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Lab On-Chip Detection of Tuberculosis

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***Abstract*— This paper presents a new method of Tuberculosis (TB) detection; a method made simpler, faster and more accurate. The blood samples of the individuals are subjected to inspection, through photonic crystal sensor to obtain the refractive index values. The sevalues are initialized into MEEP (Massachusetts Institute of Technology Electromagnetic Equation Propagation) software to obtain the flux values. A MATLAB (Matrix Laboratory) code is written employing Naive Bayesian Algorithm for classifying the test samples indicating either the presence or absence of TB. A further step is taken by us to make this user-friendly by displaying the corresponding results on a LCD using Raspberry Pi Model B+, supported by a voice message output too. The results at each stage are recorded and analyzed.**

***Keywords*—Tuberculosis (TB), MEEP (Massachusetts Institute of Technology Electromagnetic Equation Propagation) Software, Naive Bayesian Algorithm, Raspberry Pi Model B+..**

I. INTRODUCTION

Tuberculosis disease is rearing its ugly head and is becoming almost drug resistant. It remains a threat to a huge percentage of population. The World Health Organization (WHO) estimates that one-third of the population of the world isinfected with Mycobacterium **tuberculosis and** that more than 8 million new cases of active TB occur annually [1]. The estimated global annual mortality from TB is close to 2 million people [1]. Although management of TB has faced many challenges in the past, today there are two monumental threats to global TB control: the HIV epidemic and the increasing prevalence of drug resistance [2]. Tuberculosis (TB) is diagnosed by detecting the presence of *Mycobacterium tuberculosis* bacteria in a clinical specimen taken from the patient which can be blood or sputum sample. The most common tests done are Skin Test, IGRA (Interferon Gamma Release Assays), and Sputum Smear Microscopy [3]. These current TB tests take a long time to obtain results, are not very accurate, either have low sensitivity and/or low specificity, and give “False Negatives” and “False Positives”. False Negatives imply the test result suggesting that a person has not got TB when he actually has, and False Positives imply the test result suggesting that a person has TB when he actually does not have, thereby sometimes yielding a false report.

New tests are expensive for developing countries and also require significant laboratory facilities including highly trained staff. This, in turn, leads to hesitation and/or delay in the treatment. Hence, diagnosing TB remains a significant challenge, particularly in resource poor settings. Therefore, detection is made simpler, sensitive and more accurate by involving technology that is ubiquitous via machine learning process which provides acute sub-classifications of the disease under investigation.

Lab on-chip detection of Tuberculosis is a latest method proposed for a simpler, faster and more accurate detection of TB, by obtaining the blood samples of the individuals and subjecting the samples to inspection through photonic crystal sensor [4].The Photonic Crystal Sensors exhibit high sensitivity and selectivity as well as high stability, immunity to electromagnetic interference and product improvements, such as smaller integration sizes and lower costs [4]. This enables us to measure the refractive indices values of the samples under inspection with higher precision for comparing the same with reference sample values.The refractive index value so obtained is then subjected to MEEP software. This is a simulation software tool used to obtain flux values. The segregation of these values is supported by Naive Bayesian Algorithm [5] using MATLAB coding. A GUI (Graphical User Interface) windowis created for the graphical representation of the obtained MATLAB outputs.For a better hands-on experience, the corresponding result is displayed on a LCD, along with voice message support using Raspberry Pi Model B+ [6] kit which makes the entire process very much user-friendly.

II. THEORY

A. Photonic Band Gap Semiconductor Structure Description

A photonic band gap (PBG) semiconductor crystal is a structure that can manifest beams of light by several orders in magnitude, analogous to the way semiconductors control electric currents in the drain-source configuration of MOSFETs (Metal Oxide Semiconductor Field Effect

Transistors) [7] or electric potential in emitter-base configuration of BJTs (Bipolar Junction Transistor)[8]. Photonic crystals typically compose of dielectric materials, that is, materials that act as electrical insulators in which an electromagnetic field can be propagated with low loss (α>>1). Holes are drilled into the dielectric in a lattice-like structure with identical repetition at regular intervals. Light entering the perforated material will reflect and refract off the interfaces between glass and air. The complex pattern of overlapping beams will lead to cancellation of a band of wavelengths in all directions leading to prevention of propagation of light into this band of the crystal. The resulting photonic band structure can be modified by filling in some holes with a compound or elemental material from stoichiometric compositions or creating defects in the otherwise perfectly periodic system leading to many non-stoichiometric and disordered configurations whose behavior delineates from known structures. The master equation (Equation 1) which describes the propagation of light in photonic crystal is obtained by solving Maxwell's electromagnetic equations.

$$\nabla \times \left(\frac{1}{\epsilon}\nabla \times H\right) = \left(\frac{\omega^2}{c}\right) \quad (1)$$

Where, 'H' is the magnetic field , 'c' is speed of light,'ϵ' is the dielectric functionand 'ω' is the frequency of resonance.
The modeling and simulation of the Photonic Crystal Sensor [9] has been performed using a simulation tool called MIT Electromagnetic Equation Propagation (MEEP), an open source software available for installation on a Linux operating system

B. Naive Bayes Classification

Classification in data analysis is the task of assigning a class to instances of data described by a set of attributes. It includes the construction of a classifier which is trained on a set of training data that already has the correct class assigned to each data point. Bayesian classification is based on Bayes theorem. Bayes' Theorem is a statementfrom probability theory that allows for the calculation of certain conditional probabilities.

C. Bayes Theorem

If a given data set is A= $\{a_1,a_2,....a_n\}$ representing n features, then

$$P(C_k|A) = \frac{P(A|C_k)\ P(C_k)}{P(A)} \quad (2)$$

Where,
$P(C_k)$: Independent probability of C_k: priori probability
P(A): independent probability of A: evidence
$P(A|C_k)$: conditional probability of A givenC_k: likelihood
$P(C_k|X)$: conditional probability of C_k given X: posteriori probability

D. Kernel Distribution

A kernel distribution is a non-parametric representation of the probability density function (pdf) of a random variable. You can use a kernel distribution when a parametric distribution cannot properly describe the data, or when you want to avoid making assumptions about the distribution of the data. This distribution is defined by a smoothing function and a bandwidth value that controls the smoothness of the resulting density curve.

E. Kernel Density Estimator

The kernel density estimator is the estimated probability density function (pdf) of the random variable. Its formula is given by the equation

$$\hat{f}_h(x) = \frac{1}{nh}\sum_{i=1}^{n} K\left[\frac{x-x_i}{h}\right], \infty < x < -\infty \quad (2)$$

where, n is the sample size, K(•) is the kernel smoothing function, h is the bandwidth.

III. TOOLS USED FOR SIMULATION

A. MEEP Software Tool

MIT Electromagnetic Equation Propagation (MEEP) is a simulation tool developed by MIT for design, model and simulation of various photonic crystal structures[9]. It is a time domain tool and implements the FDTD (Finite Difference Time Domain) method.The FDTD method solves the time domain Maxwell's equation. The method divides the field in time and space and solves for electric and magnetic fields. We use MEEP tool for designing and simulating the photonic crystal based bio-sensor from which the flux values are obtained.

B. MATLAB

Matrix Laboratory (MATLAB) is a software bundle for great-performance numerical, arithmetic computation and visualization [10]. MATLAB's built-in functions deliver outstanding toolbox for linear algebra computations, data analysis, signal processing, optimization, and many other types of scientific computations. The basic building block of matrix laboratory is the matrix. MATLAB contains built-in functionality to help you create the Graphical User Interface (GUI) using which we can display the output more efficiently. We use MATLAB for analyzing and plotting the transmission spectrum obtained from the sensor and for Naive Bayes classification.

IV.RESULT AND DISCUSSION

A. MATLAB Output

The output from the photonic crystal sensor designed using MEEP tool is saved in MS Excel file using dot xlsx (.xlsx) format, which is used as input to MATLAB. When the MATLAB code is executed and excel files are loaded, the following GUI[11] output is obtained. Figure1 shows the output for normal test values and figure2 shows the output for TB affected test values.

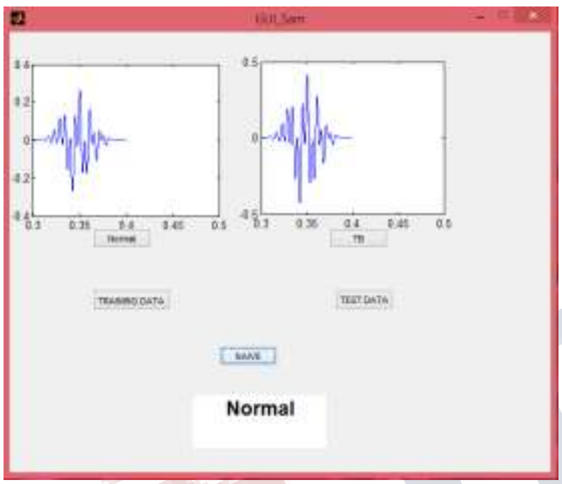

Figure1: GUI output for Normal test value

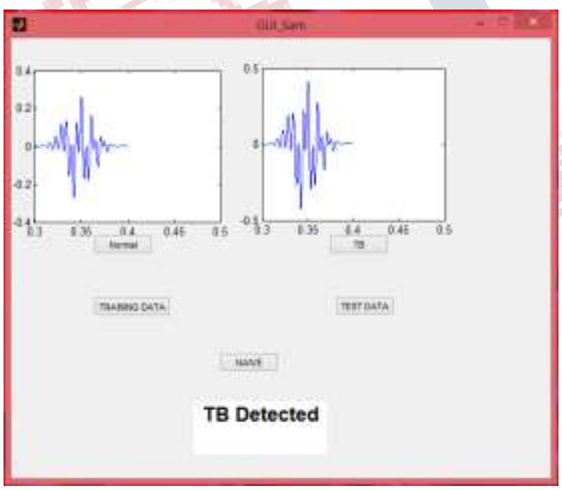

Figure2: GUI output for TB affected test value

B. LCD Output

The MATLAB output is displayed on an LCD through Raspberry Pikit. Figure3 shows the connection of the Raspberry Pi kit to a host computer.We have used the latest version i.e. Raspberry Pi Model B+ [6].

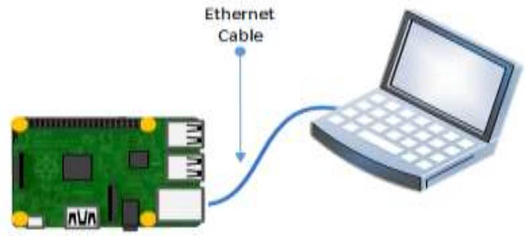

Figure3: Interfacing and configuration of Raspberry Pi Model B+ to the Host Computer Using Raspberry Pi support from MATLAB

After successfully obtaining the GUI (Graphical User Interface) output, we go to the "Add-ons" in MATLAB and select the "Get Hardware Support Packages" option. From the "Support Package Installer" window, the 'Install from Internet' option is selected to setup the installation of Hardware package. The Hardware Support Package can then be downloaded for 'Raspberry Pi. After the download is completed, the package is extracted into a folder in 'C' drive, after which 'Configure the Network' is selected by using 'Direct connection to host computer'. A 4GB or larger SD memory card is inserted into a card reader on the Host computer. The SD memory card is removed from the host computer and is inserted into the Raspberry Pi kit. One end of an Ethernet cable is connected to the Raspberry Pi kit and the other end to the Host computer. A 5V micro USB power supply is given to the board.

The LCD is interfaced to the Raspberry Pi kit by making the appropriate connections to the GPIO (General Purpose Input/output) pins [12][13]. The output obtained is as shown below in figure4 and figure5.

Figure4: LCD output for Normal test Value

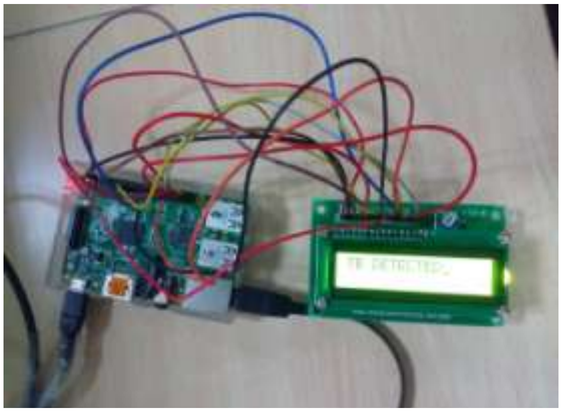

Figure5: LCD output for TB affected test value

V. CONCLUSION AND FUTURE ENHANCEMENT

Lab on-chip detection of TB has been successfully demonstrated which is reliable, simpler, sensitive, and an accurate tool for effective detection of TB. To summarize, we obtain the blood samples of individuals and subject them to inspection through photonic crystal sensor. The refractive indices so obtained from these samples are initialized into MEEP (Massachusetts Institute of Technology Electromagnetic Equation Propagation) software tool to obtain the flux values which are given as input to the MATLAB (Matrix Laboratory) , where flux values are classified using Naive Bayes algorithm. The corresponding result is displayed on LCD using Raspberry Pi along with a voice message. We have developed a system which will act as a foundation and an initial step towards the implementation of Lab on-chip detection of TB. Further, this method can be implemented as a software program on an Android platform. Different Machine algorithms can be used and compared with the one used here. Different sensor structures can be designed to increase the sensitivity and can be used to diagnose other diseases.

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