Classification of Acute Myeloid Leukaemia using Deep Learning Features

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Abstract
Acute Myeloid Leukaemia (AML) is a sub-category of leukaemia, which is prevailing among adults. One of the top ten most dangerous causes of mortality for humans is AML, which stands for Acute Myeloid Leukaemia. AML originates in the bone marrow but tends to rapidly spread to the bloodstream. In some cases, it can also affect other parts of the body such as lymph nodes, liver, spleen, central nervous system (which includes the brain and spinal cord), and testicles. Manual methods are time-consuming, and their accuracy depends on the operator's ability. However, automatic classification can improve accuracy and speed up clinical decisions for haematologists and medical experts. However, state-of-the-art mechanisms are complex and their accuracy is less than 98 percent. The objective of our research was to introduce a novel approach that utilizes a Convolutional Neural Network (CNN) for extracting CNN features from images of blood smears. Moreover, it classified the images into two classes i.e., normal and abnormal. The proposed mechanism achieves high accuracy of 99.07%.

Keywords: Deep Learning; Convolution Neural Network; Medical Images; Acute Myeloid Leukaemia; Image Classification.

Introduction

Acute Myeloid Leukaemia (AML) is a type of blood cancer that attacks mostly adults. If left untreated, this illness can lead to death. (Agaian, Madhukar, & Chronopoulos, 2018). General symptoms of AML are gums bleeding, infections, body pain, fever, shortness of breath, etc. Timely detection is crucial for the survival of patients with acute Myeloid Leukemia, which is a curable condition. Medical imaging techniques enable specialist physicians and hematologists to examine and distinguish different types of blood cells, bone cells, and soft tissues from the obtained medical images. In the medical field, a blood sample holds great significance as many blood-related disorders can be classified by studying blood smear images. Examples of such disorders include Leukaemia, Acute Leukaemia, Acute Myeloid Leukaemia, AIDS, Malaria, Anaemia, and more (Gautam & Bhadauria, 2014). There are three main classes

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of human blood cells: leukocytes, erythrocytes, and platelets, each of which belongs to unique categories within the blood. There are 5 subcategories of white blood cells (WBCs), which include Monocytes, Lymphocytes, Basophils, Eosinophils, and Neutrophils. However, for the diagnosis of AML, it is necessary to focus on a specific subclass of WBCs, namely Monocytes (Arbab, Khan, & Ali, 2022).

Despite the fact that AML is curable, early discovery is crucial for survival. Doctors need to conduct a range of tests to confirm their findings in the laboratory. While certain tests may require invasive procedures such as a lumbar puncture or bone marrow biopsy, other tests can be less invasive and only necessitate a peripheral blood sample. A minimally invasive test is the Complete Blood Count. A blood sample is run through a haematology analyser, which produces quantitative data. Abnormal results should be investigated further with a microscopic inspection. The laboratory technician conducts a cell analysis during which they enumerate the various types of cells encountered and note their characteristics, including their shape and structure. Using computer vision techniques, the proposed research analyses blood smear images for AML identification and categorization. WBCs are divided into five types: monocytes, lymphocytes, basophils, eosinophils, and neutrophils**.**

In the literature (Thanh, Vununu, Atoev, Lee, & Kwon, 2018; Zhao, Zhang, Zhou, Chu, & Cao, 2017), Features were extracted from blood smear images through the use of manual methods. These manual methods are time-consuming, and their accuracy depends on the operator's ability. In addition, automated classification has the potential to enhance accuracy and expedite clinical decisions for haematologists and medical professionals. However, state-of-the-art mechanisms are complex and their accuracy are less than 98 percent.

A computerized system has been suggested to assist hematic pathologists in detecting and Classifying Acute Myeloid Leukaemia (AML) in blood smear images, leading to more precise diagnosis with improved accuracy. The system utilizes automated detection techniques to identify and classify AML in microscopic blood smear images. Dataset used in this research is obtained from local teaching hospitals. This research aims to create a system capable of identifying abnormal blood cells in the human body, which are indicative of cancer. To detect monocytic leukaemia, we intend to apply various approaches in a certain order that would yield a satisfactory outcome about the patient(Cristianini & Shawe-Taylor, 2000). Moreover, Matlab is utilized to implement the proposed work. The contributions are shortened as follows.

1. A new computer-based framework has been developed to detect and classify AML in blood smear images, aiding hematopathologists in diagnosing AML more efficiently and accurately.
2. Testing and validation of trained model compared with other models.
3. The objective is to develop a precise model that can identify and classify immature monocytes accurately, along with computing the critical morphological features. This model will act as a base for future research on computer-assisted detection of leukaemia.
4. To promptly identify abnormal findings and make swift decisions to save lives.

Literature study

Anna Jurek et al. have conducted a research study on widely used techniques in Ensemble-Based Classification, exploring their modifications, limitations, and reviews of these techniques in detail (Jurek, Bi, Wu, & Nugent, 2014).Indira P. et al. published a research paper in 2016, presenting a model for detecting Acute Myeloid Leukemia (AML) in adults, which is a rapidly growing type of cancer. The segmentation was achieved using the "K-means clustering" technique, while spatial and spectral features were extracted for feature extraction. Although spectral features are considered more reliable and stable, much of the information is duplicated from one image to another, rendering classification insignificant. To address this issue, the researchers utilized genetic algorithm to optimize spectral features. Finally, the linear Support Vector Machine was employed for classification.(Umamaheswari & Geetha, 2019).

The authors of papers (Patel & Mishra, 2015; Thanh et al., 2018), have suggested a method that uses convolutional neural networks (CNNs) for many different area like Acute Myeloid Leukaemia (AML), text classification (Ali et al., 2022), lung nodule classification (Yar, Abbas, Sadad, & Iqbal, 2021) and pneumonia classification (Hussain, Khan, & Yar, 2019). This type of cancer can affect individuals of all ages, including both children and adults.The authors of paper (Cabrera, Legaspi, Papa, Samonte, & Acula, 2017), employed Support Vector Machine (SVM) to extract granularity features for detecting WBC, and compared the results with CNN features. They asserted that their proposed method achieved superior accuracy. The paper presents a novel approach that employs a CNN classifier for the classification of Acute Lymphocytic Leukaemia (ALL). Through experimental evaluation, the proposed technique showcases remarkable accuracy in distinguishing between normal and abnormal cells.(Mohapatra, Patra, & Satpathy, 2014).

In this work (Thanh et al., 2018), the authors have proposed filtering methods, such as k-state grouping, histogram alignment. The authors of paper (Zhao et al., 2017), have introduced a methodology that employs diverse image processing techniques for the detection of leukaemia. By utilizing the Naïve Bayes classifier, the proposed mechanism achieves an accuracy of 90.33%.In paper(Hazlyna et al., 2018), the authors have presented an algorithmic solution for the detection of leukaemia. The proposed approach delivers an average accuracy of 97.26%, as measured by the percentage of correct classifications. Paper (Macawile, Quiñones, Ballado, Cruz, & Caya, 2018), introduces a technique that enables the segmentation of different types of White Blood Cells (WBCs) from microscopic blood images. The proposed approach aims to improve the accuracy of cell counting, thereby yielding more precise results.

Paper(Gouda & Chandraprakash, 2019), presents the Jaya algorithm as a means of distinguishing between defective and non-defective cells, with features extracted from nucleus images. The experimental results demonstrate an improvement in accuracy following the optimization with the Jaya algorithm. The authors of paper (Agaian, Madhukar, & Chronopoulos, 2014) have developed a systematic approach for leukaemia detection, involving a step-by-step process that includes pre-processing, nuclei segmentation, and feature extraction. The suggested method provides a high level of precision, with an accuracy rate of 98 percent. Similarly, The Study (Goutam & Sailaja, 2015), suggests employing k-means clustering and support vector machine (SVM) for detecting leukaemia, which yields a 98 percent accuracy rate.

This study (Khalilabad & Hassanpour, 2017), details the development of an automated system for cancer detection that involves the processes of generalization, gridding, and image data extraction. The experimental findings demonstrate that the proposed system achieves a high level of accuracy, accurately identifying the cancer database at a rate of 95.45 percent. The study (Amin, Kermani, Talebi, & Oghli, 2015) introduces the k-means algorithm as a segmentation technique for leukaemia detection, followed by the use of Support Vector Machine (SVM) to classify cells as either cancerous or non-cancerous. This research (Mohamed et al., 2018), describes an application designed to aid in the early diagnosis of hematologic diseases, utilizing a random forest classifier to make the final determination. The suggested system attains an average precision rate of 94 percent.

In Paper (Khalilabad & Hassanpour, 2017), the authors present an automated methodology for the identification of cancer patients utilizing data acquired from micro-images. The framework comprises three primary components: photography, data minerals, and diagnostics. At the image analysis level, operations such as

image generalization, gridding, and image data extraction are performed. The experimental results demonstrate the effectiveness of the proposed method, achieving a high accuracy rate of 95.45 percent in identifying the cancer database. Similarly, filtering approaches such as k-state grouping, histogram alignment, and the Zack algorithm have been employed to develop a system that achieves a precision of 93.57 percent. The system has been successfully implemented in MATLAB (Panetta, Sparreboom, Pui, Relling, & Evans, 2010) .

Methodology

In order to classify AML, we need to localize Monocyte from blood smear image, and then compute set. Initially, we applied pre-processing techniques to resize images and remove noise. Then these images pass from proposed model to extract features. Finally, these images are classified into two classes i.e., normal and abnormal.

The objective of this proposed work is to analyse and process blood smear images, creating an automated technique that supports medical professionals in segmenting and identifying AML, ultimately facilitating AML diagnosis. Monocytes can be easily distinguished from the background and other blood cells in blood smear images due to their unique nuclei. However, features extraction from Monocytes is not an easy task due to variations present in cell shape, dimensions, and edges. The afflicted monocytes are known as blast cells, and they undergo additional morphological alterations as the disease progresses. Due to their irregular shapes and small indentations in the cytoplasm, blast cells are distinguishable from other blood cells. Consequently, the proposed approach identifies Monocytes in a blood smear image and differentiates them into normal and blast cells. The suggested method comprises the following stages.

1) Training phase
2) Testing Phase

In the proposed work, we use CNN method to extract features. Initially, the model is trained with training data. Moreover, about 70 percent of data is used for training. Then, features are extracted from prepared data using deep learning models called Alex Net. Finally, the detected cells are classified into two classes normal and abnormal. Similarly, testing phase consist of 30 percent of data. In testing phase we pass images through the trained model. The data is analysed and compared with stored feature of trained data. Then, cells are classified into normal or abnormal classes. Like training phase, the testing phase also involve pre-processing phase. It consists of image resize, image noise removal, image enhancement. Moreover, Leukaemia is detected only by analysing the WBC.

Therefore, the proposed study is focused on WBC to find AML in blood smear images. There are five distinct categories in which white blood cells can be classified i.e., Neutrophils, Eosinophil, Basophil Lymphocyte and Monocyte. However, our focus is on Monocytes to detect AML.

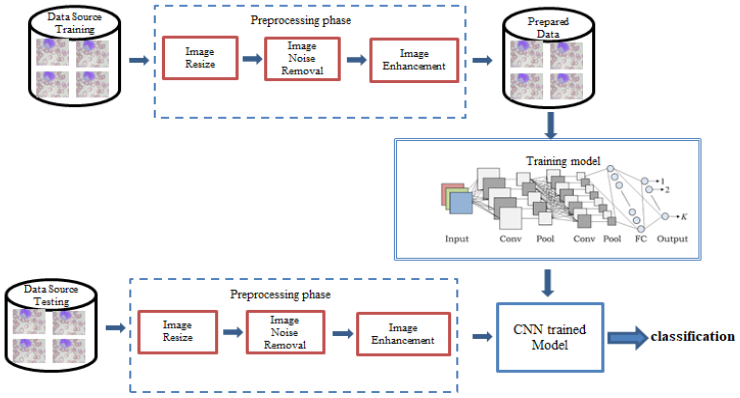

Figure 1: Dataflow Diagram

Feature Extraction and Classification

The attributes of images are used to denote their similarities. The classifier then compares different images and classifies them into specified classes using functions and their labels. CNN characteristics are used to extract discriminatory functions. The feature extraction phase is followed by classification phase. All of the classifiers use a similar approach. A decision boundary is created by dividing the dataset to classify the different categories. As suggested in this work, the trained model classifies the cells into normal and abnormal classes (Alom et al., 2018).

Deep Learning Models

Deep learning Models consists of multiple layers which is used to extract high level features from raw data. Moreover, different deep learning models i.e., VGG (Visual geometry group) Google net, Resnet, ImageNet etc., are used to extract features. However, the proposed mechanism use Alex Net model (Tawalbeh, Muheidat, Tawalbeh, Quwaider, & Abd El-Latif, 2022).

Alex Net

Alex-Net was developed by Alex Krizhevsk in 2012. Alex-Net has basically 25 convolution Layers. The acceptable size of images for efficient results should be 227 x 227 pixels(Arbab et al., 2022) (Badrinarayanan, Kendall, & Cipolla, 2017). To extract features, we introduced the Alex Net CNN architecture. AlexNet

utilizes particular operations such as convolution, pooling, and regularization to extract intricate features from image data. One input layer, five convolution layers, five regularisation levels, five down sampling layers, and three Fully Connected layers comprises the Alex Net architecture(Abounassar, El-Kafrawy, & Abd El-Latif, 2022).

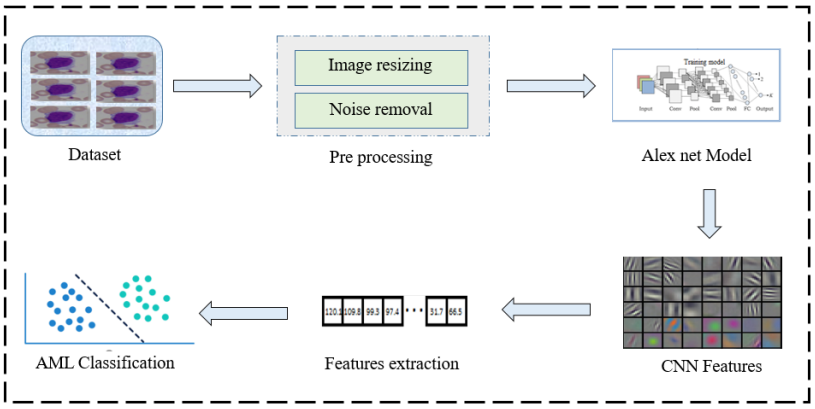

Figure 2: Proposed Framework

Convolutional Neural Network

The CNN consists of 4 layers namely the Convolutional Layer, ReLU Activation Layer, Pooling Layer, and Fully Connected Layer. To extract CNN features, we resize images for efficient results should be 227 x 227 pixels as the dataset is about circle shape recognition we have taken 4 filters of 3x3 consisting of random pixel values. The CNN working is described below.

1. In the convolutional layer four, 3x 3 matrices are iterated on the whole image and created a dot product of filter matrix and every 3x3 matrix of the image and stored in another map or array.
2. ReLU is an activation function. It replaces the negative values in the matrix with zero. After ReLU activation we have 4 matrices as we have 4 filters.
3. In the Pooling layer we selected 2x2 window size. Iterated on the whole image, took the highest value in a particular window and stored in a different matrix. So we can have a shrinked image.

These steps are repeated 2 times and made the image matrix size shorter. Now the Fully Connected Layer is implemented which stores all the pixel values of 4 outcome images into one stack. Thus, when a test image is given as input to the CNN, it executes all the above steps and compare the stack value with the predefined values. Then, it gives prediction regarding pattern recognition. After applying epoch size of and batch size of 10 the CNN model worked

on our image dataset with 100% of train accuracy and total 99% test accuracy.

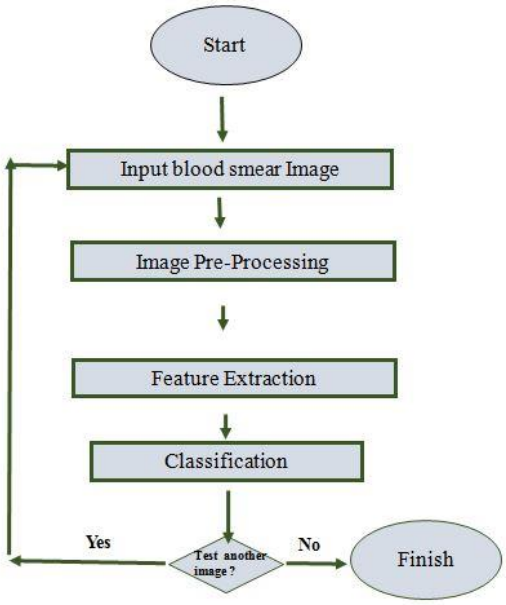

Figure 3: Testing images

Experimental Results

Dataset

The research involved the collection of 4,000 Monocytes blood smear images from Hayatabad Medical Complex (HMC) Hospital, which is situated in Peshawar, Pakistan. The dataset comprises 4000 images, out of which 2000 images are of normal Monocytes and the remaining 2000 images depict aberrant cells. These blood smears were taken with a Nikon DS-Fi2 high-definition colour camera head. All the images were saved in JPG format with a resolution of 960 x 1080 pixels. MATLB was used to reduce the image size to 227 x 227 pixels. Table 1 contains the dataset's details.

Table 1
Dataset

S.No	Human Blood Cell	No of Images
1	Normal Monocytes	2000
2	Abnormal Monocytes	2000
Total		4000

For this study, we use state-of-the-art deep convolutional neural network. Initially, the localization of monocytes from blood smear images is carried out, followed by the use of the Alex Net model for feature extraction. Furthermore, the Alex net model

identifies human blood cells as normal or malignant. The experimental data are reported, with a precision of 99.07 percent. The subjective analyses are applied to check the performance of the projected monocytes classification is performing. A team of 4 haematologists from Hayatabad Medical Complex Peshawar were requested to join the evaluation process system. The proposed approach is validated by haematologists, who compare the results with the ground truth. This rule correctly recognises and classifies AML cells. The following matrices and equations were used in the analysis of the proposed mechanism.

$$FPR = \left(\frac{FP}{TN+FP}\right) \quad (1)$$

$$FNR = \left(\frac{FN}{TP+FN}\right) \quad (2)$$

$$\text{F-Measure}=2*(FPR*FNR)/ (FPR*FNR) \quad (3)$$

$$\text{Accuracy}= (TP/\text{Total Test Images}) *100 \quad (4)$$

The extent of malignant cells correctly known is true positive. The range of unaffected cells that are indicated as effected cells is known as false positive. The number of unaffected cells that are appropriately labelled is referred to as true negative. The range of aberrant pixels wrongly labelled as unaffected is known as a false negative. The weighted mean of FNR and FPR is the F-Measure.

The proposed method has demonstrated classification results, with an F-measure that exceeds 99.07% accuracy, for the classification of 4000 microscopic images of affected and unaffected Acute Myeloid Leukaemia (AML) in blood smear samples. In order to achieve this, two parameters, namely shape and size, were taken into consideration. The visual classification results are illustrated in Figure 4, and the proposed technique is compared with various classifiers, as depicted in the same Table 2.

Classification Report

Classification Report is one of the popular method to compare algorithms. The report consists of Precision Score, Recall Score, F-1 Score.

Precision Score: Ability of a classifier not to label a positive sample when it is negative.

$$\text{Precision Score} = t\,p/ (t\,p + f\,p)$$

Recall Score: Ability of a classifier to predict all positive sample with the true value.

$$\text{Recall Score} = t\,p/ (t\,p + f\,n)$$

F-1 Score: The Weighted harmonic mean of Precision and Recall score which signifies that both the Precision and Recall scores are important.

Table 2
Comparison of proposed system with other classifiers

Classifiers	KNN	SVM	Proposed
Accuracy	80.50%	90.09%	99.07%

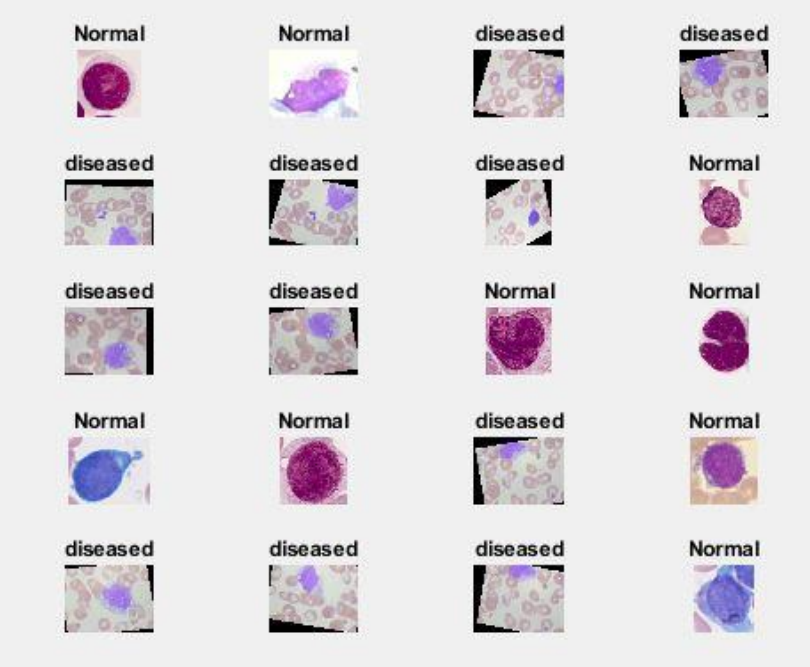

Figure 4: Visual Classification of proposed method

Performance Analysis

The presence of abnormal monocytes on microscopic inspection of a peripheral blood smear indicates AML. Monocytes are recognised from normal WBCs and, in particular, monocytes, by fine morphological differences. As a result, the test is a binary classification problem, with monocytes being positive and WBCs being negative. These characteristics are hand-picked for use in supervised machine learning models.

The dataset consisted of cell-centered images that were professionally annotated as normal white blood cells. However, noise was present in the form of surrounding red blood cells and inconsistent background lighting in the images. For this study, a PC with an Intel Core i7 2.4GHz CPU, 8GB RAM, and Windows 10 operating system was utilized to implement three traditional classifiers and CNN using Matlab 2018a. The performance of each model was assessed based on an average of six rounds of training

and testing. As the dataset was imbalanced, precision, recall, and F1-scores were presented in the report. (Table 3).

Table 3
Classifier Precision, Recall, and F1-scores

Classifiers	Precision	Recall	F-Score
KNN	0.85	0.61	0.71
NN-1	0.83	0.87	0.80
NN-2	0.78	0.87	0.82
CNN	0.88	0.90	0.89

The K-Nearest Neighbors (KNN) model demonstrated the lowest and most inconsistent accuracy rate, measuring at 81.5 percent. This outcome can be attributed to the model's dependence on the training set to recognize the nearest neighbors. This made the K-Nearest Neighbors (KNN) model susceptible to data partitioning issues, which arise when noisy images or cell populations are distributed unevenly between the training and testing sets. Despite this constraint, the K-Nearest Neighbors (KNN) model still performed well in the classification task, highlighting the significance of raw pixels as predictors in cell-centered images with noise. Additionally, due to their similar architectures, the NN-1 and NN-2 models exhibited closely-matched accuracy rates of 85.3 percent and 86.2 percent, respectively.

NN-2 exhibited relatively superior performance and less variability, which can be attributed to improved regularization through dropout and better weight initialization via batch normalization. Interestingly, adding more fully-connected layers did not have any impact on the model's performance. The models tested showed a limited improvement in full image classification following modifications. The CNN model outperformed the other models, achieving the highest accuracy rate of 92.3 percent. Interestingly, the improved accuracy can be attributed to a single convolutional layer. These results suggest that the CNN model is close to meeting clinical laboratory performance standards. The precision, recall, and F1-scores further corroborate the accuracy claims. Notably, the F1-scores demonstrate the advantages of using NNs over KNNs, as well as the superior benefits of using a CNN (Bukhari, Yasmin, Sammad, El-Latif, & Ahmed, 2022).

One of the ways to assess the effectiveness of a machine learning classification system in accurately identifying data points is by measuring its accuracy, which represents the number of correctly classified data points out of all the data points. In our study, we were able to achieve an accuracy rate of 99.07 percent. On the other hand, loss refers to the disparity between the actual values of a given problem and the predicted values generated by the model. A higher

loss value indicates greater errors produced by the model on the data, and our study's loss rate was 4 percent.

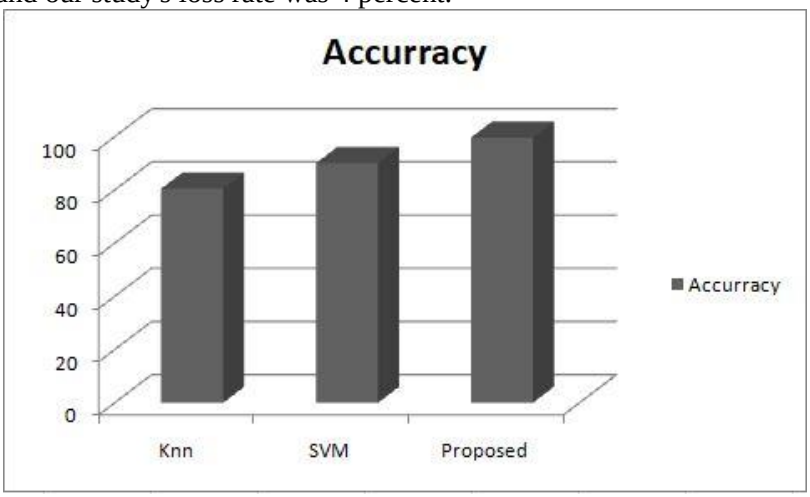

Figure 5: Comparative analysis

Conclusion

The primary focus of this study is to introduce a computerized approach that can classify AML in blood smear images with greater precision, thereby potentially saving many lives. The Main idea behind this work is to locate monocytes, extract CNN features, and carry out classification. Initially, a specific subclass of white blood cells, i.e., monocytes, is identified in the blood smear image, and a set of CNN features is extracted from the images. Through experimentation, it was discovered that the proposed method enhances the classification performance in comparison to various other advanced classification methods. The suggested system has attained a precision rate of 99.07 percent. The proposed system is an efficient way to diagnose AML early on without the need for expensive investigative procedures.

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