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Research Article

MODELING AND CONTROL OF ANAESTHETICS DURING POST SURGICAL TREATMENT

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ABSTRACT
The major constraint in automatic control of anaesthesia is patient's variability based on drug tolerance. A controller has to be designed in such way that it is robust to the actual patient's response even if the controller is designed based on a nominal patient model. Anaesthetic agent used in this study is isoflurane gas and the controlled delivery of anaesthetic agent has to be given with utmost care of great accuracy because the agents used here have narrow therapeutic uses. The importance of the robustness of the controller to be designed is that it must provide a sufficient and controlled administration of drugs to avoid the situations of under and over dosing of patients. The hemodynamic parameters that are to be measured during drug administration is Mean Arterial Pressure (MAP) and heart rate (HR), whereas another parameter to be measured during anaesthesia delivery is measure of unconsciousness of the patient called as Bi-spectral Index (BIS). In this study, the anaesthesia control system is modeled and controller design is made for patient undergoing Intensive Care Treatment (ICU) after valve replacement surgery. The background analysis is made by observing the real-time parameters such as BIS, MAP, and HR of patient undergone valve replacement surgery.

Keywords: Anaesthesia, Control, Modeling, Simulation, Surgery.

1. INTRODUCTION
There is direct measurement of hypnosis is BIS. Hypnosis is the state of unconsciousness of the patient which is achieved through the administration of anaesthetic agent. But there is no direct measurement for analgesia. Analgesia is the measure of sense to pain caused by the surgical procedure. This is measure through MAP and HR [1, 2]. When the patient is undergoing treatment after surgery in ICU, more attention and periodical monitoring is required because the tolerance of patient is completely based on their hypnotic and analgesic state. The adequate drug administration during this period helps the patient to recover fast and the number of days spent by the patient in hospital can be reduced and hence tend to be cost-effective [3, 4]. General anaesthesia process is categorized into three phases as discussed below:

1.1. Initiation Phase
In this phase, the patient's state of being conscious is changed into hypnotic state through the induction of anaesthetic agent. During this process, there will be respiratory depression which is supported using artificial ventilation and securing the airway is the important step. This phase terminates within a few minutes [5].

1.2. Maintainence Phase
This phase is the stable part where the anaesthetic state of the patient has to be maintained until the patient is completely recovered from the surgical procedure. It is this phase where the controllers play a crucial role in regulating and maintaining the drug administration [6]. Since isoflurane is an inhalation agent, it is administered along with oxygen to the patient. Isoflurane is responsible for both hypnotic and analgesic state of the patient.

1.3. Emergency Phase
During this phase, the patient will be completely switched off from drug administration if the patient had completely recovered. When the drug inhalation is stopped, the patient exhales the remaining drug present inside the lungs and slowly returns to the conscious state [7, 8].

2. MATERIAL AND METHODS

The anaesthesia control system is shown in Fig. 1 with modeling of anaesthetic agent based on compartmental approach.

2.1. Modeling of Anaesthesia Control System

The modeling is carried out by considering one central compartment (lungs), peripheral compartment II (vessel rich organ like liver), peripheral compartment III (muscles), peripheral compartment IV (other organs and tissues), and peripheral compartment V (fat tissues). A flow of isoflurane along with oxygen is supplied into patient's lungs [9]. The gas gets circulated and rebreathing of exhaled gas is prevented by using relief valves. The CO_2 absorber is used to remove CO_2 from the exhaled gas with the help of soda-lime and the fresh exhaled gas is fed into the gas. The parameters involved in modeling are shown in Table 1.

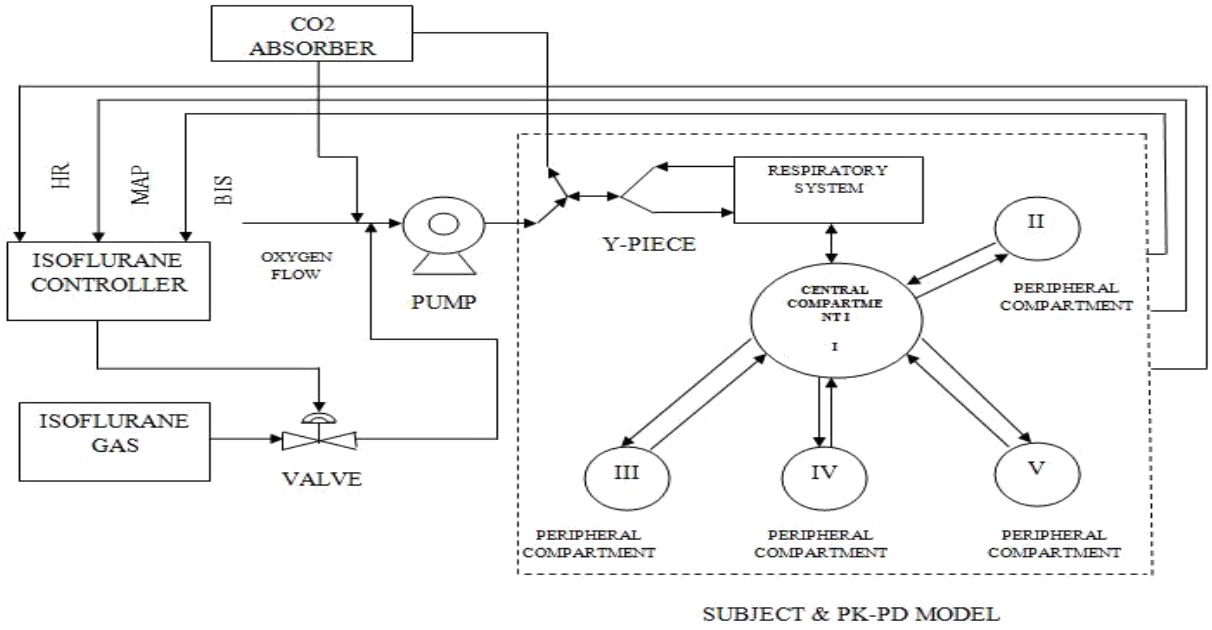


Fig. 1: Block Diagram for Anaesthesia Control System

The mass balance Eq. of the each compartment is derived as-

$$V_i \frac{dC_{i,j}}{dt} = Q_i \left(C_{ar,j} - \frac{C_{i,j}}{R_i} \right) - K_{i,j} C_{i,j} \quad (1)$$

Where, V_i is the volume of the compartment

$C_{i,j}$ is the drug concentration in the compartment

Q_i is the blood flow to the compartment

$K_{i,j}$ is the rate constant

$C_{ar,j}$ is the drug concentration in arteries

R_i is the partition coefficient between blood and tissues in the compartment

The flow rate of blood is expressed as-

$$Q_{i,out} = \frac{Q_{i,n}}{R_i}, \; Q_{i,n} = Q_i \quad (2)$$

Where, $Q_{i,n}$ is the inlet flow rate of blood

$Q_{i,out}$ is the outlet flow rate of blood

Considering the concentration of the drug in arteries is equal to the concentration of drug in the outlet flows from central compartment, the Eq. is obtained as-

$$V_i \frac{dC_{i,j}}{dt} = Q_i \left(C_{1,j} - \frac{C_{i,j}}{R_i} \right) - K_{i,j} C_{i,j} \quad (3)$$

The inhalation process of isoflurane carried out through respiratory system is modeled as-

$$V \frac{dC_{inhale}}{dt} = Q_{in} C_{in} - (Q_{in} - \Delta Q) C_{inhale} - f_R (V_T - \delta)(C_{inhale} - C_0) \quad (4)$$

Where, C_{inhale} is the concentration of isoflurane inhaled by the patient (g/ml)

C_{in} is the concentration of the isoflurane in inlet stream (g/ml)

C_O is the concentration of isoflurane in outlet stream (g/ml)

f_R is the frequency of respiration (l/min)

V_T is the tidal volume (l)

V is the volume of respiratory system (l)

δ is the physiological dead space (ml)

Q_{in} is the inlet flow rate (ml/min)

ΔQ are the losses (ml/min)

Due to the elimination of isoflurane by exhalation and metabolism by liver, the peripheral compartment II is modeled as-

$$V_2 \frac{dC_2}{dt} = Q_2 \left(C_1 - \frac{C_2}{R_2}\right) - K_{20} C_2 V_2 \quad (5)$$

Where, K_{20} is the rate of elimination of isoflurane in peripheral compartment II. The concentration of isoflurane in compartments III, IV, and V are obtained as-

$$V_k \frac{dC_k}{dt} = Q_k \left(C_1 - \frac{C_k}{R_k}\right) \; for \; k = 3, 4, 5 \quad (6)$$

The pharmacodynamic modeling is done by assuming that there is some delay between inhalation of isoflurane by lungs and isoflurane dissolving in brain tissue thereby causing hypnosis. The effect-site compartment modeling with non-linearity is usually expressed in terms of Sigmoid Hill equation. as shown in Eq. 7-9.

$$BIS = Eff_{0,b} - Eff_{max,b}\left(\frac{C_e^{\gamma}}{C_e^{\gamma} + C_{50}^{\gamma}}\right) \quad (7)$$

$$MAP = Eff_{0,m} - Eff_{max,m}\left(\frac{C_e^{\gamma}}{C_e^{\gamma} + C_{50}^{\gamma}}\right) \quad (8)$$

$$HR = Eff_{0,h} + Eff_{max,h}\left(\frac{C_e^{\gamma}}{C_e^{\gamma} + C_{50}^{\gamma}}\right) \quad (9)$$

Where $Eff_{0,b}$, $Eff_{0,m}$ and $Eff_{0,h}$ $Eff_{0,h}$ are the base value when the drug input is zero, $Eff_{max,b}$, $Eff_{max,m}$ and $Eff_{max,h}$ are the value of maximum change of concentration to the drug input.

C_e^{γ} is the effect-site concentration represented as $\frac{dC_e}{dt} = k_{e0}(C_1 - C_e)$

k_{e0} is the equilibrium time between end tidal and effect-site

C_{50}^{γ} is the half maximal effective concentration

γ is the Hill's coefficient

Table 1: Parameters Involved In Anaesthesia Modeling

Parameters	Values
Q_0	1-10 l/min
ΔQ	0.1-0.5 l/min
Δ	0.1-0.2 l
f_R	4-25 min^{-1}
V_T	0.3-1.2 l
V	4-6 l
K_{20}	0.0093±0.0137 min^{-1}
k_{e0}	0.3853 min^{-1}
γ	1.534
C_{50}^{γ}	0.7478 min^{-1}

Based on ARX modeling, the transfer functions obtained from anaesthesia-physiological model with weight as co-variate (Patient weight taken in this work is 45 kg) are shown as follows

$$\frac{BIS_{45}}{ISOFL_{45}} = \frac{-6.31}{17.075s + 1} e^{-3s} \quad (10)$$

$$\frac{MAP_{45}}{ISOFL_{45}} = \frac{-5.292}{13.409s + 1} e^{-2.134s} \quad (11)$$

$$\frac{HR_{45}}{ISOFL_{45}} = \frac{4.226}{12.385s + 1} e^{-1.355s} \quad (12)$$

3. CONTROLLER DESIGN

3.1. Proportional-Integral (PI) Controller

PI controller is also designed for the controlled drug delivery during post surgical treatment. In anaesthesia control system, PI values are tuned using Ziegler-Nichols method. This method is also called a closed loop method. Initially, the closed loops of the obtained transfer functions are formed with integral value as zero and proportional value at some constant. The response of the system should result with sustained oscillations. Until sustained oscillations are obtained, the proportional values are changed randomly [10, 11]. The proportional value corresponding to sustained oscillations are termed as ultimate gain (K_u) and the time period of oscillation determined from sustained response is termed as ultimate period (P_u). Based on these values, the tuning parameters are calculated using following equations

$$K_c = 0.45 K_u \quad (13)$$

Where, $K_u = \frac{4d}{\pi a}$, d is the value of relay and a is the half of the amplitude of sustained oscillations.

$$\tau_i = \frac{P_u}{1.2} \quad (14)$$

Where, P_u is the period of oscillation for one cycle.

4. RESULTS AND DISCUSSION

The simulated responses for the controlled inhalation rate of isoflurane using PI controller to regulate BIS, MAP, and HR are presented in following Figures for five cases with co-variate as weight. Figures 2, 3 and 4 depict the controlled response of BIS, MAP and HR during the inhalation of isoflurane by patient with 45 kg and their respective inhalation rates are 54.7 ml, 67.3 ml and 58.5 ml.

The performance of PI controller is evaluated using time domain specifications and error criteria are tabulated below.

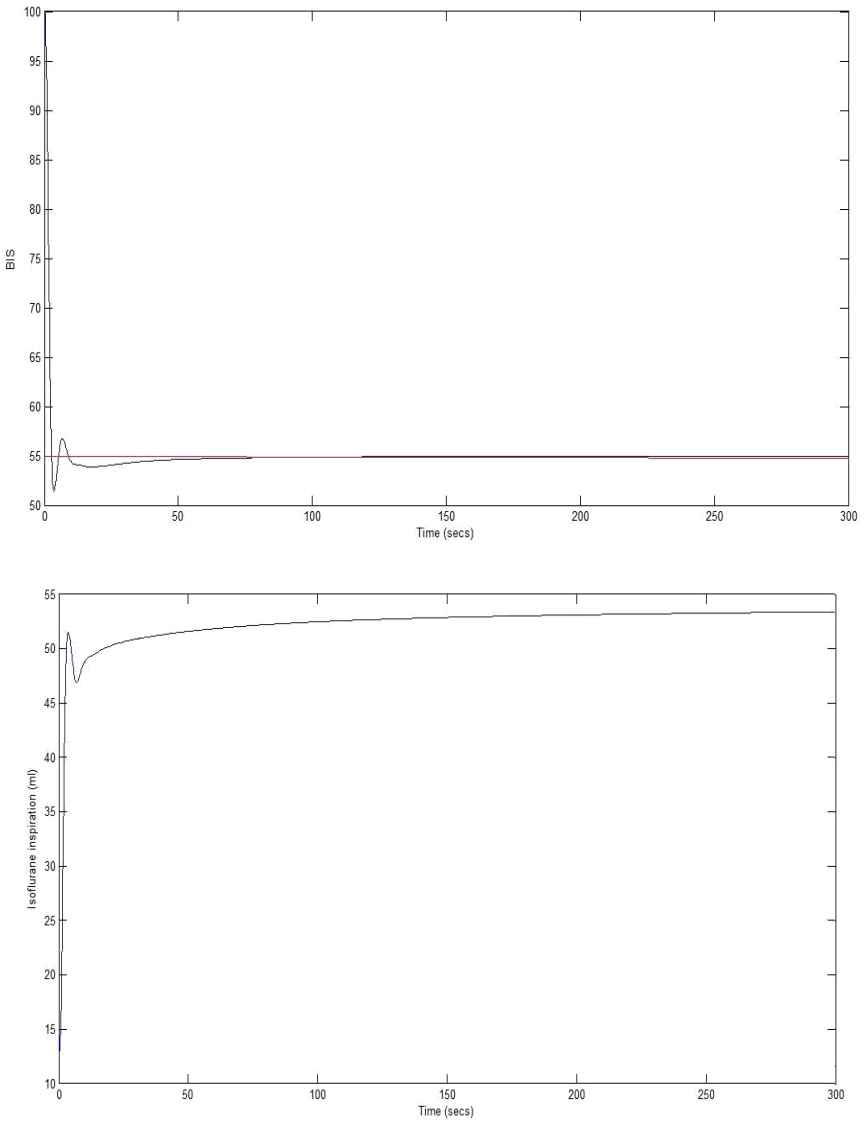
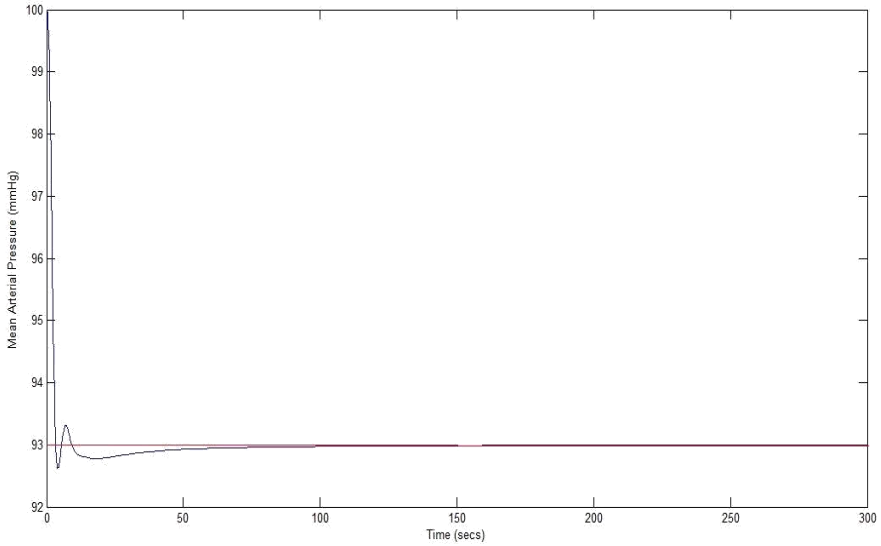


Fig. 2: BIS Response in 45 kg Patient using PI Controller



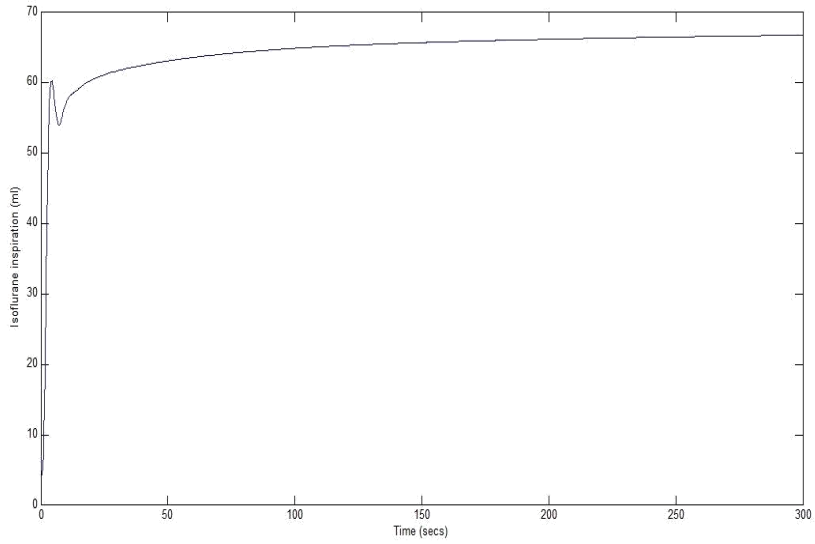


Fig. 3: MAP Response in 45 kg Patient using PI Controller

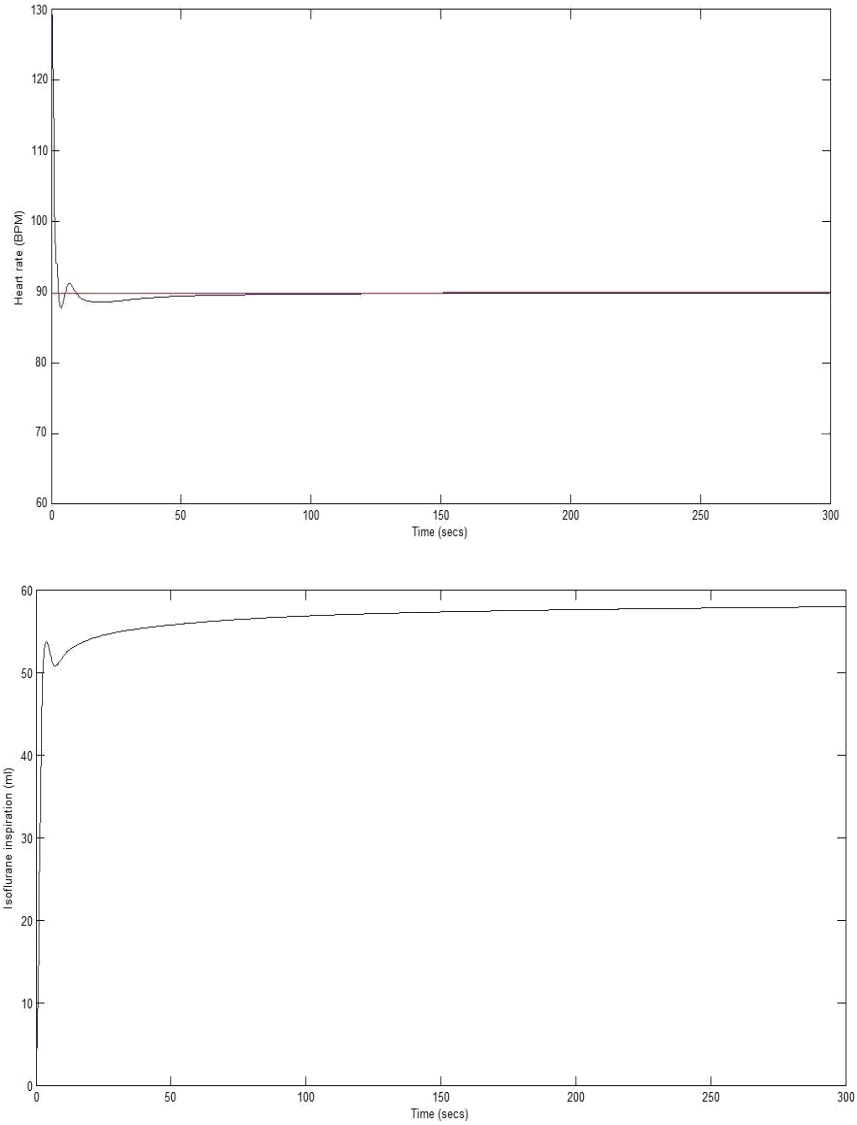


Fig. 4: HR Response in 45 kg Patient using PI Controller

Table 2: Time domain specifications for controlled isoflurane inhalation by PI controller

Patient weight	Parameter	Rise time (sec)	Peak time (sec)	Settling time (sec)
45 KG	BIS	10.8328	3.1554	63.5304
	MAP	41.0529	3.1554	217.8697
	HR	47.6125	156.7941	317.0501

Table 3: Error criteria for controlled isoflurane inhalation by PI controller

Patient weight	Parameter	Steady state error	ITAE	ISE	IAE
45 KG	BIS	0.0123	$2.97E^{-5}$	$2.434E^{-4}$	1.373
	MAP	0.0116	$9.28E^{-4}$	1.538	0.5064
	HR	0.1005	$1.017E^{-6}$	$9.814E^{-4}$	0.4335

5. CONCLUSION

Automation in medical applications plays a major role in aiding anaesthetists and physicians involved during surgery and post surgical treatment. Drug administration through manual control to patients' results in under and overdosing of drugs which leads to various life threatening consequences. Hence, in this work, an advisory system is modeled and controller is developed which helps the anaesthetist know about the state of the patient and effects of drug dosage. It also simplifies the task of anaesthetists and enhances safety of the patient.

Conflict of interest

None declared

Source of funding

None declared

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