The Power of the Pen: Development of Massively Parallel Dip-Pen Nanolithography

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ABSTRACT If one had complete control of the architecture of a surface, in terms of composition and physical structure, one could ask and answer some of the most important scientific questions in a wide variety of fields, including surface science, catalysis, and cellular biology. Unfortunately, there are few tools that allow one to tailor surface architecture with such control, and of those that exist, such as electron- and ion-beam lithographies, most are limited in terms of the environment in which they can operate, the materials that can be patterned, cost, and throughput. Toward this end, important new scanning probe technologies have been developed that have impacted fields such as electronics, optics, and medicine.

Since the invention of the scanning tunneling microscope (STM),[1] researchers have been enthralled with the idea of transitioning this high-resolution reading tool into a surface patterning tool. Indeed, in the early days of the STM, Eigler and co-workers[2,3] showed how one could manipulate atoms on a surface to create well-defined structures, including the IBM logo made of individual Xe atoms.[2] Although an impressive feat of atomic-scale control, the technique was extremely limited, since the experiment was performed at liquid helium temperatures (4 K), had to be done in an ultrahigh vacuum, and could only be carried out on a conducting surface. With the introduction of the atomic force microscope (AFM),[4] new approaches to scanning probe surface patterning were taken, including (1) anodic oxidation, in which a surface is oxidized to generate a pattern;[5] (2) nanografting, in which a monolayer is used as a resist and the tip is used to remove the monolayer to make a pattern;[6] (3) nanoelectrochemical patterning, in which the tip is used to convert the end group of a monolayer electrochemically into some functional structure that can be subsequently chemically modified;[7] and (4) thermomechanical writing, in which a tip with a localized heater is used to thermally restructure an underlying polymer substrate.[8] Interestingly, these approaches to patterning all share one common feature in that they rely on the initial delivery of *energy* rather than molecules or materials to surfaces to make patterns. This means that they are surface destructive rather than constructive techniques. This feature limits the type of patterning one can do and presents significant complexity problems in terms of creating higher throughput techniques based upon cantilever arrays (*vide infra*).

In 1999, we reported the invention of dip-pen nanolithography (DPN),[9] which was a significant departure in strategy for using a scanning probe microscope to pattern surfaces. It was the first scanning-probe-based patterning technique in which molecules could be directly transported repeatedly from a molecule-coated tip to a surface in an additive rather than a destructive manner. With DPN, molecules that serve as inks are coated on an AFM tip and transported to the surface by engaging the tip and moving it over the surface. Inks that have an affinity for a surface are typically used, so the technique often results in one-molecule-high structures with physical architectural parameters controlled by the movement of the AFM tip. DPN also utilizes the water meniscus that naturally forms at the point-of-contact between tip and surface to help control ink transport. Indeed, today most DPN is conducted in a humidity-controlled chamber that allows one to regulate ink transport.[10]

The first structures that were formed by DPN involved alkanethiols on gold, but many combinations of inks and substrates have been developed since then (Figures 1 and 2). Inks studied to date include many types of small molecules, metal ions, nanoparticles, polymers, oligonucleotides, peptides, and proteins.[10,11] In addition to gold, substrates have included glass, quartz, silicon, germanium, and gallium arsenide.[10,11,25]

Interestingly, in 1995, others attempted to transport 1-octadecanethiol on a gold surface, but they concluded that transport does not take place.[12] The reason why the experiment did not work is unclear and could be due to the instrument setup, lack of understanding regarding the role of the meniscus and humidity on ink transport, or instrumental design and imaging con -

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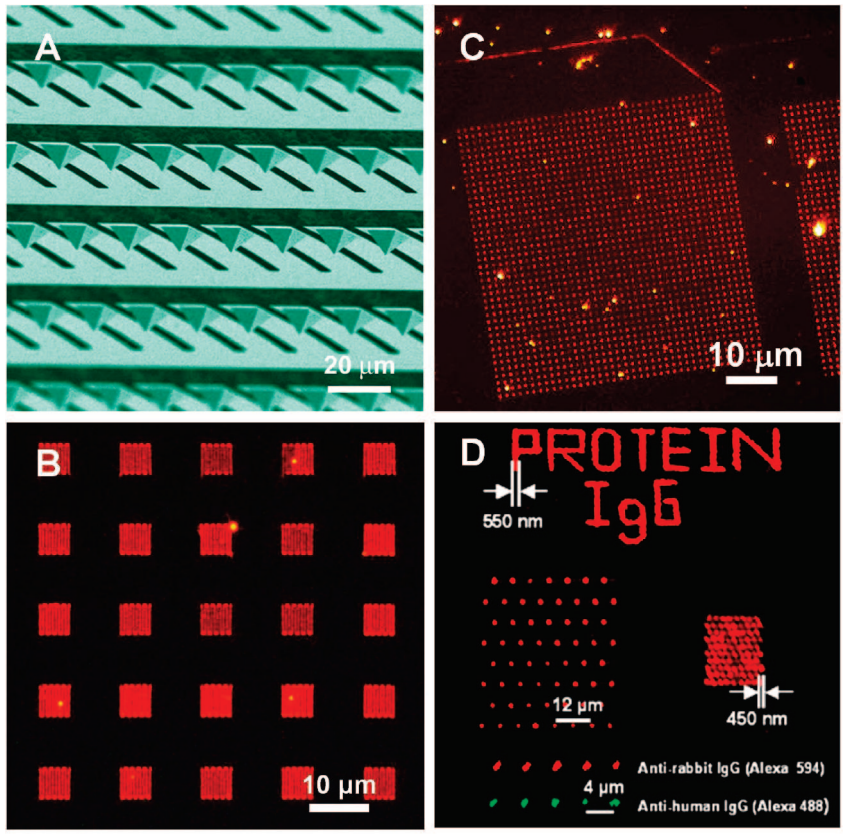

Figure 1. (A) SEM image of part of a 55,000-pen 2D array. (B) Fluorescence microscopy of 1 mol % rhodamine-labeled 1,2-dioleoyl-*sn*-glycero-3-phosphocholine. [Reproduced with permission from ref 25.] (C) Dark-field light-scattering image of gold nanoparticles hybridized to immobilized DNA patterns created by passive 26-pen arrays. (D) Fluorescence images of protein patterns generated by DPN. [Reproduced with permission from ref 26.]

straints. Regardless, this early negative result delayed the discovery, invention, and development of DPN for several years. Today, the DPN technique is used in over 20 different countries and has been transitioned into a commercial patterning tool, the NScriptor (NanoInk, Inc., Chicago, IL).[11]

One of the main challenges in the development of DPN pertains to throughput. Efforts to increase the throughput of scanning probe lithographies through the use of "multiple pen" cantilever arrays have been extensive.[13–15] However, one of the largest impediments has been that the engineering requirements and cantilever array designs intended for a given application are often intimately tied and restricted to the techniques for which they have been developed. Therefore, although impressive 50-pen linear arrays have been developed for anodic oxidation,[16] they cannot be used for DPN. Even the two-dimensional (2D) 32 × 32 probe array developed by IBM for polymer hole-making, known as the Millipede,[8] is not ideal for DPN because of the array architecture (*e.g.*, rigid cantilevers) and instrumentation requirements of the array (not a conventional AFM). Indeed, in the context of molecule-based printing, one of the major challenges in realizing a viable multiple-pen, large-area scanning probe printing technique is to maintain the soft and hard compatibility, resolution, and registration capabilities of DPN without creating a system that is prohibitively complex such that the scope of use and user base are substantially reduced due to complexity or cost barriers.

In recent years, significant advances in material-based parallel printing capabilities, in the context of a DPN experiment, have been made (Figure 1A,B and Figure 2A). In general, there are two strategies: those that involve a passive-pen array, where each pen is a duplication tool, and those that involve active arrays, where each pen in the array can be independently actuated and used to make a different nanostructure. From a device complexity standpoint, the passive-pen approach is attractive, since fabrication constraints are minimal and the array design is conceptually simple. Indeed, both linear and 2D passive arrays have been developed and are now commercially available.[17,18] These tools allow one to print molecule- and material-based structures over long distances (centimeters) or large areas (square centimeters). Effectively, what is printed at each pen is duplicated *n* times, where *n* is the number of pens in the array. Challenges in leveling have been overcome in array design and by taking into account the fact that DPN, unlike many other scanning-probe-based patterning techniques, is insensitive to tip–substrate contact force over a fairly large contact force window. Indeed, a 55,000 passive-pen array, the highest density and largest working scanning probe array ever fabricated, has been developed for DPN and allows routine patterning over large areas with sub-100 nm feature size and shape control.[17] Furthermore, it has been shown that this approach can be scaled to fabricate an array with as many as 1 million pens that occupy ~20 cm^2, although this system has not been optimized for DPN printing. Regardless, the work suggests that, in the near future, very large-area nanostructure duplication tools based upon sheets of cantilevers will be possible in the context of DPN.

This parallel DPN-based printing capability, afforded by the passive-pen approach, dispels some of the myths regarding the throughput barriers of scanning probe lithographies and makes such capabilities generally available to the nanotechnologist interested in nanofabrication, but it still does not allow one

to control surface architecture with the type of control envisioned and desired at the start of these projects. Indeed, active-pen arrays are required for ultimate patterning flexibility. Two approaches have been developed for realizing active-pen array structures. The first utilizes thermal actuation at each pen and allows one to address each tip within a linear array independently.[19] Utilizing such arrays, one can prepare many nanostructures of differing feature size and shape in a single experiment. In a proof-of-concept experiment, Bullen *et al.* showed how the digital numbers "0–9" could be written with 1-octadecanethiol-coated 10-pen arrays by moving the array in the form of a "figure 8" but only engaging each tip with the surface when it was required to write the number each was assigned to make.[19] Although the result was an impressive demonstration of the power of the active-pen array, the structures one can make thus far using this technique are far from perfect; indeed, temperature fluctuations appear to perturb the rate of transport and limit the types of inks that can be utilized. Therefore, although this demonstration stands as an important proof of concept, much work needs to be done to increase the flexibility and utility of the approach.

A second approach to active-pen arrays involves the use of electrostatic actuation at each tip.[20] This technique offers the benefit of actuation without heating the probes. It also avoids thermal cross-talk between adjacent probes and thus allows one to fabricate an array with high probe density.

Looking forward, while the future of DPN looks promising, major challenges for realizing its full potential remain. Single-pen DPN is already being evaluated as an inspection and repair tool in the context of photomasks for the electronics industry. It is one of the few techniques that allows one to locate a negative defect and to fill it. The equivalent of a nanoscale eraser has been developed that allows one to desorb molecules selectively from an imperfect molecule-based nanostructure and subsequently back-fill with the correct molecules.[21] Both the passive- and active-pen array approaches are extremely useful but for different applications. The simplicity of the passive array approach makes it attractive for making many replicas of nanostructures, which can be used to template the assembly of nanoscale building blocks (*e.g.*, carbon nanotubes,[22,23] nanoparticles, and viruses[24]) from solution or to study one class of nanostructures selectively in a statistically meaningful manner. When only a single ink is used, these passive arrays allow one to make the types of structures one can sometimes make with a stamp, but with significant advantages—each new design does not require the lengthy fabrication of a new mask or master. Essentially, one has the feature resolution afforded by an AFM with near-infinite flexibility in terms of pattern choice, with less concern about feature distortion that often accompanies the polymer-based stamping procedures used to create micro- and nanoscale features. Once strategies have been developed for independently inking each of the pens within an array, the passive arrays will be useful for building large libraries of chemically distinct structures, much in the way robotic spotters and ink-jet printing technology have opened up the field of biological microarrays (proteins and DNA). These capabilities will dramatically accelerate the ability of researchers to study important phenomena and processes in the life sciences, in-

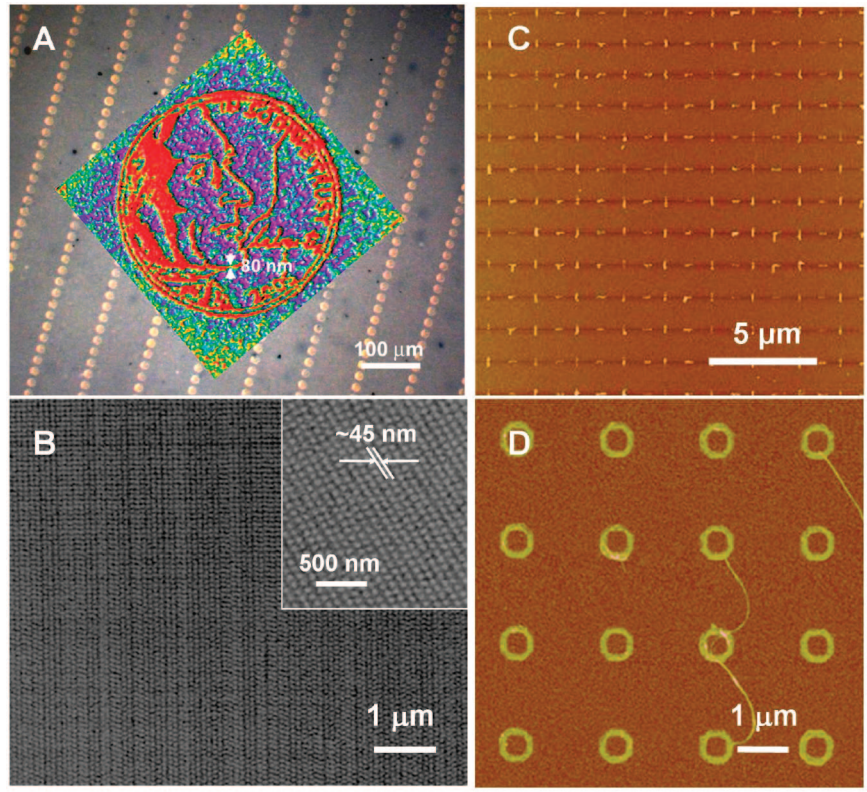

Figure 2. (A) AFM image of a miniaturized replica of the face of the five-cent coin generated by depositing 1-octadecanethiol on a gold-on-SiOx substrate followed with chemical etching. The background is an optical micrograph of a representative region of the substrate on which the approximately 55,000 duplicates were generated. [Reproduced with permission from ref 27.] (B) Silicon nanostructures by DPN patterning followed with chemical etching. [Reproduced with permission from ref 28.] (C) Tobacco mosaic virus immobilized on 16-mercaptohexadecanoic acid nanoarrays. (D) DPN-generated chemical templates as a surface manipulation tool for assembling single-walled carbon nanotubes into nanoscale rings. [Reproduced with permission from ref 29.]

It is conceivable that arrays of DNA, peptides, and sugars one day will be synthesized by DPN *in situ* using the tips of an array to deliver each of the reagents required to make a particular and desired macromolecule or nanostructure.

cluding cell–surface interactions (by using the multiple-pen DPN approach to reconstruct models of the extracellular matrix), single-particle biology (for example, feature sizes can be made so small that one can manipulate individual virus particles and perhaps, with resolution enhancement strategies, proteins[10,11]), and important issues like virus infectivity at the single-particle level.[24] In addition, by combining additional capabilities on the probe tip, such as thermal and electrostatic field control, DPN could be transformed into a "scanning probe epitaxy" tool that allows inorganic reactions to be carried out on a surface in a very localized manner. Quantum dot, nanowire, and perhaps even carbon nanotube syntheses, to name a few, are possible.

As the active-pen arrays are further developed, the complexity and sophistication of the structures one can fabricate will dramatically increase. It is conceivable that arrays of DNA, peptides, and sugars one day will be synthesized by DPN *in situ* using the tips of an array to deliver each of the reagents required to make a particular and desired macromolecule or nanostructure, much like the synthesis of DNA in a gene machine. This capability will lead to arrays of biomolecules and nanostructures with unprecedented densities and complexity. Consider the possibilities. A DNA array capable of identifying any known sequence requires 4^{17} features. With 50-μm features, this chip would be approximately the size of a tennis court and therefore impractical. With 50-nm features, it is approximately the size of a U.S. penny. A scanning-probe-based system with the flexibility and resolution to synthesize structures of the complexity of DNA would be extremely useful. It not only could dramatically decrease the cost of chip fabrication and result in a researcher-accessible technology that makes bio-array fabrication routine, it could also leap past the light-driven lithographic and ink-jet printing methods that currently are limited to micrometer-scale features and often lead to defect-ridden structures. Of course, the small feature sizes will necessitate the development of rapid reading protocols and force researchers to consider challenging issues pertaining to the reactivity of nanoscale features fabricated in this manner. Regardless, the development of such a tool will be a major step for chemists interested in learning how to control the physical and chemical architecture of a surface on a scale that opens up a myriad of possibilities on both the hard and soft matter sides of the aisle.

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