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Improvement of the Time-Domain Response of a Thermodilution Sensor by the Natural Observation System

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SUMMARY When measuring the ejection fraction for the evaluation of the ventricular pumping function by means of the thermodilution technique, the slow response a conventional thermistor has caused it to be considered unsuitable, and fast thermistors have been proposed as an alternative. However, in this paper we propose improving the time-domain response of a conventional thermistor using a signal processing technique composed of a series of first-order high-pass filters which is known as the natural observation system. We considered the rise time of the thermistor in response to a step temperature change to effect correction for the measurement of the ejection fraction. The coefficients of the natural observation system were calculated by minimizing the square error between the step-response signal of the thermistor and the band-limited reference signal. In an experiment using a model ventricle, the thermodilution curve obtained from a conventional thermistor was improved using the proposed technique, thus enabling successful measurement of the ejection fraction of the ventricles.
key words: *thermodilution, natural observation system, ejection fraction, rise time, step-response, real time*

1. Introduction

The ejection fraction of the ventricle, defined as the ratio of the stroke volume to the ventricular volume, is an index for characterizing the pumping function of the heart and it is used to compute the end-diastolic volume of the ventricle. The ejection fraction has been measured by various means such as the dye-dilution method, angiography and the heart pool-scan. However, they are not suitable for repeated use or for use with seriously ill patients because of the intracorporeal remainder of coloring matters, contrast media or radio isotopes. The thermodilution method and the impedance method are much safer than these methods and are extremely useful in examining the changes of the ventricular function with the progression of time, due to their allowing for the measurement of the cardiac output [1]. In the thermodilution method, the thermodilution curve, which shows the change in temperature over time after cooling water has been injected into the ventricle, is measured. The ejection fraction is estimated using the temperature change between successive end-diastolic times of the ventricle. The time constant of the thermistor which is used conventionally in the measurement of the cardiac output, however, is fairly large (for example, the time constant of Swan Ganz thermodilution catheter was approximately 1.33 seconds in measurement). Thus, it is difficult to detect the temperature change per heart beat at the outflow tract, and so the thermistor has never been used for the ejection fraction measurement. Instead, the fast-response thermistor was developed, which could be mounted on the catheter, allowing for the measurement of the thermodilution curve for a single heart beat [2]-[5]. The fast-response thermistor, however, is expensive and unsuitable for regular clinical examinations.

However, we propose a signal processing technique to correct the signal by accounting for the rise time of the conventional thermistor in response to a step temperature change, i.e. to improve the frequency characteristics of the measuring system. This is commonly done using Fourier analysis, however, Fourier analysis requires information of the signal from the infinite past to the infinite future time and so is unsuitable for real time processing. Conventional analog or digital filters must be used for real time processing. If the order of the system is high and many coefficients must be calculated, it is difficult to realize the system.

We use the natural observation system [6], [7] to overcome these problems. In the natural observation system as originally proposed in [6], the observed signal, considered to be the output of a first-order low-pass filter, is passed through a series of first-order high-pass filters, and the original signal is reconstructed from a linear weighted sum of the outputs of these filters and the observed signal. This method is realizable in real time, because it reconstructs the present time signal using only signals from the infinite past up to the present time. The only coefficients to be calculated are the weights of the filter outputs.

The natural observation system compensates for the time response of the thermistor by realizing a band-limited inverse filter in the frequency domain. Therefore, we obtain a signal whose rise time in response to a step temperature change is more rapid than that of the thermistor. To implement the natural observation system, the natural observation coefficients

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(i.e. the weights of the filter outputs), the time constant of each high-pass filter, and the order of system (i.e. the number of high-pass filters) must be predetermined. We calculate the natural observation coefficients by minimizing the square error between the measured signal of the thermistor in response to a physically applied step signal and a band-limited reference signal mathematically derived from a step function. The time constants and the order of the system are determined in terms of both the signal-to-noise ratio and the accuracy of the signal after the correction. Finally, estimation of the ejection fraction is carried out using the thermodilution curve restored by our method.

2. Natural Observation Method

Fourier analysis is used for signal analysis, signal processing and system identification. Fourier analysis requires signals from the infinite past to the infinite future time, making it unsuitable for real time implementation. However, the natural observation method only requires signals from the past up to the present time.

In the theory of the natural observation method, a fundamental observation operator, $\Gamma(s)$, is defined as

$$\Gamma(s)f(t)=\int_0^{\infty}\frac{1}{s}e^{-\tau/s}f(t-\tau)\,d\tau \tag{1}$$

where $f(t)$ is the original signal and s is a positive real valued time constant. A series of fundamental observed signals, $a_m(t)$, is recursively defined using $\Gamma(s)$ as

$$a_0(t)=\Gamma(s)f(t), \tag{2}$$

$$a_m(t)=\{I-\Gamma(s)\}a_{m-1}(t), \quad \text{for } m=1,2,\cdots \tag{3}$$

The original signal may be expressed as

$$f(t)=\sum_{m=0}^{\infty}a_m(t). \tag{4}$$

Equation (1) requires only the signal from the infinite past to the present time, and does not require the signal in the future time. Moreover, since the signal of the past time decays exponentially, the signal in the present time is emphasized in Eq.(1). In this manner, the natural observation method naturally expresses the present signal. That is why this system is named "the natural observation method." A structural analysis of the instantaneous waveform using the natural observation method was proposed [8], [9]. Using this analysis we can obtain a series of instantaneous amplitude coefficients and a series of instantaneous frequency coefficients of the waveform.

The above infinite-order natural observation method can express any signal. The finite-order natural observation method which uses a weighted sum of fundamental observed signals has also been proposed [10]-[12]. It is called the natural observation system, and such a system of order M can express any signal $f(t)$ for which there exist natural observation coefficients b_m $(m=0,1,\cdots,M)$ such that

$$f(t)=\sum_{m=0}^{M}b_m a_m(t) \tag{5}$$

holds, where $a_m(t)$ is as defined in Eqs.(2) and (3). Notice that although this appears similar in form to a truncated Fourier series or other basis representation, its fundamental meaning is different. For a given class of signals the natural observation coefficients will be constant. It is the $a_m(t)$ that varies with each signal in that class as they depend on $f(t)$ through Eq.(2). Examples of kinds of signal which can be represented by this system are Dirichlet series signals, periodic signals and polynomial signals. Kiryu [13] and Ohkubo [14] applied the natural observation system to the modeling of speech signals and recognition of concatenated vowels, respectively.

The natural observation system can be applied to the restoration of signals. Let $a_0'(t)$ be the observed signal and let

$$g(t)=\sum_{m=0}^{M}b_m a_m(t) \tag{6}$$

be the restored signal for a fixed set of coefficients b_m. If $a_0'(t)$ coincides with $a_0(t)$ in Eq.(2) and the original signal $f(t)$ is representable using the coefficients b_m, then $g(t)$ is a perfect restoration of $f(t)$. We have previously reported on use of the natural observation system to correct pressure waveforms in a catheter manometer system [15], [16] and to correct electrocardiograms in a Holter system [17]. In this paper, we apply the natural observation system to improve the time-domain response of the thermistor. We also have modified the method of coefficient determination so that we may acquire more precise coefficient values.

3. Thermodilution Method

Let ESV (end-systolic volume) be the volume of blood contained in the ventricle at the time of the end-systolic point. Let SV (stroke volume) be the additional volume of blood pumped into the ventricle during the time between the end-systolic point and the end-diastolic point. Let EDV (end-diastolic volume) $=ESV+SV$. The temperature of the blood is assumed to be T_0°C. Measurements of the ejection fraction and EDV by the thermodilution curve can be made in a similar manner to the measurement of cardiac output [1], [5]. The outline of the thermodilution method is shown in Fig. 1(a).

Just at the end-systolic point, cooling water is injected into the ventricle causing a drop of ΔT_1°C in the blood contained therein. This state is shown in the circle at the far left. During the time up to the next

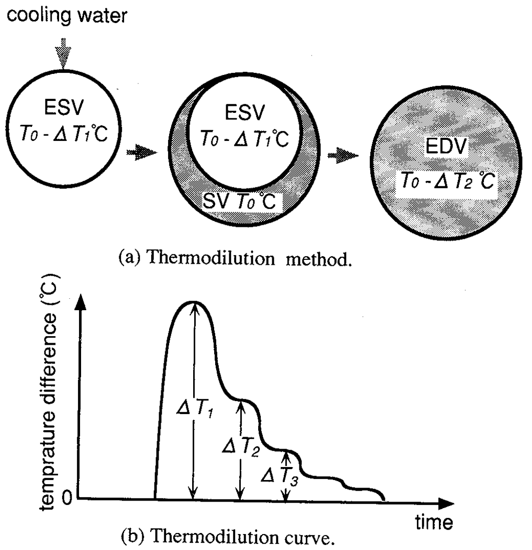

Fig. 1 Thermodilution Method. The stepwise thermodilution curve could be obtained by a fast-response thermistor. ESV= end-systolic volume; EDV=end-diastolic volume; SV=stroke volume; baseline temperature= T_0°C; $\varDelta T_1$, $\varDelta T_2$, $\cdots$ = temperature differences between the baseline and plateaus.

end-diastolic point, a volume SV of T_0°C blood will enter the ventricle. This state is shown in the two right hand circles. Let the final temperature at the end-diastolic point be $(T_0-\varDelta T_2)$°C. Then we have the following equations:

$$T_0-\varDelta T_2=\frac{(T_0-\varDelta T_1)ESV+T_0SV}{EDV}. \tag{7}$$

Equation (7) may be rewritten as

$$\frac{ESV}{EDV}=\frac{\varDelta T_2}{\varDelta T_1}. \tag{8}$$

The temperature of the blood in the ventricle gradually return to the original temperature, T_0°C, due to repeated pulsation.

If we could measure the temperature change by means of a temperature sensor with a sufficiently small time constant, then the stepwise thermodilution curves could be obtained, as shown in Fig. 1(b). From this we can obtain the ejection fraction. From Eq. (8), it is found that $\varDelta T_2/\varDelta T_1$, which is the attenuation rate per heart beat in the plateaus of the thermodilution curve, coincides with the residual rate, ESV/EDV of the ventricles. The calculated value of the ejection fraction (EFC) is defined by

$$EFC=\frac{SV}{EDV}=1-\frac{ESV}{EDV}. \tag{9}$$

It is difficult, however, to obtain the EDV in clinical cases. In practice, the following measured value of the ejection fraction using the thermodilution curve (EFTD) is used instead. From Eqs. (8) and (9),

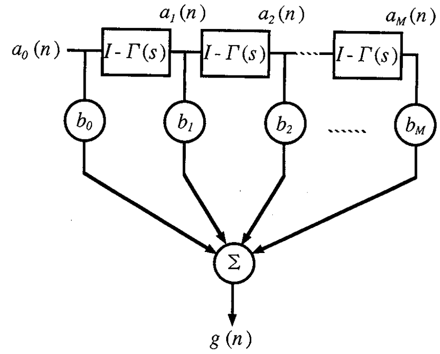

Fig. 2 Natural observation system for the correction of the thermodilution curve. $a_0(n)$=observed signal; $I-\Gamma(s)$=first-order high-pass filter with its the time constant s; $a_m(n)$ $(m=1, \cdots, M)$=output of m-th high-pass filter; b_m $(m=0, \cdots, M)$= coefficients; $g(n)$=corrected output.

$$EFTD=1-\frac{\varDelta T_2}{\varDelta T_1}. \tag{10}$$

4. Improvement of Time-Domain Response

4. 1 Correcting System

The transfer function of the conventional thermistor can be modeled by an M-th order low-pass filter [5] composed of fundamental observation operators of the form given in Eq. (1). We then define the noise free model observed signal as

$$a_0(t)=\left\{\prod_{n=1}^{M}\Gamma(s_n)\right\}f(t) \tag{11}$$

where each s_n is a complex conjugate pair or a real singlet and M is the order of observed system. Each $\Gamma(s_n)$ is a low-pass filter with a cutoff angular frequency of $1/s_n$. Note that this supersedes the previous definition of $a_0(t)$ given in Eq. (2). Just as with the $a_0(t)$ defined in Eq. (2), there are some signals which can be represented from the $a_0(t)$ defined in Eq. (11) using the finite-order natural observation method of Eq. (5). We consider a band-limited restoration of the original signal $f(t)$ when the observed signal $a_0(t)$ is the model observed signal $a_0(t)$ with added noise.

Figure 2 shows the block diagram of the natural observation system for the correction of a signal. The output signal of the natural observation system is given by Eq. (6) which can be rewritten as

$$g(t)=\sum_{m=0}^{M}b_m\{I-\Gamma(s)\}^m a_0'(t). \tag{12}$$

The value, s, of the time constants in each high-pass filter is the same. The order, M, is set to coincide with the order of the observed system.

Consider the band-limited signal

$$h(t)=\Gamma(s)^M f(t). \tag{13}$$

It is shown in the appendix that there always exist a set of coefficients b_m such that $g(t)=h(t)$ when the observed signal is noise free.

The value of the coefficients b_m depends on the transfer function shown in Eq.(11), i.e. on the time constants s_n which may be, as in our case, unknown. The b_m only need be calculated once and then the method may be used for band-limited restoration of any signal. In our experiment we use a step function for $f(t)$. The corresponding $h(t)$ is called the reference signal for the coefficient determination. The details of a method for determining s are described in Sect. 4. 2.

In the previous natural observation system [15]-[17], the coefficients were decided by minimizing the error between the original signal, $f(t)$, and the reconstructed signal, $g(t)$. The $g(t)$ derived by this method does not necessarily coincide with $h(t)$ even when the observed signal is noiseless. In the appendix it is shown that $h(t)$ is the optimal signal which can be recovered. Furthermore, because the observed step response may contain high frequency noise, the coefficients should only be used to match the band-limited part of the signal. This is also assured by using $h(t)$ instead of $f(t)$ as the reference signal.

4. 2 Relationship Between the Rise Time and the Time Constant of High-Pass Filters

We defined the rise time, t_r, of the step-response obtained by Eq.(13) as the time required to rise from 10 to 90 per cent of amplitude [18]. The amplitude-frequency characteristic of the operator $\Gamma(s)^M$ shown in Eq.(13) is given by

$$|H(\omega)|=\left(\frac{1}{\sqrt{1+\omega^2 s^2}}\right)^M \tag{14}$$

where ω is the angular frequency. Let ω_c be the cutoff angular frequency, i.e. ω_c satisfies

$$20\log|H(\omega_c)|=-3\ [\text{dB}]. \tag{15}$$

Equation (15) may be rewritten by

$$\omega_c=\sqrt{2^{1/M}-1}/s. \tag{16}$$

The relationship between ω_c and the rise time, t_r, is determined by

$$t_r\omega_c=2.2. \tag{17}$$

Finally, the relationship between t_r and s is given by

$$t_r=2.2s/\sqrt{2^{1/M}-1}. \tag{18}$$

If the order of the observation system, M, and the target rise time, t_r, are predetermined, the time constant of each high-pass filter, s, in the natural observation system is determined by Eq.(18).

4. 3 Parameter Estimation

Signals were digitized at a constant sampling rate and had a local time index n for $n=1, \cdots, N$. The corrected output, $g(n)$, shown in Fig. 2 is given by

$$g(n)=\sum_{m=0}^{M} b_m a_m(n), \quad \text{for } n=1, 2, \cdots, N, \tag{19}$$

where N is the observation window size, i.e. number of time steps over which we observed the signal, and $a_m(n)$ are the output signals of the constituent first-order high-pass filters of the natural observation system. Each high-pass filter was designed by the bilinear z-transformation. The window size N is sufficiently large to allow observation of the transient part of the observed signal. The residue $e(n)$ is given by

$$e(n)=h(n)-g(n), \quad \text{for } n=1, 2, \cdots, N. \tag{20}$$

where $h(n)$ is the band-limited reference signal. Suppose $e(n)$ is a white noise. The optimum coefficients b_m for the correction are estimated to minimize the square norm of $e(n)$ over the observation window. That is, after the observed step-response signal, $a_0'(n)$, was obtained, b_m were calculated to make the output signal of the natural observation system, $g(n)$, approximate the desired response signal, $h(n)$.

5. Experimental Procedure

5. 1 Step-Response of the Thermistor

The response of the conventional thermistor to a step temperature change was used as the observed signal. The thermistor was equilibrated in a 37°C water bath and then plunged into a 36°C water bath. The response signal, $g(t)$, was acquired by a 12 bit analog-to-digital converter with a sampling frequency of 250 Hz. The window size, N, was 2000 samples (8 seconds), which was sufficient to cover the time until the transient response converged or reached the stationary state. The band-limited reference signal was produced by substituting the step signal for $f(t)$ in Eq.(13).

5. 2 Thermodilution Measurement

In order to test our thermodilution measurement system we built a model ventricle, as shown in Fig. 3. The pump set at the top of the model ventricle was driven by a stepping motor to produce constant simulated heart beat. The stroke volume and the stroke rate were adjusted by controlling the pump stroke and the rate of the stepping motor, respectively. A waveform similar to the actual aortic pressure waveform was obtained by providing an air chamber and circulation resistance, based on the Wind-kessel model [19], at the outflow

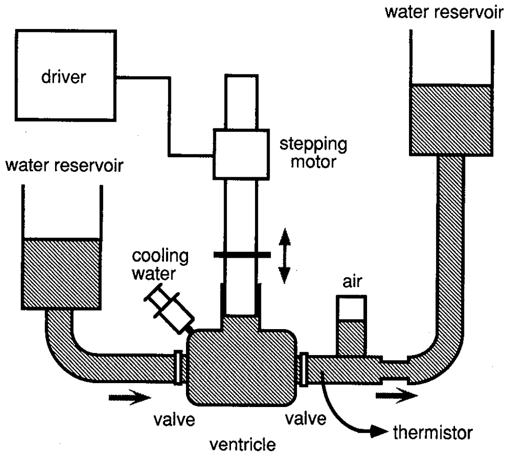

Fig. 3 Model ventricle driven by the stepping motor. The end-systolic volume (ESV) =200 ml.

port of the ventricles.

The ESV of the model ventricle was 200 ml and the experiments were carried out with two different stroke volumes (SV), i.e., 50 ml and 70 ml (corresponding to values of the EFC of 0.2 and 0.259, respectively). The stroke rate was 70 ml per minute. The measurement procedure was as follows: (1) The temperature of the water entering the model ventricle through the inflow port was kept at 37°C; (2) Cooling water (10 ml of 0°C water) was instantaneously injected into the model ventricle just at the end-diastolic phase, i.e. the peak of the piston up-stroke; (3) The outflow-liquid temperature was detected by the conventional thermistor provided at the outflow port; (4) The thermodilution curve and the pressure waveform were input into the microcomputer simultaneously through the analog-to-digital converter with 12-bit resolution and a sampling frequency of 250 Hz; (5) Then the natural observation system corrected the thermodilution curve and calculated the ejection fraction of the model ventricle.

6. Results

6. 1 Calculation of the Coefficients and Restoration of the Step-Response

Figure 4(a) shows the step-response signal, $a_0(t)$, measured by the conventional thermistor. The rise time of the step-response signal was about 2.93 seconds. Figure 4(b) shows the band-limited reference signal, $h(t)$. Figure 4(c) shows the restored step response signal, $g(t)$, obtained with the coefficients b_m set to minimize the distance to $h(t)$. A rise time of 0.44 seconds was obtained by setting s to 0.128 seconds and M to 2.

6. 2 Correction of Thermodilution Curve

Figure 5 shows the original and restored thermodilution curves. The arterial pressure waveform of the model is also shown in the lower column. The original thermodilution curve obtained directly from the thermistor was quite smooth. Thus, it was difficult to identify the effect of each heart beat. After the restoration, the temperature change for each heart beat could be clearly observed and the plateaus of the stepwise temperature change coincided with the end-diastolic phase as shown by vertical lines. Accurate measuring times were obtained using the arterial pressure waveform.

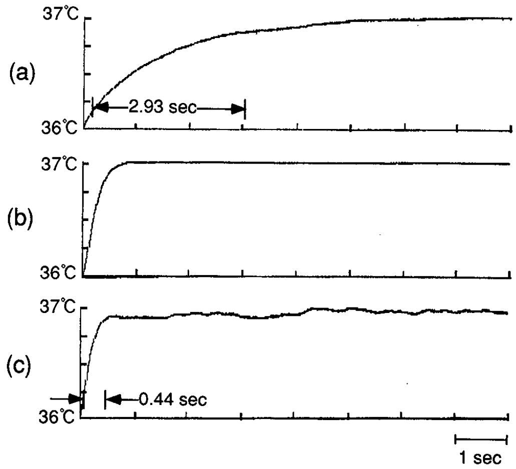

Fig. 4 (a) Step-response of a conventional thermistor. (b) The band-limited reference signal. (c) The corrected output of (a). A rise time of 0.44 seconds was achieved by setting the time constant, s, to 0.128 seconds and the order, M, to 2.

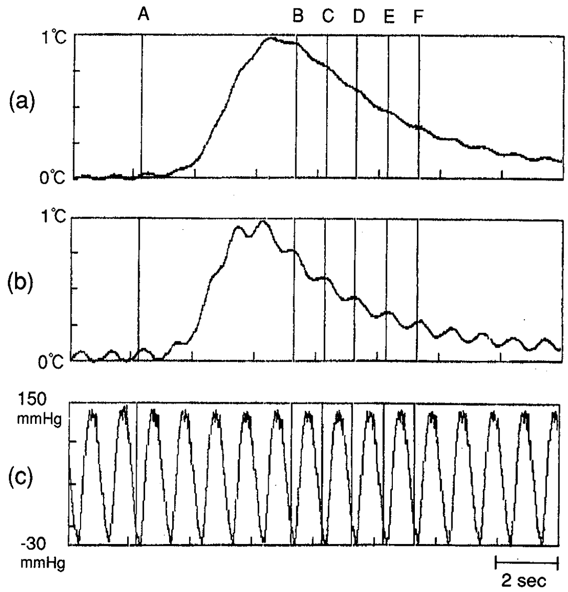

Fig. 5 Thermodilution curves (a) before and (b) after correction. Figure (c) shows the arterial pressure waveform. A: Time at when the baseline temperature is taken; B–F: Times at when the plateau temperatures for the ejection fraction measurement are taken.

Table 1 Results of ejection fraction measurement obtained from the corrected thermodilution curve from seven experiments.

	EFC = 0.200	EFC = 0.259
mean EFTD±SD	0.197±0.008	0.264±0.008
mean percent difference*	- 1.5 %	1.9 %

*(EFTD - EFC)×100 / EFC

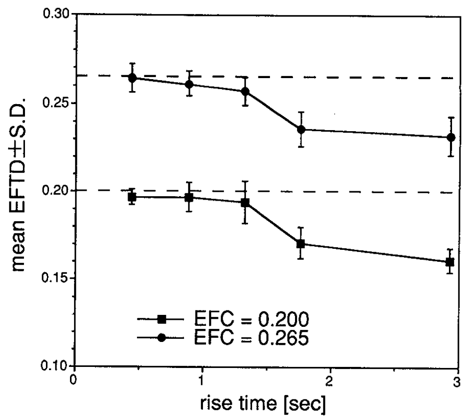

Fig. 6 Relationship between the rise time in response to the step temperature change and the ejection fraction measured by the thermodilution method (EFTD). EFC=calculated ejection fraction.

6. 3 Measurement of the Ejection Fraction

On each thermodilution curve the arterial pressure waveform was used to determine 6 consecutive end-diastolic time points at which to measure each of the corresponding temperature plateaus. The values of EFTD for six heart beats were calculated using Eq. (10), and the average value was calculated. This was done for a total of seven experiments, and the mean EFTD and the standard deviation were calculated for actual EFC values of 0.200 and 0.259. Table 1 shows the results as well as the mean value of percent difference between the EFTD and the EFC. The experimental values obtained in each measurement were very close to the set value, and the standard deviation for each set value was about 0.008. The percent differences were 1.9 per cent or less on the average.

7. Discussion

A first-order system can be completely evaluated by estimation of its time constant. However, the order of the conventional thermistor may be greater than 1. In practice, we have estimated this system as a second-order system. Thus, we have chosen to evaluate the transfer function of the thermistor using the rise time in response to a step change. The rise time of the step response restored by the natural observation system can be lessened if the time constant, s, of the natural observation system is set to a small value. A smaller s, however, may result in more emphasis on high frequency components, which in turn would lead to emphasizing noise components from the measurement system itself. Figure 6 shows the EFTD calculated using several different rise times. The order of the natural observation system, M, was set to 2. When the rise time was 1.32 seconds or greater, the ejection fraction was undervalued. However, values close to the set values were obtained when the rise time was 0.44 seconds. Rise times much lower than that resulted in very inaccurate measurements as a result of sensitivity to noise and so were not included in the graph. We expect that the rise time necessary to measure the ejection fraction accurately will depend on the value of the ejection fraction. Larger values of ejection fraction will require shorter rise times.

In our experiments, it was found that the relationship between temperature and impedance of the thermistor was not completely linear. The temperature change with respect to the impedance in the thermodilution method, however, lies in a very narrow range of about 1°C, and it was regarded to be approximately linear [20]. The measurement of the step-response was conducted in the same temperature range (from 36°C to 37°C) as that which exists in the actual thermodilution curve, avoiding the non-linearity problem.

Imai [21] reported problems with clinical measurement because the catheter is used to deliver the cooling water as well as to provide a mounting point for the thermistor. Thus, the thermistor may be cooled down below the surrounding blood temperature because of cooling water remaining within the catheter after injection. This phenomenon is closely related to the length of catheter that is inserted inside the body. In our experiment, we avoided this problem by performing the temperature detection and the injection of the cooling water with separate devices.

8. Conclusion

The thermodilution method is a method for measuring the heart function and has been used extensively in clinical cases. This method is relatively easy for patients to bear and enables measurements to be made frequently. Nevertheless, it has been limited to the measurement of the cardiac output because of the long rise time of the thermistor used in the thermodilution method.

We have focused attention on the transfer function of the thermistor, especially the rise time in response to a step temperature change. By applying the natural observation system, we improved the rise time of the thermistor to 0.44 seconds, limiting the high-frequency noise at the same time. The natural observation system realized simple operability and high reliability. Moreover, we performed the correction in real time without any modifications to the conventional thermistor. The improvement of the thermistor led to the detection of the temperature change synchronized with the heart beat, and to the attainment of an accurately restored thermodilution curve. In addition, the ejection fraction, which is the index that evaluates the heart function, was accurately obtained from the improved thermodilution curve. This demonstrates the possibility of employing the conventional thermistor, which is less expensive and widely used in clinical cases, in the measurement of the ejection fraction by the thermodilution method. The system now needs to be evaluated in clinical trials.

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Appendix

We represent the restoration in the frequency domain. The Laplace thransform of the noiseless observed signal, $a_0(t)$, shown in Eq. (11) is

$$A_0(p)=\left[\prod_{n=1}^{M}\left(\frac{1}{ps_n+1}\right)\right]F(p) \tag{A·1}$$

where p is the Laplace operator and $F(p)$ is the Laplace transform of $f(t)$. The Laplace transform of the reconstructed signal, $g(t)$, shown in Eq. (12) is

$$\begin{aligned} G(p)&=\sum_{m=0}^{M} b_m\left(\frac{ps}{ps+1}\right)^m A_0(p)\\ &=\left(\frac{1}{ps+1}\right)^M \sum_{m=0}^{M} b_m (ps)^m (ps+1)^{M-m} A_0(p)\\ &=\left(\frac{1}{ps+1}\right)^M \left[\frac{\sum_{m=0}^{M} b_m (ps)^m (ps+1)^{M-m}}{\prod_{n=1}^{M}(ps_n+1)}\right]F(p). \end{aligned} \tag{A·2}$$

The Laplace transform of the reconstructed signal, $h(t)$, shown in Eq.(13) is

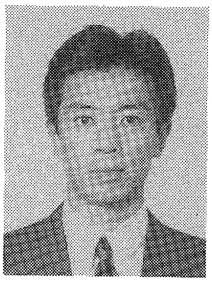
$$H(p)=\left(\frac{1}{ps+1}\right)^M F(p). \qquad (\mathrm{A}\cdot 3)$$

In Eq.(A·2), the middle product term is a fraction of M-th order polynomials in p. The polynomial in the denominator has fixed coefficients, and the polynomial in the numerator has coefficients which are a linear function of s and b_m. The time constant s is fixed, but the M natural observation coefficients b_m exist such that the numerator and denominator polynomial coefficients are the same, i.e. such that

$$\sum_{m=0}^{M} b_m (ps)^m (ps+1)^{M-m} = \prod_{n=1}^{M} (ps_n+1) \qquad (\mathrm{A}\cdot 4)$$

is satisfied, so that we obtain $G(p)=H(p)$.

We can also see from Eq.(A·2) the other two product terms are a fixed low pass filter and $F(p)$. The optimal restored signal is the one which gives the best representation of the band-limited part of $F(p)$, i.e. the one where the middle product term is 1.



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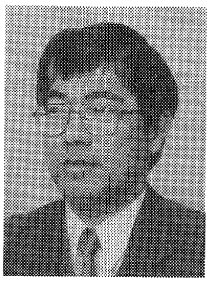

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