

no modification of cell surfaces is required, so that artifacts between the probe and the cell surface may be minimized compared with magnetic twisting cytometry and optical tweezers, in which microbeads are attached to the cell surface before measurements. However, the statistical properties of cell rheology, which are important to know the universality of cell mechanics, have not been so far investigated in the AFM method. In the present study, we measure a large number of cells in the force modulation measurements with a microarray technique. The amplitude and phase of fibroblast NIH3T3 cells ($n > 100$) were measured in the frequency range from sub-Hz up to 200 Hz, and $G^*(\omega)$ was estimated. The results indicated that the storage and loss moduli exhibited clearly a log-normal distribution. Moreover, these moduli were well fitted to a power-law model, the so-called structural damping model, and the exponent was around 0.2 with a normal Gaussian. The relationship between the rheological properties and the internal structures of cells will be discussed.

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Single DNA Molecule Reaction Based On Dip-pen Nanolithography

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Controlling a reaction at the single molecule level has attracted substantial attention from chemical, physical and biological society for its scientific importance and potential applications. Some examples have been given using small molecules by scanning tunneling microscopy (STM). Challenges still remain in control of single-molecule reactions on the soft bio-molecules, which may reveal meaningful information on biological processes. Conventional techniques including magnetic tweezers and fluorescence microscopy have been used to study the enzymatic digests of single DNA molecules. Herein we report a new technique for localized digestion of single DNA molecules on solid substrate with nonspecific endonuclease, by employing an atomic force microscope (AFM) and the concept of Dip-pen nanolithography (DPN). We choose the solution containing DNase I with Mg^{2+} ions as the ink. As we known the DNase I can catalyze the hydrolysis of DNA strands without the requirement of specific sequence when Mg^{2+} ions or Mn^{2+} ions is presented. However, in our system, when DNase I ink solution was deposited on a local position of a single DNA molecule by an AFM tip, the followed digestion location of the DNA strands could be restricted with nanometer precision, so that the site cutting reaction with nonspecific endonucleases was achieved. This AFM site-specific reaction approach, although there is certain degree of shifting and broadening due to lateral diffusion of enzymes on surface, promises a deeper understanding of molecular surgery at the molecular scale and may become very important in the emerging field of nanobiotechnology.

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High-speed, Thermo-chemical Nanolithography for Biological Applications

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Scanning probe-based chemical nanolithography has been recognized as an essential part of future nanofabrication processes. However, most of the present strategies still have significant limitations in terms of throughput, resolution and substrate variety. Recently, we have developed a new chemical nanolithography technique called thermo-chemical nanolithography (TCNL). TCNL utilizes a resistively-heated atomic force microscope tip to thermally activate a chemical reaction on an arbitrary organic or inorganic substrate surface. TCNL can write well-defined chemical features at a rate of mm/s, with sub-15 nm resolution [1]. In particular, we have demonstrated that carboxylic ester groups on a polymer surface can be deprotected by TCNL to give carboxylic acids and further modified to form anhydrides [2]. Therefore, TCNL can tune surface wettability with in situ write-read-overwrite capability. In addition, nanoarrays of TCNL-activated amine groups have been used as anchor sites to immobilize a variety of biological ligands [3]. This proves TCNL to be a powerful tool to control the physical placement of biomolecules and cells. It can be applied to a range of molecular cell biology studies such as ligand-receptor recognition and cell signaling.

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3. D. Wang, V. Kodali, W. D. Underwood, J. E. Jarvholm, T. Okada, S. J. Jones, C. Rumi, W. P. King, S. R. Marder, J. E. Curtis and E. Riedo, (2008) in preparation.

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Direct Mapping Of Surface-bound Liquid With Sub-nanometer Resolution

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At the solid-liquid interface molecules of the liquid adopt a particular arrangement which depends primarily on the interfacial energy and geometry. At the nanoscale this molecular arrangement is of central importance in a wide range of fields from molecular biology to surface physics, heterogeneous catalysis and electronics. In biology the role of interfacial liquid is further emphasized by the soft nature of most biomolecules whose conformation and dynamics depends on the surrounding medium. This is the case for protein function and folding (1), self-assembly processes and bio-electronics where a complex interplay between surface-bound liquid molecules and ions strongly affects any motion. Using amplitude modulation atomic force microscopy (AM-AFM) operated in liquid and in a particular regime, it is possible to simultaneously image the topography of the surface-bound liquid while measuring its adhesion energy to the solid investigated. We have used this method to map the binding energy of water to gold nanoparticles coated with mixed ligands, self-assembled in controlled patterns (2, 3). Such functionalized nanoparticles can mimic the typical surface of proteins (hydrophobicity, charge, surface domains) while allowing careful control of the domains' size and properties (2). Our results show that the average binding energy of water to the surface of the nanoparticles strongly depends on the spatial arrangement of the ligands molecules. The geometry as well as the size of the ligand domains both affect the local adhesion energy of the solvent in a non-linear fashion. Our findings provide experimental and quantitative insight into the interplay between solvent and surfaces in nanoscale biophysical processes.

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(2) A. Verma et al, (2008), *Nature Mat.* 7, 588-595.

(3) A. Centrone et al, (2008), *Proc. Natl. Acad. Sci.* 105, 9886-9891.

2055-Pos Board B25

Visualizing Lipid/Water and Lipid/Ion Interactions at the Biological Interfaces with Angstrom-Resolution by Frequency Modulation Atomic Force Microscopy

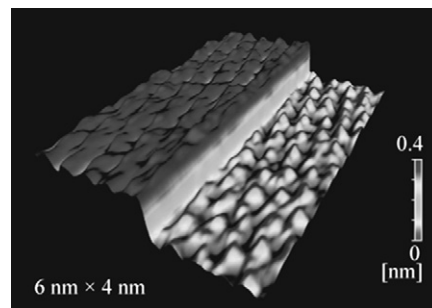
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At the interface between biological membranes and their surrounding physiological solution, various interfacial phenomena take place through the interactions between lipid headgroups and water molecules (or ions) and hence have a great impact on the functions and structure of the biological membranes. However, it has been a great challenge to experimentally access such interfacial phenomena with Angstrom resolution.

Recently, we have developed an atomic force microscopy (AFM) technique that is capable of visualizing Angstrom-scale structures and phenomena at the solid/liquid interface with piconewton order loading forces. Here we apply this technique to the investigation of the lipid/water and lipid/ion interactions at the biological interfaces.

The figure shows an AFM image taken at the interface between the DPPC bilayer on mica and PBS solution. The image shows the molecular-scale corrugations of the lipid headgroups (lower half) and their primary hydration shells (upper half), revealing the existence of a stable hydration layer on the DPPC bilayer with nanometer-scale lateral extent.



Fluorescence Spectroscopy II

2056-Pos Board B26

Improved Global Spectral Analysis Method for Simulating Excitation-Emission Maps of Semiconducting Single-Walled Carbon Nanotubes

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Recent research breakthroughs in the field of semiconducting single-walled carbon nanotubes (SWCNTs) have centered strongly around the acquisition and analysis of photoluminescence excitation-emission maps (EEMs). EEMs have been shown to provide both qualitative and quantitative information of