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AUTOMATIC CONTROL OF MECHANICAL VENTILATION. PART 1: THEORY AND HISTORY OF THE TECHNOLOGY

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ABSTRACT. Objective. In this article, automatic control technology as applied to mechanical ventilation is discussed and the techniques that have been reported in the literature are reviewed. **Methods.** The information in the literature is reviewed and various techniques are compared. **Results.** Automatic control has been applied in many ways to mechanical ventilation since several decades ago. More aggressive techniques aimed at automatic and more optimal control of the main outputs of the machine have emerged and continue to be enhanced with time. **Conclusions.** Development of more efficient automatic techniques and/or enhancement of the present methods are likely to be pursued to make this technology more compatible with future healthcare requirements.

KEY WORDS. mechanical ventilation, automation, closed-loop control.

INTRODUCTION

Closed-loop automatic techniques have been used in various forms in mechanical ventilation for several decades. The older technologies are mostly concerned with provision of a set volume and/or pressure of gas to the patient at a prescribed rate by the clinician. Correct delivery of the set volume/pressure of the inspiratory gas to the patient necessitates closed-loop monitoring of the delivered values to the patient by the machine. Modalities that embody mandatory minute volume technique (MMV) [1], various closed-loop technologies such as synchronized intermittent mandatory ventilation (SIMV), along with many variations of such modalities have been developed and used to assure delivery of a determined volume of gas to the patient in concert with his/her spontaneous breathing activity. Newer technologies utilize more aggressive methods directed at automatic control of the main outputs of ventilators in response to patient's changing requirements. The controlled outputs in these techniques include volume or pressure of the inspiratory gas, frequency of respiration, positive end-expiratory pressure (PEEP), and fraction of inspired oxygen (F_{IO2}).

The objective of this article is to discuss closed-loop control as applied to mechanical ventilation, provide an overview of the techniques developed to date, and to assess the direction and trend of this technology in view of the present and future clinical requirements.

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METHODS

What is closed-loop control?

In a closed-loop control system, the output(s) are controlled based on the present input(s) and previous output(s) and/or state variables of the system. Simply put, in a closed-loop system, some state variables and/or outputs are used to control the next output(s) of the system through feedback loops. A schematic diagram of a closed-loop control system is shown in Figure 1. In this configuration, if ''controller inputs'' are obtained by adding ''reference inputs'' to ''feedback signals,'' the system is said to be controlled by positive feedback, and if ''feedback signals'' are subtracted from ''reference inputs'' to obtain ''controller inputs,'' the type of feedback is said to be negative. Negative feedback systems can be designed to be stable, while positive feedback systems are inherently unstable.

Closed-loop control as applied to mechanical ventilation

If the concept of feedback as shown in the schematic diagram of Figure 1, is applied to mechanical ventilation, the ''reference inputs'' will be the settings provided by the clinician, ''Controller'' is normally a microprocessor that calculates the next control signal levels, ''Actuators'' are the circuits and components that receive the Controller's outputs and transform them into actuating signals to effect the pressure applied to the patient airways, and ''Plant'' is the patient. ''Transducers'' are sensors and monitors that measure volume, flow, pressure, or blood gas pressures of the patient and produce feedback signals that are in turn used to change the next inputs to the Controller. By this general definition, whenever, any parameter of the Plant (which is the patient) is measured and a signal indicative of that measurement is automatically fed back to the system input, closed-loop control is performed. Therefore, in any volume control mode where the volume of gas delivered to the patient's airway is measured and adjusted to remain at a prescribed level, or any pressure control mode in which the pressure in the patient's airway is adjusted by the machine, closed-loop control exists. Commonly used ventilation modes such as volume control (VC), pressure control (PC), SIMV, pressure support (PS), volume support (VS), etc., can be all regarded as closed-loop techniques by this general definition. In control of respiration, the actuating signals can be used to control patient's breathing on a breath-by-breath basis (i.e. interbreath control), or adjust the patient's breath during the breathing interval (i.e. intrabreath control).

As an example, in a mode called volume-assured pressure support, once a breath is triggered either by the patient or by the machine, the first portion of the breath which is pressure limited is delivered. Then the controller determines whether the target tidal volume is reachable, and if not, inspiration is continued according to peak flow setting to assure the delivery of the required amount of breathing gas. This mode represents an intrabreath, dual closed-loop control technique of breathing. Another example of intrabreath control is PS (or PSV) mode in which gas flow is controlled during the breath to provide pressure support to the patient. An example of closed-loop interbreath control is the pressure regulated volume control (PRVC) mode in which the inspiratory pressure applied by the machine is adjusted based on the patient's measured respiratory dynamic compliance to deliver a target tidal volume of gas to the patient.

Therefore, many modern ventilation techniques can be regarded as closed-loop control methods from an engineering standpoint, but with various degrees of automation.

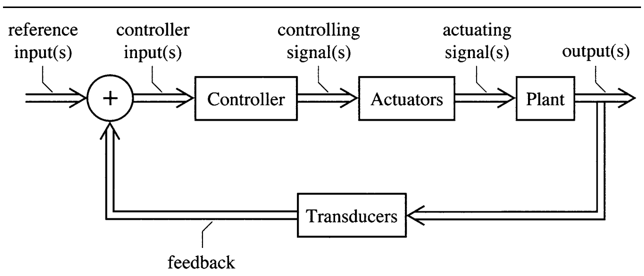

Fig. 1. A schematic diagram of a closed-loop system.

Closed-loop categories

The application of closed-loop techniques in mechanical ventilation is significantly enhanced if the machine takes over more critical aspects of treatment by using automatic control. For example, the machine can measure some of the patient's physiological parameters and automatically adjust its main outputs such as tidal volume, inspiratory pressure, or respiratory rate based on the patient's changing requirements. In other words, the ventilator determines some or all of the main targets of breathing through automatic control rather than the clinician. In that case, mechanical ventilation takes on a new dimension of automation.

Among various systems developed for control of mechanical ventilation, there are rule-based systems in which patient parameters such as airway pressure, spontaneous tidal volume and breathing rate, and end-tidal

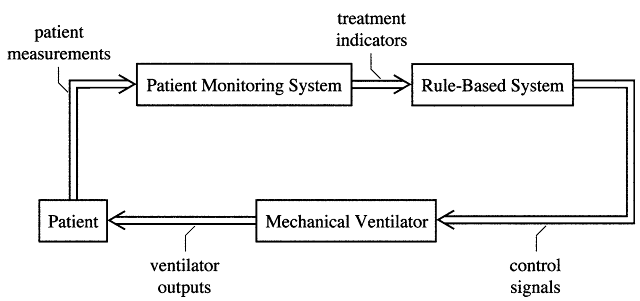

Fig. 2. A schematic block diagram of a rule-based controller.

partial pressure of carbon dioxide (P_{etCO2}) are used as indicators for adjustment of the ventilator's outputs. Figure 2 shows the schematic block diagram of such a system. The control schemes of these rule-based systems that will be described later in this article are based on clinical guidelines and protocols. Although the principles of operation of such systems can be compared to those of negative or positive feedback control systems, but they may not be regarded as feedback controlled from an engineering standpoint. In these methods, the patient's measured parameters are not used to formulate the inputs to the system and generate feedback signals to be added to or subtracted from reference inputs as shown in the diagram of Figure 1. Rather, the patient's measured parameters in these systems are used as indicators on whether some incremental changes should be made to the ventilator's output or not.

Based on the above-mentioned differences among mechanical ventilation technologies, closed-loop ventilation as discussed in this article is classified under three main categories:

1. The main ventilatory targets such as tidal volume, respiratory rate, PEEP, F_{IO2}, and the inspiratory pressure are set by the clinician and closed-loop control is used to deliver those targets.
2. Some of the ventilatory targets are periodically adjusted incrementally by the ventilator based on treatment protocols.
3. Some or all of the main ventilatory targets are computed by the ventilator and adjusted through feedback control based on formulations using ventilatory as well as patient parameters, either continuously or periodically.

The features of systems belonging to the 1st category are discussed in some detail elsewhere [2, 3] and are not the focus of this article. The discussions that follow concentrate on the 2nd and 3rd categories above. Those systems will be collectively referred to as "automatic systems." The term "closed-loop" as used in the proceeding sections denotes systems that belong to the 3rd category above. The systems in the 2nd category are identified as "protocol-driven systems."

OVERVIEW OF AUTOMATIC SYSTEMS

The first closed-loop system for mechanical ventilation was introduced in 1950s [4], in which the end-tidal P_{CO2} (P_{etCO2}) was used to control the amount of ventilation provided by the machine. In the next few decades, a series of closed-loop techniques were developed in which P_{etCO2} or the volume of expired CO_2 was measured and used to control the amount of ventilation given by the machine [5–8]. The arterial pH level was used next in another closed-loop system to control mechanical ventilation [9]. With the development of microprocessors, a system which incorporated proportional-integral-derivative control (PID) using P_{etCO2} was introduced in 1982 [10]. This was followed by another microprocessor-controlled system using the PID technique which controlled the rate and tidal volume of breaths based on P_{etCO2} monitoring [11]. The next system was a closed-loop computer-controlled system for anesthetic delivery and automatic control of ventilation [12]. In this system, a PID controller was used to adjust ventilation based on P_{CO2} monitoring.

Up-to this point, either arterial P_{CO2} or pH, measured directly or indirectly, was the main variable used to control ventilation. However, using only one variable in control of ventilation is un-natural, can be misleading, and may mask respiratory problems. In 1991, a system was introduced which used multiple patient data to control the rate and tidal volume of breaths of a mechanically ventilated patient [13, 14]. In this technique, a modified version of an equation which was based on a hypothesis in physiology presented in 1950 [15], was used to compute the optimal frequency of mechanical ventilation. The closed-loop system in the patented technique [13] was designed to regulate blood gases and used respiratory mechanics data to minimize the work rate of breathing. This system was designed to reduce the load on the respiratory muscles, mimic natural breathing, stimulate spontaneous breathing, and reduce weaning time. Shortly after the patent describing this invention was published in 1991, Hamilton Medical, a ventilator manufacturing company, contacted and subsequently met with the inventor and expressed interest in learning more about the technology and marketing it. Yet, several years later in 1994, an article was published by a group of researchers, some of them employed at

Hamilton Medical, which described the clinical evaluation results of a closed-loop system for mechanical ventilation called adaptive lung ventilation (ALV) [16]. In this system respiratory mechanics data were used to compute optimal rate and tidal volume of breathing in mechanical ventilation to minimize the work rate of breathing using the same procedure and formula that were described earlier in the patented invention [13]. Despite the fact that some of the authors of the article on ALV were quite familiar with the earlier invention also through previous meetings and discussions with the inventor, and that the fundamentals of the evaluated system in their article were the same as those described for an embodiment of the patent covering the invention, there was no reference to the patent or the publications linked to it in the article on ALV. After several years, Hamilton Medical marketed a technology for closed-loop control of ventilation called adaptive-support ventilation (ASV) which was a variation of ALV, and described by one of the more simple embodiments of US Patent 4986268 [13]. This mode was marketed under license of the patent by Hamilton Medical in later years as a result of a lawsuit that settled in 2004.

In early 1990s another patented closed-loop system for weaning from mechanical ventilation was introduced [17, 18]. This was an intrabreath technique called proportional assist ventilation (PAV). Using this method, the ventilator measured the flow rate and the volume of gas inhaled by a spontaneously breathing patient on the machine and delivered pressure support that was proportional to the elastic and resistive components of pressure developed by the patient. This system was only suitable for patients with reasonably strong spontaneous breathing effort. More details of this technique will be described in the 2nd part of this article.

In late 1980s to early 1990s a number of automatic protocol driven systems for weaning from the ventilator were introduced. The first one of those systems used the measured pressure in the endotracheal tube of the patient as an indicator of the strength of spontaneous breathing and based on that measurement adjusted the length of mandatory breaths in the intermittent mandatory ventilation (IMV) mode [19]. The next protocol-driven system for weaning was introduced in 1991 [20]. This system used a laptop computer interfaced with a pulse oximeter that continuously measured the patient's arterial oxygen saturation. The computer checked the spontaneous breathing rate, minute ventilation, and oxygen level of the patient who was placed on the SIMV + PS mode periodically. If the measured values were acceptable, first the rate of mandatory breaths was incrementally reduced, and then the level of pressure support was gradually decreased until the patient was weaned. If any of the measured data fell outside an acceptable range, the computer increased the level of support.

This was followed by another protocol-driven system for weaning [21]. In this system, three indicators were used for weaning; the spontaneous breathing rate, tidal volume, and P_{etCO2}. If these measurements were in the acceptable ranges, the level of support for the patient who was placed on the PS mode was decreased incrementally until he/she was ready for extubation. If any of the measured data fell outside the ''comfort zone,'' the level of support by the machine was increased.

The next protocol-driven system for weaning was introduced in 1993 [22]. This was a slightly modified version of the system presented in 1991 by the same researchers [20]. This system was used in a similar manner to the earlier version except that it measured tidal volume instead of minute ventilation, and although arterial oxygen saturation of the patient was still monitored continuously by use of a pulse oximeter, but oxygen was no longer used as an indicator for weaning.

In mid to late 1990s two automatic systems for mechanical ventilation that used fuzzy logic control procedures were presented. The first one introduced in 1996 [23] automatically controlled the rate and tidal volume of breathing based on measured values of P_{etCO2} during anesthesia. The second system presented in 1999 was a protocol driven technique for weaning patients on PS mode [24]. This system created fuzzy sets based on four inputs and the rates of changes of those inputs which were: heart rate, tidal volume, respiratory rate, and arterial oxygen saturation. The level of support provided by the ventilator was adjusted based on the measured indicators. This system was designed to wean patients suffering from chronic obstructive pulmonary disease (COPD) from the ventilator.

Another automatic system for mechanical ventilation was introduced in 1996 [25, 26]. In this technique the airway pressure measured 0.1 s after the onset of inspiration ($P_{0.1}$), and the alveolar ventilation were used as indicators to increase or decrease the level of support in the PS mode. In this system, if $P_{0.1}$ was lower than a preset value and alveolar ventilation was higher than a target level, level of pressure support was decreased. Otherwise, any other combination of alveolar ventilation and $P_{0.1}$ dictated an increase in the pressure support level. Setting the target values for alveolar ventilation and $P_{0.1}$ was a critical factor in successful application of this weaning technique. This system did not represent a classical continuous positive feedback control system and therefore was not inherently unstable due to the fact that the patient's airway pressure was only measured at a single distinct point during inspiration and chosen as an indicator for weaning. This system could not prevent hypoventilation and was subject to noise in the presence of disturbances such as coughing.

Another closed-loop method for control of ventilation that used an estimation of the patient's arterial CO_2 tension as control variable was presented in 2002 [27]. This was a variation of the MMV technology [1] in which the level of minute ventilation was periodically calculated by the ventilator based on the patient's estimated CO_2 level.

In parallel to many automatic systems for control of weaning and/or the amount of breathing gas supplied to the patient, many other automatic systems for control of patient's oxygenation were developed in the last several decades.

A system for automatic adjustment of F_{IO2} for neonates suffering from respiratory distress syndrome (RDS) was introduced in 1979 [28]. An intra-arterial electrode and an oxygen analyzer were used to provide the input data to the system.

Another closed-loop technique for control of F_{IO2} in neonates was introduced in 1985 [29]. This system used the neonate's oxygen level measured by transcutaneous monitoring and adaptive control procedures to calculate the required level of F_{IO2}. The next computer controlled system for improvement of oxygenation was designed to automatically adjust the level of PEEP [30]. Three algorithms were tested in the study and according to the reported findings; the one which was based on normalizing the fractional residual capacity (FRC) produced the optimal results in the shortest period of time.

A closed-loop technique for control of F_{IO2} that used arterial oxygen saturation as input was introduced in 1987 [31]. This system incorporated a proportional-integral (PI) technique and used adaptive control algorithms. Another closed-loop system for control of F_{IO2} in neonates was presented in 1988 [32]. This system used arterial oxygen measurements made by use of an intra-arterial electrode to adjust F_{IO2}.

A microprocessor-based system for control of F_{IO2} which used inputs from a pulse oximeter in neonates was introduced in 1992 [33]. This was followed by another microprocessor controlled system for adjustment of F_{IO2} in adults that also used patient's arterial oxygen saturation as input and incorporated a PI controller [34]. The next system was designed to control the levels of F_{IO2} and PEEP in adults based on measurements of arterial oxygen partial pressure or arterial oxygen saturation. This system's algorithm was based on clinical guidelines [35]. Around the same time, a closed-loop technique for control of F_{IO2} in neonates that used arterial oxygen saturation as input was presented [36]. A PID algorithm was used in the controller in this system.

Another closed-loop system for control of F_{IO2} in adults was introduced in 1997 [37]. This system used arterial oxygen saturation data as input and incorporated artifact rejection techniques. The computer algorithm used a PID procedure in this system.

The systems that have been developed more recently, tend to combine closed-loop techniques for delivery of optimal ventilation with automatic methods of controlling PEEP and/or F_{IO2} [38–40]. Some of these techniques are designed to control tidal volume, respiratory rate, inspiratory pressure, the inspiratory-to-expiratory time ratio (I:E), F_{IO2}, and PEEP by using feedback closed-loop control techniques [39]. Another recent system [40], which is the subject of a new patent application, combines the features for closed-loop control of ventilation with new features for control of more ventilatory variables such as PEEP and F_{IO2}, as well as control of weaning in adults, pediatrics, and neonatal patient populations. All these systems [38–40] include the features of a ventilation technique known as adaptive support ventilation (ASV) which was originally introduced in 1991 [13], and augment those by many added closed-loop techniques for control of other ventilatory parameters.

Table 1 shows the categories of automatic systems for control of mechanical ventilation. It shows systems that are based on closed-loop techniques from an engineering standpoint, as well as those that are protocol-driven. The technologies categorized in this table include those designed to control ventilation, weaning, and oxygenation, either individually or in combination.

Table 1. Various categories of automatic systems for mechanical ventilation

Automatic closed-loop systems	Ventilation controllers [4–14, 23, 25–27]
	Weaning controllers [17, 18]
	F_{IO2} and/or PEEP controllers [28–34, 36–39]
	Ventilation + (PEEP and/or F_{IO2}) controllers [38, 39]
	Ventilation + PEEP + F_{IO2} + weaning controllers [40]
Automatic protocol-driven systems	Ventilation/weaning controllers [19–22, 24]
	F_{IO2} and/or PEEP controllers [35]

Systems are identified by their cited reference numbers and are separated by commas.

DISCUSSION AND CONCLUSION

Many automatic systems for control of the main outputs of mechanical ventilators in the management and/or weaning phases of treatment have been developed by researchers in the field. In closed-loop control techniques, it is important not to base the technique on a single control variable such as arterial P_{CO2} or P_{etCO2}. Systems that use only one variable to control ventilation may mask respiratory problems and cause provision of inappropriate treatments. The automatic systems whether protocol-driven or closed-loop feedback controlled, need to have effective methods of artifact rejection in place to avoid propagation of errors. Furthermore, in closed-loop feedback controlled systems in particular, data abstraction and smoothing techniques may need to be incorporated to prevent abrupt and/or inappropriate treatments offered.

Closed-loop systems designed to control F_{IO2} with or without automatic titration of PEEP, need to be sufficiently robust to tackle abrupt disturbances in oxygen balance of the patient. The systems that are based on fine control algorithms such PI or PID techniques alone, will likely need to be enhanced to gain higher speed and efficiency in correcting and preventing hypoxia if the patient's oxygen level falls abruptly. Automatic systems that can be used in different phases of treatment and can control a wider range of ventilator's outputs are likely to be of more use to clinicians than more restricted systems in future. Also, neuro-fuzzy techniques may need to be further explored in control of different aspects of mechanical ventilation.

The 2nd part of this article will focus on the analysis of automatic systems that have been commercialized, and a discussion of the likely trends in the technology of mechanical ventilation in the years to come.

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