Analysis of minimum noise range for signal detection method using $2\omega_c$ harmonic frequency in biosensor signal detection

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***Abstract* - Recently, biosensors have been developed for portable biosensor system. Signals measured in the biosensor system are inevitably accompanied by a variety of internal and external noises. Thus, biosensor systems require very low-level signals detection under noisy environments. Lock-in amplifier (LIA) has been used for the detection of a weak signal concealed in an intense background noise such as thermal noise, flicker noise (1/f) and shot noise in biosensor systems. The LIA is composed of a trans-impedance amplifier (TIA), a phase sensitive detector (PSD) and filters such as low pass filter (LPF) and high pass filter (HPF). In general, output signal of the LIA is that modulated signal by the PSD is represented by the DC voltage after passing through the LPF. However, in order to improve the signal to noise ratio (SNR) and dynamic reserve, a second-order harmonic frequency ($2\omega_c$) which is double of reference frequency is used. For the detection of $2\omega_c$ signal, the minimum noise region in frequency domain should be determined. Also, this region should not be affected by the flicker noise. The total noise characteristics of a system almost depend on the first stage of cascade system by Friis formulas. Therefore, total noise figure of the LIA is determined by the noise characteristics of the TIA. In this paper, we analyzed characteristics of the TIA and found the minimum noise region for using $2\omega_c$ detection method. We implemented the LIA based on CMOS integrated circuit using 0.18㎛ process and detected the $2\omega_c$ signal for improvement of the SNR. As a result of experiment, the minimum noise region is ranged from 20 to 55 ㎑ in the TIA.**

I. INTRODUCTION

Recently, biosensors have attracted great attention for applications in the future IoT. The development of biosensors started with the invention of enzyme electrodes by Leland C. Clark in 1962. The biosensor is a biological detection system that converts a biological information into

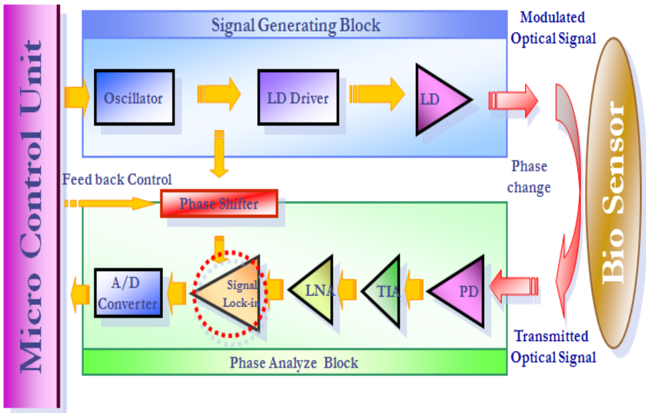

Fig. 1. Diagram of CMOS-based biosensor signal detection system.

a useful signal to obtain measured information from the bio object. The typical biosensor includes bioelements such as an enzyme, antibody and sensing element. The biosensor has advantages such as selective detection for only the target substance, rapid and continuous measurement, high specificity and fast response time. [1] Biosensors are used in various fields such as medicine, industry, military and environment. Applications of biosensors are monitoring glucose level in diabetes patients, food analysis, environmental applications, protein engineering and drug discovery applications and wastewater treatment. [2] Thus, miniaturization of system is needed for generalization of biosensor system, and a signal detection circuit of high sensitivity is required. [3, 4]

Signals measured in the biosensor system are inevitably accompanied by a variety of internal and external noises. Thus, biosensor system is required for detection of very low-level signals under noisy environments. Fig. 1 shows diagram of the signal detection in the biosensor system. Lock-in amplifier (LIA) has been used for detection a weak signal concealed in intense background noises such as thermal noise, flicker noise (1/f) and shot noise in the biosensor system. The LIA is composed of a trans-impedance amplifier (TIA), a phase sensitive detector (PSD) and filter such as low pass filter (LPF) and high pass filter (HPF). [5] The LIA have disadvantages such as very large, high price and difficulty of portability. Thus, the LIA

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is designed by technology-based on CMOS integrated circuit for low noise, high performance and portable size. [6] In general, output signal of the LIA is that a modulated signal by the PSD is represented by the DC voltage after passing through the LPF. However, a signal to noise ratio (SNR) of the LIA based on CMOS integrated circuit is reduced by a flicker noise which is one of inherent characteristics in semiconductor devices. The flicker noise is inversely proportional to frequency and exists at low frequency regions. In order to improve the SNR and dynamic reserve, a second-order harmonic frequency ($2\omega_c$) which is double a frequency of reference signal is used. [7] Dynamic reserve is used to describe the signal recovery performance of the LIA.

For detection the signal of $2\omega_c$ frequency, the frequency region of minimum noise should is determined. Also, this region should be not affected by the flicker noise. Harald T. Friis introduced in 1944 the noise figure (NF) concept which characterized the degradation in the SNR. According to the Friis formulas for noise, the total noise characteristics of system almost depend on the first stage of cascade system. [8] Therefore, total noise figure of the LIA is determined by the noise characteristics of the TIA.

In this paper, we analyzed noise characteristics of the TIA. Also, the LIA based on CMOS integrated circuit was implemented using 0.18㎛ process and the minimum noise region is determined.

II. SIGNAL DETECTION METHOD USING LOCK-IN AMPLFLIER

A. The principle of lock-in amplifier (LIA)

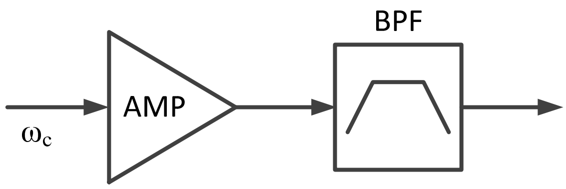


Fig. 2. General filtering using low noise amplifier and the band pass filter.

As shown in Fig. 2, general filtering using low noise amplifier and the BPF is used in order to detect a weak signal. Because general filtering increases the loss of signal and worsens the SNR, there is no good method using general filtering. The LIA is used for detection a weak signal concealed in various noise. Fig. 3 shows the block diagram of the LIA. The measurement method using the LIA requires that a frequency of reference signal fixes same frequency of input signal. As shown in Fig. 4, the input signal is amplified and multiplied with the lock-in reference signal using the PSD. The output signal of the PSD is new signal at the sum and difference frequency (ω_c) of input and reference signal. [5] Assuming that both the input and reference signal is sinusoidal, the PSD output voltage is thus

$$v_{in} = V_{sig}\cos(\omega_c t + \theta_{sig}) \quad (1)$$

$$v_{ref} = V_{ref}\cos(\omega_c t + \theta_{ref}) \quad (2)$$

$$v_{PSD} = V_{sig}\cos(\omega_c t + \theta_{sig}) \times V_{ref}\cos(\omega_c t + \theta_{ref}) \quad (3)$$

$$= \frac{1}{2}V_{sig}V_{ref}\left[\cos(\theta_{sig} - \theta_{ref}) + \cos(2\omega_c t + \theta_{sig} + \theta_{ref})\right]$$

$$\approx \frac{1}{2}V_{sig}V_{ref} + \frac{1}{2}V_{sig}V_{ref}\cos(2\omega_c t), \quad (if\ \ \theta_{sig} = \theta_{ref} = 0) \quad (4)$$

If phase difference between the input and reference signal is zero, the output signal of the PSD be maximized and contain components at the zero frequency (i.e. DC) and the 2 ω_c frequency, where ω_c is the frequency of the input and reference signal. Fig. 4 (a) shows modulated signals of time domain and (b) shows spectrum of frequency domain. After input signal is modulated by the PSD, AC signal is removed by the LPF. Therefore, we can detect the weak signal by finding the DC signal through the LPF.

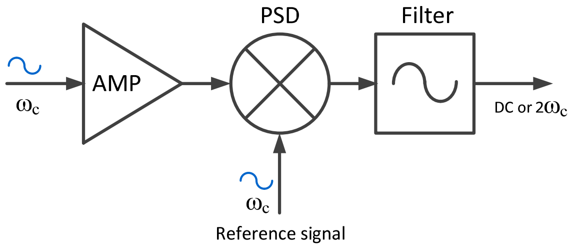


Fig. 3. Block diagram of the lock-in amplifier.

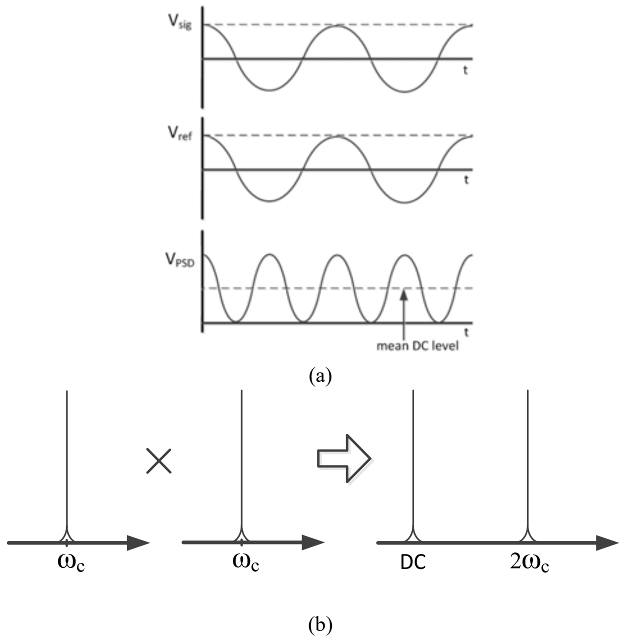


Fig. 4. Modulation result by the PSD.
(a) result of time domain (b) result of frequency domain

B. The method using second-order harmonic frequency

Fig. 5 shows signal and noise distribution according to frequency. In low frequency range, noise is increased by flicker noise. As the frequency increases gradually, influence by flicker noise is decreased and noise is equal to the white noise floor. [9, 10] Because DC component is detected using the LPF in conventional LIA, the amplitude of DC voltage and the SNR is reduced by flicker noise.

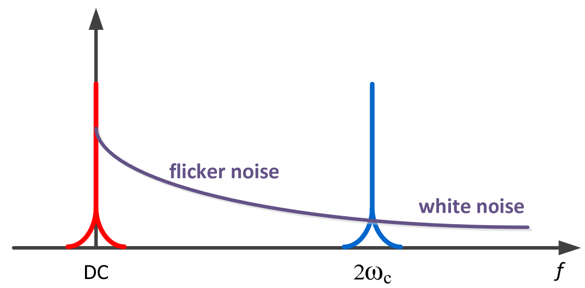


Fig. 5. Signal and noise distribution in frequency domain.

In order to resolve this problem, there is method using the second-order harmonic frequency ($2\omega_c$) which is double of a frequency. If $2\omega_c$ frequency component is detected by the BPF, the SNR is more improved than the SNR by the LPF at DC component because the flicker noise is inversely proportional to frequency and exists at low frequency regions.

Also, dynamic reserve is improved. Dynamic reserve is a term which is one of the LIA specifications and used to describe the signal recovery performance of the LIA. Dynamic reserve is defined as out of phase rejection ratio for distortion or simply as ratio of full scale signal to clipping level. It is usually expressed in decibels (dB), where

$$Dynamic\ Reserve = 20 \times \log_{10} \times \frac{Interfering\ Signal}{Required\ Signal} \quad (5)$$

Dynamic reserve is often confused with dynamic range. Dynamic range is the ratio between the peak largest and peak smallest values of signal.

III. ANALYSIS OF NOISE FIGURE IN FREQUENCY RESPONSE

A. Total noise characteristic of cascade system

The noise factor and noise figure defines how much noise is added by any amplifier which is amplifying the signal. The noise figure (NF) concept is introduced by Harald T. Friis in 1944. The noise factor and noise figure are related and expressed by following equation.

$$\text{Noise Factor (F)} = \frac{(S_i / N_i)}{(S_o / N_o)} \quad (6)$$

$$\text{Noise Figure} = 10 \times \log_{10}(\text{Noise Factor}) \quad (7)$$

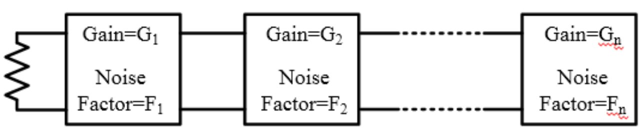


Fig. 6. The gain and noise factor of the cascade system.

As shown in Fig. 6, if several devices are cascaded, the total noise factor can be found with Friis formula and is given as

$$F_{total} = F_1 + \frac{F_2 - 1}{G_1} + \frac{F_3 - 1}{G_1 G_2} + \frac{F_4 - 1}{G_1 G_2 G_3} + \cdots + \frac{F_n - 1}{G_1 G_2 \cdots G_{n-1}} \quad (8)$$

where F_n and G_n are the noise factor and available power gain. The equation (8) shows the two important facts that gain G_1 should be sufficiently large in the first stage of a system and the total noise factor is primarily determined by the noise factor F_1 of the first stage. [8] Because the first stage in the LIA system is the trans-impedance amplifier (TIA), consequentially, the TIA is needed to have the largest gain and the smallest noise in the LIA in order to improve the SNR of the LIA.

B. The frequency region selection method in the TIA

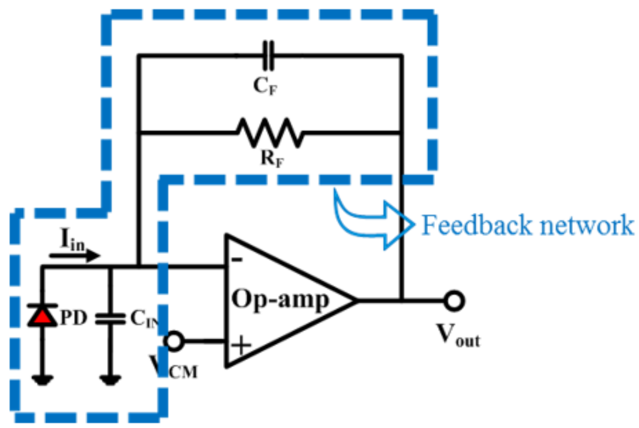


Fig. 7. Structure of the trans-impedance amplifier.

Because the signal generated from the optical biosensor is a current signal, the TIA is used as I-V converter in front-end of the LIA. Generally the TIA is designed using only feedback resistor. Because trade-off relation between gain and bandwidth exists in the TIA. In order to resolve this problem, compensation capacitor is used in feedback of the TIA. Fig. 7 shows structure of the TIA using op-amp and Fig. 8 shows transfer function of the TIA. Mathematically, gain of the TIA is decided by input impedance and feedback factor.

$$\text{Input impedance } Z_I = \frac{R_F}{1 + s(C_F + C_{IN})R_F} \quad (9)$$

$$\text{Feedback factor } \beta = \frac{1 + sR_F C_F}{1 + s(C_{IN} + C_F)R_F} \quad (10)$$

$$\text{Gain of the TIA (dB}\Omega) \ \frac{V_{out}}{I_{in}} = -Z_I \frac{A(s)}{1 + \beta A(s)} \quad (11)$$

$$= \frac{R_F}{1 + s(C_F + C_{IN})R_F} \left[\frac{A(s)}{1 + \frac{(1 + sR_F C_F)A(s)}{1 + s(C_{IN} + C_F)R_F}} \right]$$

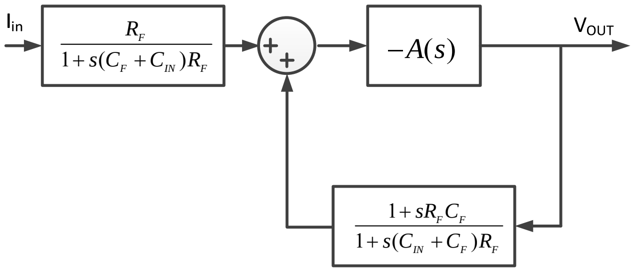


Fig. 8. Transfer function of trans-impedance amplifier.

If the impedance of feedback resistor (R_F) is very large compared to impedance of the input capacitance (C_{IN}) and feedback capacitor (C_F), the gain of the TIA can be estimated by the R_F.

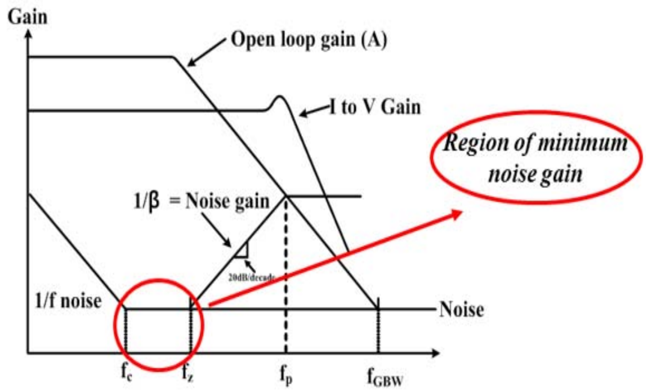


Fig. 9. Frequency response of gain and noise in the TIA.

Bandwidth of the TIA is affected not only R_F, C_{IN} and C_F but also GBWP (gain bandwidth product) of op-amp and widened according to increase of GBWP and feedback capacitor. The Fig. 9 shows frequency response of gain and noise in the TIA. Noise gain (NG) is decided by 1 over feedback factor. The point f_c is cut off by frequency of flicker noise, the point f_z is zero position of 1 over feedback factor. Noise gain is 0dB in the frequency region between f_c and f_z and increased in other regions. [11, 12, 13]

$$C_F = \frac{1}{4\pi R_F f_{GBW}} + \sqrt{\frac{1}{(16\pi R_F f_{GBW}} + \frac{C_{IN}}{2\pi R_F f_{GBW}}} \quad (12)$$

$$f_p = \frac{1}{2\pi R_F C_F} \qquad f_z = \frac{1}{2\pi R_F (C_F + C_{IN})} \quad (13)$$

$$f_{3dB} = \frac{1}{2\pi R_F C_F} = \frac{1}{2\pi R_F \sqrt{\frac{C_{IN}}{2\pi R_F f_{GBW}}}} = \sqrt{\frac{f_{GBW}}{2\pi R_F C_{IN}}} \quad (14)$$

As shown equation (12) ~ (14), the zero and pole position of the TIA can be calculated by feedback component and characteristics of op-amp. Also the SNR can be improved when signal is detected and measured in region of minimum noise gain.

IV. CHIP IMPLEMENTATION AND EXPERIMENT RESULTS

Fig. 10 shows the die microphotography of the fabricated the LIA with the size of 3800μm × 3800μm. Fig. 11 shows experiment set-up for confirmation of the minimum noise frequency range in the TIA. In the measurement system, we used a to-can laser diode with a wavelength of 680 ㎚ and high speed photo diode (S5971) in order to have enough bandwidth. Also we used a current driver (LDX-3320) to drive the to-can laser diode and current was 30 ㎃. We measured the output of the TIA according to frequency from 10 to 60 ㎑ using spectrum analyzer.

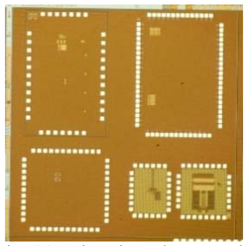


Fig. 10. Die microphotograph.

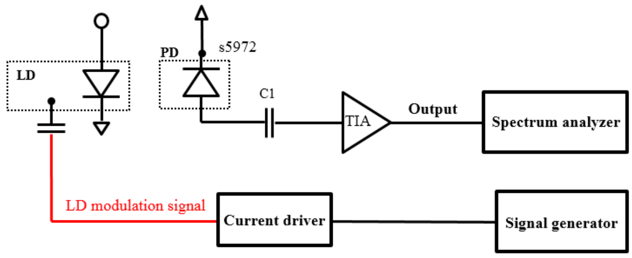
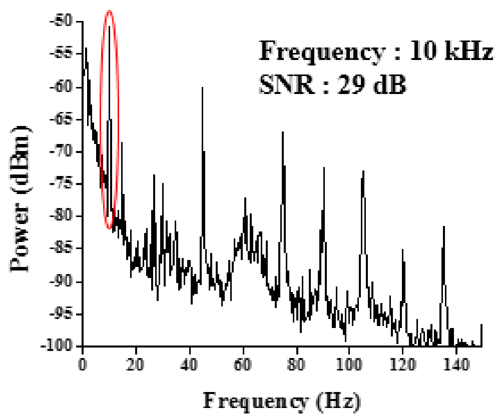
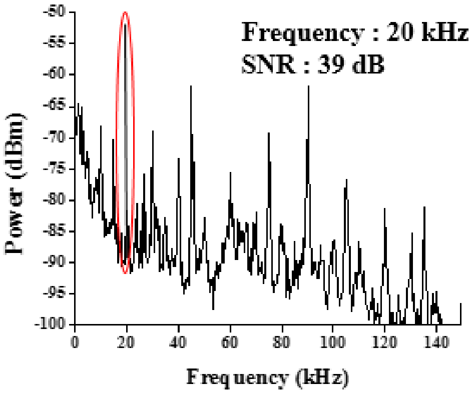


Fig. 11. Experiment set-up for confirmation of the minimum noise frequency range in the TIA.

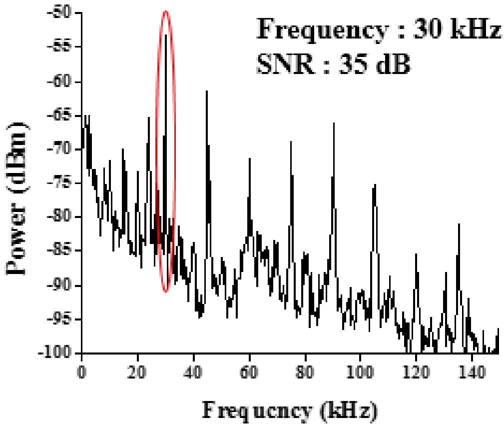
Fig. 12 shows experiment result of according to frequency from 10 to 60 ㎑. As a result, noise figure was affected by the flicker noise in the lower frequency range than 20 ㎑. In the higher frequency range than about 55 ㎑, noise was increased by characteristic of noise gain in the TIA. Therefore, minimum noise frequency region is ranged from 20 to 55KHz.



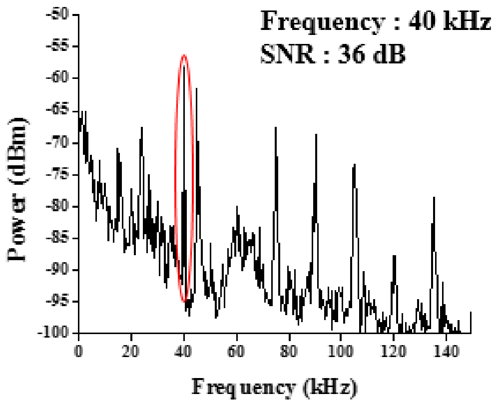
(a)



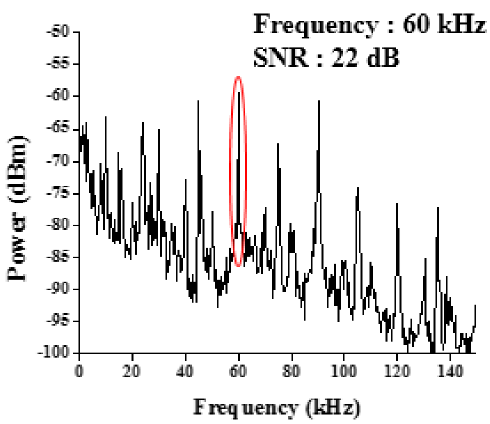
(b)



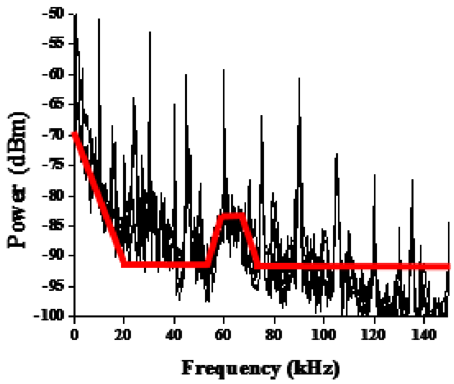
(c)



(d)



(e)



(f)

Fig. 12. The output of the TIA in frequency domain.
(a) 10 ㎑ (b) 20 ㎑ (c) 30 ㎑ (d) 40 ㎑ (e) 60 ㎑
(f) minimum noise range (from 20 to 55 ㎑)

V. CONCLUSIONS

We proposed a frequency range selection method for using $2\omega_c$ detection method in the LIA. The SNR and dynamic reserve can be improved, when the signal is detected at $2\omega_c$ frequency in the LIA. For detection the signal of $2\omega_c$ frequency, the frequency region of minimum noise should be determined. The total noise characteristics of system almost depend on the first stage of cascade system by Friis formulas. Because the noise figure of the LIA depends on characteristics of the TIA, we analyzed noise characteristics of the TIA and found the frequency region of minimum noise for using $2\omega_c$ detection method. The experimental results show that the SNR is improved more than 10 ㏈ at frequencies form 20 to 55 ㎑. The $2\omega_c$ signal detection method at minimum noise region has been successfully verified and is believed to be very useful for biosensor detection system using the LIA.

ACKNOWLEDGMENT

This work was supported by the IDEC and by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2009-0093817) and by the Pioneer Research Center Program through the NRF funded by the Ministry of Science, ICT & Future Planning (No. NRF-2014M3C1A3051969).

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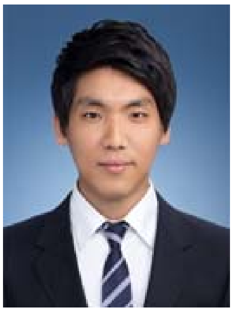

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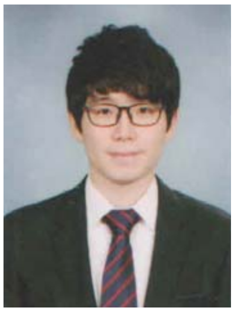

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He has authored more than 200 research papers in various international journals and conference proceedings. His current research interests are in the area of optoelectronics, optical biosensors, optical signal processing, and their circuit systems.