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A Robust Segmentation Method for Acute Lymphoblastic Leukemia Detection

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Abstract*—Acute Lymphoblastic Leukemia is a malignant disorder of lymphoid cell, which affect both children & adults between ages of 2 & 5 years. The 80% cure is possible in children by effective treatment. Pathologists use leukocytes for the identification of variousdiseases. The methods like Fluorescent in Situ Hybridization (FISH), flow cytometry, immunophenotyping are used for leukemia detection. These methods have specific roles in the diagnosis & management of various haematological neoplasms. Careful examination of blood & bone marrow is fundamental in all haematological diagnosis. The major role of cytochemistry is in the diagnosis of acute myeloid leukemia & myelodysplastic syndromes and the major role of immunophenotyping is in the diagnosis of chronic lymphoproliferative disorder & acute leukemia cytogenetic analysis has role in confirming the diagnosis of chronic granulocyte leukemia and gives important information in the acute leukemias. But these methods give slow analysis and less accuracy. This paper presents fully automatic method for identification and classification of WBCs from microscopic images. In the proposed segmentation method Otsu's thresholding method is used to segment normal and ALL lymphocytes from the blood cell component. The whole work has been done by using MATLAB software.

Keywords*—Acute Lymphoblastic Leukemia, White Blood Cells, Segmentation.

I. INTRODUCTION

In recent year's immunophenotyping,cytogenetic analysis and flow cytometry have become important in characterizing haematological neoplasm. The objective of the present study is to diagnose the clinical, haematological and genetic markers of leukemic children's. Acute Lymphoblastic Leukemia (ALL) is the most common leukemia in children of age 2 to 5 years. Morphological examination of bone marrow aspiration with cytochemical staining and immunophenotyping are the methods used for the diagnosis and classification of Acute Lymphoblastic Leukemia (ALL). Flow cytometry is the method of choice for immunophenotyping because it has several advantages such as rapid analysis and high sensitivity. Leukemia is a disease of unknown etiology and fatal termination which is characterized by uncontrolled, abnormal and widespread proliferation of leukocytes in bone marrow and blood. The term disease implies discomfort, or absence of ease within the body when disease occur it may require clinical treatment [1]. In general the diseases can be classified on basis of their cause and cell of origin that is infectious, immunological, endocrine, genetic, neoplastic and traumatic etc.

Physicians are interested in understanding the biology of the diseases and how it can be prevented and treated [2]. However all cancers are characterized by uncontrolled growth of abnormal cells, affect surrounding tissues, metastasis and killing the host [3]. Cancer can develop in individuals of any race, gender, age, socioeconomic status, or culture and involve in any type of cells, tissues and organs of human body. Generally cancer is second leading cause of death. Scientific evidence suggests that most of the cancers caused by infectious agents, smoking, heavy use of alcohol and obesity could be prevented. Early diagnosis through regular screening programs and removal of precancerous growth can provide complete cure in many cancers. Cancer is generic term which describe group of malignant diseases with cells displaying uncontrolled and invasive growth along with metastasis. It can develop in any organ or tissue, such as in blood, lymph node, bone, breast, skin, colon, or nerve tissue.

Leukemia is also known as liquid cancer which develops from cells in the blood, bone marrow and also from lymphatic systems. In leukemia, the abnormal White Blood Cells (WBC) flood the bone marrow. Disease in blood cells can result with anaemia, decrease in platelet count decreases the clotting ability of the blood and due to abnormal nature of white blood cells, and they lack the ability to fight infections. The usual symptoms of leukemia include frequent infections, fatigue and easy bleeding and bruising. Depending on the clinical course, leukemia disease can be classified as acute which is rapidly progressing disease with a highly immature blast cells or chronic which denotes slowly progressing disease with increased number of more mature cells [4]. The classification of leukemia is based on both clinical course and source of leukemic cell population is shown in Table I.

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TABLE I LEUKEMIA CLASSIFICATION

Clinical course	**Cell of Origin**	
	Lymphoid	**Myeloid**
Acute	Acute Lymphoblastic Leukemia (ALL)	Acute Myeloid Leukemia (AML)
Chronic	Chronic Lymphoblastic Leukemia (CLL)	Chronic Myeloid Leukemia (CML)

Acute LymphoblasticLeukemia (ALL) is caused by excessive production of immature lymphocytes (lymphoblast) in the bone marrow. Untreated Acute Lymphoblastic Leukemia (ALL) can cause death due to crowding out normal cells in bone marrow and by metastasizing to other essential organs through the peripheral blood. Due to advance in molecular biology and treatment modalities classification of Acute Lymphoblastic Leukemia (ALL) has become essential for prognostic assessment and suitable chemotherapy planning.

II. LITERATURE SURVEY

In last few years, many researchers have done research on the digital pathology, and contributed to the area of modem quantitative microscopy [5]. In the literature, several works done are devoted to overcome the problem of subjectivity in visual assessment of morphological characteristics in stained cell/ tissue samples. Leukocyte or WBC segmentation methods available in the literature are mostly shape, threshold, region growing, or edge based schemes. Angulo et al [6] proposed a two stage blood image segmentation algorithm based on automatic thresholding and binary filtering. This scheme exhibits good segmentation performance in terms of cytoplasm, nucleus and nucleus extraction in lymphocyte image. An automatic method is used for segmentation and border identification of all subjects that do not overlap the boundary in an image taken from peripheral blood smear slide is presented in [7]. Segmentation performed by morphological processing followed by snake balloon algorithm is presented in [8]. A WBC segmentation scheme based on colour space images using feature space clustering technique, scale-space filtering for nucleus extraction and watershed clustering for the extraction of cytoplasm is given in [9]. Use of the morphological operators and examining the scale-space properties of toggle operator to improve the segmentation accuracy is given in [10]. The automatic morphological method which is based on morphological analysis of WBC is presented in [11]. The use of teager energy operator for segmentation, nucleus based on the edges, which are detected effectively by teager energy operator is done in [12]. A multi-step segmentation method is used in [13]. The automatic thresholding method is given in [14] the following section describe the full process for the detection of leukemic cells in blood smear images. The dataset which is required for the detection of leukemia is available for download [15].

III. METHODOLOGY

A.Overview of the proposed method

The main goal of this work is the processing and analysis of microscopic images, in order to provide an automatic procedure to support the medical activity which is able to count and classify the WBC affected by ALL. Leukocytes are easily identifiable from microscopic images, as their nuclei appear darker than the background, but data extraction form WBCs can present some complications due to variations presentin cell shape, dimensions and edges. The generic term leukocyte refers to set of cells that are very different between them, which contain neutrophils, basophils, eosinophil, lymphocytes and monocytes, also distinguishable by the presence of granules in the cytoplasm and by the number of lobes in the nucleus. The lobes are the most sustainable part of the nucleus and they are connected toeach other by thin filaments. The lymphocytes which are suffering from ALL are called lymphoblast which has additional morphological changes that increase with increasing severity of the disease. Lymphocytes are present in regular shape and compact nucleus with regular and continuous edges. Otherwise, lymphoblast have shape irregularities, small cavity in the cytoplasm, cells vacuoles and spherical particles within the nucleus is called nucleoli. Therefore the proposed method, identify all types of WBCs present in the microscopic images, which requires various steps to reach the goal and then classify WBCs as suffering from ALL or not. The whole process is shown in figure. 1

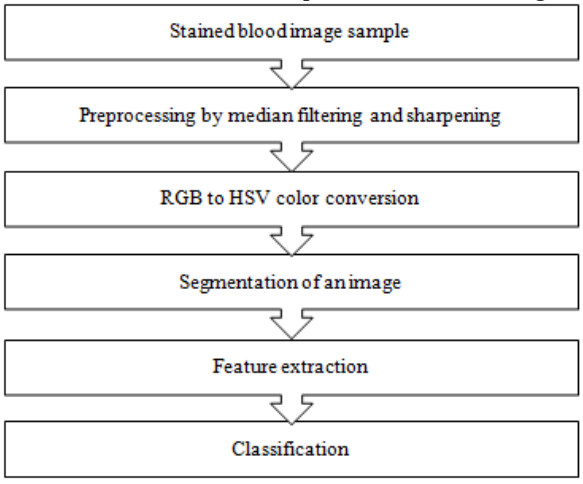

Fig. 1 Typical system overview

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The main objective of this work is to design and develop robust segmentation method for detection of blast cells. In leukemia patient number of WBC will increase. So the ratio of white blood cell to red blood cell also increases. Thus it is important to have cost effective image processing system which will help haematologists to determine the ratioof white blood cells to red blood cells for leukemia detection.

B. Leukocyte/ WBC identification system

In the proposed method the membrane is detected firstly, so that the separation of subsequent adjacent cells more accurate. The pre-processing is done by median filtering and sharpening. Median filtering is used to remove noise and sharpening is used to better enhancement of an image. WBC identification is easy and possible by using the conversion in HSV colour model. We have observed that leukocytes are more concentrated in the 'S' component of HSV colour model figure 2 shows RGB image and 'S' component image for accurate segmentation, also the redistribution of image gray levels is necessary. So the histogram equalization or a contrast stretching can be used for segmentation. We have to calculate threshold value for automatic segmentation the Otsu's methods [16] is used in which threshold value is automatically selected. To get better result it is important to remove background and it is possible to remove background by performing simple arithmetic operations. Thus to clean up the image we have used area opening operation, which allows to delete all the objects with size smaller than the structuring element.

C. Locating and segregating nucleus

Once the result of WBCs by removing other cells is obtained, it is possible to verify the overlapping of leukocytes and their separation. There are various methods present for separatingand to determining the objects in an image [17]. In the present work, we have used labelling method which labels and also finds in the image, it labels all objects are now individual cells which are segregated and used to find out the features of individual cells for feature extraction, we use regiondrops function which is present in MATLAB [18]. These region properties can compute number of useful features of each object.

D. Detection of nucleus

Once the labelled cells are obtained by using above method, the overlapped cells are removed and only non-overlapped cells are considered for the feature extraction process.

E. Feature extraction

An image feature is nothing but distinguishing the primitive characteristic or attribute of an image [19]. Some features are natural in sense such features are defined by visual appearance of an image while artificial features result from specific manipulations of an image. For feature extraction we used here shape features and densitometric features.

1) Natural features include the luminance of a region of pixels and gray scale textural regions.
2) Image amplitude histograms and spatial frequency spectrum are examples of artificial features.

In the proposed method following features of lymphocytes have been observed. These are area, perimeter, eccentricity, solidity form factor and elongation. These features are important due to shape of nucleus for differentiation of lymphoblast. These features are nothing but the shape features, these are:

1) Area: Area is nothing but total number of nonzero pixels present in an image.
2) Perimeter: It is nothing but total number of pixels which are present in boundary of an object.
3) Eccentricity:It is the roundness of an object, with value 0.0 up to 1.0.A circle is perfectly round and eccentricity means deviation of an object being circular. Circle has eccentricity 0, while line segment has eccentricity 1.To measure this the formula is in (1),

$$\text{Eccentricity} = \frac{\overline{a2-b2}}{a} \quad (1)$$

4) Solidity: It is ratio of actual area by convex null area.To measure this the formula is in (2),

$$\text{Solidity} = \frac{Actual\ \ Area}{Convex\ \ hull\ Area} \quad (2)$$

5) Form factor:It is the function of area and perimeter of an object and it changes surface irregularities. To measure this the formula is shown in (3),

$$\text{Form Factor} = \frac{4\ X\ Pi\ X\ Area}{perimeter\ \ \ xperimater} \quad (3)$$

6) Elongation:It is nothing but abnormal bulging of nucleus and it is shown in (4),

$$\text{Elongation} = \frac{Rmax}{Rmin} \quad (4)$$

The densitometric features are homogeneity, energy, correlation and entropy. These features includes,

1) Homogeneity: Here the degree of variation is measured.
2) Energy: It is used to measure uniformity.
3) Correlation: It is used to represent correlation between pixel values and its neibourhood.
4) Entropy: It is used to measure randomness using entropy.

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F. classification

For the classification of leukemia the Support Vector Machine (SVM) classifier is used. Support Vector Machine (SVM) classifier has the capability to distinguish two classes. For transforming the input data from the observation space to a higher dimensional feature space Support Vector Machine (SVM) classifier is used [20].

IV. RESULT AND DISCUSSION

A microscopic image is used and also processed for the evaluation. The various results obtained by evaluation are shown below. In the result, input RGB image and saturation component is shown in figure 2. In figure 3 the histogram of 'S' component and threshold output is shown. By using Otsu's thresholding algorithm the thresholded image and original gray image is shown in figure 4. The result of area opening operation which removes various artefacts and unwanted pixels is shown in figure5. In figure 6 the final segmented nucleus is shown their obtained nuclei are further used to extract various features and to identify the lymphoblast cells.

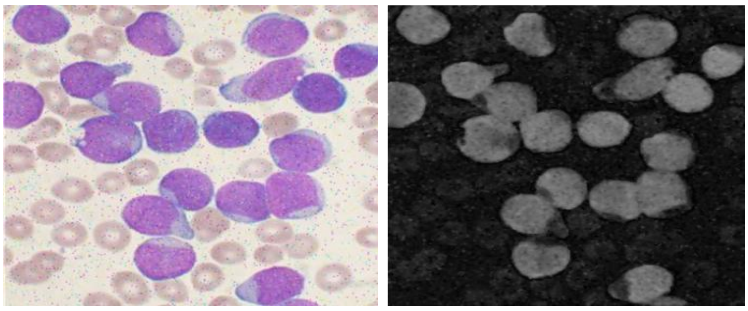

Fig. 2 Original RGB image and S component image

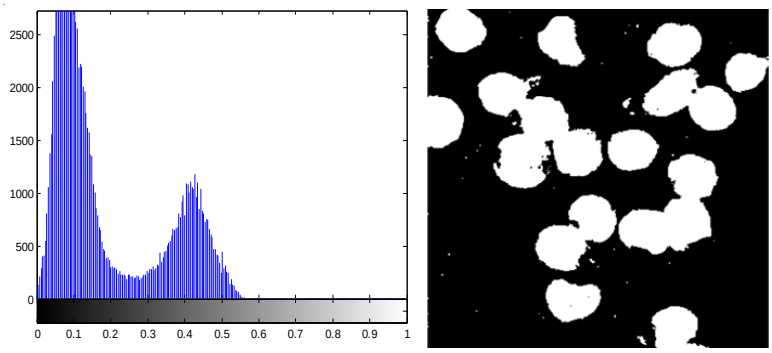

Fig. 3 Histogram of saturation component and thresholded output

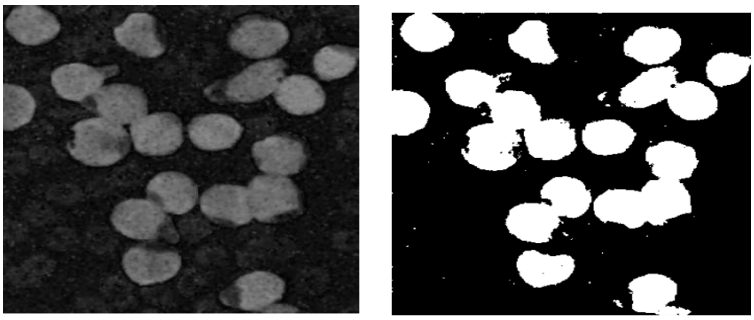

Fig. 4Original gray level image and segmentation result

Fig. 5 Background removal result and area opening result

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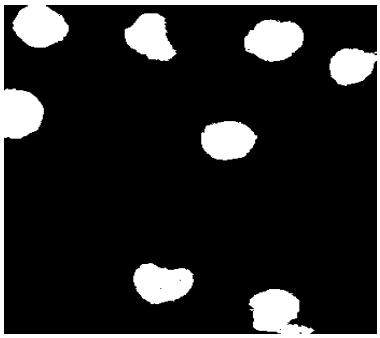

Fig. 6 Nucleus obtained for feature extraction

V. CONCLUSION

The basic aim of the proposed work is the blood smear image segmentation followed by feature extraction. We mainly considered here shape features like area, perimeter, eccentricity, solidity, form factor, elongation and densitometric features like energy, homogeneity, correlation, entropy for the detection of lymphoblast i.e. nothing but for the detection or leukemia. The proposed method performs an automated segmentation which is faster than traditional methods like Fluorescent in Situ Hybridization (FISH), Immunophenotyping, Cytogenetic analysis and Cytochemistry. Results obtained encourage the future work to develop a robust segmentation system which is independent of stains used in blood smear image.

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