

Non-invasive Detection of Hypoglycemia in Patients with Type 1 Diabetes using Electroencephalography Signals

by

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CERTIFICATE OF AUTHORSHIP/ORIGINALITY

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

I also certify that the 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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Abstract

For patients with type 1 diabetes mellitus (T1DM), hypoglycemia, or the state of abnormally low blood glucose level (BGL), is the most common but acute complication which limits their intellectual as well as physical activities. Mild hypoglycemic episodes cause sweating, nervousness, heart plumping, confusion, anxiety, etc. which can be fixed by eating or drinking glucose-rich food. However, if left untreated, severe episodes of hypoglycemia may lead to unconsciousness, coma, or even death. Nocturnal episodes of hypoglycemia are especially dangerous because sleep reduces and obscures early symptoms, so that an initially mild episode may become severe. Because of its severity, it is essential for T1DM patients to be monitored and alarmed whenever a hypoglycemic episode occurs, especially during the night.

For the purpose of hypoglycemia detection, using parameters extracted from the electroencephalogram (EEG) is one of the most promising methods. Because it depends on a continuous supply of glucose and is vulnerable to any glucose deprivation, the human brain is one of the first affected organs under the occurrence of hypoglycemia. Since the EEG is directly related to the metabolism of brain cells, a failure of cerebral glucose supply can cause early changes in EEG signals that can be utilized in hypoglycemia detecting devices.

The main aim of this thesis is to develop a computational methodology of non-invasively detecting the onset of nocturnal hypoglycemia for patients with T1DM from their EEG signals. There are two core tasks to be implemented: feature extraction and classification.

Feature extraction analyses a variety of EEG parameters to find features that significantly respond to the onset of hypoglycemia. Important features will be used as inputs of the classification in order to classify and detect hypoglycemic episodes.

Using raw EEG signals collected at four EEG channels (C3, C4, O1, O2) from five T1DM patients who participated in an overnight hypoglycemia-induced study, four EEG parameters (power level, centroid frequency, spectral variance, spectral entropy) within three frequency bands (theta, alpha, beta) are extracted by spectral analysis. Statistical analysis is applied to find parameters that significantly correlate to the transitions of patients' states during the study, from normal to hypoglycemic and then to recovery state. The statistical results show that under hypoglycemic conditions, there are early changes in the theta and alpha bands of EEG signals. The decrease in centroid alpha frequency is the most significant feature which is consistently observed in all patients at all EEG channels ($p < 0.0001$). Besides, by analysing the data from the BGL range of 3.3-3.9 mmol/l, it is established that the EEG responses to hypoglycemia only significantly occur when patients' BGLs fall to the threshold of 3.3 mmol/l. This threshold is used to distinguish between hypoglycemic state and non-hypoglycemic state for the classification purpose in this thesis. As a result of the feature extraction, two EEG features of centroid theta frequency and centroid alpha frequency are derived at two channels C3 and O2 to be used as inputs of the classification.

In terms of classification algorithm, in this thesis, the standard multi-layer feed-forward neural network is utilised as the classification unit. Three different training techniques are applied to train the developed neural network, including the LM algorithm, the LM+GA algorithm, and the LM+GA+Adaptive algorithm. The LM algorithm is based on the popular Levenberg-Marquardt algorithm and the cross-validation technique in order to direct the training process to one of local optimal solutions. The LM+GA algorithm includes two consecutive steps of global search and local search. The global search is based on a genetic algorithm which helps the training process direct to the area of the global optimal solution. The local search is based on the LM algorithm which acts as a fine tuner to get the training process closer to the final optimised solution. Lastly, the LM+GA+Adaptive algorithm is introduced, as the final neural network training procedure

proposed by this thesis. This algorithm consists of two consecutive stages including an adaptive training stage implemented after the GA+LM algorithm. The stage of adaptive training helps to adapt the optimised network yielded by the GA+LM algorithm to the new EEG patterns of unseen subjects, thus limiting effects of the EEG variability on classification results and enhancing the generalisation ability of the developed neural network.

The final classification results produced by this thesis (80% sensitivity and 60% specificity on the training set and 78% sensitivity and 62% specificity on the testing set) indicate that by applying the proposed computational methodology, nocturnal episodes of hypoglycemia can be successfully detected in patients with T1DM from their non-invasive EEG signals. With the final performance achieved by this thesis, future works will be carried out to pursue the final aim of the current research which is developing a non-invasive EEG-based system for detecting hypoglycemia that can be applied into the real clinical environment.