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Low temperature bonding of poly(methylmethacrylate) electrophoresis microchips by in situ polymerisation

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Abstract

A novel method for bonding poly(methyl methacrylate) (PMMA) electrophoresis microchips at the temperature below the glass transition temperature of PMMA based on in situ polymerization has been demonstrated. Methyl methacrylate (MMA) containing initiators was allowed to prepolymerize in an 85 °C water bath for 8 min and 15 min to produce a bonding solution and a dense molding solution, respectively. The channel plate of the PMMA microchip was fabricated by the UV-initiated polymerization of the molding solution between a nickel template and a PMMA plate at room temperature. Prior to bonding, the blank cover was coated with a thin layer of the bonding solution and was bonded to the channel plate at 95 °C for 20 min under the pressure of binder clips. The attractive performance of the PMMA chips bonded by the new approach has been demonstrated by separating and detecting dopamine, catechol, three cations, and three organic acids in connection with end-column amperometric detection and contactless conductivity detection.

Keywords: Miniaturization; Capillary electrophoresis; Amperometric detection; Conductivity detection; Poly(methyl methacrylate)

1. Introduction

During the past decade, microfluidic analytical systems fabricated on glass, silica and polymer microchips have undergone an explosive growth. Much attention has been paid to capillary electrophoresis (CE) microchips owing to their high degree of integration, portability, minimal solvent/reagent consumption, high performance and speed [1–3]. These microchip analysis systems hold considerable promise for biomedical and pharmaceutical analysis, clinical diagnostics, environmental monitoring, and forensic investigations, etc.

Most early reports on miniaturized analytical systems have relied on glass or silicon substrates in connection with the standard lithographic fabrication technology. CE microchips are mainly fabricated using glass substrates, from cheap soda lime glass to high quality quartz [4]. However, their application was limited because of high cost, harmful and complicated fabrication procedures, and the limitation on the geometric modification of the chip channel [5]. Therefore, polymers are becoming the most promising materials for the microfluidic devices because they can be produced with mass-replication technologies, such as injection molding and hot embossing. Industrial interest in utilizing plastics for the production of microanalytical systems is primarily driven by the fact that these materials are less expensive and easier to be manipulated than silica based substrates. Polymers offer attractive mechanical and chemical properties, low cost, ease of fabrication, biocompatibility, and higher flexibility [5,6]. Such plastic chips have been fabricated using in situ polymerization [7], laser ablation [8], imprinting [9], injection molding [10], etc. A wide variety of polymer materials have been evaluated for fabricating microchips instead of glass, in which poly(dimethylsiloxane) (PDMS) and poly(methyl methacrylate) (PMMA) are the two most commonly used polymers. PMMA has been particularly useful for microfluidic chips with the features of low price, excellent optic

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transparency, and excellent electric and mechanical properties [6,11,12]. It has been reported as the least hydrophobic of the commonly used plastic materials [13], and can directly generate stable electroosmotic flow (EOF) in the microchannels under the electrical field applied [8,14]. In the fabrication methods mentioned above, the imprinting approach has been commonly employed due to some attractive advantages of simple procedure, less expense, and suitableness of mass production. Usually, imprinting methods involve the commercial available hot-embossing systems and the rigid templates such as quartz [15], Si [9] and nickel [16] templates. Recently, methods based on in situ polymerization have been developed for the fabrication of PMMA chip by using Si [17,18] and metal [7] templates. The Si or quartz templates readily tend to be broken due to the different thermal expansion coefficients of the templates and the polymers in imprinting or molding process.

In comparison with glass and PDMS microchips, PMMA-based CE microchips have been developed limitedly. It is a challenge task to find a reliable sealing technique to enclose the PMMA microchannel networks without clogging. Thermal bonding techniques [9,16,19,20] under pressure are usually employed for bonding PMMA substrates. In addition, thermal lamination [10], solvent bonding [21], glue layer [12], adhesive tape [22], and PDMS films [23–25] have also been used. Among them, various thermal bonding techniques are preferable as they allow formation of microchannels with uniform surfaces composed entirely of the same polymeric materials. Prior to sealing, the PMMA substrates were heated to the temperature above its glass transition temperature (T_g, 105 °C) and positive pressures were applied on the channel plate and the cover [9]. However, slight variance of the pressures and temperature may cause microchannel deformation and affect the reproducibility and yield because of the higher bonding temperature employed. It is of high importance to decrease the bonding temperature below the T_g of PMMA. Recently, Wooley et al. have demonstrated that PMMA substrates can be bonded together to form microfluidic devices by clamping a blank piece to a channel plate and heating the assembly in a boiling water bath. Rapid, high-resolution CE separations of derivertized amino acids have been successfully carried out on devices fabricated using this method [26]. Other sealing approaches unavoidably introduce multiple materials to form microchannels with non-homogeneous internal surfaces, which leads to undesired effect on the EOF and may reduced the separation efficiency [27,28]. Solvent bonding or thermal lamination, are less satisfactory, due to possible blocking of the microchannels or swelling of the pressure-sensitive adhesive of the laminated chips, respectively.

In this paper, a novel bonding technique for the PMMA electrophoresis microchips has been developed. The channel plates of the CE chip were fabricated by ultraviolet (UV)-initiated polymerization of the prepolymerization solution of methyl methacrylate (MMA) between a nickel template and a commercially available PMMA plate under the ambient pressure. Subsequently, the PMMA channel plate and the cover were bonded together at a lower temperature (95 °C) below the T_g of PMMA with the aid of the in situ polymerization of a layer of the prepolymer of MMA coated on the cover. The ease, simplicity, versatility, and low cost of the new fabrication route thus make it extremely attractive for the mass production of PMMA electrophoresis microchips. The feasibility and performance of the PMMA chips bonded by the new method have been demonstrated by separating and detecting dopamine, catechol, three cations, and three organic acids in connection with end-column amperometric detection (AD) and contactless conductivity detection (CCD).

2. Experimental

2.1. Reagents

Methyl methacrylate (MMA), benzoin ethyl ether (BEE), and 2-2′-azo-bis-isobutyronitrile (AIBN), sodium oxalate, sodium potassium tartrate, sodium acetate, methyl ammonium, ammonium chloride, sodium chloride were all purchased from Shanghai Chemical Reagent Company (SinoPharm, Shanghai, China). The commercial MMA and AIBN should be purified prior to use. The MMA was purified by the following steps as conventional method: removing hydroqunone (a inhibitor) with 5% sodium hydroxide aqueous solution, washing with deionized water, dehydration with anhydrous magnesium sulfate, and distillation under vacuum. High-purity AIBN was prepared by recrystallization using hot methanol as solvent. Dopamine, catechol, histidine (His), and 2-(*N*-morpholino)-ethanesulfonic acid (MES), were all obtained from Sigma (St. Louis, MO, USA). Stocking solutions (10 mM) of dopamine and catechol were both prepared in doubly distilled water (Medical Center of Fudan University, Shanghai, China). Appropriate amounts of methyl ammonium, ammonium chloride, sodium chloride, sodium oxalate, sodium potassium tartrate, and sodium acetate were all dissolved in doubly distilled water to reach the final concentration of 100 mM. Other chemicals were all analytical grade. The analysis of dopamine and catechol was performed with a 10 mM phosphate buffer (pH 6.5). The run buffer for the separation of cations and organic acids was a MES/His buffer (20 mM each, pH 6.1). Samples solutions were prepared by diluting the stock solutions in the corresponding running buffer solutions. Microscopic glass slide (75 mm × 25 mm × 1 mm) were received from Shanghai Jinglun Industrial Glass Co. Ltd. (Shanghai, China).

2.2. Microfabrication procedure

The PMMA microchips (16 mm × 70 mm) had simple cross layouts, with the four-way injection cross-connected to the three reservoirs and the separation channel. The PMMA chip consisted of a 60 mm-long separation channel (between the injection cross and the detection reservoirs) and a 5 mm-