Scientific Research Publishing

Open Journal of Applied Sciences, 2025, 15(7), 2136-2148
https://www.scirp.org/journal/ojapps
ISSN Online: 2165-3925
ISSN Print: 2165-3917

Identification of Stomatocytes through Microscopic Image Analysis of Blood Smears

Alico Nango Jerôme[1], Koffi Patrice[2], Ouattara Sié[3], Wognin Joseph Vangah[4], Alain Clément[5]

[1]French Preparatory Program for Admission to Grandes Écoles (CPGE), University of San Pedro (USP), San Pedro, Côte d'Ivoire
[2]Research and Digital Expertise Unit (UREN), Virtual University of Côte d'Ivoire (UVCI), Abidjan, Côte d'Ivoire
[3]Houphouët-Boigny National Polytechnic Institute (INPHB), Yamoussoukro, Côte d'Ivoire
[4]Research and Digital Expertise Unit (UREN), Virtual University of Côte d'Ivoire (UVCI), Abidjan, Côte d'Ivoire
[5]LARIS, SFR MATHSTIC, Université d'Angers, Angers, France
Email: sie_ouat@yahoo.fr

How to cite this paper: Jerôme, A.N., Patrice, K., Sié, O., Vangah, W.J. and Clément, A. (2025) Identification of Stomatocytes through Microscopic Image Analysis of Blood Smears. *Open Journal of Applied Sciences*, **15**, 2136-2148.
https://doi.org/10.4236/ojapps.2025.157141

Received: May 28, 2025
Accepted: July 21, 2025
Published: July 24, 2025

Abstract

The analysis of microscopic images of blood smears remains crucial in medical diagnostics, aiming to reveal abnormalities related to blood cells, particularly red blood cells. These abnormalities, whether morphological or colorimetric, allow for the precise detection of both common and rare diseases, as certain anomalies are clear indicators of specific pathologies. Stomatocytes, which are the focus of our study, are red blood cells exhibiting membrane defects that, to a certain extent, lead to increased permeability to sodium and potassium. These abnormal erythrocytes generally exhibit a morphology that is overall similar to that of normal red blood cells. However, the central pale area takes on a slit-like or elliptical shape instead of the typical round form. This specific feature, which distinguishes them from other cells, is indicative of a pathology known as stomatocytosis, which may be either congenital or acquired (such as in alcoholic cirrhosis or acute alcohol toxicity). Its diagnosis relies on a series of costly biological tests. However, the blood smear remains the essential examination due to the specific morphological characteristics of stomatocytes. This paper proposes a semi-automated characterization method for the clear identification of stomatocytes in blood smear images. Developed within the MATLAB environment, the method combines K-means pixel-based classification with algorithms designed to isolate the central pallor of the stomatocyte, followed by the extraction of distinctive features enabling its differentiation. The results obtained are highly promising, as stomatocytes in blood smear images are accurately identified using the proposed approach. Thus, the identification of stomatocytes is based on compactness, eccentricity characterized by the difference between the major and minor axes, as well as the proportion of red and white pixels.

Keywords

Erythrocyte, Red Blood Cells, Morphology, Stomatocyte, Stomatocytosis, Alcoholic Cirrhosis, Algorithm, K-Means

1. Introduction

The blood smear is a routine examination in hematology. On a blood smear, red blood cells also known as erythrocytes or hematies generally exhibit similar shapes: circular with a centrally located circular pale area. Calculating the proportion of this central pallor may contribute to the classification of anemia types [1]. Any alteration in these morphological parameters typically indicates a pathological condition in hematology. Microscopic image analysis of blood smears is an essential method in hematology, as it directly reveals the appearance of blood cells under the microscope [2]-[5]. This examination, crucial for medical diagnostics, aims to highlight morphological and colorimetric abnormalities related to blood cells, particularly red blood cells. Among the morphological abnormalities observed in blood smears, stomatocytes are notable due to their distinctive shape. These abnormal erythrocytes generally appear similar to normal red blood cells in overall morphology; however, their central pale region takes on a slit-like or elliptical shape rather than the typical round form.

These abnormally shaped red blood cells, which are the focus of our study, exhibit membrane defects. While they may appear sporadically in an otherwise normal blood smear, their significant presence can indicate certain hematological disorders, such as hereditary stomatocytosis, drug-induced toxicity, or specific liver diseases (e.g., alcoholic cirrhosis) [6] [7]. Therefore, their accurate identification is essential for guiding the diagnostic process.

Stomatocyte identification traditionally relies on visual analysis by practitioners; this manual procedure is very time-consuming, subjective, and necessarily depends on the presence of an expert. Since the introduction of artificial intelligence (AI) and biomedical image analysis techniques, new approaches are being implemented for the identification and classification of blood cells [8] including stomatocytes from digitized microscopic images [9].

This document proposes a semi-automatic approach for the identification of stomatocytes by analyzing microscopic images of blood smears, emphasizing discriminating morphological parameters. This method, whose main objective is to improve the reliability and speed of diagnosis, is developed in a Matlab environment, which is a combination of the pixel classification method with the K-Means method and algorithms for isolating the target red blood cell and also the pale central area of the stomatocyte and then extracting the specific characteristics used for their identification. The results obtained are excellent, because stomatocytes in blood smear images are clearly identified with the pro-

posed method.

2. Literature Review

The recognition of red blood cells (erythrocytes) in general, and stomatocytes in particular, from microscopic images of blood smears represents a major technological and medical challenge. Image processing approaches applied to blood smears offer a promising solution for the rapid and accurate identification of red blood cell abnormalities.

In response to this major challenge, the scientific community has not remained inactive. As a result, many researchers have conducted studies on this topic to assist practitioners in diagnosing diseases related to erythrocyte abnormalities. These studies encompass a variety of methods. In the literature, numerous research efforts have employed neural networks and their various architectures for the identification and classification of blood cells [10]-[12]. Regarding red blood cell detection and classification, the authors in [13] used the Mask R-CNN model, which enables accurate segmentation of erythrocytes, thereby facilitating morphological analysis through precise segmentation masks—crucial for feature extraction in cell identification. The approach presented in [14] is based on deep learning techniques for erythrocyte classification, particularly in the context of sickle cell anemia. This method relies on transfer learning, data augmentation, and a multiclass SVM classifier. It highlights the challenges associated with accurate cell classification while achieving excellent results.

In 2017, H. A. Elsalamony employed the watershed segmentation method and circular Hough transform combined with the extraction of various morphological parameters to generate a unique signature for the identification of three red blood cell types: healthy red blood cells, sickle cells, and elliptocytes [15]. The detection of blood cells, including red and white blood cells, was the focus of the work by C. Di Ruberto *et al.* in 2019. The authors used an Edge Boxes-based approach to enable simple detection of red blood cells [16]. The segmentation and classification of red blood cells were also addressed in the research by Navya K.T. *et al.* In [17], the authors proposed an automatic segmentation and classification method using Fuzzy C-means (FCM) clustering and the SqueezeNet model. After segmenting red blood cells with FCM clustering, they used the YOLOv5 object detection model to identify red blood cells and then classified them as normal or abnormal using the SqueezeNet model, achieving an average classification accuracy of 97.9%. To further improve the accuracy of blood cell identification and classification, S. Pravinth Raja *et al.* proposed using neural networks, specifically the ResNet model, which extracts features from each segmented cell image and classifies them by type. The overall accuracy achieved by the authors' proposed method was 93.01% [18].

The accurate identification of blood cells particularly erythrocytes remains critical in the diagnosis of related pathologies. In this context, Alico J.N. *et al.* [19] developed a semi-automated method using Otsu's algorithm along with morpho-

logical and colorimetric analysis of erythrocytes in blood smear images to identify various forms of anemia. This approach highlighted the importance of precise red blood cell recognition to improve diagnosis and patient management in healthcare settings. To refine feature extraction and ensure the reliability and accuracy of cancer diagnostics, G. Chinna *et al.* adopted the Random Forest-Recursive Feature Elimination (RF-RFE) model in combination with the XGBoost algorithm [20].

It should be noted that the present study builds upon the work in [19], which was based on the analysis of 250 prepared blood smears.

At the end of our literature review, we observed that existing studies, taken as a whole, did not specifically address the identification of stomatocytes. However, this red blood cell morphology is associated with serious conditions such as hereditary stomatocytosis, drug-induced intoxications, and certain liver diseases (e.g., alcoholic cirrhosis). Therefore, we consider it essential to develop a semi-automated method for identifying these specific cell types, given their clinical significance.

In the following section, we describe the method we propose for the accurate identification of stomatocytes based on the analysis of microscopic images of blood smears.

3. The Method Proposed

In this study is divided into seven (07) steps, the first two of which were previously developed in [1] and [19]. The microscopic image acquisition process was carried out on blood smears using a setup described in [1]. In this section, the authors ALICO *et al.* collected blood samples from patients after obtaining their informed consent, following an explanation of the importance of the study. After collection, a team of biologists received the samples in the laboratory. This team was divided into two groups: the first was responsible for preparing the blood smears, while the second assessed the quality of the smears in order to select those suitable for analysis.

Step II, which results in the isolation of the initial red blood cell to be identified, begins with a semi-automated process involving a modified Otsu algorithm and a combination of the 8-connected component labeling algorithm (ARCC-8 connectivity) and the automatic threshold segmentation algorithm (ASSA), as developed in [19].

At this stage, the developed algorithm enables the selection of the red blood cell to be identified within the blood smear image. From this selection, a mask is generated, within which the erythrocyte is located. The cell is then isolated using an 8-connected component labeling algorithm (see **Figure 1** for the connected neighbors of pixel (x, y)). This process involves identifying the neighboring pixels along the cell's boundary. The algorithm evaluates each pixel's connectivity: if a pixel has all eight neighbors, it is considered to be fully inside the cell and not on its contour. Otherwise, the pixel is located on the boundary. By scanning the entire

cell in this manner, we are able to isolate the red blood cell.

(x-1, y-1)	(x, y-1)	(x+1, y-1)
(x-1, y)	**(x, y)**	(x+1, y)
(x-1, y+1)	(x, y+1)	(x+1, y+1)

Figure 1. Table showing the eight-connectivity of a pixel with coordinates (x, y).

In Step III, the isolated erythrocyte is segmented using a combination of Otsu's [19] and K-means algorithms.

3.1. Pixel-Based Classification

3.1.1. Principle of the K-means Algorithm

The K-means algorithm is a pixel classification technique that partitions data into K predefined classes. It is widely used in the literature due to its speed, simplicity of implementation, and effective classification performance.

The principle of the algorithm is as follows:

1) The algorithm begins by initializing K cluster centroids in the feature space.

2) Next, it calculates the distance between each feature (or pixel) and the centroids, assigning each feature to the nearest cluster in order to minimize this distance.

3) Then, the centroids are recalculated based on the new clusters.

4) Based on the newly formed clusters, the attributes in the feature space are reassigned to the nearest cluster.

This iterative process continues until the centroids stabilize or the mean squared error falls below a predefined threshold (see **Figure 2** below).

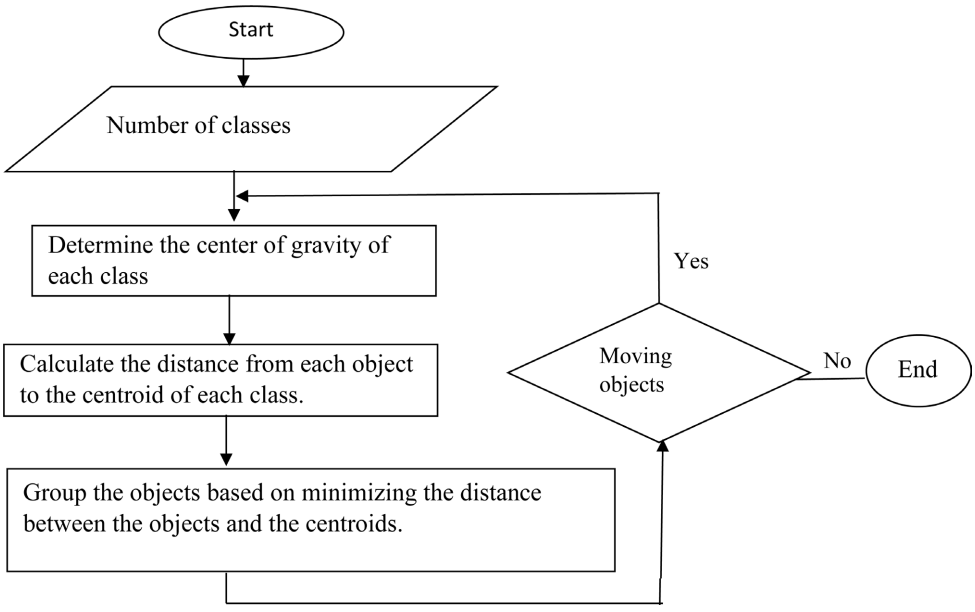

Figure 2. Description of the k-means algorithm.

3.1.2. Combination of Otsu's Algorithm with K-Means

The isolated red blood cell, which is the result of the combination of Otsu's segmentation algorithm with connected component analysis, undergoes segmentation using the K-means algorithm to group pixels into two classes based on their coloration. This combination enables the distinction of two pixel classes representing different colorations of the red blood cells (see Figure 3 below) and allows for the isolation of each class.

Figure 3. Segmentation process of erythrocytes into two classes, (a) original erythrocyte, (b) erythrocyte segmented into two classes.

3.1.3. Red and White Zone Isolation Algorithm (AIZRB)

The isolation of the different colored regions of red blood cells (see Figure 4 below) contributes to an accurate quantification of the pixels composing them. This algorithm for extracting the central white zone of the erythrocyte allows us to calculate morphological parameters such as compactness, major and minor axes, and eccentricity, whose equations are shown below in section 3.2.2. These parameters are crucial for determining the shape of the central zone, which is decisive for the identification of stomatocytes.

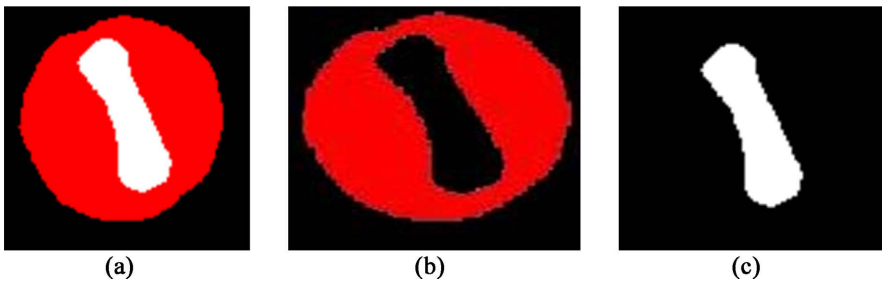

Figure 4. Isolation process of different parts of the erythrocyte, (a) image segmented into two classes (red and white), (b) isolated red zone, (c) isolated central zone.

Algorithm 1: Red and White Zone Isolation (**AIZRB**)
Input: *RGB color image of the red blood cell*
Output: *Isolated red area, isolated white area*
Begin
1. Load the color image
2. Extract the three channels: R, G, B

3. Define thresholds to detect:

a. Red pixels (high R, low G and B)

b. White pixels (high R, G, and B values)

4. Create a binary mask for the red area

- red = (R > threshold1) AND (G < threshold2) AND (B < threshold3)

5. Create a binary mask for the white area

- white = (R > threshold4) AND (G > threshold4) AND (B > threshold4)

6. Apply the masks to extract the areas:

- red_image = Image. red_mask*

- white_image = Image. white_mask*

7. Display or return the two extracted images

End

This approach enables the differentiation of the main structural components of the red blood cell through colorimetric analysis. The red region generally corresponds to hemoglobin-rich areas, while the white region may represent the central pallor or abnormal features, such as those observed in stomatocytes. By isolating these regions, more specific and reliable morphological and diagnostic analyses can be performed.

3.2. Algorithm for Estimating Colorimetric and Morphological Features

3.2.1. Estimation of Colorimetric Features

After segmenting the red blood cell into two classes (red and white) using our method to isolate the different parts of the cell and measure parameters on stomatocytes, these results will be compared with those of abnormal red blood cells characterized in [19], namely: acanthocytes, sickle cells, elliptocytes, annulocytes, as well as healthy erythrocytes. This comparison will consider the shape, the proportion of red and white areas, and the morphology of the central zone of the red blood cells. This methodology has been highly appreciated by field experts, as it enables greater accuracy in decision-making, which is crucial for patient health and care management.

Colorimetric Feature Estimation Algorithm (CFEA)

Input*: Load the segmented binary image (red/white)*

Output*: Proportion of red pixels, proportion of white pixels*

Begin

1. Initialize counters: red_count = 0, white_count = 0

2. For each pixel in the image:

a. If the pixel is red:

Increment red_count by 1

b. Else if the pixel is white:

Increment white_count by 1

3. End for

4. Compute the total number of pixels:

total_pixels = red_count + white_count

5. Compute the proportions:

red_ratio = red_count/total_pixels

white_ratio = white_count/total_pixels

End

3.2.2. Estimation of Morphological Features

The identification of objects requires an appropriate selection of discriminative features (see Table 1 below), a choice that undoubtedly follows from an effective segmentation method [21].

Table 1. Morphological parameters [19].

Parameters	Formulas		Descriptions
Area	$aire = \sum_x \sum_y f(x,y)$	(4.1)	Set of pixels covering the region represented by the cell.
Perimeter (P)	$P = \sum_x \sum_y f(x,y)$ with $x,y \in F(R)$	(4.2)	The sum of the pixels located all along the border of the cell (**R**).
Compactness (C)	$C = \frac{4\pi \cdot area}{P^2}$	(4.3)	It is a morphological feature that contributes to the characterization of certain object shapes.
Major axis	$\text{grdaxe} = \max\{\text{dst}(a,b) \mid a,b \in R\}$	(4.4)	This axis is obtained after determining the spatial centroid of the isolated and binarized red blood cell.
Minor axis	$\text{ptaxe} = \min\{\text{dst}(a,b) \mid a,b \in R\}$	(4.5)	The minor axis (ptaxe) is the smallest diameter of the cell passing through the centroid.
Axis difference	$\text{EcartAxes} = \text{grdaxe} - \text{ptaxe}$	(4.6)	The difference between the axes allows us to clearly distinguish between certain shapes of red blood cells.

4. Results and Discussion

The methodology proposed in this study (refer to Figure 5 above for illustration) begins with the extraction of discriminative features that enable the formal identification of stomatocytes, following their isolation from the blood smear image. This initial phase facilitates the computation of global morphological and colorimetric descriptors specific to the isolated stomatocytes, with the corresponding morphological formulas provided in Table 1 above.

Subsequently, the central pale area of each stomatocyte is segmented, and morphometric analysis is conducted specifically on this region. The parameters extracted from this central area, when combined with the previously derived features, enhance the ability to differentiate stomatocytes from other erythrocytes, whether normal or abnormal.

This comparative analysis considers the overall shape of the red blood cells, the relative proportions of the red and pale regions, and the geometric configuration of the central area.

The results of this analysis are summarized in the tables presented below.

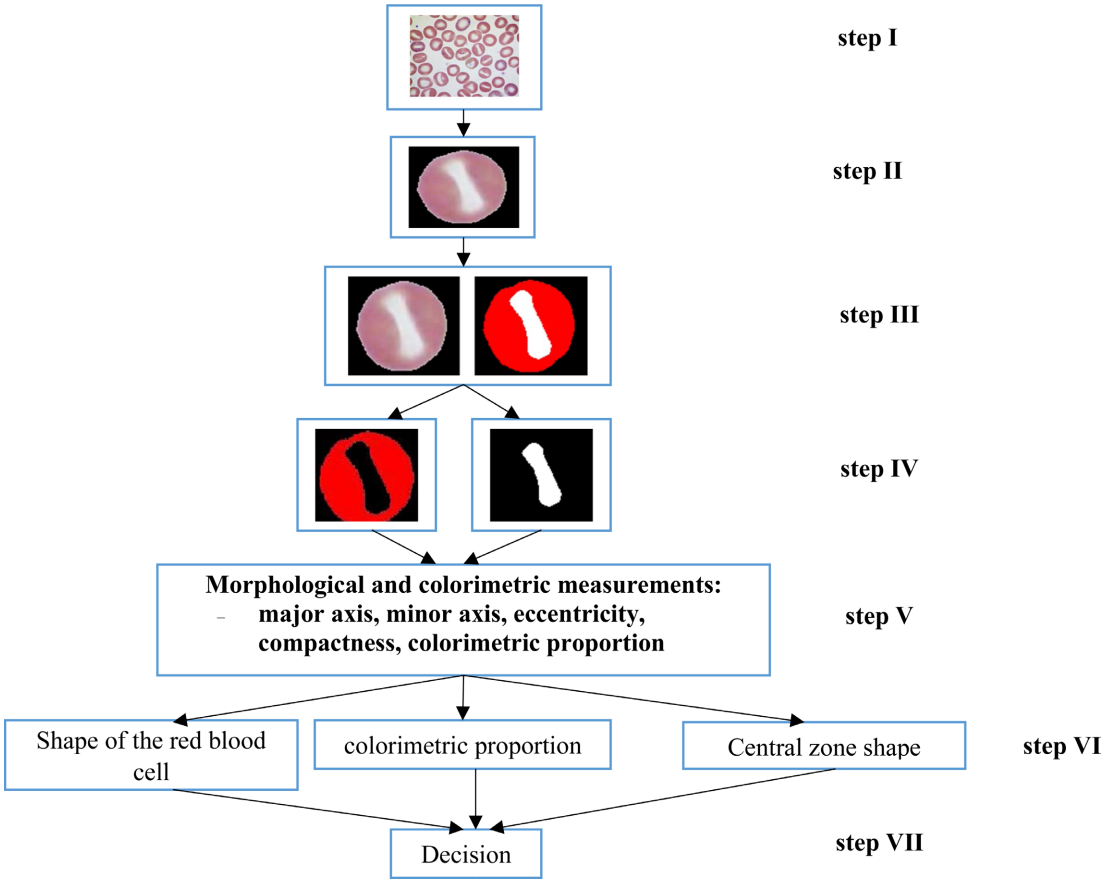

Figure 5. Proposed flowchart for the detection of stomatocytes.

Table 2. Morphological parameters of stomatocytes.

	Morphological parameters: stomatocytes				
	Compactness	minor Axis (r1)	major Axis (r2)	Axis difference	varconvex
H5_2	1.15	87	93	6	0
H5_3	1.23	77	78	1	0
H5_4	1.20	66	72	6	0
H5_5	1.17	69	74	5	0
H5_6	1.22	65	69	4	0
H2_2	1.24	78	83	5	0
H2_3	1.23	85	86	1	0
H2_4	1.23	87	91	4	0
H2_5	1.25	76	80	4	0
H3_1	1.27	77	79	2	0
H3_2	1.21	83	86	3	0
H3_5	1.26	81	86	5	0

Table 3. Summary of morphological parameter measurements for other erythrocyte types [19].

	Normal erythrocytes	Annulocytes	Elliptocytes	Sickle cells	Acanthocytes
Compactness C	1.13 < c < 1.22	0.9 < c ≤ 1.05	0.9 < c ≤ 1.09	0.53 < c ≤ 0.73	0.57 < c ≤ 0.78
Axis difference (r)	r < 7	r < 7	25 < r ≤ 29.36	32 < r ≤ 35.69	21 < r ≤ 42.02
% Red	86 < %R ≤ 92	54 < %R ≤ 66	96 < %R ≤ 100	96 < %R ≤ 100	100%
%White	10 < %B < 13	33 < %B < 45	10 < %R ≤ 100	-rare	0%
Center	circular	circular	-sometimes absent	-absent	absent

Table 4. Colorimetric parameters of stomatocytes.

	Colorimetric parameters of stomatocytes			
	Red pixels	White pixels	% White	% Red
H5_2	4195	810	0.16	0.84
H5_3	4075	820	0.16	0.84
H5_4	3082	587	0.16	0.84
H5_5	3222	675	0.17	0.83
H5_6	2982	451	0.13	0.87
H2_2	4659	543	0.10	0.90
H2_3	5034	781	0.13	0.87
H2_4	5540	896	0.14	0.86
H2_5	4340	561	0.11	0.89
H3_1	4162	650	0.14	0.86
H3_2	5083	695	0.12	0.88
H3_5	4568	723	0.14	0.86

Following the isolation of stomatocytes, we extracted and quantified parameters from the images of the initial stomatocytes. Upon analyzing the obtained results, we observed that the stomatocytes exhibit a circular shape, as reported in the literature [22]. This circularity is further supported by the compactness values ranging between 1.15 and 1.22, and by the deviation r being less than 7.

This initial analysis creates a morphological ambiguity between stomatocytes and healthy erythrocytes, which is also observed with annulocytes, as both cell types share similar morphological parameters with stomatocytes (see **Table 2** and **Table 3** above). Consequently, this suggests that stomatocytes could be both normal and abnormal, which is implausible and thus inconsistent.

Conversely, this analysis distinguishes stomatocytes from sickle cells (drepanocytes) and acanthocytes, which exhibit compactness values below 0.80, as well as from elliptocytes, characterized by an elongated shape with a deviation r ranging widely between 25 and 30 (see **Table 2** and **Table 3**).

Furthermore, by performing a colorimetric analysis of stomatocytes in comparison to healthy erythrocytes and annulocytes, stomatocytes can be distinguished from annulocytes based on the proportions of different regions within the red blood cell, specifically the number of red and white pixels. For annulocytes, the proportion of white pixels (%W) ranges between 54% and 67% of the total erythrocyte surface (see Table 3), whereas this proportion is below 18% for stomatocytes (see Table 4).

Table 5. Morphological characteristics of the central region of stomatocytes

	Morphological parameters of stomatocytes: the central slit region.				
	Compactness	Minor Axis (r1)	Major Axis (r2)	Axis difference	Excent
H5_2	0.51	21.87	76.46	54.59	0.96
H5_3	0.58	20.02	69.55	49.53	0.96
H5_4	0.51	14.93	64.15	49.22	0.97
H5_5	0.53	16.02	66.17	50.15	0.97
H5_6	0.50	12.17	55.31	43.14	0.97
H2_2	0.52	9.72	38.24	28.52	0.97
H2_4	0.72	18.07	34.28	16.21	0.91
H2_5	0.75	13.45	30.79	17.34	0.90
H3_1	0.72	12.04	34.52	22.48	0.94
H3_2	0.58	10.05	42.32	32.27	0.97
H3_5	0.84	16.86	42.01	22.15	0.93

Despite the previous analysis, confusion remains in differentiating stomatocytes from healthy erythrocytes. To resolve this issue, we completely isolated the central zone of the erythrocytes and studied their morphology (see Table 5 above). We observed that the central zones—specifically the white areas—of healthy erythrocytes conform to their overall circular shape. In contrast, the central zones of stomatocytes exhibit, on one hand, an elliptical morphology characterized by compactness values centered around approximately 0.5, and on the other hand, high axis deviations. These deviations range from 17 to 54 pixels, further confirming the elliptical shape (see Table 5 above).

5. Conclusions

The automatic identification of blood cells in general, and stomatocytes in particular, represents a promising research area. Stomatocytosis is a hematological disorder that poses a serious threat to human health, as it affects vital organs such as the liver (cirrhosis). Early, precise, and reliable diagnosis is therefore crucial.

To achieve this, we have proposed a method that enables the extraction and segmentation of red blood cells by grouping pixels into two classes. Our method

allowed us to estimate colorimetric and morphological parameters, facilitating the formal identification of any given erythrocyte, whether normal or abnormal.

Indeed, our method enabled a comparative study between stomatocytes and other red blood cells (healthy erythrocytes, annulocytes, elliptocytes, sickle cells, and acanthocytes) by relying on morphological and colorimetric parameters extracted from each red blood cell, with particular emphasis on the morphological characteristics of the central white region of each cell to resolve any ambiguities.

Thus, the identification of stomatocytes is based on compactness, eccentricity characterized by the difference between the major and minor axes, as well as the proportion of red and white pixels.

Our future work will focus on refining the features for the accurate classification of white blood cells based on their morphology and texture.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Alico, J.N., Ouattara, S. and Clement, A. (2020) A New Electronic Instrumentation Approach for the Acquisition of Microscopic Blood Smear Images for the Automatic Diagnosis of Anemia. *Advances in Bioscience and Biotechnology*, **11**, 237-255. https://doi.org/10.4236/abb.2020.116018

[2] Fenneteau, O. and Maier-Redelsperger, M. (2000) Contribution of Blood Smear Examination to the Diagnosis of Constitutional Red Blood Cell Pathology. *Revue Française des Laboratoires*, **2000**, 51-62. https://doi.org/10.1016/s0338-9898(00)80310-8

[3] Wrzyszcz, A. and Rychlik, U. (2022) Morphological Abnormalities of Erythrocytes and Platelets-Selected Issues. *Diagnostyka Laboratoryjna*, **57**, 204-212. https://doi.org/10.5604/01.3001.0016.1865

[4] Berzuini, A., Bianco, C., Migliorini, A.C., Maggioni, M., Valenti, L. and Prati, D. (2021) Red Blood Cell Morphology in Patients with COVID-19-Related Anaemia. *Blood Transfusion*, **19**, 34-36.

[5] Zitzer, N.C. (2023) The Greatness of Glass: Importance of Blood Smear Evaluation. *Veterinary Clinics of North America*: *Small Animal Practice*, **53**, 29-52. https://doi.org/10.1016/j.cvsm.2022.07.005

[6] Mohandas, N. and Gallagher, P.G. (2008) Red Cell Membrane: Past, Present, and Future. *Blood*, **112**, 3939-3948. https://doi.org/10.1182/blood-2008-07-161166

[7] da Coste, J. (2013) Symposium on Prions and Transfusion Safety. *Transfusion Clinique et Biologique*, **20**, 393-394. https://doi.org/10.1016/j.tracli.2013.05.001

[8] Font, W.D., Garcia, S.H., Nicot, M.E., *et al.* (2022) Classification of Red Blood Cell Shapes Using a Sequential Learning Algorithm. In: Bastos-Filho, T.F., de Oliveira Caldeira, E.M. and Frizera-Neto, A., Eds, 27*th Brazilian Congress on Biomedical Engineering*, Vol. 83, Springer, 2059-2065. https://doi.org/10.1007/978-3-030-70601-2_301

[9] Matek, C., Schwarz, S., Spiekermann, K. and Marr, C. (2019) Human-Level Recognition of Blast Cells in Acute Myeloid Leukaemia with Convolutional Neural Networks. *Nature Machine Intelligence*, **1**, 538-544. https://doi.org/10.1038/s42256-019-0101-9

[10] Delgado-Ortet, M., Molina, A., Alférez, S., Rodellar, J. and Merino, A. (2020) A Deep

Learning Approach for Segmentation of Red Blood Cell Images and Malaria Detection. *Entropy*, **22**, Article 657. https://doi.org/10.3390/e22060657

[11] S., A., Ganesan, K. and K., B.B. (2022) A Novel Deep Learning Approach for Sickle Cell Anemia Detection in Human RBCs Using an Improved Wrapper-Based Feature Selection Technique in Microscopic Blood Smear Images. *Biomedical Engineering/Biomedizinische Technik*, **68**, 175-185. https://doi.org/10.1515/bmt-2021-0127

[12] Tseng, T. and Huang, H. (2022) Classification of Peripheral Blood Neutrophils Using Deep Learning. *Cytometry Part A*, **103**, 295-303. https://doi.org/10.1002/cyto.a.24698

[13] Sadafi, A., Bordukova, M., Makhro, A., Navab, N., Bogdanova, A. and Marr, C. (2023) RedTell: An AI Tool for Interpretable Analysis of Red Blood Cell Morphology. *Frontiers in Physiology*, **14**, Article 1058720. https://doi.org/10.3389/fphys.2023.1058720

[14] Alzubaidi, L., Fadhel, M.A., Al-Shamma, O., Zhang, J. and Duan, Y. (2020) Deep Learning Models for Classification of Red Blood Cells in Microscopy Images to Aid in Sickle Cell Anemia Diagnosis. *Electronics*, **9**, Article 427. https://doi.org/10.3390/electronics9030427

[15] Elsalamony, A. (2017) Anaemia Cells Detection Based on Shape Signature Using Neural Networks. *Measurement*, **104**, 50-59. https://doi.org/10.1016/j.measurement.2017.03.012

[16] Di Ruberto, C., Loddo, A. and Putzu, L. (2020) Detection of Red and White Blood Cells from Microscopic Blood Images Using a Region Proposal Approach. *Computers in Biology and Medicine*, **116**, Article 103530. https://doi.org/10.1016/j.compbiomed.2019.103530

[17] K. T., N., Prakash, N., Prasad, K. and Singh, B.M.K. (2025) Red Blood Cell Segmentation and Classification Using Hybrid Image Processing-Squeezenet Model. *Multimedia Tools and Applications*. Preprint. https://doi.org/10.1007/s11042-025-20644-1

[18] Raja, S.P., Khan, S., Bhatnagar, S., Chen, T.M. and Sathiyanarayanan, M. (2025) Machine Learning Approaches for Improving the Accuracy of Blood Cell Detection and Subtypes Classification Using Smear Microscopic Images. In: Fortino, G., Kumar, A., Swaroop, A. and Shukla, P., Eds., *Proceedings of Third International Conference on Computing and Communication Networks*, *Lecture Notes in Net-Works and Systems*, Vol 977, Springer, 649-667. https://doi.org/10.1007/978-981-97-2671-4_48

[19] Alico, J.N., Ouattara, S. and Clement, A. (2020) A New Strategy for the Morphological and Colorimetric Recognition of Erythrocytes for the Diagnosis of Forms of Anemia Based on Microscopic Color Images of Blood Smears. *International Journal of Advanced Computer Science and Applications*, **11**, 488-497. https://doi.org/10.14569/ijacsa.2020.0110762

[20] Pullaiah, G.C. and P.M., A.K. (2024) Optimal Feature Selection from High-Dimensional Fusion of Blood Smear Images for Leukemia Diagnosis. *Scalable Computing: Practice and Experience*, **25**, 1980-2000. https://doi.org/10.12694/scpe.v25i3.2690

[21] Garcia-Lamont, F., Lopez-Chau, A., Cervantes, J. and Ruiz, S. (2024) Nucleus Segmentation of White Blood Cells in Blood Smear Images by Modeling the Pixels' Intensities as a Set of Three Gaussian Distributions. *Medical & Biological Engineering & Computing*, **62**, 2371-2388. https://doi.org/10.1007/s11517-024-03065-4

[22] https://www.thebloodproject.com/stomatocyte/