Abstract

The purpose of the present study is to construct a basic experimental system for automatic control of alveolar CO\textsubscript{2}-concentration during controlled and assisted respiration. This system consists of a newly developed computer-controlled respirator and its controlling devices. In the present study, ventilation rate and alveolar CO\textsubscript{2}-concentration are regarded as the input and output of the controlled object, respectively. The automatic control system of alveolar CO\textsubscript{2}-concentration is designed using an adaptive pole-placement method. The proposed system is applied to clinically basic control experiments of alveolar CO\textsubscript{2}-concentration both in controlled and assisted respiration. Furthermore, physiological experiments are made on healthy subjects during light exercise in order to ascertain the robustness of the system. Thus, the proposed system is confirmed to be useful for the control of alveolar CO\textsubscript{2}-concentration taking into account characteristic differences of the respiratory regulation system due to chronic change and individuality.

1 Introduction

A regulation system of an organic function is structured by some mutually related subsystems which have non-linear and time-varying characteristics dependent on its individuality. They function with appropriate controllers in order to maintain their homeostasis. Hence, it is not easy to control an organic function by some action from its external environment.

A respiratory regulation system with relatively well known characteristics is thought possible to control non-invasively in a real time by the appropriate choice of input and output owing to its anatomical structure. Various methods [1][2] have been proposed, including a trial by Frumin et al. to maintain a constant level of alveolar CO\textsubscript{2}-concentration [3].

Wakamatsu et al. have developed computer controlled programmable respirators suitable for the various artificial control of respiration [4][5][6][7][8]. The control of artificial respiration using the programmable respirator based on the adaptive control method has been successful with healthy subjects at rest where their alveolar CO\textsubscript{2}-concentration were accurately controlled.

In the present study, the control system based on the adaptive pole-placement method is applied to the clinically basic control experiments of alveolar CO\textsubscript{2}-concentration both in controlled and assisted respiration stages. That is, the physiological experiment is performed on healthy subjects during light exercise in order to ascertain its robustness. It is thus confirmed that the proposing system is generally useful for the control of alveolar
CO₂-concentration even taking into account the non-linear and time-varying characteristics of an individual respiratory regulation system.

2 Instrumentation and Method

2.1 Respiratory Regulation System

The regulatory mechanism of respiration is still not sufficiently understood. An attempt had been made to describe it using a mathematical model by Grodins et al. [9]. Then various kinds of models concerning respiratory rhythm and blood flow have been proposed [10]. Nevertheless, satisfactory models of respiratory regulation system have never been proposed representing its non-linearity, chronic change and differences of individuals which are remarkable in organisms.

The respiratory regulation system is widely regarded as the one composed of two subsystems; a ventilation and gas-exchange system, and a circulatory system as illustrated in Fig.1.

In this study, only the essential functions concerning above subsystems including a circulatory system are described in the figure.

![Respiratory Regulation System Diagram](image)

Fig.1 Respiratory Regulation System

In the ventilation and gas-exchange system, ventilation amount ("controlling input") is determined by the respiratory center ("controller") monitoring the partial pressures of CO₂ and O₂ (PaCO₂ and PaO₂, respectively) in arterial blood ("controlled value") in order to maintain their proper levels ("desired values"). Ventilation and gas-exchange are performed by the activation of a diaphragm and intercostal muscles ("actuators"). PaCO₂ and PaO₂ are detected by central and peripheral chemosensitive areas. Then, the proper stimuli are transmitted to the respiratory center during this process, if their pressures are not appropriate.

The non-linear and time-varying characteristics depending on individualities in a respiratory regulation system can be found, for instance, in the transportation of O₂ and CO₂ according to their dissociation curves which are modified by physiological state depending on pH, PaCO₂, body temperature and 2,3-DPG. In addition, the transportation of the gases are affected by blood flow depending on metabolic rate change. Hence, it is not easy to seize the accurate dynamic characteristics of such a respiratory regulation system with much variable characteristics.

2.2 Control of Respiratory Regulation System based on Adaptive Control Theory

The purpose of respiration is an intake of O₂ for oxidation in the body and a discharge of side-products of CO₂, which are closely related to the level of hydrogen ion concentration. It is, therefore, appropriate to design the control system of artificial respiration with PaCO₂ i.e. alveolar CO₂-concentration as a physiological indicator for its significant control.

In order to synthesize a control system, some description of a controlled object is necessary. However, it is not easy to represent a respiratory regulation system by mathematical models because of its non-linear characteristics as well as individual differences and chronic change as mentioned previously. Thus, it is not too much to say in present situation that by an artificial respiration the gas-exchange and circulatory systems cannot be controlled but only insufficiency of ventilation can be compensated.

By the way, an adaptive control method is effective in the case of controlled objects whose characteristic change cannot be well recognized. Actually, this method has ever been adopted to the control of alveolar CO₂-concentration.
In the present study, a deviation from an equilibrium point of alveolar CO$_2$-concentration is regarded as the output $y(k)$ of the controlled object. And a deviation from ventilation rate giving the equilibrium point is regarded as its input $u(k)$. The following linear auto-regressive moving average (ARMA) model is used as a mathematical model of the controlled object.

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

where

$$A(z^{-1}) = 1 + \sum_{i=1}^{n_a} a_i z^{-i}, B(z^{-1}) = \sum_{j=0}^{n_b} b_j z^{-j}$$

A mathematical model is given by

$$y_M(k) = -\sum_{i=1}^{n_a} \hat{a}_i(k)y(k-i) + \sum_{j=0}^{n_b} \hat{b}_j u(k-j) = \hat{\theta}^T(k)\zeta(k)$$

where

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

The adaptive law is given by

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

where

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

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

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

Therefore, the proposed system ensures a stable control of alveolar CO$_2$-concentration coping with the differences of individuals and chronic change of the respiratory regulation system. The block diagram of the whole control system is shown in Fig.2.

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

Here, $C(z^{-1})$ is a polynomial that provides desirable poles and $K$ is a gain to make a controlled deviation zero.

The controlling input is determined by

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

where

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

Polynomials $R(z^{-1})$ and $S(z^{-1})$ are determined so that they may satisfy

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

Hence, the proposed system ensures a stable control of alveolar CO$_2$-concentration coping with the differences of individuals and chronic change of the respiratory regulation system. The block diagram of the whole control system is shown in Fig.2.
2.3 Some Problems of Digital Control of Respiration

Recent development of mechatronic technique has made automatic control systems dealt with as discrete-time systems using digital algorithms. A discrete-time system is the one whose phenomenon is described at every sampling time where the object is usually controlled on the basis of its dynamics observed under a constant sampling interval. In the case of a controlled respiration, frequency of ventilation can be set by medical staffs. Alveolar CO$_2$-concentration is well controlled, if an appropriate sampling interval is chosen beforehand. However, in the case of an assisted respiration depending on a patient's spontaneous respiratory rhythm, there may be a disagreement of a sampling time with a measuring time of alveolar CO$_2$-concentration under a constant sampling interval. Therefore, if the data acquisition is synchronized with a respiratory rhythm, the sampling interval should be unceasingly changed. The change of sampling interval is interpreted as a change of observation time that is essential to the comprehension of the dynamic characteristics of a controlled object. Thus, the dynamic characteristics in a new sampling interval is recognized as a different one in a previous different sampling interval, even though the actual characteristics of a controlled object remains unchanged. Consequently, it becomes difficult to describe the system by a conventional discrete-time representation. There sometimes exists different recognition of the characteristics according to a different sampling interval, apart from the difference caused by its non-linearities, individuality and chronic change of a respiratory regulation system. In the case of an assisted respiration subjected to a different sampling interval, it becomes more difficult to design the control system of alveolar CO$_2$-concentration. However, an adaptive method ensures a whole control system innovated on the basis of the detection of change of the characteristics and environment of a controlled object. Then, if the change of its characteristics is regarded as the changes of parameters, an adaptive pole-placement method is thought the most appropriate method to control alveolar CO$_2$-concentration even in an assisted respiration.

2.4 Programmable Respirator

Figure 3 shows the computer-controlled respirator [8] with 2-cylindrical pumps independently driven for inspiration and expiration, which has been developed by Wakamatsu and others [4][5][6][7]. It is applied to the control system of the present physiological experiments.

![Fig.3 External View of the Respirator](image)

The hardware control system is supported by three computers (BP386SX, WACOM) for controlling alveolar CO$_2$-concentration, driving pistons, detecting fault and processing experimental data. The intermixture of inspiratory and expiratory air is avoided by a valve mounted on an air mask which moves with synchronization of respiration so that alveolar CO$_2$-concentration can be measured accurately. The whole control system of alveolar CO$_2$-concentration including the respirator and the measuring instruments are illustrated in Fig.4.

Respina 1H26(NEC SAN-EI) is used as an expired gas analyzer and Pulse-oximeter OLV-1000(NIHON KODEN) as measuring instrument of O$_2$-saturation of peripheral arterial blood.
Figure 7 shows two experimental results in an assisted respiration under the previously mentioned sampling intervals. These show that proposed system can control alveolar CO$_2$-concentration even in an assisted respiration.

3 Experiments and Results

The control of alveolar CO$_2$-concentration was performed on 9 healthy subjects (7 male and 2 female, age 27-38 years) using the control system of the respiration.

The proposed system was first supplied for the physiological experiment using healthy subjects at rest in 30[min], where the frequency of the ventilation was chosen 16 [times/min] and the sampling interval 30 [sec]. Secondly, in order to ascertain its robustness, alveolar CO$_2$-concentration of a subject during light exercise using an ergometer was controlled in 10 [min], where the frequency of the ventilation was chosen 22 [times/min]. The subjects were instructed to breathe with not own respiratory rhythm but the rhythm of the respirator. Thirdly, as the basic experiment for the control of alveolar CO$_2$-concentration in an assisted respiration, the frequency of ventilation was changed at random from 14 to 18 [times/min]. Hereby, experimental data were acquired at every 7 ventilatory period with the sampling intervals varied from 23.3 to 30.0 [sec]. The desired value of alveolar CO$_2$-concentration was given in all cases by a step-like function with decrement by 1.0 [Vol%] at 10 [min] after the start of the control experiments.

Figure 5 shows two experimental results taken out as examples from the ones on subjects at rest in a controlled respiration. These show that alveolar CO$_2$-concentration was satisfactorily controlled to follow up the given desired value.

Figure 6 shows two experimental results taking into account the metabolic rate change caused by the light exercise using an ergometer where subjects pedaled in 40 [rpm] with 30 and 50[W]. It shows that alveolar CO$_2$-concentration can be controlled irrespective of metabolic rate change.

Controlled deviations were relatively large only in a few steps from the beginning of the control or on the change in a desired value. They became smaller in accordance with proper adaptation of the control system which yielded a considerable
accurate control of alveolar CO$_2$-concentration as illustrated in Figs.5, 6 and 7.

**Fig.7 Experimental Result in Assisted Respiration**

### 4 Conclusion

A computer-based control system of the artificial respiration by the adaptive pole-placement method was proposed. It was experimentally confirmed to follow up a desired value satisfactorily irrespective of metabolic rate change and difference of individual subjects.

The proposed system is applicable to patients whose respiratory dynamic characteristics cannot be completely seized because of their individual differences and chronic changes etc., being automatically adapted to their environmental characteristic change. This is the reason why such a proposing “adaptive control system” is useful.

However, a desired value of alveolar CO$_2$-concentration still has to be set within a physiologically appropriate range depending on the state of patients, for which a proper method such an artificial intelligence is clinically required. It is remarked that conventional respirators can be substituted in the control system, although only 2-cylindrical respirator has been taken into account in the present experiments. The present control system of artificial respiration in principle will become available not only clinically but also even at home e.g. to muscular dystrophy patients who need an assisted respiration by a smaller respiratory equipment without any requirement of peculiar medical knowledge. Therefore, the further study is necessary from the methodological viewpoint to make the system smaller with simplified operation for its easier application.

In addition, as the present method ensures the objective description of the change in individual characteristics, it is applicable to various kinds of medical fields. Thus, this method will be directly applied to the control of the depth of anesthesia in the progressive process of the present study concerning the control of respiratory gas concentration, provided that appropriate indicators of the depth of anesthesia are clarified.

### References


