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Review

Plasma-assisted surface modification of organic biopolymers to prevent bacterial attachment

Kateryna Bazaka [a], Mohan V. Jacob [a], Russell J. Crawford [b], Elena P. Ivanova [b,*]

[a] Electronic Materials Research Laboratory, School of Engineering and Physical Sciences, James Cook University, Townsville, Queensland 4811, Australia
[b] Faculty of Life and Social Sciences, Swinburne University of Technology, P.O. Box 218, Hawthorn, Victoria 3122, Australia

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ABSTRACT

Despite many synthetic biomaterials having physical properties that are comparable or even superior to those of natural body tissues, they frequently fail due to the adverse physiological reactions they cause within the human body, such as infection and inflammation. The surface modification of biomaterials is an economical and effective method by which biocompatibility and biofunctionality can be achieved while preserving the favorable bulk characteristics of the biomaterial, such as strength and inertness. Amongst the numerous surface modification techniques available, plasma surface modification affords device manufacturers a flexible and environmentally friendly process that enables tailoring of the surface morphology, structure, composition, and properties of the material to a specific need. There are a vast range of possible applications of plasma modification in biomaterial applications, however, the focus of this review paper is on processes that can be used to develop surface morphologies and chemical structures for the prevention of adhesion and proliferation of pathogenic bacteria on the surfaces of in-dwelling medical devices. As such, the fundamental principles of bacterial cell attachment and biofilm formation are also discussed. Functional organic plasma polymerised coatings are also discussed for their potential as biosensitive interfaces, connecting inorganic/metallic electronic devices with their physiological environments.

1. Introduction

For decades biomaterials have played an important role in disease management and the advancement of health care. Their applications range from coatings for tablets or capsules in pharmaceutical preparations to being essential components of extracorporeal devices such as contact lenses or kidney dialyzers and in-dwelling devices and implants. Many of these materials were not originally designed for medical applications, and while they addressed many important medical issues, their use frequently led to complications, such as poor biocompatibility, time-dependent material degradation and subsequent mechanical failure, infection, inflammation and blood clot formation. The biomaterials were often selected only for their bulk properties, such as mechanical strength and inertness, and as a result many widely used biomaterials exhibited significant drawbacks. Many possessed sub-optimal surface biological properties such as high hydrophobicity and high friction, resulting in deleterious effects such as inflammation and irregular tissue responses. Recently, advanced surface characterisation techniques have allowed a better understanding of the reactions occurring at the interface between the biomaterial surface and host tissues. This has allowed an insight into the important role that the surface properties of biomaterials play with regard to the response of the biological environment to in-dwelling medical devices [1]. As a consequence, novel techniques have been developed that can impart desirable chemical, physical, and biological properties to the biomaterials. This can occur through the synthesis of a new material with desirable properties built directly into its matrix or by the modification of materials already being used by the medical industry [2]. The surface modification of biomaterials is an economical and effective method by which biocompatibility and biofunctionality can be achieved while preserving the favorable bulk characteristics of the biomaterial, such as strength and inertness. One such modification technique is plasma surface modification. This provides device manufacturers with a flexible and environmentally friendly process that allows tailoring of the surface properties of the material to suit a specific need [3–8]. In addition, exposure to plasma has been shown to irreversibly damage bacterial cells, allowing in situ sterilisation of the biomaterial during the surface modification process. For example, plasma sterilisation has been demonstrated to be effective against *Escherichia coli* [9,10], *Staphylococcus aureus* [9,11], *Pseudomonas aeruginosa* [10], *Bacillus cereus* [10], *Bacillus subtilis* [12] and *Geobacillus stearothermophilus* [13]. The resultant plasma coatings have been shown to possess spatial uniformity and strong adhesion to the substrate. They result in a smooth, defect-free surface with

* Corresponding author. Tel.: +61 3 9214 5137; fax: +61 3 9214 5921.
E-mail address: eivanova@swin.edu.au (E.P. Ivanova).

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sound chemical and physical stability [14–16]. Furthermore, coatings manufactured using plasma technologies display interesting optical and electrical properties, making them suitable candidates for integration into a range of electronic devices that can interface between organic/inorganic electronics and physiological environments [17]. This paper discusses the processes used to develop plasma-modified surfaces with morphologies and chemical structures that prevent the adhesion and proliferation of pathogenic bacteria.

2. Plasma modification

A plasma is defined as a partially or wholly ionised gas with approximately equal amount of positively and negatively charged particles. Near equilibrium plasmas are formed under high temperature conditions and are characterised by thermal equilibrium of its entire range of species. The temperatures required to generate near-equilibrium plasmas generally range between 4000 and 20,000 K, depending on the ionisation potential of the element. These extreme conditions are not likely to be appropriate for the surface modification of biomaterials constructed from polymers [1], although they can be used for the evaporation and deposition of bioactive metals and ceramics, such as natural hydroxyapatite-based bioglass–ceramic composites [18,19] and zirconia coatings [20,21] for artificial bones and hard tissues. Non-equilibrium plasmas, on the other hand, can be initiated at substantially lower temperatures, enabling their application for surface cleaning and functionalisation of polymer surfaces. The ion mobility in a low temperature plasma is significantly lower than that of the electrons that transport the energy through the electric field [22]. The plasma can also be classified according to the pressure at which it is initiated or according to the energy source used to energise the gas [23].

During plasma surface treatment the substrate is exposed to a reactive environment of a partially ionised gas comprising large concentrations of excited atomic, molecular, ionic, and free radical species Fig. 1. The nature of the interactions between the excited species and the solid surface will determine the type and degree of the chemical and physical modifications that will take place. The processing conditions, such as power, pressure, gas, etc., and the nature of the substrate will determine whether the surface modification is one of film deposition, substitution, or ablation. Plasma polymerisation can take place when a monomer, either in vapor phase or at the surface, is fragmented into reactive species that can then recombine and be deposited onto the surface of the substrate. Monomers that do not necessarily contain functionalities associated with conventional thermo-chemical polymerisation, such as unsaturation or ring structures, can be deposited in this way.

In plasma treatment gases that do not fragment into polymerisable intermediates upon excitation are used. These include air, nitrogen, argon, oxygen, nitrous oxide, helium, tetrafluoromethane, water vapor, carbon dioxide, methane, and ammonia. Exposure to such plasmas can lead to the introduction of chemical functionalities, with the nature of the functionalities being highly dependent on the chemical composition of the biomaterial and the process gas. For instance, plasma oxidation, nitration, hydrolyzation, or amination will increase the surface energy and hydrophilicity of the biomaterial, therefore changing the way in which the biomaterial interacts with its immediate physiological environment. Free radicals are also created on the surface, since the surface is being bombarded by energetic particles and high energy UV radiation. This can lead to surface ablation, cross-linking or surface activation. Ablation is a process by which lower molecular weight species, such as volatile oligomers and monomers, are desorbed. Cross-linking occurs when radicals from one chain on the surface of the polymer combine with radicals from another polymer chain to form a bond. Surface activation, however, involves the recombination of surface radicals with atoms or chemical groups that are different from those that were originally present at the surface of the biomaterial.

The surface functionalities that arise as a result of plasma treatment can serve as a platform for further surface modification processes, such as the grafting of biomolecules and other functional structures. Further surface modification can be performed in order to tailor the properties of the biomaterial to a specific application.

Despite the many advantages associated with the use of conventional plasma techniques for surface functionalisation, polymer thin films fabricated using this method are typically characterised as highly cross-linked and amorphous. Furthermore, these films retain only a limited amount of the original monomer functionality due to the high degree of fragmentation and recombination that takes place during the plasma polymerisation process. If low input power deposition and low levels of substrate heating are used the original chemical structure of the monomer can be retained to a large extent, however, a relatively low degree of cross-linking results, rendering these coatings inferior in terms of their mechanical properties and dynamic stability, hence limiting their in vivo applicability [24]. A number of papers have been published that detail the use of a pulsed plasma technique. This technique allows the precise control of chemical functionality and surface morphology and results in a coating with good stability [24–29]. The plasma

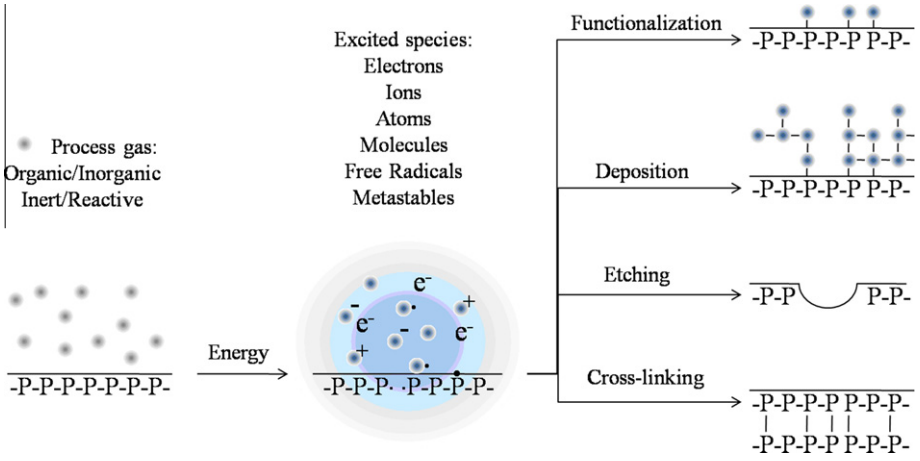

Fig. 1. Surface modification processes that can be achieved using the plasma technique.