Swellable plasma polymer films for use in hydrogel-based biomedical devices

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Abstract: Swellable plasma polymer films have been deposited on silicon wafers and hydrogels in a low-pressure PECVD system. Deposition characteristics and physicochemical characterization data of swellable oxygen-rich plasma polymerised ethylene films were studied. These films were deposited using gas flows consisting of C_2H_4 (5 sccm) and CO_2 (10-40 sccm). Using profilometry, changes in thickness of films over multiple water immersion and drying cycles were recorded. Changes in the structure and morphology of films was also evaluated by using scanning electron microscopy, dye permeation studies and atomic force microscopy. Mechanical properties of the films were studied by using nanoindentation experiments, and films with higher elastic moduli were more resistant to deformation. However, the behaviour of films was dependent on the flexibility and water content of the underlying hydrogel substrates as well. These findings pave way for creation of stable plasma polymer films on biomedical devices made from hydrogels.

Keywords: Plasma polymer films, Hydrogels, Swellable films, Water stability, Environmental stress cracking

1. Introduction

Hydrogels are common materials for fabricating biomedical devices. Surface modification of hydrogels can impart the hydrogels with enhancements like increased cell attachment [1], decreased bacterial adhesion [2] as well as the capability to graft biomolecules [3] onto the hydrogel surfaces. Plasma polymerisation provides easily reproducible, well controlled thin films on the surface of hydrogels without the use of solvents [4-6].

However, such thin films are prone to instability in conditions of water immersion. During the process of plasma polymerisation, hydrogels are relatively dry and the plasma polymer films adhere to such hydrogels. However, these hydrogels take up water after immersion and therefore the films must match the swelling of the hydrogel. If the films don't swell in a proportionate manner, internal stresses build up on the plasma polymer films. These internal stresses could manifest as fragmentation when hydrogels are placed inside water after plasma polymerisation. Other methods of surface modification, including wet treatments that use solvents, could cause changes in the bulk properties of hydrogels.

Therefore, there is an interest to study plasma polymer films (PPFs) with the ability to swell upon absorption of moisture and de-swell upon desorption. While swelling characteristics of hydrogels in bulk has been studied in detail [6, 7], swelling behaviour of thin PPFs has not been thoroughly investigated. In this contribution, we aim to study the various plasma processing conditions that lead to deposition of swellable PPFs and how the conditions affect the stability and durability of such PPFs.

2. Materials and methods

2.1 Hydrogel fabrication - Hydrogels were prepared by UV curing of a liquid monomer mixture of 2-hydroxyethyl methacrylate, ethylene glycol dimethacrylate and 2-hydroxy-2-methylpropiophenone. The monomer is denoted by the term Polymacon and falls in the FDA Group

I of low-water, non-ionic polymers. This liquid was shaped into circular discs of 1.12 cm in diameter and 0.15 cm in thickness by placing the liquid inside an aluminium mould of similar dimensions while UV curing.

	HEMA (uL)	EGDMA (uL)	Crosslinker (uL)
HYD-003	990	5	5
HYD-004	998	1	1
HYD-005	980	10	10

Table 1 Chemical formulations for different types of hydrogels

2.2 Plasma polymer film (PPF) deposition - A low-pressure capacitively coupled RF glow discharge in gas mixtures containing a source of carbon and a source of heteroatom, was used to produce the PPFs on hydrogels. The films were deposited on the circular UV-cured hydrogel discs.

-	$Flow(C_2H_4)$	Flow(CO ₂)	Working	Applied
	(sccm)	(sccm)	pressure	power (W)
			(Pa)	
PPEO-A	5	10	80	10
PPEO-B	5	15	80	10
PPEO-C	5	20	80	10
PPEO-	5	40	80	10
Low				

Table 2 Plasma processing conditions for films investigated in this study

The depositions were performed in a cylindrical stainlesssteel vacuum chamber (20 cm in diameter and 50 cm in height) with a disc shaped powered electrode ($\emptyset = 10$ cm) on which the samples were placed. A showerhead gas distributor positioned 4 cm above the powered electrode also served as grounded electrode. The chamber was evacuated to a base pressure of ~3.5 Pa. The process mixtures were introduced via mass-flow controllers (see Figure 1). The gas flow ratio, defined as R = (flow of CO₂)/(flow of C₂H₄) was one of the experimental parameters varied to control film composition. Table 1 contains a description of the various experimental parameters used in the present study.

2.3 Evaluation of thickness and swelling behavior - PPFs were deposited on silicon wafers thickness of the PPFs on

silicon wafers was measured by contact profilometry (Bruker Instruments, DektakXT, Germany). Thickness of the films after water immersion and subsequent drying was then carried out to give an idea of the relative stability of the PPFs.

2.4 Surface and Cross-sectional SEM images – To study the morphology of PPF as well as the cross-sectional image on the hydrogels surface, the treated hydrogels were examined under a FEI Helios Nanolab focused ion beam scanning electron microscope. Surfaces of treated hydrogels immediately after plasma deposition and those of hydrogel surfaces after water immersion/folding were studied. Surfaces of blank, untreated hydrogels were also studied. To prepare the hydrogel samples for SEM, hydrogels were left inside the argon-rich atmosphere of an MBraun MB 200B glovebox. They were sputter-coated with 8 nm of gold coating immediately before SEM observation.

2.5 Measurement of elastic modulus – Experiments were carried out using a hardness tester (Nanovea M1, USA) equipped with a Berkovich three-sided pyramidal indenter (Synton MDP AG, Switzerland). Single repeat indentations at a minimum of five different points on the sample were utilised to calculate hardness and apparent moduli of elasticity. Experimental conditions for the single repeat indentations were initial load – 0.03 mN, loading = unloading rate = 0.75 mN/min and peak load = 1 mN. Data analysis was done according to the Oliver-Pharr method.

2.6 Dye permeation through hydrogels/PPFs – Hydrogels were fabricated according to the method described in section 2.1, and then plasma polymers were deposited on those hydrogels by the methods described in section 2.2. After deposition, these samples were placed in between the donor and receptor chambers of standard Franz diffusion cell with receptor volume of 1.5 mL. In the donor chamber, 200 µL of 50 µg/mL TBO in water solution was pipetted. The diffusion cell was placed undisturbed for 24 hours. After 24 hours, 10 µL samples were taken from the receptor chambers. These samples were used to calculate the TBO concentrations that had diffused through the samples. The amount of diffused TBO through hydrogels with PPFs was compared to that diffused through an untreated hydrogel, and this measurement gave an indication of the relative integrity of the PPF.

2.7 Atomic force microscopy studies – PPFs were deposited on silicon wafers and on hydrogel samples by using methods described earlier in the documents. The surface morphology of the films was investigated by atomic force microscopy (AFM) using a MFP3D instrument (Asylum Research, Santa Barbara, CA, USA). All samples were measured in tapping mode using silicon cantilevers (ACTA model, AppNano) with a nominal spring constant of 37 N/m, nominal resonant frequency of 300 kHz, and nominal tip radius of 6 nm. Gwyddion 2.48 software was used to process the AFM images.

3. Results and Discussion

Deposition on both silicon wafers and hydrogels led to PPFs of varying thicknesses. As the gas flow ratio (R)

between CO_2 and C_2H_4 increased (Table 2), the thickness of PPFs decreased. This can be attributed to the increased etching effect of the carbon dioxide precursor, leading to increased bombardment and removal of material from the layers formed due to polymerisation of ethylene.



Fig. 1 Changes in thickness of swellable PPFs deposited on silicon wafers after alternate water immersion and drying cycles

After deposition on silicon wafers, the PPFs were stable in varying degrees towards exposure and immersion to water. PPFs formed using lower flow rates of carbon dioxide were more stable compared to those formed using higher carbon dioxide flow rates. All PPFs have shown the capacity to expand following immersion in water. All PPFs also displayed a cycling behaviour after immersion in water and subsequent drying. Regardless of gas flow ratios, all PPFs would undergo swelling after water immersion but would the return to the original thickness due to drying after being left in ambient conditions (Fig.1).

Despite all PPFs being able to cycle in terms of thickness before and after water immersion, there were minor differences in terms of the quality of PPFs after being subject to water immersion. All PPFs in this study were deposited at constant pressure of 80 Pa and output power of 10 W. The PPF deposited at the lowest gas flow ratio (R=2, PPEO-A) displayed a slight reduction in thickness as the number of water immersion cycles was increased. The PPF deposited at the medium gas flow ratio (R=3, PPEO-B) was relatively more stable in terms of thickness after water immersion. However, the PPF deposited at the highest gas flow ratio (R=4, PPEO-C) displayed an increase in the thickness as the number of water immersion steps was increased. In comparison, a negative control was employed in the form of a plasma polymer deposited at very high gas flow conditions (R=8, PPEO-Low) and this film did not show any changes in thickness after water immersion or drying.Changes in the shape and structure of PPFs after water immersion was also linked to the nature of the underlying hydrogel substrate (Table 1). Three types of hydrogel substrates were studied, and they varied in terms of the water content. SEM was utilised to study changes in morphology of the surface, as well as presence of cracks/fragmentation by imaging the cross-sectional nature of the PPFs on hydrogels.



Fig. 2 Cross-sectional SEM imagery of swellable PPFs on different hydrogel types

While the change in shape and structure after water immersion depends on the type of the PPF, there is an under arching effect of the water content of hydrogels. As the hydrogels become more flexible, the change in shape of the hydrogels after water immersion also translates to the change in shape of PPFs. The films on the lower water content hydrogels (HYD-005) display almost no change in structure in the cross-sectional images after water immersion (Fig. 2). These findings are useful as they provide direction on the types of PPFs that can be used as successful coatings on hydrogel-based biomedical devices that are expected to undergo exposure to human body fluids.



Fig. 3 SEM images of the surfaces of swellable PPFs on hydrogels before and after water immersion

Across the three types of swellable PPFs studied, the stability of the films towards water exposure and immersion decreased as the gas flow ratio increased with time. All films responded to the swelling of the hydrogel substrate by undergoing deformation, but the swellable film with highest flow ratio (R=4, PPEO-C) cracked after water immersion (Fig. 3).



Fig. 4 Apparent elastic moduli of an untreated hydrogel and those of swellable PPFs on hydrogel surfaces

The findings from the SEM images agree with those from nanoindentation studies. Pure, untreated hydrogel surfaces possessed the lowest elastic modulus of all samples (Fig. 4). The swellable PPFs deposited using lower and medium gas flow ratios (R=2/3, PPEO-A and PPEO-B) possessed higher elastic moduli and therefore more resistant to deformation. The PPF deposited at the highest gas flow ratio (R=4, PPEO-C) was more prone to deformation upon swelling, and therefore displayed higher incidence of deformation and cracking.



Fig. 5 Amount of TBO permeated through an untreated hydrogel as well as through hydrogels with swellable PPFs

As films become more susceptible to deformation, gaps and cracks are induced in the structure of PPFs after water immersion. Some of the material from the films might be lost during water immersion as the lower molecular weight fragments from the PPF get dissolved in water [7]. An untreated hydrogel allowed the highest amount of TBO to pass through, followed by the PPF deposited at the highest gas flow ratio (R=4, PPEO-C). This PPF had the lowest elastic modulus of all three swellable plasma polymer films. The other films displayed lesser amounts of TBO permeation (Fig. 5).

Increase in gas flow ratio leads to increased cluster formation in the gas phase inside the plasma reactor chamber. These clusters deposit on the substrate surface, with an increased cluster size and therefore increased average roughness of the surface (Fig. 6). This rough structure of the films produces a film that has gaps in between clusters of plasma polymers, and this reduces stability of films in aqueous solution as shown by the TBO permeation results.



Fig. 6 AFM images of different swellable plasma polymer films deposited on silicon wafers, with scans carried out in non-contact mode

4. Conclusion

In this study, we have shown the successful fabrication of a set of swellable plasma polymer films using different gas flow ratios of hydrocarbon and functional precursor gases at similar pressures and applied power outputs. These films were studied for changes occurring before and after water immersion, primarily by measuring thickness changes. Changes on the PPF surfaces was investigated qualitatively by comparison of longitudinal and cross-sectional SEM images before and after water immersion. Stability and integrity of the PPFs was also compared by quantifying the dye penetration through untreated as well as plasma coated hydrogels. The study concluded that all plasma processing conditions gave rise to swellable films, but the ones deposited that lower gas flow ratios are more stable. To create durable PPFs on surface of hydrogels, the choice of processing conditions also needs to be made based on the type of hydrogel being used as a substrate.

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