NON-HERMETIC PACKAGING FOR FLEXIBLE MEDICAL IMPLANTS BASED ON MULTI-STACK PARYLENE C/PDMS BILAYER THIN FILMS

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ABSTRACT

Next generation flexible hybrid electronics (FHE) devices for implant applications require highly protective, mechanically compliant, wireless-compatible coatings for packaging. Such demanding requirements are not likely to be met by a single material. To address this issue, a multilayer, all-polymer packaging technology specifically for use in chronic implantation applications was designed. Based on parylene-C/PDMS bilayer films, the encapsulation approach was developed to package flexible implantable systems that incorporate the complex topographies associated with on-board electronics, interconnects and antennas. The multilayer packaging approach was initially evaluated using microfabricated planar interdigitated electrodes and then extended to 3D devices consisting of flexible polyimide printed circuit boards with on-board wireless transmission circuitry. Accelerated lifetime testing indicates that the estimated lifetime increases with increasing bilayer stacking number. We found that a triple bilayer stack with an overall thickness of ~225 μm has an estimated lifetime of over 3.5 years at physiological conditions.

KEYWORDS

Non-hermetic packaging, flexible medical implants, PDMS, parylene-C

INTRODUCTION

Advancements in MEMS for implanted biomedical systems has stimulated the development of high-impact medical technologies with some noteworthy examples being cardiac pacemakers [1] blood pressure monitors [2], retinal prostheses [3], and glucose monitors [4]. Recent developments in flexible hybrid electronics (FHE) is enabling a new generation of highly functional implantable devices for a diverse set of applications that leverage the mechanical flexibility and small form factor associated with FHE to produce highly functional electronic circuits that can conform to the irregular topographies associated with deployment. Next generation FHE devices for implant applications require highly protective, mechanically compliant and wireless-compatible coatings for packaging. Such demanding requirements are not likely to be met by a single material.

A variety of flexible polymeric materials have been identified for encapsulation of implantable systems based on their excellent barrier properties and biocompatibility. The list of candidate materials includes polyimide, parylene, liquid crystal polymer (LCP), and polydimethylsiloxane (PDMS). These materials are less protective than metals and ceramics and thus have not been widely adopted for long-term implant applications. However, recent studies have shown promising results regarding their potential for long-term encapsulation, in particular for devices fabricated on polymeric substrates. Parylene/metal/parylene multilayer coatings have been developed for use in flexible retinal implants, exhibiting longer lifetimes than a simple silicone-coated parylene layer [5]. Unfortunately, the metallic interlayer in these coatings challenges the incorporation of wireless components. For implantable microsystems with wireless powering or transmission functions, reliable packaging approaches based on insulating materials is desired, with polymers being particularly attractive for mechanically flexible devices.

In this paper, we describe the development of a multi-layer, non-hermetic packaging technology based on a bilayer structure consisting of PDMS and parylene-C. The stacked, bilayer structure capitalizes on the fact that failure-inducing defects in a single layer are likely to be terminated at a material interface [6]. Both PDMS and parylene-C are widely used in biomedical microdevices and can be processed into thin film bilayers on both planar substrates and those with complex 3D structures. The bilayer structure leverages the outstanding moisture barrier characteristics of parylene-C with the favorable mechanical and biocompatible properties offered by PDMS. The bilayer structure leverages the favorable attributes of these two materials while simultaneously compensating for their weaknesses. The bilayer structure accommodates for the poor moisture barrier characteristics of PDMS and the poor mechanical properties of thick parylene-C by capitalizing on the favorable properties of the other material. The multi-stack, bilayer architecture yields a non-hermetic encapsulant that is both highly protective of moisture intrusion and mechanically flexible.

PACKAGING PROCESS

The multilayer packaging approach involves cleaning and pretreatment of substrate surfaces followed by sequential deposition of PDMS and parylene-C films until the desired encapsulation thickness is achieved.

Surface Cleaning

The surface cleaning step involved sequential immersion of the substrate in beakers containing acetone, IPA, and DI water for multiple cycles (5 minutes per cycle). Each beaker was placed in an ultrasonic cleaner with the bath temperature set at ~70°C. To minimize the accumulation of particulates on substrate surfaces during and after substrate cleaning, the cleaning and packaging steps were performed in a Class 100 clean room.

Pretreatment of Substrate Surfaces

Although parylene-C has better barrier properties than PDMS, it generally exhibits poor adhesion to most substrate materials including metals and polymers. Adhesion of parylene can be improved by increasing the contact area to the substrate by roughening its surface. Parylene adheres well to PDMS because the enhanced surface roughness due to native defects on the PDMS surface can be filled by vapor-deposited parylene. Therefore, the excellent barrier properties of parylene can be fully utilized while addressing the issues associated with poor adhesion. In order to reduce the possibility of delamination between PDMS and parylene-C, MED-160 Silicone primer (NuSil Technology) was used as an adhesion promoter prior to PDMS deposition. MED-160 is known to improve the adhesion of silicones to various substrates including metals, ceramics, plastics and other silicone-based materials. It is also a medical grade material which makes it potentially well-suited for devices designed for use in clinical applications [7]. It has been shown that by using MED-160 as the adhesion promoter, the moisture undercut rate between PDMS and

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parylene was reduced from 22.3 µm/day to 3.2 µm/day [8].

For the proposed packaging approach, MED-160 was applied to the substrate by dip-coating prior to the deposition of each PDMS layer. After substrate cleaning, MED-160 was applied by dip coating (L2006A1-US, Ossila) using a dip speed of 5mm/s, a withdrawal speed of 5mm/s and a dwell time of 10s. Excess primer was then removed by gentle wiping. Finally, the device was devolatilized for 2 hours at ambient temperature and humidity.

Multi-Stack Packaging

The PDMS coating process involved the following procedure. First, Parts A and B of MED-6600 were mixed at a weight ratio of 1:1 in a clean beaker. The mixture was then thoroughly stirred using a stainless steel rod to achieve a homogeneous blend. The mixture was then degassed for 3 minutes in a vacuum desiccator to remove air bubbles. The degassed PDMS was then deposited on the MED-160 coated substrate by dip coating using a dip speed of 5mm/s, a withdrawal speed of 5mm/s, and a dwell time of 60s. After the device was pulled from the PDMS mixture, it was suspended for 3 minutes to allow excess PDMS to drip off the substrate. The dip-coated device was then transferred to a fume hood for 30 minutes to evaporate the xylene solvent from the PDMS coating. This step is very important since xylene is both toxic and can inhibit the curing process. After solvent evaporation, the PDMS layer was cured at 65°C for 2 hours in an oven.

Parylene-C coatings were applied using a dedicated parylene deposition system (Model PDS 2010, Specialty Coating Systems, Inc.). The thickness of each parylene-C layer is controlled by the weight of parylene-C monomers used in each deposition process. To deposit a 5µm-thick layer, 9.54g of parylene-C monomer was used. After loading the system, the chamber was pumped down to a base pressure below 15 mTorr, after which the deposition process was initiated. The deposition process took about 2.5 hours. After deposition, the coated devices were removed from the chamber and prepared for PDMS deposition.

A multi-stack, bilayer encapsulant was produced on each substrate by repeating the deposition of MED-6600 and parylene-C films to achieve the desired number of bilayer units. Prior to each dip coating of MED-6600, MED-160 primer was dip-coated and devolatilized to enhance the adhesion between PDMS and parylene-C. Figure 1 shows a schematic of the cross-sectional view of the multi-stack, bilayer encapsulation.

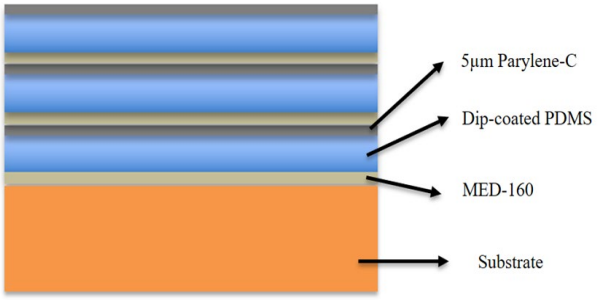

Figure 1: Schematic of the cross-sectional view of the multi-stack encapsulation.

EVALUATION USING INTERDIGITATED ELECTODES

Fabrication of Interdigitated Electrodes

For initial testing, interdigitated electrodes (IDEs) were fabricated on flexible, copper-clad polyimide substrates using a simple one mask process. The mask contained patterns for eight test coupons. Each IDE consisted of forty, 0.2 mm x 9.5 mm interdigitated electrodes and two, 2.5 x 2.5 mm^2 contact pads for hardwire connections to the data acquisition setup. The width of each electrode was 200 µm and the space between each electrode was 400 µm. The peripheral dimensions of each test coupon was 1.5 cm x 5 cm. Fabrication of IDEs test coupons utilized conventional microfabrication techniques including photolithography and wet etching. Single sided copper clad polyimide (LF8530R, DuPont) was selected as the substrate material.

Following IDE fabrication, the test coupons were packaged using the multi-stack, bilayer encapsulation described previously and illustrated schematically in Figure 2. The thicknesses of each PDMS and parylene-C layer was nominally 70 µm and 5 µm, respectively.

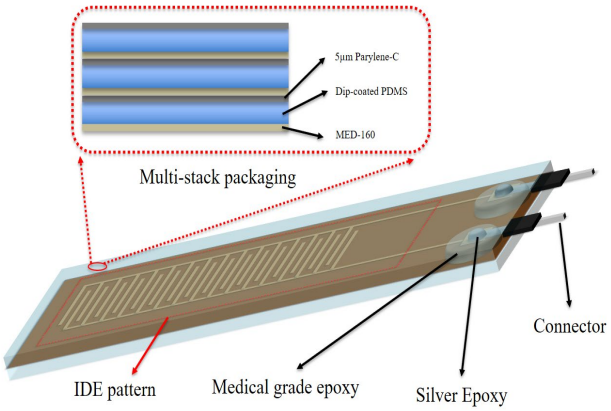

Figure 2: Schematic of a packaged IDE test specimen for accelerated lifetime testing.

Accelerated Lifetime Tests of Packaged IDEs

Standard accelerated lifetime testing was performed in order to estimate the lifetime of packaged devices under simulated physiological conditions in a practical testing period. For packaged implantable devices, accelerated lifetime tests are commonly performed by immersing test devices in heated saline (0.9%) or phosphate-buffered saline (PBS) to best simulate the body fluid environment.

The accelerated lifetime test for the packaged IDE test coupons was conducted by continuously measuring the surface insulation resistance of packaged IDEs under soak testing conditions. Three temperature baths (Isotemp 10L GP Bath, Fisher Scientific) were used to simultaneously test a total of 120 IDE test coupons at either 65°C, 75°C or 85°C. Each bath was filled with water, heated to the designated temperature and covered by an acrylic board to slow the evaporation of the bath water.

Each IDE test coupon was individually inserted in a glass vial filled with 0.9% saline and sealed by acrylic lids that had a small rectangular hole for electrical connections to the IDE. RTV sealant (Dow Corning) was applied on the lids to ensure tight sealing between the lid and glass vial as well as the electrical feedthroughs that penetrated the lid. IDE samples were then connected to a

multiplexer circuit. Multiplexers were controlled by digital signals sent from a programmed Arduino Uno board to enable automatic switching between the samples. One, 8-channel and eight, 16-channel multiplexers comprised the circuit, enabling up to 128 samples to be monitored for surface insulation resistance in sequential manner by rapidly switching between samples. Voltage signals from each sample were collected using an NI-MyDAQ™ data acquisition card and processed by a LabVIEW™ program to record the surface insulation resistance of the packaged samples. To evaluate the relationship between the effectiveness of protection and the packaging thickness, 24 samples with different bilayer stacking units were tested in each temperature bath for a total of 72 test coupons under test. For each temperature bath, test coupons were encapsulated with 1 to 3 bilayer units with 8 coupons comprising each bilayer group. Samples from each of the three bilayer groups was tested at 65°C, 75°C and 85°C. The water level in the baths was monitored to ensure that the vials remained immersed and thus the IDEs were held at a constant temperature. Plots of measured surface insulation resistance versus soak time for representative packaged IDE samples from the triple bilayer group evaluated at the three testing temperatures are shown in Figure 3.

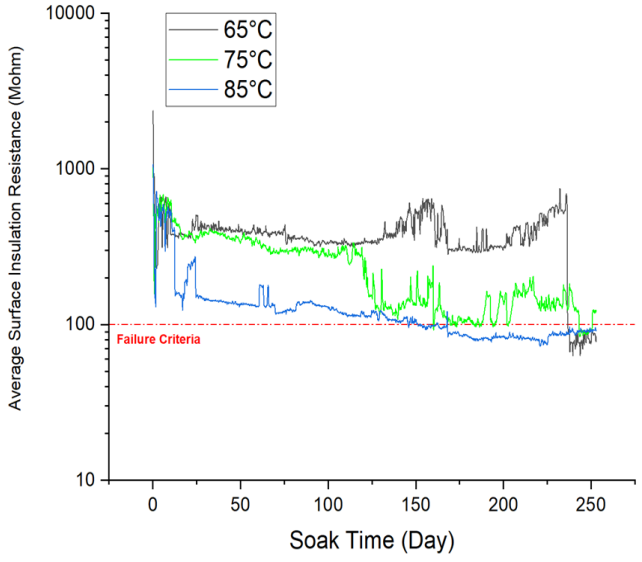

Figure 3: Representative plots of surface insulation resistance versus soak time for a set of three IDEs packaged with a triple bilayer encapsulant and tested in soak baths at 65°C, 75°C and 85°C

According to the Arrhenius equation, $\ln(t_i)$ is proportional to E_a/RT, where t_i is the time to failure at different temperatures, E_a is the activation energy, R is the gas constant and T is temperature [9]. Assuming that the degradation mechanism at 37°C is identical to the degradation mechanism at the three testing temperatures, a linear dependence enables prediction of package lifetime at physiological temperature based on the accelerated lifetime testing results. To this end, the average lifetimes were calculated for sample groups in which all 8 samples failed within the testing period and ln(t) was plotted as a function of 1/T (see Figure 4), where t is the average time to failure for a given bilayer group. For the single, double and triple bilayer groups, the package lifetime was estimated from a linear fit of the data. Based on these data, the estimated lifetimes of IDEs packaged using single, double and triple encapsulants at 37°C in saline are 2.73 years, 2.89 years, and 3.52 years, respectively. As expected, the estimated lifetime increases with increasing bilayer stacking number.

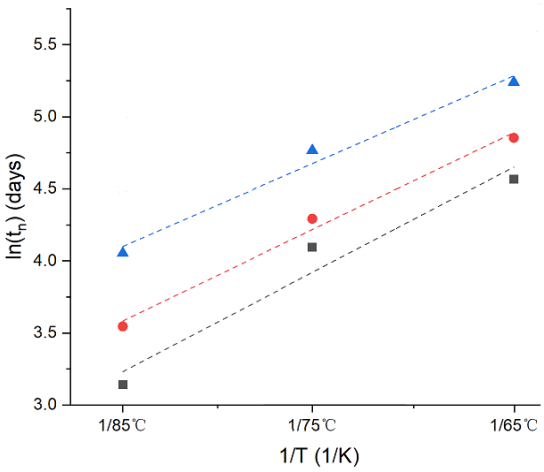

Figure 4: Plots of ln(t) vs 1/T for the single (■), double (●) and triple (▲) bilayer encapsulants.

EVALUATION USING FLEXIBLE WIRELESS DEVICES

Fabrication of Flexible Wireless Devices

Flexible wireless devices consisting of a passive amplifier circuit, programmable microcontroller, LCR circuit and associated peripherals were assembled on multilayer polyimide printed circuit boards manufactured by a commercial vendor (PCBWay). Assembly of the electronic components on these boards was performed manually. First, the flexible board was affixed to a glass slide using double-sided tape. Solder paste was then applied to contact pads on the board using a stainless steel stencil. The electronic components were then placed in their designated positions, followed by reflow soldering using a reflow oven. After soldering, the device was inspected under a microscope to ensure all electronics were soldered properly.

After an initial functionality test to verify device viability, medical grade epoxy was dispensed on the electronic components using a pressure-controlled micro dispensing system. The epoxy was then cured at 65°C in an oven for 1 hour. Medical grade epoxy offers additional reliability to the packaging in multiple ways. The epoxy serves to mechanically protect the solder joints which are likely to break when the device is bent during implantation and deployment. The epoxy does not add excessive rigidity to the device since it only covers the rigid electronics and their solder joints. Additionally, medical grade epoxy is an excellent barrier material which provides added protection from damage by moisture that may eventually penetrate through the polymer bilayers. The epoxy can also inhibit leaching of hazardous chemicals from the solder joints and electronics. These devices were packaged using a 7-bilayer encapsulant. Figure 5 shows photographs of a representative devices before and after the encapsulation process.

Accelerated Lifetime Tests of Packaged Flexible Wireless Devices

Three devices were assembled and packaged for accelerated lifetime tests. The packaging layers have an overall thickness of ~525 µm, which is much thinner than some of the discrete electronic components that comprise the device. These devices were placed in individual glass vessels and soak tested at either 65°C, 75°C or 85°C

in 0.9% PBS using the same test setup employed in the IDE study. On a daily basis, these devices were removed from the heated water baths for a short period to evaluate electrical functionality by connecting each device to a 2.5V power supply through a wired connection and collecting data using both the wired connection and the wireless circuitry. The microcontroller on the device was programmed to transmit wireless data for a period of 60 seconds after power up and successful transmission was indicated by a green indicator light on the wireless radio which continuously flashed during data successful transmission. Simultaneously, currents through the wired connection with the device in both working and sleeping modes were also measured.

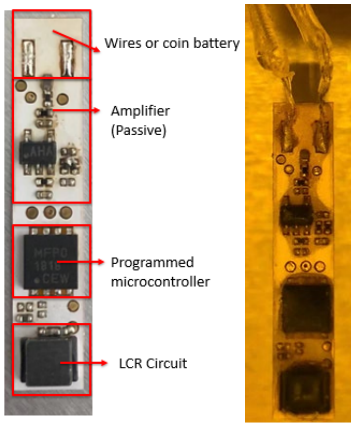

Figure 5: Photographs of an electronic device used to evaluate the multi-stack, bilayer package on 3D topographies: (left) before packaging and (right) after packaging.

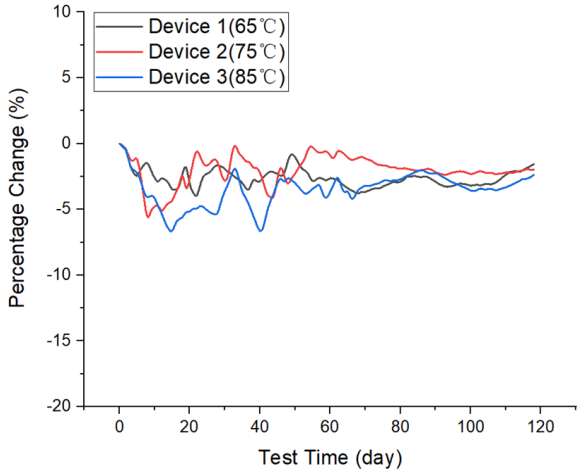

Figure 6: Percentage change in working mode supply current versus soak test time for the three externally powered devices tested at 65℃, 75℃ and 85℃.

The percentage change of average current in the working mode versus soak time for the three devices is presented in Figure 6. The maximum change of average working current was -4.21%, -6.04% and -6.83% for the devices tested at 65℃, 75℃ and 85℃, respectively. At Day 119, the percentage differences decreased to -1.55%, -1.94% and -2.83% for devices tested at 65℃, 75℃ and 85℃. These observed changes were not large enough to affect the normal operation of the microcontrollers and wireless functions. In fact, all three devices maintained wireless functionality over the entire testing period. Because these devices did not exhibit failure at the end of the testing period, a proper estimate of device lifetime could not be made. However, applying the 10°C rule to the data collected from sample tested at 85°C suggests that the equivalent lifetime could be as high as ~9 years at physiological temperature.

CONCLUSION

A non-hermetic packaging approach based on a parylene-C/PDMS bilayers for flexible implantable biomedical systems is described. Accelerated lifetime testing of IDE samples packaged using 3 units of the bilayer structure exhibited an estimated lifetime of over 3.5 years under physiological conditions using an all-polymer encapsulant that is only ~ 225 µm in overall thickness. Current and wireless functionality testing of packaged active devices suggest that the combination of medical-grade epoxy and the proposed multi-stack, bilayer package is able to provide sufficient protection for the electronic components of flexible implants designed for chronic use. For the flexible circuit packaging, accelerated lifetime tests on packaged devices reveal an acceptable level of small scale current fluctuations (less than 6%) during soak testing without any catastrophic failures of the programmed microcontroller.

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