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A Review on Digital Microscopic Images for Plasmodium Parasite Detection

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Abstract

Indonesia is one of the regions that contribute to the increasing number of malaria cases. In 2019, more than 250 million malaria cases were found in Indonesia. This phenomenon is caused by several factors, including the examination procedure. In Indonesia, the digital microscopic examination has become the gold standard procedure in detecting and diagnosing malaria, whereas this procedure requires considerable expertise. Hence, the rapid examination is difficult to ensure. In order to overcome this problem, several methods of malaria detection have been proposed with a different approach. Image processing and computer vision techniques have become a powerful approach in the development of early detection systems called computer-aided detection (CADe) and computer-aided diagnosis (CADx). Several previous findings reported their contributions in detecting Plasmodium parasites using image processing and computer vision. Recently, artificial intelligence, including machine learning and deep learning, also offered outstanding results in detecting the Plasmodium parasite. This paper aims to present a scientific review of recent image processing and computer vision applications for the development of CADe or CADx in order to assist the doctor in doing rapid detection and diagnosis.

Keywords*: CAD; early detection; malaria; medical image analysis; plasmodium parasite*

1. Introduction

Malaria is one of an epidemic health disease and well-known as a serious infectious disease (Loddo, Di Ruberto, & Kocher, 2018). Generally, malaria is infected by parasites of peripheral blood that is one of the genus Plasmodium. Because of these parasites infect the blood cells, the doctor usually uses microscopic procedure for rapid screening of malaria. The diagnostic microscopic procedure of malaria requires the three following essential tasks which should be done sequentially (Tek, Dempster, & Kale, 2010): (1) Identifying the presence or absence of Plasmodium parasite by analyzing the examined blood specimen; (2) Identifying the species of Plasmodium parasite from the detected parasites. Plasmodium parasite generally has four species, i.e. Plasmodium Falciparum, Plasmodium Vivax, Plasmodium Malariae and Plasmodium Ovale; and (3) Identifying the life-cycle-stages of the Plasmodium parasite. Plasmodium parasite has three life-cycle-stages that grows up in each

Identifying the presence or absence of Plasmodium parasite becomes the most important task particularly in the screening process. Identifying the species of Plasmodium parasite uses for giving an appropriate treatment to the patients. Life-cycle-stages detection is an essential task for accurately assessing the parasitemia which defines as an infection degree e.g. infected or uninfected cell ratio. Life-cycle-stages detection is also used by clinical research for producing respective treatment and drugs that must be analyzed before (Tek et al., 2010).

The diagnostic microscopic procedure of malaria is conducted manually and requires a considerable expertise. It was shown in several studies that this manual procedure becomes the unreliable screening method at the time when conducted by non-expert (Bates, Bekoe, & Asamoa-Adu, 2004; Coleman et al., 2002; Kettelhut, Chiodini, Edwards, & Moody, 2003). Furthermore, image modality quality also affects the detection and diagnosis process. Some artifacts that have similar characteristic with Plasmodium parasite makes the doctor

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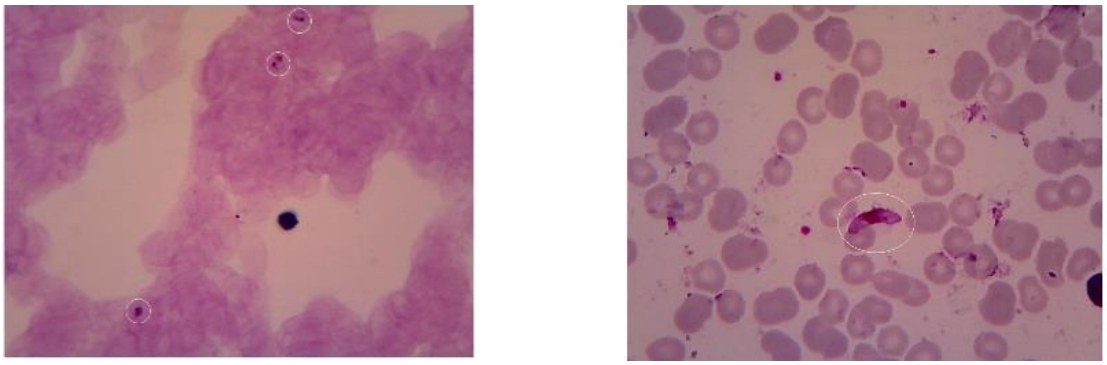

(a) (b)

Figure 1. Example of (a) thick blood smear modality and (b) thin blood smear modality with *Plasmodium* is depicted by white circle shape.

difficult to distinguish either parasite or artifact. Considering this unreliable result, image modality quality and availability of expert, computer aided detection (CADe) and computer aided diagnosis (CADx) are developed. Several researchers try to develop many algorithms and scheme for assisting doctor in screening or examining malaria.

Implementation of computer vision techniques in malaria screening detection and diagnosis becomes an interesting challenge in order to overcome some problems related to diagnostic microscopic procedure that is manual conducted by doctor (Loddo et al., 2018). This paper presents a comprehensive review and analysis of several works conducted which have implemented image processing and machine learning as a powerful method to detect and identify Plasmodium parasite. All explanation in this paper is organized as follow: section two describes about Plasmodium parasite detection method, section three describes about analysis and discussion, section four describes about gaps and issues, and finally conclusion is stated in section five.

2. Plasmodium Parasite Detection Method

This section presents the investigation of several process including different method and algorithm which have potential to be implemented in development of CADe or CADx of malaria as follow: preprocessing step, detection and segmentation step, feature extraction step, classification step, performance evaluation step. All these processes are combined to produce the powerful CADe or CADx. Extensive scientific article searching in several publishers e.g. Elsevier, IEEExplore, PubMed, Springer, etc is conducted based on keyword of "Plasmodium detection", "malaria detection and diagnosis", "CAD for malaria" up to December 2019. Since image processing and computer vision have been used in all of steps described before, the reviewed works is explained in the six following sub-sections which describes about the methodology.

2.1 Data

Digital microscopic images are an approved image modality in development of CAD for malaria. There are two types of digital microscopic images that often use in development of CAD for malaria i.e. thick blood smear images and thin blood smear images. Example of both types are depicted in Fig. 1. Each blood smear has different medical application. Thick blood smear is used in early detection process, while thin blood smear is used for identifying species and life-cycle-stages. However, several researchers use thin blood smear for developing CAD, because this modality is more completely appearing all information of Plasmodium parasite than thick blood smear.

All used data that have been reviewed in this study are provided by the local hospital of each research. However, some public datasets are available as illustrated in Table 1.

2.2 Preprocessing step

In the image processing field, particularly in development of computer-aided, preprocessing methods are an essential process in order to enhance the image quality. Preprocessing is assumed as applying several algorithms for improving the image such as normalization, unwanted noise and artifact removal, contrast enhancement, etc. All these processes are very useful in image analysis process. Generally, preprocessing process is conducted by considering the characteristic of image data. Digital microscopic images are provided by microscope examination which is affected by lighting and magnification. Hence, different dataset may need different method.

Oliverira et al. (Oliveira et al., 2017) applies artificial intelligence and modifies face detection method for identifying Plasmodium parasite. In this research work, preprocessing step is done by removing the image background around red blood cells by applying morphological erosion. Gonzalez-Betancourt et al.

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Table 1. Public dataset

Creator	Scope	Number of data
National Library of Medicine (National Library of Medicine, n.d.)	Classification case	27,558 cell images with equal instances of parasitized and uninfected cells
GEO Dataset (GEO DataSets, n.d.)	Classification case	Some cases are available
Malaria Bounding Boxes (Mader, n.d.)	Detection case	1364 images
Malaria BBC (Dharun, n.d.)	Classification case	This dataset consists of 103 leukocyte; 71,546 red blood cell; 144 gametocyte; 352 ring; 179 schizont; and 1,473 trophozoite
Cell Images for malaria Detection (Kumawat, n.d.)	Classification case	13,780 images of parasitized and 13,780 images of uninfected blood cell
BIOGSP – Malaria dataset (BioGPS, n.d.)	Some cases are available	Some cases are available

(González-Betancourt et al., 2017) proposes a Plasmodium detection system using watershed segmentation and mathematical operators. In the first process, this research work eliminates small irrelevant structures and part of noise by applying morphological operation and performs an image smoothing by applying morphological erosion and dilation with disk-shape structuring element and radius of 0.274 times smaller than radius of red blood cells.

Research conducted by Romero-Rondon et al. (Romero, Sanabria, Bautista, & Mendoza, 2016) proposes a detection scheme using morphological operation, watershed method, Hough transform and K-Means. In the initial process, this study performs noises removal by applying morphological opening and dilation with disk-shaped structuring element. Luis Rosado et al. presents an automated detection method for malaria parasite in thick blood smear. In the pre-processing, this study applies median filter for removing unwanted noise and artifact followed by Otsu thresholding for removing background (Rosado, Correia da Costa, Elias, & Cardoso, 2016).

Stephen Bias et al. presents a malaria detection based on edge detection. For the preprocessing step, this research work applies peak detection and threshold value measurement. Peak detection and threshold value are defined by considering the distribution of intensity value. The largest peak of distribution is assumed to be a background, second peak is assumed to be an object. After that threshold value is determined of middle value between background and object (Bias, Reni, & Kale, 2018).

In study conducted by Edy Victor Haryanto et al., a rapid detection algorithm for Plasmodium parasite is presented. This study only uses schizont stage of Plasmodium Falciparum as a dataset. For the pre-processing step, this study concerns in RoI determination, noise and artifact removal, contrast enhancement. RoI determination is conducted in manual process which approves by the doctor. Noise and artifact removal are conducted by applying median filter. For the contrast enhancement process, this study uses contrast adjustment function that is available on the Matlab library (Haryanto, Mashor, Nasir, & Jaafar, 2017).

Considering that digital microscopic have low contrast and some noise, Jullend Gate et al. uses median filtering to overcome these problems with windowing size of 3 by 3 (Gatc & Maspiyanti, 2018). While, Hedge et al. applies GGB color transformation to enhance quality of image. In summary, all methods that is often used in improving quality of digital microscopic images are described in Table 2 (Hegde, Prasad, Hebbar, & Singh, 2018).

2.3 Detection and segmentation step

Detection and segmentation process are the most important process in early Plasmodium detection process. According to reviewed works, detection and segmentation process can be done by two major approaches i.e. histogram-based segmentation, edge-based segmentation. The two approach are done in different way and procedure. According to several previous works, this procedure is powerful for detecting and segmenting Plasmodium parasite. This method is created based on the characteristic of red blood cells and parasite. Some researcher assume that parasite is located inside of the red blood cells. Accordingly, other object that has similar characteristic with parasite and is located outside of red blood cells is defined as not parasite. This theory is then adopted to create a detection and segmentation scheme.

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Table 2. Summary of preprocessing process

Problem	Objective	Method	Researcher
Noise removal	Removing the background around of red blood cell, noise and all unwanted object	Morphological operation	(González-Betancourt et al., 2017; Oliveira et al., 2017; Romero et al., 2016)
	Removing the unwanted noise and artifact	Median Filter	(Gatc & Maspiyanti, 2018; Haryanto et al., 2017; Rosado et al., 2016)
	Removing the background around of red blood cell and all unwanted object	Thresholding method	(Bias et al., 2018)
Image enhance-ment	Enhancing contrast of image	Contrast adjustment	(Haryanto et al., 2017)
	Enhancing quality of image	GGB color space transformation	(Hegde et al., 2018)

2.3.1 Histogram-based

Research work conducted by Dave et al. presents a red blood cells detection by using unsupervised learning technique followed by histogram based adaptive thresholding and morphological erosion and dilation for segmenting parasite object (Dave & Upla, 2017). Somasekar et al. performs a Plasmodium parasite segmentation by using thresholding method followed by morphological operation (Jalari & Reddy, 2017)(Somasekar & Eswara Reddy, 2015). Rosado et al. proposes a red bloos cells and parasite segmentation using adaptive thresholding approch followed by morphological operation with an elliptcal sructuring element (Rosado et al., 2016)(Rosado, da Costa, Elias, & Cardoso, 2017). Devi et al. proposes segmentation of red blood cells by performing marker-controlled watershed with h-minima as internal marker (Devi, Singha, Sharma, & Laskar, 2017). Romero-Rondon et al. also performs marker-controlled watershed with defining the suitable marker-controlled watershed transform in three different approach i.e. considering on morphological erosion, Hough transform and K-means (Romero et al., 2016). Edy Victor Haryanto et al. proposes a segmentation of red blood cell by using simple thresholding method initialed with transforming the input image in HIS color space (Haryanto et al., 2017). Madhu Golla performs different technique for segmenting red blood cells and parasite. In this study, type II Fuzzy combining with inverse Gaussian gradien is used to resolve segmentation problem (G, 2019).

2.3.2 Edge-based

Edge-based is defined as one of rapid detection process. This approach works based on the edge pattern of an object. Stephen Bias et al. performs an rapid malaria detection in mobile hardware suing edge-based detection technique. The segmentation process is started by segmenting red blood cells which performs by applying multithresholding method. All segmentation process is then continued by selecting the candidate are with three rules, i.e. white object that has area less than 500 pixel is removed, black object that has area less than 150 pixel is removed, other entities cells are removed by applying morphological closing with small disk-shaped structuring element. For the parasite segmentation, this research uses 8 semi-ambigous kernel. All kernels with x component are performed in the image I. If position x match with pixel 1 and 0 in the input image, pixel that match with x will be assumed as edge (Bias et al., 2018).

In summary, all detection and segmentation method in Plasmodium parasite cases are summarized based on used approach as described in Table 3.

2.4 Feature extraction step

Feature extraction is used to extract information that appear in images. In Plasmodium cases, the used features should able to describe the characteristic of Plasmodium parasite. According to the literature review, there are two approaches of feature that is often used in Plasmodium cases. The two approaches are geometry approach and statistical approach.

2.4.1 Geometry approach

Geometry approach: is method used for extracting object based on contour characteristic that can be calculated by shape and edge features such as area, roundness, slimness, circularity etc. Nugroho et al. applies some shape features such as area, circumference, compactness, roundness and slimness. All these features are used to classify Plasmodium malariae and Plasmodium ovale which have difference characteristic of contour (Nugroho, Darojatun, Ardiyanto, & Buana, 2018). Hence, shape feature is chosen in that study. Jullend Gate et al. also uses some shape features such as diameter and area. This research work uses the two

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Table 3. Summary of detection and segmentation process.

Approach	Method	Researcher
Histogram based	Simple thresholding method in specific color space	(Haryanto et al., 2017)
	Simple thresholding followed by morphological operation	(Jalari & Reddy, 2017)(Somasekar & Eswara Reddy, 2015)
	Adaptive thresholding followed by morphological operation	(Rosado et al., 2016)(Rosado et al., 2017)
	Marker-controlled watershed	(Romero et al., 2016)(Devi et al., 2017)
	Type II Fuzzy combining with inverse Gaussian gradient	(G, 2019)
Edge based	Multithresholding method followed by edge detection process	(Bias et al., 2018)

features to extract Plasmodium parasite candidate in order of detection purpose. Since shape feature consists of many feature vectors, several previous studies use them to extract the characteristic of Plasmodium parasite (Gatc & Maspiyanti, 2018). Nugroho et al. uses twelve shape features including of object area, convex area, convexity, object perimeter, convex perimeter, solidity, compactness, roundness, trimness, first invariant moment, second invariant moments and third invariant moments. All these features are expected to be a powerful combination to classifying Plasmodium falciparum and Plasmodium vivax. P. A (Nugroho, Satria Wibawa, Setiawan, Murhandarwati, & Buana, 2019). Pattanaik et al. uses geometry feature including of shape feature to extract Plasmodium parasite and detect object that has similar characteristic with Plasmodium parasite (Pattanaik, Swarnkar, & Sheet, 2017). Nugroho et al. uses seven shape features such as perimeter, area, roundness, slimness, convexity, solidity and dispersion (Nugroho, Dendi Maysanjaya, Setiawan, Murhandarwati, & Oktoeberza, 2019).

2.4.2 Statistical approach

Statistical approach: is a simple feature extraction method to describe the characteristic of object. Statistical approach works by calculating statistic parameters. Statistical approach consists of some feature such as first order of statistical feature, second order of statistical feature and third order of statistical feature. In Plasmodium cases, first order and second order of statistical feature become popular feature that is often used by several researcher. First order of statistical feature including of mean, standard deviation, entropy, skewness, energy, smoothness and kurtosis is used by (Nugroho, Satria Wibawa, et al., 2019)(Nugroho, Dendi Maysanjaya, et al., 2019). Second order of statistical feature including of grey level co-occurrence matrices (GLCM) is used by (Nugroho et al., 2018; Nugroho, Dendi Maysanjaya, et al., 2019; Nugroho, Satria Wibawa, et al., 2019).

Both geometry and statistical approach are used by considering the characteristic of data. Table 4 illustrates

Table 4. Summary of feature extraction process

Approach	Method	Researcher
Geometry approach	Shape feature	(Gatc & Maspiyanti, 2018; Nugroho et al., 2018; Nugroho, Dendi Maysanjaya, et al., 2019; Nugroho, Satria Wibawa, et al., 2019; Pattanaik et al., 2017)
Statistical approach	Histogram	(Nugroho, Satria Wibawa, et al., 2019)(Nugroho, Dendi Maysanjaya, et al., 2019)
	Invariant moment	(Nugroho, Satria Wibawa, et al., 2019)
	GLCM	(Nugroho et al., 2018)(Nugroho, Satria Wibawa, et al., 2019)(Nugroho, Dendi Maysanjaya, et al., 2019)

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the summary of feature extraction method in Plasmodium cases.

2.5 Classification step

In Plasmodium cases, classification process is used for several purposes such as detection, false positive reduction and classification. In the several previous studies conducted by (Nugroho et al., 2018)(Nugroho, Satria Wibawa, et al., 2019)(Nugroho, Dendi Maysanjaya, et al., 2019), multilayer perceptron becomes a popular classifier and obtains the highest performance compared with support vector machine and k-nearest neighbors (Nugroho, Satria Wibawa, et al., 2019).

2.6 Performance evaluation

Performance evaluation is a step for measuring how a method or algorithm is work. For detection field, several researchers use accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) as evaluator. These five parameters can be calculated by the following equations:

$$accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (1)$$

$$sensitivity = \frac{TP}{TP + FN} \quad (2)$$

$$specificity = \frac{TN}{TN + FP} \quad (3)$$

$$PPV = \frac{TP}{TP + FP} \quad (4)$$

$$NPV = \frac{TN}{TN + FN} \quad (5)$$

Performance evaluation are calculated based the objective of research. In detection cases, researcher usually use sensitivity and PPV. In segmentation and classification cases, performance evaluation is illustrated by accuracy, sensitivity, specificity, positive predictive value and negative predictive value.

3. Analysis and discussion

Applying image processing technique in identification of Plasmodium parasite is a challenge in field of computer vision. According to the review process, applying image technique in both detection and classification process needs several steps such as pre-

Table 5. Comparison results

Research	Result											
	Detection		Segmentation					Classification				
	Sen	PPV	Acc	Sen	Spe	PPV	NPV	Acc	Sen	Spe	PPV	NPV
(Oliveira et al., 2017)	-	-	-	-	-	-	-	91.00%	-	-	-	-
(González-Betancourt et al., 2017)	-	97.40%	-	-	-	-	-	-	-	-	-	-
(Romero et al., 2016)	-	-	-	98.38%	98.80%	-	-	-	-	-	-	-
(Rosado et al., 2016)	80.50%	-	-	-	-	-	-	-	-	-	-	-
(Bias et al., 2018)	-	-	-	-	-	-	-	90.06%	90.53%	84.93%	98.49%	45.29%
(Gatc & Maspiyanti, 2018)	84.43%	85.50%	-	-	-	-	-	-	-	-	-	-
(Jalari & Reddy, 2017)	-	-	-	98.00%	93.30%	98.65%	90.33%	-	-	-	-	-
(Rosado et al., 2017)	73.90% to 96.20%	-	-	-	-	-	-	-	-	-	-	-
(Devi et al., 2017)	-	-	98.02%	-	-	-	-	-	-	-	-	-
(Nugroho et al., 2018)	-	-	-	-	-	-	-	95.00%	93.00%	97.00%	-	-
(Nugroho, Satria Wibawa, et al., 2019)	-	-	-	-	-	-	-		91.70%	94.90%	-	-
(Pattanaik et al., 2017)	-	-	-	-	-	-	96.68%	88.70%	93.44%	84.13%	-	-
(Nugroho, Dendi Maysanjaya, et al., 2019)	-	-	-	-	-	-	-	97.29%	97.30%	97.30%	-	-

processing, detection, segmentation, feature extraction and classification. Each process is done by considering the characteristic of data. To summarize the review process, this research work obtains the review result as drawn in Table 5 in which "sen" defines as sensitivity, "acc" defines as accuracy, and "spe" is specificity.

4. Gaps and issues

Both preprocessing and detection or segmentation process can be done in several procedure. Based on the reviewing process that has been conducted, it can be identified several challenges that needs to be resolved. Mostly, previous research works is conducted in homogeny dataset or only particular of data for example only uses one species or life-cycle-stages of Plasmodium. Even though, each species or life-cycle-stages have differences with other species or life-cycle-stages in shape, texture, color, chromatin, etc. Hence, it becomes a challenge for the researcher to develop adaptive segmentation method in un-homogenized data.

Most of previous research works are conducted red blood cells first with the assumption that Plasmodium parasite always appears inside of the red blood cells. This procedure should be regenerated because, parasites that has area same as or closed to the red blood cells are existed. Hence, this detection procedure will not able to detect parasite.

Recently, deep learning becomes a powerful method to resolve many problems. It becomes a challenge to use deep learning approach for detecting Plasmodium parasite.

5. Conclusion

This paper performs the critical review in malaria detection which aims to analyze all potential method that support in computer-aided development. This paper is presented in several sub-section that focus on preprocessing process and detection and segmentation process. According to several previous works, preprocessing is necessary for enhancing the quality of image, while knowledge for choosing the best method is also necessary. In the detection and segmentation, there are two approaches, i.e. histogram-based and edge based. Each of them has advantages and disadvantages. All comparison results of each method have been presented. It can be useful guide for the researcher to overcome the limitation and develop further research in detecting malaria. According to the comparison table, the determination of detection method should consider the data weather it was homogeny or heterogeny.

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