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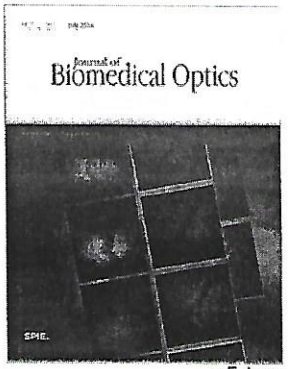

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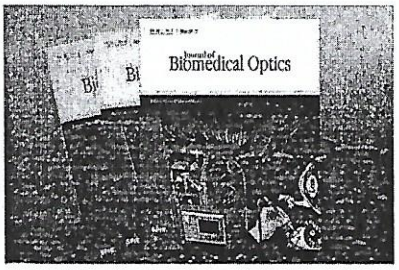

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Spectral and Statistical Parameters in Fuzzy Neural Expert Machine for Colorectal Adenomas and Adenocarcinoma Discrimination

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Abstract
This paper presents a novel method which automatically detects differences in biopsy images of the colorectal polyps, extracts the required histopathology information through Fourier and statistical images analysis of the microscopic images and then classifies the cells into normal adenomas and malignant adenocarcinoma. The images are captured by a CCD camera from a laboratory microscope slide and store in computer using the .TIF format. The new system is implemented by fuzzifying image histopathological data as shape and texture descriptors calculated from the spectral analysis and greyscale statistical co-occurrence matrix analysis of the microscopic cell images. These features are then fed into a fuzzy neural network expert classifier to differentiate the images. The novel system has been evaluated using 116 cancers and 88 normal colon polyp images collected from 44 normal patients and 58 cancer patients at random resulted in 96.435% classification accuracy. The breakthrough is that the algorithm is independent of the feature extraction procedure adopted, takes into consideration the gross and micro examination conducted by the pathologist and overcomes the sharpness of class characteristics associated with other classifiers algorithms.

BRIEF BIOGRAPHY
I received my B.Eng. in Electrical Engineering in 1996 from the University of Nigeria and my MSc in Electrical and Electronic Engineering from the University of Lagos, Nigeria in 2001 and afterwards I was employed by the same university as a lecturer.
In 2002 I was granted a three year study leave to pursue my PhD research in the School of Electrical, Electronic and Computer Engineering, University of Newcastle upon Tyne, United Kingdom, under the University's International Student Scholarship and the Department's Studentship schemes. I work in the Multimedia and Computer Vision laboratory under the Communication and Signal Processing Research group and my research interests include Neural Network, Fuzzy Logic, Medical imaging and Signal/Image Processing. I am a member of IEE and IEEE with the specialized groups of The IEEE Signal/Image Processing, Neural Network and Communications Societies.

1 Description of Purpose
Polyps are benign or malignant neoplasm derived from glandular epithelium. If found in the colon is called colon polyps [1].There are principally two types of polyps. These are the Hyperplastic (normal adenomas) and Adenocarcinoma polyps. Adenomas are precursor to all colorectal cancer (Adenocarcinoma). This is because their rate transformation to malignancy is usually very high. A biopsy is the only way to differentiate between Hyperplastic and Carcinoma polyps. This is done by a pathologist through a histopathological analysis of colon cell image slide referred to as the gross and micro examinations. The morphology and morphometric quantities measured and recorded by the pathologist for diagnosis include size, shape, texture and location and spread. But unlike many other cancer cells, the size of the tumor is not a major factor in determining the outcome of diagnosis and there is also no tumor marker that solely distinguishes colon tumor [2], [4]. Pathologists, daily, screen large numbers of slides containing cancerous cells manually, which are similar in shape, size or cells structure. This procedure becomes arduous, difficult and can affect the Pathologist's decision. It is of interest in this research to implement a routine which can automatically decide what kind of cells that a microscopic slide of the colon specimen contains by just looking at the texture through the modern advances in image processing and classifier algorithm. This routine could, among others be helpful tool in medical diagnosis of colorectal cancer.
Cancer of the large bowel is among the commonest of malignant tumours (third in the UK after lung and breast cancer) and represents the second largest cause of death from cancer in the western world. In UK over 30,000 people develop colorectal cancer each year [2]. The American Cancer society reported that about 105,500 people will have colorectal cancer in 2004 with about 57100 resulting to death in America [3]. This disease is uncommon in Asia, Africa and South America suggesting a possible dietary aetiology. High intake of animal fat increases the risk of colon cancer possibly explaining the high incidence of colorectal carcinoma (30-60 per 100000) in USA, Western Europe and Australia [2] [4].
Several classifier algorithms have been invented and tested. These include the traditional classifiers which on the average achieved 85% accuracy. [5] [6] [7] [8]. Recent research result shows that it is possible to classify tissue samples represented as digital grey images as either cancerous or normal with success rate of about 90%. Esgiar et al [9] [10] and Chen et al [11] proposed the fractal dimension algorithm for detection and classification of cancerous colonic mucosa. Fractal analysis was compared with traditional texture analysis such as entropy and correlation with improve in sensitivity and specificity but there was no great deal to the discrimination already achieved by the traditional methods. However, this result even though is good, but not good enough for an automated system working in real life situation because of its implications in case of error and worst error case is for a cancerous cell to be classified as normal. The importance of this research is therefore to investigate the possibility of classifying normal and malignant (cancerous) colon cells (tissues) using the novel Fuzzy Neural

Expert Machine (FNEM) which will effectively eliminate overlaps among the classes by clustering the feature descriptor values of the colon images as derived from co-occurrence matrix and spectral analyses. From the Fourier spectral extraction the parameters measured include spectral entropy (h), energy (e) and inertia (I) while from co occurrence matrix we calculated the following features, statistical contrast (CON), entropy (ENT), and moment (ASM) and correlation (COR).

2 Method

After tissue samples were collected through biopsy and prepared in the pathology and histology laboratories [28], slides were digitally captured through the process of image acquisition. The images were segmented to isolate and detect gland objects through morphological processes [12-23]. The images were sampled to makeup for the tissue distribution on the image, and digitized in 8 bits format with grey level ranging from 0̂ to 255in 512x512 size formats and stored in personal computer. All images are then divided into small images of 256x256 formats, all in a pre-processing operation. Then the images were filtered through various filtering and segmentation algorithms [28-30], all data sets having been turned into binary image format ready for further analysis. The experimental setup is shown in fig.1. Fig.2a is the block diagram of the FNEM classifier while the network layering is shown in fig.2b. The images were then normalized. Fig. 3a and fig.3b show samples cancer cell image and normal cell image. After all these, the Fourier power spectral and statistical analyses were performed on the captured slide images. The greyscale features were obtained by creating a co-occurrence matrix of the normalized images. The distance between pixels was set equal to one. The best feature values were obtained at angles, 0, 45, 90 and 135 degrees. We calculated the Fourier based features by integrating over circle segments with centre angles of 0, 45, 90, 135, 270 and 360 degrees using four different radii. Having obtained good features which give high degree of discrimination between different objects and give roughly the same object, we then designed a fuzzy neural network to assign the objects into defined groups described below.

This method employs Fuzzy-Neural network combined with clustering algorithm to classify cancerous colon cells.

Assuming a training set for cluster $\bar{w}_{id}$, $\left(\bar{X}_j, \bar{T}_j\right)$ where $1 \le j \ge k$ and $\bar{X}_j = (\bar{x}_{ji}, ..., \bar{x}_{jm}) \in [0,1]$ and the actual output is $Y_j = (\bar{y}_{j1}, ... y_{jn})$, $\bar{T}_j$ is the target output, the learning rule adjust it weights as

$$w_{id}(t+1) = w_{id}(t) + \alpha_{id}\left(X - \eta \Delta w_{id}(t+1)\right) \tag{1}$$

where $1 \le i \le$ 1 = 1,2,..and η is a number representing learning rate and α_{id} is a non-negative mixing factor. From (1) the fuzzified delta algorithm of the back propagation neural model is derived:

$$\bar{w}_i(l+1) = w_i(\bar{l}) + \eta\left[\sum_{j=1}^{k}\left(\bar{Y}_j - \bar{T}_j\right)\left(\bar{Y}_j\right)\left(1-\bar{Y}_j\right)\bar{X}_{ji}(l+i)\right] \tag{2}$$

To get real output is derived from (2) defuzzification.

The output from the defuzzification with respect to the class c_i is obtained as:

$$y^j = \frac{\sum_{j=1}^{n} y_i^j * \alpha_j(x)}{\sum_{j=1}^{n} \alpha_j(x)} = p_2 * \sum y_i^j * \alpha_j(x) * K_g\left(\frac{x - m_j}{h}\right) \tag{3}$$

The factor p_2 depends on x which in turn depends on the feature extraction method adopted.

A decision is obtained by choosing the class label for which equation (3) is the largest. This is an equivalent approximation of the probabilistic classifier that is asymptotically optimal in the Bayesian case. The neural networks are used to tune the fuzzy membership function involved in the decision making [20-27]. It is a simple mapping $\Im$ such that each object X in a feature space $(x_1, ..., x_n)$ is associated with one class c_i from the set $C = \{c_1, ..., c_n\}$ in our case $n = 2$, with a set of labelled training data $m_j = [m_{1j}, ...m_{nj}]^T \in \Re^n$, $\Im : \Re^n \to C$. If we denote $d_i \in \{1,2,...,n\}$ as the index of the class label among $\{c_1, ..., c_c\}$ associated with m_j and a centroidal defuzzifier, then the non linear mapping becomes $f : X \to Y$,

The FuNN training Algorithm is set below. Initialize the fuzzified weights, $w_i \in [0,1]$

1. Present the fuzzified input, $x_1, ..., x_n \in [0,1]$ and the desired output

2. Calculate the Actual outputs; using the logistic activation function,
3. Adapt weights $\bar{w}_i(t+1) = \bar{w}_i(t) + \eta[\Delta \bar{w}_i(t+1)]$
4. The weights is adjusted as, as in (1)
5. Defuzzify the output as in (3)
6. Repeat by going to step 2.

The F-NEA is a six layered feed forward network with back propagation learning algorithm. The network has two phases, the learning and decision making (validation) phases. The network is made up of fuzzy neurons that are characterized by fuzzy input signals and fuzzy weights and also implements the If –Then rules which is the implication of the neural network expert system. That is to say that it performs the mapping function as well as the expert function. The number of units in the first layer, L1 is equal to the number of input features. This layer simply transfers the input to the next layer. Membership calculation and fuzzification are performed by layers L2, L3 and L4. L2 is specifically the rule layer. L4, L5 and L6 represent the MLP feed forward network with the back propagation learning algorithm with the detailed functions of input, hidden and output respectively.

3. Results

Classification follows texture analysis and feature extraction. The images were divided into two, Training set and validation set. The first 44 normal images and 58 cancer images were used for training. The second 44 normal images and 58 cancer images were used for testing. All the images used were acquire as hospital samples captured with a light microscope in combination of a CCD camera with magnification of *40. Each acquired image has a spatial resolution of 256x256 pixels with 65536 bytes representing unit8 arrays. The algorithm is implemented using MATLAB.

Table.1 is the combined effects of the Fourier features and the co-occurrence matrix features. The overall classification rate achieved is 96.435%. Fig.4 shows that performance was achieved during training. During training the stopping criterion adopted was to halt when the rate of change of error is sufficiently small resulting in 1163 epochs and error difference of $5*10^{-4}$. The classification vector differentiation is shown in fig.5. There was no experimental misclassification. In the confusion matrix given in Table 2, the error rate could be as a result of incomplete elimination of noise in the images, medical specimen preparation or other pre-processing anomalies.

4. Novelty: In order to capture the unique texture characteristics of the benign and malignant colon polyps images several feature descriptors derived from spectral energy/inertia and co-occurrence matrix contrast, entropy, correlation inverse difference moment and angular second moment have been investigated and incorporated into our system. Finally the proposed complete colon cell image classification system contains the Detect and Extracts system with FNEM classifier to achieve automatic cell image spectral and texture feature extraction and tumor classification yielding a very low task classification error rate of missed cancer of 2.6% and sufficient for applications that need more detailed information making it better than other methods which are incapable of this type of deep understanding and accuracy. The algorithm incorporates feature analysis and selection and at the same time independent of the feature extraction procedures adopted while overcoming the sharpness of class characteristic associated with other classifier. Finally on its own the FNEM produced a highly significant results for discriminating between cancer (adenocarcinoma) and benign (adenomas) colon cells adding a small improvement to the results obtained using other classifiers .There was over 6% improvement over other classifiers which is of great value clinically. Future extension of this work will be to make this algorithm more robust to identify various different types of colorectal polyps especially distinguishing between various colon adenomas polyps. The novelty of the algorithm is that it is independent of the feature extraction procedure adopted; takes into consideration the gross and micro examination conducted by the expert pathologist and overcomes the sharpness of class characteristics associated with other classifiers algorithms.

5. Conclusion

An algorithmic system based on textural image analysis and fuzzy neural network was developed for colon cancer classification. The system consists of an automatic texture feature extraction process, image enhancement algorithm and fuzzy neural network classifier. During the process of feature extraction, colon cells were located using iterative generation of texture feature values. The experiment shows that using image spectral values and spatial grey level dependence matrices with fuzzy neural networks performs better in classification than other feature discriminators and the use of Fourier analysis features are weak discriminant in cell image analysis.

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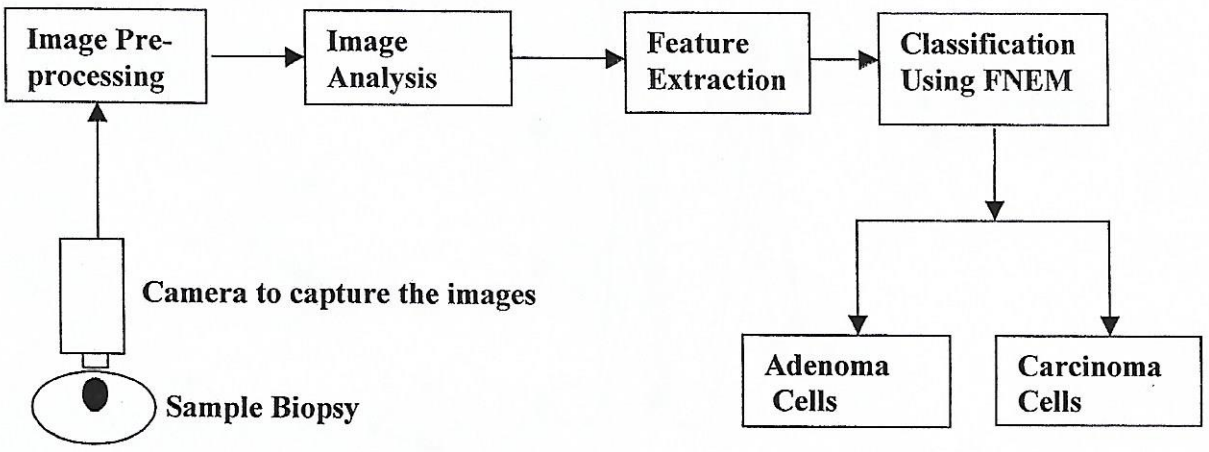


Fig.1: Experimental setup diagram.

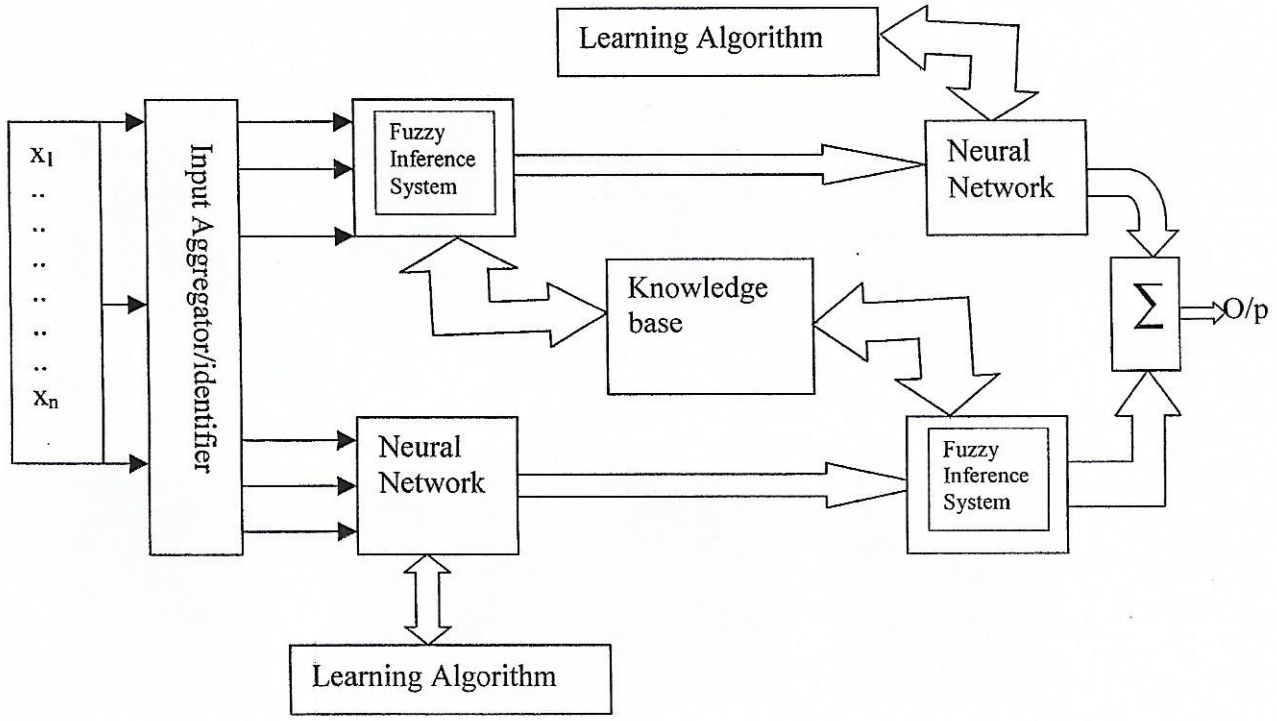


Fig.2a: Block diagram of the FNEM

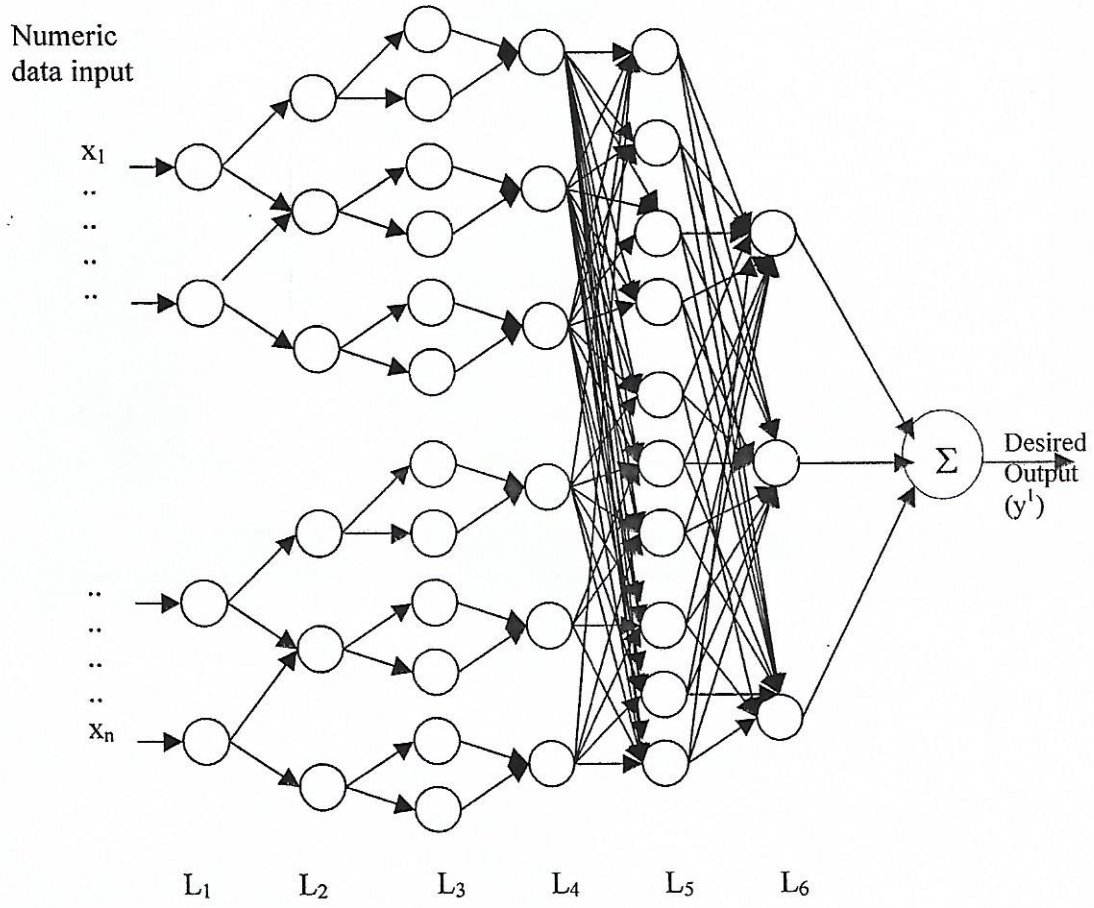


Fig. 2b: *Network Layer of the FNEM*

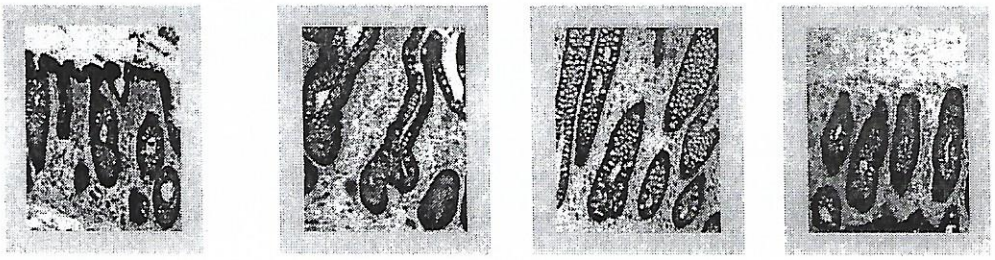


Fig.3a: Normal colon cells

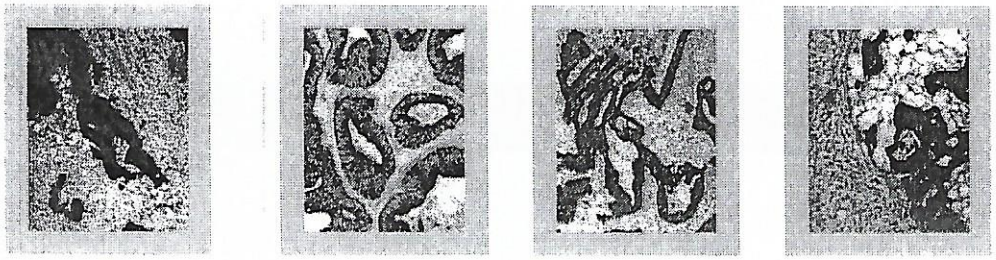


Fig (3b): Colon Cancer cells.

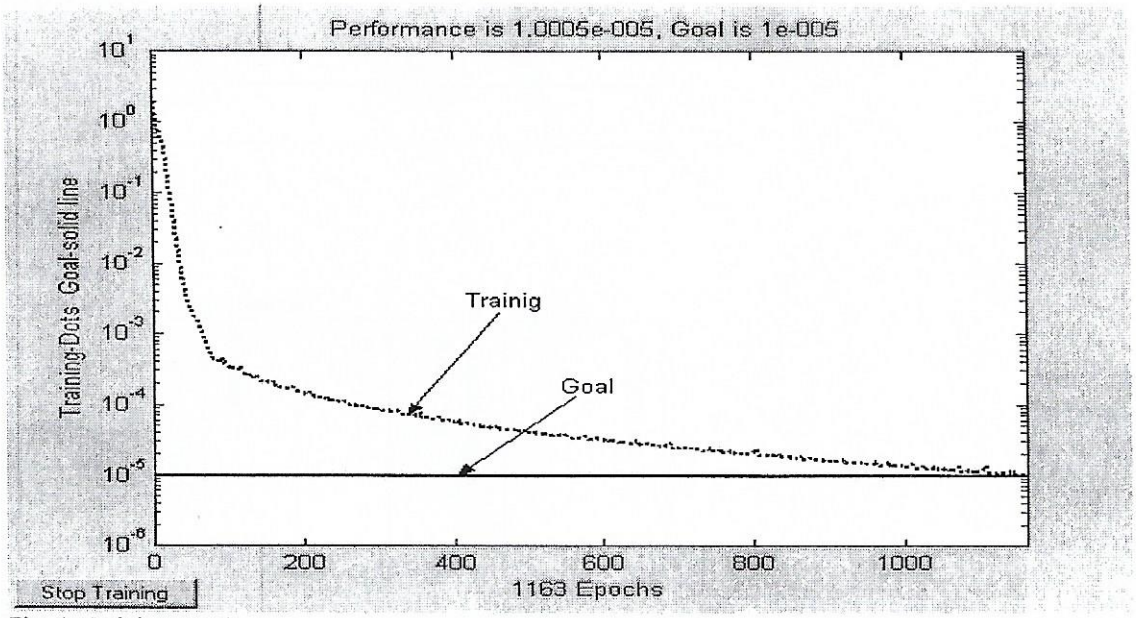


Fig: 4: Training Graph.

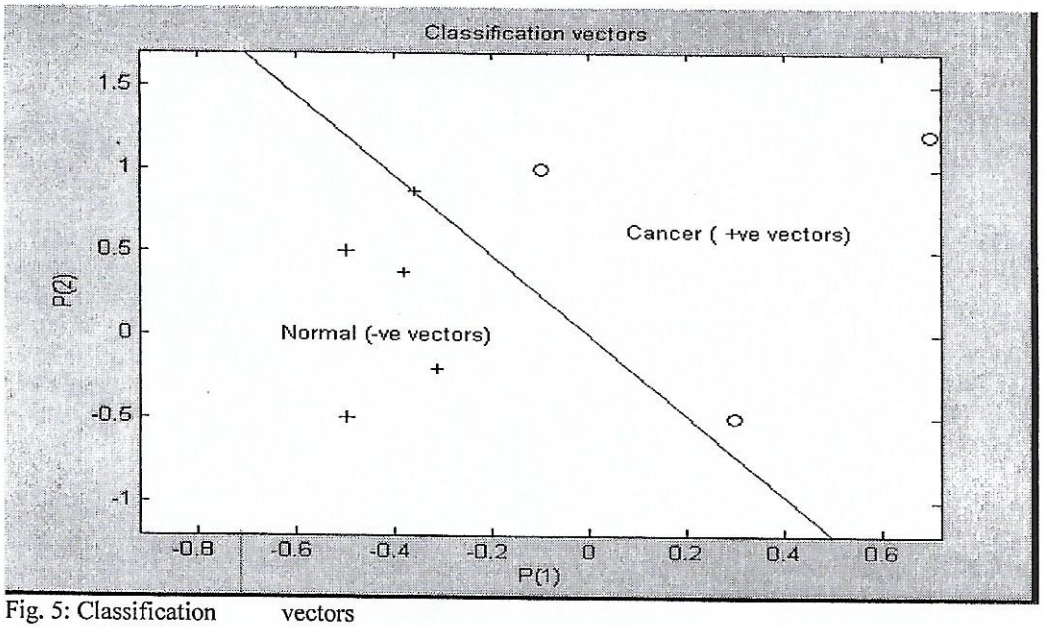


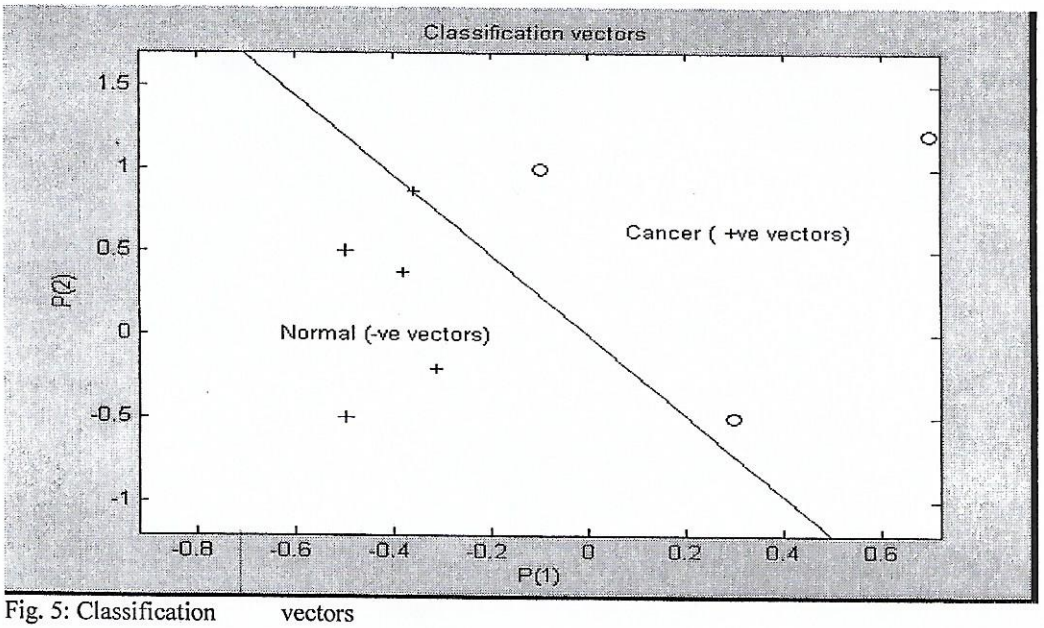
Fig. 5: Classification vectors

TABLE1: Classification for combined features

Feature combinations in the calculations	Classification Rate
I & CON	0.9625
I, CON & ASM	0.9637
I, CON, ASM & ENT	0.9641
I, CON,COR, ASM ENT & IDM	0.974

TABLE2: Confusion matrix

Classified as / **Correct classes**	**Cancer**	**Normal**	**Classification Rate (%)**	**Error Rate**
Cancer	113	3	97.414	0.026
Normal	4	84	95.455	0.045



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