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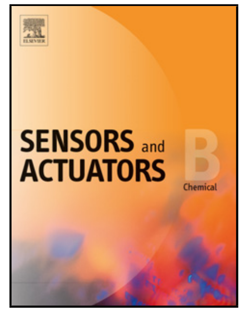

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Surface-plasmon optical-heterodyne clock biosensor

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Highlights

- A novel SPR interrogation/readout approach is implemented
- An optical method to detect chemical reaction via time/frequency measurements is demonstrated
- Performance competitive with state-of-the-art research grade SPR sensors is obtained
- The technique is well suited to integration in ultra-compact devices

Surface-plasmon resonance (SPR) sensors represent a formidable technology for molecular biology and bioanalytics applications. Here, we devise a new interrogation architecture that transforms a standard SPR chip into an optical-heterodyne clock detector comparable with the best SPR instruments. The key ingredients are (i) the conversion of refractive-index changes on the SPR chip into frequency shifts of an oscillatory electronic signal (ii) a differential probe & reference optical-cavity scheme that cancels out most source/detector noise contributions. A rigorous characterization of the sensor performance with the integration time demonstrates a refractive-index resolution on the 10^{-8}-RIU level over a 1-s timescale using a bare, unstabilized SPR element. A bio-sensing test with a functionalized surface interfaced with a microfluidic flow-cell is carried out, showing detection of streptavidin via covalent bond down to concentrations of 90 fg/mm^2.

Keywords

Surface Plasmon Resonance, Biosensing, Optical Resonator, Heterodyne detection

1. Introduction

Plasmonic sensors are a pivotal tool for detection and investigation of molecular interactions having applications in important areas, such as medical diagnostics and molecular biology [1-5]. Over the last two decades, SPR biosensors have become a mature technology and numerous optical platforms have been proposed and developed along with proper chemical functionalization protocols [6-14]. Yet, the resolution of SPR instruments is still insufficient to detect low-molecular weight analytes (< 200 Da), e.g. proteins and hormones, at very low concentration. To address these issues, a number of functionalization strategies have been proposed to amplify the binding signal of target molecules [15,16]. In parallel, novel plasmonic platforms have been developed to enhance the detection sensitivity, such as those based on localized surface plasmons with metallic nanoparticles [17-20] and hyperbolic metamaterials [21-25]. However, even with such advanced platforms, the refractive index (RI) resolution of a plasmonic sensor is still affected by fluctuations of various nature on the detected signal. Indeed, a recent comparison between a theoretical model and the best reported resolution levels [7] clearly indicates that the performance of diverse SPR set-ups is basically independent of the used excitation platform, the limiting factor being mainly attributed to intrinsic instabilities of the radiation source (intensity noise) and noise in the opto-electronic system [26-28]. Strong improvements can be obtained with interferometric phase-detection methods, applied to gas [29] and liquid sensing [30-32], albeit they rely on delicate setups and their sensitivity strongly depends on the arm length, which hardly comply with the miniaturization demand of real applications. In particular, a significant suppression of low-frequency noise is achieved with differential schemes [30, 31], where a probe and a reference field are simultaneously used for the interrogation. A higher degree of noise immunity can be obtained using heterodyne detection methods, also based on dual-polarization schemes [33, 34] and Zeeman lasers [35, 36].

Here, we present a novel optical method that transforms refractive index variations at a SPR chip into a radio-frequency oscillatory signal, i.e. an optically-generated clock. The method relies on the birefringence induced by exciting a surface plasmon on the mirror of an optical cavity, whereby two orthogonally-polarized simultaneously-resonant modes are excited and their frequency difference is measured. Compared to previous interferometric techniques [29-32], the perfect common-path propagation of the two resonant cavity modes, serving as probe and reference fields, leads to active cancellation of the cavity mechanical fluctuations. It