

Surface Functionalization of Biomaterials and Biosensors

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INTRODUCTION: The spontaneous assembly of multifunctional molecules at surfaces has become a useful technique to design hybrid interfaces for the biosensor field, model surfaces for cell-biological studies and drug carrier surfaces for medical application. While alkanethiol self-assembled monolayers on gold surfaces are routinely used today, there is a need for a wider range of reliable assembly systems that are compatible with oxide-based substrate surfaces. The general objective is to produce interfaces via cost-effective, robust techniques that allow the elimination of non-specific protein adsorption (“non-fouling” surfaces) and the addition of bioligands at controlled surface density and molecular conformation in order to direct the biological response to biomaterials and biosensor chips.^{1,2}

RESULTS: Poly(ethylene glycol)-grafted polyionic copolymers assemble spontaneously from aqueous solutions at charged interfaces resulting in well-defined, immobilized monolayers or multilayers depending on the polymer architecture. The degree of interactiveness can be controlled quantitatively through the design of the polymer architecture.³ If the polymer is functionalized with bioligands such as peptides (to mimic cell-interactive proteins), biotin (link to (strept)avidin) or NTA-Ni²⁺ (link to histidin-tagged biomolecules), biomaterial and biosensor interfaces with quantitative control over ligand density can be efficiently produced.

Cell-interactive peptides can be covalently coupled to polymeric self-assembly systems to achieve controlled surface density of ligands, which interact in a specific way through integrin- or heparin-mediated recognition and binding. Cell-adhesive, but bacteria-resistance surfaces provide a surface platform of potentially high clinical relevance.⁴ Chemical patterning of surfaces into (bio)adhesive and non-adhesive areas in the micrometer to nanometer range has become an important tool to organize biological entities such as cells and biomolecules at interfaces in a highly controlled manner (Fig. 1).⁵ Two novel surface modification techniques are presented that combine conventional microfabrication (top-down) with molecular self-organization (bottom-up approach). Biologically meaningful patterns of protein-adhesive and

non-adhesive areas in a size range from micrometers to as small as 50 nm could be produced with consistent quality and on comparatively large areas (e.g., whole 4-inch wafers).

Fluorescence microscopy, XPS, ToF-SIMS, Ellipsometry and AFM were used to control *ex situ* each surface modification step, while the kinetics of the interface reactions including the interaction with biological media were monitored in situ with an optical, evanescent field based sensor (OWLS) and the quartz crystal microbalance (QCM-D) technique.

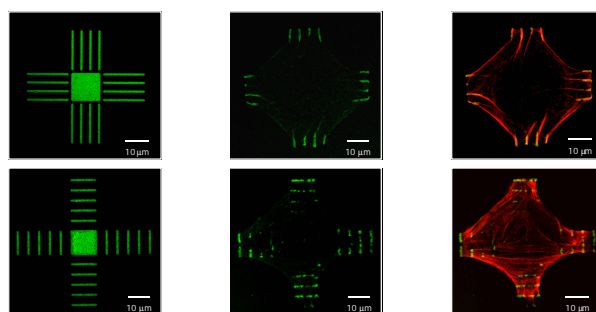


Fig. 1: Adhesive patterns produced by the selective molecular assembly patterning (SMAP) technique. Left: Confocal fluorescence microscopy of fibronectin pattern. Middle: Focal adhesions of attached single fibroblast cell (vinculin staining in green). Right: Actin fibre network of single fibroblast cell (actin staining in red). Image size: ca. 60x60 μm^2 .

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