Electrically Compensated Fourier Transform Ion Cyclotron Resonance Cell for Complex Mixture Mass Analysis

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# Electrically Compensated Fourier Transform Ion Cyclotron Resonance Cell for Complex Mixture Mass Analysis

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S Supporting Information

ABSTRACT: Complex natural organic mixtures such as petroleum require ultrahigh mass spectral resolution to separate and identify thousands of elemental compositions. Here, we incorporate a custom-built, voltage-compensated ICR cell for Fourier transform ion cyclotron resonance mass spectrometry (FTICR MS), based on a prior design by Tolmachev to produce optimal mass resolution. The compensated ICR cell installed in a custom-built 9.4 T FTICR mass spectrometer consists of seven cylindrical segments with axial proportions designed to generate a dc trapping potential that approaches an ideal three-dimensional axial quadrupolar potential. However, the empirically optimized compensation voltages do not correspond to the most quadrupolar trapping field. The compensation electrodes minimize variation in the reduced cyclotron frequency by balancing imperfections in the magnetic and electric field. The optimized voltages applied to compensation electrodes preserve ion cloud coherence for longer transient duration by approximately a factor of 2, enabling separation and identification of isobaric species (compounds with the same nominal mass but different exact mass) common in petroleum, such as C_3 vs SH_4 (separated by 3.4 mDa) and $SH_3{}^{13}C$ vs $^{12}C_4$ (separated by 1.1 mDa). The improved performance of the ICR cell provides more symmetric peak shape and better mass measurement accuracy. A positive ion atmospheric pressure photoionization (APPI) petroleum spectrum yields more than 26 000 assigned peaks, Fourier-limited resolving power of 800 000 at m/z 500 (6.6 s transient duration), and 124 part per billion root mean square (rms) error. The tunability of the compensation electrodes is critical for optimal performance.
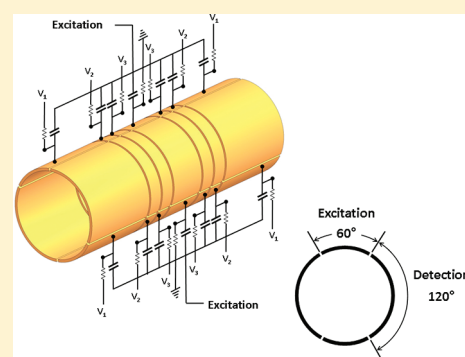
Fourier transform ion cyclotron resonance mass spectrometry (FTICR MS) provides the highest mass resolution and mass measurement accuracy of any broadband mass spectrometer[1,2] and enables confident elemental composition assignment of thousands of sample components with subpart per million (ppm) mass measurement error from a single mass spectrum.[3] Resolving power, $m/\Delta m_{50\%} \geq 400\,000$ (in which $\Delta m_{50\%}$ is the FTICR magnitude-mode mass spectral peak full width at half-maximum peak height) and mass measurement accuracy (<300 ppb rms error) up to 800 Da are now routinely provided by high-field (≥9.4 T) FTICR MS. The high performance of FTICR MS is directly related to transient duration. Factors that limit the transient duration include Coulombic interaction between ions of different m/z, electric and magnetic field imperfection, and collisions with background gas molecules.[4−8] The ultrahigh performance needed for complex mixture analysis requires careful optimization of trapping, excitation, and detection conditions.[9,10]

Various electrically compensated ICR cell designs have been proposed to more closely approximate a pure quadrupolar electric field.[11−15] Recently, Tolmachev et al.[16] described an electrically

compensated open cylindrical ICR cell based on prior work by Gabrielse et al.[17] but optimized for detection of ion cyclotron motion. The Tolmachev cell improves dc potential harmonicity at a large cell radius[16] and allows for larger optimal post-excitation ion cyclotron radius without a loss of ion cloud coherence, resulting in a higher mass resolving power, mass measurement accuracy, sensitivity, and dynamic range for a peptide mixture designed to simulate bottom-up proteomic analysis.

Here, we report implementation and performance of an ICR cell that incorporates compensation electrode geometry similar to that reported by Tolmachev et al. We increase the cell size to take advantage of a large (225 mm diameter) bore, 9.4 T magnet and apply it to FTICR MS of a petroleum crude oil, a complex natural mixture with tens of thousands of known components. The challenge for analysis of such a complex mixture is to maintain the ion cloud phase coherence for ions of all detected m/z values over a wide dynamic range for the entire transient
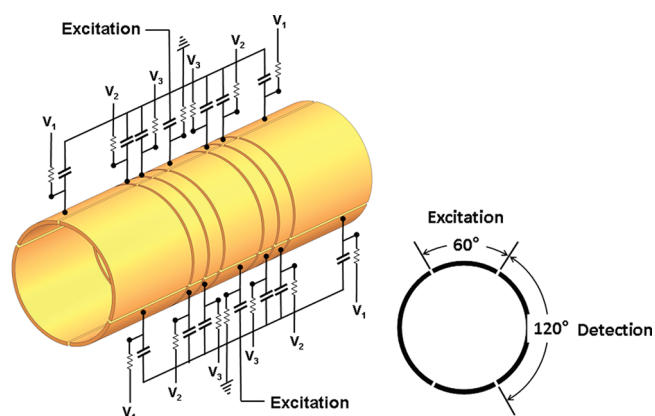
Figure 1. Schematic diagram of the compensated ICR cell, including the capacitive coupling of the excitation voltage on the inner and outer compensation electrodes. Only the central segment is currently used for detection. A transverse cross-section optimized for detection efficiency is displayed on the right.

duration. The new cell improves resolving power, mass accuracy, and dynamic range 2-fold each by increasing the transient duration. Interestingly, the compensation voltages that most closely approach a pure quadrupolar potential are not optimal for mass resolution and mass accuracy.

■ EXPERIMENTAL PROCEDURES

Crude Oil. South American heavy crude oil and a North American crude oil (~10 mg) were each diluted in 5 mL of toluene (HPLC grade, Sigma-Aldrich Chemical Co., St. Louis, MO) to make a stock solution. The stock solution was further diluted in toluene to yield a final concentration of 250 μg/mL for analysis by atmospheric pressure photoionization (APPI) or electrospray ionization (ESI) FTICR MS.

Instrumentation. Experiments were performed with a custom-built FTICR mass spectrometer equipped with a passively shielded 225 mm bore 9.4 T superconducting magnet (Oxford Instruments, Abingdon, Oxfordshire, U.K.).[18] Figure 1 illustrates the compensated ICR cell, consisting of 7 cylindrical, 94 mm i.d. segments with proportions based on the Tolmachev et al. design.[16] Specifically, the axial length of each outermost trapping segment is 93 mm; outer and inner compensation segments are each 16.3 mm; and the central segment length is 44.5 mm, with a 2.5 mm gap between adjacent segments. Cell plates constructed of oxygen-free high thermal conductivity (OFHC) copper are held in place by titanium fasteners and Macor spacers connected to an outer aluminum support shell. The angular extent of each detection and excitation electrode is 120° and 60° for an optimized detection surface area.[19] The 60° electrodes are capacitively coupled to all of the trapping segments (150 kΩ resistors and 1 nF capacitors) to minimize axial excitation.[20] The measured pressure in the ICR cell region was ~1.8 × 10^{-10} Torr. Broadband frequency-sweep excitation (720–100 kHz at a sweep rate of 50 Hz/μs and 360 V$_{p-p}$ amplitude) accelerates ions to a calculated cyclotron orbital radius of 19 mm (i.e., ~40% of the cell radius), followed by broadband detection (6.6 s data acquisition period to yield 8 Mword time-domain data with a low mass Nyquist threshold of m/z 228). 250 time-domain acquisitions were summed,

Hanning-apodized, and zero-filled once, prior to fast Fourier transform and magnitude calculation. Instrument control and data analysis were performed with a modular ICR data station.[21]

■ RESULTS AND DISCUSSION

ICR Cell Design. The internal diameter of our ICR cell was chosen to be ~57% larger than that reported by Tolmachev et al.[16] to take advantage of the large bore diameter of the magnet. Further, a larger cell diameter decreases the magnetron frequency and thus any magnetron frequency variation associated with a nonquadrupolar trapping potential. The larger cell has a greater ion storage capacity and lower charge density for the same number of ions.

Complex Mixture Analysis. The ultrahigh mass resolving power ($m/\Delta m_{50\%}$ = 450 000–650 000 at m/z 500) and accurate mass capability (<300 ppb rms mass error) of FTICR MS make it ideally suited for confident assignment of elemental composition to each of tens of thousands of crude oil components in a single mass spectrum.[22,23] However, spectral complexity can nevertheless exceed the accessible mass resolution, which is limited by pressure, magnetic and electric field imperfections, and space charge. Figure 2 demonstrates the improved performance achieved with the new cell. The transient duration of 6.6 s for analysis of crude oil is approximately 2-fold longer than routinely achievable with a three-segment open cylindrical cell with an aspect ratio of 2,[20] and more than 29 000 peaks with a peak height >6σ of baseline rms noise (228 < m/z < 1000 Da) are resolved and assigned with an rms error of 124 ppb. A mass scale-expanded segment at m/z 497 shows some common isobaric overlaps between species of the same nominal mass. The mass resolving power achieved for all assigned peaks is Fourier limited, indicating that all ion clouds maintain phase coherence throughout the entire detection period.[24] Optimized compensation voltages improve peak shape (i.e., decreased peak splitting, broadening, and asymmetry) critical for precise mass determination. Adjustment of the compensation voltages allows the ICR cell to operate as a typical three-segment cell to provide a direct comparison between compensated and uncompensated configurations (see Figure S1 in the Supporting Information). For positive electrospray ionization of a North American crude oil, the number of assigned elemental compositions nearly doubles: from 3 640 (three-segment configuration) to 6 710 (seven-segment configuration). An increase in transient duration from 3.6 s typically achieved with a conventional three-segment cylindrical cell to 6.6 s now routinely achieved with the electrically compensated cell significantly extends the upper mass limit for confident identification of elemental composition. For example, the upper mass limit for resolution of isobaric species common in petroleum (or peptides), such as C_3 vs SH_4 (separated by 3.4 mDa) increases from m/z 975 to 1325 and for $SH_3{}^{13}C$ vs $^{12}C_4$ (separated by 1.1 mDa) increases from m/z 540 to 740 (for equal magnitude peaks). The new cell promotes linear behavior throughout a longer transient duration, facilitating absorption-mode data reduction[25] and further improvement in resolving power, mass accuracy, signal-to-noise ratio, and dynamic range.

ICR Cell Operation. Ultrahigh performance requires careful tuning of compensation electrode voltages for optimal transient duration and peak shape. Experimentally determined optimal
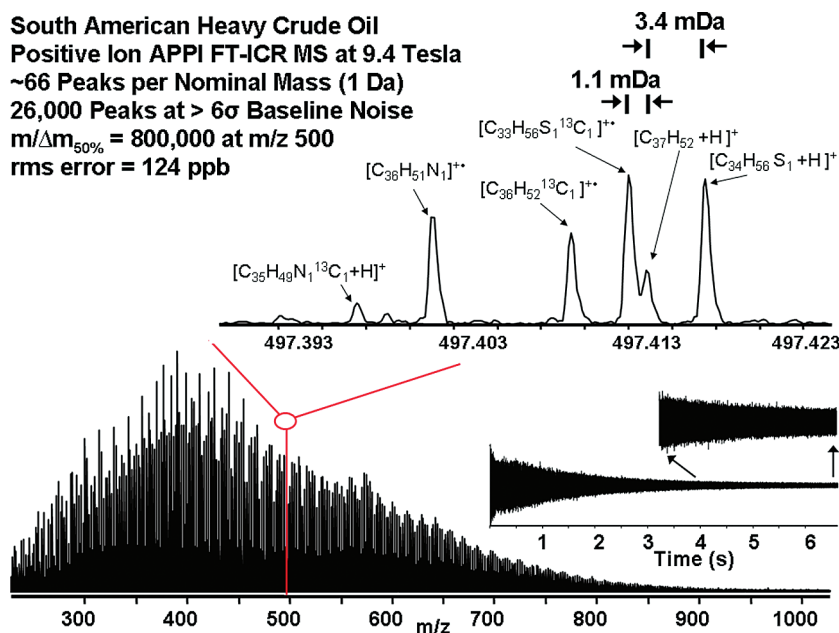
Figure 2. Broadband positive-ion APPI FTICR mass spectrum of a heavy crude oil. More than 26 000 peaks with magnitude greater than 6 times the standard deviation of the baseline noise are baseline-resolved from $228 < m/z < 1\,000$. The inset shows the peak shape along with typical mass splits observed in ultrahigh-resolution crude oil mass spectra.

voltages deviate from values (trap +0.70 V, outer segment +0.20 V, and inner segment −0.20 V) that should most closely approach a pure quadrupolar potential. Brustkern et al. have also reported that optimal performance for their electrically compensated ICR cell design was achieved with values that deviate from optimally quadrupolar.[26] A purely quadrupolar electrostatic trapping potential is optimal only for a spatially homogeneous magnetic field. However (see below), optimal performance in an inhomogeneous magnetic field may require a slightly nonquadrupolar trapping potential.[27] When the spectrometer axial position was shifted with respect to the magnet, the compensation voltages had to be reoptimized, indicating that the electrical shims compensate for magnetic field inhomogeneity. Deviation from the compensation voltage designed to most closely approach a quadrupolar trapping potential may also help to accommodate a distribution in ion axial kinetic energy. A change in compensation electrode potential by as little as ±50 mV shortens the transient duration and/or distorts the peak shape. The optimal post-excitation ion radius for complex mixture analysis is ∼40% of the cell radius, about the same as for a three-segment cylindrical cell and independent of the excitation sweep rate or peak voltage, indicating that the transient duration is limited by other factors at higher radius (e.g., magnetic field inhomogeneity or pressure). Tests are underway to elucidate the limiting mechanism. Resolution of up to thousands of elemental compositions in the most complex mixtures necessitates acquisition of a long-duration time-domain signal over a wide m/z range: hence, excitation is limited to <50% of the compensated cell radius. For less complex samples for which lower resolution suffices, ions may be excited to ∼65% of the compensated cell radius. The shorter central (detection) segment of the compensated cell reduces the detection surface area compared to a standard three-segment cylindrical cell and effectively decreases the signal magnitude. The reduction in signal magnitude depends on ion axial amplitude but is effectively recovered by a 2-fold increase in transient duration

(and thus spectral peak height) and increased radial extent of the detection electrodes. In addition, the increase of the angular extent of the detection electrodes from 90 to 120 degrees essentially eliminates third harmonic signals.[19,28]

■ CONCLUSIONS

We have applied an electrically compensated FTICR cell for complex mixture analysis (in this case, crude oil). The improved tunability of the trapping electric field results in a 2-fold increase in transient duration and associated improvement in resolving power and mass accuracy. Longer transient duration extends the mass range for confident unique elemental composition assignment. Careful tuning of the compensation electrodes results in optimal peak shape and Fourier-limited line width ($m/\Delta m_{50\%} = 800\,000$ at m/z 500) for >6.6 s detection period and ∼125 ppb mass measurement error over a wide mass range, e.g., more than 26 000 mass spectral peaks assigned in a single mass spectrum. Ultimate performance for complex mixtures is achieved for a post-excitation ion cyclotron radius equal to ∼40% of the cell radius, i.e., the same as for a three-segment cylindrical cell, presumably limited by magnetic field inhomogeneity. The experimentally determined optimal compensation voltages differ from those that most closely approximate a quadrupolar potential, also consistent with compensation for magnetic field inhomogeneity.

■ ASSOCIATED CONTENT

ⓢ Supporting Information. Time-domain ICR signals and broadband positive ESI FTICR mass spectra for a North American crude oil, acquired with a three-segment open cylindrical ICR cell and a seven-segment electrically compensated cell; almost twice as many elemental compositions could be assigned for the compensated cell. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

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