Journal of Metals, Materials and Minerals. Vol.17 No.2 pp.67-74, 2007

Surface Modification of Microfluidic Devices

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Received Sept. 19, 2007
Accepted Nov. 5, 2007

Abstract

Microfluidic is a multidisciplinary which encompasses the fields of physics, chemistry, nanotechnology, engineering, and biotechnology. It has been developed extensively for many applications such as handling biological entities such as DNA separation, immunoassay, cell sorting, biosensors, and enzymatic assays due to the potential offered by miniaturizing, high throughput of analysis, low cost of fabrication, multiplex functionality and portability. The surface modification of microfluidic devices has also been a major focus in research to help to enhance their efficiency. There is a variety of surface modification methods and in this paper we reviews and presents an overview of the surface modification techniques of microfluidic devices.

Introduction

The recent advances in fabrication technology have led to reduction in size of devices by several orders of magnitude. One area that benefits in particular from this trend is the area of microfluidic system. Microfluidic devices can be used to obtain a variety of interesting application such as DNA and protein separation(1), immunoassay(2), and biosensors. Microfluidic devices have potential in: a reduction of cost per analysis, a decreasing of sample amount, and shorter analysis time. There are many reasons for surface modification of microfluidic devices. The two main reasons are – to control electro-osmotic flow (EOF) and to reduce analyte-wall interaction. Hence, the surface modification is of great importance for enhancing the efficiency of these devices

Microfluidic Devices

Microfluidic concerns the handling and manipulation of minute amounts of fluids in micro, nano or even pico liters level. Microfluidic device can be identified by the fact that it has one or more channels with dimension in micrometer or nanometer, microfluidic devive is shown in Figure 1. Microfluidic devices are used as new tools for separating variety of compounds. The basic principles of capillary electrophoresis (CE) are used in microfluidic systems. In microfluidic devices, the fluid is driven by applying either an electric potential or an external pressure. However, applying voltage is a popular method in driven fluid in separation due to the flat flow profile. When the voltage is applied, the fluid migrated due to the Electrophoretic mobility and electro-osmotic flow.

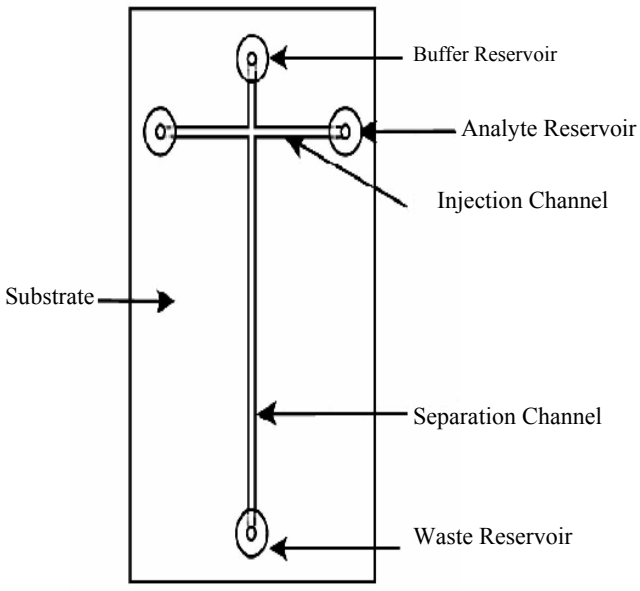

Figure 1. Microfluidic devices.

Electrophoretic Mobility[3]

The principle of electrophoresis refers to the migration of charged electrical species when dissolved, or suspended, in an electrolyte through which an electric current is passed. Cations migrate toward the negatively charged electrode (cathode) and anions are attracted towards the positively charged electrode (anode). Therefore, separation by electrophoresis relies on differences in the speed of migration (migration velocity) of ions or solutes. Ion migration velocity can be expressed as: $\nu = \mu_e E$ Where ν is ion migration velocity (ms^{-1}), μ_e is electrophoretic mobility ($m^2v^{-1}s^{-1}$) and E is electric field strength ($V\ m^{-1}$).

The electric field strength is a function of the applied voltage divided by the total capillary length.

$$E = V/L \qquad (1)$$

Electrophoretic mobility is a factor that indicates how fast a given ion or solute may move through a given medium (such as a buffer solution). Electrophoretic mobility is given by

$$\mu_e = \frac{q}{6\pi\eta r} \qquad (2)$$

Where q is the charge of the ionized solute, η is the buffer viscosity, and r is the ion radius. From equation 2 it can be seen that the migration rates depend on charge-to-size ratio. A smaller ion will migrate faster than a larger ion of the same charge. An ion with a higher charge will migrate faster than one with a lower charge, if they are the same size. Electrophoretic mobility is probably the most important concept to understand in electrophoresis. This is because electrophoretic mobility is characteristic property for any given ion or solute and will always be constant. It is the defining factor that decides migration velocities. Different types of ions or solutes have diverse electrophoretic motilities. So, they also have various migration velocities at the same electric field strength. From difference in electrophoretic mobility, it is possible to separate mixtures of various ions and solutes by using electrophoresis.

Electroosmotic Flow (EOF)[38]

In capillary electrophoresis, the buffer solution usually also moves through the capillary under the influence of an electric field. This phenomenon is termed electroosmotic flow. When a buffer is placed inside a capillary, the inner surface of a capillary acquires a charge. This may be due to ionization of the capillary surface or adsorption of ions from the buffer onto the capillary. An uncoated fused-silica, the surface silanol (Si-OH) groups are ionized to negatively charged silanoate (Si-O-) groups at pH above three. The silanoate groups attract cations from the buffer, which form an inner layer of cations at the capillary wall. These cations are not sufficient density to neutralize all the negative charges, then, outer layer of cations forms. The inner layer is tightly held by the Si-O- group, which is referred to as the rigid layer. The outer layer of cations is not tightly held because it is further away from the silanoate groups, and it is referred to as the diffused layer, as represented in Figure 2.

When a voltage is applied across the capillary, cations in the diffuse layer are free to migrate towards the cathode, carrying the bulk solution with them. The result is a net flow in the direction of the cathode.

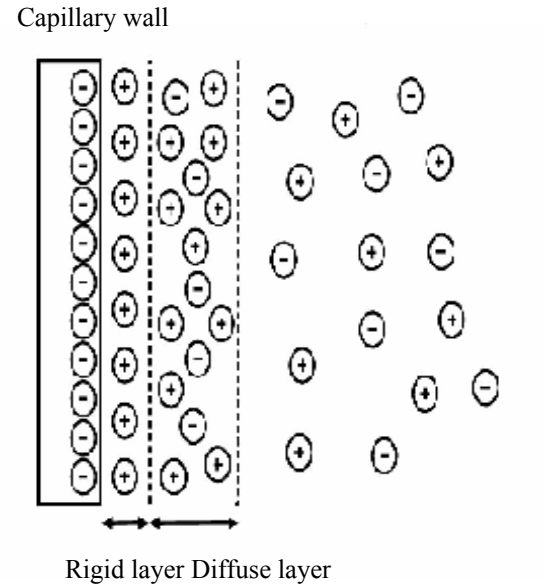

Figure 2. Schematic of double electric layer.

Electroosmotic flow has a relatively flat profile, Figure 3(a), compared to pump or laminar flow, Figure 3(b). The advantage of flat flow profile is that all of the solute molecules experience the same velocity component caused by electroosmotic flow regardless of their cross-sectional position in the capillary. They were elute as narrow bands giving narrow peaks of high efficiency, Figure 3(c). On the contrary, the solutes move through a tube under the influence of

pump flow, where the solutes in the center of the tube move faster than those nearer the wall. The result of this flow profile is relatively broad peaks, Figure 3(d).

Net Flow

In normal mode, the direction of electroosmotic flow is towards the negatively charged cathode, which means the buffer flow from the source vial, through the channel.

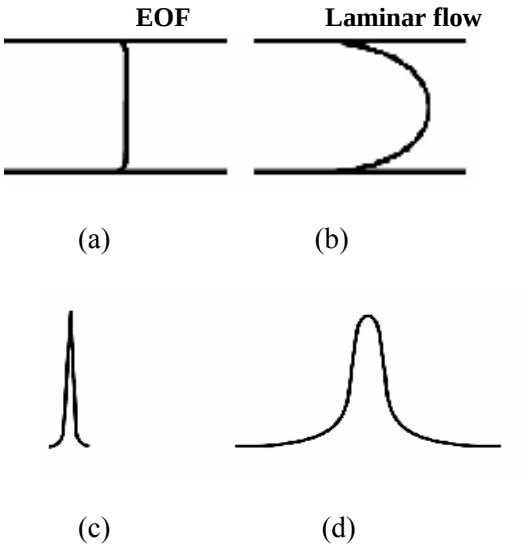

Figure 3. (a) Flat profile (b) Laminar profile (c) Peak from flat profile (d) Peak from laminar profile.

Charged solute molecules are separated due to differences in their electrophoretic mobilities, and will tend to migrate toward the electrode that has an opposite charge from the solute, Figure 4 (a). Negatively charged anions are attracted to the positively charged anode and, with no electroosmotic flow, would simply migrate into the source vial without passing through the capillary and detector. The electroosmotic flow of buffer is usually greater than the electrophoretic mobilities of negatively charged solutes so they are carried along with the buffer toward the detector. The electroosmotic flow can be strong enough to carry even small triply charged anions toward the negative electrode. Since anionic solutes are pulled back toward the source vial by the positive charge of anode, they move at the rate that is lower than electroosmotic flow. Neutral solutes are not influenced by electrophoretic mobilities, and therefore move through the capillary at the same rate as the electroosmotic flow. Positively charged solutes migrate toward the negative electrode under the influence of both electrophoretic mobilities and electroosmotic flow, and so move faster than the electroosmotic flow. It can be seen in Figure 4.

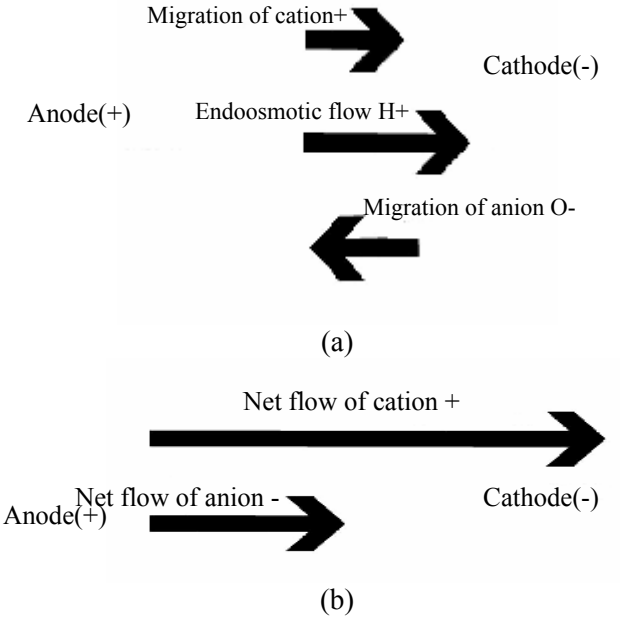

Figure 4. (a) Direction of migration ions (b) Net flow

Surface Modification

The property of surface is of great importance for chip-based microfluidic devices. Motivations of surface manipulation are similar to that of surface modification in classical CE.

There are many procedures and techniques for surface modification of microfluidic devices. However, the main of modification focused on the improved electrophoretic separation by reducing analyte-wall interactions and manipulation of electroosmosis.

It is well known that in classical CE the performance as well as the reproducibility of electrophoretic separation can be considerably improved by an appropriate surface modification. Rigid inorganic substrates such as glass, silicon, and quartz are used for microfluidic devices. Alternately, polymeric materials can also be used for fabricating microfluidic devices. In application area with a possibility of cross contamination, disposable microfluidic devices can be fabricated by using polymeric materials. Commodity polymeric materials are less expensive for large-scale manufacturing of microfluidic devices, and plastic machining technologies, including injection molding, casting, and embossing, are more versatile

and accessible. Unfortunately the surfaces of many polymeric and inorganic materials are not compatible with biological samples. Hydrophobic, electrostatic, or their interaction attracts some analytes to the surface, leading to sample adsorption and sample loss and analytical irreproducibility. Furthermore, the adsorption of some organic molecules and biomolecules to hydrophobic channel walls, which leads to an unstable EOF, has been identified as a major problem in the development of microfluidic devices in plastic materials. Therefore, it is often necessary to modify the microfluidic surface as part of the fabrication protocol. A variety of surface modification methods have been proposed for example, plasma treatment, UV grafting, surfactant coating, and self assembled thin layer. However, different procedures and techniques for surface modification of microfluidic devices are reviewed but have to select the appropriate techniques for each application. This review presents overview of surface modification techniques.

Plasma Treatment

Plasma is the most common method for modifying the surface in microfluidic systems due to the fast process. Many different types of gas-plasma reported such as air[4], oxygen[5], UV-ozone[6], H_2O[7-9] and ammonia[10] modify the polymer surface. Plasma modification processes generate new chemical properties on the polymer surface due to chemical reactions and physical reactions of surface with active gas phase species. Different molecules that display different properties can be immobilized onto the surface results in different surface properties from underlying bluk polymer.

Long and co-workers[11] reported the water-vapor plasma-based surface activation for trichlorosilane modification of poly(methyl methacrylate) (PMMA). This method involves two separation steps. First, surface activation of PMMA with water-vapor plasma introduced surface hydroxylation. Second, treatment of the plasma-treated PMMA with a substituted trichlorosilane solution to the functional surface layer. The effect of water-vapor plasma treatment was observed. With increasing plasma power, a decrease in contact angle of the PMMA surface was observed, consistent with increasing hydrophilicity from surface hydroxylation. The surface after plasma treatment was found to be stable for at least 4 h before hydrophobic recovery was observed, but all samples were utilized in less than 1 h after plasma exposure. Liu and co-workers[12] reported the modification of PMMA surface by using oxygen plasma with 2-Bromoisobutyryl bromide. Then poly (ethylene glycol) (PEG) was grafted to surface of PMMA substrates using atom-transfer radical polymerization, which reduced electroosmotic flow and nonspecific adsorption of protein on PMMA surface. The result showed fast, reproducible and efficient separations of protein and peptides on PEG-grafted PMMA capillary electrophoresis microchips.[12] Not only PMMA surface but also PDMS surface have been modified by plasma. In order to modify wetting properties many researchers reported modification method of PDMS surface by using plasma with the different kinds of polymers: poly (vinyl alcohol)[13], 2-hydroxyethyl methacrylate (HEMA)[14] and acrylic acid.[15]

UV grafting

UV polymer grafting is a one of the technique for modifying surface of microfluidic devices, which is similar to plasma technique. Different monomers such as acrylic acid, acrylamide, dimethylacrylamide (DMA), 2-hydroxyethyl acrylate and PEG-monomethoxyl acrylate were grafted onto polymer surface to increase hydrophilic properties.[16] For all monomers grafting occurred only in the presence of benzyl alcohol, which is thought to act as a chain-transfer agent. The monomers, Acrylic acid (AA), acrylamide (AM), dimethylacrylamide (DMA), 2-hydroxylethyl acrylate (HEA) and poly(ethylene glycol) monomethoxyl acrylate (PEG), were also selected based on their likely ease of attachment, past usage in biocompatible device, and display of different functional groups. All grafted surfaces exhibited a decrease in the contact angle of water compared to that of native PDMS.[16] However this method, only disassembled channels could be coated. Hu and co-workers[17] demonstrated a new method that used benzophenone as the photoinitiator. It was absorbed onto PDMS followed by UV-grafting (photografting) of monomer. After addition of a variety of monomer solutions (acrylic acid), poly(ethylene glycol) monomethoxyl acrylate or poly(ethylene glycol) diacrylate and illumination with UV light, a stable, covalently attached surface coating formed in the microchannels with distinct surface properties. The modified surfaces were enable to separate the substrate peptide, which was not separated on native or oxidized PDMS surface. Ebara and co-workers[18]

reported the smart microfluidic chips. Their channel were modified by UV-mediated graft polymerization of the temperature-responsive polymers are (poly[N-isopropyl acrylamide] or PNIPAAm), the temperature- and pH-responsive copolymers are (P[NIPAAm-co-acrylic acid (AAc)]), and a non-fouling hydrogel (polyethylene glycol diacrylate, or PEGDA). The grafting of PNIPAAm and PEGDA made the surface more hydrophilic. PEGDA grafting resulted in a more hydrophilic surface due to the nature of PEG. PNIPAAm-grafted surfaces showed large changes in contact angles in response to temperature change. P(NIPAAm-co-AAc) was also grafted onto PDMS surface for a temperature- and pH-sensitive polymer. So, the smart polymer surfaces prepared by this method demonstrated large surface wettability changes in response to temperature and/or pH. In addition, PMMA and polycarbonate(PC)[19] were modified surface by UV graft polymerization, which ozone (O_3) treatment was used to oxidize the polymer surfaces. A methacrylate functionality is introduced by reacting the oxidized surfaces by 3-methacryloxypropyltrimethoxysilane. Then polyacrylamide was UV grafted onto the chemically modified model surfaces. The results presented that the UV/O_3/silane pretreatment followed by UV surface grafting of polyacrylamide onto the microchannel walls appreciably reduce mechanical breakdown at the walls and dislodgment of the gel plug of fluid sample by electroosmotic forces.

Polymer Monolayer

One straightforward method to generate modified surfaces is by using self assembled monolayer. Deposition of self-assembled monolayer is amenable to implementation in microfluidics devices, since it only requires the flow of a solution or a gas stream of adsorbate molecules through the channels. Self assembled monolayers have been used in glass microfluidics networks to engineer surface properties with the aim of controlling liquid motions, confining and aligning of biological macromolecules and liquid crystals, stabilizing the liquid interface in an extraction system, controlling electroosmotic flow, preventing cell adhesion and protein adsorption.[20]

Mela and co-workers[21] built a sensing system by coating the surface with a self-assembled monolayer of a Rhodamine B dye in a glass micro channel and subsequently binding a fluorescent sensing molecule to the monolayer. Rhodamine B-derivatized monolayer was confined to the walls of glass-fabricated micro channels and was able to switch between a fluorescent and a non-fluorescent state reversibly, depending on the acidity of the organic solution inside the micro channel. Glass and PDMS were employed to attach Oregon Green 514 monolayer.[20] This system was able to sense the pH of aqueous solutions that flowed through the fluidics network by a change in fluorescent properties.

A positively charged poly(allylamine hydrochloride) (PAH) monolayer was coated onto a negatively charged silicon oxide surface by electrostatic self-assembly (ESA), which was shown in study of Hau.[21] The PAH was covalently conjugated with fluorescein isothiocyanate (FITC), at pH 6, which the amino functionality of the PAH was protonated and positively charged. FITC was a fluorescent molecule and would later be used to visualize PAH-coated areas. Only areas coated with FITC labeled PAH would emit light with intensity proportional to the amount of PAH coating material when excited. Uncoated areas would remain dark. This greatly facilitates the design and control of micro-flow patterns. The positively charged PAH surface coating has a thickness of about 2 nm and shows long-term stability.

Many different types of monolayer on PMMA microfluidic device have been shown in the literatures such as n-dodecyl-β-D-maltoside[23] and cationic starch derivatives.[23] Coating cationic starch derivatives and n-dodecyl-β-D-maltoside monolayer have been developed for suppression of analyte adsorption.[22,23] Modification of PDMS surface with different type of monolayer was shown such as phospholipids polymer[24], poly (acrylic acid)[25] and polyacrylamide.[26] Phospholipids polymer coating, which was dipping technique, showed to reduce unfavorable protein adsorption.[24] The surface modification of PDMS was modified with polyacrylamide through atom transfer radical polymerization. A fast separation of lysozyme and cytochrome c in 35 s was demonstrated.[26]

Polymer Multilayer

The use of polyelectrolyte mutilayers (PEMs) has been shown to be simple, reproducible method for surface modification. The PEMs surface modification was obtained by coating with

alternating layer of positively and negatively charged polyelectrolytes on any substrate (a charged surface). The use of PEMs to alter the functionalities of a surface-charged region exploited to control the flow direction and electroosmotic mobility within plastic and glass microfluidic system.[27-29] Barker and co-workers[30] reported the using PEMs for control of flow direction. Deposition of alternating layers of poly(allylamine hydrochloride) (PAH) and poly(styrene sulfonate) (PSS) on polystyrene (PS) substrate and a cationic layer of polybrene (PB) and an anionic layer of dextran sulfate(DS) on poly(dimethylsiloxane) (PDMS) channel were done for observed controlling flow direction. Sui and co-workers[29], fused silica capillaries were coated with multilayers made from poly(styrene sulfonate), PSS, as a permanently charged negative polyelectrolyte, and a mixture of poly(diallyldimethylammonium chloride), PDAD, and a random copolymer of diallyldimethylammonium and acrylic acid, PDAD-co-PAA. It shown that was controlled by the pH. Then, the pH induced switching of surface charge was minimized by diluting the pH-responsive polyelectrolyte with permanently charged polymer. Poly(diallyldimethylammonium chloride) (PDAD) is commonly used as the polycationic due to the property of strong cationic polyelectrolyte, so it can be tightly absorbed on the polymer surface by ionic interaction. Although the PEMs are easily fabricated but many factors effected to the efficiency of electroosmotic mobility such as ionic strength of polyelectrolyte, and pH. PEMs of poly(allylamine hydrochloride) and poly(styrene sulfonate) on PS and PETG microchannels substrate materials were reported that showed excellent wettability, allowing facile filling of channels. The PEMs produced reproducible results and robust enough to withstand long-term storage.[30] Poly (dimethylsiloxane) (PDMS) is a biomaterial that presents serious surface instability but various approaches have been used for modify PDMS surface. Layer-by-layer electrostatic self-assembly of PEMs is one of the good procedures to modify surface. Makamba and co-workers[31] reported using electrostatic self-assembly of polyethyleneimine (PEI) and poly(acrylic acid) (PAA) on top of a hydrolyzed poly(styrene-alt-maleic anhydride) (PSMA) base layer absorbed on PDMS. The polyelectrolyte layers were cross-linked by carbodiimide coupling and covalent attachment of poly(ethylene glycol) (PEG) chains. The PEMs produced stable, hydrophilic, protein-resistant coating, which resisted hydrophobicity recovery in air.[31] Liu and co-workers[32] reported modification of PET microchip by layer-by-layer assembly technique with alternating layers of chitosan (CS) and hyaluronic acid (HA) for trypsin immobilization in multilayer thin film, which was improved by the wetting of microchannel walls. In addition, Quinn and co-workers[33] improved wettability by using polyelectrolyte (PE) multilayer films prepared from poly(styrene sulfonate)-poly (acrylic acid) (PSS-PAA) blends, deposited in alternation with poly(allylamine hydrochloride) (PAH) on glass, gold, and silicon substrates. PEI was used as a precursor layer to homogenously coated the substrates with positive charge. In addition, PEI and PAH were the polyions used as the top layer cellular adhesion material.[34] Moreover many different types of PEM have been cited in the literatures such as polyelectrolyte multilayers of (PSS/PAH)(n)[35], PDAD/poly (sodium N-undecanoyl-(L)-leucylvalinate) [poly(L-SUIA)][36,37] and cationic poly(L-lysine)/anionic poly(L-SUIA). It can be concluded that the facile technique of LbL deposition of PEMs is a convenient and accurate mean of surface modification carried by simply altering the composition of the solutions on any substrates.

Conclusion

Microfluidic devices have immense application potential and present a bright future in the era of high technology. Surface modification techniques improve the efficiency of the microfluidic devices. Although variety of techniques have been developed for these modifications many more possibilities still remain to be explored making it a promising field for research scientists.

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