NON-INVASIVE DETECTION OF HYPERGLYCAEMIA IN TYPE 1 DIABETIC PATIENTS USING ELECTROCARDIOGRAPHIC SIGNALS

By

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CERTIFICATE OF AUTHORSHIP/ORIGINALITY

I, Linh Lan Nguyen, certify that the work in the thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that this thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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This thesis is especially dedicated to my dearest family

for their endless love, care and encouragement …

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List of Abbreviations

ANN	:	Artificial neural network
AUC	:	Area under the curve
BGL	:	Blood glucose level
CGF	:	Conjugate gradient back propagation with Fletcher-Reeves updates
CGMS	:	Continuous glucose monitoring system
ECG	:	Electrocardiography
FFT	:	Fast Fourier transform
GA	:	Genetic algorithm
GDX	:	Gradient descent with momentum
gm	:	Geometric mean
HRV	:	Heart rate variability
KNN	:	K-nearest neighbour
LDA	:	Linear Discriminant Analysis
LM	:	Levenberg Marquardt
LM-NN	:	Neural network using Levenberg Marquardt algorithm
MSE	:	Mean squared error
NIR	:	Near-infrared light
NN	:	Neural network
PC	:	Principle component
PCA	:	Principal component analysis
PCA-CGF	:	Neural network using principal component analysis and Conjugate gradient backpropagation with Fletcher-Reeves updates algorithm
PCA-GDX	:	Neural network using principal component analysis and Gradient descent with momentum algorithm
PCA-LM	:	Neural network using principal component analysis and Levenberg Marquardt algorithm
PCA-RP	:	Neural network using principal component analysis and Resilient backpropagation algorithm
PCA-SCG	:	Neural network using principal component analysis and Scaled conjugate gradient algorithm
PSO	:	Particle swarm optimisation

PSO-NN	:	Neural network using particle swarm optimisation
ROC	:	Receiver operating characteristic
RP	:	Resilient backpropagation
SCG	:	Scaled conjugate gradient
Sen	:	Sensitivity
Spec	:	Specificity
T1DM	:	Type 1 Diabetes mellitus
VIF	:	Variance inflation factor

List of Symbols

Q	:	the beginning of QRS complex
R	:	the peak of QRS complex
S	:	the end of QRS complex
P	:	the beginning of P-wave
T_P	:	the peak of T-wave
T_E	:	the end of T-wave
RR	:	the interval between two consecutive R points
PR	:	the interval from the beginning of P-wave to the beginning of QRS complex
QT	:	the interval from Q point to the end of T-wave (T_E)
QT_C	:	the corrected QT interval by heart rate (Bazett's formula)
RT	:	the interval from R point to the end of T-wave (T_E)
RT_C	:	the corrected RT interval by heart rate (Bazett's formula)
T_PT_E	:	the interval from the peak of T-wave (T_P) to the end of T-wave (T_E)
T_PT_{EC}	:	the corrected T_PT_E interval by heart rate (Bazett's formula)
MeanRR	:	mean *RR* interval
SDNN	:	the standard deviation of the *RR* interval index
RMSSD	:	the root mean square of successive *RR* interval differences
pNN50	:	the percentage of beats with a consecutive *RR* interval more than 50 ms
HRVi	:	HRV triangular index
TINN	:	baseline width of the *RR* interval histogram evaluated through triangular interpolation
VLF	:	Very low frequency
LF	:	Low frequency
HF	:	High frequency
TotalPw	:	Total spectral power
LF/HF	:	ratio between *LF* and components
p_{best}	:	best solution of the particle has achieved so far
g_{best}	:	the global best
lbest	:	the local best
w_i	:	position of the particle
v_i	:	velocity of the particle

c_1, c_2	:	acceleration constants
ω	:	inertia factor
ω_{max}	:	initial weight
ω_{min}	:	final weight
v_{max}	:	maximum allowable velocity
$v_{max\text{-}perc}$	:	velocity clamping percentage

Abstract

Hyperglycaemia is the medical term for a state caused by a high level of blood glucose, resulting from defects in insulin secretion, insulin action, or both. Hyperglycaemia is a common dangerous complication to glycaemic control in Type 1 diabetic patients. The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Therefore, reliable detection of hyperglycaemic episodes is important in order to avoid major health conditions.

Conventionally, diabetic patients need to frequently monitor blood glucose levels to determine whether they have hyperglycaemia or not. A patient has to prick their finger (finger-stick) for a drop of blood several times a day, which can therefore significantly discourage many patients from periodically checking blood glucose levels. Another choice for hyperglycaemia detection might be continuous glucose monitoring systems (CGMS), which measure the glucose level in the interstitial fluid. For patients using CGMS, finger-sticks are still required to calibrate the sensor. The main shortcoming of CGMS is that glucose levels in interstitial fluid lag temporally behind blood glucose values, normally 10-15 minutes, which absolutely limits the accuracy of the detection. There is a strong demand to have a non-invasive technique to help patients to diagnose the disease easily and painlessly. Few methods have been reported to detect hyperglycaemia non-invasively or minimally invasively such as in exhaled methyl nitrates, and early detection of ongoing β cell death. However, the purpose of these studies was on real-time glucose control rather than disease diagnosis.

Electrocardiography (ECG) is a broadly used technique to obtain a quick, non-invasive clinical and research screen for diagnosing abnormal rhythms of the heart caused by diseases. In fact, observations of ECG changes have been found in hypoglycaemia and hyperglycaemia states in T1DM, such as increased heart rate and prolongation of *QT* interval in hypoglycaemia, whereas hyperglycaemia was related to reduced heart rate variability. By using these findings in hypoglycaemia,

researchers have developed an effective and sensitive system to detect hypoglycaemia non-invasively. These excellent performances of hypoglycaemia detection using ECG is the motivation of this thesis to study the effect of hyperglycaemia on ECG signals, and based on the findings to exploit the computational intelligence on the non-invasive detection of hyperglycaemia.

This research firstly explores the changes of ECG parameters associated with the hyperglycaemic state in T1DM. The ECG parameters consist of ECG intervals relating to repolarisation phase and heart rate variability (HRV) measures. A clinical study of ten T1DM patients and ECG feature extraction process are conducted to collect ECG features. Statistical analysis is then applied to every ECG feature to estimate the significant difference between hyperglycaemic and normoglycaemic states. The results show that the selected ECG parameters in hyperglycaemia differ significantly from those in normoglycaemia ($p< 0.05$). It implies that certain ECG parameters are correlated with high blood glucose levels and they possibly contribute to the performance of hyperglycaemia detection. Thus, the ECG parameters are used for input data of hyperglycaemia classifiers in this thesis.

Furthermore, the thesis introduces novel computational intelligent methods for hyperglycaemia detection using the ECG parameters. A neural network using Levenberg-Marquardt algorithm is the first method explored for hyperglycaemia detection in this thesis, known as LM-NN. The second algorithm is the integration of principal component analysis (PCA) with a neural network utilising the Levenberg-Marquardt algorithm, which is called a PCA-LM-NN network. PCA is a useful tool for dimensionality reduction to diminish the computational requirement and overcome the problem of multicollinearity. It is employed to filter the data so that only the significant independent ECG variables responsible for the high blood glucose levels can be used as input for the network training, in order that the neural network performs well for hyperglycaemia detection. The third method is for the improvement of the second method where particle swarm optimization is included. This algorithm is a combination of PCA, PSO and neural network, which is called PSO-NN. The PSO is utilised as an effective training algorithm to optimise the weights of the neural network. The proposed methods are compared with each other and with other traditional classifiers. All the algorithms are investigated with the clinical electrocardiographic data extracted from ten T1DM patients.

The results show that the performance of PCA-LM model for hyperglycaemia detection is better than that of LM-NN (70.88% vs. 67.94%, in terms of geometric mean). In addition, the PSO-NN outperforms the PCA-LM-NN (77.58% vs. 70.88%, in terms of geometric mean). In short, the PSO-NN significantly improves the performances of both the LM-NN and PCA-LM-NN, with considerable sensitivity, specificity and geometric mean of 82.35%, 73.08% and 77.58%, respectively.