Hypoglycaemia Detection for Type 1 Diabetic Patients Based on ECG Parameters Using Fuzzy Support Vector Machine

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***Abstract*—Nocturnal hypoglycaemia in type 1 diabetic patients can be dangerous in which symptoms may not be apparent while blood glucose level decreases to very low level, and for this reason, an effective detection system for hypoglycaemia is crucial. This research work proposes a detection system for the hypoglycaemia based on the classification of electrocardiographic (ECG) parameters. The classification uses a Fuzzy Support Vector Machine (FSVM) with inputs of heart rate, corrected QT (QT_c) interval and corrected TpTe ($TpTe_c$) interval. Three types of kernel functions (radial basis function (RBF), exponential radial basis function (ERBF) and polynomial function) are investigated in the classification. Moreover, parameters of the kernel functions are tuned to find the optimum of the classification. The results show that the FSVM classification using RBF kernel function demonstrates better performance than using SVM. However, both classifiers result approximately same performance if ERBF and polynomial kernel functions are used.**

I. INTRODUCTION

Hypoglycaemia, or abnormally low blood glucose, is a common complication of insulin-dependent diabetes mellitus (IDDM) and remains a central problem [1]. In a number of studies, hypoglycaemia is one of known causes of death in the diabetic patients [2, 3]. Symptomatic hypoglycaemia is categorized as mild to severe episodes. In another study, mild hypoglycaemia occurs in 58% and severe hypoglycaemia (defined as the reactions to hospitalization or need of assistance) happens in 26% of 172 insulin-treated diabetic patients [4].

The Diabetes Control and Complications Trial (DCCT) estimated that around 55% of severe hypoglycaemia episodes occur during sleep [5]. Nocturnal hypoglycaemia can be dangerous in which symptoms may not be apparent while blood glucose level (BGL) decreases to very low level. It is reported that falling plasma glucose to 2.2 mmol/l very rarely provoke an awakening response in IDDM patients observed and it corresponds to an absence of clear-cut counterregulatory hormonal responses [6] and therefore a detection system for the onset of hypoglycaemia is crucial.

Regarding correlation between hypoglycaemia and cardiac dysrithmia, a number of studies have demonstrated that hypoglycaemia results altered ventricular repolarization or prolonged corrected QT (QT_c) interval [7-9]. QT interval represents the duration of ventricular depolarization and subsequent repolarization to occur and, in the heart's electrical cycle, is the interval from the start of the Q wave to the end of the T wave. QT_c prolongation in hypoglycaemia is predicted on account of sympathoadrenal stimulation [8]. Moreover, hypoglycaemia also induce to increase heart rate (heartbeats per unit of time) [10].

Therefore, the electrocardiography (ECG) parameters are examined in experiments for hypoglycaemia detection and have demonstrated as essential inputs for system to determine hypoglycaemia episodes. The heart rate as an ECG feature has been applied as one of inputs for detection of the onset of hypoglycaemia using the fuzzy estimator [11] and the fuzzy neural network [12]. Furthermore, heart rate and QT_c interval have been implemented for nocturnal hypoglycaemia detection using neural network algorithm [13]. Other ECG parameters: RR, RT_c, T wave amplitude, T wave skewness and T wave kurtosis have also been applied to detect onset of hypoglycaemia using artificial neural network (ANN) and linear discriminant analysis (LDA) [14]. RT_c interval and T wave amplitude have also investigated as inputs for the Rule Base for the nocturnal hypoglycaemia detection [15]. Another ECG parameter is a corrected TpTe ($TpTe_c$) interval that is the interval from the peak to the end of T wave and is a descriptor of T wave morphology [16-18].

In general, most of the aforementioned approaches for the hypoglycaemia detection employ methods to reach satisfactory level of reliability so as to act as hypoglycaemia detection system using ECG parameters. Up to now the methods still require extensive validation before they can be adopted for worldwide clinical practices. Thus, this research effort is to develop methods to achieve satisfactory of the hypoglycaemia detection. The construction methods in this research is based on classification techniques using fuzzy support vector machine (FSVM), that is not yet explored widely in the onset of hypoglycaemia detection system.

FSVM is a further classification technique of support vector machine (SVM). SVM has proved mostly good performance for classification in various application [19] including in application to classify features of cardiac signals [20-25]. Choosing SVM as a classification tool consider to its good performance and SVM classification ability to generalize well even with small size sample [26]. In the FSVM method, a fuzzy membership is introduced to each training sample of SVM and therefore different training

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points can make different contributions to the learning of decision surface. For that reason, FSVM technique can enhance traditional SVM in reducing effects of outliers and noises in data points [27, 28]. FSVM has showed better performances than SVM in applications such as classification of EEG signals using wavelet-based features [29], multi-class text categorization [30] and image classification [31].

In this paper, the performances of FSVM and SVM classifiers are compared in the classification of three ECG parameters (heart rate, QT_c and $TpTe_c$) to hypoglycaemia or normoglycaemia. Kernel functions, are implemented for mapping of the data sets to high dimensional space, are also compared to find the best performance of the classification. The kernel functions are radial basis function (RBF), exponential radial basis function (ERBF) and polynomial function. Therefore this work would contribute to demonstrate the FSVM and SVM classification for these ECG parameters in the detection of hypoglycaemia.

The rest of this paper is organized as follows. Methods consisting of features extraction of the ECG signals and the FSVM and SVM classification are described in section II. Section III presents the experimental results and the conclusion for this research is drawn in Section IV.

II. METHODS

This work consists of two main stages, feature extraction and FSVM classification (Fig 1). The main task of the feature extraction is to obtain the heart rate, QT_c and $TpTe_c$ from the ECG signals. The FSVM classification is constructed to classify the ECG signal inputs into hypoglycaemic or normoglycaemic condition.

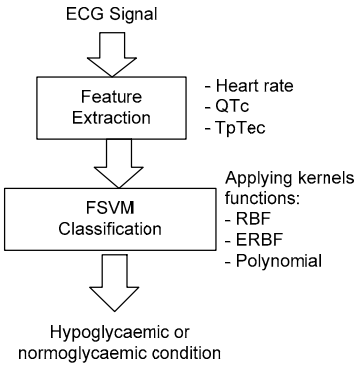


Fig. 1. FSVM classification for the ECG signals to hypoglycaemic or normoglycaemic condition.

A. Feature extraction

The three ECG parameters are estimated based on the ECG signals acquired from the diabetic patients ECG signals recorded by the Compumedics system. The estimation is created in Matlab® environment. Three interval values (RR interval, QT interval and TpTe interval) are illustrated in Fig. 2. The three intervals are then calculated to find heart rate which equals to 60/RR, QT_c which equals to $QT/(RR)^{1/2}$ and $TpTe_c$ which equals to $TpTe/(RR)^{1/2}$. The end of T wave (T_{end}) is defined using the Philips QT Interval Measurement Algorithms, that is by drawing a line segment from the top of the T wave forward in time to a point and the T_{end} is a point that has the maximum vertical distance between the point and the line segment [32]. The three ECG parameters are then used as inputs of the classification.

The inputs are labeled with –1 for hypoglycaemia and are labeled with +1 for normoglycaemia. The threshold for hypoglycaemic level used in this system is 3.3 mmol/l. It means that the ECG conditions with BGL equal or lower than 3.3 mmol/l are defined as hypoglycaemia and those of which are higher than 3.3 mmol/l are defined as normoglycaemia.

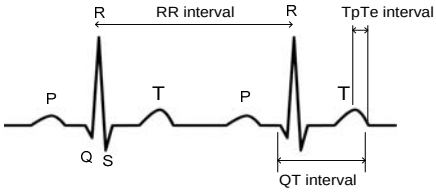


Fig. 2. RR, QT and TpTe intervals in a typical ECG signal

B. Classification using FSVM

Considering to the three parameters, the classifier is used to automatically recognize hypoglycaemia condition of the type 1 diabetic patients. This section will briefly discuss SVM and FSVM. A more detailed discussion of SVM can be found in [33, 34] and of FSVM in [28, 35].

1) SVM classifier

Fig. 3 shows the optimal hyperplane in the linearly separable binary classification problems. Suppose that there are k training data samples $(\mathbf{x}_i, y_i) \ldots (\mathbf{x}_k, y_k)$ where $\boldsymbol{x}_i \in R^N$ is an-N dimensional space and the associated $y_i \in \{+1, -1\}$ is class label. It is assumed that the samples can be separated by the hyperplane satisfying

$$\mathbf{w} \cdot \mathbf{x} + b = 0 \tag{1}$$

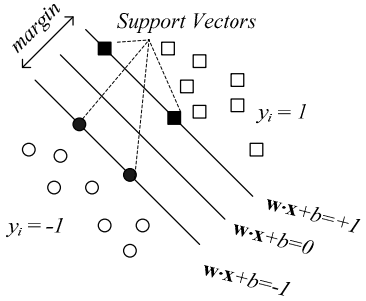


Fig. 3. SVM classification for the linearly sparable case. The lines are the hyperplanes. Squares and circles denotes training data.

where $\mathbf{w}$ is the hyperplane perpendicular vector, $|b|/\|\mathbf{w}^2\|$ is distance of the hyperplane to the origin ($|b|$ is absolute value of b and $\|\mathbf{w}\|$ is module of $\mathbf{w}$). For linearly separable case, SVM algorithm maximize margin between classes and thus all training data satisfy $\mathbf{w}\cdot\mathbf{x}_i+b \geq 1$ for $y_i = +1$ and $\mathbf{w}\cdot\mathbf{x}_i+b \leq 1$ for $y_i = -1$. These two constraints can be formulated in one expression,

$$y_i(\mathbf{w}\cdot\mathbf{x}+b)-1\geq 0\ . \tag{2}$$

The training data points that satisfy the equality in inequality (2) are called support vectors. The margin between two hyperplanes, $\mathbf{w}\cdot\mathbf{x} + b = +1$ and $\mathbf{w}\cdot\mathbf{x} + b = -1$, is $2/\|\mathbf{w}\|$. The optimum separating hyperplane can be found by maximizing the margin, minimizing $\|\mathbf{w}^2\|$, with respect to constraint (2).

It is often that in many real world problems that a separating hyperplane does not exist. Hence it is introduced positive slack variable ξ_i and then

$$y_i(\mathbf{w}\cdot\mathbf{x} + b) \geq 1-\xi_i. \tag{3}$$

The optimal separating hyperplane is determined by $\mathbf{w}$ that minimizes the functional

$$C\sum\xi_i + \tfrac{1}{2}\|\mathbf{w}\|^2\ . \tag{4}$$

The C is a user defined constant that to control the tradeoff between complexity and proportion of nonseparable points.

Searching the optimal hyperplane in (1) using Lagrange multiplier approach is to maximize

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

subject to

$$0\leq\alpha_i\leq C \text{ and } \sum y_i\alpha_i=0\ , \tag{6}$$

where α_i is the Lagrange multiplier.

In a case of imbalanced distributions, it is needed to use different error weights and in order to penalize more heavily the undesired type of error, and/or the errors related to the class with the smallest population [36]. Then (4) is modified by minimizes the functional

$$C^-\sum_{i:y_i=-1}\xi_i + C^+\sum_{i:y_i=+1}\xi_i+\tfrac{1}{2}\|\mathbf{w}\|^2 \tag{7}$$

Having determined the optimum Lagrange multiplier, the optimum solution for the vector w is given by

$$\mathbf{w}=\sum\alpha_i y_i\mathbf{x}_i \tag{8}$$

Replacing the inner-product in (5) with a kernel function $K(\mathbf{x_i},\mathbf{x_j})$ map input data to higher dimensional space so that nonlinearly separable data can be linearly classified. In this paper the classification apply three kernel functions: RBF, ERBF and polynomial functions. Parameters σ in the RBF/ERBF and d in the polynomial are tuned to obtain a high classification performance. The kernel functions are:

RBF, $$K(\mathbf{x}_i,\mathbf{x}_j)=\exp\left(-\frac{\|\mathbf{x}_i-\mathbf{x}_j\|^2}{2\sigma^2}\right);$$

ERBF, $$K(\mathbf{x}_i,\mathbf{x}_j)=\exp\left(-\frac{\|\mathbf{x}_i-\mathbf{x}_j\|}{2\sigma^2}\right);$$

and polynomial, $K(\mathbf{x}_i,\mathbf{x}_j)=\left(\mathbf{x}_i.\mathbf{x}_j+1\right)^d$

Finally, for any test vector $\mathbf{x}\in R^N$, the output of the classification is then given by

$$y=\text{sgn}(\sum\alpha_i y_i K(\mathbf{x}_i,\mathbf{x}))\ . \tag{9}$$

2) FSVM classifier

In order to enhance the training performances, fuzzy membership is introduced to each training sample. FSVM introduce a fuzzy membership $0< s_i<1$ associated with each data point x_i. The output of fuzzy membership s_i is regarded as attitude of the corresponding training points toward one class in the classification problem. The optimal hyperplane problem then can be regarded as the solution to [28]

$$\text{minimize}\quad C\sum_{i:1}^{k}s_i\xi_i+\tfrac{1}{2}\mathbf{w}\cdot\mathbf{w} \tag{10}$$

subject to (3).

The problem (10) can be transformed into,

$$\sum_{i=1}^{k}\alpha_i-\frac{1}{2}\sum_{i=1}^{k}\sum_{j=1}^{k}\alpha_i\alpha_j y_i y_j(\mathbf{x}_i.\mathbf{x}_j) \tag{11}$$

subject to

$$0\leq\alpha_i\leq s_i C \text{ and } \sum y_i\alpha_i=0\ . \tag{12}$$

In this paper, the output value of the fuzzy membership s_i is designed as shown in the Fig 4. This membership is based on the associated blood glucose level (BGL) value β of the ECG signals. The peak of s_i is at β = 3.30 mmol/l that is the boundary between hypoglycaemia and normoglycaemia. The values of 2.2201 and 6.2201 are considered to the minimum and maximum of BGL data, respectively, in this work. The both values are determined considering to the minimum and maximum value of the BGL data. The output value s_i of the membership function is described below:

$$s_i=\begin{cases}0, & \textbf{for } \beta\leq 2.2201\\ \dfrac{(\beta-2.2201)}{(3.3-2.2201)}, & \textbf{for } 2.2201<\beta<3.3\\ \dfrac{(6.2201-\beta)}{(6.2201-3.3)}, & \textbf{for } 3.3\leq\beta<6.2201\\ 0, & \textbf{for } \beta\geq 6.2201\end{cases} \tag{13}$$

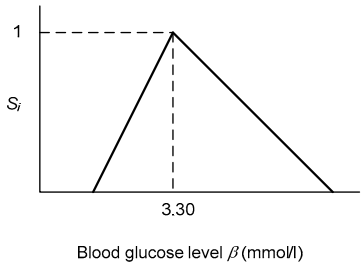


Fig. 4. The fuzzy membership of the FSVM

III. Experimental Result

The profile of the blood glucose level (BGL) of the type-1 diabetic patients acquired using the Yellow Spring Analyzer is presented in Fig. 5. The glucose level profile is started with the normal level and then the hypoglycaemic periods occur until the glucose level is less than 3.3 mmol/l. The ECG data of the five type-1 diabetic patients, with age of 16±0.7 years, are investigated for the classification in this work. Each patient data is an overnight monitoring for the natural occurrence of nocturnal hypoglycaemia. In general, the BGL was estimated every 5 minutes and the ECG signals is recorded and stored in ProFusion software (Compumedics).

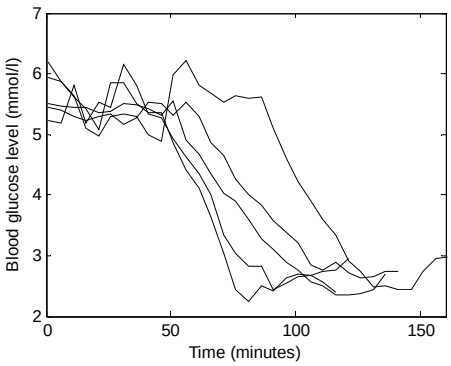


Fig. 5. Blood glucose level profile of the 5 patients

The inputs for the classifications have been obtained from the feature extraction of the ECG signals of the five patients. The data points of the input set are 134 containing both hypoglycaemic and normoglycaemic conditions. The inputs have also been classified using SVM and FSVM classification considering to the hypoglycaemic conditions.

A leave-one-out cross-validation scheme is used to evaluate the performance of the classification. In this scheme, the dataset is divided into 5 subsets with one used for testing and the remaining subsets used to train and construct the SVM decision surface. The performances are measured in terms of sensitivity, specificity and accuracy:

$$Sensitivity = \frac{TP}{TP+FN},$$

$$Specificity = \frac{TN}{TN+FP},$$

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN},$$

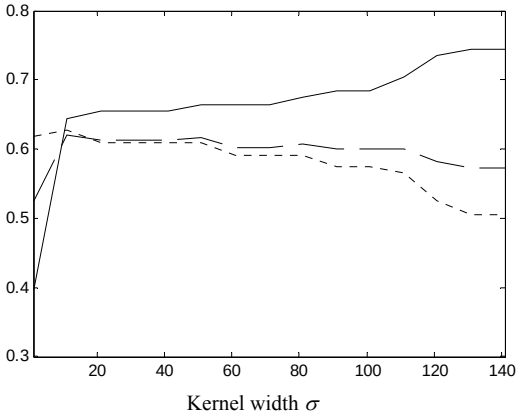
where *TP* (true positive) is number of the inputs that correspond to hypoglycaemia classified as hypoglycaemia. *FP* (false positive) is number of the inputs that correspond to normoglycaemia classified as hypoglycaemia. *TN* (true negative) is number the inputs that correspond to normoglycaemia classified as normoglycaemia. *FN* (false negative) is the inputs that correspond to hypoglycaemia classified as normoglycaemia. Average of sensitivity, specificity, and accuracy of the cross-validation are used for comparison among the classification techniques,

Each of the three kernel functions (RBF, ERBF and polynomial function) has been applied in both SVM and FSVM classification and the result of the cross-validation is described in Fig. 6 and Fig. 7. The classifiers apply the three kernels with variation of kernel parameters: σ parameter (kernel width) is for RBF and ERBF kernel function and d parameter (degree of polynomial) is for polynomial kernel function. Parameter of σ is varied from 1 to 141 with step of 10 and parameter of d is varied from 1 to 10 with step of 1. Considering to the experiments, these steps are sufficient in which the performances of the classifiers with these steps can represent the performances along these kernel parameter ranges.

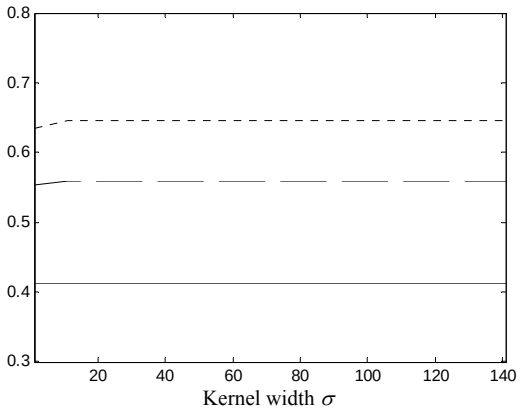
The graphs show that the choosing kernel functions in the both SVM and FSVM classifiers is crucial to find a good performance in the classification, especially in term of sensitivity for this case. In this experiment, in general, the classifiers with RBF kernel function outperform than the others. Furthermore, tuning the kernel parameters is also significant in the both FSVM and SVM classification. In the classification with RBF kernel width from 1 to 141, the sensitivity increase but the specificity decrease. Meanwhile, the sensitivity and specificity remain constant during variation of the ERBF kernel width. Using RBF kernel function, the FSVM generally outperform the SVM. Although in the RBF kernel width σ = 131 the sensitivity of both FSVM and SVM is nearly same, the specificity and accuracy of the FSVM is higher. However, both classifiers obtain almost same performance when they use ERBF kernel function. Therefore, choosing how to map the data sets to high dimensional space in SVM and FSVM is crucial.

In the cross-validation, the comparison of the optimum values of the classifications is showed in Table 1. Considering to the classification results having the highest sensitivities, the FSVM classifier with RBF kernel function outperform the SVM classifier that it is indicated by the significantly higher specificity and accuracy that is 58.54% and 63.20% respectively. However, using ERBF and polynomial kernel functions, the optimum values of both classifiers are nearly same.

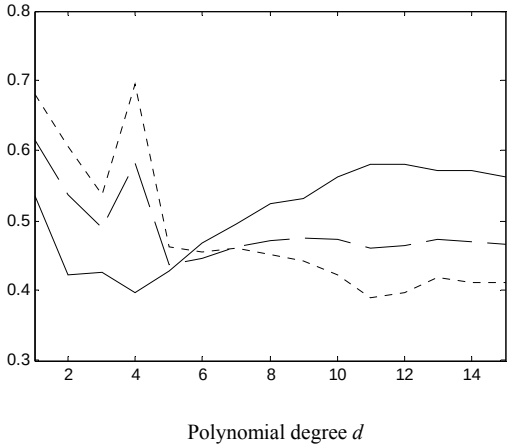
The better performances of the classification using FSVM compared to SVM are in line with the fact that there are more choices for appropriate parameters in the FSVM training than in the SVM training [28, 35]. The additional parameter is the fuzzy membership that can control the trade-off of the respective training data point. The fuzzy membership is made in the range from close to zero to 1 that consider to the associated BGL values of the ECG parameters (Fig. 4). The lower membership values for the very low and very high BGL values are regarded to the fact that not the all patients have very low or very high BGL. On the other word, the very low or very high value can not represent well of a class in the training and hence it is given the lower membership. For the future, an optimization system could be applied to determine the best of these values to find the better performance of the classification



(a) The SVM classification with RBF kernel function

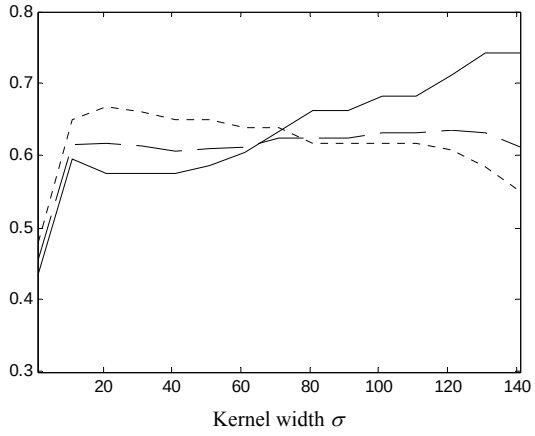


(b) The SVM classification with ERBF kernel function

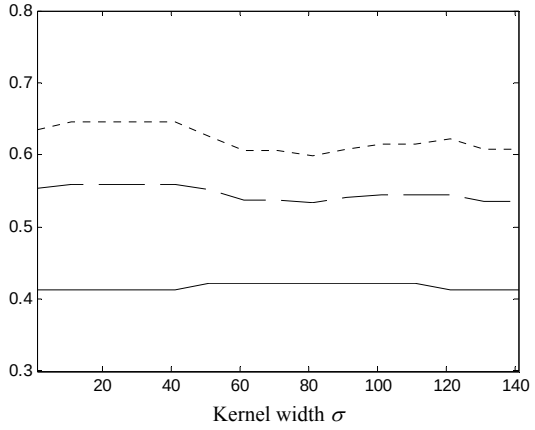


(c) The SVM classification with polynomial kernel function

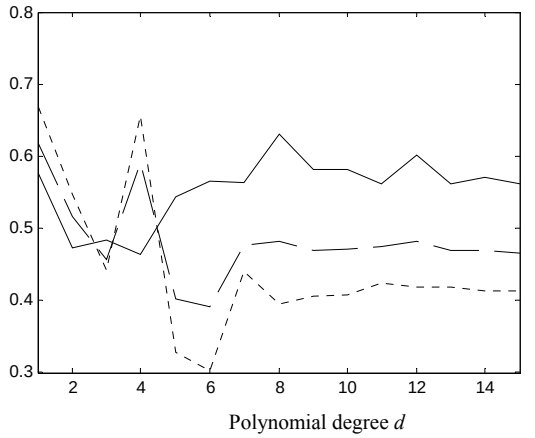
Fig. 6. Cross-validation results of the classifications using the SVM with different kernels and kernel parameters. (Solid line: sensitivity, dotted line: specificity, dashed line: accuracy).



(a) The FSVM classification with RBF kernel function



(b) The FSVM classification with ERBF kernel function



(c) The FSVM classification with polynomial kernel function

Fig. 7. Cross-validation results of the classifications using the FSVM with different kernels and kernel parameters. (Solid line: sensitivity, dotted line: specificity, dashed line: accuracy).

TABLE 1
OPTIMUM VALUE OF THE LEAVE-ONE-OUT CLASSIFICATION PERFORMANCE OF THE SVM AND FSVM

Classifier	Kernel Function	*Sens (%)*	*Spec (%)*	*Acc (%)*
SVM	***RBF***	74.43	50.50	57.34
	ERBF	41.24	64.50	55.99
	Polynomial	57.14	41.24	46.98
FSVM	***RBF***	74.19	58.54	63.20
	ERBF	42.19	62.54	5510
	Polynomial	63.05	39.60	48.25

Sens: Sensitivity; *Spec*: Specificity; *Acc*: Accuracy

IV. CONCLUSION

In this paper, the classifications for the ECG parameters using FSVM and SVM to obtain the hypoglycaemia episodes of the type 1 diabetic patients have been developed. The performances in the cross-validation of both classifiers have also been compared. In this classification, using RBF kernel function and with kernel width of 131, the FSVM demonstrate higher performance of classification than SVM. However, both classifiers applying ERBF and polynomial kernel functions have nearly same performances. In short, the FSVM with RBF kernel function gives 74.14% sensitivity and 58.54% specificity for type 1 diabetic problem.

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