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Patterned polycaprolactone-filled glass microfiber microfluidic devices for total protein content analysis

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ABSTRACT

Membrane based microfluidic devices have gained much popularity in recent years, as they make possible rapid, inexpensive analytical techniques that can be applied to a wide variety of areas. The ability to modify device hydrophilicity and hydrophobicity is critically important in fabricating membrane based microfluidic devices. Polar hydrophilic membranes, such as glass microfiber (GMF) membranes, hold great potential as they are inexpensive, chemically inert, and stable. Filling of these membranes with non-polar polymers such as polycaprolactone (PCL) converts the hydrophilic GMF into a hydrophobic medium. Controlled alteration of the surface chemistry of PCL/GMF substrates allows for the fabrication of microfluidic patterns on the surface. Using this approach, we have developed a simple and rapid technique for fabrication of highly adaptable complex multidimensional (2D and 3D) microfluidic pathways on a single membrane. PCL-filled GMF media were masked and selectively exposed to oxygen radicals so that the exposed surface became permanently superhydrophilic in its behavior. The desired microfluidic pattern was cut into the mask prior to assembly and exposure, and the mask was removed after exposure to reveal the ready-to-use microfluidic device. To verify and demonstrate the performance of this novel fabrication method, a colorimetric total protein assay was applied to the determination of protein concentrations in real samples.

1. Introduction

Wicking microfluidic analytical devices have been applied to many areas of analytical chemistry [1–3]. These analytical devices offer rapid and reliable measurements at low cost. The quality of these devices and their range of applicability are highly dependent upon the method of fabrication applied and materials of manufacture [4–7]. The basic fabrication method for devices of this kind involves patterning of a support substrate (an organic or inorganic filtration membrane) into hydrophilic channels defined by hydrophobic barriers comprised of various polymers, water resistant inks/toners or waxes [5,8,9].

As a supporting substrate, glass microfiber (GMF) membrane media is a good candidate that offers many advantages over paper. GMF is an inexpensive, temperature stable, pH resistant, and chemically inert hydrophilic membrane made up of fine microscale borosilicate fibers [10,11]. This study introduces a combination of a GMF substrate with a polycaprolactone (PCL) barrier agent as a novel platform for the fabrication of wicking microfluidic devices. The GMF substrate can be adapted for use with many different chemistries and assays when used in concert with PCL, a biocompatible and biodegradable polymer that can be used to define the hydrophobic portions of these devices [12]. PCL is a polyester with low melting and glass transition temperatures, high miscibility with other polymers, excellent solvent compatibility, and a facility for functionalization [13,14]. Hence, it is favored for use in various applications that expand device applicability [13–15].

Cost and complexity are key factors of importance in designing microfluidic devices for broad application. Therefore, development of simple and inexpensive fabrication techniques that do not require expensive chemicals or instruments is a necessity. Oxygen plasmas have been employed as microfluidic device fabrication tools, primarily to affect surface chemistry, by many groups [16–19]. These are strong plasmas that rigorously etch surfaces. On the other hand, oxygen plasma decontaminators have been widely used for gentler cleaning processes for many years [20–22]. Decontaminators are optimized to generate long lived oxygen radicals rather than strong O_2 plasmas [23]. Exposure of a polymer-coated substrate to oxygen radicals will effectively alter surface properties, such as surface free energy, which are the driving forces that dictate the hydrophilic/hydrophobic nature of the surface [24,25].

In this study, a novel, low cost, simple, and highly-adaptable microfluidic device fabrication approach was developed for PCL-filled

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GMF membranes. This fabrication approach involves selective exposure of the PCL-filled GMF membranes to oxygen radicals which is achieved using a mask made from an inexpensive tape. Changes in the mask design allow for fabrication of different channel geometries (flow-through, flow-through + lateral flow, and surface-lateral flow). Combining such different channel geometries allows for fabrication of complex multidimensional (2D and 3D) microfluidic devices on a single polymer-filled membrane, enabling unique properties and applications. Traditional approaches for fabricating 3D flow devices typically involve multistep stacking of 2D patterned layers/membranes using intermediate layers with adhesive properties [26,27]. Thus, these devices require multiple layers of materials and multiple unit operations to fabricate. In contrast, by using the selective oxygen radical exposure fabrication technique described here, microfluidic mixers, separations tools, delay circuits, and timing devices can all be fabricated on a single membrane that contains all needed 3D fluid flow pathways. Surface flow (2D) assay immobilization zones are highly useful in performing colorimetric assays. This approach allows for assay components to be immobilized on the surface the membrane and generates an increased analytical signal as it is largely free from the membrane matrix effects. This fabrication approach also allows for deposition of assay components before and/or after the fabrication of fluidic channels, as best accommodates the assay reagent requirements. In this study, we have demonstrated the compatibility and performance of the fabrication technique by analyzing real world protein unknowns using an immobilized colorimetric assay for total protein quantitation.

2. Materials and methods

2.1. PCL-filled GMF membranes

PCL solutions (w/v) were prepared by dissolving appropriate weights of PCL (Perstorp, Warrington, UK) in appropriate volumes of analytical grade toluene (Macron Fine Chemicals, Center Valley, PA, USA). Solutions were spin-coated (Laurell WS-400, North Wales, PA, USA) at 2500 rpm for 30 s on Whatman (GE Healthcare Bio-Sciences, Pittsburgh, PA, USA) glass microfiber (GF/A) membranes to ensure even application and penetration, followed by drying at 50 °C for 15 min. To date, the most impressive results have been achieved using PCL of 25000 M.W. at 15% w/v (in toluene), where the initial weight percentage of PCL: GMF was approximately 50:50 under the above conditions.

2.2. Preparation of masks

The desired mask for each surface (top and bottom) was designed using drafting software (SolidWorks 2013–2014 Education edition, Waltham, MA, USA) and cut out of tape (i tape, Intertape Polymer Group, Marysville, MI, USA) using a laser cutter (VLS 3.50, Universal Laser Systems, Scottsdale, AZ, USA) with the following settings: power = 40% speed = 100%, pulses per inch = 500, z-axis = 0.

2.3. Oxygen radical exposure (ORE) experiments

Oxygen radical exposure experiments were conducted using an Evactron (Redwood City, CA, USA) decontaminator/RF plasma cleaner installed on a home built vacuum chamber under conditions determined separately for each experiment. The pressure and forward RF power were maintained at constant values of 0.6 Torr and 13 W, respectively. Selective exposure to radicals – not to the plasma but only to radicals generated by the plasma – was accomplished by covering the area of the membrane intended to remain unexposed with a patterned mask, prepared as described above, and ensuring that the substrate was placed at a distance well below the plasma region. Exposure time was dependent on pattern requirements. The minimum demonstrated exposure time required to generate a microfluidic pattern was 5 s.

2.4. Protein analysis

Analysis of total protein content in various samples was conducted using an immobilized colorimetric assay consisting of a pH 1.8, 250 mM citrate buffer (95% ethanol: 5% water) and 3.75 mM tetra bromophenol blue (TBB) as a colorimetric indicator (Sigma-Aldrich, St. Louis, MO, USA), prepared in ethanol (Sigma-Aldrich, St. Louis, MO, USA). Assay reagents were immobilized as a 2:1 mixture of buffer solution: TBB solution using an automated solution dispenser (D300, HP Corvallis, OR) over the reagent zone (3 mm diameter) prior to

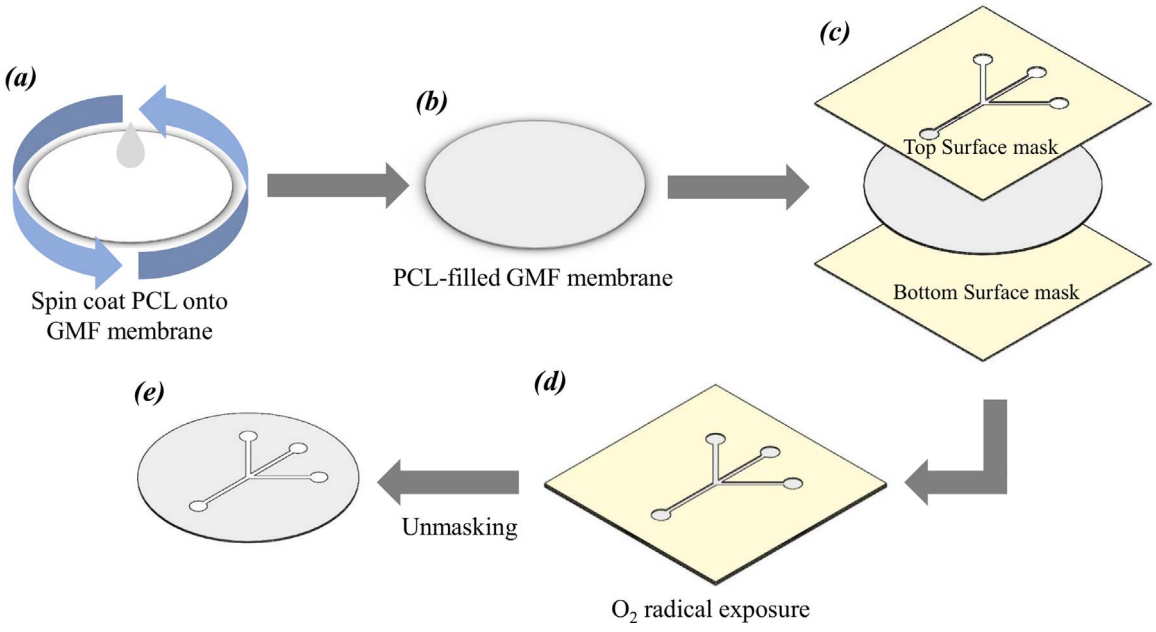

Fig. 1. Pattern fabrication mechanism: (a) PCL was spin-coated onto the GMF membrane to yield a PCL-filled GMF substrate (b). (c) The PCL filled GMF membrane was then sandwiched between the top mask (facing towards the oxygen radical source) and bottom mask (facing away from the oxygen radical source). (d) The membrane assembly was exposed to oxygen radicals. (e) Unmasking the substrate reveals the hydrophilic pattern on the PCL-filled GMF membrane.