ABSTRACT

With the ease availability and accessibility of various consumer electronic devices such as smartphones, Arduino microcontroller board (with the camera module), small single-board computers, e.g., Raspberry Pi with the camera module, CCTV, miniature display and low-cost optics modules, it brings new possibilities for the development of alternative, inexpensive, field-portable sensing and imaging platforms [1–3]. To be more specific, smartphones or mobile phones have been exploited extensively for this purpose which is a powerful pocket computing device with numerous integrated sensors and wireless connectivity. By 2020, it has been reported that there are 6.05 billion smartphone users with a penetration rate of 61.28% worldwide [4]. Such huge penetration of smartphones to this extent is possible only because of their affordability and consumer-oriented low-cost design approach. Now, with the rapid advancement in smartphone manufacturing technology, low-cost smartphone devices (also referred to as low-end devices) also offer similar sensing and processing capabilities to those of more expensive (high-end) devices. Because of this, the number of smartphone users is even increasing rapidly both in developed as well as under-developed countries, thus providing new opportunities to acquire and handle data by innovating new portable and cost-effective technologies on top of the smartphone platform. Various hardware and sensors e.g., complementary metal-oxide semiconductor (CMOS) module, ambient light sensor (ALS), display module, USB port etc. along with the software interface of a smartphone have been exploited to develop not only affordable, but also portable cutting-edge technological solutions in the field of optical imaging and sensing, surface plasmon resonance (SPR) based sensors, electrochemical and near-field communication (NFC) based biosensors [5–8].

Optical microscopic imaging is ubiquitous for biological, life science research and other laboratory applications [9]. It is the basic foundation of scientific imaging and analysis that allows the visualization of cellular and sub-cellular structures and their dynamics. Still, a microscope is the gold standard tool for diagnosis of various

diseases such as sickle cell anemia, malaria, tuberculosis etc. Commercially available standard microscopes can deliver precise imaging with high resolution. However, their bulkiness, cost, fragility, and need for skilled personal to operate limit their usability within well-established and advanced laboratory facility conditions. Again, in developing countries, due to slow acquisition and unreliable supply chains further inflate the prices, making it extremely challenging to use it as a point-of-care tool (PoCT) in resource-constrained settings [4]. Thus, it is apparent to develop portable, cost-effective microscopic imaging systems that could facilitate its deployment as a PoCT device in the regions where facilities are inadequate.

This thesis work reports the design and development of affordable and portable different microscopic imaging platforms on a smartphone for various biological, biomedical and other monitoring applications with reference to the resource-poor regions. Both $3f$ and $4f$ optical configurations have been implemented to develop the imaging platforms. The CMOS camera module has been primarily exploited as a detector in the present study. Other hardware parts such as LED flashlight of the phone, USB port (for powering and establishing communication between the smartphone and the external peripheral modules) etc., have also been utilized to make a complete standalone smartphone based microscopic imaging system. Rapid prototyping of the proposed microscopic systems has been performed using the 3D-printing technology. Along with the optics design of the imaging system, efforts have been made to make the system more versatile by developing custom-coded smartphone applications for image parameter analysis such as image enhancement, cell recognition etc.

In the first step of the thesis, a high resolution, wide-field multi-modal finite-conjugate microscopic imaging system on a single platform using a smartphone has been developed by integrating off-the-shelf optical components. The designed system utilizes the built-in camera for recording of the images and the LED flash of the phone as an optical source. Three dynamically adaptable modes of imaging, namely transmission bright-field (BF), oblique illumination dark-field (OIDF) and total internal reflection dark-field (TIRDF), have been demonstrated on a single platform. The design parameters such as magnification, resolution etc. and construction of the device have been discussed thoroughly. The applicability of the platform has been evaluated by comparing the performances with a standard laboratory microscope.

One of the major drawbacks of a finite-conjugate imaging system is that the spatial resolution of the system depends on the pixel pitch of the CMOS sensor of the smartphone due to low optical magnification. To tackle this, in the second step, a low-cost 3D-printed smartphone microscopic system with a very high optical magnification has been developed. The imaging system is based on the $4f$ optical configuration where an objective lens and a tube lens are stacked adjacently such that their focal planes coincide. Modern optical microscopes that are based on infinity-corrected objectives follow this configuration [10]. This allows the utilization of the numerical aperture at the full potential delivering enhanced resolution. An image processing algorithm has been proposed by using cloud-based services, which can be accessed anytime through a mobile broadband network. Using this facility, the quality of the captured images can be further enhanced, thus obviating the need for dedicated computational tools for post-processing of the images. Since, our primary intention is to design affordable and portable technological solutions that are meant to be used in regions where resources are very limited, hence further optimization in the design of the platform has been implemented. In the next phase, the microscopic system has been modified to operate in high-throughput BF and fluorescence modes at three different optical magnification levels that perform at par with that of a laboratory-grade microscope. The versatility of the device has been demonstrated through imaging of standard microbeads and human blood samples both in BF and fluorescence modes of imaging. Furthermore, the designed imaging platform is equipped with an on-board cell recognition feature which has been obtained through developing a smartphone application for automatic cell counting with high precision.

In the third step of the thesis, a programmable illumination smartphone microscopy (PISM) as a flexible multimodal imaging platform for contrast enhancement of various samples has been proposed using different low-cost consumer optoelectronics parts. Usually, different microscopic imaging modes require spatially modulated illumination systems, which can be obtained by introducing optical filters and physical masks into the condenser lens of the microscope. For instance, in a DF microscope, a specialized opaque disc is inserted into the aperture focal plane of the condenser lens to create a hollow cone of light. It would produce a numerical aperture larger than the objective lens so that only the scattered light from the specimen can enter the objective lens. Similarly, for phase-contrast imaging, a phase ring is inserted into the condenser's aperture plane to fit the ring-shaped phase plate inside the objective lens. To integrate all the imaging modes together in a single platform is either extremely laborious and expensive or impracticable. Herein, a miniature (0.96 inches), programmable organic light-emitting diode (OLED) display has been used as an optical source to develop the proposed PISM system. By displaying different color and binary patterns on the OLED display, six well-established imaging modes, namely BF, DF, oblique illumination (OI), Fluorescence imaging (FI), Rheinberg illumination (RI), and differential phase contrast (DPC) imaging have been demonstrated on a single optical setup. Furthermore, by incorporating additional optical components such as an optical polarizer into the setup, another imaging mode-polarized imaging has been realized with the proposed PISM system.

Finally, in the end of the thesis, a cheap and versatile one-shot BF, DF and DPC imaging solution using the off-the-shelf optical and electronics components for infield applications has been demonstrated. Currently, bulky and complex optomechanical design has been implemented to obtain various label-free multi-contrast microscopic setups. The basis for economical and versatile microscopic imaging applications is the cost-effective engineering of the illumination component. This work details the design and development of a one-shot multi-contrast microscopic imaging platform on a smartphone by generating a multiplexed color pattern on an OLED panel used as an optical source for the proposed system. The same color pattern has also been adapted to a basic laboratory microscope to transform it into a multi-contrast imaging platform. The color channel of the final image has been decomposed and subsequently computed to obtain the different contrast enhancing imaging modes. Both the systems provide three imaging modalities for every single shot, namely BF, DF, and DPC imaging on a single optical setup.

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