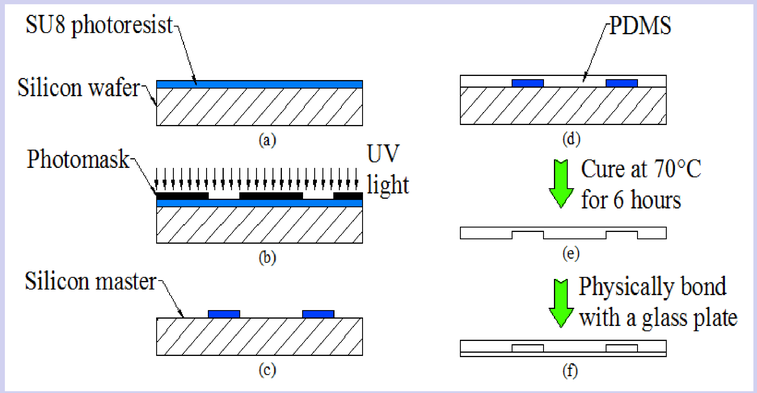
Interaction of Cancer Cells with Microposts in a Microfluidic Device Immobilized with Aptamers

Kangfu Chen[a], Teodor Georgiev[a] , Z. Hugh Fan[a, b, c]
[a]Department of Mechanical & Aerospace Engineering, [b]Pruitt Family Department of Biomedical Engineering, [c]Department of Chemistry
P.O. Box 116250, University of Florida (UF), Gainesville, FL 32611, USA

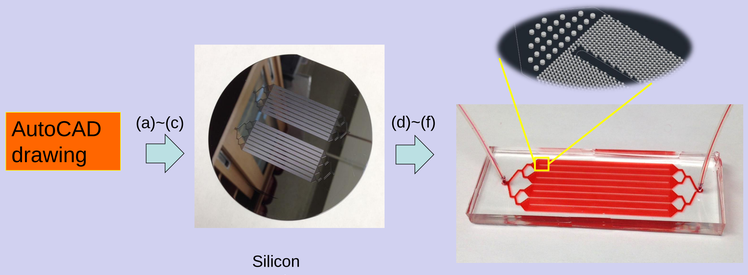
Introduction

- Circulating Tumor Cells(CTCs)
  - Cells shed from primary tumors and enter the bloodstream [1].
  - Extremely rare, comprising only a few cells out of over 10^9 hematological cells in 1 mL of blood [2].
  - Has great potential for studies of cancer metastasis [3].
- Aptamers
  - Single stranded DNA or RNA molecules that can specifically bind to target cells by folding into unique secondary or tertiary structures.
  - Can be generated using an in vitro selection process termed cell-SELEX (systematic evolution of ligands by exponential enrichment)[4].
- Advantages of Microfluidc Devices for CTC isolation
  - High CTC detection sensitivity and spatial resolution with moderate blood sample consumption [3].
  - Integrated reference system with little human intervention [5].
  - Lower examination cost, potential for disposable devices and increased portability [6].
- Objectives
  - Cancer cells capture efficiency in micropost-based devices.
  - Captured cells distribution around the microposts.
  - Simulation of the flow field in the microchannel.
  - Simulation of the interaction between cancers and aptamer functionalized microfluidic device.

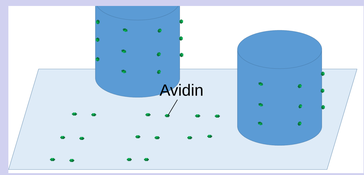
Fabrication of Microfluidic devices



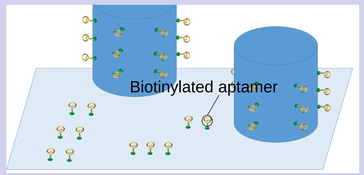
(a)~(c) Fabrication of a silicon master through photolithography; (d)~(e) Polydimethylsiloxane (PDMS) substrate with micropost array using soft-lithography; (f) The PDMS substrate bonded with a glass plate and form a micropost-based device



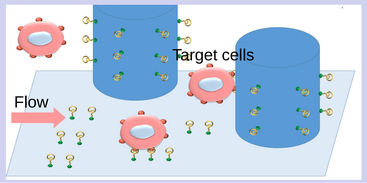
Surface Modification and Operation



Avidin immobilized on the surfaces through physical adsorption

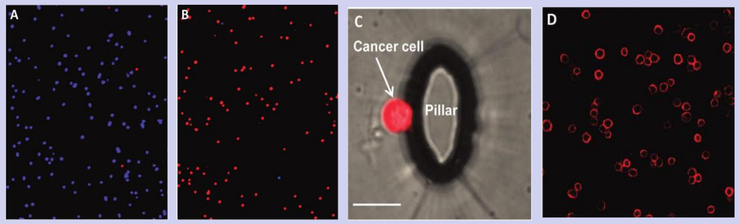


Biotinylated aptamers conjugate with avidins on surfaces



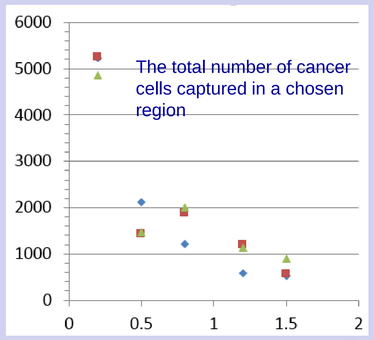
Captured target cancer cells due to the interaction between the aptamers and the receptors on cell surfaces

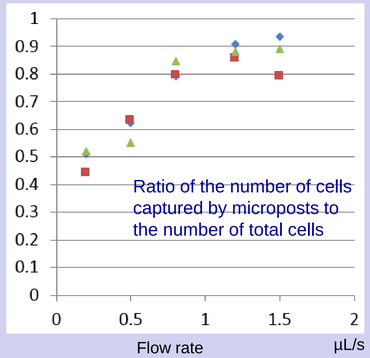
Experimental Result

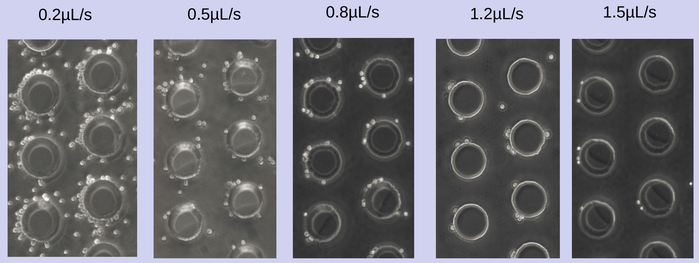


(a) Cell sample containing target cells and control cells before being infused into the microfluidic device; (b) Cells captured and enriched in the microfluidic device; (c) A cancer cell captured around a micropost; (d) Cancer cells detected using fluorescently labeled aptamers [7]

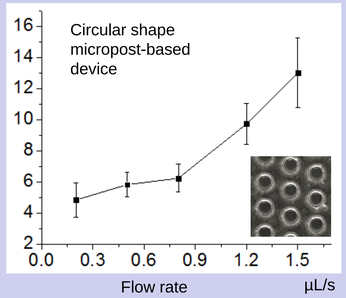
Effects of Flow Rate

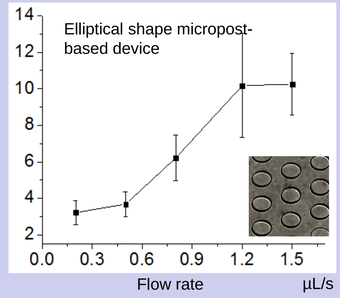






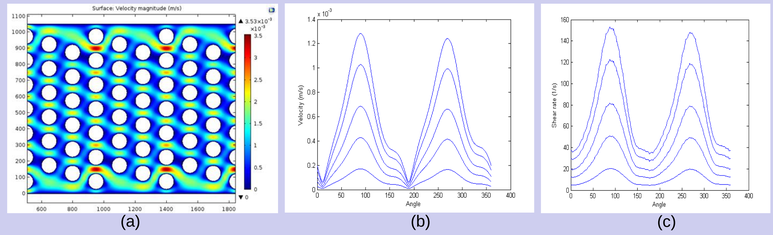
Distribution of Captured Cells Around Microposts



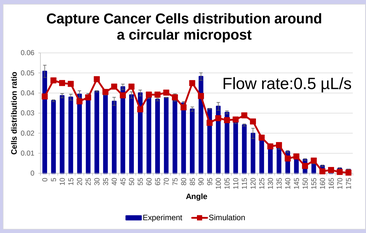


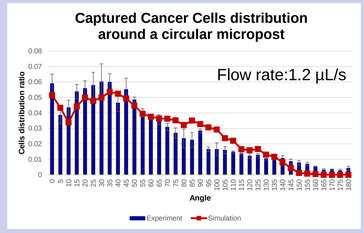
The figures above ratio of the number of cancer cells captured around the front half of microposts and the number of cancer cells captured around the back half of microposts.

Simulation Result



The figures above give the simulation result of fluid environment in the microchannel: (a) describes the velocity field in the microchannel; (b) shows the velocity distribution around a micropost; (c) shows the shear rate distribution around a micropost.





The figures above show the comparison of experimental results and simulation results: (a) Captured cancer cells distribution around a circular micropost at an infused flow rate of 0.5 μL/s; (b) Captured cancer cells distribution around a circular micropost at an infused flow rate of 1.2 μL/s.

Conclusions

- Micropost-based devices show high efficiency for cancer cells isolation, mainly due to momentum interception.
- For individual micropost in the device, cell capture efficiency in the back half is more sensitive to a higher flow rate regarding cancer cell capture.

Acknowledgement

This work is supported by National Institute of Health (K25CA149080), National Science Foundation (OISE-0968313), and UF.

Reference

[1] Fidler, I. J. Nat. Rev. Cancer 2003, 3, 453
[2] Yu, M., et al Haber, D. A. J. Cell Biol. 2011, 192, 373.
[3] Nagrath, S, et al., Nature 2007, 450, 1235.
[4] Tuerk, C.; Gold, L. Science 1990, 249, 505.
[5] Bhagat, A., et al., BME& Computing, 2010. **48**(10): p. 999-1014.
[6] Stott, S.L., et al. PNAS, 2010. **107**(43): p. 18392-18397.
[7] Sheng, Weian, et al. *Analytical chemistry* 84.9 (2012): 4199-4206.