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Blood Cancer Cell Classif cation based on Geometric Mean Transform and Dissimilarity Metrics

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ABSTRACT

Blood cancer is an umbrella term for cancers that affect the blood, bone marrow and lymphatic system. There are three main groups of blood cancer: leukemia, lymphoma and myeloma. Some types are more common than others. In this paper, a new image transform based on geometric mean properties of integral values in both horizontal and vertical image directions is proposed for leukemia cancer cell classif cation. Available classif cation methods using the classical feature extraction methods which are sensitive to rotation and deformation of the blood cells. The new transform is based on geometric mean projection, which —unlike other image transforms, such as Radon transform— is not considered all signals in an image with the same signal acquisition rate. Instead, it is general and thus applicable to all capturing signal functions to achieve suff cient invariant features. The geometric mean projection transforms (GMPT) guarantees that the detector only extracts the highly informative information from the object to achieve an invariant feature vector for an accurate classif cation process. This method has been used as cancer cell identif cation using microscopic Imagery analysis in this study. Dissimilarity metric calculation and shape analysis by using image transform has been used to extract the feature vectors of the imagery. Then, the accumulated feature vectors have been classif ed to different classes by using artif cial neural network (ANN). The proposed technique has been evaluated in the standard images sourced from USIM, Malaysia. The evaluation results indicate the robustness of the technique in different types of images available in the dataset.

Keywords: Cancer cell classification Image transform, Image processing, Pattern recognition

INTRODUCTION

The feature extraction and dissimilarity metrics have their applications in various f elds such as medical image analysis (Ismail, Hassan, & Swift, 2010; Sotiras, Davatzikos, & Paragios, 2013; Sun, Zhou, & Yang, 2012), ownership identif cation (Emami & Omar, 2010), Jawi character recognition (Nasrudin, Omar, Liong, & Zakaria, 2009) license plate recognition (Ashtari, Nordin, & Kahaki, 2011) and medical image classif cation (Hazra, Chowdhury, & Dutta, 2016). Image Classif cation is the process of identifying the objects based on their features and properties (Vennila & Gnanamurthy, 2016). Therefore, feature extraction as a basic process of medical image analysis can affect the f nal classif cation rate. Moreover, dissimilarity measurement is a fundamental task in image processing and computer vision which can affect the f nal results signif cantly (Kahaki, Nordin, Ashtari, & Zahra, 2016). Thus, improvement in these basic processes can lead the algorithms to achieve the results in a robust and eff cient manner.

Recently, considering the unique information as features extracted from medical images can be used to extract useful information such as cancer cells from medical images to assist and improve patient diagnosis (Ismail, 2012). The diagnosis of AML and its subtypes is based on the morphological analysis of peripheral blood and bone marrow (Hassan, 1996). In 1971, the diagnosis of leukaemia cells was based on their morphology and according to (Gunz, 1960) in (Hassan, 1996) it has been correct in just 70% of examinining cases. In the early 1980, 90% of acute leukaemia cases could be correctly classif ed as ALL and AML based on the French-American-British (FAB) classif cation system, prior to development of immunophenotyping (Hassan, 1996). Piuri and Scotti (2004) have concentrated on using the nucleus for classif cation through image segmentation. The sample images are extracted from an accredited image repository, the Atlas of Blood Cells Differentiation, which is highlighted by (Piuri & Scotti, 2004). Zamani and Safabakhsh (2006) proposed a colour gradient method to smooth the image is employed instead of using gray scale before applying a Gradient Vector Flow (GVF) snake based method. Scale-space f ltering and the watershed algorithm was applied to colour images for detecting nuclei by Jiang, Liao, and Dai (2003). Another technique using eigen cells for detecting white blood cells was introduced by Yampri, Pintavirooj, Daochai, and Teartulakarn (2006), but their study had limited success in correctly classify all of the white blood cells and in the case of overlapping cell there can be some weakness. Ritter and Cooper (2007) introduced a histogram of pixel counts focusing on the touching cells and an edge cutting algorithm was then applied to separate the cells. This technique can be used for touching cells but not for overlapping cells. The technique is not possible to use in this project because cutting the cells will create different morphological features which might lead to incorrect classif cation. Circle detection has been performed using genetic algorithms and sobel's method by Ayala-Ramirez, Garcia-Capulin, Perez-Garcia and Sanchez-Yanez (2006) which detected circlers, but not morphological features. Particle Swarm Optimization combined with Neural Networks was used to escape from a local optimum in an application for detecting the colour nucleus in large-scale image data by (Fang, Y., Pan, Liu, & Fang, L., 2005). Sarrafzadeh, Rabbani, Dehnavi, & Talebi (2015) proposed a novel method based on dictionary learning and sparse representation for detecting and classif cation of different sub-types of AML. For each class, two intensity and

label dictionaries are designed for representation using image patches of training samples. New image is represented by all dictionaries and the one with minimum error determine the type of class. The combination between linear contrast technique and colour segmentation based on HSI (Hue, Saturation, Intensity) colour space were used by (Nasir, Mashor, & Rosline, 2011) in order to obtain a fully segmented abnormal WBC and nucleus of acute leukaemia images. The unsupervised segmentation technique namely k-means clustering algorithm is used to ease the segmentation process (Nasir et al., 2011).

Dissimilarity measurement techniques can be used to classify the cancer cells. The most common dissimilarity measure methods include correlation coeff cient (Zhang, Deriche, Faugeras, & Luong, 1995), sum of absolute differences (SAD) (Tomasi & Kanade, 1992) and normalized cross correlation (NCC) (Nakhmani & Tannenbaum, 2013). These methods are not robust under different image deformation, especially in medical image analysis while they using point to point distance measurement of the gray level values. Previously, we optimized the mutual information measurement technique to improve the performance (Kahaki et al., 2016). In this research, we intend to investigate the information theory formulation for a new fundamental dissimilarity measure algorithm on classif cation problem and we expected to speed up and improve the performance. On the other hand, medical image analysis algorithms have signif cant dependencies to dissimilarity measurement of the features to achieve robust results under different image deformations (Sotiras et al., 2013). Feature extraction can achieve using image transform methods. One of the common image transform methods is Radon transform (Deans, 2007) which is an integral based transform using an image rotation algorithm. Radon transform is sensitive to local variation and only used single integral based function for signal acquisition. We have solved this problem using proposed mean projection transform (Kahaki, Nordin, & Ashtari, 2014) by calculating the integral values in different contour directions which shows better performance compared to recent approaches. However, the proposed method is not fast enough for real-time applications and performed based on object rotation for signal acquisition.

In this research, we intend to develop new high performance shape transform for feature extraction which is not only robust to local variation of the shape but also fast for real time needs especially for medical technology applications. The output of this research can be used in cell classif cation which is an important issue in medical image analysis while it can automatically specify or identify the region of interest in medical imagery. Therefore, the results can be used to ease the experts in classifying and determining the cancer cells in medical images. The region of interest for localization can be a cancer tissue in Pathobiology images, brain tumor in the MRI images, a crack of bone in radiology images, or text characters in a manuscript (Nasrudin et al., 2009; Redika, Omar, & Nasrudin 2008).

Dissimilarity metrics and shape analysis are employed in different algorithm as a main topic in computer vision and image analysis. It refers to the problem of extracting signif cant features of the objects inside a digital imagery such as cancer cells in microscopic medical images in order to compare the features. Numerous related methods have been introduced over the last several decades. Further research in medical image analysis is expected to improve patient care, contributing to areas such as personalized medicine with individually tailored treatment, increasing evidence-based decision making within healthcare, reducing complications during

and after surgery, and allowing a better understanding of the effects of treatments in various diseases (Ismail, 2012). Image processing in medical research is becoming a subject of prime focus due to its tremendous potential for the public health sector and the scientif c community in general. In particular, imaging applications are emerging as a new opportunity for innovation at the meeting point between medicine and computer science. Many software and research groups focus on the development of image processing applications for medical images, for example to improve feature extraction and produce an effective cancer cells classif cation (Cai et al., 2015). Collaboration with clinicians has allowed the extraction of useful information contributing to more eff cient diagnosis, especially in the treatment and study of cancer (Pak, Kanan, & Alikhassi, 2015).

Dissimilarity metrics and image transforms are fundamental process in image processing and medical image analysis f elds. These processes play an important role as one of the critical issues in medical image processing to perform diagnosis in a minimally invasive procedure. The basic process for cancer cells identif cation is to extract cell features from microscope imagery and compare the properties by using dissimilarity metrics. Previously, we improved the existing dissimilarity metrics and image transforms to achieve more accurate results using newly proposed methods (Kahaki et al., 2014; Kahaki et al., 2016).

The aforementioned methods are based on original properties of the shape contour which is not strong enough to classify the cancer cells in medical imagery due to their similar shape properties. Moreover, existing similarity measurement techniques, such as normalized cross correlation (NCC), squared sum of intensity differences (SSD) and correlation coeff cient (CC), are insuff cient for achieving adequate results under different imaging conditions. The f rst objective of this research is to introduce a robust and invariant dissimilarity metric based on mutual information. The proposed improvement of mutual information is conducted based on information theory formulation to overcome the limitation of the existing methods. Moreover, to expand the projection based shape descriptors to capture the image signals in high entropy directions, a new robust image transform is proposed. This transform used as a feature descriptor to improve the classif cation rate as the next objective. Aforementioned algorithms are expected to achieve more accurate and eff cient results in medical image analysis compare to existing methods. The signif cance of the output of this research is its applications in several different f elds, including classif cation and other medical image analysis tasks.

MATERIALS AND METHODS

In most people's minds there is no more frightening disease than cancer, often viewed as an untreatable, unbearable, and painful disease with no cure. Indeed, it is a serious, potentially life-threatening illness (King & Robins, 2006). Leukaemia is a type of blood cancer. The f rst accurate description of leukaemia was performed by Velpeau in 1827 (Olson, 1989; Velpeau, 1827). There are four general types of leukaemia, namely acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL) and chronic myeloid leukaemia (CML). This research focuses on AML, a serious illness caused by the abnormal growth and development of early nongranular white blood cells. Clinicians have to identify these abnormal cells under a microscope, in order to decide if a patient with suspected

leukaemia would need a bone marrow transplant. In addition, they have to calculate the number of blast cell to conf rm the diagnosis (Yi, Chongxun, Chen, & Li, 2006). Extracting the features and classify them based on dissimilarity metrics can achieve an automatic diagnostic system in medical image analysis f eld. Therefore, the structure of automatic cancer diagnostic system contains two main components which are feature extraction based on shape analysis and classif cation by using dissimilarity metric comparison. Review of the pertinent literature indicates that the performance strongly depends on the information produced by the feature extraction steps and the dissimilarity metric properties. Therefore, an invariant dissimilarity metric should be able to generalize the algorithm to all methods to achieve adequate result. Based on the extant literature, the most commonly used dissimilarity metrics considered are: normalized cross-correlation (NCC), zero-mean normalized cross-correlation (ZNCC), sum of square differences (SSD) and cross-correlation (CC). In computer vision applications in which the image brightness may change in both the source and the target image, the image can be normalized to achieve better performance (Khokhlov, Fischer, & Rittel, 2012). NCC is the correlation similarity method which is widely used in image registration applications and is def ned below.

$$NCC = \frac{\sum_{i=1}^{m} \sum_{j=1}^{n} r_{i,j} . t_{i,j}}{\sqrt[2]{\sum_{i=1}^{m} \sum_{j=1}^{n} r_{i,j}^2 + \sum_{i=1}^{m} \sum_{j=1}^{n} t_{i,j}^2}} \qquad (1)$$

There are several disadvantages to using NCC [35, 36]: If the position of the image energy changes, NCC can fail (Long, Fu, & Han, 2009; Wang, C., Jin, Yang, & Wang, B., 2011). NCC is sensitive to the image amplitude due to, for example, lighting changes in image sequences (Wang et al., 2011; Long et al., 2009). The correlation coeff cient or ZNCC overcomes these diff culties by normalizing the image and feature vectors to unit length, yielding a cosine-like correlation coeff cient. When the mean of both r and t patches is affected in normalized cross- correlation, better results in different grey level intensities can be obtained. This approach also makes the measurement more robust to lighting effects on the images, which can be def ned as [35]:

$$ZNCC = \frac{\sum_{i=1}^{m} \sum_{j=1}^{n} (r_{i,j} - \bar{r}) . (t_{i,j} - \bar{t})}{\sqrt[2]{\sum_{i=1}^{m} \sum_{j=1}^{n} (r_{i,j} - \bar{r})^2 + \sum_{i=1}^{m} \sum_{j=1}^{n} (t_{i,j} - \bar{t})^2}} \qquad (2)$$

The expression above is bias invariant, and is thus widely used in the estimation of the CC. If there is a linear relationship between the two sets of grey level values in the source and target images, ZNCC is more eff cient than NCC (Chambon & Crouzil, 2011), however, it may fail under high image amplitude changes.

The most common pixel-based matching cost is sum of squared intensity differences (SSD) proposed by Hannah (1974). As its name suggests, in the SSD dissimilarity metric, the

differences are squared. Thus, its computational complexity is higher compared to the sum of absolute differences (SAD) method, as it includes several multiplication operations.

$$SSD(r,t) = \sum_{i=1}^{i=m} \sum_{j=1}^{j=n} (r_{i,j} - t_{i,j})^2 \tag{3}$$

Cross-correlation-based Measures: The cross-correlation-based similarity metrics are based on scalar products and are thus also referred to as 'sliding dot product' or 'sliding inner-product'. They have many applications in pattern recognition and signal processing. The similarity-based correlation for discrete functions *f* and *g* can be def ned as:

$$f * g(n) = \sum_{m=-\infty}^{\infty} f[m]g[m+n] \tag{4}$$

Cross-correlation is common technique, as it is used to measure the degree to which different data series are correlated (Yu, Lou, Qian, & Wu, 2008). Some of the techniques used to calculate the image similarity are described. CC similarity measure is based on the sum of squared differences. Considering r and t as the reference and the target images, the difference between r and t can be found using the sum of squared differences in non-discrete cases by applying the following expression:

$$mismatch\ similarity = \iint (r-t)^2, $$
$$\iint (r-t)^2 = \iint r^2 + \iint t^2 - 2 \iint r.t \tag{5}$$

Clearly, as the mismatch similarity needs to be at the minimum in order to achieve the maximum similarity, the $\iint r.t$ needs to be maximized. Thus, $\iint r.t$ can be considered as similarity and be written as cross-correlation as follows:

$$match\ similarity = \iint r.t \tag{6}$$

In the discrete format, it can be expressed as:

$$CC = \sum_{i=1}^{m} \sum_{j=1}^{n} r_{i,j}.t_{i,j} \tag{7}$$

Cross-correlation can be used only in normalized form, and is thus known as normalized CC similarity metric (Chambon & Crouzil, 2011).

Given two sets of features $R = \{r_i\}_{i \in [1,n]}$ and $T = \{t_j\}_{j \in [1,k]}$ as reference and target features, the correspondence problem is to f nd a set C:R   T of correspondence pairs *m(r,t)* def ned as:

$$\tag{8}$$

With dissimilarity equation

$$= \quad = \tag{9}$$

where $r \in R$ and $t \in T$ are the feature vectors, $D_s(r,t)$ represented the dissimilarity index between r and t, and l is the threshold value. Existing dissimilarity algorithms are not suff cient for complicated f elds such as cancer cell images which has deformable objects. We intend to employ the information theory functionality to solve this issue to achieve an eff cient and robust algorithm.

The next process of the classif cation is to extract the features from the input images which performed based on image transform. Image transforms can be simple arithmetic operations on images or complex mathematical operations which convert images from one representation to another. A new image transform based on geometric mean properties of integral values in both horizontal and vertical image directions is proposed. The new transform is based on geometric mean projection, which —unlike other image transforms, such as Radon transform— is not considered all signals in an image with the same signal acquisition rate. Instead, it is general and thus applicable to all capturing signal functions to achieve suff cient invariant features. The geometric mean projection transforms (GMPT) guarantees that the detector only extracts the highly informative information from the object to achieve an invariant feature vector for an accurate classif cation process. Considering $F(X) = f(x, y)$ as the function of the image signal S in R, then GMPT is a function transform of S, where the geometric mean of the horizontal and vertical integral is calculated by using the proposed Equation (11):

$$GMPT = \prod_{i=1}^{n} \left(\int_{Sx} F(x, y) |dx|, \int_{Sy} F(x, y) |dy| \right) \tag{10}$$

To parametrize of any signal with respect to the arc-length and the Euclidean distance from the origin to S, GMPT can be written as:

$$\left(x(t), y(t) \right) = \prod \left[\left(t \sin(\alpha) + s \cos(\alpha) \right), \left(-t \cos(\alpha) + s \sin(\alpha) \right) \right] \tag{11}$$

Where is the angle of the vector, and (, s) are the transform parameters on $\Re^2$ for all signals, and GMPT can be represent in the aforementioned coordinates according to Equation (5):

$$GMPT = \prod_{i=1}^{n} \left(\int_{-\infty}^{+\infty} F(x(t), y(t)) |dx|, \int_{-\infty}^{+\infty} F(x(t), y(t)) |dy| \right) \tag{12}$$

RESULTS

The GMPT calculates the geometric mean of the integrals of an input image function in vertical and horizontal directions to calculate the feature vector matrix of each object. The result of feature vector calculated by using GMPT transform presented in Figure 1.
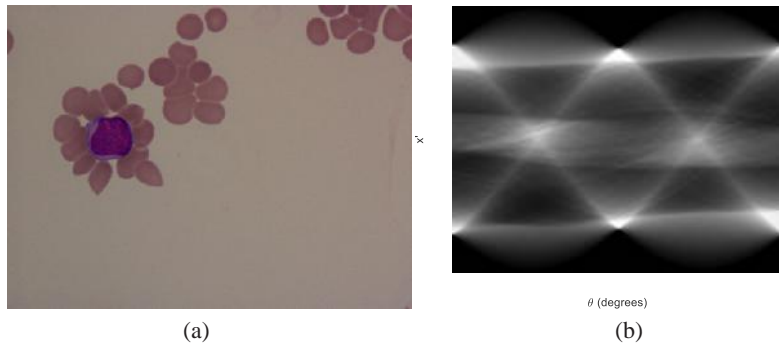

(a)   (b)

Figure 1. (a) Leukaemia Cancer Cells. (b) GMPT transform result

The data consists of 322 real images, 1280 by 960 pixels in size, all from patients suffering from AML. They were provided by the Department of Hematology in the Universiti Sains Malaysia (USM) in Kota Bahru, Kelantan, Malaysia. The subtypes described in the study are M1, M2, M3 and M5. The images were taken with the same lighting and contrast but different microscope zoom magnif cations of 100x, 40x and 60x (23).

The blood cells were extracted after the segmentation stage for classif cation in this study. The result of classif cation of different blood cells is presented in Figure 2. The result of classif cation using ANN indicates that the proposed method can successfully classify most of the blood cells in the available dataset.
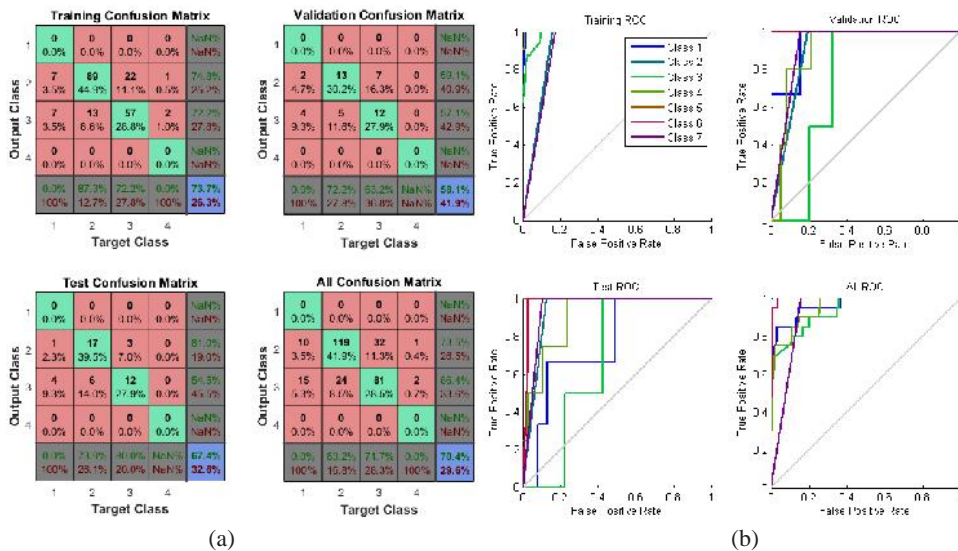

(a)   (b)

Figure 2. (a) Classif cation result. a) Confusion matrix, b) Receiver operator curve performance

Figure 2(a) present the confusion matrix of the ANN to classify four different leukaemia classes. The overal result for all classes achieved 70.4% of classif cation rate in general. Figure 2(b) presents the ROC plot for different classes in different stages such as training, validation, test and all ROC result. As depicted in Figure 2(b), all ROC plot indicates a high true positive rate and low false positive rate for all classes. This indicates a high sensitivitiy of the proposed method in deteting different types of canser cells in digital images.

CONCLUSION

Combination of the dissimilarity metrics and the geometric mean projection transforms to identify and classify different leukemia cells indicates a high classif cation performance for cancer cell identif cation. The result of classif cation for different cancer classes demonstrates higher rate for f nal stages of the process. The average result indicates that the proposed method is a reliable method for cancer cell identif cation in the available dataset.

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