# An Image Processing Application for Diagnosing Acute Lymphoblastic Leukemia (ALL)

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***Abstract***— *Leukemia, simply called "Blood cancer" is a fatal disease where the white blood cells (WBC) increases in bone marrow and peripheral blood. Acute lymphoblastic leukemia (ALL) is one of the most common types of leukemia aroused by accumulation and overproduction of immature and cancerous cells known as lymphoblasts. Presently, the diagnosis of ALL includes performing a full blood count, blood picture, bone marrow biopsy, cytochemical stain, immunophenotyping and cytogenetics. These techniques are highly tedious, costly, requires expertise of hematologists and available only in few hospitals. Therefore, as an alternative, use of image processing to diagnose ALL would become an effective solution. Although, several research groups have employed image processing to identify ALL, recognition and splitting of overlapping red blood cells (RBC) with WBC has yet been a challenging issue. This paper is about an application which includes an image processing algorithm to diagnose ALL while attempting to solve the above mentioned issue of overlapping cells. The algorithm is also extended to detect the quality devastation in blood films in terms of storing them for prolonged period. The inputs for this application are microscopic peripheral blood images of ALL patients obtained from Department of Pathology Clinic at Faculty of Medicine, University of Colombo. Then, image processing techniques; image enhancement, segmentation, feature extraction and classification are performed. For the detection and diagnosis of leukemia, segmentation using morphological operations in OpenCV Python and classification using K-Nearest Neighbour and Support vector machine implementations has been proposed in this research. It is observed that the proposed algorithm has led to a high accuracy in diagnosing ALL. The system also includes a PHP based web application that serves hematologists, doctors and patients to log in to their specific user accounts and make records, insert details and view diagnosing reports.*

***Keywords***— **Acute Lymphoblastic Leukemia, Image processing, Segmentation and Feature extraction, Classification**

## I. INTRODUCTION

Blood is one of the most important materials of the human body as it is the principle agent that make humans live. Human blood consists of two major parts; plasma and cells. The peripheral blood cells consist of three main components; Red blood cells (RBC), White blood cells (WBC) and platelets. There are five types of WBCs; Neutrophils (40-75%), Lymphocytes (20-45%), Eosinophils (1-8%), Monocytes (0-10%), Basophils (0.5-1%). Leukemia, simply called "Blood cancer" in which usually the number of WBC increase in the bone marrow and peripheral blood. These leukemic cells (usually immature) replace the normal blood cells and causes malfunction of the bone marrow and peripheral blood. Furthermore, excess amount of these cells travels to other sites such as liver, spleen to maintain normal cells production. Later, the leukemia cells also invade other organs causing them to malfunction (Hoffbrand et al, 2004).

There are two main types of leukemia according to the morphology of cells in the bone marrow. They termed as acute & chronic Leukemia. Acute leukemia involves the rapid overgrowth of very immature blood cells whereas chronic leukemia involves the overgrowth of somewhat mature blood cells in the bone marrow compared to acute type. In the French-American-British (FAB) classification (Bennett et. al, 1976), acute leukemia is further categorized into two groups based on the white blood cell from which the malignancy originates from. They are acute lymphoblastic leukemia (ALL) is caused by abnormal lymphoid cells, and acute myeloid leukemia (AML) is caused by abnormal myeloid cells in the bone marrow (Hoffbrand et al, 2004). The predominant abnormal cells in the ALL are lymphoblasts.

The detection, identification and classification of leukemia normally follow series of steps. They are full blood count, examination of blood picture, bone marrow & trephine biopsy, immunophenotyping and cytogenetics (Hughes-Jones et. al, 2004; Hoffbrand and Lewis 1995; Purohit, 2000; Cui et. al, 2004). The whole process takes about 3-4 days and also needs a well-trained experienced staff. However, early diagnosis of leukemia contributes to early treatment and proper management of patients. Furthermore, manual detection procedure stated above is a highly tedious task that involves the effort of hematologists and other supporting staff as it is intensively slow, costly, time consuming. Even though

advanced techniques are being used there may be errors especially diagnosing subtypes.

Image processing and data mining fields have provided fast, cost effective and accurate solutions in fields such as medical image management, image data mining, bioimaging, neuroimaging and virtual reality in medical visualization (Scholl et al., 2011; Hegadi, 2010). Researches have been conducted for the detection and counting of red blood cells, white blood cells and to diagnose diseases like anaemia, malaria and deficiency of vitamin B12 using blood images (Vaghela et al., 2015). Furthermore, Image Processing techniques are the used in detecting cancer cells (Patil and Jain, 2014). Image processing is also been used in diagnosing leukemic cells in blood samples. Techniques such as Image acquisition, pre-processing, segmentation, Feature extraction and classification have been used in the diagnosis.

## II. LITERATURE REVIEW

Presently, a considerable contribution has been done by researchers in the aim of ALL detection using image processing. The common flow of the image processing techniques that is used in diagnosis can be illustrated by below figure.

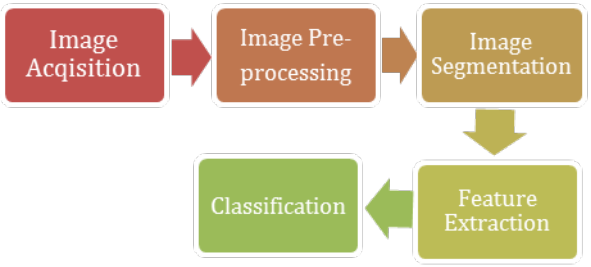


Figure 1. Flow of ALL diagnosis

The researches done so far are different from the segmentation methods and classification methods they have used. A review done on image processing techniques have been elaborated in this section.

### *A. Segmentation methods*

*1) Watershed segmentation:* "Watershed" refers to a ridge that splits areas drained by different river systems. Watershed lines are defined on the nodes, edges, hybrid lines on both nodes and edges and in continuous domain. Watershed segmentation is an easy method for the detection of WBC but requires best quality images in order to achieve a better accuracy (MAHAJA et al., 2014).

*2) Fuzzy C Means Clustering (FCM):* This data clustering technique groups a dataset into n clusters with all data points in that dataset belong to each and every cluster to a certain degree. FCM result is much accurate and it's able to measuring nucleus boundaries with shape, colour and texture, but it's difficult in classification of lymphoblast in to its sub types through this segmentation (MAHAJA et al., 2014; Viswanathan, 2015).

*3) Fuzzy K-Means Clustering in L*A*B* colour space:* K-Means method is a least squares partitioning method and it divides a collection of objects to K groups of clusters. It considers each object have a location in the space and finds partitions in the image such that objects within each cluster close to each other as likely, and as far from the objects in other clusters as possible. This method is not applicable on incremental data and it cannot give classification with labelled data (Vaghela et al., 2015). Mohapatra and the colleagues have used fuzzy based blood image segmentation for separate out leucocytes from other blood components (Mohapatra et al., 2011).

*4) Otsu's method:* This is a thresholding method and it's the easiest and fastest method used in segmentation. Thresholding is based on a clip-level named a threshold value used in converting a grayscale image into a binary image. Fabio Scotti has used Otsu's method in nucleus and cytoplasm selection in lymphoblasts and lymphocytes (Scotti, 2005). Their experiments have showed a good performance of this method in separating the nucleus from the cytoplasm.

*5) Shadowed C-means clustering (SCM):* SCM is a method of partitive clustering developed in the framework of shadowed sets. Unlike rough clustering, in SCM, the choice of threshold parameter is fully automated and the number of clusters is optimized in terms of various validity indices (Mitra et al., 2010). Shadowed clustering can handle overlapping among clusters efficiently and also it can model uncertainty in class boundaries (Mohapatra et al., 2014). The algorithm is robust in the presence of outliers too. However, fuzzy c-means clustering have problems with high dimensional data sets and a large number of prototypes (Oliveira and Pedrycz, 2007).

*6) HSI Colour based Segmentation:* HSI (Hue, Saturation, Intensity) is a common colour model used in image segmentation. HSI colour model has a good capability of representing the colours of human perception (H. D.Cheng et al., 2006). Nor Hazlyna and the team have conducted a research for ALL detection based on segmentation using HSI and RGB colour space (Nor Hazlyna et al., 2010). The results have shown that the proposed segmentation technique based on HSI has successfully segmented the acute leukemia images while preserving significant features and removing background noise. Singhal and Singh (Singhal and Singh, 2014) and Halim and his colleagues (Halim et al., 2011) are some research groups who have used HSI colour based segmentation in ALL diagnosis. They have used HSI colour based segmentation as it provides better performance than RGB colour segmentation.

*7) K-means clustering:* K-means clustering is an unsupervised learning algorithm which involves two simple processes as relegating the given data set and classifying the colligated data sets to the centroid nearest to them. K-means clustering segmentation have been used in identifying the leukemia sub types (Fatma and Sharma, 2014; Ashwini Rejintal and Aswini.N, 2016) and in AML screening systems (Agaian et al., 2014). K-means clustering does not give classification with labelled data and also not applicable on incremental data (Vaghela et al., 2015).

*8) Morphological Operations (shape-based):* Segmentation using morphological operations is a technique considering the processing of geometrical structure based on set hypothesis, topology, lattice hypothesis and arbitrary functions etc. This is the most successful segmentation method that has been used so far. Through this method it is very easy for detecting white cells, overlapping of cells and shape of cells. Thus this is based on statistics so can get approximate results.

Bhattacharjee and Saini (Bhattacharjee and Saini, 2015), Vaghela and the group (Vaghela et al., 2015) and Raje and Rangole (Raje and Rangole, 2014) are some researchers who have used morphological based image segmentation in leukemia diagnosis. They have discovered that the morphological operators used for the extraction of features have resulted in high segmentation accuracy. Segmentation using morphological operations has been used in morphological classification of Leucocytes by microscopic images (Scotti, 2005; Piuri and Scotti, 2004). There, the researchers have focused on reducing the problem of identification and classification of WBC types in microscope images using morphological operations.

*B. Classification Methods*

Classification is in charge of assigning to the unknown test vector which is a label from one of the known classes (Rege and Dr.Gawli, 2015). Mostly used classifiers are as follows.

*1) Support Vector Machine (SVM):* SVM is a discriminative classifier that is formally defined by a separating hyper plane. When labelled training data is given (supervised learning), the algorithm outputs an optimal hyperplane which categorizes new examples. Patel and Mishra (Patel and Mishra, 2015) is a research group who presented an automatic approach for leukemia detection using microscopic images. Colour, geometric, shape and statistical features have been analysed and classified under the SVM classifier in the intention of grouping the normal and abnormal cells. SVM has been used to classify leukemia types too. A three-layered framework consists of feature extraction, coding, and classification for the detection of leukemia from blood smear images has been proposed by Faivdullah and his colleagues (Faivdullah et al., 2015) leukemia types. They have employed a one-vs-all technique to convert SVM, which is a binary classifier in to a multi-class classifier.

*2) Artificial Neural Network (ANN):* This is a statistical learning algorithm defined by an interconnected set of nodes that are similar to the network of neurons found in brain. ANNs are capable of pattern recognition and machine learning, thus is mainly used in generating and estimating the output from a large number of input data set (Bhattacharjee and Saini, 2015). Mohapatra and the colleagues (Mohapatra et al., 2012) have engaged in another project in Lymphocyte image segmentation using Functional Link Neural Architecture for ALL detection (Mohapatra et al., 2012). Fatma and Sharma (Fatma and Sharma, 2014) have tried on a system to identify and classify sub types of acute leukemia using neural network.

*3) CART (Classification and Regression Trees):* CART (Classification and Regression Trees) statistical method has been used in automatic leukemia diagnosis in investigating the classification power of cell markers extracted in segmentation (Serbouti et al., 1991). This method generates classification tree diagrams with complete splitting information at each node and then produces a classification matrix, splitting cost and probability matrix for both the learning sample and the cross validation. The classification trees can be saved and used in classifying unknown specimens. Serbouti and the research team has employed CART in their research done in automatic leukemia diagnosis (Serbouti et al., 1991).

*4) K-Nearest Neighbour (KNN):* This is considered to be the best classifier in the family of nonparametric method with a good scalability. In leukemia detection kNN=1 is considered to classify between blast cells and normal lymphocytic cells (Bhattacharjee and Saini, 2015). Bhattacharjee and Saini (Bhattacharjee and Saini, 2015) in their research in diagnosing ALL have discovered that KNN is the best classifier that produced high specificity and also have the lowest computational complexity which has produced a specificity of 95.23%.

*5) Ensemble of Classifiers (EOC):* Ensemble methods are machine learning algorithms that construct a set of classifiers and then classify new data points by taking a weighted vote of their predictions (Dietterich, 2011). EOC improves of the performance of individual classifiers. The ultimate goal of classification result integration algorithms is to generate more certain, precise and accurate system results. But EOC possess some limitations also such as increased storage, increase the number of computations and decreased

comprehensibility. EOC is been an efficient classification model used in leukemia diagnosis so far. An ensemble classifier system for early diagnosis of ALL has been developed by Mohapatra and group in 2014 (Mohapatra et al., 2014). As the results they have obtained more accuracy in EOC in comparison with other classifiers employed. Scotti and Piuri (Piuri and Scotti, 2004) have used ensemble of classifiers on their research done in Morphological Classification of Blood Leucocytes by Microscope Images. The classification accuracy has been tested and a proper classifier has been chosen from a set of candidates of different classifiers.

## III. METHODOLOGY AND EXPERIMENTAL DESIGN

An automated Acute Lymphoblastic Leukemia diagnosing application would be a useful tool in diagnosing of Acute Lymphoblastic Leukemia in blood samples efficiently and accurately. The basic method for diagnosis can be divided into following steps.

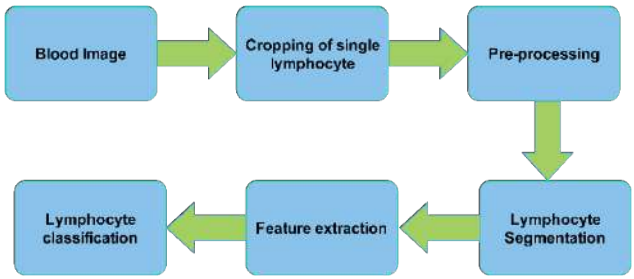


Figure 2. Basic diagram of the system

The input for the system is the Leishman's stained blood slide image, and the lymphocytes in the image are cropped and individuated manually. Firstly in the pre-processing module, the image acquisition noise and background non-uniformities are removed. Secondly image segmentation is performed using a proper segmentation technique. This is done using three consecutive steps of background removal, separating the lymphocytic cell and separating the nucleus region which has been described in this paper. In the feature extraction module, various morphological features are been sorted differently using the segmented regions of the lymphocytic cell and the nucleus. Combining the features of both cell and nucleus, some new features are also calculated. In the lymphocyte classification module the tested cells are labelled as blast or normal.

### A. Image Acquisition

The inputs for this automation process are microscopic images obtained from peripheral blood films which stained by Leishman's that has been obtained from Department of Pathology Clinic at Faculty of Medicine, University of Colombo. All the obtained images are affected from B-ALL precursor which is a major type of ALL. The images are captured from two different camera sources as Huawei GR5 2017 smartphone camera and Canon camera in the same lightning conditions, resolution and magnification. The slides are placed under a MicroTech XSZ-N207 microscope in 100 magnification. 75 of the chosen images are taken into the experiment. Microscopic images acquired from the ALL-IDB (Acute Lymphoblastic Leukemia Image Database) are used as standard. 50 images chosen from ALL-IDB2 database are used.

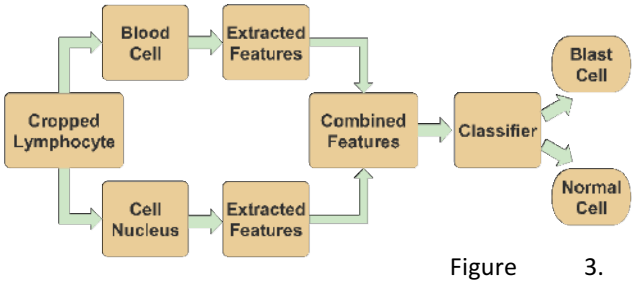


Figure 3. Block diagram of the proposed algorithm

### B. Image pre-processing

Pre-processing is essential as normal images consist of excessive staining and shadows. Image enhancement, which is used to bring out the image details that are obscured is the main task of this stage. Following three main tasks are performed in this stage.

*1) FastNlMeansDenoisingColoured technique:* This is done to remove noise and excess blurriness.

*2) Edge enhancement:* Done in order to sharpen the image by cleaning the cell/cell segments in the boundary of the image.

3) RGB splitting: The RGB image is split in to three channels; green, red and blue in order to identify the red blood cells and white blood cells separately.

4) Removing the green channel: Green channels are mostly sensitive to red blood cells. Thus, it is removed from the image in this step.

### C. Image segmentation

Segmentation process partitions an image to its constituent segments or objects known as pixels. This locates objects and boundaries (curves and lines etc.) of images and modifies the representation of an image into somewhat that is more meaningful and easier to analyse. This is a crucial step as the following feature extraction and classification results are much related with the result of the segmentation module. In this stage the following three steps are under gone.

*1) Background removal:* In this stage, canny filter is first used to reconstruct the border of the cells present in the image. Then morphological operation 'dilation' is done using a prepared structuring element. Then 'closing' is

done. Combing the images obtained from dilation and closing, a new image is obtained. Next, threshold to Zero, Inverted thresholding is performed to the image obtained from pre-processing. Then the resulted image is combined with the new image obtained from morphological segmentation and the background is now removed.

*2) Isolating the lymphocytic cell:* In the resulted image, the largest contour area is considered to be the area of the cell region. The image is then subjected to a combination of binary thresholding and Otsu's thresholding and a binary image of the cell is produced. The total blood cell's binary image is now ready for feature extraction.

*3) Isolating the nucleus:* In this step, firstly the intensity of the original cropped blood image is increased such that only the nucleus will be visible in the image. Then thresholding is done in order to separate the nucleus. Here a combination of binary thresholding and Otsu's thresholding is done. Then the nucleus region is segmented by subjecting the image to the background removal step described earlier. Then the segmented nucleus is converted to binary and it is now ready for feature extraction.

*D. Feature extraction*

In feature extraction, the acquired data from the image is transformed and labelled to a particular set of features, which is going to be used for further classification. The binary equivalent images produced by the segmentation technique of blood cell and cell nucleus are used to extract those morphological features. Using the extracted features of blood cells and nucleus, some combined features also have been calculated. Some of the features that are explored are given below.

Table 1. Parameters Obtained In Feature Extraction

| Feature | Parameters Extracted |
|---|---|
| Colour features | Mean colour values |
| Geometric features | Perimeter, Radius, Area, Compactness, Rectangularity, Convexity, Symmetry, Concavity, Elongation, Eccentricity, Solidity etc. |
| Texture features | Entropy, Energy, Correlation, Homogeneity etc. |
| Statistical features | Skewness, Variance, Mean, Gradient matrix etc. |

*E. Image classification*

For classification, K-Nearest Neighbour classifier is used.

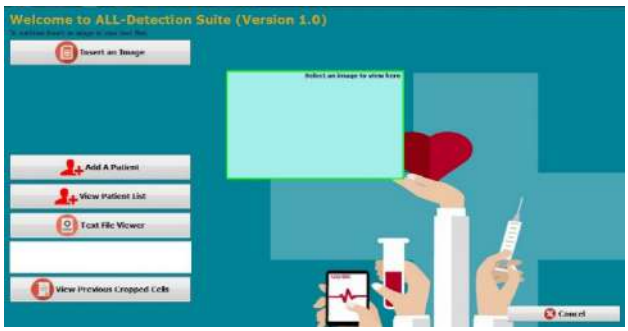


Figure 4. ALL Diagnosing Window

## IV. RESULTS

There are two main objectives that this research is focused on. One is to develop an algorithm to compare the image qualities of purely isolated cells and overlapping cells. Second one is to detect the quality devastation in blood films in terms of storing them for prolonged period. The proposed algorithm was implemented using python programming language using the OpenCV package for python. Following figures depicts a design of user interface and the results that were obtained in the segmentation, feature extraction and classification stages separately.

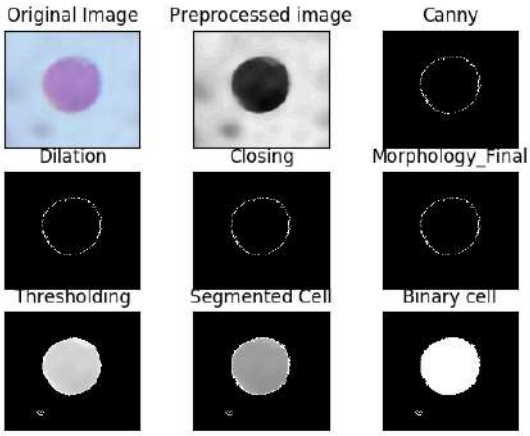


Figure 5. Segmentation results of the cell

Figure 5 elaborates the results of a lymphocyte image used for segmentation stage of the cell. In the figure firstly, original image is shown. The pre-processed image shows the result of the steps FastNlMeansDenoisingColoured technique, Edge enhancement, RGB Splitting and removing the green channel respectively. Next canny, dilation, closing and combination of dilated and closed images, thresholding for pre-processed image and binary image of the cell has been shown.

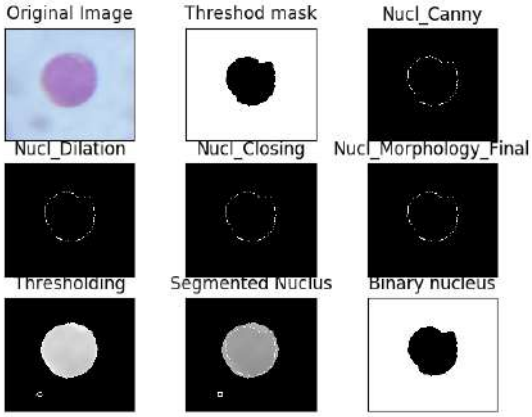


Figure 6. Segmentation results of the nucleus

Figure 6 elaborates the results of the same lymphocyte image used for segmentation stage of the nucleus. In the figure firstly, original image is shown. Then the thresholding mask image shows the result of the combination of the binary and Otsu's segmentation performed. Next canny, dilation, closing and combination of dilated and closed images, thresholding for pre-processed image and binary image of the cell has been shown.

In the feature extraction module, 12 geometric features with regard to the cell and nucleus had been extracted separately. The features extracted are area, perimeter, circularity, diameter, roundness, compactness, nucleus to cell ratio, cytoplasm area, cytoplasm to nucleus ratio, convexity and solidity. The features had been saved in a csv file. Those features extracted with respect to a one lymphocytic cell are depicted in Figure 7. In the classification stage, the features have been fed to the K-Nearest Neighbour classifier. Out of the 75 images used, 35 images have been used for the training the classifier and 40 for testing. The label 1 has been outputted for detected acute leukemic cells and label 0 has been outputted for healthy cells respectively as shown in Figure 7.

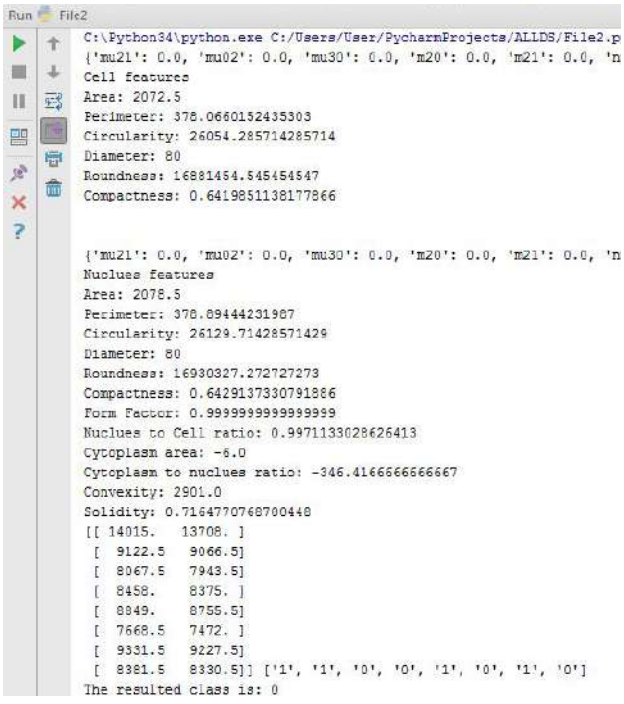


Figure 7. Feature extraction and classification results

The proposed algorithm is been tested and developed to detect features of overlapping cells and to detect the quality devastation that occurs in old blood films when they are kept for 3-6 months.

## V. CONCLUSION AND FURTHER WORK

The developing system will be extended to have good results in automatic diagnosis of the disease in the acquired human blood samples. The proposed algorithm can also be further develop to detect the granules and intra cellular components inside the cell. As per the statistical data published in future spreading of a cancer like leukemia in the world, automation procedures to detect leukemia has become an urgent need. Governments, especially in a developing country like Sri Lanka would find these automatic leukemia detection systems as cost effective solutions to implement in hospitals.

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