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The insulation performance of reactive parylene films in implantable electronic devices

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Abstract

Parylene-C (poly-chloro-p-xylylene) is an appropriate material for use in an implantable, microfabricated device. It is hydrophobic, conformally deposited, has a low dielectric constant, and superb biocompatibility. Yet for many bioelectrical applications, its poor wet adhesion may be an impassable shortcoming. This research contrasts parylene-C and poly(p-xylylene) functionalized with reactive group X (PPX-X) layers using long-term electrical soak and adhesion tests. The reactive parylene was made of complementary derivatives having aldehyde and aminomethyl side groups (PPX-CHO and PPX-CH₂NH₂ respectively). These functional groups have previously been shown to covalently react together after heating. Electrical testing was conducted in saline at 37°C on interdigitated electrodes with either parylene-C or reactive parylene as the metal layer interface. Results showed that reactive parylene devices maintained the highest impedance. Heat-treated PPX-X device impedance was 800% greater at 10 kHz and 70% greater at 1 Hz relative to heated parylene-C controls after 60 days. Heat treatment proved to be critical for maintaining high impedance of both parylene-C and the reactive parylene. Adhesion measurements showed improved wet metal adhesion for PPX-X, which corresponds well with its excellent high frequency performance.

1. Introduction

Commercially available implantable electronics, such as a pacemaker or deep brain stimulator, are typically packaged inside of a laser welded, metal canister [1]. Yet many applications require micro-scaled sensors and actuators where hermetic packaging is impractical. Next generation implantable biosensors, smart drug delivery systems, and neuroprostheses will need to maintain long-term insulation using fully exposed microfabricated structures [2]. We, for example, are attempting to develop parylene-based microfabricated electrode arrays for long-term sensing in the brain, which requires exceptionally low noise and stability [3].

Interfacial boundary layers that form between each material in a well insulated structure should be clean, have similar surface energies, and possess adequate adhesion strength to withstand the intended environment [4]. On one hand, polymers are attractive because of their diverse bulk properties and alterable surface chemistry. On the other, polymers are inherently porous to water, oxygen, and salts compared to high temperature inorganics [5,6]. As such, polymer-based devices must have interfacial boundaries that are stable in the presence of water, oxygen,

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and ions. This issue is especially important for a microfabricated structure being used in a bioelectrical application. By way of illustration, first consider a polymer coating on two suspended metal wires that form an interconnect in a generic sensor or actuator (Fig. 1A). When this device is in biological fluid or tissue, two critical electrical measurements should be known—the lateral impedance, Z_{lat} , and transverse impedance, Z_{trans} . Z_{lat} is inversely related to crosstalk in this circuit. Z_{trans} is inversely related to signal loss via “shunting”. One interfacial boundary exists for both measurements. By contrast, when a similar interconnect is created using planar microfabrication, another interfacial boundary is introduced (Fig. 1B). In the first example of coated metal wires, a poorly adhering interfacial boundary will only cause a dramatic decline in Z_{lat} or Z_{trans} if the metal begins to corrode. Otherwise, the impedance will be dominated by the geometry of the circuit (track and space width, metal and dielectric height) and the bulk properties of the material. However, in the example of a biomedical MEMS device, Z_{lat} in particular can have a striking decline in impedance if the polymer-metal and polymer-polymer boundaries are compromised, thereby enabling a low resistive pathway. This study used an interdigitated electrode to measure both Z_{lat} and Z_{trans} .

Parylene-C has a recognized issue of poor wet metal adhesion [4,7–11], which should raise caution over its use in biomedical microdevices. Nonetheless, it has many desirable properties. Parylene-C is chemically inert, has a low dielectric constant ($\epsilon_r = 3.1$), and the highest biocompatibility certification, USP Class VI. It is synthesized from a low-molecular weight dimer, dichloro[2.2]paracyclophane using a solventless polymerization process. Critically important in microfabrication, parylene-C can be deposited as conformal, pinhole free films that are subsequently dry-etched using an oxygen plasma.

Parylene-C has been used in implantable sensors and actuators. Most notably, parylene-C has been successfully used as a coating in neural recording arrays [12,13]. A few researchers have also used parylene in implantable microfabrication applications. One group used oxygen plasma to clean and roughen between parylene deposition [14,15], and more recently used heat treatment to improve long-term electrical resistivity through the parylene-C film [16,17]. Heat treatment combined with pressure was shown to improve parylene-parylene adhesion, which is believed to mechanically interlock polymer chains at the interface [18,19].

“Reactive parylene” films can be used to modify interfacial properties and by functionalizing the paracyclophane dimer with a variety of reactive chemical groups [20–22]. Recent research has used complementary reactive parylene films having aldehyde and aminomethyl groups, PPX-CHO and PPX-CH₂NH₂ respectively, to improve adhesion strength of PDMS on silicon [23]. The aldehyde and aminomethyl groups covalently react to form an imine linkage after heating at 140°C for 3 hours (Fig. 2B). We use these same complementary reactive parylene films (PPX-X) in electrical and mechanical test structures.

Wide spectrum impedance data for long-term soak tests using microfabricated parylene-C devices is lacking. This study investigates both parylene-C and reactive parylene using long-term electrical soak tests and adhesion tests. Two important techniques are utilized: (1) electrochemical impedance spectroscopy and (2) an interdigitated electrode sensor. EIS is also commonly used to evaluate the longevity and degradation kinetics of many polymer-metal systems [24], including paint and epoxy coatings. EIS is most effective when coupled with “under-coating” or interfacial measurements [25,26], which are possible with an interdigitated electrode. Broad frequency analysis provides greater relevance to a variety of bioelectrical applications, e.g. biosensors (<10 Hz frequency band) or neural recording and stimulation (500–5000 Hz frequency band).

2. Design and fabrication

2.1 Interdigitated electrode fabrication

The interdigitated electrode (IDE) structure consisted of long, widely spaced leads in a “Y” configuration. The large separation between bond pads was designed to reduce stray capacitance. The overlapping metal region was 5-mm tall $\times$ 700- μ m wide. Each electrode tine was 1.5- μ m wide and a 4.5- μ m gap. The total length of the overlapping metal trace was 292,000 μ m per half. Metal was buried in a parylene substrate, similar to a stripline configuration in printed circuit boards. An alternative geometry was 3.0- μ m track and a 3.0- μ m gap. The results for the 3/3 geometry are discussed in section 3.4.

The microfabrication for these structures required two masks and was conducted on 4” silicon wafers in the Lurie Nanofabrication Facility at the University of Michigan. For simplicity, we describe the process in four major steps (Fig. 2A). Fig. 2-A1. One micron of SiO₂ was thermally grown on the wafer. An adhesion promoter A-174 was vaporized onto the wafer surface then parylene-C was CVD polymerized (PDS2010, Specialty Coating System) on the oxide. Deposition was 2.4- μ m thick for experimental wafers, i.e. those to receive PPX-X, or 2.5- μ m thick for control wafers. Fig. 2-A2. Next the parylene-C surface was briefly etched with an oxygen plasma for 30 sec at 80W (March Asher) in preparation for the next polymerization step. Oxygen plasma etching has been reported as a technique to clean and roughen a parylene undercoating [14,15]. It has also been suggested as way to create free radicals on a polymer surface that can form covalent bonds during parylene polymerization [4]. This plasma cleaning step occurred before each CVD step throughout the process to ensure consistency between layers. Poly(4-formyl-p-xylylene-co-p-xylylene), PPX-CHO, was CVD polymerized using custom built equipment described previously [27], although could be deposited with commercial equipment as well. 90–140 nm of PPX-CHO was deposited on the experimental wafers only. Precursor synthesis was conducted in an author’s laboratory (JL) with further details described elsewhere [22,27]. The strong carbonyl stretch at 1688 cm⁻¹ in the IR spectrum was used to confirm the presence of the aldehyde group after deposition (Fig. S1A). Thickness was determined with a profilometer. Next, metal lift-off (SPR220) was used to pattern the Cr/Au/Cr (100/4000/100 Å). Metal was deposited with an e-beam evaporator (Enerjet). The resist was removed with 1112A (Shipley Microposit Remover). Following lift-off, wafers were immediately cleaned in acetone, IPA, then spin rinsed for 5 minutes. Fig. 2-A3. Poly(4-aminomethyl-p-xylylene-co-p-xylylene), PPX-CH₂NH₂, was CVD polymerized on experimental wafers. Precursor synthesis is described elsewhere [28]. Deposition of PPX-CH₂NH₂ was conducted using the same parameters as PPX-CHO, and profilometric measurements indicated film thicknesses of 90–130 nm thick. The peaks at 3361 and 3301 cm⁻¹ in the IR spectrum were used to confirm the presence of the N-H bonds after deposition (Fig. S1B). Next, parylene-C was deposited on experimental and control wafers either 2.4 μ m or 2.5 μ m, respectively. Fig. 2-A4. Titanium was deposited 1000-Å thick (evaporator) and patterned (SPR220) to define the structural mask during oxygen plasma etching (not shown). After O₂ plasma etching (Plasmatherm 790), chromium was removed from the exposed bond pads by a wet etch (Cyantek CR-14) for 8 sec. The titanium and SiO₂ (sacrificial release layer) were etched in DI:HF:H₂O₂ (3:3:1) for ~1 hour. Released test structures were filtered out and repeatedly rinsed with ~2L of DI until the pH of the rinse water was normal. Released devices were air dried and ready for assembly (Fig. 2-A4). The thickness of dielectric material over metal was 2.3 to 2.5 μ m per side for all devices.

IDE test structures were connected to a printed circuit board employing gold ball studs with thermosonic bonding [29]. A protective coating of silicone (MED-4211, Nusil Technology) was carefully applied over each end of the IDE ball bond regions. An additional 100 nm of parylene-C was deposited onto all IDEs to coat any pinhole or edge defects. “Heated PPX-X”

and “Heated CNTL” (parylene-C) samples were heated in an oven at 140°C for 3 hours. The resulting “Y” structure is illustrated in Fig. 3A.

2.2 Soak Testing

The electrochemical impedance measurements were performed using an Autolab PGSTAT 12 (Eco Chemie) with associated Frequency Response Analyzer software. The spectral range was 100,000 to 1 Hz, except dry samples which were limited to 10 Hz given the high impedance of these devices. 5 frequencies were measured per decade on a logarithmic scale (26 frequencies total). A two electrode measurement was made by connecting the counter to the reference electrode input, and the working to the sense electrode. The sinusoidal voltage amplitude was 25 mV. A 1 mm diameter platinum electrode was used as the counter electrode in measurements of Z_{trans} . All impedance measurements were carried out in a Faraday cage in order to minimize any external interference. Transverse and lateral impedance (Z_{trans} and Z_{lat}) testing was collected on the first hour, first day, and then at least every 5th day. Given the low capacitance values of dry test structures (Table 3), care was taken to ensure cables were routed and spaced in a repeatable manner throughout the study. The baseline capacitance was determined to be 3.1 pF, which included cables, connectors, and a printed circuit board (without the IDE).

A custom soak chamber was created from glass jars and a machined nylon lid. The nylon lid held the IDEs below the water level to ensure constant soaking was achieved (Fig. 3). Each lid was sealed from the outside of the jar with gasket sealer. Assembled devices were mounted through openings in the custom soak chamber lid and sealed with silicone from the top (Fig. 3). The IDE active area was completely submerged throughout the study. The soak chamber was filled with phosphate buffered saline (1X) with 0.1% sodium azide. The PBS solution was changed every twenty days to minimize the possible effects of evaporation and precipitation. Eight samples were loaded into each soak chamber. Multiple soak chambers were held at 37°C for 60 days in a large temperature-controlled water bath. The temperature range during data collection was 35–39°C.

2.3 Adhesion Testing

Two peel-test structures were fabricated and the resulting cross-section and angle of separation is illustrated in Fig. 4. Adhesion forces were measured quantitatively using a load cell (Sensotec Model 31, Honeywell). One half of each structure was fixed and the other pulled apart using a programmable piezoelectric micromotor (M-230, Physik Instrumente) as illustrated (Fig. S2). Optical examination and profilometric measurements were used to conclude the plane of separation.

Microfabrication of parylene-on-metal structure—Evaporate 500 Å of chromium on a 4" silicon wafer. CVD polymerization of parylene (PPX-CHO or parylene-C) 100-nm thick (actual 75 to 135 nm). Pattern a sacrificial separation layer of SPR220 photoresist. Surface cleaning in oxygen plasma (March Asher) for 30 sec at 80W. CVD parylene (PPX-CH₂NH₂ or parylene-C) 100-nm thick (actual 80 to 135 μm). Repeat oxygen plasma and then CVD parylene-C 5-μm thick four times for a total thickness of 20 μm. Oxygen plasma treatment was repeated between each layer. This thickness was necessary to prevent breakage during the adhesion test. The wafer was diced into 7.5-mm wide pieces. The length was greater than 20 mm. Sacrificial photoresist was removed by dipping only the resist end of the sample into acetone for 2 hours then rinsed in IPA. Samples dried at least one day before testing.

Microfabrication of parylene-on-parylene structure—This structure process was identical to the IDE structure except the inclusion of a Ti sacrificial layer and the omission of the metal electrode. After depositing the SiO₂ and first 5 μm of parylene-C, a 100-nm parylene film was deposited as before (PPX-CHO or parylene-C). Then a Ti sacrificial layer was

deposited (1000 Å). The Ti was patterned using SPR220 and a wet etchant of 20:1:1 DI:HF:H₂O₂. Another 100-nm parylene film (PPX-CH₂NH₂ or parylene-C) and 5 µm of parylene-C was then polymerized. The final structure was defined by a Ti mask, etched with an O₂ plasma, and then released in DI:HF:H₂O₂ (3:3:1) for ~1 hour. The peel test structures (3mm × 20mm) were air dried for several days.

2.4 Circuit Modeling

The impedance measurements were fitted using Boukamp's program, EQUIVCRT [30]. Analysis of the impedance measurements were performed between 1 Hz and 100 kHz. Extracted capacitance values were used to verify that the test structures had similar geometries and thus were useful for comparison (Table 3). Dry IDEs not heat treated fit best using a parallel resistor and capacitor. Heated IDEs were fit to a simple constant phase element (CPE). The impedance of a CPE is defined as:

$$Z_{CPE} = \frac{1}{Y(j\omega)^n}$$

where j is an imaginary number, ω is angular frequency (rad), n is the CPE power, and Y is the CPE constant.

3. Results

3.1 Lateral impedance

Lateral impedance, Z_{lat} , was first measured before soaking began. All dry measurements resulted in similarly high impedance (Fig. 5A, red). Capacitance of the dry IDEs was also determined to be similar (21.6 ± 5.4 pF, Table 3) after fitting to an equivalent circuit model. Dry IDEs that were not heat treated resulted in a semi-circular arc on a Nyquist plot and a modest phase shift on a Bode plot (Fig. 5A). This is indicative of a simple resistor and capacitor in parallel (average error of 6.6%). Heated IDEs resulted in an unchanging phase so a constant phase element was used to estimate capacitance (average error of 1.9%). Z_{lat} values of dry structures (Fig. 5A, red) and the modeled capacitance (Table 3) were similar, indicating that each variable had a similar geometry.

The soak response of Z_{lat} was measured in PBS 1X at 37°C over 60 days (Fig. 5A). Within one hour, all variables showed a decline in impedance in at least the low frequency spectrum. For frequencies greater than 10 kHz, the heated PPX-X cohort resulted in little impedance change whereas all other variables fell by one-third of the dry value or more. The unheated parylene-C (CNTL) and unheated PPX-X cohorts fell most dramatically in the first hour. Heating the control and PPX-X devices had an immediate and long-term beneficial effect over the entire spectrum (1–100,000 Hz). The dynamic nature of the unheated PPX-X devices was evident in the breakpoint frequency (45° phase). The breakpoint frequency shifted toward low frequencies as time progressed while impedance increased. This pattern is the reverse of a typical organic coating on metal [24].

A direct contrast of each cohort is shown at 1 hour and day 60 and includes the standard error for each (Fig. 6). The highest impedance was found in the heated PPX-X cohort (N=5) after the 60 day soak test. However, the heated parylene-C cohort (N=3) initially had higher impedance below 10 Hz. Another consistent trend is a higher impedance at higher frequencies of PPX-X devices relative to controls. Even the unheated PPX-X devices, despite the rapid decline at 1 Hz, had an order of magnitude advantage over the unheated control between 10–100 kHz. The frequency-dependent contrast between materials and the dynamic nature of the unheated PPX-X provide important clues about the physical model and failure mechanism.

A small sample of devices were individually tested in PBS 1X at room temperature to measure the immediate temporal response. The decline in impedance could be tracked on the scale of minutes (Fig. 7) which explained the difference between dry samples and the 1-hour time point. As before, the decline in impedance magnitude is greater at low frequencies.

3.2 Transverse impedance

Transverse impedance measured the resistive and capacitive nature of current through the parylene coatings and saline to a large counter electrode. Z_{trans} is plotted below Z_{lat} with the same scale to allow for a contrast of these two measurements (Fig. 5B). The temporal changes were minute relative to Z_{lat} . These results show consistent, high impedance over time for each variable. Phase was also consistent and moderately capacitive for all variables. Unheated PPX-X initially had low impedance below 10 Hz but this rebounded to normal levels by day 5. It has been reported that a small defective area will produce a large decrease in impedance magnitude, i.e., defect area has a non-linear affect on impedance [31]. Therefore, transverse impedance results indicated that parylene formed a consistent coating with few or no defects. Z_{trans} , unlike Z_{lat} , showed no clear differentiation between variables.

3.4 Adhesion force testing

Two separate adhesion tests were performed. First we tested parylene-on-metal and then parylene-on-parylene (Fig. 4). Adhesion force was quantified by using a load cell in series with a programmable piezoelectric motor (Fig. S2). The parylene-on-metal test included a stack of parylene deposited on chromium. Chromium, a commonly used adhesion layer, was also used as the metal adhesion layer in the interdigitated electrode. This test structure effectively measured the adhesion force of the weakest layer—either a parylene-parylene interface or a parylene-metal interface. Results are shown in Table 1 (N=5 for each cohort). All dry samples performed well. Samples were heated as before (3 hours at 140°C without oxygen purging) so increased brittleness was evident when the adhesion force was high. A significant difference became evident after soaking for 30 minutes in 1X PBS at 37°C. Soaked parylene-C samples could not be measured because the parylene-C stack separated from the chromium layer during handling. The wet PPX-X layers had improved adhesion, 2.4 g/mm when unheated and 14.9 g/mm after heating. Also, the separation at the Cr/PPX-CHO interface only occurred in one of these samples. Optical images (Fig. S3) and a profilometer were used to determine the plane of separation.

The second adhesion test was designed to isolate and measure the parylene-on-parylene interfaces. This test also differed from the first adhesion test in that the angle of separation was 180° and was exposed to hydrofluoric acid during processing. Wet adhesion strength was best for the heated parylene-C interface (Table 2). As before, brittleness of the sample increased presumably due to oxidation from the heat treatment. We would expect the adhesion force to be slightly underestimated when cohesive failure occurred. Only heated parylene-C samples had a high, consistent adhesion strength. The heated PPX-X, had low adhesion strength but was stable whether dry or wet (0.3 g/mm). Determining the plane of separation was not possible for the parylene-on-parylene samples and therefore not reported.

3.5 Wet Etch Testing

Two wet etching methods of buried metal were performed during the normal course of fabrication, which provided a useful technique to compare the wettability at the polymer-metal interface. Following an 8 sec chromium wet etch (ceric and acetic acid in an aqueous solution) and 2 minute rinse, exposed metal at the bond pad region was imaged (Fig. S4A). PPX-X interface had a chromium undercut of 9 μm, whereas the parylene-C interface was undercut by 40 μm indicating either greater wettability or poor wet adhesion.

The second wet etch test used DI:HF:H₂O₂ 3:3:1 to undercut the titanium sacrificial layer used in the polymer-on-polymer test structure. Unheated parylene-C and unheated PPX-X structures were removed from etchant then rinsed for 10 minutes in DI before imaging. The PPX-X and titanium interface resulted in an undercut of ~0.4 mm after 60 minutes. Parylene-C structures were undercut >1.5 mm after 10 minutes (Fig. S4B). Similar to the chromium results, the parylene-C interface had either greater wettability or poor wet adhesion to titanium.

3.6 Affect of IDE Geometry

An alternative interdigitated electrode geometry was also tested that had a metal width of 3 μm and a gap of 3 μm . Z_{lat} and Z_{trans} soak test results are included in supplementary material (Fig. S5). Given that there was a difference in geometry, fewer devices tested, and some anomalies in the Z_{lat} soak test results, we could not average these results with the original geometry. Dry impedance measurements of the two IDE geometries were fit to simple equivalent circuits to extract the capacitance values (Table 3). The 3/3 μm metal/gap width had 14% greater capacitance than the 1.5/4.5 μm metal/gap. After soaking, Z_{trans} for the 3 μm gap devices also suggested a robust, viable coating and with little differentiation between variables. Z_{lat} had similar trends as seen in the devices with the 4.5- μm gap, such as improved high frequency performance for the PPX-X devices. Unheated PPX-X devices also showed a similar “rebound” effect as before. The most noticeable drop in impedance was the heated parylene-C IDEs relative to the 4.5 μm geometry. The parylene-C 3- μm gap IDEs had an average 1 kHz impedance of 36 k Ω versus 328 k Ω , which cannot be explained by geometry alone (Table S1). All 3- μm gap IDEs had a lower average impedance relative to the 4.5- μm gap. A suggested explanation for this is discussed below.

4. Discussion

Heat treatment of either parylene-C or PPX-X devices had a beneficial and long-term effect. The mechanism by which heat treatment (3 hrs, 140°C) improved the insulation performance of parylene-C was not directly tested but the evidence suggests a polymer-polymer and not a polymer-metal interaction. According to Table 2, heat treatment directly improved the interfacial parylene-C adhesion. Conversely the adhesion tests of parylene-C on metal showed no wet adhesion with heating (Table 1) so a polymer-metal interaction is highly unlikely. Others have shown that heat treatment and pressure improves parylene-parylene bonding, and suggested the cause was polymer chain entanglement [18]. Heating may also quench hydrophilic free radicals on cleaved chain ends left over from the oxygen plasma cleaning step.

As for the heat treated PPX-X, previous research on the complementary layers of PPX-CH₂NH₂ and PPX-CHO showed that 140°C for 3 hrs created an imine bond. This reaction likely occurred here as well, but given that the processing conditions (exposure to highly acidic and basic solutions) may interfere we cannot be certain. In addition to the imine bond at the polymer-polymer interface, the PPX-X may be reacting with the chromium or native chromium oxide to form a metal-oxygen-polymer complex. For example, metal deposited onto oxygen-treated polystyrene surfaces formed a metal-oxygen-polymer complex as seen in published XPS data [32] and correlated to improved adhesion [33]. Researchers have also shown that a polymer deposited onto chromium, then heated, improved adhesion strength [34]. The chemical mechanism was suggested to be an electron transfer from the Cr to hydrophilic groups, resulting in the formation of a charge transfer complex. It could also be the interdiffusion of the chromium oxide and polymer layers. Our adhesion test results (Table 1) showed moderate dry and wet metal adhesion after heating of PPX-X, which is consistent with this mechanism but that did not occur with parylene-C test structures. The high frequency response of PPX-X also supports the theory that improved metal adhesion has occurred, otherwise metal delamination would have increased the capacitance and reduced the high

frequency impedance modulus (Fig. 5A). Finally, we see from the wet metal etch experiments (Fig. S4), the polymer-metal interface has reduced susceptibility to hydrolysis. While these data lack direct chemical mechanisms, there was a clear indication of having an improved PPX-X-chromium interface relative to parylene-C and chromium.

Unheated PPX-X devices showed a surprising reverse delamination response while soaking at 37°C. This cohort shared the same test chamber with all other variables and an antibacterial (NaN_3) was added to the 1X PBS, so these results could not have been a contamination issue. The breakpoint frequency decreased and magnitude increased in time. Breakpoint frequency and magnitude are used in organic-metal coating studies to track the temporal response of debonding or delamination [11,24]. Since the trend is in reverse for PPX-X, we interpret this as a bonding mechanism. Furthermore, PPX-CHO and PPX- CH_2NH_2 bonding alone (formation of an imine bond) would not account for a robust, high frequency impedance. It can be suggested that the cause of the increasing impedance is due in part by an interaction at the polymer-metal interface. Analytical chemistry techniques should be used in future studies to prove this hypothesis and discover the exact nature of this reaction.

Regarding the time course of these results, the rapid rate of lateral impedance decline was not initially expected. However, this response agrees with observations made by others [11]. Yasuda et al. found that water penetrates parylene-C at a rate of 15 microns/minute. This report also notes that water saturation in a thin film will occur in the first day and salt intrusion occurs on a slower time scale of days. Therefore, the saturation we see within the first day is not unreasonable and implies that, particularly for unheated devices, hydrolysis is the primary cause of delamination.

The results for PPX-X adhesion in Table 2 are not entirely consistent with those seen in Table 1. The differences in testing were the angle of separation and the amount of chemical exposure. The parylene-on-parylene test structures were processed similar to the interdigitated electrodes, which included exposure to diluted hydrofluoric acid. This strong acid may affect the aminomethyl or the aldehyde functional groups and therefore may prevent or mitigate the imine bond from forming after heating. Further investigation is needed to identify any process interactions.

Two IDE geometries were also presented. Z_{lat} was considerably lower for the heated CNTL group in the 3- μm gap geometry compared to the 4.5- μm gap. All 3- μm gap variables had a lower impedance, although this drop in impedance was most pronounced for parylene-C. What can account for this difference? Since Z_{trans} was normal for the 3- μm gap geometry, and the dry value of Z_{lat} was normal, we rule out processing defects as a cause. We do not believe the Z_{lat} difference can be accounted for by the small sample size either, especially for the heated CNTL group ($N=5$). We believe the ultra-flexible structures (5- μm total thickness) revealed a mechanical design limitation (not a chemical one) by creating considerable stress during handling. The smaller gap increased the likelihood of micro-delamination, i.e. polymer-polymer separation, because of increased local stress between metal tracks. Small regions of micro-delamination could then account for this difference. The flexible 5- μm parylene structures resulted in almost 50% loss due to open-circuit failure. These two issues, an inconsistent Z_{lat} in the narrowly spaced design and frequent open circuits, highlight the fragility of large 5- μm parylene structures. Several improvements could be made in future applications: (1) thinner metal structures will reduce local stress in the parylene, and (2) a thicker substrate will increase mechanical strength.

In a multi-channel bioMEMS device, a large decline of the trace-to-trace impedance, Z_{lat} , will cause an increase in crosstalk noise or, in the worst case, create an electrical short. Susceptibility to crosstalk can be mitigated by proper design rules. One may increase the gap between traces,

add a ground plane (if possible), or increase capacitance to the externally grounded extracellular space. Capacitive and crosstalk theory of interconnects allows us to model a variety of configurations [35] and thereby reduce susceptibility. However, those techniques affect our design space and do not address the failure mechanism. Ideally we can mitigate the decline of Z_{lat} by choosing materials and surface chemistry that minimize delamination at the interfacial boundaries (Fig. 1B). We expect heat-treated parylene-C or PPX-X devices will work for 60 days or more *in vivo* if the proper design rules are chosen. We suggest that when designing a polymer-based electrode, use a wider gap than trace width, minimize mechanical strain on the device, and design in a safety factor for the lateral and transverse impedance (Z_{lat} and Z_{trans}) of the interconnect.

5. Conclusions

We utilized an interdigitated electrode and impedance spectroscopy to investigate sensitive interfacial changes of parylene-C and reactive parylene nanofilms. Reactive parylene and heated parylene-C films used here show dramatic improvement in impedance over a broad frequency range. Furthermore, the reactive parylene nanofilms (PPX-CH₂NH₂ and PPX-CHO) showed 3–10X improvement between 100–100,000 Hz relative to the heated parylene-C. The advantage of the reactive parylene, we suggest, is derived from improving the wet metal adhesion and covalent bonds at the aldehyde-aminomethyl interface. Finally, the concept of a hydrophobic, biocompatible barrier layer (parylene-C) in combination with a reactive interfacial layer (e.g. PPX-X) provides a useful strategy for researchers when seeking to design more robust non-hermetic implants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Challenge of using microfabricated implantable electronics. (A) Cross-section of a coating over two free standing metal wires. Lateral and transverse impedance in this example are predominantly sensitive to the bulk properties, such as $\epsilon_{\text{polymer}}$. (B) A microfabricated polymer-metal-polymer structure. Z_{lat} will show far greater sensitivity to poor adhesion at the polymer-polymer or polymer-metal interface than Z_{trans} .

Fig. 2. (A1-A4) Major microfabrication steps of a parylene interdigitated electrode or IDE with reactive parylene (PPX-X) nanofilms. (A4) Released crosssection of final device. The PPX-X layers were omitted in control devices (not shown). (B) Schematic of reaction using complementary PPX-CHO and PPX-CH₂NH₂ layers. $\Delta T = 140^\circ\text{C}$ for 3 hrs. (C) Micrograph of the bottom half of an IDE. Scale = 200 μm . (D) High magnification of IDE. Trace width = 1.5 μm , space = 4.5 μm . Scale = 50 μm . Region beyond device in panels C, D cropped for contrast.

Fig. 3.

Soak test setup. Cross-section through a glass jar containing up to eight IDEs for long-term EIS measurements. (A) Lateral impedance configuration. Z_{lat} was the impedance of the interdigitated electrode. (B) Transverse impedance configuration. Z_{trans} was the impedance between one-half of the IDE and a large counter electrode in solution. Both Z_{lat} and Z_{trans} used a two electrode configuration by connecting the working electrode to sense and counter to the reference input.

Fig. 4.

Two peel-test structures used to evaluate adhesion force. (A) Parylene-on-metal structure with a photoresist sacrificial layer (not shown) and peeled at 90 degrees. (B) Parylene-on-parylene structure with a titanium sacrificial layer (not shown) and peeled at 180 degrees. Labeled dimensions are thickness $\times$ width $\times$ length. Control pull-test structures substituted parylene-C in place of PPX-amine and PPX-aldehyde.

Fig 5.

Bode plots displaying the temporal response to soaking in 1X PBS at 37°C. (A) Lateral impedance, Z_{lat} , and (B) transverse impedance, Z_{trans} . Variables from left to right are CNTL unheated, CNTL heated, PPX-X unheated, and PPX-X heated. Z_{lat} increased over time for unheated PPX-X although it never completely rebounded to the level of heated PPX-X.

Fig 6.
Single time point Bode plots of Z_{lat} at 1 hour and day 60. The shaded area around each variable represents standard error.

Fig 7.
 Example Z_{lat} impedance in first 20 minutes. (A) 10 Hz and (B) 1 kHz response of lateral impedance versus time while soaking at 22°C. First data point was the dry impedance magnitude.

Table 1
Adhesion force of parylene stack on chromium (90° separation, N=5).

	Dry Force, g/mm	Separation ^c	Wet ^d Force, g/mm	Separation ^c
Parylene-C Unheated	24.1 ± 16.0	cohesive	0	Cr/ParC
Parylene-C Heated	>39.0 ± 9.1 ^b	cohesive	0	Cr/ParC
PPX-X Unheated	33.6 ± 9.0	cohesive	2.4 ± 1.8	CH ₃ NH ₂ /ParC
PPX-X Heated	>43.8 ± 8.8 ^b	cohesive	14.9 ± 13.9	CH ₃ NH ₂ /ParC or Cr/CHO

^aWet adhesion protocol: soak structure in 1X PBS for 30 min at 37°C.
^bTearing limited the adhesion force.
^cImages available in supplemental material, Fig. S3.

Table 2
Adhesion force of parylene on parylene (180° separation).

	Dry Force, g/mm	N	Wet ^d Force, g/mm	N
Parylene-C Unheated	17.1 ± 0.9	4	1.22 ± 2.3	4
Parylene-C Heated	>8.8 ± 8.7 ^b	3	> 10.5 ± 2.4 ^b	3
PPX-X Unheated	0.14 ± 0.01	4	0.16 ± 0.05	3
PPX-X Heated	0.3 ± 0.07	5	0.3 ± 0.02	3

^aWet adhesion protocol: soak structure in 1X PBS for 30 min at 37°C.

^bTearing limited the adhesion force.

Table 3

Dry Capacitance and Geometry

	1.5/4.5 μm trace/gap Dry Capacitance, pF N = 14	3/3 μm trace/gap Dry Capacitance, pF N = 12
No Heat Treatment ^a	22.5 $\pm$ 6.1	25.4 $\pm$ 1.5
Heat Treatment ^b	21.0 $\pm$ 4.6	24.0 $\pm$ 2.3
Average Capacitance	21.6 $\pm$ 5.4	24.6 $\pm$ 2.0

^a Impedance fit to a parallel resistor and capacitor. Average error = 6.6%.

^b Impedance fit to a constant phase element. Average error = 1.9%.