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Investigation of white blood cell biomaker model for acute lymphoblastic leukemia detection based on convolutional neural network

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ABSTRACT

Acute Lymphoblastic Leukemia (ALL) is a disease that is defined by uncontrollable growth of malignant and immature White Blood Cells (WBCs) which is called lymphoblast. Traditionally, lymphoblast analysis is done manually and highly dependent on the pathologist's skill and experience which sometimes yields inaccurate result. For that reason, in this project an algorithm to automatically detect WBC and subsequently examine ALL disease using Convolutional Neural Network (CNN) is proposed. Several pretrained CNN models which are VGG, GoogleNet and Alexnet were analaysed to compare its performance for differentiating lymphoblast and non-lymphoblast cells from IDB database. The tuning is done by experimenting the convolution layer, pooling layer and fully connected layer. Technically, 70% of the images are used for training and another 30% for testing. From the experiments, it is found that the best pretrained models are VGG and GoogleNet compared to AlexNet by achieving 100% accuracy for training. As for testing, VGG obtained the highest performance which is 99.13% accuracy. Apart from that, VGG also proven to have better result based on the training graph which is more stable and contains less error compared to the other two models.

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1. INTRODUCTION

Leukemia is one of blood cancer disease that is highly related to White Blood Cell (WBC) and can cause fatal and death [1]. WBC is closely related to human immune system which helps to fight diseases and viruses [2]. Human are always surrounded by harms, bacteria and viruses every day, hence a strong immune system is needed. WBC analysis is very crucial and greatly helps to monitor our immunity level for early prevention. It is also potentially can be diagnosed with diseases such as HIV, Lymphoma and Leukemia. In this paper, Acute Lymphoblastic Leukemia (ALL) is detected from WBC region in blood smear image as illustrated in Figure 1.

WBC has five types which are Neutrophils, Eosinophils, Basophils, Monocytes and Lymphocytes as shown in Figure 2 [3]. Basically, ALL comes from the presence of Lymphoblast which is the abnormal cell of Lymphocytes. It can be differentiated by its shape irregularities, small cavity in the cytoplasm,

spherical particles within nucleus and the number of lobes in the nucleus [4]. This disease commonly attacks 25% of young children below 15 years old [5].

Conventional method of detecting ALL is by manual analysis which the pathologist needs to review the blood sample image manually [6-7]. It is highly dependent on the pathologist's skill and experience [8]. Among pathologist itself might produce different result and it creates confusion. Other than that, as the sample increase, it will be more challenging for the pathologist and it is also time consuming [9]. Blood smear image consists of non-uniform illumination which will harden the pathologist's work [10]. Automated system also can help to aid pathologist in the blood diagnosis [11]. Other than that, computer aided system by using machine learning is proposed to identify lymphoblast and detect ALL. However, machine learning consists of complicated process of segmentation, feature extraction and classification [12, 13]. It is also challenging as the classification result is highly dependent on the selection of features. If the features selected is insignificant, classification accuracy will be affected.

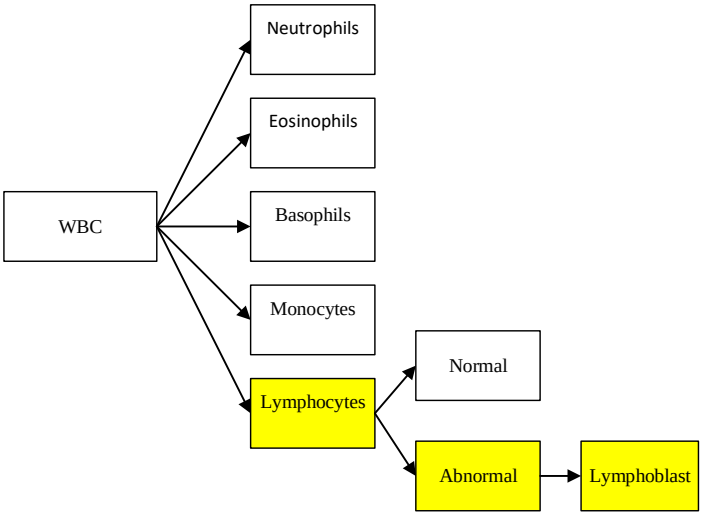


Figure 1. Structure of ALL

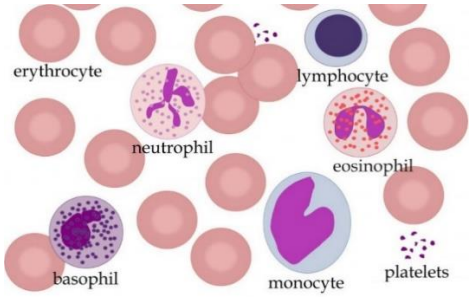


Figure 2. Illustration of five types of WBC in a blood smear image [3]

In this work, computer aided using Convolutional Neural Network (CNN) which is deep learning model is done to cater the limitations. The biggest advantage of deep learning is its ability to learn the object's features, no complex classifier design needed and its performance is high [14]. Other than that, it is widely used in medical field due to its ability to achieve impressive performance [15]. Deep learning also can be defined as a class of machine learning techniques that exploit many layers of non-linear information processing for supervised or unsupervised feature extraction and transformation and for pattern analysis and classification [16]. CNN process an input data by its multiple layers which consists of four key features: local connections, shared weights, pooling and the use of many layers [17]. Deep learning in medical benefit is exploit nowadays. There are many research and applications using deep learning that can be found previously such as image classification for Malaria diagnosis which use the AlexNet pretrained model [18]. Other than that, AlexNet of CNN is also used for fire detection and it achieved stable accuracy as reported in [19]. CNN architecture that consiste of 5 layers of convolutional, pooling and fully connected layer

is proposed to detect the subtype of WBC [20]. Face and non-face image classification is reported in [21] to shows an outstanding performance. Other than that, there are also research on ALL identification which compares the result of machine learning and CNN and CNN showed the best performance result [22]. Some works combine CNN with Recursive Neural Network (RNN) to classify types of WBC [23]. Lastly, the most related work to ours is as reported in [24] which used AlexNet pretrained model to identify lymphoblast and detect ALL. Rest of the paper is organized as follows: Section II describes the proposed framework and methodology of the process, section III presents the result of the implementation and analysis. Section IV provides the conclusion and future works.

2. RESEARCH METHOD

2.1. Dataset

Images used were from ALL_IDB which consist of public blood smear image that contains of ALL effected cell and healthy cell as shown in Figure 3. There are three main elements in the blood smear image which are Red Blood Cell (RBC), white blood cell (WBC) and the background. The deep colored purple is the WBC region while the pinkish or lighter purple is the RBC region and other than that is considered as the background. The first row shows the lymphoblast cell and the second row shows non-lymphoblast cell. It can be differentiated by its shape irregularities, small cavity in the nucleus, spherical particles within nucleus and number of lobes in the nucleus. In this paper, there are 30 images of lymphoblast and 30 images of healthy cell were examined to detect ALL. These images resolution are the same which are 257x257. However, the input size is resized based on the pre-trained model used. There are 60 images in total and 70% of it is used for training and 30% is used for testing. The software language used is Matlab with R2018b version. While for completing the algorithm, deep network designer in Matlab software is used. All the layers used for CNN model such as convolution layer, fully connected layer and pooling is in the mentioned toolbox.

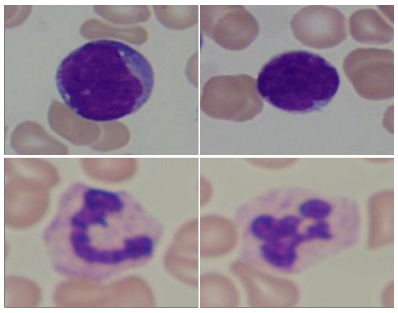


Figure 3. Lymphoblast and non-lymphoblast

2.2. Convotional neural network

In this paper, we compare the pre-trained models of AlexNet, GoogleNet and Vgg16 for ALL detection. The CNN key operation is as shown in Figure 4. After input image is extracted, the filters with learned weights to generate feature maps in done in the convolution part. Basically, image size will differ after the convolution layer. Non-linearity is often done by using Rectified Linear Unit (ReLU) to minimize the features vector. Lastly, fully connected is the classifier which act to classify the lymphoblast and non-lymphoblast cell. In every pre-trained models that were used, we changed the last fully connected to 2 class output using softmax function. The mini batch size and epoch is set to 10 and 6 respectively for all models.

- AlexNet: It contains of 8 layers which consists of 5 convolutional and 3 fully connected layers as shown in Figure 5. Input image for AlexNet is RGB image with resolution of 227x227. Firstly, 11x11 convolution mask is used over 227x227 input image followed by 5x5, 3x3, 3x3 and 3x3 convolution mask. AlexNet used ReLU for the non-linearity function.
- GoogleNet: It contains 22 layers as shown in Figure 6. Input image required for GoogleNet is slightly different from AlexNet. It requires RGB input image with 224x224 resolution. GoogleNet has addition of inception layer which is used to convolve in parallel different sizes from 1x1 to 5x5 and it is done by applying Gabor filters with different sizes. It is also widely known by its ability to cater image related problems [22].

– VGG:This pre-trained model consists of 19 layers as shown in Figure 7 and the input image is from the resolution of 224x224 which is same as GoogleNet. VGG uses 3x3 filters with stride of 1 in convolution layer and it also used the same padding in pooling layer which is 2x2 and the stride is 2.

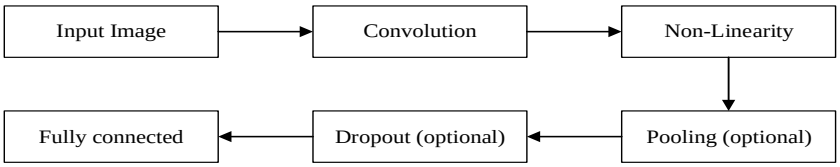


Figure 4. CNN key operation

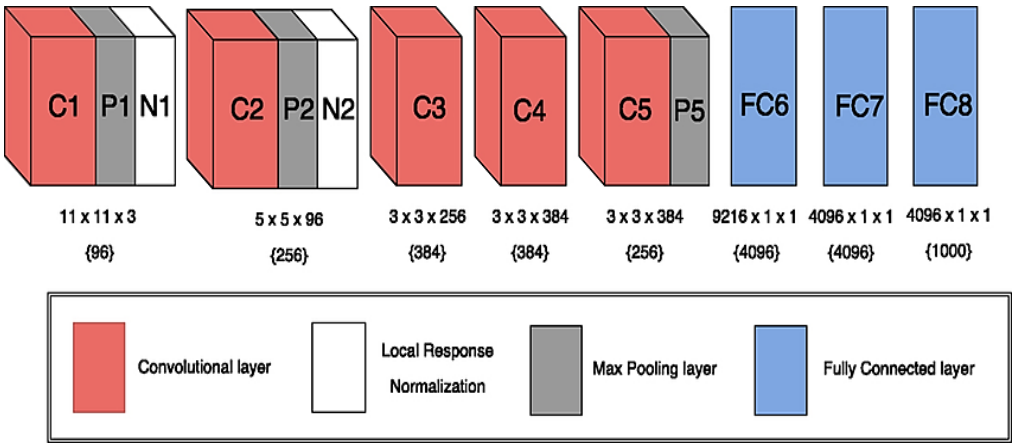


Figure 5. AlexNet architecture

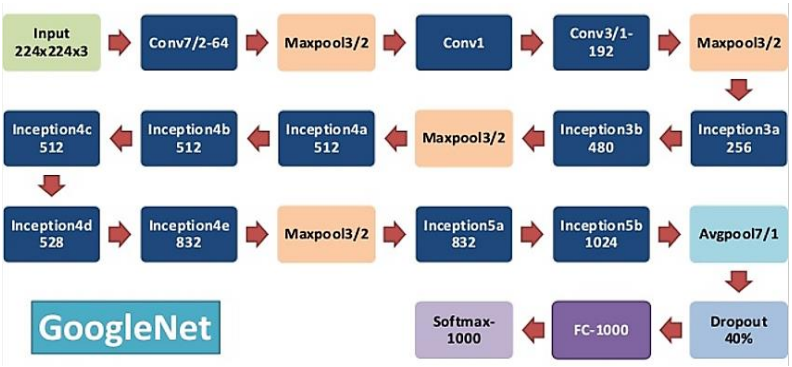


Figure 6. GoogleNet architecture

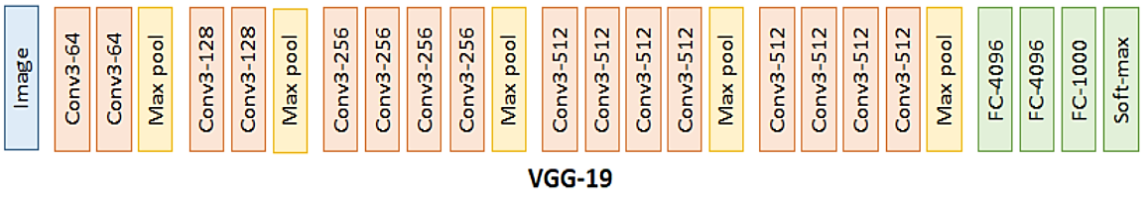


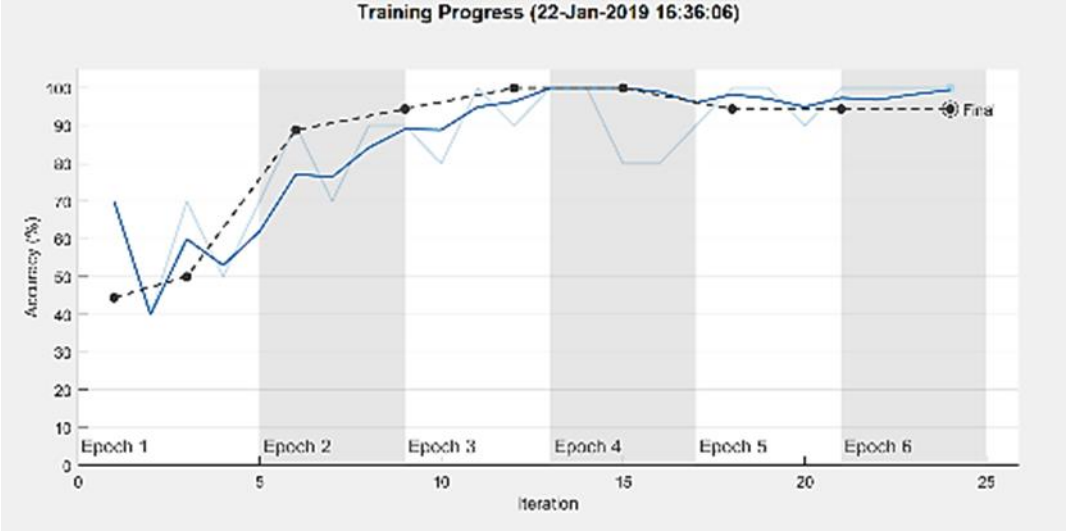
Figure 7. VGG architecture

3. RESEARCH METHOD

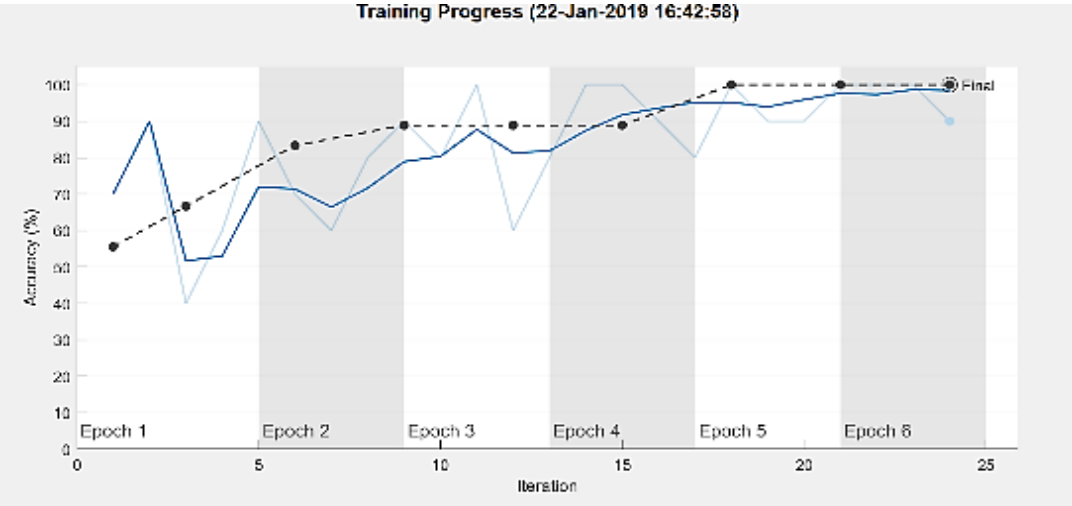
Images of two classes of Lymphoblast and Non-lymphoblast cell is trained by using 3 pre-trained models which are AlexNet, GoogleNet and VGG. The parameters such as mini batch size, epoch, iteration,

percentage of training and testing are set the same which are 10, 6, 24, 70% and 30% respectively. Figure 8 shows the training process for AlexNet, GoogleNet and VGG model. Based on the graph, VGG model is more stable as it achieves 100% validation accuracy at iteration of 12 until the rest of iteration compare to GoogleNet which is at iteration 18. It shows that VGG achieves 100 % stability faster than the other two models.

The comparison of three models is made in terms of its training and testing accuracy and the elapsed time for training process. It can be seen that training accuracy of AlexNet is 94.44% while for GoogleNet and VGG, both training achieve 100% accuracy. The result has been tabulated in Table 1. In the training process, AlexNet training accuracy is the lowest as the layer is lesser and might not be significant for ALL detection. However, the elapsed time is the shortest compared to GoogleNet and VGG. It is due because the AlexNet model has the fewest layer which is 8 layers compared to GoogleNet and VGG which are 22 and 19 layers respectively.

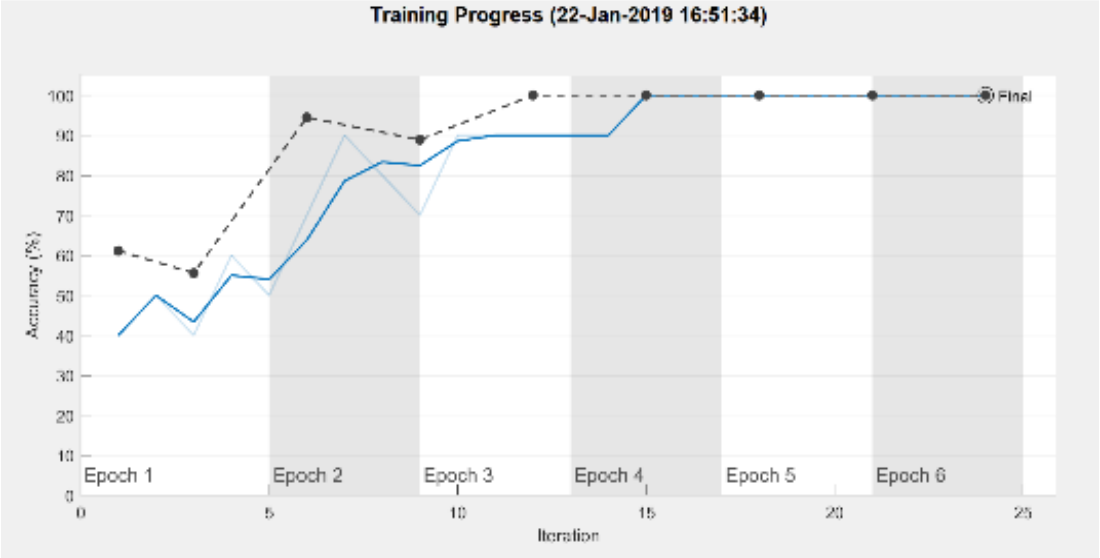


(a)



(b)

Figure 8. Training graph of, (a) AlexNet, (b) GoogleNet



(c)

Figure 8. Training graph of, (c) VGG (*continue*)

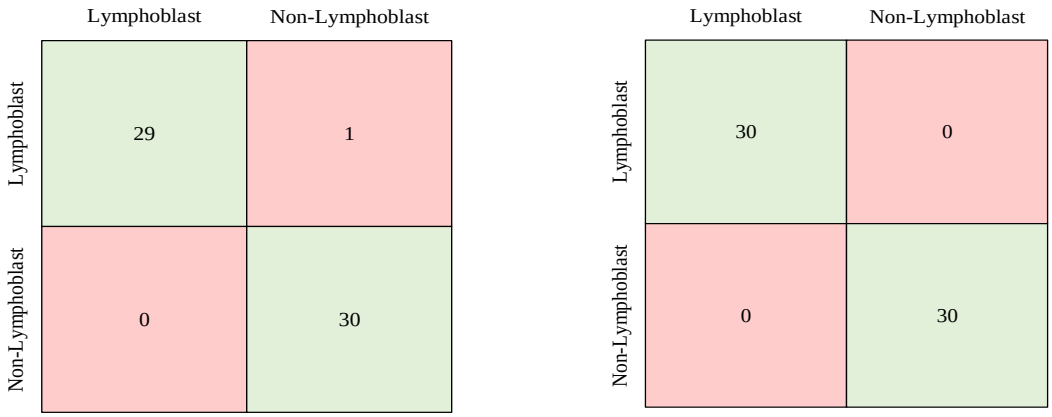
While in Table 2, comparison of testing result for lymphoblast and non-lymphoblast is tabulated. It can clearly be seen that for both lymphoblast and non-lymphoblast classification, VGG model obtains the highest accuracy. The illustration of testing classification for AlexNet, GoogleNet and VGG is depicted in Figure 9(a) and Figure 9(b) respectively. Both AlexNet and GoogleNet contains error in classifying Lymphoblast cell. In 30 images, there is one image that is misclassified. While for VGG model, all images are perfectly classified to its class and category. Best result can be achieved by a model that contains layers between 16-19 as reported in [25]. Other than that, VGG is also reported to have advantages of stacking multiples convolutional layers with small-sized kernels which can improve the effectiveness of receptive field of the network [25].

Table 1. Accuracy of training and testing

CNN Model	Training (%)	Testing (%)	Elapsed time
AlexNet	94.44	97.16	52 sec
GoogleNet	100	91.45	1 min 57 sec
VGG	100	99.13	8 min 35 sec

Table 2. Accuracy of testing for lymphoblast and non-lymphoblast

CNN Model	Lymphoblast (%)	Non-Lymphoblast (%)
AlexNet	97.66	96.66
GoogleNet	89.58	93.32
VGG	99.77	98.49



(a) (b)

Figure 9. (a) Confusion matrix of AlexNet and GoogleNet, (b) Confusion matrix of VGG

4. CONCLUSION

In this paper, comparison of three different pretrained models of AlexNet, GoogleNet and VGG was made to classify Lymphoblast cell for ALL detection. These models have different number of layer and the layers are differentiated from each other. It was compared using Convolutional Neural Network on Matlab. There were 60 images in total which consist of 30 lymphoblast images and 30 non-lymphoblast images. In this project, 70% of the images was used for training and 30% was used for testing purposes. As a result, VGG was able to classify lymphoblast and non-lymphoblast cell correctly compare to AlexNet and GoogleNet. In the training process, VGG and GoogleNet able to achieve 100% accuracy. While in the testing assessment, VGG still maintains its high accuracy by obtaining 99.13% which is the highest compared to AlexNet and GoogleNet which obtained 97.16% and 91.45% respectively. VGG also proven the best from its confusion matrix. There are no misclassification of cells by using VGG model. While for AlexNet and GoogleNet, there was one image that has been misclassified by the models.

In the future, the authors expected the system to be better by modifying the best pretrained model for WBC which is VGG to improve the result and accuracy. Next, the authors wish to increase the sample image and cater the illumination problem. Lastly, the algorithm is expected to be able to classify all five types of WBC which are lymphocyte, monocytes, neutrophils, basophil and eosinophil.

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