Overview of digital holographic deep learning of red blood cells for field-portable, rapid disease screening

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ABSTRACT

In this work we present an overview of previously published work on identification of COVID-19 red blood cells (RBCs) and sickle cell disease based on the reconstructed phase profile using deep learning framework. The video holograms for thin blood smears were recorded using a compact, low-cost and field portable, 3D-printed shear based digital holographic system. Individual cells were segmented from the holograms and then each frame was reconstructed to extract spatio-temporal signature of the cells. Morphology based features along with motility-based features extracted from reconstructed phase images, were fed to a bi-LSTM to classify between COVID-19 positive and healthy red blood cells. Based on the majority of the cell's subjects were classified as healthy or diseased.

Keywords: Digital holography microscopy, COVID-19, sickle cell disease, bi-LSTM, field portable, 3D-printed, red blood cell

SYSTEM OVERVIEW

Coronavirus disease 2019 (Covid-19) was a highly infectious disease caused by SARS-C0V-2 virus. Several symptoms like fever, respiratory problems, cough, loss of taste and smell are generally associated with the disease. The highly infectious nature of the disease and very common symptoms were called for a precise and fast diagnosis method especially in low resource and largely populated countries. Currently available diagnosis methods involve polymerase chain reaction (PCR) testing, antigen testing, antibody-based methods, and lung compound tomography (CT) based methods [1]. Except antigen testing methods, all these methods require a dedicated test facility and can take from few hours to few days for the results. Antigen tests rely on the proteins specific viruses, are fast, highly specific but lower in sensitivity and prone to false negative [2]. Recent studies have reported morphological deformation in the red blood cells (RBCs) of patients particularly in severe cases [3]. Digital holography microscopy (DHM) is a quantitative phase imaging technique which in combination with machine learning shows promising application in disease diagnosis, cell classification and cell imaging [4-5]. In this work we overview previously presented DHM setup in integration with a deep learning framework [6] as a portable compact and low-cost alternative Covid-19 diagnosis system.

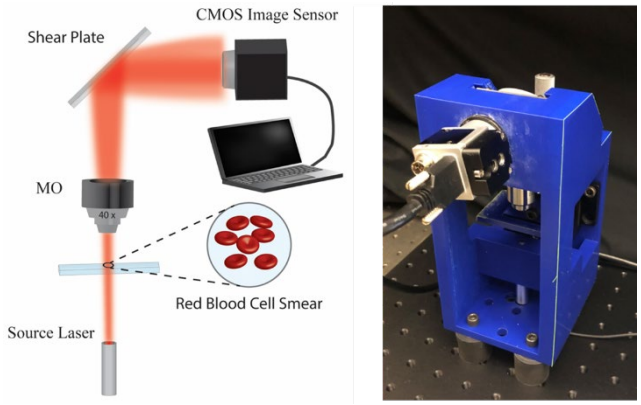

Fig.1 (a) Optical configuration and (b) 3D-printed experimental system with dimensions 94 mm x 107 mm x 190.5 mm. [6]

Fig.1. shows the shearing based common path DHM system and it's optical diagram, used for data collection. The system consist of a laser diode (1.2mW, 635nm), a microscope objective (40X, 0.65NA), a 1D translation stage, a shear glass plate and a CMOS sensor with pixel size 1.6 µm. The shear plates devides the incoming modulated signal in two beams which interefere on sensor plane to form an hologram. Video holograms of the thin blood smears were recorded.

Later, individual cells were segmented from the phase profiles. The phase profiles of the hologram were obtained using numerical reconstruction [4]. Features extracted from the phase profiles were input to the deep learning model. Features extracted for analysis include both handcrafted and transfer-learned based features. Handcrafted features focus on morphological aspects, describing the 3D shape of phase profiles, are calculated for each frame of reconstructed video data from segmented RBCs. These measurements include mean optical path length (OPL) coefficient of variation, projected cell area, optical volume, cell thickness skewness, cell thickness kurtosis, cell perimeter, cell circularity, cell elongation, cell eccentricity, cell thickness entropy, maximum and minimum cell widths, and maximum and minimum OPL values. Transfer learned featured derived from the final fully connected layer of a DenseNet-201 convolutional neural network, which has been pre-trained on the ImageNet database were also utilized. This approach yields an additional 1000 extracted features for each segmented cell. 1017 feature were extrated for each frame, which then fed to LSTM for training purpose. Fig.2 [6] shows the overview daigram for the entire process.

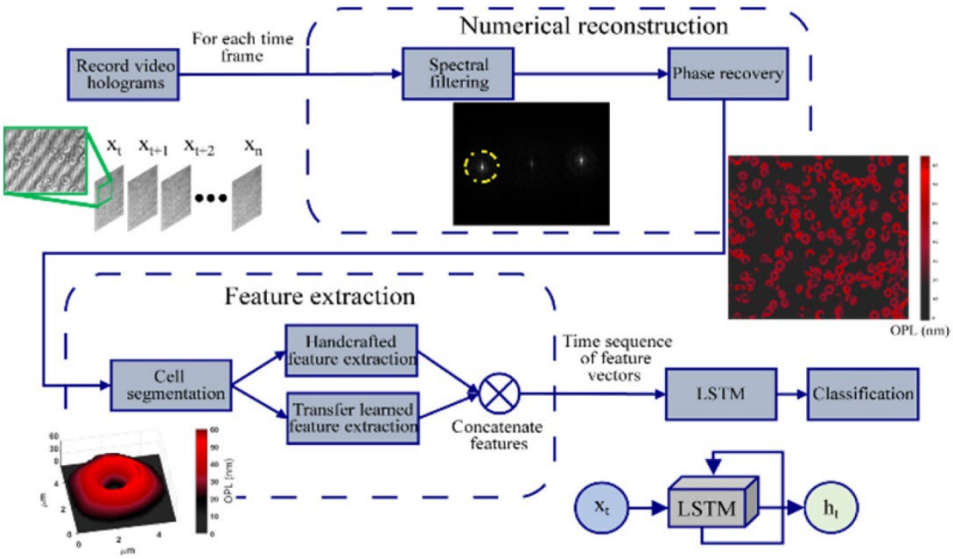

Fig.2. Overview diagram for deep-learning-based digital holo- graphic microscopy cell identification system. Video holograms are recorded using the system depicted in Fig. 1. Individual cells are seg- mented at each time frame, and features are extracted for input into a LSTM classifier. x_t and h_t denote, respectively, the input and output of a portion of a LSTM block at time-step t. LSTM, long short-term memory [6].

The training and testing dataset contains the data from 10 Covid patients and 14 healthy volunteers. The overviewed method has achieved a classification accuracy of 67.44% at cellular level. Based on the majority of cells a patient was determined to be positive or negative. By keeping the threshold to be 0.5, an accuracy of 87.5% was achieved for patient level classification [6].

CONCLUSION

In conclusion, we have overviewed a compact and field portable 3D-printed system based on shearing interferometry to distinguish between healthy disease-state RBCs as well as diagnosing patients based on the classified cells [5, 6]. The study suggests that the morphological changes in red blood cells of an infected person can be utilized as a biomarker for the classification task. B. Javidi acknowledges support from National Science Foundation grant number 2141473.

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