Research Article
Model Predictive Control of Drug Infusion System for Mean Arterial Pressure Regulation of Critical Care Patients

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Abstract: Patients recovering in critical care units are continuously monitored for their hemodynamic states and accordingly given proper medication. The widely monitored hemodynamic variable is the Mean Arterial Pressure (MAP), which is regulated by infusion of vasoactive drugs like Sodium Nitroprusside (SNP). Presently, physicians check the patients' MAP at regular intervals. This task is time-consuming and if automated, allows the physicians to attend to other critical parameters, which cannot be measured. Automation of the drug infusion based on the MAP would lead to continuous regulation of the hemodynamic variable enabling speedier recovery. This study attempts to automate the regulation of the drug infusion system using a model predictive controller. The controller's performance was tested for three types of patient models. The controller tracks the set point changes and maintains the mean arterial pressure within the required values.

INTRODUCTION

Critical care patients recovering in Intensive Care Units (ICUs) are continuously monitored for any hemodynamic instability and given proper medication. One such important parameter is the Mean Arterial Pressure (MAP), which is high in patients after a surgery. This is treated by infusing vasoactive drugs like Sodium Nitroprusside (SNP). The drug is administered either as a bolus injection or as a controlled continuous release. The second method is preferred, as it reduces the blood pressure gradually over time. The control problem is to find the correct dose that quickly lowers the blood pressure to the desired level, while avoiding a drug overdose (Hahn et al., 2002). To obtain the optimal outcomes in individual patients, physicians adjust the infusion rates or doses of the drug manually at frequent intervals (Uemura and Sugimachi, 2013).

The manual control of the MAP using the SNP is not straightforward as this pressure-controlling mechanism varies among different patients (Behbehani and Cross, 1991). In addition, manual adjustments are monotonous, hence the need to automate the drug infusion system. As the SNP is a fast acting and an extremely potent drug, control systems have been developed to automatically administer the infusion of the drug for reducing and regulating the MAP (Ying and Sheppard, 1990). The regulation of MAP has been experimented with different control algorithms (Isaka and Sebald, 1993).

Various experiments done with the automated setup have proved to be superior to the manual methods (Gao and Joo Er., 2006). Many researchers have also experimented with multidrug control where the MAP and the Cardiac Output (CO) of the patient were controlled using the SNP and the Dopamine (DP). Nirmala et al. (2011) and Nirmala and Veena Abirami (2010) have discussed the multivariable problem of controlling the MAP and the CO using two drugs namely the SNP and the DP. The authors had applied the MPC strategy to the SISO problem, but with only one patient model with constraints on the manipulated variable (Nirmala et al., 2013a, b).

The objective of this study is to study the performance of the MPC designed to control the drug infusion system for the regulation of MAP for three patient models-sensitive, nominal and insensitive patients. In addition, this performance is compared with that of the performance of an Internal Model Controller applied to the same system for the three patient models (Hahn et al., 2002).

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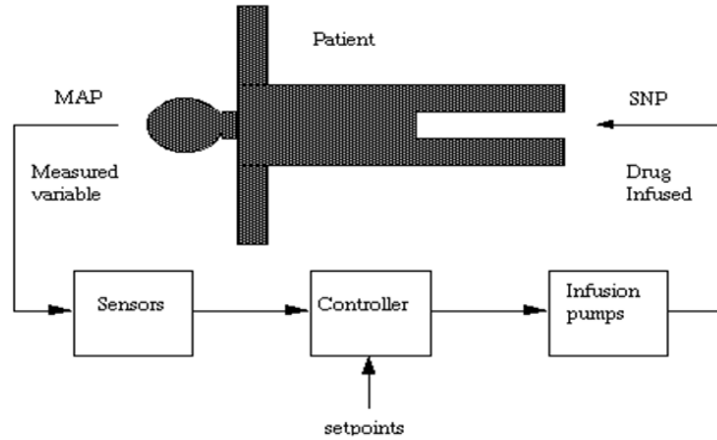
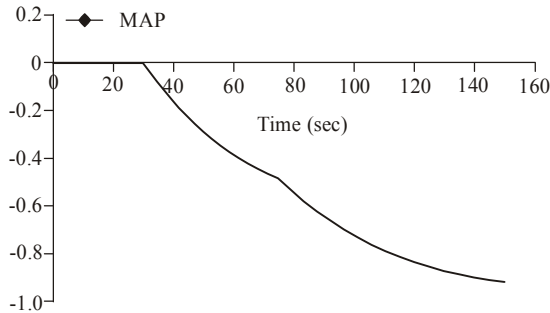Fig. 1: Schematic diagram of the proposed closed-loop drug infusion system

Fig. 2: Open loop response of the drug infusion system

MATERIALS AND METHODS

Closed loop drug infusion system: Figure 1 shows the schematic diagram of the proposed closed-loop drug infusion system. The MAP is measured and given to the MPC, which compares the measured value with the desired value and takes corrective action by regulating the rate of flow of the SNP. Medical experts decide the reference (set-point) values.

Process model: The patient is modeled by a first order transfer function with dead time as given in (1). This model has been adapted from Hahn *et al.* (2002):

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

The parameters in (1) are described in Table 1 with their range (Hahn *et al.*, 2002). The open-loop response of the drug infusion system in (1) was studied for a unit step change in SNP. Figure 2 gives the response obtained and shows that an increase in SNP decreases the MAP.

Model predictive control: In general, a predictive control algorithm solves an on-line and optimal control problem subject to system dynamics and variable constraints. The system model is given in (2):

$$x(k+1) = Ax(k) + Bu(k) + Gd_p(k)$$
$$y(k) = Cx(k) + Du(k) + Hd_m(k) \qquad (2)$$

where,
$x(k) \in \Re^{nx}$ = The states
$u(k) \in \Re^{nu}$ = Manipulated inputs
$y(k) \in \Re^{ny}$ = The measured outputs

The vectors $d_p(k)$ and $d_m(k)$ are unmeasured disturbances to the state dynamics (process noise) and the outputs (measurement noise), respectively. The controller predicts the future behavior of the actual system over a time interval defined by a lower and an upper prediction horizon, denoted by N_w and N_p, respectively. The optimal input to the plant is calculated by minimizing a cost function defined along the prediction horizon. This function is specified as a sum of quadratic future errors between the reference trajectory and predicted plant output and the predicted control effort and is given in (3):

$$J(k) = \sum_{i=N_w}^{N_p} \| \hat{y}((k+i)/k) - r(k+i) \|^2 Q(i) + \sum_{i=0}^{N_u-1} \| \Delta u((k+i)/k) \| R(i)$$
$$(3)$$

The cost function (3) is subject to the constraints specified on the inputs, outputs and inputs increments as given in (4):

$$u_{min} \le u(k) \le u_{max}$$
$$y_{min} \le y(k) \le y_{max}$$
$$\Delta u_{min} \le \Delta u(k) \le \Delta u_{max} \qquad (4)$$

where,

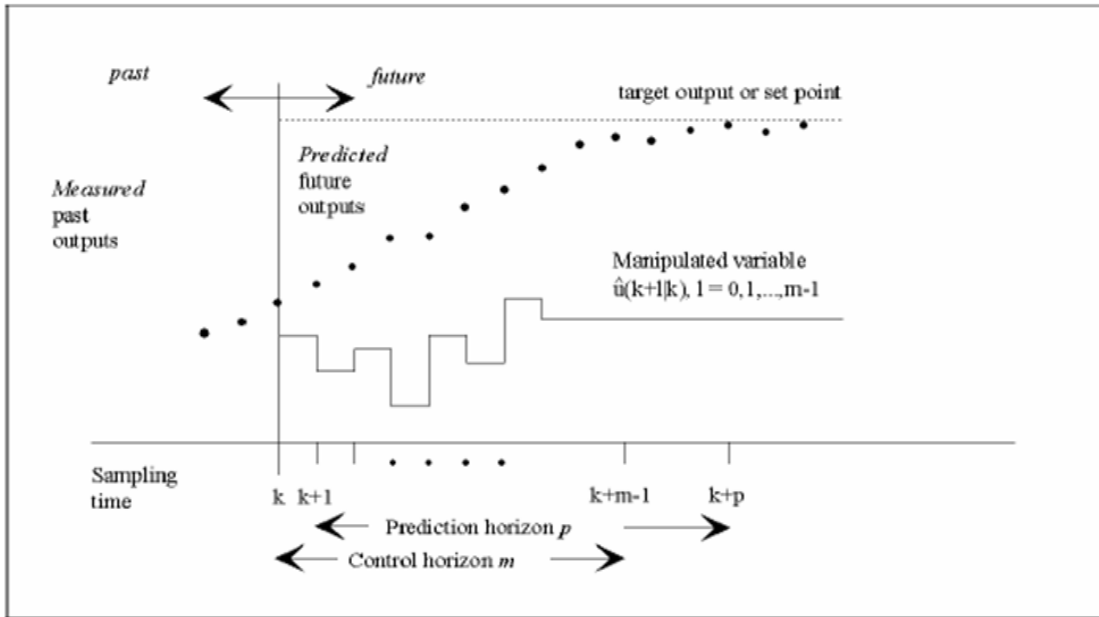|	
Q (i)	= The positive definite error weighting matrix
R (i)	= The positive semi-definite control weighting matrix
ŷ ((k + i) /k)	= The vector of predicted output signals
r (k + i)	= The vector of future set-points
Δ u ((k + i) /k)	= The vector of future control actions

Fig. 3: Basic principle of MPC strategy

Table 1: Specifications of model parameters for transfer function in (1) and their range of values

Parameter	Units	Avg.	Min.	Max.
Steady-state gain, K (1+α)	mmHg (mlh^{-1})$^{-1}$	-1.0	-0.25	-9.0
Recirculation, α	-	-	0	0.4
Initial transport delay, T_i	S	30	20	60
Recirculation time, T_c	S	45	30	75
Time constant, τ	S	40	30	60

Max.: Maximum; Min.: Minimum; Avg.: Averge

Table 2: Values of parameters in (1) for different patient models

Parameter	Units	Sensitive	Nominal	Insensitive
Steady-state gain, K (1+α)	mmHg (mlh^{-1})$^{-1}$	-9	-1.0	-0.25
Recirculation, α	-	0	0.4	0.40
Initial transport delay, T_i	s	30	20	60
Recirculation time, T_c	s	45	30	75
Time constant, τ	s	40	30	60

Figure 3 shows the basic principle of the MPC strategy. The presence of disturbances and plant/model mismatch are taken into account by implementing a feedback measurement and a receding horizon strategy, which means that only the first element of the computed control sequence is applied to the plant. At the next sampling interval, both the control horizon and the prediction horizon move one-step ahead and the entire cycle of state estimation, output prediction and optimization is repeated using the new measurements from the plant.

MPC tuning: The tuning parameters of the MPC controller are the cost function weighting matrices R and Q, the control horizon Nu, the prediction horizon Np and the sampling time Ts. The prediction horizon Np determines the number of output predictions that are used in the optimization calculation. A long prediction horizon leads to better performance and a stabilizing effect, but increases the computation burden.

The control horizon N_u determines the number of future control actions that are calculated at each optimization step. In general, a short control horizon leads to a controller that is moderately insensitive to uncertainties and modeling errors, whereas a long control horizon results in unnecessary control action and long computation time. The matrix Q penalizes the tracking errors and guides the servo performance of the control system. The matrix R is a move suppression factor that changes the aggressiveness of the controller and assures a smooth control action.

Usually the tuning of these parameters in order to guarantee good performances, stability and robustness is done by simulation, even if approaches for developing model predictive control tuning rules exists (Wojsznis *et al*., 2003).

Prediction model: For the design of a linear MPC, a linearized approximation of the nonlinear model in (1) should be obtained. In this study, the transfer function model in (1) is linearized and a linear state-space model

of the drug infusion system is obtained and used as the prediction model.

Simulation study: Simulations were done on the drug infusion model represented by (1) for three kinds of patient models: nominal, sensitive and insensitive using the MPC in closed loop. The values of the parameters in (1) are specified for the three different kinds of patient model and given in Table 2 (Behbehani and Cross, 1991). The simulations were done with an initial condition of zero, which simulates a steady-state condition. A setpoint change of -30 mmHg was given to the MAP and the response of the closed-loop system observed for the three patient models. Figure 4 shows the response of the closed-loop drug infusion system controlled by the MPC for the step change of-30 mmHg. Figure 5 shows the output of the controller for the system. The controller was tuned for a prediction horizon of 10 and a control horizon of 2. All the simulations were carried out in MATLAB/SIMULINK.

RESULTS AND DISCUSSION

From Fig. 4, it is inferred that the drug infusion system controlled by the MPC reaches the desired value of -30 mmHg within a reasonable time for all the three patient models. The results are compared with the response of the system controlled using the Internal Model Controller (IMC); another advanced control strategy developed in Hahn *et al*. (2002) and tested on the three models. The comparison based on the time domain specifications-settling time and overshoot is given in Table 3. From Table 3 it can be seen that the set-point tracking of the MPC is far better than that of the IMC. For all the three patient models, the settling time is faster when compared to the results reported in Hahn *et al*. (2002). In the case of the insensitive patient, the overshoot is larger in the case of MPC controlled system due to the fast response of the drug for the change in the set-point, which is a salient feature of the MPC.
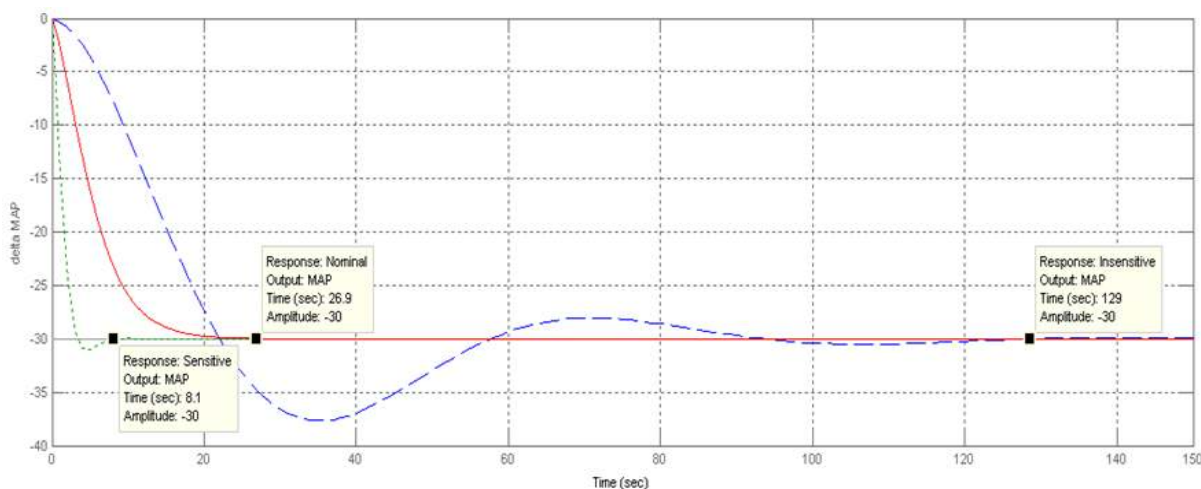

Fig. 4: Response of the closed loop drug infusion system using MPC strategy for a step change of-30 in MAP
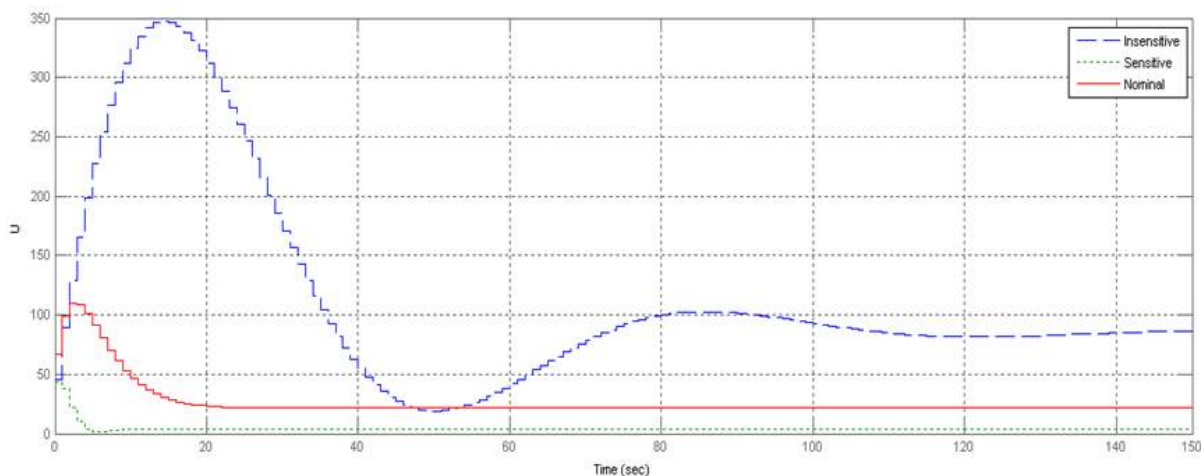

Fig. 5: Controller output for the step change of -30 in MAP

Table 3: Comparison of time-domain specifications for the drug infusion system with IMC and MPC

	Sensitive		Nominal		Insensitive	
Specification	IMC Behbehani and Cross (1991)	MPC	IMC Behbehani and Cross (1991)	MPC	IMC Behbehani and Cross (1991)	MPC
Settling time	500 sec	8.1 sec	350 sec	26.9 sec	800 sec	129 sec
Overshoot	No overshoot	No overshoot	No overshoot	3%	16%	25%

CONCLUSION

This study attempts to study the performance of the drug infusion system controlled with MPC for three different types of patient models. The nominal values for the tuning parameters, namely the prediction horizon and the control horizon were arrived to achieve the optimum values that can be applied to all the models. The results show that the MPC controller designed and applied on the drug infusion model is better with respect to the settling time, but has the drawback of overshoot being large in the case of the insensitive patient model as compared with the IMC performance.

REFERENCES

Behbehani, K. and R.R. Cross, 1991. A controller for regulation of mean arterial blood pressure using optimum nitroprusside infusion rate. IEEE T. Bio-Med. Eng., 38(6): 513-521.

Gao, Y. and M. Joo Er., 2005. An intelligent adaptive control scheme for postsurgical blood pressure regulation. IEEE T. Neural Networ., 16(2): 475-483.

Hahn, J., T. Edison and T.F. Edgar, 2002. Adaptive IMC control for drug infusion for biological systems. Control Eng. Pract., 10: 45-56.

Isaka, S. and A.V. Sebald, 1993. Control strategies for arterial blood pressure regulation. IEEE T. Bio-Med. Eng., 40: 353-363.

Nirmala, S.A. and B. Veena Abirami, 2010. Development of model predictive control strategy for monitoring and control of drug infusion for critical care patients. Proceedings of the International Conference on Innovative Research in Engineering and Technology. Park College of Engineering, Coimbatore, India, Aug 12-14, pp: 33F-1-4.

Nirmala, S.A., B. Veena Abirami, V. Dinesh Kumar and D. Manamalli, 2011. Drug infusion control for patients under critical care using model predictive control strategy. Proceedings of the International Conference on Trends in Industrial Measurements and Automation. Chennai, Jan. 4-6, pp: 211-215.

Nirmala, S.A., R. Muthu and B. Veena Abirami, 2013a. Unconstrained and constrained control of drug infusion system for patients under critical care using linear model predictive control strategy. Proceedings of the International Conference on Biosignals, Images and Instrumentation. SSN College of Engineering, Chennai, India, Mar. 14-16, pp: 118-125.

Nirmala, S.A., R. Muthu and B. Veena Abirami, 2013b. Drug infusion control for mean arterial pressure regulation of critical care patients. Proceeding of the IEEE Region 10 Conference on (31194) TENCON 2013. Xi'an, China, Oct. 22-24, pp: 1-4.

Uemura, K. and M. Sugimachi, 2013. Automated cardiovascular drug infusion system to control hemodynamics. Adv. Biomed. Eng., 2: 32-37.

Wojsznis, W., J. Gudaz, T. Blevins and A. Mehta, 2003. Practical approach to tuning MPC. ISA T., 42(1): 149-62.

Ying, H. and L.C. Sheppard, 1990. Real-time expert-system-based fuzzy control of mean arterial pressure in pigs with sodium nitroprusside infusion. Med. Prog. Technol., 16: 69-76.