DEVELOPMENT OF A NOVEL OPTOELECTRONIC SENSOR PLATFORM

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INTRODUCTION

As of now, countless sensors have been created with various applications within the health industry, to monitor the well-being of a person and to screen for diseases. However, most of these sensors have inherent limitations such as size, cost, relatively high limits of detection and they do not provide real-time- and point-of-care measurements. An ideal biosensor would be of compact and portable design and would perform non-invasive (from saliva, urine, etc.), real-time-measurements of the biomarkers of interest in a reliable and fast manner. The following concept is one attempt, to conquer this huge challenge. In this approach, two sensor techniques (SPR and FET – optical and electronic) are used to compare complement sensor responses.

BACKGROUND

Since its introduction in the 1990s, Surface Plasmon Resonance (SPR) has proven to be among the best technologies to investigate the specificity, affinity and binding/dissociation kinetics of macromolecules. SPR has also been commercialized and used for routine analysis in laboratories all over the world (e.g. Biacore, GE Healthcare). For detecting interactions with the SPR, no labels are required, which bypasses such problems, as steric hindrances or structural changes due to labeling.(*2*) The sensing principle is based on surface plasmons which are created on a flat metal-dielectric interface (in SPR sensors, usually gold is used as metal) upon radiation with a laser. In the Kretschmann geometry (Fig 1.), polychromatic light travels through a high refractive index prism at a specific angle, exciting plasmons on the surface of the metal, which drops the intensity of the light entering the detector. This angle is called a resonance angle. Upon a binding event on the surface the refractive index of the metal surface changes and thus also the resonance angle is modified.(*3*) Despite the many advantages of this method, SPR devices are usually very big benchtop systems, expensive (>10k €) and have an intrinsic size limitation of the analyte (> 3 kDa).

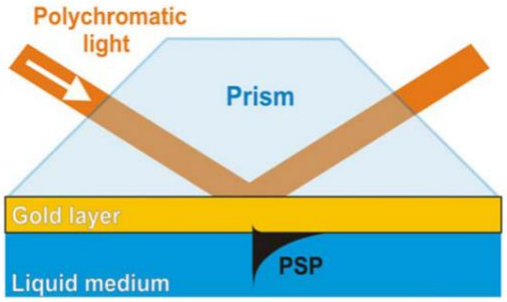

Figure 1. The excitations of PSP's in Kretschmann geometry of an ATR method by a polychromatic light (3)

In search of solving some of the above-mentioned problems, the concept of a field-effect transistor (FET)-based biosensor has attracted a lot of attention over the last decade. A FET consists of an insulator, a semiconductor and three electrodes. The *source* and the *drain* electrodes are in direct contact with the semiconductor, while the third, the *gate*, is isolated from the semiconductor by the *insulator*. (Fig 2.) By applying a voltage between the *gate* and the *source/drain*

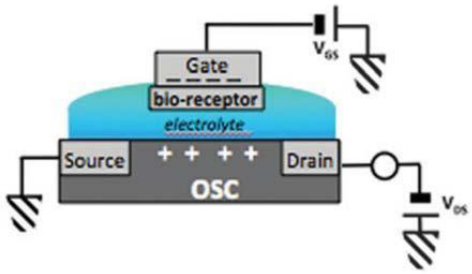

Figure 2. Schematics of an OFET. OSC designates organic semi-conductor (1)

electrodes, charges of opposite sign are induced at the semiconductor-dielectric interface. Because the charges in the semiconductor are mobile, current will flow in the channel when an additional voltage is applied between *source* and *drain*. If a biorecognition event is taking place on either the *gate* or semiconducting interface, the change in capacitance will modulate the overall source-drain current (Equation 1).(*4*) Hence, even small molecules (<200 Da) can introduce signal changes and allow for ultra-low detection. However, one of the main challenges of electronic biosensing are reproducibility and the prevention of unspecific binding events.

$$I_{DS}^{sat} = \frac{W}{2L} C_i \mu (V_{GS} - V_T)^2$$

Equation 1. The relationship between voltage and current within a FET

RESULTS AND DISCUSSION

Considering the weaknesses of both systems, the idea arose to measure optical- (SPR) and electronic (FET) sensor response, compare the results and, therefore, complementing each other and negating the drawbacks of the individual approaches. We benchmark the experimental FET sensors with more established SPR tools in order to test for the scope and limitations of the new system. In our prototype a flow cell design is used to measure the FET signal as the current between drain and source electrode and an additional flow cell for the SPR read-out on a gold surface as source of surface plasmons. An electrolyte containing the analyte is used as a dielectric material, enabling ultra-low voltage operations (Fig. 3).

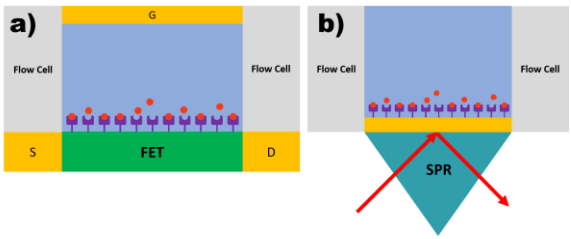

Figure 3. The scheme of the measurement set-up for FET (a) and SPR (b) read-out

In preliminary results we demonstrate the capability of the system for biotin-neutravidin as well as PNA-DNA and layer-by-layer (LBL) sensing. With our new platform we can investigate a biosensing event from an optical and electronic point of view. One advantage of this system is the possibility to obtain different analyte properties: with the SPR measuring the mass of the bound analyte and with the FET measuring its charge. Currently we also use this tool for smell sensing applications. For this, odorant binding proteins (OBPs) are used as biorecognition elements for odor molecules (<200 Da).

OUTLOOK

One could also use this system e.g. for blood analysis and obtain not only the information about the quantity and quality of selected biomarkers, but also obtain information about their biological state (isoelectronic point) and pH of the solution at the same time.

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