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Plasma assisted surface treatments of biomaterials

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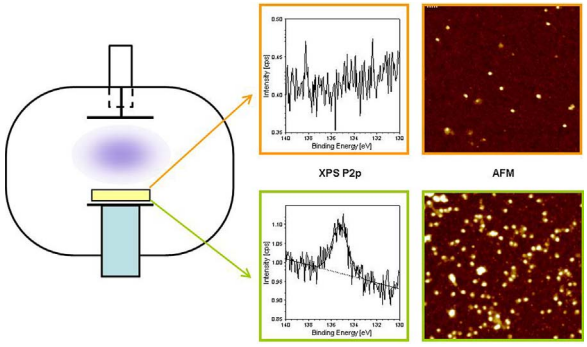
HIGHLIGHTS

- Plasma surface treatments are an effective and economical for material functionalization.
- Plasma treatments are convenient and powerful approaches for biomaterial engineering.
- The physical and chemical characteristics of the treated materials are thinly tunable by varying the plasma parameters.
- Combinatorial processes allow a single step synthesis of substrates with desired composition and thickness.

GRAPHICAL ABSTRACT



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ABSTRACT

The biocompatibility of an implant depends upon the material it is composed of, in addition to the prosthetic device's morphology, mechanical and surface properties. Properties as porosity and pore size should allow, when required, cells penetration and proliferation. Stiffness and strength, that depend on the bulk characteristics of the material, should match the mechanical requirements of the prosthetic applications. Surface properties should allow integration in the surrounding tissues by activating proper communication pathways with the surrounding cells. Bulk and surface properties are not interconnected, and for instance a bone prosthesis could possess the necessary stiffness and strength for the application omitting out prerequisite surface properties essential for the osteointegration.

In this case, surface treatment is mandatory and can be accomplished using various techniques such as applying coatings to the prosthesis, ion beams, chemical grafting or modification, low temperature plasma, or a combination of the aforementioned.

Low temperature plasma-based techniques have gained increasing consensus for the surface modification of biomaterials for being effective and competitive compared to other ways to introduce surface functionalities.

In this paper we review plasma processing techniques and describe potentialities and applications of plasma to tailor the interface of biomaterials.

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1. Introduction

Biomaterial is defined as a material that is used in specific form or structure to fabricate prostheses or biomedical devices that are intended to replace or recover an impaired body function in order to save or improve the patient's quality of life [1]. Over the past fifty years biomaterials science has investigated different types of biomaterials and their applications to replace or restore the function of compromised or degenerated tissues or organs. Every year more than 13 million prostheses/medical devices are implanted solely in the U.S.A [2].

For biomedical applications, requirements are quite severe. Materials must be biocompatible, that is they should not induce long lasting or severe negative effects on the surrounding biological tissues, likely be bioactive to trigger desired biological process (such e.g. those involved in the material integration), and should be durable or biodegradable depending on the application. In addition, they must fulfill the mechanical demand, as in prosthetic implants, likewise when employed in other devices such as biosensors [3]. Many materials possessing essential mechanical properties for the fabrication of prostheses exhibit poor integration with the human tissues, consequently inducing blood clotting or severe foreign body reactions leading to implantation failure [4]. Surface properties play a dominant role in controlling biological phenomena that occur at the interface, hence in cascade, the fate of the prosthesis. In this respect, surface engineering has become crucial for biological and biomedical applications where biocompatibility and bioactive responses are required [2,5,6]. Hundreds of different biomaterials have been investigated: synthetic and natural polymers (collagen, fibrin, chitosan, hyaluronan, heparin, cellulose, polyurethanes, polyesters, polytetrafluoroethylene, polymethylmethacrylate, hydrogels…), metals (steel, titanium, CrCoMo alloys,…) and ceramics (calcium phosphates, hydroxyapatite, alumina, zirconia…) [2,7]. These materials are utilized in a wide class of implants like in ophthalmology as intraocular lenses, wound dressings, orthopedic implants, (cardio)-vascular surgery for blood vessels, heart valves or stents and implants for dentistry [7].

The host/biomaterial interaction of any prostheses or devices follows a series of complex events. Initially, a material was considered biocompatible if it was inert, i.e., not activating any tissue responses, such as for blood-contacting applications where no-platelet or thrombus activation are major requirements, [8–10]. However, all materials implanted in a body or in contact with body fluids induce a biological response, that is responsible for the short and long term body reactions whose nature, intensity and duration can lead to the implant's integration or failure [4]. Examples of failure and of induced negative effects, which is also dependent on the specific application, include tissue necrosis, infection, calcification, extensive fibrosis and scar. The response of the human body to a biomaterial can be partially optimized by changing the chemistry of its surface. Significant amount of experimental and theoretical researches has been devoted to correctly design or modify the surface properties of biomaterials based on specific application. It is matter of a complex design of the surface processing which is called surface bioengineering [11].

Few seconds after the implantation of a prosthesis, or in general after a material encounters biological fluids, the surface that is coated by a layer of low molecular weight substances is replaced by higher molecular weight biological moieties and finally proteins. The composition of the protein layer adsorbed at the surface and their conformation can alter the biological responses of the prosthesis [6,12–14]. Cell adhesion is protein mediated occurring through the interaction of the cell integrin receptors and biomaterials surface-adsorbed body proteins, [15–18] [19–21]. The conformation of the adsorbed proteins, their composition and density drive cellular adhesion and proliferation, and can be responsible for their differentiation [17,18,22]. Biomaterials surface engineering investigates the creation of surfaces that can promote cell adhesion with signaling motifs of appropriate biological molecules while preventing the unfolding of adsorbed proteins with subsequent aggregation cascades occurring on most non-biological surfaces [23].

There are several surface engineering methods that can be categorized into two main groups: physicochemical and biological. Examples of physicochemical methods are wet chemical processing such as acid etching/oxidation, functional groups grafting, methods utilizing material irradiation such as cold plasmas, ion or electron beams, lasers, photo-lithography [24–28].

Among all techniques utilized for engineering surfaces, those based on plasma technology have been proven to be extremely efficient in improving the surface properties of a material without affecting the bulk ones, such as mechanical stiffness and robustness [29]. Surface properties may be thinly defined by varying the plasma parameters, tailored to produce different types of surfaces depending on the specific application and requirements [30]. In addition, plasma process is controllable and reproducible, it provides sterile surfaces and can be easily transferred to industrial production.

In this paper we review the plasma processes and the techniques involved in its use for the modification of materials (Section 2), while a further section is dedicated to the detailed discussion of three different applications of plasma-assisted processing of biomaterial surfaces, showing how an opportune plasma treatment can be used to tune the bioactivity of solid substrates.

2. Plasma reactors

Plasma is a confined ionized gas whose temperature and pressure may be tuned in rather wide range. Depending on these parameters cold or hot plasmas, low or high pressure plasmas can be identified. The generation of plasmas is obtained through a separation of electrons from their parent atoms or molecules which are left in an ionized status. The production and sustaining low-temperature plasmas for technological applications is generally achieved by applying an electric field to a neutral gaseous precursor. Any volume of a neutral gas always contains some molecules dissociated into ions and electrons, as a result of the interaction of gas with high-energy photons due to cosmic radiation or natural radioactive decays. The applied electric field accelerates ions and electrons and new charged particles are created when these charge carriers collide with the neutral precursor molecules thus leading to their dissociation. These charged fragments and radicals more easily react with a substrate altering its composition. Typically oscillating electric fields in the range of radio frequencies are applied to gaseous species to generate the plasma. However, coupling a microwave radio frequency (RF) source to a gaseous precursor is not immediate because of the different transmission power of the precursor (impedance) with respect to that of the source/electrical cable system. This problem can be resolved by utilizing a matching box that is able to tune the source to the plasma reactor avoiding RF reflection with loss of power. There are a few kinds of plasma instruments whose performance relies on plasma source and the specific application [31–39].

Fig. 1 represents the schematic configuration of the most popular plasma reactor systems. In capacitive coupled plasmas (Fig. 1A), an oscillating electric field is applied between two plain electrodes, one of these electrodes is the sample holder and generally is grounded. Reactors shown in Fig. 1B and C are inductively coupled. In these systems the plasma is excited utilizing a magnetic oscillating field generated by a coil connected to a microwave RF generator. Reactors (B) and (C) differ because in the former the plasma is created in the central region of the reactor chamber while in the latter the plasma is generated apart from the reactor chamber. In Fig. 1C the plasma is formed inside a plasma source and propagates through the reactor chamber to the sample surface. This is called remote plasma because the surface is not exposed directly to the RF power used for the plasma generation. This ensures efficient surface treatments with much lower thermal power transferred to the sample preserving it from damage. Reactors (A), (B) and (C) operate at low pressure that is obtained by connecting the