In-situ Fabrication of Dialysis Membranes in Glass Microchannels Using Laser-induced Phase-Separation Polymerization

Brian J. Kirby and Anup K. Singh
Sandia National Laboratories, Livermore, CA (bjkirby@sandia.gov)

Abstract

Laser-induced phase-separation polymerization of a porous acrylate polymer is used for *in-situ* fabrication of dialysis membranes inside glass microchannels. A shaped 355 nm laser beam is used to define polymer membranes of 4-14 μm thickness, which bond to the glass microchannel and form a semipermeable membrane. Differential diffusion through the membrane is observed for fluorescein molecules versus 200 nm latex microspheres, showing the potential for this technique to integrate sample cleanup into chip-based analysis systems.

Keywords: phase-separated polymer, filtration, dialysis, sample preparation, polymer monolith

1. Introduction

Complex samples (*e.g.,* cell extract) often require extensive cleanup or pretreatment before introduction to analysis channels in a miniaturized device. These pretreatment steps are often performed off-chip using large volumes of sample and other reagents, and hence often add substantially to the total analysis time and cost. Dialysis, or size-based separation of species via selective diffusion through a semipermeable membrane, is a widely used technique for cleanup of biological samples [1,2]. We have developed a technique for fabricating thin (4-14 μm) porous polymer dialysis membranes within the channels of a glass microchip. UV laser-initiated polymerization (Figure 1) is used for controlled placement of the dialysis membrane in a chip for cleanup of complex or dirty samples; this technique is rapid and inexpensive and increases the potential functionality of integrated microfluidic devices. The semipermeable membrane allows diffusion of fluorescein molecules while preventing diffusion of 200 nm latex microspheres, showing the potential for extracting a small molecular weight analyte of interest from a complex matrix.

2. Substrate

Standard cross-shaped glass microchips were obtained from Micralyne; chemicals were obtained from Aldrich and used as received. To facilitate bonding between the membrane and the glass surfaces, glass surfaces were first exposed to a 2:2:1 (by volume) mixture of water, glacial acetic acid, and 3-(trimethoxysilylpropyl) acrylate for a period of 30 minutes, covalently linking the silane to the wall and exposing the acrylate group for polymerization.

3. *In-situ* Photopatterning of Polymer Membranes

Following surface treatment, channels are filled with a monomer/solvent/photoinitiator solution of 73:27 pentaerythritol triacrylate:1-propanol (by weight) with 10 mg/ml AIBN photoinitiator. Thin (4–14 μm) porous polymer membranes are fabricated *in-situ* by shaping and focusing the 355 nm output of a 12 kHz, 800 ps-pulse, 160 nJ-pulse, frequency-tripled Nd:YAG laser into a 1-2 μm sheet and using this sheet to generate photoinitiated phase-separation polymerization [3,4] in the irradiated region (Figure 2). The thickness of the membrane is determined by the laser sheet thickness, radical diffusion, solved-phase polymer diffusion, and bulk fluid motion [5]. Laser sheet thickness was minimized by spatially filtering the focused laser output with a 2 μm slit and imaging the resulting diffraction pattern at ~0.5 magnification onto the channel. Following polymerization, the system was flushed thoroughly with acetonitrile to remove residual polymer/monomer/solvent material and then filled with aqueous solutions for testing.

4. Demonstration of Differential Diffusion

Aqueous solutions of (a) fluorescein (Exciton) or (b) 200 nm, carboxylate-modified, dye-impregnated latex spheres (Molecular Probes) were alternately used to fill channels on one side of the polymerized membrane; the other side was filled with water. Solutions were allowed to come to rest and the diffusion of species (fluorescein or latex spheres) across the membrane was observed over several minutes using fluorescence excited at 488 nm. Figure 3 shows a schematic and images for both cases. For this porous polymer, with a nominal pore size of 30 nm (measured with Hg porosimetry, BET, and SEM), fluorescein diffuses across the membrane while the latex spheres do not. In future applications, monomers and solvents may be chosen to lead to a specific pore size distribution, which can be used to engineer the molecular weight cutoff of the porous membrane for a specific application.

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References

1. N. Xu, Y. Lin, S.A. Hofstadler, D. Matson, C.J. Call, R.D.A. Smith, *Anal Chem* **70** (1998).
2. J. Lichtenberg, N.F. de Rooij, E. Verpoorte, *Talanta* **56** (2002).
3. C. Yu, M.H. Davey, F. Svec, J.M.J. Frechet, *Anal Chem* **73** (2001).
4. D.J. Throckmorton, T.J. Shepodd, A.K. Singh, *Anal Chem* **74** (2002).
5. B.J. Kirby, T.J. Shepodd, E.F. Hasselbrink, *J. Chrom A*, in press (2002).

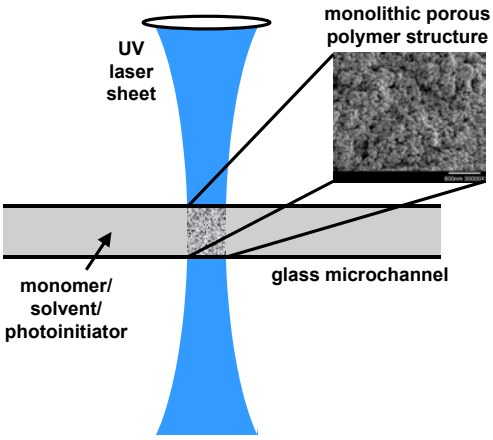

Figure 1. Phase-separation polymerization.

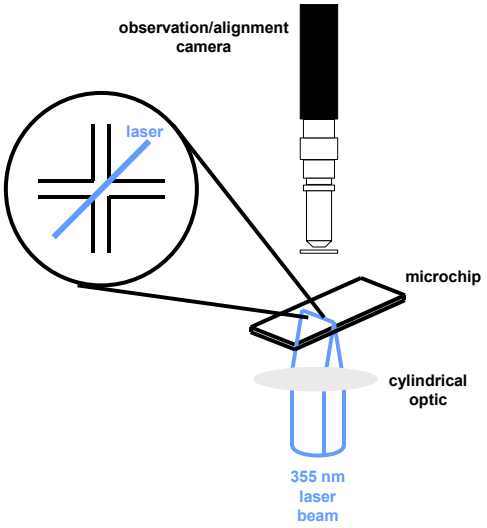

Figure 2. Beam-shaping optics for thin membrane polymerization.

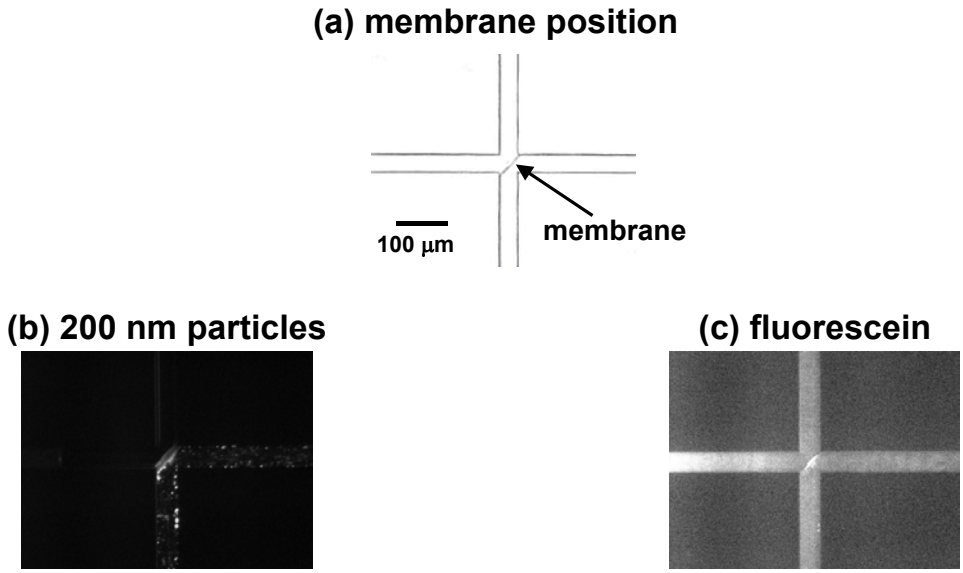

Figure 3. Images of selective diffusion across a 9 µm porous polymer membrane: (a) white light image of membrane location; (b) fluorescence image of 200 nm fluorescent spheres, which do not diffuse across the membrane; (c) fluorescence signal from fluorescein, which does diffuse across the membrane.