BIO MARKER BASED ESTIMATION OF CANCER CELL DETECTION BY HUMAN EXHALE VOC BREATH ANALYSIS USING MEMS SENSORS.

[1]A.NAGAMALLI, [2]Dr. DAISY RANI.A
[1]Research Scholar, Instrument Technology, ANDHRA UNIVERSITY, AUCE (A), VISAKHAPATNAM.
[2]Assistant Professor, Instrument Technology, ANDHRA UNIVERSITY, AUCE(A), VISAKHAPATNAM.

Abstract : Volatile Organic Compounds (**VOC)** are a wide range of carbon based organic chemical compounds which evaporate easily at room temperature referred as volatile in nature. Human exhaled breathe consists of carbon dioxide (CO_2) along with more than 3000 Volatile Organic Compounds exists like acetone, methanol, ethanol, and butane and formaldehydes etc. Out of existing several invasive methods, Exhaled breath analysis is a non-in vasive technique through which most preferable pain less procedures can be adopted for the purpose of diagnosing cancer cell/tissue detection. A MEMs based Bio-sensor design and fabrication using specific process flow methods is the main objective for detection of respiratory disease detection such as lung cancers. Many biomarkers are globally available among those only few suitable VOC gases are selected for the estimation and the level of severity or stages of Cancers. For this purpose, A MEMs VOC sensor structures must be designed using COMSOL software and suitable physics applied to achieve high sensitivity and accuracy, response time, repeatability of bio sensor. Based on the surface roughness obtained cancer cell topologies, malignancy can be predicted thereby reduce mortality.

IndexTerms - **VOC components, cell culturing, lung cancers, Bio-markers, MEMS.**

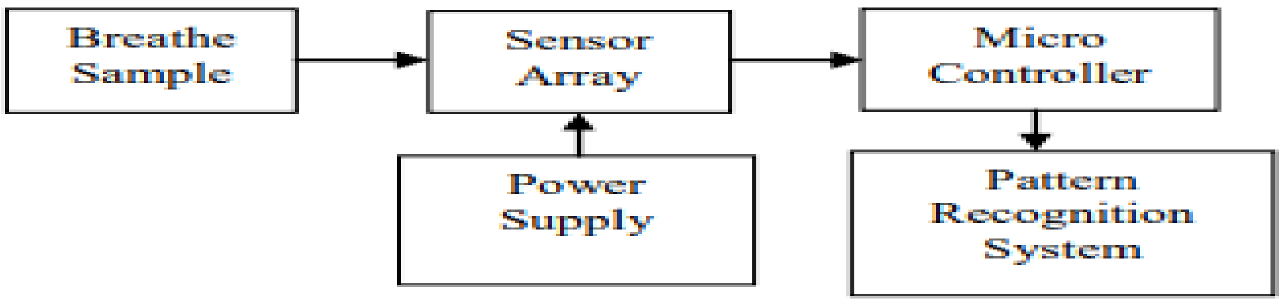
I. INTRODUCTION

Bio-chips are also referred as lab-on chip technologies with integrated multiple lab functions has wide spread over time in the field of medicines, food safety, pharmacy labs, diagnostic applications estimation and detection of glucose levels, stages of cancers. The evolution of MEMS technology has given enhancement to several new interdisciplinary fields such as bio-MEMS, optical MEMS, RF MEMS and micro fluidics are great advances in the field of engineering and research with lab on chip, and organ on chip based technologies. In the present paper bio-mems is highlighted with the fabrication of sensors suitable for medical health technologies in which drug delivery, drug efficacy estimations, tissue culturing thereby severity of diseases can be estimated with the best performance factors of bio-sensors like selectivity, sensitivity range, accuracy, response time, recovery time, life time along with amenability of portability and miniaturization of entire sensors in the wide range of operating frequencies is preferable.

There are many VOC out of which six carbonyl compounds like (Butane-C_4H_8O, $C_5H_{10}O$, $C_2H_4O_2$, $C_4H_8O_2$, $C_6H_{10}O_2$, $C_9H_{16}O_2$) few are considered as bio markers with elevated concentrations for Cancer detection. Cancer can be detected either by biomarker technique, cell culturing, cell morphology, cell cytology through image processing QD imaging , MRI, SERs, Diffusion reflect imaging, photo acoustic signalling, surface plasma device methods. Cancer levels are in 3 stages mostly initial, progression, severe stage. Severity at stage-4 will be higher. Estimation of cancer cell studies at stage 1 itself is more dominant method thereby reduce mortality.

II.**Implementation**

Generally from the previous observations VOCs in the breath of healthy individuals are isoprene (12– 580 ppb), acetone (1.2–1,880 ppb), ethanol (13–1,000 ppb), methanol (160–2,000 ppb) and other alcohols [1], [4].Several studies indicate that the health, occupational exposure, and habits (such as smoking) of individuals all strongly influence breath emissions of an individual. For example, the breath of individuals with high occupational exposures has been observed to contain significant levels of a wide variety of compounds, including chlorinated and aromatic hydrocarbons that are not normally associated with breath. Implementation methodology or basic block diagram can be as shown in below fig [1], by using pattern recognition systems either by using neural networks techniques or by data acquisition using Image processing algorithms best predictions may be obtained.



Fig[1]. Basic building block of SENSOR array for the detection of VOC [2]

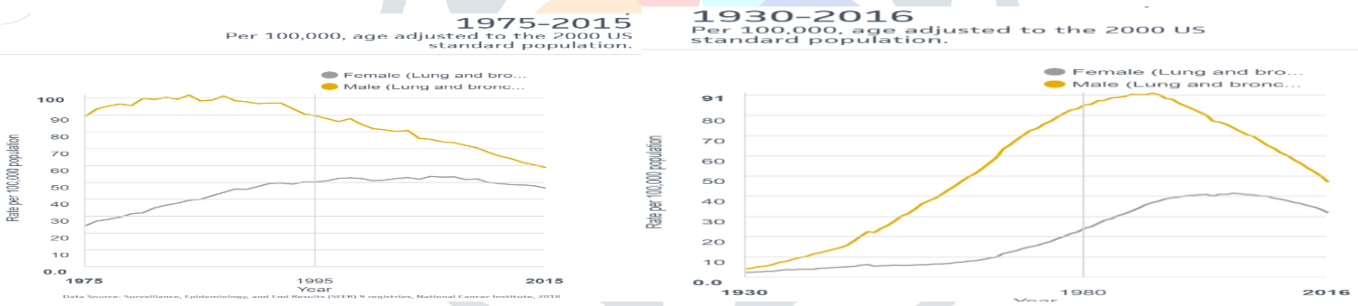
III. The challenges ahead

In order to estimate VOC component in the exhale an array of gas sensors are connected which are treated as e-nose systems, and is processed by data acquisition systems, control system each block is run with sufficient power supply unit. Chamber of sensors can be constructed with different sensors such that each sensor detects one type of VOC, 6 gases with 6 sensor array. Volatile transport system is taken from the exhale breath of human being having respiratory diseases. Based on the concentrations and typical ppm readings estimation of disease and detection of stages of cancer can be predicted. In the technical aspect Bio sensors are constructed with less than 10 um feature sizes, it is possible with advent of MEMs. Thus, mems based bio-sensor for VOC estimation is mostly challenging aspect in terms of transducers, biological detection elements, Micro-Nano Engineering techniques, and nerve cells technology aspects, signal processing systems which has to compute as fast as Human brain or at least with competence speed.

IV. The influencing factors

Lung cancer is the second most common cancer in both male and female and is the leading cause of cancer death among both genders. Each year, more mortality rate increasing coz of lung cancer than that of colon, breast, and prostate cancers combined. Worldwide estimation and statistical analysis from American cancer Society in 2019

New cases estimated are 1,762,450 and death rate is 606,880 are as shown in graphs [2-3],[15]. In developing country Lung & Bronchus Cancers are about 14% estimated in male, 13% in female and the estimated deaths are about 28% & 26% respectively according to omega Cancer Society stats 144,937new cases in the year 2015-17 and among 70,218 are died only in India.



Fig[2&3] Gender rate of population in US Affected with Lung CANCER (1975-2015) & (1930-2016)[15].

From the above graphs rate of population affected by lung cancers are maximum over the period last decade[15]. With suitable early stage detection, rate of mortality can be reduced. Also, Prevention of Lung Cancers could be possible by early stage detection and reducing smoking, second hand smoke, less often by the exposure to radon or other environmental echo factors [3]. Few lung cancers occur in humans without any known risk factors for the disease too.

V. Importance

The present paper gives the information and severity of the cancer diseases, along with need and estimation of disease early stage detections. Technological growth in Bio sensors, micro fabrication techniques, mems based gas sensors, cell or tissue culturing by measuring, diagnosing & estimation by the variation of electrical, mechanical or PH changes of cell this global health issues related to Cancers can be reduced and deduce mortality rate further.

VI. The current study

Software required for the simulations are COMSOL Multiphysics. Sensor structure is implemented by choosing COMSOL Multiphysics version COMSOL 5.0 with suitable geometry selection and material selected as lithium niobate on silicon substrate. Peizo electric device studies are chosen surface rough ness, thermal expansions, temperature studies are obtained by applying suitable physics and simulating the studies with extra fine and tetra hydral meshing.

VII. Findings and Suggestions :

Sample Measures of IDE:

Peizo electric device studies are chosen surface rough ness, thermal expansions and temperature studies are obtained by applying suitable physics and simulating the studies with extra fine and tetra hydral meshing. The following Table [1] represents the obtained results with enhanced number of elements and number of boundary elements resolved by tetrahedral meshing with minimal element quality. Symmetric matrices found. Eigenvalue solve Number of degrees of freedom solved for: 427642.

Table [1]: Tetrahedral meshing Analysis

Sno	Number of boundary elements	Number of elements	Minimum element quality
1	154	166	0.5643
2	191	1091	0.2294
3	1196	17993	0.05709
4	1997	38018	0.01082

Analysis:

Finite element estimation method is best suitable method to simulate a gas sensors, which gives best solution format for mems structures. Displacement, electric potential are measured. Number of degrees of freedom resolved for 427642. Displacement field (Material) (comp1.u): 2e-010, with Displacement Electric potential (comp1.V): 1 and Floating potential (comp1.es.fp1.V0_ode):0.44V, by using Explicit-Sparse null-space function used. As there are Finite Volume method, FEM based analysis is suggested due to fewer degrees of freedom for the same mesh, poorer current conservation, this characteristic is best suitable for Low power applications, and Multiphysics compatible.

VIII. Suggestions:

Several diagnostic methods such as NEMS, Canti-arrays, CNT, Nano wires or Nano pores can be utilized further in place of Canti levers and shear based saw gas sensors, Peizo actuators can be suggested further.

IX. Results & Conclusions:

Depends on surface roughness obtained on the MEM structure tissue or cancer cell morphologies can be estimated. If more variations occurs on surface morphology Malignancy can be predicted through which stage of diseases can be estimated. The following are the simulated Comsol structures and graphs are represented in the fig[4]. Maximum stress, temperature vs. scatter volume, total heat dissipation near the electrodes and surface roughness are measured, variable displacements under the applied stress fields are observed in the fig[5] at various Eigen frequencies.

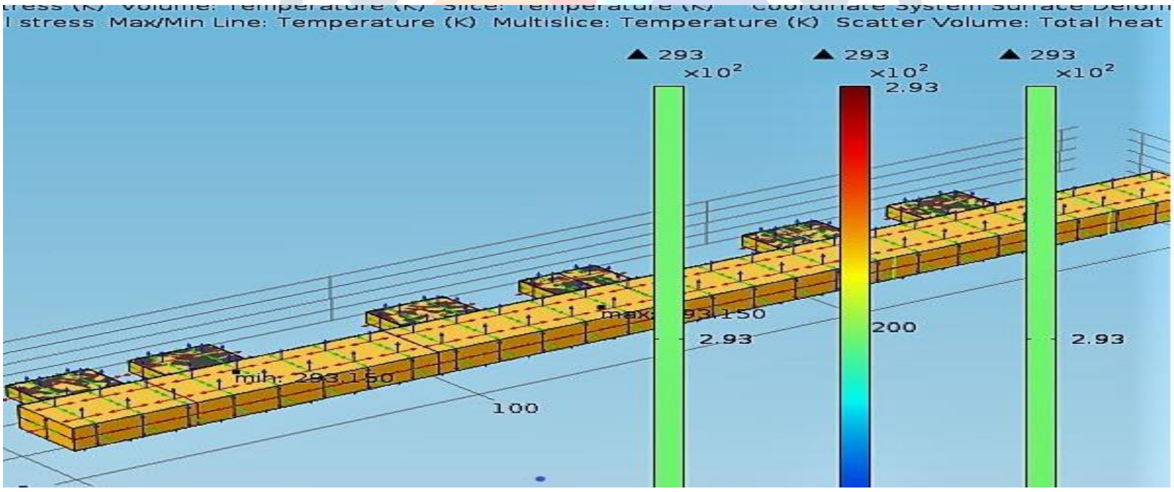


Fig [4] Comsol IDT Structure to estimate Surface roughness and Cancer Cell Progession.

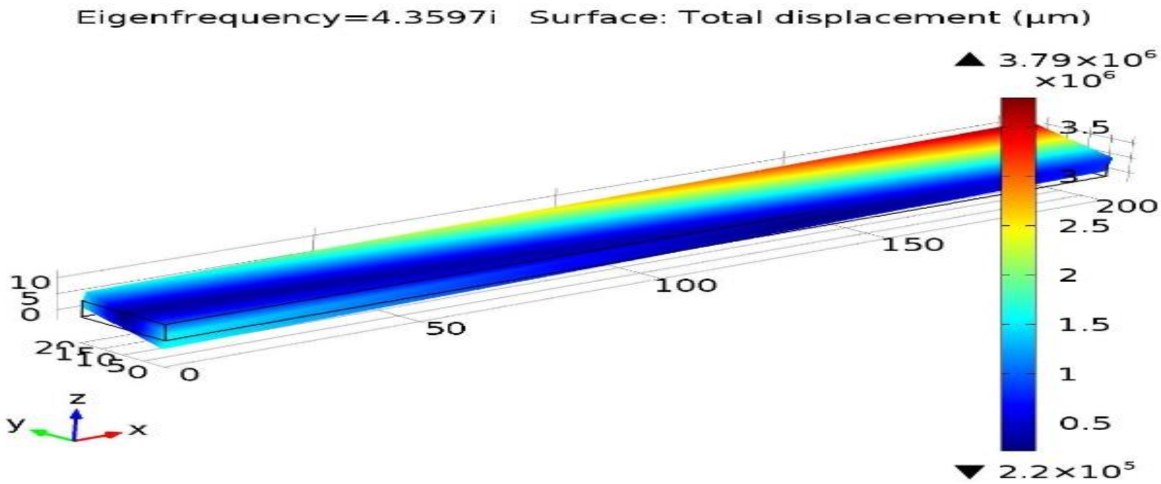


Fig [5] COMSOL Bar Structure to estimate Surface displacement at Eigen frequencies for Cancer Cell Progression.

References:

[1] Jill D. Fenske & Suzanne E. Paulson "Human Breath Emissions of VOCs", Journal of the Air & Waste Management Association, 49:5, 594-598, DOI: 10.1080/10473289.1999.10463831

[2] D. Arul, Pon Daniel ,K. Thangavel "Empirical study on Early Detection of Lung Cancer using Breath Analysis" IEEE Sponsored 2 nd International Conference on Innovations in Information, Embedded and Communication systems (ICIIECS) 2015, DOI:10.1109/ICIIECS.2015.7192869

[3] http://cdc.gov/nchs, National center for disease control and prevention, 2017.

[4] Gurusamy JT, Putrino G, Jeffery R, Dilusha Silva KKMB, Martyniuk M, Keating A, Faraone L, MEMS based hydrogen sensingwith parts-per-billion resolution, *Sensors and amp; Actuators: B. Chemical*2018).https://doi.org/10.1016/j.snb.2018.07.118.

[5] Hong-Lae Kim, Jangseop Han, Sang-Myun Lee, Hong-Beom Kwon, Jungho Hwang,Yong-Jun Kim "MEMS-based particle detection system for measuring airborne ultrafine particles"School of Mechanical Engineering, Yonsei University, 50 Yonsei-ro, Seodaemun-gu, Seoul, 03722, Republic of Koreaa© 2018 Elsevier 2018.

[6] H. K. Gatty, G.Stemme and N. Roxhed "An amperometric hydrogen sulphide sensor applicable for bad breath monitoring", Manuscript, 2015.

[7] H. K. Gatty, S. Leijonmarck, M. Antelius, G. Stemme and N. Roxhed ""An amperometric nitric oxide sensor with fast response and ppb- level concentration detection relevant to asthma monitoring", *Sensors and Actuators B: Chemical*, vol. 209, pp 639–644, 2015.

[8] G. Eranna, B. Joshi, D. Runthala, and R. Gupta, "Oxide materials for development of integrated gas sensors—a comprehensive review," *Critical Reviews in Solid State and Materials Sciences*, vol. 29, pp. 111-188, 2004.

[9] C. Bur, P. Riemann, M. Andersson, A. Schütze, and A. L. Spetz, "Increasing the selectivity of Pt-gate SiC field effect gas sensors by dynamic temperature modulation," *Sensors Journal, IEEE*, vol. 12, pp. 1906-1913, 2012.

[10] Jill D. Fenske & Suzanne E. Paulson (1999) Human Breath Emissions of VOCs, Journal of the Air & Waste Management Association, 49:5, 594-598, DOI: 10.1080/10473289.1999.10463831.

[11] Smith, D. Spanel, P. "The novel selected ion flow tube approach to trace gas analysis of air and breath," Rap. Comm. Mass Spec. 1996b, 10, 1183-1198.

[12] Lin, Y.; Dueker, S.R.; Jones, A.D.; Ebeler, S.E.; Clifford, A.J. "Protocol for collection and HPLC analysis of volatile organic carbonyl compounds in breath," Clin. Chem. 1995, 41(7), 1028-1032.

[13]G.Korotcenkov, *Handbook of Gas Sensor Materials*: Springer, 2013.

[14] Wallace, L.; Buckley, T.; Pellizzari, E.; Gordon, S. "Breath measurements as volatile organic compound biomarkers," Env. Health Persp. 1996, 104(Supp. 5), 861-869.

[15] https://cancerstatisticscenter.cancer.org/module/lCjZBQJc, American Cancer Society for Statistics and Analysis.