

CHARACTERIZATION OF TAILORED NON-FOULING POLYMER SURFACES USING TIME OF FLIGHT SECONDARY ION MASS SPECTROMETRY AND MULTIVARIATE ANALYSIS

M.S.Wagner¹, S.Pasche², D.G.Castner³, M.Textor²

¹National Institute of Standards and Technology, Gaithersburg, USA ²Dept. of Materials, ETHZ, Zürich, Switzerland ³Depts. Of Bioengineering and Chemical Engineering, University of Washington, Seattle, USA.

INTRODUCTION: Non-fouling polymeric materials are widely used in biomaterials and biosensors. In particular, adlayers of Poly(L-Lysine)-graft-Poly(Ethylene Glycol), PLL-g-PEG, on metal oxide substrates resist protein adsorption and cell adhesion [1]. In this study, static Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) was used to study the effect of surface chemistry and structure on the protein resistance of a series of PLL-g-PEG adlayers with systematically varied ethylene glycol (EG) surface densities.

METHODS: PLL-g-PEG polymers were synthesized with various PEG graft densities (i.e. number of PLL monomers per grafted PEG chain) using 1, 2, or 5 kDa N-hydroxysuccinimidyl esters of methoxy-terminated PEGs and 20 or 300 kDa PLLs and assembled onto Nb₂O₅ substrates as described previously [2]. The EG surface density and protein resistance of the PLL-g-PEG adlayers were measured using Optical Waveguide Lightmode Spectroscopy (OWLS). The surface chemistry and structure was monitored using static positive and negative ion ToF-SIMS and Principal Component Analysis (PCA) [3].

RESULTS: As the EG surface density of the PLL-g-PEG adlayers increased from 3.9 to 30.9 EG units/nm², the amount of protein adsorption decreased from ~300 ng/cm² to below the OWLS detection limit (~1 ng/cm²). Generally, changing the molecular weight of the grafted PEG chain did not affect protein resistance of the adlayers. However, changing the PLL molecular weight from 20 to 300 kDa typically increased the amount of protein adsorption.

PCA of the positive ion spectra showed two distinct trends. The relative intensities of the PEG-related peaks were positively correlated with the thickness of the adlayer and the amount of PEG at the outermost surface of the adlayer. The relative intensities of the peaks related to the methoxy endgroup of the PEG molecules were positively correlated with the amount of methoxy endgroup in the adlayers. The variance in the negative ion spectra was principally due to changes in the thickness of

the PLL-g-PEG adlayer. The results from PCA were used to generate multivariate peak ratios which corresponded with the thickness, PEG enrichment, and methoxy group enrichment of the adlayer. As the EG surface density and protein resistance increased, the adlayers became thicker and more methoxy endgroups were exposed at the outermost surface. Changing the PLL molecular weight from 20 kDa to 300 kDa increased the amount of protein adsorption of these adlayers, but did not appreciably change the positive or negative ion ToF-SIMS spectra, suggesting that long-range forces (e.g. electrostatic forces) were responsible for protein adsorption for these adlayers.

DISCUSSION & CONCLUSIONS: Protein resistance of the PLL-g-PEG adlayers was dependent on the EG surface density and the structure of the PEG chains on the surface. Tightly packed PEG chains that exposed their methoxy endgroups showed enhanced resistance to protein adsorption while less densely packed PEG surfaces revealed substrate (PLL or Nb₂O₅) sites for protein adsorption. Adlayers of PLL-g-PEG synthesized using 300 kDa PLL probably looped from the Nb₂O₅ substrates, allowing more protein adsorption than the adlayers of PLL-g-PEG synthesized using 20 kDa PLL.

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