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Microcontact printed poly(amidoamine) dendrimer monolayers on silicon oxide surface

Nikodem Tomczak, G. Julius Vancso *

Materials Science and Technology of Polymers, Faculty of Science and Technology, University of Twente, and MESA+ Institute for Nanotechnology, P.O. Box 217, 7500 AE, Enschede, The Netherlands

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Abstract

Patterning of silicon substrates with poly(amidoamine) generation 5 (PAMAM-G5) dendrimers using soft lithographic microcontact printing (μCP) is presented. μCP is shown to yield monolayers of dendrimers patterned with high level of definition over μm^2 to mm^2 areas. The patterns are stable over a period of weeks, which is attributed to the suppressed diffusion of partially charged G5 PAMAM on oxidized silicon. However, the dendrimers studied were shown to be relatively weakly bound to the substrate when subjected to lateral stresses. In aqueous conditions most of the dendrimers desorbed from the substrate.

Keywords: AFM; Dendrimer; PAMAM; Microcontact printing

1. Introduction

Dendrimers are a unique class of synthetic, nearly monodisperse polymers, which encompass hyperbranched, tree-like, covalent structures with precisely defined molecular architectures [1–4]. Their dimensions range from one to several nanometers and they exhibit increasing sizes with increasing degree of molecular branching (hereafter referred to as generation). A characteristic feature of dendrimers is the presence of well-defined, controllable functional groups at their molecular "surface" (dendrimer periphery), which determine their chemical properties, and provide synthetic versatility. Due to their exact molecular size and well-defined architecture, dendrimers have been frequently used as building blocks in bottom–up macromolecular nanotechnology. Poly(amidoamine) (PAMAM) dendrimers feature among the most commonly used, and best studied hyperbranched structures, based on ethylenediamine core [5], exhibiting various surface groups. For example "generation 5" (G5) PAMAM dendrimers have 128 accessible terminal primary amines available for derivatization. Although the synthesis and solution properties of dendrimers have been studied in depth, the knowledge of the structural and physicochemical properties of dendrimers at interfaces is still limited. Nevertheless, owing to their unique properties, dendrimers have found applications in

* Corresponding author. Fax: +31534893823.
E-mail address: g.j.vancso@tnw.utwente.nl (G.J. Vancso).

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a broad range of fields including medicinal chemistry [6], catalysis [7], and photonics [8].

During the last decade many investigations were concerned with fabrication and properties of dendrimer surface structures [9]. For the preparation of dendrimer monolayers or multilayer films, layer by layer assembly [10,11], self assembly [12], covalent linking [13,14], spin coating [15,16], soft lithography [14,17–22] and dip pen nanolithography [14,23,24] were used.

Among possible fabrication methods microcontact printing (μCP) is one of the simplest, most robust and inexpensive methods to obtain sub-50 nm dendrimer patterns over large areas [25]. However, only few studies of μCP of dendrimers were reported in the literature to date [14,17–20,22,26]. Depending on the μCP conditions, formation of monolayers [14,18,22,26], multilayered structures [17], and thin films [19] were reported. Recently, sub-50 nm patterns of dendrimers on silicon [18] and palladium [22] were achieved. The feasibility of the μCP technique to pattern stable PAMAM dendrimer monolayers on silicon substrates on larger length-scales, however, was not given considerable attention. Also the time dependent stability of the patterns in air and in liquids was not addressed.

In addition to controlled fabrication of surface patterns with dendrimers, the resulting interfaces must be well characterized, preferably with a resolution down to the diameter of the individual hyperbranched particles. Atomic force microscopy [27] (AFM) was shown to be very useful to investigate the morphology of the dendrimer assemblies at the solid–air, solid–liquid, and liquid–air interfaces. AFM images revealed the extent of dendrimer packing, aggregate formation, or the quality of monolayers [28]. AFM related experiments allowed one to elucidate the structural deformations (if any) of dendrimers deposited on various surfaces. To this end, studies of single core-shell tecto(dendrimers) on mica [16], single PAMAM (G4 and G8) on Au [29], (G5-G10) on mica [30,31] and HOPG substrates [31] were performed.

In the context of possible applications, high level of definition of the printed patterns and absence of diffusion of the dendrimeric ''ink'' on the silicon substrates can be advantageous for some chip-based analytical technologies. If e.g. G5-PAMAM dendrimers are used, part of the available amine terminal groups can interact with the silicon substrate, nevertheless, there would be still a substantial amount of NH_2 groups left for further functionalization with e.g. biomacromolecules. The usefulness of such patterns in various applications mentioned is mainly limited by the pattern stability in aqueous environments.

In this communication, we show that microcontact printing (μCP) is a relatively easy and straightforward technique to fabricate large area (μm^2 to cm^2), amino-functionalized G5-PAMAM dendrimer monolayer patterns on silicon oxide substrate. We demonstrate that AFM can be successfully used to characterize, and modify these patterns. The dendrimers adopt a flattened conformation at the surface indicating favorable interactions with the silicon oxide. Unlike for dendrimers of lower generation, G5-PAMAM patterns display a remarkable stability over a period of several weeks when stored in ambient conditions. However, when subjected to lateral stresses, the dendrimers can be ''moved'' across the surface indicating that the interactions between the dendrimer terminal amine units and the silicon oxide substrate are relatively weak. In water environment most of the dendrimers desorb from the substrate. Covalent coupling of the dendrimers to the substrates is needed for further functionalization and applications in aqueous media.

2. Experimental section

Methanolic solutions of PAMAM dendrimers of G5 (5 wt%) were obtained from Aldrich and used as received. Absolute methanol was obtained from Biosolve (The Netherlands). Silicon substrates were cut from a 4-inch silicon wafer into a $1 \times 1\ cm^2$ pieces. The substrates were cleaned by immersing in a freshly prepared Piranha solution (solution containing 70% of concentrated sulfuric acid and 30% of hydrogen peroxide) for 5 min, and rinsed with high purity Milli-Q water (Millipore Milli-Q water). Cleaned substrates were stored in an ethanolic solution. When needed for experiments, the substrates were rinsed several times with ethanol, dried in a stream of N_2 and used immediately for dendrimer deposition. PDMS stamps were fabricated by pouring a 10:1 mixture of Sylgard 184A and Sylgard 184B precursors (Sylgard 184, Dow Corning) over a cleaned and pre-patterned silicon master. The PDMS stamps were cured for 24 h at 60 °C. Cured stamps were peeled off from the master for subsequent use in μCP. Microcontact printing of dendrimers was performed according to the procedure reported in [26]. The PDMS stamps were dipped

into a methanolic solution (1 wt%) of G5-PAMAM for 2 min, rinsed with deionized Milli-Q water and blow-dried in a stream of nitrogen gas. The stamps were applied to cleaned silicon substrates for 5 to 10 s and then carefully removed.

Imaging of silicon substrates coated with dendrimers was performed with NanoScope III, and a Dimension 3100 atomic force microscope (Digital Instruments, Santa Barbara, CA). A set of V-shaped Si_3N_4 cantilevers (Nanoworld, Germany) with spring constants of 0.04–0.06 N/m, and a single beam Si cantilever with a nominal spring constant of ~40 nN/nm (Pointprobe-plus, Nanosensors, Germany) were used for imaging in the contact and tapping modes, respectively. The spring constant of the contact mode cantilevers was calibrated by monitoring the cantilever fluctuations in air, due to thermal excitations, and by applying the equipartition theory [32]. Thermal noise data acquisition and analysis was performed using a custom-written LabView (National Instruments) software. The estimated error of the spring constant determination was ~15%.

3. Results and discussion

First we describe the process of μCP of dendrimers used in this study, as shown schematically in Fig. 1a. The main steps of the μCP process included fabrication of a PDMS stamp by replication from a silicon master, inking the stamp with the dendrimer "ink" solution, "ink" transfer to the substrate by conformal contact, and finally removal of the stamp leaving behind the "ink" on the substrate. Fig. 1b shows an AFM height image of G5 PAMAM dendrimers microcontact printed onto a cleaned silicon substrate. Parts b–d of Fig. 1 show consecutive zoomed-in areas of the same patterned region to reveal the fine structure of the patterns. The lateral distance between the patterned areas is equal, on average, to 2 μm and corresponds to the contacted areas between the PDMS stamp and the surface. No contamination of the non-printed areas is observed. The edges between the stamped and not stamped sections are very sharp indicating that the deposition of the dendrimers took place in areas of conformal contact indicating high pattern fidelity. This is attributed to the low surface diffusion of the dendrimer "ink" used [33]. The average height of the printed regions is equal to 2 nm with some protruding domains exhibiting heights up to ca. 4.5 nm.

At this juncture it might be useful to consider the structure of PAMAM dendrimers at interfaces. The conformation of dendritic macromolecules will be determined mainly by the strength of interactions of the dendrimer chemical units (end-groups, branches) with the substrate and with the surrounding medium. For PAMAM dendrimers it was experimentally confirmed that the dendrimers have a rather hollow core and a densely packed outer layer with amino end-groups positioned preferably at the dendrimer periphery [34]. In solutions, PAMAM dendrimers were shown to adopt spherically symmetric, globular conformations. However, it was observed that interactions between the PAMAM dendrimers and the silicon substrate may cause significant flattening of the dendrimers shape [28]. At neutral pH all primary amines are protonated ($pKa = 9.0–10.7$) [35], thus this flattening may be due to favorable interactions between the charged PAMAM amine end-groups and the negatively charged, oxidized, silicon surface. Indeed, amino terminated G5-PAMAM dendrimers on various substrates have been studied by Mecke et al. [36] who concluded that the height and the width of the dendrimers depend on the nature and strength of the interactions between the dendrimers and the substrate. They have reported heights from 1 to 1.5 nm for isolated amine-terminated G5-PAMAM dendrimers on mica. Single dendrimer height values for NH_2 terminated PAMAM on various substrates (except silica) have also been studied by Betley et al. [37]. They conclude that as substrates are changed from hydrophobic to hydrophilic, AFM determined heights exhibit increasing and substantial deviations (flattening) from heights of ideal, spherically shaped dendrimers. Thus, we assume that molecular height data for G5 PAMAM obtained on mica can be also used for silica, i.e. in our case a single dendrimer height of 1–1.5 nm is anticipated. On the other hand, our stamped dendrimer films exhibited a height of approximately 2 nm, which slightly exceeds the height of single isolated dendrimers as discussed above. This slightly higher value can be explained by assuming well-packed structures of the hyperbranched molecules within our stamped films. Specifically, in tightly packed structures, one would anticipate a reduction of the attachment points of the NH_2 terminal groups to the substrate, which would result in reduced shape flattening. This would explain the increase of the height values we observed. We conclude that the dendrimeric films we obtained by μCP predominantly consist

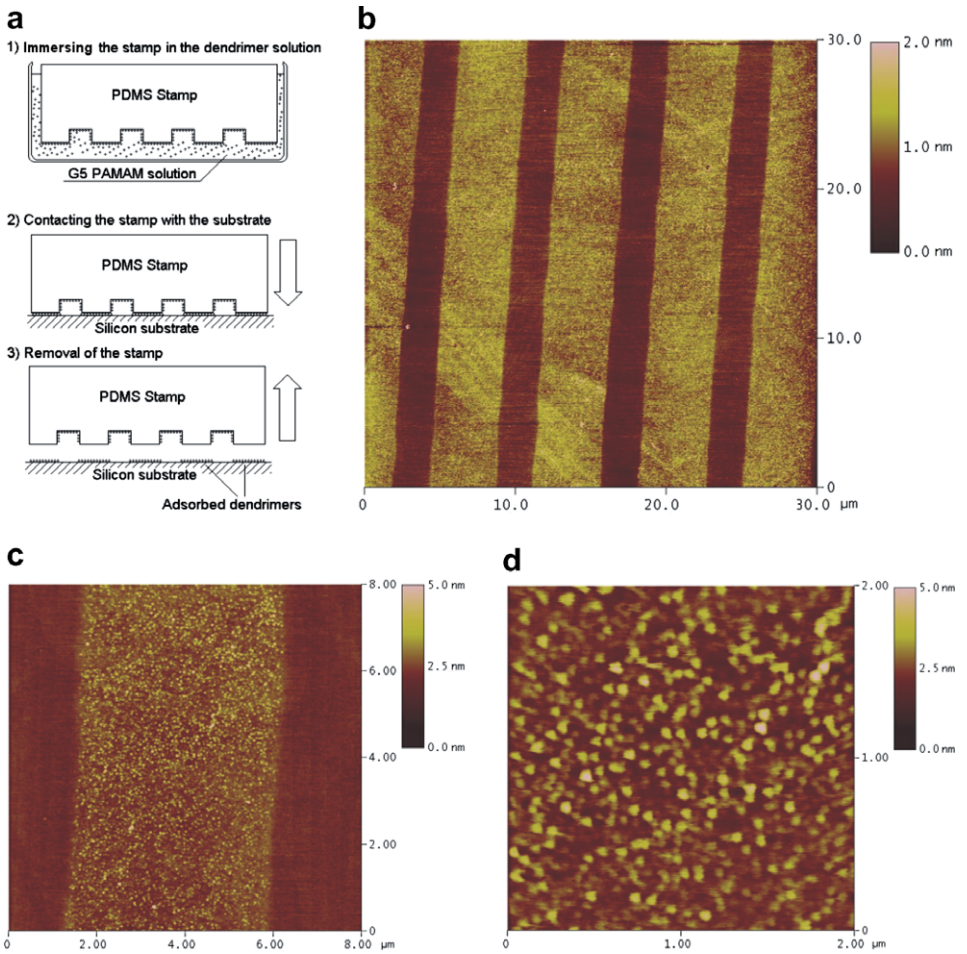

Fig. 1. (a) Scheme of the μCP method. (b)–(d) are AFM height images of microcontact printed G5 PAMAM dendrimers on silica surface.

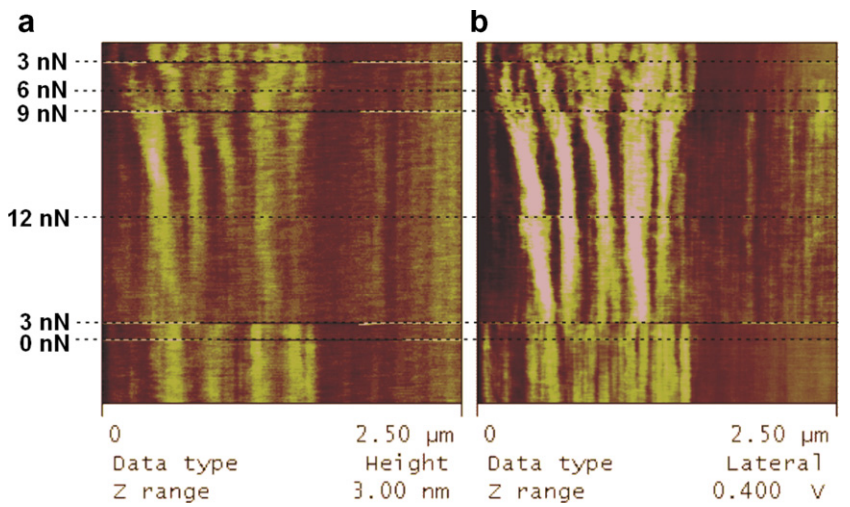

Fig. 2. Scratching the dendrimer layer with the slow-scan axis disabled under increasing load. (a) is the height and (b) the friction force image acquired during scratching. The vertical axis of the images correspond to time. The applied normal load is marked on the left side of the image.

of hyperbranched molecular monolayers. Finally, we note that occasional observation of higher features (of ca. 4.5 nm height) is likely an indication of dendrimer aggregation, stacking, or multilayer formation in the corresponding areas [10,11].

The patterned G5-PAMAM structures were stable in ambient conditions (air, at room temperature, with varying relative humidity form 30% to 50%) over a period of many weeks (the longest time interval between imaging was 5 weeks). However, the stability of G4 PAMAM dendrimer patterns on silicon in ambient conditions, as reported, was only 14 days [17]. As the stability of PAMAM patterns mainly depends on the interactions between the silicon surface and the number of terminal NH_2 groups at the PAMAM periphery, the improved stability of the patterns could be simply due to the increased number of interaction sites for dendrimers moving from G4 to G5. Apparently, the water absorbed from the ambient is not enough to cause significant dendrimer surface mobility.

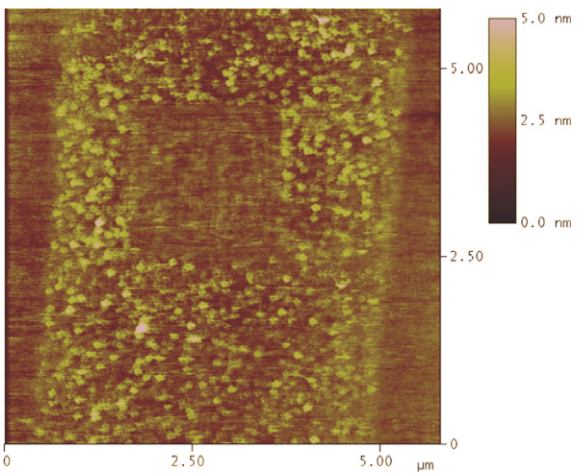

Fig. 3. AFM height image of the pattern scratched by an AFM tip. The absence of dendrimer pile-up at the area edges indicates transfer of the dendrimers to the AFM tip.

To probe the strength of the surface/dendrimer interactions we performed a simple, qualitative, "scratching test". This experiment was based on scanning one single line back and forth (with a disabled slow-scan axis) under increasing normal loads and simultaneously observing changes (if present) in the surface topography [38,39]. The temporal development of the surface along the single scanned line is shown in Fig. 2a (height) and b (lateral force signal). The vertical axis of the image corresponds here to time, and surface normal load values are marked in the image. For low normal loads, $F_n < 3$ nN, no significant changes in the monolayer structure could be detected. Under higher normal loads, $3\ \text{nN} < F_n < 12$ nN, however, the dendrimer layer was deformed and the dendrimers were pushed across the surface with the AFM tip forming well-known periodic adhesion detachment waves. After reducing the normal load, the friction images show that the dendrimer molecules begin to redistribute among the ridges. Similar experiment was performed for a two-dimensional area in the printed patterns

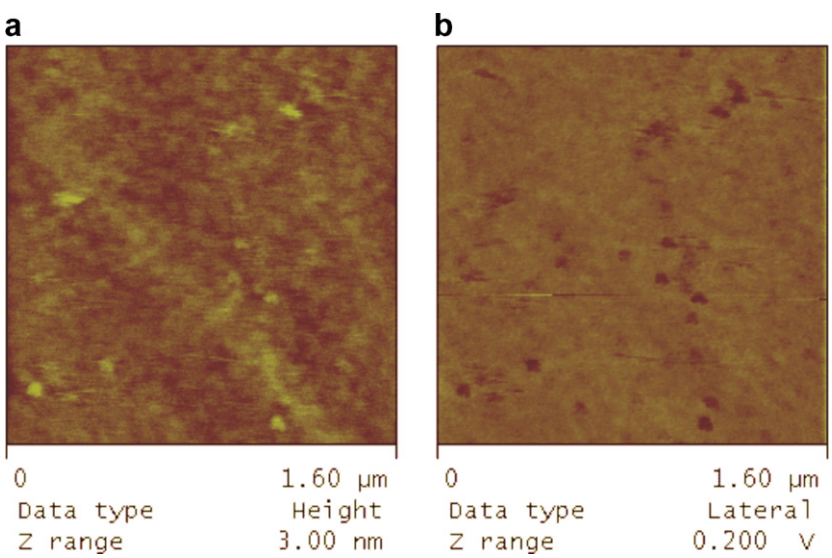

Fig. 4. AFM height (a) and lateral force (b) images of G5-PAMAM dendrimers on silicon after introduction of water. Lateral force signal reveals dendrimers that are not visible in the height image.

(Fig. 3). The tip was scanning the sample under a constant load of 10 nN. The virtual absence of piled-up dendrimers at the edges of the scratched area indicates, however, that some of the dendrimers were transferred to the AFM tip. This is similar to earlier observations for low molar mass ''inks'' like octadecanethiol [40].

To probe the stability of the patterns in biologically relevant media, we have also imaged the μCP patterns in water. Fig. 4a and b shows representative AFM height and lateral force images, respectively, of the sample after introduction of water. A number of protrusions on the height image (absent on a not printed sample imaged in water) are visible. Corresponding contrast in the measured lateral forces for the same protruding areas shows that the features visible on the height image are the remaining dendrimer molecules, or remaining dendrimer aggregates. Owing to the compositional sensitivity of the lateral force signal, dendrimers which are not visible in the height image can be identified. Imaging of the printed regions in water revealed that most of the dendrimers desorbed from the substrate immediately after introducing the solvent, and the microcontact printed patterns imaged in air could not be visualized. Therefore, for application of the printed dendrimer monolayers in aqueous media, covalent coupling of the dendrimers to the substrate will be needed to perform subsequent derivatization reactions on the available functional groups [14,24].

4. Conclusions

We have presented that micrometer scale patterns of G5-PAMAM monolayers on silicon oxide surface can be obtained over areas of up to several mm^2 by using a relatively simple microcontact printing technique. AFM images revealed that roughly a single monolayer of dendrimers was deposited onto the substrate. No contamination of the area between the patterns was observed, indicating that no surface diffusion occurred after stamping. Pattern edge sharpness indicated that the patterns were defined only by the conformal contact between the PDMS stamp and the substrate. Although the patterns were stable in air over a period of weeks, and no surface diffusion over micron length-scales could be detected, the dendrimers were shown to be relatively weakly bound to the substrate when subjected to lateral stresses. Introduction of aqueous medium caused most of the surface bound dendrimers to desorb from the substrate. Covalent coupling of the dendrimers to the substrate is needed to perform further derivatization of the printed patterns.

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