

Proportional Resonance and Fractional-order Proportional Integral Derivative-based Closed-loop Drug Infusion for the Regulation of Mean Arterial Pressure in Critical Care Patients – A Modeling and Simulation Study

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Abstract

Aim: Managing hypertensive emergencies are a common occurrence in critical care setups. Mean arterial pressure (MAP) is an important hemodynamic variable indicative of hypertensive control and its regulation and needs to be controlled by a constrained set of physiological values. **Materials and Methods:** Sodium nitroprusside is a potent vasoactive drug which is used in the critical care setups to regulate hypertensive emergencies, administered through intravenous route. Many closed-loop drug infusion systems (CL-DIS) powered by fuzzy logic, artificial neural networks, and state-space models have been used to regulate the infusion. In this work, an attempt using proportional resonance controller and fractional-order proportional integral derivative (PID) with a closed loop is modeled and simulated. **Results and Discussion:** This work proposes a CL-DIS-based proportional resonance controller and fractional-order PID controller, which will respond rationally to the changes in the patient's condition and activate drug infusion to continue the MAP at the set physiological values of 60 and 70 mmHg. **Conclusion:** The planned controller setup has potential to be used as a controller for intravenous infusion of drugs and in our work maintained the MAP constrained by set values for the time domain responses for ideal physiological set points.

Key words: Drug infusion system, fractional-order proportional integral derivative, proportional integral controller, proportional-resonant controller, sodium nitroprusside

INTRODUCTION

Drug infusion pumps are increasingly used in the delivery of the drugs intravenously and especially for the infusion of potent and hard to infuse drugs.^[1] Drug infusion pumps can be operated in a higher level of autonomy and be used in adaptive and closed-loop delivery of drugs. Control engineering models are being explored and adopted for better drug delivery and have opened up the possibility of algorithmic drug delivery affording precise control over the constraints of time and the volume to be infused.^[2] Hence, this can be adapted for closed-loop infusion and can compute the rate

and volume of the drug to be delivered resulting in a better therapeutic outcome.^[3]

Patients recuperating in critical care setups are continuously monitored for their hemodynamic parameters. Mean arterial

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pressure (MAP) is a parameter which is continually monitored and needs to be maintained in an ideal physiological value of 60–70 mmHg in most conditions. Since time to elicit a pharmacological response is low in a critical care setup, fast acting vasodilator drug sodium nitroprusside (SNP) is the drug of choice for the maintenance of MAP in critical care setups.^[4] Due to its potent action, SNP needs to be administered with caution due to its toxicity and to obtain more favorable outcomes with different pharmacological thresholds.^[5] Caregivers at critical care setups regulate the infusion rates or doses of the drug physically at frequent intervals. This adds to the fatigue and causes potential errors causing the intervention to fail or resulting in adverse drug reactions.

Many control engineering models have been adopted successfully for the drug delivery with a better degree of success and control. Closed-loop drug infusion system (CL-DIS) has been the method of choice to infuse medications, antibiotics, hormones, chemotherapeutic agents, nutrients, and anesthetics to patients in critical care setups in controlled amounts or based on the measured inputs.^[6] CL-DIS based on control engineering models is being increasingly used in critical care setup. Many types of control systems have been used to power the CL-DIS. Review of literature suggests that CL-DIS powered by proportional integral derivative (PID) and fractional-order PID (FOPID) was not available. In this work, an attempt has been made to model an infusion system to infuse potent vasoactive drug SNP based on the stated controllers.^[7] Having an algorithmic control can save time and errors of the caregiver when infusing a potent vasoactive drug.^[8]

The paper is structured as follows: Section II discusses the proposed CL-DIS block diagram and discussion of simulation; Section III describes model implementation and simulation results; and Section IV, the results obtained from the work and its suitability for the intended purpose.

MATERIALS AND METHODS

Research gap

The review of literature in this domain suggested the dearth of CL-DIS powered by PI, FOPID, and proportional-resonant controller (PRC) and found none comparing the relative merits of infusing drugs powered by these control models. This work suggests PRC for the control of CL-DIS.^[9–12] There is a need to improve the dynamic response of CL-DIS. The above papers do not talk about the enhancement of dynamic response of CL-DIS. The above literature does not deal with the comparison of PI, FOPID, and PR controlled CL-DIS. This work suggests PRC for the control of CL-DIS.

PROPOSED DIS

Figure 1 shows the schematic diagram of the CL-DIS. The controller block represents the proportional integral controller (PIC)/FOPID and PRC, which is designed to recognize set points for MAP from the medical specialist.^[13] Based on the set point and the current measured value of the MAP, the proposed system is expected to maintain the patient's MAP at the preferred value by the infusion of SNP. The modeling and simulation of control systems were done using MATLAB®TM R2017 and Simulink®TM Toolbox Version 9.1 (academic license). Simulink software is the industry-standard tool for modeling and simulating, multivariate, and dynamic responses in biological systems.^[14–16]

FOPID controller

The representation of FOPID was developed from fractional differentiation. The response with FOPID is faster than that of the corresponding PIC system. A block diagram that signifies the FOPID control structure is depicted in Figure 2. The transfer function of an FOPID controller takes the form of

$$C_{\text{FOPID}}(s) = K_p + K_i/s^\lambda + K_d s^\mu \quad (1)$$

Where λ is the order of the integral part, μ is the order of the derivative part, while K_p , K_i , and K_d are the controller as in a conventional PID controller.

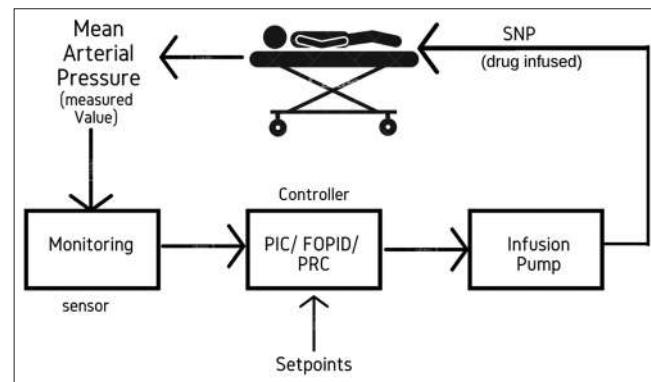


Figure 1: Schematic diagram of the proposed closed-loop drug infusion system

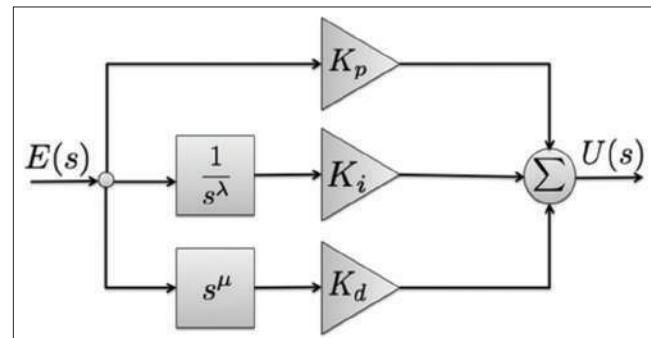


Figure 2: Block diagram of fractional-order proportional integral derivative controller

PRC

The model of the PRC and the plant is depicted in Figure 3. PRC is capable of generating a constant sinusoidal potential essential for maintaining a steady-state signal.

The transfer function of the represented by plant $G_f(s)$, which is given as follows:

$$G_f(s) = \frac{sC_f R_d + 1}{s^3 L_i L_g C_f + s^2 C_f R_d (L_i + L_g) + s(L_i + L_g)} \quad (2)$$

There is always steady-state magnitude and phase error exists while tracking a sinusoidal signal utilizing a PI

control. Alternatively, a PRC which is based on internal model principle an infinite gain at reference signal oscillating frequency. This would remove steady-state error while tracking a sinusoidal signal. The PRC $G_i(s)$ is in the form:

$$G_i(s) = K_p + \frac{K_i s}{s^2 + 2\delta\omega_0 s + \omega_0^2} \quad (3)$$

Here, K_p and K_i are the proportional and integral gain, respectively, “ δ ” is the damping factor, and ω_0 is power frequency of the grid voltage. The infinite gain of PRC is

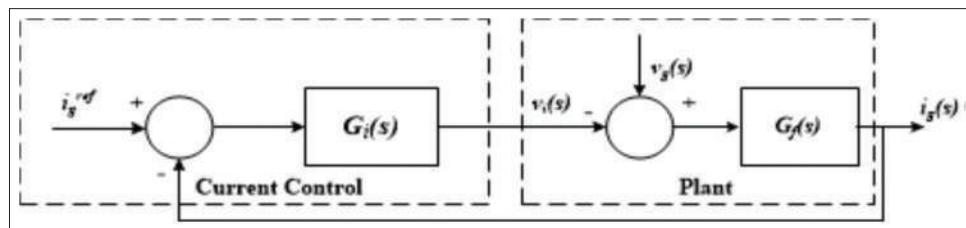


Figure 3: Block diagram of proportional-resonant controller

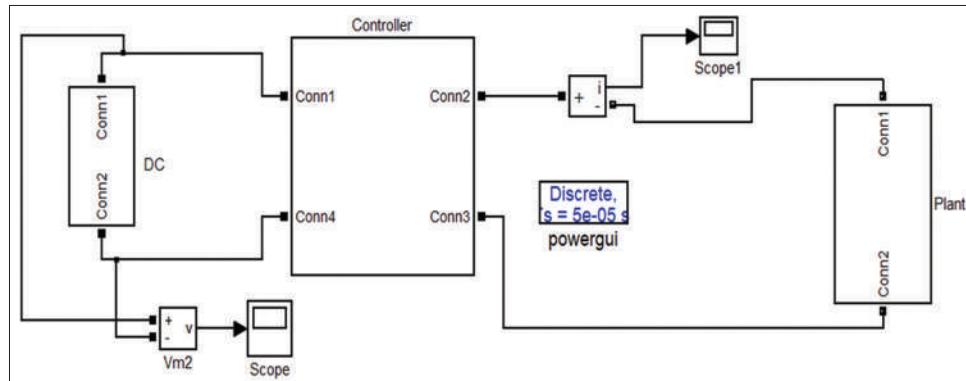


Figure 4: Diagram of drug infusion without any control

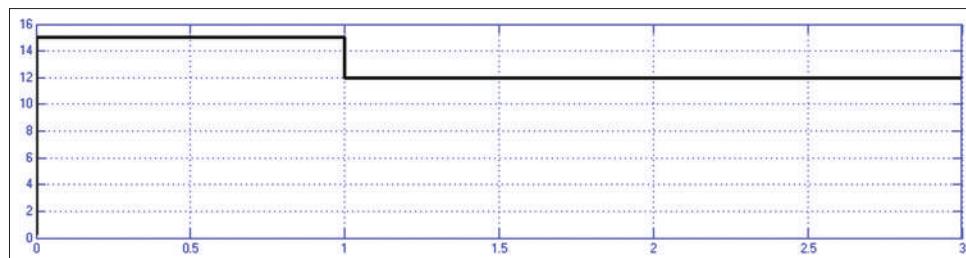


Figure 5: Response of the infusion system for unit mmHg step change in the mean arterial pressure for constrained without controller

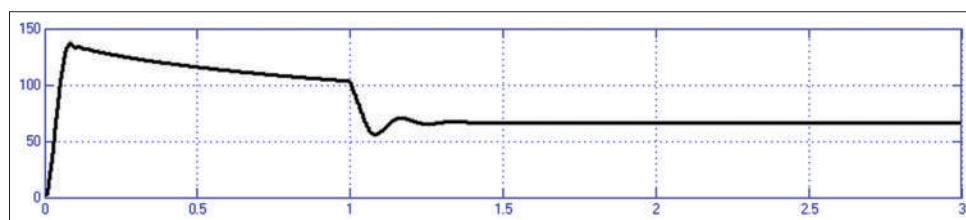


Figure 6: Drug (sodium nitroprusside) infusion without controller

reduced by damping factor δ to increase the bandwidth, and thus, dynamics of the CL-DIS remains stable.

MODELING AND SIMULATION RESULTS

Open-loop DIS

Model diagram of DIS in open-loop system without controller is shown in Figure 4. Response of the infusion system for unit mmHg step change in the MAP for constrained without controller is shown in Figure 5. Drug infusion without controller is shown in Figure 6. It can be seen that drug infusion is reduced. Rate of SNP without controller is shown in Figure 7.

CL-DIS with PI control

Closed-loop simulations are carried out for the DIS with the step fall using PIC as shown in Figure 8. The simulated values of K_p , K_i , K_r , and K_d used are as follows: $K_p = 0.01$, $K_i = 5$, $K_r = 5$, $K_d = 0.09$.

CL-DIS with the step fall using PIC is shown in Figure 8. Response of the infusion system for unit mmHg step change in the MAP for constrained PI using simulation model is shown in Figure 9 and its value is 12. Drug infusion with PIC is shown in Figure 10. It can be seen that drug infusion is brought back to original value using PIC. Rate of SNP with PIC is shown in Figure 11 and its value is 1.6.

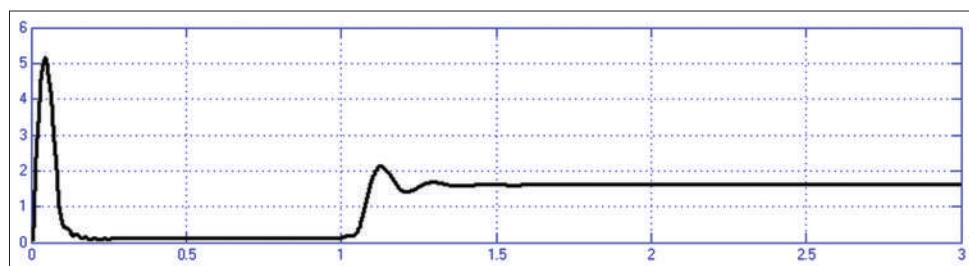


Figure 7: Rate of sodium nitroprusside infusion in open loop

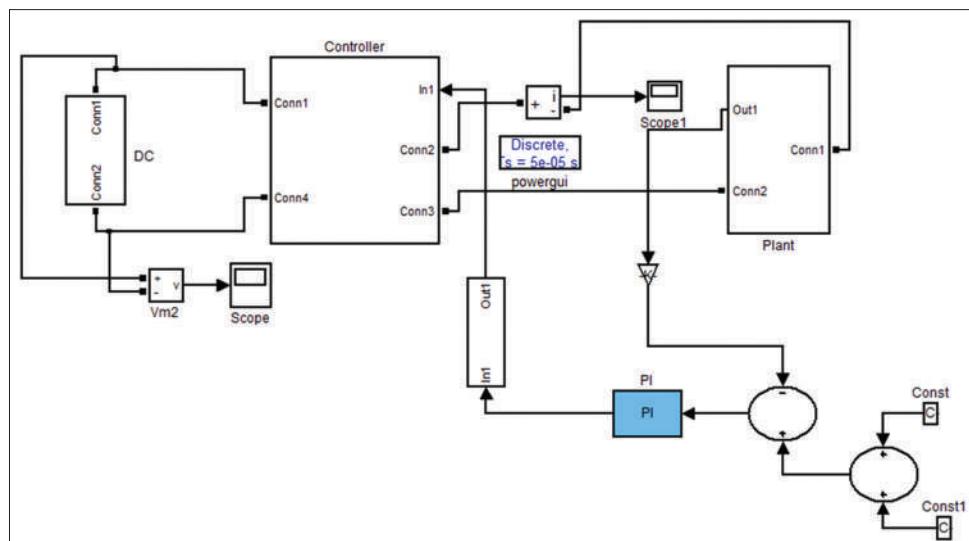


Figure 8: Model block diagram of drug infusion in closed-loop system using proportional integral controller

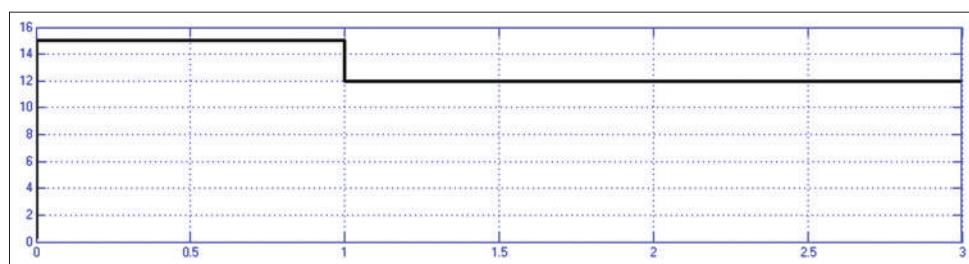


Figure 9: Response of the infusion system for unit mmHg change in the mean arterial pressure for constrained proportional integral controller using simulation model

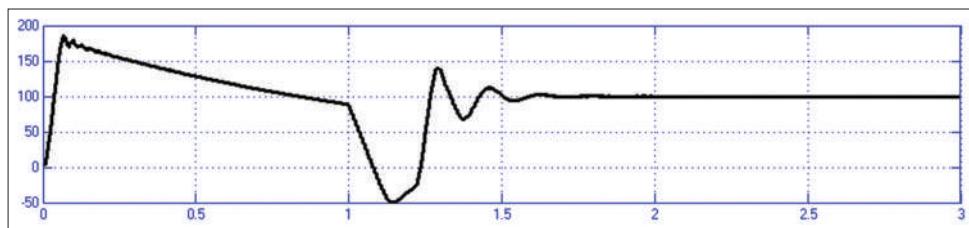


Figure 10: Drug infusion with proportional integral control

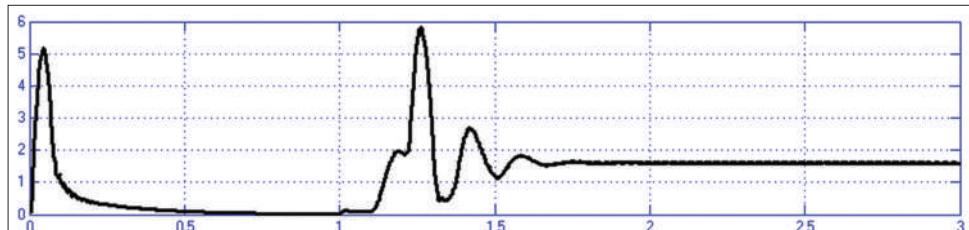


Figure 11: Rate of sodium nitroprusside infusion with proportional integral control

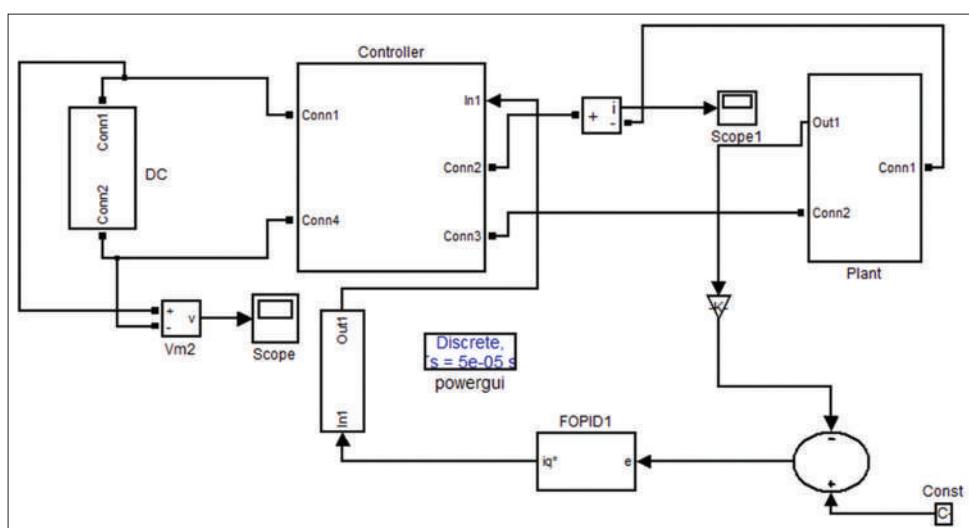


Figure 12: Model diagram of closed-loop drug infusion systems with fractional-order proportional integral derivative controller

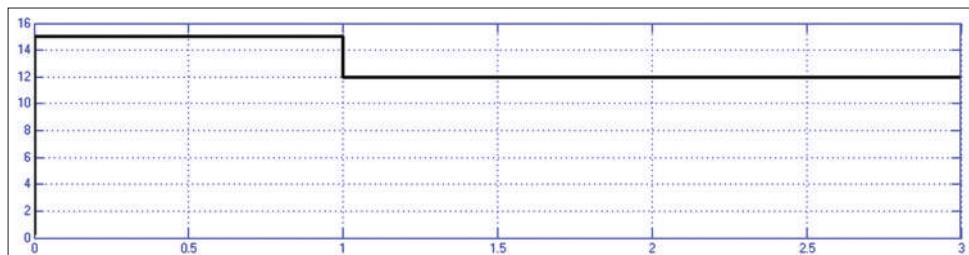


Figure 13: Response of the infusion system for unit mmHg step change in the mean arterial pressure for constrained fractional-order proportional integral derivative using simulation model

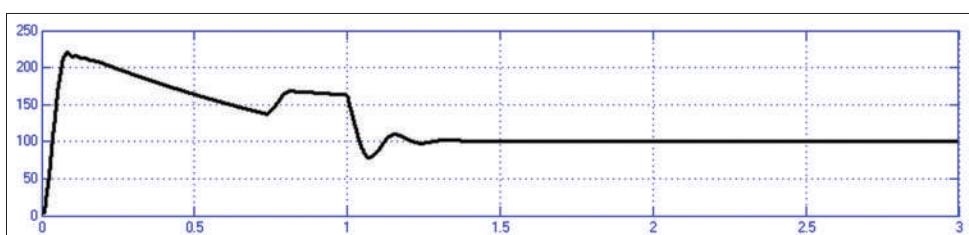


Figure 14: Drug infusion with fractional-order proportional integral derivative control

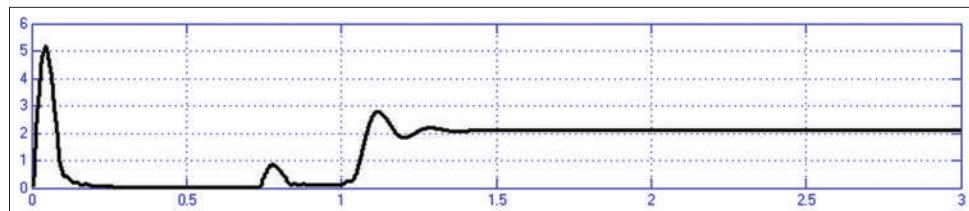


Figure 15: Rate of sodium nitroprusside infusion with fractional-order proportional integral derivative control

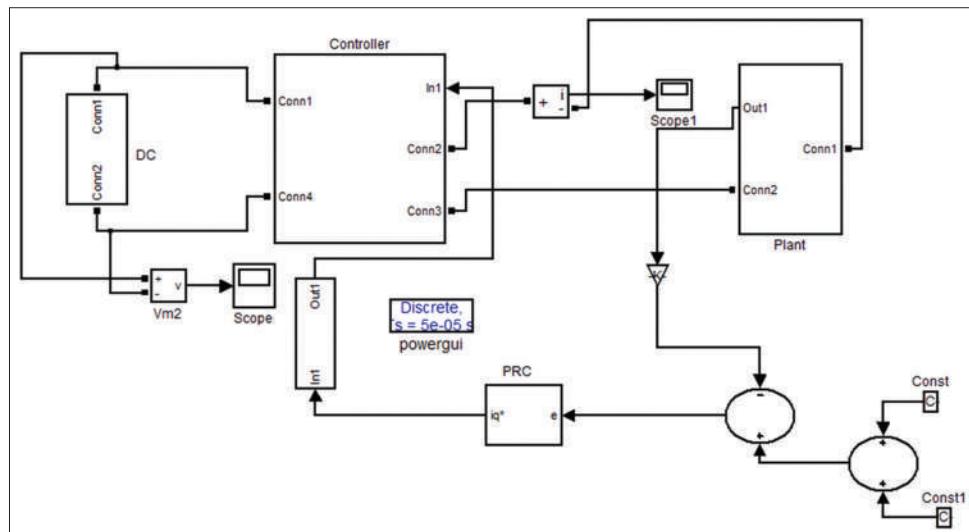


Figure 16: Diagram of closed-loop drug infusion system with proportional-resonant controller

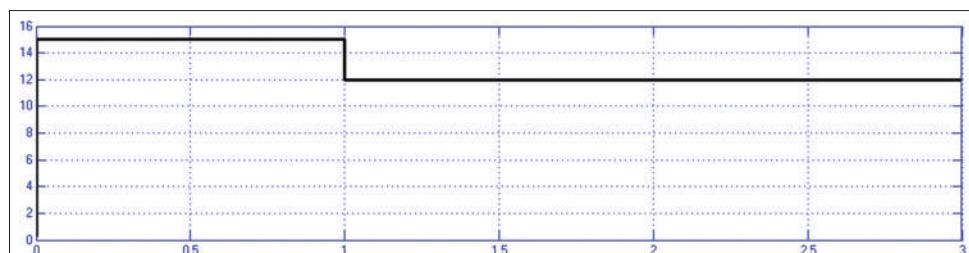


Figure 17: Response of the infusion system for unit mmHg step change in the mean arterial pressure for constrained proportional-resonant controller using simulation model

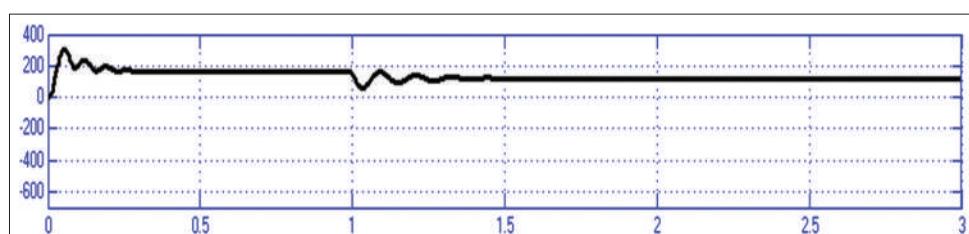


Figure 18: Drug infusion with proportional-resonant controller

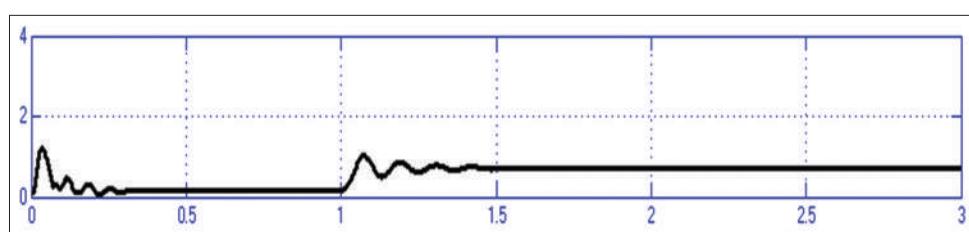


Figure 19: Rate of sodium nitroprusside infusion with proportional-resonant controller

Controller	MAP of 60 and 70 mmHg							
	Peak overshoot		Rising response time (s)		Setting time (s)		Peak regulation (s)	
	60 mmHg	70 mmHg	60 mmHg	70 mmHg	60 mmHg	70 mmHg	60 mmHg	70 mmHg
Proportional integral	9.8	9.9	1.26	1.36	1.81	1.97	1.30	1.41
Fractional-order proportional integral derivative	6.3	6.8	0.83	0.96	1.42	1.55	0.92	0.98
Proportional-resonant controller	4.4	4.9	0.81	0.88	1.34	1.39	0.85	0.89

MAP: Mean arterial pressure

CL-DIS with FOPIID control

Closed-loop simulations are carried out for the DIS with the step fall using FOPIID controller as shown in Figure 12. Response of the infusion system for unit mmHg step change in the MAP for constrained FOPIID using simulation model is shown in Figure 13. Drug infusion with FOPIID controller is shown in Figure 14. It can be seen that drug infusion is brought back to original value using FOPIID controller. Rate of SNP infusion is shown in Figure 15.

Closed-loop system with PRC

Closed-loop simulations for the DIS with the step fall using PRC are shown in Figure 16. Response of the infusion system for unit mmHg step change in the MAP for constrained PRC using simulation model is shown in Figure 17. Drug infusion with PRC is shown in Figure 18. It can be seen that drug infusion is brought back quickly to original value using PRC. Rate of SNP with PRC is shown in Figure 19.

Comparison of time domain response with MAP of 60 and 70 mmHg and with PI, FOPIID, and PRC is given in Table 1. Using PRC, peak time is reduced from 9.8 s, 6.3 s, to 4.4 s; rising response time is reduced from 1.26 s, 0.83 s, to 0.81 s; settling time is reduced from 1.81 s, 1.42 s, to 1.34 s; peak regulation is reduced from 1.30 s, 0.92 s, to 0.85 s; and noise variation is reduced from 9.7, 8.4, to 6.1.

For attaining the set point of MAP of 70 mmHg, by PRC, peak time is reduced from 9.9 s, 6.8 s, to 4.9 s; rising response time is reduced from 1.36 s, 0.96 s, to 0.88 s; settling time is reduced from 1.97 s, 1.55 s, to 1.39 s; peak regulation is reduced from 1.41 s, 0.98 s, to 0.89 s; and noise variation is reduced from 10.3 s, 9.1 s, to 6.6 s. It can be seen that the best response is obtained using PRC. The time domain response improves with the reduction in set MAP value.

CONCLUSION

DISs with PI, FOPIID, and PRC were modeled simulated and analyzed for MAP values of 60 and 70 mmHg. This study demonstrates the inherent characteristics of the PRC to handle constraints. The main application of the constraints is that the output takes a better time response to have achieved. We found the infusion characteristics of the PRC are better than the PI and FOPIID controlled DISs. We have developed a CL-DIS for algorithmic for drug infusions. Using PRC, peak overshoot, peak regulation time, and noise variable are reduced in the closed-loop system. Our system routinely restored and accurately maintained SNP and MAP at their target values with small performance error and has potential to be developed as a stand-alone CL-DIS. The contributions of the present work on CL-DIS are as follows:

1. PRC is proposed for DIS
2. Time response of DIS is improved using PRC.

The simulation of DIS can be verified using the software PSIM or PSCAD. The hardware may be implemented using digital signal processing or field-programmable gate array. Innovative protection measures can be applied to DIS. Optimized controller design can be done in future.

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