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Unsupervised Segmentation Technique for Acute Leukemia Cells Using Clustering Algorithms

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Abstract**—**Leukaemia is a blood cancer disease that contributes to the increment of mortality rate in Malaysia each year. There are two main categories for leukaemia, which are acute and chronic leukaemia. The production and development of acute leukaemia cells occurs rapidly and uncontrollable. Therefore, if the identification of acute leukaemia cells could be done fast and effectively, proper treatment and medicine could be delivered. Due to the requirement of prompt and accurate diagnosis of leukaemia, the current study has proposed unsupervised pixel segmentation based on clustering algorithm in order to obtain a fully segmented abnormal white blood cell (blast) in acute leukaemia image. In order to obtain the segmented blast, the current study proposed three clustering algorithms which are k-means, fuzzy c-means and moving k-means algorithms have been applied on the saturation component image. Then, median filter and seeded region growing area extraction algorithms have been applied, to smooth the region of segmented blast and to remove the large unwanted regions from the image, respectively. Comparisons among the three clustering algorithms are made in order to measure the performance of each clustering algorithm on segmenting the blast area. Based on the good sensitivity value that has been obtained, the results indicate that moving k-means clustering algorithm has successfully produced the fully segmented blast region in acute leukaemia image. Hence, indicating that the resultant images could be helpful to haematologists for further analysis of acute leukaemia.

Keywords**—**Acute Leukaemia Images, Clustering Algorithms, Image Segmentation, Moving k-Means.

I. Introduction

BLOOD is the red fluid that circulates around the body in the circulatory system. One of the main functions of blood is to act as body's defense system against infection and foreign materials. This function is specifically carried out by white blood cells (WBCs). WBC is produced in bone marrow through a complex process which is proliferation, differentiation and maturation.

Discordance between proliferation and differentiation of WBC by bone marrow cause a blood cancer, which is known as leukaemia. This leads to abnormal production of WBCs where they divide and grow in an uncontrolled way [1]. If the abnormality develop and progress rapidly, this is known as acute leukaemia, which tends to affect young children or older adults. Acute leukaemia can be divided into two categories which depend on their cell of origin. Leukaemia evolving from the myeloid/granulocyte cell line is called acute myelogenous leukaemia (AML) while lymphocytic precursors give rise to acute lymphoblastic leukaemia (ALL) [2].

Early detection and classification of acute leukaemia disease can assure high percentage of recovery for that particular type [3]. Therefore, a fast and accurate diagnosis technique is needed. Common technique in screening human blood is by using microscope [4]. Since this is done manually by lab technologies, it is time consuming and the accuracy depends on the operator's capabilities and tiredness [5]. In order to improve the reliability of diagnosis and reduce human dependency is by creating an automated image processing system for acute leukaemia. The performance of the system depends on proper segmentation of images. This is because image segmentation is the most important step in image processing as it will affect the post-processing stage directly.

The purpose of image segmentation is to reduce pixel data to region-based information about the objects and structure present in the image [6]. There are various segmentation methods for blood cell images that have been proposed. Among common methods used are thresholding [7], [8], watershed [9], clustering [10], [11] and mathematical morphology [12]. There are several segmentation methods that have been proposed for blood cells recognition of leukaemia images. Khasman and Al-Zgoul [3] proposed a fast and cost-effective method in identifying different forms or types of leukaemia. The study focused on developing a first phase automated leukaemia form identification system by segmenting the infected cell images. The images will first undergo thresholding in order to separate the cytoplasm and nucleus. Then, the boundaries of both regions are traced out by applying the principle of chain code. After that, the unwanted membrane was eliminated. Region filling will also be applied so that region such as area can be evaluated. Lastly, image restoration was used to the region of interest. This method has been evaluated using 120 images and managed to produce segmented accuracy of 93% to 100% for four different types of leukaemia.

Mohapatra, Patra and Kumar [11] have mentioned the importance of suitable segmentation routines in order to gain better recognition of disease. In achieving the objective, the study has manipulated two clustering methods by integrating both methods in obtaining better segmentation performance. The two clustering methods are fuzzy sets and rough sets. Integration of both methods created the hybrid rough fuzzy c-

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means algorithm for segmenting stained blood sample images of leukocytes. Fuzzy sets held the properties of being able to endow efficient handling while rough sets held the properties of being able to deal with uncertainty. To prove the efficiency of hybrid rough fuzzy c-means algorithm, other standard cluster based segmentation techniques such as k-means, k-medoid, fuzzy c-means and rough c-means have also been tested for comparison. The results show that the proposed method has achieved the lowest overall misclassification error percentage for both Cell 1 and Cell 2 images.

Agaian, Madhukar and Chronopoulos [13] has presented a simple technique for automated detection and segmentation of AML in blood smear. The images have been processed in CIELAB colour features and colour correlation in order to identify myeloblasts. Colour based clustering has been applied in order to extract the nuclei of the leukocytes by choosing clusters corresponding to nucleus, background and others. By using k-means as segmentation method, only the edges of the nuclei were obtained. Therefore, morphological filtering was applied to overcome the problem. After that, texture and shape-based features were extracted from whole images. The computer simulation will include the impact of Hausdorff dimension on the system before and after the influence of local binary pattern. The performance is evaluated by comparing the result for sub images and whole images and also the proposed system as compared to the existing systems. Results show that the proposed system is able to obtain 98% of accuracy by using SVM classification method.

Clustering algorithm is an unsupervised task which able to divide given data set into various non-overlapping of homogenous group. Moreover, it is able to represent image into cluster space. Clustering algorithm such as k-means, fuzzy c-means and moving k-means have proven their capability to produce good medical image segmentation performance [14], [15]. Therefore, this study will analyze the significant of applying these three clustering algorithms on segmenting the acute leukaemia images. The performance of the proposed auto segmentation techniques are evaluated by using pixels subtraction technique and quantitative assessment base on manual segmentation image as reference image.

II. Methodology

The proposed procedures for segmentation of acute leukaemia images are summarized as follows:

1. Capture the acute leukaemia slide images.
2. Extract the saturation component of HSI (hue, saturation, intensity) colour space from the original image.
3. Apply the clustering algorithms which are *k*-means, fuzzy *c*-means or moving k-means algorithms.
4. Apply the 7×7 pixels median filter.
5. Apply the seeded region growing area extraction algorithm [16].

Further details for image acquisition and segmentation of acute leukaemia images using the three clustering algorithms are discussed in the following sections.

A. Image Acquisition

The first step is to acquire the image of acute leukaemia blood samples. Both ALL and AML slides were provided by Hospital Universiti Sains Malaysia (HUSM). The acute leukaemia slides were analyzed using Leica DLMA microscope at 40X magnification. The 100 images were captured using Infinity-*2* digital camera at a resolution setting of 800×600 pixels and saved in bitmap (*.bmp).

B. Saturation Component Based On HSI Colour Space

In this study, the colour image segmentation for acute leukaemia images is performed based on HSI colour model. In general, the HSI colour model represents every colour with three components, which are hue (H), saturation (S) and intensity (I). Hue is a colour attribute that describes a pure colour, whereas saturation component measures the degree of white light added to pure colour. The intensity expresses the brightness of the hue and saturation [17]. Based on observation of several blood images, it is found that the *S* component image gives the best contrast in terms of saturation value between the blast and the unwanted regions in acute leukaemia image. These unwanted regions are referred to the normal RBCs and background. In addition, the normal RBCs region is less saturated in *S* component image hence decreasing its visibility. Therefore, the *S* component image is used for further segmentation process. The saturation formula can be applied on acute leukaemia image by using (1) [17].

$$Saturation = 1 - \frac{3}{R+G+B}\min(R,G,B) \tag{1}$$

C. Blast Segmentation Using Various Clustering Algorithms

After the *S* component information has been extracted from the RGB image, the next step is to segment the blast in acute leukaemia image. In order to automate the segmentation of acute leukaemia image, the current study will utilize the potential of unsupervised pixel segmentation based on clustering algorithm. In this study, three clustering algorithms which are k-means (KM), fuzzy c-means (FCM) and moving k-means (MKM) clustering are applied on saturation component image in order to perform the segmentation process. The three clustering algorithms will perform the segmentation process by segmenting the blast from the red blood cells (RBCs) and background regions in acute leukaemia image. Comparisons among the three clustering algorithms will be made in order to measure the performance of each clustering algorithm on segmenting the blast area.

In order to apply the three clustering algorithms which are KM, FCM and MKM algorithms, consider an acute leukaemia image with resolution of $X \times Y$ pixels to be clustered into nc regions. Let $p(x,y)$ as an input pixel to be clustered and c_j is the j-th centre (cluster) (x = 1, 2, …, X, y = 1, 2, …, Y and j = 1, 2, …, n_c). During performing the clustering process, each data will be clustered into 3 groups which representing the blast, RBCs and background regions. Based on these considerations, KM, FCM and MKM clustering algorithms can be implemented as described in the following sections.

1) *k*-Means Clustering Algorithm

KM is a clustering method which is one of the most popular unsupervised learning algorithms due to its simplicity. The KM clustering algorithm for image segmentation can be carried out as follows [18]:

a. Initialize the centres.
b. Assign each data to the nearest centre.
c. When all data have been assigned, recalculate the new centre position using (2):

$$c_j = \frac{1}{n_{c_j}} \sum_{i \in c_j} x_i \tag{2}$$

d. Repeat steps (b) and (c) until the centres are not significantly moved.

2) Fuzzy *c*-Means Clustering Algorithm

FCM algorithm was developed by Dunn in 1973, and improved by Bezdek in 1981. FCM clustering minimizes the following function as in (3) [19]:

$$E = \sum_{j=1}^{n_c} \sum_{i=1}^{N} M_{ij}^m \left\| v_i - c_j \right\|^2 \tag{3}$$

where, M_{ij} is the partition matrix, which represents the degree of membership between each data sample and all centre . N is the number of data, n_c is the number of cluster, v_i is i-th sample of data and c_j is j-th center of cluster. The value of m (a real number greater than one) will control the fuzziness of the membership function. The FCM clustering algorithm for image segmentation can be carried out as follows [19]:

a. Initialize the centres.
b. Calculate membership function, according to (4) and (6).

$$M_{jp(x,y)} = 1 \Big/ \sum_{k=1}^{n_c} \left(d_{jp(x,y)} / d_{kp(x,y)} \right)^2 \tag{4}$$

where,

$$d_{jp(x,y)} = \left\| p(x,y) - c_j \right\| \text{ and } d_{kp(x,y)} = \left\| p(x,y) - c_k \right\|$$

$$\left.\begin{matrix} M_{kp(x,y)} = 1 \\ M_{jp(x,y)} = 0; \text{for } p(x,y) \neq k \end{matrix}\right\} \text{if } d_{kp(x,y)} = 0 \tag{5}$$

c. Calculate the centre positions using:

$$c_j = \sum_{y \in c_j} \sum_{x \in c_j} M_{jp(x,y)}^2 p(x,y) \Big/ \sum_{y \in c_j} \sum_{x \in c_j} M_{jp(x,y)}^2 \tag{6}$$

d. Repeat steps (b) to (c) until there is no significant change in the centre positions.

3) Moving *k*-Means Clustering Algorithm

In 2000, Mashor [20] proposed a modified version of KM clustering algorithm called Moving *k*-means clustering algorithm. The MKM clustering algorithm is capable to avoid the dead centres and centre redundancy problems. In addition, this algorithm has been proven to be effective in reducing the effect of the centre from being trapped in poor local minima. The MKM clustering algorithm for image segmentation can be carried out as follows [20]:

a. Initialize α_0, and set $\alpha_a = \alpha_b = \alpha_0$ (where α_0 is a small constant value, $0 < \alpha_0 < 1/3$ and should be chosen to be inversely proportional to the number of centres).
b. Assign all pixels to the nearest centre and calculate the centre positions using:

$$c_j = \frac{1}{n_j} \sum_{y \in c_j} \sum_{x \in c_j} p(x,y) \tag{7}$$

c. Check the fitness of each centre using:

$$f(c_j) = \sum_{y \in c_j} \sum_{x \in c_j} \left(\left\| p(x,y) - c_j \right\| \right)^2 \tag{8}$$

d. Find c_s and c_l, the centre that has the smallest and the largest value of f(.).
e. If $f(c_s) < \alpha_a f(c_l)$,
 i. Assign the members of c_l to c_s if $p(x,y) < c_l$, where $x,y \in c_l$, and leave the rest of the members to c_l.
 ii. Recalculate the positions of c_s and c_l according to:

$$c_s = \frac{1}{n_s} \sum_{y \in c_s} \sum_{x \in c_s} p(x,y) \tag{9}$$

$$c_l = \frac{1}{n_l} \sum_{y \in c_l} \sum_{x \in c_l} p(x,y) \tag{10}$$

Note: c_s will give up its members before step 5a and, n_s and n_l in (9) and (10) are the number of the new members of c_s and c_l respectively, after the reassigning process in step 5a.

f. Update α_a according to $\alpha_a = \alpha_a - \alpha_a / n_c$ and repeat steps 4 and 5 until $f(c_s) \geq \alpha_a f(c_l)$
g. Reassign all pixels to the nearest centre and recalculate the centre positions using (7).
h. Update α_a and α_b according to $\alpha_a = \alpha_0$ and $\alpha_b = \alpha_b - \alpha_b / n_c$ respectively, and repeat steps (b) to (g) until $f(c_s) \geq \alpha_b f(c_l)$.

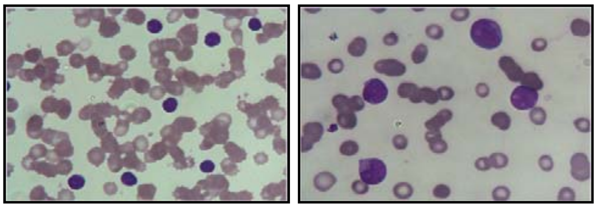
D. Image Filtering Using Median Filter Algorithm

After the segmented image has been obtained using clustering algorithm, the output image is then filtered using median filter. The *7×7* pixels median filter is applied in order to smooth the surface of the segmented blast, as well as to remove any salt and pepper noise from the image.

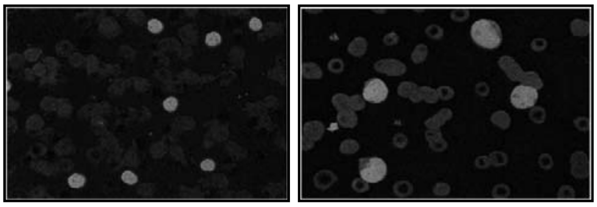
E. Seeded Region Growing Area Extraction Algorithm

After the clustering and filtering process have been performed on acute leukaemia image, there is a tendency for the unwanted regions such as segmented RBCs and platelet to be appeared on the segmented image. This is due to the properties such as colour and size in which these unwanted regions shares with the blast. Therefore, these unwanted regions should be removed from the image in order to enhance the segmentation performance as well as to avoid miss-diagnosis of the blast in further classification process. In order to reduce this problem, a modified version of conventional seed based region growing algorithm namely seeded region growing area extraction (SRGAE) [16] algorithm is applied on the segmented image.

This algorithm is applied for the two main purposes. First is to calculate the total area in pixels for the region of interest (ROI). Secondly is to remove any unwanted regions that are bigger in size in which cannot be cleaned by using the 7×7 pixels median filter. The size of the blast is one of the important morphological characteristics that can be used to verify whether the segmented blast can be considered as either ALL or AML. Therefore, the selection of ROI in SRGAE algorithm is determined based on its size. Based on analyses of the blast in several acute leukaemia images, it has been found that the size of the blast in both ALL and AML images are more than 1000 pixels. Thus, any segmented regions which are less than 1000 pixels are considered as non-blast and will be removed from the image during region growing process.



(a) (b)



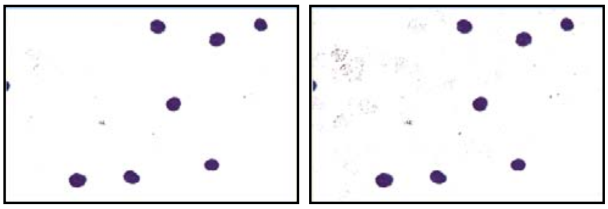
(d) (e)

Fig. 1 (a) Original ALL image, (b) original AML image, (c) *S* component on original ALL image and (d) *S* component on original AML image

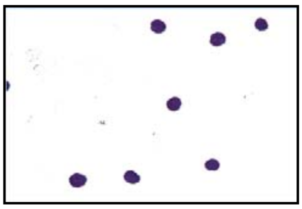
III. Results and Discussions

In this study, the proposed procedures for segmentation of acute leukaemia images have been applied and tested on 50 ALL and 50 AML images. Comparisons in terms of providing good segmentation performances have been made among the three different clustering algorithms which are KM, FCM and MKM algorithms. Figs. 1 (a) and (b) show the original images of ALL and AML, respectively. In order to perform segmentation on acute leukaemia image, the *S* component information has been extracted from the original RGB image. The *S* component images that have been extracted from original ALL and AML images are shown in Figs. 1 (c) and (d), respectively. Based on these images, the blasts appeared as the brighter part of the image (high *S* region), while the RBCs and background regions appeared as the darker part of the image (low S region). Therefore, the extraction of *S* component information will ease the clustering process as the appearance of the RBCs regions are slightly highlighted in the *S* component image.

Then, the three clustering algorithms which are KM, FCM and MKM algorithms have been applied on the *S* component image for segmenting the blast from the RBCs and background regions. The results obtained after applying the three clustering algorithms are shown in Figs. 2 and 3. Here, (a), (b) and (c) represent the resultant images of KM, FCM and MKM algorithms, respectively. Based on these resultant images, it can be seen that the three clustering algorithms are able to cluster the ALL and AML images into three main regions which are blast, RBCs and backgrounds regions. By referring to the resultant KM images, it can be seen that these images have less unwanted regions as compared to the resultant images of FCM and MKM algorithms. However, by observing the single segmented blast region of AML as shown in Fig. 4, the KM algorithm is unable to provide fully segmented blast especially on the cytoplasm area as compared to FCM and MKM algorithms.

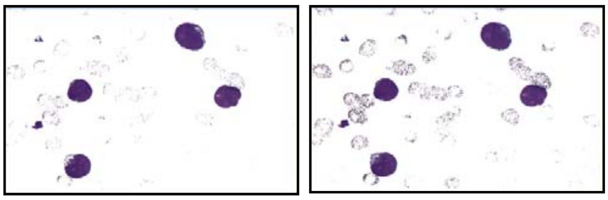


(a) KM (b) FCM

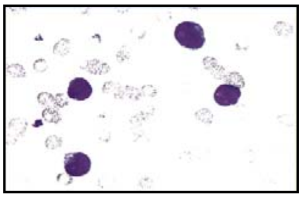


(c) MKM

Fig. 2 Results of images for ALL after applying the three clustering algorithms on *S* component image

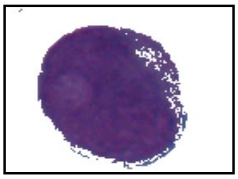


(a) KM (b) FCM

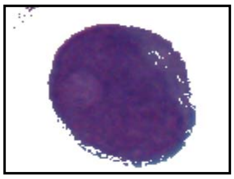


(c) MKM

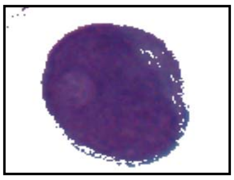
Fig. 3 Results of images for AML after applying the three clustering algorithms on *S* component image



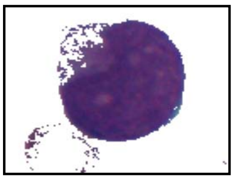
(a) KM



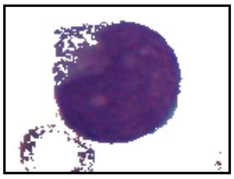
(b) FCM



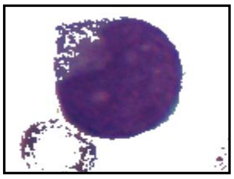
(c) MKM



(d) KM



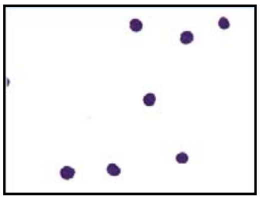
(e) FCM



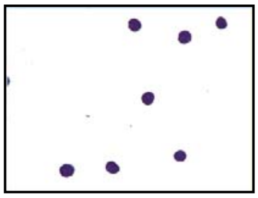
(f) MKM

Fig. 4 A single segmented blast in AML image

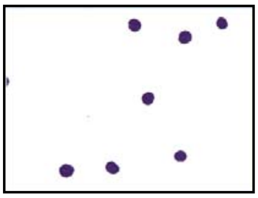
Even though segmentation using clustering algorithm is able to segment the blast in the image, however some unwanted regions such as segmented RBCs can still be seen in the image. Therefore, these images are further process with median filter and SRGAE algorithms in order to remove the unwanted regions from the image. Figs. 5 and 6 show the results of images after filtering the resultant clustering images using 7×7 pixels median filter. By filtering the image, most of the small background pixels have been removed. However, some unwanted regions which are bigger in size can still be seen in the image. In order to give better visualization results, the SRGAE algorithm has been further applied. Figs. 7 and 8 represent the resultant images after applying the SRGAE algorithm. By using the SRGAE algorithm, it can be seen that this algorithm can remove the large unwanted regions which area is less than 1000 pixels from the image, as compared to the resultant images that have been filtered using 7×7 pixels median filter. As a result, a clean segmented acute leukaemia image has been obtained by applying the combination of median filter and SRGAE algorithms.



(a) KM



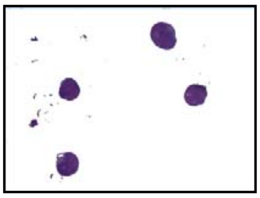
(b) FCM



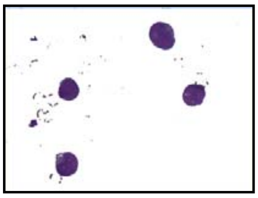
(c) MKM

Fig. 5 Results of images for ALL after applying median filter to the three clustering images

(a) KM

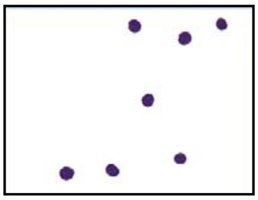


(b) FCM

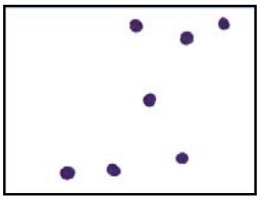


(c) MKM

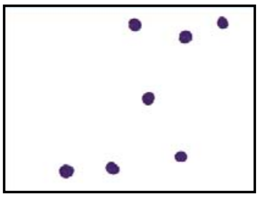
Fig. 6 Results of images for AML after applying median filter to the three clustering images



(a) KM

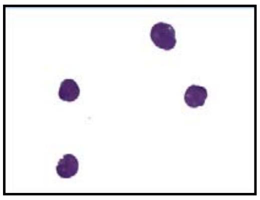


(b) FCM

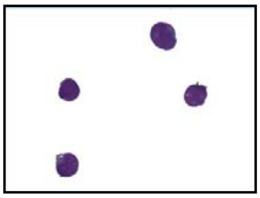


(c) MKM

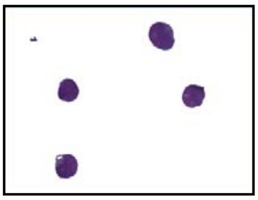
Fig. 7 Results of images for ALL after applying median filter and SRGAE algorithms to the three clustering images



(a) KM



(b) FCM



(c) MKM

Fig. 8 Results of images for AML after applying median filter and SRGAE algorithms to the three clustering images

In order to determine the quality of segmented image that have been produced using KM, FCM and MKM clustering algorithms, the assessment is performed based on pixels similarity by comparing the resultant segmented image against the manual segmented image. Table I shows the comparison of segmentation performances for 100 segmented acute leukaemia images, with a total of 50 images for each type of ALL and AML. In order to compare segmentation performance among the three clustering algorithms, this study has focused on the sensitivity value that has been obtained. This is mainly because the higher the sensitivity values of the segmented image, the better the clustering algorithm in segmenting the blast area in acute leukaemia image. Based on the segmentation performance of 100 acute leukaemia images, MKM clustering algorithm has proven to be the best in producing fully segmented blast area with sensitivity value of 86.18% as compared to segmentation results provided by KM and FCM algorithms with sensitivity values of 84.04% and 85.78%, respectively.

TABLE I
SEGMENTATION PERFORMANCES BASED ON SENSITIVITY, SPECIFICITY AND ACCURACY FOR 100 ACUTE LEUKAEMIA IMAGES

Clustering Algorithm	Analysis	Segmentation Performance (%)		
		ALL (50 Images)	AML (50 Images)	Average of 100 Images
KM	Sensitivity	87.08	81.00	84.04
	Specificity	99.72	99.23	99.48
	Accuracy	98.72	97.80	98.26
FCM	Sensitivity	89.35	82.21	85.78
	Specificity	96.17	98.26	97.21
	Accuracy	95.71	96.90	96.31
MKM	Sensitivity	89.96	82.40	86.18
	Specificity	97.13	98.72	97.92
	Accuracy	96.59	97.45	97.02

IV. CONCLUSIONS

This paper has proposed unsupervised pixel segmentation based on clustering algorithm for segmenting the blast in ALL and AML images. Three different clustering algorithms which are KM, FCM and MKM algorithms have been utilized in order to compare the performances of these clustering algorithms. The performances of these clustering algorithms have been analyzed qualitatively and quantitatively. Qualitatively, it can be seen that segmentation using MKM algorithm has proven to be the best in obtaining the fully segmented blast as compared to the results provided by KM and FCM clustering algorithms. Quantitatively, based on the best sensitivity value that has been obtained, a more convincing segmentation performance in segmenting the blast in acute leukaemia image has been achieved by using MKM algorithm as compared to KM and FCM algorithms. Thus, it is proven that MKM clustering algorithm has better performance for segmentation of acute leukaemia images. From the proposed segmentation technique, the features of AML and ALL slides images such as shape and cells size are able to be revealed. These features are essential in distinguishing the difference between ALL and AML images for further analysis by haematologists.

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