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APPLICATION OF QUADRATIC DISCRIMINANT ANALYSIS ALGORITHM FOR THE CLASSIFICATION OF ACUTE LEUKEMIA USING MICROSCOPIC IMAGE DATA

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Abstract

Acute Leukemia has drawn the attention of researchers worldwide as it is a very fatal disease and gives limited time to the patient for recovery. Moreover, it is difficult to diagnose this disease due to the lack of any specific symptoms. Hence the timely diagnosis of the disease is very important. Thus, researchers across the globe have emphasized on the development of automated models for its efficient and accurate diagnosis. This research paper provides a novel approach of acute lymphoblastic leukemia diagnosis from microscopic blood smear images by classifying it into malignant and normal using quadratic discriminant analysis (QDA). The proposed approach utilizes efficient feature extraction with the help of morphological processing. The extracted features have been classified with the help of Quadratic discriminant Analysis (QDA). Outputs of the proposed approach has been compared with other extensively used classifiers e.g., Support Vector Machine (SVM), k-Nearest Neighbour (K-NN), Decision Tree (DT) for leukemia diagnosis. It is found that QDA performed best with an accuracy of 94.4% compared to SVM (92.6%), K-NN(92.6%) and DT(91.7%).

1. Introduction

Leukemia has been used as the synonym of 'cancer of white blood cells

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(WBCs)' though it may affect red blood cells (RBCs) and platelets as well. In leukemia, uncontrolled proliferation of partially developed white blood cells, also known as blast cells, takes place. These blasts cells interfere with the functioning and development of healthy RBCs, WBCs and platelets. Leukemia can be categorized into Acute Lymphoblastic Leukemia (ALL), Chronic Lymphoblastic Leukemia (CLL) Acute Myeloid Leukemia (AML), Chronic Myeloid Leukemia (CML). Acute Lymphoblastic Leukemia (ALL) is often characterized as childhood leukemia whereas acute myeloid leukaemia (AML) is commonly found in men above 55 years of age. As per (Siegel et al., 2021), the cancer cases have been estimated to increase from 979,786 in year 2010 to 1,898,160 in America for the year 2021. The article also projects 61,090 new cases of Leukemia in America in the year 2021 and the expected deaths from leukemia are projected to be 23,660. The above statistics present the creepiness of leukemia. The disease is diagnosed when number of the blast cells is found to be more than 20%. In case of Leukemia, the white blood cell count may grow to a range of 1 - 4 lacs/μL as compared to 4000 - 11,000 / μL. Counting these many cells and looking at their shape and size is so laborious and tiring job and is thus very error-prone. The process heavily relies at the expertise of the haematologists and results may vary from one lab to other. Other tests used for diagnosis like qPCR, FISH, Flow-cytometry and cytogenetics etc. are overpriced.

To efficiently perform this task, researchers from computers and medicine fields are working together to develop automated screening system. With the advent of machine learning, though it has become possible but still the diagnosis and correct prediction has been far from reality.

The contribution of this paper is to show that the QDA can be used for the application in the current context successfully and to prove that it gives excellent results when compared to other machine learning algorithms namely K-NN, SVM, Decision Tree.

The next section throws some light on the literature survey in this field. Section 3 discusses the image processing involved in the process and Section 4 describes the classification techniques employed for the purpose. Section 5 gives an insight into the results and analysis. Finally, the last section concludes the paper.

2. Related Work

Image processing is a multi-step process involving image acquisition, enhancement, segmentation and morphological processing (Cruz and Wishart, [11], Shafique and Tehsin, [27]). Relevant features including color, shape, texture etc are extracted which are used further in classification using machine learning (Jagadev, [16], Mishra et al., [17]. Various steps involved in leukemia diagnosis from microscopic blood smear images involve image pre-processing, image enhancement, segmentation, feature extraction and classification. Various researchers have used them to develop the computer aided diagnostic models to facilitate efficient decision making for the diagnosis and identifying the sub-type of the fatal disease (Ananthi and Balasubramaniam, [3]). Image enhancements methods are used to perform contrast enhancement and colour space correction. Contrast enhancement is important as it directly effects the segmentation and thus the final prediction (Salihah et al., [25]). This is required to improve the image quality, so as to remove or suppress the undesirable noise from image and help visualize the finer details which were, otherwise not visible due to low contrast. In most cases, RGB to HSV (Abedy et al., [1]) and CIELAB (l*a*b) models have also been used for pre-processing. Next step after image enhancement is image segmentation. Segmentation is the process by which the region of interest in the image is found and separated from the background (Bhagya et al., [5]). Researchers like, (Bhuiyan et al., [7]) have used clustering-based segmentation methods in their work, whereas, watershed transformation is used by (Bhattacharjee and Saini, [6]). (elHouby, [14]) applied the common framework consisting of pre-processing, segmentation, feature extraction and classification on blood smear images to classify them as diseased or healthy for acute lymphoblastic leukemia. The classification was done using k-NN, DT, NB and SVM which yielded promising results using Decision Tree. (Setiawan, Harjoko, Ratnaningsih, Suryani, Wiharto, et al., [26]) in their work performed segmentation using K-Means with watershed distance transformation (WDT) together with other morphological operations to segment and multi-class SVM with one-versus-rest comparison for classifying cell types based on subtypes of AML e.g., M4,M5 and M7 and claimed 87.72% segmentation accuracy and very good results for classifying each cell type as myeloblast, promyelocyte, granulocyte, monoblast, promonocyte, monocyte, megakaryoblast and support cell.

In our previous works, we have demonstrated the comparison of segmentation techniques for leukemia classification (Chand and Vishwakarma, [9]) Click or tap here to enter text and also performed a comparative study of the effects of segmentation on the classification of Acute Lymphoblastic Leukemia (ALL) using SVM and the novel extreme learning machine (ELM) in (Chand and Vishwakarma, [10]) with promising results displayed by ELM.

This paper demonstrates the use of Quadratic discriminant analysis (QDA) algorithm as an efficient classifier that classifies the blood cell images into healthy and malignant one. QDA is an extension of linear discriminant analysis (LDA) that is capable of discriminating classes through quadratic boundary. Both LDA and QDA are similar in the sense that both require multi-variate normally distributed (Gaussian) data but these two differ in the assumption of co-variance matrix for various classes. The LDA, which is based on Mahalanobis distance, assumes that co-variance matrix for each output class is same whereas in case of QDA, co-variance matrix is to be calculated for each class separately. Though QDA has not been used for the detection of leukemia earlier but this algorithm has furnished excellent results for classification problems e.g., assessment of risk for cadmium in rice (Wang et al., 2018) and classifying the fuel samples based on the quality check status of data. QDA has proved to provide robust results (Tharwat, [29]).

3. Experiment

3.1. Image acquisition: To accomplish this work, image data was requested from Dr. Fabio Scotti et al. (RuggeroDonidaLabati, Vincenzo Piuri, 2011) who have organized and made the data set available for this disease. The data set is divided into two subsets. ALL-IDB1 contains 108 images of peripheral blood samples from 59 healthy persons and 49 are from ALL patients. The second subset of this data set consists of 260 lymphocytes segmented from the images in first subset. The data set images are well labelled by expert oncologists.

3.2. Image pre-processing: As the images in ALL-IDB1 are not uniformly illuminated, there is a need to pre-process them. Histogram based

method is used for image enhancements. Images were converted from RGB to gray-scale and then contrast stretching was performed to enhance the overall image. Histogram equalization was performed to enhance the contrast of nucleus before applying the segmentation.

3.3. Image segmentation: Image addition and subtractions are performed to obtain segmented image. The algorithm is as below:

Step 1. After applying contrast stretching, we get result (A).

Step 2. Histogram equalization applied to the image gives a temporary result (B).

Step 3. The temporary resultant images obtained in step 1 and 2 i.e., image A and image B are added to obtain the added image $(A + B)$ to improve the brightness of image except nucleus.

Step 4. Similarly, image subtraction was performed on A and B to obtained subtracted image $(A - B)$ that highlights the objects and marks their edges in the image.

Step 5. Finally, the added image $(A + B)$ and subtracted image $(A - B)$ are added that gives us the segmented image of blood smear with all other components removed from the image.

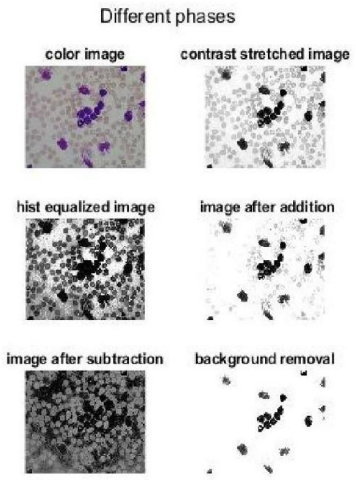

Figure 1. Different phases of image enhancement.

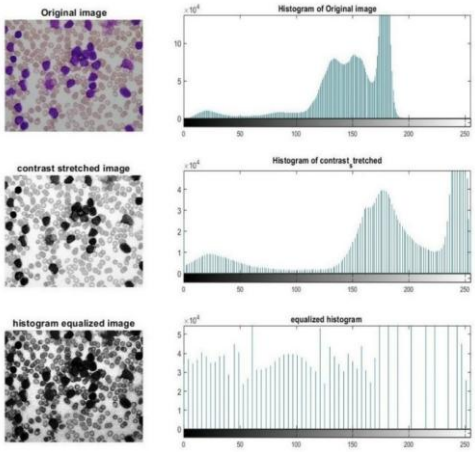

Figure 2. Images and their histograms.

Once the images were successfully segmented using the above mentioned, a total of twelve morphological or geometric features i.e., area, perimeter, major-Axis, minor-Axis, orientation, convex-Area, filled-Area, eccentricities, eq-Diameter, solidity, roundness and extent were extracted from the connected components found in the segmented images. Finally, the mean values of these features for all the components of each cell were calculated in order to find the mean of feature values for the whole image as we have not separated nucleus from cytoplasm. This is a novel approach that we have employed to increase the efficacy of extracted features and used these mean features to classify the cell to be either belonging to the healthy person or the diseased one.

3.4. Image Classification: The features thus extracted are given as input to different machine learning classifiers to classify the blood cell images into malignant and benign. To the best of our knowledge, Quadratic Discriminant Analysis has not yet been used for leukemia diagnosis. To compare the results obtained from QDA, three other extensively-used tools of machine learning viz. K-NN, Decision tree and SVM were also used to perform the categorization of peripheral blood image into leukemic or healthy cell. A leukemic cell is characterized by the presence of more than 20 percent blast cells which are the uncontrolled and abnormally "undifferentiated'' leukocytes present in blood cells. The 108 images are divided into training and test set in the ratio 70:30.

The training data is used to train the machine learning models with 10-fold cross validation and the testing data is used to test the models on unseen images.

3.4.1. Quadratic Discriminant Analysis: Discriminant analysis techniques are better recognized to provide classification and dimensionality reduction. As the name suggest, QDA is a variation of linear discriminant analysis (LDA), which is often used as a dimensionality reduction technique as well as a classifier whereas QDA can only serve as a classifier.

QDA works by estimating the co-variance matrix for each class thus providing a greater number of effective parameters as compared to LDA.

Both, the Linear discriminant analysis (LDA) and Quadratic discriminant analysis (QDA) are based on simple probabilistic models which derives the conditional distribution of the sample space represented by $P(X = x/Y = k)$ for each class k.

Let the random variable X be a vector represented as

$X = (X_1, X_2, \ldots, X_p)$, drawn from a multi-variate Gaussian distribution, divided into k classes. Given μ_k is the mean vector and Σ_k is the co-variance matrix specific to class k. Given an input sample $x \in X$, prediction of the category can be obtained by using Bayes' rule, using posterior probability as follows:

$$P(X = x/X = x) = \frac{P(X = x/Y = k) \cdot P(Y = k)}{P(X = x)} \tag{1}$$

Let $P(Y = k) = \pi_k$ (2)

For Discriminant Analysis (DA), the posterior probability $P(X = x/Y = k)$ is modelled as a multivariate normal distribution given by the density function $f_k(x)$ as

$$f_k(x) = \frac{1}{(2\pi)^{d/2} |\Sigma|_k^{1/2}} \cdot \exp\left(-\frac{1}{2}(x - \mu_k)^T \cdot \sum_k^{-1} (x - \mu_k)\right), \tag{3}$$

where d represents the dimensions of sample vector or the number of features.

Now Let us represent $P(Y = k)/(X = x)$ by $p_k(x)$ Using equations equation (1), (2) and (3), we get:

$$p_k(x) = \frac{f_k(x) \cdot \pi_k}{P(X = x)}$$

$$= C \cdot f_k(x) \cdot \pi_k, \text{ where } C = \frac{1}{P(X = x)}$$

$$= C \cdot \pi_k \cdot \frac{1}{(2\pi)^{d/2} |\Sigma_k|} \cdot \exp\left(-\frac{1}{2}(x - \mu_k)^T \cdot \Sigma_k^{-1}(x - \mu_k\right) \quad (4)$$

Where, $C_1 = C \cdot \frac{1}{(2\pi)d/2}$

Taking the log on both sides of equation 4, we get:

$$\log p_k(x) = \log\left(C_1 \cdot \pi_k \cdot \exp\left(-\frac{1}{2}(x - \mu_k)^T \cdot \Sigma_k^{-1}(x - \mu_k)\right)\right)$$

$$= \log C_1 + \log \pi_k - \frac{1}{2}\log|\Sigma_k| - \frac{1}{2}(x - \mu_k)^T \cdot \Sigma_k^{-1}(x - \mu_k)$$

Ignoring the term $\log C_1$, as it does not depend on k, we get:

$$= \log p_k(x) = \log \pi_k - \frac{1}{2}\log|\Sigma_k| - \frac{1}{2}(x - \mu_k)^T \cdot \Sigma_k^{-1}(x - \mu_k)$$

$$= \log \pi_k - \frac{1}{2}\log|\Sigma_k| - \frac{1}{2}[x^T\Sigma_k^{-1}x + \mu_k^T\Sigma_k^{-1}\mu_k] + x^T\Sigma^{-1}\mu_k$$

Thus the classifier predicts the class for the observation $X = x$ for which the value of quadratic score function, represented by $\delta_k(k)$ is maximum:

$$\delta_k(x) = \log \pi_k - \frac{1}{2}\log|\Sigma_k| - \frac{1}{2}(x - \mu_k)^T \cdot \Sigma_k^{-1}(x - \mu_k)$$

3.4.2. K-Nearest Neighbours (K-NN): It has quite often been used in literature to classify leukemia images (Mishra et al., [18], Rajpurohit et al., [20]). K-NN was implemented on MATLAB 2018b. The image data was divided into 70% and 30% for training and testing purpose. On testing K-NN with different values of neighbours that is the variable K, it was found $K = 4$ gave the best results in this case.

3.4.3. Support Vector Machine (SVM) with quadratic kernel: SVM was used to test the segmented images for classification with different kernels e.g. linear, quadratic and cubic. Quadratic SVM gave the best results. SVM is amongst the most extensively used ML algorithm for this purpose that divides the data using a hyper-plane (Rawat et al., [21], Rehman et al., [22]). The support vectors are selected in such a manner so as to maximise the distance from the hyperplane and are shown in Figure 3.

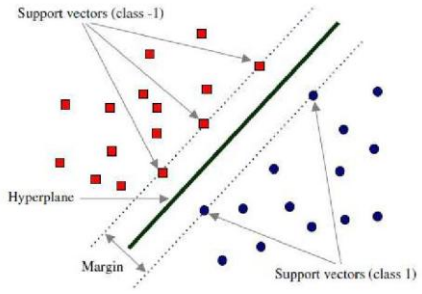

Figure 3. Classification hyper-plane in Support Vector Machine.

Image courtesy: (Baghaee and Mlaki, 2019).

3.4.4. Decision Tree: A Decision tree is a graphical representation that depicts branching into various classes based on a series of tests. Each node in the tree represents the test performed on an attribute, the branches from that node represents the various outcomes of the test while each leaf represents the class labels, i.e., the decision reached after testing all important attributes. The importance of an attribute is found on the basis of splitting criteria. We employed decision tree with at most 10 splits with split criteria as gini-index.

4. Results and Performance Analysis

The experiment was conducted with ALL-IDB1 dataset comprising of 108 images of peripheral blood smear. The images were segmented using histogram-based approach and the conventional shape features extracted from the images were used in a novel manner so as to characterize each cell image by mean values of various features. These features were then given as input to different classifiers i.e., DT, SVM, k-NN and QDA. The accuracy achieved from these classifiers as determined in the experiment are 91.70%,

92.70%, 92.6% and 94.40% respectively. The performance of the classifiers are evaluated on the basis of confusion matrix i.e. true positive (TP), true negative (TN), false positive(FP) and false negative (FN) as shown in figure 4. The confusion matrix for each classifier is shown in Figure 5.

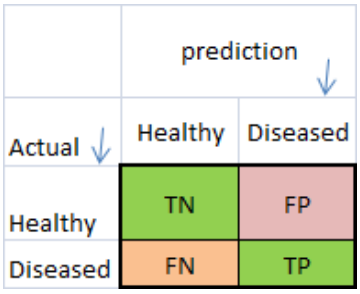

Figure 4. General Confusion Matrix.

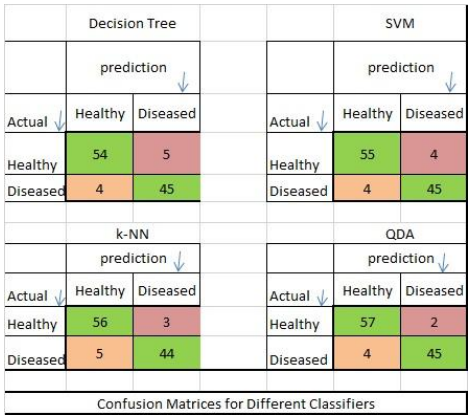

Figure 5. Confusion Matrix specific for the results by each classifier.

The performance indicators used are defined in table 1.

Sensitivity: $\frac{TP}{(TP + FN)}$	Specificity: $\frac{TN}{(TN + FP)}$	Precision : $\frac{TP}{(TP + FP)}$
Recall = sensitivity	F-Score $= 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} \times \text{Recall}}$	Accuracy $= \frac{TP + TN}{(TP + FP + TN + FN)}$

On the basis of these calculations, sensitivity, specificity. Accuracy, Precision and F-Score values are calculated for various classifiers and are summarized in table 2 below.

The results in table-2 demonstrate that QDA outperforms SVM and other machine learning models by showing an accuracy of 94.4, precision of 95%, recall of 91% and overall F-Score as 93.75%.The comparison result from the four algorithms have been summarised in the Figure 6. It is evident from the figure that QDAexhibits very promising results when compared to other machine learning algorithms.

Conclusion

This paper carried out novel experiment on 108 microscopic blood smear images from ALL-IDB1 data-set to classify them into diseased and healthy cells using quadratic discriminant analysis, which is based on Bayesian discrimination and works on multivariate normal distribution. The images went through various phases of image processing like enhancement through histogram-based processing and segmentation through thresholding. The important geometric features were extracted from cell-images using a novel approach of finding the mean values of all connected components in segmented lymphoblasts in an image as against the prevailing approach of segmenting the cytoplasm and nucleus separately and then utilising the geometric features of the nucleus and cytoplasm for further classification. The extracted features were then fed to the not yet used QDA for the detection of acute lymphoblastic leukemia from blood microscopic images. The results from QDA are then compared with other extensively used classifiers viz Decision Tree, K-NearestNeighbour(KNN), and Support Vector Machine (SVM). The accuracy obtained from DT, kNN, SVM and QDA are 91.70%, 92.6%, 92.7% and 94.40%, thus proving that QDA performs better than other mentioned classifiers.

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