene expression. For this purpose, nucleic acids are usually formulated as multifunctional nanoparticles which are designed to overcome numerous barriers on the way from an administration site to the target cells. We have developed various methods for using nucleic acids in medical applications. More recently, we have focused on “gene therapy without

genes”, that is on using messenger RNA instead of genes for making patient cells produce their own therapeutic protein. This program is intended to enter first in man application in 2015. In this presentation, challenges encountered when developing nucleic acid drugs from bench to bedside will be discussed.

## Complement Sensing at Nanoscale

S. Moein Moghimi

Centre for Pharmaceutical Nanotechnology and Nanotoxicology, Department of Pharmacy, University of Copenhagen, Universitetsparken 2, DK-2100 Copenhagen Ø, Denmark

The complement system is a complex network of plasma and membrane-associated proteins and represents one of the major effector mechanisms of the innate immune system. The function of complement in innate host defence is accomplished through highly efficient and tightly orchestrated opsonisation, lytic and inflammatory processes. Synthetic nanoparticles and particulate drug carriers (e.g., liposomes, polymeric nanoparticles and nanocapsules) by virtue of their size, shape and surface characteristics (e.g., display of architecture with repetitive epitopes such as those arising from surface projected polymers or polyanionic/polycationic clusters) may resemble many microorganisms. These 'pathogen-mimicking' properties make nanoparticles prone to interception by the complement system and a number of consequences ensue from complement activation. These comprise both beneficial and adverse reactions, depending on the extent and severity of complement activation as well as microenvironmental factors. These concepts will be discussed in relation to therapeutic applications of nanoparticles and anti-cancer nanomedicines.

[1] Hamad, I., Al-Hanbali, O., Hunter, A.C., Rutt, K.J., Andresen, T.L. and Moghimi, S.M. (2010) Distinct polymer architecture mediates switching of complement activation pathways at nanosphere-serum interface: implications for stealth nanoparticles engineering. *ACS Nano* 4: 6629–6638.

[2] Moghimi, S.M., Hunter, A.C., and Andresen, T.L. (2012). Factors controlling nanoparticle pharmacokinetics: an integrated approach and perspective. *Ann. Rev. Pharmacol. Toxicol.* 52, 481–503.

[3] Moghimi, S.M., Wibroe, P.P., Helvig, S.Y., Farhangrazi, Z.S., and Hunter, A.C. (2012). Genomic perspectives in inter-individual adverse responses following nanomedicine administration: the way forward. *Adv. Drug Deliv. Rev.* 64, 1385–1393.

[4] Andersen, A.J., Robinson, J.T., Dai, H., Hunter, A.C., Andresen, T.L. and Moghimi, S.M. (2013) Single-walled carbon nanotubes surface control of complement sensing and activation. *ACS Nano* 7: 1108–1119.

[5] Moghimi, S.M., and Farhangrazi, Z.S. (2013). Nanomedicine and complement paradigm. *Nanomedicine: Nanotechnol. Biol. Med.* 9, 458–460.

[6] Moghimi, S.M. (2014) Cancer nanomedicines and the complement system activation paradigm: anaphylaxis and tumour growth. *J. Control. Rel.* 190: 556–562.

[7] Moghimi, S.M. and Farhangrazi, Z.S. (2014) Just so stories: random acts of anti-cancer nanomedicine performance. *Nanomedicine: Nanotechnol. Biol. Med.* (in press).

## Nanoscale imaging and single-molecule detection at ultra-high concentrations using photonic antenna devices

Maria F. Garcia-Parajo

ICFO-Institute of Photonic Sciences, Mediterranean Technology Park, 08860 Barcelona, Spain & ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain

The quest for optical imaging of biological processes at the nanoscale has driven in recent years a swift development of a large number of microscopy techniques based on far-field optics. These, so called, super-resolution methods are providing new capabilities for probing biology at the nanoscale by fluorescence. While these techniques conveniently use lens-based microscopy, the attainable resolution and/or localization precision severely depend on the sample fluorescence properties. True nanoscale optical resolution free from these constraints can alternatively be obtained by interacting with fluorophores in the near-field. Indeed, near-field scanning optical microscopy (NSOM) using subwavelength aperture probes is one of the earliest approaches sought to achieve nanometric optical resolution<sup>1</sup>. More recently, photonic antennas have emerged as excellent alternative candidates to further improve the resolution of NSOM by amplifying electromagnetic fields into regions of space much smaller than the wavelength of light. In this contribution, I will describe our efforts towards the fabrication of different nano-antenna probe configurations as well as 2D antenna arrays for

applications in nano-imaging and spectroscopy of living cells<sup>2-5</sup>. I will show examples on how these devices can be exploited to detect individual molecules at micro-molar concentrations<sup>4,5</sup>, as well as our efforts towards the study of cell surface receptors in living cells with unprecedented resolution and sensitivity.

[1] P. Hinterdorfer, M.F. Garcia-Parajo, Y. Dufrene, *Acc. Chem. Res.* 45, 327 (2012).

[2] M. Mivelle, T.S. van vanten et al. *Microscopy & Research Technique*, 77, 537–545 (2014)

[3] M. Mivelle, T.S. van vanten et al. *Nano Letters* 12, 5972 (2012)

[4] D. Punj, M. Mivelle, et al. *Nature Nanotechnology* 8, 512 (2013).

[5] M. Mivelle, T.S. van Zanten et al, *Nano Letters online* DOI:10.1021/nl502393b (2014).

## How yeast adapts to a strong genetic perturbation: one function at the time

Liedewij Laan and Andrew Murray

FAS Center for Systems Biology, Harvard

Complex gene regulatory and protein networks allow yeast to grow and divide under a wide range of environments. These networks also need to be robust to genetic perturbations to buffer genotypic variation due to sexual reproduction and evolution. Nevertheless, on long evolutionary timescales mutations are essential to allow organisms to adapt. So, how robust are these networks to genetic perturbations, and what are the underlying mechanisms of robustness? We addressed these questions by deleting the nearly essential gene *BEM1* from the polarity network in budding yeast. Bem1 brings together Cdc42, a small G protein that regulates actin polymerization, and its activator Cdc24, a guanine nucleotide exchange factor, and by doing so Bem1 is an essential part of one of the positive feedback loops that create a single site of cell polarization. Cells lacking Bem1 have severe polarization defects, resulting in many very large cells that eventually explode. As a consequence, *bem1Δ* populations proliferate roughly 10-fold slower than their wild-type counterparts.

To study adaptation, we evolved 11 *bem1Δ* lines by serial dilutions for one thousand generations. At the end of the evolution, *bem1Δ* cells approached wild-type growth rate and cell size and polarization dynamics were indistinguishable from wild type. We sequenced the final time points and found mutations in three genes (*BEM3*, *NRP1*, and *BEM2*) that appeared in the same order in several independent lines. After reconstructing these mutations in a *bem1Δ* background and studying their phenotype, we suggest the following progressive mechanism of adaptation: The first mutation (inactivating *BEM3*) improves activation of Cdc42, the second mutation increases positive feedback, and the third mutation fine tunes activation of Cdc42. These experiments show that the polarization module is highly adaptable through a small number of mutations which are surprisingly efficient in recovering proper function, especially given the precision of the original network in its ability to produce one and only one site of polarization.

## Strong spin-orbit coupling of spin-3/2 holes in gallium-arsenide semiconductor nanostructures

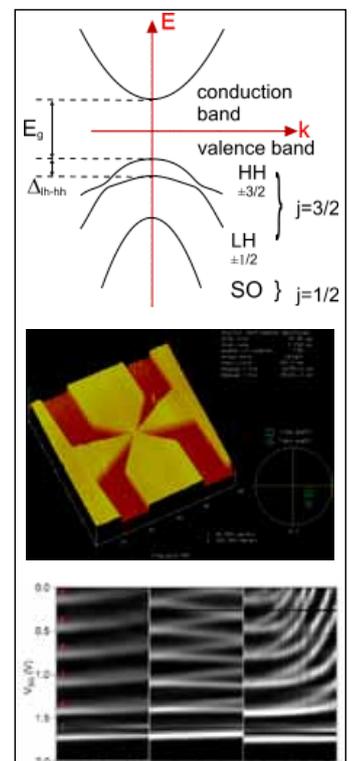
Alex Hamilton

School of Physics, University of New South Wales, Sydney 2052, Australia; [www.physics.unsw.edu.au/QED](http://www.physics.unsw.edu.au/QED)

The electrical current in a semiconductor can be carried by negatively charged electrons or positively charged holes. In undergraduate physics, we are often taught that holes in the valence band are just an absence of an electron. But they aren't. Valence band holes are spin-3/2 particles, and this gives them very different properties to spin-1/2 electrons. In recent years there has been growing theoretical interest in the possibility of using holes in semiconductor nanostructures for applications ranging from ultra-fast spin transistors through to quantum information and communication. This talk will describe where holes come from, why they are so different to electrons, and what one can do with holes that can't be done with electrons.

The differences between electron and holes are most striking when they are confined to low dimensional nanostructures. In quantum wires the interplay of spin-orbit interaction and electrostatic confinement leads to an extreme anisotropy of the Zeeman spin-splitting that is completely unlike electrons, and still not fully understood. I will present measurements mapping

out the anisotropy of the hole Lande g-tensor, and show that it is possible to directly measure off diagonal component of the g-tensor.



## Microfluidic droplets for quantitative biological studies

Charles N. Baroud

LadHyX & Department of Mechanics, Ecole Polytechnique, CNRS, 91128 Palaiseau, France

I will present a set of tools that we have developed for manipulating microfluidic droplets. These tools simplify the fluidic operations, allowing the user to work with stationary drops while the conditions are varied in time. This gives access to spatial and temporal information on the contents of the drops, which can contain molecules (DNA, enzymes,...) or cells. Different applications of this platform have been developed in our lab. I will describe measurements of enzyme kinetics on an integrated chip, allowing us to obtain full enzyme activity characterisation rapidly and using minute amounts of reagents. I will also de-

scribe the detection of rare DNA through a digital PCR device based on our microfluidic tools. This device is now being industrialized by a spinout company (Stilla Technologies). Finally, I will describe a massively parallel cell culture platform that will allow the exploration of cellular heterogeneity on a single chip. I will give examples of each of these devices and show some of the potential for droplet microfluidics for transforming the way biology is performed. I will also insist on the interest of the link between fundamental physical science and biotechnological applications.

## Non-inertial lift and its application to label-free microfluidic cell separation and sorting

T. M. Geislinger<sup>ab</sup>, M. Stamp<sup>a</sup>, B. Eggart<sup>a</sup>, S. Braunmüller<sup>a</sup>, L. Schmid<sup>a</sup>, S. Chan<sup>b</sup>, K. Moll<sup>b</sup>, M. Wahlgren<sup>b</sup>, A. Wixforth<sup>a</sup>, and T. Franke<sup>ac</sup>

a) Experimental Physics I, University of Augsburg, 86159 Augsburg, Germany

b) Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Box 280, S-171 77 Stockholm, Sweden

c) Chair of Biomedical Engineering, University of Glasgow, Oakfield Avenue, G12 8LT, Glasgow, Scotland

Reliable cell separation and sorting are important tasks in everyday's laboratory work and of increasing importance in various medical diagnoses. Widely used methods like fluorescence or magnetically activated cell sorting (FACS, MACS), however, require labelling of samples with adequate markers and/or the generation of external fields. Apart from the dimensions and the costs of such devices, any unwanted alterations of the cells by the markers potentially interfere with subsequent processes such as genetic analyses. Here, we present a simple and cheap microfluidic approach for continuous, passive and label-free cell sorting that relies on the exploitation of a hydrodynamic effect for separation: the non-inertial lift effect<sup>[1]</sup>. The non-inertial lift effect is a repulsive cell-wall interaction of purely viscous origin that acts on non-spherical and deformable objects in laminar flow fields. Generally, the lateral drift becomes stronger for larger and more deformable objects. First, we examine the influence of flow rate and external fluid viscosity on the separation of different objects (red blood cells (RBC), blood platelets and latex microspheres) and compare our results with analytical theory<sup>[2,3]</sup>. We then exploit our findings to separate RBCs from the smaller blood plate-

lets as well as blood platelets from the rigid, equally-sized latex microspheres<sup>[2]</sup>. Based on our findings, we design a microfluidic device for non-inertial lift induced cell sorting (NILICS) that operates continuously and label-free, using size and deformability as intrinsic markers. We apply NILICS to sort circulating tumor cells out of RBC solutions by size with sorting efficiencies up to 100%<sup>[4]</sup>. Furthermore, we use the much weaker dependency of the non-inertial lift on deformability to enrich RBCs infected with the malaria parasite *Plasmodium falciparum*<sup>[5]</sup>.

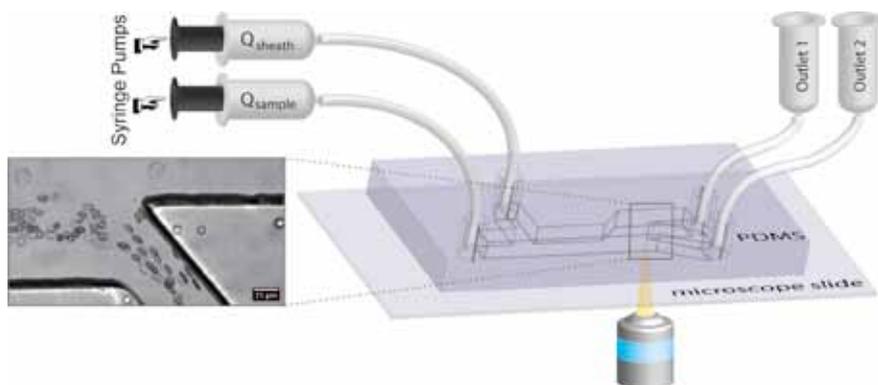
[1] Geislinger, T. M. & Franke, T. Hydrodynamic lift of vesicles and red blood cells in flow--from Fåhræus & Lindqvist to microfluidic cell sorting. *Adv. Colloid Interface Sci.* 208, 161–76 (2014).

[2] Geislinger, T. M., Eggart, B., Braunmüller, S., Schmid, L. & Franke, T. Separation of blood cells using hydrodynamic lift. *Appl. Phys. Lett.* 100, 183701 (2012).

[3] Olla, P. The lift on a tank-treading ellipsoidal cell in a shear flow. *Journale Phys. II* 7, 1533–1540 (1997).

[4] Geislinger, T. M. & Franke, T. Sorting of circulating tumor cells (MV3-melanoma) and red blood cells using non-inertial lift. *Biomicrofluidics* 7, 44120 (2013).

[5] Geislinger, T. M., Chan, S., Moll, K., Wixforth, A., Wahlgren, M., & Franke, T. Label-free microfluidic enrichment of ring-stage *Plasmodium falciparum*-infected erythrocytes using non-inertial hydrodynamic lift. (submitted)



## Single-Molecule Fluorescence on DNA Origami

G.P. Acuna, A. Puchkova, C. Vietz, D. Wang, B. Lalkens, Philip Tinnefeld

*Institute for Physical & Theoretical Chemistry - NanoBioScience, Braunschweig University of Technology, 38106 Braunschweig, Germany*

In recent years, we have combined DNA nanotechnology with single-molecule fluorescence to create functional single-molecule devices such as nanoscopic rulers for superresolution microscopy and energy transfer switches<sup>1-4</sup>. DNA origamis are also used to improve single-molecule detection by fluorescence enhancement with nanoantennas or by single-molecule placement in zeromode waveguides using nanoadapters<sup>5, 6</sup>. Especially, fluorescence enhancement with self-assembled nanoparticles holds great potential for single-molecule detection at higher concentrations but also for diagnostic applications<sup>7, 8</sup>. We will discuss recent advancement in fluorescence enhancement and how to disentangle the complex factors that influence the fluorescence of single molecules near metallic nanostructures<sup>9</sup>.

[1] J. J. Schmied, M. Raab, C. Forthmann, E. Pibiri, B. Wunsch, T. Dammeyer, P. Tinnefeld *Nat Protoc.* 2014, 9, 1367-1391.

[2] J. J. Schmied, C. Forthmann, E. Pibiri, B. Lalkens, P. Nickels, T. Liedl, P. Tinnefeld *Nano Lett.* 2013, 13, 781-785.

[3] J. J. Schmied, A. Gietl, P. Holzmeister, C. Forthmann, C. Stein-

hauer, T. Dammeyer, P. Tinnefeld *Nat Methods.* 2012, 9, 1133-1134.

[4] I. H. Stein, C. Steinhauer, P. Tinnefeld *J Am Chem Soc.* 2011, 133, 4193-4195.

[5] E. Pibiri, P. Holzmeister, B. Lalkens, G. P. Acuna, P. Tinnefeld *Nano Lett.* 2014, 14, 3499-3503.

[6] G. P. Acuna, F. M. Moller, P. Holzmeister, S. Beater, B. Lalkens, P. Tinnefeld *Science.* 2012, 338, 506-510.

[7] P. Holzmeister, G. P. Acuna, D. Grohmann, P. Tinnefeld *Chem Soc Rev.* 2014, 43, 1014-1028.

[8] P. Tinnefeld *Nature nanotechnology.* 2013, 8, 480-482.

[9] J. V. Pellegrotti, G. P. Acuna, A. Puchkova, P. Holzmeister, A. Gietl, B. Lalkens, F. D. Stefani, P. Tinnefeld *Nano Lett.* 2014, 14, 2831-2836.

## FRIDAY, SEPTEMBER 26

## Photo-Induced Charge Carrier Generation in Covalent Organic Frameworks

Florian Auras,<sup>a,b</sup> Mona Calik,<sup>a,b</sup> Laura Salonen,<sup>a</sup> Matthias Handloser,<sup>a,b</sup> Mirjam Dogru,<sup>a,b</sup> Dana Medina,<sup>a,b</sup> Veronika Werner,<sup>a</sup> Dirk Trauner,<sup>a,b</sup> Achim Hartschuh,<sup>a,b</sup> Paul Knochel,<sup>a</sup> Thomas Bein<sup>a,b</sup>

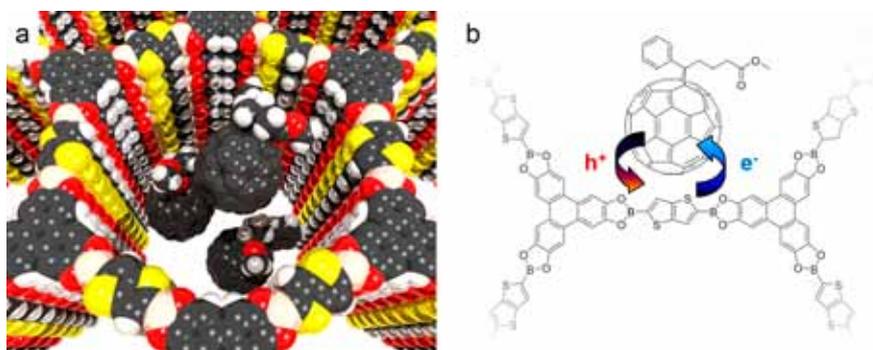
*a* Department of Chemistry, Ludwig-Maximilians-University, Munich, Germany

*b* Center for Nanoscience (CeNS), Ludwig-Maximilians-University, Munich, Germany

Covalent organic frameworks (COFs) offer a strategy to position molecular semiconductors within a rigid network in a highly controlled and predictable way. The  $\pi$ -stacked columns of layered 2D COFs enable electronic interactions between the COF layers, thereby providing a path for exciton and charge carrier transport, while the accessible porous channels allow for infiltration of guest molecules. We have constructed ordered interdigitated heterojunctions by infiltrating thin films of a thienothiophene-containing COF with [6,6]-phenyl C61 butyric acid methyl ester (PCBM) as electron acceptor (Figure 1). Photo-induced charge transfer from the COF to pore-located PCBM molecules was confirmed by strong photoluminescence quenching. Moreover, we used the COF:PCBM junctions as active layer in first COF-based photovoltaic devices.<sup>[1]</sup>

Another strategy for constructing opto-electroactive COFs, which we followed recently, is to combine two complementary semiconductors within the framework. If the energy levels and geometric arrangements are chosen adequately, the framework will consist of ordered columns of molecular donors and acceptors. We have applied this concept to construct a photovoltaic device based on a newly developed triphenylene-porphyrin COF. For the first time, we could demonstrate the generation of extractable charge carriers inside a COF upon illumination.

[1] M. Dogru, M. Handloser, F. Auras, T. Kunz, D. Medina, A. Hartschuh, P. Knochel, T. Bein, *Angew. Chem. Int. Ed.* 2013, 52, 2920-2924.



**Figure 1.** a) The porous COF framework can be infiltrated with fullerene derivatives to create well-ordered interdigitated heterojunctions. b) Upon photoexcitation, electrons are injected into the fullerene phase and holes are transferred to the COF.

## Imaging electron transport in semiconductor nanostructures on the scale of the electron wavelength

Thomas Ihn

*ETH Zurich, Switzerland*

Mesoscopic electron transport arises in semiconductor nano- and microstructures when the temperature is so low that several length scales, such as the elastic mean free path and the phase-coherence length of electrons become comparable to each other and to the system size. Since the field has matured over more than 30 years, a vast number of beautiful experiments and theories exist for understanding and describing the physics in these systems. Recently, an imaging technique has been developed that produces brilliant pictures of mesoscopic systems at the scale of the Fermi-wavelength of the electron. In this talk I will pick a few simple and basic examples from the available mea-

surements to illustrate the imaging principle of this scanning gate technique and its physical meaning. We will see that some fundamental aspects of transport, such as conductance quantization, conductance fluctuations, or adiabatic edge channel transport in the quantum Hall regime can be rediscovered with spatial resolution and that there were unanticipated surprises that still leave open questions today.

# POSTER ABSTRACTS - SESSION I (A-LEE)

<b>Effect of charge and size on molecule diffusion across basal lamina interfaces <i>in vitro</i> and <i>in vivo</i></b> <u>Fabienna Arends</u> , Sabine Sellner, Markus Rehberg and Oliver Lieleg . . . . .	20	<b>Sequence defined oligo(ethanamino)amides for folate receptor targeted pDNA or siRNA delivery: optimization and preliminary structure-activity relationship study</b> <u>Dongsheng He</u> , <u>Ana Krhac Levacic</u> , Katharina Müller, Petra Kos, Dian-Jang Lee, Ernst Wagner . . . . .	26
<b>Covalent Organic Frameworks as Photoconductive Materials</b> Mona Calik, <u>Laura Ascherl</u> , Florian Auras, Dana. D. Medina, Veronika Werner, Maria Lohse, John. T. Markiewicz, Simon Herbert, Paul Knochel and Thomas Bein . . . . .	20	<b>Equilibrium Dynamics of Helical Polymers</b> <u>Lorenz Huber</u> , Philipp Lang, Erwin Frey. . . . .	26
<b>High-throughput force-fluorescence spectroscopy in zero-mode waveguides</b> <u>Fabian Baumann</u> , Stephan F. Heucke, Magnus S. Bauer, Diana A. Pippig, Hermann E. Gaub . . . . .	20	<b>OER catalysis in tin-doped hematite photoanodes for water splitting</b> Halina Dunn, Johann M. Feckl, <u>Alexander G. Hufnagel</u> , Alexander Müller, Dina Fattakhova Rohlfing, Laurie Peter, Christina Scheu, Thomas Bein . . . . .	26
<b>Traceless pH-sensitive coating of viral and non-viral vectors</b> <u>Linda Beckert</u> and <u>Ruth Röder</u> , Jennifer Altomonte, Libor Kostka, Tomas Etrych, Ernst Wagner. . . . .	21	<b>Lipid-like nanoparticles for mRNA delivery</b> <u>Anita Jarzebinska</u> , Tamara Weber, Christian Dohmen, Christian Plank, Carsten Rudolph. . . . .	27
<b>Small Angle X-Ray Scattering for Structural Analysis of Biological Macromolecules</b> <u>Linda Bruetzel</u> and Jan Lipfert . . . . .	21	<b>High-sensitivity measurement of DNA-Protein binding energies by automated fluorescence microscopy</b> <u>Christophe Jung</u> , Peter Bandilla, Mark von Reuter, Susanne Hueneburg, Ulrich Unnerstall and Ulrike Gaul . . . . .	28
<b>Surface acoustic wave induced charge carrier dynamics in single GaAs/AlGaAs radial heterostructure nanowires</b> <u>D. Bühler</u> , M. Weiß, J. B. Kinzel, F. J. R. Schülein, D. Rudolph, M. Bichler, G. Abstreiter, J. J. Finley, A. Wixforth, G. Koblmüller and H. J. Krenner . . . . .	22	<b>Nanoscale arrangements in soft matter films revealed by IR-SNOM</b> C. Westermeier, R. Stabla, <u>D. Kalb</u> , C. Liewald, F. Keilmann, J. Rädler, and B. Nickel. . . . .	28
<b>Photophysics of hybrid organo-halide lead perovskite nanoparticles</b> <u>C. Cardenas-Daw</u> , M. Fu, N. Mutz, A. S. Urban, J. Stolarczyk, J. Feldmann. . . . .	22	<b>Radio frequency acousto-mechanical tuning of a photonic molecule</b> <u>Stephan Kapfinger</u> , Thorsten Reichert, Michael Kaniber, Jonathan J. Finley, Achim Wixforth, and Hubert J. Krenner . . . . .	28
<b>Dose response relation of triplebody mediated cell killing studied in single cell arrays</b> <u>Elisavet I. Chatzopoulou</u> , Farzad Sekhavati, Todd A. Braciak, Georg H. Fey, Joachim O. Rädler. . . . .	22	<b>Regulation of nanoparticle diffusion in the vitreous humor</b> <u>Benjamin Käsdorf</u> , Fabienna Arends, and Oliver Lieleg . . . . .	29
<b>Fourier Space Imaging of Raman Scattering Intensities in Graphene</b> Harald Budde, <u>Nicolás Coca López</u> , Xian Shi, and Achim Hartschuh . . . . .	23	<b>Heat driven selection of nucleic acids</b> <u>Lorenz M. R. Keil</u> , Simon A. Lanzmich, Moritz Kreysing and Dieter Braun. . . . .	29
<b>Ultrastable Cellulosome-Adhesion Complex Tightens Under Load</b> Constantin Schoeler, Klara H. Malinowska, Rafael C. Bernardi, Lukas F. Milles, Markus A. Jobst, <u>Ellis Durner</u> , Wolfgang Ott, Daniel B. Fried, Edward A. Bayer, Klaus Schulten, Hermann E. Gaub and Michael A. Nash . . . . .	23	<b>Infrared hyperspectral mapping of nano-composites</b> Sergiu Amarie, Dominik Kalb, <u>Fritz Keilmann</u> , Clemens Liewald, Bert Nickel, Joachim Rädler, Robert Stabla, Christian Westermeier. . . . .	30
<b>Energy transfer involving core and surface states of carbon dots</b> <u>M. Fu</u> , F. Ehrat, Y. Wang, A.L. Rogach, J.K. Stolarczyk, A.S. Urban, J. Feldmann . . . . .	24	<b>Magnetic (Torque) Tweezers Experiments to Probe the Mechanics and Interactions of Nucleic Acids</b> <u>Franziska Kriegel</u> and Jan Lipfert . . . . .	30
<b>Kramers Escape Problem for Self-Propelled Particles</b> <u>A. Geiseler</u> , P. Hänggi, and G. Schmid . . . . .	24	<b>Microfluidic assisted self-assembly of folate-targeted Monomolecular siRNA-lipid Particles</b> <u>R. Krzyszton</u> , B. Salem, G. Schwake, C. Leonhardt, K. Müller, E. Wagner, J. O. Rädler . . . . .	31
<b>A spectral method for coupled diffusion and gene regulation</b> <u>Raphaela Geßele</u> , Steffen Rulands, Johannes Knebel and Erwin Frey . . . . .	24	<b>Combination of a polymer-based transfection system with modified mRNA to enhance transfection <i>in vitro</i></b> <u>Jana Lambrecht</u> , Mehrije Ferizi, Christian Dohmen, Christian Plank, Carsten Rudolph . . . . .	31
<b>Nanostructuring for new perovskite solar cell absorber materials</b> <u>Fabian Hanusch</u> , Benjamin Mandlmeier, Alesja Ivanova, Pablo Docampo, Thomas Bein . . . . .	25	<b>A Thermal, Autonomous Replicator Made from Transfer RNA</b> <u>Simon A. Lanzmich</u> , Hubert Krammer, Friederike M. Möller and Dieter Braun . . . . .	31
<b>Detection of the Plasmonic Circular Dichroism Signal of Chiral Molecules Self-Assembled in a Plasmonic Hotspot of Gold Nanoparticles by DNA-Origami</b> E.- M. Roller, <u>C. Hartl</u> , R. Schreiber, T. Zhang, T. Liedl. . . . .	25	<b>Nanosized Polyplexes with Dual-Functional MTX Ligand for Enhanced Combined Cytotoxicity with Therapeutic Eg5 siRNA</b> <u>Dian-Jang Lee</u> , Ulrich Lächelt, Daniel Edinger, Dongsheng He, Taavi Lehto, Ernst Wagner . . . . .	32

# POSTER ABSTRACTS - SESSION I (LI-Z)

- Optical printing and injection of gold nanoparticles into living cells**  
M. Li, T. Lohmüller, and J. Feldmann . . . . . 33
- Polarimetry of Exciton Landscapes in Monolayer MoS<sub>2</sub>**  
J. Lindlau, A. Neumann, H. Yamaguchi and A. Högele. . . . . 33
- High stress levels lead to transition from heterogeneous timing to synchronized cellular response of the *E.coli* Colicin E2 operon**  
Andreas Mader, Benedikt von Bronk, Benedikt Ewald, Sara Kesel, Karin Schnetz, Erwin Frey and Madeleine Opitz . . . . . 33
- A separation of powers - force and function of the versatile cohesin-dockerin interaction**  
Lukas F. Milles, Wolfgang Ott, Ellis Durner, Markus A. Jobst, Klara H. Malinowska, Constantin Schöler, Tobias Verdorfer, Michael A. Nash, Hermann E. Gaub . . . . . 34
- Polymerization and protection of nucleic acids in a prebiotic environment**  
Matthias Morasch, Dieter Braun and Christof B. Mast. . . . . 34
- Chemiluminescence of an anthracene-based UiO-68**  
S. Wuttke, B. Rühle, E. Mühlbauer, F. Hinterholzinger, P. Roy, A. Godt, T. Bein . . . . . 35
- Mechanics of dimeric von Willebrand Factor under varied pH conditions probed by Single Molecule Force Spectroscopy (AFM)**  
Jochen P. Müller, Tobias Obser, Reinhard Schneppenheim, Martin Benoit . . . . . 35
- Conductivity in Polymeric Electrode for Roll-to-Roll Printed Organic Electronics: Evolution of Nanostructure and Molecular Orientation in PEDOT:PSS**  
C.M. Palumbiny, C. Heller, C.J. Schaffer, V. Körstgens, G. Santoro, F. Liu, C. Wang, A. Hexemer, T.P. Russell, S.V. Roth, P. Müller-Buschbaum . . . . . 36
- Identification of siloxane mechanochemistry with single molecule force spectroscopy and ab initio simulations**  
Michael F. Pill, Alfred Kersch, Martin K. Beyer, and Hauke Clausen-Schaumann . . . . . 37
- Lissajous rocking ratchet in quantum dots**  
Sergey Platonov, Bernd Kästner, Hans W. Schumacher, Sigmund Kohler and Stefan Ludwig. . . . . 37
- Facilitated diffusion mechanism of microtubule polymerases**  
Emanuel Reithmann, Louis Reese, Erwin Frey. . . . . 38
- Nanoscale DNA origami based plasmonic ring structures**  
Eva-Maria Roller, Larousse K. Khorashad, Michael Fedoruk, Robert Schreiber, Jochen Feldmann, Alexander O. Govorov, Tim Liedl. . . 38
- Novel thermoelectric films based on polymer-nanoparticle composite**  
N. Saxena, A. Greppmair, M. Coric, J. Wernecke, S. Marggraf, E. M. Herzig, M. S. Brandt, P. Müller-Buschbaum. . . . . 39
- Non-equilibrium transport through a QD using Keldysh-FRG 1**  
Dennis Schimmel, Jan Heyder, Florian Bauer, Jan v. Delft. . . . . 39
- Click chemistry – a versatile method for enzyme immobilization in large pore colloidal mesoporous silica nanoparticles**  
Alexandra Schmidt, Martina Lichtnecker, Kathrin Bader, Stefan Niedermayer and Thomas Bein . . . . . 39
- Characterizing Cell Motility and Transmigration in Ring Shaped Micro Patterns**  
C. Schreiber, F. J. Segerer, J. O. Rädler. . . . . 40
- Models for Angiogenesis on microstructured surfaces**  
Simon Schuster, Kerstin Pflieger, Florian Gegenfurtner, Max Albert, Felix Segerer, Joachim Rädler, Angelika M. Vollmar and Stefan Zahler. . . . . 40
- DNA Nanotubes as Intracellular Delivery Vehicles *in vivo***  
S. Sellner, S. Kocabey, A. K. Nekolla, F. Krombach, T. Liedl, and M. Rehberg . . . . . 40
- Tip-enhanced Raman Spectroscopy (TERS) – Excitation Power Dependence?**  
Xian Shi, Tobia Mancabelli, Harald Budde, Alexandre Bouhelier, Achim Hartschuh . . . . . 41
- Cell manipulation using Surface Acoustic Waves**  
Melanie Stamp, Christoph Westerhausen, Achim Wixforth . . . . . 41
- Game Theory on the Nanoscale**  
Georg Urtel, Dieter Braun and André Estévez-Torres. . . . . 41
- Microparticle formulation of mRNA for sustained protein production in cells**  
Maximilian Utzinger, Christian Dohmen, Christian Plank, and Carsten Rudolph . . . . . 42
- From Genes to Protein Mechanics on a Chip**  
Tobias Verdorfer, Marcus Otten, Wolfgang Ott, Markus A. Jobst, Lukas F. Milles, Diana Pippig, Hermann E. Gaub, and Michael A. Nash . . . . . 42
- Mesoporous silica nanoparticles as drug delivery platforms**  
Veronika Weiss, Alexandra Schmidt, Christian Argyo, Stephan A. Mackowiak, Stefan Datz, Constantin von Schirnding, Thomas Bein, Christoph Bräuchle . . . . . 43
- Conformational changes of Sti1 when Hsp70 or/and Hsp90 bind**  
Daniela Wengler, Alina Röhl, Jelle Hendrix, Johannes Buchner, Don C. Lamb . . . . . 44
- Double Gate Organic Thin Film Transistors on Thin Foils for Biosensing**  
Franz Werkmeister, Teru Koide, Bert Nickel. . . . . 44
- Manipulation of cell proliferation and migration using surface acoustic waves**  
Christoph Westerhausen, Manuel Brugger, Melanie Stamp, and Achim Wixforth. . . . . 45
- Synthesis of nanostructured metal oxide electrodes for electrochemical lithium insertion**  
Peter M. Zehetmaier, Ksenia Fominykh, Johann M. Feckl, Dina Fattakhova-Rohlfing, Thomas Bein. . . . . 45
- Flow and diffusion in channel-guided cell migration**  
Anna-Kristina Marel, Matthias Zorn, Christoph Klingner, Roland Wedlich-Söldner, Erwin Frey and Joachim O. Rädler . . . . . 45

## Effect of charge and size on molecule diffusion across basal lamina interfaces in vitro and in vivo

**Fabienna Arends<sup>1,2</sup>, Sabine Sellner<sup>3</sup>, Markus Rehberg<sup>3</sup> and Oliver Lieleg<sup>1,2</sup>**

<sup>1</sup> Zentralinstitut für Medizintechnik, Technische Universität München, Boltzmannstrasse 11, 85748 Garching (Germany)

<sup>2</sup> Fakultät für Maschinenwesen, Technische Universität München, Boltzmannstrasse 15, 85748 Garching (Germany)

<sup>3</sup> Walter Brendel Zentrum, Ludwig-Maximilians-Universität München, Marchioninistr. 15, 81377 München (Germany)

The permeability of the basal lamina, a biological hydrogel found at the basolateral side of the endothelium, is an important property for the design of new drug delivery systems. During inflammation, the endothelium becomes leaky and molecules can directly pass from the blood stream into the basal lamina. In such a situation, the basal lamina constitutes the main barrier against the efficient entrance of drug carriers from the blood stream into the connective tissue. Therefore, it is highly desirable to understand which parameters dictate diffusion processes across the blood-basal lamina interface. Here, we quantify the diffusion of dextran and peptides of dif-

ferent size and charge across a buffer-basal lamina interface using a microfluidics approach. As a model system for the basal lamina, we study an extracellular matrix gel (ECM) purified from the Engelbreth-Holm-Swarm sarcoma of mice. We measure the formation of a concentration gradient of solutes across the ECM phase and compare our findings with in vivo experiments obtained in living mice. From our data, we aim at deciphering the important parameters responsible for the permeability properties of the hydrogel. Our results can guide the design of new drug carriers which can efficiently diffuse from the blood stream into the connective tissue.

## Covalent Organic Frameworks as Photoconductive Materials

**Mona Calik, Laura Ascherl, Florian Auras, Dana. D. Medina, Veronika Werner, Maria Lohse, John. T. Markiewicz, Simon Herbert, Paul Knochel and Thomas Bein\***

University of Munich, Department of Chemistry and Center for NanoScience (CeNS), Butenandtstr. 5-13, 81377 Munich, Germany, Tel.: +49(0)89-2180-77623, \*E-mail: bein@lmu.de

Covalent organic frameworks (COFs) have recently been developed as a new class of porous and crystalline materials with interesting and tunable physical and chemical properties.[1] Up to now, COFs can be achieved mainly by boronate ester formation, imine condensation or  $\beta$ -ketoenimine formation. Lately, two-dimensional COFs have attracted interest as potential candidates for the production of new photoactive materials.[2] The  $\pi$ -interactions between the COF-layers allow for the formation of highly oriented films with host channels. These defined channels are accessible and can incorporate small guest molecules.[3] Here we present the two major approaches for the preparation of photoactive electron-donor-electron-acceptor COFs. The first route is based on the formation of highly ordered electron donor-acceptor interpenetrated systems, in which electron-donor COF films host electron-acceptor molecules such as C60 derivatives.[4] The second approach involves photoconductive COFs providing both electron-donating and electron-accepting subunits. Due to the  $\pi$ -stacked layers, these donor-acceptor-COFs

(D-A-COFs) exhibit highly ordered pillars of donor as well as acceptor entities that permit charge transfer within the COF and charge transport in the third dimension.[5]

[1] A. P. Côté, A. I. Benin, N. W. Ockwig, A. J. Matzger, M. O'Keeffe, O. M. Yaghi, *Science* 2005, 310, 1166–1170.

[2] M. Dogru, T. Bein, *Chem. Commun.* 2014, 50, 5531–5546.

[3] L., K. Furukawa, J. Gao, A. Nagai, T. Nakamura, Y. Dong, D. Jiang, *J. Am. Chem. Soc.* 2014.

[4] D. D. Medina, V. Werner, F. Auras, R. Tautz, M. Dogru, J. Schuster, S. Linke, M. Döblinger, J. Feldmann, P. Knochel, T. Bein, *ACS Nano* 2014, 8 (4), 4042–4052.

[5] S. Jin, K. Furukawa, M. Addicoat, L. Chen, S. Takahashi, S. Irle, T. Nakamura, D. Jiang, *Chem. Sci.* 2013, 4, 4505–4511.

## High-throughput force-fluorescence spectroscopy in zero-mode waveguides

**Fabian Baumann, Stephan F. Heucke, Magnus S. Bauer, Diana A. Pippig, Hermann E. Gaub**

Center for Nanoscience & Physics Department, University of Munich, Amalienstrasse. 54, 80799 Munich, Germany.

In the last years zero-mode waveguides (ZMW) emerged as an important tool to overcome the concentration limit of optical single-molecule detection. Via their subwavelength geometry in opaque metallic films they prohibit light propagation inside their cavity and hence are capable to confine excitation volumes of conventional optical microscopes drastically. This allows coping with high concentrations of fluorescently labeled ligands as necessary in single-enzyme experiments to monitor their biochemical activity (e.g. DNA real time sequencing). Complementary, mechanical experiments with single-molecule resolution and piconewton sensitivity provide control over a second but important parameter in molecular interactions: force.

First combinations of these strong single-molecule properties, fluorescence and mechanics, provide enormous possibilities in mechanoenzymatic research. Our group addresses the employment of nanoapertures for AFM-based force spectroscopy to establish simultaneous single-molecule fluorescence-force spectroscopy at high fluorescent ligand concentrations. In a proof-of-principle experiment the analysis of a probable single binding event in a force-activated enzyme (Titin Kinase) has been shown in a ZMW. The methodology is further improved by the implementation of non-invasive tip localization routines to provide automated data acquisition at rates similar to those in standard force spectroscopy. Whereas light incident on the

thin cantilever is transmitted with some losses, the fraction of light incident on its high-aspect ratio tip is strongly absorbed. Live superresolution methods applied on this absorption signal are able to securely and centrally navigate the cantilever into a ZMW with an accuracy of few nanometers. The application of

high-throughput force-fluorescence spectroscopy in nanoapertures is promising for investigating the mechano-activation of kinases by high-yield recording of fluorescent ATP-binding or of minimum phosphorylation peptides under mechanical stress.

## Traceless pH-sensitive coating of viral and non-viral vectors

**Linda Beckert<sup>1</sup> and Ruth Röder<sup>1</sup>, Jennifer Altomonte<sup>2</sup>, Libor Kostka<sup>3</sup>, Tomas Etrych<sup>3</sup>, Ernst Wagner<sup>1</sup>**

*1 Pharmaceutical Biotechnology, Center for System-based Drug Research, Department of Pharmacy, Butenandtstraße 5-13, Building D, 81377 München, GERMANY.*

*2 II. Medical Department, Klinikum rechts der Isar at TU Munich, Ismaningerstraße 22, 81675 München, GERMANY*

*3 Centre for Biomacromolecular and Bioanalogous Systems, Department of Biomedical Polymers, Institute of Macromolecular Chemistry Academy of Sciences CR, v.v.i., Heyrovského sq. 2, Prague, Czech Republic. E-mail:kostka@imc.cas.cz*

The successful implementation of oncolytic viruses or nucleic acids as medical agent depends on the delivery efficiency. Therefore, non-viral delivery systems have been developed to protect nucleic acids by compacting the negative charged nucleic acids into particles of virus-like dimensions. Alternatively, oncolytic virus vectors have emerged as novel natural tool to target and cause cytolysis of cancer cells [1]. Despite many advances on the vector development front, systemic delivery remains a major bottleneck. Nonspecific interactions with cells of the immune system as well as blood proteins and rapid clearance by liver and spleen have to be prevented. This can be overcome by the usage of shielding agents such as PEG (polyethylene glycol) and HPMA (N-(2-Hydroxypropyl)methacrylamide) [2]. However, irreversible surface shielding can lead to inactivation in case of oncolytic virus and endosomal entrapment in case of a polymeric carrier system. A promising method of improving the efficacy by overcoming these boundaries is the creation of vectors that are bioresponsive, so that transfer is enabled by cleavage of chemical bonds upon exposure to various physiological environments. Here, we present an approach where the delivery systems are reversible shielded with PEG or HPMA connected via a universal attachable tool called AzMMMan (azidomethyl-methylmaleic

anhydride) [3], which can be attached to any carrier via primary amino groups. After the delivery systems enter an acidic environment (tumor tissue or endosome), a pH-labile bond is broken, releasing the functional virus or the vectors endosomolytic capability. We hypothesize that this approach proposed here will significantly enhance the transduction efficiency of systemically applied viral and non-viral delivery systems by avoiding unspecific interactions, hence prolonging circulation and therefore providing a substantial benefit to the clinical translation of these vectors as potent medical agent.

[1] J. Altomonte, O. Ebert, *Sorting out Pandora's box: discerning the dynamic roles of liver microenvironment in oncolytic virus therapy for hepatocellular carcinoma*, *Front Oncol.*, 4(2014), 1-10

[2] L. Kostka, C. Konák, V. Šubr, M. Špírková, Y. Addadi, M. Neeman, T. Lammers, K. Ulbrich, *Removable nanocoatings for siRNA polyplexes*, *Bioconjug Chem.*, 22 (2011) 169-179

[3] K. Maier, E. Wagner, *Acid-labile traceless click linker for protein transduction*, *J. Am. Chem Soc.*, 134 (2012), 10169-10173

## Small Angle X-Ray Scattering for Structural Analysis of Biological Macromolecules

**Linda Bruetzel and Jan Lipfert**

*Department of Physics, Nanosystems Initiative Munich, and Center for NanoScience, LMU Munich, Amalienstr.54, 80799 Munich (Germany)*

Small angle X-ray scattering (SAXS) is a powerful technique to unravel the structure and interactions of biological macromolecules such as proteins and nucleic acids with a size of kDa up to GDa. In contrast to X-ray crystallography, the molecules are studied in solution allowing for time-resolved investigations and measurements under a broad range of solution conditions, including (near-) physiological environments. Thereby, only small sample volumes (10 - 30  $\mu$ l) and moderate protein concentrations (~ 1 mg/ml) are required. SAXS experiments are routinely performed at state-of-the-art 3rd generation synchrotron X-ray sources. As a complimentary approach we present an in-house setup for SAXS measurements, which we are currently developing in collaboration with the lab of Bert Nickel and Joachim Rädler. As a proof-of-concept, we are employing both double stranded DNA and proteins such as cytochrome c and lysozyme used previously as scattering standards.

Using SAXS we want to study the conformational changes of the large blood glycoprotein von Willebrand factor (vWF), which plays an important role in hemostasis and thrombosis. Recent studies could show that vWF undergoes regulating conformational changes at different hemodynamic conditions. SAXS measurements have the potential to provide further insight into pH-dependent structural dynamics of vWF. In addition, we describe how SAXS data can be used for the ab initio reconstruction of low-resolution (30-10 Å) 3-D models of biomolecules and their assemblies. In this context, we will perform SAXS measurements in order to characterize nucleic acids (RNA, DNA). In addition, gold nanocrystals, which can be attached site-specifically to the DNA will be utilized in order to obtain molecular distance distributions.

### Surface acoustic wave induced charge carrier dynamics in single GaAs/AlGaAs radial hetero-structure nanowires

**D. Bühler<sup>1</sup>, M. Weiß<sup>1,3</sup>, J. B. Kinzel<sup>1,3</sup>, F. J. R. Schülein<sup>1,3</sup>, D. Rudolph<sup>2,3</sup>, M. Bichler<sup>2</sup>, G. Abstreiter<sup>2,3,4</sup>, J. J. Finley<sup>2,3</sup>, A. Wixforth<sup>1,3</sup>, G. Koblmüller<sup>2,3</sup> and H. J. Krenner<sup>1,3</sup>**

*1 Lehrstuhl für Experimentalphysik 1 / Universität Augsburg, 86159 Augsburg, Germany*

*2 Walter Schottky Institut / TU München, 85748 Garching, Germany*

*3 Nanosystems Initiative Munich (NIM), 80779 München, Germany*

*4 Institute for Advanced Study (IAS) / TU München, 85748 Garching, Germany*

We investigate the influence of the dynamic electric fields induced by a surface acoustic wave (SAW) on the optical emission of single semiconductor nanowires (NW) via the use of microphotoluminescence ( $\mu$ -PL) spectroscopy. The investigated nanowires consist of a GaAs core surrounded by an AlGaAs shell containing an additional 3nm wide radial GaAs quantum well (QW). For both, the core and the radial QW, we observe clear signatures of acousto-electric exciton dissociation and convey-

ance of electrons and holes. This method enables us to locally and contactlessly observe the electrical field induced carrier dynamics and make conclusions about the underlying mobilities of electrons and holes for both the core and the quantum well of the nanowire. Moreover, at high laser excitation powers and thus high charge carrier concentrations we observe an attenuation of this effect pointing to a screening effect of the piezoelectric fields caused by an increase of the charge carrier density.

### Photophysics of hybrid organo-halide lead perovskite nanoparticles

**C. Cardenas-Daw, M. Fu, N. Mutz, A. S. Urban, J. Stolarczyk, J. Feldmann**

*Photonics and Optoelectronics Group, Ludwig-Maximilians-Universität (LMU), Munich (Germany)*

Hybrid organo-halide lead perovskites have raised great expectations in recent years due to their application as light harvesters in solar cells, resulting in promising energy-conversion efficiencies which are being improved at a remarkably fast pace. The simple and cost-effective construction of these devices appears as a viable option over current technologies which require the energy-intensive fabrication of highly crystalline materials. To understand the principles behind the performance of organo-halide lead perovskites, it is fundamental to study their photophysical properties at the single crystal level. For this purpose, we have synthesized perovskite nanoparticles by means of a

simple colloidal precipitation process. Homogeneous solutions of the precursor ions are slowly destabilized by the addition of poor solvents which are miscible with the continuous medium. This triggers the instantaneous formation of nano-sized crystals in a metastable colloidal state, which are immediately fixed to a substrate before further growth and destabilization takes place. The variation of concentrations and solvent ratios results in the formation of crystals of different sizes. This allows the photophysical study of crystals and assemblies of different sizes by means of single-particle photoluminescence spectroscopic techniques.

### Dose response relation of triplebody mediated cell killing studied in single cell arrays

**Elisavet I. Chatzopoulou<sup>1</sup>, Farzad Sekhavati<sup>1</sup>, Todd A. Braciak<sup>2</sup>, Georg H. Fey<sup>3</sup>, Joachim O. Rädler<sup>1</sup>**

*1 Faculty of Physics, Ludwig-Maximilians-University, Munich, Germany*

*2 Division of Hematology and Oncology, Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, Ziemssenstrasse 1, D-80336 Munich, Germany*

*3 Chair of Genetics, University of Erlangen-Nuremberg, Erlangen*

Monoclonal antibody therapy is a promising strategy to treat cancer with the help of the patient's own immune system. Recent studies in the case of acute myeloid leukemia (AML) have shown that single chain triplebodies that recognize two epitopes on the cancer target cell provide more effective elimination. Here we study the potency of triplebody (SPM-2) to direct NK cells against cancer using single cell arrays of model target cells. Using fluorescence indicators and time-lapse microscopy the fraction of cells killed in the presence of NK cells is determined in an automated high-throughput modality. The approach

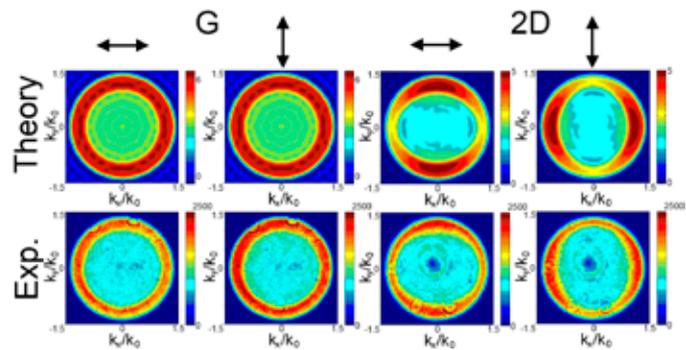
allows to determine the killing fraction as a function of SPM-2 concentration as well as a function of effector-target (ET) cell number ratio. Our results demonstrate the potential of microstructured cell arrays for quantitative studies on the interplay between the immune system and cancer cells and its antibody mediated manipulation.

## Fourier Space Imaging of Raman Scattering Intensities in Graphene

Harald Budde, Nicolás Coca López, Xian Shi, and Achim Hartschuh

Department Chemie und CeNS, LMU, München(Germany)

Raman spectroscopy has proven to be a very powerful tool for the characterization of different properties of graphene, such as identification of the number of layers, defects, strain, etc. [1]. Here, we report on the angular distribution of the emission of the Raman signal of graphene on glass. In general, the orientation of an emitting dipole is directly encoded in the spatial distribution of the emitted light. Fourier space imaging, also known as back focal plane imaging, allows to uniquely reconstruct this orientation from emission patterns [2]. The Raman emission from graphene can be explained by assuming point-dipolar emitters, despite graphene's extended two dimensional structure. Parameter free quantitative model calculations are presented in agreement with polarization dependent measurements. We observe that the intensity of the double-resonant 2D band of graphene is maximized when the excitation and detection polarizations are parallel and minimized when they are orthogonal, whereas that of the G band is isotropic. This is expected from polarization dependent Raman measurements [3]. Furthermore, the detection efficiency in microscopic Raman measurements is extracted from calculated patterns and is in agreement with the experimental data. In conclusion, our present work suggests back focal plane imaging as useful tool for studying the emission characteristics of nanomaterials.



Fourier space imaging of Raman scattering intensities in graphene. Comparison between experimental and theoretical back focal plane emission patterns for both G and 2D Raman signals. The arrows indicate the excitation polarization.

[1] Ferrari et al., *Nature Nanotechnology*, Vol. 8, April 2013

[2] Lieb et al., *J. Opt. Soc. Am. B*, Vol. 21, No. 6, 2004

[3] Yoon et al., *Nano Lett.*, Vol 8, No. 12, 2008

## Ultrastable Cellulosome-Adhesion Complex Tightens Under Load

Constantin Schoeler<sup>1,†</sup>, Klara H. Malinowska<sup>1,†</sup>, Rafael C. Bernardi<sup>2</sup>, Lukas F. Milles<sup>1</sup>, Markus A. Jobst<sup>1</sup>, Ellis Durner<sup>1</sup>, Wolfgang Ott<sup>1</sup>, Daniel B. Fried<sup>3</sup>, Edward A. Bayer<sup>3</sup>, Klaus Schulten<sup>2,4</sup>, Hermann E. Gaub<sup>1</sup> and Michael A. Nash<sup>1</sup>

<sup>1</sup> Lehrstuhl für Angewandte Physik and Center for Nanoscience, Ludwig-Maximilians-Universität, 80799 Munich, Germany.

<sup>2</sup> Theoretical and Computational Biophysics Group, Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, United States.

<sup>3</sup> Department of Biological Chemistry, The Weizmann Institute of Science, Rehovot 76100, Israel.

<sup>4</sup> Department of Physics, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, United States.

† Equally contributing.

Conversion of biomass into fermentable sugars for biofuel production currently relies on soluble free enzymes secreted by cellulolytic microorganisms. Certain bacteria, however, produce large, modular, multi-enzyme networks called cellulosomes to more efficiently degrade lignocellulose. While network assembly is enabled by protein interactions with commonplace affinities, we show that certain cell wall associated receptor-ligand interactions prove to be extremely resilient to applied force. Through single molecule force spectroscopy and steered molecular dynamics simulations, we characterized the ligand-receptor complex which tethers the cellulosome bearing bacterium *Ruminococcus flavefaciens* to its substrate. The complex withstood forces of 600-750 pN, representing the strongest bimolecular interaction reported to date, equivalent to half the mechanical strength of a covalent bond. Our findings indicate inter-domain

stabilization of the complex and suggest that certain network components serve as mechanical effectors for maintaining network integrity. This detailed understanding of cellulosomal network components could help in the future development of biocatalysts for production of fuels, chemicals, and pharmaceuticals from renewable plant-derived biomass.

## Energy transfer involving core and surface states of carbon dots

**M. Fu,<sup>1</sup> F. Ehrat,<sup>1</sup> Y. Wang,<sup>2</sup> A.L. Rogach,<sup>2</sup> J.K. Stolarczyk,<sup>1</sup> A.S. Urban,<sup>1</sup> J. Feldmann<sup>1</sup>**

*1 Photonics and Optoelectronics Group, Department of Physics and CeNS, Ludwig-Maximilians-Universität München, Amalienstrasse 54, D-80799 München, Germany*

*2 Department of Physics and Materials Science and Centre for Functional Photonics (CFP), City University of Hong Kong, Hong Kong SAR*

Carbon dots<sup>[1,2]</sup> (CDs) have attracted fast growing interest due to their exceptional advantages such as high fluorescence quantum yield, chemical stability, biocompatibility, and low toxicity. Recently the fluorescent CDs have been used for bioimaging, photocatalysis, photovoltaics, as light-emitting diodes, and for lasing. However, due to the complex structure of CDs, the intrinsic mechanism and origin of the fluorescence in CDs have not yet been completely understood. Herein, by utilizing static and transient fluorescence spectroscopy, the energy transfer mechanisms in fluorescent CDs were investigated. Our results show that the fluorescence of CDs comes from two types of states: core states, located in the carbon sp<sup>2</sup> domains inside the CDs, and surface states, located at passivated sites mainly at the surface of the CDs. After excitation of an electron-hole pair in a core-state the energy can either decay radiatively, or can trans-

fer to a surface state and then decay radiatively, albeit at a lower energy. Gradually shifting the excitation wavelength leads to an abrupt change in the emission wavelength, as the surface states can also be directly excited for wavelengths longer than 450 nm. These results provide insight into the internal structure of the CDs, in particular of their light emitting components, and will also help in applying these structures in wavelength-tunable nanolasers or light-emitting diode.

[1] S. Zhu, Q. Meng, L. Wang, J. Zhang, Y. Song, H. Jin, K. Zhang, H. Sun, H. Wang, B. Yang, *Angew. Chem. Int. Ed.* 2013, 52, 3953–3957.

[2] Y. Wang, S. Kalytchuk, Y. Zhang, H. Shi, S. V. Kershaw, A. L. Rogach, *J. Phys. Chem. Lett.* 2014, 5, 1412–1420

## Kramers Escape Problem for Self-Propelled Particles

**A. Geiseler, P. Hänggi, and G. Schmid**

*Augsburg University, Germany*

In the poster presentation, the dynamics of an active Brownian particle in an attractive harmonic potential is investigated. Within a 1D constant speed modeling of the particle's dynamics we consider the stationary probability distribution using both numerical and analytical approaches. By means of the results obtained hereby, subsequently the escape problem of a self-propelled particle from a metastable potential well is considered, which is discussed in detail in Ref. [1] for the case of a vanishing self-propulsion. Regarding the properties of the stationary state in a harmonic potential, two major timescales are found, governing each the translational and the rotational dynamics of the particle. Here, the particle radius is identified to be the essential quantity regu-

lating the ratio between those timescales. For very small and very large particle radii, as well as for weak propulsion forces, approximate analytic expressions for the stationary probability distribution of the particle are derived. These analytic results compare favorably with exact numeric outcomes. Moreover, with respect to Kramers' escape problem, the analytical approximations prove to be quite beneficial, since—within their respective range of validity—the thereby obtained expressions for the escape rate coincide well with numerical findings.

[1] P. Hänggi, P. Talkner, and M. Borkovec, *Rev. Mod. Phys.* 62, 251 (1990).

## A spectral method for coupled diffusion and gene regulation

**Raphaela Geßele, Steffen Rulands, Johannes Knebel and Erwin Frey**

*Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Department of Physics, Ludwig-Maximilians-Universität München, Germany*

The first step in the early development of an embryo is the establishment of spatial patterns of transcription factors which dictate the differentiation of cells in later stages of development. The concentration of transcription factors at cell nuclei during the development of a *Drosophila melanogaster* embryo is determined by coupled diffusion and gene regulation processes. Due to the small copy numbers of transcription factors and the random nature of reactions this morphogenesis is intrinsically stochastic. Conventionally, such a stochastic dynamics is studied by sampling from a large number of numerical simulations based on drawing pseudo-random numbers. However, for space dependent systems these methods are computationally very costly. Here we develop a method that allows inferring solutions of stochastic gene regulation cascades in a discretized space. Spe-

cifically, instead of only considering a single cell nucleus we are here interested in the behavior of many cells which are diffusively coupled. On the contrary to conventional methods the developed procedure follows an approach which solves for the probability distribution directly without sampling. Employing methods from quantum mechanics the master equation is expanded in its eigenbasis. A mapping scheme makes it possible to also solve for spatial degrees of freedom. For a system where the first gene regulates itself and also regulates the second gene at two cell nuclei coupled by diffusion of one species the spectral method has proven fruitful. This system could help the further in-depth investigation of the Bicoid-Hunchback interaction in the early embryo of *Drosophila*.

## Nanostructuring for new perovskite solar cell absorber materials

**Fabian Hanusch, Benjamin Mandlmeier, Alesja Ivanova, Pablo Docampo, Thomas Bein\***

*Department of Chemistry and Center for NanoScience (CeNS), University of Munich (LMU), Germany \*E-mail: bein@lmu.de*

Alkylammonium metal trihalide perovskite absorbers have garnered a considerable amount of interest recently in the photovoltaics community. Devices fabricated from these materials achieve very high power conversion efficiencies, already superior to amorphous Si. Although very efficient devices based on planar heterojunction architecture, where the perovskite film is sandwiched between charge selective contacts, have been recently reported,<sup>[1]</sup> the most efficient devices still require a mesoporous charge extraction layer. This is often attributed to an insufficient charge diffusion length and therefore incomplete extraction of the photogenerated charges. New perovskite materials – prepared by substituting either the halide or the metal atom – often exhibit charge collection limitations. This can be overcome by using a nano- or meso-structured titania scaffold as electron collecting anode, where the distance that needs to be travelled by the charge carriers is then reduced to the pore size of the scaffold – typical-

ly a few 10 nanometers. This could be of special importance when looking for a substitute of the toxic lead component. We propose that for new perovskite absorber material screening, it will be necessary to first incorporate them in a porous scaffold and step by step optimize the system until the charge transport properties are sufficient and there is no need for a structured electron selective layer. For this purpose we designed custom tunable titania nanostructures with pore sizes between a few 10 and hundreds of nanometers, depending on the charge carrier diffusion length in the perovskite material to be optimized.<sup>[2]</sup>

[1] Docampo et al, *Adv. Energy Mater.* 2014, DOI: 10.1002/aenm.201400355.

[2] Ivanova et al, *J. Am. Chem. Soc.* 2014, 136, 5930-5937; Mandlmeier et al, *J. Am. Chem. Soc.* 2011, 133, 17274-17282.

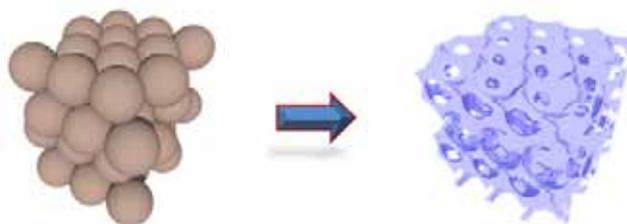
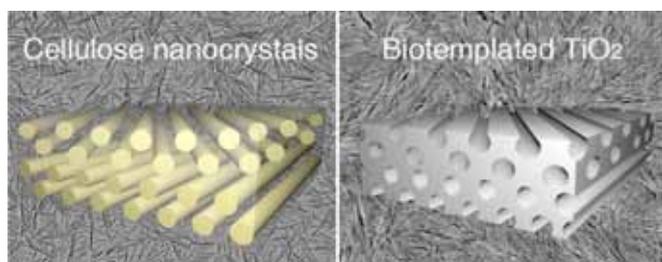


Figure 1: left: Titania structured with cellulose nanocrystals (pore size 8 – 15 nm); right: inverse opal structure of titania, templated with PMMA spheres (pore size: 20 – 200 nm).

## Detection of the Plasmonic Circular Dichroism Signal of Chiral Molecules Self-Assembled in a Plasmonic Hotspot of Gold Nanoparticles by DNA-Origami

**E.- M. Roller<sup>1</sup>, C. Hartl<sup>1</sup>, R. Schreiber<sup>2</sup>, T. Zhang<sup>1</sup>, T. Liedl<sup>1</sup>**

*1 Department of Physics and Center for Nanoscience, Ludwig-Maximilians-Universität, Geschwister-Scholl-Platz 1, 80539 München (Germany)*

*2 Department of Physics, University of Oxford, Clarendon Laboratory, Parks Road, Oxford, OX1 3PU, (U.K.)*

We designed and implemented a DNA-based plasmonic nanostructure that can pick up the circular dichroism (CD) signal of chiral molecules located in a focus point between two plasmonic nanoparticles. The detection of a CD signal from chiral molecules in the plasmonic focus points of metal nanoparticle aggregates and on metal surfaces has been described theoretically and demonstrated experimentally<sup>1,2,3</sup>. With the goal to observe a plasmonic CD for various chiral molecules, we designed DNA-origami-structures to bring a chiral molecule in the plasmonic hotspot of two gold nanoparticles. Plasmonic DNA origami antennas can be used for Surface Enhanced Raman Spectroscopy measurements<sup>4,5</sup>. By modifying the DNA origami structures employed in these experiments, we built a variety of addressable plasmonic hotspots. The first DNA origami structures consist of two- or three-layered square lattice DNA origami sheets with an aperture in the middle for the attachment of chiral target mol-

ecules. Single-stranded DNA extensions for the attachment of gold nanoparticles are positioned around the aperture on both sides of the origami sheet. Gold nanoparticles with diameters of 10 to 40 nanometers carrying complementary DNA sequences to the extension sequences are conjugated to the pre-defined binding sites on both sides of the aperture. In initial experiments, no aperture design was used which led to the presence of double-stranded DNA (dsDNA) in the center of the plasmonic focus point. CD signals are usually dominant around the absorption wavelength of a material – 260 nm for dsDNA. With our plasmonic particle dimer we were able to observe a CD signal in the visible region of the spectrum. In upcoming experiments, we will optimize the binding of each of the components and employ new methods to increase the concentration of the nanostructures to perform further CD measurements.

[1] H. Zhang and A. O. Govorov, *Phys. Rev. B* 87, 075410 (2013)

[2] J. M. Slocik et al. *Nano Lett.* 11, 701-705 (2011).

[3] B. M. Maoz et al. *Nano Lett.* 13, 1203-1209 (2013)

[4] P. Kühler et al. *Nano Lett.* 14, 2914-2919 (2014).

[5] V. V. Thacker et al. *Nat. Commun.* 5:3448 doi: 10.1038/ncomms4448 (2014).

## Sequence defined oligo(ethanamino)amides for folate receptor targeted pDNA or siRNA delivery: optimization and preliminary structure-activity relationship study

**Dongsheng He<sup>1,2</sup>, Ana Krhac Levacic<sup>1</sup>, Katharina Müller<sup>1</sup>, Petra Kos<sup>1</sup>, Dian-Jang Lee<sup>1,2</sup>, Ernst Wagner<sup>1,2</sup>**

<sup>1</sup> Department of Pharmacy and Center for NanoScience, Ludwig-Maximilians-University Munich, Germany;

<sup>2</sup> Nanosystems Initiative Munich, Germany

Cationic polymers are a versatile compound class with potential for the non viral delivery of different types of therapeutic nucleic acids. In order to achieve a successful and efficient delivery, just like the viral vectors, polymeric carriers also have to combine multiple functionalities. However despite their similar chemical nature, delivery of pDNA and siRNA has its own challenging obstacles which need to be addressed individually. Therefore a precise chemistry, site-specific placement of different modules and detailed structure-activity relationship studies are needed for a nucleic acid specific (e.g. pDNA or siRNA) optimization process. Herein we present sequence-defined oligomers comprising artificial polyamine domains for nucleic acid complexation, monodisperse polyethylene glycol (PEG) for surface shielding

and folic acid for receptor specific cellular uptake. Via utilizing solid-phase assisted synthesis, oligomers with different topologies and additional functional domains, such as histidines for endosomal escape and tyrosines or fatty acid for the further stabilization of complexes, could be obtained. *In vitro* screening of folate receptor specific pDNA and siRNA delivery were investigated. The resulting structure activity relationships identified separate beneficial modules for pDNA or siRNA delivery. In pDNA transfections transgene expression was greatly enhanced by an increased endosomal buffer capacity, whereas siRNA delivery rather showed need for complex stabilization. In sum the work demonstrates the versatility of the presented compound platform and its potential for cargo-specific optimization.

## Equilibrium Dynamics of Helical Polymers

**Lorenz Huber, Philipp Lang, Erwin Frey**

Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Department of Physics, Ludwig-Maximilians-Universität München, Germany

Biopolymers like DNA, cytoskeletal filaments or artificially designed DNA-origami fibres are famous representatives of elastic nano particles that form a helical configuration at their ground state. The handedness, radius and pitch of these helices are determined by their curvature  $\kappa$  and torsion  $\tau$ . The statistical mechanics of such filaments is described by the helical wormlike chain model, where  $\kappa$ ,  $\tau$  are identified as the filaments' intrinsic bending and twisting rates, respectively. Here we employ Brownian dynamics simulations to investigate the thermal end-to-end distance fluctuations. We find that  $\langle \delta R^2(t) \rangle$  exhibits a rich scaling behavior with varying  $\kappa$  and  $\tau$ . For  $\kappa = 0$  the initial relaxation resembles the  $t^{3/4}$ -scaling law

as predicted by semiflexible polymer theory. In contrast, helices with a low ascending pitch angle, i. e.  $\kappa > \tau$ , show power law exponents exceeding  $3/4$  due to the additional elastic modes of the spring-like polymer conformation. The crossover region with  $\kappa < \tau$  reveals a sudden intermediate relaxation regime with a scaling exponent well below  $3/4$ . With rising  $\tau$  this domain only slowly converges towards the semiflexible limiting case. Our findings demonstrate the intriguing influence of helical parameters on the dynamics of single polymer systems and can in principle help to determine structural details beyond the resolution of (static) experimental techniques.

## OER catalysis in tin-doped hematite photoanodes for water splitting

**Halina Dunn, Johann M. Feckl, Alexander G. Hufnagel, Alexander Müller, Dina Fattakhova Rohlfing, Laurie Peter,<sup>1</sup> Christina Scheu, Thomas Bein\***

Department of Chemistry and Center for NanoScience (CeNS), University of Munich (LMU), Butenandtstr. 11 E, 81377 Munich, Germany

<sup>1</sup> Department of Chemistry, University of Bath, BA2 7AY, United Kingdom

Direct utilization of sunlight for splitting water into hydrogen and oxygen is expected to be an important pillar of a future economy based largely on renewable energy. It combines harnessing the world's largest and most long-lived power source with the advantages of hydrogen as a storage medium, such as the ability to store large amounts of energy and universal usability in electricity generation as well as in chemical processes. Photoelectrochemical (PEC) water splitting at n type hematite

( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>) photoanodes is appealing because of this material's abundance, chemical stability, non-toxicity and band gap suitable for absorbing a large fraction of the solar spectrum. However, its performance is severely compromised by a short hole diffusion length as well as sluggish water oxidation kinetics at the surface. Solutions to these problems are pursued by doping hematite with other metal ions, among them Sn<sup>4+</sup>, which has led to improved water oxidation performance.<sup>1,2</sup> While most previ-

ous studies attribute this to increased bulk, we show herein that enhanced catalytic activity of the water oxidation is a more plausible explanation. We found that in the mixed oxide synthesized by a sol-gel method developed in our group, tin is preferentially incorporated close to the surface in a core-shell particle structure. Intensity-modulated photocurrent spectroscopy (IMPS) and photocurrent transient analysis showed that tin doping increases the rate constant of interfacial charge transfer, and thus the water oxidation. The highest photocurrents were observed at a doping level of 20 at% tin in the synthesis solution. Fur-

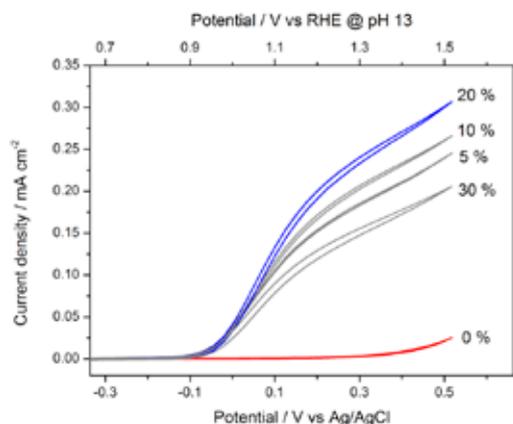


Fig. 1: J-V-Curves of  $\text{Fe}_2\text{O}_3$  with different amounts of Sn added to the precursor solution.

thermore, we showed that this doping also improves the electron collection efficiency for long electron pathways. This study shows that the working mechanisms of dopants in hematite can be complex and require detailed studies on well-defined model systems. For this purpose, photoelectrodes are now being prepared in our group by atomic layer deposition (ALD).

[1] N.T. Hahn et al. *Chem. Mater.* 2010, 22, 6474–6482.

[2] K. Sivula et al. *J. Am. Chem. Soc.* 2010, 132, 7436–7444.

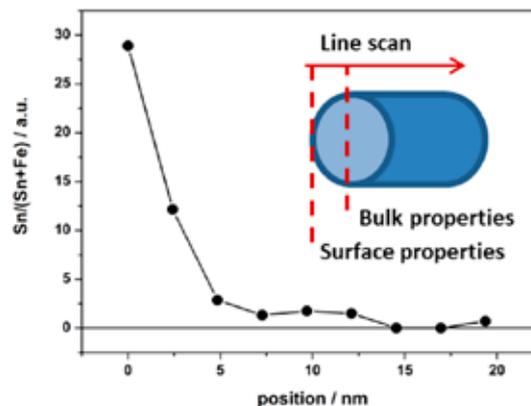


Fig. 2: Radial TEM EDX line scan across  $\text{Fe}_2\text{O}_3$  particle.

## Lipid-like nanoparticles for mRNA delivery

Anita Jarzebinska, Tamara Weber, Christian Dohmen, Christian Plank, Carsten Rudolph

Ethris GmbH, Lochhamer Str. 11, 82152 Martinsried

Ludwig Maximilian University of Munich, The Faculty for Chemistry and Pharmacy, Butenandtstr. 5-13, 81377 München

Ethris SNIM<sup>®</sup> RNA-Technology represents a novel nucleic acid therapy platform based on stabilized non-immunogenic messenger RNA (mRNA). In contrast to commonly used mRNA, SNIM<sup>®</sup> RNA can be administered repeatedly leading to sustained expression of therapeutically active proteins even at low doses. This can be used in the therapy of hereditary diseases, as an alternative to protein therapy, and in regenerative medicine. However, the mRNA's susceptibility to enzymatic degradation in cells and its negative charge create a need of efficient delivery systems for *in vivo* applications. A promising approach is the complexation of the SNIM<sup>®</sup> RNA in the lipidoid formulation. Incorporation of the cationic lipid in the formulation enables stable binding of the negatively charged molecule of mRNA. The lipidoid structure is composed of an oligoamine head group modified with C12 hydrocarbon tails. The screening of different head groups *in vitro* indicated that the alternating structure is the determining factor in terms of transfection efficiency. In three tested cell lines: NIH-3T3 (murine

fibroblasts), HepG2 (human liver carcinoma) and A549 (human lung carcinoma) the trend remained the same. We were able to proof that one reason of dramatic differences in activity between the slightly varying lipid-like structures is the buffer capacity. The acid dissociation constant in the range of pH 6.2 and 6.5 is the characteristic enabling lipid-like carriers an effective endosomal escape and, hence, efficient cell transfection. The relatively high expression of the reporter gene (Firefly luciferase) in mice after intravenous administration confirmed the utility of lipoplexes in mRNA delivery *in vivo*.

## High-sensitivity measurement of DNA-Protein binding energies by automated fluorescence microscopy

**Christophe Jung, Peter Bandilla, Mark von Reuter, Susanne Hueneburg, Ulrich Unnerstall and Ulrike Gaul\***

*Gene Center Munich, Department of Chemistry und Biochemistry, Ludwig-Maximilians-Universität München, Feodor-Lynen-Strasse 25, 81377 München (Germany)*

Transcription Factors that bind target DNA sequences are essential for the proper regulation of gene expression. The understanding of such transcription control networks is difficult and requires comprehensive and accurate information about the transcription factor binding affinities. Unfortunately, such data are often not available, as existing experimental methods for measuring binding preferences are low throughput or biased towards high-affinity sites. We developed a method based on Fluorescence Anisotropy (FA) to determine DNA-protein affinity landscapes in solution at large scale and with ultra-high sensitivity. We adapted a standard widefield fluorescent microscope for fully automated measurement of FA in 96- or 386-well plate format, with one affinity titration per single-well. This is achieved through a controlled delivery system, where the protein is incorporated within a po-

rous gel matrix and the DNA-ligand diffuses through the matrix during measurements. Using a competitive binding assay, we can measure the concentration of active protein and KDs into the sub-nanomolar range with high reproducibility. The approach successfully combines automation with low sample consumption and high accuracy. We applied this technique to determine the binding specificities of 20 transcription factors participating in the well-characterized segmentation gene network of the early *Drosophila* embryo. The resulting position weight matrices show subtle but significant differences from existing ones; we evaluate their performance in a thermodynamic model<sup>1</sup> predicting the expression of segmentation enhancers.

[1] E. Segal, T. Raveh-Sadka, M. Schröder, U. Unnerstall and U. Gaul, *Nature* 2008, 451, 535.

## Nanoscale arrangements in soft matter films revealed by IR-SNOM

**C. Westermeier, R. Stabla, D. Kalb, C. Liewald, F. Keilmann, J. Rädler, and B. Nickel**

*Faculty of Physics and Center for NanoScience (CeNS), LMU Munich*

Local ordering motives influence functional properties of soft matter systems to a large extent. In the case of proteins, folding motives such as helical are structure defining. In the case of organic thin films, molecular packing promotes the overlap of pi-orbitals and charge transfer. Since molecular vibrations are sensitive to local ordering, IR spectroscopy is a versatile technique to study local order in soft matter films; however, due to the inherently long IR wavelength, standard IR techniques lack lateral resolution in the nm range. In combination with near field techniques,<sup>1</sup> we are able to do nano-imaging and IR spectroscopy on soft matter films far beyond the diffraction limit, i.e. we are resolution limited only by the radius of an AFM tip (approx. 20 nm) illuminated an IR laser (s-SNOM setup by Neaspec). First, we use this technique to study polymorphism in highly ordered thin films of small aromatic molecules for organic electronics. For pentacene, nano-imaging was successfully accomplished and the coexistence of two sub-micron phases was experimentally verified.<sup>2</sup> Due to shifts of vibrational resonanc-

es, the s-SNOM is able to differentiate the distribution of bulk phase and thin film phase of pentacene with a spatial resolution of about 20 nm. Since pentacene is used for the fabrication of thin film transistors (TFTs), the identification of the local phase arrangement is of high interest since it may explain variations of charge mobility in TFTs. DNA-origami structures are another example of highly ordered molecular constructs. In collaboration with the group of T. Liedl, we want to image the structural order of DNA origami adsorbed to flat surfaces in future work.

[1] F. Keilmann & R. Hillenbrand in *Nano-Optics and Near-Field Optical Microscopy* (eds. A. Zayats and D. Richards), ArtechHouse, 2009.

[2] C. Westermeier, A. Cernescu, S. Amarie, C. Liewald, F. Keilmann & B. Nickel; "Sub-micron phase coexistence in small-molecule organic thin films revealed by infrared nano-imaging", *Nature Comm.* 5, 4101, doi:4110.1038/ncomms5101 (2014).

## Radio frequency acousto-mechanical tuning of a photonic molecule

**Stephan Kapfinger<sup>1,3</sup>, Thorsten Reichert<sup>2,3</sup>, Michael Kaniber<sup>2,3</sup>, Jonathan J. Finley<sup>2,3</sup>, Achim Wixforth<sup>1,3</sup>, and Hubert J. Krenner<sup>1,3</sup>**

*(1) Lehrstuhl für Experimentalphysik 1, Universität Augsburg, 86159 Augsburg; (2) Walter Schottky Institut und Physik Department, Technische Universität München, 85748 Garching; (3) Nanosystems Initiative Munich (NIM), 80799 München*

We propose and demonstrate a dynamically tunable photonic molecule (PM) formed by two L3 defect cavities defined in a GaAs two-dimensional photonic crystal membrane. To tune the optical resonances of the two cavities of the PM we employ the acousto-mechanical deformation induced by an 800 MHz surface acoustic wave (SAW) [1]. For this frequency the cavity separation matches half the acoustic wavelength. Thus, the resulting SAW-driven sinusoidal spectral modulations of the two modes are opposite in phase giving rise to a time-dependent

detuning. We monitor the mode spectrum in the time-domain by probing the time-resolved stroboscopic PL emission [2] of off-resonantly coupled quantum dots. For a PM with finite detuning, we observe for low acoustic amplitudes the established but out-of-phase spectral oscillation of two uncoupled modes. As we increase acoustic amplitudes, we resolve a characteristic anti-crossing of the two cavity modes in the time domain. From the observed splitting we are able to deduce the PM coupling strength of 180 GHz. The coupling is further confirmed in spa-

tially and time-resolved PL maps showing delocalization of the modes over both cavities at resonance.

[2] Schülein et al., *PRB* 88, 085307 (2013)

[1] Fuhrmann et al., *Nat. Photon.* 5, 605 (2011)

## Regulation of nanoparticle diffusion in the vitreous humor

Benjamin Käsdorf<sup>1,2</sup>, Fabienna Arends<sup>1,2</sup>, and Oliver Lieleg<sup>1,2</sup>

<sup>1</sup> Zentralinstitut für Medizintechnik, Technische Universität München, Boltzmannstrasse 11, 85748 Garching, Germany

<sup>2</sup> Fakultät für Maschinenwesen, Technische Universität München, Boltzmannstrasse 15, 85748 Garching, Germany

The diffusive behavior of nanoparticles in biological hydrogels is determined by the characteristics of both the gel and the particles. Hydrophobic and/or electrostatic interactions can affect the particle diffusion to a great extent. One example for such a biological hydrogel is the vitreous humor. High intravitreal mobility of pharmaceutical drugs is crucial for effective treatment of several ocular diseases. In this study we investigate the diffusive behavior of nanoparticles in ovine vitreous humor compared to

porcine and bovine vitreous humor using single particle tracking. We tune the nanoparticle diffusion in the ovine vitreous by enzymatic modifications and inducing Debye screening. By investigating the particular properties of nanoparticles and hydrogel components which are involved in regulating nanoparticle diffusion, the way can be paved for the development of efficient drug delivery systems in biological hydrogels, such as the vitreous humor.

## Heat driven selection of nucleic acids

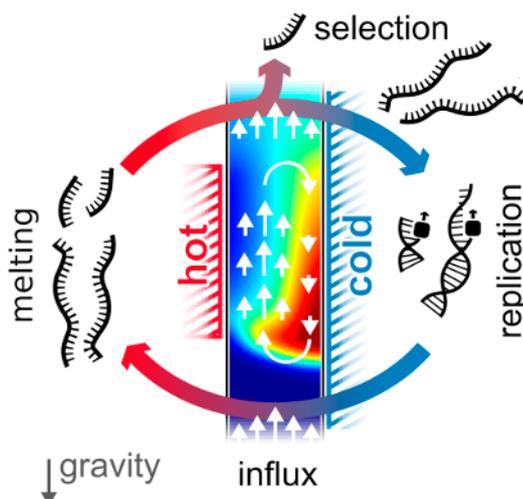
Lorenz M. R. Keil<sup>1</sup>, Simon A. Lanzmich<sup>1</sup>, Moritz Kreysing<sup>1,2</sup> and Dieter Braun<sup>1</sup>

<sup>1</sup> Systems Biophysics, Department of Physics, Center for Nanoscience, Ludwig-Maximilians-Universität München, 80799 Munich, Germany

<sup>2</sup> now: Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Environments shape living systems by selection. This also holds true for the first molecular replicators that had to stabilize against the equilibrium push towards dilution and decay. Especially problematic for the origin of life is the kinetic tendency of competing replicators to generate ever shorter genomes. We experimentally demonstrate that a basic thermal non-equilibrium between two geological heat reservoirs can accumulate replicating oligonucleotides and select them for increasing genome length. The interplay of molecular thermophoresis and laminar convection is able to actively filter exclusively long oligonucleotides from a steady flow through this open compartment. Trapped long strands are at the same time exposed to

convective temperature cycling, which allows for exponential replication by overcoming template inhibition. Two-fold shorter strands die out in the same setting as they are simply flushed out of the system. The combination of length selection and thermal cycling renders these out-of-equilibrium compartments suitable long term habitats for the evolution of replicating oligonucleotide populations towards increasing molecular complexity. Besides the origin life, this mechanism might facilitate SELEX experiments (systematic evolution of ligands by exponential enrichment), where aptamers are selected from oligonucleotide libraries. Only the bound aptamers will remain in the trap and undergo temperature oscillations, whereas the unbound bulk will be flushed out. While standard SELEX methods consist of many time-consuming steps, here the procedure can be performed in one setting.



**Heat-driven filter selecting for increased genome length.** An asymmetrically heated open pore at top and bottom allows to select oligonucleotides from a steady upward flow through the pore. The interplay of gravity and a temperature gradient is sufficient to cyclically separate double-stranded DNA and drive exponential base-by-base replication reactions.

## Infrared hyperspectral mapping of nano-composites

Sergiu Amarie\*, Dominik Kalb, Fritz Keilmann, Clemens Liewald, Bert Nickel, Joachim Rädler, Robert Stabla, Christian Westermeier

Soft Condensed Matter Group, Ludwig-Maximilians-Universität, 80539 München

\* Neaspec GmbH, Bunsenstr. 5, 82152 Martinsried

Infrared spectroscopic analysis rests on vibrations which label any chemical compound with a characteristic "fingerprint" spectrum in the 3-30  $\mu\text{m}$  wavelength region—intrinsically. Combining IR with AFM allows to perform IR chemical recognition routinely at 20 nm spatial resolution.<sup>1,2</sup> Known as scattering-type scanning near-field optical microscopy (s-SNOM) this instrument has become commercially available from a CeNS spin-off (neaspec.com). Recently, we have enhanced s-SNOM by a coherent broadband mid-infrared illumination<sup>3</sup> based on 100-fs pulses (thus even allowing nanoscale probing at ultrafast time resolution<sup>4</sup>); with this illumination, a complete IR spectrum is obtained at any sample position of the tip ("nano-FTIR"). By scanning the sample, an IR-hyperspectral line image or two-dimensional image is recorded. The technique of nano-FTIR is being applied to thin-film organic conductors where it revealed coexisting structural phases<sup>5</sup> (see also poster by D. Kalb et al. and talk by C. Westermeier). Nano-FTIR hyperspectral imaging is likely valuable in all fields of nanoscience as has already been demonstrated in studies of protein,<sup>6</sup> human bone,<sup>7</sup> and interstellar-dust nano-composites.<sup>8</sup>

[1] Knoll, B. & Keilmann, F. Near-field probing of vibrational absorption for chemical microscopy. *Nature* 399, 134 (1999).

[2] Huth, F. et al. Nano-FTIR absorption spectroscopy of molecular fingerprints at 20 nm spatial resolution. *Nano Lett.* 12, 3973 (2012).

[3] Keilmann, F. & Amarie, S. Mid-infrared frequency comb spanning an octave based on an Er fiber laser and difference-frequency generation. *J. Infrared, Millimeter, and Terahertz Waves* 33, 479 (2012).

[4] Wagner, M. et al. Ultrafast and nanoscale plasmonic phenomena in exfoliated graphene revealed by infrared pump-probe nanoscopy. *NanoLetters* 14, 894 (2014).

[5] Westermeier, C. et al. Sub-micron phase coexistence in small-molecule organic thin films revealed by infrared nano-imaging. *Nature Comm.* 5, 4101, doi:4110.1038/ncomms5101 (2014).

[6] Amenabar, I. et al. Structural analysis and mapping of individual protein complexes by infrared nanospectroscopy. *Nature Comm.*, 4, doi:10.1038/ncomms3890 (2013).

[7] Amarie, S. et al. Nano-FTIR chemical mapping of minerals in biological materials. *Beilstein J. Nanotech.* 3, 11 (2012).

[8] Keilmann, F., Hillenbrand, R. & McLeod, A. S. Nano-FTIR – the chemical nanoscope. *G.I.T. Imaging & Microscopy* 1, 26 (2013).

## Magnetic (Torque) Tweezers Experiments to Probe the Mechanics and Interactions of Nucleic Acids

Franziska Kriegel and Jan Lipfert

Department of Physics, Nanosystems Initiative Munich, and Center of NanoScience, LMU Munich, Amalienstr. 54, 80799 Munich

Magnetic Tweezers (MT) can probe single molecules using magnetic forces and torques. In the MT, a superparamagnetic bead is attached to the molecule of interest, for example double stranded (ds) DNA or a protein, while the other end is attached to the bottom of the flow cell. By controlling the position and rotation of magnets, above the flow cell, forces and torques can be applied to stretch and twist the molecules of interest. By varying the magnet configuration different fields can be applied for specific purposes. A "conventional" horizontal magnet configuration is suitable to analyze the force-extension behavior or to observe DNA supercoiling while rotating the molecules. Using cylindrical magnets in combination with a smaller side magnet, called Magnetic Torque Tweezers (MTT), offer the opportunity to measure torque of dsDNA. As an advantage compared to other single-molecule force manipulation techniques, for a given magnet position, the applied forces in the magnetic tweezers are constant, such that no feedback is required to apply constant forces even over long

periods of time. Forces in a range of 0.1 pN up to 100 pN can be reached. In particular also smaller forces (< 1 pN), characteristic of non-covalent macromolecular interactions, can readily be applied and measured. Furthermore, our MT setup is able to track multiple beads (currently up to ~20) at the same time, enabling the collection of statistics in a single measurement run. Currently, we are investigating the precise response of dsDNA to applied forces and torques at varying salt concentrations. Preliminary analysis of force-extension and torque-rotation measurements suggest that the torsional stiffness of DNA does not depend on salt concentration, in contrast to the bending persistence length. In addition, our MT setup allows us to address other biological challenges, for example to probe protein-nucleic acid interactions or the processes of folding and unfolding of proteins.

## Microfluidic assisted self-assembly of folate-targeted Monomolecular siRNA-lipid Particles

**R. Krzyszton<sup>1,2</sup>, B. Salem<sup>3</sup>, G. Schwake<sup>1</sup>, C. Leonhardt<sup>1</sup>, K. Müller<sup>4</sup>, E. Wagner<sup>4</sup>, J. O. Rädler<sup>1</sup>**

*1 Ludwig-Maximilians-Universität München (LMU), Fakultät für Physik, Lehrstuhl Prof. Rädler, Geschwister-Scholl-Platz 1, 80539 München, Germany*

*2 Graduate School of Quantitative Biosciences (QBM), Ludwig-Maximilians-University, Feodor-Lynen-Straße 25, 81377 Munich, Germany*

*3 Ludwig-Maximilians-Universität München (LMU), Department Chemie und Biochemie, Physikalische Chemie I, Butenandtstr. 11, Haus E, D-81377 München Germany*

*4 Ludwig-Maximilians-Universität München (LMU), Department Pharmazie, Zentrum für Pharmaforschung, Butenandtstr. 5-13, Haus D, 81377 München, Germany*

The design of non-viral delivery vectors is crucial for efficient gene therapy. For optimal transport within blood and extracellular matrix used nanocarriers need to be small and stable *in vivo*. Furthermore the molecular targeting into diseased cells, facilitated by introduction of cellular receptors ligands on the surface of tailored vectors, extend their specific uptake efficiency and helps to avoid uncontrolled gene release within healthy tissues. In previous work we presented the monomolecular-siRNA lipid particles (mNALP) can be form via self-assembly during solvent exchange process. However self-assembly by this method criti-

cally depends on the mixing kinetics of the solvents isopropanol and water. Here we systematically study the self-assembly of siRNA with lipids by various mixing methods, including hydrodynamic focusing in microfluidic T-junction chip. We show that physicochemical parameters like homogeneity and siRNA encapsulation turn out to be more reproducible in microfluidic devices. We furthermore investigate the stability of mNALPs in blood serum and demonstrate that addition of small amounts of folated PEG-lipid to mNALP's results in specific binding to KB cells that overexpress the folate receptor.

## Combination of a polymer-based transfection system with modified mRNA to enhance transfection *in vitro*

**Jana Lambrecht<sup>1</sup>, Mehrije Ferizi<sup>2</sup>, Christian Dohmen<sup>1</sup>, Christian Plank<sup>1,2</sup>, Carsten Rudolph<sup>1</sup>**

*1 Ethris GmbH, Martinsried, Germany*

*2 Institute of Experimental Oncology and Therapy Research, Klinikum Rechts der Isar, Technical University Munich, Germany*

Transcript therapy is based on the delivery of messenger RNA (mRNA) instead of DNA into the cytoplasm of target cells. Treating inherited genetic disorders with therapeutic mRNA is a promising alternative to DNA therapies since mRNA is translated in the cytoplasm and is only present for a period of time before being degraded. In order to create an efficient system for transfecting cells with mRNA the components of this system, vector and cargo, need to be optimized. In recent years a lot of work has been done regarding the development of non-viral polymer-based vectors, so called polyplexes, as well as the improvement of mRNA with respects to stability, expression and immunogenicity. In the present study we looked into possible synergistic effects on transfection potential and expression levels over time in NIH3T3 cells (murine fibroblasts). We combined non-toxic, poly(acrylic acid)-based vectors containing alternating pendant groups with modified mRNAs based on the SNIM® (stabilized non-immunogenic messenger RNA) technology

containing a distinct combinatorial set of 5'- and/or 3'-untranslated region introducing stabilizing elements to the mRNA. Depending on the chemical structure of the pendant group cytotoxicity of the polymeric formulations was found to be lower when compared to branched poly(ethylenimine). Also all tested mRNA constructs with the differently combined UTRs showed higher expression results than the control mRNA containing no UTRs. We were not able to find a specific system comprising of a polymer and an UTR-modified mRNA that showed synergistic effects on transfection efficiency and prolongation of protein expression. Nonetheless the best performing polymer remained the most active carrier independently on the delivered mRNA construct. In addition to that each UTR-mRNA construct showed sustained expression when transfected with the polymeric formulations compared to the results obtained by transfection with DreamFect Gold™.

## A Thermal, Autonomous Replicator Made from Transfer RNA

**Simon A. Lanzmich, Hubert Krammer, Friederike M. Möller and Dieter Braun**

*Systems Biophysics, Physics Department, Center for Nanoscience, Ludwig-Maximilians-Universität München, 80799 Munich*

Evolving systems rely on the storage and replication of genetic information. To this end, modern biology employs an RNA-dominated machinery to encode proteins, which in turn replicate genetic information. Before this interlinked machinery evolved, early life most probably replicated genes using a pool of short RNA sequences<sup>1</sup>. Here, we present an autonomous, purely thermally driven replication mechanism. Instead of the chemical base-by-base replication advocated by RNA world approaches<sup>2-5</sup>, the presented mechanism operates on successions of multi-base codons. It consists of a pool of RNA molecules that

encodes and replicates a repetitive four-letter code. The RNAs are derived from transfer RNA (tRNA), each containing the anticodon framed by two hairpin loops. The anticodons serve as sequence-encoding toeholds while the hairpins are pairwise complementary, allowing the strands to bind sequentially. To explore the concept, we have recently shown a reduced system to work<sup>6</sup>. It is built of four halves of tRNA, each strand forming a single hairpin with a toehold, and replicates a two-letter code. For replication, binding energy is initially stored by thermally quenching the tRNA molecules into monomo-

lecular hairpin states. Subsequent temperature oscillations connect the hairpins in a highly specific cross-catalytic reaction with a duplication time of 30 s, significantly faster than the untemplated reaction. Reaction kinetics were measured using a real time fluorescence signal and in good agreement with our kinetic model of the reaction network. In a sense, this is a physically driven version of the chemical ligation chain reaction<sup>7</sup> that replicates a two-letter code cross-catalytically<sup>8-10</sup>. Instead of chemical backbone ligation, matching strands are joined by physical base pairing. The approach is compatible with hydrothermal molecule traps<sup>11-13</sup> and thermal microconvection<sup>14</sup>, and might have been selected for by asymmetric hydrolysis of the strand backbone<sup>15</sup>.

[1] E.V. Koonin and A. S. Novozhilov, *IUBMB Life* 61, 99 (2009).

[2] W. Gilbert, *Nature* 319, 618 (1986).

[3] C. Guerrier-Takada et al., *Cell* 35, 849 (1983).

[4] C. Deck, et al., *Nature Chem.* 3, 603 (2011).

[5] S. Rajamani et al., *J. Am. Chem. Soc.* 132, 5880 (2010).

[6] H. Krammer et al., *PRL* 108, 238104 (2012)

[7] F. Barany, *PNAS* 88, 189 (1991).

[8] G.A von Kiedrowski, *Angew. Chem.* 98, 932 (1986).

[9] W. S. Zielinski and L. E. Orgel, *Nature* 327, 346 (1987).

[10] T. A. Lincoln and G. F. Joyce, *Science* 323, 1229 (2009).

[11] P. Baaske et al., *PNAS* 104, 9346 (2007).

[12] I. Budin et al., *J. Am. Chem. Soc.* 131, 9628 (2009).

[13] C. B. Mast and D. Braun, *PRL* 104, 188102 (2010).

[14] D. Braun et al., *PRL* 91, 158103 (2003).

[15] B. Obermayer et al., *PRL* 107, 018101 (2011).

### Nanosized Polyplexes with Dual-Functional MTX Ligand for Enhanced Combined Cytotoxicity with Therapeutic Eg5 siRNA

Dian-Jang Lee<sup>1,2</sup>, Ulrich Lächelt<sup>1,2</sup>, Daniel Edinger<sup>1</sup>, Dongsheng He<sup>1,2</sup>, Taavi Lehto<sup>1</sup>, Ernst Wagner<sup>1,2</sup>

<sup>1</sup> Department of Pharmacy and Center for NanoScience, Ludwig Maximilian University of Munich, Germany

<sup>2</sup> Nanosystems Initiative Munich, Germany

**PURPOSE:** The novel strategy that synthetic small interfering RNA (siRNA) can invoke RNAi responses is expected to be an excellent option for treating many incurable diseases such as cancer. However, efficient tissue-specific delivery of siRNA remains the major limitation in the development of RNAi therapy. By solid phase supported (SPS) synthesis, we have synthesized a series of sequence-defined polymers which include a cationic (oligoethanamino)amide core, cysteines (as bioreversible disulfide-forming units), and polyethylene glycol chain (for shielding surface charges) coupled to a terminal ligand. To recognize the target cells, the antifolate drug methotrexate (MTX) is employed as both targeting ligand for folate receptor-mediated uptake and as an anticancer therapeutic as it is toxic to the target cells by blocking de novo thymidylate and purine synthesis and consequently DNA and RNA synthesis. Besides, we exploit a therapeutic siRNA against eglin 5 (Eg5) that blocks mitosis to cause death of rapidly dividing cancer cells. Together we formulate Eg5 siRNA and MTX-conjugated polymer as a nanosized targeted siRNA polyplex with synergic antitumor effect.

**METHODS:** Size of siRNA polyplex was recorded by atomic force microscope and fluorescence correlation spectroscopy. Uptake was determined by flow cytometry and knockdown of a luciferase reporter gene was used to monitor gene silencing efficiency. To evaluate the efficacy of Eg5 siRNA, we measured toxicity by cell viability assay, mRNA expression by qRT-PCR, and aster formation of cellular DNA.

**RESULTS:** siRNA polyplexes were uniform nanoparticles with 5.4 nm of hydrodynamic diameter. These polyplexes were taken up by KB cells in a MTX-dependent manner, and this attributed to association with folate receptor. Transfections induced significant silencing of luciferase expression in KB-eGFP<sub>Luc</sub> cells. Treatments with MTX-conjugated polyplexes containing Eg5 siRNA in KB cells triggered knockdown of Eg5, resulted in typical aster formation, and caused enhanced cytotoxicity.

**CONCLUSIONS:** We developed a specific and efficient siRNA carrier system with dual-functional ligand for cellular delivery and antitumor effect. siRNA polyplexes successfully delivered cargo into the target cells mainly via folate receptor. When combined with therapeutic Eg5 siRNA and MTX, the siRNA polyplexes carried out synergistic cytotoxic activity. This highly functionalized and molecule-defined carrier system for siRNA delivery could be a potential strategy for RNAi-based cancer therapeutics.

# POSTER ABSTRACTS - SESSION II (LI-ZORN)

## Optical printing and injection of gold nanoparticles into living cells

**M. Li, T. Lohmüller, and J. Feldmann**

*Photonics and Optoelectronics Group, Faculty of Physics and Center for NanoScience (CeNS), Ludwig-Maximilian-University Munich, Amalienstr. 54, D-80799 Munich, Germany*

The active delivery of nanoscopic objects to the surface and interior of living cells with light offers promising prospects for the development of novel molecular delivery strategies or intracellular biosensor applications. Here, we show that single gold nanoparticles from solution can be patterned on the surface of living cells with a 532 nm continuous wave laser beam by means of optical forces. Furthermore, we demonstrate that in a second step the particles can be

injected into the cell by focusing the laser directly on the printed particles through a combination of plasmonic heating and the formation of nanobubbles. We find that short exposure times (within one second) are sufficient to perforate the cell membrane and inject the particles into the cell. Gold nanoparticles can be injected with a cell survival rate of > 70% depending on the laser energy which was revealed by cell viability tests.

## Polarimetry of Exciton Landscapes in Monolayer MoS<sub>2</sub>

**J. Lindlau<sup>1</sup>, A. Neumann<sup>1</sup>, H. Yamaguchi<sup>2</sup> and A. Högele<sup>1</sup>**

*1 Fakultät für Physik and CeNS, Ludwig-Maximilians-Universität, 80539 München, Germany*

*2 Materials Physics and Applications, Los Alamos National Laboratory, Los Alamos, NM 87545, USA*

Monolayer transition metal dichalcogenides such as molybdenum disulfide (MoS<sub>2</sub>) belong to a new class of truly two-dimensional materials with unique physical properties<sup>[1]</sup>. In contrast to gapless graphene monolayer MoS<sub>2</sub> is a direct band gap semiconductor with optical transitions in the visible<sup>[2]</sup> viable for potential applications in ultra-thin photosensitive electronic devices<sup>[3]</sup>. Furthermore, coupled spin and valley degrees of freedom offer a photonic approach to valleytronic applications<sup>[4]</sup>. We present the results of our optical studies of monolayer MoS<sub>2</sub> at cryogenic temperatures. In our experiments we mapped out the spatial distribution of neutral and charged excitons in large-scale monolayer MoS<sub>2</sub> flakes and identified with polarization resolving spectroscopy the relationship between exciton spin and valley degrees of freedom.

[1] K. S. Novoselov et al., *Proc. Natl. Acad. Sci. U.S.A.* 102, 10451 (2005)

[2] K. F. Mak et al, *Phys. Rev. Lett.* 105, 136805 (2010)

[3] Q. H. Wang et al., *Nat. Nanotechnol.* 7, 699 (2012); O. Lopez-Sanchez et al., *Nat. Nanotechnol.* 8, 497 (2013)

[4] H. Zeng et al., *Nat. Nanotechnol.* 7, 490 (2012); K. F. Mak et al., *Science* 344, 1489 (2014)

## High stress levels lead to transition from heterogeneous timing to synchronized cellular response of the *E.coli* Colicin E2 operon

**Andreas Mader,<sup>a</sup> Benedikt von Bronk,<sup>a</sup> Benedikt Ewald,<sup>a</sup> Sara Kesel,<sup>a</sup> Karin Schnetz,<sup>b</sup> Erwin Frey<sup>c</sup> and Madeleine Opitz<sup>a</sup>**

*a Center for Nano Science, Faculty of Physics, Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, D-80539 Munich, Germany; b Institute for Genetics, Universität zu Köln, Zùlpicher Str. 47a, 50674 Köln, Germany; c Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Department of Physics, Ludwig-Maximilians Universität München, Theresienstr. 37, 80333 München, Germany*

The production of bacteriocins in response to worsening environmental conditions is one means of bacteria to outcompete other microorganisms. Colicins, one class of bacteriocins in *Escherichia coli*, are effective against closely related Enterobacteriaceae. In a single cell study, we analyze the heterogeneous gene expression of Colicin E2, expressed from the SOS inducible *E. coli* Colicin E2 operon. We quantitatively study expression dynamics of the Colicin E2 operon in *E. coli* using fluorescence time-lapse microscopy. Different fluorescence reporter proteins allow us to observe heterogeneity in Colicin production and Colicin release separately. The fraction of cells expressing the Colicin E2 operon and the cells response times depend thereby on the strength of the applied stress

signal. While at low exogenous stress levels all cells eventually respond after a given time (heterogeneous timing), high stress levels lead to a synchronized stress response of all cells about 75 min after induction via stress. A heterogeneous response in combination with heterogeneous timing can be biologically significant. It might enable a bacterial population to endure low stress levels, while at high stress levels an immediate and synchronized response may allow elimination of closely related bacteria competing for resources. Furthermore we could demonstrate, that the amount of Colicin released is dependent on *cel* (lysis) gene expression. Future investigations will focus on transcriptional as well as post-transcriptional regulation affecting the dynamics of Colicin expression and release.

### A separation of powers - force and function of the versatile cohesin-dockerin interaction

**Lukas F. Milles, Wolfgang Ott, Ellis Durner, Markus A. Jobst, Klara H. Malinowska, Constantin Schöler, Tobias Verdorfer, Michael A. Nash, Hermann E. Gaub**

*Lehrstuhl für Angewandte Physik and Center for Nanoscience (CeNS), Ludwig-Maximilians-Universität, 80799 Munich, Germany*

How can we assemble protein networks? The answer to that question may have been discovered with the cellulosome, a modular system of numerous enzymes expressed by a multitude of thermo- and mesophilic bacteria, most prominently *C. thermocellum*. It excels at breaking down lignocellulosic biomass through hierarchical assembly. The modular basis of cellulosome network formation is the high affinity cohesin-dockerin receptor-ligand interaction. Different bacteria produce structurally different cellulosomes but exhibit homologous cohesin-dockerin pairs. We present a sampling of representative interactions, characterize their affinities and find them to be distinct to their position in the cellulosome network. Single-molecule force spectroscopy is used

to measure the force necessary to separate a cohesin-dockerin complex. The resulting force-extension traces show various unfolding pathways with a recurring fingerprint. We developed a classification algorithm to determine the most probable unfolding pathway clusters through dimensionality reduction techniques. Furthermore we demonstrate the suitability of a cohesin-dockerin system as a tag to study enzyme unfolding pathways in single molecule pulling experiments. The cellulosome's constituents hold the potential to become versatile connectors for nanoscopic protein assembly and have already proven their aptitude as reliable tags for single molecule force spectroscopy experiments.

### Polymerization and protection of nucleic acids in a prebiotic environment

**Matthias Morasch, Dieter Braun and Christof B. Mast**

*Systems Biophysics, Department of Physics, Center for NanoScience, Ludwig-Maximilians-University Munich, 80799 Munich, Germany*

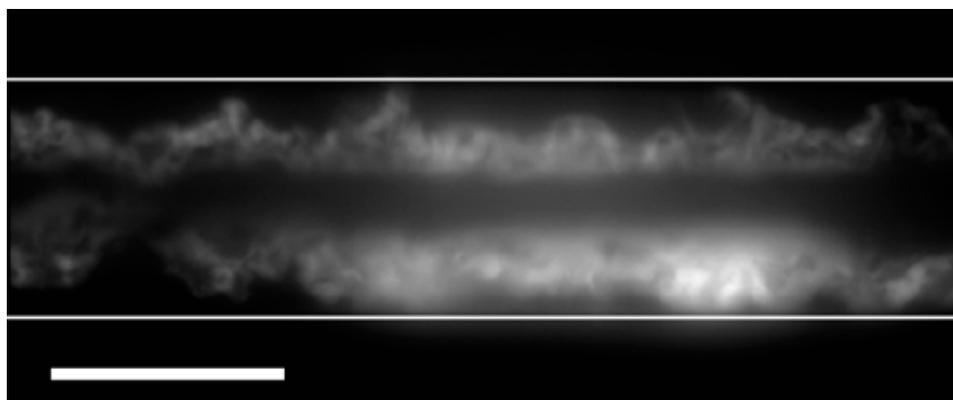
The formation of the first replicating systems capable of Darwinian evolution in an aqueous environment was likely a crucial step towards the evolution of life. Current opinions on the prebiotically plausible synthesis of single nucleotides however require multiple steps of drying and UV irradiation<sup>[1]</sup>. We therefore propose porous rock at hot springs near sea level as sites where both dry and wet conditions can be combined. A temporarily dry surface of the rock would allow reactions where the synthesis and polymerization of nucleotides can take place<sup>[1,2]</sup>. Washing these products into the pores would then enable their accumulation and further polymerization by harnessing a temperature gradient across the pore<sup>[3]</sup>. This can lead up to a point where the polymers form macroscopic structures that are even better protected against dilution. In our experiments, we show a dry polymerization of 3',5'-cyclic GMP to long nucleic acid strands without the help of catalysts or enzymes at moderate temperatures<sup>[2]</sup>. In addition, we

demonstrate the enzyme-free compaction of two-base (G & C) nucleic acid strands in a simple temperature gradient across a water-filled pore. The strands are capable of polymerization and branching via hybridization of complementary parts and form millimeter-sized structures that are stable against dilution and small water flows. This also paves the way for a selection mechanism in which only polymerizing strands are retained in the system, while others are flushed out over time. Our goal is to eventually combine dry and liquid states in one pore in order to increase the possibilities of reaction pathways in the same setting, while maintaining the advantages of a small and separated compartment.

[1] Powner MW, Gerland B, Sutherland JD (2009) Synthesis of activated pyrimidine ribonucleotides in prebiotically plausible conditions. *Nature* 459:239–242.

[2] Morasch M, Mast CB, Langer JK, Schilcher P, Braun D (2014) Dry Polymerization of 3',5'-Cyclic GMP to Long Strands of RNA. *ChemBioChem* 15:879-883.

[3] Mast CB, Schink S, Gerland U, Braun D (2013) Escalation of polymerization in a thermal gradient. *Proceedings of the National Academy of Sciences* 110:8030–8035.



**Gelation of nucleic acids.** Two-base 24mers were accumulated for ~100 min. The strands consist of three self-complementary parts that allow them to form a network. This results in a macroscopic gel that is stable against water flows and can survive for days without active accumulation. Strands were labeled with SYBR Green I in 1x PBS buffer. Scale bar: 100µm.

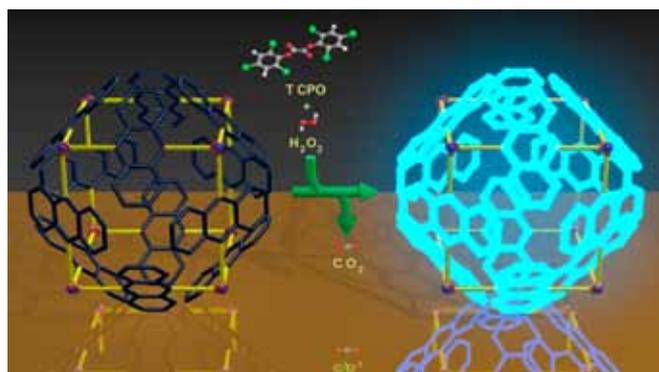
## Chemiluminescence of an anthracene-based UiO-68

S. Wuttke<sup>1</sup>, B. Rühle<sup>1</sup>, E. Mühlbauer<sup>1</sup>, F. Hinterholzinger<sup>1</sup>, P. Roy<sup>2</sup>, A. Godt<sup>2</sup>, T. Bein<sup>1</sup>

<sup>1</sup> University of Munich and Center for NanoScience (CeNS), Butenandtstraße 11, 81377 Munich, Germany

<sup>2</sup> Bielefeld University, Department of Chemistry, Universitätsstraße 25, 33615 Bielefeld, Germany

Numerous possible combinations of metals and organic linkers that comprise metal-organic frameworks (MOFs) offer great topological and chemical diversity within those structures. These features make them ideal candidates for applications in gas storage, catalysis, and chemical sensing.<sup>[1]</sup> For chemical sensing applications, luminescence represents a powerful read-out concept since the measurements are usually very sensitive and offer high resolution, with even single molecule visualization. The distinct advantage of chemiluminescence



in comparison to fluorescence is the absence of external light sources. Thus implies that the analytically relevant emission can be measured against a completely dark background, resulting in a high sensitivity of this transducer concept. In the present work, we developed a derivative of 9,10-diphenylanthracene, which is known to have chemiluminescence properties. We synthesized an UiO-68-related structure with this building block, resulting in a MOF with large pores and high surface area.<sup>[2]</sup> Strikingly, the UiO-68(anthracene) MOF shows strong chemiluminescence once exposed to a solution of bis(2,4,6-trichlorophenyl)oxalate and hydrogen peroxide. We anticipate that the implementation of a chemiluminescent transducer concept within MOFs will greatly extend the scope of MOF-based sensors.

[1] S. Kitagawa, R. Kitaura, S. Noro, *Angew. Chem. Int. Ed.* 2004, 43, 2334-2375.

[2] S. Wuttke, B. Rühle, F. Hinterholzinger, E. Mühlbauer, P. Roy, A. Godt, T. Bein, to be submitted.

## Mechanics of dimeric von Willebrand Factor under varied pH conditions probed by Single Molecule Force Spectroscopy (AFM)

Jochen P. Müller<sup>1</sup>, Tobias Obser<sup>2</sup>, Reinhard Schneppenheim<sup>2</sup>, Martin Benoit<sup>1</sup>

<sup>1</sup> Center for Nanoscience and Department of Physics, University of Munich, Amalienstraße

54, 80799 Munich, Germany

<sup>2</sup> Department of Pediatric Hematology and Oncology, University Medical Center, Hamburg-Eppendorf, Hamburg, Germany

Von Willebrand Factor (VWF) is a giant multimeric blood glycoprotein that senses shear flow irregularities in the blood stream. At sites of vascular injury, where shear forces are increased and of elongational character, VWF extends and subsequently promotes platelet adhesion<sup>[1,2]</sup>. Since formation of a platelet plug is essential for hemostasis, defects in or deficiency of VWF can lead to severe bleeding disorders, such as found in von Willebrand disease. Understanding the structural rearrangements within VWF when stretched in the blood stream is of fundamental interest from both a biophysical and medical perspective. Using AFM-based Single Molecule Force Spectroscopy, we probe the mechanical signature of VWF dimers, the smallest repeating subunits of VWF. Small peptide tags at opposite termini of the dimers allow pulling specifically and in a well-defined geometry. Varied pH conditions help to interpret the obtained force-extension profiles, as pH was shown to influence the static structure of VWF

dimers and thus facilitate their correct multimerization in the endothelial Golgi apparatus<sup>[3]</sup>. From a more medical perspective, acidic conditions are found at sites of inflammation in the blood. Overall, we report on the mechanics of dimeric VWF under physiologically relevant pH conditions.

[1] Schneider, S.W. et al. 2007 *Proceedings of the National Academy of Sciences* 104:7899-7903

[2] Springer, T.A. 2011 *Journal of Thrombosis and Haemostasis* 9 (Suppl 1):130-143

[3] Zhou, Y.F. et al. 2011 *The EMBO Journal* 30:4098-4111

## Conductivity in Polymeric Electrode for Roll-to-Roll Printed Organic Electronics: Evolution of Nanostructure and Molecular Orientation in PEDOT:PSS

C.M. Palumbiny<sup>1,2,3</sup>, C. Heller<sup>1</sup>, C.J. Schaffer<sup>1,2</sup>, V. Körstgens<sup>1</sup>, G. Santoro<sup>4</sup>, F. Liu<sup>5</sup>, C. Wang<sup>6</sup>, A. Hexemer<sup>6</sup>, T.P. Russell<sup>5</sup>, S.V. Roth<sup>4</sup>, P. Müller-Buschbaum<sup>1,2,3</sup>

<sup>1</sup> TU München, Physik-Department, Lehrstuhl für Funktionelle Materialien, 85748 Garching, Germany

<sup>2</sup> Center for NanoScience, LMU München, 80539 Munich, Germany

<sup>3</sup> Int. Graduate School of Science and Engineering, EuroTech Univ. Alliance, TU München, Germany

<sup>4</sup> Deutsches Elektron-Synchrotron, 22607 Hamburg, Germany

<sup>5</sup> Univ. of Massachusetts Amherst, Dep. of Polymer Science and Engineering, MA 01003, USA

<sup>6</sup> Advanced Light Source, Lawrence Berkeley National Lab, Berkeley, CA 94720, USA

Since the invention of organic electronics (OE), organic thin films have attracted immense interest among researchers from all over the world. The transparency and the potential of manufacturing of OE devices on flexible substrates enables numerous smart design opportunities as well as roll-to-roll (R2R) production. The performance of optimized OE devices strongly depends on the optimum length scales of the nanomorphology. In this work, the underlying morphological changes in the film volume are probed with ex-situ and in-situ X-ray scattering techniques: grazing incidence small and wide angle X-ray scattering (GISAXS and GIWAXS).<sup>[1]</sup> The brittleness of the commonly used indium tin oxide (ITO) is one of the main limiting factors for the R2R production of OEs. Flexibility however, is one of the main advantages of OE devices over conventional electronics. In this context, we show that the addition of co-solvents increases the conductivity of PEDOT:PSS polymer blend films by more than three orders of magnitude, making it suitable as an ITO replacement. The underlying structural evolution is probed with GISAXS and GIWAXS (DESY, Hamburg). As a result, the enhancement in conductivity is ascribed to fundamental morphological changes and for the first time to molecular reorientations within crystalline domains.<sup>[2]</sup>

In order to realize the goal of up-scaling, techniques such as printing are needed. Film formation typically takes place within a couple of seconds and involves complicated structure and morphology evolutions. Hence, to understand the formation of printed films, in-situ investigations are necessary. We realize the printing of PEDOT:PSS films with a self-made slot die coater, specially designed for the implementation at a synchrotron facility (ALS/LBNL Berkeley & UMass Amherst) for in-situ GIWAXS measurements. This experiment provides a comprehensive understanding of the nanomorphology evolution for directed device optimization.<sup>[3]</sup>

[1] P. Müller-Buschbaum, *Advanced Materials* 2014, DOI: 10.1002/adma.201304187.

[2] C. M. Palumbiny, C. Heller, C. J. Schaffer, V. Körstgens, G. Santoro, S. V. Roth, P. Müller-Buschbaum, *J. Phys. Chem. C* 2014, 118 (25), 13598–13606.

[3] C. M. Palumbiny, F. Liu, T.P. Russell, A. Hexemer, C. Wang, and P. Müller-Buschbaum, *in preparation*.

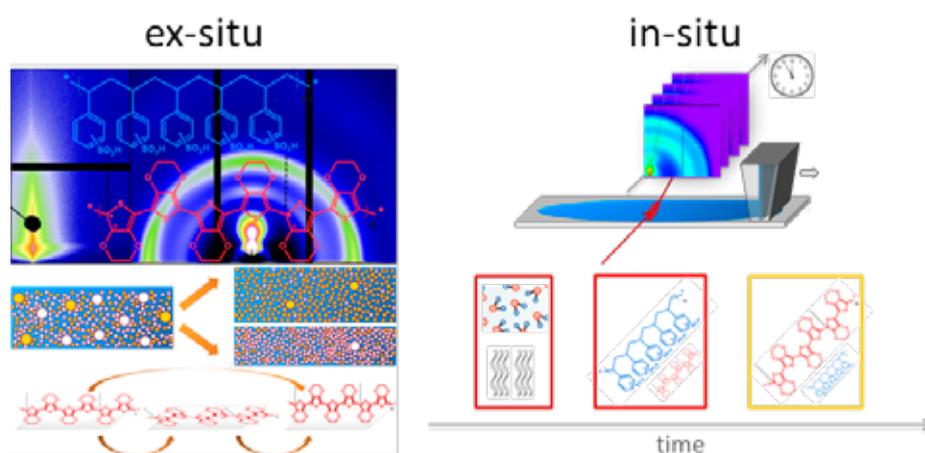


Figure 1: Ex-situ and in-situ GISAXS and GIWAXS investigations of PEDOT:PSS polymeric electrodes. The enhanced conductivity of PEDOT:PSS by co-solvents is ascribed to improved morphology and molecular orientation in crystalline domains.

## Identification of siloxane mechanochemistry with single molecule force spectroscopy and ab initio simulations

**Michael F. Pill<sup>1,2,3</sup>, Alfred Kersch<sup>1</sup>, Martin K. Beyer<sup>2,4</sup> and Hauke Clausen-Schaumann<sup>1,3</sup>**

*1 Munich University of Applied Sciences, Department of Applied Sciences and Mechatronics, Lothstr. 34, 80335 Munich, Germany*

*2 Institut für Physikalische Chemie, Christian-Albrechts-Universität zu Kiel, Olshausenstrasse 40, 24098 Kiel, Germany*

*3 Center for NanoScience (CeNS), Geschwister-Scholl-Platz 1, 80539 Munich, Germany*

*4 Institut für Ionenphysik und Angewandte Physik, Leopold-Franzens-Universität Innsbruck, Technikerstrasse 25, 6020 Innsbruck, Austria*

The mechanical stability and the degradation of individual chemical bonds can be investigated by single molecule force spectroscopy. Quantum chemical calculations of possible reactions including effects of external forces aid the interpretation of these experiments. We have investigated the force-dependent lifetime of several chemical reactions using the atomic force microscope (AFM) in force-clamp mode. Single molecules of carboxymethylated amylose (CMA) were coupled with different silanes between a glass substrate and the AFM tip.<sup>1</sup> Individual CMA molecules were stretched with different clamp forces and temperatures until a bond scission was observed. Reaction kinetics of the experiments exhibited single or bi-exponential behaviour. Bi-exponential kinetics indicates at least two separate components in the ensemble of molecules investigated: for N<sup>1</sup>-[3-(trimethoxysilyl)-propyl]diethylenetriamine (DETA), with three ethoxy groups, and 3-aminopropyl(diethoxy)methylsilane (APDEMS), with two ethoxy groups a bi-exponential behaviour was observed, while for (3-aminopropyl)-dimethyl-ethoxysilane (APDMES), with one ethoxy group, a single exponential behaviour was observed. One ethoxy group is always bond to the surface, and via the additional ethoxy groups in DETA and APDMES, the silane can form cross-links to neighbouring silane anchors, while for APDMES cross-linking to neighbouring silanes is not possible. The bi-exponential behaviour, of DETA

and APDEMS, can be explained by the fact that not at all silanes are always cross-linked. Data analysis with Arrhenius kinetic models based on a Morse potential was used to identify force independent kinetic parameters. For all three silanes one decay channel showed the same reaction parameters, which indicates a reactions at the siloxane bond, when the silane is not cross-linked. The activation energy was approximately 50 kJmol<sup>-1</sup> and the Arrhenius prefactor approximately 10<sup>8</sup> s<sup>-1</sup>. To explain the detail of the reaction pathway several possible chemical reactions were calculated using quantum chemical methods<sup>2</sup>. To obtain force dependent kinetic parameters the External Force is Explicitly Included<sup>3</sup> method was used. The base catalysed hydrolysis of the siloxane anchor exhibited nearly the same activation energy and force dependent kinetic parameters as in the experiment.

[1] S.W. Schmidt, T. Christ, C. Glockner, M.K. Beyer and H. Clausen-Schaumann, *Langmuir*, 26 (2010), 15333-38.

[2] M. F. Pill, S. W. Schmidt, M. K. Beyer, H. Clausen-Schaumann, and A. Kersch, *Journal of Chemical Physics*, (2014), 140 (4), 044321

[3] J. Ribas-Arino, M. Shiga and D. Marx, *Chemistry - A European Journal* 48 (2009), 4190-93.

## Lissajous rocking ratchet in quantum dots

**Sergey Platonov<sup>1</sup>, Bernd Kästner<sup>2</sup>, Hans W. Schumacher<sup>2</sup>, Sigmund Kohler<sup>3</sup> and Stefan Ludwig<sup>1</sup>**

*1 Center for NanoScience & Fakultät für Physik, LMU-Munich, 80539 München, Germany*

*2 Physikalisch-Technische Bundesanstalt, Bundesallee 100, 38116 Braunschweig, Germany*

*3 Instituto de Ciencia de Materiales de Madrid, CSIC, 28049 Madrid, Spain*

Symmetries are a very important concept of physics - the most famous one being the CPT symmetry. Breaking symmetries often gives rise to interesting effects and, in particular, breaking the time-reversal symmetry is a requirement for many applications such as information processing. Here we present such a concept based on a quantum dot (QD) electrostatically defined in a AlGaAs/GaAs heterostructure. We break time-reversal symmetry by periodically modulating its barriers such that a single

electron tunneling current occurs. The current direction can be controlled by introducing a phase difference between the two periodic signals. We show that our QD resembles a Lissajous ratchet. A consistent theoretical model based on scattering matrix formalism describes our experimental findings. Similar devices could be realized in a large variety of systems, for instance in nanomechanical or superconducting circuits. Possible applications include noise management, filtering and signal routing.

## Facilitated diffusion mechanism of microtubule polymerases

**Emanuel Reithmann, Louis Reese, Erwin Frey**

*CeNS, Arnold Sommerfeld Center for Theoretical Physics, LMU Munich*

The diffusive motion of proteins on filamentous structures in the cell is vital for several cellular functions like gene regulation and cytoskeletal dynamics. A targeting mechanism of the respective reaction sites that is faster than the limit imposed by three dimensional diffusion is crucial in both cases. In this respect, recent experimental studies suggested that a facilitated diffusion mechanism due to reduction of dimensionality in the diffusive motion is utilized by two key players involved in regulation of microtubule dynamics, MCAK and XMAP. To quantify this facilitated diffusion mechanism on a theoretical level we investigate a stochastic lattice gas model for enzymatic activities at microtubule ends such as polymerization and depolymer-

ization. We quantify our models using data accessible from experimental studies. This allows for a direct comparison between theory and experiment. For both proteins, we propose a model that is in excellent agreement with experimental findings. Our results show that one dimensional diffusion serves as a crucial mechanism to enhance the enzymatic activity of these proteins. We hypothesize that this mechanism ensures that regulation of microtubule dynamics by MCAK and XMAP becomes feasible under physiological conditions. Furthermore, we observe that the facilitated diffusion mechanism operates most efficiently at cellular enzyme concentrations.

## Nanoscale DNA origami based plasmonic ring structures

**Eva-Maria Roller<sup>1</sup>, Larousse K. Khorashad<sup>2</sup>, Michael Fedoruk<sup>3</sup>, Robert Schreiber<sup>1</sup>, Jochen Feldmann<sup>3</sup>, Alexander O. Govorov<sup>2</sup>, Tim Liedl<sup>1</sup>**

*1 Department of Physics and CeNS, Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, 80539 München, Germany*

*2 Department of Physics and Astronomy, Ohio University, Athens, Ohio 45701, USA*

*3 Photonics and Optoelectronics Group, Physics Department and CeNS, Ludwig-Maximilians-Universität München, Amalienstr. 54, 80799 Munich, Germany*

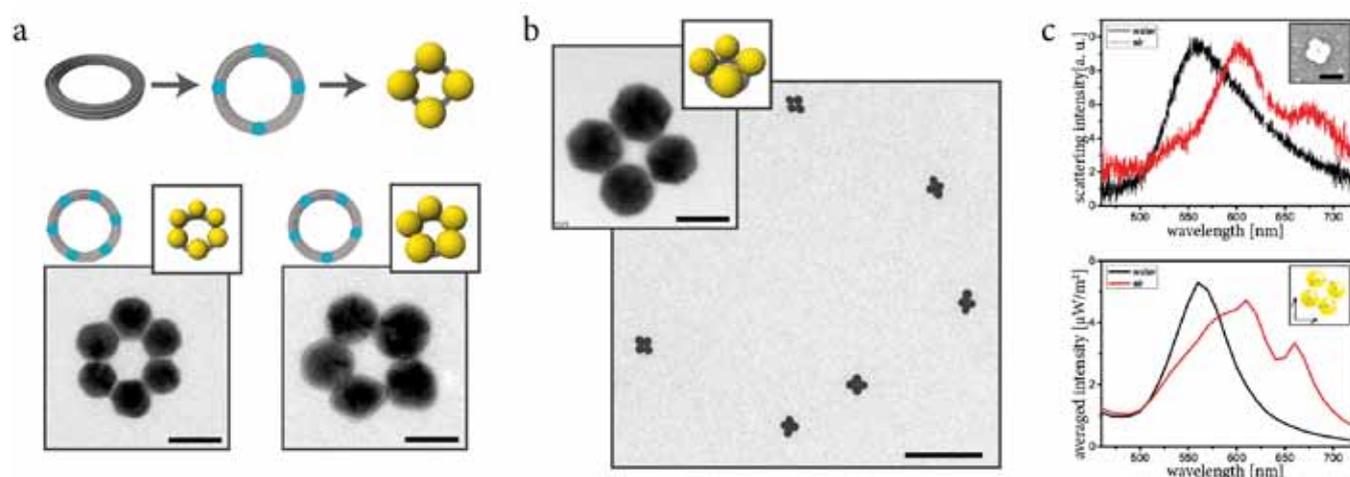
Nanoscale materials for light manipulation are of great interest due to their possible applications in signal modulation, metamaterial research and optical sensing. With the aim to control electromagnetic waves at visible frequencies, we created self-assembled nanostructures with subwavelength features that exhibit collective plasmon modes in the visible region. One concept for the experimental realization of artificial optical magnetic modes relies on the arrangement of nanoparticles in a ring structure<sup>1,2</sup>. The bottom-up strategy of DNA-self-assembly has been demonstrated to be a viable method to construct building blocks for plasmonic metamaterials<sup>3</sup>. Herein we applied this method for the fabrication of ring structures composed of four to eight precisely organized single metal nanoparticles by us-

ing a ring-shaped DNA origami structure of ~ 60 nm diameter. The optical response of these metamolecules was measured by bulk absorption spectroscopy as well as by single structure scattering spectroscopy. The unique plasmonic features were then compared to computational simulations. In conclusion we demonstrated the possibility to create fluids containing optically active metamolecules.

[1] Alù, A. *et al. Opt. Express* 14, 15557-1567 (2006).

[2] Shafiei, F. *et al. Nature Nanotech.* 8, 95-99 (2013).

[3] Kuzyk, A. *et al. Nature* 483, 311-314 (2012).



**Fig. 1:** DNA-origami – AuNP ring structures. a, Plasmonic ring structures were constructed by arranging gold nanoparticles on ring-shaped DNA origami structures with specific predefined attachment points. Scale bar 40 nm. b, Wide field TEM micrograph of the DNA-origami – AuNP hybrids. Scale bar 400 nm. Inset: Zoom in on one structure. Scale bar 40 nm. c, dark-field scattering spectra of a single structure surrounded by water (black) and air (red) and corresponding numerical simulation.

## Novel thermoelectric films based on polymer-nanoparticle composite

**N. Saxena<sup>1,2</sup>, A. Greppmair<sup>3</sup>, M. Coric<sup>4</sup>, J. Wernecke<sup>5</sup>, S. Marggraf<sup>5</sup>, E. M. Herzig<sup>4</sup>, M. S. Brandt<sup>3</sup>, P. Müller-Buschbaum<sup>1,2</sup>**

*1 TU München, Physik-Department, Lehrstuhl für Funktionelle Materialien, 85748 Garching, Germany*

*2 Center for NanoScience, LMU München, 80539 München, Germany*

*3 TU München, Walter-Schottky-Institut and Physik-Department, 85748 Garching, Germany*

*4 TU München, Munich School of Engineering, 85748 Garching, Germany*

*5 Physikalisch-Technische Bundesanstalt, BESSY II Helmholtz-Zentrum Berlin, 12489 Berlin, Germany*

Thermoelectric materials gained interest over the past years, due to a high interest in renewable, sustainable and environment-friendly technologies for energy conversion. In thermoelectrics, a temperature gradient is applied to both ends, which leads to a change in the charge carrier distribution due to their flow from the hot to the cold side, depending on the electrical conductivity of the material. It is feasible to have a low thermal conductivity, which prevents the propagation of phonons and heat through the material. A measure for the efficiency of a thermoelectric material is the so-called figure of merit ZT:

$$ZT = \frac{\sigma S^2}{\kappa}$$

$\sigma$  describes the electrical conductivity,  $S$  the Seebeck coefficient or thermopower and  $\kappa$  the thermal conductivity.  $\sigma S^2$  is also often referred to as the power factor. So far, thermoelectric materials mostly comprised inorganic components, such as bismuth and

tellurium. Although these materials show high ZT, they suffer from problems such as high energy consumption for production, or environmental concerns because of potential toxicity of the components and/or low abundance. In order to overcome these restraints, we present a hybrid approach for making thermoelectric films by combining the co-solvent-treated polymer blend PEDOT:PSS with inorganic nanoparticles. This strategy is especially appealing because of the high tailorability of polymer morphologies, the high availability of polymer materials and the possibility for solution-based processing at ambient conditions. In this context, we realized a functioning thermoelectric system and now aim for the increase of the ZT-values. Measurements were carried out regarding electrical conductivity, Seebeck coefficient and film thickness. In addition, first experiments were used to investigate the correlation of the distribution of nanoparticles within the film with the measured thermoelectric properties using resonant soft x-ray scattering.

## Non-equilibrium transport through a QD using Keldysh-fRG 1

**Dennis Schimmel, Jan Heyder, Florian Bauer, Jan v. Delft**

*Arnold-Sommerfeld-Center Munich, LMU Munich, Center for NanoScience, Nanosystems Initiative Munich*

The functional renormalization group (fRG) is a powerful resummation technique which recasts the computation of diagrams into a differential equation. We apply the non-equilibrium (Keldysh) version of it to a single impurity Anderson model. From previous studies it is known that the truncated fRG-scheme employed violates the particle-conservation law. Thus, the resulting value of a given observable, e.g. the conductance, depends on the precise representation used. We show the dependence of the differential conductance out of equilibrium on the representation for

finite bias voltage at different temperatures and magnetic fields. In future, we hope to apply this technique to a quantum point contact (QPC). The QPC is assumed to be described by a one-dimensional, inhomogeneous, interacting region coupled to non-interacting leads. So far, a different implementation of fRG has been used to explore the equilibrium properties of this model. It shows striking qualitative agreement with the measured 0.7 anomaly.

## Click chemistry – a versatile method for enzyme immobilization in large pore colloidal mesoporous silica nanoparticles

**Alexandra Schmidt, Martina Lichtnecker, Kathrin Bader, Stefan Niedermayer and Thomas Bein**

*Department of Chemistry and Center for NanoScience (CeNS), University of Munich (LMU), Butenandtstrasse 5 – 13(E), 81377 Munich, Germany*

Recently, we have developed several bare and modified colloidal mesoporous silica systems, for example uniform MSNs functionalized with numerous organic moieties.<sup>[2][4-5]</sup> However, the synthesis of MSNs with large pores (LP\_MSN) and well-defined small particle sizes is an important challenge, as the pore size of conventional silica nanoparticles (around 4 nm) is unsuitable for the adsorption of larger biomolecules such as enzymes and small interfering RNA (siRNA). The immobilization of enzymes for catalytic processes is a key application of mesoporous silica materials as the pores protect the fragile cargo from external influences such as degradation. In this contribution, we demonstrate the optimization of the pore diameter and the molecular functionalization of the mesopores in order to allow the fac-

ile diffusion and attachment of guest molecules into the host. An increase in pore diameter to values larger than 5 nm was achieved with micellar expanders, large molecular weight surfactants and novel fluorinated co surfactants.<sup>[6]</sup> The employed synthesis procedure yields homogeneous azide-functionalized LP\_MSN-N<sub>3</sub> of about 120 nm in size with ultra-large pores of 10 nm, using a direct co condensation approach to introduce the organo-functionality. The azide-moieties in the porous framework allow for a mild and biocompatible click chemistry reaction with two acetylene-functionalized enzymes of different sizes (sp cytochrome C and sp-trypsin). The catalytic activity of the immobilized enzymes was investigated with fluorogenic reactions and it was demonstrated that both enzymes are highly

active in their immobilized state compared to previous studies and free enzymes; a 2.9 times higher activity was observed for LP\_MSN-CytC compared to the free enzyme.

[1] A. M. Sauer, A. Schlossbauer, N. Ruthardt, V. Cauda, T. Bein, C. Bräuchle, *Nano Lett.* 2010, 10, 3684.

[2] S. A. Mackowiak, A. Schmidt, V. Weiss, C. Argyo, C. von Schirnding, T. Bein, C. Bräuchle, *Nano Lett.* 2013, 13, 2576.

[3] A. Schlossbauer, A.M. Sauer, V. Cauda, A. Schmidt, H. Engelke,

U. Rothbauer, K. Zolghadr, H. Leonhardt, C. Bräuchle, T. Bein, *Adv. Healthcare Mater* 2012, 3, 316.

[4] V. Cauda, A. Schlossbauer, J. Kecht, A. Zuerner, T. Bein, *J. Am. Chem. Soc.* 2009, 131, 11361.

[5] J. Kobler, K. Möller, T. Bein, *ACS Nano* 2008, 2, 791.

[6] F. Gao, P. Botella, A. Corma, J. Blesa, L. Dong, *J. Phys. Chem. B* 2009, 113, 1796.

### Characterizing Cell Motility and Transmigration in Ring Shaped Micro Patterns

**C. Schreiber, F. J. Segerer, J. O. Rädler**

*Fakultät für Physik & Center for NanoScience, Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, 80539 München*

Cell migration is important in many biological processes such as embryogenesis, wound healing, or cancer metastasis. To understand the formation of tumors and the effect of drugs, a detailed characterization of the migration behavior is important. Furthermore the ability to overcome barriers like the basement membrane is a key indicator for the aggressiveness of different cancer cells. Therefore a systematic approach for studying transmigration behavior is necessary to characterize the invasiveness. Here we study single cell migration constrained to a micro-patterned ring-shaped lane. On such tracks cells perform a 1D

persistent random walk. Analyzing large arrays of these patterns in parallel, we are able to evaluate characteristic velocities and persistence times of a cell line with high accuracy. By introducing a gap of defined size and chemical composition in the ring shaped lane we study cell behavior at defined chemical interfaces. At the chemical border cells either turn around or transigrate over the barrier. Studying the transmigration probability systematically, we find a steady decrease of transition probability with increasing barrier width. Thus, this system will allow the detailed comparison of cell lines with varying invasiveness.

### Models for Angiogenesis on microstructured surfaces

**Simon Schuster<sup>1</sup>, Kerstin Pflieger<sup>1</sup>, Florian Gegenfurtner<sup>1</sup>, Max Albert<sup>2</sup>, Felix Segerer<sup>2</sup>, Joachim Rädler<sup>2</sup>, Angelika M. Vollmar<sup>1</sup> and Stefan Zahler<sup>1</sup>**

*1 Centre for Drug Research, Department of Pharmacy, University of Munich*

*2 Department of Physics, University of Munich*

Angiogenesis, the growth and formation of novel blood vessels from preexisting vessels, is an important physiological and pathophysiological process involved in wound healing but also in cancer progression. However, dynamics of angiogenesis in general and the impact of physical factors are barely understood. We try to model different cellular processes of primary endothelial cells using micro-structured surfaces. With the help of micro contact printing we bring HUVECs (= Human Umbilical Vein Endothelial Cells) into defined cellular shape and stress conditions in order to model 3D migration, tip cell

formation and fibronectin-fibrillogenesis. All these processes have been shown to play an important role in angiogenesis. We use primary endothelial cells, which are not adapted to 2D cell culture, to establish an easy accessible model system for imitating 3D migration on a flat surface. This model has been proposed before for 3T3 fibroblast, but HUVECs show some striking differences. Our results reveal that 1D migrating endothelial cells share a lot of properties compared to 3D migrating cells, regarding their overall morphology as well as their cellular response to selected small molecule inhibitors.

### DNA Nanotubes as Intracellular Delivery Vehicles *in vivo*

**S. Sellner<sup>1</sup>, S. Kocabey<sup>2</sup>, A. K. Nekolla<sup>1</sup>, F. Krombach<sup>1</sup>, T. Liedl<sup>2</sup>, M. Rehberg<sup>1</sup>**

*1 Walter Brendel Centre of Experimental Medicine, Ludwig-Maximilians-Universität München, Marchioninistr. 15, 81377 Munich, Germany*

*2 Department of Physics & Center for NanoScience, Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, 80539 Munich, Germany*

We investigated the use of DNA-based nanotubes as carrier systems for CpG delivery and their effect on immune cells *in vivo* and in real time. DNA nanotubes were produced using the single-stranded tile assembly method by mixing 48 unique DNA strands to form 8-helix nanotubes with a length of ~40 nm and a diameter of ~8 nm. Unmethylated CpG sequences are recognized by Toll-like receptor 9 (TLR9), present on lymphocytes

and antigen-presenting cells, incl. macrophages, and thus initiate an innate immune response. To test the immune stimulation *in vivo*, CpG-decorated DNA nanotubes were microinjected into the cremaster muscle of anesthetized mice. Using *in vivo* microscopy, we observed that CpG-decorated DNA nanotubes were rapidly internalized by tissue-resident macrophages and colocalized with late endosomes/lysosomes in these cells. Only

microinjection of CpG-decorated DNA nanotubes but not of plain DNA nanotubes or CpG oligonucleotides induced a significant increase in leukocyte adhesion and transmigration in post-capillary venules of the cremaster muscle. Interestingly, CpG-decorated DNA nanotube-induced leukocyte recruitment was almost completely abolished in animals treated with an inhibitor of mast cell degranulation. Confocal microscopy of immunostained muscle tissue revealed that only after treatment with

CpG-decorated DNA nanotubes, nuclei of cells surrounding the microinjection site were positive for phosphorylated p65, indicating TLR-9-mediated activation of the NF- $\kappa$ B pathway. Taken together, these *in vivo* findings suggest that DNA nanotubes are promising delivery vehicles to target tissue macrophages. The immunogenic potential apparently depends on the decoration of DNA tubes with CpG oligonucleotides.

## Tip-enhanced Raman Spectroscopy (TERS) – Excitation Power Dependence?

**Xian Shi<sup>1</sup>, Tobia Mancabelli<sup>1</sup>, Harald Budde<sup>1</sup>, Alexandre Bouhelier<sup>2</sup>, Achim Hartschuh<sup>1</sup>**

<sup>1</sup> Department Chemie and CeNS, LMU München, Germany

<sup>2</sup> Département Nanosciences, Université de Bourgogne, France

Tip-enhanced Raman spectroscopy (TERS) utilizes the enhanced electric field in the proximity of an optical antenna to achieve nanometer spatial resolution and high detection sensitivity<sup>[1]</sup>. However, the Raman enhancement mechanism under strong local field still remains unclear. A recent report indicates a contribution from non-linear Raman scattering in the case of very strong enhancement<sup>[2]</sup>. To study this, we conduct power-dependent confocal and tip-enhanced measurements by simultaneously recording the excitation laser intensity and the corresponding Raman G-band signal of single carbon nanotubes

(CNTs) dispersed on a gold film. Here we discuss a possible contribution of stimulated Raman scattering using a single excitation laser frequency. Our results will contribute to our understanding of tip-enhanced mechanism and shed light on experimental findings.

[1] Nina Mauser and Achim Hartschuh, *Chem. Soc. Rev.*, 2014, 43, 1248.

[2] R. Zhang et al, *Nature*, 2013, 498, 82.

## Cell manipulation using Surface Acoustic Waves

**Melanie Stamp<sup>1,2</sup>, Christoph Westerhausen<sup>1,2</sup>, Achim Wixforth<sup>1,2</sup>**

<sup>1</sup> Chair for Experimental Physics I, Augsburg University, Germany

<sup>2</sup> Center for NanoScience and Nanosystems Initiative Munich, Schellingstraße 4, 80799 Munich, Germany

Studying cell proliferation and migration is crucial not only for scientific interests, but could also be used for a medical purpose. Therefore adhesion phenomena of different cell-material combinations can be examined to determine specific properties. For an optimal implementation of materials in living environments, a thorough characterization of cell adhesion properties, both kinetics and strength, is required. Here we present a miniaturized (~ 100  $\mu$ l) lab-on-a-chip implant hybrid system which allows to quantify cell (de-) adhesion under dynamic conditions mimicking those of physiological relevance. Surface acoustic

waves on optical transparent chips are used to create a microfluidic shear spectrum ranging from 0 - 400  $s^{-1}$  which the cells are exposed to. We demonstrate its applicability with a model of an osseointegration study using SAOS-2 cells on medical implant material samples. The great advantage of DANI compared to present-state cell adhesion probing systems is that it requires only very few lab consumables, live observation of the cells and arbitrary material-cell combinations. Further on, the measurement chamber allows temperature and pH-value control (e.g. to generate physiological conditions).

## Game Theory on the Nanoscale

**Georg Urtel\*, Dieter Braun\* and André Estévez-Torres\*\***

\*Systems Biophysics, Department of Physics, Center for Nanoscience, Ludwig-Maximilians-University Munich, 80799 Munich, Germany

\*\*Laboratoire de photonique et de nanostructures, LPN-CNRS, route de Nozay, 91460 Marcoussis, France

In evolutionary game theory, cyclical dominance is a simple set of rules, that can lead to spatio-temporal pattern-formation<sup>[1]</sup>. The ability of such systems to form these patterns depends on the diffusion coefficient and the system size. The DNA-Toolbox is an well-established set of enzymes (polymerase, exonuclease, nickase) and DNA-strands, where the amplification of one DNA-species can activate or inhibit the production of another species<sup>[2]</sup>. With a similar system, predator-prey-dynamics have already been observed<sup>[3,4]</sup>. Linking three DNA-species together, such that A inhibits B, B inhibits C and C inhibits A, allows cyclical dominance on the nanoscale. Using a simple model<sup>[2]</sup> and a finite element simulation software package

(COMSOL), the behavior can be simulated in 0D, 1D and 2D. In the latter case, moving patterns like spiral waves build up. The three species replace each other dynamically according to their cyclical dominance.

[1] Reichenbach, T., Mobilia, M., & Frey, E. (2007). Mobility promotes and jeopardizes biodiversity in rock-paper-scissors games. *Nature*, 448(7157), 1046-1049.

[2] Padirac, A., Fujii, T., & Rondelez, Y. (2012). Bottom-up construction of *in vitro* switchable memories. *Proceedings of the National Academy of Sciences*, 109(47), E3212-E3220.

[3] Fujii, T., & Rondelez, Y. (2012). Predator-prey molecular ecosystems. *ACS nano*, 7(1), 27-34.

[4] Padirac, A., Fujii, T., Estévez-Torres, A., & Rondelez, Y. (2013). Spatial waves in synthetic biochemical networks. *Journal of the American Chemical Society*, 135(39), 14586-14592.

### Microparticle formulation of mRNA for sustained protein production in cells

Maximilian Utzinger<sup>1,2,3</sup>, Christian Dohmen<sup>1,2,3</sup>, Carsten Rudolph<sup>1,2,3</sup>, Christian Plank<sup>1,2,4</sup>

1 Ethris GmbH, Martinsried, Germany; 2 Nanosystems Initiative Munich, Germany; 3 Center for NanoScience, Germany; 4 Institute of Experimental Oncology and Therapy Research, Klinikum Rechts der Isar, Technische Universität München, Germany

Stabilized non-immunogenic messenger RNA (SNIM® RNA) is being established as a favourable alternative for enzyme replacement or gene therapies. SNIM® RNA can be administered repeatedly leading to expression of therapeutically active proteins even at low doses. In some cases, a prolonged expression is desired to achieve this goal only with a few applications. Hence, SNIM® RNA has been compacted and concentrated into PLGA (poly(lactic-co-glycolic)acid) microparticles of adjustable sizes to increase the local sustained release of the messenger

RNA. In this work of research it is shown that a prolonged expression can be achieved by using microparticles as the delivery agent *in vitro* on mesenchymal stem cells compared to a traditional lipidic nanoparticle formulation of SNIM® RNA. The goal of this project is to develop a drug delivery system which can be used for local administration in different body tissues like bone, muscles or skin. The microparticles have been investigated by mRNA expression tests *in vitro*, and additionally by light – and electron microscopy for size analysis.

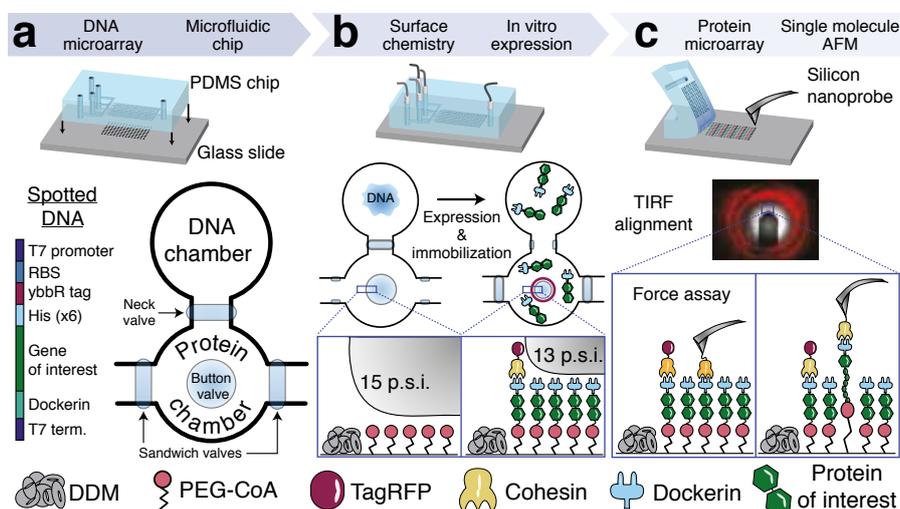
### From Genes to Protein Mechanics on a Chip

Tobias Verdorfer, Marcus Otten, Wolfgang Ott, Markus A. Jobst, Lukas F. Milles, Diana Pippig, Hermann E. Gaub, Michael A. Nash

Chair for Applied Physics, Biophysics and Molecular Materials and Center for NanoScience, LMU Munich

Mechanical forces acting on proteins play a pivotal role in biological systems. By applying forces to single molecules, conformational changes and energetic barriers along unfolding pathways can be probed by SMFS. Since low experimental throughput has significantly limited the capacity to screen libraries of proteins, we developed a versatile microfluidic system to address these issues. Our platform enables parallelized force spectroscopy utilizing cell-free *in vitro* gene expression, covalent protein immobilization and subsequent measurements of mechanical properties at the single molecule level in a streamlined format with one single cantilever. A PDMS microfluidic chip on a glass slide seals engineered DNA spots to provide micro reactors for protein synthesis. Expressed fusion proteins covalently attach to the glass surface at their N-termini and display free dockerin domains at their C-termini. With a single cohesin-functionalized cantilever, un-

folding pathways and unbinding characteristics of multiple different proteins can be probed. Our example library contained structural proteins, cytoskeletal constituents, enzymes, and fluorescent proteins, which we were able to detect by their specific unfolding fingerprints. Analysis of contour-length increments and rupture force - loading-rate data characterizes the constructs and are compared with computational methods. As an application of this novel system, mutant variants of individual receptor-ligand proteins can be constructed, immobilized and measured on a single molecule basis to screen for candidates in protein design. For example, saturation mutagenesis of single residues responsible for binding their counterpart can be performed and characterized on a single device. This method provides a unique means of comparing forced dissociation and unfolding pathway characteristics of engineered proteins.



**Method workflow.** (a) A gene array is spotted onto a glass slide and a multi-layer microfluidic chip featuring 640 unit cells is aligned to the DNA microarray and bonded to the glass slide. Each unit cell comprised a DNA chamber, a protein chamber, and superseding elastomeric control valves actuated by pneumatic pressure. (b) Control valves are utilized for spatially selective surface modification of each protein chamber with PEG-CoA, for fluidic isolation of each chamber prior to *in vitro* expression of the microspotted DNA and for fluorescent labeling with TagRFP-Cohesin. (c) After removal of the microfluidic device, the resulting well-defined, covalently attached protein microarray are accessed from above with a functionalized AFM cantilever. Single-molecule unfolding traces of each of the protein constructs are thus acquired sequentially at each corresponding array address with a single cantilever in a single experiment.

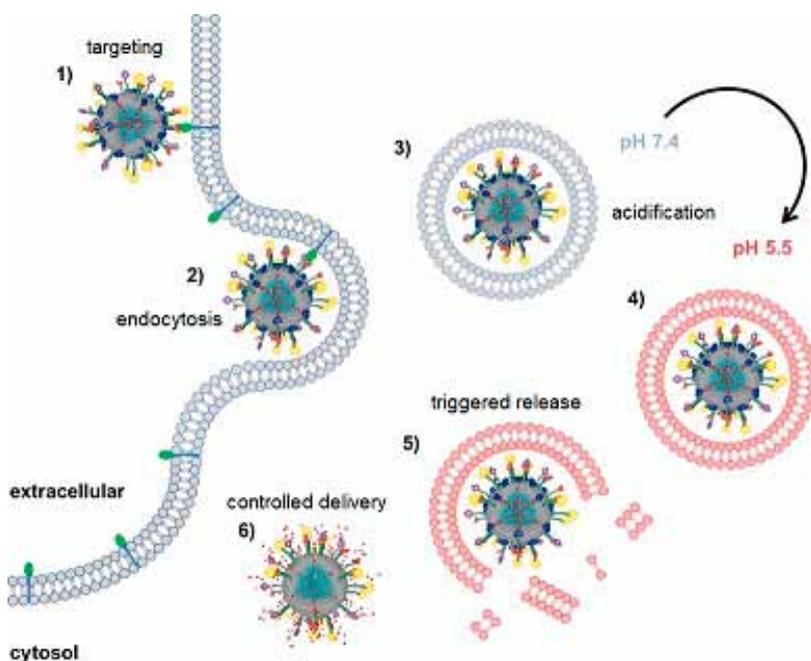
## Mesoporous silica nanoparticles as drug delivery platforms<sup>[1]</sup>

Veronika Weiss<sup>a</sup>, Alexandra Schmidt<sup>b</sup>, Christian Argyo<sup>b</sup>, Stephan A. Mackowiak<sup>a</sup>, Stefan Datz<sup>b</sup>, Constantin von Schirnding<sup>b</sup>, Thomas Bein<sup>b</sup>, Christoph Bräuchle<sup>a</sup>

*a* AK Prof. Bräuchle, *b* AK Prof. Bein, Department of Chemistry, Nanosystems Initiative Munich (NIM), Center for NanoScience (CeNS), University of Munich (LMU), Butenandtstr.11, 81377 Munich, Germany

Nano-sized mesoporous silica particles (MSN) with high colloidal stability attract growing attention as drug delivery systems for targeted cancer treatment. These MSN offer a high pore volume, a defined and tunable pore size, and various functionalization possibilities.<sup>[1,2]</sup> Recently, we have developed a strategy to incorporate molecular functionality at different locations of colloidal mesoporous silica nanoparticles. For targeted drug delivery, the triggered release of bioactive compounds at specific locations, times and conditions is highly desirable. Here, we present our recent studies on different capping and release mechanisms for

controlled and targeted delivery of model drugs into cancer cells. With live-cell spinning-disc fluorescence microscopy we were able to monitor the uptake of MSN by single cells, trigger endosomal escape by photoactivation and detect the release behavior from the particles (cf. Figure). The functionality of the targeting ligands which have been attached to our nanoparticle system was evaluated by performing competition experiments with free ligands. We investigated several delivery platforms based on MSN including a supported lipid bilayer as capping system, or pH-responsive gatekeepers such as polymer, enzyme or dendron structures. Controlled release could be demonstrated either with light activation, reduction of the pH or reductive milieu inside living cells. For demonstration of successful intracellular release of the encapsulated guest molecules we either monitored spreading of fluorescent model drugs or the destruction of fluorescently labeled cell compartments. The obtained results demonstrate that multifunctional MSN are a promising and flexible platform for drug delivery applications, such as cancer therapy.



[1] C. Argyo, V. Weiss, C. Bräuchle, T. Bein, *Chem. Mater.* 2014, 26, 435.

[2] S. A. Mackowiak, A. Schmidt, V. Weiss, C. Argyo, C. von Schirnding, T. Bein, C. Bräuchle, *Nano Lett.* 2013, 13, 2576.

[3] S. Niedermayer, V. Weiß, A. Herrmann, A. Schmidt, S. Datz, E. Wagner, C. Bräuchle, T. Bein, *submitted*.

Schematic representation of different stages of a targeted cellular uptake of a multifunctional MSN and controlled release of the cargo into the cytoplasm of cancer cells. 1) Active docking to cell surface receptor of a nanocarrier via targeting ligands; 2) process of ligand/receptor-mediated endocytosis; 3) MSN entrapped in endosome; 4) intracellular transport and acidification of endosome; 5) triggered endosomal escape of nanocarrier, thus obtaining access to the cytoplasm; 6) controlled delivery of the cargo inside the cell.<sup>11</sup>

## Conformational changes of Sti1 when Hsp70 or/and Hsp90 bind

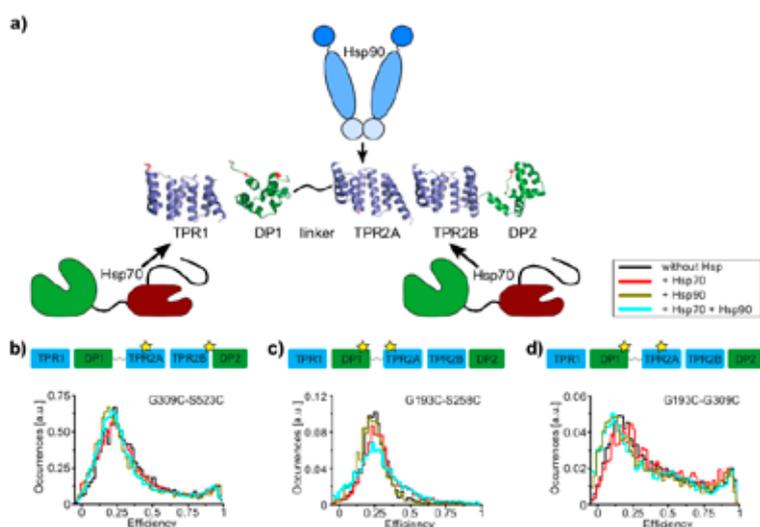
**Daniela Wengler<sup>1</sup>, Alina Röhl<sup>2</sup>, Jelle Hendrix<sup>1</sup>, Johannes Buchner<sup>2</sup>, Don C. Lamb<sup>1</sup>**

<sup>1</sup> Department Chemie, Center for Nano Science, Center for integrated protein science (CIPSM) and Nanosystems Initiative München (NIM), Ludwig-Maximilians-Universität München, Butenandtstr. 11, 81377 München, Germany

<sup>2</sup> Center for integrated protein science (CIPSM) at the Department Chemie, Technische Universität München, Lichtenbergstr. 4, 85747 Garching, Germany

Heat shock proteins like Hsp70 and Hsp90 work together as chaperones to help nascent proteins reach their final functional conformation. Understanding the underlying mechanisms of chaperone assisted protein folding may thus help to prevent diseases like Alzheimer or Parkinson. The cochaperone Sti1 helps to bring the chaperones Hsp70 and Hsp90 in contact. Sti1 has five domains, two aspartate and proline rich (DP) domains and three tetratricopeptide repeat (TPR) domains and a flexible linker. The different domains form three functional elements, a flexible N-terminal module (TPR1 and DP1), a long linker region and a rigid C-terminal module (TPR2A, TPR2B

and DP2). Sti1 has one binding site for Hsp90, in the TPR2A domain, and two binding sites for Hsp70, in the TPR1 and the TPR2B domain (Figure 1a). On a solution based setup with MFD (Multi-parameter Fluorescence Detection) in combination with PIE (Pulsed Interleaved Excitation)<sup>1</sup> we use spFRET (single pair Förster Resonance Energy Transfer) measurements to show that the two TPR2 domains are rigidly connected (Figure 1b) and the distance of the ends of the linker does not change in the presence of Hsps (Figure 1c). Furthermore, we encapsulated the protein in 200 nm large vesicles, which we then immobilized to the surface<sup>2</sup>. We could demonstrate, by using surface based spFRET with TIR (Total Internal Reflection) excitation, that Hsp90 influences where Hsp70 binds. In the absence of Hsp90, the TPR2B domain is the preferred Hsp70 binding domain. The Sti1 molecule is in a more compact conformation (Figure 1d) and Hsp70 prefers to bind to the TPR1 domain, when Hsp90 binds. Taken together, our results suggest that the presence of Hsp90 regulates the binding of Hsp70 and assures the transfer of Hsp70 between the two modules, which is maybe responsible for the efficient handover of the client protein between Hsp70 and Hsp90.



[1] Kudryavtsev, V. et al. *Chemphyschem* 13, 1060-78 (2012)

[2] Okumus, B. et al. *Biophys. J.* 87, 2798-806 (2004)

## Double Gate Organic Thin Film Transistors on Thin Foils for Biosensing

**Franz Werkmeister<sup>1</sup>, Teru Koide<sup>1,2</sup>, Bert Nickel<sup>1</sup>**

(1) Fakultät für Physik & CeNS, Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, 80539 München, Germany

(2) on leave from: Japan Patent Office, 3-4-3 Kasumigaseki, Chiyoda-ku Tokyo 100-8915, Japan

There is a need for cheap, flexible and lightweight biosensors. Biosensors based on organic electronics match these requirements. We have demonstrated a transducer based on an Organic Thin Film Transistor (OTFT). The organic semiconductor was encapsulated by a thin layer of tetratetracontane (TTC) to enable stable operation in electrolyte [1]. However, the bottom gate of this device has still been a silicon chip. We replaced the Si gate with a thin metal electrode and the silicon oxide dielectric with a biocompatible dielectric, parylene to fully realize the advantages of organic electronics. Thin foils of parylene with a thickness of ca. 2  $\mu\text{m}$  can also serve as the substrate for the OTFT, resulting in flexible devices. The electrode structures of the OTFTs are micro patterned by photolithography. Such OTFTs can be operated in electrolytes [2]. Here we show operation of OTFTs operated as double-gate thin film transistors based on parylene as substrate and bottom gate dielectric. The encapsulation has been changed from TTC to parylene-C, since these films yield a higher ca-

pacitance and are crosslinked. Measurements are done in 10 mM Dulbecco's PBS buffer solution. The threshold voltage of the top gate can be adjusted by the applied bottom gate voltage. This allows maximising the transconductance of the OTFT. The OTFTs are mounted in a commercial plastic micro fluidic flow chamber. Six individual transistors are placed in the flow channel and can be read out in parallel via hot-switching through the individual transistors. Detection of urea is demonstrated with OTFTs functionalized with the enzyme urease. Urease catalyzes the hydrolysis of urea, which results in a pH shift. This pH shift is measured by the transistor.

[1] M. Göllner, G. Glasbrenner and B. Nickel, *Electroanalysis* 24, 2012, 24, No. 2, 214-218.

[2] F. Werkmeister, B. Nickel, *J. Mater. Chem. B*, 2013, 1, 3830-3835.

## Manipulation of cell proliferation and migration using surface acoustic waves

**Christoph Westerhausen<sup>1,2</sup>, Manuel Brugger<sup>1,2</sup>, Melanie Stamp<sup>1,2</sup>, Achim Wixforth<sup>1,2</sup>**

*1 Experimental Physics I, Physics Institute, University of Augsburg, Augsburg, Germany*

*2 ;Nanosystems Initiative Munich NIM, Munich, Germany*

During tissue injury large numbers of endothelial cells are injured, destroyed or removed. After hemostasis the wound needs to be sealed. Thus, the remaining cells have to rebuild the tissue by proliferation and migration to restore its function. Here, obviously, time is a critical factor. Thus, an exciting question in biological physics is: "Can you enhance cell growth?" and, considering clinical surgery: "Can you manipulate velocity and direction of cell growth?". Beneath radiation, pressure or temperature changes to manipulate cell growth, mechanical effects are of special interest. In the past, static mechanical treatment has been shown to stimulate cell growth under specific conditions.

However, highly controllable dynamic manipulation of microscopic systems respectively living cells is enabled by the technology of surface acoustic waves. Here we demonstrate the bio compatibility and bio functionality of such a bio reactor for dynamic cell manipulation. Saos2 cells on a SiO<sub>2</sub> covered LiNbO<sub>3</sub> substrate are continuously treated with acoustic waves for 72 hours. By the combination with established wound healing assays we show significantly increased proliferation respectively migration of Saos2 osteoblasts compared to reference samples. Moreover we give an outlook on continuative experiments to explain the physical reasons of the observed effects.

## Synthesis of nanostructured metal oxide electrodes for electrochemical lithium insertion

**Peter M. Zehetmaier, Ksenia Fominykh, Johann M. Feckl, Dina Fattakhova-Rohlfing, Thomas Bein**

*Department of Chemistry and Center for NanoScience (CeNS), University of Munich (LMU), Butenandtstr. 11 (E), 81377 Munich, Germany*

The development of electrode materials offering both high energy density and high power is urgently required in the field of electrochemical energy storage. Materials with very short charging times are highly desirable for the use in electric vehicles and mobile electronics and will enable many envisioned applications. Nanostructuring is known to be one way to drastically alter the properties of materials and therefore is considered as one of the key routes towards the improvement of already commercially applied electrode materials. Using a novel solvothermal synthesis approach in tert-butanol we develop new pathways for the fabrication of different ternary metal oxide nanoparticles for the application in lithium-ion batteries. Furthermore, our research focusses on their controlled assembly into continuous networks. With this method we were able to obtain fully crystalline interconnected porous frame-

works composed of ultrasmall lithium titanate Li<sub>4</sub>Ti<sub>5</sub>O<sub>12</sub> (LTO) spinel nanocrystals.<sup>[1]</sup> These were shown to be the fastest ever-reported titanate morphologies as anode material for lithium insertion. We have found that the reduction in crystal size also leads to a change in bulk ion transport properties of the nanocrystals, explaining their extremely fast electrochemical lithium insertion rates. Here we show the extension of our successful synthesis strategy to the development of nanostructured thin films of lithium cobalt oxide LiCoO<sub>2</sub> (LCO), which was the first commercially used cathode material in lithium ion batteries. The reduction in size led to faster charge and discharge processes in nanostructured LCO compared to bulk material.

[1] J. M. Feckl, K. Fominykh, M. Döblinger, D. Fattakhova-Rohlfing, T. Bein, *Angew. Chem. Int. Ed.* 2012, 51, 7459

## Flow and diffusion in channel-guided cell migration

**Anna-Kristina Marel<sup>1,4</sup>, Matthias Zorn<sup>1</sup>, Christoph Klingner<sup>1</sup>, Roland Wedlich-Söldner<sup>2</sup>, Erwin Frey<sup>3,4</sup> and Joachim O. Rädler<sup>1,4</sup>**

*1 Fakultät für Physik & Center for NanoScience, Ludwig-Maximilians-Universität, 80539 München; 2 Institute of Cell Dynamics and Imaging, University of Münster, 48149 Münster, Germany; 3 Fakultät für Physik, Arnold Sommerfeld Center & Center for NanoScience, Ludwig-Maximilians-Universität, 80333 München; 4 Nanosystems Initiative Munich, 80799 München, Germany*

Collective migration of mechanically coupled cell layers plays a notable role during embryonic development, wound healing and cancer progression. Confluent epithelial sheets are well-studied and spontaneous formations of swirls as well as glass-like dynamic arrest as a function of cell density have been uncovered. In contrast, the flow-like properties of one-sided cell-sheet expansion in confining geometries are not well understood. We studied the short- and long-term flow of Madin-Darby canine kidney (MDCK) cells as they move through microchannels, using single cell tracking and particle image velocimetry (PIV). We found that a defined stationary cell current emerges when data is averaged over characteristic spatial and temporal scales. The averaged flow-field exhibits a velocity gradient in the direction of migration and a plug-flow-like profile across the advancing sheet. The observed flow velocity can be decomposed into two contributions, a constant term stemming from directed cell

migration and a diffusion-like contribution that scales with the density gradient. From the density gradient and the speed of front propagation, we extract the collective diffusion coefficient of this diffusive component using the Fisher-Kolmogorov model. In order to connect diffusion mediated transport to underlying cellular motility, single cell trajectories and occurrence of vorticity were studied. We discovered that the directed large-scale cell flow alters fluctuations in cellular motion at short length scales: The formation of swirls is reduced compared to resting tissues. In addition, single-cell trajectories show persistent random-walk behavior superimposed on drift, whereas cells in resting tissue did not show significant displacement beyond neighboring cells. Our work thus suggests that active cell migration manifests itself in an underlying, spatially uniform drift as well as in randomized bursts of short-range correlated motion that lead to a diffusion-like transport.

# PRESENTING AUTHORS

## A

Alberto Amo.....	8
Fabienna Arends.....	20
Laura Ascherl.....	20
Florian Auras.....	17
Phaedon Avouris.....	5

## B

Charles Baroud.....	15
Dimitri Basov.....	12
Fabian Baumann.....	20
Linda Beckert.....	21
Yaakov Benenson.....	8
Linda Bruetzel.....	21
Dominik Bühler.....	22

## C

Carlos Cardenas-Daw.....	22
Elisavet Chatzopoulou.....	22
Nicolas Coca Lopez.....	23

## D

Nynke Dekker.....	9
Ellis Durner.....	23

## F

Ming Fu.....	24
--------------	----

## G

Maria Garcia-Parajo	
Alexander Geiseler.....	24
Thomas Geislinger.....	15
Raphaela Gessele.....	24

## H

Alex Hamilton.....	14
Peter Hänggi.....	7
Fabian Hanusch.....	25
Stephen Hart.....	9
Caroline Hartl.....	25
Dongsheng He.....	26
Lorenz Huber.....	26
Alexander Hufnagel.....	26

## I

Thomas Ihn.....	15
-----------------	----

## J

Anita Jarzebinska.....	27
Christophe Jung.....	28
Ralf Jungmann.....	4

## K

Dominik Kalb.....	28
Stephan Kapfinger.....	28
Khaled Karrai.....	6
Benjamin Käs Dorf.....	29
Lorenz Keil.....	29
Fritz Keilmann.....	30
Ana Krhac Levacic.....	26
Franziska Kriegel.....	30
Rafaël Krzysztan.....	31

## L

Liedewij Laan.....	14
Jana Lambrecht.....	31
Simon Lanzmich.....	31
Dian-Jang Lee.....	32
Heinrich Leonhardt.....	8
Miao Li.....	33
Jessica Lindlau.....	33
Stefan Ludwig.....	11

## M

Andreas Mader.....	33
Muthiah Manoharan.....	6
Christof Mast.....	5
Lukas Milles.....	34
Delia Milliron.....	7
Moein Moghimi.....	13
Matthias Morasch.....	34
Erika Mühlbauer.....	35
Jochen Müller.....	35

## N

Lukas Novotny.....	10
--------------------	----

## P

Claudia Maria Palumbiny.....	36
Michael Pill.....	37
Christian Plank.....	12
Sergey Platonov.....	37

## R

Emanuel Reithmann.....	38
Ruth Röder.....	21
Eva-Maria Roller.....	38

## S

Nitin Saxena.....	39
Dennis Schimmel.....	39
Alexandra Schmidt.....	39
Christoph Schreiber.....	40
Simon Schuster.....	40
Hermann Sellier.....	11
Sabine Sellner.....	40
Xian Shi.....	41
Melanie Stamp.....	41

## T

Manuel Thery.....	4
Philip Tinnefeld.....	16

## U

Georg Urtel.....	41
Maximilian Utzinger.....	42

## V

Tobias Verdorfer.....	42
-----------------------	----

## W

Veronika Weiss.....	43
Daniela Wengler.....	44
Franz Werkmeister.....	44
Christoph Westerhausen.....	45
Christian Westermeier.....	10

## Z

Peter Zehetmaier.....	45
Matthias Zorn.....	45

# NOTES

# LIST OF PARTICIPANTS

Amo	Alberto	CNRS, Marcoussis
Arends	Fabienna	TU Munich
Ascherl	Laura	LMU Munich
Auras	Florian	LMU Munich
Avouris	Phaedon	IBM, Yorktown Heights, NY
Baroud	Charles	Ecole Polytechnique, Palaiseau
Basov	Dimitri	UC San Diego
Baumann	Fabian	LMU Munich
Beckert	Linda	LMU Munich
Bein	Thomas	LMU Munich
Benenson	Kobi	ETH Zürich
Braun	Dieter	LMU Munich
Brauns	Fridtjof	LMU Munich
Bruetzel	Linda	LMU Munich
Brugger	Manuel	University of Augsburg
Bühler	Dominik	LMU Munich
Cardenas-Daw	Carlos	LMU Munich
Chatzopoulou	Elisavet	LMU Munich
Coca Lopez	Nicolas	LMU Munich
Dekker	Nynke	TU Delft
Denk	Jonas	LMU Munich
Durner	Ellis	LMU Munich
Eckl	Maria	LMU Munich
Franke	Thomas	University of Augsburg
Frey	Erwin	LMU Munich
Fu	Ming	LMU Munich
Garcia-Parajo	Maria	ICFO, Castelldefels
Gaub	Hermann	LMU Munich
Geiseler	Alexander	University of Augsburg
Geislinger	Thomas	University of Augsburg
Gessele	Raphaela	LMU Munich
Hamilton	Alex	University of New South Wales
Hänggi	Peter	University of Augsburg
Hanusch	Fabian	LMU Munich
Hart	Stephen	UCL
Hartl	Caroline	LMU Munich
Hartschuh	Achim	LMU Munich
He	Dongsheng	LMU Munich
Hennig	Susanne	LMU Munich
Hohle	Markus	LMU Munich
Huber	Lorenz	LMU Munich
Hufnagel	Alexander	LMU Munich
Ihn	Thomas	ETH Zürich
Jarzebinska	Anita	ethris GmbH
Jung	Christophe	LMU Munich
Jungmann	Ralf	Wyss Institute Boston
Kager	Anna	LMU Munich
Kalb	Dominik	LMU Munich
Kapfinger	Stephan	University of Augsburg
Karraï	Khaled	attocube AG
Käsdorf	Benjamin	TU Munich
Keil	Lorenz	LMU Munich
Keilmann	Fritz	LMU Munich
Kotthaus	Jörg	LMU Munich
Krhac Levacic	Ana	LMU Munich
Kriegel	Franziska	LMU Munich
Krzyszton	Rafał	LMU Munich
Laan	Liedewij	Harvard University
Lambrecht	Jana	ethris GmbH
Lanzmich	Simon	LMU Munich
Lee	Dian-Jang	LMU Munich
Leonhardt	Heinrich	LMU Munich

Li	Miao	LMU Munich
Liedl	Tim	LMU Munich
Lindlau	Jessica	LMU Munich
Ludwig	Stefan	LMU Munich
Mader	Andreas	LMU Munich
Manoharan	Muthiah	Alnylam Pharmaceuticals, Cambridge
Mast	Christof	LMU Munich
Milles	Lukas	LMU Munich
Milliron	Delia	University of Texas at Austin
Moghimi	Moein	University of Copenhagen
Morasch	Matthias	LMU Munich
Mühlbauer	Erika	LMU Munich
Müller	Jochen	LMU Munich
Nickel	Bert	LMU Munich
Novotny	Lukas	ETH Zürich
Palumbiny	Claudia Maria	TU Munich
Pill	Michael	Munich University of Applied Sciences
Pinto	Marilena	LMU Munich
Plank	Christian	TU Munich
Platonov	Sergey	LMU Munich
Rädler	Joachim	LMU Munich
Rehberg	Markus	LMU Munich
Reithmann	Emanuel	LMU Munich
Röder	Ruth	LMU Munich
Roller	Eva-Maria	LMU Munich
Saxena	Nitin	TU Munich
Schimmel	Dennis	LMU Munich
Schmidt	Alexandra	LMU Munich
Schollwöck	Ulrich	LMU Munich
Schreiber	Christoph	LMU Munich
Schuster	Simon	LMU Munich
Schwille	Petra	Max-Planck-Institute of Biochemistry
Sellier	Hermann	Institut NÉEL/CNRS, Grenoble
Sellner	Sabine	LMU Munich
Shi	Xian	LMU Munich
Stamp	Melanie	University of Augsburg
Stintzing	Sigmund	LMU Munich
Thery	Manuel	Hopital Saint Louis, Paris
Tinnefeld	Philip	TU Braunschweig
Urtel	Georg	LMU Munich
Utzinger	Maximilian	ethris GmbH
Verdorfer	Tobias	LMU Munich
von Delft	Jan	LMU Munich
Wagner	Ernst	LMU Munich
Weiss	Veronika	LMU Munich
Wengler	Daniela	LMU Munich
Werkmeister	Franz	LMU Munich
Westerhausen	Christoph	LMU Munich
Westermeier	Christian	LMU Munich
Zehetmaier	Peter	LMU Munich
Zhang	Peng	LMU Munich
Zorn	Matthias	LMU Munich

## ACCOMMODATION

Accommodation for all participants is provided on San Servolo. The buildings are situated in the island's beautiful green parkland. All bedrooms have air conditioning, television, telephone and internet access. A twenty-four hour reception service is guaranteed.

## LUNCH

The cafeteria is located on the ground floor of Building 15. The Cafeteria is open every day with the following timetable:

Breakfast	7.30 am - 9.30 am
Lunch	12.30 pm - 2.30 pm
Dinner	7.00 pm - 9.30 pm

Prices: breakfast € 6.50 (*please sign the list at the counter*), lunch and dinner € 10.00 (pasta course, main course, side order of vegetables or salad, yoghurt, bread and water). There are also reduced menus for € 7.00 (pasta course, side order of vegetables or salad, water and bread) and € 8.00 (main course, side order of vegetables or salad, water and bread).

A bar is also available on campus and is located on the ground floor of Area 6 in the main building.

## WELCOME RECEPTION

The Welcome Reception will take place on Sunday, Sept. 21, at 8:00 pm.

## INTERNET

WLAN Network San Servolo: UNIVIU

username: censworkshop2014  
password: censworkshop2014

Two PC rooms with internet connection are accessible for the participants located next to the conference hall. Please ask for the keys in the conference office next to the lecture hall.

Internet activity will be monitored and recorded as required by Italian law.

## TIMETABLES

### TRAIN TO VENICE AND BACK TO MUNICH

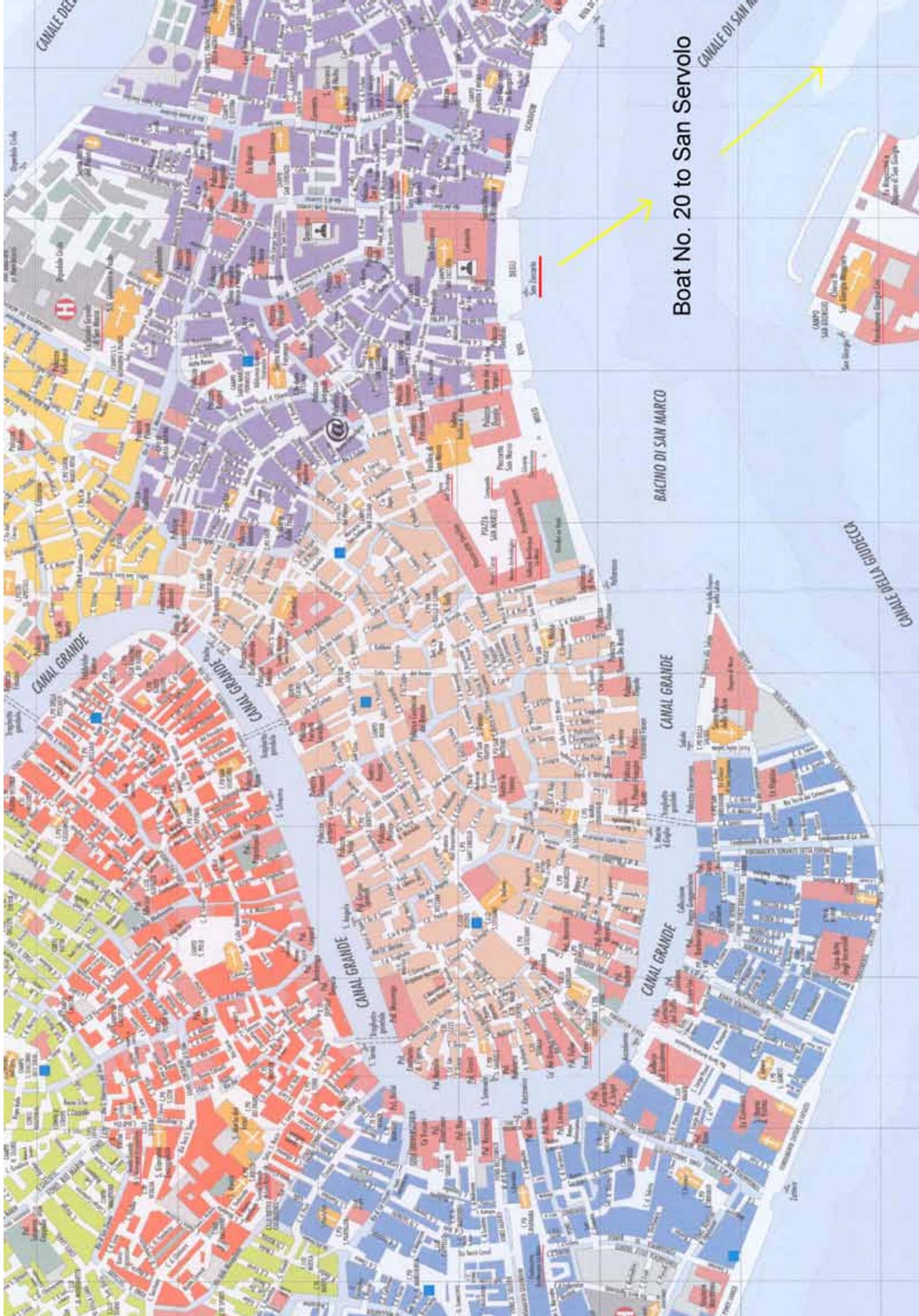
To Venice (21.09.)		Back to Munich (26.09.)	
Munich Main station	Venezia Santa Lucia	Venezia Santa Lucia	Munich Main station
11:38	18:10	13:35	20:21

### BOAT LINE 20 TO WORKSHOP LOCATION (SAN SERVULO)

The boat from Venice to San Servolo leaves from the Riva degli Schiavoni at San Marco; the stop is in front of the Londra Palace Hotel. Boat number 20 goes to San Servolo.

To San Servolo		Back to Venice	
S. Zaccaria	S. Servolo	S. Servolo	S. Zaccaria
6:55	7:05	8:35	8:45
7:15	7:25	8:45	8:55
8:15	8:20	9:10	9:20
8:35	8:50	9:40	9:50
9:00	9:10	10:00	10:10
9:20	9:30	10:50	11:00
9:50	10:00	11:20	11:30
10:30	10:40	12:10	12:20
11:10	11:20	12:40	12:50
11:50	12:00	13:30	13:40
12:30	12:40	14:00	14:10
13:10	13:20	14:50	15:00
13:50	14:00	15:30	15:40
14:30	14:40	16:00	16:10
15:10	15:20	16:50	17:00
15:50	16:00	17:30	17:40
every 40 min until		18:00	18:10
		18:50	19:00
		19:20	19:30
20:30	20:40	20:10	20:20
every hour until		20:40	20:50
23:30	23:40	21:50	22:00
0:25	0:35	22:40	22:50
1:30*	1:40		
2:10*	2:20		

\* Trip made upon request. The boarding at S. Zaccaria must be booked at least 20 minutes beforehand at the following free phone number: (+39) 041-800-845065. Remember to arrive a few minutes before departure time.



Boat No. 20 to San Servolo

BACINO DI SAN MARCO

CANAL GRANDE

CANAL GRANDE

CANAL GRANDE

CANALE DELLA GIUDECCA

CANALE DI SAN MARCO

CANALE DEL FERRO

CeNS Workshop Venice: Walk and Talk at the Nanoscale						
Time	Monday, September 22	Tuesday, September 23	Wednesday, September 24	Thursday, September 25	Time	Friday, September 26
09:00	<b>Welcome</b>	<b>09:00</b> <b>Yaakov Benenson</b> Molecular computing meets synthetic biology	<b>09:00</b> <b>Stefan Ludwig</b> 0.7-Å Anomaly in Quantum Point Contacts: Correlations in 1D	<b>09:00</b> <b>Moein Moghimi</b> Complement Sensing at Nanoscale	<b>09:00</b>	
09:15	Force Scaling in Stress Fibers	<b>09:45</b> <b>Heinrich Leonhardt</b> Studying cellular structure & function with 3D-SIM & fluorescent nanobodies	<b>09:45</b> <b>Hermann Sellier</b> Electron Interactions in Quantum Point Contacts	<b>09:45</b> <b>María García-Parajo</b> Nanoscale imaging and single-molecule detection at ultra-high concentrations using photonic antenna devices	<b>09:45</b>	<b>Florian Auras</b> Covalent Organic Frameworks
10:00	<b>Ralf Jungmann</b> Approaching the limit: Multiplexed Super-Resolution Microscopy with DNA-PAINT and Exchange-PAINT	<b>10:30</b> <b>Coffee break</b>	<b>10:30</b> <b>Coffee break</b>	<b>10:30</b> <b>Coffee break</b>	<b>10:05</b>	<b>Thomas Ihn</b> Imaging electron transport in semiconductor nanostructures on the scale of the electron wavelength
10:45	<b>Coffee break</b>	<b>11:00</b> <b>Alberto Amo</b> Quantum emulation with microcavity polaritons	<b>11:00</b> <b>Dimitri Basov</b> Surface plasmons and phonon polaritons in atomically thin van der Waals crystals	<b>11:00</b> <b>Liedewij Laan</b> How yeast adapts to a strong genetic perturbation: one function at the time	<b>10:50</b>	<b>Closing remarks</b>
11:15	<b>Christof Mast</b> Can thermal traps drive Darwinian evolution?	<b>11:45</b> <b>Nynke Dekker</b> Single-molecule studies of genome processing	<b>11:45</b> <b>Christian Plank</b> Nucleic Acid Delivery – From Academic Discovery to Drug Development	<b>11:45</b> <b>Alex Hamilton</b> Strong spin-orbit coupling of spin-3/2 holes in gallium-arsenide semiconductor nanostructures		
11:35	<b>Phaedon Avouris</b> Graphene Plasmons: Properties and Applications					
	<b>Lunch (12:20-14:15)</b>	<b>Lunch (12:30-14:00)</b>	<b>Lunch (from 12:30)</b> Boat at 12:40	<b>Lunch (12:30-14:00)</b>		
14:15	<b>Muthiah Manoharan</b> Chemical Strategies for Delivery of RNAi Drugs	<b>14:00</b> <b>Stephen Hart</b> Targeted nanocomplex formulations for gene and siRNA therapy		<b>14:00</b> <b>Charles Baroud</b> Microfluidic droplets for quantitative biological studies		Boat leaves at 11:20 / 12:10
15:00	<b>Khaled Karrai</b> Precision positioning and sensing for nano-Manipulation applications	<b>14:45</b> <b>Christian Westermeier</b> Disorder in Org. Semiconductors		<b>14:45</b> <b>Thomas Geislinger</b> Non-Inertial Lift-Induced Cell Sorting		Train to Munich leaves at 13:35 h from train station
15:45	<b>Coffee break</b>	<b>Posters session I &amp; coffee (15:05-17:00)</b>	<b>Informal discussions</b>	<b>Posters session II &amp; coffee (15:05-17:00)</b>		
16:15	<b>Delia Milliron</b> Plasmonic metal oxide nanocrystals & their near infrared electrochromism	<b>Lukas Novotny</b> Cooling and Amplification of a Vacuum-Trapped Nanoparticle		<b>Philip Tinnefeld</b> Single-Molecule Fluorescence on DNA Origami		
17:00	<b>Peter Hänggi</b> On the use and abuse of THERMODYNAMIC entropy	<b>17:00</b> <b>18:00 Guided tour on San Servolo</b>		<b>17:00</b> Single-Molecule Fluorescence on DNA Origami		<b>Boat at 18:00</b>