# Two-Tone Molecular Printing

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***Nanopipette with two chambers produces microstructures made of biomolecules.***

The emblem of the Cambridge University, a portrait of scientist Isaac Newton, rendered in microscale as a colorful, fluorescing image: are British researchers just playing around? No, it's a "finger exercise" for serious science. For modern, miniaturized analytical and diagnostic processes, it is necessary to attach microstructures made of different biomolecules to tiny supports with high precision.

David Klenerman and his team from Cambridge University and Imperial College (London) used their miniature artwork to prove that their novel "two-tone molecular printing process" is suitable for the production of very highly resolved microstructures.

The new technique is based on the same principle as scanning probe microscopy, in which an extremely fine tip travels over a surface at a very short distance. At the heart of the new "printing" process is a glass nanopipette whose interior is divided into two chambers by a membrane. The chambers can be filled with two different solutions. Each chamber contains an electrode to which a voltage is applied. This voltage is used to adjust the distance between the pipette tip and the support to be "printed" on. When the pipette gets very close to the surface, a drop of liquid comes out of the tip, which causes a current to flow between the two electrodes—a current dependent on the distance to the surface. Such a dual pipette can operate in air, unlike other voltage-based methods, which require a liquid. Only the meniscus of the drop touches the

surface of the support. The “ink” can therefore not run, and finely resolved structures can be produced.

For their tests, the researchers used an ink made of DNA molecules containing a “glue”, a molecule that binds specifically to another protein, like a two-component adhesive. This second protein was used to coat the surface of the support to be imprinted. In addition, a fluorescent dye was attached to the DNA. The two chambers of the pipette were filled with two different DNA-dye inks, one fluorescing red, the other green. How does the pipette know which ink to dispense? By means of the voltage between the electrodes in the two chambers: one electrode is negatively charged, the other is positive. The DNA molecules are attracted to the positive electrode and are retained in the chamber; only the ink in the chamber with the negative electrode can flow out. If the other color is needed, the polarity is simply reversed. The researchers thus dab the dyes onto the support pixel by pixel. Gradations in color intensity are possible in that darker spots can get multiple drops. The yellow color in the university emblem arises when the red and green dyes are applied over one another. Because both dyes come out of the same pipette tip, the work is much more precise than is possible with multiple-pipette processes.

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