Monday Morning, October 20, 2008

IPF 2008 Frontiers in Imaging: from Cosmos to Nano
Room: 312 - Session IPF-MoM

Bio-Imaging

Moderator: J. Hollenhorst, Agilent Technologies

8:20am **IPF-MoM1 Trapping Single Molecules in Water at Room Temperature**, ***A.E. Cohen***, Harvard University **INVITED**

To study a single molecule, one would like to hold the molecule still, without perturbing its internal dynamics. I will present a machine that achieves this goal. The Anti-Brownian Electrokinetic trap (ABEL trap) tracks the Brownian motion of a single molecule using fluorescence microscopy, and applies electrical kicks to the molecule that are timed to induce an electrokinetic drift that cancels the Brownian motion.[1] The ABEL trap can immobilize single biomolecules for extended observation and has been used to study the dynamics of individual DNA molecules and protein chaperonins.[2] I will give examples of new things that can be learned from trapped molecules.[3]

[1] A. E. Cohen and W. E. Moerner, "Suppressing Brownian motion of individual biomolecules in solution," Proc. Natl. Acad. Sci. USA 103, 4362-4365 (2006).

[2] A. E. Cohen and W. E. Moerner, "Principal Components Analysis of shape fluctuations of single DNA molecules," Proc. Natl. Acad. Sci. USA 104, 12622-12627 (2007).

[3] A. E. Cohen and W. E. Moerner, "Controlling Brownian motion of single protein molecules and single fluorophores in aqueous buffer," Opt. Express 16, 6941-6956 (2008).

9:00am **IPF-MoM3 Pushing Magnetic Resonance Imaging Into the Nanoscale Regime - the Quest for a Molecular Structure Microscope**, ***D. Rugar***, IBM Research Division **INVITED**

I describe our effort to extend magnetic resonance imaging (MRI) into the nanometer regime using a technique called magnetic resonance force microscopy (MRFM). MRFM achieves a billion-fold improvement in the sensitivity of magnetic resonance detection by replacing the conventional inductive pickup with ultrasensitive detection of magnetic force. This increase in sensitivity can be harnessed to greatly improve the resolution of magnetic resonance microscopy. In a series of recent experiments at IBM, we have successfully demonstrated 3D magnetic resonance imaging with spatial resolution on the order of 5 nm. The experiment operates in field gradients up to 50 gauss per nanometer (5 million tesla per meter) and makes use of the naturally occurring statistical polarization of nanoscale ensembles of nuclear spins. Understanding the unusual point spread function of MRFM is key to converting the measured 3D force map into a real-space image of the proton distribution in the sample. As a first demonstration of 3D nanoscale MRI, we have imaged individual tobacco mosaic virus particles. The long term goal of this work is to develop a "molecular structure microscope" whereby one could directly image the 3D atomic structure of macromolecules.

10:20am **IPF-MoM7 Imaging in Cell Biology**, ***T. Kirchhausen***, Harvard Medical School **INVITED**

11:00am **IPF-MoM9 Intracellular Fluorescence Imaging at Nanometer Resolution**, ***H.F. Hess***, Howard Hughes Medical Instituite **INVITED**

Fluorescence microscopy, is usually limited in its ability to resolve and focus on features smaller than the optical diffraction limit. However special photoactivated fluorescent proteins can be harnessed in a technique called Photo-Activated Localization Microscopy, PALM. Successive sparse subsets of these fluorescent proteins can be activated, imaged, individual molecules localized and their coordinates accumulated and rendered into a PALM image. Thereby the distribution of labeled endogenous proteins can be seen with the resolution of an electron microscope. PALM images of protein location and organization are illustrated with mitochondria, lysosomes, actin networks, focal adhesions and other cell structures. Another technique, an interferometric microscope, is described that can measure the vertical position of fluorescent molecules to nanometer precision with high photon efficiency. This can be combined with PALM to give full 3 dimensional molecular coordinates of proteins with ~ 20 nm resolution.

11:40am **IPF-MoM11 Retinal Imaging with MEMS-based Adaptive Optics**, ***S. Olivier***, Lawrence Livermore National Laboratory **INVITED**

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