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Detection of acute lymphocytic leukemia (ALL) with a pre-trained deep learning model

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Abstract – Acute Lymphocytic Leukemia (ALL) is a type of cancer caused by immature lymphocytes in the bone marrow. Acute Leukemia is common in both children and adults. It can also cause death if left untreated. Hematologists diagnose ALL by examining the blood and bone marrow. This method used is slow and takes more time. In this study, the diagnosis and classification of the disease was carried out using peripheral smear images with the proposed method. In the proposed method, 99.80% accuracy was obtained by using the DarkNet19 pre-trained model. Then, 1000 features were obtained from Darknet19. 521 of the obtained features were selected with Mrmr feature selection algorithm. The selected features are classified with support vector machines. An accuracy of 99.94% was achieved with the proposed method. The results show that the proposed method can be used as a tool that will certainly assist pathologists in diagnosing ALL and its subtypes.

Keywords – Acute Lymphocytic Leukemia, Darknet19, Mrmr,Feature Selection, SVM

I. INTRODUCTION

Cancer is the excessive and untimely proliferation of cells. In this process, cells escape from the eye of the immune system and spread to distant tissues (metastasis) and clone in those areas (malignant)[1]. Cancers are classified according to the cell or tissue group they originate from. Leukemia is a tumor originating from hematopoietic cells[2]. Leukemia is an increase in immature blood cells called blasts with a change in the code that occurs in the main cells in the bone marrow, which is the main production site of the blood circulating in our veins with any effect. These cells spread rapidly and involve the bone marrow, lymph nodes, spleen, liver, brain and central nervous system. Leukemia originates from hematopoietic stem cells and is divided into two groups as acute lymphoblastic leukemia (ALL) or acute myeloblastic leukemia (AML) according to the subclasses of these stem cells[3, 4]. ALL is an abnormal, uncontrolled and excessive proliferation of lymphoblasts, which occurs as a result of genetic damage to the DNA of a single stem cell. These abnormal cells, called leukemia cells, are dysfunctional, multiply rapidly, replace normal cells and form the symptoms of the diseaseLymphoblasts multiply in the bone marrow and pass from there to the blood and other organs such as the cerebrospinal cord. ALL type is 80% of childhood leukemias. In adults, it is 20% of all adult leukemias. Leukemia is diagnosed by history and physical examination. After the examination, complete blood count and peripheral smear test are performed. In the peripheral smear test, blood cells are examined under a microscope. If there are abnormal blood cells in these tests, a diagnosis of leukemia is made. However, since leukemia is a cancer originating from the bone marrow, the definitive diagnosis is made by taking the bone marrow and examining it in the pathology, genetics and flow cytometry laboratory. Today, artificial intelligence-based models have been developed in order to prevent these

situations and help doctors. Especially with the concept of "digital pathology" in the field of health, the development of artificial intelligence models has accelerated. In order to obtain better results than the existing traditional disease diagnosis methods, digital pathology images were given as input to various artificial intelligence models, the models were trained and then digital pathology images were classified and analyzed using artificial intelligence algorithms[5, 6]. Different studies have been carried out in the literature by using deep learning methods together with medical signals and images. [7-11]. The summaries of studies on pathology data using machine learning and deep learning methods, their methods, datasets and their success results according to certain metrics are given below. Das et al. [12], classified ALL using the ALLIDB1 and ALLIDB2 datasets. They used the MobilenetV2 and ResNet18 CNN models in their proposed method. With 70% training and 30% testing, they achieved 99.39% accuracy on ALLIDB1 and 97.18% on ALLIDB2. With 50% training and 50% testing, they achieved 97.92% accuracy on ALLIDB1 and 96.00% on ALLIDB2. Das et al. [13], extracted features from ALLIDB1, ALLIDB2 and ASH datasets by transfer-learning. The extracted features were classified using the SVM classifier. With 70% training and 30% testing, 99.39% accuracy in ALLIDB1, 98.21% in ALLIDB2 and 97.73% in ASH was achieved. Das et al. [14], detected ALL automatically using the pre-trained ShuffleNet CNN model. With 70% training and 30% testing, 98.00% accuracy in ALLIDB1 and 96.46% in ALLIDB2 was achieved. With 50% training and 50% testing, 95.00% accuracy in ALLIDB1 and 96.89% accuracy in ALLIDB2 was achieved. Genovese et al. [15], extracted features from the ALL-IDB2 dataset with the VGG16 pre-trained model. They obtained results of 96.84% , 97.53% and 96.15% for accuracy, sensitivity, and specificity, respectively. Kumar et al. [16], used the RESNET50 CNN network to detect ALL. They obtained results of 96.15% , 100% and 91.30% for Accuracy, sensitivity, and specificity, respectively, in the SVM classifier. With Logistics regression, they achieved 96.15% , 100% and 93.55% results for Accuracy, sensitivity, and specificity, respectively. They obtained results of 96.15% , 95.65% and 95.65% for accuracy, sensitivity, and specificity, respectively, in the random forest classifier. Kumar et al. [16], used the Resnet50 CNN network to detect ALL. In the SVM classifier, 96.15% , 100% and 91.30% results were obtained for Accuracy, sensitivity, and specificity, respectively. With Logistics regression, they achieved 96.15% , 100% and 93.55% results for Accuracy, sensitivity, and specificity, respectively. In the random forest classifier, results were obtained for Accuracy, sensitivity, and specificity of 96.15%, 95.65%, and 95.65%, respectively.

II. Materials and Method

In this section, information is given about the data set used and the proposed method.

A. *Dataset*

In the study, the data set prepared with the images obtained from the bone marrow laboratory of Taleqani Hospital (Tehran, Iran) was used. The study included 64 patients with suspected ALL diagnosed as Early Pre-B, Pre-B and Pro-B, and 25 individuals diagnosed as benign (hematogon). The dataset consists of 3562 peripheral smear images taken from 89 patients in total [17]. Images were taken under a microscope with 100x magnification using a Zeiss branded camera. In addition, the images obtained with the help of the microscope were recorded in JPG format with a size of 224x224. Example images of the four classes in the data set are given in Figure 1.

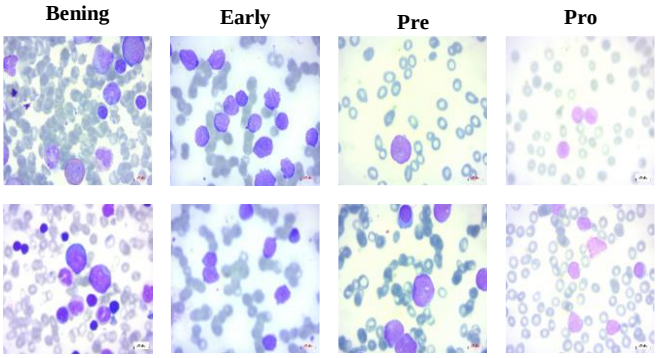

Figure 1. Samples from the datasets for each class

B. *DarkNet-19*

Darknet 19 has a Convolutional Neural Network (CNN) architecture consisting of 19 layers. This architecture is used to extract features from images and then features are fed into the next layer. These properties are used for classification in the last layer. The DarkNet19 architecture has been proposed as a new classification model to be used as the basis for YOLOv2 [18]. Similar to the VGG model, a 3x3 convolution filter is used, and the number of filters is doubled after each maximum value association layer. In the classification layer, first the mean

commonality layer is used, the feature representation is revealed between the mean commonality and the 3x3 dimensional convolution layer by using a 1x1 dimensional convolution filter[19]. The DarkNet19 architecture includes 19 convolution layers, 5 max pooling layers, 18 Batch normalization layers and 18 Leaky Relu layers, the model structure is given in Figure 2.

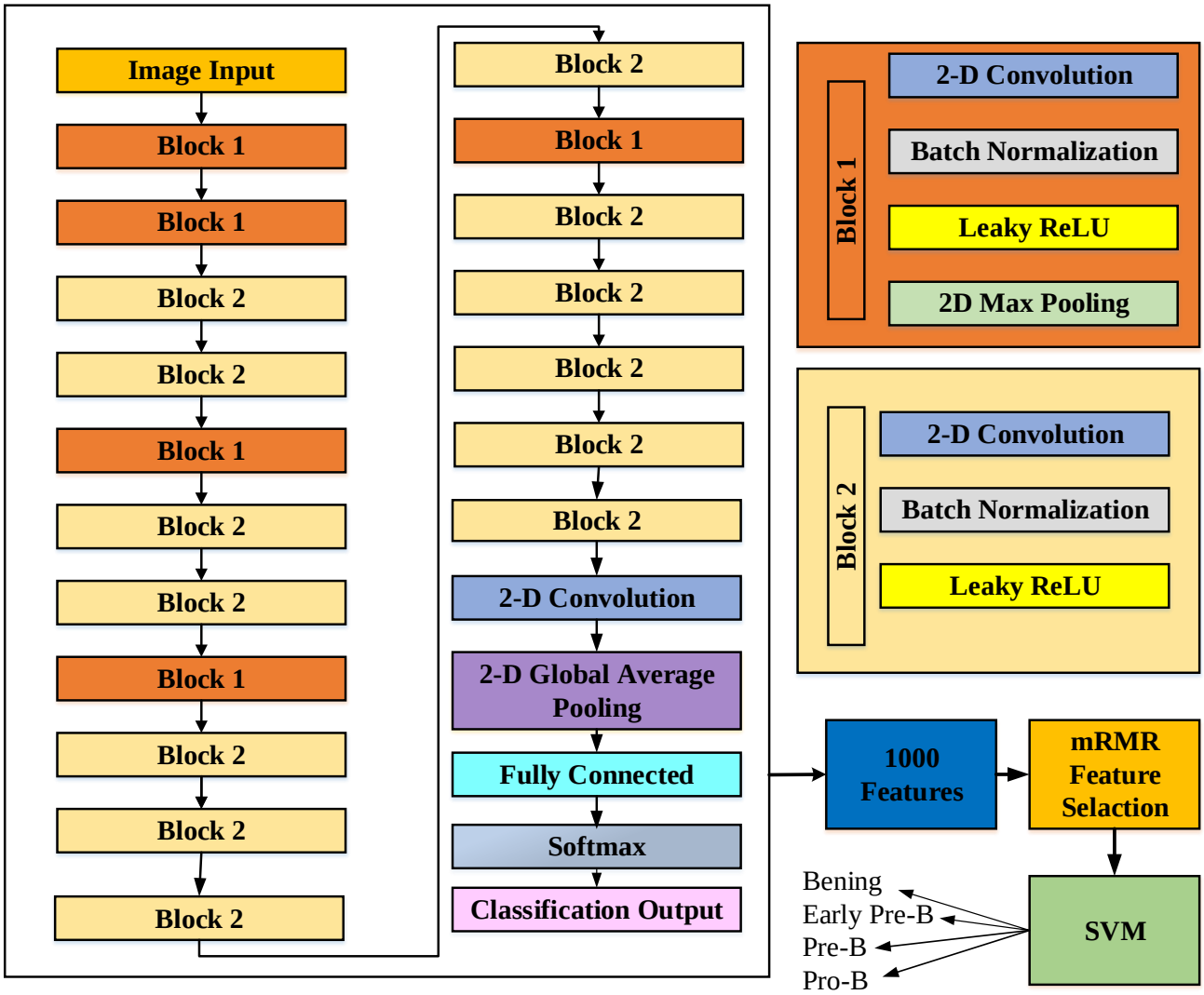

Figure 2. Block diagram of the proposed method

C. *Minimum redundancy feature selection*

Minimum redundancy feature selection mRmR is an entropy-based feature selection method with a high success rate and working speed. It is an entropy-based method, and it performs filtering by both selecting the features that contribute the most to the classification and minimizing the redundancy between the features. The idea of minimum redundancy is the selection of attributes that are neither distant nor close. Allows the minimal redundancy attribute set to better represent the entire data set [20].

D. *Classification*

The support vector machines method is used for both regression and classification purposes. However, it is generally used for classification. Being a supervised learning algorithm, SVM can classify both linear and non-linear data, but mostly it tries to classify data linearly. SVM is a highly preferred method as it produces significant accuracy with less computation [21, 22].

III. EXPERIMENTAL RESULTS AND DISCUSSION

In this study, Matlab program was used to create models and obtain results. All programs were run on PC with 11th Gen Intell® core™ i9-11900 processor and 64GB RAM. In the study, the Kaggle ALL dataset consisting of peripheral smear image of acute lymphoblastic leukemia was used. There are images belonging to 4 different classes in the data set. The network was trained by giving the

images in the dataset to the input of Darknet19. Training parameters are tabulated in Table 1.

Table 1. Training Parameters.

Solver		**Basic**		**Sequence**		**Advanced**	
Solver	sgdm	Validation Frequency	1	Sequence Length	Longest	L2 Regularization	0.0001
Initial Learn Rate	0.01	Max Epochs	30	Sequence Padding Value	0	Gradient Threshold Method	I2norm
Iteration	268	Mini Batch Size	128	Sequence PaddingDirection	right	Learn Rate Drop Factor	0.1

70% of the ALL dataset trained in Darknet 19 was used randomly for training and 30% for estimation. As a result of the training, the accuracy graph obtained for training and prediction is given in figure 3 and the loss graph in figure 4. The training time is 268 minutes 32 seconds. 99.80% accuracy was obtained.

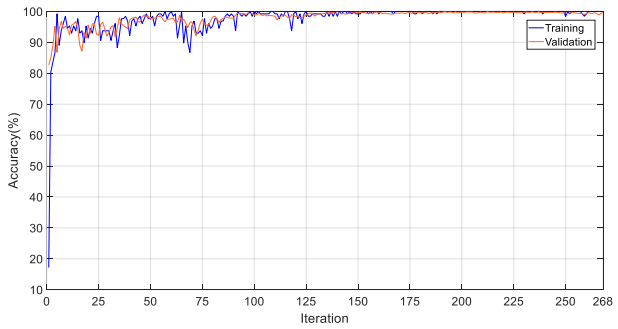

Figure 3. Accuracy performance of the model

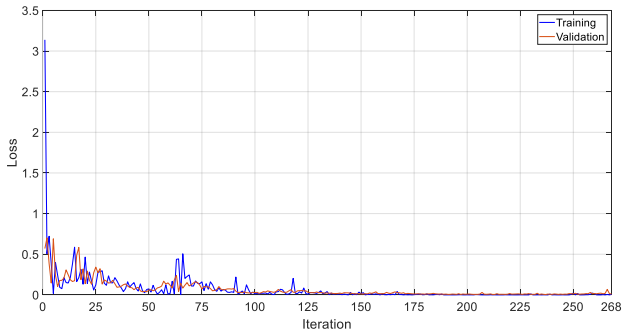

Figure 4. Loss performance of the model

1000 features were obtained by using the weights of the trained network. Obtained features were selected by mRMR algorithm. In the selected features, 521 features with weight values above 0.25 were selected.

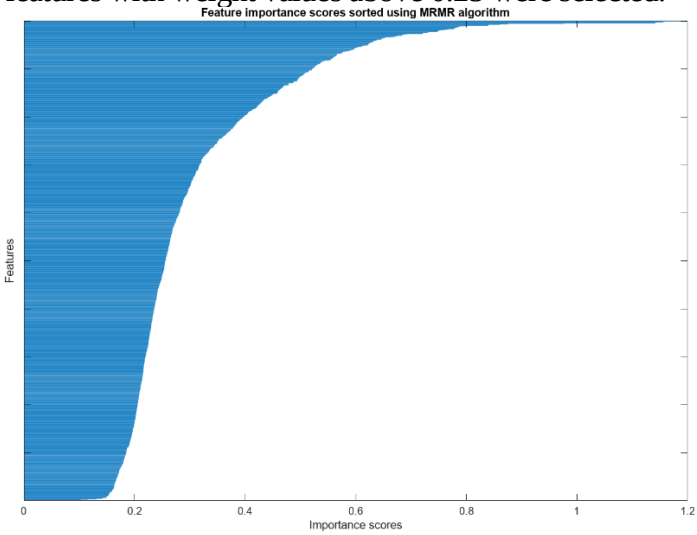

Figure 5. Feature weights calculated with the mRMR algorithm

Matlab Classification Learner was used to obtain classification results. The 10-fold cross validation results for SVM[21], ANN[23], KNN[24] and Naive Bayes[25] are tabulated in table 2. This procedure was repeated once using all features and once feature selection by mRMR.

Table 2. Classification results.

	All features	Selected features
SVM	99.6	99.9
ANN	99.5	99.9
KNN	99.5	99.9
Naive	99.1	99.4

Figure 5 shows the confusion matrices obtained by the SVM classifier and 10-fold cross validation.

Figure 6. Confusion matrices

In the study, F1-Score, Re-call and precision results were examined to measure the classification performance. Accuracy: It expresses the ratio of correctly classified classes to all classes. Precision: Used to measure correctly predicted positive patterns from the total predicted patterns in a positive class. Recall: The ratio of true positives to the sum of true positives and false negatives. Table 3 gives the experimental results.

Table 3. Classification results.

	Accuracy	F1-Score	Re-call	Precision
All Features	99.57	98.82	100.00	97.67
		99.49	98.98	100.00
		99.90	100.00	99.79
		99.75	99.50	100.00
mRMR Feature Selection	99.94	99.90	100.00	99.80
		99.95	99.90	100.00
		99.95	100.00	99.90
		99.94	99.88	100.00

Using the same dataset, the studies in the literature are tabulated in Table 4. Tusar et al.[26] used the MobileNetV2 network. It achieved 97.42% accuracy. Basymeleh et al.[27] used the VGG16 pre-trained model. The guy used the optimizer. obtained accuracy, sensitivity, specificity, and confirmation accuracy of 97.50%, 99.96%, 100%, and 98.44%, respectively.

Table 4. Comparison of current studies with the same data set[17].

Reference	Year	Method	Results
Tusar et al.[26]	2022	MobileNetV2	97.42
Basymeleh et al.[27]	2022	VGG16	97.50
Proposed Method	2023	Darknet19,mRMR,SVM	99.94

IV. CONCLUSIONS

In this study, diagnosis and classification of acute lymphoblastic leukemia disease was carried out. Kaggle ALL data set was used as the data set in the study. There are four classes in the dataset. Pre-trained DarkNet19 CNN network is used in the proposed model. The dataset is trained on the DarkNet19 CNN network. Then, 1000 features were extracted from the trained network. 521 of the extracted features were selected with the mRMR feature selection algorithm. With the SVM classifier, 99.94% accuracy was obtained with 10-fold cross validation. One of the most important conveniences of this proposed method is that the data can be used raw, that is, directly. In future studies, working with different CNN models and parameters can be discussed in more detail.

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