# CLOSED-LOOP CONTROL OF THE INSPIRED FRACTION OF OXYGEN IN MECHANICAL VENTILATION

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**ABSTRACT. Objective.** Supplemental oxygen treatment of patients on mechanical ventilation is crucial in maintaining the patients' oxygen levels in the normal range. The purpose of this study was to evaluate the effectiveness of a closed-loop controller for automatic adjustment of the fraction of inspired oxygen, $FIO_2$. More specifically, the aim of the study was to assess the robustness of the controller in correcting hypoxemia as well as its effectiveness in prevention of hyperoxemia and oxygen toxicity. **Methods.** The microprocessor-based feedback control system combines a rapid control algorithm with a proportional-integral-derivative (PID) control procedure to automatically adjust $FIO_2$. The system is designed to prevent hypoxemia by applying a stepwise control procedure in response to rapid declines in arterial oxygen saturation while fine-tuning $FIO_2$ and avoiding hyperoxemia by resuming to the PID control procedure when appropriate. The system includes a sophisticated safeguard unit which is designed to communicate any oxygenation problems or measurement artifacts to the medical personnel while keeping $FIO_2$ at a safe and sufficiently high level. The control system has been tested by using computer simulations as well as animal studies. **Results.** In response to different disturbances, the arterial oxygen saturation returned to the normal safe range within less than 20 seconds, thereby avoiding any untoward effects of hypoxemia. Under steady state conditions, the variations in arterial oxygen saturation were kept within $\pm 3\%$ of the mean value. The controller corrected hypoxemia within seconds while preventing hyperoxemia, rejecting artifacts, and minimizing exposure to high concentrations of oxygen. **Conclusion.** The results of the study attest to the reliability of the proposed closed-loop control scheme for automatic adjustment of $FIO_2$. Further evaluation of the controller will require testing the effectiveness of the system on different patient groups.

**KEY WORDS.** Closed-loop control, oxygen, mechanical ventilation.

## INTRODUCTION

Oxygen supplementation and adequate control of arterial partial pressure of oxygen are crucial to the care of patients on mechanical ventilation. Prevention of hypoxemia and avoidance of hyperoxemia are important in all patient populations. In current mechanical ventilators, $FIO_2$ is manually controlled. In acutely ill patients, achievement of stable and safe levels of arterial oxygen saturation by manual control is both difficult and time consuming and necessitates almost constant attention of the medical personnel.

There have been several attempts to automatically control $FIO_2$ in ventilatory therapy [1, 9]. In a paper by

Mitamura et al. [1], oxygen saturation of arterial blood was monitored in order to open or close an oxygen flow valve. In their system if arterial oxygen saturation fell below a certain level, oxygen was added to the inspired gas. This system could be used effectively if the variations in arterial oxygen saturation were small. Under acute conditions, the system failed to respond effectively to serious disturbances in oxygen balance of the patient. In an early article by Beddis et al. [2], a servo control system was proposed that used invasive measurement of arterial partial pressure of oxygen, $PaO_2$. The results of the study showed improvement over manual control but still the arterial partial pressure of oxygen was outside the set limits in 12.2% of the time when the servo control system was used. In another article by Sano and Kikucki, a system for adaptive control of $PaO_2$ in infants was presented [3]. The resultant plots of measured transcutaneous pressure of oxygen versus time showed long transient periods and wide fluctuations. Yu et al. [4] proposed an adaptive control system for automatic control of $FIO_2$ that used pulse oximetry for measurement of arterial oxygen saturation, $SpO_2$. In this system $SpO_2$ could be corrected to normal range within four minutes of control time. In another paper [5] a microprocessor-based system was presented to control $SpO_2$ of infants automatically. The results showed improvement over manual adjustment of $FIO_2$ but there were still large fluctuations in $SpO_2$ of infants under automatic control. In another article a proportional-integral control system was described for the automatic adjustment of $FIO_2$ that used pulse oximetry as the non-invasive technique for measuring $SpO_2$ [6]. The results of the study showed that $PaO_2$ could be brought back to the safe range within about 2 minutes of control. In another paper [7], a PID system for supplemental oxygen treatment of newborn infants was presented which used pulse oximetry for measuring $SpO_2$. The results showed that $PaO_2$ could be corrected to the safe limits within about 2.5 minutes of control time. In another article [8], a closed-loop system was presented for automatic adjustment of $FIO_2$ based on feedback control from a pulse oximeter. The system used PID control and had safeguards against erroneous measurements. According to the results shown in the study, the closed-loop controller brought $SpO_2$ to the target level within about 3 minutes.

An overview of these closed-loop control systems [1, 8] indicate that although most of them are sophisticated and microprocessor controlled, they either are not efficient in the presence of serious disturbances in oxygen balance of the patient, or they require several minutes of control time to bring $SpO_2$ back to the safe range under acute conditions which can be hazardous

when the oxygen level of the patient falls abruptly. The present paper describes an oxygen control system for automatic adjustment of $FIO_2$ which is designed to respond to hypoxemia within seconds while preventing hyperoxemia and minimizing exposure to excessive inspired oxygen levels. The system, whose design was briefly presented before [9], uses feedback of arterial oxygen saturation measured by using a pulse oximeter. It has been suggested by many researchers that pulse oximetry can provide reliable measurement of arterial oxygen saturation and is less affected by peripheral factors compared to other non-invasive techniques for measuring the oxygen level of the patient [10–14]. The system presented in this paper uses pulse oximetry for continuous monitoring of oxygen and providing input to the controller. Capnography which has also been reported to be a very useful non-invasive technique for monitoring the end-tidal carbon dioxide, $PETCO_2$, [13, 14], is used in the study to continuously monitor the patient's $CO_2$ level. In the control procedure, two different algorithms are incorporated and combined. The system is designed to prevent hypoxemia by using a rapid stepwise control system if $SpO_2$ falls abruptly. After fluctuations of $SpO_2$ are stabilized and reach the safe levels, control returns to a fine-tuned PID algorithm. If $SpO_2$ does not decline abruptly, the control will remain in the PID routine and does not resort to the rapid stepwise algorithm. The system is designed to correct hypoxemia within seconds instead of minutes. It is equipped with a fault detection and alarm unit that disregards any erroneous measurements and informs the medical personnel of any untoward condition in the patient's oxygenation. The system has been tested by using computer simulations as well as animal experiments.

## METHODS AND MATERIALS

### Description of the control system

The configuration of the $FIO_2$ control system is shown in Figure 1. The arterial oxygen saturation of the patient is continuously measured by a pulse oximeter. The output of the oximeter is provided to the $FIO_2$ controller as shown. The $SpO_2$ signal is converted to digital and processed by a microprocessor. The output of the microprocessor which is the $FIO_2$ control signal is converted to analog and is provided to the mixer regulator unit which in turn controls the oxygen flow valve and thereby the inspired fraction of oxygen, $FIO_2$, of the patient on the ventilator.
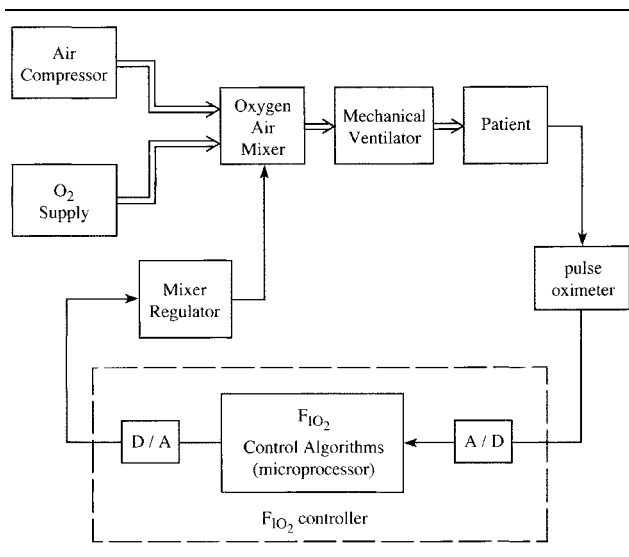
*Fig. 1. Block diagram of the FIO₂ control system.*

## Control algorithm

Figure 2 shows the steps taken in the $F_{IO_2}$ controller. The algorithm uses the combination of two different techniques to control $F_{IO_2}$. As shown in the figure, at the beginning the alarms are deactivated. Then the set-point for $PaO_2$ is defined and the initial value of $F_{IO_2}$ is sent to the output port. Next, all the threshold values for $SpO_2$ and a loop indicator called LP are defined, LP is initially set at 1.5, and the main loop is started at A. It should be noted that the set-point value for $PaO_2$ and all the threshold values for $SpO_2$, are defined at this stage by the medical personnel and are read from the input ports. These values are set based on the conditions of the patient and the desired level of oxygenation. As the main loop is started at A, the measured value of $SpO_2$ of the patient is read from one of the input ports. Next, based on the blood hemoglobin dissociation curve, $PaO_2$ is calculated. The default equation built into the algorithm for this calculation is the following [15, 16]:

$$PaO_2 = (-\ln[1 - (SpO_2)^{0.5}]/0.046) + CF \qquad (1)$$

The factor CF in the above equation is a correction factor that can be set by the medical personnel to correct and shift $PaO_2$ based on the patient's blood acidity. CF is set to zero if the patient's pH level remains in the normal range (i.e. 7.45–7.55). This factor is adjusted by 3.5 mm Hg per 0.1 deviation in blood pH from the normal range [16].

In the next step, the value of $PaO_2$ is compared to a minimum threshold value to detect the possibility of

any artifact. If $PaO_2$ turns out to be less than the minimum value, the algorithm is transferred to B, where the $SpO_2$ reading is discarded and an artifact is assumed. In this case, the routine considers $PaO_2$ to be the same as what it was defined or calculated before, and the algorithm is transferred to the next step. If on the other hand, $PaO_2$ is found to be higher than the minimum threshold level, its value is accepted and the routine continues. At this point, $SpO_2$ is compared to a minimum safe value (the first threshold value) defined initially for the patient. The algorithm is designed to prevent $SpO_2$ of the patient from falling below this minimum safe value. Therefore, if $SpO_2$ is found to be less than or equal to the minimum safe limit, a new loop is started at C and $F_{IO_2}$ is increased to 60% (or another level if adjusted initially in the software), the loop indicator LP is defined to be 2.5, the routine is continued for 0.75 seconds and then returns again to A and the procedure is repeated. If on the other hand, $SpO_2$ is found to be higher than the minimum safe value, at the next step, it is compared to a second threshold value which is higher than the first one. If $SpO_2$ is less than the second threshold value, the loop indicator LP is checked and control remains in the same loop. It should be noted that there are four loops incorporated in the main loop which starts at A. These four loops are shown at C, D, E, and F in the flow-chart of Figure 2. In the loop shown at C, $F_{IO_2}$ is set at 60%. In the loop at D, $F_{IO_2}$ is lowered stepwise to 45%. In the loop at E, $F_{IO_2}$ is further lowered to 30%, and in the loop at F, fine-tuned control is performed by using a PID control procedure. The loops C, D, and E provide most rapid, stepwise control of $F_{IO_2}$ to avoid any untoward effect of hypoxemia while reducing $F_{IO_2}$ downward if $SpO_2$ rises adequately. By using this procedure, the controller is very sensitive to abrupt falls in $SpO_2$. If such falls are detected, $F_{IO_2}$ is increased instantly to prevent any prolongation of hypoxemia. At the same time, the controller keeps watching $SpO_2$ and decreases the value of $F_{IO_2}$ step by step if $SpO_2$ improves. The PID control loop which is started at F in Figure 2, is designed to provide fine regulation of $F_{IO_2}$ in the absence of sharp and hazardous declines in $SpO_2$. It should be noted that control remains in the PID loop and does not resort to the rapid stepwise routine unless sharp declines in $SpO_2$ are detected. In the PID loop, as shown in Figure 2, the derivative, proportional, and integral errors are calculated. The equations that are used to calculate these values are as follows:

$$Y'(K) = PaO_2 \text{ (set-point)} - PaO_2 \qquad (2)$$
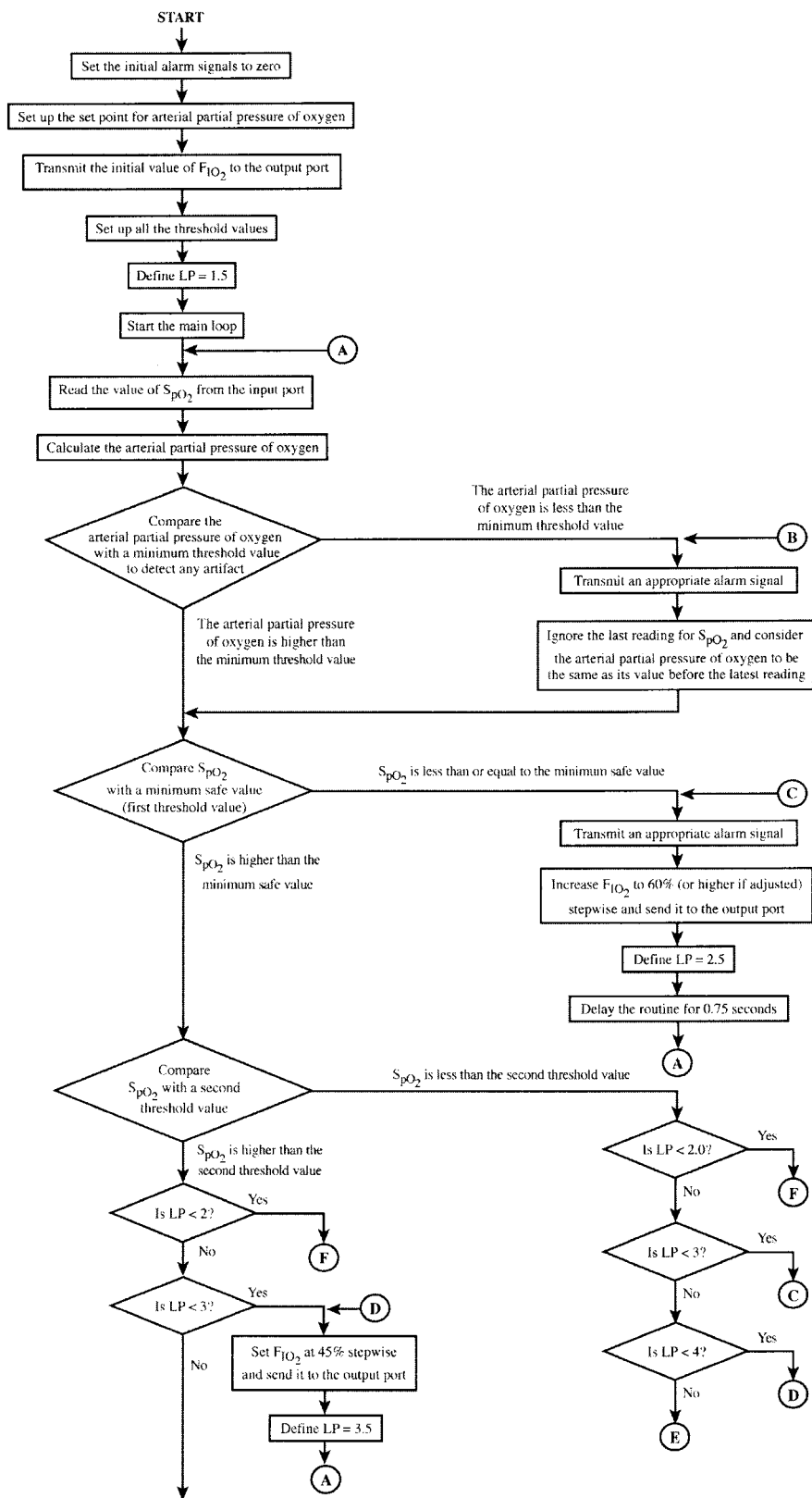
$$Y''(K) = [Y'(K) - Y'(K-1)]/T \qquad (3)$$
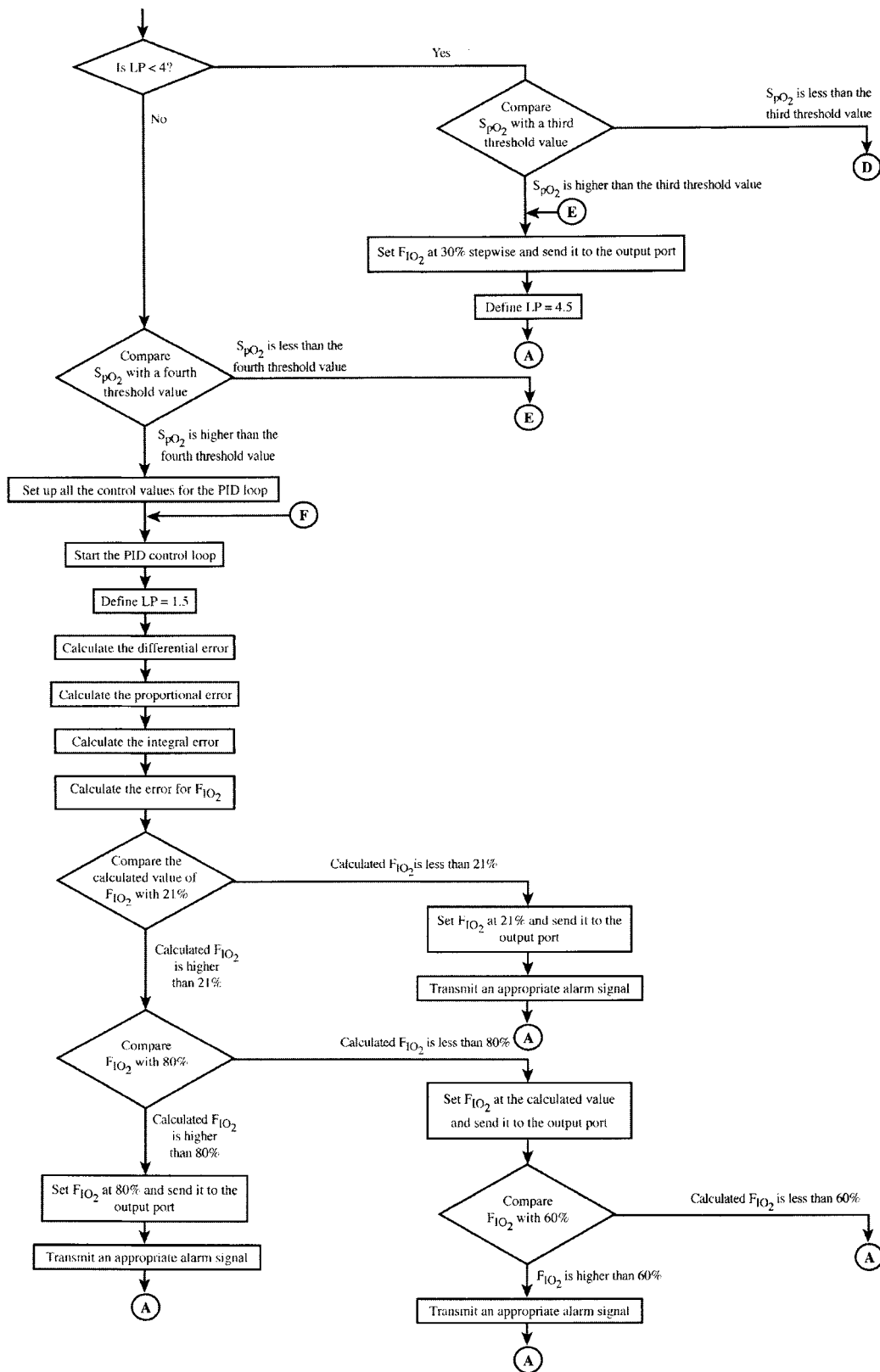
*Fig. 2a. Flow-chart of the control algorithm.*

*Fig. 2b. Flow-chart of the control algorithm.*

$$Y(K) = Y(K - 1) + TY'(K) \qquad (4)$$

$$G(K) = \alpha Y'(K) + \beta Y(K) + \gamma Y''(K) + \lambda \qquad (5)$$

In the above difference equations, $Y'(K)$, $Y''(K)$, and $Y(K)$ are the proportional, derivative, and integral components of error respectively. $G(K)$ is the calculated value of $FiO_2$ and T is a sampling interval chosen at 0.75 seconds in the program. The parameters $\alpha$, $\beta$, $\gamma$, and $\lambda$ are set at $6.45 \times 10^{-5}$, $3.22 \times 10^{-5}$, $7.29 \times 10^{-6}$, and 0.21 respectively. The values of these parameters were tuned to minimize steady-state oscillations and to keep the overshoot/undershoot in $FiO_2$ response of the PID controller below 25% of the change. The calculated value of $FiO_2$ is compared to a minimum value of 0.21 (21%) and a maximum value of 0.8 (80%) as shown in the flow-chart. If $FiO_2$ is between these two levels, its value is accepted and sent to the output port. However, if the calculated value of $FiO_2$ is too high or too low, its value is adjusted. In case the calculated $FiO_2$ turns out to be less than 80% but higher than or equal to 60%, or if it is less than 21%, appropriate alarm signals are generated and sent to the output ports.

### Computer simulation studies

The performance of the $FiO_2$ controller was investigated in a number of simulation experiments. In these tests, the patient was represented by a detailed mathematical model. The structure of this model is shown in Figure 3. The plant shown in this figure is a part of a mathematical model of the human respiratory system developed previously [17]. Since the patient in the simulation experiments is under mechanical ventilation, only the plant as shown in Figure 3 and not the respiratory controller was simulated in the experiments. The plant consists of lungs, body tissues, the brain tissue, an arterial transport delay, and cardiac output and cerebral blood flow controllers. The equations describing the plant constitute a 12th order non-linear system. The detailed description of this model and its equations can be found in Reference 17 and are not repeated here for brevity.

In the simulation tests, the delay introduced by the oxygen air mixer shown in the block diagram of Figure 1 was represented by the following equation:

$$T_1 dFiO_2/dt + FiO_2(t) = G(t) \qquad (6)$$

In this 1st order equation, $G(t)$ is the analog control signal applied to the oxygen air mixer and $T_1$ is the time constant of the mixer which was set at a typical value
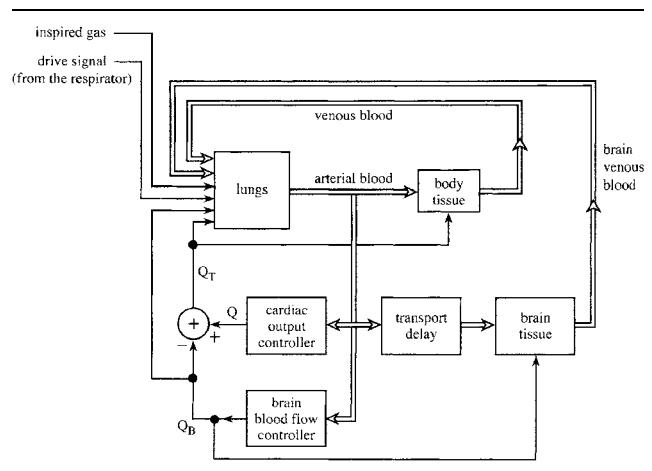


*Fig. 3. Model block diagram for the plant (patient) in the simulation experiments.* ════ : $O_2$ and $CO_2$ main blood circulation.

of 30 seconds in the simulation experiments. Using the above-mentioned model and equations, the $FiO_2$ control system of Figure 1 was simulated in a number of tests.

### Animal studies

The control system was tested on six Yorkshire pigs. All experiments were performed in accordance to the standards of the Animal Care Committee at Loma Linda University Medical Center. The animals weighed $120 \pm 12$ lbs and were aged $4.5 \pm 0.5$ months. The initial preparation consisted of atropine 0.05 mg/kg and telazol/xylazine (100 mg/ml each mixed 1:1) 0.25 ml/kg. The animals were weighed and placed in the supine position on a heated table. Pulse oximetry and ECG probes were placed. A 20 gauge angiocath was placed in an ear vein to provide vascular access for fluid replacement and sedation. The animals were tracheally intubated fiberoptically with a 7.5 mm endotracheal tube (ETT). Once the ETT was placed, the animal was sedated and paralyzed with a continuous infusion of fentanyl 30 mcg/kg/hr and pancuronium bromide 0.2 mg/kg/hr. A percutaneous arterial catheter was placed in the groin for arterial blood gas measurements and blood pressure monitoring.

### Equipment set-up for animal experiments

Figure 4 shows the set-up of the equipment for the animal experiments. It is composed of a Siemens Servo Ventilator 300A which is controlled via an external cable, a Siemens Servo Screen 390 monitor, a Nellcor

N-200 pulse oximeter, a BCI9000 capnograph, a Hewlett Packard HP78534C monitor/terminal for ECG and blood pressure, a computer system equipped with Lab-View software, and a prototype of the $F_IO_2$ controller. The $F_IO_2$ controller comprised of a Micromint BCC52 microprocessor board, A/D and D/A boards, an artifact detector and an alarm circuit designed for this system. The control algorithm was saved on an EPROM on the microprocessor board of the controller.

The Siemens Servo 300A ventilator was controlled externally via its analog I/O terminal N81. Appropriate jumpers were mounted on one of the ventilator's internal PC boards according to the service manual instructions of the ventilator. This was done in order to allow for the automatic control of the oxygen concentration from the $F_IO_2$ controller as well as to gain access to and monitor some of the ventilator's internal signals. The ventilator was set in the volume control mode and the settings, except $F_IO_2$, were manually adjusted for different animals.

The capnograph and the pulse oximeter were used to monitor the end-tidal $CO_2$ ($P_{ET}CO_2$) and $SpO_2$ of the subject continuously. The $SpO_2$ from the oximeter was provided as input to the $F_IO_2$ controller. The outputs of the capnograph and the oximeter as well as the ventilator and the $F_IO_2$ controller's outputs were provided to a computer monitoring system equipped with the Lab-View software package. The transient and steady state responses of the system were obtained and constantly monitored. This data was recorded and analyzed throughout the experiments. Statistical analysis was performed on the recorded data to determine the mean values and the standard deviations of data. A $p$-value $< 0.05$ was considered to indicate statistical significance.

## RESULTS

### Computer simulation results

Two examples of the transient response of the system in the simulation experiments are shown in Figures 5 and 6. Figure 5 shows the response of the system in hypoxemia induced initially by low oxygen breathing. The alveolar-arterial oxygen difference in this test is 20 mm Hg. As shown, in the first 100 seconds, $PaO_2$ falls under 70 mm Hg and $SpO_2$, falls to around 92%. After this initial period when the controller is turned on, $F_IO_2$ rises sharply and $PaO_2$ is brought back to the normal range within a few seconds. The $F_IO_2$ value returns to around 21% as $PaO_2$ is stabilized and $SpO_2$ settles around 95.5%.
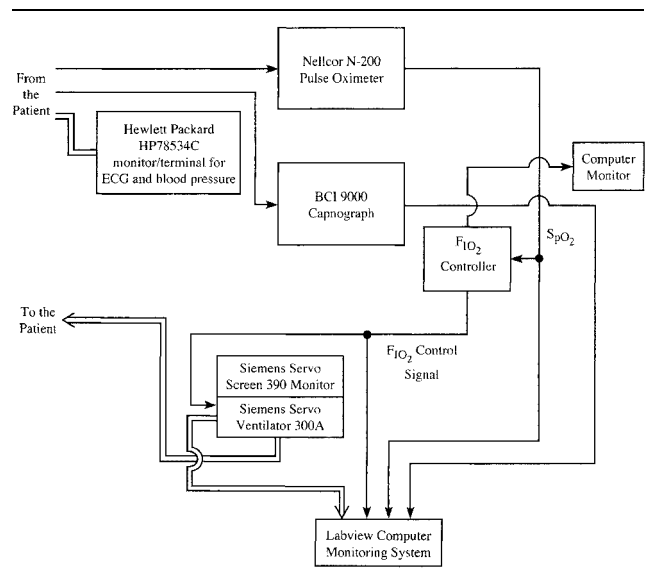
Figure 6 shows another set of simulation results. In

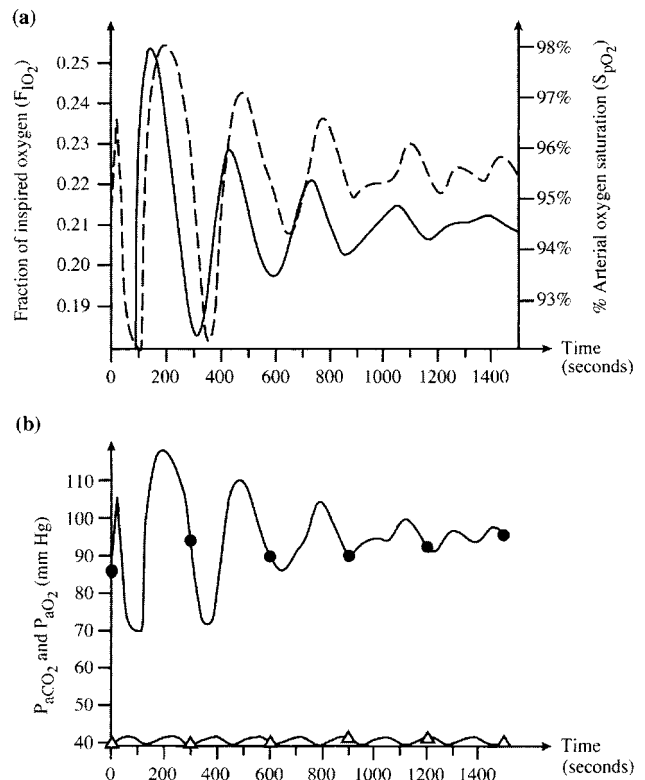*Fig. 4. General description of the equipment set-up in the animal experiments.*

*Fig. 5. Transient simulation responses of the control system to 100 seconds of 18% oxygen breathing. The alveolar-arterial oxygen difference is 20 mm Hg. The symbols − − − and —— in (a) correspond to $SpO_2$ and $F_IO_2$, and the symbols ● and △ in (b) correspond to $PaO_2$ and $PaCO_2$ respectively.*
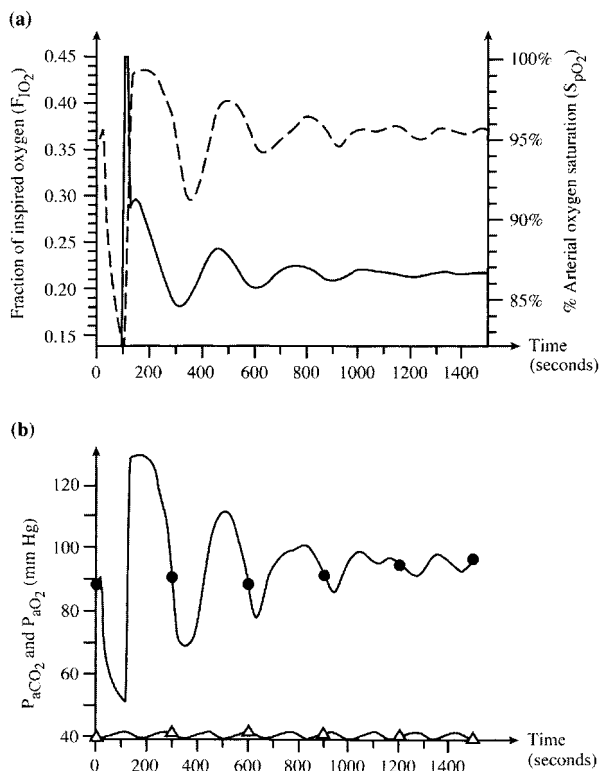
**(a)**



**(b)**



*Fig. 6. Transient simulation responses of the control system to hypoxemia induced by 14% oxygen breathing in the first 100 seconds. The alveolar-arterial oxygen difference is 25 mm Hg. The symbols – – – and —— in (a) correspond to $SpO_2$ and $F_{IO_2}$, and the symbols ● and △ in (b) correspond to $PaO_2$ and $PaCO_2$ respectively.*





*Fig. 7. An example of the response of the controller to induced hypoxemia in animal studies. $SpO_2$ falls initially to about 91% within 3.5 minutes. The controller brings back $SpO_2$ to around 93% in 10 seconds and further increases $SpO_2$ to 98% within less than 20 seconds.*

this test, hypoxemia is initially induced by 14% oxygen breathing and the alveolar-arterial oxygen difference is 25 mm Hg. As seen in the figure, $PaO_2$ falls initially to about 50 mm Hg and $SpO_2$ goes down to 82% due to low concentration of inspired oxygen. When the controller is turned on after 100 seconds, $F_{IO_2}$ rises instantly to 45% to correct hypoxemia and $PaO_2$ is brought back to the normal range within several seconds. The $F_{IO_2}$ control is returned automatically to the fine-controlled PID loop as $PaO_2$ stabilizes around the set-point of 95 mm Hg and $SpO_2$ settles around 95.5%.

As seen in the simulation tests, hypoxemia is corrected within seconds while hyperoxemia and exposure to high inspired oxygen concentrations are minimized.

## Animal experiment results

In these tests hypoxemia was induced by continuously mixing up-to 40% additional nitrogen into the ventilator's air inlet. Figures 7 and 8 show two examples of the
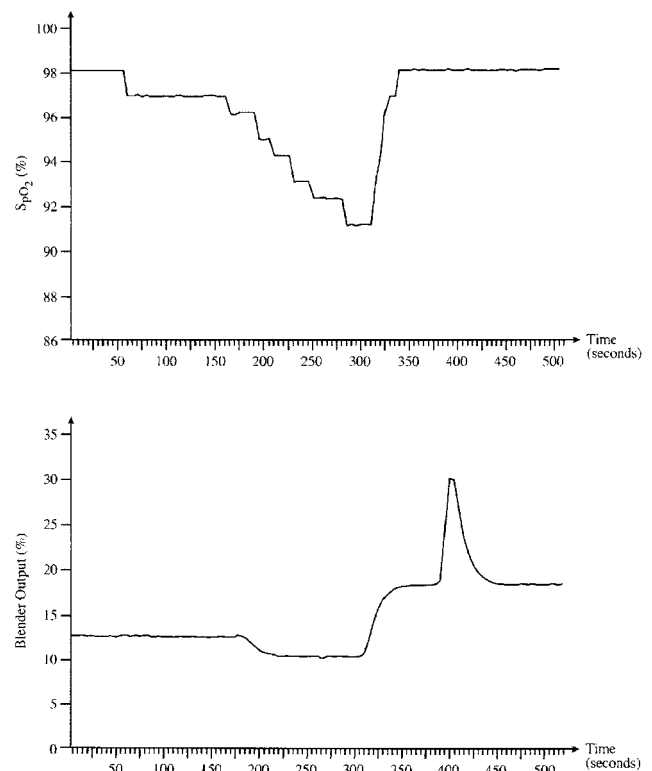
transient response of the controller. For the purpose of the experiments, the $PaO_2$ set-point was 85 mm Hg and the four $SpO_2$ threshold values were defined at 90%, 93%, 95%, and 97% respectively. As shown in Figure 7, hypoxemia is induced by low oxygen breathing. As a result, $SpO_2$ falls to about 91% within 3.5 minutes. As seen in the figure, hypoxemia is corrected promptly by the controller which brings back $SpO_2$ to around 93% within 10 seconds and further increases $SpO_2$ to 98% within less than 20 seconds. The time lag observed between the output of the mixer and $SpO_2$ is due to the typical 20–30 seconds mixing time of the blender.

In Figure 8 another example of the transient response of the system to induced acute hypoxemia is shown. As can be seen, $SpO_2$ initially falls abruptly to about 69% due to the addition of high concentrations of nitrogen to the air entering the mixer. The intervention of the controller results in the correction of hypoxemia and bringing back the $SpO_2$ level to more than 91% in about 15 seconds. As seen in the figure, despite continuous dilution of the inspired gas with high concentra-
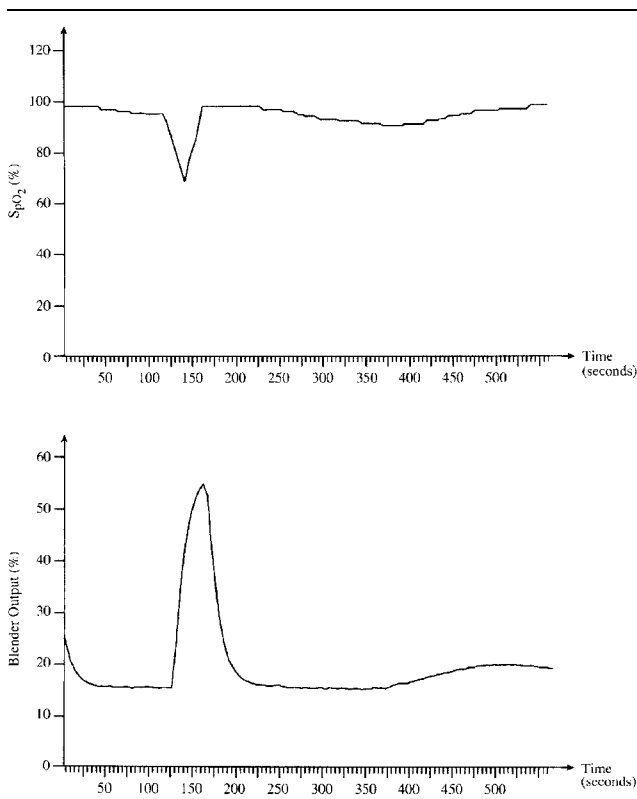
*Fig. 8. An example of animal studies. Response of the controller to induced hypoxemia. SpO$_2$ initially falls to about 69%. The controller corrects hypoxemia and brings back SpO$_2$ to around 91% in about 15 seconds. SpO$_2$ further rises to 98% within 20 seconds.*

tions of nitrogen, the controller which adjusts the flow of additional oxygen to the mixer, corrects the inspired oxygen concentration and SpO$_2$ rises to around 98% within 20 seconds and stabilizes around this value in about 5 minutes.

The summary of the steady state results of the experi-

ments is shown in Table 1. In this table, SpO$_2$, FiO$_2$ (the oxygen concentration at the mixer output under steady state conditions), PetCO$_2$, PaO$_2$, PaCO$_2$ (arterial partial pressure of CO$_2$), and blood pH results are shown. The last three columns of data were obtained by checking blood gases intermittently. It should be noted that the "air" coming into the mixer was diluted in advance by addition of high concentrations of nitrogen to induce hypoxemia. The values of FiO$_2$ listed in Table 1 represent the oxygen concentration at the output of the mixer under steady state conditions as a result of addition of the controlled concentrations of oxygen to the diluted low oxygen air coming into the mixer unit. It can be seen in the results that the variations in SpO$_2$ were quite small with the largest standard deviation of $\pm 1$. SpO$_2$ remained above 93% all of the time and above 94% most of the time ($p < 0.0028$) in the results shown in Table 1. The mean oxygen concentration at the mixer output varied from 16.2% to 31.2% depending on the animal and the ventilator settings.

## DISCUSSION

A closed-loop system for automatic control of the inspired fraction of oxygen in mechanical ventilation is proposed. The system uses the non-invasive measurement technique of pulse oximetry. Two different closed-loop control mechanisms are incorporated and combined in this system. One is a rapid stepwise control system which responds instantly to fast declines in the arterial oxygen saturation of the patient. The other is a more slow, finely controlled PID control system that provides fine control of the inspired fraction of oxygen in the absence of sharp declines in the arterial oxygen saturation. The parameters of the PID controller are tuned to minimize steady state oscillations and to keep

*Table 1. Summary of the steady state results of the animal experiments*

| Test | | | | Experimental settings | | | Experimental results | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pig nr. | Sex | Weight (lbs) | Duration of experiment (min) | VE (lit/min) | F (breaths/min) | VT (lit) | Mixer output (%) mean ± std. | SpO$_2$ (%) mean ± std. | PetCO$_2$ (mm Hg) mean ± std. | PaO$_2$ (mm Hg) | PaCO$_2$ (mm Hg) | pH |
| 1 | F | 120 | 71 | 6.5 | 11.3 | 0.58 | 18.21 ± 1.08 | 96.10 ± 1.00 | 39.86 ± 0.66 | 83 | 37 | 7.5 |
| 2 | M | 128 | 102 | 7.3 | 12.6 | 0.58 | 19.10 ± 0.21 | 96.17 ± 0.25 | 32.72 ± 1.52 | 106 | 36 | 7.48 |
| 3 | M | 132 | 77 | 8.2 | 15.7 | 0.53 | 23.40 ± 0.12 | 96.16 ± 0.21 | 32.10 ± 1.38 | 81 | 32 | 7.56 |
| 4 | F | 118 | 57 | 8.9 | 16.4 | 0.54 | 18.51 ± 0.81 | 95.00 ± 0.58 | 36.21 ± 0.87 | 76 | 33 | 7.53 |
| 5 | F | 126 | 60 | 9.3 | 15.7 | 0.59 | 16.23 ± 2.66 | 96.08 ± 0.49 | 34.10 ± 0.44 | 103 | 34 | 7.52 |
| 6 | F | 108 | 55 | 8.1 | 13.9 | 0.58 | 31.24 ± 0.95 | 95.87 ± 0.53 | 30.89 ± 0.77 | 116 | 33 | 7.51 |

the overshoot/undershoot in the $F_IO_2$ response of the controller below 25% of the change. The stepwise controller is designed with three loops, each with defined minimum and maximum $SpO_2$ threshold values. The controller switches from the PID control to the rapid stepwise algorithm only if rapid declines are observed in $SpO_2$. Once in the stepwise control mode, the controller continuously checks $SpO_2$ and reduces $F_IO_2$ to minimize the exposure of the patient to high concentrations of inspired oxygen and avoid oxygen toxicity. The system is designed to correct hypoxemia within seconds while preventing high oxygen breathing and hyperoxemia. Both the computer simulation and the animal study results show that by using this system hypoxemia as well as hyperoxemia are prevented. The arterial oxygen saturation in the experiments was brought back to the safe range within 15 seconds of the intervention of the controller. The results also show that the standard deviations of the arterial oxygen saturation were kept within $\pm 1.04\%$ of the mean value under steady state conditions in all experiments. In order to discard artifacts and to avoid masking respiratory problems, the controller is provided with a fault/artifact detection and alarm system that discards erroneous measurements and informs the medical personnel of any undesirable conditions in the patient's oxygenation.

The control algorithm enables the medical personnel to define the desired oxygenation levels for individual patients. This is done by defining a desired $PaO_2$ setpoint, by setting four threshold values for $SpO_2$, and by correcting and shifting the oxygen dissociation curve based on the patient's blood pH level.

The simulation tests were done on a detailed model for humans and the animal experiments were carried out on Yorkshire pigs weighing 108–132 lbs. Although there are significant similarities between the plant parameters in the animal experiments and those of humans, there are still some differences that need to be explored. Further studies are needed to evaluate the efficiency of the controller for different patient groups. Also, further research is recommended to combine this automatic $F_IO_2$ control system with other aspects of closed-loop control in mechanical ventilation.

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