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   HYPOTHESES

   RESEARCH METHODOLOGY

   RESULTS & DISCUSSION

   FINDINGS

   RECOMMENDATIONS/SUGGESTIONS

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- Schemenner, R.W., Huber, J.C. and Cook, R.L. (1987), "Geographic Differences and the Location of New Manufacturing Facilities," Journal of Urban Economics, Vol. 21, No. 1, pp. 83-104.

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- Garg, Sambhav (2011): "Business Ethics" Paper presented at the Annual International Conference for the All India Management Association, New Delhi, India, 19–22 June.

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THE ELECTRONIC-NOSE TECHNOLOGIES IN HEALTHCARE AND BIOMEDICINE: A CASE STUDY

M.NAVEEN KUMAR
RESEARCH SCHOLAR
PH.D IN COMPUTER SCIENCE
DRAVIDIAN UNIVERSITY
KUPPAM

ABSTRACT
This paper reviews the range of sensors used in electronic nose (e-nose) systems to date. It outlines the operating principles and fabrication methods of each sensor type as well as the applications in which the different sensors have been utilized. It also outlines the advantages and disadvantages of each sensor for application in a cost-effective low-power handheld e-nose system.

KEYWORDS
Sensors, Gases.

INTRODUCTION
There have been many developments in electronics to create real life environments with respect to sight and sound. But there are three other significant senses- smells, touch and taste which have not been experimented much with. The sensor technology of artificial olfaction had its beginnings with the invention of the first gas multi sensor array in 1982. Advances 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.

Electronic nose is being developed for military and homeland security applications in the detection of explosives and hazardous chemicals. Currently, many explosives are found by dogs and other animals with highly sensitive olfactory senses. Developing an efficient hand-held device has been a challenge because volatile explosive vapours found in large open spaces are present at low concentrations that range from parts per billion or even parts per trillion. Bomb detectors might not be very good than electronic noses because they are blind to many important environmental and olfactory chemicals. However, the diversity of today's terrorist threats (explosive, chemical, and biological) makes it increasingly apparent that there is a role for electronic noses with the ability to quickly learn and recognize threat vapours of any kind. Electronic noses are best used as investigative rather than screening tools

A few smell-sensing instruments had been proposed in narrow applications earlier in the 1960's. Moncrief developed one of the first smell detection instruments in 1961 for agricultural application, where he used a single coated thermistor as the smell sensor. In 1964, Wilkens and Hartmen developed a smell detector where an array of smell detectors was used. It was in late 1980's that the first intelligent electronic smelling system came into being. Researchers in the University of Warwick in Coventry, England, developed sensor arrays for odour detection. Pattern recognition techniques were used by Gardner to discriminate the output of electronic smell sensors. Hartfield described an integrated circuit based device that performs data acquisition from a miniature array of 32 conducting polymer gas sensors. David and Gardner designed a circuit capable of measuring signals from arrays of resistive and piezoelectric sensor types in the same board

Electronic noses were originally used for quality control applications in the food, beverage and cosmetics industries. Current applications include detection of hazardous chemicals and explosives, detection of odours specific to diseases for medical diagnosis, and detection of pollutants and gas leaks for environmental protection. The Warwick pioneers envisioned an electronic equivalent of the mammalian olfactory system and so even though it doesn't resemble its biological counterpart the least bit, the label 'electronic nose' or 'E nose' has been widely adopted.

Artificial noses have been around for more than 20 years. These devices typically consist of arrays of chemical sensors that respond to odorant molecules. Each sensor responds slightly differently to a given odor, and taken together, the sensors give an "odor fingerprint"—a characteristic response pattern, such as a series of colors to each odor.

Most of these devices have been able to identify and distinguish only between specific odors they've previously been trained to recognize, however, says neuroscientist Rafi Haddad of the Weizmann Institute of Science in Rehovot, Israel. If an artificial nose is ever to replace the real thing, he says, it will have to be able to classify odors it has never encountered before

Electronic noses use almost the same sample delivery and transfer techniques as gas-chromatography systems, but do not include columns or mass spectrometers, Warburton says. Chemical detection in most electronic noses is performed using a series of sensors, predominantly comprised of conducting-polymer, metal-oxide, and infrared sensors.

"This kind of technology can be used around the clock to analyze odor quality and can be operated by technicians who have much less training than those who operate gas-chromatography systems," says Aaron Kramer, project manager for Nordic Sensor Technologies AB, Linkoping, Sweden. Electronic nose systems are also more affordable than most GC/MS systems.

Despite these benefits, electronic nose systems are not designed to replace standard analysis systems. "When the electronic nose detects a problem or quality deviation, researchers will still need to perform traditional chemistry methods with GC/MS to learn what is causing the problem," Kramer says.

The term "electronic nose" is a bit of a misnomer and has found varied acceptance within the field. Some companies, including Nordic Sensor Technologies AB, are trying to abandon it because the technology does not simulate the exact function of a human nose.

The human nose has been used as an analytical tool in many industries to measure the quality of food, drinks, perfumes and also cosmetic and chemical products. It is commonly used for assessing quality through odour and this is carried out using sensory panels where a group of people fills out questionnaires on the smells associated with the substance being analysed. These sensory panels are extremely subjective as human smell assessment is affected by many factors. Individual variations occur and may be affected by physical and mental health as well as fatigue (Pearce et al., 2003). For this reason, gas chromatography and mass spectrometry have been employed to aid human panels to assess the quality of products through odour evaluation and identification and also to obtain more consistent results. However, these assistive techniques are not portable, they tend to be expensive and their performance is relatively slow.

The solution to the shortcomings of sensory panels and the associated analytical techniques is the electronic nose (e-nose). E-nose systems utilize an array of sensors to give a fingerprint response to a given odour, and pattern recognition software then performs odour identification and discrimination. The e-nose is a cost-effective solution to the problems associated with sensory panels and with chromatographic and mass-spectrometric techniques and can accommodate real time performance in the field when implemented in portable form.

The development and utilization of many new electronic-nose (e-nose) applications in the healthcare and biomedical fields have continued to rapidly accelerate over the past 20 years. Innovative e-nose technologies are providing unique solutions to a diversity of complex problems in biomedicine that are now coming to fruition. A wide range of electronic-nose instrument types, based on different operating principles and mechanisms, has facilitated the creation of different types and categories of medical applications that take advantage of the unique strengths and advantages of specific sensor types and sensor arrays of different individual instruments.

Electronic-nose applications have been developed for a wide range of healthcare sectors including diagnostics, immunology, pathology, patient recovery, pharmacology, physical therapy, physiology, preventative medicine, remote healthcare, and wound and graft healing. E-nose biomedical applications range from biochemical testing, blood compatibility, disease diagnoses, drug purity, monitoring metabolic levels, organ dysfunction, and telemedicine. This review summarizes some of the key technological developments of electronic-nose technologies, arising from past and recent biomedical research, and identifies a variety of future e-nose applications currently under development which have great potential to advance the effectiveness and efficiency of biomedical treatments and healthcare services for many years.

A concise synthesis of the major electronic-nose technologies developed for healthcare and medical applications since the 1980s is provided along with a detailed assessment and analysis of future potential advances in electronic aroma detection (EAD) technologies that will provide effective solutions to newly-emerging problems in the healthcare industry. These new e-nose solutions will provide greatly improved quality controls for healthcare decisions and diagnoses as well as badly needed final confirmations of appropriate patient treatments. The purpose of this chapter is to provide some detailed insights into current and future e-nose applications that will yield a variety of new solutions to detection-related tasks and difficult problems in the fields of healthcare and biomedicine. The uses of electronic-noses for quality control (QC) and quality assurance (QA) issues, associated with numerous diagnostic testing activities conducted within the medical field, also are discussed.

ELECTRONIC NOSE

The electronic nose is a system that consists of three functional components that operate serially on an odorant sample-a sample handler, an array of gas sensors and a signal processing system. The output of the electronic nose can be the identity of the odorant, an estimate of the concentration of the odorant, or the characteristics properties of the odour as might be perceived by a human.

ENS can be seen as arrays of-non specific sensors able to generate electrical signals in response to either simple or complex volatile compounds, and give through a suitable multi component analysis technique, the possibility of discrimination, recognition and classification of odours. The target compound, in gaseous form, is introduced into the sensing chamber where the sensors are exposed to the vapour. A variety of basic sensors can be used according to the nose strategy chosen. Some of them are sensitive to the mass of adsorbed species; others show sensitivities to electric charges while others are based on either surface or bulk conductivity changes due to chemically interactive materials

These changes are dependent on a complex interaction between the components of the vapour and the sensors, as each sensor responds to a number of components in a unique manner. Each sensor in the array has different characteristics (e.g., coatings, operating temperatures, etc.) and, hence, each sensor will give a different electrical response (voltage output) for a particular odour.

The pattern of response across all the sensors in the array is used to identify and/or characterise the odour. In electronic noses pattern recognition methods are required for the qualitative analysis of odours or of different compounds present in a certain mixture and multi component analysis methods are required for the quantitative determination of one or more compounds in a mixture. Commercially available analysis techniques fall into three main categories as follows:

1. Graphical analyses: bar chart, profile, polar and offset polar plots
2. Multivariate data analyses (MDA): principal component analysis (PCA)
3. Network analyses: artificial neural network (ANN) and radial basis function (RBF)

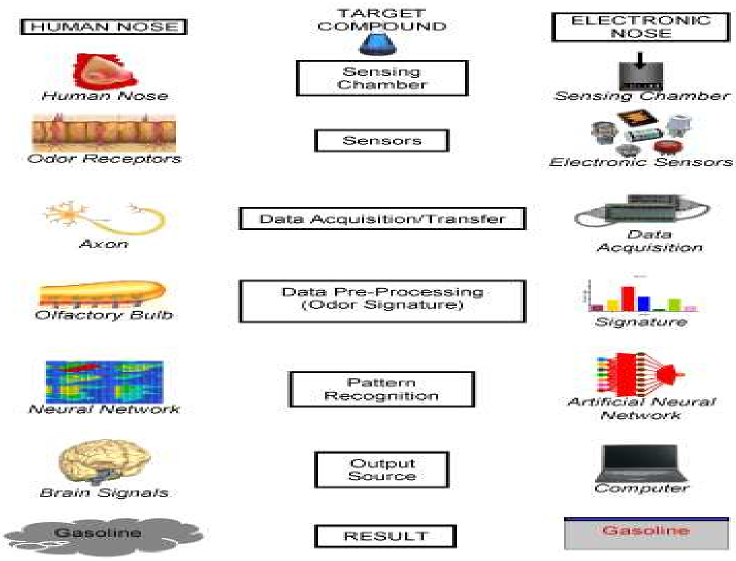
Experimental data are evaluated by a qualitative or quantitative link between output signals of an instrument and the chemical information (composition or concentration of analytes). This requires a comparison of the sensor outputs with previously recorded calibration data. When high concentrations of volatile are measured, a non-linear pattern recognition technique, such as ANN (Artificial Neural Networks), would be more appropriate.

On a very simplified and abstract level, ANN is based on the cognitive process of the human brain. ANNs are a commonly used pattern recognition technique which attempt to mimic the biological processes of the human brain.

COMPARISON OF ELECTRONIC NOSE WITH BIOLOGICAL NOSE

Each and every part of the electronic nose is similar to human nose. The function of inhaling is done by the pump which leads the gas to the sensors. The gas inhaled by the pump is filtered which in the human is the mucus membrane. Next comes the sensing of the filtered gas, which will be done by the sensors i.e., olfactory epithelium in human nose. Now in electronic nose the chemical retain occurs which in human body is enzymal reaction. After this the cell membrane gets depolarised which is similar to the electric signals in the electronic nose. This gets transferred as nerve impulse through neurons i.e., neural network which is analogous to the electronic circuitries in the electronic nose.

FIGURE 2.1: BIOLOGICAL AND ARTIFICIAL OLFACTION



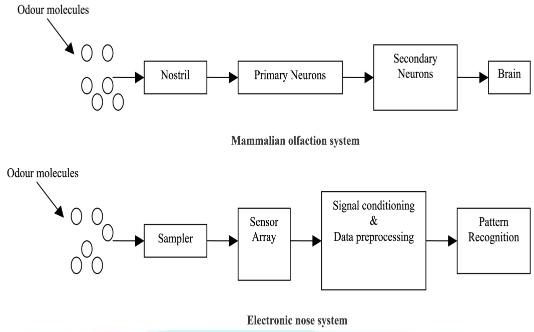
THE NEED OF ELECTRONIC NOSE

Why do we have to electronify the nose? The human sniffers are costly when compared to electronic nose. It is because these people have to be trained. This is more time consuming than the construction of an electronic nose. Also the speedy, reliable new technology of the gas sensors in the electronic nose helps in the continuous real time monitoring of odour at specific sites in the field over hours, days, weeks or even months. An electronic nose also overcomes other problems associated with the human olfactory system. For the confirmation of the values obtained from a sniffer the result obtained from the sniffer has to be compared with some other sniffer's value. And here there are great chances of difference in the values got by each individual. Detection of hazardous or poisonous gas is not possible with a human sniffer. Thus taking into consideration all these cases of individual variability, adaptation (becoming less sensitive after prolonged periods of exposure), fatigue, infections, mental state and subjectivity we can say that electronic nose is highly efficient than human sniffer

Principle of operation of e-nose systems. The e-nose attempts to emulate the mammalian nose by using an array of sensors that can simulate mammalian olfactory responses to aromas.

The odour molecules are drawn into the e-nose using sampling techniques such as headspace sampling, diffusion methods, bubblers or pre-concentrators. The odour sample is drawn across the sensor array and induces a reversible physical and/or chemical change in the sensing material, which causes an associated change in electrical properties, such as conductivity. Each "cell" in the array can behave like a receptor by responding to different odours to varying degrees. These changes are transduced into electrical signals, which are preprocessed and conditioned before identification by a pattern recognition system as shown in the below Figure. The e-nose system is designed so that the overall response pattern from the array is unique for a given odour in a family of odours to be considered by the system.

The following figure shows the Comparison of the mammalian olfactory system and the e-nose system:



APPLICATIONS OF ELECTRONIC NOSE

The advent of the electronic nose has opened a variety of applications and new possibilities in many fields where the presence of odours is the relevant phenomenon. The biggest market for the electronic nose is the food industry including quality monitoring or grading of food, beverage and fruits, inspection of food packaging materials. There are also researches being done in using the electronic nose for disease diagnosis. An electronic nose can examine odours from the body (e.g., breath, wounds, body fluids, etc.) and identify possible problems. Electronic noses are found to be effective tools in environmental management. Applications include that analysis of fuel mixtures, detection of oil leaks, testing ground water for odours, and identification of household odours. Potential applications include identification of toxic wastes, air quality monitoring, and monitoring factory emissions. Applications include that analysis of fuel mixtures, detection of oil leaks, testing ground water for odours, and identification of household odours. Potential applications include identification of toxic wastes, air quality monitoring, and monitoring factory emissions.

Others in the industry have generalized the term to pertain to all technologies that mimic the sense of smell through chemical fingerprinting, says Wayne Gagne, applications specialist with AromaScan, Hollis, N.H.

Most systems that can be categorized as electronic noses create chemical footprints by analyzing sample headspace. The gaseous release generated by odorous samples is collected from equally sized samples over a period of time, Gagne says. Once odors are analyzed by an electronic nose, the chemical footprints are placed in a library and used as a comparison for other samples.

"The machine doesn't know what any odors are – you have to give it information to correlate chemical footprints with odors," Gagne says. "We are finding that these tools are particularly important for the polymer and food industries."

Relatively new technologies, electronic noses have only been on the market for about a decade. Because of this, companies have spent a great deal of time over recent years educating clients about the need for their products. Worldwide, about seven companies are active in the market, and about as many are working to develop the technology, Warburton says.

Some electronic noses can be combined with gas chromatographs to provide more exact descriptions of the chemicals that comprise specific odorants. Despite this enhanced capability, the instruments will not notice that odors are disagreeable to humans unless they are told which chemical footprints cause unpleasant smells.

MEDICAL DIAGNOSTICS AND HEALTH MONITORING

Modern medicine faces the problem and challenge of achieving effective disease diagnoses through early detections of 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.

RESPIRATORY DISEASE DIAGNOSTICS

It is well known that exhaled human breath contains thousands of volatile organic compounds (VOCs) in gas phase, which can individually be detected by gas chromatography and mass spectrometry.

Such VOCs can potentially be used as non invasive biomarkers of various biochemical pathways that are operative in health and disease. Interestingly, it has been demonstrated that there is a link between exhaled VOC and human lung disease, in particular regarding lung cancer. An electronic nose has been developed that can diagnose respiratory infections such as pneumonia by comparing smell prints from the breath of a sick patient with those of patients with standardized readings. It is also being studied as a diagnostic tool for lung cancer.

URINARY TRACT INFECTIONS

Urinary tract infections have been thoroughly investigated by Di Natale, Aathithan and Pavlou proposed the use of the electronic nose as a potential diagnostic tool for patients affected with kidney diseases, by distinguishing traces of blood in urine samples, and for the rapid identification of E. coli, Proteus spp. and Staphylococcus spp. infections at very high levels of confidence. Aathithan analyzed 534 clinical urine specimens of which 21 % had significant bacteriuria indications. The sensitivity and specificity of the electronic nose compared with conventional cultural counts were 83.5% and 87.5% respectively, but the e-nose diagnoses were done at significantly lower costs.

ENVIRONMENTAL MONITORING

Environmental applications of electronic noses include analysis of fuel mixtures, detection of oil leaks, testing ground water for odours, and identification of household odours. Potential applications include identification of toxic wastes, air quality monitoring, and monitoring factory emissions. Air pollution and many different types of odours are common pollutants which require monitoring and quantification. The exhaust from automobiles and trucks is a very good example of environmental air pollution. Water pollution occurs where there are leaking fuel tanks or where spills have occurred and organics have entered the aquifers. Water pollution associated with rivers, lakes, and water aquifers represents approximately 60% of the world environmental problems. Because pollutants in water are volatile, water pollution can be measured simply by testing the headspace vapours above the water.

FOOD INDUSTRY

Panels of well trained tasters and smellers are daily utilized to certify the goodness of foods and their fitting with the human taste. Therefore food analysis represents also a practical field where an electronic nose can be utilized as an essential support of the human capabilities. Analysis of fruit ripeness, food and beverage quality check, grading of wines, meat quality assessment etc are some of its major areas of application in this industry. Electronic noses can be used to augment or replace panels of human experts. The Electronic nose has also been applied to both alcoholic and non-alcoholic beverages, for example in the identification of coffee bean types; instant coffee aromas during processing; the detection of diacetyl, dimethyl sulphide and amylacetates during fermentation.

ANALYSIS OF FRUIT RIPENING

Since fruit ripening is associated with an accumulation of aromatic volatiles during ripening for both climacteric and non climacteric fruit, electronic noses seem to hold a great potential in the fruit industry. Sensor signal used in the electronic nose helps to assess fruit quality and maturity. Using e noses to monitor fruit freshness and maturity level is advantageous as it can maximize profits and have better consumer satisfaction. Information from the noses can help in removal of rotten fruits at the appropriate time which can help in avoiding storage losses due to rots and fruit diseases.

ANALYSIS OF MEAT QUALITY

Meat, especially beef, reaches an acceptable state for consumption after a long period of storage at low temperature, a storage procedure known as aging. During storage, not only aging but also bacterial spoilage can occur. Consequently, to obtain appropriately aged meat, it is desirable to monitor the progress of aging and bacterial spoilage simultaneously. A direct sensing method for monitoring meat quality can be employed. The sensor is composed of an Ag/AgCl electrode and a platinum electrode on which putrescine oxidase or xanthine oxidase were immobilized to estimate bacterial spoilage or the progress of aging, respectively.

ANALYSIS OF DAIRY PRODUCTS

The shelf-life of milk also has been studied. A Fox 4000 electronic nose equipped with 18 sensors and an auto sampler was used to evaluate the growth of total bacteria in milk stored at ambient temperature and 5 °C. The results showed that measurements generated by the electronic nose could be used to detect both bacterial growth in milk and shelf-life. Gorgonzola and cottage cheese were characterized using polyperrole semiconductor sensors in the electronic noses.

ADVANTAGES OF ELECTRONIC NOSE OVER BOMB DETECTORS

A bomb detector is designed to answer the question, what something is not. For example, it is not a bomb. It provides little or no information on the identity of the object producing the odour or fragrance. Conversely an electronic nose answers the question what something is. For example, it is jet fuel. An electronic nose sees everything and misses nothing. A bomb detector is best used to detect trace amounts of explosives in the presence of high background chemical vapours. An electronic nose is best used to characterize and recognize objects by detecting the principal chemical components of the object's aroma. An electronic nose is limited in its ability to detect trace levels of explosives or chemical weapons by its inherent and finite dynamic range. Its full sensitivity can be best used when there are no high-concentration background chemicals. Electronic noses have the ability to recognize an almost limitless number of chemical vapour threats while bomb/chemical agent detectors provide the ability to detect specific target chemicals at trace levels while not being affected by high ambient concentrations of non-target compounds. Electronic noses provide a different screening capability with inherently more information gathering power than bomb detectors and help to resolve ambiguities by using a library of aroma signatures. Therefore, an electronic nose would work well screening the relatively clean air of a commercial office building, military headquarters and other enclosed spaces such as a shipping container.

CONCLUSION

An "electronic nose" is a system originally created to mimic the function of an animal nose. However, this analytical instrument is more a "multi-sensor array technology" than a real "nose". Whatever the sensor technology, it is still far from the sensitivity and selectivity of a mammalian nose. Therefore, its aim is not to totally replace either the human nose or other analytical methods. A sensory panel is necessary to define the desired product quality which can then be used to train the system. Traditional analytical methods such as GC-analysis will always be needed to determine qualitatively or/and quantitatively why one food sample differs from others. The "electronic nose" can only perform quick "yes or no" tests in comparison to other products. It could occasionally replace sensory analysis and even perform better than a sensory panel in routine work, or in cases where non-odorous or irritant gases need to be detected.

Compared to classical and other novel analytical methods, the electronic nose built offers a cheap and non destructive instrument that (if properly programmed and automated) can be operated by non specialists.

The number of measurements that can be done in a day compares favourably to other sophisticated methods, such as aromatic profile identification using chromatography (one of the newest approaches), and since the whole process is automatic, the cost of each measurement is very low. Therefore, in the near future, the electronic nose could be envisaged as a global measurement system calibrated for ripeness determination or a multi instrument system to extract the indicators for which it has been calibrated.

Food analysis is a very complex discipline. Due to its strict interaction with the quality of life it is extremely important to improve the performances of the methods in the fields. EN seems to be a new instrument that can offer the unique advantage of providing fast and low expensive qualitative analysis of many kinds of foods.

Further work needs to address important limitations. For example, a straightforward procedure should be devised to detect and correct sensor drift from year to year. Also, the initial calibration of the system for a given cultivar should take only a few measurements and be valid, at least, for some consecutive campaigns. Finally, the measurement cycle should be faster in order to increase throughput. All of these considerations are being studied and might imply the optimization of the sampling process, the use of more advanced processing algorithms, and the incorporation of new sensor technologies into the system.

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