Miniature and micro mass spectrometry for nanoscale sensing applications

S. Taylor and N. France
Department of Electrical Engineering and Electronics, University of Liverpool, Liverpool, L69 3GJ
s.taylor@liv.ac.uk

Abstract. In recent years the use of miniature and/or microscale versions of the more popular mass spectrometers have been realised. This has led to the development of portable analytical devices for a range of ‘in the field’ sensing applications in aerospace, environmental monitoring, medical diagnosis and process control. In this paper the principles underpinning the development of miniature quadrupole mass spectrometers are reviewed. Two different microfabrication methods are compared with a conventional QMS used for residual gas analysis in the range 1-100 Da.

1. Introduction
Mass spectrometry (MS) is a well known and widely used analytical technique. Its attraction is that not only is it highly sensitive, but also information rich and capable of providing information in the mass, concentration and time domains in real time. MS can monitor the presence and abundance of a single ion species (amongst many) and as such it is well suited for a wide range of nanoscale sensing applications. Medium and large scale laboratory based instruments allow both qualitative and quantitative measurements to parts-per-trillion (ppt) levels. However in the last fifteen years miniature and micro MS versions have been researched and deployed. Miniature MS though less sensitive are now used for out of the laboratory applications in the field and in harsh environments. This paper gives an overview of one type of miniature MS: the quadrupole mass spectrometer (QMS). The underlying principles of QMS operation are presented and two fabrication methods for miniature QMS realisation are described. MS in marine environments is also possible and has usually been attempted via the use of a suitable membrane to allow the sample into the MS vacuum chamber. This is known as membrane inlet mass spectrometer (MIMS) technology. The feasibility of MIMS as an environmental monitor for particular analyte molecules is considered and demonstrated.

2. Miniature mass spectrometry
In MS the mass to charge ratio of ions and/or ionic species is determined. MS is most generally used to find the composition of a (unknown) physical sample by generating a mass spectrum representing the masses of sample components. Other applications include: determining the isotopic composition of elements in a compound or substance, determining the structure of a compound by observing its fragmentation patterns, quantifying the amount of a compound in a sample using a carefully designed calibration method, studying the fundamental of gas phase ion chemistry and determination of other physical, chemical and/or biological properties of compounds.
All mass spectrometers consist of three basic components: (i) ion source (ii) mass analyser and (iii) detector system. Figure 1 shows how these are configured in the case of the QMS [1].

![Figure 1: Schematic diagram of a QMS showing ion source, analyser and detector.](image)

2.1 Ion Source and detector
The ion source is the part of the mass spectrometer that ionises the material under analysis (the analyte). The ions are then transported by an electric field to the mass analyser. Techniques for ionisation have been a key to determining what types of samples can be analysed by mass spectrometry. Electron ionisation and chemical ionisation may be used for gases and vapours and are the most common in QMS. The final element of the mass spectrometer is the detector which records the charge induced or current produced when an ion passes by or strikes a surface.

2.2 Mass Analyser
The mass analyser (mass filter) separates the ions according to their mass-to-charge ratio. All mass spectrometers are based on dynamics of charged particles in electromagnetic fields in vacuum and for this reason the MS system invariably contains a vacuum system which can be the most costly and/or bulky component in the system.

In the case of the QMS, for given voltages applied to the 4 electrodes, only ions of a particular charge to mass ratio have stable trajectories: other ions are rejected. If the voltages are scanned with a fixed ratio between DC and RF results in a mass spectrum. An ideal quadrupole field is provided by hyperbolic form electrodes. Circular electrodes are more common and may be used provided that the ratio of electrode radius (r) to inscribed radius (r₀) and is set at an appropriate value [2].

![Figure 2: End on view of the mass filter (mass analyser) for a QMS](image)
In the case of a quadrupole field the ion motion may be resolved into independent components in $x$ and $y$ directions. The equation of ion motion $x(t)$ for an ion in the electromagnetic field between the electrodes is given by:

$$\frac{d^2x}{dt^2} + \left(\frac{e}{mr_0^2}\right) [U - V \cos(\omega t)] x = 0 \quad (1)$$

where $f = \text{RF frequency}$, $\omega = 2\pi f$, $e/m = \text{ion charge/mass}$, $r_0 = \text{inscribed radius of the QMS mass filter}$ and $U, V$ are the direct and RF voltages respectively. Solution of the above equation indicates that there are an infinite number of stable operating zones but in practice only 1 or 2 of interest.

For the first stable operating zone the maximum detectable mass $m_{\text{max}} \text{ (in Da)}$ is given by:

$$m_{\text{max}} = 7 \times 10^6 \frac{V_{\text{max}}}{f^2 r_0^2} \quad (2)$$

where $V_{\text{max}}$ is the RF voltage applied between adjacent electrodes. The QMS instrument mass resolution ($m/\Delta m$) is related to number of RF cycles experienced by a particular ion ($n$):

$$m/\Delta m \approx \frac{n^2}{20} = \frac{f^2}{40 e V_z} \quad (3)$$

where $L = \text{QMS mass filter length}$ and $V_z = \text{ion energy (in eV)}$

From (2) it may be seen that $V_{\text{max}}$ falls with $r_0^2$ therefore a low voltage instrument may be obtained if instrument dimensions are reduced. From (3) it may be seen that a reduction in mass filter length $L$ is offset by increasing the RF frequency and thereby maintaining instrument resolution. This is the motivation behind microfabricated and miniature versions of the QMS.

Quadrupole mass analysers with submillimetre $r_0$ have been achieved by microfabrication in silicon [3]. Subsequent MEMS versions have shown improved performance [4] however the sensitivity of such instruments is low. Furthermore large batch quantities of such devices are necessary in order to justify the cost of microfabrication tooling. More recently a QMS mass analyser with hyperbolic form electrodes of $r_0$ of 0.4mm has been achieved using digital light processing which is a low cost rapid prototyping (RP) method [5]. The advantage of DLP is that any electrode shape (and its insulating housing) may be fabricated at mm or sub millimetre dimensions. Such QMS analysers are lightweight (compared to stainless steel) which is essential for some applications (e.g. on board spacecraft).

A comparison of the performance for a typical conventional QMS and two miniature QMS is given in Table 1. The choice of technology is also driven by application. These approaches allow the QMS to be tailored to a particular end use.

|               | Conventional QMS | MEMS QMS | RP QMS |
|---------------|------------------|----------|--------|
| Inscribed radius $r_0$ (mm) | 2.76             | 0.22     | 0.90   |
| Peak RF voltage (V) | 1000             | 35       | 200    |
| Frequency (MHz) | 2-3              | 6        | 3-4    |
| Length (mm)    | 100-125          | 10-30    | 40     |
| Mass range (Da) | 500              | 400      | 100    |
| Pressure range (mbar) | $< 2 \times 10^{-4}$ | $< 2 \times 10^{-3}$ | $< 10^{-3}$ |
| Resolution at 10% peak | 500              | 200      | 100    |

Table 1: Comparison of conventional and miniature QMS
Figure 3: QMS mass filters fabricated by conventional and microfabricated methods. Left: a conventional QMS mass analyser with stainless steel electrodes diameter 6.25mm in ceramic holders. Centre: microfabricated QMS with gold coated optical fibre electrodes diameter 0.5mm held in a silicon mount. Right: RP QMS with hyperbolic form gold coated electrodes of r₀ 0.9mm held in a PMMA electrode holder.

2.3 Results and applications

Advances in genomics, proteomics and metabolomics have revealed numerous biomarkers that indicate patient condition. In many cases, however, measurement of these biomarkers involves time consuming or expensive analysis. It is well known that exhaled breath contains thousands of chemicals, several of which have already been established as nanoscale biomarkers for disease. Breath analysis has been used for screening for metabolic disorders (diabetes and cholesterol handling problems), pulmonary disease, asthma, heart disease, diabetes and cancer. Figure 4 shows results from human patient breath samples taken using a conventional QMS. The mass spectral peak at m/z = 44 corresponds to the carbon dioxide present in the breath sample. The ratio to m/z = 32 (O₂) may be used to provide a real time monitor of the patient respiratory quotient (RQ) under exercise and non-exercise conditions providing e.g. data on patient pulmonary and/or heart condition. Figure 5 shows a mass spectrum taken over the same mass range but this time using a miniature instrument with r₀ = 0.9mm (hyperbolic form electrodes). The gas mixture in this case is Helium /Air /Argon and mass spectral peaks occur at the appropriate points on the mass scale. The resolution is reduced compared to the conventional QMS (as expected) but still adequate for many applications.

Figure 4: Mass spectrum of an exhaled breath from a human patient obtained using a conventional QMS.
One of the advantages of miniature instruments is the ability to operate at higher pressures than their conventional counterparts. This is due to the shorter distance travelled by the ion between the source and detector which means that a higher mean free path length can be achieved before instrument performance is compromised. Operation of the MEMS QMS has been demonstrated showing a linear increase in ion current with pressure up to $10^{-2}$ mbar for $m/z = 14$ (N$^+$ ions).

2.4 QMS simulation

Instrument simulation is usually desirable and in the case of high performance QMS essential in order to optimise performance. Motion of ions through the ioniser has been simulated using a 4th order Runge Kutta numerical integration of equation (1) [2]. Ion injection is randomised in space and time relative to the RF field and by calculation of $10^5$ ion trajectories for each point on the mass scale ($10^7$ - $10^8$ ions in total) a mass spectrum may be determined.

In the case of a non quadrupolar field (e.g. for non ideal electrode geometry, or in the case of displaced electrodes [6]), ion motion may be defined by:

$$eE_x = m\left(\frac{\partial^2 x}{\partial t^2}\right) \text{ and } eE_y = m\left(\frac{\partial^2 y}{\partial t^2}\right)$$

(4)

where $E_x$ and $E_y$ are the electric field components in $x$ and $y$ directions respectively. Calculation of the electric fields may be achieved using finite difference or finite element methods. However the boundary element method (BEM) is faster and allows 3D effects to be incorporated.

3. Conclusions

Miniature and microscale versions of all of the main mass spectrometer types have been realised. In the case of the QMS, loss of instrument performance due to scaling down in size may be recovered somewhat via operation at higher frequencies. Instrument resolution and sensitivity is reduced compared to a larger scale conventional QMS but remains adequate for many nanoscale sensing applications in environmental monitoring, medical diagnosis and for process control.

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