A Strategy for the Chemical Synthesis of Nanostructures

Wolfgang T. Müller, David L. Klein, Thomas Lee, John Clarke, Paul L. McEuen, Peter G. Schultz*

Highly localized chemical catalysis was carried out on the surface groups of a self-assembled monolayer with a scanning probe device. With the use of a platinum-coated atomic force microscope tip, the terminal azide groups of the monolayer were catalytically hydrogenated with high spatial resolution. The newly created amino groups were then covalently modified to generate new surface structures. By varying the nature of the catalyst and the chemical composition of the surface, it may be possible to synthesize molecular assemblies not readily produced by existing microfabrication techniques.

Approaches for the chemical synthesis of nanostructures with complex molecular architectures and interconnections are still in their infancy. Molecular self-assembly provides one strategy for generating stable, structured assemblies on the nanometer scale (*1*). Another approach that offers considerable promise is the use of scanning tunneling or force microscopy to manipulate atoms and molecules on surfaces (*2*, *3*). A logical next step is to adapt the scanning probe devices to carry out highly localized nanochemistry on self-assembled monolayers (SAMs) to generate more complex structures.

Here, we report that an atomic force microscope (AFM) can be used to chemically modify the surface of a SAM in a spatially defined fashion when the AFM scanning tip is coated with a catalyst. Scanning with a platinum-coated AFM tip over a SAM surface containing terminal azide groups results in the catalytic conversion of the azide groups to amino groups (Fig. 1). The amino groups formed by this process can be selectively modified with a variety of reagents in a second step to generate more complex structures. Spatial resolution is achieved by localization of the catalyst with the scanning probe; covalent attachment of the SAM to the support maintains structural integrity. The use of a catalyst rather than an electrochemical process allows the use of a variety of scanning probe devices and surfaces, requires no potential between the tip and surface, and may significantly expand the range of surface transformations that can be explored (*4*).

The catalytic hydrogenation of azides to amines was chosen for this study. This reaction is known to have a very low activation energy and yields no by-products that could inactivate the catalytic tip (*5*). Because metal-bound hydride is likely the reactive species, catalysis is expected to occur only at those sites where the tip contacts the surface (*6*). The free amino groups generated in the catalytic reaction can be derivatized in high yield by a variety of molecules, including acids, aldehydes, and metal complexes (*7*). Both the catalytic step and subsequent chemical modification steps were carried out in solution to ensure compatibility with the largest number of possible chemistries.

Formation of the SAM with surface azide groups was achieved by means of self-assembly of 11-bromoundecyltrichlorosilane in dicyclohexyl onto glass slides and subsequent displacement of the bromide with sodium azide (*8*, *9*). To unambiguously identify the areas that had been scanned with the AFM, we used etched glass slides containing a pattern of 600 μm by 600 μm squares. For all of the AFM experiments, the samples were glued with cyanoacrylate to circular glass cover slips and mounted in a sealed liquid cell (*10*). The catalytic probe was fabricated by evaporating a 7-nm layer of platinum onto a silicon AFM tip that had been coated with an adhesion layer of chromium (3 nm) in an electron-beam evaporator (*11*). Such tips have been found to be electrically conductive, which indicates that congruent coverage of the entire AFM tip with metal has occurred (*12*). Because thin metal layers (10 nm) do not significantly change the imaging properties of the AFM cantilever (thickness ~800 nm), controlled scanning of the sample surface during catalysis was possible.

After assembly of the liquid cell with the SAM substrate and platinum-coated AFM tip, the cell was flushed with isopropanol that had been saturated with hydrogen gas. Scanning was performed at a speed of 1 μm s^{-1} and a force of ~400 nN (*13*, *14*). After scanning, the sample was removed from the liquid cell, rinsed with ethanol and water, and then covalently modified with either fluorescein-labeled, aldehyde-modified latex beads (diameter 290 Å; Molecular Probes, Eugene, Oregon) (*15*) or 3-(2-furoyl)quinoline-2-carboxaldehyde (ATTO-TAG; Molecular Probes) (*16*, *17*). The latter compound forms a highly fluorescent isoindole on reaction with primary amino groups. ATTO-TAG itself is not fluorescent but reacts with primary amines in the presence of cyanide ions to form an isoindole derivative with an excitation maximum at 486 nm and a fluorescence emission at 591 nm. Consequently, detection of a fluorescence signal demonstrates unequivocally the conversion of the surface azide groups to primary amino groups. The samples were then imaged by fluorescence microscopy with a confocal scanning laser microscope.

Conditions for derivatizing the amine surfaces with the fluorescent latex beads or the fluorogenic reagent (ATTO-TAG) were optimized to yield maximum fluorescence intensities with SAMs formed from aminopropyltriethoxysilane (*18*). Control experiments with azide surfaces showed very little nonspecific binding of the beads

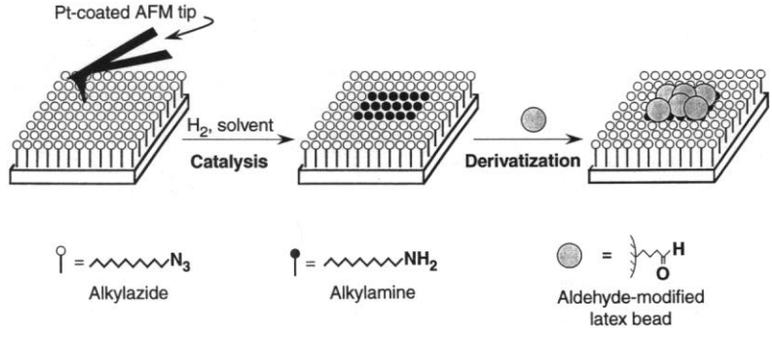

Fig. 1. Scanning with a platinum-coated AFM tip over a SAM surface containing terminal azide groups in the presence of H_2 leads to the reduction of azide groups to primary amino groups. Derivatization of the resulting amine surface with aldehyde-modified latex beads or ATTO-TAG results in specific labeling of the reduced areas.

W. T. Müller and P. G. Schultz, Department of Chemistry, University of California, Berkeley, CA 94720, USA, and Lawrence Berkeley Laboratory, Materials Sciences Division, Berkeley, CA 94720, USA.
D. L. Klein, T. Lee, J. Clarke, P. L. McEuen, Department of Physics, University of California, Berkeley, CA 94720, USA, and Lawrence Berkeley Laboratory, Materials Sciences Division, Berkeley, CA 94720, USA.
*To whom correspondence should be addressed.

and no detectable nonspecific labeling with ATTO-TAG. The fluorescence signal on these control surfaces resembled the dark current of the photomultiplier tube used for the fluorescence detection. When pure amine control surfaces were derivatized with the beads or ATTO-TAG reagent, the signal strength was more than 10 times that of the azide control surfaces.

Catalytic "imaging" was carried out by scanning of the azide-terminated SAM surface in hydrogen-saturated isopropanol with the platinum-coated AFM tip. Subsequent derivatization with fluorescent latex beads or ATTO-TAG reagent resulted in brightly fluorescent squares (Fig. 2, A and B). The structures are exactly the same size as the area scanned with the catalytic AFM tip (here, 10 μm by 10 μm). Scanning of the azide-terminated surface in hydrogen-saturated isopropanol with an untreated, fresh silicon tip or a tip coated with gold (a catalytically inactive metal) did not result in any detectable structures after derivatization with either fluorescent latex beads or ATTO-TAG reagent (Fig. 2C). A low-force scan (*19*) of the surface that was previously scanned with the platinum-coated tip during catalysis was also performed before derivatization with the beads or ATTO-TAG reagent. No differences were observed between the scanned and surrounding unscanned areas; this finding indicates that the tip did not significantly perturb the SAM (*20*).

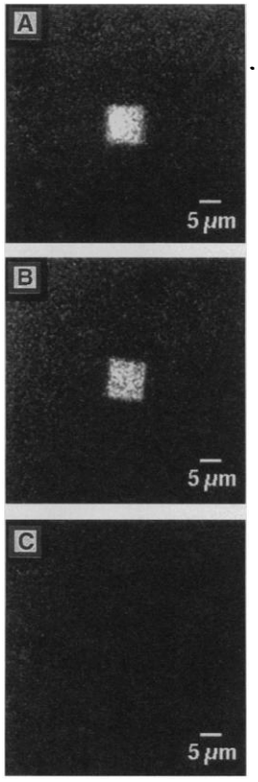

Fig. 2. Fluorescence micrographs of surface azide groups derivatized after scanning under different conditions in the AFM. (**A**) A 10 μm by 10 μm area was scanned with a platinum-coated AFM tip in hydrogen-saturated isopropanol and derivatized with fluorescent aldehyde-modified latex beads. (**B**) A 10 μm by 10 μm area scanned as in (A), but derivatized with ATTO-TAG reagent. (**C**) A 10 μm by 10 μm area scanned with a silicon AFM tip under the same conditions as in (A) and (B) and derivatized with ATTO-TAG reagent (the same picture was obtained when the surface was derivatized with aldehyde-modified latex beads).

These results indicate that during scanning with the platinum tip, the surface azide groups of the SAM are catalytically reduced to amino groups. These groups can then be covalently labeled with either fluorescent latex beads or ATTO-TAG reagent in a spatially defined fashion. To estimate the degree of hydrogenolysis of the surface azide groups in the scanned areas, we derivatized the amine and azide control surfaces as well as the catalytically reduced surfaces with ATTO-TAG reagent and quantified the fluorescence intensities. These measurements indicate that roughly 10% of the total surface azide groups are converted to amino groups by the scanning catalyst tip. Improvements in yield may result from changes in tip morphology, reaction conditions, or the nature of the surface (*21*). AFM images of surfaces derivatized with latex beads showed edges defined with 400 Å resolution for the catalytically modified areas; this observation indicates that resolution is thus far limited only by the size of the derivatization agent used (here, 400 Å). The ultimate resolution of this technique has yet to be determined.

Given the large number of heterogeneous catalytic reactions involving transition metal catalysts, the approach described above may provide a general strategy for performing chemistry on a nanometer scale. The development of such a synthetic approach should allow the defined variation of surface properties by chemical conversion of surface groups and subsequent covalent attachment of molecules to these modified surface groups (for example, interconnected metal and semiconductor quantum dot arrays). Finally, this approach may allow more detailed investigation of reaction parameters (such as reactant distance, contact times, and orientation) and other characteristics of catalytic processes.

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9. The glass slides were immersed for 4 min in a solution of 35 μl of 11-bromoundecyltrichlorosilane in 3.5 ml of dicyclohexyl. The resulting bromide surface groups were converted to azide groups by overnight stirring with 80 mg of NaN_3 in 3.5 ml of dimethylformamide. After rinsing with deionized water, ethanol, and chloroform, the samples were stored in sealed amber glass vials under nitrogen until use in the catalysis experiments.
10. The AFM was an Autoprobe CP (Park Scientific Instruments, Sunnyvale, CA).
11. The silicon AFM tips were Ultralevers (Park Scientific Instruments) with an apex radius of 100 Å.
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13. A force on the order of 400 nN has been shown to be necessary to penetrate solvation layers between a Pt-coated AFM tip and a conducting substrate so as to achieve ohmic conductivity (*12*).
14. Use of a faster scanning speed or a reduced pressure of the tip on the surface during catalysis led to a decrease in the number of reduced azide groups, as indicated by a weaker fluorescence signal after derivatization. A complete scan of a square 10 μm by 10 μm (256 lines) required 42 min; because each of these squares was scanned three times before derivatization, the complete scanning required 126 min.
15. The sample was immersed in 3 ml of morpholinoethane sulfonic acid buffer (MES; 50 mM, pH 6.5), and 30 μl of an aqueous solution of fluorescein-labeled, aldehyde-modified latex beads (2% solids in H_2O, mean diameter 29 nm; Molecular Probes) was added. The solution was mixed thoroughly and allowed to stand for 3 hours in the dark.
16. The sample was immersed in 1 ml of phosphate buffer (50 mM, pH 8.2), and 50 μl of a solution of 20 mM ATTO-TAG in methanol and 25 μl of an aqueous solution of 300 mM KCN were added. The mixture was allowed to stand for 1 hour in the dark.
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19. A force of 3 to 5 nN and a scanning speed of 1 μm s^{-1} were used.
20. Comparable forces do not visibly damage a covalently linked SAM similar to the one used here [V. V. Tsukruk, L. M. Lander, W. J. Brittain, *Langmuir* **10**, 996 (1994)].
21. The catalytically active contact area between the Pt tip and the SAM may be less than the total contact surface area. This difference in size would contribute to incomplete conversion of the entire scanned area and thus a low overall yield.

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