Monday Morning, November 4, 2002

Biomaterials
Room: C-201 - Session BI-MoM

Theoretical Studies of Biosurfaces/Biotribology and Biorheology
Moderator: R.A. Latour, Clemson University

9:00am **BI-MoM3 Molecular Simulation Studies of Orientation of Antibodies Adsorbed on Charged Surfaces**, *J. Zhou, J. Zheng,* ***S. Jiang***, University of Washington

Antibodies have found many applications in biotechnology and clinical medicine, including diagnostic assays, environmental testing, and process monitoring. It is well-known that Fab fragment of an antibody can bind its antigen with a very high specificity. Therefore, it is desirable to control the antibody orientation for immunoassay applications. In this work, Monte Carlo simulations are performed to study and predict the adsorption and orientation of antibodies as a function of surface and solution properties using hierarchical models, a simplified Y-shape 12-bead model antibody, a united-residue model, and an all-atom model. For all these three models, simulation results show that higher surface charge density and lower solution ionic strength favor narrower orientation distribution of adsorbed antibodies. Simulation results further show preferred antibody orientation under controlled surface and solution conditions, which are verified by our SPR and ToF-SIMS experiments. For the 12-bead model, it allows us to quickly map out the general trends of the orientation behavior of antibodies on surfaces. For the residue model we developed, more detailed residue-distribution information of antibody near surfaces can be achieved. For the all-atom model, the conformation change of an adsorbed antibody was obtained with a proposed hybrid method. The fundamental understanding of antibodies on surfaces of this work will facilitate the effort to develop better biosensors.

9:20am **BI-MoM4 Mapping the Free Energy State of Water in Hydration Layers and Its Importance for Ligand-Receptor Binding**, ***G.W. Grahek****, R.A. Latour, S.J. Stuart*, Clemson University

The thermodynamic contributions of solvent molecules during ligand-receptor binding are generally believed to be very important, but relatively little is actually understood regarding how the entropy, enthalpy, and free energy of hydration layers change as a ligand approaches and docks with its receptor. We assume that both ligands and receptors perturb the thermodynamic state of their localized hydration layers, and that these effects must be superimposed on the intervening water layers as a ligand approaches its receptor. It is hypothesized that this effect may have a significant influence on the height of the activation barrier for ligand-receptor binding, and thus may serve as an important medium-range modulator of ligand-receptor binding. Based on this underlying hypothesis, we are investigating the development of statistical mechanics based molecular modeling methods to calculate the entropy, enthalpy, and free energy values of water as a function of position surrounding a designated solute molecule. Simulations have been conducted using both molecular dynamics (AMBER 6.0) and Metropolis Monte Carlo (BOSS 4.2; OPLS) methods using TIP3P and TIP5P water, respectively, and periodic boundary conditions surrounding a centralized solute molecule. Entropy, enthalpy and free energy are then mapped on a 3-dimensional grid. The simulations indicate that distinct changes do occur in the calculated free energy state of water molecules in the first two hydration layers surrounding the solute compared to bulk water. Further studies are being planned to investigate the effect of solute-solute separation distance on the intervening water layers. Following final development, these methods will be applied to actual ligand-receptor systems for the purpose of predicting the influence of water structure on binding. It is believed that these simulations may provide new insights that will facilitate drug design for specific receptor targets.

9:40am **BI-MoM5 Growth of a Polymer Brush from Solution: Adsorption, Desorption, Conformational Conversion and Charging**, ***H.J. Kreuzer***, Dalhousie University, Canada **INVITED**

Going beyond mean field theory we develop a model of a polymer brush that allows for inhomogeneity, confinement and lateral interactions. The model is developed for freely rotating chains and a realistic Interacting Chain Model for poly(ethylene glycol). The parameters in the latter are obtained from a first principles theory based on (i) ab initio (density functional theory) calculations of the potential energy surfaces of the polymer conformers, and (2) the proper statistical mechanics for which we succeeded to formulate and solve a Green's function approach (transfer matrix method) in the presence of an external force field. We set up kinetic equations for the time evolution of the growth of a brush from solution. For PEG a detailed analysis and discussion of recent data is made that identifies two time regimes of pancake adsorption and collision-induced conformational conversion to stretched moeities, respectively. Lastly we discuss the possibility that auto-ionization of water in contact with the brush may lead to preferential adsorption of hydroxide and hydronium ions depending on the pH.

H.J. Kreuzer, R.L.C. Wang, and M. Grunze, New Journal of Physics 1, 21.1 (1999). R.L.C. Wang, H.J. Kreuzer, and M. Grunze, Phys. Chem. Chem. Phys. 2, 3613 (2000). L. Livadaru, H.J. Kreuzer, and R.R. Netz. Interacting Chain Model for Poly(ethylene glycol) from First Principles. Macromolecules (in press). Kreuzer, H.J.; Payne, S.H.; Livadaru, L. Biophysical Journal 2001, 80(6), 2505-2514. Kreuzer, H.J.; Grunze, M. Europhys. Lett. 2001, 55(5), 640-646. M. Himmelhaus, T. Bastuck, S. Tokuitsu, M. Grunze, L. Livadaru and H.J. Kreuzer. Growth of a polymer brush from solution, (preprint).

10:20am **BI-MoM7 Puzzles of Fluid Flow in the Biomaterials Environment**, ***S. Granick***, University of Illinois, Urbana-Champaign **INVITED**

In areas from blood flow to biosensor applications, it is essential to predict fluid flow. The standard model states that fluid velocity is zero at solid surfaces, but evidence is accumulating against this in many situations, especially regarding aqueous solutions and surfaces coated with polymer cilia. We have studied flow of aqueous solutions containing variable amounts of monovalent and divalent electrolyte past solid surfaces whose charge was varied and whose 'softness' was varied by polymer cilia. Deviations from the standard model are observed when the wall shear stress exceeds a critical level whose magnitude depends on the system studied. In some respects this is understood, in other respects it is not. The puzzles will be emphasized.

11:00am **BI-MoM9 Hydration Forces on a Switchable Bioactive Surface**, ***B.-I. Kim****, M.A. Samara, D.L. Huber, J.E. Houston, B.C. Bunker*, Sandia National Laboratories

Poly(n-isopropyl acrylamide) (PNIPAM) monolayers can be thermally switched between hydrophobic and hydrophilic states at a phase transition temperature of 35°C. Protein adsorption studies indicate that the hydrophilic state represents an anti-fouling state, while biomolecules form adherent monolayers on the hydrophobic state. We have used a scanning probe system called the interfacial force microscope (IFM) to probe the mechanisms for protein adsorption on this switchable polymer surface. With the IFM, we have simultaneously measured both normal and friction forces between a silica tip and a surface functionalized with PNIPAM as a function of separation distance. The results show that at room temperature, there is a repulsive hydration force between the tip and the substrate. As the phase transition temperature is approached, the repulsive force collapses, allowing the tip and substrate to come into adhesive contact. The transition from repulsive to attractive adhesive forces is accompanied by a doubling in lateral friction forces. IFM results obtained at different tip speeds at different temperatures suggest that the repulsive hydration force observed at room temperature is associated with the presence of ordered water structures within the polymer that break down at higher temperatures. Experiments are in progress with chemically-functionalized tips to provide us with fundamental insights of the parameters controlling the stability of this ordered water and its role in protein adsorption.

11:20am **BI-MoM10 Structural Properties of Nucleosomal DNA Characterized by Atomic Force Microscopy**, ***M.E. Greene****, M.A. Ratner, J. Widom, M.C. Hersam*, Northwestern University

One of the fundamental problems in contemporary molecular biology involves whether a sequence dependence exists in nucleosomal DNA which gives the molecule certain structural properties leading to the formation of nucleosome with histone octamer. A way to approach the solution is to look at the isolated DNA molecules to discern the native structural properties in the absence of histones. Interfacing biological molecules with inorganic substrates and probing them using atomic force microscopy (AFM) allows for such study. AFM has been used to image surfaces with adsorbed biological molecules for over a decade, and in particular DNA has been characterized to an extent that imaging artifacts interfering with proper analysis have been identified. Several technical difficulties have been resolved as well, including substrate selection and a reproducible surface binding protocol, opening the door for AFM to be used as a powerful tool to investigate problems of genuine biological importance. In this investigation, a 342-bp strand of synthetic dsDNA dubbed "601" shown by Lowary and Widom to have a high affinity for binding to histone octamer is examined. This sequence is thought to mimic the behavior of DNA sequences found in chromatin. Preliminary analysis of AFM data of a natual nucleosomal DNA sequence isolated from chicken erythrocyte suggests agreement with the worm-like chain (WLC) model. Attention is given to the quantities of end-to-end distance, contour length, and intrachain bend angles in order to assess the persistence length, bendedness, and bendability of the sequence. AFM data is currently being gathered using Si cantilevers tipped with multiwalled carbon nanotubes as well as high aspect ratio Si tips with a nominal radius of curvature of 2 nm to obtain better lateral resolution and detailed measurements of bends and curvature fluctuations in the chains. An automated analysis methodology to allow the handling of large data sets will be introduced as well.

Authors Index

Bold page numbers indicate the presenter