

# **The Review of Microscopic Image Analysis and Computer Aided Malaria Parasite Infected Erythrocyte Detection**

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## **Abstract**

Gold standard test has been the traditional test conducted for malarial diagnosis, wherein the process of preparing a blood smear on a glass slide, staining it and examining them under a microscope for observing parasite genus plasmodium takes place. Despite of numerous other diagnostic test solutions being available, still there are many shortcomings observed in the microscopic analysis. Currently, the treatments are profoundly carried out based on symptoms and if any false negatives take place, it could be fatal and could create varied implications. With numerous cases of malaria related deaths being reported, there is intrinsic need for early detection of the malarial infection in individuals. In this manuscript, review of recent contributions pertaining to computer aided and microscopic image processing for malaria detection strategies are discussed from contemporary literature.

## **1. INTRODUCTION**

Malaria is an epidemic health disease and has significant implications on the health of individuals. Globally, in many countries people are facing the risk of malaria and as per the reports of WHO (World Health Organization), every year millions of people are dying due to malaria. It is estimated that every year 250 million infections are taking place due to parasites of genus plasmodium, with more than 98% deaths resulting because of plasmodium falciparum. In the current techniques used for diagnosis of infections from P.falciparum, manual process is highly adapted, categorically even in the case of developing countries. Despite of some advanced methods being in existence, still the process of manual microscopy of blood films over slides is considered as a golden standard solution. Manual microscopy has significant advantage than the other techniques because of sensitivity and specifics. Among the disadvantages of using the manual microscopy methods, the need for

human intervention to the process is high, and there are potential chances that it could lead to late and also erroneous diagnosis.

Usage of microscope needs extensive training for gaining adequate expertise in diagnosis and also the sheer volume of samples that are to be analyzed could lead to inconsistency in the reports. Also, the other impacting factors are the blood smear, stain quality and the quality of microscope that is used for analysis, in addition to expertise of the pathology professionals.

Usage of microscope needs quality training for gaining expertise in diagnosis. Taking in to consideration, the quantum of samples that have to be analyzed, the microscopic method might be inconsistent. Also, the factors like blood smear, stain quality, microscopic quality and the domain expertise of professionals play a vital role in effective diagnosis. If the computer aided diagnostic methods like the image-based diagnosis methods are adapted, it can certainly support in addressing the limitations envisaged in manual process.

In this paper, the aim is to study the semi-automatic diagnosis method based on image processing and the ones that provide effective and reliable solution. It is imperative that numerous studies were carried out and varied range of computer vision or image based algorithms has been proposed in the past. But many of those algorithms are supervised and complex solutions, and it requires manual intervention and calibration. Considering the rate at which the disease is impacting and the volume of samples that are to be analyzed, there is integral need for more effective and robust solution which needs less human intervention.

In such conditions, solutions that are computer aided, can help in more consistent and accurate diagnosis of true malaria cases and ensure that appropriate diagnosis of malaria symptoms in the case samples are performed. Process of Manual microscopy is performed to investigate under the microscope, the thin blood films on slides for observing ratio of infected red blood cells (iRBCs) called as Parasitemia over 100 microscopic fields. Pathologists have to study parasite morphology by varied life cycle stages for specification advocated by WHO practical microscopy guide.

Giemsa staining method is commonly used method for highlighting the parasites. Among the disadvantages of adapting the Giemsa method, it stains the other blood film features like the platelets, WBC, and slide artifacts. Such other stained objects could lead to implications while analyzing results using manual microscope.

Globally, with the rising population, even the risk of people prone to malaria disease is also rising alarmingly and every year the rise of malaria prone deaths are also increasing.

Malaria Parasitemia is used as a parameter for affirming the quantum of parasites in the patient's blood and also be considered as key indicator of the malarial infection levels in a human body. Manual process of evaluating thin blood smears using the microscope is tedious and also consumes considerable time and also has scope of human errors. Despite the fact that the automated assessments can address some of the

limitations, still the inability in terms of evaluating cases that are varying from standard model, are turning out to be a challenge.

Though, a microscope malaria parasite is detected in blood slides, detection and recognition of plasmodium is possible by the method of staining (Giemsa), which is a chemical process. The process highlights life treating plasmodium parasites, WBC, RBCs.

### 1.1 Microscopic Image Processing

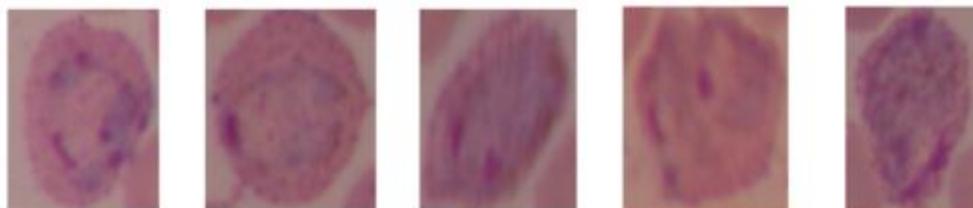
Microscopic images are vividly used in molecular biology and medical domain. As the image modalities are manifold, numerous issues arise after the initial data acquisition step. In this manuscript, several algorithms are reviewed to observe existing solutions and propose critical pipeline of microscopic image compression/storage, and the ones that can be analyzed more efficiently.

## 2. NOMENCLATURE OF THE ERYTHROCYTE FEATURES

Erythrocyte a cell observed in the blood and has life of about 120 days. Microscopic image analysis of blood cells are performed to diagnose varied diseases like malaria, cancer, etc. [1]. Using the texture, size and the color, the differences between a normal and abnormal erythrocyte can be observed. In the normal conditions, mature erythrocytes are usually round, biconcave disc-shaped, the nuclear cell contain around 7-8 microns in diameter. The erythrocytes that are normal are termed as normocytic and the ones that are comprising malarial infection will have changes in features as represented in Fig.1



(a) Normal Erythrocyte



(b) Infected Erythrocyte

**Figure 1:** Normal and Infected Erythrocytes

## 2.1 Feature extraction from Microscopic Blood Smear Images

Feature extraction is an approach of assessing the images for identifying objects or region of interest and analyze tissues in the pathology slides for structure and other features. To ensure right features are adapted for analysis, appropriate selection of subgroup is essential for improving accuracy of classification and reducing any kind of complexities. For distinguishing the infected and non-infected erythrocytes, varied features are used from different array, and computation of new variables are carried out.

Feature sets as detailed above comprise factors to distinguish variance for class and within class of feature vector space, i.e. differentiating classes by the set of features. Morphological features, texture features and intensity features are certain example of set of features resourceful in distinguishing between infected and non-infected erythrocytes.

Morphological features signify the size and shape of a erythrocyte without taking in to account the density, and profoundly in the case of P.Vivax and P.Ovale infections, the erythrocytes are enlarged, but erythrocyte remains the same in case of P.falciparum. Numerous factors like the area, perimeter, eccentricity, compactness ratio, minor axis of best fit ellipse, bending energy, major axis of best fit ellipse, roundness ratio [2] are certain features that are significant with Morphological features. Spatial distribution of intensity in a specific range is provided by texture features exploration. GLCM (Gray level co-occurrence matrix) is integral part of intensity and texture features, local binary pattern, saturation histogram, laplacian and gradient textures [3] [4] [5].

Researchers have focused upon numerous features for classifying the infected and non-infected erythrocyte. F.BorayTek et.al has used the feature set comprising color histogram, areagranuometry, auto-correlogram, relative shape measurements, for diagnosing the malaria parasite infection in erythrocyte [4]. In [5], for detection of erythrocyte observation, the method of automated image processing methods are proposed.

In [6], semi-automated method for quantification and classification of malaria infected erythrocytes has been proposed. Certain key features adapted in the model are sobel histogram, gray scale histogram, saturation level histogram.

Spirngl et.al has proposed the mode of automatic malaria diagnosis using microscopic imaging process. Some of the key features selected in the model are Hu set of invariant moment, intensity histogram, flat texture, run-length matrix, gradient features, co-occurrence matrix, for classifying the erythrocytes [7].

In [8] Perimeter area, and form factor are used for digital analysis of changes by plasmodium vivax and followed by, in [9] content based retrieval approach that relies on features like intensity histogram, Hu moment as key features has been proposed.

Color as well the statistical features comprise area, perimeter, grey scale histogram, saturation histogram, metric are mainly used in [10] for malaria detection. In [11] researchers used the feature sets like the nuclear density, Nucleo cytoplasmic ratio for detection of malaria parasite stages, in automated manner. In [12], quantum of pixels comprising chromatin dot stain, standard deviation related to value channel of HSV representation for each ROI, are selected as features for classifying erythrocytes that are malaria infected. In [13], the researchers have focused upon developing web based frame work for classification based on texture and automated storage of malaria parasite images, using certain features like the fractal dimension, run length matrix ,gray level co-occurrence matrix and local binary pattern.

Features like the Hu moment, color histogram, color auto-correlogram, relative shape measurement that relies on Mobile support for Diagnosis of Communicable Diseases in Remote Locations were proposed [14]. In [15] has proposed the image analysis system that depends on feature sets like gray level texture, color attributes and geometric features for automatic detection and classification.

Multi-scale laplacian of Gaussian and Gabor filter based model has been proposed in [16]. The process of quantitative characterization for plasmodium vivax in the infected erythrocytes has been proposed in [17] by M. Gosh et.al.

Automatic screening of malaria parasite on the basis of machine learning comprising 96 features including entropy, fractal dimension, histogram based features, haralick texture, gray level run length matrix, and many other such features sets, were proposed in [18].

Malaria Parasite Detection in Giemsa-Stained Blood Cell images that are reliant on features, has been proposed in [19]. In [20], morphological features based diagnosis of malaria infections was proposed. In [21] researchers have proposed an effective tool for automatic classification of vivid blood diseases using the digital image processing techniques. In it, the histogram based features for various color channels like the hue, intensity and saturation are used for identifying the normal and infected erythrocytes. In [22], automatic detection of malaria parasite is performed using histogram of color channel and fractal dimension. Malaria disease symptom analysis, using histogram and image processing features has been proposed in [23]. In [24], morphological feature and also the textural features based solution has been proposed for rapid diagnosis of malaria.

Diagnosis of malaria over thin blood smears has been proposed, in which the features like standard deviation, energy, skewness, phase of image, energy etc. are used [25]. N. Linder et.al [26] has proposed the model of computer vision screening of plasmodium falciparum candidate areas in the blood smears. Feature sets like local binary pattern rotation invariant local contrast, scale invariant feature transformation are used for analysis. Automatic characterization based analysis of microscopic

images of thin blood smears had been proposed comprising around 16 morphological features and 80 texture feature sets.

### 3. REVIEW OF LEARNING BASED MALARIA DETECTION STRATEGIES

Makkapati and Rao [27] has supported the segmentation of HSV color space, wherein the Red Blood Cells, WBCs and Parasites are color space segmented in addition to estimating optimal saturation thresholds. The process has resulted with 83% sensitivity, and operates in HSV space. The challenge with the solution is that it can only detect the optimum threshold but do not determine any kind of local or global threshold. The solution reflects upon the color image processing techniques.

Ravi raja and et.al [28] has proposed the models of blood image processing, with detection of malarial parasites comprising infected erythrocytes. After usage of statistical based approach for classifying. Varied range of information like the infected blood color, size and shape are used for analysis. Once the images are compared to the infected images, image transformation process is carried out using scaling and shaping, for reconstructing the image.

Morphological approach technique is introduced by Ruberto et.al [29], in which the segmentation of cell images are more accurate than the traditional watershed based algorithm. As the non-flat disk-shape structuring elements are adapted for improving the accuracy of normal watershed oriented algorithm, the performance has been more effective. Such methods has resulted in better understanding of RBC structure, in an existing watershed based algorithm.

Sadeghian et.al [30] has demonstrated a framework, in which digital image processing is used for segmenting white blood cells. Gray level image processing is used for classifying it to two parts. One as morphological analysis based nucleus segmentation and the other as cytoplasm segmentation relying on thresholding of pixel intensity. In [27], processes that are dependent on RGB color space which segments RBC's and malarial parasites are discussed. In the experiments of this solution, the images are taken from the Leishman-stained blood smears and 83% of sensitivity has been observed in the model.

In [28], automated image analysis based solution has been proposed. The process is based on detection of parasite boundaries and edge detection for representing cell. Steps like pre-processing, edge detection, edge linking and clump split are used for effective processing of proposed solution.

In [31], S P Premaratnea et.al has proposed the solution of digital images using microscopic slides. For the training sets, feed forward back propagation neural network has been used. 64 X 64 pixel images are used for training the data set and segmentation in to digital image.

Image retrieval based solution is proposed by Chen Pan et.al [32], and its classifying cell of the image comprise high image databases. Two types of histogram are used for

the process. KPCA (Kernel Principal Component Analysis) is used for extracting effective features from the feature vector.

In [33] researcher has proposed method of automatic detection and classification of MCCs. The method of block region growing and k-means clustering is adapted for extracting the region, and accordingly, the blanket method is applied for identifying MMCs clusters and the solution has attained 95% high classification and around 93% detection rate.

Amit and P U [34] has introduced segmentation of infected cells in blood smear images comprising adoptive threshold which is performed using Otsu algorithm, and it can give better result when compared to averaging technique.

RDTs (Rapid Diagnostic Tests) [35] are used in immune chromatographic methods, for detecting the antigens derived from malaria in lyses blood. Such tests are currently adapted in detection of Histidinerich protein II, and Parasite lactate dehydrogenizes (pLDH). In [36], Histidinerich protein II is produced by trophozoites and young gametocytes of P.

QBC (Quantitative Buffy Coat) speed [35] proposed in detecting malarial parasites has definitive advantage in laboratories and it comprises large number of samples. It is observed that there is hardly any loss of parasites, from the procedure. In [36], emphasis over the other advantage of QBC model is imperative. Technicians can carry out the QBC test and detect the malaria parasite in less than a day. However, the constraints are relatively higher costs of conducting the model, and scope of leak or breakage of blood filled QBC tubes. Also, lack of scope for managing the permanent record of test is the other key disadvantage in the model [37].

QBC techniques reflect a higher levels of sensitivity and specificity in the laboratory tests, than in the field level tests, in comparison to blood smears approach.

It is imperative that Otsu algorithm approach is very effective when compared to the other models, and the key advantage of the algorithm is despite of many evaluations, less time is consumed in the process. Among all the data science strategies considered for performing on feature sets, computer vision of microscopic images offers better quality of outcome. It is emphatic from the review that there is significant scope for improving the feature optimization strategies for disease diagnosis, by applying data science strategies on computer vision of microscopic images.

#### **4. CONCLUSION**

In this manuscript, the review of data science strategies like machine learning, mining, heuristic and statistical approaches that are applied over the microscopic image features like the texture, local binary patterns, and morphological features, for achieving disease prediction in the early stages. Emphasis has been more on understanding the scope and implications envisaged in computer vision of microscopic image analysis that should be able to observe parasitemia counts in sub-standard smears.

In the review, certain limitations like the lack of optimal feature set optimization methods, search strategies accuracy are observed in the existing methods of contemporary literature. Some of the suitable description features constituting discriminative properties for classifying the blood smears as erythrocytes and parasite infected erythrocytes are also reviewed. Efficient features must be adapted for analysis to improve the process outcome. Key areas like the feature extracting methods, image research and classification strategies that can be very significant for future research.

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