The Classification of Abnormal Red Blood Cell on The Minor Thalassemia Case Using Artificial Neural Network and Convolutional Neural Network

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ABSTRACT
The morphological disorder of the red blood cell is one of the indications of a certain type of diseases. On the minor thalassemia, such cases like the erythrocyte having a nucleus, a few number of the fragment cell and the target cell will be seen. This research study aimed at classifying four types of abnormal blood based on the shape, texture, and colour which was obtained from the image of the peripheral blood smear. The preprocessing stage using histogram equalization, segmentation stage using morphological operation, until feature extraction had been done. On the classification stage, the best accuracy to classify the blood into five types using algorithm of momentum backpropagation neural network was 93.22%, while the result of classification using the convolutional neural network (CNN) was 92.55%.

CCS Concepts
• ***Computing methodologies → Artificial intelligence → Computer Vision → Computer Vision Problem → Object Identification.***

Keywords
Thalassemia; abnormal erythrocyte; classification; ANN; CNN.

1. INTRODUCTION
Thalassemia is a type of genetic inherited disorder. It is caused due to the incomplete gen to form the alpha and beta globin protein, or one or two protein forming the globin protein is diminished which causes the decreasing production of globin. However, if two beta globin gens or three alpha globin gens are gone, the production of globin will decrease drastically, so the red blood cells cannot be produced perfectly and red blood cells cannot distribute enough oxygen to the body. This condition will affect seriously towards somebody's health. When the four alpha gens are gone, the stillbirth usually occurs.

Thalassemia is one of the most frequent diseases in the world, and Indonesia is included on the belt of thalassemia. Based on National Institute of Health Research and Development (NIHRD) Indonesia in 2008 , there were some provinces in Indonesia which had higher prevalence of thalassemia compared to the national prevalence, they were Aceh 13.4%, Jakarta 12.3%, and Sumatera 5.4% [1]. Ginsberg *et al.* states that the prevention of this disease is more useful than curing the disease [2]. Until nowadays, the curing of thalassemia is done only by a supportive way, which is done by blood transfusion regularly, while the gen therapy is still on the stage of development, and the prevention of thalassemia which can decrease the number of thalassemia prevalence is by thalassemia screening.

The thalassemia screening is divided into complete blood check (CBC), reviewing the morphology of erythrocyte, and the analysis of hemoglobin. The related research study about the classification of thalassemia using the complete blood check data had been done on the research [3][4][5] by using the classification algorithm SVM, KNN, MLP and ANN. Then, the research was developed into the review of erythrocyte morphology. The related research study, in this case, has been done recently. The classification of the abnormal blood cell became the main objectives of the research study.

On the application of digital image processing technology, there are some stages, those are image acquisition, image preprocessing, image segmentation, features extraction, and classification. The image acquisition is a sample digitalization process of the patient blood by using camera on the microscope lenses. The preprocessing stage is aimed at improving the quality of the image obtained from the image acquisition. The segmentation stage is done to separate the object and the background to obtain the ROI. The image extraction is done to obtain the statistic score from ROI which will be conducted on the classification.

The previous research study commonly dealt with the drawback especially on the stage of segmentation in which they were not able to separate the overlapping cells which could affect the accuracy of the classification [6][7][8]. The other research, however, decided not to include the overlapping cells on the classification stage [9][10][11][12]. After the segmentation stage, the next challenge is the feature extraction because on this stage,

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the research must obtain the most representative feature; the fewest feature found but the most distinguish. Das *et al*. did the statistic analysis using ANOVA towards the geometric and moment invariant feature to obtain the representative feature, and he found six values of moment invariants which were more representative than geometric feature [13]. Bhowmick *et al*. did the ranking towards three features and he obtained that the area of perimeter, major axis, and minor axis was the highest rank [14]. The geometric and texture features were also used on the research [11][12] while the colour feature was used in the research [9] [15][16]. And The radiant signature feature was also selected as the representation of the blood cell shapes on the research [8] and [17].

On the classification stage, some algorithm classifier has been used to differentiate the type of normal erythrocyte and the abnormal one on the thalassemia case. Bayesian classifier was chosen by Bhowmick *et al.* to distinguish the abnormal erythrocyte based on the size (macrostic, microstic, and normal) obtaining the accuracy value up to 88.99% [14]. Some other classifiers used by researchers were KNN, SVM, ANN, Decision tree classifier, and fuzzy logic [8][9][11][12][17]. Nowadays, at the age of machine learning, there has been a growing interest towards deep learning which can research the features automatically to be classified. The same case happens on the medical care, the application of deep learning has been developed. Liang *et al.* [18] applied CNN to help malaria diagnosis, Anthimopoulos *et al.* [19] also applied CNN on CAD (computer aided diagnosis) system for interstitial lung diseases (ILDs). This research focused on image classification of four types of abnormal blood and normal blood cells based on shape, texture and colour features.

2. METHODOLOGY

The methodology applied on this research to classify the blood cells shown on the Figure 1. The input was the peripheral blood smear images resulted from the acquisition which later proceeded to preprocessing and segmentation to obtain the sub-image of the single erythrocyte. After gaining the sub-image, the features extraction was done to obtain the statistic values of the sub-image by applying some extraction methods which could represent the shape, texture, and colour features of the erythrocyte. After obtaining the value of features, the normalization and classification was conducted.

2.1 Image Acquisition

The data acquisition is a process of taking the data of blood microscopis image which derived from the blood preparat through microscope using additional special camera for microscope (Optilab). The process of selecting the image was assisted by a laboratorian to get the image of red blood cells which used for this research study. The dry blood preparat was obtained from the Clinic Pathology Laboratory of Medical Faculty UGM, Indonesia. The dry blood preparat was obtained from the thalassemia patients, ADB patients, and normal individuals. Based on the obtained images from the acquisition image, the Region of Interens (ROI) was selected manually to obtain the single blood cell which was proceeded on the next step. The sampel of red blood cells ROI is shown on the Figure 2 which has 400x400 pixel in size. On the minor thalassemia case, there would be some red blood cell cases such as erythrocyte having the nucleous, few fragment cells, and target cell.

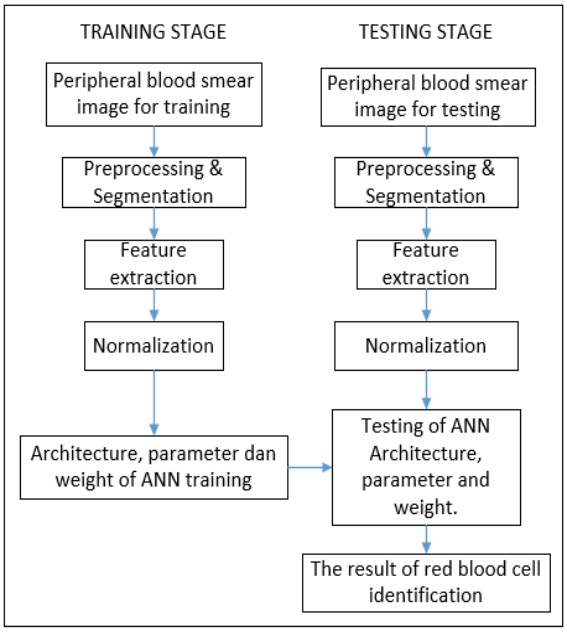

Figure 1. Flowchart of experiment

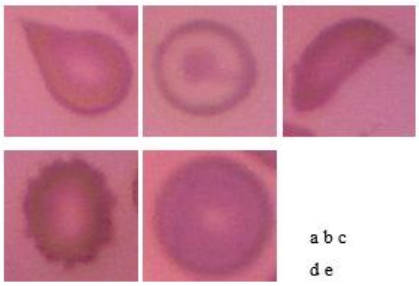

Figure 2. The image of red blood cells: a. tear drop, b. target cell, c. sigar cell, d. acantocyte, e. normal cell

2.2 Preprocessing

The preprocessing stage was conducted to improve and adapt the result of acquisition image so that the next stage of image processing obtained a correct image. The preprocessing stage conducted on this research was resized images which were done by converting the RGB image to grayscale colour, enhancing the image intensity using histogram equalitation and binarization of the image. The preprocessing stage is shown on the Figure 3.

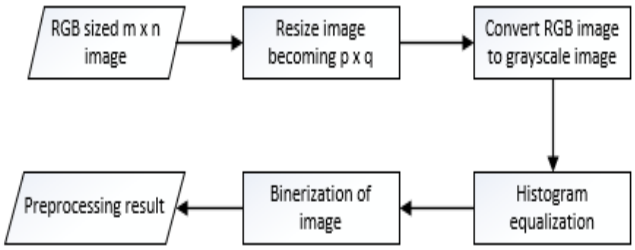

Figure 3. Flowchart of preprocessing

2.3 Segmentation

This stage was conducted to gain the sub-image which only had the red blood cells. The methods used on this stage were

binerization, morphology operation, hole filing operation, and image multiplication operation.

2.4 Feature Extraction and Normalization

The next stage is the feature extraction. The features which could be extracted from the peripheral blood smear image of the thalassemia patients were the shape and texture of the red blood cells. The method conducted to extract the shape feature at this stage was Invariant Moments, and the method conducted to the extraction of the texture feature was GLCM. Meanwhile, the colour feature which was extracted was the mean, standard deviation, and skewness from the pixel values. The followings are feature values obtained from the feature extraction:

1. The feature extraction using Invariant Moments was obtained and the 7 insensitive invariant moments towards translation, scale changing, and rotation were used. In addition, geometry parameter as a part of shape features: area perimeter, major axis, and minor axis would were as well. From the shape feature, 11 features were obtained.
2. The extraction of texture feature using GLCM obtained 4 features namely contrast correlation, homogeneity, energy on each angle 0 °, 45 °, 90 °, and 135 °, so 16 features would be gained.
3. The colour feature by calculating the colour moments namely mean, standard deviation, curtosis, and skewness on the grayscale image and on every colour channel from the RGB images. From colour features, 16 features would be obtained.

From the feature extraction, 43 values of feature would be obtained for one erythrocyte on one sub-image of the segmentation result. After that, the data was normalized into same range (0-1).

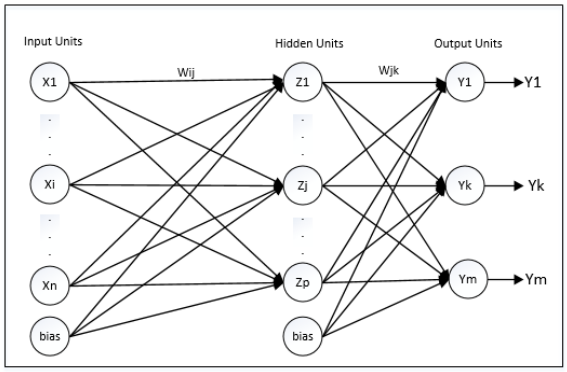

Figure 4. The architecture of ANN multilayer

2.5 Classification

After obtaining the normalized feature values, the next step was identification whether the type of sub-image used machine learning. Algorithm which was applied on this research study was artificial neural network (ANN) and convolutional neural network (CNN). Algorithm of ANN and CNN consisted of two processes; they were training stage and testing stage. Those two stages are identical (doing the same process), the difference of those two is the used of input data. The data of the testing stage is the image which has not been used on the training stage. On the application of ANN algorithm, the implementation of the precise parameter is very influential towards the result of the identification, so the research dealing with the precise parameter for this case would be conducted. On this stage, the assessment or early validation towards the result of system identification would be conducted. The multilayer ANN architecture is shown on the Figure 4. This research used momentum backpropagation neural network refers to research by Harjoko et al. [20] for Acute Myeloid Leukemia (AML) classification. Some influential ANN parameters are the number of hidden layers and the number of neuron in the hidden layer, while the number of neuron on the input layer depends on the number of feature which is used as the input, and the number of neurons on the output layer depends on the number of data class. The other parameters which need to be sought are the value of learning rate and epoch. The result of the training stage is the obtained the architecture, parameter, and the weight of every node.

Not far different from ANN, the classification of CNN was also affected by the used architecture and parameter. Different from the ANN, the input of the CNN was images which proceeded on the convolution and sub sampling to obtain the feature map containing the pixel value which was the representation from the most important features of the image input. The CNN architecture suggested by LeCun *et al.* [21] is shown on Figure 5 called as LeNet-5. The architecture consists of two convolution layers, two sub-sampling layers, and two fully connection layers, and ended by Gaussian connection. Convolution was conducted by using certain numbers and certain size of kernel. The number of kernel used was based on the features which would be obtained. On the convolution layer of C1 and C2, 5x5 kernel size was used, and on the sub sampling layer, 2x2 kernel size was used. The feature map as a result of both convolution layers and sub-sampling layer were used as the input of fully connected layer which classified the feature maps to certain classes.

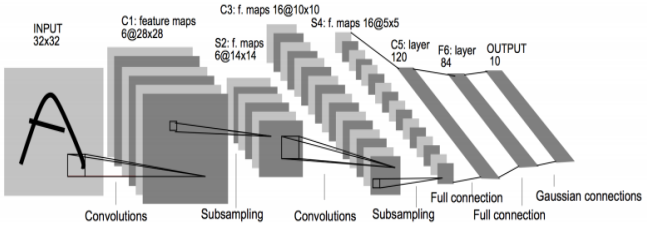

Figure 5. The architectur of LeNet-5, convolutional neural network for digit recognition [21]

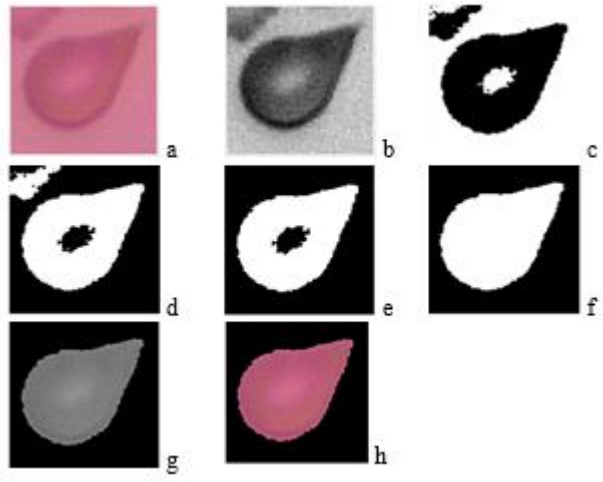

Figure 6. The result of preprocessing and segmentation on tear drop cell image

3. RESULT

In this study, the proposed method was tested using 256 images consisting of four types of abnormal red blood cells and normal red blood cells. Figure 6 shows the result of preprocessing (a-c) and the result of the segmentation process (d-h). In preprocessing stage, original image (a) was converted to grayscale colour and enhanced the image intensity using histogram equalization (b). After that binarization applied on the image (c). The segmentation started with the process of erosion morphology operation (d) continued by removing small objects by comparing the area (the number of white pixels) of the detected object (e). Then the candidate object would be subjected to hole filling morphology operation to fill the empty area inside the object, so the solid erythrocyte form was obtained (f). The last stage was performing multiplication operations between binary images (f) and grayscale images (b) to obtain sub-images of erythrocyte cells in grayscale colour (g), while sub-image in RGB colour (h) was obtain by performing multiplication operations between (f) and (a).

After the object in the form of erythrocyte image was obtained, the extraction feature to obtain the statistical value of texture characteristics, shapes and colors was conducted. The normalization process was performed on the value of the acquired feature to equalize the range of values in the range 0-1. All the features were, then, used in the classification phase using backpropagation neural network momentum with variation of epoch parameter, learning rate, number of neuron in hidden network, and momentum. The architecture of the used network neurons consisted of one hidden layer with variations of 4, 6, 8 and 10 neurons. The variation of learning rate and the used of momentum values was 0.01, 0.05 and 0.1, while the number of epoch used in the training phase was 5000 and 10000.

Test results with the best accuracy on 5000 epochs are shown in Figure 7, while the best accuracy of 10000 epochs is shown in Figure 8. Figure 7 is a graph of comparison of accuracy which gained from learning rate variation and number of neurons in the hidden layer, at epoch = 5000 and momentum = 0.1. From the four trained neural network architectures at 5000 epochs, the highest accuracy was 91.79% which was generated by the architecture that had 8 neurons in the hidden layer and the learning rate = 0.05. At 0.05 learning rate (orange colored bars), the addition of the number of neurons in the hidden layer from 4 neurons to 8 neurons increased the accuracy of 78.74% to 91.79%. The accuracy, however, decreased when neurons were added to 10.

Figure 8 shows a comparison graph of neural network architecture on 10000 epochs with parameters that produce the best accuracy. At the momentum value 0.05, the best accuracy is 93.24% with the other parameters used such as learning rate = 0.1 and 6 neurons in the hidden layer. In the neural network architecture that has 6 neurons in the hidden layer, it produced accuracy which was proportional to the increase of the given learning rate, while the architecture which had neuron 8 on the hidden layer showed the best accuracy on learning rate 0.05, and it decreased when the learning rate increased to 0.1. All test data on neural network against some parameters is shown on table 1 and table 2. Table 1 shows the results of back-propagation neural network momentum testing at 5000 epochs and 10000 epochs.

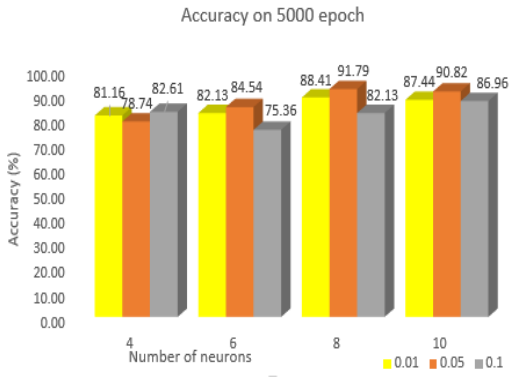

Figure 7. The comparison of accuracy on epoch = 5000 and momentum = 0.1

In addition to using momentum back propagation neural network, this study compared the classification results with the convolutional neural network (CNN). CNN is one of the classification methods that has the ability to characterize learning automatically. The input received by CNN was the same RGB image used in the training of the backpropagation momentum method. The image, however, was resized to 32x32 pixels for CNN input. The CNN architecture which was used in this study referred to the LeNet-5 architecture [21] with slight modifications. The CNN architecture in this study consisted of two convolution layers and one fully connected layer. Figure 9 shows the CNN architecture used in this study. The convolution filter kernel size used in both convolution layers was 5x5, and the mask size at the pooling stage was 2.2. Whereas in fully connected layer, the researchers used 100 node at hidden layer and the dropout value was 0.5

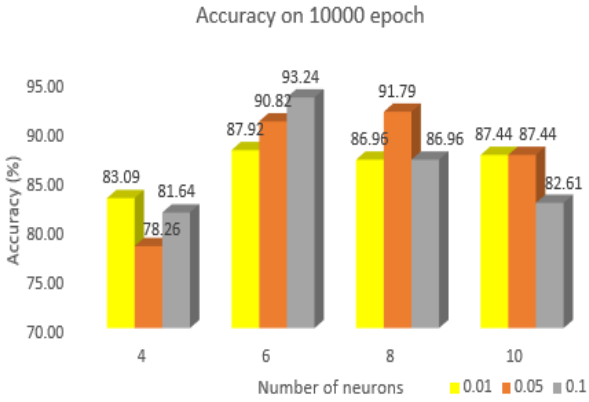

Figure 8 The comparison of accuracy on epoch = 10000 and momentum = 0.05

Table 1. The accuracy of testing result at 5000 epoch and 10000 epoch

No	Learning Rate	Neurons in hidden layer	Momen-tum	Accuracy (%)	
				5000 epc	10000 epc
1	0.01	4	0.01	80.68	80.68
2	0.05	4	0.01	78.26	78.74
3	0.1	4	0.01	84.06	85.51
4	0.01	6	0.01	84.06	84.54
5	0.05	6	0.01	84.54	84.54
6	0.1	6	0.01	84.54	87.44
7	0.01	8	0.01	80.19	82.13
8	0.05	8	0.01	84.54	85.99
9	0.1	8	0.01	84.54	86.96
10	0.01	10	0.01	80.19	81.16
11	0.05	10	0.01	84.54	85.02
12	0.1	10	0.01	86.96	87.44
13	0.01	4	0.05	83.09	83.09
14	0.05	4	0.05	77.29	78.26
15	0.1	4	0.05	81.64	81.64
16	0.01	6	0.05	86.96	87.92
17	0.05	6	0.05	89.37	90.82
18	0.1	6	0.05	90.82	93.24
19	0.01	8	0.05	86.96	86.96
20	0.05	8	0.05	90.82	91.79
21	0.1	8	0.05	81.16	86.96
22	0.01	10	0.05	85.51	87.44
23	0.05	10	0.05	85.51	87.44
24	0.1	10	0.05	82.13	82.61
25	0.01	4	0.1	81.16	81.64
26	0.05	4	0.1	78.74	80.68
27	0.1	4	0.1	82.61	84.54
28	0.01	6	0.1	82.13	82.61
29	0.05	6	0.1	84.54	85.51
30	0.1	6	0.1	75.36	75.36
31	0.01	8	0.1	88.41	89.86
32	0.05	8	0.1	91.79	92.75
33	0.1	8	0.1	82.13	82.61
34	0.01	10	0.1	87.44	89.37
35	0.05	10	0.1	90.82	91.79
36	0.1	10	0.1	86.96	90.34

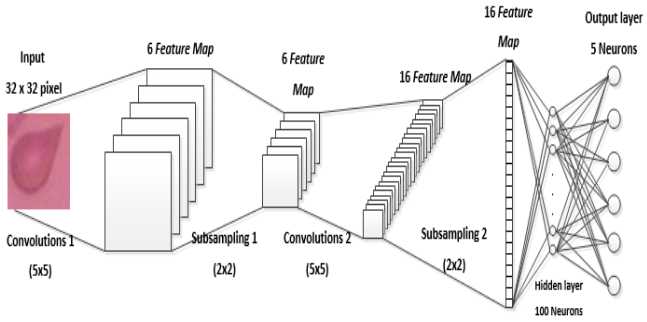

Figure 9. The CNN architecture for erythrocyte classification

The result of CNN architecture classification on Figure 9 is shown on Table 3. The epoch variations used in this research was 1000 and 5000, while the used learning rates were 0.1 and 0.01. The highest accuracy of CNN classification was 92.55% which was obtained from 5000 epoch parameter and learning rate =0.01. Figure 10 shows the comparison the accuracy of classification testing using CNN trained on 1000 epoch and 5000 epoch. At the 0.01 learning rate, the accuracy reached higher than 90% for both epochs, while at the 0.1 learning rate, the accuracy of 1000 epoch reached 89.41%, and 89.81% for 5000 epoch. This finding shows that the smaller the learning rate was given, the higher the accuracy was obtained.

Table 3. The Result of Blood Classification Testing using CNN

No	Conv. Layer 1	Conv. Layer 2	Epoch	Learning rate	Av. Accuracy (%)
1	6 @ 5x5	16 @ 5x5	1000	0.1	89.41
2	6 @ 5x5	16 @ 5x5	5000	0.1	89.81
3	6 @ 5x5	16 @ 5x5	1000	0.01	90.19
4	6 @ 5x5	16 @ 5x5	5000	0.01	92.55

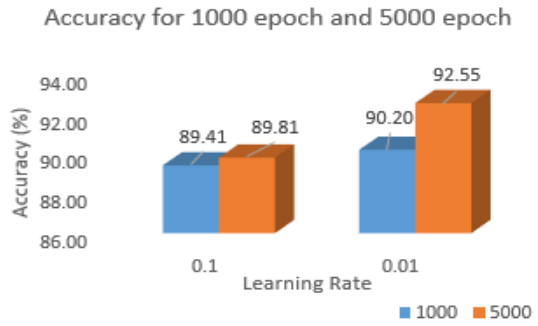

Figure 10. The comparison result of CNN accuracy at 1000 epoch and 5000 epoch

4. CONCLUSION

In this study, an abnormal red blood cell classification method had been developed based on extracted traits. This study used 43 characteristics which are a combination of the features of shape, texture and color. The best accuracy obtained for classification of red blood cells into five classes was 93.24% using the momentum backpropagation neural network architects with 6 nodes in the hidden layer, learning rate 0.1, and momentum 0.05. While the accuracy obtained from the CNN architecture is 92.55%. Both architectures used in this study provide good results for the classification of 4 types of abnormal and a normal erythrocytes. In the next research, the researcher expected to develop an automatic segmentation method on the peripheral blood smear image and perform the selection of traits to obtain better accuracy results. In addition, further research is also expected to increase the number of images used in the study.

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