ON THE USE OF KNOWLEDGE-BASE INFERENCE TO CLASSIFY EARLY STAGES OF EYE DISEASE

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Abstract: **Processing medical data requires the analysis of a large amount of information that must be assembled, evaluated, and prioritized.**

The overall objective of the research presented in this paper is to develop a framework that will make the activities of information retrieval, information classification and information analysis more efficient. The final result of this on-going effort will be an automated knowledge-base eye disease classification and diagnosis system that integrates image analysis, feature extraction, fuzzy-neural inference and data mining. By employing such techniques, one is able to compensate for noisy or incomplete information and learn about the underlying domain knowledge associated with the data. Human expertise can be captured and integrated as part of the knowledge base. In this paper, preliminary results are presented; a discussion of the use of fuzzy neural inference to select some of the classification parameters is also provided.

Keywords: **knowledge-based systems, classifiers, image analysis**

I. Introduction

Currently, detecting and successfully treating eye diseases depends on the ophthalmologist's ability to identify, classify, and verify retinal features from 35mm photographs obtained from a Fundus camera. The primary goal of the on-going project discussed in this paper is to reduce the time in diagnosing and treating eye diseases by creating a new image analysis system to fully automate the classification of diabetic retinopathy from digitized images. Retinal disorders pose a significant health threat; for example, it is estimated that 2.3 million Americans have glaucoma and over 10 million more are susceptible. Worldwide about 50 million people suffer from this disorder. Diabetic retinopathy, a complication associated with diabetes, has become a leading cause of blindness in the Western world. At Duke Eye Center, for example, it is estimated that approximately 50% of eye patients suffer from glaucoma, diabetes, or both.

When blood vessels in the retina leak fluid or bleed, they cause the retina to swell and form deposits (*exudates*). Unknown factors cause macular degeneration, the physical disturbance of the macula. Macular degeneration occurs with the formation of new blood vessels and exudates (*drusen*) from blood vessels in and under the macula. Macular holes, another form of macular degeneration, is characterized by tears or holes in the macula.

Examining photographs of the optic Fundus is the primary means of diagnosis of ophthalmic diseases by ophthalmologists. Using Fundus photographs (60 degrees, including the macula and the disk), an ophthalmologist focuses on identifying abnormal features on the retina, white spots in the macula, finding new blood vessel growth, determining the tortuosity of the normal present vessels, and then identifying any significant amount of ocular pathology. There are a number of diseases that can be evaluated by analyzing a Fundus photograph for diabetic retinopathy, vein occlusion, and epiretinal membrane. Automating the process of annotating and even analyzing these images offers the hope of computerized patient pre-screening, automatic tracking of disease progression, automatic defect detection, and decreased inter-observer variance in morphometric analyses of retinal features.

Fundus photographs are, by their nature, noisy and of poor-contrast [12]. This makes low-level image processing difficult. High-level interpretation of image features is impeded by the substantial degree of variation in the appearance of structural features across patients. A high degree of generalization is required to identify and segment features of the retina (e.g., blood vessels, the optic nerve and exudates) since they may appear very different in different patients due to differences in photographic equipment, photographer, condition of the eye, lighting conditions or the digitization process. Of these features, the most readily identifiable one is the network of blood vessels on the surface of the retina. Within these images, blood vessels are easily distinguishable to the human observer, despite the obvious differences in color and lighting between the two images.

II. Retinal Image Processing and Medical Data Mining

For the automated classification of eye diseases from optical images, researchers have used numerous methods. For example, Brigatti et. al. [4] use neural networks for detecting glaucoma. Further, the ambitious Structured Analysis of the Retina (STARE) project at the University of California at San Diego [5,7,9] is attempting to diagnose diseases from digitized Fundus photographs. They have produced filters that appear somewhat liberal in what they accept, requiring post-processing for re-classification. Also, their feature classifier is trained on expert labeled data, such as blood vessels, and bright and dark spots. After feature extraction and post-processing, the remaining features set is used to generate probabilities of the existence of human-readable symptoms. This is done using Bayesian belief networks.

III. The Knowledge-based Inference System: Work to Date and Preliminary Results

In our preliminary work to develop a knowledge-base classifier to detect eye disease, we made use of specific elements of robot vision, but modified to analyze 2D images of diseased retinas. The work primarily concentrated on tracing blood vessels, because finding evidence of new growth can indicate the onset of a disease. Similarly, the presence of exudates can also imply the onset of a disease.

In our demonstration of the principle, the major goal was to extract and show as many blood vessels as was possible using a thinning algorithm developed for the purpose, and to show where bifurcations occur in blood vessels occurred. Being guided by an ophthalmologist, we also knew that the fovea, the optic cup, and exudates had to be located within an image. Given these attributes, we needed to extract data, particularly with the exudates. This was done by developing an interactive user interface. The prototype system of Scoggins [13] provides an interactive GUI's that allows medical experts to annotate large distributed databases of medical images [6]. This figure shows an image and the interactive GUI. Behind is captured the selection of the "expert" and the data associated with the selection. This is the information we would use to extract "knowledge-based" information, and hence automate the process. Fig. 2 illustrates the overall concept of the knowledge-base inference system.

First, data from the Fundus camera is captured in a database. To date we have already constructed a retinal image database consisting of 116 images with 16 normal, 24 glaucomatous, 26 diabetic retinopathy, 28 macular degeneration, and 22 macular holes. These were scanned from 35mm slides of Fundus photography provided by the Duke University Eye Center.

Then, the image data is processed to obtain feature information. We have applied a *curl* topographic method [10] to retinal images, because it gives topographical information and geometrical relationships between objects in images to retinal images (see Fig. 3) Although this is preliminary work, the *curl* method shows promise in terms of speed and computational efficiency, compared to the conventional methods used to do the same task.

The research direction taken in this preliminary study is adopted from that discussed in [1]. This method makes use of the fact that the transect grey-level profile of blood vessels in the green plane of the color Fundus photograph appear roughly Gaussian. When blood vessels are subjected to this method they appear darker than their background because the Gaussian-like profile of the vessel is inverted. A promising way to locate blood vessels in an image is to convolve the image with a kernel whose pixel values are the ID Gaussian distribution function evaluated at the pixel's coordinates.

The kernel has two dimensions: the first dimension is the ID Gaussian function, and the second dimension is simply a repeated replication of the Gaussian function. In order for the filter response to be equal to zero in areas of constant greylevels, the filter is shifted by the mean of all pixel values in the kernel. In addition, the blood vessels may appear at any orientation in the image, therefore the kernel must be repeatedly convolved with the image at multiple orientations.

After convolving the green plane of the input image with the matched blood vessel filter at 12 orientations, the maximum response of the filter at each pixel location is recorded in the resulting image. Through applying this operation at a single block to a retinal image, we have shown that all edges respond to the filter.

Following this, we obtained results using this filtering method on a much larger scale. We noted that while the noise is lessened, the response to the blood vessels is significantly blurred. What we concluded was that a method was needed that get the benefits of both large and small scale analysis; the small scale provides detailed responses to small blood vessels, while the large scale is less sensitive to noise. If asked where are the blood vessels located, we concluded they would be located in areas of intense response to a filter of *all* scales.

After thresholding, a multi-scale filter is applied using a number of scales. The threshold is set to the mean filter response and is used to detect the pixels on the medial axis. This technique has been found to work well in practice, although it is somewhat contrived. More research is needed into knowledge-based thresholding algorithm for this work so as to ascertain the effect thresholding has on the final result. One approach that is being investigated is the use of an adaptive fuzzy neural inference system (ANFIS). The ANFIS can be trained off-line (supervised learning) using several images to learn about the resolution and threshold values and how such parameters as the SNR, the edge strength and edge density effect their selection. Then the ANFIS may applied on-line (unsupervised learning) to select these two parameters for other images. One can select the consequent and premise parameters in several ways [14]. The learning mechanisms require a forward pass and a backwards pass to find estimates of the premise and consequent parameter sets and one can modify the effects of old data using an exponential weighting as new data become available. This approach has been implemented successfully in [11] to select the threshold and resolution parameters in the edge detection problem.

After thresholding, the connected components are labeled and sorted by area. The largest connected component will typically contain the most information, i.e. the largest blood vessels. This was thinned and then overlaid on the original image. We then proceeded toward finding smaller vessels, at each step performing whatever analysis was necessary. After a predefined processing time to reach a conclusion has passed, the search is stopped. In this way, the best sources of information about the blood vessel network are searched for first, and the less informative (and possibly incorrect) sources are searched for last (see Fig. 4.

To classify the data, rule induction can alleviate the knowledge elicitation from a human expert [1]. Two families of automatic rule induction algorithms have been successful in inducing classification rules from examples; these are ID3 and AQ [3, 8, for example]. While the original ID3 was successfully applied to chess endgames, later derivatives (e.g., C4.5 and NewID) have been used for medical applications [2, 6]. Similarly, AQ was used first to classify soybean diseases, whereas later derivatives, like CN2 [3], have also been used in medical diagnosis [6]. We initially use these algorithms to classify diabetic retinopathy because the features extracted meet Bloomfield's criteria for using rule-induction in such an application [1].

Rule-based inductive learning is a technique that derives classification rules from a training set of examples that are the input to the system. The training set consists of a set of attributes and the desired outputs, known as classes. The attributes, paired with the particular class, represent the output expected by an ideal system. The system should give expected outputs on new inputs if a good, comprehensive training set is used. During the learning process the rules are continuously modified under strictly defined conditions to reduce the outputs between the actual outputs produced by the rules and the desired output [6]. An ANFIS may also be integrated in the rule induction process to compensate for uncertainties and noise. This work on developing the rule base for classification is continuing.

VI. Concluding Remarks

The goal of the project discussed here is to reduce the time to diagnose and treat a common eye disease, diabetic retinopathy. In this on-going project, we are creating new image analysis and data mining software algorithms and building a system to automatically detect the disease. High-resolution 2D digitized retinal images obtained from a Fundus camera are employed. We have already developed segmentation filters based on both image processing and topographical methods. Both methods extract blood vessels and blood vessel features. Currently, we are building the system, using the same images, from within which an ophthalmologist will select and label specific retinal features. The objectives are to automatically classify a retina condition based on this labeling and to evaluate the classifier efficiency for accurately detecting diabetic retinopathy.

Future research work includes an investigation into the temporal progression of the disease using images obtained from regular patient screening. Since our diagnostic analysis is based on 2D representations of 3D features, we will ensure through experimentation with geometric analysis that feature accuracy is not lost through the 3D to 2D translation. Further, we will explore the benefits of using 3D image analysis and sensory integration in diagnosing diabetic retinopathy, and extend the coordinate geometry concept to include 3D analysis.

Part of the on-going work is to determine the level of acceptability for thresholding. Since determining threshold will be based on shape descriptors, e.g. area or bounded rectangle size, experiments are being conducted to identify the most efficient shape descriptor for the task; the ANFIS is a promising approach.

An alternative to thresholding using shape descriptors would be to use statistical information from pixels, through counting the pixels of a connected component. To re-classify connection by this second method would require computing the mean and standard deviation of the colors of the pixels corresponding to that component (yielding a normal distribution with a 3x3 covariance matrix for an RGB image). This approach is also being investigated.

VII. References

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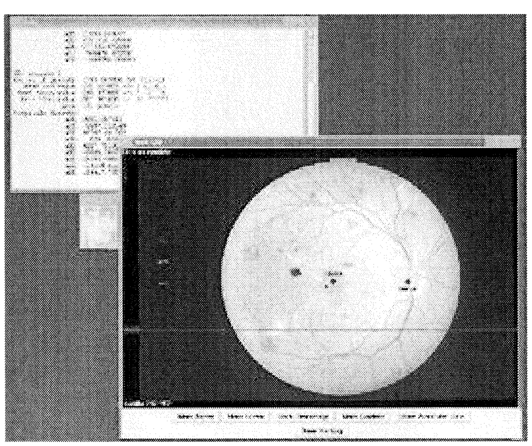

Fig. 1: The Image and Graphics User Interface

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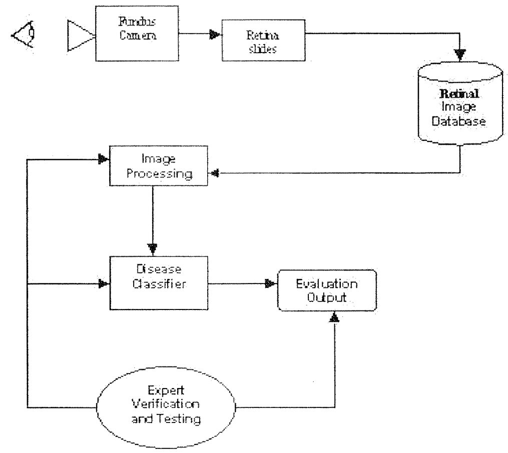

Fig. 2: Overall Diagram of the Inference System

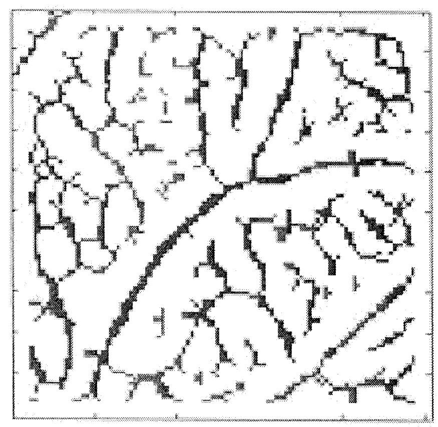

Fig. 3: Processed Image Using the *curl* Method

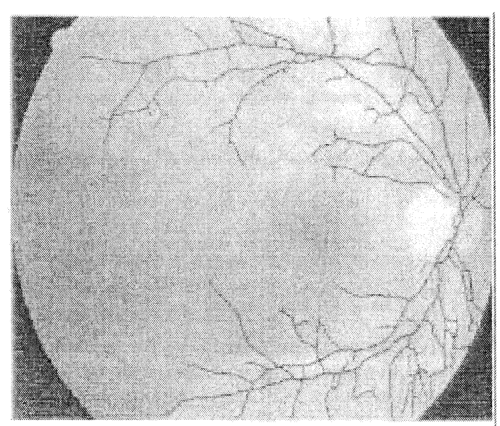

Figure 4: Vessel Analysis Result