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Computer Aided Diagnostic System for Detection of Leukemia using Microscopic Images

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Abstract

In present scenario, hematological disorders of leukocyte (WBC) are very frequent in medical practices. This work proposes a novel technique to differentiate ALL (acute lymphoblastic leukemia) lymphoblast cells from healthy lymphocytes. The technique first separate leukocytes from the other blood cells and then lymphocytes are extracted. In this context, a novel computer aided diagnostic system (CAD) is designed for detection of hematological disorders like leukemia (blood cancer) based on Gray level co–occurrence matrices (GLCM) and shape based features. The features thus extracted classified by the auto support vector machine (SVM) binary classifier to find the presence of lymphoblast cell (leukemic cells). GLCM texture feature with feature vector length 13 reveals, classification accuracies of 86.7\% and 72.4\% for cytoplasm and nucleus respectively while for shape based features illustrated, classification accuracies of 56.1\% and 72.4\% respectively for a feature vector length 11 in both regions of lymphocyte. The classification accuracy of combined texture-shape feature is 89.8\% with feature vector length 37 which shows better results as compared to an individual.

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Keywords: Haematology; Acute lymphoblastic leukaemia (ALL); Gray level co–occurrence matrices (GLCM); SVM classifier; Shape based features.

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1. Introduction

The medical community has been established to take care of human health with knowledgeable and proficient experts like a clinician, chemist, hematopathologists, and many others which are specialized in health science. Because of the advancement in technology, technology provides an opportunity for having faster and more accurate tools (X-ray machines, CBC machines, MRI). These automated medical tools are essential for diagnosing patients and their future prognoses of the conditions. For the prediction of the blood disorders, needs to study the structure of blood and its malignancy.

1.1 Blood and Its Malignancy

Blood is a fluid connective tissue, which circulates through the lymphatic system of the body around the heart and blood vessels. Leukocyte cells are an important element of the immune system, responsible for protection against bacteria, fungi, viruses, invading parasites and infections. The process of blood cell formation in bone marrow is known as haemopoiesis. Initially, all blood cells originate from pluripotent stem cells and undergo several developmental stages before the formation of distinct cell of different type.

For the treatment of the blood related disorders, pathologist desires to study the structure of blood that is known as hematology. In hematology, experts deal with the discrepancy of blood with essentials of blood and the tissues for the blood formation. Hematology is used to identify and examine the cure for polycythemia, anemia, sepsis, purpura simplex, leukemia's and hemophilia. Visual inspection of microscopic blood smear images is an error prone labor-intensive repetitive and time consuming task. It is the broadly used technique in India for identification of the cell structure of leukocyte. Hematological tests are performed by hematopathologists for assurance of certain treatments such as cancer chemotherapy. Hematological diseases lead to discomfort, or absence of ease within the body. Basically disease can be discriminated on the basis of their cause and cell of origin.

Table 1: Estimated deaths (all age groups) from all types of leukemia, 2014(USA), American cancer society

| Type                     | Total | Male  | Female |
|-------------------------|-------|-------|--------|
| Acute lymphoblastic leukemia | 1440  | 810   | 630    |
| Chronic lymphocytic leukemia  | 4600  | 2800  | 1800   |
| Acute myeloid leukemia     | 10460 | 6010  | 4450   |
| Chronic myeloid leukemia   | 810   | 550   | 260    |
| Other leukemia             | 6780  | 3870  | 2910   |
| Total                    | 24090 | 14040 | 10050  |

By the advancement of quantitative microscopic techniques such problems can be overcome by facilitating the PBS (peripheral blood smear) analysis and by developing intelligent CAD systems for early prediction of malignant disease like leukemia. In India and even in many developed countries, leukemia is one of the most common hematological malignancies. Data as reported by the American Cancer Society is shown in table 1 for different kind of leukemia. It describe an estimated deaths rate in USA for all age groups from all types of leukemia(ALL, AML, CML and CLL).

Hematological malignancies like leukemia and lymphomas are a heterogeneous group of cancers of the blood, bone marrow and lymph node. However, all cancers are characterized by uncontrolled cell division. Myelogenous leukemia, myelodysplastic syndromes and myeloproliferative diseases are from the myeloid cell lineage, while myeloma, lymphocytic leukemia, and lymphomas have a lymphoid call origin. Leukemia is also known as liquid cancer which does not produce solid mass or tumors. It occurs due to abnormal growth of the white cell division in bone marrow and the balance of the blood system will be disrupted because of flooding of cells.

Suspicious and careful microscopic examination of stained blood smear is the only way to diagnose the leukemia effectively. Due to the complex nature of white blood cells, manual examination lead to variation in slide preparation that resulting in non standardized, inconsistent and subjective reports. So a cost effective and robust automated system is required to full fill the demand of correct diagnosis without being influenced by hematologists experience, tiredness and operator’s fatigue.
The proposed CAD system is capable to handle the conflict nature of white blood cells shown in figure 1. It consists of four different modules: (1) Preprocessing for removing outliers (2) Segmentation (3) Feature extraction of cytoplasm and nucleus region and (4) classification of selective features. The detailed description of literature and work carried for leukemia detection on microscopic images by different authors is shown in table 2.

The rest of the paper is organized as follows: Section 2 describes material and methods with the framework of the proposed method and Section 3 presents an experimental result and detailed analysis of the results obtained. Finally in Section 4 remarks are concluded.

| Author(s), Year | Goal | No. of images | Feature extraction method | Classifier |
|----------------|------|---------------|---------------------------|------------|
| S. Mohapatra et al., 2012 | Unsupervised Blood Microscopic Image Segmentation and Leukemia Detection using Colour-based Clustering | 108 | Fractal dimension, shape features including contour signature and texture, colour features | SVM |
| M. Madhukar et al., 2012 | New Decision Support Tool for Acute Lymphoblastic Leukemia Classification | 98 | Fractal dimension, shape features | SVM |
| S. Mohapatra et al., 2011 | Fuzzy based Blood Image Segmentation for Automated Leukemia Detection | 108 | Hausdorff Dimension and contour signature | SVM |
| S. Mohapatra et al., 2012 | Lymphocyte Image Segmentation Using Functional Link Neural Architecture for Acute Leukemia Detection | 96 | Colour based method | ANN |
| S. Mohapatra et al., 2011 | Automated Leukemia Detection in Blood Microscopic Images using Statistical Texture Analysis | 108 | Fractal, shape and texture features | SVM |
| N. Chatap et al., 2014 | Analysis of blood samples for counting Leukemia cells using Support vector machine and nearest neighbour | 121 | Shape features | SVM, KNN |
| L. Putzu et al., 2014 | Leukocyte classification for leukaemia detection using image processing techniques | 267 | Shape, colour, texture features | SVM |
| M. Joshi et al., 2013 | White Blood Cells Segmentation and Classification to Detect Acute Leukemia | 108 | Shape features | KNN |
| Nasir et al., 2013 | Classification of Acute Leukaemia Cells using Multilayer Perception and Simplified Fuzzy ARTMAP Neural Networks | 500 | Shape and colour based features | FNN, Bayesian classifier |
| R. Devi et al., 2015 | Classification of Acute Myelogenous Leukaemia in Blood Microscopic Images Using Supervised Classifier | 160 | Shape based features | PNN |
| L. Faivdullah et al., 2015 | Leukemia Detection from Blood Smears | 100 | Shape based features | SVM |

2. Material and Methods

2.1 Database description

All microscopic blood images in the datasets have a native resolution equal to 2592 × 1944 are in JPG format, captured with a power shot G5 camera. The ALL-IDB database has two distinct versions are ALL-IDB1 and ALL-IDB2, respectively. The ALL-IDB1 dataset is composed of 108 images. The total number of candidate lymphoblast presents in the ALL-IDB1 is equal to 510. The ALL-IDB2 image set contains 260 images and the 50% of these represent lymphoblast.
2.2 Segmentation

Segmentation of leukocytes (White blood cell) will follow the steps to pre-process the nucleus and cytoplasm region by enhancement of input image, then segmentation is performed by Image processing steps. Initially, to make the image processing reliable for the analysis, the original source coloured input images are converted into gray level images then image pre-processing is applied. Image enhancement is applied to improve the image quality and to make that processable by another modules. Then various filtering operations are applied. In figure 2, there is a sample image taken from the ALL-IDB in which segmentation process is applied and various processed images are shown.

2.3 Feature Extraction and Selection

The extraction of prominent features plays an important role in the performance increment of the classifier and for reducing the computational complexity as compared to a high dimensional features space. Generation of features of blood cells is the most important problem that distinguishes them with different blast types with the highest accuracy. In this study, work is carried out on shape features of cytoplasm and nucleus as Euler number, area, parameter, diameter, solidity, major axis, minor axis, eccentricity, orientation, convex area, extent of malignant cell as well as healthy cells and texture features are calculated with GLCM like contrast, correlation, energy, homogeneity and entropy statistics are derived from the GLCM matrix of the nucleus and cytoplasm region.

According to hematopathologists the contour of the nucleus is a vital feature for discrimination of lymphoblast from lymphocyte. For contour analysis of the nucleus part, shape based features on region and boundary are extracted. All the extracted features from the binary equivalent image of the nucleus part with none zero pixels represents the nucleus region. Two classes of features region and boundary are extracted from the nucleus for quantitative evaluation.

Based on the morphology, there are different types of leukemia as described in table 1 like ALL (Acute lymphoblastic leukaemia) is small, blast cell of leukocytes is uniform, and cytoplasm part is scanty, round and usually contains single nucleoli inside nucleus. While in AML (Acute myeloid leukaemia), the blasts are larger and irregular form and are usually multiple nucleoli with the presence of Auer rode. The white blood cell appears rather darker than the background while red blood cell (erythrocytes) appears in an intermediate intensity level.
There are 13 feature vectors of Gray level co-occurrence matrices (GLCM) and shape contains 11 feature vectors. Some of these are here described.

\[
\text{Energy} = \sum_{i,j=0}^{n-1} (p_{i,j})^2
\]  
\[
\text{Contrast} = \sum_{i,j=0}^{n-1} n^2 \left( \sum_{i,j=1}^{n} p_{i,j} \right) \left| i - j \right| = n
\]  
\[
\text{Correlation} = \frac{\sum_{i,j} (i,j)p_{i,j} - \mu_1 \mu_2}{\sigma_1 \sigma_2}
\]  
\[
\text{Homogeneity} = \sum_{i,j} \left( \frac{1}{1+|i-j|^2} \right) p_{i,j}
\]  
\[
\text{Area} = \sum_{i=1}^{x} \sum_{j=1}^{y} f(x, y)
\]  
\[
\text{Perimeter} = 2 \pi r
\]  
\[
\text{Diameter} = \sqrt{4 \text{Area} / \pi}
\]  
\[
\text{Euler’s no} = e = \lim_{n \to \infty} \left( 1 + \frac{1}{n} \right)^n
\]  
\[
\text{Solidity} = \frac{\text{area}}{\text{convex area}}
\]
2.4 Classification Module

Classification is to associate the appropriate class label (type of texture) with the blood test sample by using the measurements. The selection of prominent features plays an important role in reducing the computational complexity of a classifier. For detection of leukemia from the complex morphological background of tissue section images of leukocytes, a vast number of artifacts/noise are also extracted and large amounts of multivariate data is generated. This multivariate data degrades the performance of a classifier to discriminate between leukocytes and artifacts/noise. Based on the output of classifier, each feature vector is assigned a class label (predefined integer value) depending on the number of classes. Each classifier is configured such that the application of a set of inputs produces a desired set of outputs. The entire specific data is divided into training and testing data sets. The training data are used for updating the weights. Nonlinear mapping functions transform the nonlinear separation problem in the input plane into a linear separation problem in feature space, facilitating easier classification in the high dimensional feature space.

The classification is performed by using auto Support Vector Machines binary (SVM) that has the capability to discriminate two classes. In a dataset of 130 ALL infected images, first 65 images is used for training and next half are used for testing of the proposed system. Similarly, the first half is used for training and next half is used validating purpose for 66 images of the nucleus as well cytoplasm of healthy images. SVM first uses a nonlinear mapping function for transforming the input data from the observation space to a higher dimensional feature space, and then creates a maximum margin hyper plane to separate the two given classes.

3. Result and Discussion

Initially, all the GLCM texture features, angular second moment (energy), contrast, correlation, sum of squares known as variance, inverse difference moment (homogeneity), sum, average, sum variance, sum entropy, entropy, difference variance, difference entropy, information measures of correlation are calculated for the nucleus and the cytoplasm region of lymphocyte. The classification accuracy for the nucleus and cytoplasm of lymphocytes and lymphoblast based on the texture and shape features describes in table 3. Similarly, Shape features area, parameter, diameter, Euler number, solidity, major axis, minor axis, eccentricity, orientation, convex area, extent are calculated. All possible TFVs are calculated for the nucleus and cytoplasm regions of both malignant lymphocytes (lymphoblast) and healthy lymphocytes. From table 3, it is clear that the accuracy of developed computer aided diagnosis system is 72.4 % and 86.7 % for nucleus and cytoplasm respectively in case of GLCM texture features. For shape features, the achieved accuracy is 72.4 % and 56.1 % of nucleus and cytoplasm respectively.

| TFV (L) | CMN (%) | CMN (%) | OCA (%) | OCA (%) |
|---------|---------|---------|---------|---------|
| GLCM (13) | HWBC | IWBC | HWBC | IWBC | HWBC | IWBC | HWBC | IWBC |
| HWBC | 7 | 26 | 27 | 6 | 72.4 | 86.7 |
| IWBC | 1 | 64 | 7 | 58 |
| SHAPE BASED (11) | HWBC | IWBC | HWBC | IWBC | HWBC | IWBC | HWBC | IWBC |
| HWBC | 16 | 17 | 3 | 30 | 72.4 | 56.1 |
| IWBC | 10 | 55 | 13 | 52 |

Note: TFV: Texture feature vector; L: Length of feature vector; CM: Confusion Matrix; OCA: overall classification accuracy for nucleus; OCA: overall classification accuracy for cytoplasm; HWBC: Healthy white blood cells; IWBC: Infected White blood cells.

The texture features of cytoplasm are combined with texture features of nucleus then and are tabulated in table 4. The combined GLCM and shape features calculated accuracies are 76.5 % and 67.3 % respectively. When the texture and shape features are combined, then obtained accuracy is 87.7 %. Table 4 also describes the individual classification accuracy for healthy and malignant cells. In case of individual classification accuracy of 60.6 %, 84.6 % are obtained for healthy white blood cells and infected white blood cells in case of texture features. For shape feature based classification accuracies calculated are 42.4 % and 80.0 % for healthy and infected white blood cells. When the shape and texture features of cytoplasm and nucleus are combined the calculated accuracies are 75.76 %.

Table 3: Classification accuracy for nucleus and cytoplasm based on texture and shape features.
and 93.85\% for healthy and malignant white blood cells respectively as shown in table 4 fourth row.

Table 4: Classification details for healthy and infected WBC using combination of cytoplasm and nucleus texture features.

| TFV (L)        | CM<sub>CN</sub> | Accuracy (%) |
|----------------|------------------|--------------|
| GLCM (26)      |                  |              |
| HWBC           | 20               | 76.5         |
| IWBC           | 13               | 60.6         |
|                |                  | 84.6         |
| SHAPE BASED (22)|                  |              |
| HWBC           | 14               | 67.3         |
| IWBC           | 19               | 42.4         |
|                |                  | 80.0         |
| GLCM+SHAPE (48)|                  |              |
| HWBC           | 25               | 87.7         |
| IWBC           | 8                | 75.7         |
|                |                  | 93.8         |

Note: TFV: Texture feature vector; L: Length of feature vector; CM<sub>CN</sub>: Combined confusion matrix for cytoplasm and nucleus; OCA: overall classification accuracy; ICA<sub>HWBC</sub>: Individual classification accuracy for healthy white blood cells; ICA<sub>IWBC</sub>: Individual classification accuracy of infected white blood cells; HWBC: Healthy white blood cells; IWBC: Infected White blood cells.

The importance of shape features of nucleus stated in table 5 and can be verified by result. After combining the texture features of cytoplasm and nucleus with shape features of cytoplasm, obtained accuracy is 76.5\%. It shows that the obtained results are not too much affected. When the shape of the nucleus of the combined texture feature of the cytoplasm and the nucleus is added, it shows better results as shown in the second row of table 5. It also shows affect on results when collective texture feature of cytoplasm, nucleus and collective shape features of cytoplasm, nucleus are combined.

Table 5: Classification details for healthy and infected WBC using a combination of texture features of cytoplasm and nucleus with shape based features.

| TFV (L)       | CM<sub>CN</sub> | Accuracy (%) |
|---------------|------------------|--------------|
| GLCM<sub>CN</sub>_SHAPE<sub>C</sub> (37) |                  |              |
| HWBC          | 13               | 77.5         |
| IWBC          | 2                | 63           |
| GLCM<sub>CN</sub>_SHAPE<sub>N</sub> (37) |                  |              |
| HWBC          | 28               | 89.8         |
| IWBC          | 5                | 84.8         |
| GLCM<sub>CN</sub>_SHAPE<sub>CN</sub> (48) |                  |              |
| HWBC          | 28               | 89.8         |
| IWBC          | 5                | 84.8         |

Note: TFV: Texture feature vector; L: Length of feature vector; CM<sub>CN</sub>: Combined confusion matrix for cytoplasm and nucleus; OCA: overall classification accuracy; ICA<sub>HWBC</sub>: Individual classification accuracy for healthy white blood cells; ICA<sub>IWBC</sub>: Individual classification accuracy of infected white blood cells; HWBC: Healthy white blood cells; IWBC: Infected White blood cells; GLCM<sub>CN</sub>_SHAPE<sub>C</sub>: GLCM texture feature of cytoplasm, nucleus and shape features of cytoplasm; GLCM<sub>CN</sub>_SHAPE<sub>N</sub>: GLCM texture feature of cytoplasm, nucleus and shape features of nucleus; GLCM<sub>CN</sub>_SHAPE<sub>CN</sub>: GLCM texture feature of cytoplasm, nucleus and shape features of cytoplasm, nucleus.

4. Conclusion

A computer aided diagnostic system is illustrated for detection of acute lymphoblastic leukaemia (ALL) by analyzing shape and texture features. Auto SVM binary classifier is used for better detection accuracy. The overall accuracy of developed CAD system is 72.4\% and 86.7\% for nucleus and cytoplasm region respectively for the GLCM texture feature. For shape features, achieved accuracy is 72.4\% and 56.1\% of nucleus and cytoplasm region respectively. Combined classification accuracy for GLCM texture-shape feature of the nucleus - cytoplasm region is 89.8\% which gives better result than individuals. It concludes that shape of the nucleus is more important than the shape of cytoplasm for detecting the leukemic immature lymphocyte from the healthy mature lymphocyte.
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