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AUTOMATIC IDENTIFICATION OF MALARIA THROUGH MICROSCOPIC IMAGES

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Abstract

Malaria is a leading cause of death and disease in many developing countries, where young children and pregnant women are the most affected groups. In 2012, there were an estimated 207 million cases of malaria, which caused approximately 627 000 malaria deaths. Around 80% of malaria cases occur in Africa, where the lack of access to malaria diagnosis is largely due to a shortage of expertise, being the shortage of equipment the secondary factor. This lack of expertise for malaria diagnosis frequently results on the increase of false positives, since prescription of medication is based only on symptoms. Thus, there is an urgent need of new tools that can facilitate the rapid and easy diagnosis of malaria, especially in areas with limited access to quality healthcare services. Methods: Various image processing and analysis approaches already proposed on the literature for the detection and segmentation of malaria parasites in blood smear microscopic images were collected and reviewed. This timely review aims to support the increasing interest in the development of low cost tools that can facilitate the rapid and easy diagnosis of malaria, especially in areas with limited access to quality healthcare services. Results: Malaria parasites detection and segmentation techniques in microscopic images are, in general, still in need of improvement and further testing. Most of the methodologies reviewed in this work were tested with a limited number of images, and more studies with significantly larger datasets for the evaluation of the proposed approaches are needed. Despite promising results reported during the past years, the great majority of the computer-aided methods found on the literature for malaria diagnosis are based on images acquired under well controlled conditions and with proper microscopic equipment. However, one should take into account that 80% of malaria cases occur in Africa, where this type of equipment is scarce or even nonexistent in common healthcare facilities. Conclusion: This work collects and reviews various image processing and analysis approaches already proposed on the literature for the detection and segmentation of malaria parasites in blood smear microscopic images. This timely review aims to support the increasing interest in the development of image processing-based systems to be used in rural areas of developing countries, which might be the next future trend in malaria computer-aided diagnosis.

Keywords: Malaria, computer-aided diagnosis, image analysis, segmentation, feature extraction, classification.

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1. Introduction

Malaria is one of the most severe public health problems worldwide. It is a leading cause of death and disease in many developing countries, where young children and pregnant women are the groups most affected. In 2012, there were an estimated 207 million cases of malaria, which caused approximately 627 000 deaths. An estimated 3.4 billion people continue to be at risk of malaria, mostly in Africa and Southeast Asia. Around 80% of malaria cases occur in Africa [1]. It is worth taking into account that the number of malaria cases and their geographical distribution are not stable because of several factors, like the increasing prevalence in some areas due to expanding drug resistance; the widespread availability of fake and substandard medicines; global warming and expansion of malaria into favorable areas at higher elevations; and population mobility of different kinds [2]. The increasing interest in the development of computer aided diagnosis (CAD) systems for malaria diagnosis is closely related with common practical difficulties experienced in under-resourced health facilities of developing countries, such as the excessive workload due to shortage of staff. Image processing approaches are often used in CAD systems to reduce the dependence of manual microscopic examination of blood smears, which is an exhaustive and time consuming activity, simultaneously requiring a considerable expertise of the laboratory technician. During the last years, several image processing techniques have been proposed for malaria diagnosis using microscopic images, addressing the detection of a wide variety of different malaria parasites, in different growth stages and using images acquired from different types of blood smears. Under the scope of this paper, various image processing and analysis approaches already proposed on the literature for the detection and segmentation of malaria parasites in blood smear microscopic images were collected and reviewed. This timely review aims to support the increasing interest in the development of low cost tools that can facilitate the rapid and easy diagnosis of malaria, especially in areas with limited access to quality healthcare services.

2. Malaria Disease Characterization

Malaria is caused by a parasite in the blood and can be seen only under a microscope with high magnification. For the visualization of the parasites, a blood film must be made, dried, stained and examined under the microscope. When the microscopist sees stained parasites, the diagnosis of malaria is confirmed by identifying the stage and species of the malaria parasite, as well as the infection density [2].

2.1. Malaria Parasites Stages

In the human host, malaria parasites pass through 3 different growth stages that can be detected in the peripheral blood: the trophozoite stage, the schizont stage and the gametocyte stage. Trophozoites are often called the ring stage, being the most commonly seen stage, appear incomplete in thick films, and can vary from small to quite large within the host cell. Usually, trophozoites have one chromatin dot, but two are common for the P.falciparum species. The cytoplasm takes different shapes, from a well-defined, fine ring to forms that are irregular or bizarre, sometimes called ‘amoeboid’ [1]. The schizont stage begins when the trophozoite has

reached its full capacity and the parasite starts to divide into daughter cells called merozoites. Several more divisions of the chromatin follow, which mark the growth of the schizont, until there are many chromatin bodies, each with its accompanying cytoplasm. The number of chromatin and merozoite divisions helps to identify the species. These clearly delineated new parasites are now ready to leave the host cell to invade new red blood cells [2]. Gametocytes are round or banana-shaped, depending on the species. The way in which the parasite takes up the stain helps to identify the sex of the parasite in thin films, being difficult to differentiate between male and female in thick films [3].

2.2. Malaria Parasites Species

Four species of Plasmodium can infect and be transmitted by humans: the P.falciparum, P.vivax, P.ovale and P.malariae. P.falciparum is the commonest species in the tropical parts of the world and can evolve rapidly to severe illness and death if not recognized and treated with effective medicines [2]. It is the species responsible for most cases of severe malaria and death. P.vivax is the commonest species in the cooler parts of the tropics, being the largest of the human malaria parasites and the cause of much illness and absenteeism from work and school [2]. P.ovale is considered a rare species, but relatively common in West Africa and other parts of the African continent. Because of morphological similarities, P.ovale is sometimes mistaken for P.vivax by less experienced microscopists [2]. Moreover, the existence of a new genotype for P.ovale has been recently hypothesized [4]. P.malariae is found worldwide and causes a chronic infection that in some cases can last a lifetime. In some chronically infected patients, P.malariae can cause serious complications such as the nephrotic syndrome [5]. As a final note, P.knowlesi is a malaria parasite that is found in nature in macaques, and naturally acquired human infections were thought to be extremely rare, however a large focus of human infections was reported in 2004 [6].

3. Malaria Diagnosis Characterization

Malaria infection can be suspected based on the patient's symptoms, travel history or physical findings at examination. However, for a definitive diagnosis, laboratory tests must be made to prove the presence of the malaria parasites. The microscopy examination remains the gold standard for laboratory confirmation of malaria, which consists in preparing a blood smear, staining it (most often with the Giemsa stain) and examining it through a microscope [5]. The importance of reliable malaria diagnoses cannot be overstated, since false negatives can be potentially fatal, and false positives increase the drug resistance of the patients, leading consequently to unnecessary economic burden [7]. Laboratory diagnosis of malaria can be made through microscopic examination of two kinds of blood smears, thin and thick, taken most often from a finger prick. Thick blood smears are 20-40 times more sensitive in detecting malaria parasites because the blood is more concentrated, which allows for a greater volume of blood to be examined. The thick smear is approximately 6-20 times as thick as a single layer of red blood cells, which results in a larger volume of blood being examined. However, thick smears are more difficult to read, so thin smears aid in parasite species identification and quantification. Malaria Parasites Stages the images used on the reviewed works can be divided in two different groups

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according to their characteristics: full view images (FV) and manually cropped sub-images (CS). FV consists on images corresponding to the entire microscopic field of view (see Figs. 1 and 2).

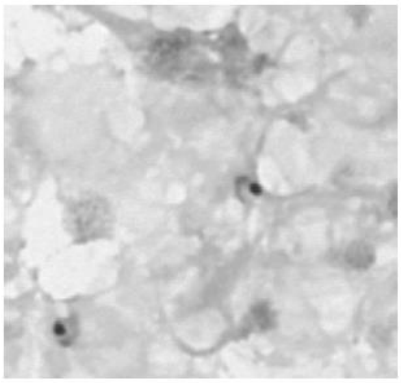

Fig. (1). Example of full view image on thick smear

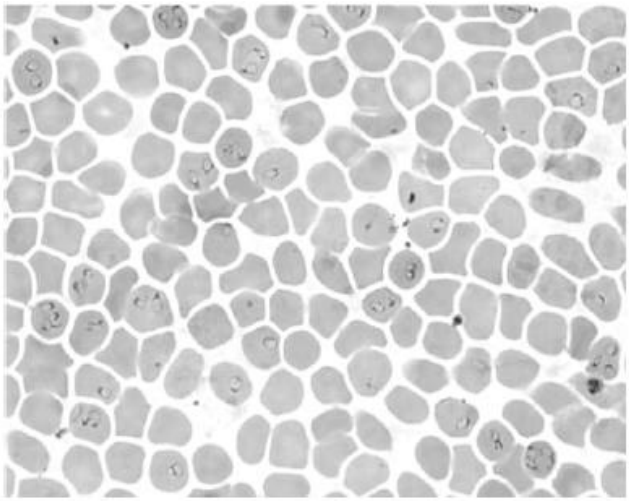

Fig. (2). Full view image on thin smear

CS consists on cropped patches of the FV images, corresponding to regions of interest manually cropped (see Figs. 3 and 4). Moreover, the vast majority of the proposed approaches found on literature use high quality equipment in the acquisition process, particularly commercial cameras that are specifically customized for the acquisition of microscopic images, for instance easily attached to microscopes. The exception is [7], which uses a smartphone built-in camera to acquire images (see Fig. 5).

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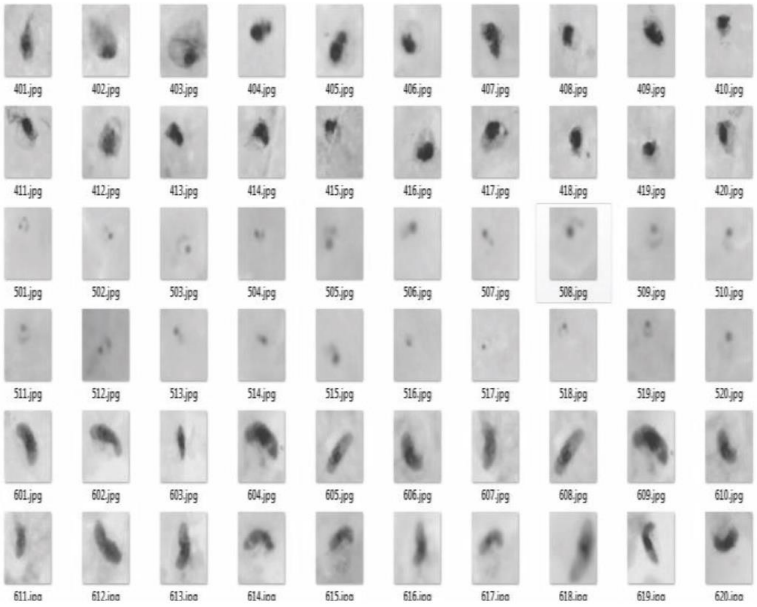

Fig. (3). Cropped images on thick smear

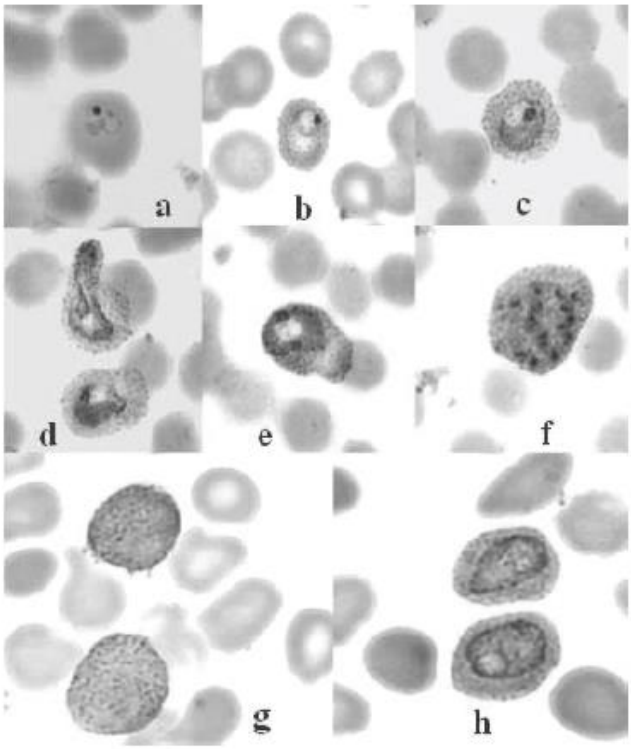

Fig. (4). Cropped sub-images on thin smear

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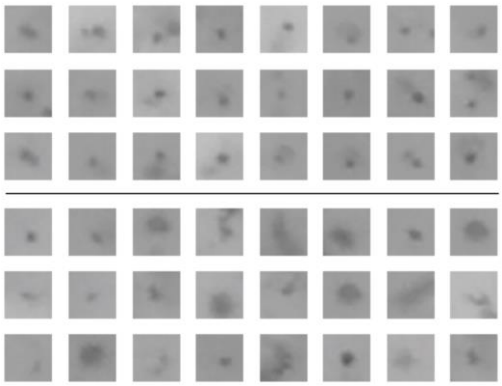

Fig. (5). Mobile acquired image patches on thin smear, with positive cases at the top and negative cases at the bottom

3.2. Performance Metrics

The classification results of the reviewed works are usually presented in terms of two metrics ordinarily used for this purpose: 1) Sensitivity (SE), i.e. the percentage of structures correctly classified as positive cases of malaria parasites; and 2) Specificity (SP), i.e. the percentage of structures correctly classified as negative cases of malaria parasites.

4. Image Processing Techniques

This section critically reviews the main studies found in the literature regarding the analysis of malaria infected blood smears using image processing and analysis. Since typical approaches usually comprise four different image processing and analysis tasks, the reviewed works were divided into the following sub-sections: 1) Segmentation; 2) Feature Extraction; 3) Feature Selection; and 4) Classification.

4.1. Segmentation

Image segmentation is the process that partitions a digital image into disjoint (non-overlapping) regions, each of which typically corresponds to one object. Once isolated, these objects can be measured and classified, as discussed in the following sub-sections. This sub-section groups and reviews the methods proposed on the literature for the segmentation of malaria-stained components on thin and thick blood smears.

4.2. Feature Extraction

The primary objectives of feature extraction are reducing the computational complexity of the subsequent process and facilitating a reliable and accurate recognition for unknown novel data, being the last objective particularly important for computer vision and pattern recognition systems. Moreover, the in-depth understanding of the domain-specific knowledge gained by

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human experts on the problem being addressed can be of extreme importance for the design of a reliable and effective feature extraction engine [8].

4.3. Feature Selection

In order to build a good classification model, the reduction of the number of attributes used on the classification process may not only have positive impact in terms of the processing time, but also in terms of the classification results. Feature selection techniques play an important role in this context, and they can be organized into three categories: filter methods, wrapper methods and embedded methods [9]. Filter Methods rank each feature according to some univariate searching function and select the highest-ranking features, where the scoring should reflect the discriminative power of each feature. Some of the most common univariate filter methods includes Bayesian Network, Information Gain, Signal-to-Ratio, Euclidean Distance or Correlation Squares (R2). Filter methods are usually very efficient and fast to compute, but comprise some significant drawbacks like the redundancy of the selected features, which can carry the same information. Another important disadvantage of the filter methods is the fact that this selection does not consider some important relationships between features, since features can receive a low score by the ranker algorithm when used by itself, but be very useful when combined with other features. Opposite to filter techniques that consider the ranking of each feature independently, Wrapper and Embedded Methods are specific to a given machine-learning algorithm. In the Wrapper Method, a search is conducted using a specific classifier in order to find the subset of features with which the classification algorithm performs the best. For instance, using forward selection, the Wrapper Method estimates the accuracy of adding each unselected feature to the feature subset, and the feature that most improves the accuracy is selected. These methods typically terminate when the estimated accuracy of adding any feature is less than the estimated accuracy of the feature set already selected [10].

4.4. Classification

In machine learning and statistics, classification is the problem of identifying to which of a set of categories (subpopulations) a new observation belongs, on the basis of a training set of data containing observations (or instances) whose category membership is known. In the terminology of machine learning, classification is considered an instance of supervised learning i.e.learning where a training set of correctly identified observations is available [11]

5. Conclusion

Malaria parasites detection and segmentation techniques in microscopic images are, in general, still in need of improvement and further testing. Most of the methodologies reviewed in this work were tested with a limited number of images, and more studies with significantly larger datasets for the evaluation of the proposed approaches are needed. Despite promising results reported during the past years, the great majority of the computer-aided methods found on the literature for malaria diagnosis are based on images acquired under well controlled conditions and with proper microscopic equipment. However, one should take into account that 80% of

malaria cases occur in Africa, where this type of equipment is scarce or even nonexistent in common healthcare facilities. Furthermore, the analysis of thin blood smears is much more addressed in the literature when compared with thick blood smears. This is probably because the image processing tasks required on thick blood smears analysis are considerably more challenging, given the fact that thin blood smears consist on a single layer of blood elements. Thus, several additional image artifacts are avoided in thin blood smear analysis, like the overlap of blood elements or the recurrent appearance of unfocused structures caused by the location of those structures in different focal planes. Thick blood smears are considered 20-40 times more sensitive in detecting malaria parasites, and therefore should be equally addressed, despite the additional image processing challenges. This work collects and reviews various image processing and analysis approaches already proposed on the literature for the detection and segmentation of malaria parasites in blood smear microscopic images. This timely review aims to support the increasing interest in the development of image processing-based systems to be used in rural areas of developing countries, which might be the next future trend in malaria computer-aided diagnosis. The development of new mobility-aware microscopic devices (and ideally low cost) is an area that can greatly improve the chances of the successful deployment of computer vision CAD solutions for malaria diagnosis in the field. Taking into account the high customs taxes and import duties currently in practice in most of the African countries, the easy replicability of these microscopy devices in third world countries should also be an issue to address. Several others additional requirements for this type of microscopic devices can be equally considered, like automating the device as much as possible, discarding the need of considerable expertise and train of the technician in terms of maneuvering the microscope, or supplying the energy needed for the illumination and/or any type of automation through the mobile device battery, thus discarding the need of an additional power source. The mobile phone is currently Africa's most important digital technology, and is boosting African health as it emerges as a platform for diagnosis and treatment. In 2000, few Africans had a phone, but today about three-quarters do [12]. Just as African telecommunications largely skipped over landline infrastructure and went straight to mobile phones, some experts say African medicine can skip over centralized labs [13]. Considering the recent significant improvements of the new generation of mobile devices in terms of image acquisition and processing power, if a reliable automatic diagnostic performance is ensured through the usage of those devices, one would dramatically reduce the effort in the exhaustive and time consuming activity of microscopic examination. Moreover, the lack of highly trained microscopists on malaria diagnosis in rural areas could then be complemented by a significantly less specialized technician that knows how to operate the system and prepare blood smears. The usage of mobile devices in the system architecture can also bring significant improvements in terms of portability and data transmission. Finally, malaria diagnosis might be just one element of a suite of diagnostic software tests running on this type of system. Several other tests could simultaneously be carried out using the same images, for instance cell counting or detection of other hemoparasites like microfilaria or trypanosoma.

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