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An intuitive thermal-induced surface zwitterionization for versatile, well-controlled haemocompatible organic and inorganic materials

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ABSTRACT

In this study, a facile and effective strategy is presented for the preparation of a series of zwitterionic poly(sulfobetaine methacrylate) (pSBMA)-grafted organic and inorganic biomaterials with well-controlled haemocompatibility via intuitive thermal-induced graft polymerization. The research focused on the effects of zwitterionic surface packing density on human blood compatibility by varying the SBMA monomer concentration on the silanized silicon wafer substrates. A 0.2 M SBMA monomer solution was found to not only produce Si wafer surfaces with ideal zwitterionic surface packing density and uniform, evenly distributed pSBMA grafting coverage but also yield optimal hydrophilicity and haemocompatibility. SBMA monomer concentrations lower and greater than 0.2 M yielded a zwitterionic surface with low grafting coverage. This study also demonstrated that the same, intuitive thermal-induced graft polymerization strategy could be applied to a variety of organic polymeric, inorganic ceramic and metal oxide biomaterials to improve haemocompatibility. Among the tested organic and inorganic materials, however, it was found that inorganic biomaterials demonstrated greater resistance to protein and platelet adhesions. It was hypothesized that the ozone treatment, which generated an abundance of hydroxide groups on inorganic substrate interfaces, might have given the inorganic biomaterials a more stable silanized layer yielding a preferable reaction state and resulted in sturdier and more durable pSBMA grafting.

1. Introduction

Haemocompatibility of biomaterials is an essential aspect in the development of biomedical apparatus; however, despite great effort put into ameliorating blood compatibility of biomaterials [1], little consensus has been reached on "blood compatibility" in biomaterials. As biomaterials are introduced into human blood, some are susceptible to adhesion and adsorption of biological molecules while others remain inert and display few interactions with their surroundings. The adhesion and adsorption of biomolecules can cause functional defects of the materials, which may result in serious physiological responses including blood clotting, immune rejection, chronic inflammation, etc. Furthermore, blood and biomaterial interactions may sometimes stimulate a convoluted cascade of processes such as proteins, platelets and leucocytes adhesion/activation which are immensely interlinked [2].

Modifications to biomaterial surfaces, such as plasma-induced surface grafting [3,4], surface-initiated atom transfer radical polymerization [5,6], etc., as means to improve haemocompatibility have been proposed in recent years. While these modifications are effective in improving blood compatibility of materials, the processes involved remain both intricate and expensive; as a result, a robust, cost-effective protocol for enhancing blood compatibility via surface modification is necessary for practical and commercial purposes. For instance, organosilanes, with the structure $(OR)_3$-Si-R′, are common coupling agents used to modify ceramic biomaterial surfaces in coatings [7], where in a silanization reaction, organosilanes are covalently bounded to amorphous silica or alumina surfaces [8,9]. In earlier studies, stable covalent bonding between the inorganic material and the polymer layer interface was suggested as the primary factor for enhancing interfacial adhesion. The hydrolysis process of the alkoxide groups with silanols initiates the condensation of the stable siloxane bonds with other silanol groups on the material surface [10,11] while the organofunctional group is covalently bonded to the polymer matrix, creating a stable interface.

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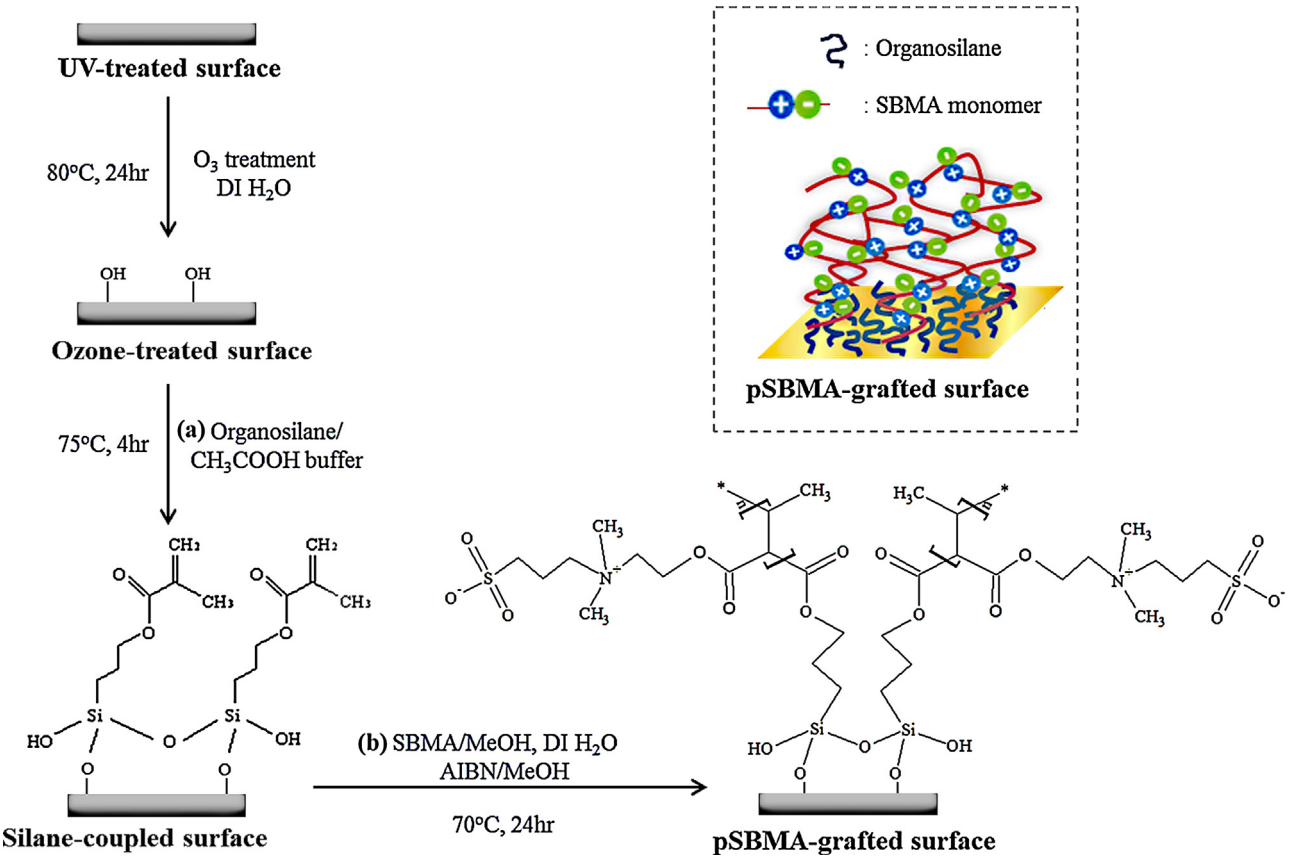
Thermal-induced polymerization is a common method for polymer synthesis where excited radical monomer is polymerized to form legitimate polymers. It is a traditional well-known grafting approach in surface modification, without using a catalyst and a toxic solvent. This method of polymerization has revealed new and simplified techniques to modify material surfaces. Over the years, this technique has also been employed by researchers to modify biomaterial surfaces to have desirable characteristics such as biological and blood compatibility. In 2004, Jiang et al. demonstrated the potential of reducing biological molecule adhesion via zwitterionic-modified surfaces [12]. Zwitterionic polymers with a neutral tail group in which both a positive and negative charge located at their tails exhibit good blood compatibility. The surface modifications involving zwitterionic molecules, such as polysulfobetaine with $[-N^{+}(CH_2)_nSO_3^{-}$, $n = 3,4]$, have attracted a growing interest for their potential in advancing the evolution of non-thrombogenic biomaterials [13–16]. From here, the applicability of this approach was investigated to solve universal surface treatment, i.e., for target application such as creating antifouling layers on general surfaces ranging from organic polymeric surfaces to inorganic ceramic and metal oxides, without involving the convoluted synthesis of intricate linkers and toxic processes.

In this study, a facile and effective strategy to modify the inorganic silicon (Si) wafer surfaces with zwitterionic poly(sulfobetaine methacrylate) (pSBMA) polymer grafting via thermal-induced polymerization is proposed. During this polymerization, the initiator organosilane molecules were chemically bounded to the Si wafer surfaces and the pSBMA polymers were formed in situ onto the substrates in a subsequent thermal-induced polymerization reaction. A series of pSBMA-grafted Si wafer surfaces with varying polymer thicknesses and packing densities were prepared by changing the concentration of the monomer (SBMA) solution. The relationships between the pSBMA grafting density, the physicochemical properties and the biointeractions of the modified Si wafer surfaces with protein and blood cells were investigated. This protocol was further employed on various polymeric, ceramic, and metal biomaterial surfaces including porous and dense poly(tetrafluoroethylene) (PTFE), dense poly(propylene) (PP), poly(vinylidene fluoride) (PVDF), aluminium oxide (Al_2O_3), silicon dioxide (SiO_2), biomedical grade titanium (Ti) and stainless steel (SUS) to evaluate the universal applicability of pSBMA grafting on a wide range of organic and inorganic biomaterials.

2. Materials and methods

2.1. Materials

Polished silicon wafers were purchased from the Wafer Works Corporation. Aluminium oxide (Al_2O_3) was purchased from YIA CHUAN International Co., Ltd. Silicon dioxide (SiO_2) was purchased from KINIK Co. Polished biomedical grade titanium (Ti) and stainless steel (SUS 316L) were purchased from Titanium Industries Asis, Inc. and Walsin Lihwa Corporation, respectively. Porous and dense poly(tetrafluoroethylene) (PTFE) and poly(vinylidene fluoride) (PVDF) membranes were purchased from Millipore Co. Polypropylene (PP) membrane was purchased from Membrane Solutions LLC. 3-Trimethoxysilyl propyl methacrylate was purchased from ACROS Organics. The 2,2′-azobis-isobutyronitrile (AIBN), [2-(methacryloyloxy)ethyl]dimethyl(3-sulfopropyl)-ammonium hydroxide (sulfobetaine methacrylate, SBMA) macro monomer was purchased from Monomer-Polymer & Dajac Laboratories, Inc. Bovine serum albumin (BSA), tetrahydrofuran (THF, HPLC grade) and ethanol (absolute 200 proof) were purchased from Sigma–Aldrich. Fibrinogen (fraction I from human



Scheme 1. Schematic description for the surface modification of Si wafer: (a) silanization with 3-aminopropyl trimethoxysilane and (b) graft polymerization with SBMA via thermal-induced radical polymerization.