MaculaTEST - Computer Aided Diagnosis System for Macular Diseases

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Abstract — Bordering on important domains – engineering, medicine and informatics, involving not only knowledge regarding the biosystems structure and functionality, but also knowledge and skills from technical and IT systems, the paper presents the results of some researches on biological human visual structures concerning the diagnosis of visual diseases, namely the macular ones. This is a highly important transdisciplinary topic; it combines aspects from biosystems (human visual system), image acquisition and processing (medical imagistic), artificial intelligence techniques (neural networks) and information management (databases). Starting from classical or digital retina images, using neural networks image recognition algorithms, the Computer Aided Diagnosis (CADx) system identifies macular diseases with high precision. Images are stored in databases together with patient personal details and treatments and diagnosis information. The software includes image processing modules, databases and neural networks that can be trained for recognizing images of new diseases. The Computer Aided Diagnosis reduces the doctor's level of incertitude regarding some diseases, improves the initial and evolutional identification precision of disease, allows to monitor the health status of the patient during new treatment methods, stores images in digital format and generates diagnosis databases that can be used in research, medical practice and specialized teaching.

Key-Words: — computer aided diagnosis, neural networks, image processing, ophthalmology, retina

1 Introduction

Macula is a sensitive area in the central part of retina, responsible for focusing central vision in the eye and controlling our ability to read, drive a car, recognize faces or colors and see objects in fine detail [1].

There are different eye conditions in which it can be damaged, often causing loss of central vision. Macular diseases, especially AMD (Age related Macular Degeneration) are an increasing problem worldwide, because they are irreversible, so it is very important that the process to be early identified and stopped. Macular degeneration is caused by the deterioration of the central portion of the retina, the inside back layer of the eye that records the images we see and sends them via the optic nerve from the eye to the brain.

Such problems may occur at a higher age, but in the last years it was observed at the second part of life (40 – 60 years old persons).

Current treatment options can delay progression and research continues into ways of reversing retinal damage.

2 Problem Formulation

The Computer Aided Diagnosis (CADx) system for macular diseases is a very useful tool for doctors and researchers due to the following advantages:

- A diagnosis recognized by the computer will reduce the doctor's level of incertitude.
- It offers speed, accuracy, consistence and a high confidence coefficient in results interpreting.
- It allows monitoring the health status of the patient during new treatment methods.
- The diagnosis can be stored in a digital format (image file for the retina and a record in a patient database).
- The image can be analyzed and processed on-line or off-line.
- The system generates a diagnosis database useful for researchers, for medical practice and for specialized teaching purposes.
- A database with patient personal and care information can be developed, having local or remote access.

- The long treatment costs, the supplementary tests and the number of surgical intervention are significantly reduced.
- The quality and accessibility of medical services are increased.

2.1 The structure of the CADx system

The CADx system has to analyze the image of the patient's macula and classify it, offering a response that contains four possible diagnosis, order by a level of certitude. Initially, the system was trained to recognize the normal macula and a certain set of diagnosis, but it can be also further trained to learn more.

The structure of the system is presented in Fig.1.

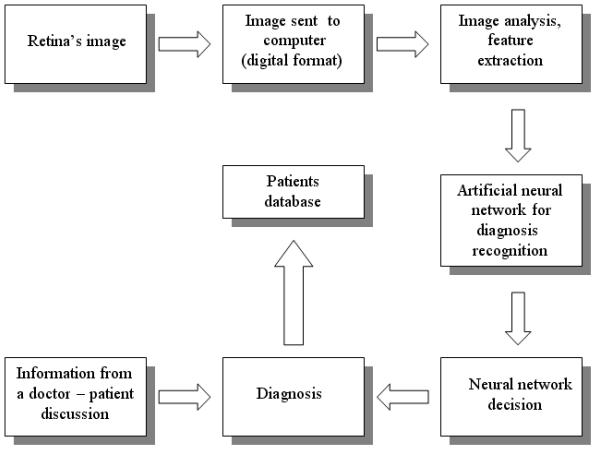

Fig.1. Structure of the Computer Aided Diagnosis System

3 Problem Solution

Retina's image can be acquired directly from a retinal investigation camera that offers a digital image or a classical one on color-reversal film. These last pictures have to be processed on a photo processing machine and then digitized using a scanner. The system is ready to work with any image of the retina, in digital format. The file format of the image used for recognition, in this software release, has to be a *jpg* one.

3.1 Image analysis and features extraction

Having the image on the computer screen, the doctor can analyze and process it, so that to emphasize the elements which identify the diagnosis.

For doing this, specialized software was designed. A Graphical User Interface (GUI) developed in Matlab by the authors, offers access to an image processing module. It contains two special menu options for image processing, namely *"One Image Analysis"* and *"Images Comparison"*.

Different options are available for user (Fig.2): opening a file, saving it in the same or other format, viewing the original image, the Red, Green and Blue components, transforming from RGB to Gray. Histograms for R, G and B components can be computed and plotted for a number of maximum 255 bins. User can zoom and pan the image. Options as *Vertical Zoom, Horizontal Zoom, Unconstrained Zoom, Vertical Pan, Horizontal Pan, Unconstrained Pan* and *Reset to Original View* are available. The image can be horizontal and vertical mirrored or rotated.

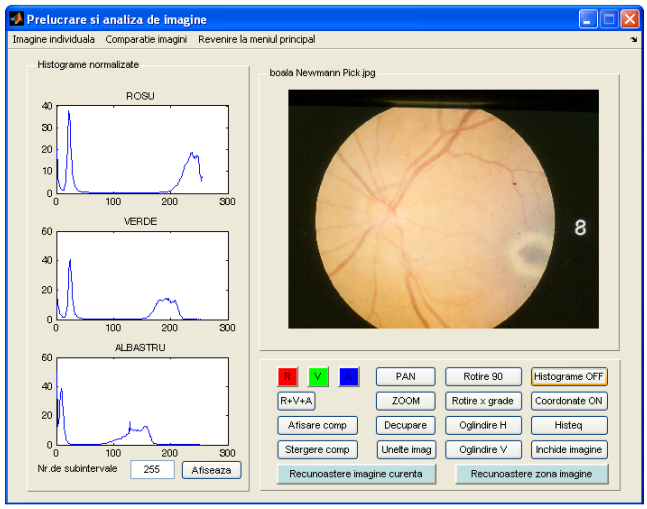

Fig.2 *"One image analysis"* menu option

The contrast can be enhanced using histogram equalization. Doctor can select and crop an interest part of image and save it.

All of these tools are used for emphasizing some image characteristics so that the diagnostic to be easy recognized.

The possibilities for viewing end editing an image are very useful for the user, especially for doctor, but they were very important in the design phase of the Computer Aided Diagnosis system. They gave the possibility to generate a database with images of diagnosis used for training an artificial neural network in the image recognition process. Another database was used for testing the network. We can see if a rotated image, or a mirror one can be correctly recognized, if it is better to use gray images or RGB images or contrast enhanced images for neural network inputs.

The other option from *"Image Analysis"* module is the *"Two Images Comparison"*.

Two image files can be opened and analyzed together, visual or using normalized histograms or values that represent features. User can zoom and pan images and also plotted histograms. Regarding features, a set of 2D moment invariants can be computed and also a set of six values that describe a region by quantifying its texture content [2]. The six

descriptors are based on statistical properties of the intensity histogram, namely on statistical moments and they are: *mean* – a measure of average intensity, *standard deviation* – a measure of average contrast, *smoothness* of the intensity in that region, *third moment* – a measure of skewness of a histogram, *uniformity* and *entropy*.

Special user functions were developed in Matlab for computing the values above [3]. The set of seven 2D moment invariants are computed using the equations below.

For a digital image having a *f(x,y)* intensity distribution, the two dimensional moment of order $p+q$ is defined as [2]

$$m_{pq} = \sum_x \sum_y x^p y^q f(x,y) \tag{1}$$

for $p, q = 0, 1, 2,...$ and x, y are the values of image coordinates.

These moments in general are not invariant to any distortions and therefore the corresponding central moments are defined as

$$\mu_{pq} = \sum_x \sum_y \left(x - \bar{x}\right)^p \left(y - \bar{y}\right)^q f(x,y) \tag{2}$$

where we denoted

$$\bar{x} = \frac{m_{10}}{m_{00}} \quad \text{and} \quad \bar{y} = \frac{m_{01}}{m_{00}} \tag{3}$$

The central moments are known to be invariant under translation. It can be demonstrated that the first four orders of central moments from equation (2) can be expressed in terms of the ordinary moments defined in equation (1).

$$\begin{aligned}
\mu_{00} &= m_{00} \\
\mu_{10} &= \mu_{01} = 0 \\
\mu_{11} &= m_{11} - \frac{m_{10} m_{01}}{m_{00}} \\
\mu_{20} &= m_{20} - \frac{m_{10}^2}{m_{00}} \\
\mu_{02} &= m_{02} - \frac{m_{01}^2}{m_{00}} \\
\mu_{12} &= m_{12} - m_{02}\bar{x} - 2m_{11}\bar{y} + 2m_{10}\bar{y}^2 \\
\mu_{21} &= m_{21} - m_{20}\bar{y} - 2m_{11}\bar{x} + 2m_{01}\bar{x}^2 \\
\mu_{03} &= m_{03} - 3m_{02}\bar{y} + 2m_{01}\bar{y}^2 \\
\mu_{30} &= m_{30} - 3m_{20}\bar{x} + 2m_{10}\bar{x}^2
\end{aligned} \tag{4}$$

Often it is desirable to normalize the moments with respect to size. This may be accomplished by using the area, μ_{00}.

The **normalized central moment of order (p + q)** is defined as

$$\eta_{pq} = \frac{\mu_{pq}}{\mu_{00}^{\gamma}} \quad \text{for} \quad p, q = 0, 1, 2, \ldots \tag{5}$$

and

$$\gamma = \frac{p+q}{2} + 1 \quad \text{for} \quad p + q = 2, 3, \ldots \tag{6}$$

From above equations, a set of seven **2D moment invariants**, insensitive to translation, change, scale, mirroring and rotation can be derived:

$$\begin{aligned}
\phi_1 &= \eta_{20} + \eta_{02} \\
\phi_2 &= (\eta_{20} - \eta_{02})^2 + 4\eta_{11}^2 \\
\phi_3 &= (\eta_{30} - 3\eta_{12})^2 + (3\eta_{21} - \eta_{03})^2 \\
\phi_4 &= (\eta_{30} + \eta_{12})^2 + (\eta_{21} + \eta_{03})^2 \\
\phi_5 &= (\eta_{30} - 3\eta_{12})(\eta_{30} + \eta_{12}) \cdot \\
&\quad \cdot \left[(\eta_{30} + \eta_{12})^2 - 3(\eta_{21} + \eta_{03})^2\right] + \\
&\quad + (3\eta_{21} - \eta_{03})(\eta_{21} + \eta_{03}) \cdot \\
&\quad \cdot \left[3(\eta_{30} + \eta_{12})^2 - (\eta_{21} + \eta_{03})^2\right] \\
\phi_6 &= (\eta_{20} - \eta_{02})\left[(\eta_{30} + \eta_{12})^2 - (\eta_{21} + \eta_{03})^2\right] + \\
&\quad + 4\eta_{11}(\eta_{30} + \eta_{12})(\eta_{21} + \eta_{03}) \\
\phi_7 &= (3\eta_{21} - \eta_{03})(\eta_{30} + \eta_{12}) \cdot \\
&\quad \cdot \left[(\eta_{30} + \eta_{12})^2 - 3(\eta_{21} + \eta_{03})^2\right] + \\
&\quad + (3\eta_{12} - \eta_{30})(\eta_{21} + \eta_{03}) \cdot \\
&\quad \cdot \left[3(\eta_{30} + \eta_{12})^2 - (\eta_{21} + \eta_{03})^2\right]
\end{aligned} \tag{7}$$

The other six values representing image's features are also computed with the GUI [4]. An important approach for describing a region is to quantify its texture content. A frequently used method for texture analysis is based on statistical properties of the intensity histogram.

Let us consider z_i a discrete random variable that corresponds to the intensity levels of an image and let us denote $p(z_i)$ the corresponding normalized histogram, with $i = 0, 1, 2, \ldots, L-1$ and L – the number of possible intensity values.

One of the principal approaches for describing the shape of a histogram is via its ***central moments*** (also called ***moments about the mean***) [2], which is defined as

$$\mu_n = \sum_{i=0}^{L-1} (z_i - m)^n p(z_i) \tag{8}$$

where n is the moment order and m is the ***mean***:

$$m = \sum_{i=0}^{L-1} z_i p(z_i) \quad (9)$$

The ***mean*** *(m)*, a measure of average intensity, is the **first image feature** in a vector of such values. Due to the fact that histogram is assumed to be normalized, the sum of its all components is 1.

The second moment is called the ***variance***

$$\mu_2 = \sum_{i=0}^{L-1} (z_i - m)^2 p(z_i) \quad (10)$$

Standard deviation *(σ)*, a measure of average contrast, is used also as an image feature.

$$\sigma = \sqrt{\mu_2(z)} = \sqrt{\sigma^2} \quad (11)$$

The third image feature is the ***smoothness*** *(R)*. It measures the relative smoothness of the intensity in a region. In practice, the variance is normalized to the range [0, 1] by dividing it by $(L-1)^2$.

$$R = 1 - 1/\left(1 + \sigma^2\right) \quad (12)$$

The fourth image feature is the ***third order moment*** *(μ_3)*. It measures the skewness of a histogram. If the histogram is symmetric than $\mu_3 = 0$, if it is skewed to the right of the mean than $\mu_3 > 0$, and if it is skewed to the left of the mean than $\mu_3 < 0$. Values of this measure are brought into a range of values comparable to the other five measures by dividing μ_3 by $(L-1)^2$.

$$\mu_3 = \sum_{i=0}^{L-1} (z_i - m)^3 p(z_i) \quad (13)$$

The fifth image feature is ***uniformity*** *(U)*. It is maximum when all the gray levels are equal (maximally uniform) and decreases from there.

$$U = \sum_{i=0}^{L-1} p^2(z_i) \quad (14)$$

The last value in our vector of features is ***entropy*** *(e)*, a measure of randomness.

$$e = \sum_{i=0}^{L-1} p(z_i) \log_2 p(z_i) \quad (15)$$

All of these values are computed in Matlab with a user defined function. In the image processing module of the Graphical User Interface developed for diagnostic recognition, the option *"Two Images Comparison"* allows to compute and to compare them. The computed values are scaled by the vector [1 1 10000 10000 10000 1].

Using the GUI it was made a comparison between images using R, G, B components, gray image and the corresponding multidimensional one [4]. It was observed that differences between 2D moment invariants values are not significant, excepting the multidimensional image. It is normal because the multidimensional image is obtained by concatenating the 3 two dimensional arrays (of RGB image) in a 2D array. The rotated multidimensional image is made by 3 two dimensional images rotated before, not by rotating directly the entire multidimensional image. So it is better to use the RGB image or the gray one when extracting features, instead of multidimensional images.

3.2 Artificial neural network for image recognition

An image is made by pixels. Depending on the image format and knowing that each pixel has associated a number of values, the total number of values can be a huge one. It is impossible to associate a neuron for each value in the neural network structure. It is almost impossible to find two identical retina images at the pixel level. That is why for the image recognition with artificial neural networks we have to use at inputs a vector of values extracted from image features.

A multilayer perceptron network was used for diagnosis recognition [5]. System administrator can design, train, test and optimize it for improving the system performance. All these steps are executed using another GUI designed also in Matlab (fig.3).

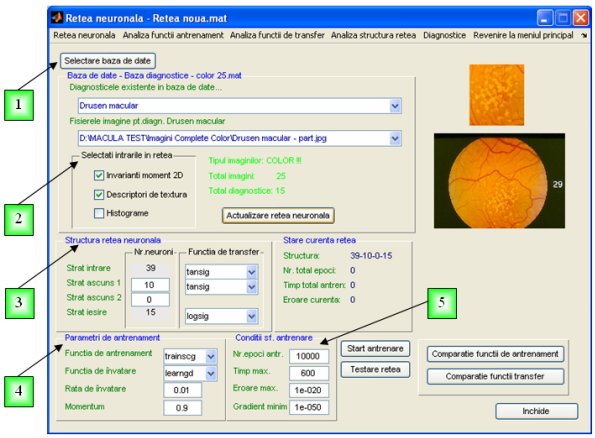

Fig.3 Main window for neural network designing, training, testing and optimizing

For doing this, a training set can be generated form a database that contains information about macular diseases images [6]. The number of values representing features will determine the number of inputs in the neural network and it can be selected

from the main window (fig.3). Using RGB images and seven 2D moment invariants plus six texture descriptors, the number of inputs was 39. The number of diagnostics from the database will determine the number of outputs. The structure of the network (hidden layers) can be modified and also the training parameters. Learning is a supervised one. Best results were obtained with a feedforward multilayer perceptron network, trained with a scaled conjugate gradient backpropagation algorithm [7]. After 10.000 training epochs, all 25 images from a database with 15 diagnostics, were classified [6]. Then, more images were appended to the database and the training process continued. After the successful training process, the network was tested with a set of images some of them representing similar diagnostics or normal macula status. Finally, the specificity obtained was 90,91%.

The neural network can be used to recognize images inside the image processing module and inside the diagnosis database module (fig.4).

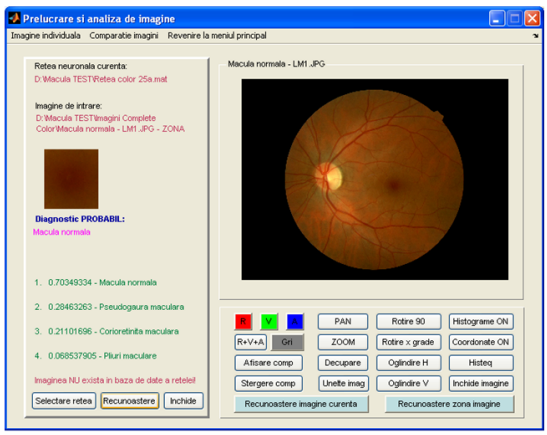

Fig. 4. Image recognition using neural networks, from the image processing module

A list of 4 possible diagnostics, ordered by a certitude coefficient, is displayed.

3.3 PATIENTS' DATABASE

The doctor receives the decision from the Computer Aided Diagnosis system and after a discussion with the patient about pathological antecedents, other diseases, different medical treatments, will establish the final diagnostic. This can be stored in the patients' database.

Patient's record contains the following information: name of the patient, patient's ID which is used for uniquely identify of the same person, if it is male or female, patient age, working domain, the date when the record was added or diagnosis date, name and full path of the image file, what the diagnosis is about, a history of patient health status or past diagnosis, the treatment recommended for him and some special remarks [8].

Because of the size of the database, we considered that it is more useful to store only the path and the name of the retina image file. All the image files can be stored in a separate folder on the hard-disk for example. It is an advantage because these images can be viewed, analyzed or transferred independently of the database itself, instead of embedding them in the database. From the patients' database, a diagnostics database can be extracted.

Data have additional value beyond supporting the care of specific patients. For example, subsets of individual patient care data can be used for research purposes, quality assurance purposes, developing and assessing patient care treatment paths (planned sequences of medical services to be implemented after the diagnoses and treatment choices have been made), assessments of treatment strategies across a range of choices, and assessments of medical technologies in use.

The software is supplied in an executable format, so it can be installed on every computer without having to install Matlab.

4 Conclusion

Entire software for this Computer Aided Diagnosis system was developed by the authors. The doctor will use the program in a so called *user* mode, that does not contain all the facilities above, and that can be set from the *Settings* menu option. The system is an open one, allowing to create new databases with diagnosis images, new neural networks, to train and optimize them, by an administrator which will have access to all the facilities (*administrator* mode), so that to have the possibility to recognize new diagnosis and to continue the training process for improving system performance.

The graphical interface is a user friendly one.

Starting from classical or digital retina images, using neural networks image recognition algorithms, the Computer Aided Diagnosis (CADx) system identifies macular diseases with high precision. Images are stored in databases together with patient personal details and treatments and diagnosis information. The software includes image processing modules, databases and neural networks that can be trained for recognizing images of new diseases. The Computer Aided Diagnosis reduces the doctor's level of incertitude regarding some diseases, improves the initial and evolutional identification precision of disease, allows to monitor the health status of the patient during new treatment methods, stores images in digital format and generates diagnosis databases that can be used in research, medical practice and specialized teaching.

New development directions for the system will focus on:

- Embedding the system so that to be implemented in a retinal digital investigation camera
- On-line retina's image analysis on the computer.
- Integration in a database server for different types of diagnostics, with remote access for researchers, doctors, teachers and students.
- Adapting the system for using it to recognize images from other domains (industrial for example).
- Improving the system by adding new image features that can be used as inputs in the neural network.
- The possibility to compare more than two images, for better observing the evolution of a disease, side by side or superposed, using transparency

References:

[1] www.macular.org – American Macular Degeneration Foundation.

[2] Gonzales R., Woods R., Eddins S, *Digital Image processing using Matlab*, Pearson Prentice Hall, 2004.

[3] Luculescu, M., Lache, S., Barbu, D., Barbu, I., Feature Extraction Methods Used for Images of Macular Diseases – Part I, *The 1st International Conference on Computational Mechanics and Virtual Engineering – COMEC 2005*, Braşov, Vol. II, 2005, pp. 48-54.

[4] Luculescu, M., Lache, S., Barbu, D., Barbu, I., Feature Extraction Methods Used for Images of Macular Diseases – Part I, *The 1st International Conference on Computational Mechanics and Virtual Engineering – COMEC 2005*, Braşov, Vol. II, 2005, pp. 55-60.

[5] Luculescu, M., Macular Diseases Recognition Using Neural Networks, *The First National Conference of Optometry and Medical Engineering – COPTOMIM 2006*, Braşov, 2006, pp. 155-158.

[6] Luculescu M, *Researches on Biological Human Visual Structures Concerning the Diagnosis of Macular Diseases*, PhD Thesis, 2007.

[7] Moller, M.F., A Scaled Conjugate Gradient Algorithm for Fast Supervised Learning, *Neural Networks,* Vol. 6, 1993, pp. 525-533.

[8] Luculescu, M., Enache C., Patients' Management Software For Ophthalmologic Office, *The First National Conference of Optometry and Medical Engineering – COPTOMIM 2006*, Braşov, 2006, pp. 159-162