Magnetic Marker and High $T_c$ Superconducting Quantum Interference Device for Biological Immunoassays

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SUMMARY Magnetic immunoassays utilizing magnetic marker and high $T_c$ superconducting quantum interference device (SQUID) have been performed. In this magnetic method, binding-reaction between an antigen and its antibody is detected by measuring the magnetic field from the magnetic marker. First, we discuss the magnetic property of the marker, and show that Fe$_3$O$_4$ particles with diameter of 25 nm can be used for remanence measurement. We also show a design of the SQUID for sensitive detection of the magnetic signal from the marker. Next, we developed a measurement system utilizing the SQUID and a reaction chamber with very low magnetic contamination. Finally, we conducted an experiment on the detection of the biological materials called IL8 and IgE. At present, a few atto-mol of IL8 and IgE has been detected, which shows the high sensitivity of the present method.

key words: immunoassay, high $T_c$, SQUID, magnetic marker, magnetic nanoparticle, remanence

1. Introduction

Biological immunoassay is the detection of biological materials called antigen. Recently, magnetic immunoassay utilizing a magnetic marker and a superconducting quantum interference device (SQUID) has been developed [1]–[10]. In this application, binding reaction between an antigen and its antibody is magnetically detected by using the so-called magnetic marker. The magnetic field from the marker that couples to the antigen is detected with the SQUID. Three methods have so far been developed for the detection of the magnetic signal from the marker, i.e., remanence [1], [2], relaxation [3]–[7] and susceptibility [8]–[10] measurements. Compared to the conventional optical system, the SQUID system is expected to have high sensitivity and capability of detection in the liquid state.

For the application to immunoassay, the magnetic marker is required to generate a large magnetic signal in order to improve the sensitivity of the system. The marker is usually made of Fe$_2$O$_3$ or Fe$_3$O$_4$ particles whose diameter is a few 10 nanometers. In this case, the magnetic property of the particle is significantly degraded by the thermal noise, and the degradation depends strongly on the size of the particle [11], [12]. Moreover, the size of the particles is not uniform but distributes in the practical case where assembly of particles is used. Therefore, it is necessary to quantitatively clarify the magnetic signal from the assembly of the nanoparticles.

In developing the immunoassay system, the SQUID should efficiently collect the magnetic signal from the marker. Since the spatial variation of the magnetic field from the marker is large in this application, it is necessary to design the SQUID by taking account of this point. For example, the size of the pickup coil should be optimized, and close distance between the SQUID and the room temperature sample should be achieved. It is also necessary to develop a reaction chamber that has very low magnetic contamination in order to avoid the magnetic noise.

In performing the immunoassay, the marker has to satisfy good dispersion in the liquid in order to guarantee efficient binding reaction between the antigen and its antibody. It is also necessary to develop a protocol for the magnetic immunoassay since sensitivity of the immunoassay also depends on the experimental procedures, such as sample preparation. Although the protocol has been established in the case of optical immunoassay, there have been very few studies in the case of magnetic immunoassay.

In this paper, we show our recent results on the immunoassay utilizing the magnetic marker and the SQUID. In Sec. 2, magnetic signal from the assembly of the nanoparticle is shown for the case of remanence, relaxation and susceptibility measurements. In Sec. 3, design of the SQUID for sensitive detection of the magnetic signal from the marker is shown when spatial distribution of the magnetic field is taken into account. In Sec. 4, measurement system utilizing the high $T_c$ SQUID and the reaction chamber with very low magnetic contamination is shown. In Sec. 5, exper-
imental results on the detection of the biological materials called IL8 and IgE are shown. At present, a few atto-mol of IL8 and IgE is detected, which shows the high sensitivity of the present method.

2. Property of Magnetic Marker

2.1 Remanence of Magnetic Nanoparticles

In Fig. 1, magnetic immunoassay utilizing the magnetic marker and the SQUID is schematically shown. In the immunoassay, antigen is detected by using its antibody that selectively couples to the antigen. The antibody is labeled with the marker made of magnetic nanoparticle with diameter $d$. The binding reaction between the antigen and its antibody is detected by measuring the magnetic field from the marker. Since the magnetic signal from the marker depends on the magnetic property of the nanoparticle, we first study its property.

It is well known that the magnetic property of the nanoparticle is strongly affected by the thermal noise, i.e., relaxation of magnetization occurs due to thermal noise [11]. Using the anisotropy energy density $K$ and the volume $V = (4\pi/3)d^3/2$ of the particle, we can express the relaxation time $\tau$ as

$$\tau = \tau_0 \exp(KV/k_B T)$$

where $\tau_0 = 10^{-9}$ s is the characteristic time. For typical value of $K=13\text{kJ/m}^3$, the relaxation time becomes $\tau = 2.6 \times 10^{-7}$ s for $d=15$ nm and $T=300$ K. In this case, remanence cannot be kept, and the particle shows the so-called super-paramagnetic property. On the other hand, the relaxation time becomes as long as $\tau = 144$ s when the size is increased to $d=25$ nm. In this case, the particle can keep remanence after magnetization. Therefore, detection method of the nanoparticle must be chosen depending on the size of the particle. As will be shown later, we choose the Fe$_3$O$_4$ nanoparticle with $d=25$ nm in order to use the remanence measurement method.

2.2 Effect of Size Distribution of Magnetic Nanoparticles

In practical cases, the size $d$ of the magnetic particle distributes in the sample. Therefore, we study the effect of the size distribution on the magnetic signal from the sample. For this purpose, we consider the simple case when the energy $KV$ in Eq. (1) distributes uniformly from $KV=0$ to $KV=50k_BT$ due to the distribution of the volume of the particle, as shown in Fig. 2(a). This distribution corresponds to the distribution of the diameter from $d=0$ to $d=32$ nm when we assume the value of $K=13\text{kJ/m}^3$.

We made a numerical simulation of the magnetization of the sample when an external field $H$ is applied for $t = t_{mag}=1$ s, and then turned off for $t > t_{mag}$. Details of the simulation will be presented elsewhere. In Fig. 2(b), magnetization of the sample is shown as a function of time. Here, the vertical axis shows the magnetic moment $\langle m \rangle$ averaged over the sample. The moment $\langle m \rangle$ is normalized by the value of $N M_s(V)$, where $N$, $M_s$ and $\langle V \rangle$ are the total number, saturation magnetization and average volume of the particles, respectively. The result is calculated for the normalized field $h = H/H_s = 0.05$, where $H_s = 2K/\mu_0 M_s$ is the coercive field.

When the field $h$ is applied for $0 < t < t_{mag}$, magnetization increases with time. After the field $h$ is turned off, the magnetization decrease sharply with very short time, and then decreases slowly with time, i.e., relaxation of magnetization occurs. However, the magnetization still remains after the long passage of time, i.e., remanence also occurs.

In order to study the magnetic signal from the particle for different measurement methods, we define three values as follows. The magnetic moment at $t = t_{mag}$ is defined by $\langle m(0) \rangle = \langle m(t_{mag}) \rangle$. This value gives the magnetic signal in the case of susceptibility measurement. The amplitude of

![Fig. 1](image1.png)

**Fig. 1** Schematic figure of the magnetic immunoassay using the SQUID. The antibody is labeled with the magnetic marker made of Fe$_3$O$_4$ nanoparticle. The binding reaction between an antigen and its antibody is detected by measuring the magnetic field from the marker.

![Fig. 2](image2.png)

**Fig. 2** (a) Distribution of the energy $KV$ in the sample. The energy $KV$ distributes uniformly from $KV=0$ to $KV=50k_BT$, which corresponds to the distribution of the diameter of the particle from $d=0$ to $d=32$ nm for the case of $K=13\text{kJ/m}^3$. (b) Magnetization process of the assembly of the particles when the excitation field $h=0.05$ is applied for $0 < t < 1$ s, and then turned off for $t > 1$ s.
the relaxation is defined by $\Delta(m) = \langle m(t = t_{mag} + 0.01) \rangle - \langle m(t = 2) \rangle$, where sharp drop of $\langle m \rangle$ just after $t = t_{mag}$ is excluded since this drop cannot be measured in the practical measurement. The remanence is defined as $\langle m \rangle_r = \langle m(t = 2) \rangle$, i.e., the magnetization that remains 1 s after the field is turned off.

In Fig. 3, the dependences of the magnetic signal on the applied field $h$ are shown. The results for small and large values of $h$ are shown in Figs. 3(a) and 3(b), respectively. As shown, susceptibility signal $\langle m \rangle_{sus}$ increases with the field $h$. The signal is the highest among three methods. However, it must be noted that the susceptibility signal $\langle m \rangle_{sus}$ must be measured in the presence of the excitation field. In practical measurements using the SQUID, the value of $h$ is limited by the noise caused by the excitation field [12]. The maximum value of $H$ was reported to be $\mu_0H = 2$ mT, which corresponds to $h = 0.04$ if we assume the value of $\mu_0H_c = 50$ mT for Fe$_3$O$_4$.

The relaxation signal $\Delta(m)$ increases with the field $h$ when $h$ is smaller than $h = 0.04$. In this region, the relaxation signal is comparable to the susceptibility signal $\langle m \rangle_{sus}$, and is larger than the remanence signal $\langle m \rangle_r$. However, the relaxation signal becomes saturated when the field becomes larger than $h = 0.04$. If we assume the value of $\mu_0H_c = 50$ mT, the value $h = 0.04$ corresponds to $\mu_0H = 2$ mT. The saturation of the relaxation signal above $\mu_0H = 2$ mT was experimentally observed in [7].

The remanence $\langle m \rangle_r$ is small when the field $h$ is small. However, the signal increases with $h$, and the remanence signal $\langle m \rangle_r$ becomes very large compared to the relaxation signal when the large field is applied. It must be noted that the excitation field can be applied outside the SQUID system in this case. Therefore, we can apply large excitation field without increasing the noise of the SQUID system.

In the present system, therefore, we choose the Fe$_3$O$_4$ nanoparticle with nominal diameter of $d = 25$ nm, and use the remanent measurement method. We note that the diameter of the particles used in the experiment ranged from 18 nm to 32 nm with averaged value of 25 nm.

2.3 Fabrication of Magnetic Marker

The maker was prepared by two-step reactions as shown in Fig. 4. i.e., the polymer coating and the immobilization of antibody. The polymer coating was carried out by a radical polymerization, followed by the adsorption of poly(N-vinylpyrrolidone) macromonomer in methanol. A typical run was as follows. To 20 cm$^3$ methanol solution of 0.2 g vinylphencyle-terminated poly(N-vinylpyrrolidone), Monomer; acryloyl-L-glutamic, Crosslinker; tr(1-acyloxyethyl)amine hydrochloride, THF; tetrahydrofurane, AIBN; 2,2’-azobis (isobutylonitrile), WSC; 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide.

![Fig. 4 Magnetic marker made of Fe$_3$O$_4$ nanoparticles with diameter of 25 nm. The magnetic particle is covered with the copolymer layer whose diameter is typically 80 nm, and 2.1 antibodies are immobilized on the single maker. Here, Macromonomer; vinylphencyle-terminated poly(N-vinylpyrrolidone), Monomer; acryloyl-L-glutamic, Crosslinker; tr(1-acyloxyethyl)amine hydrochloride, THF; tetrahydrofurane, AIBN; 2,2’-azobis (isobutylonitrile), WSC; 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide.](image-url)
Fe₃O₄, 0.01 g 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and 5 cm³ phosphate buffer (0.01 M). After the mixture was stirred at 0°C for one hour, 10 mg human IgE was added. The resulting solution was further stirred at a room temperature for 6 hours. The antibody-immobilized particles were separated by a centrifugation from the phosphate buffer five times. The antibody was immobilized 6.6 mg/g, which was corresponding to 2.1 antibodies on each particle.

3. Design of SQUID for Sensitive Detection

3.1 Spatial Distribution of the Magnetic Field

In Fig. 5(a), a SQUID system for the magnetic immunoassay is schematically shown. Here, we assume a square sample with side length 2a. The number of the magnetic particles in the sample is N, and the volume of each particle is V. In the remanence measurement, the sample is magnetized in the z direction outside the SQUID system, and each particle has the magnetic moment M per unit volume. In this case, the magnetic moment mₜ per unit area is given by \( mₜ = NVM/(2a)^2 \).

For the SQUID, we consider the directly coupled SQUID, as shown in Fig. 5(b). The pickup coil is made of thin film with width \( w_p \), and outermost side length is 2b. The distance between the SQUID and the sample is z, and the z-component of the magnetic field \( B_z \) is detected. In Fig. 6, spatial distribution of the magnetic field \( B_z(x, 0, z) \) along the x direction is shown. The calculation is made for the sample size 2a=5 mm and different values of the distance z. As shown, spatial distribution of \( B_z \) is large, i.e., \( B_z \) is concentrated around the sample. This result indicates that the conventional design of the SQUID that is developed for the case of the uniform magnetic field cannot be used in the present case. It is necessary to design the SQUID so as to efficiently measure the magnetic field shown in Fig. 6.

Therefore, we develop the simulation method that can treat the case when the spatial change of the magnetic field is large. Using the simulation, we can obtain the relationship between the signal flux \( \Phi_s \) detected with the SQUID and the number N of the particle in the sample. Details of the simulation will be described elsewhere [14].

3.2 Magnetic Flux Detected with the SQUID

In Fig. 7(a), solid lines show the dependence of the signal current \( I_s \) on the size 2b of the pickup coil. Here, \( I_s \) is the current flowing through the SQUID inductance of the directly coupled SQUID. The simulation is made for the sample size 2a=5 mm and the distance z=1 mm. In the simulation, the ratio between 2b and the film width \( w_p \) is fixed as \( w_p/2b = 1/3, 1/6 \) and 1/2. As shown, the signal current \( I_s \) increases, reaches maximum, and then decreases when the size 2b increases. For the cases of \( w_p/2b = 1/12 \) and 1/6, we obtain a clear peak of \( I_s \), while a broad peak is obtained for the case of \( w_p/2b = 1/3 \). The value of 2b that maximizes \( I_s \) is the optimum size of the pickup coil.

We note that the peak value of \( I_s \) increases with the increase of the ratio of \( w_p/2b \) as shown in Fig. 7(a). The value of \( I_s \), on the other hand, can be shown to be saturated for \( w_p/2b > 1/3 \). Therefore, the ratio of \( w_p/2b = 1/3 \) gives the maximum signal current \( I_s \) in this case. This behavior is similar to the case of the uniform magnetic field [15].

In Fig. 7(b), the optimum size of the pickup coil 2b is shown when the sample size 2a and the distance z are given. In the calculation, the ratio of \( w_p/2b \) is fixed as \( w_p/2b = 1/3 \), and the sample size is changed from 2a=1 mm to 2a=5 mm. The symbols, \( \triangle \), \( \bigcirc \) and \( \square \) show the results for z=0.5 mm, 1 mm and 2 mm, respectively. The broken lines show the optimum size 2b of the pickup coil that gives the maximum value of \( I_s \). As shown, optimum values of 2b are nearly the same between z=0.5 mm and z=1 mm. The value of 2b, however, becomes large for the case of z=2 mm. This is due to the broadening of the magnetic field when the distance z becomes large.

Since the \( I_s \)-2b curve shows a broad peak in the case of...
Fig. 7  
(a) Dependence of the signal current $I_s$ on the size $2b$ of the pickup coil. Simulation is made for the sample size $2a=5\,\text{mm}$ and the distance $z=1\,\text{mm}$. Note that the value of $2b$ that gives the maximum value of $I_s$ is the optimum size of the pickup coil. (b) Optimum value of $2b$ of the pickup coil for different values of $2a$ and $z$. The broken lines show the optimum value of $2b$ that gives the maximum value of signal current $I_s$. The solid lines show the value of $2b$ that gives 90% of the maximum value of $I_s$.

$w_p/2b=1/3$, as shown in Fig. 7(a), we also study the value of $2b$ that gives 90% of the maximum value of $I_s$. Solid lines show the results. As shown, the size $2b$ of the pickup coil can be considerably reduced if we allow a 10% decrease of the signal current $I_s$. The decrease of the size $2b$ is large for the case of $z=1\,\text{mm}$ or large values of $2a$. In this case, the size $2b$ of the pickup coil becomes comparable to the sample size $2a$. Details will be described elsewhere [14].

In Fig. 8, dependence of the signal current $I_s$ on the distance $z$ is shown for different sample size $2a$. Note that the vertical axis represents the value of $I_s/(\mu_0 N MV)$. This means that the number $N$ of the particle in the sample is fixed even when the sample size $2a$ is changed.

Fig. 8  
Dependence of the signal current $I_s$ on the distance $z$ for different sample size $2a$. Note that the vertical axis represents the value of $I_s/(\mu_0 N MV)$. This means that the number $N$ of the particle in the sample is fixed even when the sample size $2a$ is changed.

dependence becomes larger when the sample size $2a$ becomes smaller. In the case of $2a=1\,\text{mm}$, the distance should be less than 0.5 mm in order to obtain large signal.

It must be noted that the signal current $I_s$ becomes larger for smaller sample size $2a$ when the number of the particle $N$ is fixed. Therefore, we should use smaller size $2a$ and shorter distance $z$ for the increase of the signal current $I_s$.

4. SQUID System

4.1 Reaction Chamber

In developing the system for magnetic immunoassay, magnetic contamination in the reaction chamber should be as small as possible. Since we use the remanence measurement method for the detection of the magnetic marker, remanent field from the chamber must be kept as small as possible after the excitation field of about 0.1 T is applied. Unfortunately, commercial chambers have large magnetic contamination, which result in the large remanent field after the excitation field is applied. An example is shown in Fig. 9(a).

In this case, the reaction chamber is magnetized with the field of 0.1 T outside the SQUID, and the resulting remanent field from the chamber is measured with the SQUID. In the measurement, the chamber is moved under the SQUID with a distance of 1.5 mm, and the waveform of the magnetic flux detected with the SQUID is recorded. As shown, remanence of the chamber gives the magnetic flux of $40\,\mu\Phi_0$. This value is too large to measure the weak magnetic signal from the magnetic marker.

Therefore, we develop the reaction chamber that has low magnetic contamination by controlling the fabrication process. In Fig. 9(b), the magnetic noise from the new chamber is shown. In this case, remanence of the chamber gives the magnetic flux less than $0.4\,\mu\Phi_0$, which is comparable to the noise of the SQUID system. Therefore, we can detect the weak magnetic signal from the marker by using the new chamber.

As discussed in Sec. 3, close distance between the
SQUID and the room temperature sample is required in order to obtain large magnetic signal. When the SQUID is set under the reaction chamber, thickness of the base of the chamber should be kept as thin as possible in order to realize close distance between the sample and the SQUID. For this purpose, thickness of the base is chosen as 0.4 mm, which gives the distance of $z=1.5$ mm in the present case. The diameter of the chamber is 5 mm and the volume is 300 µl, which are the typical values of the chamber used for the immunoassay.

4.2 SQUID System

Previously, we showed a basic SQUID system for magnetic immunoassay [8], [9]. Recently, we have been developing a new system to investigate the performance and usability of the magnetic immunoassay in an ordinary environment at a medical facility. Figure 10 shows a schematic drawing of the developed immunoassay system.

In this measurement system, disk-shape reaction chamber (sample disk) was used. The sample disk is made of magnetic free material described in the previous subsection. Twelve reaction cells were formed along a concentric circle with a diameter of 150 mm. Therefore, twelve samples could be examined in one measurement sequence. A position marker was formed at the outer edge of the sample disk and detected by position sensor. The signal from position marker was used as a trigger for data accumulation.

The directly coupled thin film gradiometer, which can reduce the spatially uniform external noise, was used as a sensor. The gradiometric pickup coil consists of two $5 \times 5$ mm$^2$ superconducting loops, i.e., $2b=5$ mm and $w_p=2b/3$ in Fig.5(b). We note that the value of $2b=5$ mm is not an optimum value, but was chosen due to the limited space of the substrate. In this case, the signal flux detected with the SQUID becomes 90% of the optimum design, as shown in Fig. 7(b).

The gradiometer was fabricated by the conventional patterning process using YBa$_2$Cu$_3$O$_y$ high $T_c$ superconducting thin film deposited on a bicrystal SrTiO$_3$ substrate ($15 \times 15$ mm$^2$). The gradiometer was placed in vacuum for thermal insulation and cooled by liquid nitrogen through a sapphire/Cu rod. The magnetic signal generated from sample was measured through a thin sapphire window (0.3-mm-thick). The distance between sample and SQUID is about 1.5 mm. The gradiometer is controlled using a flux locked loop circuit with ac bias method. Typical flux noise of the gradiometer was $70 \mu \Phi_0/\text{Hz}^{1/2}$.

The SQUID and sample are surrounded with three layers of permalloy magnetic shield in order to reduce the disturbance from the environmental magnetic noise. SQUID and magnetic shield were set in an aluminum box that acts as an RF shield (Fig. 10). In addition, the gradiometric pickup coil can reduce the spatially uniform environmental noise by 2-3 decades.

By rotating the sample disk, reaction cells pass through above the SQUID gradiometer one after the other. Thus, twelve samples can be measured in one rotation cycle. The rotation speed of the sample disk was 15–60 rpm and more than 100 times accumulation was performed for averaging. The measurement procedure including the sample rotation, measurement and subsequent data averaging could be set and controlled by a computer.

In Fig. 11(a), an example of the measurement signal is shown. In this case, the rotation speed of the sample disk was 15 rpm, i.e., time for one rotation was 4 s. The signal is averaged for 100 measurements. Analogue filters of 5-Hz high-pass and 40-Hz low-pass are used to improve the signal-to-noise ratio. As shown, signals from twelve samples can be clearly measured.

In Fig. 11(b), the signal from the 100 pg of Fe$_3$O$_4$...
nanoparticles is shown. The diameter of the Fe$_3$O$_4$ particles is 25 nm, and the remanent signal from the particle was measured. The magnetic signal of about 1 m$\Phi_0$ was clearly detected under the ordinary laboratory environment. We note that it is accurate to represent the signal in terms of the magnetic flux $\Phi_s$, since the magnetic field from the particle spatially distributes in the area of the pickup coil of the SQUID, as shown in Fig. 6. The average magnetic field at the pickup coil was $B=18$ pT for $\Phi_s=1$ m$\Phi_0$ in the present case.

We note that the signal was measured in the unshielded laboratory environment at Kyushu University Hospital in order to investigate the system performance in a medical facility. At present, the detecting limit of this system is about 30 pg of Fe$_3$O$_4$ nanoparticles, which is limited by some external noise. It will be possible to improve the system performance to detect less than 10 pg Fe$_3$O$_4$ nanoparticles since the flux noise of the gradiometer was $70 \mu\Phi_0/\text{Hz}^{1/2}$.

5. Experimental Result

5.1 Preparation of Sample

We conducted an experiment to detect the binding reaction between the antigen and its antibody. The sample used in the experiment is schematically shown in Fig. 12, where two antigens called IL8 and human IgE were used. The sample was prepared using the following standard procedure [2]. First, a substrate was coated with capturing antibody called MAB208 for IL8 or A116UN for IgE. Next, a blocking material (Block Ace) was coated to prevent nonspecific binding of the antigen to the substrate. Then, serially diluted antigen (IL8 or IgE) was added and incubated at room temperature for 1 hour. A 200$\mu$l solution of antigen was used in the experiment. Finally, the magnetically labeled antibody, i.e., magnetic marker shown in Fig. 4, was added and incubated for 30 min. After finishing the binding reaction, unbound markers were washed out. Size of the sample was 5 mm in diameter.

5.2 Immunoassay Experiment

When the sample is made, direction of the magnetic moment of each marker is random. In order to align the direction of the moment and to generate remanence of the sample, a field of 0.1 T was applied in perpendicular to the substrate outside the SQUID system. Then, the sample is inserted into the SQUID system, and the remanence field of the sample is measured, where time interval between magnetization and measurement is about 1 minute. We note that the experiment was done using the previously developed SQUID system, whose details were described in [8] and [9].

In Fig. 13(a), the relationship between the signal flux $\Phi_s$ and the weight $w$ of the antigen is shown. The horizontal axis represents the weight of IL8 and IgE, while the vertical axis shows the signal flux $\Phi_s$. The triangles show the results of IL8, while the circles show the results of IgE. As shown, good relationship between $\Phi_s$ and $w$ was obtained for both samples. We can detect IL8 and IgE down to 0.03 pg and 0.3 pg, respectively. These results demonstrate the high sensitivity of the present method.

Since the signal flux $\Phi_s$ is proportional to the number of antibodies that couple to the antigens, it will be more accurate to represent the quantity of antigen in terms of molecular concentration, rather than the weight. Taking account that the molecular weight of IL8 and IgE is $10^4$ and $1.8\times10^5$, respectively, we plot the signal flux as a function of molecular concentration, as shown in Fig. 13(b). Here, the horizontal axis represents the molecular concentration of IL8 and IgE. As shown, signal flux becomes almost the same between IL8 and IgE when the molecular concentration is the same. This result is quite reasonable since the signal flux is proportional to the number of antigens. At present, a few atto-mol of IL8 and IgE has been detected.
6. Conclusion

Recent our results on the magnetic immunoassay utilizing the magnetic marker and the SQUID are presented. First, magnetic signal from the assembly of magnetic nanoparticles is studied for different measurement methods. It was shown that we can obtain large magnetic signal by using the remanence of the Fe3O4 particle with diameter of 25 nm. We also show the design of the SQUID for sensitive detection of the magnetic signal from the marker. Next, the system utilizing the SQUID and the reaction chamber with very low magnetic contamination is shown for the measurement of multiple samples. Finally, we detected the biological materials called IL8 and IgE, and showed that a few atto-mol of IL8 and IgE can be detected, which shows the high sensitivity of the present method.

Acknowledgments

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References

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