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Classification of Prostate Cell Nuclei using Artificial Neural Network Methods

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***Abstract*—**The purpose of this paper is to assess the value of neural networks for classification of cancer and noncancer prostate cells. Gauss Markov Random Fields, Fourier entropy and wavelet average deviation features are calculated from 80 noncancer and 80 cancer prostate cell nuclei. For classification, artificial neural network techniques which are multilayer perceptron, radial basis function and learning vector quantization are used. Two methods are utilized for multilayer perceptron. First method has single hidden layer and between 3-15 nodes, second method has two hidden layer and each layer has between 3-15 nodes. Overall classification rate of 86.88% is achieved.

***Keywords*—**Artificial neural networks, texture classification, cancer diagnosis.

I. Introduction

CANCER is one of the biggest problems of the human beings and in many developed countries, prostate cancer is one of the commonly diagnosed cancer in men. Risk factor of the prostate cancer depends on age, genetic background, and ethnical character.

Diagnosis of prostate cancer requires the tissue and cell specimens. These specimens (as shown in Fig.1) are screened and analyzed by a pathologist using a microscope. Optimum medical treatment is decided according to this information gathered by the pathologist. In some cases, correct diagnosis is very hard and there can be 30-40% difference between pathologists' decisions [1]. Dramatic results about wrong diagnosis of cancer cases from biopsy slides can be found in [2].

Prostate cancer is evaluated using to staging systems: the Jewett-Whitmore system and the TNM (tumor, node, metastases) system. In the Jewett-Whitmore system, prostate cancer is classified according to anatomical view and spread. A and B are early stages. In these stages there are few cancerous cells and they are in the prostate tissue. In the later stages (C and D) cancer invades most of the prostate and spreads to other organs/tissues. In TNM system, T refers to the size of the primary tumor, N will describe the extent of lymph node involvement, and M refers to the presence or absence of metastases.

Artificial neural networks are commonly used for the diagnosis of the prostate cancer. In these studies, various types of data are used, such as prostate specific antigen (PSA) levels [3], clinical and biochemical criteria [4], ultrasonic echo signals with PSA [5]. Neural networks are utilized in this kind of biomedical applications because of their ability to perform more accurately than other classification techniques. Basic advantages of the neural network method over traditional classifiers are; easy adaptation to different types of data and use of its complex configuration to find the best nonlinear function between the input and the output data.

II. Data Collection

A. Image Acquisition

The specimen images are x100 magnified by the Leica microscope. An oil immersion objective was used. The analog image signal was acquired with a color camera and with a s-video connection the signal was transmitted to the computer. The images are digitalized in 768x576 pixel 24bit/pixel format and saved.

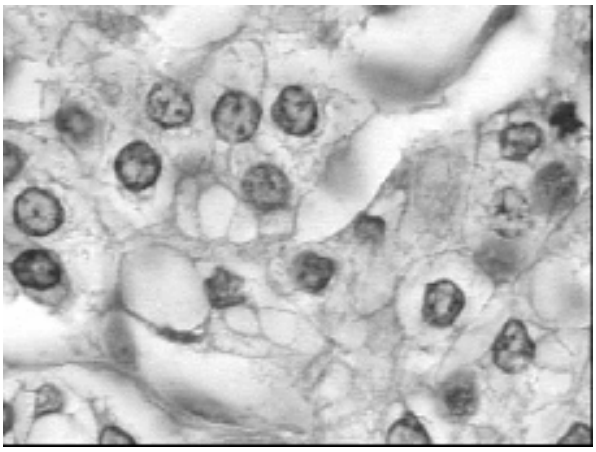

Fig. 1 Prostate tissue containing cancerous cell nuclei

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B. Histology

Microscopic slices are the radical prostatectomy materials belonging to the patients who had a surgical operation because of prostate cancer. The radical prostatectomy materials are fixed in 10% formalin for 24-48 h. to preserve the biologic structure. Routine tissue inspection was applied to the entire structure. Paraffin blocks prepared from the tissue cut into 5-μm thick slices and stained with heamatoxylin and eosin.

III. Feature Extraction

Image texture of the prostate cell nuclei are mathematically modeled using three different methods:

- Gauss-Markov random field model (GMRF) [6]-[7].
- Fourier transform based relative entropy [8].
- Stationary wavelets [9].

GMRF model parameters are estimated using maximum likelihood method. Neighborhood systems between 1 and 9 are used for the extraction of feature set. Sample correlation function on the lattice, defined as the lossless feature set [6]. 5x5, 7x7, and 9x9 lattices are used on the image blocks. In relative entropy method [8], the set of relative entropy parameters of the normalized energy spectrum is calculated from discrete Fourier transform of the image. Nucleus images of prostate cells are mathematically modeled by stationary wavelet transform [9]. Daubechies, Coiflet, biorthogonal, and symmetric spline wavelets [10] with different orders are used for the transforms. Feature vectors are calculated from the energy, entropy, and mean deviation representations of each channel output.

A 28 element feature vector is calculated for each of the nucleus image. The feature vector consists of 12 elements from GMRF, 7 from Fourier entropy, and 9 from wavelet transform. Statistically significant ($p<0.001$) features are selected using t-test. After all, sequential forward selection method is used to select best features and to reduce the dimension of the feature vector. The resultant feature vector has 3 elements, one from each model.

IV. Classifiers

The aim of the classifier is to distinguish (label) the normal and cancerous prostate cell nuclei. Images are classified using the following classifiers.

A. Multi layer perceptron (MLP)

The MLP is a feedforward network which is able to partition the pattern space using nonlinear boundaries for classification problems [11]-[13]. In our work, two MLP models are used. In the first model (MLP1) there is only one hidden layer, and in the second (MLP2) there are two hidden layers in the network. For both of these layers, the number of nodes is changed from 3 to15 to calculate the performance. The network's hidden nodes have sigmoid activation function, and the outputs have linear activation function.

TABLE I
Classifier Performances

	Classifier			
	MLP2	**MLP1**	**RBF**	**LVQ**
Sensitivity (%)	88.75	88.75	85.00	82.50
Specificity (%)	85.00	78.75	77.50	77.50
Overall (%)	86.88	83.73	81.25	80.00

B. Radial Basis Function (RBF) network.

The RBF is special kind of feedforward network which has a high dimensional hidden layer with Gaussian basis (kernels) [11]-[13]. Output nodes form a linear combination of the basis functions computed by the hidden layer nodes. The basis functions are formed (learned) from the training samples. These basis functions produce a localized response to input stimulus. In this work, different multivariate Gaussian width (spread) parameter is used to train and test the network.

C. Learning vector quantization (LVQ) network

Learning Vector Quantization (LVQ) is a classifier based on Kohonen's work [14]. This classifier approximates the Bayes classifier regardless of the underlying distribution of parameter vectors. To accomplish this, input feature vectors are quantized (mapped) to smaller number of reference vectors using nearest neighbor rule in the training stage. In our study, LVQ network is utilized with 3 to 15 nodes in the hidden layer.

V. Results

In this work, neural networks which have the highest performance for analysis and classification of prostate cells have been investigated to aid for diagnosis to the pathologist. Performance evaluation is based on 4 criteria:

- Sensitivity
- Specificity
- Overall performance
- Receiver operating characteristic (ROC) curve

Sensitivity is the correct classification rate of cancerous cells, specificity is the correct classification rate of normal cells, and overall performance is the correct classification rate of both normal and cancerous cells. Leave-one-out method is used for calculation of sensitivity, specificity, overall performance values, and ROC curves of the neural network classifiers. In leave-one-out method, total group of cases is divided into a subgroup of n-1 training cases, and this subgroup is used for training of the neural network. The test group (which contains the leaved case) is used to test the classifier. The procedure is repeated for each case in the group to calculate the performance criteria values. Calculated performance values of the classifiers are summarized in Table I.

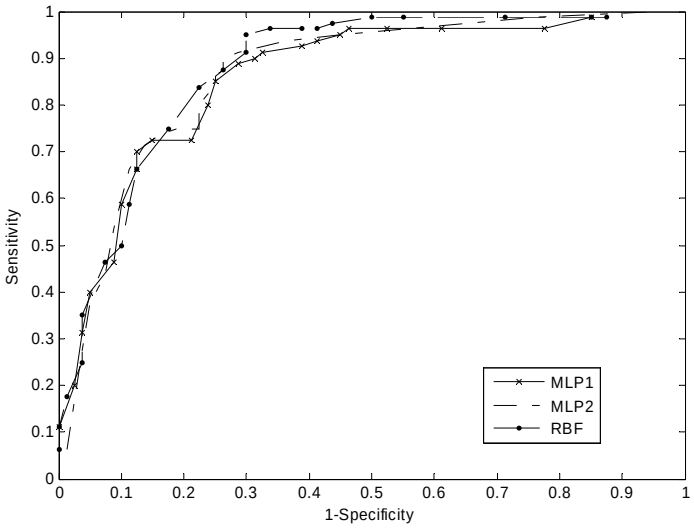

Fig. 2 ROC curves of classifiers

Best performance values are calculated with 11, 11-3, and 3 neurons in the hidden layer(s) for MLP, MLP2, and LVQ respectively. ROC curves for the neural network classifiers are given in Fig. 2. Area under the ROC curve is an important criterion about classifier performance. Best area under curve value is 0.80422 for MLP2. Area under curve values for MLP1 and RBF are 0.71062, and 0.75352 respectively.

VI. Conclusion

In this work, performance of neural network based pattern recognition methods are demonstrated for prostate cell nuclei classification. Future work will focus on real time classification application in a pathology laboratory. Additional methods and data will be used to increase the classification performance. A high performance, accurate and real time diagnosis system will greatly aid to the pathologist and to the patients.

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