Software-based Diagnostic Approach for Detection of Malaria Parasite in Blood

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ABSTRACT

Malaria is a serious global health problem. Its diagnosis is prevalently done manually using conventional compound light microscopy. However, this traditional approach is time consuming, tiresome, gives variation in results and requires skilled personnel which may not be available everywhere and anytime. To overcome these challenges and provide a reliable alternative, a software-based approach is proposed. The approach is underpinned by image analysis techniques; it aims the detection and diagnosis (or screening) of malaria infection in microscopic images of stained thin blood film smears. Thus, the proposed approach combines selected pre-processing, segmentation, feature extraction and edge detection schemes to distinguish malaria cells in order to identify malaria parasites in stained plasmodium images. Ninety-two (92) images of infected and non-infected plasmodium parasites were acquired (in three categories: downloaded, snapped and digitally acquired images), pre-processed, segmented, relevant features extracted and diagnosis made based on features extracted from the images. The accuracy of the approach was tested. Results show that this approach achieved 91.3% accuracy level, 96.6% sensitivity, and 94.4% positive predictive value. The level of outcome suggests that the software approach can be successfully used for malaria detection.

General Terms

Digital Diagnosis, Image Processing, Malaria Parasite.

Keywords

Algorithm, Feature Extraction, Image Processing, Malaria, Malaria Cell, Parasite Count, Plasmodium, Pre-processing, Segmentation.

1. INTRODUCTION

Malaria is a hazardous disease of the blood that is caused by the Plasmodium parasite, which is transmitted from person to person via the bite of an infected female of the Anopheles mosquito. According to World Health Organization (WHO) most recent malaria report [1], malaria constitutes one of the most life-threatening diseases with about 228 million cases recorded and responsible for an estimated405,000 deaths globally in year 2018 alone. Also, the latter report suggests no sign of global gains in reducing new malaria cases and deaths in the period 2014 to 2018. Plasmodium falciparum is however considered predominant among the malaria species; it accounts for 99.7% malaria cases and responsible for the majority of malaria deaths in Africa [2], [3].

Early detection of malaria infection enables timely prescription of appropriate medication. However, malaria diagnosis involves identification of its parasite or antigens/products in the blood of the patient. Malaria diagnosis through blood examination can be divided into microscopic and non-microscopic tests.

Among the popular and WHO recommended blood-based malaria diagnosis techniques are: the conventional manual microscopy method and rapid diagnosis test (RDT) [2], [4], [5]; also in use for malaria diagnosis are the urine malaria test (UMT) and the polymerase chain reaction (PCR) [6], [7], [8].

Urine test method is a newer method of detecting malaria parasites. It involves the collection of infected person's urine sample, which is then subjected through a series of medical processes before the malaria parasite is detected. While PCR method, unlike urine test, involves the collection and analysis of blood sample; its more accurate than urine test, RDT and microscopy examination; and also, its expensive and requires a specialized laboratory.

Conventional manual microscopy technique makes use of the blood drawn from a patient, which is then used to make a smear on a glass slide. This smear is then stained with a chemical called Giemsa. Staining helps to differentiate between Plasmodium parasites and red blood cells. The most limiting factors of this technique are that it is time consuming, the results obtained are difficult to reproduce and the personnel that conduct the test should be skilled. The last challenge can be quite serious in areas where the disease is endemic or has limited number of skilled human capacity.

Despite the extensive use of above methods and those unmentioned, the conventional manual microscopy examination of peripheral blood smears is still regarded the prime standard and the most prevalent diagnostic technique for malaria [9], [10].

Since most of the available methods are manual, time consuming and dependent on the expert's expertise, thus in order to improve detection rate and accuracy, an easier, faster and less time consuming method is needed. The foregoing thus necessitates a software-based method for detecting malaria infection.

2. RELATED WORKS

Asha et al. [11] deploys an automated malaria parasite detection process that combines a set of image processing techniques. The process is said to curb human error while detecting the presence of malaria parasites in blood samples. In achieving the study goal, the detection process involves image median filtering for noise removal, histogram equalisation, colour based feature extraction of cells, intensity adjustment, image conversion to binary form, and application of a set of morphological operations. Thereafter, infected cells are counted, and then superimposed on original image. Similarly, Diaz et al. [12] utilises a technique for detection, quantification of parasitemia and parasite life stages. Pixel

colour features are extracted and used to train classifiers for detection. Furthermore, Anand et al. [13] investigates detection of plasmodium infected erythrocytes using a technique called holography.

2.1 Malaria Parasite

There are five parasitic species that can cause human infection, namely: Plasmodium falciparum, Plasmodium vivax, Plasmodium knowlesi, Plasmodium ovale, and Plasmodium malariae [4], [14]. Sample images of these species are shown in figure 1 below. They constitute human malaria species that are spread from one person to another via the bite of female mosquitoes of the genus Anopheles [15]. Recent information shows that P. falciparum and P. vivax are the most dominant malaria parasites [2], distributed all over "malarious" areas of different countries and accounting for 60-70% and 30-40% cases respectively in areas like Ethiopia [16].
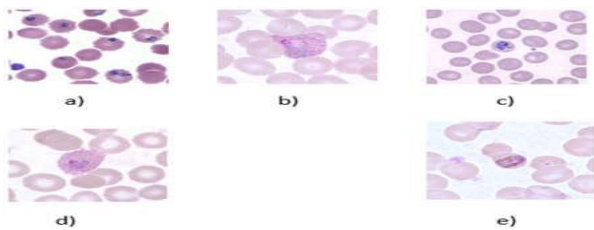

Figure 1: Species of malaria parasite: (a) P. falciparum; (b) P. ovivax; (c) P. Knowlesi; (d) P. ovale; (e) P. malariae [14]

2.2 Malaria Detection

Malaria diagnosis is generally the process of testing the existence of malaria parasites in a patient. Based on earlier discussed literatures, malaria detection is still prevalently manual [2], [6], [8]. However, recent works show efforts made towards automatic detection of malaria, instances are [11], [12], [13] and [17]. Thus, both approaches are reviewed below.

2.2.1 Manual-based malaria detection

As earlier mentioned, the manual process includes microscopic process examination and rapid diagnostic test (RDT). Microscopic examination of blood film is still regarded the most common method or gold standard of malaria diagnosis [10]. A few newer methods for manual detection of malaria such as: the polymerase chain reaction (PCR) [8] [18], [19], [20]; RDT [21], [22] and others (see [23]) have been developed. Although, as earlier stated, PCR method is more accurate than microscopic examination and RDT, it is expensive and requires a specialized laboratory [19]. As a result, microscopic examination of blood films remains the gold standard for laboratory diagnosis of malaria because it is economical and a reliable method.

In respect of microscopic method, diagnosis initially requires observing blood smeared slide under the compound light microscope in order to detect presence or absence of parasites. Practitioners generally observe two types of slides using fast Giemsa stain protocol to highlight the parasites. One blood slide is thick smeared, while the other (or second) is thin smeared; the violet coloured dots within the red blood cell (RBC)are then considered the identified stained parasites.

The probability of detecting parasite in thick blood smeared slides is higher because of the larger volume of blood observed. If the expert suspects the presence of malaria parasite in thick blood smeared slides; then the diagnosis process is followed by examination of a thin smeared blood slide.

The thin blood smear slide is used for the enumeration of the infection. The process of enumeration requires manual count of the number of RBCs in the observed microscopic field; this is followed by manual counting of number of infected RBCs. Apart from enumeration, medical laboratory specialists also need to report the life cycle and the species causing the infection. Thus, the process of diagnosis is extensively dependent on experts.

2.2.2 Automated malaria detection

The automatic based malaria detection might involve the design of an information system for the purpose of detecting malaria parasite. This can be realized through deployment of digital image analysis technique to: detect the occurrence of malaria parasite inside red blood cell (RBC); and determination of the density of parasite inside patient's body which is called percentage of parasitemia or simply parasitemia.

However, detection of malaria parasite using image processing can be challenged by false malaria parasite detection and lack of better measurement in estimating parasitemia. This can be attributed to the fact that the colour of parasites, red blood cell (RBC) and background regions vary depending on the pH of the buffer used for smear preparation [24]. Also, incorrect microscopic settings and poor staining process do results in poor recognition or even in total loss of information. Therefore, a good staining procedure is considered key in order to acquire quality microscopic image that will be processed to detect malaria automatically.

3. METHODS: DIAGNOSIS PROCESS

The proposed software-based diagnostic approach is a five-phase process. The study approach involves: image acquisition, pre-processing, segmentation, feature extraction, and comparison and classification as shown in figure 2. The stated phases are further explained below.
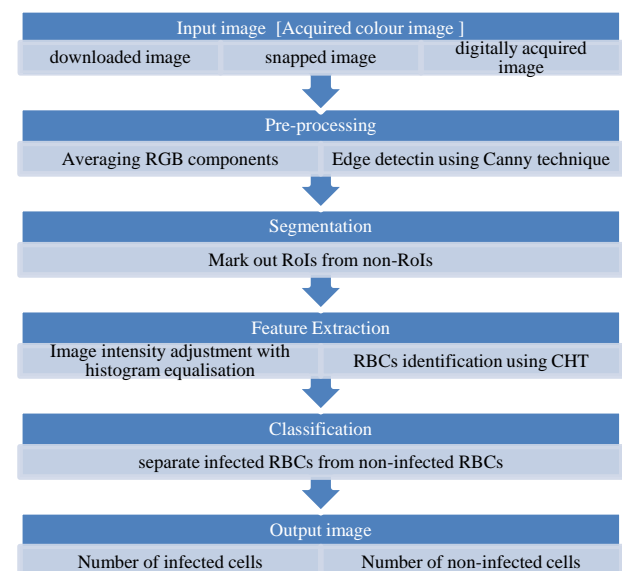

Input image [Acquired colour image]		
downloaded image	snapped image	digitally acquired image

Pre-processing	
Averaging RGB components	Edge detectin using Canny technique

Segmentation
Mark out RoIs from non-RoIs

Feature Extraction	
Image intensity adjustment with histogram equalisation	RBCs identification using CHT

Classification
separate infected RBCs from non-infected RBCs

Output image	
Number of infected cells	Number of non-infected cells

Figure 2: The software diagnosis approach architecture

3.1 Image Acquisition

Images are acquired from three sources: downloaded images from the Centre for Disease Control (CDC) website [25] with sample shown in (a); snapped images as shown in (b); and

digitally acquired images as presented in (c) of figure 3 below.

(a)   **(b)**   **(c)**
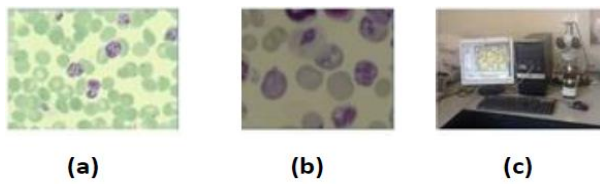
(a) Downloaded image (b) Snapped image (c) Digitally acquired image

Figure 3: Sources of acquired images

3.2 Image Pre-processing

Pre-processing of acquired image(s) is/are undertaken on completion of the image acquisition process. This phase involves converting the original digital colour image into gray scale image. This enables reduction in the processing time; also, it enhances extraction of the image's hue and saturation information, as well as removal of inherent spurious noise.

The colour image to gray scale conversion process involves averaging the components that make up the colour image (that is, R=>Red, G=>Green and B=>Blue) [26]. Figure 4 below depicts the result of averaging of R, G and B into gray scale.
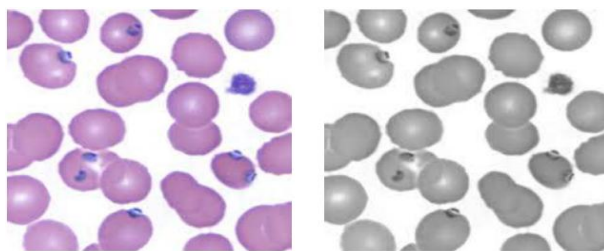
(a) Original image   (b) gray scale image

Figure 4:Color (or RGB) to gray scale conversion

The resulting gray scale image is further processed to detect edges using one of the available standard edge detection methods, which includes: Sobel, Zero-cross, Canny, Laplacian of Gaussian (log) methods [27], [28], [29], among others. Accordingly, this study utilised canny method because it enables the use of two thresholds; thus enables the detection of, as well as distinguishes, strong edges from weak edges. Unlike other methods, canny provides excellent edges detection result [30]. Also, the latter method is less likely to be deceived by noise, and more likely to detect real weak edges [29]. Operationally, the canny method looks for the local maxima of the gradient of an image to determine image edges. Gradient is computed by utilizing the derivative of a Gaussian filter [28], [29].

3.3 Image Segmentation

Segmentation is usually carried out on pre-processed images. Part of the purpose of segmentation is to know and distinguish the RBCs present, and also count the number of red blood cells in images. When an image is segmented, the regions of interest (ROIs) can be distinguished from the non-ROI portion [26], [31]; generally, creating a binary mask of what to be qualified, quantified, or tracked.

In achieving the foregoing, this work utilized a standard segmentation technique known as watershed [32], in preference over other available techniques (see [31]).

Watershed is capable of identifying the region of interest corresponding to object shape and size, provides close contour, and its computationally efficient [31], [32]. Also, the technique enables identification and separation of overlapping cells [33]. Watershed is a form of transformation algorithm that takes an input gray scale image and operates on it like a topographic map. The algorithm considers the brightness of each point in the gray scale image as its height, and then identifies the lines that run along the tops of ridges.

3.4 Feature Extraction

Infected and non-infected red blood cells can be distinguished by extracting a set of features from an image array; thereafter, a set of new variables are computed with relevant information concentrated into separate classes [35]. The goal of this phase, therefore, is to extract features that discriminate between infected and non-infected red blood cells, as much as possible. The extracted features should contain only relevant information, unlike the raw image that has high morphology variations and contains large amount of data with relatively little useable information. Also, features extraction should be robust enough, such that the outcome is reproducible for newly collected samples. The features extraction process is discussed in following sub-sections.

3.4.1 Finding number of RBCs in an image

To find the RBCs in an image there is need to start with questioning how many circles are there in the concern image. By finding out how many circles are there in an image, the number of cells in an image can be determined. There are a number of techniques that can be used to find a circle in an image (see [35]); however, extended Hough transform, known as the Circular Hough transform (CHT) method [36] [37], was employed to count the number of circles. The choice of the latter method is due to its proven capability to accurately count standalone, as well as overlapped cells in an image [36]. Figure 5 shows the result gotten on application of CHT method on a sample image.
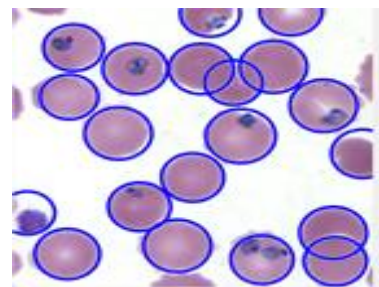

Figure 5: Cells detection
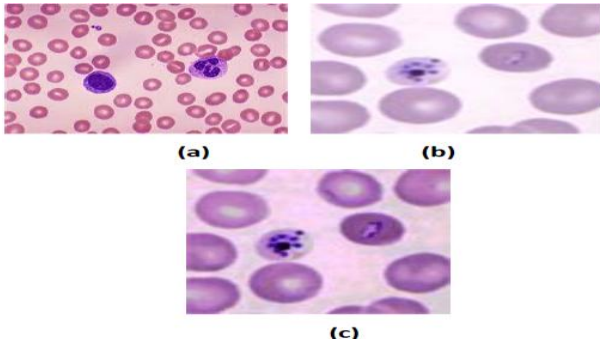
3.4.2 Intensity

There is a need for image intensity adjustment in order to properly identify infected malaria cells therein [36]. Prior to commencement of the identification process, image intensity is adjusted due to likely presence of heterogeneous data with varying intensity. The foregoing is an effective technique; it ensures speedy identification of infected cells since infected images usually have darker regions with high threshold value [38].

Intensity adjustment is undertaken by adjusting target image such that its histogram matches that of a reference image. For instance in MATLAB, the function "*imhistmtch*" accepts an input gray scale image (or True Colour image as appropriate), "I_{image}", then transform such that the histogram of its output image, "O_{image}" approximately matches that of the reference

image, "R_{image}", on the assumption that the same number of bins are utilized for both histograms, thus:

$$O_{image} = imhistmatch\left(I_{image}, R_{image}\right) \qquad (1)$$

However, when the input is a TrueColour image, each colour channel (i.e. R, G or B channel) of the I_{image} is independently matched to corresponding colour channel of its reference image, R_{image}. Figure 6 below shows the result of a sample image intensity adjustment.

(**a**)Reference image (**b**) Target image (**c**) Histmatched image

Figure 6: Intensity adjustment

By adjusting intensity of an image, the pixel value of the infected pixel cells can be determined, thereafter determines the threshold value of the infected cells.

Figure 7 below shows that infected cells have higher pixel value, while other regions of no interest have lower pixel value; this thereby informs the threshold value to use to identify infected cells in an image.
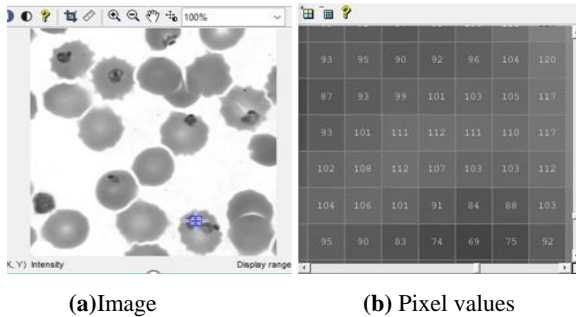

(**a**)Image   (**b**) Pixel values

Figure 7: Threshold for infection and pixel values

3.5 Classification

After step by step application of selected techniques as discussed in earlier phases above, it was possible to classify infected from non-infected cells in an image. Thus, figure 8 represents a sample image with malaria infected cells.
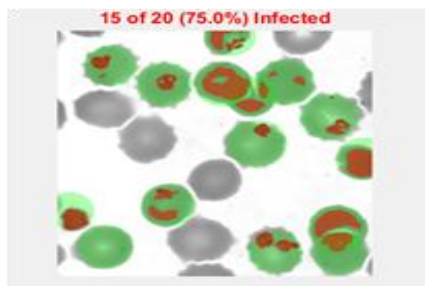

Figure 8: Identified infected cells

4. RESULT ANALYSIS

In order to determine the performance of the proposed software-based diagnostic approach, manual detection was compared with software-enabled detection both at image and cell levels.

For the detection of parasite present at image level, a comparison of software-enabled detected images and manual detection was done for a total of 92 plasmodium images (Downloaded, Snapped and Digitally acquired images).

Some experimental data / results can be seen below:

Table 1: Downloaded images

Image (S/N)	Number of cells present (Cell count)			Number of cells infected (Parasite count)			Malaria detection (If parasite is seen or not)		
	Software	Manual Count	Difference	Software	Manual Count	Difference	Software	Manual Count	Difference
IM-01	1	18	17	0	4	4	Absent	Present	1
IM-02	16	19	3	1	1	0	Present	Present	0
IM-03	4	11	7	0	2	2	Present	Absent	1
IM-04	27	27	0	1	1	0	Present	Present	0

Table 2: Digitally acquired images

Image (S/N)	Number of cells present (Cell count)			Number of cells infected (Parasite count)			Malaria detection (If parasite is seen or not)		
	Software	Manual Count	Difference	Software	Manual Count	Difference	Software	Manual Count	Difference
DIM-01	28	28	0	0	0	0	Absent	Absent	0
DIM-02	25	25	0	1	1	0	Present	Present	0
DIM-03	21	24	4	0	0	0	Absent	Absent	0
DIM-04	20	20	0	1	0	0	Present	Absent	1

Table 3: Snapped images

Image (S/N)	Number of cells present (Cell count)			Number of cells infected (Parasite count)			Malaria detection (If parasite is seen or not)		
	Software	Manual Count	Difference	Software	Manual Count	Difference	Software	Manual Count	Difference
SIM-01	98	102	4	1	2	1	Present	Present	0
SIM-02	111	103	-8	5	5	0	Present	Present	0
SIM-03	126	150	24	4	4	4	Present	Present	0
SIM-04	92	100	8	6	7	1	Present	Present	0

Note that the above compared images comprise of those that have infected cells and those not infected. Out of the 92 images, 84 detections were made correctly. A graphical result analysis of this is shown below.
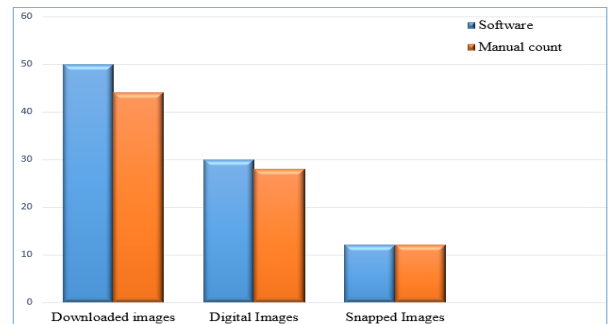

Figure 9: Comparison of manual and software detection at image level.

Out of 50 downloaded images, software detected 44 correctly; and out of the 30 digital images, software detected 28 correctly. However, software detected correctly all the 12 snapped images.

Meanwhile, the 8 images where the software got it wrongly, was due to overlapped cells which results in enlargement of the size. Thus, an accuracy level of 91.3% was achieved using equation 2 below as in Harris et al.[36]. Note, accuracy is the extent to which the value of a measure is close to the true or actual value.

$$Accuracy = \frac{Software\ Detected}{Actual\ Data} \times 100\% \qquad (2)$$

At cell count level, the total of cells (infected and non-infected ones) counted by manual method, as against those counted by software are 2193 and 2020 respectively.

The breakdown of the foregoing manual and software cell counts according to image types is shown graphically below.
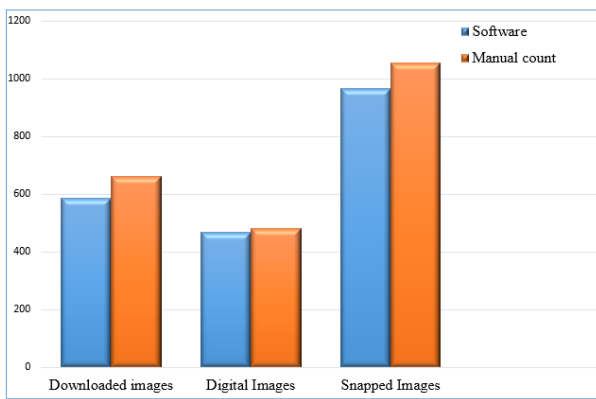

Figure 10: Comparison of manual and software detection at cell level.

Regarding manual versus software cell counts for the downloaded images, digitally acquired images and snapped images, the counting recorded are: 660 as against 586; 480 as against 467; and 1053 as against 967 respectively.

That is, the number of software detected cells is less than total cells in manual detection. Hence, the malaria ratio will be 0.92 (i.e. 92%) using equation 3 below as adapted from Harris et al. [36].

$$Mal.Ratio = \frac{Software\ Detected}{Manual\ Counted\ Cells} \times 100\% \qquad (3)$$

Where conflicts are noticed in cells detection, these were caused by overlapping cells that the related algorithm (in the software) could not resolve (or distinguish it from single cells). Also, the detection of parasites in eight (8) images was erroneous due to overlapped cells thus resulted in cell size enlargement. However, these conflict situations can be eliminated or reduced drastically with a carefully/well prepared blood smears.

In view of the above, the performance of the software approach should be evaluated. According to Bashir et al. [14] and Altman et al. [40], a diagnostic approach's performance can be assessed using some measures such as: sensitivity, specificity and accuracy. Sensitivity is the percentage of true positives correctly determined (or ability to correctly detect parasite(s) in the presence of the symptoms or disease); specificity is the percentage of true negatives correctly detected; while accuracy is as earlier defined above (*see equation 2 above*). Also, the predictive positive value (PPV)

which is defined as the precision rate of an approach can be measured.

Computationally, sensitivity measure can be expressed thus:

$$Sensitivity = \frac{TP}{TP + FN} \times 100\% \qquad (4)$$

While predictive positive value (PPV) as:

$$PPV = \frac{TP}{TP + FP} \times 100\% \qquad (5)$$

From the above equations (4) and (5), TP represents "True Positive", FN implies "False Negative", while FP represents "False Positive".

Thus, based on above reported results (84 detections out of 92 images, with 8 images wrongly diagnosed) and using equations (2) to (5), a summarized result analysis is hereby presented in table 1 below:

Table 1: Summary of all cases for parasitic detection

Description	Units
Total cases tested for parasite presence	92
True Positive (TP)	84
False Positive (FP)	5
False Negative (FN)	3
Accuracy	91.3 %
Malaria Ratio	92 %
Sensitivity analysis (%)	96.6 %
Positive Predictive Value (%)	94.4 %

5. CONCLUSION

Currently, what is regarded as gold standard in the detection of malaria parasite is the manual use of microscopes. This manual approach requires highly skilled personnel which may not be available everywhere and anytime. Also, the manual approach is prone to false detection resulting from human error which can worsen or lead to fatal health condition of patients.

Hence, with the outcome in section 4 above, the proposed software-based approach utilizing image processing techniques (such as *segmentation, feature extraction, edge detection, etc.*) and couple with carefully stained smear, has capability to eliminate or reduce drastically the challenges of the manual approach.

The software-based approach is robust; it recorded high sensitivity ratio, accuracy, positive prediction value, and precise/actual classification of infected cells.

While this study focuses on detection of malaria infected cells, future work can be carried out to predict different stages of infected cells or different kinds of diseases (e.g. cancer) using software-based approach that implements machine learning techniques.

6. ACKNOWLEDGMENT

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