Back-propagation Artificial Neural Network for Early Diabetic Retinopathy Detection Based On A Priori Knowledge

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ABSTRACT. Purpose: We aim to develop a back-propagation artificial neural network (BP-ANN) improved by a priori knowledge and to compare its efficacy with other methods in early diabetic retinopathy (DR) detection.

Methods: A total of 240 fundus images, composed of 120 early-stage DR and 120 normal images, were obtained with the same 45° field of view camera, with the macula at the center, as a cohort for further training. All retinal images were processed, and a priori knowledge features such as blood vessel width and tortuosity were semi-automatically extracted. An improved BP-ANN with a priori knowledge was developed, and its efficacy was compared with that of the traditional BP network and SVM. Besides, k-fold cross validation method was conducted to demonstrate the efficiency of the proposed methods. We also developed a graphical user interface of our proposed BP-ANN to aid in DR screening.

Results: Our 10 randomization and 5-fold cross validation results of SVM, traditional BP, and improved BP were compared. The results indicated that the BP-ANN with a priori knowledge can achieve better detection results. Besides, our results were also comparable with other reported state-of-art algorithms. During the training stage, the epoch in the improved BP-ANN was less than that in the traditional BP group (109 vs 254), indicating that the time cost was shorter when using our improved BP-ANN. Furthermore, the accuracy and epoch of both the traditional BP and our improved BP network obtained better performances when the number of hidden neurons was 20.

Conclusions: A priori knowledge-based BP-ANN could be a promising measure for early DR detection.

CCS: Information system→Expert system

1. INTRODUCTION

The incidence of diabetes has increased globally each year [1-2], and one its complications is diabetic retinopathy (DR), which usually causes blindness at its late stage. The use of non-invasive optical fundus imaging techniques, such as the fundus camera, has allowed screening for early DR detection.
to be performed by experienced health care providers. However, the growing number of diabetes patients and relatively limited number of image analyzers have led to difficulty in meeting the demand for fundus image diagnosis. Thankfully, due to advances in machine learning techniques, computer-aided detection (CAD) of early DR provides a way to close this gap between supply and demand.

Artificial neural network (ANN) is a machine learning model simulating brain anatomic neuron connections, the effects of which have been validated in industry and scientific studies, such as data processing, pattern recognition, system control, and medical diagnosis [3-6]. However, ANN has some limits, including over-fitting and generalization faults, in its application. Previous work found improvements in ANN generalization when a priori knowledge was incorporated into ANN to model complex systems [7,8]. Therefore, we aimed to combine feature extraction from fundus images with a doctor’s a priori knowledge in the diagnosis of early diabetic retinal vascular changes and construct an early DR diagnostic BP-ANN model. We then compared the efficacy of our novel method with that of the traditional BP-ANN method and support vector machine (SVM).

2. MATERIALS AND METHODS

2.1 Dataset and Experiment Design
A total of 240 fundus images with the macula at the center were obtained by the same 45° field of view camera. These images were collected from 120 early-stage DR and 120 normal participants in a cohort for further training. The study protocol was conducted in accordance with the ethical guidelines of the 1995 Declaration of Helsinki, and this study was approved by the Ethics Committee of Nantong University. All image sizes were normalized to 565×584 pixels to ensure consistency for further width calculation tests. Our experimental method incorporated a priori knowledge into the feature extraction and network construction of the traditional BP-ANN process (Fig. 1).

![Fig. 1 The flow diagram of the experiment](image)

2.2 Retinal Image Processing and Feature Extraction
All fundus images were normalized for illumination, size, and color by different cameras during the imaging process. A robust fuzzy clustering algorithm based on texture features was used to automatically segment the retinal blood vessels [9] (Fig. 2).

In this study, a priori knowledge was defined as geometric features of blood vessels, such as width and tortuosity, after consulting experienced ophthalmologists about their diagnostic experience. For automatic labeling of major arteriole and venule trees, the optic disk (OD) was detected using the self-adaptive distance regularized level set evolution method proposed in our previous work [10]. After the OD was segmented, the OD centroid was automatically identified for further image processing. A self-adaptive round mask with its center at the centroid of the OD was utilized to obtain the initial seeds by subtracting the mask from the vessel centerline network. Once the seed points were identified, they were classified into venule and arteriole seed points.
Automatic tracing algorithms were then developed to annotate the whole retinal vessel skeleton network as arteriole and venule trees (Fig. 3). The obtained tracing results were then compared with those identified by ophthalmologists.

Next, the superior retinal temporal artery (SRTA), superior retinal temporal vein (SRTV), inferior retinal temporal artery (IRTA), and inferior retinal temporal vein (IRTV) were labeled and selected for further quantitative analysis. After vessel labeling, geometric features, such as the width [11] and tortuosity of retinal segments at each order, were extracted. Herein, a retinal vessel topological order framework was chosen for feature extraction: the first order segment was defined as the part where the retinal tree originates from the outline of the OD, then two daughter segments were marked as the second order, and the orders of offspring topological branches were added accordingly until the automatic tracing was completed [12]. In this manner, a total of 72 features of retinal vessel segments at each hierarchical order from the four major retinal vessels (IRTA, IRTV, SRTA, and SRTV) were extracted and prepared for further analysis. To compare the efficiency of our a priori knowledge-based features, the commonly-utilized computer vision extracted features, such as mean, variance, homogeneity, contrast, dissimilarity, entropy, angular second moment, and correlation features from gray-level co-occurrence matrix, were extracted from the same dataset for further classification.
2.3 Improved BP Neural Network Classifier and Performance Analysis
The framework of our BP-ANN was designed as follows (Fig. 4):
the hidden layer input $H_{in}(j)$ was defined as:
\[ H_{in}(j) = \sum_{i=1}^{M} \omega_{ij} x_i + a_j \]  
(1)
where $x_i$ was input features, $\omega_{ij}$ was the weights between the neurons from the input layer and hidden layer, and $a_j$ represents the threshold for hidden layer neurons.

For a traditional BP network, $\omega_{ij}$ is randomly assigned, but in this study, we regulated $\omega_{ij}$ to $\omega'_{ij}$ based on our previous regression modeling coefficients of the input features [13,14]. Its estimates are defined as follows:
\[ \beta = \arg \min_{\beta} \| y - \sum_{j=1}^{p} \beta_j x_j \| + \lambda \sum_{j=1}^{p} |\beta_j| \]  
(2)
in which $\lambda$ is a non-negative regularization parameter, $x$ is the width and tortuosity of retinal segments at each order, $Y$ is the average accuracy of two models, and the $\beta$s are the coefficients of the regression model.

The optimal number of neurons in the hidden layer was referenced as follows:
\[ h < -1 \]  
\[ h < \sqrt{(m + n)} + a \]  
(3) (4)
where $n$ was the number of input layer neurons, $h$ was the number of neurons in the hidden layer, $m$ was the number of neurons in the output layer, and $a$ was a constant between 0 and 10. In this study, $n$ was set as 72, $m$ was set as 2, and $h$ ranged from 11 to 20. The training function for BP-ANN was the moment gradient descent method [15]. The epoch of training, sensitivity, specificity, and accuracy were separately recorded for each test.

The results with the traditional feature extraction method based on computer vision were compared with the improved a priori knowledge-based BP-ANN. Additionally, the same features were used as input to the SVM classifier with radial basis function as kernel to compare its performance with our proposed BP classifier. Besides, k-fold cross validation method was conducted to demonstrate the efficiency of the proposed methods.

2.4 DR Detection Application Development
Here, to facilitate the application of our method to DR screening, a graphical user interface of the DR classifier based on our improved BP-ANN was designed and developed (Fig. 5).

The image processing algorithms, including fundus image importing, blood vessel segmenting, feature extracting, ANN training, and automatic classifying, were embedded. When a fundus image was imported, it was firstly validated by an ophthalmologist whether or not it showed DR. The
features such as blood vessel width and tortuosity were then extracted, saved, and further used as input values for BP-ANN training. Before clicking on the “Train” button, training parameters were manually configured for BP-ANN construction. The training process was kept iterative until the network performance achieved its best and the training confusion matrix was displayed to confirm the performance of the network. Subsequently, the trained network structure was stored for use in detecting the DR status of unclassified fundus images. When the “Auto Classify” button was clicked, the results of the classification would display.

Fig. 5 BP network construction

3. RESULTS
In this study, the SVM, traditional BP-ANN, and our improved BP-ANN were each utilized to detect the status of normal and DR fundus images. For k-fold cross validation, k was set as 5 in this experiment, and 10 random times of validation results were analyzed for 240 labeled original samples. Our 10 randomization and 5-fold cross validation results were seen in Table 1.

Table 1 K-fold cross validation results for SVM

| No. | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 |
|-----|----|----|----|----|----|----|----|----|----|----|
| Acc. (%) | 88.33 | 90.00 | 90.33 | 90.83 | 91.33 | 91.67 | 92.67 | 92.5 | 93.17 | 93.67 |

While for BP-ANN and a priori knowledge BP-ANN, the average accuracy of 10 randomization tests with different hidden neurons were listed (Table 2 and 3), indicating that the BP-ANN with a priori knowledge can achieve better detection results.

We found that the epoch decreased as the number of neurons in the hidden layer increased, and the epoch was remarkably lower in the improved BP group than in the traditional BP group (109 vs 254) (Fig. 6A), indicating that the time cost was shorter when using our improved BP-ANN. When the number of hidden neurons reached 20, the accuracy and epoch of both the traditional BP-ANN and our improved BP-ANN were enhanced, but the improved BP-ANN achieved a superior performance compared with the traditional BP-ANN (Fig. 6B).

Table 2 K-fold cross validation results for BP-ANN with different hidden neurons

| Hidden neurons | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  |
|----------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Mean Acc. (%)  | 88.85 | 90.77 | 92.31 | 93.85 | 93.46 | 94.23 | 94.23 | 96.38 | 97.31 | 96.15 |

Table 3 K-fold cross validation results for a priori knowledge based BP-ANN with different hidden neurons

| Hidden neurons | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  |
|----------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Mean Acc. (%)  | 92.38 | 92.62 | 93.69 | 93.77 | 93.85 | 96.38 | 96.31 | 97.31 | 97.77 | 98.46 |
Fig. 6 The comparison of epoch between traditional BP and BP with a priori knowledge (A: Epoch for different hidden neurons; B: accuracy for different hidden neurons)

The classifier utilized in this study was a modified ANN, which requires a training process that is usually regarded as a kind of supervised machine learning protocol. Different from this type of supervised classifier, Abràmoff et al. [16] used a non-supervised k-NN classifier for classification by extracting three features of microaneurysms (hemorrhages, exudates, and cotton wool spots) which obtained a sensitivity of 90% and a specificity of 47.7%. Likewise, Dupas et al. [17] also used a k-NN classifier for DR detection, and they achieved a higher specificity of 72.7% but a lower sensitivity of 83.9%. However, similar to our study, Shahin et al. [18] used a supervised ANN classifier for the automated classification of normal and abnormal retinal images by automatically detecting the blood vessels, hard exudate microaneurysms, entropy, and homogeneity. They obtained an average accuracy of over 92%, a sensitivity of over 88%, and a specificity of 100%, which were comparable to those obtained by our study. Furthermore, Acharya et al. [19] utilized SVM, which is another popular supervised classifier for DR classification, by extracting four features: retinal blood vessels, exudates, microaneurysms, and hemorrhages. They obtained a detection accuracy of 86%, and a sensitivity and specificity of 82% and 86%, respectively, in contrast to the accuracy, sensitivity, specificity of our study, which were 92.19%, 92.50%, and 91.67%, respectively. A detailed comparison between the above-mentioned studies and our protocol was provided in Table 4.

Table 4. Comparison of our study with other published studies

| Studies             | Features extracted | Methods | Dataset size | Performance measure |
|---------------------|--------------------|---------|--------------|---------------------|
| Abràmoff et al. [16]| MA, HEM, exudates, and CWS | k-NN    | 1670         | Sensitivity-90%, Specificity-47.7% |
| Dupas et al. [17]   | MA, HEM, and exudates | k-NN    | 761          | Sensitivity-83.9%, Specificity-72.7% |
| Shahin et al. [18]  | Blood vessels, hard exudates, MA, entropy, and homogeneity | ANN     | 340          | Accuracy-92%, Sensitivity-88%, Specificity-100% |
| Acharya et al. [19] | Blood vessels, exudates, MA, and HEM | SVM     | 331          | Accuracy-86%, Sensitivity-82%, Specificity-86% |
| Our method          | Blood vessels      | modified BP-ANN | 240          | Accuracy-95.01%, Sensitivity-95.08%, Specificity-95.73% |

MA: Microaneurysms; HEM: Hemorrhages; CWS: Cotton wool spots

4. DISCUSSION

DR detection is an important machine learning research topic for fundus image analysis [20-22]. In Table 2, we compared our results with those of other DR detection studies that applied different feature extraction and machine learning methods.

Here, we used the extracted features as input values for BP-ANN. Compared with the traditional feature extraction method that is based on machine vision, the method of combining feature extraction with a priori knowledge could better highlight the nature of a fundus image and improve the ANN classification result. The epoch decrease in our study was largely due to the fact that a priori knowledge-based weight initiation can optimize the further convergence calculation and lessen the time cost for optimal value searching in BP-ANN. This might prevent the neural network over-fitting phenomenon and improve both the network training speed and the efficiency of classification. Besides a priori knowledge input of features that we designed, other retinal image geometric features have
been developed for BP-ANN classification [23-26]. Furthermore, OCT images have recently been utilized to extract features from different intraretinal layers to diagnose glaucomatous eye and DR [27,28], and these features could be taken into account in our further studies. In this study, we modified ANN by incorporating our previous reported a priori knowledge [13] and gained an improved DR classification performance. Besides, there are many other forms of a priori knowledge that could be incorporated into a BP neural network classifier, such as improving the network structure [29], setting the activation function, setting the initial weight [30], and image preprocessing [31], the method described in this study mainly incorporated a priori knowledge into our BP neural network classifier by setting the initial weight and performing image preprocessing. However, it is common for a priori knowledge based BP-ANN classifier to have different performance when being applied into different fundus image datasets, which might limits the generalization of our algorithm in real clinical scenario. Additionally, the sample size is relatively small in this work. Our future studies will assimilate additional types of a priori knowledge into our model and access our method on more large size samples.

5. CONCLUSION
The proposed a priori knowledge-incorporated BP-ANN was able to detect early DR images better than the traditional BP-ANN and could be a promising measure for early DR detection.

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