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Image Recognition of Malaria-infected Red Blood Cells among Other Normal and Cancer-Mutated Cells Using CNN

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Abstract

Malaria is a contagious infectious disease that is still threatening human life. Malaria morbidity when viewed by province shows that Eastern Indonesia is the area with the highest Annual Parasite Incidence (API), namely Papua, West Papua, NTT, and Maluku. This is a concern for the continued efforts to control and eliminate malaria in these high malaria-endemic areas. There are many strategies to help and prevent, include the possibility of innovation in the diagnostic process. Therefore, to answer how to provide innovation in technology to accelerate the elimination of malaria, this study aims to identify the image of red blood cells which infected with malaria among other normal and leukemia cancer-mutated cells (non-malaria) by making improvements through the proposed new model used. This model is meant to do deep learning using Convolutional Neural Network (CNN). The results obtained in this study show that the success of using the proposed model is influenced by the pre-processing stage, the dropout regularization function, learning rate, and momentum value used. The accuracy value obtained is 0.9660, 0.9693 precision, 0.9626 recall, and an F1 score of 0.9659.

Keywords: Deep learning, CNN, Malaria disease, Cancer-mutated cells, Dropout regularization.

1. Introduction

Malaria is a serious infectious disease that threatens human life. This disease is caused by the plasmodium from the Anopheles mosquito which is transmitted through the bite of the mosquito. Plasmodium carried from the bite of female Anopheles mosquitoes will live and multiply in human red blood cells which, if not handled quickly and appropriately, can cause death (Widiawati et al., 2016)(Liang et al., 2017) (Quan et al., 2020)(Dong et al., 2019). Based on data from the World Health Organization (WHO), malaria cases worldwide until 2018 reached 228 million with a total death rate of 405,000 per year which includes the Southeast Asian region, especially Indonesia(World Health Organization, 2019b).

Through the Center for Data and Health Information of the Ministry of the Republic of Indonesia, information on malaria trends in Indonesia has continued to decline since 2011, which shows that the government's countermeasures and control programs have been quite successful. However, malaria morbidity is determined by the Annual Parasite Incidence (API) when viewed by province, showing that Eastern Indonesia is the region with the highest API, namely Papua, West Papua, NTT, and Maluku. This is what continues to be a concern for the elimination program, especially in these high malaria-endemic areas (Pusat Data Kesehatan dan Informasi, Indonesia, Kementerian Kesehatan Republik, 2016).

The finding of malaria cases is done through laboratory confirmation using a microscope or rapid diagnostic test, which until now is the main method used for malaria diagnosis. Diagnosis is made based on clinical symptoms such as chills, fever, headache, weakness, etc., blood tests, and other tests(Jan et al., 2018). Various tools and strategies in malaria control will be very good at accelerating the progress of efforts to eliminate and reduce cases of malaria deaths, including the possibility of innovations and new tools for the diagnosis process and more effective antimalarial drugs (World Health Organization, 2019a)(Gopakumar et al., 2018).

If this is related to the current field of technology, Artificial Intelligence (AI) is one that also contributes to innovation in the medical field, through various studies using large medical data sets to do both data grouping, image analysis with

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machine learning (Poostchi et al., 2018) or another computer-based automatic diagnosis of malaria(Jan et al., 2018)(Madhu, 2020). In this connection, deep learning is one part that also produces various studies(Khedkar et al., 2020). This is because in medical image analysis, this method is considered attractive and the most effective to use, besides that it is a supervised machine learning approach which is a variation of the neural network model but with considerable equivalence to the human brain(Razzak et al., 2018)(Voulodimos et al., 2018).

Therefore, to answer how to provide innovation with a large medical dataset in helping malaria elimination efforts, this study aims to identify the dataset in the form of images of malaria infected and non-malaria (normal cells and leukemia cancer-mutated cells) as a means of malaria diagnosis, using a Deep Learning model algorithm which is Convolutional Neural Network (CNN). As a deep learning model, CNN is specifically designed to study two-dimensional (2D) data such as images and videos (Liang et al., 2017) that can be used in the recognition and classification process (Suriya et al., 2019). By conducting this research, it is hoped that in its future development it can help in decision making and efforts to eliminate malaria, especially in Eastern Indonesia.

Technological innovations provided through science in the medical field are now growing. Starting from big data analytics, image analysis with machine learning, early detection of various diseases, to the classification and grouping of medical data through the field of Artificial Intelligence (Fatima & Pasha, 2017)(Chen et al., 2017).The use of medical images is one that is considered important in the detection process for a particular disease(Razzak et al., 2018) (Mustafa et al., 2018) including malaria. So, in this case, various studies were carried out to support the development of the world of health for this.

2. Literature Review

Research contributed by designing a new Visual Geometry Group (VGG) -SVM network with transfer learning. Where this network is introduced with the BTrain top layer and freezes the other layer transfer learning strategies. VGG acts as a pre-trained model, while SVM is the target classifier. The object used in this study was Infected Malaria Falciparum Parasite which resulted in a classification accuracy of 93.1% (Vijayalakshmi A & Rajesh Kanna B, 2020)

The same research was conducted by (Shekar et al., 2020) who used thin blood smears as their object. Using 10 cross-validation layers from CNN by comparing three types of CNN models based on their accuracy then selecting the right and high level of accuracy. The three of them are Basic CNN which produces an accuracy of 94.3%, VGG-19 Frozen CNN 94.3%, and VGG-19 Fine Tune CNN with the highest accuracy of 96.4%. Raising the problem of malaria prevention through early detection with the same dataset as previous researchers, consider a critical problem in rural areas that depend on the experience of pathologists, using a CNN deep learning model with 5-fold cross-validation and 20 epochs as well obtained a fairly good accuracy of 95% (Shekar et al., 2020). Whereas Liang et al., with their new 16 layer CNN model achieved 97.37% accuracy in their research(Liang et al., 2017).

Presenting three new stages in the diagnosis process of malaria, this research used red blood cells to apply the Segmentation Neural Network (SNN) for image segmentation with 93.72% accuracy and the CNN method for image classification 87.04% (Delgado-Ortet et al., 2020). Unlike the case with Suriya et all., who proposed a Deep Convolutional Neural Network that focuses on comparing validation loss and accuracy by setting hyper-parameters to classify images and calculating the Kappa coefficient and Matthew's correlation coefficient (Suriya et al., 2019). The accuracy obtained is 98.9%. Dong et al., came up with a similar study by evaluating three well-known CNN types including LeNet, AlexNet, and GoogLeNet, and the SVM method was used as a comparison. It produces LeNet accuracy of 96.18%, AlexNet 95.79%, GoogleLeNet 98.13%, and SVM 91.66% (Dong et al., 2017). Transfer Learning ResNet 50 as one of CNN's pre-trained learning methods is also proposed with an accuracy of 95.4%.(Sai Bharadwaj Reddy & Sujitha Juliet, 2019).

Another contribution was given in their study that proposed a diagnosis process using a smartphone. Where the stages of identification of parasite candidates use the Iterative Global Minimum Screening (IGMS) method and for the classification process an adjusted Convolutional Neural Network (CNN) is used (Yang et al., 2019). At the patch level and patient level, the accuracy rates were 97% and 78%, respectively. Another study also proposed the use of the 12 layer CNN model by applying gamma correction and logarithmic correction at the pre-processing stage of data obtaining accuracy in the training of 99.71% and accuracy of test data of 98.23% (Kumar et al., 2018).

Kumar et all, have proposed the use of a new and strong CNN-based kernel dilation aimed at the classification process of infected and uninfected red blood cells. This was followed by the use of the Multi-Magnification Deep Residual Network (MM-ResNet) method which contributed to including multi-magnifying erythrocyte classifiers using deep CNN and the MM-ResNet framework with an accuracy of 98.08% by (Pattanaik et al., 2020)

Based on previous studies, this research focuses on how images of malaria-infected red blood cells and non-infected which is normal cells and leukemia cancer-mutated cells can be identified using the algorithm and how the validation of accuracy results from the recognition carried out consider improvements of the data processing and algorithms used. Besides, this study proposed a new CNN model that used kernel constraint as another use of dropout regularization on model learning.

3. Material and Methods

To support this research, a public dataset was used as experimental material. The data collection process and the pre-processing stage will be described in the following sections. Likewise, with the stages used in research starting from the process of reading the dataset, pre-processing data, initializing the model, to the training and testing process. The architectural model proposals in detail will be presented in different sections.

The required data collection is taken from the Kaggle dataset, which is a jpg and bmp image format. Malaria image dataset which consists of two types of classes, namely parasitized and uninfected red blood cells. To make naming easier, the researchers used the word "infected" to represent images of malaria parasites. The number of images in the original dataset was 27,579 images in two different folders according to their respective classes. The dataset of each class contains 13,780 images. Besides, blood cells infected with leukemia cancer were also used in addition to the identification process of 6054 images, which were included in the class of not infected cells with malaria cells with the aim that the learning model could distinguish these images well. Figure 1 below shows an example of a red blood cell (blood smear) that is infected and not infected with Malaria (normal) and blood cells mutated by leukemia cancer.

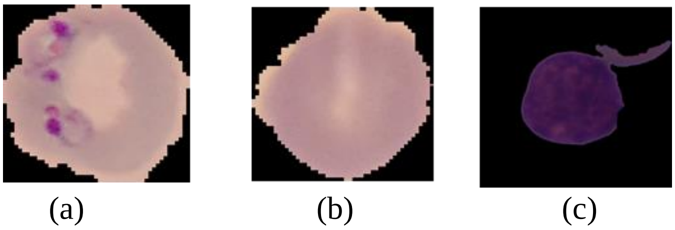

Fig. 1. Thin blood smear samples (a) malaria-infected cells and (b) malaria uninfected cells (c) leukemia cancer-mutated cells

After the identification process was carried out on the entire data, the images in the non-malaria-infected image folder, which originally numbered 13,779, became 7.745 images adding by leukemia cancer-mutated cells as many as 6054. So, the total data in the "uninfected" folder is 13.779. Whereas in the class folder that was infected, the number of images is 13,779 images. So, the total images to be used in this study were 27,558.

The pre-processing stage is a supporting step that also plays an important role in this research. Because the entire data consists of different pixel sizes, this research will also initialize one fixed size (resizing data) which is fed into the model used as well as the rescale or feature mapping process in the range of 0 to 1(Pattanaik et al., 2020)(Rahman et al., 2019) Data augmentation is also implemented to help improve model performance(Kumar et al., 2018). The following parameters in data augmentation applied to training data can be seen in Table 1.

Table 1. Augmentation Table

Augmentation Type	Parameters
Zoom range	0.2
Shear range	0.2
Horizontal flip	True
Fill mode	Nearest

3.1. Research Steps

The implementation of the algorithm used in the study follows several stages which are described in Figure 2. There are seven steps must be taken into consideration.

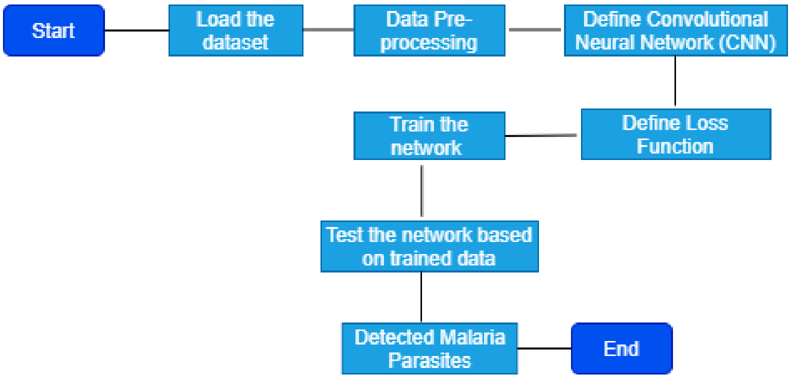

Fig. 2. Research steps diagram

As seen in Figure 2, the initial steps taken in this study began with the preparation and reading of the dataset followed by the pre-processing stage described in the previous sub-chapter. Next is the creation of the CNN model which will be explained in the sub-chapter of the proposed model architecture. The loss activation function in this study is categorical cross-entropy with the stochastic gradient optimizer as the optimization algorithm also, this study uses Keras-TensorFlow. The details will be explained in the next section.

3.2. Proposed Model

The initialization of the model customization with the Convolutional Neural Network (CNN) algorithm was proposed as a learning model used in the study (Figure 3). This proposed model is applied to the training process and network testing. This model uses image input data that has been changed from its original size to a size of 100x100 pixels.

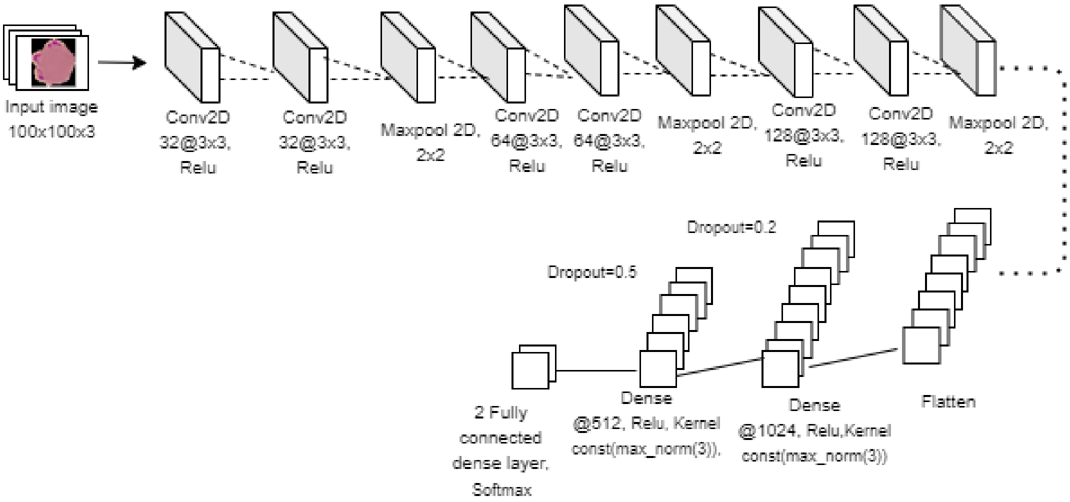

Fig. 3. Proposed CNN Model Architecture

The proposed learning model consists of 15 layers including 6 convolutional layers, 3 max polling layers, one flattened layer, and 3 dense layers. Also, the two layers between them which are a dropout function of 20%, and 50% of the input data at one dense layer to reduce overfitting on the existing learning network (Rahman et al., 2019). The dense layer (fully connected dense layer) also includes applying kernel constraint into the matrix with max_norm (3) which performs well with the dropout function. Each of the existing convolutional blocks uses the Relu activation function.

In the feature extraction layer process, a convolutional layer and a pooling layer are used. A convolutional operation consists of 32, 64, and 128 filters with a 3x3 kernel size with the same set of padding. Pool size 2x2 is used for all Max pooling layers in the model. The implementation of the dropout function in the hidden layer is randomly discarded by 20% and 50% of the input data. This is followed by 512, 1024, and the dense layer output. At the end of the classification stage, the output from the dense layer is entered into another activation function, namely softmax. The use of softmax activation in this study as a probability function where this function predicts the output of a particular class with a predicted value(Mustafa et al., 2018). As previously described, we used categorical cross-entropy to determine the activation loss function, with an optimization algorithm, namely the stochastic gradient optimizer (SGD)(Sunarko et al., 2020). The adjustment of the learning rate is 0.001 and momentum 0.5. The optimizer is possible to converge faster by absorbing more unwanted dimensions with the use of momentum (Dang et al., 2018).The batch size was 32 samples and continued for 25 epochs.

4. Result and Discussion

The experiment on the red blood cell image used was started by arranging the dataset for the folder name and categorizing the class labels. The categories were divided into two classes, namely "infected" and "uninfected". The dataset consists of three folders, namely train, validation, and test. Randomly checking the test folder, if it contains files then all of them will be moved into the train folder, which is then divided into two datasets in the train folder with a percentage of 80:20, where 80% of the data is used for training and 20% which was moved previously used in the testing process.

5-fold stratified k-fold cross-validation was used in the study. The distribution of each data set per fold applies to the train and test (validation) processes. Randomly, the image of blood cells is divided into 5 available folds. More details can be seen in the Table 2.

Table 2. Description of the value of the stratified k-fold-cross-validation.

Description Value
Fold 1
17650 images belonging to 2 classes.
4413 images belonging to 2 classes.
Fold 2
17650 images belonging to 2 classes.
4413 images belonging to 2 classes.
Fold 3
17650 images belonging to 2 classes.
4413 images belonging to 2 classes.
Fold 4
17650 images belonging to 2 classes.
4413 images belonging to 2 classes.
Fold 5
17652 images belonging to 2 classes.
4411 images belonging to 2 classes.

The declaration of variables representing the two categories in different classes is carried out, then the matrix values are converted into a two-dimensional array to facilitate the training process. Stratified k-fold cross-validation is used to divide the data in the train folder so that it can be repeatedly recognized as many as 5 folds, and validation afterward of all data in the training process.

The use of images of blood cells mutated by leukemia cancer is also added to the category of “uninfected” class with the aim that the learning model can identify both images of malaria-infected and non-malaria (normal cells and leukemia cancer-mutated cells). Validation of training data was also carried out. 5-fold stratified k-fold cross-validation was used in the study. Also, for the pre-processing stage, normalization, data augmentation, and resizing of the image size were performed.

4.1. Modeling and Training

In the proposed model, as in general, there are two important stages, namely feature extraction and classification. The extraction feature of the image begins with a convolution process at the input and filter values as specified. Dropout regularization is used in the existing proposed model, in which it selects random neurons to ignore during network training. The use of this function is applied to hidden layers.

This can be seen when the result of the convolution process with the second 32 x 32-pixel filter is carried out, the feature map is obtained and the convolution result value is subject to the activation function and the max-pooling layer. As much as 20% and 50% of neurons are dropped from the network in the hidden layer are applied afterward. For each hidden layer, a limit is imposed to ensure that the maximum norm of weight does not exceed the value of 3. A loss activation categorical cross-entropy function is then applied.

The training stage is carried out by the existing learning network. Evaluation of the performance of the results of the validation of existing training is also carried out. The training performance and evaluation are described by the graph in Figure 4.

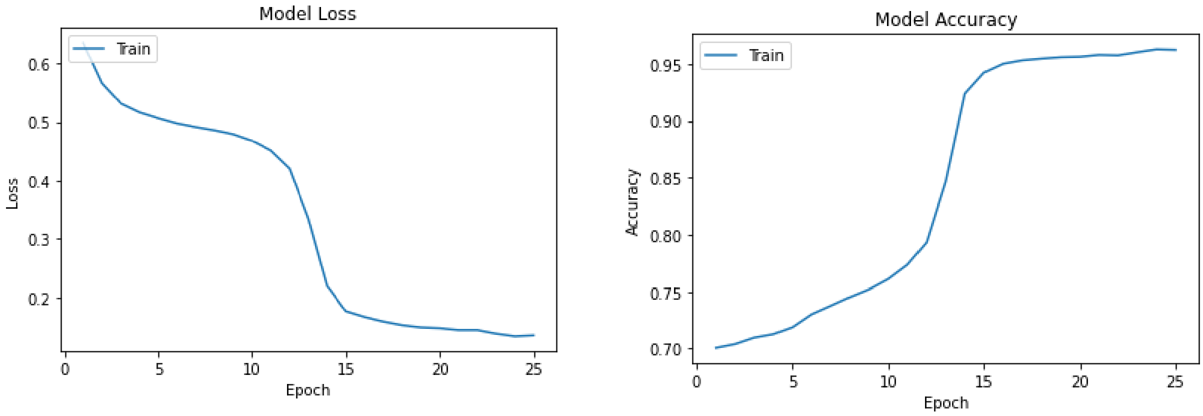

Fig. 4. Loss and accuracy model

The analysis is shown in the loss model graph and accuracy during the training process, showing a fairly good performance. Loss model from condition 0.6573 slowly decreases, back up on the 21st epoch, which is 0.1473 which is higher than the previous epoch value then decreases and stabilizes to 0.1462 in the last iteration. Likewise, the accuracy performance which started with 0.6669 or 66.69% slowly began to increase but decreased slightly in the 18th iteration then increased and stabilized at an accuracy rate of 0.9583. The validation test of the training data produces a fairly good predictive value in the confusion matrix, with an accuracy value of 0.96554 (96.55%), and the time required for the training process is 24889.18 seconds.

4.2. Testing and Evaluation Matrix

The next testing process is carried out. With the models and networks that have been studied in training, a dataset of 5513 images in each class is then tested. The results obtained are shown in the evaluation matrix as shown in Table 3.

Table 3. Confusion Matrix

Prediction Value	**Actual Value**	
	Positive Class (Malaria-Parasitized)	**Negative Class (Malaria-Uninfected)**
Positive Class (Parasitized)	2655[1]	103[2]
Negative Class (Uninfected)	84[3]	2617[4]

[1]TP (True Positive) ; [2] FN (False Negative); [3] FP (False Positive) ; [4] TN (True Negative)

Table 3 shows the process of identifying red blood cell images, as many as 2655 images of parasites were correctly predicted by the tissue as blood cells infected with malaria. The actual value of malaria-infected images predicted as uninfected cells was 84, then 103 blood cells with the actual value not infected with malaria were identified as infected images and 2671 images that belonged to the uninfected class were correctly identified.

This study shows that the proposed learning model used runs quite well in network training and testing. Apart from the use of dropout regularization, activation and optimizer functions are also supported. No less important than the pre-processing stage. All aspects from the start to the run of the model play an important role to obtain an accuracy value of 0.9660, precision 0.9693, recall of 0.9626, and an F1 score of 0.9659.

5. Conclusion

Based on the results of the experiments that have been carried out in the study, it can be concluded that:

a) Malaria-infected red blood cells and uninfected (non-malaria) which is normal cells and leukemia cancer-mutated cells can be identified properly by the proposed model used in the learning network.
b) The use of dropout regularization as a way to improve the network through the existing proposals gives good results. The value that resulted from using a dropout with max-norm regularization was inseparable from the learning rate and momentum values. This is indicated by the accuracy obtained in the evaluation of 0.9660 or 96.60%.
c) The pre-processing and data augmentation stages also provided another important influence in the success of image recognition of malaria-infected red blood cells among other normal and leukemia cancer-mutated cells in this study.

As a suggestion for future research, development can be done by trying to compare the use of other activation functions with the proposed model, various CNN pre-trained networks, and their implementation using applications connected to smartphones to make it easier in the future.

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