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Capacitive biosensor based on vertically paired electrode with controlled parasitic capacitance

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ABSTRACT

A capacitive biosensor based on vertically paired electrodes with controlled parasitic capacitance is presented to improve the sensitivity of capacitive measurement. The vertically paired electrodes were fabricated with a parylene film as a dielectric layer, with the distance between the electrodes less than hundreds of nanometer. The problem of parasitic capacitance owing to the electrode configuration was analyzed according to the superposed area of the electrode. In this work, two kinds of vertically paired electrodes were fabricated to control the parasitic capacitance—square-type and circular-type electrodes with different superimposed areas of 21.8 (100%) and 9.3 (42%) mm^2 and the same electrode area of 9.4×10^{-5} mm^2, respectively. The effect of superimposed area of the vertically paired electrodes on capacitive measurement was analyzed using the electrodes. The sensitivity of capacitive measurement was observed to increase with a decrease in superimposed electrode area and frequency. Further, the effect of parasitic capacitance was estimated by computer simulation of the sensitivity of impedance and capacitive measurement when 10% change in R_S or C_S occurred. The results showed that adsorption of proteins could be sensitively measured when the parasitic capacitance decreased. Finally, the effect of superimposed area of the vertically paired electrodes was measured from the interaction between antigens (human serum albumin, HSA) and immobilized antibodies (anti-HSA antibodies).

1. Introduction

Capacitive biosensors for non-labeled detection of protein adsorption use two- or three-electrode systems [1–3]. Particularly for application in immunoassays [4–6], such capacitive biosensors are used to detect specific interaction between antigens and antibodies [7–10]. Capacitance is defined by the equation $C = \varepsilon \cdot A / d$, where ε, A, and d represent the dielectric constant, area of the electrode, and distance between the electrodes, respectively [11,12]. In principle, capacitance change can occur from the change in dielectric constant of the electrodes of capacitive biosensors upon replacement of water molecules ($\varepsilon_{water} = 80$) on the electrodes by proteins ($\varepsilon_{protein} = 20$), as shown in Fig. 1. As the area of electrode as well as the distance between the electrodes affects the sensitivity of capacitive measurement, the sensitivity can be improved by reducing the distance between the electrodes [13–15]. Among the various kinds of electrodes, interdigitated electrodes (IDEs) with many pairs of finger electrodes are frequently used for capacitive measurements [16–19]. In IDEs, the distance between finger electrodes affect the sensitivity of capacitive measurement. Although the sensitivity of capacitive measurement for non-labeled detection of proteins could be significantly improved by using IDEs with the electrode distance in sub-micrometer scale, the fabrication of such IDEs requires expensive processes based on e-beam lithography and stepper process [16,20,21].

Recently, a simple fabrication method for vertically paired electrodes was reported for capacitive detection of the interaction between antigens and antibodies, which could effectively reduce the distance between the electrodes to several hundred nanometers [22]. The vertically paired electrode was fabricated by sequential deposition of two gold electrodes, and a parylene film layer was used as a dielectric layer between the top and bottom electrodes. To expose the top and bottom electrodes, the constituent layers were sequentially etched from top to bottom, as shown in Fig. 2(a). As the parylene film could be deposited with a thickness of several hundred nanometers with high electric isolation, the vertically paired electrodes could be effectively fabricated. The exposed electrodes of the vertically paired electrodes were

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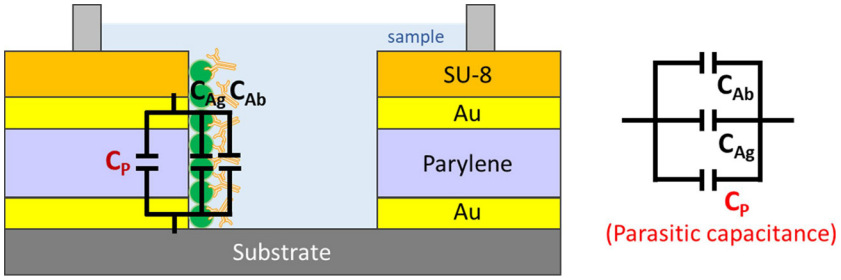

Fig. 1. Schematic view of capacitive biosensor based on vertically paired electrodes and the analog circuit for the capacitive detection of protein adsorption.

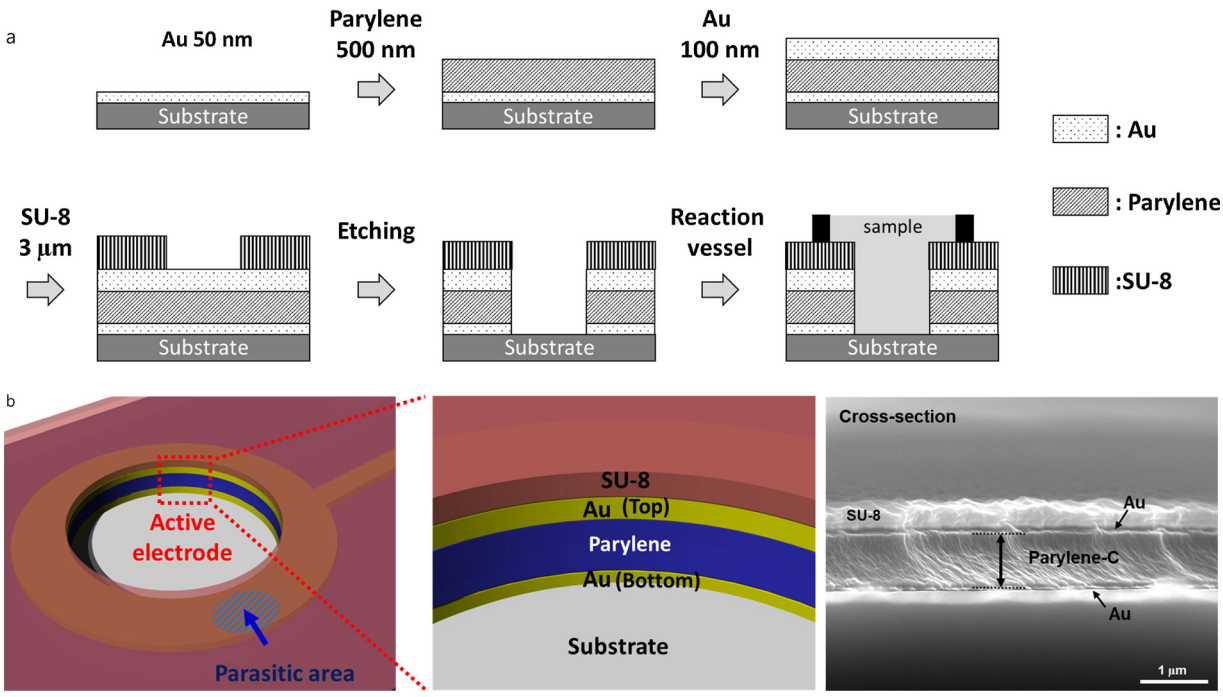

Fig. 2. Fabrication of vertically paired electrodes. (a) Schematic view of the fabrication process of the vertically paired electrode by sequential deposition and etching processes. (b) Side view of the vertically paired electrode with two exposed electrodes and a parylene film as a dielectric layer.

used for the capacitive measurement of specific interactions between antigens and antibodies. In vertically paired electrodes, a part of the electrodes, which are positioned in parallel and are unexposed to the sample solution, is called the "superimposed electrode area." As the parylene film dielectric layer was intercalated between the vertically paired electrodes, the electrode structure corresponded to a capacitor that generated a parasitic capacitance (C_p). When the capacitance of the exposed electrodes changed (ΔC) due to the adsorption of proteins from the selective antigen-antibody interactions, the parasitic capacitance from the parylene film was inevitably measured together with the capacitance change of the exposed electrodes (C_{signal}), as shown in Fig. 1. Therefore, the reduction of parasitic capacitance could improve the sensitivity of measurement of capacitance change on the surface of the exposed electrodes from the specific interaction between antigens and antibodies.

In this work, the effect of parasitic capacitance on capacitive measurement was analyzed by using two kinds of vertically paired electrodes with controlled parasitic capacitance and by computer simulation with the commercial software COMSOL™. Finally, the change in the sensitivity of capacitive measurement was estimated from the reaction between the immobilized antigens and antibodies using the two kinds of vertically paired electrodes.

2. Materials and methods

2.1. Materials

Human serum albumin (HSA), 3,3′,5,5′-tetramethylbenzidine (TMB), and other analytical grade chemicals were purchased from Sigma-Aldrich (Seoul, Korea), and anti-HSA antibodies were purchased from AbCam (Cambridge, UK). A negative photoresist (SU-8 2002) was purchased from MicroChem. Co. (Westborough, MA, USA), parylene-C dimers were purchased from Femto Science Co. (Korea), and Ag/AgCl reference electrodes were purchased from Warner Instruments LLC (Hamden, CO, USA). A Pt wire with 2-mm diameter was used as a counter electrode for cyclic voltammetry.

2.2. Electrode fabrication

Square-type and circular-type vertically paired electrodes were prepared on a soda lime glass substrate by sequential deposition of gold electrode (50 nm), parylene-C film (550 nm), gold electrode (100 nm), and SU-8 layer (2 μm). Two gold layers were sputtered by using metal masks to design square-type superimposed area (5×5 mm^2) and circular-type superimposed area (outer diameter = 4 mm), as shown in Fig. 2(b). Between the gold layers, a 550-nm-thick parylene-C film was thermally deposited by the following polymerization steps: 1) evaporation of parylene dimers at 160 °C, 2) pyrolysis at 650 °C for the