

Lab-on-a-Chip Application: Tumor Cell Immunocapture on a Microfluidic Device with Automated Sample Loading

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The manipulation of biological samples for diagnostic purposes requires reproducibility and simplicity to be useful in practice. As microfluidic devices transition towards use in medical diagnostics, traditional handheld syringe pumps can be too bulky and laborious for medical procedures that require quick turnaround times. Here, we discuss the evaluation of a portable breadboard platform that includes a microfluidic device for detection of prostate cancer through cell capture technology. The breadboard platform from LabSmith included uProcess™ software, an SPS01 miniaturized programmable syringe pump and CapTite™ manual valve and connectors. In addition to comparable performance, the LabSmith pump, valve, and connectors allow for accurate and automated sample loading, a valuable feature in clinical settings. The LabSmith pump and related components can also be mounted on to the LabSmith breadboard, creating a stable diagnostic system in any desired orientation. These features make the LabSmith miniaturized pump an effective and convenient addition to any microfluidic device in both experimental and clinical settings.

INTRODUCTION

Microfluidic devices are a promising approach for efficiently diagnosing complex diseases such as metastatic cancer, which can be difficult to detect at early stages. Cell capture technologies with demonstrated efficacy in isolating circulating tumor cells (CTCs)¹⁻² are based on binding specific proteins that are expressed on CTCs in the blood. The microfluidic platform contains an array of posts functionalized with antibodies specific to the proteins on the circulating tumor cells, selectively binding and enriching these rare populations while maximizing interactions with particles the size of CTCs (15-25 μm diameter). Subsequently, the immunocaptured target cells can be analyzed. One system utilizing the specifically optimized GEDI (Geometrically Enhanced Differential Immunocapture) chip was able to capture 85% of the model prostate CTCs that were flowed through the device²⁻³, a promising result for the future of cancer diagnostics (Figure 1).

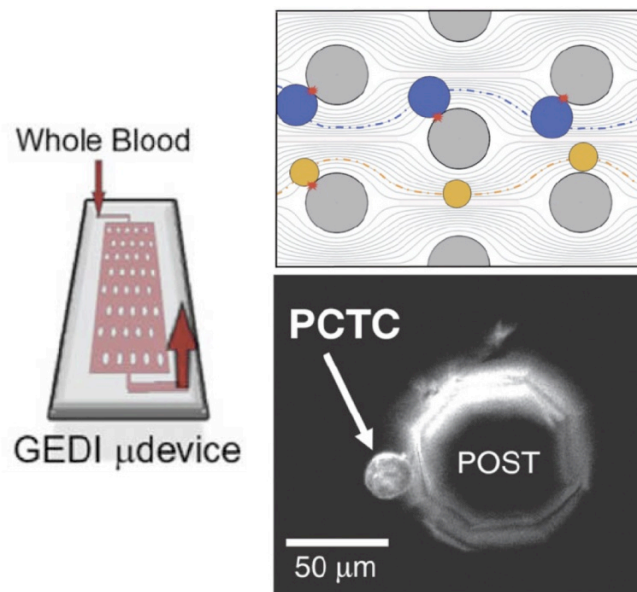


Figure 1. The GEDI μdevice design selectively binds circulating tumor cells. Left, a depiction of the blood sample containing circulating tumor cells flowing through the GEDI chip. Top right, the strategic placement of the antibody-coated posts increases the number of collisions with larger cells (blue) while smaller cells (yellow) are more likely to flow through without binding. Bottom right, a prostate circulating tumor cell (PCTC) shown bound through immunoaffinity to a post on the GEDI chip. Images adapted from Gleghorn et al. and Kirby et al.

The success of the GEDI chip in capturing CTCs in the laboratory provided a strong basis to improve upon as the technology moved towards a clinical setting. One roadblock to this transition was the lack of a reliably reproducible method for loading the biological samples on to the microfluidic chips. In the laboratory studies, sample loading was performed using manually loaded syringe pumps. While standard syringe pumps are suitable for lab settings, they are labor-intensive and bulky, making them less desirable for clinics that require results rapidly and with minimal manipulation.

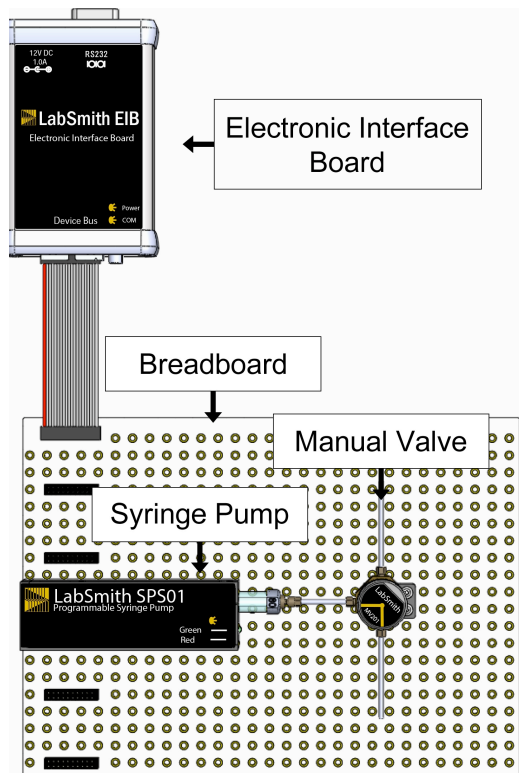
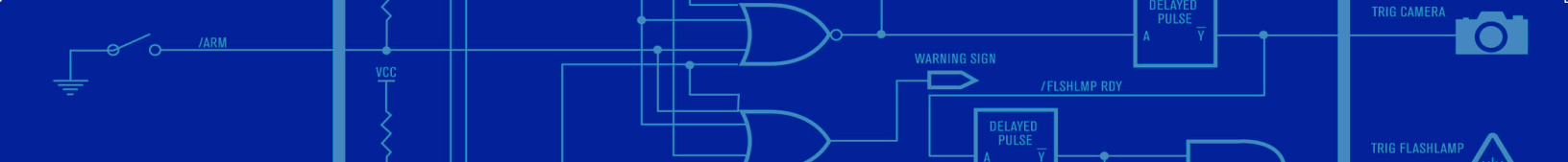


Figure 2. LabSmith programmable syringe pump with automated valve attached to the LabSmith uProcess breadboard.

To achieve these goals, we have turned to the LabSmith [uProcess™](#) programmable [SPS01 syringe pump](#) breadboardable system to efficiently automate and package the sample loading process and simultaneously decrease the opportunity for human error (Figure 2). The zero dead volume [CapTite™ manual valves](#), with all wettable components identical to the automated valve, was used for testing. The goal of these tests was to determine if any component reduced capture efficiency. No blood samples were used for this testing. Model prostate cancer cells were seeded in PBS and cells were counted while on the GEDI chip.

EXPERIMENT AND RESULTS

The LabSmith [SPS01 syringe pump](#) provides the automation desired for use in a clinical setting. Its bidirectional capability, facilitated by an automatable valve and [uProcess™ software](#) allows for programmed withdrawal of the sample from a collection tube and subsequent delivery on to the analysis chip. The rates of both sample withdrawal and sample loading can be programmed separately to optimize both loading and run times. The pump is compatible with different

syringe volumes to optimize the flow rate of biological samples, which are often sensitive to cell shearing. Furthermore, due to the upright position of the experiment, the secure attachment of the LabSmith miniaturized syringe pump and valve to the LabSmith [uProcess™ breadboard](#) increases the stability of the sample flow and allows for reliable sample loading and analysis (Figure 3).

In head-to-head comparisons, the diagnostic GEDI system performs at comparable levels when using either a standard syringe pump or an optimized LabSmith miniaturized pump system. The capture efficiency, defined as the percentage of cells captured on the GEDI chip from the total number of cells seeded, was statistically indistinguishable between the two pumps (Figure 3). When the LabSmith pump was used in combination with flexible tubing that reduced cell shearing, cell viability also remained comparable to standard syringe pump system. The data further verifies that there is no loss in capture efficiency or cell viability with the inclusion of the valve component. These results confirm that the LabSmith [uProcess™](#) software, automated [SPS01 syringe pump](#), [CapTite™ fittings](#), breadboard and valve create a suitable automatable platform for biological sample loading. Combined with its ease of use, the LabSmith pump, valve, breadboard and connectors will be an advantageous component to include in current and future microfluidic diagnostic devices.

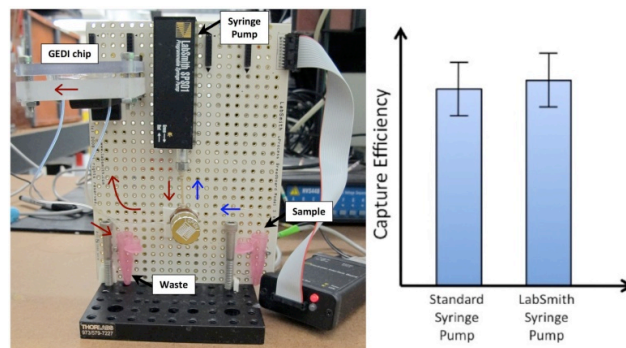


Figure 3. Setup of LabSmith [uProcess™](#) and [CapTite™](#) components delivering sample to the GEDI chip. Blue arrows, sample flow during withdrawal phase. Green arrows, sample loading on to GEDI chip. Right, capture efficiency of the GEDI chip when used with a standard syringe pump or the LabSmith [uProcess](#) syringe pump.

REFERENCES

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