

## ***DECLARATION***

---

I, hereby, declare that the thesis entitled “***Design and implementation of an inexpensive, handheld microscopic imaging and analytical system for biomedical and laboratory applications***”, submitted to the School of Sciences, Tezpur University (TU), in partial fulfillment of the requirements for the award of the Doctor of Philosophy in Physics, has been carried out by me at the Department of Physics, TU, Assam, India-784028, under the supervision of ***Prof. Pabitra Nath*** (Supervisor). The contents of this work is original except where specific reference is made to the works of others and has not been submitted in whole or in part for consideration for any other degree or qualification in this or any other university or institute.

---

Diganta Rabha

---

Date



## TEZPUR UNIVERSITY

(A central University established by an Act of Parliament)

### DEPARTMENT OF PHYSICS

Tezpur-784028, Assam, India

---

## CERTIFICATE OF THE PRINCIPAL SUPERVISOR

This is to certify that the thesis entitled “*Design and implementation of an inexpensive, handheld microscopic imaging and analytical system for biomedical and laboratory applications*”, submitted to the School of Sciences, Tezpur University in partial fulfillment for the award of degree of Doctor of Philosophy in Physics, is a record of research work carried out by **Mr. Diganta Rabha** under my guidance and supervision.

All help received by him from various sources have been duly acknowledged. No part of this thesis has been submitted elsewhere for award of any other degree.

**Date:**

**Place:**

**Prof. Pabitra Nath**

Department of Physics

Email: pnath@tezu.ernet.in

Ph. no. +91-3712-275575

Fax. +91-3712-267006



## TEZPUR UNIVERSITY

(A central University established by an Act of Parliament)

Tezpur-784028, Assam, India

---

### CERTIFICATE OF EXTERNAL EXAMINER AND ODEC

This is to certify that the thesis entitled “*Design and implementation of an inexpensive, handheld microscopic imaging and analytical system for biomedical and laboratory applications*”, submitted by Mr. Diganta Rabha to Tezpur University in the Department of Physics under the School of Sciences in partial fulfillment of the requirement for the award of degree of Doctor of Philosophy in Physics has been examined by us on ..... and found satisfactory.

The committee recommends for the award of the degree of Doctor of Philosophy.

**Principal Supervisor**

**Date:**

**External Examiner**

**Date:**

## ***ACKNOWLEDGMENT***

---

As I have achieved another milestone in my academic carrier, I would gladly take this moment to express my eternal feelings to those few individuals without whose help and support my research work would not reflect in the form of this thesis. First of all, I would like to express my deepest and sincerest gratitude to my supervisor, ***Prof. Pabitra Nath***, who believed in me and was the constant pillar of support at every step of this PhD journey in the most real sense. His research enthusiasm and dedication to the pursuit of physics have been a precious source of motivation and inspiration for me. I feel fortunate to be a researcher under his supervision, who always ensured and inspired me by building confidence to carry out the research work with flying colors. Apart from being a supervisor, he is a person of high caliber and a great human being. His encouraging, caring and nourishing nature made me grasp a lot of lessons and his suggestions on scientific learning will remain a beacon of light guiding me throughout my entire life.

I would like to show my sincere appreciation and thanks to my doctoral committee members, ***Prof. Gazi Ameen Ahmed*** (Department of Physics) and ***Prof. Manabendra Mandal*** (Department of Molecular Biology and Biotechnology) for their support, insightful comments and cherished suggestions that helped me to carry on my research work by building a proper scientific temperament. They provided me with access to their laboratory facilities without a second thought whenever I needed it. Because of which, it was possible for me to carry out my research in such an interdisciplinary field. I want to sincerely acknowledge and express my deepest sense of gratitude to the faculty members of the Department of Physics for providing me with the opportunity to pursue my PhD degree. I will be always grateful to *Prof. A. Kumar, Prof. J. K. Sarma, Prof. N. Bhattacharya, Prof. N. Das, Prof. P. Deb, Prof. M. K. Das (Head), Dr. D. Mohanta, Dr. S. K. Das, Dr. Arup J. Choudhury* and *Dr. R. Sarmah*. I am blessed and grateful for their academic support and encouragement since my joining to this department. I must also acknowledge the technical officers and staffs of the department, *Dr. Kishore Boruah, Mr. Umesh Patir*, and *Mr. Narayan Sarma*, for their unconditional support in official works and also my deepest thanks to all other non-academic staffs for their help at times.

I owe my sincere thanks and gratitude to *Dr. Amrit Sarmah*, Department of Pathology, Tezpur Medical College & Hospital, for his invaluable lessons and training on biomedical imaging, without whose my research work would be incomplete. My profound thanks to *Dr. Jacob Engelberg* from Applied Physics Department, Hebrew University of Jerusalem, Israel, for performing the optical simulation in Zeemax

software of one of my research works.

It is with immense pleasure I confess that no words would be sufficient to express my gratitude towards my lab members for their unconditional support and cheering all throughout my staying in the lab. I will be always grateful to my senior lab members, *Nabadeep da* and *Iftak da*, for their encouraging words throughout my PhD tenure. I want to express my thoughtful thanks to my current lab members, *Diganta Hati*, *Priyanka*, *Sritam*, *Dipjyoti*, *Biprav*, and *Rupam*, for all the stimulating discussions, their helping hands whenever needed, and for all the fun times we had together.

This journey would not be such delightful without the presence of constant support from friends and seniors. I would take this moment to thank *Pritam*, *GVS Bhagyaraj*, *Bichitra*, *Dhruba*, *Ankur*, *Aftab*, for always being there to support. I cannot find words to express my appreciation to my department seniors, *Rajib da*, *Rocktopal da*, *Dipankar da*, *Pratikshya ba*, *Happy ba*, *Prarthana ba*, for guiding and supporting me in every possible way. I express my warmest thanks to all my department colleagues and friends for their excellent company throughout the journey.

I am deeply indebted to **Maa-Deuta** for their endless, unconditional support and love, and it can't be expressed in words how grateful I am to them for all the sacrifices that they have made on my behalf. Their enormous faith in me is the only reason I am able to move forward, no matter how the harsh situation is. I am also grateful to the Almighty for giving me such a wonderful twin sister and brother, *Sangita* and *Chinmoy*, in my life. Their support and love are everything to me. I express my deepest thanks to *Jyotshna* for being there with me in every situation of my life. I solely owe this thesis to them. I feel blessed to have such a supportive family for tremendous love and comfort by my side.

I am always thankful to the **Indian Council of Medical Research (ICMR)**, New Delhi for providing me the project fellowship to carry out my research work without any economic hurdle. Finally, I would like to acknowledge and thank to the entire fraternity of Tezpur University for providing all types of facilities and gifting me these beautiful and memorable times of my life, which I will cherish forever.

*(Diganta Rabha)*

## LIST OF FIGURES

1.1	A basic BF microscope and its components . . . . .	3
1.2	Schematic of different microscopic techniques; (a) BF setup, (b) DF setup, (c) PC setup, and (d) fluorescence imaging setup. . . . .	5
1.3	Smartphone market penetration during the period 2015-2020 in the world and in India. . . . .	8
1.4	The development of different inexpensive microscopic imaging platforms on smartphone; (a) a mobile microscopy by utilizing conventional optical elements, reproduced from [26] with permission from Public Library of Science (PLOS), (b) demonstration of smartphone based fluorescent microscope for detection of water-borne parasites like giardia lamblia cysts, reproduced from [27] with permission from Royal Society of Chemistry, (c) prototype of a video microscopy on smartphone for blood-borne filarial parasites detection, reproduced from [28] with permission from American Association for the Advancement of Science, (d) demonstration of a smartphone microscope using color compound polymer lenses, reproduced from [29] with permission from Nature Publishing Group, and (e) demonstration of a chip scale lens-free microscope using ambient light, reproduced from [30] with permission from Royal Society of Chemistry. . . . .	11

1.5	The development of different spectroscopic platforms on smartphone; (a) the working principle of a smartphone based fluorescence spectroscope for biological assays, reproduced from [60] with permission from American Chemical Society, (b) demonstration of a smartphone based dual wavelength spectroscope based on absorption and fluorescence, reproduced from [58] with permission from Optica Publishing Group, and (c) prototype of the smartphone platform reflectance spectrometer using optical fiber, reproduced from [59] with permission from Optica Publishing Group. . . . .	14
1.6	Demonstration of smartphone based colorimetric detection platforms; (a) optical scheme of the colorimetric analyzer platform for detection of proteins and enzymes, reproduced from [66] with permission from Wiley Online Library, (b) prototype of the smartphone based colorimetric detection of saliva alcohol concentration, reproduced from [67] with permission from Optica Publishing Group, and (c) demonstration of the smartphone based albumin tester in urine, reproduced from [68] with permission from Royal Society of Chemistry. . . . .	15
1.7	Different smartphone based optical sensing platform; (a) an optical biosensor for screening of osteoarthritis, reproduced from [74] with permission from Royal Society of Chemistry, (b) demonstration of a photometric sensor for fluoride level detection in drinking water, reproduced from [75] with permission from American Chemical Society, and (c) turbidity measurement using smartphone, reproduced from [76] with permission from Royal Society of Chemistry. . . . .	17
1.8	Demonstration of smartphone based SPR sensing platforms; (a) an illustration of the SPR sensing device on smartphone for chemosensing, reproduced from [77] with permission from Wiley Online Library, (b) a prototype of the SPR imaging platform for on-site bio-detection, reproduced from [78] with permission from Elsevier, and (c) demonstration of the smartphone based LSPR sensing platform for bio-conjugation detection, reproduced from [79] with permission from Royal Society of Chemistry. . . . .	18

1.9	Smartphone based electrochemical biosensor; (a) demonstration of a rapid electrochemical analyzer using the USB port of a smartphone for quantitative biomolecular detection, reproduced from [87] with permission from Royal Society of Chemistry, (b) potentiometric electrochemical biosensor for PoC applications using audio jack of smartphone, reproduced from [88] with permission from Elsevier, and (c) an smartphone electrochemical sensor for nitrite contamination in water, reproduced from [89] with permission from Elsevier. . . . .	20
1.10	Smartphone platform NFC sensing systems; (a) demonstration of a smartphone based NFC sensing device for gas sensing, reproduced from [90] with permission from National Academy of Sciences, and (b) a smartphone based NFC wound monitoring device, reproduced from [91] with permission from Elsevier. . . . .	21
2.1	Evolution of smartphone sensors from 1992 to 2020 . . . . .	36
2.2	Typical illustration of the development of the smartphone based optical imaging and sensing platforms. . . . .	38
2.3	Schematic optics design of the smartphone camera. . . . .	40
2.4	Schematic representation of the Bayer pattern formation and digital color image recognition by the CMOS sensor of a smartphone. . . . .	40
2.5	Different sensor architectures of modern smartphone camera. (a) Standard Bayer Pattern, (b) 4-cell configuration, and (c) 9-cell configuration. . . . .	41
2.6	Smartphone camera module. (a) Imaging sensors integrated into a phone in different size format, and (b) aspheric compound lens module detach from the phone camera module. . . . .	42
2.7	Experimental setup to measure the RGB spectral response of the smartphone cameras. . . . .	43
2.8	RGB spectral response measurement of (a) Moto G5 Plus, (b) Samsung Galaxy C9 Pro, and (c) AxioCam 105 color camera used in laboratory microscope, respectively. . . . .	43
2.9	Emission spectra of the LED flash of three different variant smartphones used in this thesis work. . . . .	44
2.10	Powering and establishing serial communication with peripheral electronic device using USB-OTG protocol. . . . .	45
2.11	Powering an external LED directly using the phone battery through the USB port. . . . .	45
2.12	Android sensor hub system . . . . .	46
2.13	User interface (UI) of the Android Studio platform with essential components. . . . .	47



3.1	Basic optical configuration of the Köhler illumination setup. . . . .	52
3.2	Realization of a finite-conjugate optical configuration on smartphone. . . . .	54
3.3	Schematics of the proposed smartphone microscopic imaging system. (a) BF illumination, (b) OIDF illumination and (c) TIRDF illumination respectively. The inset in figure (c) shows the guided light from the optical fibers propagates in the lateral direction of the glass slide through the process of total internal reflection. . . . .	55
3.4	Smartphone microscopic device. 3D layout of the smartphone platform imaging system (a) in BF mode, (b) in TIRDF mode, (c) in OIDF mode, and (d) represents the photo image of the designed setup developed for the present work. . . . .	57
3.5	Characterization of the designed tool for evaluation of spatial resolution and FoV. Image of 1951 USAF resolution test target captured by the designed tool under BF illumination (a) without using digital zoom, (b) with 4× digital zoom and (c) after considering 10× digital zoom of the camera app. (d) represents the intensity profiles of the lowest resolving group (group 7 elements 1 - 6). . . . .	58
3.6	Comparison of imaging characteristics by standard optical microscope (10×/0.25NA objective lens) and the designed BF smartphone microscopic setup. (a), (b) 5 μm silica beads. Scale bars are 40 μm. (c), (d) images of Leishman stained blood smear. Scale bars are 100 μm. And (e), (f) unstained HECC cells. Scale bars are 100 μm. . . . .	60
3.7	Applications of smartphone microscopic device for imaging of biological samples under different DF illumination mode. Zoomed-in and cropped images of microbeads captured (a) under OIDF illumination, (c) under TIRDF illumination mode. Scale bars are 50 μm. (b) and (d) represents the intensity profiles of the inset figure in (a) and (c) respectively. Zoomed-in and cropped images of HECC cells under (e) OIDF illumination mode and, (g) TIRDF illumination mode while (f) and (h) show the intensity distribution of the marked region respectively. Scale bars are 100 μm. . . . .	61
3.8	(a) TIRDF imaging of AuNPs using the designed smartphone microscopic system and (b) SEM image of the imaged AuNPs. . . . .	62

3.9	Applications of smartphone microscopic system for imaging of microorganisms. (a), (b) and (c) are the cropped and zoomed-in images of <i>C. albicans</i> acquired using a 10×/0.25NA objective lens, smartphone BF and OIFD imaging mode respectively. Scale bars are 50 μm. (d), (e) and (f) are the images of <i>B. subtilis</i> acquired using a 40×/0.45NA objective lens, smartphone BF and OIFD imaging mode, respectively. Scale bars are 20 μm. . . . .	63
4.1	Two possible microscopic configurations on smartphone. (a) Optical setup of a 3 <i>f</i> imaging system, (b) 4 <i>f</i> optical imaging setup where Fourier-optics is employed to predict the behavior of the system. . . .	70
4.2	Schematic illustration of the working steps of the proposed optical microscope. . . . .	72
4.3	Optimized optical design of the proposed smartphone microscopic imaging system. . . . .	73
4.4	Ray tracing simulation of the optical schemes. (a) Zeemax model of the proposed smartphone microscope, and (b) its MTF at the object plane. . . . .	74
4.5	Smartphone based microscope: (A) the optical layout, (B) the 3D printed prototype installed on an android smartphone device. . . . .	74
4.6	Development of an image processing algorithm to enhance the captured images using Matlab mobile application. . . . .	75
4.7	Images of USAF Resolution test target (A) obtained from standard optical microscope (Carl Zeiss’s Primo Star), (B) with the designed smartphone based optical microscope, (C) its corresponding processed image and (D) intensity profile of the selected region. Scale bars are 10 μm. . . . .	76
4.8	Processed smartphone microscope image of thin blood smear. (A) Smartphone microscope image, (B) corresponding image of a cropped region, (C) corresponding processed image of the cropped region (D) a 40×/0.65 NA traditional microscope image of the blood sample and (E) zoomed version of the same region of interest (ROI) of the traditional microscope. Scale bars are 20 μm. . . . .	78
4.9	Design of the proposed BF and fluorescence microscopic device. (a) Optical layout diagram of the system; (b) 3D design of the system; (c) Fully assembled device in working condition. . . . .	82

4.10	Characterization and performance testing of the microscopic device. (a) Image of a USAF-1951 resolution test target acquired under BF illumination showing spatial resolution of the microscopic system up to Group 7 Element 6 (2.19 $\mu\text{m}$ ); (b) Represents the intensity profile of the horizontal and vertical element bars of Group 7 indicated in dotted red line in fig. (a); (c) 12 images of the PSF in x-y direction of 1 $\mu\text{m}$ microbeads focused from $-z$ direction to $+z$ direction; (d) Reconstructed PSF from (c) in y-z and x-z direction; (e) Measurement of the FWHM of the PSF in lateral direction by taking average values of 10 microbeads within a single FoV. . . . .	86
4.11	Applications of the microscopic device for imaging of biological specimen. (a) Leishman stained blood smear image captured using the proposed device under BF illumination. Scale bar is 20 $\mu\text{m}$ ; (b) BF image of the Acridine orange stained blood; (c) Fluorescence image of the same region in (a); (d) Overlaid image of the BF and fluorescence image of blood shown in fig.(b) and (c). Scale bars are 50 $\mu\text{m}$ ; and (e) a large FoV of the fluorescence image of whole blood. Scale bar is 200 $\mu\text{m}$ . . . . .	88
4.12	Application of the microscopic device for morphological study. (a) Comparison of images of five types of WBCs (Neutrophil, Eosinophil, Basophil, Monocyte, and Lymphocyte), RBCs and platelets acquired using the proposed microscopic system and a laboratory-grade microscope, respectively. (b) Scatter plot of the cellular intensity variance against cell diameter to perform a three-part WBC differential where black color represents the granulocytes, red for monocytes, and blue for lymphocytes. . . . .	89
4.13	Application of the microscopic system for cell concentration counting. (a) 3D layout design of the DIY chamber; (b) Assembled chamber; (c) Fabricated sample loading chamber chip; (d) BF image of diluted RBCs captured under low magnification of the proposed microscopic system. Inset image shows the zoom-in view of the ROI marked in red square. Scale bar is 100 $\mu\text{m}$ ; (e) BF image of diluted WBCs. Inset image shows the zoom-in view of the ROI marked in red square. Scale bar is 200 $\mu\text{m}$ . . . . .	90

4.14	Development of the cell recognition and counting algorithm and the interface of the android application. (a) BF image of cells in a single FoV; (b) Implementation of the Sobel operator to recognize the cell boundaries; (c) Thresholded image; (d) Recognized cells after the removal of noisy artifacts; (e) Cell number estimation using contour detection algorithm; (f) initial interface of the android app; (g) BF image read-in; (h) Output results. . . . .	92
4.15	Comparison of our developed automatic microscopic system counting results with the manual hemocytometer count that traditionally used in clinics. (a) Results for red blood cells counting where red line represents the line of perfect prediction for both the cases. (b) Counting results for white blood cells. A consistent count of both RBCs and WBCs are observed. . . . .	93
5.1	Schematic of the rapid prototyping of the PISM system. . . . .	102
5.2	Design and fabrication of the microscopic system. (a) schematic of a $3f$ optical configuration, (b) $3f$ configuration for the present PISM system comprises of camera phone lens as an objective and the internal lens of the phone as tube lens, (c) Schematic illustration of the optical arrangement of the PISM system with different illumination patterns, (d) 3D rendering of the PISM system and (e) Prototype of the developed microscopic system. . . . .	103
5.3	Circuit diagram for controlling the OLED display module. The OLED display has been connected to the Arduino Nano microcontroller board and established a serial communication to the smartphone app “Serial USB Terminal” via USB-OTG protocol. The USB port of the phone provides a 5V power which is sufficient to power-up the microcontroller board. . . . .	105
5.4	User interface (UI) and working of the open-source app “Serial USB Terminal”. (a) The app on the home screen of the phone, when the Arduino is connected via USB-OTG cable, a pop-up message appears on the screen and (c) the app will open after clicking the ‘OK’ button, (d) connect the device, (e) send data to the microcontroller to display patterns on the OLED screen, (f) disconnect the device when the task is completed. . . . .	106

5.5	Adjusting the illumination NA by varying the diameter of a white circular pattern on the OLED display to match the NA of the objective lens. The dotted red circles represent the objective NA. (a) $NA_{ill} = 0.3NA_{obj}$ , (b) $NA_{ill} = 0.45NA_{obj}$ , (c) $NA_{ill} = 0.8NA_{obj}$ , (d) $NA_{ill} \cong 1.0NA_{obj}$ . . . . .	107
5.6	Characterization of the PISM system. (a) The photograph of the OLED display panel showing a bright circle, employed in the PISM as an illumination source, (b) Spectral response of the OLED display when a white, blue, green, and red circle is displayed on the panel, (c) image of a USAF-1951 resolution test target acquired by the PISM, showing spatial resolution of the microscopic system up to Group 7 Element 6 ( $2.19 \mu\text{m}$ ), (d) represents the intensity profile of the entire Group 7 indicated in red line in fig.(c), (e) and (f) show the BF and DF image of $1 \mu\text{m}$ diameter microbeads captured by the PISM. (f) bottom panel represents the x-y, y-z and x-z views of the point-spread function reconstructed for the imaged micro bead labeled as 2 in the figure and (g) Measurement of full width at half maximum (FWHM) of the PSF in lateral direction by taking average values of 10 microbeads within the FoV of the PISM. . . . .	108
5.7	3D-printed XYZ translational stage of the PISM designed to hold a conventional microscopic slide of dimension $75 \text{ mm} \times 25 \text{ mm} \times 1 \text{ mm}$ . (a), (b) 3D rendering of the stage in two different views. (c) 3D-printed stage loaded with a sample slide. . . . .	110
5.8	Image acquisition by the PISM system under different modes of imaging. Standard $5 \mu\text{m}$ beads sample have been imaged under (a) BF, (b) DF, (c) OI, (d) fluorescence, (e) RI (yellow/blue), and (f) DPC modes of the PISM. One can clearly see the artifacts and debris that present on the microscopic slide in DF and DPC modes that are not visible in any other modes of imaging. Scale bar is $50 \mu\text{m}$ . . . . .	113
5.9	Applications of the PISM for multimodal imaging of unstained and stained HECC cells. Zoomed-in image of the unstained HECC cells under (a) BF, (b) DF, (c) DPC, and (d) fluorescence image of HECC cells stained with acridine orange dye. Scale bar is $50 \mu\text{m}$ . . . . .	114

- 5.10 Differential phase contrast (DPC) imaging capability of the PISM. The above figures explain the computation for generation of DPC images of unstained HECC cells. Consecutive left, right, top and bottom-half circle illumination patterns are displayed on the OLED display panel and the corresponding images ( $I_l$ ,  $I_r$ ,  $I_t$ , and  $I_b$ ) are being recorded respectively. The final phase images are being calculated using the equation (1) along the horizontal axis by taking normalized difference of  $I_l$  and  $I_r$ , and along the vertical axis by taking normalized difference of  $I_t$  and  $I_b$ . These are given in the bottom row of the figure. The inset plots of the DPC images represent the intensity fluctuations of the marked cells along red line. Scale bar is 100  $\mu\text{m}$ . . . . . 115
- 5.11 Applications of the PISM system for imaging in OI and RI modes. Figure (a) shows the BF image captured by the PISM (b) represents the OI mode of image of the sample while (c) and (d) are the RI images with different color combination (blue/yellow and dark/yellow) in the display panel of the OLED. Scale bar is 50  $\mu\text{m}$ . . . . . 116
- 5.12 Performance evaluation of the PISM system while imaging in DPC mode. (a) and (b) show the BF and DPC images of *C. albicans* respectively when the sample is stained with methylene blue. The hyphae formation in *C. albicans* can be clearly seen in DPC mode. Scale bar is 50  $\mu\text{m}$ . . . . . 117
- 5.13 Application of the PISM system for histopathology applications. (a) and (b) represent the images of H & E stained nerve cell tissue captured with the PISM and a laboratory microscope (10 $\times$  objective lens, NA 0.25) respectively under BF mode. The bottom panel in these figures represents the zoomed-in view of the same regions indicated in red squares of (a) and (b). Scale bar is 50  $\mu\text{m}$ . Figure (c) and (d) show the BF images of Leishman stained blood sample acquired by the PISM and the laboratory microscope. Inset figures in (c) and (d) the showed the zoomed-view of the region indicated in squares. Scale bar is 50  $\mu\text{m}$ . 118
- 5.14 Application of the DPC imaging capability of the PISM to histopathology applications by imaging Leishman stained human blood smear. An enlarged view of the red blood cells and white cells indicated in the red box are shown and for comparison to the BF mode of imaging, the same region of interest has been provided on the right hand sight of above figure. Scale bar is 50  $\mu\text{m}$ . . . . . 119

5.15	Polarized mode of imaging with the designed PISM (a) Polarized imaging of starch sample, and (b) tissue paper. The birefringence natures of the test samples are clearly visible with the PISM system. Scale bars are 50 and 100 $\mu\text{m}$ , respectively. . . . .	119
6.1	Schematic illustration of the color-multiplexed illumination scheme and reconstruction of the respective BF, DF and DPC images. . . . .	128
6.2	Schematic representations of the imaging systems. (a) optical layout of the proposed cmSM system, (b) cmLM setup, (c) photograph of the mini OLED display with the displayed color-multiplexed illumination pattern, and (d) spectral emission profile of the OLED display. . . . .	129
6.3	Prototype design and characterization of the cmSM system. (a) 3D rendering of the device, (b) developed device attached to a phone, (c) PSF of 1 $\mu\text{m}$ bead in the lateral direction of x-y, y-z and x-z, (d) BF image of the same bead shown in (c), (e) intensity profiles of 10 beads in lateral direction, and (d) imaging of 1951 USAF test target. The intensity profiles of the line elements of group 7 marked in red line is shown on the right side. . . . .	130
6.4	Graphical representation of the algorithm to reconstruct the multi-contrast BF, DF and DPC images on Matlab mobile platform. . . . .	133
6.5	Imaging of biological unstained specimens with the proposed microscopic systems. (a) HECC cells captured in BF, DF, and DPC (x and y-direction) with cmSM and cmLM respectively, (b) human blood under BF, DF, and DPC (x and y-direction) captured using the both systems respectively. Scale bars are 20 $\mu\text{m}$ . . . . .	134
6.6	Applications of color-multiplexed DPC imaging of the cmSM system for biomedical imaging. (a) One-shot DPC imaging of hyphae formation of <i>C. albicans</i> without staining. Scale bar is 100 $\mu\text{m}$ . (b), (c) and (d) the enlarged view of the ROI indicated in red square in (a), corresponding BF and DF images of the same ROI respectively. Scale bars are 20 $\mu\text{m}$ . (e) DPC image of unstained human blood smear captured using the proposed smartphone multi-contrast system. Scale bar is 100 $\mu\text{m}$ . (f), (g) and (h) are the enlarged regions marked in (e) respectively. Scale bars are 20 $\mu\text{m}$ . . . . .	136

LIST OF TABLES
----------------

2.1	Most commonly used sensors in different variant smartphones. . . . .	37
2.2	Imaging sensor specifications comparison of three different smartphones.	39
4.1	Comparison of the figure of merits between a standard optical microscope and the designed smartphone microscope. . . . .	80
4.2	List of essential components for the construction of the proposed smartphone microscopic system. . . . .	94
5.1	Specifications of the lenses evaluated for use as an objective lens in the PISM. . . . .	104



## *List of abbreviations*

ALS	Ambient Light Sensor
BF	Bright-field
CAD	Computer-aided Design
CFA	Color Filter Array
cmLM	color-multiplexed Laboratory Microscope
CMOS	Complementary Metal-Oxide Semiconductor
cmSM	color-multiplexed Smartphone Microscope
CPU	Central Processing Unit
DF	Dark-field
DIY	Do-it-Yourself
DPC	Differential Phase Contrast
FDM	Fused Deposition Modeling
FI	Fluorescence Imaging
FWHM	Full Width Half Maximum
GPU	Graphics Processing Unit
GUI	Graphical User Interface
HECC	Human Epithelial Cheek Cell
IDE	Integrated Development Environment
IF	Infrared Filter
LED	Light Emitting Diode
LSPR	Localized Surface Plasmon Resonance
MTF	Modulation Transfer Function
NA	Numerical Aperture
NFC	Near-field Communication
OI	Oblique Illumination
OIDF	Oblique Illumination Dark-field
OLED	Organic Light Emitting Diode
OS	Operating System
OTG	On-The-Go
PISM	Programmable Illumination Smartphone Microscopy
PoCT	Point-of-Care Tool
PSF	Point-Spread-Function
RI	Rheinberg Illumination
SLM	Spatial Light Modulator
SNR	Signal-to-Noise Ratio
SPR	Surface Plasmon Resonance

STL	Standard Tessellation Language
TIRDF	Total Internal Reflection Dark-field
USAF	United State Air Force
USB	Universal Serial Bus
WHO	World Health Organization

*Dedicated to Maa-Deuta*  
*(Charu Rabha & Deva Kanta Rabha)*