2DOF PID-Based Controller for Chemotherapeutic System

Disha Mondal, Asha Rani, and Vijander Singh

Abstract This paper aims to analyze the capability of 2DOF PID controller while dealing with multiple and conflicting objectives problem. A basic PID control system fails to track the reference input and reject the disturbance simultaneously. This problem may be better dealt with the use of a two-degree of freedom controller which combines the effect of two controllers in separate loops to meet the two criteria. The problem considered in this study is the drug dose control in chemotherapy. In this study, multi-objective GA and multi-objective swarm optimization algorithms are implemented to obtain the optimum amount of the drug delivery for chemotherapeutic treatment. The designed controller is compared with the conventional PID controller. Various analyses like step response analysis, bode analysis, parameter perturbation analysis and disturbance analysis are carried out to justify the performance of the designed controller.

Keywords 2DOF · NSGA-II · Step response · Disturbance · Parameter perturbation

1 Introduction

Proportion integral and derivative (PID) controller is a common control algorithm used in almost every engineering process for the effectiveness and simplicity of the controllers. PID controller is the basic controller that has been in use since decades. With time many advancements are made in the PID control scheme for better performance. These controllers are tuned using several methods and algorithms. A

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conventional PID controller fails to effectively reject the system disturbance which causes sudden change in the system dynamics. Such changes affect the output of the system. Such disturbing effects may be countered by a two-degree of freedom PID controller (2DOF PID).

A 2DOF PID controller uses two control loops which lead to a robust control system. Taguchi and Araki [1] provided several configurations of a 2DOF PID controller. Another study [2] shows the supremacy of a 2DOF PID over conventional PID controller in the field of power electronics. In several other studies, 2DOF controllers are preferred over the conventional ones [3]. The controller performance for a particular application depends upon the tuning parameters. The most classical techniques used are the Zeigler-Nichols and Cohen-Coon method of tuning. With the advancement of intelligent techniques, the controllers may be efficiently tuned using the intelligent optimization algorithms [4, 5]. The problem considered in this study is the control of drug dose in chemotherapeutic treatment. This problem deals with two conflicting objective functions. The multi-objective evolutionary algorithms, i.e., multi-objective GA and multi-objective swarm optimization, are incorporated to control the drug delivery in the crucial chemotherapy problem [6–8]. The supremacy of the 2DOF PID controllers are established using several validation techniques.

The study shows cancer model and its description in Sect. 2. The controller design is shown in Sect. 3 followed by the validations in Sect. 4. The conclusion is mentioned in Sect. 5.

2 Cancer Model

Chemotherapeutic drug control deals with two objectives which are in opposition to each other. The drug injection in the body increases the drug content of the body which successfully kills the cancer cells, however, with the cancer cells the normal cell are also killed due to the harmful effect of the drug. Thus, regulating the drug content to control the harmful effect of drug in the body is equally important. A master slave cascade control system is implemented to achieve both the targets where two individual controllers are used to control the two parameters [9].

The model reported by Martin is used quite often to understand the proliferation of cancer cells. The model is represented in terms of ODE [9] (Eq. 1–3).

$$\frac{d}{dt}Z(t) = -\lambda Z(t) + k(D(t) - \alpha)H(D(t) - \alpha), \tag{1}$$

$$\frac{d}{dt}D(t) = u(t) - \gamma D(t), \tag{2}$$

$$\frac{d}{dt}T(t) = D(t) - \eta T(t),$$

λ, γ, α, η and k are tumor growth rate ($1.5*10^4$ cells/day), drug decay rate (0.27 per day), drug threshold level (10 drug days), elimination rate constant (0.4 per day) and cells killed/time/drug concentration ($9.9*10^{-3}$ per day per drug unit). $D(t)$ and $T(t)$ are drug concentration and toxicity level. Z is the transformed variable. Two conflicting objectives are achieved by introducing the following constraints in the modeling:

- The drug concentration should be regulated between 10 and 50 drug unit.
- The harmfulness or toxicity of the body should be below 100 drug unit.

3 2DOF Proportional Integral Derivative Controller

The degree of freedom of a controller gives the number of closed loops that can be adjusted independently. A two-degree of freedom controller attempts to produce the desired output and reject any disturbance in the system simultaneously. Thus, it is more robust as compared to a single degree of freedom PID controller. A 2DOF PID controller is implemented in the system that deals with multi-objective problem. Literature [1] reports the design of several configurations of 2DOF PID controller. The configuration considered in this study is a conventional PID controller and a feedback compensator. The conventional PID controller tracks the reference point, and the feedback compensator handles the disturbances. The feedback compensator consists of proportional and derivative control action along with the derivative filter. The derivative filter is used to avoid the derivative kick. The block diagram of the 2DOF PID-based control system is given in Fig. 1.

where K_{por} = proportional control action, K_{int} = integral control action, K_{der} = derivative control action and s_1 and s_2 are the set point weights. The control action of the controller is obtained by multi-objective algorithm tuned controller. The multi-objective genetic algorithm, non-dominated sorting genetic algorithm-II and multi-objective PSO are used to tune the controller. The output obtained is analyzed using various methods to study the effectiveness of the 2DOF PID controller and chooses the best tuned 2DOF PID controller for the desired drug control. The objective functions are

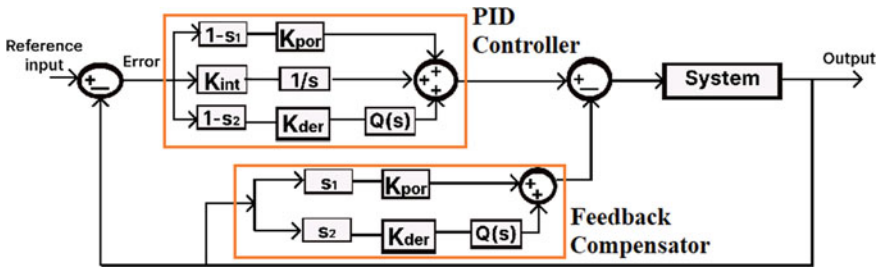

Fig. 1 2DOF PID controller

1. Sum of absolute error in toxicity level of the body, $\sum |E1(nT)|$,
2. Sum of absolute error between actual and desired drug concentration in the body, $\sum |E_2(nT)|$.

4 Validation

Four types of validation analysis are done in this paper using MATLAB Simulink. The methods include step response analysis for the toxicity of the body, bode analysis to find the stability of the system, disturbance analysis and parameter perturbation to study the effect of parameter changes on the number of cancer cells killed.

4.1 Step Response Analysis

Initially, time response analysis is carried out by considering the constraint on maximum allowable toxic level of the body as a step function with a step size of 100. The quality of the step response is measured in terms of various parametric values listed in the Table 1. A step signal is treated as a sudden input and the response of the controller to this sudden change is recorded. Step response gives the information about the stability of the controller and its ability to switch from one state to another state. The step response obtained using different 2DOF PID controllers and the conventional PID controller is shown in Fig. 2, and the quantitative analysis is given in Table 1.

It is observed from the results that the 2DOF PID controller provides a significantly better response than PID in terms of rise time, settling time and peak value. Further, the output for 2DOF PID controller settles faster than the PID controller. Further, the toxicity level of the body is best limited by NSGA-II tuned 2DOF PID controller. As the increase in toxicity in the body above 100 can be lethal for cancer patients,

Table 1 Step response analysis of the controllers

2DOF PID	Rise time (days)	Settling time (days)	Peak time (days)	Peak value	Steady state value
NSGA-II	4.723	18.420	13.954	99.96	99.96
MOGA	5.594	20.068	14.102	100	100
MOPSO	5.482	19.094	14.033	99.97	99.97
PID					
NSGA-II	6.410	21.961	14.200	100	100
MOGA	5.355	21.100	15.000	100	100
MOPSO	5.918	20.365	15.979	100.6	100

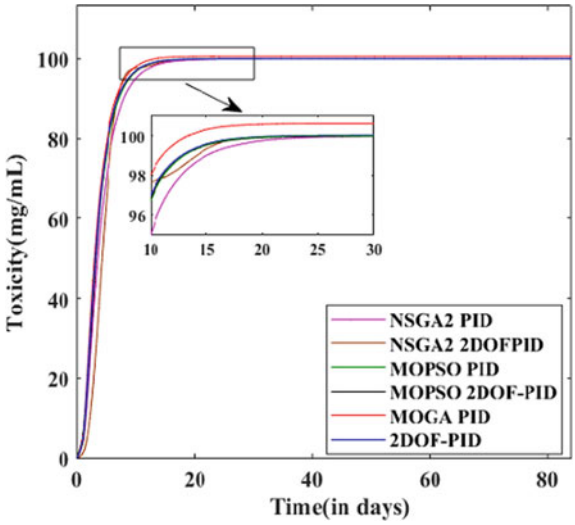

Fig. 2 Step response for toxicity level

hence the controller with minimum overshoot must be considered to control the drug injection.

4.2 Bode Analysis

Bode analysis is done to study the dynamics of the system. Bode plot measures the magnitude and phase of the output as a function of frequency. The gain and phase margin of the 2DOF PID controllers is evaluated. The values for gain margin are 70.7 dB, 54.2 dB and 53.3 dB for controllers tuned by NSGA-II, MOGA and MOPSO, respectively. Similarly, the phase margin for the controllers are 179 degrees for NSGA-II and 180 degrees for the other designed controllers. It is observed from the analysis that all the designed controllers lead to a stable system. However, NSGA-II tuned controller is more stable as compared to other controllers (Fig. 3).

4.3 Parameter Perturbation

While the treatment is carried out the model parameters are considered as fixed and constant. However, the parameter values can change owing to any physiological change or model approximation. Thus, a small change in the parameters can cause a prominent effect on the final output of the system. This issue is analyzed by observing the variation of maximum cancer cells reduced with the parametric change. The model parameters are perturbed from their nominal values (Table 2).

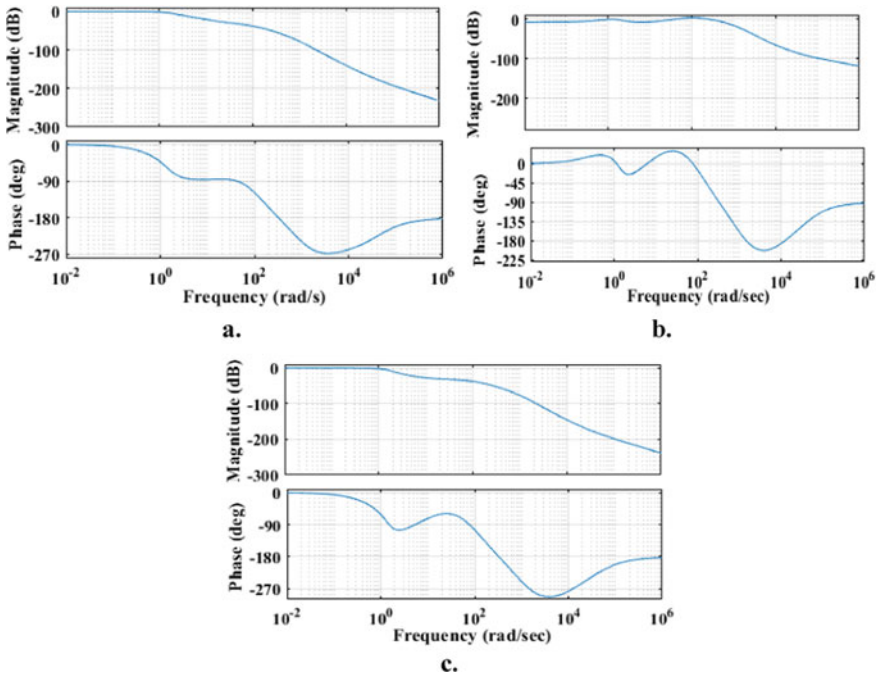

Fig. 3 Bode plot of 2DOF PID using **a**. NSGA 2, **b**. MOGA and **c**. MOPSO

Table 2 Variation of cancer cells with disturbance signal

2DOF PID (10^9)	5% decrease	10% decrease	5% increase	10% increase
NSGA -II	7.663	87.62	0.0518	0.0027
MOGA	9.029	93.04	0.0577	0.0033
MOPSO	8.914	89.64	0.0565	0.00731
PID (10^9)				
NSGA -II	10.44	133.38	0.0941	0.0067
MOGA	11.66	134.38	0.0986	0.00731
MOPSO	11	135.55	0.0972	0.00692

The toxicity obtained using different controllers is given in Table 3. It is revealed from the results that the change in body toxicity does not vary much with the changes in parameters for the 2DOF controller. Further, NSGA-II tuned 2DOF PID controller proves to be the most robust as compared to the other controllers.

Table 3 Peak value of toxicity level with disturbance in drug dose

2DOF PID controller	Sin (3,3,1)	Sin (3,15,1)	Pulse of amplitude 0.5	Pulse of amplitude 1
NSGA-II	100	99.98	99.98	100.01
MOGA	100.35	100.01	100.01	100.01
MOPSO	100.20	100.15	100.14	100
PID controller				
NSGA-II	100.42	100.10	100.17	100.26
MOGA	100.54	100.15	100.14	100.14
MOPSO	101	100.75	100.23	100.80

4.4 Disturbance Analysis

Disturbance is a common phenomenon in a practical control system. A well-designed controller must be able to handle the disturbance without causing any deviation in the desired output. Thus, disturbance analysis provides information about controller response to an unknown disturbance. In a chemotherapeutic treatment, the disturbance can arise while the drug is injected in the body using dc motors. Four different cases of disturbance are considered in this study, and the final toxic level is noted. For a better control, the controller should be able to restrict the peak and final toxic level to 100 and lesser output depicts better disturbance rejection. The disturbance signals are introduced halfway in the treatment period, i.e., on 42nd day of the treatment. Sinusoidal and pulse waves are used as disturbance in the drug dose (Fig. 4).

The variation in the output because of these disturbance signals are shown in Table 3. The waveforms of corresponding output responses are shown in Fig. 3.

Results reveal that the toxic content of the body rises above the safe threshold level in the presence of different disturbance signals. However, the rise in toxicity for 2DOF PID controller-based system is less as compared to the PID controller (Table 4).

5 Conclusion

This article presents the 2DOF PID control system for a multi-objective problem. The advantage of 2DOF PID controller is that it gives more robust performance by utilizing two feedback loops. During step change in PID controller, there is a rapid change caused due to proportional and derivative actions, which can be better handled by 2DOF PID controller. In this paper, the 2DOF PID controller is used in cascade configuration to control two objections which are conflicting with each other. The controller parameters are tuned using optimization algorithms. The stability and robustness of 2DOF PID controllers are validated using four validation techniques, i.e., step response analysis for body toxicity measurement, bode plot analysis for

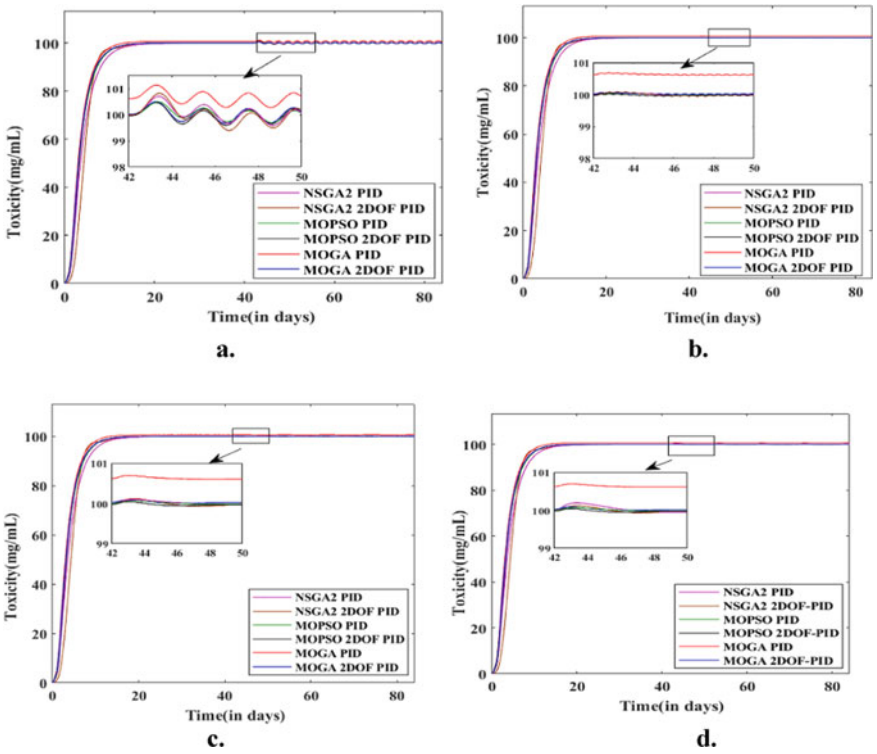

Fig. 4 Toxicity regulation by the controllers in response to **a**. pulse disturbance of 0.5 width, **b**. pulse disturbance of 1 width, **c**. 3Sin3t disturbance signal and **d**. 3Sin15t disturbance signal

Table 4 Controller parameters for the designed controllers

	Controller parameter	NSGA 2 2DOF PID	NSGA 2 PID	MOPSO 2DOF PID	MOPSO PID	MOGA 2DOF PID	MOGA PID
	Kpor	0.1381	0.3598	1.6122	1.8605	1.8612	1.9996
	Kint	1.2024	0.7228	0.8443	0.6287	1.0206	0.5402
C1	Kder	0.1758	0.2294	0.6630	0.7021	0.6381	0.2294
	s1	0.9411	–	0.3223	–	0.2083	–
	s2	0.2084	–	0.4376	–	0.1127	–
	Kpor	0.5673	1.1279	1.6850	1.8736	1.9910	1.9766
	Kint	0.6234	0.2615	1.5467	0.4977	1.3271	0.6944
C2	Kder	0.0172	0.0002	0.1051	0.2832	0.0393	0.0003
	s1	0.8354	–	0.3880	–	0.2017	–
	s2	0.0172	–	0.4139	–	0.3712	–

stability, disturbance analysis to check the robustness of the controllers and parameter perturbation to study the count of tumor cells with parameter variation. It is revealed from the complete analysis that 2DOF PID controller performs better than the conventional PID controller. Further, the 2DOF PID controller is best tuned by NSGA-II algorithm. Hence, it is concluded that the introduction of fractional order to conventional PID controller provides the robust and efficient control of drug delivery for chemotherapeutic treatment.

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