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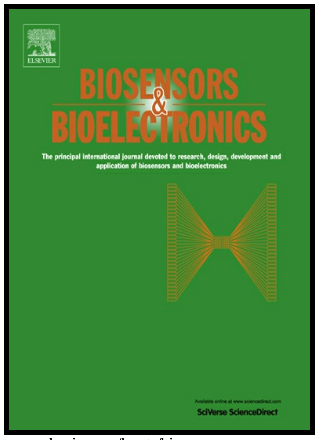

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A label-free cardiac biomarker immunosensor based on phase-shifted microfiber Bragg grating

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Abstract—Fiber optics evanescent field based biosensor is an excellent candidate for label-free detection of cardiac biomarkers which is of great importance in rapid, early, and accurate diagnosis of acute myocardial infarction (AMI). In this paper, we report a compact and sensitive cardiac troponin I (cTn-I) immunosensor based on the phase-shifted microfiber Bragg grating probe which is functionalized. The fine reflective signal induced by the phase shift in modulation significantly improves the spectral resolution, enabling the ability of the sensor in perceiving an ultra-small refractive index change due to the specific capture of the cTn-I antigens. In buffer, a log-linear sensing range from 0.1 to 10 ng/mL and a limit of detection (LOD) of 0.03 ng/mL (predicted to be as low as 10.8 pg/mL) are obtained. Furthermore, with good specificity, the sensor can be applied in test of cTn-I in human serum samples. The proposed sensor presents superiorities such as improved integratability and portability, easy fabrication and operation, and intrinsic compatibility to the fiber-optic network, and thus has a promising prospect in "point-of-care" test for cardiac biomarkers and preclinical diagnosis.

Keywords—Optical microfibers; Phase-shifted Bragg gratings; fiber optical immunosensors; Cardiac troponin I; Acute myocardial infarction diagnosis

1. Introduction

Cardiovascular diseases (CVD) killed 17.5 million lives in 2012 and the number keeps growing, according to the newest report of the World Healthy Organizer (WHO, 2015). The acute myocardial infarction (AMI) or heart attack has been the one of the leading culprits of the mortality worldwide (Thygesen et al., 2012), which attributed to the blockage of the coronary arteries, triggering the scarcity of blood supply to the heart. AMI causes irreversible damage to the myocardial cells within a short time and probably brings out various complications, severely threatening the patient safety (White and Chew, 2008). Therefore, test of cardiac biomarkers which specifically reflect the damage of the heart muscle in patient's blood is of utmost importance depending on not only the capability of filling the absences in traditional diagnosis, such as the electrocardiograph (ECG) (Mahajan and Jarolim, 2011; Mohammed and Desmulliez, 2011), but also the potential of prognosticating the AMI at very early stage (Fathil, et al., 2015).

Labeling immunoassay techniques, including enzyme-linked immunosorbent assay (ELISA) and fluorescence immunoassay are frequently-used and powerful tools for detection of cardiac biomarkers with high sensitivity. However, the requirements of complicated and professional labeling process, large amount of the samples as well as reagents, and considerably long turn-around-time (TAT)(Tuteja et al., 2016; Fan et al., 2008) barricade the progress of those methods towards AMI diagnosis which needs simple and quick test results for making clinical decision as well as providing medical care to patients. As a consequence, label-free biosensors are developed recently to satisfy the yearning of rapid, accurate, and "point of care" (POC) test solutions for AMI diagnosis and early screening (King et al., 2016).

The label-free biosensors for detection of cardiac biomarkers mainly rely on the transducers which are generally categorized by mechanisms including optics (Wu et al., 2017; Diware et al., 2017; El-Said et al., 2016; Pawula et al., 2016; Zhang et al., 2014; Tang and Casas, 2014), electrics (Jo et al., 2017; Kim et al., 2016; Tuteja et al., 2016; Shin et al., 2016), magnetics (Meyer et al., 2007), and acoustics (Lee et al., 2011), presenting good performances and potentialities due to their simplicity in tests.

As an important optical method of detection which is fast developing and maturing, the fiber optics based biosensor becomes an eligible candidate for *in-situ* test of cardiac proteins by virtue of its distinguished advantages such as accepted cost, small and smart structure, high accuracy, biological compatibility, electromagnetic immunity, free of light coupling and telemeasurement (Wang and Wolfbeis, 2016). Based on the evanescent or plasma wave on the fiber surface, the immunoreactivity of cardiac biomarkers could be directly transduced by the resonant wavelength shift via the change of the surface refractive index (Luo et al., 2017; Sridevi et al., 2015; Masson et al., 2004).

Microfiber, which was defined as the fiber with a diameter below 10 micron, allowed the transmitting light to further interact with the surrounding medium because of the larger evanescent field (Ismaeel et al., 2013; Tong et al., 2003). Bragg grating written in

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