Molecular Simulation of Non-Fouling SAM surfaces

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Statement of Purpose: While significant advances in biocompatible and environmentally sound materials have been made, one of the significant and still challenging issues is surface resistance to protein and cell adhesion. Much experimental guess-and-check work has been conducted that have succeeded in producing a number of low and non-fouling materials and coatings. However, the mechanisms for protein resistance are very poorly understood and the majority of new material breakthroughs still come by luck. Some examples of fortuitously discovered non-fouling surfaces include ethylene glycol, phosophocholine, and some sugar aditols. The protein surface interface is frequently difficult to study experimentally. The region of interest is buried; there are many complex components and interactions that frequently cannot be separated with laboratory techniques. Molecular Modeling provides a unique tool to separate the intermingling interactions and look directly at the buried interfaces. Thus, the purpose of this work is to study the non-fouling mechanism using MC and MD simulations in the hopes of reaching an understanding sufficient enough for intelligent design.

Methods: In this work two simulation techniques, Monte Carlo (MC) and Molecular Dynamics (MD) are used to study the interaction between Lysosyme (PDB ID - 7LYZ) and SAM surfaces of functionalized alkanethiols. Monte Carlo simulation is used to determine the optimal protein orientation over the surface of interest. While molecular dynamics is used to determine the interaction forces and water characteristics. All simulations are conducted with one of two programs: CHARMM and BIOSURF. CHARMM is a commonly used, commercially available simulation package that has both MC and MD capabilities. BIOSURF is a Fortran-based, MD package developed by a group member. Both programs use an all-atom potential force field to describe the atomic interactions. The simulation system is analyzed about every 100ps to monitor its approach to equilibrium and any properties or forces of interest. BIOSURF contains analytical subroutines including: water radial distribution function, g(r); tracking hydrogen bonding between the SAM and water molecules; determining the water residence time in layers through the structure; and many others.

Results / Discussion: Simulation results through 1ns are completed for OEG SAM systems. The results show a strong link between non-fouling behavior and the ability of the surface to interact with water. Figure 1 highlights the force between the SAM surface and the protein as a function of separation distance. Figure 2 shows number of hydrogen bonds and SAM flexibility as a function of surface composition. The surfaces with more OEG bind more water and also create a larger force on the protein in solution[2]

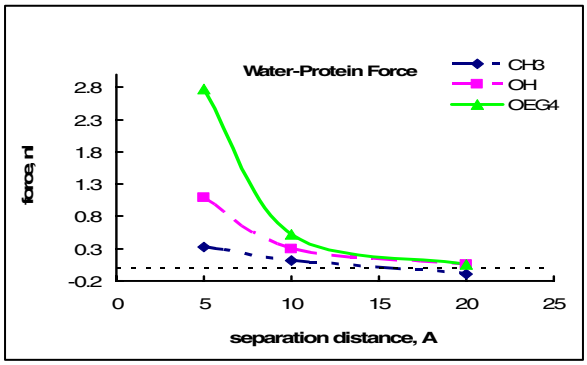

Figure 1: Force on protein from water vs. distance

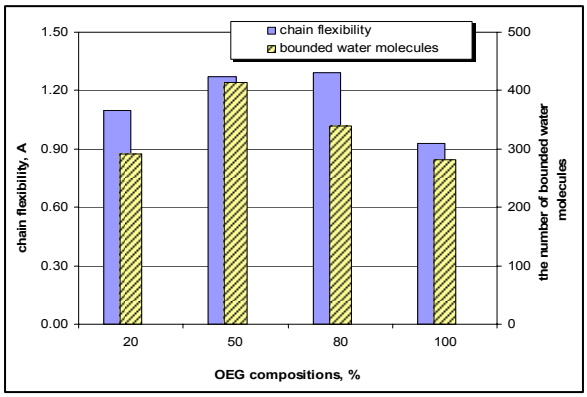

Figure 2: SAM flexibility and Hydrogen bonding vs. OEG composition

In addition to the data presented above, other analytical methods, like water residence time and layer-by-layer force, as well as other non-fouling surfaces, PC and sugar aditols are being used to investigate and verify the non-fouling mechanism.

Conclusions: A surfaces ability to resist protein adhesion is intimately linked to its ability to bind water. This conclusion is supported by our simulation work as well as others experimental findings[1]. It is generally thought that surfaces that are charge neutral and strong hydrogen bond acceptors but not hydrogen bond donors will be protein non-fouling[1]. While this conclusion is supported by our OEG work, our early results with PC and sugar aditol SAMs indicate the non-fouling mechanism maybe more complicated and still rather incompletely described. Our results show that non-fouling surfaces are those that strongly bind water regardless of that binding mechanism. By expanding the scope of our analysis and non-fouling surfaces we will further strengthen this claim and move us towards intelligent design based on the better mechanistic understanding.

References: 1. Ostuni, E.; Chapman, R.G.; Holmlin, E.; Takayama, S.; Whitesides, G.M. *Langmuir* **2001,** *17*, 5605-5620. 2. Zheng, J.; Li, L.; Chen, S.; Jiang, S. *Langmuir* **2004**, *20*, 8931-8938.