Plasma Induced Grafting Polymerization of 2-Methacryloyloxyethyl Phosphorycholine Onto Silicone Hydrogels to Reduce Surface Hydrophobicity and Protein Adsorption

Plasma Induced Grafting Polymerization of 2-Methacryloyloxyethyl Phosphorycholine onto Silicone Hydrogel to Reduce Surface Hydrophobicity and Protein Adsorption

By Zhaowen Dong, B.ASc. Material Engineering

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AUTHOR: Zhaowen Dong, B.ASc. (University of Toronto)
SUPERVISOR: Professor Heather Sheardown

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ABSTRACT

Silicone hydrogels have been widely utilized in ophthalmic applications due to the comfort of hydrogels, their excellent biocompatibility, high oxygen permeability and transparency. For use as a contact lens, the silicone hydrogel interacts with the tear film, cornea, and eyelid; thus surface properties of the gel are crucial. The high oxygen permeability of silicone hydrogel contact lens materials mainly relies on the incorporation of siloxane functional groups. However these groups are extremely mobile and surface active, which can result in an increase in the lens surface hydrophobicity, as well as protein and lipid deposition. Therefore, there is a need for surface modification of silicone hydrogel contact lenses. Otherwise users may choose to decrease the frequency and wear duration of silicone contact lenses due to dryness or bio-fouling related issues.

A novel biomimetic methacrylate monomer which contains a phosphorylcholine group, 2-methacryloyloxyethyl phosphorycholine (MPC) was grafted onto the surface of novel silicone hydrogel materials to create a thick hydration layer in order to enhance the protein resistance and surface wettability. Low temperature air plasma was chosen to initiate grafting polymerization of MPC monomers onto silicone hydrogel substrates. Hydrogels were treated with plasma and exposed to air flow to yield hydroperoxides on the surface; the peroxide group acted as a photo-initiator for further thermal MPC grafting polymerization.

After surface modification, the silicone hydrogels were characterized by XPS and ATR-FTIR to confirm the structure and elemental composition. A significant amount of phosphorus was found on the XPS spectra of the modified materials, demonstrating that the MPC monomers were successfully grafted onto the gel surface. According to water contact measurement results, the modified samples possessed very hydrophilic surfaces, with advancing angles of about 27°, compared the unmodified samples at around 110°. After surface grafting, between a 20% and 50% reduction in protein deposition was observed, which aligned with water contact angle results. Other properties such as oxygen permeability, transparency, water equilibrium, and elastic modulus remained unchanged after the air plasma exposure and thermal MPC polymerization.

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LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
ATR-FTIR	Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy
BSA	Bovine Serum Albumin
CW	Continuous Wear
Dk	Oxygen Permeability
DMA	N,N-Dimethylacrylamide
EWC	Equilibrium Water Content
FDA	Food and Drug Administration
GPC	Giant Papillary Conjunctivitis
HEAM	Hydroxyethyl Methacrylate
PL	Isoelectric Point
MA	Methacrylic Acid
MMEQ	Monomethyl Ether Hydroquinone
MPC	2-Methacryloyloxyethyl Phosphorycholine
NVP	N-Vinyl Pyrrolidone
PBS	Phosphate Buffered Saline
PDMS	Polydimethylsiloxane
PEG	Poly(ethylene glycol)
PLTF	Pre-Lens Tear Film
PMMA	Poly(methyl methacrylate)
POLTF	Post-Lens Tear Film
PVP	Polyvinylpyrrolidone
RGP	Rigid Gas Permeable
SCCM	Standard Cubic Centimeters Per Minute
TFLL	Tear Film Lipid Layer
TRIS	3-[Tris(trimethylsiloxy)silyl]propyl Methacrylate
UV	Ultraviolet
XPS	X-Ray Photoelectron Spectroscopy

1. INTRODUCTION

Contact lenses have become important for people who wish to see the world clearly without glasses and heavy steel frames. Contact lenses are indeed a masterpiece of the history of healing art, and they have a remarkable long history that goes back more than five centuries. Leonardo da Vinci is often considered as the first conceptual pioneer of contact lens. In 1508, he tried to manipulate corneal power by inserting a small water filled glass hemisphere over the corneal surfaces of patients (Mannis & Heitz, 2004). The glass-blown scleral lens remained as the one and only choice until the 1930s when the polymethyl methacrylate (PMMA) was invented (Key, 2007). Compared with glass, the new plastic material was thinner and more comfortable to be fitted over the ocular surface, but there were plenty of aspects that could be improved including gas permeability, flexibility, and surface wettability. As the manufacturing technology progressed, the hydroxyethyl methacrylate (HEMA) based soft water containing lens was first marketed in 1971 (Kemsley, 2008). This hydrogel successfully inherited the soft and comfort from the water content or the hydrophilic materials.

Nevertheless, limited gas permeability remained as an unsolved problem for all types of contact lenses which was necessary for lenses to be worn overnight. Corneal oxygen entirely relies on exchange with the outside environment, so the contact lens must be sufficiently gas permeable to avoid hypoxia-related problems.

Since the late 1970s, silicone elastomers have become a popular material choice for many types of medical devices due to its chemically inert, physically flexible, and highly transparent nature (Sweeney, et al., 2000). Silicone elastomers have excellent oxygen permeability due to the extremely mobile siloxane back groups (Sweeney, et al., 2000). The studies also have shown that the level of overnight corneal edema for the lens user (during eye closure) was significantly lower compared conventional hydrogel lens (Holden and Mertz, 1984). However, the first but very unsuccessful commercial attempt to create a silicone lens was made by Bausch & Lomb in 1984 as a 30 day extend wearing lens indicated by the FDA (US Food and Drug

Administration). Despite the exceptionally high oxygen permeability, the dry silicone lens surface tended to adhere onto the ocular surface due to insufficient ion and fluid transport (Chou, 2009). In addition, due to the very hydrophobic nature of silicone, it was not only very difficult for the lens to absorb wetting agents but caused rapid lipids and proteins deposition (Chou, 2009).

In fact, the first silicone hydrogel contact lens was not marketed until 2002, with the entry of Pure Vision lens by Bausch & Lomb, which ushered a new era of silicone hydrogel contact lenses. By 2016, the global contact lens market was worth about $7.2 billion with an anticipated 5% annual growth. Silicone hydrogels occupy 68% of the worldwide lens market share (Nichols, 2017). The silicone hydrogel lens became such a popular choice because it combines the benefits of highly oxygen permeable silicone-based monomers (like 3-methacryloxypropyl trimethylsiloxy silane (TRIS)) with highly wettable and ion permeable hydrophilic monomers (such as HEMA or N-N, Dimethyl Acrylamide (DMA)) (Goda and Ishihara, 2006). On the other hand, the siloxane functional groups are extremely mobile and surface active, so they can easily rotate to the lens surface. This will significantly lower the surface wettability which is usually associated with an uncomfortable wearing experience, dryness, redness, or other mechanical irritations (Tighe, 2013). Besides, low lens surface wettability leads to rapid surface and lipid deposition, which causes fouling or diminishes visual clarity and lens lifetime, and it can further induce corresponding immunological responses (Thissen, 2010).

In the current project, a novel type of silicone copolymer contact lens material was synthesized by UV-induced photoinitiation using silicone based (methacrylate polydimethylsiloxane (PDMS) and TRIS) and hydrophilic monomers (DMA) to achieve a relatively high-water equilibrium content and oxygen permeability. Multiple surface modification techniques can be applied to modify the hydrophobic disadvantage of the silicone-based lens such as plasma oxidation and coating, internal wetting agent, and surface graft polymerization. Surface graft polymerization was chosen for this project due to its chemical stability of covalent binding and lower risk of protein deposition (Sun, 2011).

In order to achieve better surface wettability and antifouling properties, a biomimetic monomer, MPC, was selected to graft onto the silicone hydrogel. The double bonded methacrylate group allows various types of reactions to be conducted, and zwitterionic phosphorylcholine side chain creates a thick hydration layer, which improves surface wettability and non-specific protein adhesion resistance significantly (Monge,2011). Low pressure air plasma is the one of most versatile and preferable graft polymerization techniques. It can generate reactive sites rapidly at room temperature, does not alter the hydrogel's bulk material properties or involve any catalytic contamination on the gel surface (Goda.T, 2006). Plasma treatment was applied to generate active peroxide radicals on the gel surface, which can be viewed as the "pre-grafted photo-initiators" for initiating graft polymerization on top of silicone hydrogel samples.

In the scope of this project, the MPC modified and unmodified silicone hydrogels were characterized by static water contact angles, lysozyme and bovine serum albumin (BSA) protein deposition measurements. The evidences of covalently bind MPC grafting layer were confirmed by XPS and ATR-FTIR techniques. Other important factors such as water equilibrium content, oxygen permeability, ion transmissivity, elastics modulus, and light transmissivity will be also investigated in this project.

2.LITERATURE REVIEW

2.1 OCULAR ENVIRONMENT FOR CONTACT LENSES

The human eye is a fragile and extremely complex organ which is directly exposed to the outside environment. It is very particularly sensitive and vulnerable to external threats such as air pollutants, infectious microorganisms, or even large variations in temperature and humidity (Wolkoff, 2010). The complicated tear film and lens interaction place very high demands on the performance of the contact lens as an "ophthalmic compatible" material. As an ophthalmic compatible device, the lens must help to maintain a stable, continuous tear film for visual clarity. In addition, it should trigger a minimal amount of tear film deposition or denaturation. Moreover, the lens should sustain normal hydration for the comfort of the user, must be sufficiently oxygen permeable to maintain normal corneal metabolism, and possess sufficiently high ion transmissivity to allow smooth, comfortable, non-irritating ocular movement under the contact lens (Nicolson, 2001). Therefore, it is extremely crucial to understand the surrounding ocular environment for contact lens design.

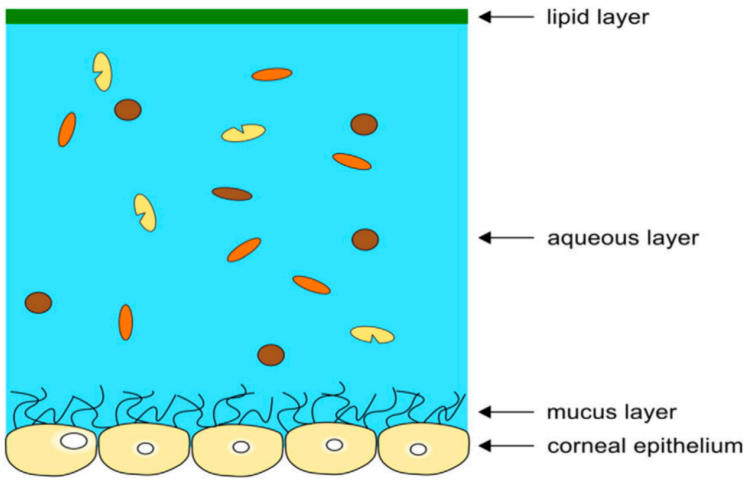


Figure 1. Human tear film structure, image adopted from (Cwiklik, 2016).

As shown in Figure 1 above, tear film is the liquid layer which covers the cornea, acting as a physical barrier between the eye and the outside environment. It is not one homogenous aqueous phase but can be divided into three distinct layers, containing

many insoluble components (Cwiklik, 2016). The outermost layer of the tear film, predominantly composed of lipids, is known as the Tear Film Lipid Layer (TFLL). It helps to reduce the surface tension of the tear film, re-spreading tear film after blinking, and prevent excess liquid evaporation (Cwiklik, 2016). Thus, TFLL plays a critical role in maintaining tear film stability.

The second layer is an aqueous layer which contains many water soluble and insoluble components including electrolytes, proteins, peptides, and small molecule metabolites (Zhou, 2012). The primary roles of the aqueous components include presenting a smooth layer of light refraction, providing lubrication during blinking, nourishing corneal cells underneath and preventing dehydration and adhesion of dust particles and pathogens (J.P. McCulley,1997). According to a previous protein study, more than hundred types of protein can be found in this aqueous layer, with the most abundant proteins are tear lipocalin and lysozyme (A. Kijlstra,1994). Lipocalin assists with tear film spreading and lysozyme inhibits microbial activities (A. Kijlstra,1994).

The posterior layer is a mucin layer, which is mainly composed of sugar-rich glycosylated proteins produced by the epithelial cells to anchor epithelium (Cwiklik, 2016). Moreover, this mucin lay is easily wettable due to its gel-like structure, and the layer can also assist in re-spreading of the liquid after blinking (King-Smith, 2004).

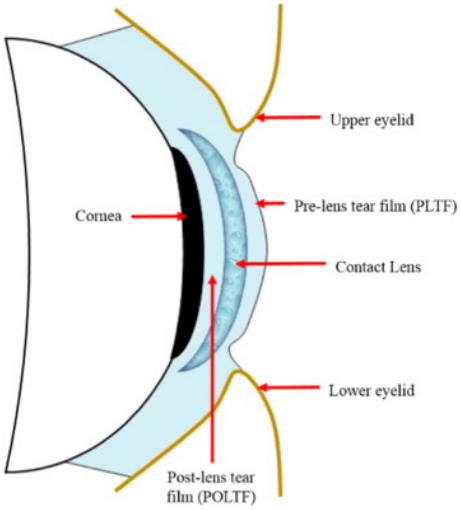


Figure 2. Schematic illustration of the insertion of a contact lens within the tear film, image adapted from (Gause, 2015).

The tear film plays a vital role in maintaining visual clarity and ocular surface health. However, the tear film is actually very thin about 6.5-9μm, compared with any type of contact lens which typically ranges from 60 to 200μm (Lira, 2015). It is desirable for the contact lens to disrupt the stability of tear film as little as possible. After insertion of a contact lens, the tear film will be divided into two layers, the Pre-Lens Tear Film (PLTF) and Post-Lens Tear Film (POLTF). The PLTF layer provides a uniform and smooth coating layer over contact lens (Gause, 2015). If this layer becomes rough, irregular, or even depleted, it causes light scattering at the lens surface and reduces the image quantity (Timberlake, et al., 1992). In addition, a stable PLTF can provide extra lubrication to palpebral conjunctiva (see Figure 3) during blinking. Furthermore, the PLTF layer, specifically the superficial lipid film, can reduce evaporation, which helps to maintain hydration of the lens (Nichols, 2003). If the PLTF is altered by insertion of the lens, the lens will be quickly dehydrated after evaporation of PLTF. This is followed by POLTF depletion by absorption into the dry contact lens, resulting in contact lens related dry eye (Sharma A, 1985). As illustrated in Figure 2, POLTF acts as lubrication layer and cushion zone between the lens and the corneal and conjunctival epithelium, which is vital to comfort and smooth ocular movement under the lens (Gause, 2015). Also, the POLTF can also help to remove cellular and inflammatory debris from this layer through tear exchange (Little SA & Bruce AS, 1994). Therefore, depletion of this layer may lead to infection, inflammation, and other mechanical irritations.

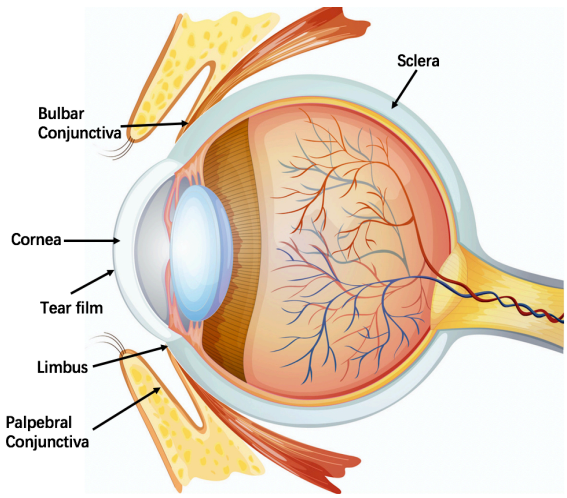


Figure 3. Schematic illustration of the eye structure with the exterior part captioned, image adopted from https://www.vectorstock.com/royalty-free-vector/human-eye-cross-section-vector-1854832

To understand the exterior structure of the eye or the ocular coat is extremely important to contact lens design because contact lens will be fitted over the exterior region of the eye. The ocular coat is composed of dense connective tissues, the sclera and the cornea. The cornea not only protects the eye from infections and structural damage to the deeper parts but also plays a critical role in the transmission and refraction of light to the lens and retina (Meek, 2015). Since the cornea is avascular, the nutrient supply is entirely dependent on the exchange of tear film and aqueous humor (Meek, 2015 &Yiallouro, 2016). Similarly, oxygen can be only received via permeation from the surrounding environment; thus the contact lens must be oxygen permeable enough to avoid hypoxia related problems (Macrae,1987). The sclera forms a white colored connective tissue coating layer over the entire eyeball surface, and helps the eye to maintain its shape, as well as protecting the eye from either external or internal forces (Willoughby, 2010). The conjunctiva is a thin and transparent mucous layer which can be distinguished into two segments. It covers part of the front surface of the eye and part of inner surface of the eyelid, making it impossible for the lens to move behind the eye (Heiting, 2017). The conjunctiva also keeps the inner surface of eyelid moist, so the eyelid can open and close smoothly without too much friction (Heiting, 2017). Lastly, limbus is not only the connective tissue between cornea and sclera but also contains the pathway of aqueous humor outflow (Buskirk,1989).

2.2 SILICONE HYDROGEL BASED CONTACT LENSES

The oxygen permeability or Dk which has a unit of barrer $=10^{-10}\frac{\text{ml O2}\times\text{cm}}{\text{sec}\times\text{cm2}\times\text{mmHg}}$, is one of the most important factors to validate the performance of silicone hydrogels because it is inevitable that contact lens acts as a barrier to reduce oxygen to the anterior cornea (Sweeney, 1999). In the open eye, the oxygen level is determined by the oxygen transmissibility (Dk/t) of the lens material; the eyelid further reduces

oxygen concentration as an additional barrier in the closed eye (Covey, Sweeney, et al., 2001)

Soft extended overnight wear lenses became commercially available in the late 1970s. However, the performance of the early lenses were not satisfactory to either the patient or the practitioner. Due to their limited oxygen permeability, many (up to 30% over a period of 12 months) suffered from chronic or acute hypoxia induced corneal epithelial complications such as blurry version, inflammation, edema, and epithelial microcysts (Sankaridurg, 2000). The daily disposable lens was introduced in the 1990s to provide safe and convenient wearing on a daily basis. However, up to 15% of the users sleep in with these lenses, which only designed for daily wear (Holden,1988). In addition, 97% of users have expressed the desire to wear lenses continuously at least six nights per week, and 85% of patients believed that extended wear was also an essential determining factor in their choice of contact lens (Holden,1988). Thus, there was a significant need for a more gas permeable contact lens material.

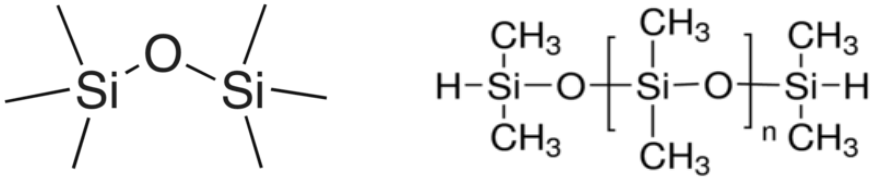


Figure 4. Siloxane functional group and chemical structure of Polydimethylsiloxane monomer (PDMS).

Silicone hydrogel contact lenses are also known as Continuous Wear (CW) soft hydrogel contact lenses. CW soft hydrogel lens can be defined as the lenses that rely on silicon or fluorine (siloxane or fluoroalkyl groups) to enhance the oxygen permeability rather than the relying on the water content from the hydrophilic polymers to control oxygen permeability (Nicolson, 2003). For example, silicone-based commercialized contact lens Lotrafilcon-A (24%) has a significant lower Equilibrium Water Content (EWC) compared with its conventional HEMA based counterpart etafilcon-A (58%). The Lotrafilcon-A (140 Dk) has 4 times higher oxygen permeability compared with etafilcon-A (28 Dk) (White, 2013). It has been

suggested that the minimum Dk requirements to avoid end of day and end of seventh-day edema are 24 and 35 barrers (Mertz GW.,1980). In addition, the minimal (less than 4 % corneal edema) Dk requirement for the overnight lens wear is 87 barrers (La Hood,1988). If oxygen permeability can reach 125 barrers, then it is possible to completely avoid overnight edema and other hypoxia symptoms (La Hood,1988). In fact, the high-water content puts a low upper limit onto lens' oxygen permeability. The water oxygen permeability limit is 80 barrers, which is significantly less than 300 Dk, the oxygen permeability of PDMS (Alvord,1998).

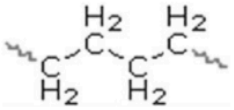
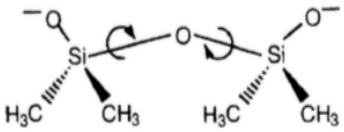
		
Chain Structure		
Bond length (nm)	0.154	0.163
Bond angle (°)	112	130
Energy to rotate (kJ/mol)	15	1

Table 1 Comparative properties of silicon-oxygen and carbon bonds, image adopted from (Tighe, 2013).

As Table 1 illustrates, the uniqueness of silicone hydrogel lenses compared with conventional lenses is due to the structure difference between carbon-carbon and silicon-oxygen bond (see Figure 4). Compared with carbon-carbon bonds, silicon bonds are significantly longer, flatter, and consume less energy to rotate (Tighe, 2013). There is a very interesting analogy, siloxane oxygen bonded segments are like an eel taken out from the water. It will wriggle and writhes, because it's inherent nature (mobility) it can always find its way to water (surface or hydrophobic environment) (Tighe, 2013) as shown in Figure 5. The exceptionally high oxygen permeability of silicone hydrogel lens is due to the extremely flexible siloxane backbones from the silicone-based macromer components, which rotates and transmits oxygen easily through the lens substrate (Goda & Ishihara, 2006). Due to its high oxygen permeability, silicone-based hydrogel soft lens has quickly dominated the global lens market, occupying more than 68% of the market share and a

significant percentage of first-time wearer refits from other types of contact lens (Morgan PB,2015).

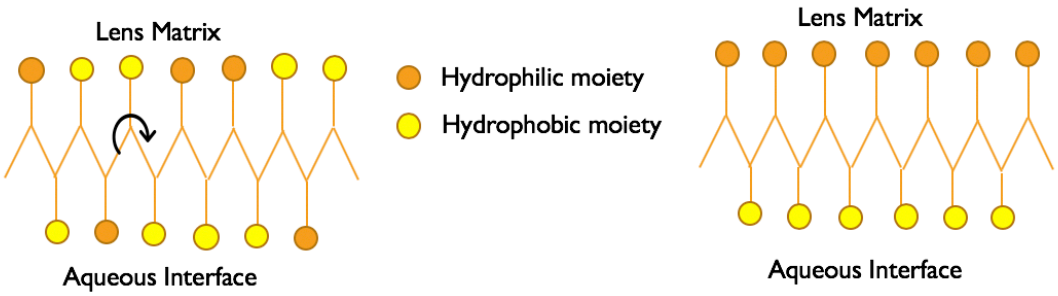


Figure 5. Siloxane bonds rotation after aerial exposure

As discussed in the previous section, tear film is very critical to ocular health and contact lens wearing comfort due to its anti-microbial and lubrication roles. Studies have shown even for high water content soft contact lenses (>50%) that lens wear will still disrupt the stability of tear film, which ultimately leads to lens dehydration and dry spot formation (Nichols, 2004). This inevitable problem even exists for the thinnest contact lenses because it is still about more than 9 times thicker than the tear film. The outermost layer of PLTF or lipid film layer which mainly prevents excess tear film evaporation is likely to experience longer exposure times and break down risk to the atmosphere and ultraviolet light than non-lens wearing condition (Jones, 2012). Moreover, silicone hydrogels have a significantly higher lipid deposition and lipid denaturation compared with hydroxyethyl methacrylate (HEMA) based soft hydrogel due to its relatively hydrophobic nature (Jones L, 2003). The reason is the siloxane groups are extremely dynamic inside of the soft water containing hydrogel network, so they can move freely move to the lens surface. This phenomenon is referred as “like attracts like”, the siloxane groups are attracted by the same hydrophobic air (Nicolson, 2003). After lens insertion, the thin PLTF layer will be exposed longer to the air condition, so the dry spots will be more likely to form on the lens surface after over top tear draining (Bruce, 1996). Then hydrophobic siloxane groups will migrate to the lens surface after air exposure. This potentially accelerates the deposition of the lipids (hydrophobic lipid tails), and can leads to total breakdown of the lipid film layer which ultimately causes drainage of PLTF and POLTF and eye dryness (Little, 1994). It is worth mentioning that this problem does not happen with

silicone-acrylate rigid gas permeable (RGP) lenses. The RGP lens has a glassy and rigid matrix, so the siloxane does not have the same degree of motion in the hydrogel (Tighe, 2004).

2.3 SURFACE MODIFICATION OF SILICONE HYDROGEL LENSES

The initial design emphasis back to 1990s on silicone hydrogel contact lenses can be generally broadened into two different regions; daily open eyewear, and highly oxygen permeable overnight wear (Morgan PB, 2010). Therefore, balancing the components of silicone hydrogel materials for different purposes are very critical to wearing comfort. For instance, there is a general trend that shows that when the hydrophilic components or water content increases, the oxygen permeability and young's modulus decreases (Truong, 2014). Thus, silicone hydrogel lenses are unique in many ways including in water content, Young's modulus, and oxygen permeability.

As a result, silicone hydrogel lens often is divided into first-, second-, and third-generation rather than one cohesive group. Each new generation does not necessarily replace or build on the previous one, but has different substrate components, surface treatments, or polymer chemistry (Flynn, 2008).

Balafilicon A (PureVision, Bausch & Lomb) and Lotrafilcon A (Night & Day, CIBA Vision) are the most representative marketed first-generation silicone hydrogel lenses. Balafilcon A has a Dk of 99 barrers and 36% water content, is composed of TRIS and N-Vinyl Pyrrolidone (NVP) (Tighe, 2006). For Balafilicon A, plasma oxidation is conducted inside of a gas chamber to convert hydrophobic TRIS on the surface into hydrophilic glassy islands of silicate, which acts as the "water attracting bridges" covering the hydrophobic substrate underneath (Nicolson, 2003). On the other hand, Lotrafilcon A involves copolymerizing of TRIS, DMA, and a large amount of fluoro-siloxane macromers, so it results in a much higher Dk of 144 barrers and a lower water content of 24% (Chou, 2008). Plasma coating is subsequently conducted on the surface of Lotrafilcon A lens to create an ultra-thin (25 nm) hydrophilic layer. This

layer helps to cover the hydrophobic silicone components below, which enhances the surface wettability of the lens (Nicolson, 2003).

The second generation silicone hydrogel Galyfilcon A (Acuvue Advance, Vistakon) and Senofilcon A (Acuvue Oasys) involves using siloxane macromers, hydrophilic monomers (HEMA or DMA), and the "Tanaka monomer" which is a more hydrophilic TRIS derivative (Chou, 2008). This monomer was originally invented in 1979, at the Toyo Contact Lens Company by Kyoichi Tanaka. Compared with the first generation, both brands have a significantly higher water content (Galyfilcon 47% and Senofilcon 38%) but a relatively low Dk (Galyfilcon 60 barrers and Senofilcon 103 barrers) (Tighe, 2004). Due to the high-water content and surface wettability, no additional surface treatment is required for the Galyfilcon and Senofilcon lens. In order to maintain a high degree of hydration of the lens throughout the wearing day, a long chain and high molecular weight monomer; Polyvinyl-pyrrolidone (PVP) is incorporated into the matrix of both silicone hydrogel lenses as the internal wetting agent (Jones, 2006). The PVP serves as a humectant, meaning it attracts and retains moisture inside of the lens substrate (Jones, 2006).

The latest generation or the most recent marketed silicone hydrogel lens; Comfilcon A (Biofinity, CooperVision) and Enfilcon A (Avaira, CooperVision), uses a unique long-chain siloxane macromer combining with other hydrophilic components (Jones, 2006). These two lens materials are referred to as "inherently wettable", and requires no internal wetting agent or surface treatment (Chou, 2008). Oxygen can be transmitted efficiently through the silicone component, so more hydrophilic components can be incorporated into the hydrogel matrix. Thus, this breaks the traditional reverse relationship between water equilibrium and oxygen permeability. For example, Comfilcon A has a water content of 48% and a Dk of 128 barrers, while Enfilcon A has a water content of 46% and a Dk of 100 barrers (González-Méijome, 2006). Compared with previous generations, these numbers are unexpectedly high-water content for corresponding Dk values.

As previously mentioned, the contact lens will interact intensively with the surrounding biological environment such as the tear film, cornea, and the eyelid.

Thus, the silicone hydrogel material's surface characteristics like wettability, friction coefficient, and protein resistance are crucial to ocular health and comfort. Surface properties can be modulated by deposition of ultrathin polymer layers onto the substrate material, and this modification can be achieved by either physical adsorption or covalently bonding (Zydrko, 2011). Moreover, this modification method will not alter the bulk properties of the material (Xu, 2009). The physical absorption method, a reversible process, involves the adsorption of the desired polymer chains onto the substrate. However, this bonding layer is thinner and more unstable, and it can be physically exfoliated from the surface (Zhao, 2000). Furthermore, the grafted layer is not stable in the extremely complex ocular environment. In addition, the segments that are removed might trigger other mechanical and immunological complications (Tian, 2016).

On the contrary, the covalent bonding method can introduce a high density of grafted chains onto the substrate surface in a more precise and controlled manner (Bhattacharya A, 2004). In addition, the covalent bonds can minimize chain delamination, improving the long-term stability, and thus this also makes grafting different polymer on the same substrate possible (Minko S, 2008). Therefore, most silicone hydrogel lenses are modified by covalent grafting (Edmondson, 2004). Lastly, the covalent polymer grafting can be accomplished by the "graft from" and "grafting to" method (Figure 6).

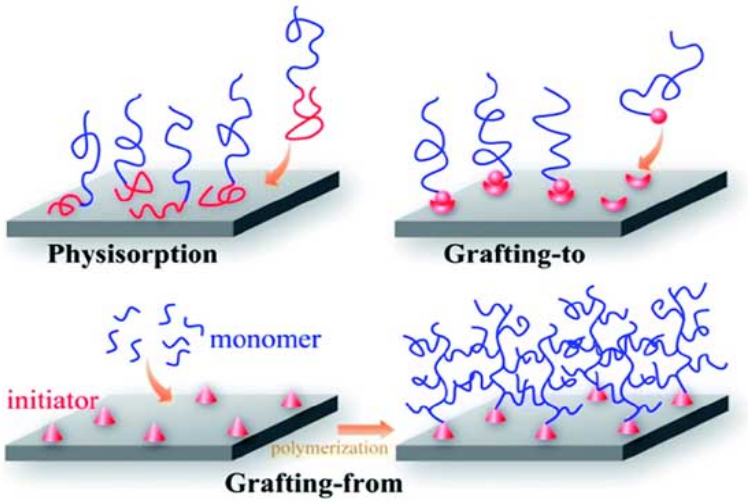


Figure 6. Schematic illustration of "physisorption", "grafting to", and "grafting from" surface modification procedures, image adapted from (Rohit R, 2015)

In the "grafting to" approach, the functionalized polymer chains will react with the reactive sites on the substrate surface (see figure 6). The grafting polymer chains can be synthesized through various polymerization technique such as controlled radical, anionic, and cationic polymerization (Zydrko, 2011). As a result, a well-defined polymer grafting layer with low molecular weight distribution can be obtained (Zydrko, 2011). Moreover, the "grafting to" approach can be conducted on various types of substrates such as flat (Luzinov, 2000), porous structure (Burtovyy, 2007), fiber/textiles (Ramaratnam, 2007), or even nanoparticles (Reukov,2009). The "grafting to" approach has used widely in early days due its simplicity (Ito, 1997). However, the major drawback of this method is limited grafting layer thickness. In other words, only a certain amount of polymer chains can be immobilized onto the substrate surface, because grafting polymer segments have to diffuse through the existing grafted layer (Lemieux M, 2003). This disadvantage limits the grafting space and potential reactive sites, which further constrains the grafting density and thickness.

On the other hand, the "grafting from" approach has attracted a significant amount of attention in recent years (Motornov & Lemieux, 2003). To be specific, the "grafting from" approach utilizes pre-existing initiators on the substrate surface to initiate chain polymerization growth, and then monomers can easily migrate to and grow from the initiating sites (Gupta, 2010). For this project, the initiators on the hydrogel surface are generated by low-pressure air surface plasma treatment, which will be discussed in detail in the next section. Depending on different grafting requirement, multiple techniques can be applied from, surface-initiated anionic and cationic, ring opening, atom transfer radical, and conventional free radical polymerization (Tian, 2016). Therefore, the "grafting from" approach can provide thicker and denser covalently grafted layer in a more flexible and controllable manner.

Plasma, a quasi-neutral gas, is also described as the 4th aggregate state of matter because plasma behaves differently from solid matter, liquids, and gases (Fromme, 2010). Plasma consists of neutrons, electrons, ions, and other atomic and molecular species, which moves freely around and interacts with each other (Chu, 2002). The

gas inside of plasma chamber is activated by the high frequency of waves for generating ions, electrons, and radicals. Depending on the types of gas and wave frequency used, different surface properties can be obtained (Kisling, 2007). At present, low pressure and temperature plasma treatment techniques dominate the contact lens surface treatment market due to their higher plasma generating efficiency and the fact that they will not alternate bulk properties of the lens materials (Slow, 2006). Any solid phase material compatible with low-medium vacuum level can be treated with low pressure plasma (Favia, 1998). Moreover, plasma surface treatment is a very rapid, economically effective, and environment friendly lens processing technique (Baumann L, 2013). In addition, besides creating active surface species, it also can be used to clean contaminants from the polymer surface, so it has become increasingly popular in the contact lens manufacturing industry (Baumann, 2013).

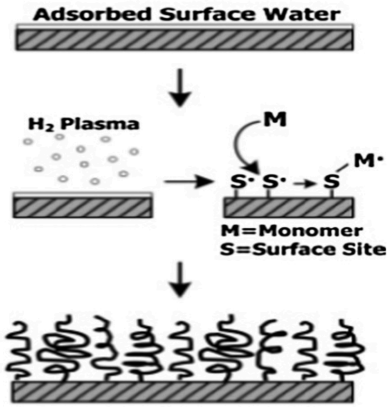


Figure 7. The process illustration of hydration, hydrogen plasma initiation, and chain growth on the surface silicone hydrogel substrate, image adopted from (Tian, 2016).

Several studies have shown that plasma-induced grafting polymerization is an effective and desirable method to functionalize the lens surface interface for further monomer immobilization (Wavhal, 2002, Gupta, 2002). To be specific, plasma induced polymerization is a two-step process. First, the reactive sites and functional groups are be created on the silicone hydrogel surface. The density of the radicals can be controlled through the treatment time and radio frequency power (Lewis et al., 2007). Second, the addition of the monomers on the reactive sites initiates chain polymer growth on the silicone hydrogel surface. This results in a high density of covalently linked polymer chains that are directly initiated from the substrate surface,

so it further enhances the grafting stability under thermal and chemical stresses (Drummond C, 2004). On the other hand, the plasma-initiated surface grafting might not be able to achieve sufficient surface initiation level for the inorganic species (due to the native surface oxides) and substrates with very large surface area (Kai T, 2006).

2.4 2-METHACRYLOYLOXYETHYL PHOSPHORYLCHOLINE

Numerous attempts had been made to improve the oxygen permeability and water content of the lens materials. However, little consideration has been paid to other critical characteristics such as surface wettability and anti-biofouling properties. Recently, biomimetic phospholipid grafting polymers have demonstrated good cell and protein adhesion resistance, high surface wettability, and excellent biocompatible properties, which means that they can play a vital role in contact lens surface modifications (Goda & Ishihara, 2006).

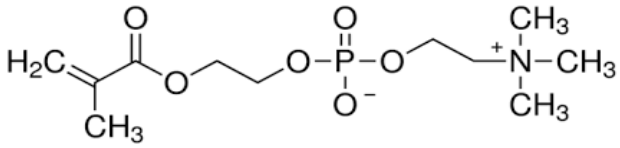


Figure 8. Chemical Structure of 2-Methacryloyloxyethyl Phosphorylcholine

Research into synthetic phospholipid monomers actually started back in the 1980s, based on the idea to mimic the structure of the cell membrane. The phospholipid is the fundamental unit of the cell membrane, which is consisted of a hydrophobic alkyl tail and a hydrophilic polar head (Goda & Ishihara, 2006). In 1990, Ishihara and his colleagues successfully synthesized MPC, a biomimetic zwitterionic monomer with a zwitterionic polar head and methacrylate tail (Ishihara, 1998). The reactive double bonds in the methacrylate tail allows for easy copolymerization with hydrophilic or hydrophobic substrate lens materials. The most representative phospholipid product is 2-methacryloyloxyethyl phosphorylcholine (MPC) shown in Figure 8 above. Many studies have shown that surface wettability of silicone-based products has increased significantly, while not altering the oxygen permeability of the silicone substrate (Ishihara, 1997& Sawada, 2003 & Moro T, 2004).

Zwitterionic means that the monomer contains both positive and negative charge, while maintains overall charge neutrality. Both charge units can bind with water molecules, which leads to the formation of a thick hydration layer around the p-MPC chains as shown in Figure 9. The tightly bonded hydration layer acts as a physical and energetic barrier (avoiding the entropic effects of surface dehydration) to prevent non-specific protein bonding (Chen et al. 2010).

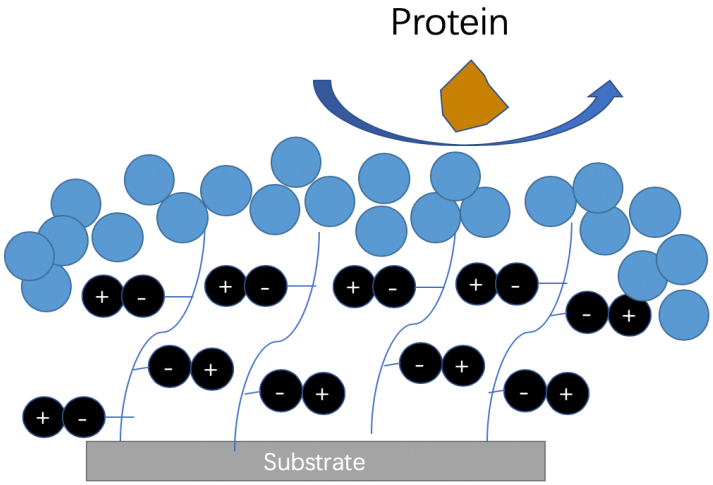


Figure 9. illustration of the working mechanism of MPC induced hydration layer repelling protein adhesion onto silicone hydrogel substrate

There are two types of anti-biofouling water soluble materials: polyhydrophilic and polyzwitterionic, which are often confused. Indeed, both material classes share some similarity in anti-biofouling behaviors such as electrical neutrality and hydrophilic nature (Chapman, 2000 & Ostuni, 2001). To be specific, proteins have randomly charged residues on their surface, and they tend to adhere to either positively or negatively charged surfaces (Chen et al., 2010). In addition, if the protein and polymer only share/bound by a small fraction of water molecules, then denaturation and tightly adherence will be more likely to happen (Ishihara, 1998).

Hydrophilic monomers like polyethylene glycol (PEG) based materials attract water through hydrogen bonding, and then water molecules penetrate into the polymer to form a hydrogen bonded network with polymers (Chen, et al., 2010). Since the hydrogen bonds can be easily broken, and thus the hydrophilic grafting layer might

experience the transition from non-biofouling to biofouling under dehydrated conditions (Gil, 2004). On the contrary, both positively and negatively charged units of the zwitterionic materials can bind water molecules more strongly and tightly via electrostatically (ionic solvation) induced hydration (Chen, et al., 2010). Studies also have shown that there is a clear correlation between the thickness of the hydration layer and non-specific protein resistance ability (Zheng, 2005, Herrwerth, 2003, Chen, 2000). Kitano also found that more bound water molecules around the surface of zwitterionic materials than the hydrophilic materials (Kitano, 2005).

Finally, it is worth to mentioning that chain length and flexibility will also impact the protein resistance of the grafted material. Longer chains under protein compression cause a greater level of steric repulsion to resist protein attachment (Jeon 1991).

2.5 PROTEIN ADSORPTION ONTO SILICONE HYDROGELS

As previously mentioned, silicone hydrogel contact lenses represent a relatively new generation of bio-materials that incorporate siloxane functional groups which substantially improves the oxygen permeability of the lens. Many clinical studies have demonstrated that these lenses lead to fewer cases of overnight associated physiologic complications compared with the conventional soft lens materials (Sweeney, 2000, Covey, 2001). However, there were also concerns about the silicone hydrogel lens' protein deposition behavior due to its relatively hydrophobic surface. For instance, there are more cases of immune complications such as giant papillary conjunctivitis (GPC) being reported with silicone-based lens compared conventional soft lens (Skotinitsky, 2002). Clinically, protein deposition on contact lens is extremely important, especially for the silicone hydrogel lens which are intended in overnight or longer period of use (Jones, 2003). Excessive protein adsorption and denaturation can result in a reduction of comfort, vision clarity, and increased inflammatory responses (Jones, 2003). Despite the fact that a definitive protein deposition and denaturation mechanism still remains unclear, many studies have confirmed that a number of factors can influence the silicone hydrogel lens' protein deposition and denaturation such as material surface charge, water equilibrium content, degree of hydrophilicity, and wearing time (Tighe,1998, Jones, 2000, Garrett 1996).

The surface characteristics of silicone hydrogel lens can substantially impact protein resistance of the lens, and other relevant factors such as protein charge, protein concentration, and protein structure will also influence protein deposition onto the silicone hydrogel lens (Luensmann, 2012). The primary contact lens protein adsorption source is the human tear film. Proteins are major components of the human tear film with a total concentration between 6.5-9.0 mg/ml depending on the individual, and some contact lens studies have shown that time of day, age, and the material of the lens can also greatly affect the tear film protein concentration (Tighe, 1993, Ng, 2000, Sack, 1992). The human tear film proteins perform a variety of tasks such as protection from an excessive amount of tear evaporation and interaction with outside pollutants, nourishing corneal epithelial cells, regulating immune responses, antioxidation, and metabolism (Green, 2008, De Souze, 2006). Proteins in the human tear film typically range from 10 kDa to 2360 kDa, and approximately 80% of proteins have a size less than 100 kDa (De Souze, 2006). Moreover, tear film proteins generally range in charge from isoelectric point (pl) of 1 to 11 (Zydney, 1996). It is worth mentioning that most of the tear film proteins have a pI that is significantly greater or smaller than the physiological pH 7.4, which helps to improve the solubility of proteins in the tear solution (Nuyken, 2005, Bajpai, 2004). If the solution environment is too close to the pl of proteins, and then leads to increases in protein aggregation and deposition (Nuyken, 2005, Bajpai, 2004). For instance, lysozyme (14.3 kDa, pI of 11.0) and BSA (66 kDa, pI of 4.7), are the most representative and commonly used proteins for contact lens protein deposition studies, because both of proteins have abundant concentration (1.9 mg/ml and 0.5mg/ml) and play significant roles (anti-inflammatory and transporting insoluble molecules) in the human tear film (Rezwan, et al. , 2005, Tighe, 1993). Since the average pH of the human tear film is around 7.4, so the lysozyme is positively charged, and albumin is negatively charged (Fullard,1990, Sack, 1993).

Proteins are three dimensional complex copolymers that are arranged into four structural levels. Each amino acid will have a specific type of side chain on the backbone, which gives specific functionality (Brandon, 1999). Accordingly, amino

acids can be subcategorized into polar, non-polar, and positively or negatively charged (Brandon, 1999). The primary structure can be further organized into more complicated three-dimensional structures, and proteins are typically folded together in a three-dimensional structure by hydrophobic forces, hydrogen bonds, and van der Waals forces (Voet, 2004). Typically, the non-polar (hydrophobic) amino acids are buried inside of the protein molecules, and the polar and charged (hydrophilic) amino acids are exposed, interacting with the surrounding environment (Luensmann, 2012). In an aqueous solution like the human tear film, most protein structures are in the metastable state, because there is a lack of accessible surface with which the non-polar amino acids can interact (Luensmann, 2012). Thus, the Gibbs energy increases, so energetically it is unfavorable for conformational changes to happen (Norde, 1992). However, once the protein is exposed to a solid hydrophobic surface like a dry lens surface, then the protein tends to reorganize its structure from inward so the free energy decreases (Roach P, 2005). Consequently, the protein will be unfolded or coiled into a new random structure, and thus deposition and denaturation are more likely to happen. As a result, this conformational change prevents proteins from performing their natural roles or interacting with other cells and proteins (Lindgren, 2005). Hence, this can trigger bio-fouling, including a loss of optical clarity and in extreme cases, immune responses such as GPC for the users (Allansmith, 1977). In addition, if the charged side chains of the amino acid contact with an oppositely charged lens surface, then protein surface deposition will be further enhanced. As mentioned in the previous section, this is also the reason that electrical neutrality of the grafting polymer is preferred for contact lens applications. Lastly, besides lens surface wettability, the other factors might impact protein stability are summarized in Table 2 below.

Table 2: The characteristics of surface and protein that affects protein adsorption on lens materials. Adapted from (Dee, 2002).

Property	**Effect**
Protein size	Larger the protein molecules have more bonding sites, so easier to bonded with the lens substrate.

Protein charge	Protein molecules near the physiological pH of the tear film, generally adsorb more readily onto the lens substrate.
Protein structure stability	Less stable proteins have smaller amount of intramolecular cross-linkings, so the proteins can be unfolded to a greater extent, which also means more bonding sites.
Surface potential	Surface potential will not only enhance the bonding with opposite charged amino acids, but also influences the ion distribution inside of the tear film.
Surface heterogeneity	Non-uniform surface characteristic domains can cause interaction with multiple types of protein
Surface topography	Greater degree of surface texture, exposes more surface area to interact with the proteins

Furthermore, Jones and colleagues have conducted protein deposition and denaturation measurements on two types of first-generation silicone hydrogel lens (Lotrafilcon and Balafilcon) and one conventional HEMA lens (Etafilcon). Etafilcon only had roughly one-third and one-fourth lysozyme denaturation amount compared to Balafilcon and Lotrafilcon respectively (Jones, 2003). Moreover, regardless of lipid type, silicone lens absorbed much higher lipid amount compared with the etafilcon lens (Jones, 2003). As previously mentioned, proteins are tending to adhere on the more hydrophobic surface. Despite the surface treatments used to modify silicone hydrogels, Lotrafilcon and Balafilcon are still more hydrophobic compared with their conventional counterpart (Lee, 2001 & Garrett, 1999 & Jones, 2001). Based on this fact, more protein deposition and denaturation should be expected on less wettable surface materials (Jones, 2001, 2003).

3. EXPERIMENTAL

3.1 SILICONE HYDROGEL PREPARATION

In this project, silicone hydrogel were prepared by copolymerization of the hydrophobic monomer 3(Tris (trimethylsiloxy) silyl) propyl methacrylate (TRIS) (98%, Sigma-Aldrich), the hydrophilic monomer N, N-dimethyl acrylamide (DMA) (99%, Sigma-Aldrich), and silicone macromer methacryloxypropyl terminated polydimethylsiloxane (10 cSt, Gelest Inc.). The TRIS and DMA monomers were chosen as the substrate materials, because they were already widely used in Lotrafilcon A and B silicone hydrogel contact lenses. Before the hydrogel synthesis, TRIS and DMA were all injected through a column containing inhibitor remover for the removal of the monomethyl ether hydroquinone (MMEQ) (99%, Sigma-Aldrich). 1050 mg of methacrylated PDMS (35 wt%), 900 mg of TRIS (30 wt%), and 1050 mg of DMA (35 wt%) were added into a 10 ml glass vial, and 400 mg of 1-hexanol was injected into the mixture as a diluent which helped to mix the hydrophobic and hydrophilic phases. In addition, 30 mg of Darocur 1173 photoinitiator (99%, Sigma-Aldrich) was added into the solution. This solution was then mixed by a magnetic stirring bar for a period of 20 minutes until homogenous. After the pre-polymerization mixing stage, the mixture solution was then injected into a mold for further polymerization.

The mold consisted of two acrylic photomask plates separated by a 1.0 mm thick Teflon spacer. Two polyester sheets were placed between the spacer and the photomask plates in order to prevent polymer adhesion onto the acrylic plates. The entire mold was bolted tightly together to avoid solution leakage inside of the Ultraviolet (UV) oven. Once the pre-polymer injection step was completed, the mold was then transferred inside of UV chamber (Cure Zone 2 Control-cure, USA) with a 400 W metal halide lamp at a wavelength of 365 nm curing for 15 minutes. After photopolymerization, the silicone hydrogel remained inside of the mold for 24 hours and was then placed inside of the fume hood overnight for removal of any remaining 1-hexanol. The silicone hydrogel was further soaked in ethanol for another 24 hours

to remove the unreacted monomers. Finally, the hydrogel films were stored at 37°C in MilliQ-water until further use.

3.2 PLASMA INDUCED SURFACE GRAFTING OF P-MPC CHAINS

Before surface modification, the silicone hydrogel sheets were punched into circular discs with a diameter of 6.35 mm (1/4”). Different weights of 2-methacryloyoxyethyl phosphorycholine (MPC) (97%, Sigma Aldrich) powder were dissolved in 10ml glass vials with 4 ml Milli-Q water and passed through a column of inhibitor removers. The MPC solutions were then purged with nitrogen in order to eliminate the presence of dissolved oxygen. The hydrated silicone hydrogel discs were placed in a plasma chamber for surface radical activation (Expanded Plasma Cleaner, PDC-002 (230 V), Harrick Plasma, USA), and air flowrate, vacuum pressure, and gas mixing (if second gas was needed) were controlled and monitored by PDC-VCG2 digital meter (Harrick Plasma, USA). In order to initiate the plasma system, the chamber was vacuumed to a pressure of 80 mTorr. Once the pressure reading had stabilized, air was then used as the medium of glow discharge plasma with a flow rate of 30 SCCM (standard cubic centimeters per minute). Both sides of the silicone hydrogel discs were treated with plasma for about 120 seconds at 45 W, because both of slides of the hydrogel contact lenses will interact tear film intensively.

The schematic illustration of plasma induced grafting polymerization of MPC onto the silicone hydrogel is shown in Figure 10 below. MPC aqueous solutions were prepared at three different concentration, 0.1 M, 0.5 M, and 1.0 M. The plasma treated silicone hydrogels were immersed into glass vials containing the MPC aqueous solution, and then the sealed glass vials were placed into a hot water bath for 24 hours. The hydroperoxides were thermally decomposed into radicals, initiating the chain growth of MPC monomers onto the surface of silicone hydrogel discs. Lastly, the modified silicone hydrogel discs were washed with ethanol solution on a shaker for 24 hours to remove all the unbounded MPC homopolymers from the hydrogel samples.

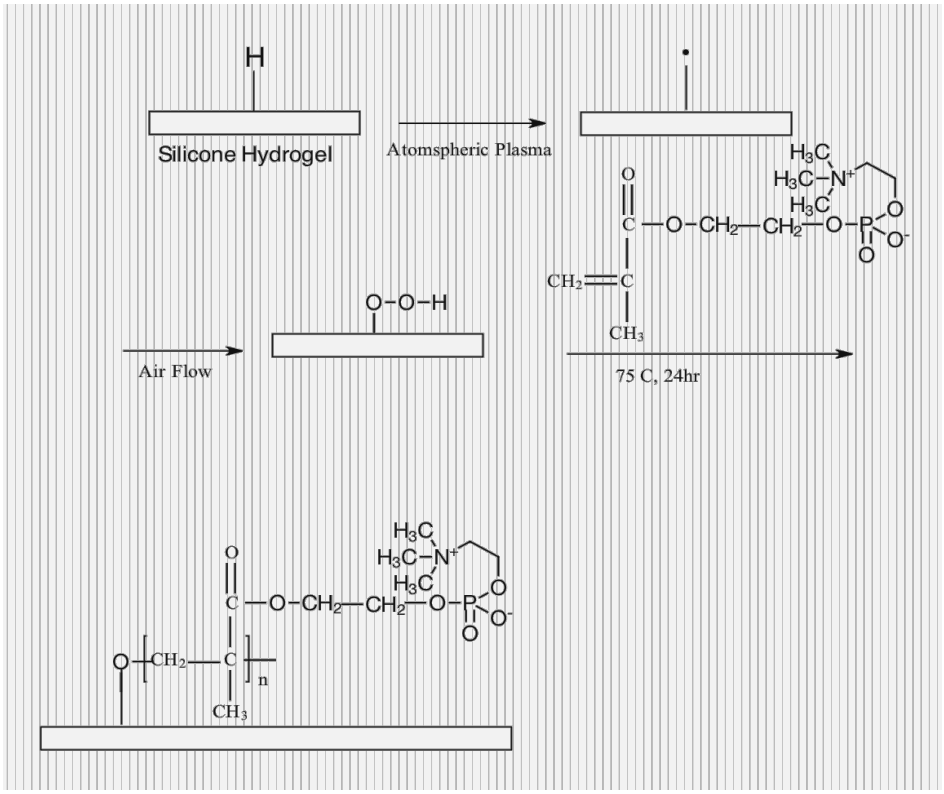


Figure 10. Schematic illustration of plasma induced radical surface grafting polymerization.

3.3 SURFACE WETTABILITY

Surface wettability of the modified and unmodified silicone hydrogels was evaluated by static water contact angles through the sessile droplet measurement technique. The measurement was performed by the Drop Shape Analyzer-DSA25 (Kruss, Germany) at room temperature and humidity. The dispensed water droplet was viewed and analyzed by the software provided with the instrument. Prior to the experiment, the hydrogel discs were stored in Milli-Q water for at least 72 hours to maintain full hydration, and then a Kimwipe was used to wipe excess water from the hydrogel surfaces. As mentioned previously, peroxides were generated by air plasma induction on the surface of the silicone hydrogel, and then radicals were created upon thermal decomposition of the peroxide bonds (-O-O or -O-O-H). The grafting (photo-initiator) density can be determined by many treatment parameters, such as plasma treatment time, radio frequency power, and other polymerization conditions (Lewis et al., 2007). Therefore, sessile droplet tests were performed on 0.5 M MPC modified

silicone hydrogel discs to investigate whether a 120 second treatment time was sufficient or not. The 0.5 M MPC modified silicone hydrogel discs (n=5) were plasma treated with a different period of time, 0s, 15s, 30s, 60s, 90s, 120s, 180s, and 240s.

In addition, five different groups of 2 min plasma treated silicone hydrogel samples were used for evaluating the impact of MPC grafting layer on surface wettability; unmodified, only with plasma treatment (no MPC grafting), modified with 0.1 M, 0.5 M, and 1.0 M MPC. For each group, five silicone hydrogel discs were used (n=5). At day 0, 10, 20, 30, 40, and 50 the water contact angles of these hydrogel samples were measured again in order to investigate the stability of the grafting layer over a long period of time.

3.4 SURFACE CHARACTERIZATION

Before the surface characterizations, all the samples were triple rinsed in ethanol and then dehydrated at 70℃ for 48 hours. Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR) was used to confirm the presence of covalently bonded p-MPC chains on the surface of the silicone hydrogel discs. A Nicolet 6700 FT-IR Spectrometer was used to carry out the hydrogel surface chemical analysis (Thermo Electron Corporation, USA). In addition, the Smart DuraScope (diamond as the ATR crystal) was aligned to conduct the infrared attenuated reflection measurement on the hydrogel discs, and then IR adsorption spectrum was collected and plotted by OMNIC v7.3 Series Software (Thermo Fisher Scientific, USA) with a spatial resolution up to 10 microns.

X-Ray Photoelectron Spectroscopy (XPS) was used to further confirm the presence of p-MPC and as well as to quantitatively determine the surface elemental composition of the hydrogel discs. XPS experiments were performed on a Thermofisher Scientific Escalab 250Xi (Thermofisher Scientific, UK). Samples were affixed to sample platen with double-sided carbon tape. The photoelectrons were collected with a spot size of 900 microns, a probing depth between 1-10 nm, at a taking off angle of 30˚.

Charge-compensation was supplied using the combined e/Ar+ flood gun, and binding energy of the main C-C peak was shifted to 285 eV. The spectra were initially

obtained with a pass energy of 100 eV and then followed by high resolution scans of the spectral regions at a pass energy of 20eV. Data processing was carried out by the instrument complementary software Advantage v.5.957.

3.5 PROTEIN ADSORPTION

The unmodified and p-MPC modified silicone hydrogel discs were immersed in a phosphate buffered saline (PBS pH 7.4) solution for 48 hours in order to achieve complete hydration. The silicone hydrogel discs were gently washed and wiped with a KimWipe and then placed vertically inside a 96-well plate. BSA and lysozyme were chosen as model proteins. Both proteins were radiolabeled with ^{125}I using the iodine monochloride method. The unbound ^{125}I was removed by passing the solution through AG 1-X4 resin (Bio-Rad, CA). The concentration of BSA and lysozyme were both set to 1.0 mg/ml in order to approximately mimic human tear film protein concentration. 250μL of BSA and lysozyme with 10% radiolabeled protein content were placed into each well. There were four types of hydrogel discs; unmodified, modified with 0.1M, 0.5 M, and 1.0 M MPC solution. Four silicone hydrogel discs were used for each type of protein at each concentration.

The silicone hydrogel discs were incubated in the protein solution at room temperature, for periods of 3, 12, 24, and 48 hours. After the incubation, the hydrogel discs were triple rinsed with PBS solution for 10 minutes each to remove the loosely bounded proteins from the surface of the hydrogels. Lastly, the amount of protein adsorption was determined through comparing radioactivity of each disc, which counted by the Automatic Gamma Counter Wizard 31480 (PerkinElmer, USA) with a counting time of one minute each sample, and then the deposition amount will be calculated based on the sample surface and radioactive background counts.

3.6 EQUILIBRIUM WATER CONTENT

Lens Equilibrium Water Content (EWC) is not just a simple parameter to measure the degree of swelling of the hydrogel lens upon hydration. In fact, distinct relationships

exist between EWC, oxygen permeability, and stiffness of the hydrogel lens (Flynn, 2006). For instance, in Morgan and Efron's study, the oxygen permeability and water content of 17 commercial brands of hydrogel contact lens were measured and used to derive a simple exponential formula (Morgan & Efron, 1997). Therefore, the EWC is also a critical manufacturing control factor which can assist in the performance evaluation of a silicone hydrogel lens. Modified and unmodified silicone hydrogel discs were fully immersed in Milli-Q water for at least 48 hours at room temperature (n=6). The samples were then blotted gently with Kimwipe to remove excess water from the sample surface. The hydrated mass (M_H) of lenses was then determined. After weighting, the hydrogel samples were thermally dehydrated for a period of 48 hours at 70℃. Lastly, the lenses were weighted again to obtain the dehydrated mass (M_D), and then the equilibrium water content was determined based on the equation below.

$$\text{Water Equilibrium Content (\%)} = \frac{M_H - M_D}{M_H} \times 100\% \quad (1)$$

3.7 Tensile Testing

The elastic modulus of a lens material determines the materials' resistance performance to deformation under tension. In the simple term, a higher modulus contact lens is commonly described as "stiffer" or vice versa. Elastic modulus is extremely important for lenses comfort. If the modulus of lens' material is too high, it may cause mechanical irritation or "edge-fluting" (the stiffer lens doesn't drape over the cornea surface properly, causing the edge part of the lens to sit up), which subsequent reduces the comfort of the users (Jones, 2006, Sweeney, 2004). On the contrary, if the modulus was too low, then it might be harder for the users to handle and negatively impacting the durability of the lens (Jones, 2005, Tighe B, 2006). The elastic modulus of the silicone hydrogel samples was measured at room temperature by performing tensile tests. The 1 mm thick fully hydrated samples were cut into dog bone coupon shape with a total width of 15 mm, a total length of 40 mm, a gauge length of 20 mm, and a gauge width of 5 mm. Prior to testing, the hydrogel strips were gently blotted with a Kimwipe to remove excess surface water, and then the tops

of the hydrogel strips were wrapped with paper tape to prevent specimen slippage and clamping damage. The tests were conducted by the INSTRON 3366 Universal Testing System (INSTRON, USA) with a strain rate of 1 mm/min, maximum load of 50 N; the elastic modulus calculation was based on 2% of the total strain. All data processing and plotting was completed by the INSTRON Series IX/s Automated Materials Tester v.8.33.00 (INSTRON, USA).

3.8 LIGHT TRANSMITTANCE

Contact lens light transmittance characteristics are critical to the users and practitioners because it determines the visual performance and quality of the contact lens. The electromagnetic spectrum is a collection of widely diverse waves including infrared, X-rays, gamma rays, and short waves. The visible light spectrum ranges from approximately 390 to 700 nm. For this project, the light transmittance performance of the silicone hydrogel discs and the influence of grafting layer were evaluated. A DU 640 Spectrophotometer (Beckman Instruments, CA) was used to investigate the ability of the modified and unmodified silicone hydrogel samples to maintain light transmissivity ranging from 350 nm to 800 nm (n=6). Silicone hydrogel samples were blotted with a Kimwipe to remove the excess surface water, and then the thickness of discs was also measured by Electronic Thickness Gauge Model ET-3 (Rehder Development, USA). The hydrated silicone discs were loaded into a cubic prism, and then Milli-Q water was poured to immerse the disc. Lastly, the prism was then mounted in the sample compartment inside of the spectrum machine for visibility measurements.

3.9 ION PERMEABILITY

The ionic permeability is used as a quality control factor of contact lens material by many lens manufacturers. The parameter commonly refers to the ability of ions to pass through the polymeric matrix of the lens material. It has been shown that the

smoothness of contact lens movement over ocular surface is greatly affected by the ion permeability of the lens material (Silva et al., 2015). In this report, the ion permeability of the modified and unmodified silicone hydrogel membranes was measured by using a two-chamber diffusion device as shown in Figure 11 below.

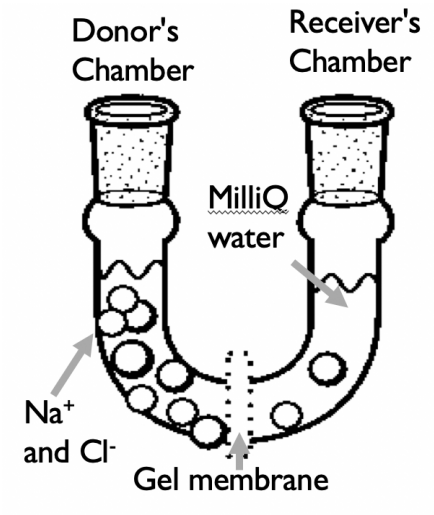


Figure 11. The schematic illustration of the permeation device

Silicone hydrogel membrane was punched into about 0.9 cm diameter discs in order to cover the ion exchange channel between the two chambers. The silicone hydrogel discs were swollen in MilliQ-water (deionized) for 48 hours, and this experiment was conducted at room temperature. After mounting the silicone disc into the device, one side of the chamber was filled with water and left overnight to check for leakage. The thickness of the hydrogel discs was again measured and recorded by the Electronic Thickness Gauge Model ET-3 machine. The ion permeability of the silicone hydrogel membranes was evaluated by the CDM 83 Conductivity Meter (Ascent Concept & Technology, USA). For lens permeation measurement, the donor chamber was filled with 10 ml of 1.0 M NaCl/MilliQ solution, and the receptor cell was also filled with the equal volume of fresh MilliQ-water. The ion concentration of the receptor solution was measured and plotted over a period of approximately 12 hours (n=3 for each silicone hydrogel group). Prior to the permeation tests, a linear relationship between the electrical conductivity and ion concentration was derived by using the meter to measure conductivity of corresponding concentration of NaCl solutions. This linear equation was used to identify ion concentration inside of the

receptor cell. Lastly, the ion permeability of the lens material was calculated based on the equation below.

$$\ln\left(1-\frac{2C_{R(t)}}{C_{D,0}}\right) = -\frac{2\cdot A\cdot P}{V\cdot L}(t-t_0) \quad (2)$$

C_R: Solute concentration in receiver cell at time t

$C_{D,0}$: Initial concentration inside of Donor cell

A: Surface area of the silicone hydrogel membrane

P: Coefficient of ion permeability

V: Chamber volume

L: Member thickness

T: permeation time

3.10 OXYGEN PERMEABILITY

Oxygen permeability of the unmodified and modified silicone hydrogel was measured by Permeometer Model 210T (Createch Group, USA). The components of the permeometer are shown in Figure 13 below. Prior to oxygen permeability tests the

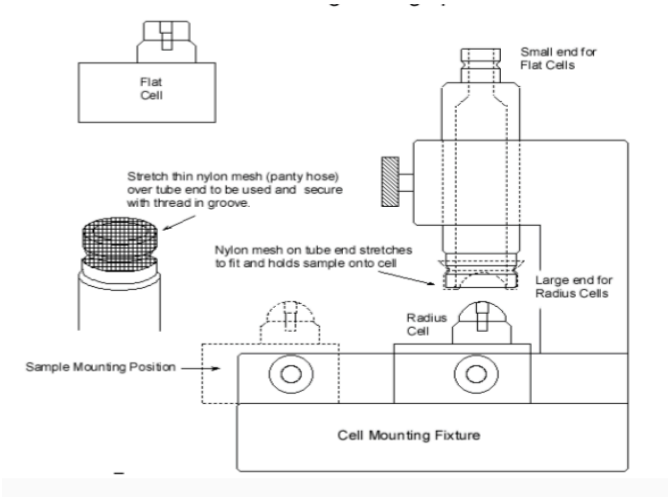


Figure 12. Dissection view of Permeometer Model 210T, image adapted from (I. Fatt, 1987).

silicone hydrogel films were punched into 1 cm diameter disks, and then soaked in MilliQ-water for a period of 48 hours. The thickness of the hydrogel discs was

measured by the Electronic Thickness Gauge Model ET-3 machine. For oxygen permeability testing, first a few drops of saline buffer solution were dispensed onto the central part of the gold/silver electrode sensor. The hydrogel disc was then placed on top of the flat shape sensor, and a thin nylon mesh was pressed above the silicone surface to avoid gel wrinkling or clamping damage from the fixture. The cell holder (the hollow vertical tube fixture) was lowered down and pressed tightly onto the surface of the hydrogel. The oxygen permeability experiment should be conducted at room temperature about 90% to 100% humidity (preventing gels from dehydration). The oxygen was reduced at the golden cathode on the sensor, thus a current reading would be generated on the device. After sample mounting steps, a period of at least 10 minutes was given before starting to read the current. For highly oxygen permeable hydrogel (> 50 Dk), the difference in gel thickness might also affect the current reading (Fatt, 1987), so the five groups of silicone hydrogel with different thickness ranging from approximately 0.25 mm to 1.5 mm were used to obtain a more accurate oxygen permeability of the sample. The permeability test was repeated three times (n=3). The electrochemical reaction happening at cathode and the equations for calculating oxygen permeability are listed below, and detailed oxygen permeability coefficient calculations can be found in the appendix C.

The electrochemical reaction at the cathode: $4e^- + O_2 + 2H_2O = 4OH^-$

Fick's law of diffusion: $J = A(\frac{Dk}{L})(P_1 - P_2)$ (3)

Farday's law of current flow : $i = n \cdot F \cdot J$ (4)

Rearranging the equations above $\frac{Dk}{L} = \frac{i}{A \cdot n \cdot F \cdot P_{O_2}}$ (5)

Dk: Oxygen permeability F: Faraday constant i: Current

L: Hydrogel thickness A: Area of the cathode

P_{O_2}: Oxygen tension on the open surface of the hydrogel

n: Number moles of electrons to reduce one mole of oxygen

3.11 STATISTICAL ANALYSIS

Statistical analyses were performed by using a single factor analysis of variance (ANOVA) and Turkey's range test on Statistica 11.1 (StaSoft, USA), with a confidence range of 95% ($p<0.05$) was established for statistically significant results.

4. RESULTS AND DISCUSSION

4.1 WATER CONTACT ANGLE MEASUREMENT

In this project, the contact angle between a solid surface (hydrogel discs) and the liquid phase (dispensed water droplet) was measured using the sessile drop technique. The higher the water contact angle, the more hydrophobic and less wettable the sample surface is. The results of static water contact angle measurements can be seen in Figures 13 and 14.

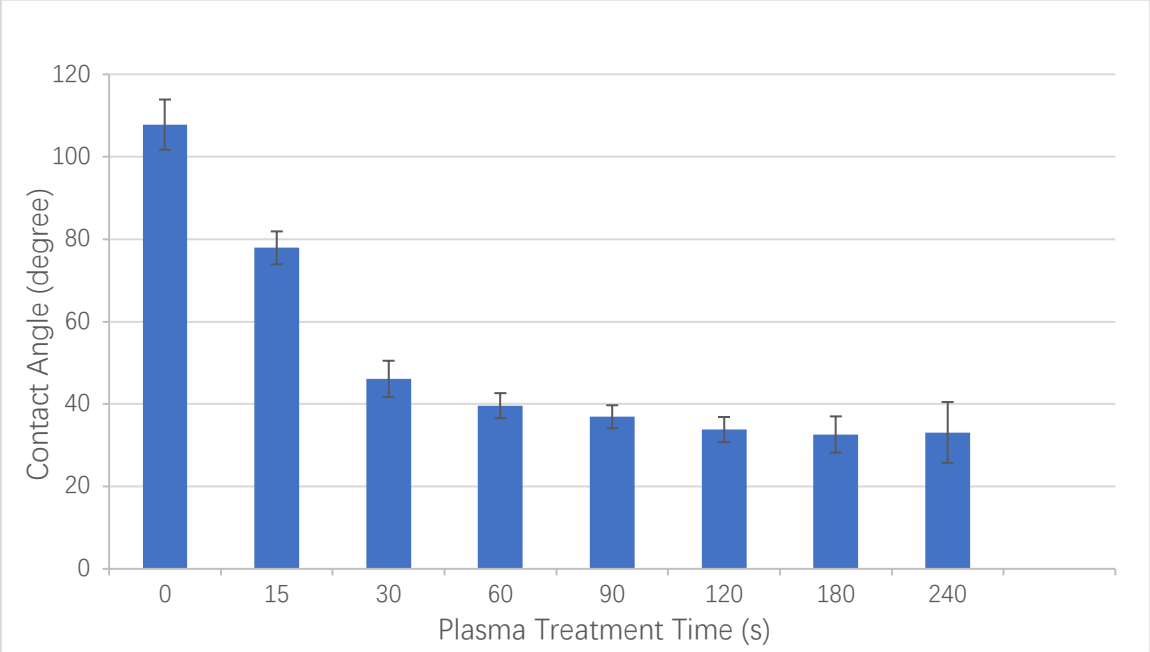


Figure 13. The impact of plasma treatment time on the water contact angles of 0.5 M MPC modified silicone hydrogel samples at day 0. The results are shown in mean ± standard derivation (n=5).

As shown in Figure 13, two minutes of plasma treatment resulted in much more wettable surface behavior, leading to a relatively low water contact angle of 33.8°, compared to the 15 seconds sample which had a contact angle of 77.9°. In contrast, three and four minutes of plasma exposure had illustrated similar wettability behavior to the two minute samples, which had water contact angles of 32.6° and 33.1° respectively. It was not surprising to see high water contact angles with less plasma treatment time, because it would be expected that there would be fewer peroxides (grafted on photo-initiators) as active sites on the surface of silicone hydrogels to

initiate chain polymerization growth of MPC monomers. Since the silicone surface was not fully covered by the MPC polymers, the resulting surfaces were less wettable. On the other hand, the two, three, and four minutes of plasma treated samples showed similar static water contact angles. It was very likely that only certain amount of peroxides groups could be generated on the surface of the silicone discs, thereby MPC grafting intensity was similar between these different groups, and thus there was no significant difference in water contact angles. Therefore, two minutes of treatment time was selected for the remaining studies.

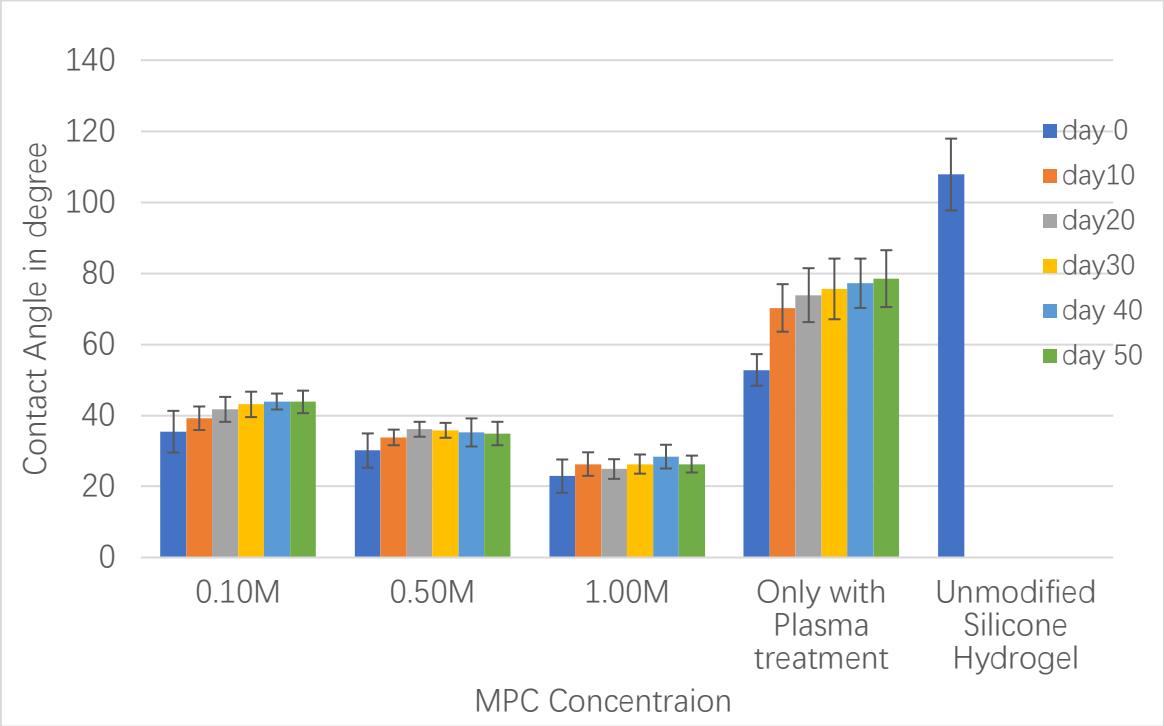


Figure 14. Water contact angles changes of five different groups of silicone hydrogel samples over a period of 50 days, including three MPC modified, unmodified, and only plasma treated silicone hydrogel sample groups. The results are shown in mean ± standard derivation (n=5).

As shown in Figure 14, the unmodified silicone hydrogel was the least wettable among all of the five groups with a water contact angle of about 107°. The relatively high hydrophobicity was likely due to the presence of hydrophobic silicone domains on the surface of the silicone hydrogels. On the contrary, the MPC modified samples demonstrated much more wettable behavior due to the grafted-on p-MPC chains. For instance, the 0.1 M modified silicone samples had a contact angle approximately 47°

at 50 days, which was about a factor of two less than the water contact angle of the unmodified silicone samples. Among the MPC modified groups, 1.0 M MPC modified samples possessed the lowest contact angle of around 26° at 50 days compared with the significantly less hydrophilic 0.1 M (~47°) and 0.5 M (~35°) groups. In fact, the 1.0 M MPC group had the most monomer concentration inside of the reaction batch. Thus, it was more likely for all the active sites (radicals) to react with the MPC monomers, which definitely resulted a higher chain length and grafting density. Since the surface was covered by a denser and thicker hydration layer (induced by the zwitterionic p-MPC chains), it is not surprising that the samples would give a lower water contact angle. It is also worth noting that after only plasma treatment the water contact angle of unmodified samples dropped dramatically from 107° to 53°. This is due to the formation of hydrophilic polar groups such as hydroperoxides, hydroxyl, and carbonyl groups on hydrogel surface after plasma treatment (Everaert, 1995). However, only after 10 days, the water contact angle increased back to ~71°, indicative of the instability of these surface polar groups over a long-term period of time. In contrast, the covalently bonded p-MPC chains demonstrated good stability over a period of 50 days. For all three MPC groups, there was only a slight contact angle increase at day 10 or 20, which was likely caused by the hydrophobic recovery of silicone based materials . This meant that the covalently bonded MPC grafting layer could maintain the surface hydrophilicity of the silicone hydrogel lenses over a long period of time.

4.2 ATTENUATED TOTAL REFLECTANCE FOURIER TRANSFORM INFRARED SPECTROSCOPY

Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR) technique was used to identify the presence of the chemical functional groups near the surface of the silicone hydrogel sample discs. The entire infrared spectrum and all the relevant peaks of interest are shown in Figure 15. The chemical structure of the unmodified silicone hydrogel substrate was confirmed. Silicone methyl groups were located at the peaks of 800 cm^{-1} and 1250 cm^{-1}. There was also a small peak at about 1725 cm^{-1}, which represented the carboxyl functional group from the silicone

components, and the stretch of amide functional group from the DMA component was observed at the peak around 1640 cm^{-1}. Surprisingly, there was no new peak observed for the 0.1 M MPC modified samples. This could be explained as the lower spatial resolution of the ATR-FTIR (much less sensitive than XPS), and the grafting layer was too thin for ATR-FTIR machine to read. On the other hand, the presence of MPC grafting layer was observed from 0.5 M and 1.0 M MPC modified samples. In both spectra, small peaks at approximately 1270 cm^{-1} were discovered, which was attributed by the vibration of -$POCH_2$ groups from the MPC grafting layer.

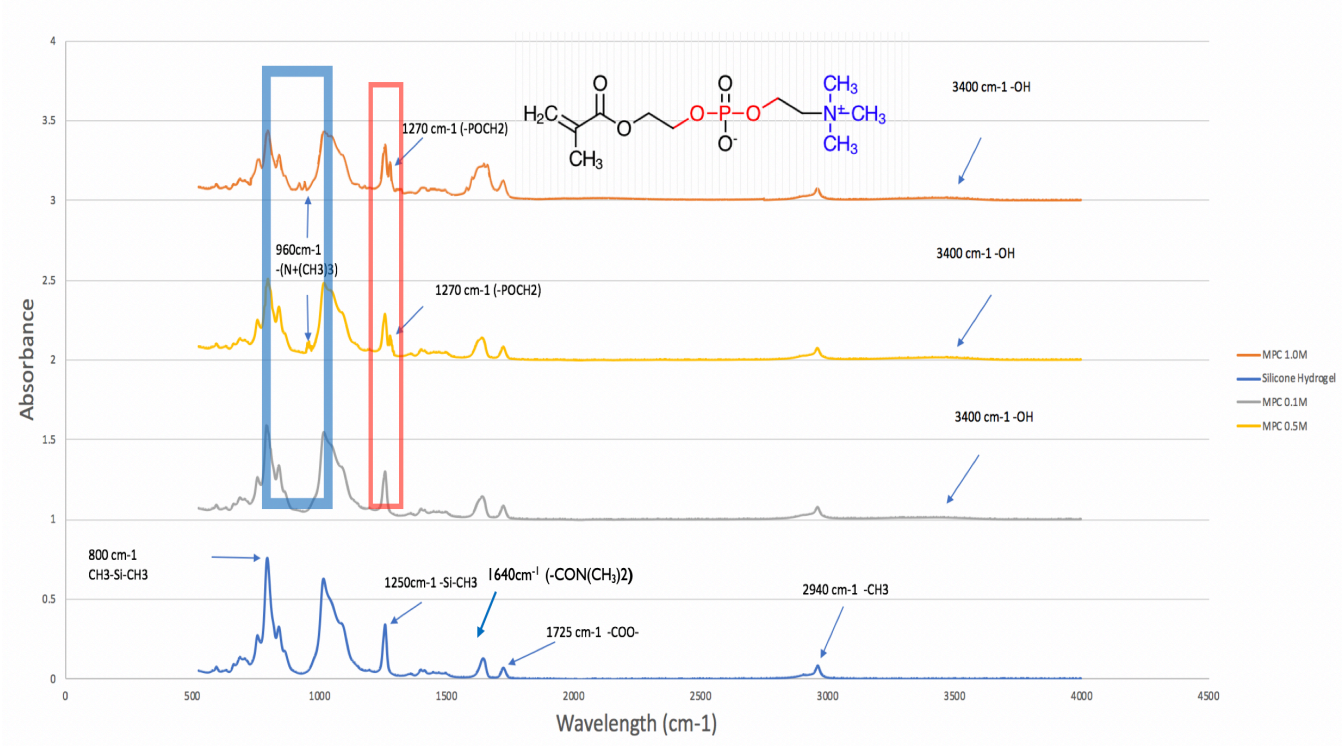


Figure 15. The ATR-FTIR spectrum of MPC modified and unmodified silicone hydrogel sample discs

Furthermore, the peaks located at about 960 cm^{-1} in both spectra represented the stretch of amine groups. It is important to note that both amine and phosphorus group could be found on the zwitterionic head part of the MPC monomer as shown above. Therefore, the presence of these chemical functional groups on the infrared spectrum provided evidence of the successful grafting of the MPC layer on the silicone hydrogel sample surfaces. Lastly, hydroxyl groups usually corresponded to the stretch from 3200 cm^{-1} to 3600 cm^{-1}, and a small fluctuation appeared at around 3400 cm^{-1}

for all four spectra. Since the hydrogels were dehydrated before the ATR-FTIR tests, this can likely be attributed to moisture absorption.

4.3 X-RAY PHOTOELECTRON SPECTROSCOPY

X-Ray Photoelectron Spectroscopy (XPS) was conducted to measure the elemental composition of the surface of the silicone hydrogel discs, providing further evidence of the successful grafting of the p-MPC chains onto the surface of the hydrogels. Table 3 below summarizes the surface composition of the unmodified and modified silicone hydrogels (see Appendix A for all XPS spectra). It is very important to note that there was no phosphorous content on the hydrogel substrate materials. After grafting, it increased from 0% to 0.52% and 1.94% for the 0.1 M and 1.0 M MPC modified surfaces. In this project, the only phosphorous containing monomer was the MPC, thus the presence of P (2p) demonstrated that MPC had been successfully grafted onto the hydrogels. As previously mentioned, XPS is a much more sensitive surface analysis technique with a probing depth of 1 to 10nm, whereas ATR-FTIR's spatial resolution is in term of microns. Therefore, the evidence of presence of the p-MPC chains on 0.1 M MPC modified hydrogel demonstrated by XPS.

On the other hand, the percentage of silicon decreased rapidly from 16.52% to 13.59% and 10.53% after grafting modification. This decrease in the silicon content was caused by the MPC modification covering up the underlying surface. The probe depth was between 1 and 10nm, and there was still significant Si content after surface grafting. Therefore, the thickness of the grafting MPC layer under the vacuum conditions to the XPS can be estimated to be between 1 and 10 nm. Moreover, the 1.0 M MPC modified hydrogels should have denser and thicker MPC grafted based on the higher percentage of phosphorous. This explains the superior surface wettability of these samples based on the static water contact angle measurements. On the contrary, the nitrogen content was insignificant in both substrate or MPC monomer, and thus there was no significant percentage variation. Finally, oxygen percentage also increased quickly after MPC grafting due to the significantly higher elemental ratio inside in of the MPC monomer (see MPC structure) compared with the hydrogel substrate monomers.

Table 3. Low resolution spectrum XPS data of elemental composition at a take off angle of 30°

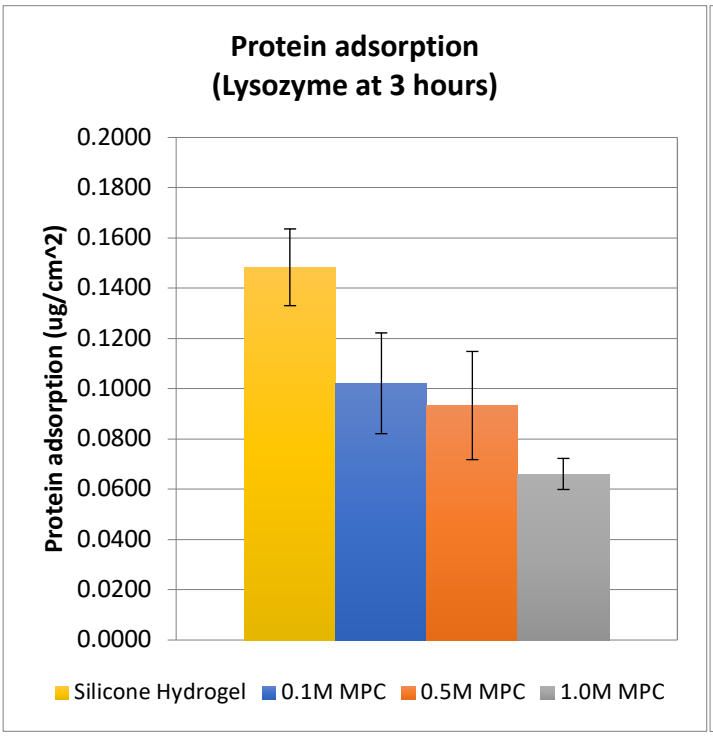
Peaks	Si (2p)	P (2p)	C (1s)	N (1s)	O (1s)
position	Rel.At. %	Rel.At. %	Rel.At. %	Rel.At. %	Rel.At. %
Unmodified	16.52	-	58.21	2.71	22.11
0.1M MPC	13.59	0.52	53.64	2.89	28.04
1.0M MPC	10.53	1.94	54.10	3.46	29.80

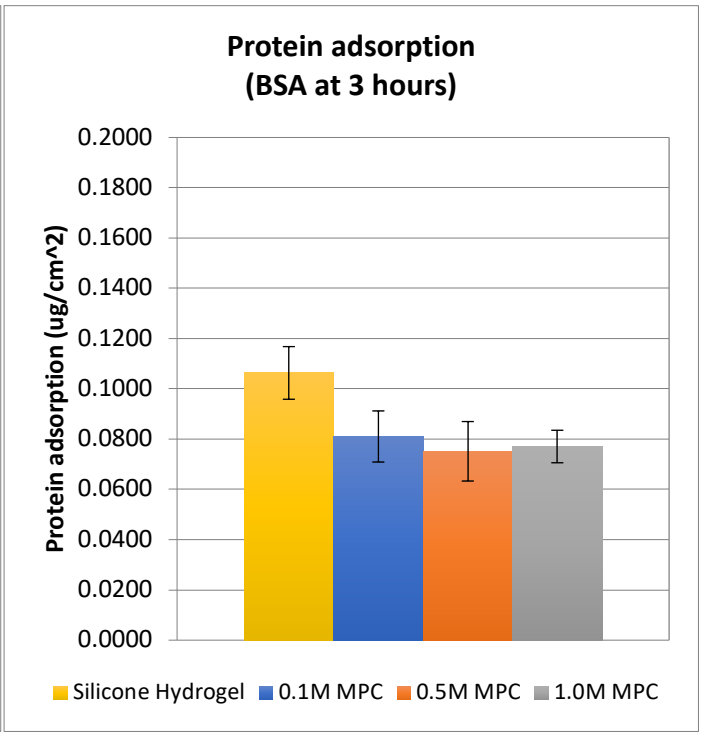
4.4 PROTEIN ADSORPTION

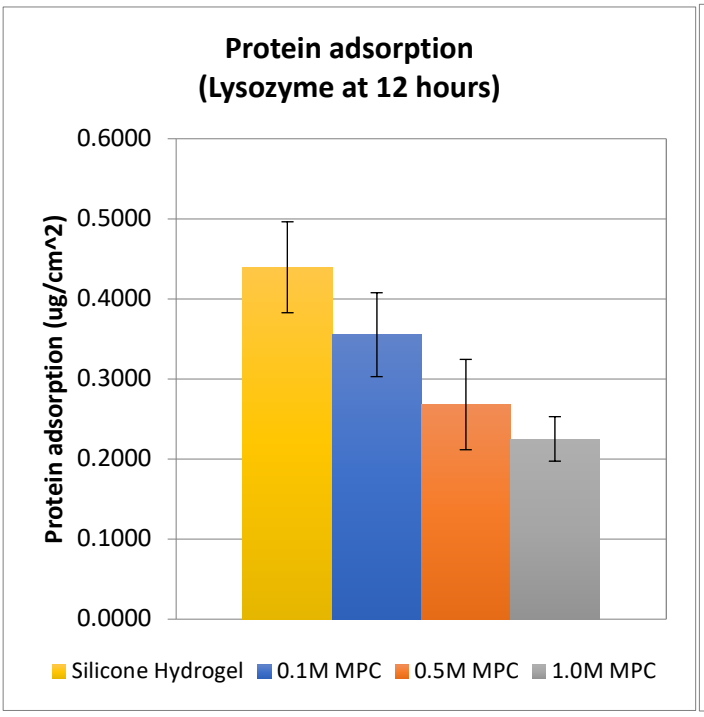
Lysozyme and bovine serum albumin (BSA), two of the most well studied and abundant proteins in tears were selected to assess the protein resistance performance of the p-MPC modified silicone hydrogel lens inside of human tear film. Lysozyme and BSA were chosen as the study proteins not only due to their abundant concentration and significant role inside of tear film, but also considering their opposite isoelectric point and size which could potentially demonstrate different types of protein adsorption behavior.

As shown in Figure 16 and 17, the total adsorption amount of both proteins increased rapidly over first 24 hours, and then the trend of increase gradually slowed between 24 hours and 48 hours. This could be ascribed as the dilution of the protein solutions due the PBS washing step, or simply reaching the adsorption limit of the silicone hydrogel discs. It was also important to note that an approximately 20-50% of reduction in protein adsorption was achieved after MPC surface modification for all groups of hydrogels. For instance, after 3 hours of deposition, the lysozyme adsorption of 0.1 M MPC modified silicone hydrogel was reduced by about 31.1% compared with unmodified hydrogel decreasing from 0.148 $\mu g/cm^2$ to 0.102 $\mu g/cm^2$. In addition, the higher concentration of MPC modified groups trended to have a greater lysozyme and BSA reduction percentage. For example, after 24 hours' BSA adsorption, the 0.1 M MPC modified hydrogel adsorbed 0.698 $\mu g/cm^2$, while the 0.5M MPC modified hydrogel only adsorbed 0.563 $\mu g/cm^2$.

It is believed that protein resistance of MPC units was mainly coming from the hydration layer generated by the zwitterionic MPC monomers, which repelled the protein adhesion from the hydrogel surface (Herrwerth, et al., 2003, Chen, et al., 2010). Thus, the higher MPC concentration resulted a denser MPC grafting layer, which eventually led to a more wettable surface (see section 4.1) and stronger protein adhesion resistance. It was surprising to see a higher BSA overall protein adsorption for all groups of the silicone hydrogel samples. At 48 hours, the unmodified hydrogel adsorbed 0.652 $\mu g/cm^2$ of lysozyme, which was 0.194 $\mu g/cm^2$ or about 22.9% less than the BSA deposition on the unmodified hydrogels. Lysozyme was much smaller in size and expected to have a higher amount of deposition according to previous protein studies, because it could be folded into tightly packed single layer; and penetrated further into the bulk of hydrogels compared with BSA molecules (Jadi, et al., 2012 and Luensmann, et al., 2007). It is also worth to note that equal (1.0 mg/ml) protein solution concentrations were used rather than conventional experiment settings (1.9 mg/ml's lysozyme and 0.5 mg/ml's BSA). Lastly, large standard derivations and some inconsistency in reduction percentage were observed due to the non-living nature of the free radical polymerization, so there was little control over the molecular weight, polydispersity, and more importantly the chain length of the p-MPC grafting chains, which affected the consistency of the water barrier layer on top of the silicone hydrogel substrates, hence ultimately led to different protein resistance performance (Hawker and Hedrick, 1995).







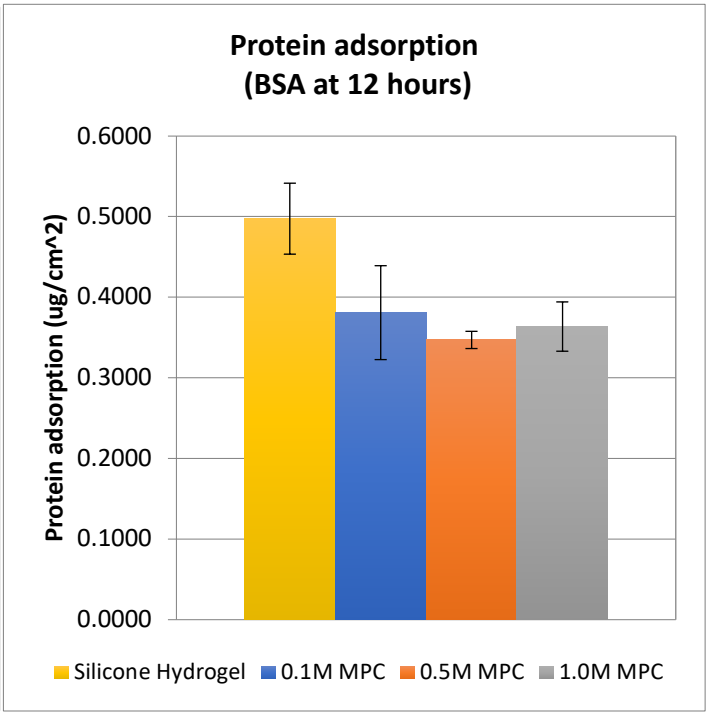
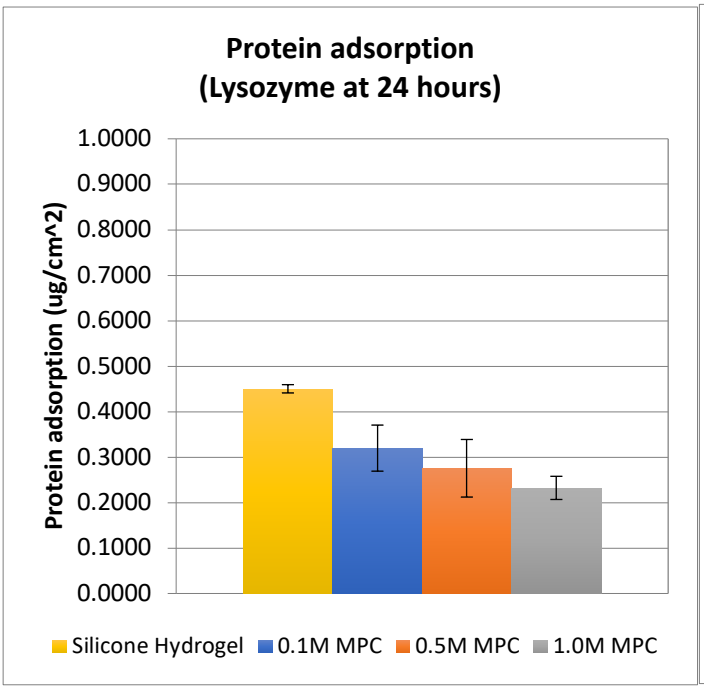
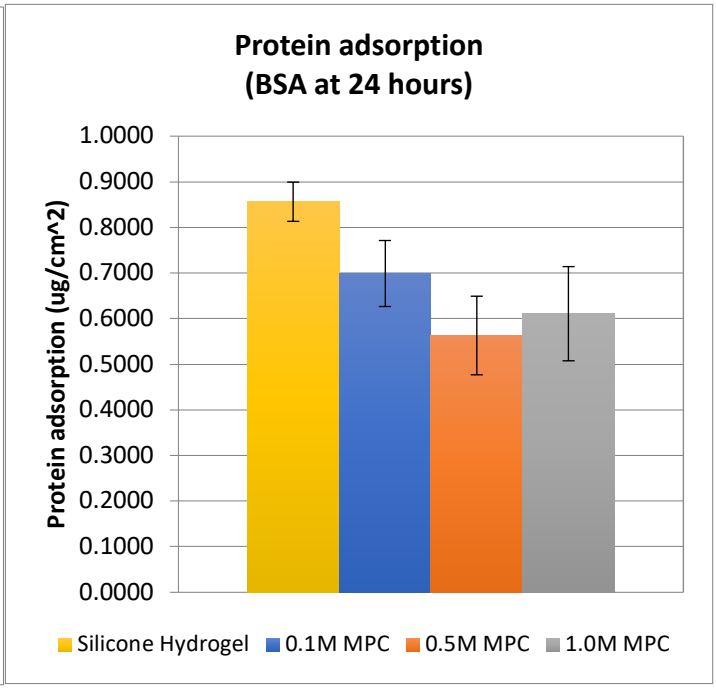
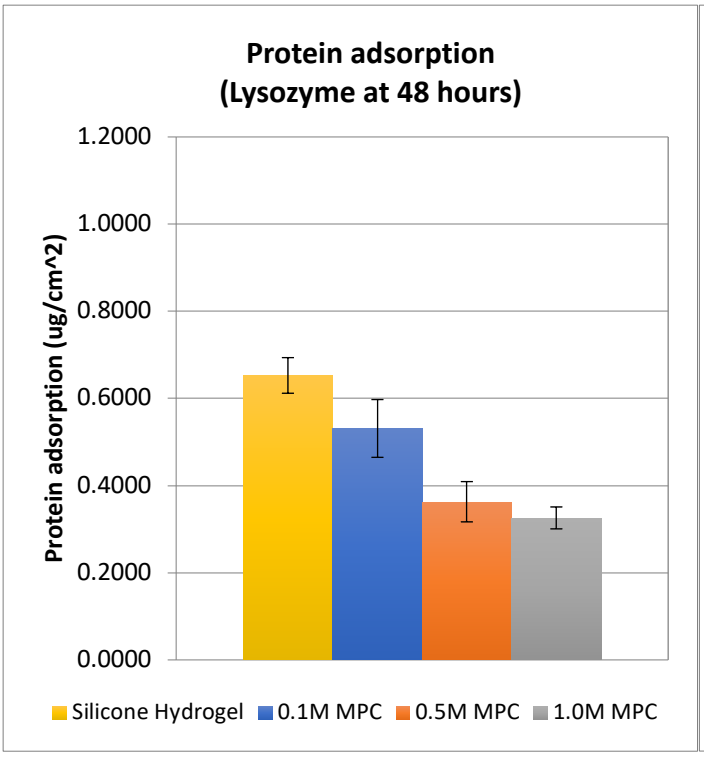


Figure 16. The amount of lysozyme and bovine serum albumin (1.0mg/ml) absorbed by the modified and unmodified silicone hydrogel discs after immersing inside of the protein solutions for 3 hours and 12 hours. The results are shown in mean ± standard derivation (n=4).







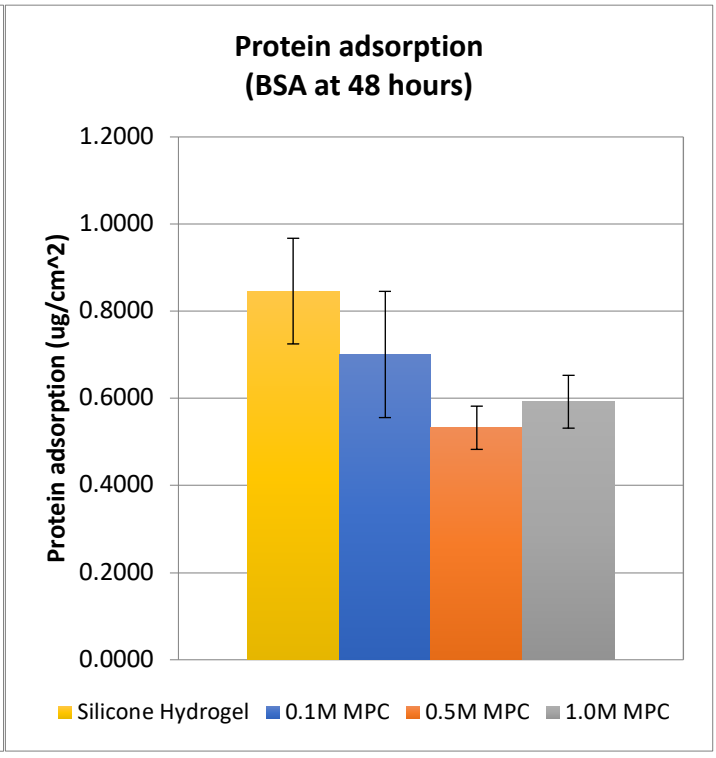


Figure 17. The amount of lysozyme and bovine serum albumin (1.0mg/ml) absorbed by the modified and unmodified silicone hydrogel discs after immersing inside of the protein solutions for 24 hours and 48 hours. The results are shown in mean ± standard derivation (n=4).

4.5 EQUILIBRIUM WATER CONTENT

Equilibrium water content is an important manufacturing control factor because EWC can greatly influence the lens' mechanical and transportation characteristics (see section 3.6). For all the commercial soft silicone hydrogel contact lens, the EWC typically falls into a range of approximately 20% to 35% (Efron, Morgan, et al., 2007), and it is essential to compare the EWC of sample hydrogels with the commercial ones, to give a better understanding of potential wear performance. As demonstrated in Table 4 below, the unmodified silicone hydrogel had 21.1% of EWC, which was on the low side of acceptable range of hydrogel contact lens. However, it was not surprising to see a relatively low EWC number, because nearly 65wt% of the substrate materials were hydrophobic components. In addition, after the various concentrations of MPC surface grafting, the EWC increased slightly by about 0.5%, 1.4%, and 2.1% for the 0.1, 0.5 and 1.0 M samples respectively.

As mentioned in section 2.4, the zwitterionic MPC monomers induce electrostatic binding with large amount of water molecules. Consequently, a thick hydration layer will be formed on the surface of 1.0 M silicone hydrogel. On the other hand, the grafting layer of 0.1 M silicone hydrogel is relatively thin(see section 4.2), and therefore only slight increases in the EWC are noted after modification.

Table 4. Equilibrium water content of all groups of silicone hydrogel samples. The data above are indicated in mean ± standard derivation (n=6).

	Equilibrium Water Content
Unmodified Silicone Hydrogel	21.1 ± 0.2%
0.1 M MPC Modified Hydrogel	21.6 ± 0.3%
0.5 M MPC Modified Hydrogel	22.5 ± 0.4%
1.0 M MPC Modified Hydrogel	23.3 ± 0.4%

4.6 TENSILE TESTING

Elastic modulus is another important design factor, which contributes greatly towards contact lens fitting over the ocular surface and lens durability (see section 3.7).

Commercial silicone hydrogel contact lenses tend to have higher elastics modulus ranging from 0.5 MPa to 1.5 MPa compared with conventional soft lenses which range from 0.2 MPa to 0.5 MPa (French and Jones, 2016). The results of tensile tests are shown in Table 5 and show that were no significant modulus changes after plasma treatment and MPC thermal grafting, demonstrating that the surface modification had no effect on the bulk properties of the materials. On the other hand, the elastic modulus of the samples was about 1.5 MPa higher than the maximum expectation. This could be explained by the substantial portion (65wt%) of siloxane in the hydrogels, which resulted a higher modulus (French and Jones, 2016). In addition, despite using a diluent to help mixing, microgel particles or microphase separation were still suspected to exist in the polymeric matrix due to the very opposite hydrophilicity between the PDMS and DMA (Lipatov and Tatiana, 2007). The degree of segregation depended on the size of these microgels, and a higher degree of segregation would have resulted a higher elastic modulus when the coefficient of segregation less than 0.3. (Lipatov, 2007 and Guidi, 2014).

Table 5. Elastic Modulus of all groups of hydrogel samples. The above data are shown in mean ± standard derivation (n=6).

	Elastic Modulus
Unmodified Silicone Hydrogel	3.30±0.40MPa
0.1 M MPC Modified Hydrogel	3.11±0.31MPa
0.5 M MPC Modified Hydrogel	3.25±0.44MPa
1.0 M MPC Modified Hydrogel	3.21±0.20MPa

4.7 LIGHT TRANSMITTANCE

Light transmissivity of the contact lens material can greatly affect the visual quality of the lens and the user's wearing experience. The transmittance of visible range of light (390-700nm) of all groups of silicone hydrogels was measured and is shown in Figure 18. Overall, all groups of silicone hydrogel materials prepared demonstrated excellent light transmissivity ranging from around 90% to 94%. In addition, there was no significant change in light transmissivity observed after the plasma induced p-MPC grafting step. However, the conventional soft hydrogel lens has a higher visible light

transmittance. For example, the light transmittance of p-HEMA lenses ranges from about 98.5 to 100% and p-(DMA-co-TRIS) hydrogels ranged between 97% and 100% (Guidi, et al., 2014). Lower light transmittance can be ascribed to the microphase separation existing inside of the polymeric matrix of the silicone hydrogel (Nicolson and Vogt, 2001).

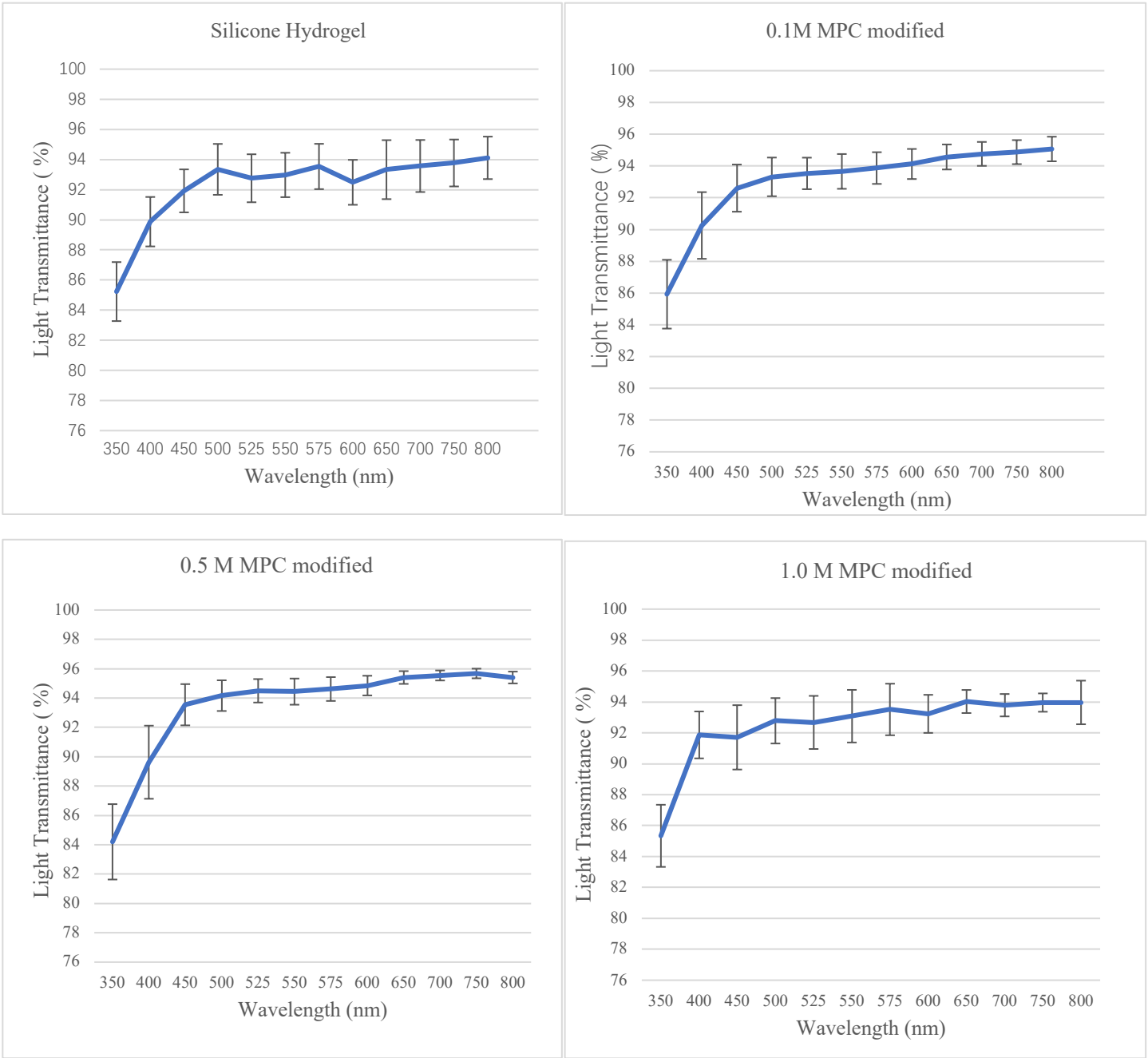


Figure 18. The light transmittance of all groups of silicone hydrogel samples over the visible range of light. Data are shown as mean ± standard derivation (n=6).

4.8 ION PERMEABILITY

Ion permeability of contact lens materials is considered as a quality control factor by some lens manufacturers because it is believed that the movement of contact lens over the corneal surface will be affected when the ion permeability coefficient lower than $2.40 \times 10^{-7} cm^2/s$ (Tighe and Sweeney, 2000). This parameter is usually measured by the ability of Na^+ and Cl^- ions to pass through the polymeric matrix. In this project, a conductivity meter was used to determine the ion concentration inside of the receptor chamber as a function of time. An example of calculation of ion permeability coefficient was listed in the Appendix B. As Table 6 illustrates, all groups of silicone hydrogel samples had ion permeability values that were greater than minimal ion permeability requirement. In addition, there was also no significant ion permeability change that happened after the MPC grafting. Thus, the ocular movement of the MPC modified silicone hydrogel lens over the corneal surface would not be hindered. Lastly, there is no evidence that a large ion permeability will affect contact lens performance (Silva, 2015).

Table 6. The ion permeability coefficients of all groups of silicone hydrogel samples. The data are shown as mean ± standard derivation (n=3).

	Ion Permeability
Unmodified Silicone Hydrogel	$1.36 \pm 0.11 \times 10^{-6} cm^2/s$
0.1 M MPC Modified Hydrogel	$1.55 \pm 0.14 \times 10^{-6} cm^2/s$
0.5 M MPC Modified Hydrogel	$1.38 \pm 0.18 \times 10^{-6} cm^2/s$
1.0 M MPC Modified Hydrogel	$1.45 \pm 0.10 \times 10^{-6} cm^2/s$

4.9 OXYGEN PERMEABILITY

Oxygen permeability (Dk) is a very important contact lens design factor, because the corneal oxygen supplement relies entirely on permeation from the outside environment (see section 2.1 and 2.2). In this project, oxygen permeability of the

silicone hydrogel samples was measured in Barrer (1 barrer $=10^{-10}\frac{\text{ml O2}\times\text{cm}}{\text{sec}\times\text{cm2}\times\text{mmHg}}$) by polarographic method (mentioned as Fatt's method in section 3.10), which measured the amount of oxygen passing through the silicone hydrogel from the atmosphere to the sensor electrodes.

As summarized in the Table 7 below, the Dk value of unmodified silicone hydrogel was 102.9 barrers, almost 5 times higher as that for conventional HEMA based Etafilcon A (21.4 barrers) (Efron, et al., 2007). This demonstrates that the silicone hydrogels prepared in this work are excellent mimics for commercially available materials, satisfying both the requirement for avoiding end of day edema (> 35 barrers) and for overnight wear (> 87 barrers) (Mertz, 1980, La Hood, 1988). However, the oxygen permeability of this material is still not sufficient (>125 barrers) to fully obviating overnight hypoxia symptoms (Mertz, 1980, La Hood, 1988). In addition, after plasma induced MPC grafting, the Dk values of all groups of silicone hydrogels did not change significantly. An example of calculation of the Dk can be found in the Appendix C.

Table 7. The oxygen permeability coefficients of all groups of silicone hydrogel samples presented in Dk's unit of barrers. The above data were shown in mean ± standard derivation (n=3).

	Oxygen Permeability (Dk, Barrer)
Unmodified Silicone Hydrogel	102.9±5.2
0.1 M MPC Modified Hydrogel	105.7±2.8
0.5 M MPC Modified Hydrogel	100.8±3.3
1.0 M MPC Modified Hydrogel	104.0±4.8

5. CONCLUSIONS AND RECOMMENDATIONS

In conclusion, silicone hydrogel materials were prepared which mimic the properties of commercially available silicone hydrogel materials in terms of transparency, oxygen and ion permeability and water content. Thus these materials are excellent mimics when evaluating surface modification or other modifications.

Air plasma induced MPC surface grafting technique was shown to have significant potential for improving surface characteristics of these silicone hydrogel materials without negatively affecting the bulk or transport properties. The surface wettability of the silicone hydrogels improved substantially after p-MPC surface grafting. The static water contact angle of the MPC modified samples was as low as 27°, and the grafting layer maintained this value at a stable level over a period of at least 50 days while the plasma modification alone reverted quite rapidly. A small increase in the EWC of the silicone hydrogels was observed (0.5%-2.1%) after MPC surface modification, which likely resulted from the zwitterionic polymers inducing a hydration layer on the hydrogel surfaces. Furthermore, protein adsorption was also reduced significantly for all groups of modified silicone hydrogel samples. In comparison of the unmodified silicone discs, lysozyme adsorption decreased by as much as 50.5% and BSA adhesion declined by as much as 37.1%. Moreover, the presence of covalently bonded p-MPC chains was further confirmed by ATR-FTIR and XPS. ATR-FTIR spectra showed peaks, which corresponded to the presence of amine and phosphorus groups on hydrogel surface. XPS was followed next to analyze the changes of surface elemental composition after MPC grafting. The level of silicon on the surfaces decreased significantly after MPC surface grafting while the presence of phosphorous was noted on the modified surfaces. The air plasma induced grafting technique did not adversely impact the bulk properties of the materials; mechanical strength, and permeation characteristics basically remained as the same after the surface modification.

Since micro-phase segregation remained as a minor problem with the silicone hydrogels, which resulted in relatively stiffer and less visibly light transparent substrates, it may be useful to replace the siloxane used in these studies with a more

hydrophilic siloxane monomer such as TRIS-OH. In addition, a longer protein deposition period should be conducted in future work. As noted in Section 4.4, the lysozyme molecules might not have enough time to unfold themselves into the tightly packing form on the silicone hydrogel surface. For the future studies, lipid deposition should also be included, because lipid molecules play a vital role in preventing an excessive amount of tear evaporation and keeping lens hydrated. The ocular environment is extremely complex, and blinking for example, will exert forces on the contact lens which results consequent motions in all directions. Thus, the frictional properties of the silicone hydrogel contact lens against different surfaces should be investigated in the future work as well.

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APPENDIX A: XPS SPECTRUMS

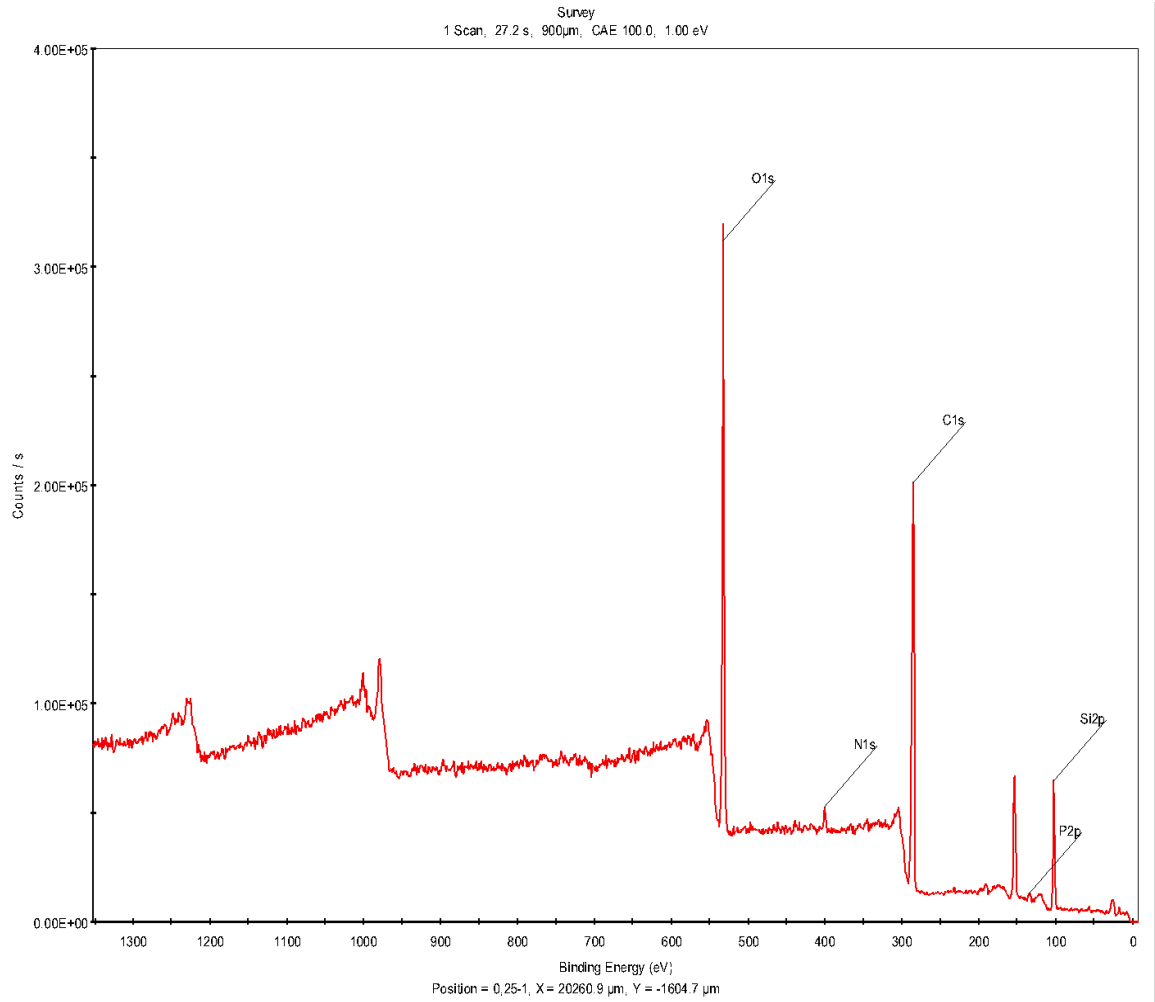

Figure A-1. The low-resolution spectrum of unmodified silicone hydrogel sample with a taking of angle of 30°

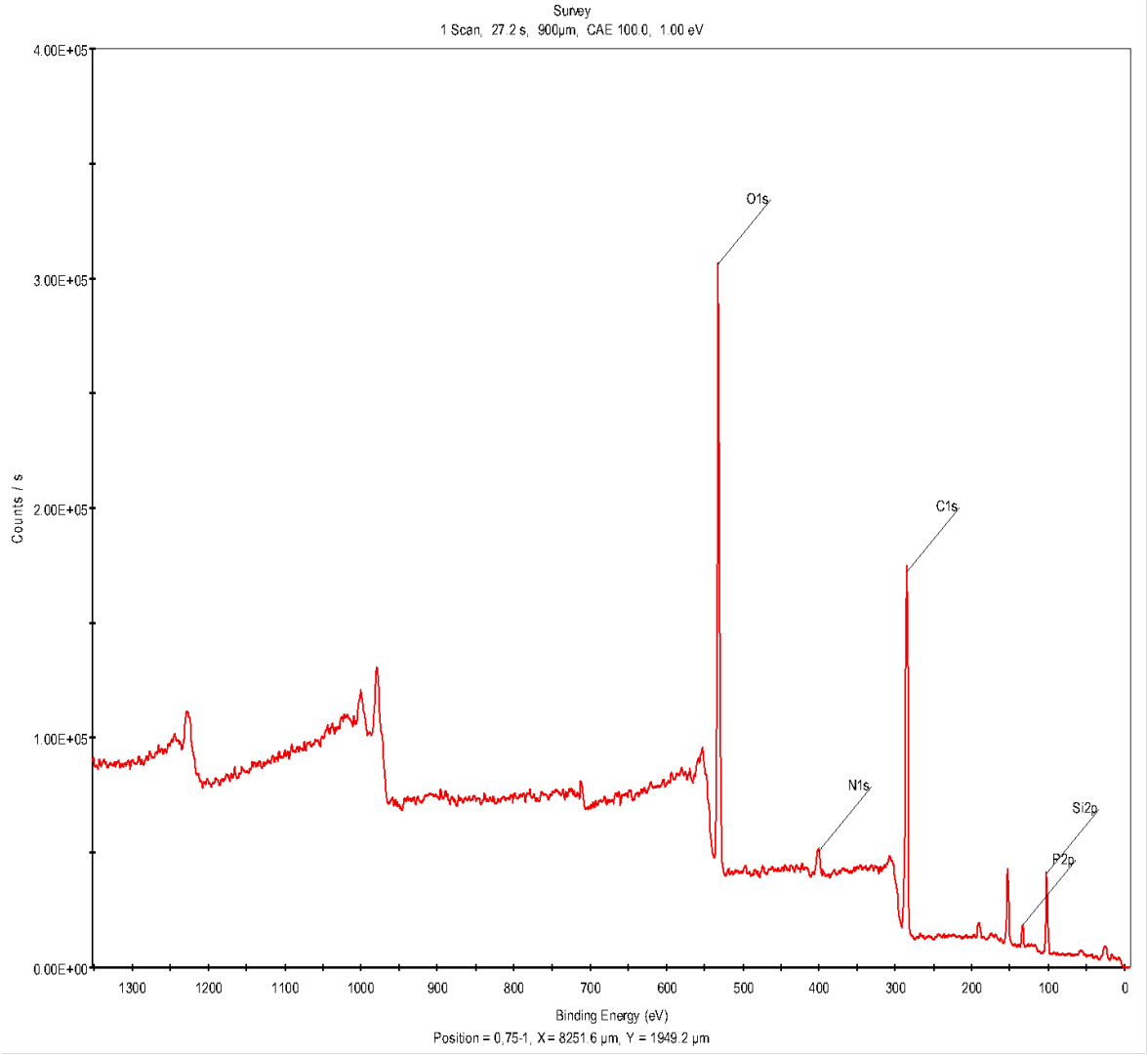

Figure A-2. The low-resolution spectrum of 0.1 M MPC modified silicone hydrogel sample with a taking of angle of 30°

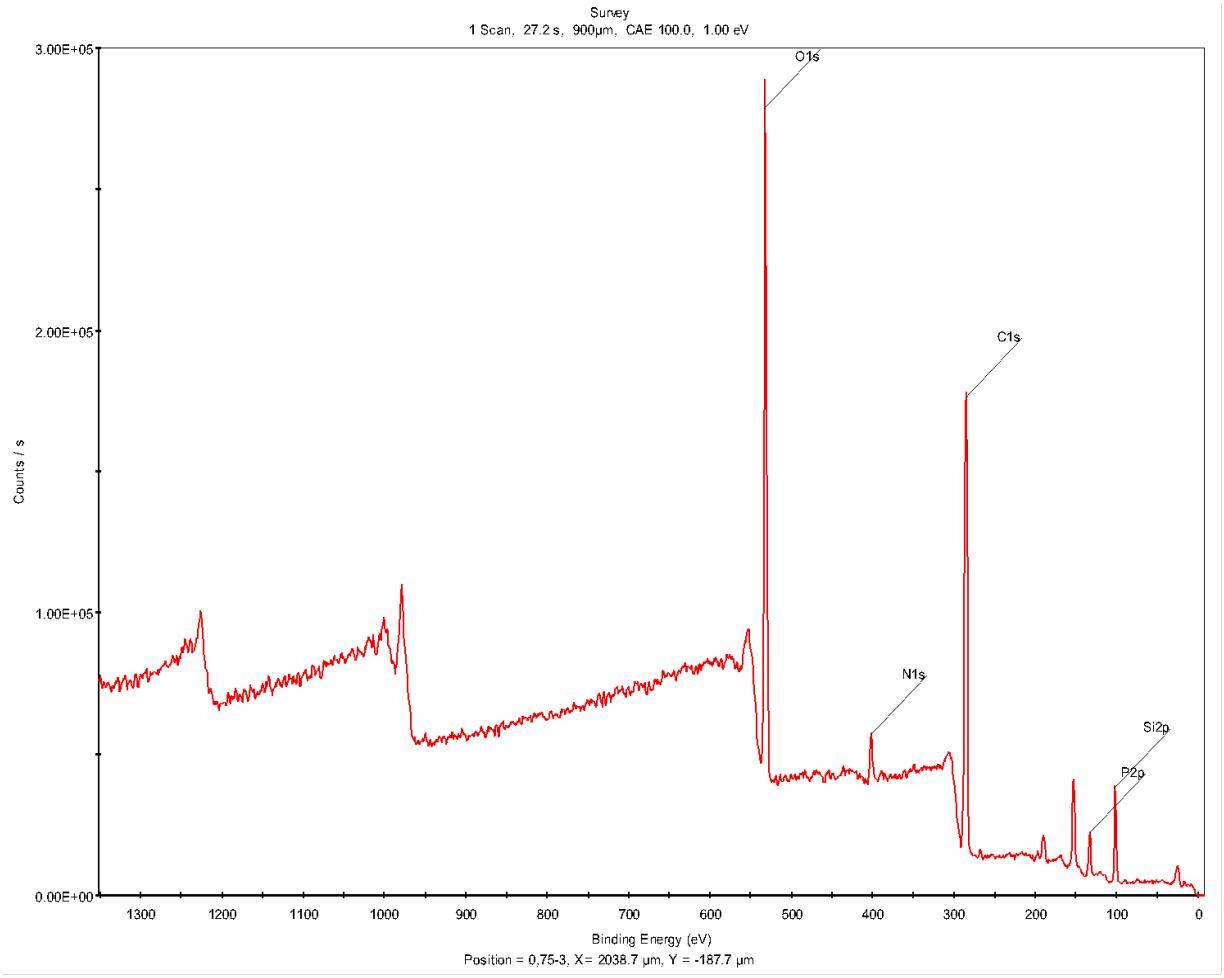

Figure A-3. The low-resolution spectrum of 1.0 M MPC modified silicone hydrogel sample with a taking of angle of 30°

Appendix B: Example of Ion Permeability Calculation

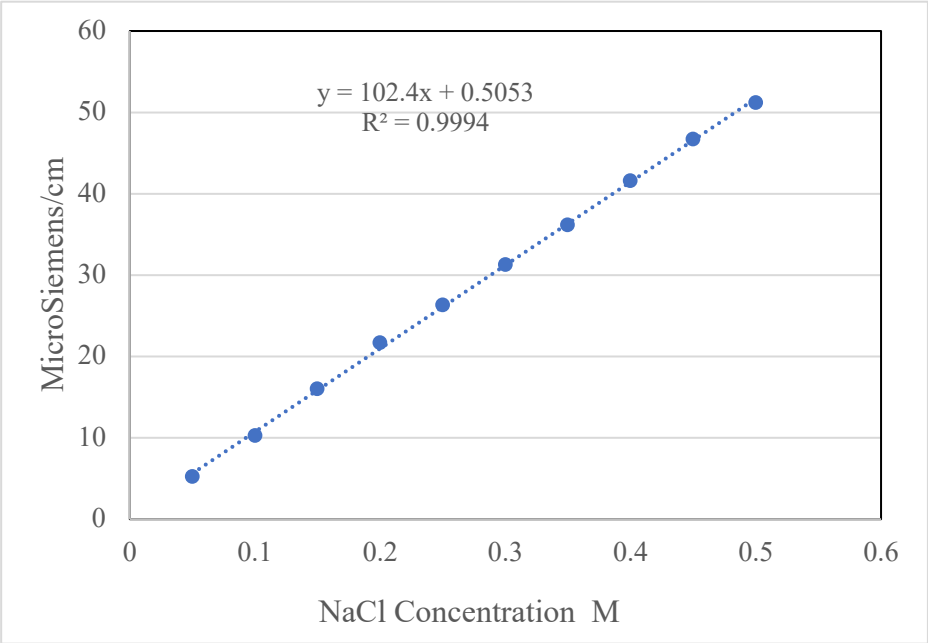

Figure B-1. The solute conductivity measurement, a linear relationship between ion concentration and corresponding electrical conductivity was derived based the plot above. Then, the ion concentration can be found according to the conductivity values obtained by CDM 83 Conductivity Meter.

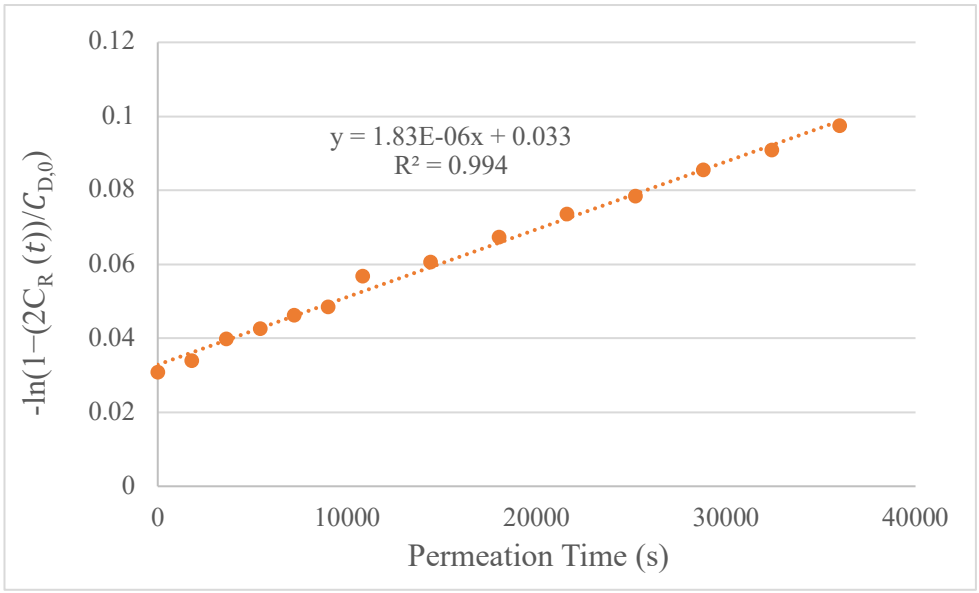

Figure B-2. The Ion permeation test of 0.1M MPC modified silicone hydrogel, a linear relationship between was derived based on the ion concentration inside of the receiving chamber and the permeation time.

Ion permeability Calculation

Solution volume in each chamber: V=10 cm^3

Thickness of membrane: 0.096 cm (0.96mm measured according to the Thickness Gauge Model ET-3)

Channeling membrane area: $A=0.45 \times 0.45 \times 3.14 = 0.636 cm^2$

$$\ln\left(1 - \frac{2C_{R\,(t)}}{C_{D,0}}\right) = -\frac{2 \cdot A \cdot P}{V \cdot L}(t - t_0)$$

C_R: Solute concentration in receiver cell at time t

$C_{D,0}$: Initial concentration inside of Donor cell

A: Surface area of the silicone hydrogel membrane

P: Coefficient of ion permeability

V: Chamber volume

L: Member thickness

T: permeation time

Based on the B-2 figure above, a linear equation between ion concentration and permeation time was derived. The linear equation constant $k=1.83x10^{-6}$ equals to the constant terms $\frac{2 \cdot A \cdot P}{V \cdot L}$ in the B1 equation above.

Thus, $1.83x10^{-6} = \frac{2 \cdot A \cdot P}{V \cdot L}$, the ion permeability coefficient,

$$P = \frac{K \times V \times L}{2 \times A} = \frac{0.096cm \times 1.83x10^{-6}\frac{1}{s} \times 10cm^3}{2 \times 0.636cm^2} = 1.38 \times 10^{-6}\ \frac{cm^2}{s}$$

Appendix C: Example of Oxygen Permeability Calculation

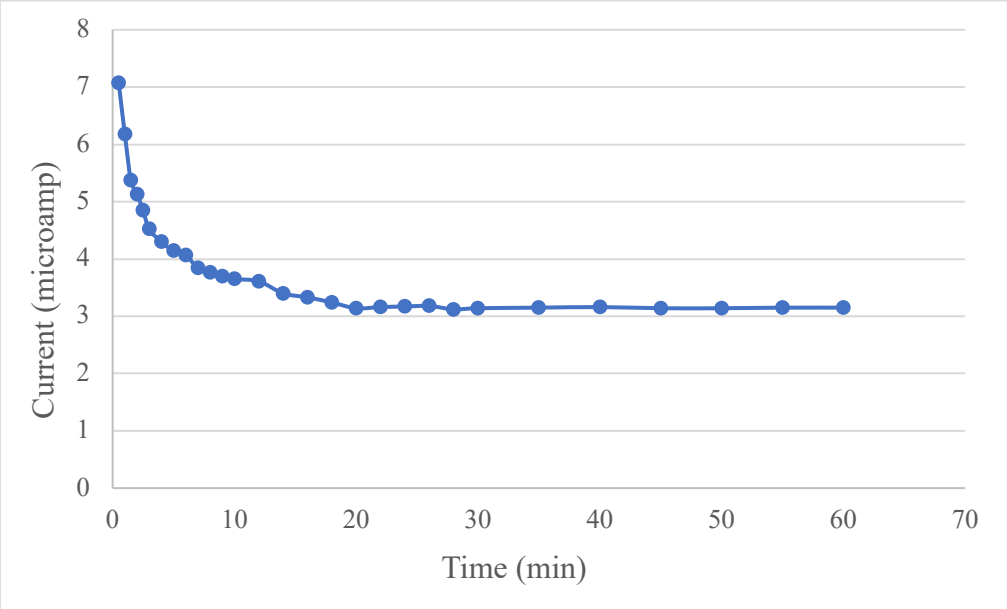

Figure C-1. The current reading of 0.20 mm thick unmodified silicone hydrogel during the polarographic oxygen permeation test, readings obtained from the Permeometer Model 210T.

Oxygen permeability Calculation

The electrochemical reaction at the cathode: $4e^- + O_2 + 2H_2O = 4OH^-$

Fick's law of diffusion: $J = A(\frac{Dk}{L})(P_1 - P_2)$

Farday's law of current flow : $i = n \cdot F \cdot J$

Rearranging the equations above $\frac{Dk}{L} = \frac{i}{A \cdot n \cdot F \cdot P_{O_2}}$

Dk: Oxygen permeability F: Faraday constant i: Current

L: Hydrogel thickness A: Area of the cathode

P_{O_2}: Oxygen tension on the open surface of the hydrogel

n: Number moles of electrons to reduce one mole of oxygen

Area of the gold cathode: $A=0.2cm^2x0.2cm^2x3.14=0.1256cm^2$ (d=0.4 cm)

Number of electrons used to reduce one mole of oxygen: n=4

Oxygen tension on the open surface of the hydrogel sample: $P_{O_2} = 155mm\ Hg$

Thickness of the silicone hydrogel sample: L=0.02cm (0.20 mm measured according to the Thickness Gauge Model ET-3)

Current reading from Permeometer Model 210T: i=3.15-0.06= 3.09μA
The 0.06μA was subtracted as the dark or background current. In addition, the initial decreasing in reading was due to exhausting of the oxygen pre-existing inside of buffer solution or hydrogel.

The unit of oxygen transmissibility is $\left(\frac{\mathrm{DK}}{\mathrm{L}}\right) = \frac{\mathrm{cm}}{\mathrm{sec}} \frac{\mathrm{ml O_2}}{\mathrm{ml \times mmHg}}$

The unit of oxygen permeability is $\mathrm{Dk} = \frac{\mathrm{cm^2}}{\mathrm{sec}} \frac{\mathrm{ml O_2}}{\mathrm{ml \times mmHg}}$

Dk has a non-SI unit: Barrer, 1 barrer = $1 \times 10^{-10} \frac{\mathrm{cm^2}}{\mathrm{sec}} \frac{\mathrm{ml O_2}}{\mathrm{ml \times mmHg}}$

$$\frac{\mathrm{Dk}}{L} = \frac{\mathrm{i}}{\mathrm{A \times n \times F \times P_{O_2}}}$$

$$= \frac{3.09 \times 10^{-6}\mathrm{A} \times 22400 \ \frac{\mathrm{cm^3}}{1 \text{ of mole}}}{0.1256\mathrm{cm^2} \times 4 \ \frac{\text{mole electrons}}{1 \text{ mole}} \times 96500 \frac{\mathrm{s \cdot A}}{\text{mole of electrons}} \times 155\text{mm Hg}}$$

$$= 9.21 \times 10^{-9} \frac{\mathrm{cm}}{\mathrm{s \times mm\ Hg}} \text{ or } \frac{\mathrm{cm \times ml O_2}}{\mathrm{s \times mm\ Hg \times ml}}$$

$$\frac{\mathrm{L}}{\mathrm{Dk}} = 1.08 \times 10^{8} \ \frac{\mathrm{s \times mm\ Hg \times ml}}{\mathrm{cm \times ml O_2}}$$

Both demominator and numerator are mutiplyed by $\mathrm{cm^3}$ because Dk is usually given in forms of $\mathrm{D} = \frac{\mathrm{cm^2}}{\mathrm{s}}$ and $\mathrm{k} = \frac{\mathrm{ml\ O_2}}{\mathrm{ml \times mm\ Hg}}$. Furthermore, repeated the above calculation steps for four more silicone hydrogel samples with different thickness

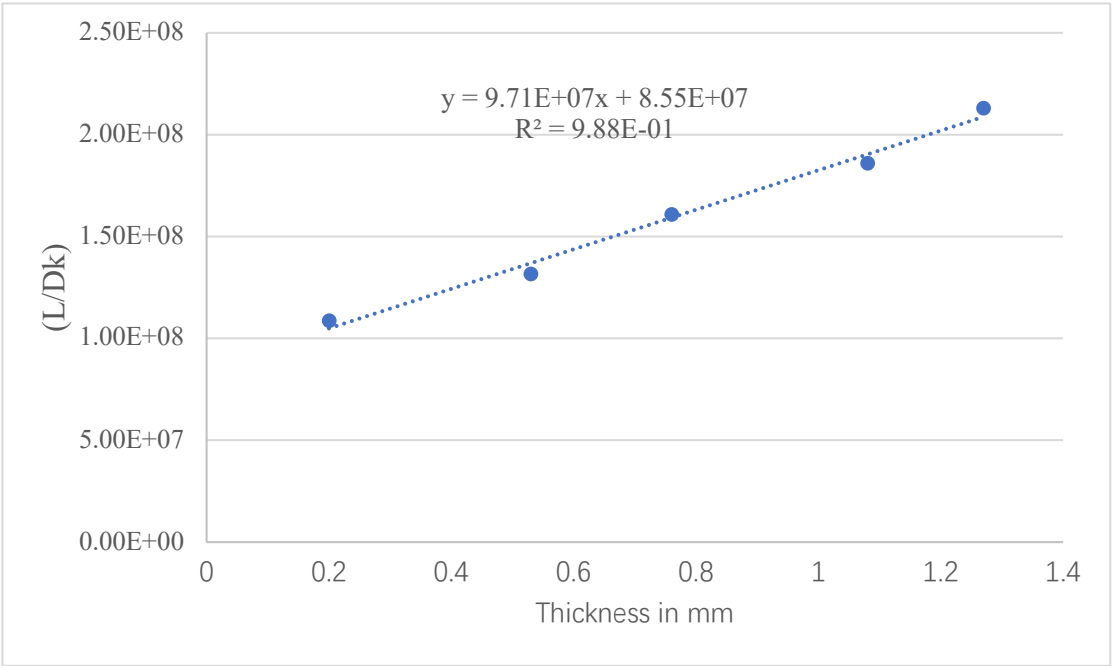

Figure C-2. Oxygen permeability measurement for the unmodified silicone hydrogel, and five different sample thickness were used to derivate the Dk of the hydrogel.

As the figure C-2 demonstrated above, the slope k of the linear line equals to

$k=\frac{L}{Dk}\times\frac{1}{L}=\frac{1}{Dk}$ or

$Dk=\frac{1}{k}=\frac{1}{9.71\times10^{-7}}=1.029\times10^{-8}\ \frac{cm^2\times mlO_2}{s\times mm\ Hg\times ml}$ or 102.9 barrers