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Automatic Leukocytes Classification using Deep Convolutional Neural Network

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ABSTRAK

Sel darah putih atau leukosit adalah salah satu bagian darah yang bertanggung jawab untuk sistem kekebalan tubuh. Penghitungan setiap jenis leukosit merupakan hal yang krusial untuk menentukan status kesehatan. Sel darah dihitung menggunakan hematology analyzer. Namun, perangkat ini hanya tersedia di laboratorium klinik pusat atau rumah sakit. Saat ini masih banyak clinician yang melakukan perhitungan manual dengan memperkirakan jumlah leukosit menggunakan mikroskop. Hal ini berpotensi menimbulkan kesalahan perhitungan yang tinggi. Oleh karena itu, penelitian ini mengusulkan suatu sistem yang dapat mengklasifikasikan jenis-jenis leukosit. Metode convolutional neural network (CNN) dengan arsitektur VGG-19 digunakan dalam klasifikasi leukosit. Beberapa skenario pengujian dengan mengubah parameter epoch dan ukuran batch diterapkan untuk mendapatkan akurasi terbaik. Hasil simulasi model pembelajaran yang digunakan dapat menghasilkan akurasi hingga 100% untuk mengklasifikasikan neutrofil, eosinofil, monosit, dan limfosit. Hasil ini dicapai dengan menggunakan pengoptimal Adam, Epoch=5 dan batch size=60.

***Kata kunci**: leukosit, klasifikasi, CNN, VGG-16*

ABSTRACT

White blood cells or leukocytes are one of the blood components responsible for the body's immune system. Counting each type of leukocyte is a crucial thing to determine the health status. Blood cells were counted using a hematology analyzer. However, this device is only available in central clinical laboratories or hospitals. Currently, there are still many clinicians doing manual calculations by estimating the number of leukocytes using a microscope. This has the potential to generate high errors in calculations. Therefore, this study proposes a system that can classify the types of leukocytes. The convolutional neural network (CNN) method with VGG-19 architecture was employed in leukocyte classification. Several test scenarios by changing the epoch and batch size parameters were applied to obtain the best accuracy. The results of the simulation of the learning model used can generate accuracy up to 100% for classifying neutrophils, eosinophils, monocytes, and lymphocytes. This result was achieved using Adam optimizer, epoch=5 and batch size=60.

***Keywords**: leukocyte, classification, CNN, VGG-16*

1. INTRODUCTION

Blood is an essential component of the human body **(Farley et al., 2012)**. Blood circulates nutrients and oxygen to all cells and tissues in the body **(Marenzana & Arnett, 2013)**. Blood also carries information about health status. If there is an infection in the body, it can also be analyzed through a blood sample. Blood components include blood plasma, red blood cells, white blood cells, and platelets **(Kuan et al., 2018)**. The composition of blood plasma is about 55%, and the rest is blood cells and platelets **(Weber et al., 2018)**. They must be inappropriate portions so that the body is healthy. Blood components have specific functions. White blood cells or leukocytes have an essential role in the body's immunity **(Nicholson, 2016)**. A key symptom of blood leukemia is aberrant alterations in the number, shape, and texture of white blood cells or leukocytes.

Leukocytes circulate along the walls of blood vessels to look for foreign bacteria and then destroy them. If analyzed in more detail, leukocytes consist of eosinophils, lymphocytes, monocytes, neutrophils, and basophils. They have their respective roles to work together to maintain the body's immune system. The normal proportion of each leukocyte component is 40 to 60% neutrophils, lymphocytes 20 to 40% monocytes 2 to 8%, eosinophils 1 to 4%, and basophils 0.5 to 1%. If an inappropriate amount is found, it is suspected that there is an infection in the body.

Analyzing the calculation of blood components, especially white blood cells, becomes an important job because it is related to infectious diseases. The medical instrument for the blood cell count is a hematology analyzer. However, these devices are only available at large health care centres or laboratories. You can only take a blood sample at the clinic and then send it to a hematology analyzer laboratory. Another way is to estimate manually on microscopic images of blood cells, but it will take a long time and be tedious. Another problem is that the device settings and image quality greatly determine accuracy **(Reyes-cadena, 2014)**. Currently, digital image processing has a major role in pattern recognition, object detection, and classification of medical images **(Gavet & Debayle, 2019)**. The classification of blood cells or blood cell count has been reported in numerous studies **(Fitri et al., 2020)**. Feature extraction methods combined with machine learning have been proposed for blood cell recognition **(Hodneland et al., 2009) (Putzu & Ruberto, 2013)**. The detection method using traditional machine learning produces high accuracy. However, it requires selecting of a reliable feature extraction method **(Falcón-ruiz et al., 2010) (Mourtada et al., 2019)**. Another issue is the need for big data or analysis on a large number of datasets in a relatively short time **(Al-Dulaimi et al., 2018)**. The deep learning (DL) approach is a significant advance in image recognition and can provide a solution to this problem **(Beyeler, 2017) (Tsihrintzis et al., 2018)**.

Therefore, this study proposes a white blood cell classification method using the DL approach. The major focus of this work is to classify the white blood cells into Neutrophils, Eosinophils, Monocytes, and Lymphocytes, which is a frequent difficulty that most biomedical engineering researchers confront. The Convolutional Neural Network (CNN) method as a form of DL was employed in this study. To achieve the optimum performance, the CNN architecture used is VGG-16 with adjusted parameters. Accuracy, precision, recall, and the F1-score are all measured as part of the suggested method's performance evaluation. With this proposed method, it is hoped that it can be developed in the application of blood cell counting.

2. MATERIAL AND METHODS

2.1 White Blood Cells Dataset

The white blood cells images used in this study were collected from the Kaggle open dataset https://www.kaggle.com/datasets/paultimothymooney/blood-cells. The white blood cells types include Neutrophil, Eosinophil, Monocyte, and Lymphocyte in *.jpeg form. Figure 1 presents samples of white blood images of each type used in this study. 2,487 images were simulated, consisting of 624 Eosinophil, 620 Lymphocyte, 620 Monocyte, and 623 Lymphocyte. The proposed method was based on CNN architecture with the VGG-16 model and an adam optimizer. The model in this study was simulated in Google Colaboratory with Python, as seen in Figure 2.

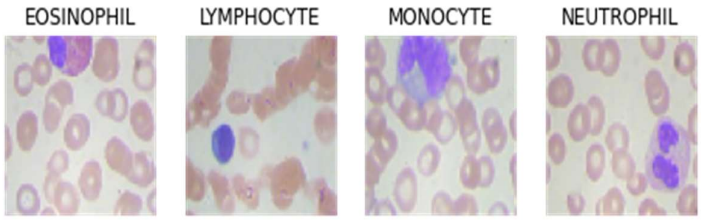


Figure 1. The sample of white blood cells dataset

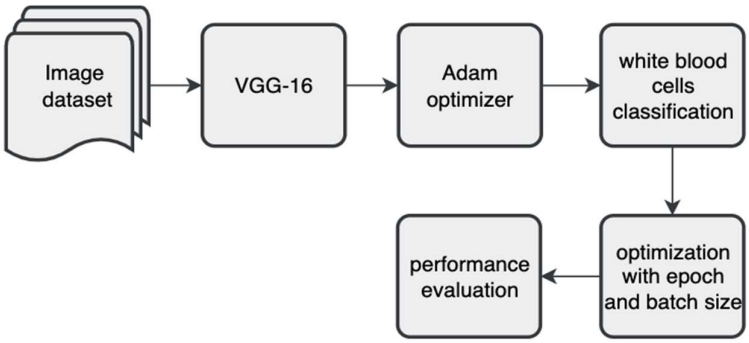


Figure 2. Proposed method

2.2 VGG-16 (Visual Geometry Group-16) Architecture

The Convolutional Neural Network (CNN) is a feature extraction and classification technique. Yann Lecun was the first to launch CNN in 1988 **(Zhang et al., 2019)**. CNN is one of the methods that paved the way for the developing of Deep Learning. Regarding image classification, CNN takes the input image and processes it before classifying it into specific categories (e.g., face, motorbike, dog, helmet). CNN uses VGGNet, Alexnet, DenseNet, ResNet, and other designs. Input, convolutional, activation, pooling, fully linked, and output layers are the essential components of CNN **(Abou El-Seoud et al., 2020) (Ali & Ali, 2021)**, as shown in Figure 3 **(Aulia et al., 2021)**.

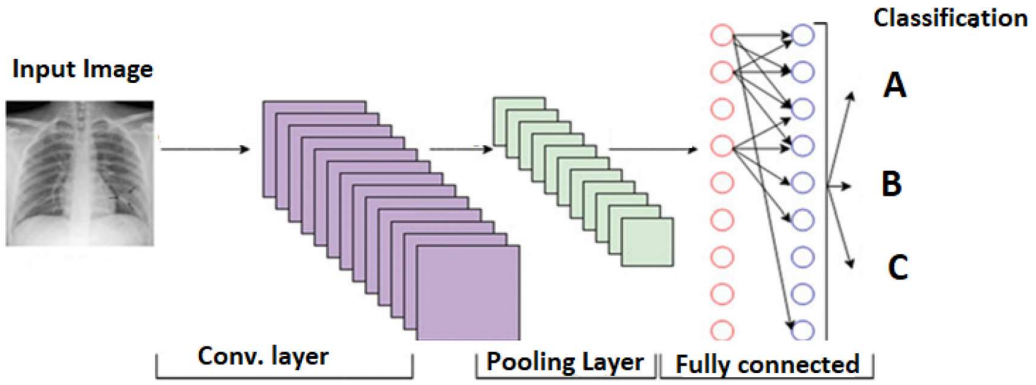


Figure 1. The architecture of convolutional neural network (Aulia et al., 2021)

The convolutional layer extracts features, while the pooling layer builds new filters using rules **(Widhiyasana et al., 2021)**. In the meantime, a fully linked layer at the output stage contains many neurons that act as decision-makers. The CNN transfer learning model **(Elnakib et al., 2020)** is a general computer vision approach for developing transfer learning systems. Transfer learning is a method for dealing with the problem of large-scale data collection. Instead of beginning with a blank slate, the data collection process uses trained models. In this study, we used transfer learning VGG16 models that were previously trained on ImageNet. The goal of the testing design is to determine how robust the proposed model.

VGG is a large and complex network. It is the result of combining 16 convolution layers, each convolution layer's number of filters increases from 64 to 512. VGG-16's architecture is depicted in Figure 4. A twodimensional convolution with a kernel size of 3x3 is applied to the input RGB image of 224x224 pixels during the training phase. The layers that make up the VGG16 network have the following specifications **(Bendarkar et al., 2021) (Maysanjaya, 2020) (Nanditha et al., 2021)**:

a) Conv. box-1: consists of two conv. layers, each with 64 filters and 224x224x64 of size.
b) Max pool-1: the Max-pooling layer and it produces the following results: 112x112x 64.
c) Conv. box-2: consists of two conv. layers, each with 128 filters and 112 x 112 x 128 of size
d) Max pool-2: This layer resulting has dimensions 64x64x128.
e) Conv. box-3: consists of three conv. layers, each with 256 filters and 56 x 56 x 256 pixels size.
f) Max pool-3: This is also a Max-pooling layer, resulting in the following dimensions: 28x28x256.
g) Conv. box-4: consists of three conv. layers, each of which includes 512 filters and 28x28x512of size.
h) Max pool-4: Maximum pooling layer (14x14x512).
i) Conv. box-5: consists of three conv. layers, each of which includes 512 filters and 14x14x512 of size.
j) Max pool-5: Maximum pooling layer, resulting in: 7x7x512.
k) Fully Conn. Layer 1 (FC1): 1x1x4096 of size
l) Fully Conn. Layer 2 (FC2): 1x1x4096 of size.
m) Predictions for output: 1x1x1000 of size.

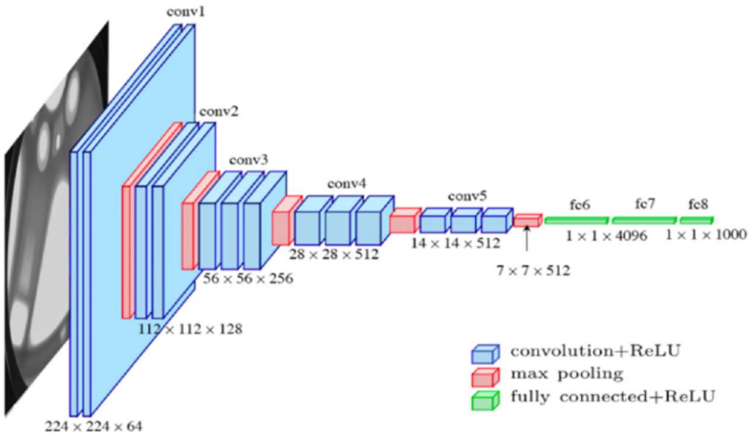


Figure 4. The architecture of VGG-16 (Nanditha et al., 2021)

2.3 Performance Evaluation

A confusion matrix is a tool that represents an algorithm's performance. It is sometimes referred to as an error matrix. The parameters of the confusion matrix are used as assessment parameters to assess the experiment results. As shown in Table.1, the confusion matrix has four cases: True Positive (TP), False Positive (FP), True Negative (TN), and False Negative (FN) **(Samreen et al., 2020**). The circumstances where both the forecast and actual values are positive and negative are referred to as TP and TN. FP denotes a positive prediction with an actual negative value, while FN denotes a negative prediction with an actual positive value **(Sunario Megawan & Wulan Sri Lestari, 2020)**.

Table 1. Confusion matrix

	Predicted yes	**Predicted no**
Actual yes	*True Positive* (TP)	*False Negative* (FN)
Actual no	*False Positive* (FP)	*True Negative* (TN)

The F-score, also called the F1-score, is a measurement of a model's precision on a certain dataset. It is employed to evaluate binary categorization schemes that assign examples to either positive or negative groups. The F-score is a technique for combining the model's recall and precision. The harmonic mean of recall and precision is used in the calculation of the F1 score. With the formula in equation 4, an F-score can have a maximum value of 1.0, signifying optimal precision and memory, and a minimum value of 0 if neither precision nor recall are zero. Precision-Recall serves as a useful indicator of classification success when the classes are significantly out of balance. In data extraction, recall measures the number of relevant results returned, whereas precision evaluates the relevancy. Equations 2 and 3 define the precision and recall, respectively.

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{TN} + \text{FP} + \text{FN}} \quad (1)$$

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \quad (2)$$

$$\text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}} \quad (3)$$

$$\text{F1score} = \frac{2 * \text{Precision} * \text{Recall}}{\text{Precision} + \text{Recall}} \quad (4)$$

For various thresholds, the precision-recall curve depicts the tradeoff between precision and recall. A large area under the curve denotes high recall and precision, with high precision denoting a low false-positive percentage and high recall denoting a low false-negative percentage. High scores for both indicate that the classifier is producing accurate (high precision) results and that the majority of all positive outcomes are being produced (high recall). A system with high recall but low precision returns a large number of results when compared to the training labels, but the majority of its projected labels are incorrect. A system with high precision but low recall produces very few results when compared to the training labels, yet the majority of its predicted labels are accurate. A perfect system with great precision and recall will produce many results, all of which will be correctly labeled.

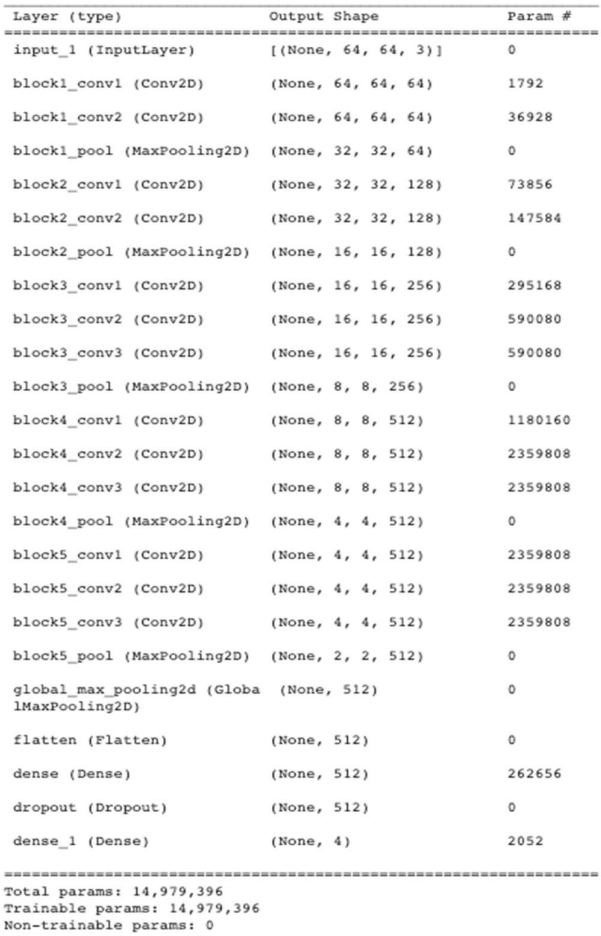
3. RESULTS AND DISCUSSION

Paul Mooney provided the dataset used in this study, an open source that could be downloaded on https://www.kaggle.com/datasets/paultimothymooney/blood-cells. We used 2,487 images of white blood cells in the form .jpeg that were organized into four folders according to cell type: Neutrophil, Eosinophil, Monocyte, and Lymphocyte. We split the dataset for training and testing with a comparison of 80:20, respectively. The number of images for each class represents in Table 2.

Table 2. Sharing Images f Blood Cells on The Dataset

Image Class	Training set	Testing set	Total images
Eosinophil	499	125	624
Lymphocyte	496	124	620
Monocyte	496	124	620
Neutrophil	498	125	623
Total	1,991	496	2,487

Based on Table 2, from a total dataset of 2,487 images, we split into 1,991 for the training set and 496 for the testing set. Our experiment was simulated on Google Colaboratory. Transfer learning parameters were used in the training and testing (batch size and epoch variations). Figure 5 shows the VGG-16 modeling architecture used in this work. Based on the experiment, the most excellent accuracy value of 100% for classifying blood cells images into neutrophil, eosinophil, monocyte, and lymphocyte was discovered using the proposed VGG-16 model in Figure 4. This result was conducted on epoch=5 and batch size=60, as shown in Table 3.



Layer (type)	Output Shape	Param #
input_1 (InputLayer)	[(None, 64, 64, 3)]	0
block1_conv1 (Conv2D)	(None, 64, 64, 64)	1792
block1_conv2 (Conv2D)	(None, 64, 64, 64)	36928
block1_pool (MaxPooling2D)	(None, 32, 32, 64)	0
block2_conv1 (Conv2D)	(None, 32, 32, 128)	73856
block2_conv2 (Conv2D)	(None, 32, 32, 128)	147584
block2_pool (MaxPooling2D)	(None, 16, 16, 128)	0
block3_conv1 (Conv2D)	(None, 16, 16, 256)	295168
block3_conv2 (Conv2D)	(None, 16, 16, 256)	590080
block3_conv3 (Conv2D)	(None, 16, 16, 256)	590080
block3_pool (MaxPooling2D)	(None, 8, 8, 256)	0
block4_conv1 (Conv2D)	(None, 8, 8, 512)	1180160
block4_conv2 (Conv2D)	(None, 8, 8, 512)	2359808
block4_conv3 (Conv2D)	(None, 8, 8, 512)	2359808
block4_pool (MaxPooling2D)	(None, 4, 4, 512)	0
block5_conv1 (Conv2D)	(None, 4, 4, 512)	2359808
block5_conv2 (Conv2D)	(None, 4, 4, 512)	2359808
block5_conv3 (Conv2D)	(None, 4, 4, 512)	2359808
block5_pool (MaxPooling2D)	(None, 2, 2, 512)	0
global_max_pooling2d (GlobalMaxPooling2D)	(None, 512)	0
flatten (Flatten)	(None, 512)	0
dense (Dense)	(None, 512)	262656
dropout (Dropout)	(None, 512)	0
dense_1 (Dense)	(None, 4)	2052

Total params: 14,979,396
Trainable params: 14,979,396
Non-trainable params: 0

Figure 5. The VGG-16 model summary used in this work

Table 3. The Training And Testing Result Of White Blood Cells Classification

Epoch	Batch size	Accuracy(%)		Loss(%)	
		Training	Testing	Training	Testing
1	30	98.99	76.91	2.74	23.54
2	30	96.38	98.39	10.58	4.46
3	30	99.20	98.59	2.64	5.11
4	30	97.59	98.59	7.55	2.04
5	30	97.85	98.60	7.87	2.68
1	60	97.18	91.77	7.82	31.52
2	60	97.29	99.00	7.73	3.31
3	60	98.44	98.80	6.29	5.08
4	60	97.84	99.80	7.96	1.23
5	60	99.90	100	0.54	0.49
Average		98.07	96.15	6.17	7.95

Based on Table 3, we reach the highest accuracy of 100% on epoch=5 and batch size=60. As for the accuracy rate on training and testing processes, our method achieved 98.07% and 96.15%, respectively. And for the loss rate on training and testing processes, our method achieved 6.17% and 7.95%, respectively.

The performance of the proposed method is then compared with the previous study, which used the same dataset and classification class. The results show that the present research outperformed the study by El-Seoud **(Abou El-Seoud et al., 2020)**, which simulated using Google Colaboratory, Keras as the library, and TensorFlow as the backend engine. The previous study suggested CNN model achieved a 96.78 % accuracy rate in recognizing different types of white blood cells. In addition, the test data used in the present study is larger than the reference study **(Abou El-Seoud et al., 2020**) 496 and 125, respectively.

The detail of the performance evaluation includes the precision, recall, and F1 score for each class represented in Figure 6.

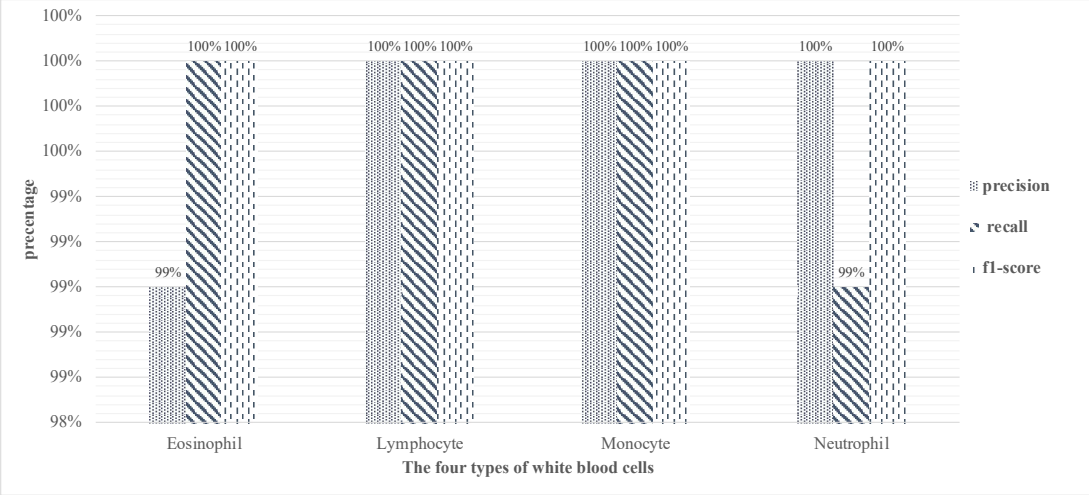


Figure 6. The performance evaluation includes the precision, recall, and F1 score for each class

Based on Figure 6, the average precision, recall, and F1-score are 99.5%, 100%, and 100%, respectively. Our proposed method achieved the F1 score of 100% or equal to a maximum value of 1.0, that means our performance indicates an ideal precision and recall in classifying the white blood cells images into four folders according to cell type: Neutrophil, Eosinophil, Monocyte, and Lymphocyte. Precision is calculated by dividing the true positives by anything predicted as a positive. Our system reaches 99.5% precision, meaning there are 0.5% False Positive detected or 0.5% detected incorrectly. As seen in Figure 7, there is one image classifying the eosinophil as neutrophil from a total of 125 testing images. The precision refers to the percentage of true positive (TP) over the actual results (TP+FP). On the other hand, recall means the percentage of true positive (TP) over the predicted results (TP+FN), out proposed method achieved an ideal recall rate of 100%.

The result conducted by the confusion matrix in Figure 7 shows our proposed method is expected to be developed for automatic white blood cell count.

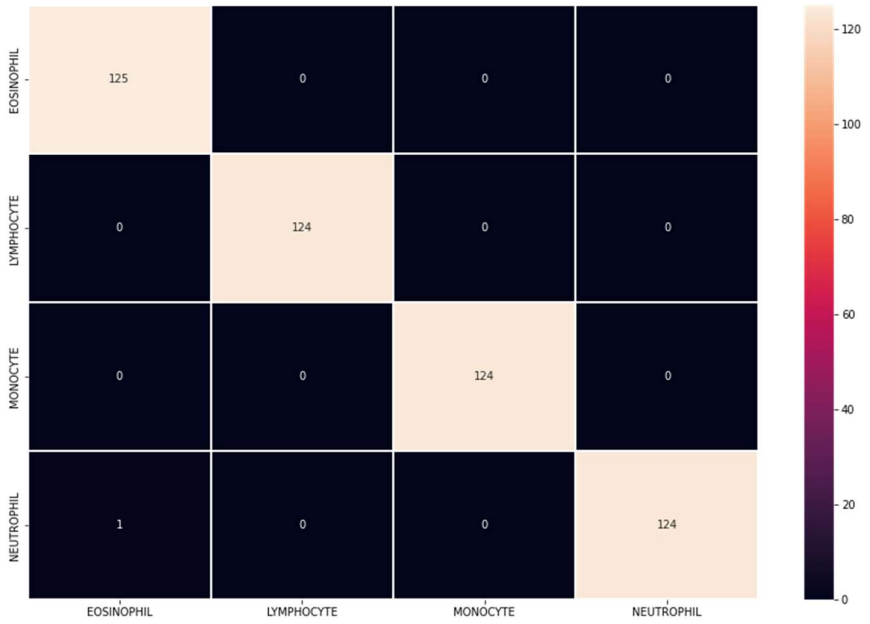


Figure 7. The Confusion matrix of the best result of blood cells classification using VGG-16.

4. CONCLUSION

Leukocytes have an important role in maintaining the body's immunity. The number of leukocytes determines the condition of human health. Leukocytes have various types where each type has a specific function. The limited number of hematology analyzer devices in health services then becomes a challenge in developing a classification system for leukocyte types. This system will facilitate automatic calculations based on microscopic blood samples. This study succeeded in simulating a deep learning model for leukocyte classification. CNN method with VGG-16 architecture was employed to extract the essential features and perform the classification function. The simulation results show an accuracy of 100% for classifying neutrophils, eosinophils, monocytes, and lymphocytes. The excellent result was achieved with Adam optimizer, epoch=5 and batch size=60. The results of the current study also outperform previous studies. The proposed method is expected to be developed for automatic white blood cell count.

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