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Overview: e-Nose device for THC detection

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CONTENTS

1 Development of a Low-Cost Portable Sensor for Detection of Tetrahydrocannabinol (THC) in Saliva [1]

1.1 Introduction

A possible solution for determining THC impairment includes a measuring device, which analyzes saliva to determine the user's THC level of toxicity using mouth swabs. The THC concentration of the sample taken from the user is evaluated by determining the cannabinoid vapour pressure, if the vapour exceeds the legal level set, the individual would be considered as impaired.

1.2 Methodology

The devices utilizes a gas sensor to measure the concentration of THC in vapour emitted from a saliva sample. The sensing element uses a metal oxide semiconductor layer formed on alumina substrate of a sensing chip, with an integrated heater for detection of solvent vapours. As the sensor is exposed to THC, the resistance of the sensor decreases based on the THC concentration.

The components used within the case are a gas sensor (Figaro, TGS2620), an arduino Uno REV 3 SMD, LCD screen, 12V battery, breadboard, SPDT slide switch, Piezo buzzer, three LED's and a 3D printed poly-carbonate enclosure with testing channel attached to the bottom section of the device. The testing utilized a Δ9-Tetrahydrocannabinol solution at 1.0 mg/mL in methanol to simulate saliva containing THC.

1.3 Results and Discussion

THC concentration testing was carried out using a swab, present at 5mm from the sensor testing channel, held at the inlet and then removed. Different concentrations of THC dissolved in water were tested. Baseline trials were carried out to show the effect of a sensor readings when a dry swab and a wet swab soaked in pure water approached the sensor.

The prototype successfully differentiates among THC, ethanol, wet and dry swab. For this test, the swab was removed from the inlet after 40 s. The detector can differentiate among different concentrations of THC.

1.4 Conclusion

The design demonstrates the ability to detect various volatile compounds through swab/saliva prototype. At this stage the device is unable to differentiate the compounds that are being detected but can determine the concentration.

2 Detecting Cannabis use on the Human Skin Surface via an Electronic Nose System [2]

2.1 Introduction

An electronic nose system (e-Nose) could be a low-cost, portable and non-invasive alternative for drug testing. An e-Nose is an instrument which comprises an array of electronic chemicals sensors with partial specificity and an appropriate pattern-recognition system capable of recognizing simple or complex odors. The most widely used gas sensors are metal oxide gas sensors (MOS) piezoelectric crystal sensors (PCS) and conducting polymer sensors (CPS).

A portable e-Nose for identification of cannabis-based drugs was already developed, however, they investigated the drugs directly as opposed to the metabolites occurring after the drug use. The objective of this study was to developed and apply e-Nose to distinguish on-site between regular tobacco and cannabis, use by analyzing human body odour directly from the skin surface

2.2 Methods

2.2.1 Electronic Nose Set up

Customized sensors from the company UST Geschwend. On the sensor surface, a type of interaction is ensured between gas molecules and these sensor layers by changing their conductivity, these changes are measured over time. The sensor material consists of semiconducting oxides applied to a a ceramic carrier substrate, incorporating a plate heater to control the sensor temperature.

By modifying the effective sensor layer and the chip temperature, it is possible to vary the types of gases that can be detected, as well as the sensors sensitivity, although certain physical and chemical limitations can apply.

Metal oxide Gas sensors are sensitive towards a wide spectrum of gas species with a somewhat wide overlapping of sensitivities. The configuration of the used e-nose is depicted in figure 2.1

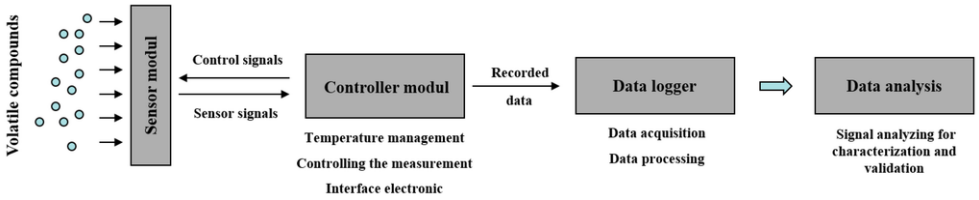

Figure 2.1: Configuration of the used electronic nose system

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The sensor unit is followed by a control unit responsible for controlling the temperature of the sensor heating system and for handling the data recording and data storage. Finally, a data logger collects the sensor data (sensor curves) and specific patient data; this logger contains also a reference data base for specific sensor curves (not used in this study).

2.2.2 Data processing and Analysis

All data preprocessing and data analyses were performed using MATLAB R2009b; statistical analyses were performed either with MATLAB or SPSS 19.

Sensor data (changes in conductance over different heating temperatures) were interpolated to obtain equidistant temperature values. These values were further averaged to get representative curves for each sensor layer. The data and statistical analyses are divided into two main parts and methods.

1. Analysis of the sensor curves (**A**).
2. Analysis of features extracted from sensor curves (**B, C** and **D**).

A: Directly analyzes the three sensor signals using principal component analysis (PCA), followed by discriminate function analysis (LDA and/orr QDA).

B, C, D: Method based on extracted features (time and frequency domains) from the sensor curves and uses classification methods either **B** PCA followed by LDA/QDA, **C**, stepwise discriminant function analysis (SDS) or **D**, support vector machines (SVM).

2.3 Patients and Study Design

The study population was recruited from the LWL-University Hospital of Bochum and included two groups of health volunteer subjects.

2.4 Results and Discussion

Test	**Sensitivity**	**Specificity**	**Accuracy**
A	85%	50%	67.5%
B	80%	50%	65.0%
C	80%	85%	82.5%
D	95%	90%	92.5%

Table 2.1: Summarized results.

2.5 Conclusions

This study shows that an electronic nose system has the ability to differentiate between human body odour of subjects using cannabis and normal tobacco-smoking subjects.

3 Chemistry, Metabolism, and Toxicology of Cannabis: Clinical Implications [3]

3.1 Chemical Components of Cannabis

The cannabis plant contains more than 421 chemicals of which 61 are cannabinoids. Some of the major cannabinoids present in cannabis are listed in tables 3.1 and 3.2. Δ^9 Tetrahydrocannabinol (THC) is considered as the most psychoactive component contributing to behavioural toxicity of cannabis.

Name	**Effects**
Δ^9 Tetrahydrocannabinol	Main psychoactive component. Causes physiological and behavioural effects.
Δ^8 Tetrahydrocannabinol	Less psychoactive than Δ^9-THC.
Cannabinol (CBN)	Less powerful than Δ^9-THC.
11-hydroxyΔ^9-THC	Liable for psychological effects of cannabis. Imitates activity of Δ^9-THC and other cannabinoids that interact cannabinoid receptors.

Table 3.1: Cannabinoids and their properties: Psychoactive components

Name	**Effects**
Cannabidiol (cBD)	Lacks psychoactive properties, has anti-convulsant action.
Cannabichromene	Not psychoactive
(-)Δ^{8-}THC-oic acid	Not psychoactive, has analgesic activity

Table 3.2: Cannabinoids and their properties: Non-psychoactive components

3.1.1 Pharmacological Actions of Cannabinoids

Δ^9-THC is volatile viscous oil with high lipid solubility and low aqueous solubility and acid dissociation constant (pKa of 10.6). It is present in cannabis as a mixture of mono-carboxylic acids, which gets readily and efficiently de-carboxylated upon heating. It decomposes when exposed to air, heat or light and readily binds to glass and plastic. Therefore, Δ^9-THC is usually stored in basic or organic solvents in amber silicate glassware to avoid loss during analytical procedures.

3.2 Pharmacokinetics of Cannabis

Δ^9-THC which is highly lipoliphic get distributed in adipose tissue, liver, lung and spleen. Hydroxylation of Δ^9-THC is rapidly absorbed through lungs after inhalation, it quickly reaches high concentration in blood.

3.2.1 Metabolism and Elimination of Δ^9-THC

The average plasma clearances rates have been reported to be 11.8 ± 3 L/hour for woman and $14.p \pm 3.7$ L/hour for men.Others have determined approximately 36 L/hour for naïve cannabis

users and 60 L/hour for regular cannabis users.

3.2.2 Detection and Analysis of Cannabinoids by Different Analytical Techniques

Cannabinoids can be detected in saliva, blood, urine, hair and nail. The cut off value for detect on of cannabinoids recommended by the Substrate Abuse and Mental Health Services Administration and European threshold of 50ng/ml was found to be consistent with recent heavy cannabis abuse. False negative and false positive results occur from structurally related drugs that are recognized by the antibodies or occasionally artifacts such as adulterants affecting the pH, detergents and other surfactants. For this reason, any positive result must be confirmed by chromatographic techniques. Cannabis has a long half-life in humans, in chronic cannabis users it is particularly difficult to determine whether a positive result for cannabis represents a new episode of drug use or continued excretion of residual drug.

3.3 Conclusions

Research in the future should focus on the molecular changes induced by acute and long-term exposure to cannabis and the contribution of individual psychoactive components.

4 Drug Testing in Oral Fluid [4]

4.1 Introduction

The use of alternative specimens to blood or urine for establishing exposure to drugs has become a significant direction in clinical and forensic toxicology. The alternative specimens include hair, sweat and oral fluids; oral fluids has been seen as a non-invasive alternative to blood but also as an alternative to urine.

The last decade has also seen a significant development in the understanding of the target drugs and their pharmacokinetics in oral fluid. This has applied particularly to he abused drugs and what concentrations may or may not relate to blood concentrations. This review outlines the roles and applications of testing for drugs in oral fluid, describes the relative advantages and disadvantages of this form of testing and illustrates applications of oral fluids testing for specific drugs.

4.2 Scope of Review

This paper reviews the developments and applications of drug testing in oral fluid particularly over the last ten years.

4.3 Source of Oral Fluid

Oral fluid is excreted primarily by three glands: the parotid, sub-maxillary and sublingual and by other smaller glands. It has a low protein content (0.3%) and can vary in flow rate from zero to several mL per minute depending on influences from various factors, including emotional state and hunger. Dry mouth syndrome is relatively common and can be caused by the anxiety of the collection procedure or even by lack of proper hydration of the individual.

4.4 Collection Techniques and Adulterants

Expectoration, or spitting, provides neat oral fluid, but this is relatively viscous and can be difficult to work with in the laboratory. It may also be contaminated with food and require centrifugation. Some collector available use some form of proprietary diluent or mix with the collected oral fluid (Table 4.1).

Oral fluid production is stimulated by use of agents such as citric acid candy, chewing gum or other agents. This will inevitably change pH and concentration of drug in the oral fluid. A number of drugs are known to affect the secretion of oral fluid, including cannabis. There is significant intra- and inter-subject variation in relation to drug concentrations depending on the technique used, the physiology of the person and the influence of factors affecting drug concentration in oral fluid.

Since the collection of oral fluid specimen can be viewed by a second person without infringing privacy it does not suffer from the same issues regarding possible adulteration or substitution as for urine. The consumption of beer immediately smoking marijuana joint appeared to lower concentrations of THC in oral fluid at 1 hour post dose. Since the oral fluid in the mouth is rapidly turned over, a wait of several minutes should allow re-equilibration of drug in the surrounding tissues.

Name of collector	**Method of operation**
DrugWipe	Swipe only (tongue or skin)
Cozart collector	Absorbent foam pad plus diluent
Dräguer DrugTest	Absorbent foam pad with diluent
Intercept	Absorbent foam pad with diluent
OralScreen	Absorbent foam pad only, drops applied to device
OralLab	Absorbent foam pad, collector squeezed to apply oral fluid into test cartridge
OraLine	Direct application to oral cavity, or use of other collectors
OraTect	Absorbent directly connected to device
Quantisal	Absorbent foam pad plus diluent
SalivaScreen	Absorbent foam pad, drops applied to device
Salivette	Cotton wool swab which is then filtered and centrifuged
Toxiquick	Absorbent bud, oral fluid squeezed into syringe and applied to device

Table 4.1: Selection of collection devices reported in literature.

4.5 Recovery of Drugs from Collectors

Cozart and The Quantisal collection devices have a good recovery for THC.

4.6 Applications of Oral Fluid Drug Testing

Oral fluid has the advantage over blood in that it can be obtained non-invasively in a situation where adulteration or substitution is difficult. A review of the advantages and disadvantages of specimens is available.

4.7 Pharmacokinetics

There is almost no carboxy metabolite of THC present in oral fluid. In the case of most drugs, the oral fluid concentration can be estimated from pH of oral fluid and blood, the protein binding of the drug an its pKa. For acid drugs the equilibrium favours blood, hence oral fluid concentrations are less than for blood, while for basic drugs higher oral fluid concentrations occur.

The average concentration ratio for Alcohol and THC are on table 4.2. In the absorptive phase there are often higher concentrations in the oral fluid due to local absorption effect in the mucous membranes of the buccal cavity, This local absorption effect is probably highest for THC due higher fat solubility and ease of penetration through membranes and the very low partitioning from blood to oral fluid.

Drug (type)	**Average oral fluid to blood concentration ratio**
Alcohol (Ethanol)	1.07
Δ^9-Tetrahydrocannabinol (Neutral)	1.a2

Table 4.2: Average oral fluid to blood concentration ratio for selected drugs.

4.8 Initial Testing Techniques

4.8.1 Field Testing

A number of devices are available for field use, unfortunately, there is no consistency in the specifications applied to these devices. The apparent sensitivity is often not defined in terms of consistency of detection in oral fluid specimens. This means that at the present moment there is no objective way to assess performance of these devices or cartridges.

In laboratory, terms such as false positive (FP) and false negative (FN) are used. FP refers to a situation when a presumptive initial rest result is not confirmed, FN refers to a situation when a confirmation rest finds a drug present that was not detected by the initial test.

Sensitivity is often used in defining performance of initial testing kits and refers to the relative detectability of the kit or device in question over a comparison method. On other hand, specificity refers to the percentage of negative results using the kit or device compared to the total number of negative specimens using a comparison method. The comparison method is usually a Gas Chromatography-Mass spectrometry o LC-MS method.

4.8.2 Confirmatory Analytical Techniques

The recommended minimum detectable concentrations of THC in oral fluid according to Substance Abuse & Mental Health Services Administration in the USA (SAMHSA), the European Union roadside assessment testing study (ROSITA) and the Australian Draft Standard for the collection, detection and quantification of drugs of abuse in oral fluid can be found on table 4.3

Drug	**SAMHSA cut-offs (ng/mL)**	**ROSITA cut-offs (ng/mL)**	**Standard Australia proposed target concentrations (ng/mL)**
THC	2	1.9	10

Table 4.3: Recommended minimum detectable concentrations of drugs in oral fluid.

It is possible that some international agreement may exist in the future regarding minimum detectable concentrations (or cut-offs), however, this is unlikely since there are still significant differences in cut-offs in urine between countries after over 30 years of testing. Moreover, inadverted exposure may limit the concentrations that can be used to prove deliberate use. In the case of cannabis, a study has found that THC concentrations for a short period following high passive exposure in an unventilated room of up to 26 ng/mL.

4.9 Conclusions

The use of oral fluid has been found to offer significant promise when detection of relatively recent use of drugs is sought in a non-invasive manner. Technological advances do allow on-site detection of drugs, but there are technical issues in relation to collection of oral fluid and in the variability of drug concentrations in this fluid.

5 Correlation of Breath and Blood Δ^9-Tetrahydrocannabinol Concentrations and Release Kinetics Following Controlled Administration of Smoked Cannabis [5]

According to the National Forensic Laboratory Information System's 2017 report, Δ^9-THC was the second most frequently identified drug in drug related incidents. THC impairs both motor and cognitive functions, decision-making, impulse control and memory. Performance impairment is associated with time since last use and has been shown to peak within 1 hour of smoking marijuana, declining over 2 to 3 hours after cannabis use, therefore, reliable testing requires detection throughout the 3 hour impairment window.

Exhaled breath has been suggested as an alternative matrix in which detection of cannabinoids may more closely correspond to the window of impairment. In the first study publication in 1983, THC was detected only in breath at 10 min after smoking and was below analytical limit detection at 20min. Three decades later, an alternative sampling procedure followed by quantification using LC-MS/MS was evaluated for the detection of cannabinoids in breath samples. In 1 study, THC was detected in 13 chronic smokers at 30 min, 1 hour and two hours following controlled administration. THC was not detectable 3 hours after cannabis use in all chronic smokers but became detectable again for 1 individual at 4 hours.

5.1 Materials and Methods

All breath samples were collected using a handheld device with a baffle-based saliva trap (Alcohol Countermeasures Systems) incorporated in the mouthpiece to remove oral fluid.

5.1.1 Sample preparation for breath and whole-blood samples

Samples captured from exhaled breath were eluted from the breath-capture module with 1.0mL of methanol.

5.1.2 LC-MS/MS Method For Breath and Whole-Blood Samples

LC-MS/MS analysis was performed using a Shimadzu Prominence LC-20ADXR and QTRAP 4500 triplequadrupole mass spectrometer (Sciex).

5.1.3 Statistical Analysis

Were performed using R. Linear regression with ordinary least squares was use to calculate the fit coefficients. For each data set, corresponding to a single individual and sample matrix (breath or blood) time points after smoking were considered for analysis. For a selected data set, linear regression was performed for $log(C)$, where C is the THC concentration as a function of time.

5.2 Results

Δ^9-THC was detected in exhaled breath for all individuals at baseline through 3 hours after cannabis use. THC concentrations in breath were highest at the 15-min timepoint (median = 17.8 pg/L) and declined to< 5% of this concentration in all participants 3 hours after smoking. The decay curve kinetics observed for blood and breath were highly correlated within individuals and across the population.

5.3 Conclusions

THC can be reliably detected throughout the presumed 3 hours impairment window following controlled administration to smoked cannabis. The findings support breath THC concentrations as presenting a physiological process and are correlated to blood concentrations, albeit with a shorter window of detection.

6 PHARMACOLOGY AND EFFECTS OF CANNABIS: A BRIEF REVIEW [6]

6.1 Sources of Cannabinoids

Cannabinoids are present in the stalks, leaves, flowers and seeds of the plant, and also in the resin secreted by the female plant. The THC content varies tremendously between different sources and preparations of cannabis, table 6.1.

Form	**Source**	**THC content**
Marijuana (USA) Cannabis (UK)	Dries leaves/stalks/flowers/seeds	
(Herbal cannabis)	Traditional cigarette (reefer) of 1960s and 1970s	1 – 3% THC (~ 10 mg/reefer)
	Modern cigarette (joint) of 1980s; result of intensive cultivation and more potent subspecies	6 – 20% THC (60 – 200 mg/joint)
Hashish (USA) Cannabis resin (UK)	Resin, secreted by plants	
	Bricks, cakes, slabs	10 – 20%THC
Hashish oil	Product of extraction by organic solvents	15 – 30%THC

Table 6.1: Preparation of cannabis (USA and UK)

Cannabis can be smoked as joints, from pipes or "buckets", by inhaling from a mass of plant or resin ignited in a sawn-off plastic bottle/ It can also be eaten, baked into cookies or cakes or occasionally drunk as an extract.

6.2 Prevalence of Cannabis Use

A survey oh 3075 university students from UK universities found that about 60% had some experience with cannabis, nearly 25% had tried it more than once or twice and 20% of students reported regular use. Among 785 second-year medical students from seven UK medical schools surveyed in 1996, 46% reported cannabis use and 10% were taking it at least once a week.

A survey of 90 house officers found that nearly 30% reported current cannabis use and 11% used it weakly or monthly.

6.3 Pharmacokinetics of Cannabinoids

About 50% of the THC in a joint of herbal cannabis is inhaled in the mainstream smoke; nearly all of this is absorbed through the lungs, rapidly enters the bloodstream and reaches the brain within minutes. Bioavailability after oral ingestion is much less; blood concentrations reached are 25−30% of those obtained by smoking the same dose, partly because of first-pass metabolism in the liver.

Once absorbed, THC and other cannabinoids are rapidly distributed to all other tissues at rates dependent on the blood flow. Because they are extremely lipid, soluble, cannabinoids accumulate in fatty tissues, reaching peak concentrations in 4-5 days. They are then slowly released back into other body compartments, including the brain. Because of the sequestration in fat, the tissue elimination half-life of THC is about 7 days, and complete elimination of a single dose may take up to 30 days.

Because of the pharmacokinetics characteristics of cannabinoids - both the sequestration in fat and the presence of active metabolites - there is very poor relationship between plasma or urine concentrations and degree of cannabinoid-induced intoxication.

6.4 Conclusions

Cannabis is not, as widely perceived, a harmless drug but poses risks to the individual and to society.

7 New Digital Metal-Oxide (MOx) Sensor Platform [7]

Even though selectivity of MOx sensors can be tuned and notably improved, long-term stability in the presence of siloxanes will deteriorate their accuracy over time or even male it impossible to use sensors in applications with high siloxane loads such as mobile phones. Moreover, most available sensors do only offer a simple analog interface, the output signal is provided in form of a resistance for which additional circuitry has to be implemented.

In order to take the unique challenges for a gas sensing IoT and mobile applications, Sensirion developed the Sensirion Gas Platform (SGP) multi-pixel sensor. Multiple sensing elements are combined with a siloxane resistance, which is unprecedented for a commercially available MOX sensor. The sensing elements are integrated with a digital interface into a small surface mount device (SMD). In combination with the on-chip calibration data, the digital interface greatly simplifies the integration of the SGP into different applications, since the output signal can be directly used by costumers for air-quality indication without further processing.

7.1 Materials and Methods

7.1.1 Sensor architecture

The SGP offers a complete gas sensor system integrated into a very small 2.45x2.45x 0.9mm^3 flat no-lead (DFN) surface mount package. Sensirions proprietary CMOSens technology allows the co-integration of analog and digital electronics together with a micro-hotplate and the sensing elements on a single chip. Four MOX sensing elements based on layer of MOX nano-particles are deposited on a micro hot-plate, each sensing element can be measured separately by read-out electrodes. To guarantee stable operation independent of the surrounding temperature, a heater and a temperature sensor are integrated on the hotplate to actively control its operating temperature.

The signals from the four sensor elements are measured by an optimized amplifier covering a measurement range of eight orders of magnitude. The signal-processing addition, individual calibration parameters are written during production into an on-chip one-time programmable memory. This allows conversion of the sensor raw signals into calibrated output signals such as those for concentrations of volatile organic compounds.

7.1.2 Manufacturing Process

The entire process is tightly monitored at every step and strict grading ensures that only sensors which adhere to specifications and can be readily used by the customer are shipped. The process flow can be seen in figure 7.1

7.1.3 Experimental Methods

The sensors were reflow soldered on either custom printed circuit boards (PCBs) or flexible PCBs. Because the sensor chips contain all the necessary circuitry, the read-out electronics have been kept simple. Apart from stable 1.8V power supply, only an i^2c bridge and, in the case of the multi-sensors boards, an i^2c multiplexer chip, is required. The entire electronics were designed in-house.

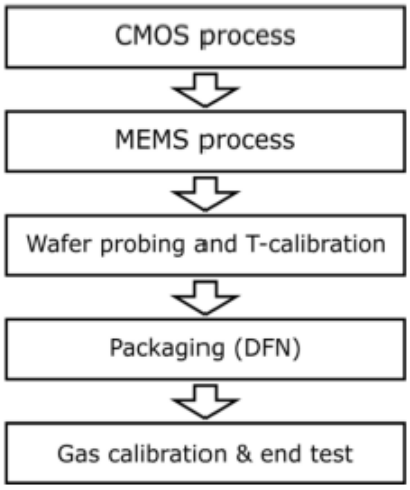

Figure 7.1: SGP gas sensor manufacturing process flow

For the field measurements, the read-out electronics were connected to a miniature computer which controlled the data- acquisition and the data upload via Wifi.

In the laboratory measurements, gas mixing systems with up to 8 channels were employed. Each channel was controlled with a sensirion mass flow controller. For the dry channel, air generated by a zero-air generator was used. In the wet channel, the zero air was passed through a water bubbler. To avoid errors due to incomplete saturation of the air in the bubbler, the ratio of dry and wet channel was controlled in a closed loop using a Sensirion SHT temperature and humidity sensor.

7.2 Results

7.2.1 Siloxane Stability

The degradation caused by siloxanes typically translates into a significant decrease in VOC sensitivity and a strong increase of the response time, potentially caused by silicone dioxide formation , Unfortunately, silicon-containing compounds are found in many products used in everyday life, such as cosmetics, cleaning agents or plastic parts and, therefore, siloxanes are present in all relevant operational environments The overall siloxane background concentration determines the time scale of degradation and, therefore, the total sensor lifetime.

The core technology of the SGP, provides the sensor with a unique robustness against contamination by silixanes. This is achieved by a combination and optimization of the sensing material, operation mode, and the on-chip evaluation of multiple signals from different sensing elements.

7.2.2 Total Volatile Organic Compounds (tVOC)

The term tVocs refers to the total concentration of VOCs present simultaneously in the air. Global consensus has resulted in the emergence of guidelines for tVOCs standards of indoor air quality issued by governmental organizations in different countries. The maximum tVOC levels that are considered as acceptable range from ~ 0.6 to ~ 1 mg/m^3.

Laboratory techniques to determine VOC concentrations, such as flame ionization detectors, or gas chromatography-mass spectrometry, are either too expensive, too power-intensive or to large to be applicable in compact and affordable IA1 devices in e.g., smart home applications. For these applications MOX sensors are preferred technology due to their high sensitivity and broadband-sensing capabilities. The signal is calibrated such that the sensor output S_{out} follows equation 7.1.

$$ln\left(\frac{c}{c_{ref}}\right) = \frac{S_{ref} - S_{out}}{a} \tag{7.1}$$

Were c is the applied ethanol concentration, S_{ref} the value of S_{out} at a reference concentration c_{ref} and $a = 512$ a scaling factor. The SGP shows a high sensitivity to different VOCs, even in the sub-ppm concentration range which is most relevant for most indoor air-quality applications.

7.3 Conclusions

The new SGP platform represents a milestone in the commercial application of MOX technology. The unique combination of sensor and electronics integration, multi-pixel platform and long-term stability opens a pathway to novel applications for metal-oxide gas sensors in consumer products like mobile phones, wearables and IoT devices.

8 FUNDAMENTALS OF METAL OXIDE GAS SENSORS [8]

8.1 Introduction

All started after metal oxides were identified as possible sensitive materials, there were brought to the market by Taguchi, who founded the still largest manufacturer of SMOX sensors, namely Figaro Engineering. They were so successful because they are inexpensive, integrate into arrays and low power when realized on the appropriate transducer structures.

In air, at temperatures between $150-400^{\circ}C$, oxygen is adsorbed at the surface of the metal oxides by trapping electrons from the bulk with the overall effect of increasing the resistance of the sensor, for n-type materials, or decreasing it for p-type materials. The occurrence of a target gas in the atmosphere, which reacts with the pre-adsorbed oxygen or directly with the oxide, determines a change of the sensor resistance, which is recorded as a sensor signal and the magnitude of which is correlated to the concentration of the target gas.

In this contribution we will examine more in detail the way in which the actual SMOX based gas sensors function, taking into consideration all their relevant parts.

8.2 Overview of Sensing

For an SMOX gas sensor based on SnO_2, realized by screen printing the sensing material onto an Al_2O_3 substrate provided with Pt electrodes. The parts that could influence the sensing properties are:

1. The SnO_2 grains at the surface of the layer of which the reactions with the ambient gases are taking place and between which the transport of the free charge carriers takes place.
2. Different materials synthesis methods will result in different bulk and surface properties which both have an influence on the sensor's performance.
3. At the surface of the SnO_2 grains noble metal additives can be/are present.
4. The noble nature of the electrodes makes it impossible for them to play an active chemical role. This means that their nature but also micro-structure and morphology will have an impact on gas sensing performance.

As result one can say that the sensor is more than the "algebraic" sum of its parts.

8.3 Operando Investigations

- DC resistance measurements (the normal way to characterize gas sensors) give information about the changes in the concentration of free charge carriers induced by surface reactions.
- AC impedance spectroscopy allows identifying the presence of surface space charge layers or electrode-metal oxide contacts and of the nature of free charge carriers. In combination with work function changes in the surface dipole concentration.
- Hall Effect measurements in combination with the modeling of the conduction will allow to deconvolute the 2 standard components: the charge carrier concentration and their drift mobility of the conductivity.
- Work function change measurements by the Kelvin method provide insight about relative changes in the work function determined by surface reactions. In combination with conductance measurements it allows for the discrimination between localized chemisorption and ionosorption.

- On-line gas analysis of exhaust composition after the sensor reactor allows to identify reactions products of solid-gas interaction and yields information about possible reaction mechanisms.
- Diffuse Reflection Infrared Fourier Transformed Spectroscopy (DRIFTS) measurements identify adsorbed surface species which are involved in the gas solid reaction.
- X-ray absorption spectroscopy studies which allow finding out the chemical state, the surrounding and possible changes in the chemical state.

8.4 Conclusions

The processes involved in gas sensing with SMOX based gas sensors are extremely complex and their understanding, which is needed for being able to develop in an intelligent manner better sensors, asks for very performing investigation techniques that are to be applied in operation conditions.

9 ALTERNATIVE SPECIMENS FOR WORKPLACE DRUG TESTING [9]

Since 1970s urine has been the most common technique for detecting drug use in the workplace. Although widely utilized, problems such as the lack of long-term drug detection, the inability to correlate urine drug test results with drug impairment and blood drug concentrations, opiate source differentiation, specimen adulteration by donors and privacy issues continue to affect the industry. Therefore, the testing of urine alone may not continue to guarantee a drug-free workplace. The selection of specimen for drug analysis is influenced by a variety of factors, principally ease of specimen collection, analytical and testing considerations, and interpretation of results. Recently, interest has shifted from urine towards other specimens that can provide distinct advantages.

Specimen	**Advantages**	**Disadvantages**
Urine	• Drugs and drug metabolites are highly concentrated • Extensive scientific basis for testing methodology • Performances testing is liberally practiced • Results are frequently accepted in court • Uniform testing criteria establish • Easily tested commercial screening methods	• Period of detection 2-3 days • No dose-concentration relationship • Drug concentration influenced by amount of water intake • Susceptible to adulteration and substitution
Oral Fluid	• Useful in detection of recent drug use • Results may be related to behaviour/performance • Ready accessible for collection • Observed collection • Detect parent drugs metabolites	• Detection window might be shorter • Contamination following oral, smoked and intranasal routes of drug administration • Collection volume may device dependent • Performance testing under development
Hair	• Provides longer estimate of time usage • Detects parent drugs metabolites • Observed collection • Ease of obtaining, storing and shipping specimens • Second specimen can be obtained from original source	• Inability to detect drug use • Potential hair color bias • Possible environmental contamination for some drug classes • Susceptible to adulteration by treatment prior to collection • Performance testing under development
Sweat	• Provides cumulative measure of drug exposure • Ability to monitor drug intake for a period of days to weeks • Detects parent drugs and metabolites • Noninvasive specimen collection • Collection device is relatively temper-proof	• Large variation in sweat production • Specimen volume unknown • Limited collection devices • High inter-subject variability • Risk of accidental removal • Risk of contamination during application/removal • Cannot detect prior exposure Performance testing under • development

Table 9.1: Summary of advantages and disadvantages of Urine, Oral Fluid, Hair and Sweat

alter

These specimens include oral fluid (saliva), hair and sweat. Oral fluid was previously limited to aspects of therapeutic drug monitoring and insurance testing, but the introduction of several laboratory-based drug test systems and on-site devices have expanded drug testing capabilities.

Confirmation of presumptive positive test results require very sensitive and specific methodology. The majority of laboratories currently utilize gas chromatography-mass spectrometry (GC-MS) for the confirmation and quantitation of drugs and drug metabolites in oral fluid, hair and swear. However, many more challenging assays (e.g., cannabis) require MS-MS technology to achieve the required limits of detection.

The analytes recommended for workplace testing, in case of marijuana are shown in table 9.2

Specimen	**Analyte**
Urine	Marijuana metabolites THCA
Oral Fluid	THC and metabolite THC Parent drug
Hair	Marijuana metabolites THCA
Sweat	Marijuana metabolites THCA

Table 9.2: Recommended Aalytes for Various Specimens

In summary, oral fluid, hair and seat appear to sufficiently meet the requirements to be added to workplace drug testing, particularly laboratory-based programs. There are adequate analytical methods, and the relevant drugs and metabolites have been identified.

10 Analytical methods for abused drugs in hair and their applications [10]

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Hair has been used as an alternative specimen to blood and urine for documentation of use or exposure to drugs, because hair analysis can provide information on drug intake for a long time after the drug has been eliminated from the body. Hair is preferable as a biological sample because of its stability and ease for sampling and storing compared with conventional biological samples such as blood and urine. Hair analysis consists of several steps, such as sampling, washing for decontamination, extraction of target compounds from hair, and instrumental analysis.

Δ^9-THC, an active constituent of cannabis, was determined to distinguish abuse of marijuana or hashish. Especially hair analysis which can detect long-term exposure is important in the theory test for the issue of driving license and for workplace testing. THC is metabolized to 11-hydroxy-Δ^9-THC by hepatic enzymes and is oxidized further to 11-nor-Δ^9-Tetrahydrocannabinol-9-carboxylic acid (THC-COOH)) (figure 10.1), his one has a low rate of incorporation into hair and it is not highly bound to melanin, resulting in a lower concentration in hair compared with other drugs abuse. Therefore, sensitive determination of these substances in hair by GC-MS method was performed.

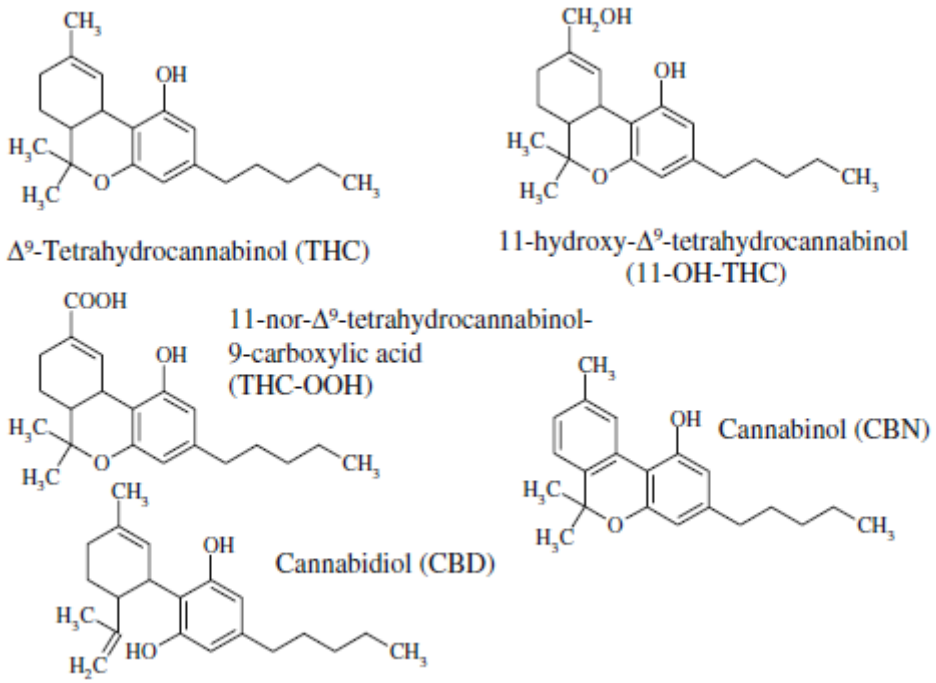

Figure 10.1: Chemical structures of cannabinoids

11 A BRIEF HISTORY OF ELECTRONIC NOSES [11]

11.1 Introduction

11.1.1 The human olfactory system and odours

Smell is the dominant factor in our sensation of flavour and so can often be used alone to profile the flavour of various products. The sense of smell arises from the stimulation of the human olfactory system by odorant molecules emitted from an object. The odorant molecules are drawn up into the nasal cavity and across the olfactory area (epithelium) below the olfactory bulb.

First, there is a thin aqueous mucus layer into which extend the olfactory hairs or cilia from olfactory cells. G-receptor binding proteins are located at the surface of the cilia and acts as chemosensory receptors. There are believed to be relative small number of receptor proteins (≈ 100) so that the receptor cells have partially overlapping sensitivities. There are about 100 million olfactory cells, which are believed both to amplify the signal and generate secondary messengers. The messengers control ion channels and thus generate signals that travel down axons from the olfactory nerves to about 500 glomeruli nodes in the olfactory bulb. These signals are then further processed by about 100000 mitral cells and then finally sent via a granular cell layer to the brain.

11.1.2 Machine olfaction

The physicochemical properties of some products are measured using conventional equipment, such as GC and MS. these (mechanical) methods are not only time-consuming but results are often inadequate. There is an enormous demand for an electronic instrument that can mimic the human sense of smell and provide low cost and rapid sensory information.

An electronic nose is an instrument, which comprises an array of electronic chemical sensors with partial specificity and an appropriate pattern-recognition system, capable of recognizing simple or complex odours

This definition restricts the term electronic nose to those types of intelligent chemical array sensors systems or chemical sensoric array devices that are specifically used to sense odorant molecules in an analogue to the human nose. However, the architecture of an electronic nose also applies in the field of gas sensing detection of individual components or mixtures of gases/vapours

11.2 Electronic nose technology

11.2.1 Sensors

The generic structure architecture of an e-nose is shown in figure 11.1. An odour j is presented to the active material of a sensor i, which converts a chemical input into an electrical signal. The requirement for the sensors in an electronic nose is that they have a partial sensitivity, i.e, that they can respond broadly to a range or class of gasses rather than to a specific one. Considerable research effort has been directed to the use of inorganic semiconducting materials such as oxides and catalytic metals. With oxide materials the odorant molecules react with chemisorbed oxygen species and thus modulate the conductivity.

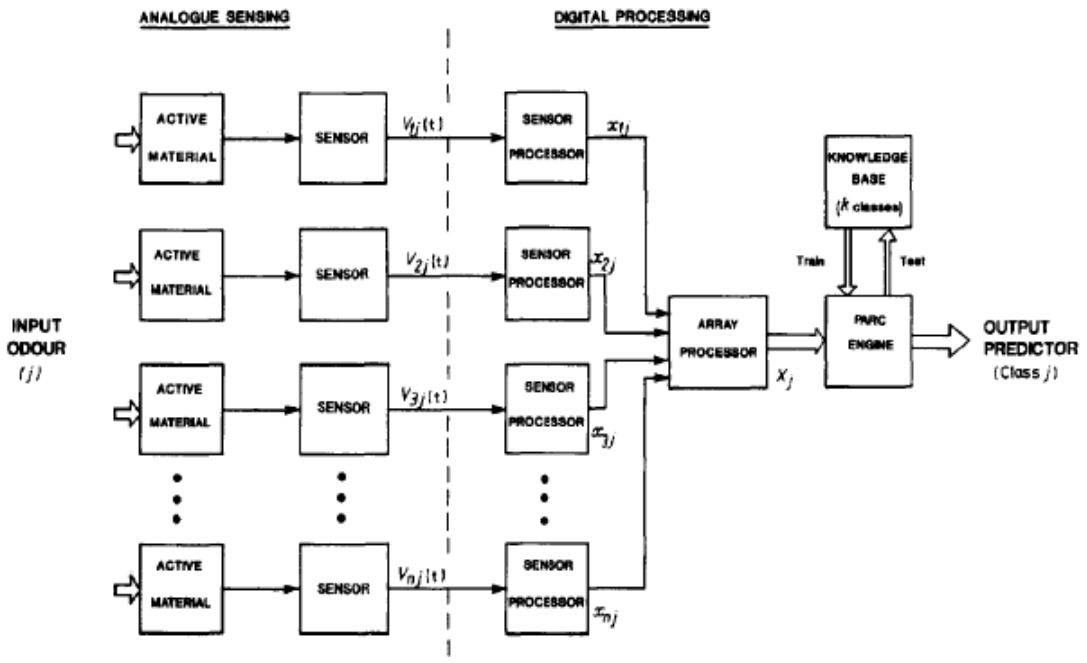

Figure 11.1: Generic architecture of an electronic nose

11.2.2 Signal preparation

The individual sensors i within the e-nose produce a time-dependant electrical signal $V_{if}(t)$ in response to an odour j. The rise and decay time of the sensor signals will depend upon one or more of the following parameters.

1. The flow delivery system that carries the odour from the source to the sensor array.
2. The nature of the odour, e.g, type, concentration.
3. The reaction kinetics of the odour and the active material.
4. The diffusion of the odour within the active material.
5. The nature of the sensing material.
6. Ambient conditions.

11.2.3 Pattern-recognition techniques

The response generated by the sensor array are then analyzed using patter recognition (PARC) engine. In most cases there are two stages used in the PARC process. First, the output of the sensor array is trained by the PARC method using mathematical rules that relate the output from a known odour to a set of descriptors (k classes) held in a knowledge base. This process is known as a supervised learning. Then the response from an unknown odour is tested against the knowledge base and the predicted class membership is given.

Table 11.1 lists some of the supervised learning PARC methods that have been applied to the responses from odour sensing arrays. Some of these are linear techniques and assume arrays. Some of these are linear techniques and assume that the response vectors are well described in Euclidean space. In general this is not true unless the sensor output have been linearized or the odour concentration is low, so that the chemical response is naturally linear.

PARC method	**Linear**	**Parametric**
Principal component analysis	Yes	No
Discriminant function analysis	Yes	Yes
Template marching (usually least squares)	Yes	Yes
Back propagation neural network	No	No
Learning vector quantization	No	No

Table 11.1: Some supervised learning PARCs used in electronic noses

More recently supervised learning artificial neural-networking techniques have been used. These methods are quite attractive because they can handle non-linear data, they are tolerant to senor drift or noise ($\approx 10\%$) and tend to produce lower predictive error rates than chemometric techniques. Moreover, the artificial neural network is attractive as it, to certain extent, mimics the olfactory system. There are also PARC methods that do not need a separate training stage but learn to discriminate between the response vectors automatically. These are unsupervised learning methods and are closer to the way brain works, the principal methods used so far are listed in table 11.2

PARC method	**Linear**	**Parametric**
Euclidean cluster analysis	Yes	No
Other cluster analysis	No	No
Kohonen network	No	No

Table 11.2: Some unsupervised learning PARCs used in electronic noses

11.3 Current status of electronic nose technology

11.3.1 Applications

Table 11.3 summarizes some of the different applications of electronic noses that have been reported to date.

Application	**Array type**
Grading of coffee blends or beans	MOX
Roasting level of coffees	MOX
Grading of Whiskys	Piezoelectric
Grading of lagers and beers	MOX
Off-flavours in lagers	Polymer
Freshness of fish	MOX
Freshness of meat	MOSFET
Quality of grains	Electrochemical
Quality of air	Polymer
Perfumes	Piezoelectric

Table 11.3: Some applications of electronic noses

11.4 The outlook for electronic noses

There is a plethora of potential applications of electronic noses today. Besides de assessment of various foodstuff and beverages, there is considerable scope in the field of environmental monitoring. Odour control is of increasing importance in our lives. This environmental application area is particularly important because the architecture for an electronic nose could be trained to recognize hazardous chemicals as well as odours. Finally, its quite likely that there will be increasing interest in the use of electronic noses in the medical field.

12 CANNABIS AND SPORT [12]

The consumption of substances derived from cannabis such as hashish (resin) and marijuana ("grass", "pot"), particularly in the from of joints, is widespread. The relatively high incidence of cannabinoids detection in urine reflects the high incidence of cannabinoids detection in urine reflects the high prevalence of cannabis use among young adults.

Renaud and Cornier showed that marijuana smoking reduce maximal exercise performance; when 12 healthy young adults cyded to exhaustion 10 minutes after smoking, exercise duration decreased from 16 to 15 minutes. Driving and piloting skills are also negatively affected, and point to the dangers of cannabis exposure when high level of alertness and quick reflexes are required, such as in automobile sports. The main feature recreational use of cannabis is that it produces a feeling of euphoria with decreased anxiety and increased sociability, which may alleviate the stress generated by competition. However, cannabis can also produce dysphoric reactions, including severe anxiety and panic disorders, paranoia and psychosis. Because cannabis diminishes alertness, and has relaxing and sedative properties, it may be used to improve sleeping time and sleep quality.

12.1 Cannabis Analysis in Urine

According to the World Anti-Doping Agency (WADA) standards, urine samples are considerd positive for cannabis exposure if the sum of the concentrations of free and conjugated carboxy-THC is greater than $15\mu g/l$, when determined by gas-chromatography/mass spectrometry.

12.2 Effects of cannabis consumption

Isolated or infrequent consumption can lead to:

- Mild intoxication
- Sedative effect on behaviour.
- Slower reaction times.
- Memory problems.
- tendency towards drowsiness.

In terms of the effect on the body, although heightened sensory perception can be expected, THC also engenders a certain heaviness, marked relaxation, and excessive fatigue of the limbs. As the dose increases, the user may experience hallucinations, an alteration of the perception of reality and a marked reduction in concentration.

As regards psychological and social behaviour, cannabis accentuates the mood. So user may become carefree, happy, and relaxed, but also risks becoming stressed, depressed, or paranoid. Other effects on a user include reduce inhibition and developing a certain indifference. Regular consumption leads to psychological dependence, a chronic sedative effect, and even social detachment.

13 Development of a Highly Selective Single Sensor Microfluidic Based Gas Detector [13]

13.1 Introduction

The state of the art technology available in the industry today for real time gas detection is the electronic nose or e-nose, which functions based on sensor arrays coupled with pattern recognition systems.

13.2 Odor and sense of smell

Odor is a sensation generated when odorant 8gas) molecules interact with receptors in the olfactory neurons in the (human) nose which can sense more than 10000 different odors. The nose is the only external part of our olfaction system, the odorant molecules enter through the nasal cavity and reach the olfactory receptors which are placed between our eyes. The receptors neurons are connected to the olfactory bulb which is part of our brain and the olfactory bulb is connected to the olfactory cortex which is in charge of signal analysis and patter recognition on different smells. While the air goes through the nasal cavity, the temperature of the air reaches the temperature of body, in the presence of any odorant in the air the molecules of the odorant react with the olfactory receptors and that results into the sense of smell.

In essence the olfactory receptors are the main part of the smelling process since they produce the electrical pulse which is transferred through the olfactory bulb to the neurons and hence the brain for signal analysis and pattern recognition. Olfactory receptors are neuron cells which are placed in epithelium, there are more than 10 million olfactory receptor cells in epithelium which has a surface area of 2-4 cm^2 and is cover with a 10-40 μm thick layer of mucus. The gas molecules are adsorbed to this later, diffuse into, and reach the olfactory receptors, the end of each cell reaches the surface of the epithelium through tiny hairs which are called cilia.

Each olfactory receptor responds only to certain gas molecules, therefore, by exposing the olfactory system to a chemical compound, some of the olfactory receptors get activated and the rest are deactivated. In essence, if there are "n" receptors and each has two modes (active and non-active) 2^n scenarios migth occur. The results in encoding different smells in the olfactory system.

13.3 Machine Olfaction

Gas chromatography (GC) and mass spectrometry (MS) are the most commonly used "macro" systems developed for analysis of Volatile Organic Compounds, VOCs. Although GC and MS have high accuracy and reliability, these methods are expensive and time consuming and require bulky devices and highly skilled personnel to run them. Also the sample extraction and experimental process involved using these methods are sophisticated and time consuming. The miniaturization of the system such as gas chromatography and mass spectrometry in a low-cost fashion has not been realized yet. These methods are not called e-nose as their operation principle is not similar to the biological model.

13.3.1 Gas Chromatography - Mass Spectrometry - Electronic Nose

- Gas Chromatography: A GC is an analytical instrument that measures the content of a mixture of different gas components in a sample, the sample injected into the instrument is transported by a stream of gas (carrier gas) into a separation channel known as the column, different components are then separated along the column. The detector placed at the end of the column measures the quantity of the components that exit the column.
- Mass Spectrometry: The sensitivity of this method is high, and it is usually used in series which a GC to identify different compounds of components in a gas mixture.
- Electronic nose (e-nose): Operate based on sensor arrays coupled with patter recognition systems, as for the sensory part, an array of several sensors are used. The goal of the first e-nose was to develop portable device for detection of flammable gases.

The name of the e-nose is chosen because of its similarity to the human nose. Five stages of smell detection sing human olfaction system are:

1) Sniffing the smell during which the odorant molecules are adsorbed to receptor cells and stimulate them;
2) Stimulation of the olfactory receptors and producing an electrical pulse;
3) Transferring the electrical signal to mitral cells through glomerulus, which is part of the olfactory bulb;
4) Sending the neuron signals to the brain through the mitral cells;
5) Performing signal analysis and pattern recognition in the brain, resulting in smell detection.

The five components of smell detection using an e-nose are:

1) Sample extraction and delivering the gas molecules to the chamber where the the sensor array is located;
2) Reaction of the gas molecules with the sensor sensing pallet, resulting in electrical signals;
3) Amplification and recording of the electrical signals using interface circuit;
4) Converting the recorded signals to digital data that is fed to a computer;
5) Analyzing the data, extracting the features from the signals, and recognizing the pattern of each signal (using different pattern recognition techniques), resulting in smell detection.

The analyte is extracted in the chamber where the conditions of the sample (temperature and humidity) are controlled. If the components of the sensor array are correctly chosen the responses of the different sensor to the analyte are different which results in a general finger print for the examined sample.

13.3.2 Sensors in e-nose

Gas sensors are devices which perform based on changing one or few of their physical characteristics (such as mass, conductivity or capacitance) when they are exposed to a gas. Converting these changes to electrical signals results in producing the response of the sensor to different gases. Gas sensors are evaluated based in their performance indicators which are as follows:

- **Sensitivity:** Shows how precise the sensor can detect the target gas.
- **Detection limit:** The minimum volume concentration of the target which can be detected by gas sensor, showing how sensitive is the sensor.

- **Selectivity:** The ability of the gas sensor to distinguish between different components of a mixture and detect a single specific gas.
- **Response time:** The time which is required for the sensor to create a signal from reaction to a specific concentration of the target gas.
- **Recovery time:** The time which takes for the sensor response to return to its baseline.
- **Power consumption:** The power dissipated by the sensor heater and sensing pallet.
- **Dynamic range:** The difference between the maximum concentration of the gas that could be detected and minimum detection limit.
- **Life cycle:** The period of time which a sensor can operate without stopping.
- **Drift:** The gradual change in the sensing capability of a gas sensor over time.

The most frequently used type of gas sensors is metal oxide semiconductor (MOS), in the basic configuration of MOS sensors, figure 13.1, a chemo-resistor is made by deposition of a thick film metal oxide pallet ant thick film thermo-resistor micro-heater on opposite surfaces of a millimeter-scale ceramic substrate.

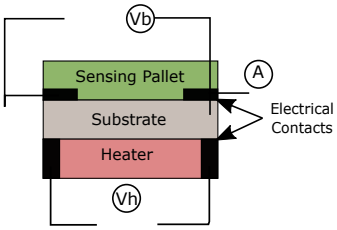

Figure 13.1: MOS Gas Sensor Schematic

The behaviour of a MOS sensor in DC bias can be modeled as a variable resistance R_s, figure 13.2, the value of this resistance depends on the type of gas molecule, the gas concentration and temperature of the sensing pallet. The resistance of the sensor resistance of the sensor in the clean air R_{air} (baseline) The sensitivity (S) of such a sensor is defined by equation 13.1

$$S = \frac{R_{air}}{R_{gas}} \tag{13.1}$$

in which R_{air} and R_{gas} are the resistances of the sensing pallet measured in the clean and contaminated air, respectively.

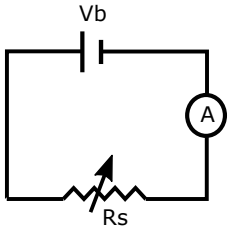

Figure 13.2: MOS Gas Sensor Electrical Circuit in DC Bias

The selectivity between two gases (i, j) is defined by equation 13.2. Current gas sensors are either made to be evenly sensitive to different gases or fabricated for detecting a specific target.

$$Sel(i, j) = \frac{S_i}{S_j} \tag{13.2}$$

Hence, differentiating among different gases or a mixture of gases using single sensor is very challenging, if not impossible as the transient responses of the sensor to two different gases are almost the same.

13.3.3 Feature extraction methods

The process of extracting information from the responses of the sensor components of an array of sensors is called feature extraction. The goal is to relate the extracted features from the responses to the type, concentration or a characteristic of the examined gas.

Difference feature extraction methods are used and reported in the literature. For instance, the maximum level of the response, difference between maximum and minimum levels, area underneath the response curve, signal curve, signal peak time, maximum of the differentiation with respect to time, and slope of the response. There are different methods used to reduce the dimensions ot the extracted features, these include: Principal Componen Analysis (PCA), Linear Discriminant Analysis (LDA), Kernel Principal Component Analysis (KPCA, non-linear), and Generalized Discriminant Analysis (GDA, non-linear).

Different methods such as k-nearest neighbor (KNN), neural network (NN) and support vector machine (SVM) are used for data classification, and hence gas identification, in the feature space. KNN is one of the most commonly used methods for sample identification, in this one the distances of each feature vector to different clusters are measured and based on the measured distances the appropriate cluster is selected (the minimun distance). This method is simple but computationally expensive, and it needs mathematical analytical tools as the distance of the feature vector from all other points in the feature map is required to be measured and compared.

13.3.4 E-nose Application

Application	**Example**
Food Industry	Coffee, Meat, Fish, Oil, Dairy, Bread
Agriculture	Fruit, Cereal, Vegetable, Plant, Poultry
Medical	Disease diagnosis, Breath analysis, Hospitals
Beverage	Fruit juice, Wine
Air quality	Pollutant, Toxic
Environment	Contamination in water and soil
Military	Explosives, Chemical Warfare Agents, Counter terrorism
Robotic	Remote sensing, Odor source localization
Space	Shuttle, International Space Station
Multimedia	Virtual olfactory interfaces
Fire & Safety	Fire detection, Leakage detection, Combustible
Biology	Bacteria, Fungal, Microbial Recognition
Cosmetic	Fragrance, perfume
Geology	Soil, Volcanic gases
Petroleum	Fuel Quality, Fuel Leakage, Oil
Other Industries	Automotive, Paper quality, Cigarette

Table 13.1: Different applications of electronic noses, recreated from [13]

14 Early Detection of Illicit Drug use in Teenagers [14]

The objective is to review the literature on illicit drug use in teenagers and highlight the risk factors for teen involvement. The authors also review the warning signs that a teen is using illicit drugs.

14.1 Introduction

Illicit drug use among teenagers has been well documented, and it appears to be more widespread than parents and guardians may suspect. There is statistical evidence that teens are getting involved in drug use as early as 12 to 14 years old. The data and statistics on illicit drug and alcohol use and the consequences of such activities among teenagers are very frightening. Several authors have reported the association between alcoholism and illicit drug use among teenagers and motor vehicle accidents, risky sexual behaviours, increase suicidality, homicides, mental health problems, and high rate of school dropout.

14.2 Risk factors

- **Family risk factors:** Inadequate parental supervision, poor communication, family tension and conflicts, inconsistent or unduly severe parental discipline, broken homes, and family history of parental alcohol or drug abuse.
- **Individual risk factors:** History of early childhood negative and aggressive behaviour, history of physical or sexual abuse, being male, Caucasian, and an older adolescent, emotional, social, or academic difficulties, poor impulse control, unstable emotions, thrill-seeking behaviours, and very low perception of the dangers inherent in drug use.
- **Miscellaneous risk factors** Low socioeconomic status, level of education, living in a high crime and drug-use neighbourhood, ease of drug availability, peer group pressure, and history of mental illness.

14.3 Warning signs

Some of the warning signs are: Frequent change of friends, withdrawal from usual family bonding, routines and activities, unusual and violent behaviours, impairment of the sense of judgment and desinhibition, difficulties in verbal expression (such as limit in his or her communication or become unusually talkative with incoherent words and sentences) , deterioration of school grades and skipping of classes, lack of motivation, apathy, poor morale, low productivity, lack of self control, aggressive behaviour, difficult temperament, poor interactions, neglect of personal hygiene and appearance and adoption of unusual dress habits, deception and disrespect to authority figures, lying, manipulative and secretive traits, they may become irritable and verbally abusive, they might threaten to quit school or destroy family property, depression, mood instability, suicidal.

The appearance of bloodshot eyes, widely dilated pupils, or pin-point pupils are very indicative of drug use. There may be noticeable changes in body habitus such as unexplained and sudden weight loss, weight gain or poor oral hygiene.

14.4 Conclusion

There is an urgent need for parents, school teachers and healthcare providers to be familiar with the early signs and symptoms of drug and substance abuse to be able to implement preventive measures.

15 THE EFFECT OF DRUG USE ON WORKPLACE ACCIDENTS [15]

15.1 Introduction

In the last thirty years, there has been a significant decrease in the growth rate of labour productivity in the United States. Coinciding with the decline in productivity has been an increase in illicit drug use by the employed population. In response to these perceived losses, the government and private sector have undertaken an extensive campaign to reduce drug use in the workplace. As if 1990, 46 percent of all firms with 250 or more employees had a drug-testing program and 79 percent if these firms had a formal employee assistance plan. Act of 1988 requires federal government contractors to maintain drug free workplace policies.

The purpose of this paper is to examine the relationship between drug use and productivity in a more systematic way than that found in prior studies. In particular, this paper will investigate the relationship between drug use and workplace accidents. Assuming that drug use affects the probability of having an accident, it can be shown that wages and workers' compensation benefits will have a significant impact on drug consumption levels. The logic underlying this hypothesis is relatively simple: *An accident results in a loss of income the size of which is determined by the difference between wages and workers' compensation benefits.*

15.2 Conclusion

The first examined the effect of drug use on workplace accidents directly by testing weather drug use was significantly correlated with workplace accidents, the second analysis was less straightforward and focused on individual consumption choices. Specifically, we tested whether workers' compensation benefit and wages, the determinants of the financial loss associated with workplace accident, were significantly related to drug use.

The results are mixed. For the female sample, the evidence supports the conclusion that on average, drug use is not significantly related to the incidence of workplace accidents. This result is not surprising for two reasons. First, women work predominantly in occupations that are less hazardous, and where on-the-job accidents are less frequent. Second, woman have relatively low levels of drug use and are less likely to be impaired by such use. Both of the facts may explain the absence of a significant effect of drug use on workplace accidents for the female sample. Among males, however, direct estimates of the effect of drug use on workplace accidents indicate that drug use raises the probability oh having a workplace accident by approximately by 25 percent.

16 BEATING DRUG TESTS AND DEFENDING POSITIVE RESULTS [16]

16.1 Introduction

Alcohol and drug abuse is a serious public health issue worldwide. In one report published in 1999, an estimated 60 million Americans smoke, 14 million people were abusing alcohol and another 14 million people were taking illicit drugs, as a result 590,000 deaths, about 25% of all deaths in the United States were caused by addictive substances. 105,500 from alcohol abuse 446,000 from tobacco use and 39,000 from addictive drugs in 1995. In addition, such addictions cause 40 million illnesses and injuries each year and the economic burden of such abuse is estimated to be over $400 billion including health care cost, low worker's productivity and crime. Drugs and alcohol abuse are risk factors for crime, family violence, accidents, birth defects, divorce and disability

16.2 Workplace Drug Testing

The overall testing process under mandatory testing consists of proper collection of specimen, initiation of chain of custody and finally analysis of specimen by a SAMHSA (substance Abuse and Mental Health Services Administration, an agency under Department of Health and Human Services on the United States Government) certified laboratory.

The confirmation should be performed by a second technique, preferably GC/MS. It is estimated that approximately 20 million employees are screened each year in the US for illicit drugs.

16.3 How People Try to Beat Drug Tests

There are several ways people try to beat drug tests. Synthetic and drug free human urine, various detoxifying agents are available through the Internet and the manufacturers of these products claim that these agents are effective in flushing out drugs from the body. Certain adulterants should be added in vitro to pass a drug test.

Drug testing laboratories routinely perform "specimen submitted for workplace drug testing. These tests include creating, specific gravity, temperature and pH specimen. All values should be within acceptable limits in order for the specimen to be processed further for workplace drug testing. Substituting one's urine with drug free urine is a sure way to pass the drug test unless the laboratory testing such a specimen can identify it as a substituted specimen due to its unacceptable temperature. People also add various household chemicals to urine in vitro in order to invalidate workplace drug testing.

Several precaution are taken by the personnel of the collection site to avoid such adulteration of submitted specimens such as asking the donor to remove outer garments that may contain concealed adulterating substances. The collector should ensure that all personal belongings such as a purse or a briefcase stay with the collector. When a donor is unable to provide a urine specimen, the donor may have intentionally urinated prior to arriving at the collection site, has a physical disability making it impossible to provide a specimen, or has a "shy bladder". If they can't provide the specimen, the donor is given a reasonable amount of fluid to drink distributed reasonably through a period of up to 3h or until the donor has provided a new sufficient amount of urine specimen, the collection procedure is discontinued and deemed a "refusal to test".

17 OVERVIEW ON SNIFFPHONE: A PORTABLE DEVICE FOR DISEASE DIAGNOSIS [17]

Handy and easy-to-use device that allows the non-invasive detection of gastric diseases.

17.1 Introduction

In this paper, we present an approach to tackle these requirements by integrating heterogeneous micro- and nano- technologies into autonomous smart system that can be coupled to a mobile phone and analyze disease markers from exhaled breath.

17.2 Sniffphone

17.2.1 Overall Concept

Figure 17.1 shows a scheme of the sniffphone concept. (A) is transferred wirelessly via the phone's internet, (B)to an external server for remote analysis of the collected signals, (C) Pattern recognition and statistical methods are then applied on the received data, while considering other clinical information of the same patient. Upon the completion of the analysis, a clinical report including the diagnosis results is sent back to clinical doctor for diagnosis and tracking (D) along with a brief feedback to the user (E).

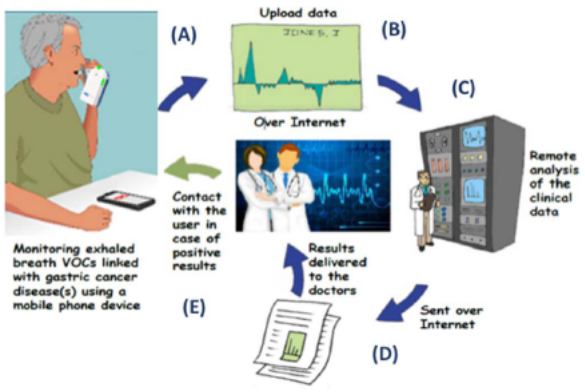

Figure 17.1: Illustration of the Sniffphone concept

17.2.2 Using Sniffphone

The user creates an account on the sniffphone server, with login and password along with some personal information. For the breath analysis the user logs into the account, fills a brief questionnaire regarding his/her life style at the time of the measurement and triggers the measurement process. Once the measurement is finished, the sniffphone device sends the measurement data to the smartphone, which in turn sends it to the data analysis server along with the given questionnaire information. Finally, the user receives a feedback message in his/her smartphone related to the result of the data analysis.

17.3 Materials and Methods

The device consists of several units: microfluidics, pumps, collection chamber, gas sensor array, auxiliary environmental sensors, breath detectors, electronic unit, all integrated in a case.

The device operates in two steps first the ambient air is measured for reference and then the user exhales at a short distance from the inlet of the device. When the user exhales, the beginning and end of his/her breath is detected by a breath detector sensor (NV sensors by Nanovation). Then the microfluidic system directs the breath sample to the sensors chamber, where the gas sensor array is located.

The breath sampling protocol is designed to sample the deep alveolar end-tidal part of the breath. Thus, the first part of the exhaled breath is discarded by pumping the sample during the first few seconds, determined by the NV sensors. Then, two valves enclose the target part of the breath ample in the sensors chamber, where the sensors are measuring during few seconds until they reach stability. Finally, the sample is pumped out and the chamber is cleaned.

The sensor array contains a chip with eight Gold Nanoparticles (GNP) gas sensors developed at the Technion Institute and specifically designed for detecting gastrointestinal diseases and cancer. The GNP sensor technology is an advanced approach for detecting VOCs profiles present in breath, which in this application are the VOC biomarker profiles of the gastrointestinal diseases with risk of developing cancer. Other environmental sensors monitor for the measurement conditions, and their responses can also be considered in the posterior data analysis.

18 SNIFFING THE UNIQUE "ODOR PRINT" OF NON-SMALL-CELL LUNG CANCER WITH GOLD NANOPARTICLES [18]

18.1 Abstract

A highly sensitive and fast-response array of sensors based on gold nano-particles, in combination with pattern recognition methods, can distinguish between the odour prints of non-small-cell lung cancer (NSCLC) and negative controls with 100% accuracy, with no need for pre-concentration techniques.

18.2 Introduction

We report an array of 18 molecularly modified gold nano-particles (Au NPs)in combination with a pattern recognition method that can sense and identify patterns of odorant molecule(s), such as VOCs emitted from seven different types of NSCLC, with no need for pre-concentration of the lung cancer bio-markers. The molecules surrounding the Au NPs are of the same chemical groups as the VOCs emitted from the NSCLC, and thus show high sensitivity to biomarkers of lung cancer cells.

18.3 Results and Discussion

GC-MS analysis identified 350-400 different VOCs that had been either synthesizes or catabolized in at least one cell line. The compounds that were chosen for both the NSCLCs and the medium were those with >0.08% of the total amount detected by GC-MS.

Figure 18.1 shows the average abundance ratio of the 55 volatile biomarkers identified with SPME-aided GC-MS. Forty common VOCs were founded in the head space of the NSCLCs and the control cell lines, at distinctly different concentration mixtures. VOCs 41-55 were found only in the head-space of NSCLC samples.

Based on these results we designed and used an array of 18 chemiresistors for detecting the head space of NSCLC and a control medium. In this configuration, each sensor is widely responsive to a variety of odorants. Hence, each analyte yields a distinct signature from the array of broadly cross-reactive sensors. Patter recognition algorithms can be applied to the multidimensional set of signals, obtained simultaneously from all the sensors int he array, to yield information about the identify, properties, and concentration of the vapour exposed to the sensor array.

The functionalities of Au NPs were chosen, based on the GC-MS analysis presented in figure 18.1, as having structures similar to the lung-cancer-related biomarkers to maximize the sensitivity to the target. Chemiresistors are based functionalized Au NPs combine the advantages of organic specificity with the robustness and processability of inorganic materials.

Sensors of Au NPs that are mostly coated with hydrophobic functionalities are almost insensitive to water and hence are particularly suitable for breath testing, sicne exhaled breath contains $\approx 80\%$ relative humidity.

Prior to exposure to the sample head space, we examined the response $\Delta R/R_B$ (where R_B, typically, $\approx 1M\Omega$ is the baseline resistance of the sensor in the absence of analyte and ΔR is the baseline-corrected steady-state resistance change upon exposure of the sensor to analyte) of each sensor to some representative lung cancer biomarkers.

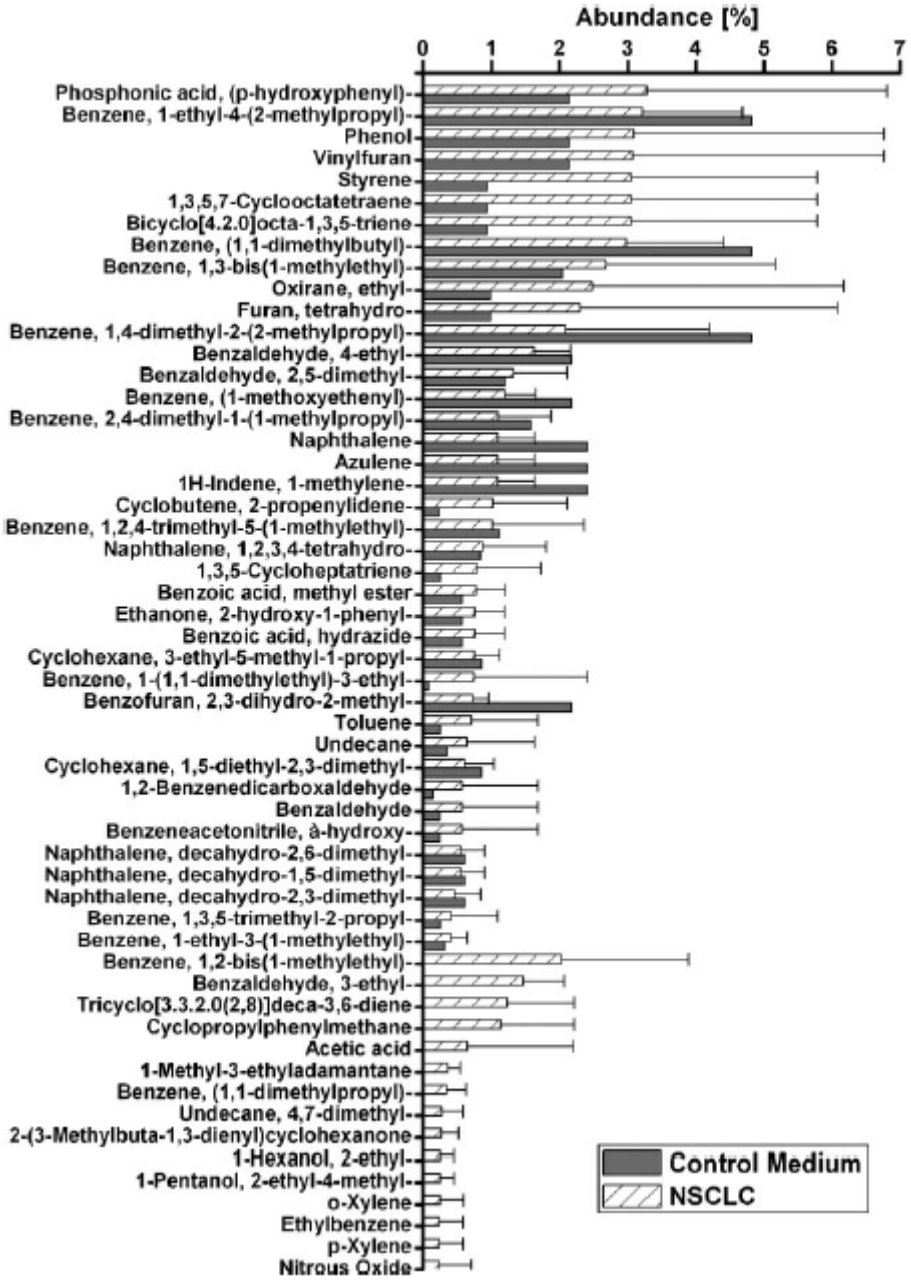

Figure 18.1: Average abundance ratio of the 55 volatile biomarkers identified with SPME-aided GC-MS.

The biomarker concentrations were $P_a/P_o + 0.0001 - 0.05$ where P_a and P_o are the pressure and vapour pressure of the analyte at room temperature ($\approx^\circ$ 21C), respectively. We found that the sensors response was rapid upon exposure to the simulated vapour analyte, fully reversible upon switching back to purified dry air, responsive to a wide variety of concentrations, and showed satisfactory signal-to-noise ratio.

For the tpical response of three of our sensors. The sensors showed either a decrease in resistance (ten sensors) or an increase in resistance response (eight sensors).The physical mechanism responsible for the electronic response of NP films to analyte exposure is still subject to controversy. It is well known that the response of chemiresistors made from metalcore NPs and capping monolayers can be either positive (increased resistance) or negative (decreased resistance). These changes could be attributed to one or both of the following mechanisms: 1) swelling, which may increase the resistance due to an increased interparticle tunnel distance; or 2) an increase in the permittivity of the organic matrix surrounding the metal cores may decrease the resistance due to a reduction of the potential barriers between the metal cores, thereby decreasing the tunneling decay constant.

No overlap for the NSLC and the control patterns is seen, and the clusters were separeted with 100% success, clear discrimination was achieved with the sensor array without preconcentration or dehumidification of the cell line sample.

18.4 Conclusions

We have identified 40 common VOCs that appear in >85

NSCLCs and in the control medium and 15 VOCs that appear only in NSCLC, but not in the control medium. Based on this knowledge, we fabricated an array of highly sensitive, simple-to-use, and inexpensive cross-reactive sensors and exposed them to NSCLC and the control medium. Analysis of the responses from the array of sensors using PCA showed 100% separation between the clusters of NSCLC and the control medium, without using any preconcentration technique. Success in this endeavor would ultimately provide a launching pad for initiatives for immediate diagnosis of fresh (frozen) tissues of lung cancer in operating rooms, where a dichotomic diagnosis is crucial for guiding surgeons during surgery.

19 A REVIEW OF DRUG DETECTION TESTING AND AN EXAMINATION OF URINE, HAIR, SALIVA AND SWEAT [19]

19.1 Introduction

Large scale biological testing for illicit drug use was developed during the occupation of Japan by the United States after WWII. The need to develop a reasonably inexpensive and accurate urine tests resulted in chromatographic procedures that were able to detect small amounts of opiates in urine.

The demand for drug testing products created a highly competitive market. The resulting technological advances can be seen in the products reviewed in the appendices of this document. Hair, swat and saliva are showing potential as testing mediums with advantages in detection times, ease of collection and resistance of tampering balancing possible reductions in test accuracy and higher laboratory costs.

A very large number of substances can be routinely measured in the different biological matrices. This paper will primarily restrict itself to a discussion of the detection of the five classes of commonly abused drugs. These include opiates, methadone, cocaine, sympathomimetic amines, cannabis and benzodiazepines.

19.2 Methodology of this review

Journal publications and conference presentations on drug detection and on the use of urine, hair, saliva and sweat for the detection of drugs in humans were identified through a comprehensive search of the electronic database Medline. In addition, Australian experts involved in the analysis of urine, hair and sweat were contacted for unpublished reports, policy documents and related information

19.3 Identifying Drug use

Identification of drug use is a two-step process that involves a screening test which, if found to be positive, is followed by a confirmatory test. The screening test is designed to be sensitive to the presence of a class of drug while often sacrificing the ability to specifically identify the particular drug present. The confirmatory test, conducted only on a positive sample, is used to identify the specific drug and/or metabolites present thus to ensure that the sample is truly positive for the targeted drug.

19.3.1 Result Interpretation

Drug Metabolites

Half-life, Time taken for 50% of the drug to be removed from the body by either metabolism or excretion. After a substance is consumed it is broken down, or metabolized, by the body into other chemicals that after excretion, can be detected in the biological specimen .

In many cases metabolites have significantly longer half-lives than their parent drug, and are thus more likely to be detected. Accurate identification of relative metabolite concentrations is often essential in the determination of the actual drug used, as different drugs can have the same metabolites.

Table 19.1 summarizes the relative occurrence of parent drug and metabolites in urine, saliva, sweat and hair. The parent compound is more likely to be detected in hair, sweat and saliva than in urine.

Drug	**Urine**	**Saliva**	**Sweat**	**Hair**
Amphetamine	Amphet	Amphet	Amphet	Amphet
Methamphetamine	Metham> Amphet	Methamphetamine	Methamphetamine	Metham> Amphet
Cocaine	BE>EME> Cocaine	Cocaine>BE≈ EME	Cocaine>EME> BE	Cocaine>BE> EME
Heroin	MO-glucuronide> MO	Heroin ≈ 6-MAM >MO	Heroin ≈ 6-MAM> >MO$^{\diamond}$	Heroin ≈ MO
Codeine	CO-glucuronide CO>norcodeine	CO	CO	CO>MO
Methadone	EDDP	Methadone	Methadone	Methadone
Marijuana	Carboxy-THC	THC	THC	Carboxy-THC

Table 19.1: Relative occurrence of parent drug and metabolite(s) in urine, saliva, sweat and hair

Qualitative Results

Test that indicates whether a sample is positive or negative for a specified drug. There are four possible results of a qualitative drug test, table 19.2.

Test Result	**Yes**	**No**
Positive	True-positive	False-positive
Negative	False negative	True-negative

Table 19.2: Four possible results of a qualitative drug test

Interpreting a Positive Test Result

A positive result indicates that the specific drug is present at or above the designated cut-off level. Typically, the cut-of concentration is st to the lowest concentration the drug can be reliably detected following consumption.

False-Positive: Occur when a benign substance in the biological sample mimics the chemical effect of the targeted substance on the test. The test indicates a positive result even though the target drug was absent.

Interpreting a Negative Test Result

The drug and its metabolites are absent in the biological sample. The amount of drug present in the sample at the time of sample collection and thus whether a positive result is obtained, is determined by a number of factors.

False-Negatives: It is possible for sub-cut off levels of a drug to be detected in a sample and for it still to be reported as negative. There are a number of actions an individual can take, depending on the sample being taken, to increase the likelihood of a false-negative result.

Quantitative Results

Determination of the specific concentrations of a parent drug and/or its metabolite(s) in a sample.

19.4 Methods of Drug Testing

19.4.1 Screening Tests

Immunoassay is the most commonly used method for the screening of illicit drugs in biological samples. Commercially available immunoassays are sold as kits. Each test kit contains a precise quantity of the drug or metabolite it is measuring and a precise quantity of antibodies designated to detect and destroy the drug or drug metabolite. The three main limitations of immunoassay screening tests are sensitivity, specificity and cross-reactivity.

- Sensitivity: Measure of a test's ability to identify the presence of a drug when it is, in fact, present.
- Specificity: Refers to the extent to which the test can discriminate between different drugs.
- Cross-reactivity: Occurs when the test is unable to distinguish between substances that are unrelated but chemically similar.

19.4.2 Confirmatory tests

The confirmation should be made using a different technique of equal or greater sensitivity (GC/MS).

19.5 Biological indicators of Drug Use

The presence of drugs can be assessed in a variety of biological matrices. The applicability and usefulness of these matrices which include urine, blood, hair, saliva and sweat vary depending on the context in which they are applied and the results required. The mos significant way in which the matrices differ is the time range or window period for which drug use can be detected

19.5.1 Urine Analysis

Most widely used biological specimen for the analysis of illicit drugs and their metabolites. Despite a number of persistent shortcomings, such as its susceptibility to tampering.

The Physiology of Urine Production

Produced by the kidneys and is an ultra-filtrate of blood. During urine production the kidneys reabsorb essential substances. Excess water and waste products, such as urea, organic substances and inorganic substances, are eliminated from the body.

Incorporation of drugs into Urine

When a drug is smoked or injected absorption is nearly instantaneous and excretion in urine begins almost immediately. Absorption is slower when a drug is orally administered and excretion may be delayed for several hours. Generally a urine specimen will contain the highest concentration of parent drug and metabolite within 6 hours of administration.

For most illicit drugs a dose will be eliminated almost completely within 48 hours.

Specimen Collection

The ease with which a urine sample can be manipulated to increase the probability of a false-negative result means that significant measures must be taken to ensure the integrity of the specimen. There is a complete guideline to ensure a good collection.

Advantages and Disadvantages of urinalysis

Advantages

- Urine is generally available in sufficient quantities to make confirmation testing or sample retesting a simple process.
- Parent drug and/or metabolites are available in higher concentrations than other matrices making laboratory analysis a simpler process than other mediums.
- Good on-site tests are available, making screening a relatively quick process.

Disadvantages

- Urine has a relative short window of detection compared to hair and sweat.
- Samples are relatively easy to tamper. Collection sites should be appropriately designed and supervised to make adequate observation possible.
- Urine collection is relatively invasive and often reported to be humiliating for the donor and the observer.
- Good on-site tests are often more expensive than laboratory tests.

19.5.2 Hair Analysis

Wide window of detection. In contrast to urine, hair may be used to comment on a person's drug-use history spanning up to several months. Wide range of applications, such as workplace testing, neonatal testing, exposure assay and insurance cases. It has also been successfully used in forensic and law enforcement applications.

Incorporation of Drug into Hair

Although not fully understood, a more complex model of drug incorporation into hair has been accepted where drugs are incorporated not only from capillaries but also from the secretions of the sebaceous glands, apocrine glands and eccrine glands that coat the hair shaft. Inter-individual differences in hair structure and porosity, hair growth, melanin content, hair hygiene and use of cosmetic hair treatments and bleaching have also been shown to have significant effects on the observed concentrations of drugs in hair further increasing the difficulty of inter-individual comparison.

Specimen Collection

Specific guidelines and recommendations regarding sample collection:

- Sample collection should be performed by a responsible authority respecting the legal, ethical and human rights of the person being tested for drug use.
- Hair samples should be obtained in an environment free of drugs of abuse.
- Hair samples should be obtained in an environment free of drug contamination.
- Hair samples should be collected by an appropriately trained individual, not necessarily a physician.
- Hair should be tied together and cut as close to the skin as possible.
- A sufficient amount of hair should be taken so that a repeat analysis or confirmation analysis can be performed by another laboratory if needed. The weight of the specimen should be approximately 200 mg.
- For shipment and storage, the hair sample should be wrapped in aluminum foil to maintain integrity and avoid contamination.
- Specimens can be stored under dry conditions at room temperature.

Methodological Criteria for Obtaining Hair Test Results

- Standard hair analysis should be performed on a measured segment of hair.
- All hair samples should undergo a decontamination procedure.
- The washes should be analyzed for the drug under investigation, so as to allow comment on external exposure (passive contamination), if necessary.
- All positive screening test should be confirmed by alternate methods, for example by chromatography coupled by mass spectrometry or any other technology comparable or greater specificity and selectivity.

Analytical Techniques

- Point-of Collection Hair Tests: No commercially available on-site tests for drugs in hair.
- Methods of extracting drugs from hair.
  - Preparation: Hair is either left intact, finely cut, powdered or homogenized prior washing and extraction.
  - Washing: Hair should be washed to remove external drug contamination and excess dirt grease from the surface of the hair. Avoid over washing.
  - Extraction: Three main extraction modes: alkaline digestion, acid extraction and enzymatic treatment.
- Laboratory-Based Immunoassay Screening Tests: Immunoassays are typically not suitable for hair but some methods have been developed. Marijuana detection is still possible though more difficult because most commercial immunoassays are specific for the carboxylic acid metabolite of THC, which is found in hair in concentrations below detection limits.
- Chromatographic Confirmation Test: The analytical method most frequently used for hair analysis is gas chromatography/mass spectroscopy

Advantages and Disadvantages

Advantages

- Hair analysis has the widest window of drug detection.
- Hair may have utility when observing changes in drug use over time within an individual.
- Hair collection is non-invasive. It is also easy to store and ship specimens.
- Very low risk for disease transmission in the handling of the samples.

- It is generally easily to obtain sufficient hair for confirmation testing or reanalysis.
- Hair is difficult to substitute or adulterate.

Disadvantages

- Hair analysis cannot be used to determine levels of drug use.
- Hair analysis cannot detect recent drug use because of its slow growth rate.
- Complexities of drug incorporation and stability of drugs in hair male accurate and reliable interpretation difficult.
- It is generally not possible to use hair analysis to reliably detect very low drug use.

REFERENCES

[1] M. Boertien, R. Smith, B. Stewart, W. Mazyan, N. Bressan, and A. Ahmadi, "development of a low-cost portable sensor for detection of tetrahydrocannabinol (thc) in saliva," *CMBES Proceedings*, vol. 41, 2018.

[2] A. Voss, K. Witt, T. Kaschowitz, W. Poitz, A. Ebert, P. Roser, and K.-J. Bär, "Detecting cannabis use on the human skin surface via an electronic nose system," *Sensors*, vol. 14, no. 7, pp. 13 256–13 272, 2014.

[3] P. Sharma, P. Murthy, and M. S. Bharath, "Chemistry, metabolism, and toxicology of cannabis: clinical implications," *Iranian journal of psychiatry*, vol. 7, no. 4, p. 149, 2012.

[4] O. H. Drummer, "Drug testing in oral fluid," *Clinical Biochemist Reviews*, vol. 27, no. 3, p. 147, 2006.

[5] K. L. Lynch, Y. R. Luo, S. Hooshfar, and C. Yun, "Correlation of breath and blood δ9-tetrahydrocannabinol concentrations and release kinetics following controlled administration of smoked cannabis," *Clinical chemistry*, vol. 65, no. 9, pp. 1171–1179, 2019.

[6] C. H. Ashton, "Pharmacology and effects of cannabis: a brief review," *The British Journal of Psychiatry*, vol. 178, no. 2, pp. 101–106, 2001.

[7] D. Rüffer, F. Hoehne, and J. Bühler, "New digital metal-oxide (mox) sensor platform," *Sensors*, vol. 18, no. 4, p. 1052, 2018.

[8] N. Barsan and U. Weimar, "Fundamentals of metal oxide gas sensors," *Tagungsband*, pp. 618–621, 2012.

[9] Y. H. Caplan and B. A. Goldberger, "Alternative specimens for workplace drug testing," *Journal of Analytical Toxicology*, vol. 25, no. 5, pp. 396–399, 2001.

[10] M. Wada, R. Ikeda, N. Kuroda, and K. Nakashima, "Analytical methods for abused drugs in hair and their applications," *Analytical and bioanalytical chemistry*, vol. 397, no. 3, pp. 1039–1067, 2010.

[11] J. W. Gardner and P. N. Bartlett, "A brief history of electronic noses," *Sensors and Actuators B: Chemical*, vol. 18, no. 1-3, pp. 210–211, 1994.

[12] M. Saugy, L. Avois, C. Saudan, N. Robinson, C. Giroud, P. Mangin, and J. Dvorak, "Cannabis and sport," *British journal of sports medicine*, vol. 40, no. suppl 1, pp. i13–i15, 2006.

[13] M. Paknahad, "Development of highly selective single sensor microfluidic-based gas detector," Ph.D. dissertation, University of British Columbia, 2017.

[14] S. Ali, C. P. Mouton, S. Jabeen, E. K. Ofoemezie, R. K. Bailey, M. Shahid, and Q. Zeng, "Early detection of illicit drug use in teenagers," *Innovations in clinical neuroscience*, vol. 8, no. 12, p. 24, 2011.

[15] R. Kaestner and M. Grossman, "The effect of drug use on workplace accidents," *Labour Economics*, vol. 5, no. 3, pp. 267–294, 1998.

[16] A. Dasgupta, "Beating drug tests and defending positive results: A general overview," in *Beating Drug Tests and Defending Positive Results*. Springer, 2010, pp. 1–10.

[17] C. Jaeschke, M. Padilla, E. Turppa, I. Polaka, O. Gonzalez, K. Richardson, J. Pajukanta, J. Kortelainen, G. Shani, G. Shuster *et al.*, "Overview on sniffphone: a portable device for disease diagnosis," in *2019 IEEE International Symposium on Olfaction and Electronic Nose (ISOEN)*. IEEE, 2019, pp. 1–2.

[18] O. Barash, N. Peled, F. R. Hirsch, and H. Haick, "Sniffing the unique "odor print" of non-small-cell lung cancer with gold nanoparticles," *Small*, vol. 5, no. 22, pp. 2618–2624, 2009.

[19] D. Rouen, K. A. Dolan, and J. Kimber, *A review of drug detection testing and an examination of urine, hair, saliva and sweat.* National Drug and Alcohol Research Centre, University of New South Wales Sydney, 2001.