A chronically stable polymer adhesive for bioelectronics

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***Abstract*—In biomedical applications, strong, long-term adhesion onto wet tissue is necessary for device-to-biological tissue positioning. Current methods often employ the use of crosslinked hydrogels that swell and lose mechanical and adhesion properties over time during in vivo conditions. To overcome the above limits of hydrogel biointerfaces, this paper aims to design a chemically stable polymer adhesive to achieve a chronically stable and strong adhesive for biomedical device applications. The long-term stability of this polymer adhesive will not be compromised by dehydration or excess swelling, which are the two main shortcomings of conventional hydrogels. Therefore, it shows a promising future for long-term implantable applications in biomedical devices.**

***Index Terms*—Tissue adhesion, bioelectronic interface, hydrogel, elastomers, polymer adhesives**

I. Introduction

Implantable and wearable bioelectronics contribute greatly to the development of diagnostic and therapeutic biomedical applications. In most of the cases, hydrogels are used as such bioelectronic interface to attach a device to tissue [1]. Hydrogel, which is composed of polymer network and water, has many unique advantages compared to other polymers. For example, the high-water content and various polymer structure enables a wide range of modulus and a flexible incorporation of different functional groups for various application such as adhesion.

However, when the structure of hydrogels enables unique properties such as softness and adhesion, it also leads to the intrinsically instability under dynamic wet *in vivo* conditions. For example, hydrogels used for implantable devices *in vivo* lose the mechanical integrity due to over-swelling by body fluids, while those used for wearable devices on skin lose adhesion and softness due to dehydration. In both instances, this instability stems from the intrinsic properties of hydrogels, which impose material-based limitations on their long-term applicability.

On the other hand, polymer matrices like poly-dimethylsiloxane (PDMS) are chemically stable and they will not swell during *in vivo* conditions due to its hydrophobicity [2]. But unfortunately, they are not as soft and adhesive as hydrogels. To develop a chronically stable adhesive for the long-term *in vivo* biological-to-device attachment, this paper offers a solution by modifying the mechanical property, *i.e.*, softness and adhesion, of PDMS through synthetic chemistry. In the following sections, the significance of achieving tissue-like softness and the crucial role of adhesion in enhancing device performance and biocompatibility will be first emphasized. After understanding these fundamental principles, we can delve deeper into the mechanisms and approaches employed to fine-tune these properties. Finally, we can use characterization techniques to quantify and to validate the outcomes, providing a comprehensive understanding of the process and its potential implications from a material-level for bioelectronic technology.

II. Background

To attain a polymer adhesive suitable for bioelectronic applications, two primary aspects must be addressed: reducing the modulus to match tissue-level properties and enhancing adhesion to wet tissues.

A. Significance of tissue-like softness for biointerfaces

Extremely soft materials are advantageous by minimizing the mechanical mismatch that often arises between electronic devices and the human skin or underlying tissue. Unlike traditional rigid materials, which can induce discomfort and limited flexibility, soft materials exhibit mechanical properties that more closely resemble those of biological tissues. This inherent similarity enables better conformability, fostering seamless integration with the complex and curved surfaces of the human body. Such enhanced conformability establishes a crucial foundation for various medical applications, particularly in wearable and implantable devices, which facilitates the accurate and reliable transmission of signals between the device and biological systems.

More importantly, tissue-like softness plays a pivotal role in reducing foreign-body responses, which are the body's immune reactions to foreign materials introduced during medical procedures [3]. The immune system's response to rigid materials can lead to inflammation, fibrosis, and encapsulation, compromising the performance and longevity of bioelectronic devices. In contrast, soft materials are better tolerated by the body, minimizing adverse reactions, and promoting a more biocompatible interface.

B. Hydrosilylation reaction of poly-dimethylsiloxane (PDMS)

Poly-dimethylsiloxane (PDMS) is a widely used elastomer in the field of bioelectronics due to its exceptional biocompatibility, softness, and versatility. PDMS is composed of repeating siloxane units, resulting in a highly flexible and

elastic structure. This unique molecular arrangement contributes to its remarkable softness, making it an ideal candidate for biointerfaces, where mechanical compatibility with biological tissues is of utmost importance.

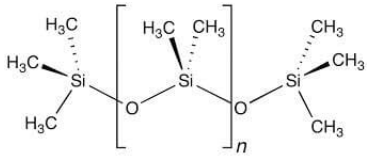

Figure 1. Chemical Structure of PDMS

However, while PDMS outperforms many of its counterparts, it is worth noting that the Young's modulus of the most widely used commercial PDMS variant, Sylgard 184 and Ecoflex, is still significantly higher—two to three orders of magnitude—than that of conventional hydrogels.

The mechanical property of PDMS is determined by chemistry. The synthesis of the PDMS matrix involves a chemical reaction termed as "hydrosilylation", which occurs between vinyl-terminated polymers and hydride functional polymers, allowing for precise control over the PDMS's softness, toughness, stretchability, and elasticity.

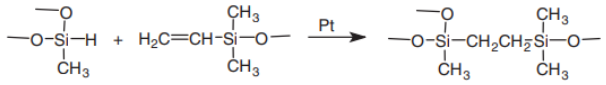

Figure 2. Hydrosilylation reaction between vinyl-terminated polymers and hydride functional polymers

To tune the mechanical properties, the ratio between the vinyl-terminated polymers and hydride functional polymers can be adjusted. PDMS with multifunctional groups usually act as crosslinkers and makes material harder. For example, increasing the proportion of divinyl-terminated polymers, which can act as crosslinkers, relative to hydride functional polymers tends to result in a more rigid and less stretchable PDMS elastomer. On the other hand, a higher proportion of monohydride functionalized or monovinyl-terminated polymers relative to divinyl-terminated polymers will lead to a softer and weaker PDMS matrix.

C. *Crucial role of wet tissue adhesion*

Adhesion is another crucial factor to ensure a successful and effective communication between electronic or medical devices and living tissues. Robust tissue adhesion ensures close physical contact and integration with the body's intricate structures, allowing for reliable signal transduction, efficient energy transfer, and accurate data collection. Moreover, strong tissue adhesion minimizes the risk of device displacement, slippage, or migration, ensuring the sustained functionality and longevity of implanted or wearable bioelectronic devices. Additionally, robust tissue adhesion is instrumental in reducing the risk of adverse immune responses and inflammation, enhancing the biocompatibility and tolerability of implanted devices. For applications such as biosensors, drug delivery systems, and neural interfaces, where precise interactions with biological systems are crucial, achieving strong and biocompatible tissue adhesion is vital to unlocking the full potential of bioelectronics and advancing medical treatments and healthcare technologies.

D. *Mechanism of wet tissue adhesion*

Compared to dry adhesion, achieving adhesion to wet surface is more challenging due to the existence of interfacial water.

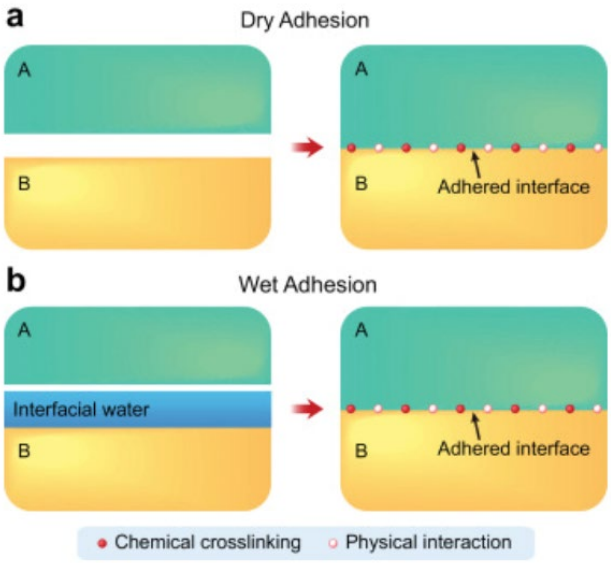

Figure 3. Different mechanism for dry and wet adhesion [4]

There are two main stages involved in achieving wet tissue adhesion. In the first stage, the material should be able to absorb the interfacial water by rapid swelling or hydration. In the second stage, the material will then be able to reach the tissue surface and build adhesion through intermolecular forces such as hydrogen bonds, electrostatic interactions and van der Waals interactions [5]. Consequently, the design principles for materials targeting wet tissue adhesion encompass two essential aspects: (1) rapid hydration capacity to facilitate interfacial water absorption, and (2) incorporation of functional groups that can establish favorable interactions with the tissue.

To incorporate tissue adhesion to PDMS elastomer, this paper introduced effective functional groups by chemical surface modification. A commonly used polymer in hydrogel applications is the crosslinked polyacrylic acid (PAAc) [1]. By using in situ polymerization to introduce a layer of PAAc onto the surface of PDMS, it may lead to an adoption of a brush-like orientation due to the steric hindrance of each polymer string against each other as seen in Figure 5 [6]. Therefore, unlike a crosslinked network, this conformation allows the polymers to absorb water without over swelling to a loss of mechanical properties.

In conjunction with the PAAc grafts that offer hydrogen bonding to enable adhesion, another functional group, PAAc grafted with N-hydroxysuccinimide ester (PAAc-NHS) can lead to greater adhesion through the formation of covalent bonds with primary amines in the tissue [7] as seen in Figure 6. Utilizing a copolymer of PAAc and PAAc-NHS leads to absorption of the interfacial water, hydrogen bonding adhesion, and strong covalent bonds between the polymer and the tissue.

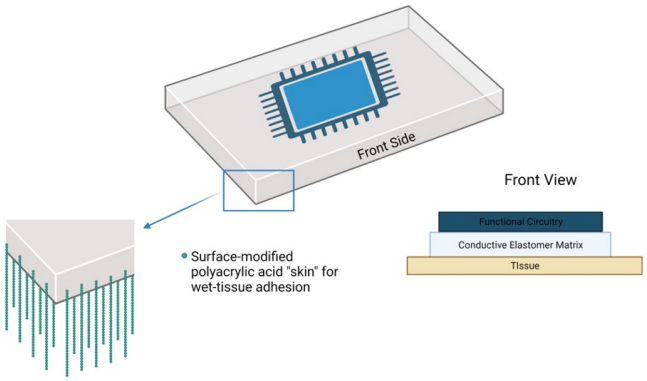

Figure 5. Surface grafted polymers onto an elastomer matrix of PDMS. The surface grafter polymer groups for a linear chain by repelling forces upon each other.

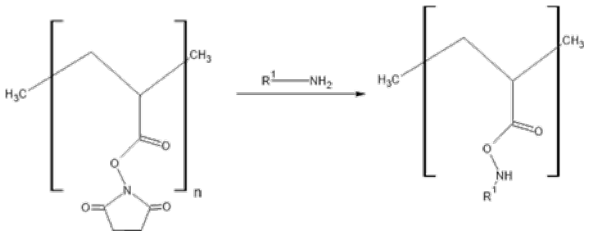

Figure 6. Reaction between the PAAc-NHS group with primary amines in tissue, resulting in covalent bonding between tissue and the polymer.

III. Methods and Materials

Ecoflex™ Gel Platinum Silicone Gel, Smooth-On. Benzophenone, TCI. Acetone >99.5+, thermoscientific. Acrylic Acid, stabilized with MEHQ, TCI. 2,5-Dioxopyrolidin-1-yl acrylate (AAc-NHS), BLD Pharm. N,N'-Methylenebisacrylamide (MBAA), TCI. α-Ketoglutaric acid, Sigma Aldrich. Gelatin from porcine skin, Sigma Aldrich. Chitosan, Sigma Aldrich. Gelatin Methacrylate (300 bloom, degree of substitution 60%), TCI. *Ex Vivo* tissue was obtained from local supermarkets. Mechanical Testing was completed on Instron 5564 Tabletop Universal Testing Machine.

i. Preparation of Silicone Gel

For creating the PDMS rubber, the standard 1:1 weight ratio of parts A and B were measured and mixed. After mixing, the pre-polymerized mixture was added to molds and degassed in a vacuum chamber for 10 minutes. The molds were then cured in an oven at 90 °C for 5 minutes.

To tune the modulus of PDMS elastomer, the mixing ratio between A and B varied from 1:10 to 10:1 in weight.

ii. Surface modification of PDMS

The PDMS substrate first immersed in a 10% (w/v %) benzophenone solution in acetone to introduce photo-initiator then dried to remove extra solvent. Two set of monomer solution was used to test the adhesion property. For the pure acrylic acid monomer solution, it contained 50% (v/v%) acrylic acid in water. To introduce covalent bonding with tissue, the other set of monomer solution incorporated acrylic acid grafted with N-hydrosuccinimide ester (AAc-NHS), containing 35% (v/v %) acrylic acid monomer and 15% AAc-NHS (w/v %) in water. The monomer solution was drop-cast onto PDMS substrate and initiated by UV illumination under nitrogen. For the 100 W UV lamp, the exposure time was about 5 minutes. After polymerization, the product was then washed in hot water bath to remove unreacted monomer. Finally, the product was dried and stored in room temperature for use.

iii. Tensile Tests

The samples were loaded onto the universal tensile machine with pressurized clamps, and the dimensions of the sample were measured. The test was completed with a 10 N load cell, and the tensile test was run with constant 200 mm/min extension.

Data analysis of this testing was performed in Excel utilizing linear regression.

iv. 180 Degree Peeling Tests

The surface-modified PDMS was adhered to Kapton tape as backing layer before applying to chicken heart. 180 degree peeling tests were conducted 30 minutes after the application. A 2 kN load cell was used for the testing and the extension was maintained at 50 mm/min. The interfacial toughness was calculated by 2 times plateau force divided by sample width.

Data analysis of this testing was performed in MatLab, and the resulting adhesion energy was calculated by taking the average force of the identified plateau region and dividing by double the width of the sample.

v. Chronic stability tests

The surface modified PDMS was adhered to squid tissue and stored in PBS at 4°C for long-term adhesion tests.

IV. Experimental Results

A. Tuning mechanical properties of PDMS

The commercial PDMS consist two parts A and B, where one part usually contains vinyl-terminated siloxane, and the other contains hydride functional siloxane. By varying the ratio between vinyl group and hydride group, PDMS with a wide range of moduli could be obtained.

The softness of a material can be quantified by Young's modulus, which describes the material's resistance to deformation under an applied force. Mechanical testing machines can be used to test the modulus of a material by applying controlled forces to the sample and measures its corresponding deformation to obtain a stress-strain curve. The slope of the linear region is used to determine the modulus. Stiffer material has a higher Young's modulus, while softer material has a lower value. Therefore, for the application of neural tissue and other soft organs, the elastic moduli must be in the 0.5-10 kPa range [1]. In Figure 5, lowering the ratio of A:B to 1:10 increased the modulus while decreasing the ratio to 10:1 made the material to soft to be loaded on the sample stage for tensile tests.

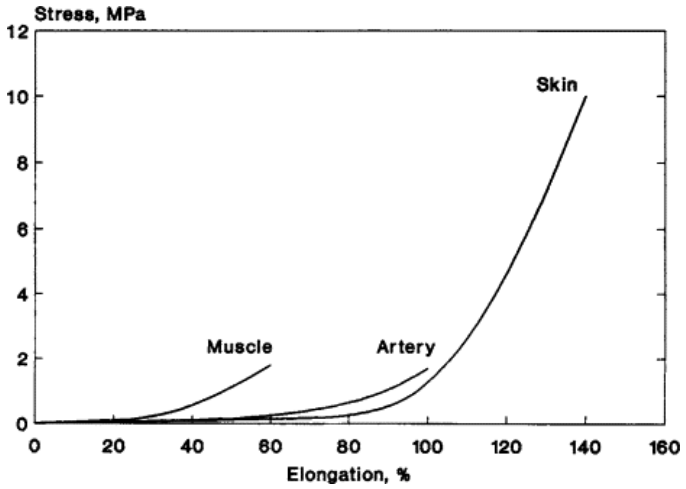

Figure 7. The graph shows the stress versus elongation plot for different biological tissues. The notable characteristics are low elastic moduli and elastic stiffening with increasing loads [8].

In addition to softness, another feature of the mechanical property of biological tissues is strain-stiffening effect as can be seen in Figure 7. Strain-stiffening refers to a mechanical behavior in which certain materials become stiffer or more resistant to deformation as they are stretched or deformed. In another word, the modulus of a strain-stiffening material increases as it is being stretched. In Figure 5, the different slopes of the blue and red region indicated the increased modulus of PDMS during stretching, which is another tissue-like property contributing to conformal attachment under dynamic conditions.

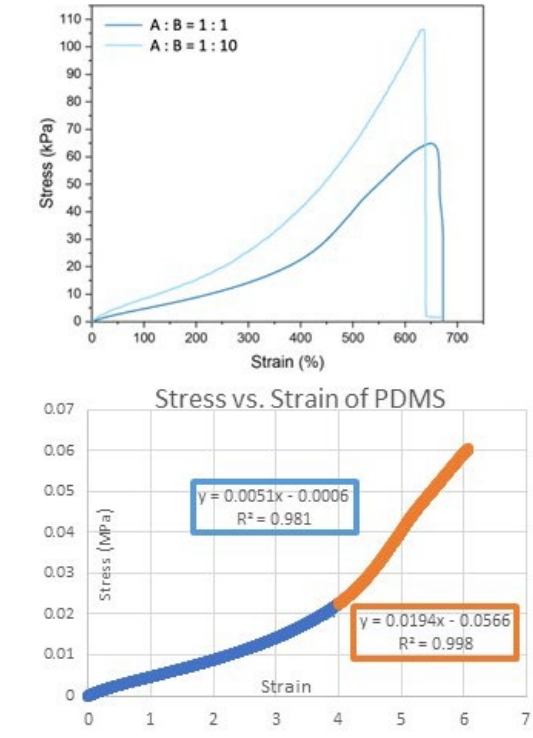

Figure 8. The upper plot shows the different modulus of PDMS with different mixing ratio. The lower plot shows the increased modulus during stretching. Both plots demonstrate that the PDMS matches the low elastic modulus of biological tissue and the moduli stiffening of biological tissues.

The stress-strain curve provides additional insights into two other important material parameters: toughness and stretchability. Toughness quantifies a material's capacity to absorb energy before fracturing, making it a critical consideration for bioelectronics. High toughness ensures superior resistance to mechanical wear and tear, thereby enhancing the overall durability and reliability of bioelectronic devices. This characteristic can be evaluated by calculating the area under the stress-strain curve. Stretchability, on the other hand, can be determined by observing two key aspects of the stress-strain curve: elongation at break and reversible elongation in the elastic region. Achieving high elongation at break and wide elastic region is crucial as it allows the material to accommodate movements and deformations without material fracturing or constraining natural motions. This flexibility is essential for ensuring the integrity and longevity of bioelectronic interfaces when subjected to dynamic mechanical stresses. In Figure 5, the PDMS showed excellent toughness and stretchability.

B. Surface modification of PDMS

Unmodified PDMS elastomer exhibited no adhesion to tissues primarily due to its hydrophobic nature, which hindered its ability to absorb interfacial water and establish effective interactions with tissue surfaces. To enhance the hydrophilicity and introduce functional groups, we polymerized a layer of acrylic acid on the PDMS surface. The carboxyl groups in the acrylic acid facilitated adhesion by forming hydrogen bonds and electrostatic attractions with the tissue surface. However, this interaction proved to be unstable and susceptible to disruption by water. To achieve long-term adhesion, we introduced AAc-NHS, enabling the formation of covalent bonds with the tissue. Surprisingly, even before immersing the sample into water, the initial adhesion of PDMS containing AAc-NHS on the surface surpassed that of PDMS composed solely of pure AAc. This unexpected result in Figure 9 highlights the significant improvement achieved by incorporating AAc-NHS, promising enhanced and lasting tissue adhesion for our bioelectronic interfaces.

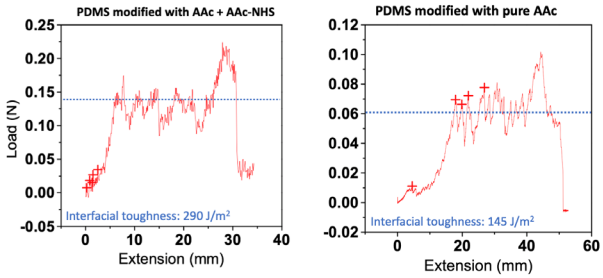

Figure 9. Comparison of interfacial toughness of PDMS modified with AAc + AAc-NHS and AAc.

The strong interfacial toughness (290 J/m^2) enabled by chemistry modification of PDMS proved the initial success of the strategy. To test the long-term adhesion, modified PDMS was attached to tissue and stored in PBS at 4°C. As a control group, we synthesized a hydrogel that was reported by Yuk *et al.* to be highly adhesive to wet tissue. However, although showing fast and strong adhesion when first applied, the hydrogel swelled significantly after four days in PBS at 4°C, as can be seen in Figure 10. The excess swelling led to mechanical

degradation and weak attachment which could be easily disturbed by gentle touching. On the contrary, our surface modified PDMS didn't show any observable swelling after 6 weeks in PBS. The adherence remained robust and strong even under violent vortexing.

Figure 10. These photos show the different thickness of a typical hydrogel system by Yuk et al. [9] before attachment and after attachment for 4 days stored in PBS. Additionally, the hydrogel does not stay adhered to tissue after a minimal load due to a lack of mechanical properties.

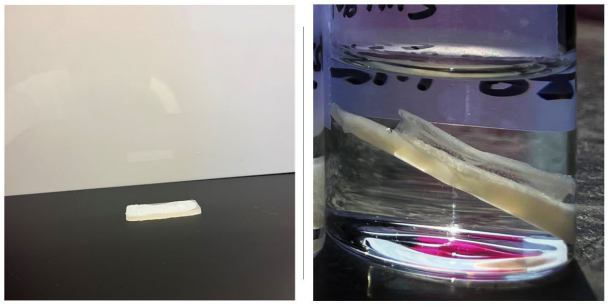

Figure 11. These photos show the continued adherence of the surface-modified PDMS to biological tissue after 6 weeks. The photo on the left shows the surface-modified PDMS elastomer before adherence, and the photo on the right shows the robust adherence to tissue and lack of swelling of the system after 6 weeks in PBS.

V. Discussion and Conclusion

In this study, we have successfully developed a novel polymer adhesive with exceptional properties tailored for bioelectronic interfaces. The main idea of the paper is to combine the advantage of hydrogel in terms of softness and adhesion with the chemical stability of PDMS elastomer. Through strategic tuning of the PDMS modulus and surface modification with a layer of polyacrylic "skin", we achieved an "all-in-one" polymer adhesive with tissue-like softness, wet tissue adhesion, and long-term stability. This innovative adhesive presents a significant advancement in addressing the challenges of achieving robust adhesion to wet tissues while preserving tissue-like softness, a critical factor for biocompatibility and overall device performance.

The potential applications of this polymer adhesive in real-world biomedical scenarios are promising. Future investigations on its biocompatibility, mechanical reliability, and long-term stability *in vivo* will be essential to ensure its safety and efficacy. Additionally, further integration with the device may expand its applicability in various biomedical fields.

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