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Evaluation of medical grade infusion pump parameters using Gaussian Process Regression

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Abstract

Prediction techniques are extensively used in medical applications and health devices. The prediction of the infusion flow rate and its speed in a smart wireless infusion pump is necessary to provide precise drug flow. This paper has developed the prediction model to predict the lag time and infusion pump speed using the Gaussian process regression (GPR) technique with a squared exponential kernel. The present smart wireless infusion pump is usually incorporated with its smart drug library. The required parameters such as drug dosage, drug flow rate are utilized as inputs to predict the pump speed, minimize start-up delays using proposed regression techniques. The evaluation of prediction models is done by the coefficient of determination (R^2), mean absolute error (MAE), and root-mean-squared error (RMSE). These prediction results are verified for predicting lag time and infusion pump speed for two different carrier flowrates, 10 ml/hr, 50 ml/hr. The study's outcome indicates that the regression model GPR has better prediction accuracy with a mean coefficient of determination of 0.99. Hence, the GPR technique can achieve quick infusion speed with minimized lag time, the optimal flow rate for smart infusion pumps.

Keywords: GPR, start-up delay, prediction, smart drug library.

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1. Introduction

Significant improvement in the medical field has developed smart medical devices for the health care system. Smart drug delivery devices are one among them. Smart infusion pump usage relies on the different categories available. The syringe infusion pump, portable infusion pump, an ambulatory infusion pump are based on the mechanism adopted for each device [1]. The flow rate of these medical devices is based on pressure variation, motor movements, a revolution of the peristaltic pump and rotary pumps. Controlling these actions is essential to deliver the required drug dosage for the patients. The patients can be in the hospital or home. The usage of pumps varies as per the requirement for the patient. It can be used for dialysis, chemotherapy, infusion of nutrients, saline, anaesthesia, blood infusion for cardio-related issues [2]. For all types of medical pumps, the usage and concept of the actuation to obtain a precise infusion of the fluid with the required flow rate are essential. Significant improvement in information technology, electronics, communication has led many to undergo research in all the fields with these growths [3]. Physiological control systems with medical devices to enable interoperability, network connectivity, safety measures are vital [4]. The integration of artificial intelligence, such as prediction techniques, fuzzy logic, etc., with control system concepts for smart medical devices is gaining popularity [5]. Predictive optimal control can be achieved and ensures safety for the patient [6]. The utilization of smart medical pumps

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includes drug administration, pumping of blood, administration of anaesthesia [7]. Research has been handled to estimate blood flow rate in blood pumps using the Gaussian process regression model and estimate viscosity, and a pressure difference is concentrated [8]. The drug parameters such as coefficient of viscosity and ambient temperature impact the flow rate in an infusion pump. A comparison on temperature variation, viscosity for continuous infusion of FOLFOX6 and FOLFIRI for chemotherapy patients has been performed. It is inferred from this study that duration of the drug concentration and infusion is based on the coefficient of viscosity and temperature changes [9]. The analysis for this study was performed with the regression methods. In addition to this, research on the impact of viscosity, volume of infusion on subcutaneous and the tolerance of the pain is analysed [10]. For patients with type I diabetes, a control algorithm for insulin dosage to maintain blood glucose level is carried with a hybrid approach named backstepping sliding mode Gaussian controller [11]. The modelling and control of the infusion pump are designed for anaesthesia based on the pharmacokinetic representations. The depth of anaesthesia is regulated using optimal control and model predictive control strategies. The authors focused on the mathematical model of the insulin infusion pump and synthesized optimal parameters for meal bolus calculation [12], [13]. The approach was evaluated for optimization of usage of pump-related parameters. The drug flow rate is calculated as per the type of pump used for each medical application. Research work on different pump actuation mechanisms has been carried out [14], [15].

Effective fluid actuation is attained by proper selection, pumps, valves, reservoirs, and catheters. The pump and its technology should be selected based on its usage and should minimise drug alterations [16]. In recent times, the micropumps design has made it suitable for implantable systems. Peristaltic rotary pumps are built for precise drug delivery, with low voltage actuation, easy sealing, and minimal impact on fluid properties. Study and analysis on the pump performance for rotational speed, lag time which leads to minimized start-up delay, are carried out. In this study, two different pump designs with variation in rollers, the angle between rollers are regulated to perform accurate drug delivery about the operating speed and time duration.

The smart infusion pump is designed with a suitable pumping actuation unit, microcontrollers to activate the fluid dispensing with the aid of software. The software triggers the hardware with the smart drug library, its template, and algorithms associated with it [17]. In ICUs and the hospital environment, the patient dosage requirements, health records are maintained as electronic health records in a secured manner. This is enabled by utilizing wireless-enabled medical devices, and the information is stored in a web server located remotely [18]. This framework assists the nurses to handle each patient as per the need. These days smart medical equipment can perform the desired process by integrating patients, nurses' stations, remote servers, and physicians [19]. Detection of a malicious attack on the automated insulin pump to avoid overdosage has been examined using regression techniques and supervisory learning methods [20]. The implementation of prediction, regression techniques are widely implemented in the medical sector in different directions. The focus towards handling physiological time-series signals is handled by the Gaussian multitasking process (MTGP) [21]. For radiotherapy and patient monitoring, results from the MTGP model are compared with other machine learning methods. It is demonstrated that gaussian methods provide better results in terms of statistical performance. The utilization of machine learning algorithms such as K-Nearest Neighbour, Support Vector Machines are used for accurate decision, the anticipation of opioid infusion rate as per analgesia nociception index in general anaesthesia [22]. Several prior types of research were carried out on the design, modelling, and control of smart infusion pumps using relevant techniques. The prediction and classification using different ANN, Machine learning, fuzzy logic techniques solely and in hybrid are implemented [23]. The literature illustrates that the infusion pump parameters are critical for the drug delivery, blood infusion for the patients using its specified hardware and smart drug library incorporated [24].

In this paper, the verification of statistical parameters using regression methods such as GPR and optimized GPR is modelled for the smart infusion pump. The parameters such as speed of the pump, lag time, infusion flow rate are considered. The prediction of lag time is essential as it relates to the start-up delay. Lesser the start-up delay, the faster the infusion, and it can be achieved by accurate actuation of the speed of the pump employed with the motor [25].

2.Materials and methods

The tremendous improvement of computational methods leads to a focus on implementing prediction, control, modelling techniques for smart infusion pumps. The smart infusion pumps used nowadays can be used in different ways for several medical applications [26]. These devices are designed with a smart drug library with the required database placed in the local or remote server. Literature leads with evidence that the drug library template is built with the drug name, dosage information, infusion flow rate, the concentration of the drug, dosage units, hard and soft alarm limits [27]. In this paper, an enhanced smart drug library template has been considered for several drugs: carrier flow, lag time, speed of the infusion pump for the drug dosage, and its infusion flow rate. The enhanced smart drug library has been developed based on the drug information available on the website eMC (electronic Medical Compendium). A synthetic dataset of drug libraries is created for 7 different drugs with a range of drug dosage and concentration. In the dataset, the total infusion flow rate, lag time, speed of the infusion pump for the specific condition of gear position with 10 rev/min is considered for the calculation. The lag time for the smart pumps is calculated as

$$Lag\ time = {V_d}/{Q_t} \tag{1}$$

where V_d is the dead volume and Q_t is the total infusion flow rate.

The total infusion flow summarises carrier flow rate (Q_c) and drug flow rate (Q_d).

Data set of the drug dosage, its flow rate in terms of ml/hr for the adults weighing averagely 60 kgs, and Q_c of 10ml/hr and 50 ml/hr is considered. Based on (1), the lag time for the device

is calculated with the dead volume of 1.5 ml/hr. Further, the speed of the pump is obtained as per the motor's rotational speed and the number of gears. The calculations will vary to control the speed of the pump according to the different types of motors employed, the number of gears used.
the speed of the infusion pump θ_i with its flow rate Q_t is calculated as

$$\theta_i = Q_t \times 10 \text{ rev/ml} / 60 \text{ min/hr} \quad (2)$$

From equations (1) and (2), it is significant that θ_i is inversely proportional to lag time, and hence if the speed of the infusion pump is controlled, the infusion flow rate is ensured with minimum lag time for an infusion pump.
The methodology followed in this paper is shown in figure 1. The concept considered is applicable for the continuous and intravenous infusion of IV fluids.

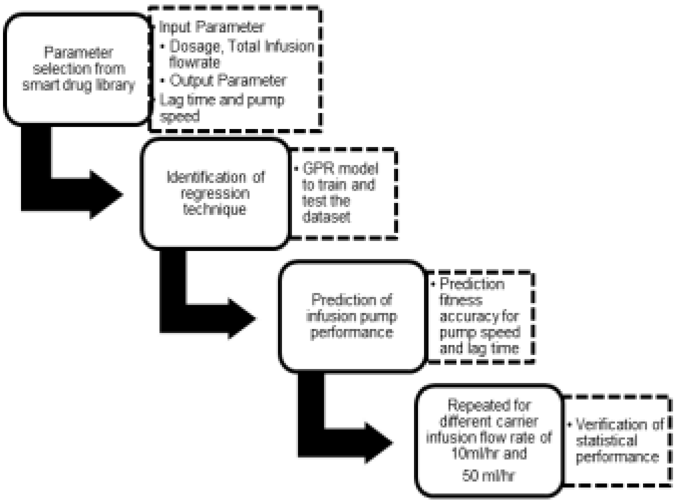


Figure 1. Graphical representation of the proposed method.

The popular machine learning technique GPR is used to model the system parameters in forecasting the speed, the lag time for the dosage to be delivered. The statistical parameters are verified for the proposed enhanced drug library data set. The optimization, training, verification of results is carried out using MATLAB.
The analysis based on the different studies has been performed.
Study 1: Initially, dosage, flow rate as input is considered to forecast pump speed.
Study 2: For the same set of inputs as in study 1 is considered, the output parameter is lag time.
Study 1 and 2 is performed for Q_c values 10 ml/hr and 50 ml/hr.
The GPR model and optimized GPR implemented for both the conditions and are discussed below.

2.1 Gaussian process regression

The Gaussian process is a machine learning regression model widely used to predict the expected values of a given model as per the input data. This regression model can be employed for multivariable parameters. GP models are implemented for several applications and used in health care for single input or multiple input modes. In general, this model is a Bayesian modelling technique used as classification, regression, and dimensional reduction process [28]. GPR has the advantage that functional behaviour to prior information can be expressed. GPR is preferred in this work to forecast the required output when noise or external disturbance occurs [29]. In smart infusion possibility of the noise will be based on the measurement noise or other internal disturbances. In this approach, the influence of the input variables varies the lag time and speed, and hence the focus is to predict the optimal speed of the pump and reduced start-up delay even noise prevails. In this scenario, the Gaussian process is preferred. The important component of GPR is a kernel. Several kernel functions are available, and each has its significance.

A Gaussian process (GP) is defined with its probability distribution functions for the range of input variable x as:

$$f(x) \sim gp\left(m(x), k(x_i, x_j)\right) = N\left(m(x), k(x_i, x_j)\right) \quad (3)$$

where $m(x), k(x_i, x_j)$ are the mean and covariance function with i,j indicates inputs in a given dataset and smart drug library input for a finite set of input dosage concentration it is gaussian as the resultant of the infusion pump is susceptible to the process noise.
The component here is the choice of the covariance function, which is also called a kernel. Different kernels available are squared exponential, Matern, rational quadratic. In this work, squared exponential is considered because the fitness values and the accuracy are better when compared to other kernel functions [30].
The squared exponential kernel is given as

$$k(x_i, x_j) = \theta_k^2 \exp\left(\frac{1}{\theta_l^2}\|x_i - x_j\|^2\right) \quad (4)$$

where θ_k, θ_l are scaling parameters of y and x, respectively. Once the kernel function is defined, the regression computation is performed with the kernel, and the prediction of the dependent variables is obtained [31]. The prediction accuracy is checked by calculating the coefficient of determination R^2, Root mean square error, mean square error and mean absolute error. Further, the GPR kernel is combined with a Bayesian optimizer which minimizes the cost function.

Steps followed:

1. Identify the x, y data set
2. Selection of kernel
3. Execute the GPR with prior parameter
4. Simulate to predict the y data set with optimization and without optimization method
5. Verification.

The prediction of y values for Q10 (Q_c=10ml/hr) and Q50 (Q_c=50ml/hr) is verified for GPR without Bayesian optimizer and with Bayesian optimizer.

3. Results

3.1 Performance of GPR

The paper is intended to investigate the impact of prediction errors for smart infusion pump speed and lag time for different carrier infusion rates at 10 ml/hr and 50 ml/hr. The input dosage, total carrier flow rate for predicting speed and lag time as output using the GPR model. The verification is obtained for two different studies based on the carrier infusion flow rates.
The verified statistical performance parameters are listed in table 1 and table 2. In table 1, the GPR with exponential kernel and an optimized GPR approach to predict pump speed output for the carrier flow rate of 10 ml/hr and 50 ml/hr. From the predicted infusion pump speed data trained, it is observed that R^2 is 1, which is required for a better regression model. Further, the obtained error values are lesser when GPR is employed. The error values are obtained as per the required prediction accuracy. Similarly, the statistical parameters are found for the lag time for 10 ml/hr and 50 ml/hr carrier flow rate, as shown in table 2.

Study 1: The predicted output – speed

Using GPR regression and variation of GPR with Bayesian optimizer is shown to predict the infusion pump speed with performance attributes. The prediction of the infusion pump speed is significant for a smart infusion pump as the precise flow of the drug and fluid will be delivered appropriately to the patient.

Table 1. Study 1- Statistical performance of infusion pump speed

Regression method	Carrier flow rate	RMSE	R^2	MSE	MAE
GPR with exponential kernel	10 ml/hr	0.0038	1	1.479 $\times10^{-7}$	8.28 $\times10^{-5}$
	50 ml/hr	0.00046	1	2.177$\times10^{-7}$	9.18$\times10^{-5}$
Optimized GPR with exponential kernel	10 ml/hr	0.00038	1	1.473 $\times10^{-7}$	8.29 $\times10^{-5}$
	50 ml/hr	0.00565	1	3.19$\times10^{-5}$	0.00115

The prediction and residual responses verified for infusion pump speed using GPR models for the carrier flow rate of 10ml/hr and 50 ml/hr are shown in figure 2. The residual responses signify the true error between the true and the predicted speed (output). The correlation for the predicted output is better in the responses, which is scattered around zero with a better distribution factor in both the GPR models evaluated.

Study 2: The predicted output – lag time

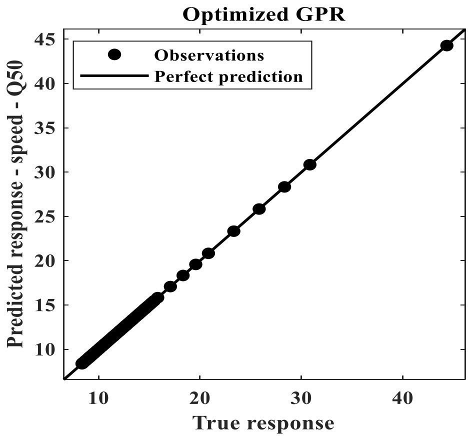
The appropriate infusion of fluid to the patients can be made possible when the start-up delays are reduced in the smart infusion pump. The important criteria to have minimized start-up delay for an infusion pump is identifying and predicting lag [illegible]ed for two different carrier flow rates for the corresponding dosage and infusion flow rate. Two different carrier flow rates are identified as in many situations when the patient undergoes chemotherapy, multiple infusion is administered. In multiple infusion start-up delays, lag time is prominent, and hence the prediction of lag time is essential. The statistical parameters are analysed using GPR models and tabulated in table 2. Further, the GPR model with different kernel variants is applied, and prediction of the lag time is performed for the set of dosages for the drug data set identified from the eMC website. The predicted and residual responses are shown in figure 3, which signify the relationship with predicted output lag time and thus the prediction accuracy.

Table 2. Study 2 - Statistical performance of infusion pump's lag time

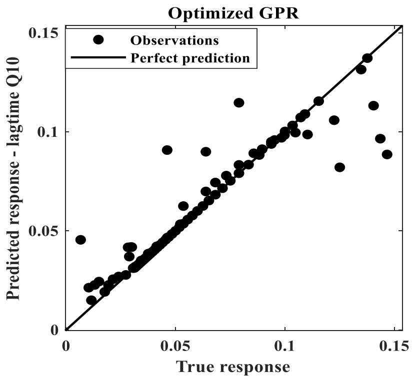
Regression method	Carrier flow rate	RMSE	R^2	MSE	MAE
GPR with exponential kernel	10 ml/hr	0.0157	0.81	0.00246	0.00657
	50 ml/hr	0.00132	0.94	1.75$\times10^{-6}$	0.000612
Optimized GPR with exponential kernel	10 ml/hr	0.0136	0.86	0.000185	0.00605
	50 ml/hr	0.001147	0.96	1.317$\times10^{-6}$	0.000516

3.2 Prediction response

The prediction responses between the true variable and predicted variable, such as speed of infusion pump and lag time for carrier flow rate 10ml/hr (Q10) and 50 ml/hr (Q50), are verified. The responses for lag time are shown in figure 2. The predicted response is better in the case of optimized GPR in both studies.



(a)



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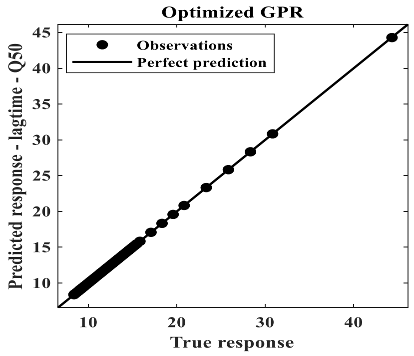
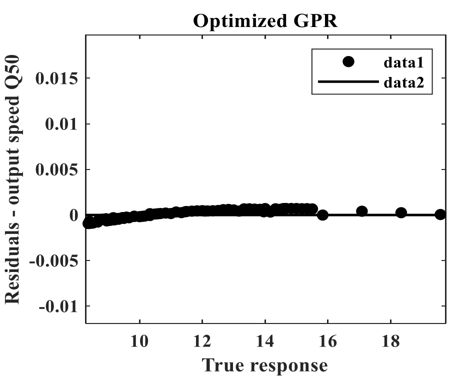


(c)

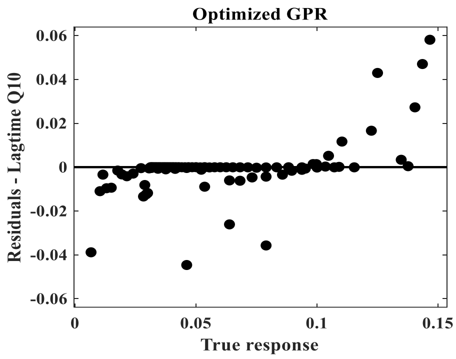
Figure 2. Prediction of infusion speed (a) and lag time (b), (c) for Q10 and Q50

3.3 Residual responses

The minimization of the error between the true variable and the predicted variable can be observed from the residual output. The residues have to be around zero to obtain a better distribution factor. From figure 3, it is apparent that the error is minimum. The minimized error results as the regression model used are GPR. The GPR model with the exponential kernel is better for the smart infusion pump to reduce start-up delay with speed and lag time predictions. The residual results obtained are shown in the figure below for two variants of the GPR model for both the studies considered in this work.



(a)



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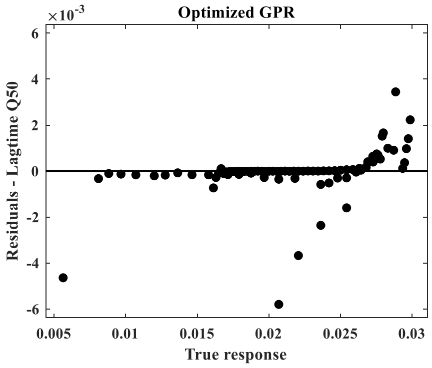


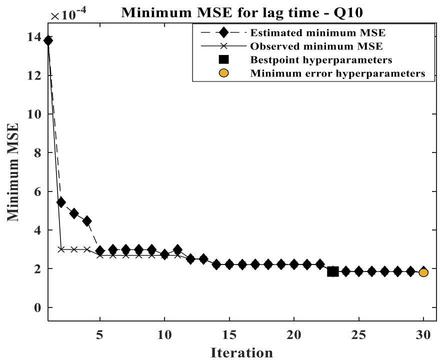
(c)

Figure 3. Prediction accuracy of infusion speed (a) and lag time for Q10 (b), Q50 (c) with residuals

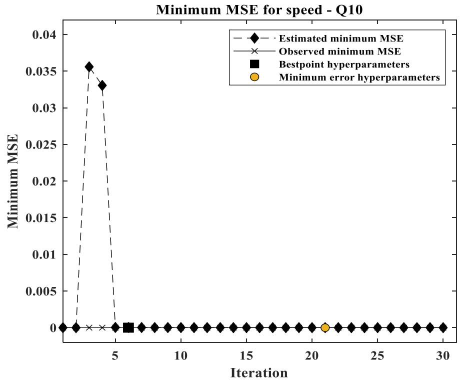
3.4 Optimized minimum MSE

The best fit of the lag time and speed for the infusion pump based on the smart drug library has been verified by identifying the minimum MSE. The minimum MSE can be achieved by selecting an optimizer that selects the best and minimum error hyperparameters. In this work, a Bayesian optimizer is used to perform this [32],[30]. Based on the hyperparameter values, the balancing of variance is found, and the model will not be overfitted or underfit. Figure 4 shows the optimized resultant for few iterations. The minimum MSE for both the studies with different carrier flow rates Q10 and Q50 are shown.

The optimization of MSE is indeed needed as the performance of the smart infusion pump is solely dependent on the speed of the infusion pump. In the proposed work, GPR and the optimized GPR show better results in terms of prediction accuracy statistically. To obtain these results statistically, it can be correlated with the minimization of MSE with a better regression model. The lag time's hyperparameter for Q10 and Q50 is 0.000185 and 1.317×10^{-6}. Similarly, the pump speed hyperparameter for Q10 and Q50 is 2.17×10^{-7} and 1.47×10^{-7}. Further, the relationship between the predicted lag time, speed for the required infusion flow rate is shown in figure 5.



(a)



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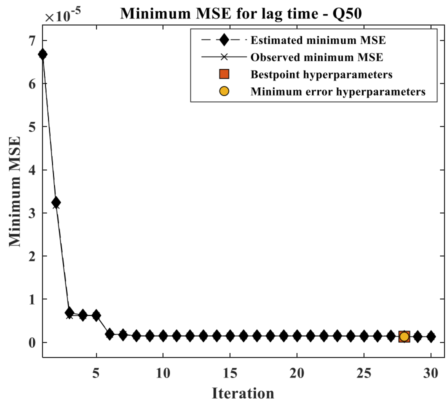

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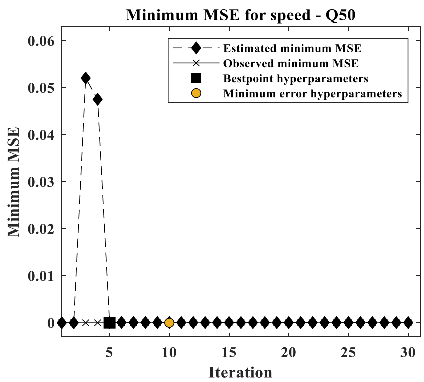

(d)

Figure 4. Optimized MSE of (a) Q10 lag time, (b) Q10 speed, (c) Q50 lag time and (d) Q50 speed.

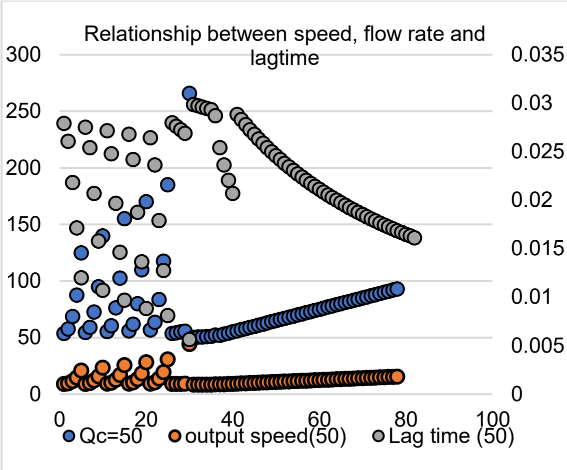

Figure 5. Relationship between the infusion pump speed, lag time and flow rate.

4. Discussion

The GPR model considered here can be used for a smart infusion pump that can be implemented as a standalone device or a wireless smart infusion pump. The smart library and its algorithm can follow these machine-learning regression techniques to forecast the desired speed and lag time. Hence, the start-up delay and time infusion of the drug fluid will be delivered to the patient. The results of performance indices of the regression model are iterated for many drug datasets. The correlation coefficient for carrier flow rate of 10 ml/hr in GPR, optimized GPR are 0.81, 0.86 while RMSE is 0.157, 0.0136 and for 50 ml/hr it is 0.94, 0.96 and RMSE is 0.00132, 0.00114 for predicting lag time. Similarly, the performance indices are identified in predicting the infusion pump speed with the R^2 value as 1 for 10 ml/hr while RMSE is 0.0038. Further, the R^2 values are 1 for 50 ml/hr, and RMSE is 0.00046, 0.00565 for both variants of the GPR model.

5. Conclusion

This paper proposed the concept of providing the required dosage for the patient with a smart infusion pump. The system's performance could be verified for its quick infusion pump speed and minimum lag time to reduce start-up delay. The smart pump's reliability depends on the predicted speed, the lag time for the specified dosage, total infusion rate with carrier flow rate for a different drug. The prediction is performed using GPR regression for the infusion pump, wherein it is feasible to implement continuous infusion of fluid for different pumping mechanisms. The pumping actuation of the infusion pump can be controlled using different control algorithms. The perception of this work to provide a better regression model using pump-related parameters for stable continuous infusion for different carrier infusions. The proposed study results are obtained for carrier infusion rate of 10ml/hr, 50 ml/hr. This is performed by predicting the required output parameters of the smart infusion pump for the specific volume of the drug dosage. The statistical performance indices obtained in this study indicate that the mean coefficient of determination is 0.99, and the average root mean square errors are less. The fitness response, a residual response, is better. The result indicates that the performance of GPR is preferable for the smart infusion pump when used with the primary or secondary infusion.

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