# Closed-Loop Nanopatterning of Liquids with Dip-Pen Nanolithography

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High-throughput experimentation techniques, such as microtiter plates, enable chemists and biologists to simultaneously perform thousands of experiments in an automated fashion by taking advantage of miniaturization to reduce reaction volumes and reagent quantities. While transformatively smaller than the vials used by the prior generation, the typical working volume for microtiter plates is in the range of few microliters and there are still far too many compounds to study even with this degree of miniaturization. [1]

Dip-Pen Nanolithography (DPN) could provide a path to continuing this miniaturization in fluid handling as it encompasses approaches to pattern fluids with volumes at least 10 orders of magnitude smaller than what is achievable in microtiter plates. While the patterning of such sub-fL volumes has been demonstrated with various different materials over the years, to achieve controlled and reliable experimentation with DPN, it is crucial to have precise control over the size of features and amount of fluid that is transferred in real time. Here, we enable closed-loop control over the fluid transferred using DPN by combining a novel process for quantifying the fluid on a cantilever, the utilization of a tip-less cantilever architecture, and a control strategy for adjusting writing parameters *in situ*. Specifically, we employ a two harmonic mode inertial sensing algorithm to reliably quantify the amount and location of fluid on the cantilever. Critically, sensing the mass of liquid on the cantilever before and after a fluid transfer event allows us to monitor the deposited amount with precision approaching the fL scale. This capability allows us to investigate the fundamental mechanisms and characteristics of fluid transport at this scale. Taking inspiration from experiments of fluid transfer between macroscopic parallel plates, we find that the fraction of the liquid that is transferred from the cantilever to the substrate is only a function of speed of the cantilever and surface energies of the substrates. Based on this discovery, we show that the amount of fluid that will be transferred can be predicted based on the amount of ink on the cantilever, and transferred amount can be precisely controlled by selecting writing parameters. With this insight in hand, we develop a closed-loop process for writing patterns with designed feature sizes. Given the versatility of scanning probes to characterize fluids once they are patterned, this work lays the foundation for multifunctional research systems in which chemical experiments are set up, performed, and evaluated at the nanometer scale.

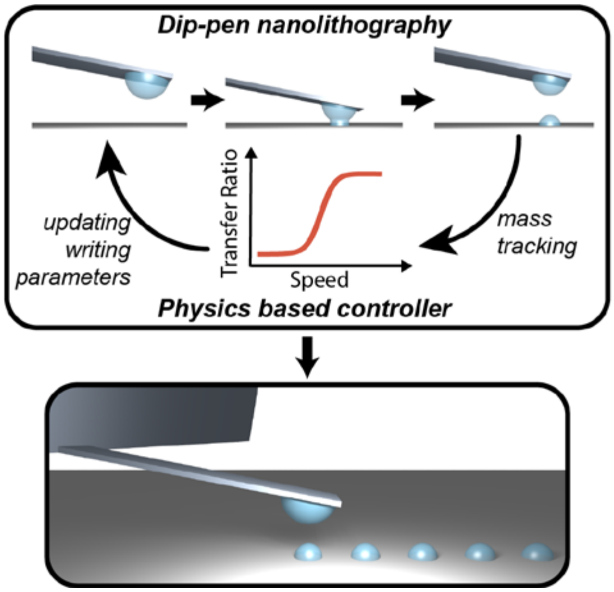


Figure 1. Schematic showing how mass tracking and a physics-based model of liquid transfer can be used together with a tipless atomic force microscope (AFM) probe to realize closed-loop dip-pen nanolithography (DPN).

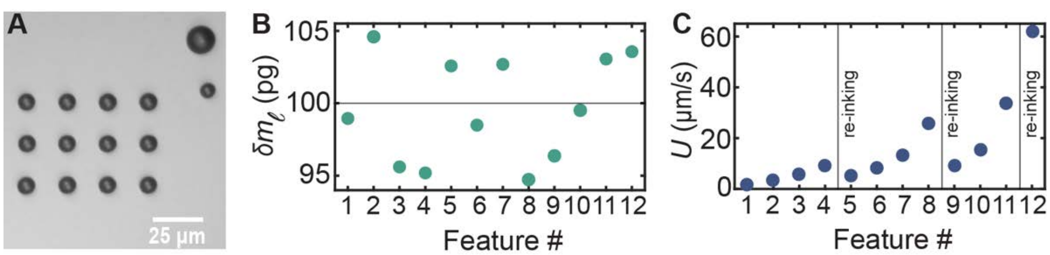


Figure 2. A grid of features with controlled masses patterned by closed-loop DPN. (A) Optical micrograph of the final pattern showing twelve written features with remaining liquid reservoirs in the top right. Features were written row-wise from the bottom right to the top left with the probe being re-inked in between features 4 and 5, between 8 and 9, and between 11 and 12. (B) Mass $\delta m_\ell$ of each feature calculated *in situ*. Here, the target feature size was 100 pg. (C) Controller-chosen withdrawal velocity ($U$) for each feature with re-inking events marked as grey lines.