Trends in Health Informatics

www.thi.reapress.com

THI. Vol. 2, No. 2 (2025) 116–126.

Paper Type: Original Article

Robust Unsupervised White Blood Cell Nucleus Segmentation Using Intuitionistic Fuzzy Divergence Thresholding in the Lab Color Space

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Citation:

Received: 11 November 2024 *Revised: 15 February 2025* *Accepted: 27 March 2025*	Zooghi, S. (2025). Robust unsupervised white blood cell nucleus segmentation using intuitionistic fuzzy divergence thresholding in the lab color space. *Trends in Health Informatics, 2*(2), 116-126.

Abstract

White Blood Cell (WBC) nucleus segmentation is a fundamental step in automated hematological image analysis, as the accuracy of subsequent feature extraction and classification largely depends on precise nucleus localization. However, variations in staining protocols, illumination conditions, and image acquisition systems often reduce the robustness of conventional grayscale-based segmentation methods. This paper presents a robust and fully unsupervised framework for WBC nucleus segmentation based on Intuitionistic Fuzzy Divergence (IFD) thresholding in the Lab color space. Unlike the conventional IFD approach, which performs thresholding on grayscale images, the proposed method applies the IFD optimization process to the a-channel of the Lab color space, where leukocyte nuclei exhibit significantly higher chromatic contrast than surrounding blood components. The optimal threshold is determined by minimizing the IFD, and the extracted binary mask is subsequently used to delineate nucleus regions. The proposed method was evaluated on three independent peripheral blood smear image datasets acquired under different staining protocols and imaging conditions. Experimental results demonstrate that the proposed framework maintains consistent segmentation performance across heterogeneous datasets. Visual comparisons further indicate that the proposed approach produces more reliable nucleus segmentation than conventional grayscale-based IFD thresholding. Owing to its unsupervised nature, low computational complexity, and robustness to imaging variations, the proposed framework provides an effective preprocessing solution for computer-aided leukocyte analysis and automated hematological diagnosis.

Keywords: White blood cell, Segmentation, Intuitionistic fuzzy divergence, Lab color space, Medical image processing.

1 | Introduction

White Blood Cells (WBCs) are among the most important components of the human immune system and play a critical role in defending the body against infections and pathological conditions. Quantitative and morphological analysis of WBCs is routinely employed in the diagnosis of hematological disorders, leukemia,

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https://doi.org/10.22105/thi.v2i2.49

inflammatory diseases, and immune deficiencies [1]. Traditionally, WBC analysis is performed manually by hematologists through microscopic examination of peripheral blood smear images. However, manual inspection is labor-intensive, time-consuming, and prone to inter-observer variability, motivating the development of automated computer-aided blood analysis systems [2].

Accurate segmentation of WBCs is one of the most critical stages in automated hematological image analysis because the performance of subsequent feature extraction and classification modules strongly depends on the quality of segmentation [3]. Nevertheless, reliable WBC segmentation remains a challenging task due to variations in staining protocols, illumination conditions, image acquisition devices, cell morphology, overlapping cells, and the presence of Red Blood Cells (RBCs) and artifacts [4].

Numerous segmentation approaches have been proposed in the literature. Early methods mainly relied on thresholding techniques because of their simplicity and low computational cost. Otsu-based thresholding and histogram analysis methods were widely adopted to separate leukocyte regions from the background [5]. However, these methods often exhibit poor performance when dealing with heterogeneous images acquired under different laboratory conditions.

To overcome these limitations, color-based segmentation approaches have been extensively investigated. Various color spaces including RGB, HSV, HSI, YCbCr, and Lab have been employed to enhance the contrast between nucleus, cytoplasm, RBCs, and background regions [6]. For instance, color-space-based clustering methods have demonstrated that transforming blood smear images into alternative color spaces can improve segmentation accuracy compared with direct processing in the RGB domain [6]. Nevertheless, the performance of color-based approaches is highly dependent on the selected color space and often deteriorates when staining conditions vary significantly.

Clustering-based algorithms such as K-means, Fuzzy C-Means (FCM), and possibilistic clustering have also been applied to WBC segmentation [7]. These methods exploit color and intensity distributions to group pixels into homogeneous regions. Although clustering approaches can achieve satisfactory segmentation results, they usually require parameter tuning and may be sensitive to initialization conditions and image quality variations.

Fuzzy set theory has emerged as an effective tool for handling uncertainty in medical image segmentation. Chaira proposed a fuzzy divergence-based leukocyte recognition framework in which fuzzy membership functions were employed to improve nucleus extraction [8]. Subsequently, Ghosh et al. [9] developed a hedge-operator-based fuzzy divergence measure for leukocyte segmentation in chronic myelogenous leukemia images. To further improve robustness against uncertainty, Khan et al. [10] introduced an Intuitionistic Fuzzy Divergence (IFD)-based thresholding algorithm for automatic leukocyte nucleus segmentation, where the optimal threshold is determined by minimizing the divergence between the original image and an ideal segmented image. Later, Chaira [11] proposed a leukocyte segmentation method based on Intuitionistic Fuzzy Sets (IFS) and interval type-II fuzzy theory, demonstrating improved segmentation accuracy under uncertain imaging conditions.

In recent years, deep learning architectures, particularly convolutional neural networks and U-Net-based models, have achieved remarkable performance in medical image segmentation tasks [12]. Despite their success, these approaches generally require large annotated datasets, extensive training procedures, and considerable computational resources. Furthermore, their generalization capability may decrease when images are acquired under staining and imaging conditions different from those used during training [13].

A careful review of the literature reveals several research gaps. First, many existing studies focus exclusively on nucleus segmentation while neglecting complete WBC segmentation including cytoplasm extraction. Second, most conventional methods utilize a single color space throughout the segmentation process, limiting their ability to exploit complementary color information. Third, the majority of reported methods are evaluated on a single dataset, making their robustness against inter-dataset variations difficult to assess. Finally,

although IFD has proven effective for nucleus extraction, its integration within a complete multi-stage and multi-color-space WBC segmentation framework has received limited attention.

To address these limitations, this paper proposes a robust framework for WBC segmentation based on IFD and multi-color-space analysis. The proposed method employs the a-channel of the Lab color space to enhance nucleus discrimination and performs nucleus extraction using IFD-based thresholding. Simultaneously, the CMYK color space is utilized to identify background regions and suppress irrelevant structures. Subsequently, RBCs are detected and removed, cytoplasm regions are extracted, adjacent WBCs are separated, and spurious objects are eliminated through a sequence of post-processing operations. Unlike many previous studies, the proposed framework aims at complete WBC segmentation and is validated on three independent datasets acquired under different staining and imaging conditions.

The main contributions of this work are summarized as follows:

I. A robust multi-color-space framework for complete WBC segmentation is proposed.

II. IFD thresholding is integrated with the Lab color space for accurate nucleus extraction.

III. Complementary information from the CMYK color space is utilized for background suppression.

IV. A complete segmentation pipeline including nucleus extraction, cytoplasm extraction, RBC elimination, separation of touching cells, and artifact removal is developed.

V. The proposed method is evaluated on three independent blood smear datasets to investigate its robustness and generalization capability.

The remainder of this paper is organized as follows. Section 2 presents the theoretical background of IFD and color-space analysis. Section 3 describes the proposed segmentation framework. Section 4 presents the experimental setup and evaluation metrics. Section 5 discusses the results and comparative analyses. Finally, Section 6 concludes the paper and outlines future research directions.

2 | Theoretical Background

2.1 | Color Space Analysis in Blood Smear Images

Color information plays a significant role in the segmentation of WBCs from peripheral blood smear images. Different staining protocols produce characteristic color distributions in blood components, allowing color-based segmentation algorithms to distinguish nucleus, cytoplasm, RBCs, and background regions more effectively than grayscale approaches [14].

The RGB color space is the most commonly used representation in digital imaging. However, its channels are highly correlated and often fail to provide sufficient discrimination between blood components under varying illumination and staining conditions. Consequently, alternative color spaces have been investigated for hematological image analysis [15].

Among them, the Lab color space has attracted considerable attention because of its perceptual uniformity and ability to separate luminance information from chromatic information. The transformation decomposes an image into three channels:

I. L*: Lightness component.

II. a*: Green-to-red chromatic component.

III. b*: Blue-to-yellow chromatic component.

In stained blood smear images, leukocyte nuclei generally appear as dark purple regions. Since purple coloration is strongly represented within the a* channel, this channel often provides enhanced contrast between nucleus pixels and surrounding structures [16].

Another color representation frequently used in image analysis is the CMYK color space. Unlike RGB, CMYK describes image colors using cyan (C), magenta (M), yellow (Y), and black (K) components. The conversion from RGB to CMYK is expressed as:

$$\begin{aligned} K &= 1 - \max(R,G,B), \\ C &= (1 - R - K)/(1 - K), \\ M &= (1 - G - K)/(1 - K), \\ Y &= (1 - B - K)/(1 - K), \end{aligned} \quad \textbf{(1)}$$

where R, G, and B are normalized RGB values in the range [0,1].

The CMYK representation provides additional information regarding background and non-cellular regions, making it useful for separating blood cells from the slide background under varying acquisition conditions [17].

2.2 | Intuitionistic Fuzzy Sets

Classical fuzzy set theory introduced by Zadeh [18] represents uncertainty through a membership function only. However, in many practical image segmentation problems, uncertainty cannot be adequately described using a single membership value.

To address this limitation, Atanassov introduced the concept of IFS, which characterize each element using both membership and non-membership degrees [18].

Let $X=\{x1,x2,\ldots,xn\}$ be a finite universe of discourse.

An IFS A is defined as:

$$A=\{\langle x,\mu_A(x),\nu_A(x)\rangle : x\in X\}, \quad \textbf{(2)}$$

where

$\mu A(x):X\rightarrow[0,1]$ denotes the membership degree and $\nu A(x):X\rightarrow[0,1]$ represents the non-membership degree.

These values satisfy

$$0 \leq \mu_A(x)+\nu_A(x)\leq 1. \quad \textbf{(3)}$$

The uncertainty associated with element x is represented by the hesitation degree:

$$\pi A(x)=1-\mu_A(x)-\nu_A(x). \quad \textbf{(4)}$$

The hesitation component provides additional information regarding ambiguity and uncertainty, making intuitionistic fuzzy theory particularly suitable for medical image segmentation tasks where boundaries are often ill-defined [19].

2.3 | Intuitionistic Fuzzy Divergence

The similarity or dissimilarity between two IFS can be quantified using an IFD measure.

Suppose A and B are two IFS defined over the same universe X.

For each element x, the corresponding membership and non-membership values are represented as $(\mu A(x),\nu A(x))$ and $(\mu B(x),\nu B(x))$ respectively.

The IFD proposed by Jati et al. [20] measures the discrepancy between two intuitionistic fuzzy representations and can be employed as an objective criterion in image thresholding problems.

The divergence becomes minimum when the segmented image closely resembles the ideal segmentation and increases as the discrepancy between the two representations grows.

This property makes IFD particularly suitable for determining optimal threshold values in image segmentation applications.

2.4 | Intuitionistic Fuzzy Divergence-Based Thresholding

Thresholding aims to partition image pixels into meaningful regions according to their intensity distributions. In IFD-based thresholding, an image is first represented as an IFS. Assume that the image is partitioned into K regions. The mean intensity of the kth region is defined mk. For a pixel with intensity value xi the membership function is computed as [20]:

$$\mu(x_i) = \exp\left(-\frac{(x_i - m_k)^2}{2{\sigma_k}^2}\right), \quad (5)$$

where σk denotes the standard deviation of the corresponding region. The non-membership value is then determined by Yager's complement:

$$v(x_i) = \frac{1 - \mu(x_i)}{1 + \lambda\mu(x_i)}, \quad (6)$$

where λ>0 is a controlling parameter.

After obtaining the intuitionistic fuzzy representation, divergence values are computed for all candidate threshold combinations.

Let D(t1,t2) denote the IFD corresponding to thresholds t1 and t2

The optimal thresholds are selected according to:

$$(t_1^*, t_2^*) = \operatorname{argmin} D(t_1, t_2). \quad (7)$$

The selected thresholds are subsequently used to generate the segmented image.

Because the optimization process is based on divergence minimization rather than histogram shape alone, the method generally exhibits greater robustness against intensity variations and noise compared with conventional thresholding approaches [20].

The theoretical concepts described in this section constitute the foundation of the proposed WBC segmentation framework. The integration of color-space analysis and IFD-based thresholding for robust WBC segmentation is presented in the next section.

3 | Proposed Nucleus Segmentation Method

The objective of the proposed method is to achieve robust WBC nucleus segmentation in peripheral blood smear images acquired under different staining protocols, illumination conditions, and image acquisition systems. Since nucleus segmentation represents the foundation of subsequent hematological image analysis, any segmentation error can significantly affect the performance of higher-level diagnostic systems.

The original IFD thresholding algorithm proposed by Jati et al. [20] has demonstrated promising performance for leukocyte nucleus extraction. However, the original method operates on grayscale images, which often fail to adequately represent chromatic characteristics of blood smear images. Consequently, dark RBCs, staining artifacts, and other image structures may exhibit intensity distributions similar to those of leukocyte nuclei, resulting in false detections.

To overcome this limitation, the proposed method incorporates color-space analysis into the IFD framework. Instead of applying the thresholding process to the grayscale image, the algorithm exploits the a-channel of the Lab color space, where nucleus regions exhibit significantly higher contrast relative to surrounding blood components.

The overall framework consists of three major stages:

I. Transformation of the RGB image into the Lab color space and extraction of the a-channel.

II. IFD-based threshold optimization.

III. Binary nucleus mask generation using the optimal threshold.

The complete workflow of the proposed nucleus segmentation framework is illustrated in *Fig .1*.

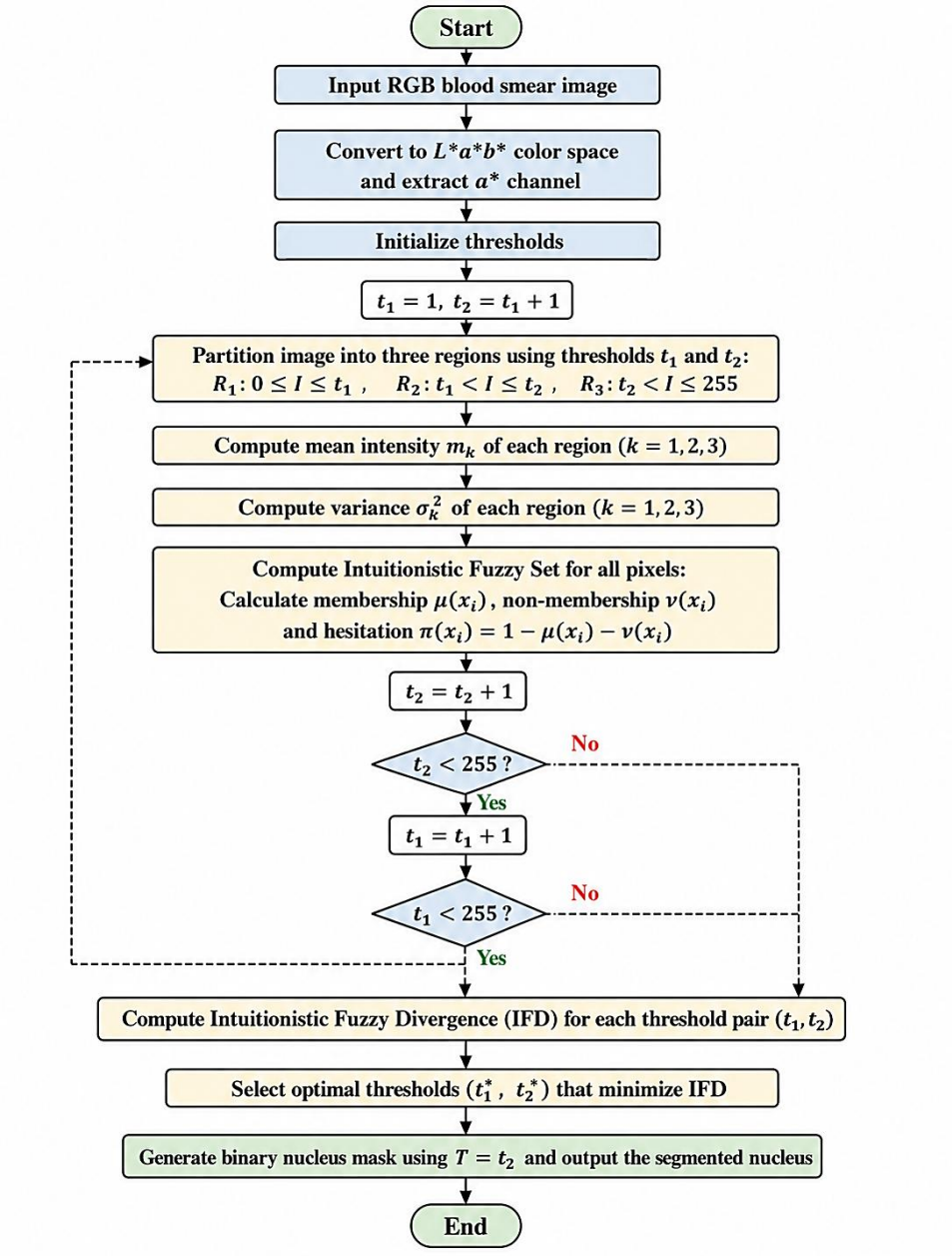

Fig. 1. Flowchart of the proposed WBC nucleus segmentation method.

After color-space transformation according Section 2.1, the extracted a-channel is subjected to IFD thresholding. Given that microscopic images of blood smears typically comprise three primary color regions, a minimum of two threshold values is necessary for effective segmentation of these regions. Consequently, for each pair of thresholds varying between 0 and 255, the image is partitioned into three distinct regions. If the brightness intensity values within each region r_i are denoted by $f(r_k)$, the following holds:

$$0 \le f(r_1) \le t_1 \le f(r_2) \le t_2 \le f(r_3) \le 255. \quad (8)$$

The mean brightness level for each of the three segmented regions is then calculated and expressed as m_k. For every pixel in the image, the degree of membership is determined using *Eq. (5)*. Using the membership function, the non-membership function is also computed *Eq. (6)*. In this study, the value of λ is set to 2.

The IFD between two images A and B is given by

$$\mathrm{DIF} = \frac{1}{2}\sum_{i=1}^{M-1}\sum_{j=1}^{N-1}\begin{bmatrix} 4 - \{1-\mu_A(a_{ij})\} + \mu_B(b_{ij})\}e^{\mu_A(a_{ij})-\mu_B(b_{ij})} \\ -\{1-\mu_B(b_{ij})\} + \mu_A(a_{ij})\}e^{\mu_B(b_{ij})-\mu_A(a_{ij})} \\ -\{1-v_A(a_{ij})\} + v_B(b_{ij})e^{v(a_{ij})-v_B(b_{ij})} \\ -\{1-v_B(b_{ij})\} + v_A(a_{ij})\}e^{v_B(b_{ij})-v_A(a_{ij})} \end{bmatrix}. \quad (9)$$

The original image is represented as a fuzzy set. Let the original image in its fuzzy form be denoted by A, and the ideal segmented image by B. Then, $\mu_B = 1$ and $v_B = 0$, the IFD between A and B is calculated using *Eqs. (3)* and *(4)* as follows:

$$\mathrm{IFD} = \frac{1}{2}\sum_{i=1}^{M}\sum_{j=1}^{N}\begin{bmatrix} 4 - \{2-\mu_A(i,j)\}e^{\mu_A(i,j)-1} - \mu_A(i,j)e^{1-\mu_A(i,j)} \\ -\{1-v_A(i,j)\}e^{v(i,j)} - \{1+v_A(i,j)\}e^{-v_A(i,j)} \end{bmatrix}. \quad (10)$$

The value of IFD is computed for all possible threshold pairs (t_1, t_2). The pair of thresholds that yields the minimum IFD value is selected as the optimal thresholds. The value $T = t_2$ is taken as the final threshold for nucleus segmentation and extraction of its binary mask.

4 | Simulation Results

4.1 | Datasets

In this paper, images from three different datasets with varying characteristics were employed to evaluate the different stages of the proposed method. Details of each dataset are described below.

Dataset 1: This dataset consists of 400 images acquired from 100 peripheral blood smears. The blood smears were stained using the Giemsa-Wright method. The images were captured by a digital camera (SONY model No. SSC-DC50AP) mounted on an optical microscope (Microscope-Axioskope 40) equipped with a colorless lens at 100× magnification. All images are color images of size 720 × 576 pixels with 24 bits per pixel, stored in BMP format. The images were collected at the Hematology-Oncology Research Center of Imam Khomeini Hospital (Tehran, Iran) and classified into different types of WBCs by a hematologist. In addition, the nuclear and cytoplasmic regions of the WBCs were manually segmented by an expert. The images in this dataset exhibit significant variation in brightness intensity. This dataset is suitable for nucleus and cytoplasm segmentation of WBCs as well as for the classification of different types of leukocytes [21].

Dataset 2: The microscopic images in this dataset were acquired using a KODAK EasyShare V803 digital camera mounted on a Leica microscope at 100× magnification with an oil-immersion lens. The required blood smears were stained with Giemsa. The images are color images of size 3264 × 2448 pixels with 24 bits per pixel, stored in JPG format.

These images were collected by the specialized Hematology Center at Dr. Juan Bruno Zayas Alfonso Hospital in Santiago, Cuba. Healthy and pathological RBCs were classified by a specialist in this dataset. This database can be used for blood smear image segmentation and RBC classification methods.

Dataset 3: The images in this dataset were captured using a CANON Power Shot G5 digital camera attached to a laboratory microscope with variable magnification (ranging from 300× to 500×). The images are color images with 24 bits per pixel, stored in JPG format. This dataset was prepared at the M. Tettamanti Research Center in Monza, Italy, for the detection of Acute Lymphoblastic Leukemia (ALL) using blood sample image processing techniques. It consists of two subsets: ALL-IDB1 and ALL-IDB2.

The first subset (ALL-IDB1) contains 108 images of size 2592 × 1949 pixels, encompassing a total of 3900 blood elements. Overall, there are 510 lymphoblasts across all images, whose center coordinates were determined by an expert. In each image, the presence or absence of at least one lymphoblast is also indicated. The number of images containing lymphoblasts is equal to the number of images without lymphoblasts. This subset can be used to evaluate the algorithm's performance in blood smear segmentation and separation of overlapping cells. Moreover, due to the availability of labeled lymphoblasts, it is suitable for assessing the classification power of the system in ALL detection at both image and cell levels.

4.2 | Results

In blood smear images, WBC nuclei typically appear as dark purple structures due to the staining process. Although grayscale conversion simplifies image representation, it also removes valuable chromatic information that can facilitate nucleus discrimination. *Fig. 2* presents representative segmentation results obtained using the original grayscale-based IFD approach. It can be observed that the method performs satisfactorily on certain images but fails when RBCs or other structures exhibit intensity levels comparable to those of the nucleus.

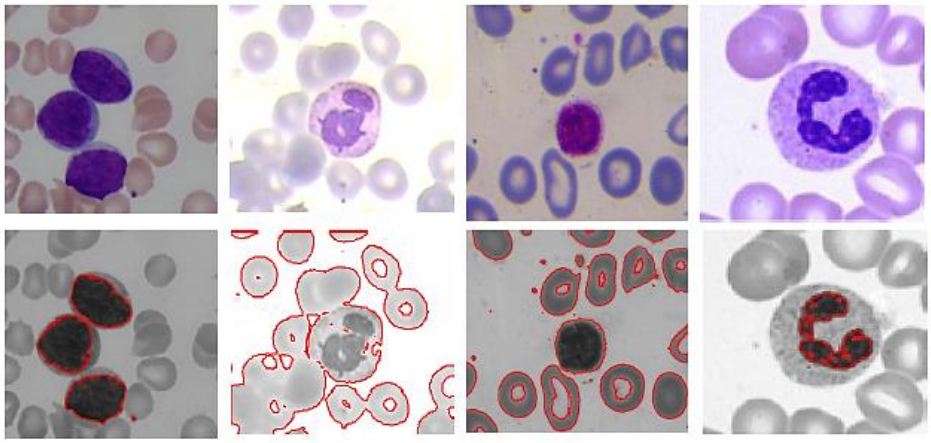

Fig. 2. Results of intuitionistic fuzzy divergence-based thresholding on the grayscale image.

To improve segmentation robustness, the RGB image is transformed into the Lab color space. The Lab representation separates luminance information from chromatic information and has been widely employed in medical image segmentation due to its perceptual uniformity. Among the three channels of the Lab color space, the a-channel provides the strongest contrast between nucleus regions and surrounding structures. Since leukocyte nuclei are predominantly purple, their chromatic characteristics are more effectively represented within this channel.

Fig. 3 demonstrates the segmentation results obtained by applying IFD thresholding to the a-channel. Compared with grayscale processing, the proposed strategy substantially reduces false detections and improves nucleus localization across different datasets.

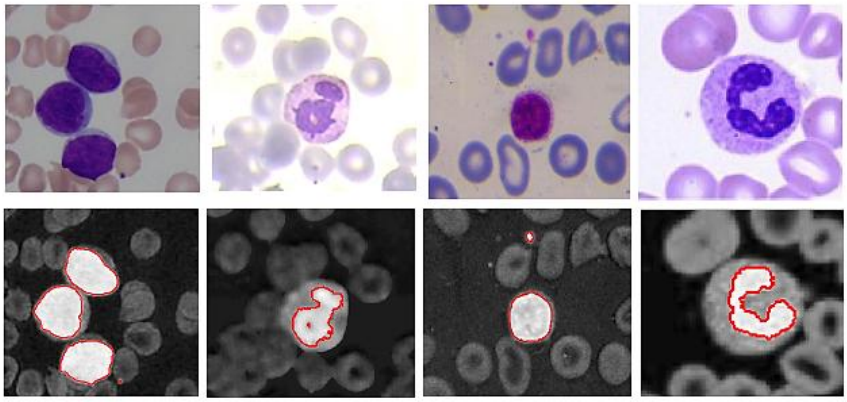

Fig. 3. Results of the intuitionistic fuzzy divergence-based thresholding on a channel of the L*a*b* color space.

Fig. 4 provides a visual comparison of the performance of the four nucleus segmentation algorithms on three representative images acquired from Datasets 1, 2, and 3, respectively.

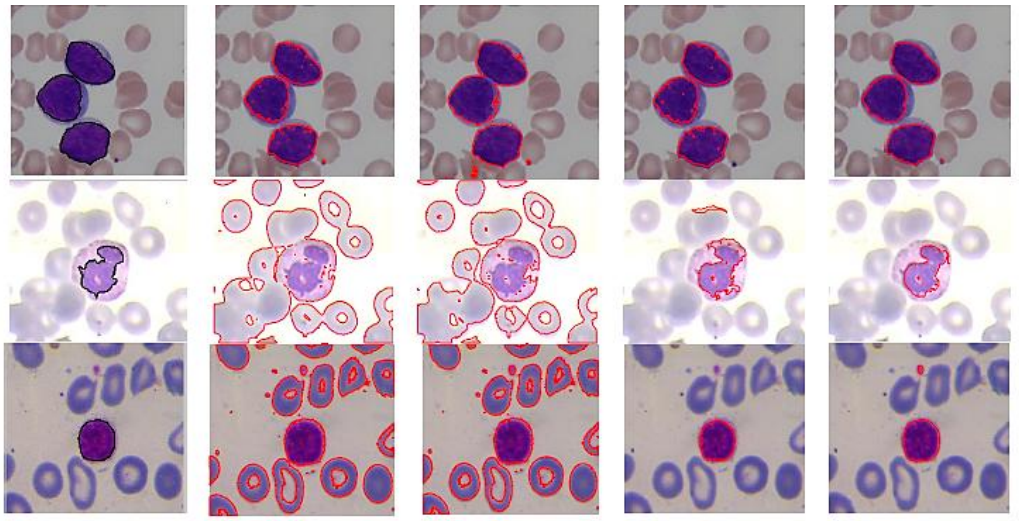

Fig. 4. Performance comparison of the proposed algorithm with other competing algorithms.

It is observed that the proposed algorithm exhibits greater robustness compared to the three other methods and produces segmentation results closer to the expert's ground-truth segmentation.

5 | Conclusion

In this paper, a robust and fully unsupervised method for WBC nucleus segmentation in peripheral blood smear images was presented. The proposed approach combines IFD thresholding with the a-channel of the Lab color space to improve nucleus discrimination under different staining and image acquisition conditions. Unlike the conventional IFD approach, which performs thresholding on grayscale images, the proposed method exploits chromatic information to enhance the contrast between leukocyte nuclei and surrounding blood components, thereby reducing false detections caused by RBCs and staining artifacts.

The proposed framework was evaluated on three publicly available blood smear image datasets containing considerable variations in staining protocols, illumination conditions, and image quality. Experimental results demonstrated that the proposed method consistently produced accurate nucleus segmentation across all datasets without requiring any training stage or parameter tuning for individual datasets. Visual comparisons confirmed that the proposed approach generated segmentation results closer to expert annotations than conventional grayscale-based thresholding methods.

Compared with existing thresholding-based segmentation techniques, the proposed method preserves the computational simplicity of IFD while significantly improving its robustness through an appropriate color-space representation. Furthermore, unlike supervised deep learning approaches, the proposed algorithm does not require large annotated datasets or computationally expensive training procedures, making it suitable for practical laboratory environments and resource-constrained medical systems.

Future research will focus on extending the proposed framework by incorporating adaptive color-space selection, automatic parameter optimization, and comprehensive evaluation using widely adopted segmentation metrics such as the Dice Similarity Coefficient and Jaccard Index. In addition, the segmented nuclei obtained by the proposed method can be employed as a reliable preprocessing stage for automated WBC classification and computer-aided hematological diagnosis.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Availability

All data are included in the text.

Conflicts of Interest

The authors declare no conflict of interest.

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