ICIC Express Letters
Volume **17**, Number **1**, January **2023**

ICIC International ©2023 ISSN 1881-803X
pp. **103–111**

ERYTHROCYTE CLASSIFICATION USING ALEXNET AND SIMPLE CNN

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Received January 2022; accepted April 2022

Abstract. *One examination method to support thalassemia diagnosis is a blood morphological examination of the patient's peripheral blood smear. However, manual analysis of peripheral blood smears requires time, unique expertise, and expert eye fatigue. This paper proposes a computer vision method using deep learning to assist experts in examining peripheral blood smears. The dataset consists of nine erythrocyte types that appear in thalassemia patients. The image size normalization was conducted before the deep learning model used the image. Data augmentation was used to increase the number of data in the datasets. The transfer learning approach is used to improve classification results. The erythrocyte classification result using Alexnet and simple CNN has been compared. The best performance of the Alexnet model reached 95.92% accuracy, 91.46% sensitivity, and 99.48% specificity.*

Keywords: Erythrocyte classification, Deep learning, Thalassemia, Alexnet, CNN

1. **Introduction.** Several abnormal erythrocytes that appear on peripheral blood smears can indicate certain diseases. One of them is thalassemia, a type of anemia that can be genetically inherited. One examination method to support thalassemia diagnosis is a blood morphological examination of the patient's peripheral blood smears. Manual inspection of peripheral blood smears requires a lot of time and special skills. Besides, manual erythrocyte examination is also affected by eyestrain from the observer. Therefore, we need a way to help medical personnel examine erythrocytes in peripheral blood smears.

The computer vision technology method can help the process of examining erythrocytes. In this case, the computer will allow the observer to process and analyze the patient's peripheral blood cells to obtain clinically significant abnormal cells. Image of peripheral blood cells were obtained from the microscope using a camera. The existing processes include improving image quality, object segmentation, and object feature extraction. Then proceed with the learning process with artificial intelligence.

Some examples of research related to computer vision in the medical field that has reported are

- Automatic segmentation of overlapping cervical smear cells [1].
- Automated detection of retinal nerve fiber layer for glaucoma evaluation [2].

DOI: 10.24507/icicel.17.01.103

- Analysis of shape, texture, and color characteristics for erythrocyte classification [3].
- Toolkits for cardiovascular research (CemrgApp) [4].
- Acute lymphoblastic Leukemia detection [5,6].
- Enhancement of Digital Imaging and Communications in Medicine (DICOM) brain images [7].
- Retinopathy disease classification [8].
- Amniotic fluid segmentation [9].
- Dysarthria speech classification [10].

Deep learning is a learning method that is popularly used today. The advantage of using deep learning is that there is no need to do a manual feature selection process. This method will generate features automatically from the existing convolution layer. In the medical field, the implementation of deep learning has been used in various medical cases, for example, the white blood cell classification [11,12], red blood cell classification in cases of sickle cell anemia [13,14], and lung pattern classification for interstitial lung diseases [15]. Multi deep learning with the majority vote technique has been applied to diagnosing COVID-19 on X-Ray images of the lungs by Fibriani et al. [16]. The combination of CNN and hand-crafted features has been done by Zhou et al.; however, the results were not significant [17].

Tyas et al. classified nine types of erythrocytes in thalassemia based on hand-crafted features [3]. The features used are morphological, texture, and color features. The classifier used is MLP with one hidden layer. The experimental results show that combining these three features provides the best performance at 98.11% for accuracy, 86.67% for sensitivity, and 99.75% for specificity. However, the highest sensitivity is achieved when shape features only are employed. In this case, the accuracy is 95.23%, the sensitivity is 92.69%, and the specificity is 99.40%. Deep CNN has been used by Xu et al. to classify eight types of erythrocytes. The study conducted automatic erythrocyte segmentation and separated overlap erythrocytes. The CNN architecture consists of 10 layers, including three convolutional layers, three pooling layers, two dropout layers, a fully connected layer, and an output layer. The mean accuracy of the classification results for eight types of erythrocytes was 87.50% [13].

Alzubaidi et al. classified erythrocytes into three categories: circular or normal, elongated or sickle cells, and other blood content classes. Their research used three types of datasets and three architectural models. The dataset consists of single cell cropped images. The first model has 40 layers with nine layers of convolution (3 series, six parallel) followed by batch normalization and Rectified Linear Unit (ReLU) in each layer. The second model has eight convolution layers (2 series, six parallel) and two fully connected layers, while the third model has six convolution layers (2 series, four parallel) and two fully connected layers. The accuracy obtained based on the proposed method is 99.54% on the erythrocytesIDB dataset. The accuracy of the proposed model combined with the multiclass SVM classifier is 99.98% on the erythrocytesIDB dataset, whereas the accuracy obtained on the collected dataset is 98.87% [14].

The Alexnet with transfer learning model was used by Aliyu et al. to classify erythrocytes in sickle cell anemia [18]. There are 15 types of erythrocytes used in the study. The performance obtained is 95.92% accuracy, 77% sensitivity, 98.82% specificity, and 90% precision. Quan et al. [19] proposed an Attentive Dense Circular Net (ADCN) for classifying erythrocytes in malaria diseases. The comparison result of ADCN performance and the CNN model's performance has shown ADCN as superior to other CNN models.

It is necessary to recognize certain types of erythrocytes in certain medical cases. In several previous studies, excellent performance has been obtained, but erythrocytes have not been classified based on the actual type. On the other hand, studies that have classified erythrocytes based on actual type can still be improved. This study classifies nine types of

erythrocytes based on actual types from thalassemia cases using Alexnet and simple CNN. This study's contribution is to get the evaluation results according to the convolution features for erythrocyte classification and obtain the best architecture for simple CNN and Alexnet for erythrocyte classification. The advantage of this study is the improvement in the accuracy and specificity of the classifier. The rest of this paper is organized as follows. Section 2 describes the dataset and deep learning model used in this paper. Section 3 describes the experiment and result of the proposed method. Finally, Section 4 presents the conclusion of this paper.

2. **Proposed Methodology.** This study compares the results of erythrocyte classification using the Alexnet architecture and the simple CNN architecture. Some of the steps carried out are preprocessing, data augmentation, and classification.

2.1. **Dataset and preprocessing.** The dataset used in this study is a dataset from Tyas et al. [3]. The dataset consisted of 7108 single erythrocyte images from thalassemia, iron deficiency anemia, and normal individuals. Images in the dataset [3] have diverse sizes. Therefore, it is necessary to normalize the image size to 227 × 227. The process carried out is shown in Figure 1. Based on the input image size (M × N), the first step is to add zero paddings to the row or column to obtain the largest image size (M × M or N × N). Then the image is converted into a size of 227 × 227.

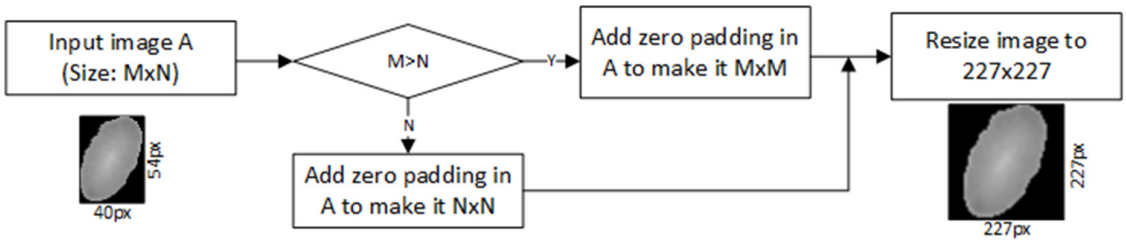

FIGURE 1. Preprocessing: Size normalization in the dataset

2.2. **Data augmentation.** Training a deep learning model on a more significant amount of data can improve the model's capabilities. In this study, we apply data augmentation techniques. Data augmentation techniques modify the existing dataset's image. Some ways to be done in data augmentation are rotation, translation, reflection, scaling, and brightness. In this study, data augmentation with translation and reflection techniques was used.

2.3. **Transfer learning using Alexnet.** Alexnet has been trained using more than 1 million images. This model can classify images into 1000 object categories. By applying the transfer learning method, we use Alexnet and then change the final layer as needed. After that, retraining must be conducted using the new image dataset. The transfer learning process is shown in Figure 2. The first step is to load a pretrain network, which is a network that has been trained for classifying 1000 object classes. The network input is an image, and the output is a label of the object in the image. The early layers of this network learned the lower-level features of the image, while the final layers studied more specific features. The next stage is replacing the final or last three layers as needed. The last layers consist of a fully connected layer, a SoftMax layer, and a classification output layer. In this study, the fully connected layer is adjusted to have the same size as the number of new data classes (nine classes). The next step is to train the network using the erythrocyte image train dataset and then classify the validation images and evaluate their performance. Then we retrain the network using the training and the validation data combined to improve the network and get maximum performance.

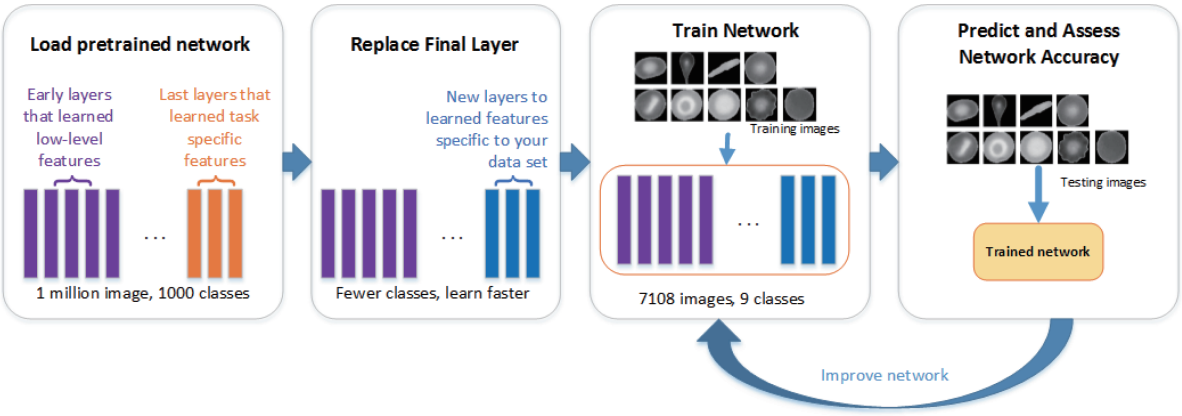

FIGURE 2. Transfer learning using Alexnet

The Alexnet architecture used in this study is shown in Figure 3. The Alexnet input is a grayscale image of 227 × 227 size. The model consists of four layers of convolution (Conv) followed by the Rectified Linear Unit (ReLU) and batch normalization (Norm). Then, the max-pooling layer is followed by the second convolutional layer, the max-pooling layer again, and the third to the fifth layers of the convolution layer. After that, the fifth convolutional layer's output is forwarded to the max-pooling layer and becomes the input for the Fully Connected (FC) layer. There are 3 FC layers and two dropout layers between the FC layers to avoid overfitting. Detailed information regarding the filter size and stride used for each layer is shown in Table 1.

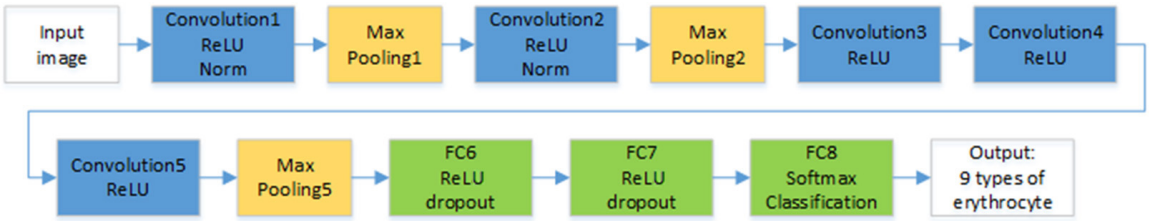

FIGURE 3. Alexnet architecture

TABLE 1. Filter size and stride in Alexnet architecture

Name of layers	Filter Size (FS) and Stride (S)
Input layer	–
Conv1, ReLU1, Norm1	FS = 11 × 11, S = 4
Max Pooling	FS = 3 × 3, S = 2
Conv2, ReLU2, Norm2	FS = 5 × 5, S = 1
Max Pooling	FS = 3 × 3, S = 2
Conv3, ReLU3	FS = 3 × 3, S = 1
Conv4, ReLU4	FS = 3 × 3, S = 1
Conv5, ReLU5	FS = 3 × 3, S = 1
Max Pooling	FS = 3 × 3, S = 2
FC6, ReLU6	4096
Drop6	Learning rate: 0.5
FC7, ReLU7	4096
Drop7	Learning rate: 0.5
FC8	9
Softmax and classoutput	9 classes

2.4. **Classification using simple CNN.** The second architecture is simple CNN architecture, which is simpler than Alexnet, shown in Figure 4. The architecture consists of three convolutional layers, followed by two pooling layers and one fully connected layer. Detailed information regarding the filter size and stride used for each layer is shown in Table 2.

FIGURE 4. Simple CNN architecture

TABLE 2. Filter size and stride in simple CNN architecture

Name of layers	Filter Size (FS) and Stride (S)
Input layer	–
Conv1, Norm1, ReLU1	FS = 3 × 3, S = 1
Max Pooling	FS = 2 × 2, S = 2
Conv2, Norm2, ReLU2	FS = 3 × 3, S = 1
Max Pooling	FS = 2 × 2, S = 2
Conv3, Norm3, ReLU3	FS = 3 × 3, S = 1
FC8	9
Softmax and classoutput	9 classes

3. **Result and Discussion.** This section describes the evaluation and analysis of erythrocyte classification performance.

3.1. **Parameter evaluation.** This study evaluated the classification result based on accuracy, sensitivity, and specificity. The classification results are shown in the confusion matrix, and the accuracy (a), sensitivity (b), and specificity (c) values can be calculated based on Equations (1)-(3), where TP is a true positive, TN is a true negative, FP is a false positive, and FN is a false negative.

$$\mathrm{a} = \frac{TP + TN}{TP + FP + FN + TN} \tag{1}$$

$$\mathrm{b} = \frac{TP}{TP + FN} \tag{2}$$

$$\mathrm{c} = \frac{TN}{TN + FP} \tag{3}$$

3.2. **Performance analysis.** This study split the data into 70% for the training process and 30% for the testing process. The results of the erythrocyte classification based on AlexNet architecture are shown in Table 3. The maximum accuracy is 96.16%, and the maximum specificity is 99.50% obtained from Alexnet (No. 4) with a learning rate of 1e-4 and epoch of 100. The maximum sensitivity is 91.46%, obtained from Alexnet (No. 2) with a learning rate of 1e-3 and epoch of 100. The accuracy of Alexnet No. 2 is 0.24% lower than No. 4, the specificity of Alexnet No. 2 is 0.02% lower than No. 4. In comparison, the difference in sensitivity values for model No. 2 is 4.09% higher than model No. 4.

Table 4 shows the classification results using simple CNN. The best performance is obtained when the learning rate and epoch are 1e-3 and 100, respectively. The model achieves 88.66% accuracy, 75.87% sensitivity, and 98.52% specificity. The results for simple CNN show that a lower learning rate gives lower classification performance. The experiments showed that a lower learning rate did not improve classification performance.

Table 3. Classification performance based on Alexnet transfer learning

No	Learning rate	Epoch	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	1e-3	80	94.98	88.50	99.36
2	1e-3	100	95.92	**91.46**	99.48
3	1e-4	80	95.50	88.81	99.41
4	1e-4	100	**96.16**	87.37	**99.50**
5	1e-5	80	92.78	82.67	99.07
6	1e-5	100	94.19	84.99	99.25
7	1e-6	80	86.26	66.11	98.15
8	1e-6	100	89.50	76.14	98.59

Table 4. Classification performance based on simple CNN

No	Learning rate	Epoch	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	1e-3	80	87.90	75.07	98.37
2	1e-3	100	**88.66**	**75.87**	**98.52**
3	1e-4	80	85.70	73.89	98.14
4	1e-4	100	85.84	74.30	98.16
5	1e-5	80	85.00	69.44	98.02
6	1e-5	100	83.45	65.17	97.84
7	1e-6	80	77.82	56.29	97.08
8	1e-6	100	78.80	58.96	97.20

A too-small learning rate affects a longer training time. However, in some instances, it can cause training to stop in solutions that are not optimal, so that the model's performance is also not optimal [20].

The experimental result shows that the transfer learning approach gives better results than building a model from scratch. Additional layers of the architectures improve the classification results. Alexnet with more layers provides better performance when compared to the simpler architecture in the second experiment. Based on Table 4, model No. 2 and model No. 4 provide good performance. Table 5 and Table 6 show the confusion matrix with sensitivity and specificity values for each class. Table 5 uses the Alexnet architecture model No. 2, while Table 6 uses the Alexnet architecture model No. 4. The

Table 5. Confusion matrix of classification result using Alexnet model No. 2

Class/ Erythrocyte class			Output class									Total	Sensitivity (%)	Specificity (%)
			O	TD	P	N	ST	T	H	A	SP			
Target class	1	O	**332**	1	1	10	3	5	7	3	1	363	**91.46**	99.66
	2	TD	1	**622**	0	0	0	0	0	0	0	623	**99.84**	99.93
	3	P	2	0	**5**	0	0	0	0	0	0	7	71.43	99.95
	4	N	0	0	0	**414**	1	1	10	1	1	428	**96.73**	98.48
	5	ST	2	0	0	10	**98**	5	0	0	0	115	85.22	99.70
	6	T	0	0	0	0	1	**251**	1	0	2	255	**98.43**	98.99
	7	H	1	0	0	4	1	4	**57**	0	0	67	85.07	99.03
	8	A	0	0	0	0	0	0	1	**105**	0	106	**99.06**	99.80
	9	SP	0	0	0	2	0	4	1	0	**162**	169	**95.86**	99.80
Total												2133		
Mean													**91.46**	**99.48**
Accuracy (%)													**95.92**	

Note: oval cell (O); teardrop cell (TD); pencil cell (P); normal cell (N); stomatocyte (ST); target cell (T); hypochromic (H); acanthocyte (A); spherocyte (SP).

TABLE 6. Confusion matrix of classification result using Alexnet model No. 4

Class/ Erythrocyte class			Output class									Total	Sensitivity (%)	Specificity (%)
			O	TD	P	N	ST	T	H	A	SP			
Target class	1	O	**354**	1	1	3	0	2	2	0	0	363	**97.52**	99.21
	2	TD	1	**622**	0	0	0	0	0	0	0	623	**99.84**	99.74
	3	P	2	2	**3**	0	0	0	0	0	0	7	42.86	99.95
	4	N	3	0	0	**411**	0	2	10	1	1	428	**96.03**	99.00
	5	ST	7	1	0	11	**77**	17	0	1	1	115	66.96	100.00
	6	T	0	0	0	0	0	**254**	1	0	0	255	**99.61**	98.56
	7	H	1	0	0	3	0	5	**57**	1	0	67	85.07	99.32
	8	A	0	0	0	0	0	0	1	**105**	0	106	**99.06**	99.85
	9	SP	0	0	0	0	0	1	0	0	**168**	169	**99.41**	99.90
Total												2133		
Mean													**87.37**	**99.50**
Accuracy (%)													**96.16**	

Note: oval cell (O); teardrop cell (TD); pencil cell (P); normal cell (N); stomatocyte (ST); target cell (T); hypochromic (H); acanthocyte (A); spherocyte (SP).

sensitivity of the classification of oval cells, teardrop cells, normal cells, target cells, acantocyte cells, and spherocytes cells in Table 5 and Table 6 are above 90%. The sensitivity of models No. 2 and No. 4 in classifying hypochromic cells is 85.07%.

Furthermore, the sensitivity of model No. 2 in recognizing pencil cells was 71.43%, while model 4 was 42.86%. The sensitivity of model No. 2 in identifying stomatocyte cells is also 18.26% higher than model No. 4. The recognition of pencil cells and stomatocyte cells in model No. 2 is superior to model No. 4. The differences in total accuracy, average specificity, and average sensitivity of models No. 2 and No. 4 are 0.24%, 0.02%, and 4.09%. Therefore, Alexnet model No. 2 can be chosen as the best solution for erythrocyte classification.

An example of erythrocyte classification based on the Alexnet model No. 2 is shown in Figure 5. The numbers above the cell represent the class code and the prediction

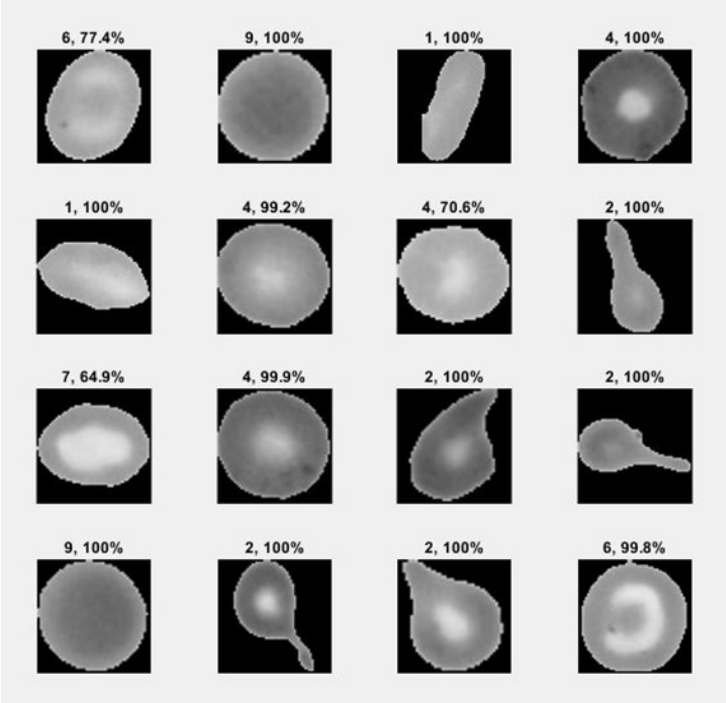

FIGURE 5. Example of classification result based on Alexnet (model No. 2)

probability. Consider only the cells in the first column. The first row says that the cell is predicted as the target cell (6) with a probability of 77.4%. The second row says the cell is predicted as an oval cell (1) with 100% probability. The third and fourth rows show that the cells are predicted as the hypochromic cell (7) and spherocytes cell (9) with the likelihood of 64.9% and 100%, respectively. Although the probability is not 100%, the cells are predicted correctly.

Classification using hand-crafted features has been carried out in previous study [3]. Table 7 compares the performance results from the previous study with this study based on the same dataset's highest sensitivity performance. The proposed method's accuracy and specificity (Alexnet No. 2) are slightly superior to performance of [3]. However, the sensitivity of [3] was 1.23% higher than the proposed method. That condition shows that there is a chance that the erythrocyte classification using the deep learning method produces better performance than [3]. Therefore, it is necessary to increase the number of data and obtain balanced data for each class.

TABLE 7. Comparative analysis of erythrocyte classification in the same dataset

Method	**Accuracy (%)**	**Sensitivity (%)**	**Specificity (%)**
MLP [3]	95.23	92.69	99.40
Alexnet (No. 2)	95.92	91.46	99.48
Simple CNN (No. 2)	88.66	75.87	98.52

4. **Conclusions.** This study aims to classify erythrocytes based on the characteristics resulting from the convolutional layer. Based on the research results, we can conclude that the Alexnet architecture with the transfer learning method produces better performance than the simpler CNN architecture. The best performance obtained from Alexnet is 95.92% for accuracy, 91.46% for sensitivity, and 99.48% for specificity. The proposed method shows improved performance, although not significantly. This research indicates that the deep learning method may improve erythrocyte classification results considerably by providing a balanced dataset.

Acknowledgment. This work is partially supported by the Universitas Gadjah Mada under Grant number 197/J01.1.28/PL.06.02/2020.

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