



Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/complbiomed

Modeling the control of the central nervous system over the cardiovascular system using support vector machines



José Díaz^{a,*}, Jesús Acosta^b, Rafael González^a, Juan Cota^a, Ernesto Sifuentes^a, Àngela Nebot^c

^a Dept Ingeniería Eléctrica y Computación, Instituto de Ingeniería y Tecnología, Universidad Autónoma de Ciudad Juárez, 32310, Ciudad Juárez, Mexico

^b Dept Instrumentación y Control, Universidad Politécnica Territorial de Falcón "Alonso Gamero" (UPTAG), 4101, Coro, Venezuela

^c Dept Computer Science, Universitat Politècnica de Catalunya, 08034, Barcelona, Spain

ARTICLE INFO

Keywords:

Central nervous system
Cardiovascular system
Modeling
Support vector machine
Fuzzy inductive reasoning

ABSTRACT

The control of the central nervous system (CNS) over the cardiovascular system (CS) has been modeled using different techniques, such as fuzzy inductive reasoning, genetic fuzzy systems, neural networks, and nonlinear autoregressive techniques; the results obtained so far have been significant, but not solid enough to describe the control response of the CNS over the CS. In this research, support vector machines (SVMs) are used to predict the response of a branch of the CNS, specifically, the one that controls an important part of the cardiovascular system. To do this, five models are developed to emulate the output response of five controllers for the same input signal, the carotid sinus blood pressure (CSBP). These controllers regulate parameters such as heart rate, myocardial contractility, peripheral and coronary resistance, and venous tone. The models are trained using a known set of input-output response in each controller; also, there is a set of six input-output signals for testing each proposed model. The input signals are processed using an all-pass filter, and the accuracy performance of the control models is evaluated using the percentage value of the normalized mean square error (MSE). Experimental results reveal that SVM models achieve a better estimation of the dynamical behavior of the CNS control compared to others modeling systems. The main results obtained show that the best case is for the peripheral resistance controller, with a MSE of 1.20e-4%, while the worst case is for the heart rate controller, with a MSE of 1.80e-3%. These novel models show a great reliability in fitting the output response of the CNS which can be used as an input to the hemodynamic system models in order to predict the behavior of the heart and blood vessels in response to blood pressure variations.

1. Introduction

One of the most important systems of the body is the cardiovascular system (CS), which is almost fully controlled by the central nervous system (CNS). The CNS generates regulatory signals which are transmitted by bundles of nerves through the autonomic nervous system (sympathetic and parasympathetic) to the heart, blood vessels, kidneys, and other body parts; this allows to maintain an appropriate blood flow that follows the hemodynamic changes, which are mainly due to variations of the arterial blood pressure. Also, the CNS controls other global functions in the CS, such as the cardiac output, blood flow redistribution, and arterial pressure to name a few [1].

Most of the control systems in the CS are carried out in the vasomotor center, the bulbar respiratory center, and other suprasegmental structures of the brain [2]. The vasomotor center processes integral

information from visceral sensors, such as baroreceptors of cardiac cavities and large vessels, and chemoreceptors. The reflex function of baroreceptors is very important in the rapid control of blood pressure since it modulates efferent signals directed to the heart and blood vessels; moreover, baroreflex actions produce rapid changes in renal sympathetic nervous activity, which plays a very important role in the short term control of the blood pressure performing a variety of functions like mediating renin secretion, tubular reabsorption of water and sodium, and renal intravascular resistance [3,4].

The hemodynamic behavior of the CS has been widely studied, and there are many mathematical and computational models that fairly and accurately simulate the performance of hemodynamic variables of this system [5–7]. However, modeling the control response of the heart and blood vessels in the hemodynamic system represents an important challenge due to the high complexity of the CNS.

* Corresponding author. Tel.: +52 1 6565294828.

E-mail addresses: david.roman@uacj.mx (J. Díaz), ajesus@uptag.edu.ve (J. Acosta), rafael.gonzalez@uacj.mx (R. González), jcota@uacj.mx (J. Cota), esifuent@uacj.mx (E. Sifuentes), angela@cs.upc.edu (À. Nebot).

<https://doi.org/10.1016/j.complbiomed.2017.12.008>

Received 28 March 2017; Received in revised form 22 November 2017; Accepted 13 December 2017

A simplified diagram of the cardiovascular system proposed by Vallverdú [7] is shown in Fig. 1. In this diagram, the hemodynamic system (HS), controlled by a branch of the CNS, both make up the cardiovascular system. The branch of the CNS that controls the HS is composed of five controllers that produce efferent signals leading changes in the peripheral resistance, the cardiac output and the coronary circulation. The HS controllers are: heart rate (HR), myocardial contractility (MC), peripheral resistance (PR), venous tone (VT), and coronary resistance (CR). The afferent signal that regulates these controllers is represented by the carotid sinus blood pressure; this signal is originated from the arterial carotid sinus baroreceptors [7].

In the last few decades, important contributions related to support vector machine (SVM) approaches have been produced, in both theory and practice. These approaches have led to the development of methodologies that are useful in the design of efficient algorithms with applications focused to practical problems in classification and regression tasks [8–10]. For instance, linear and non-linear SVM regression for time series prediction have been widely used in many real world applications, such as financial market, weather and electric utility, network traffic, among others [11]; however, at the best of our knowledge, there are few works that describe approaches to predict biomedical signals. In one of these studies, Shen et al. [12] developed a predictor model based on a wavelet kernel function using a SVM to predict multichannel electroencephalogram signals. Many studies have shown that SVMs capture effectively the behavior of dynamic systems which are typically nonlinear, non-stationary and not defined *a-priori*.

The purpose of this study is to predict the response of five CNS controllers in the cardiovascular system model proposed by Vallverdú [7] employing regression models of SVMs. Previous investigations have employed a variety of schemes for the same target, like nonlinear autoregressive moving average with external inputs (NARMAX) models [13], neural network techniques [14], fuzzy inductive reasoning (FIR) algorithms [13,15], genetic fuzzy systems (GFS) or hybrid techniques such as genetic-FIR algorithms (GA-FIR) [16], and automatic constructions of linguistic rules methodologies based on FIR (CARFIR) [17]. Although some of these models have reported good results, in the present study the authors intend to explore the potentialities of SVMs in the prediction of five CNS controllers in the CS model; due to its complexity, this task represents a big challenge for any nonlinear regression model. In this way, the authors propose a new predictive model derived from SVMs

which uses digital signal processing and offers an alternative to build a model that can be as robust and efficient as others already mentioned. Thus, to evaluate the prediction performance of the proposed SVM model, it is compared with those studies.

2. The support vector machines methodology

The target of traditional techniques for pattern recognition consists of minimizing an empirical risk to optimize the performance of a training data set; however, according to the theory of SVMs, this last technique minimizes an upper bound of an expected risk (i.e., the structural risk) that provides a great ability to generalize any model, the main goal in the statistical learning.

There are three important characteristics of SVMs [18]:

- 1) The learning technique can generalize a model with few training data points; and from this training data set, the generalization error limit can be estimated.
- 2) There is only one variable acting as a regularizing parameter (associated to the penalty for misclassification) [19], which determines a balance between generalization performance and resolution [20].
- 3) The algorithm finds a decision surface that maximizes the margin between the classes of a training set to obtain the best performance with new data that must be classified.

Support vector machines determinate the output as a linear combination of samples in the training data, in which the data points with nonzero coefficients are called “support vectors”. In the next lines, it is described the mathematical formulation of the support vector machines.

Given a set of data training of l attribute-label pairs (x_i, y_i) , $i = 1, \dots, l$; where $x_i \in R^n$ and $y_i \in \{1, -1\}$, the SVM for classification purposes needs to solve the optimization problem presented in Eq. (1) [21]:

$$\begin{aligned} \min \quad & \Phi_{(w,\xi)} = \frac{1}{2}w^T w + C \sum_{i=1}^l \xi_i \\ \text{subject to} \quad & y_i(w^T \phi(x_i) + b) \geq 1 - \xi_i \\ & \xi_i \geq 0 \end{aligned} \tag{1}$$

The vector w determines the optimal generalized separating hyperplane, ξ_i represents a measure of the misclassification errors, and $C > 0$ (a settable parameter) is the cost parameter of the error term. The training vectors x_i are mapped by the function ϕ into a higher dimensional space. $K(x_i, x_j) \equiv \phi(x_i)^T \phi(x_j)$, represents a kernel function which makes a nonlinear mapping of the input space into a feature space. In this higher dimensional space (the feature space), SVM finds a linear separating hyperplane with the maximal margin.

Popular kernel functions commonly used for pattern recognition are the followings:

$$K(x, y) = (1 + x \cdot y)^p \tag{2}$$

$$K(x, y) = \exp\left(-\frac{\|x - y\|^2}{2\sigma^2}\right) \tag{3}$$

$$K(x, y) = \tanh(kx \cdot y - \delta) \text{ for some } k \text{ and } \delta \tag{4}$$

Equation (2) represents a polynomial kernel and provides a classifier using a p th-degree polynomial function over the data. Eq. (3) gives a classifier based on Gaussian radial basis functions, and Eq. (4) represents a kind of special neural network kernel of a hide layer with sigmoid activation functions. Most of kernel functions are detailed in Refs. [18,22,23].

The solution to the optimization problem of Eq. (1) is equivalent to determine the point at which the gradient of the Lagrangian (Φ), shown in Eq. (5), is zero:

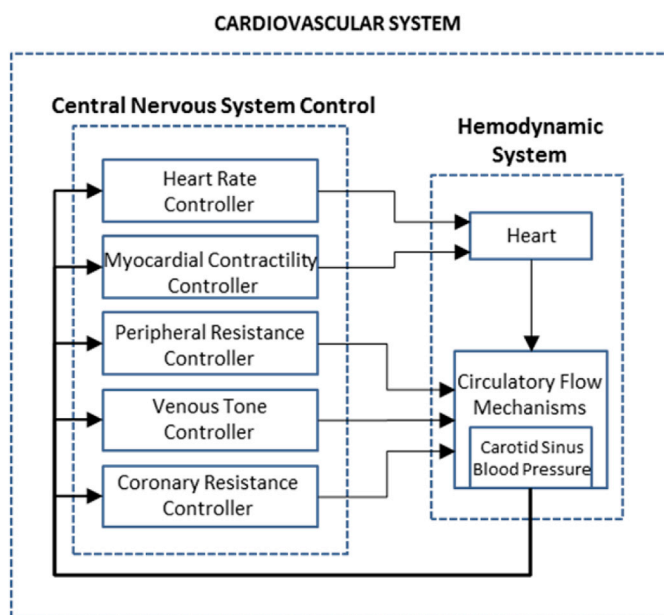


Fig. 1. A simplified diagram of the cardiovascular system model composed of the CNS control and the hemodynamic system [7].

$$\Phi_{(w,b,\alpha,\xi,\beta)} = \frac{1}{2} \|w\|^2 + C \sum_{i=1}^l \xi_i - \sum_{i=1}^l \alpha_i [y_i (w^T \phi(x_i) + b) - 1 + \xi_i] \sum_{i=1}^l \beta_i \xi_i \tag{5}$$

where the parameters α, β are the Lagrange multipliers. Solving Eq. (5) requires huge computational capabilities; however, this primal problem can be transformed in a dual problem to optimize time processing and computational operations. This is done by minimizing the Lagrangian with respect to w, b, ξ , and maximizing it with respect to α, β as described below in Eq. (6).

$$\max_{\alpha} W(\alpha, \beta) = \max_{\alpha, \beta} \left(\min_{w, b, \xi} \Phi(w, b, \alpha, \beta, \xi) \right) \tag{6}$$

Equation (7) shows how to obtain the minimum value of the Lagrangian Φ with respect to w, b and ξ :

$$\begin{aligned} \frac{\partial \Phi}{\partial b} = 0 &\Rightarrow \sum_{i=1}^l \alpha_i y_i = 0 \\ \frac{\partial \Phi}{\partial w} = 0 &\Rightarrow w = \sum_{i=1}^l \alpha_i y_i \phi(x_i) = 0 \\ \frac{\partial \Phi}{\partial \xi} = 0 &\Rightarrow \alpha_i + \beta_i = C \end{aligned} \tag{7}$$

Then, the solution of the optimization problem of Eq. (7) becomes:

$$\alpha^* = \underset{\alpha}{\operatorname{argmin}} \frac{1}{2} \sum_{i=1}^l \sum_{j=1}^l \alpha_i \alpha_j y_i y_j K(x_i, x_j) - \sum_{k=1}^l \alpha_k \text{ subject to } \begin{cases} 0 \leq \alpha_i \leq C, & i = 1, \dots, l \\ \sum_{j=1}^l \alpha_j y_j = 0 \end{cases} \tag{8}$$

Solving Eq. (8) allows to find the Lagrange multipliers, α and β . Finally, Eq. (9) establishes the classifier for the optimal separating hyperplane in the feature space.

$$f(x) = \operatorname{sgn} \left(\sum_{i=1}^l \alpha_i y_i K(x_i, x) + b \right) \tag{9}$$

For regression problems, SVMs include an alternative loss function [24] that must be modified to introduce a measure of distance. Four kinds of loss functions commonly implemented for SVM regression models are presented in Refs. [23,24]. Below, it is described the mathematical formulation of the support vector regression (SVR).

In regression tasks, given a training set of l data points, (x_i, z_i) , $i = 1, \dots, l$; where $x_i \in R^n$ is an input, and $z_i \in R^1$ is its corresponding output, the optimization problem to be solved becomes [18]:

$$\begin{aligned} \min_{w,b,\xi,\xi^*} & \frac{1}{2} w^T w + C \sum_{i=1}^l \xi_i + C \sum_{i=1}^l \xi_i^* \\ \text{subject to} & (w^T \phi(x_i) + b - z_i) \leq \varepsilon - \xi_i \\ & (z_i - w^T \phi(x_i) - b) \leq \varepsilon - \xi_i^* \\ & \xi_i, \xi_i^* \geq 0, \quad i = 1, \dots, l \end{aligned} \tag{10}$$

where C is a pre-specified value (cost parameter of the error term, similar to the classifier in SVMs), and the parameters ξ_i, ξ_i^* are looseness variables that set the upper and the lower limits in the output system.

When using a ε -insensitive loss function [23], the dual problem of Eq. (10) can be expressed as:

$$\begin{aligned} \min_{\alpha, \alpha^*} & \frac{1}{2} (\alpha - \alpha^*)^T Q (\alpha - \alpha^*) + C \sum_{i=1}^l (\alpha_i - \alpha_i^*) + \sum_{i=1}^l z_i (\alpha_i - \alpha_i^*) \\ \text{subject to} & \sum_{i=1}^l (\alpha_i - \alpha_i^*) = 0 \\ & 0 \leq \alpha_i \\ & \alpha_i^* \leq C, \quad i = 1, \dots, l \end{aligned} \tag{11}$$

where $Q_{ij} = K(x_i, x_j) \equiv \phi(x_i)^T \phi(x_j)$; α and α^* are the Lagrange multipliers, which are obtained by solving Eq. (11). Thus, the regression function can be expressed as:

$$f(x) = \sum_{i=1}^l (\bar{\alpha}_i - \bar{\alpha}_i^*) K(x_i, x) + \bar{b} \tag{12}$$

where

$$\begin{aligned} w^T \phi(x_i) &= \sum_{i=1}^l (\alpha_i, \alpha_i^*) K(x_i, x) \\ \bar{b} &= -\frac{1}{2} \sum_{i=1}^l (\alpha_i, \alpha_i^*) (K(x_i, x_r) + K(x_i, x_s)) \end{aligned} \tag{13}$$

The optimization criteria for other loss functions are similar to those

ones obtained in Ref. [24]. The ε -insensitive loss function has the quality of working with few support vectors. This provides a computational advantage over other loss functions as the Huber, quadratic and Gaussian approaches.

In this research, SVR models are implemented in Matlab[®] (R2012a) using the LIBSVM tool developed by the Taiwan University [25]. All Matlab simulations are made with a Core 2 Duo computer with a 2.1 GHz processor.

3. Cardiovascular control of the central nervous system

The specific data used in the present study correspond to the same signal sets used by Vallverdú in Ref. [7], where a generic model of the CS is identified and validated. In order to validate that model, cardiac catheterization of patients is employed to obtain physiological data; this led to the simplified cardiovascular system model shown in Fig. 1. In this model, the branch of the CNS that controls the hemodynamic system is composed of five controllers that produce efferent signals that bring about changes in the peripheral resistance, cardiac output and coronary circulation; these controllers are: heart rate, myocardial contractility, peripheral resistance, venous tone, and coronary resistance. The afferent signal that regulates these controllers is represented by the carotid sinus blood pressure, originated from the arterial carotid sinus baroreceptors [7]. Sensibility analysis shows that the baroreceptor parameters that have the most influence on the output variables in the CS model come from the carotid sinus baroreceptors; therefore, the influence of the baroreceptors of the aortic arch is neglected [7]. It is important to notice that, in this CS model, the regulatory mechanisms of the renal function that response to changes of the renal sympathetic nerve activity (RSNA), mediated by baroreflex action, are not assessed due to the fact that RSNA data is not available.

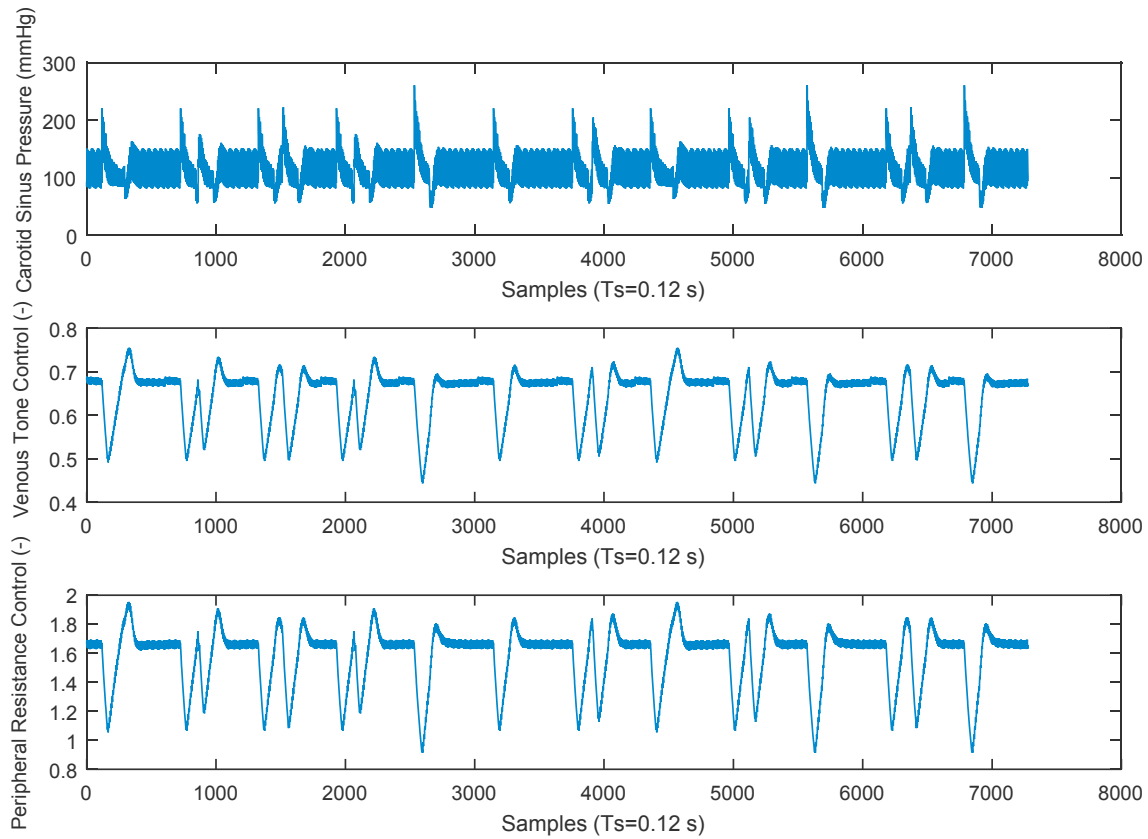


Fig. 2. Carotid sinus blood pressure (upper trace), and the output signals of the controllers of venous tone (middle trace) and peripheral resistance (lower trace), used for training the SVR models.

The input and output signals of the Vallverdú’s model are obtained simulating a model with differential equations of the central nervous system [7]. The model of differential equations is tuned in order to represent patients with different percentages of coronary arterial obstruction (between 30% and 70%). It is done by matching the four physiologic variables of the model (i.e., heart rate, aortic pressure, right auricular pressure, and coronary blood flow) with measurements taken from the patients. Simulations of the differential equations for each model employed a sampling rate of $F_s = 8.33$ Hz (sampling period $T_s = 0.12$ s) [7]. Each model is identified based on the output response of the systems to the same input signal (7279 data samples as shown in the upper trace of Fig. 2). Thus, the same quantity of data samples in the output of each model is obtained; these input-output signals constitute the training dataset. Figs. 2 and 3 show the training signals of the input variable (CSBP) and the output variables of the controllers.

To evaluate the models of each controller, a test dataset with six signal segments (not employed in training) is used, where each test data segment has a size of about 600 samples. Each dataset contains signals with specific morphologies, derived from executing six different exhibitions of the Valsalva maneuver with different duration and relative intensity. A detailed explanation of the test datasets can be found in Refs. [7,13,15]. For instance, Fig. 4 shows the output signals (test dataset) of the heart rate controller.

3.1. Training process

Before to start with the training process, the kernel function of the SVM needs to be established. Many tests made to different kernel schemes as the RBF, polynomial and sigmoid were evaluated employing a whole training dataset. The former one, exhibited the best prediction performance and also was faster than the others during the training processes. For the initial models, there was used $C = 10$ and $\sigma = 10$.

Preliminary attempts using the input signal CSBP (and different processed version of this signal) for training the SVR models presented a very poor performance. For this reason, a second input signal for each model had to be added to improve the prediction output in every model as depicted in Fig. 5.

An all-pass filter (two pole/cero pairs) with flat magnitude response and pole magnitude of $1/\sqrt{2}$ is used to create the second signal with a time delay (phase compensation) where the CSBP signal is used as the input. To adjust the pole/cero pair spacing of the filter, the start and the end frequencies are primarily determined. It is used a coarse-grained searching of 0.1π step in the frequency plane $[0 - \pi]$ to find the pair of frequencies that provides the minimal error between expected and predicted output signals. Once this pair of frequencies are found, a fine-grained searching of 0.01π step is carried out around them to improve estimation accuracy.

The performance of each model at each iteration is analyzed by computing the percentage value of the normalized mean square error (MSE). The metric used to compare the predicted output ($\hat{y}_{(n)}$) and the expected output ($y_{(n)}$) is shown in Eq. (14):

$$MSE = \frac{E \left[\left(y_{(n)} - \hat{y}_{(n)} \right)^2 \right]}{y_{var}} \cdot 100\% \tag{14}$$

where y_{var} is the variance of $y_{(n)}$, given by Eq. (15):

$$y_{var} = E \left[y_{(n)}^2 \right] - \{ E[y_{(n)}] \}^2 \tag{15}$$

A cross validation process is accomplished in order to adjust the parameters of the SVR models. To do this, the training dataset of each controller composed of 7279 samples is segmented in subsets of 4279 data samples, where 3679 samples (about 50.5% of the total training

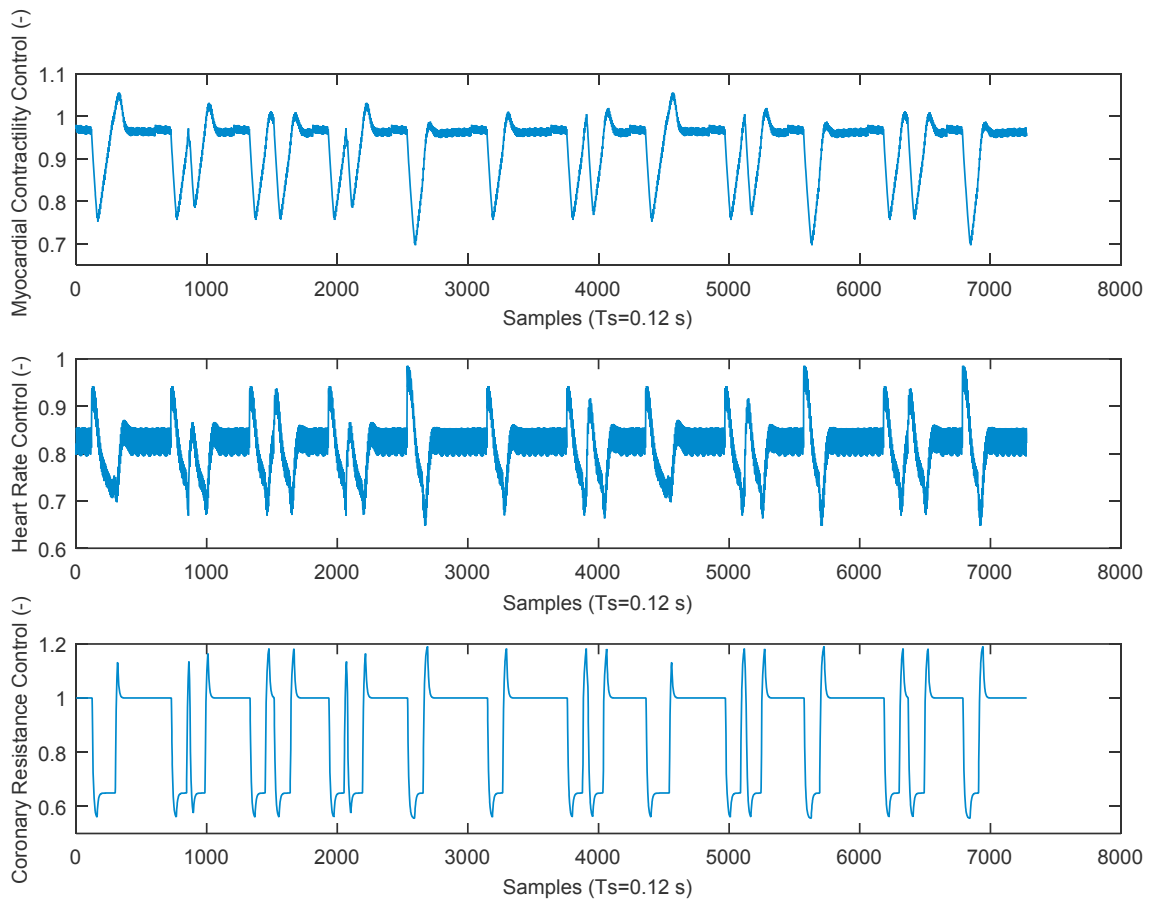


Fig. 3. The output signals of the controllers of myocardial contractility (upper trace), heart rate (middle trace), and coronary resistance (lower trace), used for training the SVR models.

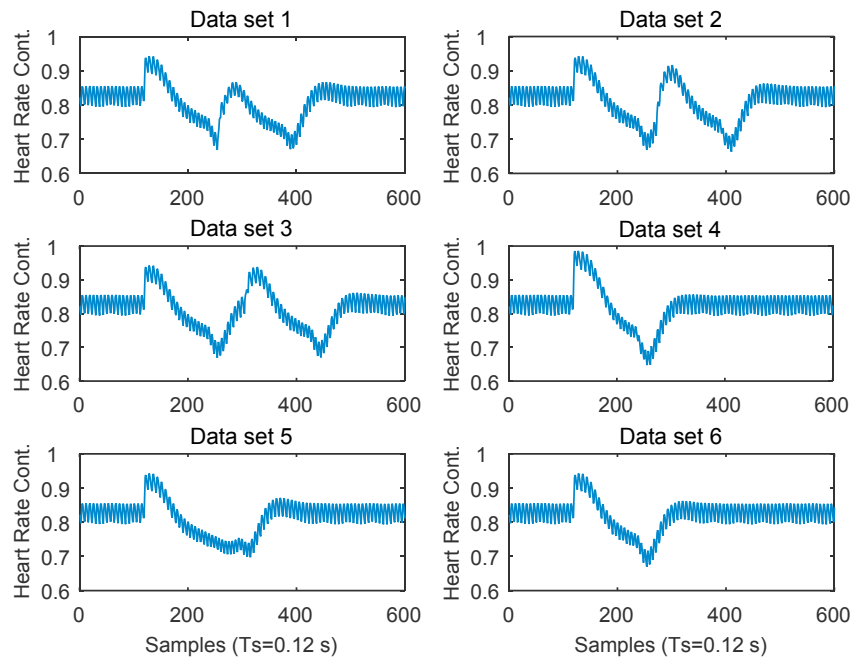


Fig. 4. Output signals for the heart rate controller of the test dataset.

dataset) are used for training the model, and the other 600 samples for testing purposes. In order to avoid discontinuities in the signal processing, only continuous segments of the training dataset are considered. In

total, twelve subsets of data are formed sliding the 4279 samples from the beginning to the end of the data in steps of 600 samples, where 3679 samples are overlapped in each case. In six cases, the test segment is

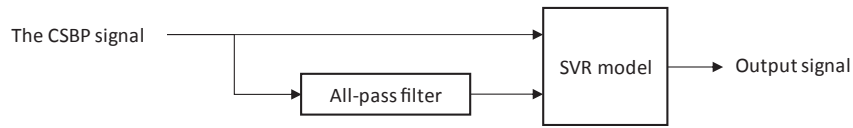


Fig. 5. General scheme to improve the prediction performance of the five models of the CNS.

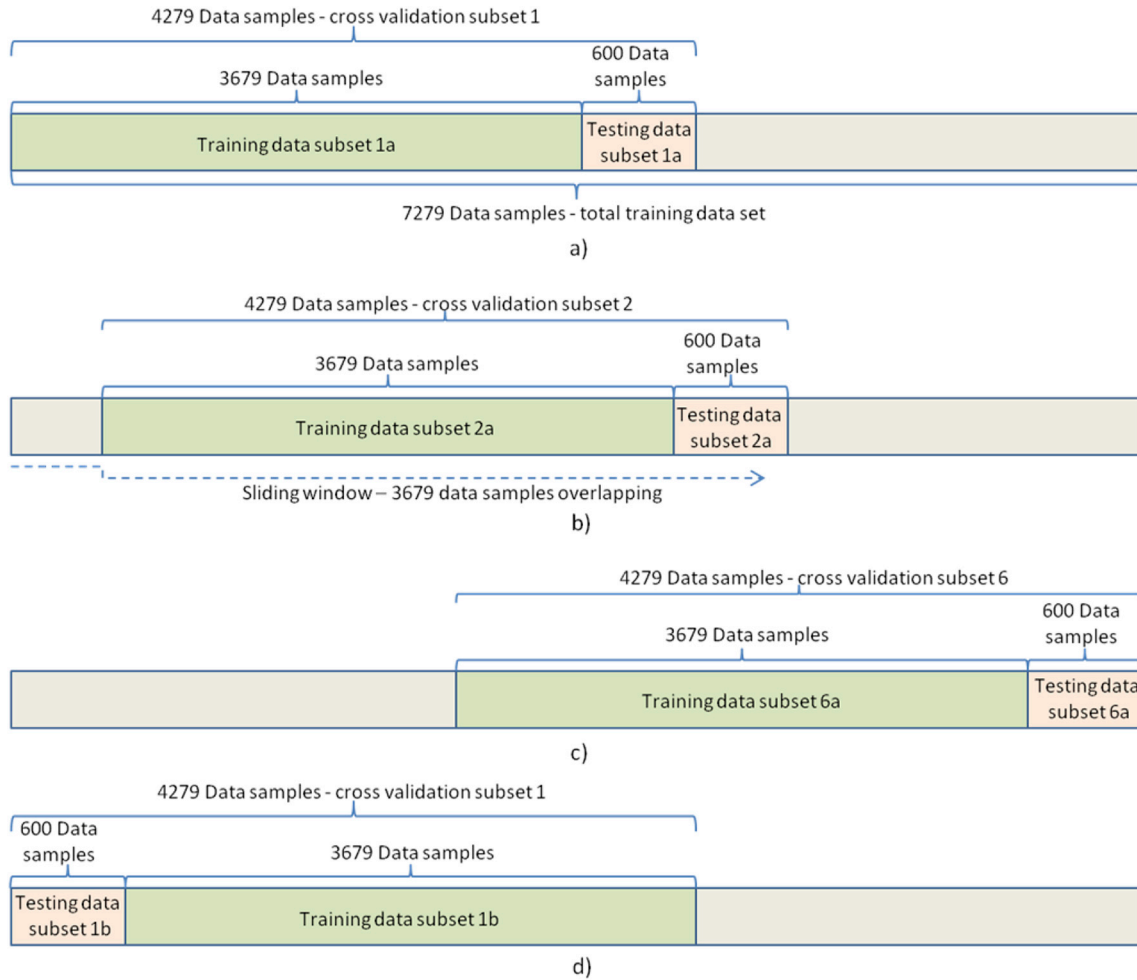


Fig. 6. Data segmentation for the cross validation process.

Table 1
Parameters used in the all-past filter and SVM for each controller.

		HR	PR	MC	VT	CR
All-pass filter	Start - stop frequency [π rad]	.01–.11	.01–.13	.01–.13	.01–.11	.01–.13
	SVM					
	C	10	10	10	5	5
	σ	10	53	60	58	60

located at the end of each data subset (called testing data subset “a”, as shown in Fig. 6 a–c), and in the remaining cases, the test segment is positioned at the beginning of the data subset (called testing data subset “b”, as shown in Fig. 6 d). Thus, twelve iterations of cross validation process are performed.

Using the grid-search procedure, as suggested in Ref. [26], the MSE average of the 12 iterations in the cross validation process is computed to optimize the parameters C and σ of the SVR models.

Table 2
MSE of each control model using SVR.

	HR (%)	PR (%)	MC (%)	VT (%)	CR (%)
Training data	1.7e-3	1.14e-4	6.38e-4	7.05e-4	1.36e-4
Dataset 1	1.7e-3	1.10e-4	5.34e-4	6.06e-4	1.05e-4
Dataset 2	1.5e-3	1.10e-4	4.61e-4	5.81e-4	0.99e-4
Dataset 3	1.5e-3	0.89e-4	4.97e-4	4.55e-4	1.08e-4
Dataset 4	1.6e-3	1.03e-4	5.32e-4	5.98e-4	1.39e-4
Dataset 5	2.0e-3	1.31e-4	7.44e-4	7.55e-4	1.57e-4
Dataset 6	2.8e-3	1.83e-4	9.42e-4	1.10e-3	1.80e-4
Average Error	1.8e-3	1.20e-4	6.18e-4	6.81e-4	1.36e-4

3.2. Validation process

Once the optimized parameters, C and σ , and the starting and the ending frequencies of the all-pass filter are found as shown in Table 1, a final model is built using the whole training dataset (7279 samples) for each controller.

Finally, the SVR models of each CNS controller are then evaluated

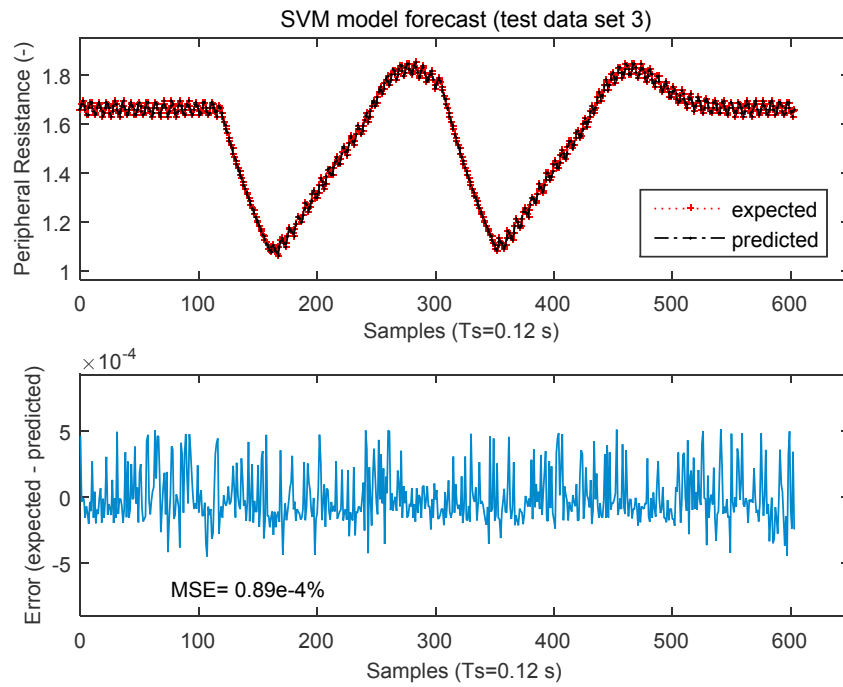


Fig. 7. Predicted result versus reference output using the test dataset 3 of the PR controller.

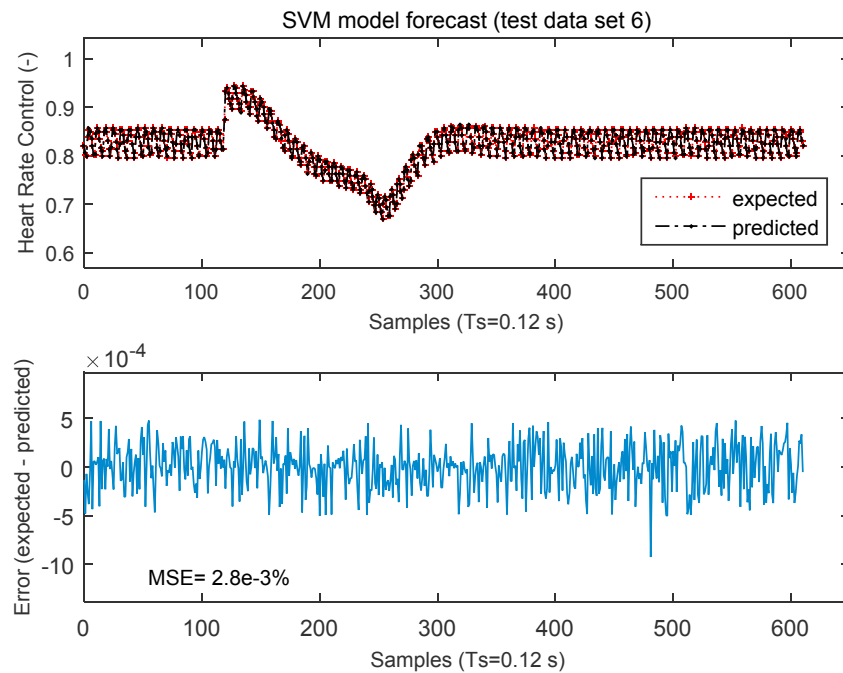


Fig. 8. Predicted result versus reference output using the test dataset 6 of the HR controller.

using the testing dataset, where the MSE of each controller is reported in the next section.

3.3. Results

This section shows the prediction performance of each control model. For each model, six test datasets are processed, and every output is compared with its respective pattern. The MSE formula is used to evaluate the performance of the models. Also, the worst and the best MSE cases are graphically depicted, and processing times of the tuning

algorithms are analyzed and discussed.

Table 2 presents the MSE of the five control models. It can be seen that the largest average error is 1.8e-3%, which corresponds to the HR controller.

Fig. 7 shows the best predicted result corresponding to the test dataset 3 of the peripheral resistance controller with a MSE = 0.89e-4%, as shown in Table 2. In the upper trace of Fig. 7, both the expected and the predicted output signals are depicted in the same frame, showing a good coincidence between these two signals, demonstrating the excellent performance of the proposed model. Such differences are shown in the

Table 3
MSE of different regression methods when predicting the test datasets against the proposed SVR model.

	HR (%)	PR (%)	MC (%)	VT (%)	CR (%)
NARMAX [13]	9.8	14.89	17.21	16.89	31.69
FIR [13]	1.37	1.49	1.41	1.47	0.09
TDNN [14]	15.35	33.76	34.02	34.04	55.69
RNN [14]	18.31	31.16	35.16	34.77	57.12
FIR ^a [15]	7.3e-5	7.0e-4	7.6e-6	7.9e-4	3.0e-4
GFS (GA-FIR) [16]	0.10	0.15	0.30	0.28	9.47e-30
CARFIR [17]	11.02	9.97	5.00	5.01	2.64
SVR (this study)	1.8e-3	1.20e-4	6.18e-4	6.81e-4	1.36e-4

^a Patient four of five participants.

lower trace of Fig. 7.

The worst predicted result is shown in Fig. 8, which corresponds to the test dataset 6 of the heart rate controller. Even in this case, differences between expected and predicted signals are not distinguishable, which means a great accuracy of our model.

It is also important to notice that the processing times for the cross validation process (in the worst case) are the next: to set the frequencies of the all-pass filter about 4992 s are required and to find the best parameters C and σ , 44256 s are employed.

3.4. Discussion

This section analyzes the performance of the proposed SVR models with those obtained in previous studies.

Table 3 summarizes the prediction results reported for the same problem when using NARMAX, TDNN,¹ RNN,² FIR, GFS (GA-FIR), CARFIR and the proposed SVR models. This table specifies the MSE average for each controller, it is done by comparing the expected-predicted outputs to each controller when the test dataset is used. As it is noted, the row six presents the best performance obtained by Nebot et al. [15]. In that research, a database that includes signals of five different patients is used, where the best result corresponds to the model built for the patient four. The average error of the proposed models, when compared with the same patient of [15], is slightly higher, but the former presents better MSE results in three of the five controllers.

The SVR model of the HR controller presents the highest error of the five proposed models (MSE average of 1.8e-3% against 7.3e-5% of Nebot). The main contribution to this error is due to the test dataset six which shows a MSE = 2.8e-3% (see Table 2); however, this error when compared with Nebot is considerably lower, which presented a MSE = 32.1e-3%. The SVR models show a narrow variation margin of the errors in the predicted responses. This indicates that our proposed models can reproduce the behavior of the five controllers with less error variability.

It should also be noted that, although the prediction for the CR controller in our study (see Table 3, last column) is better than that reported by Nebot [15], it does not overcome that obtained by the GFS technique [16]. However, it should be taken into account the computational cost required to use that hybrid technique. The total execution time for tuning the parameters and training the SVR model of each controller is less than 14 h. Acosta reported an average time of more than 357 h to find the best parameters of the GFS models, employing a computer with a 0.6 GHz processor [16]. Although, the computer processor used in our simulations is 3.5 times faster than that used in Ref. [16], the required lapse to build each SVR model is close to 25.5 times shorter; it means a computational savings around 7.3 times.

As described above, changes in blood pressure cause variations in the afferent baroreceptor signal (the input signal of the models). The outputs of our models should activate the effector elements of the hemodynamic

system (heart and blood vessels), which in turn modify the blood pressure, forming the control system of the cardiovascular system. However, we must remark that the purpose of the present study was to predict the control responses of the CNS to changes in blood pressure (as those caused by Valsalva maneuvers) using SVM regression models, and the model of the hemodynamic system has not been the focus of this research.

4. Conclusions

In this paper, support vector machines have been used to model a portion of the human central nervous system, which is in charge of controlling the hemodynamic behavior of the cardiovascular system. The controllers of heart rate, myocardial contractility, peripheral resistance, venous tone and coronary resistance have been modeled in order to predict their responses.

A detailed methodology to adjust important values of signal processing filtering and SVM parameters of the proposed models have been described. It was found that the choice of a second input signal, which merges from a delayed version of the original input signal, was the key factor to obtain an optimal performance of the SVR models.

The strategy to implement the training methodology of the SVR models resulted in a low computational cost when it was compared with other optimization techniques implemented in other models used for the same purpose of regression.

Support vector machines represent an efficient and powerful technique that have shown a great reliability in estimating the control outputs of the CNS over the cardiovascular system, and it could be useful in models of the hemodynamic system to predict the behavior of the heart and blood vessels in response to variations of the blood pressure.

Acknowledgements

This paper has been partially supported by the Universidad Autónoma de Ciudad Juárez (UACJ) and the Program for Professional Teacher Development (PRODEP) under the project UACJ-PTC-371.

References

- [1] A.C. Guyton, J.E. Hall, in: *Tratado de Fisiología Médica*, tenth ed., Mc-Graw Hill Interamericana, Mexico, 2006.
- [2] J.H. Coote, Landmarks in understanding the central nervous control of the cardiovascular system, *Exp. Physiol.* 92 (2007) 3–18.
- [3] U.C. Kopp, *Neural Control of Renal Function*, Morgan & Claypool Life Sciences, San Rafael (CA), 2011.
- [4] C. Julien, Baroreflex control of sympathetic nerve activity and blood pressure variability, *Clin. Exp. Pharmacol. Physiol.* 35 (2008) 512–515.
- [5] J.E.W. Beneken, V.C. Rideout, The use of multiple models in cardiovascular system studies: transport and perturbation methods, *IEEE Trans. Biomed. Eng.* 15 (1968) 281–289.
- [6] K. Sagawa, *Cardiac Contraction and the Pressure-volume Relationship*, 1988. New York.
- [7] M. Vallverdú, *Modelado y simulación del sistema de control cardiovascular en pacientes con lesiones coronarias*, Universitat Politècnica de Catalunya, Barcelona, 1993.
- [8] Y. Ma, G. Guo, *Support Vector Machines Applications*, Springer, New York, 2014.
- [9] N. Deng, Y. Tian, C. Zhang, *Support Vector Machines: Optimization Based Theory, Algorithms, and Extensions*, CRC press, 2012.
- [10] R.G. Brereton, G.R. Lloyd, Support vector machines for classification and regression, *Analyst* 135 (2010) 230–267.
- [11] N.I. Sapankevych, R. Sankar, Time series prediction using support vector machines: a survey, *IEEE Comput. Intell. Mag.* 4 (2009) 24–38.
- [12] M. Shen, L. Lin, J. Chen, C.Q. Chang, A prediction approach for multichannel EEG signals modeling using local wavelet SVM, *IEEE Trans. Instrum. Meas.* 59 (2010) 1485–1492.
- [13] A. Nebot, F. Cellier, M. Vallverdú, Mixed quantitative/qualitative modeling and simulation of the cardiovascular system, *Comput. Meth. Progr. Biomed.* 55 (1998) 127–155.
- [14] J. Cueva, R. Alquezar, A. Nebot, Experimental comparison of fuzzy and neural network techniques in learning models of the central nervous system control, in: *EUFIT'97, 5th European Congress on Intelligent Techniques and Soft Computing*, Aachen, 1997, pp. 1014–1018.

¹ Time Delay Neural Network.

² Recursive Neural Network.

- [15] A. Nebot, F. Mugica, F. Cellier, M. Vallverdú, Modeling and simulation of the central nervous system control with generic fuzzy models, *Simulation* 79 (2003) 648–669.
- [16] J. Acosta, Aprendizaje de Particiones Difusas para Razonamiento Inductivo, Departament d'Enginyeria de Sistemes, Automàtica i Informàtica Industrial, Universitat Politècnica de Catalunya, Barcelona, 2006.
- [17] P. Gómez, A. Nebot, F. Mugica, Automatic construction of fuzzy rules for modelling and prediction of the central nervous system, in: Workshop de minería de datos y aprendizaje automático en el marco de la 8th Iberoamerican Conference on Artificial Intelligence Sevilla, 2002, pp. 23–32.
- [18] V. Vapnik, *Statistical and Learning Theory*, John Wiley & Sons, INC, New York, 1998.
- [19] F. Girosi, M. Jones, T. Poggio, Regularization theory and neural networks architectures, *Neural Comput.* 7 (1995) 219–269.
- [20] M. Pontil, A. Verri, Properties of support vector machines, *Neural Comput.* 10 (1998) 955–974.
- [21] C. Cortes, V. Vapnik, Support-vector networks, *Mach. Learn.* 20 (1995) 273–297.
- [22] F. Girosi, An equivalence between sparse approximation and support vector machines, *Neural Comput.* 10 (1998) 1455–1480.
- [23] S.R. Gunn, *Support Vector Machines for Classification and Regression*, ISIS Technical Report, 14, 1998.
- [24] A.J. Smola, Regression Estimation with Support Vector Learning Machines, Master's thesis, Technische Universität München, 1996.
- [25] C.-C. Chang, C.-J. Lin, LIBSVM: a library for support vector machines, *ACM Trans. Intell. Syst. Technol. (TIST)* 2 (2011) 27.
- [26] C.-W. Hsu, C.-C. Chang, C.-J. Lin, *A Practical Guide to Support Vector Classification*, Department of Computer Science, National Taiwan University, 2003.



Rafael González received the Engineer in Electronics degree in 1997 from the Rafael Belloso Chacín University, Maracaibo, Venezuela, and the Ph.D. in Biomedical Engineering degree in 2008 from the Universitat Politècnica de Catalunya, Barcelona, Spain. He has been Associated Professor at the Francisco de Miranda University, Coro, Venezuela, since 1999, teaching courses in analog electronic and biomedical sensors. Currently he is working at the Department of Computer and Electrical Engineering, UACJ (Universidad Autónoma de Ciudad Juárez), Mexico. His current research areas include biomedical sensors and analog signal processing, noise and interference in electronic circuits and noninvasive physiological measurement.



Juan Cota received his Ph.D. in Electrical and Computer Engineering at the University of Texas at El Paso (UTEP), in 2011. Currently, he works as a full research professor at the Autonomous University of Ciudad Juárez (UACJ) Mexico, since 2003. He has national and international publications on the fields of electrical engineering, and he is holder of a national patent. His current research interests include Wireless Sensor Networks, Smart Sensors, Numerical Optimization, and Digital Signal Processing.



Ernesto Sifuentes was born in Durango, Mexico, in 1976. He received the B.S. degree from Technological Institute of Durango (ITD), Mexico, in 2000, the M.S. degree from Technological Institute of Chihuahua (ITCH), Mexico, in 2002, and the Ph.D. degree from Universitat Politècnica de Catalunya (UPC), Barcelona, Spain, in 2009, all in electronic engineering. Since August 2002, he has been a titular professor at the Department of Computer and Electrical Engineering, UACJ (Autonomous University of Ciudad Juárez), Mexico. His current research interests include sensor interface circuits, virtual instrumentation, embedded systems, autonomous sensors, and wireless sensor networks.



Ángela Nebot received her Ph.D. degree in computer science from the Polytechnical University of Catalonia (UPC), Barcelona, Spain, in 1994. She joined the Department of Llenguatges i Sistemes Informàtics, UPC, in 1994 as an Assistant Professor, and since March 1998 she has been Associate Professor in the same department. She is currently the head of the Soft Computing research group of the UPC. Her current research interests include fuzzy, neuro-fuzzy and genetic-fuzzy systems. The application areas include medicine, biology, atmospheric sciences and e-learning. She has published 17 articles in international research journals, more than 10 book chapters and more than 60 papers in international congresses. Dr. Nebot collaborates as a reviewer in several international journals: *Artificial Intelligence Communication*, *Artificial Intelligence in Environmental Engineering*, *Neurocomputing*, *IEEE Transactions on Fuzzy System and Fuzzy Sets and Systems*. Is a member of the Editorial Board of the *International Journal of General Systems and Simulation: Transactions of the Society for Modeling and Simulation International* journal.



José Díaz was born in Venezuela in 1976. He got an Electronic Engineer degree at the Polytechnic Institute of the National Armed Forces (Maracay, Venezuela) in 1997. He received his Ph.D degree in 2008 from Simón Bolívar University (Caracas, Venezuela). Between 1998 and 2016 he was part of the Electromedicine - Biomedical Engineering Program of the National Experimental University Francisco de Miranda in Coro, Venezuela. He is currently Professor attached to the Department of Computer and Electrical Engineering of the Autonomous University of Ciudad Juárez, Chihuahua, Mexico. His interest in teaching and research includes: Electronic and biomedical instrumentation, analog and digital signal processing, and machine learning.



Jesús Acosta was born in Coro-Estado Falcón, Venezuela. He received his Ph.D. degree in control engineering from the Polytechnical University of Catalonia (UPC), Barcelona, Spain, in 2007, and his M.S. degree in process engineering (cum laude) from the *Universidad Nacional Experimental Politécnica "Antonio José de Sucre"* (UNEXPO), Barquisimeto, Venezuela, in 2000. He received his B.S. in computer science (cum laude) from the *Universidad Tecnológica del Centro* (UNITEC), Guacara, Venezuela, in 1995. He joined the Department of *Instrumentación y Control*, *Universidad Politécnica Territorial de Falcón "Alonso Gamero"* (UPTAG) in 1996. He is currently a member of the Soft Computing research group of the UPC. His current research interests include fuzzy, neuro-fuzzy and genetic-fuzzy systems, also automation, pattern recognition and machine learning. The application areas include medicine, biology, atmospheric sciences, e-learning and control process. He has published 4 articles in international research journals and more than 20 papers in international congresses. Mr. Acosta collaborates as a reviewer in several international journals: *IEEE Transactions on Industrial Electronics* and *Revista Ciencias Sociales y Educativas*. He received a Ph.D. fellowship in 2001–2003 from the Agencia Española de Cooperación Internacional (Spain) and he was a research fellow from 2004 to 2006 at the UPC.