

Influence of the Molecular Charge of PEG-Conjugated Catechol Equivalents on the Formation of Self-Assembled Adlayers

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INTRODUCTION: Highly controlled physicochemical surface properties are key factors in the development and optimization of new biomaterials such as load bearing hard-tissue (i.e. bone) implants or catheters, as well as biosensor surfaces that have regular contact with complex protein mixtures. In recent works, L-3,4-dihydroxyphenylalanine (DOPA), a catechol which is believed to be the key residue in mussel adhesive proteins (MAPs), was attached to monomethoxy-terminated poly(ethylene glycol) (mPEG) for the purpose of rendering surfaces protein resistant [1]. By using an adhesion foot consisting of three repeating DOPA units, Dalsin *et al.* showed that protein adsorption could be reduced up to 99% [1]. However, the fact that DOPA is a non-proteinogenic amino acid which carries a negative charge at physiological pH values and that at the same conditions most metal oxide surfaces are negatively charged as well, electrostatic repulsion effects could impede adsorption processes and decrease the stability of adsorbed molecules with only one or two DOPA groups per PEG chain.

In order to investigate the influence of the charge of the surface binding group on the adsorbed adlayer, its stability and subsequent protein resistance upon serum exposure, we developed new single-side catechol derivatives (neutral, negative and positive charged) and coupled them to PEG chains.

The design of the positively charged compound was inspired by a natural product evolutionary selected by cyanobacteria to bind Fe(III). Indeed, these organisms evolved sophisticated strategies for iron sequestering and the iron chelator anachelin was evolutionary optimized to effectively bind to Fe(III) [2]. We wondered whether this exceptional binding phenomenon could be extended to bind as well to *metal oxide surfaces* [3].

METHODS: The molecules were/will be investigated in terms of adsorption behavior and subsequent resistance against serum adsorption, using variable angle spectroscopic

ellipsometry (VASE), optical waveguide lightmode spectroscopy (OWLS) and X-ray photoelectron spectroscopy (XPS). For polymer adsorption standard conditions were defined as follows: 1 mg/ml resp. 0,1 mg/ml of polymer dissolved in cloud-point buffer, adsorption at 50°C for 4 hours. Adsorptions were done on TiO₂ coated silicon wafers for VASE and XPS experiments and on TiO₂ coated waveguides for OWLS measurements.

RESULTS: Our preliminary results demonstrate that the charge of catechol PEG conjugates has a major influence on polymer adsorption and stability. In order to confirm these observations further results, including long term stability study will be presented.

DISCUSSION & CONCLUSIONS: VASE and OWLS experiments revealed that neutral and positive charged mPEG-DOPA derivatives show an enhanced adsorption on TiO₂ and lead to a superior protein resistance compared to negatively charged mPEG-DOPA₁ used in a related work by Dalsin *et al.* [1].

REFERENCES: [1] J.L Dalsin, *et al* (2005) *Langmuir* **21**: 640-646. [2] Selected examples: K. Gademann, (2005) *ChemBioChem* **6**: 913. [3] K. Gademann, Y. Bethuel, (2004) *Org. Lett.* **6**: 4707. K. Gademann, Y. Bethuel, (2004) *Angew. Chem., Int. Ed.* **43**: 3327.[3] D. Wäckerlin (2005) *Biomimetic Surface Modifications with Differently Charged PEG-conjugated Catechol Derivatives. Diploma Thesis, Dept. of Material, ETH Zürich*, soon available at www.textorgroup.ch