Clinical Diagnosis using Array Sensors

Siva Shanthini E G
MSc (IT) First Year
IIITM-Kerala
Trivandrum, India
sivavisva04@gmail.com

Vishnu G
MSc (IT) First Year
IIITMK-Kerala
Trivandrum, India
vishnu.g2989@gmail.com

Abstract*— Sensor technologies have been advanced and it is used in many fields and one of the prominent field is clinical diagnosis. It can be used to identify the specific components of an odor and analyze its chemical makeup. An electronic nose (e-nose) consists of a mechanism for chemical detection, such as an array of electronic sensors, and a mechanism for pattern recognition, such as a neural network . The e-nose can be used to identify many deadly diseases such as cancer, respiratory diseases, urinary diseases etc.

***Keywords*—e-nose,array sensors, neural network**

I INTRODUCTION

With the invention of the first gas multisensory array in 1982 a new breakthrough in the use of sensor technology in artificial olfaction began. Advancements in aroma-sensor technology, electronics, biochemistry and artificial intelligence made it possible to develop devices capable of measuring and characterizing volatile aromas released from a multitude of sources for numerous applications. These devices, known as electronic noses, were engineered to mimic the mammalian olfactory system. It is an instrument designed to obtain repeatable measurements, allowing identifications and classifications of aroma mixtures. The device allow the identification of mixtures of organic samples as a whole (identifiable to a source that released the mixture) without having to identify individual chemical species within the sample mixture. This property or technology of e-nose can be used in diagnosis of disease in medical field. Animals such as dogs, rats etc. are being used for detecting diseases like cancer, tuberculosis. Around 70% of efficiency is achieved through these animals. This method along with the e-nose technology can be used in medical diagnosis to achieve almost 95% accuracy. Studies have proved that dogs can detect lung and breast cancer via whiff of a patients breath, ovarian cancer from smelling blood, melanoma from the scent of skin, and colorectal cancer from the stink of stool samples. e-nose is a combination of multiple array sensors and pattern recognizing system. Clinical diagnosis using array sensors uses a collection of array sensors together to form a e-nose structure. There for convenience we use e-nose as the building unit.

IJERT

II HUMAN OLFACTORY SYSTEM

The olfactory system is the sensory system used for olfaction, or the sense of smell. Most mammals and reptiles have two distinct parts to their olfactory system: a *main olfactory system* and an accessory olfactory system. The main olfactory system detects volatile, airborne substances, while the accessory olfactory system senses fluid-phase stimuli. Behavioral evidence indicates that most often, the stimuli detected by the accessory olfactory system are pheromones.

A. Function

Olfactory system of humans consists of mainly two parts, a peripheral and a central one. The main function of the peripheral one is to sense an external stimulus and encoding it as an electrical signal in neurons, where as that of central one is to integrate and process central nerve system. Fig (1) shows a human olfactory system.

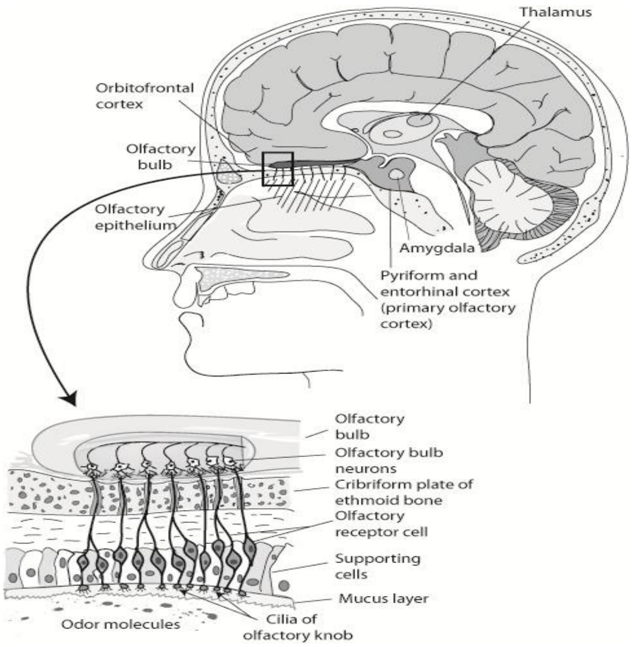

Fig1: human olfactory system

B. Peripheral

In mammals, the main olfactory system detects odorants that are inhaled through the nose, where they contact the main olfactory epithelium, which contains various olfactory receptors. These olfactory receptors are membrane proteins of bipolar olfactory receptor neurons in the olfactory epithelium. Rather than binding specific ligands like most receptors, olfactory receptors display affinity for a range of odor molecules. Olfactory neurons transduce receptor activation into electrical signals in neurons. The signals travel along the olfactory nerve. The olfactory nerve, similar to the optic nerve, is not part of the peripheral nervous system but is defined as a part of the brain. This nerve terminates in the olfactory bulb, which also belongs to the central nervous system. The complex set of olfactory receptors on different olfactory neurons can distinguish a new odor from the background environmental odors and determine the concentration of the odor. Further activities are done by the central system.

C. Central System

Axons from the olfactory sensory neurons converge in the olfactory bulb to form tangles called glomeruli. Inside the glomerulus, the axons contact the dendrites of mitral cells and several other types of cells. Mitral cells send their axons to a number of brain areas, including the anterior olfactory nucleus, piriform cortex, the medial amygdala, and the entorhinal cortex.

The piriform cortex is probably the area most closely associated with identifying the odour. The medialamygdala is involved in social functions such as mating and the recognition of animals of the same species. The entorhinal cortex is associated with memory, e.g. to pair odours with proper memories. The exact functions of these higher areas are a matter of scientific research and debate.

IJERT

In the central nervous system, odours are represented as patterns of neural activity. These representations may be encoded by space (a pattern of activated neurons across a given olfactory region corresponds to the odour), time (a pattern of action potentials by multiple neurons corresponds to the odour) or a combination of the two. Scientists debate whether the odour code is primarily temporal or spatial.

It is remarkable that humans can recognize more than 10,000 different order but they should at least differ about the 30% before they can be distinguished. This recognition of different order is made possible by the huge number of different odorant receptor. The gene family for the olfactory receptor is infecting the largest family studied so far in mammals. On the other hand the neural net of the olfactory system's provide with their 1800 glomeruli a large two dimensional map in the olfactory bulb that is unique to each odorant.

Animals also have a similar olfactory system like humans. Animals such as dogs, rats have sharp systems which can recognise order in a more precise manner. Animals like dogs, giant African pouched rats (*Cricetomys gambianus*) are used operationally to detect land mines, poison and even in detecting various kind of disease. Animals can sense a wide variety of smell. Comparing to humans animals can distinguish each smell with a slight change. It is proved that elephants can even smell water. Variety of animals like dog, fruit fly, mouse etc. is used to find presence of diseases as well as in military purpose. This sensitivity of animals is researched to derive or an electronic dive, which can be programed to sense and identify various smells and to give some inference.

III ELECTRONIC NOSE USING ARRAY SENSORS

Over the last decade, "electronic sensing" or "e-sensing" technologies have undergone important developments from a technical and commercial point of view. Electronic sensing mainly means the capability of reproducing human senses using collection of sensors called sensory arrays and pattern recognition system. Inputs such as odor molecules are fed into the chemical sensory array which is then processed with the help of pattern recognition system and the output is produced. Such an electronic sensing system can be used to identify the smell to detect the diseases in humans. e-nose can have a wide variety of application, including applications in defense.

E-nose is an electronic mimic of human nose. Similar to the central and the processing systems in humans, e-nose contains sensory array and pattern recognition system. The electronic device is not exactly a replacement to the human olfactory system but it goes beyond that. The conventional olfactory laboratory relies on human nose. But the main problem faced in this situation is human nose get tired with more and more sample. Since e-nose is an electronic system there is no such problem as multiple measurements can be taken from a single sample provided.

IV COMPONENTS AND INSTRUMENTS IN E-NOSE

An electronic nose is first defined as a device which comprises of an array of chemical sensors with different selectivity, a signal pre-processing unit and a pattern recognition system.
The list of necessary components (as follows):

- An aroma delivery system, which transfers the volatile aromatic molecules from the source material to the sensor array system.
- A chamber where sensors are stored, which has usually fixed temperature and humidity, which otherwise would affect the aroma molecules adsorption.
- An electronic transistor which converts the chemical signal into an electrical signal, amplifies and conditions it.
- A digital converter that converts the signal from electrical (analog) to digital.
- A computer microprocessor which reads the digital signal and displays the output after which the statistical analysis for sample classification or recognition is done.

Sensors play an important role in gathering data from the sample. There are a collection of sensors used to built the e-nose system that is why the diagnosis is mainly said as diagnosis using array sensors. Quartz crystals Micro Balances (QMB), Surface Acoustic Wave Sensors (SAW), Metal Oxide Semiconductor Sensors are some of the sensors used in the process.

A. Sensors Used In Enose

A sensor is a converter that measures a physical quantity and converts it into a signal which can be read by an observer or by an (today mostly electronic) instrument. For example, a mercury-in-glass thermometer converts the measured temperature into expansion and contraction of a liquid which can be read on a calibrated glass tube. A thermocouple converts temperature to an output voltage which can be read by a voltmeter. For accuracy, most sensors are calibrated against known standards.

1) Metal Oxide Semiconductor (Mos) Sensor

MOS sensors are one of the most commonly utilized sensor systems as they possess a broad range of electronic, chemical, optical and physical properties that are often stable to vary with the composition of surrounding gas atmosphere. The oxide materials in MOS sensors contain chemically adsorbed oxygen species, which can interact with gaseous molecules on the metal oxide surface thus altering the conductivity of the oxide. The change in resistance depends on the VOC that interacts with the adsorbed oxygen on the semiconductor, the metal oxide grain size and the temperature at which the sensing takes place. MOS sensors have the advantage of being inexpensive, robust, long lasting and rapidly responsive; nevertheless, they require high-temperature material processing, generally functioning at 300-500˚C, to allow rapid and reversible reactions at the sensor surface and avoid formation of a layer of chemisorbed water that would inhibit the reaction with VOCs. These results in large power consumption especially in traditional MOS sensors configured as single crystals, thin/thick films and ceramics.

2) Optical Sensors

An optical sensor in detection system comprises four basic components: a light source, suitable optics for directing light to and from the sensor, sensing materials or sensor and a photo detector for detecting light signals coming from the sensor. A wide selection of light sources are available for optical sensors, including highly coherent gas and semiconductor diode lasers, broad spectral band incandescent lamps, and narrow-band, solid-state, light-emitting diodes (LEDs) [7]. Photo-diodes, CCD and CMOS cameras can be employed to detect output signals, but the choice must be made carefully and take into account the specifications required, such as sensitivity, detective power, noise, spectral response, and response time. Optical sensors can generally be categorized into two types, i.e. intrinsic optical and extrinsic optical sensors.

3) Piezoelectric Sensors

Piezoelectric sensors rely on the piezoelectric effect, discovered by the Curie brothers in 1880, which states that certain crystals generate an electrical potential proportional to an applied mechanical stress. Inversely, when an electric potential is applied, piezoelectric crystals undergo a mechanical deformation which can in turn create a mechanical pressure. In these sensors, piezoelectric crystals have a resonant frequency which is highly sensitive to the mass change applied to the crystals.

V ENOSE WORKING

E-nose work with the help of different variety of sensors. The array sensors used in the e-nose help to sense data which is then analyzed and processed. A schematic diagram of electronic nose is shown below, fig(2):

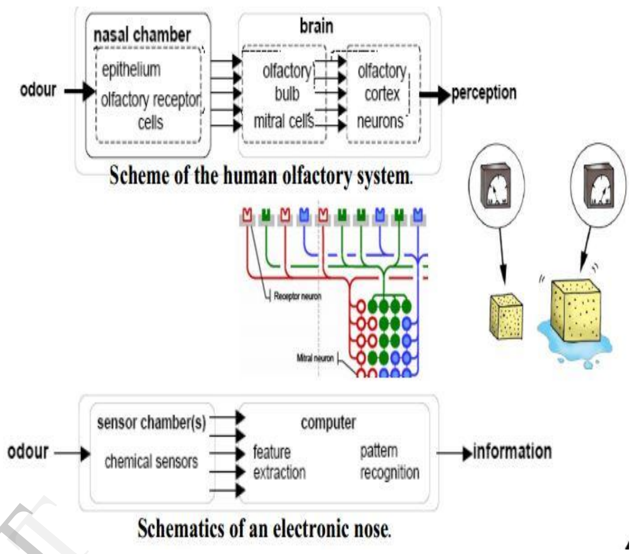

Fig2: schematic diagram

IJERT

Order or sample which is inhaled as molecular particle goes into the sensor chambers or chemical chambers. In humans this activity is done in the nasal chamber which contains olfactory receptor cells. The sensor chamber contain array of sensors. These arrays of sensors are responsible for identifying and collecting data based on the sample. Humans have brain to analyze the input and take decision. Olfactory neurons play a vital role in this activity. Similar to human brains e-nose uses computer which contain pattern recognition system stored program etc.

A functional block diagram, fig (3), shows the control flow and working of an e-nose that contain array sensors. Artificial neural network can be used to analyze information in a much simpler method. The output from the array sensors are given to the pattern recognition unit where the order is recognized based on the data from array sensors and stored program.

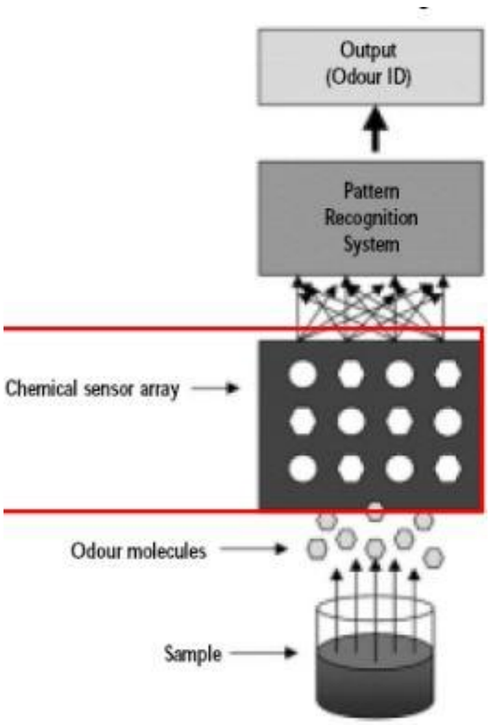

Fig3: Functional block diagram

VI ELECTRONIC-NOSE APPLICATIONS

Electronic-nose systems have been designed specifically to be used for numerous applications in many different industrial production processes. A wide variety of industries based on specific product types and categories, such as the automobile, food, packaging, cosmetic, drug, analytical chemistry and biomedical industries utilize e-noses for a broad and diverse range of applications.

The defense sector also has some wide application for the array sensors as well as the e-nose. It mainly includes the detection of land mine, and other investigation purpose. Some individual examples of electronic nose applications in each of these individual industries and product areas are discussed in more detail in the following sections.

A. Medical Pathology

Modern medicine faces the problem and challenge of achieving effective disease diagnoses through early detections of pathogenesis or disease conditions in order to facilitate the application of rapid treatments, but at the same time dramatically reducing the invasiveness of diagnostic treatments. Chemical analysis of human biological samples, such as breath, blood, urine, sweat and skin, are the most common means of diagnosing most pathological conditions. The traditional method where dog and flies are used to detect diseases such as cancer, TB etc., which can be identified in more accurate way using the array sensor enabled e-nose.

1) Cancer Detection Using Enose

It is already proved that dogs have the capability to detect cancer by sniffing the patient's breath which is termed as canine cancer detection. The sensitivity of dogs in olfactory sensing is much high compared to that of humans. They can identify specific alkanes and aromatic compounds at low concentrations in breath created by a tumor that circulates from the patient's blood to the lungs. Similarly, electronic noses can detect disease marker substances from the human body, thus having the potential of early stage detection for different types of cancers. The array sensors which are present in the e-nose can collect the input from the breath of the patient. The input that is collected in the array sensors are recognized by the pattern recognizer. The stored information and the analyzed pattern are compared to detect whether the person is having cancer or not.

Recent results showed utility of an electronic nose to smell chemicals related to lung, breast, brain, prostatic, melanoma and pancreatic cancers. However, few biomarkers are available for cancer detection at the present time due to the difficulty in determining which specific VOCs correlate with a cancer type among a vast myriad of possible compounds detected. The detection of lung cancer accounts for most cancer diagnosis by electronic noses since important biomarkers for this disease have been discovered in numerous investigations of VOCs identified from exhaled breath of lung cancer patients. Although studies have supported the correlation between the composition of breath and lung cancer, many other diseases can alter the breath composition and interfere with detection, so it is necessary not only to detect generic alterations, but also those specifically consequent to cancer. The analysis of artificial breaths is compared with those of breaths exhaled by patients and healthy controls. Results have shown that the data points of the artificially altered breath samples tend to drift toward the lung cancer group, proving the significance of the role played by these volatile com- pounds in contribution to lung cancer [93]. Researchers are dedicated to applying electronic noses to other types of cancer.
The JPL e-nose consisted of 16 sensors with uniquely coated polymer-carbon composite films and sensed the air in the head space above the cells based on a change in conductivity. The results showed that the JPL E-Nose was able to distinguish between two types of tumor cells and between two types of organ tissue, which could be used as part of multi-modality intraoperative approach for detection and treatment of brain cancers. Research has showed up to 93% accuracy on using e-nose method to detect cancers than using dogs.

2) Urinary Tract Infections

A urinary tract infection (UTI) (also known as acute cystitis or bladder infection) is an infection that affects part of the urinary tract. It is one of the most prevalent infectious diseases with 3 million UTI cases each year in the USA alone. The urinary system includes the kidneys, ureters, bladder and urethra. UTI, when it affects the lower urinary tract it is known as a simple cystitis (a bladder infection) and when it affects the upper urinary tract it is known as pyelonephritis (a kidney infection). Most UTI affects the

IJERT

lower urinary tract, which is not serious unless it spreads to the upper tract and develops into pyelonephritis; thus, early diagnosis for UTI is important and the application of an electronic nose opens the gate for on-line and simple UTI diagnosis. Electronic noses can diagnose UTIs by examining the volatile compounds produced by bacterial contaminants in urine samples. The researches has shown the potential for early detection of microbial contaminants related to UTI using an electronic nose, which might be applied in rapid systems for use in clinical practice .

3) Respiratory Diseases

The extensive research for non-invasive respiratory disease markers has led to the development of an electronic nose which can distinguish diseases that affect the airway or pulmonary parenchyma. The respiratory disease like tuberculosis, asthma can be identified in its preprimary stage using the e-nose technology. The analysis of exhaled breath has been proposed as the main option for detection and identification of respiratory diseases, although other approaches exist, e.g. the analysis of blood samples and bacterial culture samples. The breath prints produced by an electronic nose are associated with airway inflammation activity, and provide a molecular basis for disease detection and a personalized pharmacological treatment.

Two studies were conducted to estimate the diagnostic accuracy of the Diagnose analysis, I.e., a Proof of Principle Study (30 participants) and a Validation Study (194 participants). The results showed that the electronic nose can differentiate between TB patients and healthy controls with a sensitivity of 76.5% and specificity of 87.2% when identifying TB patients within the entire test population. The research has demonstrated a possibility of an electronic nose as a portable and fast- time-to-result device to screen search for TB cases in rural areas, without the need for highly-skilled operators or a hospital center infrastructure.

Thus e-nose opens a new diagnosis method in detecting diseases in clinical industry.

4) Food Freshness, Quality, Ripeness And Shelf-Life

It is one of the important fields to be considered in today’s situation. Freshness of food material is an important concern. Quality and freshness of the food including both cooked as well as the uncooked food can be detected and certified using array sensor application.

The age of fruits (ripeness or maturity level) determines the shelf life and future rate of quality loss due to changes in flavor, firmness and color. Harvesting fruits at an optimal physiological condition ensures good quality at a later stage (when evaluated by the consumer) by enhancing a number of quality characteristics that extend the shelf-life, slow the rate of decline in firmness or texture, and maintain a preferred level of flavor and overall appearance.

There for e-nose can play a vital role in food and food product industries.

VII CONCLUSION

Array sensors or electronic sensors are used in many application areas where olfactory plays a major role. Breath analysis is an attractive procedure for electronic noses to predict disease because it is non-invasive and sampling methods are simple. However, one of the major proficiencies of diagnostic breath analysis is the difficulty in discovering the relationship between identified marker compounds with a pathology, since in most cases specific metabolic pathways are unknown [102]. Once these difficulties are resolved, the application of electronic noses could make up a vital part in monitoring disease epidemiology.

REFERENCES

[1] Persaud, K.C.; Dodd, G. Analysis of discrimination mechanisms in the mammalian olfactory system using a model nose. Nature 1982, 299, 352-355.J. Clerk Maxwell, A Treatise on Electricity and Magnetism, 3rd ed., vol. 2. Oxford: Clarendon, 1892, pp.68-73.

[2] I.S. Jacobs and C.P. Bean, “Fine particles, thin films and exchange anisotropy,” in Magnetism, vol. III, G.T. Rado and H. Suhl, Eds. New York: Academic, 1963, pp. 271-350.

[3] J. W. Gardner and P. N. Bartlett, “A Brief History of Electronic Noses,” Sensors and Actuators B, Vol. 18-19, No. 1-3, 1994, pp. 211-220

[4] Gardner, J.W.; Bartlett, P.N. A brief history of electronic noses. Sens. Actuat. B: Chem. 1994, 18, 211-220.

[5] http://en.wikipedia.org/wiki/Sensor

[6] A. Kolmakov and M. Moskovits, “Chemical Sensing and Catalysis by Onedimensional Metal-Oxide Nanostruc- tures,” Annual Review of Materials Research, Vol. 34, 2004,pp.151-180. doi:10.1146/annurev.matsci.34.040203.112141

[7] S. Kladsomboon, M. Lutz, T. Pongfa and T. Kerdcharoen, “An Optical Artificial Nose System for Odor Classifica- tions Based on LED Arrays,” Proceedings of the 8th In- ternational Conference on Electrical Engineering/Elec- tronics, Bangkok, 17-19 May 2011, pp. 145-148.

[8] M. Schaechter, G. Medoff and B. I. Eisenstein, “Mecha- nisms of Microbial Disease,” Lippincott Williams & Wil- kins., Baltimore, 1999.

[9] A. K. Pavlou, N. Magan, C. McNulty, J. M. Jones, D. Sharp, J. Brown and A. P. F. Turner, “Use of an Elec- tronic Nose System for Diagnoses of Urinary Tract Infec- tions,” *Biosensors and Bioelectronics*, Vol. 17, No. 10, 2002, pp. 893-899. doi:10.1016/S0956-5663(02)00078-7

IJERT