Evolved Fuzzy Reasoning Model for Hypoglycaemic Detection

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***Abstract* – Hypoglycaemia is a serious side effect of insulin therapy in patients with diabetes. We measure physiological parameters (heart rate, corrected QT interval of the electrocardiogram (ECG) signal) continuously to provide early detection of hypoglycemic episodes in Type 1 diabetes mellitus (T1DM) patients. Based on the physiological parameters, an evolved fuzzy reasoning model (FRM) to recognize the presence of hypoglycaemic episodes is developed. To optimize the fuzzy rules and the fuzzy membership functions of FRM, an evolutionary algorithm called hybrid particle swarm optimization with wavelet mutation operation is investigated. All data sets are collected from Department of Health, Government of Western Australia for a clinical study. The results show that the proposed algorithm performs well in terms of the clinical sensitivity and specificity.**

I. Introduction

HYPOGLYCAEMIA (low blood glucose) in diabetic patients has the potential to become dangerous. In general, the blood glucose in men can drop to 3 mmol/l after 24 hrs of fasting and to 2.7 mmol/l after 72 hrs of fasting. In women, glucose can be low as 2 mmol/l after 24 hrs of fasting. Blood glucose levels below 2.5 mmol/l are almost always associated with serious abnormality. In many cases of hypoglycaemia, the symptoms can occur without the patient being aware [3] and at any time, such as while driving or during sleep. In severe cases, the patient can lapse into a coma and die. Nocturnal episodes are potentially dangerous and have been implicated when diabetic patients have been found unexpectedly dead in their beds.

Diabetes Control and Complications Trial (DCCT) Research Group reported [1] that hypoglycaemic episodes are defined as those in which the patient had blood glucose levels < 3.33 mmol/l (60mg/dl). Nocturnal hypoglycemia is particularly dangerous because sleep reduces and may obscure autonomic counter-regulatory responses, so that an initially mild episode may become severe. The risk of severe hypoglycemia is high during sleeping at night, with at least 50% of all severe episodes occurring during that time [9].

This paper will make a significant contribution to knowledge in the modeling with physiological responses using a fuzzy reasoning system. We have developed a hybrid particle swarm optimization based fuzzy reasoning model for the early detection of hypoglycaemic episodes using physiological parameters such as heart rate and corrected QT interval of electrocardiogram signal. Fuzzy reasoning model (FRM) [4], [6] is good in representing some expert knowledge and experience in some linguistic rules which can be easily understood by human being. By introducing FRM, the performance in terms of sensitivity and specificity of the detection system is significantly improved. To optimize the fuzzy rules and membership functions of FRM, an evolutionary algorithm called hybrid particle swarm optimization with wavelet mutation (HPSOWM) [5] is introduced. Particle swarm optimization is a powerful random global search technique to handle optimization problems. It can help find the globally optimal solution over a domain. In HPSOWM, wavelet mutation is introduced to overcome the drawback of possible trapping in the local optima in PSO. A case study is given to show the proposed system is successful in detecting the hypoglycaemic episodes in T1DM.

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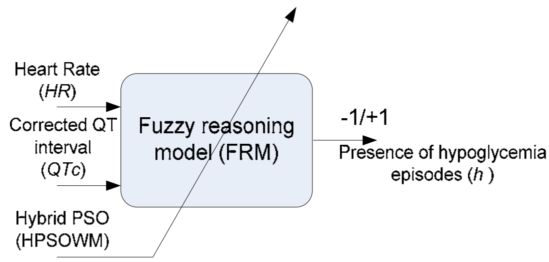

Fig. 1. PSO based fuzzy reasoning model for hypoglycaemia detection.

II. Methods

To realize the early detection of hypoglycaemic episodes in T1DM, an evolved fuzzy reasoning model (Fig. 1) is developed. It is a 2 inputs and 1 output system. The physiological inputs are the heart rate (*HR*) and corrected QT interval of the electrocardiogram signal (QT_c), and the output is the presence of hypoglycaemia (*h*) (+1 represents hypoglycaemia and –1 represents non-hypoglycaemia). In this proposed system, the fuzzy membership functions and fuzzy rules are optimized by HPSOWM [5]. The details of the FRM and, HPSOWM are discussed as follows:

A. Fuzzy reasoning model

Referring to Fig. 1, the FRM is used to realize the correlation between the physiological parameters (*HR* and QT_c) and the presence of hypoglycaemia (*h*). In this FRM, there are three parts and called fuzzification, reasoning by if-then rule, and defuzzification.

1. Fuzzification

The first step is to take the inputs and determine the degree of membership to which they belong to each of the appropriate fuzzy sets via membership functions. In this study, there are two inputs, heart rate (*HR*) and corrected QT interval (QT_c).

The degree of the membership function shows in Fig. 2 for input HR $\mu_{N_{\mathrm{HR}}^k}(HR(t))$ is a bell-shaped function as given by:

when $m_{\mathrm{HR}}^k \neq \max\{\mathbf{m}_{\mathrm{HR}}\}$ or $\min\{\mathbf{m}_{\mathrm{HR}}\}$

$$\mu_{N_{\mathrm{HR}}^k}(HR(t)) = e^{\frac{-(HR(t)-m_{\mathrm{HR}}^k)^2}{2\sigma_{\mathrm{HR}}^k}}, \tag{1}$$

where $\mathbf{m}_{\mathrm{HR}} = \begin{bmatrix} m_{\mathrm{HR}}^1 & m_{\mathrm{HR}}^2 & \dots & m_{\mathrm{HR}}^k & \dots & m_{\mathrm{HR}}^{m_f} \end{bmatrix}$, k=1, 2,…, m_f, m_f denotes the number of membership function, t=1, 2, …, n_d, n_d denotes the number of input-output data pair, parameter m_{HR}^k and σ_{HR}^k are the mean value and the standard deviation of the member function, respectively.

when $m_{\mathrm{HR}}^k = \min\{\mathbf{m}_{\mathrm{HR}}\}$

$$\mu_{N_{\mathrm{HR}}^k}(HR(t)) = \begin{cases} 1 & \text{if } HR(t) \leq \min\{\mathbf{m}_{\mathrm{HR}}\} \\ e^{\frac{-(HR(t)-m_{\mathrm{HR}}^k)^2}{2\sigma_{\mathrm{HR}}^k}} & \text{if } HR(t) > \min\{\mathbf{m}_{\mathrm{HR}}\} \end{cases} \tag{2}$$

when $m_{\mathrm{HR}}^k = \max\{\mathbf{m}_{\mathrm{HR}}\}$

$$\mu_{N_{\mathrm{HR}}^k}(HR(t)) = \begin{cases} 1 & \text{if } HR(t) \geq \max\{\mathbf{m}_{\mathrm{HR}}\} \\ e^{\frac{-(HR(t)-m_{\mathrm{HR}}^k)^2}{2\sigma_{\mathrm{HR}}^k}} & \text{if } HR(t) < \max\{\mathbf{m}_{\mathrm{HR}}\} \end{cases} \tag{3}$$

Similarly, the degree of the membership function for input QT$_c$ ($\mu_{N_{\mathrm{QT}}^k}(QT(t))$) is same as HR.

2. Reasoning by if-then rules

With these fuzzy inputs (HR and QT_c) and fuzzy output (presence of hypoglycaemic, y), the behavior of the FRM is governed by a set of fuzzy if-then rules in the following format:

Rule γ: **IF** $HR(t)$ is $N_{\mathrm{HR}}^k(HR(t))$ **AND** $QT_c(t)$ is $N_{\mathrm{QT}}^k(QT(t))$

THEN $y(t)$ is w_γ (4)

where $N_{\mathrm{HR}}^k(HR(t))$ and $N_{\mathrm{QT}}^k(QT(t))$ are fuzzy terms of rule γ, γ=1, 2, …n_r; n_r denotes number of rules and n_r is equal to $(m_f)^{n_{in}}$ where n_{in} represents the number of input of the FRM; $w_\gamma \in [0\ 1]$ is the fuzzy singleton to be determined.

3. Defuzzification

Defuzzification is the process of translating the output of the fuzzy rules into a scale. The presence of hypoglycaemia $h(t)$ is given by:

$$h(t) = \begin{cases} -1, & y(t) < 0 \\ +1, & y(t) \geq 0 \end{cases}, \tag{5}$$

where

$$y(t) = \sum_{\gamma=1}^{n_r} m_\gamma(t) w_\gamma \text{, and} \tag{6}$$

$$m_\gamma(t) = \frac{\mu_{N_{\mathrm{HR}}^\gamma}(HR(t)) \times \mu_{N_{\mathrm{QT}}^\gamma}(QT(t))}{\sum_{\gamma=1}^{n_r}\left(\mu_{N_{\mathrm{HR}}^\gamma}(HR(t)) \times \mu_{N_{\mathrm{QT}}^\gamma}(QT(t))\right)} \text{, and} \tag{7}$$

All the parameters of FRM ($\mathbf{m}_{\mathrm{HR}}$, $\boldsymbol{\sigma}_{\mathrm{HR}}$, $\mathbf{m}_{\mathrm{QT}}$, $\boldsymbol{\sigma}_{\mathrm{QT}}$, and $\mathbf{w}$) are tuned by the hybrid particle swarm optimization with wavelet mutation [5].

B. Hybrid particle swarm optimization with wavelet mutation

To optimize the fuzzy reasoning model, an evolutionary algorithm called hybrid particle swarm optimization with wavelet mutation (HPSOWM) [5] is investigated. It is a novel optimization method developed by Ling et. al. [5]. It models the processes of the sociological behavior associated with bird flocking. It uses a number of particles that constitute a swarm. Each particle traverses the search space looking for the global optimum. Wavelet mutation is introduced to overcome the drawback of tapping local optima of conversional PSO. The HPSOWM is shown in Fig. 3.

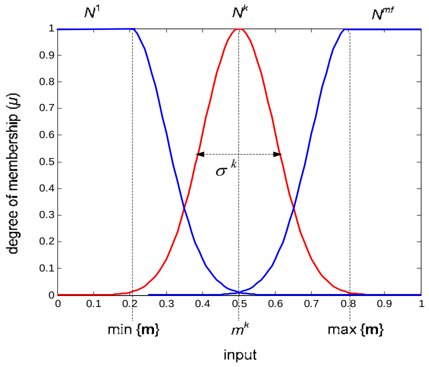

Fig. 2. Fuzzy inputs.

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begin
  $t \rightarrow 0$ // iteration number
  Initialize $X(t)$ // $X(t)$: swarm for iteration t
  Evaluate $f(X(t))$ // $f(\cdot)$: fitness function
while (not termination condition) **do**
  begin
    $t \rightarrow t+1$
    Update velocity $\mathbf{v}(t)$ and position of each particle $\mathbf{x}(t)$ based on (8) – (11) 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 μ_m
      Update $\bar{x}_j^p(t)$ based on (12) – (14)
    Reproduce a new $X(t)$
    Evaluate $f(X(t))$
  end
end

Fig. 3. Pseudo code for HPSOWM.

From Fig. 3, X(t) is denoted as a swarm at the t-th iteration. Each particle $\mathbf{x}^p(t) \in X(t)$ contains κ elements $x_j^p(t) \in \mathbf{x}^p(t)$ at the t-th iteration, where p = 1, 2,... , γ and j = 1, 2,… , κ; γ denotes the number of particles in the swarm and κ is the dimension of a particle. First, the particles of the swarm are initialized and then evaluated by a defined fitness function. The objective of HPSOWM is to minimize the fitness function $f(X(t))$ of particles iteratively. The swarm evolves from iteration t to t +1 by repeating the procedures as shown in Fig. 3. The operations are discussed as follows.

The velocity $v_j^p(t)$ (corresponding to the flight speed in a search space) and the position $x_j^p(t)$ of the j-th element of the p-th particle at the t-th generation can be calculated using the following formulae:

$$\begin{aligned} v_j^p(t) = k\Big(& w \cdot v_j^p(t-1) + \varphi_1 \cdot r_1 \cdot \left(\tilde{x}_j - x_j^p(t-1)\right) \\ & + \varphi_2 \cdot r_2 \cdot \left(\hat{x}_j - x_j^p(t-1)\right)\Big) \end{aligned} \tag{8}$$

and

$$x_j^p(t) = x_j^p(t-1) + v_j^p(t) \tag{9}$$

where

$\tilde{\mathbf{x}} = [\tilde{x}_1 \quad \tilde{x}_2 \quad ,... \quad \tilde{x}_\kappa]$ and $\hat{\mathbf{x}} = [\hat{x}_1 \quad \hat{x}_2 \quad ,... \quad \hat{x}_\kappa]$,

$j = 1, 2, \ldots, \kappa,$

the best previous position of a particle is recorded and represented as $\tilde{\mathbf{x}}$; the position of best particle among all the particles is represented as $\hat{\mathbf{x}}$; w is an inertia weight factor; φ_1 and φ_2 are acceleration constants; r_1 and r_2 return a uniform random number in the range of [0,1]; k is a constriction factor derived from the stability analysis of equation (9) to ensure the system to be converged but not prematurely. Mathematically, k is a function of φ_1 and φ_2 as reflected in the following equation:

$$k = \frac{2}{\left|2 - \varphi - \sqrt{\varphi^2 - 4\varphi}\right|} \tag{10}$$

where $\varphi = \varphi_1 + \varphi_2$ and $\varphi > 4$.

Generally, w can be dynamically set with the following equation:

$$w = w_{\max} - \frac{w_{\max} - w_{\min}}{T} \times t \tag{11}$$

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

In (8), the particle velocity is limited by a maximum value $v_{\max}$. The $v_{\max}$ determines the resolution with which regions are to be searched between the present position and the target position. From experience, $v_{\max}$ is often set at 0.1 to 0.2 of the dynamic range of the element on each dimension.

Next, the mutation operation is used to mutate the element of particles. The wavelet mutation (WM) operation exhibits a fine-tuning ability. Every particle element of the swarm will have a chance to mutate governed by a probability of mutation, $\mu_m \in [0 \quad 1]$. For instance, if $\mathbf{x}^p(t) = [x_1^p(t), \quad x_2^p(t), \quad \ldots \quad , x_\kappa^p(t)]$ is the selected p-th particle and the element of particle $x_j^p(t)$ is randomly selected for mutation (the value of $x_j^p(t)$ is inside the particle element's boundaries $[\rho_{\min}^j, \rho_{\max}^j]$), the resulting particle is given by $\bar{\mathbf{x}}^p(t) = [\bar{x}_1^p(t), \quad \bar{x}_2^p(t), \quad \ldots \quad , \bar{x}_\kappa^p(t)]$

$$\bar{x}_j^p(t) = \begin{cases} x_j^p(t) + \sigma \times (\rho_{\max}^j - x_j^p(t)) \text{ if } \sigma > 0 \\ x_j^p(t) + \sigma \times (x_j^p(t) - \rho_{\min}^j) \text{ if } \sigma \le 0 \end{cases}, \tag{12}$$

where $j \in 1, 2, \ldots \kappa$, κ denotes the dimension of particle and the value of σ is governed by Morlet wavelet function:

$$\sigma = \psi_{a,0}(\varphi) = \frac{1}{\sqrt{a}} \psi\left(\frac{\varphi}{a}\right) = \frac{1}{\sqrt{a}} e^{-\left(\frac{\varphi}{a}\right)^2 / 2} \cos\left(5\left(\frac{\varphi}{a}\right)\right) \tag{13}$$

The amplitude of $\psi_{a,0}(\varphi)$ will be scaled down as the dilation parameter a increases. This property is used to do the mutation operation in order to enhance the searching performance.

According to (13), if σ is positive approaching 1, the mutated element of the particle will tend to the maximum value of $x_j^p(t)$. Conversely, when σ is negative ($\sigma \le 0$) approaching –1, the mutated element of the particle will tend to the minimum value of $x_j^p(t)$. A larger value of $|\sigma|$ gives a larger searching space for $x_j^p(t)$. When $|\sigma|$ is small, it gives a smaller searching space for fine-tuning.

As over 99% of the total energy of the mother wavelet function is contained in the interval [–2.5, 2.5], φ can be generated from $[-2.5, 2.5] \times a$ randomly. The value of the dilation parameter a is set to vary with the value of t/T in order to meet the fine-tuning purpose, where T is the total number of iterations and t is the current number of iterations. To perform a local search when t is large, the value of a should increase as t/T increases so as to reduce the significance of the mutation. Hence, a monotonic increasing function governing a and t/T is proposed as follows.

$$a = e^{-\ln(g) \times \left(1 - \frac{t}{T}\right)^{\zeta_{wm}} + \ln(g)} \tag{14}$$

where ζ_{wm} is the shape parameter of the monotonic increasing function, g is the upper limit of the parameter a. After the operation of wavelet mutation, a new swarm is generated. This new swarm will repeat the same process. Such an iterative process will be terminated if the pre-defined number of iterations is met.

C. Fitness function and training

In this system, HPSOWM is employed to optimize the fuzzy rules and membership functions by find out the best parameters m_{HR}^k, σ_{HR}^k, m_{QT}^k, σ_{QT}^k, w_γ, of the FRM.

The function of the fuzzy reasoning model is to detect the hypoglycaemic episodes accurately. To measure the performance of the biomedical classification test, sensitivity (ς) and specificity (η) are used [1].

The objective of the system is to maximize the sensitivity and the specificity, thus, the fitness function is defined as follow:

$$f = \lambda\varsigma + (1-\lambda)\eta + \beta \text{, and} \tag{15}$$

$$\beta = \begin{cases} 10 & \text{if } \varsigma > 0.7, \eta > 0.5, \\ 0 & \text{otherwise} \end{cases} \tag{16}$$

where $\lambda \in [0 \ 1]$ is a constant value to control a balance of the sensitivity ς and specificity η. In this clinical study, λ is set at

TABLE I . CLINICAL RESULTS FOR HYPOGLYCAEMIC DETECTION WITH DIFFERENT NUMBER OF MEMBERSHIP FUNCTION

m_f	Training		Testing	
	Sensitivity	Specificity	Sensitivity	Specificity
3	75.56%	52.32%	72.41%	50.98%
5	76.67%	51.23%	65.52%	51.96%
8	73.33%	52.59%	75.86%	50.98%

0.58 where the ratio between the sensitivity and specificity is 0.58 : 0.42. It is important to keep a higher value of the sensitivity then that which represents the abnormal condition. In (15) and (16), β is a penalty function to force ς >0.7 and η >0.5 during training and it satisfies the requirement of the diagnosis. Since the objective is to maximize the fitness function of (15), a larger fitness value will be generated by β =10 is given if the requirement (ς >0.7 and η >0.5) is met.

III. EXPERIMENTAL RESULTS AND DISCUSSIONS

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

We measured the required physiological parameters, while the actual blood glucose levels (BGL) are collected as reference using Yellow Spring Instruments [7], [8]. The main parameters used for the detection of hypoglycaemia are the heart rate and corrected QT interval. The responses from 16 T1DM children exhibit significant changes during the hypoglycaemia phase against the non-hypoglycemia phase. Normalization is used to reduce patient-to-patient variability and to enable group comparison by dividing the patient's heart rate and corrected QT interval by his/her corresponding values at time zero.

The overall data set consisted of a training set and a testing set, each with 8 patients randomly selected. For these, the whole data set which included both hypoglycemia data part and non-hypoglycemia data part are used. By using HPSOWM which is used to find the optimized fuzzy rules and membership functions of FRM, the basic settings of the parameters of the HPSOWM are shown as follows.

Swarm size γ : 50;
Constant c_1 and c_2 : 2.05;
Maximum velocity $v_{\max}$: 0.2
Probability of mutation μ_m : 0.7;
The shape parameter of wavelet mutation ζ [5] : 2;
The constant value g of wavelet mutation [5] : 10000;
Number of iteration T : 500.

The clinical results for hypoglycaemic detection with different number of membership function m_f are tabulated in Table I. In this table, we can see that the best testing sensitivity is 75.56% with specificity 50.98% when the m_f is set at 8. For comparison purpose, feed-forward neural network (FFNN) [11] and multiple-regression (MR) [10] are given. Both approaches are trained with HPSOWM. The comparison result is tabulated in Table II. We can see in this table that the FRM performs better than FFNN and MR in term of the sensitivity and specificity. Only FRM can meet the requirement of the diagnosis (sensitivity > 70% and specificity > 50%)

TABLE II. TESTING RESULTS FOR HYPOGLYCAEMIC DETECTION WITH DIFFERENT APPROACHES

m_f	Sensitivity	Specificity
FRM	75.86%	50.98%
FFNN	64.26%	52.50%
MR	62.31%	53.10%

IV. CONCLUSION

In this paper, hybrid particle swarm optimization based fuzzy reasoning model is developed to detect the hypoglycaemic episodes for diabetes patients. Fuzzy reasoning model is investigated to detect the presence of hypoglycaemia. To optimize the fuzzy rules and membership functions, a hybrid particle swarm optimization with wavelet mutation is presented. As concluded, the testing performance of the proposed algorithm for detection of hypoglycaemic episodes for T1DM is satisfactory, as the sensitivity is 75.86% and specificity is 50.98%.

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.

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