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# Non-invasive Detection of Hypoglycemic Episodes in Type1 Diabetes Using Intelligent Hybrid Rough Neural System

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*Abstract*— **Insulin-dependent diabetes mellitus is classified as Type 1 diabetes and it can be further classified as immune-mediated or idiopathic. Through the analysis of electrocardiographic (ECG) signals of 15 children with T1DM, an effective hypoglycemia detection system, hybrid rough set based neural network (RNN) is developed by the use of physiological parameters of ECG signal. In order to detect the status of hypoglycemia, the feature of ECG of type 1 diabetics are extracted and classified according to corresponding glucose levels. In this technique, the applied physiological inputs are partitioned into predicted (certain) or random (uncertain) parts using defined lower and boundary of rough regions. In this way, the neural network is designed to deal only with the boundary region which mainly consists of a random part of applied input signal causing inaccurate modeling of the data set. A global training algorithm, hybrid particle swarm optimization with wavelet mutation (HPSOWM) is introduced for parameter optimization of proposed RNN. The experiment is carried out using real data collected at Department of Health, Government of Western Australia. It indicated that the proposed hybrid architecture is efficient for hypoglycemia detection by achieving better sensitivity and specificity with less number of design parameters.**

## I. INTRODUCTION

Hypoglycemia is the medical term for a state produced by lower level of blood glucose. It represents a significant hazard in Type 1 diabetes and can even lead to neurological damage or death. It is well known as death-in-bead syndrome. Several cases have been reported that patients with type 1 diabetes found dead in an undisturbed bed [1]. It can also result in physical and psychosocial morbidities such as brain damage, loss of consciousness, depression and low self-esteem [2]. Early detection and prevention on one set of hypoglycemia become the number one diabetic treatment goal. To achieve this, much more efforts need to provide to improve design and technology in detection of hypoglycemic episodes in type 1 diabetes.

A number of studies have been reported that the possibility of hypoglycemia is mainly effected by prolongation of QT interval (starting from Q point to the end of T-wave) in Type1 diabetes patient [3] [4]. Considering such correlation between physiological parameters of ECG signal and hypoglycemia, the presence of hypoglycemia is detected by the use of computational intelligence technologies. In [5] [6], fuzzy inference system and fuzzy neural network estimator are developed through the changes of heart rate (HR) and skin impedance parameters. Based on the physiological parameters of ECG signal, heart rate (HR), corrected QT interval (QTc) and skin impedance, bayesian neural network has been tested and introduced in detection of hypoglycemia in patients with T1DM [7] [8].

In addition, to identify the presences of hypoglycemic episodes in Type 1 diabetic patients, the hybridization technologies, such as genetic algorithm based neural network system [9], evolved fuzzy reasoning model [10], swarm based support vector machine [11] and statical multiple regression with fuzzy inference system [12], have been successfully applied to the development of hypoglycemia monitoring system. Even though satisfactory performances are found by the use of intelligent computational techniques, to the best of knowledge, none of the above has been adopted as hypoglycemia monitoring system in practise.

In this paper, a hybrid rough set based neural network (RNN) has been developed for detection of hypoglycemic episodes by the use of physiological parameters of ECG signal. A traditional neural network with a common structure still have the problems in managing architecture of the network and accelerating the training of the network [13]. In the proposed RNN, using rough set properties, the preprocessing stage is firstly carried out by partitioning the applied input signal into predictable (certain) part and random (uncertain) part. In this way, the neural network is designed to deal only with the boundary region which mainly consists of the random part of the applied input signal. Such approach improved classification accuracy and achieved better sensitivity and specificity with less number of design parameters.

The organization of this paper is as follows: in Section II, an RNN and its training procedures by the use of hybrid particle swarm optimization with wavelet mutation (HPSOWM) is introduced. To show the effectiveness of our proposed methods, the results of early detection of nocturnal hypoglycaemia episodes in T1DM are discussed in Section III and a conclusion is drawn in Section IV.

## II. METHODS

The hybridization technology using rough sets concepts and neural computing for decision and classification are presented in this paper. Neural network has been widely used as a universal function approximator due to its excellent

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property in dealing with complex function approximation [14]. However longer training time and complexity in neural computation become limiting factors to handle neural network in every applications [15]. Recently much of attention have been given to accelerate the process of neural network learning and reduce complexity by carrying out pre-process stage before the network training.

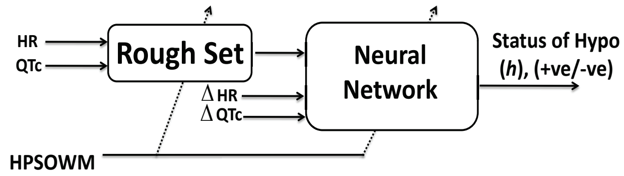


Fig. 1. Detection of Hypoglycemic Episodes Using Rough Neural Network

In the proposed RNN detection system in Fig.1, the pre-processing stage is firstly performed by using defined *lower region* and *boundary region* based on the rough set properties. The applied physiological inputs (HR and QTc) are partitioned into predictable (certain) part and random (uncertain) part by the use of defined rough regions. In rough set, the lower region mainly captures definite or certain part while boundary region mainly deal with random part of applied input signal.

Once lower and boundary segregation are taken place, feed forward neural network in Fig.1 will deal with boundary region consisting of randomness and uncertainty to reduce inaccurate modeling of data. Such architecture is able to reduce size of NN input and scaled down whole structure of the network [16]. It satisfies with the fact that a smaller network usually requires shorter learning time. To obtain optimized network parameters A global training algorithm, hybrid particle swarm optimization with wavelet mutation (HPSOWM) is introduced in this paper.

## A. Rough Set Theory

The rough set offers as a effective method that is applicable in many branches of artificial intelligence (AI) technologies. Its soundness and usefulness has been proven in many real life applications.

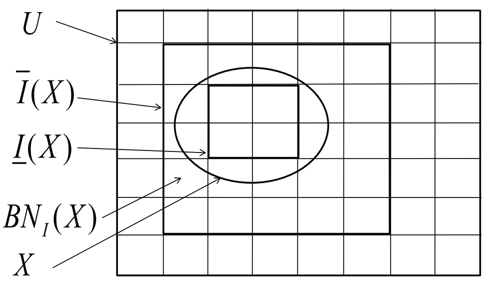


Fig. 2. Rough Set Approximation

In the rough set (Fig. 2), the universe, $(U)$ be a finite, nonempty set with, $I$, being an equivalence relation called the indiscernibility relation on $U$. $I(x)$ would then be described as an equivalence class of the relation $I$ containing the element $x$. The concept of an indiscernibility relation brings about the fact that not all elements in the universe, $U$ can be discerned given the information available. Further, such an indiscernibility relation is used to determine the *lower*, *upper* and *boundary* approximations which is expressed as:

$$\bar{I}(X) = \{x \in U : I(x) \subseteq X\} \tag{1}$$

$$\underline{I}(X) = \{x \in U : I(x) \cap X \neq 0\} \tag{2}$$

$$BN_I(X) = \bar{I}(X) - \underline{I}(X) \tag{3}$$

where $\bar{I}(X)$ and $\underline{I}(X)$ are defined as the *lower* and *upper region* of approximation region while the *boundary region* is denoted as the disjoint between lower and upper approximation. Decision rules are describing data patterns which represent in the form: $IF\ \alpha\ THEN\ \beta$, where $\alpha$ is the condition part and $\beta$ is the predicted class.

The optimized lower and upper boundaries parameters are obtained by using a global learning algorithm, HPSOWM which the boundary parameters, $\delta \in \left[\bar{I}(X), \underline{I}(X)\right]$ are encoded as elements of particle and gives the optimal values for those encoded elements of particle.

## B. Feed Forward Neural Network Architectures

A multi layer feedforward neural network becomes the most famous due to its good approximation in any smooth and continuous nonlinear separation functions in a compact domain to arbitrary accuracy [17]. For each input $u_i$, $i =$

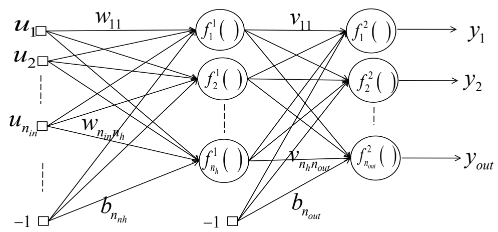


Fig. 3. A three layer feedforward neural network archicture

$1,2,\ldots,n$ has its associated weights $w_j$, $j = 1,2,\ldots,m$ which can be modified to model synaptic learning. The input-output relationship of a fully connected feedforward neural network in Fig. 3 is calculated as follows:

$$y_h = f_h^2\left(\sum_{j=1}^{n_h} v_{jh} f_j^{n_{in}}\left(\sum_{i=1}^{n_{in}} w_{ij}u_i - b_j\right) - b_h\right), h = 1,2,\ldots,n_{out} \tag{4}$$

where $u_i$, $i = 1,2,\ldots,n$ are the input variables, $n_{in}$ is the number of inputs while $n_h$ denotes the number of hidden notes. $w_{ij}$, $j = 1,2,\ldots,n_h$ is defined as the weight which is linked between the $i^{th}$ input and $j^{th}$ hidden nodes, $v_{jh}$ is the weight of link between the $j^{th}$ hidden and $h^{th}$ output nodes, $b_j$ and $b_h$ are the biases for hidden and output nodes.

The transfer function $f_j^1(\cdot)$ and $f_h^2(\cdot)$ are used as the activation function in the hidden nodes and output nodes. The hyperbolic tangent sigmoid transfer function $\tan sig(\theta) = \frac{2}{1+e^{-2\theta}} - 1 \in [0 \quad 1]$ and linear transfer function $pureline(\theta) = \theta$ are commonly used in the neurons of hidden and output layers. To find the optimized boundary, structure and weights of RNN, each particle of HPSOWM [19] defined with the boundary parameters of rough set $\delta$ and weights $(w_k^l)$ which is in the form of $\mathbf{x} = [w_k^l \ \delta]$.

### *C. Hybrid Particle Swarm Optimization with Wavelet Mutation (HPSOWM)*

For HPSOWM, a dynamic mutating space is introduced by incorporating a wavelet function. The detail Algorithm is presented in [19]. In HPSOWM, the wavelet is used as a tool to model seismic signals by combining the dilations and the translations of a simple oscillatory function (the mother wavelet) of finite duration. Thus, the mutating space of PSO is dynamically varying along the search based on the properties of the wavelet function. The resulting wavelet mutation operation aids the HPSOWM to perform more efficiently than the other hybrid PSO and genetic algorithm methods.

To find the optimized boundary, structure and weights of RNN, each particle of HPSOWM defined with the boundary parameters of rough set $\delta$ and weights $(w_k^l)$ which is in the form of $\mathbf{x} = [w_k^l \ \delta]$. In HPSOWM, a swarm $X(t)$ is constituted with the number of particles. Each particle $\mathbf{x}^p(t) \in X(t)$ contains $\kappa$ elements $x_j^p(t)$ at the $t$-th iteration, where $p = 1,2,...,\theta$ and $j = 1,2,...,\kappa$; $\theta$ denotes the number of particles in the swarm and $\kappa$ 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 (cost function) $f(X(t))$ of particles iteratively. The position $x_j^p(t)$ and velocity $v_j^p(t)$ of HPSOWM are given as follows:

$$\begin{aligned} x_j^p(t) &= x_j^p(t-1) + v_j^p(t) \\ v_j^p(t) &= k.\left(w.v_j^p(t-1) + \ _1 r_1\right).\left(\tilde{x}_j - x_j^p(t-1)\right) \\ &+ \ _2 r_2\left(\hat{x}_j - x_j^p(t-1)\right) \end{aligned} \tag{5}$$

where$\tilde{x}^p = \left[\tilde{x}_1^p, \tilde{x}_2^p, \ldots, \tilde{x}_k^p\right]$ and $\hat{\mathbf{x}} = [\ \hat{x_1} \ \hat{x_2} \ ,...\hat{x_\kappa}\ ]$, $j = 1,2,...,\kappa$.

The best previous position of a particle is recorded and represented as $\tilde{x}$; the position of best particle among all the particles is represented as $\hat{x}$; $w$ is an inertia weight factor; $r_1$ and $r_2$ are acceleration constants which return a uniform random number in the range of [0,1]; $w$ is inertia weight factor and $k$ is a constriction factor which detail derivation is discussed in [19].

$$\tilde{x}_j^p(t) = \begin{cases} x_j^p(t) + \sigma \times \left(\rho_{\max}^j - x_j^p(t)\right) & ,\sigma > 0 \\ x_j^p(t) + \sigma \times \left(x_j^p(t) - \rho_{\min}^j\right) & ,\sigma < 0 \end{cases} \tag{6}$$

where $j \in 1,2,\ldots,\kappa$ and $\kappa$ denotes the dimension of particles. The value of $\sigma$ is governed by Morlet wavelet function as presented in [19].

### *D. Performance Evaluation*

In clinical study, the sensitivity and specificity are used to measure the performance of biomedical classification test. In [20] sensitivity and specificity are defined as: $sensitivity\ (\xi) = \frac{TP}{TP+FN}$ and $specifity\ \ (\eta) = \frac{TN}{TN+FP}$ in which $N_{TP}$ is the number of true positive, $N_{FN}$ is the number of false negative, $N_{FP}$ is the number of false positive , and $N_{TN}$ is the number of true negative.

The objective is to maximize the fitness function of (7) which equivalent to maximize the sensitivity and the specificity. To meet the objective of the system the fitness function $f(\xi,\eta)$ is defined as follow:

$$f(\xi,\eta) = \xi + \eta \tag{7}$$

where $\xi$ and $\eta$ are sensitivity and specificity and $\eta$ is defined as: $\eta = \begin{cases} 1 & if\ \eta \geq \eta_{\max} \\ 1 - \left(\frac{\eta_{\max} - \eta}{\eta_{\max}}\right) & if\ \eta < \eta_{\max} \end{cases}$

$\eta_{\max}$ is a upper limit of the specificity and it is used to fix the region of specificity to find the optimal sensitivity in this region. Particularly, $\eta_{\max}$ can set from 0 to 1 and different sensitivity with different specificity values can be determined.

In this study, hypoglycemia episodes (BGL $\leq 3.3 mmol/l$) is detected using proposed hybrid rough set based block neural network as presented in Fig. 3. The construction process of proposed RNN is presented as follows:

1) Partitioning of the input data to certain (predictable) or uncertain (random) parts based on rough regions which is make up of a combination of lower region and boundary region, (1) - (3). In order to meet with the objective of clinical application, lower region (1) is defined as positive lower region, $\underline{I}_+(X)$ and negative lower region, $\underline{I}_-(X)$ in order to perform output prediction.
2) Prediction of output (status of hypoglycemia (+/−) by using (+/−) lower region) simplify the neural network input i.e., if the applied input signal is within the positive lower region, the approximated output is given as + hypoglycemia whereas it approximates as − hypoglycemia if the applied input signal is within the negative lower region.
3) The rest of the elements which is associated with randomness and uncertainty are categorized under the boundary region (3) and simultaneous classification task is performed by feedforward neural network (FWNN) in Section II-B.
4) The output of RNN, $y$ is calculated by (4) and it is defined as positive when the status of hypoglycemia $h$ is positive which expressed as:
$$h = \begin{cases} +1, & y \geq 0 \\ -1, & y < 0 \end{cases}.$$
5) Network training is performed by the use of HPSOWM [19] to obtain optimized parameters. Each particle $x_j^p(t)$ in the swarm $X(t)$ is encoded with network parameters and rough boundary parameters as $[w_k^l \ \delta]$.

After the training process, the optimal boundary parameters, $\delta$ in (1)-(3), weight parameters in (4) is obtained and the process is repeating until no improvement in classification performance have been achieved.

## III. RESULT AND DISCUSSION

To study the natural occurrence of nocturnal hypoglycemia, 15 children with T1DM is monitored for the 10-hour overnight at the Princess Margaret Hospital for Children in Perth, Western Australia, Australia. The required physiological parameters are measured by the use of non-invasive monitoring system [7] while the actual blood glucose level (BGL) are collected using Yellow Spring Instruments to use as a reference. All the data are collected at the same time and the duration for each patients varies from 360 minutes to 480 minutes.

In the actual blood glucose profile for 16 T1DM children [8], the significant change of 15 T1DM children responses can be distinctly seen during they hypoglycemia phase against non-hypoglycemia phase. The presence of hypoglycemia are estimated at sampling period $k_s$ and the previous data at sampling period $k_s - 1$. In general, the sampling period takes about 5 to 10 minutes and approximately 35-40 data points are used for each patient. Since normalization is carried out, patient-to-patient variability is reduced and group comparison is enabled by dividing the patient's heart rate (HR), corrected QT interval (QTc) by their corresponding value at time zero.

The BGL $< 3.3mmol/l$ was considered hypoglycemic episodes and the observation on changes in HR and QTc during hypoglycemia is carried out. From this group of patients [8], the normalized HR, QTc and their associated hypoglycemia revealed that there was a significant increment in HR $(1.082 \pm 0.298$ *vs*. $1.033 \pm 0.242)$ and QTc $(1.060 \pm 0.084$ *vs*. $1.031 \pm 0.086)$ by giving $p$ value of $HR < 0.06$ and $QTc < 0.001$.

Among 15 patients, 12 T1DM patients were found to experience hypoglycemic episodes as their BGL threshold levels were less than $(3.3mmol/l)$, while 3 T1DM patients did not experience hypoglycemia events as presented in Table I. This is because no natural occurrence of hypoglycemia episodes were presented during measurement or they may not have been valid with the defined BGL threshold level. For the clinical application in this study, BGL $< 3.3mmol/l$ was considered a hypoglycemic episode.

Based on these changes, HR and QTc are considered as an essential inputs to proposed hypoglycemia monitoring system (Fig. 1) while $\Delta HR$ and $\Delta QTc$ are used to improve the sensitivity. The overall data set consist of both hypoglycemia data and non-hypoglycemia data part was organized into a training set (5 patients with 184 data points), a validation set (5 patients with 192 data points) and a testing set (5 patients with 153 data points) which are randomly selected. In detail, 5 patients for the training sets are patients number 1, 2, 3, 9 and 10, where as patients number 4, 5, 11, 12, 13 and 6, 7, 8, 14, 15 are selected for validation and testing sets. The hypoglycemia episodes (BGL $\leq 3.3mmol/l$) are detected by the use of HPSOWM based RNN.

In clinical study, the sensitivity of detection system is more important than the specificity because it mainly represents the performance of classifier. Thus, the training specificity, $\eta_{\max}$ is set to 40% and analyze the sensitivity at the define $\eta_{\max}$. As can be seen in Table II, the average (mean) testing result of proposed RNN is found to be satisfactory with sensitivity, 76.28% and specificity, 50.40% compared to other methods, WNN with sensitivity, 71.39% and specificity, 44.37% and FWNN with sensitivity, 68.84% and specificity, 48.34%.

For evaluation purpose, $\gamma$ analysis is introduced in this paper, i.e., $\gamma = \theta\xi + (1-\theta)\eta$, ($\theta$ varies $0.1 \to 1$). In this study, to achieve minimum requirement of proposed monitoring system (sensitivity $\geq 60\%$ and specificity $\geq 40\%$ ), $\theta$ is set to 0.6 (which is equivalent to sensitivity 60%). Thus, $\gamma = 0.6\xi + 0.4\eta$. The obtained mean sensitivity and specificity are evaluated by means of $\gamma$ analysis in Table II in which the proposed RNN outperforms other comparison methods with $\gamma$ is 68.84%

As can be seen in Table III, the proposed RNN achieves better sensitivity and acceptable specificity value of 76.74% and 52.73 % whereas conventional FWNN with no rough approximation only gives 69.77% of sensitivity and 49.09% of specificity.

From results in Table II-III, it is quite evident that hypoglycemia episodes in T1DM children can be efficiently detected non-invasively and continuously from the real-time physiological responses. The proposed RNN model has been designed in such a way that the proposed approach improves classification performance and results in early convergence of the network.

## IV. CONCLUSIONS

In this paper, a new hybrid rough neural network detection algorithm is developed to recognize the presence of hypoglycemia. The rough approximation property is adopted by defining *lower* and *boundary region* and implemented those defined regions within neural network framework. To optimize the design parameter of proposed RNN system, a hybrid particle swarm optimization with wavelet mutation (HPSOWM) operation is used. The performance of proposed detection algorithm is found to be satisfactory with best sensitivity and specificity. The above results indicated that hypoglycemic episodes in T1DM children can be detected non-invasively and continuously from real time physiological responses. It also reveled that the proposed detection algorithm is efficient in obtaining better sensitivity with less number of design parameters.

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TABLE I
THE 15 PATIENTS AND THEIR ASSOCIATED HYPOGLYCEMIA AND NON-HYPOGLYCEMIA EVENTS

| Patient Number | No.of Hypo Episodes | Duration of Episodes(min) |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 8 | 40 |
| 3 | 7 | 45 |
| 4 | 10 | 50 |
| 5 | 4 | 20 |
| 6 | 14 | 75 |
| 7 | 9 | 45 |
| 8 | 11 | 55 |
| 9 | 17 | 105 |
| 10 | 0 | 0 |
| 11 | 0 | 0 |
| 12 | 9 | 45 |
| 13 | 9 | 85 |
| 14 | 13 | 70 |
| 15 | 7 | 70 |

TABLE II
MEAN VALE OF TRAINING VALIDATION AND TESTING RESULTS: SET MAXIMUM SPECIFICITY, $\eta_{\max}$= 40%

| | | RNN | WNN | FWNN |
|---|---|---|---|---|
| **Training** | **Sensitivity** ($\xi$) | 84.85 % | 84.12 % | 83.64 % |
| | **Specificity** ($\eta$) | 40.35 % | 40.63% | 40.50 % |
| **Validation** | **Sensitivity** ($\xi$) | 87.34 % | 80.44 % | 79.07 % |
| | **Specificity** ($\eta$) | 40.13 % | 40.94 % | 41.38 % |
| **Testing** | **Sensitivity** ($\xi$) | 76.28% | 71.39 % | 68.84 % |
| | **Specificity** ($\eta$) | 50.40 % | 44.37 % | 48.34 % |
| | **Gamma** ($\gamma$) | 65.56 % | 60.58 % | 60.04 % |

TABLE III
BEST TESTING RESULTS: SET MAXIMUM SPECIFICITY, $\eta_{\max}$= 40%

| **Methods** | Parameters | Sensitivity($\xi$) | Specificity($\eta$) | Gamma($\gamma$) |
|---|---|---|---|---|
| **RNN** | 25 | 76.74 % | 52.73 % | 67.14 % |
| **WNN** | 78 | 72.09 % | 45.45 % | 61.43 % |
| **FWNN** | 45 | 69.77 % | 49.09 % | 61.50 % |