A Study and Development of Auto Tuning Control in a Perfusion System for Extracorporeal Membrane Oxygenator

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ABSTRACT
In this study and the development of auto tuning control in a perfusion System for Extracorporeal Membrane Oxygenation (ECMO) support is described. ECMO is a temporary life support system used for patients who's Heart or Lungs is not working properly. This system must be managed by a Perfusionist to maintain proper blood flow and blood pressure to the patient. In this paper, the control of blood-gas process of an ECMO system is modeled in a detailed approach in MATLAB Scripts. Experimental results show a good agreement in static and frequency domain measurements.

Keywords
Extracorporeal Membrane Oxygenation (ECMO),cardio Pulmonary Blood Gases (CPB), partial Oxygen (pO_2), partial Carbon dioxide pressure (pCO_2).

1. INTRODUCTION
Extracorporeal support, in general refers to a medical procedure that occurs outside the human body, most often applied to circulatory procedures. Examples include Hemofiltration, Hemodialysis, Extracorporeal Membrane Oxygenation (ECMO), and Cardio Pulmonary Bypass. This particular study is focused on the use of advanced control methodologies to regulate the arterial partial pressures of O_2 and CO_2 during an ECMO process. Extracorporeal Membrane Oxygenation (ECMO) is a temporary life support system used when Heart or Lungs is not working properly. ECMO is a modified form of Heart Lung Machine and it can be used for a longer period. ECMO system must be managed by a Perfusionist to maintain proper blood flow and blood pressure. Much of the time, the Perfusionist makes small adjustments to the pumps in the ECMO system to maintain flow and pressure, due to the nature of the procedure this process can be tedious and is prone to human error. By introduction of automatic control in ECMO system the variables are perfectly controlled.

2. EXTRACORPOREAL MEMBARANE OXYGENATATION
The concept of Cardio Pulmonary Bypass was developed in the nineteen fifties. In1972, the first case of ECMO was reported. [3-4] ECMO has been used for treatment of cardiac and pulmonary failure.ECMO system takes over the function of wounded Heart or/and Lungs and makes them to rest for a fast recovery. The main components of a typical ECMO system includes a membrane oxygenator, pump, fluids and heparin administration interfaces, heat exchanger, pressure monitor, and blood gas sensors.[6] Schematic Diagram of ECMO system is shown in Figure.1

The ECMO system provides temporary cardiac and pulmonary support. Here blood is pumped through arterial and venous cannulation. Blood from the cannula drains passively into a small venous reservoir. The ECMO pump draws blood from the venous reservoir, which works like the right atrium. The function of this reservoir is to prevent negative pressure from pulling the vessel wall into the cannula and reducing the risk of damage to the vena cava. The tubing from the bladder leads to ECMO pump, which is usually a roller pump. The blood leaving from the roller pump enters the membrane oxygenator. The membrane oxygenator functions as an artificial Lung by mixing O_2 and removing CO_2 in the blood. In addition to oxygenating the blood, it also maintains the blood temperature at the appropriate level with the help of a heat exchanger. The blood returns to the patient from the heat exchanger.

The Blood aspirated from vents and suction systems enters a separate cardiotomy reservoir, through a microfilter, to the venous reservoir. A secondary pump, the cardioplegia pump may be used to deliver blood and drugs directly to the heart. Heparin drug is given as a continuous infusion in the system to stop the blood from clotting. Air bubbles entering in the arterial blood can cause systemic embolization, so a bubble detector used which gives a warning and the bridge present allows bubbles to circulate down to the bladder where they can be easily aspirated. Sensors are used for monitoring pressure, pH, Oxygen saturation, blood gases, and temperatures. Real time set up of ECMO system is shown in Figure.2

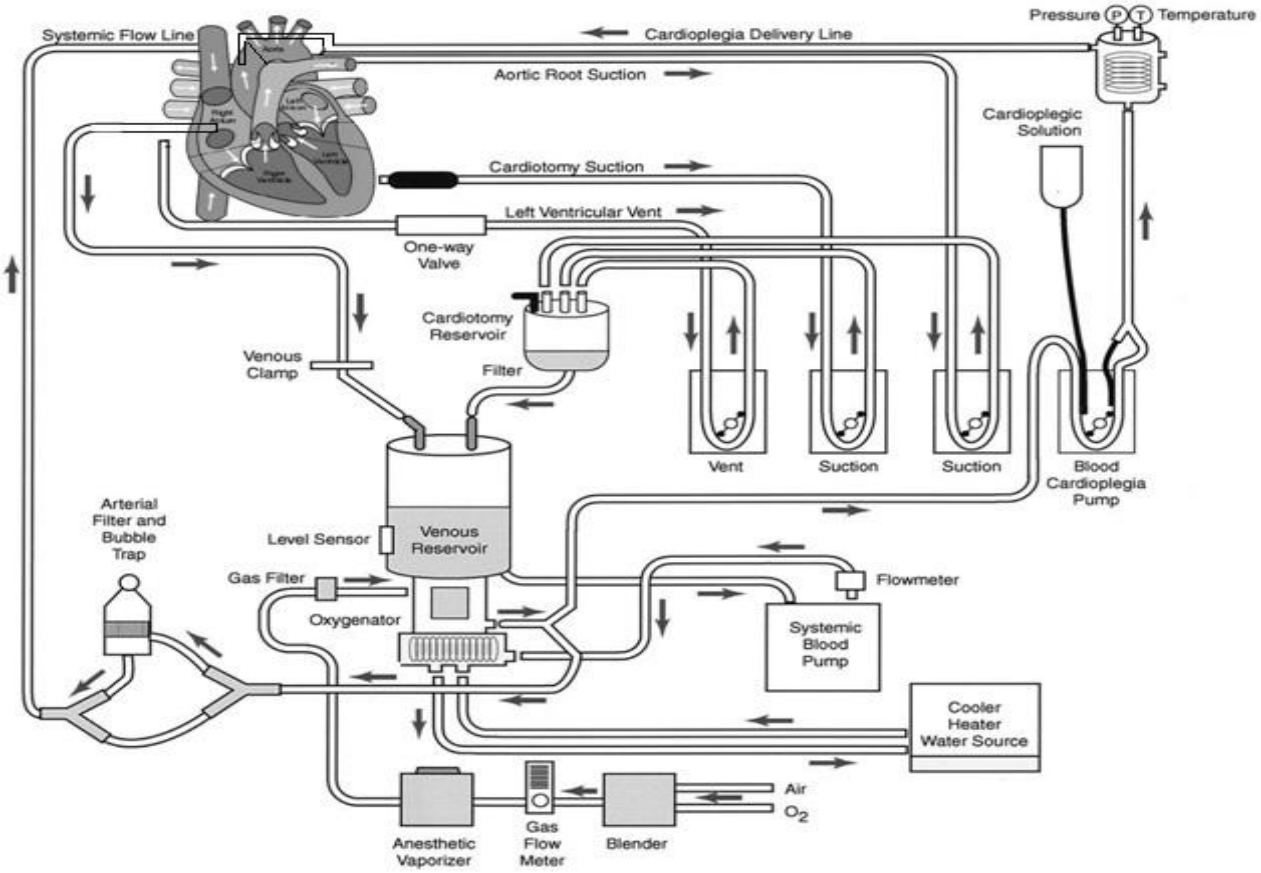

Figure 1. Schematic Diagram of ECMO system

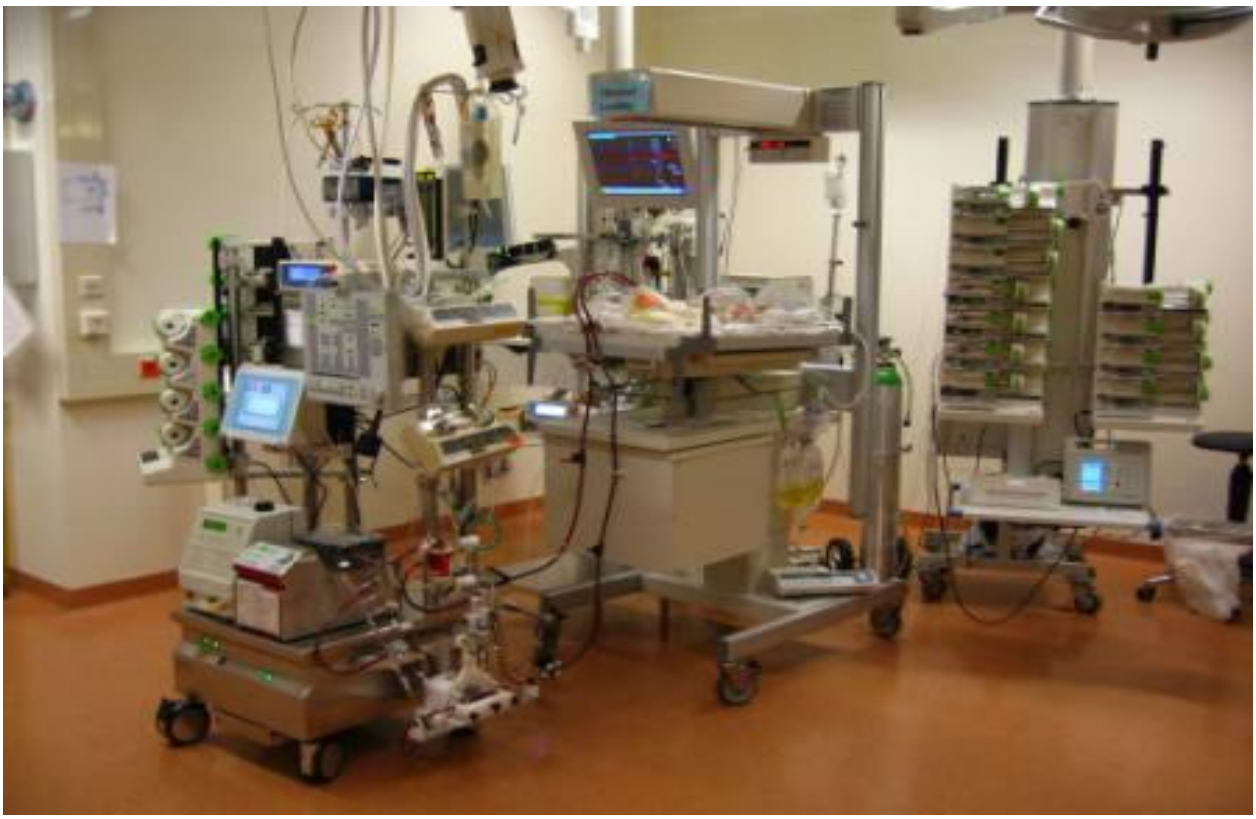

Figure 2. Real time set up of ECMO system

3. MEMBERANE OXYGENATOR

In this study, only the membrane oxygenator and the blood gas sensors need to be considered for quantifying the system under consideration. The membrane oxygenator replicates the functionality of the human lungs in that it exposes the blood to regulate amount of O_2 and CO_2 for assimilation. Firstly, the choice of membrane is critical, since the material should be impermeable to blood, but permeable to O_2 and CO_2. The polymethyl pentene, nonporous hollow fibre oxygenators, are now widely used, provide very efficient gas exchange.Membrane oxygenator is shown in figure.3.

Figure 3. Memberane oxygenator

Membrane oxygenator consists of porous hollow fibres, which are arranged in mats or bundles in axial orientation. Gas entering on top inside the fibres while the blood is flowing first down through a heat exchanger and then up through the gas exchanger. Gas exchange between gas and blood-phase is a very complicated process involving position dependent quantities and partially nonlinear mechanisms which include gas transport and diffusion in blood or the diffusion across the membrane. Membrane oxygenator and the way by which the O_2 and CO_2 Gases are introduced into the oxygenator for mixing is shown in figure 4.

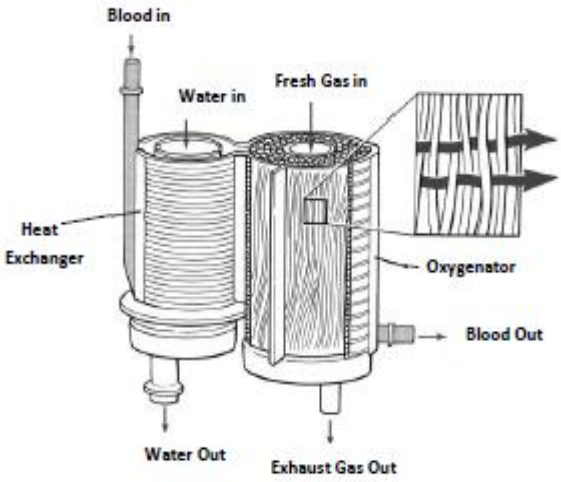

Figure 4. Memberane oxygenator

4. TRANSPORT OF CARDIO PULMO - NARY BLOOD GASES

In physiological circulation the de-oxygenated Cardio Pulmonary Blood Gases is circulated through the lung, where Carbon dioxide is removed and Oxygen is added. In Cardio Pulmonary Bypass, the Heart and Lungs are at rest; Lung function is taken over by an oxygenation device. The transport of Oxygen and Carbon dioxide is mainly accomplished by the haemoglobin which is contained in the erythrocytes. The haemoglobin and other buffer systems of the blood plays a certain role in the regulation of the acid-base management.

4.1 O_2-Transport

Oxygen (O_2) in the Cardio Pulmonary Blood Gases (CPB) is transported in a physically dissolved or chemically bound condition. About 30 to 100 times as much Oxygen can be transported in chemical binding to the haemoglobin than physically dissolved Oxygen in the (CPB) plasma. After the diffusion process over the membrane of the Lung cells (pulmonary alveoli), the O_2-molecule becomes physically dissolved in the water of the blood and then can react to the haemoglobin. The amount of physically dissolved oxygen is dependent on the partial pressure of the Oxygen in the gas.

4.2 CO_2-Transport

Carbon dioxide (CO_2) is transported in the blood as physically dissolved CO_2, as chemically bound bicarbonate (HCO_3^-) and as carbamate ($Hb*CO_2$). The chemical binding process for carbon dioxide is far more complex than that for Oxygen, as it also influences the acid-base balance, and vice versa.

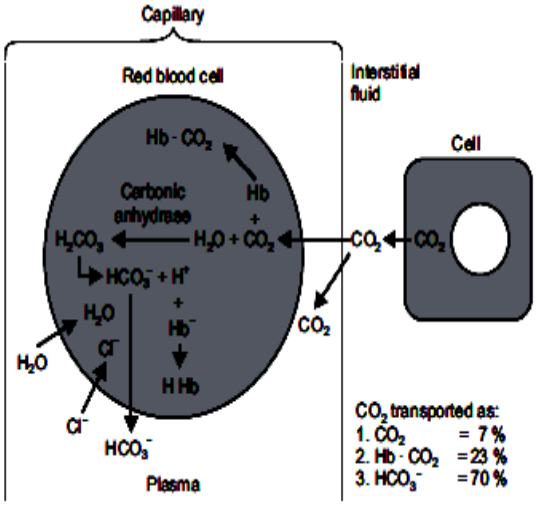

Figure 5. Carbon dioxide transport and reaction

Transport of Carbon dioxide, even in abnormal conditions is not a problem because much greater quantities of Carbon dioxide than Oxygen can be transported. Figure 5 shows the Carbon dioxide transport process. The Carbon dioxide diffuses from the tissue cells in gaseous form through the cell membrane. From there it enters the capillary and the blood, where it initiates the following physical and chemical reactions.

5. CONTROLLER CIRCUITS OF ECMO

The control strategy proposes the simultaneous control of both O_2 and CO_2 partial pressures in the arterial blood. For feedback control, a blood–gas analyzer and a gas blender are used. Since these components are used in a modern ECMO system [3]. The control input values, the O_2-fraction (FiO_2) of

the inert gas (nitrogen N_2) is used for partial Oxygen pressure (pO_2) control and the gas flow to the oxygenator is used for partial Carbon dioxide pCO_2 control. The components of the Extracorporeal Cardio Pulmonary Bypass circuit, with the HLM to the left and the patient's vascular system to the right is shown in Figure. 6

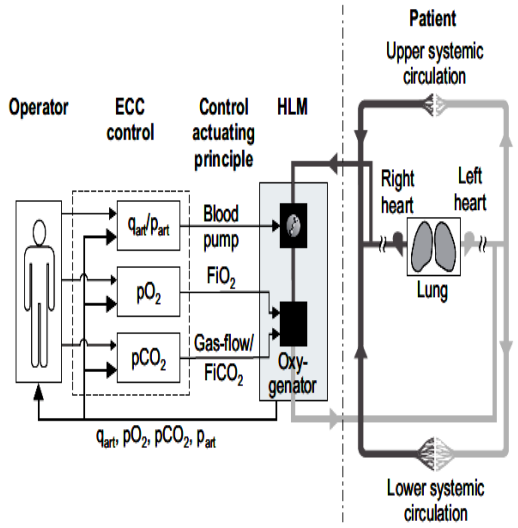

Figure 6. The Extracorporeal (CPB) circuit

6. SYSTEM MATHEMATICAL MODEL OF BLOOD GASES

When physical parameters measured with an instrument a numerical value is obtained, this value is to be checked to know how close is to the true value. The error is difference between the measured value and the true value, since the exact error is never known, it can only be estimated. The estimate of the error is called the uncertainty. It includes both bias and precision errors [2].All the potential significant errors are to be identified for the instrument(s).All measurements should be given in two parts Mean value and Uncertainty. An external linear controller CELC was gain-scheduled in dependence of the blood flow through the oxygenator. This is because of the changing linear system gain in dependence of the blood flow. [1]-[2] The requirements for the external linear controller are robustness and performance in the face of Uncertainties as shown in Fig. 8, whether in the degrading plant or the prediction and linearization routines.

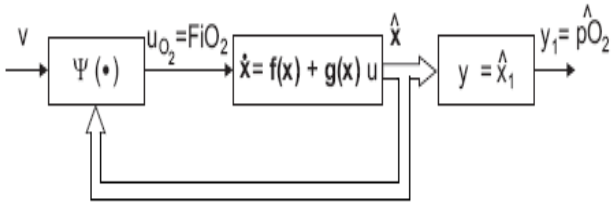

Figure 7. Linearization loop for nonlinear O_2 plant without time delay

Step 1
Uncertainty was assumed for the linearised system in the form of unstructured multiplicative and without time delay uncertainty. The unstructured multiplicative uncertainty was modeled with the nominal model $G_{lin}(s)$, which is the linear transfer function, obtained by the state linearization.

$$G_p = G_{lin}(S)\,(1 + l_m(S)) \qquad (1)$$

Step 2
Describes a member of the family of plants, with lm(s) the unstructured multiplicative uncertainty. The family of plants is then given by

$$\Pi = \left\{ \frac{G_p(s) - G_{lin}(s)}{G_{lin}(s)} \le l_m(w) \right\} \qquad (2)$$

Step 3
Multiplicative uncertainty was assumed in terms of bound $l_{m1}(s)$. $l_{m1}(s)$ is composed of uncertainties of the linearisation and the state estimation process and is described by the 'worst case' transfer function Worst case uncertainty of the third order transfer function is given as

$$\hat{G}(s) = \frac{\alpha_{wo}}{\beta_3 s^3 + \beta_2 s^2 + \beta_1 s + \beta_0} \qquad (3)$$

Table I Transfer function Parameter

Symbol	β_{w3}	β_{w2}	β_{w1}	β_{w0}	α_{w0}
Values	1	0.9	0.27	0.027	0.324

This is the linearised Transfer Function with static gain and high frequency gain uncertainty, where it is assumed that all Transfer function of the plant praramete will vary with table 1. Note that the linearised TF is of third order, because of the relative degree of the linearisation process. [1]

Step 4
The uncertainty $\mathbf{l_{m1}(s)}$ follows to

$$l_{m1}(s) = \frac{\hat{G}(s) - G_{lin}(s)}{G_{lin}(s)} \qquad (4)$$

Step 5
Phase lag compensator is used to compensate or reduce the oscillatory of input oxygen flow (FiO_2).The first order transfer function zeros were numerator part and poles were denominator part with multiplication of the gain margin given as

$$\hat{l}_{m2}(s) = K_{m2}\,\frac{s + \alpha_{m2}}{s + \beta_{m2}} \qquad (5)$$

Table II Phase lag Compensator transfer function Parameter

Symbol	K_{m2}	$\propto_{m2}$	β_{m2}
Values	2.5	0.08	0.4

Step 6
The process is linearised for input/output behaviour, but the process gain changes occur at different blood flows q_b. Since the pO_2 controller was tuned with high static gains in the lower operating area of blood flows.

$$k_p(q_b) = \begin{cases} 3k_{p0}(q_b - 1.5) \; \forall q_b \geq 1.504 l/min \\ 0.1k_{po} \qquad\qquad \forall q_b < 1.504 l/min \end{cases} \quad (6)$$

Step 7
The total system multiplicative unstructured uncertainty is then lumped as [7]

$$l_m(s) = l_{m1}(s) + \hat{l}_{m2}(s)(1 + l_{m1}(s)) \quad (7)$$

Step 8
The above uncertainty of the lumped model can be converted into inverse model. So Input Oxygen Gas obtained as

$$FiO_2 = l_m^{-1}(s) = \frac{1}{l_m(s)} \quad (8)$$

Step 9
Partial pressure of Oxygen (pO_2) can be obtained by the multiplicative unstructured uncertainty lumped inverse model with total blood flow q_b.

$$pO_2 = l_m^{-1}(s) * q_b \quad (9)$$

7. SIMULATION RESULTS

A simultaneous control strategy was chosen, for the Oxygen delivery and Carbon dioxide removal in the Blood Gases, to control the partial pressures of Oxygen (pO_2) in the Blood Gases, adjust the input gas Oxygen fraction (FiO_2). For pO_2 Control the Input flow u = FiO_2 and output flow y = pO_2.

In this simulation results, only input Oxygen flow (FiO_2) control is designed and output flow of Oxygen (pO_2) for Perfusion system will be automated. Step responses of the input Oxygen flow (FiO_2) versus time. Maximum limit 0.06 is tuned for the input control variable correspondingly change over the output flow of partial pressure of Oxygen (pO_2) maximum limit was of 1.01 mmHg.

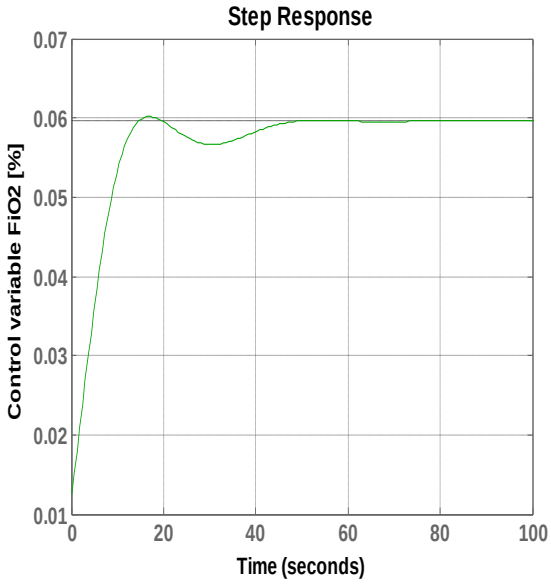

Figure 8. Phase lag compensator Response for Input Oxygen flow (FiO_2) control

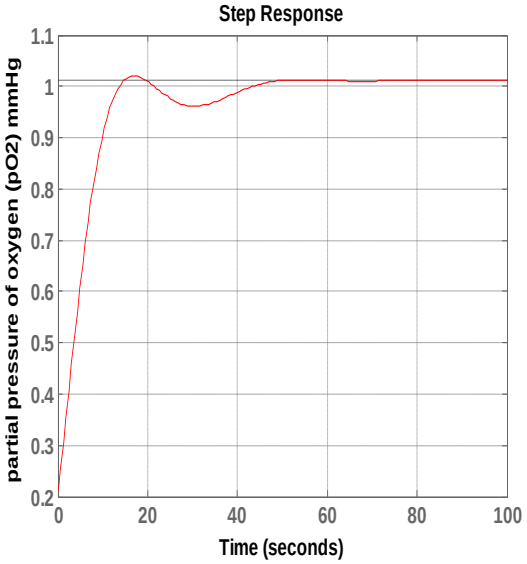

Figure 9. Phase lag compensator Response for pO_2 control

Table III Evaluation table for pO_2 controller design

Step input (mmHg)	Rise time(Tr) (sec)	Settling time(Ts) (sec)	Overshoot (%)
1	1.61	47.6	0.1

8. DISCUSSION

Pressure of Oxygen (pO_2) is obtained by Evaluation table will help us to model and development of the real time parameter observation of pO_2 plant family. The system model of the Blood Gases without the time delay is considered. This model is a (SISO) single-input single-output without time delay of uncertainty. The goal of this system is to control the partial pressure of Oxygen (pO_2), using the ratio of the input set point of Oxygen (FiO_2).

9. CONCLUSION

The system is linearised into a third-order system without time-delay. With help of uncertainty model a Phase lag compensator is chosen to control the dynamics of the input Oxygen gas (FiO_2). Then Compensator technique is used to reduce overshoot of the inspired Oxygen gas (FiO_2). Blood Gas parameter Partial pressure of Oxygen (pO_2) must vary with the input flow rate of Oxygen (FiO_2).Generally the Blood pump is used to control the pressure level of oxygen with the manual help of the perfusion system. By the introduction of this time varying responses an Automatic Controller can be designed for an ECMO system in future.

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