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Truly “exact” mass: Elemental composition can be determined uniquely from molecular mass measurement at ~0.1 mDa accuracy for molecules up to ~500 Da

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Abstract

At sufficiently high mass resolution, not all molecular masses are possible, even for arbitrary elemental composition. Here, we consider all possible elemental compositions, $C_cH_hN_nO_oS_s$, c unlimited, h unlimited, $0 < n < 5$, $0 < o < 10$, $0 < s < 3$, for even-electron ions $(M+H)^+$ and $(M-H)^-$, of molecular mass, 300–500 Da. Masses are then sorted into “bins” of width, 5, 1, 0.5, and 0.1 mDa, with inclusion (or not) of up to two ^{13}C’s. The number of different elemental compositions per bin varies from 0 to ~20 for 5 mDa bins, dropping to 0–2 for 0.1 mDa bins (including one ^{13}C) and 0–1 for 0.1 mDa bins (not including ^{13}C). Thus, for molecules up to ~500 Da in mass, mass resolution and accuracy of ~0.1 mDa generally suffice to yield a unique elemental composition for molecules in even the most complex natural mixtures (namely, petroleum crude oil), and higher mass resolution and accuracy are not necessary. The required resolution and accuracy are now becoming available with high-field (9.4–14.5 T) Fourier transform ion cyclotron resonance mass spectrometry.

Keywords: Fourier transform mass spectrometry; Ion cyclotron resonance; ICR; Petroleum; Accurate mass

1. Introduction

This special issue of the *International Journal of Mass Spectrometry* celebrates Jürgen Kluge’s accomplishments, many of which feature ultraprecise determination of ions of a single mass or mass-to-charge ratio, *m/z* (analogous to weighing macroscopic objects on a single-pan balance). Recently, it has become possible to extend such measurements to the analog of a double-pan balance by trapping ions of two different *m/z* values simultaneously [1]. Although such measurements achieve extraordinary precision and accuracy predicted to approach 1 part in 10^{12}, the experiments are necessarily conducted at liquid helium temperature, for ions whose *m/z* values are nearly identical, so as to limit the frequency bandwidth (and thus noise) in the measurement. In this paper, we consider the analytical chemical problem of *broadband* accurate mass measurement, for complex organic mixtures whose mass spectral *m/z* values ranging over a factor of 2–10. Those experiments are typically conducted by Fourier transform ion cyclotron resonance mass spectrometry [2,3].

Accurate mass measurements offer a means to determine the chemical composition of complex organic mixtures such as petroleum [4,5], coal [6], humic/fulvic acids [7], and vegetable oils [8]; to identify proteins [9], and to assign amino acid compositions of peptides [10] and nucleic acid compositions in DNA and RNA [11]. For example, Spengler has shown how to apply accurate mass constraints to MS and MS/MS data, so as to improve the speed and accuracy of protein identification based on mass analysis. All of these methods basically rely on mass defects of various nuclides.

Every isotope of every chemical element has a different mass defect (i.e., difference in Daltons between its exact mass and the nearest integer mass) [12]. Moreover, because no two mass defects are integer multiples of each other, a molecule’s

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elemental composition, e.g., $C_cH_hN_nO_oS_s$, may be determined from sufficiently accurate measurement of its mass [13,14]. However, mass accuracy alone is not enough—it is necessary to *resolve* the masses of all components of a mixture in order to be sure that the measured mass corresponds to just one elemental composition.

Recently ultrahigh-resolution ($m/\Delta m_{50\%} > 300{,}000$, in which m is mass and $\Delta m_{50\%}$ is the mass spectral peak full width at half-maximum peak height) electrospray ionization (ESI) Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS (3)) has resolved more than 10,000 different elemental compositions in a single mass spectrum of petroleum crude oil [15] or coal [6], the most compositionally complex mixtures analyzed to date. Here, we establish the minimal mass resolution required to distinguish essentially all chemically possible (and chemically reasonable) elemental compositions for $C_cH_hN_nO_oS_s$ molecules of 300–500 Da, as encountered in fossil fuel mixtures. Because fossil fuel mixtures are the most compositionally complex, with tens of thousands of different elemental compositions spanning a relative abundance dynamic range of only ~10,000, they provide the most stringent test for mass resolution—all other organic mixtures will have fewer components and thus be easier to identify.

2. Methods

2.1. Computation methods

Possible elemental compositions within a stated mass range were calculated by use of a program compiled with Lab Windows/CVI version 6.0 (National Instruments Co., USA). A calculated list of compositions was saved in comma separated value format (.csv format) and processed by use of the Origin 5.0 program (OriginLab Corp., USA).

2.2. Chemical constraints

Not all possible elemental compositions are chemically possible. For example, the valence rules of chemical bonding lead to the "nitrogen rule" [16]. For even-electron ions, such as $(M + n\mathrm{H})^{n+}$ or $(M - n\mathrm{H})^{n-}$ generated by electrospray ionisation:

Even-mass ions have odd number of nitrogen atoms (1a)

Odd-mass ions have even number of nitrogen atoms (1b)

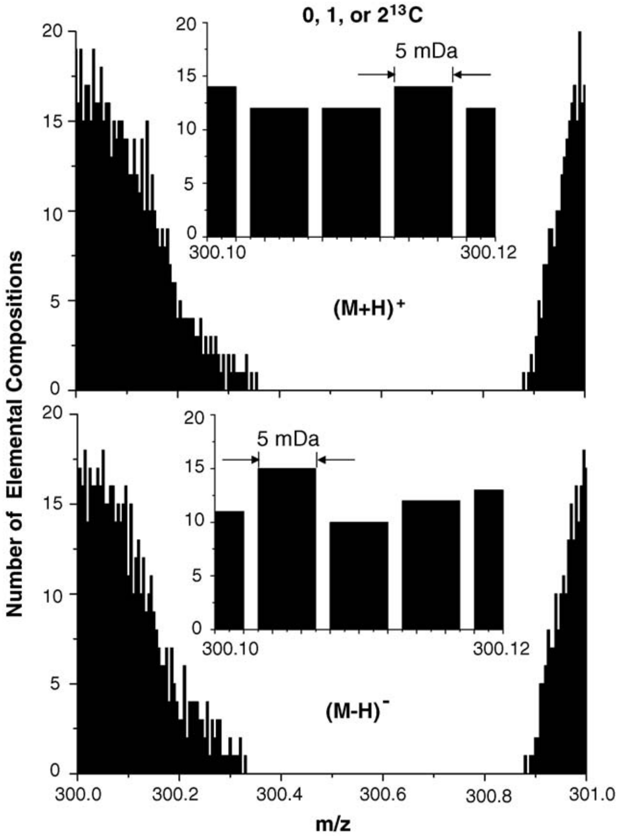

Fig. 1. Number of elemental compositions ($C_cH_hN_nO_oS_s$, c unlimited, h unlimited, $0 < n < 5$, $0 < o < 10$, $0 < s < 3$, including species containing up to two ^{13}C's) as a function of mass, in 5 mDa mass segments, for even-electron ions between 300 and 301 Da. *Top*: $(M + \mathrm{H})^+$ ions. *Bottom*: $(M - \mathrm{H})^-$ ions. *Insets*: mass scale expansion from 300.10 to 300.12.

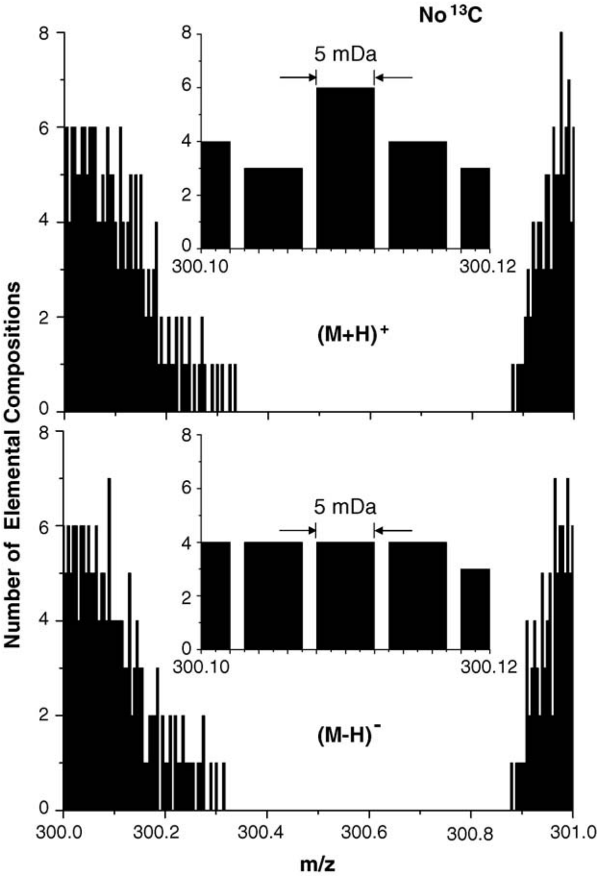

Fig. 2. Number of elemental compositions ($C_cH_hN_nO_oS_s$, c unlimited, h unlimited, $0 < n < 5$, $0 < o < 10$, $0 < s < 3$, excluding species containing ^{13}C) as a function of mass, in 5 mDa mass segments, for even-electron ions between 300 and 301 Da. *Top*: $(M + \mathrm{H})^+$ ions. *Bottom*: $(M - \mathrm{H})^-$ ions. *Insets*: mass scale expansion from 300.10 to 300.12.