



A Review of Computer-Assisted Techniques Performances in Malaria Diagnosis

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Abstract. Malaria belongs to the class of the deadliest infectious diseases in the world. The generally available tools to diagnose this disease, the microscopy and rapid diagnostic test (RDT), have many limitations. Alternative diagnostic techniques with superior results are inaccessible to developing countries with more prevalent cases. Early detection of the infection is critical. Computer-assisted methods are needed. This study surveys the performance of the computer-assisted techniques used in malaria diagnosis and the preprocessing techniques to render the data usable. The survey illustrates, compares and discusses computer-assisted methods results, considering different performance metrics. It highlights how artificial intelligence can strengthen the fight against disease.

Keywords: Malaria · Diagnosis · Machine learning ·
Computer-assisted techniques · Performance metrics · Deep learning

1 Introduction

Malaria is an ancient disease whose first trace dates from the 5th century before Jesus Christ [1]. The parasite of this disease was discovered in 1880 by Alphonse Laveran, doctor and, French military [2]. Five Plasmodium species cause malaria in humans: Plasmodium falciparum, Plasmodium vivax, malariae Plasmodium, oval Plasmodium, and Plasmodium knowlesi. The most severe species is the Plasmodium falciparum, which causes the most significant number of deaths and is responsible for 97% of malaria cases globally. The World Health Organization (WHO) report of 2020 reported that malaria affected 229,000,000 people in 2019 while causing the death of 409,000 people [3]. To effectively treat this disease, it is imperative to go through an accurate diagnosis, given that its symptoms are found in many other febrile illnesses. Different diagnostic tools have been developed. The microscopic examination of the thick and thin blood smear is a reference used since 1904 to diagnose malaria [4]. However, the resulting performance depends on the quality of the smear (both light and thick), the availability of high quality and well-maintained optical microscope,

and the practitioner’s expertise. With these sensitive requirements, WHO recommends using RDTs, especially in limited resource areas [5]. However, more than 90 % of commercially available RDTs target the *Plasmodium falciparum* histidine-rich protein-2 (PHRP-2), a specific protein of *Plasmodium falciparum*. On the one hand, false negatives are common because of the parasites that can detect of the PHRP-2 gene. On the other hand, false positives can result from PHRP-2 presence in the blood 30 days after the elimination of the infection [6]. Polymerase chain reaction (PCR), and loop-mediated isothermal amplification (LAMP) molecular diagnostic tests have been developed and offer ultrasensitivity in the field. However, PCR is limited to well-equipped laboratories distant from the remote endemic areas and is not ideal for quickly treating malaria cases [1, 7]. As for the LAMP method, it requires moderately qualified personnel and presents a complex design of primers. In addition, there is no documentation for malaria LAMPs as a diagnostic tool in the population, and the price is high for commercial LAMP kits [1, 6, 8]. Overall, computer-assisted techniques are desirable to meet the requirements for early detection of the disease. In this study, we present the performance of the computer-assisted methods used for the early diagnosis of malaria via the images of a blood smear to encourage their uses in the fight against malaria. The rest of this document is organized as follows. Section 2 presents related works, and Sect. 3 describes the materials and methods used. Section 4 deals with the data acquisition process, while Sect. 5 discusses the images’ pretreatment. In Sect. 6, the methods used to classify the malaria parasites are shown. Section 7 presents the discussions and the conclusion follows in Sect. 8.

2 Related Works

This part presents some survey studies on malaria diagnosis using computer-assisted techniques. Each survey was presented according to the authors’ objectives. Thus, this study [9] presents an overview of the computer vision studies used to diagnose malaria while seeking to solve specific problems in the field. The authors of this survey [10] identified 112 articles addressing the diagnosis of malaria assisted by the computer published between 2000 and 2015. In addition, the study discussed various image-processing algorithms for blood smears, recognition forms, and malaria detection. [11] presents the analysis of different researchers’ work in detecting malaria parasites using computer vision. This study examined the image processing methods, the classification of malaria parasites and their stages of life while discussing possible research prospects on existing challenges. Furthermore, [12] presents an investigation into the image acquisition process’s different stages to classify the red blood cells infected with the malaria parasite. This study was carried out to supplement prior investigations in the diagnosis of malaria assisted by the computer and to provide the last update of state of the art in this area as it presents at the end of 2017. Each of these surveys has been presented to meet the objectives of the respective authors. But in general, there is a presentation of an overview of computer vision studies

used for the diagnosis of malaria while detailing image processing methods, classification of infected and non-infected red blood cells with the malaria parasites then the solutions found. In our case, the objective is to present the performance of computer-assisted techniques used for the diagnosis of malaria and then to propose a process to achieve this performance to motivate decision-makers to invest in this area to get rid of malaria, which causes several deaths each year.

3 Materials and Methods

As part of this work, we collected more than 300 articles, including 229 articles uploaded directly in to web of science database and other publications were found by searching Google Scholar using the following research strings:

- methods of malaria diagnosis performed in laboratories;
- malaria diagnostic kits
- malaria diagnoses using machine learning
- image preprocessing techniques for malaria diagnosis.

We sorted all the publications to keep 102 publications relevant to this work. These publications were published in sources such as: The American Journal Of Tropical Medicine And Hygiene, Malaria Journal, Plos One, ScienceDirect, IEEE Access, Springer Link, International Journal of Advanced Research in Computer Science & Technology, Journal of Microscopy, Journal of Physics: Conference Series, IEEE Journal of Biomedical and Health Informatics, Open Access Freely Available Online, Neural Computing & Applications, International Conference of Advanced Computer Science and Information Systems, United States National Library of Medicine.

4 Data Acquisition

Data acquisition is essential for implementing any efficient malaria prediction system through blood smear images. Indeed, most prediction errors are due to how the data were acquired. Many samples have information that contributes to prediction errors. For example, before applying operations to the blood drops on the slides, the variation of blood volumes on the slides used for training and those used for testing causes prediction errors, as illustrated in the case of a study in Peru [13]. It is also crucial to take suitable precautions in blood preparation. As indicated here [12], inadequate blood preparations often lead to artefacts commonly confused with malaria parasites, leading to false positives. In addition, there is a possibility that errors come from the devices used to acquire the images (as in [14], where it is specified that the lighting in a microscope can considerably modify the information captured by the image sensor. Thus, a microscope can substantially change the data captured by the image sensor) and/or preprocessing not applied to the data. This section will give an overview of the steps used in the literature to acquire the data.

4.1 Coloring Methods

To diagnose malaria based on the colors of blood components, it is essential to use a staining method. Thus, the staining method will stain the parasites to identify them on the microscopic images of the blood smears. Various staining methods have been used in the literature to identify malaria parasites. Therefore, our objective is not to present an exhaustive list of staining methods but instead to overview the most commonly used ones.

Giemsa Coloring Method

The Giemsa coloring method was developed in 1904 by Gustav Giemsa. This method has allowed blood smear microscopy to be the golden standard for diagnosing malaria [15]. The Giemsa solution is a mixture of eosin and methylene blue (azure). The eosin colors the chromatin of the parasite in red, while the methylene blue colors the parasitic cytoplasm in blue. This method has been recommended for coloring thin and thick blood smears [16]. Although widely used, this coloring method has disadvantages such as the need for much work with a delay that can exceed 45 min to have the result [17]. Nevertheless, referenced publications here [18–25] used the Giemsa coloring method to highlight the parasite of malaria.

Leishman Coloring Method

Although the Leishman staining method is less widely used than the Giemsa staining method, it offers better visualizations and sensitivity while taking less time than the Giemsa staining method to detect malaria parasites [26–28]. In addition, studies like [29–31] have used Leishman staining to identify malaria parasites in blood smears.

Fluorochrome Coloring Method

This coloring technique also performs better than Giemsa's coloring in detecting malaria parasites with thin and thick blood smears. However, the problem with this technique is that standard epi-lighted mercury vapor fluorescence microscopes are expensive, especially for tropical countries where malaria is endemic [32–34].

Acridine Orange Coloring Method

The orange coloring method with acridine also is better than the Giemsa coloring method. However, the disadvantage of this method is that the sensitivity depends on the parasitic density and the differentiation of space is often difficult [17]. Nevertheless, studies like [35–38] used the acridine orange coloring methods for blood smear coloring to diagnose malaria.

Wright Coloring Method

This technique (often combined with the Giemsa coloring technique) makes malaria parasites visible [39]. For malaria diagnosis, various studies, such as [40–43], used this technique to highlight the parasites.

Digitization of Blood Smear

After the blood smear coloring using an effective method, we move on to the scanning process of the blood smear using a digital camera. At this level, different tools were used to collect the images that would be processed before moving on to the learning phase. These references [11, 17, 44–47] indicate the example of some studies that described the various methods and tools used to acquire the images of blood smears.

5 Pretreatment of Images

The objective of the pretreatment process is to obtain images with low noise and a high contrast compared to the original images for the subsequent processing [48, 49]. The pretreatment process contains operations such as the removal of unwanted noises, the increase in the picture contrast, the colors' conversion, the image's sharpness, the image filtering stretch [44, 47, 50], the correction of the bottom lighting of the microscopic images of a peripheral blood smear, that varies from one slide to another due to the variation of coloration [51]. [52] specified the need for pre-treatment to eliminate white blood cells confused with red blood cells by the implemented algorithm for the best classification of malaria parasites. Even with Convolutional Neural Networks (CNN) that are algorithms designed for image recognition tasks, which have been successfully applied in different areas as detailed in [53, 54], the authors went from poor performance to excellent performance by using preprocessing on the data as shown in [55]. The process of image preprocessing is so crucial that it is found in almost all studies involving artificial intelligence with image data. For example, these references [52, 56–59] present studies that have used some preprocessing methods to improve the quality of images. Concerning the state of the data, some of the techniques below will be used to have better performances.

5.1 Segmentation Methods

A microscopic image of a thin blood smear contains various blood components such as erythrocytes, leukocytes, platelets, and staining artefacts. Segmentation of a digital image allows the separation of the image into constituent regions. It aims to isolate individual erythrocytes from the rest of the blood constituents and then locate the probable plasmodium parasites from infected erythrocytes. It provides the ability to detect the object of interest in blood cell images while allowing separation of the foreground (object) from the background, i.e., red blood cells, blood cells, other components, and parasite from the image's background help separate overlapping malaria parasites. This is one of the most challenging tasks in image processing because it determines the success or failure of the subsequent classification process [50, 57, 60–62]. Some examples of specific segmentation methods usage are given in [11, 47–49, 63].

5.2 Feature Extraction Methods

Malaria parasite infection causes microstructural changes in erythrocytes. Thus, feature extraction selects appropriate parameters that correctly describe the image information. These parameters are grouped in vector form and are called feature vectors. Parasites and other colored components are flexible objects with significant shapes, sizes, and morphologies. Therefore, color information is valuable but insufficient to distinguish between other colored things, such as Plasmodium, and different species. Nevertheless, geometric features are still essential for recognizing complex shapes, and many researchers have used them to identify parasites [11, 50, 64]. In studies like [30, 47, 57, 61, 65], examples of the use of feature extraction methods have been presented.

5.3 Feature Selection Methods

As specified in the previous section, malaria infection causes shape changes in red blood cells. Thus, feature selection plays a crucial role in finding the most significant features among many extracted features in pattern recognition. In addition, this technique reduces redundant and irrelevant data to increase predictive performance, as the original feature set may contain unrelated data leading to an overlearning problem [30, 57, 64].

6 Classification Methods

After the ready-to-use data is acquired, an algorithm will be trained to create a model capable of classifying infected and uninfected red blood cells. Depending on the literature, machine learning and/or deep learning methods were used for classification. Therefore, we present the performance of different methods used in classifying red blood cells in the tables below. Each table line gives essential information to gauge the performance of automatic or deep learning methods used for detecting of malaria parasites on the blood smear images (Tables 1 and 2).

Table 1. The performance of machine learning technologies

References	Methodologies	Number of samples	Accuracy (%)	Sensitivity (%)	Specificity (%)	Precision (%)	Recall (%)	F1 Score (%)	MCC (%)	AUC (%)
[71]	ANN	70	99	–	–	88	91	90	–	–
[56]	Bayesian approach	600	84.0	–	–	–	–	–	–	–
[71]	Bag of Features and SVM	27 558	85.6	–	–	–	–	–	–	93.2
[67]	CNN-SVM	26 161	98.93	99.16	–	99.21	–	99.18	–	–
[67]	CNN-KNN	26 161	99.12	99.23	–	99.11	–	99.28	–	–
[73]	C4.5	500	–	99.2	–	–	–	99.0	–	100.0
[75]	GB, RF and SC	27 558	96	–	–	97	97	97	–	–
[57]	hybrid classifier	200	98.50	95.68	98.81	–	–	93.82	–	–
[73]	IB1	500	–	99.8	–	–	–	99.0	–	99.0
[57]	KNN	200	97.35	83.64	99.07	–	–	88.05	–	–
[76]	KNN	9	93.3	72.4	97.6	–	–	–	–	–
[57]	Naive Bayes	200	97.23	95.68	97.38	–	–	89.21	–	–
[73]	Naive Bayes	500	–	84.5	–	–	–	87.0	–	95.0
[74]	RF	27 558	–	–	–	82	86	84	–	–
[66]	SVM	47	–	99.0	99.8	–	–	–	–	–
[56]	SVM	600	83.5	–	–	–	–	–	–	–
[68]	SVM	2565	91.66	–	–	–	–	–	–	–
[53]	SVM	765	–	92.95	93.82	–	–	–	44.35	–
[69]	SVM	450	–	94	99.7	–	–	–	–	–
[57]	SVM	200	98.38	94.59	98.81	–	–	93.12	–	–
[70]	SVM	15	–	93.12	93.17	–	–	–	–	–
[72]	SVM	70	98	–	–	83	91	87	–	–
[77]	SVM	60	93.33	93.33	–	–	–	–	–	–
[44]	VGG19-SVM	1530	93.13	93.44	92.92	89.95	–	91.66	–	–
[44]	VGG16-SVM	1530	89.21	89.80	89.81	84.47	–	87.05	–	–

Table 2. The performance of deep learning technologies

References	Methodologies	Number of samples	Accuracy (%)	Sensitivity (%)	Specificity (%)	Precision (%)	Recall (%)	F1 Score (%)	MCC (%)	AUC (%)
[68]	AlexNet	2 565	95.79	–	–	–	–	–	–	–
[71]	AlexNet	27 558	96.4	–	–	–	–	–	–	99.2
[67]	Autoencoder	26 161	99.5	98.80	99.17	99.29	–	99.51	–	–
[78]	CNN	27 578	97.37	96.99	97.75	97.73	–	97.36	94.75	–
[53]	CNN	765	–	97.06	98.50	–	–	–	70.33	–
[79]	CNN	27 558	98.85	98.79	98.90	98.90	–	–	–	–
[71]	CNN	27 558	96.0	–	–	–	–	–	–	99.1
[80]	Custom CNN	27 558	99.09	–	–	99.56	–	99.08	98.18	99.3
[55]	CNN	27 558	99.96	–	–	100.0	99.928	99.96	–	–
[85]	CNN	27 558	97.30	–	–	97	97	97	94.17	97.04
[86]	CNN	27 558	98.23	96.44	99.99	99.09	–	97.74	–	–
[75]	CNNs and mini-VGGNet	27 558	–	–	–	99	96	97	–	–
[71]	DenseNet	27 558	96.6	–	–	–	–	–	–	99.1
[82]	DenseNet12 1	10 000	95.6	94.8	96.5	–	–	–	–	99.0
[88]	DBN	4 100	–	97.60	95.92	–	–	89.66	–	–
[84]	Faster R-CNN (InceptionV2)	643	–	–	–	72.29	93.03	–	–	–
[89]	FLANN/SSAE	1 182	89.10	93.90	83.10	–	–	94.50	–	–
[68]	GoogLeNet	2 565	98.13	–	–	–	–	–	–	–
[80]	InceptionResNet	27 558	98.79	–	–	99.56	–	98.77	97.59	99.2
[82]	InceptionV 3	10 000	92.8	92.5	93.0	–	–	–	–	97.6
[82]	InceptionResNetV2	10 000	93.5	93.2	93.8	–	–	–	–	98.0
[68]	LeNet-5	2 565	96.18	–	–	–	–	–	–	–
[82]	MobileNet V2	10 000	94.8	94.1	95.5	–	–	–	–	98.7
[71]	ResNet	27 558	96.0	–	–	–	–	–	–	99.2
[81]	ResNet-50	27 558	95.4	–	–	–	–	–	–	–
[82]	ResNet50V 2	10 000	93.8	93.5	94.0	–	–	–	–	98.2
[84]	RetinaNet (SSD ResNetFPN)	643	–	–	–	86.97	60.86	–	–	–
[80]	SqueezeNe t	27 558	98.66	–	–	99.44	–	98.64	97.32	98.85
[84]	SSD (InceptionV 2)	643	–	–	–	91.50	37.53	–	–	–
[71]	VGG-16	27 558	96.5	–	–	–	–	–	–	99.3
[80]	VGG-19	27 558	99.32	–	–	99.71	–	99.31	98.62	99.31
[82]	VGG19	10 000	95.9	95.6	96.3	–	–	–	–	99.1
[82]	VGG16	10 000	96.0	95.6	96.4	–	–	–	–	99.2
[90]	WELM/ AlexNet_FC 7	23 248	96.18	–	–	–	–	–	–	–
[82]	Xception	10 000	94.6	94.3	94.8	–	–	–	–	97.9

6.1 Interpretation of Results

The main objective of this study is to present the performance of computer-assisted techniques used to diagnose malaria to motivate their use in the fight against malaria. Therefore, we have collected in tables the results of several articles illustrating the performance of computer-assisted techniques in identifying malaria from blood smear images. Each row of a table gathers the essential information to judge the ability of a machine learning or deep learning methodology to identify malaria parasites. Each table has eleven columns: the first one represents the reference of the different papers, the second one shows the methods used, the third one represents the number of image samples used in the study, and from the fourth to the last one, we have different results of performance metrics according to the publications. These performance metrics are defined as follows:

- Accuracy: accuracy is a standard metric that is the percentage of the number of correct predictions [90].
- Sensitivity or Recall: the rate of correctly identified true positive predictions to all positive outcomes [90].
- Specificity is the rate of correctly identified negative predictions to all negative outcomes [90].
- Precision: the precision is the fraction of the correctly classified instances from the total classified instances [91].
- F1-score: this score is a harmonic mean of precision and sensitivity; it can be used as an overall performance metric [90].
- MCC: Matthew’s correlation coefficient (MCC) is a metric formulated to evaluate the quality of binary classification; it was designed to be used as a balanced measure that can be used on imbalanced datasets [90].
- AUC: the area under the receiver operating characteristic curve (AUROC) is the area under an angle of true positive rate versus false-positive rate that can be used as a metric for methods working on imbalanced datasets [90].

These performance metrics provide the information expected by the doctor to make good decisions in the fight against malaria while pushing to replace existing tools. These continue to show their failings while plunging the world into more serious consequences. Indeed, the report on malaria published on December 6, 2021, by the WHO showed that the number of cases and deaths from malaria increased by 14,000,000 and 69,000 respectively in 2020 compared to the number of cases respectively. and the number of deaths observed in 2019 [96]. Moreover, according to WHO data, a few years ago, there was a shortage of more than 7 million doctors worldwide, and in 2035 this shortage will reach 13 million. This will mean that almost half of the world’s population will not be able to get medical help, and access to a specialist will take a few weeks or more, even in the world’s richest countries [97].

Therefore, computer-assisted techniques are urgently needed in the eradication of this disease. When data of sufficient quality and quantity are available, computer-assisted techniques offer better results than even the most advanced human expertise. These techniques have the quality of allowing the prediction of the parasite density which is essential information to know the severity of the infection to better guide the doctor in the choice of the appropriate treatment. The convincing results of these techniques and their successful use in various fields have made it possible to estimate that the proportion of professional tasks performed by intelligent robots will reach 52% in the world by 2025 [98].

7 Discussions

Techniques to eradicate malaria require an accurate diagnosis of the disease. Most failures in the fight against malaria are caused by an incorrect diagnosis of this disease, presenting the same symptoms as other febrile diseases. Misdiagnosis is widespread with all the tools currently available. As

reported in [75], studies have shown that 46 laboratory professionals diagnosed 6 malaria slides for *Plasmodium falciparum* and *Vivax* with an error rate of 43.5% and 37%, respectively. Another similar study reported an overall malaria diagnosis error rate of 40.4%. The microscope has been used for more than a century. However, such a tool gives results that depend on the microscopist's expertise. More than half of all malaria diagnoses worldwide are performed by microscopy [72], mainly because of its low cost. The creation of rapid RDT tools has circumvented the problem of test performance being dependent on human expertise. However, RDTs can present many false positives with the detection of the pHRP-2 protein which can be present in the blood for up to 30 days after clearance of the infection. In addition, RDTs cannot detect malaria infections with very low parasitemia. RDTs have gained popularity mainly because of their ease of use [92], despite these weaknesses. The ultra-sensitives diagnostic tests like the PCR and LAMP tests are not practical for the reasons indicated in the introduction. The World Health Organization has recommended a minimum standard of sensitivity and specificity of 95% so diagnostic tools are clinically helpful when assessing patients infected with *Plasmodium falciparum* densities of 0.0002% [93]. Computer-assisted techniques provide much more advanced performance than these indications when data is used in quality and in sufficient quantity on deep learning algorithms.

Obtaining the best performance for malaria diagnosis using these techniques depends entirely on the data quality. In addition, many challenges affect the data depending on their acquisition conditions. These challenges have inhibited the achievement of the best performance in various studies. The best way to overcome this problem is to apply preprocessing on the data before running it through the chosen algorithm for training. As an illustration, in this study [55], the impact of pretreatment has considerably changed the performance measures in detecting malaria parasites, as presented in Table 3 below.

Table 3. Example of the impact of images preprocessing

Model	Accuracy	Precision	Recall	F1-score
Stacked CNN-5 layers with preprocessing	99.879	99.976	99.783	99.879
Stacked CNN-5 layers without preprocessing	49.61	50.14	50.14	50.14

In other cases, the effect of pretreatment [94, 95] improved the accuracy and F1-score in detecting malaria parasites via blood smear images. In some cases, the performance of computer-assisted techniques presented in the performance of machine learning or deep learning technologies sections has shown undeniable capabilities in the early identification of malaria, facilitating its eradication. In this sense, the present manuscript tries to draw the attention of the primary decision-makers to control deadly diseases such as malaria to invest in research using machine learning techniques for early and accurate malaria diagnosis. The lack of diagnostic experts further supports the integration of these techniques

into easy-to-use tools. This problem has been considered in some studies that have developed malaria diagnostic systems that can be used in smartphones. In addition, studies like [45, 52, 67, 72, 87, 99–101] have shown the possibilities of integrating diagnostic systems with smartphones and achieving better performance.

8 Conclusion

Malaria is one of the deadliest diseases worldwide. The performance of neural networks for malaria diagnosis through blood smear images is unbeatable in this era of Big Data. In some publications, the maximum potential of neural networks has not been reached, mainly because of some gaps in the available data. However, studies that consider the preprocessing operations on the data obtained rates are trending towards 100% on specific performance metrics. With these results, if the diagnostic method is easy to use, this will provide a compelling way to rid the world of malaria. Our future work will implement all processes to develop an efficient and usable system for diagnosing malaria.

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