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Using Machine Learning-Based Control Co-Design for Feedback Control of Medication Delivery

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Abstract

This study investigates the highs and lows associated with the formation of addiction and focuses on developing a feedback control loop for an infusion pump that optimizes drug concentration in the bloodstream according to specific criteria. To achieve this, the system's mathematical model was analyzed to derive an open-loop transfer function, which was then used to apply a PID (Proportional-Integral-Derivative) controller for feedback regulation. In addition to traditional control methods, both machine learning (ML) and deep learning (DL) techniques were explored as classifiers to assist the pump in administering accurate doses. The target drug concentration in the patient's bloodstream was determined to be 7.55 mg/ml, which served as the steady-state setpoint for the transfer function. By incorporating the PID tuner into the feedback loop, the system was optimized to meet design requirements, including a rise time of less than 25 minutes and a maximum overshoot of 5% above the setpoint concentration. Machine learning classifiers, including Naïve Bayes (NB), Decision Trees, and Support Vector Machines (SVM), achieved an impressive classification accuracy of 100%. Additionally, a deep learning (DL) model was successfully developed to predict patient classification based on their metabolic profile. This research lays the foundation for the development of a feedback-driven infusion pump and an algorithm capable of classifying patients according to their metabolism. The goal is to provide doctors with a tool that customizes the pump's dosage for each patient, ensuring they receive the correct amount of medication tailored to their individual needs.

Keywords: Addiction modeling; PID controller; Infusion pump optimization; Machine learning classifiers; Personalized drug dosage

1. Introduction

After the emergence of the virus in 2020, the deaths due to opioid overdoses have increased dramatically. In response to the escalating difficulty of this matter, cutting-edge solutions are being developed that will autonomously evaluate the quantities of drugs in an individual's circulation, determine the necessary dosage according to a specific concentration, and administer the medication in minimal doses. This specific dosage will be adequate to stop the individual from feeling unease, while still being minimal enough to steer clear of

the pleasure associated with addiction. In order to preserve equilibrium among these tiers, the apparatus will utilise an artificial intelligence model through its response regulation framework.

A gadget similar to this drug distribution mechanism, crafted to autonomously evaluate and release the necessary amount, is an intelligent insulin pump [1]. The device is now capable of operating automatically due to the addition of a detector. This cohesive framework persistently observes sugar concentrations and autonomously adjusts the individual's insulin as necessary. Additionally, it can adopt strategies to help prevent elevated glucose levels and offers adjustments for relaxation and exercise. An important issue with this pump intended for the novel drug administration apparatus is that its cartridge holds only 3 mL of medication, which falls far short of the 40 mL needed for the drug delivery device in this research [2].

A distinct healthcare device that utilises feedback control is an Implantable Cardioverter Defibrillator (ICD) [3]. This device operates by continuously monitoring and regulating the individual's pulse. When the individual's pulse drops beneath a set threshold, the device will send an electrical signal to the heart, encouraging it to beat and produce a heartbeat, similar to how a defibrillator operates. The prompt detection of the heart allows a gadget such as this to successfully preserve an individual's life, since the jolt will be delivered the instant a pulse is missing. Although there are benefits, it is crucial to recognise specific risks linked to the utilisation of an ICD apparatus, including internal haemorrhaging, injury to blood vessels, and possible rupture of cardiac tissue. As these concerns stem from the apparatus being situated inside the body, they could potentially be resolved by transitioning the ICD to an outside defibrillator, maintaining a discreet design similar to the drug administration device mentioned in this study. Another benefit of an outside gadget is the ease of removing or replacing it, since no medical procedure is necessary.

In addition to analysing similar tools, previous research played a beneficial role in the progress of the ML investigation that will be discussed later. This piece discusses the effects of the educational and evaluation methods, the significance of data segmentation in artificial intelligence, the prediction of blood sugar levels, an investigation into advanced learning uses, and other subjects. [4] [5] [6] [7] [8]. An essential aspect of artificial intelligence is the ratio of preparation to evaluation that is applied to analyse information. In an article exploring the effects of training/testing ratios on machine learning within biomedical engineering, Uçar et al. observed that when faced with a small number of samples in a dataset, or when there is minimal confidence in the dataset, it is recommended to select ratios of 90/10 or 80/20. Considering a significant volume of information, and to assess "under the most difficult conditions," a balanced proportion of 50/50 was indicated to be ideal [8]. However, only a single one of the four analysed papers arrived at a similar finding of 90/10 concerning forecasting capability when compared to 70/30 and 80/20 [7]. The last three decided that the 70/30 division was the best option. [/4/ /5/ /6/].

Gadze and associates investigated various deep learning frameworks, including a convolutional neural network (CNN) and long-short term memory (LSTM). This research focused on the systems' development of an artificial intelligence framework to detect and mitigate a distributed denial of service assault on software-defined networking controllers. When evaluated against specific linear-oriented machine learning frameworks, the LSTM framework showed similar precision and proved to be an effective classification tool for DDoS identification. Within the analysed linear frameworks, the k-nearest neighbour (KNN) framework exhibited remarkably elevated precision (99.4%) in this investigation, positioning it as a formidable option for choosing a classification model [4].

Every reference examined provides significant perspectives on how multiple elements can affect the machine

learning model, the accuracy of diverse frameworks, and other considerations; nonetheless, three of them are unrelated to medical uses, which limits the applicability of the data shared. This research may act as a comprehensive source in the domain of medical uses, especially emphasising the investigations that focus on these uses. [5] [8]. In order for a gadget of this kind to operate successfully, it needs a well-adjusted response management framework and artificial intelligence method, allowing it to correctly obtain, evaluate, and generate exact information. Employing a response regulation system, the device should obtain a measurement of substance concentrations in the bloodstream, evaluate the amount of treatment needed, and finally, administer the treatment. Although this seems to operate on its own, the mechanism must uphold a certain level and ought to be able to adapt to changes in the individual's physical actions. This is the moment when the computational learning process becomes crucial. The framework is capable of classifying individuals based on their metabolic speeds, aiding the doctor in identifying the suitable setpoint levels and PID settings needed. This ensures that the individual obtains a suitable dosage of the treatment, preventing surplus or shortage. The process begins by recognising the unrestricted loop transfer function, adjusting it as necessary to improve its precision, and integrating a PID controller. During every phase, the accuracy of the system and different measurements are assessed. The main goal is to incorporate artificial intelligence into a responsive control mechanism that will allow the drug dispensing apparatus to function at peak performance and assist in mitigating the persistent opioid epidemic.

Design and Methods

The goal of this initiative is to create a mechanism that guarantees a consistent delivery of pharmaceuticals to the circulatory system. The method utilised in this scenario is a regulatory mechanism, with the concentration of drugs in the circulatory system acting as the main variable of the mechanism. To ensure a consistent level of medicine in the blood, a control mechanism will consider the amount that can be administered at one time, biological resistance elements, possible disruptions, and the maximum concentration allowed. The diagram presented in Figure 1 depicts the progression of the machine learning algorithm's creation.

The diagram presented earlier demonstrates that the assessment includes administering the medication to the individual and measuring the concentration of the substance in the circulatory system. This collection of details demonstrates how an individual responds to the therapy. The data is then employed to train and evaluate a machine learning model designed to classify the patient based on their metabolic response to the treatment and how the treatment is metabolised for each specific patient. This artificial intelligence method can later be incorporated into the management system and utilised in the drug dispenser to accurately administer drugs at a pace that lessens discomfort for the individual and avoids the emergence of a peak, thus lowering the chance of forming a dependency on the drug.

Deriving the Open Loop Transfer Function

The most important component of this project is to create an open loop transfer function that correctly models the concentration of medication. Figure 2 below

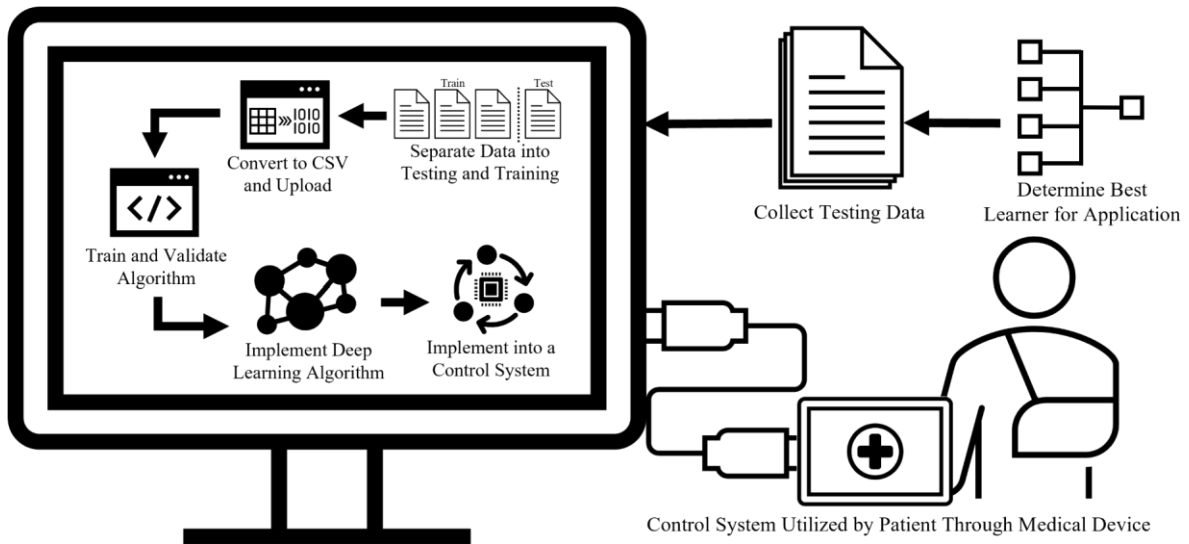


Figure 1. Schematic diagram showing the process of machine learning algorithm development.

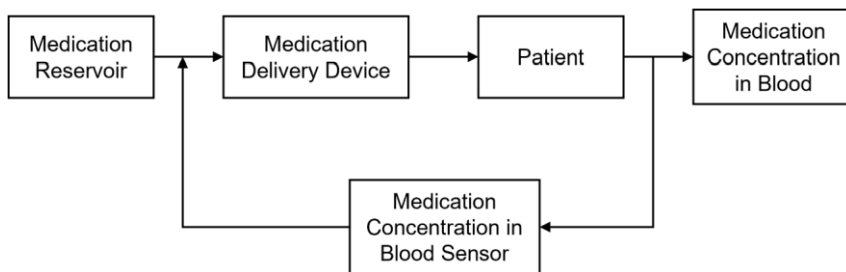


Figure 2. Flow Chart representing feedback control system in medication delivery device.

presents an unrestricted loop transfer function that illustrates a representation of the medication concentration within the bloodstream. The input in this feedback cycle is the amount of medication to be delivered into the bloodstream. The result produced by the system indicates the level of medication present in the blood circulation. The loop's transfer function will be established using a mathematical model as shown in Equation (1) below.

$$mx \square \square + + = bx \square \square kx \quad f t () \quad (1)$$

Once the open loop transfer function has been established, the goal is to refine it with a PID tuner to meet the design specifications informed by earlier experimental findings. The specified standards are employed to enhance the efficiency of the device in question. The apparatus must achieve 90% of the ideal medication concentration in less than 25 minutes, must not surpass the ideal medication concentration by over 5%, and once the ideal concentration is attained, it should not vary by more than 2% from its designated concentration value [9].

Machine Learning Implementation

Our initiative mainly centres around artificial intelligence to comprehend how various situations influence the speed at which the body processes drugs. This encompasses examining interruptions like active motions—such as running, upright positions, and lying down—and their effects on the body's metabolic processes. These modifications in bodily movement influence the speed at which compounds are handled, either hastening or decelerating the drug's breakdown. In order to explore this, we employed multiple collections of input information to forecast possible results, aiding us in enhancing our comprehension of how various elements, such as physical actions and dietary practices, influence drug levels. The provided information encompasses factors like the rate at which the medication diminishes in the circulatory system, the permissible level of the medication, the body's tolerance to a specific amount, and the influence of dietary consumption.

In the setup for the artificial intelligence model, we gathered information from a hundred individuals. Seventy percent of this information is utilised for educating the algorithms, whereas the leftover thirty percent is set aside for verification. The information resides in a CSV document, which is brought into MATLAB for examination. We will utilise the Classification Learner tool within MATLAB to implement artificial intelligence techniques. Every individual is categorised (A, B, C, D, or E) according to the fluctuation in medication levels throughout a 10-hour duration following the delivery of 20 mg of treatment. These classifications function as tags, with the 10 intervals of density assessments acting as signals for the educational systems.

Four algorithms for machine intelligence are evaluated: a decision tree, k-nearest neighbours (KNN), Gaussian Naïve Bayes, and cubic support vector machine (SVM). The frameworks are created utilising 5-fold cross-checking. The effectiveness of the algorithms is assessed through a comparison of training and validation accuracies. The model exhibiting the smallest disparity between training and validation accuracy is deemed the most effective. The outcomes from this framework will subsequently be evaluated against a more extensive collection of 1000 individuals, sourced from the initial reduced group. Advanced neural networks are likewise employed in Simulink to forecast drug concentrations in the circulatory system. In this scenario, the resulting information from the apparatus design acts as a feed for the neural network. An MLP architecture is developed using the identical data set applied for computational learning, preserving the 70/30 division between training and validation. The CSV document has been altered to eliminate the patient name field and relocate the category field to the extreme right, guaranteeing that the data entries occupy the initial 10 columns. The arrangement of the system is illustrated in Figure 3.

The profound learning architecture relies on the characteristic network from [10] and comprises 7 tiers. The structure comprises an entry layer featuring 10 attributes, all of which are standardised using z-scores. Next, there is a dense layer comprising 50 units, succeeded by a normalisation layer, an activation layer using rectified linear units, another dense layer containing a single unit (indicating the output of the classifier), a softmax layer, and a concluding classification layer. The system is optimised utilising the Adam algorithm with a small batch size of 10, randomising at every epoch, while training advancement is displayed, and detail level configured to false. The developed system is incorporated into an independent MATLAB/Simulink framework utilising a forecasting component. It is crucial to confirm that MATLAB version 2020b or later is utilised, since the deep learning components are exclusively accessible from this version forward.

The gathered information illustrates the disparity between the intended medication level and the real level present in the blood. This difference is increased by 10,000 to enhance its visibility to the system. The information is subsequently arranged into a temporal sequence characteristic of dimension 11 utilising a

MATLAB application for additional examination.

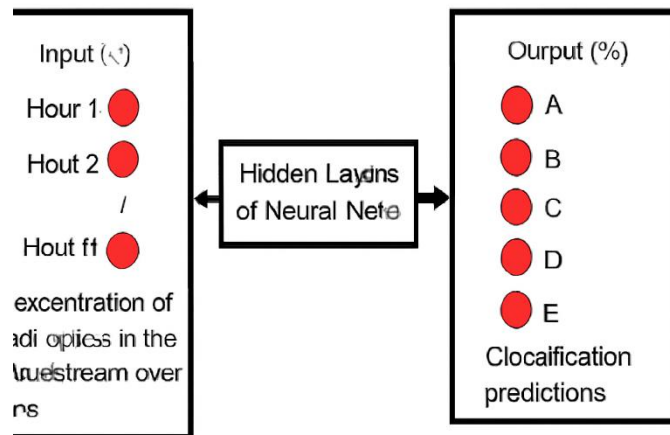


Figure 3. Structure of neural network.

document (MLP networks exclusively accept information that is structured as a feature). The system that has been created eliminates an entry from the attribute, resulting in the attribute's size being 10, which corresponds to the number of samples collected during the 10-hour duration. The structured attribute is subsequently altered through a matrix transpose process in the updated MATLAB/Simulink model, allowing the transposed attribute to be employed by the prediction block. Once the Simulink model completes its execution, the outcome is a validation prediction accuracy derived from the input data.

Results and Discussion

The initial phase of crafting our apparatus entails identifying the unrestricted transfer function that characterises the level of medication within the circulatory system. Prior to concluding this segment of the initiative, numerous essential factors were assessed, including the volume of the drug storage, the lowest dosage, and both the standard and peak medication levels. Table 1 presents the computed figures and the techniques employed for their assessment. Analysing this information, we note that the necessary target value for the control mechanism is 7.55 mg/ml, indicating the desired level of the drug in the circulatory system. The least quantity indicates the tiniest portion of the medication given for each individual operation of the straight actuator. In relation to this endeavour, the least amount of movement for the actuator has been established at 0.05 mm. The peak dosage threshold represents the utmost permitted concentration within the individual's circulatory system that does not induce damage. This relates to the 5% excess in the control circuit, which was outlined in the design specifications. As a result, the highest allowable level of the drug in the bloodstream is 7.95 mg/ml. Once these preliminary figures and project specifications are established, the open-loop transfer function may be computed. In Formula (1) from the design approach, the parameters m , b , and k denote particular constants, whereas $x(t)$ signifies the system's output. The result shows the drug level in the blood, thus $x(t)$ is replaced with $c(t)$. The entry to the operation, $f(t)$, relates to the quantity of medicine added to the system.

In order to determine the transfer function, we utilise the Laplace Transform on the function and condense

the equation into a fraction representing output over input. This formula includes four established parameters: the mass of blood, which is 8 kg, the resistance coefficient of blood (0.0006 N·s/m or 0.0006 s·ml), and the rigidity coefficient, which corresponds to the blood capacity as the blood holds the energy of the medication. The total amount of blood is calculated by taking the mass and dividing it by the blood's density (1060 kg/m³), resulting in an overall blood volume of 7.55 litres or 7550 millilitres. The indication, $u(t)$, denotes the quantity of material introduced into the circulatory system through one actuator operation. The least amount is 22.5 mg. The overall weight of the system can be determined by utilising Formula (3).

This transfer function illustrates a mechanism that remains unrefined or adjusted, missing amplification elements that could enhance the feedback mechanism's efficiency. Consequently, the mechanism displays fluctuations prior to settling at the optimal level. This unrestricted transfer function serves as a numerical representation of the drug levels in the user's circulatory system, as previously mentioned.

A straightforward Simulink representation of the open-loop configuration is depicted in Figure 4. This equation illustrates the concentration of drugs within the circulatory system. The medication quantity adheres to a sequential pattern, illustrating the perfect level of treatment to be given for guaranteeing patient well-being and maximum ease. The amount was established via trials in the Simulink simulation, resulting in a figure of 92 mg. In excess of 1500 ticks (roughly 25 moments), 92 mg of treatment needs to be administered to achieve the desired level. In addition to the medication component, a step function named "Concentration Setpoint" was added to the model to serve as a benchmark for the transfer function graph. The ultimate amount for this phase was determined to be 7.55 mg/ml. The framework extends from time equals zero to time equals fifteen hundred seconds, with the related chart displayed in Figure 5.

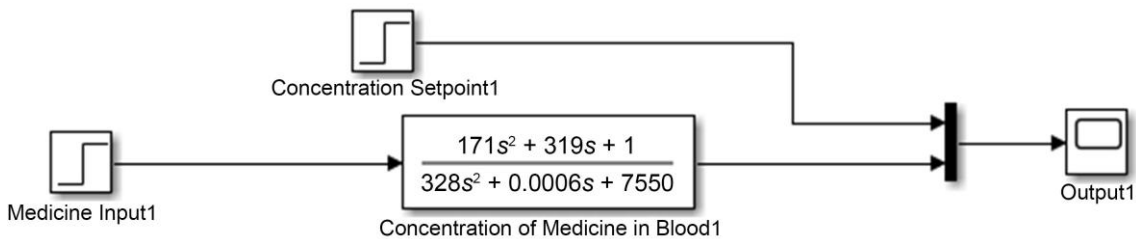


Figure 4. Open loop system model in MATLAB/Simulink.

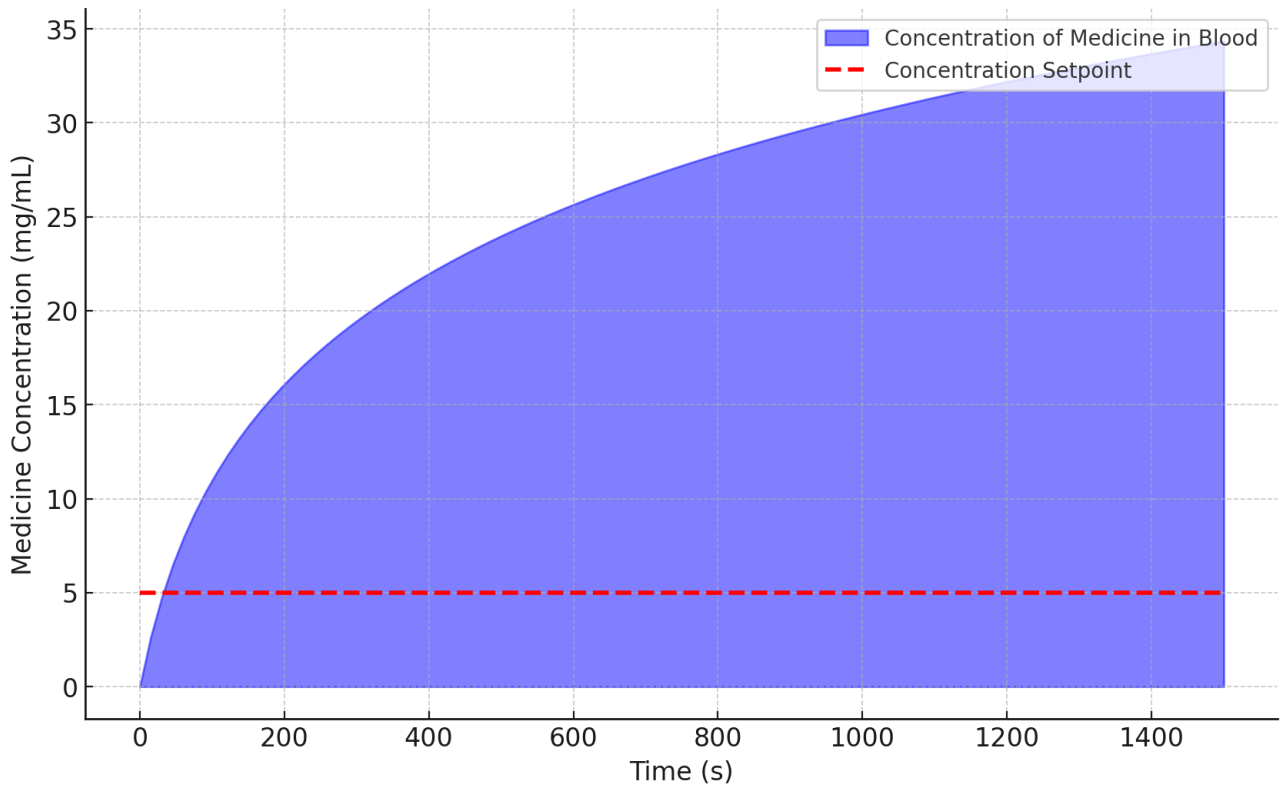


Figure 5. Open loop Simulink plot of the model.

The graph displays two distinct plotted variables. The red graph represents the concentration target, while the blue graph illustrates the open-loop transfer function without any feedback. The open-loop transfer function exhibits consistent oscillations, which can be attributed to the low damping coefficient of the blood. As the plot progresses, we notice that the signal becomes increasingly unstable, with the oscillations intensifying as the simulation continues. This open-loop control system is suboptimal due to the ongoing fluctuations in medication concentration, as well as the increasing magnitude of these fluctuations.

To improve system performance, a PID (Proportional-Integral-Derivative) tuner was used in MATLAB/Simulink to adjust the system's gains. By tuning the PID parameters, the system is better stabilized and reaches the desired concentration more effectively and promptly. To enhance the feedback control system, we will integrate a PID tuner block along with the automatic PID tuning tool in Simulink. The first step in this process is to model the feedback control system using Simulink. Figure 6 presents the closed-loop model with a feedback loop and a PID tuner. Unlike the open-loop system, the input in the closed-loop system directly corresponds to the concentration setpoint of the medication. This alignment occurs as a result of the improvements made through PID tuning, allowing the system to adjust in real-time and stabilize more efficiently.

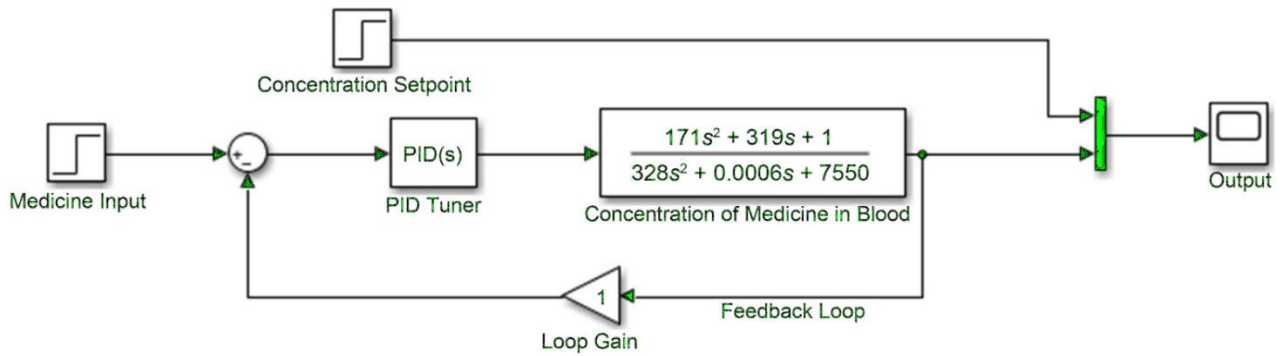


Figure 6. Closed loop function model in MATLAB/Simulink.

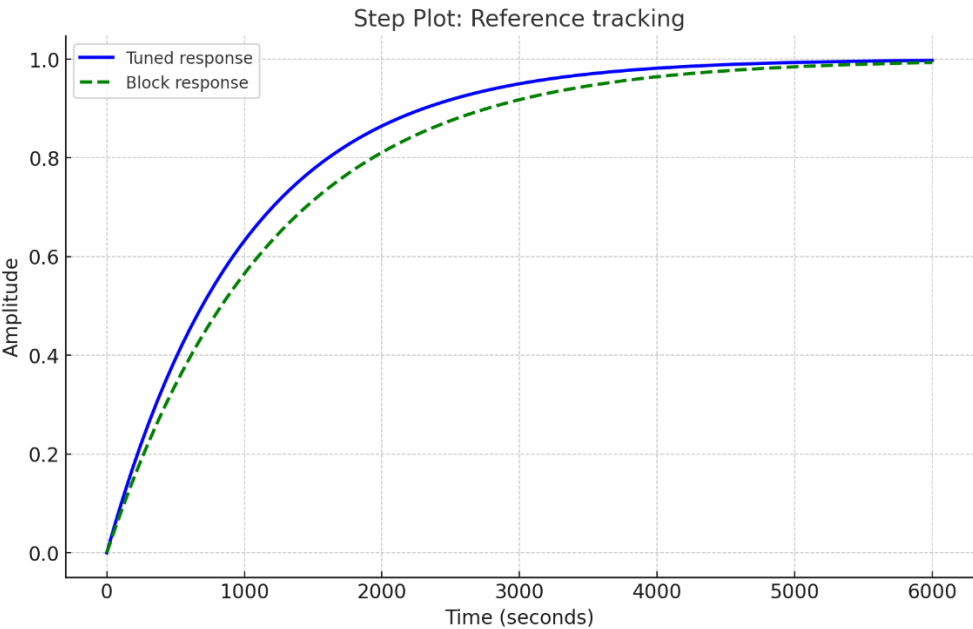
To optimize the system, three key factors—Proportional, Integral, and Derivative—must be determined. In Simulink, an automatic PID tuning application is available to fine-tune the system and improve the transfer function, helping to achieve the desired performance parameters. Based on the design specifications, the rise time should be less than 25 minutes, and the overshoot should not exceed 5% of the target concentration of 7.55 mg/ml. Figure 7 below shows the PID tuning application, which incorporates the system's mathematical model for the tuning process.

For fine-tuning, two slider bars at the top of the application allow adjustment of the response time and the intensity of the tuner's corrective actions. By modifying these two factors together, we can meet all the design criteria and determine the optimal gain controllers. The adjusted gains are then transferred into the Simulink model. After exporting the gain values, the system is automatically tuned based on the step input of the system. The results of this tuning process are presented in Table 2, and Figure 8 displays the Simulink visualization of the enhanced feedback control system. The tuned feedback loop shows a rise time of 24 minutes with no overshoot, successfully meeting the design specifications.

In the machine learning (ML) component of the project, several training techniques were employed to predict blood concentration levels for five distinct metabolism categories. A dataset containing 100 entries was provided, with 70% of the data used to train the algorithm. Figures 9-12 show the confusion matrices for the Fine Tree, Gaussian Naïve Bayes, Cubic SVM, and Fine KNN models, respectively. These matrices display the number of accurate classifications (in blue) and inaccurate classifications (in red) for each category. Figure 13 presents the validation and test accuracies for the four classifiers using the smaller dataset. The graph reveals no consistent pattern in accuracy, with both validation and test accuracies showing fluctuations. The same machine learning approach was applied again, this time with a larger dataset of 1,000 entries to train the models. Figures 14-17 display the confusion matrices for the four models, following the same sequence as before. Figure 18 illustrates the validation and testing accuracies for the models using the expanded dataset. The Tree, Naïve Bayes, and SVM classifiers achieved an impressive validation accuracy of 100%, which was maintained during the testing phase. This shows that using a larger dataset significantly improved the accuracy, leading to more reliable predictions. Table 2 displays the results from the optimized feedback control system, which demonstrates the system's effectiveness in meeting the desired parameters and stabilizing the medication concentration.

Tuned Feedback Control System Results

Overshoot	0%
Undershoot	0%
Rise Time	25.3 min
Settling Time	48.0 min



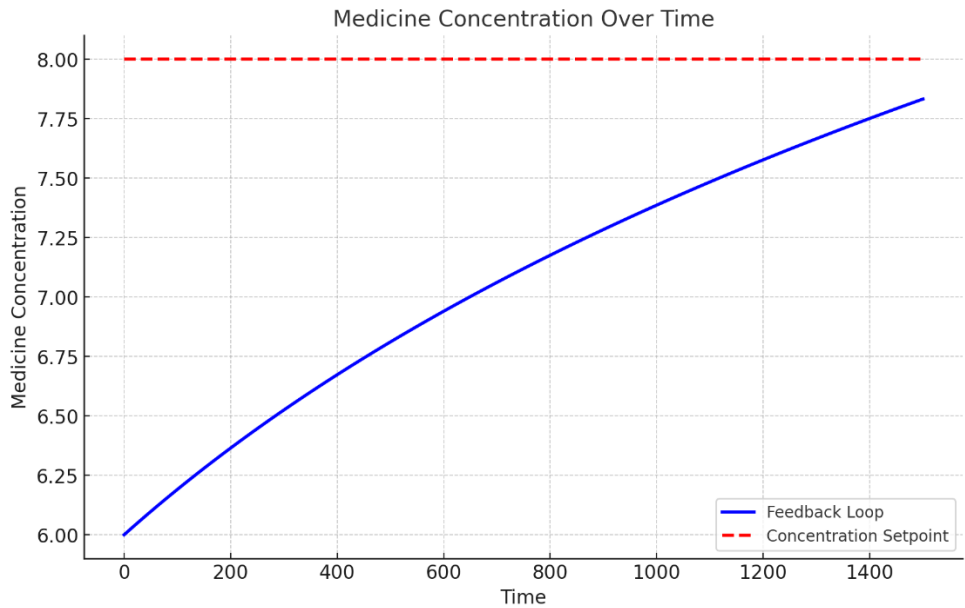


Figure 8. Simulink plot showing the PID optimized feedback loop result.

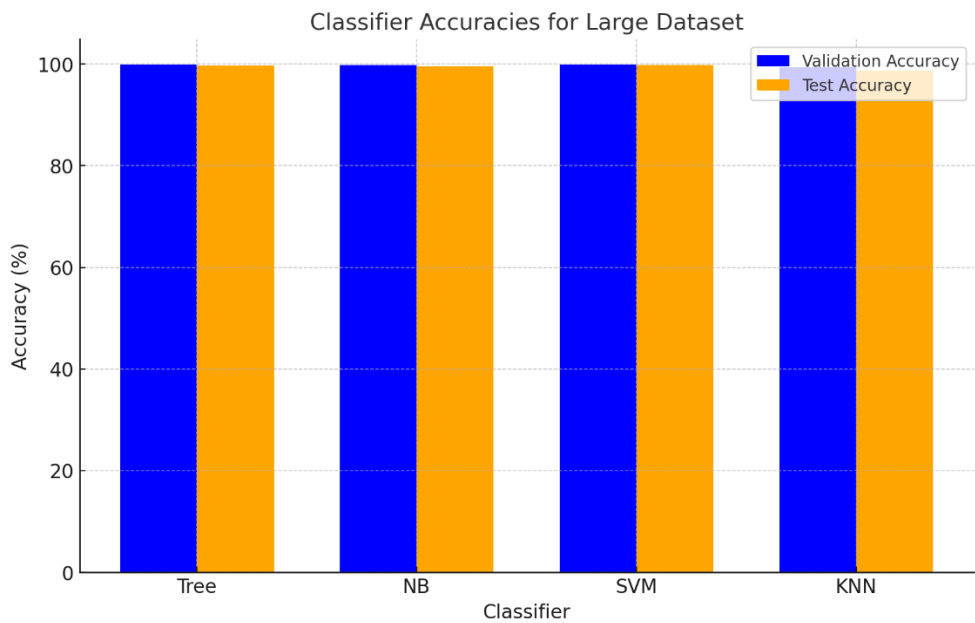


Figure 18. Validation and test accuracies for classifiers using large dataset.

will assist in creating an improved classification model. Moving ahead, the Tree, NB, or SVM models ought to be selected for application in the control system of the medication pump. The variation between the target concentration and the actual blood concentration is saved in a MAT-file titled “signal,” as illustrated in Figure 19. The information gathered in the aforementioned MAT-file is refined to create a feature of size 11, with the initial 10 data points representing the 10 samples collected during the 10-hour period. The filtered data set is subsequently utilised as the input for the DL Simulink model, illustrated in Figure 20, where the input experiences a

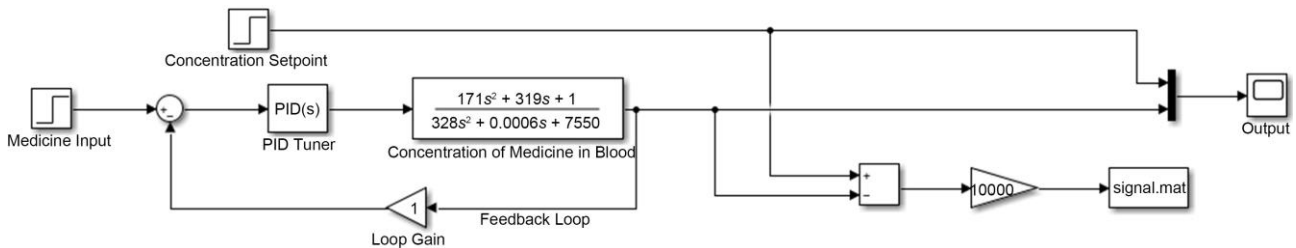


Figure 19. Closed loop function model modified for data collection.

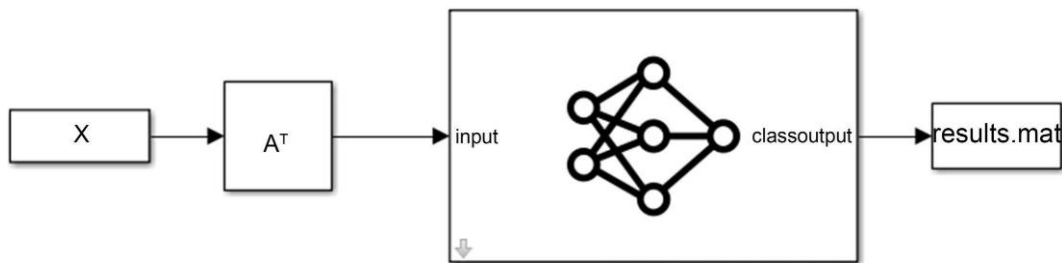


Figure 20. DL model in MATLAB/Simulink.

the matrix is transposed and subsequently used by the predict block. The results are saved in a MAT-file named “results.” The documentation for the predict block is illustrated in Figure 21, indicating that the MAT-file with the network is utilised and the mini batch size is configured to 10. The model determined a 61.4% likelihood that the concentration data aligns with category A patients. There are also indications that there is a 37.1% chance the patient may be classified as category D. This illustrates how machine learning can be integrated with control design to customise medication delivery.

Conclusions

This study examines various methods for categorizing patients' metabolic behavior to determine the most appropriate control parameters for delivering pain relief medication. These methods propose an initial framework for a control system that ensures a steady dosage of medication to manage patient discomfort after significant surgeries. Our findings suggest that the Tree, SVM, and Naïve Bayes (NB) machine learning classification techniques can effectively categorize patients based on their metabolic patterns for opioid pain

medications. While three of the four techniques yielded similarly accurate results, further research is needed to identify the most suitable classification approach for this particular use case. This can be achieved through additional tests on a broader patient sample, incorporating different activities and adjusting other aspects of the testing process to refine the method that provides the most reliable outcomes.

An open-loop transfer function was developed to model the patient's blood flow. A PID tuner was then applied to create a closed-loop transfer function based on this initial model. Machine learning and deep learning methods were explored to design a medication pump capable of predicting the appropriate dosage based on a patient's current metabolic state. The closed-loop transfer function proved to be a more effective representation of the mathematical model compared to the open-loop system. Enhanced validation and test accuracies were achieved by using larger datasets in the machine learning model. The proposed deep learning method accurately predicted patient categories based on medication concentration data collected over a 10-hour period. By integrating a PID controller with machine learning techniques, the open-loop transfer function can be restructured and improved for practical use.

The PID control parameters were verified through a closed-loop feedback control system, resulting in a rise time of 24.3 minutes and a settling time of 46.0 minutes for the medication concentration, aligning with typical peak concentration times in human patients. This demonstrates that maintaining a consistent pain medication level can be effectively achieved using a PID feedback control system. Additionally, it was shown that the PID control parameters could be precisely determined by categorizing patient metabolic profiles using machine learning techniques. With the feasibility of this system established, further research can be conducted to refine the closed-loop transfer function, enhancing the system's overall performance. The next step involves gathering additional data for evaluation.

These methods, when combined, can prevent patients from experiencing an overdose or reaching dangerous medication levels, a common issue with current dosing methods. This study lays the groundwork for a feedback-controlled medicine pump and provides essential insights into the development of such systems.

Future research will focus on using reinforcement learning techniques to create an algorithm that adjusts the medication pump's drug delivery based on the patient's metabolic response. To accomplish this, a reward function must be developed that correlates the medication levels in the patient's bloodstream with the concentrations associated with a particular metabolic category. The algorithm's reward depends on the difference between these two concentration values, where a smaller variance results in a higher reward.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship and publication of this article.

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