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A highly sensitive and label free biosensing platform for wireless sensor node system

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ABSTRACT

In this paper, we propose a radio-frequency (RF) biosensor platform based on oscillation frequency deviation at 2.4 GHz. Its feasibility is experimentally demonstrated with the well-known biomolecular binding systems such as biotin–streptavidin and deoxyribonucleic acid (DNA) hybridization. For a basic principle of our biosensing system, the impedance of a resonator with the biomolecular immobilization is at first varied so that the corresponding change results in frequency change of an oscillator. Especially, to enhance the sensitivity of the proposed system, a surface acoustic wave (SAW) filter having a high-Q factor (~2000) is utilized. From the resulting component, even a small change of oscillation frequency can be transformed into a large output amplitude variation. According to the experimental results, it is found that our system shows the low detectable limit (~1 ng/ml) and fast response time (~real-time) for different target biomolecules, i.e. streptavidin and complementary DNA (cDNA). As a result, we find that our device is an effective biosensing system that can be used for a label-free and real-time measurement of the biomolecular binding events.

1. Introduction

During the last decade, radio-frequency (RF) systems for bio/medical applications received a lot of attention due to their suitability for non-invasive, non-contact, and non-destructive detection capability as well as their low cost and low power consumption characteristics (Buchli et al., 1989; Shen et al., 1997; Zhang et al., 2001). In recent years, the RF biosensor platforms have been expansively investigated for the diverse healthcare applications associated with wireless communication system including radio-frequency identification (RFID), sensor node and so on (Kim et al., 2006; Farahi et al., 2007; Sun et al., 2009; Malhotra and Chaubey, 2003). However, suitable biosensing devices and circuits have not been investigated at microwave frequencies. For this reason, various RF biosensing schemes have been introduced for sensing of the antigen-antibody reaction as well as of cells. For examples, the biosensing devices utilizing interdigital capacitors (IDCs), single-walled carbon nanotubes (SWCNTs) and metamaterial elements have been studied for the detection of label-free biomolecular interactions (Lee and Yook, 2008; Lee et al., 2010a, 2010b; Kallemudi and Gurbuz, 2011). In addition, the microelectromechanical system (MEMS)-based RF biosensors for living cell detection have been also studied (Dalmay et al., 2010a, 2010b; Grenier et al., 2010). These approaches reveal clear possibilities in RF biomolecular sensing, but they still bear key disadvantages, such as need of expensive equipment, complex measurement system, which is a RF probe system associated with vector network analyzer (VNA), and sophisticated micro-fabrication process. In case of metamaterial inclusions for biosensing, to enhance sensitivity of the biosensing scheme, a resonator of high-Q performance has been essentially required.

In the present work, an RF active sensing system based on oscillation frequency deviation (OFD) at 2.4 GHz (Kim et al., 2012) is applied for detection of well-known and important biomolecular binding systems, such as biotin–streptavidin and DNA hybridization. These coupling systems were employed as following reasons: the biotin–streptavidin coupling system can be utilized to study a wide variety of biological structures and processes. Actually, it has proven to be particularly useful in the detection and localization of antigens, glycoconjugates, and nucleic acids by employing biotinylated antibodies, lectins, or nucleic acid probes. Meanwhile, DNA hybridization is a molecular biology technique that can measure the degree of genetic similarity between pools of DNA sequences. In addition it is usually used as molecular diagnostic agents.

2. Materials and methods

2.1. Principle and configuration of system

Fig. 1(a) shows the operating principle of the proposed RF biosensing system. The system consists of an oscillator, a SAW filter, and a power detector. The biosensing mechanism of our system is as

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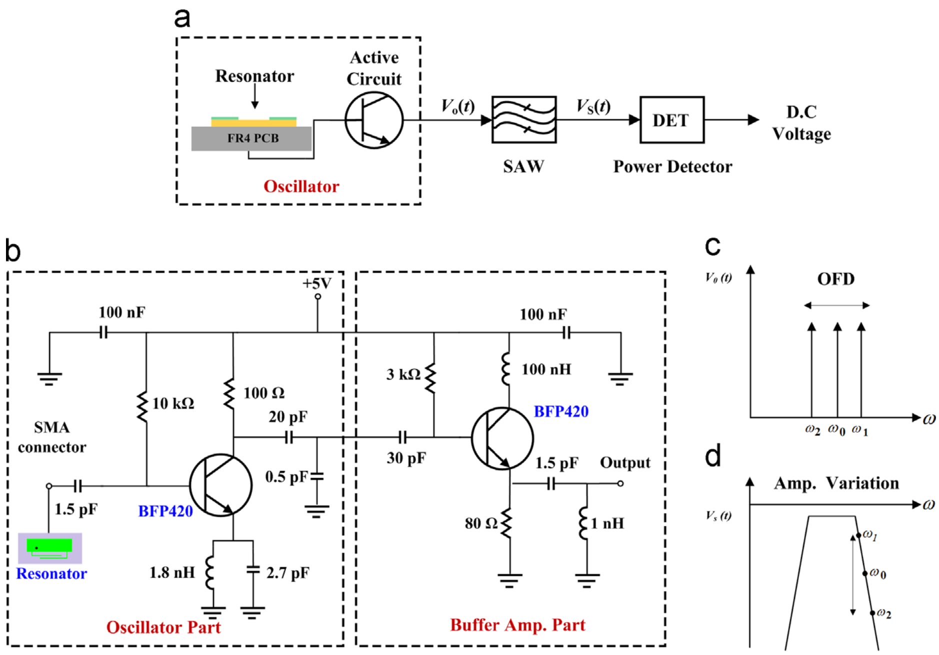

Fig. 1. Schematic diagram of proposed RF biosensing system. (a) Operating principle of the biosensing system. (b) Schematic of oscillator and buffer amplifier. Output spectra of the oscillator (c) and of the SAW filter (d).

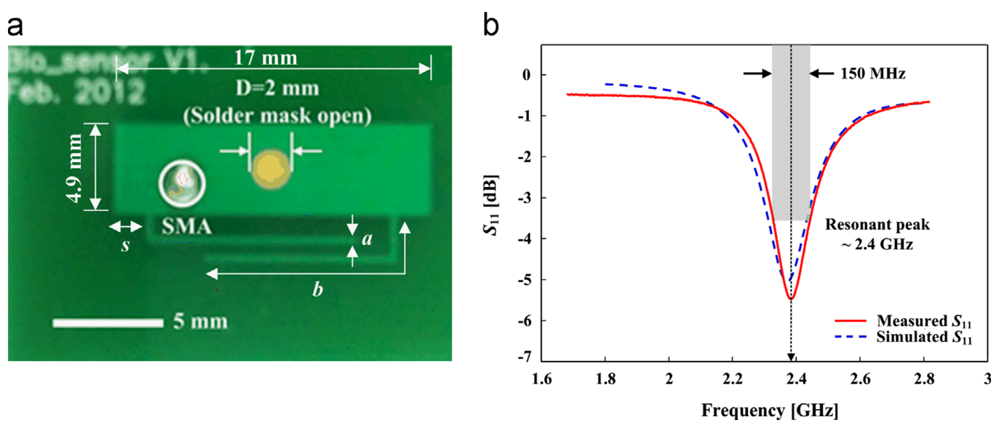

Fig. 2. Fabricated resonator for biosensing system and its resonant characteristic. (a) The fabricated resonator coated with masking layer (green) except sensing part. The length and width of the rectangular patch are 17 mm and 4.9 mm, respectively. The dimensions of the two folded arms are $a=0.3$ mm and $b=12.2$ mm, and these are symmetrically located at the corners of the rectangle at an offset of $s=0.3$ mm. (b) Simulated and measured result of the resonator. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

follows: first, the oscillation frequency is changed by the impedance variation of the planar resonator due to the biomolecular immobilization. Here, the immobilization has an effect on the surface characteristic of the resonator, thus changing the resonator impedance component, such as resistive (*R*), inductive (*L*), and capacitive (*C*). Moreover, the resonator plays important roles in sensing as well as feedback component in our system. Since the target biomolecules are much small in size and weight-mass, the frequency deviation due to the immobilization is extremely small. For above reason, with conventional circuit topologies the detection capability is not sensitive enough for medical applications. To overcome this difficulty, a surface acoustic wave (SAW) filter is used at the oscillator output to increase the sensitivity of the system. Assuming that the impedance variation and resulting frequency deviation are in the locking range of the oscillator, the amplitude of the SAW filter output can be maximized in the skirt frequency region. As a result, even though the frequency deviation is small, it can be transformed into a large output amplitude variation by the SAW filter. In the last stage, an RF power detector is adapted in the output of the SAW filter to transform the frequency deviation of the oscillator to the variation of DC voltage, which can be easily digitized for digital signal processing. With this approach, the oscillation frequency deviation can be eventually used for biosensing as illustrated in Fig. 1(a). In particular, Fig. 1(b) shows in detail the schematic diagram of the 2.4 GHz amplifier and the cascade type resonator combined with an emitter follower-type buffer amplifier (Takaoka and Ura, 1980; Regis et al., 1998). Here, the buffer amplifier of the emitter follower-type is used to prevent a strong mutual interaction between the oscillator and the filter because the oscillation condition can be changed by the rapid impedance variation at the skirt frequency range of the SAW filter. Fig. 1(c) and (d) represents the output spectra of the oscillator and the SAW filter, respectively.

2.2. Simulation and fabrication of sample

Fig. 2(a) shows the fabricated resonator associated with the oscillator in our system. This is fabricated on a dielectric substrate