

ENGN2706 Research Methods

Tuning Selectivity of Semiconductor Metal- Oxide Gas Sensors Using Metal Organic Frameworks to Improve Acetone Sensing for Applications in Type 1 Diabetes

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Abstract

Acetone sensing is a promising area of breath analysis that poses the potential to provide non-invasive diagnosis and monitoring for a life-threatening complication of type 1 diabetes known as diabetic ketoacidosis. In particular the use of chemical sensors has been of recent interest due to their portability and high potential for miniaturisation. Selectively detecting this acetone amongst the hundreds of other gases present in exhaled breath poses a major difficulty for chemical sensors. This paper explores the use of metal-organic frameworks (MOFs) as filtration membranes as a solution to this problem. A review of the most recent experimental research surrounding MOF use in gas sensing was conducted as part of this research, to identify the various properties of MOFs that may be manipulated to enhance selectivity towards acetone. The MOFs that were investigated included: ZIF-8, ZIF-71, ZIF-67, ZIF-CoZn, and HKUST-1. It was found that the pore size, chemical affinity between gas and MOF, oriented growth, thickness of the MOF and the stacking of multiple MOFs were all related to increasing the selectivity of chemical sensors towards a target gas. Further experimental research is needed to both validate and expand on the key findings discussed in this paper.

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Introduction

Breath analysis offers exciting scope to improve the quality of current medical instrumentation, through the use of semiconductor metal oxide gas sensors (SMOs); an easy to construct, low in cost, and most importantly, non-invasive diagnostic and monitoring device. SMOs are a type of chemiresistive sensor that are able to detect gas molecules in the breath, to reveal information about metabolic processes. Important parameters of SMOs that contribute to sensor performance include sensitivity, morphology, operating temperature, response time and selectivity. Improving the selectivity of SMOs towards particular analytes remains a major obstacle in the field of breath analysis. Typically, selectivity is enhanced by chemically altering the metal oxide layer with catalytically active additives such as gold, or by doping the sensor material with other metal oxides like zinc or silicon. More recently, however, with rapid developments in nanotechnology, metal-organic frameworks (MOFs) have been incorporated into SMO technology. MOFs behave as a coating above the sensing layer inside SMOs, with malleable gas filtration properties that allow it to act as a sieve to isolate target analytes from a breath sample and ultimately improve selectivity.

A major application of breath analysis that requires advancements in the selectivity of SMOs lies with acetone sensing, which would help minimise the impact of a life-threatening diabetic condition known as diabetic ketoacidosis. This paper will provide a review of the current MOF technology being used to filter confounding compounds¹ from a breath sample, while providing an analysis of key findings to identify potential pathways for improving MOF use in acetone sensing. Section 1 will provide an introduction into the basic functionality of breath sensors along with a discussion on its fundamental parameters. Typical approaches for improving the selectivity of SMOs will be explored, along with the scope for real-life application that exists in monitoring and treating diabetic ketoacidosis through improving SMO selectivity. Section 2 will introduce MOFs and their functionality, as well as present the opportunity for MOFs to greatly improve the selectivity of SMOs. Section 3 will then explore the current MOF technology being used in breath sensing and present an organised summary of the important properties of these MOFs. Finally, Section 4 will involve a critical evaluation of the findings from Section 3, ultimately providing recommendations for how MOFs can be explored in future experimental research to further improve the selectivity in current acetone sensing.

¹ **Confounding compound:** an interfering gas compound

Section 1: Introduction to Breath Sensors

Given the current global movement to transform the healthcare system according to “P4 medicine” – that is, a predictive, preventive, personalised and participatory approach – breath analysis presents enticing potential as a means of achieving this [Flores et al., 2013]. Breath analysis is a promising field of medicine that offers the benefits of non-invasive disease diagnostics with a variety of diagnostic breath tests having already been developed for a plethora of applications. These include the urea breath test for diagnosis of *H. pylori* infection, CO₂ monitoring for use of anaesthesia in intensive care and FeNO monitoring to detect asthma [Lourenco et al., 2014; Righettoni et al., 2015]. There is potential, however, to increase this scope and help with the early diagnosis and continuous monitoring of many other diseases such as lung cancer, kidney disease and type 1 diabetes [Righettoni et al., 2015].

1.1 Types of Breath Sensors

Various techniques are currently used for breath analysis which may be categorised into 3 groups based on: (1) mass spectrometry (MS), (2) laser-absorption spectroscopic techniques and (3) chemical sensing [Righettoni et al., 2015].

The majority of the most sophisticated analytic methods such as proton transfer reaction mass spectrometry (PTR-MS) and flame ionisation detectors (FID) fit under the first two categories [Lourenco et al., 2014]. These techniques are typically excellent in terms of sensitivity, stability and response time; however, their major limitations lie in their need for large, expensive machinery that requires trained operators to function. The use of chemical sensors provides a probable solution to many of these challenges.

Chemical sensors generally offer low manufacturing cost, a high miniaturization potential, simplicity in its use, and portability [Righettoni et al., 2015]. Furthermore, the increased portability of these devices also enables the future distribution of this technology to remote areas and developing countries [Tung et al., 2019; Güntner et al., 2019]. There are several technologies within this category of chemical sensors that have varying sensing mechanisms such as quartz crystal microbalances (QCM) and surface acoustic wave (SAW). Albeit, the focus of this report will be on chemiresistive sensing through SMOs [Haghighi et al., 2019].

1.1.1 Semiconductor Metal Oxide Gas Sensors

SMOs are sensors that measure and detect the chemical properties of an analyte through two elemental components: the sensing layer and the transducer (Appendix A). The sensing layer is fabricated using nanostructures of metal oxides, which can either be placed in series with two electrodes (Figure 1) or coated on a set of interdigitated electrodes [Salunkhe et al., 2017]. A potential difference is then applied across the electrodes, allowing for the resistance of the

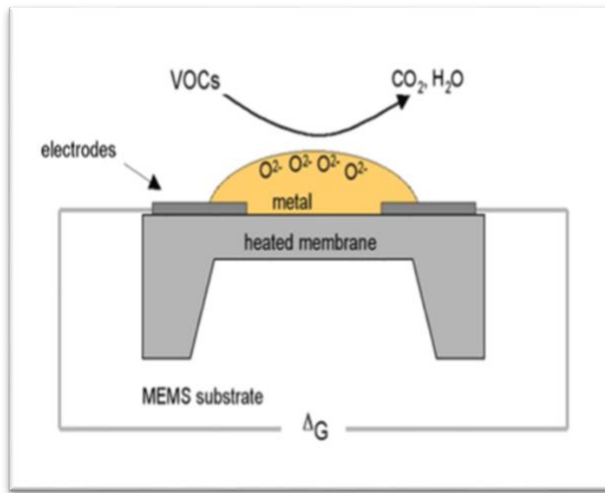


Figure 1 - Schematic of semiconductor metal-oxide gas sensor [BaseApp, 2018]

sensing material to be measured. Oxygen in the air combines with the metal forming various oxygen species such as O_2^- , O^- , O_2^- on the metal oxide surface layer. When reducing gases interact with these oxygen species, there is a redox reaction that releases electrons which creates either hole accumulation regions for p-type SMOs or electron depletion regions for n-type SMOs [Koo et al., 2019 which ultimately changes

the electrical resistance measured across the

electrodes [Jang et al., 2017]. This change to the state of equilibrium of the metal oxide sensing material is interpreted by the transducer as a change in resistance of the surface material [Righettoni et al., 2015; Haghighi et al., 2019]. The metric for the response of SMOs is therefore resistance.

Typically, SMOs detect a group of chemicals called volatile organic compounds (VOCs) such as acetone and ethanol, which are particularly useful for understanding individual metabolic conditions [Güntner et al., 2019]. VOCs appear in trace concentrations in exhaled breath, anywhere between the range of parts-per-million (ppm) and parts-per-trillion (ppt) [Lourenco et al., 2014; Saasa et al., 2018]. Therefore, in order to detect the true concentration of a target VOC in a sample of exhaled breath, SMOs must be highly sensitive. Moreover, exhaled breath contains hundreds of other interfering VOCs [Fu, 2016] which can cause a false positive response - consequently, SMOs must also be highly selective. In other words, strong selectivity and sensitivity are vital to achieve strong accuracy and precision, respectively, in breath analysis. While highly sensitive SMOs have been successfully engineered, attaining high selectivity has posed more challenges and has led to difficulties in the commercialisation of SMOs [Haghighi et al., 2019].

1.2 Characteristics of Current Breath Sensing

The following section explores the central characteristics of breath sensors, necessary for optimising sensor performance. While they are not all directly related to selectivity, they are important parameters that need to be considered to assure the overall success of SMOs. Furthermore, an understanding of the following parameters is relevant for later discussions in Section 3.

1.2.1 Sensitivity

The response (R) of a SMO is often defined according to the ratio of the change in resistance to the initial resistance and is represented by the following equation:

$$R = \frac{R_f - R_o}{R_o} \quad (1)$$

R_f is the resistance of the sensing layer in the presence of the analyte, and R_o is the initial resistance of the layer [Koo et al., 2019]. The sensitivity of a SMO is defined as the rate of a change of the response (R) with respect to the concentration (C) of a given gas and is represented by the following equation:

$$S = \frac{dR}{dC} \quad (2)$$

Further sensitivity can be achieved by adding noble metals, dopants and foreign oxides to the sensing layer [Righettoni et al., 2015].

1.2.2 Morphology of the Sensing Layer

The nanostructures of the metal oxide sensing layer (morphology) can be manipulated into various shapes such as spheres, rods, wires and core-shell structures, each with varying surface areas (Figure 2) [Righettoni et al., 2015; Koo et al., 2019]. Increasing the surface area of the sensing layer can contribute to a superior response when measuring a target VOC due to the increased adsorption of analyte molecules onto the sensor surface. Hence, morphology alteration during the synthesis process can contribute to increased sensitivity [Güntner et al., 2019; Koo et al., 2019].

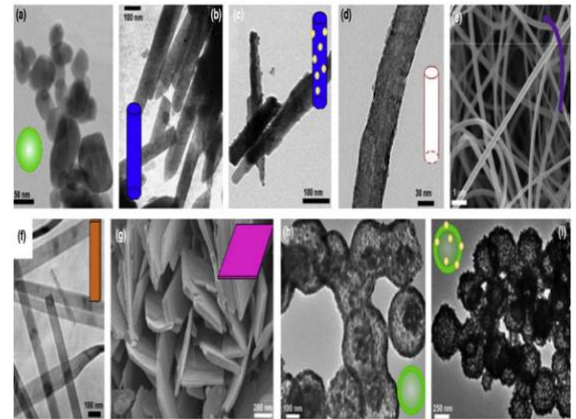


Figure 2 – Various nanostructures of sensing layer: (a) nanoparticles, (b) nanorods, (c) nanorods, (d) nanotubes (e) nanofibers, (f) nanobelts, (g) nanoplatelets (sheets), (h) hollow spheres, and (i) hollow spheres [97] [Righettoni et al., 2015]

1.2.3 Operational Temperature

Typical operating temperatures of SMOs are in the range of 200 to 500 °C [Güntner et al., 2019]. At low temperatures, the thermal activation energy of the target gas molecules is too low to react optimally with the sensing material, resulting in a lowered overall response. When the optimal operating temperature is reached, the adsorption ability of gas molecules is in the maximum state. Increasing temperature beyond this leads to excessive activation energy which causes desorption to become a more dominant process than adsorption which once more, negatively affects sensitivity [Righettoni et al., 2015; Haghighi et al., 2019; Koo et al., 2019]. Thus, optimal sensitivity can be achieved in part by evaluating temperature-response profiles for each material-analyte combination through experimentation [Güntner et al., 2019].

1.2.4 Response and recovery time

The response time is defined as the time taken for the sensor response to decrease from R_0 to 10% of $(R_0 - R_f)$ when the sensor is exposed to the target analyte. The recovery time is defined as the time taken for the response to increase from R_f to 90% $(R_0 - R_f)$ when the sensor is no longer exposed to the target analyte.

1.2.5 Other considerations

Furthermore, the sensors must be able to function at high relative humidity's (RH) as exhaled breath has RH levels of approximately 90%. This is typically measured using the coefficient of variation (CV) which describes the effect of humidity on responses, which is defined as:

$$CV = \frac{R_{SD}}{R_{avg}} \times 100$$

Where RSD and Ravg are the standard deviation and average value of responses with different humidity. A higher CV value for a given gas suggests less susceptibility to humidity fluctuations and vice versa for low CV values. For clinical applicability, the long-term stability of the SMO is also important to ensure the reliability of results. Stability can be determined by measuring the variation in response of a SMO to an analyte over an extended period.

1.2.6 Selectivity

For a SMO being exposed to various VOCs simultaneously, the subsequent response will be based on the interaction between this variety of VOCs and the sensor, and there is no indicator for how much of the response may be attributed to each individual VOC. Selectivity is defined as a SMO's ability to distinguish between a target VOC and any other molecule which is important to assure the validity of the response. Selectivity is usually explored through

analysing the cross-sensitivity of a sensor to a variety of VOCs at varying concentrations. Points to consider when assessing selectivity include the exploration of any competition mechanisms that may exist between gases reaching the grain surface as well as consideration of different diffusion rates of different gases through the sensing layer [Righettoni et al., 2015].

There are many prospective approaches for addressing this issue of selectivity including improving sampling methods, modifying sensor composition, using sensor arrays as well as using filtration layers, as will be discussed.

Careful breath sampling may aid in enhancing selectivity as various VOCs in exhaled breath come externally from the environment through inhalation, food ingestion and skin absorption [Güntner et al., 2019]. Ensuring the breath sample has as few exogenous² VOCs can reduce the number of interfering gases present and hence, improve selectivity.

The nanostructured sensing materials of SMOs often struggle with poor thermal stability at high operating temperatures [Righettoni et al., 2015]. Many studies have found that thermally stabilizing the sensing materials at a nanoscale is possible with the addition of dopants to inhibit particle and crystal growth and consequently improve selectivity [Xu et al., 1992; Righettoni et al., 2015; Tricoli et al., 2008; Wang et al., 2008]. This idea is further supported by Righettoni et al. who found that doping WO₃ with Cr- or Si- using flame aerosol synthesis significantly increased selectivity to acetone [Righettoni et al., 2012].

Using an array to combine various sensors is a common method for overcoming the limitations in the selectivity of individual sensors. Each sensor can be designed to have a different response to each gas in a sample and a mathematical signal analysis of these separate responses can enable an alternate means of analysing complex gas mixtures [Lourenco et al., 2014]. Multiplexing these sensors into an array increases orthogonality³ and hence improves the ability to distinguish between gases. In fact, one such array which consisted of Si-doped WO₃, Ti-doped ZnO, and Si-doped MoO₃ sensors together with RH and CO₂ sensors detected concentrations of acetone with unprecedented precision; down to 21 ppb [Güntner et al., 2018]. Therefore, these sensor arrays have great potential to overcome the selectivity limitations of single sensors. The major limitation associated with arrays is the substantial power consumption involved.

² **Exogenous:** growing or originating from outside an organism

³ **Orthogonality:** the accuracy of a response to an analyte.

Another approach to increasing selectivity is to introduce filters above the sensing layer, to modify the gas composition reaching the sensing element such that interfering gases are removed. Limitations of using filters include an increased cost and complexity of the system, a potential reduction in sensitivity, increased response and recovery time and potential degradation of the filter material during operation [Lourenco et al., 2014]. Nevertheless, this idea of filtration has been tested and found to be very successful [Güntner et al., 2019] and recently, microporous materials known as metal-organic frameworks (MOFs) have been found to be particularly effective for this application. MOFs will be further discussed in Section 2.

1.3 Acetone Sensing and Diabetic Ketoacidosis

Acetone is one of the major VOCs found in the breath. Measuring the concentration levels of acetone present in exhaled breath facilitates the diagnosis and monitoring of diseases such as type 1 diabetes and more specifically, diabetic ketoacidosis (DKA). DKA is a life-threatening complication of type 1 diabetes developed due to the excessive levels of ketones in the blood, and acetone is an example of a ketone [Saasa et al., 2018; Lourenco et al., 2014]. Generally, the management of DKA is poor as patients respond to the condition on an emergency basis when symptoms arise. This is largely due to the invasive, inconvenient manner of monitoring ketone levels; patients must prick themselves approximately 4 times each hour to get stable readings [Saasa et al., 2018]. Alternatively, a Continuous Glucose Monitor (CGM) can be used to get instantaneous readings of ketone levels in the blood. Due to lacking affordability of the product, however, patients are often deterred from this solution. Considering type 1 diabetes affects almost 5% of the Australian population with a growing patient pool, there is an increasing need for new non-invasive and affordable technologies to help in the management of the disease [AIHW, 2019].

Numerous studies have found a positive correlation between high concentrations of acetone in the breath and an increased risk of suffering from DKA [Turner et al., 2009; Minh et al., 2011]. In particular, acetone concentrations in the breath of a healthy human can vary anywhere from 0.15 to 2.7 ppm [Turner et al., 2006] while acetone concentrations can get as high as 1250 ppm for those suffering from DKA [Anderson, 2015]. Therefore, SMOs offer an attractive solution, that is both non-invasive and affordable, solving both limitations of the current methods mentioned above [Lourenco et al., 2014; Nejentsev et al., 2007; Noble et al., 2002]. In regards to the standard of current acetone sensing, one study found that 1 ppm of acetone could be detected in the background of other VOCs present in normal breath using a nanosized gamma iron sesquioxide (γ -Fe₂O₃) sensor [Chakraborty et al., 2008]; however, higher selectivity is necessary to detect acetone in the sub-ppm range. This can be achieved by utilising the gas separation properties of MOFs which will be thoroughly explored in the next section.

Section 2: Introduction to Metal-Organic Frameworks

MOFs are a group of porous, organic-inorganic hybrid crystalline materials with large specific surface areas, which offer more unique structural diversity than most other porous materials. This has led to the application of MOFs in high capacity storage of H₂, water filtration, catalysis, photovoltaics and in relation to this paper, gas separation [Koo et al., 2019; Zhou et al., 2012]. They consist of a one-, two- or three-dimensional network of secondary building units (SBUs) – typically metal ions or clusters coordinated by oxygen or nitrogen – held in place by various organic molecules [Butova et al., 2016]. The SBUs act as the nodes that are linked together by the organic molecules which act as edges. This pattern repeats, forming a cage-like structure [Li et al., 2012]. Different combinations of metals and organic ligands will create different

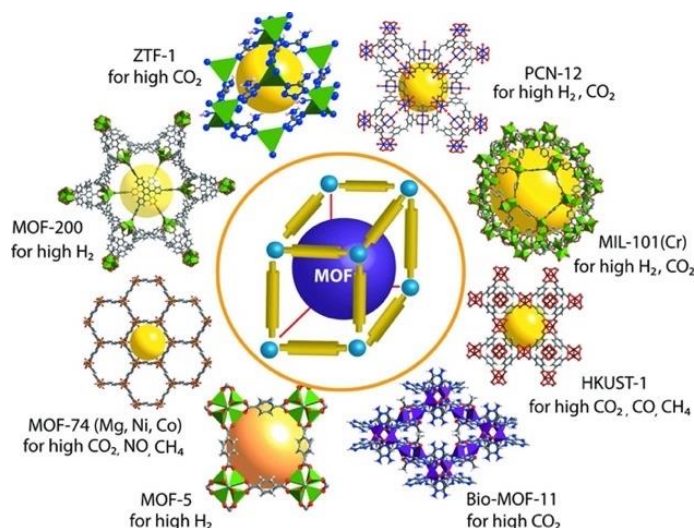


Figure 3 - Diversity in morphology of MOFs [GalusAustralis, 2020]

MOFs. For example, combining zinc nitrate ($\text{Zn}(\text{NO}_3)_2$) and 2-Methylimidazole ($\text{CH}_3\text{C}_3\text{H}_2\text{N}_2\text{H}$) as a metal salt and organic linker respectively will result in the formation of Zeolitic Imidazolate Framework (ZIF) 8, a popular design in MOF technology.

MOFs have many compelling features such as extremely high porosity - meaning they have up to 90% free volume; an extraordinary degree of variability in their structure such as tuneable pore size; and flexibility in both network geometry and chemical functionality. Figure 3 depicts a number of different MOFs, which portrays the extreme versatility in the network geometries that can be achieved in MOF membranes. Furthermore, since MOFs are formed through the covalent and dipole interactions between metal nodes and organic ligands, they are quite chemically and thermally stable [Li et al., 2012]. The most prominent of these properties, however, is their extraordinarily large internal surface area. Research has shown that MOFs have the highest surface area of known materials [Wei et al., 2013], internal surface areas as great as 7000m²/g [Farha et al., 2012]. This is far greater than that of materials such as graphene used competitively for similar applications, which have maximum theoretical specific surface areas of 2360m²/g [Zhang et al., 2020]. The combination of all these features enables substantial tunability of adsorption selectivity. In particular the pore size is controlled by the carbon chain length of the organic linker whereas the chemical properties of the pores are determined by the use of different substituents and functional groups into the organic linker [Butova et al., 2016].

2.1 Metal-Organic Frameworks as Selective Filtration Membranes

MOFs have been investigated deeply in the field of chemical gas sensors, and are applicable in 3 sub-areas: (1) the development of pure MOFs as a new generation of chemiresistive sensing materials, (2) the use of MOFs as sacrificial templates to, once more, form new sensing materials and finally, (3) exploiting the unique gas adsorption characteristic of MOFs to form selective filtration membranes on top of conventional sensing materials [Koo et al., 2019]. While the first two applications do offer ways to improve selectivity, the focus of this research is in the last application of selective membrane filtration. The general idea of this application is to combine the high sensitivity of nanostructure SMOs with the high selectivity of MOF membranes into a single SMO@MOF material that selectively ushers target analytes and rejects confounding gases from reaching the sensing layer [Yao et al., 2016].

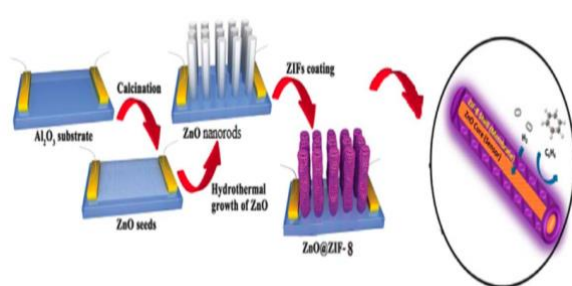


Figure 4 – Mechanism diagram of ZnO@ZIF-8 gas sensor [Khudiar et al., 2020]

MOFs have an excess of active sites such as metal nodes and functional groups in ligands [Koo et al., 2019] that enable gas molecules to be easily adsorbed. The diffusion of gas molecules through the MOF membrane is determined by physical and chemical parameters such as molar adsorption potential,

kinetic diameters of molecules and the pore size of MOFs [Koo et al., 2019; Haghighi et al., 2019]. By specifically synthesising MOFs with consideration to these characteristics, a target analyte can be selectively separated from other confounding molecules in a sample as shown in Figure 4, where C_6H_6 is filtered out while H_2 is allowed to pass through the membrane. This presents the most likely solution to achieving the selectivity needed in acetone-specific SMOs to enable commercialisation.

2.2 Motivation of My Research

Before acetone-specific SMOs may be transferred from a laboratory-based device into clinical practice, many issues must be addressed; primarily the need to improve their selectivity [Güntner et al., 2019]. With advances in nanotechnology, there are many methods to systematically tailor the selectivity of a SMO such as: changing their composition (morphology), using dopants, combining different selective sensors into an array and finally, using microporous filters known as MOFs. My research will present the latest advancements in the application of MOFs as filtration membranes for SMOs and provide recommendations for future experimental work that may potentially enable greater sensor selectivity towards acetone.

Section 3: Application of Metal Organic Frameworks in Current Breath Sensors

The MOFs that will be investigated in this section primarily include: ZIF-8, ZIF-71, ZIF-67, ZIF-CoZn and HKUST-1. Note; the following studies are not all primed towards acetone sensing, albeit, there are interesting findings from each of the presented papers that may be analysed and applied towards acetone sensing.

3.1 ZIF-8

Zeolitic Imidazolate Frameworks (ZIFs) are a class of MOF that consists of zinc and cobalt metal ions, surrounded by tetrahedra made of nitrogen atoms which are connected by imidazolate organic linkers [Zhou et al., 2018]. ZIFs are the most popular type of MOF under current investigation, due to their high thermal and chemical stability, and inherently high surface area properties [Jafari et al., 2019]. Various ZIF's will be explored as part of this research.

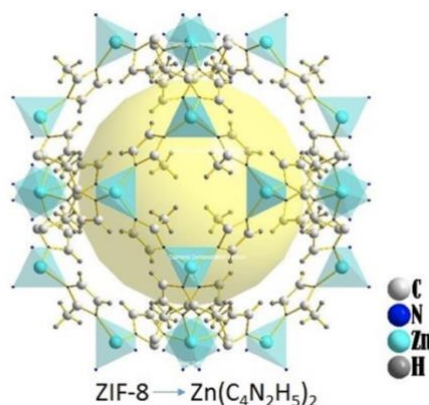


Figure 5 – Structure of ZIF-8 [Matatagui et al., 2017]

ZIF-8 is the most popular of the ZIF family of MOFs. It forms a SOD zeolite-type structure which is composed of $\text{Zn}(\text{2-methylimidazole})_2$ and has a small aperture diameter ranging from 3.4\AA to 4.0\AA and a large aperture diameter of 11.6\AA (Figure 5 and Figure 6). The membrane thickness of ZIF-8 is between 70-100nm [Zhou et al., 2018] and the structure typically has a surface area of up to $1900\text{m}^2/\text{g}$ [Wei, 2013]. Another important characteristic of ZIF-8 is the structural flexibility of its “gate openings”, which occurs as a result of $-\text{CH}_3$ and imidazolate linkers swinging. This mechanism ultimately facilitates the diffusion of gas through the membrane [Jafari et al., 2019]. The addition of ZIF-8 as a filtration membrane to the sensing layer increases the density of pores, the overall surface area and the number of active metal sites, enabling enhanced gas diffusion. Since the relative humidity of exhaled breath is upward of 80%, fluctuations in humidity poses a significant hindrance to sensor performance. Therefore, the hydrophobicity of ZIF-8 due to the non-polar nature of its apertures boasts its ability to be used in breath sensing while maintaining insensitivity to humidity fluctuations [Jafari et al., 2019].

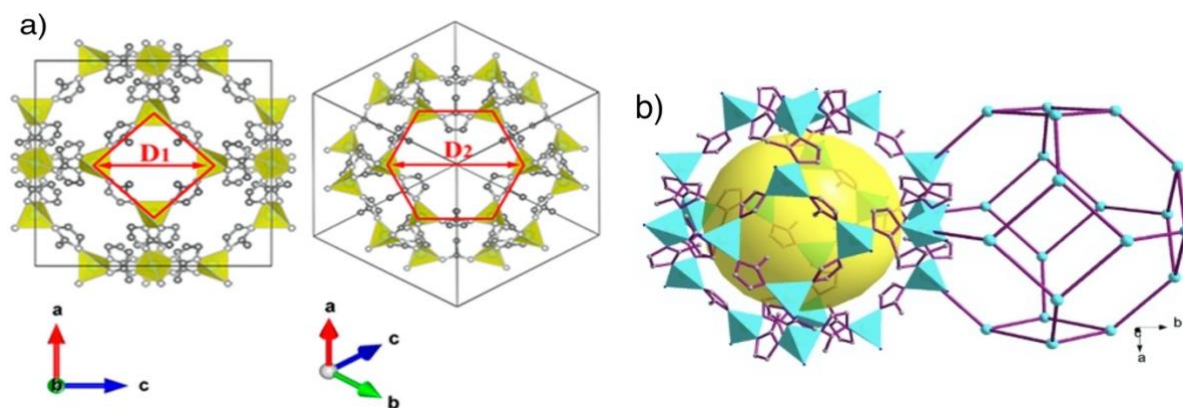


Figure 6 – a) visual representation of how a small and large aperture size integrates into a single MOF structure, b) 3D isometric view of small and large apertures [Tian et al., 2016]

3.1.1 Research by Tian et al. (2016)

Tian et al. synthesised ZnO nanorods coated with a layer of ZIF-8 and found that this material improved the selectivity of the sensor towards formaldehyde when compared to acetone, ethanol, methanol, ammonia and toluene [Tian et al., 2016]. Formaldehyde has a kinetic diameter of 3.73\AA (Appendix B) which is approximately the same as the pore size of ZIF-8. This enables the formaldehyde to pass through while the other VOCs in this experiment had kinetic diameters larger than that of the ZIF-8 pore size, causing them to be effectively filtered out by the membrane. An exception to this was that ammonia, which has a smaller kinetic diameter than the ZIF-8 pore size, did not pose a strong response. This was concluded to be a result of the low chemical affinity of the ZIF-8 layer to ammonia. There was no discussion on what exactly about the ZIF-8 layer was the cause for the low affinity between the ZIF-8 membrane and ammonia; hence, this is a point for future exploration.

3.1.2 Research by Drobek et al. (2016), Khudiar et al. (2020) & Jafari et al., (2016)

Drobek et al. and Khudiar et al. found that ZnO@ZIF-8 nanowires could drastically improve cross sensitivity of hydrogen when compared to benzene and toluene due to the smaller kinetic diameter of hydrogen compared to benzene and toluene (Appendix B) [Drobek et al., 2016; Khudiar et al., 2020]. Jafari et al. produced a nanocomposite of ZIF-8 using multi-walled carbon nanotubes (MWCNTs) and silver nanoparticles (AgNPs). They found when testing the cross-sensitivity of ethanol, methanol, acetone, acetonitrile and n-hexane using their ZIF-8/MWCNT/AgNP sensing nanomaterial, ethanol and methanol produced the greatest response. It is worth noting that this study investigated the aforementioned VOCs in liquid form which decreases the applicability of these findings to the purpose of the current research. Nevertheless, the unique nanostructure used was not found to have been previously synthesised and so, may be a point of exploration for future research on improving gas selectivity through MOFs.

For all three of these studies, the major explanation for the observed selectivity is the filtration effect of the pore size of the MOFs similar to that of Tian et al.'s findings. Therefore, the idea that utilising the pore size of the nanostructured MOF-metal oxide materials as an effective way of providing spatial confinement to limit the diffusion of interfering gases through the membrane is highly supported by a plethora of studies [Wu et al., 2017]. When considering the applicability of these findings to acetone sensing, a limitation arises given that all interfering gases in these studies had a larger molecular size than both the target analyte and the pore size of the ZIF-8 layer. Acetone has a midrange kinetic diameter of 4.60\AA , meaning there are many interfering VOCs in exhaled breath that are smaller in size than acetone such as nitrogen and carbon dioxide (Appendix B). This suggests that pore size filtration of molecules larger than acetone will not be enough to achieve the required selectivity. Therefore, physical properties of the MOF layer alone are likely not enough and there is a need to take into consideration chemical properties of the MOF as a means of repelling other gases or inversely, attracting acetone to the MOF membrane.

3.1.3 Research by Tian et al. (2020)



Figure 7 – SEM image of ZnO@ZIF-8 hollow nanofibers [Tian et al., 2020]

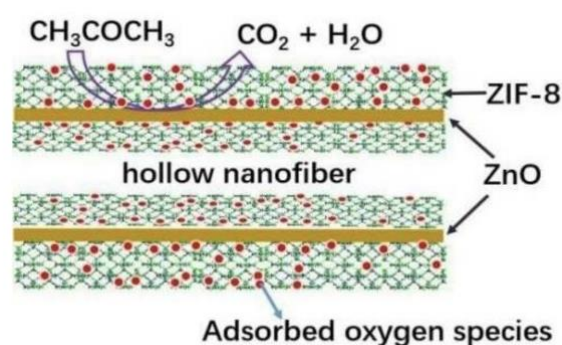


Figure 8 – Schematic illustration of sensing mechanism of ZnO@ZIF-8 hollow nanomaterial [Tian et al., 2020]

Tian et al. aimed to develop a new hollow nanofiber structure by coating ZIF-8 onto the inner and outer surface of ZnO hollow fibers to improve selectivity of ZnO based SMOs to acetone (Figure 7 and Figure 8). They synthesised their ZnO@ZIF-8 nanomaterial by calcining electrospun $\text{Zn}(\text{AC})_2$ fibers at 650°C for 2 hours and then combining the resulting ZnO hollow fibers with 2-methylimidazole. It was found that for the range of gases tested - acetone, hydrogen, methanol, formaldehyde, toluene and ammonia - the sensor exhibited the greatest cross sensitivity towards acetone; approximately 0.542 ppm^{-1} . This selectivity towards acetone may be primarily attributed to the oriented growth of the ZIF-8 layer along the (211) plane on the ZnO fibers. The acetone sensitivity of a nanostructure with (110) reflection was compared to that with a (211) reflection, and it was found that the latter showed a higher acetone response.

At an operating temperature of 263°C, the sensor response was 60 at an acetone concentration of 100 ppm. This is a substantial improvement from the initial response of 9.6 from the pure ZnO material, and also a drastic improvement in comparison to similar work by other studies [Tian et al., 2020]. This can be attributed to the increased permeability on both sides of the hollow fibers due to the ZIF-8 coating. The study also investigated controlled experiments to determine how significant the hollow morphology was for sensing performance. It was found that a non-hollow structured ZnO@ZIF-8 sensor had an optimal response of 34 at 312°C. This result was 43.3% worse than a hollow nanostructure's optimal response of 60 at 263°C, and also required higher operating temperatures to achieve it. This emphasises the significance of the morphology of the sensing layer. By having hollow nanofibers, they are able to essentially double the surface area for which the sensor can make readings which suggests there is a need for further work to be done on sensing layers adopting a hollow morphology.

3.1.4 Research by Ren et al. (2019)

Ren et al. synthesised a ZnO@ZIF-8 core-shell microsphere nanomaterial and tested the cross sensitivity of acetone, ammonia, carbon monoxide, hydrogen, ethanol and sulphur dioxide to the sensor. It was found that ethanol posed a significantly higher response than the other test gases due to its strong chemical affinity to the ZIF-8 membrane (Figure 9). Interestingly, the dominant mechanism in determining the sensitivity of gases to the material in this study was the affinity as opposed to the physical size of the molecule in relation to the aperture of the ZIF-8 framework. There was no discussion, however, on the specificities of the ZIF-8 membrane that may have caused this affinity, which is a gap in the literature that requires further experimental research. Furthermore, there was a clear distinction between the level of acetone and ethanol detected which is a remarkable finding since distinguishing between acetone and ethanol is one of the major issues in acetone sensing, as they are physically and chemically very similar compounds [Güntner et al., 2019]. These findings suggest that there is a need for future research to explore the synthesis procedure, chosen morphology of the metal oxide, and the operating conditions of this study, by replicating it with slight alterations, in order to discern what is so unique about this particular nanomaterial that enabled it to distinguish between acetone and ethanol.

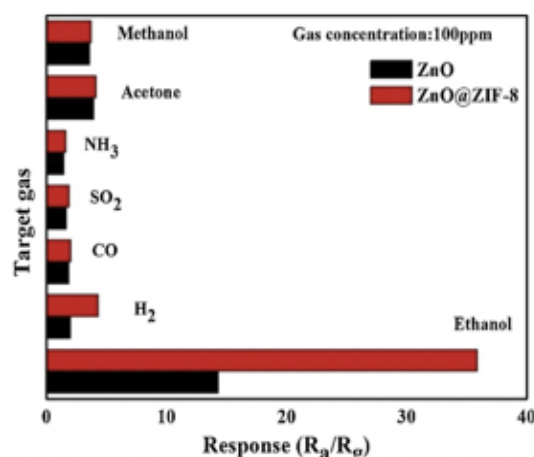


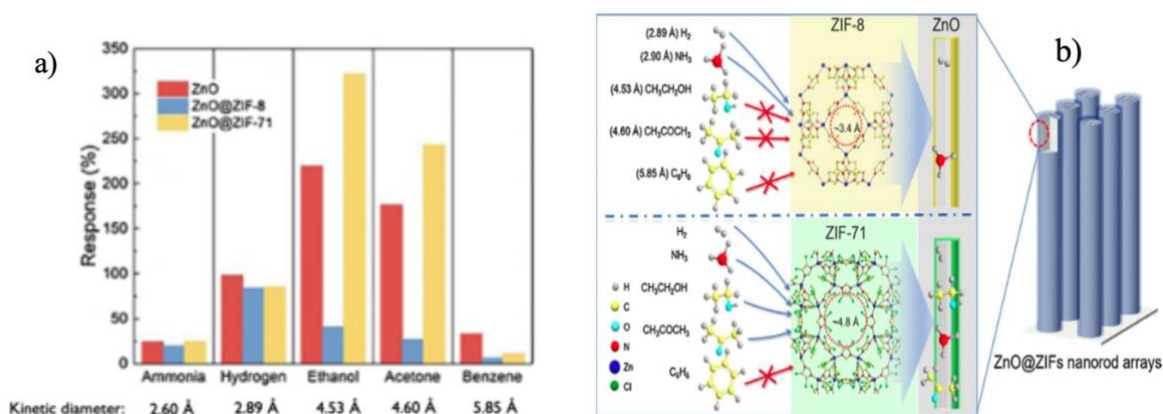
Figure 9 – Cross sensitivity of ZnO microspheres and ZnO@ZIF-8 microspheres to various gases at 100ppm concentration

Based on this study, it may be concluded that the chemical composition of the target analyte contributes significantly to design choices around which MOF layer will induce the strongest analyte-MOF interaction. For example, carbon dioxide will mainly experience electrostatic interactions with MOFs due to its strong quadrupolar effect. The MOFs ability to interact electrostatically in this way is determined by its pore structure. On the contrary, for methane, the main mode of interaction with a MOF membrane is through the dispersion potential of the gas, and the MOFs ability to interact in this way is determined by its active sites [Ren et al., 2019].

3.2 ZIF-71

ZIF-71 forms a RHO zeolite-code structure which is composed of $\text{Zn}(4,5\text{-dichloroimidazole})_2$ and has a small aperture diameter ranging from 4.8\AA to 5.4\AA and a large aperture diameter of 16.8\AA . The membrane thickness of ZIF-71 is approximately 50nm [Zhou et al., 2018]. Similar to ZIF-8, ZIF-71 also demonstrates a strong insensitivity to humidity fluctuations.

3.2.1 Research by Zhou et al. (2018)



Zhou et al. found that when comparing three sensing materials - pure ZnO nanorods, ZnO@ZIF-8 nanorods and ZnO@ZIF-71 nanorods - ZnO@ZIF-71 had a higher response to ethanol and acetone than both the pure ZnO nanorods and the ZnO@ZIF-8 nanorods (Figure 10a). The accessibility of ammonia and hydrogen through both SMO@MOF composites and the inaccessibility of benzene through both composites demonstrates the previously discussed physical filtration effect of the MOF, seeing as ammonia and hydrogen are both smaller than the pore size and benzene is larger than the pore size (Figure 10b). It was concluded that the selectivity towards acetone and ethanol was most likely caused by the similarity between the kinetic diameter of ethanol and acetone, which are 4.53\AA and 4.60\AA respectively, and the pore

size of the small cavities in the ZIF-71 membrane which ranges between 4.8Å and 5.4Å. The listed gases in Figure 10a are presented in order of smallest to largest kinetic diameter and it is evident that as the similarity of the pore size and the kinetic diameter of a gas increases, the sensor response also generally increases. Therefore, it may be concluded that the gas adsorption selectivity of gas sensors towards molecules with midranges kinetic diameters such as acetone, may be enhanced by modifying the pore size of MOFs to match that of the target molecule. A subsequent complication arises however, when the kinetic diameter of the target molecule is similar to that of interfering gases. For example, in the case of acetone and ethanol - using this proposed strategy of pore size screening is ineffective as acetone and ethanol have kinetic diameters that vary by 0.07Å. Thus, there is a need for other properties of MOFs to be exploited in order to achieve ideal selectivity towards a target analyte, as mentioned.

3.2.2 Research by Zhou et al. (2019)

Zhou et al. explored the ways in which a ZnO@ZIF-71 nanorod material would react to acetone and ethanol and conducted a thorough study into other important characteristics of the breath sensor that are modified by the incorporation of the ZIF-71 layer. This was a follow-on study from Zhou et al.'s 2018 paper. They found that the sensor, once modified with ZIF-71, demonstrated a higher response to ethanol over acetone. It was also found that the sensor could operate at lower operating temperatures (150°C) and had a lower detection limit of 3ppb for acetone when compared to the pure ZnO material. The range of humidity values tested in the study was 20 - 80% relative humidity and the CV values for ethanol and acetone respectively were 4.49% and 5.02%, which are both relatively low.

The response and recovery times of the sensor were also improved through the use of the ZIF-71 membrane. The response and recovery time decreased by 40% and 31% respectively (Appendix C). Given the increase in the specific surface area of the sensor as a result of the ZIF-71 incorporation, more gas molecules are adsorbed and hence the sensitivity of the sensor to acetone was improved from 4.44 ppm⁻¹ to 7.33 ppm⁻¹. The major contributing factor to both of these results was that the ZIF coating guided adsorbed gas molecules to the sensing layer which increased the likelihood of contact between the gas and the sensing layer needed for a response to be detected. This induced both a higher sensitivity and response/recovery time.

Furthermore, the DFT simulation involved the calculation of the adsorption energies between adsorbates and ZIF-71, which is an estimation of the potential interaction energy that exists between organic molecules. This was determined using the following equation, and other complex mathematical processes that are not relevant for the scope of this project.

$$E_{ads} = E_{complex} - (E_{ZIF-71} + E_{adsorbate}) \quad (3)$$

It was found that ethanol-1, acetone-1 and acetone-3 have negative values for E_{ads} which indicates that both acetone and ethanol may be adsorbed onto the structure of ZIF-71. Since ZIF-71 had larger adsorption energies for ethanol as opposed to acetone (Appendix D), it would be expected that the sensor response to ethanol would be enhanced when compared to acetone and this was evident in the results.

The increased number of open Zn^{2+} metal sites present in the structure of ZIF-71 partially explain the results as they increased the interactions of the ZIF-71 framework with ethanol and acetone. These metal sites are charge-dense binding sites that interact strongly with molecules with great polarisability such as acetone and ethanol [Zhang et al., 2013]. This presents another mode of tuning the selectivity towards acetone.

Ultimately, this paper demonstrates the overall strength of their $ZnO@ZIF-71$ nanorod sensor for acetone and ethanol sensing as they achieved a very high response, quick response/recovery times, and insensitivity to humidity fluctuations. However, there is still a need to improve the ability of sensors to distinguish between acetone and ethanol.

3.3 ZIF-67

ZIF-67 is composed of Co^{2+} cations as SBUs and a 2-methylimidazole ligand. ZIF-67 has a three-dimensional zeolite-like structure with SOD topology and has a specific surface area of $1832.2\text{m}^2\text{g}^{-1}$ (Figure 11) [Chen et al., 2014]. It also has a high thermal stability as the framework is stable at temperatures of up to 260°C in normal air.

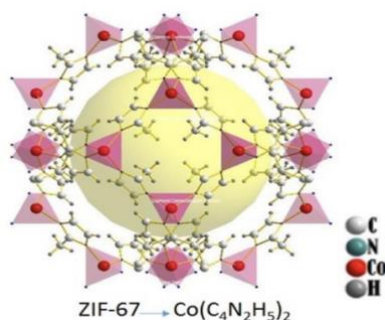


Figure 11 – Structure of ZIF-67 [Matatagui et al., 2017]

3.3.1 Research by Matatagui et al. (2017)

Matatagui et al. explored how combining ZIF-8 and ZIF-67 in a single sensing device would affect the sensor response to hydrogen gas and found that there was a much stronger response towards hydrogen when using both MOFs in unison as opposed to ZIF-67 on its own; the former being 4.5 times larger than the latter. There were, however, many lacking details in this paper with regards to the synthesis process and the procedure used for analysis, suggesting that further research is required to ensure the reproducibility and reliability of these findings.

3.3.2 Research by Kwon et al. (2015)

Kwon et al. designed a ZIF-67 polycrystalline membrane grown on top of a ZIF-8 sensing layer through a newer modification method known as heteroepitaxial growth. Heteroepitaxial growth is an approach for modifying MOFs that combines different crystalline systems via molecule-level connections. This enables the favourable properties of materials to be combined without sacrificing the intrinsic features of the individual crystals which is unlike other MOF modification techniques such as metal/ligand exchange [Kwon et al., 2015]. With this technique, the first intergrown membrane of ZIF-67 grown on ZIF-8 seeds was achieved. That is, a ZIF-8@ZIF-67 nanomaterial as well as a ZIF-8@ZIF-67@ZIF-8 nanomaterial. Evidently, this involved using the MOF material as both the sensing material as well as using it as a filtration membrane. The nanomaterials were used to perform gas separation experiments on propylene/propane mixtures in ambient conditions. Given the chemical similarity between propylene and propane, not to mention that their kinetic diameters vary by only 0.20Å, separating these gases poses a significant challenge to researchers. The ZIF-8@ZIF-67 material demonstrated a strong propylene/propane separation capability. With the incorporation of another layer of ZIF-8, the ZIF-8@ZIF-67@ZIF-8 material showed even higher separation capabilities, with a separation factor of approximately 200. This was a result of the reduced membrane thickness as well as the enhanced grain boundary structure from adding the ZIF-8 overlay. This effect is not specific to ZIF-8 overlays as using ZIF-67 as the overlay on a ZIF-67 membrane produced an enhanced separation factor as well, although it was not as large as that from the ZIF-8 overlay. Interestingly however, overlaying a ZIF-8 membrane with either ZIF-8 or ZIF-67 did not yield a significant result in comparison to using ZIF-67 as the primary membrane. It was also found that the presence of a methanol cosolvent in the growth solution for forming the ZIF-67 membrane was responsible for decreasing the membrane thickness as well as enhancing the reproducibility of the material. These results may be redirected towards separating acetone and ethanol seeing as they share a similar relationship to that of propylene and propane. Therefore, future research should investigate how these nanomaterials perform when distinguishing between ethanol and acetone.

3.3.3 Research by D'Mello et al. (2018)

D'Mello et al. investigated a SnO₂ nanoparticle encapsulated in a ZIF-67 membrane to assess the selectivity to carbon dioxide. The SnO₂@ZIF-67 nanomaterial demonstrated a response that was twice that of the pure SnO₂ nanoparticles. While there was no discussion on the cross sensitivity of the sensor in relation to gases besides carbon dioxide, this study provides a successfully synthesised SMO@MOF combination of SnO₂ with ZIF-67 that should be explored in future research since there are not many similar studies that used the same nanomaterial to explore selectivity towards acetone [Koo et al., 2019].

3.4 ZIF-CoZn

ZIF-CoZn is a bimetallic MOF which benefits from the strengths of both ZIF-8 and ZIF-67, where the metal nodes are made of both zinc (Zn) and cobalt (Co). The zinc metal nodes provide thermal stability and hydrophobicity while the cobalt enables excellent thermal catalytic ability. The crystal structure of the material is isostructural to ZIF-8 and ZIF-67 [Koo et al., 2019; Jian et al., 2020].

3.4.1 Research by Yao et al. (2016)

Yao et al. formed a pure ZnO, a ZnO@ZIF-8 and a ZnO@ZIF-CoZn nanowire material to assess the sensitivity and selectivity of the material toward acetone under various humidity conditions. Water vapour is the major interfering gas molecule found in exhaled breath and so, this paper's exploration into the direct interaction between acetone and water vapour in a gas sensor is very useful. By altering the precursor (2-methylimidazole) concentration, various thicknesses of the ZIF frameworks were synthesised and investigated between the range of 5–100 nm (Figure 12).

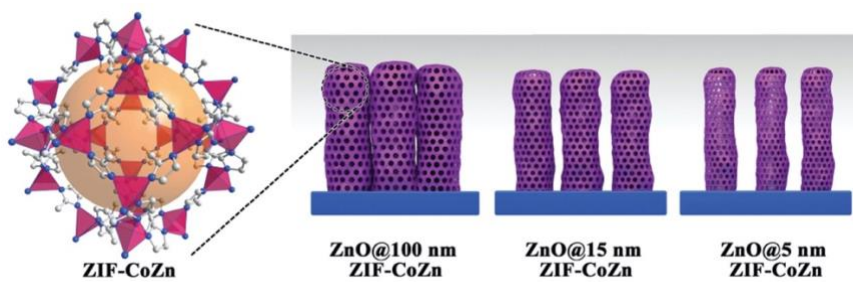


Figure 12 – Visual representation of varying thicknesses of ZIF-CoZn membrane [Yao et al., 2016]

When compared with ZnO and ZnO@ZIF-8, ZIF-CoZn has better sensitivity to acetone - the response was enhanced by almost 20 times. It was also found to be able to work at lower temperatures than the other two materials. Furthermore, there was a CV rating of 7.4% for a relative humidity range of 0% to 90% which is a strong result. The response and recovery time

were both decreased by 48% and 470%, respectively and improved response and stability was also observed, all as a result of the excellent catalytic property of the Co_2+ in ZIF-CoZn which can activate oxygen molecules from the air to accelerate the oxidation of acetone. Moreover, it was concluded that decreasing the thickness of the MOF layer from 100nm to 5nm directly correlated with increased cross sensitivity towards acetone. Therefore, it may be concluded that the thickness of a MOF layer may contribute to increased selectivity towards acetone. Figure 13 shows an image from the supporting information document of the study, which suggests that they did explore how other gases interact with the synthesised MOF; however, there was no discussion provided to explain these results which is a limitation that should be build off in future experimental research. It was evident, nonetheless, that the sensor was most selective towards acetone which is a promising result. Ultimately, the paper presents promising findings for highly sensitive and selective acetone sensing in the presence of water vapour.

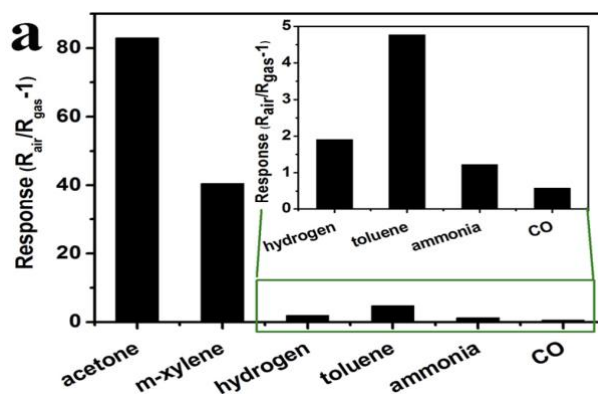


Figure 13 – Cross sensitivity of ZnO@ZIF-CoZn to various gases [Yao et al., 2016]

3.5 HKUST-1

The HKUST-1 framework is composed of copper (II) “paddle wheel” cations as SBUs and benzene-1,3,5-tricarboxylate (BTC) ligand molecules [Van Assche et al., 2014]. It has one of the highest densities of metal sites with a multi-cage porous network that consists of two large cages and one small cage (Figure 14). The small cage (S1) is formed by four BTC linkers and has an opening diameter of 4.5Å [Van Assche et al., 2014; Chevalier et al., 2019]. The large cages, L2 and L3, both have an opening diameter of approximately 9Å and internal diameters of 13.2Å and 11.1Å respectively. They are oriented in an alternative fashion around S1 pockets and the only difference between them is that L3 cages contain all the free Cu_{2+} metal sites, while L2 has none (Figure 14) [Van Assche et al., 2014].

3.5.1 Research by Chevalier et al. (2019)

Chevalier et al. developed a HKUST-1 sensing nanomaterial and explored the cross sensitivity of the material to toluene, o-Xylene, ethanol, acetone and acetaldehyde under realistic indoor air conditions. Unlike any other previous research, experiments were conducted in both mono-pollutant and multi-pollutant mixtures of the aforementioned gases in order to assess its behaviour in realistic conditions (i.e. in the presence of a mixture of pollutants).

The adsorption capacity at saturation (C_{ads}), which is the mass of adsorbed VOC per unit weight of adsorbent (m_{ads}), was defined as follows:

$$C_{ads} = \frac{Q \cdot \int_{t_i}^{t_f} (C_{in}(t) - C_{out}(t)) dt}{m_{ads}}$$

Where Q is the total flow rate, C_{in} and C_{out} are the concentrations at the inlet and the outlet of the adsorption column respectively, t_i is the time when the pollutant is introduced and t_f is the time when saturation is reached.

It was found that the adsorption capacities for toluene, o-xylene, ethanol, acetone and acetaldehyde under mono-pollutant conditions were 23.8, 14.7, 16.5, 5.0 and 1.4wt% respectively which was concluded to be largely a result of chemical properties of the gases, such as the boiling point and polarity. A higher boiling point enables easier adsorption of gases by the HKUST-1 layer, due to the stronger intermolecular forces that exist between them. There was an exception, however, in that the absorption of o-xylene under mono-pollutant conditions was lower than expected given its very high boiling point which suggests that there were also physical properties contributing to the adsorption capacities.

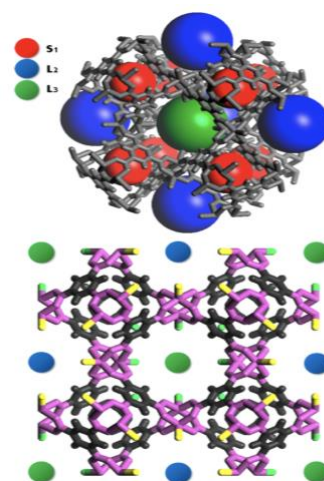


Figure 14 – (Top) HKUST-1 structure with cages S1, L2, and L3. (Bottom) From view of the upper panel showing the paddlewheel (purple) and free metal sites in the L3 cages pointing towards the lower plane (light green) and the upper plane (yellow) [Chevalier et al., 2019]

The competition mechanisms that existed in binary gas mixtures were also investigated. To do so, they developed a mathematical expression to represent the selectivity of the sensor to a binary gas mixture containing two compounds which is defined as follows:

$$\alpha_{A/B} = \frac{C_{ads,A} \cdot C_B}{C_{ads,B} \cdot C_A}$$

Where $\alpha_{A/B}$ is the selectivity of a mixture of two gases (A and B), $C_{ads,A}$ and $C_{ads,B}$ are the adsorption capacities of the compounds A and B respectively and C_A and C_B are the molar concentrations of the compounds respectively. If $\alpha_{A/B}$ has a value greater than 1, the framework is more selective towards compound A and for a value less than 1, compound B is preferred.

Three gas combinations were investigated: o-xylene/acetone, toluene/acetone and toluene/o-xylene with a concentration of 1.25 ppm of each gas injected into the sensing system. The

order of highest to lowest adsorbed VOC was o-xylene, acetone and toluene. The selectivity for each binary gas mixture may be seen in Table 1. Acetone was expected to fit into the small 4.5Å S1 pocket due to its smaller kinetic diameter (Appendix B), while the large molecules of o-xylene and toluene (Appendix B) were expected to migrate towards the larger apertures of the HKUST-1 framework [Terencio et al. 2013; Chevalier et al., 2019]. For the o-xylene/toluene comparison, the expected behaviour was observed and both gases were competitively adsorbed into the larger cages; however, due to higher boiling point and polarity of o-xylene in comparison to toluene, it was preferentially adsorbed by the HKUST-1 framework. This reveals an interesting characteristic about the adsorption mechanisms of MOFs being primarily driven by physical properties, followed by chemical properties.

For the o-xylene/acetone experiment, it was expected that o-xylene would dominate acetone in adsorption due to its kinetic diameter being more similar to that of the large pores. Nevertheless, the acetone was adsorbed into the side pockets as well as on the free metal sites inside the L3 pockets due to strong chemical interactions between Cu₂₊ metal ions and acetone, contributing to a very similar selectivity between the gases. Ultimately, the o-xylene was observed to be slightly more selective than acetone (Table 1). Finally, for the toluene/acetone experiments, a similar phenomenon was observed as in the o-xylene/acetone experiment; however, the affinity of acetone to the metal sites enabled it to have a greater selectivity than toluene.

Table 1: Selectivity in multi-gas experiments from Chevalier et al. (2019)

	o-Xylene (A) / Acetone (B)	Toluene (A) / Acetone (B)	Toluene (A) / o-Xylene (B)
Selectivity ($\alpha_{A/B}$)	2.0	0.7	9×10^{-4}

This paper investigated an area that very few papers have explored in the past; that is, the competition mechanisms that exist when sensing binary gas mixtures. It may be concluded that both the kinetic diameter, and the chemical properties of a gas can be equally important in the driving mechanism of the observed selectivities. The paper was also published in 2019, suggesting that these findings are not out of date and have scope to be further investigated. A limitation of this study, however, is that the sensor requires low RH levels to function correctly, which significantly decreases the applicability of these findings for the relevant application of breath analysis. Therefore, further research is needed to firstly increase the reliability of these findings since there are not many papers to support the findings of this one, and secondly, to identify ways of improving the sensors susceptibility to humidity fluctuations.

Section 4: Recommendations for Future Research

4.1 Discussion of Findings

In this section, general recommendations will be made for future experimental research based on the findings and gaps identified in the papers presented in Section 3. Recommendations specific to certain studies will generally not be discussed here as they were already discussed in Section 3, where more context was also provided. Nevertheless, we will categorise the different factors that were discovered to seemingly affect selectivity and discuss the general things that may be done in future research to explore these avenues.

4.1.1 Pore Size

The most common method for enhancing the selectivity of a sensor towards acetone is by manipulating the pore size of the MOF layers to physically limit the diffusion of interfering gases through the membrane. This idea is highly supported by a variety of studies [Drobek et al., 2016; Khudiar et al., 2020; Jafari et al., 2016]. All of these studies suggested that the smaller the kinetic diameter of a molecule, the more sensitive it will be to the sensor.

Contrastingly, Zhou et al. (2018) suggested that for molecule smaller than the pore size of the aperture of the MOF, the closer the kinetic diameter of the molecule was to the pore size, the higher the selectivity. That is, the biggest molecule that can fit through the pore will have the highest selectivity. This reveals an interesting contradiction between findings of various MOFs and should be a point of future research in order to determine whether either proposal holds any validity. Regardless, it is still ideal for pore apertures to be engineered to match the size of acetone because if it were any smaller, the acetone molecules would be unable to pass through and if it were any bigger, other larger confounding molecules would be allowed to pass through. In order to more closely evaluate the relationship between the pore size of the MOF membrane and the gases' kinetic diameter, gases with more marginal differences in kinetic diameters should be used for experimentation as opposed to the large differences in kinetic diameter in the gases used for most current studies.

4.1.2 Chemical Affinity

The boiling point and polarity of molecules were found to have an impact on the adsorption selectivity. A higher boiling point of a molecule will correspond to greater intermolecular forces between the molecule and the MOF layer [Chevalier et al., 2019]. Zhou et al. (2019) also found that the open metal sites present in the MOF structure were involved in increasing the interactions between the MOF layer and molecules with large. Acetone is one such

molecule with large polarisability, and so, this concept of exploiting the open metal sites of the MOF structure to enhance selectivity should be directly applied to acetone sensing. These metal sites can be manipulated by varying the ratio of H₂O or DMF in the solvent used during synthesis.

Finally, as mentioned, a pressing issue in acetone sensing is distinguishing between ethanol and acetone due to their chemical and physical similarity. Ren et al. (2019) found there was a clear distinction between the level of acetone and ethanol detected by their ZnO@ZIF-8 core-shell microsphere-based sensor which was attributed to the strong chemical affinity between the ZIF-8 membrane and ethanol. Future investigations should replicate this study to firstly ensure its reproducibility, but also to aim to identify the specific mechanism that enabled such a difference between the ethanol and acetone response. If this detail is identified, it may conversely allow for selectivity towards acetone over ethanol to be achieved.

4.1.3 Oriented Growth

It was also found that the oriented growth of the MOF layer can directly affect the selectivity towards acetone. Tian et al. (2020) found that the (211) reflection enabled greater selectivity towards acetone when compared to the (110) reflection. This is a remarkable finding seeing that it is directly applicable to future testing for acetone sensing. The orientation growth may be controlled in a similar way to how the number of metal sites are controlled; by manipulating the ratio of DMF and H₂O in the solvent used during synthesis. More specifically, increasing the concentration of H₂O in the solvent enabled the enhancement of the (211) reflection as opposed to the (110) reflection of the nanostructure. Future work should explore this idea and experimentally determine an ideal ratio to maximise acetone selectivity with consideration to both mechanisms that are affected by this ratio – number of open metal sites and oriented growth.

4.1.4 Combination of MOFs

The stacking of MOF layers on top of each other was found to be another interesting approach for enhancing acetone selectivity. Matatagui et al. (2017) in particular, found that adding a ZIF-67 layer on top of a ZIF-8 membrane enhanced selectivity towards hydrogen. The findings from this paper may potentially be used in unison with those of Tian et al. (2020) who found that a specially modified pore size of a ZIF-8 framework was highly selective towards acetone. Combining the ZIF-67 with Tian et al.'s particular ZIF-8 structure may allow for even fewer interfering gases to interact with the sensing layer.

4.1.5 Thickness of MOF Layer

Continuing from the idea of combining MOFs to enhance selectivity, Kwon et al.'s ZIF-8@ZIF-67@ZIF-8 nanomaterial showed unprecedentedly high propylene/propane separation capabilities which was a remarkable finding given the extreme similarity between the gases. This was a result of the reduced membrane thickness on top of the effect of combining MOFs. The study identified that the presence of a methanol cosolvent in the growth solution for forming the ZIF-67 membrane, decreased the membrane thickness. Therefore, future work should investigate how varying the methanol concentration in the solvent involved in synthesis affects MOF thickness and hence, the separation capability towards acetone and ethanol since they are also very difficult to separate. The findings of Yao et al. (2016) also support the conclusion that decreasing the thickness of a MOF layer may contribute to increased selectivity towards acetone.

Table 2 shows a summary of all the studies that were analysed as part of this research, which highlights the MOF property responsible for the selectivity observed in that study as well as the gases that were sensed.

4.2 General Recommendations

Ultimately, based on these findings about how altering the properties of the MOF can influence selectivity, a MOF should be synthesised in future work that is compliant with the following recommendations. A ZIF-8@ZIF-67@ZIF-8 nanomaterial should be produced, as done by Kwon et al., as stacking MOFs were found to enhance the propylene/propane separation capabilities. Note, this may not apply for acetone sensing which can be determined through experimentation. The pore size should be specially engineered to match the size of acetone molecules in accordance with Zhou et al.'s findings. It should be oriented on the (211) reflection with a maximum number of active metal sites present on its structure by optimising the ratio of DMF to H₂O in the solvent used for synthesis. Furthermore, the thickness should be minimised as much as possible, again by manipulating the ratio of DMF to H₂O. Finally, the hollow nanofiber adopted in Tian et al.'s 2020 study should be the chosen morphology of the sensing layer as this enabled the largest response to acetone of all the studied sensors.

It was clear that the ZnO@ZIF-71 nanorod material synthesised by Zhou et al. (2019) and the ZnO@ZIF-8 hollow nanomaterial synthesised by Tian et al. (2020) posed the greatest selectivity towards acetone specifically. Therefore, these two experiments in particular are strongly recommended to form the foundations for future work in acetone sensing.

Table 2: Summary of all MOFs analysed through this research

Note: the highlighted gases in the ‘Gases sensed’ column are the prominent gases that were sensed

MOF	Nanomaterial	Gases sensed	MOF Property Responsible for Selectivity	Results	Ref.
ZIF-8	ZnO@ZIF-8 nanorods	Hydrogen , benzene	Pore size	Small aperture allowed restriction of benzene.	Khudiar et al., 2020
	ZnO@ZIF-8 hollow nanofibers	Acetone , hydrogen, formaldehyde, methanol, toluene, ammonia	Orientation growth	Enhanced selectivity towards acetone over other gases due to orientation growth of ZIF-8 on ZnO.	Tian et al., 2020
	ZnO@ZIF-8 core-shell microspheres	Acetone, ammonia, carbon monoxide, hydrogen, ethanol , sulphur dioxide	Chemical affinity	Strong affinity of material to ethanol contributed to enhanced response.	Ren et al., 2019
	ZnO@ZIF-8 nanorods	Acetone, ethanol, methanol, formaldehyde , ammonia, toluene	Pore size + chemical affinity	Small diameter of formaldehyde allowed significant adsorption (4 times more than other VOCs)	Tian et al., 2016
	ZnO@ZIF-8 nanowires	Benzene, hydrogen , toluene	Pore size	Enhanced selectivity for H ₂ at 300C	Drobek et al., 2016
	ZnO@ZIF-8/MWCNT/Ag NPs cubic nanostructure	Ethanol , methanol , acetone, acetonitrile, n-hexane	Pore size + unique sensing layer morphology	Small pore size is a large contribution to this. This paper used liquid VOCs as opposed to gas VOCs, however, the unique nanostructure used may be explored by future papers.	Jafari et al., 2019
ZIF-71	ZnO@ZIF-71 nanorods	Ammonia, hydrogen, acetone , ethanol , benzene	Pore size	The similarity in pore size between acetone, ethanol and the ZIF-71 layer enabled enhanced selectivity towards these gases over the other gases. big things are more likely to interact with the MOF layer	Zhou et al., 2018
	ZnO@ZIF-71 nanorods	Ethanol , acetone, water vapor	Pore size + chemical affinity	The increase of active open metal sites enabled a stronger chemical affinity to ethanol and acetone	Zhou et al., 2019
ZIF-67	ZIF-8@ZIF-67	Hydrogen	Composition of 2 MOFs	Increased sensitivity through combination of MOFs	Matatagui et al., 2017
	ZIF-8@ZIF-67 & ZIF-8@ZIF-67@ZIF-8	Propylene, propane	MOF thickness + composition of 2 MOFs	Stacking MOFs was found to increase propylene/propane separation capabilities .	Kwon et al., 2015
	SnO ₂ @ZIF-67	Carbon dioxide	Unique sensing layer morphology	Presents a unique SMO@MOF combination for future study	D’Mello et al., 2018
ZIF-CoZn	ZnO@ZIF-CoZn	Acetone , water vapor	Thickness of MOF	Decreasing thickness of membrane from 100nm to 5nm increased selectivity to acetone	Yao et al., 2016
HKUST-1	HKUST-1 nanomaterial	Toluene, o-xylene , ethanol, acetone, acetaldehyde	Pore size + chemical affinity	High boiling point was correlated with stronger selectivity. Explored unprecedented binary gas mixture experiments.	Chevalier et al., 2019

Section 5: Future Work

Many avenues for future work related to improving selectivity by utilising MOF technology have already been discussed as part of Section 4. Albeit, there are other important findings that came as a result of this research which revolve less around improving selectivity and more around generally improving the overall quality of acetone sensors by utilising MOFs. This poses many routes for future investigation. For instance, Zhou et al. (2018) found that the ZIF-71 membrane on top of their ZnO sensing layer, aided in guiding adsorbed gas molecules to the sensing layer. This increased the likelihood of contact between the gases and the sensing layer, which induced both a higher sensitivity and response/recovery time. This result is not widely supported by other studies and so, there is lacking reliability with this result. Hence, further work is necessary to investigate this result as it presents an appealing strategy to simultaneously increase both sensitivity and selectivity with the use of MOFs.

Another interesting point for future research is extending on the work of Chevalier et al. who explored the competition mechanisms that exist when sensing binary gas mixtures through a MOF membrane – an idea that has little to no previous work. While checking cross-sensitivity is a good starting point for measuring selectivity towards gases, it neglects to take into consideration the competition mechanisms that exist between the hundreds of gases present in exhaled breath, as was done in this study. Therefore, further implementations of this work would allow for another measurement of selectivity to be used in testing sensors to allow for more reliable results.

Additionally, it's a very rare occurrence for studies to be conducted with collections of more than 10 testing VOCs. This should be a future area for inquiry because there are 100's of VOCs present in the breath that need to be analysed and checking the selectivity of acetone against the same gases repeatedly will not improve our ability to be certain that acetone is what is being detected by the breath sensors.

Numerous studies have also found the significance of the sensing layer on selectivity. Tung et al. (2019) synthesised three MOFs by combining pristine graphene (pG) as the sensing material with: copperbenzene-1,3,5-tricarboxylate to create pG-Cu BTC; zirconium 1,4-dicarboxybenzene to create pG-Uio 66; and 2-methylimidazole zinc salt to create pG-ZIF-8. These pG-MOF hybrid materials were particularly selective towards chloroform and methanol among the tested gases. It was concluded that the chloroform, a nonpolar molecule, has favourable interaction energy with organic linkers in the pG-Cu BTC composite allowing a

strong analyte-MOF interaction. That is, there was a strong affinity of chloroform molecules for hydrogen bonding to the Cu-BTC. Furthermore, methanol, a highly polar molecule, most likely interacts with the MOF layer by forming a coordination bond with Cu^{2+} ions in pG-Cu BTC, once more enabling a strong response. While acetone was not adsorbed as much as chloroform and ethanol, this study presents a new branch of sensing layers combined with MOFs, that may be explored with modifications made to potentially enable greater acetone sensing.

On that note, very recently, Zhang et al. (2020) synthesised ultrafine $\text{W}_{18}\text{O}_{49}$ nanowires (UFNWs) by using WCl_6 as a precursor and absolute ethanol as a solvent. It was found that the material has excellent selectivity to acetone which was confirmed through DFT analysis. The calculated results are in agreement with the experimental results, further confirming the ultrahigh selectivity of $\text{W}_{18}\text{O}_{49}$ UFNWs to acetone. The above results demonstrate that the high selectivity of $\text{W}_{18}\text{O}_{49}$ UFNWs to acetone is due to the exposure of its single crystal plane (010). Similarly, Liu et al. (2019) synthesised a one-dimensional (1D) porous platinum (Pt)-doped In_2O_3 nanofiber structure for acetone sensing. They observed very high selectivity toward acetone against other interfering gases. These results demonstrate that improving the quality of the sensing layer in combination with a MOF membrane poses promising potential significantly increase selectivity towards acetone in exhaled breath.

Other possible approaches to increasing selectivity include: gas pre-separation to remove confounding compounds from a sample prior to being exposed to a sensors, and computer simulations as a means of increasing the reliability of findings and modelling gas-MOF interactions in order to be able to change variables by miniscule increments (unlike most real-world experiments) to see the effect on selectivity. Finally, using MOF derivatives to create the actual sensing layer by using a MOF as a self-sacrificial template is another possibility.

The present study may have been improved had a more thorough investigation into computer simulation experiments been conducted as part of this research. This may have yielded other interesting findings to either support or contradict the findings that are presented in this paper, which could have been further analysed to make more informed recommendations.

Conclusion

In summary, this paper provided a review of the current literature surrounding the use of MOF membranes to increase selectivity of chemical sensors towards acetone. A collection of 5 MOFs were investigated including ZIF-8, ZIF-71, ZIF-CoZn, ZIF-67 and HKUST-1. There were useful findings from each paper that were discussed in detail in Section 3, however, generally speaking the following conclusions were drawn about a MOF that may be designed in future to enhance selectivity towards acetone. The pore size of this MOF should ideally be tailored to the size of acetone molecules. The ratio of DMF to H₂O in the solvent used during synthesis should be chosen such as to maximise the number of open metal sites in order to exploit the chemical affinity between acetone and the MOF layer, while also minimising the MOF thickness as much as possible. The MOF layer should be oriented along the (211) reflection plane. Finally, ZIF-71 and ZIF-8 should form the primary membrane as they showed the greatest potential towards enabling greater acetone selectivity and a secondary ZIF-67 layer should be synthesised on top of the first membrane as this was also found to increase selectivity. Ultimately, these findings stand to enable future experimental research to achieve greater selectivity toward acetone through semiconductor metal oxide gas sensors, which can, in turn, contribute to speeding up the commercialisation of acetone sensors as a medical tool for monitoring type 1 diabetes and DKA.

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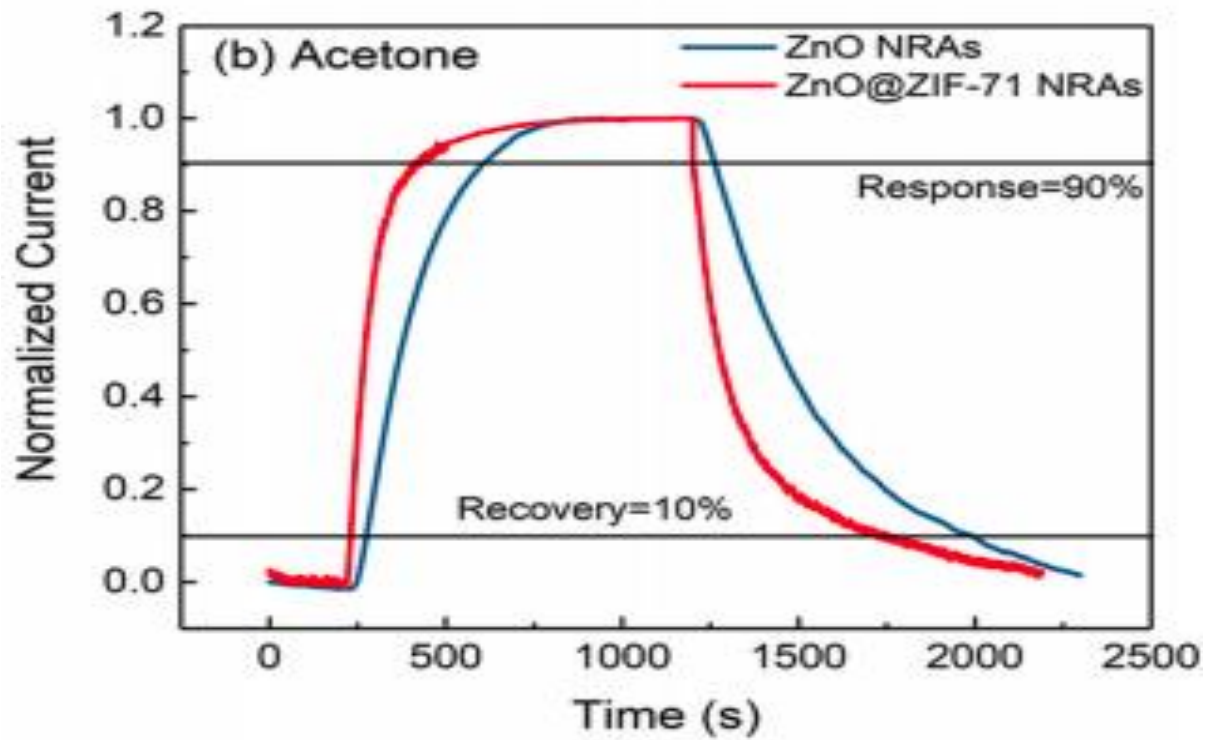
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Appendix B: Kinetic Diameters of VOCs

Gas	Chemical Formula	Kinetic diameter (Å)	Reference
Helium	He	2.60	Pechar, et al., 2020
Hydrogen	H ₂	2.89	Scholes et al., 2010
Ammonia	NH ₃	2.60	Ismail et al., 2015
Water	H ₂ O	2.65	Scholes et al., 2010
Nitrous oxide	N ₂ O	3.30	Ismail et al
Dichloromethane	CH ₂ Cl ₂	3.30	
Carbon dioxide	CO ₂	3.30	Pechar, et al., 2020
Acetylene	C ₂ H ₂	3.30	Matteucci et al., 2006
Methanol	CH ₃ OH	3.63	Hu et al., 2019
Nitrogen	N	3.64	Pechar, et al., 2020
Carbon monoxide	CO	3.76	Matteucci et al., 2006
Formaldehyde	CH ₂ O	3.73	Noël et al., 2019
Methane	CH ₄	3.80	Pechar, et al., 2020
Propane	C ₃ H ₈	4.30	Matteucci et al., 2006
Propylene	C ₃ H ₆	4.50	Matteucci et al., 2006
Ethanol	C ₂ H ₅ OH	4.53	Zhou et al., 2018
Acetone	C ₃ H ₆ O	4.60	Hu et al., 2019
2-propanol	C ₃ H ₈ O	4.70	Haghighi et al., 2019
Toluene	C ₇ H ₈	5.25	Tian et al., 2020
Pyridine	C ₅ H ₅ N	5.7	Bräuer et al., 2017
Benzene	C ₆ H ₆	5.85	Noël et al., 2019
Chloroform	CHCl ₃	5.90	Voyles et al., 2015
o-Xylene	C ₈ H ₁₀	6.80	Chevalier et al., 2019

Appendix C: Normalised current curves for a acetone concentration of 5 ppm to compare response and recovery time of ZnO nanorods against ZnO@ZIF-8 nanorods



[Zhou et al., 2019]

Appendix D: Summarized DFT Results Simulation of Possible Adsorption Site Configurations between ZIF-71 and Two Kinds of Adsorbed Gases

	ethanol-1	ethanol-2	ethanol-3	acetone-1	acetone-2	acetone-3
adsorption site	C=O...Zn	O-H...Cl	O-H...Cl	C=O...Zn	C=O...Cl	C=O...Cl
E_{ads} (kJ/mol)	-12.50	5.39	93.48	-6.82	3.06	-2.81
adsorption	√	×	×	√	×	√

[Zhou et al., 2019]