White Blood Cell Types Classification Using Deep Learning Models

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Abstract
Classification of different blood cell types is an essential task for human's medical treatment. The white blood cells have different types of cells. Counting total White Blood Cells (WBC) and differential of the WBC types are required by the physicians to diagnose the disease correctly. This paper used transfer learning methods to the pre-trained deep learning models to classify different WBCs. The best pre-trained model was Inception ResNetV2 with Adam optimizer that produced classification accuracy of 98.4% for the dataset comprising four types of WBCs.

Keywords: *Deep Learning, Blood Cells Classification, Transfer Learning*

1. Introduction

Every minute the heart is pumping five litres of blood to the body and represent 7% of the bodyweight [1]. It trans- ports oxygen, eliminates carbon dioxide, protects the body's immune system from viruses and bacteria, and maintains the body temperature. All these tasks make the blood essential for life [2]. The blood consists of crucial components; Plasma is the liquid component that contains all other blood components such as Red blood cells, White blood cells, and Platelets [3]. Counting red blood cells and white blood cells has vital importance in detecting abnormalities and diagnosing diseases. Distribution of various cell types in the white blood cells indicates problems in the immune system [4]. There are five major types of white blood cells: Neutrophils, Lymphocytes, Eosinophils, Monocytes, and Basophils. The Neutrophils is the first line of defence in the body and the biggest in number. It fights with different types of infections created by bacteria, fungi, or inflammations. Eosinophils deal with parasitic infections and helps the body's interaction with various allergic reactions. Lymphocyte creates a defence from harmful invaders such as viruses by generating antibodies. Monocyte makes more defence toward the body by killing any dangerous bodies that can affect the immune system. This type of cell can last for a longer time than other cell types. The Basophils provides short-term inflammatory response and react to the body's sensitivity and allergies by releasing a chemical called histamine. Comparing to the cell types as mentioned earlier, the Basophils are the lowest population in cells counts [5]. The number of white blood cells (WBC) present in the blood is one of the vital indicators of different

diseases. A Normal range of the WBC count varies according to the age of the human. It is between 4,000 to 10,000 per cubic millimeter of blood in an adult, whereas infants may have a higher number of WBCs ranging from 5000 to 38000 [6], [7]. Abnormal WBC count indicates different types of medical conditions. Leukocytosis represents an abnormally high WBC count, whereas, in the case of Leukopenia, a patient has a low WBC count. A high WBC count may be due to allergic response, inflammatory conditions, and infections. A low WBC count may indicate autoimmune disorders, bone marrow damage, leukemia, etc. Along with total WBC counts, the differential is also performed on the WBCs. Differential provides information about health issues to the healthcare provider. A particular type of WBC count may lead to the cause of infection or inflammation. A normal range of these types of WBC is Neutrophils (40 to 60%), Eosinophils (1 to 4%), Basophils (0.5 to 1%), Monocyte (2 to 8%), and Lymphocytes (20 to 40%) [8]. Abnormal differential counts indicate a health problem, and hence it is important to identify these cells in the blood sample and count them. In this paper, the classification of these blood cell types is optimized through deep learning methods. Deep learning algorithms (DL) simulate the human brain in terms of structures and functions. Deep neural networks similar to artificial neural networks (ANN) contain a large number of neuron layers. One main difference between ANN and DL is the process of features extraction. In ANN, the step of features extraction represents an essential step before constructing the model, while in deep learning models, it is an implicit step that takes place during the training of the model. [9]. Deep learning algorithms require a large amount of training data to train the model correctly. If the training examples for a new problem are insufficient, it is impossible to adequately train deep learning architectures. Transfer learning uses the knowledge earned from a previously trained DL model instead of collecting many training examples. Creating new DL models by fine-tuning previously trained models refers to the transfer learning process. Some examples of pre-tuned models are VGG16, ResNet50, InceptionV3, which had been trained on a massive dataset of images [10]. Extracting meaningful information from the images of a blood cell and recognizing different types of cells is helpful to detect multiple kinds of illness. An automatic WBC identification will help in reducing the working load of the technicians in the clinical laboratories. In the remote areas with lesser medical expertise and availability of the trained technicians, proposed methodology will help in quick reporting of the clinical lab results.

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The main objective of this paper is to use the concept of transfer learning on the classification of white blood cell images. We have compared four pre-trained models, namely MobileNetV2, VGG16, Xception, and InceptionResNetV2, and summarized the classification performance. Two optimization methods are applied to tune their parameters. The remainder of the paper is divided as follows: related work is discussed in the section 2, materials and methods are explained in section 3, Results and discussions in section 4 and finally, the paper is concluded in section 5.

2. Related Works

Wang et al. [4] extracted spatial features based on morphology and spectral features of five types of WBC. They have achieved a classification accuracy of more than 90% using the Support Vector Machine (SVM) classifier. Rezatofigi and Zadeh [11] applied image processing algorithms to extract various features after segmentation. Essential features are selected using the sequential forward selection method. The perfor- mance of two algorithms, ANN and SVM, are tested on a smaller dataset of 254 images and obtained 96% classification accuracy. Prinyakupt and Pluempitiwiriyawej [12] extracted morphological features after segmentation from blood smear images and applied linear and Bayes classifiers to classify five types of WBCs. Classification accuracy was above 97% for both classifiers. Lots of research exists on the segmentation of blood cells in the images [13]–[15]. Mathur et al. [16] used active contours to segment the WBC nucleus and cytoplasm. Cellular, nuclear, and cytoplasmic features are used to train a Na¨ıve Bayes classifier. Training (80% of images) and testing (20% of images) on 237 images produced classification accu- racy of 92%. Shahin et al. [17] proposed a deep convolutional neural network called WBCsNET to classify five types of healthy WBCs. They have used the concept of transfer learning in which off-the-shelf features from several pre-trained models are selected for the training on the WBCs images. Overall classification accuracy was found to be 96%. Reddy et al. [18] classified microscopic cell-images into infected with malaria or uninfected cells. The results showed that transfer learning produced a good performance in classifying the malaria cells. For the same purpose, researchers in [19] proposed the CNN architecture model (Inception-v3) to determine whether new image datasets through Transfer Learning will function best in terms of accuracy and performance or not. White blood cells classification proposed in [20], first solving the imbalance problem in the dataset by creating a synthetic image using classic data augmentation and Deep Convolutional Generative Adversarial Networks (DCGAN). After that, the ResNet50 model is trained on a dataset with two different scenarios. The first is taking synthetic images and the real images with a 70 to 30% ratio and obtained an accuracy of 80.4%. In contrast, the second scenario with a 50 to 50% image ratio got 82.5% accuracy. Segmentation and Classification of the White Blood Cells to Detect Acute Leukemia is provided by [21], where they applied segmentation to the blood slide image and extract the features from the image to detect leukemia based on KNN classifier to obtain an overall accuracy of 93%. Despite the high performance and accuracy obtained by using CNN to classify the blood cells, Liang et al. [22] proposed a hybrid method to enhance the overall performance. The new approach depends on combing features extracted from the CNN model with the features extracted from the RNN model. This method produced 90% classification accuracy. Baydilli et al. [23] combined images of WBCs from different datasets and used the concept of transfer learning to classify the types of WBCs. The total number of images from 10 datasets is more than 1500 images of various sizes. After trying different ratios for training and testing, the best classification accuracy was 98%. Wang et al. [24] proposed a 3D attention network that can learn spatial and spectral features of the images collected from microscopy hyperspectral images to classify WBCs. Classification results on a dataset of about 5900 images showed that a 3D attention network could produce a classification accuracy of 97% on five types of WBCs.

3. Materials and Methods

The dataset was collected by several contributors for the Barcelona Clinic Hospital, where microscopic images of eight types of cells were taken, including the white blood cells used in this paper [25]. The images have a size of 360 x 363 pixels. The dataset contains 17,092 images from eight different cell types (neutrophils, eosinophils, basophils, lymphocytes, monocytes, immature granulocytes, erythroblasts, and platelets). We have selected four cell types from this dataset, namely neutrophils, eosinophils, lymphocytes, and monocytes. The number of images for these cell types is highest in the dataset and better for the training and testing. The dataset for these four WBC types contains 10,469 images divided into train, validation, and test sets. Training dataset contains 70%, whereas testing and validation datasets contain 20% and 10% respectively. The following table illustrates the distribution for each dataset (Table 1). Figure 1 shows sample images from all four classes.

Data augmentation is considered the most powerful solution for the problem of data size limitation. Many medical image datasets suffer from this issue due to the non-availability of sufficient samples. This approach encompasses several techniques that tend to enhance the quality and size of images, such as: transforming the geometric, augmenting colour space and feature space, image mixing, erasing randomly, and many others [26]. Hence, we have increased the training dataset by image augmentation. The number of total images in the training dataset after data augmentation is given in table 2.

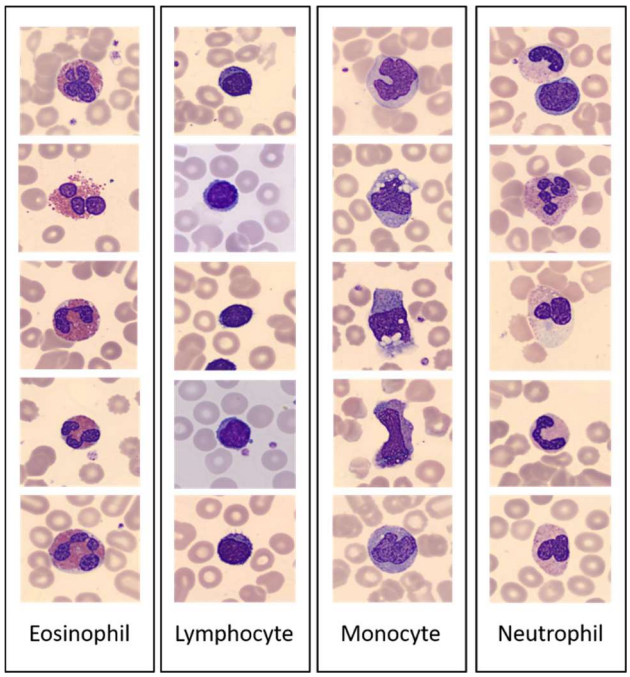

Figure 1. Sample images from the Dataset

Table 1. Distribution of the WBC Dataset

Data	Train 70%	Validation 20%	Test 10%
Eosinophil	2039	509	318
Lymphocyte	1554	388	243
Monocyte	1818	454	284
Neutrophil	2036	508	318

Table 2. Number of training images after data augmentation

Cell Types	Before Augmentation	After Augmentation	Total
Eosinophil	2039	4078	6117
Lymphocyte	1554	3108	4662
Monocyte	1818	2639	4457
Neutrophil	2032	4072	6104

3.1 Pre-trained Models

This experiment depends on transfer learning approach, where pre-trained models are imported in order to use its wights. Four pre-trained models are considered in this experiment which are: MobileNetV2 [27], VGG16 [28], Xception [29], InceptionResNetV2 [30]. These models were chosen specially because of the high performance and amount of data they had been trained on. Four pre-trained models are considered in this paper which are MobileNetV2 [27], VGG16 [28], Xception [29], InceptionResNetV2 [30]. These models were chosen due to their high performance, and they have trained on a large amount of data.

MobileNetV2 by Google is a deep convolutional neural network that can perform better on mobile devices [27]. It contains two types of blocks, residual blocks with the stride of 1 and residual blocks with the stride of 2 for downsizing. The architecture of MobileNetv2 comprises 2D convolutional layers and residual bottleneck layers. Residual blocks provide a skip connection from the start to the end of a convolutional block.

VGG16 achieved an accuracy of 92% on the Imagenet dataset having 14 million images. K. Simonyan and A. Zisserman of the University of Oxford proposed the VGG16 convolutional neural network model. The architecture of VGG16 consists of 16 layers, including convolutional layers, pooling layers, and fully connected layers.

Xception model is an extension of the Inception architecture. It replaces the standard Inception modules with depth-wise separable convolutional layers with residual connections. A strong feature extraction base comprises 36 convolutional layers followed by a logistic regression layer. A fully connected layer before the logistic regression layer is optional.

Inception-ResNet-v2 is a very deep convolutional neural network. This model is trained on ImageNet database comprising more than a million images. The model consists of 164 layers. The model has learned numerous representations of features from a wide variety of images [31]. This model combines the Inception architecture with residual connections, where each Inception block is followed by a filter expansion layer (1 × 1 convolution without activation). The performance of this model has been established by several kinds of research where it showed the highest classification accuracy compared with other models [32], [33]. Table 3 compares the number of layers and number of parameters for each model.

Table 3. Pre-trained deep learning models

Model	Number Of layers	Number Of parameters (millions)
Mobile NetV2	53 layers	3.5
Vgg-16	16 layers	138
Xception	71 layers	22.9
InceptionResNetV2	164 layers	55.9

3.2 Optimization Methods

An optimization method is needed that updates the weights to get optimal cost function with minimum error. The stochastic gradient descent (SGD) method uses the cost function gradient information with momentum and scheduling of the learning rate [34], [35]. Adam (Adaptive moment estimation) is one of the most commonly used optimization methods built on the adaptive estimation of the first and second-order moments [36]. This method is computationally efficient and has low memory requirements. Furthermore, it is invariant to diagonal re-scaling of the gradients.

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3.2 Performance Measures

Classifier performance can be expressed in terms of accuracy, precision, recall, and F-measure. Precision is defined as the number of truly positive instances (TP: True Positive) divided by the total number of positive instances (including True Positive and False Positive).

$$Precision = \frac{TP}{TP + FP}$$

Recall or Sensitivity is defined as the number of instances truly classified as positive (TP: True Positive) divided by the total Positive instances including TP and FN (False Negative).

$$Recall = \frac{TP}{TP + FN}$$

F-measure is the combination of precision and recall and defined as,

$$F - measure = \frac{2 \times Precision \times Recall}{Precision + Recall}$$

4. Results and Discussion

The last four trainable layers were removed from the pre- trained models. Then, two fully connected layers are added in the pre-trained models. The last layer is the classification layer, where the Softmax function is applied for classification. The images are resized to 224 x 224 pixels size. Some parameters like learning rate, momentum rate for SGD optimizer only, and epsilon (used to avoid nearly zero gradient case) for Adam optimizer only are fine-tuned to get the best results. Two values of the learning rate, 0.01 and 0.001, are considered. After several trials, a momentum term of 0.9 performed better than all other values. For the value of epsilon in Adam optimizer, 0.01 is found to be the best as recommended in [37] also. A batch size of 32 is used for all the models.

Table 4. Classification accuracy for all four models

Base Model	Opt. Method	LR	Train	Validation	Test
Mobile NetV2	SGD	0.01	97.77	95.37	79.79
	Adam	0.001	97.77	94.84	**89.85**
Vgg-16	SGD	0.001	94.20	94.46	90.28
	Adam	0.001	95.54	95.21	**94.23**
Xception	SGD	0.01	96.43	91.66	**90.37**
	Adam	0.001	88.84	85.26	82.20
Inception ResNetV2	SGD	0.01	98.21	95.80	**96.21**
	Adam	0.001	96.88	94.35	94.32

Table 4 demonstrates the classification accuracy for all models. The best result is in bold text. It summarizes the performance of all four models with different learning rates (LR) and optimizers. It can be noted that the Inception ResNetV2 model outperformed all the models and produced the best result in terms of classification accuracy (98.4% for testing dataset).

Figure 2 shows confusion matrix for Mobile NetV2 model using Adam optimizer. Eosinophil class is confused with Lymphocyte class (25 instances) and Neutrophil class (14 instances). Similarly, Monocyte and Neutrophil classes are also confused with Lymphocyte class. Confusion matrix for Xception model with SGD optimizer is shown in Figure 3. Classification of Eosinophil and Lymphocyte classes is improved considerably but Monocyte class is confused with Lymphocyte class in higher number (46 instances). Moreover, Neutrophil class is confused with Eosinophil class in 31 instances.

Figure 4 shows confusion matrix for all four classes. It is clear from the figure that most instances of all four classes are classifier correctly. Some instances of the Monocyte cell type are confused with Lymphocyte and Neutrophil cell types. Overall classification accuracy is highest among all models (Classification accuracy is 96.21%). In figure 5, confusion matrix of VGG-16 model is tabulated for Adam optimizer. Monocyte class is confused with Lymphocyte class (24 instances) and classification of Eosinophil class is improved. The VGG-16 model with Adam optimizer showed slightly lower performance (classification accuracy is 94.2%). The confusion matrix for this model is shown in figure 5. The confusion matrix shows that some Neutrophil cell types are also confused with Eosinophil and Monocyte cell types.

It is difficult to decide which optimizer is the best between Adam and SGD optimizers. SGD optimizer performed better for Xception and Inception ResNetV2 models whereas Adam optimizer outperformed SGD optimizer in case of Mobile NetV2 and VGG-16 models.

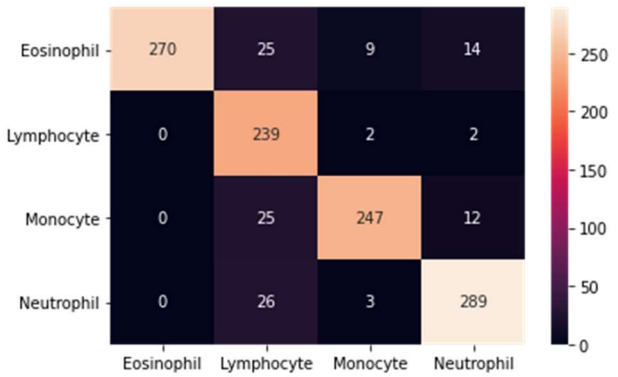

Figure. 2 Confusion Matrix for Mobile NetV2 with Adam Optimizer

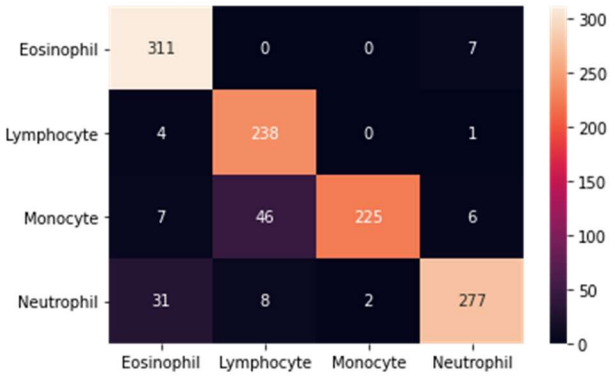

Figure. 3 Confusion Matrix for Xception with SGD Optimizer

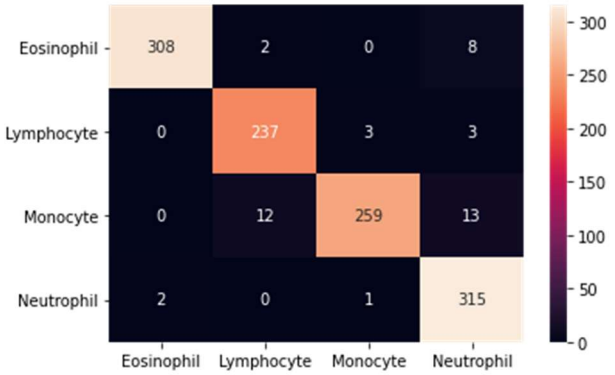

Figure. 4 Confusion Matrix for Inception ResNetV2 with SGD Optimizer

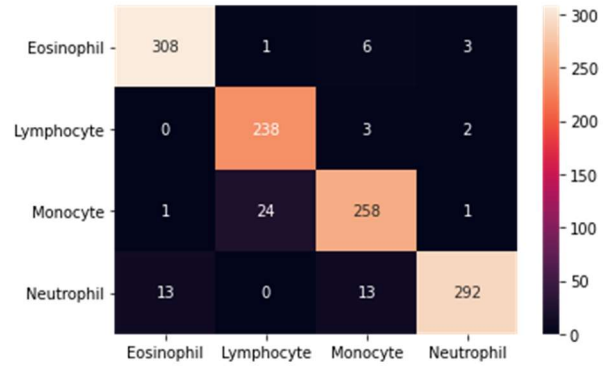

Figure. 5 Confusion Matrix for VGG-16 with Adam Optimizer

Table 5. Inception RESNETV2 performance on testing dataset for SGD optimizer and learning rate of 0.01

Class Name	Precision	Recall	F-measure
Eosinophil	99.00%	97.00%	98.00%
Lymphocyte	94.00%	98.00%	96.00%
Monocyte	98.00%	91.00%	95.00%
Meutrophil	93.00%	99.00%	96.00 %

Inception ResNetV2 model produced the best results among all four models. For the learning rate of 0.01 and SGD optimizer showed promising results with highest classification accuracy among all combinations (Classification accuracy is 96.2%). Adam optimizer with learning rate of 0.001 also got a classification accuracy of 94.3% which is near to the best accuracy. Precision, Recall, and F-measure of the Inception ResNetV2 model are listed in table 5 for all four classes. Measurements show high percentage values for all the classes that offer good performance of the pre-trained Inception ResNetV2 model on the WBCs dataset. F-measure combines both precision and recall measures. F-measure of Eosinophil class is highest with a value of 98% whereas, f-measure for other classes is near 96%.

5. Conclusion

Transfer learning is one of the most promising deep learning methodologies for real-life applications related to image classification. In this paper, different pre-trained models are used to classify images of WBCs by transfer learning. A comparison between four powerful pre-trained models with two optimization methods is presented in this paper. All four models have shown good classification accuracy on the WBCs dataset, but the Inception ResNetV2 model outperformed the rest of the models. SGD optimizer and Adam optimizer performed equally well for Inception ResNetV2 model.

6. Future Work

In future work, this model will be applied to more classes, including different pathologies. Moreover, more data collection will improve the training of the deep learning model and the results presented in this paper shows the efficacy of the deep learning models in automatic identification of the WBC classes. Recently many research works are present in the literature that focused on non-traditional optimization methods like particle swarm optimization [38,39], genetic algorithms [40] etc to optimize the parameters of deep learning models. Our future work will focus on application of such optimization methods to optimize deep learning models on a larger dataset of WBCs.

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