Hybrid Particle Swarm - based Fuzzy Support Vector Machine for Hypoglycemia Detection

Nuryani Nuryani, Sai Ho Ling, Hung T. Nguyen
Centre for Health Technologies, Faculty of Engineering and Information Technology
University of Technology Sydney, Australia
nnuryani@eng.utd.edu.au; Steve.Ling@uts.edu.au; Hung.Nguyen@uts.edu.au

Abstract—Severe hypoglycemia is potentially life-threatening. This article introduces a novel hypoglycemia detection strategy using a hybrid particle swarm - based fuzzy support vector machine (SFisSvm) technique. The inputs of this system are six electrocardiographic (ECG) parameters. The system parameters of SFisSvm are optimized using a particle swarm optimization method. The proposed hypoglycemia detector system is a combination of two subsystems, namely, fuzzy inference system (FIS) and support vector machine (SVM). Two most significant inputs, heart rate and RTpc are fed to FIS, and its output is used for input of the SVM. The other ECG parameters and the output of FIS are fed to SVM and, then, are classified to indicate the presence of hypoglycemia. In this study, three and five membership functions are investigated for FIS. Furthermore, radial basis function (RBF), sigmoid and linear kernel functions are employed for mapping the inputs to high dimensional space in SVM. Performances of SFisSvm with different kernel functions are compared. As conclusion, the performance of SFisSvm is found with 75.19%, 83.71% and 79.33% in terms of sensitivity, specificity and geometric mean.

Keywords-component; hypoglycemia; electrocardiography, fuzzy logic; support vector machine.

I. Introduction

Severe hypoglycemia is a potentially serious problem in life which remits significant morbidity and mortality. In correlation with cardiovascular conditions, it could cause atrial fibrillation [1, 2], ventricular ectopics, sustained ventricular tachycardia, ventricular fibrillation and asystole [3]. Hypoglycemia in type 1 diabetic patients which happens during sleep was associated as the cause of the "dead in bed" syndrome [4].

In recent years, hypoglycemia detection methods have been interesting fields studied by research groups [5-7]. The detection is essentially employed to provide an early warning that hypoglycemia is happening, and then patients or their carers can perform appropriate actions to achieve normoglycemia. These appropriate actions could help patients to reduce hypoglycemic complications.

Based on invasiveness, there are three types of hypoglycemia detections, which are invasive, minimally invasive and noninvasive [8]. Obviously, the noninvasive type is a preferable choice because it is more convenient for patients to use this type of detection. Furthermore, noninvasive hypoglycemia detections mostly can be used for continuously hypoglycemic monitoring.

One of the interesting methods to detect hypoglycemia noninvasively is by means of physiological effects of hypoglycemia. In studies, hypoglycemia detection have been developed by means of hypoglycemic physiological effects on the heart [6], [9], [10], brain [5], [11], and skin [12].

Studies of hypoglycemia detection employed algorithm techniques to process ECG parameters to find a high performance of hypoglycemia detection. Several algorithms have been investigated for hypoglycemia detection; neural network [9], [13], fuzzy neural network [14], self-organizing fuzzy estimator [15], and genetic-algorithm-based multiple regression [6].

In general, those studies employ methods to reach satisfactory level of reliability in hypoglycemia detection using ECG parameters. Until recently, to the best of our knowledge, hypoglycemia detections using ECG parameters still require extensive validation before they can be adopted for worldwide clinical practices. Therefore, the presentation of this paper is an effort to develop a method to find hypoglycemia detection having high performance. The construction method in this paper is based on the classification techniques using hybrid particle swarm - based fuzzy support vector machine (SFisSvm).

SVM has proved good performance in general for classification in various application [16] including in application to classify features of cardiac signals [17-20]. Choosing SVM as a classification tool consider to its good performance and SVM classification ability to generalize well even with small size sample[21]. FIS also has showed good performance in many applications, including in medical field [22].

Swarm based SVM (SSvm) algorithms have also been studied for hypoglycemia detection using ECG parameters [23]. The proposed algorithm might improve the performance of the SSvm hypoglycemia detection by including fuzzy inference system (FIS) in the SSvm, arising SFisSvm.

This paper proposes a novel hypoglycemia detection strategy using hybrid particle swarm - based fuzzy support vector machine (SFisSvm). This hypoglycemia detection strategy employs six electrocardiographic (ECG) parameters as inputs and was constructed by two subsystems, FIS and SVM. Two most significant ECG parameters are fed to the FIS, and the other ECG inputs are fed directly to the SVM; the two most

significant ECG parameters are found from [23], which are the ECG parameters resulting the highest performance in hypoglycemia detection. The output of the FIS is also used as the input of the SVM; thus, there are five inputs for the SVM module. FIS is the famous system employing fuzzy logic and fuzzy set theory[24]. Its frameworks are based on the concepts of fuzzy set theory, fuzzy if-then rules, and fuzzy reasoning. The advantages of FIS include its ability to handle linguistic concepts and universal approximator, performing nonlinear relation between inputs and outputs. Thus, by applying FIS to the two ECG parameters a hypoglycemic index can be found from the two ECG parameters and the index is used for input of SVM.

The parameters of FIS and SVM are optimized using hybrid particle swarm optimization with wavelet mutation (HPSOWM) [25] which could find the optimal model of hypoglycemia detection with the best performance. Furthermore, the performances of SFisSvm using different kernel functions in hypoglycemia detection are presented; in addition these performances are also compared with the performance of the SSvm hypoglycemia detection [23].

The rest of this paper is organized as follows. Section II presents the construction of the proposed strategy; by describing FIS, SVM and HPSOWM. Section III presents the experimental results, and the conclusion for this research is drawn in Section IV.

II. METHOD

This paper presents hypoglycemia detection strategy by employing SFisSvm with inputs or ECG parameters, shown in Fig. 1. The ECG parameters used are HR, RTp_c, QT_c, TpTe_c, ToTe_c and QTp_c (Fig. 2); the output is binary level, which is hypoglycemic or nonhypoglycemic level. In this system, HPSOWM [25] is used to optimize the parameters of FIS and SVM.

The ECG parameters are extracted form ECG signal (Fig. 2)). Heart rate is 60/RR in which RR is the interval of the consecutive R peaks. The six ECG parameters of HR, RTp_c, QT_c, QTp_c involve ventricular depolarization and repolarization. TpTe_c and ToTe_c involve only repolarization. The index of c in the parameters is to indicate that the ECG parameters are corrected using Bazett formula.

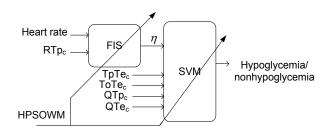


Figure 1. SFisSvm for hypoglycemia detection with input of ECG parameter

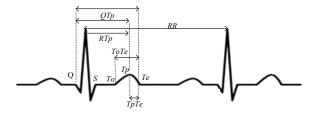


Figure 2. ECG parameters used for the input of the hypoglycemia detection

A. FIS

As in the Fig. 1, FIS is used to find the approximating function between the two ECG parameters (HR and RTp_c) and hypo-index η . The output FIS η becomes one of the input of SVM.

The first step of FIS is to find the degree of membership function for these two ECG parameters. The membership function adopts the Gaussian membership function. The membership degree of HR can be expressed as

$$\mu_{N_{\rm HR}^k}\left(HR(i)\right) = e^{\frac{-\left(HR(i) - m_{\rm HR}^k\right)^2}{2\sigma_{\rm HR}^k}} \tag{1}$$

In which, for three membership functions, $\mathbf{m}_{HR}^k = \begin{bmatrix} m_{HR}^1 & m_{HR}^2 & m_{HR}^3 \end{bmatrix}$ and i = 1, 2, ..., k, k denotes the data points number. m_{HR}^k and σ_{HR}^k are the mean value and the standard deviation of the membership functions, respectively. The membership degrees of the other input, RTp_c, are obtained using by similar way.

The second step is the mapping between the inputs and hypoindex η created by means of the fuzzy if-then rules as in the following rule:

Rule
$$\rho$$
: **IF** HR(*i*) is $N_{HR}^k(HR(i))$ **AND** RTp_c(*i*) is $N_{RTp_c}^k(RTp_c(i))$

THEN
$$\eta(i)$$
 is w_{ρ_2} (2)

in which $N_{\rm HR}^k(HR(i))$ and $N_{\rm RT_{PC}}^k({\rm RT_{PC}}(i))$ are fuzzy terms of rule ρ . $\rho=1,2,...,n_r;\ n_r$ denotes the number of rules. In the case of three membership functions, n_r is 9 which is $(m_f)^p$; m_f (= 3) is the number of membership functions, and p (= 2) is the number of inputs.

The third step of FIS is defuzzification, to find the hypoindex η , which uses the following formula

$$\eta(i) = \frac{\sum_{\rho=1}^{n_r} w_\rho \left[\mu_{N_{\text{HR}}^{\rho}} \left(\text{HR}(i) \right) \times \mu_{N_{\text{RTpc}}^{\rho}} \left(\text{RTpc}(i) \right) \right]}{\sum_{\rho=1}^{n_r} \left(\mu_{N_{\text{HR}}^{\rho}} \left(\text{HR}(i) \right) \times \mu_{N_{\text{RTpc}}^{\rho}} \left(\text{RTpc}(i) \right) \right)}$$
(3)

B. SVM

In Fig. 1, SVM is used to classify five inputs; four ECG parameters $TpTe_c$, $ToTe_c$, QTp_c , QTe_c and η (output of FIS). The output of SVM is the hypoglycemic level, which is hypoglycemic or non-hypoglycemic state. SVM is a classifier that constructs an optimal hyperplane which separates binary

class data. Let $\mathbf{X}=(\mathbf{x}_i,y_i)$ be a set of training data which can be linearly separated, where $\mathbf{x}_i \in R^m$ is an m dimensional space and the associated $y_i \in [-1\ 1]$ is class label, i=1,2,...,k, kn_d is the number of data. 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. The training data satisfy $y_i(\mathbf{w} \cdot \mathbf{x} + b) - 1 \ge 0$, in which training data lie in the equality of this equation are support vectors. The optimum hyperplane can be determined through maximizing distance, 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 $2/\|\mathbf{w}\|$.

For many real world problems, such separating hyperplane does not exist. Hence slack variable ξ_i is introduced and then $y_i(\mathbf{w}\cdot\mathbf{x}+b)\geq 1-\xi_i$. The optimal separating hyperplane is determined by minimizing

$$C\sum_{i=1}^{k} \xi_i + \frac{1}{2} \left\| \mathbf{w} \right\|^2 \tag{4}$$

where *C* is a *cost* constant that is used to control the tradeoff between margin size and error.

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

$$L(\alpha) = \sum_{i=1}^{k} \alpha_i - \frac{1}{2} \sum_{i=1}^{k} \sum_{j=1}^{k} \alpha_i \alpha_j y_i y_j (\mathbf{x}_i \cdot \mathbf{x}_j)$$
 (5)

subject to

$$0 \le \alpha_i \le C \text{ and } \sum_{i=1}^k y_i \alpha_i$$
 (6)

where α_i is the Lagrange multiplier.

In a case of imbalanced distributions between two class data, a higher error weight $(w_0 \text{ or } w_I)$ need to be given to the class with the smallest population [26]. Then (4) is modified by minimizing

$$w_0 C \sum_{i:y_i=-1}^k \xi_i + w_1 C \sum_{i:y_i=-1}^k \xi_i + \frac{1}{2} \| \mathbf{w} \|^2$$
 (7)

The inner-product in (5) 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, three kernel functions are adopted;

Radial basis function (RBF),

$$k(\mathbf{x}_{i}, \mathbf{x}_{j}) = exp\left(-\gamma \left\|\mathbf{x}_{i} - \mathbf{x}_{j}\right\|^{2}\right); \tag{8}$$

Sigmoid,
$$k(\mathbf{x}_i, \mathbf{x}_j) = (\gamma(\mathbf{x}_i, \mathbf{x}_j) + 1);$$
 (9)

linear,
$$k(\mathbf{x}_i, \mathbf{x}_j) = \mathbf{x}_i \cdot \mathbf{x}_j$$
; (10)

In this paper, C, w_0 , w_1 in (7) and γ in (8) and (9) are parameters which are optimized using HPSOWM [25]. Finally, the class prediction for any test vector $\mathbf{x} \in R^N$ is given by

$$f(\mathbf{x}) = sgn(\sum \alpha_i y_i k(\mathbf{x}_i, \mathbf{x}) + b), \tag{11}$$

in which sgn is a signum function; the value of $f(\mathbf{x})$ which is greater than 0 is associated with +1 class and the negative one is associated with -1 class.

```
begin
      t \rightarrow 0
                          // iteration number
      Initialize Z(t)
                         // Z(t): swarm for iteration t
      Evaluate f(Z(t)) // f(\cdot): fitness function
while (not termination condition) do
        begin
               Update velocity \mathbf{v}(t) and position of each particle \mathbf{z}(t) based
              on (12) - (15) respectively
                     if v(t) > v_{max}, v(t) = v_{max} end
                     if v(t) < -v_{max}, v(t) = -v_{max} end
               Perform wavelet mutation operation with \mu_m
                     Update \bar{z}_i^p(t) based on (16) – (18)
               Reproduce a new Z(t)
               Evaluate f(Z(t))
         end
end
```

Figure 3. Pseudo code for HPSOWM

C. Hybrid particle swarm optimization with wavelet mutation

SFisSvm parameters are optimized to find the best performance of the hypoglycemia detection. The SFisSvm parameters are FIS parameters, which are mean value and the standard deviation of the membership functions in (1), and SVM parameters, which are C, w_0 , w_I in (7) and γ in (8) and (9). To optimize the parameters, HPSOWM is investigated. HPSOWM performs optimization considering an evolutionary technique based on the movement of swarms and inspired by the social behavior of bird flocking and fish schooling [27] with wavelet mutation.

The algorithm of HPSOWM can be expressed as in the Fig. 3. The particles of the swarm Z(t) are initialized and then are evaluated by a defined fitness function. The objective of HPSOWM is to minimize the fitness function f(Z(t)) of particles iteratively. The swarm evolves from iteration t to t+1 by repeating the procedures.

Particles fly through a search space with adjusted velocity and position. The velocity is adjusted as

$$v(t) = q(\varphi v(t-1) + c_1 r_1 (z_p - z(t-1)) + c_2 r_2 (z_g - z(t-1)))$$
(12)

and

$$z(t) = z(t-1) + v(t)$$
(13)

Where z_p is the best previous position of a particle, and z_g is the best particle position among the all particle. r_1 and r_2 are random functions in the range [0 1], and φ is inertia weight factor. c_1 and c_2 are acceleration constants. q is a constriction factor to ensure the system to be converged but not prematurely, which is formulated is in the following:

$$q = \frac{2}{\left| 2 - c - \sqrt{c^2 - 4c} \right|} \tag{14}$$

where $c = c_1 + c_2$ and c > 4. In general, φ can be formulated as in the following:

$$\varphi = \varphi_{max} - \frac{\varphi_{max} - \varphi_{min}}{T} \times t \tag{15}$$

where t is the current iteration number, T is the total number of iteration, φ_{max} and φ_{min} are the upper and the lower limits of the inertia weight, and are set to 1.2 and 0.1, respectively.

In the wavelet mutation operation, every element of particle has a chance to be selected to find mutation such that

$$\overline{z}(t) = \begin{cases}
z(t) + \sigma \times (\rho_{max} - z(t)) & \text{if } \sigma > 0 \\
z(t) + \sigma \times (z(t) - \rho_{min}) & \text{if } \sigma \le 0
\end{cases}$$
(16)

where

$$\sigma = \frac{1}{\sqrt{a}} e^{-\left(\frac{c}{a}\right)^2/2} \cos\left(5\left(\frac{c}{a}\right)\right) \tag{17}$$

and ρ_{max} and ρ_{min} are the upper and lower boundary of the element of particle. The dilation parameter a is set to vary with the value of t/T as in the following:

$$a = e^{-\ln(g) \times \left(1 - \frac{t}{T}\right)^{\alpha_{wm}} + \ln(g)}$$
(18)

where α_{wm} is the shape parameter of the monotonic increasing function, g is the upper limit of the parameter a.

The objective function of The HPSOWM is as in the following

$$\phi = -\left(\alpha \mathcal{G}_t + \left(1 - \alpha\right) \eta_t + \alpha \mathcal{G}_v + \left(1 - \alpha\right) \eta_v\right) + \sigma \tag{19}$$

where θ_t and η_t are the sensitivity and specificity, respectively, obtained from the hypoglycemia detection model which is tested by using a training data set; and θ_v and η_v are the sensitivity and specificity, respectively, obtained from the hypoglycemia detection model which is tested by using a validation data set. The inclusion of θ_v and η_v in the fitness function is to reduce the risk of overtraining [28]. α is set as 0.58 to avoid risk of low sensitivity.

To force a high sensitivity in the detection, σ is given by using the following definition,

$$\sigma = \begin{cases} 10 & if \quad \theta_t > 0.7, \eta_t > 0.4, \theta_v > 0.7, \eta_v > 0.4 \\ 0 & \text{Otherwise} \end{cases}$$
 (20)

The σ definition in (20) is to force the sensitivity and specificity to be higher than 70% and 40%, respectively.

III. RESULT

The proposed hypoglycemia detection strategy using SFisSvm was investigated using the ECG parameters resulted from a hypoglycemia study. The hypoglycemia 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. Five patients with type-1 diabetes voluntarily participated for this study.

The ECG parameters used in the study are (i) $TpTe_c$, (ii) $ToTe_c$, (iii) RTp_c , (iv) QTe_c , (v) QTp_c , and (vi) HR. Index of c in the parameters indicates that the heart rate correction for the variables uses the Bazett's formula [29], which is normalized using square root of RR interval. The detail of procedure to obtain these ECG parameters from the patients' ECG signals is referred to [23].

The resulted ECG parameters are 1327 and 399 data points of non-hypoglycemia 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 optimized membership functions of the SFisSvm which employed RBF (SFisSvmR) are plotted in Fig. 4 and the tabulated fuzzy rule is presented in Table I. Three Gaussian fuzzy terms are used; the terms are L (low), M (medium) and H (high). The optimized fuzzy singleton for different fuzzy terms is presented in Table I. Fuzzy if-then rules (9 rules) can be presented using the singletons, such as: IF HR(i) is "H" AND RTp_c is "H", THEN $\eta(i)$ is "H" (or δ = 0.9132).

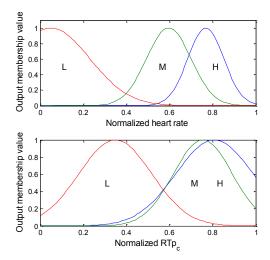


Figure 4. Fuzzy membership function of heart rate and RTpc.

TABLE I.	FUZZY RULE TABLE		
HR			
RTpc	L	M	Н
L	0.7408	0.5360	0.7631
M	0.6854	0.5547	0.9500
Н	0.0500	0.1083	0.9132

The other optimized parameters are the parameters relating to SVM; they are C, g, w_o , w_I as presented in Table II. These parameters relates to SFisSvm using RBF kernel function. The optimized w_0 and w_I are 0.0987 and 0.9917, respectively. These values show that to find the optimal performance the hypoglycemic class uses far higher weight factor (w_I) than non-hypoglycemic class weight factor (w_0) . As mentioned above, the data number of hypoglycemic class is around a third of nonhypoglycemic class, and thus it needs higher weight factor. Furthermore, the training used 250 iterations with population size of 50. The values of the fitness function during the optimization of SFisSvmR are plotted in Fig. 5.

TABLE II. OPTIMIZED SVM PARAMETERS

Parameter	Value
С	39394.4265
g	51.6522
w_0	0.0987
w_I	0.9917

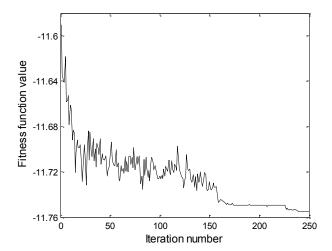


Figure 5. Fitness function values during the optimization of the SFisSvm which employed RBF kernel function (SFisSvmR),

The performances of the hypoglycemia detections using the SFisSvm which employed RBF (SFisSvmR), sigmoid (SFisSvmS) and linear kernel (SFisSvmL) functions are described in Table III. The performances are presented in terms of sensitivity, specificity and geometric mean (gm). Geometric mean or gm equals to the square root of the multiplication of sensitivity and specificity [31], or $gm=\sqrt{(\beta.9)}$. The geometric mean is suitable to indicate performance of imbalanced data. This work used an imbalanced data in which data number of nonhypoglycemia is about triple of the number of

hypoglycemia data. The presented result involves the performance in training, validation and testing. For comparison purpose, the result of the detection using swarm based SVM algorithm [30] is also presented in Table III. The algorithm involves the swarm based SVM applying RBF kernel function (SSvmR), sigmoid kernel function (SSvmS) and linear kernel function (SSvmL).

As indicated in Table III, SFisSvmR outperform SFisSvmS and SFisSvmL in all three terms, which are sensitivity, specificity and geometric mean. The outperformance includes in training, validation and testing. Furthermore, the proposed methods outperform to the associate SVM without fuzzy inference system (SFisSvmR vs. SSvmR and SFisSvmSL vs. SSvmL) in all three terms of training, validation and testing. The performances of SFisSvmS and SVMS are nearly same. Thus, in general the proposed algorithm which is hybrid fuzzy SVM is higher than SVM without fuzzy. SFisSvmR was also investigated using five membership functions (tabulated in Table IV), and the resulted performance is nearly same with that uses three membership functions. The best performances of the proposed hypoglycemia detection strategy are 75.19%, 83.71% and 79.33% in terms of sensitivity, specificity and gm.

TABLE III. PERFORMANCES OF THE HYPOGLYCEMIA DETECTION ALGHORITHMS

		SSvm [30]		SFisSvm			
		SSvmS	SSvmL	SSvmR	SFisSvmS	SFisSvmL	SFisSvmR
Training	Sens.	88.72	53.38	96.99	88.72	78.20	100.00
	Spec.	64.93	95.25	84.84	66.74	81.67	90.05
	gm.	75.90	71.31	90.71	76.95	79.92	94.89
Validation	Sens.	83.46	45.86	70.68	84.96	75.94	78.20
	Spec.	61.76	92.31	76.02	63.35	76.47	81.67
	gm.	71.80	65.07	73.30	73.36	76.20	79.92
Testing	Sens.	79.70	53.38	70.68	79.70	74.44	75.19
	Spec.	61.31	88.69	81.45	61.54	77.60	83.03
	gm.	69.90	68.81	75.87	70.03	76.00	79.01

Values in %

TABLE IV. PERFORMANCES OF SFISSVMR USING 3- AND 5- MEMBERSHIP FUNCTIONS

		SFisSvmR		
		3 membership function	5 membership function	
Training	Sens.	100.00	100.00	
	Spec.	90.05	90.27	
	gm.	94.89	95.01	
Validation	Sens.	78.20	76.69	
	Spec.	81.67	83.26	
	gm.	79.92	79.91	
Testing	Sens.	75.19	75.19	
	Spec.	83.03	83.71	
	gm.	79.01	79.33	

Values in %

IV. CONCLUSION

This article has presented the strategy of SFisSvm implemented for hypoglycemia detection. HPSOWM has been employed to optimize the fuzzy and SVM parameters. Compared to the hypoglycemia detection strategy by using SVM algorithm only, the proposal hybrid fuzzy and SVM system has an improvement in term of the performance of the hypoglycemia detection. Furthermore, three kernel functions for the SVM, and three- and five- membership functions have been investigated for this strategy. The best performance of the hypoglycemia detection found in the experiment is 75.19%, 83.71% and 79.33% in terms of sensitivity, specificity and geometric mean. A further study could be conducted by implementing the proposed algorithm in a real time device.

ACKNOWLEDGMENT

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

REFERENCES

- A. Collier, D. M. Matthews, R. J. Young, and B. F. Clarke, "Transient atrial fibrillation precipitated by hypoglycaemia: two case reports.," *Postgraduate Medical Journal*, vol. 63, pp. 895-897, 1987.
- [2] M. A. Baxter, C. Garewal, R. Jordan, A. D. Wright, and M. Nattrass, "Hypoglycaemia and atrial fibrillation," *Postgraduate Medical Journal*, vol. 66, p. 981, 1990.
- [3] B. J. Burke and T. K. Kearney, "Hypoglycaemia and cardiac arrest," Practical Diabetes International, vol. 16, pp. 189-190, 1999.
- [4] R. B. Tattersall and G. V. Gill, "Unexplained death of type 1 diabetic patients," *Diabetic Medicine*, vol. 8, pp. 49-58, 1991.
- [5] K. H. Claus B. Juhl, Rasmus Elsborg, Mikael Kjær Poulsen, Peter E. Selmar, Jens Juul Holst, Claus Christiansen, Henning Beck-Nielsen, "Automated detection of hypoglycemia-induced EEG changes recorded by subcutaneous electrodes in subjects with type 1 diabetes—The brain as a biosensor," *Diabetes Research and Clinical Practice*, vol. 88, pp. 22 28. 2010.
- [6] S. S. H. Ling and H. T. Nguyen, "Genetic-algorithm-based multiple regression with fuzzy inference system for detection of nocturnal hypoglycemic episodes," *IEEE Transactions on Information Technology* in *Biomedicine*, vol. 15, pp. 308-315, 2011.
- [7] M. T. Ryan, V. W. Savarese, B. Hipszer, I. Dizdarevic, M. Joseph, N. Shively, and J. I. Joseph, "Continuous glucose monitor shows potential for early hypoglycemia detection in hospitalized patients," *Diabetes Technology & Therapeutics*, vol. 11, pp. 745-747, 2009.
- [8] N. S. Oliver, C. Toumazou, A. E. G. Cass, and D. G. Johnston, "Glucose sensors: a review of current and emerging technology," *Diabetic Medicine*, vol. 26, pp. 197–210, 2008.
- [9] C. Alexakis, H. Nyongesa, R. Saatchi, N. Harris, C. Davies, C. Emery, R. Ireland, and S. Heller, "Feature extraction and classification of electrocardiogram (ECG) signals related to hypoglycaemia," in *Proceeding of Computers in Cardiology*, 2003, pp. 537-540.
- [10] H. T. Nguyen, 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," in Proceeding of the 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2008, pp. 1311 - 1314
- [11] H. T. Nguyen and T. W. Jones, "Detection of nocturnal hypoglycemic episodes using EEG signals," in 32th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2010, pp. 4930-4933.
- [12] K. Johansen, S. Ellegaard, and S. Wex, "Detection of nocturnal hypoglycemia in insulin-treated diabetics by a skin temperature skin

- conductance meter," *Acta Medica Scandinavica*, vol. 220, pp. 213–217, 1986
- [13] H. T. Nguyen, N. Ghevondian, S. T. Nguyen, and T. W. Jones, "Detection of hypoglycemic episodes in children with type 1 diabetes using an optimal bayesian neural network algorithm," in *Proceedings of the 29th Annual International Conference of the IEEE EMBS*, 2007, pp. 3140-3143.
- [14] N. Ghevondian, H. T. Nguyen, and S. Colagiuri, "A novel fuzzy neural network estimator for predicting hypoglycaemia in insulin-induced subjects," in *Proceeding of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 1997, pp. 1371-1374.
- [15] G. Hastings, N. Ghevondian, and H. Nguyen, "A self-organising fuzzy estimator for hypoglycaemia monitoring in diabetic patients," in Proceeding of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1998, pp. 1371-1374.
- [16] D. Meyer, F. Leisch, and K. Hornik, "The support vector machine under test," *Neurocomputing*, vol. 55, pp. 169-186, 2003.
- [17] N. Acir, "A support vector machine classifier algorithm based on a perturbation method and its application to ECG beat recognition systems," *Expert Systems with Applications*, vol. 31, pp. 150-158, 2006.
- [18] S. S. Mehta and N. S. Lingayat, "Application of support vector machine for the detection of P- and T-waves in 12-lead electrocardiogram," computer methods and programs in biomedicine, vol. 93, pp. 46-60, 2009
- [19] A. H. Khandoker, M. Palaniswami, and C. K. Karmakar, "Support vector machines for automated recognition of obstructive sleep apnea syndrome from ECG recordings," *IEEE transactions on information technology in biomedicine*, vol. 13, pp. 37-48, 2009.
- [20] S. Osowski, L. T. Hoai, and T. Markiewicz, "Support vector machine-based expert system for reliable heartbeat recognition," *IEEE Transactions on Biomedical Engineering*, vol. 51, pp. 582-589, 2004.
- [21] R. P. W. Duin, "Classifiers in almost empty spaces," in *Proceeding of the 15th International Conference on Pattern Recognition*, 2000, pp. 1-7 vol.2.
- [22] S. H. Ling, H. H. C. Iu, K. Y. Chan, H. K. Lam, B. C. W. Yeung, and F. H. Leung, "Hybrid Particle Swarm Optimization With Wavelet Mutation and Its Industrial Applications," *IEEE Transactions on Systems, Man, and Cybernetics, Part B: Cybernetics*, vol. 38, pp. 743-763, 2008.
- [23] N. Nuryani, S. Ling, and H. Nguyen, "Electrocardiographic Signals and Swarm-Based Support Vector Machine for Hypoglycemia Detection," *Annals of Biomedical Engineering*, vol. 40, pp. 934-945, 2012.
- [24] L. A. Zadeh, "Fuzzy Sets," Information and Control, vol. 8, pp. 338-353, 1965
- [25] S. H. Ling, H. H. C. Iu, K. Y. Chan, H. K. Lam, B. C. W. Yeung, and F. H. Leung, "Hybrid Particle Swarm Optimization With Wavelet Mutation and Its Industrial Applications," *IEEE Transactions on Systems, Man, and Cybernetics, Part B: Cybernetics*, vol. 38, pp. 743-763, 2008.
- [26] R. Batuwita and V. Palade, "FSVM-CIL: fuzzy support vector machines for class imbalance learning," *IEEE Transactions on Fuzzy Systems*, vol. 18, pp. 558-571, 2010.
- [27] J. Kennedy and R. Eberhart, "Particle swarm optimization," in *IEEE International Conference on Neural Networks* 1995, pp. 1942-1948.
- [28] M. L. Astion, M. H. Wener, R. G. Thomas, G. G. Hunder, and D. A. Bloch, "Overtraining in neural networks that interpret clinical data," *Clinical Chemistry*, vol. 39, pp. 1998-2004, 1993.
- [29] A. J. Moss, "Measurement of the QT interval and the risk associated with QTc interval prolongation: A review," *American Journal of Cardiology*, vol. 72, pp. B23-B25, 1993.
- [30] M. H. Zweig and G. Campbell, "Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine," *Clinical Chemistry*, vol. 39, pp. 561-77, 1993.