SYSTEMS AND METHODS FOR MASS CALIBRATION

FIELD

[0001] The present disclosure generally relates to the field of mass spectrometry including systems and methods for mass calibration.

INTRODUCTION

[0002] Mass spectrometry relies upon the measurement of physical values that can be related to the mass-to-charge ratio (m/z) to determine a mass of an ionic species or a compound within a sample. High mass accuracy requires calibration of the measured physical values against species of known m/z or mass. Calibration is generally accomplished with the use of a calibration mixture that produces multiple ionic species of known m/z. However, the choice of ions suitable for use in a calibration mixture may be limited.

[0003] From the foregoing it will be appreciated that a need exists for improved calibration methods for mass spectrometry.

SUMMARY

[0004] According to a first aspect of the present invention, there is provided a method including: producing ions from one or more calibrant species and delivering the ions to a mass analyzer; measuring a first set of mass related physical values for the ions from the one or more calibrant species; producing ions from a sample and delivering the ions to a mass analyzer, the sample including ion species of unknown mass and a first sample ion species of known mass, the first sample ion species having a mass-to-charge ratio outside of the range of the mass-to-charge ratios of the calibrant ion species; measuring a second mass related physical value for the first sample ion species; calculating a calibration curve based on the first set of mass related physical values for the plurality calibrant ion species and second mass related physical value for the first sample ion species; and modifying at least one instrument parameter based on the calibration curve.

[0005] In various embodiments of the first aspect, the mass analyzer can include a Fourier transform mass analyzer. In specific embodiments, the instrument parameter can be selected from the group consisting of a coefficient relating m/z to ion frequency, a frequency range for an image current, a digitizing rate, a filter bandwidth for an image current, and any combination thereof.

[0006] In various embodiments of the first aspect, the mass analyzer can include a quadrupole mass analyzer or a quadrupole ion trap mass analyzer. In specific embodiments, the instrument parameter can be selected from the group consisting of an RF voltage, a DC voltage, and any combination thereof.

[0007] In various embodiments of the first aspect, the mass analyzer can include a time-of-flight mass analyzer. In specific embodiments, the instrument parameter can be selected from the group consisting of a coefficient relating m/z to flight time, an acquisition time window, a flight tube clearing pulse time, and any combination thereof.

[0008] In various embodiments of the first aspect, the sample can be provided by a gas chromatographic instrument.

[0009] In various embodiments of the first aspect, the sample can be provided by a liquid chromatographic instrument.

[0010] In various embodiments of the first aspect, the method can further include providing a second sample including a second sample ion species to the mass spectrometer; operating the mass spectrometer using the modified instrument parameter from the calibration; and measuring a third mass related physical value for the second sample ion species.

[0011] In specific embodiments, the method can further include shifting the calibration curve based on a measured mass-to-charge ratio of a third sample ion species within the second sample to account for scan specific drifts in the calibration curve, wherein the instrument parameter is not changed based on the shifting of the calibration curve. In specific embodiments, the second sample ion species can have a mass-to-charge ratio within the range of the mass-to-

charge ratio of the first sample ion species and the mass-to-charge ratio of at least one of the calibrant ion species.

[0012] In various embodiments of the first aspect, the first sample ion species can have a mass-to-charge ratio above the range of the mass-to-charge ratios of the calibrant ion species.

[0013] In various embodiments of the first aspect, the first sample ion species can have a mass-to-charge ratio below the range of the mass-to-charge ratios of the calibrant ion species.

[0014] According to a second aspect of the present invention, there is provided a mass spectrometer, including: an ion source configured to form ions from one or more calibrant species and from a sample, the sample including ion species of unknown mass and a first sample ion species of known mass, the first sample ion species having a mass-to-charge ratio outside of the range of the mass-to-charge ratios of the calibrant ion species; a mass analyzer configured to measure a mass related physical value for an ion; a controller configured to: obtain a first set of mass related physical values for ions from the one or more calibrant species; obtain a second mass related physical value for the first sample ion species; calculate a calibration curve based on the first set of mass related physical values, the second mass related physical value, and known mass-to-charge ratios of the ions from the one or more calibrant species and the first sample ion species; and modify the operation of the mass analyzer based on the calibration curve.

[0015] In various embodiments of the second aspect, the mass analyzer can include a Fourier transform mass analyzer. In specific embodiments, modifying the operation of the mass analyzer can include modifying a coefficient relating m/z to ion frequency, a frequency range for an image current, a digitizing rate, a filter bandwidth for an image current, and any combination thereof.

[0016] In various embodiments of the second aspect, the mass analyzer can include a quadrupole mass analyzer or a quadrupole ion trap mass analyzer. In specific embodiments, modifying the operation of the mass analyzer can include modifying an RF voltage, a DC voltage, or any combination thereof.

[0017] In various embodiments of the second aspect, the mass analyzer can include a time-of-flight mass analyzer. In specific embodiments, modifying the operation of the mass analyzer can include modifying a coefficient relating m/z to flight time, an acquisition time window, a flight tube clearing pulse time, or any combination thereof.

[0018] In various embodiments of the second aspect, the mass spectrometer can further include a gas chromatograph for supplying a sample to the ion source.

[0019] In various embodiments of the second aspect, the mass spectrometer can further include a liquid chromatograph for supplying a sample to the ion source.

[0020] In various embodiments of the second aspect, the controller can be further configured to operate the ion source to provide a second sample including a second sample ion species to the mass spectrometer; operate the mass spectrometer using the modified instrument parameter from the calibration; and obtain a third set of mass related physical values for the second sample ion species. In specific embodiments, the controller can be further configured to shift the calibration curve based on a measured mass-to-charge ratio of a third sample ion species within the second sample to account for scan specific drift in the calibration curve, wherein the operation of the mass analyzer is not changed based on the shifting of the calibration curve.

[0021] In various embodiments of the second aspect, first sample ion species can have a mass-to-charge ratio above the range of the mass-to-charge ratios of the calibrant ion species.

[0022] In various embodiments of the second aspect, first sample ion species can have a mass-to-charge ratio below the range of the mass-to-charge ratios of the calibrant ion species.

DRAWINGS

[0023] For a more complete understanding of the principles disclosed herein, and the advantages thereof, reference is now made to the following descriptions taken in conjunction with the accompanying drawings, in which:

[0024] Figure 1 is a block diagram of an exemplary mass spectrometry system, in accordance with various embodiments.

CLAIMS

1. A method comprising:

producing ions from one or more calibrant species and delivering the ions to a mass analyzer;

measuring a first set of mass related physical values for the ions from the one or more calibrant species;

producing ions from a sample and delivering the ions to a mass analyzer, the sample including ion species of unknown mass and a first sample ion species of known mass, the first sample ion species having a mass-to-charge ratio outside of the range of the mass-to-charge ratios of the calibrant ion species;

measuring a second mass related physical value for the first sample ion species;

calculating a calibration curve based on the first set of mass related physical values for the plurality calibrant ion species and second mass related physical value for the first sample ion species; and

modifying at least one instrument parameter based on the calibration curve.

2. The method of claim 1, further comprising:

providing a second sample to the mass spectrometer, the sample including a second sample ion species;

operating the mass spectrometer using the modified instrument parameter from the calibration; and

measuring a third mass related physical value for the second sample ion species.

3. The method of claim 2, further comprising:

shifting the calibration curve based on a measured mass-to-charge ratio of a third sample ion species within the second sample to account for scan specific drifts in the calibration curve, wherein the instrument parameter is not changed based on the shifting of the calibration curve.

4. The method of claim 2, wherein the second sample ion species has a mass-to-charge ratio within the range of the mass-to-charge ratio of the first sample ion species and the mass-to-charge ratio of at least one of the calibrant ion species.

5. The method of claim 1, wherein the first sample ion species has a mass-to-charge ratio above the range of the mass-to-charge ratios of the calibrant ion species.

6. The method of claim 1, wherein the first sample ion species has a mass-to-charge ratio below the range of the mass-to-charge ratios of the calibrant ion species.

7. A mass spectrometer, comprising:

an ion source configured to form ions from one or more calibrant species and from a sample, the sample including ion species of unknown mass and a first sample ion species of known mass, the first sample ion species having a mass-to-charge ratio outside of the range of the mass-to-charge ratios of the calibrant ion species;

a mass analyzer configured to measure a mass related physical value for an ion;

a controller configured to:

obtain a first set of mass related physical values for ions from the one or more calibrant species;

obtain a second mass related physical value for the first sample ion species;

calculate a calibration curve based on the first set of mass related physical values, the second mass related physical value, and known mass-to-charge ratios of the ions from the one or more calibrant species and the first sample ion species; and

modify the operation of the mass analyzer based on the calibration curve.

8. The mass spectrometer of claim 7, wherein the mass analyzer includes a Fourier transform mass analyzer or a time-of-flight mass analyzer.

9. The mass spectrometer of claim 8, wherein the controller is configured to modify the operation of the mass analyzer by modifying a coefficient relating m/z to ion frequency, a frequency range for an image current, a digitizing rate, a filter bandwidth for an image current, and any combination thereof.

10. The mass spectrometer of claim 7, wherein the mass analyzer includes a quadrupole mass analyzer or a quadrupole ion trap mass analyzer.

11. The mass spectrometer of claim 7, wherein the controller is configured to modify the operation of the mass analyzer by modifying an RF voltage, a DC voltage, or any combination thereof.

12. The mass spectrometer of claim 7, wherein the mass spectrometer further includes a gas chromatograph for supplying the sample to the ion source.

13. The mass spectrometer of claim 7, wherein the mass spectrometer further includes a liquid chromatograph for supplying the sample to the ion source.

14. The mass spectrometer of claim 7, wherein the controller is further configured to:

operate the ion source to provide a second sample to the mass spectrometer, the sample including a second sample ion species;

operate the mass spectrometer using the modified instrument parameter from the calibration; and

obtain a third set of mass related physical values for the second sample ion species.

15. The mass spectrometer of claim 14, wherein the controller is further configured to:

shift the calibration curve based on an measured mass-to-charge ratio of a third sample ion species within the second sample to account for scan specific drift in the calibration curve, wherein the operation of the mass analyzer is not changed based on the shifting of the calibration curve.

16. The mass spectrometer of claim 7, wherein the first sample ion species has a mass-to-charge ratio above the range of the mass-to-charge ratios of the calibrant ion species.

17. The mass spectrometer of claim 7, wherein the first sample ion species has a mass-to-charge ratio below the range of the mass-to-charge ratios of the calibrant ion species.