Biologically active surfaces using chemical vapor deposition polymerization

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Statement of Purpose: Future biomedical implant devices will use advanced surface engineering technologies to actively modulate tissue integration. Towards this goal, vapor-based polymer coatings have been interesting candidates for the coating of implant devices, because of their advanced processibility and their excellent intrinsic biocompatibility. For instance, a specific vapor-deposited polymer (parylene) is already used in FDA approved drug-eluting stents. The commercially available coatings lack however, anchor groups for further modification and therefore do not allow for immobilization of biomolecules or the implementation of protein-resistancy.Herein, we describe the usefulness of the CVD polymerization process to create functionalized, biologically active surfaces.

Methods: *[2.2]Paracyclophane synthesis:* Chemicals were purchased from Aldrich and were used without further purification. Friedel-Crafts acylization of [2.2]paracyclophane with the corresponding acid anhydride, or acid chloride, using an excess of aluminum chloride resulted in keto-functionalized [2.2]paracyclophanes in high yields.

CVD polymerization: 4-Benzoyl[2.2]paracyclophane was synthesized via a three-step synthesis.4 The starting material was sublimed under vacuum and converted by pyrolysis into reactive species, which polymerize upon condensation. A constant argon flow of 20 sccm was used as carrier. Sublimation temperatures were kept at 110-130 °C followed by pyrolysis at 800 °C. Subsequently, polymerization occurred on a rotating, cooled sample holder placed inside a stainless steel chamber with a wall temperature of 130 °C. The coating pressure was 540 μbar. The exit of the chamber was connected via a cooling trap to a mechanical pump. X-ray photoelectron spectroscopy, (Axis Ultra, Kratos), and FTIR spectroscopy (Nicolet 6700) were used for characterizing the resulting polymers.

Photopatterning of CVD coated microfluidic devices. After surface modification via CVD polymerization, the coated substrates were immersed in an aqueous solution of polyethylene glycol (PEO, 10.000 g/mol, 3 weight-%). In these studies, both star-PEO and linear chain PEO were compared. For patterning, a photomask was brought in close proximity to the outside surface of the device (the depth of the microchannel was 50 μm). Samples were then exposed to broad-range UV radiation of about 320 nm wavelength for 30-60 min. DI-water was used to separate excess PEO. For protein adsorption studies, samples were incubated with protein solutions for 5 min.

Results / Discussion: A conformal film of PPX-CO-Ph was deposited on the sample surfaces using CVD polymerization. The chemical structure of the resulting polymer coatings was verified by grazing-angle FTIR spectroscopy and XPS spectroscopy. The FTIR spectrum was in accordance with previous findings and reveals characteristic bands of the C=O stretches at 1612 and 1665 cm-1. X-ray photoelectron spectroscopy was used to confirm the results of the FTIR study. The XPS survey spectrum and the high-resolution spectra of oxygen and carbon indicate 95.5 atom-% carbon and 4.5 atom-% oxygen, as compared to the theoretical value of 95.8 atom-% carbon and 4.2 atom-% oxygen. The high-resolution C1s spectrum further reveals characteristic signals for aliphatic and aromatic carbon (C-C, C-H) normalized to 285 eV, C-C=O at 285.9 eV, C=O at 286.1 eV, and a signal indicating a $\pi \rightarrow \pi^*$ transition at 291.5 eV. The latter signal is characteristic for aromatic molecules and has been previously reported for similar poly-p-xylylenes.The excellent accordance between both data sets suggests that side-reactions, such as decomposition of functional groups, can be largely excluded under the conditions used for CVD polymerization. This is important for surface engineering applications, where CVD coatings form reactive interfaces for subsequent, often complex immobilization steps. In an application example, a polymer-based microchannel was first coated with the photoreactive coating via CVD polymerization followed by the incubation with an aqueous solution of PEO. For this purpose, the PEO solution was filled into the microchannel for 30 min. Next, the solution was removed, tried with a stream of argon and the photomask was placed on bottom side facing the luminal surface of the microchannel. After UV exposure, the non-bound PEO was removed and the entire channel was incubated with the protein solution. Although the pattern is clearly observable, the features are less sharp on the deeper luminal surface than on the shallow surface. The reduced contrast for the deeper channels is a result of the wider distance of the surface from the mask. Nevertheless, fibrinogen is adsorbed only to the PEO-free squares establishing a discontinuous protein pattern within the microchannel.

Conclusions: We have demonstrated the feasibility of using these reactive polymers to control non-specific protein adsorption on different substrates. More importantly, experiments have also been conducted with 3-D patterning in a PDMS-based microfluidic channel demonstrating the creation of spatially controlled non-fouling surfaces in 3-D geometries. In addition, the photopatterning method overcomes the continuous patterns in laminar flow patterning. This novel technique consists of two steps: (1) CVD polymerization of the photodefinable coating, and (2) photopatterning. This generic surface engineering protocol is widely applicable to a range of biomaterials and even hybrid devices, because of the substrate independence of the CVD coating step. With the precise control of non-specific protein adsorption and the ease of photopatterning technique in three dimensions, we foresee the technology to be useful for the design of novel biomaterials or for "BioMEMS" applications.

References:

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