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Review

Patterned and switchable surfaces for biomolecular manipulation

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Abstract

The interactions of biomolecules and cells with solid interfaces play a pivotal role in a range of biomedical applications and have therefore been studied in great detail. An improved understanding of these interactions results in the ability to manipulate DNA, proteins and other biomolecules, as well as cells, spatially and temporally at surfaces with high precision. This in turn engenders the development of advanced devices, such as biosensors, bioelectronic components, smart biomaterials and microarrays. Spatial control can be achieved by the production of patterned surface chemistries using modern high-resolution patterning technologies based on lithography, microprinting or microfluidics, whilst temporal control is accessible through the application of switchable surface architectures. The combination of these two surface properties offers unprecedented control over the behaviour of biomolecules and cells at the solid–liquid interface. This review discusses the behaviour of biomolecules and cells at solid interfaces and highlights fundamental and applied research exploring patterned and switchable surfaces.

Keywords: Surface patterning; Switchability; DNA adsorption; Spatial control; Temporal control

Contents

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1. Introduction

Advanced biodevices that are able to control the behaviour of biomolecules at surfaces in both space and time are promising tools for elucidating solutions to many biologically based problems and are of particular interest in terms of medical devices and technologies. The biomolecules of interest include proteins and shorter peptide chains, DNA, RNA, oligonucleotides (oligonucleotides are short (2–50) bp of typically single stranded DNA), lipids and polysaccharides, as well as larger assemblies of these biomolecules, in particular living cells. Examples of such devices can be found in microarray technology, in "smart" drug delivery, biosensing, bioelectronics and tissue engineering [1–6]. The development of a number of high-resolution patterning techniques coupled with functional surface chemistry has enabled the formation of surfaces that offer stringent control over the adsorption of biomolecules and cells in space [7]. Furthermore, the development of switchable surfaces that are responsive to a particular signal and that switch between disparate properties, such as hydrophobic/hydrophilic, positive/negative net charge or even swollen/condensed layers, has added a new dimension to biomolecule manipulation. Individually, these processes have enabled the production of a number of advanced biodevices. More recently these patterning and switching techniques have been combined, producing devices that are able to control biomolecules and cells in both space and time, offering an unprecedented ability to manipulate biomolecular behaviour [8].

The manipulation of biomolecules at interfaces is an important field of investigation for the creation of biodevices, and has been dominated by work on DNA and proteins. This review, therefore, focuses on studies conducted using DNA and proteins. Several techniques are highlighted that lead to patterned or switchable surfaces, with a particular focus on techniques that allow the manipulation of biomolecules in both space and time. Furthermore, this review looks at the manipulation of living cells at interfaces, an area that is dependent on the ability to manipulate biomolecules.

2. Surface manipulation of biomolecules and cells

The ability to control biomolecules at the solid/liquid interface requires a sound knowledge of the behavioural characteristics of biomolecules. The manipulation of biomolecules is significantly different from the manipulation of smaller molecules or synthetic polymers. Weak forces, such as hydrophobic interactions, are able to play a significant role given the ability of these biomolecules to form multivalent interactions. The size of these molecules also plays a considerable role in regard to their behaviour at surfaces; for example, larger molecules tend to have a lower rate of surface adsorption when compared with smaller molecules, which adsorb, desorb and diffuse more readily from and to the surface [9]. Due to the significance of these issues in a variety of biomedical applications, a significant body of work has examined the forces that determine the fate of biomolecules at surfaces and how their shape and structure influences the thermodynamics and kinetics of surface adsorption. The adsorption of DNA to a surface is governed by three types of non-covalent interactions associated with the functional groups of DNA: electrostatic forces mediated by the negative charge of the phosphate groups, and hydrophobic effects and hydrogen bonding mediated by the nucleobases [10,11]. Thus, a common approach to adsorb DNA to a surface consists in the provision of positively charged coatings [12,13].

The essence of how proteins behave at surfaces depends largely on their primary structure, that is, the sequence of amino acids making up the protein. There are four main properties of amino acids that influence the behaviour of proteins: polar, non-polar, anionic and cationic. Thus, the main two interactions of proteins with surfaces, like in the case of DNA, are electrostatic and hydrophobic interactions. Living cells exist in nature within the extracellular matrix (ECM), which is a network of biomolecules forming the framework that cells attach to and are supported by. This matrix is composed largely of polysaccharides and various proteins; and it is these proteins, in particular collagen (CN), fibronectin (FN) and vitronectin, that cells use to attach to the ECM. Thus, the adhesion of cells to a tissue is mediated by proteins that are already present on that tissue or that the cell produces itself. Likewise, in vitro cell–surface interactions can be controlled via the control of biomolecule–surface interactions as most cell–surface interactions depend on the presence of an interfacial biomolecule layer, with proteins playing the most important role [7].

As well as chemically initiated cell attachment, the effects of topographical cues to initiate and control the