

VIRAL SEPARATIONS USING A MICROFABRICATED ELECTRICAL SPLIT SYSTEM

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Abstract

This paper reports the use of a microfabricated electrical split-flow lateral-transport thin separation cell for the separation of tobacco mosaic virus from contaminants. Basic theory and function of the system is presented.

Keywords: Viral separations, sample preparation, process monitoring, SPLITT

1. Introduction

Several research groups are working on the development of instruments that could quickly identify and sort biowarfare agents and other environmental samples, but the major limitation of almost all the systems is that they need a prepared sample before any kind of analysis can be performed to reach a definite conclusion. The microfabricated SPLITT (split-flow lateral-transport thin separation cell) system presented in this paper has this capability and has distinct advantages over similar systems including the fact that it does not need any kind of prepared sample and most importantly works in a continuous mode (critical for detection of biowarfare agents and environmental hazards). Because of the systems ability to function continuously, it also has potential in process monitoring, especially of bioreactors and nanoparticle (colloid)

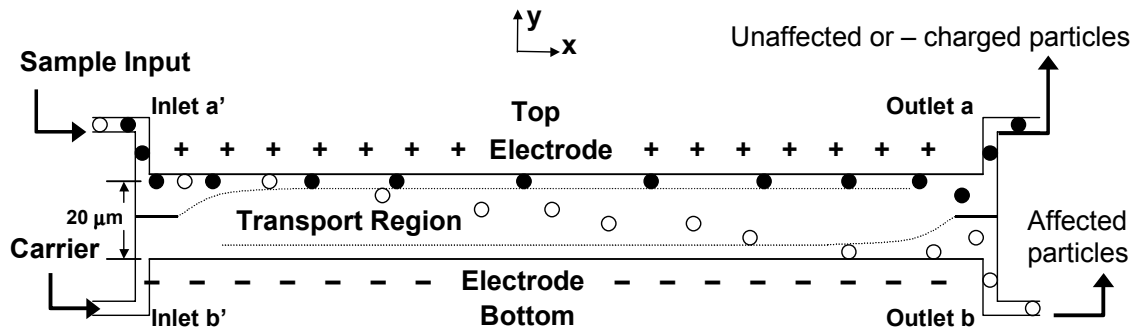


Figure 1. Diagram of electrical SPLITT cell showing transport of particles across the small dimension of the channel due to the effect of the electric field. Uncharged, negatively charged, or relatively unaffected particles will remain along the top edge of the channel while particles of interest will be transported across the channel and removed at outlet b. By adjusting the applied field and the flow rates at each of the inlet and outlet ports will determine which particles elute at which outlet.

manufacturing systems. A miniaturized SPLITT system would also be ideal for continuous sample preparation in micro total analysis systems now being developed by a wide range of researchers. The basic operation of a SPLITT system is shown in Figure 1.

2. Theory

The initial work for this project involved developing analytical and numerical models of the function of the systems to determine how they would function after being scaled down to the microscale domain. The results of these models were used to design the physical prototypes which were then fabricated. The basic equation for estimating function in the SPLITT system is

$$F_b = \frac{BL\mu V / w + \dot{V}(a)}{\dot{V}(a) + \dot{V}(b)}, \quad (1)$$

where B is the channel breadth, L is the channel length, μ is the electrophoretic mobility of the particles, V is the applied voltage, w is the thickness of the channel, and $\dot{V}(a)$ and $\dot{V}(b)$ are the flow rates through the respective outlets. [1]

3. Experimental

For the prototype test phase of this project, a number of differently sized channels were fabricated on 100 mm <100> Si wafers. The materials used to make up the channels in the SPLITT system were epoxy based negative resist SU-8-25 (used to form the sidewalls of the channels), titanium, and gold (served as the electrodes). The complete fabrication process is shown in Figure 2. Once the SPLITT System was fabricated, integration with other instruments such as syringes, pumps and detectors was performed as shown in Figure 3.

4. Results and Discussion

Characterization of the system was done using standard particles (polystyrene samples) and viruses such as TMV (Tobacco Mosaic Virus). Figure 4 shows how adjusting the applied voltage in the system affects the percentage of injected sample collected at one

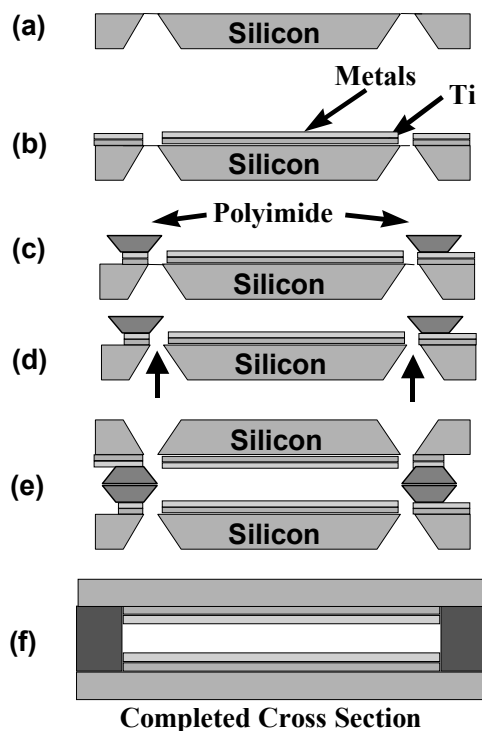


Figure 2. Fabrication steps for miniaturized electrical SPLITT system. (a) KOH etching is used to etch ports in silicon wafers (b) Metals deposited to form electrodes using metal evaporation system (c) Photosensitive polyimide patterned in shape of channel and underexposed to generate overarching shape (d) Silicon nitride membranes are removed in plasma etch (e) Two substrates are bonded together using liquid polyimide and then cured. (f) Completed cross-section through center of channel.

of the two outlets for a bolus of polystyrene spheres injected into the system. Experiments to determine the effect of voltage, flow rates, channel size, and carrier solution were all carried out, but not presented here do to space considerations.

The sample preparation capabilities of the system were demonstrated by separating a mixture of tobacco mosaic virus (TMV) and polystyrene particles. The results of some of these experiments are shown in Figure 5. Figure 5 shows an optical absorption spectrum taken from each of the outlet collection syringes showing that the TMV has been completely separated from the mixed polystyrene spheres. Figure 6 shows the abrupt loss of TMV in the detector by reversing the polarity of the applied electric field.

5. Conclusions

Overall, a novel microfabricated system for the separation and analysis of nanoparticles, viruses and other colloids has been demonstrated. The completed system demonstrated high resolution and a robust nature with application to a variety of fields.

Acknowledgments

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Reference

1. Fuh, C Bor "Split Flow Thin Fractionation" *Anal Chem.* Vol 72, pp 266-271, 2000.



Figure 3. Photograph of completely assembled system

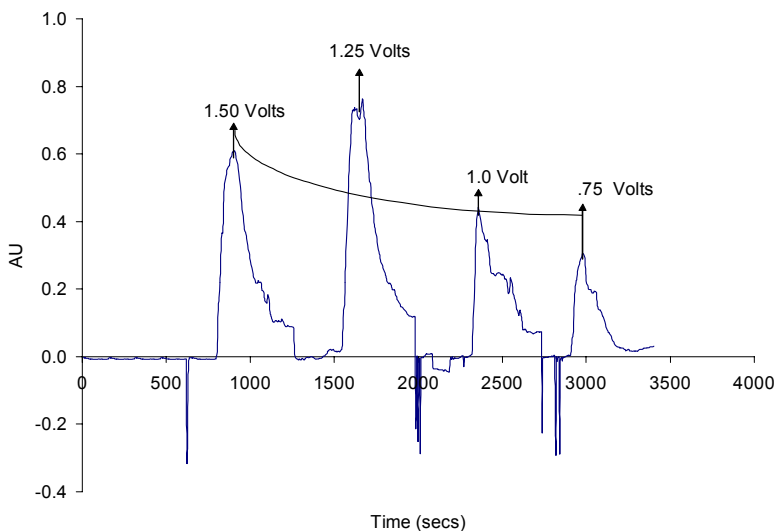


Figure 4. Detector trace showing how changing the applied voltage in the system affects the amount of polystyrene collected at outlet b.

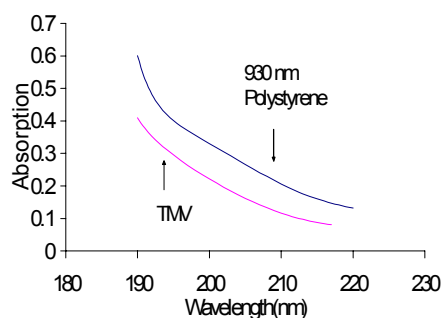


Figure 5. Adsorption spectra for two outlets during TMV separation showing polystyrene in one syringe and TMV in the other with little or no mixing.