Extending the potential of Polydimethylsiloxane microchips

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Abstract

The search for microchannel wall modifications of simple use, that provide the desired functionality while the nonspecific adsorption is reduced to a minimum, has allowed the development of new wall coatings. Specifically, the study of modifications that will enable to create robust microfluidic devices for the direct analysis of complex samples in which no sample pretreatment is required, are becoming a very important field of research, since they will allow microfluidic devices to become the analytical tool of choice for pharmaceutical and bioanalytical research fields.

Resumen

La búsqueda de modificaciones a superficies de microcanales de fácil empleo, que provean la funcionalidad deseada y a la vez reduzcan la adsorción no específica, ha permitido el desarrollo de nuevos recubrimientos superficiales. Específicamente, el estudio de aquellas modificaciones que permitan la creación de dispositivos de microfluidos para el análisis directo de muestras complejas, donde no se necesite tratamientos preliminares, se están convirtiendo en un campo muy importante de investigación, puesto que el dispositivo de microfluidos constituirá una importante herramienta de selección para la investigación en estudios farmacéuticos y bioanalíticos.

Introduction:

Miniaturization of analytical instruments utilizing microfabrication technology has attracted a wide interest in analytical chemistry for the past 15 years. The concepts of «Micro-Total Analytical Systems» (mTAS) and «Lab-on-a-Chip» (LOC) refer to develop integrated micro devices which are able to achieve complete analysis cycles (e.g. sample pretreatment and analysis) in a small space.[1]

Typical planar analytical microchips can be microfabricated from different substrates: glass, silicon, or polymers ranging in overall size from mm- to cm- scale with structural units (e.g. separation channels, reaction chambers, mixing chambers, etc.) in mm-scale.[2, 3] These microchips are currently used in pharmaceutical and bioanalytical research, and they are especially developed for the fields of proteomics, genomics, clinical diagnostics, and drug discovery.

Glass and quartz are frequently used for fabricating mTAS and LOC devices. They are attractive materials for microfluidic devices due to their excellent optical properties, high insulating properties, and due to their lack of reaction toward a variety of different solvents.[3]

Recently, several scientific groups have been applying polymers as well for building micro devices, since they provide a wider choice in microfabrication techniques, and also because they are more attractive for commercial applications.[3]

The microfluidic devices usually employs electroosmotic pumping for moving analytes and reagents through their channels; therefore, the understanding and total control of electroosmotic flow (EOF) becomes a central parameter for the assessment of the analytical processes and reactions that occur inside the devices.[3]

A fundamental parameter for characterizing the EOF is the Zeta potential (z-potential), as well as the electric double layer (EDL) which generates it (Fig.1). The EOF is produced when an electric field (E) is introduced down the length of an electrolyte-filled microchannel and it induces a net charge in the EDL to migrate, carrying the rest of the fluid by viscosity action.[4]

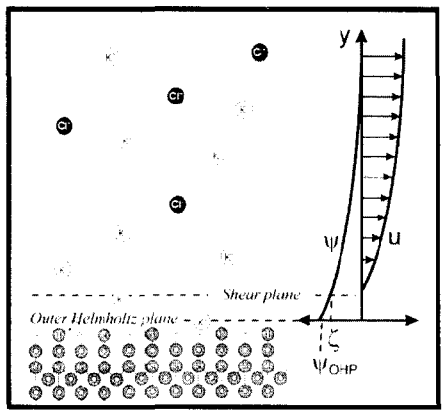

Figura 1. Diagram of the electric double layer.[4]

Since the EDL is normally only a few nanometers thick, the velocity profile in a uniform microchannel becomes uniform as well (with exception of the boundary region inside the EDL). Therefore, this pumping system introduces a minimum amount of band broadening during the analytic process, improving the separation efficiency of the microfluidic device, especially in comparison to microfluidic devices which use pressure-driven flow (Fig.2). [5]

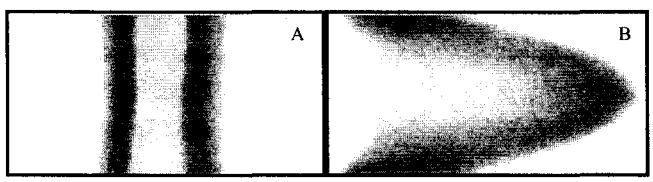

Figure 2. Flow profiles. (A) Electroosmotic flow profile, (B) Pressure driven flow profile.[5]

However, even when using EOF, band broadening can occur if there are any variations in solution conductivity, heterogeneous values of z-potential along the surface, and/or viscosity/permittivity variations of the fluid or of the wall surface. Localized changes of these properties produce local heterogeneities on the flow streamlines (Fig.3), consequently creating eddy migrations which leads to a lower separation resolution (either band broadening or tailing).[4]

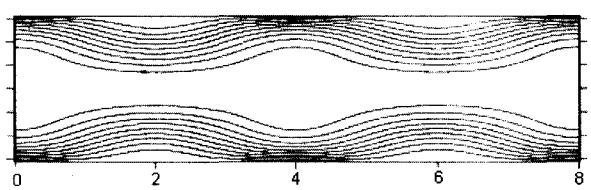

Figure 3. Simulation of flow streamlines produced by sinusoidal variations in the z-potential in direction of the capillary axis $z = z_o[1 + sin(2px)]$.[4]

These variations may happen more often in polymeric-based micro devices where EOF has been seen to vary from vendor-to-vendor and/or device-to-device (as it can be notice in literature). In particular, for those microfluidic systems based on polymers that show low surface charge density (i.e. hydrophobic polymers), since their EOF are often induced by surface charges generated either by unknown sources or by the microfabrication process.

Therefore, internal capillary coatings are applied in order to control the EOF by perfectly matching the z-potential on the microchannel surface.[4] Microfluidic coatings can be separated in two categories: permanent and dynamic coatings (the latter one is usually subdivided in dynamic and semi-dynamic coatings).

Finally, surface modifications are also of great importance in microfluidic technologies to suppress analyte-wall interactions which may lead to nonspecific adsorption of the sample to the wall, and may locally change the z-potential to generate specific mixing zones where axial dispersion can occur, which can cause the introduction of additional functional groups (e.g. stationary phases) or it can immobilize reagents (e.g. antibodies, enzymes, etc.) for improving the overall separation process.[4]

Why is the measurement of complex sample such as blood proteins so difficult in a microfluidic chip?

Microchips offer various possibilities for performing biological assays since they are based on the same principle of capillary electrophoresis (CE), that is, a capillary system to which an electric field is applied. Therefore, most of the applications known to CE could be transferred to microchips.[3]

However, microfabricated instrumentation may not be as robust as expected by researchers and final users, consequently several technical issues must be solved first. For example, the high surface area-to-volume ratio of the microfluidic devices may be a drawback when studying biomolecules (e.g. peptides and proteins), which may be adsorbed on the surface. The adsorption of these biomolecules to the walls of microfluidic devices have a wide range of repercussions, from local changes in z-potential which introduces band broadening (its consequences have been explained before) to the complete clogging of the system.

The interactions of proteins with the surface can be divided in: nonspecific and biospecific. The term nonspecific refers to

general Van der Waals forces, as well as electrostatic interactions (i.e. coulombic interactions), on the other hand, the term biospecific refers to those interactions which are highly specific and rely on a close complementary interaction between protein and surface.[6]

Although, until now the agreement of the mechanism for nonspecific interaction is based on a favorable change of free energy of the system, and a great amount of data have been accumulated by several groups around the world, the specific mechanistic steps behind the nonspecific interactions are not yet totally understood.[6]

In the case of a nonspecific interaction between a protein and a hydrophobic surface, the agreed mechanism is entropically driven and it may be described as follows[6]:

1) Diffusion of the protein to the surface
2) Reversible adsorption on the surface
   a. Removal of the solvatation layer
   b. Removal of water/ion molecules off the surface
   c. Hydrophobic or other interactions between the protein and surface
   d. Structural rearrangements of the protein
   e. Structural rearrangements of the excluded molecules
3) Irreversible de-naturalization of the protein on surface

Process (a)-(c) are responsible for the largest contribution to the overall free energy changes. In addition, the p-p interactions, which can also occur between protein and surface, contribute to the binding enthalpy (e.g. protein and a phenyl-derived surface). Moreover, the change of free energy due to the irreversible adsorption of the protein to the surface will be related to the denaturalization, which itself will be related to the thermodynamic stability of the folded protein.[6]

In this case, the reaction parameters that can influence the proposed mechanism are[6]:

1) The strength of interactions between protein and surface
2) Structure that the protein adopts on the surface
3) Ionic strength and salt/solvent properties

On the contrary, in a nonspecific interaction between a protein and a polar/charged surface, the mechanism is mainly enthalpy driven. In this case, we can consider the same mechanism used for hydrophobic proteins; however, we should consider the following extra interactions[6]:

1) Dipole interactions
2) Ionic interactions
3) Hydrogen bridges

Therefore, the overall effect on the change of free energy of interaction will depend on a balance between electrostatic attraction and repulsion forces (enthalpy).[6]

However, in reality, a single protein can exhibit both biospecific and nonspecific interactions with a surface, for example, protein A can strongly bind to immunoglobulins and also be adsorbed nonspecifically on many surfaces.[7]

Moreover, the nonspecific interactions themselves are far from simple. For example, a protein at a solution with a pH above their pI will show an overall negative charge, these conditions will avoid the protein from being adsorbed on negatively charged surface (due to charge repulsion); nevertheless, the protein may still have sections with a localized positive charge (lysyl or arginyl residues) that can interact with the negatively charged wall.[6]

Therefore, the complexity of the wall-analyte interaction at a molecular level, in particular for the case of proteins, makes then impossible to predict in advance which surface modification will be the most appropriate for each particular application.[6]

The following parts of this review will be focus in one specific polymeric material that is commonly use in microfabrication, which is polydimethylsiloxane or PDMS (Fig 4, courtesy of Mr. Michael Jacobs, Dipl.-physiker).

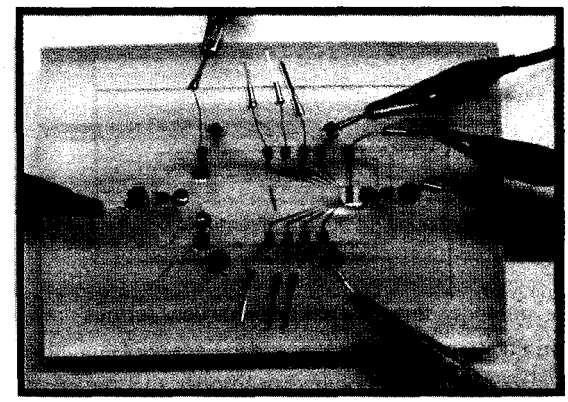

Figure 4. Polydimethysiloxane microfluidic chip. Courtesy of Michael Jacobs, Dipl.-physiker

Citing Doherty et al. [6] «Since polymeric microfluidic devices have tremendous potential as disposable bed-side, or on-site, devices, the development of simple modifications of these polymer microchannel surfaces to regulate EOF and to prevent the adsorption of proteins and other complex biomolecules that would be present in a raw biological sample will be critical.»

Poly(dimethylsiloxane) microfluidic devices

PDMS is one of the most popular polymers for the fabrication of microfluidic chip devices due to its transparency (down to 280 nm), high insulating properties, its inertness toward a variety of different solvents, and due to the microfabrication techniques used with this material, which it is called soft lithography, specifically rapid prototyping and replica molding (Fig.5). [8]

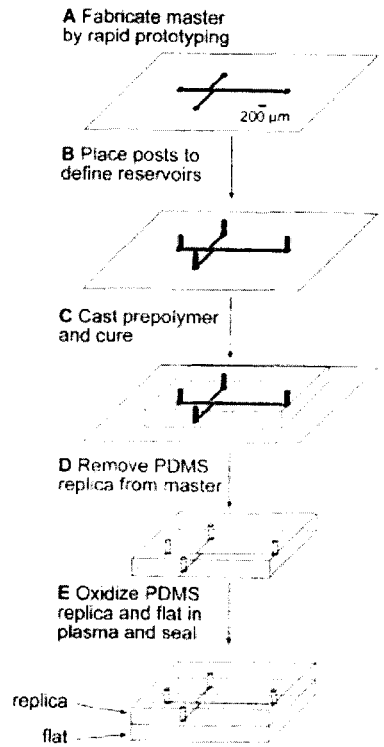

Figure 5. Fabrication of PDMS microfluidic device by replica molding. [8]

Nevertheless, this material presents very serious drawbacks. Native PDMS possesses a low surface energy (similar to those shown by fluorinated polyhydrocarbons), this means that the material surface is hydrophobic [9] and therefore it adsorbs nonspecifically proteins on the surface.

Surprisingly, native PDMS have been reported to also support EOF, especially considering that there are no charged groups that could form an EDL. Researchers attributed this unusual behavior to the adsorption of charged groups onto the surface, the presence of polymerization catalysts, and charges produced by acid-base chemistry of the surface that generates silanol groups. [10]

To enhance the hydrophilic behavior and to improve the EOF in a PDMS microchip, researchers have been using hybrid microfluidic devices with separation channels made from PDMS and a flat substrate of different materials, such as glass or poly(methylmethacrylate). [11] However, side-effects may be introduced due to the nonuniformity of surface charge density at the walls of the channels (as mentioned before in the introduction).

Other option includes high energy sources such as oxygen plasma, ultra-violet light and corona discharge, which have been used to create hydrophilic PDMS surfaces by oxidation (Fig.6).[12] In most cases, the surface of the PDMS is simultaneously subjected to many high-energy species which include electrons, ozone, radiation, and ions. The presence of these species form a SiO_x silica-like layer on the surface of the PDMS.

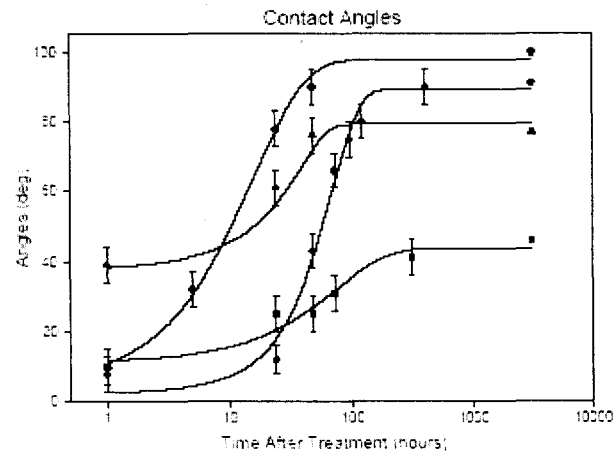

Figure 6. Contact angles vs. time (logarithmic scale). Traces: (•) 14 m PDMS membrane treated with UV/ozone for 60 min; (♦) bulk PDMS treated with RF oxygen plasma for 1 min; (■) bulk PDMS treated with UV/ozone for 30 min; and (▲) is the 14 m PDMS membrane with 120 min UV/ozone exposure.[12]

The oxidized PDMS is hydrophilic and even supports EOF. Moreover, it can form an irreversible seal with another flat surface by condensation, if it comes in contact with it in a

period of a minute or less after being activated. However, the surface of oxidized PDMS is known to recover its hydrophobicity after the oxidation (although the mechanism is still not well defined, it is known that the process usually takes 3 hours).

Therefore to obtain long-term effects, researchers have also explored the field of surface coatings on PDMS microfluidic devices, to make the channel surface more hydrophilic, to stabilize the EOF, and to reduce the nonspecific absorbance of proteins to the walls. As mentioned before, surface coatings can be divided in permanent and dynamic coatings. In the case of permanent coatings, chemical compounds are covalently bound to functional groups of the surface to become insoluble in the electrolyte. Meanwhile for dynamic coatings, surface-active compounds (SA compounds) are dissolved in a solution which is flushed through the microchannels, where they are strongly adsorbed to the surface modifying its properties.

In the latter case, the adsorption/desorption process is often reversible; therefore, the SA compounds must be re-introduced to the system to guarantee the stability of the coating in time. The subdivision in the dynamic category (dynamic or semi-dynamic) is based in the frequency in which the coating must be re-applied.

True dynamic coatings is usually applied to SA compounds as part of the background electrolyte (constantly replenishing the surface), on the other hand, the semi-dynamic coatings just requires the introduction of the SA compounds between runs to stabilize the coating. When using high molecular weight compound for semi-dynamic coatings, the results can be similar to those of static coatings since they are irreversibly adsorbed to the surface without a covalent bond.

Possible surface modifications on Poly(dimethylsiloxane) microfluidic devices:

a. Dynamic coatings:

Surfactants, in particular those under their critical micelle concentrations, can easily adsorb to hydrophobic surfaces. In the specific case of PDMS, the hydrophobic tail of the surfactant is expected to strongly interact with PDMS, while the charged head stretches out of the surface and changes the surface charge density (i.e. EDL), consequently generating a constant EOF.

Dou et al. observed that the addition of MES surfactant in NaOH solution enhances the separation of arginine, glucose and glycine by reducing the EOF in a PDMS microfluidic device (Fig.7). Although, the real mechanism is not yet clear and further experiments are needed according to the authors, they showed that MES has different effects on the plate height for each analyte. The explanation given by the author was that the addition of MES to the background electrolyte affects the system in two different ways: (1) it reduces the EOF by blocking the active groups that generates it on the surface, and by increasing the viscosity of the running buffer; and (2) the addition of MES to the solution eliminates the adsorption of analytes on the PDMS surface by coulombic forces. [13]

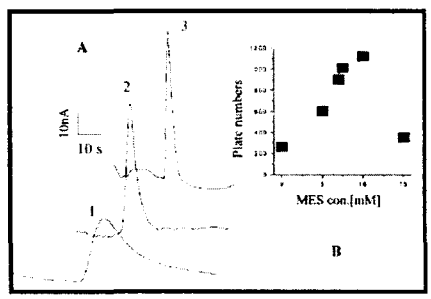

Figure 7. (A) Electropherograms of Arg. in 20 mM NaOH with different MES concentration (con.). (1) 0 mM MES, (2) 5 mM MES, (3) 7.5 mM MES. (B) Theoretical plate numbers of Arg. at different MES con. Sample, 0.5 mM Arg.; separation voltage, 1500 V; injection, double T (800 V, 8 s). [13]

In addition to this work, Harrison's group proved that the use on a surfactant is suitable for separating proteins with significant differing hydrophobicity and varying pI values on a PDMS-coated capillary (Fig.8). The coating in this case was based on the nonspecific polar/charged model mechanism. [14]

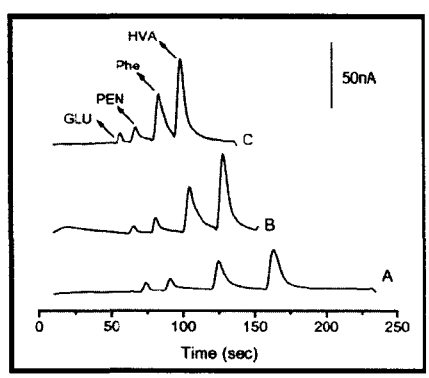

Figure 8. Electropherograms showing the effect of the presence of surfactants on the separation of 2 mM glucose, 0.6 mM penicillin, 0.9 mM phenol, and 1 mM homovanillic acid. (A) No surfactant added; (B) 1.2 mM SFS; (C) 1.3 mM DOCh. Other conditions: EDET = 0.7 V; 5 mM borate buffer, pH 12.0; E = 1500 V, TINJ = 5 s. [15]

In both cases presented for dynamic coatings, in order to achieve a good separation, the pH of the running buffer solution was kept over the pI of the individual analytes to be separated. In this way the repulsion forces between the protein and the surface become predominant.

b. Semi-Dynamic coatings:

Polyelectrolyte multilayers (PEMs) are thin composite films that are fabricated by coating the surface with successive layers of polyelectrolytes with opposite charges. This process has two important consequences: (1) an opposite charged polyelectrolyte can be adsorbed in the subsequent step; and (2) the adsorbed polyelectrolyte repels equally charged molecules from the surface.

Henry's group proved that the use of PDMS coated with a PEM, which consisted in a first layer of polybrene and a second layer of dextran sulfate, stabilized the EOF, as well as it improves the separation efficiency of dopamine and hydroquinone, which are taken as model components for electrochemical detection (Fig.9). [16]

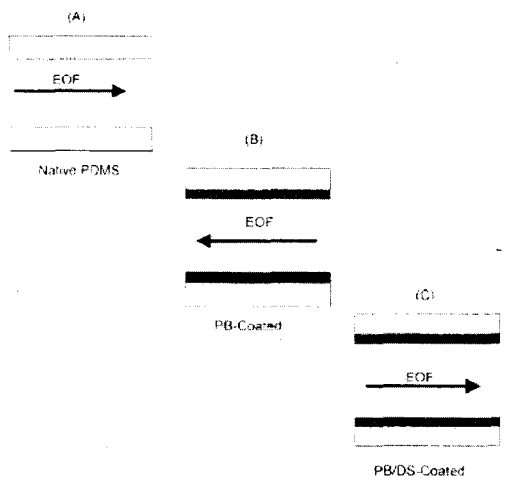

Figure 9. Successive multilayer coating procedure: (A) preconditioned channel containing negative surface groups, (B) first layer coating with a 5% PB, (C) second layer coating with a 3% DS. Arrows indicate the relative direction of EOF. [16]

It is also possible to use multilayers of proteins to decrease the nonspecific interactions between PDMS and different proteins. For example, Eteshola and Leckband used a BSA-based blocking buffer, for reducing the nonspecific adsorption of proteins on an ELISA-type assay on PDMS microchannels, by modifying the charge density on the surface (Fig.10). To improve the signal-to-noise ratio, the authors also modified the PDMS channels with protein A to obtain an IgM binding platform, which helped them to optimize the IgM position toward the analyte.[7]

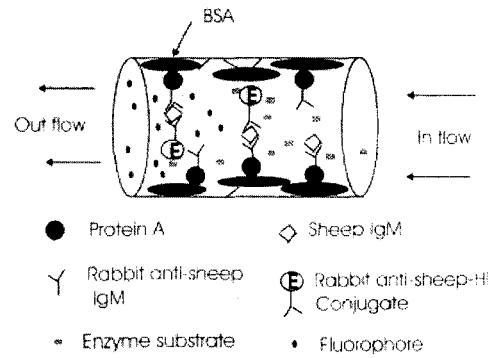

Figure 10. Schematic of the sandwich ELISA developed by Eteshola and Leckband.[7]

Another protein multilayer approach was developed by Linder et al. They presented a modification based on three layer biotin-neutravidin sandwich coating, made of biotinylated IgG, neutravidin, and biotinylated dextran, where the negative charge present in the latter layer repels the negative charged proteins (Fig.11). Moreover, the authors proved that by using electroosmotic flow to confine the reaction in a specific zone and by replacing the biotinylated dextran layer with any biotinylated reagent, the modified surface can be functionalized with bioactive groups. [17]

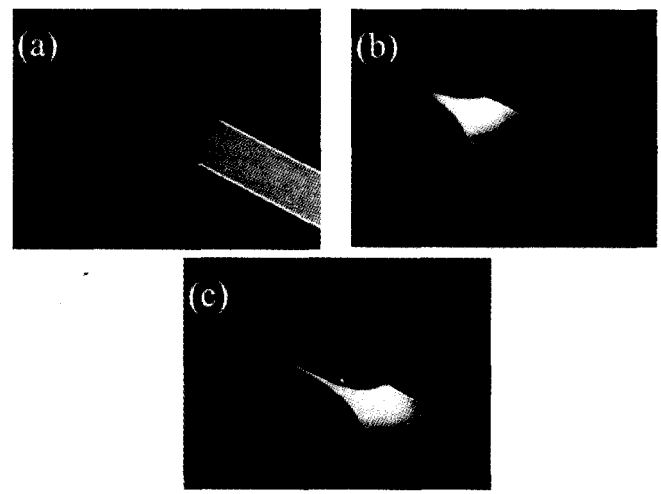

Figure 11. (a) Antibodies are patterned on the neutravidin surface using laminar flows. (b) Fluorescently labeled antigen is electrokinetically transported towards the immobilized antibodies. (c) Unbound antigen is electrokinetically removed, and fluorescence arising from the immunocomplex can be quantified.[17]

Another method for creating well-defined patches of active species inside a PDMS microfluidic device was developed by Cremer's group (Fig.12). [18] First, a passivating protein layer (e.g. fibrinogen) was adsorbed to the walls and floor of a poly(dimethylsiloxane)/glass microchannel. The channel was then filled with an aqueous biotin-linked dye solution, which is bleached to create highly reactive species (i.e. photopatterning). These activated molecules subsequently attached themselves to the adsorbed proteins on the microchannel walls and floor via a singlet oxygen-dependent mechanism, leaving a modified protein resistant layer with active biotin sites for modification.

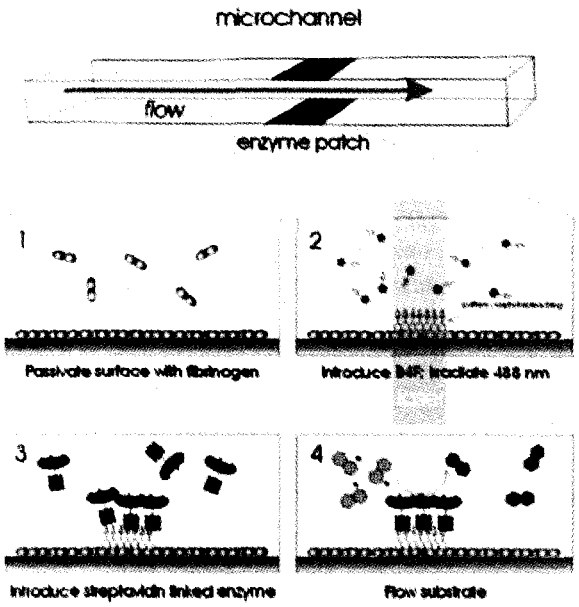

Figure 12. Schematic diagram of the photoimmobilization process. (Top) Enzyme patches are formed on the top and bottom of a microchannel using the following procedure: (1) Passivation of the surface with a fibrinogen monolayer is followed by (2) biotin-4-fluorescein surface attachment. This is accomplished by photobleaching with a 488-nm laser line. (3) Next, the binding of streptavidin-linked enzymes that can be exploited to immobilize catalysts and (4) monitor reaction processes on-chip.[18]

Multilayer coating can also be achieved by using lipids. Phospholipids for example are able to generate a self-assembled bilayer film on the surface of the oxidized-PDMS. This bilayer film is advantageous because it offers a simple surface modification procedure for oxidized-PDMS, while it retains the protein-resistant headgroups and lipid interior regions of their biological counterparts.

Phillips and Cheng used a phospholipids-based modification for improving the wettability of oxidized-PDMS microfluidic channels, and reducing protein adsorption by electrostatic interactions between the lipid headgroups and charged proteins. Moreover, they were able to functionalize the oxidized-PDMS surface, by introducing vesicles with different lipid reagents, to perform a microfluidic heterogeneous immunoassay of a cholera toxin (Fig.13). [19]

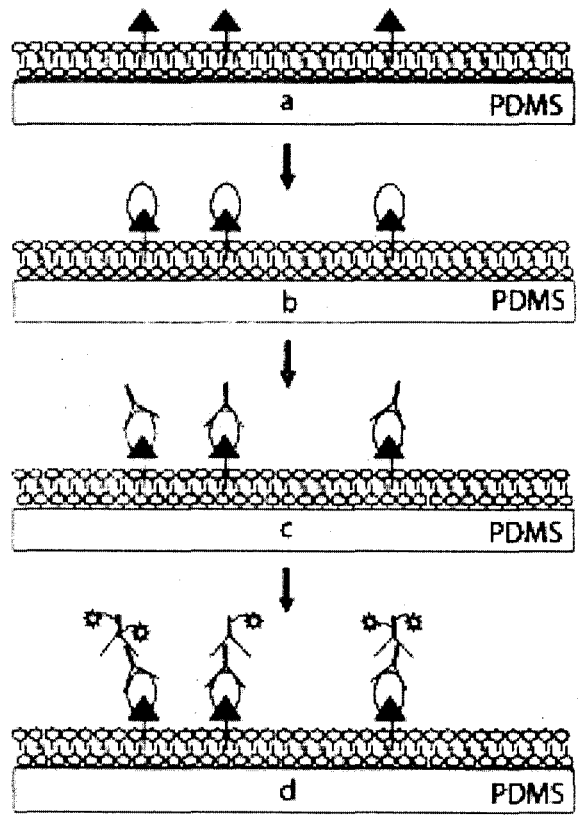

Figure 13. For immunoassay, (a) vesicle fusion to form GM1 integrated SBMs, (b) capture of CT on the membrane, (c) binding of rabbit anti-CT, (d) binding of Alexa 532-tagged goat anti-rabbit for fluorescent detection.[19]

Although increasing the hydrophilicity and the protein repellency of a material by introducing charges in the surface has become a common trend, as we have seen in the previous examples for dynamic and semi-dynamic modifications, it is not always useful for studying complex sample mixtures, where the adsorption of ions of opposite charge from the sample can produce local inhomogeneities on the z-potential; consequently, creating eddy migrations leading to a lower separation resolution (either band broadening or tailing). [20]

Therefore to improve the separation of these complex sample mixtures, researchers have also used neutral hydrophilic polymer layers. For example, poly(vinyl) pyrrolidone (PVP) is

a neutral polymer which is water soluble, and less hydrophilic than poly(vynil) alcohol (PVA), which means that PVP is a better candidate to modify PDMS than PVA; although, both polymers exhibit self-coating properties and reduce electroosmotic flows to negligible levels (i.e. this coatings allowed the separation to be completely dependant on the proteins' electrophoretic mobility).

Following this trend, McCormick used a modified PVP capillary to separate 15 proteins with molecular weights ranging from 12K to 77K and different pI values (from 4.5 to 11) by keeping the running buffer at a lower pH than the lower pI value to allowed all the proteins to migrate in the same direction. [21]

c. *Static coatings:*

Static coatings can be considered as the real «ideal» coatings, since they will change completely and irreversibly the surface properties of a material to obtain those that the researchers desire (i.e. enhance the biospecific interactions, and reduce the nonspecific interactions), without modifying the bulk material.

However, static coatings in general depend on arduous chemical processes (e.g. graft polymerization, silanization reactions, and chemical vapor deposition), which not always present a 100% of yield; making them less favorable if compared to the dynamic and semi-dynamic surface modifications.

The following paragraphs are some examples of static coatings procedures, were a good compromise between increasing the selectivity of the system toward a specific analyte or group of analytes, reducing the nonspecific interactions, and the time required for their fabrication can be observed.

In most cases, the static coating just provide a highly reactive functional group such as amine functionalities on the surface for the consecutive deposition of different biomolecules or polymeric layers, which provide the selectivity desire.

Graft polymerization is widely used in polymer chemistry to vary the surface properties of polymers (Fig.14). Typically it involves creation of reactive sites (radicals) on the polymer surface by using UV light, ionizing radiation or chemical reagents (e.g. Ce[IV]), followed by covalent linkage of monomer or a preformed polymer that can then be used as the initiation site for a new polymeric chain.

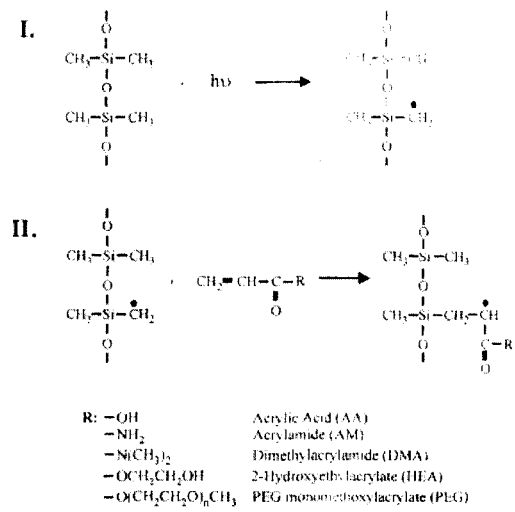

Figure 14. Reaction scheme for UV graft polymerization on a PDMS surface. Step I illustrates the formation of radicals on the PDMS surface by UV light. Step II displays the initiation step in the polymerization reaction. R is the monomer side group.[22]

Albritton's group used a grafted-polymerization based on UV light to modify the surface of the PDMS microfluidic devices with poly(ethylene glycol)monomethoxyl acrylate (PEG), which it is known to be an hydrophilic coating that reduces the electroosmotic flow (EOF) and the nonspecific adsorption of proteins to the glass walls, allowing them to enhance the separation of two fluorescent-labeled kinase-activity biomarkers, F-PKC and F-src (Fig.15). [22]

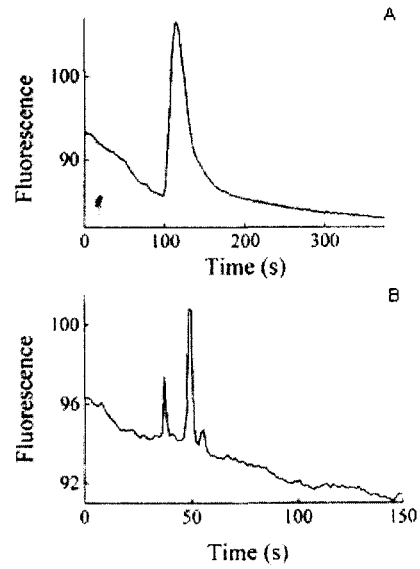

Fig. 15. Electrophoresis of F-PKC and F-src on an oxidized-PDMS and PEG-grafted-PDMS devices. (A) The two halves of a PDMS device were oxidized by exposure to an oxygen plasma. (B) Conditions are identical to that in (A) except that the two halves of a PDMS device were grafted with PEG (25 ig/cm²).[22]

It was noticed that after PDMS was oxidized, some of its functional groups on the surface were converted to $Si(OH)_{4-n}O_n$. The presence of silanol groups on the surface provides the oxidized-PDMS devices similar surface properties to those observed in glass-based devices (i.e. hydrophilic surface and a higher EOF compared to native-PDMS). Therefore, researchers concluded that the surface of the oxidized PDMS can be modified with the same reagents that are typically used to modify glass surfaces through condensation reaction (e.g. silanol reagents).

For example, Matsubara et al. immobilized g-aminoprolpyltriethoxysilane by dipping a plasma-oxidized PDMS chip for 45 min. into acetone including 1% (v/v) g-APTES (Fig.16). Then, the PDMS was rinsed twice in acetone and dried under a stream of nitrogen. Since, the immobilized g-APTES had its propyl amine group exposed to the surface, it was possible to the authors to attached mast cells to the surface of the now hydrophilic PDMS. [23] Although, the authors reported that this surface modification method made the cells inactive, it can be applied for other applications.

Fig. 16. Mast cells incubated on the PDMS. The left side of the PDMS shows the non-treated surface («), and the right side shows g-APTES treated surface.[23]

Finally, the chemical vapor deposition (CVD) polymerization consists in the vacuum-deposition of a polymer coating, where a solid precursor (monomer or oligomer) is first vaporized (Fig.17); the resulting gas is then heated to 600±800 C to yield an active species. In the last step, the active precursor gas is adsorbed as it polymerizes on the substrate creating a stable polymer coating.

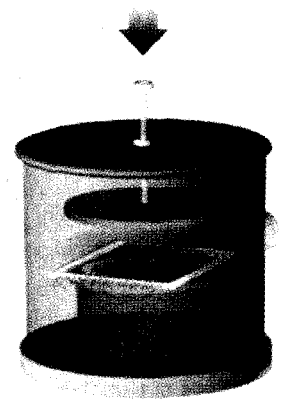

Figure 17. Schematic of the Hot-Wire Chemical Vapor Deposition (HWCVD) chamber. Showing gas inlet through upper showerhead, pyrolysis on square filament array, and deposition onto a wafer substrate resting on the bottom electrode.[24]

Langer's group used CVD to adsorb a reactive coating, PPX-PPF (poly(p-xylylene carboxylic acid pentafluorophenolester-co-p-xylylene)), on the surface of the chemically inert PDMS (Fig.18). [25] The reactive coating has three main chemical features that makes it a promising candidate for surface modification of PDMS microfluidic devices: (1) it establishes a chemical interface with high reactivity for primary amino groups, while preventing the underlying PDMS from swelling; (2) amino terminated biotin ligands substitute the pentafluorophenol groups, forming chemically stable amide bonds; and (3) the poly(p-xylylene) backbone accounts for chemical inertness and insolubility.

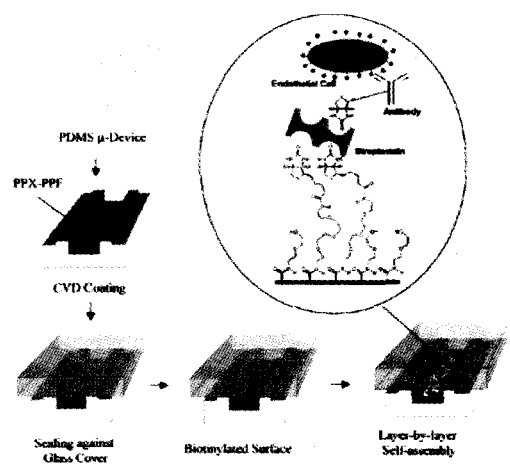

Figure 18. PDMS is first modified with a reactive coating, which is then used to bind biotin ligands and to self-assemble streptavidin. Biotin-labeled Human Anti-Integrin (HAI) is then bound to the modified PDMS surface and used to study cell surface receptor activity.[25]

Conclusions

Microfabricated planar devices have great potential for use at the point-of-care or in central laboratories, especially for Genomics and Proteomics studies, due to the benefits related to miniaturization.

Wall modifications based on physically adsorbed molecules provide a quick and efficient answer to avoid non-specific adsorption. However, their interactions with the analytes (i.e. proteins) are not specific, since they are based on hydrophobic or charge repulsion interaction, making them unsuitable for creating robust microfluidic devices for the direct analysis of complex samples.

On the other hand, semi-dynamic and static coatings are well-suited for more complex applications, due to the possibility of providing the desired functionality while the nonspecific adsorption is reduced to a minimum.

It is my opinion, that the future prospect of this research is to develop, easy-to-fabricated static coatings as the one presented by Marquette & Blum (entrapment of biological active beads during the polymerization of PDMS)[26] in combination with protein resistant buffers that will aim to reduce the nonspecific adsorption to the walls. Therefore combining the best of two worlds.

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