DDF annual report

Title of Investigation:

A Micro-fabricated Hematology Analyzer

Principal Investigator:

Dr. Brian G Jamieson (Code 553)

Other In-house Members of Team:

Barney Lynch (Code 553) and Steve Cagiano (Code 699)

Other External Collaborators:

Dr. Bradley Layton and Ms. Stephanie Sullivan (Drexel University)

Initiation Year:

FY 2005

Aggregate Amount of Funding Authorized in FY 2004 and Earlier Years:

None

Funding Authorized for FY 2005:

$60,000

Actual or Expected Expenditure of FY 2005 Funding:

In-house, $40,000; Contracts, $20,000 (Drexel University)

Status of Investigation at End of FY 2005:

To be continued in FY 2006 with an additional $30,000 in FY 2006 DDF funding.

Expected Completion Date:

September 2006

Purpose of Investigation:

The ability to monitor astronaut health is critical for successful long-term human space exploration. The complete blood count (CBC) is a routine medical test that counts red blood cells, white blood cells and platelets, as well as various cell subtypes in a sample. The CBC is performed in a

clinical laboratory using a hematology analyzer, a piece of equipment that currently is unsuitable for spaceflight due to its large size and power consumption. The goal of our research is to develop a very small, accurate, and easy-to-use analysis chip that would provide a CBC for astronauts on long-duration space flights. We are developing this chip using standard semiconductor micro-fabrication methods that are available in-house at the Goddard Space Flight Center (GSFC).

Accomplishments to Date:

We have developed a repeatable and controllable process for fabricating the desired micron-scale silicon filters (Figure 1).

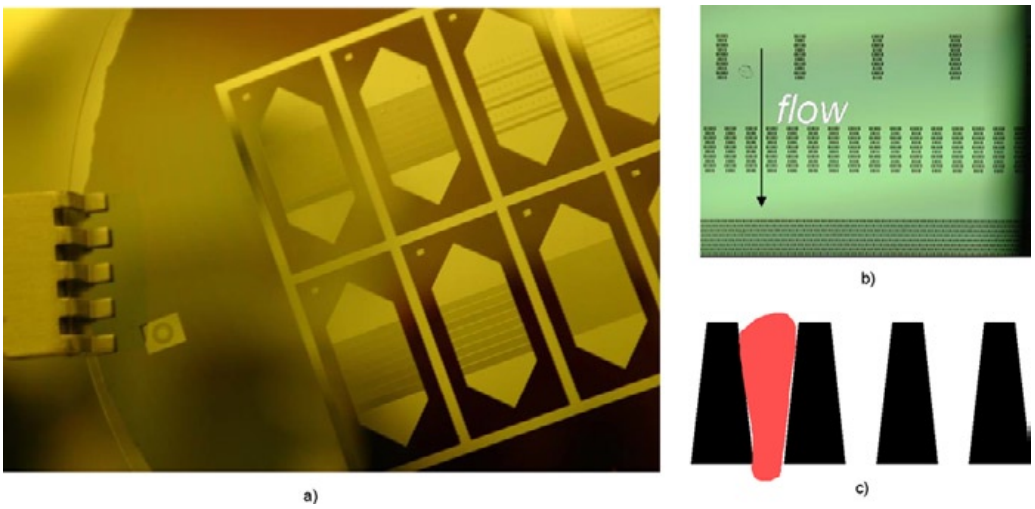

Figure 1. Photograph of four-inch silicon and Pyrex wafer containing 10 fabricated devices (a). Details of a single trapezoidal filter bed are shown in (b), with a schematic illustration of the red blood cell trapping principle (c)

We have tested these devices using calibrated polystyrene microspheres that are between 3 to 12 microns wide. We also have demonstrated differential trapping by size in the differently sized filter regions.

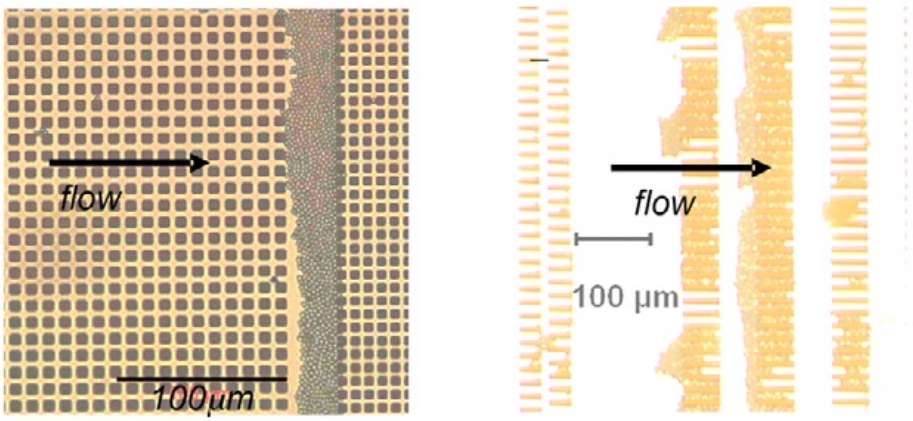

Figure 2. Two regions of 6-micron filter beds (square, at left and trapezoidal at right) illustrating trapping of calibrated polystyrene microspheres

We have worked out key parameters for the successful operation of the device, such as flow rates and dilutions, and have developed a method for connecting devices under test to an external, commercially available syringe pump. We also have tested a device with whole blood, and have observed red blood cells trapping in the filter beds (Figure 3). Work to quantify the degree of differential trapping (i.e. differences in trapping probability with size) is in progress. With computer and mathematical modeling, we have made progress on developing an approach to cell counting with electrical impedance methods.

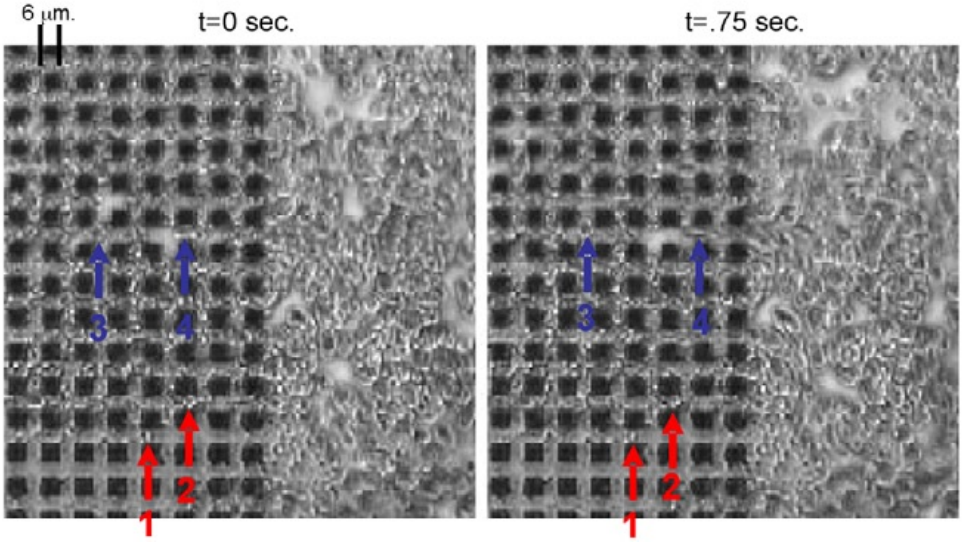

Figure 3. Images with .75-second elapsed time (left to right), showing red blood cells (RBCs) flowing through the device. Red arrows mark location of putative wedged RBCs (1&2), which have not moved between first and second frame. Blue arrows follow RBCs as they travel vertically (3) and horizontally (4) through filter bed.

Journal Articles:

Layton, B.E., Sullivan, S.M., Gadia, V., Singh, R., Koluch, N., Jones, D., Galas, J.P., Yang, C. Jamieson, B.G., "A Space-Based Electrical Impedance Hematology Analyzer," in preparation for *Lab on a Chip.*

Conference Presentations:

Layton, B.E., Jamieson, B.J., Sullivan, S.M. 2005. "A Micro-Fabricated Electrical-Impedance-Based In-Flight Hematology Analyzer," 3rd Annual Conference on Microchannels and Minichannels. June 13–15, Toronto, Canada.

Sullivan, S.M., Layton, B.E., Jamieson, B.G. Velasquez, J. 2005. "A Micro-Fabricated Electrical-Impedance-Based In-Flight Hematology Analyzer," BMES Fall Meeting, Baltimore, MD, September 29, 2005.

Layton, B.E., Sullivan, S.M., Jamieson, B.G., 2005. "A Micro-Fabricated Electrical-Impedance-Based In-Flight Hematology Analyzer,"ASME International Mechanical Engineering Congress and Exposition, Orlando, FL, November 5–11, 2005.

Planned Future Work:

We currently are working to integrate parallel plate capacitors into the filter devices to test the concept of cell counting with electrical impedance. We are working to improve the resolution of our captured images to quantify the degree of red blood cell sorting by size. We also plan to explore platelet and white blood cell trapping with whole blood samples. As a result of observations made during our investigations so far, we are exploring a second strategy for cell sorting by size. This approach utilizes boundary effects in the regions between filters to partially "pre-sort" the cells before entering the filter regions. This may be a method of decreasing the analysis time or it may be a valuable tool for cell-size sorting in its own right.

Key Points Summary:

Project's innovative features: This research has the potential for producing an inexpensive and autonomous method for performing a complete blood count (CBC) in the space environment. Our basic approach is "sort and count," meaning that we use a series of successively finer filter beds to separate blood cells by size. A series of parallel plate capacitors then "counts" the number of cells in each size bin. Using this information it is possible to derive most of the key CBC parameters. Our approach dodges many of the pitfalls of competitive approaches, such as the large lasers of optical discrimination and high rate of reagent use in Coulter counting. We know of no other commercial or private research group attempting a similar approach.

Potential payoff to Goddard/NASA: A miniature, disposable hematology analyzer will significantly advance the state-of-the-art in autonomous medical care for human spaceflight, in support of the President's Exploration Initiative. More generally, this work will allow Goddard to develop expertise in the area of lab-on-a-chip technology. These techniques have potential applications anywhere that portable chemistry is needed. Two examples include astrobiology or *in situ* resource characterization.

The criteria for success: This is a challenging problem and will not be solved in its entirety under the DDF program or any other research program. Our goal is to demonstrate the basic working principles of the approach. In particular, our goal is to develop a device that will demonstrate the ability to:

1. Sort blood cell types (i.e. red blood cells, white blood cells, and platelets)
2. Sort red blood cells by size
3. Count cells (to within 10s of cells) based on an electrical impedance measurement

If we are able to meet these goals, we believe that the next step should be to identify a viable commercial partner to help us develop a device that meets NASA's long-term needs.

Technical risk factors: Other groups have proposed and developed miniature hematology analyzer chips. However, we believe that we are the first to mechanically sort cells by size, and then count them with an electrical impedance-based method. As with any novel research approach, the technical risk lies in the need to demonstrate that the underlying principles are feasible and practical. On the sorting end of things, our main technical challenge is to show that the filter will select cells by size and not just by mechanical compliance. For the impedance-based read-out, the main challenge is to achieve sufficient sensitivity in a very noisy environment.