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Feature Article

Surface-initiated controlled radical polymerization enhanced DNA biosensing

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ABSTRACT

The surface chemistry at the DNA recognition and binding interface plays an important role in determining the performance of DNA microarrays and DNA biosensors. Surface-initiated controlled radical polymerization (SI-CRP) reactions represent a powerful toolbox to generate microarray and biosensor surfaces with enhanced DNA recognition and binding properties or to amplify and transduce these events. Surface-initiated polymerizations generate thin films in which all polymer chains are tethered with one chain end to the underlying surface and are also referred to as polymer brushes. SI-CRP reactions possess a number of features that make them highly attractive to engineer the properties of biosensor interfaces. First of all, the thickness of the films can be precisely adjusted to match the requirements of the specific biosensor format. Secondly, the grafting density of these films can be tuned to optimize binding kinetics and capacity. Finally, being a bottom-up technique, SI-CRP can also be used to modify complex, patterned or structured biosensor substrates with a conformal DNA recognition and binding interface. This article provides an overview of the state-of-the-art on the use of SI-CRP techniques to enhance or facilitate DNA biosensing. On the one hand, SI-CRP techniques have been used to generate high binding capacity surface coatings. On the other hand, these reactions have also been demonstrated to be powerful tools to amplify DNA recognition and binding and allow visual detection. The examples discussed in this article not only underline the potential of SI-CRP reactions to engineer the properties of biosensor interfaces, but also, together with future advances in these polymerization techniques, provide exciting opportunities to further enhance the performance of DNA microarrays and DNA biosensors.

Contents

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1. Introduction

DNA microarrays [1] and biosensors [2] are analytical devices that explore the unique sequence selectivity of the DNA hybridization process to detect target DNA sequences [3]. This is of great relevance for medical diagnosis [4,5], for forensic investigations [6] as well as for fundamental studies, such as e.g. gene expression analysis [7–10].

In essence, for both DNA microarrays and DNA biosensors, target detection is the outcome of a 3-step process that involves (i) immobilization of the probe DNA; (ii) hybridization of the probe DNA with the target sequence and (iii) detection; i.e. transduction of the hybridization event into a measurable signal [11,12]. In case of a DNA biosensor, probe immobilization takes place directly on the transducer surface [2]. The hybridization of the target sequence depends on the stability, accessibility and reactivity of the surface-bound DNA. As a consequence, the immobilization of the probe DNA and the surface chemistry at the DNA recognition and binding interface are critical aspects in the development of DNA biosensors [13].

A variety of strategies has been developed for the immobilization of probe DNA, which includes the use of electrostatic interactions (e.g. using positively charged surfaces), non-specific adsorption (e.g. on graphite surfaces), highly specific non-covalent interactions (e.g. using avidin/streptavidin–biotin binding) as well as covalent surface attachment [11]. The latter approach typically involves the use of surfaces that present aldehyde or epoxy groups, which can undergo reactions with amino-modified probe DNA, or explore the chemisorption of thiol modified probe DNA on gold substrates. In addition to immobilizing the pre-synthesized nucleotides, arrays of surface-attached probe DNA can also be prepared via *in-situ* synthesis from appropriately functionalized surfaces [12,14].

In addition to two-dimensional substrates such as e.g. glass slides [15–17] or carbon or gold electrode surfaces [18–22], there has also been an increased interest in the use of polymer-based DNA immobilization platforms for the development of DNA biosensors or microarrays. The main attractive feature of these polymer-based interfaces is that they provide a three-dimensional platform with a much higher probe binding capacity as compared to the typical two-dimensional substrates. Examples of such polymer based three-dimensional substrates that have been used include nitrocellulose films [23,24], as well as various hydrogel based coatings [25–47] which can be prepared either *in situ* or by deposition of pre-synthesized polymers.

The aim of this article is to illustrate the opportunities that are provided by surface-initiated controlled radical polymerization (SI-CRP) techniques for the development of DNA biosensors or DNA microarrays. SI-CRP generates densely packed assemblies of polymer chains that are tethered to the surface with one chain end and which are commonly referred to as polymer brushes [48–51]. SI-CRP techniques possess a number of unique characteristics that make them ideally suited for the development of three-dimensional polymer-based DNA biosensor and microarray interfaces. First of all, the controlled/"living" nature of the SI-CRP process allows to precisely control the thickness of the polymer interface, which can be advantageous e.g. for waveguide-based sensors [52]. Secondly, a variety of strategies is available that can be used to tune the grafting density of polymer brush thin films, which allows to engineer the accessibility and probe binding capacity of the interfaces. Finally, being a "bottom-up" methodology, SI-CRP can also be used to generate well-defined and conformal biosensor and microarray interfaces on geometrically complex substrates, such as e.g. (nano)porous membranes [53,54]. In addition to "bottom-up" synthesis via surface-initiated controlled radical polymerization, polymer brushes can also be prepared via the so-called "grafting-onto" strategy, which involves coupling pre-synthesized polymers to an appropriately functionalized surface. This strategy has also been successfully used to prepare DNA binding and detection interfaces [55–59]. As compared to surface-initiated polymerization strategies, the grafting-onto approach generally leads to polymer brush films with lower grafting densities and is restricted to relatively thin polymer brush films. This article exclusively concentrates on polymer brushes obtained via the "grafting from" strategy using SI-CRP methods.

The remainder of this article is organized in three sections, each of which highlights one specific class of polymer brush based DNA biosensing or microarray platforms. First, the use of SI-CRP to generate polymer brush interfaces that can covalently bind probe DNA will be discussed (Fig. 1). The second class of polymer brush

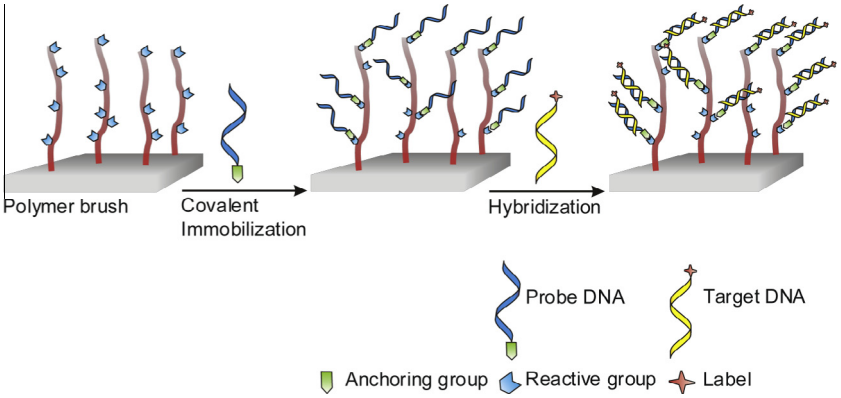

Fig. 1. Covalent immobilization of probe DNA on a polymer brush.

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