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Towards the design of universal immunosurfaces for SPR-based assays: A review

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ABSTRACT

Surface biofunctionalization, including chemical activation and attachment of the bioreceptor, is an essential step to provide reliable detection of biomolecular binding events monitored by Surface Plasmon Resonance (SPR), the most employed optical biosensor, and other biosensor techniques. Recent progress in the area of immobilization procedures are aimed at producing reproducible interfacial surfaces that enable the sensitive and specific recognition of the analyte. Antibodies are still the most employed bioreceptors for SPR assays. A wide range of strategies have been proposed to maximize the SPR immunosensor performance by controlling the stability and orientation of the immobilized antibody. This article reviews the most recent advancements in random and oriented antibody immobilization approaches for SPR biosensing applications, with a special focus on the research that have been done to find universal linkers, which can allow the use of the same functionalized surface for different applications.

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1. Introduction

The interest on Surface Plasmon Resonance (SPR) biosensor as a label-free tool for monitoring binding events in real time has been growing exponentially since the first publications expanding to clinical, environmental and food analysis applications [1,2]. Although SPR technology primarily focused on the improvement of the design and the miniaturization of the technological platforms [3], the feasibility of high performance SPR devices relies mostly on the correct incorporation and functionalization of the biological receptor recognition layer [1].

SPR biosensors commonly use antibodies as bioreceptors to recognize its complementary target. Although recent progress in biotechnology have led to the design of new recognition molecules as aptamers or imprinted polymers [4], theoretically able to replace antibodies, antibody-based assays are still the first choice for studying biomolecular interactions due to their superior performance. The production of antibodies can be directed against a large variety of molecules ranging from low to high molecular weight, as pesticides, hormones drugs and intact cells. Antibody

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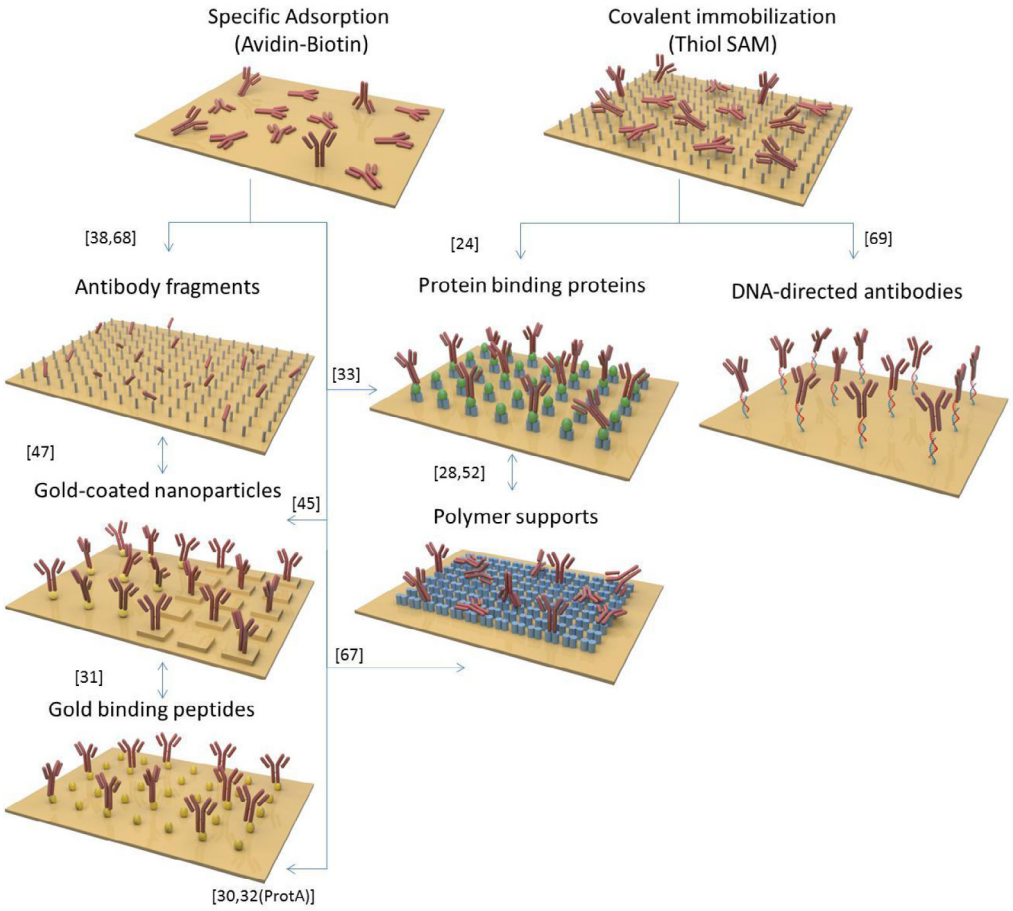

Fig. 1. Novel immobilization strategies based on combinations of common and recent developments of surface functionalization.

production can be dedicated and expensive but the excellent properties of antibodies like affinity, selectivity and stability make immunoassays one of the most robust molecular biorecognition systems.

The selection of the immunoassay format frequently relies upon the nature and characteristics of the analyte which has to be determined. In a typical enzyme-linked immunosorbent assay (ELISAs) antibodies need to be labeled in order to obtain a detectable signal, whilst immunosensors as SPR allow direct determinations in real-time without the need of labels or additional steps [5]. Monitoring of immunoresponses by SPR biosensor can be obtained by using either the antigen or the antibody as ligands. For analytes with a molecular weight over 1000 Da, the use of antibodies as ligands is preferred so that the antibody immobilized onto the sensor surface may recognize its complementary antigen in a simple, fast and direct manner.

A number of immobilization models have been reported for the achievement of maximum immunosensor consistencies while preserving the biological activity of immobilized antibodies. The immunosurface stability is crucial since it prevents antibody denaturation and non-specific binding during the immunointeraction. The formation of well-ordered interfaces without damage of the immobilized antibodies is also an essential aspect for the achievement of reliable and sensitive biosensor platforms. The search for a universal immobilization method is still beyond our reach and many new immobilization techniques have been studied during the last years to achieve this goal. Fig. 1 shows common and recent developments of surface biofunctionalization strategies.

Immobilization designs can exploit random or orientated formats in order to obtain the maximal functionality by enhancing the immunosensor capacity and/or the orientation of the antibody binding sites. Discussion on random and orientated antibody immobilization strategies has been addressed in some studies [6]. In general, random immobilization formats succeed in achieving higher surface coverages while strategies based on the orientation of antibodies provide better sensitivities for analyte detection. Random orientation of antibodies can be affected by steric hindrance and non-specific protein adsorption, resulting in antibody inactivation and lowest antigen binding capacity [7]. As a consequence, the oriented immobilization of antibodies, from site-directing methods to protein-binding proteins, is preferable since it affords chemical stability and optimal availability of the functional groups. The analytical performance between several random and oriented immobilization strategies is compared in Table 1.

The concern on the value of selecting the appropriate immobilization method for measuring antigen-antibody interactions [8] is demonstrated by the number of publications released every year. This review focuses on the recent advances of SPR immobilization strategies for immunoanalytical formats. In particular, we concentrate on the current trends based on the combination of traditional and novel biotechnological alternatives, like fusion proteins, polymer brushes and intact-fragmented antibodies, recently developed for the design of universal interfaces. Special attention has been paid to the functionalization of SPR biosensor surfaces with major applications in clinical diagnostics and real-time analysis.