

An Automated Leucocyte Classification For Leukemia Detection

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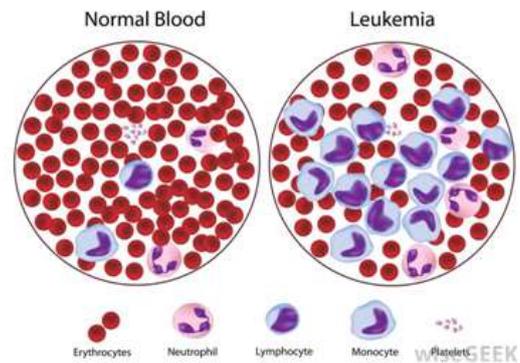
Abstract - Acute lymphoblastic leukemia is a form of blood cancer caused due to the abnormal increase in the production of immature white blood cells in the bone marrow, mostly affecting children below 5 years and adults above 50 years of age. Here a system is proposed to detect acute lymphoblastic leukemia from a standard dataset of ALLIDB1. Two methods were proposed for recognition of the disease based on the image processing techniques. First method is based on the traditional feature extraction method where the features like area, perimeter, major axis, minor axis and number of nucleus are extracted and given to the classifier for classification. In this method the images are subjected to segmentation by adaptive kmeans for extracting the nucleus before feature extraction. In the second method the images from the dataset is subjected to CNN based deep neural network. A comparative analysis of classification such as SVM (Support Vector Machine) and ANN (Artificial Neural Network) is done with features extracted from the first method. First method provides a recognition efficiency of 89.47% with SVM and 92.10% with ANN. CNN (Convolutional Neural Network) based feature extraction method provides recognition efficiency of 93%.

Key Words: WBC; ALL; SVM; ANN

1. INTRODUCTION

The counting and classification of blood cells from microscopic images allow evaluation and diagnosis of many diseases. Leukemia is a blood cancer that can be detected through the analysis of WBCs or leukocytes. Leukemia can be of two types: acute and chronic. According to the French-American-British (FAB) classification model, acute leukemia is classified into two subtypes: acute lymphoblastic leukemia

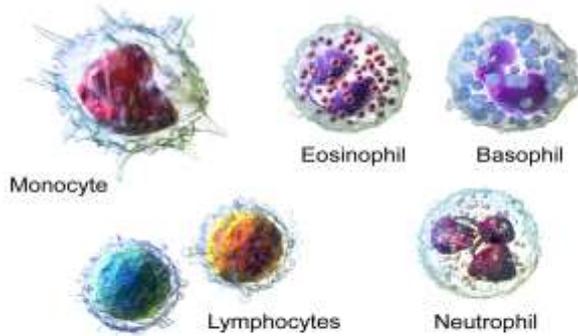
(ALL) and acute myeloid leukemia (AML). In this paper we consider only the ALL, that affects a group of leukocytes called lymphocytes. The ALL primarily affects children and adults over 50 years and due to its rapid expansion into the bloodstream and vital organs can be fatal if left untreated. Therefore, it becomes crucial early diagnosis of the disease for patient's recovery, especially in the case of children.



The use of image processing techniques can help to count the cells in the human blood and, at the same time, provide information on the cells morphology. These techniques require only one image and are therefore less expensive, but at the same time more scrupulous in providing more accurate standards. The main goal of this work is the processing and analysis of microscopic images, in order to provide a fully automatic procedure to support the medical activity, able to count and classify the WBCs affected by ALL.

White blood cells are one of the cells the body makes to help fight infections. It is also called Leukocytes. Leukocytes are easily identifiable from microscopic images, as their nuclei appear darker than the background, but data extraction from WBCs can present some complications due to wide variations in cell shape, dimensions and edges. The generic term leukocytes refers to a set of cells that are very different between them, which includes neutrophils,

basophils, eosinophils, lymphocytes and monocytes, also distinguishable by the presence of granules in the cytoplasm and by the number of lobes in the nucleus. The lobes are the most substantial part of the nucleus and are connected to each other by thin filaments.

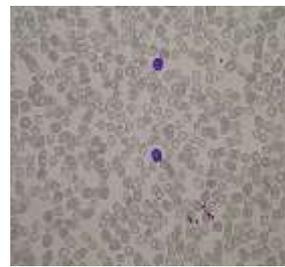


White Blood Cells

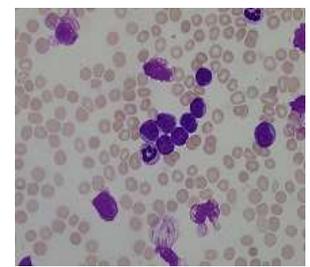
Furthermore lymphocytes suffering from ALL, called lymphoblasts, have additional morphological changes that increase with increasing severity of the disease. In particular, lymphocytes present a regular shape, and a compact nucleus with regular and continuous edges. Instead, lymphoblasts present shape irregularities, small cavity in the cytoplasm, called vacuoles, and spherical particles within the nucleus, called nucleoli. Therefore, in this paper, we present a method to identify all types of WBCs present in the microscopic images, which need various steps to reach the goal, and then classify WBCs as suffering from ALL or not.

The usage of Image processing techniques for identification and counting of cells of interest opens a wide plethora of applications for early detection of vast number of ailments. Analysis of human blood samples provides data that can be used to detect and predict many diseases, which can be treated successfully if diagnosed early. Acute lymphoblastic leukemia is one such disorder mostly affecting children of age less than 5 years and adults greater than 50 years. Acute lymphoblastic leukemia (ALL) is caused due to the over production of immature white blood cells called lymphoblasts (also known as blast cells), which inhibit the production of normal white blood cells (WBCs).

The term acute means ALL can progress at an alarming rate to other parts of the body like central nervous system, spleen, liver and lymph nodes and if left untreated it can pose danger to life in a few months. This makes early detection of the disease of paramount importance to prevent further damage to the body. Presence of lymphoblasts in a blood sample is a sure way of knowing if the patient is tested positive for the disease. This paper presents a method to automatically identify and count the lymphoblast cells in a given blood sample, so as to eliminate human errors and most importantly facilitate earlier detection of acute lymphoblastic leukemia.



Normal Sample



Affected Sample

The implementation is done in MATLAB by using the image processing toolbox. The input database consists of 108 samples of image taken from healthy and infected patients captured with an optical laboratory microscope along with a Canon PowerShot G5 camera. The images are in .JPG format with a 24 bit color depth and a resolution of 2592x1944. The blood sample consists of three types of blood cell components: Red blood cells, white blood cells and platelets. Red blood cells (RBCs) also known as erythrocytes make up around 40 percent of bloods volume.

RBCs contain hemoglobin, which enables it to carry oxygen to other cells. White blood cells are fewer in number compared to the RBCs and are primarily responsible in defending the body against external infections. The WBCs are classified into neutrophils, lymphocytes, monocytes, eosinophils and basophils. Platelets are smaller in number compared to RBCs and WBCs. They help in the clotting process by coagulation. In case of an infected blood sample,

there is a large presence of immature lymphocytes (known as lymphoblasts). The number of lymphoblasts is a strong indicator of the disease, thus detection and counting of lymphoblast is the most trusted way of diagnosis.

2. LITERATURE SURVEY

This literature discusses techniques for the detection of leukemia via image processing methods. In general, the technique of detecting leukemia through microscopic images of a blood sample was divided into three stages:

- Leukocyte Cell Image Segmentation
- Feature Extraction of Leukocyte Cell Image
- Detection and Classification of Leukemia Cell

2.1 Leucocyte Cell Image Segmentation

Segmentation [17] is the essential step for image analysis and image processing of ALL. Various methods of image segmentation used in literature available such as thresholding method, clustering, region growing, and others. In [1] used a color based segmentation method in L^*a^*b color region through Fuzzy C-Means clustering method which clustered White Blood Cells into four groups. This L^*a^*b color region is used because it has a two-dimensional region of color when compared to the three-dimensional RGB color. Based on research [2] used Otsu thresholding method. To get the effective segmentation, Linear Contrast Enhancement, and Histogram Equalization was applied followed by image arithmetic operation that could eliminate blood components other than white blood cells effectively.

In [3] made a comparison between three segmentation methods: K-Means clustering, Fuzzy C-Means and modification of K-Means namely Moving K-Means. This approach was applied in HSI color space. Segmentation was performed on these three segmentation algorithms, and each has different performance, where the highest classification accuracy is Moving K-Means. In [4] applied segmentation with K-Means method in a grayscale color space with $k = 4$, segmentation process divided blood into four clusters.

Clustering was done by minimizing the sum of the square of the distance data and the associated centroid. In [6] also used K-Means segmentation but segmentation is done using the value of H and S in HSV color space. Regarding [5] used $L^*a^*b^*$ color space as in [1] with K-Means Clustering method to get the nucleus lymphocytes followed by Otsu thresholding to obtain a binary image which is equipped with a morphological filter to remove the undesired region and get optimal nucleus images for classification.

In [7] used color segmentation in HSI color space after preprocessing process using contrast enhancement technique to facilitate segmentation results. Based on [8] utilized thresholding in the HSI color space on the value S with median filtering method and region growing method were applied to improve the quality of segmentation. In [9] proposed color segmentation method approach in the HSI color space with Discriminating region based on the white blood cells. The idea is constructing a Discriminating region for the scatter plot of pixels belonging to the white blood cells. By checking whether a pixel lies inside the region Discriminating, white blood cells can be segmented effectively.

Research on [10] used two methods for the Segmentation technique which are Active Contour and Watershed Transformation. They found that watershed transformation gives a better result for segmenting the nucleus, and can segment more region and the computational cost is low rather than the Active Contour Technique. In [12] used threshold value based on Zack Algorithm. Based on their study, Zack Algorithm is effective when the histogram displays clear valleys between high and weak peaks present in the Y component histograms generated from leucocytes and red blood cells. According to [13] proposed a dual-threshold method for segmenting White Blood Cells. This approach used two threshold values which obtained from golden section search algorithm, where two threshold values were applied in different color space: gray-scale image and HSV color space.

2.2 Feature Extraction

Feature extraction [17] is used most in the research include morphological features that characterize the shape of the cell. Other features used are a fractal dimension, color feature, texture feature. In [1] used a variety of features for lymphoblasts classification. Features that used fractal dimension is Hausdorff dimension, signature contour, shape features which include area, perimeter, compactness, solidity, eccentricity, elongation, and form factor. To improve the accuracy of detection, a color feature which is the average value of color and texture features such as homogeneity, energy, correlation, and entropy is also used. Research [2] proposed a method of Fisher's Discrimination Ratio (FDR) followed by Exhaustive Search to get the most efficient feature extraction for leukemia detection.

They obtained three most distinctive features: diameter of the nucleus, the nucleus cluster Prominence and the minor axis of the ellipse bounding. Based on [4], [12] used LDP operator to extract features from the nucleus that were segmented. Features obtained through histogram generated from the LDP operator. According to [10] utilized basophilia intensity texture features based on the LAB color space. Moreover, they propose a novel method to characterize the cytoplasmic profile. It estimates the projections of the cytoplasm using the peripheral region around the cell segmented by WT. This feature is obtained by using thresholding segmentation to the green component and counting the pixels of this region.

2.3 Detection And Classification Of Leukemia Cells

Only a few studies have focused on specific classification techniques [17] to detect leukemia cells. Despite the classifying type of white blood cell and blast cell, Acute Lymphoblastic Leukemia was divided into three classes which consist of ALL-L1, ALL-L2, and ALL-L3. This type of classification problem is included in this part to be explained more. Research in [2] used k-nearest neighbor classification

with Euclidean Distance. Some misclassification resulted from the similarity between the morphological features of normal lymphocyte cells with lymphoblast cells. In [5] used sequential neural network classifier with two stages, where the first stage is to distinguish normal cells with abnormal cells, while the second stage is to differentiate between ALL and AML. However, due to the shortage of input image database, they only discussed step one to distinguish between normal cells and lymphoblast cells.

Next research which same with [6], research [11] performed improvement using HSV and FCM to detect cancerous and non-cancerous cells. Based on research [7], they compared two methods for classification of white blood cells, the Multilayer Perceptron (MLP) as in [8], but here they used two algorithms for training, called Lavenberg-Marquardt algorithm (LM) and Bayesian Regulation (BR). Another method used for the classification is ARTMAP Simplified Fuzzy Neural Network (SFAM). The results obtained indicate where the MLP with trainer BR algorithm produces the highest accuracy is 95.70 percent as compared to other methods which used 100 training epochs and six hidden nodes. [9] also compared three methods for classifying white blood cells, in here MLP obtains the highest degree of accuracy compared with SVM and HRCNN.

The detection of leukemia through image processing focusing on segmentation preceded by preprocessing to get better segmentation results. The results of the cell nucleus segmentation are crucial in lymphoblast classification accuracy. Besides, the classification method used also determines the level of detection accuracy lymphoblast. The steps of detecting leukemia is divided into three stages, namely Segmentation, Feature Extraction and Classification. At the stage of segmentation, The results mostly had a relatively high degree of accuracy above 90 percentage. K-Means method and Fuzzy C-Means are segmentation methods that were often used. At the stage of feature extraction, features used are the texture, color, and

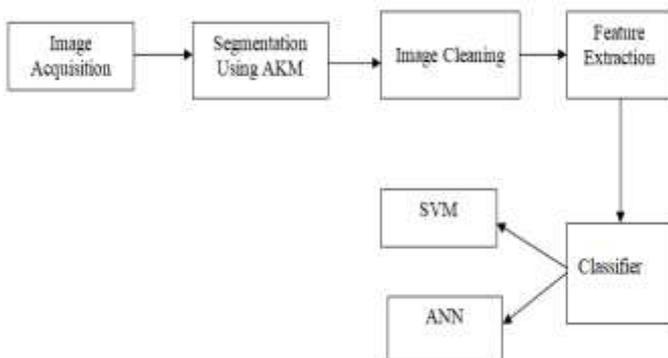
geometrical features. In the classification stage, the accuracy results are quite high by using SVM and MLP methods.

3. PROPOSED WORK

In the proposed methodology, the image of blood smear goes through different stages. First the input image undergoes segmentation. Then the image cleaning operation is performed. After that features are extracted from the image. Finally these features are classified by a classifier. The objectives of the proposed method are developing an automated and accurate method to find whether the blood image is leukemia affected or not. It includes identification and classification of leucocytes. Also find the best method which classifies the leucocytes among three classification methods. The proposed method also aims in analyzing the performance of SVM, ANN, and CNN.

3.1 METHODOLOGY

3.1.1 Shallow Feature Extraction Method Based Recognition System



i. Image Acquisition

The database consists of images of blood samples taken from healthy and infected patients and which are appropriately marked by an expert oncologist. This forms the reference for computing the results for the implementation. The dataset images are microscopic images from the laboratory through Canon Power Shot G5 camera.

Hence all images have 24-bit color depth in JPG format and 2592 × 1944 resolution with different magnifications.

ii. Segmentation

Image segmentation is a process in which divides an image into different parts as like mathematical differentiation. It helps to make over the overall appearance of an enhanced image into more meaningful and easier image for a system to further process. Hence the images are segmented based on a set of homogeneity criteria. Many segmentation [14] techniques have there such as threshold, Otsu method, edge based, etc. K-means is one of the most simple and important algorithm capable for solving the almost all types of clustered problems.

Also, segmentation by k-mean clustering has some disadvantages. In k-means, some random points are selected as centroids. Programmer has to specify the number of clusters. For a better segmentation result Adaptive k-means clustering is used. This adaptive K-Means method which proposed recently was originally based on the standard K-Means algorithm for better segmentation [15]. During initialization step, the placement of the k-centroids is very crucial because different location will give different result. The standard K-Means method uses the randomly choose k-centroids which leads to accuracy degradation in segmentation. This may cause inconsistent result in the image segmentation.

Despite of using the normal randomly choose initial k-centroids, this adaptive method manipulates the local minimum and maximum values based on the RGB colour space during the initialization step. The enhanced initialization method returns a two-element array with minimum and maximum RGB values from the whole pixel area. The operator computes the maximum and minimum pixel values for each band of a rendered image within the region of interest. The adaptive method is an iteration-based clustering that produces an optimal value of initial k-centroids by minimizing the objective function α . The

initial k-centroids can be obtained by using the following objective function:

$$\alpha = \sum_{i=1}^c \sum_{k=1}^n \partial(\mu_{min}, \mu_{max})$$

where α is the Euclidean distance between minimum RGB value μ_{min} and maximum RGB value μ_{max} , n represent the number of image pixels and c is the total number of cluster.

iii. Image Cleaning

It is necessary to clean up the image to get more better result. It is done through the process of area opening, it can remove all the objects with a smaller than the structuring element in which structuring element has a circular shape and its size value can be assumed as the average size of objects in the image. After area opening followed by morphological dilation performed. This will fill the vacant area in the cell structure and get a clear separated image. The number of nucleus is calculated by labeling the connected components.

iv. Feature Extraction

This is the process of extracting the features as the descriptors from observable images to which the experts refer and at the same time it is most appropriate step for the classification. For that shape descriptors and number of nucleus present in the image is used. A set of numbers which can characterize a given shape is known as shape descriptors. The basic shape descriptors such as area, major and minor axis, perimeter are used. Area descriptor is a vector that represents the number of pixels in the labeled region. Perimeter containing an estimate of the perimeter length in pixels for each blob. Major axis and minor axis descriptors are the vectors that represents the length of major axis and minor axis of ellipses respectively.

v. Classification

Classification is a process of assigning a known class for a unknown vector. Here the classification is done by the feature vectors to the ALL affected or not. Naive Bayesian, KNearest Neighbour, Decision Trees, SVM are the major standard classifiers. In these each classifier will set up the process in which there is a set of inputs and produce a desired set of outputs with deserved class. For the leukaemia detection system SVM classifier is used and it classifies the image in to one of the two classes ALL affected or not. In addition to SVM, two layer feed forward network and CNN network is used. Here we are finding which method gives the better classification.

a) Support Vector Machine(SVM)

SVM(Support Vector Machine) one of the important classifier, in which the method is that the entire data set is divided in to two sets which are training and testing. Training data is the learning paradigm section. In these the process of training the vectors and updating of parameters are takes place while the test data used to approving the classifier in which deserve the vector. Here SVM classifies by labelling each lymphocyte as ALL affected or not based on the feature vector from the feature extraction phase. The process takes for each image and train and assign the class by accordance with the experts and produce deserving output as whether ALL patient or not. In SVM classification the entire measured data is divided into training and testing data sets. The training data is used for updating the weights and the process of training the network is called learning paradigms.

The remaining test data are used for validating the classifier performance. SVM classifies by labelling each lymphocyte sub image as normal or malignant sample based upon a set of measured feature. There are different SVM classifiers are there such as linear, quadratic, radial etc. For the work, SVM with linear kernel is used. The work compares the class predicted by the classification model for a certain WBC with the class assigned to it by an expert haematologist. In a binary problem, the instances are subdivided in healthy

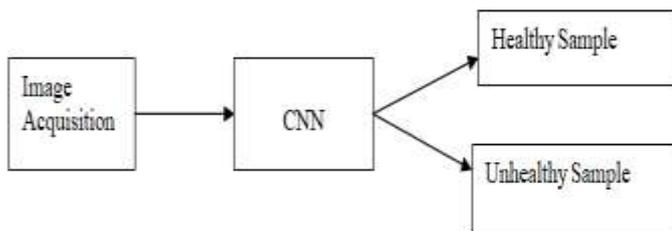
and unhealthy. For this the instances as unhealthy when the WBCs were affected by leukaemia and healthy when the WBCs were not suffering from leukaemia. By this the accuracy value is calculated.

b) Artificial Neural Network(ANN)

Neural network is a system designed for the purpose of information processing and uses biological nervous system for inspiration (like brain processes information) for it. An ANN is composed of huge counts of reciprocally connected elements which are called neurons. These neurons act as processing elements and they work like a single entity. Artificial Neural Network learns from examples. Learning is the process of training the neural network in order to make the network capable of performing the classification. There are two types of processes that can be used to train the neural network, supervised learning & unsupervised learning. Here a two layer feed forward network is used, which gives highest accuracy than SVM classifier.

3.1.2 Convolution Neural Network(CNN) Based Recognition System

a) Basic Structure



b) CNN

Convolution Neural Networks (ConNets or CNNs) are a category of neural networks that have proven very effective in areas such as image recognition and classification. Convolutional Neural Networks are very similar to ordinary Neural Networks, they are made up of neurons that have learnable weights and biases. Each neuron receives some inputs, performs a dot product and optionally follows it with a non-linearity. The whole network still expresses a single

differentiable score function: from the raw image pixels on one end to class scores at the other.

And they still have a loss function (e.g. SVM/Softmax) on the last (fully-connected) layer and all the tips/tricks we developed for learning regular Neural Networks still apply. ConvNet architectures make the explicit assumption that the inputs are images, which allows us to encode certain properties into the architecture. These then make the forward function more efficient to implement and vastly reduce the amount of parameters in the network. This network provides better classification results than the other classification method.

CNN is composed of various convolutional and pooling layers. Let's see how the network looks like. We pass an input image to the first convolutional layer. The convoluted output is obtained as an activation map. The filters applied in the convolution layer extract relevant features from the input image to pass further. Each filter shall give a different feature to aid the correct class prediction. In case we need to retain the size of the image, we use same padding (zero padding), otherwise valid padding is used since it helps to reduce the number of features. Pooling layers are then added to further reduce the number of parameters. Several convolution and pooling layers are added before the prediction is made. Convolutional layer helps in extracting features.

As we go deeper in the network more specific features are extracted as compared to a shallow network where the features extracted are more generic. The output layer in a CNN is a fully connected layer, where the input from the other layers is flattened and sent so as to transform the output into the number of classes as desired by the network. The output is then generated through the output layer and is compared to the output layer for error generation. A loss function is defined in the fully connected output layer to compute the mean square loss. The gradient of error is then calculated. The error is then backpropagated

to update the filter(weights) and bias values. One training cycle is completed in a single forward and backward pass.

A CNN consists of an input and an output layer, as well as multiple hidden layers. The hidden layers of a CNN typically consist of convolutional layers, pooling layers, fully connected layers and normalization layers. Convolutional layers apply a convolution operation to the input, passing the result to the next layer. Convolutional networks may include local or global pooling layers, which combine the outputs of neuron clusters at one layer into a single neuron in the next layer. ReLU is the abbreviation of Rectified Linear Units.

This layer applies the non-saturating activation function.

The performance of the proposed work is compared using Convolutional Neural Network (CNN) to analyze which of these will give best results. A convolutional neural network (CNN) is a class of deep, feed-forward artificial neural networks that use a variation of multilayer perceptron designed to require minimal preprocessing. Here, CNN with two layers is used. CNN performs its work accurately using 10,000 images. In this work only 108 images are used and accuracy is found to be more than 92.86%. If there were more images, the accuracy would be much more. According to the study, it is concluded that if there is availability of more images, then CNN is found to produce the best results with high accuracy.

4. EXPERIMENTAL RESULTS

For the proposed work, 47 images are used for training and 35 images are used for testing. The performance measures of the current existing automated method and the proposed work is being analyzed and it is found that the proposed method gives greater accuracy. Fig 4.1 shows the input RGB image of blood cells which is affected by leukemia.

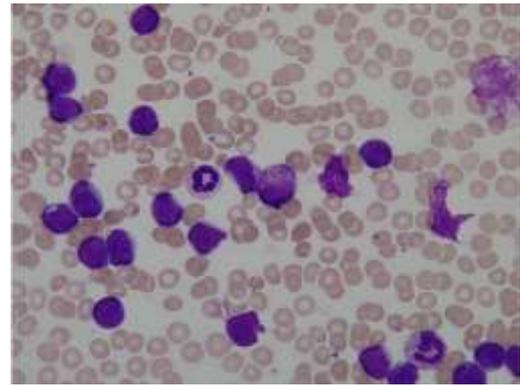


Fig.4.1 Input Image

Then the image is segmented using Adaptive k-means. Thus the nucleus are extracted from the image. Fig. 4.2 shows the image after segmentation.

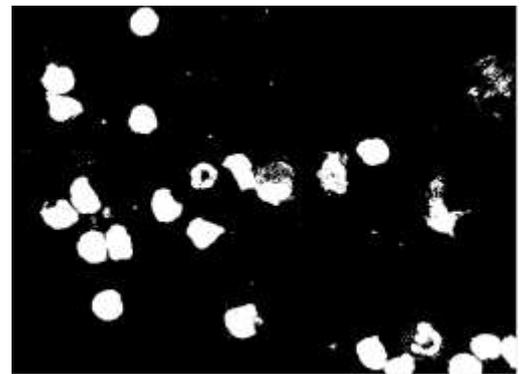


Fig.4.2 Image after segmentation

After segmentation image cleaning operations are performed. Which includes area opening and morphological dilation. Fig 4.3 shows the image after area opening.

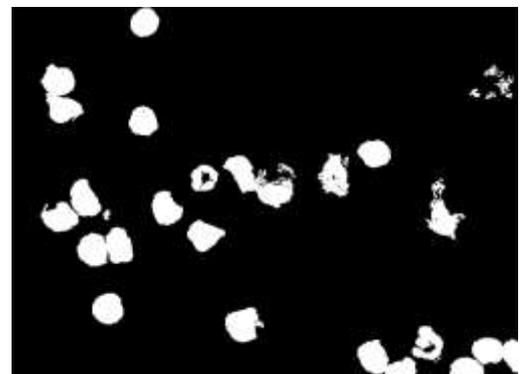


Fig.5.3 Image After Area Opening

Area opening is followed by morphological dilation. Fig.4.4 shows the image after morphological dilation.

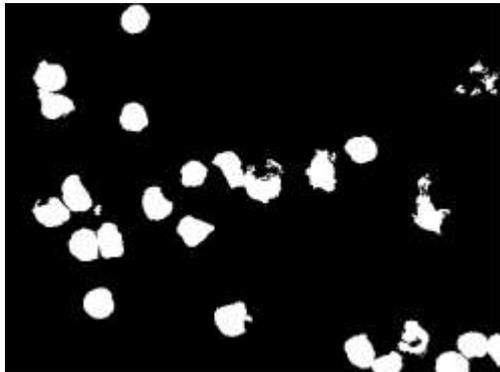


Fig.5.4 Image After Morphological Cleaning

After image cleaning feature extraction is done. The basic shape descriptors such as area, major and minor axis, perimeter are used. In addition to this number of nucleus present in the images are counted. In classification stage, the presence of leukemia in the image sample will be checked and then it is classified into unhealthy or healthy sample using Support Vector Machine (SVM). Then, the classification is implemented using Artificial Neural Network (ANN). The performance of SVM is compared with that of ANN. The results of ANN are found to be better than that of SVM. The proposed work is also implemented using Convolutional Neural Network (CNN). Comparison table which shows the comparison between Shallow methods and CNN is shown below.

Rates	SVM	ANN	CNN
Accuracy	0.8947	0.9210	0.9300
Error rate	0.1053	0.0791	0.0520
Sensitivity	0.7778	0.8333	0.8834
FP rate	0	0	0
Specificity	1	1	1
Precision	1	1	1
Prevalence	0.4737	0.1300	0.0999

Table 4.1: Comparison between Shallow methods and CNN

5 CONCLUSIONS

In this work a system for diagnosing leukemia using microscopic images of blood samples is developed. Here a

novel technique of segmenting the infected area using adaptive kmeans clustering is developed. The detection is carried out based on two methods. First, based on shallow features and second based on deep CNN network. The detection of leukemia in the blood samples requires more accuracy and for that the number of features considered play a vital role in it.

Features like major axis, minor axis, area, perimeter and number of nucleus which are extracted from the images gives more accuracy in the proposed method. Thus the proposed method will be able to identify and classify the blood smear images more accurately. Then this shallow feature extraction method based recognition system is compared with CNN based recognition system.

This procedure will be a stepping stone in leukemia diagnosis, as it avoids the usual ways of segmenting the cells first and then segmenting the nucleus from the image. In this work initially the nucleus are extracted using adaptive kmeans clustering. The proposed method has been implemented in the Mat lab environment, for flexibility and speed of prototyping the image processing options. This method not only classifies leukemia infected and non infected but also studies the classification using SVM and ANN and finds that ANN is better classifier than SVM for proposed work.

It also studies the implementation of proposed work using CNN and concludes that CNN provides best result than other classifier. Shallow feature extraction method based recognition system produce an efficiency of 89.47% with SVM and 92.10% with ANN. CNN based feature extraction method produce an efficiency of 93%. Therefore it is concluded that in shallow recognition system ANN is better as compared to SVM. And CNN based feature extraction method is better than the shallow recognition system, as it produces more accuracy.

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