Microfluidic System for Solution-Array-Based Bioassays

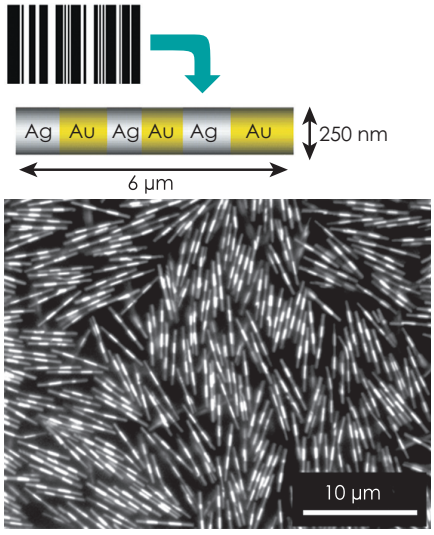

Figure 1. Optical microscope image of Nanobarcodes™ particles.

We are developing an integrated, reconfigurable microfluidic system for performing user-specified multiplexed biomarker assays for the early detection of disease-causing agents, using solution array technology. Solution arrays are similar to gene and protein chips, but use surface-functionalized particles in solution, rather than the binding of biomolecules to a fixed surface. Instead of correlating fluorescence with location, as in a chip format, the particles are encoded for identification. Results are read by examining particles for their encoded type and for the presence or absence of the fluorescence indicative of a positive binding event. The flexibility of solution arrays means that different types of functionalized particles can be added as desired by an end user, and particles for DNA, RNA, and protein detection can be used simultaneously in a single low-cost format.

The particles used in this project are Nanobarcodes™ particles (Fig. 1), short metallic nanowires that bear patterns of light and dark stripes analogous to the stripes in a supermarket barcode. These particles offer unique advantages in their ability to be identified using standard light microscopy, avoiding the need for complicated spectroscopic or flow cytometry methods. Surface functionalization of metal particles is understood, and the Nanobarcodes™ can be made with magnetic materials, opening new possibilities for manipulating, transporting, and trapping the particles using magnetic and electric fields.

Project Goals

The goal of the project is to demonstrate a prototype bioassay system based on Nanobarcodes™ particles. This system will be capable of performing simultaneous assays for several biowarfare-agent simulants. Along the way, we expect to achieve a number of important scientific goals, advancing the state of the art in particle-based biochemical assays and in the manipulation and control of metallic nanoparticles within aqueous solutions.

Relevance to LLNL Mission

Biodefense is a major research focus at LLNL, in support of technology needs for homeland security and national defense. The technology developed in this project will also benefit medical diagnosis and treatment of disease.

FY2005 Accomplishments and Results

In this final year of the project, many of the lines of research we pursued in earlier stages were completed and brought together.

The development of the multiplex immunoassay was advanced to the point that we could obtain full dose-response curves of the entire multiplex assay to different concentrations of biowarfare-agent simulants, such as *Bacillus globigii* bacterial spores (Fig. 2). These results showed that the assay itself is mature, with very low background and cross-talk.

The studies of the physical properties of the particles were completed, yielding a great deal of new information. This included measurements of the relative physical effects of several different self-assembled monolayer (SAM) coatings,

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plus the addition of coatings of antibodies and other proteins used in the immunoassay process. The Nanobarcode™ particle synthesis process was successfully modified to include ferromagnetic nickel stripes, 25 to 75 nm in length, allowing the particles to be captured and collected using magnetic fields. This important advantage of Nanobarcodes™ was further developed through studies of the rate of travel under magnetic field attraction and the evaluation of techniques for performing magnetic capture within microchannels.

This knowledge has been leveraged to develop an integrated microfluidic system for carrying out automated Nanobarcode™-based multiplexed assays, using a low-cost microfluidic card (Fig. 3).

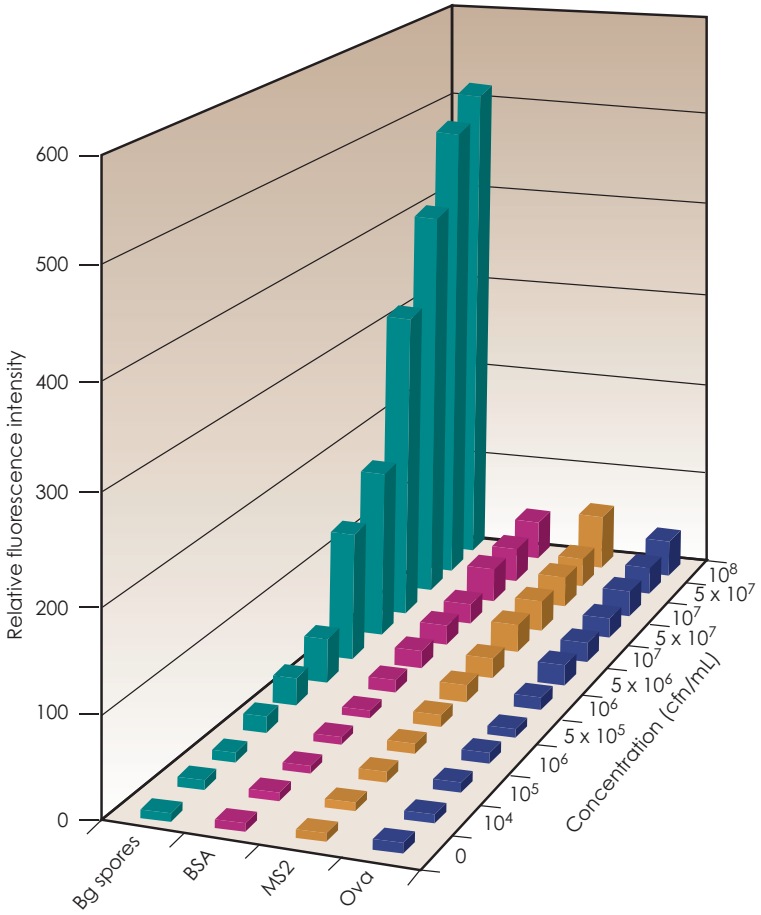

Figure 2. Nanobarcodes™-based multiplex bioassay results for a four-plex biodetection panel.

Related References

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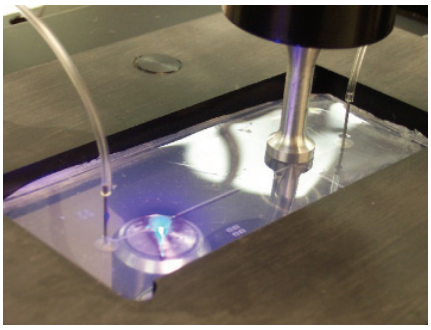

Figure 3. Microfluidic card in use. The card interfaces with the microscope, automated fluidics, an ultrasonic transducer for mixing, and a capture electromagnet with focusing cone (located beneath the card).