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Acute Mylogenous Leukemia Detection in Blood Microscopic Images

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Abstract— Image Processing and Analysis can be defined as the act of examining images for the purpose of identifying objects and judging their significance. In current days, image processing techniques are widely used in many medical areas for improving earlier detection and treatment stages. The microscopic images of the blood cells are observed to find out many diseases. Changes in the blood condition show the development of diseases in an individual. Leukemia can lead to death if it is left untreated. Leukemia is detected only by analyzing the white blood cells. So our study is focused only on the white blood cells (WBCs). In a manual method of Leukemia detection, experts check the microscopic images. This is lengthy and time taking process which depends on the person's skill and not having a standard accuracy. In this paper we are focusing, automated approach of leukemia detection. The automated Leukemia detection system analyses the microscopic image it extracts the required parts of the images and applies some filtering techniques. K-means clustering approach is used for white blood cells detection.

Keywords— Segmentation, filtering techniques, K-Means clustering algorithm

I. INTRODUCTION

The microscopic images of the blood cells are observed to find out many diseases. Changes in the blood condition show the development of diseases in an individual.[8] Leukemia can lead to death if it is left untreated. Based on some statistics it is found that the leukaemia is the fifth cause of death in men and sixth cause of death in women. Leukemia originates in the bone marrow. Each bone contains a thin material inside it which is also known as a bone marrow. The components of blood are Red Blood Cells (erythrocytes), White Blood Cells (leucocytes), platelets and plasma. Leukemia is detected only by analyzing the white blood cells. So our study is focused only on the white blood cells (WBCs).The cells in the bone marrow start changing and they get infected and become leukemia or infected cells. These leukemia cells are having strange properties than the normal cells. Their growth is abnormal and survival time is more than the normal cells. They interrupt normal cells to carry out their work. After a certain amount of time normal cells die while leukemia cells don't. The old leukemia cells last for a long time and new leukemia cells produce in an abnormal way. The rate at which the leukemia cells progress is different according to the type of leukemia.

In this work, automated approach of leukemia detection is proposed. In a manual method of Leukemia detection, experts check the microscopic images. This is lengthy and time taking process which depends on the person's skill and not having a standard accuracy. The automated Leukemia detection system analyses the microscopic image and overcomes these drawbacks. It extracts the required parts of the images and applies some filtering techniques. K-mean clustering approach is used for white blood cells detection.

The field of image processing continues, as it has since the early 70s, on a path of dynamic growth in terms of popular and scientific interest and number of commercial applications. Considerable advances have been made over the past 30 years resulting in routine application of image processing to problems in medicine, manufacturing, entertainment, law enforcement, and many others. Examples include mapping internal organs in medicine using various scanning technologies automatic fingerprint recognition.

White blood cells are bigger in size than the red blood cells. The concentration and composition of the white blood cells provide some important information which helps us to find out many diseases [9] and [13]. Acute Myeloid Leukemia (AML) is produced in the white blood cells. When the non-granular white blood cells develop early and in the abnormal growth, it results in the AML. The blast cells in the bone marrow are developed to form granulocytes which is the white blood cells having small granules or particles.[11] The blast in the stem cells which causes AML doesn't mature. These AML blasts become large in bone marrow and also in the blood. When these cells become large in number, the body cannot stop bleeding and cannot fight against infection. Therefore, the treatment of this

disease becomes mandatory as soon as possible after the detection of this disease. To find out the appropriate treatment and the stage of the illness, we have to look at the blast cells in the bone marrow. These abnormal cells are going to be identified using the microscope by clinicians. Depending on the number of blast cells counted and the type of blast in the bone marrow, the disease is classified for the treatment.

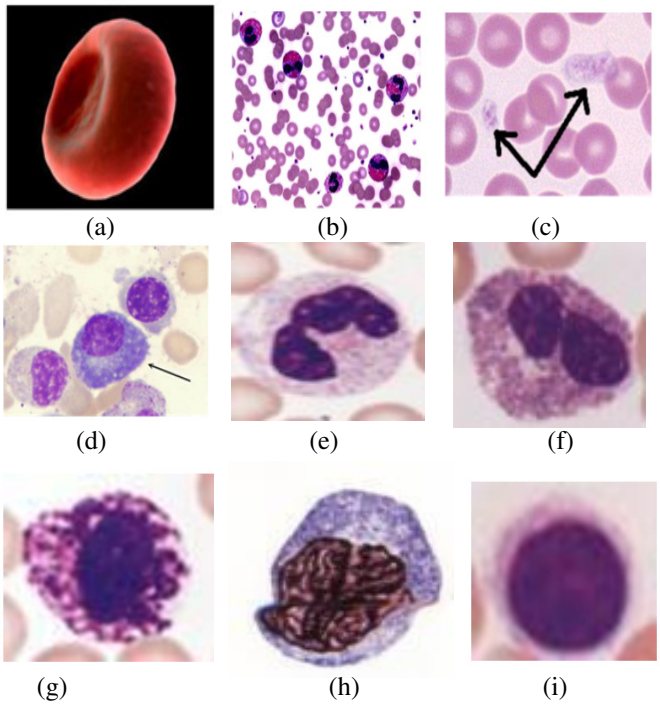

Figure 1.(a)Red Blood Cells,(b) White Blood Cells, (c) Platelets, (d) Plasma, (e) Neutrophil, (f) Eosinophil, (g) Basophil, (h) Monocyte, (i) Lymphocyte

The red blood cells are transport oxygen from the lungs to organs and peripheral site. The white blood cells are defensive role in destroying invading organisms, e.g. bacteria and viruses and assist in the removal of dead or damaged tissue cells. This cell is having the nucleus which is containing the cytoplasm. The granules of it are of two types – primary and secondary. Primary granules are seen at the pro-myelocyte stage while the secondary granules are seen at the myelocyte stage. The diameter of it is 12-15 µm. These look very similar to the neutrophils. The only change is in the cytoplasmic granules which are red. They insert seditious exudates. They react to the allergies. The diameter of it is 12-15 µm. Basophils can be found only in the normal peripheral blood. Basophils are having more no of cytoplasmic granules in it. These granules overlie nucleus. The diameter of it is 9-10 µm. Monocytes are generally bigger than the leucocytes. In the bone marrow, the ancestors of the monocytes, promonocytes and monoblasts, are very tough to differentiate from the myeloblasts. Monocytes are present in the bone marrow for very short time. After 20-40 hours they get matured and perform their duties. The diameter of it is 16-20 µm. Lymphocytes are responsible for our body health. They fight against any kind of intruders and infection. This is called are immune system. In the case of any kind of attack, our immune system generates the antigenic specificity to protect our body. The diameter of it is 8-10 µm.

II. EASE OF USE

A. *Acute Myeloid Leukemia (AML)*

Acute Myeloid Leukemia (AML) is produced in the white blood cells. When the non-granular white blood cells develop early and in the abnormal growth, it results in the AML. The blast cells in the bone marrow are developed to form granulocytes which is the white blood cells having small granules or particles. The blast in the stem cells which causes AML doesn't mature. These AML blasts become large in bone marrow and also in the blood [2]. When these cells become large in number, the body cannot stop bleeding and cannot fight against infection. Therefore, the treatment of this disease becomes mandatory as soon as possible after the detection of this disease [3]. To find out the appropriate treatment and the stage of the illness, we have to look at the blast cells in the bone marrow. These abnormal cells are going to be identified using the microscope by clinicians. Depending on the number of blast cells counted and the type of blast in the bone marrow, the disease is classified for the treatment.

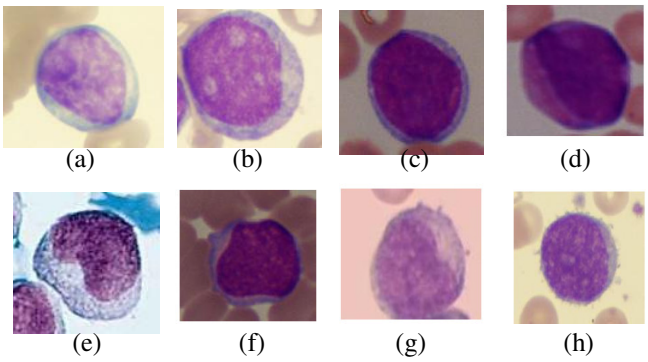

Figure 2. (a) M0: Minimally differentiated acute myeloid leukaemia, (b) M1: Myeloblastic without maturation, (c) M2: Myeloblastic with maturation , (d) M3: Promyelocytic, (e) M4: Myelomonocytic, (f) M5: Monoblastic monocytic, (g) M6: Erytheroleukemia, (h) M7: Megakaryocytic

The blast cells are large and quite heterogeneous with the absence of Auer rods. 90% of myeloid cell lines are blasts. The blast cells show few granules but may show Auer rods. 30-89% of myeloid cell are blasts. >10% are promyelocytes 20% are monocytes. Show multiple

cytoplasmic granules. Hypergranular promyelocytes with heavy to dust like granules, frequent Auer rods, nucleus often blooded; microgranular variant may occur. Blast cells show multiple Auer rods. 30-80% of myeloid cell lines are myeloblasts plus maturing neutrophils. 20-80% of myeloid cell lines are monocytic lineage. Blasts have some monocytoid differentiation >80% of a myeloid cell line are monoblasts, promonocytes or monocytes.[3] In M5a 80% of myeloid cell lines are monoblasts; in M5b, <80% were monoblast and the remainder are promonocytes or monocytes >=50% of bone marrow cells are erythroid precursors. > 30% of non-erythroid myeloid cell lines are blasts. Showing preponderance of Erythroblast Blasts in marrow or blood are identified as megakaryocytic lineage[2]. If marrow is undesirable, biopsy shows large tumour of blasts, frequently increased numbers of megakaryocyte and reticulin

B. Bone Marrow

Bone marrow can be found inside some large bone in body. It is a special kind of a tissue which contains stem cells.[4] Stem cells are the cells which are transformed into any kind of cells which our body requires. Stem cells are transformed into white blood cells, platelets and red blood cells each of them are having various types of roles to be performed to make the body healthy. Inside the tissue, immature stem cells with extra irons exist [5]. Figure 3 shows the cells in the bone marrow while a patient is having leukemia.

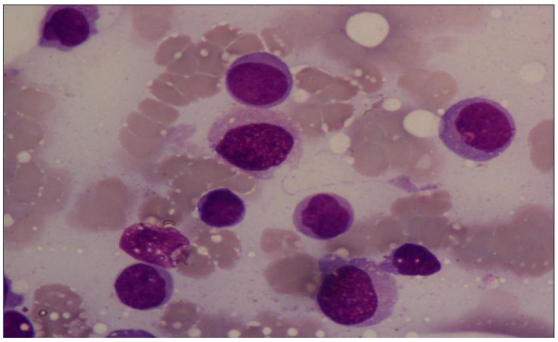

Figure 3. Bone Marrow sample in M2 AML case

III. ALGORITHM ANALYSIS

It has been observed from the literature that much number of schemes have been developed in counting the blood cells automatically from the microscopic images. Many people are still working in the automated blood cells counting. The literature on the leucocyte segmentation, it is noticed that large number of methods are only working on the extraction of nucleus but there are very few methods available which are extracting the cytoplasm and even with less accurately. The main reason behind the less accuracy in the cytoplasm extraction is that most of the researchers are using the grey level color for the extraction of cytoplasm which is not easily separable from the other colors.

It is noticed in the literatures that different approaches are used for the white blood cells detection. Some have used KNN approach, threshold techniques, EM algorithm, Fuzzy rules, watershed transform, GVF model, trained neural network [7]. Fuzzy c-mean clustering, computer morphometric system and many more. From the literature studied, it has been observed that there are many ways we can make a better system for the identification of leukemia from the microscopic blood image. None of the researchers has used the K-mean clustering for the segmentation of the white blood cells from the microscopic blood image. In this thesis [3]. K-mean clustering approach has been used on the clean microscopic blood image followed by image cleaning and the extraction of the nucleus and cytoplasm with a good accuracy.

A. Clustering

Cluster analysis is one of the major data analysis methods widely used for many practical applications in emerging areas[9].Clustering is the process of finding groups of objects such that the objects in a group will be similar (or related) to one another and different from (or unrelated to) the objects in other groups. A good clustering method will produce high quality clusters with high intra-cluster similarity and low inter-cluster similarity [7] and [11]. The quality of a clustering result depends on both the similarity measure used by the method and its implementation and also by its ability to discover some or all of the hidden patterns [8].

B. K-Means Based Algorithm

Step 1: The region number and the region centers are initialized, using the output of the max min algorithm.

Step 2: For every pixel p, the distance D (p,ri) between p and all region's intensity and spatial centers is calculated. The pixel is then assigned to the region for which the distance is minimal. Normalization of the spatial distance with the area of each region is necessary in order to enable the creation of large connected regions. Otherwise [6] pixels would tend to be assigned to smaller rather than larger regions due to greater spatial proximity to their centers. In this case, large objects would be broken down to more than one neighboring smaller regions instead of forming one single, larger region.

Step 3: Region centers are recalculated. Regions with areas below the threshold size are dropped.

Step 4: The number of regions is also recalculated, taking into account only the remaining regions.

Step 5: If the number of regions K is equal to the one calculated in the previous iteration and the difference between the new centers and those in the previous iteration is below the corresponding threshold for all centers, then stop, else go to Step 2 [9]. Since there is no certainty that the

K suppressed mean algorithm will converge for any given image, the maximum allowed number of iterations here was chosen to be 20.

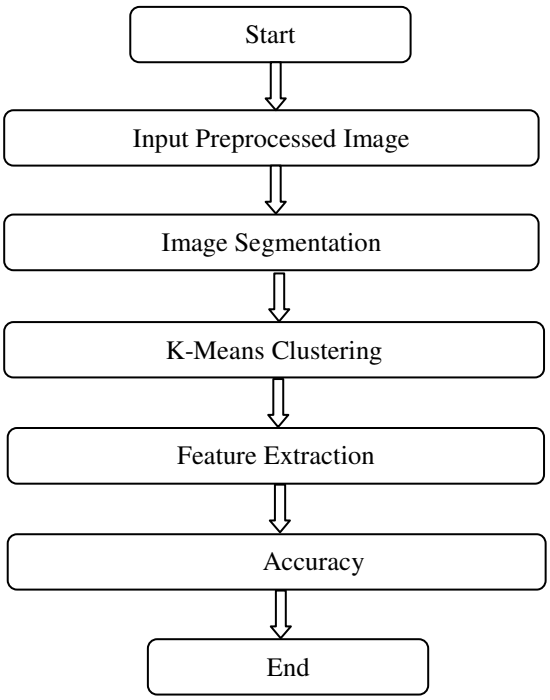

Figure 4.System Architecture

In this phase we try to extract some of the features from the processed image. Here, we try to find out the features of the nucleus [13] of myelocytes and lymphocytes. Feature extraction is the process of converting the image into data so that we can check these values with the standard values and finally we can differentiate between the cancerous and non-cancerous data.

Color Features – The mean color values of the grey images are acquired. Geometric Features – The perimeter, radius, area, rectangularity, compactness, convexity, concavity, symmetry, elongation, eccentricity, solidity are obtained. Texture Features – The entropy, energy, homogeneity, correlation are obtained. Statistical Features – The skew ness, mean, variance and gradient matrix are obtained.

Elongation shows the way of an object elongation. Rectangularity shows how well the bounding box is filled. Eccentricity is the ratio of the major axis length and the foci of the ellipse. Convexity shows the relative amount of difference of object from its convex object. Compactness is the ratio of the area of an object and area of circle having same perimeter. In this final phase, the features extracted are used to provide the final answer [12]. All feature extracted are listed into the different columns with their values. When we give any image as an input to the proposed system then we first calculate the feature values. The values of the test image features are checked with the previously calculated values Based on the values of the input image the SVM classifier classifies that test image into either infected or not infected class.

The method mentioned in this paper for WBC extraction and counting is color based clustering method by focusing on image intensity level. There are several steps needed to be done in this method to get the desired result. The block diagram of flow processes involved in this research. It shows that this research and study is started by importing the input image. Then the image will be transformed into grayscale image by using specified function called grayscale conversion.

C. Steps For Clustering

1. Read the image.
2. Convert image from rgb to lab color space.
3. Convert data type to double.
4. Arrange the above data into column vector.
5. Define variable which contains total number of clusters.
6. Apply k-means clustering on the above data.

D. Steps For Object Counting

1. Read the image.
2. Extract the blue plane from the image and store it into a variable.
3. Convert image from RGB to gray.
4. Subtract the gray scale image from extracted blue plane image.
5. Calculate the threshold of subtracted image.
6. Convert the subtracted image into black and white image.
7. Calculate all the connected objects.

E. Nucleus and Cytoplasm Selection

The leucocytes identified in above steps can now be used to extract the nucleus and cytoplasm. To carry out this step, we crop the image with the bounding box size. This size is the rectangle which can properly fit the component so that we can isolate each components of an image. We have to separate out each leucocyte by this method. The borders of every sub-image obtained like this have to be cleaned up before we proceed. Now the portion outside the leucocyte has to be cropped which will help us in getting the cytoplasm. This method completely removes the artefacts. We have used Cseke's observation to find out nucleus in our method. The observation says that the white blood cells nuclei are more in contrast on the green component of the RGB color space. So, we can get nucleus by using the threshold.

IV. FEATURE EXTRACTION

In this phase we try to extract some of the features from the processed image. Here, we try to find out the features of the nucleus [13] of myelocytes and lymphocytes. Feature

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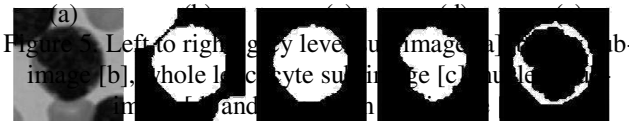

Figure 3. Left to right, grey level [illegible] image [a], [illegible] sub-image [b], whole leucocyte sub-image [c], [illegible] image [d] and [illegible]

Geometric Features – The perimeter, radius, area, rectangularity, compactness, convexity, concavity, symmetry, elongation, eccentricity, solidity are obtained. Texture Features – The entropy, energy, homogeneity, correlation are obtained. Statistical Features – The skew ness, mean, variance and gradient matrix are obtained.

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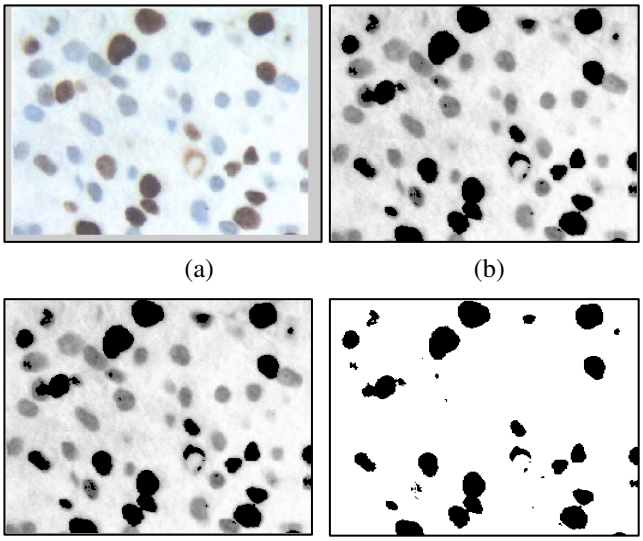
V. EXPERIMENTAL RESULTS AND ANALYSIS

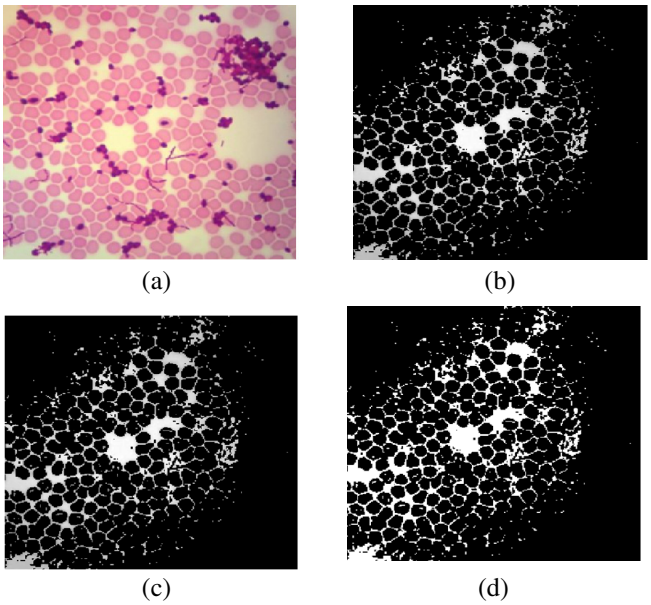
The microscopic image has been sent to the proposed system. The system then gives the subsequent images as the result. The image we got as input is modified by the system by removing the noise [16]. The identification of grouped leucocytes and image cleaning operations are performed on the image and then after it is going to be converted into the grey scale image. Next the cluster index image which is important for applying the K-means algorithm. Cluster index image defines cluster to the each component of the image. The K-means clustering is applied on the figure Background, Red blood cells cluster and white blood background of the image [20]. The proposed system is tested by the different microscopic images and the accuracy is also calculated. The images are different in many terms of lightening, magnification and resolution. Thirty-three images are fetched from the whole ALL-IDB dataset which are taken from the same camera and same lightening conditions. The proposed system also shows the percentage of the infection present in the blood image.



(a) (b) (c) (d)

Figure 4. (a) Original image, b) Gray scale image, (c)Denoised image, d) Segmented Image

The symptoms of AML are caused by replacement of normal bone marrow with leukemic cells, which causes a drop in red blood cells, platelets, and normal white blood cells [18]. These symptoms include fatigue, shortness of breath, easy bruising and bleeding.



(a) (b) (c) (d)

(a) Original Image, (b) Gray Scale Image, (c) Denoised Image, (d)Segmented Image

The microscopic images of the blood cells are observed to find out many diseases. Changes in the blood condition show the development of diseases in an individual. Leukemia can lead to death if it is left untreated. Based on some statistics it is found that the leukemia is the fifth cause of death in men and sixth cause of death in women. Leukemia originates in the bone marrow. Each bone contains a thin material inside it which is also known as a bone marrow.

Table1: white blood cells identification

age	Manual Count	Auto Count	Accuracy
Image1	12	1	91%
Image2	9	5	55%
Image3	7	4	57%
Image4	8	8	70%
Image5	24	19	79%
Image6	18	18	50%
Image7	7	7	60%
Image 8	17	16	96%
Image9	7	7	72%
Image10	12	12	50%
Image11	15	12	80%
Image12	12	12	40%
Image13	10	7	70%
Image14	5	3	60%
Image15	17	17	90%

VI. CONCLUSION

The major part of this work is to segment the lymphocytes and myelocytes white blood cells for leukemia detection. The first phase of the proposed system is dealing with the image cleaning and noise removal for making the image ready for the further and accurate study. The second and major phase is the leucocytes identification from the image. The third phase is dealing with the nucleus and cytoplasm extraction from the image which can finally be used for the feature extraction in the last phase of the proposed system. This model has been tested against 33 images taken under same lightening condition and the accuracy achieved is 93.57% [19]. We can also use the proposed system to find out the percentage of leukemia infection in microscopic image.

We hope this approach will be beneficial for today's fast life and early detection of leukemia without any need of costly tests and with a better accuracy.

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