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An Electrical Signal Detection System for a Microbiochip with Gold Nanoparticles

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Abstract. In this paper, an electrical signal detection system for microbiochips is proposed to overcome the limitations of conventional optical systems such as bulky system size and high manufacturing cost. An electrical detection system with interdigitated microelectrodes is fabricated using MEMS technology. High conductive nano size gold particles were selected for the system to detect biological reactions between bio materials in the microbiochip. Experiments were performed with variations of particle densities and electrode gaps. In addition, a simulation to predict the electrical resistance of the microbiochip was developed. Both the simulation and experimental data show that the conductivity increases as the gap becomes narrower and the particle density higher.

Introduction

Most microbiochip detection systems commonly use a fluorescent marker and optical peripheral apparatus in order to sense bio reactions such as DNA hybridization and immunoassay [1,2]. Optical apparatuses, for example, the confocal laser scanning microscope, are usually not small enough to be carried. Therefore, miniaturization, an advantage of the microbiochip, is restricted. In addition, optical detection systems are generally expensive. However, by using electrical signal sensing instead of fluorescent sensing, such limitations can be overcome [3]. However, advanced techniques in the design and microfabrication of a sensing chip along with the data acquisition and processing of minute signals are needed to put the detection system to practical use.

Recently, nanoparticles have been effectively utilized for electrical signal detection [4,5,6]. The feasibility of the electrical signal detection of the micro bio-reaction using conductive nanoparticles was studied. Firstly, a microelectrode sensor that can detect the electrical signal was designed and fabricated. To evaluate the performance of the microelectrode sensor, simulations and experiments were conducted. The influences on the resistance and conductivity of the electric signal with the nanoparticle density and the gap between sensor electrodes were then examined.

Microelectrode sensor for electrical signal detection

The principle of bio-reaction detection by electrical signal using nanoparticles [3] is shown in Fig. 1. Electrical signal sensors are composed of two sensing microelectrodes. For the detection system, bio capture probes were immobilized between the microelectrodes and bio targets were coated on gold nanoparticles. Provided that the nanoparticles coated with the target are injected on the sensor, the targets are able to react with the immobilized probe. The gold nanoparticles are fixed between the micro electrodes as the capture probe and the target are bound together. The electric current can then flow through the fixed nanoparticles. Hence, the reaction between the target and the capture probe can be detected by the occurrence of the electric current between the sensing microelectrodes.

Photographs of microelectrode sensors for the experiment to evaluate the electro signal detection using nanoparticles are shown in Fig. 2. In order to sense the electrical signal using the nano-

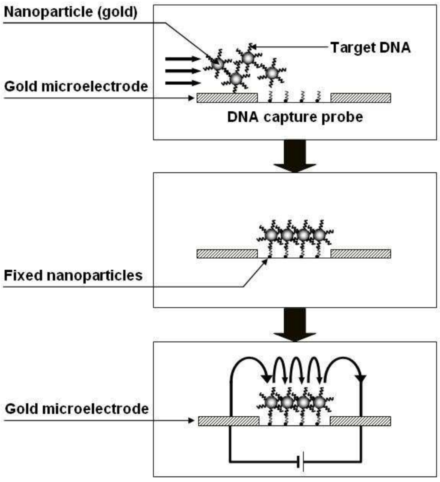
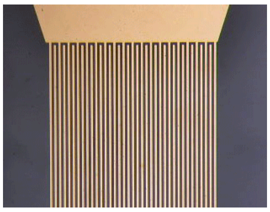
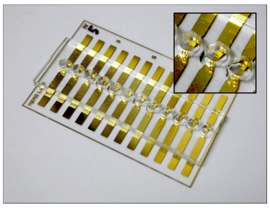


Fig. 1 Concept for detecting electric signals



(a) Detection zone & electrodes



(b) Biosensors with PDMS well

Fig.2 Photographs of the biosensors

particles, two gold electrodes on the glass substrate were designed to be on opposite sides to act as a switch. The center of the sensor or electrical signal detection zone is designed in the shape of a comb to increase the sensing area. The PDMS well is fabricated to precisely inject biomaterial into the detection zone. The microelectrode sensor was fabricated with gaps between the sensing electrodes, 3, 5, and 7 µm to study the effect of the gap on the electrical signal detection. In order to fabricate the microelectrode sensor, firstly, 200 Å Cr and 3000 Å Au were thermal evaporated on the glass substrate. A positive photo resist (AZ1512) was spin coated over the evaporated Au thin film. The photo resist was patterned by photolithography. The gold microelectrodes were made by the wet-etching of the Cr/Au thin films with photo resist masking. Finally, the remaining photo resist was removed.

Electrical Sensing Simulation

Electric conductivity with nanoparticle distribution was analyzed by simulation. As illustrated in Fig. 3, each gold nanoparticle was randomly distributed on the multi layer hexagonal lattices. Next, the nanoparticles that connected the sensing microelectrodes were sought out. Six intersections among the hexagons were assumed to be the electrical connection points between the nanoparticles. The electric conductivity was calculated if the electrodes were connected through contact by the nanoparticles. The electrical resistance (R) can be evaluated by the equation

$$R = \rho \frac{l}{A} \quad (1)$$

where A and l are the cross-sectional area and length of nanoparticles, respectively. As the length of a column in the lattice can be regarded as the area per unit length, the area (A) can be evaluated by counting the number of contact points. In addition, as the specific resistance (ρ) and l values are constant, a simplifying constant K (=ρl) is introduced.

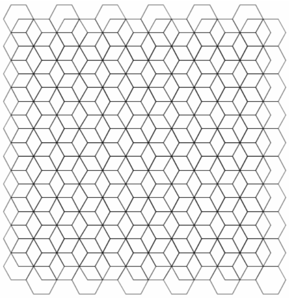
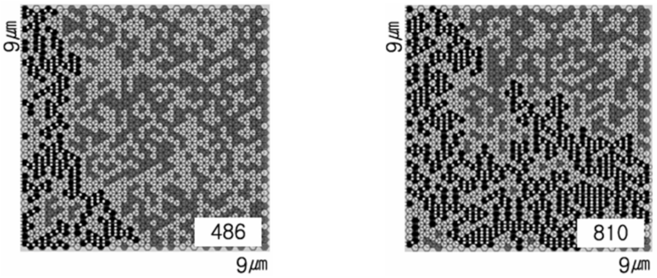


Fig. 3 Hexagon lattices between electrodes for simulation



(a) electrically disconnected (b) electrically connected

Fig. 4 Electrically charged gold particles in the detection zone (uniform random distribution)

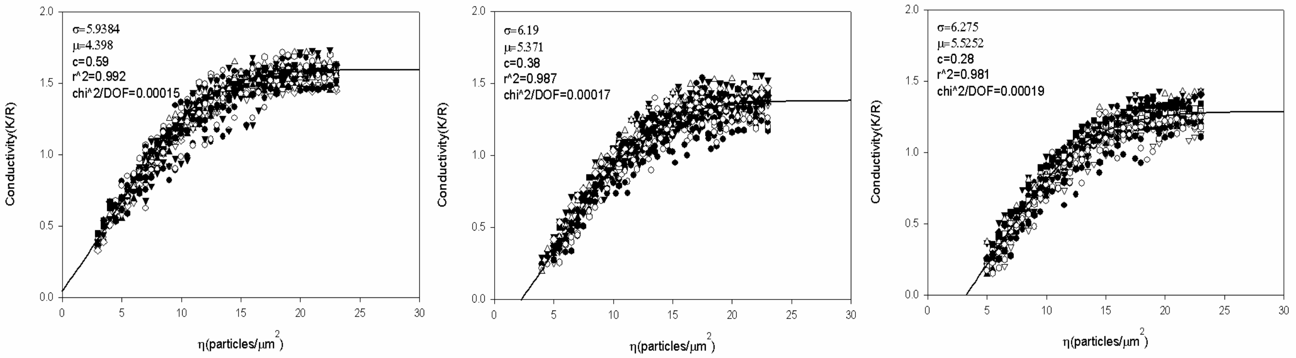
Fig. 4 is the simulation result that shows whether the nanoparticles are charged with electricity as the density of the nanoparticles (η) in the detection zone increases. The simulation was performed for the 486 (= 6 particles/μm^2) and 810 (= 10 particles/μm^2) nanoparticles, whose size was 250 nm, in 9 μm × 9 μm detection zone. The results show that the electrified nanoparticles, black particles in Fig. 4, increase as the nanoparticle density increases so that the probability of electricity transmission through the sensing microelectrodes increases.

The results of the simulation, the effect of nanoparticle density on the K/R is shown in Fig. 5. The K/R increases as the density increases. At the same nanoparticle density, the K/R increases as the gap between the electrodes becomes smaller. The dependence of the conductivity K/R on the nanoparticle density η was approximated by the shape of the cumulative distribution function as follows:

$$\frac{K}{R}=\frac{1}{\sqrt{2\pi\sigma}}\int_0^{\eta} e^{-(\eta-\mu)^2/(2\sigma^2)}d\eta \quad (2)$$

where, the nanoparticle density η is a random variable, σ is the variance, and μ is the mean.

When the variation of K/R according to η is curve-fitted by the cumulative distribution function of Eq. (2), the correlation coefficient is greater than 0.96. Applying the chi-square goodness-of-fit, each value of the chi-square over degree of freedom is less than 0.05 regardless of the gap between the electrodes. Hence, the electric conductivity K/R is regarded as the normal distribution. According to the simulation results, electrical signal detection becomes more efficient as the nanoparticle density increases and the gap between the electrodes decreases.



(a)gap between electrodes:3μm (b)gap between electrodes:5μm (c)gap between electrodes:7μm

Fig. 5 Conductivity of the nanoparticles between sensing electrodes (Simulated)

Electrical sensing experiment

Experiments were performed to measure the conductivity (resistance) with the nanoparticle density and the gap between the electrodes in the detection zone of the microelectrode sensor. The resistance was measured using the wheatstone bridge circuit as in Fig. 6. The fabricated microelectrode sensor chip was mounted on the wheatstone bridge circuit board, and nanoparticles were then injected on the detection zone of the microelectrode sensor. Gold nanoparticles of 250 nm diameter were used as a conductible nanoparticle. In order to make various densities of the nanoparticles, colloidal nanoparticles in buffer, which were purchased, were extracted by a

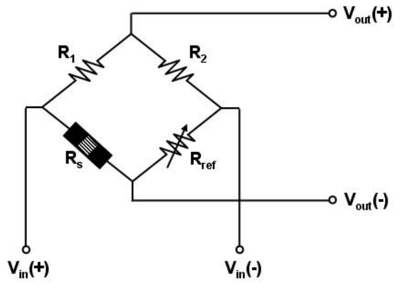


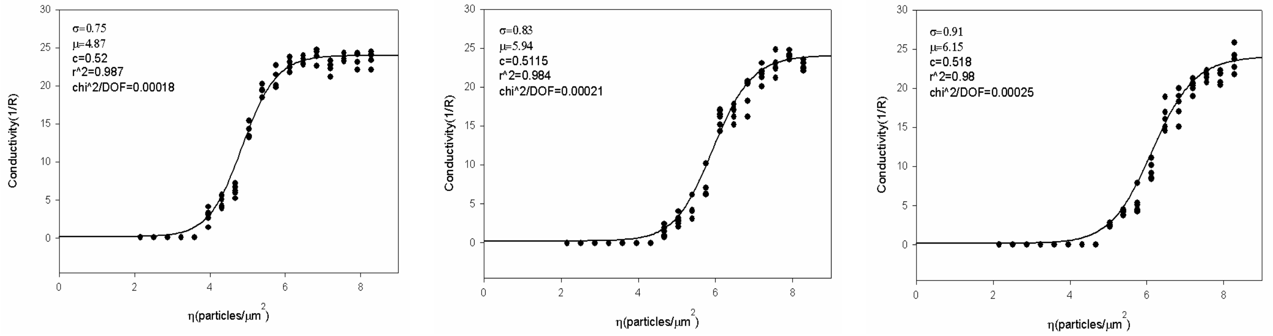
Fig. 6 Electric circuit for signal detection

gap	μ [particles/ μm^2] (simulated)	μ [particles/ μm^2] (experimented)	Difference [%]
3 μm	4.39	4.87	9.7%
5 μm	5.37	5.94	9.6%
7 μm	5.53	6.15	10.2%

Table. 1 Differences between sim. and exp.

centrifugal separator and then diluted to the desired density of the nanoparticles. When the diluted solution was injected into the detection zone and then dried, the nanoparticles remain in the detection zone.

Measured conductance is as in Fig. 7. The variation of the conductance according to the nanoparticle density was curve-fitted by Eq. (2). The result shows that the variation of the conductance can be approximated by the cumulative distribution function, the same as the simulation results. The average, μ, of Eq. (2) represents the minimum nanoparticle density that makes electrical signals stochastically stable. The average becomes larger as the gap between the sensing microelectrodes increases and the conductance becomes reasonable as the density of nanoparticles increases. Therefore, in order to increase the reliability of the electrical signal from the microelectrode sensor, the gap between the sensing electrodes must be as small as possible and the density of the nanoparticles must be increased. Differences in the average in results between simulation and experiment are below 10.2 % as shown in Table. 1.



(a)gap between electrodes:3μm (b)gap between electrodes:5μm (c)gap between electrodes:7μm

Fig. 7 Conductivity of the nanoparticles between sensing electrodes (experimented)

Conclusion

Electrical signal detection using conductible nanoparticles was proposed for microbiochip applications. The microelectrode sensor chip was designed and fabricated to examine the feasibility of electrical signal detection using nanoparticles immobilized by the detection zone of the sensor. The modeling of the electrical signal detection by the distribution of the nanoparticles and the algorithm of the conductivity estimation was developed. The results of the simulation and experiments showed that the variation of the conductivity according to the nanoparticle density for each electrode gap was approximated by the cumulative normal distribution function. From the experiments and simulation results, it can be concluded that the proposed system is readily applicable to microbiochips.

Acknowledgment

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