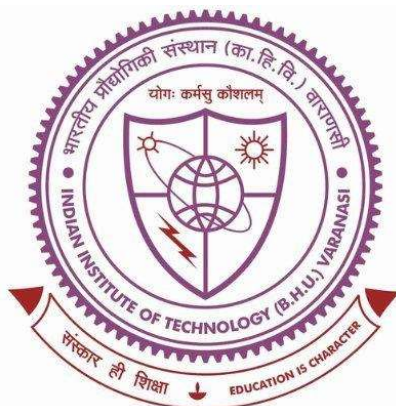


**FABRICATION OF POLYMERIC MICROSTRUCTURES  
HARNESSING THIN-FILM INSTABILITIES AND ITS  
APPLICATION IN POINT-OF-CARE OPTICAL SENSING**



A thesis submitted in partial fulfillment  
for the award of the degree

Doctor of Philosophy

by

Shubham Mishra

**DEPARTMENT OF CHEMICAL ENGINEERING  
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2022



To the one and all.

*LORD RAMA*

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## LIST OF ABBREVIATIONS AND SYMBOLS

<i>PDMS</i>	Poly dimethylsiloxane.
<i>PS</i>	Polystyrene.
<i>MEK</i>	Methyl Ethyl Ketone
<i>OLED</i>	Organic Light Emitting Diode.
<i>n</i>	Refractive Index
<i>T<sub>g</sub></i>	Glass Transition Temperature.
$\mu m$	Micrometer.
<i>NA</i>	Numerical Aperture.
<i>MP</i>	Mega Pixel.
<i>PPI</i>	Pixel Per Inch.
<i>OPD</i>	Optical Path Difference.
<i>a<sub>t</sub></i>	Shift Factor.
<i>T<sub>r</sub></i>	Reference Absolute Temperature.
<i>T</i>	Absolute Temperature.
$\mu$	Absolute Viscosity.
$\rho$	Density.
$\gamma_{sg}$	Surface Energy at solid gas Interphase.
$\gamma_{sl}$	Surface Energy at solid-liquid Interphase.
$\gamma_{lg}$	Surface Energy at liquid gas Interphase.
<i>E<sub>s</sub></i>	Elastic modulus of the substrate.
<i>E<sub>f</sub></i>	Elastic Modulus of film.
$\epsilon_{pre}$	Strain developed in Prestretched film.
$\lambda_0$	The wavelength of Wrinkles in small deformation.

$A_0$	Amplitude of Wrinkles in small deformation.
$h_f$	Thickness of the Film.
$\nu_s$	Poissons Ratio of the substrate.
$\nu_f$	Poissons Ratio of film.
MPa	Mega Pascal.
$\lambda$	Wavelength of Wrinkles in finite deformation.
$A$	Amplitude of Wrinkles in finite deformation.
$\varepsilon_c$	Critical Strain above which buckling/wrinkling occurs.
$\varepsilon_{mem}$	Membrane strain
$\varepsilon_{peak}$	Maximum Strain.
$\sigma$	Stress-induced in the thin film.
$T_s$	Thickness of Substrate.
$T_f$	Thickness of Film placed over Substrate.
$k$	Curvature of the substrate.
$R$	Radius of the Curved Substrate.
SERS	Surface Enhanced Raman Spectroscopy.
CV	Crystal Violet Dye.
UA	Uric Acid Biomarker.
POC	Point-of-Care.
$A/\lambda$	Ratio of Amplitude to the Wavelength of the SERS device Design.
$D_1, D_2, D_3$	Design of Microfluidic Devices.
$J_1, J_2, J_3$	Different Junctions in Microfluidic Device.
$MI$	Mixing Index.
PVP	PolyVinylPyrolidine.

UV	Ultra Violet Spectroscopy.
FTIR	Fourier Transform Infra Red Spectroscopy.
TEM	Transmission Electron Microscopy.
AgNp	Silver Nanoparticle.
DI	De-ionized.
IPA	Iso Propyl Alcohol.
XRD	X-Ray Diffraction Spectroscopy.
$K$	Dean Number.
$D_h$	Hydraulic Diameter.
$R_e$	Reynolds Number.
RSD	Relative Standard Deviation.
EF	Enhancement Factor
LoD	Limit of Detection.
$I_{sers}$	Intensity on SERS substrate.
$I_s$	Intensity in an aqueous sample.
$C_{sers}$	Number of Molecules Probed on SERS sample
$C_s$	Number of Molecules probed in an aqueous sample.
$\sigma_{sers}$	Standard Deviation of a SERS peak.
$d$	Slope of the Calibration Curve.
PDMS Substrate	Crosslinked PDMS substrate



## PREFACE

India's theme of the G-20 presidency is "One Earth, One Family, One future", a vision seen by our honorable Prime Minister Shri Narendra Modi ji. The vision of our prime minister is to provide sustainable growth with, basic lifestyle facilities such as food shelter clothing Education, and health available to all globally. To participate in this noble vision, the scientific community is focused on developing sustainable development programs for all. An important component of sustainable development is the availability of healthcare facilities to all. Development of conventional healthcare infrastructure requires extensive capital and trained manpower, thus an alternate healthcare ecosystem with lesser capital and a semi-skilled labor force is evident. An important component of such an alternate healthcare ecosystem is low-cost equipment, with simple operating protocols that can be used in resource-limited settings by semi-skilled labor. The nascent advances in microfluidic technology and global emphasis on the development of alternate healthcare ecosystems to provide healthcare facilities in resource-limited settings have forced to development of point-of-care testing devices. Point-of-Care testing devices are defined as the equipment, which is used to find significant information for primary diagnosis and prognosis at the point of sample collection. Despite several attempts to develop Point-of-care devices, there are limited aspects of diagnosis where such devices are helpful. The most crucial aspect of point-of-care testing devices is the miniaturization and complex integration of different engineering aspects in one place. Various attempts for developing point-of-care testing devices have focused on a particular aspect of technology development. A wholesome study of complete device development is vital for the development of commercially viable technology.

It was observed that the estimation of the number of specific biological markers in a sample is of crucial importance. Such as red blood cells, platelets, white blood cells, and bacteria in water sources are a few examples that prove to be crucial in remote locations and resource-limited settings. Conventional methods, such as electrochemical, Enzyme-linked immunosorbent assay (ELISA) methods are costly, sophisticated, and more importantly, require sophisticated user profiles. Looking at the increasing smartphone user base and cell phone-based monitoring applications, it is very much viable to develop an optical sensor that can be used by a standard smartphone. Thus optical sensing techniques embedded in microfluidic device setup will be proved to be very robust instrumentation for transportation and operation.

This study attempts to develop an optical sensor based on thin-film microstructures to quantify the number of transparent micro-particles of size more than 3 micro-meter. Thin-film-based optical microstructures in a microfluidic device provide an extremely robust and contamination-free setup for the controlled detection of samples. The detection of particles was demonstrated to be more resolved with better contrast using thin-film optical microstructures. Further, devices and techniques were evolved to use this setup for on-field applications. All the problems encountered in transferring this lab-based technology to on-field application were addressed and solved using a different mechanism of soft material processing and surface interaction techniques. Further, an understanding of microfluidics was utilized to develop a detection setup for biomarkers using the surface-enhanced Raman spectroscopy SERS technique.

An exact understanding of thin-film instabilities for the formation of different structures and harnessing their potential for different optical applications is vital for the development of the cell phone-based optical sensing device. The understanding of problems at different stages of transferring a technology developed in the lab to on-field

applications helps to explore a practical scientific solution. Thus in this research work, we have promulgated the-

- Understanding the thin-film instabilities, dewetting phenomena, and harnessing the potential of dewetted structures as microlenses and their capability to resolve sub-micron objects.
- A framework for embedding such microlenses in microfluidic channels and observation of moving microparticles of 3 micrometers using a standard microscope.
- Image processing of the image captured to identify and estimate the number of particles.
- Understanding the free volume adjustment of polymer chains, to shape them into an optical tool to be used with a cell phone camera to provide an alternative to the standard microscope.
- Diffusion of light through a gradient patterned substrate, to provide a different intensity of diffused light from different points of the substrate.
- Understanding the mixing in a microchannel with different passive micromixers, and utilizing effective mixing for SERS enhancement and detection of the biomarker.

This thesis work is divided into four major chapters. The first chapter deals with the understanding of thin-film instabilities and dewetting of the thin film. The dewetted structures were used as the microlenses to observe the submicron pattern and moving particles in the microchannel. Images of moving particles in the microchannel were subjected to image processing and the number of particles in the sample was estimated. The next two chapters are subsequently developed to transfer this technology from the lab to on-field applications. In the second chapter, we developed a polymer macro lens, used

with the cell phone camera to obtain better magnification and resolution than inbuilt facilities. This development may allow us to obviate the use of a standard microscope in the remote and resource-limited setup. The third part deals with the imaging problem where a substrate with a gradient pattern was developed using thin-film buckling with gradient mechanical stress induced in the substrate. This gradient spacing wrinkled pattern allows us to use the cellphone flash light for sample illumination and imaging in a reflection mode. The first three chapters develop a fully operational device for the on-field application. However, imaging protocols and more sophisticated image processing techniques need to be developed, which is kept for future development. Further, the understanding of microfluidics was used to develop a device to bring analyte and plasmonic nanoparticles into close vicinity to get SERS enhancement. The SERS enhancement in a continuous flow microfluidic device was used to detect the biomarkers and disease monitoring. Finally, a chapter concluding the above works with an assessment of development and future possibilities of development of various technologies is discussed.