# 7 CONCLUSIONS

## 7.1 Discussion and further work

This thesis has been concerned with the characterisation, optimisation and evaluation of a novel FAIMS sensor. The Owlstone solution represents a reduction, by an order of magnitude, in the geometry of the sensor otherwise employed within FAIMS systems. Given such a change in design, the performance of the sensor was expected to be influenced differently to changes in operational parameters. This was investigated by first considering the theory underpinning the operation of FAIMS but predominantly through empirical investigations centred on current and potential applications of the technology. This final chapter considers the outcomes of the work presented within this thesis and highlights potential avenues for further investigation.

### 7.1.1 Theory related to FAIMS

Through the review of FAIMS theory it became apparent that in optimising the performance of a system there were inherent trade-offs between the parameters controlling FAIMS operation. As a consequence, the eventual design of a FAIMS sensor will result from a specific chemical sensing requirement or emphasise on a particular system property (*e.g.* sensitivity). The development of FAIMS has been driven primarily by the desire to miniaturise the technology for field practical applications or *in situ* analysis. This has resulted in a compromise between the eventual primary application of the FAIMS sensor and its performance with regard to sensitivity, selectivity and the resources required by the system.

It had previously been demonstrated that sensitivity generally suffers from a reduction in the gap height, because of increased losses attributable to diffusion, and a reduced effective gap height. These losses can be countered through a low residence time of ions and ensuring that the waveform is applied with a high frequency, respectively.

Sources in the literature had previously reported a dependence of the compensation voltage position on the magnitude of flow rate, which was challenged in Chapter 2. This was initially based on theoretical considerations but was later tested and the hypothesis supported by experimental results reported in Chapter 5. These findings were obtained when investigating the dependence of ion response upon the characteristics of the carrier flow in Chapter 5.

Empirical studies have also indicated that further developments of the ionisation theory is required as existing mechanisms present in the literature do not fully explain all experimental findings. It would be of interest to explore the characteristics of ionisation by a $^{63}$Ni source, independently from a separation region. In particular, a better understanding of the influence of the residence time within the source and changes in humidity upon the resulting ion species. Not only would this improve any study with which $^{63}$Ni is used but potentially also impact the design of future FAIMS systems.

Having considered the different ways in which the sensor geometry can influence the properties of a FAIMS device it is recommended the effect of extending the length of the separation region, while increasing the flow rate to maintain an equivalent residence time be investigated. Diffusion loss within the separation region can be approximated to be dependent upon the residence time and gap height only. Maintaining these two quantities should ensure that the sensitivity remains relatively unchanged, while extending the length restricts the acceptance angle of ions reaching the detector. This will lead to greater filtering, placing a tighter constraint upon the acceptable ion trajectories and increasing selectivity. Considering geometry factors only, a doubling of the length should result in 50% of the ions not possessing the correct mobility being removed, compared to when the length is unmodified[1].

### 7.1.2 Peak fitting

One consequence of the smaller geometry of the separation region used in an Owlstone FAIMS device was that it was more likely that ion signals would become mixed. In response, peak fitting algorithms were investigated to recover some of the lost resolution. Final peak fitting was completed by a single procedure (unconstrained non-linear optimisation) but three separate preliminary methods for obtaining estimations of the different major ion species were also investigated. It was found that each of the three different methods had their own biases and each proved most effective in different situations. The approach described as Successive Gaussians was an entirely original method for estimating the parameters of ion responses. It would be of interest to continue the investigation of the three methodologies to discover the full potential of what can be achieved.

[1] In an Owlstone FAIMS sensor the maximum acceptance angle is 6.65 °, $\gamma = \tan^{-1}(g/l)$. Doubling $l$ will approximately halve the acceptance angle and tripling $l$ will result in ~1/3 of the ions previously able to pass on to detection, despite not possessing the correct mobility, being neutralised.

### 7.1.3 Characterisation of parameters

A systematic study of the influence of changing the pressure, humidity and magnitude of carrier flow on the performance of the sensor for the detection of DMMP was undertaken. This work represented the first systematic study of this type with the Owlstone FAIMS sensor. It was found that the sensitivity of the device increased with greater humidity and magnitude of the carrier flow, for both the monomer and dimer product ions. It was observed that the CV positions of the monomer and dimer have different dependencies. This was attributed to the occurrence of clustering; it had been previously reported in the literature that the monomer molecular-ion is capable of solvation with additional humidity molecules under low field conditions, while the dimer is not. In agreement with the literature, the likelihood of clustering was attributed as being dependent upon the occurrence of an analyte colliding with a water molecule within the low field portion of the applied asymmetric waveform. It was found that an average of 0.34 collisions between monomer ions and water, in the duration of a low field region of the asymmetric waveform, was required to observe the on-set of clustering.

Through this study a greater understanding of how humidity affects the sensitivity of this sensor was obtained. However, owing to the difficulty in isolating the effects dependent upon either the ionisation or separation regions, it was not possible to conclusively identify the specific cause of the observed behaviour (although the saturation of water in the ionisation region was suggested). As with the proposed further work arising from the theory chapter there would be value in experimentally testing the variation of parameters relating solely to the ionisation region (*e.g.* residence time, humidity concentration).

### 7.1.4 Detection of ethyl acetate in wine

The second case study was a new application for FAIMS; an evaluation of its potential to detect compounds present within wine, specifically ethyl acetate. To aid with the analysis a GC unit was linked to the FAIMS sensor which facilitated orthogonal separation of compounds and therefore enabled better resolution between compounds, which otherwise would have been difficult to isolate by FAIMS alone. The outcome was that ethyl acetate was shown to be detected in solutions of wine (without pre-treatment) at concentrations below the human perception threshold (120 mg/l).

While the monitoring of ethyl acetate in wine was the focus of the study, the modification of the carrier flow (as explored in Chapter 5) was applied to overcome the attenuating effects of the more abundant ethanol. This is likely to be relevant to other investigations where there is a more plentiful constituent which may prevent the full ionisation of the target analyte. Most samples, when taken *in situ* and with a minimum of pre-treatment are likely to experience competitive ionisation. The methods employed within this study have allowed optimisation which has effectively countered the initial reduction in performance.

With respect to furthering the study undertaken, it has been suggested that a more complete way of quantifying how the modifications affected analysis could be obtained through the introduction of an internal standard. Ideally an internal standard should have similar characteristics to the compounds under study so that it experiences comparable conditions while being independently detected for assessment. A complication to including an internal standard within the study was that competitive ionisation was required to assess the benefit obtained through the modification of the carrier flow. An internal standard would therefore affect the ionisation, resulting in a situation dependent upon its presence. Selection of a suitable candidate for such a standard is therefore a complicated task as it needs to form an ion for detection but does not interfere with the ionisation of the target analyte.

Now that a single component of wine has been isolated it is also a natural extension of the study to investigate the capability of detecting additional compounds. Every additional compound successfully resolved and quantified within wine increases the likelihood that a GC-FAIMS device will be successfully adopted within the wine industry.

## 7.2 Concluding remarks

This thesis has investigated the application of the Owlstone FAIMS sensor, both through theory and practical case studies. The results obtained can be generally applied to a wide range of applications. Furthermore, peak fitting has been described which explored the potential of data analysis, allowing increased detail to be realised. Beyond the normal operation of a FAIMS sensor (*e.g.* dispersion field strength, mode of operation) when approaching any application it is now realised how critical it is to consider the following:

- *The ionisation method employed.* Will any target compounds be preferentially ionised compared to others and does it minimise potential ion response from the background?
- *The humidity present.* Is it likely to vary across data acquisition, can it be exploited to provide greater sensitivity and selectivity, how does the quantity expected effect the expected generation of ions?
- *The polarity of generated ions.* Can different target compounds be assessed in separate polarities, providing greater specificity and potentially increased sensitivity through avoiding background response?

- *The background*. If the ion response from background compounds limits the ability to detect and specify target compounds at the levels required (after optimisation of ionisation, humidity and polarity has been exhausted) is an additional sampling or separation technique required (*e.g* gas chromatography)?
- *The carrier flow*. Will modifying the carrier gas (pressure, flow rate) supplied to the FAIMS system enhance its operation, how will it affect any hyphenated systems?

When considering new applications for FAIMS the above represents the most immediate questions to be addressed, but, it does not constitute a definitive list.

In conclusion, FAIMS represents an analytical technique which is in the ascendancy. Primarily, this is as (1) a pre-filter for mass spectrometers within the laboratory (not investigated in this thesis) and as (2) a stand alone technology, which is capable of operating as an *in situ* sensor. Specifically, the Owlstone FAIMS sensor has been investigated. Through the characterisation of the novel sensor, and its evaluation for non-traditional applications, a deeper understanding of FAIMS and its operation was obtained. This led to the development of new tools and methods which can aid investigations beyond those studied, ultimately enhancing the capability of the sensor for more diverse applications.