19. Self-Assembled Monolayers for Diagnostics and Sensing

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Objective: Use self-assembled monolayers (SAMs) as model systems to develop fundamental, quantitative knowledge of generic molecular recognition and sensing reactions of ultrathin films. Develop and apply ultrathin film measurement methods to correlate molecular-scale structure of films with their diagnostic and sensing performance.

Problem: Biosensors and diagnostics are being developed to perform rapid, accurate, and low-cost multi-analyte measurements, e.g., DNA and protein chips. These two-dimensional diagnostic arrays are revolutionizing health care, biomedical research, and drug discovery. While the feasibility of this technology has been demonstrated, there is still little known about factors such as molecular conformation and structure that influence hybridization of surface-bound probes. To better understand these systems it will be necessary to develop novel measurement methods for correlating biomolecular layer structure with molecular recognition properties.

Approach: We prepare biologically active films by derivatizing biomolecules with a thiol group, and self-assembling the thiol-modified biomolecule on Au surfaces. Current studies are focussed on establishing a detailed molecular-level picture of thiol-derivatized DNA monolayers. Surface density, hybridization activity, and molecular conformation of surface-bound DNA probes are characterized with a variety of surface-sensitive methods, including electrochemical techniques, surface plasmon resonance (SPR), ^{32}P radio-labeling, x-ray photoelectron spectroscopy, ellipsometry, and scanning tunneling microscopy (STM).

Results and Future Plans: Efforts in FY00 focussed on determining the effect of target length on hybridization efficiency, particularly when target sequence lengths exceed those of the DNA probes. Probe length was held constant at 25 bases and the target lengths of 25, 40, 60, and 100 were examined. Hybridization efficiencies were determined using two independent methods, SPR and a NIST-developed electrochemical technique, chronocoulometry. Results from both methods indicate that hybridization efficiency decreases dramatically with increasing length of target DNA for a defined probe sequence of 25 bases. The significance of this result is that DNA detection and quantitation may be biased by DNA strand length.

Fundamental structural characterization of SAMs was also investigated to understand and control nano-and meso-scale monolayer structure. Using variable temperature STM, a two dimensional phase diagram of the monolayer decanethiol on Au(111) was established, a first for alkanethiol SAMs. Four triple point temperatures were determined that define phase melting points and the temperatures above which SAM phases are metastable. An understanding of 2D SAM phase behavior also led to the development of a protocol to produce nearly defect-free SAMs over large areas that may aid in the assembly of structures for molecular electronic applications (See Fig. 1). The establishment of a phase diagram paves the way for true thermodynamic studies of the effect of chain-length and end-group on alkanethiol SAMs.

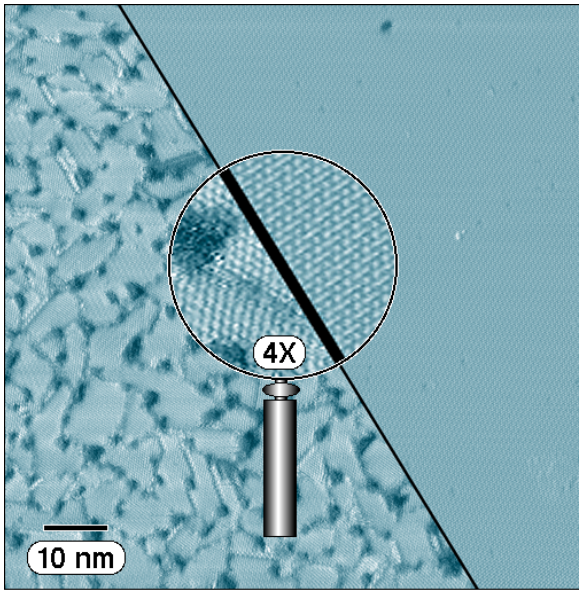

Figure 1:STM images of decanethiol SAMs formed on Au (111) prepared by conventional self-assembly methods (left) and new method (right) derived from understanding of phase behavior. The new method yields nearly defect-free monolayers.

Future work DNA monolayers will exploit microhotplate measurement technology.