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# THE CNST NEWS

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## INSIDE

CONTROLLING NANOWIRE POSITION USING USING FLUID FLOW

CNST HOSTS WORKSHOP ON *IN SITU* TRANSMISSION ELECTRON MICROSCOPY

IMPROVING FLUORESCENCE-BASED MICROARRAYS FOR DISEASE DETECTION

**NIST**  
National Institute of  
Standards and Technology  
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# MARYLAND STARTUP IMPROVES FLUORESCENCE-BASED MICROARRAYS FOR DISEASE DETECTION

Working with CNST NanoFab engineers, researchers from Plasmonix, Inc., have built prototype plasmonic substrates for use in fluorescence-based microarrays. By allowing light to interact with metal nanoparticles, these plasmonic substrates increase the intensity of fluorophores (fluorescent molecules) by several orders of magnitude, improving the sensitivity of existing fluorescence-based protein microarray assays. Their device has the potential to expand the useful range of fluorescence for applications in clinical diagnostics and drug development without adding significant experimental time or operating costs.

Fluorescence is one of the most prevalent molecular and cellular detection technologies used today in medical research and clinical diagnostics (including immunology, pathology, cytogenetics, and microbiology). Protein microarrays, which allow parallel simultaneous detection of many disease-causing agents, use fluorescing molecules that are selectively bound to detection molecules in order to assess the state of a variety of diseases, including cancer.

Unfortunately, fluorescence signals are often too weak for detecting low abundance targets. This low signal strength has limited fluorescence's usefulness for onsite clinical diagnostic tests and for cost-effective drug development. The typical solution to this problem, when possible, has been to use complex molecular signal amplifiers that require additional time and cost.

Leveraging techniques developed at the University of Maryland, School of Medicine Center for Fluorescence Spectroscopy, the Plasmonix team, led by James Russo and Sean Higgins, has developed a device to enhance microarray fluorescence signals with only minimal increases in the background signal. The device consists of multilayered thin-films whose surface contains metal nanoparticles and is fabricated on a conventional glass or plastic microscope slide, allowing it to drop into existing commercial microarray systems. The top layers are plasmonic and excite fluorophores on the device's surface, while the lowest layer is photonic and carries light into the system.

Built on conventional microscope slides, the Plasmonix device is intended to work with existing commercial microarray systems. Designed and fabricated in the NanoFab, they enhance fluorescence by approximately a factor of a hundred over background signal.

When exposed to light of a certain wavelength, nanoparticles in the plasmonic layer excite localized surface plasmons (a type of electromagnetic field) which can interact with nearby fluorophores on the device's surface. The field makes the fluorophores brighter by altering the photo-physics of fluorophores. One key effect is that fluorophore lifetimes are decreased, reducing the time for undesired reactions to occur. Collectively, these effects contribute to increasing the fluorescence signal without increasing the background signal.

The system, which has been tested with a variety of standard fluorescence-based assays, enhances the fluorescence signal by a hundred-fold over the background signal, resulting in a corresponding improvement in assay sensitivity.

In June 2013, Plasmonix was chosen as the Maryland Incubator Company of the Year for Technology Transfer. Based in the bwtech@UMBC incubator, a research and technology park set up by the University of Maryland, Baltimore County, Plasmonix focuses on improving disease detection assays. The researchers credit their success in translating research ideas into a fabrication process to help from NanoFab staff members Vince Luciani and Gerard Henein. According to Jim Russo, "We started with a 'recipe' from an academic setting and ended up with a product that

is close to commercialization. It is hard to find the type of support for developing processes that we have found at NIST in any other facility." Russo explains, "having multiple instruments, including electron beam evaporators, sputtering tools, and metrology equipment, lets us develop processes and determine the right way to build our devices without having to raise millions of dollars of investor money for process development, which would be difficult."

Based on their results, Russo believes the company has developed a practical platform that lends itself to manufacturing with product costs comparable to conventional microarray slides.

Plasmonix is now working with commercial microarray technology partners to beta-test their device in typical microarray settings. They are also scaling up the process for production. They are preparing to move the fabrication to a contract manufacturing organization that can prepare the surfaces. They have also taken cost estimates for building their own facility with their own electron beam evaporator and sputtering unit, and are investigating vendors of thin-film coatings in order to increase their capacity.