Micromachining of Parylene C for bioMEMS

Brian J. Kim and Ellis Meng*

ABSTRACT: Recent advances in the micromachining of poly(p-xylylenes), commercially known as Parylenes, have enabled the development of novel structures and devices for microelectromechanical systems (MEMS). In particular, Parylene C (poly[chloro-p-xylylene]) has been explored extensively for biomedical applications of MEMS given its compatibility with micromachining processes, proven biocompatibility, and many advantageous properties including its chemical inertness, optical transparency, flexibility, and mechanical strength. Here we present a review of often used and recently developed micromachining process for Parylene C, as well as a high-level overview of state-of-the-art Parylene hybrid and free film devices for biomedical MEMS (bioMEMS) applications, including a discussion on its challenges and potential as a MEMS material. Copyright © 2015 John Wiley & Sons, Ltd.

Keywords: poly(p-xylylene); Parylene C; micromachining; deposition; etching; MEMS; bioMEMS

INTRODUCTION

Parylene, the trade name for poly(p-xylylene) offered by Specialty Coating Systems (SCS, Indianapolis, IL), is a semicrystalline, thermoplastic polymer that was commercialized by the Union Carbide Corporation in 1965. Following the discovery of an optimized chemical vapor deposition (CVD) process to produce the polymer with high yield, Parylene was employed as an encapsulation layer for electronics because of its chemical inertness, high dielectric strength, and conformal, pin-hole free coating at room temperature. With the development of micromachining techniques of Parylene, specifically selective Parylene etching processes, the material has gained popularity as a structural material for microelectromechanical systems (MEMS) in a broad variety of applications, including biomedical devices and coatings. A review of Parylene as a material for biomedical MEMS (bioMEMS) devices is presented, beginning with an introduction to the polymer, its variants, and noteworthy material properties. A discussion of major and recently introduced micromachining processes developed for a specific Parylene variant typically selected for use in biomedical applications, namely, Parylene C, is then reviewed in depth. Lastly, examples of state-of-the-art Parylene bioMEMS devices that highlight the use of Parylene as a structural and free-film material are examined, concluding in a discussion of the limitations and challenges of micromachining Parylene C and the use of the material for biomedical applications.

INTRODUCTION TO PARYLENE

Poly(p-xylylene), initially described as a "snake-skin" like polymer, was first synthesized by Michael Mojzesz Szwarc in 1947 in a study of the by-products of thermal decomposition of p-xylene.[1] However, this process suffered from poor yield as well as secondary gaseous byproducts, and thus was difficult to scale. Improvements to the deposition process were made through the work of William Gorham at Union Carbide,[2] who developed a stable dimer precursor and optimized a CVD polymerization process that facilitated a commercially viable form of the material.

This Gorham process for poly(p-xylylene) deposition (Fig. 1), which is carried out under vacuum to increase the mean free path to the substrate to be coated, begins with a granular dimer precursor, di-p-xylylene (or [2.2] paracyclophane). This precursor is vaporized and then pyrolyzed at a temperature above 550°C to cleave the dimer into its reactive radical monomer. Within the deposition chamber (at room temperature), the reactive monomer adsorbs to all exposed surfaces and begins to spontaneously polymerize to form conformal poly(p-xylylene) films. The Gorham process enables the control of deposition parameters (e.g. vaporizer and pyrolysis temperatures, and chamber pressure) and also allows for the full conversion of the dimer into the polymer film without any byproducts. Another advantage of this process is that the substrate is coated at room temperature, allowing compatibility with thermally sensitive materials. For a thorough review of the deposition and polymerization process, as well as a proposed chemical model, the reader is referred to by Fortin et al.[3]

Currently, the commercial market for poly(p-xylylenes) is dominated by two industry leaders, Specialty Coating Systems (SCS; "Parylene" trade name) and Kisco Conformal Coating LLC ("diX" trade name), with each manufacturing their own dimer sources. For both companies, the breakthrough of the Gorham process to efficiently produce poly(p-xylylenes) contributed to the synthesis of other chemical variants of poly(p-xylylenes) with added functional groups on the monomer unit. Although these variants utilize the same Gorham polymerization process (but with different starting dimers), they have different material properties because of the functional groups and are thus used for different applications. There are more than 10 commercially available variants of poly(p-xylylenes) to date (Fig. 2). The most commonly used types as reported in the research literature are Parylene N (the same

* Correspondence to: Ellis Meng, Department of Biomedical Engineering, University of Southern California, 1042 Downey Way, DRB-140, Los Angeles, CA 90089-1111, USA.
E-mail: ellis.meng@usc.edu

B. J. Kim, E. Meng
Department of Biomedical Engineering, University of Southern California, 1042 Downey Way, DRB-140, Los Angeles, CA, 90089-1111, USA
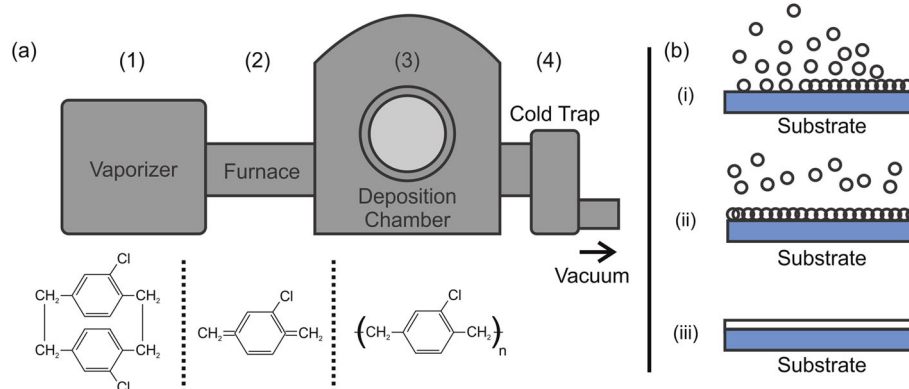
Figure 1. (a) A schematic overview of the Gorham deposition as demonstrated for depositing poly(chloro-p-xylylene). (1) The precursor dimer is evaporated. (2) In the furnace, the dimer is pyrolyzed to cleave the dimer into monomer units. (3) The reactive monomers adsorb to the substrate within the deposition chamber, coating all exposed surfaces with polymer. (4) A cold trap is also used within the setup to trap stray unreacted monomer from entering the vacuum pump. (b) Schematic representation of deposition of Parylene on one side of a substrate within the deposition chamber beginning with (i) adsorption of monomer radical units on the surface of the substrate, and (ii) subsequent polymerization from these radical units to form a (iii) conformal film by the end of the deposition process. This figure is available in colour online at wileyonlinelibrary.com/journal/pat
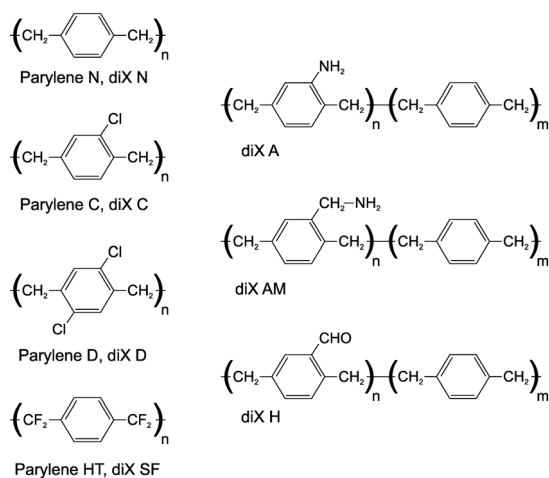

Figure 2. Chemical structure of poly(p-xylylene) variants with both SCS (Parylene) and Kisco (diX) trade names.

poly[p-xylylene] discovered by Szwarc), Parylene C (poly[chloro-p-xylylene]), Parylene D (poly[dichloro-p-xylylene]), and Parylene HT, also named AF-4 (poly[tetrafluoro-p-xylylene]), all from SCS. A brief comparison of the material properties of these four polymers is found in Table 1. In short, Parylene N is primarily used as a dielectric and has been shown to have excellent crevice penetration ability, but has the slowest deposition rate. Parylene C has been the most popular for biological applications because it was the first variant to attain the ISO 10993, USP class VI rating (the highest biocompatibility rating for plastics), and has excellent water and gas barrier properties compared with Parylene N. It is important to note that Parylene N and Parylene HT have also since received the ISO-10993, USP Class VI rating. Parylene D has greater thermal stability but otherwise similar properties to Parylene C and more recently has been replaced in some applications with Parylene HT. Parylene HT is becoming more popular, largely because of its improved properties: lower dielectric constant, higher ultraviolet stability, better crevice penetration, higher thermal stability, and lower moisture absorption. However, the material requires substrate cooling for acceptable deposition rates and yield.[4]

There are other, more reactive p-xylylenes, with functional groups that make them ideal for specific applications, such as Parylene A (diX A and diX AM from Kisco)[5,6] that contain amine groups for better adhesion performance with biological specimens. Others have synthesized polymer films with other active functional groups such as a carbonyl,[7] aldehyde,[8] ester,[9] anhydride,[9] alkyne,[10,11] alcohol,[12] and photoactivable pheylacetyl[13] that can provide improved material properties and under additional chemical reactions, further chemically modify the polymer surface. One of note, Parylene E consists of ~69% diethylated and ~25% monoethylated p-xylylene to form a film that is soluble within common solvents such as methylene chloride, chloroform, and toluene.[14] In addition to its solvent solubility, Parylene E is ideal for optics applications (e.g. waveguides) because of its near isotropic optical properties and little to no loss. Overall, many chemical poly(p-xylylene) variants have been produced for different applications, but the polymer predominantly used for bioMEMS is Parylene C because of its widespread availability and properties, which are discussed in the next session, and thus is the focus of the rest of the review.

Parylene properties

Regardless of the variant, Parylenes have ideal properties for barrier applications as their benzene backbones make them chemically inert, and the conformal, uniform deposition process allows for optimal coverage for encapsulation. Because of these characteristics, in addition to its high dielectric strength, Parylene C first found use as a coating for implantable electronics,[15,16] following early experiments that validated the polymer's biocompatibility.[15] After the introduction to the MEMS community in 1997 as a coating material for fluidic interconnects,[17] Parylene C gained popularity as a MEMS material because of the advantages of its deposition process and compatibility with standard micromachining and photolithographic processes. Its gas phase, pinhole-free polymerization at room temperature and effective gap fill made the coating process compatible with a variety of MEMS materials and structures for applications as a coating (e.g. antistiction coating because of Parylene C's low coefficient of friction) and a structural material. Parylene C has also been shown to deposit with low to no intrinsic stress,

Table 1. Material properties of Parylene N, C, D, and HT (adopted from[182])

Property	Parylene N	Parylene C	Parylene D	Parylene HT
Dielectric strength (V/mil), 1 mil film	7000	5600	5500	5400
Dielectric constant				
60 Hz	2.65	3.15	2.84	2.21
1 kHz	2.65	3.10	2.82	2.20
1 MHz	2.65	2.95	2.80	2.17
Young's modulus (GPa)	2.413	2.758	2.62	2.551
Index of refraction	1.661	1.639	1.669	1.559
Yield strength (MPa)	42.06	55.16	62.05	34.47
Elongation to break (%)	Up to 250	Up to 200	Up to 200	Up to 200
Coefficient of friction				
Static	0.25	0.29	0.33	0.145
Dynamic	0.25	0.29	0.31	0.130
Density (g/cm^3)	1.10-1.12	1.289	1.418	1.32
Melting point (℃)	420	290	380	>500
Thermal conductivity at 25℃ (W/[m·K])	0.126	0.084	—	0.096
Gas Permeability at 25℃, (cc·mm)/(m^2·day·atm)				
N_2	3.0	0.4	1.8	4.8
O_2	15.4	2.8	12.6	23.5
CO_2	84.3	3.0	5.1	95.4
H_2	212.6	43.3	94.5	—
Water absorption (% after 24 hours)	<0.1	<0.1	<0.1	<0.01
Specific heat at 20℃ (cal/g·C)	0.20	0.17	—	1.04

although stresses in the film can increase following processing methods that apply heat and plasma.[18] These stresses, however, can be decreased by limiting the exposure to elevated temperatures during processing,[19] as well as treating the free films at elevated temperatures[20] followed by controlled cooling.[21] In addition, the ability to form smooth films that incur little optical scattering and high transmittance in the visible spectrum makes Parylene C amenable to applications requiring transparency.[22–25] Currently, free film Parylene C devices are increasing in popularity compared with other polymer (e.g. poly-imide and poly[di-methyl] siloxane [PDMS]) devices because of its simpler deposition process, and combination of high flexibility and mechanical strength.

Specifically for bioMEMS, Parylene C has been widely adopted for its proven biocompatibility and chemical and solvent inertness, which are imparted by its chemical structure. As the deposition process does not require any additives (unlike epoxies) and has no harmful by-products, Parylene C has been the standard for the coating of implantable devices as well as a structural MEMS material for biomedical devices. Numerous published studies have tested the biocompatibility of Parylene C both *in vitro*[26] and *in vivo*,[16] and its biostability, low cytotoxicity, and resistance against hydrolytic degradation have been strong arguments for its use as a biomedical material.[27–29]

However, certain properties of Parylene C, arising from its polymeric structure, must be considered when working with the material. First, changes in deposition conditions can significantly alter the material properties described in the preceding texts; there has been work within literature to vary the deposition parameters (vaporizer temperature and chamber pressure), to polymerize Parylene C with different mechanical and chemical properties.[3,30,31] Overall, faster deposition rates were found to increase the surface roughness of Parylene C.[31] Second, photooxidation of Parylene C occurs at $\lambda > 250$ nm, resulting

in film discoloration as well as a degradation of mechanical properties because of chain scission and chemical substitutions.[32–34] This chemical modification, however, was found to predominantly affect the surface of the film (top 25%), with a majority of the reactions occurring in the top 5% of 3 μm thick films.[34]

In addition, Parylene C is thermally sensitive (more-so than the other Parylenes) because of its low glass transition point (T_g) (60–90℃[35]) and undergoes thermal oxidative degradation (i.e. loss of material) when exposed to temperatures greater than 125℃ in an oxygen-rich environment.[36,37] Annealing of Parylene C at these temperatures must carried out in a vacuum environment to prevent degradation; vacuum annealed films exhibited no chemical difference from as-deposited samples.[38] Lastly, although the water and vapor permeability may be lower than other materials, soaking of Parylene C films results in water vapor penetration[39,40] and ion permeation.[41] A similar phenomenon is observed during solvent soaking, as Parylene C swells to a degree largely determined by solvent type, molecular size of the solvent, and thickness of the film.[42] Consideration of these effects is key in the development of fabrication processes as well as choice of sterilization techniques for Parylene C or Parylene C-coated biomedical devices.[43] Further considerations as well as possible counter strategies for these shortcomings will be discussed in the last section.

FABRICATION TECHNIQUES

Of the different Parylenes developed, Parylene C is the most widely used in MEMS with the majority of the applications in bioMEMS. Thus, the remainder of the review focuses specifically on fabrication techniques developed for use with Parylene C. These include discussion on etching/removal techniques, unique

deposition strategies, surface modification processes, and thermal treatment.

Etching processes

Etching techniques for Parylene C (hereon referred to as Parylene) are limited to physical and dry processes largely because of the high solvent inertness of the polymer. There have been reports of the wet etching of Parylene using chloronapthelene or benzoyl benzoate,[44] but only at extreme temperatures (>150°C), which can make this process incompatible with photolithography steps. Dry etching techniques have been found to be the most effective and practical to etch Parylene; for a more detailed review of plasma etching of Parylene, the authors refer the reader to Meng et al.[45] Parylene etching can be accomplished using oxygen-based plasma etching,[45–48] reactive ion beam etching,[49] and reactive ion etching (RIE/deep RIE or DRIE).[45,50,51] For these methods, the etching mechanism is thought to be similar to that of oxygen plasma etching of Parylene N, involving benzene ring opening using reactive oxygen radicals to form volatile carbon dioxide or carbon monoxide products (Fig. 3a).[52,53] For methods that include a physical component in addition to chemical etching (e.g. RIE and DRIE), ion bombardment of the film aids in bond breakage and radical formation to further increase etch rates[54] (Fig. 3b).

Dry etching techniques for Parylene tend to produce an isotropic etch profiles, as RIE methods can achieve aspect ratios of 2:1, while plasma etching is limited to a 1:1 ratio. A switched chemistry etch that involves cycling through (1) deposition of C_4F_8-based Teflon-like polymer as a sidewall passivation layer, (2) etching in SF_6 plasma, and (3) etching in O_2 plasma, similar to DRIE, was found to improve the anisotropy to produce fairly vertical sidewalls.[45] One technique using a DRIE tool and cooling the Parylene to 5°C, achieved fast etch rates (1 μm/min) with aspect ratios of 9:1.[55] Many materials have been explored as protective etch masks for Parylene including photoresists, aluminum, oxides, spin on glass, nitride, and α-silicon,[45,56–58] but photoresist and sputtered aluminum remain the most popular, because of ease of patterning and hard mask qualities, respectively. However, the etch selectivity between photoresist and Parylene is very low (1:1) and may not be optimal when etching thick Parylene layers (>10 μm).[45] Aluminum etch masks are not compatible with DRIE processes, as they can sputter and redeposit during the etch process.[55] It is important to consider these factors during process design.
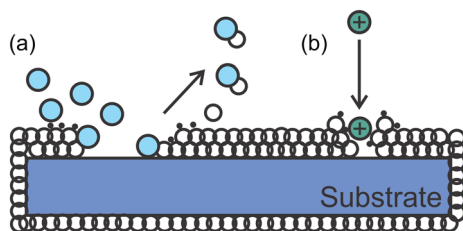

Figure 3. Schematic diagram illustrating the (a) chemical and (b) physical etching mechanisms during the O_2 plasma based dry etching of Parylene. Reactive oxygen radicals react with the carbon atoms of the benzene ring structure to cause ring opening and formation of volatile gaseous products. For etch processes that also include a physical component (e.g. reactive ion etching), ion bombardment causes the formation of reactive radicals on the surface following bond breakage to increase etch rate. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

Another method for Parylene removal includes laser ablation (266 nm)[59–61], one of the first techniques employed for Parylene etching to expose electrode sites. Infrared (800 nm) and UV (248 nm) laser ablation of Parylene films (100 nm thickness) on wafer for direct writing were investigated for precise cell patterning.[62] However, UV laser ablation was found to induce UV-based photooxidation of the Parylene substrate and render the surface unideal for cell patterning applications.[62] Manual removal of Parylene films has also been demonstrated, where a pre-coating of release agents, such as 2% Micro-90 lab cleaning solution (International Products Corporation, Burlington, NJ) on the substrate as well as immersion in water[63–65] aided in the removal of the film without damage.

Deposition processes

As the CVD of Parylene is a relatively simple and tunable process, many variants of the routine coating method have been investigated to achieve novel films and structures. A prominent technique within literature is the deposition of Parylene onto molds to create structures. One method to form a high aspect ratio (HAR, e.g. 20:1) Parylene channel embedded in silicon, used DRIE etching to form a HAR trench, and subsequent Parylene deposition to construct the embedded channel and seal the trenches.[66] A similar process was used to construct HAR Parylene beams to create suspended structures that are capable of large in-plane displacement.[67] The conformal deposition of Parylene onto molds was also manipulated to coat copper mesh or micro-aperture grids to produce micropore membranes by ceasing the deposition of Parylene prior to covering the each cell of the grid.[68]

Other three-dimensional (3D) devices have also been constructed by depositing Parylene onto structural molds (e.g. photoresist, silicon) to form hemispherical, bump electrodes (Fig. 4a),[69] pockets for silicon chips,[70] and 3D micro electrode arrays.[71,72] One work of note utilized a two-photon polymerization process to create 3D nano/microstructures out of photoresist with high resolution (<100 nm) and coated the structures with Parylene to form precise 3D Parylene structures.[73] Superhydrophobic Parylene films (contact angles of ~155°) were also constructed by depositing Parylene onto a silicon mold with micro/nanostructures to attain advantages of a super-hydrophobic surface while maintaining the transparency and flexibility of Parylene.[74] Other works have looked into the use of more inexpensive PDMS molds to develop bond-less, tape-capped Parylene-based microfluidics[75] as well as 3D penetrating microelectrodes.[76]
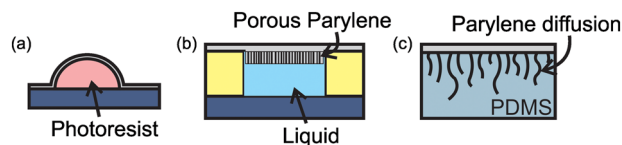

Figure 4. Representative cartoons of examples of Parylene deposition onto different surfaces. (a) Deposition of Parylene onto a hemispherical photoresist structure to form 3D electrodes.[69] (b) Deposition of Parylene onto a liquid substrate to form a porous film on the side in contact with the liquid.[80] (c) Deposition of Parylene onto PDMS substrates with low deposition rates to allow for the diffusion of the polymer into PDMS. The bottom image indicates a reduction of the diffusion of the dye into the channel wall following caulking of the PDMS using Parylene.[82] This figure is available in colour online at wileyonlinelibrary.com/journal/pat

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Beyond molds, Parylene deposition onto different surfaces has also been used to fabricate unique films, such as the Parylene on liquid deposition technique,[77] also known as the solid on liquid deposition process,[78] involving the deposition of Parylene on liquids (Fig. 4b). By depositing Parylene on a low vapor pressure liquid between 1 and 7 Pa (e.g. glycerin and silicone), Parylene encapsulated liquids were formed, which were used for complex optical devices, including microliquid lenses,[23] liquid prisms,[24] and a micro-droplet array for displays.[22] Alternatively, the liquid also served as a sacrificial layer to fabricate microfluidic devices without the need for molds, polymer sacrificial structures, or channel bonding.[79] A closer inspection of the polymer interface between the Parylene and liquid revealed a rough, porous surface, unlike the planar, smooth surface on the other side, the properties of which can vary with the liquid substrate that was coated.[80] These porous surfaces have been utilized to form gas exchange membranes.[80]

Parylene deposition onto other polymers has also been explored to create hybrid soft-devices. For microfluidic technologies, the integration of PDMS and Parylene enabled devices with improved chemical inertness by using Parylene as a barrier coating to reduce the diffusion of analytes into the PDMS microchannel sidewalls. However, a uniform Parylene coating within a long PDMS microchannel is difficult because of Parylene's diffusion-limited deposition process.[81] One group improved this shortcoming by synthesizing Parylene caulked PDMS (pcPDMS), where the deposition rate of Parylene was slowed to allow for the Parylene monomers to diffuse into the bulk PDMS prior to the formation of the microchannel via bonding (Fig. 4c).[82] Removal of excess Parylene on the surface of the PDMS chips using oxygen plasma allowed for bonding of the PDMS parts to form microfluidic channels while maintaining the low permeability of the Parylene coating.[82]

A more in-depth look at the CVD and polymerization of Parylene C reveals that the deposition reaction is under kinetic control. That is, the rate-limiting steps for the reactions are (1) the adsorption of the monomer onto the substrate, (2) surface migration and bulk diffusion of the monomer, and (3) chemical reactions involving the initiation or propagation of the polymer.[3] By devising deposition strategies that interfere with these steps, films with variant properties were synthesized including: a porous Parylene film for use as an ultrafilter that uses evaporating glycerin vapors during the deposition process to hinder polymer growth[83] and the formation of Parylene nanofibers using oblique angle polymerization (OAP), a deposition technique that directs the monomer to the substrate at an angled flux to leverage self-shadowing to create Parylene nanostructures.[84] In another example, von Metzen et al used an aperture to impede the diffusion of monomer units, as a technique for controlled, tapered deposition of Parylene.[85]

Furthermore, processes that inhibit these deposition mechanics can enable the selective deposition of Parylene. In most cases, heat was used to prohibit the deposition of Parylene using heaters fabricated on the substrate,[86,87] as a localized temperature increase (>140°C[87]) can reduce the deposition rate in that region.[88,89] Another technique utilized deposited transition metals (e.g. iron, gold, silver, and platinum) in the form of evaporated thin films, salts, and organometallic complexes to delay the initiation and propagation steps of Parylene polymerization.[90] The mechanism for this form of inhibition relies on deactivation of the radical monomers once they are adsorbed to the metal surface, prohibiting initiation of polymer growth.[90] The

efficacy of this method varies with the choice of transition metal (group 8 transition metals were the most effect at inhibiting polymer growth) and is relevant only for thin film (<1.7 μm) Parylene deposition.[91] For thicker films, Parylene polymerization continues as secondary monomers adsorb on top of the deactivated monomer layer, and conformality is reasserted.[90]

A quick note is mentioned here on the adhesion of Parylene onto different materials. Although Parylene deposition results in strong adhesion for many substrates, this bond strength is not universal; adhesion can be improved through the use of a silane-based adhesion promoter, A-174 ([[gamma-(methacryloyloxy)propyl]trimethoxysilane). A-174 has been found to greatly increase the adhesion of Parylene for silicon devices[92] as well as platinum surfaces.[93] However, the typical immersion-based A-174 treatment process readily dissolves common positive photoresist materials, which must be considered during process design.

Parylene as a masking material

Because of the chemical inertness of Parylene, as well as its simple deposition and patterning methods, Parylene C has also been utilized as a masking material for various etchants. Parylene has been used as an etch mask for common wet etching processes (e.g. hydrofluoric acid, nitric acid, and acetic acid; potassium hydroxide; and tetramethylammonium hydroxide[94]), as well as an etch stop layer for hydrofluoric acid (HF) vapor etching of silicon.[95] Recrystallization of the Parylene by treating the film at high temperatures (350°C) under vacuum[94] and integration of thin film metal layers[95] was shown to improve the quality of the etch mask. One technique devised to fabricate metal nanowires involved a POP (Parylene C on photoresist) masking process, where nanotraces of Parylene were used as an etch mask for metal.[96] In this work, a dual-layer photoresist structure was patterned onto a surface with an undercut in the bottom photoresist layer subsequently filled by CVD deposited Parylene. Removal of the Parylene and photoresist revealed Parylene nanotraces within the undercut region that were masked from the etch process; these nanotraces were then used as etch masks for a metal layer underneath the original structure. Beyond micromachining, Parylene has been used as a removable ("peel-off") and reusable polymer shadow mask to pattern proteins and cells for cell chips.[55,97] For a more thorough review of Parylene for cell patterning and stamping, the reader is referred to Tan et al.[98]

Surface modification

Modification of the surface of Parylene C can result in useful functionalization as well as improvements in the material's performance for specific applications. Plasma treatments of Parylene surfaces have been explored to improve the adhesion of various materials to Parylene. These techniques are advantageous as they modify only the surface properties of the polymer without affecting the bulk. Oxygen plasma and ion beam treatment of Parylene prior to gold deposition was found to increase adhesion properties largely because of the added carbonyl functional groups following the process as well as mechanical interlocking because of increased roughness.[99] Pre-plasma treatment of various polymers prior to Parylene coating have also been shown to improve adhesion. In a study observing in situ plasma treatment (i.e. plasma treatment within the Parylene

deposition chamber) of poly(tetrafluoroethylene), poly(propyl-ene), poly(methylmethacrylate), and glass substrates during Parylene deposition, argon, oxygen, and methane plasma treatment all contributed to a qualitative increase in adhesion; however, the mechanisms for improved adhesion were different for each chemistry.[100] Methane plasma treatment was found to be the most consistent method to increase adhesion,[100] because of the deposition of a hydrophobic surface layer with additional free radical sites during methane plasma treatment. This was also supported by a study involving the deposition of another hydrophobic plasma polymer (trimethylsilane) to increase adhesion of Parylene to metal surfaces.[101] Oxygen plasma treatment of PDMS has also been observed to increase Parylene adhesion up to a four-fold improvement.[102]

Plasma treatment can also be used to change the surface energy of Parylene C, normally hydrophobic (native contact angle = ~80°), to create films that are either more hydrophilic or hydrophobic, depending on the treatment parameters and the gases involved. Oxygen plasma was used to create hydrophilic Parylene surfaces by introducing oxygen-related polar functional groups (e.g. carboxyl and hydroxyl) onto the surface, but the hydrophobic nature of Parylene was found to revert after a week to 40–50% of its initial state.[103] However, compared with PDMS, Parylene has better hydrophilic stability following plasma treatment largely because of differences in T_g; PDMS has a lower T_g than Parylene, which induces polymer chain reorganization back to a normal hydrophobic surface more quickly.[104] In addition, consecutive O_2-SF_6 plasma treatment was found to achieve contact angles of 169.4° to create super-hydrophobic surfaces, through a combination of oxygen plasma induced surface roughening and fluorine-based chemical modification of the surface with SF_6.[105]

For biomedical applications, plasma treatment of Parylene C surfaces was shown to improve cell adhesion, typically poor for untreated Parylene surfaces.[26,106] The oxygen plasma surfaces aid in cellular adhesion because of increased hydrogen bonding between the surface and water molecules of the cellular material. Another method to improve cellular adhesion is to adhere proteins onto as-deposited Parylene films (e.g. horse serum, bovine serum albumin, immunoglobulin G, fibronectin, and Matrigel) by soaking the films within the solution.[26,107] However, pre-treatment of the Parylene film with oxygen plasma in this case has been found to decrease protein adsorption.[26] In cases where protein adhesion is required within Parylene lumen structures, a pre-coating of poly(d-lysine) was found to improve the wettability of the Parylene surface and to wick protein mixtures.[108] Other methods for surface modification of Parylene C for biomedical applications involve UV-induced photoxidation (1 or 2 h of treatments) to create a hydrophilic surface by

producing carboxyl and aldehyde groups.[107] The addition of other functional groups to the polymer surface using Friedel-Crafts acylation to add thiol and poly(N-isopropylacrylamide) (pNIPAM) groups for improved gold film and tissue adhesion respectively[7] has also been demonstrated.

Thermal treatment

Parylene C is a thermoplastic material and is susceptible to thermal treatment during or after fabrication. Post-fabrication thermal annealing of Parylene can increase crystallinity and stiffness[31] and reduce water vapor permeation[39] in the annealed film. Application of temperature and pressure also facilitates Parylene to polymer bonding for unique applications, such as forming microchannel structures. By exposing Parylene-polymer constructs to high temperatures (greater than the glass transition point of Parylene, 60–90°C, but below its melting temperature, 290°C[35]) while applying a bonding pressure, mechanical fusing of Parylene into the second polymer can be achieved and aid in bond formation.[35] Plasma activation of the Parylene C layer to create radical species can further aid in this process. This mechanism can be used to create Parylene to SiO_2 bonds at 280°C with oxygen plasma treatment,[109] as well as Parylene to photoresist (SU-8, AZ 4620) bonds, for temperatures greater than 90°C with oxygen plasma treatment (Fig. 5a).[110] Bonding strength was found to increase with increased bonding temperature.[110] Parylene–Parylene bonding has also been demonstrated at both die[111] and wafer[112–114] levels to construct devices or to achieve an intermediate glue layer for wafer-level bonding.

Other techniques leveraging the thermoplastic property of Parylene includes a hot-embossing process, where a nickel mold was pressed into Parylene films at 150°C to form an imprint with <2.32% dimensional deviation (Fig. 5b).[115] Thermal forming of Parylene free films has also been demonstrated by annealing multi-layer Parylene devices with varying thickness or differing Parylene variants (Parylene C and N layers) to create residual stress differences to form self-curling films.[116–118] Metal molds have also been used to thermally shape Parylene planar films into curved (Fig. 5c)[119,120] and 3D structures.[121]

One technique utilizing the thermal treatment of Parylene is the pyrolysis of the polymer to form conductive films.[122–125] In this process, Parylene is used as a carbon source and is pyrolyzed at 900–1200°C under nitrogen atmosphere to form a conductive thin film for use as an electrode surface. This technique, however, has been observed to produce a 15–20% reduction in thickness following pyrolysis.[122] By leveraging the conformal deposition and patternable properties of Parylene, planar, and 3D carbon electrodes and structures can be constructed by first
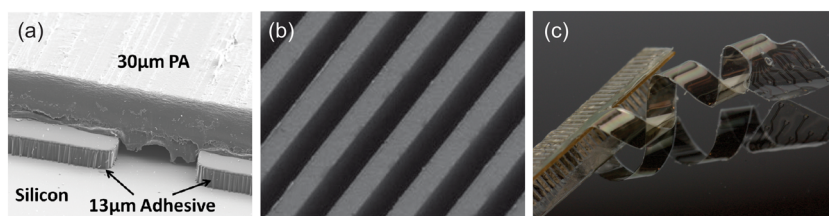

Figure 5. Examples of thermal treatment of Parylene to form novel structures and devices. (a) Bonding of Parylene C (PA) onto silicon using a 13 μm SU-8 adhesive (©2013 IEEE. Reprinted, with permission, from Reference 110). (b) SEM of hot-embossed Parylene surface illustrating the clean ridges formed following the process (© IOP Publishing. Reproduced by permission of IOP Publishing from Reference 115. All rights reserved). (c) Coiled Parylene cable formed via thermal shaping. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

fabricating the Parylene structures and then undergoing the pyrolysis process.

State-of-the-art Parylene C devices for bioMEMS

In this section, a high-level overview of Parylene-based hybrid (i.e. Parylene-based structural elements) and free-film (i.e. Parylene substrate, released from wafer) devices is presented to demonstrate the use of aforementioned processing techniques to create novel devices for bioMEMS applications.

Hybrid structures

In addition to its use as an encapsulation coating to protect implanted devices,[92,126–128] Parylene C is frequently deposited and patterned on more typical MEMS materials (e.g. silicon) to form hybrid devices that take advantage of its conformal deposition, optical transparency, and biocompatibility. For many devices, Parylene is simply used to form flexible cables integrated with implantable electrodes[120,129–131] to untether the implant from a larger secondary unit that comprises electronics; this isolation has been shown to improve chronic performance of implanted devices within the cortex.[132] In some instances, PDMS is coated around the cables to provide mechanical robustness while maintaining biocompatibility.[120,130]

More recently, Parylene hybrid devices have been employed to construct novel neural probes to record electrical signals from the cortex. These devices combine the biocompatible and flexible nature of Parylene with rigid silicon,[72,133,134] metal,[135] or SU-8[136] regions to add stiffness for easier insertion into cortical tissue. These Parylene hybrid neural probes take advantage of the compatibility of Parylene with standard MEMS processes to combine both the surface micromachining of Parylene with other polymers or with the bulk micromachining of silicon to form rigid islands integrated in a Parylene device. Similar techniques have been used for retinal prosthetics such as a Parylene microtube array in silicon to deliver neurotransmitters to retinal ganglion cells (Fig. 6a).[137]

Hybrid microfluidic devices have explored various techniques to produce closed Parylene microchannels using sacrificial wax or photoresist[138] and liquid structures[79] that involved the direct deposition of Parylene on these structural materials to form channels with sufficient adhesive strength for fluid flow. A photoresist sacrificial structure technique was also employed to form a Parylene neurocage array on a glass substrate with integrated electrodes for a neural cell chip.[139] The same technique was utilized to form a Parylene microchannel-based electrospray device with performance similar to conventional fused silica or glass-based devices.[140] Another more common technique involved the bonding of Parylene-Parylene[35,111] or Parylene-silicon layers, either using adhesive layers[110] or without,[109] to form microfluidic devices. In addition, the deposition of thin (<1 μm) Parylene films has added semipermeable functionality to these microfluidic devices to provide media diffusion for cell chips[141] and act as a membrane for pH sensing.[142]

Parylene's flexibility was also leveraged to improve more traditional silicon-based devices, such as a comb-drive actuator[143] or a micromotion amplifier,[144] to enable larger displacements at lower driving forces. Membrane-based pressure sensors that leverage Parylene's flexibility for larger deflections (compared with other more common materials, e.g. silicon) as a sensing mechanism with a rigid substrate has also been demonstrated via the deposition of Parylene onto a sacrificial material like ferrofluid.[145] Parylene bellows were also constructed to provide
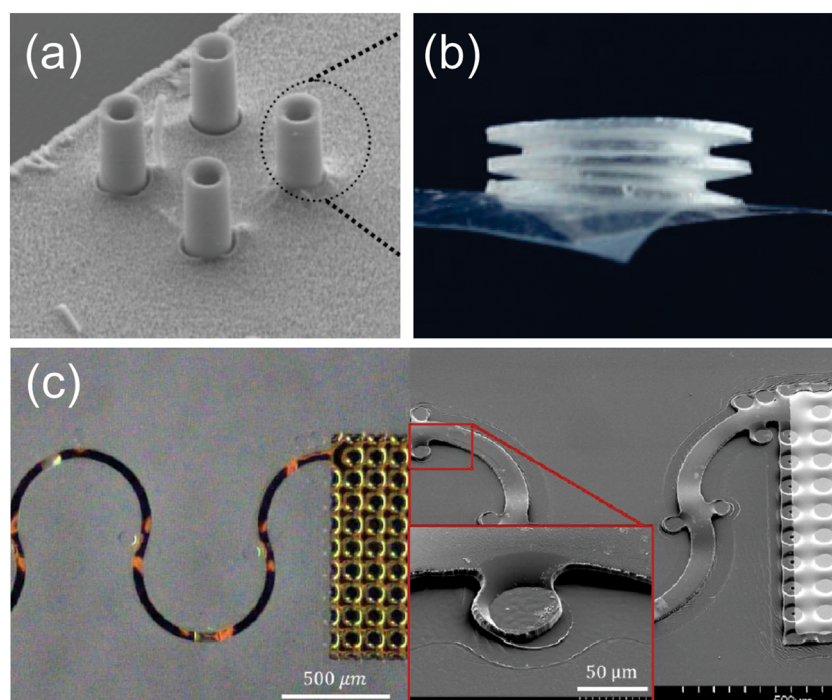

Figure 6. Examples of hybrid Parylene devices: (a) Parylene microtube array on a silicon substrate for delivery of neurotransmitters to retinal ganglion cells (© IOP Publishing. Reproduced by permission of IOP Publishing from Reference 137. All rights reserved). (b) Parylene bellows to be attached to glass substrate as an actuator for drug delivery (Reproduced with kind permission of Springer Science and Business Media from Fig. 4b in Reference 148) (c) Suspended Parylene-metal-Parylene flexible trace on a PDMS substrate for use as a strain sensor (Reprinted from Reference 149 with permission from SPIE). This figure is available in colour online at wileyonlinelibrary.com/journal/pat

large diaphragm deflections using a low-power electrolysis-based actuator for drug delivery (Fig. 6b).[146–148] In one report, Parylene–metal–Parylene electrode structures were anchored to a PDMS substrate to produce a strain sensor that withstood significant elongation without electrical disconnection (Fig. 6c).[149] In this work, Parylene electrodes were suspended using a sacrificial photoresist layer over the PDMS substrate, enabling detection of bending and twisting and not just axial stretching.

Free film devices

Increasingly, MEMS comprising micro-machined Parylene structures released entirely from carrier substrates, so-called free film devices, have become more prevalent for biomedical applications. These free film devices are normally released from a carrier substrate (e.g. silicon) using sacrificial layers (e.g. silicon, oxides, photoresist, and aluminum) that are removed following the final process steps. Mechanical peeling, assisted by water immersion, has also facilitated the release of devices without damaging the structure.[63–65] Free film devices are favored for implantable MEMS as their inherent flexibility helps minimize damage during implantation and allows for conformal attachment to surrounding tissue. Additionally, free film Parylene devices can integrate transducer, electrical components (e.g. coils,[150,151] discrete electronics,[152] and chips[70,152]), and flexible electrical connections into a single, encapsulated structure, minimizing unnecessary complexity.

As a material for implantable sensors, Parylene has been used as the responsive membrane for capacitive pressure sensors for intraocular implants.[153] A similar sensing mechanism has been demonstrated in electrolyte-filled, Parylene microchamber-based, force sensors that utilized changes in electrochemical impedance to measure deflections of Parylene membranes.[154,155] Another Parylene-based pressure sensor utilized a unique microbubble-based sensing mechanism to measure hydrostatic pressure.[156,157] In this device, a microbubble was formed within a Parylene microchamber using electrolysis, and corresponding pressure-induced changes to microbubble size was assessed using electrochemical impedance measured between electrodes on either side of the chamber. Parylene-based chemical sensors for glutamate detection using electrodes modified with deposited glutamate oxidase[158] and pH sensors using plasma modified Parylene films as a proton sensor[159] have also been demonstrated. In one effort, submicron Parylene films (20–200 nm), known to contain pinholes, were used as elution membranes for Parylene-based drug delivery patches by encapsulating dried drug plugs; elution rates were controlled by the thickness of the permeable Parylene membrane, where thicker films were found to elute slower.[160]

There has been considerable work using Parylene as a substrate material for implantable neural prostheses because of Parylene's high compatibility, low Young's modulus, and amenability to metal electrode deposition processes. Specifically for cortical recording and stimulation applications, Parylene has been used to develop both penetrating (Fig. 7a)[64,65] and non-penetrating microelectrode arrays.[25,161,162] In one device, the transparency of Parylene was leveraged to allow for optical stimulation of cortical cells for optogenetics while maintaining electrical recording functionality using transparent, indium tin oxide electrodes.[25] By sandwiching multiple layers of Parylene and metal traces, high-density neural probes with 256 electrodes on a single shank have been produced.[161] Parylene-based cuff electrodes for recording from nerve fibers in the peripheral nervous system have also been developed that utilize thermal curling[118] or built in ratcheting structures[163] to create conformal wrapping around fibers for improved signals. Planar Parylene spinal cord stimulators have also been fabricated and chronic performance demonstrated in rat animal models.[164]

In the field of sensory neural prosthetics, Parylene has become a popular material for retinal implants that involve electrical stimulation of retinal ganglion cells to induce image percepts. High electrode density, curved retinal implants were demonstrated using both a multi-Parylene-metal layer process and thermal shaping of the finished device to match the curvature of the retina (Fig. 7b).[165] In addition to exploiting thermal stress to curl Parylene devices, the inclusion of thin, "score" lines enabled an "origami-like" manipulation of film shape.[166] An all-inclusive, wireless Parylene retinal implant was also demonstrated that incorporated stimulation electrodes, discrete electronic components, and a radio frequency inductive powering coil, on a single Parylene substrate (Fig. 7c).[152] In one design, 3D penetrating electrodes for the retina exploited a micromachined silicon mold to form sharp Parylene needle-like structures.[71] Thermal curling of a planar Parylene electrode array was also demonstrated to match the spiral structure of the cochlea, while using Parylene as a thin, flexible substrate to enable a higher density of electrodes than the current state of the art for cochlear implants (Fig. 7c).[116]

CHALLENGES WITH PARYLENE C FOR BIOMEMS

Although the potential for Parylene for bioMEMS is considerable, Parylene-based devices have many limitations, largely stemming from its polymeric nature. Within this section, an overview of the issues associated with Parylene micromachining and
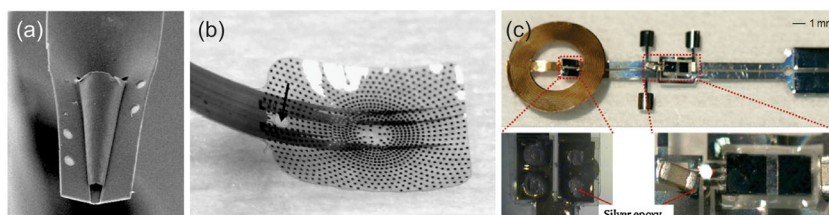

Figure 7. Examples of free film Parylene devices: (a) thermoformed Parylene sheath electrode for electrical recording from cortical neurons (© IOP Publishing. Reproduced by permission of IOP Publishing from Reference 64. All rights reserved). (b) Thermally shaped Parylene-based retinal implant with high electrode density (Reprinted from Reference 165 with permission from Elsevier). (c) All-inclusive packaged retinal stimulator with electrodes, discrete electronics, and inductive coil integrated on a Parylene substrate (Reprinted from Reference 152 with permission from Elsevier). This figure is available in colour online at wileyonlinelibrary.com/journal/pat

performance as devices as well as efforts to improve them are presented.

Processing limitations

The comparatively narrow range of processing temperatures compatible with Parylene remains one of the largest obstacles when developing bioMEMS with the material. Parylene is a semi-crystalline polymer and thus is very sensitive to temperature. As mentioned previously, any process that nears the T_g of Parylene can induce bulk material changes that can impede processing.[35] For example, standard soft bake temperatures for photoresists spun on silicon wafers are ~120°C; for Parylene, this temperature must be reduced. It follows that certain recipes developed for silicon are not compatible with Parylene. There are additional small nuances in processing Parylene; for example, during O_2 plasma dry etching, cooling or rest steps must be included to prevent Parylene being exposed to temperatures above its T_g for long periods of time because of heating from the plasma exposure. These thermal considerations extend to optimal operating conditions of Parylene C devices; mismatch of coefficient of thermal expansion between Parylene and the coated substrate has been found to create mechanical failure for devices under relatively high-temperature soaking conditions.[167] UV exposure of a large area of unmasked positive photoresist (e.g. in the fabrication of micro-sacrificial structures) during photolithography can also be detrimental to Parylene processing. Upon exposure, the UV-initiated chemical reaction of Novolak-based photoresists (AZ) can create an increase in temperature of 200°C[168] that can affect the underlying Parylene, such as in the creation of bubbles during this process that diffuse through the Parylene layer and causes points of delamination.[169]

Wet adhesion issues

It is also well established that the adhesion between Parylene-Parylene layers and Parylene-metal (e.g. thin film gold, titanium, and platinum) layers can be compromised during long term soaking conditions (Fig. 8), with devices lasting from days[38,150,170,171] to more than a year.[92] Before analyzing the underlying mechanism, it is helpful to define the nature of

polymer-polymer and polymer-metal adhesion. Adhesion between two surfaces can generally be categorized as: (1) mechanical interlocking of one surface to the other at size-scales ranging from molecular to polymer chain lengths or (2) ionic or covalent bonding between the molecules at the interface.[172]

For Parylene–Parylene layers formed during CVD, the interactions between the bottom Parylene surface and the top can comprise a combination of these two mechanisms.[3] The top layer forms when vaporized monomer units either physically adsorb to the surface or bond chemically with free radicals. Parylene monomer units can then propagate from these sites to finish polymerizing to create a top layer that is adhered to the bottom layer. Parylene–metal or metal–Parylene layer interactions are predominantly chemical, primarily resulting from first and second order bonds between the carbon atoms of Parylene monomer units and the various metal atoms (titanium and oxygen atoms of titanium-oxides, gold trimer units, and electronegative platinum atoms).[173] For both Parylene–Parylene and Parylene-metal adhesion, bonds are susceptible to failure under chronic soak conditions. Proposed mechanisms for soak delamination include water intrusion physically weakening mechanical adsorption and accentuating slight differences in surface energies between the two layers.[100]

Soaking induced delamination is strongly dependent on the presence of voids or contaminants at the bond interface.[174] Water vapor transport through the Parylene C layer condenses at these void sites underneath the coating and leads to eventual delamination.[175] This motivates additional cleaning processes prior to Parylene deposition (e.g. dilute HF bath[176]) to prevent void formation. The thickness of the Parylene has also been shown to affect adhesion; thicker Parylene coatings ($>10\,\mu m$) reduce and slow water vapor permeation[177]; however, water penetration and subsequent delamination of layers up to $40\,\mu m$ thick have been observed.[178] Increases in Parylene layer thickness will improve the lifetime of the device, but will not prevent its eventual failure.

The inevitable failure of these Parylene–Parylene and Parylene–metal devices have prompted the development of a variety of adhesion techniques that focus on improving both the mechanical and chemical interactions between the layers. To improve the mechanical interface, the following two strategies have been explored: namely, (1) generating additional
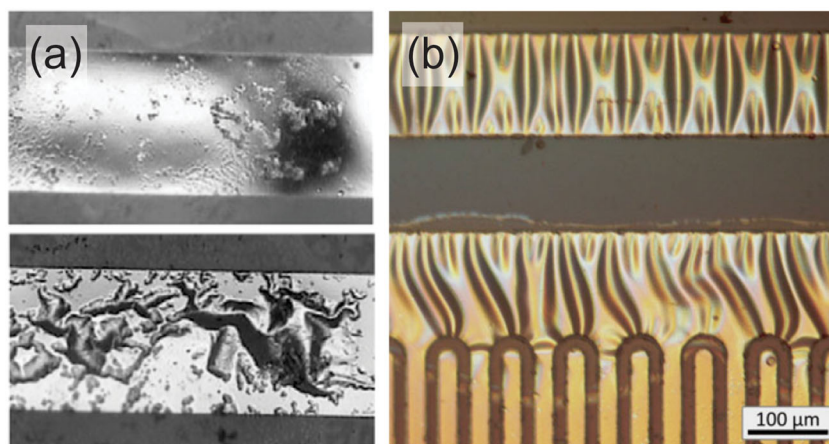

Figure 8. Examples of soak induced delamination of metal traces demonstrated via bubble formation and rippling of a Parylene-metal-Parylene free film structure: (a) after 1 or 2 days soaking in saline (Reproduced by permission of The Electrochemical Society from Reference 170), (b) after a few hours soaking in saline (Reproduced with kind permission of Springer Science and Business Media from Fig. 8 in Reference 38). This figure is available in colour online at wileyonlinelibrary.com/journal/pat

polymer chains interweaving the top and bottom layers of Parylene by using high-temperature (above the T_g) annealing during deposition using *in situ* heating[179] as well as a post-treatment,[119,164,165] and (2) using macro-level surface roughness, substrate porosity, or mechanical anchor points to provide additional regions for mechanical interlocking of the top layer.[180] To improve the chemical interface, treatments (e.g. argon, methane, and oxygen[93,100,101]) or chemical coatings (e.g. propylene carbonate[176]) to functionalize the Parylene and metal surfaces and add functional or reactive groups to create more hydrophobic surfaces prior to Parylene deposition have been investigated.[7,171,181] In one study, the use of oxygen plasma treatment on Parylene and platinum surfaces prior to Parylene deposition was found to decrease the adhesion.[93] The integration of plasma sources within the deposition chamber[100,101] to plasma treat the substrates prior to Parylene deposition without breaking vacuum have yielded promising results in improving adhesion.

It is important to note that the use of these treatments for implantable devices presents another hurdle, as the process should not only be compatible with Parylene, but also not compromise the overall biocompatibility of the device, especially for these plasma-based or chemical coatings. Overall, although there have been many efforts, Parylene–Parylene and Parylene–metal adhesion still remains an issue and a large deterrent for using Parylene as a device material.

CONCLUSION

Parylene C provides many advantages as a material for micromachined bioMEMS devices, but there is still room for additional research and improvement. Its wide range of beneficial features including flexibility, optical transparency, and chemical inertness, in addition to its room temperature, conformal deposition process hold promise for the construction of novel structures and devices, as observed through the state-of-the-art Parylene technologies presented. However, the polymeric nature of Parylene is a double-edged sword; it is important to recognize the thermal and adhesion related issues when working with the polymer. Despite this, Parylene C remains a promising material and is increasing in popularity in both biomedical and MEMS applications. Further development of reliable low-temperature micromachining processes for Parylene and improved wet-adhesion is necessary to realize reliable Parylene bioMEMS.

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