

Hypoglycemia Detection using Fuzzy Inference System with Genetic Algorithm

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Abstract—In this paper, we develop a genetic algorithm based fuzzy inference system to recognize hypoglycemic episodes based on heart rate and corrected QT interval of the electrocardiogram (ECG) signal. Genetic algorithm is introduced to optimize the membership functions and fuzzy rules. A practical experiment based on data from 15 children with T1DM is studied. All the data sets are collected from the Department of Health, Government of Western Australia. To prevent the phenomenon of overtraining (over-fitting), a validation strategy that may adjust the fitness function is proposed. Thus, the data are organized into a training set, a validation set, and a testing set randomly selected. The classification results in term of sensitivity, specificity, and receiver operating characteristic (ROC) analysis show that the proposed classification method performs well.

Index Terms—Diabetes, Fuzzy logic, Genetic algorithm, Hypoglycemia.

I. INTRODUCTION

Episodes of hypoglycemia for Type 1 diabetes mellitus (T1DM) patients, which can result in unconsciousness, seizures or even death, are common and can cause serious side effect in insulin therapy [1]. At least 50% of all severe episodes of hypoglycemia occur during night time [2] because usual insulin preparations do not adequately mimic the normal patterns of endogenous insulin secretion [3]. However, it is impossible in practice to monitor the episodes of hypoglycemia by measuring the blood glucose levels around the clock. Based on the physiological parameters of heart rate and QT interval of the ECG signal, the glucose levels of the T1DM patients can be determined and thus the episodes of hypoglycemia can be diagnosed [4].

A significant contribution is made by the use of fuzzy inferencing to realize the modeling and design of a non-invasive hypoglycemia monitoring system based on physiological responses. The classification models for numerous medical diagnosis such as diabetic nephropathy [5], acute gastrointestinal bleeding [6] and pancreatic cancer [7] have been developed by the use of the statical regression methods [8]. However, statical regression models are only accurate over the range of patients' data. In addition, it can only be applied if the patients' data are distributed based on the developed regression model, and the correlation between dependent and

independent variables does not exist. If the patients' data are irregular, the developed regression models would have an unnaturally too wide possibility range.

To carry out modeling and classification for medical diagnosis purposes using the ECG and EEG signals [9]–[11], much attention has been devoted to computational technologies such as fuzzy system [12], support vector machine [13], and neural networks [14]. Apart from EEG and ECG classification, advanced computational intelligence techniques have been applied to cardiovascular response [15], breast cancer and blood cell [16], skull and brain [17], etc. Each technology has its own advantages; for example, fuzzy system is famous for its decision-making ability. Thanks to its ability of representing expert knowledge, the system's output can be determined by a set of linguistic rules which can be understood easily. As discussed in [18], neural networks (NNs) have been used as universal function approximators thanks to their good approximation capability. To develop classification models for medical diagnosis purpose [19], NNs are good to use because of their ability in addressing both the nonlinear and fuzzy nature of patients' data. In [20], the support vector machine (SVM) has shown good performance for doing classification. It has been used in many applications. Thanks to its capability of tackling binary classification problems, SVM has been used in classifying the features of the cardiac signal [21].

Since traditional optimization methods like the least square algorithm and gradient descent methods have the potential problem of trapping in local optima, evolutionary algorithms such as particle swarm optimization (PSO) [22], genetic algorithm (GA) [23], differential evolution (DE) [24], and ant colony optimization [25] were considered. They are efficient global optimization algorithms particularly good for handling multimodal problems. As discussed in [10], [26], [27], the combination of optimization methods and evolutionary algorithms can eventually give good performance in clinical applications.

In this paper, a genetic algorithm based fuzzy inference system is developed for the detection of hypoglycemic episodes using the physiological parameters of heart rate (HR), cor-

rected QT interval (QT_c) of the electrocardiogram (ECG) signal, change of heart rate, (ΔHR), and change of corrected QT interval of the electrocardiogram signal (ΔQT_c). Fuzzy inference system (FIS) [12], [28] is good at representing expert knowledge in linguistic rules that can be easily understood by human beings. In this paper, we prove that the overall performance of the hypoglycemia detection system is distinctly improved in terms of sensitivity and specificity by using an FIS. To optimize the fuzzy rules and fuzzy membership functions of the FIS, the global searching algorithm of Genetic Algorithm (GA) [23] is investigated. GA is a powerful random global search technique to handle optimization problems. It can help find the globally optimal solution over a domain. A real application is given to show the proposed algorithm is useful to detect the hypoglycaemic episodes in T1DM children. Besides, a validation strategy is introduced to reduce the effects of overtraining [29].

The organization of this paper is as follows: In Section II, the details of the development of the genetic algorithm based fuzzy inference system are presented. To show the effectiveness of our proposed methods, the results of detecting nocturnal hypoglycemic episodes in T1DM patients are discussed in Section III. A conclusion is drawn in Section IV.

II. METHODOLOGY

To realize the detection of hypoglycemic episodes in T1DM patients, a GA based fuzzy inference system (FIS) is developed. The 4-input 1-output system is shown in Fig. 1. The physiological inputs are the heart rate (HR), corrected QT interval of the electrocardiogram signal (QT_c), change of heart rate (ΔHR), and change of corrected QT interval of the electrocardiogram signal (ΔQT_c). The output is the binary status of hypoglycemia (h), with +1 representing hypoglycemia and -1 representing non-hypoglycemia. The FIS plays a main role in modeling the correlation between the physiological parameters (HR , QT_c , ΔHR , and ΔQT_c) and the presence of hypoglycemia (h).

In this system, the fuzzy membership functions and fuzzy rules are optimized by GA. The details of the GA-based FIS, the performance measurement, and the fitness function that is associated with a validation strategy are discussed as follows:

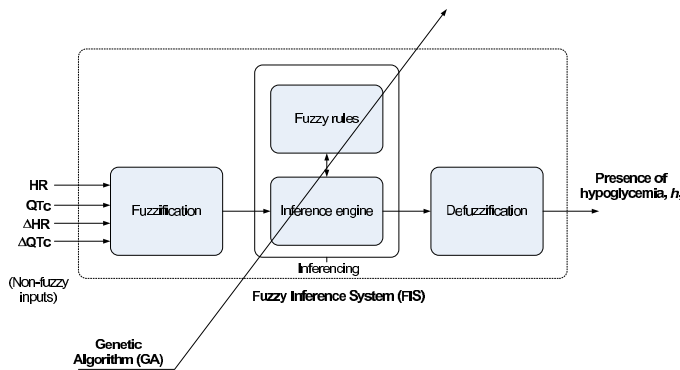


Fig. 1. Hypoglycemia detection system.

A. Fuzzy Inference System

Referring to Fig. 1, an FIS is used to model the hypoglycemic detection based on the physiological inputs (HR , QT_c , ΔHR , and ΔQT_c). The physiological inputs are treated as linguistic variables and given membership values that allow fuzzy detection. The fuzzy detection system consists of three components: fuzzification, inferencing, and defuzzification.

1) *Fuzzification*: The first step is to take the inputs, and determine the degree of membership they belong to each of the appropriate fuzzy sets. The membership function is defined as $\mu_{N_z^k}(z(t))$, which is a bell-shaped function given by:

$$\mu_{N_z^k}(z(t)) = e^{\frac{-(z(t)-m_z^k)^2}{2\zeta_z^k}}, \quad (1)$$

where $z(t)$ is any one of the following 4 signals: $HR(t)$, $QT_c(t)$, $\Delta HR(t)$, $\Delta QT_c(t)$; $z(t)$ denotes the non-fuzzy input, $k = 1, 2, \dots, m_f$; m_f denotes the number of membership functions, $t = 1, 2, \dots, n_d$; n_d denotes the number of input-output data pairs. The parameters m_z^k and ζ_z^k are the mean value and the standard deviation of the k -th membership function, respectively. If the input value is less than the minimum of the mean value or higher than the maximum of the mean value, the corresponding degree of membership is set as 1.

2) *Inferencing*: The task of the inferencing process is to map the fuzzified inputs to the rule base, and to produce a fuzzified output for each rule. The fuzzy if-then rules in the rule base are of the following format:

$$\begin{aligned} \text{Rule } \gamma : & \text{IF } HR(t) \text{ is } N_{HR}^k(HR(t)) \text{ AND} \\ & QT_c(t) \text{ is } N_{QT_c}^k(QT_c(t)) \text{ AND} \\ & \Delta HR(t) \text{ is } N_{\Delta HR}^k(\Delta HR(t)) \text{ AND} \\ & \Delta QT_c(t) \text{ is } N_{\Delta QT_c}^k(\Delta QT_c(t)) \text{ THEN } y(t) \text{ is } w_\gamma. \end{aligned} \quad (2)$$

where $N_{HR}^k(HR(t))$, $N_{QT_c}^k(QT_c(t))$, $N_{\Delta HR}^k(\Delta HR(t))$, and $N_{\Delta QT_c}^k(\Delta QT_c(t))$ are fuzzy terms, $\gamma=1, 2, \dots, n_r$; n_r denotes number of rules and n_r is set to $(m_f)^{n_{in}}$, where $n_{in} = 4$ is the number of inputs to the FIS. From the fuzzification process, the inference engine obtains the values of $\mu_{N_{HR}^k}(HR(t))$, $\mu_{N_{QT_c}^k}(QT_c(t))$, $\mu_{N_{\Delta HR}^k}(\Delta HR(t))$, $\mu_{N_{\Delta QT_c}^k}(\Delta QT_c(t))$. Aggregation is then used to obtain the output of each rule γ as a fuzzy value. The output for each rule is defined as:

$$\begin{aligned} \mu_\gamma = & (\mu_{N_{HR}^k}(HR(t))) \times (\mu_{N_{QT_c}^k}(QT_c(t))) \\ & \times (\mu_{N_{\Delta HR}^k}(\Delta HR(t))) \times (\mu_{N_{\Delta QT_c}^k}(\Delta QT_c(t))), \end{aligned} \quad (3)$$

$\gamma = 1, 2, \dots, n_r$.

3) *Defuzzification*: Defuzzification is the process of translating the outputs of the fuzzy rules into a value. The output of the defuzzification process is given by:

$$y(t) = \frac{\sum_{\gamma=1}^{n_r} w_\gamma \mu_\gamma}{\sum_{\gamma=1}^{n_r} \mu_\gamma}, \quad (4)$$

where $w_\gamma \in [0, 1]$ is the fuzzy singleton in Rule γ . If the output $y(t)$ is positive, hypoglycemia is present ($h(t) = +1$).

B. Genetic Algorithm

To optimize the fuzzy membership functions and rules (the values of m , ς and w), the Genetic Algorithm (GA) is investigated. The GA process is shown in Algorithm II.1. First, a population of chromosomes P is created. Each chromosome $\mathbf{p}_i$ contains a set of genes p_{ij} , where $i = 1, 2, \dots, n_p$, $j = 1, 2, \dots, n_g$; n_p and n_g denote the population size (number of chromosomes) and the number of genes respectively. Second, the chromosomes are evaluated by a defined fitness function $f(\mathbf{p}_i)$. The form of the fitness function depends on the application. The better chromosomes are those returning higher fitness values in this process. Third, some of the chromosomes are selected to undergo genetic operations for reproduction by the method of normalized geometric ranking [30]. It is a selection based on a non-stationary penalty function which is a function of the generation number. As the number of generation increases, the penalty increases that puts more and more selective pressure on the GA to find the feasible solution. In general, a higher-rank chromosome will have a higher chance to be selected. Fourth, the genetic operation of crossover is performed. The crossover operation is mainly for exchanging information from the two parents, chromosomes $\mathbf{p}_1$ and $\mathbf{p}_2$, obtained in the selection process with a defined probability of crossover μ_c . This probability gives an expected number of chromosomes that undergo the crossover. In this paper, Blend- α [31] is used as the operation of crossover, which has a good searching ability and can handle multimodal and separability problem effectively. For the Blend- α crossover, the resulting offspring is chosen randomly from the interval $[X_j^1, X_j^2]$ following the uniform distribution, where

$$\begin{aligned} X_j^1 &= \min(p_{1j}, p_{2j}) - \alpha d_j \\ X_j^2 &= \max(p_{1j}, p_{2j}) + \alpha d_j \end{aligned} \quad (5)$$

$d_j = |p_{1j} - p_{2j}|$, p_{1j} and p_{2j} are the j -th element of $\mathbf{p}_1$ and $\mathbf{p}_2$, respectively, and α is a positive constant.

After the crossover operation, the mutation operation follows. The mutation operation is to change the genes of the chromosomes in the population such that the features inherited from their parents can be changed. A probability of mutation, μ_m , is defined to govern the operation. It gives an expected number of genes that undergo the mutation. Non-uniform mutation [23] is used, which is an operation with a fine-tuning capability. The mutated gene is given by,

$$\hat{p}_{ij} = \begin{cases} p_{ij} + \Delta(\tau, \delta_{\max}^j - p_{ij}) & \text{if } r_d = 0 \\ p_{ij} + \Delta(\tau, p_{ij} - \delta_{\min}^j) & \text{if } r_d = 1 \end{cases}, \quad (6)$$

where r_d is a random number equal to 0 or 1 only. $\delta_{\max}^j$ and $\delta_{\min}^j$ are the upper and lower boundary of the gene. The function $\Delta(\tau, y)$ return a value in the range $[0, y]$ approaches 0 as τ increases. It is defined as follows.

$$\Delta(\tau, y) = y \left(1 - r^{(1-\tau/T)^\varsigma} \right), \quad (7)$$

where r is a random number in range of $[0, 1]$, τ represents the current generation number, T represents the total number

of iteration and ς is a shape parameter that determines the degree of non-uniformity. After going through the mutation operation, the new offspring will be evaluated using the fitness function. The new population will be formed when the new offspring replaces the chromosome with the smallest fitness value. A global best chromosome $\hat{\mathbf{p}}_g$ that has the best fitness value will be stored if the current best chromosome $\hat{\mathbf{p}}(\tau)$ is better than the global one in the current generation. The newly formed population will repeat the same process. Such an iterative process will be terminated when a defined termination condition is met. Finally, the best chromosome (solution) $\hat{\mathbf{p}}_g$ will be found.

Algorithm II.1: PSEUDO CODE FOR GA()

```

 $\tau \leftarrow 0$ 
Initialize  $P(\tau)$ 
output ( $f(P(\tau))$ )
while <not termination condition>
     $\tau \leftarrow \tau + 1$ 
    Select 2 parents,  $\mathbf{p}_1$  and  $\mathbf{p}_2$  from  $P(\tau - 1)$ 
    Perform crossover operation (5) with  $\mu_c$ 
    Perform mutation operation (6) – (7) with  $\mu_m$ 
    do
        if  $\hat{\mathbf{p}}(\tau) > \hat{\mathbf{p}}_g$ 
            then  $\hat{\mathbf{p}}_g = \hat{\mathbf{p}}(\tau)$ 
        output ( $P(\tau)$ )
        output ( $f(P(\tau))$ )
    return ( $\hat{\mathbf{p}}_g$ )
comment: return the best chromosome (solution)

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C. Performance Evaluation and Fitness Function

In this system, GA is employed to optimize the fuzzy rules and membership functions by finding out the best parameters m , ς and w . The function of the fuzzy inference system is to detect the hypoglycemic episodes accurately. To measure the performance of the biomedical classification test, sensitivity and specificity are introduced [32]. The sensitivity measures the proportion of actual positives which are correctly identified and the specificity measures the proportion of actual negatives which are correctly identified. The definitions of the sensitivity (ξ) and the specificity (η) are given as follows:

$$\xi = \frac{N_{TP}}{N_{TP} + N_{FN}}, \quad (8)$$

$$\eta = \frac{N_{TN}}{N_{TN} + N_{FP}}, \quad (9)$$

where N_{TP} is number of true positives which means the sick people are correctly diagnosed as sick; N_{FN} is number of false negative which means the sick people are wrongly diagnosed as healthy; N_{FP} is number of false positives which means healthy people are wrongly diagnosed as sick; and N_{TN} is number of true negatives which means the healthy people are correctly diagnosed as healthy. The values of ξ and η are within 0 to 1.

The objective of the system is to maximize the sensitivity and the specificity; thus, the fitness function is designed to maximize both values. A fitness function with a constant value and a penalty function is given in [33]. The constant value is used to control the balance between the sensitivity and specificity. The penalty function is used to force the sensitivity and the specificity to a required condition. However, on using this approach, only the training set and testing set are considered, which will risk the occurrence of overtraining [29]. Overtraining refers to the reduction of the generalization ability that can occur as the system is trained. To overcome this problem, a validation strategy that may adjust the fitness function is proposed in this paper to reduce the risk of overtraining.

Fig. 2 shows the idea of the proposed method to solve the overtraining problem. In this figure, the two curves represent the training performance and validation performance respectively. To overcome the overtraining problem, a validation set is introduced for the proposed fitness function. The x -axis represents the iteration number and T denotes the total number of iteration (as introduced in (7)), the y -axis represents the classification performance (in this paper, the performance is governed by sensitivity and specificity). The objective of the proposed validation strategy is to train the training set and test the trained results with the validation set with respect to a target region. The target region is a performance requirement related to sensitivity and specificity, for example, $\xi > 0.7$ and $\eta > 0.5$. As illustrated in Fig. 2 at T_a , we can see the performance of the training set has reached a very good result; however, the performance of the validation set cannot meet the minimum requirement of the target region. The testing performance will have a high chance to be out of the target region. It is an overtraining phenomenon; the model is over-fit with the training set and has the generalization performance reduced. At time T_b , the performance of both the training set and the validation set are within the target region; the testing result will have a good chance meeting the performance requirement. The parameters of the FIS will be stored at this time. In this paper, the termination condition of the GA is met when $\tau = T$. When both sets have reached the target region and $\tau < T$, such as $\tau = T_b$, we will update the target region (increase the requirement level). For example, increase $\xi > 0.7$ to $\xi > 0.75$. At time T_c , both the training and validation performance are in the updated target region, the model parameters will then be updated.

Algorithm II.2: FITNESS FUNCTION($\bar{\xi}_t, \bar{\eta}_t, \bar{\xi}_v, \bar{\eta}_v$)

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 $\eta_l \leftarrow \eta_d$ 
 $\xi_l \leftarrow \xi_d$ 
output ( $\bar{\xi}_t, \bar{\eta}_t, \bar{\xi}_v, \bar{\eta}_v$ ) based on (8) and (9)
output ( $f_{fit}$ ) based on (10)
if ( $\xi_t > \xi_l$  &  $\eta_t > \eta_l$  &  $\xi_v > \xi_l$  &  $\eta_v > \eta_l$ )
  then  $\xi_d = \xi_d + \sigma$ 

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Based on the above concept, the process of formulating the fitness function is shown in Algorithm II.2. First, a target region will be defined, the lower boundary of the sensitivity and specificity are defined as ξ_l and η_l respectively; the upper boundary for them is 1 (maximum performance). The initial values of the lower boundary for ξ_d and η_d are given. Second, based on (8) and (9), the training sensitivity ξ_t , the training specificity η_t , the validation sensitivity ξ_v , and the validation specificity η_v are evaluated. Referring to Fig. 2, the training performance is the result of ξ_t and η_t . Similarly, the validation performance is the result of ξ_v and η_v . Next, the fitness function, f_{fit} is calculated as follow:

$$f_{fit} = \bar{\xi}_t + \bar{\eta}_t + \bar{\xi}_v + \bar{\eta}_v, \quad (10)$$

where

$$\bar{\xi}_t = \begin{cases} 1 & \text{if } \xi_t \geq \xi_l \\ 1 - \frac{\xi_l - \xi_t}{\xi_l} & \text{if } \xi_t < \xi_l \end{cases},$$

and

$$\bar{\xi}_v = \begin{cases} 1 & \text{if } \xi_v \geq \xi_l \\ 1 - \frac{\xi_l - \xi_v}{\xi_l} & \text{if } \xi_v < \xi_l \end{cases},$$

and

$$\bar{\eta}_t = \begin{cases} 1 & \text{if } \eta_t \geq \eta_l \\ 1 - \frac{\eta_l - \eta_t}{\eta_l} & \text{if } \eta_t < \eta_l \end{cases},$$

and

$$\bar{\eta}_v = \begin{cases} 1 & \text{if } \eta_v \geq \eta_l \\ 1 - \frac{\eta_l - \eta_v}{\eta_l} & \text{if } \eta_v < \eta_l \end{cases}.$$

In (10), the maximum fitness value is equal to 4 (when $\bar{\xi}_t, \bar{\eta}_t, \bar{\xi}_v, \bar{\eta}_v$ all equal 1), which implies that both the training and validation performance have met the defined requirement. Finally, if the target region ($\xi_t > \xi_l$ and $\eta_t > \eta_l$ and $\xi_v > \xi_l$ and $\eta_v > \eta_l$) is reached, ξ_d will be updated by $\xi_d + \sigma$, where the value of σ is normally between 0.01 and 0.05. For finding out the optimal sensitivity with a fixed specificity value, only ξ_d will be updated during the training process.

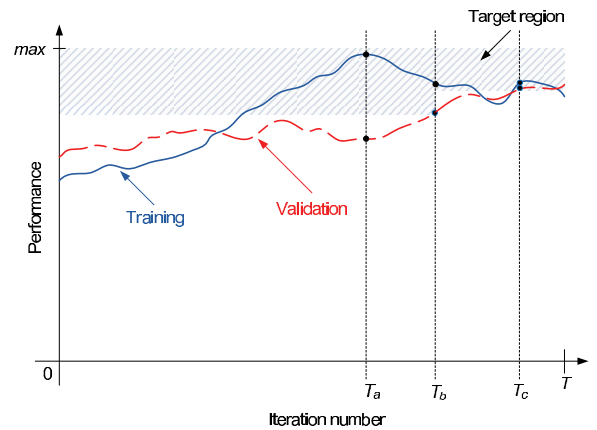


Fig. 2. Fitness function with validation strategy

III. RESULTS AND DISCUSSION

Fifteen children with T1DM (14.6 ± 1.5 years) volunteered for the 10-hour overnight hypoglycemia study at the Princess Margaret Hospital for Children in Perth, Western Australia, Australia. Each patient was monitored overnight for the natural occurrence of nocturnal hypoglycemia. Data were collected with approval from Women's and Children's Health Service, Department of Health, Government of Western Australia, and with informed consent.

A comprehensive patient information and consent form was formulated and approved by the Ethics Committee. The consent form included the actual consent and a revocation of consent page. Each patient received this information consent form at least two weeks prior to the start of the studies. He/She had the opportunity to raise questions and concerns with any medical advisers, researchers and the investigators. For the children participating in this study, the parent or guardian signed the relevant forms. We measured the required physiological parameters, while the actual blood glucose levels (BGL) were collected as reference using Yellow Spring Instruments. The main parameters used for the detection of hypoglycemia are the heart rate, corrected QT interval, change of heart rate and change of corrected QT interval. The responses from 15 T1DM children exhibited significant changes during the hypoglycemia phase against the non-hypoglycemia phase. Normalization is used to reduce patient-to-patient variability and to enable group comparison. The normalization is done by dividing the patient's heart rate and corrected QT interval by his/her corresponding values at time zero.

In this paper, the meaning of hypoglycemia is suggested as $BGL < 3.3$ mmol/l. The detection of hypoglycemic episodes using these variables is based on the proposed GA-based fuzzy inference system developed using the obtained clinical data. In effect, it estimates the presence of hypoglycaemia at sample period k_s based on the data at sampling period k_s and the previous data at sampling period $k_s - 1$. In general, the sampling period is 5 minutes and approximately 35-40 data points are used for each patient. The whole data set consists of a training set, a validation set and a testing set, each with 5 patients randomly selected. With these 15 patients, the number of data points for training, validation, and testing is 199, 177, and 193 respectively. The whole data set, which includes both the hypoglycemia data part and non-hypoglycemia data part, is used to build the classification and measure the classification performance in terms of sensitivity and specificity.

For comparison and analysis purposes, 4 approaches are used to tackle the same T1DM problem. They are: i) Evolved fuzzy inference system with 4 inputs (EFIS4) (4 inputs: HR , QT_c , ΔHR , and ΔQT_c) with the proposed fitness function and validation strategy considered; ii) Evolved fuzzy inference system with 2 inputs (EFIS2) (2 inputs: HR and QT_c only) with the proposed fitness function and validation strategy considered; iii) Evolved fuzzy inference system with 4 inputs without the proposed fitness function and validation strategy (EFIS4-V), the fitness function in [33] is applied; and iv) Evolved multiple regression with 4 inputs (EMR4).

GA is used to find the optimized fuzzy rules and membership functions of EIFS4, EFIS2, EFIS4-V, and the model parameters of EMR4. The parameter values of the GA are shown as follows.

- Population size θ : 100;
- Probability of crossover μ_c : 0.8;
- Constant value of crossover α : 0.5;
- Probability of mutation μ_m : 0.3;
- Shape parameter of mutation ζ : 2;
- Number of iteration T : 1000;
- Number of runs : 20.

In the fuzzy inference system, the number of the membership functions is set at 3 ($m_f = 3$); thus, the total number of fuzzy rules n_r is equal to 81 ($n_r = n_f^{n_{in}} = 3^4 = 81$). The best training, validation and testing results in term of the sensitivity (ξ) and specificity (η) are tabulated in Table I. For the proposed fitness function, the initial ξ_l and η_l are set at 0.7 and 0.4 respectively. The σ for sensitivity is set at 0.02. From Table I, we can see that the testing performance of EFIS4 outperform the other approaches, and the testing sensitivity is 86.05% with 42.73% specificity. The sensitivity of EFIS4 (86.05%) is significantly better than the sensitivity of EMR4 (67.44%). To illustrate the effectiveness of the proposed fitness function and validation strategy, evolved fuzzy inference system with 4 inputs (EFIS4-V) without the proposed fitness function and validation strategy is used. In EFIS4-V, there are only 2 data set (training and testing), 10 patients (combining the training and validation set of EFIS4) are selected for training and 5 patients are selected for testing. We can see from the results that the testing sensitivity of EFIS4 shows an increase from 81.40% to 86.05%. Furthermore, on comparing EFIS4 and EFIS2, the testing sensitivity with 4 inputs is better, which reflects that ΔHR ; ΔQT_c are useful physiological information to enhance the sensitivity.

The Receiver Operating Characteristic (ROC) [34] analysis is tabulated in Table II and the ROC plot is shown in Fig. 3. ROC analysis is commonly used in medical decision making, and is a useful technique for visualizing the diagnostic performance of a test. In an ROC curve the sensitivity is plotted against the false positive rate (1-specificity). A test with perfect discrimination has an ROC plot that passes through the upper left corner (100% sensitivity, 100% specificity). Thus, the closer the ROC plot is to the upper left corner, the higher the overall accuracy of the test. In Table II, the corresponding Area Under the Curve (AUC) of EFIS4 for testing is 0.7502 with a 95% confidence interval of (0.6578, 0.8426). With these results, we can see that the diagnostic performance of EFIS4 for testing is the best.

IV. CONCLUSION

A genetic algorithm based fuzzy inference system is developed to detect hypoglycemia. Experimental results indicate that hypoglycemia can be detected from the physiological responses of heart rate, corrected QT interval, change of heart rate and change of corrected QT interval. To optimize the fuzzy rules and membership functions, the genetic algorithm is

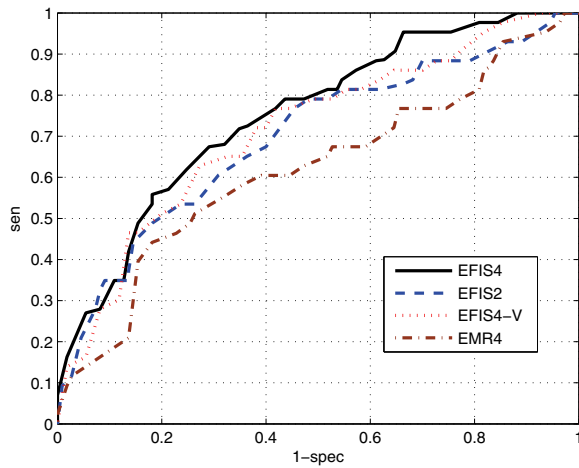


Fig. 3. ROC curve for testing.

		Method			
		EFIS4	EFIS2	EFIS4-V	EMR4
Training	ξ	82.76%	79.31%	89.23%	62.07%
	η	40.59%	38.82%	39.87%	39.41%
Validation	ξ	97.22%	97.22%	-	86.11%
	η	43.97%	41.84%	-	39.72%
Testing	ξ	86.05%	81.40%	81.40%	67.44%
	η	42.73%	40.91%	41.82%	40.91%

TABLE I

SIMULATION RESULT FOR EFIS4, EFIS2, EFIS4-V AND EMR4 AS $\eta_l = 0.4$ (ξ -SENSITIVITY, η -SPECIFICITY).

used. To avoid the over-training problem, a validation strategy that may adjust the fitness function is proposed. A clinical study is given to illustrate that the system with the proposed fitness function and validation strategy offers better results as compared with those from a fuzzy inference system of only 2 inputs, a fuzzy inference system without considering the over-training problem, and an evolved multiple regression algorithm in terms of sensitivity and specificity.

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	AUC	Standard Error (S.E)	95% Confidence Interval	
			min	max
EFIS4	0.7502	0.0472	0.6578	0.8426
EFIS2	0.6976	0.0498	0.6001	0.7952
EFIS4-V	0.7146	0.0490	0.6185	0.8107
EMR4	0.6183	0.0520	0.5164	0.7203

TABLE II
ROC CURVE ANALYSIS.

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