CHAPTER 4

Development of hydrophilic Polydimethylsiloxane (PDMS) microchannels for SPR microfluidic application

Contents

4.1 Introduction

This chapter addresses the issue of inherent hydrophobicity of Polydimethylsiloxane (PDMS) polymer that hinders its application in microfluidic based biosensing applications. In the beginning, the chapter provides a brief review of the various surface modification strategies to improve the hydrophilicity of PDMS. Thereafter, the chapter presents the investigation of Atmospheric Pressure Dielectric Barrier Discharge oxygen (APDBD O_2) plasma for the development of hydrophilic PDMS microchannels for plasmonic biosensing. The PDMS samples are fabricated using a standard technique and exposed to APDBD O_2 plasma treatment. The plasma treated PDMS is used to fabricate an SPR biosensor for the investigation of biomolecular interaction. The effect of the plasma treatment on the wettability, surface energy and hydrophilicity retention capacity of PDMS was determined using contact angle measurements and Fourier Transform Infrared (FTIR) analysis, whereas the bulk structural property and optical transparency were studied using X-Ray Diffraction (XRD) and Ultraviolet-Visible (UV-Vis) Spectroscopy respectively.

PDMS, a silicon-based organic polymer, has emerged as a popular choice of material, particularly in the field of microfluidics owing to its properties like high optical transparency, flexibility and inertness, biocompatibility and non-toxicity, ease of fabrication etc. [1, 2]. It is a promising material for the manufacturing of miniaturized electronic gadgets such as flexible and wearable devices, implantable microfluidic devices, bioassays and drug delivery systems, bioreactor and patterned cell culture, cytometric detection systems etc. [3-6]. However, the inherent hydrophobicity of PDMS (water contact angle >90°) hinders its efficacy due to the poor wettability of the polymer restricting fluidic free flow through the micro/nano channels. The hydrophobicity of PDMS also results in the undesired adsorption of proteins on its surface, thereby affecting the detection sensitivity of the sensor, particularly in biological assays and biosensors [7-8].

Several surface modification techniques have been reported by authors to render PDMS hydrophilic and resistant to the adsorption of protein and other biomolecules. Some of these approaches involve high-energy treatments using O_2 plasma, Ultraviolet (UV)/ozone treatments or corona discharges, chemical modification methods such as plasma enhanced chemical vapour deposition, silanization, formation of self-assembled

monolayers and polymer brushes via grafting methods [9-12]. Among these approaches, O_2 plasma treatment is the most widely used approach owing to its short treatment time, non-toxicity, limited depth of surface modification etc. without affecting the bulk properties of the material [13]. Results reported in the literature indicate that low-pressure thermal O_2 plasma has been utilized by many for the surface modification and functionalization of PDMS [7, 13-18]. However, the non-thermal atmospheric pressure plasma treatment process has a lower risk of damage to the surface of PDMS due to non-aggressive surface treatment. It also has the advantages of reduced equipment and maintenance costs, ease of operation, non-requirement of expensive vacuum systems and clean-room facilities. In this regard, APDBD O_2 plasma is an efficient and promising tool for non-thermal plasma treatment at atmospheric pressure [19, 20]. APDBD O_2 plasma is envisaged to be an effective and alternative method in the development of hydrophilic microfluidic channels resistant to protein adsorption for plasmonic sensing applications.

4.2 Materials and Methodology

The PDMS based microfluidic flow cells were prepared from a 3D printed mould and subjected to APDBD O_2 plasma treatment for different exposure times to study the effect of plasma on the hydrophilicity of PDMS surface. Thereafter, the plasma treated PDMS was used to fabricate an SPR biosensor using a novel bonding protocol, as reported in the previous chapter, to bond PDMS microchannels with gold (Au). Human Immunoglobulin-G (H-IgG) antigen was immobilized on the surface activated Au substrates through the inlets of the PDMS microchannels of the SPR biosensor and exposed to polyclonal antibodies viz; Mouse anti Human Immunoglobulin-G (M-aHIgG), Goat anti Human Immunoglobulin-G (G-aHIgG) and Rabbit anti Human Immunoglobulin-G (R-aHIgG) of different concentrations. The effect of the plasma treatment on the wettability of PDMS samples was characterized using the contact angle, surface energy measurements and FTIR whereas the bulk structural and optical transparency of PDMS was characterized using XRD and UV-Vis. The interaction capacity of the SPR biosensor towards antibody proteins was investigated using the SPR measurement prototype. Figure 4.1 schematically illustrates the surface modification of the PDMS sample upon exposure to APDBD O_2 plasma treatment followed by the fabrication of an SPR biosensor using plasma treated PDMS.

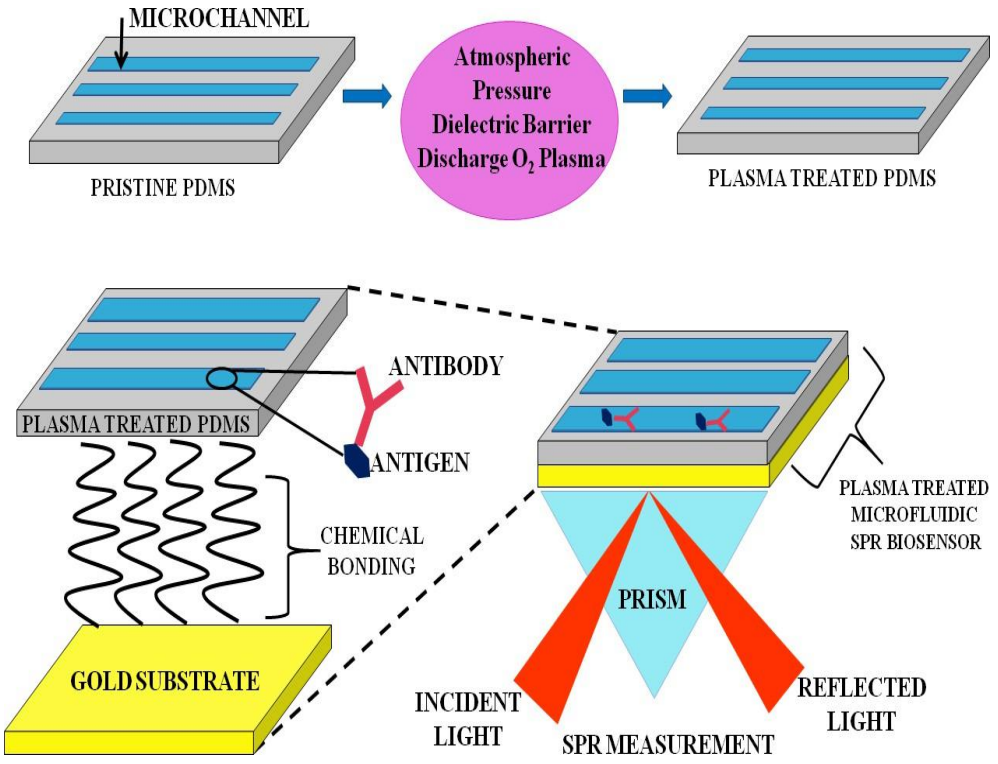

Figure 4.1: Schematic illustration of the exposure of PDMS sample to APDBD O_2 plasma treatment followed by the fabrication of an SPR biosensor using plasma treated PDMS

4.2.1 Materials

Sylgard 184, 11-Mercuptoundecanoic acid (MUA), 1-ethyl-3 (3-dimethylaminopropyl) carbodiimide (EDC), N-hydroxysuccinimide (NHS), Ethanolamine, Phosphate-Buffered Saline (PBS) were obtained from MilliporeSigma, USA. M-aHIgG, G-aHIgG, R-aHIgG and H-IgG were purchased from GeNei, Bangalore, India. 3-Aminopropyltrimethoxysilane (APTMS) was procured from Thermo Fisher Scientific, USA. Ultra pure Deionised (DI) water was used throughout the experiments. The raw chemicals were of analytical grade and used without further purification.

4.2.2 Fabrication of plasma treated multichannel microfluidic flow cell

Figure 4.2a shows the schematic representation of the fabrication process of the multichannel microfluidic flow cell. A master mould was first 3D printed which acts as a stamp for the construction of three microfluidic channels (length = 20 mm and diameter = 1.5 mm) on PDMS. Sylgard 184 was used to fabricate the microfluidic flow cell by

mixing its two constituents; silicone elastomer base (10 parts) and curing agent (1 part). The mixture was vacuum desiccated for repeated cycles of 10 min till the disappearance of all the bubbles. Then the resulting mixture was poured on top of the 3D printed master mold. The poured mixture was cured at 65˚C for 2 h in an oven. It was then cooled for 45 min at room temperature followed by peeling off from the master mould after complete curing. Finally, separate inlets and outlets were created for each microchannel using a biopsy punch.

The APDBD O_2 plasma system (Figure 4.2b) consisted of two square plane-parallel copper electrodes with a thickness of 5 mm each and a surface area of 250 mm x 250 mm. Quartz glass plates with a thickness of 3 mm and an area of 250 mm x 250 mm were used to cover the electrodes to act as a dielectric. The sample was placed on the grounded electrode which had a provision to adjust the discharge gap. O_2 gas based plasma was produced between the electrodes (covered with glass) at a discharge gap of 6 mm with a gas flow rate of 2 slpm regulated using a mass flow controller (Alicat Scientific, USA). An applied voltage of 15 kV with a discharge gap of 6 mm between the two electrodes produced a homogeneous and uniform discharge of plasma at atmospheric pressure covering the whole cross-section of the quartz plates [21-22]. This process of APDBD O_2 plasma treatment invokes hydrophilic properties in PDMS due to the introduction of polar silanol (OH) groups replacing the methyl (CH_3) groups. The strong interaction of the polar groups with the water molecules results in the reduction of the water contact angle. The schematic illustration of the effect of APDBD O_2 plasma on PDMS is shown in Figure 4.2c.

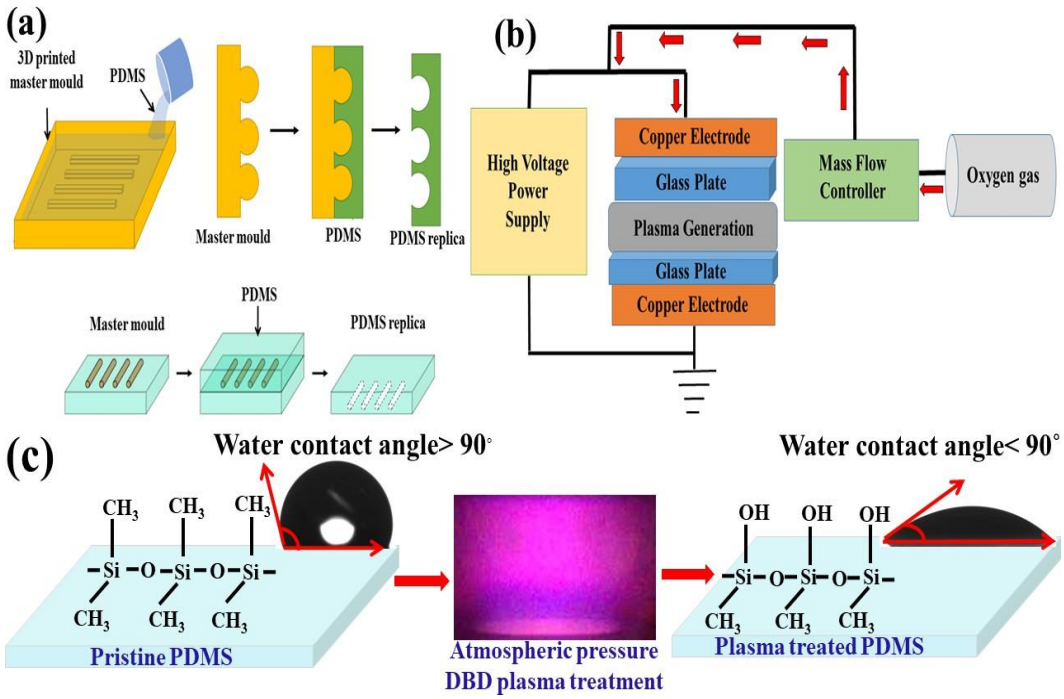

Figure 4.2: Schematic illustration of (a) Fabrication of multichannel microfluidic flow cell (b) Experimental arrangement for APDBD O_2 plasma treatment process (c) Effect of APDBD O_2 plasma on hydrophilicity of PDMS surface

4.2.3 Characterization Techniques

The effect of APDBD O_2 plasma on the hydrophilicity of the PDMS surface was studied using water contact angle measurements. The PDMS samples were subjected to plasma exposure at 40 W (15 kV, 2.67 mA) for a duration of 0-10 min, subsequently followed by water contact angle measurement on their surface. A water sessile droplet of size ~2 µL was poured atop the PDMS sample using a micro-syringe placed on the X and Y adjustable platform of the contact angle measurement setup (Dataphysics OCA15EC, Germany). A 6.5-magnification camera with a manual focus mounted on another platform adjustable in the Z-direction was used to take the images of the water sessile droplets on the surface of PDMS and analyzed using the Software Composition Analysis tool.

The surface energy is an important factor in assessing the wettability of a solid surface which determines the quantum of attractive or repulsive intermolecular force a surface can exert on another. The high surface energy of a wet surface exerts a strong attractive force on the liquid droplet forcing it to spread out resulting in a low contact

angle. The surface energies of PDMS samples were evaluated using Owens-Wendt-Rabel-Kaelble (OWRK) method using equation 4.1 [23].

$$\Upsilon_s = \Upsilon_s^D + \Upsilon_s^P \quad (4.1)$$

where γ_s^D is the dispersive and γ_s^P is the polar component of surface energy Υ_s.

To determine Υ_s from equation 4.1, first, the contact angles of DI water (a polar liquid) and diiodomethane (a non-polar liquid) were evaluated (as shown in the inset of Figure 4.4b) and then the two surface energy components ($\Upsilon_s^D, \Upsilon_s^P$) were calculated using equation 4.2.

$$\sqrt{\gamma_s^D \gamma_l^D} + \sqrt{\gamma_s^P \gamma_l^P} = \frac{1}{2}[\gamma_t(1 + \cos\Theta)] \quad (4.2)$$

where γ_l^D and γ_l^P are the dispersive and polar components of surface tension of the testing liquid, γ_t is the surface tension of the testing liquid and Θ denotes the contact angle made by the testing liquids with the PDMS surface [For water, γ_l^D=26.4 mN/m, γ_l^P= 46.4 mN/m, γ_t=72.8 mN/m. For diiodomethane, γ_l^D=50.8 mN/m, $\gamma_l^P = 0$ mN/m and γ_t= 50.8 mN/m].

The chemical compositions of the untreated and APDBD O_2 plasma treated PDMS samples were analyzed using FTIR spectroscopy (Impact 410, Nicolet, USA) in the spectral range of 4000–650 cm^{-1} in the transmittance mode. The effect of APDBD O_2 plasma on the structural composition of PDMS was investigated using XRD. Bruker Focus D8 diffractometer with Cu Kα, radiation source at 1.5406 Å was used for the investigation of the XRD data. The optical transparency of the untreated and APDBD O_2 plasma treated PDMS samples was analyzed using UV-Vis spectroscopy. A spectrophotometer (UV-2600, Shimadzu Europe) was used to record the UV-Vis transmittance spectra in the spectral range of 200-700 nm.

4.2.4 SPR biosensor fabrication

The APDBD O_2 plasma treated PDMS sample was used to construct a SPR biosensor using a novel bonding protocol to bond PDMS microchannels with Au as schematically illustrated in Figure 4.3. Step I involves plasma treatment at 40 W (15 kV, 2.67 mA) to generate the hydroxyl group terminated surface of the PDMS sample. Thereafter, the PDMS surface

was functionalized by immersing in a 10% (v/v) ethanolic solution of 3-APTMS for 1 h. In Step II, ~50 nm Au coated substrate was functionalized with a 5 mM ethanolic solution of 11-MUA followed by surface activation using a 1:1 mixture of ethanolic solution of 400 mM EDC and 100 mM NHS. In Step III, the plasma treated PDMS surface with the terminal NH_2 group was bonded with the carbodiimide activated Au surface at room temperature. In Step IV, the H-IgG antigen (1000 ng/ml) prepared in PBS was introduced through the three individual inlets of the microchannels and immobilized over the carbodiimide activated Au to fabricate the SPR biosensor. Thereafter the microchannels were washed with PBS and the unreacted NHS esters were capped with 1 M ethanolamine. Polyclonal antibodies produced in mouse, goat and rabbit (M-aHIgG, G-aHIgG and R-aHIgG) were separately injected through each of the three microchannels of the fabricated biosensor at varied concentrations (20 ng/ml–100 ng/ml) prepared in PBS to study the SPR response. An SPR biosensor was also prepared in a similar procedure with plasma untreated PDMS to compare the result with the SPR biosensor fabricated with treated plasma.

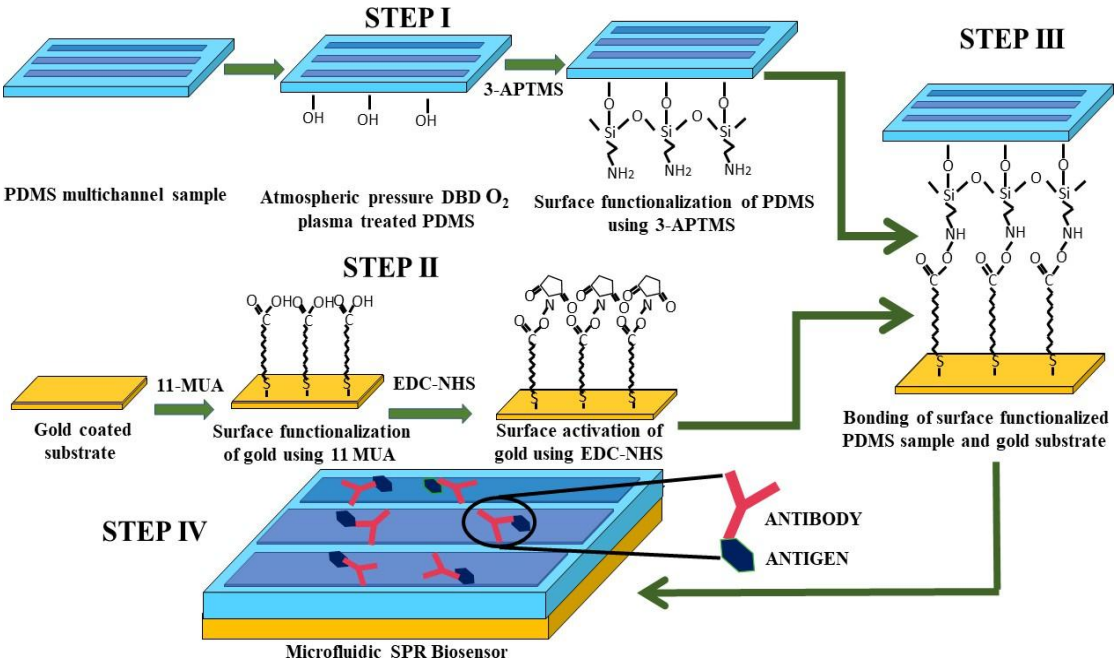

Figure 4.3: Schematic representation of the APDBD O_2 plasma treated SPR biosensor

4.3 Results and Discussion

4.3.1 Contact Angle and Surface Energy

Figure 4.4a illustrates the variation in the water contact angle of the plasma treated PDMS samples versus plasma exposure time. The results show a sharp reduction in the contact angle from 115.3˚±0.1˚ for pristine PDMS [inset of Figure 4.4a] to 35.15˚± 3.65˚ for the sample treated with plasma for 6 min [inset of Figure 4.4a]. The reduction of contact angle for plasma treated samples reveals increased wettability of the samples suggesting the replacement of methyl groups with polar functional groups on the PDMS surface following treatment. The strong interaction between these polar functional groups and water molecules results in the decrease of contact angle [24]. However, the effect of plasma saturates at 6 min of exposure time and the declining tendency of contact angle is suppressed. The obtained results are also comparable to the contact angles measured by some of the low-pressure thermal O_2 plasma based works [13-14].

Figure 4.4b shows the variation of the surface energy of PDMS versus plasma exposure time. It is evident from the figure that the untreated PDMS is strongly hydrophobic in nature with a low surface energy of 19.71 mN/m. The surface energy of the sample is enhanced with the rise in plasma exposure time with a maximum of 62.83 mN/m at 6 min. The high surface energy of PDMS surface due to plasma treatment is an indication of the changes in surface property from hydrophobic to hydrophilic. The obtained results are better and comparable to the surface energies measured by some of the low-pressure thermal O_2 plasma based works [13, 18]. For further experiments, only the PDMS sample treated for 6 min was used.

The plasma treated PDMS recovers its hydrophobicity over a period limiting its use immediately after plasma treatment. This is primarily due to the diffusion of the pre-existing low molecular weight chains from the bulk to the surface to provide stability, reorientation of the polar groups from the surface to the bulk and the condensation of the hydroxyl groups [25-28]. The rate of PDMS hydrophobic recovery is strongly affected by the storage medium and is more pronounced in the air compared to the aqueous medium. Therefore, the retention of PDMS hydrophilicity was examined by storing the plasma treated PDMS in aqueous mediums viz; DI water and PBS. The measured contact angle against the number of days of storage in DI water and PBS is plotted in Figure 4.4c which is a measure of the hydrophilicity retention capacity of the PDMS. It is observed that PDMS can retain good hydrophilicity with a contact angle of 74.86˚±3.29˚ for 50 days in PBS as compared to only 5 days in DI water. This could be attributed to the presence of salts and ions in PBS which can form ionic interactions with the polar functional groups on the PDMS surface promoting enhanced wettability and hydrophilicity [29].

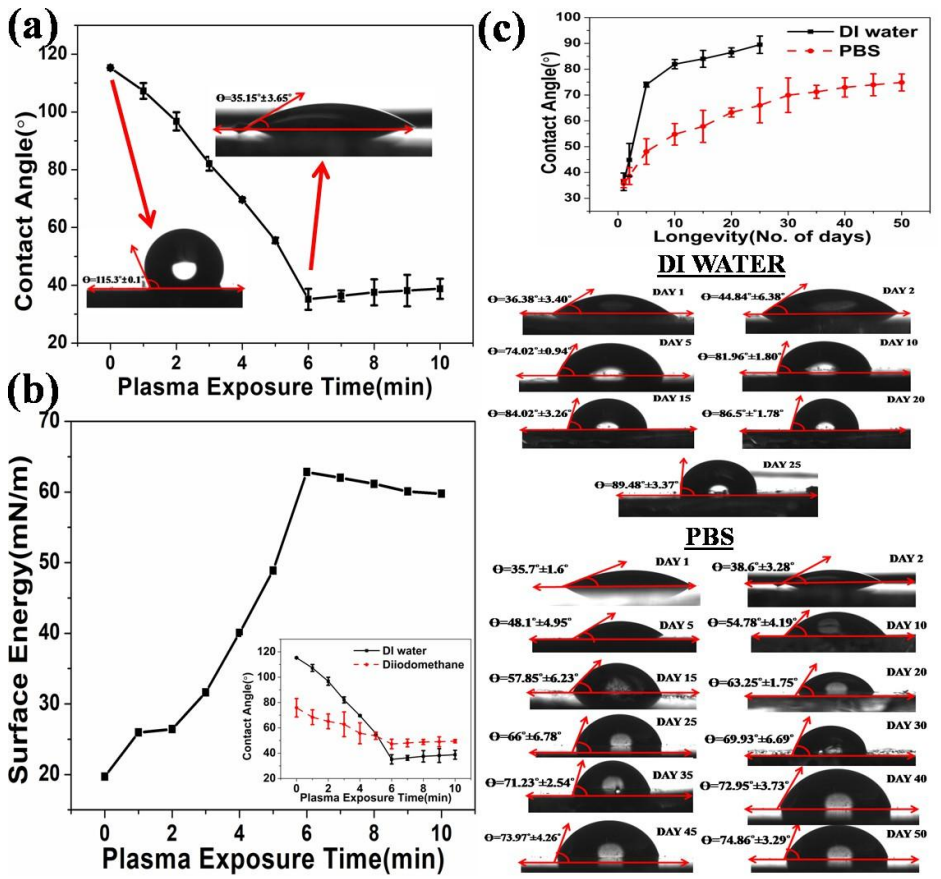

Figure 4.4: (a) Variation of water contact angle on PDMS with plasma exposure time. **Inset:** Contact angle images of untreated and plasma treated PDMS (6 min) (b) Variation of the surface energy of PDMS with plasma exposure time. **Inset:** Variation of contact angle of water and diiodomethane on PDMS surface with plasma exposure time (c) Hydrophilicity retention capacity of plasma treated PDMS stored in DI water and PBS and the corresponding images showing the respective contact angle values

4.3.2 Material Characterization

Figure 4.5a shows the FTIR data of the pristine and plasma treated PDMS samples. Pristine PDMS exhibited characteristic infrared bands viz, 2950−2970 cm^{-1} (asymmetric $-CH_3$ stretching in $Si-CH_3$), 1245−1270 cm^{-1} (symmetric $-CH_3$ deformation in $Si-CH_3$), 1000−1100cm^{-1} (stretching vibration of Si−O−Si bonds), 785−815 cm^{-1} ($-CH_3$ rocking and Si−C stretching vibrations in $Si-CH_3$). Similar data is reported earlier by other authors [13, 30, 31**]**. For the plasma treated PDMS, an additional broad band appears around 3000-3650 cm^{-1} corresponding to OH stretching vibration, indicating the introduction of polar functional groups. In addition, the generation of reactive O_2 species (O, O_2, O_2^- etc.) during APDBD O_2 plasma causes the

removal of hydrogen from the alkyl groups resulting in the reduction in the intensity of the absorption peak observed at around 1250 cm^{-1} [32]. The other absorption peaks of the plasma treated PDMS are similar to the untreated PDMS. The FTIR spectra thus clearly demonstrate that the oxygenated functional groups produced during APDBD O_2 plasma incorporate onto the PDMS surface giving it a hydrophilic nature. These polar groups account for the enhancement in the wettability and surface energy of PDMS which is consistent with the contact angle measurement data illustrated in Figure 4.4a and Figure 4.4b.

Figure 4.5b illustrates the XRD data of the untreated and plasma treated PDMS samples. Both the XRD curves show two diffraction halos; a larger one at approximately 12.8˚ and a smaller and broader one at around 22.6˚ [29]. The obtained results demonstrate the similarity in the XRD spectra of pristine and plasma treated PDMS confirming that APDBD O_2 plasma treatment does not change the bulk or structural properties of PDMS.

The UV-Vis transmittance data for untreated and plasma treated PDMS samples are shown in Figure 4.5c. Pristine PDMS shows a transmittance of 96% which is consistent with previously reported results [33, 34]. The PDMS samples treated with plasma exhibited a transmittance of 94% demonstrating no significant change in the optical transparency due to plasma treatment.

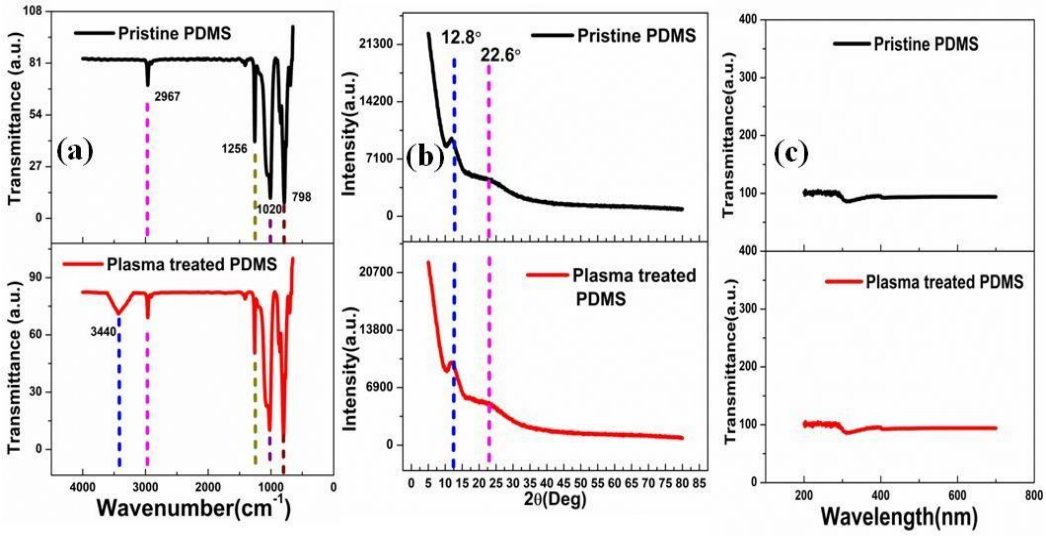

Figure 4.5: (a) FTIR spectra indicating the functional groups on pristine and plasma treated PDMS (b) XRD spectra showing the structural composition of pristine and plasma treated PDMS (c) UV-Vis transmittance spectra illustrating the optical transparency of pristine and plasma treated PDMS

4.3.3 SPR Response

Figure 4.6(a-b) shows the variation of the SPR resonance angle with concentration of antibody proteins (20 ng/ml -100 ng/ml) for the pristine and plasma treated SPR biosensors. The binding of the H-IgG antigen with the antibodies (M-aHIgG, G-aHIgG and R-aHIgG) results in a change in the local refractive index at the surface of the sensor producing shifts in the angles of resonance proportional to the concentration of the antibody proteins. The sensitivities and LoDs of the pristine and plasma treated SPR biosensors are determined from Figure 4.6a and Figure 4.6b respectively and presented in Figure 4.6c and Figure 4.6d. It is observed from Figure 4.6c that the plasma treated SPR biosensor exhibits enhanced sensitivities of 16.8˚/(µg/ml), 13.5˚/(µg/ml) and 16.65˚/(µg/ml) towards M-aHIgG, G-aHIgG and R-aHIgG respectively than pristine SPR biosensor exhibiting sensitivities of 10.5˚/(µg/ml), 11.15˚/(µg/ml) and 11.3˚/(µg/ml). Thus the plasma treated SPR biosensor demonstrates sensitivity enhancement of 60%, 21.07% and 47.34% over the pristine SPR biosensor for M-aHIgG, G-aHIgG and R- aHIgG respectively. Figure 4.6d illustrates that the plasma treated SPR biosensor exhibits LoDs of 7.13 ng/ml, 5.91 ng/ml and 1.47 ng/ml towards M-aHIgG, G-aHIgG and R-aHIgG respectively which is significantly lower than that of pristine SPR biosensor exhibiting LoDs of 18.64 ng/ml, 19.75 ng/ml and 17.32 ng/ml. Thus the plasma treated SPR biosensor demonstrates LoD improvement of 61.74%, 70.07% and 91.51% over the pristine SPR biosensor for M-aHIgG, G-aHIgG and R-aHIgG respectively. The improvement in the capacity to detect low concentrations of protein and sensitivity of the plasma treated SPR biosensor is due to the reduced adsorption affinity of the PDMS microfluidic channels towards antibody protein. APDBD O_2 plasma treatment modifies the surface of PDMS into hydrophilic by introducing polar silanol groups replacing the methyl groups. The hydrophilic nature of the surface suppresses the adsorption of protein on the surface of the microchannel, resulting in improved sensitivity and LoD of the biosensor fabricated with plasma treated PDMS.

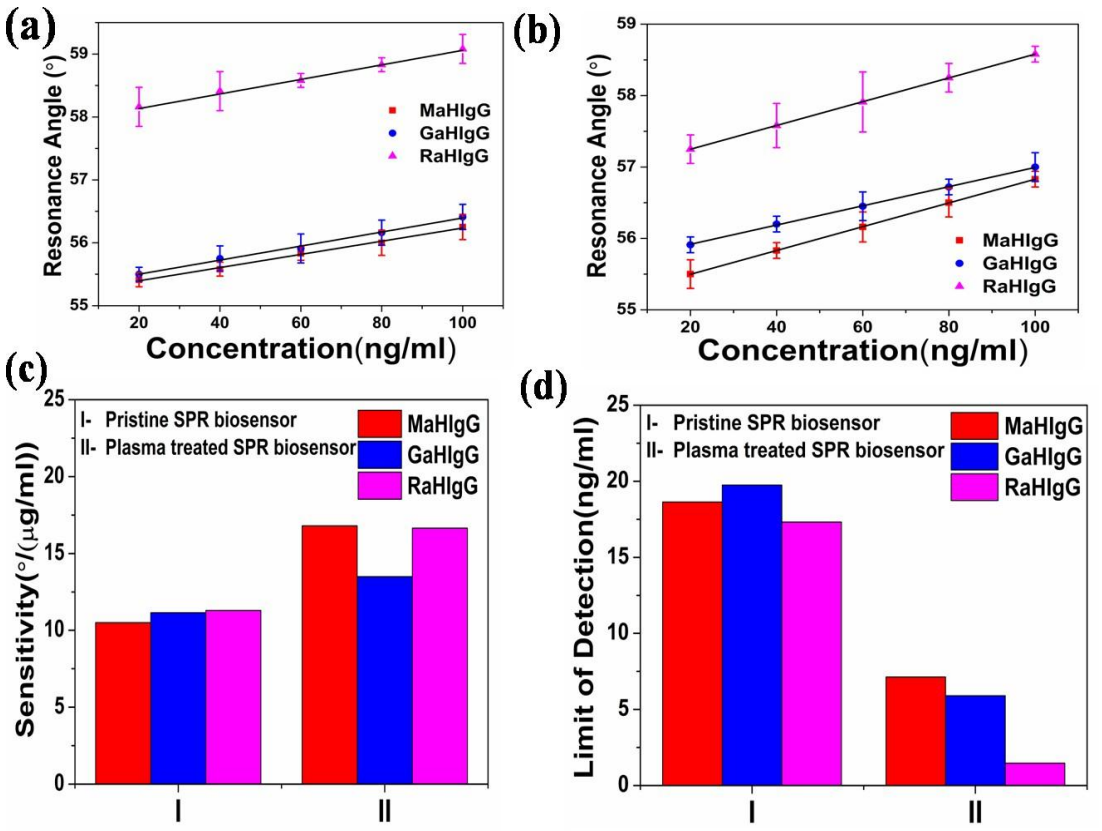

Figure 4.6: Variation of SPR resonance angle with the concentration of protein for (a) pristine SPR biosensor and (b) plasma treated SPR biosensor (c) Sensitivities of the pristine and plasma treated SPR biosensors (d) LoDs of the pristine and plasma treated SPR biosensors

4.4 Summary

This chapter investigates APDBD O_2 plasma for the development of hydrophilic PDMS microchannels for SPR biosensing. The PDMS microchannels were fabricated from a master mould using a standard technique and exposed to plasma discharge at atmospheric pressure. The plasma treated PDMS were used to fabricate an SPR biosensor using a novel bonding protocol to bond PDMS microchannels with Au and the results were compared with an SPR biosensor fabricated with pristine PDMS. The effect of plasma treatment on the wettability, surface energy and hydrophilicity retention capacity of PDMS was determined using contact angle measurements. The PDMS sample exposed to APDBD O_2 plasma for 6 min demonstrated the lowest contact angle of 35.15˚, surface energy of 62.83 mN/m and hydrophilicity retention capacity of more than 50 days in PBS. The treatment of PDMS with plasma induces surface hydrophilicity

due to the introduction of polar functional groups as evinced by FTIR analysis without compromising the bulk structure and optical properties of PDMS which were confirmed by XRD and UV-Vis spectroscopy measurements. The complementary effect of improved hydrophilicity and higher surface energy due to plasma treatment also contributed to the reduced adsorption of proteins on its surface as evinced by the improved sensitivities (16.8˚/(µg/ml), 13.5˚/(µg/ml) and 16.65˚/(µg/ml) and lower LoDs (7.13 ng/ml, 5.91 ng/ml and 1.47 ng/ml) of the plasma treated SPR biosensor as compared to pristine SPR biosensor. Thus, APDBD O_2 plasma treatment serves as a simple, rapid and effective modification strategy to render PDMS microchannels hydrophilic and suited for plasmonic biosensing applications.

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