Effects of Zwitterionic Polymer Brush Density and Chain Length on Resisting Protein Adsorption

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Statement of Purpose: Insulin catheters fail after 2-3 days due to occlusion by cell and collagen accumulation. To reduce the extent of occlusion and thus increase the device lifetime, we have developed a nonfouling coating to resist protein adsorption—most likely the triggering event to the catheter failure. In this work, we have investigated the effects of brush density and chain length in minimizing protein adsorption for a surface-grafted zwitterionic polymer coating.

Methods: A polymer brush coating of sulfobetaine methacrylate (SBMA)—a nonfouling material for biomaterials—was grafted to the surface of PTFE substrates after surface functionalization by radio frequency plasma deposition. Atom transfer radical polymerization (ATRP) was used to polymerize the SBMA. Sodium chloride was investigated to increase the resulting SBMA coating thickness. The polymer brush density was varied by changing the amount of bromine—the ATRP initiator—grafted to the surface. X-ray photoelectron spectroscopy (XPS) was used to confirm the presence of SBMA on the surface. Ellipsometry and profilometry were used to determine the film and initiator thicknesses. An *in vitro* radiolabeled protein adsorption assay was used to determine the effectiveness of the SBMA coating. Additionally, sum frequency generation (SFG) vibrational spectrometry was used to relate the water structure at the surface, due to the extremely hydrophilic SBMA, to the amount of protein adsorbed.

Results:

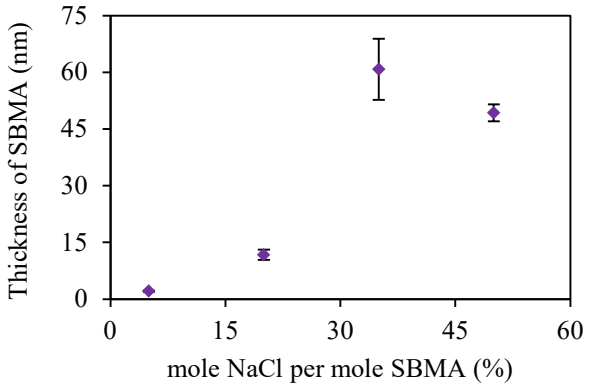

Figure 1: Thickness of SBMA film due to amount of NaCl added to the reaction solution.

The thickness of the SBMA film is correlated to the amount of NaCl added to the polymerization (Figure 1). For increasing amount of NaCl added, the critical solution temperature was lowered thereby increasing the solubility of polymerized SBMA and allowing for increased chain growth. We suspect that the SBMA chain length should be balanced with the chain density to provide a coating that is the most sterically-favorable for water binding to limit protein adsorption for biomaterials. The polymer brush density of the SBMA coating is most related to the initiator density on the surface, as measured using XPS. With increased brush density, protein adsorption was lowered for reactions with no salt addition (Figure 2). Here, the SBMA polymerized chain length was limited due to lowered solubility in water.

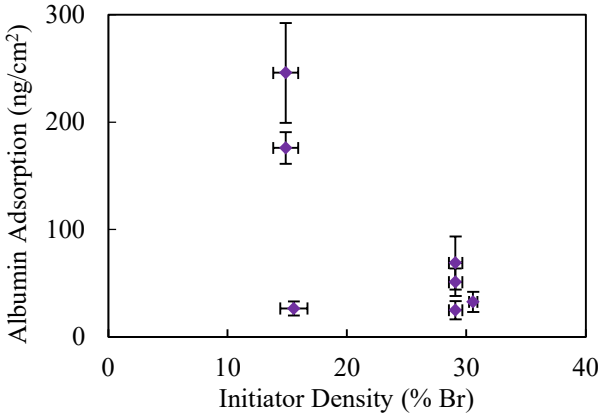

Figure 2: Protein adsorption for various initiator densities.

Ultimately, the brush density and length should be balanced to bind water with the most affinity. The resulting structured water was measured using SFG, showing a larger tightly-bound water-to-loosely-bound water ratio for higher brush density than for lower brush density (Figure 3). These brushes were limited in length due to no salt addition and lowered solubility.

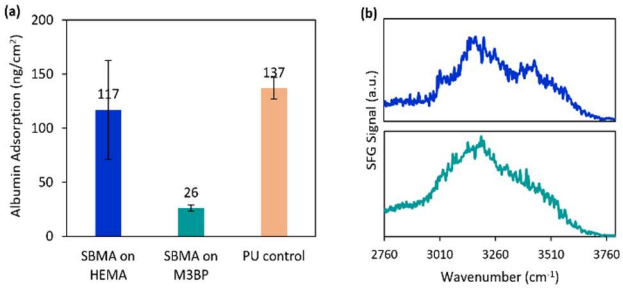

Figure 3: (a) Protein adsorption for various initiator densities, 5% (dark blue) and 30% (teal) and (b) corresponding SFG signal in the -OH region.

Conclusions: To produce the ultimate nonfouling coating for biomaterials—in this case insulin catheters—the polymerized SBMA brush length should be balanced with the chain length to be sterically favorable for binding for extracellular matrix water—the natural barrier for protein attachment and subsequent occlusion of a medical device. In future work, we will investigate the effect of salt addition for varying initiator densities.