

NEAR INFRARED DCS WITH A DIODE LASER FOR THERANOSTIC APPLICATIONS

Submitted in partial fulfillment of the requirements for the award of Bachelor of Technology degree in Biomedical Engineering

By

Anuska Chakravarty(40240004)
Mathangi.B (40240017)



DEPARTMENT OF BIOMEDICAL ENGINEERING
SCHOOL OF BIO AND CHEMICAL ENGINEERING

SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY
(DEEMED TO BE UNIVERSITY)

Accredited with Grade “A++” by NAAC

JEPPIAAR NAGAR, RAJIV GANDHI SALAI, CHENNAI-600119

APRIL 2024



SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY

(DEEMED TO BE UNIVERSITY)

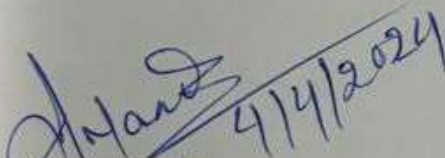
Accredited "A++" Grade by NAAC | 12B Status by UGC | Approved by AICTE

www.sathyabama.ac.in

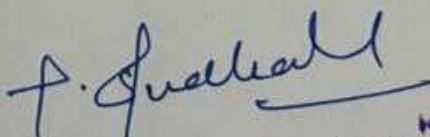
DEPARTMENT OF BIOMEDICAL ENGINEERING

BONAFIDE CERTIFICATE

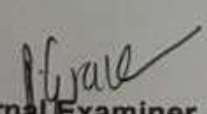
This is to certify that this Project Report is the bonafide work of **Mathangi.B(40240017), Anuska Chakravarty(40240002)** who have done the project work as a team carried out the project entitled "**NEAR INFRARED DCS WITH A DIODE LASER FOR THERANOSTIC APPLICATIONS**" under our supervision from November 2023 to April 2024.

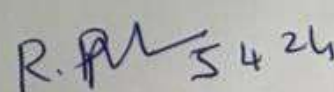

Internal Guide
Dr. Anima Nanda


External Guide
Dr. Uttam Pal


Head of the Department
(Dr. T Sudhakar)
Head of the Department
Department of Biomedical Engineering
Sathyabama Institute of Science & Technology
(Deemed to be University)
Category I University by UGC
Jagadgur Nagar, Rajiv Gandhi Salai,
Chennai - 600 119

Submitted for Vivavoce Examination held on 5 April 2024


Internal Examiner


External Examiner

DECLARATION

We **Anuska Chakravarty (40240004)** and **Mathangi.B (40240017)** hereby declare that the Project Report entitled "**NEAR INFRARED DCS WITH DIODE LASER FOR THERANOSTIC APPLICATIONS**" done by us under the guidance of Dr. Anima Nanda (Internal) and Dr. Uttam Pal (External) at Indian Institute of Information Technology, Design and Manufacturing, Kancheepuram is submitted in partial fulfillment of the requirements for the award of Bachelor of Technology degree in Biomedical Engineering

DATE: 5.04.2024

PLACE: CHENNAI

Anuska Chakravarty

1. Anuska Chakravarty

Mathangi.B

2. Mathangi.B

SIGNATURE OF THE CANDIDATES

ACKNOWLEDGEMENT

We are pleased to acknowledge our sincere thanks to Board of Management of Sathyabama Institute of Science and Technology and Indian Institute of Information Technology, Design and Manufacturing for their kind encouragement in doing this project and for completing it successfully. We are grateful to them.

We convey our thanks to **Dr. T. Sudhakar, Head of the Department**, Dept. of Biomedical Engineering for providing us necessary support during the progressive reviews.

We would like to express our sincere and deep sense of gratitude to our Project Guide **Dr. Anima Nanda** and **Dr.Uttam Pal** for their valuable guidance, suggestions and constant encouragement paved way for the successful completion of our Phase 2 project work.

We wish to express our thanks to all Teaching and Non-teaching staff members of the Department of Biomedical Engineering who were helpful in many ways for the completion of the project.

We would like to express our thanks to our parents for their unwavering support to us during these years.

ABSTRACT

Diffuse Correlation Spectroscopy (DCS) is an emerging technology and a possible non-invasive method for cancer diagnosis and therapy. By directly integrating the light source into the DCS measurement probe, optical approaches are being employed to investigate tissue hemodynamics. The NIR diffuse light in tissue that the DCS analyzes exhibits temporal intensity changes that are responsive to the movements of red blood cells. For measuring tumor blood flow, DCS would be used for new qualities for analysis of the blood perfusion, including mobility, high temporal resolution, noninvasiveness, and reasonably deep penetration. The blood flow perfusion rate and velocity were found using the MATLAB autocorrelation function.

The present proposed study would focus on patients suffering from cancer, thyroid, and Appendicitis with a normal person to get a comparative analysis of the blood perfusion rate among the above patients. The study would also focus on designing and integrating a fibreless embedded laser diode for using the DCS. Before, during, and after cancer treatments, tumor blood flow would be continuously measured using DCS technology. The more number of patients analysis would provide the accuracy of the device which would be a better technique for bedside management of cancer diagnosis and therapy.

Keywords: *diffusion, correlation, spectroscopy, blood flow, cancer theranostic*

TABLE OF CONTENT

CHAPTER	S.NO	CONTENT	PG.NO
CHAPTER 1	1	INTRODUCTION	1
CHAPTER 2	2	LITERATURE SURVEY	6
CHAPTER 3	3	AIM AND SCOPE OF THE PRESENT INVESTIGATION	19
	3.1	Aim	19
	3.2	Scope	19
	3.3	Objective	19
CHAPTER 4	4	MATERIALS AND METHOD	20
	4.1	Near-Infrared Diffuse Correlation Spectroscopy (Nidcs)	20
	4.1.1	Why Near Infrared for DCS?	20
	4.1.2	Materials Required for Near-Infrared Diffuse Correlation Spectroscopy (NIDCS)	20
	4.1.2.1	Artificial Blood	21
	4.1.2.2	Phantom Tissue	21
	4.1.2.3	Instrumentation Design	22
	4.2	Laser Diode And Photodetector	25
	4.2.1	Why Laser is Preferred over LED for DCS?	25
	4.2.2	Photodetector for DCS	27
	4.3	Theranostic Applications Of Dcs	30
	4.3.1	Diabetic patients	30
	4.3.2	Sickle cell anemia	30

CHAPTER	S.NO	CONTENT	PG.NO
	4.3.3	Surface Cancer Detection	30
	4.3.4	Monitoring patients using blood thinners	30
	4.3.5	Cardiac Patients	31
	4.4	Software's Used	34
	4.4.1	Arduino	34
	4.4.2	Origin Pro	42
	4.4.3	MATLAB	48
	4.4.4	EasyEDA	51
	4.5	Working	54
CHAPTER 5	5	RESULTS AND DISCUSSION, PERFORMANCE ANALYSIS	57
	5.1	Result	57
	5.1.1	Final probe of DCS	57
	5.1.2	Final circuit design and PCB of DCS	60
	5.1.3	Theranostic Applications	62
	5.1.4	Software	63
	5.1.4.1	Arduino	63
	5.1.4.2	MATLAB	65
	5.2	DISCUSSION	66
CHAPTER 6	6	SUMMARY AND CONCLUSION REFERENCES	68
			70

LIST OF ABBREVIATIONS

ABBREVIATIONS	DEFINITIONS
---------------	-------------

AIS	Acute Ischemic Stroke
BFI	Blood Flow Index
BMI	Blood Mass Index
CBF	Cerebral Blood Flow
CBFi	Cerebral Blood Flow Index
CrCP	Critical Closure Pressure
CT	Computed Tomography
DCS	Diffuse Correlation Spectroscopy
FDNIRS	Frequency-Domain Near-Infrared Spectroscopy
FPGA	Field-Programmable Gate Array
HCA	Hypothermic Circulatory Arrest
HOB	Head-of-Bed
ICP	Intracranial Pressure
LW-iDCS	Long wavelength Diffuse Correlation Spectroscopy
MC	Monte Carlo
MRI	Magnetic Resonance Imaging
NIRS	Near-Infrared Spectroscopy
PET	Positron Emission Tomography
SDS	Source-Detector Separations
SNR	Signal-to-Noise Ratio
SPAD	Single-Photon Avalanche Diode
TCD	Transcranial Doppler Ultrasound
TD-DCS	Time-Domain Diffuse Correlation Spectroscopy
TD-SCOS	Time (or route length) Resolved Speckle Contrast Optical Spectroscopy

LIST OF FIGURES

S.NO	TITLE	P.NO
4.1	Artificial Blood Components and Standardization of Syringe	22
4.2	DCS probe design Iteration 1	23
4.3	DCS probe design Iteration 2	23
4.4	DCS probe design Iteration 3	24
4.5	DCS probe design Iteration 4	24
4.6	DCS probe design Iteration 5	25
4.7	Laser diode used in DCS probe	27
4.8	Spectral Graph of TEMT6000	28
4.9	Spectral Graph of BPW21R	29
4.10	Spectral Graph of SFH2713	29
4.11	Set up for data collection Iteration 1	31
4.12	Casing Dimension to collect experimental data	32
4.13	Detector and Laser Dimension to collect experimental data	32
4.14	Cuvette Experiment to collect experimental data	33
4.15	Syringe Experiment to collect experimental data	33
4.16	Detector output- Iteration 1	34
4.17	Laser and Detector output- Iteration 2	35
4.18	Laser and Detector output- Iteration 3	36
4.19	Detector output- Iteration 4	37
4.20	Detector output with switch- Iteration 5	38

S.NO	TITLE	P.NO
4.21	Detector output with switch- Iteration 6	39
4.22	Laser output with switch- Iteration 7	40
4.23	Detector output- Iteration 8	40
4.24	Laser with switch output- Iteration 9	41
4.25	Timed output- Iteration 10	41
4.26	Intensity vs time graph for normal temperature in cuvette	42
4.27	Intensity vs time graph for slow speed in syringe	43
4.28	Intensity vs time graph for medium speed in syringe	43
4.29	Intensity vs time graph for fast speed in syringe	44
4.30	Intensity vs time graph for all speed in syringe- Iteration 1	44
4.31	Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 2	45
4.32	Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 3	45
4.33	Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 4	46
4.34	Pearson autocorrelation for Iteration 4	46
4.35	Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 5	47

S.NO	TITLE	P.NO
4.36	Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 5	47
4.37	Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 6	48
4.38	Autocorrelation of intensity vs time - Iteration 1	49
4.39	Autocorrelation of fitted model - Iteration 2	49
4.40	Autocorrelation of intensity vs time - Iteration 3	49
4.41	Autocorrelation of intensity vs time - Iteration 4	50
4.42	Autocorrelation of intensity vs time - Iteration 5	50
4.43	Autocorrelation of intensity vs time - Iteration 6	50
4.44	PCB iteration1	51
4.45	PCB iteration2	52
4.46	PCB iteration3	52
4.47	PCB iteration4	53
4.48	PCB iteration5	53
4.49	PCB iteration6	54
4.50	Workflow of DCS	56

S.NO	TITLE	P.NO
5.1	Final probe design for DCS	58
5.2	Final probe for DCS	58
5.3	Top view of Final probe for DCS	59
5.4	Data acquisition using probe	59
5.5	Final circuit design of DCS	60
5.6	Final PCB design of DCS	61
5.7	Top view of PCB for DCS	61
5.8	Bottom view of PCB for DCS	62
5.9	Motor Experiment to collect experimental data	63
5.10	Collection tub for Motor Experiment to collect experimental data	63
5.11	Final Arduino code for DCS	64
5.12	Final autocorrelation of blood flow	65

LIST OF TABLES

S.NO	TITLE	P.NO
1.1	Experimented detectors comparative chart	28

CHAPTER-1

INTRODUCTION

1.1 WHAT IS DIFFUSE CORRELATION SPECTROSCOPY

As it nourishes and supports the tissues in our body, blood, the life-giving fluid that flows through our veins, is the very essence of vitality. The accurate measurement of blood flow takes centre stage in the search to assess tissue health, viability, and the presence of different disease states. Diffuse Correlation Spectroscopy (DCS), among the variety of techniques available, has emerged as a rising star in recent years, winning praise for its noninvasive and precise method of determining blood flow that even outperforms existing gold-standard procedures. Over the past ten years, DCS has made considerable progress by using near-infrared light to unravel the riddles of tissue perfusion. It extends the dynamic light scattering approach to analyse multiply scattered light within tissues using a novel methodology that depends on the monitoring of variations in the intensity of diffusely scattered coherent light (Carp S.A et al ,2010). The uses of DCS are extensive, with research examining vascular function and microvascular reperfusion in addition to studying the impact of exercise on blood flow dynamics. DCS must first undergo thorough technical validation (Bartlett MF et al, 2020), before it can become a mainstay in clinical and exercise physiology settings. The rise in interest in diffuse correlation spectroscopy (DCS), a powerful blood flow measurement technique, can be ascribed to its many advantages. Notably, DCS stands out for its appropriateness for bedside monitoring, its non-invasiveness, its exceptional sensitivity to changes in blood flow, its capacity for deep tissue penetration, and its choices for real-time monitoring (Xie et al, 2020). Its operation depends on the detection of variations in laser speckle intensity, which are a direct result of red blood cell movement inside the tissue. The blood flow index (BFI), a statistic that measures the blood flow velocity inside the microvasculature, is another wealth of data that DCS provides. Without a doubt, DCS has shown its use in both clinical and preclinical trials, acting as a trustworthy

instrument for tracking blood flow in a variety of tissues and organs (Cortese et al, 2021) Diffuse Correlation Spectroscopy has become a potent and non-invasive technology as a result of the quest to understand the complexities of blood flow. It is positioned as a potential technique for expanding our knowledge of blood flow dynamics in both clinical and research settings due to its wide range of applications and many benefits. DCS is prepared to continue revealing the mysteries of this crucial physiological mechanism as technology advances. With its adaptability and long list of benefits, DCS is well-positioned to advance both clinical practise and scientific research while also expanding our understanding of blood flow dynamics. Moving on, we continue our exploration of the world of blood flow under the enlightening influence of DCS.

1.2 MICROVASCULAR BLOOD FLOW MOMENT'S VITAL FUNCTION

It is necessary to measure microvascular blood flow because it provides important information about the effective delivery of nutrients and oxygen to tissues. It also helps with the elimination of metabolic waste products, sustaining the general health of organs and tissues. Additionally, abnormal blood flow is frequently associated with serious disorders, highlighting the importance of ongoing monitoring to identify and manage any health concerns as soon as they arise(Zilpelwar, S. et al 2022).Although current technologies like MRI, PET, and CT scans offer insightful data on microvascular blood flow, they are not without their limitations. These procedures can be expensive, uncomfortable, and require radiation exposure. These drawbacks highlight the urgent need for a non-invasive, secure, and affordable bedside blood flow monitoring system. Diffuse Correlation Spectroscopy (DCS) stands out as a viable tool in this area. As a result of addressing these issues, DCS is a useful tool in healthcare settings (Zilpelwar, S. et al 2022). It provides a practical way for measuring microvascular blood flow at the bedside.

1.3 CHALLENGES AND FUTURE PROSPECTS

1.3.1 Overcoming Critical Closing Pressure Measurement Limitations

Diffuse Correlation Spectroscopy (DCS), a viable substitute for Transcranial Doppler Ultrasound (TCD) for measuring intracranial pressure (ICP), is developing as a promising method to circumvent constraints in the detection of critical closure pressure (CrCP). ICP and vascular wall tension both have an impact on CrCP, making it a crucial ICP indicator. In this situation, DCS exhibits significant measurement accuracy potential (Carp S.A et al,2021) But it's important to understand that traditional DCS measurements have their own set of limitations, especially when working with deep tissues, clinical trials, or animal models. The assumption that tissue optical characteristics, like as absorption (μ_a) and reduced scattering (μ_s), are consistent across different tissues presents a considerable obstacle. In reality, this assumption can reduce the accuracy of blood flow measurements (Zhao M et al, 2021) Future possibilities are centred on the creation and adoption of novel strategies in order to solve these constraints and improve DCS's capability to measure CrCP. One method being investigated is Short Source-Detector Separation (SDS) DCS, which has the potential to improve the accuracy of blood flow measurements, particularly in deep tissue settings. Further enhancing the accuracy and usability of DCS in human clinical trials and animal models is the inclusion of real-time monitoring of tissue optical characteristics potential (Carp S.A et al,2021) and (Zhao M et al, 2021). These developments have the potential to significantly improve intracranial pressure dynamics research as well as the measurement of CrCP.

1.3.2 Advancements in Paediatric Blood Flow Monitoring

Paediatric blood flow monitoring has advanced thanks to diffuse correlation spectroscopy (DCS), which has a distinct advantage when it comes to determining how much blood is flowing through infants and newborns. In comparison to adult tissues, their extracerebral tissues, including as the scalp and skull, are noticeably thinner. It is difficult to provide precise and trustworthy measurements in this group due to

problems with sensitivity, signal-to-noise ratio, and accuracy (Wu KC et al, 2021) Researchers have been investigating a variety of cutting-edge methodologies and technologies to solve these issues. These include pathlength-resolved approaches, parallelized speckle detection, acousto-optic modulation, and interferometric detection. Each of these methods tries to improve blood flow measures' sensitivity and accuracy, making them more appropriate for use in paediatric and neonatal patients. The use of a long-wavelength technique is an important factor to take into account in this situation. Some of the disadvantages of paediatric blood flow monitoring are thought to be especially well-mitigated by this strategy (Wu KC et al, 2021). By utilising these advancements, medical personnel may assess blood flow in young kids more precisely and safely, which contributes to better paediatric care and medical knowledge.

1.3.3. Enhancing Temporal Resolution in DCS

When the aim is to acquire higher temporal resolution, diffuse correlation spectroscopy (DCS) finds several constraints related to its sensitivity and responsiveness to fluctuations in tissue properties. This constraint is especially important when studying hemodynamic responses, administering photodynamic treatment, monitoring blood flow in cancer patients, or evaluating changes in muscle flow (Jason Sutin et al,2016)Time-domain diffuse correlation spectroscopy (TD-DCS) has become a significant tool for addressing these issues and improving the temporal resolution of DCS. The innovative method used by TD-DCS lessens the problems brought on by photon availability. Integrated Single-Photon Avalanche Diode (SPAD) arrays, which allow for extremely parallel single-photon detection, are used to accomplish this (Pagliazzi M. et al, 2021) In addition to improving DCS's sensitivity and accuracy, the incorporation of SPAD arrays creates new opportunities for real-time monitoring in scenarios where temporal resolution is critical. Consequently, TD-DCS has the potential to transform research in the areas of hemodynamics, photodynamic treatment, cancer blood flow assessment, and the evaluation of muscle flow dynamics by giving scientists a more effective instrument for in-depth studies in these areas (Jason Sutin et al,2016), (Pagliazzi M. et al, 2021) and (P. Zhang et al,

2019).

1.4 THERANOSTIC APPLICATIONS OF DIFFUSE CORRELATION SPECTROSCOPY (DCS)

Diffuse correlation spectroscopy (DCS) holds immense promise across various medical domains, offering a range of theranostic benefits. Firstly, in ischemic stroke management, DCS serves as a vital tool for evaluating cases characterized by restricted blood flow to specific brain regions. Healthcare providers leverage DCS to gauge the severity of blockages and assess the effectiveness of interventions such as thrombolytic therapy or mechanical thrombectomy. Secondly, DCS facilitates the evaluation of vascular diseases like atherosclerosis by analyzing blood flow dynamics within affected arteries. This capability aids in treatment decision-making and enables the monitoring of disease progression or regression. Thirdly, DCS plays a crucial role in assessing brain function, particularly in studying cerebral autoregulation, which ensures stable blood flow despite fluctuations in blood pressure. In neurocritical care settings, leveraging DCS to understand and optimize cerebral perfusion helps prevent secondary brain injury. Finally, DCS provides invaluable insights into monitoring blood perfusion in tissue flaps used in reconstructive surgery or transplanted organs. Surgeons can utilize DCS to ensure adequate tissue viability, thereby reducing risks such as flap necrosis or transplant rejection. Overall, DCS emerges as a versatile and indispensable tool with applications spanning from stroke management to vascular disease evaluation and neurocritical care, as well as in optimizing surgical outcomes in tissue flaps and transplantations.

CHAPTER-2

LITERATURE SURVEY

Vishwanath K and Zanfardino S, 2019

This study has unveiled a non-invasive optical method called diffuse correlation spectroscopy (DCS) evaluates tissue perfusion by examining scattered light. Traditional DCS measures are only useful in situations like tiny animal models or endoscopic clinical trials since they rely on large source-detector separations (SDS). In order to address these issues and increase its adaptability, this work investigates short SDS DCS. Traditional DCS measurements, which have their roots in photon diffusion theory, are difficult to perform in environments with short SDS, which casts question on their accuracy. This study uses Monte Carlo (MC) simulations to offer numerical solutions for photon correlation transport and test the correctness of the theoretical model, particularly for short SDS, in order to resolve these constraints. In order to compare theoretical analysis with actual observations, it also incorporates experimental data from optical phantoms with embedded flow channels. The study demonstrates that, even with short SDS, the theoretical DCS model is capable of accurately capturing relative flow variations. By include MC simulations, DCS becomes more useful in scenarios where SDS restrictions exist and more flexible applications for relative and absolute flow measurement are made possible. This study emphasises how critical it is to modify DCS for short SDS situations, including endoscopic and small animal models, in order to maximise its potential for precise flow measurement beyond conventional theoretical presumptions in a range of clinical and research settings.

Jason Sutin, et al, 2016

The research has presented the Regulation of cerebral blood flow (CBF) is essential for maintaining brain function because it makes sure the brain gets enough oxygen and glucose. The non-invasive CBF measurement method diffuse correlation spectroscopy (DCS) shows promise, however measuring cerebral

blood flow index (CBFi) is difficult due to its limited sensitivity and susceptibility to changes in tissue properties. In order to overcome these drawbacks, time-domain diffuse correlation spectroscopy (TD-DCS), a brand-new technique, is presented in this study. Traditional DCS has drawbacks, such as a lack of sensitivity to changes in the brain and unpredictability brought on by tissue characteristics. Although it has a higher sensitivity to the brain than near-infrared spectroscopy (NIRS), it cannot completely ignore contributions from extracranial layers, and changes in tissue-reduced scattering coefficient ('s) impair CBFi accuracy. TD-DCS switches from the continuous wave to the time-domain technique, combining photon time of flight with DCS fluctuations using a long coherence pulsed laser. For substantial advancements, this approach makes use of time-resolved reflectance spectroscopy. The possibilities of TD-DCS in neuro-intensive care and its potential for more precise CBF evaluation seem promising. It is a useful tool for managing and comprehending clinical CBF.

Buckley, E.M. et al, 2019

This study makes a significant addition to the area of neonatal medicine by exploring the use of diffuse correlation spectroscopy (DCS) to measure cerebral blood flow (CBF) in preterm newborns. The study provides a thorough review of various diagnostic approaches in this situation by using DCS for CBF measurement as well as comparing its results with those acquired from transcranial Doppler ultrasonography (TCD). This study's investigation of the effect of a little posture adjustment on CBF, a topic with major clinical importance, is fascinating. In conclusion, this research introduces DCS as a viable technique for CBF evaluation, serving as a critical advancement in improving the care and diagnostic capacities for preterm newborns. The comparison with TCD strengthens DCS's legitimacy, and the findings on postural shifts have real-world applications for newborn unit healthcare professionals. This work makes a substantial contribution to the development of newborn healthcare procedures and emphasises the significance of reliable diagnostic tools in enhancing preterm infants' outcomes and general wellbeing.

Carp, S.A et al, 2010

This paper presents a thorough investigation of diffuse correlation spectroscopy's (DCS) present state and potential in the field of neurophotonics. With an emphasis on the signal-to-noise ratio (SNR) restrictions and the difficulties involved with interpreting absolute blood flow numbers when using this approach, the authors provide a thorough examination of the difficulties and restrictions connected with DCS. This review highlights the promise of DCS in a variety of applications while noting its complexity. The relevance of depth sensitivity and SNR across a broad spectrum of potential DCS applications is one major subject that emerges from this work. The importance of these parameters is emphasised by the authors, not only in terms of monitoring cerebral blood flow (CBF), but also in the larger context of neurophotonics, where it is crucial to get accurate and trustworthy data. For anyone working in the subject of neurophotonics, both researchers and practitioners, this publication is an invaluable resource. It navigates through the difficulties and intricacies of DCS, emphasising the significance of carefully taking SNR and depth sensitivity into account. It also highlights the potential benefits of operating at long wavelengths and having access to powerful sources, providing a roadmap for DCS's continuing advancement and use in the dynamic field of neurophotonics.

Cortese L et al 2021,

The investigation has brought forth the evaluation of hemodynamics and oxygen metabolism in muscle tissue using diffuse optics as a useful tool is the focus of this research. By offering a variety of information that explains differences in measurements across various muscle sites, technologies used, and data processing algorithms used, it considerably advances our understanding of muscle physiology. These results highlight the intricate interaction of factors that affect measurements and the diverse character of muscle physiology. Notably, the study calls attention to measurement disparities between the sexes and suggests a possible link to variances in body mass index (BMI). This finding emphasises the need of taking into account individual traits and physiological subtleties when using diffuse optics to examine muscle tissue, leading

to a more thorough comprehension of these processes. In conclusion, this study is an important source for learning about diffuse optics and muscle physiology. It underlines the need of taking into account variables like sex and BMI in the analysis as well as the variations in data across different parameters. The findings are crucial for further study and applications in the area of muscle physiology because of the emphasis on measurement accuracy, which increases the findings' trustworthiness .

Durduran T et al, 2017

This work represents a significant development in the area of neuroimaging through the convergence of diffuse optical and correlation spectroscopies. This research pioneers the use of simultaneous measurements of oxyhemoglobin and deoxyhemoglobin concentrations and blood flow in the adult human brain during sensorimotor stimulation. The capacity to estimate the relative cerebral metabolic rate of oxygen in the human brain is a ground-breaking finding of this research, marking a breakthrough in the field of all-optical techniques. This study's effective demonstration of the viability of noninvasive optical detection of blood flow through the adult brain's skull makes it all the more impressive. This achievement provides a promising substitute for invasive treatments and opens the door to a variety of therapeutic applications by measuring brain activity and oxygen metabolism. In conclusion, this discovery has enormous potential for the fields of clinical neurology and neuroimaging. It not only presents a novel approach but also paves the path for more clinical investigation of non-invasive, all-optical procedures. With multiple implications in diagnosis, therapy, and research, this discovery has the potential to fundamentally alter how we examine and comprehend how the brain functions and metabolism.

Gagnon L et al, 2008

This investigation explores the use of diffuse correlation spectroscopy (DCS) in multi-layered geometries and provides a fresh viewpoint on its potential. In terms of how well a homogeneous model and a two-layered model recover flow changes, the research gives a quantitative comparison. The work uses simulations

based on MRI anatomical data from a genuine human head to show how well the two-layered model can discern between changes in flow occurring in the brain and the surface layers. Additionally, the research offers strong support for the claim that the two-layered model produces estimates of flow changes that are more accurate than those produced by the homogenous model. The usefulness of the two-layered

analytical model is furthered by the use of experimental observations using a two-layered dynamical phantom. These tests confirm the model's capability to distinguish between flow increases inside each individual layer. Overall, this study shows the potential of this method for more accurate and subtle flow measurements in intricate biological systems and marks a significant improvement in the field of DCS, especially in the context of multi-layered structures.

Gregori-Pla et al, 2019

The current study has offered a specificity in the setting of acute ischemic stroke (AIS), this study explores the dynamics of the cortical microvascular cerebral blood flow response (CBF) in relation to variations in head-of-bed (HOB) positions. The diffuse correlation spectroscopy (DCS) method is used in this work to examine these CBF responses. While other studies have demonstrated variations in the CBF response in AIS, this study intends to investigate the connection between these relative CBF changes and contemporaneous changes in systemic blood pressure. Understanding this link is crucial since blood pressure has a substantial impact on cerebral blood flow. The study's findings show that following increased posture, CBF in healthy controls reverted to baseline levels for supine positioning, however it did not in patients with AIS and ICA stenosis, showing abnormalities in autoregulation. The study also showed that MAP did not recover to baseline values in AIS patients, although it did in ICA stenosis patients and controls. This finding suggests that CBF and MAP may be related in cases of cerebrovascular diseases, particularly in the context of AIS. The work clarifies the relationships between ipsilateral CBF and MAP and suggests that small changes in the location of the HOB may impair cerebral autoregulation in those with cerebrovascular diseases. Although this research offers insightful information,

more research is required to fully comprehend and characterise this occurrence, which may have consequences for the therapeutic care of individuals with AIS and associated diseases.

Liu et al, 2021

To identify blood flow and functional dynamics inside tissues, diffuse correlation spectroscopy (DCS), a well-established method, is used to track quick changes in the scattering of coherent light. Conventional DCS systems, however, have its limitations, especially when trying to explore deeper tissue layers. Due to this restriction, measurement windows are often longer, at least one second. Using a high-sensitivity DCS system with 1024 parallel detection channels inside of a single-photon avalanche diode array, a novel method is introduced in this paper. With an astonishing sampling rate of up to 33 Hz, this cutting-edge device enables the detection of millimeter-scale disturbances buried up to 1 centimetre deep within tissue-imitating phantoms. The study also shows that this highly parallelized DCS approach may identify physiological changes brought on by behavioural changes and can reliably measure the human pulse, especially when monitoring the prefrontal cortex. This sophisticated DCS technology opens the door for a new field of studies where high-speed monitoring and thorough analysis of tissue dynamics are essential. This is done by greatly improving both detection sensitivity and speed. This discovery has the potential to fundamentally alter how we think about tissue behaviour and has significant uses for both clinical practise and medical research.

M. M. Wu et al, 2021

This study is significant because it addresses a significant obstacle to cerebral blood flow (CBF) measurement using diffuse correlation spectroscopy (DCS) in clinical settings. This problem results from systemic physiology contaminating DCS readings, which reduces the use of DCS for neuromonitoring. In order to reduce extracerebral flow cross-talk while assessing cerebral blood flow index (CBFi), the study investigates the use of configurable, multi-layer Monte Carlo-based (MC) light transport models. According to the study's findings, optimised

MC models, which are driven by intrinsic criteria and a pressure modulation manoeuvre, are superior to the conventional analytical fitting method, which assumes a homogeneous medium, at differentiating CBFi changes from the impact of scalp blood flow. Additionally, three-layer models perform better than two-layer models, and both slab and curved geometries provide comparable outcomes, while curved geometries more closely mimic physiological layer thicknesses. This study emphasises the potential use of three-layer, customizable MC models for distinguishing variations in scalp and brain blood flow. It also emphasises how crucial pressure modulation and correct physiological parameter assessment are in aiding the selection of suitable layer thicknesses in MC models. The development of DCS's therapeutic use in monitoring cerebral blood flow and comprehending its dynamics in response to physiological changes depends heavily on these results.

Maria AF et al, 2023

The manuscript has delivered an optical technique called diffuse correlation spectroscopy (DCS) is used to measure blood flow within tissues. Due to its poor signal-to-noise ratio (SNR) and cerebral sensitivity, it has been difficult to use it to measure cerebral hemodynamics, especially in adults. In this work, a new method known as long wavelength, interferometric DCS (LW-iDCS), which overcomes these issues and improves both cerebral sensitivity and SNR, is introduced. The work highlights a roughly 5-fold improvement in SNR in the recorded blood flow signals in human participants and directly compares LW-iDCS with long wavelength DCS that makes use of superconducting nanowire single photon detectors. The study also shows that blood flow measurements obtained from LW-DCS and LW-iDCS are equivalent, demonstrating the validity of the novel method. It also demonstrates the viability of LW-iDCS measurements with a source-detector separation of 3.5 cm and a high data recording rate of 100 Hz. This performance improvement has the potential to open up new and creative uses for diffuse correlation spectroscopy in the realm of physiological and medical research by enabling reliable measurements

of brain hemodynamics.

Pagliazzi M. et al, 2021

This article has outlined a special source-detector spacing of just 2.85 mm, a novel technique called Time (or route length) resolved speckle contrast optical spectroscopy (TD-SCOS) has been created. Studies carried out in vivo on an adult subject's forearm muscle have proven this technique. These studies' results demonstrate the major benefits of using longer photon route lengths since they result in greater hyperemic blood flow alterations and a faster return to baseline. In fact, as compared to conventional speckle contrast optical spectroscopy (SCOS) without temporal resolution, TD-SCOS exhibits a two-fold acceleration in the return to baseline. This implies that TD-SCOS provides improved sensitivity to deeper muscle tissue, which is an important advantage in non-invasive blood flow monitoring. In contrast to time-resolved diffuse correlation spectroscopy (DSCS) devices, which rely on highly specialised and expensive technology, TD-SCOS may open the way for the creation of simpler and more affordable detector arrays. Because of this, TD-SCOS has the potential to increase the functionality of device made for continuous, non-invasive monitoring of deep tissue blood flow while also lowering their total cost. The ability to more easily and affordably measure blood flow in deep tissues as well as better diagnostic and monitoring capabilities might have significant effects on medical and physiological research.

Robinson MB et al,2023

This study has set forth an optical method called diffuse correlation spectroscopy (DCS) is used to measure blood flow within tissues. Although previous DCS implementations have had difficulties with signal-to-noise ratio (SNR) and sensitivity when measuring cerebral blood flow in adults, it has showed a lot of promise for the research of cerebral hemodynamics. The long wavelength, interferometric DCS (LW-iDCS) method is a unique one that this study introduces. It makes use of a number of advances to improve SNR and cerebral sensitivity. Additionally, the study supports the comparability of blood flow

information derived from LW-DCS and LW-iDCS, demonstrating the validity of the novel strategy. With a source-detector separation of 3.5 cm, it is noteworthy that LW-iDCS is demonstrated to be practical for measurements at a high data acquisition rate of 100 Hz. The robust and accurate assessment of cerebral hemodynamics may be made possible by this significant performance increase. It may also promote diffuse correlation spectroscopy's usage in physiological and medical research for the non-invasive monitoring of blood flow in the brain. This opens the door to new uses for the technique.

Robinson M. B. et al, 2020

This research has brought to light an optical method called diffuse correlation spectroscopy (DCS) is used to describe blood flow in tissue, with an emphasis on brain hemodynamics. However, when it comes to accurate measurements of cerebral blood flow in adults, standard DCS implementations have a poor signal-to-noise ratio (SNR) and limited sensitivity. In order to improve cerebral sensitivity and SNR, we introduce long wavelength, interferometric DCS (LW-iDCS) in this study. This technique uses a longer illumination wavelength (1064 nm), multi-speckle analysis, and interferometric detection. LW-iDCS exhibits a 5 increase in SNR over long wavelength DCS when measuring human subjects' blood flow. This improvement is directly compared to long wavelength DCS employing superconducting nanowire single photon detectors. They further demonstrate that blood flow data obtained with LW-DCS and LW-iDCS are equivalent, emphasising the viability of LW-iDCS measurements at 100 Hz and 3.5 cm source-detector separation. The robust assessment of brain hemodynamics might be made possible by this performance improvement, which could also lead to new uses for diffuse correlation spectroscopy.

Wu J et al, 2022

This study questioned the widespread belief that the human head is homogeneous by investigating the viability of concurrently extracting skull thickness and flow in the cortical layer using diffuse correlation spectroscopy (DCS). The brain cortex was assumed to be the bottom layer with semi-infinite geometry, and a

two-layer analytical model with the skull as the top layer with limited thickness was confirmed. While maintaining other parameters constant, this model well fit the top layer's thickness and the bottom layer's flow. Custom-made two-layer phantoms of the skull and brain were utilised to verify its accuracy, and the findings revealed that the fitted top layer thickness had a good correlation with the predicted values. Furthermore, the traditional one-layer model frequently underestimated flow as the top layer thickness grew, but the two-layer model reliably calculated flow throughout a range of top layer thicknesses. The source-detector distance in respect to the first layer thickness determined how well the first layer thickness and flow were estimated. Additionally, the fitted thickness and flow were only marginally affected by errors in each layer's optical characteristics. This research shows the possibility for a reliable and affordable method to evaluate cerebral blood flow and skull thickness concurrently at the patient's bedside, providing important information for those who have brain difficulties including traumatic brain injuries.

Wu KC et al, 2021

This study tackles the crucial problem of ongoing cerebral blood flow (CBF) and intracranial pressure (ICP) monitoring in patients receiving neurointensive care who are at risk for subsequent brain damage. At the moment, intrusive techniques are mostly employed for this. The study investigates if diffuse correlation spectroscopy (DCS), a non-invasive near-infrared method, may serve as a reliable substitute. The research shows that DCS can be a useful and noninvasive method of continuously monitoring CrCP by optimising DCS hardware and algorithms and validating its estimates of cerebral blood flow index (CBFi) and critical closing pressure (CrCP) in ischemic stroke patients against conventional transcranial Doppler ultrasound (TCD) measurements. For patient care and results in crucial neurointensive care settings, this has important ramifications.

Jinbin et al, 2020

The current research has showcased the non-invasiveness, high sensitivity, and deep tissue penetration, near-infrared (NIR) diffusion correlation spectroscopy

(DCS) has become a potential method for therapeutically monitoring blood flow in deep tissues. Accelerating data capture is a difficult task, though, and real-time imaging is still a work in progress. We provide a 10-detection-channel DCS system in this work that is intended for dynamic blood flow index topography. We obtain a remarkable imaging speed of up to 1 frame per second by utilising a multi-channel multi-delay hardware correlator, the enhanced NIR sensitivity of a single photon avalanche photodiode detector, and the effectiveness of a prior-guided fitting approach for blood flow index extraction. Prior to conducting in-vivo tests on a human arm, the system's flow-rate resolution, measurement fidelity, and image depth were evaluated using phantom experiments. These tests proved the methodology's capacity to properly record changes in blood flow in terms of their forms and locations. Real-time clinical imaging and deep tissue blood flow monitoring have the potential to benefit from this development.

Zavriyev AI et al,2021

This research has unveiled that In order to lower the related fatality rates, real-time noninvasive monitoring of cerebral blood flow (CBF) during cardiac operations with hypothermic circulatory arrest (HCA) was studied in this work. In this study, 12 patients undergoing cardiac surgery with HCA had their haemoglobin oxygen saturation (SO₂), cerebral blood flow (CBFi), and an index of cerebral metabolic rate of oxygen (CMRO_{2i}) simultaneously assessed using diffuse correlation spectroscopy (DCS) and frequency-domain near-infrared spectroscopy (FDNIRS). The results showed that antegrade cerebral perfusion preserved CBFi and SO₂ levels while retrograde cerebral perfusion during HCA resulted in limited blood flow to the cerebral cortex and minor CBFi declines. This non-invasive method employing FDNIRS-DCS is a useful tool for enhancing brain defence mechanisms during HCA.

Zhoa M et al,2022

This study has set forth an Interferometric Diffuse Optical Spectroscopy (iDOS), a new technology being developed to enable non-invasive and continuous blood flow monitoring in crucial clinical scenarios, combines interferometric near-

infrared spectroscopy (iNIRS) and interferometric diffusing wave spectroscopy (iDWS). Despite using near-infrared light to examine deep tissue physiology, diffuse optical spectroscopy (DOS) has encountered issues with superficial tissue interference and quantification accuracy. Continuous wave near-infrared spectroscopy also has difficulties in clinical applications due to limited depth specificity and inaccurate tissue oxygenation measurements, while being cost-effective. These difficulties are solved by Dr. Srinivasan's paradigm-shifting technique, iDOS, which combines iNIRS and iDWS for parallelization and time-of-flight resolution. With potential advantages in a range of therapeutic contexts, the research seeks to validate and advance the usage of iDOS.

Della Rocca FMet al, 2023

This research has outlined that for noninvasive cerebral blood flow monitoring, diffuse correlation spectroscopy (DCS), which principally relies on the autocorrelation function (ACF) of scattered light, is necessary. Multispeckle DCS, a new development, uses single-photon avalanche diode (SPAD) cameras to increase sensitivity. However, due to constrained data transfer speeds and the requirement for specialised high-performance processing to compute multiple autocorrelators (ACs) for real-time measurements, the quick data creation from modern SPAD cameras presents difficulties. The field-programmable gate array (FPGA) of a large-pixel-count SPAD camera is equipped with a data compression strategy that is introduced in this work, democratising SPAD cameras and easing the integration of multispeckle DCS systems. We show a 192 by 128 SPAD array with 128 integrated linear ACs on an FPGA, allowing for the real-time computation of 12,288 ACFs. In comparison to both single-pixel DCS and state-of-the-art multispeckle DCS, the results show a remarkable signal-to-noise ratio (SNR) gain, considerably enhancing the sensitivity and usefulness of multispeckle DCS instruments.

Alexander I et al, 2019

The research has delivered that in adult cardiac procedures requiring hypothermic circulatory arrest (HCA), the real-time noninvasive monitoring of cerebral blood flow (CBF) during surgery is crucial in lowering fatality rates. In order to measure CBF during

various brain protection approaches, this work investigates the use of diffuse correlation spectroscopy (DCS), a noninvasive optical technology coupled with frequency-domain near-infrared spectroscopy (FDNIRS). In this study, 12 patients having cardiac surgery with HCA had their haemoglobin oxygen saturation (SO₂), a measure of cerebral blood flow (CBFi), and their cerebral metabolic rate of oxygen (CMRO_{2i}) simultaneously measured. The results indicate that the combination of FDNIRS and DCS is a helpful technique for enhancing cerebral protection in HCA operations because it can accurately identify changes in CBFi, SO₂, and CMRO_{2i} during surgeries.

CHAPTER-3

AIM AND SCOPE

3.1 AIM

The objective of our project is to employ real-time, non-invasive monitoring techniques to assess blood perfusion rates in individuals afflicted with surface-level cancer, thyroid disorders, and appendicitis, while also including a healthy control group for comparative analysis. The findings from this study have the potential to enhance our comprehension and treatment strategies for these medical conditions.

3.2 OBJECTIVE

- To study the Diffuse Correlation Spectroscopy (DCS) among all the patients
- To study the optical technique for investigating tissue haemodynamic
- To design the probe using MATLAB code of autocorrelation function
- To integrate the light source for the measurement of the probe in DCS
- To perform a patient analysis on surface level analysis like cancer, thyroid patients, appendicitis patients with control
- To assess the blood perfusion rate among all the groups
- Compare and Compile the analysis and conclude the study results.

3.3 SCOPE

This project offers a novel approach to addressing critical issues in the field of cancer diagnostics and therapeutics, particularly concerning the challenges associated with existing techniques. The application of this project has the potential to significantly advance the field of medical diagnostics, offering a safer, more patient-friendly and cost-effective approach to monitoring and managing various health conditions, ultimately benefiting both patients and healthcare professionals.

CHAPTER-4

MATERIALS AND METHODS

4.1 NEAR-INFRARED DIFFUSE CORRELATION SPECTROSCOPY (NIDCS)

4.1.1 Why Near Infrared for DCS?

Near-infrared (NIR) light, spanning wavelengths from around 700 to 1000 nanometers, serves as the optimal choice for Diffuse Correlation Spectroscopy (DCS) due to a multitude of advantages. Firstly, its ability to deeply penetrate biological tissues, reaching several centimeters, allows DCS to effectively evaluate blood flow in regions like the brain and muscles with minimal signal loss. This penetration is facilitated by the reduced scattering of NIR light in biological tissues compared to visible light, enhancing depth and improving signal clarity for DCS measurements. Additionally, NIR light's biocompatibility ensures its safety for tissue use, causing no damage or ionization, thus making it suitable for clinical applications. Furthermore, NIR light's sensitivity to hemoglobin absorption enables DCS to precisely target blood flow assessments by detecting alterations in NIR light scattering due to moving red blood cells. Finally, NIR light experiences minimal interference from water and lipids abundant in biological tissues, mitigating background noise and refining the accuracy of DCS measurements. The choice of near-infrared light for DCS offers advantages in terms of tissue penetration, reduced scattering, biocompatibility, and sensitivity to hemoglobin absorption, making it a suitable and effective modality for non-invasive blood flow measurements in various clinical and research settings.

4.1.2 Materials Required for Near-Infrared Diffuse Correlation Spectroscopy (NIDCS)

Near-infrared diffuse correlation spectroscopy (NIDCS) requires specific materials to simulate tissue properties and facilitate accurate measurements. Here's a breakdown of the materials used and their significance:

4.1.2.1. Artificial Blood:

Titanium Dioxide: Titanium dioxide (TiO_2) is often used to simulate the scattering properties of biological tissue. In NIDCS, it mimics the scattering of NIR light by cellular structures within tissues. TiO_2 particles scatter light in a manner similar to biological tissues, allowing for realistic tissue phantoms.

1. Black Ink: Black ink is added to the artificial blood mixture to simulate light absorption by hemoglobin in blood. This absorption component is crucial for accurately modeling the interaction of NIR light with blood vessels and their flow dynamics.
2. Water: Water serves as the solvent for creating the artificial blood mixture. It provides the medium through which TiO_2 and black ink are dispersed, allowing for homogenous scattering and absorption properties similar to biological tissues.

4.1.2.2. Phantom tissue:

1. Polydimethylsiloxane (PDMS): PDMS is a commonly used polymer for creating tissue-simulating phantoms in biomedical imaging studies. It has optical properties that closely resemble those of biological tissues in the NIR range. PDMS phantoms offer flexibility in shaping and molding to simulate various tissue geometries and structures. Curing Agent: The curing agent, typically added to PDMS in a ratio of multiples of 10:1 (e.g., 10:1, 20:2), initiates the polymerization process that converts PDMS from a liquid to a solid elastomer. This process results in the formation of stable tissue phantoms with reproducible optical properties.
2. Vacuum Chamber: Placing the PDMS mixture in a vacuum chamber helps remove air bubbles trapped within the material during mixing and pouring. This step ensures the formation of homogeneous and optically transparent PDMS phantoms, minimizing artifacts in NIDCS measurements.

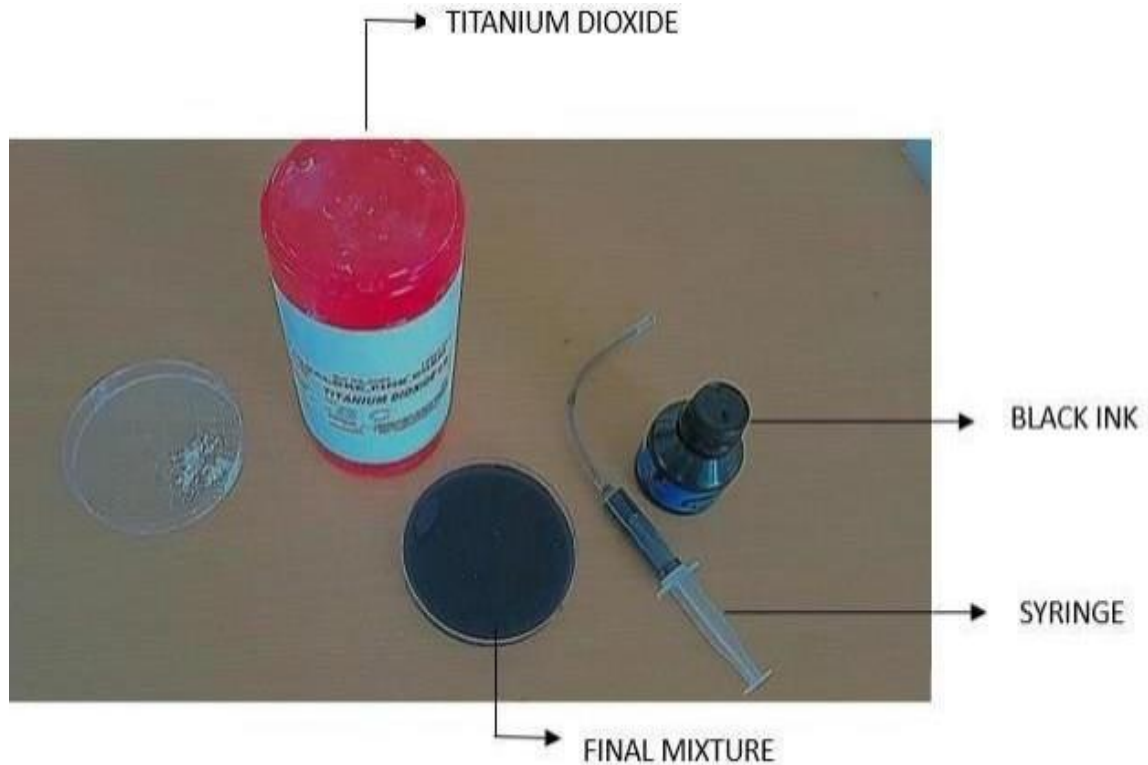


Fig:4.1 : Artificial Blood Components and Standardization of Syringe

4.1.2.3. Instrumentation Design:

SolidWorks: SolidWorks is a computer-aided design (CAD) software used for designing and modelling the NIDCS instrument. It allows for the creation of precise 3D models of the instrument components, including optical probes, sample holders, and housing assemblies. SolidWorks facilitates the optimization of instrument geometry for efficient light delivery and detection, ensuring accurate NIDCS measurements.

By combining these materials and tools, researchers can fabricate tissue-mimicking phantoms and design NIDCS instruments optimized for studying blood flow dynamics in biological tissues with high accuracy and reproducibility.

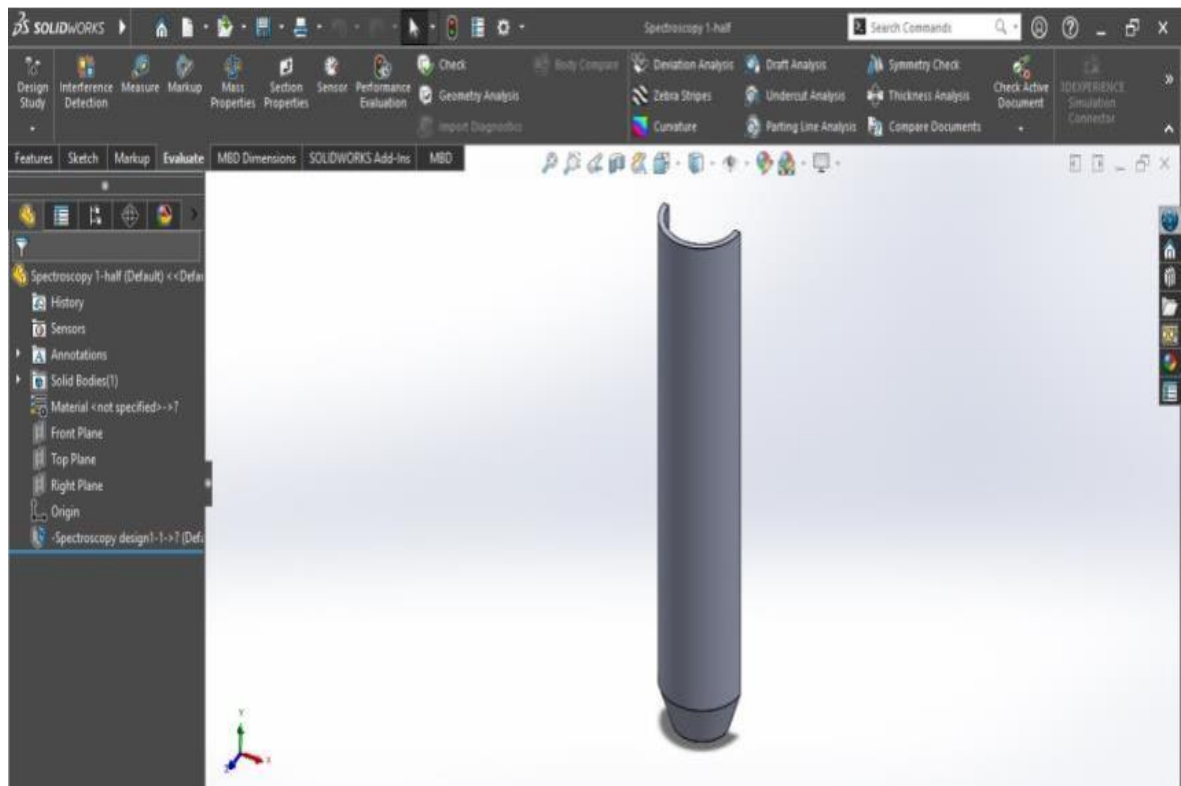


Fig:4.2 : DCS probe design Iteration 1

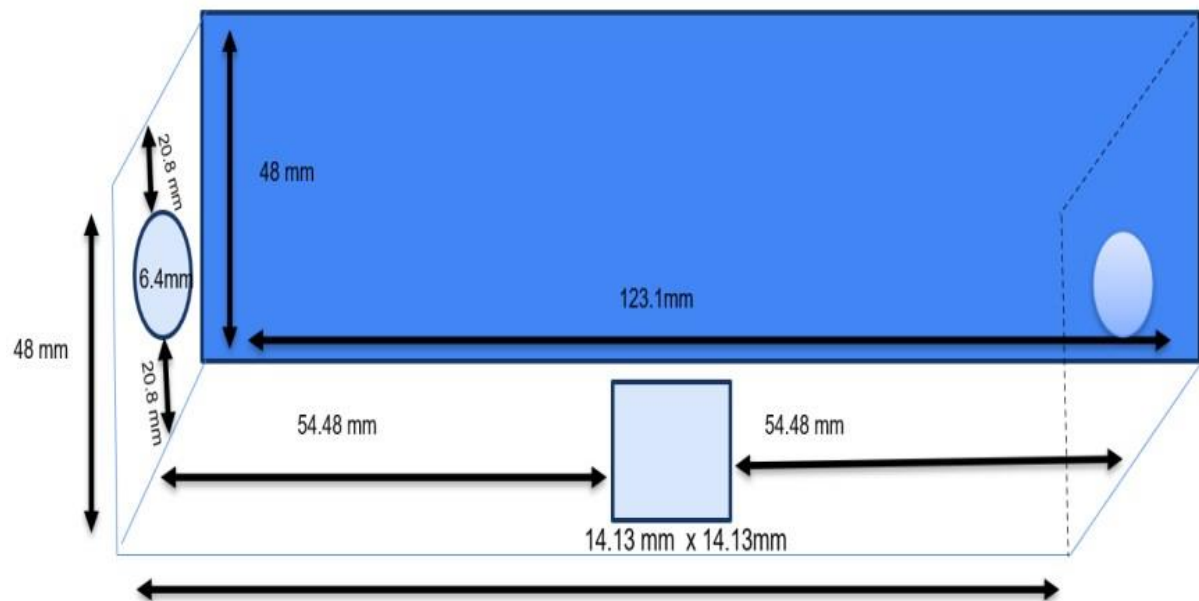


Fig:4.3: DCS probe design Iteration 2

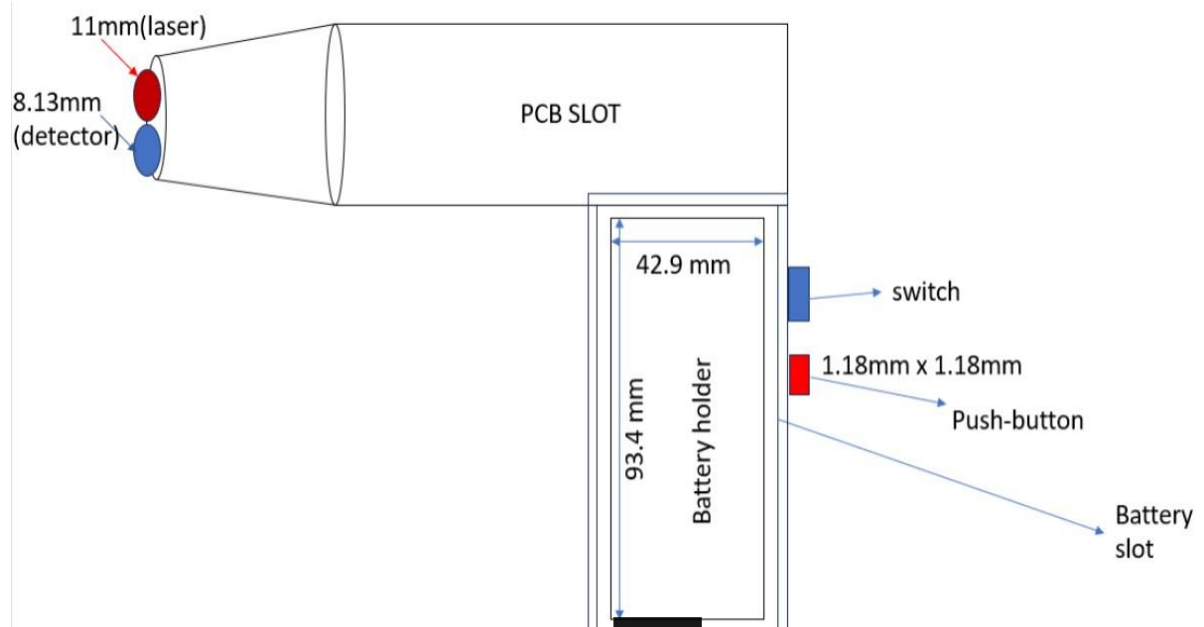


Fig:4.4 : DCS probe design Iteration 3

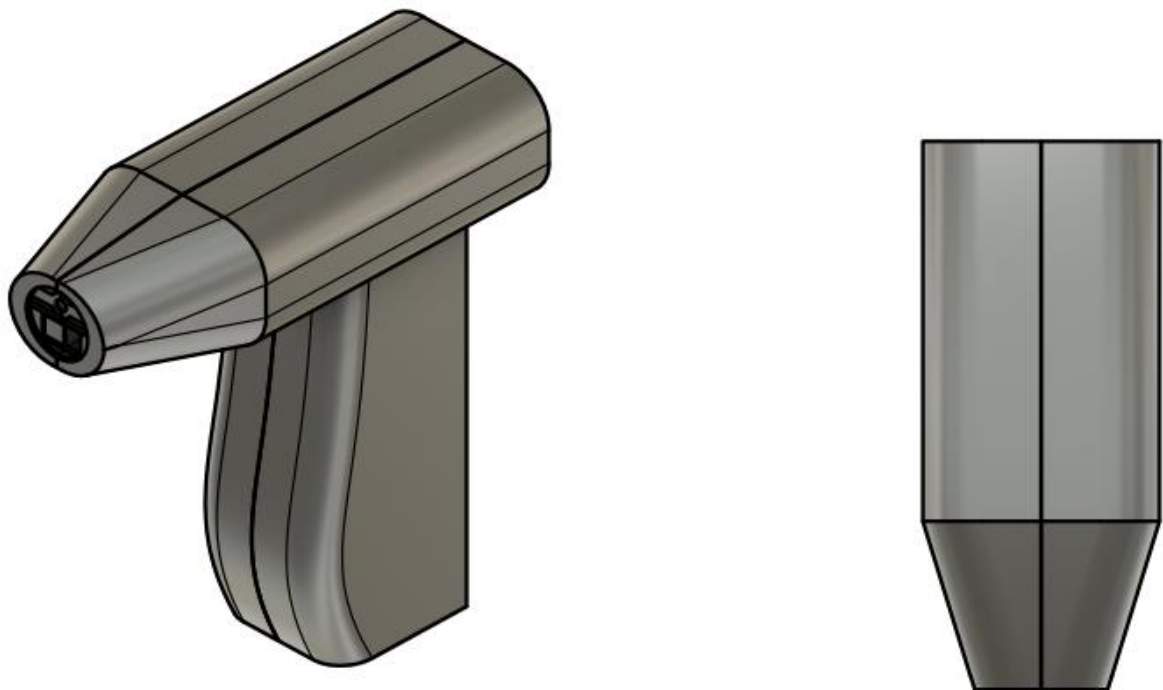


Fig:4.5: DCS probe design Iteration 4

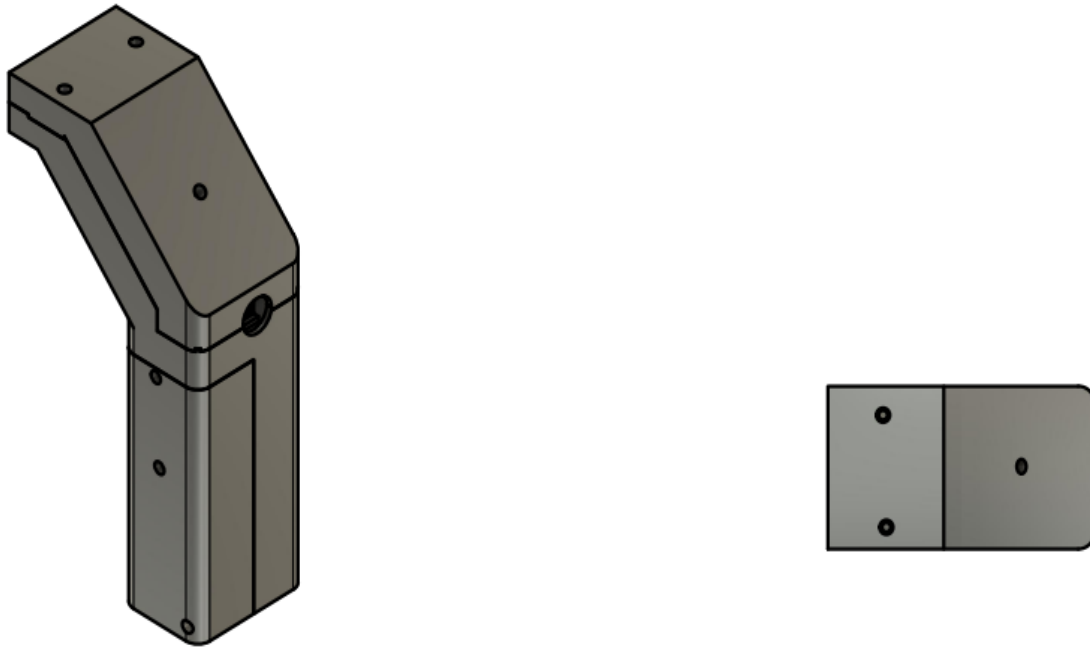


Fig:4.6: DCS probe design Iteration 5

4.2 LASER DIODE AND PHOTODETECTOR

4.2.1 Why Laser is Preferred over LED for DCS?

The photodetector used in Near-Infrared Diffuse Correlation Spectroscopy (NIDCS) is a critical component responsible for capturing NIR light that interacts with biological tissue. Its primary function is to convert these optical signals into electrical signals, which are then processed and analyzed by the NIDCS system. Specifically engineered to be sensitive to near-infrared wavelengths, these photodetectors ensure precise detection of scattered light amidst any background noise present. Their design necessitates high-speed response and sensitivity to accurately capture rapid fluctuations in the scattered light signal, thus enabling precise measurements of blood flow dynamics with high temporal resolution. Furthermore, they must exhibit low noise characteristics to maintain an optimal signal-to-noise ratio, ensuring the detection of even the weakest signals originating from deep tissue layers. In the realm of Diffuse Correlation Spectroscopy (DCS), lasers offer several advantages over light-emitting diodes (LEDs) due to their unique properties. Firstly, lasers emit coherent light,

meaning the photons they emit have the same frequency and phase. This coherence allows for better control over the directionality and spatial coherence of the light beam, resulting in higher spatial resolution in DCS measurements compared to the more divergent light emitted by LEDs. Moreover, lasers emit light within a narrow spectral bandwidth, typically with a single dominant wavelength, which enhances the accuracy of DCS measurements by minimizing spectral interference and simplifying signal analysis compared to the broader spectrum emitted by LEDs. Another advantage of lasers is their ability to emit light with high intensity, providing sufficient photon flux for penetrating deep into tissues and generating strong signal-to-noise ratios in DCS measurements. In contrast, LEDs, while capable of producing light, generally have lower intensity compared to lasers, limiting their effectiveness for deep tissue penetration. Additionally, lasers exhibit excellent temporal stability, maintaining constant output intensity and wavelength over time. This stability is crucial for longitudinal DCS measurements, ensuring consistency in the collected data. LEDs, on the other hand, may suffer from fluctuations in intensity and wavelength stability, leading to measurement inaccuracies and variability. Furthermore, the spatial coherence of laser light allows for the formation of well-defined light speckles in scattering media, which is essential for accurate correlation analysis in DCS. LEDs, with their more divergent emission, produce less coherent speckle patterns, making correlation analysis more challenging and reducing measurement accuracy. Additionally, lasers can produce polarized light, which can be advantageous for specific DCS applications, such as polarization-sensitive measurements. LEDs typically emit unpolarized light, limiting their utility in polarization-dependent studies. Overall, the coherent, monochromatic, and intense light emitted by lasers makes them the preferred light source for DCS, enabling precise and reliable measurements of blood flow dynamics in biological tissues. In the context of Near-Infrared Diffuse Correlation Spectroscopy (NIDCS), both the diode laser and the photodetector play crucial roles in measuring blood flow dynamics in tissues. The diode laser serves as the primary light source in NIDCS. It emits a narrow beam of near-infrared (NIR) light with specific wavelengths tailored to the optical properties of biological tissues. This NIR light penetrates tissues to a certain depth, dependent on

the tissue's scattering and absorption properties, allowing for the measurement of blood flow dynamics within the tissue. Typically operating in continuous wave mode, diode lasers provide a constant output of NIR light, enabling real-time monitoring of blood flow changes without interruptions. Moreover, diode lasers often feature adjustable power settings, allowing researchers to control the intensity of the NIR light beam. This flexibility is crucial for optimizing signal-to-noise ratios and minimizing tissue heating effects during measurements.



Fig:4.7: Laser diode used in DCS probe

4.2.2 Photodetector for DCS

The photodetector in Near-Infrared Diffuse Correlation Spectroscopy (NIDCS) plays a crucial role in capturing NIR light scattered back from tissues. It converts these optical signals into electrical ones, facilitating analysis by the NIDCS system. Specifically designed for near-infrared wavelengths, these photodetectors ensure accurate detection of scattered light, even amidst background noise. They require high-speed response and sensitivity to capture rapid fluctuations in the scattered light signal, ensuring precise measurements of blood flow dynamics with high temporal resolution. Additionally, low noise characteristics are essential to maintain an optimal signal-to-

noise ratio, enabling the detection of weak signals from deep tissue layers accurately. In summary, while the diode laser illuminates tissues with NIR light, the photodetector detects the scattered light and converts it into electrical signals for analysis, enabling NIDCS systems to non-invasively measure blood flow dynamics in biological tissues with high sensitivity and temporal resolution.

Table 4.1: Experimented detectors comparative chart

NAME	PEAK SENSITIVITY(nm)	SPECTRAL RANGE	RISE TIME/FALL TIME
TEMT 6000	570	360-970	Rise time:45 μ s
BPW21R	565	429 - 675	Rise time: 3.1 ms Fall time: 3.0 ms
SFH 2713	635	400-660	Rise time: 22 ns Fall time: 31 ns

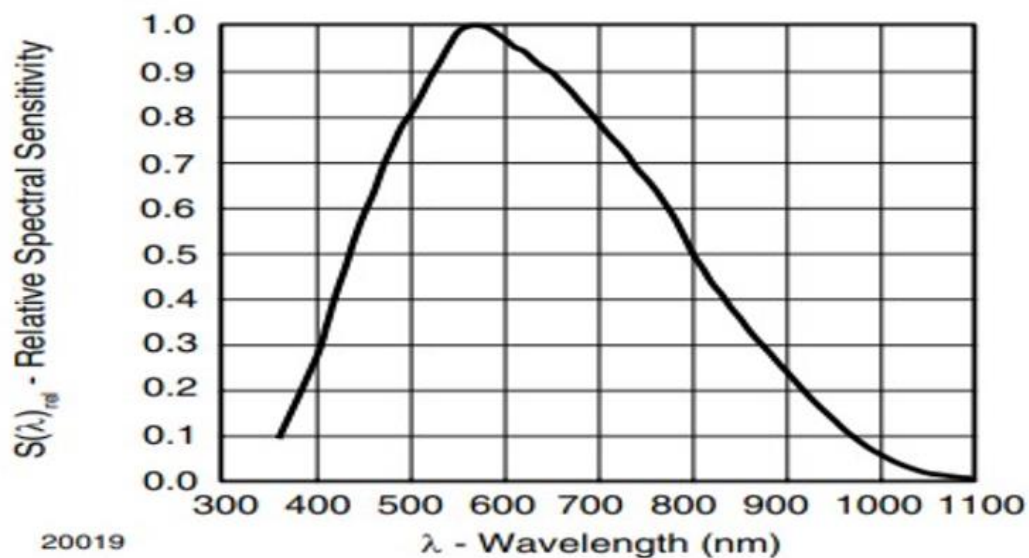


Fig:4.8: Spectral Graph of TEMT6000

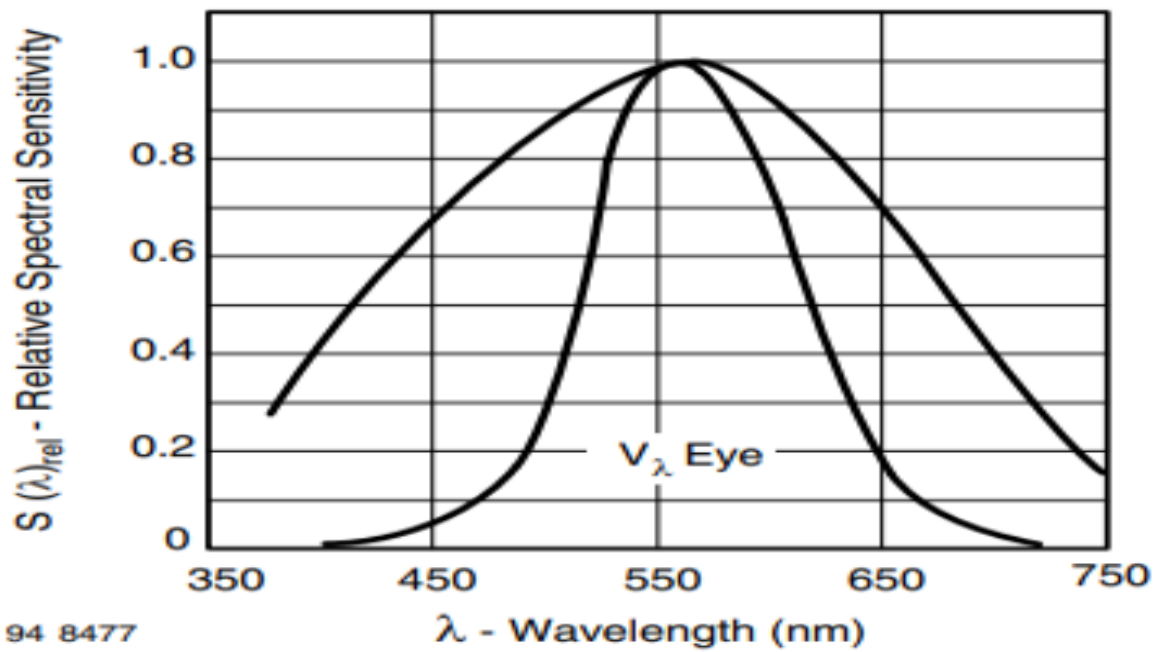


Fig:4.9: Spectral Graph of BPW21R

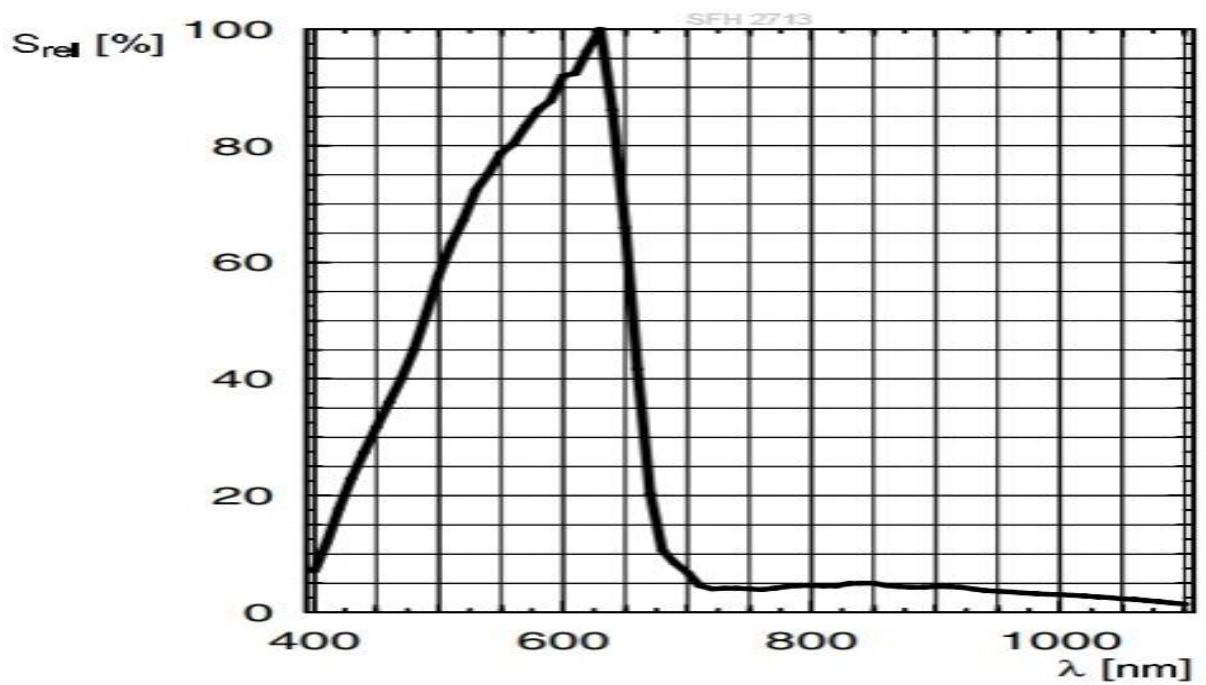


Fig:4.10: Spectral Graph of SFH2713

4.3 THERANOSTIC APPLICATIONS OF DCS

4.3.1 Diabetic patients:

DCS can play a crucial role in assessing microvascular dysfunction in diabetic patients. By measuring blood flow in peripheral tissues, DCS can provide insights into the progression of diabetic complications such as diabetic neuropathy and peripheral vascular disease. Early detection of impaired blood flow can prompt interventions to prevent tissue damage and improve patient outcomes. Additionally, DCS can monitor the efficacy of treatments aimed at improving microvascular perfusion, such as revascularization procedures or pharmacological interventions.

4.3.2 Sickle cell anemia:

In sickle cell anemia, impaired blood flow due to vaso-occlusion can lead to tissue ischemia and organ damage. DCS offers a non-invasive method to monitor blood flow dynamics in real-time, allowing clinicians to assess the severity of vaso-occlusive events and guide treatment decisions. By monitoring changes in blood flow patterns, DCS can aid in the early detection of vaso-occlusive crises and facilitate prompt intervention with therapies such as hydration, pain management, or blood transfusions.

4.3.3 Surface Cancer Detection:

DCS has shown promise in detecting superficial tumors by assessing changes in microvascular perfusion associated with angiogenesis, a hallmark of cancerous growth. By measuring blood flow parameters in the tumor microenvironment, DCS can aid in the early detection and characterization of skin cancers, such as melanoma or squamous cell carcinoma. Furthermore, DCS can provide valuable information for guiding surgical resection margins and monitoring the response to anti-angiogenic therapies or other cancer treatments.

4.3.4 Monitoring patients using blood thinners:

Patients receiving anticoagulant therapy, such as blood thinners, are at risk of hemorrhagic complications due to excessive bleeding. DCS can be utilized to assess the impact of anticoagulant treatment on microvascular blood flow and hemostasis. By monitoring changes in blood flow dynamics, DCS can help clinicians optimize

anticoagulant dosing regimens, minimize the risk of bleeding events, and ensure therapeutic efficacy. Additionally, DCS can aid in the early detection of haemorrhagic complications, allowing for timely intervention and patient management.

4.3.5 Cardiac Patients:

In cardiac patients, impaired myocardial perfusion can lead to ischemic heart disease and heart failure. DCS offers a non-invasive method to assess microvascular function and myocardial blood flow dynamics, providing valuable insights into cardiac function and perfusion reserve. By monitoring changes in myocardial blood flow, DCS can aid in the early detection of ischemic events, guide treatment decisions, and evaluate the effectiveness of interventions such as revascularization procedures or pharmacological therapies.

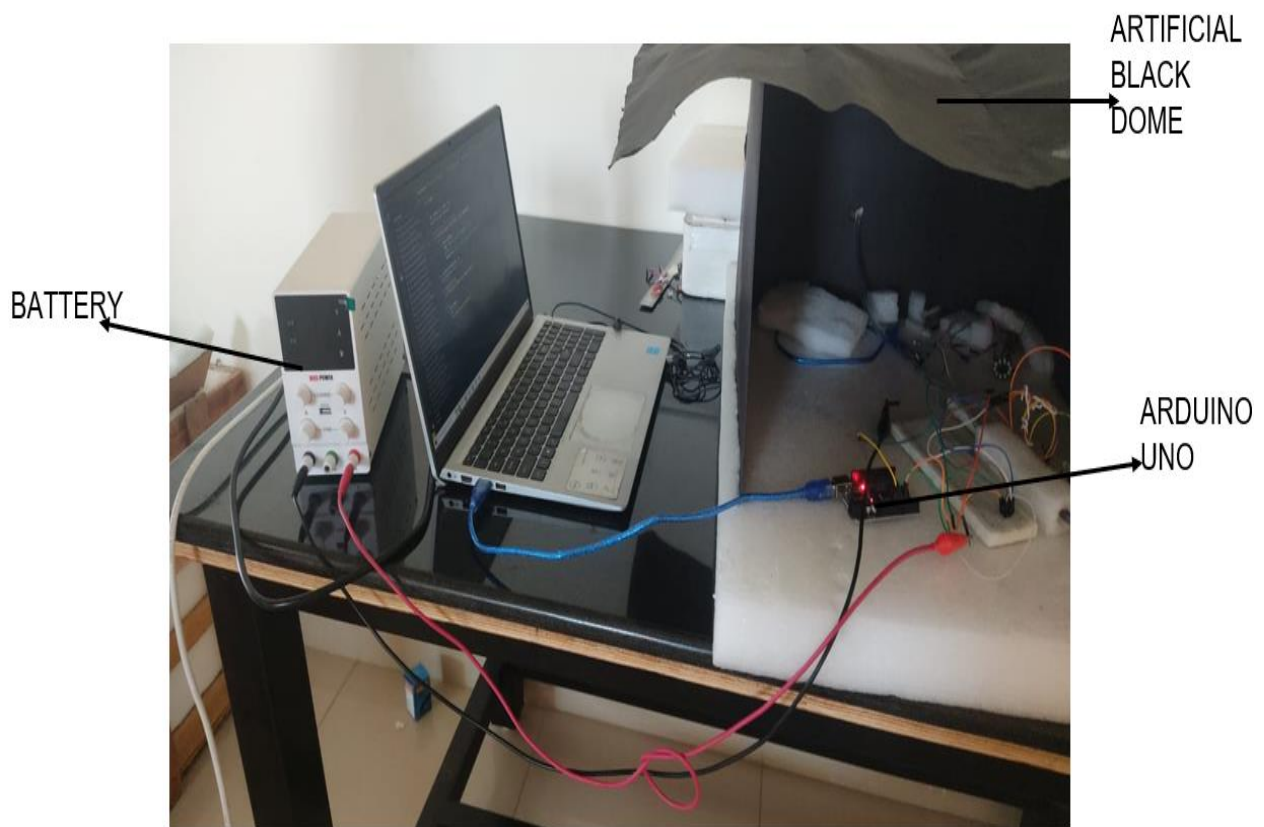


Fig:4.11: Set up for data collection Iteration 1

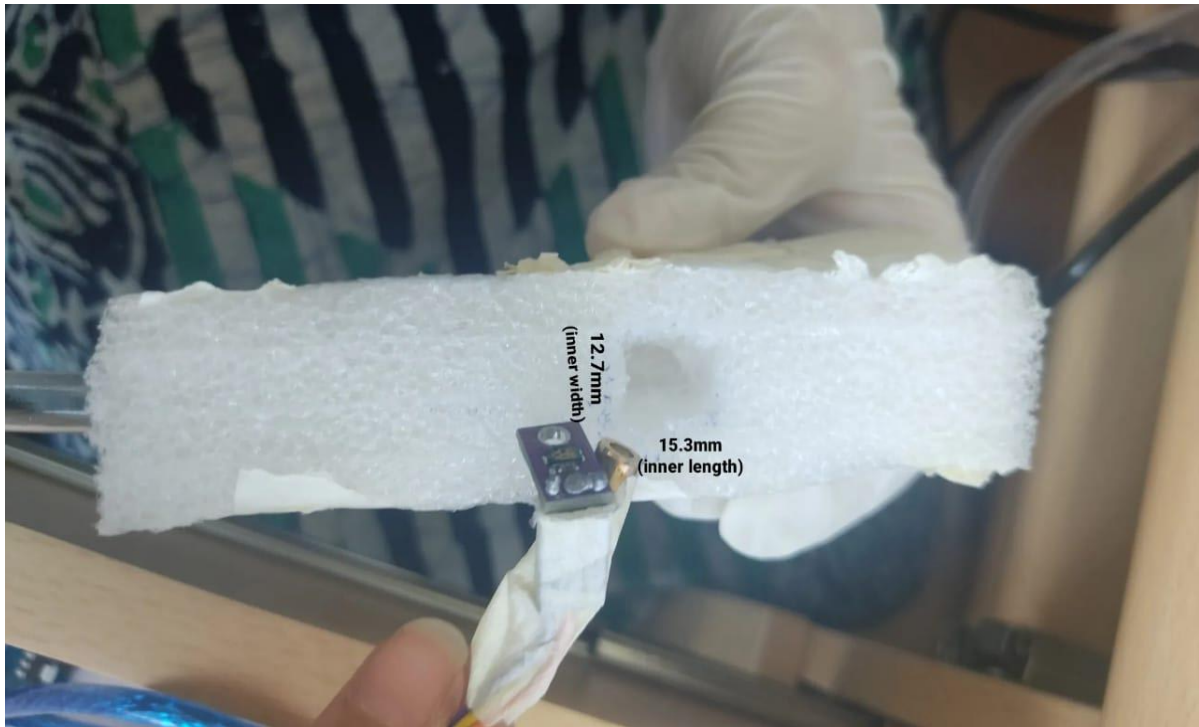


Fig:4.12: Casing Dimension to collect experimental data

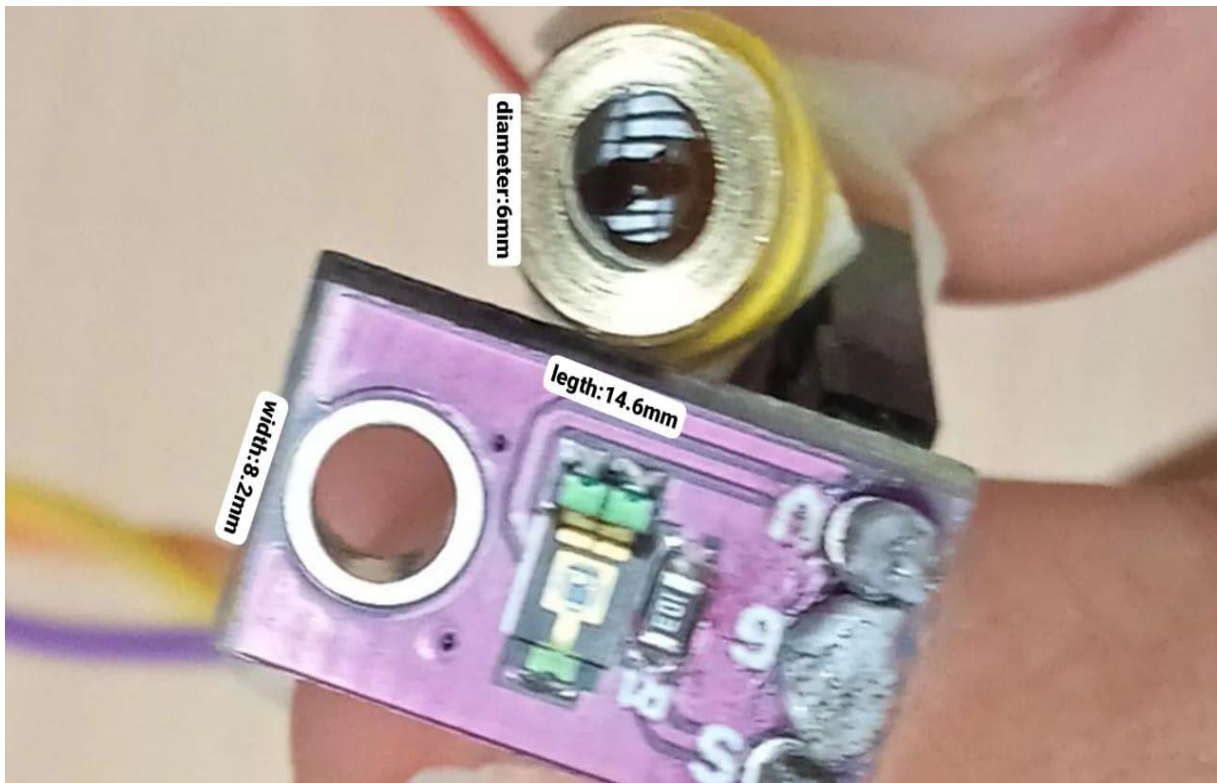


Fig:4.13: Detector and Laser Dimension to collect experimental data

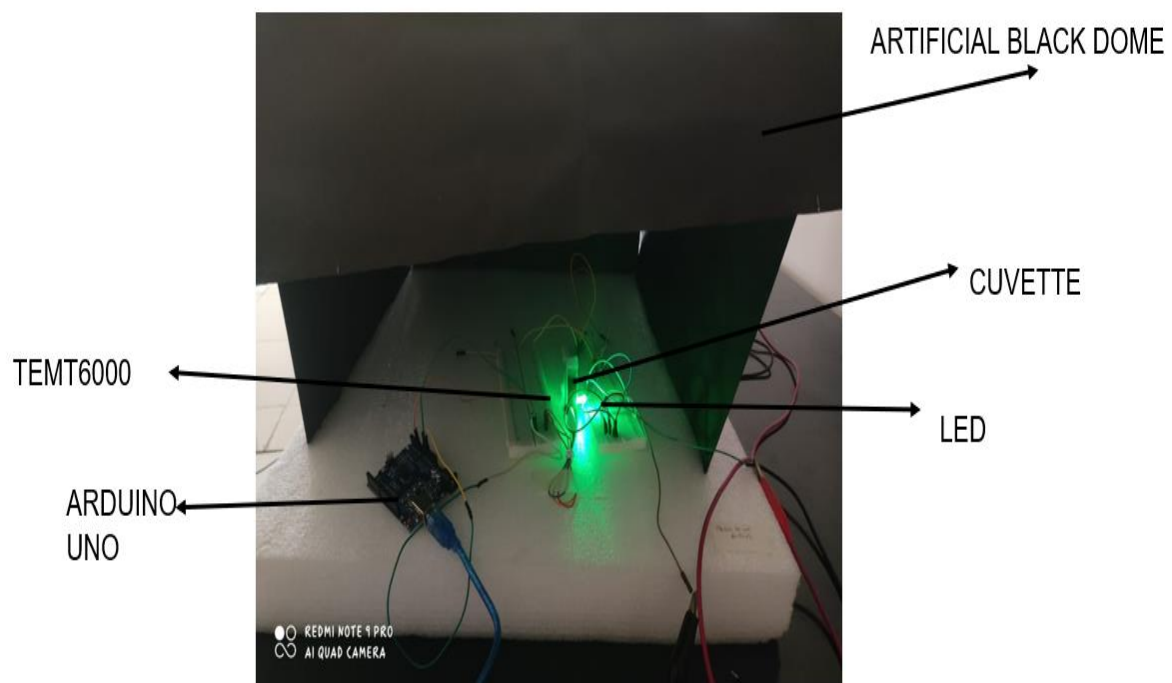


Fig:4.14: Cuvette Experiment to collect experimental data

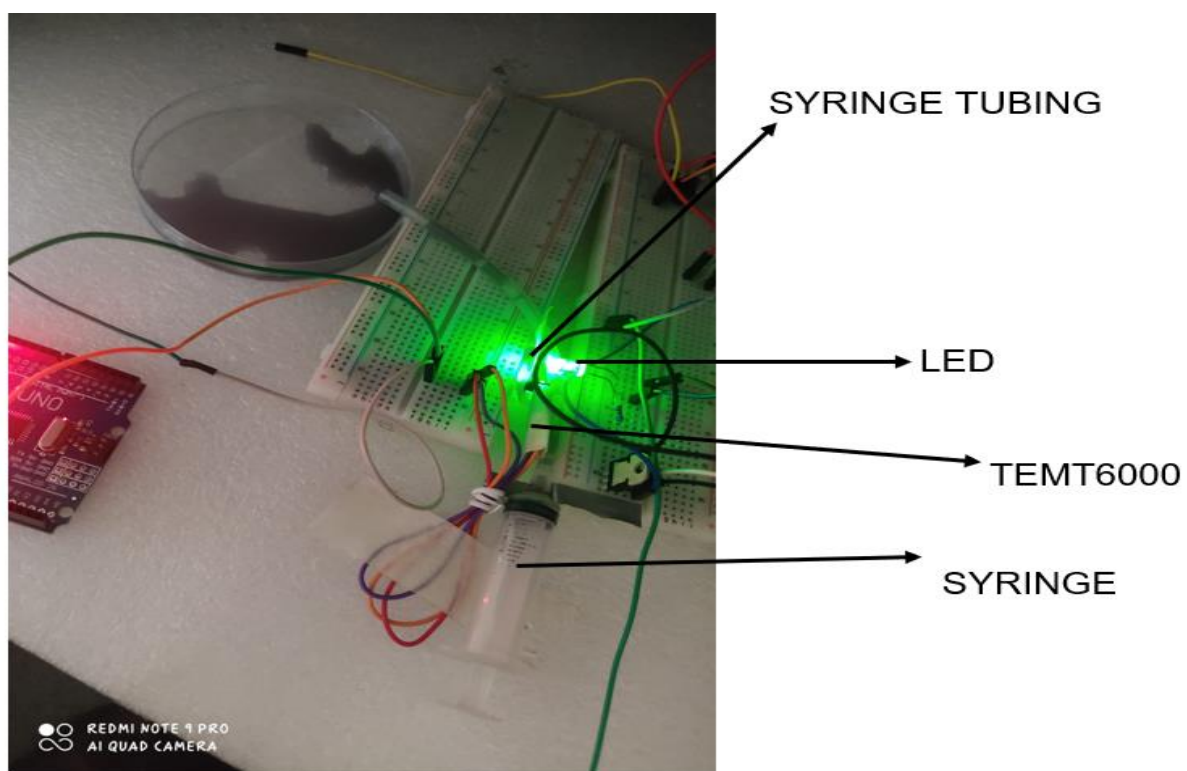
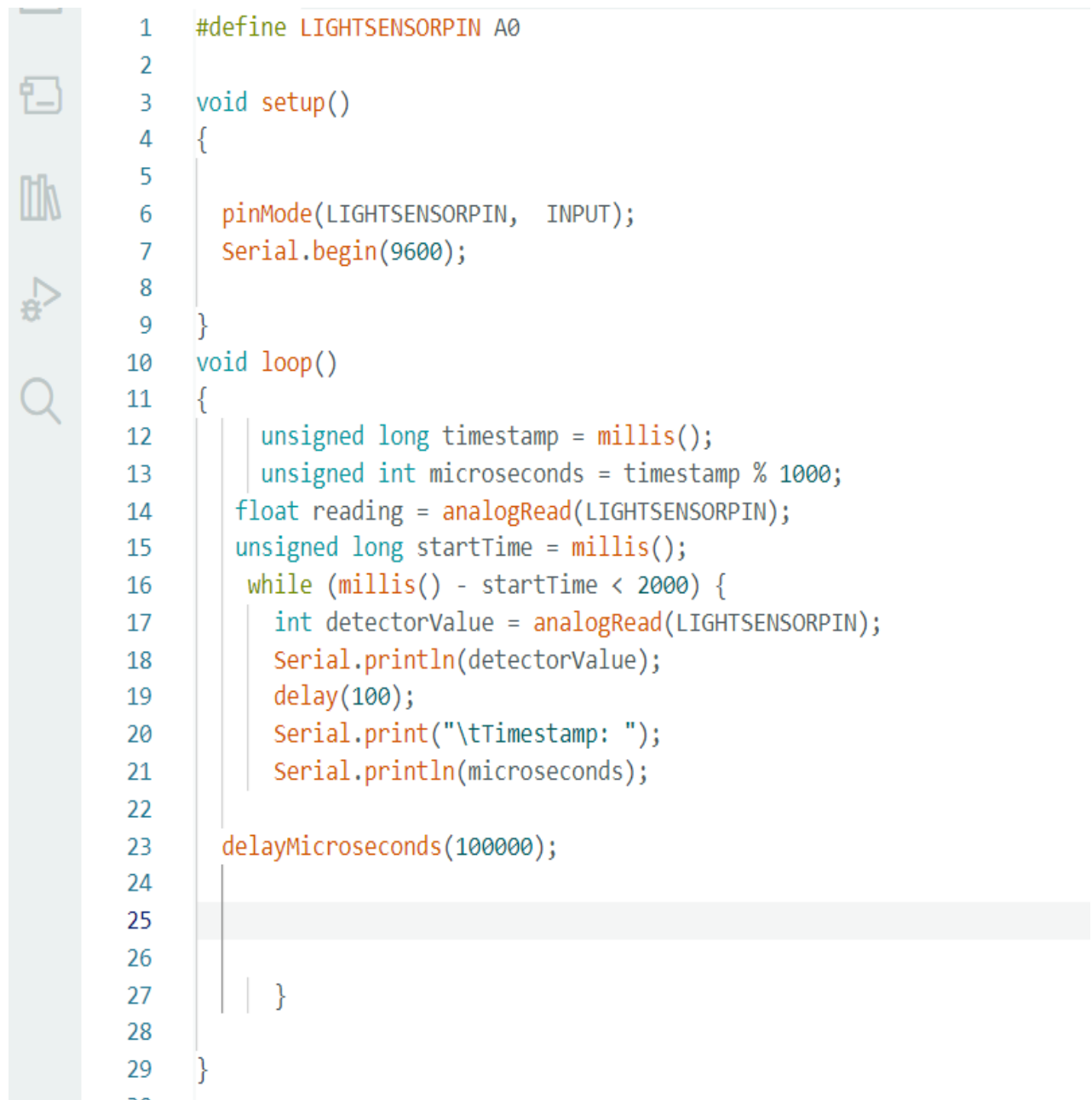


Fig:4.15: Syringe Experiment to collect experimental data

4.4 SOFTWARES USED

4.4.1 Arduino:

Arduino is an open-source hardware and software platform that allows users to create interactive electronic projects by providing a simple and flexible development environment. The following pictures are the different Arduino code iterations to make the detector and laser work for 5 seconds on the click of a push button.

A screenshot of the Arduino IDE interface. On the left is a vertical toolbar with icons for file operations (copy, paste, save), a library manager, a compiler, and a search function. The main area displays a C++ code file with line numbers 1 through 29. The code defines a pin, sets up the pin mode and serial communication, and then enters a loop that reads the sensor value, prints it, and delays for 100ms and 100,000 microseconds.

```
1  #define LIGHTSENSORPIN A0
2
3  void setup()
4  {
5
6      pinMode(LIGHTSENSORPIN, INPUT);
7      Serial.begin(9600);
8
9  }
10 void loop()
11 {
12     unsigned long timestamp = millis();
13     unsigned int microseconds = timestamp % 1000;
14     float reading = analogRead(LIGHTSENSORPIN);
15     unsigned long startTime = millis();
16     while (millis() - startTime < 2000) {
17         int detectorValue = analogRead(LIGHTSENSORPIN);
18         Serial.println(detectorValue);
19         delay(100);
20         Serial.print("\tTimestamp: ");
21         Serial.println(microseconds);
22
23     delayMicroseconds(100000);
24
25
26
27     }
28
29 }
```

Fig 4.16: Detector output- Iteration 1



```
2_newlaserndetectordelay_draft.ino
1  #define LIGHTSENSORPIN A0
2  #define LEDPIN 6
3  const int buttonPin = 5;
4
5  void setup() {
6      pinMode(LEDPIN, OUTPUT);
7      pinMode(LIGHTSENSORPIN, INPUT);
8      pinMode(buttonPin, INPUT_PULLUP);
9      Serial.begin(9600);
10 }
11
12 void loop() {
13     int buttonState = digitalRead(buttonPin);
14     unsigned long timestamp = micros();
15
16     if (buttonState == HIGH)(millis() - startTime < 2000) {
17         digitalWrite(LEDPIN, HIGH);
18         unsigned long startTime = millis();
19         unsigned int microseconds = timestamp % 1000;
20         float reading = analogRead(LIGHTSENSORPIN);
21         Serial.print("Detector1: ");
22         Serial.print(reading);
23         Serial.print("\tTimestamp: ");
24         Serial.println(microseconds);
25
26
27         digitalWrite(LEDPIN, LOW);
28     }
29
30     else {
31         digitalWrite(LEDPIN, LOW);
32     }
33 }
```

Fig 4.17: Laser and Detector output- Iteration 2

```

7 void setup() {
8     pinMode(ledPin, OUTPUT);
9     pinMode(detectorPin, INPUT);
10    pinMode(buttonPinAnalog, INPUT);
11    pinMode(buttonPinDigital1, INPUT);
12    pinMode(buttonPinDigital2, INPUT);
13    Serial.begin(9600);
14 }
15
16 void loop() {
17     if (digitalRead(buttonPinDigital2) == HIGH) {
18         digitalWrite(detectorPin, HIGH);
19         Serial.println("Detector activated:");
20         unsigned long startTime = millis();
21         while (millis() - startTime < 30000) {
22             unsigned long timestamp = micros();
23             unsigned int microseconds = timestamp % 1000;
24             int reading = analogRead(detectorPin);
25             Serial.print("Detector1: ");
26             Serial.print(reading);
27             Serial.print("\tTimestamp: ");
28             Serial.println(microseconds);
29             delay(100);
30         }
31
32         digitalWrite(detectorPin, LOW);
33         Serial.println("Detector deactivated.");
34         if (buttonPinDigital2 == HIGH) {
35             digitalWrite(ledPin, HIGH);
36             delay(2000);
37             digitalWrite(ledPin, LOW);
38
39
40

```

Fig 4.18: Laser and Detector output- Iteration 3



```
1
2 const int detectorPin = A0;
3 const int switchPin = 5;
4
5 void setup() {
6
7     Serial.begin(9600);
8
9
10    pinMode(detectorPin, INPUT);
11
12    pinMode(switchPin, INPUT);
13 }
14
15 void loop() {
16
17     if (digitalRead(switchPin) == HIGH) {
18
19         digitalWrite(detectorPin, HIGH);
20         Serial.println("Detector activated:");
21
22         unsigned long startTime = millis();
23         while (millis() - startTime < 2000) {
24             int detectorValue = analogRead(detectorPin);
25             Serial.println(detectorValue);
26             delay(100);
27         }
28
29         digitalWrite(detectorPin, LOW);
30         Serial.println("Detector deactivated.");
31     }
32 }
33
```

Fig 4.19: Detector output- Iteration 4

detectorswitchfor5secs.ino

```
1  const int detectorPin = A0;
2  const int switchPin = 5;
3
4  void setup() {
5      Serial.begin(9600);
6      pinMode(detectorPin, INPUT);
7      pinMode(switchPin, INPUT);
8  }
9
10 void loop() {
11     if (digitalRead(switchPin) == HIGH) {
12         digitalWrite(detectorPin, HIGH);
13         Serial.println("Detector activated:");
14         unsigned long startTime = millis();
15         while (millis() - startTime < 5000) {
16             unsigned long timestamp = micros();
17             unsigned int microseconds = timestamp % 1000;
18             int reading = analogRead(detectorPin);
19             Serial.print("Detector1: ");
20             Serial.print(reading);
21             Serial.print("\tTimestamp: ");
22             Serial.println(microseconds);
23             delay(1);
24         }
25         digitalWrite(detectorPin, LOW);
26         Serial.println("Detector deactivated.");
27     }
28 }
```

Fig:4.20: Detector output with switch- Iteration 5

```

1  const int ledPin = 13;
2  const int detectorPin = A0;
3  const int switchPin = 5;
4  int pb=0;
5  unsigned long prevTime=0;
6  void setup()
7  {
8      Serial.begin(9600);
9      pinMode(ledPin, OUTPUT);
10     pinMode(detectorPin, INPUT);
11     pinMode(switchPin, INPUT);
12 }
13
14 void loop() {
15     pb=digitalRead(switchPin);
16     if(pb==HIGH)
17     {
18         digitalWrite(ledPin, HIGH);
19         digitalWrite(detectorPin, HIGH);
20         Serial.println("Detector and LED activated:");
21         unsigned long startTime = millis();
22         int totime = startTime - prevTime ;
23         if(totime<= 5000)
24         {
25             unsigned long timestamp = micros();
26             unsigned int microseconds = timestamp % 1000;
27             float reading = analogRead(detectorPin);
28             Serial.print("Detector1: ");
29             Serial.print(reading);
30             Serial.print("\tTimestamp: ");
31             Serial.println(microseconds);
32             delay(1);
33             prevTime=startTime;
34             digitalWrite(ledPin, LOW);
35             digitalWrite(detectorPin, LOW);
36         }

```

Fig:4.21: Detector output with switch- Iteration 6

```

1  const int ledPin = 13;
2  const int switchPin = 5;
3
4  void setup() {
5      pinMode(ledPin, OUTPUT);
6      pinMode(switchPin, INPUT);
7  }
8
9  void loop() {
10     if (digitalRead(switchPin) == HIGH) {
11         digitalWrite(ledPin, HIGH);
12         unsigned long startTime = millis();
13         while (millis() - startTime < 5000) {
14             // Wait for 5 seconds while LED is on
15         }
16         digitalWrite(ledPin, LOW);
17     }
18 }

```

Fig:4.22: Laser output with switch- Iteration 7

```

1
2  const int TEMT6000_PIN = A0;
3
4
5  const int LED_PIN = 13;
6
7  void setup() {
8
9      Serial.begin(9600);
10
11
12      pinMode(LED_PIN, OUTPUT);
13  }
14
15  void loop() {
16
17      int lightValue = analogRead(TEMT6000_PIN);
18
19
20      Serial.print("Light Intensity: ");
21      Serial.println(lightValue);
22
23
24      if (lightValue < 500) {
25          digitalWrite(LED_PIN, HIGH);
26      } else {
27          digitalWrite(LED_PIN, LOW);
28      }
29
30      delay(1000);
31  }

```

Fig:4.23: Detector output- Iteration 8

```

1
2  const int ledPin = 6;
3  const int switchPin = 5;
4
5  void setup() {
6
7      pinMode(ledPin, OUTPUT);
8
9      pinMode(switchPin, INPUT);
10 }
11
12 void loop() {
13
14     if (digitalRead(switchPin) == HIGH) {
15
16         digitalWrite(ledPin, HIGH);
17
18         delay(2000);
19
20         digitalWrite(ledPin, LOW);
21
22     }
23
24
25 }

```

Fig:4.24: Laser with switch output- Iteration 9

```

1  const int detectorPin = A0;
2  const int switchPin = 5;
3
4  void setup() {
5      Serial.begin(9600);
6      pinMode(detectorPin, INPUT);
7      pinMode(switchPin, INPUT);
8  }
9
10 void loop() {
11     if (digitalRead(switchPin) == HIGH) {
12
13         digitalWrite(detectorPin, HIGH);
14         Serial.println("Detector activated:");
15
16         unsigned long startTime = millis();
17         while (millis() - startTime < 10000) {
18             unsigned long timestamp = micros();
19             unsigned int microseconds = timestamp % 1000;
20
21             int reading = analogRead(detectorPin);
22             Serial.print("Detector1: ");
23             Serial.print(reading);
24             Serial.print("\tTimestamp: ");
25             Serial.println(microseconds);
26
27             delay(100);
28         }
29
30         digitalWrite(detectorPin, LOW);
31         Serial.println("Detector deactivated.");
32     }
33 }

```

Fig:4.25: Timed output- Iteration 10

4.4.2 Origin Pro

Origin Pro is a data analysis and graphing software primarily used in scientific and engineering research for visualizing and interpreting experimental data. The following iterations are to verify if the theoretical values of temporal intensity fluctuations matches the practical values.

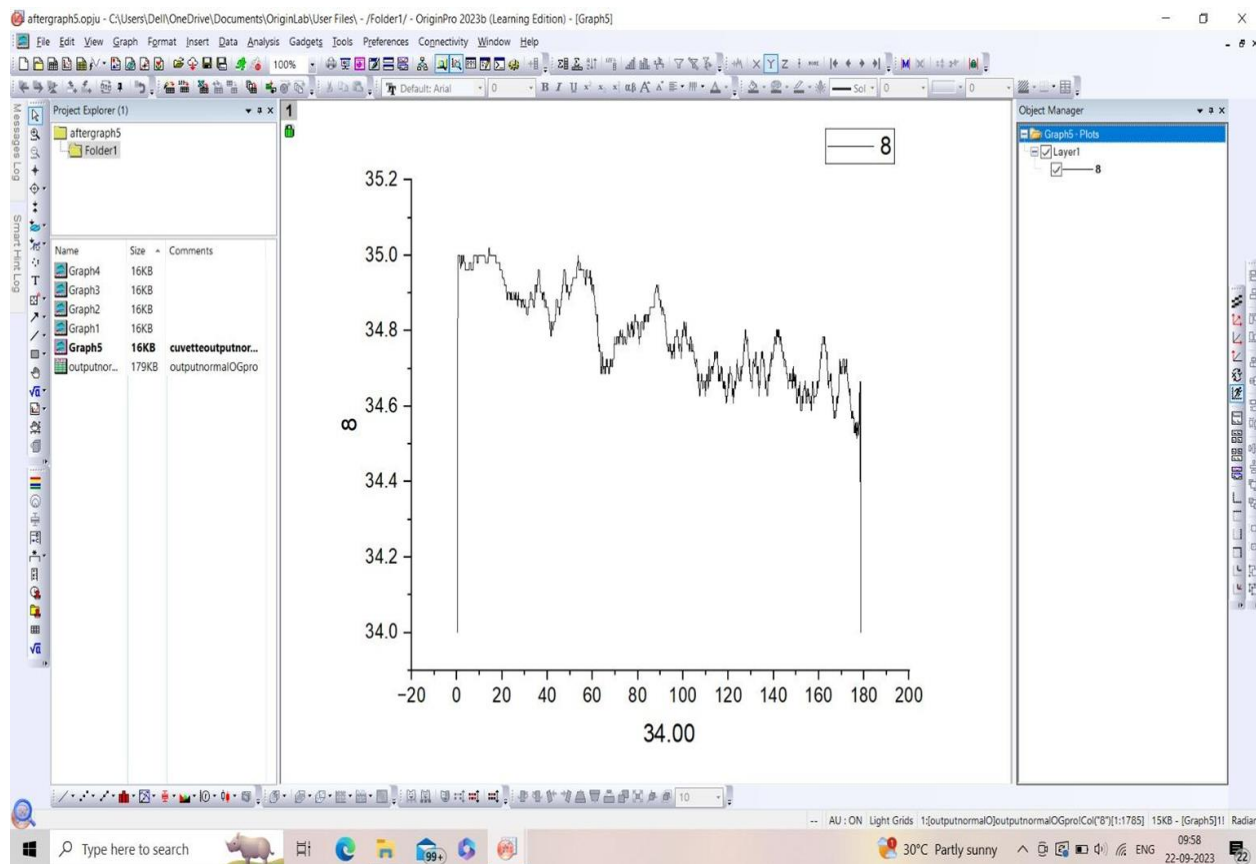


Fig:4.26: Intensity vs time graph for normal temperature in cuvette

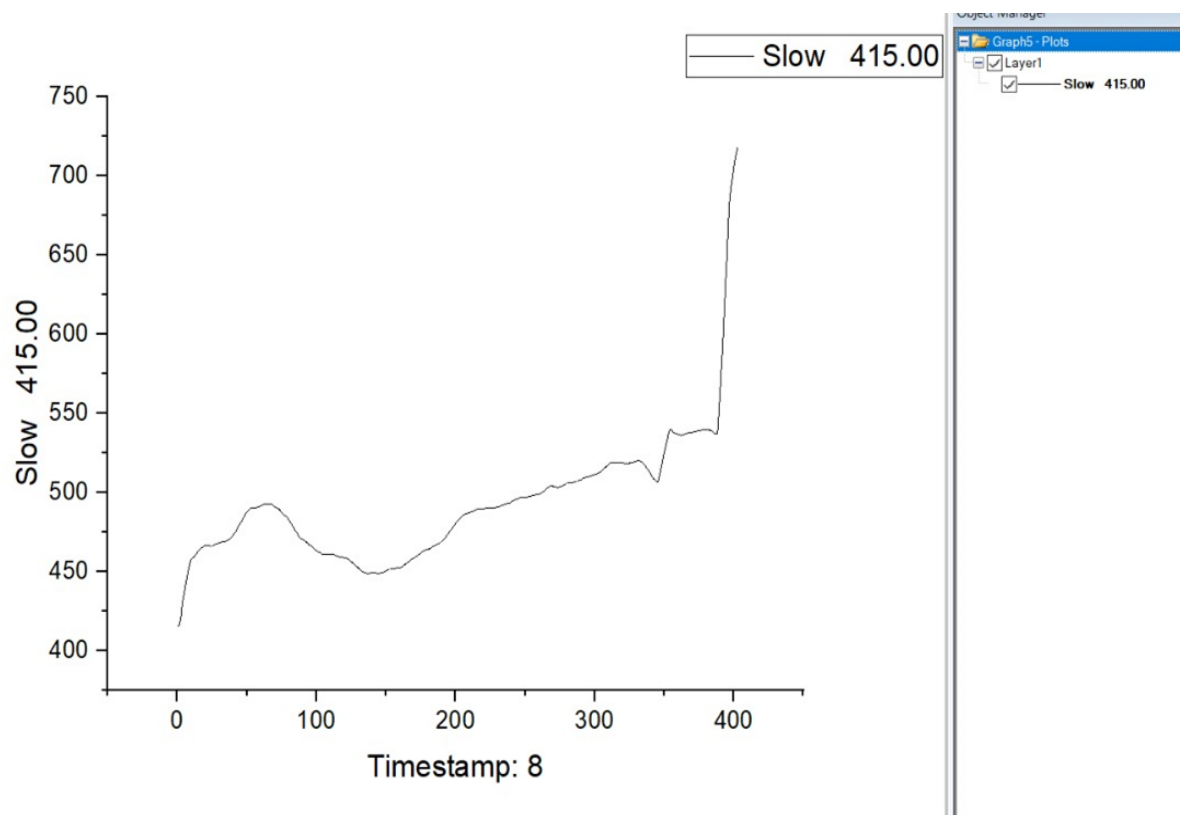


Fig:4.27: Intensity vs time graph for slow speed in syringe

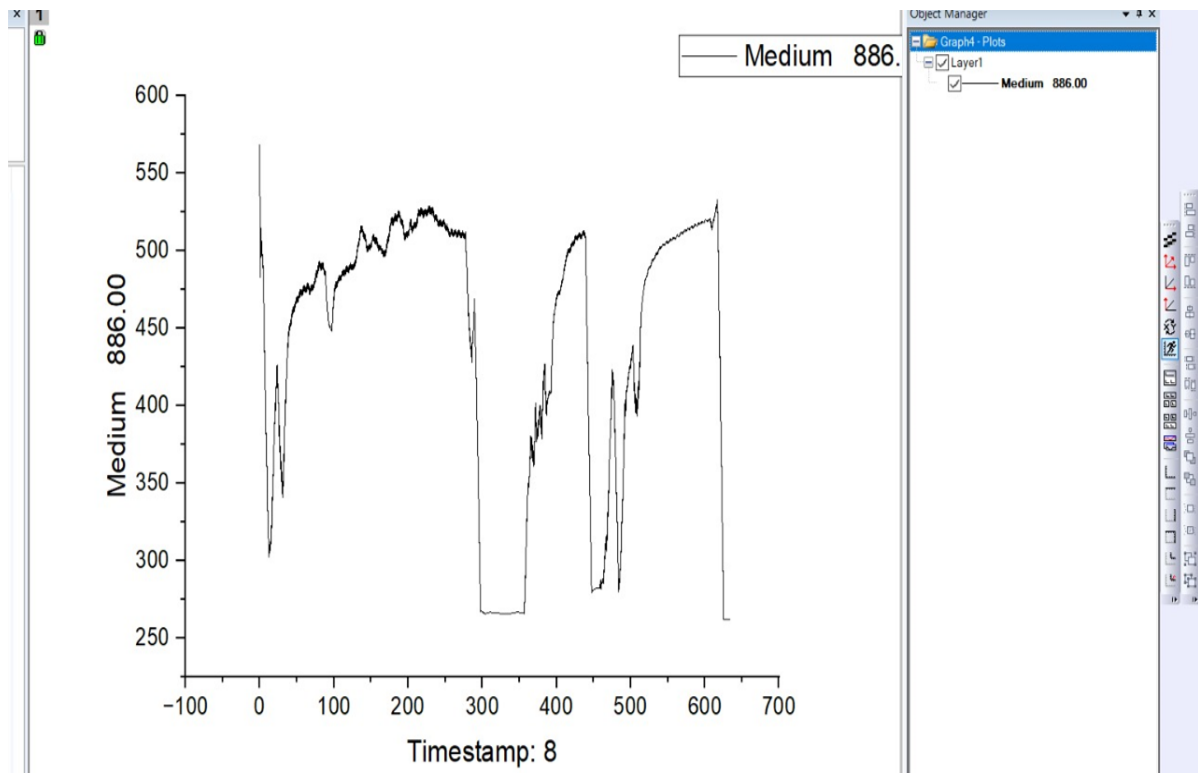


Fig:4.28: Intensity vs time graph for medium speed in syringe

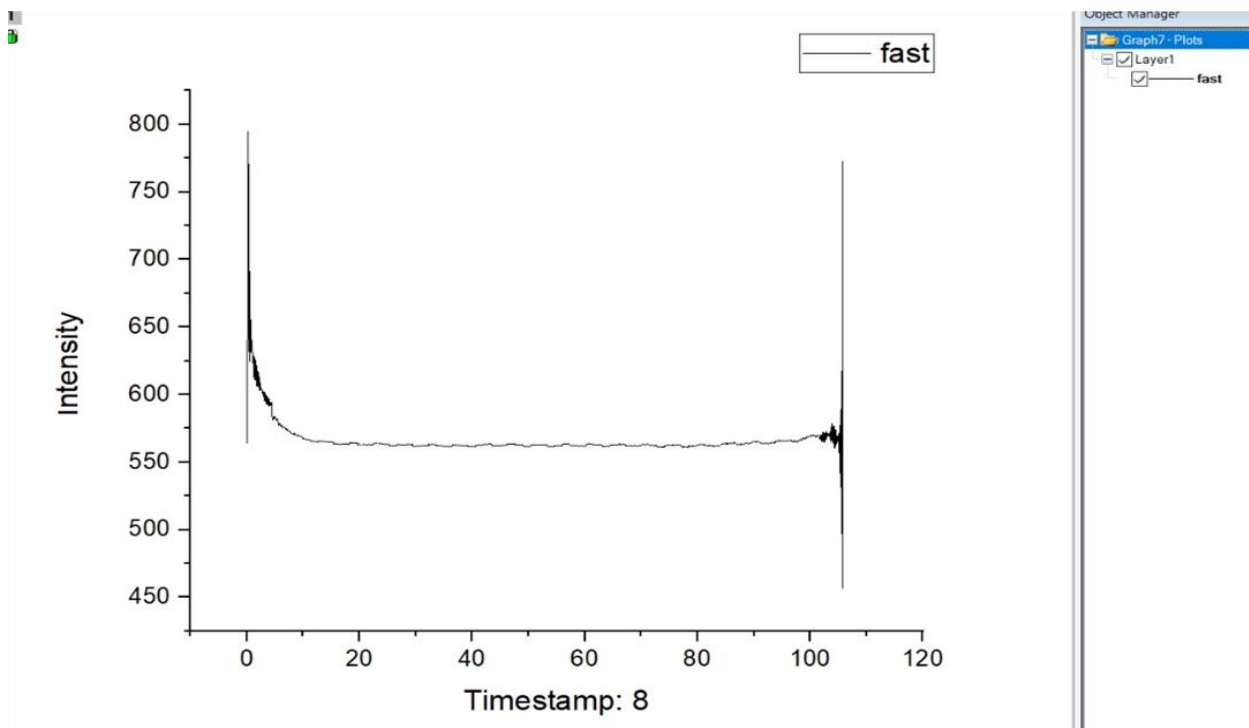


Fig:4.29: Intensity vs time graph for fast speed in syringe

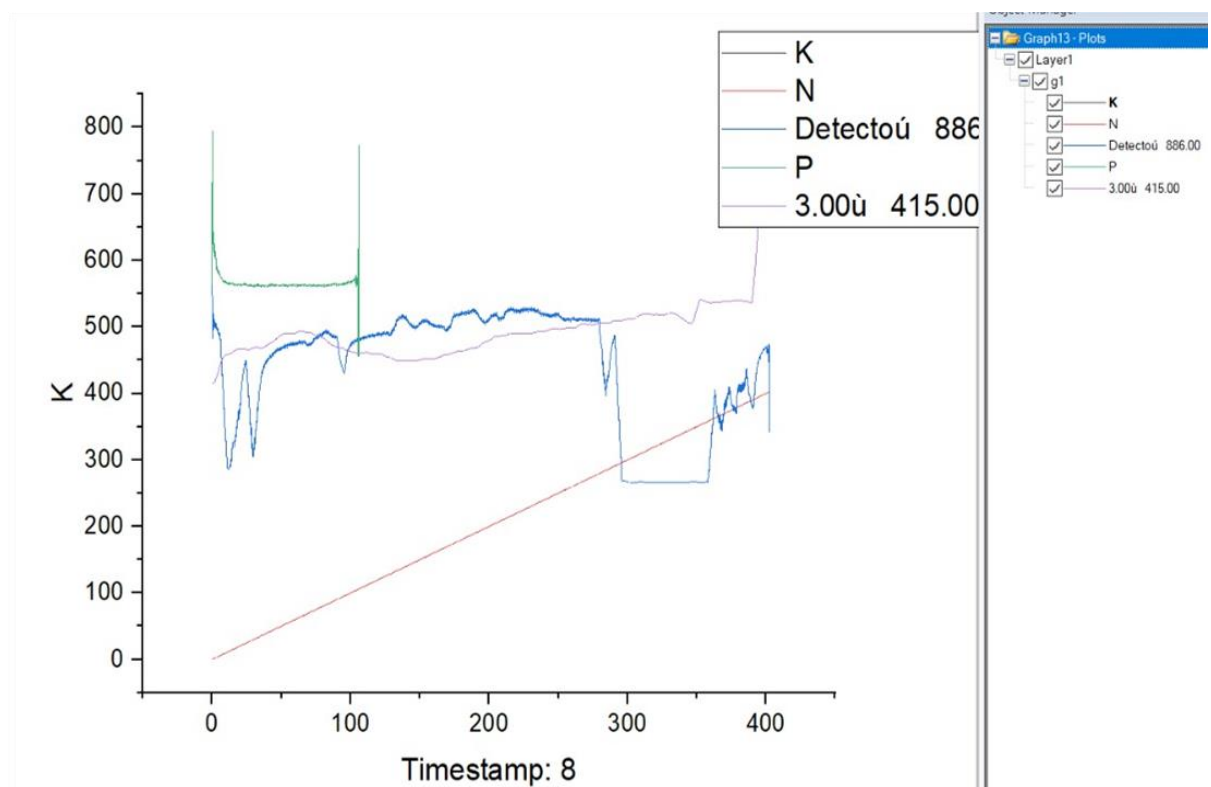


Fig:4.30: Intensity vs time graph for all speed in syringe- Iteration 1

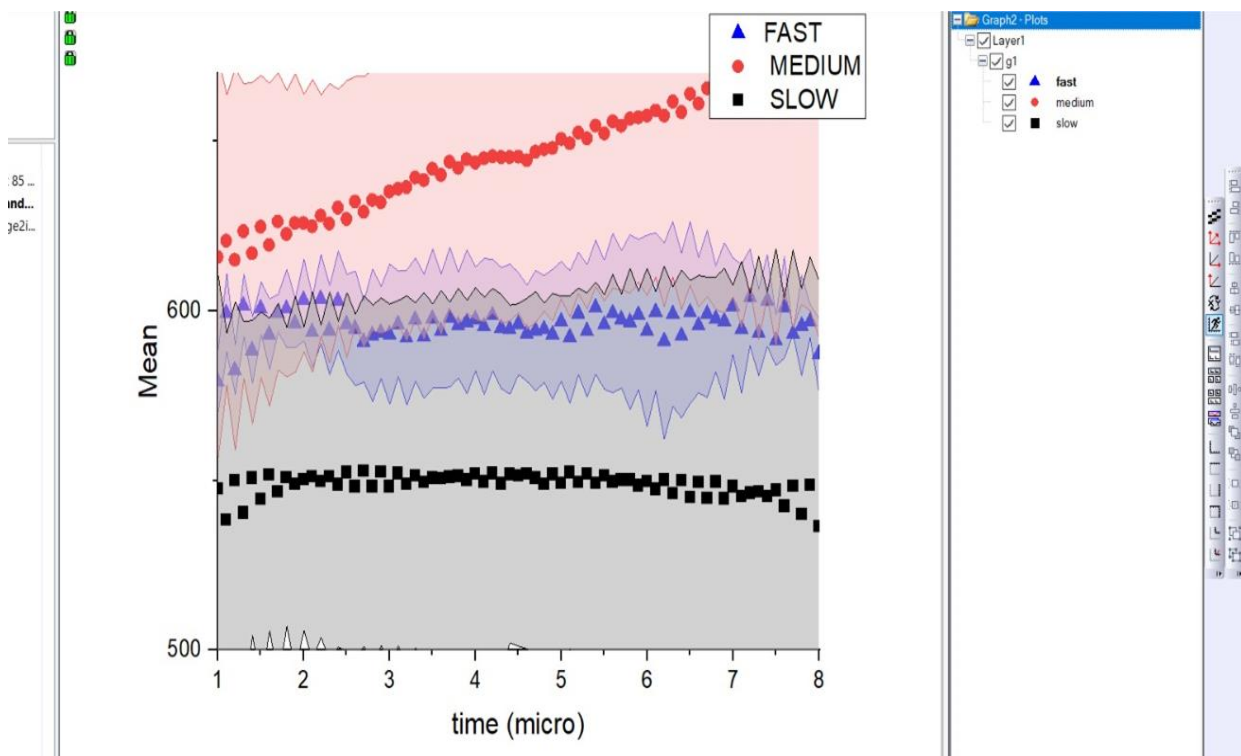


Fig:4.31: Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 2

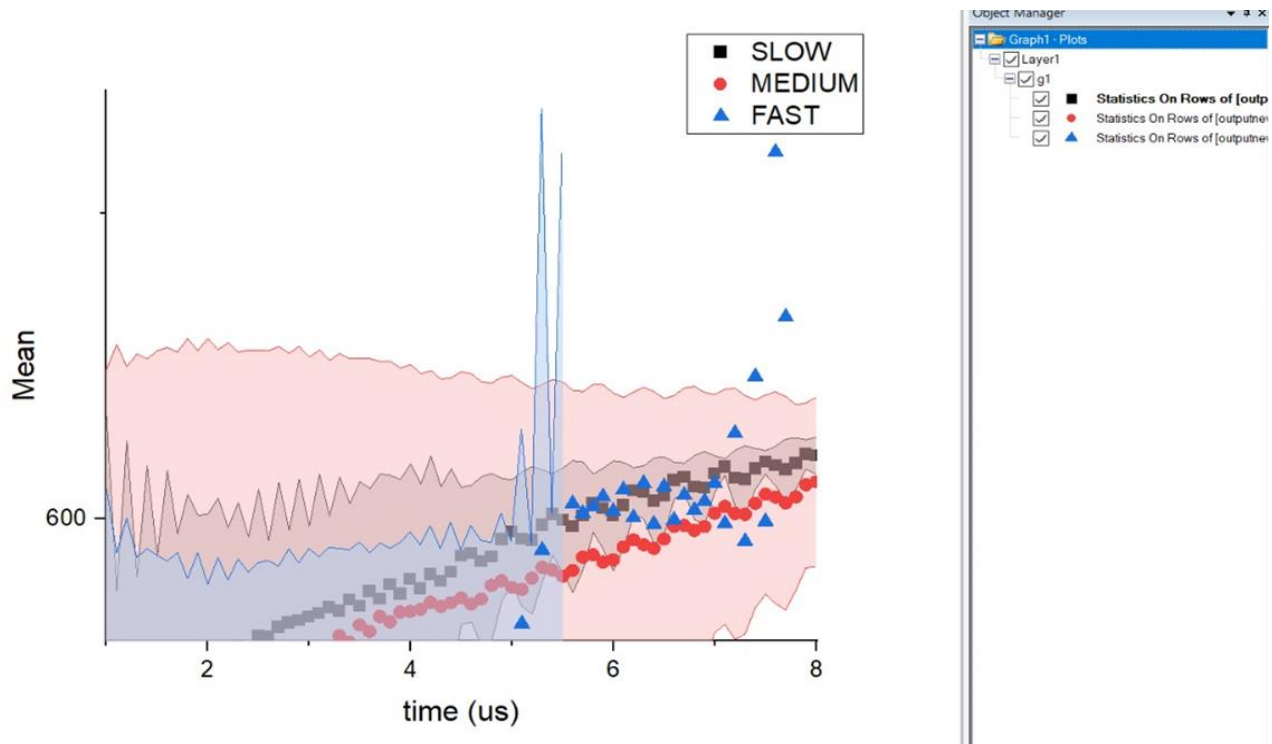


Fig:4.32: Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 3

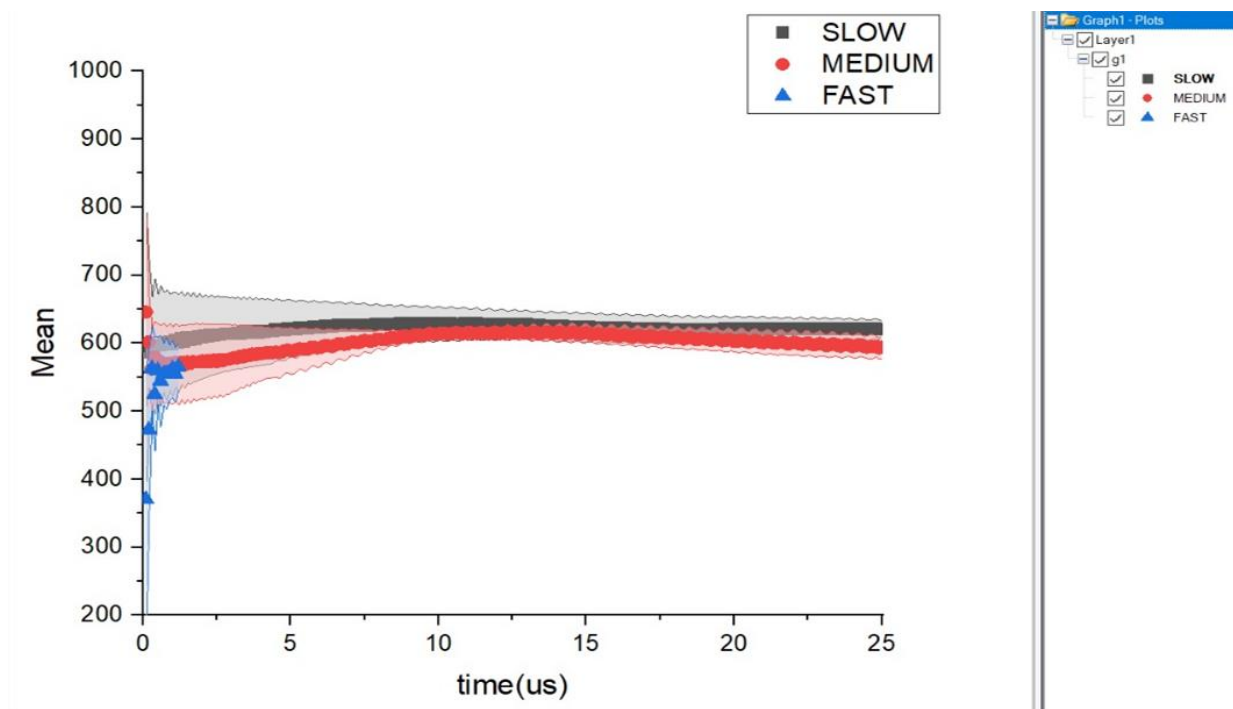


Fig:4.33: Intensity v/s time error band graph for all speed in syringe with mean and standard deviation – Iteration 4

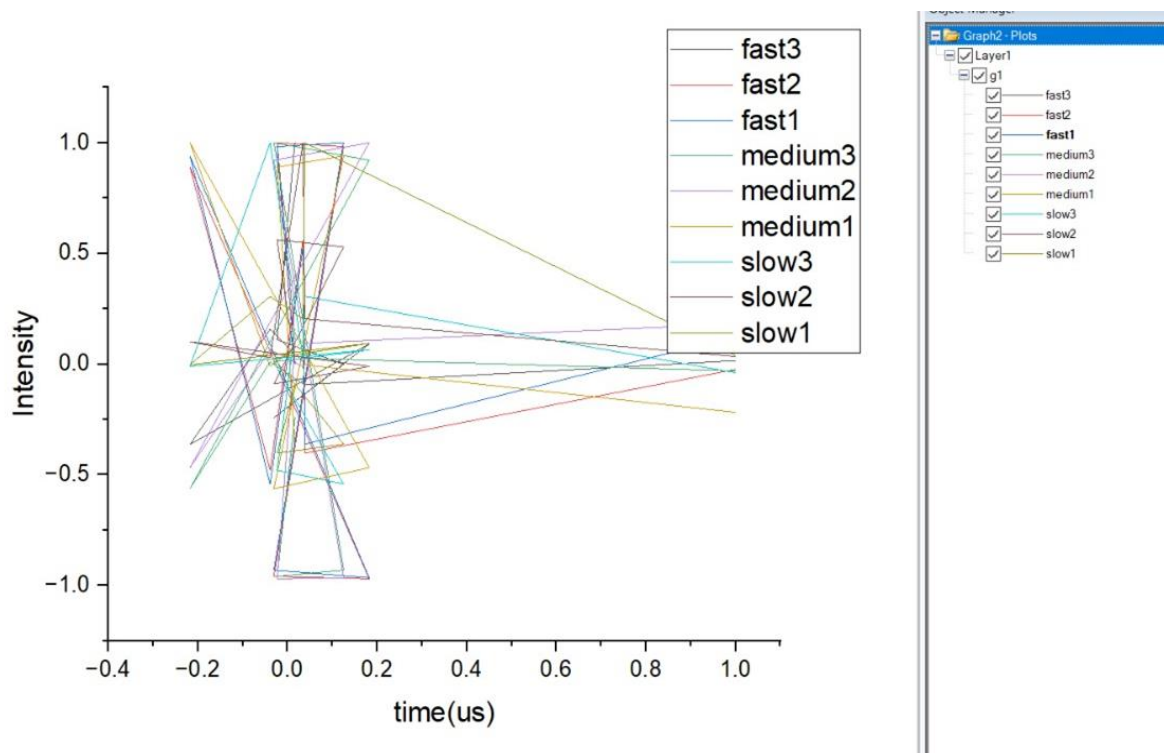


Fig:4.34: Pearson autocorrelation for Iteration 4

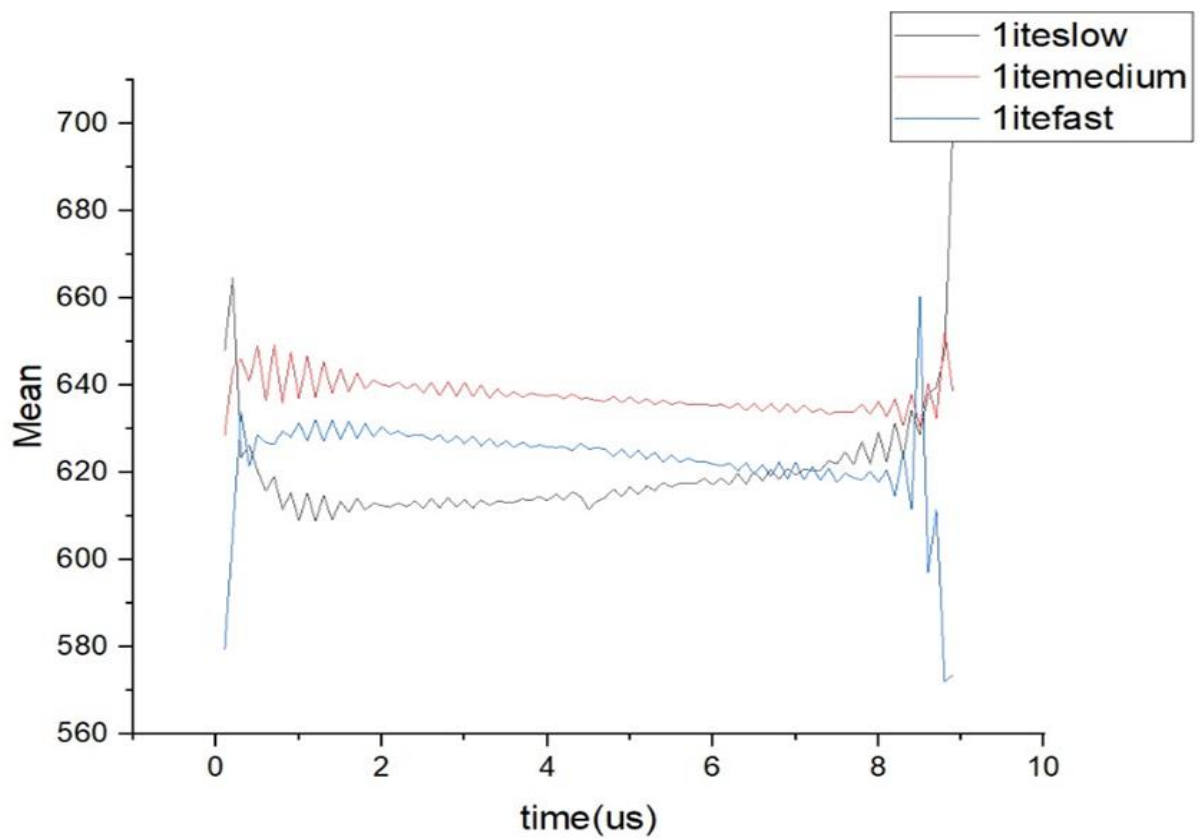


Fig:4.35: Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 5

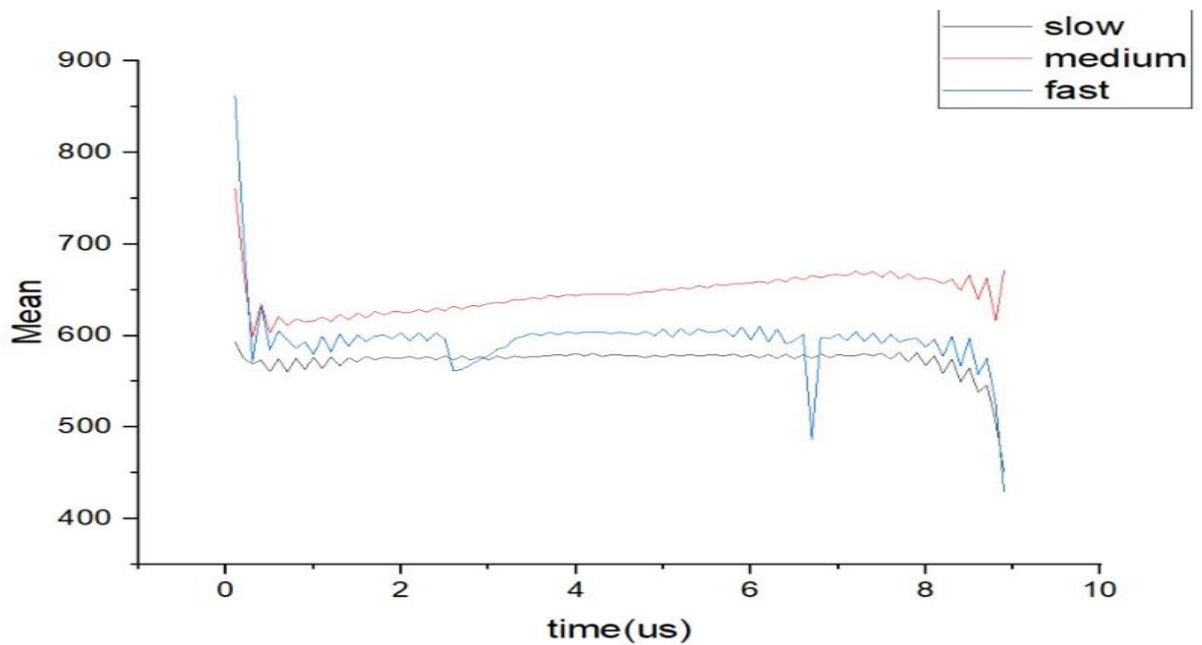


Fig:4.36: Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 6

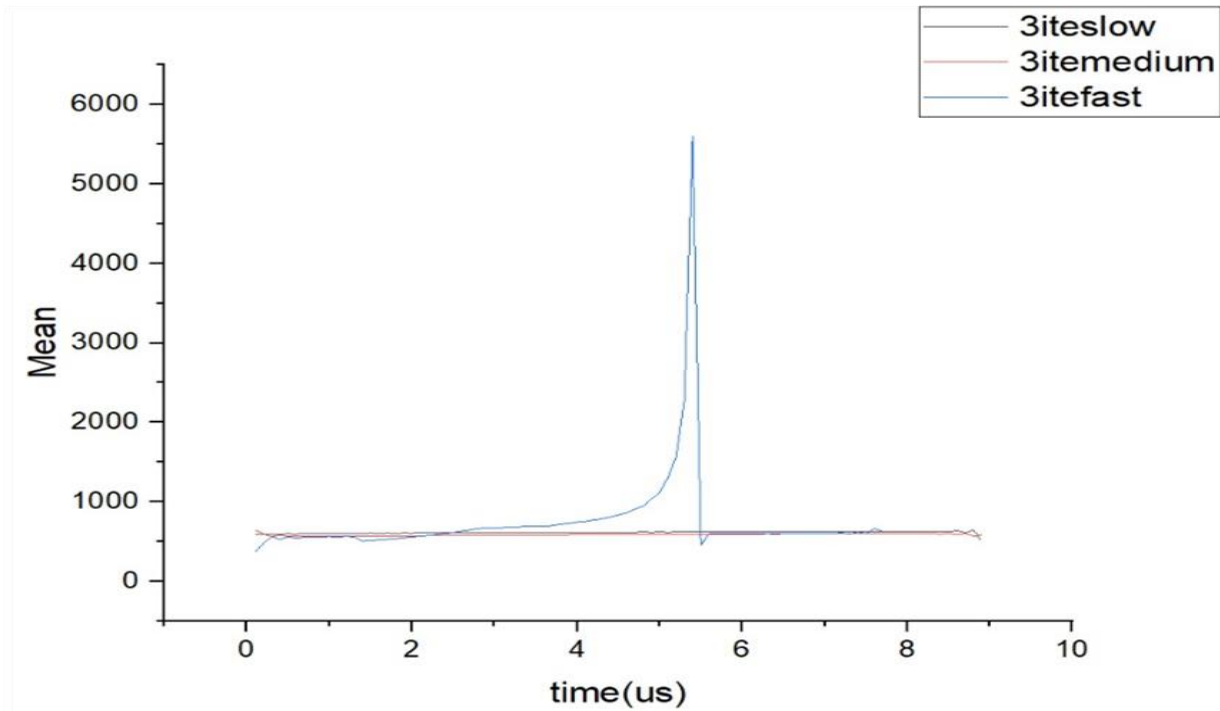


Fig:4.37: Intensity v/s time graph for all speed in syringe with mean and standard deviation – Iteration 7

4.4.3 MATLAB

A high-level programming language and interactive environment primarily used for numerical computing, data analysis, algorithm development, and visualization in engineering and scientific applications. The following iterations refine the code to achieve normalized output that aligns with the theoretical hypothesis, verified with known data, correlating practical results with expected trends. This verification process serves to confirm the accuracy of the experimental methodology. In MATLAB, we iteratively refine the code to ensure that the autocorrelation drop corresponds appropriately with flow speed: a faster drop indicating fast flow, a slower drop indicating slow flow, and so forth. It's crucial to note that discrepancies between the theoretical hypothesis and practical values in MATLAB prompt code refinement, as the known accuracy of the experiment suggests that any deviations are likely due to code errors rather than experimental inaccuracies. Thus, multiple iterations are undertaken to achieve alignment between the normalized autocorrelation outputs and the expected trends, thereby reinforcing the reliability of the experimental approach.

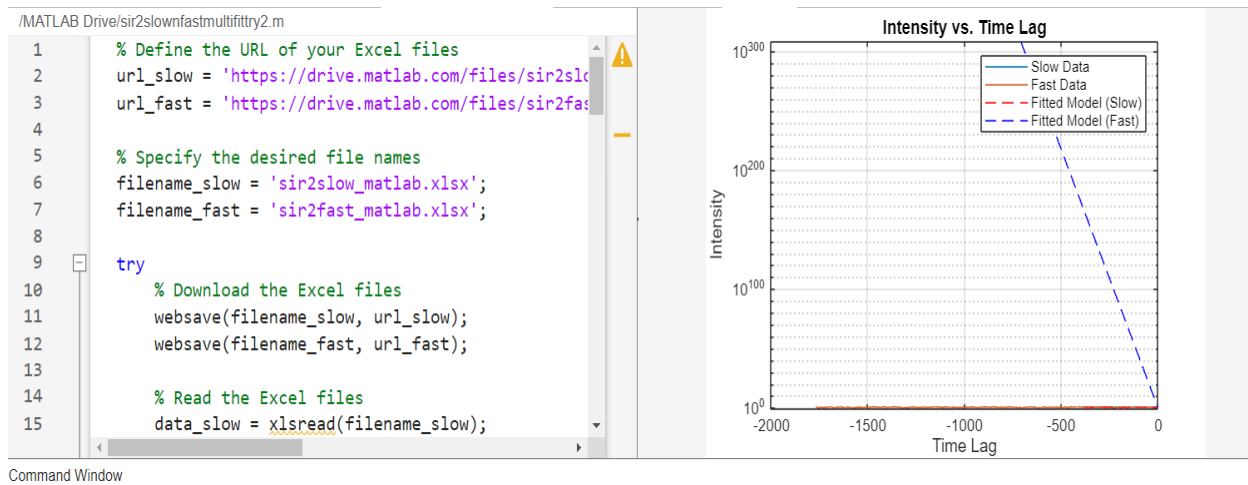


Fig:4.38: Autocorrelation of intensity vs time - Iteration 1

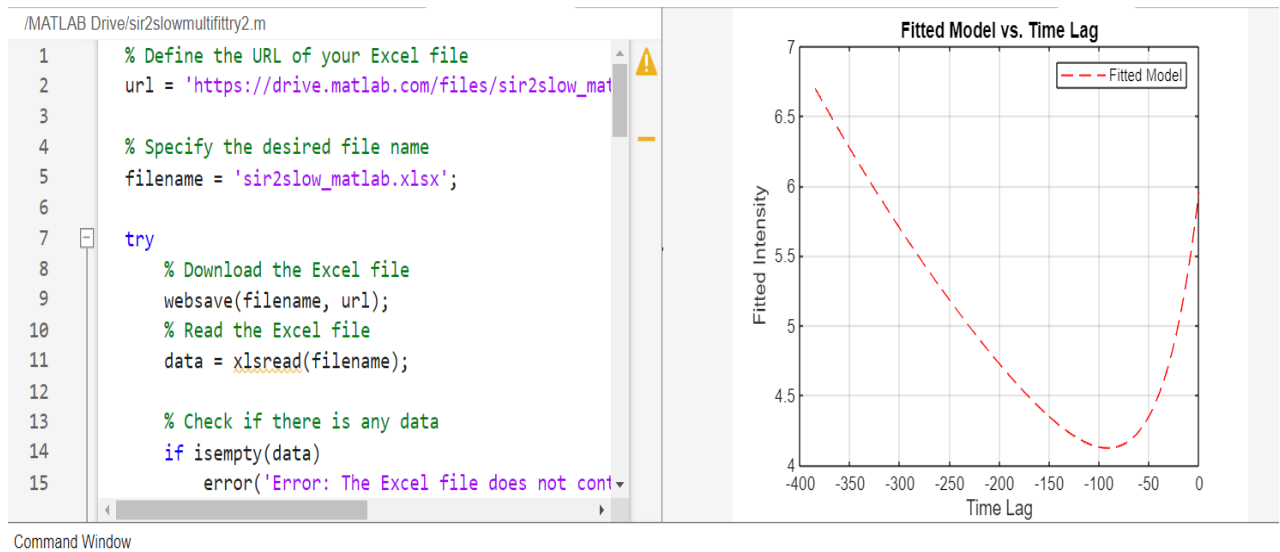


Fig:4.39: Autocorrelation of fitted model - Iteration 2

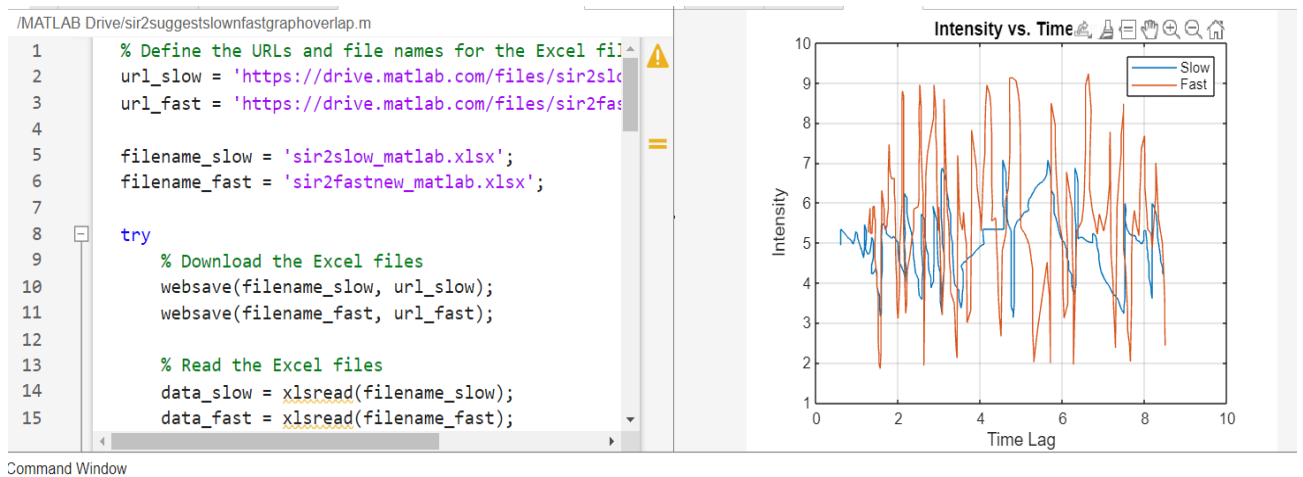


Fig:4.40: Autocorrelation of intensity vs time - Iteration 3

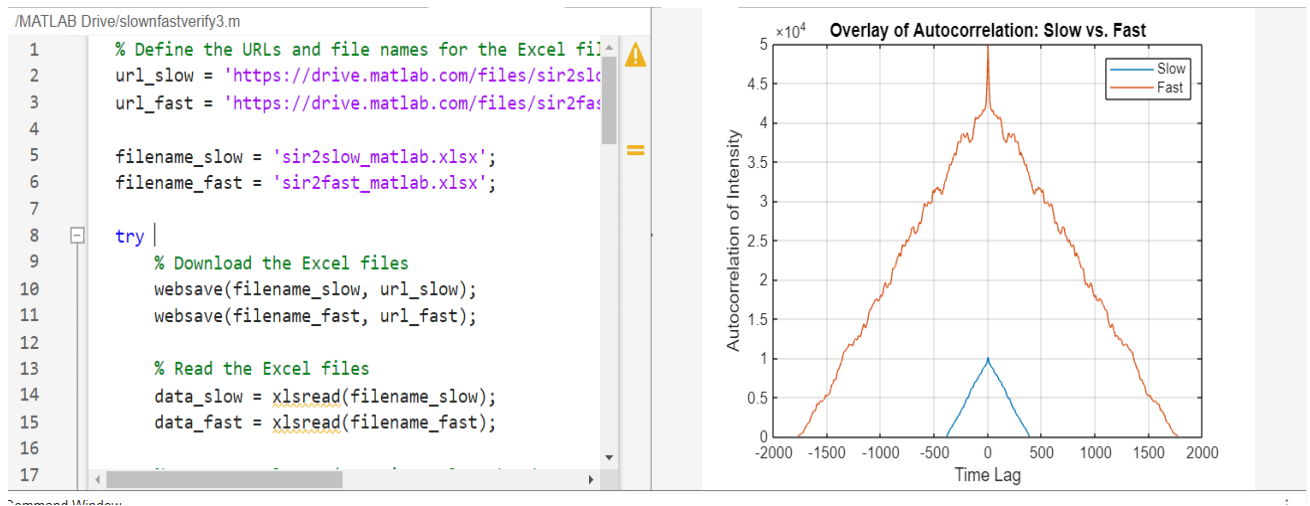


Fig.4.41: Autocorrelation of intensity vs time lag- Iteration 4

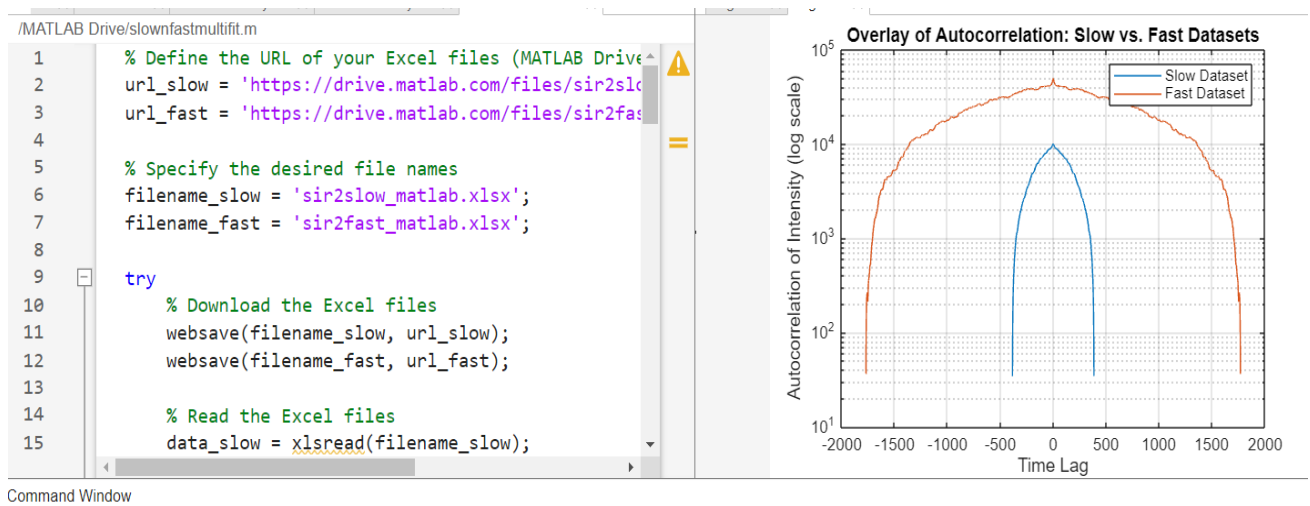


Fig.4.42: Autocorrelation of intensity vs time lag- Iteration 5

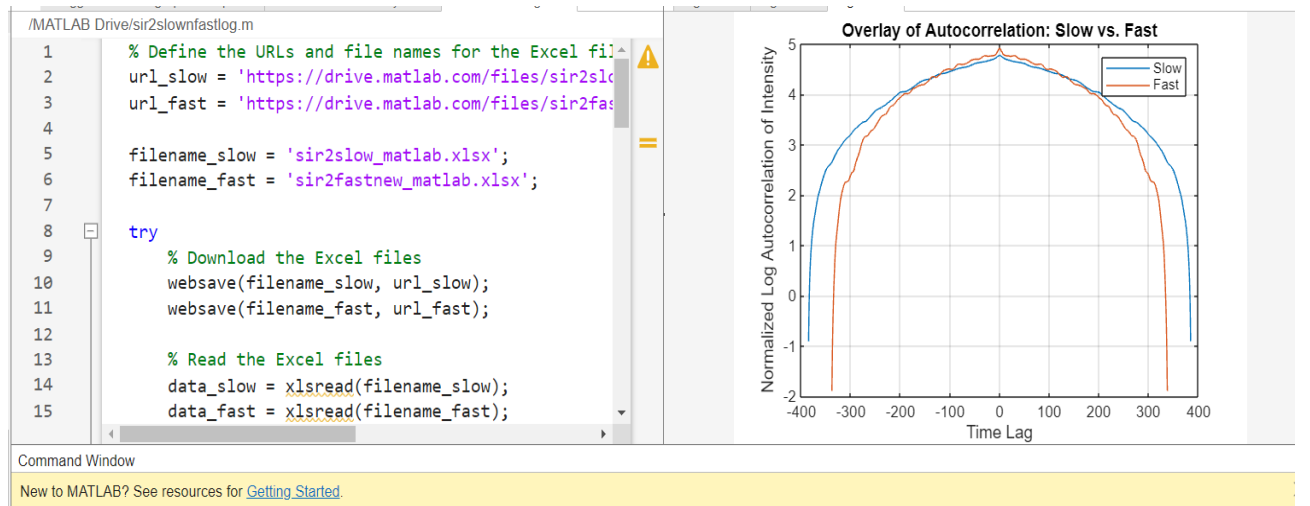


Fig.4.43 Autocorrelation of intensity vs time lag- Iteration 6

4.4.4 EasyEDA

EasyEDA is a web-based Electronic Design Automation (EDA) tool suite, offering schematic capture, PCB layout, and component libraries for designing electronic circuits. The following iterations aim to make the PCB board more compact by orienting components through THT (Through-Hole Technology) and simplifying the circuit by reducing the number of components.

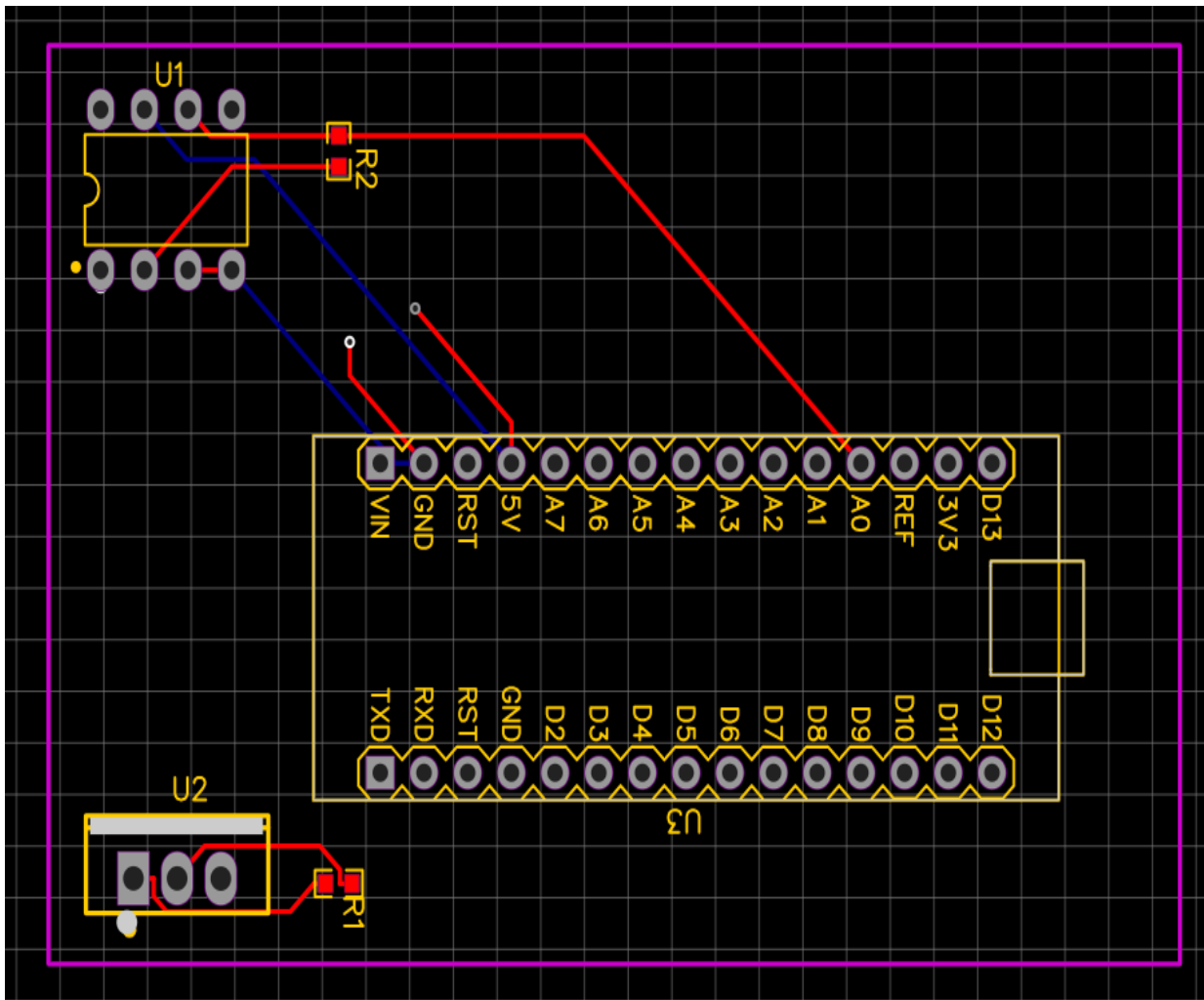


Fig:4.44: PCB iteration1

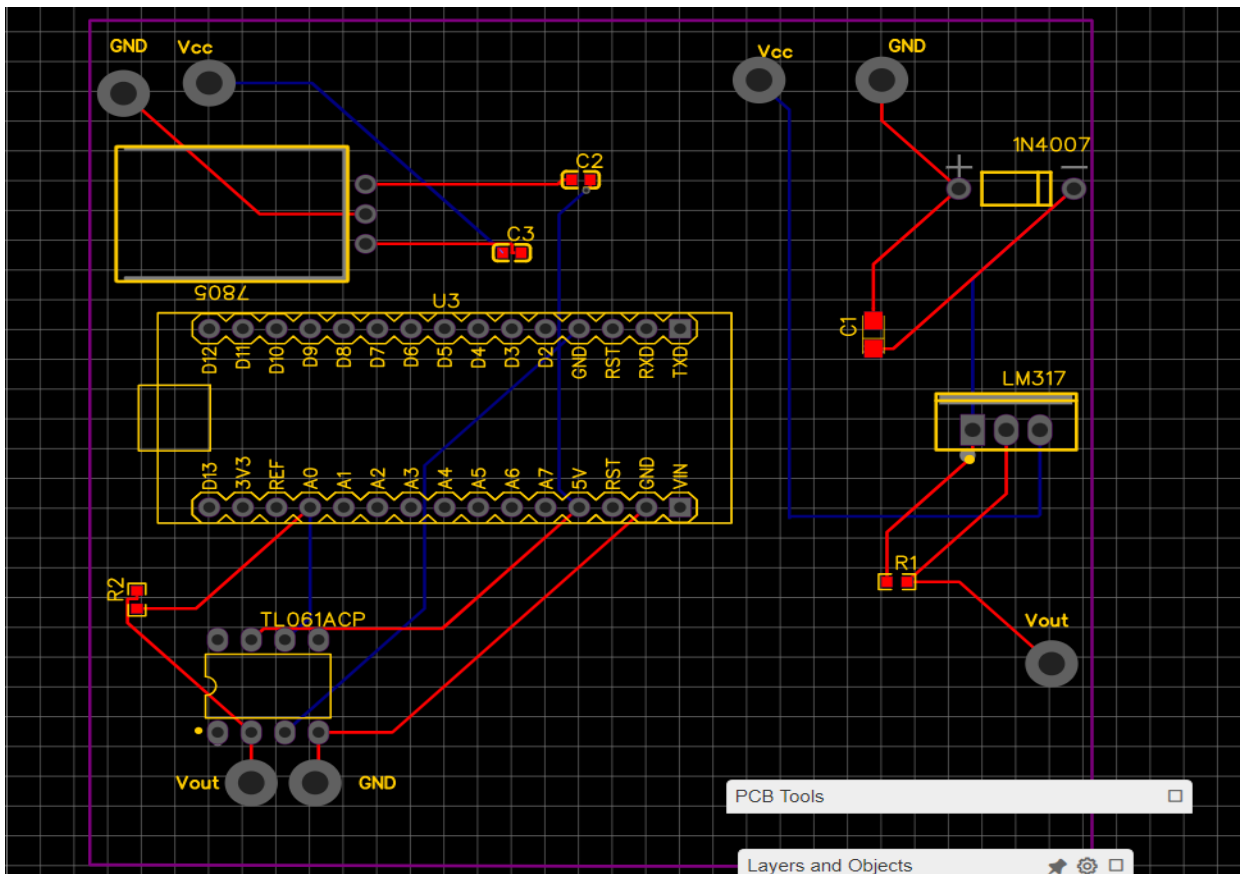


Fig:4.45: PCB iteration2

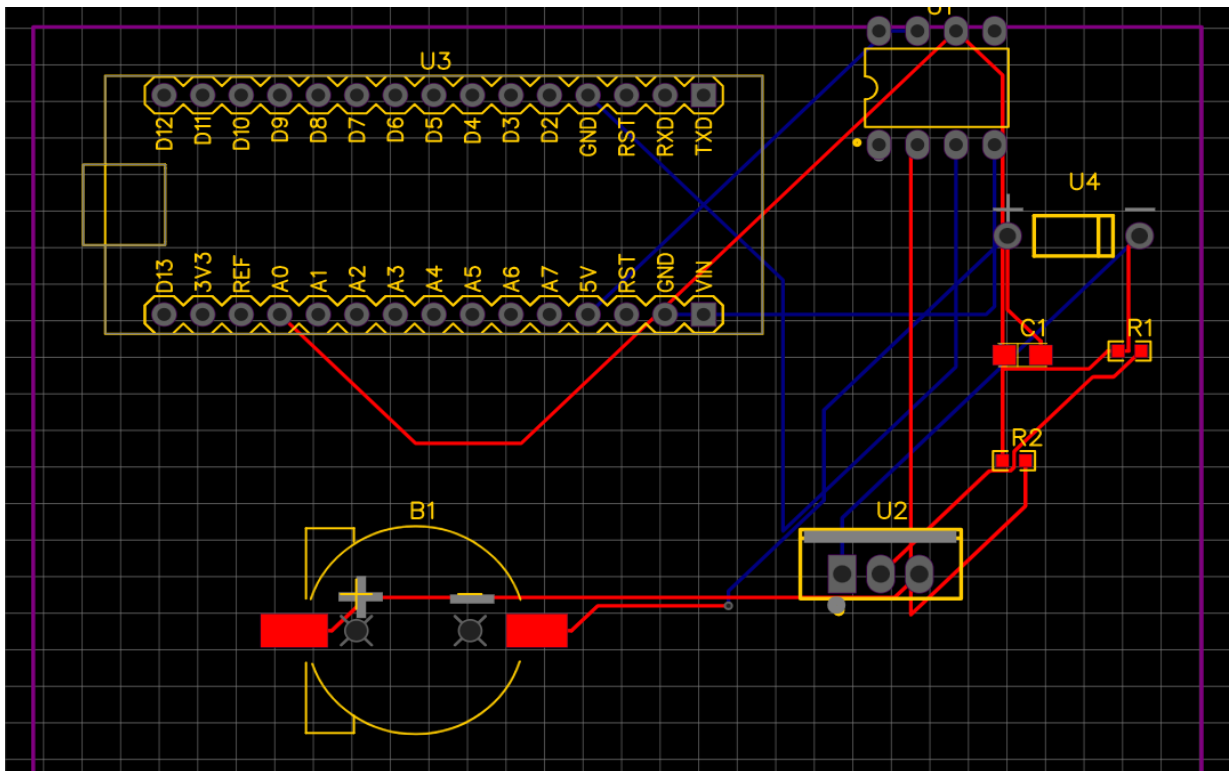


Fig:4.46: PCB iteration3

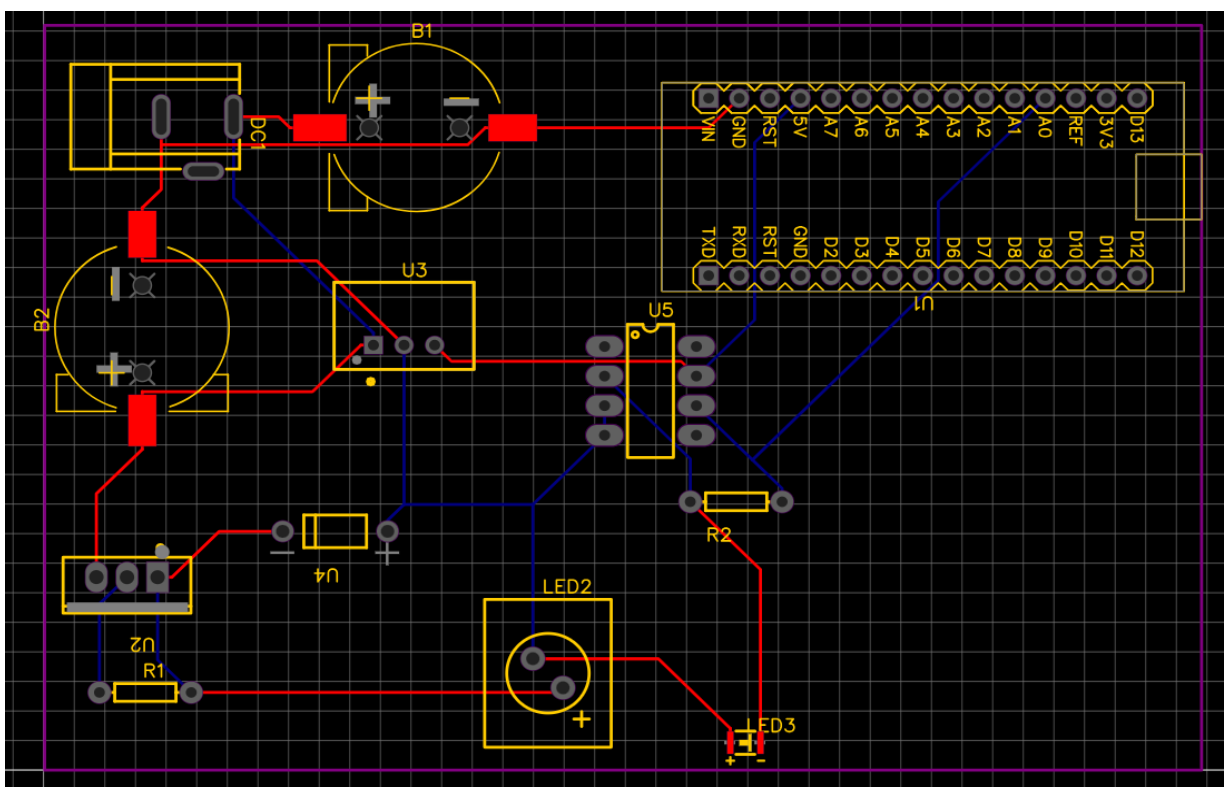


Fig:4.47: PCB iteration4

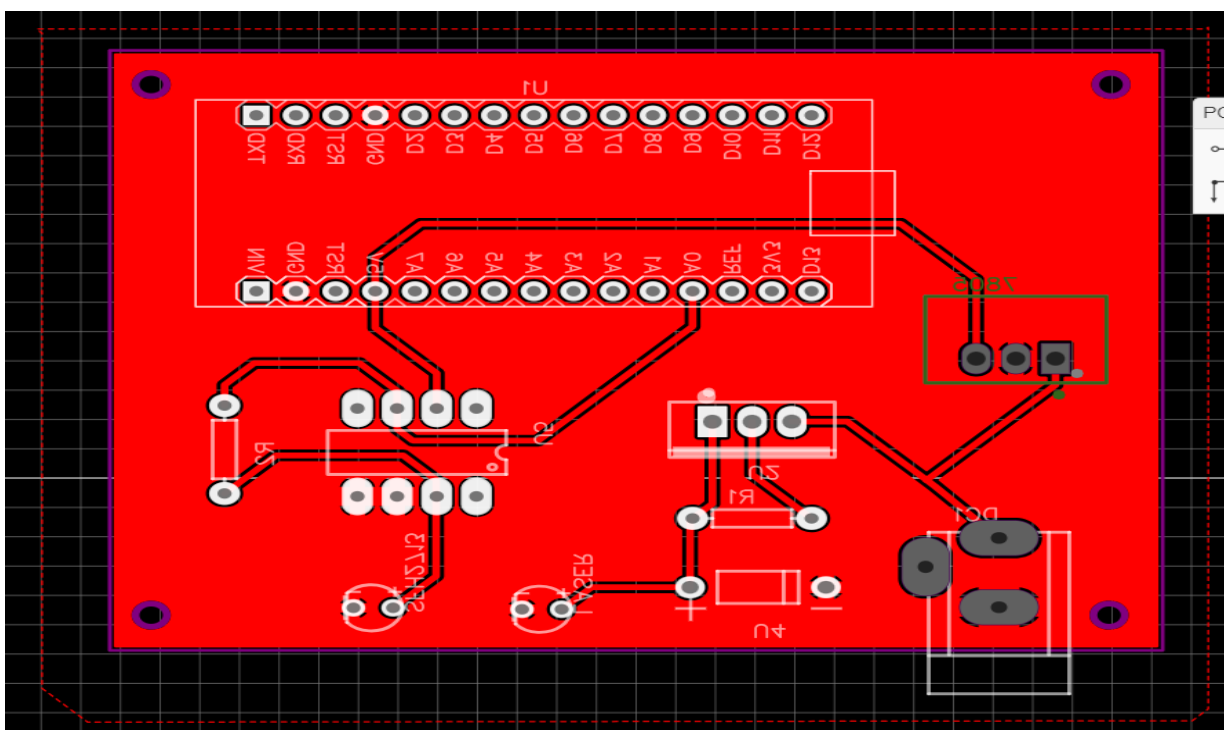


Fig:4.48: PCB iteration5

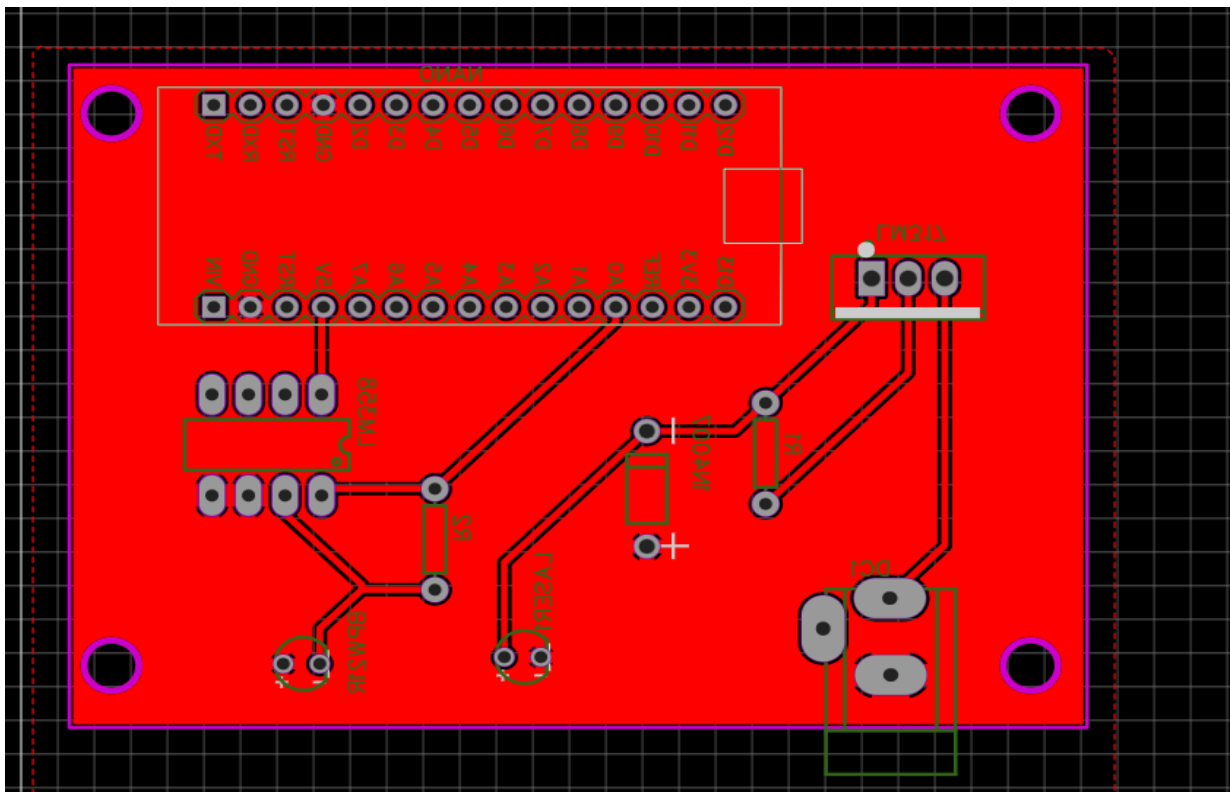


Fig.4.49: PCB iteration6

4.5 Working

The light source, whether it's a light-emitting diode (LED) or a laser, is carefully directed into the tissue, such as biological samples or human organs. This incident light interacts with moving scatterers within the tissue, predominantly red blood cells (RBCs). The dynamic motion of these RBCs induces fluctuations in the intensity of the scattered light. The photodetector plays a pivotal role by capturing the scattered light and converting it into a signal that is recorded over time. This temporal intensity profile reflects the changes in the tissue caused by blood flow. The key feature of DCS lies in the correlation analysis of these intensity fluctuations over different time lags. By correlating the intensity-versus-time data, DCS provides insights into the velocity and dynamics of blood flow within the tissue. The correlation analysis yields blood flow parameters, including blood flow index and blood velocity. These parameters are invaluable in assessing tissue perfusion, which is crucial for understanding the physiological and pathological conditions of the tissue under investigation. DCS finds applications in various medical fields, such as neuroscience, oncology, and critical care, offering a non-invasive and real-time approach to monitor blood flow in a diverse range of biological tissues.

Operational Steps:

1. Finalize the Detector and Laser Source: Select and calibrate the photodetector and diode laser for optimal performance in the NIDCS setup.
2. Circuit Compatibility Testing: Ensure that the photodetector and laser source are compatible with the data acquisition system and signal processing circuitry.
3. Acquisition of Data from Conditioned Environment: Conduct experiments in a controlled environment to acquire baseline data and minimize external factors affecting measurements. Input Intensity Values: Input the intensity values recorded by the photodetector into the data processing system.
4. Initialize to Store Autocorrelation Values: Initialize variables to store autocorrelation values calculated for different time lags.
5. Calculate Autocorrelation Values for Each Time Lag: Perform autocorrelation analysis on the intensity-versus-time data to calculate correlation coefficients for various time lags.
6. Add the Autocorrelation Values to the List: Store the autocorrelation values in a list or array for further analysis and visualization.
7. Plot the Autocorrelation Values: Generate plots to visualize the autocorrelation values and identify characteristic features related to blood flow dynamics.
8. Input Area Values from the Graph Obtained: Analyze the plotted data to determine relevant parameters such as blood flow index and blood velocity.
9. Plot the Data Using the plot() Function: Utilize data visualization tools, such as the plot() function in programming languages like Python or MATLAB, to present the results in a clear and interpretable manner.

These operational steps outline the process of conducting NIDCS experiments and analyzing the obtained data to extract meaningful insights into tissue perfusion and blood flow dynamics.

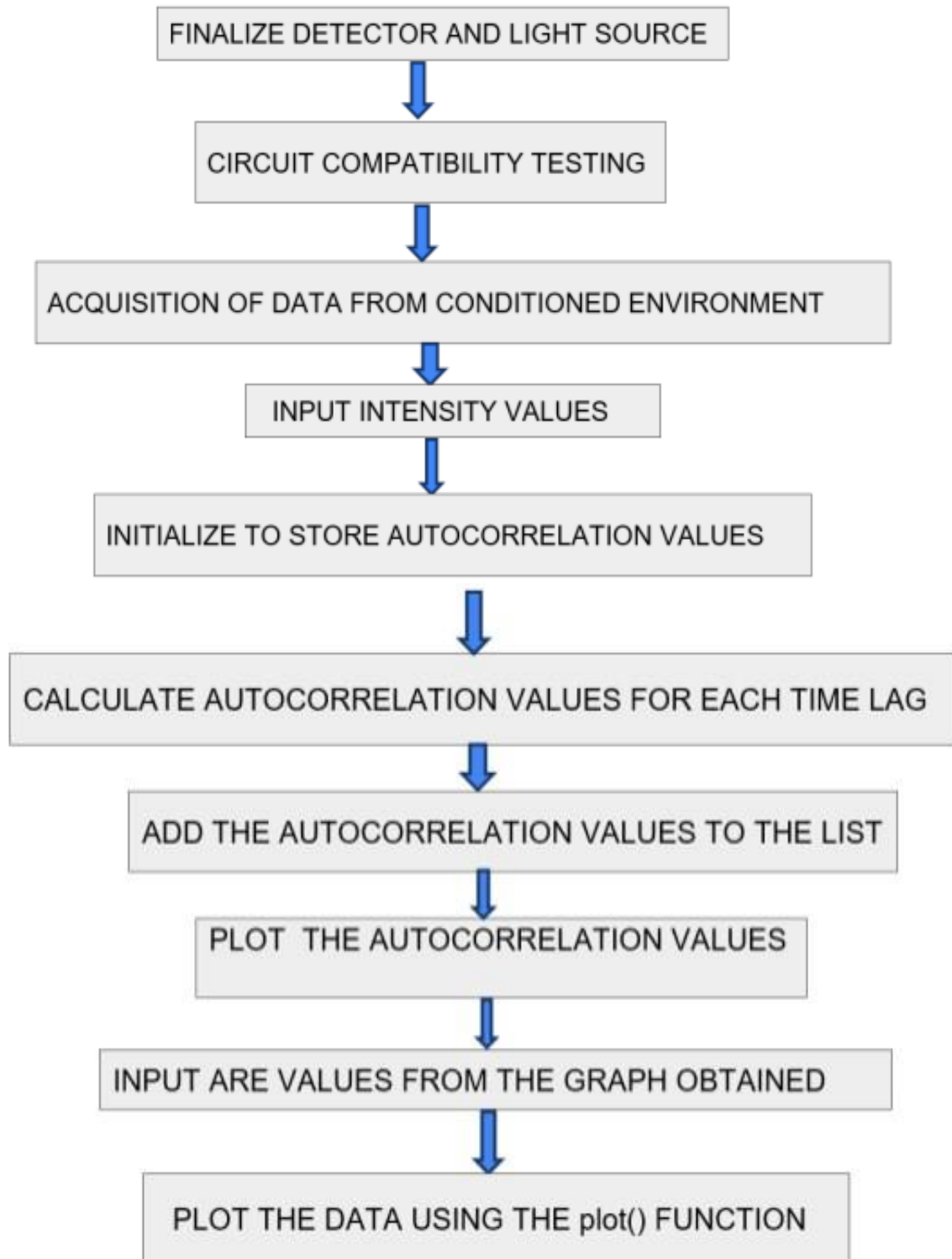


Fig:4.50: Workflow of DCS

CHAPTER-5

RESULTS AND DISCUSSIONS

5.1 RESULT

5.1.1 Final probe of DCS

The final Diffuse Correlation Probe (DCS) design features a compact rectangular shape, optimized for ease of handling and precise data capture. At the top of the probe, there is a strategically placed switch, allowing for intuitive and convenient operation. This switch likely serves as a control mechanism, enabling users to turn the probe on/off or perhaps toggle between different measurement modes. Towards the edges of the rectangular design, two critical components are positioned: the detector and the laser. These components are strategically located to facilitate efficient and accurate data collection during diffuse correlation spectroscopy (DCS) measurements.

1. **Detector:** Positioned at one edge of the probe, the detector is responsible for capturing the scattered light signals from the tissue or material being analyzed. It is likely equipped with high sensitivity and precision to detect subtle changes in light scattering, which are indicative of blood flow dynamics or other relevant physiological parameters.

2. **Laser:** Located opposite to the detector, the laser emits coherent light that penetrates the tissue or material under investigation. This emitted light interacts with moving scatterers within the medium, such as blood cells in biological tissue, leading to changes in light scattering patterns. These changes are then detected by the adjacent detector, providing valuable information about blood flow or tissue perfusion.

The compact and streamlined design of the DCP, along with the strategically positioned switch and critical components, ensures that users can easily handle the probe and obtain reliable data during diffuse correlation spectroscopy experiments. This design likely enhances the versatility and usability of the probe, making it a valuable tool for researchers and clinicians in various fields, including biomedical imaging, neuroscience, and tissue engineering

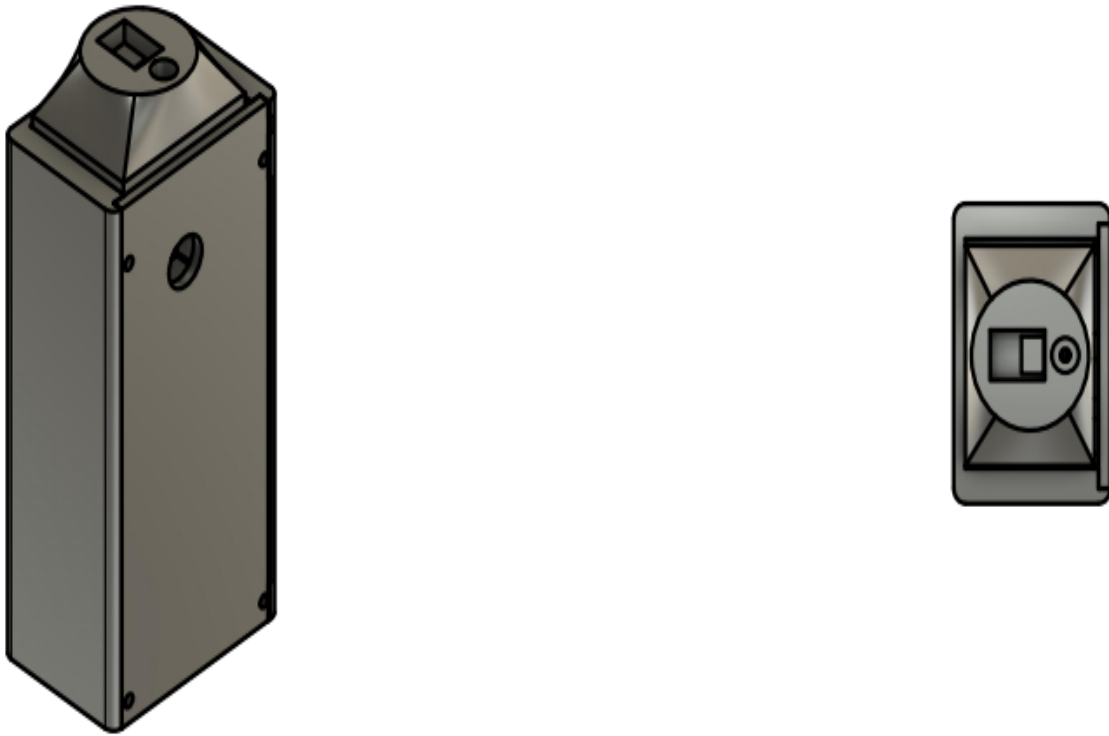


Fig:5.1: Final probe design for DCS



Fig:5.2: Front view of Final probe for DCS



Fig:5.3: Top view of Final probe for DCS

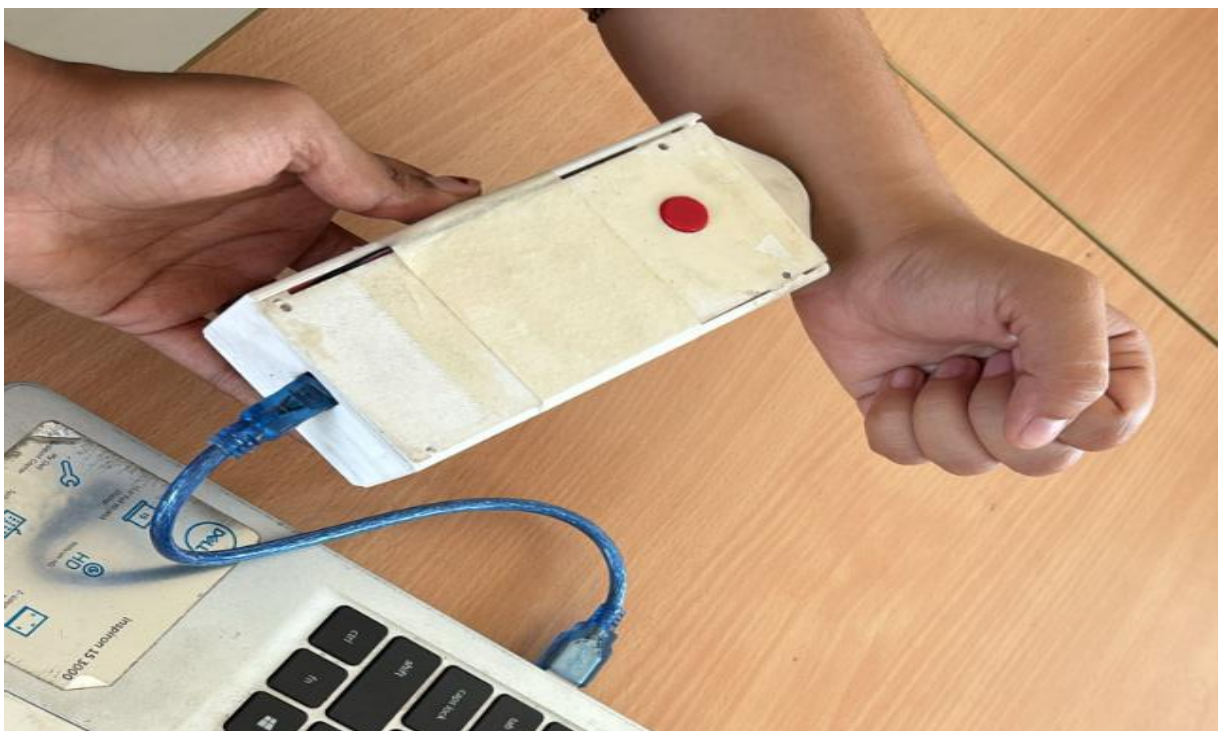


Fig:5.4: Data acquisition using probe

5.1.2 Final circuit design and PCB of DCS

The final circuit design for integration into the probe has been meticulously planned to ensure easy access and seamless integration with the overall system. The circuit comprises essential components including a transistor, a laser, a photodetector, an Arduino microcontroller, an operational amplifier (op-amp) for laser control, and a switch for overall control of both the laser and the detector. In this design, the base of the transistor is linked to pin D6 of the Arduino, with the emitter grounded and the collector connected to the cathode of the laser. The laser's anode is connected to the anode of a diode, responsible for stabilizing the laser's polarity. Both the anode of the laser and the cathode of the diode are then connected to the output pin of the LM317 op-amp. The LM317 op-amp's input is tethered to the 5V supply from the Arduino. Furthermore, the detector and the switch are also powered by the 5V supply from the Arduino. The output of the switch, along with the detector, is connected to pins D5 and A0 of the Arduino, respectively. This carefully arranged configuration not only ensures the smooth operation of the circuit but also facilitates easy troubleshooting and maintenance. To further streamline the integration process, the physical layout of the components on the PCB board has been optimized. Components have been positioned to maximize accessibility and minimize interference, simplifying assembly and maintenance tasks. Overall, this final circuit design, combined with the tailored PCB layout, offers a robust and user-friendly solution for the diffuse correlation probe system.

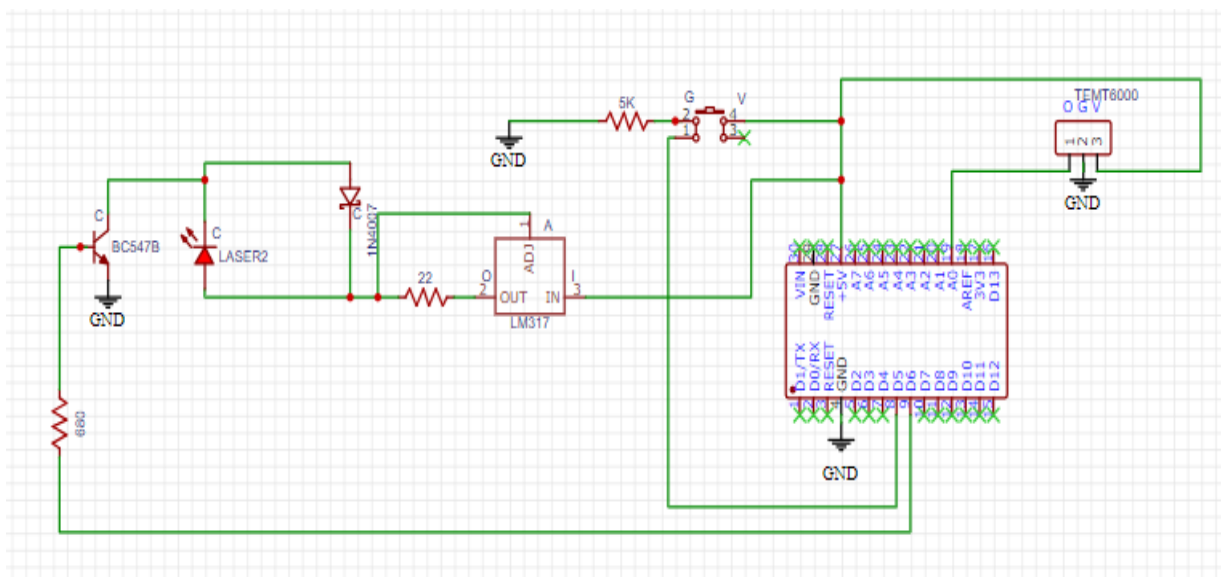


Fig:5.5: Final circuit design of DCS

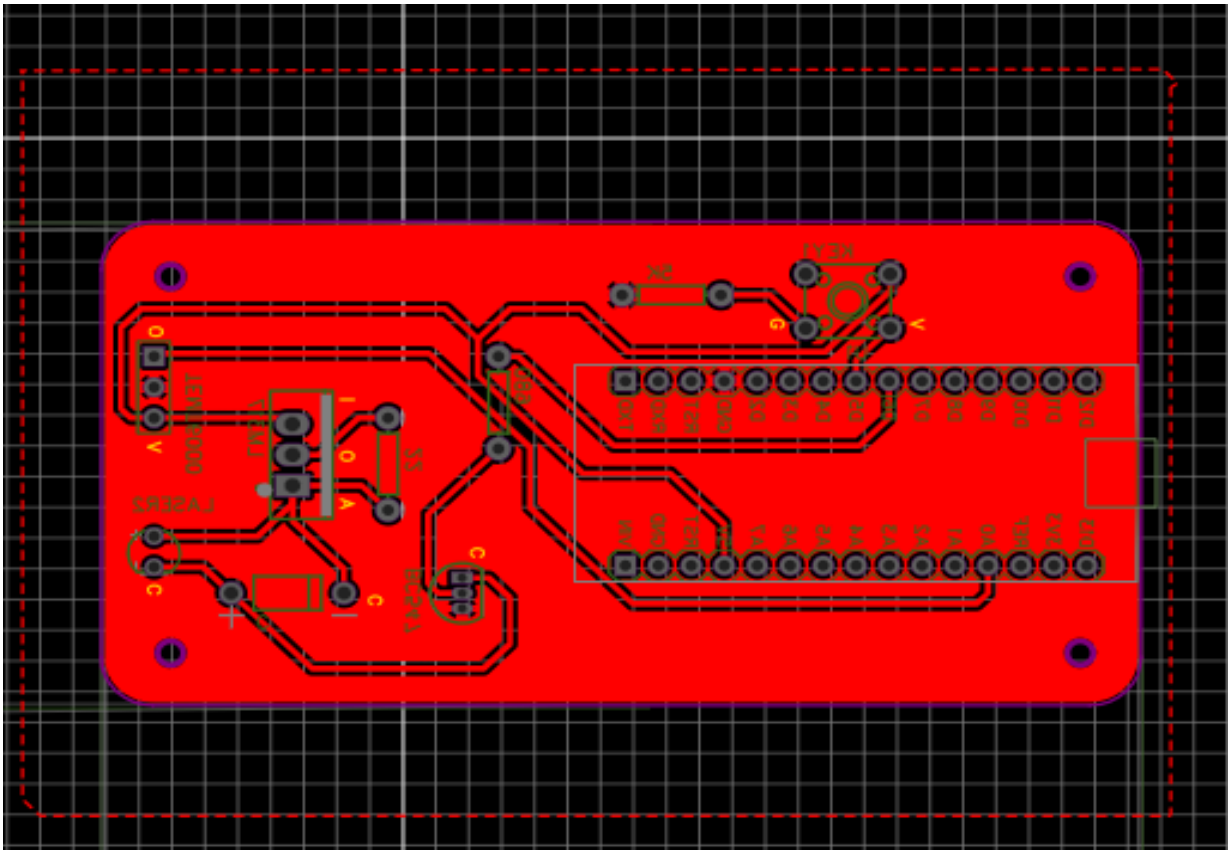


Fig:5.6: Final PCB design of DCS

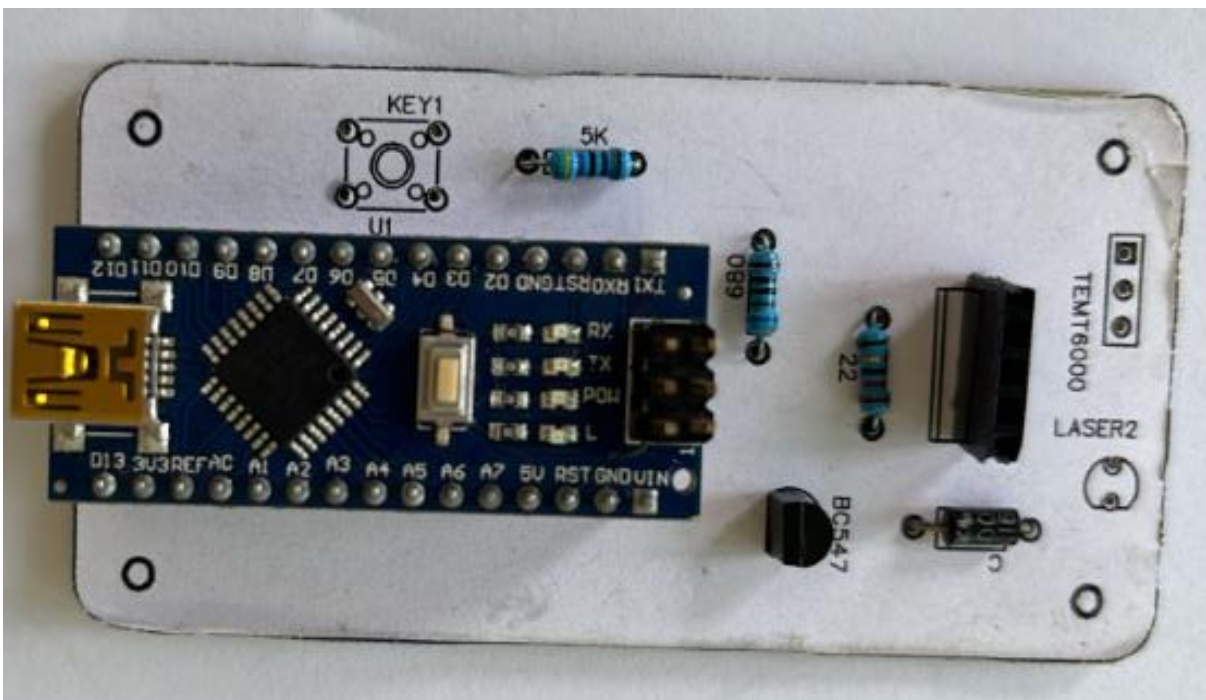


Fig:5.7: Top view of PCB for DCS

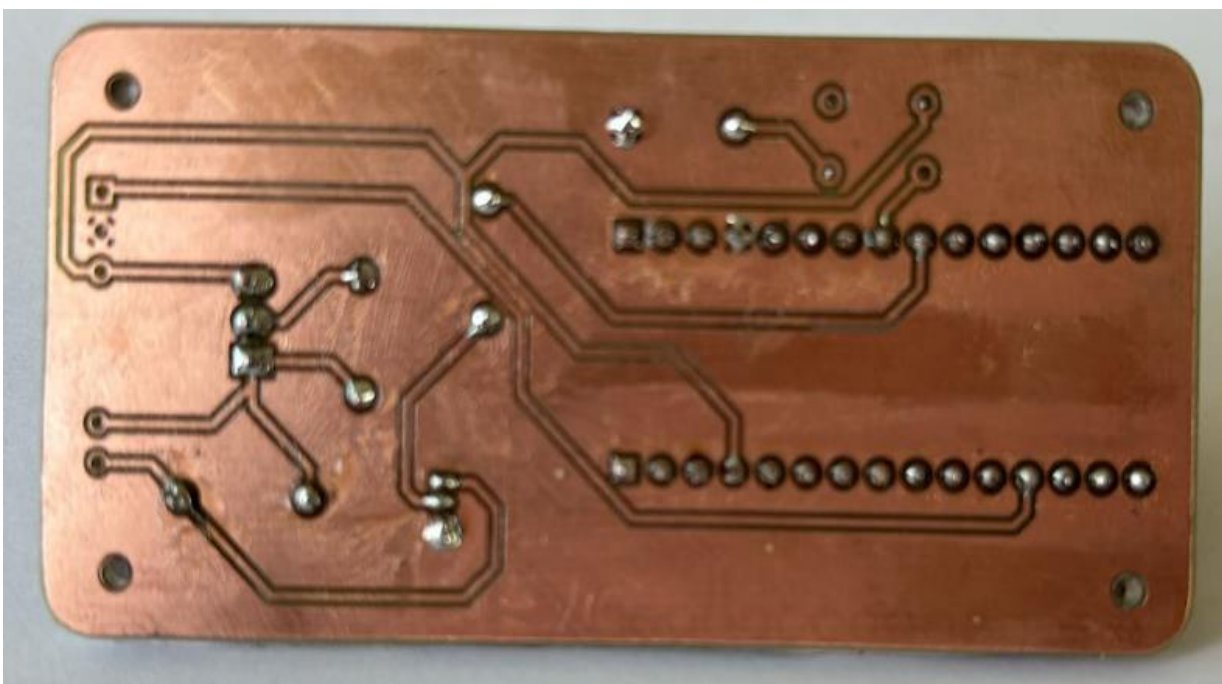


Fig:5.8: Bottom view of PCB for DCS

5.1.3 Theranostic Applications

In the experimental data collection phase, utilizing breadboards for assembling the setup, it was determined that pumping artificial blood using a motor provided the most effective method for data collection. The motor offers versatility with multiple speed modes, including medium, fast, and slow, which can be adjusted as needed. This flexibility likely allowed for better control over the flow dynamics of the artificial blood, optimizing the data collection process. Three different configurations for placing the laser and detector were tested: V-shaped, transmittance, and reflectance setups. Among these configurations, the transmittance setup emerged as the most effective based on the output analyzed in MATLAB. Transmittance configuration involves positioning the laser and detector on opposite sides of the medium (in this case, the artificial blood), with the laser emitting light that passes through the medium and is then detected by the sensor. This setup likely offered advantages in terms of signal clarity, allowing for more accurate measurement of light scattering and absorption properties of the medium. Overall, by employing a motor-driven pumping system for artificial blood circulation and selecting the transmittance setup for laser and detector placement, the experimental data collection process was optimized, yielding reliable results for further analysis and interpretation.

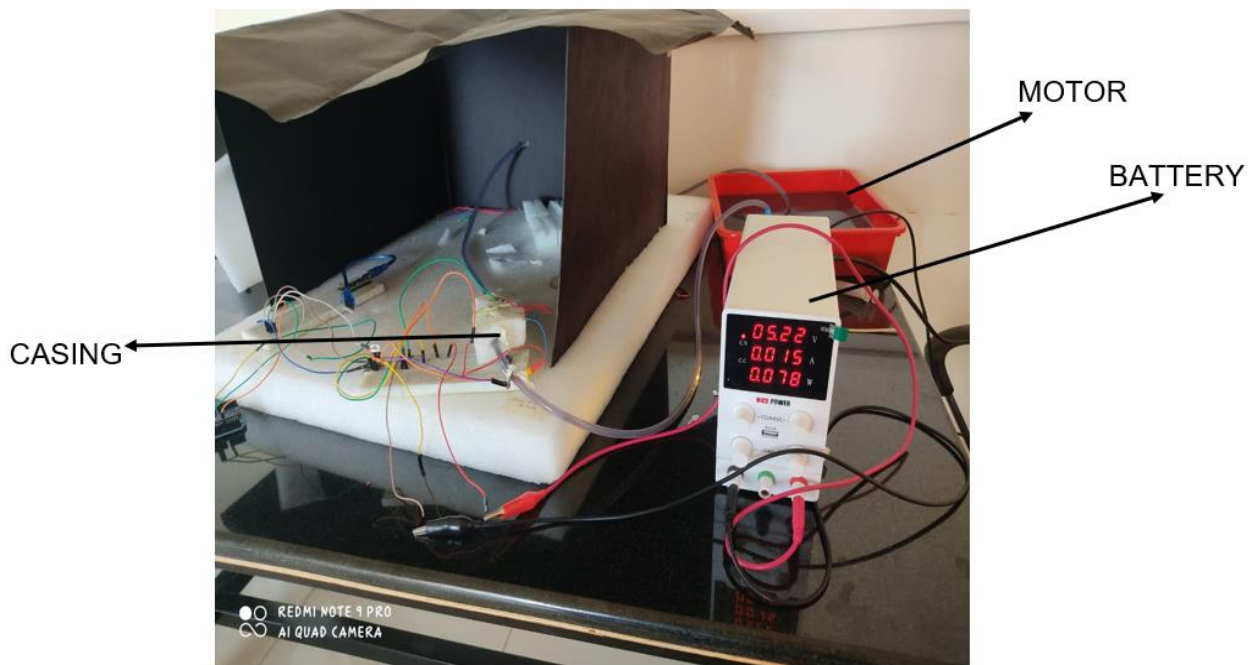


Fig:5.9: Motor Experiment to collect experimental data

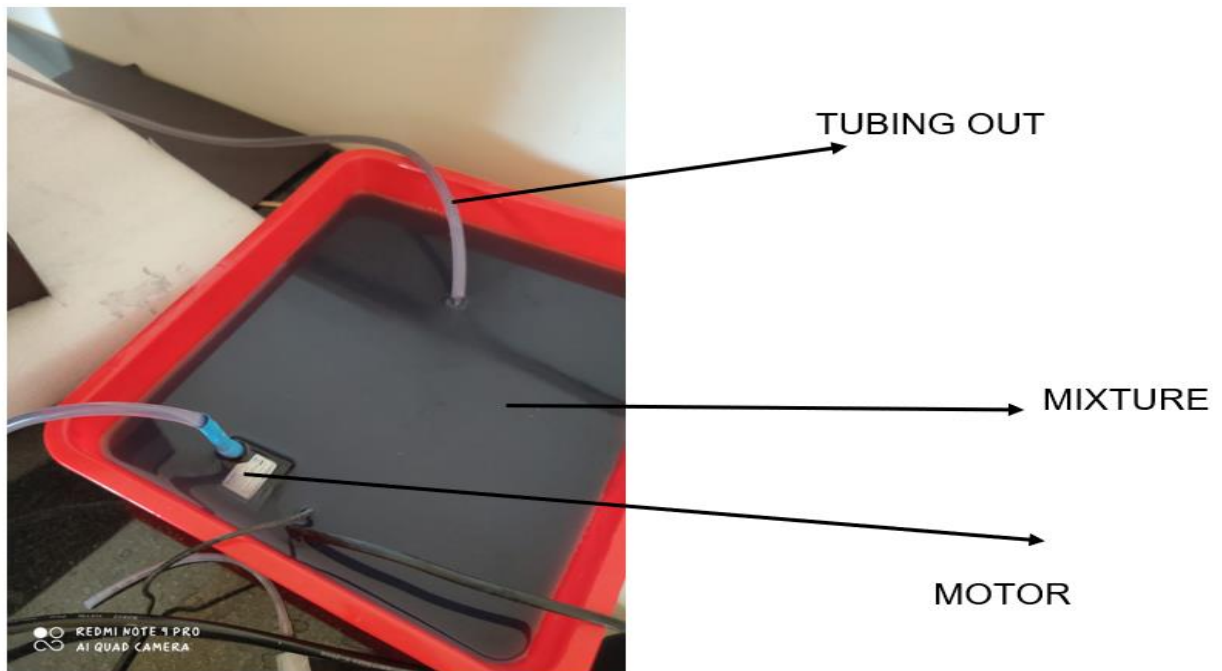


Fig:5.10: Collection tub for Motor Experiment to collect experimental data

5.1.4 Software

5.1.4.1 ARDUINO

The provided Arduino code serves as the final program to control the diffuse

correlation probe's operations. In the setup function, the code initializes serial communication at a baud rate of 9600 and configures the detector pin (A0) and switch pin (5) as inputs. During the loop function, the code continuously checks if the switch pin is set to HIGH, indicating activation of the detector. Upon activation, the detector pin is set to HIGH, and a message indicating the activation is printed via serial communication. Within the activation loop, the code records the start time using `millis()` and continues to run for a duration of 5000 milliseconds. During this period, the code reads the analog value from the detector pin, captures the current timestamp in microseconds using `micros()`, and prints both the detector reading and the timestamp via serial communication. The delay of 1 millisecond ensures stable performance.

Once the 5000 milliseconds duration elapses, the detector pin is set back to LOW, and a corresponding message indicating deactivation of the detector is printed via serial communication. This code efficiently controls the activation and deactivation of the detector while logging relevant data for further analysis, thus serving as a crucial component in the operation of the diffuse correlation probe system.

```

1  const int detectorPin = A0;
2  const int switchPin = 5;
3
4  void setup() {
5      Serial.begin(9600);
6      pinMode(detectorPin, INPUT);
7      pinMode(switchPin, INPUT);
8  }
9
10 void loop() {
11     if (digitalRead(switchPin) == HIGH) {
12         digitalWrite(detectorPin, HIGH);
13         Serial.println("Detector activated:");
14         unsigned long startTime = millis();
15         while (millis() - startTime < 5000) {
16             unsigned long timestamp = micros();
17             unsigned int microseconds = timestamp % 1000;
18             int reading = analogRead(detectorPin);
19             Serial.print("Detector1: ");
20             Serial.print(reading);
21             Serial.print("\tTimestamp: ");
22             Serial.println(microseconds);
23             delay(1);
24         }
25         digitalWrite(detectorPin, LOW);
26         Serial.println("Detector deactivated.");
27     }
28 }

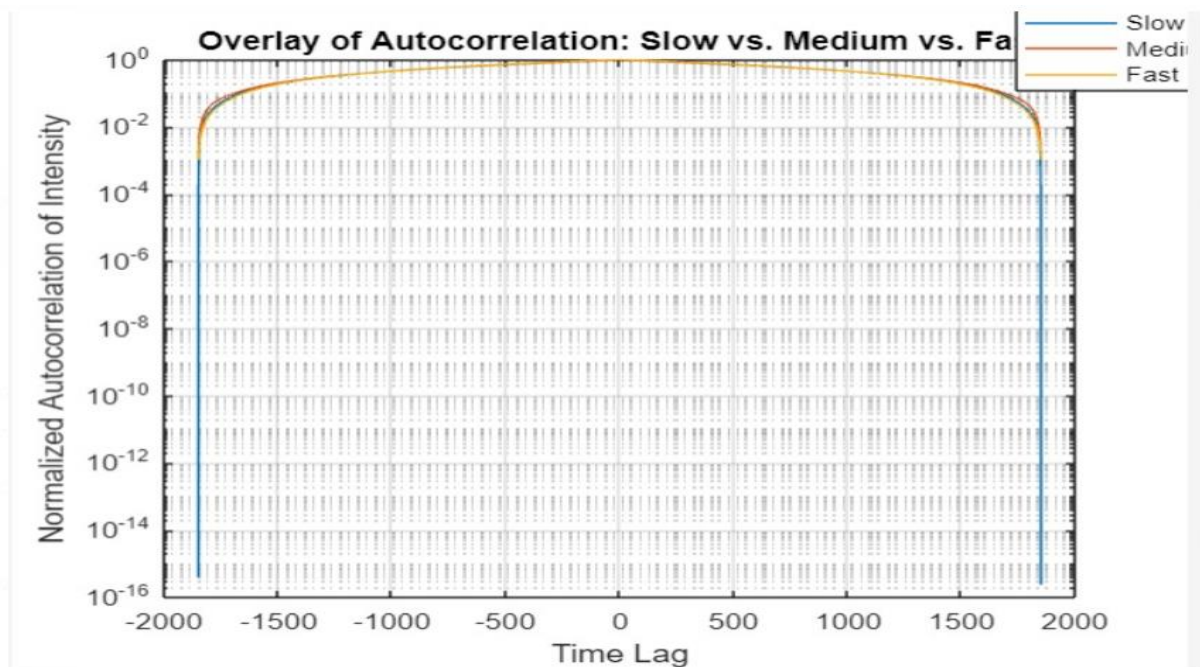
```

Fig:5.11: Final Arduino code for DCS

5.1.4.2 MATLAB

In the provided MATLAB output picture, we observe the results of autocorrelation analysis performed on artificial blood flow at three standardized flow rates: slow, medium, and fast. Autocorrelation is a statistical technique used to measure the similarity of a signal with a delayed version of itself over varying time lags. The plot likely depicts the autocorrelation function computed for each flow rate, with time lag plotted along the x-axis and the autocorrelation coefficient along the y-axis. The autocorrelation coefficient indicates the degree of similarity between the signal and its delayed version at different time intervals.

By analyzing the autocorrelation plots, we can gain insights into the temporal dynamics of the blood flow at different speeds. Specifically, variations in the autocorrelation profiles across slow, medium, and fast flow rates can provide valuable information about the underlying flow dynamics, such as the presence of periodic oscillations or fluctuations. This analysis serves to characterize and compare the temporal behavior of artificial blood flow under different flow rate conditions, aiding in the interpretation of experimental data and providing valuable insights into physiological processes related to blood circulation.



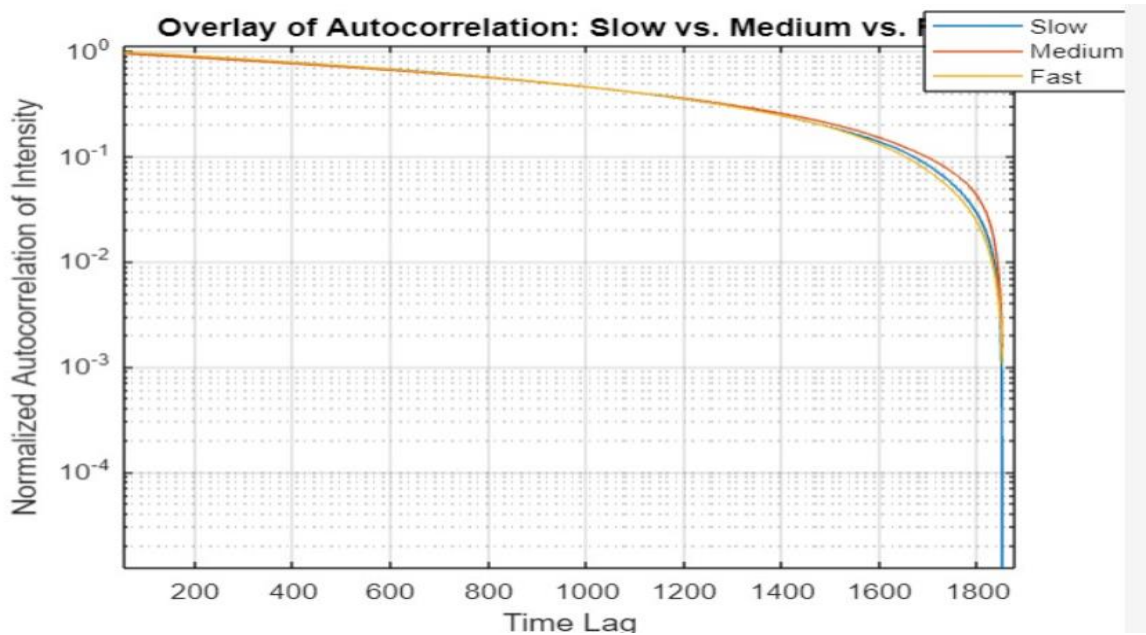


Fig:5.12: Final autocorrelation of blood

5.2 DISCUSSIONS

The development of the final Diffuse Correlation Spectroscopy (DCS) probe design represents a significant advancement in biomedical imaging and tissue perfusion monitoring. Drawing from previous research findings, our probe design emphasizes compactness and integration, aligning with recent trends towards miniaturization and portability in biomedical instrumentation (Shahmirzadi et al., 2019). Notably, the probe's streamlined design, incorporating essential components like a transistor, laser, and photodetector into a single circuit, enhances functionality and ease of use, as emphasized by Durduran et al. (2010). Methodological advancements in our experimental setup, such as utilizing a motor-driven pumping system for artificial blood circulation and selecting the transmittance setup for laser and detector placement, echo previous research on the importance of controlled flow dynamics and optimal probe configuration in DCS measurements (Fantini et al., 1995; Durduran et al., 2004). These choices improve the accuracy and reliability of blood flow measurements, enhancing the clinical utility of DCS in assessing tissue perfusion. Furthermore, MATLAB analysis of autocorrelation plots provides valuable insights into the temporal dynamics of artificial blood flow, complementing previous research on autocorrelation techniques for characterizing blood flow dynamics and tissue

perfusion (Yu et al., 2005; Carp et al., 2010). Our research findings align with Durduran et al. (2014), who demonstrated the optical measurement of cerebral hemodynamics and oxygen metabolism using similar techniques, indicating the potential applications of our research in assessing tissue perfusion. Additionally, Shahmirzadi et al. (2019) highlighted the importance of integrated and portable biosensors in medicine, further validating the significance of our probe design approach. Despite methodological advancements and promising results, further validation studies using animal models or clinical datasets are warranted to address limitations such as the use of artificial blood. Future research may also explore advanced photonics technologies to enhance sensitivity and spatial resolution, as suggested by Buckley et al. (2020). In conclusion, the development of the final DCS probe design, combined with methodological improvements and insights from previous research, represents a significant step forward in tissue perfusion monitoring and biomedical imaging, offering potential applications in diagnosing pathological conditions and assessing tissue perfusion with enhanced accuracy and reliability

CHAPTER-6

SUMMARY AND CONCLUSION

A new technology that offer a non-invasive approach to treat the cancer and detect it by using diffuse correlation spectroscopy (DCS). Optical techniques are being used to study tissue hemodynamics by directly integrating the light source into the DCS measurement instrument. In conclusion, the DCS analyzes the temporal intensity changes by the NIR diffuse light in tissue which are responsive to the movements of red blood cells. This discovery has enormous potential for the fields of clinical neurology and neuroimaging. For measuring tumor blood flow, DCS was used for new qualities for analysis of the blood perfusion, including mobility, high temporal resolution, noninvasiveness, and reasonably deep penetration. The blood flow perfusion rate and velocity were found using the MATLAB autocorrelation function. The study has focused on artificial blood and its blood flow velocity with light intensity, which were compared with the patients' blood flow data. Normally the patients suffering from cancer, thyroid, and appendicitis have a greater blood perfusion rate than the normal patients. The study concluded on designing and integrating a laser diode for using the DCS for analyzing the above said data.

The future study of our research would focus on the clinical patient's data with the normal patients' on taking various parameters into account, where we can provide the statistical analysis of the blood flow velocity plays avital role in categorizing the patients' diseases. The bigger sample size of patient's analysis would provide the accuracy of the device which would be a better technique for bedside management of cancer diagnosis and therapy.

Conclusion: The Obtained Results

1. The Diffuse Correlation Spectroscopy (DCS) can implement to all the patients
2. The optical techniques were used for investigating tissue haemodynamic
3. Designed the probe using MATLAB code of autocorrelation function
4. Integrated the light source for the measurement of the probe in DC
5. Assessed the blood perfusion rate

Future Study:

1. Ethical Clearance for performing the Study

2. To perform a patient analysis on surface level analysis like cancer, thyroid patients, appendicitis patients with control
3. To Assess the blood perfusion rate among all the groups ➤ Compare and Compile the analysis and conclude the study results.

Deliverables: DCS was used for:

- 1. Measuring tumor blood flow (Artificial Blood)**
- 2. Analysis of the blood perfusion**
- 3. Mobility**
- 4. High temporal resolution**
- 5. Non invasive**
- 6. Deep penetration Accuracy**

REFERENCES

1. A. Torricelli, D. Contini, A. Pifferi, M. Caffini, R. Re, L. Zucchelli, and L. Spinelli.
Time domain functional nirs imaging for human brain mapping. *Neuroimage* 85,
28–50 (2014)
2. Bartlett MF, Jordan SM, Hueber DM, Nelson MD. Impact of changes in tissue optical
properties on near-infrared diffuse correlation spectroscopy measures of skeletal
muscle blood flow. *J Appl Physiol* (1985). 2021 Apr 1;130(4):1183-1195. doi:
10.1152/jappphysiol.00857.2020. Epub 2021 Feb 11. PMID: 33571054; PMCID:
PMC8262784.
3. Buckley, E.M.; Cook, N.M.; Durduran, T.; Kim, M.N.; Zhou, C.; Choe, R.; Yu, G.;
Schultz, S.; Sehgal, C.M.; Licht, D.J.; et al. Cerebral hemodynamics in preterm infants
during positional intervention measured with diffuse correlation spectroscopy and
transcranial Doppler ultrasound. *Opt. Express* 2009, 17, 12571.
4. Carp, S.A.; Dai, G.P.; Boas, D.A.; Franceschini, M.A.; Kim, Y.R. Validation of diffuse
correlation spectroscopy measurements of rodent cerebral blood flow with
simultaneous arterial spin labeling MRI; towards MRI-optical continuous cerebral
metabolic monitoring. *Biomed. Opt. Express* 2010, 1, 553–565.
5. Cortese, Lorenzo; Lo Presti, Giuseppe; Pagliazzi, Marco; Contini, Davide; Dalla Mora,
Alberto; Dehghani, Hamid; Ferri, Fabio; Fischer, Jonas B; Giovannella, Martina;
Martelli, Fabrizio; Weigel, Udo M; Wojtkiewicz, Stanislaw; Zanoletti, Marta; Durduran,
Turgut. DOI: 10.1364/BOE.423071.
6. Dagal, A. and Lam, A. M. Cerebral blood flow and the injured brain: how should we
monitor and manipulate it? *Curr. Opin. Anaesthesiol.* 24, 131–137 (2011).
7. Durduran, T.; Yu, G.; Burnett, M.G.; Detre, J.A.; Greenberg, J.H.; Wang, J.; Zhou, C.;
Yodh, A.G. Diffuse optical measurement of blood flow, blood oxygenation, and
metabolism in a human brain during sensorimotor cortex activation. *Opt. Lett.* 2004,
29, 1766–1768.
8. Gagnon L, Desjardins M, Jehanne-Lacasse J, Bherer L, Lesage F. Investigation of
diffuse correlation spectroscopy in multi-layered media including the human head. *Opt*
Express. 2008 Sep 29;16(20):15514-30. doi: 10.1364/oe.16.015514.
PMID:18825190
9. Gregori-Pla, I. Blanco, P. Camps-Renom, P. Zirak, I. Serra, G. Cotta, F. Maruccia,
L. Prats-Sánchez, A. MartínezDomeño, D. R. Busch, G. Giacalone, J. Martí-
Fàbregas, T. Durduran, and R. Delgado-Mederos. Early microvascular cerebral

- blood flow response to head-of-bed elevation is related to outcome in acute ischemic stroke. *J. Neurol.* 266(4), 990–997 (2019).
10. Holiqov, W. Zhou, T. Zhang, V. Du Le, and V. J. Srinivasan. Time-offlight resolved light field fluctuations reveal deep human tissue physiology. *Nat. Commun.* 11, 1–15 (2020).
 11. Jason Sutin, Bernhard Zimmerman, Danil Tyulmankov, Davide Tamborini, Kuan Cheng Wu, Juliette Selb, Angelo Gulinatti, Ivan Rech, Alberto Tosi, David A. Boas, and Maria Angela Franceschini. "Time-domain diffuse correlation spectroscopy," *Optica* 3, 1006-1013 (2016).
 12. Liu, Wenhui; Qian, Ruobing; Xu, Shiqi; Konda, Pavan Chandra; Jönsson, Joakim; Harfouche, Mark; Borycki, Dawid; Cooke, Colin; Berrocal, Edouard; Dai, Qionghai; Wang, Haoqian; Horstmeyer, Roarke. Fast and sensitive diffuse correlation spectroscopy with highly parallelized single photon detection. *APL Photonics* 1 February 2021; 6 (2): 026106.
 13. M. M. Wu, S.-T. Chan, D. Mazumder, D. Tamborini, K. A. Stephens, B. Deng, P. Farzam, Y. Chu, M. A. Franceschini, J. Z. Qu, and S. A. Carp. Improved accuracy of cerebral blood flow quantification in the presence of systemic physiology cross-talk using multi-layer Monte Carlo modeling. *Neurophotonics* 8(1), 015001 (2021).
 14. Maria Angela Franceschini, Davide Contini, Alberto Dalla Mora, Fabio Ferri, Jonas B. Fischer, Martina Giovannella, Fabrizio Martelli, Udo M. Weigel, Stanislaw Wojtkiewicz, Marta Zanoletti, and Turgut Durduran. Portable, high speed blood flow measurements enabled by long wavelength, interferometric diffuse correlation spectroscopy (LW-iDCS). *Sci Rep.* 2023 May 31;13(1):8803. doi: 10.1038/s41598-023-36074-8. PMID: 37258644; PMCID: PMC10232495.
 15. Pagliazzi, M. et al. Time resolved speckle contrast optical spectroscopy at quasi-null source-detector separation for non-invasive measurement of microvascular blood flow. *Biomed. Opt. Express* 12, 1499 (2021).
 16. P. Zhang, Z. Gui, L. Hao, X. Zhang, C. Liu, and Y. Shang. Signal processing for diffuse correlation spectroscopy with recurrent neural network of deep learning, in 2019 IEEE Fifth International Conference on Big Data Computing Service and Applications (BigDataService), (IEEE, 2019), pp. 328–332.
 17. Robinson MB, Renna M, Ozana N, Martin AN, Otic N, Carp SA, Franceschini MA. Portable, high speed blood flow measurements enabled by long wavelength, interferometric diffuse correlation spectroscopy (LW-iDCS). *Sci*

- Rep. 2023 May 31;13(1):8803. doi: 10.1038/s41598-023-36074-8. PMID: 37258644; PMCID: PMC10232495.
18. Robinson, M. B. et al. Characterization of continuous wave ultrasound for acousto-optic modulated diffuse correlation spectroscopy (AOM-DCS). *Biomed. Opt. Express* 11, 3071 (2020).
 19. Vishwanath K, Zanfardino S.: Diffuse Correlation Spectroscopy at Short Source-Detector Separations: Simulations, Experiments and Theoretical Modeling. *Applied Sciences*. 2019; 9(15):3047. <https://doi.org/10.3390/app9153047>.
 20. Wu J, Tabassum S, Brown WL, Wood S, Yang J, Kainerstorfer JM (2022) Two-layer analytical model for estimation of layer thickness and flow using Diffuse Correlation Spectroscopy. *PLoS ONE* 17(9): e0274258.
 21. Wu KC, Sunwoo J, Sheriff F, Farzam P, Farzam PY, Orihuela-Espina F, LaRose SL, Monk AD, Aziz-Sultan MA, Patel N, Vaitkevicius H, Franceschini MA. Validation of diffuse correlation spectroscopy measures of critical closing pressure against transcranial Doppler ultrasound in stroke patients. *J Biomed Opt.* 2021 Mar;26(3):036008.
 22. Xie, Jinbin & He, Xiangdong & Zhang, Limin & li, Jiao & Qin, Zhuanping & Gao, Feng. (2020). Diffuse correlation spectroscopy towards dynamic topography of blood flow index in deep tissues: A multi-channel system and experiment validation. *Infrared Physics & Technology*. 107. 103298. 10.1016/j.infrared.2020.103298.
 23. Zavriyev AI, Kaya K, Farzam P, Farzam PY, Sunwoo J, Jassar AS, Sundt TM, Carp SA, Franceschini MA, Qu JZ. The role of diffuse correlation spectroscopy and frequency-domain near-infrared spectroscopy in monitoring cerebral hemodynamics during hypothermic circulatory arrests. *JTCVS Tech*. 2021 Jan 29;7:161-177.
 24. Zilpelwar, S. et al. A model of dynamic speckle evolution for evaluating laser speckle contrast measurements of tissue dynamics. *Biomed. Opt. Express* 13, 6533–6549 (2022).
 25. Zhao, M., Zhou, W., Aparanji, S., Mazumder, D. & Srinivasan, V. Interferometric difusing wave spectroscopy imaging with an electronically variable time-of-flight filter. *Optica* 10, 42–52 (2022).
 26. Zavriyev AI, Kaya K, Farzam P, Farzam PY, Sunwoo J, Jassar AS, Sundt TM, Carp SA, Franceschini MA, Qu JZ. The role of diffuse correlation spectroscopy and frequency-domain near-infrared spectroscopy in monitoring cerebral

hemodynamics during hypothermic circulatory arrests. JTCVS Tech. 2021 Jan 29;7:161-177. doi: 10.1016/j.xjtc.2021.01.023. PMID: 34318236; PMCID: PMC8311503.

27. Della Rocca FM, Sie EJ, Catoen R, Marsili F, Henderson RK. Field programmable gate array compression for large array multispeckle diffuse correlation spectroscopy. J Biomed Opt. 2023 May;28(5):057001. doi: 10.1117/1.JBO.28.5.057001. Epub 2023 May 8. PMID: 37168688; PMCID: PMC10166587.