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Automatic Drug Delivery System for The Drug Adrenaline using Pi, Pid, Imc & Mpc Controllers

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Abstract - Continuous specialist care and controlling of Mean Arterial Blood Pressure (MABP) of the patients for the period of postoperative cardiac surgery is the most problematic task for the medical personnel. Drug adrenaline is used to normalize the low blood pressure of the patients to the preferred level and manual control of the drug infusion rate of the patients may also be a challenging one. To mitigate this problem an automatic drug delivery system is designed, particularly if it is adjusted to the deviations in the patient's model. The main objective of this paper is to control the MABP by injecting the drug adrenaline automatically into the patient's body using four different control schemes such as PI, PID, IMC, and MPC controllers. These controllers effectively control the blood pressure of the patients to the preferred level and carry out strongly in the occurrence of deviations in the patient response. The efficiency of the proposed work is assessed by the simulation for the purpose of an automatic drug delivery scheme to control the MABP.

Keywords: Drug infusion level, Blood pressure, Control schemes, Patient model.

I. INTRODUCTION

Blood pressure is one of the main parameters in several medical applications. For instance, its variation resembles the depth of anesthesia (i.e. Unconsciousness) during the surgical process. Specifically, the MABP is considered as the most consistent parameter to be controlled to keep up the suitable anesthesia to confirm patient safety. MABP of life-threatening care patients must be supervised during and after the open heart surgery. After the conclusion of the cardiac surgery, some patients develop low blood pressure (hypotension) and the amount of postoperative hypotension is common between the cardiac patients. Such hypotension should be cured appropriately to avoid severe problems. Uninterrupted infusion of drug adrenaline would increase the blood pressure, more or less immediate. Specialist care of medical staff is essential. Most of the time, the injection of adrenaline is done manually by medical staff, for instant, nurses, which is always poor in quality. For this purpose, an automatic drug infusion control scheme is intended to effectually inject the drug adrenaline into the patient's cardiovascular system to increase the blood pressure. MABP of the patients is regulated as a result of the continuous infusion of drug adrenaline. Drug adrenaline would help to keep up the MABP of patients to the normal level. The indication of an automated scheme for the drug adrenaline infusion motivates the control engineers to stand up by means of more sophisticated schemes that can handle the optimal delivery of anesthetic drugs to the patients. A well-tuned controller must be designed to control the blood pressure that can handle rapid decreases in MABP due to disturbances.

The extensive research regarding the patient model response of Single Input Single Output (SISO) system of the drug sodium nitroprusside has been developed in [1]. This model is then implemented by a nonlinear adaptive digital PID controller to normalize Mean Arterial Blood Pressure [2]. These control techniques most probably offer appropriate results only when the plant dynamics will not be changeable and separate control parameters are tuned correctly. These controllers cannot accomplish the preferred result in the complete system for the reason that the nonlinear nature of the patient response and dissimilar patient sensitivities towards the drug [3]. The control scheme based on an IMC approach in which performance criterion considering factors like maximum peak overshoot, steady-state offset and robust stability is satisfactory for simulated patients, containing those who showed extreme sensitivity to drug infusion [4]. A similar internal model control system using a Genetic Algorithm (GA) optimization technique is utilized to calculate the parameter values of the controller [5] [6]. The self-tuning control scheme that helps to reduce the variations of the MABP from the preferred value and also enhances the amount of drug managed [7]. A microprocessor established controller has been achieved to control the MABP in [8]. The microprocessor controls the drug infusion rate required to bring back the patient's blood pressure level from its present value towards the preferred value. A general review of a SISO system for the closed-loop feedback control mechanism of the blood pressure control has been detailed in [9]. It contains an enormous selection of control schemes, including PID control and its variants, optimal control, adaptive control, rule-based control including, neural network control and fuzzy control. An adaptive PI controller discussed in [10] can commendably update the changes in patient's dynamics and offer reasonable performance in the regulation of blood pressure for hypertensive patients.

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To maintain the MABP at the anticipated level, a novel PI controller is implemented in [11] with white noise as a disturbance. This control system was able to normalize MABP in the proper time. An adaptive blood pressure controller using a parallel least square estimation procedure for the purpose of critical regulation of the MABP in hypertensive patients has been recognized in [12]. This adaptive controller performance is acceptable over an enormous range of patient gains and the controller achieved reasonable performance with disturbances. The control of blood pressure for the dogs and rabbits is tested automatically in [13]. Their controller did not deliberate the delay considered in the patient response clearly and formed an oscillatory response in certain circumstances. A Model Predictive Controller is proposed in [14] [15] to control the MABP automatically by reason of its recognized capability of assessing an ideal control action and dealing by means of input, state constraints and with disturbances. An MPC control strategy developed in [16] using a particle swarm optimization algorithm was compared with the traditional control approaches for the purpose of controlling the MABP.

In this paper, an automatic drug delivery scheme for the drug adrenaline using the SISO model to control the MABP of the patients has been proposed. The objective of this closed-loop control feedback technique is to regulate the infusion level of drug adrenaline by means of feedback MABP from cardiac patients. A control system is developed using PI, PID, IMC, and MPC controllers to solve the problems related to identify the exact dose which rapidly increases the blood pressure of the patients to the preferred level and also to avoid the drug over dosage. This system will take along the MABP of the patients as near as possible to the chosen suitable MABP so as to avoid difficulty caused by postoperative hypotension. An automatic drug infusion scheme will be very useful for the medical staff by means of time-consuming and the medical staff can focus more on controlling the additional parameters.

II. PATIENT MODEL

Many scientists and researchers have done extensive research studies to define a model for the patient. Finally, slate et al [2] designed a patient model that describes the correlation between the change in blood pressure and the infusion rate of the drug. The patient response to the drug adrenaline is modeled by first order with a dead time transfer function as expected in the equation (1).

$$G_p(s) = \frac{\Delta P(s)}{I(s)} = \frac{ke^{-T_i s}(1+\alpha e^{-T_c s})}{\tau s + 1} \qquad (1)$$

Where, $\Delta P(s)$ is the change in MABP (mmHg), $I(s)$ is the drug infusion rate (ml/h), k is the sensitivity, α is the re-circulation constant, τ is the time constant (s), T_i is the initial time delay (s), and T_c denotes the recirculation time delay (s). The values of a patient model may not same all the patients for the reason of its diverse sensitivity and the patient model parameter values are tabulated in Table 1. However, in real time the patient is subjected to the linear along with nonlinear disturbances due to physical activities of patient reflex response and respiratory effects which leads to a decrease in blood pressure.

Table 1: Patient Model Parameters

Parameter	Range
k	-9
α	0
T_i	20
T_c	30
τ	30

A. *Drug Infusion Criteria*

Drug infusion controller considered [3] should be simple in addition to solve the problems concerning the drug infusion level and capable of showing a suitable response in a real-time medical environment. The performance standards listed below, which is used to estimate the controller performance criteria:

1) Set point is -30 mmHg.
2) Settling time should be below 1200 s.
3) Overshoot has to be less than 10 mmHg.
4) No steady-state offset, but with an error acceptance of 5 mmHg.

III. GENETIC ALGORITHM

This algorithm is a heuristic search process that is usually used to produce appropriate solutions to optimization and search problems. This technique offers a complete search method for optimization. Genetic Algorithm (GA) motivated by Darwin's principle of evolution theory. The individuals in a population are denoted by chromosomes; each of them relates to a fitness value. The chromosomes are exposed to an evolutionary process that proceeds numerous sequences. The basic procedures are selection, reproduction, crossover, and mutation. Parent selection provides further reproductive chances to suitable individuals. During crossover, some reproduced individuals cross and interchange their genetic characteristics. Mutations cause an arbitrary change in the genetic material, thus subsidizing to bring together a change in the population. The evolution process monitors the GA over further satisfactory sections in the search space. GA is one of the top ways to resolve a problem for which little is recognized. The Genetic Algorithm (GA) flow chart is presented in Figure 1. Genetic Algorithm involves the following three rules:

1) Individual population (i.e.) parent is nominated that subsidize to the population in the successive generation.
2) Children's are designed by merging two parents by using crossover methods.

3) Mutation relates that deviations are applied to individual parents to preclude premature convergence.

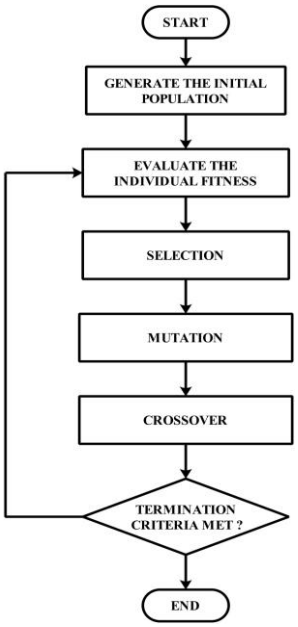

Figure 1: Genetic Algorithm Flow Chart

IV. PI CONTROLLER

Proportional-integral (PI) controller, a recognized conventional output feedback control for SISO systems is commonly used in real-time control problems, due to its ease, strength, and effective practical applications, despite many progressive controllers. PI controller uses a mechanism of closed-loop feedback, extensively used in industrialized control systems. The controller computes an error value as the difference between a measured process variable and an ideal set point of the blood pressure level. The error value is applied to the input of the controller. The controller takes the effort to lessen the error by means of regulating the process over the use of an operating variable. The output of the controller is adjusted until we get the desired MABP response. The process diagram of the PI controller for a patient model with disturbance is shown in Figure 2. The PI controller uses proportional gain and integral gain. Genetic Algorithm (GA) optimization process is used to acquire the gain values as represented in Table 2. The PI controller generalized equation is specified as follows in (2)

$$u(t) = k_p e(t) + k_i \int_0^t e(t) \tag{2}$$

Where, *u(t)* refers to the control signal, k_p denotes the proportional gain, k_i mentions the integral gain, and *e* is the error between set-point and process output.

Table 2: Gain values of PI Controller

Parameter	Gain values
k_p	0.0450
k_i	0.0020

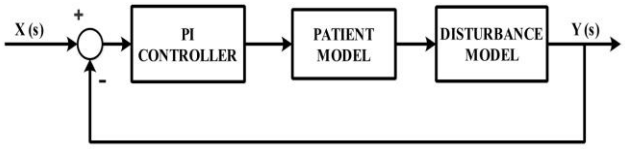

Figure 2: Process diagram for a patient model using PI Controller

V. PID CONTROLLER

Proportional Integral Derivative (PID) controller is mostly recognized and frequently used the controller in industrial applications for the reason of its simplicity, good solidity, and quick response. They are basically simple and display robust performance in excess of an extensive range of operating conditions. The controller determines an "error" value as the difference between a measured process variable and a desired set point of the blood pressure level. The controller tries to decrease the error as a result of altering the process control inputs. Based on the level of patient blood pressure the drug adrenaline will infuse to the patient's body automatically by the controller action. This process carries on until the error signal gets to zero or process variable equal to the chosen set point. The three main parameters involved in the PID controller are the proportional gain, integral gain, and derivative gain. These three coefficients are different in the PID controller so as to get optimal response. Figure 3 indicates the control arrangement of the PID controller with a patient model in the presence of the disturbance. Genetic Algorithm (GA) optimization process is used to generate the gain values for the PID controller and the values are displayed in Table 3. The PID controller error equation (3) is stated as:

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$$u(t) = k_p e(t) + k_i \int_0^t e(t) + k_d \frac{de(t)}{dt} \tag{3}$$

Where, *u(t)* refers the control signal, k_p denotes the proportional gain, k_i mentions the integral gain, k_d is the derivative gain, and *e* is the error between set-point and process output.

Table 3: Gain values of PID Controller

Parameter	Gain values
k_p	0.0005
k_i	0.0011
k_d	0.0045

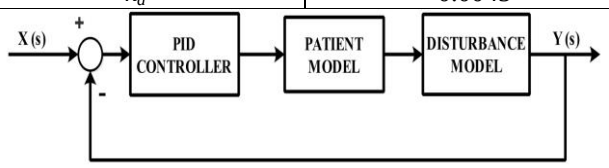

Figure 3: Process diagram for a patient model using PID Controller

VI. IMC CONTROLLER

The Internal model control (IMC) scheme is the innovative control scheme generally used in the process control industries and easy to handle. The Internal model control (IMC) scheme consists of three parts. The important part of the control scheme is accustomed to estimate the process output of the scheme. The next part of the control scheme is the internal loop which is accustomed to distinguish the internal model output and the process output. The last part of the control scheme is used to control the error and calculate the future values of the process outputs. The difference between the output of the internal model and the process output is used as the input to the controller to produce the error. This assists to decrease the impact of the disturbances on the system. IMC gain value *k* is regulated by the Genetic Algorithm (GA) optimization method and the gain value is revealed in Table 4. Figure 4 illustrates the IMC scheme of a patient model for the blood pressure control with disturbance.

Table 4: Gain value of IMC Controller

Parameter	Gain value
k	5.9437

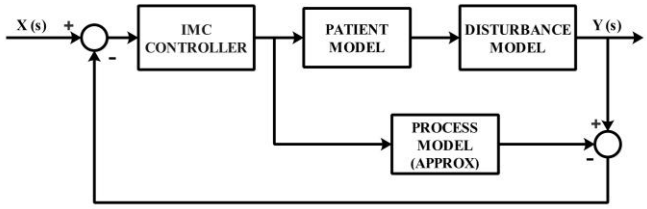

Figure 4: Process diagram for a patient model using IMC Controller

VII. MPC CONTROLLER

Model Predictive Controller (MPC) is the process control expertise that uses the scheme of the process model and open loop optimal feedback. The process model is accustomed to predicting the values of the process output. The controller computes a residue as the difference between the model output and process output. The residue is applied to the input of the controller for the purpose of controlling the drug infusion level of the patients. The recent state of the system is guessed by the past outputs and inputs for each sampling time. The controller comprises of two operations, for instance, estimation and optimization. MPC controller is tuned by the tuning parameters such as the control horizon m, prediction horizon p, sampling time T_s, weight matrices X and Y. The control horizon 'm' states the number of upcoming control actions that are considered at each optimization step. The prediction horizon 'p' defines the number of output predictions that are used in the optimization calculation. The weight matrices X and Y, which penalizes the tracking errors and control signal movement of the system respectively. Figure 5 exhibits the MPC closed-loop block diagram for a patient model with disturbance. Lesser sampling time T_s demands additional violent control, while higher sampling time results in a lesser amount of violent actions.

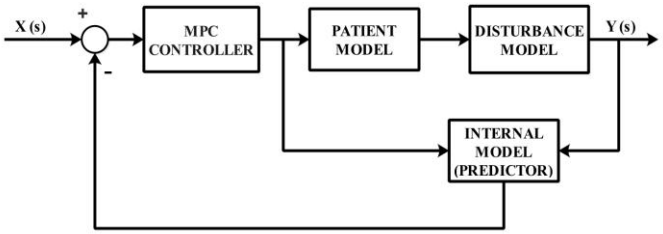

Figure 5: Process diagram for a patient model using MPC Controller

VIII. SIMULATION STUDIES

The simulation was done by means of Matlab/Simulink for the PI, PID, IMC, and MPC controllers. This model is established to study the patient's MABP response to the drug adrenaline during the simulation periods. Performance analysis is made on the four different controllers for automatic control of the drug infusion scheme of the patient with disturbances. From the results, it was detected that the entire four controllers were studied for a patient model with their MABP response and drug infusion level response.

A. MABP response

The MABP response of a patient model with disturbance is verified with the set point of -30 mmHg. Figure 6 displays the time span by the MABP response to reach the set value of -30 mmHg. The blood pressure response settled down at the time of 136, 225, 295 & 404 seconds for the PI, PID, IMC and MPC controllers respectively. There is no overshoot in the MABP response of the four different controllers. The settling time of the MABP response using the PI controller is less than that of the remaining PID, IMC, and MPC controllers. Table 5 represents the settling time and overshoot of the four different controllers.

Table 5: Four Different Controllers Performance Analysis

Parameter	PI	PID	IMC	MPC
Settling time	136	225	295	404
Overshoot	0	0	0	0

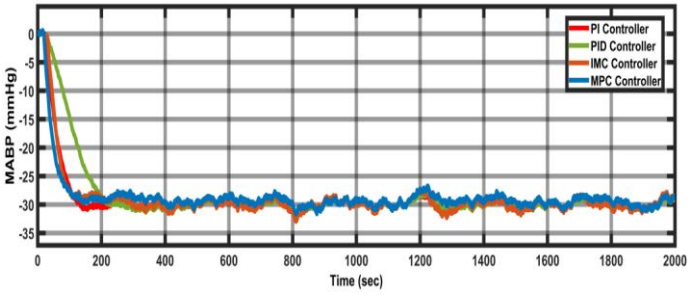

Figure 6: MABP response of Four Different Controllers

B. Drug infusion rate

The drug infusion level of the patient is up to 10 ml/h recommended by the experienced medical expert.

The rise in the quantity of adrenaline leads to the formation of cyanide owing to metabolic activities which are poisonous to humans and a decrease in the quantity of adrenaline leads to let down the MABP which causes circulatory collapse or reduced blood flow rate. Therefore, the anticipated limit of the adrenaline has to be maintained to adjust the MABP. The drug infusion level of the patient is to be maintained at the exact rate to manage the anticipated level of MABP. The large deviations in the drug infusion level of adrenaline for the patient are due to different patient sensitivity. The drug infusion level response of drug adrenaline is tested with the PI, PID, IMC, and MPC controllers respectively. The drug infusion level of a patient using PI, PID, IMC, and MPC controllers is revealed in Figure 7.

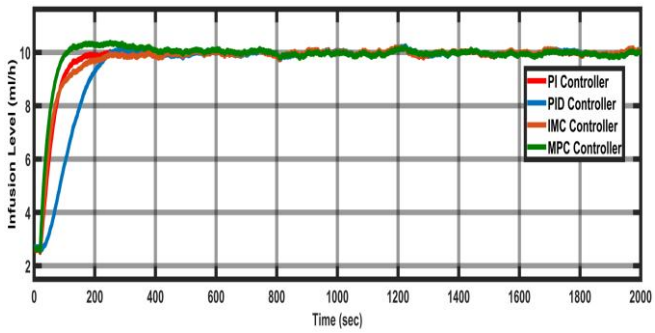

Figure 7: Drug Infusion Levels of Four Different Controllers

IX. CONCLUSION

The blood pressure regulation during and after the cardiac surgery for the hypotensive patients are analyzed. The performances of the four different controllers for the purpose of controlling the MABP of the patients are also discussed at this point. From the results, it is revealed that the controllers can effectively regulate the MABP towards the preferred level for a patient model with broadly flexible sensitivity. Simulation results are related particularly from the time approach since it is an important factor in such circumstances. This automatic MABP control system satisfied the condition mentioned in the drug infusion criteria by achieving a settling time of below 1200 seconds and ensuring an overshoot of not exceeding 10 mmHg of the MABP. The automatic control of MABP by the drug adrenaline takes less time to complete the workload of the medical staff that handles the operation manually and gives him time to take care of other features during surgery. The control approach should be verified in experimental estimations to find its strength for patient protection and proficiency in future work.

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