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Diagnosis of Acute Lymphoblastic Leukemia using Microscopic Blood Cell Images

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Abstract: **Acute Lymphoblastic Leukemia (ALL) is a kind of blood illness attributable to the surprising ascent in the development of unhealthy WBCs in the spongy tissues of the bone, prompting blood malignant growth. It may be seen in children and aged people too.**

The study of microscopic images proves a substantial role in the evaluation of leukemia and its effective detection. The existing techniques are of traditional type and somewhat depend on human intervention, which is laborious. So, an automated leukemia diagnostic system is very much needed that reduces manual intrusion and provides more precise medical information.

This paper describes an automated system developed, based on image processing techniques for the detection of acute lymphoblastic leukemia in blood cells. Here a system is proposed to detect ALL by examining microscopic blood cell images obtained from a standard dataset. In our research work, two image processing techniques are suggested for the detection of the illness. The first technique depends on the conventional feature extraction procedure where the features like region, edge, quantity of nuclei etc., are separated. Data is then sent to the classifier to be categorized. Prior to feature filtration, the images are processed by an adaptive k-means segmentation algorithm to separate the nucleus. The input image is fed to DNN in the other technique.

The overall appraisal of the presentation of classifiers like SVM ANN is performed with features obtained from the first technique. The first technique furnishes a detection efficacy of 89.37% with SVM and 92.16% with ANN. The CNN-dependent feature extraction technique offers a detection efficacy of 93.36%.

Index Terms**: Microscopic Blood Cell Images, acute Lymphoblastic Leukemia (ALL), SVM, ANN, CNN, automated leukemia detection**

I. Introduction

Medical imaging has become one of the foremost necessary visual images and interpretation strategies in biology and medicine over the past decade. Now, it has witnessed incredible progress of new, powerful instruments for processing and analyzing medical images. This has directed to a huge growth in the application of digital image processing tools [1] for resolving medical issues. The foremost difficult facet of medical imaging lies within the development of integrated systems for the utilization of the clinical sector. Model development, execution, and authentication of modern medical systems need strong partnership between doctors and engineers. The main objective of image processing is to collect data, detection of diseases, diagnose diseases, manage medical care, observation, and analysis [2].

Presently, the identification of blood illness is beyond visual survey of microscopic blood cell images. The detection of blood disorders may be useful for the classification of a variety of diseases connected to blood**.** One of the most feared human syndromes is cancer. Leukemia is a type of blood cancer, and if it is detected late, it'll lead to death. The images of normal blood cell and Leukemia blood cell is shown below in Figure 1

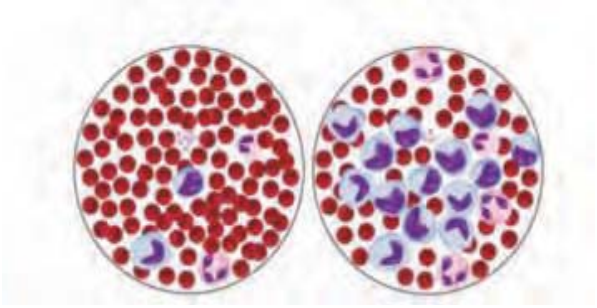

Figure 1. (a) Normal blood (b) Leukemia

White blood cells (WBCs) are one of the cells that help the body to fight infections. Having the generic term as leukocytes, the WBCs are classified based on their appearance into neutrophils, basophils, eosinophils, lymphocytes, and monocytes. The structure of different types of WBC is shown in Figure 2.

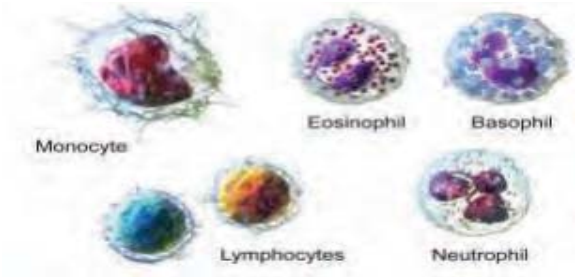

Figure 2. Composition of White Blood Cell

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Leukemia occurs when a lot of abnormal lymphocytes are produced by bone marrow due to which, the balance of the blood system will be disrupted. Leukemia can be termed as a group of haematological malignancies that are demonstrated by the tumorous proliferation or increased life span of immature white blood cells in the bone marrow [3]. The extreme production of these cells named as lymphoblasts or leukemic cells progressively dislocates healthy cells in the bone marrow and even extend to vital organs such as the liver, lymph nodes, spleen, and nervous system causing complications in fighting infections, transporting oxygen [4,5].

Clinically, leukemia is classified based on the speediness of the disease progression to acute and chronic forms. Whereas the acute kind of leukemia develops quickly and therefore the number of leukemic cells rises rapidly, chronic leukemia develops slowly over time [6]. In keeping with the sort of affected cells from that the malignancy develops, acute leukemia is again divided into two classes: acute lymphoblastic leukemia and acute myeloid leukemia [7]. In our research work, we are considering Acute lymphoblastic leukemia (ALL), which is the second most common type of blood disorder leading to leukemia in adults above fifty years and the most common type of childhood malignancy for the age less than five years, accounting for around one-third of all paediatric cancers [8].

The quantity of lymphoblasts could be a strong sign of acute lymphoblastic leukemia. For this, the blood sample is taken and scrutinized by haematologists. Microscopic images are inspected visually by haematologists and so, the method is time intense and laborious [9], [10], [11]. The method is vulnerable to errors because of human physical capability and necessitates human professionals. Moreover, it is difficult to get steady results from microscopic visual inspection. The recently used diagnostic methods rely on analyzing immune phenotyping, fluorescence in situ hybridization (FISH), cytogenetic analysis dan cytochemistry [12], [13].

The immediate and quick classification of the leukemia considerably aids in delivering the proper medication for it [14]. An automatic microscopic imaging system is greatly needed which can carry away related limitations in the visual microscopic inspection.

The system developed here is based on microscopic images to acknowledge the type of leukemia. With this system, more images can be screened, decrease evaluating time, eliminate the effect of subjective factors, and enhance the precision of the diagnosis process at the same time [15].

The execution is completed in MATLAB by utilizing an image processing toolbox. The input database is taken from public benchmark datasets: ALLIDB2. It is publicly open to download the dataset available online [10]. They provide high-quality images

In our work, we considered 108 samples of images taken from healthy and infected patients as shown in Figure 3, taken with a sophisticated optical microscope together with a high-resolution camera. The images are in a digital photographic structure having a resolution of 5.04MP pixels.

In this paper, two techniques are suggested for the detection of the illness. The first technique depends on the conventional feature extraction procedure where the features like region, edge, quantity of nuclei etc, are separated. Next, the data is given to the classifier for categorization. Here, the images are exposed to segmentation by adaptive k-means for separating the nucleus prior to feature extraction.

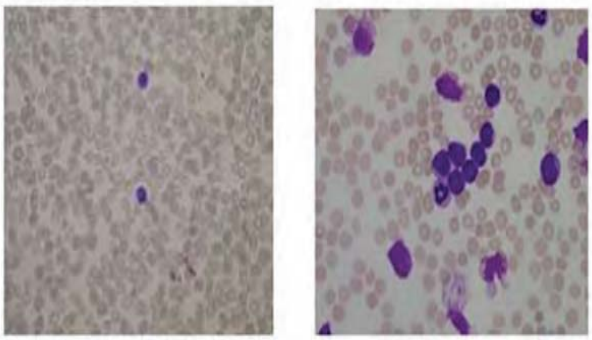

Figure 3. (a) Healthy Sample (b) Infected Sample

In the other technique, the image from the dataset is exposed to CNN- based DNN. The overall appraisal of the presentation of classifiers like SVM ANN is performed with features obtained from the first techniques. The first technique furnishes a detection efficacy of 89.37% with SVM and 92.16% with ANN. The CNN-dependent feature extraction technique offers a detection efficacy of 93.36%.

II. Literature Review

In this section, the work demonstrated by different experts on several techniques for the diagnosis of leukemia using microscopic blood cells is discussed. Normally, the study of Leukocyte cell images has been done under three headings:

A. Image Segmentation
B. Feature Extraction
C. Detection and Classification

A. Image Segmentation

[16] used a color-based division technique in the L * a * b color region instead of a Fuzzy C-Means clustering to divide WBCs into 4 classes. This region is utilized since it is a two-dimensional color region.

Analysis [17] uses the Otsu thresholding technique to get an effective segmentation. The author employed an arithmetic algorithm to competently eliminate all the blood components excluding WBCs.

In [18], a comparison of three strategies is made: K-Means clustering, Fuzzy C-Means, and K-Means modification. The same technique was utilized in HSI color space. It is noticed that each has a unique performance.

In [19] segmentation with the K-Means technique is used in greyscale color space and this divided blood into 4 groups.

In [20], the nucleus lymphocytes were obtained using the L * a * b * color space and the K-Means Clustering approach, tracked by thresholding technique developed by Otsu. They got a digital image with a structural filter to remove the undesired area and get the best nucleus images feasible for classification. The same methodology is utilized by the researcher in [21].

Color segmentation in the HSI color space was employed in [22] after a pre-processing procedure that used a contrast improvement methodology to enable segmentation findings.

To improve the quality of segmentation, [23] applied thresholding within the HSI color space on the value S, along with a median filtering technique and a region-expanding method.

[24] suggested a color segmentation technique in the HSI color space with a white blood cell discriminating area. The idea is to create a discriminating region for the scatter plot of pixels that are related to white blood cells. White blood cells can be identified by evaluating if a pixel falls inside the Discriminating zone.

Active Contour and Watershed Transformation were two approaches used in [25] for segmentation. They discovered that watershed transformation provides a promising result for nucleus segmentation, as it can segment more regions and has a lower computational cost than the Active Contour Technique.

The threshold value utilized in [26] was calculated using the Zack Algorithm. Their research shows that the Zack Algorithm is effective when the Y- Component histograms formed from leucocytes and red blood cells show obvious dips between high and weak peaks.

A dual threshold technique for segmenting White Blood Cells was proposed by [27]. Two threshold values were generated from the search method and implemented in many color spaces -grayscale and HSV.The step for image analysis and image processing of A LL is explained in [28]. Image segmentation methods such a s thresholding, clustering, region expanding, and others have been employed in the literature.

B. Feature Extraction

[16] used a variety of parameters to classify lymphoblasts. Hausdorff dimension, signature contour, shape features that incorporate area, perimeter, and form factor are examples of fractal dimension features. A color characteristic that is the normal value of color, as well as texture features like homogeneity and entropy are utilized to improve recognition accuracy.

To obtain the most effective feature extraction for leukemia identification, researchers [17] proposed a Fisher's Discrimination Ratio (FDR) technique followed by extensive analysis. They discovered the three most distinguishing features: nucleus diameter, nucleus prominence, and the nucleus axis.

[25] uses the LDP operator to abstract features from the segmented nucleus, based on [19]. The LDP operator provided a histogram, which revealed the features.

Basophilic intensity texture features were established in the LAB color space, according to [26]. They also talked about a new way to visualize the cytoplasmic profile. It assesses the cytoplasm's prognoses utilizing the WT-segmented periphery region around the cell. The green component is segmented using thresholding, and the pixels in this zone are counted.

C. Detection and Classification

Only a few studies have focused on specific classification strategies.

[17] employed k-nearest neighbor classification with Euclidean Distance in their analysis. The physical similarities between normal lymphocyte cells and lymphoblast cells resulted in some misinterpretation.

In [20], a sequential neural network classifier with two stages was utilized, the first of which was used to distinguish between normal and abnormal cells, while the second stage was used to distinguish between ALL and AML. However, due to a lack of input picture databases, they only explored step one, which involves distinguishing between normal and lymphoblast cells. The next study [21] accomplished advancement using HSV and FCM to identify cancerous and non-cancerous cells.

They used two algorithms for training, the Lavenberg-Marquardt algorithm (LM) and Bayesian Regulation, based on research [22]. They related two methods for classification of white blood cells, the Multilayer Perceptron as in [23], but they used two algorithms for training, the Levenberg-Marquardt algorithm, and Bayesian Regulation. The ARTMAP Simplified Fuzzy Neural Network is the second classification method. The results show that when compared to other approaches that employed 100 training epochs and six hidden nodes, the MLP with trainer BR algorithm produces the highest accuracy of 95.7 percent.

[23] also discussed three methods for categorizing white blood cells, with MLP achieving the highest level of accuracy when compared to SVM and CNN. The diagnosis of leukemia using image processing with a focus on segmentation and preprocessing to improve segmentation results. The accuracy of lymphoblast classification depends on the results of cell nucleus segmentation. Furthermore, the lymphoblast detection accuracy is determined by the classification technique used.

The processes of recognizing leukemia are divided into three phases, according to the literature survey: segmentation, feature extraction, and classification. During the segmentation phase, the results often exhibited a relative maximum degree of accuracy of more than 90%. Segmentation techniques such as the K-Means approach and Fuzzy C-Means are widely employed. The texture, color, and geometrical properties are utilized during the feature extraction process. Using SVM and MLP algorithms, the accuracy grades in the classification phase are quite high.

III. PROJECTED METHODOLOGY

The blood smear image is exposed to various steps in the projected method. To start with, the image is exposed to division in segmentation process. Later, the image improvement activity is executed. Next features are separated from the image. Ultimately, the feature elements

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are arranged by a classifier. The goal of the suggested method is to foster a mechanized and exact technique to analyze whether or not the blood image is impacted by leukemia. It incorporates the identification and characterization of leucocytes. Additionally, find the best strategy which classifies the leucocytes amongst the current strategies. The projected approach conjointly points in examining the exhibition of SVM, ANN, and CNN

Based on the literature, we have added the following steps to our methodology as shown in Figure 4.

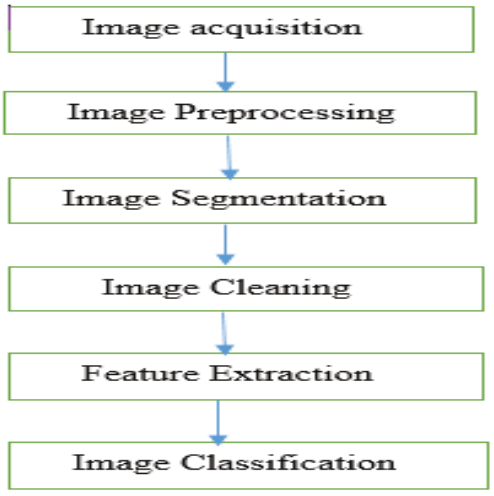

Figure 4. Steps involved in Proposed System

1.Image Acquisition

Image slides of blood samples obtained from normal and abnormal patients are included in the input, which are appropriately differentiated by an expert professional. This will be the source for evaluating the execution's outcomes. Microscopic images from the clinic are fed into the system via the higher-end camera. As a result, most of the images have a 5.04MP pixel resolution with various modifications.

2.Image Prepossessing

During image acquisition and too much staining, the images are going to be disturbed by noise. The noise could also be because of brightness or darkness that makes the region of interest (ROI) looks like a blurry image region. The background is going to be removed as our ROI is going to be white blood cells. Throughout this pre-process, image augmentation is going to be done since the contrast augmentation method is skilled to increase the medical image quality [29].

3.Segmentation

Image segmentation is a technique by which an image is divided into totally unique components. It assists with making over the overall type of the enhanced images into a more expressive and clearer image for a framework to additionally investigate. In this manner, the pictures are sectioned alluding to a bunch of consistency measures. A few division strategies have bases like threshold, edge-based, and so on [30]. K-means is one of the easiest algorithms skilled for resolving every kind of clustered issue. moreover, division by k-mean clustering has a few inadequacies. A couple of arbitrary spots are chosen as centroids in k-means technique. We ought to indicate the number of clusters. Adaptive k-mean clustering is used to provide an incredibly further developed division result. The K-Means approach is a multipurpose technique that can be used in a variety of situations. In the arranging step, the position of the k-centroids is very vital since different positions will contribute to different outcomes. The standard K-Means strategy utilizes the erratically picked k-centroids that end up in the ill-advised division. This might prompt temperamental outcomes in image division.

Despite using the standard arbitrarily chosen on k-centroids, this adaptable methodology handles the local's least and most noteworthy characteristics reliant upon the RGB coloring space during the sorting. The further created sorting out strategy yields a two-element bunch with the least and most prominent RGB regards from the whole pixel region. We register the best and least pixel regards for each band of an isolated image inside the ROI. This technique is a cycle-based grouping that yields an ideal worth of starting k-centroids by diminishing the genuine capacity.

The below-mentioned objective function can be used to get the underlying k-centroids:

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

Where α is the Euclidean distance among minimum and maximum RGB values, n is the quantity of image pixels and c is the quantity of bunches.

4. Image Cleaning

It is expected to clean up the image to further develop results. It is accomplished using the area opening methodology, which can wipe out all of the things with a smaller size than the organizing component, which has a round structure, and its size value can be assumed to represent the typical size of items in the image. As a result, the region was opened followed by morphological enlargement. This may fill the unfilled region inside the cell structure and get an unmistakable segregated image. The quantity of the nucleus is determined by marking the associated items.

5. Feature Extraction

This is the most typical method of removing characteristics as descriptors from observable images, as recommended by specialists, and it is also the most appropriate stage for classification. Shape descriptors and the amount of nucleus in the image is utilized for this purpose. Shape descriptors are a group of statistics that can be used to characterize a certain shape. The essential shape descriptors like area, major and minor turn, the edge is utilized.

6. Classification

Classification is a method of assigning a known class to an unknown vector. In this research, feature vectors are used

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to classify whether an individual is infected or not. The most often used classifiers include K-Nearest Neighbor, Decision Trees, and SVM. Each classifier will figure out how to build a required bunch of yields with defended class using a strategy in which there are a number of information sources. A SVM classifier is used in the leukemia conclusion system, and it sorts the images into one of two categories: impacted or not impacted. A double-layer feed-forward network and CNN network are used in addition to SVM. We're curious to see which strategy provides the best results.

A. Support Vector Machine (SVM)

In this classifier, the total input data is parted into 2 sets that are prepared and tested. Preparing data is the learning worldview that will prepare the vectors and update the boundaries. Then again, the test information is used to verify the classifier and approve the classifier execution along these lines. Presently, SVM classifies every lymph cell as intestinal sickness impacted or unaffected relying upon the element

vector got in the component extraction stage. The system is rehashed for each image to prepare and designate the class and produce meriting yield. SVM incorporates numerous characterization strategies like straight, quadratic, spiral, and so on. In a computerized structure, the image tests are isolated into normal and abnormal. For instance, the samples are normal once the WBCs are not experiencing leukemia and abnormal once the WBCs are impacted by leukemia. This likewise assists us with assessing the exactness.

B. Artificial Neural Network (ANN)

A neural network is a tool that makes use of the biological anxious system to trigger and is designed input processing. An ANN is constructed using a number of neurons that are mutually connected. The same neurons act as processing elements and as an integrated unit. ANN is a smart system that learns from images. Learning is the technique of instilling know-how into a neural community to better put together to execute categorization obligations. There are forms of training methods for neural networks: supervised and unsupervised. In this paper, a double-layer feed-forward network is used which gives more accuracy than SVM.

C. CNN Based Recognition System

Figure 5 shows the basic framework of CNN. It is a type of neural network that has been proven to be very effective in identifying and classifying images. Each neuron picks up information, generates dots, and then tracks it indirectly. However, the complete network shows one distinctive function, ranging from unprocessed images to processed images on the other side.

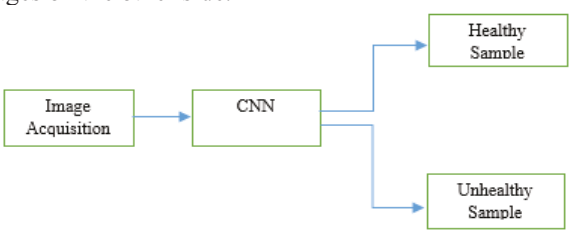

Figure 5. Basic structure of CNN

But these have a loss function in the final layer, however, each technique that we developed here is still adequate. The CNN design creates a certain impression that the information sources are images, which grants us scrambling properties into the design. As a result, the forward function becomes more efficient, and the number of parameters in the network decreases. The CNN network outperforms other categorization algorithms when it comes to grouping.

CNN has a lot of convolutional and pooling layers. The tangled yield is obtained as an actuation map at the point when we give an information image to the principal convolution layer. The convolution layer's filters remove the image's legitimate attributes from the image. Each filter will produce a distinct character to aid in the accurate prediction of elegance. In case we are intrigued to keep up with the size of the picture, we should utilize zero cushioning since it helps to diminish the assortment of attributes. To limit the quantity of characters, pooling layers are utilized. Numerous convolutions and pooling layers are incorporated preceding making the forecasts.

Many unique and advanced characters are extracted in CNN compared to SVM and ANN. The input is flattened and routed in CNN to convert the output into the wide range of categories that the network anticipates. The output layer is then used to create the output, which is then compared against the output layer to determine the error. A single forward and backward flow is termed one training cycle.

The implementation of the submitted work is evaluated by utilizing CNN to have a look at which of these three can provide the best outcomes. A CNN is a form of deep, feed-forward ANN that uses convolutional neural networks with the divergence of a multilayer model designed to minimize pre-processing. In this study, a 2- layered CNN is used. Generally, CNN will work efficiently with a huge quantity of images. But in our study, we have used 120 images and we got an accuracy of about 92.86%. if the quantity of images is increased, then definitely we will get accuracy more than this value.

IV. Experimental Results

In this proposed work, the input database is taken from a standard public benchmark dataset ALL_IDB1. It is publicly open to download the dataset available online [31]. They provide high-quality images. we have used sixty images for training and forty-five images for testing. The proposed technique is assessed with the other existing models and noticed that the submitted technique is more précised and accurate. The microscopic color image of an infected blood cell which acts as an input to our model shown in Figure 6.

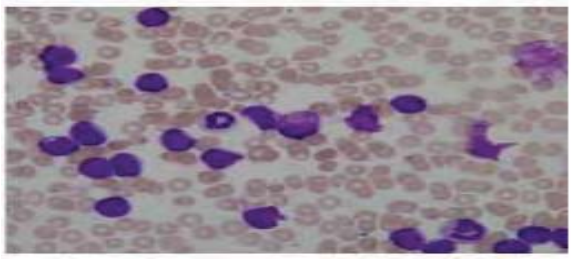

Figure 6. Input Image

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The input image is then subjected to a segmentation process by means of an adaptive k-means algorithm. Thus, in this stage, the nuclei are separated from the image. The output image obtained from the segmentation process is depicted in Figure 7.

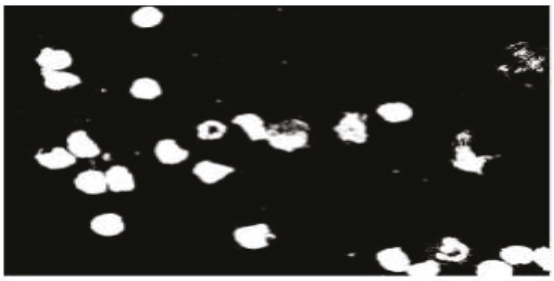

Figure 7. Image after segmentation

Next, image cleaning is carried out. In this stage, we perform two processes: area opening and structural expansion. In this stage, the small objects are filtered out from the focal point of an image. Figure 8 shows the image after the area opening

Figure 8. Image After area opening

The structural expansion uses the elements for expanding the shapes contained in the input image. Here, the pixels are added to the boundaries of objects in the image. The number of pixels added depends on the size and shape of the structuring element that is employed to process the image. The outcome of structural expansion is shown in Figure 9.

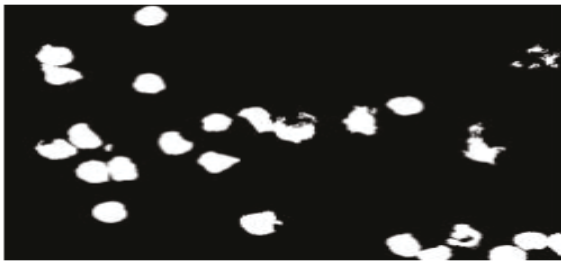

Figure 9. Image After structural expansion

After image cleanup, the feature extraction process is carried out. The basic form descriptors such as area, major and minor axis, the boundary, etc., are applied. Aside from that, the quantity of nuclei in the image sample is counted. The existence of leukemia in the sample will be evaluated in the classification step, and the sample will then be classed as healthy and unhealthy. The classification is accomplished utilizing SVM, ANN, and CNN. The performance of all the three is evaluated based on the parameters like accuracy, error, sensitivity, precision, and specificity. Usually, an image region is said to be positive or negative, depending on the data type. Moreover, a decision for the detected result will be either true or false. So, the prediction will be one of four possible types: true positive (TP), true negative (TN), false positive (FP), and false negative (FN).

Accuracy: It gives the ability of the performance of the whole classifier. It is defined as

$$\text{Accuracy} = \frac{\text{Number of correct predictions}}{\text{Total number of predictions}} \quad (2)$$

Accuracy can also be defined in terms of positive and negative for binary classification as given below:

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (3)$$

Precision: It is described as the ratio of the quantity of true positive observations to the total quantity positive observations

$$\text{Precision} = \frac{TP}{TP+FP} \quad (4)$$

Similarly, we can write the equation for

$$\textbf{Sensitivity} = \frac{TP}{TP+FN} \quad (5)$$

$$\textbf{Specificity} = \frac{TN}{TN+FP} \quad (6)$$

$$\textbf{Error} = \frac{FP+FN}{T} \quad (7)$$

Where T= TP+TN+FP+FN

The Table which describes the comparison between SVM, ANN, and CNN are illustrated below in table 4.1.

TABLE I.
COMPARISON BETWEEN SVM, ANN AND CNN

Rates	SVM	ANN	CNN
Accuracy	0.89	0.92	0.93
Specificity	1.00	1.00	1.00
Sensitivity	0.72	0.83	0.88
Precision	1.00	1.00	1.00
Error	0.10	0.05	0.04

Depiction of measure of performance parameters of SVM, ANN and CNN in 3D Clustered Column is shown below in Figure 10.

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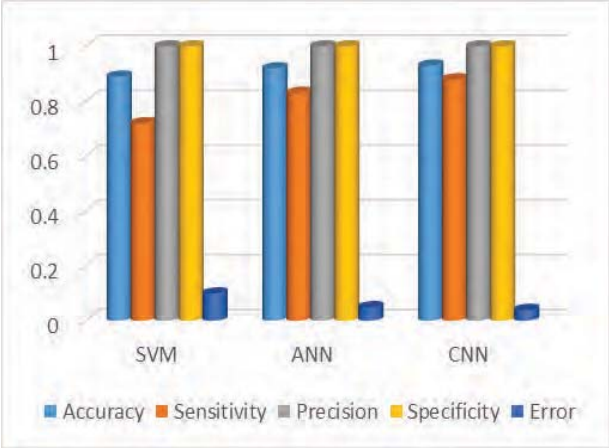

Figure 10. 3D Clustered Column

We can easily observe that CNN yields the best prediction results since it has the highest accuracy, sensitivity, and less error amongst the three approaches.

V. Conclusions

A technique for diagnosing acute lymphoblastic leukemia based on microscopic blood cell images is devised in this study. The diseased area is segmented using adaptive K-means clustering, which is a unique technique. The diagnosis is accomplished by using two techniques. The first uses SVM and ANN, whereas the second uses a DCNN. The finding of leukemia in blood image sample requires more precision.

Along with other parameters, the features like boundaries, region, and the quantity of nuclei recovered from the images will contribute to the accuracy of the projected methodology. As a result, our approach will be able to diagnose and classify input samples with greater precision.

Since it evades the common practice of first segmenting the cells and then the nucleus from an image, the projected methodology will be a watershed moment in leukemia diagnosis. Adaptive K-means clustering is used to separate the nucleus at the initial stage of this work. For flexibility and speed of prototyping image processing options, the proposed methodology is implemented in the MATLAB environment. Along with classifying leukemia into infected and non-infected, this proposed approach investigates classification using SVM, ANN, and CNN and concludes that CNN is a better classifier than the other two for the present research.

It's worth mentioning here that we recorded an efficiency of 89.37% with SVM, 92.16% with ANN and 93.36%. with CNN-based diagnosing technique. Hence, it is observed that CNN based diagnosis technique of Leukemia using microscopic blood cell images is superior because it provides the highest accuracy and sensitivity.

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