assay using full-length and truncation mutants of the SNARE proteins: syntaxin-1A, SNAP-25B and synaptobrevin, which have 0-4 cysteines. With this assay we are able to quantitatively measure the number of cysteine residues modified in reactions such as palmitoylation and oxidation. This assay is as simple as running an ELISA or western and should allow greater elucidation of the chemistry of cysteine residues in proteins cysteine due to its high resolution.

250-Pos Board B129

A Microfluidic Platform for the Culture & Analysis of Single Cells

Eric Hall, Samuel Kim, Richard N. Zare.
Stanford University, Stanford, CA, USA.

In modern biology, it is often assumed that populations of cells are composed primarily of average cells; cells that do not deviate significantly from an observational mean. This assumption is empirically convenient and until recently was necessary due to technological limitations. However, it is possible that ignorance of cellular individuality may lead one to draw incorrect conclusions, especially when the population under study is heterogeneous. Cells that exhibit significant deviation from the mean behavior can reveal important information which would be normally obscured by ensemble averaging techniques.

We have developed an array of microfluidic analytical techniques capable of studying the biochemistry of single cells [1,2,3]. Our current effort focuses on the development of a microfluidic device capable of sustaining a cell culture of a unicellular microorganism, Synechococcus, which can be resolved at the single-cell level. In our microchip, cells are captured hydrodynamically via a pressure-driven cross-flow of nutrient media. With efficient manipulation of the cellular microenvironment, the individuality of the cells' adaptive responses to stress conditions such as nutrient deprivation can be studied quantitatively using fluorescence microscopy. The design of imaging system with controlled illumination source as well as the use of different pumping mechanisms is described.

1. Wheeler, A.R., Throndset, W.R., Zare, R.N. et al. Anal Chem 75, 3581-3586 (2003).
2. Wu, H., Wheeler, A. & Zare, R.N. Proc Natl Acad Sci U S A 101, 12809-12813 (2004).
3. Huang, B., Wu, H., Zare, R.N. et al. Science 315, 81-84 (2007).

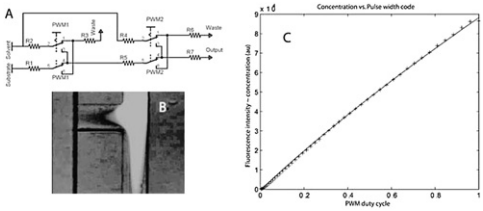
251-Pos Board B130

A Pulse Width Modulated Microfluidic Diluter

Alar Ainla, Aldo Jesorka, Owe Orwar.
Chalmers University of Technology, Göteborg, Sweden.

The preparation of solutions of different concentrations is often an essential part of chemical or biological assays. We have developed a pulsed microfluidic dilution concept, suitably for flexible programming of an accurate output solution concentration. Only minute amounts of chemicals are needed and dilution series with high resolution can be generated. The concept of our dilution chip is similar to digital analog conversion in electronics, using pulse width modulation (PWM).

By means of PDMS replica molding, a multi-stages PWM diluter has been constructed. Fluorescence imaging protocols with microscope/SLR camera as well as electrochemical probing with microelectrodes were employed for characterization and calibration, showing that the design allows for accurate dilution over 2 orders of magnitudes with high controllability, and at the same time minimal external components. This device concept can be applied in stand-alone diluter circuits or as a component in more sophisticated fully integrated analytical devices.



252-Pos Board B131

Controlled Near Infrared Laser-Activated Liposome Release

Guohui Wu, Claudia Gottstein, Alexander Mikhailovsky, Htet A. Khant, Joseph A. Zasadzinski.
University of California, Santa Barbara, CA, USA.

Liposomes have been evaluated as drug delivery vehicles for decades. However, it is hard to prepare liposomes to both balance enhanced drug retention and rapid and targeted content release. The challenge is to initiate the release of encapsulated drugs at the diseased site at a controlled rate. We recently developed a novel photo-activated approach by which near-complete contents release from liposomes can be completed within seconds by irradiating encapsulated or tethered hollow gold nanoshells (HGN) with a near infrared (NIR) pulsed laser. The rapid heating of the gold nanoshells leads to unstable microbubble formation and collapse, the same type of cavitation events associated with ultrasound. Our approach is conceptually analogous to the use of optically triggered nano-''sonicators'' deep inside the body for drug delivery. We demonstrate that even though the local temperature surrounding HGNs can be very high, the bulk temperature of the solution only rises by ~1°C. Results from electrophoresis and quantitative PCR all show no damage to DNA molecules mixed with HGNs after NIR irradiation. These results confirm the potential of using this optical approach to permeabilize lipid membranes and facilitate the cellular uptake of DNAs for gene therapy. Since DNAs are relatively robust macromolecules, we also investigated the more delicate dye molecule, carboxyfluorescein (CF), which contains a double bond; liquid chromatography followed by mass spectral analysis shows that ~95% of CF molecules are intact. These results agree well with our hypothesis that only an few nanometer thick layer surrounding HGNs reach temperatures above the explosive boiling temperature (~ 650 K), so that only CF molecules close to HGNs are damaged. Other NIR responsive materials, such as carbon nanotubes and solid gold nanoparticles were used as triggering agent for liposome release, and their release efficiencies are compared with those of HGNs.

253-Pos Board B132

The Collaboratory for Structural Nanobiology

Alvaro M. Gonzalez-Ibanez[1], Fernando Gonzalez-Nilo[1], Raul Cachau[2].
[1]Universidad de Talca, Talca, Chile, [2]Advanced Biomedical Computing Center, Advanced Technology Center, SAIC-F, NCI., Frederick, MD, USA.

Manufactured nanobiomaterials exploit the unusual properties of nanomaterials to develop new forms of intervention in biological systems. Nanobiotechnology is the field of science focused on the design, synthesis, characterization and application of nanomaterials and nanodevices to biological and biomedical problems. The success of nanobiotechnology hinges on our ability to characterize, predict, and control the biological properties of nanobiomaterials. Nanoinformatics is a collection of multi-disciplinary approaches to catalog, correlate, and model nanomaterial properties. CaNanoLab (http://cananolab.abcc.ncifcrf.gov) is an early example of a nanobioinformatics portal dedicated to foster the rapid dissemination of nanobiological information across the scientific community. Nanobioinformatics studies are complex because they must simultaneously deal with the large dispersion of chemical formulations of nanobiomaterials (ranging from polymer to metal oxide particles), the lack of a common language across contributing disciplines, and the lack of a low level language that can be used across nanoparticles. We could argue that, in lieu of a sequence space, similar to that available to bioinformatics studies of peptides and nucleotide sequences, we could build a structure based annotation and analysis of nanobioparticles that could help us cross-analyze their properties. Computer characterization of nanobioparticles is key to build a structure-based nanoinformatics infrastructure. We are in the process of building a nanobioinformatics service dedicated to the collection, curation, and correlation of structural, physico-chemical, and biological, and biomedical data: the Collaboratory for Structural Nanobiology (CSN http://csn.ncifcrf.gov). We have used CSN to explore nanobioparticles data storage, retrieval, and analysis in the context of nanobiological studies. This work has been funded in part with funds from the NCI-NIH (Contract No. NO1-CO-12400 and HHSN261200800001E). The contents of this publication do not necessarily reflect the views or policies of the DHHS, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

254-Pos Board B133

Tunable Delivery Of Chemical Gradients Over Large Cell Culture Substrates Using Microfluidic Stacked Flows

Christopher G. Sip, Albert Folch, Hoyin Lai.
University of Washington, Seattle, WA, USA.

Biomolecular gradients play an essential role in studying various biological phenomena such as development, cancer, inflammation, and wound healing. This paper reports a novel microfluidic device for generating tunable biomolecular gradients over large areas on cell culture surfaces. Laminar streams are stacked above the surface to generate a steady-state gradient via diffusion in the direction orthogonal to the flow and to the surface. Finite-element modelling was used to predict negligible shear forces at the range of gradients possible by tuning flow rates. The surface gradients were characterized with fluorescence microscopy; image analysis verified the presence of a one-dimensional gradient across a 2x2 mm area. Fig. 1 shows a variety of surface gradients obtained simply by changing the inlet configuration and pressure settings. Superimposed onto these images are the linescans taken across 4 different regions of the device which demonstrate lateral uniformity (excluding edge