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Global and Local Entropy Based Segmentation Model for Detecting Leukemia in Blood Images

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Abstract—The advancement of digital image processing classification is considered an emerging field of disease diagnosis. Various literature concentrated on classification of Leukemia in single white blood cells of smear images. This paper aimed to propose an effective machine learning mechanism for segmentation of leukemia in blood smear. The segmentation is based on estimation of local and global entropy. The proposed technique is stated as Global Local Entropy Histogram Equalization (GLEHE) for classification of leukemia in blood. The GLEHE segments leukemia in blood smear with image histogram. Both global and local features histogram is estimated based on mutual information (MI) for segmentation of blood clot in WBC's. Further, the proposed GLEHE incorporates geometric feature examination for accurate segmentation of leukemia in blood. For experimental analysis, data were collected from AA-IDB2 database. The parameters considered for analysis are TPR, TNR and accuracy. Existing technique NN, KNN, Random Forest, ACNN, SVM, Chrono-SCA_ACNN and DCNN provides 59.01%, 62.04%, 63.2%, 68.12%, 74.9%, 80% and 80.25% of accuracy. However, the proposed GLEHE provides improved accuracy of 84.64%. Simulation results demonstrated that proposed GLEHE exhibits higher accuracy, TNR and TPR rate than existing technique.

***Keywords*—GLEHE, Histogram, Global Entropy, Local Entropy, Mutual Information**

1. INTRODUCTION

Cancer is now widely accepted as a global epidemic without a global cure. In 2017, the global burden of Disease Cancer Alliance estimated that 9.7 million people died of cancer, ranking cancer as second leading death after cardiovascular diseases [1]. In blood cells, leukemia refers to cancer, and leukemia cells are produced by the bone marrow, which is irregular white blood cells. Leukemia is a form of cancer affecting individuals irrespective of era. Major types of leukemia consist of ALL; AML; CLL; CML and common lymphoma [2].

Usually leukemia has been identified by two schemes, French-American-British (FAB) and the WHO [3]. Peripheral blood blast cells and Acute Myeloid Leukemia (AMLs) characterized consist of seven types of blast cells (M1-M-7). The blood under a light microscope is studied microscopically by hematologists. This method is rather tedious, long-term and not sufficient to examine many cells. However, some mathematical methods and techniques for the discrimination of blood cells have been developed and the photo-preparation stage is important for the extraction and identification of leukemia [4].

ALL, which affects a leukocyte community known as lymphocytes. ALL can be fatal if left unchecked due to its accelerated expansion into the bloodstream and vital organs [5]. Early diagnosis of this illness is therefore critical for the rehabilitation of patients, particularly infants. ALL diagnosis is focused on the morphological identification of microscopic Lymphoblasts and the immunophenotypic evaluation of lineage commitment and flow cytometry stage of growth [6]. The classification of leukemia can be viewed as a daunting task, as the RBCs/platelets can be detected in organs. Microscopic blood smear Images of human blood have recently been observed for examination [7]. For the proper recognition of the subclass, the multiclass environment needs to be created. The primary role of the tumor is to segment the WBC from microscope images of blood sources. Blood images are primarily influenced by the tumor [8]. This role is either manually segmented or automatically segmented. While affected by leukemia, the nucleus in the WBC displays substantial shifts in character and hence nucleus region is isolated from WBC [9]. Due to the presence of human labor, it is difficult to carry out nucleus segmentation from WBC by manual process, vulnerable to mistakes, and time consuming. Also, experts use specialized devices, which can not be implemented in rural areas, for manual segmentation. Also, manual nucleus segmentation requires skilled supervision. Automated segmentation methods have been developed in recent years to

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overcome these problems. Automated segmentation as initial step, as most images have different sizes and forms, requires preprocessing [10].

Appropriate characteristics are extracted from images after segmentation via the advanced clustering or other classification. The image is taken from various image characteristics, such as Gradient Histogram (HoG), edges, texture features, geometric characteristics and statistical features [11]. Different methods, such as image sharpening, contrast correction, and noise reduction, require pre-processing. For conducting the segmentation, certain methods may prefer image enhancement. Various methods, such as manual thresholding, FCM, OTSU binarization and AC carry out image segmentation [12]. Most researchers prefer the Active Contour (AC) segmentation model since it distinguishes the image by initializing the curve to prevent information loss during image segmentation. Using the unsupervised clustering process, FCM performs the segmentation [13].

This paper, proposed a Global Local Entropy Histogram Classifier (GLEHE) for accurate segmentation of leukemia in blood. The proposed approach incorporates segmentation using MI with FCM for improved segmentation performance. The proposed GLEHE estimates the global and local entropy of image for elimination of noises. In next phase, geometric features of image are estimated for histogram normalization. Through proposed GLEHE Leukemia can be identified effectively. The comparative results stated that proposed GLEHE exhibits improved TPR, TNR and accuracy than existing technique. Paper is organized as: In section II existing literature conducted based on classifier is presented and described challenges in existing techniques. In section III research method adopted for proposed GLEHE is presented with architecture diagram with other segmentation and entropy estimation. In section IV overall simulation setup for proposed GLEHE is presented along with comparison. Finally, overall conclusion about proposed GLEHE is stated.

2. RELATED WORKS

The literature on the diagnosis of leukemia is discussed in this section. **Khashman and Abbas** [14] using images from ALL database, NN based method for detection was developed. The method used extraction steps for local features and thus reduced the time during classification. From the image tests, the NN-based scheme failed to resolve distinct forms of leukemia. **Patel and Mishra**[15] developed an SVM classifier for detection of leukemia in blood images. This technique examines the microscopic images and performs manual detection of leukemia. **Mishra S. et al.,** [16] developed a KNN classifier for addressing multiple problems in tumor detection. The proposed provides higher exactness with reduced accuracy. **Srisukkham et al.,** [17] developed a Random Forest classifier with hybrid segmentation. This classifier is utilized for better geometric feature identification for medical diagnosis. **Li et al.,** [18] developed a ACNN with thresholding for blood smear image segmentation. **Zhao et al.,** [19] proposed DCNN for image segmentation and classification. The proposed DCNN uses RF for classification but it fails to detect all white blood count. **Jha K. K and Dutta H. S** [20] developed a Chronological SCA based Deep CNN classifier. Study indicates that proposed classifier has progressed relatively well and identifies bloodstream images for leukaemia.

In existing leukemia detection different classifier subjected to distinct challenges those are stated as follows:

• Leukemia cells are identified manually and time intensive. Some researchers have developed statistical methods for leukemia detection but have had trouble discriminating against blood cells [17].

• Segmentation methods evolved in last few years are focused on differentiation, the segmentation of nuclei as well as cytoplasm region. Segmentation provides important diagnostic characteristics and hence it is important to pick main characteristics for classification from segmented images [5].

• In [19], For automated cell sorting, RF-based technology has been introduced, although the technique does not separate any of WBC from blood smear images.

• An review of current literature in general reveals that the use of several classification features increases training time of a classifier and hence the deep learning schemes must be adopted to make full use of features derived from segmented images. Motive is to look at the inconveniences of existing leukemia detection.

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2. PROPOSED ENTROPY SCHEME FOR SEGMENTATION OF LEUKEMIA IN BLOOD

This section defines proposed GLEHE for leukemia segmentation from single smear blood images. Initially, the proposed GLEHE involved in segmentation of smear images of blood through MI with identification of nucleus and WBC's.

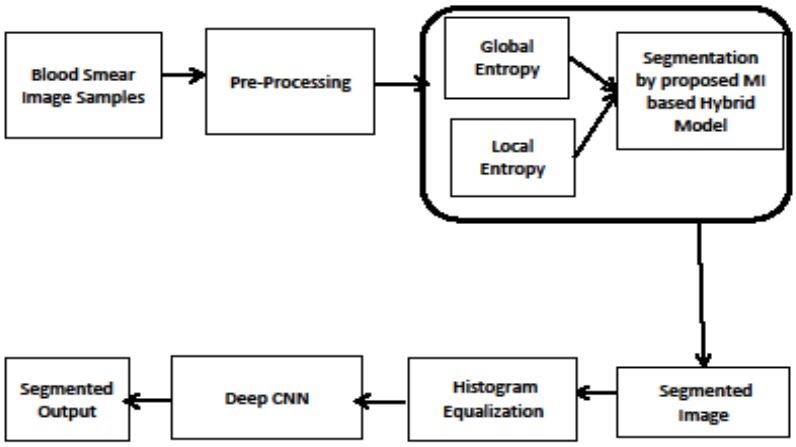

Fig.1 Overall Architecture of Proposed GLEHE

The components of images are estimated based on the global and local entropy. Based on the estimated entropy the deep learning network is trained with feature parameters. Finally, the segmented output gives detected leukemia in blood.

The single cell blood smear samples in archive are sent for pre-processing, where photographs are resized, as seen in figure 1 above. Proposed MI-based hybrid model is pre-processed and parts of heart and cytoplasm region of sample are segmented on preprocessed imaging. This model utilizes MI for segmentation of AC samples as well as FCM. GLEHE Deep CNN classifier suggested estimates and executes segmentation optimum weights for the Deep CNN.

2.1 DEEP CONVOLUTIONAL NEURAL NETWORK FOR SEGMENTATION OF BLOOD CLOT

On a broad natural image database with 1000 categories, called ImageNet, CNNs pre-trained the network. There are also photos of lymphocytes and lymphoblasts within these groups in the database. GLEHE incorporates AlexNet for classification of leukemia in blood images. These models have similar structure, and difference lies in convolutional layer and neuron size. The description about incorporated AlexNet is stated as follows:

Alexnet: This is architecture for ILSVRC-2010 competition to carry out training as well as classification of in-built ImageNet database. In this research with pre-trained model ALL-IDB2databse is utilized for processing. It contains 8 trained layers, 5 convolutional layers with filters image size of 5 × 5 and 7 × 7, followed by 3 fully-connected layers, as well as max-pooling layers. The image above the filter size is not considered for analysis, this will impact the accuracy of the system. In figure 2 CNN network utilized for training and testing of neural network is illustrated.

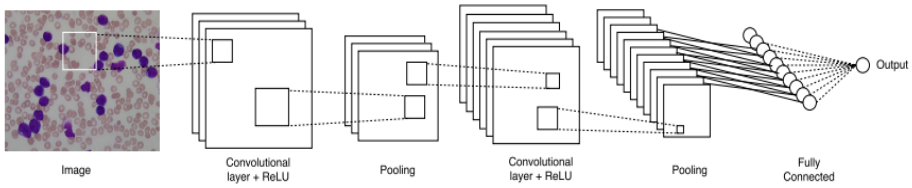

Fig 2: Architecture of CNN

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3.2 MI SEGMENTATION AND FCM CLUSTERING FOR GLEHE

The proposed GLEHE includes MI for identification of parameters with FCM classifier for segmentation of blood clots. The FCM algorithm uses the fugitive components to measure the cluster centers and split. By reducing number of distances between objects as well as corresponding cluster core, FCM clusters data into classes. Dimension of FCM method is stated in equation (1).

$$F = \{F_1, F_2, \ldots\ldots, F_{h,\ldots\ldots,} F_z\} \tag{1}$$

Clustering is happens based on objective function *F*, and function is considered as less issue, and it is shown in equation (2),

$$M_{\mu} = \sum_{i=1}^{q} \sum_{h=1}^{r} d_{ih}^{\mu} \times E_{ih} \tag{2}$$

Where, $E_{ih} = \left\| e_i - F_h \right\|$. The cluster centers are evaluated based on MF using equation (3),

$$F_h = \frac{\sum_{i=1}^{u} d_{ih}^{\mu} . e_i}{\sum_{i=1}^{u} d_{ih}^{\mu}} \tag{3}$$

FCM technique carries out task until segmenting all images as well as segmented images are shown as, $Q_{u,v}^{FCM}$.

Here, the proposed GLEHE uses Mutual Information (MI) for segmentation with this nucleus and WBC's are identified. For effective classification of image components MI is designed based on consideration of certain selection conditions. The segmentation of proposed GLEHE is examined based on the consideration of following equation (4).

$$Q_{u,v} = \begin{cases} Q_{u,v}^{A}; & if\ Q_{u,v}^{A} == Q_{u,v}^{FCM} \\ M; & if\ Q_{u,v}^{A} \neq Q_{u,v}^{FCM} \end{cases} \tag{4}$$

Where, $Q_{u,v}^{A}$ is segmentation output and $Q_{u,v}^{FCM}$ is FCM. By setting MI criteria, the term M refers to segment achieved. Above equation states that suggested hybrid MI model equates pixel values in MI and FCM segments, and if pixel values are same, the section will be taken into account. If not, the range would differ according to the MI criteria M. MI for both FCM and AC segments is determined for measurement M. The MI in the image specifies the proximity to the other pixel and thus it is more fitting to consider the image with a high MI value. MI of AC is estimated with following equation (5):

$$M^{A} = MI\left(Q_{u,v}^{A}\right) \tag{5}$$

Where, $MI\left(Q_{u,v}^{A}\right)$ is MI segments from AC, and it is estimated by applying two windows W_1, W_2. Window size W_1 is 3 × 3, and window size W_2 is 4 × 4. Standard formula for MI estimation is based on equation (6),

$$MI(W_1, W_2) = E(W_1) + E(W_2) - E(W_1, W_2) \tag{6}$$

Where, $E(W_1)$ refers to entropy of window W_1, and $E(W_2)$ indicates entropy of window W_2. Term $E(W_1, W_2)$ signifies joint entropy of windows (W_1, W_2). Expression for global entropy and local entropy features with joint probability is represented in equation (7) and (8),

$$E(W_1) = -\sum_{u} pw_1(u) \log pw_1(u) \tag{7}$$

$$E(W_1, W_2) = -\sum_{u,v} p_{w_1, w_2}(u, v) \log pw_1 w_2(u, v) \tag{8}$$

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Where, $pw_1(u)$ refers to conditional probability. Similarly, MI segments value from FCM is estimated and it is represented in equation (9),

$$M^{FCM} = MI\left(Q_{u,v}^{FCM}\right) \tag{9}$$

Finally, MI criterion for segmentation M is estimated as using equation (10),

$$M = \begin{cases} Q_{u,v}^{A}; & if\ Q_{u,v}^{A} == Q_{u,v}^{FCM} \\ Q_{u,v}^{FCM}; & \text{else} \end{cases} \tag{10}$$

The following formula notes that hybrid model proposed preserves segments with largest MI and segments from hybrid model dependent on the MI proposed which is represented as F = {F1, F2}.

3.3. GLEHE FOR HISTOGRAM BASED SEGMENTATION IN BLOOD CELLS

Histogram of image provides color balance of blood clot images for identification of clots in human. Once the global entropy and local entropy are estimated then the histogram is estimated for elimination of noises in the image pixels. The intensity distribution of images for identification of leukemia in blood images. The intensity distribution is denoted using equation (11)

$$S_1^{k.c} = \left[D_G^{red} \quad D_G^{green} \quad D_G^{blue}\right] = D\left[Q_{u,v}^{R}\right] \tag{11}$$

where, κ ∈ {1, 2}, S[F _x0005_ u,v] is histogram of κ^{th}segment belongs to v^{th} image and Sred G , S green G , and Sblue G is histogram probabilities of red, green, and blue. Further, to estimate leukemia in blood other geometric features are calculated in proposed GLEHE. With incorporation of geometric features accurate classification of leukemia in smear images. Estimation of geometric features of images is calculated based on consideration of following basic parameters such as mean, variance and standard deviations.

Mean: Statistical data in image is defined by mean parameter and it is represented in equation (12) ,

$$D_2^{k.c} = \eta = \frac{1}{p} \times \sum_{b=1}^{p} Q_{u,v}^{R.p} \tag{12}$$

Where, P shows dimension with size of (∃ 1 × ∃ 2) and F _x0005_, P u, v denotes pixel count in κ^{th}segment of j^{th} image.

Variance: The variance also contains predictive evidence and is thus calculated based on the mean value. It is represented in equation (13),

$$D_3^{k.c} = \frac{\sum_{b=1}^{p}\left(Q_{u,v}^{R.c} - \eta\right)}{P} \tag{13}$$

Where, η denotes mean of segment.

Standard Deviation: It calculates the variance by the pixels in the section and is very precise because the data distribution is not affected using equation (14).

$$D_4^{k.R} = \sqrt{\frac{\sum_{b=1}^{p}\left(Q_{u,v}^{R.P} - \eta\right)^2}{P-1}} \tag{14}$$

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Algorithm 1: Proposed GLEHE for leukemia segmentation

Begin
Select each element in image from C_o- 0; where o =1
Examine every image $c \in C_{o,}$ where, $\mu k(o,c) > 0 - Q$
while $Q = \varphi$
do
eliminate entropy c *from set of entropy present in* Q
$fval \leftarrow \max_{d \in c_0} [\min(f_0(d), \mu_k(c,d))]$
if $f_{val} > f_o(c)$ *then*
$f_o(c) \leftarrow f_{val}$
evaluate entropy of image
$\mu_k(c,e) > 0; f_{val} > f_0(e) f_{val} > f_0(e)$ *and* $\mu_k(c,e) > f_0(e)$
endif
endwhile
end
Select each histogram element in image from C_o- 0; where o =1
examine $o - Q$
while $Q = \varphi$
if $f_o(c)$ *is maximal remove voxel Q*
for each histogram in image $\mu_k(c,e) > 0$
do
$f_{val} \leftarrow \min(f_0(c), \mu_k(c,e))$
if
$f_{val} > f_0(e)$ *for* $f_0(e) \leftarrow f_{val}$
Estimate every histogram Q in every element e
endif
endfor
endwhile
end

4. RESULTS AND DISCUSSION

The findings obtained by the GLEHE proposed for leukemia classification are seen in this section. The work takes images from the ALL-IDB2 site into consideration.

4.2 DATABASE DESCRIPTION

ALL-IDB2 Database gathers single blood cell samples for the study of the proposed GLEHE. The ALL-IDB2 database includes a broad group of cropped regular and blast cell segments. Almost similar to the ALLIDB1, but with large dimensions, are the grey level properties of the ALL-IDB2 database. The database comprises of 442 images in those 203 is utilized for training and 239 is utilized for testing.

4.3 PERFORMANCE METRICS

Performance of proposed GLEHE is estimated based on metrics, such as accuracy, TNR and TPR.

Accuracy: It defined closeness of classification made by classifier as represented in equation (15).

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN} \tag{15}$$

TPR: It calculates positive samples found correctly by GLEHE represented in equation (16).

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$$TRP = \frac{TP}{TN + FP} \tag{16}$$

TNR: It calculates negative samples correctly rejected by GLEHE stated in equation (17).

$$TNR = \frac{TN}{TN + FP} \tag{17}$$

Dice Coefficient:

Dice similarity coefficient (DSC) or Dice coefficient is defined as performance measure used to measure segmented region results and ground truth value. The DSC is computed using equation (18) as follows:

$$DSC = \frac{2TP}{(FP + 2TP + FN)} \tag{18}$$

4.4 COMPARATIVE METHODS

This research considers following works for comparative analysis: NN[14], KNN [16], Random Forest [17], ACNN [20], SVM [15],Chrono-SCA_ACNN [20], and DCNN [19] .The above mentioned techniques are comparatively examined with proposed GLEHE.

4.5 SIMULATION RESULTS

After segmentation process outer portion are evaluated for extraction of features. In truth, even zero pixels are known to be very different from true feature values. Using a new method for estimating the function using the previously determined binarymask, the problem can be solved by measuring the amount of background pixel and discharging it from the histogram and the feature measurement. In figure 3 input image provided for analysis of proposed GLEHE is presented.

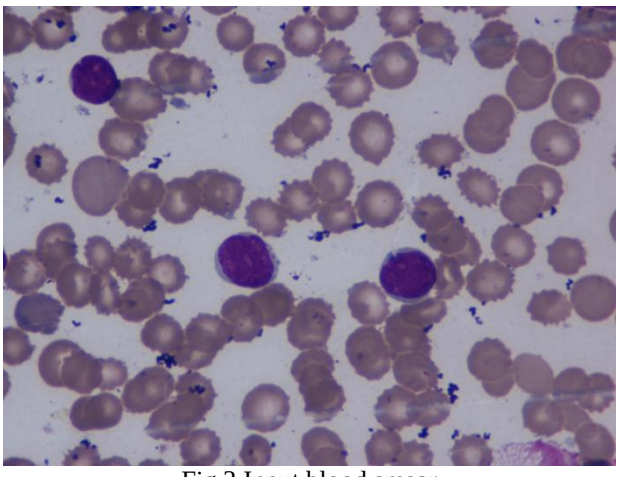

Fig.3 Input blood smear

In figure 4, entropy estimated for input image is presented after processing through MI for estimation of components in input images sequences.

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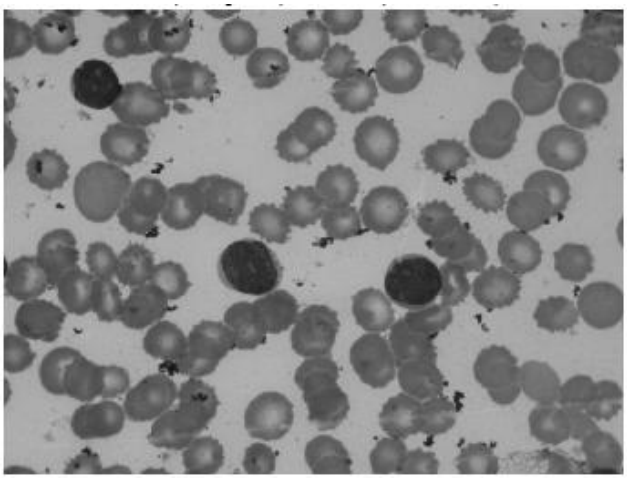

Fig.4 Entropy Estimated Image

For the segmentation of leukemia by one subsample for the validation of the model and the remaining samples of k-1 per period for the training results. Finally, the 10 folds provide an average output to meet a single prediction. Once the prediction of the instances expected by the classification model is accomplished, the accuracy can be assessed by comparing the actual class of instance, in which the class predicted in the segmentation model for a certain WBC is compared to that assigned by the expert hematologist. In figure 5 background estimated image for identification of clot is presented. Similarly, in figure 6 highlighted region for estimation of leukemia is illustrated as follows.

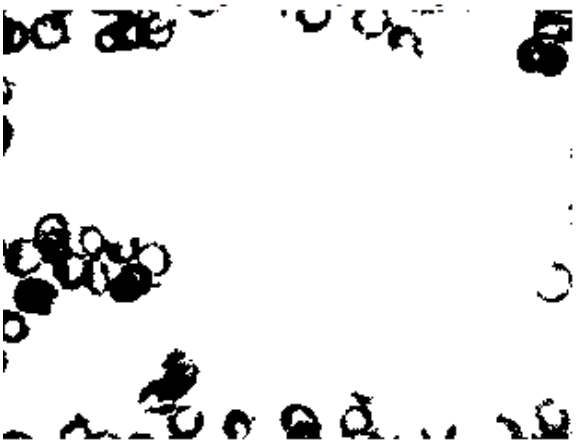

Fig.5 Histogram Normalized with GLEHE

Fig.6 Histogram of segmented Leukaemia with GLEHE

The instances of leukemia impacting the WBCs were described as positive and the correct value was determined from the WBCs without leukemia and dependent on the description. Although accuracy is the most commonly used metric, it is equally important for any class. The estimated entropy based

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classification is involved in estimation of correct classification of positive instances. For this purpose, sensitivity value is used. In table 1 time required for segmentation of cancer are presented.

Table I. Segmentation Time for GLEHE

Dataset Image	Size(Pixels)	Time for Segmentation (sec)
1	150x220	9.56
2	240x210	11.45
3	220x290	10.73
4	145x230	7.3
5	240x470	13.26

The segmentation time measured for proposed GLEHE with consideration of different dataset images are presented. The analysis stated that proposed GLEHE exhibits minimal segmentation time for identification of Leukemia in WBC's. In table II presented about TPR measured for proposed GLEHE comparatively with existing techniques. In figure 7 comparison of TPR is presented along with existing techniques.

Table II. Analysis of TPR for different validation

K-fold	NN	SVM	KNN	Random Forest	ACNN	DCNN	Chrono-SCA-DCNN	Proposed GLEHE
4	61	62	64	69.4	72.7	78	82.6	86
5	63	65	69.7	74	79	80	87	89
6	66	72	76	78	83	84	85	89
7	69	75	80	84.6	86	87	88	90
8	75	79	81.6	84.2	88	88	89	91

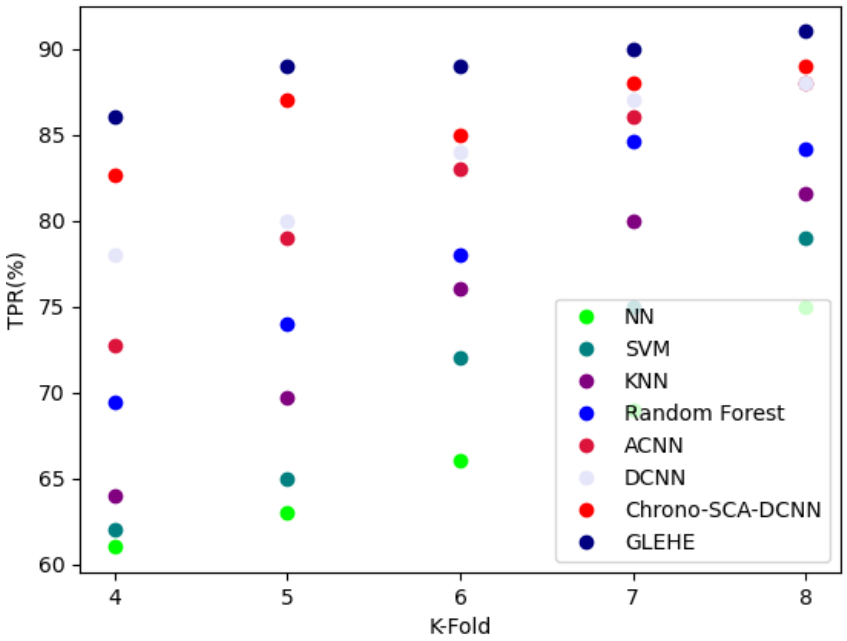

Fig.7 Comparison of TPR

Through analysis it is observed that enhance in k-fold value increases the TPR of proposed GLEHE. Among existing technique Chrono-SCA-DCNN provides higher value than conventional NN,

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SVM, KNN, Random Forest, ACNN and DCNN. However, the proposed GLEHE exhibits improved performance than existing techniques. In table 3 comparison of TNR is presented.

Table III. Analysis of TNR for different validation

K-fold	NN	SVM	KNN	Random Forest	ACNN	DCNN	Chrono-SCA-DCNN	Proposed GLEHE
4	56.8	58	61.2	71.2	77	83	85	89
5	53	61.6	66	74	76	84	86	87
6	55.6	67.3	70	76	81	86	87	88
7	57.8	74.2	75	77	80.6	85.5	88	89
8	58.8	80	83	85	86	88	89	90.2

The figure 8 TNR is comparatively analyzed for proposed GLEHE with existing NN, SVM, KNN, Random Forest, ACNN , DCNN and Chrono-SCA-DCNN.

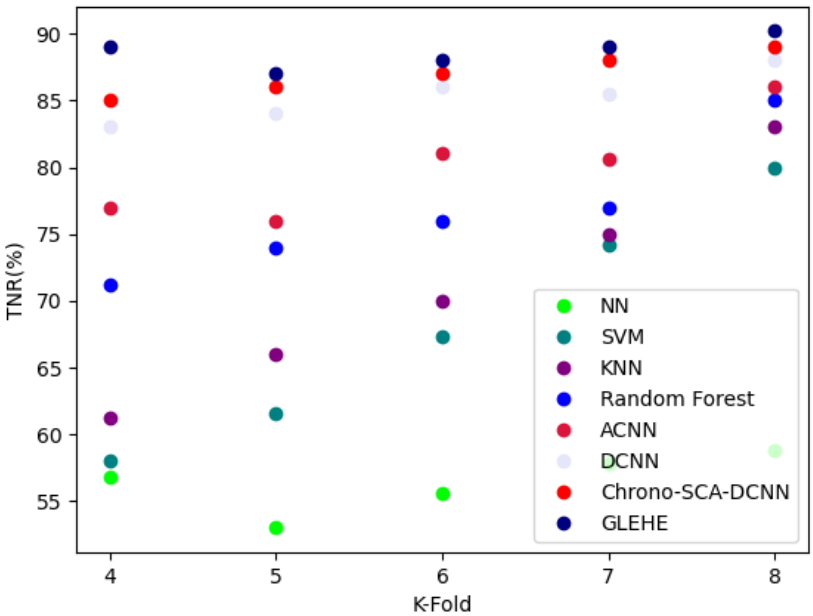

Fig.8 Comparison of TNR

The analysis of results stated that proposed GLEHE provides higher TNR rate rather than existing technique. The comparative analysis stated that estimation of global and local entropy of image increases the segmentation accuracy of proposed GLEHE. In table IV comparison of accuracy for proposed GLEHE with existing techniques are presented. Similarly, in figure 9 comparison of proposed GLEHE with existing technique are plotted.

Table IV. Analysis of Accuracy for different validation

K-fold	NN	SVM	KNN	Random Forest	ACNN	DCNN	Chrono-SCA-DCNN	Proposed GLEHE
4	45	49	53	62	69	71	74	79
5	52.34	56.2	61	65.7	71.34	73.65	77.26	80
6	64.2	66	63.60	68.5	74.63	81.26	82	84.6
7	65	69	67.29	70.83	78.49	88	83	89
8	69	70	71.2	73.6	81.1	86.3	85	90.6

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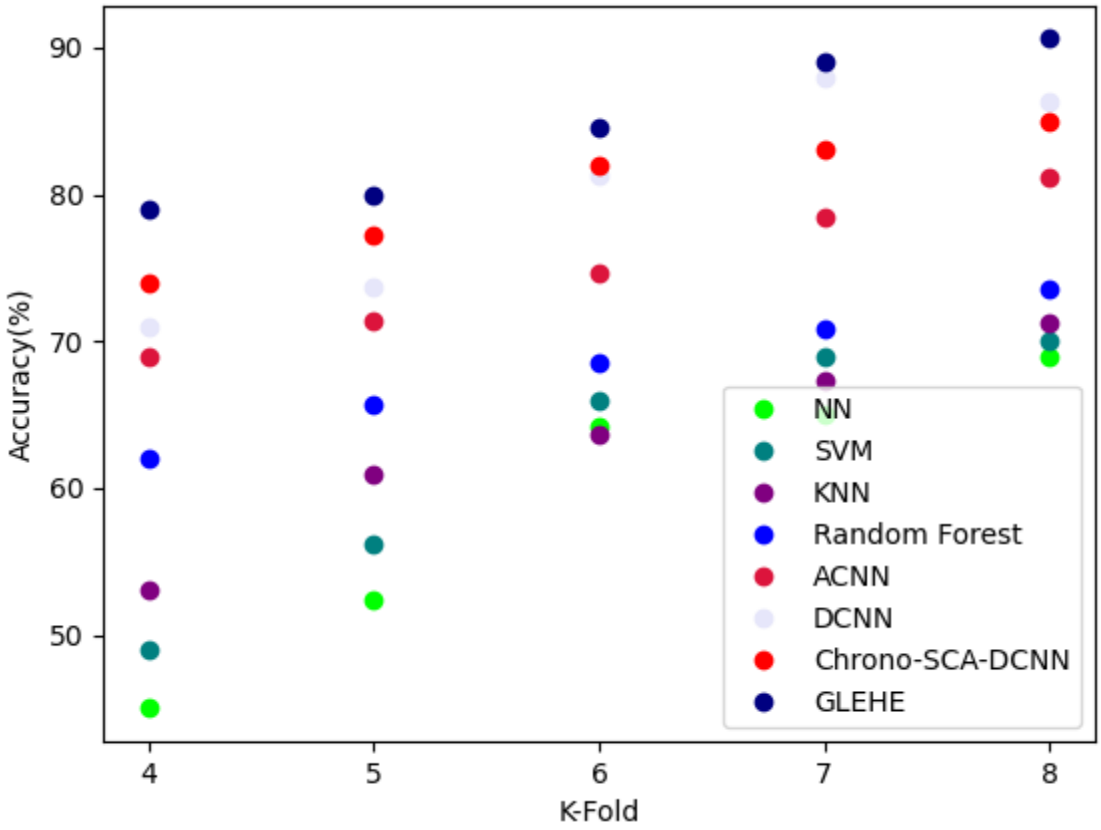

Fig.9 Comparison of Accuracy

The comparative analysis of proposed GLEHE exhibited that, accuracy measurement of proposed GLEHE is significantly higher than existing techniques. The proposed GLEHE utilizes global and local entropy which eliminates the noises and histogram normalization estimates the variation in components, this leads to increase in accuracy of proposed GLEHE. In table V, overall comparison of proposed GLEHE with NN, SVM, KNN,RF, ACNN, DCNN and Chrono-SCA-DCNN is presented.

Table V. Overall Comparative Analysis

Methods	**Dice Coefficient**	**TPR %**	**TNR %**	**Accuracy%**
NN	77.67	66.8	56.4	59.1
SVM	79.45	70.6	68.22	62.04
KNN	81.34	74.2	71.04	63.2
Random Forest	83.56	78.04	76.64	68.12
ACNN	82.56	81.7	80.12	74.9
DCNN	84.92	83.4	85.3	80
Chrono-SCA-DCNN	83.56	86.3	87	80.25
Proposed GLEHE	86.57	89	88.6	84.64

The existing technique NN, SVM, KNN, RF. ACNN, DCNN and Chrono-SCA-DCNN provides the accuracy of 59.01%, 62.04%, 63.2%, 68.12%, 74.9%, 80% and 80.25% respectively. However, the proposed GLECH provides accuracy value of 84.64% which is approximately 4% higher than that of other technique.

In figure 10 comparative analysis of proposed GLEHE in comparison with existing is illustrated.

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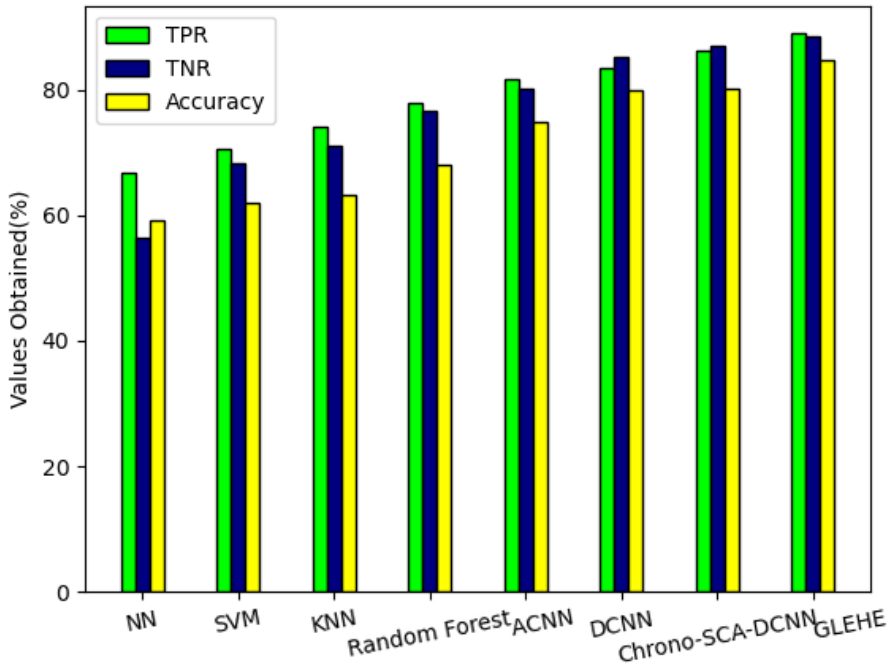

Fig.10 Overall Comparison

The comparison of proposed GLEHE with existing technique is based on the consideration of higher values. The performance evaluation of proposed GLEHE exhibits higher TPR, TNR and accuracy value than existing NN, SVM, KNN, Random Forest, ACNN, DCNN and Chrono-SCA-DCNN. The analysis confirmed that proposed GLEHE exhibits improved performance.

5. CONCLUSION

This study incorporates the methodology of segmentation of leukaemia, to evaluate blood cells effectively. The proposed GLEHE involved in two stage process like estimation of entropy and histogram Equalization. The proposed GLEHE estimate the global entropy and local entropy of image for elimination of noise. At first, the proposed GLEHE involved in segmentation of image using FCM. In next stage, based on estimation of geometric features histogram of image is estimated for background elimination for increasing performance accuracy of proposed GLEHE. The analysis of results illustrated that proposed GLEHE exhibits improved performance in terms of higher TPR, TNR and accuracy then NN, SVM, KNN,RF, ACNN, DCNN and Chrono-SCA-DCNN classification techniques. The proposed GLECH exhibits 89%, 88.6% and 84.64% for TPR, TNR and accuracy respectively.

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