

Title: A method of performing a routine on a mass spectrometer

Background to the invention

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The present invention relates to a method of performing a routine on a mass spectrometer; and to a mass spectrometer.

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Gas chromatography (GC) is a well-known analytical separation technique. A column containing a stationary phase is arranged in a GC oven. A sample is introduced into the column along with a mobile phase (carrier gas) and heated by the GC oven. The sample interacts with the stationary phase in the column and the components of the sample elute from the end of the column at different rates depending on their chemical and physical properties and affinity to the stationary phase. The mobile phase may comprise, for example, an inert or non-reactive gas such as helium or nitrogen.

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It is known to interface the GC oven with a mass spectrometer (MS) - a so-called GC/MS system arrangement - for analysis of the separated components of the sample.

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Generally speaking, a mass spectrometer comprises an ion source, a mass analyser and a detector.

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The ion source of a mass spectrometer of the type referred to in this specification includes an inner source assembly and an outer source assembly. The incoming components of the sample, for example from a GC unit, are first introduced into the inner source assembly. Here, they are ionised by colliding with electrons emitted by one or more filaments in the inner source assembly and are then emitted towards the outer source assembly which guides the ions through a series of ion lenses (extraction lens stack) towards an analyser and detector of the mass spectrometer. The terms 'inner source' and 'outer source' are used herein, in line with the above general definition, to increase clarity. Nevertheless, the respective components of the inner and outer source assemblies are likewise components of the source assembly as a whole.

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There are different types of ion source, including electron ionisation (EI) and chemical ionisation (CI). The sample enters the ion source from the gas chromatography column into a volume of an inner source housing adjacent one or more filaments. Electrons emitted by the filament(s) interact with the sample molecules which serve to ionise them. A charged repeller then repels the ions towards the lens stack of the outer source assembly.

The mass analyser of the type described herein comprises a tandem mass spectrometer, including first and second mass filters arranged either side of an ion guide (for example a collision cell). The mass filters comprise first and second quadrupoles.

In one example, the first mass filter may be tuned for the selective transmission of ions within a narrow range of mass-to-charge from the total population of ions introduced from the ionization source. The first mass filter may be tuned to select parent ions of interest. The collision cell arranged downstream of the first mass filter may fragment the selected parent ions. The second mass filter then analyses the daughter ions which emerge from the collision cell. Ions may be fragmented in the collision cell by Collision Induced Decomposition (CID) wherein ions undergo multiple collisions with gas molecules in the partially enclosed collision cell. A tandem mass spectrometer may be operated in one of several modes known in the art, including daughter (product) ion scan, parent (precursor) ion scan, neutral loss scan and selected reaction monitoring (SRM).

The detector measures the intensity, number and/or current of the ions passed to it by the mass analyser. Various types of detectors are known, including electron multipliers. A photomultiplier tube (PMT), also known as an ion-to-photon detector, may alternatively be adopted as part of a detection system. A benefit of a PMT over an electron multiplier is that it is more robust. In an electron multiplier the surfaces may be exposed to background contamination and further contamination each time the system is vented. Moreover, the first surface of the multiplier may become degraded over time by the ion beam. In a PMT arrangement, the initial ion strike is onto a metal dynode to create electrons. The electrons then strike a phosphor screen to create photons which then go into the sealed PMT to get converted back into electrons and multiplied. Advantageously, the multiplying sections of the PMT are never exposed to the instrument environment and the primary ion strike is made against conventional metal.

Using the data from the detector, the mass spectrometer (or an associated data processing system) can create a mass spectrum which illustrates the relative abundance of ions across the m/z range of interest. Consequently, a mass spectrum produced from a GC/MS arrangement allows for the qualitative and quantitative analysis of a sample.

Mass spectrometers are highly sensitive and accurate pieces of apparatus, and require regular maintenance to maintain their optimal conditions of operation. One of the problems associated with operating a mass spectrometer is that it can be difficult for an inexperienced operator to determine whether or not the mass spectrometer is in a correct operational state. Even if a problem with the mass spectrometer is detected by the operator, they may lack the specialist knowledge required to recalibrate and/or tune the mass spectrometer for subsequent operation.

It is important to ensure that the mass spectrometer instrument is measuring, collecting and displaying data correctly before being used to analyse a sample.

5 A mass spectrometer can be configured by initially producing a test mass spectrum for a known reference sample (a calibrant). The measured abundance of ions in the test mass spectrum across the detected m/z range can then be compared against a verified 'master' mass spectrum for that reference sample.

10 There is an increasing desire to provide mass spectrometers which are more 'user friendly', which reduce the burden on the operator to detect any problems and perform the required maintenance.

It is known that various configurations of the components of the mass spectrometer affect the
15 accuracy of various characteristics of the mass spectrum produced. For example, adjusting the voltages applied to the quadrupoles affects the width and position of the measured peaks. Adjusting the voltages applied to the various components of the source affect the relative ratios between peaks and the shape of the peaks.

20 It is known for some mass spectrometers, such as the 7000C triple quadrupole GC/MS system by Agilent, CA, USA, to automatically run a predetermined procedure of various adjustments to the components of the source and the mass analyser of the mass spectrometer at the operator's request. On initial start-up, the Agilent mass spectrometer initiates a predetermined configuration workflow which configures the mass analyser (the first and second quadrupole
25 mass filters) to optimize the detected peak widths and peak positions, configures the gain of the detector and optionally tunes the source voltages.

The full procedure is performed without any prior determination of the system condition.

30 A problem with such a known arrangement is that it performs a comprehensive adjustment of various components of the mass spectrometer, even if they do not need to be adjusted. This unnecessarily increases the time taken for the instrument to initialise.

The present invention seeks to provide an improved mass spectrometer and a method of setting
35 up a mass spectrometer for operation.

Summary of the invention

Accordingly, there is provided a method of performing a routine on a mass spectrometer, comprising:

- 5 providing a reference sample having known chemical properties;
 generating a test mass spectrum from the reference sample using the mass spectrometer;
 comparing predetermined characteristics of the test mass spectrum to predetermined performance criteria;
- 10 performing an autotune procedure on the mass spectrometer if a first characteristic of the test mass spectrum is deemed not to meet corresponding predetermined performance criteria;
- performing a resolution adjustment and calibration procedure on the mass spectrometer if a second characteristic of the test mass spectrum is deemed not to meet corresponding
- 15 predetermined performance criteria.

In at least one embodiment, the first characteristic includes at least one of: the relative intensity of at least one peak of the test mass spectrum; and the shape of at least one peak of the test mass spectrum.

- 20 In at least one embodiment, the first characteristic includes the relative intensity of each the peaks of the test mass spectrum.

- 25 In at least one embodiment, the first characteristic includes the shape of each of the peaks of the test mass spectrum.

In at least one embodiment, the second characteristic includes at least one of: the width of at least one peak of the test mass spectrum; and the position of at least one peak of the test mass spectrum.

- 30 In at least one embodiment, the second characteristic includes the width of each of the peaks of the test mass spectrum.

- 35 In at least one embodiment, the second characteristic includes the position of each of the peaks of the test mass spectrum.

In at least one embodiment, the autotune procedure comprises adjusting the voltages applied to at least one of the components of a source assembly of the mass spectrometer.

In at least one embodiment, the resolution adjustment procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer.

- 5 In at least one embodiment, the calibration procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer.

In at least one embodiment, the method further comprises:

- generating a confirmation mass spectrum from the reference sample following an
10 autotune and/or resolution adjustment and calibration procedure; and
comparing predetermined characteristics of the confirmation mass spectrum to the
predetermined performance criteria.

- 15 In at least one embodiment, a predetermined performance criterion is that a characteristic of the test mass spectrum is within a predetermined range of the corresponding characteristic of a stored mass spectrum for the reference sample.

In at least one embodiment, the reference sample is Perfluorotributylamine (PFTBA).

- 20 In at least one embodiment, the method further comprises detecting a leak in the mass spectrometer and providing an indication of the detected leak to an operator.

In at least one embodiment, the step of detecting a leak comprises:

- generating a background mass spectrum of the mass spectrometer background;
25 detecting the presence of at least one of water and air;
providing an indication of a detected leak to an operator if the amount of water and/or air
is higher than a predetermined level.

- 30 In at least one embodiment, the step of detecting a leak comprises providing an indication of a detected leak to an operator if the ratio of water to nitrogen, nitrogen to argon and/or oxygen to argon is higher than a predetermined level.

- In at least one embodiment, the method further comprises generating a report of the
predetermined characteristics measured and indicating whether the corresponding
35 predetermined performance criteria were met.

Another aspect provides a mass spectrometer, comprising:

- an inlet to receive a reference sample having known chemical properties;

an ion source configured to receive the reference sample and ionize it;
a detector to generate a test mass spectrum from the reference sample;
a controller configured to:

compare predetermined characteristics of the test mass spectrum to
predetermined performance criteria;

perform an autotune procedure on the mass spectrometer if a first characteristic
of the test mass spectrum is deemed not to meet corresponding predetermined performance
criteria;

perform a resolution adjustment and calibration procedure on the mass
spectrometer if a second characteristic of the test mass spectrum is deemed not to meet
corresponding predetermined performance criteria.

Description of the drawings

Embodiments of the present invention will now be described, by way of non-limiting example
only, in which:

Figure 1a illustrates part of a test mass spectrum;

Figure 1b illustrates an enlarged view of one of the peaks in the test mass spectrum of Figure
1a;

Figure 2 illustrates a first stage of a routine according to at least one embodiment of the present
invention;

Figure 3 illustrates a second stage of a routine according to at least one embodiment of the
present invention;

Detailed description of the invention

In a first aspect of the present invention, there is provided a method of performing a routine on a
mass spectrometer, comprising providing a reference sample having known chemical properties
and generating a test mass spectrum from the reference sample using the mass spectrometer.

In at least one embodiment, the reference sample is Perfluorotributylamine (PFTBA), referred
to in the art as Heptacosa and available from Waters Corporation, MA, USA. PFTBA has
multiple peaks, some of the largest peaks including those around 69, 131, 219, 264, 414 and

502 m/z. Other reference samples may be used, so long as they are stable and have chemical properties which are repeatable and readily detectable, making them suitable as calibrants.

The repeatability of a reference sample allows for it to be used to reliably determine whether a mass spectrometer is set up correctly, by comparing a test mass spectrum produced by the mass spectrometer using that reference sample to the mass spectrum that would be expected from a notionally 'ideal' mass spectrometer.

When the mass spectrometer is first assembled, initial settings are applied to the mass analyser and detector. Specifically, initial settings are applied to the first and second mass filters (e.g. the quadrupoles) of the mass analyser. For example, setting up the first and second mass filters may include adjusting the offset, slope and linearity of the scan line of the associated mathieu stability diagram. This procedure sets up the resolution peak positions under factory conditions. The detector may be adjusted to optimise the linearity in its response.

In a method according to a first aspect of the present invention, the test mass spectrum generated from the reference sample is analysed. Predetermined characteristics of the test mass spectrum are compared with stored predetermined performance criteria. If a predetermined characteristic of the test mass spectrum differs by a predetermined extent from an ideal value, or falls outside of a range of acceptable values, a further procedure to adjust the relevant settings of the mass spectrometer to cancel out or reduce the difference is performed.

Adjustments may be made to various components of the mass spectrometer, including the ion source and the quadrupoles. Adjusting the ion source may include adjusting the voltages applied to the ionisation source chamber, ion repeller and any of the lens elements of the ion source. This affects the peak ratios and/or peak shape of a spectrum generated by the mass spectrometer. The voltage applied to the first mass filter (quad) may be adjusted along with any adjustments to the ion source.

Adjusting the quadrupoles affects the range of ions which are allowed to pass through. Adjusting the RF and DC ramp rate of the quadrupole can affect the upper and lower limits of which ions may pass, thus adjusting the range of m/z values allowed to pass.

The present invention relates generally to only adjusting the components of the mass spectrometer which are able to correct the error(s) detected in the test mass spectrum.

Specifically, the method according to one aspect of the present invention comprises performing an autotune procedure on the mass spectrometer if a first characteristic of the first mass spectrum is deemed not to meet corresponding predetermined performance criteria.

- 5 The first characteristic includes at least one of: the relative intensity of at least one predetermined peak of the test mass spectrum; and the shape of at least one peak of the test mass spectrum.

The autotune procedure comprises adjusting the voltages applied to at least one of the components of a source assembly of the mass spectrometer.

Further, the method according to one aspect of the present invention comprises performing a resolution adjustment and calibration procedure on the mass spectrometer if a second characteristic of the test mass spectrum is deemed not to meet corresponding predetermined performance criteria.

The second characteristic includes at least one of: the width of at least one peak of the test mass spectrum; and the position of at least one peak of the test mass spectrum.

- 20 Both the resolution adjustment procedure and calibration procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer.

The resolution adjustment procedure sets how wide the measured peaks are. The calibration procedure adjusts the measured position of the peaks. Adjusting the width of the measured peaks tends to affect the measured position of that peak. Accordingly, the resolution adjustment procedure and calibration procedure are run together.

Peak shape

- 30 In at least one embodiment, the first characteristic includes the shape of at least one peak of the test mass spectrum. For example, a method according to at least one embodiment assesses the shape of a peak either side of the apex and compares it to predetermined performance criteria. In one embodiment, the predetermined performance criteria associated with the peak shape is whether the peak is substantially symmetrical about its apex.

35 A method according to at least one embodiment may characterise a peak with a value related to the extent to which the peak is asymmetric. In at least one embodiment, the area under the peak to the left of the apex may be compared to the area under the peak to the right side of the

apex to mathematically characterise any asymmetry. The area may be calculated by integrating the peak either side of the apex.

In at least one embodiment, predetermined reference criteria stored in connection with the mass spectrometer may denote the minimum peak shape which is acceptable.

An undesirable peak shape may include one in which a peak is followed by a pronounced spike on the high mass side (i.e with a higher m/z) of the peak.

Figure 1a illustrates an example of what may, in at least one embodiment, be determined to be undesirable peak shapes at 69, 219, 264, and 502 m/z . Figure 1b is an enlarged view of the peak at 264 m/z .

In at least one embodiment, a method of characterising a peak shape includes:

- identifying the maximum intensity in a predetermined region of m/z ;
- setting a target intensity as a predetermined percentage of the maximum intensity identified;
- identify any candidate peak(s) within the predetermined region having an intensity above the target intensity;
- characterising the peak shape as acceptable if only one candidate peak is identified;
- charactering the peak shape as unacceptable if two or more candidate peaks are identified.

A peak shape characterised as acceptable meets the predetermined performance criteria. A peak shape characterised as unacceptable does not meet the predetermined performance criteria.

In at least one embodiment, the predetermined region may be ± 1 m/z either side of a target m/z value. In at least one embodiment, the predetermined percentage may be 50%. In at least one embodiment, a candidate peak is only identified if the height of the candidate peak relative to the trough between the candidate peak and the point of maximum intensity is greater a predetermined percentage (e.g. 5%) of the height of the maximum intensity from the trough.

In Figure 1b, the predetermined region of m/z is identified with label A. The maximum intensity is labelled with line B. The target intensity is labelled with line C. The two candidate peaks are labelled D1 and D2. The trough between D1 and D2 is labelled E. The height of the candidate peak D1 from the trough E is labelled F1. The height of the candidate peak D2 from the trough

E is labelled F2. In at least one embodiment, $C \geq (0.5)B$. In at least one embodiment, $F2 \geq (0.05)F1$.

A peak shape which does not meet predetermined performance criteria may indicate that the ion source is not tuned optimally. Accordingly, in a method according to at least one embodiment, if the shape of at least one peak of the test mass spectrum does not meet the predetermined performance criteria, an autotune procedure is performed.

10 Relative intensity

In at least one embodiment, the first characteristic includes the relative intensity of at least one predetermined peak of the test mass spectrum.

15 The relative intensity of a peak in a mass spectrum is the ratio of the height of the peak relative to the height of the tallest peak (the base peak). The base peak itself therefore has a relative intensity of 100.

In at least one embodiment, the relative intensity of more than one peak is analysed.

20 When the reference sample used is PFTBA, only the relative intensity of some of the peaks may be measured. For example, only the peaks at 69, 219, 264 and 502 m/z may be analysed. This is because those selected peaks provide a reasonable representation of the peaks across the spectrum. In another embodiment, all the peaks of PFTBA may be analysed.

25 The relative intensity of the key peaks of interest in PFTBA is shown in Table 1.

Mass (m/z)	Relative intensity	Target relative intensity (MS1)
69	100.00	100.00
219	38.07	15.00-135.00
264	8.38	5.00-70.00
502	1.90	1.00-25.00

Table 1. Actual and target relative intensities of PFTBA

As the table shows, the relative intensity of peak 69 of PFTBA is 100.00. The relative intensity of peak 219 is 38.07. The relative intensity of peak 264 is 8.38. The relative intensity of peak 502 is 1.90.

In a test spectrum generated by a mass spectrometer, the measured relative intensities of the peaks of PFTBA may differ. Some variation in the measured relative intensity is acceptable. Accordingly, in at least one embodiment of the present invention, the predetermined performance criteria define acceptable ranges within which the measured relative intensities may fall. The upper and lower limits of the range may be asymmetric about the actual relative intensity of a given peak. For example, for peak 219, which has an actual relative intensity of 38.07, a measured relative intensity falling within the range of 15.00 to 135.00 may be deemed acceptable.

In at least one embodiment, the target relative intensity of the 219 peak is 15.00 – 135.00. In at least one embodiment, the target relative intensity of the 264 peak is 5.00 – 70.00. In at least one embodiment, the target relative intensity of the 502 peak is 1.00 – 25.00. The target relative intensity of the 69 peak, being the base peak, is inherently 100.

Accordingly, in a method according to at least one embodiment, if the relative intensity of at least one peak of the test mass spectrum does not meet the predetermined performance criteria, an autotune procedure is performed.

Autotune procedure

The inner source assembly of the source assembly includes an ionisation chamber and a repeller. The outer source assembly includes a plurality of lens elements arranged in a stack which serve to guide the ionised analyte molecules into the first mass filter. The various components of the inner and outer source assembly may each be held at substantially different voltages.

As part of an autotune procedure, the voltages at which the ionisation chamber, repeller and/or the lens elements is held may be adjusted, to optimise the intensity and shape of the peaks of a mass spectrum generated by the mass spectrometer.

For example, if the shape and/or relative intensity of at least one peak of the test mass spectrum does not meet the predetermined performance criteria, the autotune procedure adjusts the relevant settings (e.g. voltages) of the source assembly so that if the mass spectrometer is used to generate a further mass spectrum of the reference sample, the shape and/or relative intensity of the at least one peak of the test mass spectrum will meet the predetermined performance criteria.

The autotune procedure consists only of adjusting the parameters of the components of the source assembly. It is independent of the resolution and calibration procedure and is intended to optimise the intensity and peak shape.

5 Peak width

In at least one embodiment, the second characteristic includes the width of at least one peak of the test mass spectrum. The width may be the full width of the peak at half maximum (FWHM).

10 In at least one embodiment, the second characteristic includes the width of more than one peak of the test mass spectrum.

In at least one embodiment, the second characteristic includes the width of all of the peaks of the test mass spectrum.

15 When the reference sample used is PFTBA, only the width of the peaks at 69, 219, 264 and 502 m/z may be analysed. In another embodiment, all the peaks of PFTBA may be analysed.

20 In at least one embodiment, the predetermined performance criterion is that the measured peak width (FWHM) is 0.75 +/- 0.15. Thus, a measured peak width of 0.59 or lower, or 0.91 or higher, will fall outside of the acceptable range and therefore not meet the predetermined performance criteria.

25 Accordingly, in a method according to at least one embodiment, if the width of at least one peak of the test mass spectrum does not meet the predetermined performance criteria, a resolution adjustment and calibration procedure is performed.

Peak position

30 In at least one embodiment, the second characteristic includes the measured position of at least one peak of the test mass spectrum.

The predetermined performance criteria for an assessment of the measured position of at least one peak may be that it is within a predetermined target range, e.g. +/- 0.1 Da.

35 Accordingly, in a method according to at least one embodiment, if the measured position of a peak in the test mass spectrum falls outside of an acceptable range, a resolution adjustment and calibration procedure is performed.

Resolution adjustment and calibration procedure

Both the resolution adjustment procedure and calibration procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer. In at least one embodiment, the resolution adjustment procedure and calibration procedure comprises adjusting the voltages applied to a first and second quadrupole.

The resolution adjustment procedure sets how wide the measured peaks are. The calibration procedure adjusts the measured position of the peaks. Adjusting the width of the measured peaks tends to affect the reported position of that peak.

The resolution adjustment procedure may include adjustment of the peak width by adjusting a small subset of the slope of the line in the mathieu stability diagram (i.e. a voltage rate). The resolution adjustment is independent of any adjustment of the source parameters. The resolution adjustment alters the precision of the mass measurement. It does affect calibration.

The calibration procedure is to correct the mass position, and so improves the accuracy of the mass measurement. The calibration does not include adjusting the voltage applied to the quadrupoles but is rather a mathematical (polynomial) correction to the acquired data.

In summary, a method according to at least one embodiment is configured to assess the width, position, relative ratio and shape of at least one peak in a test mass spectrum. Those predetermined characteristics may be assessed in that order, or in any order. The order in which the predetermined characteristics are assessed may be configured such that the predetermined characteristic which has the highest probability of not meeting the corresponding performance criteria may be assessed first.

It is possible that, for a given test mass spectrum, none of the predetermined characteristics do not meet the corresponding predetermined performance criteria. Alternatively, only one predetermined characteristic may fail to meet the predetermined performance criteria. In at least one embodiment, when at least one predetermined characteristic is deemed not to meet corresponding performance criteria, the method may immediately perform the corresponding autotune or resolution adjustment and calibration procedure, without assessing any other of the predetermined characteristics. In another embodiment, all of the predetermined characteristics are compared to the predetermined performance criteria before performing any corresponding autotune or resolution adjustment and calibration procedure. A benefit of such an arrangement

is that all accuracy issues with the mass spectrometer are identified at the same time, before remedial action can be taken to address them all.

In at least one embodiment, the method further comprises generating a report of the predetermined characteristics measured and indicating whether the corresponding predetermined performance criteria were met. The report may be displayed to an operator on a user display. A visual indication may be provided to indicate whether each of the predetermined characteristics was deemed to meet the predetermined performance criteria. For example, a green 'tick' or other indicia may be displayed in association with any predetermined characteristics which were deemed to meet the predetermined performance criteria, and a red 'cross' or other indicia may be displayed in association with any predetermined characteristics which were deemed not to meet the predetermined performance criteria.

In at least one embodiment, the method may compare determined characteristics of the test mass spectrum to predetermined criteria and determine whether those characteristics either meet or fail those criteria – a binary assessment. In at least one other embodiment, a qualified determination may be made, e.g. a 'close pass' or a 'close fail'. Alternatively, the determination may adopt a traffic-light/signal system, in which a characteristic which comfortably meets predetermined performance criteria may be denoted by a 'green' status; a characteristic which meets the predetermined performance criteria with a small margin with an 'amber' status; and a characteristic which does not meet the predetermined performance criteria with a 'red' status. Such statuses may be displayed in the report.

In at least one embodiment, the method further comprises generating a confirmation mass spectrum from the reference sample following an autotune and/or resolution adjustment and calibration procedure. The method includes comparing predetermined characteristics of the confirmation mass spectrum to the predetermined performance criteria. This step verifies whether the adjustments made as part of the autotune and/or resolution adjustment and calibration procedures have corrected the accuracy of the mass spectrometer to operate within predetermined limits.

In at least one embodiment, the method includes storing in a database the test and/or confirmation mass spectrum, and/or details of the adjustments made as a result of the autotune and/or resolution adjustment and calibration procedure. Accordingly, this stored information may be associated with any mass spectra subsequently produced by the mass spectrometer in operation, and effectively acts as a verification certificate. Historical information may be interrogated and analysed to determine any long-term degradation or drift in the predetermined characteristics. Although the value of those predetermined characteristics may meet

predetermined performance criteria, any detectable degradation/drift over time can be used to predict when those predetermined characteristics may no longer meet the predetermined performance criteria. Pre-emptive measures may then be taken, for example the early performance of an autotune procedure or resolution adjustment and calibration procedure.

5 In at least one embodiment, the method further comprises detecting a leak in the mass spectrometer and providing an indication of the detected leak to an operator.

10 Leak detection is performed by generating a background mass spectrum of the mass spectrometer background and analysing the background mass spectrum for the presence of at least one of water and air. The presence of air may be determined by analysing the background mass spectrum for at least one of the components of air, such as nitrogen. The background mass spectrum may be generated before or after the test mass spectrum.

15 In at least one embodiment the leak detection step includes calculating the relative abundance of water to nitrogen; nitrogen to argon; and oxygen to argon. If the relative abundance of either water, nitrogen or oxygen is higher than a predetermined level, an indication of a detected leak is provided to an operator. For example, if the relative abundance of nitrogen and oxygen detected is substantially the same as the relative abundance of nitrogen and oxygen in the
20 atmosphere, this is indicative of an air leak. If the relative abundance of water to nitrogen is higher than a predetermined level, this may indicate unacceptable levels of water outgassing from components within the vacuum chamber.

If a leak is detected, a method according to at least one embodiment alerts the operator and
25 advises that remedial action should be taken, which may include tightening of any fluid connections to the mass spectrometer.

Figures 2 and 3 illustrate an example flow diagram of a method according to at least one embodiment of the invention.

30 At step 1, the routine 'the mass spec check' is initiated, either by a user or automatically upon turning ON the mass spectrometer. Next, a background scan 2 is performed, which may comprise generating a background mass spectrum. Next, an air and water ratio check 3 is performed, which may identify a possible leak into the vacuum chamber. If a leak is detected,
35 an indication or report 4 is provided to the control system and/or a user. In one embodiment, if a leak is detected, the routine may terminate and require the leak first to be investigated and remedied, before restarting the procedure.

Next, at step 5, a test mass spectrum is generated for the first quadrupole and, optionally, at step 6, a further test mass spectrum is generated for the second quadrupole.

The test spectrum/spectra is/are then analysed at step 7, by comparing predetermined characteristics of the test mass spectrum to predetermined performance criteria. The results of the comparisons are then indicated in a report 8 to the control system and/or in a report 9 to a user.

Figure 3 illustrates how the results of comparing predetermined characteristics of the test mass spectrum to predetermined performance criteria are then processed.

Following the generation of a report 9 of whether the predetermined performance criteria were met, the method performs a series of checks and initiates various procedures in response. First, an air and water ratio check 10 may be performed. This may be in addition to, or as an alternative to, the air and water ratio check at step 3. If the check 10 indicates a leak, the user is prompted to investigate and/or fix the leak at step 15.

Next, at step 11, the shape of at least one peak of the test mass spectrum is compared to predetermined performance criteria. If it is deemed not to meet corresponding predetermined performance criteria, an autotune procedure 16 is run.

At step 12, the relative intensity (ratio) of at least one peak of the test mass spectrum is compared to predetermined performance criteria. If it is deemed not to meet corresponding predetermined performance criteria, an autotune procedure 16 is run.

At step 13, the position of at least one peak of the test mass spectrum is compared to predetermined performance criteria. If it is deemed not to meet corresponding predetermined performance criteria, the resolution adjustment and calibration procedure 17 is run.

At step 14, the width of at least one peak of the test mass spectrum is compared to predetermined performance criteria. If it is deemed not to meet corresponding predetermined performance criteria, the resolution adjustment and calibration procedure 17 is run.

Both of steps 11 and 12 may be performed before initiating the autotune procedure 16. Likewise, both of steps 13 and 14 may be performed before initiating the resolution adjustment and calibration procedure 17.

Finally, at step 18, if any tests have been performed and remedial action taken (leak fixed, autotune or resolution and calibration procedures run) a confirmation mass spectrum may be generated and a comparison made of predetermined characteristics of the confirmation mass spectrum to the predetermined performance criteria. If any predetermined performance criteria are deemed not to be met, the entire procedure may be run again.

In at least one embodiment, the settings of the ion guide (e.g. collision cell) are not adjusted during the resolution and calibration and/or autotune procedures. In at least one embodiment, the voltage supplied to the source is not adjusted as part of the resolution and calibration procedure.

When used in this specification and claims, the terms "comprises" and "comprising" and variations thereof mean that the specified features, steps or integers are included. The terms are not to be interpreted to exclude the presence of other features, steps or components.

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately, or in any combination of such features, be utilised for realising the invention in diverse forms thereof.

CLAIMS

1. A method of performing a routine on a mass spectrometer, comprising:
providing a reference sample having known chemical properties;
5 generating a test mass spectrum from the reference sample using the mass spectrometer;
comparing predetermined characteristics of the test mass spectrum to predetermined performance criteria;
performing an autotune procedure on the mass spectrometer if a first characteristic of
10 the test mass spectrum is deemed not to meet corresponding predetermined performance criteria;
performing a resolution adjustment and calibration procedure on the mass spectrometer if a second characteristic of the test mass spectrum is deemed not to meet corresponding predetermined performance criteria.
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2. A method according to claim 1, wherein the first characteristic includes at least one of: the relative intensity of at least one peak of the test mass spectrum; and the shape of at least one peak of the test mass spectrum.
- 20 3. A method according to claim 2, wherein the first characteristic includes the relative intensity of each the peaks of the test mass spectrum.
4. A method according to claim 2 or 3, wherein the first characteristic includes the shape of each of the peaks of the test mass spectrum.
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5. A method according to any preceding claim, wherein the second characteristic includes at least one of: the width of at least one peak of the test mass spectrum; and the position of at least one peak of the test mass spectrum.
- 30 6. A method according to claim 5, wherein the second characteristic includes the width of each of the peaks of the test mass spectrum.
7. A method according to claim 5 or 6, wherein the second characteristic includes the position of each of the peaks of the test mass spectrum.
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8. A method according to any preceding claim, wherein the autotune procedure comprises adjusting the voltages applied to at least one of the components of a source assembly of the mass spectrometer.

9. A method according to any preceding claim, wherein the resolution adjustment procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer.

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10. A method according to any preceding claim, wherein the calibration procedure includes adjusting the voltages applied to at least one quadrupole of the mass spectrometer.

11. A method according to any preceding claim, further comprising:

10 generating a confirmation mass spectrum from the reference sample following an autotune and/or resolution adjustment and calibration procedure; and
comparing predetermined characteristics of the confirmation mass spectrum to the predetermined performance criteria.

15 12. A method according to any preceding claim, wherein a predetermined performance criterion is that a characteristic of the test mass spectrum is within a predetermined range of the corresponding characteristic of a stored mass spectrum for the reference sample.

13. A method according to any preceding claim, wherein the reference sample is
20 Perfluorotributylamine (PFTBA).

14. A method according to any preceding claim, further comprising detecting a leak in the mass spectrometer and providing an indication of the detected leak to an operator.

25 15. A method according to claim 14, wherein the step of detecting a leak comprises:
generating a background mass spectrum of the mass spectrometer background;
detecting the presence of at least one of water and air;
providing an indication of a detected leak to an operator if the amount of water and/or air
is higher than a predetermined level.

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16. A method according to claim 15, comprising providing an indication of a detected leak to an operator if the ratio of water to nitrogen, nitrogen to argon and/or oxygen to argon is higher than a predetermined level.

35 17. A method according to any preceding claim, further comprising:
generating a report of the predetermined characteristics measured and indicating whether the corresponding predetermined performance criteria were met.

18. A mass spectrometer, comprising:

an inlet to receive a reference sample having known chemical properties;

an ion source configured to receive the reference sample and ionize it;

5 a detector to generate a test mass spectrum from the reference sample;

a controller configured to:

compare predetermined characteristics of the test mass spectrum to
predetermined performance criteria;

10 perform an autotune procedure on the mass spectrometer if a first characteristic
of the test mass spectrum is deemed not to meet corresponding predetermined performance
criteria;

perform a resolution adjustment and calibration procedure on the mass
spectrometer if a second characteristic of the test mass spectrum is deemed not to meet
corresponding predetermined performance criteria.

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