Covenant Journal of Informatics & Communication Technology. Vol. 10 No. 2, 2022
ISSN: ***print*** **2354 – 3566** ***electronics*** **2354 – 3507 DOI:**

An Open Access Journal Available Online

Model Predictive Control of Blood Pressure and Urine Production Rate for a Physiological Patient Model

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Received: 6.08.2022, Accepted: 7.11.2022

Publication: December 2022

Abstract— The research proposes the design of a model predictive control (MPC) for automatic drug dosing to regulate high blood pressure and urine production rate in an elderly patient. Combining hydrochlorothiazide and oxybutynin is commonly used for regulation of blood pressure in elderly patients. The patient's model tries to captures the responses to the drugs as the blood pressure and urine production rates attains their various set-points. Hence, this research aims at improving the control scheme which ensured that these two physiological variables are regulated. Simulation was done in MATLAB/Simulink environment with the use of MPC Toolbox, and the controlled variables were constrained to operate at 80mmHg for blood pressure and between 24-49 ml/kg/hr for urine production rate respectively while the manipulated variables remained unconstrained. From the simulation results, the MPC controller achieved good set-point tracking and disturbance rejection, which is an indication of a healthy level of regulation within acceptable tolerances.

Keywords/Index Terms—Blood Pressure, urine production rate, MPC, patient model, set-point tracking

1. Introduction

Phishing human body is complex, and can be considered as a multivariable system, whose stability is maintained by the influence of the automatic nervous system through dynamic interaction of multiple systems (El-Samad & Khammash, 2000; Iberall *et al.*, 1975; Shafer, 1975). There is a fundamental relationship involving sensory inputs and perceptions, neural function and networks, cellular and molecular biology (Averina *et al.*, 2012), any of which may adversely affect the other, if it is not properly regulated. One of such interactive systems is the relationship between blood pressure and urine production rate. There have been debates on the causes of chronically-elevated arterial blood pressure (hypertension) (Ismail *et al.*, 2021). This phenomenon is currently modeled based on the assumption that the long-term regulation of blood pressure depends on the ability of the kidney to excrete sodium. However, this assumption leads to the conclusion that hypertension could be caused by kidney dysfunction (Averina *et al.*, 2015; Cortés-Ríos & Rodriguez-Fernandez, 2021).

Therefore, a method of addressing hypertension is to ensure proper functioning of the kidneys or find ways of complementing their functions as individuals grow older, which invariable could be viewed as a control and regulation problem (Abayomi-Alli *et al.*, 2022).

Modern control methods mostly depend on the availability of relevant control models, that is particularly very important for critical systems such as the human body, which is been discussed by several research articles related to physiological patient models scale (Shafer, 1975), and a controller for such a system needs to be robust to uncertainties and parameter changes, because physiological systems are usually unknown and difficult to analyze. They exhibit strong coupling among the different physiological control system variables (Oyewola *et al.*, 2022). When using controllers, negative feedback in the physiological system is typically embedded in the plant characteristics so that the controllers will rely on the feedback from the pump and cardiovascular system in order to function properly (Averina *et al.*, 2012; Bhardwaj *et al.*, 2021; González *et al.*, 2010; Kos & Umek, 2018; Vasilyev *et al.*, 2019). In biological systems such as the human body, control mechanisms maintain homeostasis at all levels of organization in the hierarchy of living systems (Ayeni *et al.*, 2019). However, due to aging, the functioning of the organs and tissues is gradually weakened as both diseases and accident contribute to impairing the proper function of living systems. An attempt to complement the functioning of such organs to attain similar or close to their natural performance can be achieved through drug dosing and assistance of medical devices to recover natural control mechanism (Huang & Chung, 2014; Simon, 2012).

This paper explores a control solution for addressing the physiological needs of elderly patients. To achieve this, a physiological patient model was adopted and model predictive control (MPC) was used as a solution for the considered control problem (Misra, 2020). The paper is structured as follows. Section 1 discusses the introduction, while section 2 present the methods of blood pressure control and urine production rate. Section 3 gives the adopted model and the MPC algorithm used to solve the problem of blood pressure and urine production rate. Section 4 discuss design of the MPC for the physiological patient, while the results and discussion are presented in section 5, and finally, conclusion is given in section 6.

2. Blood Pressure Control and Urine Production Rate

To reduce the blood lost during operation, a blood pressure regulation system is important. The main method is the infusion of the sodium nitroprusside in order to lower blood pressure in patients who have undergone surgery. Typically, the bolus injection can rapidly decrease blood pressure, but has disadvantage that the effect diminishes rapidly and can only be applied periodically in order to avoid cyanide poisoning (Bakouri *et al.*, 2022; Giridharan & Skliar, 2006; Pauls *et al.*, 2016). The control release method, which is often adopted has the advantage of achieving lower blood pressures over longer periods of time. However, the main challenge is finding the appropriate dose, which quickly lowers the blood pressure to the desired level while avoiding a drug overdose (Simanski *et al.*, 2007).

Adapting several parameters, especially in a nonlinear coupled system can lead to undesired behavior. Predicting the behavior of such closed loop system over the entire operating range is non-trivial. Previous research on the analysis of the model parameters has shown that an internal model controller (IMC) that can meet robust stability and performance criteria can be designed for variations in all of the system parameters. In the work of (Furutani *et al.*, 1995), a state predictive controller to cope with the dead time associated with the drug delivery response was considered. Other researchers considered the use of adaptive control to regulate the main arterial pressure through the intravenous infusion of sodium nitroprusside (Cavalcanti & Maitelli, 2015; Haamed & Hameed, 2020; Maitelli & Yoneyama, 1997; Ng *et al.*, 2017; Silva *et al.*, 2018).

Several controllers have been designed for blood pressure regulation using adaptive parameters that resolves the effect of uncertainties within the system. Due to the fact that the ultimate goal is to design a controller that can be used in the medical environment, the controller should be as simple as possible (Bosworth *et al.*, 2006; Caldwell *et al.*, 2020; Gross *et al.*, 2003). Biofeedback has also been employed for detecting and controlling physiological states like the heart rate, electroencephalogram (EEG) and muscle activity. From the control theory point of view, the controller of biofeedback system is often the patient’s brain. The pertinent thing is to create a feedback path. The three stages of biofeedback system which is the feedback presentation, data collection and signal conditioning is shown in Figure 1.

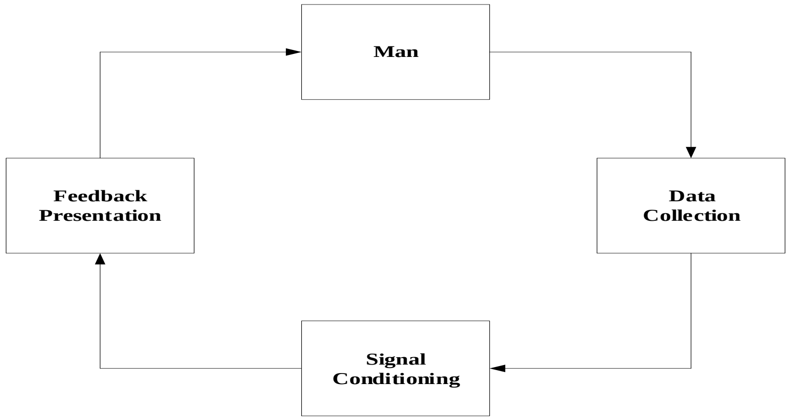

Figure 1: Biofeedback Control System

2.1 Control Schemes Employed

When variability is not considered, the hybrid explicit/multi-parametric model predictive control (mp-hMPC) requires the solution of a novel multi-parametric mixed-integer quadratic problem. In the presence of variability, however, robust explicit MPC techniques were incorporated within the overall hybrid explicit MPC strategy (Huang & Chung, 2014; Pauls *et al.*, 2016). The resulting mp-hMPC controller was tested and observed to address offset correction when compensated by making the control robust or using estimation techniques. The results show a high efficiency optimal dosage and robustness of the model predictive control algorithm to induce and maintain the desired bi-spectral index reference while rejecting typical disturbances from surgery (Ivy & Bailey, 2014; Sandeep *et al.*, 2022; Sharma & Kumar, 2022; Silva *et al.*, 2019). There are some advantages of using mp-hMPC for drug delivery systems which are suitable for portable applications, testing off-line of different scenarios to ensure the patients safety and the advantages of MPC over other control designs (Baum & Brown, 2021; Ewing, 2010).

2.2 Problem Definition

The combination of two drugs (hydrochlorothiazide and oxybutynin) is commonly used to regulate blood pressure in elderly patients. These two drugs mainly affect two physiological variables; the patient’s blood pressure and urine production rate. This research aims to develop an improved control scheme which ensures the regulation of the two physiological variables.

3. Model Predictive Control (MPC)

The equation of the patient’s mathematical model is given as (Simon, 2012):

$$\begin{bmatrix} Y_1 \\ Y_2 \end{bmatrix} = \begin{bmatrix} \dfrac{0.004e^{-0.1s}}{0.11s+1} & \dfrac{0.0005e^{-0.15s}}{7.05s+1} \\ \dfrac{0.22}{0.12s+1} & \dfrac{-0.02}{0.21s+1} \end{bmatrix} \begin{bmatrix} u_1(s) \\ u_2(s) \end{bmatrix} \tag{1}$$

Y_1 is the normalized blood pressure, Y_2 is the normalized urine production rate, u_1 is the rate of hydrochlorothiazide ingestion, u_2 is the rate of oxybutynin ingestion.

Equation (1) can be represented in the state space format, and it takes into account the effect of plant model mismatch, disturbances and other uncertainties, the state space model with augmented disturbances is used in this article.

3.1 Disturbance Model

This augmented state space model with model mismatch and disturbances entering the plant is given as (Maeder & Morari, 2010; Simon, 2012):

$$\begin{bmatrix} x(t+1) \\ d(t+1) \end{bmatrix} = \begin{bmatrix} A & Bd \\ 0 & Ad \end{bmatrix} \begin{bmatrix} x(t) \\ d(t) \end{bmatrix} + \begin{bmatrix} B \\ 0 \end{bmatrix} u(t) \quad (2)$$

$$y(t) = \begin{bmatrix} C & C_d \end{bmatrix} \begin{bmatrix} x(t) \\ d(t) \end{bmatrix} \quad (3)$$

Where $d(k) \in \Re^{nd}$, $A_d \in \Re^{nd \times nd}$, $B_d \in \Re^{nx \times nd}$, $C_d \in \Re^{ny \times nd}$

In order to capture patient-model mismatch, the disturbance model contains a model of the reference dynamics. An additional model can however be added to reject specific disturbance dynamics which are not part of the reference signal. Both types of models need to be added for every output channel. Defining the following parameters A_d incorporates an internal model of A_r if the following holds: A_d contains all unique eigenvalues of A_r; the geometric multiplicity of every eigenvalue of A_d is n_y; every Jordan chain of A_d corresponding to the eigenvalue $\lambda \in \sigma(A_d)$ is of the same length as the longest Jordan chain in A_r corresponding to this eigenvalue.

To counteract the effect of disturbances and to follow reference signals, the model needs to be output-controllable with respect to the models given by A_d and A_r. The mathematical condition for this is given as (Maeder & Morari, 2010):

$$rank \begin{bmatrix} A - \lambda i & B \\ C & 0 \end{bmatrix} = n_x + n_y, \ \forall \lambda_i \in \sigma(A_d) \quad (4)$$

3.2 Controller

The MPC which achieved the target tracking is presented in this subsection. In the regulation problem, the objective is that the system state to be brought to the origin, where the system is in equilibrium (Umar *et al.*, 2022). When tracking an unstable reference signal, it is customary to allow some modes to be non-zero. This is achieved by introducing the notion of target trajectories (Umar *et al.*, 2017). The target trajectory is defined as a sequence of states and inputs yielding the desired output for a given reference and disturbance signal. It is defined for all future time instances $t^I \geq t$. The future disturbance is given based on the current estimate.

3.3 MPC Algorithm

The set of predicted input variables are defined by (Maeder & Morari, 2010; Yusuf *et al.*, 2018):

$$U_t = \left\{ u_t(k) \right\}_{k=0}^{N-1} \quad (5)$$

The decision variables introduced by the target trajectory problem are (Maeder & Morari, 2010; Sha'aban, 2022):

$$T_t = \bigcup_{i=1}^{m} \bigcup_{j=0}^{Pj} \left\{ \left(\overline{x}_{t,j}^{\lambda i}(k), \overline{u}_{t,j}^{\lambda i} \right) \right\}_{k=0}^{N} \quad (6)$$

The MPC optimization problem is then posed as follows (Maeder & Morari, 2010; Sha'aban *et al.*, 2013):

$$\min_{U_t, T_t} \sum_{k=0}^{N-1} \left\| x_t(t) - \bar{x}_t(k) \right\|_Q^2 + \left\| u_t(k) - \bar{u}_t(k) \right\|_R^2 + \left\| x_t(N) - \bar{x}_t(N) \right\|_P^2$$
$$\begin{aligned} s.t \quad & x_t(k) \in \mathrm{X}, \quad k = 1, \ldots, N, \\ & u_t(k) \in \mathrm{U}, \quad k = 0, \ldots, N-1, \\ & x_t(k+1) = Ax_t(k) + Bu_t(k) + B_d \bar{d}_t(k), \\ & k = 0, \ldots, N \\ & x_t(0) = \hat{x}(t) \end{aligned} \tag{7}$$

Where P, Q, R and N are arbitrarily selected for the nominal closed loop system to be stable, and a feasible optimization problem for all time instants. The framework which was used for the operation of the controller is the MPC Toolbox in MATLAB environment. This involves the design of an equivalent Simulink model that will accurately represents the multivariable relationships presented by the patient's model. The patient's model was linearized before an appropriate controller was developed. The approximate model should decrease computational complexity and also retain adequate information to enclose the system dynamics.

4. Design

The design of an MPC for the physiological patient model problem was developed in MATLAB/Simulink environment, which is shown in Figure 2.

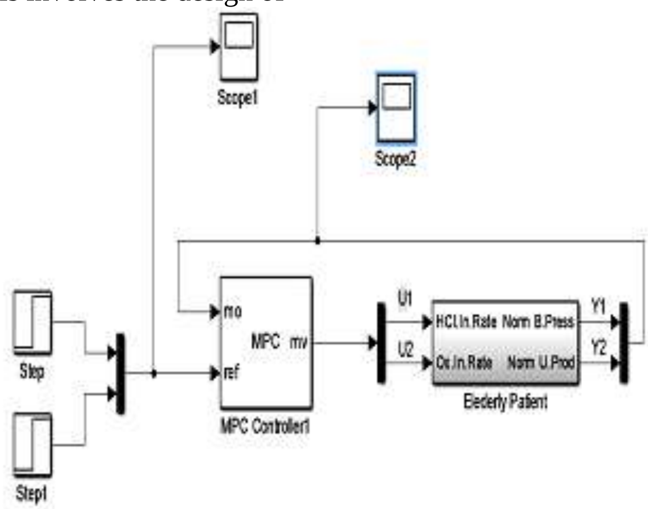

Figure 2: Simulink Block of the Controlled System

The control objective is to minimize the weighted squared error between the required set-point and the output without causing unacceptably large oscillations in the input. The controller determines the inputs at the equivalent sampling times before minimizing the performance index, which is given as (Ionescu *et al.*, 2021; Voss *et al.*, 1987):

$$J = \left[y* - y(t+k+d) \right]^T W \left[y* - y(t+k+d) \right] \tag{8}$$

Where $y*$ is the required set-point, y is the output, W is the diagonal weighting function on the relative importance of maintaining each required set-point and output, d is the minimum possible plant dead time and k is a positive integer number.

5. Result and Discussion

The results of this simulation was achieved from MATLAB/Simulink environment, which was carried out based on the estimated weighting parameters. Scenario 1 was built around MPC1 operating at an interval of 1 second, MPC open plant 1 under forced input and output constraints for a duration of 360 seconds. The output signals were constrained to constant values of 80 and 49 for ports 1 and 2 respectively. Unmeasured unit step disturbances were fed to the system for the duration of 1 second each starting from 0 units, this is shown in Figure 3.

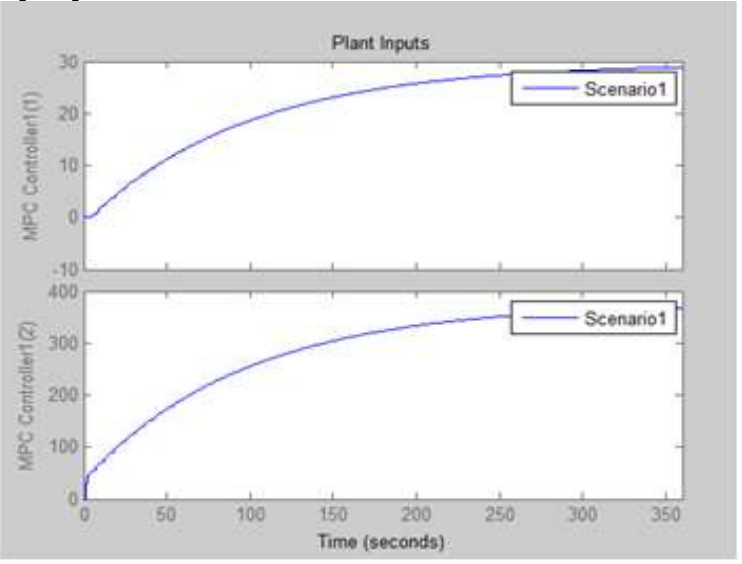

Figure 3: System Input Signal Plot

From Figure 3, which is the offset-free reference tracking and disturbance rejection of constrained systems by means of an MPC controller. The result considered disturbance and reference signals to signals generated by arbitrary unstable linear models. The MPC controller stabilized the system at about 200 secs, which stabilizes the blood pressure and urine production rate as fast as possible. The important points of the methods are the choice of a disturbance model satisfying the internal model condition, and an addition of target trajectory conditions to the MPC problem. The method removes offset under the assumptions of stability and feasibility of the closed loop.

The systems response to the developed control scheme is shown in Figure 4.

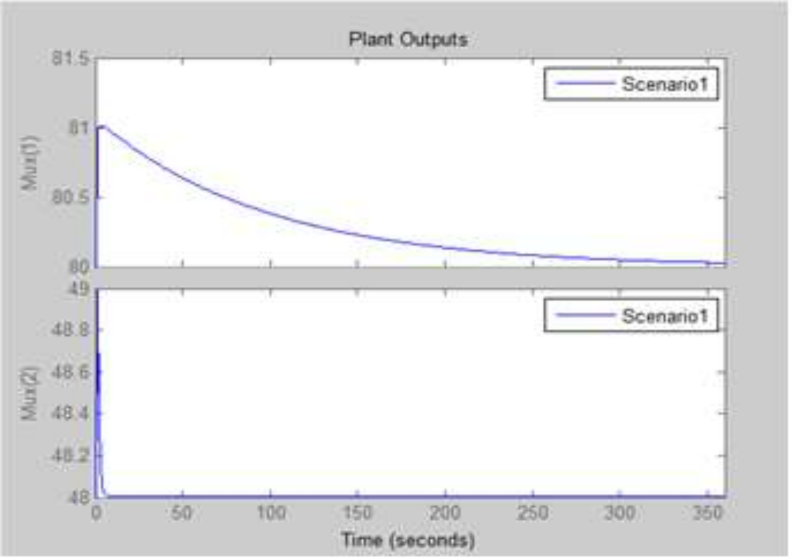

Figure 4: Systems Output Signal Plot

From Figure 4, the controller was designed to supply the patient with the appropriate doses for medication in the event that either one or both of the outputs is not satisfactory. From Figure 4, it can be seen that the signal from output one attained a mercury rate of 80 mmHg for blood pressure, while for output two is 49 ml/kg/hr for the urine production rate respectively. This shows that the patient’s response to the drugs is highly nonlinear and time varying, while the output also varies.

This is addressed by the accuracy of the estimator in correctly satisfying the linearized plant for the controller to perform satisfactorily. These uncertainties often account for the large variations to the system response, even as the initial controls to the set-point changes.

6. Conclusion

The problem of controlling blood pressure and urine production rate of an elderly patient model by a suitable control scheme has been presented. The combination of hydrochlorothiazide and oxybutynin is common for the regulation of blood pressure in elderly patients. It is observed that good tracking was achieved when disturbances was rejected. A good patient’s model of the patient captures responses to the drugs, as the blood pressure and urine production rates eventually reached their respective set-points. Simulation was done in MATLAB/Simulink environment using MPC Toolbox. The controlled variables were constrained to operate at 80 mmHg for blood pressure and between 24-49 ml/kg/hr for urine production rate respectively. The results showed a satisfactory performance in terms of set-point tracking and disturbance rejection. However, this research demonstrated the feasibility of implementing a multivariable drug delivery system in medical applications. It should be noted that the cardiac output cannot yet be continuously monitored in routine clinical environments, creating room for improved technological innovations for the future. More can be achieved by developing systems that will be safer and more effective to current clinical challenges. Estimating the background level, optimizing model order and the control interval, bounding the parameter estimates, initiating control without prior open-loop estimation of the patient's response to drug therapy, further research can be focused on providing an overall supervisory algorithm to the control system.

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