Process Control and Plasma Modification of Polymers

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The utilization of flow pressure plasma technology for some industrial applications in the field of polymer modification for biomedical applications is described. The use of process control diagnostics for implementing on-line processes will be discussed. The following processes will be discussed: deposition of super-hydrophobic and nano- micro-structured coating, non fouling and bacterial resistant coatings, -COOH functional coatings, micropatterned surfaces, anti-bacteric coatings.

Keywords: plasma modification of polymers, biomaterials, process control

1. Introduction

Low Pressure Plasmas (LPP) are largely utilized for plasma processing of polymers, *i.e.* deposition, treatment and etching, for many important applications since almost a couple of decades. The versatility of LPPs relies in the fact that the concentration of the reactive species, and the energy and density of positive ions can be varied in a wide range. This has allowed to design an entirely novel class of materials with variable stoichiometry and customized properties, which has contributed to solve many important industrial problems involving materials. The fields of applications are numerous and include sectors such as car, aerospace and naval components, glass, paper, plastics, packaging, biomedical devices, optics, textiles, shoes components, etc., besides to microelectronics, obviously.

Among the features of plasma processes, most attractive for surface-modifying biomedical polymers, it is worth to mention: a) their ability of modifying *in continuo*, in a controlled and unique way, surface chemistry and properties of materials, without altering their bulk; b) their intrinsic sterility; c) the possibility of scaling up plasma processes to industrial sizes and throughputs, with a variety of substrates (webs, inside of tubes, fabrics, non woven materials and foams, lenses ...) of different shapes and nature; d) the environment friendly approach, alternative to conventional processes mostly confined to unsafe procedures.

Plasma deposition, treatment and etching processes have been recently utilized also to transfer geometric micro- and nano-metric patterns at the surface of biomedical polymers, with the aim of driving the behaviour of cells (contact guidance) in tissue engineering experiments.

Different uses of plasma-processes are being investigated in the biomedical field since many years; Plasma Enhanced Chemical Vapor Deposition (PE-CVD) of organic films and Plasma Treatment, (*i.e.* grafting of chemical functionalities) are the most utilized processes, as listed in Table 1.

2. Super-Hydrophobic and nano- micro-structured coatings

Radiofrequency tetrafluoroethylene (C_2F_4) glow discharges modulated with duty cycles lower than 10%, and a total period of 100 ms, lead to the formation of thin amorphous films, highly fluorinated (F-to-C ratios over 1.7), and with crystalline ribbon-shaped structures. These Teflon-like ribbons are many microns long and tens of nanometers thick and exhibit spectacular hydrophobicity (water contact angles 160-175°).

The gas phase diagnostics has been performed by IR absorption spectroscopy and time resolved emission spectroscopy during the time-ON period, in order to evaluate the effect of CF_2 precursors in the plasma. The material characterization has been made by XPS, SEM, AFM and X-ray diffractometry [1,2].

TABLE 1. Deliverables and applications of plasma processes in the field of biomaterials

DELIVERABLES	APPLICATIONS
Coatings	
Blood-compatible	Vascular grafts, heart valves, catheters, cardiovascular devices, immobilization of non thrombogenic molecules
Protective, inert	Devices, prostheses
Barrier, gas-permeable, drug-releasing, leach control (ions, additives, catalysts)	Drug delivery systems, filters, devices membranes, oxygenators
Non fouling, hydrophilic	Infection-resistant surfaces, IOL's, prostheses, devices, catheters
Nanostructured fluorinated coatings	Superhydrophobic materials
Functional (selected chemical groups)	Cell growth, biosensors, immobilization of Biomolecules
Hydrophobic, superhydrophobic	Non wettable
Surfaces (PE-CVD, Treatments)	
Hydrophilic-hydrophobic	Cell growth, change of wettability
Micro-, nano-patterned substrates	Cell guidance, tissue engineering
Surfaces with selected chemical groups	Cell growth, biosensors, immobilization of biomolecules
Etching processes	
Sterilization, cleaning	Sterilization of surgical tools and devices

Figure 1 shows a typical SEM morphology of the nanosized μm -long ribbons of crystalline Teflon-like. This picture has gained an international reputation and it

is evident, from an inspection, the reason for the appellation "*fettuccine-like*" which is always given to the material.

Fig. 1 Tens of nanometers thick, several μm long ribbons of highly fluorinated crystalline Teflon-like obtained in modulated discharges fed with C_2F_4 with duty cycles $<10\%$

3. Non fouling coatings

Polyethyleneoxide (PEO)-like coatings with non fouling properties for cells, proteins and biological systems can be deposited from continuous [3, 4] and modulated [5] PE-CVD processes fed with volatile monomers like glycols (e.g. DEGDM or TEGDM, Di (tri) Ethyl Glycol Di Methyl Ether, $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_3$, $n = 2/3$, or crown ethers, characterized by $-\text{CH}_2\text{CH}_2\text{O}-$ ethylene oxide (EO) units in their structure. Mild fragmentation conditions are generally utilized in this process in order to keep as high as possible the fraction of intact EO moieties (PEO character) in the coating, a feature which is correlated to non fouling properties. The PEO character, and the non fouling properties, are associated, with good approximation, to the relative content of the ether groups (C1 component, about 286.5 eV of Binding Energy) in the C1s XPS signal, and can be quantified quite easily. Emission spectroscopy (see Figure 2) can be used as an online diagnostics allowing to control the process (see also next paragraph for this point).

4. $-\text{COOH}$ functional coatings

Glow discharges fed with vapors of acrylic acid (AA), or of other carboxylic organic compounds, allow to deposit thin organic films characterized by a good density of $-\text{COOH}$ and other oxygen-containing chemical functionalities. These functional coatings can be utilized in engineering biomedical surfaces to improve the spreading and growth of certain cells [8], and to immobilize biomolecules (enzymes, peptides, non thrombogenic, etc) by means of "apacer arm"

Fig. 2- Actinometric Optical Emission density trends of CO detected in glow discharges for deposition of PEO-like (A- TEGDME/Ar; B- DEGDME/Ar), Ag/PEO-like (C- DEGDME/Ar, in presence of Ag sputtering) and of -COOH functional (AA/Ar) coatings in different experiments. The trends are reported as a function of the PEO character (C1 component of the C1s ESCA signal) and of the surface density of -COOH groups (C3 component), respectively.

species [9] of a certain length, that keep them tethered at the surface with their biological activity unaltered.

The fragmentation of the monomer in the plasma, as usual for organic species, is reflected in the composition of the coating, and has to be kept low when the retention of the monomer structure is requested for the coating (e.g., a high density of -COOH groups from AA feeds). The surface chemistry of -COOH functional coatings can be adjusted easily by tuning the experimental parameters under spectroscopic control of the plasma phase. As for PEO-like coatings, in fact, it has been found, that surface density of -COOH groups is well correlated with the actinometric density of CO in the plasma [7, 10], which can be considered a "marker" of AA fragmentation. This is clearly shown in Fig. 2. When more CO is revealed in the plasma, a more intense fragmentation is experienced by AA, and the density of -COOH groups in the coating is decreased.

5. Plasma processes for micro-patterning biomedical surfaces

Random and geometrical patterns (morphological, chemical domains) at micrometric and nanometric scales can be transferred onto biomedical polymers, since it is known their ability, in certain contexts, to drive the behaviour of cells in a number of extremely interesting ways for fundamental and practical studies, e.g. biosensors, diagnostic kits, tissue engineering. We have utilized PE-CVD and plasma treatment processes on substrates covered with "physical masks" [11] in order to transfer different chemical domains (e.g. stripes of PEO-like coatings onto zones grafted with N-containing groups) in geometrical micro-patterns. This has allowed to alternate, at the micron scale, non fouling and adhesive zones for cells, as shown in Fig. 3. Physical masks are micron-thick polymer or metal foils where holes of the proper size and shapes are precisely drilled (e.g. by laser techniques); when properly fixed at the surface of the polymer under modification, and utilized with selected plasma treatment, etching of deposition processes, physical masks allow to transfer thin films or grafted groups onto selected zones of flat polymer samples with a space resolution of a few microns.

The adhesion between the substrates and the coating is a key issue, and can be guaranteed also in wet conditions for cell culture, when the substrates are properly plasma pre-treated (as in NH_3 discharge), to provide hydrophilicity to their surface. The pre-treatment is extremely important if hydrophobic substrates are to be coated with hydrophilic coatings (like PEO-like and pdAA).

Fig. 3. Alignment of NCTC 2544 Keratynocytes on micro-structured samples (cell-adhesive NH_3 treated tracks about 30 μm wide, cell-repulsive PEO-like domains).

The effects of both surface chemistry (PEO-like, pdAA or NH₃ treated) and topography (edge of the tracks) have been recorded on cell adhesion, confirming that cells can “feel” both surface features in culture conditions, as it is shown in figure 4. These features allows to design substrates with proper anisotropic tracks of live cells surrounded by cell repellent domains.

Native

Native + Ag/PEO-like

Fig.4- Micrographs illustrating the bacterial adhesion to native PVC (up) and Ag/PEO-like coated PVC (down). The reader should be aware that the mosaic pattern observed on the Ag/PEO-like micrograph does not correspond to bacterial cells, but is the morphology of Ag/PEO-like coated PVC.

6. Ag/PEO-likes as anti-bacteric coatings

In a properly configured parallel plate reactor (asymmetric with a cathode covered by a silver plate), under certain conditions, we have shown [6] that it is possible to couple the deposition of PEO-like coatings with the sputtering of silver atoms from the cathode. This way Ag/PEO-like coatings

results, *i.e.* PEO-like coatings with embedded Ag clusters, which show marked bacterial resistant properties. This is an important feature for catheters and other devices, and is due to the slight and slow release of Ag⁺ ions in wet conditions. PEO character and Ag content of PEO-like and Ag/PEO-like coatings are correlated with the actinometric densities of CO (monomer fragmentation, see Fig. 2) and of Ag atoms present in the plasma [6, 7]. This is a simple way to predict and control the composition of the coating by means of *in situ* spectroscopy.

This material does not allow the proliferation of bacteria, such as *Pseudomona Aeruginosa* and *Staphilococcus Aureous*. In fact, a reduction of up to 6 orders of magnitude has been observed [14]. Figure 4 clearly shows the anti-bacteric effect. This put the material in position of paramount importance as anti-bacteric coating for prostheses and for food packaging applications.

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