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Whole Site

Google Search

Home Biology Medicine Technology Products News Definition Dictionary Movies Links Tags Search RSS

Navigation Links

- Biology News
- Medicine News
- Biology Products
- Medicine Products
- Biology Definition
- Medicine Definition
- Biology Technology
- Medicine Technology
- Biology Dictionary
- Medicine Dictionary

Biology Navigation

- AIDS/HIV
- Bioinformatics
- Biotechnology
- Biochemistry
- Cancer
- Cell Biology
- Developmental Biology
- Ecology
- Environment
- Evolution
- Food Technology
- Gene
- Genetics
- Genomics
- Health/Medicine

Medical Navigation

- Abortion
- Aches
- ADHD
- Addiction
- Alcohol
- Allergy
- Alternative Medicine
- Alzheimer's Dementia
- Anxiety/Stress
- Arthritis
- Autism
- Bacteria
- Blood
- Bird Flu/Avian Flu
- Bones

HOME >> [BIOLOGY](#) >> [TECHNOLOGY](#) **M**

Researchers write protein nanoarrays using a fountain pen and electric fields

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EVANSTON, III. ---
 Nanotechnology offers unique opportunities to advance the life sciences by facilitating the delivery, manipulation and observation of biological materials with unprecedented resolution. The ability to pattern nanoscale arrays of biological material assists studies of genomics, proteomics and cell adhesion, and may be applied to achieve increased sensitivity in drug screening and disease detection, even when sample volumes are severely limited.

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 Unfortunately, most tools capable of patterning with such tiny resolution were developed for the silicon microelectronics industry and cannot be used for soft and relatively sensitive biomaterials such as DNA and proteins.

Now a team of researchers at Northwestern University has demonstrated the ability to rapidly write nanoscale protein arrays using a tool they call the nanofountain probe (NFP).

"The NFP works much like a fountain pen, only on a much smaller scale, and in this case, the ink is the protein solution," said Horacio Espinosa, head of the research team and professor of mechanical engineering in the McCormick School of Engineering and Applied Science at Northwestern.

The results, which will be published online the week of Oct. 13 in the *Proceedings of the National Academy of Sciences* (PNAS), include demonstrations of sub-100-nanometer protein dots and sub-200-nanometer line arrays written using the NFP at rates as high as 80 microns/second.

Each nanofountain probe chip has a set of ink reservoirs that hold the solution to be patterned. Like a fountain pen, the ink is transported to sharp writing probes through a series of microchannels and deposited on the substrate in liquid form.

"This is important for a number of reasons," said Owen Loh, a graduate student at Northwestern who co-authored the paper with fellow student Andrea Ho. "By maintaining the sensitive proteins in a liquid buffer, their biological function is less likely

Contact: Megan Fellman
fellman@northwestern.edu
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1
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Page: **1 2 3**

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Biology News
Medicine News
Biology Products
Medicine Products
Biology Definition
Medicine Definition
Biology Technology
Medicine Technology
Biology Dictionary
Medicine Dictionary

Biology Navigation
AIDS/HIV
Bioinformatics
Biotechnology
Biochemistry
Cancer
Cell Biology
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Ecology
Environment
Evolution
Food Technology
Gene
Genetics
Genomics
Health/Medicine

Medical Navigation
Abortion
Aches
ADHD
Addiction
Alcohol
Allergy
Alternative Medicine
Alzheimer's Dementia
Anxiety/Stress
Arthritis
Autism
Bacteria
Blood
Bird Flu/Avian Flu
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HOME >> [BIOLOGY](#) >> [TECHNOLOGY](#) [M](#)

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substrate, they could control the transport of protein to the substrate. Without the use of electric fields, protein deposition was relatively slow and sporadic. However, with proper electrical bias, protein dot and line arrays could be deposited at extremely high rates.

"The use of electric fields allows an additional degree of control," Espinosa said. "We were able to create dot and line arrays with a combination of speed and resolution not possible using other techniques."

Positively charged proteins can be maintained inside the fountain probe by applying a negative potential to the NFP reservoirs with respect to a substrate. Reversing the applied potential then allows protein molecules to be deposited at a desired site.

To maximize the patterning resolution and efficiency, the team relied on computational models of the deposition process. "By modeling the ink flow within the probe tip, we were able to get a sense of what conditions would yield optimal patterns," says Jee Rim, a postdoctoral researcher at Northwestern.

Espinosa collaborated closely with Neelesh Patankar, associate professor of mechanical engineering at Northwestern, and Punit Kohli, assistant professor of chemistry and biochemistry at Southern Illinois University, Carbondale.

"We are very excited by these results," said Espinosa. "This technique is very broadly applicable, and we are pursuing it on a number of fronts." These include sin

Contact: Megan Fellman
fellman@northwestern.edu
847-491-3115
[Northwestern University](#)
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1

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Page: [1](#) [2](#) [3](#)

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Biology News	
Medicine News	
Biology Products	
Medicine Products	
Biology Definition	
Medicine Definition	
Biology Technology	
Medicine Technology	
Biology Dictionary	
Medicine Dictionary	
Biology Navigation	
AIDS/HIV	
Bioinformatics	
Biotechnology	
Biochemistry	
Cancer	
Cell Biology	
Developmental Biology	
Ecology	
Environment	
Evolution	
Food Technology	
Gene	
Genetics	
Genomics	
Health/Medicine	
Medical Navigation	
Abortion	
Aches	
ADHD	
Addiction	
Alcohol	
Allergy	
Alternative Medicine	
Alzheimer's Dementia	
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Bacteria	
Blood	
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gle-cell biological studies and direct-write fabrication of large-scale arrays of nanoelectrical and nanoelectromechanical devices.

"The fact that we can batch fabricate large arrays of these fountain probes means we can directly write large numbers of features in parallel," added Espinosa. "The demonstration of rapid protein deposition rates further supports our efforts in producing a large-scale nanomanufacturing tool."

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fellman@northwestern.edu
847-491-3115
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Page: [1](#) [2](#) [3](#)

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