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DOI: 10.3969/j.issn.1003-501X.2017.02.003

Research progress in applications of LSPR biosensor for clinical medicine detection

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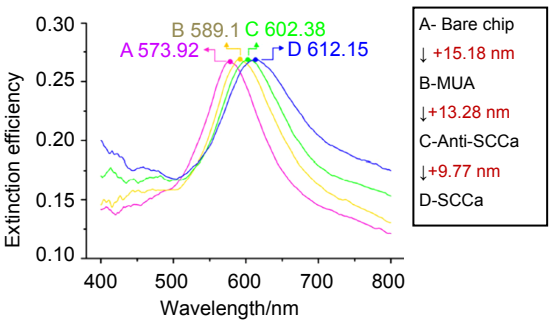

LSPR spectra for processing steps of immobilization and detection of 100 pM SCCa.

Abstract: Tumor biomarker plays an important role in early diagnosis, treatment evaluation, and prognosis prediction for human medicine and cancers. At present, the human serum tumor biomarker detection methods have defections, such as radioactive contamination, complicated operation, long detection time and high cost, which limit the widespread applications in clinic screening. The LSPR biosensor, a novel type of optical fiber-based biosensor, uses an optical fiber or optical fiber bundle to transform biological recognition information into analytically useful signals in the LSPR spectrum, which is suitable for clinical detection because of the advantages of high sensitivity, high specificity, label free, portable equipment and lower cost. In this paper, the principle and research progress of local surface plasmon resonance biosensor, especially the main findings of our study group, are reviewed.

In this work, the physical characteristics of metal nanostructure were calculated and simulated by discrete dipole approximation (DDA). Combining with reactive ion etching (RIE), nanosphere lithography (NSL) was applied to produce the triangle nanostructures. Eventually, a triangle silver nanostrure array with high refractive index sensitivity was produced. Meanwhile, a primitive ultraviolet-visible spectrometer was constructed to make spectro-analysis. An effective biological sensitive layer was fabricated on the surface of nanostructures by means of 11-mercaptoundecanoic acid (MUA) amine couple method.

To explore the clinical applications of this LSPR biosensor, we firstly used it to detect the microalbuminuria. The anti-human albumin antibody was immobilized on the sensor surface. Different concentrations of commercial albumin and albumin in urine samples from patients were determined according to the peak of LSPR extinction spectra. The biosensor displayed a detection limit of 1 ng/ml and wide dynamic range from 1 ng/ml to 1 mg/ml. Secondly, the anti-HE4 antibody as a probe, which could distinctly recognize HE4, an important ovarian tumor marker, was effectively assembled onto the nanochip surface. Human serum samples were detected and compared using an enzyme-linked immunosorbent assay. The linear range was between 10 pM and 10000 pM, with a detection limit of 4 pM and an excellent correlation between it and enzyme-linked immunosorbent assay. Thirdly, we made a functionalized chip surface with monoclonal anti-SCCa antibodies on the silver nanoparticles for distinct detection of SCCa. Different concentrations of SCCa were successfully tested in both buffer and human serum, with a linear quantitative detection range of 0.1~1000 pM. Lastly, the specific DNA probe was immobilized on the nanochip surface. Wild-type and mutant p53 DNA was detected. The low detection limit was 10 nM, with a wide dynamic range (10 nM~10 μM). Importantly, this sensor could effectively discriminate against single base mutations. By comparing with traditional methods, the advantage of the LSPR biosensor, such as wider detection range, label free, simple operation and short time was clear. It could provide a promising platform for developing clinical diagnostic applications.

Keywords: localized surface plasmon resonance; biosensor; clinical medicine; tumor biomarker

Citation: Duan Ruiqi, Yu Xiuzhang, Lan Zhu, *et al*. Research progress in applications of LSPR biosensor for clinical medicine detection[J]. *Opto-Electronic Engineering*, 2017, **44**(2): 152-160.

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