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Hand Portable Apparatus to Test Blood Cells Under Gold Standard of Microscope

Dhruva Iyer[1]; Nirvaan Sen[2]; Shekhar Jain[3]; Reetu Jain[4]

Arya Vidya Mandir (CICSE Board), JHUU[1]; Jamnabai Narsee International School[2]; Own Technology Private Limited, Mumbai[3,4]

Abstract – Our biggest war was not against COVID-19 but against insufficient testing kits — one of the vital components to confirm the infection and its spread. While we do not know when the COVID pandemic will end, and when another one will hit. Timely testing and prevention are the only two key strategies that will save the day. Taking lessons from COVID-19 which caused widespread loss of lives, we have developed a simple apparatus that will enable testing of blood samples without dependency on huge diagnostic centers or experienced senior doctors duringsuch pandemics. We took Malaria as a case study for two reasons – there is a huge amount of data with respect to people suffering from this disease and blood cell image datasets for processing and testing our hypothesis on Malaria. Many people die from malaria in rural areas even though they have many RPD (Rapid Diagnostic Testing), but the gold standard of testing is a microscope which is not easily available, and therefore we continued to find a more dependable and efficient way of detecting Malaria. The setup consists of a smart mobile microscope which is a simple equipment that consists of ball lens, polarized sheets, LED light and a blood sample that works on the principle of standard microscope that will give you enlarged image of blood cells of parasites and with Deep Learning acting on this data we will get instant results of classification into parasitized and non-parasitized cells. The mobile phone is trained to read and process blood samples with the help of Deep Learning and image processing algorithm to give you a quick result of whether the patient is having malaria or not without any prior knowledge in understanding blood cells. We use the fourth order moment as an image processing technique to get the segmented images of malarial blood cells.

Keywords **– Malaria, Diagnosis, Rural Areas, Handheld Device, Deep Learning, Image Processing, Fourth order moment.**

1. I. INTRODUCTION

Microorganisms are observed everyday, in the hope of finding diseases, developments that will help gain new insights into human health. Doctors, pathologists, scientists, share data through their findings and observations. The data gathered through microscopes is essential to analysis and conclusions. This data needs to be accurate and actually available at the right time.

The classic example of Malaria pandemic and then Covid-19 proved the need for immediate scanning

Malaria is caused by protozoan parasites of the family Plasmodium that are transmitted through the bites of infected female Anopheles mosquitoes and

that infect the red blood cells.It takes almost 30 years from the end of the Global Malaria Eradication Programme (in 1969) for malaria to re-emerge as a public health priority in global health and development discussion. Although data from 1969 to 2000 are scarce, this period was characterized by a sense of failure and abandonment in the fight against malaria. During these 3 decades, hundreds of millions of people were infected with malaria, tens of millions – mostly in sub-Saharan Africa – died, millions of households failed to emerge out of poverty as they struggled with catastrophic health expenditures, hundreds of thousands of pregnant women died during delivery due to malaria-related complexities, and millions of children were born with low birth weight, potentially leading to early death or lifetime disability. Millions of children who survived struggled with studying as they dealt with frequent absenteeism due to multiple episodes of malaria, chronic anemia, seizures, or cognitive impairment – consequences of infection and critical disease. Huge blows were dealt to the growth of already weak post-independence national economies, and their attempts to build viable health systems were hampered by lost productivity and high demand for health care.

Against this background, the first 2 decades of the 21st century represent a golden era in the history of malaria control. The world drew together to fight malaria, delivering one of the biggest returns on investment in global health. By the end of 2019, about 1.5 billion malaria cases and nearly 7.6 million deaths had been averted since the beginning of the century.In recent years, however, progress has stalled, at a time when we are still dealing with very high levels of malaria burden, re-emphasizing the need to do a lot more to sustain the gains, accelerate progress and achieve the global ambition of a malaria free world.[1]

According to the World Health Organization (WHO), Globally, there were an estimated 229 million malaria cases in 2019 in 87 malaria-endemic countries, decreasing from 238 million in 2000 (Table 1.1[a]) across 108 countries that were malaria endemic in 2000 (Fig. 1.1). At the *GTS* (Global technical strategy for malaria 2016–2030) baseline of 2015, there were 218 million estimated malaria cases. The proportion of cases due to P. vivax (Plasmodium vivax) reduced from about 7% in 2000 to 3% in 2019.[1]

Figure 1.1. depicts countries with indigenous cases in 2000 and their status by 2019 Countries with zero indigenous cases over at least the past 3 consecutive years are considered to have eliminated malaria. In 2019, China and El Salvador reported zero indigenous cases for the third consecutive year and have applied for WHO certification of malaria elimination; also, the Islamic Republic of Iran, Malaysia and Timor-Leste reported zero indigenous cases for the second time. Source: WHO database.

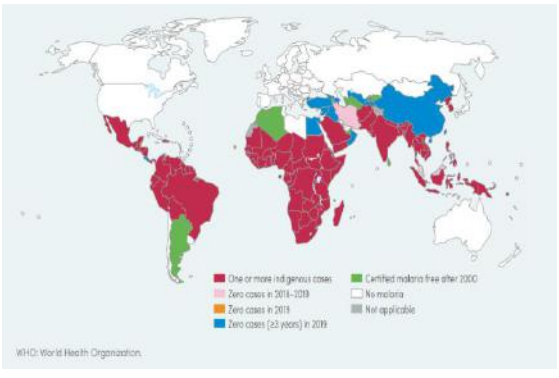


Fig 1.1.

Countries with indigenous cases in 2000 and their status by 2019.[1]

Table 1.1.[a] and Table 1.1.[b] depicts global estimated malaria cases and deaths, 2000–2019 Estimated cases and deaths are shown with 95% upper and lower confidence intervals. Source: WHO estimates.[1].

TABLE 1.1.[a]:

Year	Number of cases (000)			
	Point	Lower bound	Upper bound	% P. vivax
2000	238000	222000	259000	6.90%
2001	244000	228000	265000	7.40%
2002	239000	223000	260000	7.10%
2003	244000	226000	268000	7.80%
2004	248000	227000	277000	8.00%
2005	247000	229000	272000	8.30%
2006	242000	223000	268000	7.20%
2007	241000	222000	265000	6.80%
2008	240000	222000	264000	6.50%
2009	246000	226000	271000	6.50%
2010	247000	226000	273000	7.00%
2011	239000	218000	262000	7.20%
2012	234000	213000	258000	6.60%
2013	225000	206000	248000	5.30%
2014	217000	201000	236000	4.30%
2015	218000	203000	238000	3.90%
2016	226000	210000	247000	4.00%
2017	231000	213000	252000	3.40%
2018	228000	211000	250000	3.20%
2019	229000	211000	252000	2.80%

TABLE 1.1.[b]:

Number of deaths		
Point	Lower bound	Upper Bound
736000	697000	782000
739000	700000	786000
736000	698000	783000
723000	681000	775000
759000	708000	830000
708000	662000	765000
716000	675000	771000
685000	644000	735000
638000	599000	685000
620000	572000	681000
594000	546000	658000
545000	505000	596000
517000	481000	568000
487000	451000	538000
471000	440000	511000
453000	422000	496000
433000	403000	478000
422000	396000	467000
411000	389000	458000
409000	387000	460000

Malaria case number (i.e.cases per 1000 population at risk) reduced from 80 in 2000 to 58 in 2015 and 57 in 2019 (Fig. 1.2.[a]). Between 2000 and 2015, malaria case incidence declined by 27% and then by less than 2% in the period 2015–2019, indicating a slowing of the rate of decline since 2015 (Fig. 1.2[a]). Malaria deaths have reduced steadily over the period 2000–2019, from 736 000 in 2000 to 409 000 in 2019(Table 1.1.[a][b]).

The percentage of total malaria deaths among children aged under 5 years was 84% in 2000 and 67% in 2019. The number of deaths in 2015, the GTS baseline, was about 453 000. The malaria

fatality rate (i.e. deaths per 100 000 population at risk) decreased from about 25 in 2000 to 12 in 2015 and 10 in 2019, with the slowing of the rate of decay in the latter years similar to that seen in a number of cases (Fig. 1.2. [b]).

Of the 87 countries that were malaria endemic in 2019, 29 accounted for 95% of malaria cases globally (Fig. 1.2.a). Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%), Mozambique (4%) and Niger (3%) accounted for about 51% of all cases globally. About 95% of malaria deaths were in32 countries. Nigeria (23%), the Democratic Republic of the Congo (11%), the United Republic of Tanzania (5%), Burkina Faso (4%), Mozambique (4%) and Niger (4%) accounted for about 51% of all malaria deaths globally in 2019. [1].

Figure 1.2. depicts [a] malaria case incidence rate (cases per 1000 population at risk),[b] mortality rate (deaths per 100 000 population at risk), 2000–2019 [1]

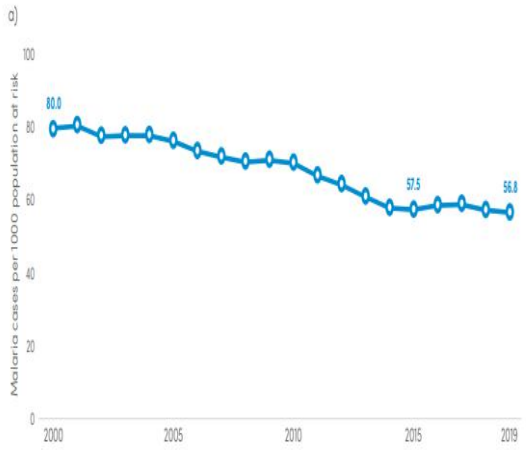


Fig1.2.[a]

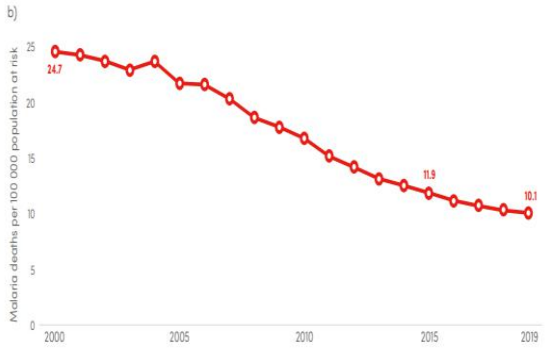


Fig 1.2.[b]

Africa, where a child dies nearly every minute due to malaria, and where malaria is a foremost cause of childhood neuro-disability. With an estimated 215 million malaria cases and 384 000 malaria deaths in 2019, the WHO African Region accounted for about 94% of cases and deaths globally. 27 of the 29 nations that consider for 95% of malaria cases globally are in the WHO African Region.[1]. Even though numbers decreased, you can see from statistics number of cases are not zero. African countries still face the challenge to eradicate malaria.

Hundreds of millions of blood films are tested every year for malaria, which involves eye and hand-operated counting of parasites and infected red blood cells by a qualified microscopist. Correct parasite counts are essential not only for malaria diagnosis. They are also essential for testing for drug-resistance, measuring drug-effectiveness, and classifying disease severity. However, microscopic diagnostics is not standardized and depends heavily on the judgment and skill of the microscopist.[2]. It is usual for microscopists in low-resource environments to work in isolation, with no precise system in place that can assure the maintenance of their abilities and thus diagnostic quality. [2]. This leads to incorrect diagnostic decisions in the

field.For false-negative cases, this leads to unnecessary use of antibiotics, a second consultation, missing days of work, and in some cases rise into severe malaria. For false-positive cases, a misdiagnosis entails unnecessary use of anti-malaria drugs and suffering from their likely side effects, such as nausea, abdominal pain, diarrhea, and sometimes severe complications.

This moderate analysis of malaria diagnosis has implied aims to perform malaria diagnosis automatically using computer aided technology. Automatic parasite counting has several benefits compared with manual counting: (1) it provides a more authentic and standardized interpretation of blood films, (2) it enables more patients to be served by reducing the workload of the malaria field workers, and (3) it can diminish diagnostic costs.

Malaria is a curable disease, with drugs available for treatment, including drugs that can help prevent malaria infections in travelers to malaria-prone regions. However, there exists no effective vaccine against malaria yet, although this is an area of active research and field studies. Once infected, malaria is a rapidly progressing disease, with a serious risk of developing into severe and cerebral malaria with neurologic symptoms for P. falciparum infections. Therefore, a timely diagnosis of malaria is veryimportant. Although malaria can be diagnosed in many ways, there is room for improvement for current malaria diagnostic tests including reducing cost, increasing specificity, and improving ease of use.

Detecting the presence of parasites is the key to malaria diagnosis. In addition, identifying the parasite species and presence of potentially mixed infections is important, as well as the observation of the stage development of P. falciparum parasites in relation to the severity of the disease. Counting parasites for determining the level ofparasitemia is not only important for identifying an infection and measuring its severity, it also allows monitoring patients by measuring drug efficacy and potential drug resistance.

Light microscopy. The current gold-standard method for malaria diagnosis in the field is light microscopy of blood films. Although other forms of diagnosis exist and have become popular in recent years, RDTs, microscopy remains the most popular diagnostic tool, especially in resource-poor settings. With microscopy, all parasite species can be detected. It allows computing the level of parasitemia, clearing a patient after a successful treatment, and monitoring drug resistance. Furthermore, it is less expensive than other methods and widely available. However, its biggest disadvantages are the extensive training required for a microscopist to become a proficient malaria slide reader, the high cost of training and employing, maintaining skills, and the large component of manual work involved.

To diagnose malaria under a microscope, a drop of the patient's blood is applied to a glass slide, which is then immersed in a staining solution to make parasites more easily visible under a conventional light microscope, usually with a 100× oil objective. Two different types of blood smears are typically prepared for malaria diagnosis: thick and thin smears.[3].A thick smear is used to detect the presence of parasites in a drop of blood. Thick smears allow a more efficient detection of parasites than thin smears, with an 11 times higher sensitivity.[4] On the other hand, thin smears, which are the result of spreading the drop of blood across the glass slide, have other advantages. They allow

the examiner to identify malaria species and recognize parasite stages more easily.

The actual microscopic examination of a single blood slide, including quantitative parasite detection and species identification, takes a trained microscopist 15–30 minutes. Considering that hundreds of thousands of blood slides are manually inspected for malaria every year, this amounts to a huge economic effort required for malaria diagnosis.

Rapid diagnostic tests. The main advantage of microscopic malaria diagnosis lies in its low direct cost, which gives it a distinct advantage in resource-poor settings.1 Other existing diagnostic methods, and any new method, must prove that they can provide the same ease of use and price point as microscopy given the limited financial resources typically available in malaria-prone regions. Arguably the only and main competitor in this sense are RDTs. They detect evidence of malaria parasites (antigens) and take about 10–15 minutes to process. Their detection sensitivity is lower but comparable with manual microscopy, and they do not require any special equipment and require only minimal training.

Although RDTs are currently more expensive than microscopy in high-burden areas,[5] a valid question is whether these tests can replace microscopy soon. At the time of this writing, according to WHO,[2] more country use microscopy more than they uses RDTs.[6] RDTs are used more in rural areas where microscopy is not available. About 47% of malaria tests in malaria endemic countries worldwide were made by RDT.[6].

The use of RDTs, however, does not eliminate the need for malaria microscopy. A major disadvantage is that RDTs do not provide quantification of the results. Therefore, now, microscopy and RDTs are more complementing each other than one replacing the other.

Polymerase chain reaction (PCR).A molecular method called PCR has shown higher sensitivity and specificity than conventional microscopic examination of stained peripheral blood smears. [7]In fact, it is consideredthemostaccurateamongalltests.Itcandetect exceptionally lowparasiteconcentrationsinthebloodandcan differentiate species. However, PCR is a complex high-cost technology that takes many hours to process by trained staff. According to [7]PCR is not routinely implemented in developing countriesbecauseofthecomplexityofthetestingandthe lack of resources to perform these tests adequately and routinely. Quality control and equipment maintenancearealsoessentialforthePCRtechnique,soth at itmaynotbesuitableformalariadiagnosisinremote rural areas or even in routine clinical diagnostic settings.

Flow cytometry. This is a laser-based cell counting and detection method that allows to profile thousands of cells per second. Although flow cytometry offersautomatedparasitemiacounts,thisisoffsetby a rather low sensitivity. Flow cytometry is less suit-able as a diagnostic technique in the field when a direct answer is required for treatment decisions. However,indevelopedcountries,itcanbeappliedin the clinical setting for accurate counting of parasite numbers, for instance in the follow-up of drug treatment. [8].

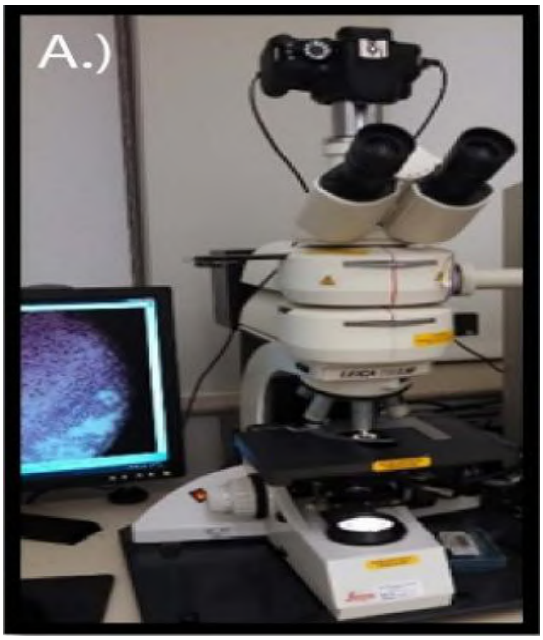
2. II.Working Principle

The ideal hardware solution for microscopic malaria diagnosis in resource-poor settings would be a small portable slide reader into which a blood slide could be inserted, and which would then output the parasitemia. Although modern technology is heading this way, we are still far from having a field-usable device. In particular, the relatively high optical magnification needed (up to 1000×) for malaria diagnosis in combination with oil immersion is a major miniaturization obstacle, unless alternatives are found. The next best solution are small camera-equipped computing devices, such as smartphones, which can be attached to a magnifying device and can then compute the parasitemia automatically, using image analysis and machine learning and deep learning.Modern smartphones have become powerful computing devices and their cameras provide sufficient resolution for malaria diagnosis. Moreover, Android phones have become relatively cheap and are often already in the possession of health-care workers, even in resource-poor settings. Although cellular network connectivity can help with the information exchange between field workers and hospital, it is not immediately needed for malaria diagnosis and the actual cell counting.Small magnifying devices that can be attached to a smartphone's camera, allowing true optical magnification compared with mere digital zooming, are commercially available. However, from different authors' experience, these devices are still lacking in the image quality provided. Therefore, a more practical approach is to simply attach the smartphone to the eyepiece of a regular microscope with an adapter so that blood slide pictures can be taken with the smartphone's camera.The idea is as shown in the following pictures in the figure 2.1[a], [b].

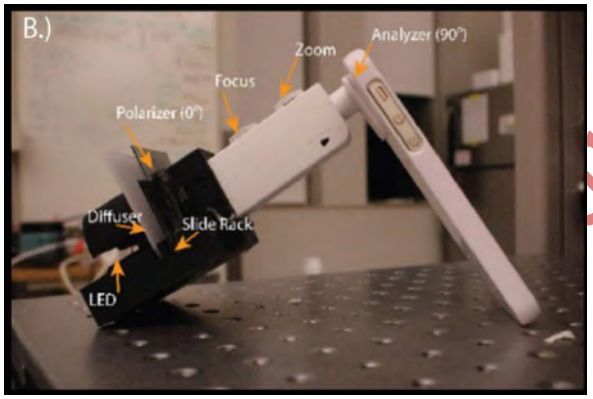
Figure 2.1.[a] Leica DMLM polarized white light microscope used as reference for comparison in this study; and [b] a microscope lens combination implemented into a 3D-printed fitting to allow similar function to a traditional polarized laboratory microscope. The MOPID system was configured in transmission mode with a magnification designed for 40X when using a mobile phone camera. An iPhone 5s was used with polarizer sheets added and a 3D-printed fitting to hold the light source, diffuser, sample slide, and microscope attachment.[9].

The working principle is as explained with the help of the block diagram shown in the figure 2.2.

Image acquisition: The first step is getting the image data.The first step is usually the acquisition of digital images of blood smears, which largely depends on the equipment and materials being use. The Image acquisition section breaks down the different approaches for the different types of microscopy, blood slides (thin or thick), and staining. Here to train the deep learning model we use separate data set of images which are easily available. [10]. Before training the Deep learning model the preprocessing is done to improve the test accuracy of the model. In real-time, we will use a ball lens attached to the mobile device or hand device cell phone to capture the images. Which forwarded for further Image Preprocessing (Image segmentation) and then to already learn the Deep Learning model for binary classification.



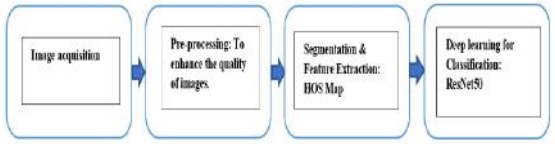
[a]



[b]

Preprocessing: Following image acquisition, most systems perform one or several preprocessing methods to remove noise and to normalize lighting and color variations inherent in the image acquisition and staining process. Preprocessing is mainly applied to improve the quality of the image and to reduce variations in the images that would unnecessarily complicate the subsequent processing steps. Three key objectives can be identified: noise removal, contrast improvement, illumination, and staining correction.For noise removal, the most popular approaches have been well-established filters, such as mean and median filters, or Gaussian low-pass filtering. In addition, applying morphologic operations is very popular. For contrast improvement, contrast stretching techniques and histogram equalization, have been the most popular approaches.[11][12]. Here we can use these techniques if necessary, but as our portable handheld device uses a high-definition camera with a flashlight and ball lens we can skip these steps.Further for segmentation and feature extraction, we use a HOS map which will take care of these tasks.[13].

Figure 2.2: shows the high-level block diagram of the entire system.



Segmentation and Feature Extraction: The next step usually involves the detection and segmentation (outlining) of individual blood cells and maybe other objects that can be visible in a blood slide image, such as parasites or platelets.Next cell segmentation is followed by the computation of a set of features, which describe the visual appearance of the segmented objects in a mathematical succinct way. To perform the image segmentation and to get the object of interest we are using a color-based HOS (Higher-Order Statistics) map [13], which is explained in detail in the technology section. The results are shown in the figure 3.1.1 and figure 3.1.2.

Deep learning for Classification: Deep learning is the latest trend in machine learning, which has already boosted the performance in many

nonmedical areas. Deep learning is an extension of the well-known multilayer neural network classifiers trained with back-propagation, except that many more layers are used. There are also different kind of layers that are used in typical successions. Deep learning typically requires large training sets. This is the reason why medical applications have been among the last applications to adopt deep learning, as annotated training images are significantly harder to obtain because of expert knowledge requirements and privacy concerns.This is an ideal application for deep learning because images of segmented red blood cells are a natural input for a convolutional neural network. Deep learning does not require the design of handcrafted features, which is one of its biggest advantages. Here we are employing the ResNet50 a Deep Convolutional Neural Network (DCNN) [14] that is already pre-train. We will modify the last layers ResNet50 for binary classification and this approach is called transfer learning. The segmented images are fed to the network to train the Deep Convolutional Neural Network (DCNN) model and get the test accuracy binary classification. The detail of the ResNet50 and how to use this network as transfer learning is given in the Technology section under the heading Transfer learning using ResNet50.

3. III. TECHNOLOGY:

1. HOS (Higher Order Statistics) explanation:

Our algorithm uses Colour Based-Higher Order Statistics (HOS) map for image segmentation. The image segmentation takes place in this manner: We transform the image into an appropriate feature space, consisting of spatial distribution of the high-frequency components. This is conducted by computing higher-order statistics (HOS) for all pixels in the low DOF image. The HOS are compatible for solving detection and classification problems because they can suppress Gaussian noise and preserve some of the non-Gaussian information. We try to exploit three colour channels for obtaining a better HOS map. In detail, the fourth-order moments are calculated for all pixels in the red, green, and blue channels. For instance, the fourth-order moment at (x, y) in a red channel is defined as follows:

where $\eta(x, y)$ is a set of neighbouring pixels cantering at (x, y),$\hat{m}_R(x, y)$ is the sample mean of red channel $I_{red}(x, y)$ of $I(x, y)$ that is:

$$\hat{m}_R(x, y) = \frac{1}{N_\eta} \sum_{(s,t)\in\eta(x,y)} (I_{red}(s, t)),$$

and N_η is a size of η. We take the maximum value among the moments from all the channels, $\hat{m}_R^{(4)}(x, y), \hat{m}_G^{(4)}(x, y), \hat{m}_B^{(4)}(x, y)$ in the following way:

$$tempHOS(x, y) = max(\hat{m}_R^{(4)}(x, y), \hat{m}_G^{(4)}(x, y), \hat{m}_B^{(4)}(x, y))$$

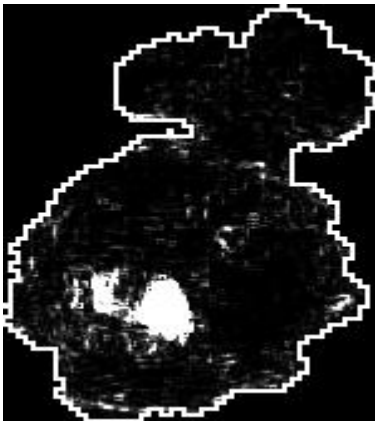
Since the dynamic range of the HOS values is huge, the value for each pixel is downscaled and limited by 255 such that each pixel takes a value from [0, 255]. The normalized outcome is called a colour based HOS map. A pixel value of (x, y) in the color-based *HOS* map, $colorHOS(x, y),$ is defined as follows:

$$colorHOS(x, y) = min(255, tempHOS(x, y)/DSF),$$

Where DSF denotes downscaling factor to reduce the dynamic range. We use a value of 300 as a downscaling factor to reduce the dynamic range as it

gives an appropriate result for segmentation.[11]. Following figure shows the HOS result for malaria parasite and non-parasite.

Figure 3.1.1. depicts [a], [b] image segmented of malaria parasite blood cell image using HOS (Higher Order Statistics).

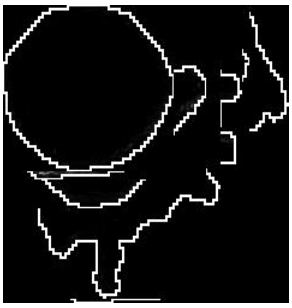


[a]

[b]

Fig 3.1.1

Figure 3.1.2. depicts [a], [b] image segmented of malaria non-parasite blood cell image using HOS (Higher Order Statistics).



[a]

[b]

Fig 3.1.2

2.Transfer learning using ResNet50:

As we are going to use ResNet50 [14] in image classification with two sets of blood cell image data - parasitized and non-parasitized. The HOS map segmented images of two types of blood cells are then fed to the convolutional neural network i.e., ResNet50. Network architecture of ResNet50 should result in 2 output class labels-parasite and non-parasite. For this purpose, we need to update the network, because ResNet50 is pre-trained for 1000 classes, the final classifier label that is Linear () is having 1000 nodes at the output layer. This last linear layer is coded only for two nodes along with fine-tuning the weights of the pre-trained network by continuing the backpropagation. The weights take update by implementing stochastic gradient

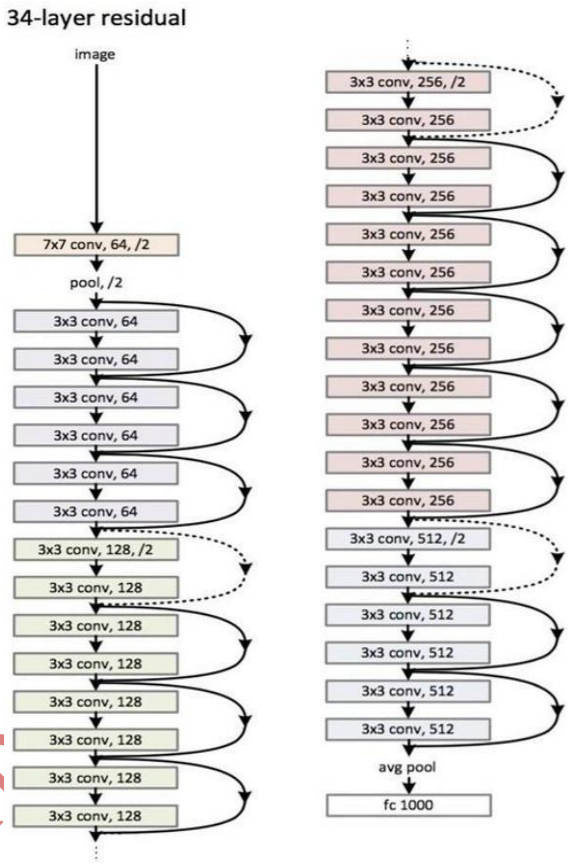
descent (SGD) algorithm as an optimizer along with cross-entropy as a loss function.

To train ResNet50, Using PyTorch, the dataset is randomly divided into training, validation, and testing where 70% of the dataset is for training,20% for validation, and 10% for testing. The batch size for training data is 64, validation and testing batch size is 32. SGD with 25 epochs and a learning rate of 0.001 is used to train the model. Unseen test data images are utilized by the trained model to get the classification accuracy.

ResNet50 architecture contains the following element:

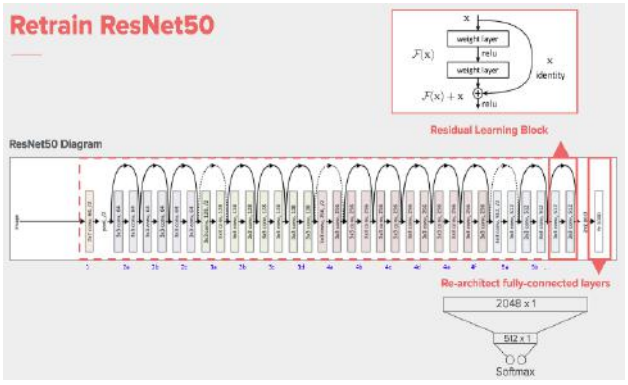
- Convolution with a kernel size of 7 * 7 and 64 different kernels all with a stride of size 2 giving us **1 layer**.
- Next, we see max pooling with also a stride size of 2.
- In the next convolution, there is a 1 * 1,64 kernel following this a 3 * 3,64 kernel and at last, a 1 * 1,256 kernels, these three layers are repeated in total 3 times so giving us **9 layers** in this step.
- Next is the kernel of 1 * 1,128 after that a kernel of 3 * 3,128 and at last a kernel of 1 * 1,512 this step was repeated 4 times so giving us **12 layers** in this step.
- After that, there is a kernel of 1 * 1,256 and two more kernels with 3 * 3,256 and 1 * 1,1024 and this is repeated 6 times giving us a total of **18 layers**.
- And then again, a 1 * 1,512 kernel with two more of 3 * 3,512 and 1 * 1,2048 and this was repeated 3 times giving us a total of **9 layers**.
- After that, we do an average pool and end it with a fully connected layer containing 1000 nodes and at the end a SoftMax function, so this gives us **1 layer**.

We do not count the activation functions and the max/average pooling layers. So, totalling this it gives us a 1 + 9 + 12 + 18 + 9 + 1 = 50 layers Deep Convolutional network.



[a]

Figure 3.2.1 [a] displays arcResNet50.



[b]

Figure 3.2.2 [b]displays idea of the Retrain ResNet50.

3.Use of Simulation software:

1. Image Segmentation - This is done by implementing the HOS in Octaves-5.2.0.
2. Deep Learning libraries - ResNet50 is imported as a deep learning neural network/model to perform classification using PyTorch.[15]
3. Platform - The experiments were performed using a computer equipped with a Core i5 processor, 16 GB DDRAM, and NVIDIA GeForce GTX 1050 Ti graphical processing unit. The proposed method is coded using PyTorch 1.6.0, where the executed version is coded using CUDA 11.0 to be run using the GPU.

4. IV. Detailed Working

A]Use of Mobile Phone Technology for Medical Diagnosis in Remote Areas:

In general, mobile phones offer an ideal platform for creating a field-based, modular polarized microscope. Currently, over 6 billion cell-phone subscriptions exist worldwide (accounting for approximately 75% of the world having access to mobile phone networks), [16][17] with the vast majority of these users (~5 billion) located in developing countries. Utilizing the existing mobile infrastructure allows for significant reduction in cost and size of mobile based designs as compared to traditional microscopes. Additionally, the number of active mobile phone subscriptions is continually increasing, particularly in low-resource settings and is expected to surpass the world population by the end of 2014 [18]. Due to the large volume of wireless communication users, mobile phones continually remain at relatively low costs even with constant advancements in hardware and software specifications on new models. Because of increased access to these mobile networks and the fact that many mobile phones currently available are equipped with advanced camera features and other technologies, they have become an ideal platform for many advanced imaging and sensing mHealth applications resulting in several portable field ready point-of-care (POC) devices. These mobile point-of-care (POC) platforms offer great opportunities for improved healthcare throughout the world by offering high quality alternatives to existing imaging modalities that are low-cost, portable and energy efficient. This is particularly important for the clinic and field in remote areas and in low resource settings, where the medical infrastructure is often limited or non-existent.

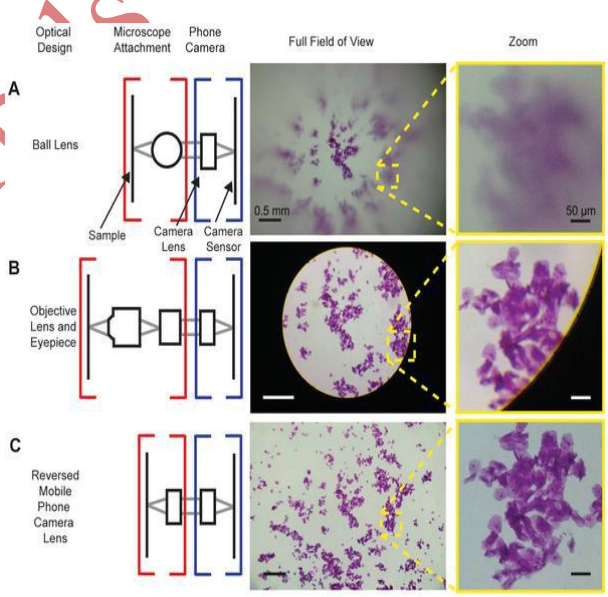


Figure 4.1 shows the Lens-less phone-based microscopy.

Mobile phone-based microscopy approaches can be broken down into three specific design areas including:

1. Lens-less approaches,
2. on-lens approaches and
3. attachment based approaches.

Research in each of these design categories has produced promising scientific approaches towards cell-phone microscopy designs capable of significantly affecting healthcare standards in developing countries, particularly in single cell resolution for disease diagnosis.

Using a lens less design approach can allow for more compact designs and eliminates the need for optical alignment. Additionally, this technique allows for decoupling of the relationship between field-of-view (FOV) and resolution, thus allowing for significant improvements in large FOV imaging without sacrificing system resolution as compared to traditional microscopy techniques.

The second approach uses on-lens device design configurations typically employing a refractive element directly attached to the cell-phone camera at the focus, or a ball lens mounted in front of the camera lens. This approach allows for a low-cost alternative and produces comparable resolution to other reported cellphone-basedmicroscope systems. The ball lens creates a spherical focal plane; thus, the technique only allows for a small FOV of a captured image to be in focus. The out of focus areas in the FOV then need to be adjusted using image processing correction techniques. [19][20][21][22][23].

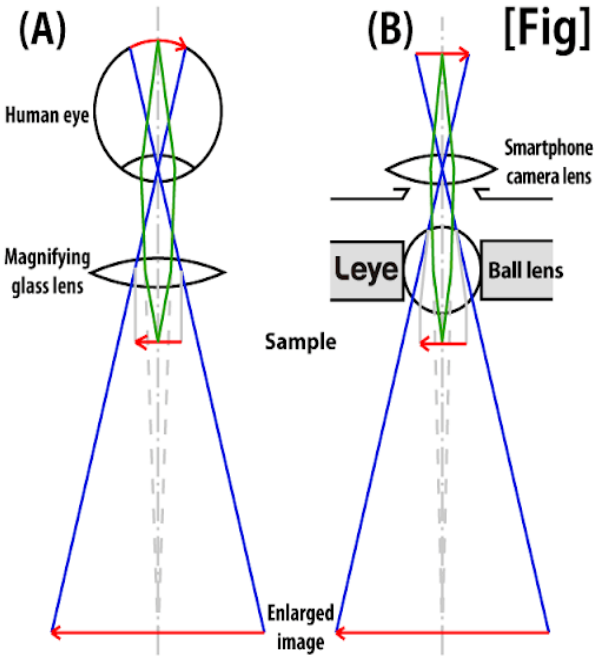


Figure 4.2 shows field View of the Lens.

We describe the design of a low-cost, lightweight, high quality mobile-optical-machine learning equipment that allows see gold standard microscope view in mobile by advance machine learning detection that going to reduce the time and effort for diagnosis of malaria in rural areas.

B] Materials and Methods:

For the MOML system the optical setup and components consisted of a commercial cellular phone, customized attachable mount, two polarizer sheets (that could be removed for non-polarized imaging), low-power high efficiency white light emitting diodes (LEDs) and a plastic lens assembly configuration allowing for appropriate magnification, resolution and FOV for diagnosing the presence of the malaria parasite.

Phone details:

Following the adjustable multiple lens microscope assembly in the MOPID design, a snap on 3D-printed cartridge had individual compartments that allowed for polarized microscopy. The cell-phone 3D-printed cartridge attachment consisted of PLA plastic using a fused deposition modeling 3D-printer (MakerBot Industries, New York NY). The attachment included slotted areas to insert the sample microscope slide, a rotatable polarizer sheet, titanium dioxide chip diffuser plate (RTP Company, Winona, MN) and white LEDs (COAST, Portland, OR) to illuminate the sample. The ability to rotate the analyzer, varying the degree of polarization, allows for both conventional histology and crossed polarized light imaging for birefringence measurements from the hemozoin crystal.

The portable commercial microscope lens assembly consisted of two separate plastic lens modules and had a numerical aperture (NA) value of 0.65. The MOPID design incorporated white light LEDs placed at a distance from the sample, allowing for even field illumination. The individual LEDs were chosen because of their low-cost, low power, durability, and long lifetime; all characteristics ideally suited for use in low-resource settings. In the designed system, the white light LED total power was 66 lumens after the light passes through a TiO_2 diffuser plate. The diffuser plate is utilized to allow for homogenous illumination across the sample and was followed by a polarizer sheet generating linearly polarized light prior to transmission through the sample. is the location where the blood smear or histological slide is inserted into the optical train. This slit is located such that the sample is optimally positioned at approximately one focal length of the imaging system. Utilizing a multi-position insert the slide can be manually moved past the camera from left to right in incremental steps. The final component prior to the mobile phone surface in the optical path is a second polarizer, an analyzer, capable of being oriented either at 45 or 90 degrees with respect to the initial polarizer orientation

Method for Polarized Light Microscopy Imaging:

Polarized images acquired with the MOPID and Leica microscope setups described above allowed for comparison between the two systems. The two systems were comparatively evaluated based on the following criteria: 1) Resolution, 2) Field of view (FOV), 3) Magnification and 4)

Illumination quality:

The depth of focus, illumination beam quality and divergence angle on the FOV, was calculated for each system. Additionally, the predicted system magnification was determined for the MOPID combination. Similarly, the NA of the system was calculated and compared to the reported data. Using this number, the diffraction limited resolution was calculated for the MOPID and reference design setup described above. Utilizing each hardware configuration and the different lens combinations, USAF resolution target images were acquired in addition to images of prepared samples on microscope slides.

Procedure:

For malaria diagnosis, a drop of blood from an infected person is taken. This drop is put on a glass slide and then is stained with a suitable solution to highlight the parasites. This whole preparation is called a smear. Blood smears are taken most often from a finger prick.

Thick and thin blood smears will let doctors know the percentage of red blood cells that are infected

(parasite density) and what type of parasites are present.

- Thick blood smears are most useful for detecting the presence of parasites because they examine a larger sample of blood. (Often there are few parasites in the blood at the time the test is done.)
- A thin blood smear is a drop of blood that is spread across a large area of the glass slide. Thin blood smears help doctors discover the type of species of malaria is causing the infection.
- After the blood samples are taken from the patient, we then put the sample in a 3d design cover that has the ball lens, LED. These 3d design covers will hold the blood samples in 90 degree and will help to view the blood samples as a standard microscope view and will give you a detailed view of the blood samples.
- After the blood sample is viewed on the phone screen, the segmented of same image is given to the trained deep learning model, which will then diagnose whether the patient has malaria or not.
- A deep learning model is to use the approach of transfer learning, so it is pre-trained already. Which in-turn gives you proper detection and classification of blood cell samples.
- The execution of the deep learning model (ResNet 50) on the edge device like a mobile phone is a challenge that we may face.
- After the results are arrived, we then do the next patient and go on with this procedure. This will solve the time and efficiency in detection of the blood cells in parasites and improve the growth of cell detection.

V. Future Scope:

The system uses an image processing technique i.e. Color-based HOS map to get the segmentation and then a deep learning algorithm. These two things can be done together with the help of Deep Learning only. Second, the deep learning model deployment on the cell phone is a challenging task and needs more attention.

VI. Conclusion:

We successfully devised a tool to carry out an effective and accurate diagnosis of malaria using a mobile phone. For getting an appropriate image with perfect zoom and nice quality to carry out image segmentation, we use a 6mm diameter ball lens and a 1mm diameter polarizing sheet to neglect different light intensities, respectively. Now, image segmentation is carried out using the HOS (High Order Statistics) map. We conveniently utilised ResNet50 architecture using transfer learning to classify the obtained blood sample images into categories namely: parasitized and non-parasitized. The accomplished test accuracy for binary classification by using a pre-trained deep learning network - ResNet50 - on the segmented images of the malaria parasite is 86%.

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VIII. Authors

First Author:

Dhruva Iyer

Pursuing secondary education from ARYA VIDYA MANDIR (CICSE Board), JHUU. Currently in 10th grade.
Email ID:dhruvakiyer@gmail.com

Second Author:

Nirvaan Sen

Completed secondary education from Jamnabi Narsee International School (IGCSE Board), JUHU. Currently 11th grade in the same school (IBDP Board).
Email ID:nirvaan10@gmail.com

Third Author:

Reetu jain

Chief-Mentor and Founder of On My Own Technology Private Limited Mumbai, reetu.jain@onmyowntechnology.com

Fourth Author:

Shekhar jain

Chief Executive Officer and Co-founder of On My Own Technology Private Limited Mumbai, shekhar.jain@onmyowntechnology.com