SUB-TERAHERTZ SENSING AND IMAGING TECHNIQUES FOR NON-INVASIVE GLUCOSE MEASUREMENT AND TUMOR MARGIN ASSESSMENT APPLICATIONS

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by

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Under the inspiration of Almighty God, this thesis is dedicated to my parents

CERTIFICATE

This is to certify that the thesis entitled **"SUB-TERAHERTZ SENSING AND IMAGING TECHNIQUES FOR NON-INVASIVE GLUCOSE SENSING AND TUMOR MARGIN ASSESSMENT APPLICATIONS"** being submitted by **Miss. Priyansha Kaurav** to the **Indian Institute of Technology Delhi**, for the award of the degree of **Doctor of Philosophy**, is a record of the bonafide research work carried out by her. She has worked under my supervision and guidance and has fulfilled the requirements, which to my knowledge, have reached the requisite standard for the submission of the thesis. The results presented in this thesis have not been submitted in part or full for the award of any degree or diploma in any other University or Institute.

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ABSTRACT

In recent years, THz spectrometers and imaging systems have become part of standard laboratory tools thanks to the advancements in THz source and detector technology. Applications include explosive and concealed weapon detection, non-destructive testing, pharmaceutical quality control, and biomedical imaging. Sub-THz (0.1-0.3 THz) and THz (0.3-10 THz) radiation, which are non-ionizing and highly sensitive, have recently garnered great interest in tissue diagnostics and screening applications in vivo and ex vivo.

The use of electro-optical pulses into Time-domain Spectrometers (TDS) has become increasingly common for analyzing biological samples because they produce a broad spectrum of spectral responses. The electro-optic sampling-based TDS setups are cumbersome and expensive, so it is not practical to use this technology to develop portable and affordable imaging and sensing devices. Furthermore, the setup lacks accuracy in the sub-THz region due to the inefficiency of the laser source. Electronics based on sub-THz technology have eliminated this barrier, allowing the development of compact, robust, and easy-to-use devices for biological applications.

In addition, some biomedical applications of the electromagnetic spectrum require monitoring of real-time parameters associated with human physiological states. In these applications, signal processing of biomedical signals requires advanced computational methods that can be parallelized using high-performance platforms like GPUs and TPUs. The use of these computer technologies has enabled huge amounts of data to be modeled through machine learning. The aim of this thesis is to combine sub-THz technology with machine learning in order to develop an automated diagnostic strategy for obtaining and interpreting data from electronic sub-THz measuring equipment.

In this regard, the thesis discusses two important applications in which sub-THz electronics improve upon existing approaches for non-invasive blood glucose measurement and surgical tumor margin assessment. In the first application of non-invasive glucose measurement, S parameters' response from glucose samples of varying concentrations is measured using sub-THz waveguide probe sensors. The proposed sensor system has a sensitivity of 2 dB for a change in glucose concentration of 15 mg/dl, which is within the clinical range for non-invasive diabetes monitoring devices. As a result of including machine

learning in the system, the readability of the measuring system is improved because of the non-linear relationship established between S parameters and glucose concentration readings.

In the second application, a highly sensitive, highly efficient, and cost-effective sub-THz waveguide iris probe is designed for the detection of tumor margins during lumpectomies. This probe can detect both positive and negative margins over a frequency range of 110-170 GHz, suggesting its application in intraoperative tumor margin assessment. It is accomplished by placing the scanning probe in direct contact with the excised breast tissue. For both applications, numerical phantoms and physical phantoms are used to test the sensors' performance and accuracy at sub-THz frequencies. A demonstration of automation of imaging set up in a second application illustrates the importance of system automation for accelerating data acquisition and processing.

सार

हाल के वर्षों में, THz स्रोत और डिटेक्टर प्रौद्योगिकी में प्रगति के कारण THz स्पेक्ट्रोमीटर और इमेजिंग सिस्टम मानक प्रयोगशाला उपकरणों का हिस्सा बन गए हैं। अनुप्रयोगों में विस्फोटक और छिपे हुए हथियार का पता लगाना, गैर-विनाशकारी परीक्षण, फार्मास्युटिकल गुणवत्ता नियंत्रण और बायोमेडिकल इमेजिंग शामिल हैं। उप-THz (0.1-0.3 THz) और THz (0.3-10 THz) विकिरण, जो गैर-आयनीकरण और अत्यधिक संवेदनशील हैं, ने हाल ही में विवो और पूर्व विवो में ऊतक निदान और स्क्रीनिंग अनुप्रयोगों में बहुत रुचि प्राप्त की है।

टाइम-डोमेन स्पेक्ट्रोमीटर (टीडीएस) में इलेक्ट्रो-ऑप्टिकल दालों का उपयोग जैविक नमूनों के विश्लेषण के लिए तेजी से सामान्य हो गया है क्योंकि वे वर्णक्रमीय प्रतिक्रियाओं का एक व्यापक स्पेक्ट्रम उत्पन्न करते हैं। इलेक्ट्रो-ऑप्टिक सैंपलिंग-आधारित टीडीएस सेटअप बोझिल और महंगे हैं, इसलिए पोर्टेबल और सस्ती इमेजिंग और सेंसिंग डिवाइस विकसित करने के लिए इस तकनीक का उपयोग करना व्यावहारिक नहीं है। इसके अलावा, लेज़र स्रोत की अक्षमता के कारण सेटअप में उप-THz क्षेत्र में सटीकता का अभाव है। उप-टीएचजेड प्रौद्योगिकी पर आधारित इलेक्ट्रॉनिक्स ने इस बाधा को समाप्त कर दिया है, जिससे जैविक अनुप्रयोगों के लिए कॉम्पैक्ट, मजबूत और उपयोग में आसान उपकरणों के विकास की अनुमति मिलती है।

इसके अलावा, इलेक्ट्रोमैग्नेटिक स्पेक्ट्रम के कुछ बायोमेडिकल अनुप्रयोगों में मानव शारीरिक अवस्थाओं से जुड़े वास्तविक समय के मापदंडों की निगरानी की आवश्यकता होती है। इन अनुप्रयोगों में, बायोमेडिकल संकेतों पर आधारित सिग्नल प्रोसेसिंग के लिए उन्नत कम्प्यूटेशनल विधियों की आवश्यकता होती है जिन्हें GPU और TPU जैसे उच्च-प्रदर्शन प्लेटफार्मों का उपयोग करके समानांतर किया जा सकता है। इन कंप्यूटर प्रौद्योगिकियों के उपयोग ने बड़ी मात्रा में डेटा को मशीन लर्निंग के माध्यम से मॉडलिंग करने में सक्षम बनाया है। इस थीसिस का उद्देश्य इलेक्ट्रॉनिक सब-टीएचजेड माप उपकरणों से डेटा प्राप्त करने और व्याख्या करने के लिए एक स्वचालित नैदानिक रणनीति विकसित करने के लिए मशीन लर्निंग के साथ सब-टीएचजेड तकनीक को जोड़ना है।

इस संबंध में, थीसिस दो महत्वपूर्ण अनुप्रयोगों पर चर्चा करती है जिसमें उप-THz इलेक्ट्रॉनिक्स गैर-इनवेसिव रक्त शर्करा माप और सर्जिकल ट्यूमर मार्जिन मूल्यांकन के लिए मौजूदा दृष्टिकोणों में सुधार करते हैं। गैर-आक्रामक ग्लूकोज माप के पहले आवेदन में, अलग-अलग सांद्रता के ग्लूकोज नमूनों से एस पैरामीटर प्रतिक्रिया को उप-टीएचजेड वेवगाइड जांच सेंसर का उपयोग करके मापा जाता है। प्रस्तावित सेंसर सिस्टम में

15 मिलीग्राम/डेसीलीटर की ग्लूकोज सांद्रता में बदलाव के लिए 2 डीबी की संवेदनशीलता है, जो गैर-आक्रामक मधुमेह निगरानी उपकरणों के लिए नैदानिक सीमा के भीतर है। सिस्टम में मशीन लर्निंग को शामिल करने के परिणामस्वरूप, एस पैरामीटर और ग्लूकोज एकाग्रता रीडिंग के बीच स्थापित गैर-रैखिक संबंध के कारण माप प्रणाली की पठनीयता में सुधार हुआ है।

दूसरे आवेदन में, एक अत्यधिक संवेदनशील, अत्यधिक कुशल और लागत प्रभावी उप-टीएचजेड वेवगाइड आईरिस जांच को लम्पेक्टोमी के दौरान ट्यूमर मार्जिन का पता लगाने के लिए डिज़ाइन किया गया है। यह जांच 110-170 गीगाहर्ट्ज़ की आवृत्ति रेंज में सकारात्मक और नकारात्मक दोनों मार्जिन का पता लगा सकती है, जो इंट्राऑपरेटिव ट्यूमर मार्जिन मूल्यांकन में इसके आवेदन का सुझाव देती है। यह स्कैनिंग जांच को छांटने के सीधे संपर्क में रखकर पूरा किया जाता है। दोनों अनुप्रयोगों के लिए, उप-THz पर सेंसर के प्रदर्शन और सटीकता का परीक्षण करने के लिए संख्यात्मक प्रेत और भौतिक प्रेत का उपयोग किया जाता है। एक दूसरे अनुप्रयोग में स्थापित इमेजिंग के स्वचालन का एक प्रदर्शन डेटा अधिग्रहण और प्रसंस्करण में तेजी लाने के लिए सिस्टम ऑटोमेशन के महत्व को दर्शाता है।

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