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RBF kernel based support vector regression to estimate the blood volume and heart rate responses during hemodialysis

Faizan Javed, Gregory S. H. Chan, Andrey V. Savkin, Paul M. Middleton,
Philip Malouf, Elizabeth Steel, James Mackie and Nigel H. Lovell

Abstract— **This paper uses non-linear support vector regression (SVR) to model the blood volume and heart rate (HR) responses in 9 hemodynamically stable kidney failure patients during hemodialysis. Using radial bias function (RBF) kernels the non-parametric models of relative blood volume (RBV) change with time as well as percentage change in HR with respect to RBV were obtained. The ϵ-insensitivity based loss function was used for SVR modeling. Selection of the design parameters which includes capacity (C), insensitivity region (ϵ) and the RBF kernel parameter (σ) was made based on a grid search approach and the selected models were cross-validated using the average mean square error (AMSE) calculated from testing data based on a k-fold cross-validation technique. Linear regression was also applied to fit the curves and the AMSE was calculated for comparison with SVR. For the model based on RBV with time, SVR gave a lower AMSE for both training (AMSE=1.5) as well as testing data (AMSE=1.4) compared to linear regression (AMSE=1.8 and 1.5). SVR also provided a better fit for HR with RBV for both training as well as testing data (AMSE=15.8 and 16.4) compared to linear regression (AMSE=25.2 and 20.1).**

I. INTRODUCTION

Hemodialysis is regarded as a life sustaining therapy for kidney failure patients. It removes the excess fluid accumulated in the patient's body using the process of ultrafiltration. Despite technological advances in the development of devices that can continuously monitor the hemodynamic state of patients during hemodialysis, the under-lying complications due to progressive reduction in blood volume are still not fully understood. In modern hemodialysis machines, devices to continuously measure the hemoconcentration of blood constituents are usually employed, allowing the indirect estimation of relative blood volume (RBV) change [1], [2]. Previous studies generally showed a decreasing trend in RBV [3], [4] which reflected the effect of fluid removal on the circulating blood volume.

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Faizan Javed, Gregory S. H. Chan and Andrey V. Savkin are with the School of Electrical Engineering and Telecommunications, The University of New South Wales, Sydney, NSW, 2052, Australia (phone: +61 (2) 9385 6359; fax: +61 (2) 9385 5993). faizan@student.unsw.edu.au; [gregchan,a.savkin]@unsw.edu.au

Paul M. Middleton, Philip Malouf, Elizabeth Steel and James Mackie are with the Prince of Wales, Hospital, Sydney, NSW, 2031, Australia pmmiddleton@ambulance.nsw.gov.au, p.malouf@UNSWalumni.com,lizsteel@yahoo.com.au, James.Mackie@sesiahs.health.nsw.gov.au

Nigel H. Lovell is with the Graduate School of Biomedical Engineering, The University of New South Wales, Sydney, 2052, NSW, Australia N.Lovell@unsw.edu.au

In order to maintain the stability of patients during fluid removal, compensatory responses that include peripheral sympathetic vasoconstriction and modest heart rate (HR) increase are believed to play an important role [5], [6]. A study by Krepel [7] has found a weak but significant linear correlation between the reduction in RBV and the HR increase in stable patients during hemodialysis. However we believe that during hemodialysis the HR shows a non-linear response, as the patient goes from a state of hypervolemia to normovolemia or mild hypovolemia. To accurately model this non-linear HR response a more sophisticated non-linear curve fitting technique is required compared to a simple linear regression. In this paper, we propose a non-linear curve fitting approach known as support vector regression (SVR) to assess the RBV and HR responses during the course of hemodialysis. SVR is an efficient non-parametric non-linear regression technique based on support vector machines which was first introduced by Vapnik [8]. SVR has recently been applied in the biomedical field to model the heart rate response to various workloads during treadmill exercise [9], [10] and to assess the non-linear cardiovascular response to metabolic demand during cycle exercise [11].

To our knowledge, this is the first study to model the response of RBV and HR during hemodialysis using support vector regression. We applied SVR to model the response of RBV with respect to time as well as the percentage change in HR to RBV in hemodynamically stable patients during hemodialysis with ultrafiltration. A Radial Bias Function (RBF) kernel was used to model these two responses with the SVR parameter selection based on a grid search approach. The selected models were tested using a k-fold cross-validation technique. These modeled curves can be used as a reference response for stable patients undergoing hemodialysis and can be utilized to monitor the stability of patients as any deviations from these generalized curves can give an early indication of complications in the patients. They can also be utilized in designing feedback control systems to guide the actual changes in RBV and HR by automatically adjusting the input variables.

II. MATERIALS AND METHODS

This study was conducted at the hemodialysis unit, Prince of Wales Hospital, Sydney, Australia. A group of 12 hemodynamically stable renal failure patients with no symptoms of intradialytic hypotension for the last three months were asked to participate in the study. All patients were routinely dialyzed three times weekly for 4-5 hours. All patients

were dialyzed using an AK200S (Gambro, Lund, Sweden) machine with a polyflux 210H (Gambro, Lund, Sweden) dialyzer. The blood flow rate ranged from 300-350 ml/min, the dialysate flow rate was 500 ml/min and the dialysate temperature was set at 36^{o}C. The physical characteristics of the patients included in this study are represented as mean $\pm$ standard deviation and are given as: subjects (n=12), age in years (66 $\pm$ 11), height in cm (164 $\pm$ 10), length of time on dialysis in months (13.3 $\pm$ 8.5), dialysis duration in hours (4.55 $\pm$ 0.42), pre-dialysis weight in kilograms (89.3 $\pm$ 20.5), post-dialysis weight in kilograms (86.3 $\pm$ 20), and fluid removed in litres (3 $\pm$ 1.2). The sydney area health service human research ethics committee gave their approval in the study and an informed consent was obtained before the data collection.

The participating patients were asked to arrive in the dialysis unit around 15 minutes before the start of the routine dialysis time. After an initial rest of 5 minutes, the data recording was started while the patient rested in a semi-recumbent position on the dialysis chair. Continuous ECG was measured in lead II configuration using a bio-amplifier (ST4400, ADInstruments, Sydney, Australia) and was digitized at a sampling rate of 1000 Hz using a Powerlab data acquisition system (ADInstruments, Sydney, Australia). RBV was monitored throughout dialysis at 10 minutes intervals using a blood volume sensor (BVS) embedded into the dialysis machine. The BVS uses an ultrasonic device to measure the blood density. RBV was displayed as the percentage change relative to the start of dialysis calculated by the following formula:

$$RBV_t(change\ in\ percentage) = [\frac{Ht_t}{Ht_0} - 1] \times 100 \quad (1)$$

where Ht_0 is the hematocrit at the start of dialysis and Ht_t is the hematocrit level at time t during hemodialysis. Synchronous to each RBV measurement, a 4 minute segment of ECG was selected and mean HR was calculated by taking the inverse of RR interval using an R-wave peak detection algorithm, which involves low-pass filtering, differentiation, and threshold peak detection.

III. MODELING

A. Support vector regression

The SVR technique is based on a support vector machine (SVM), which was first introduced by Vapnik in 1995 and is firmly grounded in the framework of statistical learning theory or Vapnik-Chervonenkis (VC) theory [12]. The basic idea is to map the input data into a high dimensional feature space using non-linear mapping and then a linear regression problem is obtained in the feature space. A detailed theoretical background of SVR can be found in [12]. However in this section a brief overview of ϵ-insensitivity SVR based modeling is given [9].

Consider a training data set of input vector $\{x_i\}_{i=1}^N$ along with corresponding output vector $\{y_i\}_{i=1}^N$ where N is the number of data points. Support vector regression aims to find a function $f(x)$ that has at most ϵ deviations from the actually obtained targets for all the training data and is as flat as possible. The function has the following form:

$$f(x) = \langle \omega, \phi(x) \rangle + b \quad (2)$$

where $\langle\rangle$ is the dot product and $\{\phi(x_i)\}_{i=1}^N$ represents the high-dimensional feature spaces which are non-linearly transformed from x. The coefficients ω and b are estimated by minimizing the regularized risk function:

$$R(\omega) = \frac{1}{2}\|\omega\|^2 + C\frac{1}{N}\sum_{i=1}^{N} L_\epsilon(y_i, f(x_i)) \quad (3)$$

The first term $\frac{1}{2}\|\omega\|^2$ is the regularized term that is used as a flatness measurement of $f(x)$, C is a fixed constant determining the tradeoff between the training error and the VC dimension of the model, and L_ϵ is the ϵ-insensitivity loss function defined as:

$$L_\epsilon(y_i, f(x_i)) = \begin{cases} |y_i - f(x_i)| - \epsilon & |y_i - f(x_i)| > \epsilon \\ 0 & otherwise \end{cases} \quad (4)$$

This defines an ϵ-tube. The radius ϵ of the tube and the regularization constant C are user defined. The parameter ϵ controls the width of the ϵ-insensitive zone, used to fit the training data.

By solving the above constrained optimization problem, we have:

$$f(x) = \sum_{i=1}^{N} \beta_i \phi(x_i) \cdot \phi(x) + b \quad (5)$$

where the coefficients β_i corresponds to each (x_i, y_i) and is non zero only for a small subset of the training data named as support vectors. In SVR, by only using the support vectors, the same solution can be obtained as using all the training data points.

A kernel function can be introduced to estimate the inner product in feature space, this way all the computations can be performed directly in the input space. By using the kernel function: $k(x_i, x_j)$, the above equation can be written as:

$$f(x) = \sum_{i=1}^{N} \beta_i k(x_i, x) + b \quad (6)$$

For nonlinear SVR, a number of kernel functions have found to provide good generalization capabilities, such as linear, polynomial, radial basis function (RBF) and sigmoid. In this paper, we have used the RBF kernel to model both the change in RBV with respect to time as well as HR response to RBV during hemodialysis. The RBF kernel is given by:

$$k(u, u') = \exp(-\frac{\|u - u'\|^2}{2\sigma^2}) \quad (7)$$

A brief introduction of SVR can be found in [12], [8], [9]. Details about the selection of radius ϵ of the tube, kernel function and regularization constant C can be found in [13], [8].

B. Parameter selection and model verification

The modeling was based on 9 out of 12 patients with similar RBV and HR profile during the course of hemodialysis. The other three patients were excluded from the modeling as they all had a decreasing trend in heart rate. One patient was hypertensive at the start of dialysis and her blood pressure kept high throughout dialysis while other two had fluctuations in RBV with a total drop of only 5% by the end of dialysis.

To select the best optimized parameters for SVR and to verify the model, a grid search was combined with a k-fold cross-validation technique. For cross validation, the selected data set of nine patients was divided into 3 sections. Two sections served as training set and the third section was used to test the model. The test section changed for the next iteration so after three iterations of testing and training, each sample was tested once.

A grid search approach was used to choose the best combination of SVR parameters. First the range of parameters C, σ, and ϵ was specified. The selected parameter ranges were C (1, 50, 500, 5000), σ (2, 10, 50, 100, 200, 300, 500) and ϵ (1, 1.5, 2, 2.5) for modeling the RBV with respect to time and C (1, 50, 500, 5000), σ (1, 2, 4, 8, 10, 100) and ϵ (3, 4, 4.5, 5) for modeling the HR response to RBV change. Next, cross validation was carried out for every group of parameters (C, σ, ϵ). The average mean square error of the test data was calculated three times for each group of parameters (C, σ, ϵ). Finally the group of parameters which minimized the average mean square error was chosen as the parameter for SVR. In simple mathematical terms, we solved the following objective function:

$$min_{C,\epsilon,\sigma}(\sum_{i=1}^{n} MSE_i) \tag{8}$$

where n is the number of sections, MSE is the mean square error calculated from the true output y_j and the estimated output $\hat{y}_j$ is given by:

$$MSE = \frac{1}{n}\sum_{i=1}^{N}(y_j - \hat{y}_j)^2 \tag{9}$$

Linear regression was also applied to fit the curves and AMSE was computed to compare it with SVR.

IV. RESULTS AND DISCUSSION

Fig. 1(a) shows the SVR model identification for RBV with respect to time using RBF kernel with the parameters listed in table I using the training data. Fig. 1(b) shows the model verification based on testing data. The AMSE for the test as well as training data set is tabulated in table II.

Linear regression curves for the same testing and training data are also estimated and the corresponding AMSE is also reported in table II. Based on the SVR model, the change in RBV during the course of hemodialysis can be divided into two distinct phases: 1) a fast initial drop during the first 60 mins, 2) a slower drop as the dialysis process reaches its final stages. The initial sharp fall in RBV may be driven by

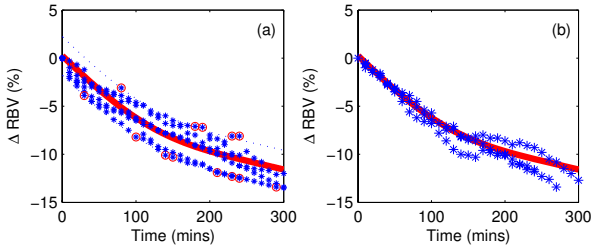

Fig. 1. RBF kernel based SVR model for RBV with time: (a) model identification based on training data (n=6) and (b) model verification based on testing data (n=3).In (a) the solid line represents the estimated input-output regression curve. The * are the actual training data points. The dotted lines represent the ϵ-insensitivity tube and the circled * points are the support vectors.

TABLE I
SELECTED MODEL PARAMETERS FOR RBF KERNEL BASED SVR

Parameter	RBV versus Time	HR versus RBV
ϵ	2	5
C	500	5000
σ	200	10
Support vectors	10(12%)	27(32%)

a rapid unloading of blood volume from the central veins due to high central venous pressure in the hypervolemic state, whereas the later slower fall may indicate an increased refilling of central circulation with blood volume shift from the peripheral microcirculation.

Fig. 2(a) and 2(b) shows the SVR model identification and verification for HR with respect to RBV using training and testing data respectively. SVR parameters that minimize the AMSE are reported in table I. The average mean square error for training and testing data are given in table II. For comparison the average mean square error for linear regression is also tabulated in II.

Based on SVR, the modeled HR response to changes in RBV during hemodialysis showed a slowing trend at the initial rapid drop in RBV to about 5% and a subsequent rise as the RBV falls further. In comparison with other haemodialysis studies, a similar biphasic HR change over the dialysis period has been observed in some [3], [14], while others showed an increasing trend in HR without the initial drop [15], [16]. We believe that the initial slowing down of HR can be regarded as a transition from hypervolemia to normovolemia whereas the augmentation of HR at the later stages can be regarded as a transition from normovolemia to

TABLE II
COMPARISON OF AMSE FOR SVR AND LINEAR REGRESSION CURVES FOR RBV WITH TIME

	RBV versus Time		HR versus RBV	
	Linear	RBF	Linear	RBF
Testing error	1.8	1.5	20.1	16.4
Training error	1.5	1.4	25.2	15.8

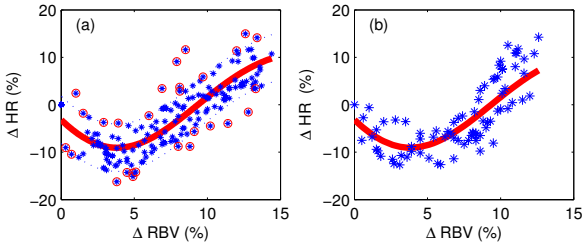

Fig. 2. RBF kernel based SVR model for HR with RBV: (a) model identification based on training data (n=6) and (b) model verification based on testing data (n=3).

hypovolemia. These mean curves can be further tuned by varying the SVR parameters to fit the individual patients response which can be utilized to design controllers for automated regulation of physiological variables.

V. CONCLUSIONS

This paper used RBF kernel based support vector regression to model the RBV response with respect to time as well as HR response to RBV in 9 hemodynamically stable patients with similar HR profile during regular hemodialysis. The SVR parameters were selected based on a grid search approach and the model was verified using a k-fold cross-validation technique. These modeled curves can be used as reference inputs to a controller that can guide the actual changes in RBV and HR by adjusting some control input like ultrafiltration rate (UFR). Such feedback control systems can help to ensure the stability of patients by automatically adjusting the UFR in case the actual changes in RBV or HR deviates from these reference curves.

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