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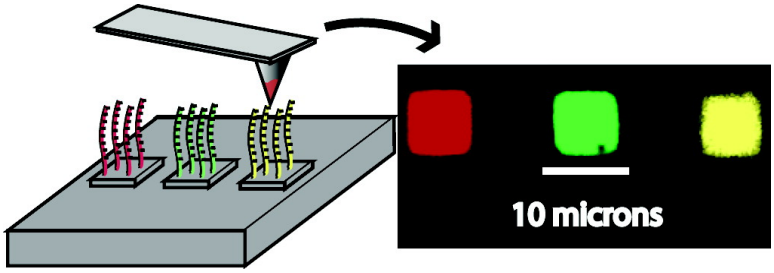


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# Single-Feature Inking and Stamping: A Versatile Approach to Molecular Patterning

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Many emerging fields of science and technology rely on precise patterning of functional molecules on surfaces. Examples include the creation of DNA and protein microarrays and other bioanalytical sensors, the formation of functional biomaterial interfaces, and the creation of molecular-scale electronics devices. A variety of patterning techniques exist that allow the patterning of substrates on the micrometer to nanometer scale, including scanning tunneling microscopy (STM),[1] dip-pen nanolithography (DPN),[2−4] microcontact printing ($\mu$CP),[5,6] photolithography,[7,8] nanopipet,[9] etc. However, patterns of arbitrary complexity remain a difficult problem. For example, the need to create patterns containing multiple components, small patterns separated by large distances, or large patterns next to small patterns motivates us to develop more versatile patterning capabilities. In this paper, we demonstrate an alternative patterning technique, which we refer to as single *f*eature *ink*ing and *s*tamping (SFINKS). Notably, SFINKS can pattern multiple components with complex structures and without cross-contamination.

SFINKS combines elements of DPN and $\mu$CP in order to generate patterns otherwise impractical to create. Figure 1 illustrates SFINKS' procedures. First, we dip an atomic force microscopy (AFM) cantilever into an "ink" solution and then deposit the ink onto a patterned elastomer stamp feature (Figure 1A). In step 2, we turn the stamp over and allow it to make conformal contact with a substrate. In the final step, the stamp is removed, leaving a patterned substrate (Figure 1B). SFINKS inks individual features on the stamp and can therefore ink multiple components on a single stamp without cross-contamination. It can also ink features tightly spaced or over large distances (2 $\mu$m to 1 cm), and it can ink both large and small features (2 to >300 $\mu$m).

As a first demonstration, we show that SFINKS can pattern multiple components in close proximity, with precision, and without cross-contamination. We inked three consecutive 8- × 8-$\mu$m square stamp features with three different 20mer probe ssDNA, identified as follows: **1**, (amino C6)-GCGATAGTAGTCTAGACAAC; **2**, (amino C6)-GGATTATTGTTAAATATTGA; and **3**, (amino C6)-ACGCAGGCTCCTCCATCACT). We then printed the DNA features onto a CodeLink glass slide (Amersham) and incubated with a solution containing the three complementary DNAs, each labeled with a different fluorphore (**1**, Cy5; **2**, Cy3; and **3**, Oregon Green). As shown in Figure 2, three distinct squares were created, and each square specifically hybridized the cDNA.

This procedure should be easily adaptable to situations requiring the patterning of many more components than demonstrated here. In addition to DNA, we have successfully patterned proteins (see Supporting Information). Our inking solution typically contains glycerol that helps to wick the ink over the pillar top when the AFM tip is brought into contact with the pillar. Therefore, unlike DPN, where excess glycerol limits the resolution of the pattern, glycerol used in SFINKS allows us to readily ink a single feature simply by bringing the tip into contact with the top of a feature.

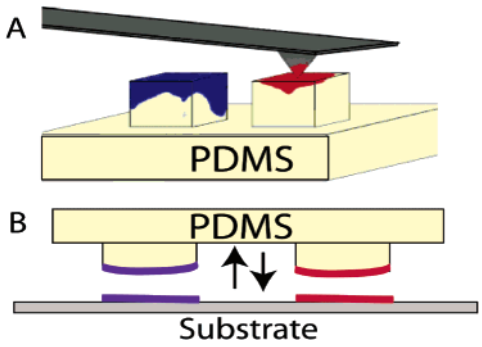


***Figure 1.*** SFINKS' procedures. (A) Inked cantilevers deposit ink to individual stamp features. (B) The stamp is turned over and printed onto a substrate. Stamps were fabricated according to standard procedures with poly(dimethylsiloxane) (PDMS). See Supporting Information.

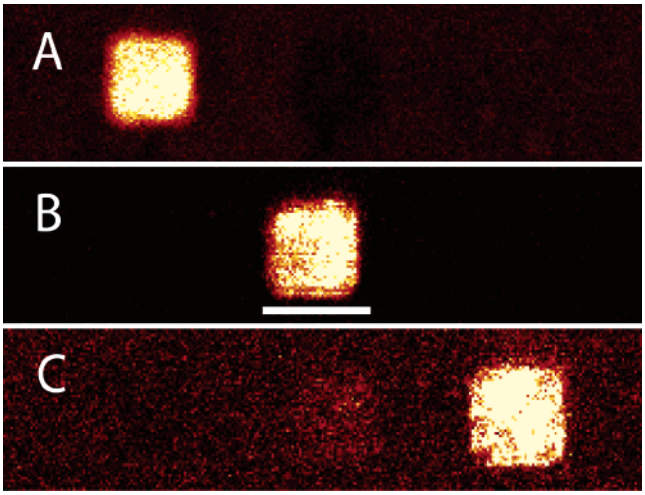


***Figure 2.*** Scanning fluorescence microscopy images of three different fluorescently labeled cDNA sequences specifically bound to their complementary probe DNA. The probe DNA was patterned with SFINKS onto a CodeLink slide. All three images correspond to scans over the same region but with different laser excitation wavelengths and detection filters that preferentially detect the fluorophores: (A) Cy5, (B) Cy3, and (C) Oregon Green. Scale bar = 10 $\mu$m. See Supporting Information.

The difference lies in the fact that the resolution of SFINKS is defined by the stamp features, and not by the deposition of the ink. We have found that patterns as large as 300 $\mu$m are easily inked with a fully dipped tip. Also, unlike DPN, because the glycerol−stamp interaction predominates, SFINKS is less tied to the tip−analyte interactions. We believe that anything soluble in glycerol can be readily inked without tip-coating procedures. Important to protein patterning, glycerol[10] is an antidesiccant, allowing us to pattern many components over several hours without loss of activity.


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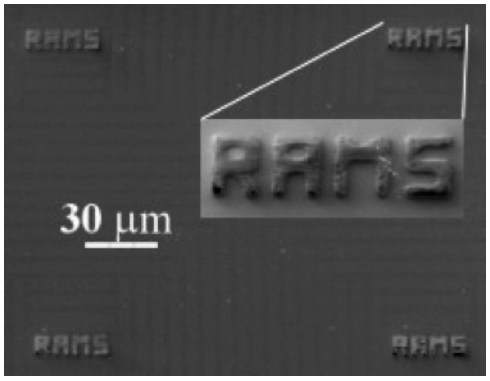


***Figure 3.*** SEM images of patterned fluorinated silane on a HF etched silicon wafer. We inked four "RAMS" features separated by 140 and 170 $\mu$m and then stamped them onto a wafer. The inset shows a higher resolution scan of a single "RAMS" consisting of 2 $\mu$m lines. See Supporting Information.

Only a few techniques can pattern multiple components at single micrometer resolution, each with drawbacks. Photolithography has been demonstrated, but it suffers from cross-contamination.[7,11,12] Nanopipet[9] is a versatile new method allowing grayscale patterning and subnanometer resolution. However, SFINKS is better suited for patterns with distinct borders, and it more readily patterns multiple components, especially when patterns differ in size. While DPN has proven to be a very versatile patterning technique, certain limitations still exist. DPN can pattern multiple components but requires either a substrate registry[2] to define relative positions or an array of cantilevers each inked with a different component.[13] The latter approach is still under development for more than two components.[14] SFINKS is advantageous because the pattern resolution and component registry are defined by the stamp features. Also, the ink deposition is straightforward. Multiple-component patterning has been demonstrated using conventional $\mu$CP.[15,16] However, only two-component patterning has been achieved at the micrometer scale.[15]

To further demonstrate SFINKS' patterning versatility, we patterned small features separated by large distances. Patterns such as these are difficult, if not impossible, to create with traditional stamping and scanning probe techniques. With stamps the structure tends to collapse.[17] Overcoming this collapse is a major limitation of the technique and an area of active research.[18] With scanning techniques, the working distance typically covers only $100 \times 100$ $\mu$m$^2$, and stages larger than that are prohibitively expensive. In a self-promoting fashion, we patterned the word "RAMS" (our school mascot) four times onto a silicon wafer with tridecafluoro-1,1,2,2-tetrahydrooctyl-1-trichlorosilane.[19] In this case, the fluorinated silane has properties similar to those of glycerol. Therefore, the ink solution consisted only of the fluorinated silane dissolved in hexane. In a manner similar to DPN, we deposited the ink by scanning the tip across the "RAMS" features. SFINKS overcomes stamp collapse because the features not inked serve as stamp support. SEM images (Figure 3) clearly reveal the four stamped patterns. The inset shows a close-up view of one of the "RAMS". For this demonstration, we chose to ink features separated by only $\sim$150 $\mu$m, but feature spacing up to centimeters is also possible. On the basis of the results of Rodgers et al.,[20] one can expect pattern resolution to be 1 $\mu$m or less over 1 cm$^2$ areas, depending on the stamp material.

These results suggest several possibilities for the future development of SFINKS. For example, the inking of multiple features is the slow step because it relies on serial operation of differently inked AFM probes. This is a problem for other forms of scanning probe lithography as well. However, it has been shown that one can create multiple stamped surfaces from a single inked stamp.[21−23] For example, Lange et al.[22] created multiple patterns of 20mer DNA from a single elastomeric stamp similar to the one described here. Furthermore, affinity contact printing ($\alpha$-CP) should be possible with SFINKS. Delamarche et al.[23,24] have demonstrated that this technique can print >10 times after a single stamp derivatization step. Therefore, after a relatively slow inking step, multiple patterns could be repeatedly created in a very quick and simple stamping step. Used in such a manner, SFINKS holds the possibility of being an extremely efficient and versatile patterning technique.

In summary, SFINKS patterns multiple components with greater versatility than existing methods. We patterned multiple components consisting of DNA or streptavidin and proved that they remain active. SFINKS will extend our abilities to create multiplexed biological arrays and molecular electronics devices.

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**Supporting Information Available:** Experimental details and control experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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