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Machine Learning Techniques for Automatic Detection of Sickle Cell Anemia using Adaptive Thresholding and Contour-based Segmentation Method

Chayashree Patgiri*, Amrita Ganguly

Abstract

Automatic diagnosis of diseases in the medical field using image processing techniques has evolved tremendously in recent times. Sickle cell anemia (SCA) is a kind of disease connected with red blood cells (RBCs) present in the human body in which deformation of cells take place. The purpose of this work is to propose an automatic image processing technique for the detection of this disease from microscopic blood images. This paper mainly focuses on automatic detection of SCA using a novel segmentation method encompassing local adaptive thresholding and active contour-based algorithm. For the detection of sickle cells, supervised classifiers such as Artificial Neural Network (ANN) and Support Vector Machine (SVM) are used. Here, geometric features of healthy and unhealthy RBCs are calculated and applied to these classifiers. In this approach, performance is found slightly greater in SVM classifier than the ANN classifier trained with scaled conjugate gradient back-propagation (BP) algorithm and with hidden layer of ten neurons. The proposed approach achieves a maximum of 99.2% accuracy with SVM classifier. The performance is also studied for seven different training algorithms in the ANN classifier by varying the numbers of hidden layer neurons. Comparative analysis of the performances of these algorithms shows that, resilient BP algorithm and 10 numbers of hidden neurons gave moderately better performance in ANN with 99% accuracy. ANN and SVM classifier with adaptive thresholding and active contour technique is an efficient approach for the classification of patients with SCA.

Keywords: Active contour, Adaptive thresholding, Artificial neural network, Image processing, Support vector machine

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Introduction

Sickle cell anemia (SCA) is a common inherited disease where red blood cell (RBC) becomes unhealthy resulting less oxygen supply to the body, since healthy RBCs are made for providing oxygen to every cell of the entire human body. SCA causes serious problems such as clogging of blood vessels, swelling in hands and feet, nerve pain, life-threatening infections, and arthritis. RBCs in the body become abnormal as their shape changes from round and flexible to rigid and crescent or sickle. In SCA, RBCs change their shape because of a constituent protein of RBCs called hemoglobin (Hb). There is alteration in the constituent chains of the Hb that cause sickle cell disease. In SCA or homozygous type of sickle cell disease, which is most commonly seen sickle cell disease, both subunits of β-globin in Hb are replaced with Hb S. If in Hb only one such subunit is replaced by Hb S then that causes other variants of sickle cell disease. The other subunit of β-globin is substituted by another abnormal variant, like Hb C. In sickle-Hb C disease, both the subunits of β-globin are replaced by Hb S as well as Hb C. If mutation occurs between beta thalassemia and Hb S, then individuals suffer Hb S-beta thalassemia disorder. An individual is called suffering in sickle cell trait if he/she has one defective gene Hb S and one normal gene. This type of person may live normal life without much complication, but they can inherit the defective gene of Hb S to their next generation. In view of these complications related to SCA, a proper automatic, precise, and faster diagnosis of the disease is very much crucial and important. For automatic diagnosis, techniques using digital image processing are very much beneficial and have gained popularity among other method now-a-days. Here, in this work some of the supervised learning methods along with active contour based and thresholding segmentation techniques are studied and applied for proper automatic classification of the disease.

Department of Electrical Engineering, Assam Engineering College, Guwahati, Assam, India

Corresponding Author: Chayashree Patgiri, Department of Electrical Engineering, Assam Engineering College, Jalukbari, Guwahati - 781 013, Assam, India. E-mail: chayashreepatgiri21@gmail.com

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This work focuses on applying a new segmentation technique comprising adaptive thresholding and active contour-based method for microscopic blood images of SCA patients. Here, NICK's local adaptive thresholding is employed. After extracting various shape features from the segmented images, classification is performed by using ANN and SVM techniques. ANN is also trained with different back-propagation (BP) algorithms for evaluating better performance of the system. A comparative study is carried out for different machine learning supervised classifiers with Otsu's global thresholding and NICK's adaptive thresholding method.

Related work

In this section, we will consider some recent quality works which are related to SCA detection. In the first section, some of the local and adaptive thresholding approaches researchers are working with will be discussed. After that different supervised learning methods which have been applied over the years in this field are discussed.

Yeruva *et al*. presented a comprehensive study and characteristics of SCA with proper details of signs, symptoms, complications and treatment of the disease. This paper also highlights about the technological usage including feature extraction, detection using neural networks (NNs), and SVM for the identification of the disease.[1]

Researchers have investigated several segmentation methods for medical image analysis over the years. Among these methods, four categories of segmentation methods are mostly used. These methods are segmentation based on thresholding, edge, region, and clustering.[2-4] Thresholding based segmentation techniques are of two varieties. Those are global thresholding and adaptive or local thresholding.[5,6] Among the segmentation methods based on global thresholding, Otsu's thresholding is one of the popular method among the researchers for normal and abnormal RBC detection.[7-9] Aliyu *et al.* have applied different segmentation techniques such as Otsu thresholding, Sobel, Laplacian of Gaussian and watershed on 30 SCA microscopic blood images and they obtained highest accuracy in Otsu's thresholding for SCA classification.[10] A system is presented that detects the types of RBC disorders using microscopic blood sample images.[11] The authors applied Otsu's thresholding for Thalassemia disease and diffused expectation maximization method for sickle cell detection. Although global thresholding is easy and simple to implement and best for uniform images, it has some drawback in certain image conditions. For images with varying levels of regional contrast differences or image having histogram that does not contain distinctive peaks, local, or adaptive thresholding became widely useful for segmentation process now-a-days. Roy *et al.* carried out a comparative study on adaptive thresholding techniques for selecting correct method for segmenting an image based on some properties of an image.[12] A work is illustrated about qualitative and quantitative analysis of adaptive thresholding methods such as Wolf's, Niblack's, NICK's, Sauvola's, and Darek Bradley's thresholding with real world images.[13] A number of work has been reported where edge based segmentation techniques are used for medical disease diagnosis. These methods segregate the image into several distinct regions by reason of the boundaries. For abnormal RBC detection, edge based segmentation methods such as Sobel detector,[10,14,15] Roberts detector, Prewitt detector,[16] Canny detector,[17] and Laplacian edge detector[10] are used extensively. Savkare *et al.* discussed a clustering based segmentation technique for automatic blood cells segmentation. They have tested K-mean clustering method on 60 microscopic images and watershed transform for separating the cluster of cells present in the images.[18] Researchers have also used K-means clustering in segmentation step for finding abnormal cells in leukemia, Thalassemia, and sickle cell anemia patients.[19-21] Region based segmentation methods are also popular among the researchers. Different region based detection methods such as region growing, contour based technique, and region based level set technique are implemented on medical images.[22-24] Other popular methods proved very useful are, namely, watershed transform,[10] improved watershed algorithm,[8,25] marker controlled watershed technique,[26] and circular Hough transform (CHT).[27-32]

In recent years, application of NN in classification and detection of medical images has increased significantly because of its high accuracy and less computation time.[29,30] Khalaf *et al.* presented a work on the utilization of different types of models of neural networks for detecting biomedical dataset for sickle cell disease. They considered four different types of NN approaches: Feed-forward NN, functional link NN, radial basis NN and voted perception classifier, and applied for classification to determine medication dosage for SCD patient.[31] Elsalamony proposed an algorithm for detecting anemia causing abnormal RBCs from microscopic images with the help of CHT and morphological operations. After that, using NN the resulting data of detection process is analyzed. Author achieved effectiveness rates of 98%, 100%, 100%, and 99.3% in 21 microscopic images using artificial NNs for detecting elliptocytosis RBCs, sickle cells, microsite RBCs, and unknown shaped RBCs, respectively.[32] The support vector machine classifier was trained for automatic detection of SCA.[33] This system delivered accuracy and sensitivity of 95% and 96.55%, respectively. Another work presented the use of different machine learning techniques like ANN trained with Levenberg-Marquardt algorithm, random forest classifier, Elman and Jordan recurrent NN (RNN) classifier, hybrid RNN, combining the Elman and Jordan networks, and SVM classifier for the classification of SCD.[34] Elsalamony discusses about three machine learning algorithms back propagation NN, SVM, and self-organizing map using ten geometrical information of cells for detection of anemia disease. For detecting normal blood cells, CHT has used, whereas shape signatures are used for deformed cells of anemia such as sickle, burr, and elliptocytosis cells.[35]

Proposed Methodology

The methodology in the form of a block diagram is given in Figure 1. Five major blocks of the methodology are as follows: (a) Input data, (b) pre-processing of the input images, (c) active contour-based segmentation with adaptive thresholding and morphological operations for image segmentation, (d) feature extraction, and (e) ANN and SVM classifiers for classification. The descriptions of these blocks are as follows.

Image Data Sample

For input data, we have considered microscopic blood images of sickle cell anemic patients. A total of 10 such sample is collected from online library.[36] These microscopic images have both round and sickle shaped RBCs. After collecting these data, pre-processing is done in the next step.

Pre-processing

At this step, first the image is changed from RBG to gray scale and then enhancement is done on gray level images for boosting its quality. The principal objective of the preprocessing is to make the data sample of the image more appropriate for further processing.

Segmentation

Image thresholding is the simplest type of image segmentation process, because it partitions the image into two zones of pixels, that is, foreground and background. To recognize the region of interest is main task of medical image segmentation. Here, the segmentation methods divide the normal and abnormal RBCs from the background. In this paper, local adaptive method of

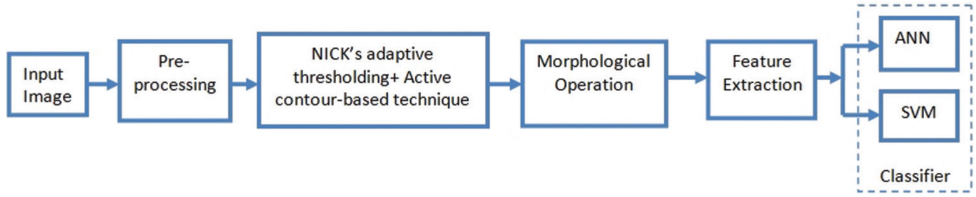

Figure 1: System block diagram

thresholding along with active contour-based segmentation is used on the pre-processed microscopic images. A brief description of segmentation methods are given below.

Active contour-based segmentation

Active contour model is used for image segmentation and boundary tracing when first employed by Kass *et al.* in 1988.[37] It is a region based iterative boundary detection method starting with an initial contour for target boundary and then changing the contour so that it reaches the final desired boundary of the object with some defined criteria. Active contour model uses the energy constraints and forces for partitioning the region of interest in the image. It creates a contour or parametric curve for borders of object. Different contour techniques using internal and external forces are employed for determining the curvature of the model. The energy function is linked with curve of the image. The sum of forces applied to the image to control the contour position on the image described the external energy. Internal energy is used to control the deformable changes. The desired contour will be defined by least energy function. This model is proved very effective for segmentation of variety of medical images.[38]

Adaptive thresholding

In local adaptive thresholding, more than one threshold value is considered for sub images of the whole image. Some characteristics of local image areas are used to choose a different threshold for distinct image parts. Various adaptive thresholding methods are used for segmentation of biomedical images which includes Niblack's, Sauvola's, Bernsen's, and NICK's thresholding. Niblack thresholding algorithm computes the threshold in accordance with the local mean and standard deviation over a particular size of window throughout each pixel position in the image.[39] The equation of NICK's thresholding is derived from Niblack's thresholding.[40] Among these mentioned thresholding methods, NICK's thresholding method is utilized with active contour-based segmentation on the pre-processed images followed by some morphological operations to obtain the final segmented images. The key objective of applying morphological operation is to remove the unwanted distortions or incomplete objects from the thresholded image.

Feature Extraction

Mostly morphological features are used to classify healthy and unhealthy RBCs for recognition of sickle cell disease. From each detected cell of the image, seven geometrical features are extracted, that is, area, perimeter, circularity, major axis, minor axis, eccentricity, and solidity. Then aspect ratio is calculated as given by the Eq. (1).

$$\textit{Aspect ratio} = \frac{\textit{Major axis length}}{\textit{Minor axis length}} \tag{1}$$

The value of aspect ratio is nearly equal to 1 whereas because of crescent shape of sickle cell, the value is much >1. Circularity or metric value or effect factor is calculated from area and perimeter using formula:

$$\textit{Circularity or Metric Value} = \frac{4\pi \text{area}}{\textit{perimeter}^2} \tag{2}$$

The value of this factor is 1 and approximately <0.7 for normal and sickle RBCs, respectively. Eccentricity is the measure of how much the object is deviated from being circular. For normal RBCs, its value is 0 as they are round in shape. Solidity for an object with regular boundary and with irregular boundary is 1 and <1, respectively.

$$\textit{Solidity} = \frac{\textit{Area}}{\textit{Area of convex hull}} \tag{3}$$

Classification using ANN and SVM

The features extracted from all healthy and unhealthy cells for each of the image in dataset are utilized for formation of the feature vector for different classifiers. One such feature vector is shown in Table 1 for a normal and sickle cell. The table shows the differences in feature values for normal RBC and sickle RBC. The feature vector for all normal and sickle cells for ten images of the dataset are derived from segmentation method and applied to train ANN and SVM classifier one by one. After that performance measures are studied for the two classifiers. Furthermore, different training algorithms are used to train the ANN and results were studied. The BP algorithms considered are: Scaled conjugate gradient BP, Gradient descent with adaptive learning rate BP, Levenberg-Marquardt BP, Gradient descent with momentum BP, Bayesian regularization BP, Gradient descent with momentum and adaptive learning rate BP, and resilient BP.

Results and Discussion

In this work, machine learning methods ANN with BP algorithm and SVM are employed for efficient detection of normal and sickle cells. For the purpose of training and testing the ANN, eight input layer features, 10 numbers of intermediate layer neurons, and two output layer neurons is used along with scaled conjugate gradient BP algorithm. The total data sample is divided into three divisions: 70% used for training, 15% for validation, and rest 15% for the testing purpose. In case of SVM classifier, 70% samples are used training and 30% samples are considered for testing.

For performance analysis of the ANN and SVM classifiers, the evaluated parameters are explained below:

Table 1: Example of feature vector for a normal and sickle cell

RBC type	*Features*							
	Major Axis	*Minor Axis*	*Aspect ratio*	*Solidity*	*Area*	*Perimeter*	*Circularity*	*Eccentricity*
Normal	88.99	85.77	1.04	0.99	5993	272.77	1.01	0.27
Sickle	102.61	45.46	2.26	0.97	3575	239.45	0.78	0.90

RBC: Red blood cell

$$Accuracy = \frac{TP + TN}{TP + FN + FP + TN} \quad (4)$$

$$Sensitivity = \frac{TP}{TP + FN} \quad (5)$$

$$Specificity = \frac{TN}{TN + FP} \quad (6)$$

$$Precision = \frac{TP}{TP + FP} \quad (7)$$

where, TP =True Positive = Quantity of positive class (sickle cell) correctly identified as positive in numbers.

TN =True Negative = Quantity of negative class (normal RBC) properly detected as negative in numbers.

FP =False Positive = Quantity of negative class (normal RBC) inaccurately detected as positive (sickle cell) in numbers.

FN =False Negative= Quantity of positive class (sickle cell) incorrectly detected as negative (normal RBC) in numbers.

Here, sensitivity or recall or true positive rate is a ratio of correctly detected sickle cell and the total unhealthy cells. Higher value of sensitivity of a classifier signifies better ability of the classifier to classify unhealthy cells over other methods. Specificity or true negative rate is a fraction of accurately classified healthy cells and the total healthy cells. Higher value of specificity signifies better ability of the classifier to classify healthy cells over other methods. Accuracy is the proportion of accurately detected cells and the total number of cells detected. It measures correct classification rate of the classifier. Precision is a proportion of total numbers of correctly identified sickle cells and the total numbers of predicted sickle cells. It specifies correctness achieved in detection of sickle cells.

Table 2 shows the performance of ANN and SVM classifiers using NICK's thresholding and active contour segmentation. It clearly shows better performance of SVM classifier over the ANN type for sickle cell detection. The proposed method gives accuracy of 99.2% and 98.8% for SVM and ANN classifier with Scaled conjugate gradient BP algorithm, respectively. The performance of the system is also experimented by replacing NICK's thresholding with global Otsu's thresholding and results are shown in Table 3. It can be concluded that NICK's adaptive thresholding performs better than global Otsu's thresholding.

Next, the performance of the ANN classifier is evaluated with different training algorithms with varying numbers of hidden layer neurons. The overall accuracy of seven different training algorithms to train the ANN classifier is shown in Table 4. Resilient BP algorithm gives highest accuracy of 99% with ten numbers of neurons in the hidden layer among all BP methods.

The classification approach used in this work is compared with other existing methods for SCA detection and shown in Table 5. In this table, results of SVM classifier with NICK's thresholding and active contour-based segmentation method have been presented and are compared with other existing SCA detection techniques which are based on global thresholding segmenting method. The comparison clearly shows an improvement in performance of ANN and SVM classifiers using local adaptive thresholding method.

Table 2: Results of ANN and SVM classifier using NICK's and active contour-based segmentation

Classifier	*Accuracy*	*Sensitivity*	*Specificity*	*Precision*
ANN	98.8	99.4	98.6	97.3
SVM	99.2	98.7	98.7	98.3

ANN: Artificial neural network, SVM: Support vector machine

Table 3: Results of ANN and SVM classifier using Otsu's and active contour-based segmentation

Classifier	*Accuracy*	*Sensitivity*	*Specificity*	*Precision*
ANN	96.8	98.7	96.1	87.9
SVM	97.4	97.9	98.9	98.8

ANN: Artificial neural network, SVM: Support vector machine

Table 4: Overall accuracy of ANN classifier with different training algorithms and varying hidden layer neurons

S. No.	*ANN training Algorithm*	*Number of hidden layers*			
		5	*10*	*50*	*100*
1.	SCGBP	98	98.8	97.3	96.8
2.	GDMBP	97	97.3	95.7	93.7
3.	GDALBP	95.9	97	94.7	93.5
4.	GDMALBP	98	98.2	97.4	96.5
5.	LMBP	97.8	98.5	96.3	95.8
6.	BRBP	96.9	97.8	97.4	96
7.	RBP	98.7	99	98.3	97.5

ANN: Artificial neural network, SVM: Support vector machine, SCGBP: Scaled conjugate gradient back-propagation, GDMBP: Gradient descent with momentum back-propagation, GDALBP: Gradient descent with adaptive learning rate back-propagation, GDMALBP: Gradient descent with momentum and adaptive learning rate back-propagation, LMBP: Levenberg-Marquardt back-propagation, BRBP: Bayesian regularization back-propagation, RBP: Resilient back-propagation

Table 5: Performance comparison of proposed system with other techniques

Technique	*Accuracy*	*Sensitivity*	*Specificity*	*Precision*
This paper (SVM classifier)	99.2	98.2	98.5	98.3
Albayrak *et al.*[9]	91.1	79	-	92.9
Aliyu *et al.*[10]	93	94	80	-
Rakshit and Bhowmik[15]	95.8	-	-	-
Chy and Rahaman[33]	95	96.5	-	-

Conclusion

This work was carried out with a clear motive of making the process of detection of SCA automatic with appropriate segmentation methods. This study considered the application of machine learning techniques such as ANN and SVM for effective detection of sickle cells. For segmentation, NICK's adaptive thresholding with active contour-based methods are used. From the evaluated results it is seen that, both the classifiers give satisfactory classification rate with NICK's and active contour segmentation. In terms of accuracy and other considered performance parameters, ANN and SVM classifiers gave better output in case of NICK's adaptive thresholding methods than Otsu's global thresholding technique.

The results are further extended for comparing performances of ANN with seven unique training algorithms, which shows that resilient BP algorithm gave moderately better accuracy. Comparison of the reported approach with other similar SCA detection methods are also provided, which give favorable results. Thus it can be concluded that, for both the normal non-overlapping and the sickle RBCs, by applying ANN and SVM classifiers with adaptive thresholding and active contour technique is an efficient approach for classification of patients with SCA.

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