Regulating Detectable Optical Domain in Sensing Technology Using Metal Mesh Devices and Detection of Submicron-size Particles

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A metal mesh device has a structure in which through-holes of the same shape are periodically placed on a thin metal film, and the selection of such a structure makes it possible to sense objects of various sizes. In this study, we showed the structure of the metal mesh device and the relationship between the detectable optical domain and the size of the objects to be measured. In addition, from measurement of changes in electromagnetic wave transmission characteristics of the metal mesh device due to specific adsorption of particles with a mean diameter of 100 nm with surface modification with Streptavidin to a metal mesh device fixed with biotin, we showed that even large particles can be sensed. Based on these examinations, we showed that, by using a metal mesh device with detectable optical domain corresponding to the size of objects, even objects that are larger than protein can be sensed.

Keywords Metal mesh device, sensing technology, submicron-size particles

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Introduction

A metal mesh device (MMD) is a structure in which through-holes of the same shape are periodically placed on a thin metal film. The MMD has optical characteristics corresponding to the periodic structure of these through-holes. The optical properties of an MMD are similar to a band pass filter, and electromagnetic waves of a certain frequency band can pass through. The frequency of this transmission band is determined by the period of through-hole; thus, by changing the structure of the MMD, a wide frequency range can be regulated from the microwave region to the visible light region.

The electromagnetic wave transmission characteristic of MMDs is called an extraordinary optical transmission, and from the 1960s to the present, studies have been conducted to elucidate its mechanism. On the other hand, there is hardly any industrial use of this optical characteristic and, until recently, almost no pioneering achievements have been made in regard to the same, other than band pass filter in the microwave to submillimeter wave regions. However, Miyamaru et al. in 2006 and Yoshida et al. in 2007 showed that, when a substance becomes adhered to the MMD, the electromagnetic wave transmission characteristic changes. This change in the electromagnetic wave transmission characteristic was due to the impact of a substance adhering to the MMD in terms of the optical characteristic, utilizing the optical characteristic of the MMD. It showed that the amount of the adhered substance could be measured, and applied research for a sensor began. As for sensing technology that uses MMDs, our research group reported on the sensing principle in 2011, on quantitative measurement results of protein in 2013, and on quantitative examination results of protein sensing in 2017 (Fig. 1).

As a technology to quantitatively detect a trace amount of a substance, surface plasmon resonance (SPR) of the visible light region, which is a similar optical technology as MMDs, is being used, especially in the field of biopolymers. However, while SPR has an advantage in regard to its sensitive detection ability, it also has a disadvantage that the detectable optical domain from the sensor surface is extremely small at 100 nm or less. In contrast, an MMD is able to create electromagnetic wave transmission characteristics over various frequencies from the microwave region to visible light regions, and if this property can be applied to detection technology, the size of various objects can be standardized with their wavelength. In other words, if the MMD structure is designed to suit the size of the object, with a sensing method using changes in the electromagnetic wave transmission characteristic of the MMD, objects of various sizes can be measured. The detectable optical domain of SPR is about 100 nm, but the MMD has the advantage of a changeable detectable optical domain depending on the size of an object based on the principle of the structure design; thus, it can be called an optical detection technology that has not been seen before.

However, in past reports on MMD sensing technology, most have used protein as measurement objects, and there is
little work on objects that are large enough that detection with SPR would be difficult. In other words, there was insufficient discussion on the advantage of MMDs by selecting the MMD structure and detectable optical domain, even objects that are larger than protein can be detected in a similar manner to protein. In this study, we used silica and polystyrene spherical particles with a diameter of 100 nm as a model of large objects such as viruses, bacteria, and cells. The electromagnetic field simulation provided the relationship between the structure of the MMD and the detectable domain, and we selected an MMD structure that suited the model particles. It was shown that objects larger than proteins can be detected with the MMD system, where the specific adsorption of silica and polystyrene was performed based on the biotin-streptavidin interaction.

The industrial significance of sensing technology that uses MMDs is the low cost of MMDs. An MMD is produced by electroforming, which allows for mass production; thus, MMDs can be provided as a disposable sensor. Since the measurement device for SPR is expensive, it is recycled through a recycling process, but with MMDs, such a process is unnecessary. Thus, it may be able to provide a new method in industrial fields that require a large number of measurements such as basic screening technology for drug development.

**Experimental**

*Experimental samples*

We prepared an MMD in which through-holes were periodically placed in a square lattice pattern on a thin metal film. Figure S1 (Supporting Information) shows definitions of the MMD structure, period $P$, hole dimension $D$, and thickness $T$. The dimensions were as follows: period $P = 2.6\ \mu m$, length of one side of a square through-hole $D = 1.9\ \mu m$, and thickness of the thin metal film $T = 0.8\ \mu m$. The parameter $P$ is strongly related to the transmission wavelength, frequency and depth of electric field (Fig. S2, Table S1). We prepared the MMD so that the frequency of the electromagnetic waves passband would be close to 100 THz. Using electroforming, we prepared an Ni MMD with an outer diameter of 6 mmφ. Furthermore, we performed Au electroless plating on the Ni MMD to prepare an MMD with its whole surface covered by dozens of nm of Au layer.

In this experiment, the dip wavelength and MMD parameters follow the equation:

$$P = 0.85 \times \lambda_0$$

(1)

MMD properties including dip frequency and dip wavelength are determined by period $P$, hole dimension $D$ and aperture ratio, where the MMD has almost 50% aperture ratio. In the case of 50% aperture ratio, the dip wavelength and frequency is determined by the above equation. The MMD was designed based on $P$ (Fig. S2 and Table S1, Supporting Information).

**Adsorption operation of particles**

For adsorption of silica and polystyrene particles by the MMD, we used specific adsorption of biotin and streptavidin. We used Au-thiol bond for MMD with Au surface to fix biotin molecules. We soaked the MMD in an ethanol solution of HS-(CH$_3$)$_3$:NH-CO-biotin (ProChimia, FT 005) with a concentration of 0.5 mg mL$^{-1}$ at room temperature for 16 h.

For objects larger than protein, we used spherical silica particles (Micromod, 43-19-102) and spherical polystyrene particles (Micromod, 01-19-102) with a mean diameter of 100 nm, where the surface of the particle was modified with streptavidin. Adsorption reaction of these particles to the MMD fixed with biotin was performed by soaking the biotin-fixed MMD in a PBS solution of particles adjusted to the desired concentration (mg mL$^{-1}$) and shaking at room temperature for 16 h.

In an experiment that confirmed specific adsorption of particles to the MMD, the MMD was soaked in a silica particle solution with a concentration of 2.5 mg mL$^{-1}$ and a polystyrene particle solution with a concentration of 1.0 mg mL$^{-1}$ for adsorption before and after fixing biotin molecules, and the change in the electromagnetic wave transmission characteristic was compared.

In an experiment that examined concentration dependence, we performed adsorption with silica particle solutions with concentrations of 0.025, 0.25, and 2.5 mg mL$^{-1}$ and polystyrene particle solutions with concentrations of 0.010, 0.10, and 1.0 mg mL$^{-1}$, and measured the changes in the electromagnetic wave transmission characteristic. As a result, the volume of particle was obtained assuming particles as spheres, then the mass of each particle was obtained using a silica density of 2.2 g cm$^{-3}$ and a polystyrene density of 1.05 g cm$^{-3}$, then converting the mass concentration of mg mL$^{-1}$ to the particle number concentration of mol L$^{-1}$.

**Measurement of electromagnetic wave transmission characteristics**

The electromagnetic wave transmission characteristic of the MMD was measured using FT-IR (BrukerOptics, ALPHA). For the same MMD, first, the electromagnetic wave transmission characteristic of the MMD before particle adsorption was measured, followed by measurement of the electromagnetic wave transmission characteristic of the MMD after particle adsorption and, based on the difference, we obtained the change in the electromagnetic wave transmission characteristic due to particle adsorption. To obtain the amount of change, we defined the bottom of the wave where transmittance in the passband drops as the dip point, and obtained the change in frequency at the dip point.

![Fig. 1 Schematic illustration of biosensing with MMD. The change of dip frequency is observed by the addition of objects on the MMD surface.](image-url)
Calculation by electromagnetic field simulation software

To examine the validity of the size of the detectable optical domain of MMD and the mean diameter of object particles of 100 nm in this study, we performed computations with electromagnetic field simulation software (CST, MICROSTripES). Figure S3 (Supporting Information) shows the computational model. The origin of the figure is the center of the hole in the MMD, with X and Y axes in the plane of the MMD, and Z axis perpendicular to the plane. In addition, the MMD in the figure is equivalent to the unit lattice in the MMD, and for period P, hole dimension D, and thickness t, we used the same dimensions as the actual sample. Boundary conditions were calculated with periodic boundaries being a \( Y = \pm P/2 \) plane and \( X = \pm P/2 \) plane that surround unit lattice of the MMD. The wave source was set \( 2P \) from the MMD front plane in the +Z direction, and a planer wave with a polarized wave in the Y-direction was applied perpendicular to the MMD plane. The detection plane was placed \( 2P \) from the MMD back plane in the –Z direction. In measurements with FT-IR, the incident light is not a linear polarized wave but light without a polarized wave plane, and it is also not parallel light but condensed light. The dip waveform of the MMD forms due to characteristics of this incident light; thus, under incident light conditions of Fig. S3 (Supporting Information), the dip waveform does not form. To solve this problem, in computation, the dip waveform was generated by breaking the symmetry of hole with the minute convex structure of the MMD shown in Fig. S4 (Supporting Information). The wave source was set \( 2P \) from the MMD front plane in the +Z direction, and a planer wave with a polarized wave in the Y-direction was applied perpendicular to the MMD plane. The detection plane was placed \( 2P \) from the MMD back plane in the –Z direction.

In the computation, we first obtained the spatial extent of the resonant electromagnetic field at the dip point of the MMD through energy calculation. Figure S4 (Supporting Information) shows the computational model. As shown by the green line in the figure, the space near the MMD is divided into minute spaces with a width of 50 nm in the +Z direction from the origin, and energy (J) of the resonant electromagnetic field in each minute space is calculated. By dividing with the volume \( (m^3) \) of each minute space, the energy density for each minute space \( (Jm^{-3}) \) is calculated. By obtaining the relationship between the Z-direction position (at the center of the 50-nm width) and the energy density of the minute space, the spatial extent of the resonant electromagnetic field of the frequency at the dip point of the MMD was examined. Next, to understand the change in the sensing performance of the MMD based on the size of an object, a planar virtual substance with a thickness \( t_0 \) was placed on the plane on the +Z size of the MMD plane. We calculated changes in the frequency at the dip point of the MMD when the thickness \( t_0 \) of a virtual substance was changed. Figure S5 (Supporting Information) shows the computational model. The planar structure in the brown part in the figure shows a virtual substance, and material characteristics induced a relative permittivity of 3, and dielectric loss of 0. The thickness of the virtual substance, \( t_0 \), was changed within the range of 0 to 1000 nm for computation. The three dimensional electromagnetic distribution was obtained based on the model, which is shown in Fig. S6 (Supporting Information).

Results

Comparison of measurement results and computational results of electromagnetic wave transmission characteristic of MMD

Figure 2 shows a comparison of measurement results for the electromagnetic wave transmission characteristic of the MMD before fixing biotin through FT-IR, and computational results for the electromagnetic wave transmission characteristic of the MMD through three-dimensional electromagnetic field simulation software. The horizontal axis in the figure represents frequencies (THz) while the vertical axis represents transmittance (%). Furthermore, the solid line in the figure represents the measurement results and the dotted line represents the computational results. The results showed that the passband was in the vicinity of 100 THz for both results, the frequency measurement result at the dip point in the passband was 97.4 THz, while the computational result was consistent at 97.6 THz.

Computational results of spatial extent of resonant electromagnetic field of MMD for dip point frequency

Using the computational model of Fig. S3 (Supporting Information), the space near the MMD is divided into minute spaces with a width of 50 nm in the +Z direction from the origin as in Fig. S4 (Supporting Information) to calculate the energy density of the resonant electromagnetic field for a minute space at the dip point frequency. Figure 3 shows the computational results. The horizontal axis of the figure represents the position of the minute space in the Z direction \( Z_m \), while the vertical axis is the energy density of the minute space at that location \( E_{d_0} \) (arb.unit) (Fig. 3, and Fig. S6 (Supporting Information)).
The energy density was standardized with the maximum energy density for the overall minute spaces. We added a red dotted line on the vertical axis from the maximum energy density to 1/e. These results show that the energy density is the highest near the MMD plane ($Z_m = 400$ nm), the energy density is relatively high ($0.73 - 1.00$) in the holes of the MMD ($0 \text{ nm} \leq Z_m < 400$ nm), the energy density attenuated with the distance from the MMD plane outside of the MMD ($Z_m > 400$ nm), and around $Z_m = 700$ nm, it reached the depth of 1/e. If we define the region where the energy density becomes the maximum (1/e) as the resonant electromagnetic field space, these results showed that the resonant electromagnetic field space at the frequency of the MMD dip point extended from inside the holes to outside the plane to about 300 nm perpendicular to the plane. When converting using wavelength $\lambda_0$ of the frequency at the MMD dip point shown in Fig. 2, this distance of 300 nm was equivalent to $0.10 \times \lambda_0$.

**Computational results of frequency change at the dip point with virtual substance thickness**

Using the computational model of Fig. S2 (Supporting Information), as shown in Fig. S5 (Supporting Information), we placed a planar virtual substance with a thickness of $t_d$ on the MMD plane, and calculated the changes in frequency $\Delta f$ at the MMD dip point when the thickness $t_d$ was changed. Figure 4 shows the computational results. The horizontal axis in the figure shows the thickness of the virtual substance, $t_d$ nm, while the vertical axis shows changes in the frequency ($\Delta f$, THz) at the MMD dip point by a virtual substance when the lack of a virtual substance is standard. We performed primary regression for seven plot points within the range of 0 nm $\leq t_d \leq 300$ nm, and showed the results as a solid line. Results showed that, in the range of 0 nm $\leq t_d \leq 300$ nm, the thickness of virtual substance $t_d$ and change in frequency $\Delta f$ at the MMD dip point were nearly proportional, and their correlation coefficient was $R^2 = 0.993$. In addition, at $t_d > 300$ nm, as the thickness of the virtual substance $t_d$ increased, the rate of change in frequency $\Delta f$ at the dip point decreased, showing that it diverged away from the previously mentioned linear relationship.\(^{12}\)

**Confirming specific adsorption of particles with surface modification with streptavidin to MMD fixed with biotin molecules**

We prepared MMDs with or without fixing biotin molecules, and performed adsorption using silica solution with a concentration of 2.5 mg mL$^{-1}$ and polystyrene particles with a concentration of 1.0 mg mL$^{-1}$ (Table 1). Then, we compared the presence and absence of specific adsorption of particles from changes in frequency at the MMD dip point ($\Delta f$). For samples (1) to (5), Table 1 shows the results of comparing changes in the frequency at the dip point ($\Delta f$). Samples (2) and (3) show the results of the silica particle solution, where (2) is the MMD before fixing biotin and (3) is absorption to the MMD after fixing biotin. In addition, samples (4) and (5) are the results of the polystyrene particle solution, where (4) is the MMD before fixing biotin and (5) is the result of adsorption to the MMD after fixing biotin. Sample (1) is the result when a biotin-fixed MMD was processed with the PBS solution alone. We measured MMDs for all the five samples, and showed the mean and standard deviation. These results showed that both silica and polystyrene particles had low $\Delta f$ to the MMD without fixing biotin, while it increased after fixing biotin. The ratio was about 9 times for silica particles and 8 times for polystyrene particles.

**Changes in frequency at MMD dip point by particle adsorption when adsorption reaction was performed by changing particle solution concentrations**

By performing the adsorption reaction by changing the concentration of silica particles and polystyrene particles, we examined the concentration dependence of changes in frequency at the MMD dip point due to particle adsorption. Figure 5 shows the measurement results. The horizontal axis in the figure shows the particle solution concentration ($M$, mol L$^{-1}$) while the vertical axis shows the frequency changes at the dip point ($\Delta f$, THz). For each condition, we took 10 measurements of MMD, and plotted the mean and standard deviation of silica particles with blue, and polystyrene particles with red. Furthermore, we showed the fitting results of silica particles in blue and polystyrene in red with Langmuir’s equation when the dissociation constant is $K_D$ mol L$^{-1}$ and the change in saturated frequencies is $\Delta f_{\text{max}}$ (THz). These results showed that, for silica particles, as the particle solution concentration $M$ increased, the amount of change in frequency at the dip point ($\Delta f$) increased. In addition, with polystyrene particles, when particle solution concentration $M$ increases from $3.0 \times 10^{-11}$ to $3.0 \times 10^{-10}$ mol L$^{-1}$, the amount of change in frequency ($\Delta f$) increases, but when particle solution concentration $M$ increases from $3.0 \times 10^{-10}$ to $3.0 \times 10^{-9}$ mol L$^{-1}$, the amount of change in frequency at the dip point ($\Delta f$) barely changed. With the Langmuir’s equation fitting, it was shown that for silica particles, dissociation constant $K_D$ was $4 \times 10^{-10}$ mol L$^{-1}$ and the amount of change in saturated frequencies $\Delta f_{\text{max}}$ was 2.30 THz, while with polystyrene particles, dissociation constant $K_D$ was $8 \times 10^{-11}$ mol L$^{-1}$ and the

| Name | Sample conditions | $\Delta f$/THz | Average | SD |
|------|------------------|----------------|---------|----|
| (1)  | (None) After immobilizing biotin | -0.02 | 0.05 |
| (2)  | Silica Before immobilizing biotin | 0.23 | 0.16 |
| (3)  | Silica After immobilizing biotin | 2.02 | 0.26 |
| (4)  | Polystyrene Before immobilizing biotin | 0.15 | 0.18 |
| (5)  | Polystyrene After immobilizing biotin | 1.27 | 0.31 |

a. Concentrations used are 2.5 mg mL$^{-1}$ silica and 1.0 mg mL$^{-1}$ polystyrene solutions.

Fig. 4 Computational results of change in the amount of frequency at the dip point ($\Delta f$) due to change in the thickness $t_d$ of the virtual substance.
amount of change in frequency $\Delta f_{\text{max}}$ was 1.43 THz.

To confirm the particle adsorption, we performed SEM observation of the MMD surface after measurement. As an example, Fig. S7 (Supporting Information) shows SEM photographs of the MMD after adsorbing silica particles. The figure shows photographs of four types of MMD that went through the adsorption process with particle solution concentrations of 0 (PBS only), 0.025, 0.25, and 2.5 mg mL$^{-1}$ at 50000 magnification. Results showed that, as particle solution concentration $M$ increased, the number of silica particles adsorbed on the surface of the MMD increased.

**Discussion**

**Estimate for detectable optical domain of MMD**

In this study, we verified the advantage of MMDs in that, by selecting the MMD structure and detectable optical domain, objects larger than protein can be detected. Here, let us discuss the relationship between the MMD structure and detectable optical domain, which is the foundation of the concept, based on the results of electromagnetic field simulation.

Figure 2 shows the comparison between measurement results and computational results for the electromagnetic wave transmission characteristics of the MMD, and that these two are mostly consistent. As such, based on the computational model of this study, the behavior of an MMD toward electromagnetic waves, and discussions on the detectable optical domain of an MMD derived from such behavior was deemed possible.

Figure 3 shows the spatial extent of the resonant electromagnetic field for the frequency at the MMD dip point. MMD sensing technology uses changes in the resonance characteristics due to the presence of an object in the resonant electromagnetic field space of the MMD. In other words, as long as it is an object with a size that allows for it to enter the resonant electromagnetic field space, it can be measured. Large objects that only allow for a part to enter the space, and objects that are outside of the resonant electromagnetic field space, would lead to errors in measurement results or may not be measured at all. Therefore, the detectable optical domain with an MMD means this resonant electromagnetic field space. Figure 3 showed that, with MMD with a frequency at the dip point of 97.6 THz, if wavelength is $\lambda_0$, the resonant electromagnetic field space is extended to the inside of the holes, and about 0.10 $\times \lambda_0$ outside of the plane. In electromagnetic field phenomenon, scaling law is established; therefore, these results are established with any resonance frequencies (wavelengths) by changing the MMD structure, and explain the relationship between the MMD structure and the detectable optical domain. This means that by regulating the resonance wavelength $\lambda_0$ by changing the MMD structure, a detectable optical domain ($0.1 \times \lambda_0$) that is able to contain objects of various sizes can be set up.

To verify the detectable optical domain of the MMD indicated by Fig. 3, we examined the changes in frequency ($\Delta f$) at the MMD dip point due to change in thickness $t_d$ of the virtual substance with sensing of the virtual substance using the MMD as the model (Fig. 4). Results showed that, in sensing a virtual substance with a thickness of $0 \leq t_d \leq 300$ nm that fits in the resonant electromagnetic field space that extends to about 300 nm outside of the plane, thickness $t_d$ and change in frequency at the MMD dip point ($\Delta f$) are mostly proportional. This showed that the linearity, which is an important property in quantitative sensing, is secured. In sensing a virtual substance with thickness of $t_d > 300$ nm so that part of it is outside of the resonant electromagnetic field space, since the contribution to the sensing results of the virtual substance that is outside of the space decreases, its deviation from the previously discussed proportional relationship increases (Figs. S8 and S9 (Supporting Information)). Based on these results, we confirmed that the detectable optical domain of the MMD shown in Fig. 3 is a valid estimate.

**Examination of the potential for detection of objects that are larger than protein by MMDs**

From the discussion in the previous section, it was estimated that the detectable optical domain of the MMD used in this study extends to inside of the holes, and about 300 nm outside of the plane. Here, based on experimental results that used silica and polystyrene particles with a mean particle diameter of 100 nm that fit inside the detectable optical domain, we discussed the potential for detecting large objects that are larger than protein using an MMD.

Based on the results of comparing the adsorption of particles that were surface modified with streptavidin to the MMD before and after fixing biotin molecules (Table 1), for both silica particles and polystyrene, the adsorption to the MMD after fixing with biotin was eight to nine times higher compared to before fixing with biotin. As such, using specific adsorption of biotin and Streptavidin, both particles specifically adsorbed onto the MMD.

Figure 5 shows changes in frequency at the MMD dip point due to changes in particle solution concentration of silica and polystyrene particles. These results show that, similar to the equilibrium curve obtained from the sensing of protein using specific adsorption, an equilibrium curve that can be approximated with Langmuir’s equation was confirmed between the concentration $M$ mol L$^{-1}$ and the change in frequency at the MMD dip point ($\Delta f$) for both particles. Since results that indicate specific adsorption between particles have been obtained with the MMD (Table 1), these results were valid. From comparison of changes in saturated frequency $\Delta f_{\text{max}}$ THz of silica and polystyrene particles, we found that the silica particles were 1.6 times larger $\Delta f_{\text{max}}$ than the polystyrene particles. The reason for this was assumed to be because silica has higher relative permittivity than polystyrene based on the sensing principle of the MMD. The particles of 100 nm in diameter were selected as the larger objects than protein. Particles with diameters of 200 - 300 nm were also examined (Fig. S8). The frequency
shift ($\Delta f$) was dependent on the detectable optical region (depth). The frequency shift ($\Delta f$) was dependent on the substance deposition position on the MMD due to the electromagnetic field distribution.

These results show that, in sensing technology using MMDs, if we design the MMD structure so that even objects that are larger than protein can fit in the detectable optical domain, it could be detected in a manner similar to protein.

Conclusions

In this study, we verified the advantage of MMDs that, by selecting the MMD structure and detectable optical domain, even an object larger than protein can be detected through computations and experiment. Computation showed that the detectable optical domain of an MMD is a space inside the hole, and about $0.10 \times \lambda_0$ outside of the main surface if the wavelength of the frequency at the MMD dip point is $\lambda_0$. Using silica and polystyrene particles with a mean diameter of 100 nm assumed to be included in the detectable optical domain, we measured changes in frequency at the dip point due to specific adsorption of these particles that were surface modified with streptavidin to a biotin-fixed MMD. We found that the relationship of the particle solution concentration mol L$^{-1}$ and change in frequency at the dip point THz is an equilibrium curve that can be approximated with Langmuir’s equation. Particles used in this study are models that assumed viruses, bacteria, and cells as objects larger than protein. In addition, detection of these objects assumes collection by specific adsorption using antibodies, sugar chains, etc., and in this experiment, we constructed an experimental system on the specific adsorption of particles to the MMD. Examination in this study showed that even objects that are larger than protein could be measured by selecting the MMD structure and detectable optical domain that suits the size of the objects.

Supporting Information

We showed the detailed explanation of calculation conditions and the state of adsorption of particles to the MMD. This material is available free of charge on the Web at http://www.jsac.or.jp/analsci/.

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