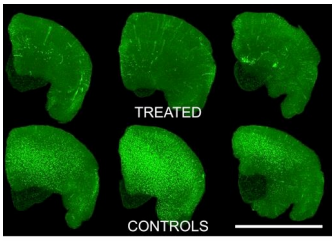

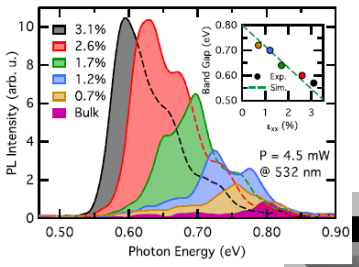

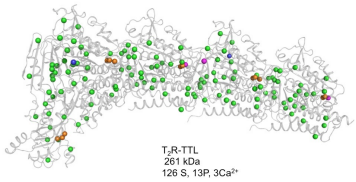

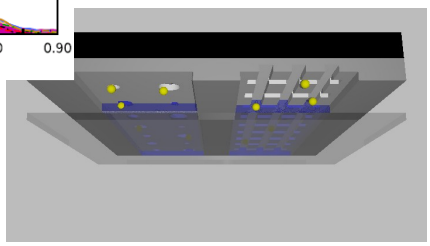

SLS Symposium on

Interdisciplinary Research

Tuesday, September 2, 2014

10:00 to 12:15, WBGB/019

10:00 High Sensitivity Assessment Of Antibody Treatment Against Amyloid Plaques Using X-Ray Differential Phase Contrast Tomographic Microscopy
Alberto Astolfo, B. Schneider, A. Lathuilière, V. Laversenne, B. Bohrmann and M. Stampanoni

10:30 High-throughput and passive trapping of nano-objects using electrostatic forces
Michael A. Gerspach, Nassir Mojarad, Thomas Pfohl and Yasin Ekinci

11:00 Coffee

11:15 Infrared synchrotron determination of excess carrier lifetimes in strained Ge micro bridges
Richard Geiger, M. J. Süess, H. Sigg, R. Spolenak, J. Faist, J. Frigerio, D. Chrastina and G. Isella

11:45 Fast native SAD phasing for routine macromolecular structure determination
Tobias Weinert, V. Olieric, S. Waltersperger, E. Panepucci, L. Chen, H. Zhang, D. Zhou, J. Rose, A. Ebihara, S. Kuramitsu, D. Li, N. Howe, A. Pautsch, K. Bargsten, A.E. Prota, P. Surana, J. Kottur, D.T. Nair, F. Basilico, V. Cecatiello, S. Pasqualato, A. Boland, O. Weichenrieder, C. Dekker, B.C. Wang, M.O. Steinmetz, M. Caffrey, M. Wang

HIGH SENSITIVITY ASSESSMENT OF ANTIBODY TREATMENT AGAINST AMYLOID PLAQUES USING X-RAY DIFFERENTIAL PHASE CONTRAST TOMOGRAPHIC MICROSCOPY

A. Astolfo[1], B. Schneider[2], A. Lathuilière[2], V. Laversenne[2], B. Bohrmann[3], M. Stampanoni[1-4]

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4 Institute of Biomedical Engineering, University and ETH, Zurich, Switzerland

Abstract
Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a progressive and irreversible deterioration of cognitive functions, ultimately leading to death. Nowadays there are few drugs available for the treatment of AD with some partial efficacy on disease symptoms. One of the major AD hallmarks is the widespread presence of microscopic amyloid β (Aβ) deposits throughout the brain. It has been suggested that Aβ accumulation plays a fundamental role in the pathogenesis of AD indicating that an immunization against Aβ may constitute an effective strategy to stop disease progression [1]. Our research is focused on the development of an encapsulated cellular implant producing recombinant antibodies directed against Aβ. The capsule is loaded with mouse myoblast cells that secrete the recombinant antibody. It diffuses out of the device, penetrate the mouse brain, bind amyloid accumulating in plaques, and clear the pathogenic forms of the protein. The capsule has the dual role of confining the cells and protecting them from the host immune rejection (Fig. 1). The efficacy of the antibody treatment can be examined measuring the amount of Aβ plaques deposited in the brain. Histology combined with fluorescence microscopy offers the possibility to measure accurately the Aβ plaques load. However, only a fraction of the brain can be visualized in a reasonable time frame in 2D slices.

One technique available that offers the opportunity to measure in 3D the volume, shape, position and density of the Aβ plaques with sufficient spatial resolution and sensitivity without sectioning the brain is x-ray Differential Phase Contrast (DPC) microscopy [2]. Aβ plaques are completely invisible in conventional x-ray attenuation CT therefore only using phase contrast techniques it is possible to image Aβ plaques. We exploited the setup available at TOMCAT beamline (Swiss Light Source) at 25 keV, III Talbot distance, 6.5 μm pixel size. Thanks to DPC microscopy we measured the effective capability of our method to clear the Aβ plaques (Fig. 2) demonstrating that it could be an attractive way to possible control AD.

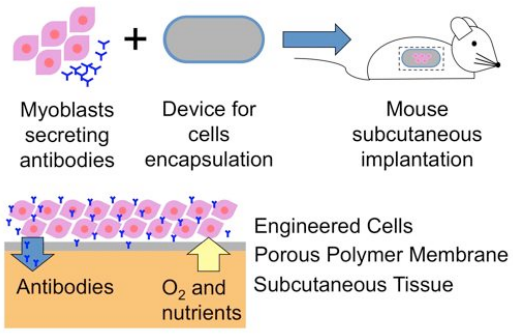

Figure 1: Schematic description of the Encapsulated Cells Device procedure.

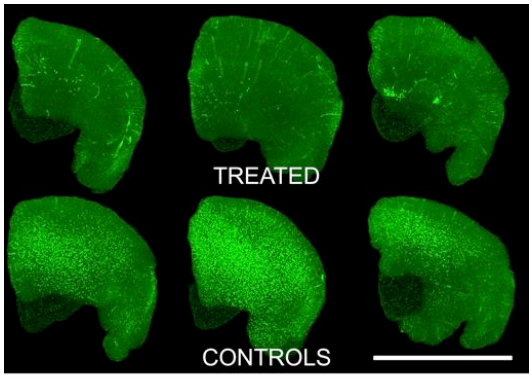

Figure 2: 3D Plaques DPC signal projected in one slice of some representative samples (bar 7 mm).

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High-throughput and passive trapping of nano-objects using electrostatic forces

Michael A. Gerspach [a,b], Nassir Mojarad [b], Thomas Pfohl [a,c], Yasin Ekinci [a,b]

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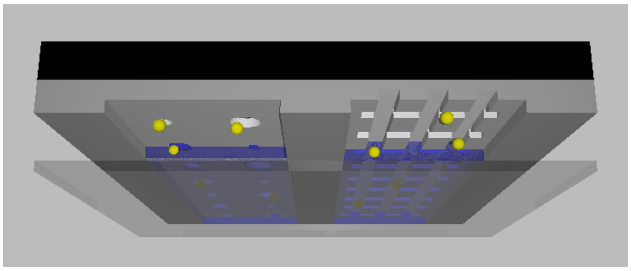
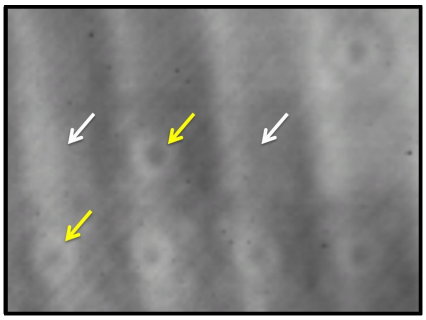
Micro- and nanofluidic systems are used in various fields of biology, physics and chemistry for applications such as studying of polymer dynamics, sorting, detecting molecular reactions, and investigating the structure and functionality of large biomolecules [1]. One way of investigating such dynamics is trapping of nano-objects in solution. Although several methods have been developed, such as optical and magnetic tweezers, electro- and dielectrophoresis, stable and high throughput trapping of nanometer-sized particles in a straightforward manner remains challenging. Our approach of trapping charged nano-objects is "geometric induced electrostatic trapping" [2]. This method is based on altering the surface topology of nano-channels that are negatively charged when exposed to water.

In this talk, the principles and fabrication of the nanofluidic devices are explained. Using nanofluidic channels with a height of 130 to 160 nm, we show trapping of 60 nm gold particles in water without any externally applied forces. Our detection scheme is interferometric scattering detection (iSCAT) microscopy, that provides high signal to noise ratios. Increasing the salt concentration of the solution leads to screening of the surface charges by free counter ions. Therefore, the traps become weaker and the residence times (τ) of the particles (the average time a particle dwell in a trap [3]) become shorter. We show that the residence time of 60 nm gold particles decreases from about 3 s at low salt concentration of < 0.02 mM to about 0.05 s at salt concentration of 1 mM NaCl solution. By improving the channel geometry, the residence time of the 60 nm gold particles can be increased to more than 180 s at low salt concentration of 0.02 mM.

These devices will enable simple and high-throughput trapping of nano-objects for studying their behavior and interactions in aqueous environment. We will employ this method for fundamental studies of soft matter systems and single biological entities.



Design of a silicon based geometric induced electrostatic trapping device.



60 nm gold particles trapped in 200 nm wide pockets (yellow arrows) and not occupied pockets (white arrows).

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Infrared synchrotron determination of excess carrier lifetimes in strained Ge micro bridges

R. Geiger[a], M. J. Süess[a,b], H. Sigg[a], R. Spolenak[b], J. Faist[b]
J. Frigerio[c], D. Chrastina[c], G. Isella[c]

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Optical interconnects are the key to overcome the limitations of today's metal wiring on CMOS chips. However, an efficient on-chip light source is required in order to complete the envisioned photonic circuit. Germanium gained a lot of attention as a possible candidate due to its compatibility with Si technology and its "nearly" direct band gap with an offset of only 140 meV from the L-valley states forming the indirect band gap. This drawback can be overcome by either alloying Ge with Sn[1], or by applying a high tensile strain[2] which results in both cases in a reduced conduction band offset between the direct Γ- and the indirect L-valleys.

In the first part of the talk, I will present our approach to create a high uniaxial tensile strain in Ge microstructures[2]. The method relies on local strain enhancement in a biaxially tensile strained layer by patterning structures with large outer cross sections ('pad') and a narrow central cross section ('constriction'). The advantageous modification of the electronic band structure can be seen in photoluminescence measurements, where the integrated emission intensity for 3.1% strain (achieved by multiplying the internal strain by approx. 20×) increases by 25× compared to bulk Ge (c.f. Fig. 1). With this technique, the theoretical limit to achieve fundamental direct band gap Ge could already be surpassed[3].

In the second part, previous[4-6] and the recent[7] pump-probe experiments related to gain and carrier lifetimes, respectively, will be reviewed. For the latter, the Ge samples were pumped with a pulsed Nd:YAG laser and probed with the broadband synchrotron radiation. Due to the photo-excited charge carriers, the refractive index of Ge changes which modifies the Fabry-Perot oscillations observed in transmission measurements (Fig. 2). Following these dynamics in time allowed to extract the carrier decay time. A comparison of differently prepared Ge layers revealed the defective Ge/Si interface to be the main non-radiative recombination channel[7]. In conclusion, our pump-probe method performed at the infrared beamline X01DC enables to experimentally access most essential parameters required for a realistic modeling of the performance of a semiconductor laser.

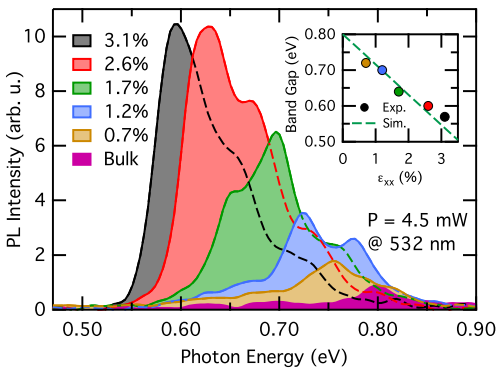

Fig. 1: PL spectra for Ge bridges with varying strain. The inset shows the PL onset of the spectra together with the simulated direct band gap energy.

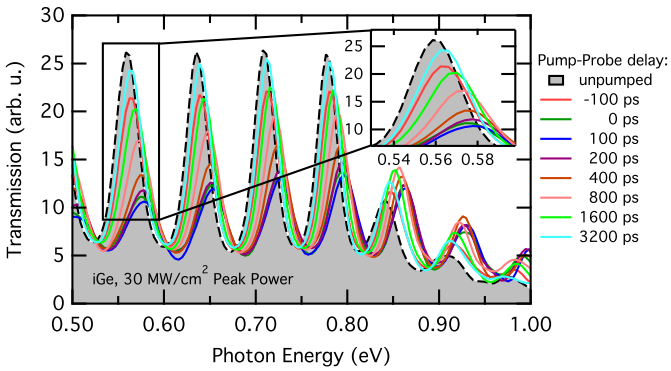

Fig. 2: Transmission spectrum for an intrinsic Ge layer on SOI at varying delay times between pump- and probe pulses.

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Fast native SAD phasing for routine macromolecular structure determination

T. Weinert[1] V. Olieric[1] S. Waltersperger[1], E. Panepucci[1], L. Chen[2], H. Zhang[2], D. Zhou[2], J. Rose[2], A. Ebihara[3], S. Kuramitsu[4], D. Li[5], N. Howe[5], A. Pautsch[6], K. Bargsten[7], A. E. Prota[7], P. Surana[8], J. Kottur[8], D. T. Nair[8], F. Basilico[9], V. Cecatiello[9], S. Pasqualato[9], A. Boland[10], O. Weichenrieder[10], C. Dekker[11], B.-C. Wang[2], M. O. Steinmetz[7], M. Caffrey[5], M. Wang[1]

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The phase problem is a major obstacle in macromolecular crystallography. It can be solved with several different approaches, each of which has specific difficulties. The simplest structure solution method is native SAD phasing, which makes use of sulfur or other light anomalous scatterers that are intrinsically present in proteins and protein crystals[1]. Because of the too small anomalous differences these elements produce at the wavelengths that are routinely accessible at macromolecular crystallography beamlines, up to now comparatively few structures have been solved using native SAD. However, due to recent advances in older techniques such as multi crystal averaging[2,3], native SAD phasing can be applied to an increasing number of cases. We developed a new data collection strategy at the bending magnet beamline X06DA at the Swiss Light Source, which is equipped with the in-house developed multi-axis goniometer PRIGo and the PILATUS 2M[4] detector. This strategy has been successfully applied to several real-life examples, including the largest structure ever solved by native SAD phasing.

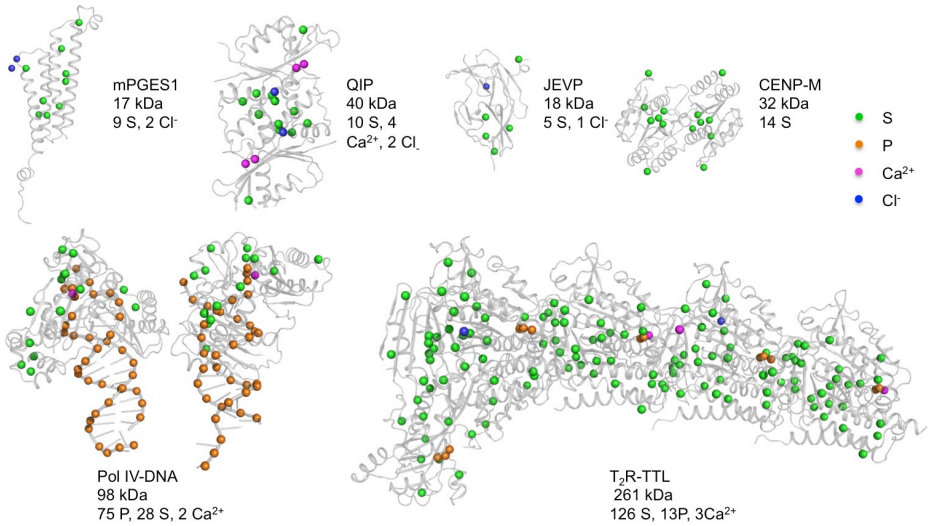

Figure 1: Some examples of structures solved at X06DA and their intrinsically present anomalous scattering substructures.

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