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ORIGINAL ARTICLE

A Simulation Study on Optimal IMC Based PI/PID Controller for Mean Arterial Blood Pressure

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Abstract
Purpose Blood pressure of postoperative patient, especially adult cardiac patient, increases due to hypertension which can be lowered by injecting an anti-hypertension vasodilator drug sodium nitroprusside (SNP). Monitor and control of dose of drug infusion on patient is necessary to reduce the blood pressure to a prescribed level, which is an important issue in biomedical engineering drug delivery problems. So, there is a need of advanced control system which improves the health of patient in less time and also reduces clinical expenses.
Methods In literature, patient's response to the infusion of drug (SNP model) is modelled. This model has five parameters that vary from patient to patient depending upon his sensitivity to drug. The main objective of our proposed work is to design a robust controller based on internal model control (IMC) structure that works effectively with different types of patient. Here, IMC based one-degree-of-freedom proportional integral (ODF-PI) and two-degree-of-freedom proportional integral derivative (TDF-PID) controllers are designed by utilizing the optimal value of SNP model gain k. Unlike the conventional PI/PID controllers, IMC based PI/PID controller has only one tuning parameter λ which is tuned on the basis of the maximum sensitivity M_S.
Results The resulting controllers achieve better robust performance criteria for nominal as well as sensitive and insensitive patients.
Conclusions The proposed technique is stable, accurate and applicable to a wide range of physiological variations in patient parameters.

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Keywords Internal model control, Mean arterial blood pressure (MABP), PI/PID tuning, Robust control, Sodium nitroprusside infusion (SNP)

INTRODUCTION

The development of mathematical models of living beings has attracted a great deal of interest to use automation and control engineering tools to biomedical drug delivery problems over a past few decades. After the rise of advanced computing platforms and availability of data from advanced sensors, the simulation of biological models have helped medical practitioners to provide optimized dose of drug for blood pressure and anesthesia control [1, 2], cancer chemotherapy treatment [3], insulin delivery to diabetic patients [4], human HIV models [5], and many more. The intensive research is needed due to the fact that the modelling biological processes should be such that when treating human diseases, the main objective is to cure or manage the disease at the same time minimizing negative side-effects associated with therapy.

There are many instances in healthcare where patient has a higher than a desired blood pressure. Generally, postoperative or critical care patients, especially adult cardiac patients have higher blood pressure, which increase due to hypertension, particularly after coronary artery bypass grafting procedures, valve replacements and lung surgery [6]. So, blood pressure (BP) regulation is very necessary to limit bleeding during surgery. An anti-hypertension vasodilator drug sodium nitroprusside (SNP) is one of the powerful medications to lower mean arterial blood pressure (MABP) [7]. The manual control of MABP by clinical personnel using SNP, is often rigorous, tiring, and of poor quality due to variations in patient response to this pressure-controlling drug and controlled release of drug over long period of time. Besides,

the simultaneous use of different drugs and the emotional state of the patient also influence the blood pressure. As a result, the clinical personnel must have good knowledge of patient's sensitivity to the drug, and changes in patient characteristics with time. Apart from this, more time needs to be spent in monitoring patients and adjusting the infusion rate of drug [1]. So, there is a need of automatic feedback control system which manipulates the rate of drug infusion in postoperative patients to avoid drug overdose, hazardous oscillations in the level of MABP, thereby causing effective care and early healing.

One of the earliest investigators Koivo *et al*. [8] and Sheppard *et al.* [9] studied the automatic control of blood pressure in living systems, which produces oscillatory response. Slate *et al.* [10] established the input-output relationship for the effect of SNP on mean arterial blood pressure as a linear single-input, single-output (SISO) model with five parameters that exhibit large variations in order to describe the response of different type of patients to the drug. In their findings, model-based control scheme did not work well with patients of high or low sensitivity [11]. After investigating the need of adaptive controller, many researchers used model-based adaptive or self tuning control scheme to accommodate variations in the patient's response [12-14]. All these research efforts conclude that the ultimate goal is to design an advanced controller that can adapt several parameter uncertainties in patient's model and yield stability, pre-defined transient and steady-state performance of the controller. Hahn *et al*. proposed an adaptive robust control strategy based on pure internal model control (IMC) strategy in which performance criterion considering factors like, maximum peak overshoot, steady-state offset and robust stability are satisfactory for several simulated patients including those who showed extreme sensitivity to drug infusion [15]. The same control strategy has also been adapted in [16], where genetic algorithm (GA) as an optimization technique is utilized to calculate the optimal value of parameters of the IMC controller, and the performance has been compared with the conventional PID controller.

Since, the living systems are imprecise and vulnerable to stochastic disturbances in the form of various physiological activities and mental state, so the robustness of the controller for such system is a prime issue. Therefore in this present study, we aim to accomplish research study on designing simple, optimal and robust controller via internal model control (IMC) design. The design strategy has been explained in the next section.

PROPOSED IMC BASED PI/PID CONTROLLER DESIGN SCHEME

In this proposed approach, we adopted a simple, efficient, intuitive, and generic scheme of advanced control technique known as internal model control technique [17]. The design and synthesis of IMC is actually based on model predictive control theory, and provides both robust and optimal performance in a straightforward manner as reported in [18, 19]. The structure pertaining to IMC has been evolved from classical feedback control system which is as shown in Fig. 1. The schematic representation of existing IMC structure is presented in Fig. 2. These Figs. 1 and 2 are reported in [17]. This IMC structure can be converted into classical feedback control system and vice-versa, through set of equations:

$$Q(s)=\frac{C(s)}{1+G_M(s)C(s)} \tag{1}$$

$$C(s)=\frac{Q(s)}{1-G_M(s)Q(s)} \tag{2}$$

In Fig. 1, the IMC structure denotes a control device as illustrated by a box with rounded corner. This structure represents a control device consisting of the feedback controller $Q(s)$, the real plant $G(s)$, and a predictive model of the plant $G_M(s)$ (i.e., the internal model). The internal-model loop uses the difference between the outputs of the process $G(s)$ to be controlled and of the internal model $G_M(s)$. This difference (i.e., error) $E'(s)$ characterizes the effect of disturbances $D(s)$ and plant/model mismatch if exists. From Fig. 2, the controlled variable $Y(s)$ is related as

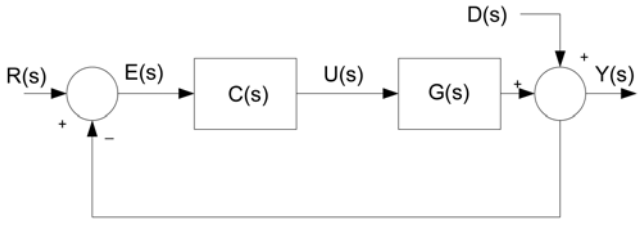

Fig. 1. Classical feedback controller.

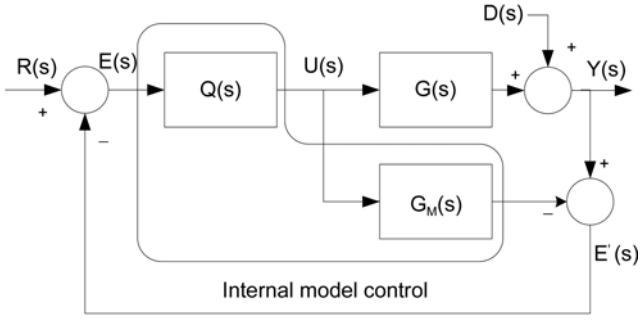

Fig. 2. Basic IMC structure.

$$Y(s)=\frac{G_M(s)Q(s)}{1+Q(s)(G(s)-G_M(s))}R(s)+\frac{(1-G_M(s)Q(s))}{1+Q(s)(G(s)-G_M(s))}D(s)\,. \tag{3}$$

For the nominal case, $G(s) = G_M(s)$ (i.e., no plant/model mismatch), the set-point and disturbance responses are simplified as: $Y(s)/R(s) = G_M(s)Q(s)$ and $(1-G(s)Q(s))$. Ideally, a control system should track the reference input rapidly, and negate the disturbance well, i.e., $Y(s) = R(s)$, and $Y(s)/D(s) = 0$. Here, in the case of IMC, this condition can be accomplished by considering $Q(s) = G_M^{-1}(s)$ and $G(s) = G_M(s)$. These relations imply that the IMC design brings guaranteed closed-loop stability by testing only the stability of controller and plant. However, defining IMC controller as the plant inverse may often creates problem of instability, prediction, or non-causality (i.e., physically unrealizable controller if derivative action is not allowed). So, the inverse model is followed by a filter $F(s)$, and for perfect control, $\lim_{s\to 0} F(s) = 1$.

The two-step procedure for designing IMC controller is given below

Step 1 Factor the model as

$$G_M(s) = G_{M+}(s)G_{M-}(s), \tag{4}$$

such that $G_{M+}(s)$ is non-minimum phase part which contains all time delays and RHP zeros. As a result, $G_{M-}(s)$ is a minimum phase and stable part, and also does not include any predictor action.

Step 2 Define the IMC controller as

$$Q(s) = G_{M-}^{-1}(s)F(s), \tag{5}$$

where $F(s)$ is a low-pass filter, commonly of the form

$$F(s) = \frac{1}{(1+\lambda s)^n}\,. \tag{6}$$

In above Eq. (6), λ is an only tuning parameter, commonly known as the IMC filter factor or closed-loop time constant. This parameter judges the speed of response of a closed-loop system, and also removes plant/model mismatch which generally occurs at high frequency, thus responsible for robustness. And, n is an integer chosen such that $Q(s)$ becomes proper/semi-proper for physical realization. Here, an effective robustness measure and most recent analytical approach, the maximum sensitivity M_s specification defined by

$$M_s = \max_{0\le\omega<\infty}\left|\frac{1}{1+C(j\omega)G(j\omega)}\right| \tag{7}$$

is the basic strategy for tuning technique [20]. To estimate λ for IMC design of first order plus dead time (FOPDT) system, apply [20]

$$\lambda = \frac{1.508-0.451M_s}{1.45M_s-1.508}T_i \tag{8}$$

A small value of M_s ensures high stability margin. So, the typical values of M_s are generally adjusted in the range of 1.2 to 2.0.

Design of IMC based PI/PID controller

In spite of tremendous innovations in advanced control technique, PI/PID type feedback controllers are still most popular and widely used in process control. It is already discussed that the IMC controller can be converted into feedback controller using (2). Thus, substituting (5) into (2) gives

$$C(s) = \frac{G_M^{-1}(s)}{(1+\lambda s)^n - G_{M+}(s)} \tag{9}$$

The feedback controller $C(s)$ in (9) usually does not have a simple structure. The standard form of ODF-PID controller is

$$C(s) = K_P + \frac{K_I}{s} + K_D s = K_P\left(1+\frac{1}{T_I s}+T_D s\right) \tag{10}$$

where K_P, $K_I = K_P/T_I$, and $K_D = K_P T_D$ are proportional gain, integral gain, and derivative gain, respectively. T_i and T_D are integral and derivative time constants for PID controller. In order to obtain standard PI/PID of the form (10), we approximate $C(s)$ using Taylor series expansion as

$$C(s) = \frac{f(s)|_{s=0}}{s} = \frac{1}{s}\left(f(0)+f^{(1)}(0)s+\frac{f^{(2)}(0)}{2!}s^2+....\right) \tag{11}$$

Consequently, the PID parameters are evaluated as

$$K_P = f^{(1)}(0)\,,\ T_I = f^{(1)}(0)/f(0)\,,\ T_D = f^{(2)}(0)/2f^{(1)}(0) \tag{12}$$

Since $Q(s)$ has only one tuning parameter λ, consequently $C(s)$ has the same tuning parameter, and correspondingly, its approximated version of PID too have single parameter. Thus in this approach, the IMC based PI/PID tuning parameters become functions of λ, and we can obtain all PID control parameters via single parameter λ. Moreover, in order to smooth set-point response, TDF-PID structure is obtained by augmenting set-point filter (pre-filter) $K(s)$ expressed by [21]

$$K(s) = \frac{\gamma\beta s+1}{\beta s+1} \tag{13}$$

Apart from this, the IMC based one-degree-of-freedom PI (ODF-PI) and two-degree-of-freedom PID (TDF-PID) controllers have not been reported yet to best of our knowledge in

biomedical applications. Hu *et al.* [21] established the relationship between IMC based PI/PID parameters and tuning parameter λ. Motivated by findings in [18], the goal of this section is to show that the IMC design procedure leads naturally to PI/PID-type controller as a simple drug infusion controller. Unlike the conventional PI/PID control, where all three terms viz. K_P, K_I, K_D are tuned individually, the proposed PI/PID has only one tuning parameter λ, and hence K_P, K_I, K_D are the functions of λ as listed in Table 1 [20, 21]. Table 1 clearly explains that all the promising features of conventional robust IMC based controller are transferred to IMC based ODF-PI and TDF-PID controller having only one tuning parameter λ instead of tuning all three parameters viz. K_P, K_I and K_D, individually.

PATIENT MODEL

The control-relevant modelling of a variety of biomedical engineering drug delivery problems [22-24] is a very complex, dynamic and challenging work. Similar to a system modelling, Slate [25] has developed the dynamic model of patient's response to the SNP infusion using correlation analysis with pseudo-random binary signal (PRBS). The input-output behaviour for the effect of SNP on MABP of a patient is modelled as

$$G(s) = \frac{\Delta P_d(s)}{I(s)} = \frac{ke^{-T_i s}(1+\alpha e^{-T_c s})}{\tau s + 1} \tag{14}$$

where $\Delta P_d(s)$ refers to the change in MABP in units of mmHg, $I(s)$ is the infusion rate of the drug in ml/h, k is the sensitivity of the patient to the drug in mmHg/(ml/h), α is the dimensionless recirculation coefficient, T_i is the initial transport delay, T_c is the recirculation transport time delay, and τ is a lag time constant. All time constants of model are measured in seconds. The patient's model can be classified into three categories-the nominal, the sensitive, and the insensitive model. Table 2 depicts patient's model parameters for all three cases [16]. It should be noticed that parameters of model are not exactly same for each type of patient. These values are approximated and in fact vary from person to person.

However, the real time patient model is also influenced by the linear as well as nonlinear disturbances which originate due to [26]:

(i) Stochastic activity and respiration effects.
(ii) A patient's reflex response due to a drop in blood pressure.

Table 1. Setting of controller parameters.

ODF-PI	TDF-PID
$K_P = \frac{\tau}{k(\lambda + T_i)}$	$K_P = \frac{1}{k}\left(\frac{\tau}{2\lambda + T_i - \beta}\right)$
$T_I = \tau$	$T_I = \beta + \tau + \frac{0.5T_i^2 - \beta T_i - \lambda^2}{2\lambda + T_i - \beta}$
	$T_D = \frac{\tau\beta}{T_I} + \frac{0.5\beta T_i^2 - T_i^3/6}{\tau(2\lambda + T_i - \beta)} + \frac{0.5T_i^2 - \beta T_i - \lambda^2}{2\lambda + T_i - \beta}$
	$\beta = \tau\left[1 - (1 - \lambda/\tau)^2 e^{\frac{-T_i}{\tau}}\right]$

Table 2. Parameters value of patient's model.

Parameter	Sensitive	Nominal	Insensitive
k	-9	-0.7143	-0.1786
α	0	0.4	0.4
T_i	20	30	60
T_c	30	45	75
τ	30	40	60

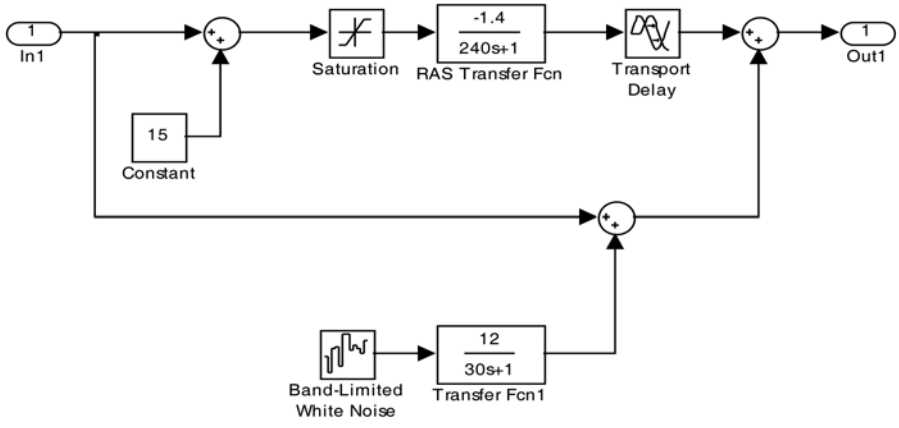

Fig. 3. Model of disturbances.

The MATLAB Simulink model of disturbances is shown in Fig. 3 [16].

DRUG INFUSION CONTROLLER

Control objectives

The objective of a control strategy is to design a simple structure of blood pressure controller capable of showing satisfactory response in a real time clinical environment. Slate *et al.* [25] suggested that controller must meet the following performance criterion:

(i) Set-point is -30 mmHg,
(ii) Settling time within 300-1200 sec,
(iii) Overshoot less than 10 mmHg and thus maximum peak of sensitivity function M_s = 1.66,
(iv) No steady-state with an error tolerance of 5 mmHg.

In addition to above tighter regulations, controller also has some clinical constraints. There must be a maximum allowable infusion rate to avoid cyanide poisoning. This rate depends upon patient's weight and drug concentration [27]. Moreover, there should be limited increase in infusion rate to avoid rapid decrease in MABP which can cause little blood flow or circulatory collapse.

Basic IMC controller design

The conceptual IMC structure for the SNP model patient is shown in Fig. 2. The IMC technique requires internal model of the process in order to design a controller. So, the original transfer function of the SNP model described in (14) is approximated to FOPDT process as stated in (15), where, T_i = 30, τ = 40, and k = –1 are considered initially for controller design [15].

$$G_M(s) = \frac{ke^{-T_i s}}{\tau s + 1} \tag{15}$$

As mentioned earlier in Table 2, the steady state gain $k(1+\alpha)$ varies from patient to patient. Moreover, it is not possible to design a robust controller which accommodates all the parameter variations. Hahn *et al.* [15] proposed a controller which is robust with respect to variations in α, T_i, T_c and τ but not for k. In their findings, it is shown that k is the only parameter which affects the stability and robustness of the control system. So, the value of k is given by

$$k = \frac{\Delta P_d(s)}{I(s)} \frac{\tau s + 1}{e^{-T_i s}} \tag{16}$$

which is obtained from nominal model defined by (15) has to be self tuned during online operation. After thorough research, it was found that certain adaptation laws for the problem of adaptive IMC were proposed in [15], [16]. Once the value of k is obtained, the IMC controller $Q(s)$ given by (5) is nothing but the inverse of $G_M(s)$ described in (15) followed by IMC filter defined by (6). Thus, IMC drug infusion controller is

$$Q(s) = G_M^{-1}(s)F(s) = \frac{\tau s + 1}{k(\lambda s + 1)^2} = \frac{40s + 1}{k(\lambda s + 1)^2} \tag{17}$$

where

$$F(s) = \frac{1}{(\lambda s + 1)^2} \tag{18}$$

SIMULATION STUDIES

In conventional PID control, manual tuning is done whenever, the dynamics of the system varies or operating conditions are changing. The schematic diagram of various types of control systems are described in Figs. 4, 5, and 6. In our simulation studies, the controller is designed for three different categories of patients. It has been already discussed that the dynamics of model of patient's response to SNP drug infusion varies from patient to patient. As mentioned earlier, the gain k of the patient model in (16), is assumed to be known for the

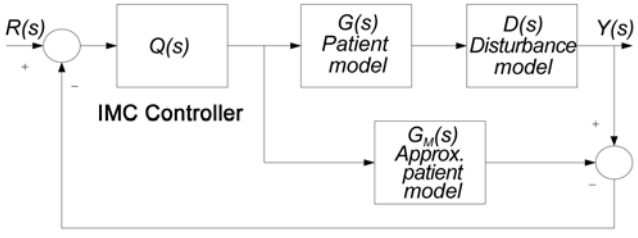

Fig. 4. IMC structure of patient.

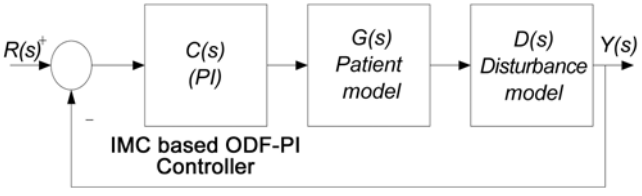

Fig. 5. Equivalent ODF-PI control system.

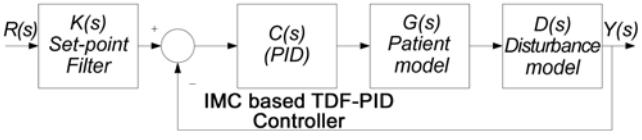

Fig. 6. Equivalent TDF-PID control system.

Table 3. Optimized gain k of patient model.

Patient's Type	k
Sensitive	-4.5437
Nominal	-0.5746
Insensitive	-0.2792

Table 4. Optimal PI/PID parameters.

Patient's Type	ODF-PI		TDF-PID		
	K_P	K_I	K_P	K_I	K_D
Sensitive	-0.0561	-0.0019	-.0001	-0.0010	-0.0039
Nominal	-0.5450	-0.0136	-0.0006	-0.0077	-0.0307
Insensitive	-1.3625	-0.0227	-0.0012	-0.0159	-0.0631

IMC controller design. So, the prior knowledge of patient drug sensitivity k can be identified online using any adaptive algorithm described in [15] and [16]. In our proposed work, we have not applied any online adaptive algorithm but utilized the optimum gain k from [16] which satisfies the entire performance criterion based upon the nominal model of the system. So, we propose IMC controller in the design scheme which requires the optimum gain of the IMC controller. Table 3 lists the optimum values of k for different type of patient model [16].

For a given sensitivity specification of FOPDT model of (14), the tuning parameter λ of an IMC based PI/PID controller can be evaluated using (8) [20]. To design the proposed optimal ODF-PI and TDF-PID controller and to meet robust performance requirements, maximum sensitivity specification $M_s = 1.26$ is selected to evaluate tuning parameter λ which gives $\lambda = 97.727$. As suggested in [21], the value of tuning parameter λ should be two to three times of the system delay to ensure robustness and satisfactory performance. Here, λ is approximately three times of the system delay (T_i) thereby resulting in stronger robustness of the controller. The IMC based ODF-PI and TDF-PID parameters corresponding to λ using Table 1 for the nominal, sensitive and insensitive patient models are given in Table 4. To evaluate set-point filter, $\gamma = 0.4$ is selected and the value of β is found to be 0.6434.

Fig. 7 is the MATLAB simulation results of the (nominal, sensitive and insensitive type) patients' responses to a step decrease of -30 mmHg in SNP drug infusion rate using IMC based ODF-PI and TDF-PID controllers and their SNP drug infusion rate, respectively. It is clear from the Fig. 7(a,c,e) that settling time of nominal, sensitive and insensitive patients are approximately 600, 800, 720 sec for TDF-PID and less than 500 sec in all type of patients for ODF-PI, which are within the prescribed range. This also illustrates that blood pressure of a nominal patient takes about 600 sec (10 min) to settle down thereby causing no risk of circulatory collapse

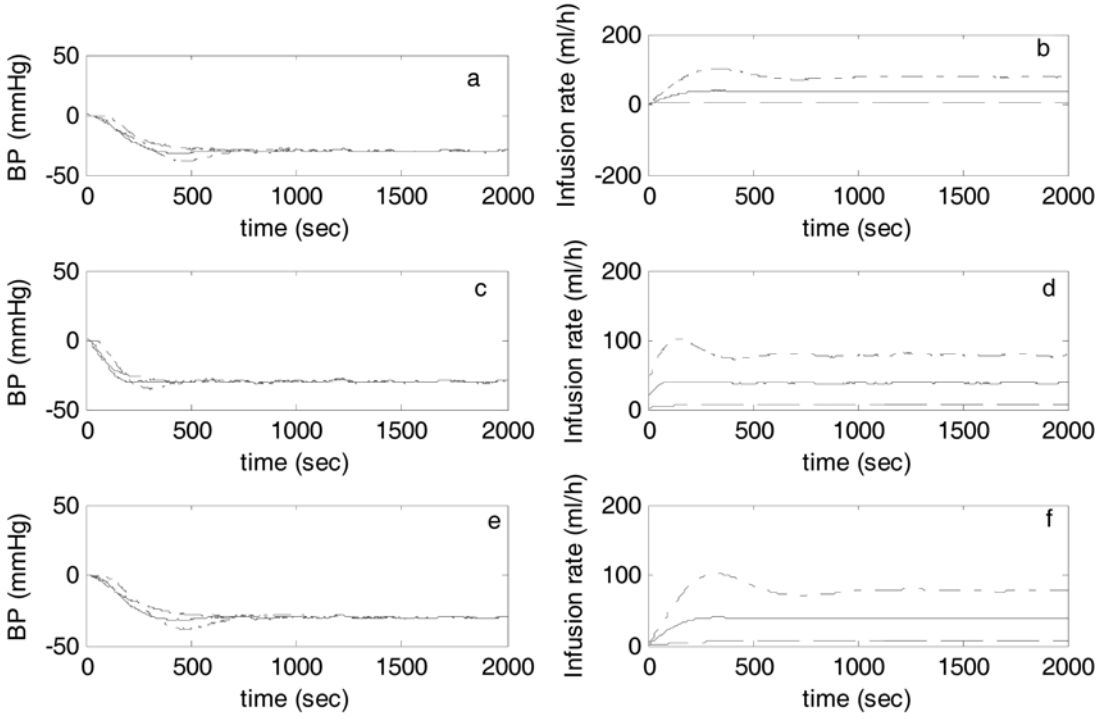

Fig. 7. (a), (c) and (e) are the blood pressure (BP) responses and (b), (d) and (f) are SNP drug infusion rate for IMC based TDF-PID, ODF-PI and conventional IMC controller, respectively. (Solid line denotes nominal patient, Dash line denotes sensitive patient, Dash-dot line denotes insensitive patient).

as suggested by clinical physician. It should also be noted that the nominal patient has least model mismatch between the assumed and the real model and therefore, depicts the shortest settling time. The overshoots calculated for nominal, sensitive and insensitive patients are 2.491, 1.3131 and 9.0747 mmHg respectively, using TDF-PID and negligible for all type of patients using ODF-PI. This confirms that overshoots are within the specified range for both type of controller and obviously better in case of ODF-PI type controller.

Fig. 7(b,d,f) exhibits the dynamics of the controller output corresponding to SNP drug infusion rate. As expected, the drug infusion rate for sensitive patient is approximately 8 ml/h and obviously higher for insensitive patient. The maximum value of the infusion rate does not exceed 300 ml/h even for the insensitive patient which satisfies the findings suggested in [28]. The large variations in infusion rate for different type of patients are due to varying patient's sensitivity response to drug. Slate *et al*. investigated that this rate can differ by as much as 36-fold from patient to patient [10].

Minimization of the performance indices like, ISE, IAE and ITAE by adjusting the closed-loop time constant λ of IMC controller provides good compromise between reduction of rise-time to check the large initial error, peak overshoot and settling time to reduce the effect of small error lasting for a long time. Furthermore, a control system is said to be optimum when the performance indices are minimum. Fig. 8 shows that the error between actual and desired output at each instant for IMC is quite large in magnitude as compared to ODF-PI and TDF-PID. Moreover, the error tends to zero in proposed PI/PID which is the basic requirement of any good controller. In Table 5 and Fig. 9, the corresponding control performance indices of IMC based ODF-PI, TDF-PID and conventional IMC controller are compared, which shows that each type of index for PI and PID is approximately ten times less than that for basic IMC control system.

Thus, all the simulations results justify that the proposed IMC based ODF-PI and TDF-PID controller are superior to basic IMC controller and are able to regulate mean arterial blood pressure regardless of whether it occurs in the transient or at steady state.

CONCLUSIONS

The tremendous motivation behind the use of control

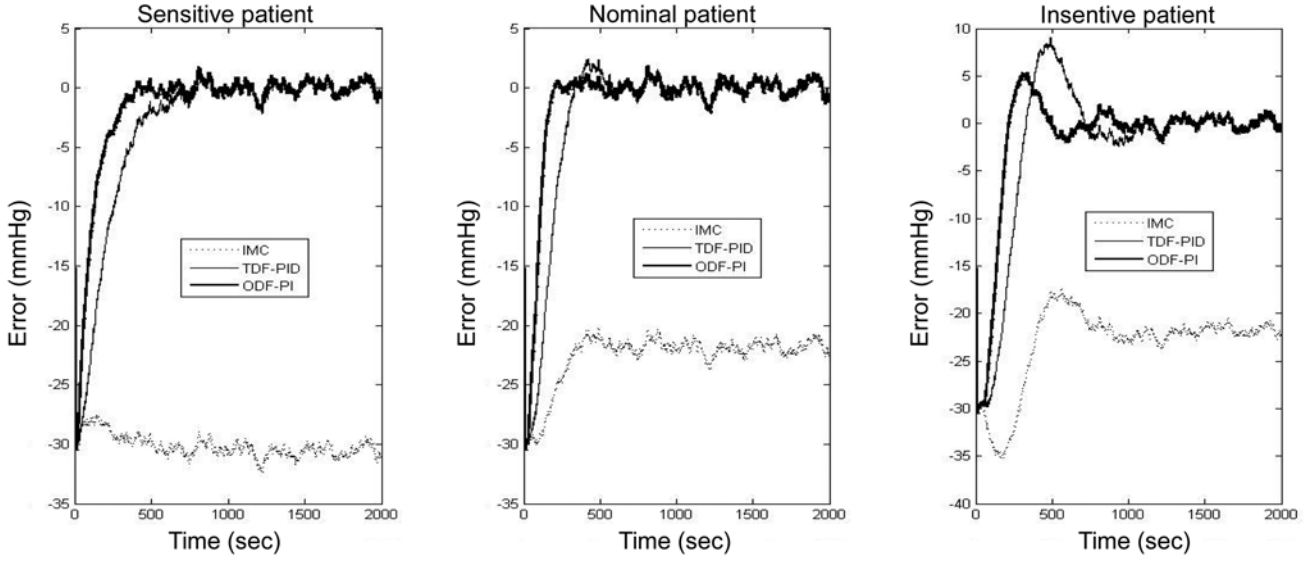

Fig. 8. Error vs. time for different categories of patient during control operation.

Table 5. Performance indices for patient's model.

Patient's category	IMC based ODF-PI			IMC based TDF-PID			Conventional IMC		
	IAE ($\times 10^3$)	ITAE ($\times 10^6$)	ISE ($\times 10^5$)	IAE ($\times 10^3$)	ITAE ($\times 10^6$)	ISE ($\times 10^5$)	IAE ($\times 10^4$)	ITAE ($\times 10^7$)	ISE ($\times 10^6$)
Sensitive	4.220	1.216	0.626	7.265	1.959	1.239	6.0280	6.094	1.189
Nominal	3.729	1.204	0.645	6.161	1.557	1.183	4.5190	4.380	1.031
Insensitive	5.821	1.666	1.033	9.318	2.893	1.707	4.6410	4.388	1.113

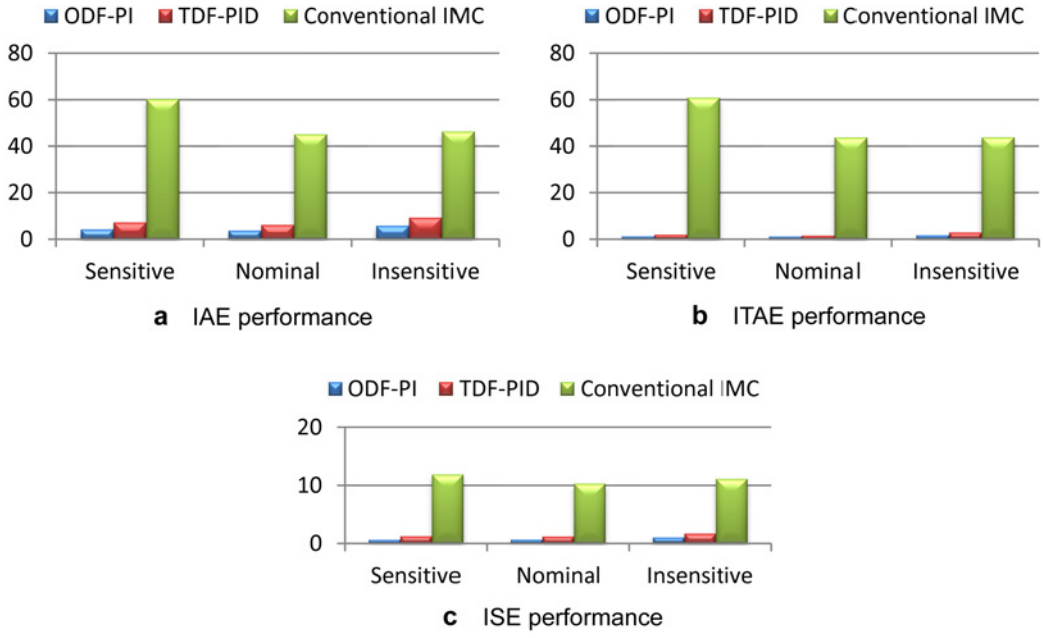

Fig. 9. Comparison of various techniques using IMC design.

engineering tools for biomedical drug delivery problems in treating human diseases is to minimize the negative impacts of the side-effects related to therapy. Plenty of research has been conducted in investigating an advanced automatic means of controlling blood pressure and has confirmed the improvement that the number of control strategies can offer in biomedical applications. The problem demonstrated in this paper is a SISO control problem which has perturbations in the model parameters, some of which show multi-fold uncertainty. But the researchers after thorough investigations described that it is possible to design a robust controller for all parameters except one.

The results in this paper demonstrate that the optimal internal model control based ODF-PI and TDF-PID controller for drug infusion are stable, accurate and applicable to a wide range of physiological variations in patient parameters. Under the influence of nonlinear disturbances due to physiological activities and mental state of patient generated by surgery or some kind of trauma (e.g., heart attack), the controller provides a good trade-off between a quick response and one without excess overshoot for all possible patients. The proposed control technique also optimizes the total amount of infused SNP dose which can be useful for treatment of pregnant women with toxemia or patients with severe chronic hypertension [7]. This control technique is superior as controller is in conventional PI/PID form with only one adjustable parameter. Nonetheless, a drawback in this design is its dependency on the prior knowledge of patient drug sensitivity. A more systematic approach to evaluate patient drug sensitivity is needed to perform online optimum parameter estimation and adaptive control strategy simultaneously; that can also be a scope for future work. Particle swarm optimization, ant-colony optimizations are certain optimization techniques which can be utilized in adaptation algorithm for finding IMC controller gain k. Some new schemes pertaining to IMC technique can also unfold opportunity in controller design for biological systems [29].

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