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An efficient machine learning approach for diagnosis of paraquat-poisoned patients

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ABSTRACT

Numerous people die of paraquat (PQ) poisoning because they were not diagnosed and treated promptly at an early stage. Till now, determination of PQ levels in blood or urine is still the only way to confirm the PQ poisoning. In order to develop a new diagnostic method, the potential of machine learning technique was explored in this study. A newly developed classification technique, extreme learning machine (ELM), was taken to discriminate the PQ-poisoned patients from the healthy controls. 15 PQ-poisoned patients recruited from The First Affiliated Hospital of Wenzhou Medical University who had a history of direct contact with PQ and 16 healthy volunteers were involved in the study. The ELM method is examined based on the metabolites of blood samples determined by gas chromatography coupled with mass spectrometry in terms of classification accuracy, sensitivity, specificity and AUC (area under the receiver operating characteristic (ROC) curve) criterion, respectively. Additionally, the feature selection was also investigated to further boost the performance of ELM and the most influential feature was detected. The experimental results demonstrate that the proposed approach can be regarded as a success with the excellent classification accuracy, AUC, sensitivity and specificity of 91.64%, 0.9156%, 91.33% and 91.78%, respectively. Promisingly, the proposed method might serve as a new candidate of powerful tools for diagnosis of PQ-poisoned patients with excellent performance.

1. Introduction

Paraquat (1,1′-dimethyl-4,4′-bipyridium dichloride, PQ), the most widely used herbicides in the world, has been deemed as the most highly toxic pesticide for human [1]. Its mortality rate is highly correlated with plasma PQ concentrations [2]. Acute ingesting 7–8 mL PQ can cause serious symptoms such as liver, lung, kidney, and heart failure that directly leads to death if without getting prompt treatment [3]. Although few of PQ poisoning appeared in developed countries, there are thousands of people died of PQ poisoning every year in developing countries [4]. For example, PQ accounts for most fatal poisonings, with 500 or more deaths per year in Korea [5].

PQ intoxication is associated with reactive oxygen species and free radicals that cause early multiorgan failure and late pulmonary fibrosis with respiratory failure [5,6]. The current treatment strategies of PQ poisoning are increasing the elimination of PQ from the body, administration of antioxidants and the maintenance of vital functions, which is an entirely different from other intervention of intoxication [1,7]. And earlier the treatment initiated, more effective in reducing mortality, particularly hemoperfusion (HP) within 2–4 h after intoxication [4]. Therefore, diagnosis is very important in treatment of PQ-poisoned patients.

Till now, the diagnosis of PQ poisoning mainly is according to the PQ concentration in blood. However, PQ is absorbed poorly from the stomach and small intestine ($<5\%$) and distributed into all organs in the body within 5 h, which means it is difficult to detect PQ in blood after poisoned 5 h [1,8]. And in some cases, the patients cannot provide a clear contact history of PQ poisoning, such as disturbance of consciousness or language. This poses a more serious problem for diagnosis. How to develop a new diagnosis method of PQ poisoning is becoming an important topic in medicine.

In this study, patients with acute PQ intoxication were involved and determined by gas chromatography coupled with mass spectrometry (GC–MS). According to their plasma metabonomics, a rapid diagnosis method was developed based on the extreme learning machine (ELM) technique [9], a new learning algorithm for a single hidden layer feed-forward neural network (SLFNs). Different from the common parameter tuning strategy of neural network, ELM tries to choose input weights and hidden biases randomly, and the output weights are analytically determined by using Moore–Penrose (MP) generalized inverse. It not only learns much faster with higher generalization performance, but

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also keeping very few parameters for tuning. Thanks to its good properties, ELM has found its applications in a wide range of fields such as cancer diagnosis [10], image quality assessment [11], face recognition [12], land cover classification [13] and hyperspectral images classification [14]. To the best of our knowledge, there is no research work dealing with the problem of PQ poisoning from the machine learning perspective. Therefore, an attempt was made in this study to explore the potential of the performance of ELM in discriminating the PQ-poisoned patients from the healthy controls. For comparison purpose, the support vector machines [15] (SVM) was also taken for diagnosis of PQ poisoning. In addition, the effectiveness of feature selection was investigated as well. The efficient and commonly used feature selection method, maximum relevance minimum redundancy (mRMR) [16], was employed for pre-processing before the classification models were constructed. mRMR is a filter type feature selection method that seeks to choose features which are relevant to the target class (maximum relevance) and come up with the feature subset containing as non-redundant features as possible (minimum redundancy). The effectiveness of the proposed approach is examined in terms of classification accuracy, AUC, sensitivity and specificity respectively on the diagnosis of PQ-poisoned cases whose samples were collected from The First Affiliated Hospital of Wenzhou Medical University. Promisingly, the developed ELM based approach has achieved high diagnosis accuracy, AUC, sensitivity and specificity of 91.64%, 0.9156%, 91.33% and 91.78%, respectively.

The remainder of this paper is organized as follows. Section 2 offers brief background knowledge on ELM. The detail of the ELM method is described in Section 3. Section 4 presents the detailed experimental designs. The experimental results and discussion of the proposed method are presented in Section 5. Finally, conclusions and recommendations for future work are summarized in Section 6.

2. Extreme learning machine (ELM)

A brief description of ELM is given in this section, for more details, one can refer to [9,17]. Given a training set $\aleph = \{(x_i, t_i) | x_i \in R^n, t_i \in R^m, i = 1, 2, \ldots, N\}$, where x_i is the $n \times 1$ input feature vector and t_i is a $m \times 1$ target vector. The standard SLFNs with an activation function $g(x)$ and $\tilde{N}$ hidden neurons can be mathematically modeled as follows [9]:

$$\sum_{i=1}^{\tilde{N}} \beta_i g(w_i x_j + b_i) = o_j, \quad j = 1, 2, \ldots, N \tag{1}$$

where w_i is the weight vector between the ith neuron in the hidden layer and the input layer, b_i means the bias of the ith neuron in the hidden layer; β_i is the weight vector between the ith hidden neuron and the output layer; and o_j is the target vector of the jth input data. Here, $w_i \cdot x_j$ denotes the inner product of w_i and x_j.

If SLFNs can approximate these N samples with zero error, we will have $\sum_{j=1}^{N} || o_j - t_j || = 0$, i.e., there exist β_i, w_i, b_i such that $\sum_{i=1}^{\tilde{N}} \beta_i g(w_i \cdot x_j + b_i) = t_j, \; j = 1, 2, \ldots, N$. The above Equation can be reformulated compactly as:

$$\mathrm{H}\beta = \mathrm{T} \tag{2}$$

where

$$H(w_1, \ldots, w_{\tilde{N}}, b_1, \ldots, b_{\tilde{N}}, x_1, \ldots, x_N) = \begin{pmatrix} g(w_1 \cdot x_1 + b_1) & \ldots & g(w_{\tilde{N}} \cdot x_1 + b_{\tilde{N}}) \\ \vdots & \ddots & \vdots \\ g(w_1 \cdot x_N + b_1) & \cdots & g(w_{\tilde{N}} \cdot x_N + b_{\tilde{N}}) \end{pmatrix}_{N \times \tilde{N}} \tag{3}$$

$$\beta = \begin{bmatrix} \beta_1^T \\ \vdots \\ \beta_{\tilde{N}}^T \end{bmatrix}_{\tilde{N} \times m} \text{ and } \mathrm{T} = \begin{bmatrix} t_1^T \\ \vdots \\ t_N^T \end{bmatrix}_{N \times m} \tag{4}$$

As named by Huang et al. [18], H is called the hidden layer output matrix of the neural network, with the ith column of H

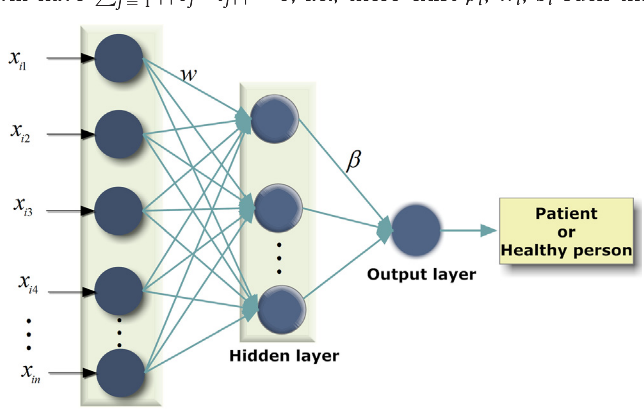

Fig. 1. The diagnosis model of PQ poisoning based on ELM.

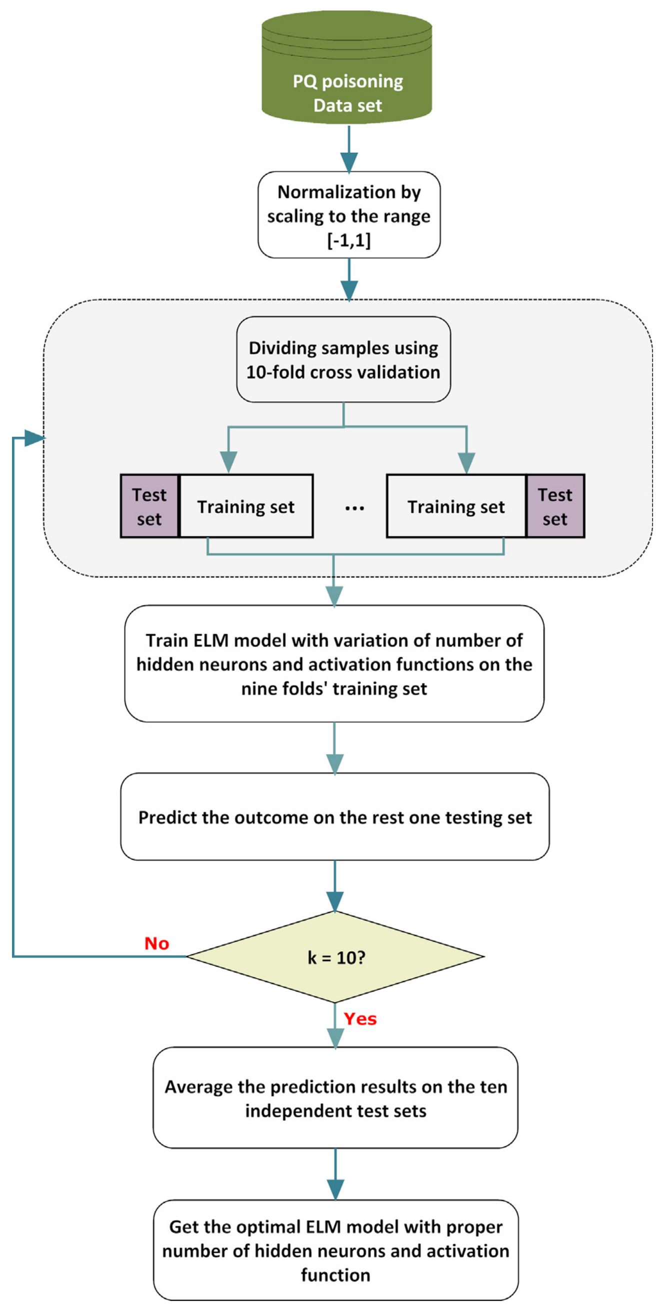

Fig. 2. The flowchart of the proposed diagnosis model.