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Microwave dielectric resonator biosensor for aqueous glucose solution

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We report a near-field microwave biosensor based on a dielectric resonator to detect glucose concentration. A microwave biosensor with a high Q dielectric resonator allows observation of the small variation of the glucose concentration by measuring the shift of the resonance frequency and the microwave reflection coefficient S_{11}. We observed the concentration of glucose with a detectable resolution up to 5 mg/ml at an operating frequency of about $f=1.68$ GHz. The change in the glucose concentration is directly related to the change in the reflection coefficient due to the electromagnetic interaction between the dielectric resonator and the glucose solution. © *2008 American Institute of Physics.* [DOI: 10.1063/1.2968115]

There is a wide spread need for highly sensitive and stable glucose biosensors in clinical monitoring, biological research, and in the food processing industry.[1,2] Glucose biosensors have taken several forms, based on electrochemical, optical, piezoelectrical, thermal, or mechanical principles.[3–6] Amperometric enzyme electrodes hold a leading position among present glucose biosensor systems and have already found a large commercial market. However, the device is largely limited to monitoring patterns and trends and is invasive. Techniques with high sensitivity and efficiency for the detection of glucose concentration using a noninvasive technology are therefore of importance in biosensor construction. In order to better characterize the concentration of glucose, we take advantage of the evaluation capabilities using a microwave dielectric resonator. Microwave sensing techniques with high sensitivity have been developed.[7–10] The changes of glucose concentration due to a change in permittivity of the glucose solution were investigated by measuring the reflection coefficient S_{11} and fractional change in resonant frequency of the resonator. The change in the glucose concentration is directly related to the change in the reflection coefficient and resonant frequency shift due to an electromagnetic interaction between dielectric resonator and the glucose solution.

The glucose biosensor consisted of a dielectric resonator with cylindrical air gap coupled to a microstrip line at an operating frequency $f=1.68$ GHz, as shown on Fig. 1. The $\lambda/4$ dielectric resonator consists of a high temperature ceramic sample with a dielectric permittivity of 88 and dimensions of $14\times5\times7$ mm^3. A network analyzer was used in measuring the reflection coefficient S_{11} and the resonant frequency. All measurements were done at temperature of 25 °C. Glucose solution was dropped directly into the gap of the dielectric resonator. A metal strip on the dielectric resonator is used as an electrode that excites the TE_{01} mode in the dielectric waveguide.

The operation principal could be explained by the plane-wave solution model. An interpretation of the S_{11} magnitude in terms of medium parameters is written as[11]

$$S_{11} = 20\log\left|\frac{Z_{\rm in}^R - Z_0}{Z_{\rm in}^R + Z_0}\right|, \tag{1}$$

where Z_0 is the effective impendence of the microstrip line and equal to 50 Ω and Z_{in}^R is the real part of complex input impedance of the dielectric resonator with glucose solution. The dependence of permittivity on solute glucose concentration is approximately linear and is often expressed as the molar increment δ.[12] The permittivity of glucose solution is complex with $\varepsilon_g=(\varepsilon_w'+c\delta')-j(\varepsilon_w''+c\delta'')$, where ε_w is the permittivity of water ($\varepsilon_w'=77.75$ and $\varepsilon_w''=6.4$ for 1.7 GHz at 25 °C),[13] c is the concentration of the glucose solution, $\delta=\delta'-j\delta''$ is the increase in permittivity when the glucose concentration is raised by 1 unit [$\delta'=0.0577$ (mg/ml)$^{-1}$ and $\delta''=0.0015$ (mg/ml)$^{-1}$ at 25 °C].[9] The real part of the complex input impedance is estimated as

$$Z_{\rm in}^R = Z_a\varepsilon_d^{1/2}(1+\varepsilon_d k_a^2 l_d^2)\frac{[1+(\varepsilon_w'+c\delta')V_g\cdot k_a^2/(\pi h_g)]\cdot[\varepsilon_d+(\varepsilon_w'+c\delta')^2V_g\cdot k_a^2/(\pi h_g)]}{\varepsilon_d^3k_a^2l_d^2[1+(\varepsilon_w'+c\delta')V_g\cdot k_a^2/(\pi h_g)]^2+[\varepsilon_d+(\varepsilon_w'+c\delta')^2V_g\cdot k_a^2/(\pi h_g)]^2}, \tag{2}$$

a)Author to whom correspondence should be addressed. Electronic mail: klee@sogang.ac.kr.

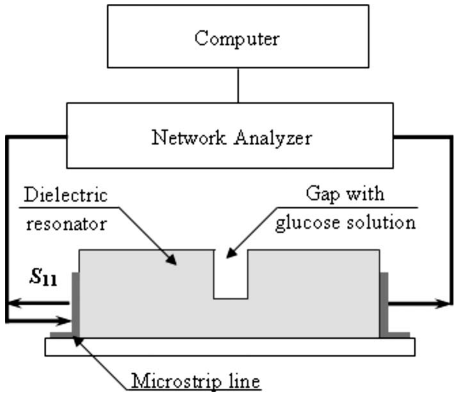

FIG. 1. Schematic structure of $\lambda/4$ dielectric resonator with cylindrical air gap coupled to a microstrip line.

where Z_a is the impedance of air (Z_a=377 Ω), k_a is the wave vector of air (k_a=36 m^{-1} at 1.7 GHz), l_d is the half width (l_d=2.5 mm), and ε_d is the dielectric permittivity (ε_d=88) of the dielectric resonator, h_g is the height (h_g=2 mm), and $V_g = \pi h_g l_g^2/4$ is the volume of the cylindrical gap in dielectric resonator (l_g=1.6 mm is the diameter of gap).

Inserting a dielectric gap in the resonator can be considered as a perturbation source in dielectric resonator cavity. The fractional change in the resonant frequency can be expressed, using perturbation theory,[11] as

$$\left|\frac{\Delta f}{f_0}\right| = \frac{\int_{V+\Delta V}([\mu+\Delta\mu]|H_0|^2 - [\varepsilon+\Delta\varepsilon]|E_0|^2)dv}{\int_V(\mu|H_0|^2+\varepsilon|E_0|^2)dv}, \qquad (3)$$

where ε, μ, and V are the unperturbed dielectric permittivity, susceptibility, and volume, E_0 and H_0 are the unperturbed electric and magnetic field, and $\Delta\varepsilon$, $\Delta\mu$, and ΔV are changes in the dielectric permeability, susceptibility, and volume, respectively. This relation indicates that the resonant frequency changes, depending on where the perturbation is located in the resonant cavity. Thus, the fractional change in resonant frequency depends on the interaction between the dielectric resonator and the aqueous glucose solution. The fractional change in the resonant frequency de-ionized (DI) water and glucose solution with different volumes and concentrations can be written as

$$\left|\frac{\Delta f}{f}\right| = \frac{2c\delta' V_g}{\varepsilon_d V_d}, \qquad (4)$$

where V_d is the volume of the dielectric resonator (V_d =490 mm^3).

We measured the microwave reflection coefficient S_{11} profile of aqueous glucose concentrations ranging from DI water to 300 mg/ml glucose concentration with increment of 50 mg/ml. The volume of glucose solution was 4 μl. As the glucose concentration increased, the dielectric permittivity of the glucose solution increased and the intensity of the reflection coefficient S_{11} increased and, at the same time, increased the fractional change in resonant frequency, as shown on Fig. 2. The theoretical curves were derived by using Eqs. (1) and (4). The permittivity of the aqueous glucose solution may be estimated by the intensity of the reflection coefficient and the resonant frequency shift. We found a good agreement with theory between the variation of reflection coefficient S_{11} and the frequency shift $|\Delta f/f|$ on the glucose concentration.

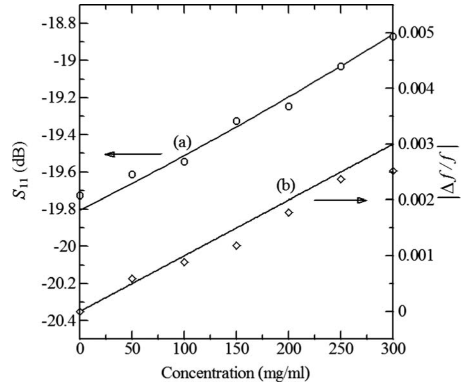

FIG. 2. Microwave reflection coefficient S_{11} (a) and resonant frequency shift $\Delta f/f$ (b) plotted as a function of the glucose concentration from DI water to 300 mg/ml with increment of 50 mg/ml. The solid lines show a fit to (a) Eqs. (1) and (b) (4), respectively.

From the linear relationship as a function of glucose concentration, as observed at lower glucose concentrations $\Delta S_{11}/\Delta c$=0.000 04 1/(mg/ml) in the linear scale. The root-mean-square statistical noise in reflection coefficient S_{11} was about 5×10^{-7} in the linear scale.[8,9] The measured signal-to-noise ratio (SNR) was about 38 dB. The smallest detectable change in concentration based on a criterion of SNR of 38 dB was about 10 mg/ml.

The reflection coefficient S_{11} and resonant frequency shift $|\Delta f/f|$ of glucose solution also depended on the volume of solution. As the volume of glucose solution increased, the reflection coefficient decreased while the frequency shift increased, as shown on Fig. 3. As the volume further increased up to 5 μl, the reflection coefficient and the frequency shift become saturated. The theoretical curves were derived by using Eqs. (1) and (4). We found a good agreement with theory between the variation of reflection coefficient and resonant frequency shift $|\Delta f/f|$ on the volume of glucose solution.

Figure 4 shows the reflection coefficient S_{11} (left axis) and resonant frequency shift (right axis) dependences on the temperature for the glucose concentration for (a) 1, (b) 10, and (c) 100 mg/ml. Due to the sensitivity of the permittivity of the glucose solution to temperature, the reflection coefficient S_{11} and resonant frequency shift are strongly dependent on temperature of the glucose solution. Note that the permit-

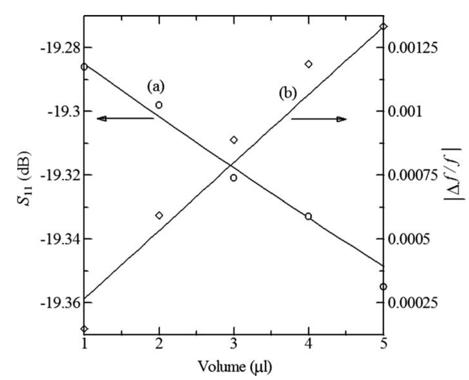

FIG. 3. Microwave reflection coefficient S_{11} (a) and resonant frequency shift $\Delta f/f$ (b) plotted as a function of the glucose volume from 1 to 5 μl with increment of 1 μl. The solid lines show a fit to (a) Eqs. (1) and (b) (4), respectively.

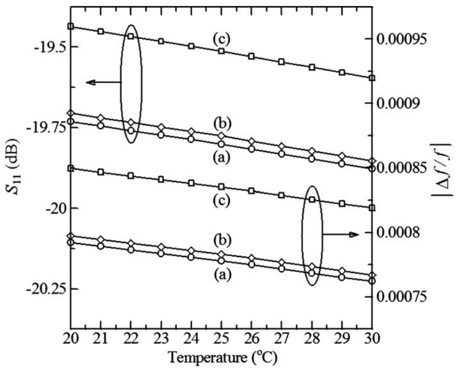

FIG. 4. Measured reflection coefficient S_{11} (left axis) and resonant frequency shift $\Delta f/f$ (right axis) dependences on temperature for glucose concentrations of (a) 1, (b) 10, and (c) 100 mg/ml. The glucose solution volume was 4 μl.

tivity changes on the orders of 0.41, 0.4, and 0.38% $^\circ C^{-1}$ for the real part and 3.56, 3.55, and 3.48% $^\circ C^{-1}$ for the imaginary part at the 1, 10, and 100 mg/ml glucose concentration, respectively. When the temperature of the glucose solution increased, reflection coefficient and frequency shift decreased due to the decrease of permittivity of glucose solution. We observed that the temperature coefficient variations of reflection coefficient for 1, 10, and 100 mg/ml glucose solution were about 0.076, 0.078, and 0.087%/°C, respectively, and the temperature coefficient variations of frequency shift were about 0.45, 0.42, and 0.38%/°C, respectively. As the glucose concentration increased, temperature coefficient of the microwave reflection coefficient S_{11} increased and the temperature coefficient of the resonant frequency shift $|\Delta f/f|$ decreased. Note that, as the temperature of the glucose solution increased, the imaginary part of the permittivity ε'' of glucose decreases more rapidly than that of real part ε', hence the loss tangent decreased. The observed temperature coefficient variations of losses for 1, 10, and 100 mg/ml glucose solution were about 3.17, 3.14, and 3.11%/°C, respectively.

We demonstrated the measurement of aqueous glucose concentration by using a microwave dielectric resonator biosensor. The reflection coefficient S_{11} and the resonant frequency shift $|\Delta f/f|$ are very sensitive to the concentration of glucose. These results clearly show the sensitivity and usefulness of this dielectric resonator for glucose biosensing using a noncontact and label-free technique without the added complications of sample treatment.

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