# Electrocardiographic Signals and Swarm based Support Vector Machine for Hypoglycemia Detection

Nuryani, Steve S.H. Ling and H.T. Nguyen

Faculty of Engineering and Information Technology, University of Technology Sydney City campus, 15 Broadway Road, Ultimo, NSW 2007, Australia

Address correspondence to Nuryani, Faculty of Engineering and Information Technology, University of Technology Sydney, City campus, 15 Broadway Road, Ultimo, NSW 2007, Australia. Electronic mail: nnuryani@eng.uts.edu.au *Abstract*— Cardiac arrhythmia relating to hypoglycemia is suggested as a cause of death in diabetic patients. This paper introduces electrocardiographic (ECG) parameters for hypoglycemia detection. In addition, a hybrid technique of swarm-based support vector machine (SVM) is introduced for hypoglycemia detection using the ECG parameters as inputs. In this technique, a particle swarm optimization (PSO) is proposed to optimize the SVM to detect hypoglycemia. With experiment using medical data of patients with type 1 diabetes, the introduced ECG parameters show significant contributions to the performance of the hypoglycemia detection and the proposed detection technique performs well in terms of sensitivity and specificity.

*Key Terms*—ECG parameter, Support vector machine (SVM), Particle swarm optimization (PSO), Hypoglycemia detection.

#### **INTRODUCTION**

Extreme hypoglycemia is one of known causes of death in diabetic patients. A survey reported that hypoglycemia caused 4% of the death of diabetic patients with age of less than fifty years<sup>33</sup>. A death review described that 4.2% of the diabetic deaths happened because of hypoglycemia<sup>9</sup>. Moreover, hypoglycemia unawareness could result that the diabetic patients do not recognize well hypoglycemia symptoms, and falling plasma glucose to very low level rarely provokes an awakening response in type-1 diabetic patients<sup>31</sup>. For these facts, an effective detection system for hypoglycemia is crucial.

This paper contributes to the development of hypoglycemia detection system by introducing electrocardiographic (ECG) parameters as inputs for hypoglycemia detection. The other contribution is that a hybrid particle swarm optimization (PSO) based SVM model has been developed for the detection of hypoglycemic episodes with inputs of ECG parameters.

Hypoglycemia is a disorder characterized by an abnormally-low blood glucose level (BGL) in the body. It is the most acute and common complication of Type 1 diabetes and is a limiting factor in a glycemic management of diabetes. Essentially, diabetic patients pursue intensive insulin therapy in attempting to control their glycemic level to prevent diabetic complications. Maintaining blood glucose level in normal range is a central issue in diabetes management and it monitors blood glucose level continuously and also employs an alarm of a hypoglycemia onset<sup>17</sup>.

A number of studies showed that hypoglycemia could result in electrocardiographic (ECG) alterations.  $QT_c$  interval, that is the interval from Q point to the end of T-wave in electrocardiogram, was longer in hypoglycemia than in euglycemia<sup>26</sup>. The mechanism of  $QT_c$  lengthening caused by hypoglycemia was proposed as sympathoadrenal response which might

relate to the rise in circulating adrenaline (epinephrine)<sup>19</sup>.

Considering to such correlation between electrocardiographic parameters and hypoglycemia, some ECG parameters, accompanied by the appropriate techniques, have been investigated for hypoglycemia detection as inputs. Heart rate (HR), one of ECG parameters, was applied for the onset detection of hypoglycemia using fuzzy estimator<sup>13</sup> and fuzzy neural network<sup>12</sup>. The other technique implemented *HR* and  $OT_c$  interval for inputs of the hypoglycemia detection using neural network<sup>28</sup> and fuzzy inference system<sup>21</sup>. The other ECG parameters: RR(interval from R-point to R-point), RT<sub>c</sub> (interval from R-point to the peak of T-wave), T-wave amplitude, T-wave skewness and T-wave kurtosis were applied to detect the onset of hypoglycemia using artificial neural network (ANN) and linear discriminant analysis (LDA)<sup>1</sup>. The other strategy was by using  $RT_c$  interval and T-wave amplitude as inputs of the Rule Base for nocturnal hypoglycemia detection<sup>2</sup>. Hypoglycemia detection strategy based on arrhythmia, which is as a hypoglycemic effect, using ECG parameters has an advantage which enables noninvasive technique instead of invasive techniques such as automatic implantable cardioverter defibrillator (AICD). AICD could monitors arrhythmia using a device inserted under skin or in upper chest muscles.

In short, the hypoglycemia detections based on ECG parameters employ ECG parameters and suitable techniques to reach a satisfactory performance. So far, to the best of our knowledge, none of them has been worldwide adopted for everyday clinical practices and it still requires comprehensive validations. Thus, one of the main contributions in this paper is to introduce new ECG parameters for input of hypoglycemia detection. As a second contribution, this paper introduces a swarm-based support vector machine (SVM) for hypoglycemia detection. The parameters of the SVM are optimized by the particle swarm optimization (PSO) method. Performance comparisons of the hypoglycemia detections using different ECG parameters and different SVM kernel functions are also the contribution provided by this paper.

*TpTe* interval, which is not yet widely explored in hypoglycemia detection, is used as an input for hypoglycemia detection in this work. In an ECG signal, *TpTe* interval is the descending part of T-wave or is the period from the peak of T-wave to its end. It was suggested that TpTe interval was independent of  $QT_c$  in the studied patient of Long QT Syndrome (LQTS)<sup>6</sup>. The congenital LQTS patients have longer TpTe than the control group<sup>22</sup>. QTp, as interval from Q point to the peak of T-wave, and T-wave width are also introduced for the hypoglycemia detection in this work. QTp and T-wave width correlate with ventricular repolarization, which was the interesting part in correlation with hypoglycemia in clinical studies<sup>29</sup>.

SVM is a classification technique which is successfully employed in many applications<sup>4</sup> including a cardiac signal classification<sup>11</sup>. Their advantages in classifications motivate us to select it as classifier in this paper. SVM requires optimal parameters to obtain the optimal classification. Particle swarm optimization is investigated to obtain the optimal parameters in this paper. PSO is a population-based stochastic-optimization method inspired by the social behavior, such as bird flocking and fish schooling. PSO has been used successfully for optimization in intelligent techniques, such as fuzzy system<sup>35</sup>, neural network<sup>20</sup> and fuzzy-neural network<sup>18</sup>. Hybrid PSO-SVM showed a high performance for detection of atrial premature beat, ventricular premature beat, right bundle branch block, left bundle branch block, and paced beat<sup>24</sup>. The other work used genetic algorithm (GA) for SVM parameters optimization to classify ECG arrhythmia using MIT-BIH database<sup>27</sup>.

The rest of this paper is organized as follows. The second section describes support vector machine, the proposed optimization using PSO and the generation of input. The obtained

ECG parameters and the hypoglycemia detection performances are presented and discussed in the third section. Finally, the fourth section is the conclusion.

#### METHOD

The proposed hypoglycemia detection system is developed by using a swarm-based SVM, as is described in Figure 1. The system uses inputs of ECG parameters and has binary output, hypoglycemia or nonhypoglycemia. In the system, PSO performs optimization to find the optimal values of the SVM parameters.

### Support Vector Machine

The description of SVM in more detail can be found in the tutorial by Burges<sup>7</sup>. Essentially, an SVM is a classifier which works through deciding a hyperplane which optimally separates two class data. Suppose there are *k* linearly-separable training-data  $\{\mathbf{x}_i, y_i\}$ , where  $\mathbf{x}_i \in \mathbb{R}^N$  is an *N* dimensional space and the associated  $y_i \in \{+1, -1\}$  is class label. The optimal hyperplane can be defined by  $\mathbf{w} \cdot \mathbf{x} + b = 0$ , which maximally separates the training data.  $\mathbf{w}$  is the hyperplane perpendicular vector and  $|b| / || \mathbf{w}^2 ||$  is distance of the hyperplane to the origin.

For linearly-separable data, training data satisfy  $y_i(\mathbf{w}\cdot\mathbf{x}+b)-1\geq 0$ , in which support vectors lie in equality of this equation. The SVM algorithm determines the optimum separating hyperplane that maximize distance, which is referred as margin, between two hyperplanes:  $\mathbf{w}\cdot\mathbf{x}+b=+1$  and  $\mathbf{w}\cdot\mathbf{x}+b=-1$ . The margin between those two hyperplanes is  $2/\|\mathbf{w}\|$ .

It is often that in many real world problems such separating hyperplane does not exist. Hence it is introduced positive slack variable  $\xi_i$  and then

$$y_i(\mathbf{w} \cdot \mathbf{x} + b) \ge 1 - \xi_i \tag{1}$$

The optimal separating hyperplane is determined by minimizing

$$C\sum_{i=1}^{k} \xi_i + \frac{1}{2} \left\| \mathbf{w} \right\|^2 \tag{2}$$

The *C*, called soft margin parameter, is a constant that is used to control the tradeoff between complexity and a proportion of nonseparable points.

Searching the optimal hyperplane is performed using Lagrange multiplier approach through maximizing

$$L(\alpha) = \sum_{i=1}^{k} \alpha_{i} - \frac{1}{2} \sum_{i=1}^{k} \sum_{j=1}^{k} \alpha_{i} \alpha_{j} y_{i} y_{j} \left( \mathbf{x}_{i} \cdot \mathbf{x}_{j} \right)$$
(3)

subject to

$$0 \le \alpha_i \le C \max_{i=1}^k y_i \alpha_i$$
(4)

where  $\alpha_i$  is the Lagrange multiplier.

In a case of imbalanced distributions between two class data, it is needed to use different error weights,  $w_0$  and  $w_1$ , to penalize more heavily the undesired errors related to the class with the smallest population<sup>5</sup>. Then (2) is modified by minimizing

$$w_0 C \sum_{i:y_i=-1}^{k} \xi_i + w_1 C \sum_{i:y_i=-1}^{k} \xi_i + \frac{1}{2} \left\| \mathbf{w} \right\|^2$$
(5)

The inner-product in (3) is replaced by a kernel function  $K(\mathbf{x}_i, \mathbf{x}_j)$  to map input data to higher dimensional space so that nonlinearly separable data can be linearly classified. In this paper, four kernel functions are adopted;

tion, 
$$K(\mathbf{x}_{i},\mathbf{x}_{j}) = exp\left(-\gamma \left\|\mathbf{x}_{i} - \mathbf{x}_{j}\right\|^{2}\right);$$
 (6)

RBF, radial basis function,

polynomial, 
$$K(\mathbf{x}_i, \mathbf{x}_j) = (\mathbf{x}_i, \mathbf{x}_j + 1)^d$$
; (8)

linear, 
$$K(\mathbf{x}_i, \mathbf{x}_j) = \mathbf{x}_i \cdot \mathbf{x}_j$$
; (9)

Values of  $\gamma$  in (6) and (7) and *d* in (8) are chosen to obtain a high classification performance through an optimization using PSO<sup>10</sup>. Finally, the class prediction for any test vector  $\mathbf{x} \in \mathbb{R}^N$  is given by

$$y = sgn(\sum \alpha_i y_i K(\mathbf{x}_i, \mathbf{x}) + b), \tag{10}$$

in which sgn is a signum function; the value of y greater than 0 is associated with +1 class and the negative one is associated with -1 class.

### **Optimization for SVM parameters using PSO**

The SVM parameters are optimized to find the best performance of the hypoglycemia detection. The SVM parameters are the soft margin parameter *C*,  $w_o$  and  $w_I$  in (5),  $\gamma$  in (6) and (7) and *d* in (8). To optimize the parameters, PSO is developed. PSO performs optimization considering an evolutionary technique based on the movement of swarms and inspired by the social behavior of bird flocking and fish schooling<sup>10</sup>. Particles of swarm (or population) fly through an *n*-dimensional solution space with adjusted velocity and position. The velocity is adjusted according to the historical of particle best-position and the neighborhood best-position, which are derived according to a user defined fitness function. The position of particle  $z_m$  and its velocity  $v_m$  at iteration *t* are<sup>10</sup>:

$$z_m(t) = z_m(t-1) + v_m(t)$$
(11)

$$v_{m}(t) = \varphi v_{n}(t-1) + c_{1}r_{1}(t-1)(z_{bm}(t-1) - z_{m}(t-1)) + c_{2}r_{2}(t-1)(z_{gm}(t-1) - z_{m}(t-1))$$
(12)

where  $z_{bm}$  is the best position and  $z_{gm}$  is the best global position of particle of the swarm. The best position is the best in a "subset" and the global best position is the best of the best positions. In the other words, the best position of a particle is recorded so far from the previous iteration; the position of best particle among the all particles is called the best global position.  $r_1$ () and  $r_2$ () are random functions in the range [0 1] for weighting acceleration constants,  $c_1$  and  $c_2$ , and  $\varphi$  is inertia weight. Those velocity and position are iterated until the convergence is reached.

The objective of the PSO optimization is to maximize the performance of the hypoglycemia detection. The performance is measured in terms of sensitivity  $\mathcal{G}$  and specificity  $\eta$ ; sensitivity is defined as the ratio of correct detection of hypoglycemia to the actual number of hypoglycemia cases, and specificity is defined as the ratio of correct detection of nonhypoglycemia to the actual number of nonhypoglycemia cases. Thus, the PSO optimization is essentially to maximize sensitivity  $\mathcal{G}$  and specificity  $\eta$  using the following fitness function;

$$f = \beta \mathcal{G}_{tr} + (1 - \beta_r)\eta_{tr} + \beta \mathcal{G}_{val} + (1 - \beta)\eta_{val} + \sigma, \tag{13}$$

where  $\mathcal{G}_{tr}$  and  $\eta_{tr}$  are the sensitivity and specificity, respectively, obtained from the hypoglycemia detection model which is tested by using a training data set; and  $\mathcal{G}_{val}$  and  $\eta_{val}$  are the sensitivity and specificity, respectively, obtained from the hypoglycemia detection model which is tested by using a validation data set. The inclusion of  $\mathcal{G}_{val}$  and  $\eta_{val}$  in the fitness function is to reduce the risk of overtraining<sup>3</sup>. The higher sensitivity than specificity is considered in the fitness function by setting  $\beta$  to 0.58. This strategy is to prevent the risk of the low sensitivity of the hypoglycemia detection. To force the high sensitivity in the detection,  $\sigma$  is

also given by using the following definition.

$$\sigma = \begin{cases} 10 & if \quad \mathcal{G}_{tr} > 0.7, \eta_{tr} > 0.4, \mathcal{G}_{val} > 0.7, \eta_{val} > 0.4 \\ 0 & \text{Otherwise} \end{cases}$$
(14)

The  $\sigma$  definition in (14) is to force the sensitivity and specificity to be higher than 70% and 40%, respectively.

### Generation of inputs

The proposed swarm-based SVM technique used ECG parameters in the input. In this experiment, the technique was examined using the ECG parameters which were obtained from five diabetic-patients in the age of 16±0.7 years. The ECG signals were captured during an overnight hypoglycemia study. The hypoglycemia study, which was a clamp study, was performed at Princess Margaret Hospital in Perth, Australia, with approval from Women's and Children's Health Service, Department of Health, Government of Western Australia, and with informed consent. Each study consisted of five phases approximately: one hour of baseline, three hours of euglycemia, one hour of ramp, one and half hours of hypoglycemia and four and half hours of recovery.

The ECG signals were recorded continuously using the Siesta<sup>™</sup> from Computedics with the sampling rate of 512 Hz; this work used single lead, which was lead II. The correlated blood glucose level was found by using Yellow Spring Instruments in each five minute. The resulted ECG signals were then exported to the form of text file.

The ECG parameters, as described in Figure 2, were obtained from the patient's ECG signals, which were in the form of text file, using a program written in Matlab. The resulted ECG signals from the Siesta did not have high noises and therefore a simple signal processing

was enough to tackle the noises. In the signal processing, the ECG signals were filtered by using a low pass filter with cut-off frequency of 80 Hz, to omit high frequency noises, and were filtered using a 50 Hz notch filter, to remove noise of power line interference. The signals were also filtered using a high pass filter with cut-off frequency of 0.7Hz to omit baseline wander. The R peak of each beat of the ECG signals was obtained by finding the peak having higher amplitude than a threshold value<sup>23</sup>. Similar method was used to obtain the T-wave peak Tp of each beat of the ECG signals that it was by obtaining the peak having higher amplitude than a threshold value in the segment on the right side of R peak<sup>30</sup>. The T-wave end Te was determined by the Philips QT Interval Measurement Algorithm<sup>32</sup>. In the algorithm, in a beat of the ECG signals, a line segment was drawn from  $T_p$  forward in time to a point in the ECG signal and the Te was a point that has the maximum vertical distance between the point and the line segment. The beginning of T-wave To was obtained by similar method to find Te with the difference that the used line segment was in the left side of the Tp. The resulted annotation was checked visually. The improper annotation, mostly because of the improper ECG signals, was not used. If a U wave presented before the T wave returned to baseline, the end of the T wave was defined as the nadir between T and U waves. The Phillips method has advantage compared to the other methods, such as tangent method, which use ECG baseline. The methods could result variability on account of the arbitrariness of the ECG baseline choosing and are sensitive to ECG baseline drift<sup>32</sup>.

To reduce patient-to-patient variability, a normalization was performed. In a patient, the ECG parameters were normalized using the patient's ECG parameter which was in the beginning of study<sup>28</sup>. The more detail, supposing that an ECG parameter at time *i* is  $x_i$  and the ECG parameter at the beginning study is  $x_0$ , normalized ECG parameter  $\bar{x}$  equals to  $x_i/x_0$ .

The resulted ECG parameters were arranged to a matrix form having rows representing data point number and column representing ECG parameters, such as  $QTe_c$ . Each row (or data point) was the average of 30 consecutive-beats of the ECG.

The ECG parameters used in the study are (i)  $TpTe_c$  (interval from the peak of T-wave Tp to the end of T-wave Te), (ii)  $ToTe_c$  (interval from the beginning of T-wave To to the end of T-wave Te), (iii)  $RTp_c$  (interval from R point to the peak of T-wave Tp), (iv)  $QTe_c$  (interval from Q point to the end of T-wave Te), (v)  $QTp_c$  (the interval from Q point to the peak of T-wave Tp), (vi)  $STo_c$  (the interval from S point to the beginning of T-wave To) and (vii) HR (heart rate that is 60/RR). The descriptions of the variables are shown in Fig. 2. Index of c in the parameters indicates the heart rate correction for the variables using the Bazett's formula<sup>25</sup>, which is normalized using square root of RR interval.

#### RESULT

The hypoglycemia detection which is based on a swarm-based SVM has been developed. The detection has been examined using the electrocardiographic parameters obtained from five diabetic-patients. In the study, the patients had nonhypoglycemic phase in the beginning and then their blood glucose decreased to hypoglycemic phase, as are described in Figure 3.

#### The Resulted ECG Parameters

The comparison of the patients' ECG parameters obtained in the hypoglycemic phase (BGL < 3.0 mmol/l) against in the nonhypoglycemic phase is presented in Table 1. The ECG parameters are presented in the form of (mean  $\pm$  standard deviation) with the associated significance value *p*, which is resulted from a *t* test. The comparison shows that the ECG

parameters in hypoglycemia differ significantly from those in nonhypoglycemia (p<0.01) except  $STo_c$  (p<0.1).  $STo_c$  is the interval from the S point to the beginning of the T-wave  $T_o$  of ECG signal. Therefore,  $STo_c$  is not used for input in the hypoglycemia detection. Those ECG parameters having significant difference are higher in hypoglycemia than in nonhypoglycemia. The higher QTc in hypoglycemia is confirmed in the other study<sup>19</sup> and the higher heart rate in hypoglycemia is also confirmed<sup>14</sup>. The higher values of the other ECG parameters;  $RTp_c$ ,  $QTp_c$ ,  $TpTe_c$ ,  $QTe_c$ , and  $ToTe_c$  in hypoglycemia, might be considered that these parameters are as part of repolarization, in which repolarization prolongs in hypoglycemia<sup>29</sup>.

#### (Table 1)

#### Hypoglycemia Detection by Using the Swarm-based SVM

The experiment for the hypoglycemia detection has been performed using the swarmbased SVM and the ECG parameters as inputs. The experiment used the ECG parameters obtained from the hypoglycemia study having 1327 and 399 data points of nonhypoglycemia and hypoglycemia, respectively. The data points were randomly divided to three subsets having same size; thus each subset consists of 575 data points of nonhypoglycemia and 133 data points of hypoglycemia. The three subsets were used as training, validation and final testing data sets. The training data set was used during the training to create a hypoglycemia detection model. The validation and training data set were used to test the hypoglycemia detection model during the optimization. The testing data set was used to test the best hypoglycemia detection model obtained from the optimization.

The hypoglycemia detection techniques using the swarm-based SVMs employ different kernel functions: RBF, sigmoid, polynomial and linear kernel functions have been examined.

PSO has been used to automatically obtain the optimal values of the parameters considering to the fitness function in (13) in the optimization. The range of values of the parameters was created as the following; *C*: 1 to  $10^5$ ,  $w_0$ ,  $w_1$ :  $10^{-4}$  to 1,  $\gamma$ : 0.01 to 100, *d*: 1 to 50. In the PSO algorithm, population size was set at 100, acceleration constants  $c_1$  and  $c_2$  were set at 2 and the inertia weight *w* was 0.9.

The performances of the hypoglycemia detections using the swarm-based SVM which employed RBF kernel functions are described in Table 2 and in Figure 4. For the comparison of the performances, a geometric mean  $m^{11}$  gm is also used. The geometric mean equals to the square root of the multiplication of sensitivity and specificity, or  $gm = \sqrt{(\beta, \beta)}$ . The geometric mean is suitable to indicate performance of a detection system with imbalanced data. This work used an imbalanced data in which data number of nonhypoglycemia is about triple of hypoglycemia data number. The table indicates that each ECG parameter shows a significant contribution to the performance of the hypoglycemia detection. In the testing, the contribution is indicated by the performance of the detection which uses single ECG parameter having performance with sensitivity of more than 73% and geometric mean of more than 49%. In terms of the geometric mean, the performance of the detection using heart rate is the highest among the detection performances which use single ECG parameter; it is consistent in training, validation and testing. In the same terms, the second and the third highest performances are the detections which use  $RTp_c$  and  $QTe_c$ , respectively. Using the all ECG parameters in the input, the best performance is found with the testing performance is 70.68, 81.45 and 75.87, respectively, in terms of the sensitivity, specificity and geometric mean.

Table 3 and Figure 5 show the performance of the hypoglycemia detection using different techniques with the same input that is the all six ECG parameters. The techniques are the swarmbased SVM applying different kernel functions; RBF, polynomial, sigmoid and linear kernel functions, which are called as SBSR, SBSP, SBSS, SBSL, respectively. The optimal parameters which were found from the optimization are presented in Table 4. In terms of the geometric mean, the performance of hypoglycemia detection using SBSR is the best compared to the other three techniques. The second, third and fourth highest performances, in the same terms, are obtained by the detections use SBSP, SBSS and SBSL techniques, respectively.

#### (Table 3)

#### (Table 4)

The proposed swarm optimization using the constraint provided in the fitness function, equation (13), to obtain the sensitivity and specificity of more than 70% and 40%, respectively, can work successfully in the experiment. It can be seen in Table 3 in which the sensitivities and specificities in training, validation and testing are more than 70% and 40%, respectively, except the sensitivities of SBSL. As comparison, the performances of the detection techniques using SVM which did not use the proposed swarm optimization, which are grouped in a technique called as rSVM in this paper, are presented in Table 5 and in Figure 6. The rSVM technique involves SR, SP, SS and SL, which are the SVM technique employed RBF, polynomial, sigmoid and linear kernel functions, respectively, without the proposed optimization. The presented performances of the detection using the rSVM techniques are the average of 100 repeated detections in which the detection parameters are randomly selected. In terms of the geometric

mean, the performances of the rSVM are comparable to the performances of the swarm-based SVM, but their sensitivities are less than 70%, which is not directed in a biomedical application. The specificities of the detections use the rSVM are higher against the swarm-based SVM. It might happen because the rSVM tend to obtain as high as possible of the total sensitivity and specificity without consideration of more 70% in sensitivity. Therefore, the proposed swarm-based SVM might be suitable to prevent low sensitivity in hypoglycemia detection with the input of ECG parameters. In addition, for comparison, linear multiple regression (LMR) was also used. The performance of LMR was low in sensitivity (less than 50%) in training, validation and testing. The geometric mean of LMR was less than 70%.

#### (Table 5)

#### DISCUSSION

TpTe, a descending part of the T-wave, was suggested as transmural dispersion in the myocardium, as the deviation between endocardial and the M cells action potentials, during repolarization<sup>34</sup>. The geometric mean of around 50% in the detection using only  $TpTe_c$  shows that  $TpTe_c$  has meaningful contribution for hypoglycemia detection. This meaningful also parallel with result of the statistical *t* test indicating that  $TpTe_c$  is higher in hypoglycemia than in nonhypoglycemia with p<0.01.  $ToTe_c$  might also have contribution to hypoglycemia detection. To $Te_c$  correlates with T-wave morphology which is possibly affected by hypoglycemia<sup>15</sup>. The difference of  $ToTe_c$  and  $TpTe_c$  with the other four ECG variables is that the two variables represent repolarization only in which the other four variables involve depolarization and repolarization. In evaluation of repolarization, excluding the QRS complex may be needed so

that the evaluation is independent from depolarization<sup>8</sup>. Relation of hypoglycemia with interval from R-peak to the peak of-T wave (RTp) is confirmed in the other study<sup>2</sup>. In estimation of repolarization, RTp is easier to be estimated than the other parameters in which it is marked by the sharp R peak and the peak of T-wave. This easier estimation could reduce error estimation of repolarization.

In this work, SVM using RBF kernel function showed the highest performance. SVM-RBF could tackle well for a nonlinear data, in which the relation between class labels and input features is nonlinear, as the data used in this work, and thus the SVM-RBF has a good generalization which resulting a good performance. In the other hand, linear kernel function could not tackle well a nonlinear data and thus its performance is low. SVM using linear kernel function could be a special case of SVM-RBF<sup>16</sup> in which SVM-linear using an SVM soft margin parameter *C* could have performance with SVM-RBF which uses a parameter value of  $\gamma$ . Because this work has limited features, which are six inputs, a mapping using kernel function is important to find a high dimensional space.

The optimal values for hypoglycemia detections have been found as in Table 4. The values of  $w_2$  are higher than  $w_1$ ; it is automatically directed to find that the error of hypoglycemia data is low which result the high sensitivity, as it is desired. In other word, the automatic selection of weight parameters performs well. Regarding *C* values, although the *C* values are high of more than 9,000, it is not overfitting which is indicated that the generalization of the detection techniques is still good; it is indicated by the testing performance is still high.

The proposed hypoglycemia detection strategy using inputs of ECG parameters and using swarm base support vector machine technique has been presented. This hypoglycemia detection strategy could have benefit for patients having risk of hypoglycemia. This strategy could be applied in a small ambulatory ECG to obtain a portable hypoglycemia detection system. Thus, by using the system, the hypoglycemia events could be monitored continuously and noninvasively in which this noninvasive method has benefit to find a painless clinical test.

#### CONCLUSION

The detection of hypoglycemia using a swarm-based SVM technique with inputs of electrocardiographic parameters has been developed in this work. The electrocardiographic parameters  $TpTe_c$ ,  $ToTe_c$ ,  $RTp_c$ ,  $QTp_c$ ,  $QTe_c$  and HR show significant contributions to the performance of the hypoglycemia detection. The various detection techniques which employ the proposed swarm optimization and the technique without the proposed optimization have been developed and compared. In general, the hypoglycemia detection using the swarm-based SVM-RBF technique outperforms the other methods. Using all six ECG parameters as inputs, this novel swarm-based SVM-RBF hypoglycemia detection algorithm yields the best performance with a sensitivity of 70.68% and specificity of 81.45%.

#### ACKNOWLEDGMENT

This work was supported by a grant from Juvenile Diabetes Research Foundation. The authors would like to thank Dr. Nejhdeh Ghevondian and Assoc. Prof. Timothy Jones for their contribution.

#### **CONFLICT OF INTEREST STATEMENT**

The authors have no conflict of interest related to this work and the manuscript presented in this article.

#### REFERENCES

- <sup>1</sup>Alexakis, C., et al. Feature extraction and classification of electrocardiogram (ECG) signals related to hypoglycaemia. *Proc. of Computers in Cardiology*. 30:537-540. 2003
- <sup>2</sup>Alexakis, C., et al. A Knowledge-Based Electrocardiogram-Monitoring System for Detection of the Onset of Nocturnal Hypoglycaemia in Type 1 Diabetic Patients. *Proceeding of Computers in Cardiology*. 33:5-8. 2006
- <sup>3</sup>Astion, M. L., M. H. Wener, R. G. Thomas, G. G. Hunder and D. A. Bloch. Overtraining in neural networks that interpret clinical data. *Clin. Chem.* 39:1998-2004, 1993
- <sup>4</sup>Barakat, N. H., A. P. Bradley and M. N. H. Barakat. Intelligible support vector machines for diagnosis of diabetes mellitus. *IEEE Trans. Inf. Technol. Biomed.* 14:1114-1120, 2010
- <sup>5</sup>Batuwita, R. and V. Palade. FSVM-CIL: fuzzy support vector machines for class imbalance learning. *IEEE Transactions on Fuzzy Systems*. 18:558-571, 2010
- <sup>6</sup>Benhorin, J., et al. Long QT syndrome. New electrocardiographic characteristics. *Circulation*. 82:521-527, 1990
- <sup>7</sup>Burges, C. A Tutorial on support vector machines for pattern recognition. *Data Mining and Knowledge Discovery*. 2:121-167, 1998
- <sup>8</sup>Can, I., K. Aytemir, S. K<sup>.</sup>ose and A. Oto. Physiological mechanisms influencing cardiac repolarization and QT interval. *Card. Electrophysiol. Rev.* 6:278–281, 2002
- <sup>9</sup>Connell, F. A. and J. M. Louden. Diabetes mortality in persons under 45 years of age. *Am. J. Public Health.* 73:1174-1177, 1983
- <sup>10</sup>del Valle, Y., G. K. Venayagamoorthy, S. Mohagheghi, J. C. Hernandez and R. G. Harley. Particle swarm optimization: basic concepts, variants and applications in power systems. *IEEE Transactions on Evolutionary Computation*. 12:171-195, 2008

- <sup>11</sup>Georgoulas, G. and C. D. Stylios. Predicting the risk of metabolic acidosis for newborns based on fetal heart rate signal classification using support vector machines. *IEEE Trans. Biomed. Eng.* 53:875-884, 2006
- <sup>12</sup>Ghevondian, N., H. T. Nguyen and S. Colagiuri. A novel fuzzy neural network estimator for predicting hypoglycaemia in insulin-induced subjects. *Proceeding of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society.* 1371 -1374. 1997
- <sup>13</sup>Hastings, G., N. Ghevondian and H. Nguyen. A self-organising fuzzy estimator for hypoglycaemia monitoring in diabetic patients. *Proceeding of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*. 1371 - 1374. 1998
- <sup>14</sup>Heger, G., K. Howorka, H. Thoma, G. Tribl and J. Zeitlhofer. Monitoring set-up for selection of parameters for detection of hypoglycaemia in diabetic patients. *Med. Biol. Eng. Comput.* 34:69-75, 1996
- <sup>15</sup>Ireland, R. H., R. T. C. E. Robinson, S. R. Heller, J. L. B. Marques and N. D. Harris. Measurement of high resolution ECG QT interval during controlled euglycaemia and hypoglycaemia. *Physiol. Meas.* 21:295-303, 2000
- <sup>16</sup>Keerthi, S. S. and C.-J. Lin. Asymptotic behaviors of support vector machines with gaussian kernel. *Neural Comput.* 15:1667–1689, 2003
- <sup>17</sup>Klonoff, D. C. The need for hypoglycemia detection and prevention in type 1 diabetes.
   *Diabetes Technology & Therapeutics*. 3:3567-570, 2001
- <sup>18</sup>Kuo, R. J., S. Y. Hong and Y. C. Huang. Integration of particle swarm optimization-based fuzzy neural network and artificial neural network for supplier selection. *Appl. Math. Model.* 34:3976-3990, 2010

- <sup>19</sup>Lee SP, et al. Influence of autonomic neuropathy on QTc interval lengthening during hypoglycemia in type 1 diabetes. *Diabetes*. 53:1535-1542, 2004
- <sup>20</sup>Lin, C.-J. and Ming-HuaHsieh. Classification of mental task from EEG data using neural networks based on particle swarm optimization. *Neurocomputing*. 72:1121-1130, 2009
- <sup>21</sup>Ling, S. H., Nuryani and H. T. Nguyen. Evolved fuzzy reasoning model for hypoglycaemic detection. *Proceeding of the 32nd Annual International Conference of the IEEE EMBS*. 4662-4665. 2010
- <sup>22</sup>Lubinskj, A., et al. New Insight into Repoiarization Abnormalities in Patients with Congenital Long QT Syndrome: the Increased Transmural Dispersion of Repoiarization. *Pacing Clin. Electrophysiol.* 21:172-175, 1998
- <sup>23</sup>Manriquez, A. I. and Q. Zhang. An algorithm for QRS onset and offset detection in single lead electrocardiogram records. *Proceeding of the 29th Annual International Conference of the IEEE EMBS*. 541-544. 2007
- <sup>24</sup>Melgani, F. and Y. Bazi. Classification of electrocardiogram signals with support vector machines and particle swarm optimization. *IEEE Trans. Inf. Technol. Biomed.* 12:667-677, 2008
- <sup>25</sup>Moss, A. J. Measurement of the QT interval and the risk associated with QTc interval prolongation: A review. *Am. J. Cardiol.* 72:B23-B25, 1993
- <sup>26</sup>Murphy, N. P., et al. Prolonged cardiac repolarisation during spontaneous nocturnal hypoglycaemia in children and adolescents with type 1 diabetes. *Diabetologia*. 47:1940-1947, 2004

- <sup>27</sup>Nasiri, J. A., M. Naghibzadeh, H. S. Yazdi and B. Naghibzadeh. ECG arrhythmia classification with support vector machines and genetic algorithm. *Conf, Proc. of the 2009 Third UKSim European Symposium on Computer Modeling and Simulation*. 187-192. 2009
- <sup>28</sup>Nguyen, H. T., N. Ghevondian and T. W. Jones. Detection of nocturnal hypoglycemic episodes (natural occurrence) in children with type 1 diabetes using an optimal bayesian neural network algorithm. *Proc. of the 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*. 1311 - 1314 2008
- <sup>29</sup>Robinson RTCE, et al. Mechanisms of abnormal cardiac repolarization during insulin induced hypoglycemia. *Diabetes*. 52:1469-1474, 2003
- <sup>30</sup>Schneider, R., A. Bauer, P. Barthel and G. Schmidt. Challenge 2006: QT interval measurement. *Proceeding of Computers in Cardiology*. 325-328. 2006
- <sup>31</sup>Schultes, B., et al. Defective Awakening Response to Nocturnal Hypoglycemia in Patients with Type 1 Diabetes Mellitus. *PLoS Med.* 4:e69, 2007
- <sup>32</sup>Sophia, H. Z., D. H. Eric, M. L. James, E. G. Richard and Q. F. Dirk. Philips QT interval measurement algorithms for diagnostic, ambulatory, and patient monitoring ECG Applications. *Ann. Noninvasive Electrocardiol.* 14:S3-S8, 2009
- <sup>33</sup>Tunbridge, W. M. G. Occasional Survey. Factors contributing to deaths of diabetics under fifty years of age. On behalf of the Medical Services Study Group and British Diabetic Association. *The Lancet.* 318:569-572, 1981
- <sup>34</sup>Yan, G.-X. and C. Antzelevitch. Cellular basis for the normal T wave and the electrocardiographic manifestations of the long-QT syndrome. *Circulation*. 98:1928-1936, 1998

<sup>35</sup>Zhao, L., F. Qian, Y. Yang, Y. Zeng and H. Su. Automatically extracting T–S fuzzy models using cooperative random learning particle swarm optimization. *Applied Soft Computing*. 10:938-944, 2010

The comparison of the ECG parameters obtained in hypoglycemic phase against in

ECG	Nonhypoglycemia	Hypoglycemia	<i>p</i> -value
Parameter			
HR	$1.052\pm0.061$	$1.197\pm0.128$	< 0.0001
$QTe_c$	$1.040\pm0.031$	$1.074\pm0.054$	< 0.0001
$TpTe_c$	$1.031\pm0.032$	$1.074\pm0.071$	< 0.0001
$QTp_c$	$1.058\pm0.071$	$1.106\pm0.096$	< 0.005
$ToTe_c$	$1.058\pm0.071$	$1.106\pm0.096$	< 0.005
$RTp_c$	$1.044\pm0.039$	$1.068\pm0.056$	< 0.01
$STo_c$	$0.994 \pm 0.141$	$0.940\pm0.193$	<0.1

nonhypoglycemic phase

The performance of the hypoglycemia detection using the developed swam-based SVM-RBF

	Training			 Validation				Testing			
Inputs	Sens.	Spec.	gm	Sens.	Spec.	gm		Sens.	Spec.	gm	
	(%)	(%)	(%)	(%)	(%)	(%)		.(%)	(%)	(%)	
HR	88.72	61.31	73.75	 86.47	57.69	70.63		82.71	57.01	68.67	
$QTe_c$	81.20	57.47	68.31	78.95	56.56	66.82		75.19	57.47	65.73	
$TpTe_c$	91.73	24.43	47.34	89.47	22.17	44.54		87.97	28.05	49.68	
$QTp_c$	83.46	45.70	61.76	77.44	47.06	60.37		78.20	49.10	61.96	
$ToTe_c$	79.70	53.17	65.10	75.19	55.88	64.82		73.68	52.04	61.92	
$RTp_c$	81.20	59.28	69.38	78.95	60.18	68.93		78.20	57.92	67.30	
$HR, QTe_c, TpTe_c$	06 00	84 84	00 71	70.68	76.02	73 30		70.68	81 45	75 87	
$QTp_c, ToTe_c, RTp_c$	70.77	04.04	<u>70.71</u>	70.08	70.02	<u>73.30</u>		/0.00	01.45	15.01	

# and the ECG parameter as input

Sens: sensitivity, Spec: specificity

The performance of the hypoglycemia detection using different techniques and using the same

	,	Training			alidatio	n		Testing		
Detection technique	Sens.	Spec.	gm	Sens.	Spec.	gm	Sens	Spec.	gm	
teeninque	(%)	(%)	(%)	(%)	(%)	(%)	.(%)	(%)	(%)	
SBSR	96.99	84.84	90.71	70.68	76.02	73.30	70.68	81.45	75.87	
SBSP	87.97	68.33	77.53	83.46	64.03	73.10	78.95	63.12	70.59	
SBSS	88.72	64.93	75.90	83.46	61.76	71.80	79.70	61.31	69.90	
SBSL	53.38	95.25	71.31	45.86	92.31	65.07	53.38	88.69	68.81	

input that is the all six ECG parameter

SBSR: Swarm-based SVM-RBF, SBSP: Swarm-based SVM-Polynomial,

SBSS: Swarm-based SVM-Sigmoid, SBSL: Swarm-based SVM-Linear.

Detection	Input	Optimal SVM parameters							
Technique	mput	С	y/d	$w_0$	<i>W</i> <sub>1</sub>				
	HR	25,453	48.74	0.12	0.87				
	$QTe_c$	38,063	51.96	0.24	1.00				
	$TpTe_c$	61,561	78.34	0.24	1.00				
SBSR	$QTp_c$	12,099	61.05	0.24	1.00				
	$ToTe_c$	100,000	85.07	0.17	0.87				
	$RTp_c$	93,924	54.94	0.21	1.00				
SBSR	All parameters	43,460	6.29	0.18	1.00				
SBSP	All parameters	47,239	30.74	0.11	0.59				
SBSS	All parameters	92,720	0.01	0.13	1.00				
SBSL	All parameters	9,436	-	0.31	0.56				

The optimal parameters which were found from the optimization using swarm technique

SBSR: Swarm-based SVM-RBF,

SBSP: Swarm-based SVM-Polynomial,

SBSS: Swarm-based SVM-Sigmoid,

SBSL: Swarm-based SVM-Linear.

All parameters: HR, QTe<sub>c</sub>, TpTe<sub>c</sub>, QTp<sub>c</sub>, ToTe<sub>c</sub>, RTp<sub>c</sub>

The performance of the hypoglycemia detections without PSO (input: all six ECG parameter)

	Training				Validatior		Testing			
Detection	Sens.	Spec.	gm	Sens.	Spec.	gm	Sens	Spec.	gm	
technique	(%)	(%)	(%)	(%)	(%)	(%)	.(%)	(%)	(%)	
SR	82.62	99.03	90.45	49.38	88.97	66.28	53.50	90.90	69.74	
SP	53.32	96.48	71.73	44.51	92.98	64.33	49.35	94.20	68.19	
SS	24.08	75.40	42.61	24.21	75.41	42.73	24.18	75.33	42.68	
SL	53.58	95.27	71.45	44.12	92.98	64.05	48.87	92.29	67.16	
LMR	45.11	95.93	65.78	38.35	92.76	59.64	45.86	94.57	65.86	

SR: SVM-RBF, SP: SVM-Polynomial, SS: SVM-Sigmoid, SL: SVM-Linear,

LMR: Linear multiple regression

Figure 1: Hypoglycemia detection using a swarm-based SVM technique and input of ECG parameters

Figure 2: The intervals: *TpTe*, *ToTe*, *RTp*, *QTe*, *QTp* and *RR*. These parameters are then corrected by heart rate, or *RR*, using the Bazzet formula.

Figure 3: The profile of the blood glucose levels of the diabetic patients.

Figure 4: The performance of the hypoglycemia detection using the developed swam-based SVM-RBF and the ECG parameter as input.

Figure 5: The performance of the hypoglycemia detection using different techniques and using the same input that is the all six ECG parameter.

Figure 6: The performance of the hypoglycemia detections which do not use the swam optimization; they use the same input that is the all six ECG parameter











