Micron 56 (2014) 17–28

Contents lists available at ScienceDirect

Micron

journal homepage: www.elsevier.com/locate/micron

A novel algorithm based on visual saliency attention for localization and segmentation in rapidly-stained leukocyte images

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ARTICLE INFO

Article history:
Received 2 January 2013
Received in revised form
25 September 2013
Accepted 25 September 2013

Keywords:
Average absolute difference
Cytoplasm enhancement
Leukocyte localization
Visual attention

ABSTRACT

In this paper, we propose a fast hierarchical framework of leukocyte localization and segmentation in rapidly-stained leukocyte images (RSLI) with complex backgrounds and varying illumination. The proposed framework contains two main steps. First, a nucleus saliency model based on average absolute difference is built, which locates each leukocyte precisely while effectively removes dyeing impurities and erythrocyte fragments. Secondly, two different schemes are presented for segmenting the nuclei and cytoplasm respectively. As for nuclei segmentation, to solve the overlap problem between leukocytes, we extract the nucleus lobes first and further group them. The lobes extraction is realized by the histogram-based contrast map and watershed segmentation, taking into account the saliency and similarity of nucleus color. Meanwhile, as for cytoplasm segmentation, to extract the blurry contour of the cytoplasm under instable illumination, we propose a cytoplasm enhancement based on tri-modal histogram specification, which specifically improves the contrast of cytoplasm while maintaining others. Then, the contour of cytoplasm is quickly obtained by extraction based on parameter-controlled adaptive attention window. Furthermore, the contour is corrected by concave points matching in order to solve the overlap between leukocytes and impurities. The experiments show the effectiveness of the proposed nucleus saliency model, which achieves average localization accuracy with F1-measure greater than 95%. In addition, the comparison of single leukocyte segmentation accuracy and running time has demonstrated that the proposed segmentation scheme outperforms the former approaches in RSLI.

1. Introduction

Differential counting of white blood cells (WBC or leukocytes) plays a crucial role in indicating lots of vital diseases such as hepatitis, leukemia and AIDS (Ghosh et al., 2010). Over the past few years, development of automated cell counter has transferred the time-consuming job from human subjects to automated systems (Bikhet et al., 2000). And it is the cell segmentation that plays a key role in these systems, whose running speed and accuracy are directly influenced by image quality. In image acquisition stage, Wright or Giemsa staining is widely used to facilitate the differentiation of blood cell types. Though traditionally-stained leukocyte images (TSLI) are colored stably with clear details, they have two problems which limit their application. One is the slow dyeing speed, which is not conducive to analyze large numbers of images. The other is the frequent overlap among blood cells (Wang and Wang, 2006), resulting in very time-consuming and challenging segmentation.

To settle the two problems, our team has recently developed a hematology reagent for both rapid leukocyte staining and erythrocyte lysing, which takes only about ten seconds and greatly eliminates the overlap among erythrocytes and leukocytes. However, the dyeing effect is not as good as that of the traditional staining. There are mainly two new problems in rapidly-stained leukocyte images (RSLI). The first is the emergence of substantial dyeing impurities, whose appearances are akin to that of nuclei, makes leukocyte localization difficult. The second is the varying color and illumination, which result in instinct boundaries, become a great challenge in segmentation.

Leukocyte localization is to extract the whole leukocyte from a complicated background. There are many leukocyte localization methods, most of which are realized by thresholding based on a nucleus saliency map (Ghosh et al., 2010; Huang et al., 2012; Jiang et al., 2006; Ko et al., 2011; Kovalev et al., 1995; Madhloom et al., 2010), because the nuclei have the most salient color in TSLI. However, since the nuclei are not the only salient objects in RSLI where dyeing impurities exists, the previous methods failed to precisely locate leukocytes in RSLI.

Segmenting every leukocyte into morphological components such as nucleus and cytoplasm is an essential and important

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http://dx.doi.org/10.1016/j.micron.2013.09.006

issue, which attracts the most attention in automatic differential blood counter systems. The pixel-based classification methods, have achieved good segmentation results in TSLI (Fang et al., 2005; Guo et al., 2007; Pan et al., 2012; Theera-Umpon, 2005). However, there is no obvious color difference between cytoplasm and background in RSLI, as well as between nucleus and cytoplasm. With color variation and no spatial information taken into account, these methods cannot get the whole cell region. The boundary-based segmentation methods (Ko et al., 2011; Lin et al., 2005; Sanpanich et al., 2008) are able to get ideal contours in TSLI. However, the cytoplasm boundaries in RSLI are too weak to be precisely obtained.

To sum up, the frequently-used algorithms would not be able to effectively extract and segment each leukocyte in RSLI, for RSLI are more challenging than TSLI. In this paper, we focus on developing a fast and precise leukocyte localization and segmentation approach, which could handle the new problems in RSLI.

2. Nucleus saliency model based on average absolute difference (AAD) and Leukocyte localization

RSLI is a complex scene which is flooded with erythrocytes fragments and dyeing impurities, containing a few scattered leukocytes. According to the visual attention mechanism, despite the tiny area of the leukocytes when compared with the whole image and the diversity of color and illumination, human eyes will quickly pick out leukocytes while ignore the others. In RSLI, the impurities and nuclei are both salient objects, very alike in their intensity and color. However, human eye can distinguish nuclei from impurities easily. The main reason is that we know the leukocyte has a round shape, with nucleus lobes in the center. Meanwhile, there is an upper limit to the size of it. Thus there is obvious contrast between nucleus and its local neighborhoods. But the impurities are amorphous and most of them don't possess the local saliency. So we define the average absolute difference (AAD) to enhance nuclei while suppressing impurities. AAD is defined as follows:

$$AAD(x,y) = \max_{\forall \Theta} \left\{ \Delta D | \Delta D = \frac{1}{N_\Omega} \sum_{x,y \in \Omega} I(x,y) - \frac{1}{N_\Theta} \sum_{x,y \in \Theta} I(x,y) \right\} \quad (1)$$

where Θ and Ω are the object and background windows as shown in Fig. 1, N_Θ, N_Ω are the sum of Set Θ and Ω respectively, $I(x, y)$ represents the gray-scale of the pixel (x, y). By computing the maximum differences between the surrounding points and the center points, the AAD operator simulates the sensitivity to local spatial discontinuities of visual receptive fields in human visual mechanism to enhance the nuclei. When both Set Θ and Ω cover only background, ΔD is quite small; when only the object is covered in Θ and Ω covers the background, ΔD has the maximal value. Given a fixed Ω, AAD can adaptively find the location of Θ which shows the maximal contrast between Θ and Ω. Therefore, Θ and Ω can best cover the object and background respectively.

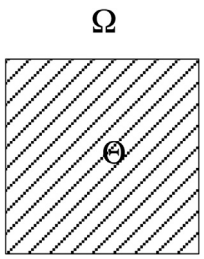

Fig. 1. Object and background windows of AAD.

When AAD is used in RSLI, the impurities are restrained effectively while the contrast between nuclei and background is retained, as shown in Fig. 2. Though the impurities are salient in the entire scene, the local contrast is low. So they can be suppressed by AAD when Ω is a little bigger than the maximum size of leukocytes.

To further suppress noises of small area and make the histogram present a more obvious double-peak, we apply the AAD operator into a well-known saliency model proposed by (Itti et al., 1998). The model is based on a biologically-plausible visual attention architecture which is related to the feature integration theory, explaining human visual search strategies. But this saliency model is not adequately suitable for RSLI because it is in a purely bottom-up manner with no top-down features. According to AAD operator, we make the best use of the two task-dependent features of leukocytes: the darker color of nuclei, the circular shape and the fixed size of leukocyte. Thus the modified saliency model based on AAD is more efficient for detecting nuclei and suppressing impurities. The architecture comparison between the proposed nucleus saliency model and Itti's saliency model is shown in Fig. 3.

The biggest difference between Itti's saliency model and our nucleus saliency model is that the color, intensity and orientation features are replaced by AAD feature in our model. Itti's model is a general model which has to consider different types of features in order to surely include all kinds of salient objects. But for leukocyte localization, we only need to consider the features which can highlight nuclei. Since the nuclei appear dark purple, green channel can best represent the contrast between nuclei and others. In brief, by means of integrating top-down and bottom-up attention, our model is able to perform better than Itti's model. We can see from Fig. 4 that the saliency map gained from our nucleus saliency model can better suppress impurities and highlight nuclei compared with Itti's saliency map.

Another difference is that the purpose of the Itti's model is to shift the focus of attention (FOA) by sorting its saliency, but we just care about the location of each region of interest (ROI) regardless of the saliency order of each ROI So we replace the "winner-take-all" neural network with an automatic binaryzation such as Otsu threshold (Otsu, 1979).

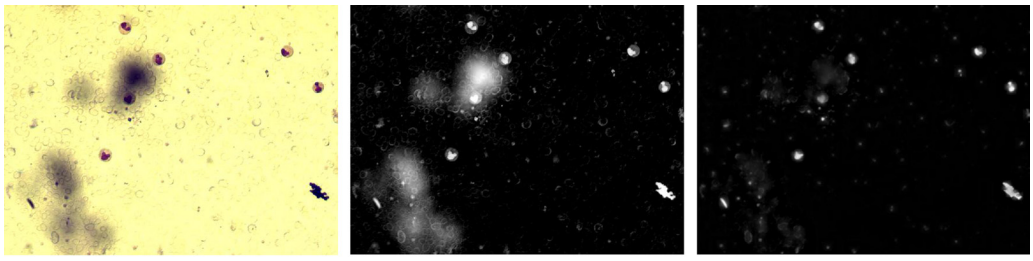

Fig. 2. (a) Original image, (b) green channel of (a), (c) AAD map of (b). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)