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A Deep Learning–Driven Framework For Automated Segmentation Of Acute Leukemia In Peripheral Blood Smear Microscopic Images

Dr. N. Sandhya[1] , Dr.K.Nandhini[2] , Ramya Selvaraj[3] , R. Naveenkumar[4] , Ishita Mishra[5] , Dr.B.Senthilkumaran[6] , Dr. Elavarasan K[7]

[1]Professor, Department of CSE-AIML&IoT, Vallurupalli Nageswara Rao Vignana Jyothi Institute of Engineering &Technology, Bachupally, Hyderabad, India. Email: sandhyanadela@gmail.com https://orcid.org/0000-0003-4962-2647
[2]Associate Professor, CSE(AI&ML), Sridevi Women's Engineering College, Hyderabad, nandhukk28@gmail.com 0009-0002-9814-6499
[3]Assistant Professor, Department of Community Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Chennai, Tamil Nadu, India Email Id: ramyas.smc@saveetha.com Orcid Id: 0000-0002-3613-2115
[4]Dept of CSE, School of Engineering and Technology, CGC University Mohali-140307, Punjab India. drnk1983@gmail.com 0000-0001-9033-9400
[5]Grade 12, Student at Excellence College, Hyderabad, Telangana India. Email: Ishitamish10@gmail.com
[6]Associate Professor, Department of Computer Science and Engineering, Vel Tech Rangarajan Dr.Sagunthala R&D Institute of Science and Technology Chennai. skumaran.gac16@gmail.com Official: drsenthilkumaranb@veltech.edu.in 0000-0002-7111-1950
[7]Assistant Professor, Department of Mathematics, Vel Tech Rangarajan Dr.Sagunthala R&D Institute of Science and Technology, Chennai, India. Official Email id: drelevarasank@veltech.edu.in / elavarasank2@gmail.com

Abstract: Early detection of acute lymphoblastic leukaemia symptoms can considerably improve patient's health condition. Detection or diagnosis of disease at the earlier stage is necessary for treating the patient. The microscopic image analysis requires subject experts and medical professionals. To meet the need, research on leukaemia has done by diverse scientist and the computational algorithms utilised for image analysis are highly influenced by the certain complexities. Occurrence of noise and blur edge portion necessitates diversified segmentation technique. Image segmentation is a way of breaking down an image information into several subdivisions that is determined as Image segments in order to reduce the image's complexities and make future processing or evaluation easier. This article research article focusses on the process of segmentation and the complexity is minimized by deep learning based convolutional neural network (CNN). The performance of the CNN is compared is compared with existing state-of-art technique whereby the CNN outperforms existing approaches.

Keyword: Segmentation, neural network, activation function, leukaemia, pre-processing, and accuracy.

1. Introduction

Leukaemia is a cancerous tumour that affects both the blood and bone marrow. The creation of abnormal white blood cells in the human body causes leukaemia. Blood is a liquid that is made up of millions of cells that consists of Red Blood Cells (RBCs), White Blood Cells (WBCs), Platelets, and Plasma, which are all components of blood cells. It helps to transport water and nutrients to the tissues [1]. Leukaemia can be classified in one of two ways: It can be characterised as acute or chronic based on how quickly the cells proliferate. Acute leukaemia is characterised by the rapid growth of abnormal white blood cells, and it is the most prevalent kind seen in children [2].

The blast cells in chronic leukaemia proliferate slowly. It is most common among the elderly, but it can afflict people of any age range [3]. Second, leukaemia is categorised as lymphoid or myeloid based on the type of white blood cells (WBC's) that have transformed into malignant cells. Leukaemia is divided into four forms based on these categories: acute lymphoblastic leukaemia (ALL), acute myelogenous leukaemia (AML), chronic lymphocytic leukaemia (CLL), and chronic myelogenous leukaemia (CML). Diverse categories of leukaemia and their description is given in Table 1 [4].

Table 1. Categories of Leukaemia

Cell Growth	Type of WBCs	Category	Description
Acute	lymphoid	Acute Lymphoblastic Leukaemia (ALL)	It is the most prevalent type of cancer found in children. In this case, the lymphocytes cannot fight against infection and they proliferate rapidly
	Myeloid	Acute Myeloid Leukaemia (AML)	It is a more common type of leukemia occurring in both men and women. In this case, large numbers of myeloid cells are produced
Chronic	lymphoid	Chronic Lymphocytic Leukaemia (CLL)	It frequently occurs in men of age group in 60s. It seldom occurs in children. In this case, lots of lymphocytes are produced and they grow slowly
	Myeloid	Chronic Myeloid Leukaemia (CML)	It is frequently found in adults of 50 year age group but rarely seen in children. In this case, large number of myeloid cells are produced

In the diagnosis of leukaemia, visual inspection of peripheral blood samples is an essential diagnostic. In telemedicine applications, automated systems based on computer vision algorithms can speed up this procedure while also improving accuracy and uniformity of response. The microscopic examination of peripheral blood is one of the phases in diagnostic methods for ALL detection [6]. White cells with abnormalities owing to the presence of malignancy are inspected.

Analysis has been done by skilled human workers for decades, who primarily do two types of analysis: cell categorization and cell counting. The crucial and fascinating aspect of this morphological examination of peripheral blood smears is that it does not require a blood sample because it may be completed with only one image. As a result, the approach is appropriate for low-cost, high-accuracy automatic detection system. Computerized and specialized tests namely immunophenotyping and cytogenetics, as well as morphological cell categorization performed by trained operators using blood/marrow microscopy images, may now be used to diagnose leukaemia. Those approaches aren't used in large-scale screening programmes, and they're only used when typical symptoms show up in a normal blood test [7, 8].

Subject expertise and medical professionals are required for microscopic image analysis [9, 10]. To fulfil the need, several scientists have conducted study on leukaemia, and the computer techniques used for image investigation are heavily impacted by specific complexity. The presence of noise and blurry edge portions demands the use of a multi-segmentation approach. Image segmentation is a method of breaking down an image's information into numerous subdivisions, known as Image segments, in order to decrease the image's complications and facilitate subsequent processing or assessment. The complexity of the segmentation process is lowered by using a deep learning-based convolutional neural network in this research report (CNN). The CNN's performance is compared to existing state-of-the-art techniques, and the CNN outperforms previous methods.

The remainder of the article is organized as follows: related works in leukaemia detection is given in Section 2, proposed segmentation and its methodology is given in Section 3, segmentation results are discussed and illustrated in Section 4, and the article is concluded with future research suggestion in Section 5.

2. Segmentation of Leukaemia Lymphocytes

Image segmentation is an essential step in medical image analysis pipelines, in which the main goal is to cut an input image into semantically relevant, and sometimes anatomically corresponding, pathologically relevant, regions. Segmentation accuracy also plays a significant role in determining the accuracy of future analysis activities which may include feature extraction, disease classification and clinical decision support. Hence, a powerful segmentation process is needed to clearly outline image structures and maintain spatial continuity and contextual data. In the given paper, a self-structured feed-forward Convolutional Neural Network (CNN) with the application of deep learning is utilized to perform segmentation. The architecture proposed has a total of nine computation layers with the first six of those layers conducting feature extraction using convolution and pooling algorithms, and the other three layers conduct high-level representation learning using fully connected layers. The general architecture aims to learn hierarchical spatial characteristics that can be used to make proper segmentation to medical images.

CNN Architecture for Segmentation

The suggested CNN architecture receives the medical image input and processes this input by various convolutional layers capturing local spatial patterns and structural correlation between neighboring pixels in a progressive way. The network structure consists of the following steps:

1. **Input Layer**
2. **Convolution Layer 1**
3. **Pooling Layer 1**
4. **Convolution Layer 2**
5. **Pooling Layer 2**
6. **Convolution Layer 3**
7. **Pooling Layer 3**
8. **Fully Connected Layer**
9. **Output Layer**

The convolution and pooling layers are performed in the order to obtain low-level, mid-level, and high-level visual features. These layers acquire discriminative spatial patterns to discriminate target and anatomic parts in the background structures.

Convolutional Layer

Convolutional layer is the fundamental element of the CNN architecture. Strong spatial correlations between neighboring pixels are common in medical images because the continuity of anatomical structure defines the continuity of medical image. The convolutional operation capitalizes on this correlation by imposing filters, which are to be learnt, on the local areas of the image. Each filter analyzes the image by sliding the window mechanism and computing feature activation which captures the spatial patterns in the form of edges, textures or structural contours.

Assume that the input image is a nxn dimensional matrix and the filter size is fxf. The convolution operation produces a feature map that highlights regions where the filter pattern matches the local pixel arrangement. Multiple filters are applied in each convolutional layer in order to capture different feature representations. If a convolutional layer contains Nfilters, then Nactivation maps are generated. These activation maps are stacked along the depth dimension to form the output tensor of the convolutional layer. The dimensionality of the resulting feature maps depends on several parameters including padding, stride, and kernel size.

Padding (P)

During convolution, the spatial dimension of the image tends to shrink because the convolution kernel cannot be centered on border pixels without exceeding image boundaries. However, edge regions may contain clinically significant information. To address this limitation, padding is applied by surrounding the input image with additional pixels whose values are typically set to zero.

Padding ensures that:

- Boundary pixels are included in convolution operations.
- Spatial information at image borders is preserved.
- Output feature map dimensions remain consistent with the input dimensions when required.

Stride (S)

Stride represents the number of pixels by which the convolutional filter moves across the image during each operation. A stride value greater than one causes the filter to skip certain positions, thereby reducing the spatial resolution of the output feature map and decreasing computational complexity.

Given an input image of dimension $n \times n$, kernel size $f \times f$, padding P, and stride S, the spatial dimension of the resulting feature map after applying a single filter can be computed as:

$$\left\lfloor \frac{n + 2P - f}{S} + 1 \right\rfloor \times \left\lfloor \frac{n + 2P - f}{S} + 1 \right\rfloor$$

If Nfilters are applied in the convolutional layer, then the total number of output feature maps becomes Ntimes the above dimension. In most CNN architectures, odd kernel sizes (e.g., 3×3, 5×5) are preferred because they maintain a central pixel around which symmetric convolution can occur.

Pooling Layer

After convolution, pooling is used to downsample the spatial resolution of feature maps, but the most informative features are selected. Pooling carries out down-sampling operations with the aim of reducing the number of network parameters and computation costs. Translational invariance is also improved by pooling by computing the sum of local neighborhood feature activations.

Max-pooling is mostly used in this work since it is found to be effective in picking the most dominant activation in every local region. The highest activation value is chosen and passed on to the subsequent layer, as far as each non-overlapping sub-region of the feature map is concerned. This is done to guarantee that strong feature responses are maintained and less informative activations are eliminated.
Individual features maps are pooled and the pooling is usually done using a 2 x 2 window at a stride of 2. This operation halves the amount of space and retains the depth of the feature representation.
Depending on the scenario of application, the alternative pooling strategies like the average pooling and weighted average pooling can be employed. But max-pooling is, in general, more effective in segmentation tasks since it points at the most discriminative spatial features.

Fully Connected Layer
The last layer of the CNN architecture is the fully connected (dense) layer. The feature vectors of the previous layers are flattened in this layer into a single dimensional feature vector. Every neuron of the fully connected layer is related with all the activations of the previous layer, thereby allowing the network to learn relationships of features globally.
These layers do feature integration in high level and make classification decisions as the combination of the spatial features obtained in the previous layers. Although, in strongly semantic segmentation models, fully connected layers are usually not used since they eliminate spatial positional information. However, in the proposed architecture they are used in the learning of complex feature dependencies and then the final segmentation output is made.

Optimization Strategy Learning.
CNN model training entails the learning of network parameters that will optimize a given loss. The loss function is used to measure the variation between the output of predicted segmentation and the ground truth labels.
The output layer is a Softmax classifier, which is used to approximate the probability distribution across the segmentation classes. The Softmax is another function that transforms unscaled raw output scores into normalized probabilities.
The probability of class c_i for an input sample X is computed as:

$$p(c_i \mid X) = \frac{e^{z_i}}{\sum_{j=1}^{c} e^{z_j}}$$

where z_i represents the output score for class i and c denotes the total number of classes.
The learning objective is formulated using the **cross-entropy loss function**, defined as:

$$E = -\frac{1}{N}\sum log\ P(c_n \mid X)$$

where N represents the number of training samples.

Proposed Methodology
Image segmentation is one of the basic medical image analysis tasks that consist of dividing an image into several significant parts of an image representing anatomical structures or pathological localities. Segmentation aims at simplifying the image representation enabling the extraction of relevant information that can be used in the later diagnostic or other analysis procedures. Segmentation accuracy is a very important issue in automated medical image analysis system since any error in segmentation would be directly transferred to the feature extraction and classification phases. Thus, it is critical that an effective segmentation framework can be developed that will be able to format spatial dependencies and contextual relationships in medical images. The framework of the deep learning-based segmentation is applied in this study to rely on a self-structured feed-forward Convolutional Neural Network (CNN). The architecture is composed of nine layers of computation with the first six layers conducting hierarchical feature extraction with convolution and pooling operations whereas the other three layers conduct higher level representation learning with fully connected layers.
The CNN architecture aims at extracting local and global structural information of medical images. The input image is taken to the network, which then takes on the input image and transmits it through a series of convolutional layers, which extracts the discriminative features. Such features are then down-sampled with pooling layers in order to reduce the computation complexity and maintain some necessary spatial properties.

Convolutional Layer
The main computing unit of the CNN architecture is the convolutional layer. There is high level of spatial correlation between the neighbor pixels in medical images as the anatomy features are continuous and the

texture patterned. Convolution operation takes advantage of these correlations by filtering the image using the local parts of the image with learnable filters. A convolutional filter is passed over the input image and the resulting pixel intensity weighted sums are calculated to create feature maps that highlight significant spatial patterns in the form of edges, textures, and structural boundaries.

Let the input image be represented by a matrix $I(x, y)$of size $n \times n$, and the convolution kernel be represented by a filter $K(i, j)$of dimension $f \times f$. The convolution operation producing the feature map $F(x, y)$can be mathematically expressed as:

$$F(x,y) = \sum_{i=0}^{f-1} \sum_{j=0}^{f-1} I(x+i, y+j) \cdot K(i,j)$$

This operation is repeated across the spatial dimensions of the image. In each convolutional layer, multiple filters are employed to capture different feature representations. If Nfilters are applied, the convolutional layer generates Nactivation maps that are stacked depth-wise to form the output tensor.

The spatial dimension of the resulting feature map depends on parameters such as padding, stride, and kernel size.

Padding

During convolution, the output feature map typically becomes smaller than the input image because the convolution kernel cannot be centered on edge pixels without exceeding the image boundary. To preserve border information, padding is applied by adding additional rows and columns of zero-valued pixels around the input image.

If the original image size is $n \times n$, kernel size is $f \times f$, padding size is P, and stride is S, the spatial dimension of the resulting feature map is calculated as:

$$O = \left\lfloor \frac{n + 2P - f}{S} + 1 \right\rfloor$$

Therefore, the output feature map dimension becomes:

$$O \times O$$

For Nconvolution filters, the total output tensor dimension becomes:

$$O \times O \times N$$

Padding ensures that important information located near image boundaries is not lost during convolution operations.

Activation Function

After convolution, a nonlinear activation function is applied to introduce nonlinearity into the network. The Rectified Linear Unit (ReLU) is commonly used due to its computational efficiency and ability to mitigate the vanishing gradient problem.

The ReLU activation function is defined as:

$$f(x) = max(0, x)$$

For each feature map element z, the activation output becomes:

$$a = max(0, z)$$

This operation ensures that negative activations are suppressed while positive activations are preserved.

Pooling Layer

Pooling layers are used to progressively reduce the spatial resolution of feature maps while retaining the most important information. This down-sampling process decreases the number of parameters and reduces computational complexity. Pooling also improves robustness to small translations and distortions in the input image.

Among different pooling techniques, max-pooling is widely used because it captures the strongest activation within each local region. For a pooling window of size $k \times k$, the max-pooling operation is defined as:

$$P(x,y) = \max_{(i,j) \in k \times k} F(x+i, y+j)$$

If the pooling stride is S_p, the spatial dimension of the pooled feature map becomes:

$$O_p = \left\lfloor \frac{n - k}{S_p} + 1 \right\rfloor$$

Thus, the resulting pooled feature map dimension becomes:

$$O_p \times O_p$$

Pooling is applied independently to each feature map, thereby preserving the depth dimension.

Fully Connected Layer

The fully connected layer is located at the final stage of the CNN architecture. In this layer, multidimensional feature maps obtained from previous layers are flattened into a one-dimensional vector. Each neuron in the fully connected layer is connected to all activations from the preceding layer.

If the flattened feature vector is represented as $x = [x_1, x_2, \ldots, x_n]$, and the weights are represented as $w = [w_1, w_2, \ldots, w_n]$, then the neuron output is calculated as:

$$y = \sum_{i=1}^{n} w_i x_i + b$$

where $b$denotes the bias parameter.

Softmax Classification and Loss Function

The output layer employs a Softmax function to convert the raw output scores into class probability distributions. For a classification problem with Cclasses, the Softmax probability for class $i$is given by:

$$p(c_i \mid X) = \frac{e^{z_i}}{\sum_{j=1}^{C} e^{z_j}}$$

where $z_i$represents the predicted score for class i.

The network parameters are optimized by minimizing the cross-entropy loss function, defined as:

$$E = -\frac{1}{N} \sum_{n=1}^{N} \sum_{i=1}^{C} y_{ni} \, log(p_{ni})$$

where y_{ni}denotes the ground truth label and p_{ni}represents the predicted probability.

Optimization Using Stochastic Gradient Descent with Momentum

The CNN parameters are updated using Stochastic Gradient Descent (SGD) with Momentum, which accelerates convergence and stabilizes learning.

The parameter update equations are defined as:

$$\phi_t = \gamma \phi_{t-1} - \eta \nabla G(w_{t-1})$$
$$w_t = w_{t-1} + \phi_t$$

where $w_t$represents updated weights, $\eta$is the learning rate, γdenotes the momentum coefficient, and $\nabla G(w_{t-1})$represents the gradient of the loss function.

Through iterative optimization, the CNN learns optimal parameters that minimize segmentation error and produce accurate delineation of image regions.

3. Result and Discussion

This section discusses about the information about dataset, performance metrics that investigates the performance of the proposed segmentation technique, and numerical outcome of the proposed as well as existing technique is compared.

3.1. Dataset Description

All of the photos in the ALL-IDB dataset were acquired with a PowerShot G5 camera in JPG format with 24 bit colour depth and a native resolution of 2592*1944. The photos correspond to different microscope magnifications (ranging from 300 to 500). The ALL-IDB database has two distinct versions namely: ALL-IDB1 and ALL-IDB2 focused on segmentation and classification of the Lymphocyte cells respectively.

Table 1. Dataset Description

Image Acquisition Setup	
Camera	CanonPowerShot G5
Image format	JPG
Color Depth	24 but
Magnification of the microscope	300 to 500
ALL-IDB1 ALL-IDB2	
Images	109260
Elements	39000260
Candidate lymphoblasts	510130

Resolution	2592*1944 257*257

3.2. Performance Metrics

Effectiveness and accuracy of the CNN based segmentation is compared using metrics such as Nucleus segmentation error, Tanimoto Index, computational time & Jacard coefficient.

Jacard Similarity: Given two sets A and B, the Jacard's similarity is defined as

$$JS(A,B) = \frac{|A \cap B|}{|A \cup B|} = \frac{|A \cap B|}{|A| + |B| - |A \cap B|}$$

The intersection between two sets A and B is denoted by A ∩ B which shows items that are present in both sets. The union between two sets A and B is given by A∪B and it reveals the elements which are in either sets. The Jacard index value lies between 0 and 1 where the value is equal to 0 if the two sets are totally different and if the jacard index value is one, it means that the two sets are one and the same. In this research work, effort has been taken to segment the nucleus from the dataset images as it is needed for subsequent feature extraction and in final Leukaemia detection.

Tanimoto Index: Tanimoto Index is a measure used for measuring similarity which happens to be an extension of Jacard coeffient where both the values represent binary similarity measure. When two binary feature vectors X_i and X_j are assumed, the binary Tanimoto coefficient is represented as

$$T(X_i, X_j) = \frac{X_i, X_j}{\|X_i\|^2 + \|X_j\|^2 - X_i . X_j}$$

Nucleus Segmentation Error: The Nucleus Segmentation Error of the Lymphocyte Images is calculated by comparing the segmentation results of automated methods with that of nucleus segmented by experts. Nucleus segmentation error of Lymphocytes is calculated by using the relation

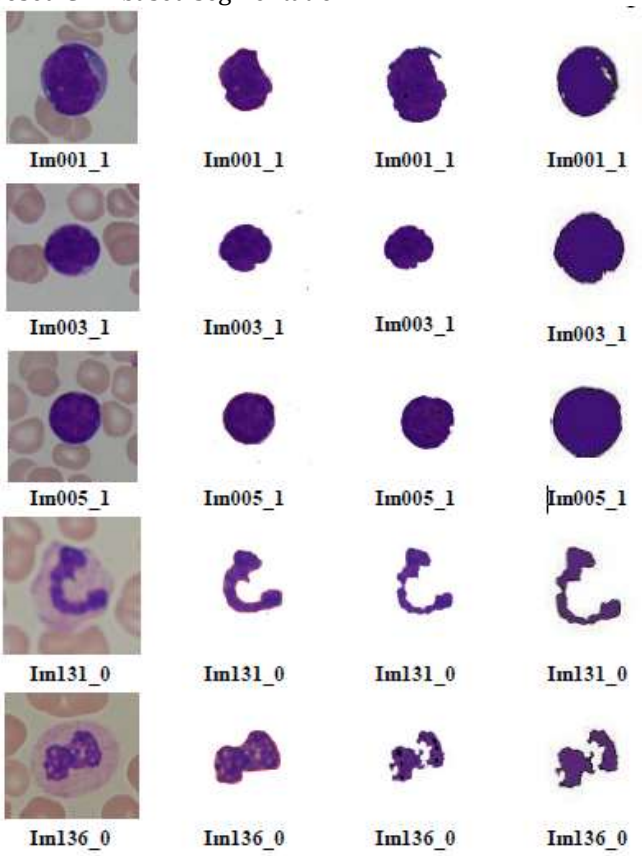
$$\varepsilon = \frac{Entire\ count\ of\ misclassified\ pixels}{Entire\ count\ of\ pixels\ in\ the\ image} * 100$$

where misclassified pixels refer to pixels not related to the nucleus region.

Segmentation Computation Time: Segmentation Computation Time refers to the time by the specified algorithm to perform nucleus segmentation from the Lymphocyte Images.

3.3. Discussion of Segmentation Outcome

This section shows the segmentation of leukaemia image and numerical outcome of existing segmentation approaches namely k-means clustering, fuzzy-c means clustering, which is further compared with proposed CNN based segmentation.



(a) (b) (c) (d)

Figure 1. Segmented Lymphocyte Nuclei

Figure 1(a) input leukaemia image, 1 (b) indicate the CNN, 1 (c) indicate the k-means clustering and 1 (d) fuzzy c means clustering.

Table 2. Comparison of Jaccard Similarity

Algorithm	K-Means Clustering	Fuzzy C Means	CNN
Im001_1	0.95	0.97	0.99
Im003_1	0.97	0.99	1.05
Im005_1	0.98	0.99	1.2
Im014_1	0.96	0.98	1.32
Im017_1	0.88	0.93	0.96
Im020_1	0.89	0.95	1.1
Im029_1	0.71	0.88	0.99
Im040_1	0.89	0.94	0.98
Im085_1	0.77	0.87	0.96
Im122_1	0.81	0.91	0.98

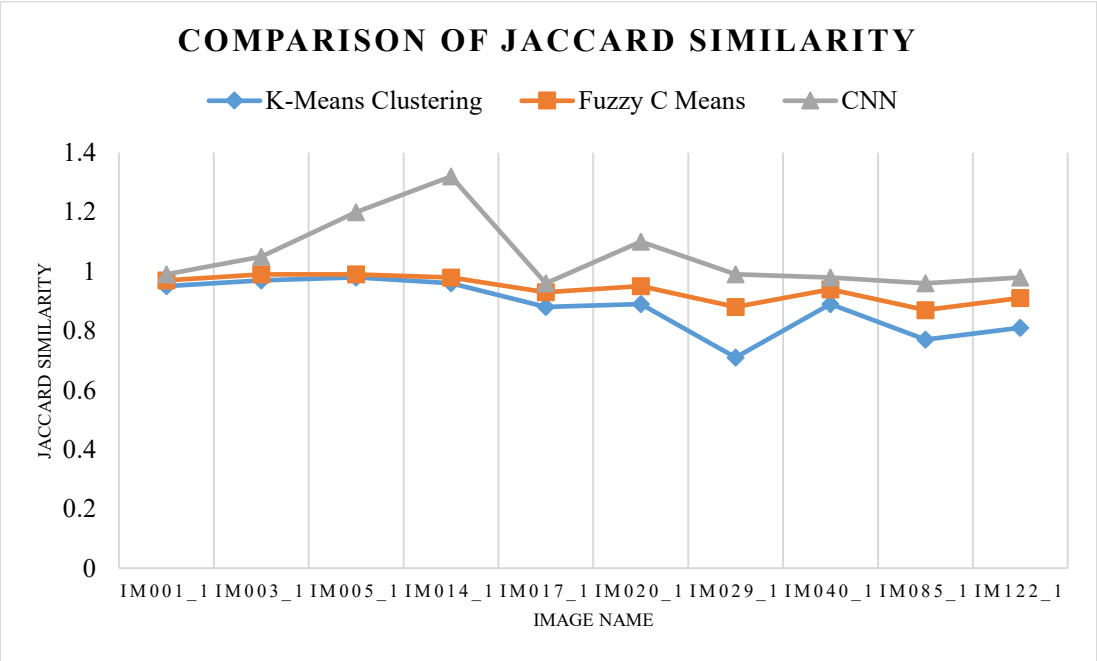


Figure 2. Comparison of Jaccard Similarity

Table 3. Comparison of Tanimoto Index

Algorithm	K-Means Clustering	Fuzzy C Means	CNN
Im001_1	0.74	0.81	0.88
Im003_1	0.76	0.78	1.05
Im005_1	0.88	0.82	1.24
Im014_1	0.86	0.87	1.12
Im017_1	0.73	0.80	0.86
Im020_1	0.88	0.89	1.04
Im029_1	0.71	0.83	0.91
Im040_1	0.88	0.89	0.96
Im085_1	0.75	0.87	0.86
Im122_1	0.81	0.81	0.88

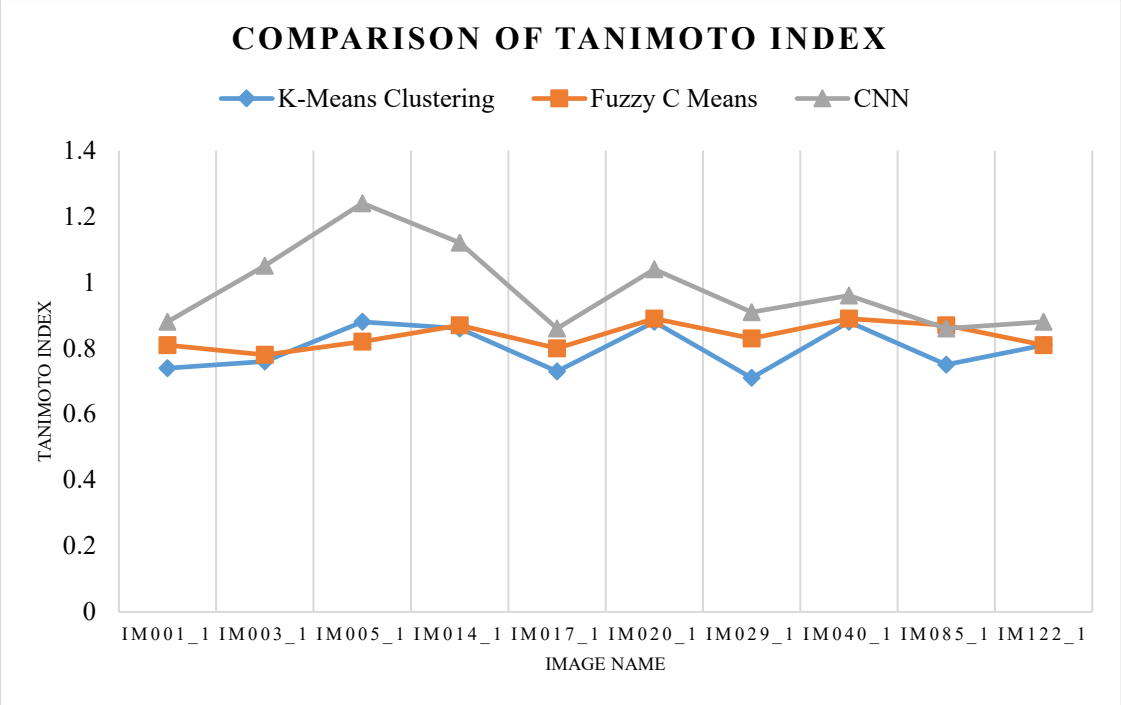


Figure 3. Comparison of Tanimoto Index

Table 4. Comparison of Nucleus segmentation error

Algorithm	K-Means Clustering	Fuzzy C Means	CNN
Im001_1	42	39	35
Im003_1	56	51	39
Im005_1	57	56	41
Im014_1	58	52	38
Im017_1	48	46	37
Im020_1	59	51	45
Im029_1	61	57	38
Im040_1	63	57	36
Im085_1	64	56	33
Im122_1	65	59	35

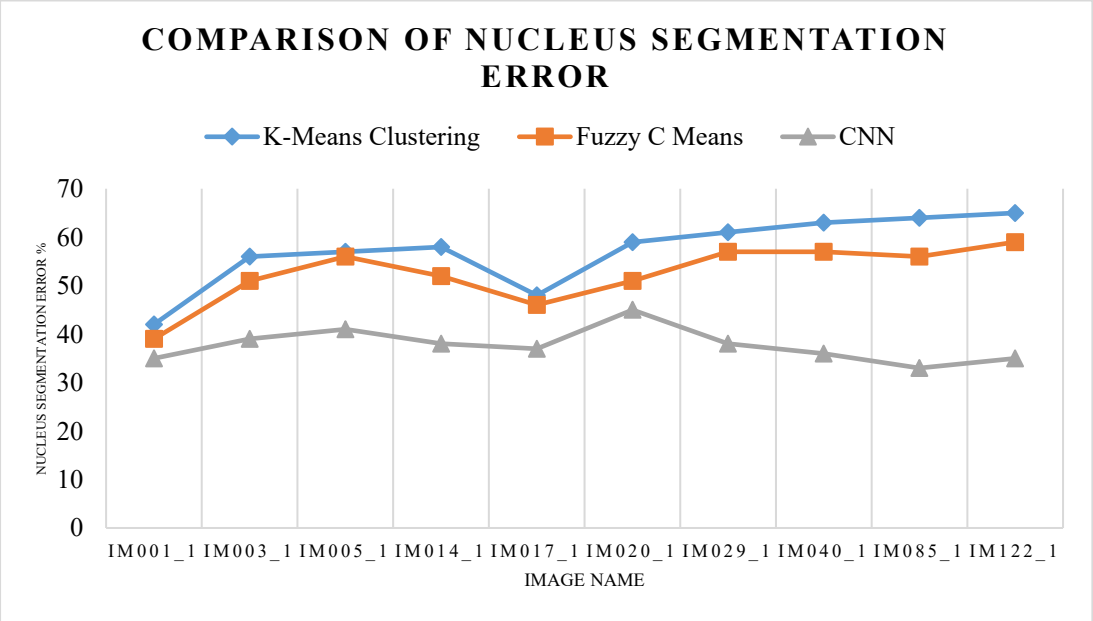


Figure 4. Comparison of Nucleus segmentation error

Table 5. Comparison of Computational Time

Algorithm	K-Means Clustering	Fuzzy C Means	CNN
Im001_1	62	59	47
Im003_1	66	61	49
Im005_1	65	63	61
Im014_1	78	72	58
Im017_1	68	66	57
Im020_1	79	71	67
Im029_1	61	59	58
Im040_1	63	57	46
Im085_1	66	56	43
Im122_1	67	68	47

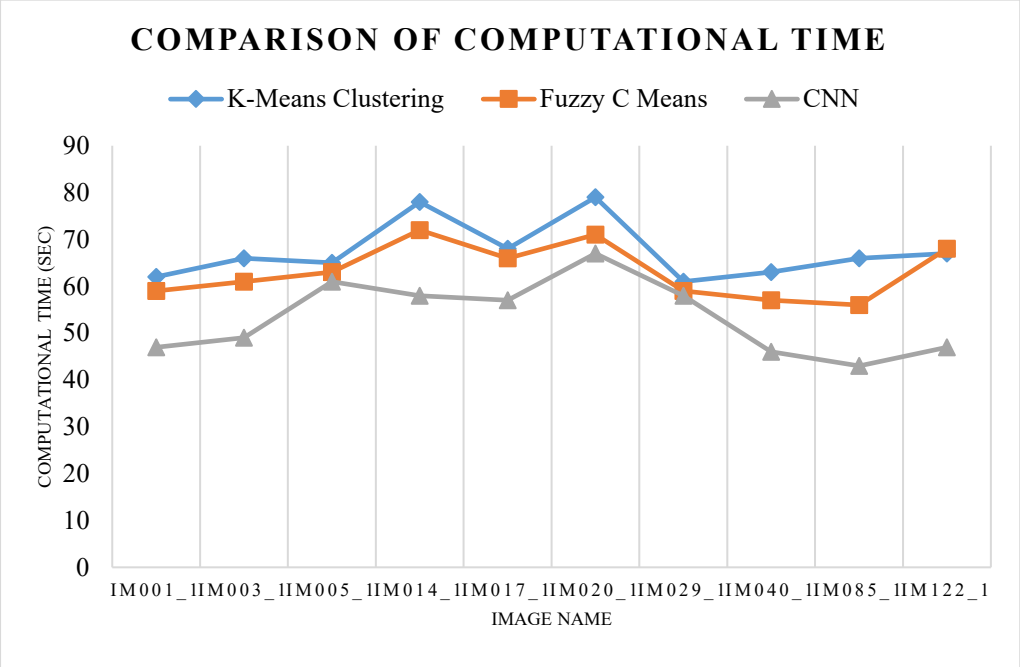


Figure 5. Comparison of Computational Time

From the observation of numerical outcome, it is identified that the proposed approach is highly effective. The computational time for image segmentation is minimum in proposed approach and the occurrence of segmentation error also minimum.

4. Conclusion

In this research article, existing automated methods namely the K-Means clustering method and Fuzzy C-Means clustering method were used to segment the nucleus of Lymphocyte Images that is compared with the proposed convolutional neural network (CNN). For evaluating the efficiency of automated segmentation methods employed, they were compared with the output generated by manually segmenting the Lymphocyte nuclei with the help of an expert hematopathologist. It is found that the CNN outperformed the K-means clustering method and Fuzzy C-means clustering method, which is investigated with the assistance of performance metrics such as Jacard index, Tanimoto index, Nucleus segmentation error and computation time. CNN for nucleus segmentation of lymphocytes is highly effective and in future segmented image can be classified with other deep learning approaches, which in turn increase the process of classification.

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