

SICKLE CELL IDENTIFICATION USING IMAGE PROCESSING AND RED
BLOOD CELL MORPHOLOGICAL CHARACTERISTICS

UMAR TURAKI ABDUL-MALIK

UNIVERSITI TEKNOLOGI MALAYSIA

SICKLE CELL IDENTIFICATION USING IMAGE PROCESSING AND RED
BLOOD CELL MORPHOLOGICAL CHARACTERISTICS

UMAR TURAKI ABDUL-MALIK

A project report submitted in partial fulfilment of the
requirements for the award of the degree of
Master of Engineering (Computer and Microelectronic Systems)

School of Electrical Engineering
Faculty of Engineering
Universiti Teknologi Malaysia

FEBRUARY 2021

DEDICATION

This thesis is dedicated to my parents, who taught me that the best knowledge is that which benefits the humanity.

ACKNOWLEDGEMENT

Alhamdulillah. Indeed, all praise is due to Allah. We praise Him and seek His help and forgiveness. We seek protection with Allah from our soul's evils and our wrong conducts. He whom Allah guide, no one can misguide; and he whom He misguides, no one can guide.

I wish to express my deepest gratitude to my supervisor, Prof. Madya Ts. Ir. Dr. Nasrul Humaimi Mahmood, who has continuous guidance, encouragement, support, and fatherly advice during the period of my project and writing of the dissertation. Indeed, without his help, the goal of this project would not have been realized.

May I also thank my fellow postgraduate students for their tips, kindness, and profitable relationship. I extend appreciation to all my colleagues in the department and others who have assisted in various circumstances. Their suggestions were useful indeed. Unfortunately, it is not possible to list all of them in this limited space.

Finally, I am grateful to all my family members and friends for their prayers and endurance.

May Allah reward every one of you with paradise, Amin.

ABSTRACT

Blood is the most vital liquid that helps sustain the healthiness and life of the human body. Biologically, normal red blood cells have circular shapes and play a key role in transporting oxygen and nutrient to tissues. Red blood cells are bendable, which allows them to pass through the veins and arteries smoothly. Sadly, there are exceptional individuals with abnormal blood cells call sickle cell disease. The physical shape of the abnormal blood cells is in sickle/crescent form. Sickle cell disease is hereditary, and a person becomes affected if at least one of the parents has the abnormal haemoglobin S gene. The danger of sickle cells is that they inflict many severe health conditions such as pain, tiredness, jaundice, kidney problem, and other critical illnesses. For many years, managing and diagnosing sickle patients is performed by collecting blood samples to manually observe the irregular shapes of the red blood cells using a microscope. This process is time-consuming and results in errors for large samples of blood. In this thesis, a compelling image processing method is proposed to optimize the detection of abnormality in human blood cells with the deep learning technique. Ten images of red blood cells were randomly collected from the online source using the Google search engine. Each image was analyzed using MATLAB codes for image processing using the blood cell area, eccentricity, diameter, extension, and form factor as input parameters. The study results show that the proposed technique has 71 – 100 percent accuracy, far higher than what is obtainable in the manual method. This technique can serve and enhance the current manual method of sickle cell segmentation because it is faster and more accurate.

ABSTRAK

Darah adalah cecair yang paling penting yang membantu mengekalkan kesihatan dan kehidupan tubuh manusia. Secara biologi, sel darah merah normal mempunyai bentuk bulat dan memainkan peranan penting dalam mengangkut oksigen dan nutrien ke tisu. Sel darah merah dibengkokkan, di mana membolehkannya melancarkan urat dan arteri dengan lancar. Malangnya, ada individu yang luar biasa dengan sel darah yang tidak normal yang disebut penyakit sel sabit. Bentuk fizikal sel darah yang tidak normal adalah dalam bentuk sabit / sabit. Penyakit sel sabit turun temurun dan seseorang akan terjejas sekiranya sekurang-kurangnya salah seorang ibu bapa mempunyai gen hemoglobin S yang tidak normal. Bahaya sel sabit adalah bahawa mereka menimbulkan banyak keadaan kesihatan yang teruk seperti sakit, keletihan, penyakit kuning, masalah ginjal, dan penyakit kritikal lain. Selama bertahun-tahun, pengurusan dan diagnosis pesakit sabit dilakukan dengan mengumpulkan sampel darah untuk memerhatikan secara manual bentuk sel darah merah yang tidak teratur menggunakan mikroskop. Proses ini memakan masa dan mengakibatkan kesilapan ketika sampel darah yang besar akan diuji. Dalam kajian ini, kaedah pemprosesan gambar yang berkesan dicadangkan untuk mengoptimumkan pengesanan kelainan pada sel darah manusia dengan bantuan teknik pembelajaran mendalam. Sepuluh gambar sel darah merah dikumpulkan secara rawak dari sumber dalam talian menggunakan mesin carian Google. Setiap gambar dianalisis menggunakan kod MATLAB untuk memproses gambar menggunakan luas sel darah, eksentrik, diameter, pemanjangan, dan faktor bentuk sebagai parameter input. Hasil kajian menunjukkan bahawa teknik yang dicadangkan memiliki ketepatan 71 - 100 peratus, yang jauh lebih tinggi daripada yang diperolehi dalam kaedah manual. Teknik ini dapat berfungsi dan meningkatkan kaedah manual segmentasi sel sabit kerana lebih cepat dan tepat.

TABLE OF CONTENTS

	TITLE	PAGE
	DECLARATION	iii
	DEDICATION	iv
	ACKNOWLEDGEMENT	v
	ABSTRACT	vi
	ABSTRAK	vii
	TABLE OF CONTENTS	viii
	LIST OF TABLES	xi
	LIST OF FIGURES	xii
	LIST OF ABBREVIATIONS	xiii
	LIST OF APPENDICES	xiv
CHAPTER 1	INTRODUCTION	1
	1.1 Problem Background	1
	1.2 Problem Statement	3
	1.3 Objectives of the Study	3
	1.4 Research Scope	3
	1.5 Significance of the Study	4
	1.6 Chapters Organization	4
CHAPTER 2	LITERATURE REVIEW	5
	2.1 Introduction	5
	2.2 Blood Diseases and SCA	6
	2.2.1 SCD Complications	6
	2.3 Detection of SCD	7
	2.4 Digital Image Separations of RBC Cluster for SCD	10
	2.5 Blood Cell Image Segmentation	11
	2.5.1 Blood Cells Extraction using Colour Based Segmentation Technique	11

2.5.2	Abnormal Finding in Human RBC in Diagnosing Sickle Cell Anaemia Using Image Processing.	11
2.5.3	Robust and Efficient Approach to Diagnose Sickle Cell Anemia in Blood	12
2.5.4	Image Processing-Based Diagnosis of Sickle Cell Anemia in Erythrocytes	12
2.5.5	Detection of Sickle Cell Anemia and thalassemia using image processing techniques	14
2.6	Review on Identification of Red Blood Cells by Image Processing	15
2.7	Image Processing Based Diagnosis of Sickle Cell Anemia in erythrocyte	15
2.8	Image Validation	16
2.9	Summary	17
CHAPTER 3	RESEARCH METHODOLOGY	19
3.1	Project Overview	19
3.1.1	Input image	19
3.2	Image Segmentation	21
3.2.1	Filling of the holes	22
3.2.2	Removing Undesired Borders	22
3.2.3	Labelling of Images	23
3.2.4	Thresholding in Image Segmentation	23
3.2.5	Estimation of Image Properties	24
3.3	Image Processing Parameters	25
3.4	Summary	26
CHAPTER 4	RESULTS AND DISCUSSION	27
4.1	Introduction	27
4.2	Blood Sample Image 1	27
4.3	Blood Sample Image 2	28
4.4	Blood Sample Image 3	29
4.5	Blood Sample Image 4	30
4.6	Blood Sample Image 5	31

4.7	Blood Sample Image 6	32
4.8	Blood Sample Image 7	33
4.9	Blood Sample Image 8	34
4.10	Blood Sample Image 9	35
4.11	Blood Sample Image 10	36
4.12	Discussions	37
CHAPTER 5	CONCLUSION AND RECOMMENDATIONS	41
5.1	Conclusion	41
5.2	Future Works	42
REFERENCES		43
Appendices A - B		47 - 58

LIST OF TABLES

TABLE NO.	TITLE	PAGE
Table 3.1	Definition of image parameters utilized in characterizing SCA cells from Mathworks	24
Table 3.2	MATLAB output parameters for the primary blood sample	25
Table 3.3	Secondary image processing parameters	26
Table 4.1	Results of ten (10) samples of secondary RBC images processed	38

LIST OF FIGURES

FIGURE NO.	TITLE	PAGE
Figure 1.1	An example of (a) SCD condition and (b) hereditary chain from parents to a child	2
Figure 2.1	Flowchart showing RBC classification [20]	8
Figure 2.2	RBC segmentation methods [7]	10
Figure 3.1	Stages of image conversions	19
Figure 3.2	input blood image in RGB form	19
Figure 3.3	RGB blood image converted into grayscale	20
Figure 3.4	Binary image of blood cells converted from grayscale	20
Figure 3.5	Image segmentation procedures and detection SCA	21
Figure 3.6	A (a) binary image filled to generate (b) a filled-image	22
Figure 3.7	Labelled objects in a cell image	23
Figure 3.8	Detected SCA (abnormal cell images)	25
Figure 4.1	Processed blood image of sample 1	28
Figure 4.2	Processed blood image of sample 2	29
Figure 4.3	Processed blood image of sample 3	30
Figure 4.4	Processed blood image of sample 4	31
Figure 4.5	Processed blood image of sample 5	32
Figure 4.6	Processed blood image of sample 6	33
Figure 4.7	Processed blood image of sample 7	34
Figure 4.8	Processed blood image of sample 8	35
Figure 4.9	Processed blood image of sample 9	36
Figure 4.10	Results of all images processed from sample 10	37

LIST OF ABBREVIATIONS

HbA	-	Adult Haemoglobin
HbS	-	Sickle Haemoglobin
RBC	-	Red Blood Cell
SCA	-	Sickle Cell Anaemia
SCD	-	Sickle Cell Disease

LIST OF APPENDICES

APPENDIX	TITLE	PAGE
Appendix A	Implementation of MATLAB Image Processing	47
Appendix B	MATLAB Code	50

CHAPTER 1

INTRODUCTION

1.1 Problem Background

Sickle cell disease (SCD) is an inheritable abnormality in the human red blood cell (RBC). In a healthy person, the RBCs are circular and perform the function of transporting oxygen and nutrients to all parts of the body. On the contrary, persons with SCD have their blood cells in a sickle-shaped/crescent appearance. This abnormality in the RBC shape is known as sickle cell anaemia (SCA) [1, 2]. In individuals with SCA, the red blood have unbendable shapes. They have a rigid structure that clogs the veins and arteries, thereby restricting the smooth flow of blood in the body. For this reason, people with SCA suffer from different health abnormalities and complications such as slow growth, fatigue, fast heart rate, jaundice, and other related sicknesses [3, 4].

In the field of biochemistry, "haemoglobin is the conjugated protein, consisting of haem and the protein globin, that gives red blood cells their characteristic colour" [5]. The haemoglobin undergoes an irreversible reaction with oxygen to form oxygenated blood transported to all body tissues. Unlike other non-communicable diseases, the SCD is heritable. When a person is affected with SCD, the victim has inherited an abnormal haemoglobin gene (haemoglobin S gene) from a parent. Patients with SCD naturally inherit at least one-abnormal haemoglobin from any of the parents [6]. The categories of SCDs are:

- a) Haemoglobin S β 0 thalassemia
- b) Haemoglobin S β + thalassemia
- c) Haemoglobin SC
- d) Haemoglobin SD

- e) Haemoglobin SE
- f) Haemoglobin SS (also known as the SCA)

The example of SCD condition and how it is inherited from parents is shown in Figure 1.1.

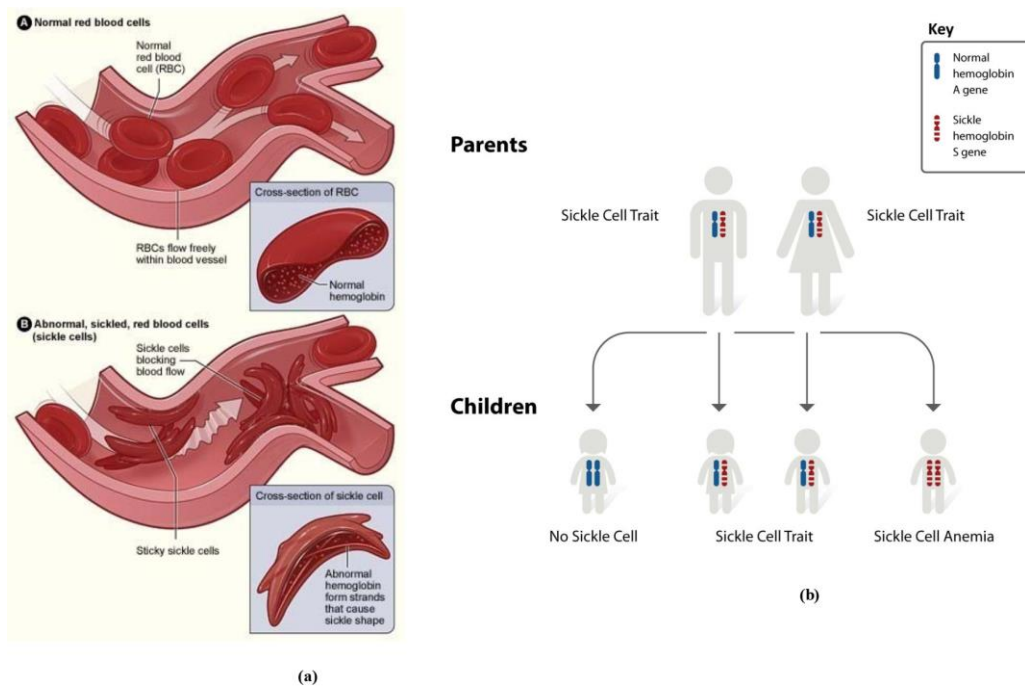


Figure 1.1 An example of (a) SCD condition and (b) hereditary chain from parents to a child

Over the past decades, the classification of sickle cells using the manual technique to observe and classify abnormal RBCs using microscopes. The manual method of RBC segmentation has several drawbacks. It is time-consuming, tedious, and accuracy is low when the blood image samples are many [7]. In the past years, image processing using deep learning has gained numerous applications in medicine and healthcare services. For instance, by employing deep learning algorithms, many RBC images can be segmented promptly. Besides, the level of accuracy and effectiveness is improved [8-12].

In this study, the metric and implemented algorithm is employed to identify normal and abnormal RBCs. The classification of RBCs is performed based on image

properties such as colour, shape, and texture. Through image segmentation, it is possible to categorize RBCs based on the area of the cell, eccentricity, and form factor.

1.2 Problem Statement

The manual identification of normal and abnormal RBCs under the microscope is cumbersome and results in undesirable RBC classification errors. Many studies have proposed deep learning for biomedical image processing of RBCs. This research aims to identify the characteristics of SCA by using red blood cell morphological characteristics using component analysis and comparison to segregate the sickle cells based on their characteristics such as area, eccentricity, diameter, extension, and form factor. The method is simple and straightforward without the need for medical experience to identify abnormal RBCs from many blood samples.

1.3 Objectives of the Study

The objectives of the study are:

- a) To identify and count numbers of sickle cells in the input image.
- b) To identify the best medical image algorithm for recognizing SCA.
- c) To detect the presence of abnormalities in blood smear image by a deep learning algorithm

1.4 Research Scope

To accomplish the stated objectives, previous studies are reviewed to determine the most suitable image processing algorithm. MATLAB 2019a is employed for coding and designing an algorithm that would optimize the images of the selected RBCs to detect abnormalities and observe changes in the cells' physical features. All images utilized are from online secondary sources.

REFERENCES

- [1] Centers for Disease Control and Prevention. "Sickle Cell Disease (SCD)." <https://www.cdc.gov/ncbddd/sicklecell/facts.html> (accessed January 10, 2021).
- [2] R. E. Ware, M. de Montalembert, L. Tshilolo, and M. R. Abboud, "Sickle cell disease," *The Lancet*, vol. 390, no. 10091, pp. 311-323, 2017.
- [3] Centers for Disease Control and Prevention. "Complications and treatments of sickle cell diseases." (accessed January 10, 2021).
- [4] M. T. Gladwin, "Cardiovascular complications and risk of death in sickle-cell disease," *The Lancet*, vol. 387, no. 10037, pp. 2565-2574, 2016.
- [5] Farlex Inc. "The Free Dictionary." <https://www.thefreedictionary.com/> (accessed January 10, 2021).
- [6] National Heart, Lung, and Blood Institute,. "Sickle Cell Disease." <https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease#:~:text=Sickle%20cell%20disease%20is%20a%20genetic%20disorder%20caused%20by%20mutations,in%20pain%20and%20organ%20damage.> (accessed January 10, 2021).
- [7] P. K. Das, S. Meher, R. Panda, and A. Abraham, "A review of automated methods for the detection of sickle cell disease," *IEEE reviews in biomedical engineering*, vol. 13, pp. 309-324, 2019.
- [8] H. A. Aliyu, M. A. A. Razak, and R. Sudirman, "Segmentation and detection of sickle cell red blood image," in *AIP Conference Proceedings*, 2019, vol. 2173, no. 1: AIP Publishing LLC, p. 020004.
- [9] L. Alzubaidi, M. A. Fadhel, O. Al-Shamma, J. Zhang, and Y. Duan, "Deep learning models for classification of red blood cells in microscopy images to aid in sickle cell anemia diagnosis," *Electronics*, vol. 9, no. 3, p. 427, 2020.

- [10] M. Zhang, X. Li, M. Xu, and Q. Li, "RBC semantic segmentation for sickle cell disease based on deformable U-Net," in *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 2018: Springer, pp. 695-702.
- [11] M. Zhang, X. Li, M. Xu, and Q. Li, "Automated Semantic Segmentation of Red Blood Cells for Sickle Cell Disease," *IEEE Journal of Biomedical and Health Informatics*, vol. 24, no. 11, pp. 3095-3102, 2020.
- [12] M. Zhang, X. Li, M. Xu, and Q. Li, "Image segmentation and classification for sickle cell disease using deformable u-net," *arXiv preprint arXiv:1710.08149*, 2017.
- [13] W. William P. "A Brief History of Sickle Cell Disease." <http://www.sicklecell.howard.edu/ABriefHistoryofSickleCellDisease.htm> (accessed January 20, 2021).
- [14] Center for Sickle Cell Disease. "Sickle Cell Disease Information." <http://sicklecell.howard.edu/information.htm> (accessed January 15, 2021).
- [15] V. Acharya and K. Prakasha, "Computer Aided Technique to Separate the Red Blood Cells, Categorize them and Diagnose Sickle Cell Anemia," *Journal of Engineering Science & Technology Review*, vol. 12, no. 2, 2019.
- [16] Z. Huang *et al.*, "Fusion high-resolution network for diagnosing ChestX-ray images," *Electronics*, vol. 9, no. 1, p. 190, 2020.
- [17] S. Nurmaini, A. Darmawahyuni, A. N. Sakti Mukti, M. N. Rachmatullah, F. Firdaus, and B. Tutuko, "Deep learning-based stacked denoising and autoencoder for ECG heartbeat classification," *Electronics*, vol. 9, no. 1, p. 135, 2020.
- [18] F. B. Piel and T. N. Williams, "Sickle cell anemia: history and epidemiology," in *Sickle cell anemia*: Springer, 2016, pp. 23-47.
- [19] V. Aparna, T. Sarath, and K. Ramachandran, "Simulation model for anemia detection using RBC counting algorithms and watershed transform," in *2017*

- International Conference on Intelligent Computing, Instrumentation and Control Technologies (ICICICT)*, 2017: IEEE, pp. 284-291.
- [20] M. Gonzalez-Hidalgo, F. Guerrero-Pena, S. Herold-García, A. Jaume-i-Capó, and P. D. Marrero-Fernández, "Red blood cell cluster separation from digital images for use in sickle cell disease," *IEEE journal of biomedical and health informatics*, vol. 19, no. 4, pp. 1514-1525, 2014.
- [21] S. Rexcy, V. Akshaya, and K. Swetha, "Effective use of image processing techniques for the detection of sickle cell anemia and presence of plasmodium parasites," *International Journal of Advance Research and Innovative Ideas in Education*, vol. 2, no. 2, pp. 701-706, 2016.
- [22] T. S. Chy and M. A. Rahaman, "Automatic sickle cell anemia detection using image processing technique," in *2018 International Conference on Advancement in Electrical and Electronic Engineering (ICAEEE)*, 2018: IEEE, pp. 1-4.
- [23] R. Adollah, M. Y. Mashor, N. M. Nasir, H. Rosline, H. Mahsin, and H. Adilah, "Blood cell image segmentation: a review," in *4th Kuala Lumpur international conference on biomedical engineering 2008*, 2008: Springer, pp. 141-144.
- [24] E. R. Dougherty, *Digital image processing methods*. CRC Press, 2020.
- [25] M. Bhatt and S. Prabha, "Detection of abnormal blood cells using image processing technique," *International Journal of Electrical and Electronics Engineers (IJEEE)*, vol. 7, no. 01, pp. 89-94, 2015.
- [26] M. A. Joshi, *Digital image processing: An algorithmic approach*. PHI Learning Pvt. Ltd., 2018.
- [27] M. González-Hidalgo, F. A. Guerrero-Peña, S. Herold-García, A. Jaume-i-Capó, and P. D. Marrero-Fernández, "Red Blood Cell Cluster Separation From Digital Images for Use in Sickle Cell Disease," *IEEE Journal of Biomedical and Health Informatics*, vol. 19, no. 4, pp. 1514-1525, 2015, doi: 10.1109/JBHI.2014.2356402.

- [28] I. Chintawar, M. Aishvarya, and C. Kuhikar, "Detection of sickle cells using image processing," *International Journal of Science Technology Engineering*, vol. 2, no. 9, pp. 335-339, 2016.
- [29] Mathworks. "Image Processing Toolbox." <https://www.mathworks.com/products/image.html> (accessed January 05, 2021).
- [30] J. Li, H. Mu, and W. Xu, "A method of using digital image processing for edge detection of red blood cells," *Sensors & Transducers*, vol. 159, no. 11, p. 1, 2013.
- [31] V. Zharkova, *Artificial intelligence in recognition and classification of astrophysical and medical images*. Springer Science & Business Media, 2007.
- [32] K. Deep, A. Nagar, M. Pant, and J. C. Bansal, *Proceedings of the International Conference on Soft Computing for Problem Solving (SocProS 2011) December 20-22, 2011: Volume 2*. Springer, 2012.
- [33] L. Alzubaidi, M. A. Fadhel, O. Al-Shamma, and J. Zhang, "Robust and efficient approach to diagnose sickle cell anemia in blood," in *International Conference on Intelligent Systems Design and Applications*, 2018: Springer, pp. 560-570.
- [34] Mathworks. "Image Processing Toolbox." <https://www.mathworks.com/help/images/ref/im2bw.html> (accessed January 14, 2021).
- [35] H. A. Aliyu, R. Sudirman, M. A. A. Razak, and M. A. Abd Wahab, "Red blood cells abnormality classification: Deep learning architecture versus support vector machine," *International Journal of Integrated Engineering*, vol. 10, no. 7, 2018.