Site-Directed Exchange Studies with Combinatorial Libraries of Nanostructures

Albena Ivanisevic, Kim V. McCumber, and Chad A. Mirkin*

Contribution from the Department of Chemistry and Institute for Nanotechnology, Northwestern University, 2145 Sheridan Road, Evanston, Illinois 60208

Received March 15, 2002

Abstract: We describe a new combinatorial method for studying the exchange between solution adsorbates and nanoscale features within libraries generated via dip-pen nanolithography. Four different compounds, 1-octadecanethiol, 16-mercaptohexadecanoic acid, ferrocene (11-mercaptoundecyl), and ferrocene (11-mercapto-1-oxoundecyl), are studied on amorphous and single-crystal gold substrates. This series of adsorbates allows us to compare the exchange properties of patterns of nanoscale features as a function of composition, feature size, and type of underlying substrate. Moreover, these properties can be compared and contrasted with bulk SAM properties. The novel strategy provides not only a method for initiating site-specific exchange processes but also a way of extracting kinetic information about the rate of such processes in situ.

Introduction

The fundamental characteristics of nanomaterials largely depend on their sizes and shapes.[1] However, studies of nanoscale structures are often limited by the availability of tools for their direct evaluation and comparison. Herein, we report a way to directly study exchange processes involving multiple types of self-assembled monolayers (SAMs) of alkanethiols on gold surfaces under one set of environmental conditions. We use dip-pen nanolithography (DPN) as a tool for generating libraries of SAMs, which consist of arrays of nanostructures that are systematically varied with respect to composition, size, shape, and position on a surface (terrace versus grain boundary).[2] Furthermore, we show that one can initiate site-specific exchange on features within the libraries of nanostructures by using an atomic force microscope (AFM) tip that has been coated with an exchange reagent. Simultaneously acquired lateral force microscopy (LFM) images allow one to compare and evaluate multiple exchange phenomena occurring within one library on one surface. In this way, one can serially dose a surface or nanostructure with the exchange reagent and obtain a stepwise kinetic map of the exchange process. SAMs are becoming important components of high-performance surfaces for sensors, light-emitting diodes (LEDs), and resists for lithographies and anticorrosion studies; an understanding of the factors that control SAM stability both on the macro- and on the nanoscopic length scales is essential for scientists to reap their full potential.[3]

Experimental Section

1-Octadecanethiol, **1**, and mercaptohexadecanoic acid, **2**, were purchased from Aldrich Chemical Co. and used as received. The ferrocenyl alkanethiols **3** and **4** were synthesized using literature procedures.[4] The amorphous gold films used in this study were prepared by Au evaporation onto silicon substrates with 150 Å of Ti as an adhesion promoter.[5] Au(111)/mica was purchased from Molecular Imaging (Phoenix, AZ) and annealed in a hydrogen flame prior to use.

Substrate Preparation. Si(100) wafers (4" (1-0-0) wafers; 3−4.9 Ω/cm resistivity; 500−550 μm thickness, native oxide layer) were purchased from Silicon Quest International, Inc. (Santa Clara, CA). Thermal evaporation of 10−15 nm of Ti (99.99%; Alfa Aesar; Ward Hill, MA) followed by 60 nm of Au (99.99%; Alfa Aesar; Ward Hill, MA) was accomplished using an Edwards Auto306 Turbo Evaporator equipped with a turbopump (Model EXT510) and an Edwards FTM6 quartz crystal microbalance to determine film thickness. Au and Ti depositions were conducted at room temperature at a rate of 1 nm/s and a base pressure of 5×10^{-7} mbar.[6]

DPN Procedure and AFM Imaging. All of the data described herein were taken using a ThermoMicroscopes CP AFM, equipped with a 90 μm scanner and conventional Si₃N₄ cantilevers (ThermoMicroscopes sharpened Microlever A, force constant = 0.05 N/m). Writing with **1** was done via literature procedures.[5,7] In the case of **2**, tips were immersed for 60 s in an acetonitrile solution saturated with the adsorbate

* To whom correspondence should be addressed. E-mail: camirkin@chem.nwu.edu.

(1) Alivisatos, A. P. *J. Phys. Chem.* **1996**, *100*, 13226−13239.

(2) Piner, R. D.; Zhu, J.; Xu, F.; Hong, S.; Mirkin, C. A. *Science* **1999**, *283*, 661−663.

(3) (a) Maoz, R.; Frydman, E.; Cohen, S. R.; Sagiv, J. *Adv. Mater.* **2000**, *12*, 424−429. (b) Maoz, R.; Frydman, E.; Cohen, S. R.; Sagiv, J. *Adv. Mater.* **2000**, *12*, 725−731. (c) Li, Y.; Maynor, B. W.; Liu, J. *J. Am. Chem. Soc.* **2001**, *123*, 2105−2106. (d) Fuierer, R. R.; Carroll, R. L.; Feldheim, D. L.; Gorman, C. B. *Adv. Mater.* **2002**, *14*, 154−158. (e) Noy, A.; Miller, A. E.; Klare, J. E.; Weeks, B. L.; Woods, B. W.; DeYoreo, J. J. *Nano Lett.* **2002**, *2*, 109−112.

(4) Chidsey, C. E.; Bertozzi, C. R.; Putvinski, T. M.; Mujsce, A. M. *J. Am. Chem. Soc.* **1990**, *112*, 4301−4306.

(5) Weinberger, D. A.; Hong, S.; Mirkin, C. A.; Wessels, B. W.; Higgins, T. B. *Adv. Mater.* **2000**, *12*, 1600−1603.

(6) Xia, Y.; Zhao, X.; Kim, E.; Whitesides, G. M. *Chem. Mater.* **1995**, *7*, 2332−2337.

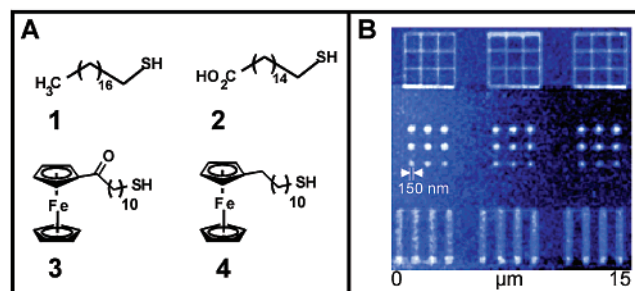(7) Hong, S.; Zhu, J.; Mirkin, C. A. *Science* **1999**, *286*, 523−525.

Figure 1. (A) Molecular inks used to generate the combinatorial libraries used in the study. (B) LFM image of a combinatorial library generated with three different molecular inks. The features on the first row were generated with **2**, the dots on the second row were drawn with **3**, and the last row of line features was written with **4**. The LFM image was collected with a tip coated with **1** at 4 Hz and contact force of 0.5 nN (24 °C, 40% relative humidity).

and then blown dry with compressed difluoroethane. Prior to writing with **3** and **4**, tips were soaked in ~5 mM chloroform solutions of the desired ink for ~30 s and blown dry with compressed difluoroethane. Unless otherwise noted, all patterning experiments were conducted in a glovebox under 40% relative humidity at 24 °C with a tip–substrate contact force of 0.5 nN. Subsequent imaging and exchange studies of the generated patterns were performed under the same conditions.

Results and Discussion

Combinatorial Library Design and Patterning. As a proof-of-concept, we used four different alkanethiols to prepare our DPN-generated libraries, Figure 1A. These molecules were chosen because (1) they allow one to probe the importance of different substituent effects (e.g., sterics, hydrophobicity, hydrogen bonding capabilities) on the exchange process, and (2) they have been the focus of several studies involving SAMs, and, therefore, there is a body of data which can be used for comparison purposes with the data provided herein.[4,8] The redox-active molecules are particularly important because of their role in studying and understanding interfacial electron-transfer processes.[4]

To determine the appropriate parameters for the AFM-tip mediated exchange process, DPN-generated arrays, consisting of dots or lines of **2**–**4**, were generated in a 15 × 15 μm area of an amorphous gold substrate, Figure 1B. The exchange process involving **1** and the arrays consisting of **2**–**4** were initially evaluated by immersing the substrates in ethanol solutions of **1** of varying concentration. The arrays were studied by AFM as a function of immersion time and solution concentration by periodically removing the slides from solutions of **1** and rinsing them with ethanol prior to imaging. By comparing the LFM images of the arrays, before and after exposure to **1**, we discovered that nanoscale features drawn with **3** and **4** can be completely exchanged in a matter from 10 s to 2 min, depending on solution exchange reagent concentration (0.1 to 1 mM solutions were studied; higher concentrations corresponded with shorter exchange times). However, such exchange processes involving bulk solutions were difficult to control, quantify, and monitor continuously. Note that we and others have used LFM to study some of the different stages of SAM growth on a variety of surfaces.[9]
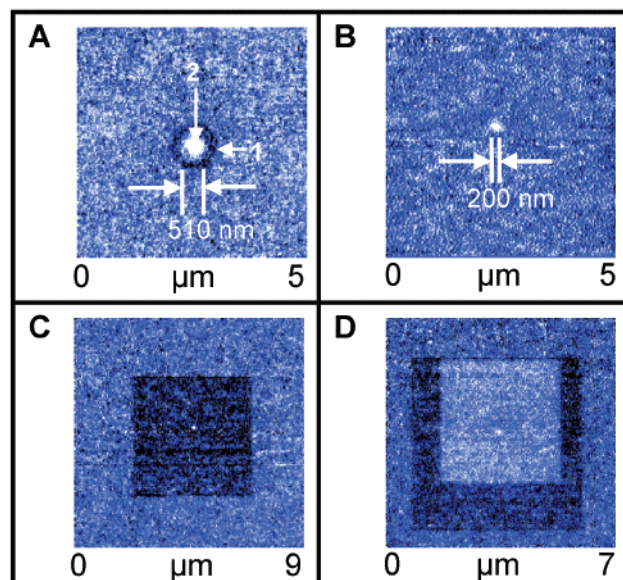

Figure 2. Exchange methodology via an AFM tip. (A) LFM image of the initial feature comprised of two different inks: the light contrast part of the feature in the middle is composed of **2**, and the outer dark region is made of **1**. (B) LFM image of the region shown in A after a tip coated with **1** was scanned across it 23 times at 4 Hz. (C) A larger scan size area of the region shown in part B. The dark square corresponds to the total area of part B. (D) LFM image after exchange was carried out with a tip coated with **2** inside the smallest, light contrast square (24 °C, 40% relative humidity).

Site-Directed Combinatorial Exchange with an AFM Tip. To gain control over the process and to quantify the order of exchange of different chemical functionalities, we initiated the exchange process using an AFM tip coated with a desired alkylthiol exchange reagent. Our protocol for site-directed exchange of nanofeatures can be demonstrated with two different molecular inks, **1** (dark contrast, low lateral force) and **2** (light contrast, high lateral force), Figure 2.[7] We initiate the experiment by designing and patterning a set of nanoscopic structures which are duplicated 44 times to generate a library that provides statistically significant data. For the example provided herein, each component of the library consists of a central dot of **2** and a ring of **1**, Figure 2A. The area surrounding the two-component nanostructure is bare gold (intermediate contrast). This structure was chosen to study the rate of exchange between **2** adsorbed to the gold surface and **1** from an AFM tip. Toward this end, the ring of **1** is used as an internal lateral force standard to help monitor the exchange process. To study the exchange process involving this nanostructure, the **1**-coated AFM tip is raster scanned across the patterned surface at a desired frequency, which controls the rate of the exchange process (4 Hz in the case of Figure 2). After raster scanning over the surface 23 times, one can see that the contrast between the gold and the ring comprised of **1** is no longer evident and the diameter of the dot composed of **2** has significantly decreased (by 39%), Figure 2B. The exchange process and deposition of **1** can be verified by expanding the scan area and comparing the LFM image of the area where we have scanned with the coated tip to the bare

(8) (a) Ohtsuka, T.; Sato, Y.; Uosaki, K. *Langmuir* **1994**, *10*, 3658−3663. (b) Weber, K.; Hockett, L.; Creager, S. E. *J. Phys. Chem. B* **1997**, *101*, 8286−8291. (c) Chung, C.; Lee, M. *J. Electroanal. Chem.* **1999**, *468*, 91−97.

(9) (a) Liu, Y.; Wolf, L. K.; Messmer, M. C. *Langmuir* **2001**, *17*, 4329−4335. (b) Sauer, B. B.; McLean, R. S.; Thomas, R. R. *Langmuir* **1998**, *14*, 3045−3051. (c) Ta, T. C.; Kanda, V.; McDermott, M. T. *J. Phys. Chem. B* **1999**, *103*, 1295−1302. (d) Peach, S.; Polak, R. D.; Franck, C. *Langmuir* **1996**, *12*, 6053−6058. (e) Hong, S.; Zhu, J.; Mirkin, C. A. *Langmuir* **1999**, *15*, 7897−7900.
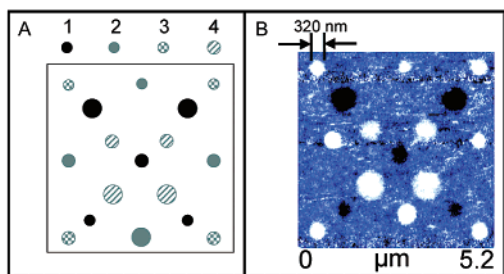
Figure 3. (A) Schematic representation of the combinatorial library design consisting of the four different molecular inks. (B) LFM image of the library described in part A, collected with a clean tip at 4 Hz and contact force of 0.5 nN (24 °C, 40% relative humidity).

gold surface surrounding it, Figure 2C. One can repeat the exchange with a tip coated with **2** and selectively replace molecules of **1** already on the surface with a monolayer of **2**, Figure 2D.

To further demonstrate the capabilities of this approach for studying surface exchange issues involving SAM nanostructures, we designed a library comprised of compounds **1**−**4**, Figure 3A. The features in this library are intentionally designed via DPN to vary in composition, size, and spacing so that we could identify some of the important issues pertaining to the exchange processes involving these molecules. Although all of these molecules bind to the gold via the same type of thiol functionality, the monolayers they form presumably have different degrees of stability due to their tail structures. This has been proposed and supported by individual exchange studies involving SAMs that cover macroscopic portions of a gold surface.[4,8] The LFM image of **1** of the 44 identical cells that make up the library shows that DPN can cleanly generate the desired set of nanostructures, Figure 3B. These types of libraries can then be used to study adsorbate exchange as a function of adsorbate molecule on the type of underlying surface (e.g., amorphous gold versus single-crystal substrates).

LFM "snapshots" of an exchange experiment carried out with a **1**-coated tip at a scan frequency of 3 Hz clearly allow one to observe the exchange process and to determine the relative stabilities of the three nanostructures comprised of **2**, **3**, and **4**, respectively, Figure 4. Indeed, as the experiment progresses, the LFM contrast associated with **2**, **3**, and **4** decreases, but in a nonuniform manner, Figure 4A−D. One can see that exchange takes place from the periphery of the nanostructures toward their centers and that the nanostructures exhibit kinetic stabilities that correlate with feature size and composition. In general, large dots exchange more slowly than small dots, and the following stability trend is observed: **2** > **4** > **3**, Figures 4 and 5. The relative stabilities can be quantified by generating kinetic plots of the exchange process (defined here as feature size as a function of tip exposure time, measured in number of scans at a designated frequency), which show that adsorbates **3** and **4** exchange completely with **1** after 17 and 25 scans, respectively, Figure 5A and B. Note that this analysis does not quantify the amount of exchange that takes place in the bulk area of a nanofeature, which is a slower but not insignificant process on amorphous gold (see Figure 2D, and note the different levels of LFM contrast for the central dot (richest in **2**), the exchanged area (a mix of **2** and **1**), and the surrounding pure **1**-modified area). In contrast, the patterns of **2** show some exchange after 30 scans, but a large percentage of the structures remain intact,
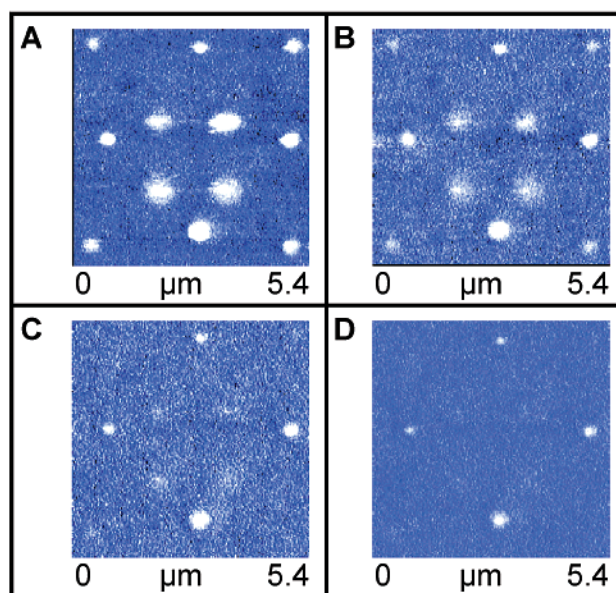

Figure 4. (A) LFM image of the library described in Figure 3, after two scans at 3 Hz with a tip coated with **1**. (B) LFM image of the library described in Figure 3, after 10 scans at 3 Hz with a tip coated with **1**. (C) LFM image of the library described in Figure 3, after 25 scans at 3 Hz with a tip coated with **1**. (D) LFM image of the library described in Figure 3, after 35 scans at 3 Hz with a tip coated with **1** (24 °C, 40% relative humidity).

Figure 5C. If a similar experiment is carried out with a **2**-coated tip, qualitatively similar data are obtained, and these data can be used to deduce the relative stabilities of SAMs composed of all four molecules: **2** > **1** > **4** > **3**. Significantly, the exchange process can be accelerated or decelerated simply by controlling the scan frequency and, therefore, tip−nanostructure contact time. For example, it takes 21 scans at 4 Hz as compared with only 13 scans at 3 Hz to achieve complete exchange of 420 nm diameter nanostructures of **3** with a **2**-coated tip. The order of SAM exchange can be understood on the basis of the different types of tail groups. Compounds **1** and **2** are the most stable because they are linear alkanes and pack into crystalline lattices.[4,10] The increased stability of **2**, as compared with **1**, is likely due to the fact that **2** can undergo hydrogen bonding within the SAM, whereas **1** cannot. These two trends might be predicted on the basis of bulk solution studies of macroscopic SAM features.[10] However, the relative stabilities of SAMs formed from **3** and **4** are neither obvious nor easily extracted from literature studies. Indeed, it appears that simply replacing a methylene unit in **4** with a carbonyl group can substantially decrease the stability of the SAM structure. This is likely due to steric effects that lead to a more disordered structure and greater susceptibility to exchange.

While the method reported herein does not directly probe the mechanism of the exchange process, it does appear that exchange predominately occurs at defect sites, such as those which may be found at the periphery of the nanostructures used in this experiment. As molecules desorb from the surface into the water meniscus, they are replaced by ink molecules, which are presumably at higher concentrations due to the reservoir on the tip. In these experiments, the susceptibility to exchange is primarily determined by tail group and overall monolayer

(10) Collard, D. M.; Fox, A. M. *Langmuir* **1991**, *7*, 1192−1197.
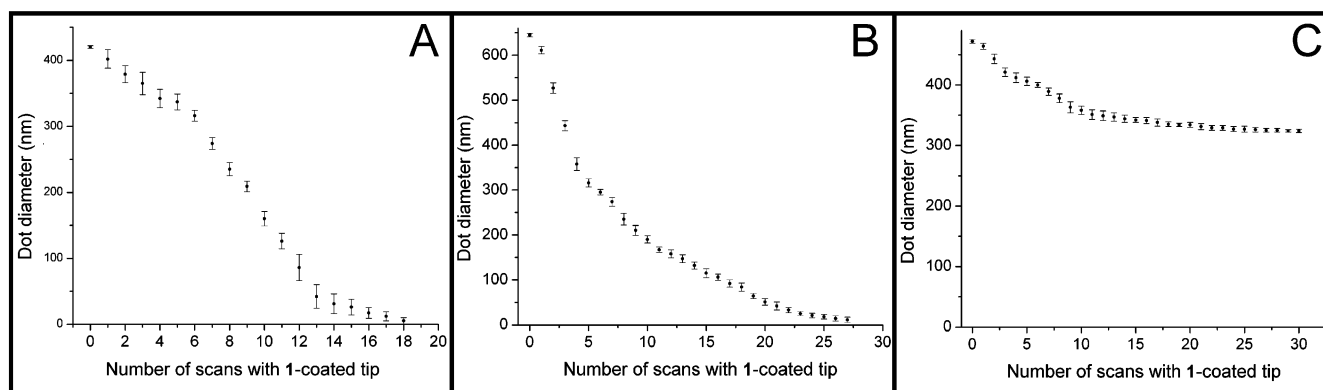
Figure 5. Plot of dot diameter as a function of number of scans at 3 Hz with a **1**-coated tip for (A) **3**, (B) **4**, and (C) **2**. The library studied is in Figure 3B. In all cases, the scan size was 5.4 μm × 5.4 μm.

structure, because the chain lengths and headgroups for the chosen molecules are similar. The results observed herein are consistent with those observed by Poirier et al., who concluded that monolayer exchange can be mediated by defects in domain boundaries in mixed monolayer systems, and also those of Marye Anne Fox and co-workers, who concluded that exchange is a dissociative rather than associative process.[10,11]

Other possible contributing factors to the exchange processes in these experiments are the contact and capillary forces. While Liu et al. have used high contact forces to promote exchange, the contact forces used in these experiments (0.5 nN) were approximately an order of magnitude lower than the ones used in their exchange experiments (5−10 nN).[12] Liu concluded that contact forces in the 5−10 nN regime are sufficient to disturb the structure of a monolayer, introducing additional defect sites in the system, thus promoting exchange with adsorbate molecules from an alkylthiol-coated tip. If the tip is facilitating exchange in these studies, it should be a fairly uniform effect, which is normalized by studying all molecules within the context of one library under identical conditions.

The capillary force may also play a role in the exchange process. An assumption implicit in the arguments made herein is that it plays a relatively minor role and is comparable from system to system. This is not necessarily the case, especially when considering monolayers of substantially different hydrophobicities. However, the area of the meniscus extends well beyond the feature sizes in these experiments.[13] Therefore, a large component of the surface being sampled is bare gold.

Exchange on Amorphous versus Single-Crystal Gold. Finally, a key question in the study of SAMs pertains to structural and stability differences as a function of substrate. For example, are SAMs on single-crystal gold substrates more stable or resistant to exchange than ones on amorphous gold? This is an issue that is difficult to address with bulk substrates using bulk solution exchange methods, because a bulk substrate that consists of a single terrace does not exist.[10,14] However, it is relatively straightforward to address this question using the approach described above. For example, one can use DPN to
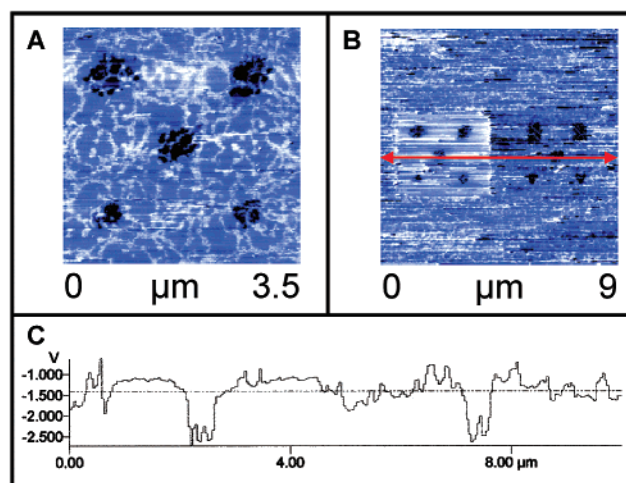

Figure 6. (A) Five dots on an Au(111)/mica substrate generated with a tip coated with **1**. (B) LFM image of two sets of the original array of dots comprised of **1**. A tip coated with **2** was scanned over the array on the left (180 times at 4 Hz, 0.5 nN contact force, 5.56 μm scan size). The array on the right side was used as a control and was never exposed to a coated tip. (C) LFM profile across the arrow marked region in part B (24 °C, 40% relative humidity).

generate an array of different diameter nanofeatures comprised of **1** on the terraces of an Au(111)/mica substrate,[15] Figure 6A. One can then raster scan across such an array with a **2**-coated tip (0.5 nN contact force, 4 Hz) and monitor the exchange process. Significantly, with such an array, very little exchange is observed after 9 h of scanning (180 times at 4 Hz, 0.5 nN contact force, 5.56 μm scan size), Figure 6B (left side). Indeed, the diameters of the dots only decrease by 12 ± 1%, and there is no appreciable change in lateral force at the center of the dots as compared with the control array, which was not exposed to the **2**-coated tip, Figure 6B (right) and C. One learns two important facts about the exchange process from these studies. First, SAMs are dramatically more stable on single-crystal substrates as compared with amorphous substrates, and, second, the exchange process on single-crystal terraces occurs primarily at the edge of a monolayer. In other words, in the case of the single-crystal substrates, the exchange process takes place almost exclusively at the perimeter of the nanostructure and moves inward, as demonstrated by the loss of contrast at the periphery of the nanostructures with little change in the central portion of the monolayer structures in the LFM images.

(11) (a) Poirier, G. *Chem. Rev.* **1997**, *97*, 1117−1127. (b) Poirier, G.; Pylant, E. D. *Science* **1996**, *272*, 1145−1148.
(12) (a) Wadu Mesthridge, K.; Song, X.; Amro, N. A.; Liu, G. Y. *Langmuir* **1999**, *15*, 8584−8589. (b) Xu, S.; Miller, S.; Laibinis, P. E.; Liu, G. Y. *Langmuir* **1999**, *15*, 7244−7251. (c) Amro, N. A.; Xu, S.; Liu, G.-y. *Langmuir* **2000**, *16*, 3006−3009.
(13) Piner, R. D.; Mirkin, C. A. *Langmuir* **1997**, *13*, 6864−6868.
(14) Creager, S. E.; Rowe, G. K. *J. Electroanal. Chem.* **1997**, *420*, 291−299.

(15) Walczak, M. M.; Popenoe, D. D.; Deinhammer, R. S.; Lamp, B. D.; Chung, C.; Porter, M. C. *Langmuir* **1991**, *7*, 2687−2693.

Conclusion

We have presented a straightforward and versatile method for generating combinatorial libraries of nanostructures and studying their exchange processes via DPN, under one set of environmental conditions. This approach allows one to study adsorbate−adsorbate exchange on the nanoscopic level in a combinatorial stepwise fashion. It provides key information regarding the kinetic stabilities of SAMs and can be generalized for a wide variety of substrates and adsorbates, thereby providing important fundamental information about SAM structures, much of which cannot be extracted from bulk methods. The limitation of the approach is that, at present, the exchange processes are studied in the water meniscus,[16] and, in principle, the tip and contact force applied can influence the exchange process. In practice, we have yet to see a dependence on contact force (with the forces used in these studies), and because all of the exchange processes are occurring with one tip on one library under the same tip−substrate contact force, the effects are spread uniformly over all of the nanofeatures, and their influence should be minimized in our analysis of relative stabilities. Efforts to extend the combinatorial approach in different environments are currently underway.

Supporting Information Available: Exchange data involving a **2**-coated tip (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0203871

(16) Although others have questioned the role of the meniscus in DPN (a), recent work has confirmed its existence and utility in a variety of patterning scenarios (b) and (c): (a) Sheehan, P. E.; Whitman, L. J. *Phys. Rev. Lett.* **2002**, *88*, 156104−156101/156104−156104. (b) Weeks, B. L.; Miller, A.; Noy, A.; De Yoreo, J. J. *Phys. Rev. Lett.* **2002**, *88*, 25505-4−255505-4. (c) Demers, L.; Ginger, D. S.; Park, S. J.; Li, Z.; Chung, S. W.; Mirkin, C. A. *Science* **2002**, *296*, 1836−1838.