Real-Time Quantitative Phase Imaging

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Abstract—The following is an introduction to a real-time blood testing system with minimal human intervention. The device tested is the first documented real-time quantitative phase imaging (QPI) system ever reported. The ultimate purpose of the device is to allow for accurate blood testing in economically challenged countries.

I. INTRODUCTION

The motive behind the quantitative phase imaging (QPI) device is to allow economically challenged countries and rural areas to gain access to modern blood testing. According to a 2012 study, “39 of 159 countries, which collected 92 million blood donations every year, were not able to run blood screens.” [1] To address this problem, researchers have been taking advantage of commercial technology, and have produced miniaturized and inexpensive devices for cell imaging in low resource settings. Instead of focusing on lowering the cost of such devices, researchers in this team prioritized the quality of data collected by their device. This QPI device offers accurate blood screens with little human interaction, allowing for an increase in blood screening due to a decrease in human labor going into each test.

II. METHODS

The blood sample is first diluted in PBS solution with 0.1% albumin to a concentration of 0.2% whole blood in solution. “The index of refractive depends linearly on the hemoglobin concentration of red blood cells as $n_0 = \beta C + n_w$, where $\beta$ is the refractive increment, C the hemoglobin concentration of the cell, and $n_w$ is the refractive index of water.” [1] Because the optical pathlength (or phase) contains information about both the sample refractive index and thickness, QPI has been used to provide measurements of red blood cell volumes, cell dry mass, dynamics, cell tomography, tissue scattering.

A grating is placed at the image plane of a commercial microscope (the dashed box) to create different diffraction orders. Filter masks are projected onto a spatial light modulator placed at the back focal plane of a Fourier lens $L_1$ to low pass filter the 0th order beam, and allow the entire 1st order beam (imaging field) to pass through. Another Fourier lens $L_2$ recombines the two beams to create an interferogram on a CCD. A Hilbert transform is then used to reconstruct the phase information from the interferogram.

The first parameter calculated is the projected area, obtained by multiplying the number of pixels of each cell with the pixel area. In order to obtain other 2D and 3D morphological parameters, the phase map $\phi(x,y)$, is converted to a height map, $h(x,y)$, as $h(x,y) = \frac{i\phi(x,y)}{2\pi\Delta n}$, where lambda is the wavelength of the light source and $\Delta n = n_e - n_0$ is the refractive index difference between RBCs and the surrounding medium. Once the height information is retrieved, the volume of each cell is calculated by integrating the height map over the projected area as $V = \int h(x,y)dx\,dy$.

III. RESULTS

The results of testing with this device are shown in the figure to the left. The figure shows the distributions of RBCs’ volumes for three patients. “The MCV values for normal, microcytic and macrocytic patient are 92.5 fl, 67.4 fl and 125.6 fl, respectively.” [1] These numbers agree very well with the data acquired by the clinical impedance counter” [1], which are 92.2 fl, 64.4 fl and 121.8 fl, respectively. The results shown also give adequate support for the device’s precision in its measurement.

IV. DISCUSSION

This experiment demonstrated a quantitative phase imaging system dedicated to blood screening, which reconstructs phase images, analyzes and calculates a number of morphological parameters of red blood cells at single cell level, all in real time. The system is capable of very high throughput imaging and allows analyzing thousands of cells per sample easily. Operating in remote and under-developed areas also involves operation under tough conditions. Of course, working under difficult circumstances requires further testing. However, the intrinsic stability of this system promises to fulfill these constraints.
References

