CHAPTER 2

ELECTRONIC NOSE – A REVIEW

2.1 INTRODUCTION

The sense of smell is extraordinarily powerful. For years, engineers worldwide have been working to develop mechanical systems that can mimic the human senses of smell, since it is one of the most subtle and most powerful features of mammalian existence. From the comprehensive review of literature made, it is proposed to apply this machine olfaction (Electronic nose) technology for the present investigation on medical diagnosis. This chapter gives an introduction to the how and why of Electronic noses.

2.2 CONCEPT OF ELECTRONIC NOSE

The Standard approach to odour analysis is to employ analytical chemistry instruments such as Gas Chromatography and Mass Spectrometry (GC/MS). These are helpful in quantifying smells, but they are time-consuming, expensive and seldom performed in real-time in the field (Troy Nagle 1998). This paved the way for the development of an alternative device so called “E-nose” with advancements in odour sensing technology and pattern recognition techniques. The main motivation behind this is the development of qualitative, low cost, real-time and portable device to perform reliable, objective and reproducible measures of volatile compounds and
odours. The E-nose draws its motivation from biology. In order to develop an E-nose it is useful to examine the physiology behind olfaction as it is necessary to achieve a reliable, subjective and analytically acceptable system (Keller 1999).

2.3 PRINCIPLES OF BIOLOGICAL OLFACITION

One of the most incredible natural systems is the mammalian olfactory system. A specialised tissue in the nose called olfactory epithelium contains olfactory receptor cells. These nerve cells interact with the odourant molecules and thus cause the sensation of smell (Craven 1996, Bartlett 1997b, Pearce 1997). The olfactory cell consists of number of cilia, where G receptor binding proteins are located at the surface of the cilia. These G receptor binding proteins cause excitation in the neurons. They have partially overlapping sensitivities to odourants and are about 100 million olfactory cells, which amplify the signal and generate secondary messages (Gardner 1994). Thus the sensory cells in the epithelium respond by transmitting signals along axon in the olfactory bulb, where it terminates in a cluster of neural network called glomeruli. These signals are further processed in about 100000 mitral cells and then finally sent via a granular cell layer to the brain (Keller 1999). In the brain, the signals are decoded using a kind of pattern recognition (Figure 2.1).
Figure 2.1 Flowchart of Natural Olfactory System
(Adapted from Giorgio 2004, Figure 1.2.2)
Thus the human olfactory system can discriminate aromas without separating mixtures into individual compounds. The three basic elements, namely the olfactory receptor cells, the olfactory bulb and the brain formed the basis for the development of the artificial olfaction devices. In 1980s, by using an array of gas sensors and pattern recognition techniques, machine olfaction was invented as Electronic nose (E-nose), for distinguishing a variety of odours (Gardner 1999).

2.4 ELECTRONIC NOSE SYSTEM

Electronic nose System is an artificial olfactory system, where the olfactory receptor cells are replaced by a chemical sensor array. The sensors generate a time-dependent electrical signal in response to the interaction of an odour with the sensor itself. The olfactory bulb is represented by a data pre-processing unit, which compensates for sensor drift and noise. The final stage in artificial olfaction is the pattern recognition system, which is corresponding to the human brain (Gardner 1999).

Pavlou et al (2000b) identified three key parameters for gas-sensing based diagnostics viz, a mechanism for generating volatiles together with gas injection system as sampling unit and sensorial detection system and complex pattern recognition system (Figure 2.2). The forthcoming sections discuss the utilization of these three key parameters throughout this investigation.
Figure 2.2 Flowchart of Artificial Olfactory System
(Adapted from Giorgio 2004, Figure 1.3.1)
2.5 SAMPLING UNIT

To analyse any substance with an E-nose, the sample has to be brought into the sensor chamber. The role of the sampling unit is to collect the sample, condition it and transfer it into the sensor chamber and then to restore the sensor by means of a cleaning procedure. The design of the sampling unit should maintain all factors such as temperature, humidity etc., that are capable of influencing sensor responses. These factors are kept under required parameters, so that only the composition of odour is retained in the sample. This type of design of sampling unit ensures good stability, repeatability, fast sensor responses and high amplitude signals. These factors are highly desired, as sampling is the first fundamental step of data acquisition and hence its execution influences all successive steps.

Sample handling techniques can be divided into two main categories: with and without pre concentration depending upon the application and nature of sample (Pearce 2003) (Table 2.1). If great difference exist between the samples, sampling method without pre-concentration is sufficient. On the other hand for trace analysis, pre concentration of the sample is necessary.

Table 2.1 Different sampling techniques

<table>
<thead>
<tr>
<th>Without Pre concentration</th>
<th>With Pre concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample flow system</td>
<td>Dynamic Head Space Sampling</td>
</tr>
<tr>
<td>Static Head Space Analysis</td>
<td></td>
</tr>
<tr>
<td>Semi Static Head Space Analysis</td>
<td>Thermodesorption</td>
</tr>
</tbody>
</table>
For E-nose, there are two main methods to treat the sample of measurement, i.e., headspace sampling and online measurement. The differences in these two strategies are mainly due to a different point of view; in the case of headspace sampling the ‘sampling action’ is to deliver the sample to the E-nose; in the case of on-line measurement the ‘sampling action’ is to introduce the E-nose in the sample environment.

2.5.1 Head Space Sampling

In head space sampling method, the head space should be sampled with maximum possible efficiency without altering its composition. The Head Space (HS) of a sample contains volatile organic compounds. The measure of head space by the chemical gas sensors reveals the information about the nature and the composition of the sample. This head space or the volume of gas is brought into the sensor chamber by the sampling unit for further analysis.

A correct and effective application of this method is obtained with a careful monitoring of partition coefficient \(k\) and phase ratio \(\beta\). The partition coefficient \(k\), is given by the Equation (2.1)

\[
k = \frac{C_i(s)}{C_i(g)} \tag{2.1}
\]

where the concentrations of the analyte \(i\) in the gas phase is \(C_i(g)\) and liquid/solid sample phase is \(C_i(s)\). Compounds that have low \(k\) values will tend to partition more readily into the gas phase and have relatively high responses and low limits of detection.
Another important parameter to match with the partition coefficient is the phase ratio ($\beta$), defined as the relative volume of the headspace ($v_g$) compared to volume of the sample ($v_s$) in the sample vial as given in Equation (2.2).

$$\beta = \frac{v_g}{v_s}$$  \hspace{1cm} (2.2)

Lower values for $k$, $\beta$ (i.e., larger sample size) will yield higher responses for volatile compounds (Snow 2002, Iguchi 2000).

2.5.2 Online Measurement

On the other hand, the need of online sampling can be due to direct monitoring of particular application. Some important on-line measurement techniques like diffusion method, permeation method, bubbler method and sampling bags (Ohnishi 1992, Phillips 1997).

2.6 GAS SENSOR ARRAY

The gas sensor array is considered as the main and most important part of an E-nose as it is similar to the olfactory nerves in the human olfactory system. It consists of an array of gas sensors, where each sensor can be described as a device. This device when exposed to a gaseous chemical compound or mixture of chemical compounds, it alters one or more of its physical properties. The physical property may be the mass of the sensor, electrical conductivity, or capacitance that can be measured and quantified directly or indirectly (Harwood 2001). Sensors can be classified according to their operating principles, each class having a different sensitivity and selectivity. The array of sensors is designed by the principle that avoids the
combinations of sensors which produce the same information by different means, e.g. pH and conductivity.

The E-nose system requires more than one sensor so that it can give unique smell print for each particular class of compounds and can be discriminated from other sample. If there is any requirement to screen a particular class of compounds whose exact composition would vary, then a combination of sensors are required. One sensor of which, is sensitive to a particular compound of interest, while the others detect only the functionality of the compound. For example, 2, 4-dinitrophenyl-hydrazine reacts with all ketones and a sensor based on this reaction would give the total concentration of all ketones present in that sample. However, a polypyrrole-based sensor can distinguish between different ketones based on the minor differences in their polarity. A third sensor can use the principle of molecular size to restrict the ketones detection. Combination of these three sensors will provide definitive information on the mixture to which they are exposed (Troy Nagle 1998, Harwood 2001).

By providing enough plasticizer to the sensors results in fast response regardless of the concentration of the gas being analyzed (Bartlett 1997b). This is very important as it allows to continuously monitoring the sample of interest with real-time variations in the concentrations. The sensory array should be designed to have high sensitivity and low selectivity (Gardner 1992). Sensors are allowed to reach equilibrium after making measurement of odour. The resulting response vectors are time dependent and represent absolute change in sensor signal with a measured odour (Dickinson 1998). The various kinds of sensor technology are listed in the Table 2.2.
### Table 2.2 Gas Array Sensor Technology

<table>
<thead>
<tr>
<th>Sensor Type</th>
<th>Principle of Operation</th>
<th>Sensitivity</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal Oxide Semiconductor (MOS)</td>
<td>Conductivity</td>
<td>5 – 500 ppm</td>
<td>Inexpensive, micro fabricated, high sensitive, short recovery time, good resistance to corrosive gases and humidity</td>
<td>Operates at high temperature</td>
<td>Borjesson 1996, Bartlett 1997a</td>
</tr>
<tr>
<td>Conducting polymer (CP)</td>
<td>Conductivity</td>
<td>1-100 ppm</td>
<td>Operates at room temperature, micro fabricated</td>
<td>Very sensitive to humidity, temperature, suffer from baseline drift</td>
<td>Lonergan 1996, Bartlett 1997a</td>
</tr>
<tr>
<td>Quartz Crystal Microbalance (QCM)</td>
<td>Piezoelectricity</td>
<td>1.0-ng mass change</td>
<td>Well understood technology</td>
<td>MEMS fabrication, interface electronics</td>
<td>Bartlett 1997a</td>
</tr>
<tr>
<td>Surface Acoustic Wave (SAW)</td>
<td>Piezoelectricity</td>
<td>1.0-ng mass change</td>
<td>Differential devices can be quite sensitive</td>
<td>Interface electronics</td>
<td>Grate 1993</td>
</tr>
<tr>
<td>Metal Oxide Semiconductor Field Effect Transistor (MOSFET)</td>
<td>Capacitive charge coupling</td>
<td>Low ppm</td>
<td>Integrated with electronic interface circuits</td>
<td>Odorant reaction product must penetrate gate</td>
<td>Morvan 2000</td>
</tr>
</tbody>
</table>

(Adapted from Troy Naggle 1998)
2.7 DATA PROCESSING AND PATTERN RECOGNITION UNIT

The multivariate response of the sensors can be utilized as an “electronic smell print” to characterize a wide range of volatile compounds by means of pattern recognition techniques. Pattern recognition may be defined as “the mapping of a pattern form a given pattern space into a class-membership function”. It exploits the cross relation and extracts information present in the sensor outputs ensemble by feature extraction. The choice of feature can be considered for subsequent multivariate data analysis.

2.7.1 Pre-processing

When performing measurements with a multi sensor system such as an E-nose, a large amount of data is generated. From each sensor more signal parameters can be calculated for describing the dynamics of each sensor’s response to the headspace of the sample. Thus large amount of data are generated necessitating required reduction depending upon the properties of interest. Hence the data extracted from the sensor responses often have to be pre-processed. Techniques used for pre-processing include weighting, standardising and normalising of the sensor responses.

2.7.2 Pattern Recognition Methods

The term pattern recognition can be defined as the transformation of an input data set, such as sensor signals from an E-nose to an output set of attributes, such as the type of sample or concentration. The complete pattern recognition consists of two steps: exploration and prediction.

In the exploration step, the objective is to get an overview of the data by finding the relationship among the measurements and the signals
obtained from the sensor and by further identifying the measurement errors. It is done by explorative and regression methods. The explorative methods allow to ‘explore’ the sensors’ responses set in a particular application, looking for relationship between these data set and possible existing structure or classification. Regression methods, instead, are devoted to establishing correlation between an input and an output data set. The various explorative and regression methods are Principal Component Analysis (PCA), Principal Component Regression (PCR), Partial Least Squares (PLS) and Multivariate Linear Regression (MLR).

In the prediction step, the objective is to find mathematical models of interesting properties or characteristics of the samples. The prediction model can be obtained by soft computing methods especially by hybrid artificial neural networks.

Comparing to the classical techniques, Artificial Neural Networks (ANN) are far superior. These are widely used for the design and analysis of adaptive, intelligent systems for a number of reasons including: potential for massively parallel computation, robustness in the presence of noise, resilience to the failure of components, amenability to adaptation and learning and sometimes resemblance to biological neural networks. These networks are also capable of recognising spatial, temporal or other relationships and performing tasks like classification, prediction and function estimation. There are several other advantages in applying ANN as opposed to any other mathematical or statistical techniques. For instance their generalisation abilities are particularly useful because data are often noise, distorted and incomplete in a practical problem. In cases where making decision is sensitive to small changes in the input, neural network plays an important role.
2.8 NEURAL NETWORK AS A PATTERN RECOGNISER

A neural network is a massively parallel distributed processor made up of simple processing units, which has a natural property for storing experiential knowledge and making it available for use. It resembles the brain in two respects:

1. Knowledge is acquired by the network from its environment through a learning process.

2. Interneuron connection strengths, known as synaptic weights, are used to store the acquired Knowledge.”

The artificial neuron is the heart of every neural network. It receives input signals, $x_i$, from $n$ number of neurons and aggregates them by using the synaptic weights, $w_i$. Finally, it passes the result after suitable transformation (transfer function) as the output signal $y_i$ (Figure 2.3). Important transfer functions are given in Figure 2.4.

Figure 2.3 Artificial Neuron
These individual neurons are aggregated to layers. A general neural network consists of an input layer, one or more hidden layer(s) and an output layer. These layers are usually fully connected.

Neural network learning algorithms can be divided into supervised and unsupervised:

- **Supervised neural networks** need an external "teacher" during the learning phase, which goes before the recalling (utilization) phase.

- **Unsupervised neural networks** "learn" from correlations of the input.

Neural networks are used for both regression and classification. In regression, the outputs represent some desired, continuously valued transformation of the input patterns. In classification, the objective is to assign the input patterns to one of several categories or classes, usually represented...
by outputs restricted to lie in the range from 0 to 1, so that they represent the probability of class membership.

Pattern recognition is formally defined as the process whereby a received pattern or signal is assigned to one of prescribed number of classes. Pattern recognition performed by neural network is statistical in nature, with the patterns being represented by points in multi dimensional decision space. The decision space is divided into regions, each one of which is associated with class. The decision boundaries are determined by the training process. The construction of these boundaries is made statistical by the inherent variability that exists within and between classes (Haykin 2009). Pattern recognition machines using neural network can take any one of two forms:

One form is that the machine is split into two parts: an unsupervised network for feature extraction and a supervised network for classification. The second form is that the machine is designed as a single multi layer feed forward neural network using supervised learning algorithm and the task of feature extraction is performed by the computational units in the hidden layers of the network. Depending upon the application of interest any one of the approaches is adopted.

2.9 APPLICATIONS

Harnessing E-nose technology finds application over broad spectrum of fields, ranging from food to modern medicine (Dickinson 1998).

2.9.1 Non Medical Applications

With advancement in this technology, number of applications have been developed such as devices to replace sniffer dogs in Defence department (Schmiedeskamp 2001), to monitor the quality of food, ripeness of fruit

2.9.2 Medical Applications

One of the most important applications emerging today out of E-nose system is in the medical field for diagnosis. It is not yet been commercialized but still showing promising results in research. As the sense of smell is an important sense to the physician, E-nose has the applicability as diagnostic tool. With E-nose both infectious and non infectious diseases can be diagnosed. It has also been proved that E-nose can be used for detecting TB, Diabetes, Gastroesophageal disease, Pneumonia, general illness, etc (Gibson 2000, Pavlou 2000 b, Ritaban 2002, Parry 1995, Pavlou 2004, Thaller 2005, Di Natale 2000). They also show promising results in detecting lung cancers (Di Natale 2003, Hao 2003, Xing 2005, Chan 2009). Recently, a conducting polymer sensor array based E-nose was applied successfully to monitor haemodialysis (Di Natale 1999, Yuh-Jiuan 2001, Fend 2004). Silvano et al (2007) predicted asthma using E-nose. Rapid diabetic diagnosis was also made possible by this technology (Ping 1997, Mohamed 2002).
2.10 COMMERCIAL ELECTRONIC NOSE

In 1964, Wilkins and Hatman tried to mimic human nose (Gardner 1994). However in 1987, the first E-nose, as an intelligent system, was introduced by Persaud and Dodd at Warwick University (Gibson 2000). The first commercial E-nose was launched in the early 1990s (Gibson 2000). Today, many commercial E-noses are available in the market including those listed in Table 2.3.

Table 2.3 Commercially available E-noses

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Country</th>
<th>Sensor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arisense Analysis GmbH</td>
<td>Germany</td>
<td>MOS</td>
</tr>
<tr>
<td>Alpha MOS</td>
<td>France</td>
<td>CP, MOS, QCM, SAW</td>
</tr>
<tr>
<td>Aromascan</td>
<td>UK</td>
<td>CP</td>
</tr>
<tr>
<td>Bloodhound Sensors Ltd</td>
<td>UK</td>
<td>CP</td>
</tr>
<tr>
<td>EEV Ltd</td>
<td>UK</td>
<td>CP, MOS, SAW</td>
</tr>
<tr>
<td>Nordi Sensor Techs AB</td>
<td>Sweden</td>
<td>MOS, QCM</td>
</tr>
<tr>
<td>Sawtek Inc</td>
<td>USA</td>
<td>SAW</td>
</tr>
<tr>
<td>Cyranose</td>
<td>USA</td>
<td>CP</td>
</tr>
<tr>
<td>LibraNOSE</td>
<td>USA</td>
<td>QCM</td>
</tr>
</tbody>
</table>

(Adapted from Troy Nagle 1998 and Gibson 2000)