Innovations in Medical Functional Surfaces via Plasma Surface Treatment

Manufacturers of medical devices ranging increasingly rely on plastics to lower cost, reduce weight and improve performance. These devices include catheters, stents, implants, surgical instruments, pipettes, prosthetic devices, artificial hips/knees, surgical gloves, and bandages.

The basic components of plastic and elastomeric materials are polymers. For any given polymer type, there can be hundreds of grades manufactured by multiple resin manufacturers with distinctly different properties. Often the device manufacturer faces tradeoffs in performance or ease of manufacturing since choosing a material that maximizes one property frequently requires compromises in others.

For example, according to Rob Bodor, Vice President and General Manager of Proto Labs, one of the leading providers of machined and molded plastic medical device parts, liquid silicone rubber (LSR) is a material that meets medical device challenges in terms of both performance and regulatory requirements.

Bodor notes that LSR can be an ideal material for medical applications. Nearly every grade of LSR is biocompatible, and the material is available in grades specifically developed and approved for implants and similar medical applications. LSR is extremely stable and can withstand high levels of heat and exposure to cleaning and disinfecting chemicals. Its heat resistance also makes it suitable for heat-related treatment applications such as cauterization, in which it can be used as safety shields on cauterizing tools.

But while LSRs have been used in medical device manufacturing for many years, the introduction of high performance substrates along with new 2-shot injection molding techniques makes adhesion of LSRs challenging due to both surface contamination and surface chemistry. Common substrates including PC, PEI, PPSU, PEEK, and PAEK have low surface energies that impede adhesion of LSRs. Self-adhering LSRs are expensive (often four times the cost of normal LSRs) and still require a clean starting surface. Alternatively, plasma surface treatment has been adopted as a safe, environmentally sound, cost-efficient and technically proven means to successfully modify plastic surfaces and enable LSRs to be used with a wide range of medical device applications (Photo1).
The Basics of Plasma Generation

Plasma is a state of matter. Most people are familiar with the solid, liquid and gaseous forms of matter. As energy is applied to a solid it melts, and as energy is applied to a liquid it becomes a gas. If even more energy is applied to a gas, the atoms in the gas can be broken down further into ions, radicals, and electrons in a conductive gaseous state called plasma. For example, Figure 1 shows the effect of creating a plasma from simple oxygen.

All plasma starts with an energy source. Most commonly, a pair of electrodes supplies radio-frequency (RF) or microwave energy to a gas. These gas molecules become excited to higher energy levels, or ionized as their electrons are shed and a plasma is created. Many of these charged species become unstable or meta-stable molecules. To return to equilibrium, they form covalent bonds with other particles or atoms on surface of a plastic present.

Atmospheric and low pressure plasmas produce the greatest density of energetic species. Atmospheric plasma jets utilize clean compressed air for the cleaning and activation of metals and polymers. In most cases treatment is line of sight, the residence time is short, and the jet nozzle is integrated in-line with relative ease.

Another work-horse manufacturing technology is low pressure gas plasma. This method requires a controlled volume, vacuum pump, and choice gas or vapor species. The control over the gas composition enables the greatest versatility in surface chemistry addition. Furthermore the low pressure method is well-suited for batch operation and the treatment of complex 3D geometry. Both the atmospheric jet and low pressure plasma chamber provide angstrom-level precision in their surface treatments. Photo 2 illustrates the components of a plasm system including the plasma jet, and the plasma control unit. A wide range of systems from this simple benchtop model to multi jet systems with more sophisticated controls and sensors is available to accommodate a wide range of manufacturing needs.
An attractive attribute of low pressure plasma in the biomedical and life sciences is the ability to tailor surface chemistry. To achieve this end chemists and engineers introduce specific gas or vapor combinations into their plasma reactor. Liquid and gas flow is regulated by a respective mass flow controller. In general, only a modest number of species are required for complete exposure of a surface. The process is extremely lean and the consumables negligible in contrast to a wet or dip processes. The exact chemical formulation of gas plasma may vary from simple to complex and there is rarely a single route to achieve a desired surface functionality.

**Wet Chemistries versus Gaseous Plasma**

Although wet chemistry methods are used for modifying and grafting of species, gas plasma offers significant benefits to liquid treatment. These include lower cost, greater ability and flexibility to modify and activate a broad range of inert surfaces, and scalability of the process to high speed commercial production.

A chemical bath such as liquid-phase silanization requires that a silane be dissolved in a solvent before a clean part is added to the solution. This method requires process times often exceeding several hours [1]. Liquid-phase silanization is also a temperamental process due to the difficulty in restricting the amount of water present in the solution. Too little water results in incomplete monolayers while an excess of water results in homopolymerization or surface aggregation [2].

By contrast, gas-phase treatment using low-pressure plasma allows for greater control of moisture, thereby eliminating unwanted surface formation. The high permeability of gas molecules facilitates the action of nano-scale features or porous structures whereas the action of liquid solutions is limited by the effects of capillary action.

What follows are a few select examples that illustrate how low pressure and atmospheric plasma are being used to modify the surfaces of medical grade materials to solve problems commonly encountered in medical device manufacturing.

**Dry Lubricity and Anti-Blocking**

Without surface treatment, a number of elastomers adhere to themselves or other surfaces when exposed to pressure, temperature, or humidity. Anti-blocking refers to the ability of a surface to not stick. For medical devices, anti-blocking agents such as waxes and oils are often unacceptable solutions due to the potential for elution into a working fluid or disruption of organism function.

Plasma polymerized coatings form densely crosslinked polymer networks that are covalently bound to a surface. Some of these coating chemistries have also been optimized for performance as flexible gas and/or liquid barriers [3]. Figure 2 demonstrates plasma processes
which reduce static friction as deposited on a fluoroelastomer surface. Plasma treated components exhibit as much as a threefold decrease in the coefficient of friction.

Figure 2: Friction reducing plasma surface treatments. The coatings are leach free and some exhibit good compatibility in oil.

**Device Hydrophilization**

Product evolution and market forces continue to drive material selection towards the use of low cost commodity polymers such as polypropylene and polyethylene. Many of these plastics, however, lack the surface polarity that makes the part surface compatible with aqueous solutions or biological reagents.

There is sometimes confusion about the relationship between wetting, surface energy, and chemical functionality. A misconception is that a surface energy of 70 dynes/cm is synonymous with a hydrophilic surface. However, dyne solutions are not composed of water but rather solvent mixtures. Functional groups of the plasma treated samples may interact with the hydroxyl, ether, or amine groups present in these solvents [4].

A study conducted on polyethylene (a hydrophobic polymer) varied the exposure of power and pressure using three plasma chemistries known to add oxygen moieties. Figures 3 and 4 present measurements made at the beginning and end of a 48 hour interval.
The measurements compare readings on the polyethylene surface using a surface dyne solution and contact angle using distilled water. In most cases greater hydrophilicity is accompanied by a high surface dyne level, however, as can be seen some samples exhibit poor hydrophilicity but with high dyne values. Thus, relying on contact angle or dyne solution measures alone is not always an accurate guide for wettability.

![Graph: Contact angle measurements conducted on polyethylene after exposure to various plasma processes](image)

*Figure 3: Contact angle measurements conducted on polyethylene after exposure to various plasma processes*
Bioactive Surfaces

Dynamic interactions exist between surfaces and living organisms. Biocompatibility is loosely achieved if a device functions without eliciting an unfavorable response in a living system. A number of surface properties including surface energy, ionic interaction, and intermolecular forces play a role in the adsorption of proteins. A host’s immune system may respond to implanted devices by marking the surface with communicative molecules. Immunological response may be suppressed by altering surface chemistry. Kane et al. demonstrate the feasibility of creating plasma polymerized polyethylene glycol (PEG)-like hydrogels on the surfaces of implantable ultra high molecular weight polyethylene (UHMWPE) [5].

Figure 5 compares the protein adsorption by surfaces of varying plasma deposition using optical fluorescence. There is a significant, and positive correlation between plasma coating thickness and protein resistance. The ether (C-O) content in the plasma coated hydrogel was measured at between 82.1% and 83.2%. This rate nearly matches the 100% ether content of conventional bulk polymerized polyethylene glycol. Additionally, some mechanical properties of the ultra-thin film were characterized using atomic force microscopy (AFM). Unlike alternative hydrogels, the plasma deposited coating can be covalently coupled to the surface.
Controlled Surfaces with Enhanced Binding

Active microfluidic devices, sensors and implantable devices often require a specific binding property or binding capacity in order to change reactions with an environment or biological fluid. The most common systems utilize specific functional groups such as amine, hydroxyl, or carboxyl for conjugation to proteins, molecules, integrin, or adhesive components.

Gas plasma removes organic surface contaminants by reducing them to volatile compounds. The nascent surface is subsequently reacted to process specific plasma chemistry.

Table 1
Amine Incorporation (XPS Measurement)

<table>
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<tr>
<th>Sample</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>Cu</th>
<th>Zn</th>
<th>Au</th>
<th>F</th>
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<tbody>
<tr>
<td>Control</td>
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<td>---</td>
<td>10.8</td>
<td>1.6</td>
<td>---</td>
<td>39.7</td>
<td>---</td>
</tr>
<tr>
<td>Amine</td>
<td>72.9</td>
<td>16.5</td>
<td>8.1</td>
<td>0.1</td>
<td>---</td>
<td>2.2</td>
<td>---</td>
</tr>
<tr>
<td>Amine Washed</td>
<td>73.6</td>
<td>15.7</td>
<td>10.0</td>
<td>---</td>
<td>0.4</td>
<td>0.1</td>
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*Table 1: Amine incorporation onto a gold surface. The modification is permanently bound to the surface and persists after a solvent wash.*

Figure 5: Protein adsorption on the surface of PEG-like plasma polymerized coatings as a function of increasing deposition times.
The intensity and duration of a plasma process impacts the resulting surface functionality and density. If the density of a functional moiety is either too high or too low this may hinder an intended surface reactivity. Table 1 illustrates the percentage of elemental nitrogen detected on a gold surface as measured by XPS before and after plasma functionalization [6].

This amine is covalently bound to the surface meaning it is permanently incorporated onto the surface. This is exemplified by the persisting nitrogen composition post solvent wash. Figure 6 illustrates different amine densities resulting from varying plasma process intensity and exposure. It is noteworthy that plasma processing is rarely a linear phenomenon. Note that additional power or time may not translate into denser species loading.

Figure 7 illustrates impact of variation in elemental composition to plasma power and precursor concentration for a quartz nano-pipette. The nano-pipette is a device used for electrical detection of DNA-functionalized nanoparticles [7]. The ability to tailor surface properties of such nano-scale devices is essential to avoiding undesirable adsorption of biological material onto the walls of a nano-channel. Such adsorption could adversely affect flow properties as well as electrical characteristics of the channel.

Plasma-enhanced chemical vapor deposition (PECVD) of mercaptopropyltrimethoxysilane was investigated as an alternative method to silanize the internal surfaces of these nano-pipettes. The mercaptosilane in a subsequent step was coupled to bovine SA.
An interesting feature is observed. Sulfur content appears to reach its maximum relative composition at a power of 50 Watts (W). A minimum in C:S ratio of 3.3 is found at 50 W and increases with power suggesting that higher plasma power lead to extensive fragmentation of the carbon-sulfur bond in mercaptopropyltrimethoxysilane.

![Figure 7: (Left) The impact of power on sulfur species incorporation on a glass nano-pipette, and (Right) Sulfur content as a percentage of time and concentration](image)

**Depositing Ultra-Thin Coatings Using Plasma Polymerization**

This process of depositing ultrathin coatings using a plasma reactor is termed plasma enhanced chemical vapor deposition (PECVD).

Ultrathin coatings offer a permanence that other plasma methods may not provide because polymeric surfaces usually have some degree of chain mobility or rotation that effectively reduces the surface treatment over time. Reorientation of polymer chains disturb the accessibility of surface functionality.

Figure 8 compares methods for loading heparin on an elastomeric copolymer. Only the plasma-grafted surface exhibited no loss in heparin density following seven-day incubation. All trials show initially good heparin loading compared with the control surface. Methods in which plasma was not employed experienced at least a 50% reduction in heparin over the period.

![Figure 9: Heparin density following gas plasma conjugation and liquid-phase conjugation of a after undergoing 7-day incubation](image)
Changing Surface Morphology with Plasma

Varying the energy applied to gas plasma affects the surface morphology. At high energy, ablation dominates, and the substrate becomes rigorously etched or nano-roughened. At lower power regimes, gas plasma is a primarily additive process and the conditions are amenable to film formation.

An ultrathin PECVD coats surface features with an atomically smooth layer. If the energy is delivered in pulsed periods, the plasma yields nano-patterned film morphology. Figure 9 compares atomic force microscopy images of three PECVD fluorocarbon coatings on a glass microscope slide. The pulsed power conditions yield bumpy textures. In a PECVD of fluorocarbon, a surface pattern increases the surface area, thereby providing greater hydrophobicity.

Contact angle measurements using deionized water results in approximately 110° for the continuous power process and greater than 130° in the case of a pulsed power condition. Fluorocarbon coatings are noted for their properties of super hydrophobicity, resistance to protein adsorption, and anticorrosion [8]. Morphology plays a big role in these surface interactions.

Another attribute of low-pressure gas plasma is its ability to develop custom PECVD surface chemistry that resembles conventional material systems. Polyethylene glycol (PEO) is a polyether compound with applications in manufacturing and medicine. Characteristics include biocompatibility, nonfouling, and nonimmunogenicity [9].

Inspection via FTIR-ATR confirms an ether content of greater than 80%. The coating is both hydrophilic and resistant to protein adsorption. PECVD of a PEO-like film offers the advantages of being conformal, covalently bound, and chemically cross-linked for improved wear resistance. Other experiments have reported application of comparable PECVD chemistry in combination with lithographic patterning for directed cell growth [10]. Cell attachment may be both assisted and inhibited by surface treatment.

Figure 9. 5 × 5–μm contact mode AFM demonstrates the different surface morphology resulting from continuous [left], low-pulsed [middle], and high-pulsed [right] plasma power conditions on a PECVD coating.
Conclusion

As illustrated by the detailed examples above and the applications depicted in Figure 10, Plasma is a versatile tool that is capable of designing controlled interfaces on a variety of materials used in medical device manufacturing. This includes replacing conventional multi-step wet chemistries. Plasma gives the medical device designer freedom to separate mechanical, optical, and fabrication techniques from the surface requirements that often require compromises in cost and performance. Plasma surface treatment can be tailored to provide the desired properties across a wide range of polymers, elastomers, adhesives, sealants, coatings and other materials to provide a versatile new chemistry tool box.

References


Figure 10. Plasma is routinely being used for surface treatment and thin film deposition is being across a wide range of medical device applications.


