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Modeling and control of Automatic Drug Delivery System for infusing Cardiac Drug

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Abstract - *Monitoring and control of physiological variables during surgeries is a difficult task since the manual infusion of drugs leads to complications in patients. Cardiovascular systems play an important role in maintaining proper blood flow in living beings. The blood flow inside the human body is usually maintained at some desired pressure. This pressure is called the Mean Arterial Pressure (MAP). During cardiac surgeries and post surgical treatments, the control of MAP is a great challenge for anaesthetist. This is mainly done by injecting vasodilator and vasoconstrictor drugs intravenously. Since this is done manually, control of drugs is of low accuracy and time consuming. Hence an Automatic Drug Delivery System (ADDS) is modeled and controlled. This paper presents the modeling of ADDS and control of MAP by implementing controllers for regulating the infusion rate of cardiac drugs sodium nitroprusside (SNP).*

Key Words: MAP, SNP, Drug Delivery and control.

1. INTRODUCTION

The blood circulation in humans is done by the cardiovascular system. Therefore proper blood flow is very essential for the well being of the humans. Now days, humans are prone to diseases such as cardiac arrest and other heart-related ailments. This is usually rectified by undergoing various surgical treatments. The blood flow inside the human body is normally maintained at certain pressure. Hence during the cardiac surgeries and post surgical treatments, there will be fluctuations in the Mean Arterial Pressure (MAP). This variation leads to further complications during the treatment. So the MAP is to be maintained at the limited range. The MAP is made to remain stable by the addition of vasodilators and vasoconstrictor drugs. Some of the commonly used drugs are Sodium Nitroprusside (SNP), Noradrenaline (NAR), Halotheane, Hexamethonium, Pentolinium, Dopamine, Trimethaphan and Nitroglycerine (NG). These drugs are infused intravenously using the syringe pump with rate limiters. Vasodilators are the drugs which are used to widen the blood vessels which in turn reduce the MAP. Vasoconstrictors are the drugs that are used in narrowing the blood vessels to increase the MAP. Most commonly infused drugs are Sodium Nitroprusside (SNP), Nitroglycerine (NG), Dopamine (DPM) and Noradrenaline (NAR).The infusion rates of these drugs are controlled by the anaesthetist.

Thus the automation of drug infusion system will be of great aid to anaesthetist and to concentrate more on other parameters. During the surgery, blood pressure will not be normal and there will be variations due to surgical procedure done by the surgeons. In order to maintain a proper blood pressure, various vasoconstrictors and vasodilators will be infused based on the nature and sensitivity of the patient. This study is mainly focussed on modeling the drug kinetics and dynamics and controlling the parameter such as MAP (Mean Arterial Pressure) by inducing the control action to the respective syringe pump of the sodium nitroprusside with infusion rate of 0-10 µg/kg/min at a continuous manner.

2.MODEL DESCRIPTION

The modeling of the human is done based their sensitivity to the drugs and the disturbances that contribute to the changing conditions in the body. Real-time data such as the drug infusion rate (ml/hr), systolic pressure (mmHg), diastolic pressure (mmHg) and the time duration (secs) during the Coronary Artery Byepass Grafting (CABG) are taken into account for the modeling of the patient response. Here the MAP is calculated from the systolic pressure and diastolic pressure obtained during the treatment. The patient model is estimated to be the transfer function of MAP to that of the drug infusion rate. The transfer functions of patient model is developed by correlation analysis as a linear first order system with a system delay (due to transport of drugs from injection site) and lag time which is responsible for uptake, distribution and biotransformation of the drugs as shown in (1).

$$\frac{\mathrm{MAP}(S)}{\mathrm{SNP}(S)} = \frac{\mathrm{K}(1+\tau_3 S)\mathrm{e}^{-\Delta s}}{[(1+\tau_3 S)(1+\tau_2 S)-\alpha](1+\tau_1 S)} \quad (1)$$

Where

K- drug sensitivity

Δ- system delay

τ_1- time constant for drug action

τ_2- time constant for pulmonary circulation

τ_3- time constant for systematic circulation

α- recirculation constant

2.1.1 PK Modeling

The patient model developed in (1) is then combined with the pharmacokinetic (PK) – pharmacodynamic (PD) model of the SNP drug model based on compartmental approach. Drug model is compartmented into one central compartment a nd four peripheral compartments as shown.

2.1.2 Central Compartment

The infusion of intravenous drugs in the central compartment is modeled as

$$V_1 \frac{dC_1}{dt} = \sum_{i=2}^{5} (Q_i(\frac{C_i}{R_i} - C_1)) + C_{inf} - \frac{1}{\tau_{1/2}} C_1 V_1 \quad (2)$$

where C_{inf} is the flowrate of the drug infused

V_i is the volume of the compartment i

$\tau_{1/2}$ is the half life of the drug

2.1.3 Peripheral Compartment

Since the drugs decay naturally in the body, the peripheral compartments are modeled as

$$V_i \frac{dC_i}{dt} = Q_i(C_1 - \frac{C_i}{R_i}) - \frac{1}{\tau_{1/2}} C_i V_i, \quad i=2,....,5 \quad (3)$$

where $Q_i = Q_{i0}(1 + \Delta_{flowi} C_{in}), i = 2,3,4,5$

$$Q_1 = \sum_{i=2}^{5} Q_i$$

where
Δ_{flowi} is the ratio of flow rate change in the i^{th}compartment

C_{in} is the concentartion of drug

2.1.4 PD Modeling

$$\frac{dEff}{dt} = k_1 C_1^N (Eff_{max} - Eff) - k_2 Eff \quad (4)$$

where Eff_{max} is the maximum elastance

k_1 and k_2 are rate constants

C refers to concentration of either NAR or NG

N is the non-linearity constant

2.2 CONTROLLER DESIGN

2.2.1 Proportional-Integral-Derivative (PID) Controller

Most widely used controller in the field of process control because of its simplicity and robustness is the three term controller called as Proportional-Integral-Derivative Controller (PID). The common tuning method for closed loop response of PID controller is Zeigler-Nichols method. Zeigler-Nichols tuning method is applied to obtain the K_p, T_i and T_d values of the closed loop transfer function of the converter. The proportional gain is slowly increased by giving small periodic disturbance to the process. At one point of time, closed loop response tends to produce sustained oscillations and Table 1 shows the tuning parameters. From the oscillations obtained, the ultimate gain (K_u) and the period of oscillation known as ultimate period (P_u) are calculated. Figure 1 shows the closed loop block diagram of PID controller.

Table 1 Tuning parameters

Controller	K_c	T_i	T_d
PID	$K_u/1.7$	$P_u/2$	$P_u/8$

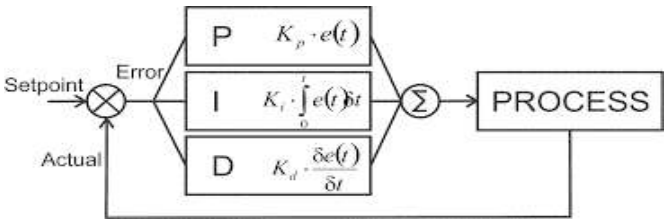

Figure 1 Schematic representation of PID controller

2.2.2 Internal Model Controller (IMC)

The IMC structure generally consists of three blocks such as controller, internal model and internal model loop. The IMC principle is that the control can be achieved only if the control system encapsulates, either implicitly or explicitly, certain representation of the process to be controlled. In particular, if the control scheme has been developed based on an exact model of the process, then perfect control is theoretically possible. In practice, however, process model mismatch is common; the process model may not be invertible and the system is often affected by unknown disturbances. The open loop control arrangement will not

be able to maintain output at set point. Nevertheless, it forms the basis for the development of a control strategy that has the potential to achieve perfect control. This strategy is called as Internal Model Control. The internal model controller is shown in Figure 2.

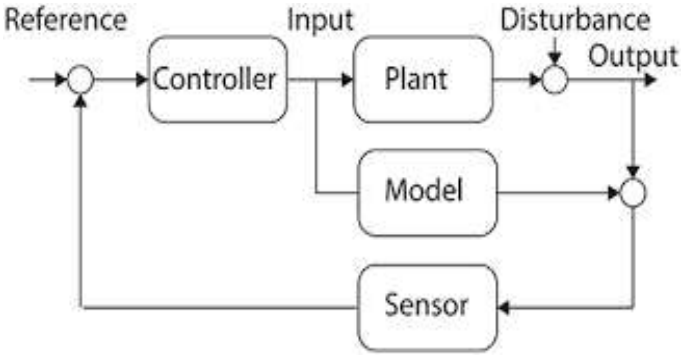

Figure 2 Schematic representation of internal model controller

3. RESULTS AND DISCUSSION

The closed loop control action by PID and IMC are discussed in this section. The variability in the patient model is implemented based on the sensitivity of the patient such as sensitive, normal and insensitive patient.

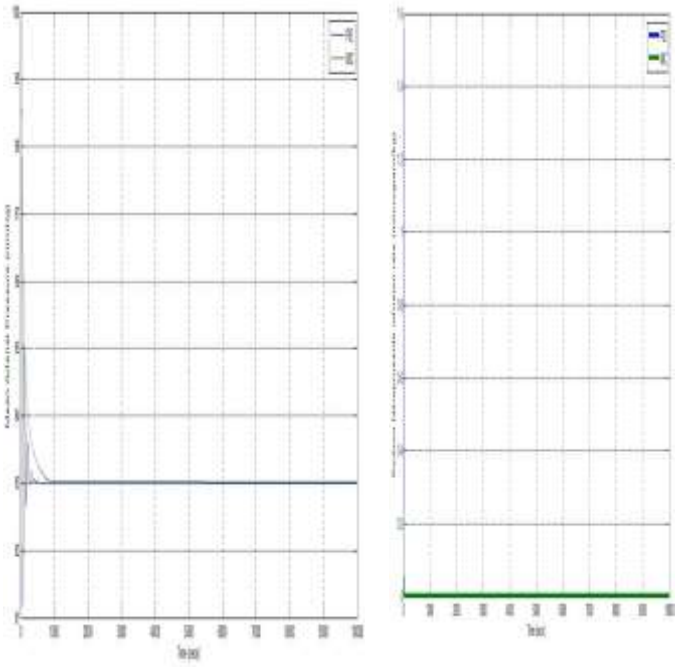

Figure 3 MAP response and SNP infusion rate obtained using PID and IMC in sensitive patient model

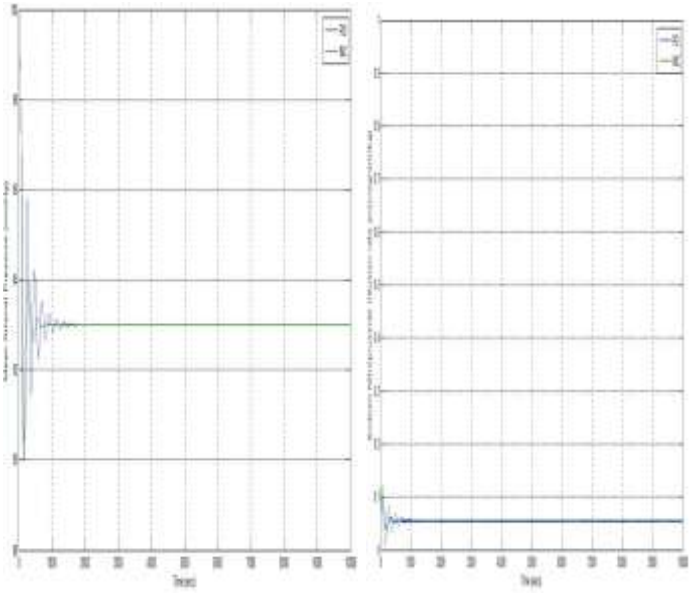

Figure 4 MAP response and SNP infusion rate obtained using PID and IMC in normal patient model

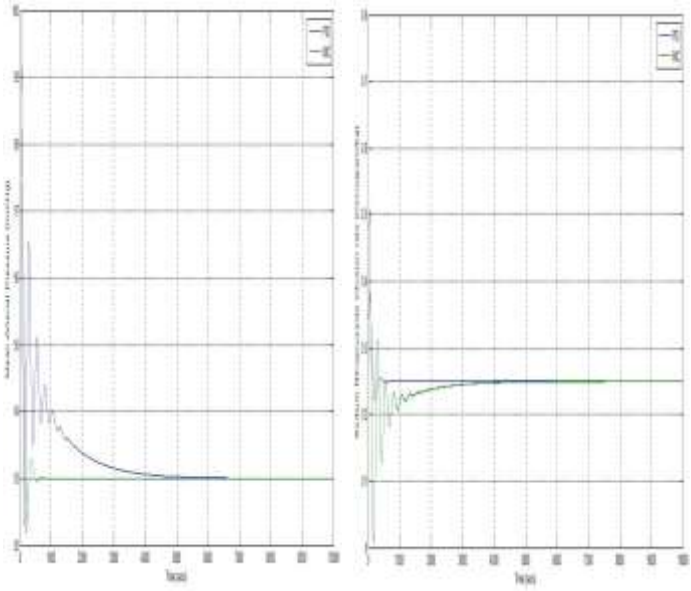

Figure 5 MAP response and SNP infusion rate obtained using PID and IMC in insensitive patient model

4. CONCLUSION

The modelling of ADDS and control of MAP by implementing PID and IMC controller for regulating the infusion rate of cardiac drugs sodium nitroprusside (SNP). The analysis was made with three categories of patient sensitive, normal and insensitive. From the results it is observed that the IMC controller produces smoother response for all the three cases.

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