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Original Article

Adaptive Control of Respiration to Deal with Differences in Individual Characteristics

Hidetoshi WAKAMATSU and Kenji TAKAHARA*

ABSTRACT

Clinical technology for coping with differences in individuals is discussed on the basis of adaptive control theory, taking into account the automatic control of alveolar CO_2-concentration in both controlled- and assisted-respiration. An experimental system is proposed which consists of a newly developed respirator and controlling and measuring devices. The control system requires safe and accurate operation under different experimental contitions of controlled- and assisted-respiration depending on patterns of ventilatory rhythms. In order to satisfy both requirements, a control system is designed on the basis of an adaptive pole assignment method, which is capable of compensating for characteristic and environmental changes in the controlled object. It yields, thus, a stable control of alveolar CO_2-concentration dealing with equipment problems and mainly with the different characteristics of the respiratory regulation system inclusive of its individual differences such as nonlinearity and chronic change. From clinical experiments on healthy subjects, the control system is confirmed to maintain a given desired alveolar CO_2-concentration with assurance of its clinical safety. This kind of adaptive control is confirmed to lead to a useful concept and method for the control of organic function on the basis of its less exact recognition because of its time-varying and ambiguous characteristics.

Key words: control of respiration, adaptive control system, pole assignment, alveolar CO_2-concentration

1. INTRODUCTION

Proper ventilation and gas-exchange in respiration is essential in order to maintain the internal biochemical environment of organisms. In cases of malfunction of ventilation, artificial respiration is known as the most effective method for the maintenance of life. Various studies on artificial respiration have been conducted along with the progress of pathologic physiology of the respiratory and circulatory systems.[1)]

Automatic control for artificial respiration is classified into two categories, (a) automatic realization of various ventilatory patterns inclusive of the studies of flow patterns, pressure of gases given by a respirator and/or assisted-respiration[2)] and (b) control of the respiratory function i.e. automatic control of CO_2 partial pressure in arterial blood or alveolar CO_2-concentration. Various methods have been proposed,[3-6)] since it was tried to maintain a constant level of alveolar CO_2-concentration.[7)] However, most methods for automatic

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Tokyo Medical and Dental University, Graduate School of Health Sciences

* Faculty of Engineering, Muroran Institute of Technology

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control of alveolar CO_2-concentration have not always been clinically available because the characteristics of the respiratory regulation system depend on differences in individuals, and due to its nonlinearity and chronic change. This is why not only respiratory regulation systems but also organic systems in general are not easy to control in their stable state. Thus, it is of primary importance to solve these problems.

In recent years, however, control of artificial respiration has been attempted with healthy subjects in rest, resulting in satisfactory control of alveolar CO_2-concentration.[8–11] In the present study, a control system based on the adaptive pole assignment method is applied to the clinically basic control of alveolar CO_2-concentration both in controlled and assisted respiration. The necessity of an adaptive method is described, which is effective for its control from the systematic comprehension of an ambiguous respiratory regulation system. Physiological effects of the proposed system using a programmable respirator newly developed for the present study are explained on the basis of clinical experiments of the control of alveolar CO_2-concentration under different conditions.

2. DIFFICULTY IN DESCRIPTION AND MANIPULATION OF THE RESPIRATORY REGULATION SYSTEM

2.1 Difficulty in modeling of the respiratory system

It is generally necessary for the control of organic functions to have their description by some mathematical model.[12] Many models relating to respiratory rhythm and blood flow have been proposed. Nevertheless, no satisfactory models have been proposed representing nonlinearity and chronic change of its characteristics and individual differences, which are peculiar to organisms. For the maintenance of partial pressure of CO_2 ($PaCO_2$) and O_2 (PaO_2) in arterial blood within proper ranges of values, physiological controllers perform natural appropriate ventilation. They rely on the activation of the diaphragm and intercostal muscles, which are driven by orders of the pons and medulla oblongata with feedback signals from the sensors of the aortic and carotid bodies during their inappropriate pressures. It is remarked that the characteristic change of ventilation rate is affected by differences in $PaCO_2$ and PaO_2, and that the transportation of CO_2 and O_2 is affected by the blood flow depending on metabolic rate change and their dissociation curves. Nonlinear characteristics can be seen in both dissociation curves that are modified by physiological state depending on pH, $PaCO_2$, body temperature and 2,3-diphosphoglycerate. It is, thus, not easy to seize the accurate dynamic characteristics of such an ambiguous respiratory regulation system.

2.2 Possibility to activate the respiratory system

The respiratory control function is forced to work according to the control law generated from the controller under artificial respiration, although it would work depending on the physiological control law characterized essentially by CO_2-concentration and occasionally by O_2-concentration when O_2-concentration sinks to an extremely low level.[13] It is here proposed to design a generally applicable and effective control system which activates the whole respiratory function for the realization of a proper level of $PaCO_2$ or alveolar CO_2-concentration.

Figure 1 is an illustration of the natural control system of respiration. The system is a complete one including self-controlled subsystems in which there must be a restriction to choose the possible method of control. Thus, it can be said that the whole gas-exchange system is inclined to be insufficiently controlled by only inadequate ventilation according to

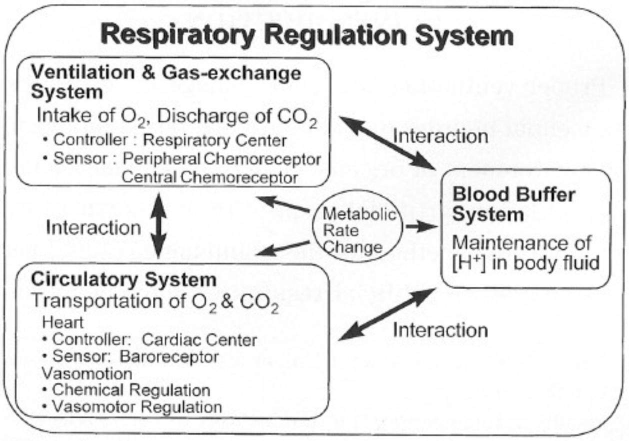

Fig. 1 Concept of the respiratory regulation system.

conventional methods. A respiratory system is in general much dependent on the total volume of alveoli, equivalent volume of body tissue and blood flow rate, which are individually different and difficult to estimate exactly. In addition, there exist numerous unknown factors affecting its dynamics. Thus, the necessary information for the synthesis of control systems cannot be obtained beforehand, because the exact physiological function cannot be known in any case. That is, it is practically not possible to design a control system for all patients with their own environments, as there always exist difficulties in the synthesis of the control system by conventional methods, which requires sufficient knowledge about the structure of controlled systems and their parameters. In other words, there are substantial theoretical difficulties of facilities resulting from imperfect recognition. Such problem, however, must be solved by some method, if organic functions are really to be controlled clinically. Hence, a suitable control method of the respiratory regulation system, including its appropriate description, has been strongly required for the robust control of CO_2-concentration. However, no appropriate methods have been proposed, which can deal with such difficulties, except for fuzzy and adaptive control methods.*1 In fact, insufficient recognition of the controlled systems, including even complicated characteristics of the experimental equipment, are of no concern, so long as an adaptive control method is applied, which is significant in the present situation because of the non-explicit parameter estimation.

2.3 Sampling difficulty in the control system of respiration

In order to realize flexible algorithms, the dynamics of a discrete-time system is usually described at every sampling time with a constant sampling interval. That is, the control system is designed on the basis of its observed dynamics in every regular sampling interval. Hence, conventional control methods are not suitable for systems with nonlinear characteristics as well as individual differences and chronically different characteristics, because they are only applicable to cases in which the parameters of individual patients are remain unchanged. By the way, they are not considered inappropriate in the case of controlled-respiration, usually for unconscious patients lying on a bed, as an appropriate sampling interval can be arbitrarily determined according to the frequency of ventilation. However, in the case of assisted-respiration depending on a patient's own respiratory rhythm, there may always be disagreements between the respiratory end-tidal timing and the controlling time of ventilation in a constant sampling interval. The sampling interval must be synchronized with the respiratory rhythm because the dynamic characteristics at a new sampling time are recognized as different from those at the previous sampling time. That is, the characteristics of a controlled object are differently recognized in every different sampling interval, even if the actual characteristics remain unchanged. Consequently, in the case of assisted-respiration with variable different respiratory rhythm, it becomes much more difficult to design a control system, because of the difficulty in its description by a conventional discrete-time representation.[14]

3. INSTRUMENTATION AND METHODS

3.1 Technological assumption coping with ambiguous knowledge about the respiratory regulation system

It is noted that knowledge about a respiratory system is not particularly required for the design of an adaptive control system. It is capable of so-called absorption of the effects of chronic changes and individual differences in the respiratory system and environmental changes inclusive of the experimental equipment, which may be fatal to the patient. Hence, the control system of respiration is designed only on the assumption of its description by an appropriate mathematical model that may represent the essential characteristics of the respiratory system including the characteristics of the experimental equipment as follows[8]:

[1] The dynamics of a respiratory system are assumed to be characterized by the relation of input (ventilation rate) and output (alveolar CO_2-concentration).

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*1 Fuzzy control is not for time-varying system, although some system deviation can be absorbed by verbal description and membership function.

[2] No consideration of the effect of interaction of the ventilation rate with the metabolic rate on alveolar CO_2-concentration.

[3] Contribution of metabolic rate change to output is regarded as a characteristic change resulting from parameter deviation.

In the present study, ventilation rate and alveolar CO_2-concentration are regarded as the input and output of the controlled object, respectively, from the viewpoint of its automatic control. The nonlinearity of the respiratory regulation system and its characteristic changes are regarded as deviations of the parameters of the mathematical model.6) Metabolic rate can be monitored as a physiologically inner-causal change according to the irregular state change of a patient. But, its contribution to alveolar CO_2-concentration is here regarded as resulting from parameter change of the controlled object. That is, the parameter change is treated as a function of metabolic rate change. As for the contribution of the ventilation rate, only the linearity and finite memory structure are assumed, although the effect of its interaction with unknown metabolic rate change on alveolar CO_2-concentration should be physiologically taken into account.

3.2 Application of an adaptive method to controlled- and assisted-respiration

An adaptive control method is effective in the case of a controlled object whose characteristic changes cannot be well recognized, making a whole control system innovated on the basis of the detection of changes in its characteristics and environment. Actually, it has been applied to the control of alveolar CO_2-concentration with considerable success.4,6,8–10)

By the way, the adaptive pole assignment method allows the whole control system to have its required characteristics in advance by the appropriate assignment of poles used as indicators of response speed and stability of the system. As all the possible changes of its characteristics inclusive of environment are regarded as changes of parameters, this method is considered the most appropriate one to control alveolar CO_2-concentration not only in controlled- but also even in assisted-respiration. That is, the method is thought suitable in order to hold stability of the control system in its adaptation process and to ensure the control of alveolar CO_2-concentration coping with the differences in individuals and chronic changes of the respiratory regulation system, even in variable sampling intervals. The concept of the proposed adaptive control system of alveolar CO_2-concentration is illustrated in Fig. 2.

3.3 Mathematical formulation of the control system by adaptive pole assignment method

For the design of a control system, the input-output relation is described as a deviation around the equilibrium state of alveolar CO_2-concentration, which is determined from the end-tidal alveolar CO_2-concentration under constant ventilation rate. It can be theoretically obtained under constant ventilation and metabolic rate, inspiratory CO_2-concentration and other constants determined by air pressure and operating range of CO_2-dissociation curve. However, it is of no concern that this is always implicitly taken into account in the adaptive pole assignment method.

The variable $y(k\tau)$ is the deviation from the equilibrium point of alveolar CO_2-concentration and $u(k\tau)$ is the deviation from the ventilation rate giving the equilibrium point, where k is the sampling number and τ is the sampling interval. They are discrete variables with respect to time $k\tau$ (abbr. k, hereafter). The aime is to determine a controlling input $u(k)$ so that the output $y(k)$ asymptotically realizes a reference $u_r(k)$ given as the desired value. The adaptive control mechanism regulates system parameters automatically, detecting changes of the controlled object and/or its environ-

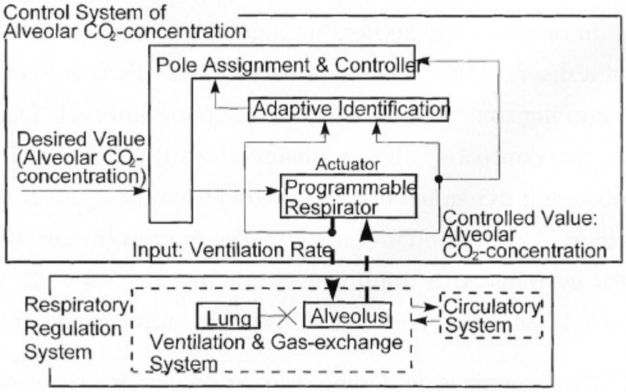

Fig. 2 Block-diagram of the control system of alveolar CO_2-concentration.

ment by an adaptive law, in which system performance is maintained within a certain degree of allowance.[15] The following linear autoregressive moving average model (ARMA-model) is used as a mathematical model[10] by which the characteristics of a respiratory system are regarded as including those of the experimental equipment:

$$A(z^{-1})y(k) = B(z^{-1})u(k) \tag{1}$$

where

$$A(z^{-1}) = 1 + \sum_{i=1}^{n_a} a_i z^{-1}, \quad B(z^{-1}) = \sum_{i=1}^{n_b} b_i z^{-i}$$

The output from the mathematical model $y_M(k)$ based on eq. (1) is given by parametric representation as

$$\begin{aligned} y_M(k) &= -\sum_{i=1}^{n_a} \hat{a}_i(k)y(k) + \sum_{i=1}^{n_b} \hat{b}_i(k)u(k-i) \\ &= \hat{\theta}^T(k)\,\zeta(k) \end{aligned} \tag{2}$$

where

$$\hat{\theta}^T(k) = [-\hat{a}_1(k), \ldots, -\hat{a}_{n_a}(k), \hat{b}_d(k), \ldots, \hat{b}_{n_b}(k)]$$

$$\zeta^T(k) = [y(k-1), \ldots, y(k-n_a), u(k-d), \ldots, u(k-n_b)]$$

are the estimated parameter vector and the state variable vector at time k, respectively. Parameters of the mathematical model are regulated so that error

$$e(k) = y(k) - y_M(k) \tag{3}$$

of the actual output $y(k)$ from the value $y_M(k)$ asymptotically converges to zero, where $\hat{a}_i(k)$ $(1 \leqq i \leqq n_a)$ and $\hat{b}_i(k)$ $(d \leqq i \leqq n_b)$ are estimates of unknown parameters, n_a and n_b are the length of memories of AR- and MA-parts and $d(\geqq 1)$ is dead time.

Let

$$C(z^{-1})y(k) = KB(z^{-1})u_r(k) \tag{4}$$

be given so that it may contain appropriate poles which satisfy stability of the closed loop system seen from the reference input $u_r(k)$ to the output $y(k)$, where $C(z^{-1}) = 1 + c_1 z^{-1} + \cdots + c_{n_c} z^{-n_c}$ (n_c indicates the length of the polynomial) and K is a gain constant given by $K = C(1)/B(1)$ to make its controlled deviation zero.

The controlling input $u(k)$ is determined from Eq. (5)

$$R(z^{-1})u(k) = Ku_r(k) - S(z^{-1})y(k) \tag{5}$$

where

$$R(z^{-1}) = 1 + \sum_{i=1}^{n_r} r_i z^{-i}, \quad S(z^{-1}) = \sum_{i=0}^{n_s} s_i z^{-i}$$

The polynomials $R(z^{-1})$ and $S(z^{-1})$ with their length given by n_r and n_s are determined so that

$$C(z^{-1}) = A(z^{-1})R(z^{-1}) + B(z^{-1})S(z^{-1}) \tag{6}$$

may be satisfied using estimated parameters of the controlled object. The adaptation algorithm is given by

$$\hat{\theta}(k) = \hat{\theta}(k-1) + \Gamma(k-1)\,\zeta(k)\,\varepsilon(k) \tag{7}$$

$$\varepsilon(k) = \{y(k) - \hat{\theta}^T(k-1)\,\zeta(k)\}/\{1 + \zeta^T(k)\,\Gamma(k-1)\,\zeta(k)\}$$

The constant-trace algorithm is adopted for a parameter regulation law for a time variant and/or nonlinear system as follows[14]:

$$\begin{aligned} \Gamma'(k) &= \Gamma(k-1) - \{\Gamma(k-1)\,\zeta(k)\,\zeta^T(k)\,\Gamma(k-1)\}/ \\ &\qquad \{1 + \zeta^T(k)\,\Gamma(k-1)\,\zeta(k)\} \\ \Gamma(k) &= \{1/\lambda(k)\}\,\Gamma'(k) \\ \lambda(k) &= tr\Gamma'(k)/tr\Gamma(0), \quad tr\Gamma(0) > 0 \end{aligned} \tag{8}$$

The basic structure of the adaptive control system by the pole assignment method is illustrated in Fig. 3.

3.4 Experimental equipment

Figure 4 is an illustration of data processing and control of respiration, clarifying the data and information flow in the experiment. The concentrations of end-tidal CO_2 and inspiratory O_2 are measured at every sampling time by gas-analyzer for controlling and monitoring the experimental process. The patient wears an air mask with a 1.0 [mm] diameter sampling tube of expiratory gas whose components are measured with the response of less than 1.0 [sec]. The tube is the

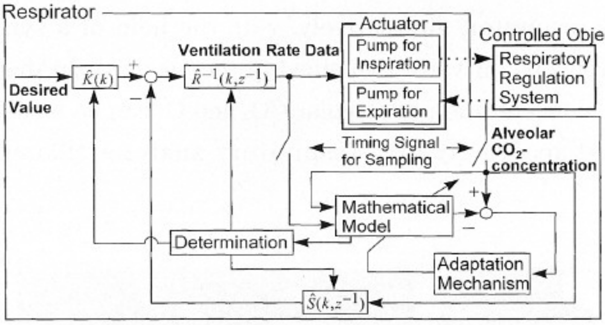

Fig. 3 Block diagram of an adaptive control system of respiration using the pole assignment method.

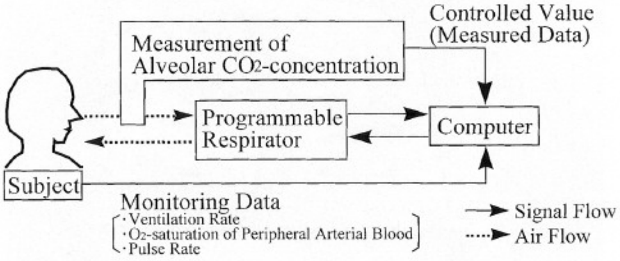

Fig. 4 Outline of the control system of artificial respiration.

short enough to make the mechanical dead space as small as possible. The wide-open end of the capsule is covered with an air cushion to keep the inside airtight. The air mask is connected to a respirator with appropriate valves to avoid contamination of inspiratory and expiratory gases. For the necessity of various kinds of physiological controls of respiration, an all-built-in-one type programmable respirator has been developed which is shown in Fig. 5.[8–10,16] The respirator is controlled by its operational parameters, which are manually given or automatically set by signals from computers. In order to supply an accurate ventilation rate, the respirator has 2 cylinders, whose movements are independently controlled actively to ventilate at every sampling time. Not only the stroke and frequency of its piston movement are readily controlled by outside signals but also the inspiratory (expiratory) wave form is controlled by setting a cycle percent ratio of inspiratory (expiratory) duration and pause of the respirator. The rhythm of the respirator can be set using the respiratory interval of the patient, because the piston movement of the respirator can be triggered by the signal from his/her diaphragm movement. The independent operations of inspiration and expiration ensure easy respiration for patients. The air is inspired from the respirator to the alveoli and expired from the alveoli to the respirator, alternatively, with the help of a synchronizing air valve contained in the air mask so that the concentration of alveolar CO_2 and O_2 can be measured accurately by a respiratory analyzer (Sanei, RESPINA 1H26). For the monitoring of an experimental state, ventilation amount is obtained by an integrator (Nihon Kohden, AQ-601G) of air flow velocity measured by a flow resistance tube, a difference pressure transducer and an amplifier (Nihon Kohden, TV-112T, TP-602T, AG-601G) and an oxygen saturation of peripheral arterial blood and pulse rate are measured by using a pulse-oximeter (Nihon Kohden, OLV-1200).

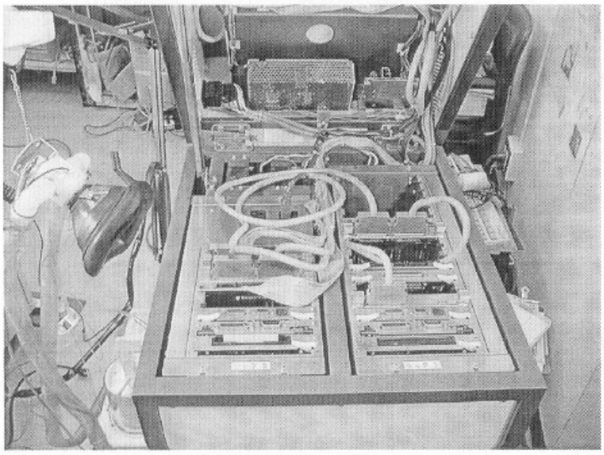

Fig. 5 Inner-view of the all-built-in-one type respirator.

4. EXPERIMENTS AND RESULTS

4.1 Experimental procedure and conditions for artificial respiration

The experiments were performed according to the theory explained in the previous section. A subject lies on his back on the bed. The concentrations of CO_2 and O_2 are measured by the gas-analyzer and acquired into the CPU for further digital processing and for monitoring of the state of the subject. Control is performed by adaptive calculation of the controlling input to realize the given reference dynamics. The controlling input is transformed into a stroke change in the movement of the piston of the respirator subjected to the number of generated pulse sequences according to the instructions of the computer. Then, it finally gives an actual ventilation rate change within its physiologically appropriate range of value.[*2]

4.2 Experimental results from artificial respiration

In order to clarify the features of the proposed method, 9 healthy adults (7 men and 2 women, 27–38 years of age) were subjected to experiments in 30 [min]. Considering clinical control of respiration, follow-up control of alveolar CO_2-concentration is taken into account under the existence of metabolic rate change caused by irregular body movement. The desired value of alveolar CO_2-concentration in both experiments was chosen as a step-like function with decrement by 1.0 [Vol%] at 10 [min] after the start of the control experiments. The poles corresponding to quick response of the system were chosen at the origin of the z-plane as $C(z^{-1}) = 1$.[10] The parameters were chosen as memory lengths $n_a = n_b = 2$ and dead time

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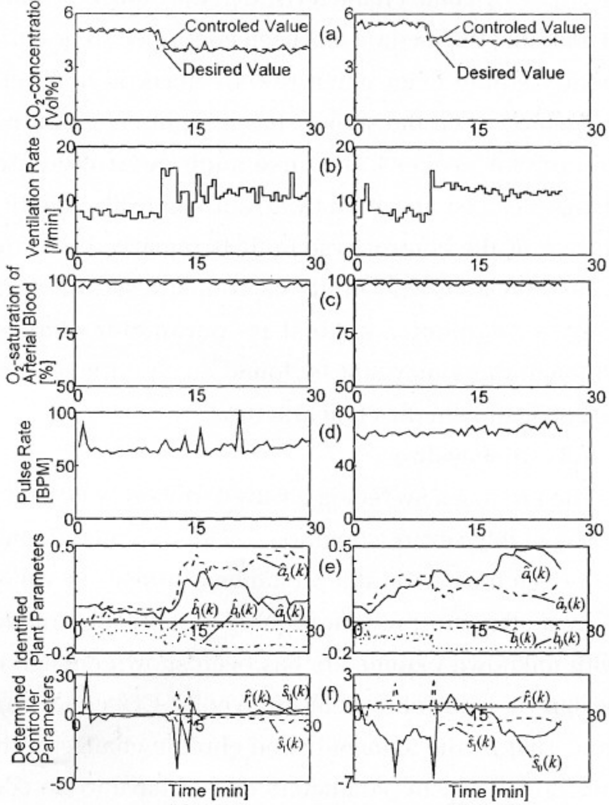
[*2] Upper and lower limits of ventilation amount are given by software and hardware mechanism.

$d=1$, taking into account the length of the tube to the gas-analyzer and its response time. The frequency of the ventilation was chosen 16 [times/min] and the sampling interval 30 [sec] in the case of controlled-respiration. The subjects were instructed to breathe not with their own respiratory rhythm but with the rhythm of the respirator. In the case of control of assisted-respiration, its equivalent environment was realized by changing the frequency of ventilation at random from 14 to 18 [times/min]. Hereby physiological data were acquired at every 7 ventilatory periods with the sampling intervals varying from 23.3 to 30.0 [sec].*3 Figure 6 shows two experimental results as examples of controlled- and assisted-respiration in 9 subjects under the previously mentioned conditions.

Control performances of artificial respiration can be graphically seen in detail, (a) Alveolar CO_2-concentration, (b) Ventilation rate, (c) O_2-saturation of peripheral arterial blood, (d) Pulse rate, (e) Estimated system parameters and (f) Parameters of controller. These show that alveolar CO_2-concentration was satisfactorily well controlled with safety of the subjects to follow-up the given desired value in both cases. The average normalized errors of the measured alveolar CO_2-concentration from the desired value according to

$$e=(1/m)\sum_{k=1}^{m}\left[|u_r(k)-y(k)|/u_r(k)\right] \tag{9}$$

were 1.69[%] in controlled-respiration and 0.28[%] in assisted-respiration, evaluating good performance of the proposed system in both cases.*4 The error distributions of the controlled output from the desired value are given in Fig. 7. They indicate proper adaptation of the control system, which yielded a considerable accurate control of alveolar CO_2-concentration. Thus, the proposed control system was experimentally confirmed to follow-up a step-like change in desired value satisfactorily as the basic controls of alveolar CO_2-concentration in controlled- and assisted-respiration in different subjects.*5 In other words, the proposed method is appropriate enough to control alveolar CO_2-concentration to follow-up a given characteristic coping with the differences in individual subjects and their physiological states and chronic changes, although there has not been explicitly found a really



(1) (2)

Fig. 6 Experimental results (1) in controlled-respiration and (2) in assisted-respiration.

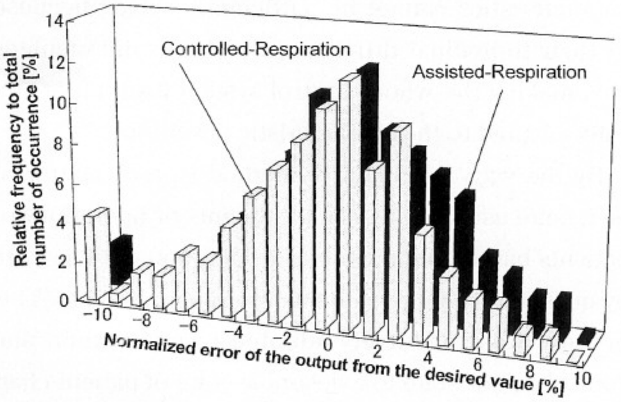


Fig. 7 Distribution of errors of the outputs from the desired values.

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*3 For easy operation, the sampling interval was at random changed, which is equivalent to the random change of a respiratory period.

*4 The physiological data are not usually observed without deviations in organism. It is desirable that the controlled values frequently cross over and remain around the desired values in both cases.

*5 The desired value may be hereby substituted by any sequential data interpreted as physiologically appropriate by medical doctors.

desirable dynamic characteristic in the clinical setting. In addition, the method has been confirmed to be sufficiently stable even when the air mask is not tight enough or when the subject has a slight cough during its control process, because such environmental changes can be absorbed by an automatically adaptive change of the control system. It is remarked that the control system also holds its robustness in a wide range of dynamics against its parameter change, although there may still be found some difficulties in its application in the clinical setting.

4.3 Discussion

The proposed system is ensured to work well under considerably severe conditions, seldom required clinically, such as with steep changes in desired value. Only a structural assumption of a controlled object with unknown parameters has been shown enough to design the control system of alveolar CO_2-concentration. That is, the ambiguity and chronic change of the concerned system parameters do not have to be considered in practice, which has been a most serious problem in such physiological control. It is thus widely applicable to patients whose respiratory dynamic characteristics cannot be sufficiently seized because of their individual differences and chronic changes etc., making the whole control system itself automatically adapted to the characteristic deviations.

By the way, the adaptive method is, as a matter of fact, quite usual in medical treatments or operations of patients based on the gradual recognition of their state by questioning, tapping, medical examination etc. This process was practically adopted to understand and control a poor state to a desirable state of patient characteristics, in which various techniques as a rule rely on the special knowledge and experience of medicine. It cannot be of course easily generalized to everyone. However, the proposed method is widely applicable to understand the state of patients and to realize its control, which does not require any special medical technique, despite its coping with differences in individuals and chronic changes of the state of patients. That is, it may be able to cover the essential ideas of individuality and generality of characteristics of organic functions, which are often disputed as contradictory concepts to each other in medical treatment. This is the reason why such a proposed adaptive control system is emphasized to be useful in the field of medicine.

5. CONCLUSION

A computer-based artificial respiratory control system has been developed to control alveolar CO_2-concentration, which has been investigated from the basic viewpoint of less necessary and less concrete knowledge about the controlled object. The control system by the adaptive pole assignment method has been successful in basic experiments on healthy subjects and clinically confirmed safe and efficient using a newly developed respirator, by which alveolar CO_2-concentration can be accurately measured and controlled. However, the desired value of alveolar CO_2-concentration still has to be determined within a physiologically appropriate range depending on the state of patients, for which a proper method such as artificial intelligence will be clinically required. The proposed artificial respiratory control system in principle will be available not only clinically but also even at home, e.g. to muscular dystrophy patients who need assisted-respiration by appropriate respiratory equipment without any medically special assistance and knowledge. Therefore, further study is required from methodological viewpoints to make the system smaller with simplified operation for its application to such cases. In addition, as the present method ensures essential description of differences and changes in individual characteristics, it is emphasized to be applicable to various kinds of medical themes, for instance, to the control of depth of anesthesia in the pertinent progressive process of such control of respiratory gas-concentration, provided that appropriate indicators of depth of anesthesia are clarified.

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