

Efficient Diagnosis of Acute Lymphoblastic Leukemia using Transfer Learning

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Abstract: Leukemia, as the most prevailing form of blood cancer, impacts both adults and children. This demands timely detection for effective intervention. However, the traditional manual diagnostic methods suffer from time-consuming processes and are prone to skill-dependent variations. In our work, we employ transfer learning techniques, which leverage information gained from models trained on enormous scale datasets, resulting in significant reductions in the need for large amount of labeled data as well as computational resources for the specialized task of ALL detection, thereby improving efficiency in terms of both time and cost. This study proposes an innovative automated Leukemia detection system utilizing advanced Machine Learning (ML) techniques, particularly deep learning-based Convolutional Neural Networks (CNNs) and Transfer Learning. Here we have proposed a model with CNN layers added to Transfer Learning Architectures in which the model with EfficientNetB3 gives the best results with a Training Accuracy of 100% and Testing Accuracy of 96.87%, F1-Score of 96.9%, Recall of 96.24% and precision of 97.58% making it the one of the promising model among other evaluated CNN architectures earlier on C-NMC-2019 ALL Dataset. The proposed system addresses the crucial need for early leukemia diagnosis. It overcomes the drawbacks of manual methods by efficiently analyzing microscopic images, extracting essential features, and applying filtering techniques to enhance accuracy. This automated approach promises to improve blood cancer detection by providing an accurate tool for clinicians and healthcare professionals, thereby significantly contributing to the enhanced patient care and management of ALL.

Keywords: Leukemia, CNN, ALL, machine learning, microscopic images

1. Introduction

Leukemia is the most common kind of blood cancer, especially among children. Leukemia is a type of cancer that affects the body's blood-forming tissues, such as the bone marrow and the lymphatic system. Leukemia is caused by the fast proliferation of abnormal white blood cells. This uncontrollable growth occurs in the bone marrow, which produces most of your body's blood. These aberrant white blood cells are unable to fight infection and impair the bone marrow's ability to produce red blood cells and platelets. Typically, leukemia cells are immature white blood cells that are still developing. In contrast to other types of cancer, leukemia doesn't generally form a mass (tumor) that shows up in imaging tests, such as X-rays or CT scans.

Leukemia does not form strong tumors, but it does produce many abnormal white platelets that crowd out normal platelets [2]. Leukemia is a fatal disease that affects many people worldwide and puts their lives in danger. Acute and

chronic leukemia are two types. Compared to acute leukemia, which needs to be treated right away, chronic leukemia advances more slowly. Acute leukemia is further subdivided into acute lymphoblastic leukemia (ALL) and acute myelogenous leukemia (AML), whereas chronic leukemia is further divided into chronic myelogenous leukemia (CML) and chronic lymphocytic leukemia [3]. Leukemia affects both adults and children.

Our work focuses on acute lymphoblastic leukemia, a type of cancer that is quite common in children. However, this may even develop in adults, and the chances of a treatment being found later are low [7]. It can be fatal if left untreated since it spreads quickly to many important organs [4]. White blood cell function is severely compromised by this lymphoid blood cell malignancy, which begins in the bone marrow and progresses swiftly [4, 7]. It is typified by the production of immature lymphocytes. As a result, leukemic individuals experience challenges with their bodies' defense against infections, affecting the immune system. ALL multiplies quickly, damaging lymphocytes and transforming them into lymphoblasts. It can sometimes be deadly, affecting the liver, spleen, and other organs. It might have symptoms like fever, stomach pains, fatigue, and vomiting [4]. Under a microscope, it might be challenging to tell juvenile leukemic blasts from normal cells because of their similar physical characteristics.

Leukemia refers to all forms of blood malignancies, which account for 8–10% of total cancer incidence rates globally.

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Every year, over 900,000 people worldwide are diagnosed with blood cancer. However, leukemia diagnosis is challenging as many people are unaware of their condition because the early symptoms are like common fever and fatigue, which have always been a problem for researchers, physicians, and hematologists [1, 8]. Early disease diagnosis with appropriate treatment facilities can improve health conditions and save lives [4]. Early detection of cancer will improve patient survival rates because it is very resistant to treatment [1]. Early and accurate diagnoses could effectively reduce treatment costs, increase the probability of remission, or even prolong the lives of patients [2]. Therefore, developing reliable and precise cancer detection techniques is essential for effective early treatment.

Leukemia can arise from several causes, such as exposure to radiation and certain chemicals, as well as family history. Diagnosis is performed by a physician to detect the presence or absence of a certain disease in a patient according to a particular dataset, which may include signs, symptoms, medical images, and exams. A wrong finding can have antagonistic results, for instance, prescription of medications with side effects, on a patient's health. Incorrect diagnosis might complicate treatment processes while also raising treatment expenses. Diagnoses can be performed via a variety of tests, such as physical examination, blood test, blood count, and bone marrow biopsy. It is thought that microscopic analysis is the most economical method for making preliminary diagnoses; nonetheless, it is often carried out by hand by an operator who may become fatigued from doing several tests in one day. Furthermore, because manual diagnoses are laborious, time-consuming, and susceptible to interobserver differences, they are inherently unreliable. Therefore, it is necessary to develop low-cost, automated systems that can accurately distinguish between healthy and diseased blood smear pictures without the need for human involvement [2].

Initially, scientists created a few diagnosis systems that mostly used conventional machine methods. The system process normally begins with the preprocessing of the input image and progresses to procedures like segmentation, feature extraction, and eventually classification. But nowadays, convolutional neural networks, or CNNs, are used to boost the system's efficiency. To accomplish classification, classic machine learning-based algorithms typically employ hand-crafted features. On the other hand, deep features are directly extracted from the raw input photos using contemporary CNN-based algorithms. CNN is one of the most alluring advancements in computer vision. Face recognition, picture categorization, visual search, object identification, and illness diagnosis are just a few of the real-world uses of CNN [4]. Deep learning algorithms are widely used in leukemia treatment to determine whether a patient has leukemia. Deep learning and image analysis techniques are being used more often in automated diagnosis systems

because of their high accuracy in a range of health diagnostic domains.

In recent years, many automated methods for diagnosing ALL have been presented. The ability to differentiate between the characteristics of healthy and blast cells is essential for achieving reliable and efficient computerized diagnosis [2]. This research paper proposes a high-accuracy classification algorithm based on transfer learning that can distinguish between abnormal and healthy blood smear images. One of the primary justifications for using transfer learning is the dearth of data on certain jobs, since labeling and collecting data may be costly and time-consuming, and using genuine user data is challenging due to recent privacy concerns [5]. This study explores the application of deep learning, specifically leveraging the EfficientNetB3 architecture, for the automated detection of leukemia in medical images. Google's EfficientNet design recently surpassed previous state-of-the-art architectures like DenseNet and ResNet on the ImageNet classification test, while requiring fewer parameters and epochs to converge [6]. We have used the C-NMC 2019 dataset from Kaggle, which contains a total of 15,135 images from 118 patients with two labeled classes: normal cells and leukemia blast. First, we performed preprocessing on the images, including data augmentation. Further, we used EfficientNetB3, which is a pre-trained deep learning model for feature extraction. Then batch normalization, dense layers, and dropout are added on top of the base model to fine-tune for the leukemia detection task. We have also compared the performance of EfficientNetB3 with other architectures like MobileNet and VGG16. Our results show that under similar training conditions, EfficientNetB3 can converge faster and outperform other models, achieving 96.87% test accuracy. This method might be applied in the pre-screening phase to identify leukemia cells during peripheral blood testing and complete blood counts (CBCs) [7].

2. Related Work

With the development of medical technology, the ability to identify white blood cells more precisely has become crucial for correct disease diagnosis and the administration of extra therapy. Over the years, numerous machine learning studies have attempted to tackle the problem of image classification using massive ALL cell image datasets, such as ALL-IDB, the ASH image bank, and the ISBI 2019 C-NMC challenge dataset. The CNMC dataset is now one of the largest single cell ALL image datasets available. This is highly suitable for machine learning since the greater the dataset, the more patient case variation that can be considered for diagnosis.

The CNMC dataset contains varying amounts of data for each type. More pictures can be added to one of the classes using image augmentation techniques.

To increase the number of photos in the healthy cell class, E. Mauricio de Oliveira and D. O. Dantas [9] proposed adding

vertical and horizontal reflection, 60-degree rotations, 17 x 17-pixel Gaussian blur, salt and pepper noise, and a shear factor of 0.3 to the data.

To improve the information, Kasani et al. [10] scaled the data to 380×380 pixels and included brightness, intensity, and flips. Images are resized from their original 450×450 pixels to eliminate unnecessary black borders.

An alternative to the need for big training datasets is transfer learning, which uses a pretrained network for either direct feature extraction or refinement on a different dataset. In [11] and [12], pretrained AlexNet is used to classify different ALL subtypes. In [13], feature extraction, feature selection, and ensembling are used to diagnose B-ALL. A trained VGG-F architecture is used for feature extraction. The next step involves using principal component analysis to choose the features that an ensemble of classifiers will employ. Based on neural networks initial success in image classification, several varieties of CNNs were developed. ResNet, AlexNet, and GoogLeNet [14] are the CNN kinds that are most frequently used. Xception and VGG16 are two examples of more traditional neural networks that J. E. Mauricio de Oliveira and D. O. Dantas [9] attempted to use excessively complex design to achieve high accuracy. Several ensemble model combinations were employed by Kasani et al. [10] to determine the precise prediction.

The softmax technique is used in the output layer of VGGNet models to generate 1000 neurons. Oliveira and Dantas [9] replaced the global average pooling layer of neurons with repaired linear units (ReLU). The softmax function was then used to couple two fully connected layers with 512 neurons to a prediction layer with two neurons. A dropout layer was also applied to prevent overfitting of the data.

Kasani et al. [10] removed five layers from the MobileNet and applied an average pooling layer application to each of them. Their overall accuracy rating was 96.17%.

In Prellburg and Kramer's [15] proposed model, there was a factor of two in spatial downsampling between each of the five convolutional phases. After adding global pooling and a linear classifier, the model achieved an overall accuracy of 89.91%.

Honnalgere and Nayak [16] used two Inception ResNets that had been trained on ImageNet before, using a mixed-model architecture for training at each training stage. The outputs from each model were then combined and fed into a pair of neurons for classification.

Yarlagadda et al. [17] expressed CNN layer features using the Inception-v3 and ResNet models in conjunction with R-MAC global descriptors. The Inception-ResNet model uses less expensive inception blocks and residual connections to increase efficiency at the expense of accuracy. Spatial areas are utilized to generate an image representation of the CNN features using the R-MAC global descriptors. Using the

dataset, CNN was trained over 940 epochs. To determine the closest commonality, they used their closest neighbours. Their accuracy rate with this strategy was 94.6%.

With the advancement of medical knowledge, the ability to accurately identify white blood cells has become increasingly important for diagnosis. Alharbi et al. [18] used the UNET architecture of a convolutional neural network (CNN) to segment and classify WBCs.

To identify WBC from blood smears, Yentrapragada [19] employs a hybrid approach that combines CNN and deep learning. 12,500 images were selected from the Kaggle image collection. The hybrid optimization technique is used as a feature extractor, and CNN paired with LSTM is used as a classifier.

Munir et al. [20] used an auto-encoder for the classification of images pertaining to breast cancer. A total of 569 samples were obtained using the Wisconsin Diagnostic Data Collection; 357 of these samples had benign characteristics and 212 had malignant characteristics. The MATLAB R2017 platform was then used to do the recommended work.

By applying machine learning methods, many researchers also tried to solve image classification tasks. The authors, T.S. Furey [21], used the Support Vector Machine (SVM) to determine whether the blood cells contained leukemia. The nuclei of the leukocytes were recovered utilizing color-based clustering and k-means clustering (KMC)-based segmentation. Numerous attributes, such as shape and fractal dimension, were obtained from the segmented pictures. They also used the SVM classifier using cross-validation techniques.

Kashef [22] suggested several machine learning algorithms, including XGBoost, SVM, gradient boosting machine, RF, decision tree, linear discriminant analysis, and multinomial linear regression, where XGBoost demonstrated the best outcomes. Deep learning methods are commonly used for leukemia classification.

A VGG-16 network was proposed by Honnalgere and Nayak [16]. It was pre-trained on the ImageNet dataset and then improved further using batch normalization. Marzahl et al. [23] combined two augmentation techniques with a pre-processing step based on normalization to create a DL-based framework. They employed an extra regression head that helped in predicting the bounding box for categorization using the ResNet-18 network.

The authors of [24] proposed an ensemble model based on DCT for the purpose of differentiating cancerous cells from normal cells. CNN-RNN is the result of merging recurrent and convolutional neural networks. An RNN and a pre-trained CNN were used in their hybrid model to extract features from the dynamic spectral domain.

Ding et al. [25] showed three different deep learning-based architectures, Inception-V3 [26], InceptionResNet-V2 [28], and DenseNet-121 [27], for the classification of microscopic images of white blood malignancy. Additionally, they showed off an ensemble neural network framework and proved that their custom layering model performed better than a lot of other single-class models.

In [29], the authors compared three different deep learning-based algorithms, such as AlexNet, VGG, and GoogleNet [30], to classify lymphocytic cells.

Our proposed model uses EfficientNetB3, which is commonly used in image classification, because these are designed in such a way that they have a balance between accuracy and efficiency in convolutional neural networks (CNNs) through a strategy called compound scaling.

Ahmed Adil Nafea [31] used EfficientNetB3 for lung cancer detection, and its results were 2.13% better than the best-trained classifier. Ahmad Huri [32] used the EfficientNet model to optimize and increase the accuracy of the classification of brain tumor MRI images. The proposed system consists of two main phases. first preparing the images using many methods, then classifying the preprocessed images using CNN. Of the 3064 images used in this study, three distinct types of brain tumors—gliomata, meningiomas, and pituitary—were visible. This investigation yielded an accuracy of 98.00%, a precision of 96.00%, and an average recall of 97.00% using the model that the researcher utilized. In [33], Sudhir D. and the authors of this study provide an improved and refined version of the EfficientNetB3 model for the classification of malignant skin lesions, based on the concept of fine-tuning transfer learning. A comparative analysis of pre-trained deep learning models, including EfficientNet B0-B2 models, ResNet50, InceptionV3, and InceptionResNetV2, has been done. The investigation's findings suggest that refined EfficientNetB3 can help with melanoma diagnosis and the development of computer-aided diagnostic systems.

3. Methods

A. Dataset Description

The dataset used was made available for the C-NMC 2019 [19] medical imaging challenge, which was hosted by the IEEE International Symposium on Biomedical Imaging (ISBI) and included 118 patients, 49 of whom were Hem patients and 69 ALL patients. Table 1 displays the dataset's comprehensive information.



Fig 1. ALL (I) and Hem (II) image

Data Categories	Subjects-Cancerous (ALL)	Subjects-Normal (Hem)	Subjects-Total	Images (ALL)	Images (Normal)	Images (Total)
Train Set	47	26	73	7272	3389	10661
Preliminary Test Set	13	15	28	1219	648	1867
Final Test Set	9	8	17	1761	825	2586

Table I

B. Methodology

1) Data Augmentation:

One important tactic to improve the efficiency of the neural network technique is to train the network on a large volume of data. Small datasets are used for the majority of computer vision jobs, which results in poor classification models. Prior-trained deep learning models, trained on a large-scale dataset such as ImageNet, can show considerable performance improvements. By expanding the quantity of training data, we utilize the data augmentation strategy to produce an efficient leukemia classification model. Data augmentation [23] is a technique that involves making minor adjustments to the existing data to purposefully boost the total. The One important tactic to improve the efficiency of the neural network technique is to train the network on a large volume of data. Small datasets are used for the majority of computer vision jobs, which results in poor classification models. Prior-trained deep learning models, trained on a large-scale dataset such as ImageNet, can show considerable performance improvements. By expanding the quantity of training data, we utilize the data augmentation strategy to produce an efficient leukemia classification model. Data augmentation [23] is a technique that involves making minor adjustments to the existing data to purposefully boost the

total number of training data copies, all without actually gathering new data.

Augmentation Technique	Parameters
Horizontal Flip	True
Vertical Flip	True
Rotation range	30
Width Shift Range	0.25
Height Shift Range	0.25
Zoom Range	0.3
Shear Range	0.2
Fill Mode	Nearest
Channel Shift Range	10

Table II

Image augmentation is one of the most widely used techniques to improve deep learning model performance and reduce over-fitting problems.

In our study, we utilized various data augmentation techniques, including horizontal flip, vertical flip, rotation_range, width_shift_range, height_shift_range, zoom_range, shear_range, fill_mode, and channel_shift_range, as illustrated in Table II.

2) Transfer Learning:

Transfer learning is a machine learning methodology whereby the knowledge acquired from problem-based training is applied to task or field specific training [24, 25]. The initial layers of deep learning are learned to define the properties of the image. The final few levels of the learned network can be eliminated during the transfer learning process. After that, a new layer on the desired image can be used to retrain the network. When employing this transfer learning approach in the present assignment, there is a significant speed and accuracy improvement over training a model from scratch, which makes use of extensive visual input along with previously learned network knowledge.

3) Proposed Framework:

After the application of data augmentation to the leukemia cell image dataset, detailed parameters are mentioned in Table II, followed by the implementation of the transfer learning model. We implemented many models, like MobileNet, VGG16, and ResNet, but got our best results on the EfficientNetB3 model.

The EfficientNetB3 version is what we propose as a compromise between outstanding performance and operating time. Google Research developed the EfficientNet [26] family of convolutional neural network topologies. One of the models in the EfficientNet family, which is regarded as a balanced and effective mode, is EfficientNet-B3.

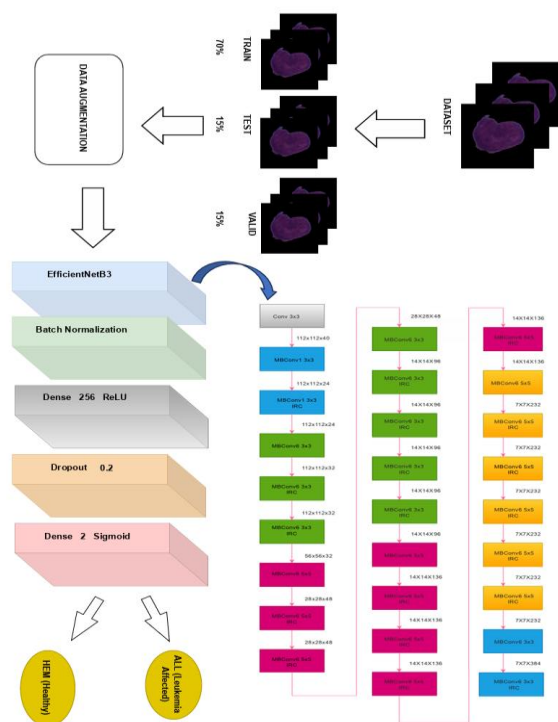


Fig 2. Methodology and Model Architecture

One of the key aspects of EfficientNet-B3 is its automated architectural scaling, which takes the resolution of the input photos into account. It makes it possible for the model to have a greater number of layers altogether and more filters, or depth and breadth, within each layer. The third model in the EfficientNet family, the EfficientNet-B3, has 1.3 times the resolution and is 1.2 times broader than the EfficientNet-B0, which has the same depth. If each layer in the input photos has additional filters and the images have a greater spatial resolution, the model can gather additional details from the photos.

In our work the EfficientNetB3 architecture is extended with batch normalization, a dense layer, a dropout layer, and another dense layer.

Batch normalization is introduced to normalize the outputs of a layer within each mini-batch. Higher learning rates and quicker convergence are possible when the learning process is stabilized by normalized inputs. Batch normalization enhances generalization performance and lessens overfitting. As batch normalization reduces the network's sensitivity to weight initialization values, this makes hyperparameter tuning easier. These are the reasons why batch normalization plays an important role in our proposed architecture.

Then we added a dense layer with L1 and L2 regularizers. This dense layer's kernel weights have an L2 regularizer added to them. During training, it penalizes the sum of squares of these weights and has a tendency to reduce all weights to zero in order to provide a smoother decision boundary. This tends to promote robustness by reducing sensitivity to noise or outliers. This dense layer's activations and biases were subjected to the L1 regularizer. The total

absolute value of these items is penalized by the L1 regularizer. In order to efficiently carry out feature selection, it is inclined to set certain weights to zero. This makes our model more interpretable by eliminating less important features.

The dropout layer is then included because, during training, it sets a specific percentage of neurons within each hidden layer to zero. In effect, this drops out those neurons, making the surviving neurons pick up more resilient and autonomous properties. The network develops better generalization representations and is less likely to memorize training material by keeping each neuron from becoming dependent on properties. The dense layer creates a dense connection structure that, generated by a dense layer, enables complex interactions and feature extraction. In this layer, each input connection to a neuron has a weight value assigned to it. The learning algorithm modifies these weights throughout training to maximize the network's prediction accuracy. The hyperparameters of our proposed model are presented in Table III.

Layers	Hyperparameters and Value
Base Model-- EfficientNetB3	Input Shape= (224,224,3)
Batch Normalization	Axis=-1
Dense Layer 1	Units= 256 kernel_regularizer=L2 regularizer for l=0.016 activity_regularizer=L1 regularizer for l=0.006 bias_regularizer=L1 regularizer for l=0.006 Activation=ReLU
Dropout Layer	Rate=0.2
Dense Layer 2	Units=2 Activation=Sigmoid
Compiler	Optimizer: Adamax (learning rate is 0.003) Loss: Binary Crossentropy Metrics: Accuracy
Batch size	40

Table III

4. Results and Model Evaluation

Before validating the performance of the proposed model, we used various performance metrics to assess its effectiveness, including precision, accuracy, F1-score, and recall.

The following parameters are calculated in the evaluation metric.

- True Positive (TP): It is the total count having both predicted and actual values of ALL (cancer).
- True Negative (TN): It is total counts having both predicted and actual values, which are Hem (normal).
- False Positive (FP): It is total counts having prediction as ALL while it is Hem..
- False Negative (FN): It is total counts having prediction as Hem while it is ALL.

Ob-serve	Equations	Description
Ac-cu-racy	$TP+TN/TP+TN+FP+FN$	The ability of the classifier to correctly classify the class label.
Pre-ci-sion	$TP /TP+FP$	This metric indicates number of positive classes with correct answers.
Re-call	$TP /TP+FN$	This metric shows the proportion of all positive classes that were correctly classified.
F1-Score	$2*(Precision*Re-call)/(Precision+Recall)$	This metric use a percentage of the balance between recall and precision.

Table IV

Our proposed model has an accuracy of 96.87%, an F1-score of 96.9%, a recall of 96.24%, and a precision of 97.58%, making it one of the most promising models.

We experimented with various common CNN architectures, which are mentioned in Table V. In this table, modified architecture (ex., Modified MobileNet) means following the same proposed architecture, only the base model has been changed.

CNN Architectures	Accuracy
VGG-16	83.78
InceptionV3	84
EfficientNet	84.5
MobileNetV2	88.89
DenseNet121	89

ResNet18	89.33
ResNet50	90
Modified VGG-16	93.46
Modified MobileNet	95.87
Modified EfficientNetB3 without L1 and L2 regularizers	94.43
Proposed EfficientNetB3	96.87

Table V: The performance of the proposed modified architecture vs. common CNN architectures.

Model	F1 Score (%)
Kaiqiang Ma & Lingling Sun (2019) [34]	85.80
Yongsheng Pan & Mingxia Liu (2019) [35]	91.0
Ekansh Verma & Vijendra Singh (2019) [36]	89.4
Jonas Prellberg & Oliver Kramer (2019) [37]	88.9
Fenrui Xiao & Ruifeng Kuang (2019) [38]	88.5
Ying Liu & Feixiao Long (2019) [39]	87.6
Yifan Ding & Yujia Yang (2019) [40]	85.5
Atmika Hinnalgere & Gaurav Nayak (2019) [41]	91.7
Puneet Mathur & Mehak Piplani (2020) [42]	91.89
Shiv Gehlot & Anubha Gupta (2020) [43]	94.86
Shubham Goswami & Suril Mehta (2020) [44]	95.26
Jose de Oliveria & Daniel Dantas (2021) [9]	92.60
William Lamberti (2022) [45]	90.10
Pradeep Das & Biswajeet Sahoo (2022) [46]	91.48
Adel Sulaiman & Sheifali Gupta (2023) [47]	92.90
Proposed	96.90

Table VI: The performance of the proposed method vs. previous methods

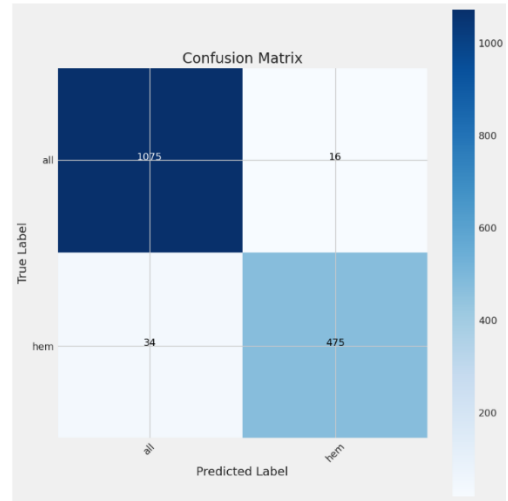


Fig. 3. Confusion Matrix of Proposed Architecture for 1600 unseen test samples

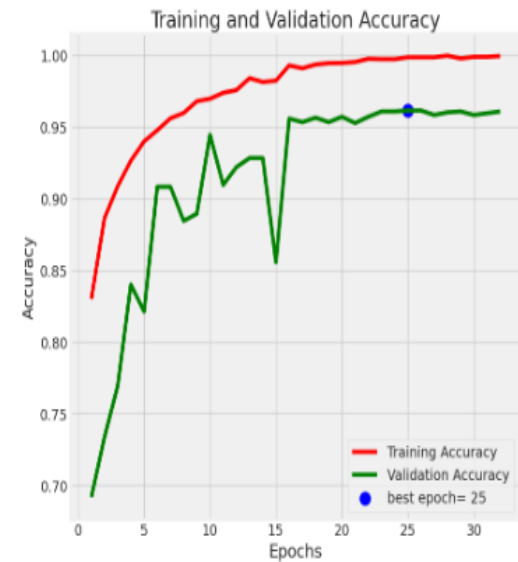


Fig. 4. Accuracy Curve of Proposed Architecture

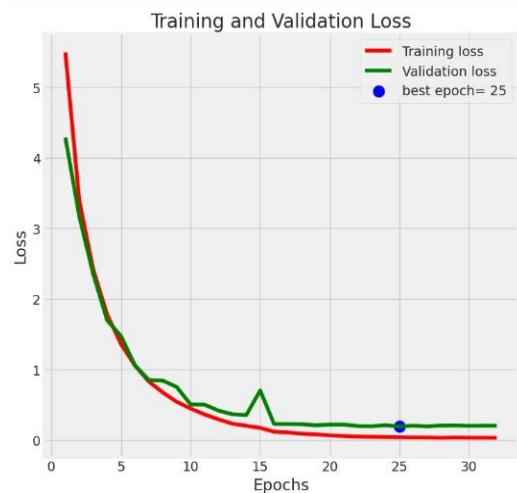


Fig. 5. Loss Function Curve of Proposed Architecture

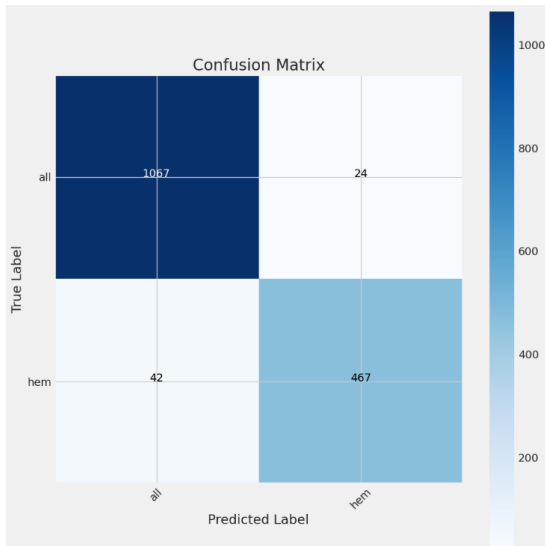


Fig. 6. Confusion Matrix of modified MobileNet Architecture for 1600 unseen test samples

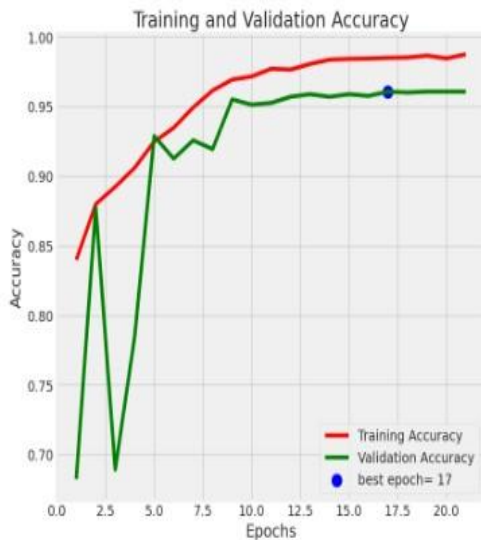


Fig. 7. Accuracy Curve of modified MobileNet Architecture

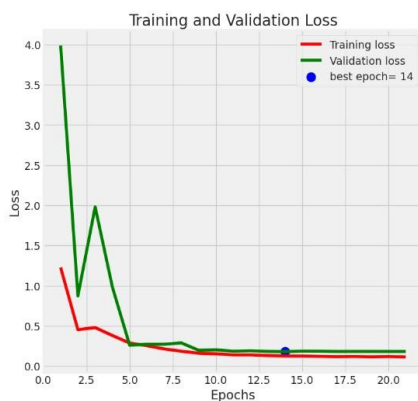


Fig. 8. Loss Function Curve of modified MobileNet Architecture

5. Conclusion

The main issues in the field of illness diagnostics are the early diagnosis and detection of leukemia and the accurate and affordable identification of malignant leukocytes in the early

stages of the disease. Labor-intensive processes and inadequate flow cytometer equipment are present in laboratory diagnosis institutes, despite the high frequency of leukemia. Treatment for leukemia can be more successful if it is discovered early. We offer a competitive and efficient approach to the classification of healthy cells and leukemia-affected cells, which is useful even when there is a lack of available data. In this paper, we propose a modified CNN architecture by adding appropriate layers at the end with L1 and L2 regularizations in the dense layer. It was experimentally proven that, due to the additional layers, this model outperforms the other researchers and simple CNN architectures to accurately distinguish normal cells from cancer cells. Based on our findings, the suggested approach effectively manages intricate images and performs better on unobserved data. Therefore, the proposed modified architecture enhances its effectiveness across diverse applications of image classification.

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