# Fluidic Platform for DNA Microarrays

**John M. Dzenitis**
(925) 422-6695
dzenitis2@llnl.gov

This project demonstrates a combined fluidic and imaging platform for DNA microarray experiments. This will be a new tool for biological countermeasures and sciences. The fluidic platform will enable new studies of microarray reuse directed at reducing the cost of the technique and new studies of kinetics to reduce the processing time. These are major steps on the way to new microarray applications in assays, environmental detection, and medical diagnostics. In addition, the platform itself could be a component of proposals to external sponsors for instrumentation work. The system will include the microarray flow cell (MFC), modified laser scanner, thin-film heater, and data acquisition capabilities.

Current detection approaches using DNA methods have good utility in predictive value, but the number of sequence signatures or probes that can be evaluated in practice is very limited. This is due to the fact that the material and labor costs per test are high, and the number of probes evaluated per test is low. For example, real-time PCR using TaqMan can assess up to four probes in a test; this approach is limited to testing for a specific agent. In an improvement, new suspension arrays can use 100 to 500 probes per test; this approach enables testing for a panel of known, fixed threat agent signatures. This approach is used on LLNL's Autonomous Pathogen Detection System.

The next stage of molecular diagnostics for biological threats is to look much more broadly for emerging threat biosignatures, such as virulence elements or natural and engineered mutations.

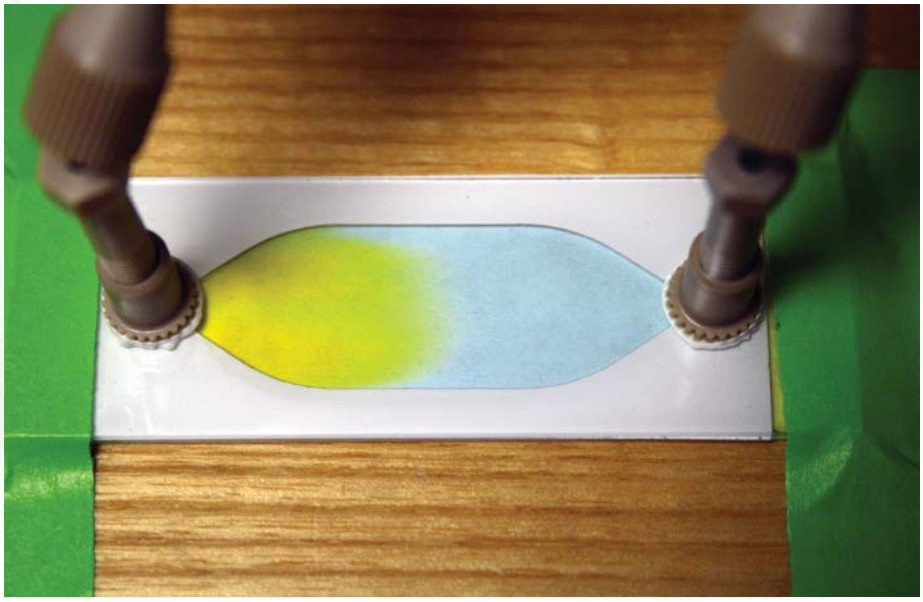

**Figure 1.** Dye visualization experiment testing liquid exchanges in the MFC.

This capability is targeted against new natural pandemics and engineered biological warfare agents to enable prompt countermeasures. High-density DNA microarrays have the capability to provide this broad type of search, using on the order of over 100,000 to 1,000,000 probes, depending on the platform. A group at the Naval Research Laboratory used high-density, short-probe microarrays to identify genetic variations of influenza viruses in clinical samples. A group at LLNL used high-density, long-probe microarrays to identify virulence elements in spiked environmental samples.

## Project Goals

The goal of this effort is to demonstrate a combined fluidic and imaging platform for DNA microarray experiments.

## Relevance to LLNL Mission

This project will be of great use to LLNL in its global security mission and ongoing efforts in detection methods against biological terrorism by providing the micro-fluidic "backbone" for these efforts.

## FY2008 Accomplishments and Results

The implementation of the MFC, thin-film heater, and modified scanning platform was completed. The next step is to characterize the system and use it for experiments directed at reducing the cost and processing time of the technique.

Our results, illustrated in Figs. 1 and 2, include the following:

1. fabrication and assembly of a MFC;
2. modification of commercial (GenePix) microarray reader optics, stage, and housing to accommodate the MFC;
3. assembly, programming, and validation of fluidics test bed;
4. demonstration of fluidic control with fully assembled MFC system;
5. fabrication and characterization of a flexible polyimide heater with integrated heat spreader; and
6. performance of initial visualization experiments of a typical test microarray in the MFC.

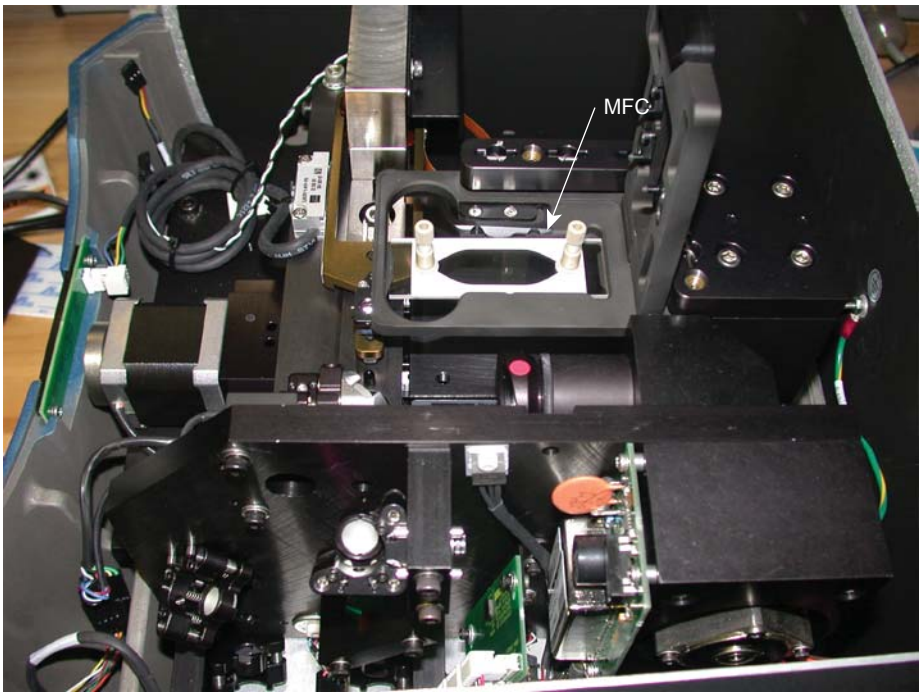


**Figure 2.** MFC integrated into a modified microarray laser scanner during a fit check.

## Related References

1. Jaing, C., S. Gardner, K. McLoughlin, N. Mulakken, M. Alegria-Hartman, P. Banda, P. Williams, P. Gu, M. Wagner, C. Manohar, and T. Slezak, "A Functional Gene Array for Detection of Bacterial Virulence Elements," *PLoS ONE*, **3**, 5, p. 2163, 2008.

2. Wang, Z., L. T. Daum, G. J. Vora, D. Metzgar, E. A. Walter, L. C. Canas, A. P. Malanoski, B. Lin, and D. A. Stenger, "Identifying Influenza Viruses with Resequencing Microarrays," *Emerging Infectious Diseases*, **12**, 4, pp. 638–646, 2008.

3. Regan, J. F., A. J. Makarewicz, B. J. Hindson, T. R. Metz, D. M. Gutierrez, T. H. Corzett, D. R. Hadley, R. C. Mahnke, B. D. Henderer, J. W. Breneman, IV, T. H. Weisgraber, and J. M. Dzenitis, "Environmental Monitoring for Biological Threat Agents Using the Autonomous Pathogen Detection System with Multiplexed Polymerase Chain Reaction," *Anal. Chem.*, **80**, 19, pp. 7422–7429, 2008.