

Neural Network and Control for Arterial Oxygen Saturation in Neonatal Infants

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Abstract: This study describes the blood Oxygen Saturation (SpO₂) for neonatal infant's by modeling and control methods. Out of analyzing and study the biological and modeling system, the mechanisms of ventilation helped the blood to be oxygenated. The oxygenation of the blood affected by Fraction of inspired Oxygen (FiO₂), rate of respiratory and rate of heart had an effect on the oxygenation. The SpO₂ was modeled by two different methods. The models discussed are a neural network model and mathematic model. The best acting model was mathematic model because it was capable to detect to changes the biological in the infant's and precisely predict the SpO₂ for an extended time and is related to apply input FiO₂. Two different controllers were designed. The controllers are PI and PID controller and they were designed by using the model of dynamic in mathematical way and with neural network. The controllers were structured to control the SpO₂ with altering the values of FiO₂. The control of two models were tested to get the response of output for SpO₂ at zero steady state error, minimum peak overshoot and minimum rise time. The control of two models were tested on data to be simulated. The controllers for two models was got to be PID to get SpO₂ at 80-90% with changing values of the FiO₂ is at 20-30%. The values of SpO₂ and FiO₂ submitted are contrast between value of the nominal actual and value of comparing which is the best for controllers.

Key words: Mathematic model, neural network, control, oxygenated, infant's, minimum peak

INTRODUCTION

Arterial oxygen saturation: A most problem in neonatal infants is Respiratory Distress Syndrome (RDS), caused by absence of a protective substance surfactant which helps the lungs increase and stay off the air sacs from collapsing (Merenstein and Gardner, 2006). The infant is to be located on the device with support of respiratory to permit the lungs of infant to additional progress. The controlled fraction of inspired oxygen (FiO₂) of infant is supplied when on the device of respiratory to be supported. The nurse Controlled the input FiO₂ for the infant. The management is done by screening the SpO₂ and adjusting the FiO₂ as required. The management of FiO₂ is focused on agreed nurses' judgment and medical practices. By management a Fraction of inspired Oxygen (FiO₂), the output SpO₂ can be managed. The range of SpO₂ is from 85-92% (Keim *et al.*, 2009). If the range of SpO₂ is <80% the tissue will be damaged, brain injury and even death by affecting a state of hypoxia. On the other hand, the risk of infant is at of prematurity retinopathy that is concomitant with blindness and even damage of vision if the range of SpO₂ is >95% (Keim *et al.*, 2009). The neonatal infants has seen was spent only 50% of the time within the acceptable levels under manual control of the FiO₂ (Laptook *et al.*, 2006; Hagadorn *et al.*, 2006). The limits of safety are control to notify the nurses when the infant is outside of the acceptable level.

Gray (1945) he proposed a model only able to take into account the output of the steady-state of the system to CO₂ inhalation, arterial anoxemia and metabolic disturbances. Grodins *et al.* (1967) added dynamics and transport delay into the respiratory system model in 1967. This was done through a system of nonlinear equations that can be used to predict changes in the blood gases during conditions of hypocapnie and hypercapnia. Grevisse developed a predictive global model of the pulmonary functions using only physically accessible variables. His system consisted of sub-systems that modeled different parts of the pulmonary system (Grevisse *et al.*, 1975). Yu developed a model that mapped the relationship between the arterial oxygen partial pressure (PaO₂) and FiO₂ (YU *et al.*, 1986). This system allowed the model to adapt to different infants and thus better model the infants response to increases in FiO₂. In this work Grevisse's idea of sub-systems was combined with Yu's idea of an adaptive model to create a robust model of the infant's biological system.

Tehrani and Bazar (1991) designed a proportional, integral, derivative controller For the control of the ventilation of premature neonatal infants in 1991. The controller examines the oxygen concentration of the inspired gas to permit for adequate oxygenation of the blood. The oxygenation was detected to stave off damaging effects of oxygen toxicity. Yu used a Multiple Model Adaptive Controller (MMAC) to regulate the

arterial oxygen saturation (SaO₂) by adjusting the FiO₂ (YU *et al.*, 1986). The MMAC assumes that the system can be represented by a finite number of models. A controller was then designed for each model to give an acceptable closed-loop response to get zero steady-state error. Keim developed a single robust controller based on a linear model (Keim *et al.*, 2009). The robust controller was designed based on an error model and performance specifications. Keim also developed an adaptive controller based on estimated parameters and disturbances (Keim *et al.*, 2009). The controller attempted to regulate the FiO₂ while mitigating the affect of the disturbances.

Morozoff and Smyth (2009) performed an experiment in which they used a PID (Proportional-intergran differential) controller to control the FiO₂ level of oxygen to supply to neonates. The controller made use of the SpO₂ measured from an oximeter as input and the output was the FiO₂ level delivered to neonates which is calculated based on the error between the current and target SpO₂. The target SpO₂ range was between 90 and 96%.

Granelli *et al.* (2005) he proposed a study of cohort with children about 39,800 had saturation in oxygen that tested by pulse oximeter (SpO₂) in the top and bottom edges and a proved reasonable measure precise for the perception of CCHD. Granelli *et al.* (2009) they studied the case of 10,000 newborns babies and declared the same.

Committee of the Advisory US in Newborns and Children Advisory on Heritable Disorders Committee on Hereditary Diseases discovered that there was comfortable verification of using a pulse oximetry to recommend screening. The defects of heart that can be perceived are mainly the following injuries: tetralogy of Fallot, syndrome of hypoplastic left heart, tricuspid atresia, pulmonary atresia, anomalous pulmonary venous return, truncus arteriosus and large vessels transposition. Screening can also perceive: arch of interrupted aortic, critical aortic stenosis, aortic valve stenosis, pulmonary valve stenosis. In addition, screening of pulse oximetry is commonly used for the perception of other conditions with hypoxemia of neonatal is like disorder of respiratory, sepsis of neonatal and hypertension of pulmonary (Hu *et al.*, 2017; Thangaratinam *et al.*, 2012).

MATERIALS AND METHODS

Mathematic model: Oxygen saturation, SaO₂ is a relative measure of the amount of oxygen molecules bound to Hemoglobin (HB). Hemoglobin consists of four iron-porphyrin molecules attached to a protein. Each heme

molecule can combine with one oxygen molecule in a reversible reaction. In other words, the maximum number of oxygen molecules that can combine with a hemoglobin molecule is:



Oxygen saturation is the ratio of the amount of oxygen carried by hemoglobin present in 100 mL of blood to the total amount of oxygen that could be carried by the hemoglobin in the same volume of blood:

$$SO_2 = \frac{HbO_2}{Hb+HbO_2}$$

Oxygen saturation is normally in the range of 95-98% in the arterial blood and between 60-80% in venous blood. Blood oxygen content refers to the total amount of oxygen present in 100 mL of blood and is normally expressed in vol%, or mL of oxygen per decilitre of blood (ml/dl). Oxygen content in blood is normally calculated by adding the amount of the gas liquefied in the blood plasma and the amount conveyed by hemoglobin. The coefficient of solubility for oxygen in plasma is 0.0031 and the amount of oxygen dissolved in the liquid is got by multiplying the PO₂ by 0.0031. On the other hand, the amount of oxygen carried in the blood as oxyhaemoglobin is determined by multiplying the mass of hemoglobin present in 100 mL of blood by the oxygen saturation and 1.38 where 1.38 represents the ml of oxygen that can combine with 1 gram of hemoglobin:

$$CO_2 = O_2\text{dissolved}+O_2\text{bounded toHb} = PO_2 * 0.0031+Hb*SO_2 * 1.38$$

The normal amount of hemoglobin present in 100 mL of blood is about 15 g for an adult whose arterial saturation level can be assumed to be about 97%. Therefore:

$$CaO_2 = 0.97*15*1.38 = 15.5 \text{ vol\%}$$

The oxygen saturation in the venous blood returned to the lung is about 75% and based on this value:

$$CvO_2 = 0.75*15*1.38 = 15.5 \text{ vol\%}$$

Based on the CaO₂ and CvO₂ values calculated above, the tissues only uses 25% of the oxygen delivered to them. Oxygen transport is the amount of oxygen delivered to the tissues per unit time. Oxygen transport is dependent of the ability of the lungs to oxygenate blood that goes through the pulmonary capillary network.

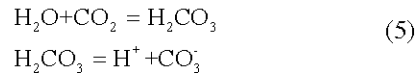
The Arterial transport will be:

$$O_2 = \text{Cardiac output} * 10 * C_{aO_2}$$

The Venous transport will be:

$$O_2 = \text{Cardiac transport} * 10 * C_{vO_2} \quad (4)$$

The concentration of hydrogen ion in a medium determines the acidity and hence, pH of the medium:



the rate of change of the volume of carbon dioxide in the lungs is calculated. The amount of CO₂ expired is given by the Eq. 6:

$$\text{Expired carbon dioxide} = (F_{iCO_2} - F_{ACO_2}) * V_A \quad (6)$$

Where:

- V_A = Alveolar Ventilation
- F_A = Alveolar molar Friction part
- F_{iCO_2} = Friction of inspired Carbon Dioxide

In order to find out how much carbon dioxide is transferred into the lungs, it is a simple matter of finding the difference in carbon dioxide concentration in these two blood vessels. This is shown:

$$\text{Carbon dioxide in to the lungs} = (C_{vCO_2} - C_{ACO_2}) * Q \quad (7)$$

Where:

- Q = Output of the cardiac
- C_{vCO_2} = Vanous blood Concentration
- C_{ACO_2} = Pulmonary blood Concentration

The rate of change of CO₂ in the lungs is:

$$\frac{dV_{ACO_2}}{dt} = V_A * (F_{iCO_2} - A_{ACO_2}) + (C_{vCO_2} - C_{ACO_2}) * Q \quad (8)$$

By Dalton's law, we get:

$$F_{ACO_2} = \frac{P_{ACO_2}}{P_{AT} - P_w} = \frac{V_{ACO_2}}{M_{iCO_2}} \quad (9)$$

$$F_{iCO_2} = \frac{P_{iCO_2}}{P_{AT} - P_{WT}} = \frac{V_{iCO_2}}{LV} \quad (10)$$

Where:

- F_{CO_2} = Fraction of inspired Carbon
- P_{CO_2} = Partial pressure of inspired Carbon

The relationship between P_{igaz} and F_{igaz} is:

$$P_{igaz} = F_{igaz} * (P_{AT} - P_w) = F_{igaz} (760 - 47) \quad (11)$$

By arranging Eq. 9 and get:

$$P_{ACO_2} = (P_{AT} - P_w) * \frac{V_{ACO_2}}{M_{iCO_2}} \quad (12)$$

By combination Eq. 8 and 12, we get:

$$\begin{aligned} \frac{dV_{ACO_2}}{dt} &= \{(P_{AT} - P_w)(C_{vCO_2} - C_{ACO_2}) * Q + \\ & (P_{iCO_2} - P_{ACO_2}) * V_A\} * \left(\frac{1}{M_{CO_2}}\right) \end{aligned} \quad (13)$$

The rate of change of the partial pressure of oxygen in the lung is:

$$\begin{aligned} \frac{dP_{aO_2}}{dt} &= (P_{iCO_2} - P_{ACO_2}) * V_A + 863Q [C_{vCO_2} - C_{ACO_2}] * \\ & \left(\frac{1}{M_{LCO_2}}\right) \end{aligned} \quad (14)$$

The Lung compartment is:

$$\begin{aligned} \frac{dP_{aO_2}}{dt} &= (P_{iCO_2} - P_{ACO_2}) * V_A + 863Q K_{CO_2} \\ & [P_{vCO_2}(t - \tau_v) - P_{ACO_2}(t)] * \left(\frac{1}{M_{LCO_2}}\right) \end{aligned} \quad (15)$$

The brain compartment is:

$$\frac{dP_{B_{CO_2}}(t)}{dt} = \frac{Q_B (P_{aCO_2}(t - \tau_B) - P_{B_{CO_2}}(t))}{M_{B_{CO_2}}} + \frac{MR_{B_{CO_2}}}{M_{B_{CO_2}} K_{B_{CO_2}}} \quad (16)$$

The tissue compartment is:

$$\frac{dP_{T_{CO_2}}(t)}{dt} = \frac{Q_T (P_{aCO_2}(t - \tau_T) - P_{T_{CO_2}}(t))}{M_{T_{CO_2}}} + \frac{MR_{T_{CO_2}}}{M_{T_{CO_2}} K_{T_{CO_2}}} \quad (17)$$

As mentioned the central and peripheral controllers. A model was found based on questions above provided:

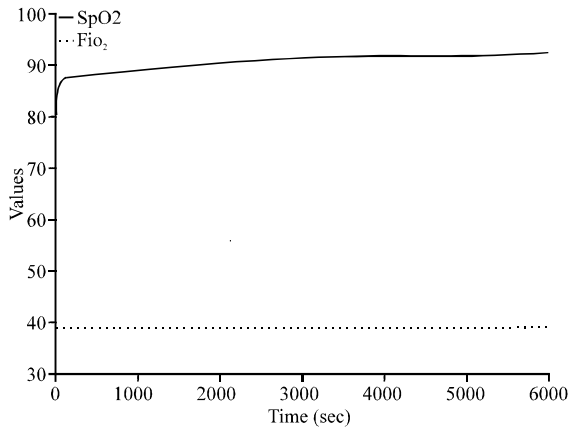


Fig. 1: The output of SpO2 according to supply input FiO₂

$$V_i = GP * (-0.05 * P_{aO_2}(t - \tau_a)) * (P_{aCO_2}(t - \tau_a) - I_p) + GC * P_{B_{CO_2}}(t) - \frac{MR_{B_{CO_2}}}{Q_B * K_{CO_2}} - I_c \quad (18)$$

Where:

GP and GC = The peripheral and central gain factors, respectively
 I_c and I_p = The apnea thresholds

A baseline PCO₂ is necessary for breathing to occur and is known as the apneic threshold. If PCO₂ is below this threshold, it results in apnea.

The model is implemented in MATLAB and has been used extensively for this paper. The mathematical model is very close to what we see in real life and is further enhanced to suit this paper. The FiO₂ range can be easily changed in the model and all the necessary information can be easily plotted, the information of particular interest was the FiO₂ range, the oxygen saturation SpO₂ and the pressure of oxygen in the blood. Figure 1 shows the amplitude of SpO₂ according to supply input FiO₂. For more accuracy for the output SpO₂, Fig. 2 displays with levels with time in 400 sec.

Neural network modeling: In order to study the output and input and output of plant to get a model with nonlinear method, the model of neural network was selected in this problem. This permits for perception of connection between the independent with dependent variables (Dayhoff and DeLeo, 2001). The model design includes the feed-forward network in two layers with layer of neuron of a linear output and layer of sigmoid hidden. The function of sigmoid was selected for layer of the first hidden of the capability of nonlinearity relationship between the output and input of neuron. The sigmoid function prevents the system from interpolate

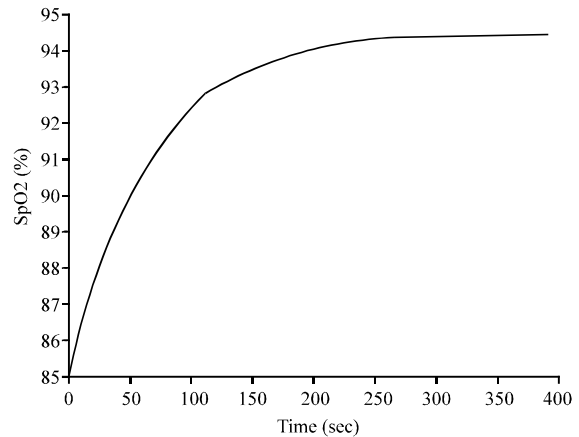


Fig. 2: Output SpO₂ from the linear system models when supplying FiO₂ step input

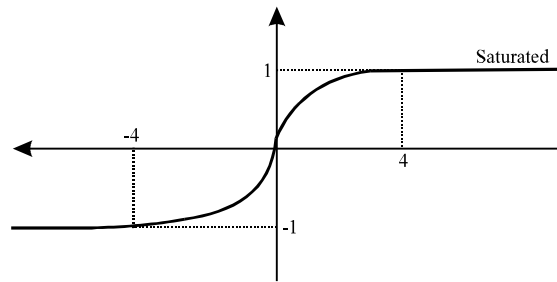


Fig. 3: Sigmoid function saturation

after any data that be trained. The inability to extrapolation is resulted by affecting the saturation of the sigmoid function that can be seen in Fig. 3 were any value above 4 produce a value of 1 and any value below 4 produces a value of 0. The layer of second hidden was selected to get a function in scaling in linear way that the values to ranges of SpO₂. Scaling the values the same amount because any values is necessary to be new scaled for one neuron that used in the layer of second hidden with the same value. The incorporation the layers of two hidden to permits to estimate functions by neural network that is given an educate figure out of neurons that be seen in the layer of first hidden (Dayhoff and DeLeo, 2001). For the neural network, the inputs are HR, FiO₂, RR and for each one can we take first derivative. The dynamics properties is so comfortable for neural network by calculation first time derivative for each one. The structure of model will be shown in Fig. 4.

By Levenberg-Marquardt backpropagation, the model was trained by using Anonymous (2005). This method was selected for its capability to access the speeds of training of second order training and don't want to calculate matrix by the Hessian method. Second-order

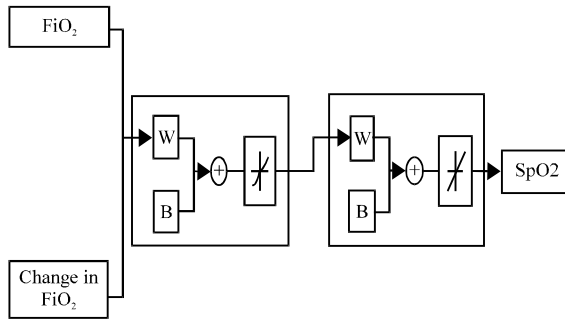


Fig. 4: Neural network model

training speeds is important since it can be time consuming and difficult to calculate the second-order derivative. Because the format of square's sum for network, the matrix in the method will be estimated with:

$$H = J^T J \tag{19}$$

where, J can be described as matrix of Jacobian and that makes the errors of neurons is comfortable by the first derivatives with respect to biases and weights. The matrix of Jacobian can be calculated by techniques of ackpropagation method. The gradient of the network was computed as:

$$g = J^T e \tag{20}$$

where, e is the network errors' vector. By combination Eq. 19 and 20 given as:

$$X_{K+1} = X_K - \frac{J^T e}{J^T J + \mu I} \tag{21}$$

where, μ is value of the step size and I is the identity matrix. To adjust between gradient descent and Newton's method the step size is adjusted. For example, when the value of μ is large enough, Eq. 20 a gradient descent method will be turns. But then, method of Newton will be turns when the value of μ is small. The main aim is to attach value of small μ due to the method of Newton works faster. A small value of μ is attained by decreasing of values of μ the error is declined every time. The prediction of the simulated SpO2 with the actual SpO2 was discovered by using method error of mean squared. Mathematic model was estimated as late as improving generalization stopped and this was completed to inhibit the neurons to be overtraining. Generalization recognized with perceiving when the value error of mean squared method is increasing samples of the

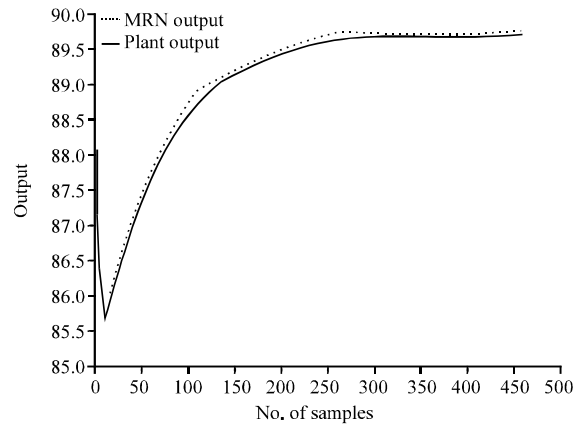


Fig. 5: Epoch = 1, learning rate = 0.005

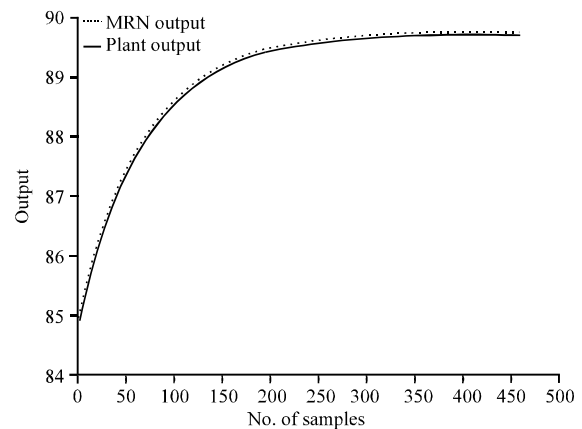


Fig. 6: Epoch = 10, learning rate = 0.0055

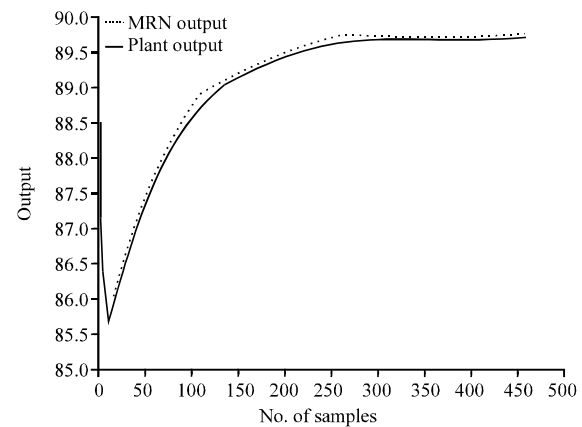


Fig. 7: Epoch = 1, learning rate = 0.015

validation samples. By using Neural network modeling algorithm with changing the values of learning rate and number of Epoch we can get the best model at Fig. 5-11.

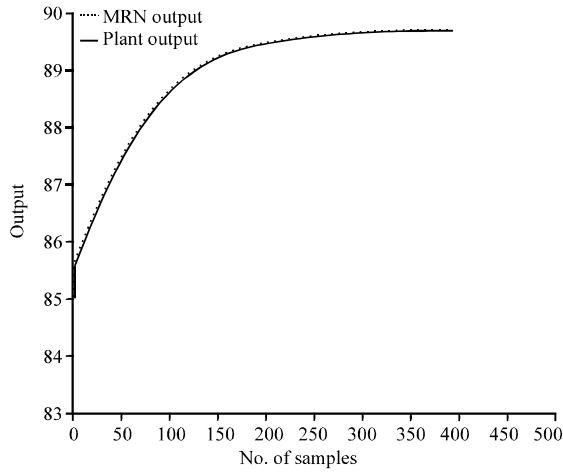


Fig. 8: Epoch = 100 with learning rate = 0.0055

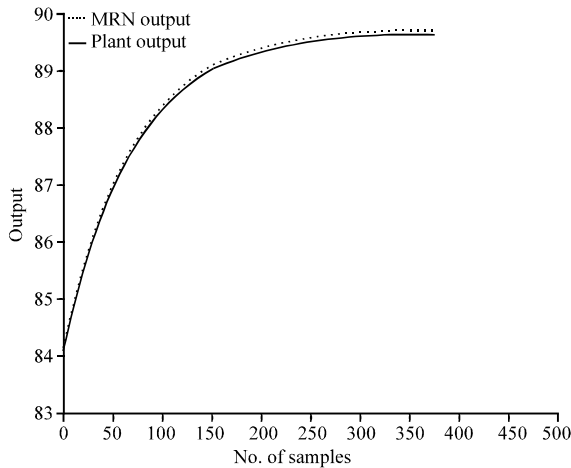


Fig. 9: Epoch = 100 with learning rate = 0.015

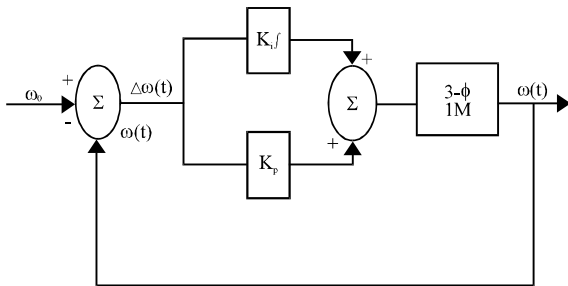


Fig. 10: Block diagram of PI controller

Control with pi and pid controller: At present, the PI controller is to the highest degree widely adopted in industrial application because its simple structure and easy to design. For all these benefits, the PI controller be unsuccessful when the controlled object is highly nonlinear and uncertain. PI controller will remove the steady state error and oscillations resulting for on-off

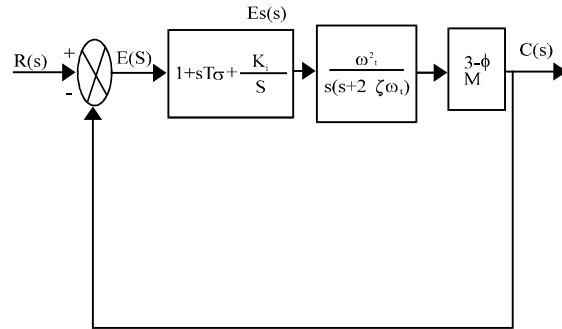


Fig. 11: Block diagram of PID controller

controller and P controller, respectively. However, for integral mode has an opposing effect on the stability and speed of the response of the system. Thus, PI controller will not change the speed of response. It can be expected because PI controller does not have means to estimate what will happen with the error in near future. This problem can be solved by applying derivative mode which has ability to estimate what will happen with the error in near future and thus to drop a reaction time of the controller. PI controllers are rarely used in industry, especially when speed of the response is not the problem of the system. A control without applying D mode is used when 1. Speed response of the system is not required 2. Large noise and disturbances are attend during operation of the process 3. There is energy storage in process 4. There are large transport response period will delay in the system. Consequently, we would like to retain the benefits of using a controller is like PI controller as shown in Fig. 5. The output of controller is

$$u(t) = K_p e(s) + K_i \int e(t) dt$$

The block diagram of PI controller is a compensation scheme of integral error, the output response relies on some way upon the actuating signal integral. The PI controller is put using a controller that makes the signal of output including of two terms, the first one is proportional to the integral signal and the other second one is proportional to the signal of actuating. Such that the controller is named proportional plus integral controller (PI).

The controller of Proportional Integral Derivative (PID) Controller as in Fig. 6. Most of controllers use to optimize a particular control system. A mathematic scheme of PID controller is most usual widely industry systems. The algorithm of PID controller used for algorithm in designing of speed. The dynamics of PID controller has the essentially functions: error of suitable action inside control to remove oscillations (P mode), raise control

signal to make error towards zero (I mode) and speed of reaction on alteration of the controller input (D mode):

$$u(t) = K_p e(t) + K_i \int e(t) dt + K_d \frac{de(t)}{dt}$$

The error signal put to the controller of combination of P,I and D. A proportional controller (K_p) will have the effect of decreasing the rise time, but never remove. The control signal is proportional to the integral of error and the integral gain If an integrator is added. Integral control signal will have the effect of reduced the error in assential, to zero value. Derivative control is used to estimate the future behavior of the error signal by using corrective actions based on the rate of change in the error signal. The control signal is proportional to the derivative of the error and K_d is the derivative gain. Derivative control will have the impact of raising the stability of the system, decreasing the overshoot and improving the transient response. The PID controller produces a control loop respond faster with less overshoot and most popular method of control by a great margin.

RESULTS AND DISCUSSION

In the first time, we did a mathematical model for arterial oxygen saturation in neonatal system to get the output of SpO2 according to the input FiO2 applying FiO2 with a value of 20-30%, we got the response of SpO2 between 84-95% and this value is the actual value for Oxygen saturation for neonatal infants as in Fig. 12-16. In the case of Neural network modeling with changing the values of epoch and learning. Neural network identifies the real system with the best values of number of epoch and learning rate and the results we got the best value for SpO2 as in Fig. 9. We used the controllers such as PI and PID and comparing which one is the best for the system to get the best response of minimum steady state error, improving transient response and decreasing peak overshoot. By using PI and PID controller to get a good response of SpO2 by tuning the values of K_p , K_i and K_d . Mathematic and Neural network model have the same response of the system for any control as in Fig. 17-22 and the best values of K_p , K_i and K_d are 10, 0.15 and 1, respectively. We note when change the values of K_p , K_i and K_d , the response of SpO2 are approximately the same for mathematic model and neural network model.

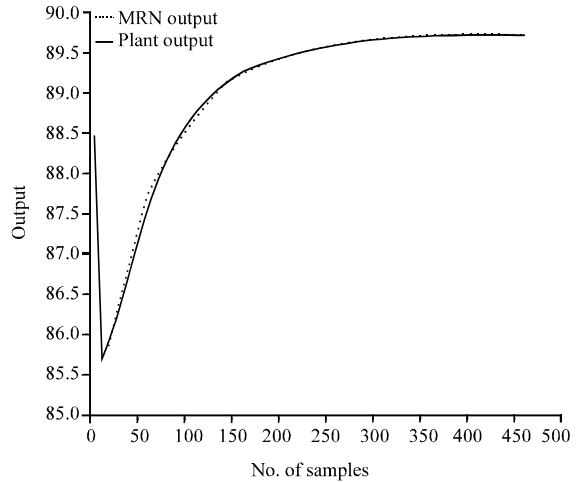


Fig. 12: Epoch = 1, learning rate = 0.005

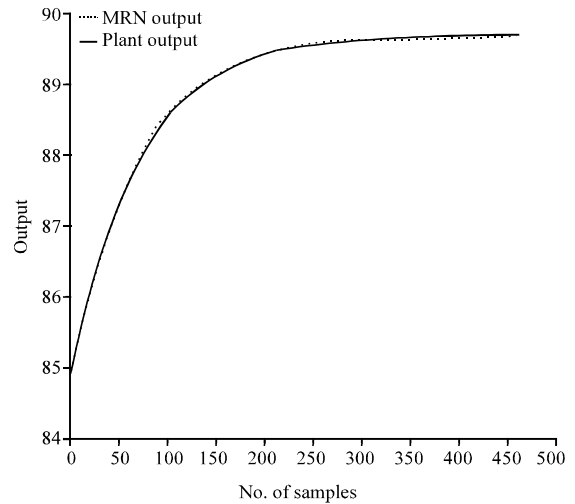


Fig. 13: Epoch = 10, learning rate = 0.0055

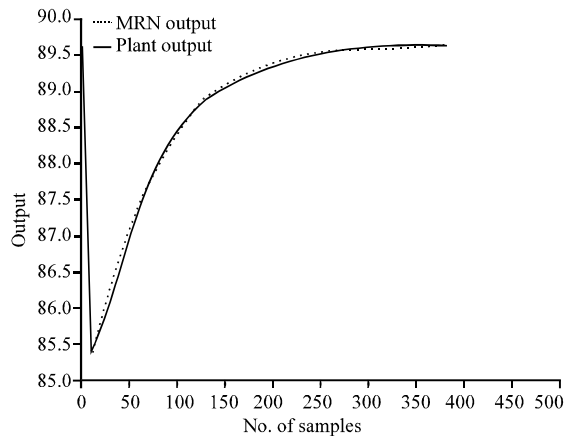


Fig. 14: Epoch = 1, learning rate = 0.015

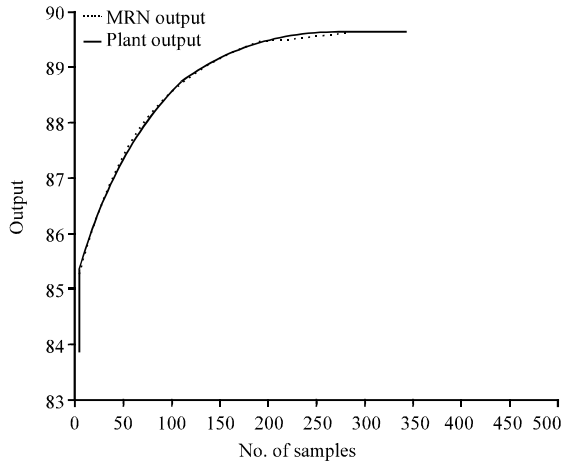


Fig. 15: Epoch = 100 with learning rate = 0.0055

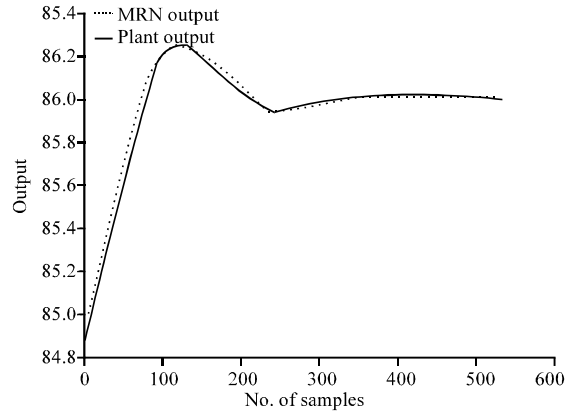


Fig. 18: $K_p = 0.1$, $K_i = 0.01$, Epoch = 10, learning rate = 0.015

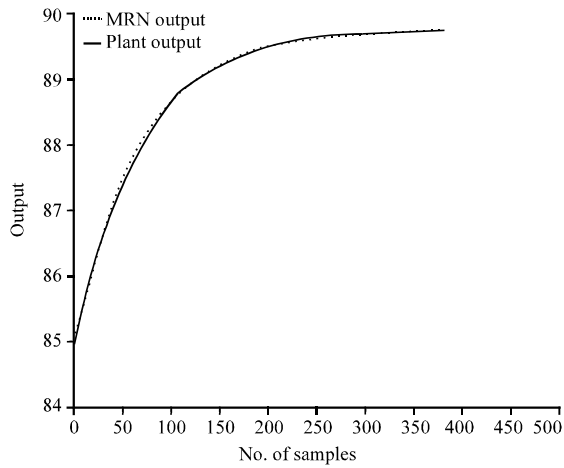


Fig. 16: Epoch = 100 with learning rate = 0.015

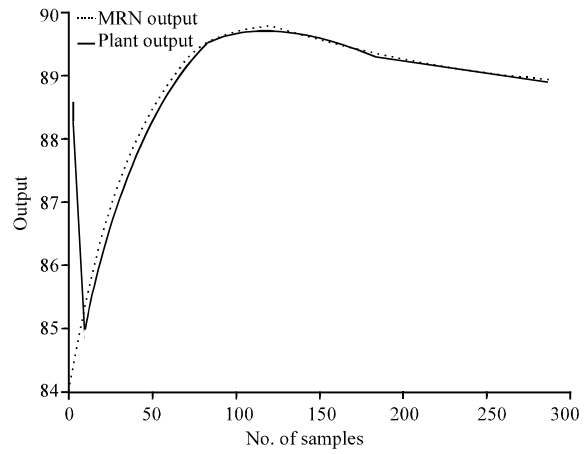


Fig. 19: $K_p = 1$; $K_d = 0.05$, Epoch = 100, learning rate = 0.015

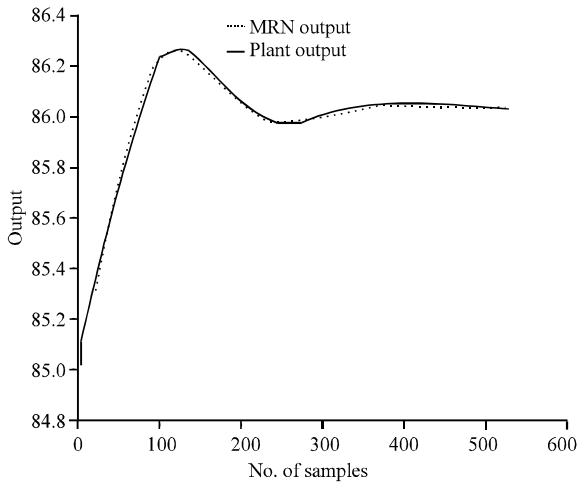


Fig. 17: $K_p = 0.1$, $K_i = 0.01$, Epoch = 100, learning rate = 0.015

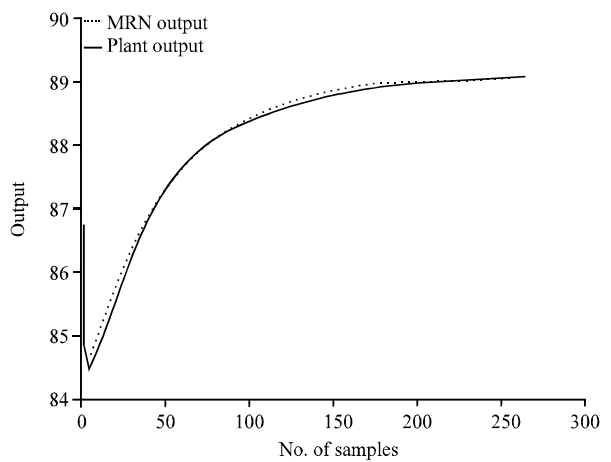


Fig. 20: $K_p = 5$; $K_d = 0.05$, Epoch = 100, learning rate = 0.015

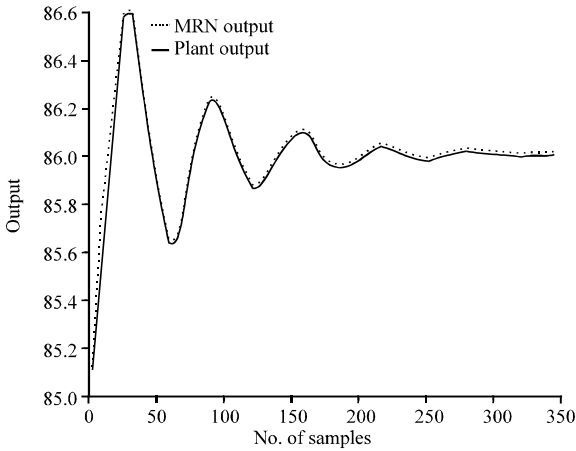


Fig. 21: $K_p = 1$; $K_p = 1$; $K_d = 1$ Epoch = 100; learning rate = 0.015

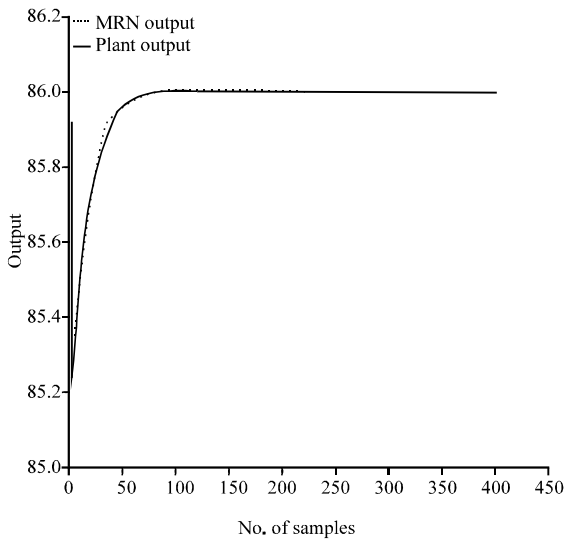


Fig. 22: $K_p = 10$, $K_i = 0.15$, $K_d = 1$, Epoch = 100, learning rate = 0.015

CONCLUSION

Currently when infants are put on a respiratory support device the nurses manually adjust the blend valve to control the amount of FiO_2 applied to the infants based on the infants SpO_2 . The infant may not receive instant attention when the desaturation event occurs. This can cause perilously low SpO_2 levels which can command to brain damage and even death. On the other hand if the SpO_2 level is high to infant is at danger for Respiratory Distress Syndrome. The aim of this paper is to design a controller that can control the infants SpO_2 and reduce the time the infant is outside of the agreeable safe range of SpO_2 . The main topics in

this paper are the investigation of the biological system, modeling and do controlling of the infant's SpO_2 .

The biology of infant's system was examined to see how the blood is did oxygenate and what measurable parameters will permit insight into the SpO_2 levels. It was discovered to oxygenate the blood during the ventilation mechanism, diffusion and aspirate. Two different modeling methods were used to model the infants SpO_2 . The first type was the updating models. This modeling type was chosen for its ability to have a generalized model of the SpO_2 while allowing the model to be updated when needed. The models examined are a neural network and mathematic model. The models were tested on two types of simulated data sets. All of the models were able to adequately estimate future values if the system had fixed parameters. This is to be expected since the model is linear. The neural network model were cable of adjusting to the change in parameter and predict the future values precisely. The mathematic model was selected to permit the mathematic model to be better model a system with variable parameters. The model was tested on the same simulated data sets and was able to adequately model both data sets. The two different controllers were selected relied on the mathematic model and the predicted range of gains and time constants. The controllers selected are a linear quadratic regulator PI and PID controller. The controllers were tested using simulated data. All controllers attempted to keep the SpO_2 at a given set point. The PI controller was the least affective at controlling the SpO_2 with changing the values of K_p and K_i but the best response of SpO_2 was time 250 sec at minimum peak overshoot with zero steady state error. The PID controller was the best controller than PI because it made the response of the system fast and the SpO_2 was time 100 sec at minimum peak overshoot with zero steady state error.

RECOMMENDATIONS

In future research, the performance of the mathematic model could be increased. The performance could be increased by introducing transport delay time into the model. By introducing the transport delay time into the system, the model would be less likely to produce negative gains for the HR and RR. Another improvement to the mathematic model would be to decrease the calculation time. The calculation time could be decreased by trying different global optimization methods.

REFERENCES

- Anonymous, 2005. Levenberg-Marquardt. The Math Works, Inc, Natick, Massachusetts, USA.
- Dayhoff, J.E. and J.M. DeLeo, 2001. Artificial neural networks: Opening the black box. *Interdiscip. Intl. J. Am. Cancer Soc.*, 91: 1615-1635.
- Granelli, A.D.W., M. Mellander, J. Sunnegardh and I. Ostman-Smith, 2005. Screening for duct-dependent congenital heart disease with pulse oximetry: A critical evaluation of strategies to maximize sensitivity. *Acta Paediatrica*, 94: 1590-1596.
- Granelli, A.D.W., M. Wennergren, K. Sandberg, M. Mellander and C. Bejlum et al., 2009. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: A swedish prospective screening study in 39 821 newborns. *BMJ.*, 1: 1-12.
- Gray, J.S., 1945. The Multiple Factor Theory of Respiratory Regulation. Army Air Force School of Aviation Medicine, Dayton, Ohio, Pages: 38.
- Grevisse, P., H. Lecocq and M. Demeester, 1975. A pulmonary model for the automatic control of a ventilator. *IFAC. Proc.*, 8: 295-302.
- Grodins, F.S., J. Buell and A.J. Bart, 1967. Mathematical analysis and digital simulation of the respiratory control system. *J. Appl. Physiol.*, 22: 260-276.
- Hagadom, J.I., A.M. Furey, T.H. Nghiem, C.H. Schmid and D.L. Phelps et al., 2006. Achieved versus intended pulse oximeter saturation in infants born less than 28 weeks gestation: The AVIOx study. *Pediatr.*, 118: 1574-1582.
- Hu, X.J., X.J. Ma, Q.M. Zhao, W.L. Yan and X.L. Ge *et al.*, 2017. Pulse oximetry and auscultation for congenital heart disease detection. *Pediatr.*, 140: 1-12.
- Keim, T., R. Amjad and R. Fales, 2009. Modeling and control of the oxygen saturation in neonatal infants. Proceedings of the ASME 2009 International Conference on Dynamic Systems and Control, October 12-14, 2009, ASME, Hollywood, California, USA., ISBN:978-0-7918-3860-0, pp: 105-112.
- Laptook, A.R., W. Salhab, J. Allen, S. Saha and M. Walsh, 2006. Pulse oximetry in very low birth weight infants: Can oxygen saturation be maintained in the desired range?. *J. Perinatology*, 26: 337-341.
- Merenstein, G. and S.L. Gardner, 2006. Handbook of Neonatal Intensive Care. Mosby Elsevier, Maryland Heights, Missouri, ISBN:9780323033008, Pages: 1039.
- Morozoff, E.P. and J.A. Smyth, 2009. Evaluation of three automatic oxygen therapy control algorithms on ventilated low birth weight neonates. Proceedings of the EMBC 2009 Annual International Conference on Engineering in Medicine and Biology Society, September 3-6, 2009, IEEE, Minneapolis, Minnesota, USA., pp: 3079-3082.
- Tehrani, F.T. and A.R. Bazar, 1991. An automatic control system for oxygen therapy of newborn infants. Proceedings of the Annual International Conference on Engineering in Medicine and Biology Society Vol. 13, October 31-November 3, 1991, IEEE, Orlando, Florida, USA., pp: 2180-2182.
- Thangaratinam, S., K. Brown, J. Zamora, K.S. Khan and A.K. Ewer, 2012. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: A systematic review and meta-analysis. *Lancet*, 379: 2459-2464.
- YU, C., W.G. He, J.M. So, R. Roy and H. Kaufman, 1986. Improvement in arterial oxygen control using multiple-model adaptive control procedures. *IEEE. Trans. Biomed. Eng.*, 34: 567-574.