

MODELLING AND CONTROL OF ARTERIAL OXYGEN SATURATION IN NEONATAL INFANTS

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ABSTRACT This paper presents design a closed loop oxygen controller for the supplement oxygen to the newborn infant. The most problem for premature infants is respiratory distress syndrome (RDS), also called neonatal respiratory distress syndrome, or respiratory distress syndrome of newborn. Due to Respiratory Distress Syndrome, the infant requires mechanical to increase the inspired oxygen. We must keep the range of the Arterial Oxygen Saturation (SpO_2) is between 82 – 95% to help the premature infants to get oxygen. If the blood oxygen saturation is more than 95% or less than 82%, the infant is at risk for retinopathy of prematurity. Since each infant is different, the control system must be robust to achieve control of the percentage of oxygen in inspired to supply to the patient. An error model is created using the resulting ranges of system gains and time constant [18]. The μ -synthesis controller is developed to control the oxygen percentage of inspired air and performance specifications are defined. The H_∞ method is used to determine the robust stability and robust performance are achieved with the system uncertainty that described by the error model.

1. INTRODUCTION

The most problem for premature infants is respiratory distress syndrome (IRDS), also called neonatal respiratory distress syndrome [1] or respiratory distress syndrome of newborn, previously called hyaline membrane disease (HMD), and is a syndrome in premature infants caused by developmental insufficiency of surfactant production and structural immaturity in the lungs. It can also result from a genetic problem with the production of surfactant associated proteins. IRDS affects about 1% of newborn infants and is the leading cause of death in preterm infants. The incidence decreases with advancing gestational age, from about 50% in babies born at 26–28 weeks, to about 25% at 30–31 weeks. The syndrome is more frequent in infants of diabetic mothers and in the second born of premature twins. RDS is more common in premature infants because their lungs aren't able to make enough surfactant. Surfactant is a liquid that coats the inside of the lungs. It helps keep them open so that infants can breathe in air once they're born. Surfactant reduces the surface tension and allows alveoli to stay open [2].

Respiratory distress syndrome occurs in infants born prematurely and is a consequence of immature lung anatomy and physiology. In premature of stressed infants, atelectasis from the collapse of the terminal alveoli resulting from lack of surfactant appears after the first few hours of life. In premature infant, surfactant production is limited and store are quickly depleted. Surfactant production may be further diminished by other unfavorable conditions such as high oxygen concentration, poor pulmonary drainage, excessive pulmonary hygiene, or effects of respirator management [3].

The arterial oxygen saturation (SpO_2) must be kept within a certain range which is usually 85-92%. The clinic is providing alarm to notify medical personal if the premature infant is outside of the range of safety of SpO_2 . If the SpO_2 level is maintained above 92%, a state of

hypoxia could result in visual impairment or blindness. If the SpO_2 level is maintained below 85%, a state of hypoxia could result in tissue damage and brain injury. Research has shown that the neonatal infants spend only 50% of the time within the acceptable ranges under manual control of the FiO_2 . The remaining 20% is spent below the acceptable SpO_2 range and 30% above the acceptable SpO_2 range. However it has been shown that the safety limits are often set outside the recommended ranges [4, 5].

The goal of this paper is to design controller of the FiO_2 to regulate the measured SpO_2 . The controller H_∞ depends on the parameter ranges from [30] was then used to create an error model for the system. Performance requirements for the controller were defined and used to conduct robust control design to find a control system that could achieve robust stability and performance with uncertainty described by the error model.

The following researchers have developed models for the human respiratory system. The first formulation was made by Roa L., Ortega-Martinez J.I. (1997) [6]. They considered the two external process included in the term respiratory system as the absorption of O_2 and the removal of CO_2 from the body and internal respiratory, the gaseous exchanges between the cells and their fluid medium. Their mathematical model have been designed for the analysis of the response of the organism to different pathological situations.

F. Tehrani et al. [7] presented a mathematical model in 1993 which used to study the effects of prematurity of peripheral chemoreceptors on the respiratory function in the newborn period and to simulate the neonatal respiratory control system. In this model, using a wide range of stimuli and the transient and steady state behavior were examined.

S. Sands, B. Edwards, V. Kelly [8] presented a model analysis of the rate of arterial oxygen desaturation during apnea demonstrate that pre-apneic ventilation, lung volume, cardiac output, hemoglobin content and blood volume exert unique effects on rate of arterial oxygen desaturation throughout the time-course of desaturation, while metabolic oxygen consumption is uniformly influential throughout the process. They have provided a mathematical framework for quantifying the relative importance of key cardiorespiratory factors on the rate of arterial oxygen desaturation during apnea, with particular relevance to preterm infants.

C.L. Yu [9] presented a model that considered a linearization of the oxygen dissociation curve to change the partial pressure of oxygen in the artery to the oxygen saturation percent. This oxygen dissociation curve was the first proposed by Severinghaus and it is used to convert partial pressure of oxygen to oxygen saturation in blood.

There are many control systems have been presented in literature. Tehrani et al. proposed a PID controller using a feedback signal of arterial oxygen saturation of the premature infant were used to adjust the concentration of inspired oxygen under the incubator in(1991)[10]. They used a computer simulation and the performance of the control system was evaluated under different test conditions to investigate the performance of the control system. The concentration of oxygen in the inspired gas (FiO_2) of the neonate was adjusted to provide for sufficient oxygenation of the blood and was low enough to prevent the damaging effects of oxygen toxicity. They calculated the values of parameters of gain PID controller after a number of preliminary simulation experiments. The effect of PID controller on the system is to make arterial pressure to reach to the set point with low time period. The results were stable and indicative of effectiveness of the controller under two different tests.

2-THE RESPIRATORY SYSTEM MODEL

A model that is based on prior research completed by Yu [12]. This model was a nonlinear model to describe the relationship between SpO_2 with the input FiO_2 . In this thesis, we will take modeling by Yu with the effect of heart rate (HR) and respiratory rate (RR) as a disturbances. The model describes the relationship between SpO_2 with the input FiO_2 .

A diagram of the device will be clinical setting can be seen in Fig (1).

The differential equation of respiratory model is

$$\frac{V_A}{\dot{V}_A + 8.63 \dot{Q}_P L T_c} \Delta S p O_2 s + \Delta S p O_2 = \frac{(1-x_d) \dot{V}_I (1-y_s) \beta_c (P_B - P_{H_2O})}{(8.63(1-y_s) Q \beta_a + (1-x_d) \dot{V}_I) L T_a} D C_{O_2} \Delta F i O_2 \quad (1)$$

The equation above represent three parts, the first part is the time constant τ and gain G_p as below

$$\tau = \frac{V_A}{8.63 (1-y_s) \dot{Q}_P \beta_c + (1-x_d) \dot{V}_I} \quad (2)$$

$$G_p = \frac{\Delta P_A \Delta P_a \Delta P_I}{\Delta P_I \Delta P_A \Delta F_I} = \frac{(1-x_d) \dot{V}_I}{8.63 (1-y_s) Q \beta_c + (1-x_d) \dot{V}_I} \frac{(1-y_s) \beta_c}{\beta_a} (P_B - P_{H_2O}). \quad (3)$$

The nominal value for the parameter β_c in the linear model is 0.0105 vol%/mm Hg and the nominal value for the parameter β_a in linear model is 0.0166 vol%/mm Hg. These β parameters vary for the nonlinear model. Now, we can compare the linear and nonlinear models when supplying 0.1% $F_i O_2$ step input is chosen for the first simulation, and an 8% $F_i O_2$ is chosen for the second. The step input occurs in the simulation at 5 seconds. The nominal conditions for the system parameters are taken from Yu and Batzel and can be seen in Table 1[16].

Now, the parameters in Table above put to Eq(1) to get the output $S p O_2$ from the linear system model when supplying a $F_i O_2$ step input as in Fig (2).

3-PROPORTIONAL INTEGRAL DERIVATIVE (PID) CONTROLLER

The developed system uses a pulse oximeter for blood oxygen feedback signals and a computer program with a PID controller design as shown in Fig (3). It then sends a signal to a modified oxygen blender which delivers a specified $F_i O_2$ level to a newborn infant. The differential equation of continuous PID controllers is

$$u(s) = K_p e(s) + \frac{K_i}{s} e(s) + K_d s e(s) \quad (4)$$

Using bilinear equation to transfer continuous to discrete equation by

$$s = \frac{2z - 1}{Tz + 1}$$

The discrete equation of the digital PID controller is

$$u(n) = n(n - 2) + (T k_p + 0.5 T^2 k_i + 2 k_d) e(n) + (T k_i - 4 k_d) e(n - 1) + (2 k_d + 0.5 T k_i - T k_p) e(n - 2) \quad (5)$$

where $u(n)$ is control unit that put to the plant, T is the sampling time to convert the continuous to discrete time and it was 0.1 sec. We got after simulation and by tuning values of K_p , K_i and K_d good performance and zero steady state error as in Fig (9) because the zero steady state error is zero and settling time is 0.1 sec.

3-ROBUST CONTROL ORIENT MODELING

The first step in robust control oriented modeling is to get a model of the plant uncertainty using knowledge of the likely range of parameter variations. The system gain and time constant parameter ranged were shown in [18] the gain was from 1.6 to 6 and time constant from 0.1 to 200. The ranges of parameters are found from transfer function model obtained by Krone. In order to account for perturbation in the system parameters, a multiplicative uncertainty transfer function weight, W_l , was added to the system. The multiplicative uncertainty error is defined as

$$E_I(s) = \frac{G_p(s) - G_{nom}(s)}{G_{nom}(s)} \quad (6)$$

where G_{nom} is the nominal plant and G_p is the perturbation plant from the nominal. The nominal plant had a system gain of 1.6 and a time constant of 0.5561 seconds. The G_{nom} was calculated by gain uncertainty multiplied the nominal plant. The line solid plotted in Fig (4.b) is the W_I uncertainty weight bounding the maximum error for all values of frequencies by plotting the multiplicative uncertainty transfer function and we can see that in Fig (4.a) and (4.b). A block diagram with uncertainty can be seen in Fig (5). The transfer function for the multiplicative uncertainty is

$$w_I = \frac{0.8s + 0.2}{s + 0.375} \quad (7)$$

ROBUST CONTROL DESIGN

The nominal model was chosen for control design. The safe level SpO2 is 92% for a neonatal infant. The controller was designed to reject disturbances that tend to drive the SpO2 from the nominal set point conditions. The desired bandwidth frequency, ω_b , 1 radians/second obtained by finding the bandwidth frequency of the nominal model. A performance weight, $w_p(s)$, is multiplied by the error signal that corresponds to a maximum allowed 1% error at frequencies below the w_b and 50% error at high frequencies. The performance weight, $w_p(s)$, is defined as

$$w_p(s) = \frac{\frac{1}{M} s + \omega_b}{s + A \omega_b}$$

where M is high frequency, A is the low frequency error, and ω_b is band width for $\left| \frac{1}{w_p(j\omega)} \right|$.

The $|S(j\omega)|$ is the magnitude of error the system and $\left| \frac{1}{w_p(j\omega)} \right|$ be upper bound on S or largest acceptable error is

$$|S(j\omega)| < \left| \frac{1}{w_p(j\omega)} \right| \forall \omega$$

and for condition above we can get parameters of $w_p(s)$ as

$$w_p(s) = \frac{\frac{1}{2} s + \omega_b}{s + 0.1 \omega_b} \quad (8)$$

In Fig (6) shows the Bode diagram of the performance weight and w_u , is added onto the control signal to limit its maximum value.

The block diagram in Fig (5), was transformed to form a diagram of the form in Fig (7). The generalized plant matrix, \mathbf{P} , the P matrix for this system is

$$\begin{bmatrix} y_\Delta \\ z_1 \\ z_2 \\ v \end{bmatrix} = \begin{bmatrix} 0 & 0 & w_I \\ -GCw_P & w_P \frac{1}{G_P} G & -GCw_P \\ 0 & 0 & w_u \\ -GC & G \frac{1}{G_P} & -GC \end{bmatrix} \begin{bmatrix} u_\Delta \\ d \\ u \end{bmatrix} \quad (9)$$

$$P_{11} = \begin{bmatrix} 0 & 0 \\ -GCw_P & w_P \frac{1}{G_P} G \\ 0 & 0 \end{bmatrix} \quad (10)$$

$$P_{12} \begin{bmatrix} w_I \\ -GCw_P \\ w_u \end{bmatrix} \quad (11)$$

$$P_{21} = \begin{bmatrix} -GC & G \frac{1}{G_p} \end{bmatrix} \quad (12)$$

$$P_{22} = \begin{bmatrix} -GC \end{bmatrix} \quad (13)$$

where G_p is the nominal system gain, G is the nominal plant transfer function, the output z_1 is connected to the weighted error signal, and output z_2 is connected to the weighted control signal. The block diagram of the P matrix will be seen in Fig (7).

The μ - synthesis controller optimization is needed since a structure $\hat{\Delta}$ matrix is considered where when the performance and uncertainty are included in the controller optimization. The $\hat{\Delta}$ matrix can be defined as

$$\hat{\Delta} = \begin{bmatrix} \Delta & 0 \\ 0 & \Delta_p \end{bmatrix} \quad (14)$$

where Δ_p is the performance uncertainty and Δ is the model uncertainty.

There is one input y_Δ , and one output u_Δ for matrix Δ . There are two inputs z_1 and z_2 and one output, d for matrix Δ_p . The configuration of $N - \Delta$ can be seen in Fig (8) and it is combined of P matrix and controller and using the lower fractional transformation (LFT) as

$$N = P_{11} + P_{12}K(I - P_{22}K)^{-1}P_{21} \quad (15)$$

In Matlab, dksyn.m was used to conduct the μ - synthesis design. The controller has one input, v , and one output, u . The resulting controller transfer function is

$$k = \frac{633.2s + 1146}{s^2 + 490.7s + 24.53}$$

4- RESULT

In the respiratory system, we need to supply the fraction of inspired oxygen FiO_2 as step input to the system with range 0.21- .25 to get arterial Oxygen Saturation SpO_2 as output with range between 85 – 94% to keep the premature infant in live. In the control design, we need to design control action to the system to keep output range.

In PID Controller, the control design in digital controller by transfer the differential equation to discrete equation by using Bilinear equation to get control action (n). By tuning K_p and K_i we can get good performance and minimum peak over shoot and zero steady state error for SpO_2 output. The control action in Eq(5) is simulated with tuning K , K_i and K_d by trial and error by Matlab codes and applied as input FiO_2 to the plant to get SpO_2 with ranging from 85%–93%. In this test, the response is in Fig (9) because there is no steady state error and minimum settling time and the value of SpO_2 after 2.1 sec.

In Robust control, the conditions were checked for robust stability and performance and nominal stability and performance we must take the matrices N and P. For the nominal stability, the closed-loop system must be in the left - half plane, so the system is nominally stable. Nominal performance checks to see if the controller performs according to the performance criteria under nominal conditions. The test for nominal performance is given as,

$$NP = |W_P(j\omega)(1 + KG)^{-1}|_\infty$$

To check the nominal performance, the inequality must hold for frequencies[19].

$$\|N_{22}\|_\infty \leq 1 \quad (16)$$

The system is nominally stable if only if the values of N_{22} less than one and can be seen the nominal performance by plotting the H-infinity norm in Fig (10).

For the robust stability, N_{11} is less or equal one for all frequencies and that the system is robust stable[19]. The equation for robust stability is

$$RS = |W_i(j\omega)KG(1 + KG)^{-1}|_\infty$$

The inequality

$$\|N_{11}\|_\infty \leq 1 \quad (17)$$

To achieve robust stability the maximum value from Eq(4.12) must be less than one.

The h-infinity norm of N_{11} can be seen in Figure (11).

Robust performance checks to see if the controller performs according to the performance criteria over a range of input. Robust performance can be checked using Eq(18).

$$RP = |W_P(j\omega)(1 + KG)^{-1}|_{\infty} + |W_i(j\omega)KG(1 + KG)^{-1}|_{\infty} \quad (18)$$

For robust performance, the structured singular value of N must be below one for the entire frequency range and can be defined by the inequality

$$\mu(N, \hat{\Delta}) < 1 \quad (19)$$

The μ -synthesis controller is found to have robust performance which can be seen in Figure (12). We can see that the amplitudes of max singular value and μ -synthesis are less than one and that means that the robust controller is found that is able to achieve desirable performance given the level of uncertainty in the system that was modeled.

5-CONCLUSION AND DISCUSSION

In this model for neonatal infants by Yu was selected because there is one input that is FiO_2 and other modes depend on lumped parameter and invasive measurements models. The main problem is how we can introduce FiO_2 to produce SpO_2 between 85% to 93% to keep the infants in a live without suffering of hypoxemia. In this paper, we designed PID and Robust PID controller to compare between them which is the best from each other. In PI digital controller, we got good response for output without zero steady state and minimum settling time was 2.1 sec but that needs more estimating values for K_p , K_i and K_d after convert the control law from continuous domain to discrete domain. We show that the output of SpO_2 reach to 2.1 sec with $K_p = 0.1$, $K_i = 550$ and $K_d = 0.0001$. In Robust analysis, was introduced with PID controller using the range of parameters found from Bradley thesis [18]. An error model was created using multiplicative uncertainty. A robust controller, error model was created a μ - synthesis controller optimization routine. The main goal of the robust controller was analyzed for performance and stability. It was shown to be nominal stable and have nominal performance and robust stability and performance. We showed that the result of controller can guarantee stability and performance for whole range of model parameters.

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Table 1. The nominal parameters

Parameter	Nominal value
V_A (volume of the lung)	0.491 L
\dot{V}_A (volume rate of respiratory air)	4 – 6 L/min
Q(total blood flow)	5 L/min
x_d (dead zone ratio)	5%
y_s (shunt ratio)	5%
P_B (barometric pressure)	760 torr
P_{H_2O} (water vapor pressure)	47 torr

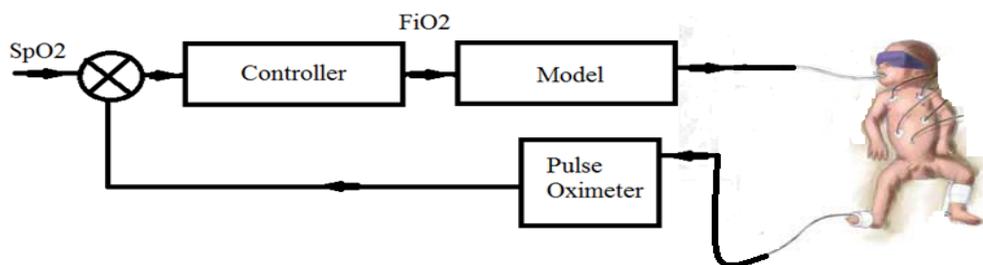


Figure (1) Diagram of the respiratory control device

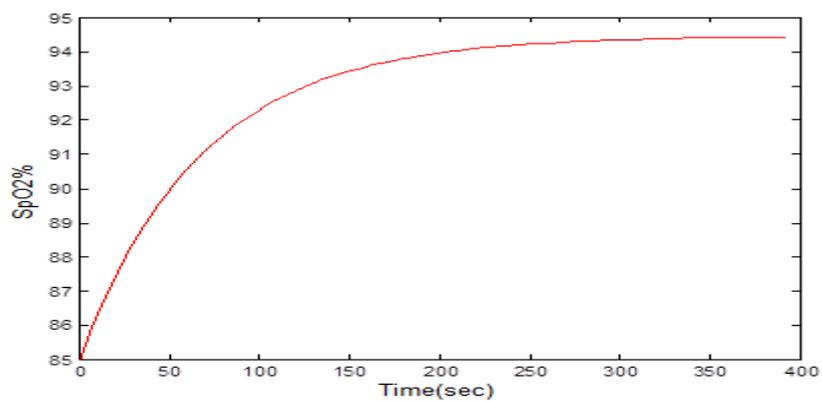


Figure (2). Output SpO2 from the linear system models when supplying FiO2 step input.

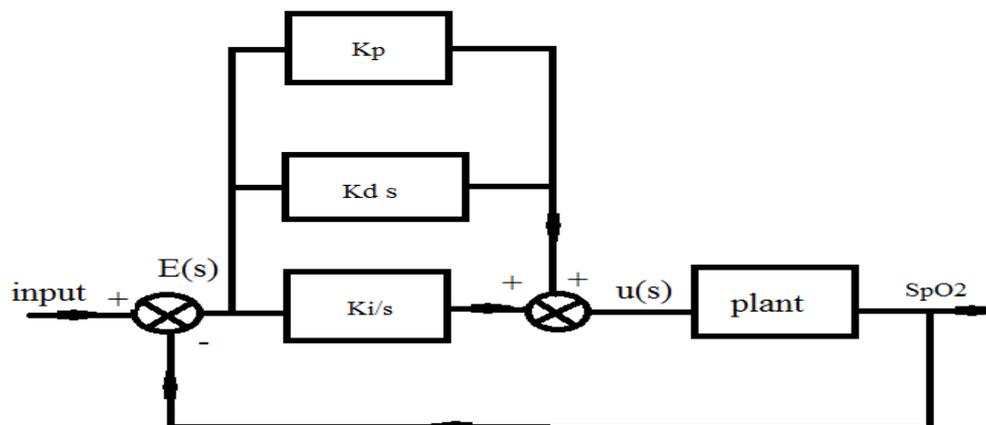
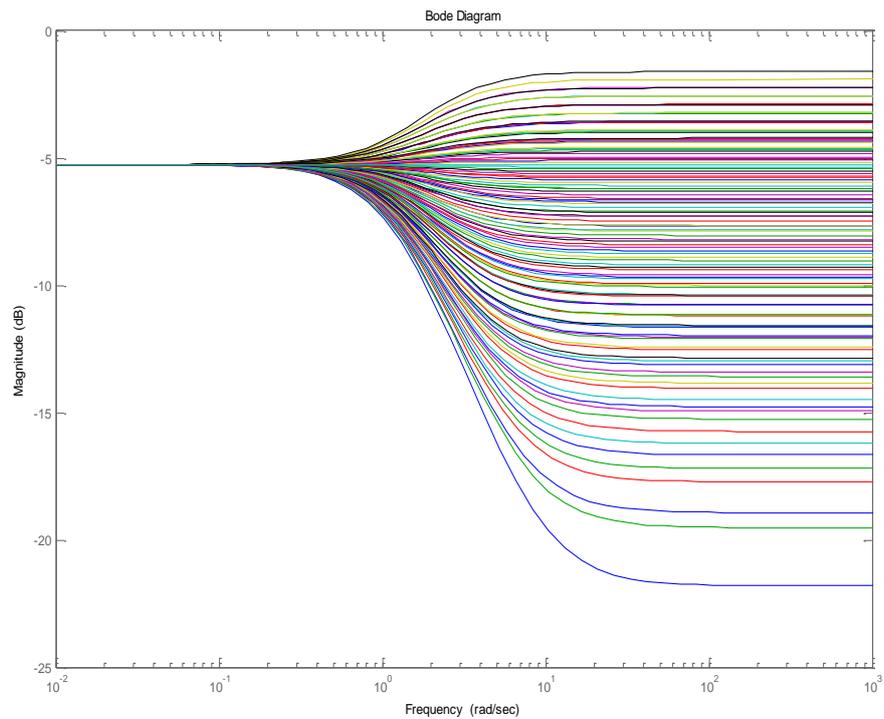
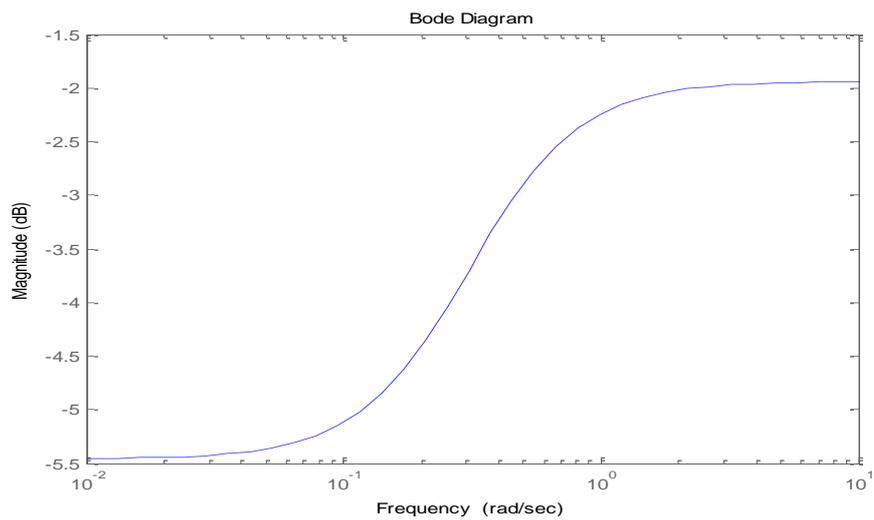


Figure (3). The block diagram of PID controller



(a)



(b)

**Figure (4). (a) Multiplicative uncertainty transfer function bounding the maximum error for the set parameter range
(b) Bode plot for transfer function of w_1 .**

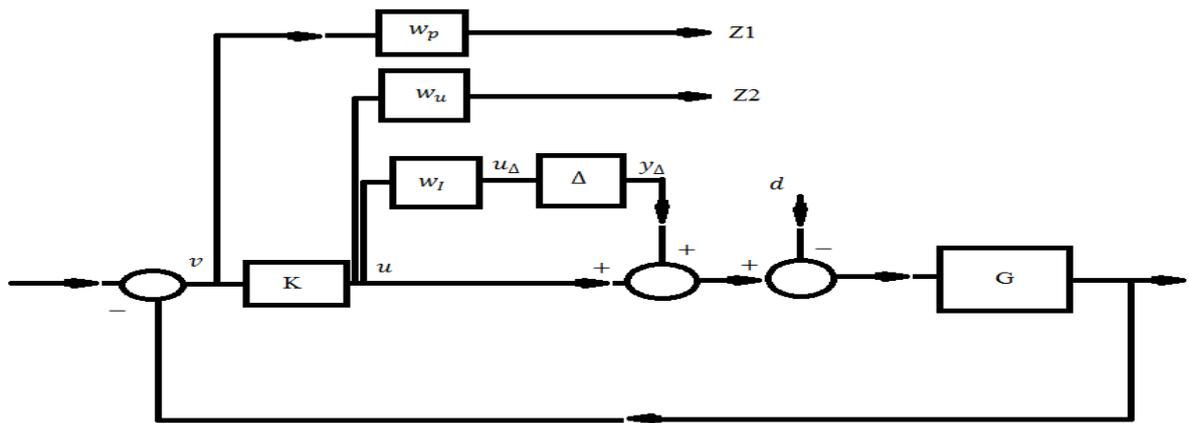


Figure (5). Block diagram of robust control model with multiplicative uncertainty

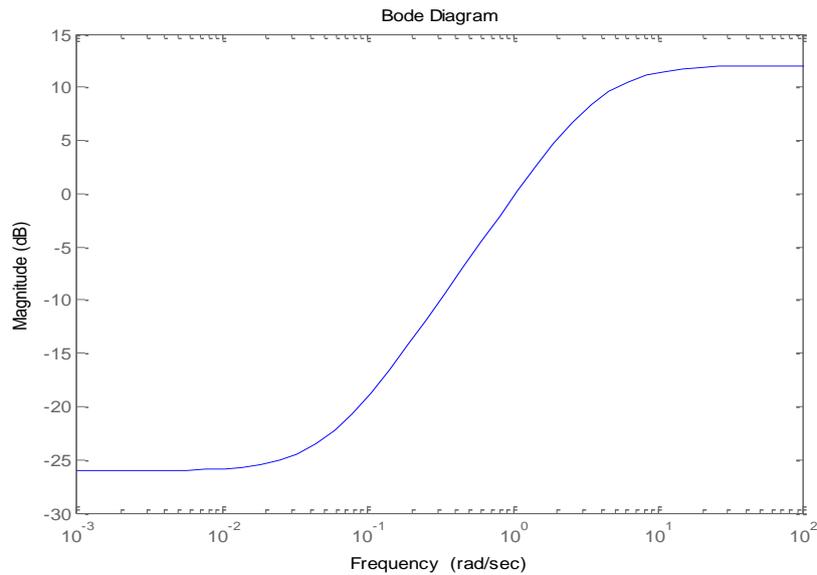


Figure (6). Bode diagram of the w_p performance weight.

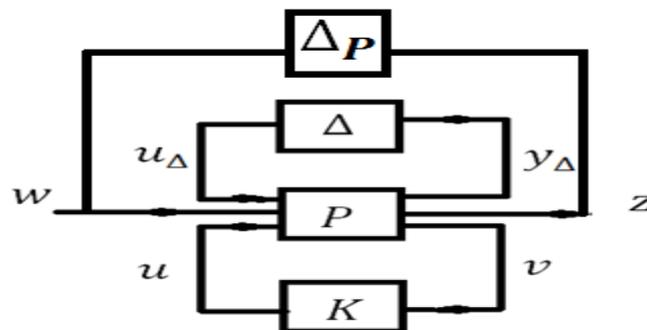


Figure (7). Block diagram of the P matrix structure

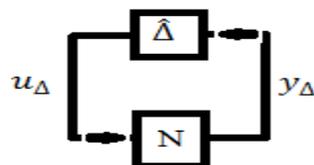


Figure (8). Block diagram of the $N - \Delta$ configuration

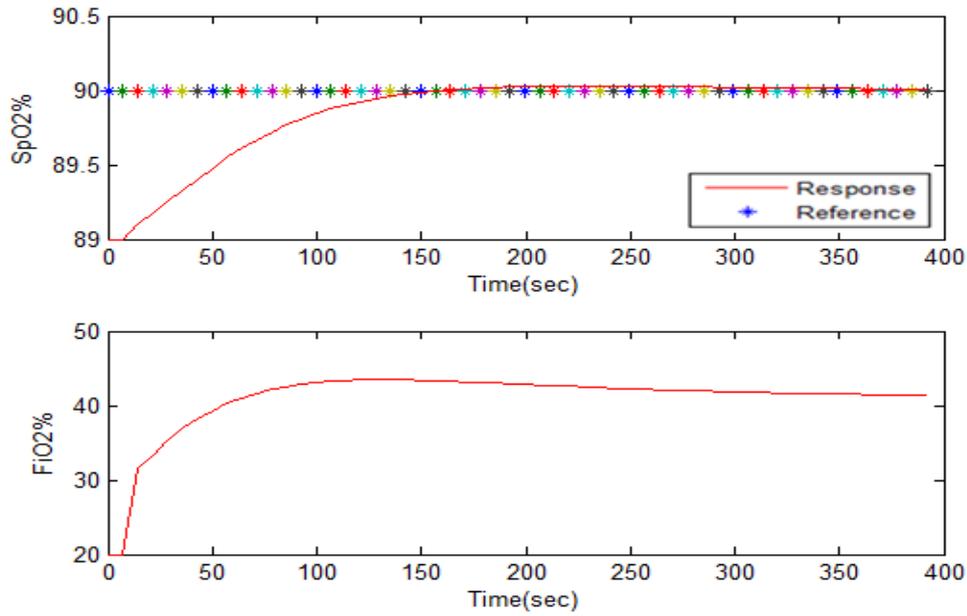


Figure (9). Simulated closed – loop SpO2 with $K_p = 0.1$, $K_i = 300$, and $K_d = 0.0001$.

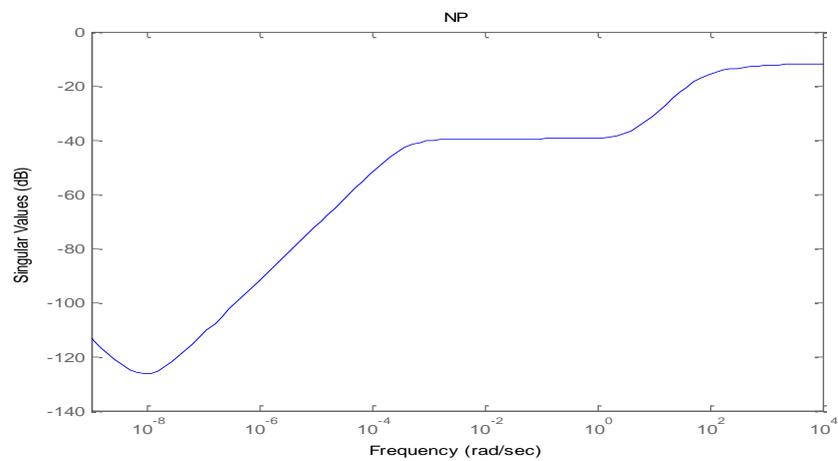


Figure (10). The H-infinity norm of N_{22} is less than one for all frequencies.

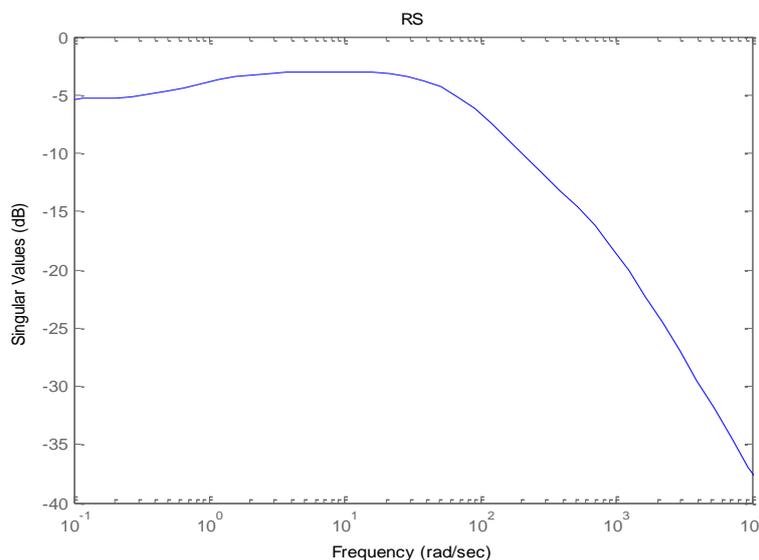


Figure 11. The H-infinity norm of N_{11} is less than one for all frequencies for the μ -synthesis controller .

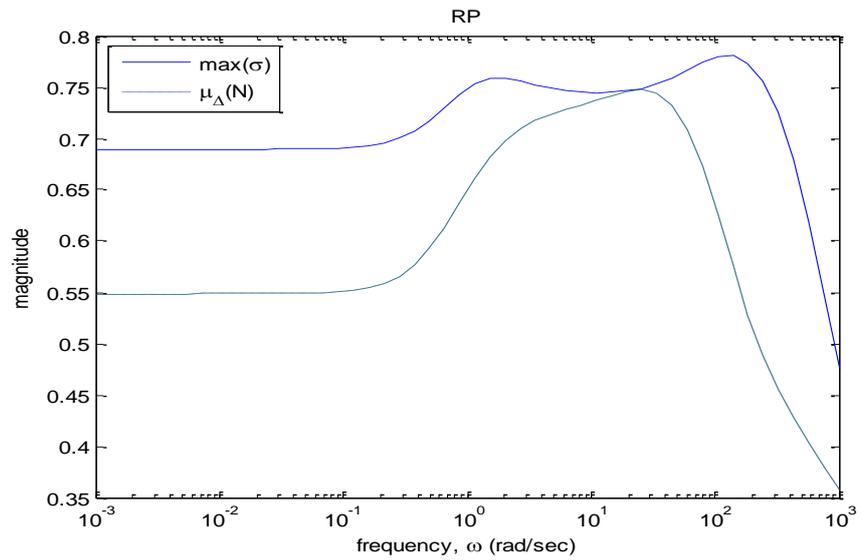


Figure (12). The maximum singular value and structured singular value of the N matrix is less than one for all frequencies.