SUSPENDED, POROUS CELLULOSE ACETATE MEMBRANES FOR MICRODIALYSIS USE

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Abstract

Porous cellulose acetate membranes were suspended over 75 micron wide silicon microchannels. The microchannels are formed when a viscous polymer lacquer is directly spin cast onto etched silicon cavities (Fig. 1). Standard fabrication processes are used to create the channel, preventing the need for adhesives, substrate bonding, or other complex assembly procedures. These microchannels can allow the isolation and concentration of specific biological molecules.

Keywords: cellulose acetate, membrane, microdialysis, porous

1. Introduction

In the area of in vivo bioanalytical measurement techniques, microdialysis involves the use of a porous material to recover biomolecules from tissue [1]. Microdialysis is a sampling method for studying localized metabolic events by monitoring the chemistry of the extracellular space around a point of interest. Conventional microdialysis involves a small polymeric probe with a porous membrane at its tip, which can be used for *in vivo* or *in vitro* studies. When a physiological salt solution is slowly pumped through the microdialysis probe (usually called the perfusate), the solution equilibrates with the surrounding fluid on the other side of this membrane. Currently, conventional microdialysis probes are hand assembled, have limited useable lifetime, and can't provide the necessary temporal resolution for analytical tools due to large dead volume issues.

Porous materials have gained interest in the fields of filtration, drug delivery, protein separation, and microdialysis. Microfluidic devices that serve these application areas are usually obtained by integrating pre-fabricated porous materials into the final device, either by using adhesives or bonding. These fabrication procedures need to include microchannels as well, the fundamental component of most microfluidic systems. This paper presents a novel fabrication method used to create a monolithic microdialysis chip.

Figure 1. Cross sectional view of a suspended cellulose acetate membrane across a 75 micron wide silicon microchannel. Inset is a top view of the suspended membrane. Dotted lines are used to show the boundaries of the microchannel.

2. Fabrication

A lithography step using photoresist first defines the location where the microchannel will be formed (Figure 2). The silicon is then etched isotropically using either sulfur hexafluoride or xenon difluoride; the photoresist is subsequently removed using acetone. A viscous polymer lacquer, 10% w/v cellulose acetate in solvent,
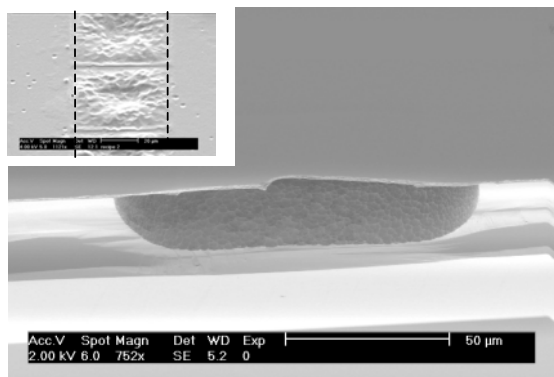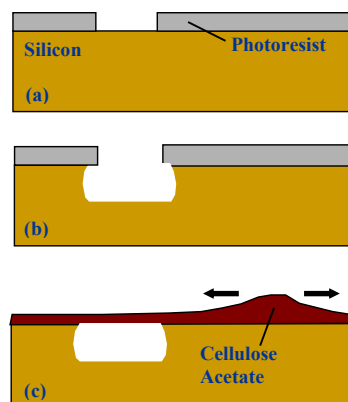
Figure 2. The fabrication process involves (a) using lithography to define the microchannel (b) silicon etching using xenon difluoride with subsequent removal of the photoresist, (c) spin coating cellulose acetate film onto the substrate.

is deposited onto a spin chuck while stationary. The 10% w/v lacquer is formed by mixing cellulose acetate (Eastman Chemicals, CA398-3) with the solvent N,N-dimethylacetamide (DMAc). A spin speed of 2500 RPM for 40 seconds is used to create a 20 micron thick cellulose acetate membrane; thickness can be varied with speed. The sample is then immediately transferred to a room temperature deionized water bath. The polymer undergoes precipitation in the non-solvent water, as the solvent is displaced from the film. The sample is left in the bath overnight to remove any remaining solvent in the film and then allowed to air dry. A semi-clear, conformal polymer coating on the silicon substrate is formed.

2. Theory

Pores are formed in the polymer film by the phase separation process. During the immersion precipitation, the composition of the polymer enters the two-phase region in the ternary phase diagram and phase separation occurs, producing a polymer-rich phase, containing mainly polymer and less solvent, and a polymer-lean phase, containing mainly solvent and less polymer [2]. The polymer-rich phase represents the structural walls of the coating while the polymer-lean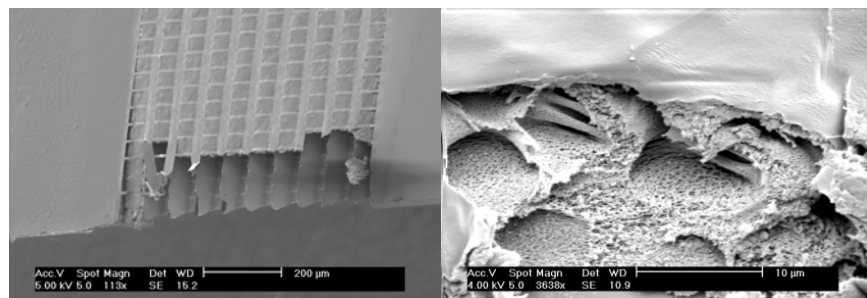 phase represents the porous regions in the coating. An asymmetric film is formed that contains a dense top layer that has minimal visible pores and a sparsely porous interior (Figure 3, right). By varying the polymer concentration, the precipitation medium and temperature, a large variety of pore sizes can be attained.

The polymer's wetting characteristics are largely responsible for its ability to fill or span across a cavity. The main force driving the polymer into a cavity is from capillary action. This is a function of the surface tension of the liquid-gas interface, the contact angle, and the size of the cavity. The main opposing forces include the cohesive forces within the polymer as well the pressure of trapped gas in the cavity. Viscosity has little effect on the ability of the polymer to enter a cavity, yet it does have an effect on the speed at which the polymer enters the cavity.

Stress in these phase separation films are from constrained in-plane shrinkage of the film during drying. The stress when using DMAc as a solvent seems to be lower as compared to using acetone. This is due to the lower volatility of DMAc, causing it to be retained in the coating until the latter stages of drying [3]. Similar coating experiments with acetone resulted in significant cracking and peeling of the polymer film from the substrate. The DMAc may be acting as a plasticizer, keeping the coating modulus lower.

3. Experimental

The cellulose acetate polymer was coated onto microchannels of various widths. The polymer successfully spanned across a microchannel of up to 75 microns in width. It was not possible to span larger openings since tears and openings appeared on the polymer surface as shown in Figure 4. To create long microchannels it was necessary to place periodic microbridges across the channel. These microbridges are undercut during the etching process (Figure 3, left). Using SEM and BET adsorption analysis, it was determined that the average pore size is approximately 50nm.

Figure 3. (Left) A cleaved chip showing a set of ten microchannels (50 microns width) are shown coated with cellulose acetate. Periodic microbridges are spaced every 75 microns along a channel. (Right) The immersion precipitation process creates an asymmetric film that has a dense top layer over a sparsely porous interior.

Fluidic interconnect was attached to the inlet/outlet ports to interface with the microchannels. A syringe pump provided a 0.3 µL/min flowrate of PBS buffer while various proteins of different molecular weight were placed above the cellulose acetate to determine its permeability. The outlet port was fractionated and collected for later analysis. The cellulose acetate showed significant permeability to myoglobin (MW=17 kDa) and soybean trypsin inhibitor (20 kDa). Large molecular weight molecules were not able to pass through the cellulose acetate.

5. Conclusions

A porous cellulose acetate film was suspended over a silicon channel using a standard fabrication process of spin coating. Although the polymer undergoes considerable stress during drying, a 75 micron wide cavity was spanned. Permeability tests indicate the ability of low molecular weight molecules to pass through the 20 micron thick cellulose acetate.

Acknowledgements

Figure 4. Film stress due to in-plane shrinkage from polymer drying.

References

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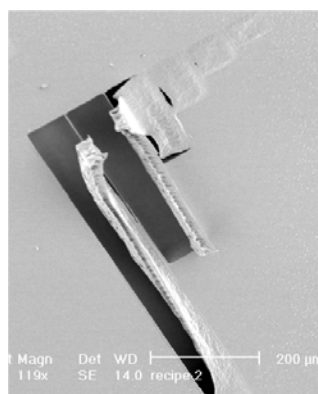[3] Vaessen, D., McCormick, A., Francis, L., Polymer 43(8) 2267-2277 (2002)