

Construction of a Biomimetic Surface on Microfluidic Chips for Biofouling Resistance

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A biomimetic surface has been formed on the poly(methyl methacrylate) (PMMA) microfluidic chips for biofouling resistance on the basis of a simple modification. Accordingly, an amphiphilic phospholipid copolymer of 2-methacryloyloxyethyl phosphorylcholine and *n*-butyl methacrylate (PMB) was developed to introduce the phosphorylcholine functional groups onto the PMMA surface via the anchoring of hydrophobic *n*-butyl methacrylate units. The 2-methacryloyloxyethyl phosphorylcholine segments could form hydrophilic domains, considered to be located on the surface, to provide a biocompatible surface. X-ray photoelectron spectroscopy and Fourier transform infrared spectra confirmed the success of surface functionalization. The PMB-modified microchips containing phosphorylcholine moieties exhibited more stable electroosmotic mobility compared with the untreated one. In addition to being characterized for minimized nonspecific adhesion of serum proteins and plasma platelets, the PMB-functionalized microchannels have been exemplified by electrophoresis of proteins. This one-step procedure offers an effective approach for a biomimetic surface design on microfluidic chips, which is promising in high-throughput and complex biological analysis.

Microfluidic devices are becoming powerful tools for performing chemical or biological assays due to the increased speed and reliability at reduced sample consumption.^{1,2} For the requirement of commercial manufacture, the material used in chip fabrication is developed from glass and silicon to polymer so that the cost and the manufacturing procedures could be decreased.³ However, their applications in microfluidics and biology have been limited since their relatively low surface energy makes them present a relatively hydrophobic surface, which may have a negative effect on the adhesion of coatings and biocompatibility. Nonspecific adsorption of analytes onto the surfaces is a common problem of polymer-based microstructures leading to the fouling of microchannel surfaces. Thus, the continuing progress in microfluidics

would partly rely on the development of surface modification technologies in a simple and reliable fashion to control the adsorption and ensure optimized biocompatibility of the microchips as a platform for improving reproducible and efficient bioanalysis.⁴

Many approaches to reduce the surface interaction have been explored including dynamic coating and chemical modification.^{5–12} The variety of polymers that are commercially available and capable to tailor the structural, physical, and chemical properties has given polymers unique advantages over other materials as surface coatings.¹³ To improve the physicochemical property, surface modification with biocompatible polymers would be a promising technique to provide an excellent interface on the conventional polymer surface. Lee et al. described a technique in which 2-bromoisobutyl bromide was immobilized on poly(methyl methacrylate) (PMMA) substrates preactivated using oxygen plasma, and then poly(ethylene glycol) (PEG) was grafted by atom-transfer radical polymerization for electrophoretic separations of proteins and peptides.⁹ Allbritton et al. demonstrated a procedure to covalently link polymer PEG to the surface of poly(dimethylsiloxane) (PDMS) microchannels by ultraviolet graft polymerization.¹⁴ These PEG coatings have been generally used to minimize nonspecific protein adsorption on glass and plastic devices. Whereas they might cause some secondary reactions in blood samples,¹⁵ alternative strategies are being studied. Using a sol–gel method, PDMS microchips were fabricated with SiO₂

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particles.¹⁶ Cheng et al. fabricated the stable and fluid-supported bilayer membranes by fusion of positively charged ethylphosphocholine vesicles into PDMS microchannels.¹⁷ Besides covalent binding and physical adsorption utilized to design PDMS microfluidic devices, a copolymer of *n*-butyl methacrylate (BMA) and γ -(methacryloxy)propyltrimethoxysilane was synthesized to directly introduce the silane functional groups onto the PMMA chip surface for fabricating protein stationary phases to allosteric analysis and protein identification by our group.^{11,12}

As nature biomolecules, phospholipids are found in various cellular membranes. Recently, much attention has been devoted to the polymeric phospholipid analogues containing phosphatidylcholine moieties that exist on the surface of the phospholipid bilayer.^{18,19} Using phospholipids to modify the polymer surfaces has attracted considerable interest as a means of improving their biocompatibility and inhibiting protein adsorption or cell adhesion. A series of phospholipid polymers shows excellent biological properties at the interface to develop various new biomaterials useful in biotechnology.¹⁸ 2-Methacryloyloxyethyl phosphorylcholine (MPC) is the most commonly used monomer for phospholipid polymers. With the polymerizable methacrylate moiety, it can readily be copolymerized with different comonomers and enable the design of numerous polymers having a wide variety of molecular architectures.²⁰ The phospholipid polymers can easily form a thin layer on substrates such as metals, glass, and polymers, onto which the phosphorylcholine groups are self-assembled.²¹ The most significant property of the phospholipid polymer is the higher free water content on its surface so that the adsorption induced by hydrophobic interaction between the polymer surface and biologically relevant materials is suppressed. Up to now, it has been widely used in tissue engineering and pharmaceutical applications.^{18,20,21} An alternative application which we investigated here was focused on the introduction of MPC domains onto the polymeric microchips to obtain a robust hydrophilic and biofouling-resistant surfaces for biological analysis.

PMMA is widely used in the microfabrication of microfluidic devices. However, its hydrophobic and inert chemical properties make it necessary for the exploration of routine, simple, and well-defined protocols to improve its surface property.²² Copolymerization with a functional monomer offers an effective approach to incorporate new properties while retaining the desirable properties into existing polymers.²³ In this present research, an amphiphilic copolymer, poly(MPC-co-BMA) (PMB), was synthesized to introduce the phosphorylcholine functional groups onto the PMMA chip surface via the hydrophobic BMA units. Such one-step modification is convenient to achieve a biomimetic surface within the PMMA microchannel, which has the feature of dense polymer

brushes effectively against biomolecular adsorption. The modified microchips show better wettability, biocompatibility, and stable electroosmotic mobility and display reproducible separation of proteins compared with the native ones. The physicochemical properties and the resistance to biofouling have been characterized. Such an approach provides an effective means for simple microchip modification, which may hold potential in clinical diagnosis and protein separation applications.

EXPERIMENTAL SECTION

Chemicals and Materials. BMA and 2,2'-azobisisobutyronitrile (AIBN), both of analytical reagent grade, were purchased from Shanghai Chemical Reagent Co., Ltd. (Shanghai, China). BMA was purified by passing through basic alumina followed by a distillation under reduced pressure. AIBN was recrystallized in anhydrous ethanol before use. MPC was synthesized and purified as reported.²⁴ Bovine serum albumin (BSA), fluorescein isothiocyanate (FITC), and FITC-conjugated BSA (FITC-BSA) were purchased from Sigma Chemical Co. (St. Louis, MO). FITC-lysozyme was obtained from the Sino-American Biotechnology Co. (Luoyang, Henan Province, China). The human blood serum protein solution from healthy volunteers was kindly supplied by Changhai People's hospital (Shanghai, China). Blood used for the scanning electron microscopy experiment was drawn from healthy rabbits. All of other chemicals were of analytical grade and purchased from Shanghai Chemical Reagent Co. Ltd. PMMA pieces were obtained from Shanhu Chemical Factory (Shanghai, China).

Synthesis of Poly(MPC-co-BMA) and Modification of the PMMA Microchannel Surface. PMB was synthesized via free radical reaction from MPC and BMA with AIBN as initiator. In brief, 0.03 mol of MPC and 0.07 mol of BMA were dissolved in 100 mL of ethanol with 50 μ g of AIBN, and the solution was reacted at 60 °C under a nitrogen atmosphere for 24 h. The product, expressed as PMB, was precipitated in petroleum ether twice for purification.

PMMA microfluidic chips for electrophoresis study were purchased from Dalian University of Technology (Dalian, China). The sectional diagram of the microchannel figured as a trapezoid form with the dimensions as 60–100 μ m width and 40 μ m depth. Four reservoirs were aligned to the channel ends to create buffer, sample, or two waste reservoirs. The microchannel was filled with 1wt % PMB ethanol solution and allowed to stand for 5 min so that PMB could be adsorbed onto the PMMA surfaces. The solution was then removed, and the microchannel was allowed to dry. The procedure was repeated once more. As a result, a modified layer formed on the PMMA channel surface.

Characterization of PMB-Modified PMMA Surface. The static contact angle of the surface was measured by a JC2000A contact angle analyzer (Shanghai Zhongchen Digital Technology & Equipment Co. Ltd., Shanghai, China). After 6 μ L of water was placed on the substrate, the surface image was taken. Every datum was the mean of the left and right contact angles of the water drop and was collected 10 times to get an average value. X-ray photoelectron spectroscopy (XPS) measurements were obtained using Al K α radiation (1486.6 eV) on an ESCA system (Perkin-

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Elmer PHI 5000C) with a base pressure of 1×10^{-9} Torr. After being degassed in the pretreatment chamber for 2 h, samples were removed into the test chamber for XPS examination. Peak positions were normalized to the carbon peak at 284.5 eV. Fourier transform infrared (FT-IR) spectra were obtained with a Nexus-470 FT-IR spectrometer (Nicolet) equipped with an Omnic sampler in the wavenumber range of 500–4000 cm^{-1} . Control experiments were made on untreated PMMA substrate.

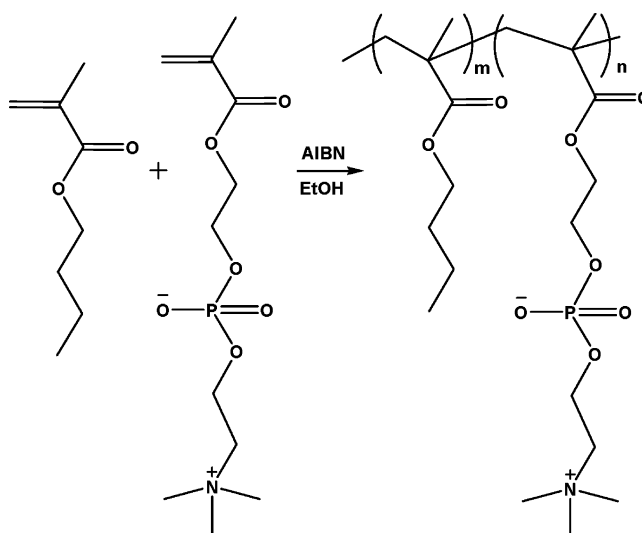
The measurement of electroosmotic flow was performed following Harrison's current monitoring method.^{25,26} Briefly, the inlet/outlet reservoirs and the fluidic channels were filled with the desired sample buffer, and the contents of the inlet reservoir were replaced with a buffer of reduced ionic strength. The electrical current in the fluidic channel was monitored after an electrical field was applied to the channel. The current decreased gradually until it reached a constant level after the content of the entire channel was replaced with a lower ionic strength buffer. The time required for the current to reach constant level was recorded using a digital real-time oscillograph (Tektronix TDS 220), and EOF velocity was calculated by dividing the channel length by the buffer replacement time. The measurements were performed by electrokinetically pumping 20 or 16 mM phosphate-buffered saline (PBS, pH from 3.0 to 9.0) through the channel with electric field strength of 250 V/cm (Shanghai Institute of Nuclear Research, Shanghai, China). The electroosmotic mobility (μ_{EOF}) was normalized by dividing EOF rate by the field strength.

Characterization of Biomolecule Adsorption and Protein Electrophoresis on Microchips. Confocal fluorescence microscopy measurements were used to evaluate the protein adsorption on the microchannels. FITC–BSA solution (2 mg/mL, 20 mM PBS, pH 7.0) was filled through the channels for 2 h and then washed extensively with buffer running for 30 min. A confocal system (TCS NT, Leica) was used to take the confocal fluorescence microscope images of the channels.

XPS measurements were used to study the protein adsorption from human serum albumin samples. PMMA substrates were soaked in the healthy human serum samples with a total protein content of 45 mg/mL for 1 h and followed by washing with buffer. The substrates were then characterized in a XPS system for the nitrogen content measurements. Scanning electron microscopy images were used to test the platelet adhesion on microchip surfaces from plasma. PMB was spin-coated on PMMA substrates, with an unmodified PMMA sheet as control. Blood was drawn from the healthy rabbits and mixed with sodium citrate solution (3.8 wt %) by a factor of 1/9 (v/v). Platelet-rich plasma, obtained by centrifugation of the anticoagulated blood at 1200 rpm for 5 min, was placed on the substrates and incubated at 37 °C for 2 h. After being washed with PBS (20 mM, pH 7.2) the substrates were immersed into 1% (v/v %) glutaraldehyde at 4 °C for 60 min to fix the adhered platelets. The samples were air-dried and sputter-coated with gold (Jeol JFC-1600 auto fine coater) prior to observation under a scanning electron microscope (Jeol JSM-5600LV).

The microchip electrophoresis of proteins was carried out using a laser-induced fluorescence (LIF) detection system and

Scheme 1. Synthesis Route of Poly(MPC-co-BMA)



the setup for data acquisition, which were home-built according to standard research systems. The sampling rate for data collection was 20 Hz. Voltages to reservoirs adjustable in the range of 0–5 kV were provided by the multichannel CDY-500L microchip high-voltage power supply (Instrument Graduate School of Shandong Province Chemistry & Industry Research Institute, Shandong, China). Channel conditioning was performed before separation. The sampling separation mode was similar to that reported previously.^{27,28} Samples were injected electrokinetically at a constant voltage of 600 V at the positive side for a fixed period of time. All separation experiments were carried out with an applied voltage of 1.0 kV.

Safety Considerations. The electrophoresis used high voltage and special care should be taken when handling the electrophoresis electrodes.

RESULTS AND DISCUSSION

Deposition of Poly(MPC-co-BMA) onto the PMMA Surfaces. This study aims at developing a simple protocol for the modification of the PMMA microchannel surface to improve its hydrophilicity, biocompatibility, and resistance to the nonspecific adsorption, making use of microchips in bioassays more convenient. Accordingly, a facile procedure was introduced to deposit a phosphorylcholine-functionalized copolymer synthesized from *n*-butyl methacrylate and 2-methacryloyloxyethyl phosphorylcholine onto the PMMA surface. The synthesis route is shown in Scheme 1 using a radical polymerization technique. PMB is amphiphilic, having two functional domains: hydrophilic MPC units for protein resistance and hydrophobic BMA segments for anchoring onto PMMA surfaces from the solution. As a member of the polyacrylates, poly(butyl methacrylate) (PBMA) has a structure similar to PMMA and is normally adopted as an adhesive in macromolecular research.¹⁰ For the surface adsorption between PBMA and PMMA, the synthesized copolymer of BMA and MPC

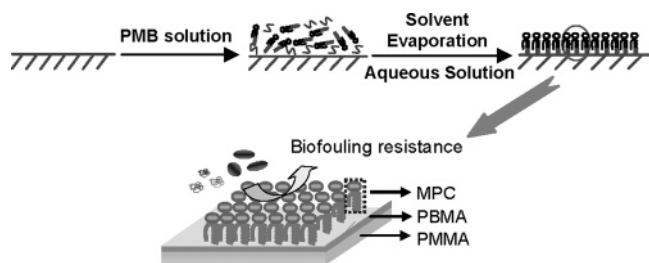
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Scheme 2. Schematic Illustration of Biomolecule Resistance of PMB-Modified Surface



is supposed to be deposited onto the relatively hydrophobic PMMA substrate easily via PBMA serving as the binding site while the hydrophilic MPC moieties are exposed to the outer surface and are oriented toward the aqueous solution due to the phase segregation. Therefore, the PMMA substrate could be effectively covered with the copolymer chains bearing phosphorylcholine groups. The proposed procedure of surface functionalization is described in Scheme 2.

The PMB-deposited layer and certain chemical elements on the PMMA surfaces have been characterized by XPS measurements. Figure 1 shows the XPS spectra recorded from the modified and native substrates. For the PMB-modified surface, six main peaks, belonging to phosphorus (P_{2s}), phosphorus (P_{2p}), oxygen (O_{KLL}), oxygen (O_{1s}), carbon (C_{1s}), and nitrogen (N_{1s}), were identified with the molar ratios C 68.72%, O 27.45%, N 1.56%, and P 2.26%, respectively (Figure 1b). According to the above results and the chemical formula of PMB, $(C_{11}H_{22}O_6NP)_m - (C_8H_{14}O_2)_n$, the molar composition of the two monomers on the surface was calculated as m/n of $\sim 1.4:1$, larger than the value calculated from theoretical prescription and element analysis ($\sim 0.4:1$) of the copolymer, indicating that the outside superficial layer contained a higher amount of MPC domains. With the affinity between BMA segments and PMMA substrate, rearrangement of PMB copolymer molecules might occur on the surface, which results in the enrichment of MPC moieties posing toward the exterior surface.

Surface Properties of PMB-Modified Microchip. Since the nonspecific adsorption is often driven by the hydrophobic interaction between biomolecules and polymer surface, sensor performance could be improved by reducing the hydrophobic interaction through surface modifications. PMB possessing both hydrophilic and hydrophobic components, its rearrangement on the PMMA surface in aqueous solution could cause an obvious change in the surface region. The static contact angle for the PMB-coated PMMA surface was measured to be $\sim 43^\circ$, while the value for untreated substrate was $\sim 72^\circ$.¹² The decrease in contact angle after modification indicates that the distinct change in wettability and surface chemistry of PMMA has taken place. This PMB-coated hydrophilic microchannel, easier to be filled, demonstrated improved compatibility with aqueous solution.

To verify the presentation of relevant chemical groups on the chip surface, FT-IR spectra of untreated and modified PMMA surfaces were investigated as shown in Figure 2. The spectrum of native PMMA substrate correlated well with the literature.²⁹

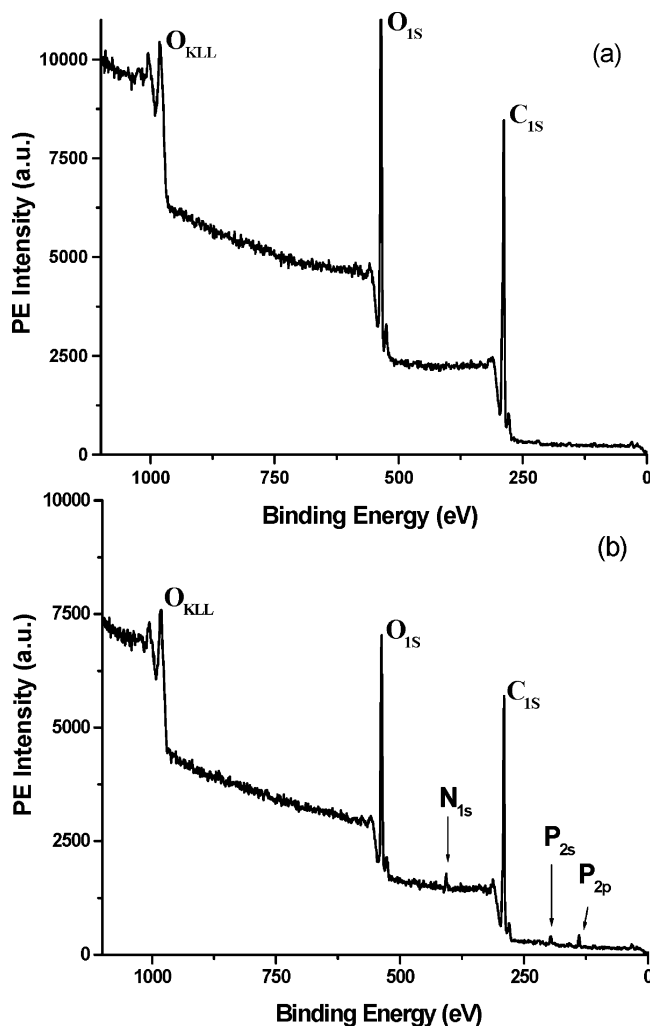


Figure 1. XPS spectra of (a) the untreated and (b) PMB-modified PMMA substrates.

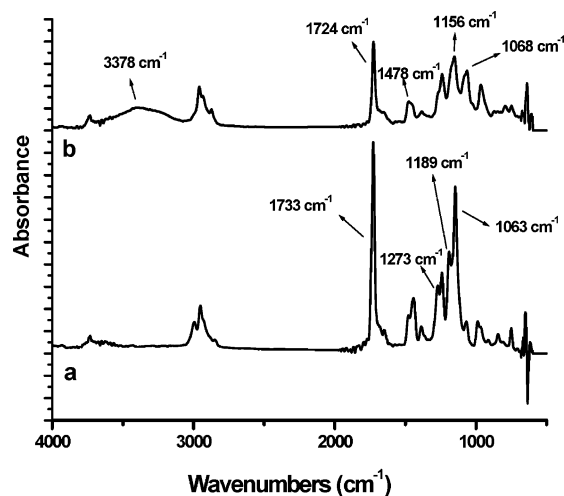


Figure 2. FT-IR spectra of (a) untreated and (b) PMB-modified PMMA substrates.

The prominent band was the carbonyl stretch, $\nu(C=O)$, at $\sim 1733\text{ cm}^{-1}$. This position was characteristic of methyl esters, particularly of those found for the films of PMMA. The remaining vibration bands observed were characteristic of the alkane and ester moieties present in PMMA. In the FT-IR spectrum of PMB-

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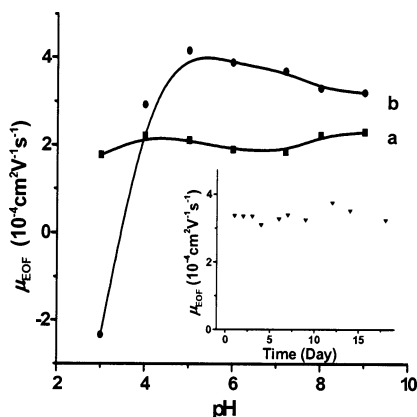


Figure 3. Influence of pH on the electroosmotic mobility of (a) native PMMA and (b) PMB-modified PMMA microchannels. Inlet figure is the stability of μ_{EOF} for PMB-coated PMMA microchannels.

modified PMMA substrate, new absorption peaks at around 1240 and 1068 cm^{-1} were observed. The peak at 1240 cm^{-1} was identified as O–P–O[−] antisymmetric stretching in MPC units, and the peak at 1156 cm^{-1} was from the overlap of C–O–C symmetric stretching from ester groups and C–O stretching from free carboxyl groups. In addition, a broad band centered at ~ 3378 cm^{-1} was present and was tentatively assigned to the $\nu(\text{O–H})$ absorption possibly associated with the H₂O adsorbed onto the MPC hydrophilic domain. FT-IR spectra of native PMMA displayed no absorption bands between 3600 and 3100 cm^{-1} . The spectroscopic results confirmed that PMB had been successfully deposited onto the PMMA substrate by the anchoring of PBMA segments.

The fluid behavior in microfluidic systems is dominated by the surface properties. Finding ways to functionalize the surfaces of polymer microchannels remains a challenge but offers great promise for modulating the electroosmotic mobility and improving the performance of microfluidic devices. The electroosmotic mobility values as a function of pH for the native and PMB-modified microchannels were measured as shown in Figure 3. Obviously, the resulting EOF values in PMB-modified channel changed from -2.3×10^{-4} to $4.6 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ over a pH range of 3.0–9.0. The EOF was reversed between pH 3 and 4 in the case of the PMB-modified PMMA channel perhaps due to the pK_a of the ionizable groups on MPC-modified surfaces. At low pH, EOF was negative and reaching a value of $-2.3 \times 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ at pH 3.0, while the EOF in native PMMA channel was independent of solution pH. The EOF in PMB-modified channels was higher than in native ones under the same electric field at neutral pH, which could be interpreted in terms of the available surface charge. On the other hand, the coating stability over extended periods of time is a general concern.¹⁵ During more than a two-week storage, no obvious EOF value changes were observed on the PMB-modified microfluidic chips, indicating that such surface functionalization coating was stable and reproducible (Figure 3 inset).

Characterization of Biofouling Resistance and Protein Electrophoresis on PMB-Modified Microchips. Fouling can occur on the hydrophobic substrates such as PMMA via hydrophobic interactions, and nonspecific adsorption is the first event in biological analysis. One way to overcome fouling at the

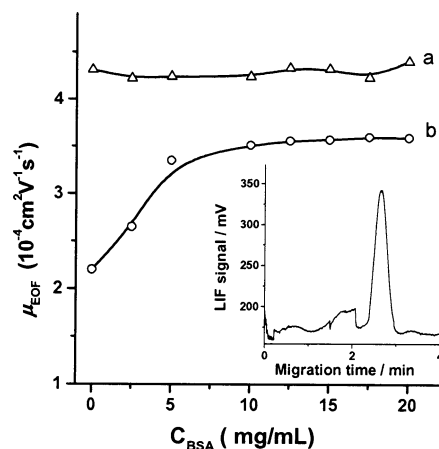


Figure 4. Stability of μ_{EOF} on (a) PMB-modified and (b) untreated PMMA microchannels for adsorption of certain concentrations of BSA. Inset figure is electrophoresis of BSA at 50 $\mu\text{g/mL}$ on PMB-modified microchip.

material–sample interface is to modify the surface of the material.¹⁵ MPC, a monomer containing phosphorylcholine headgroups, exhibiting a property that resists nonspecific interaction with plasma proteins and cells, has been developed as an attractive alternative biomimetic in biomembrane structures or phospholipid analogues.³⁰ Here we demonstrate that incorporation of phosphorylcholine groups onto the microchip surface is an effective method to reduce biofouling.

Various experiments were carried out to determine how the PMB coatings influence the adsorption of biologically relevant components onto the PMMA surface. FITC–BSA was selected as a reference compound to evaluate the effect of the PMB-modified PMMA layer for nonspecific adsorption. FITC–BSA was introduced into the untreated and PMB-modified microchannel for 2 h and then rinsed with running water for 30 min. Confocal fluorescence images of the microchannels were performed with the excitation source of 488 nm. The results indicated that FITC-labeled BSA adsorbed strongly onto the surfaces of the untreated PMMA channels. In contrast, the adsorption of FITC–BSA was significantly minimized on the modified channel surface as shown in Figure S1 (in Supporting Information).

Another result of nonspecific adsorption on the microchannel surface is that the ζ potential might be altered, which could affect the stability and reproducibility in analysis. Electroosmotic mobility values versus the adsorption of BSA are presented in Figure 4. It is shown that EOF values on PMB-derived PMMA microchannels before and after BSA adsorption are more stable than those of untreated ones, further indicating that the PMB-coated surface is more fouling-resistant. The symmetry in electrophoresis peak of BSA observed on the modified microchip (Figure 4 inset) indicates the homogeneity in the ζ potential, attributed to the uniformity of the PMB coating.³¹ For the unmodified microchannels, the EOF values changed rapidly with BSA in the low concentration range. At higher concentrations, the values leveled off. This is the so-called prefouling procedure, a usual option for

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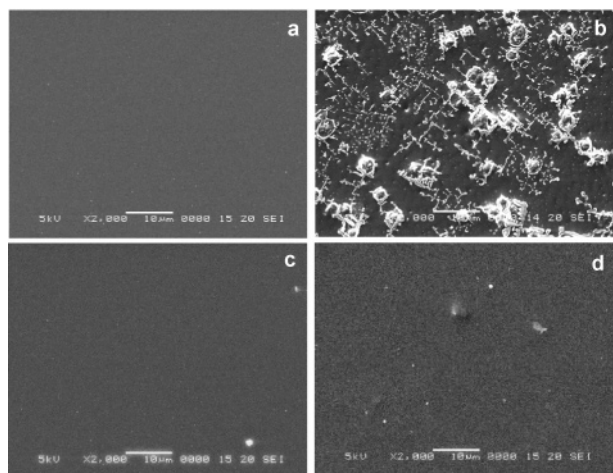


Figure 5. SEM images of (a) native PMMA and (c) PMB-modified PMMA substrates, and their adsorption of platelet (b, d) after exposure in healthy rabbit plasma.

glass or polymer devices before use. The surfaces that would normally adsorb analytes from samples are covered with a coat of inexpensive protein such as BSA to change EOF or reduce nonspecific adsorption.¹⁵ Here this procedure could be avoided by the application of microchips based on PMB modification.

MPC is amphiphilic and contains the phosphorylcholine (PC) headgroup that has been shown to have strong affinity to water as a result of its zwitterionic structure. A possibility for the enhanced protein resistance in the PMB-modified PMMA microchip might be related to the extreme hydrophilicity of the PC headgroups contained within the PMB coating. When hydrophilic polymers are in contact with water, they can hydrate and undergo a surface rearrangement.²⁰ Water contact angle of the PMB-modified PMMA surface is $\sim 43^\circ$ and thus supports the hypothesis that the excellent protein resistance of these surfaces might be due to the rearrangement of their PC headgroups in water.

Furthermore, interference from background proteins and other biological samples could limit microchip-based bioanalysis in complex media, such as blood serum or plasma, more complicated than the standard analytical systems and buffers. In such a practical condition, nonspecific adsorption can severely contaminate microchannel surfaces or block bioactive sites resulting in separation efficiency being reduced and background noise increased. The native and modified PMMA substrates were tested after exposure to the human serum and rabbit platelet-rich plasma samples, respectively. SEM images and XPS results showed that the adsorption of biorelated samples and platelets on the PMB-coated PMMA surfaces were obviously depressed compared with the untreated ones (Figure 5 and Figure S2 in Supporting Information). The results coincide with the previous research that the surface covered with the MPC-containing copolymers could alleviate protein adsorption and cell adhesion.^{18,20} It is proposed that phosphorylcholine groups on the surface adsorb phospholipids rapidly from blood due to their similar structures and then possibly rearrange to construct a biomimetic membrane that repels protein and cells.^{20,32} Compared with the untreated channel, MPC-associated H_2O would work as

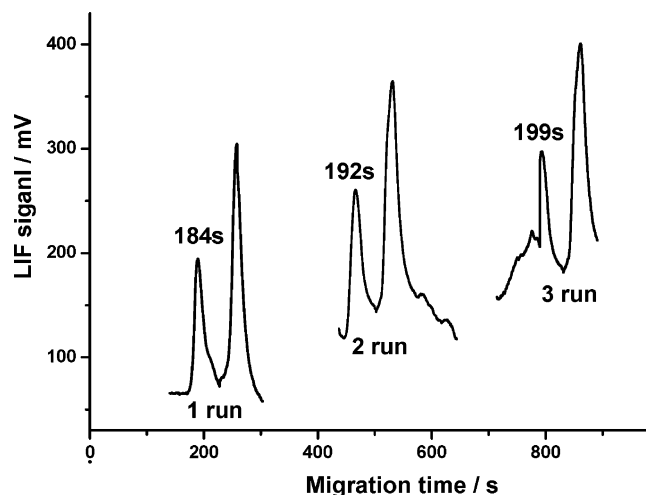


Figure 6. Electropherograms of separation of $0.35 \mu\text{M}$ FITC-lysozyme and $0.19 \mu\text{M}$ FITC-BSA on PMB-modified microchip. Running buffer solution: 10 mM Tris-HCl ($\text{pH } 8.8$). Field strength for separation: 250 V/cm . The first peak corresponded to FITC-lysozyme, and the second one to FITC-BSA.

a repelling force against nonspecific interaction on the wall of PMB-coated channel. The behavior of the reduced biofouling surfaces would make the microchip a useful platform to expediently detect biomolecules in complex matrixes, an important tool in diagnosing for clinical applications and large-scale separation of biological samples.

The electrophoresis of proteins was exemplified here to explore the purpose of the microchip modification scheme. Figure 6 shows the fluorescence peaks of FITC-BSA and FITC-lysozyme during the continuing injections on the PMB-modified PMMA microchip. They were well analyzed with the theoretical plates about 11 200 and 20 000 plates/m, respectively. Recognizing the favorable minimal adhesion characteristics of the PMB-modified microchip surface, electrophoresis separation of proteins was achieved with good reproducibility. In the control experiment, nearly no obvious LIF signal was observed in the first injection on the native PMMA microchip; in the following injections, the broad and skew peaks were detected with longer elution time and poor reproducibility, which might be attributed to the severe surface adsorption of the untreated PMMA channel (Figure S3 in Supporting Information). When the adsorption happens, the resultant inhomogeneities in ζ potential cause band broadening due to differing electroosmotic flow velocities along the varied surface status at different position in channels.^{31,33} Considering that the control of surface properties is important in achieving efficient separation and sensitive biosensing while minimizing nonspecific interaction, such chip modification protocol could be widely used in biological analysis via the phospholipid copolymer functionalization.

CONCLUSIONS

A simple phosphorylcholine-functionalized surface has been achieved within a PMMA microfluidic channel through the modification of a copolymer of PMB. The incorporation of phosphorylcholine groups onto polymer substrates might be an

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effective method for the biocompatible surface design to reduce biofouling and host responses. One of the unique features of this method is to generate a hydrophilic and antifouling surface with stable electroosmotic flow compared with the native PMMA substrate, an important issue to make polymer microchips in complex biological matrixes more straightforward to use. On account that bioactive components could be constructed onto the phospholipid polymer backbone through the modification of special functional groups, it would provide a good bioconjugate environment for selective recognition of proteins, peptides, and cells of interest. In terms of achieving highly efficient separation and analysis while minimizing biofouling from blood serum and plasma with the microchannel surfaces, the fabrication of PMMA microchips with MPC moiety coating could provide a platform

for clinical assays, pharmaceutical screening, affinity biosensing, and proteomics applications.

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SUPPORTING INFORMATION AVAILABLE

Additional information as noted in text. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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