Substrate-Independent Dip-Pen Nanolithography Based on Reactive Coatings

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Abstract: We report that nanostructuring via dip-pen nanolithography can be used for modification of a broad range of different substrates (polystyrene, Teflon, stainless steel, glass, silicon, rubber, etc.) without the need for reconfiguring the underlying printing technology. This is made possible through the use of vapor-based coatings that can be deposited on these substrates with excellent conformity, while providing functional groups for subsequent spatially directed click chemistry via dip-pen nanolithography. Pattern quality has been compared on six different substrates demonstrating that this approach indeed results in a surface modification protocol with potential use for a wide range of biotechnological applications.

Substrates displaying controlled surface patterns with features in the micrometer and nanometer regime have been of broad scientific interest for technical and biomedical applications. Among the available patterning methods, dip-pen nanolithography (DPN), a scanning probe microscopy-based nanolithographic technique that delivers "chemical inks" to substrates, offers a number of important advantages, such as the ability to produce patterns with nanometer resolution in a direct writing mode (no need for stamps and other auxiliaries) and patterning of large surface areas by parallelizing the writing process with 1D or 2D cantilever arrays.[1−3] DPN is also free of UV or ion-beam radiation and avoids harsh chemical treatments compared to the uses of conventional photolithographic methods.[4] With optimized DPN process conditions, such as homogeneous inking, the dwell time during the writing process, temperature, and humidity,[5,6] sub-50-nm resolution has been reported.[2,6] Inks such as organic molecules,[1,3,7−11] alkylthiols,[12] polymers,[13−15] DNA,[16,17] proteins,[18−21] peptides,[22,23] lipid layer,[24−26] metal ions,[27,28] sols,[29,30] and nanoparticles[31,32] have been processed in the past.[2,4,6] Even some click chemistry approaches were reported recently.[33,34] The potentially biggest limitation of DPN is the limited number of substrates/ink combinations that are compatible with the DPN process. Many of the more common substrates in DPN, such as Au and Si, may be considered model surfaces rather than biomedically or technically useful materials.

We herein address this challenge by developing a more generalizable surface modification protocol based on DPN on functionalized poly-*p*-xylylene coatings. Functionalized poly-*p*-xylylenes act as *Reactive Coatings*, which essentially establish interfaces equipped with chemically reactive groups that can be selected from amines, alcohols, aldehydes, activated carboxylic acids, alkynes, and anhydrides.[35−38] The coatings are deposited in a solventless process by chemical vapor deposition (CVD) polymerization and can be applied to a wide range of different substrate materials, if they are stable under moderate vacuum.[39] The CVD polymerization process tends to maintain an unaltered substrate topology, provides pinhole-free coverage even for sub-10-nm thick films, and can coat complex geometries.[40−42]

Prior to DPN, a range of different substrate materials were coated with poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene), via CVD polymerization of 4-ethynyl[2.2]paracyclophane.[38] Next, the ability of these substrates to support DPN nanopatterning was confirmed via spatially controlled Huisgen 1,3-dipolar cycloaddition. This reaction involves ethynyl groups presented on the CVD coating, which spontaneously convert with azides in the presence of a copper catalyst. We selected this "click" reaction, because we expected rapid conversion in high yields at room temperature to be critical for the formation of patterns with sufficient quality.[43] The coated substrates were transferred into a DPN chamber, and a 1D cantilever array containing 26 Si_3N_4 pens, which was first treated with oxygen plasma to ensure proper wetting of the azide-containing ink, was incubated in a solution of fluorescence-labeled azide ink (Figure 1). Successful Huisgen 1,3-dipolar cycloaddition was confirmed based on the formation of 1,2,3-triazoles[44] that selectively formed on poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene) coatings, but not on unfunctionalized poly-*p*-xylylene surfaces (Figure S4). The results indicated efficient transfer of azide molecules to the surface (Figure 1c,e). During the printing step, tight control of humidity at 60% was crucial in order to maintain the water meniscus and ensure the delivery of azide molecules to the solid surfaces. We also examined the dependence on writing speed vs fluorescence intensity in the range 35 to 1.75 μm/s and found a decreased writing speed to result in increased fluorescence intensity (see Supporting Information). In addition, a nanoparticle pattern was created by first conducting DPN writing of biotinylated azide molecules onto a poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene)-coated silicon substrate. Second, spatially directed self-assembly of streptavidin-conjugated gold nanoparticles resulted in patterns, which were analyzed by atomic force microscopy (AFM) (Figure 1d). To demonstrate applicability to a wide range of technically relevant substrates, DPN writing after CVD polymerization was repeated on different substrates (Figure

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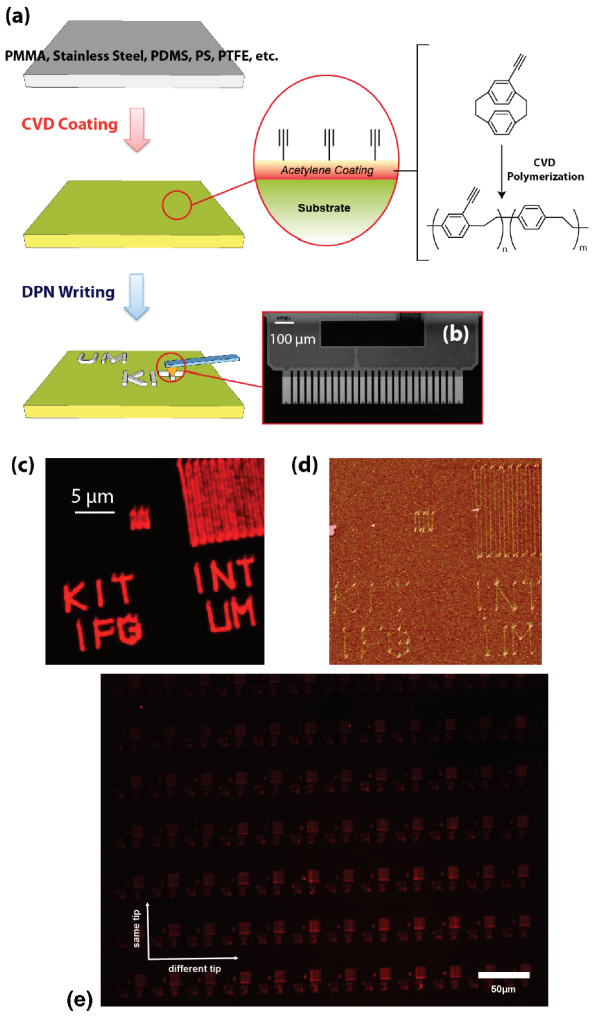

Figure 1. (a) Schematic illustration of the DPN writing process modified for CVD-coated substrates. The ethynyl-presenting polymer, poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene), is used as an example; inking molecules are covalently attached via click chemistry. (b) Micrograph of a 1D cantilever array with 26 pens. (c) Fluorescence micrograph of a poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene)-coated gold surface after DPN writing; features consist of 300-nm lines to form texts and rectangular boxes. (d) AFM image (tapping mode topography) showing self-assembled gold-streptavidin particles after DPN-based click reaction. (e) Fluorescence image of a large-scale DPN pattern, where features in the *x*-direction were written by different tips of the 1D cantilever array and repeated in the *y*-direction.

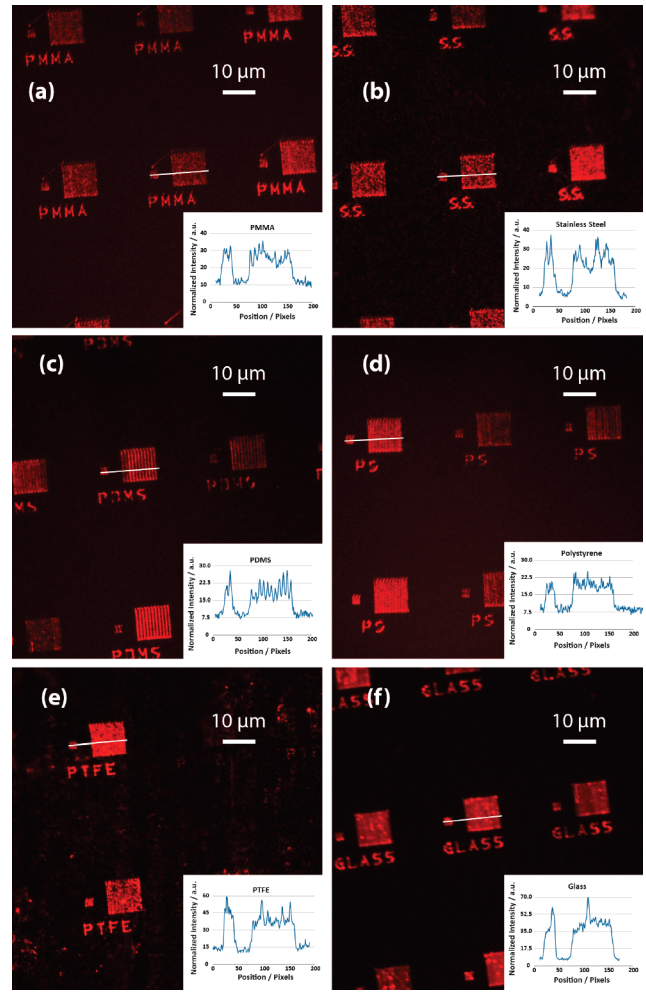

Figure 2. Fluorescence micrographs showing DPN writing process on CVD polymer coating, poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene), on various substrates of (a) poly(methyl methacrylate) (PMMA), (b) stainless steel (S.S.), (c) poly(dimethylsiloxane) (PDMS), (d) polystyrene (PS), (e) poly(tetrafluoroethylene) (PTFE), and (f) glass. Fluorescence intensity profile (bottom-right corner) is showing a reproducible presentation of the DPN writing process on different substrates along the reference line (white line) as indicated in each figure.

2a−f). In all cases, the anticipated surface patterns were clearly detected by fluorescence microscopy. This procedure is equally applicable to hard surfaces (e.g., glass, silicon) and elastomers, such as PDMS, spanning a significant range of substrate properties. Noticeably, although substrates varied with respect to surface roughness, the satisfying pattern quality was only slightly reduced on the roughest samples (stainless steel, PTFE) compared to gold or silicon.

In summary, a protocol for modification of substrates based on DPN-based click reactions on poly(4-ethynyl-*p*-xylylene-*co*-*p*-xylylene) has been established. This simple, yet versatile approach is based on the use of CVD polymerization to deposit functionalized poly-*p*-xylylenes with highly reactive groups. Beyond ethynyl groups, other CVD coatings with a wide range of functional groups are known[45] and can potentially be used (DPN based on hydrazone formation on poly(4-formyl-*p*-xylylene-*co*-*p*-xylylene)-coated silicon substrates has been demonstrated in Figure S5 of the Supporting Information). This important detail highlights the possibility of extending DPN beyond Huisgen 1,3-dipolar cycloaddition.

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Supporting Information Available: Experimental section. This material is available free of charge via the Internet at http://pubs.acs.org.

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