PARTICLE-IN-CELL SIMULATIONS OF ION MOTION IN NOVEL FTICR-MS ANALYZER CELL DESIGNS

by

JOSHUA A. DRIVER

(Under the Direction of I. Jonathan Amster)

ABSTRACT

Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) is based on the measurement of an ion’s cyclotron frequency. This measurement is based on the interaction of ions with the magnetic and electric fields present in the analyzer. These can be applied fields or space-charge resulting from ions being confined in the analyzer cell. Recently, several new analyzer cell designs have been developed, aiming at improving mass resolving power, mass accuracy, or both. These new analyzers change ion motion and detection in different ways, and understanding these changes can help guide experiment design and aid in the development of newer analyzer cells. Multi-particle simulations provide insight to the manner in which the new cell designs improve performance. Particle-in-cell (PIC) simulations offer a computationally tractable method for understanding ion motion in an FTICR-MS analyzer cell. In the presented work, PIC simulations are extended to include accurate modeling of image charge forces, and used to understand ion motion in new analyzer cells with unique detection schemes.
INDEX WORDS: Particle-in-cell, Fourier transform ion cyclotron resonance mass spectrometry, ion trajectory calculations, multiparticle simulations
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JOSHUA A. DRIVER

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by

JOSHUA A. DRIVER

Major Professor: I. Jonathan Amster
Committee: Josh Sharp
Ron Orlando

Electronic Version Approved:

Suzanne Barbour
Dean of the Graduate School
The University of Georgia
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DEDICATION

To Nicki and my family.
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CHAPTER 1
INTRODUCTION AND LITERATURE REVIEW

The work presented in this dissertation extends the capabilities of particle-in-cell simulations to include accurate image charge detection and forces for Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) and applies them to novel modes of ion detection. It focuses on computational comparisons of different FTICR-MS analyzer cell geometries and their effects on mass accuracy and resolution. FTICR-MS offers the highest mass accuracy and resolving power of any mass spectrometer [1]. Its analytical capabilities and versatility have made it an important tool in many areas of study including proteomics, metabolomics, and petroleomics [2-7]. FTICR-MS can be used to obtain elemental compositions [8], structural information via tandem mass spectrometry [9-13], and to examine ion-ion/ion-molecule chemistry [14-16]. As FTICR-MS technology has improved, there has been increasing interest in the development of new analyzer cells, designed to obtain the highest possible resolving power and mass accuracy [17-20].

History of FTICR-MS

The theory of ion cyclotron resonance (ICR) was first developed in 1930 by E. O. Lawrence [21]. The goal in these experiments was to accelerate protons, and later light ions, to study atomic properties [22]. The principle of ICR is that an ion in motion perpendicular to a magnetic field will move in a circular orbit with a frequency that is independent of its velocity. The radius of this orbit could be increased by applying an on-resonance radiofrequency (RF) electric field to electrodes orthogonal to the magnetic field. Due to conservation of angular
momentum, an increase in radius resulted in higher velocity ions. Increasing the ion’s orbital radius will later be referred to as excitation, and is a critical aspect of modern FTICR-MS. This can be seen in Figure 1.1.

Figure 1.1. Diagram of Lawrence’s cyclotron. An alternating electric field is applied to two semi-circular electrodes which are inserted into a magnetic field. The magnetic field is scanned and when an ion’s cyclotron frequency comes into resonance with the alternating electric field the ion’s orbital radius increases along with its velocity.

The next major advancement toward FTICR-MS came in 1949, when the principle of ICR was used in the omegatron mass spectrometer to precisely determine the value of a faraday [23]. The same group later showed that the instrument could be used to determine the mass to charge ratio ($m/z$) of gases present in their vacuum system [24]. This system functioned by continuously applying an RF electric field and scanning the magnetic field. When the RF field matched an ion’s orbital frequency, the radius of orbit would increase and the ion would strike a collection plate. The ion’s $m/z$ can be derived from the strength of the magnetic field when the ion strikes the plate. In the 1960s, these types of instruments were being used to study ion-
molecule reactions in several laboratories, including Wobschall [25], Llewellyn [16], and Baldeschwieler [26]. During this era, Wobschall showed that an ion could be measured by its resonant power absorption rather than by striking a collection plate. Ernst et al. showed how Fourier transform methods borrowed from nuclear magnetic resonance techniques could be applied to ICR to decrease time required to record a spectrum and increase the sensitivity [27].

The beginning of modern FTICR-MS came in 1974 with developments by Comisarow and Marshall [28]. This first experiment used a fixed frequency RF to excite CH$_4^+$ ions, detected and digitized the signal, then used discrete Fourier transform to create a frequency-domain spectrum. This achieved a higher signal-to-noise ratio and resolution than previous methods and paved the wave for further developments. This quickly led to the application of a fast frequency sweep for excitation of multiple ionic species [29] and development of electronics to handle broadband detection in FTICR-MS [30]. These experimental techniques (frequency sweep excitation and broadband detection followed by Fourier transform of the signal) are still the basic experimental design of modern FTICR-MS experiments [1].

**Forces Affecting Ions in FTICR-MS**

The fundamental principles of FTICR-MS are based on relatively simple physics and are the subject of several reviews in the literature [1, 31-33]. If we consider an ion in a magnetic field, we can employ Newtonian mechanics to determine the Lorentz force experienced by the ion as follows:

\[ F = ma = m \frac{dv}{dt} = q(v \times B) \]  

Equation 1.1

Where \( m, q, \) and \( v \) are ionic mass, charge, and velocity and \( B \) is the magnetic field strength. This includes a cross product since the magnetic field only exerts a force on an ion if a component of
the velocity is perpendicular to the magnetic field. The Lorentz force results in an ion’s trajectory being curved into a circular orbit of radius \( r \). Since angular acceleration \( = \frac{dv}{dt} = \frac{v^2}{r} \), the equation then becomes

\[
\frac{mv^2}{r} = qvB
\]

Equation 1.2

Which can be expressed in terms of angular frequency, \( \omega = \frac{v}{r} \), as:

\[
m\omega^2r = qB\omega r
\]

Equation 1.3

And then rearranged into the basis for ion cyclotron resonance, the well-known cyclotron equation:

\[
\omega_c = \frac{qB}{m}
\]

Equation 1.4

This equation shows that the cyclotron frequency of an ion depends only on its mass, charge, and the strength of the magnetic field. SI units are \( \omega_c \) in rad/s, \( q \) in Coulombs, \( B \) in Tesla, and \( m \) in kg. It is often easier however to express the cyclotron frequency in terms of Hertz, and the mass to charge ratio \( (m/q, \text{ often expressed } m/z) \) in terms of Daltons per multiple of the elementary charge:

\[
f_c = \frac{\omega_c}{2\pi} = \frac{1.535611 \times 10^7 B}{m/z}
\]

Equation 1.5

Therefore, if an ion in a magnetic field of 1 T is determined to have a cyclotron frequency of 100 kHz, we know the mass to charge ratio of the ion is 153.56. Importantly, all ions of a given \( m/z \) will orbit at this same cyclotron frequency regardless of ion velocity. This means unlike other mass spectrometry methods, there is no need to perform energy focusing steps to improve resolution.

Unfortunately, this is only true for a single ion in a magnetic field without any other fields present. Since the magnetic field has no effect on ion motion parallel to the magnetic field, other forces (in this case electric fields) must be applied to keep the ion from drifting out of the
detector. A typical FTICR-MS analyzer cell is a Penning trap, with ions confined radially by a magnetic field and axially electric fields. Now equation 1.1 becomes:

\[ F = ma = m \frac{dv}{dt} = q(v \times B) + q(E) \]  \hspace{1cm} \text{Equation 1.6}

Where \( E \) is the applied electric fields. Application of electric fields perturbs ion motion and introduces two interrelated modes of motion. The first is straightforward, the application of trapping voltages induces a simple harmonic oscillation perpendicular to the trapping plates. This is known as ‘trapping’ or ‘axial’ motion and its frequency (\( \omega_z \)) can be described by:

\[ \omega_z = \sqrt{\frac{2qV\alpha}{ma^2}} \]  \hspace{1cm} \text{Equation 1.7}

Where \( V \) is the trapping voltage, \( \alpha \) is a constant based on the geometry of the analyzer cell, and \( a \) is the distance between the trapping plates of the analyzer cell.

The second mode of motion, known as ‘magnetron’ motion, arises from the combination of the magnetic and electric fields. The trapping field produces an axial force, but it also produces a radially repulsive force. Figure 1.2 shows the potential gradient at the center of an analyzer cell. Effectively there exists a potential ‘hill’ that forces the ions to drift away from the center of the analyzer cell. Physically, the ions are progressing around the potential hill at their magnetron frequency while simultaneously undergoing cyclotron motion as shown in Figure 1.3. The magnetron frequency can be determined by:

\[ \omega_m = \frac{2aV}{a^2B} \]  \hspace{1cm} \text{Equation 1.8}

It is important to note that \( \omega_m \) is independent of mass and charge, but depends instead on trapping voltage. Since the ions are being pushed radially outward by the electric fields, and the magnetic field is confining the ions radially, these forces act in opposition. The result is an apparent weakening of the magnetic field strength. From equation 1.4 we can see that a weaker
Figure 1.2. The isopotential surface present at the center of the analyzer cell due to the application of trapping electric fields. A radially repulsive electric field pushes ions away from the center of the analyzer cell. *(Adapted from Amster 1996 [1])*

Magnetic field results in a lower cyclotron frequency. In fact, the reduced cyclotron frequency \( \omega_c \), sometimes observed cyclotron frequency, \( \omega_o \), is related to \( \omega_c \) by equation 1.9:

\[
\omega_c = \omega_o + \omega_m \text{ or } f_c = f_o + f_m
\]  
Equation 1.9

This allows for calibration of the data to obtain the actual \( m/z \) of ions in the mass analyzer. New designs of mass analyzer can also help to moderate these effects and will be the primary subject of discussion in a later section.
Figure 1.3. An ion trajectory in a cylindrical analyzer cell that shows both cyclotron and magnetron motion. Magnetron motion causes the center of cyclotron motion to process around the potential hill, following one isopotential contour (red lines). The magnitude of magnetron radius relative to cyclotron radius is shown much larger than normal operating conditions for clarity.

An ion contained by a magnetic field and electric fields then has three modes of motion: cyclotron motion, axial motion, and magnetron motion. Additionally, an ion can undergo collisions with neutral molecules in an ICR, leading to damping of ion motion. A collision with a neutral will result in a loss of velocity and kinetic energy for that ion. This will affect all three modes of ion motion. Loss of velocity will cause an ion’s cyclotron radius to shrink since it is directly proportional to velocity. Axial motion will be dampened and ions will condense toward the axial center of the cell. Magnetron radius will increase as a lower velocity ion will fall further down the potential hill. Eventually, this will result in ions striking the electrodes and being neutralized. In general, collisions produce negative results in an ICR, so the pressure is usually held very low ($10^{-9}$ to $10^{-10}$ Torr) to prevent them. However, there are some applications that use
higher pressures to accomplish tasks such as fragmenting ions in the cell (in-cell collisionally activated dissociation) or taking advantage of physics to convert magnetron motion into cyclotron motion (quadrupolar axialization excitation) [1].

Primarily, the forces acting on the ions are the result of applied electric and magnetic fields. In an actual FTICR-MS experiment there are many ions present in the analyzer. Ions of the same m/z grouped together in space is called an ion cloud. Each ion cloud will have some amount of charge associated with it, and these charges influence the trapped ions, resulting in perturbations of ion motion. This effect is known as space charge, and can introduce shifts in the observed frequency and a spread in the frequency of an ion cloud, resulting in a loss of resolution [34, 35]. As ion clouds of different m/z values pass close to each other in space their like-charges repel each other leading to a temporary reduction in the observed frequency. If there are many ions clouds of different m/z, each ion cloud is experiencing many different temporary shifts during the timeline of an experiment. The frequency shift caused by space charge is dependent upon the ion cloud density, \( \rho \), and shape of the ion cloud, defined by the constant \( G_i \), and can be calculated by the following equation:

\[
\frac{q \rho G_i}{\varepsilon_0 B} \quad \text{Equation 1.10}
\]

Although this force can’t be removed, it can be accounted for through external calibration methods that include considerations for space charge [36-40]. Furthermore, these effects can be moderated by limiting the number of ions allowed into the analyzer cell through automated gain control (AGC) [41].

Traditionally, space charge frequency shifts are only observed when two or more ion clouds are present in the mass spectrometer [42]. However, it has been shown that increasing the number of ions in the analyzer cell will cause a frequency shift even in the case of a single ion.
cloud [43]. This effect is caused by ions interacting with the charge that they induce upon the metal surfaces of the analyzer cell [44-46]. Since this is the smallest of the forces presented here, these forces (called image charge forces) are not usually directly accounted for in FTICR-MS experiments, although calibration methods have been used that include considerations for ion abundance or involve walking calibration which could indirectly account for image charge forces [36, 47, 48]. Image charge forces are usually considered as a subset of space charge forces.

All the fields (magnetic and electric) affect the ways ions move in an FTICR mass analyzer. Now that the basics of ion motion have been covered, the experimental configuration used to measure the $m/z$ of an ion will be described.

**Ion Measurement in an FTICR Mass Analyzer**

In a typical FTICR mass analyzer, ions are constrained by a Penning trap and measurement of the signal is facilitated by two pairs of opposing plates (electrodes) as shown in Figure 1.4. One set of electrodes (excitation plates) is used to excite ions to higher cyclotron orbital radii, while the other set of plates is used for detection. With most other types of mass spectrometers, detection is performed using electron multipliers, and the ions are neutralized in the process. In contrast, FTICR-MS measures the image current caused by the oscillation of image charge, and the detection plates act as antennae for this image charge. Image charge is a slight misnomer, since it refers to one method of solving a class of problems dealing with the interaction of charges and conductors, the method of images. Actually, what it refers to is the distribution of induced charges on an electrode surface by an ion or ion cloud.
Figure 1.4. A typical ICR cell design with pairs of electrodes for excitation and for detection. E1 and E2 are excitation plates, and D1 and D2 are detection plates.

First consider a single ion with a positive charge executing a cyclotron orbit within the analyzer in Figure 1.4. As the ion approaches plate D1, it will attract electrons to the plate generating a negative image charge. As it continues its orbit, it will approach plate D2 and attract electrons to that plate. The alternating current between these two plates, the image current, is sinusoidal and can be detected by an RC circuit. If the ion were negatively charged, it would repel electrons from each plate generating a positive image charge, but would essentially work the same way. The frequency of the image current is then the observed frequency of the ion.

Now consider 1000 ions of the same m/z. Initially, ions introduced into the mass analyzer will have incoherent cyclotron orbits, which would not produce any signal as the charge from one ion will cancel the charge from another. The first step necessary for detection is to make the
ions orbit coherently. This is achieved by applying a sinusoidal RF voltage to the excitation plates with a frequency equal to the ions’ cyclotron frequency. The ions are attracted to each excitation plate in turn, and the cyclotron radius of all ions are increased, bringing the ions closer to the detection plates, with a coherent cyclotron motion. The frequency of the ion cloud is measured, and the signal is proportional to the number of ions present in the cloud. Applying a single RF frequency to excite ions of a single $m/z$ is called burst excitation.

![Time domain Signal](image)

**Time domain Signal**

![Frequency domain spectrum](image)

**Frequency domain spectrum**

Figure 1.5. Broadband detection in FTICR-MS results in a time domain transient (top). By applying a Fourier transform, the individual frequency components can be determined, generating a frequency domain spectrum (bottom). This spectrum shows multiple charge states of cytochrome C, with an inset showing frequencies for the individual isotopes present in one charge state.
In an actual experiment, there are many ion clouds with different \( m/z \) values. To measure many ion clouds at once, i.e. broadband detection, it is necessary to excite all the ions present. This is accomplished by applying an RF voltage of many frequencies during the excitation event. By starting at a high frequency and rapidly sweeping to lower frequency, the unique ion frequencies will be part of the signal. By applying this RF ‘chirp’, all ions of interest will be excited to an approximately equal cyclotron radius and will be moving in coherent motion with all other ions of the same \( m/z \) value. Each of the ion clouds will produce a sinusoidal image current, and the signal will be the superposition of these sinusoidal waveforms of differing frequencies and amplitudes. This signal is then digitized and becomes the time domain transient or free inductive decay (FID) and Figure 1.5 shows an example of a transient. The frequencies and the respective intensities can be resolved from the complicated time domain transient by applying a Fourier transform [27, 28].

Application of the Fourier transform results in a frequency spectrum. The frequency spectrum cannot be directly converted to the mass spectrum via the cyclotron equation due to the frequency shifts caused by magnetron motion and space charge forces. It is necessary to calibrate the data based on known masses. This can be done with an external calibrant, using a sample of known mass to set the calibration constants before acquiring a spectrum of the sample of interest. Alternatively, since FTICR-MS can measure many masses at once, the data can be calibrated using an internal calibrant, a peak in the spectrum of known mass. The simplest calibration equation that includes consideration of space charge is shown in equation 1.11:

\[
\left( \frac{m}{z} \right)_i = \frac{A}{f_i} + \frac{B}{f_i^2} + C \left( \frac{I_i}{f_i^2} \right) \quad \text{Equation 1.11}
\]

Where \( A \) and \( B \) are empirically derived constants based on the magnetic field and trapping field, \( C \) is another derived constant that considers space charge forces, and \( f \) and \( I \) are the frequency
and intensity respectively of the data point [49]. As mentioned previously, it is possible to perform calibration in a walking manner, calibrating short sections of the frequency spectrum with different constants, to improve mass accuracy [48]. This accounts for local frequency shifts caused by space charge forces.

The basic sequence of an FTICR experiment involves four events. The sequence can be visualized as a series of pulses. The first pulse is called a quench, which is an asymmetric voltage applied to the trapping plates of the analyzer cell, so that all ions present in the analyzer are removed. Next, ions are created with an ionization event. FTICR-MS originally used matrix assisted laser desorption ionization (MALDI) [50] or electron ionization (EI) [51] to generate ions inside the magnetic field. This was done to circumvent the fact that ions were prevented from entering the magnetic field by the magnetic mirror effect [28, 52]. Since that time, various methods have been developed to allow for ion injection, making FTICR-MS compatible with nearly any ionization method [53-55].

Once the ions are in the analyzer cell, the third pulse, excitation, is used to excite ions into coherent motion to generate an image current. We have previously discussed RF burst and RF chirp excitation, but these commonly used techniques have some limitations. A RF burst excites primarily a single ion, but can induce some off-resonance excitation in ions with similar cyclotron frequency. The RF chirp suffers from poor excitation resolution as well as well as an uneven power distribution. A more ideal excitation waveform can be generated by using a technique known as stored waveform inverse Fourier transform (SWIFT) [56]. With this method, the excitation properties are defined in the frequency domain. An inverse Fourier transform can then convert the frequency spectrum into a time domain signal, which, when applied to the excitation plates, excites ions in a precise manner. A comparison of the frequency domain of a
SWIFT excitation and an RF chirp excitation is shown in Figure 1.6. This technique has even been used to purposefully excite ions to different excitation radii to reduce the ion density and resulting space charge effects [57].

![Figure 1.6. Excitation power for a chirp excitation (blue) and SWIFT excitation (red). Chirp excitation has poor resolution and uneven power, in this case even applying excitation at 0 Hz which will induce magnetron motion. SWIFT excitation has even power distribution and perfect excitation resolution.]

The final pulse or event is ion detection. This is achieved by detecting the alternating current between two opposing detection plates, known as dipolar detection. Current hardware allows for the detection of very long transients. However, as the names transient and free inductive decay suggest, the signal of a given ion cloud is limited in duration. Originally, the cause of this limitation was thought to be collisions with neutrals resulting in dampening of ion motion followed by neutralization of the ions [1]. Now however, it is understood that, while collisions do cause some loss of signal, the primary loss of coherence is due to imperfect
trapping electric fields [58]. Novel analyzer cells have been developed to help mitigate this problem, and they will be discussed in detail later.

**Mass Accuracy, Mass Resolution, and Resolving Power**

Resolution, in all types Fourier transform spectroscopy, is usually defined as the full spectral peak width at half of the peak’s maximum intensity ($\Delta\omega_{50\%}$ or $\Delta m_{50\%}$) and is usually expressed in Daltons (mass resolution) or Hertz (frequency resolution). This is done because two peaks of equal height and shape tend to first develop a noticeable valley when the distance between two peaks is slightly more than $\Delta\omega_{50\%}$. Resolving power is defined as $\omega/\Delta\omega_{50\%}$ or $m/\Delta m_{50\%}$ which is particularly useful as these two values are equal. Resolving power can be obtained from a frequency spectrum or a mass spectrum. This can be confusing as this is directly contrary to the IUPAC definitions of resolution and resolving power for mass spectrometry [59]. By the definitions used in FTICR-MS, higher resolving power provides better separation between peaks. In an ideal case, i.e. the transient doesn’t decay to zero during the acquisition, peak width will be the same for all $m/z$. However, since ICR frequency is inversely related to mass, the peaks will be closer together at higher $m/z$. Mass accuracy is the difference between the measured mass and the true mass and is usually reported in ppm or millidaltons. Although the correct units for $m/z$ is Thompsons, Daltons are often used, assuming a single charge for an ion.

The high resolving power of FTICR-MS is directly related to the number of cyclotron orbits an ion cloud undergoes during the acquisition. One way to maximize resolving power is to increase the field strength of the magnet. A one second acquisition with a 1 Tesla magnet will measure an ion with $m/z$ 400 approximately 38,390 times, giving a resolving power of 31850 and a mass resolution of 0.0126 Da. If the magnetic field strength is increased to 9.4 Tesla the same ion is measured approximately 288390 times, leading to a resolving power of 360,860, and
a mass resolution of 0.0011 Da. Theoretically this is enough to measure the difference between a molecule with 2 C$^{13}$ isotopes and a molecule with one O$^{18}$ isotope. Observing this isotopic fine structure can provide the exact elemental composition of a compound of interest, which is extremely helpful in its identification [7, 8]. The resolving power increases linearly with magnetic field strength. It is important that the area of the magnetic field that ions occupy is homogeneous, otherwise an ion’s cyclotron frequency will change as it orbits and undergoes trapping oscillations. Fortunately, this is not usually a limiting factor in FTICR MS because the requirements for nuclear magnetic resonance (NMR) magnets exceed those of FT-ICR. Since NMR is such a common tool in science today, the manufacturing of magnets has developed quite well. Currently, the highest field FTICR magnets are the 21 Tesla magnets at the National High Magnetic Field Laboratory and at Pacific Northwest National Laboratory [60, 61].

The cost associated with higher field magnets can be prohibitive [1]. One method of increasing resolution without expensive hardware changes is to apply signal processing methods that can increase resolution. Absorption mode, commonly used in Fourier transform nuclear magnetic resonance techniques, can increase the resolving power of an FTICR mass spectrum by nearly a factor of two without any hardware changes [62]. A Fourier transform of a time domain signal produces a complex output with real and imaginary terms. Normal operation, known as magnitude mode transformation, requires no knowledge of the phase shift of the signal in computing the Fourier transform. Absorption mode uses phase information to plot the real portion of the signal, granting an increase in resolving power, mass accuracy and the signal to noise ratio (S/N) [63]. Unfortunately, the typical design of FTICR-MS experiments makes obtaining the phase information difficult, as the phase varies throughout the spectrum. Some software has been developed that attempts to solve the phase function for a given spectrum,
allowing absorption mode FTICR-MS, but the computation can be time consuming [64]. Other ‘super-resolution’ data processing methods exist, but they all have a computational cost involved, and, thus, are only used in cases where extremely high resolving power is required [65-67].

Another method to maximize resolving power is to measure a transient for a longer period. However, as mentioned before, the coherence of a given ion cloud is limited in duration. It is important to use as low pressure as possible for the analyzer region of the mass spectrometer, to avoid collisional damping of ion motion. Of equal importance, it is necessary to use an analyzer cell that maximizes the potential resolving power. Although FTICR-MS can provide the highest resolving power and mass accuracy of any mass spectrometer, proper experiment design is necessary to attain best performance.

**Types of Trapping Electric Fields**

The first FTICR-MS experiments used an ion trap with an orthorhombic geometry [28, 29]. Later this design was modified to a cubic cell for use in solenoidal magnets [68]. Eventually, rectilinear geometry gave way to close-ended cylindrical cells, since a cylinder could make fuller use of the cylindrical bore of the superconducting magnets used in FTICR-MS [69]. One problem with these analyzers is that they alter the excitation field lines, introducing an axial component to ion excitation [70]. This led to ions being ejected from the cell axially. One remedy for this problem involved the introduction of an open-ended cylindrical analyzer with capacitive coupling between the excitation plates and the trapping plates [71, 72]. Another option which maintained the closed-cell geometry was the ‘Infinity Cell’ [73]. With this analyzer, the trapping plates are segmented preventing the abrupt termination of field lines that caused axial ejection. Both the open-ended cylindrical cell and the Infinity Cell are commonly used in
FTICR-MS today. While these cells maintain homogeneous excitation fields, they do not have an ideal trapping field due to their effects on magnetron motion.

Magnetron motion depends upon the trapping voltage. Equation 1.12 shows a simplified derivation of the magnetron frequency:

\[ \omega_m = \frac{2}{B} \cdot \frac{E_r}{r} \]  

Equation 1.11

where \( E_r \) is the radial electric field and \( r \) is the ion’s radial displacement from the z-axis. For most commonly used analyzer cells, there is a spatial gradient in the ratio of \( E_r/r \), leading to a change in magnetron frequency across the analyzer cell [1]. Since the observed frequency is dependent upon the magnetron frequency, the result of this changing frequency is that ions of the same \( m/z \) in different parts of the cell will be orbiting at different frequencies and those ions will eventually lose coherence. In an ideal 3D quadrupolar trapping potential, \( E_r/r \) is constant, therefore magnetron frequency is constant over the full volume of the cell. Several analyzer cell designs have been presented to address the effects of trapping fields on ion motion.

A 3D hyperbolic trap can produce a nearly ideal hyperbolic field, but the design introduces other issues. Because the region that ions can occupy is much smaller than the bore of the magnet, the charge capacity and dynamic range of the analyzer will be greatly reduced. Additionally, the distance between an ion and the detection plates will vary as a function of axial position, which introduces a change in detection amplitude as the ions oscillate along the z-axis. These shortcomings led to the development of other techniques for creating an ideal hyperbolic electric field.

With modern cell design, static or dynamic harmonization is used to shape the electrical field of a cylindrical analyzer cell to closely approximate the ideal trapping field. Static harmonization makes use of compensation rings to alter the trapping potential. Compensation rings are annular
electrodes that are placed inside the trapping electrodes and are set to potentials that shape the
trapping field. There have been several statically harmonized analyzer cells introduced in recent
years that differ mainly in the number of compensation electrodes used. The Gabrielse and
Tolmachev designs used 2 and 4 compensation electrodes respectively and were designed to
make the radial electric field constant across the trapping region of the analyzer cell [19, 74]. The
Rempel-Gross cell design used 6 compensation electrodes and was designed to make the radial
electric field equal to zero at across the trapping region for ions at 40% of the cell radius [20].
These designs create an electric field that approximates that of an ideal electric field, but because
there are a finite number of electrodes, these are imperfect.

Dynamically harmonized analyzer cells (DHCs) approximate an ideal electric field via
radial averaging. As an ion undergoes cyclotron motion, it ‘sees’ an average electric field that
corresponds to a 3D hyperbolic field. The Boldin-Nikolaev design achieves this by shaping the
cylindrical electrodes into a series of alternating leaf and hourglass shapes [18]. The trapping
voltage is applied across the hourglass electrodes which creates the dynamically harmonized
trapping potential. The externally shimmed ‘window’ cell introduced by the Environmental
Molecular Sciences Laboratory at Pacific Northwest National Laboratory uses a series of ring
electrodes to create a trapping well, much like a statically harmonized cell, then uses a
‘windowed’ internal cylindrical cell for excite and detect [75].

Another analyzer of interest is the Narrow Aperture Detection Electrodes (NADEL) cell
[76]. The NADEL is named for the two flat electrodes that extend in toward the center of the
analyzer cell as shown in Figure 2. This design was originally implemented to alter the function
of the ion transient from the normal sinusoidal function to a ‘sha’ function. This would provide
an opportunity to use signal processing options other than the Fourier transform as a method to
increase resolution. Upon testing this cell, the designers discovered that these electrodes, along with a DC offset on the excitation electrodes cause the ions to move in an unusual manner. One side effect of this unusual ion motion is that a Fourier transform of the resulting transient shows the unperturbed cyclotron frequency, which has several advantages. A SIMION model for each of the described analyzer cells is shown in Figure 1.7. Full understanding of these analyzers can help guide future cell and experiment designs.

Figure 1.8. SIMION models of various analyzer cell designs.

**Simulation of Ions in FTICR-MS**

Even in the early days of FTICR-MS, the theory of ion motion in the analyzer cell was an important area of research, and many groups in both FTICR and charged particle physics
attempted to analyze ion dynamics [32, 74, 77-79]. The theoretical understanding of ion dynamics is limited due to the difficulty of handling different analyzer geometries and ion-ion interactions [80]. When SIMION was developed and made widely available, it simplified simulation of a single ion in different analyzer geometries [81]. SIMION can provide much useful information, but it does not have appropriate capabilities for simulating space charge and image charge forces on ions.

It is therefore necessary to use specialized simulation software to gain improved understanding of ion motion. Multi-particle simulations provide a useful approach for studying collective ion motion in an FTICR analyzer cell, and to accurately model the influence of subtle effects such as space-charge and ion-image charge interactions [44, 82-86]. Simulations provide the ability to test the effects of parameters that are difficult to control experimentally such as the precise number and spatial distribution of ions in an analyzer cell [87]. The design of high-performance Fourier transform mass analyzers can be assisted by multiparticle simulations, which can predict the improvements in coherence of ion motion, mass resolving power, and mass accuracy resulting from novel cell designs [18]. More importantly, better understanding of the forces acting on ions in the analyzer cell can assist in designing experiments.

Simplified 2D simulations were used in the late 80s and 90s to understand coulombic interactions in FTICR-MS [88, 89]. The first attempts at a 3D simulation involving multiple particles were performed by Miluchichin et al. in 1993 [90]. These simulations used a parallel computer with 1024 processors to calculate the trajectories of 512 ions with the same $m/z$ to demonstrate the ion cloud’s evolution in a non-uniform electric field including the effects of space charge, though neglecting image charge forces. To account for space charge effects, the force of each ion must be evaluated for every other ion. The implementation difficulty of this
model comes from the number of calculations, which grows with the square of the number of ions. In 1999, Dale Mitchell circumvented this problem by using a particle-in-cell (PIC) method, borrowed from the plasma physics community, which offers a computationally tractable way to examine the motion of realistic numbers of ions while maintaining an accurate account of space charge [91]. It avoids the need for calculating $N^2/2$ pairwise forces between $N$ different ions. Instead, the PIC method determines the charge density at each node of a computational mesh, then uses this charge density to determine the forces acting on each ion. The number of such calculations scales with $N$ using the PIC approach, rather than $N^2$ for the particle-particle approach, greatly reducing the computational effort when modeling the behavior of large populations of ions. This approach allowed Mitchell to simulate 350,000 ions while incorporating the major forces on the ions including magnetic field, trapping field, space charge, image charge and ion-neutral collisions. PIC was further optimized by Nikolaev’s group allowing $10^7$ interacting ions to be simulated for $5 \times 10^8$ time-steps.

PIC simulations have been applied to aide in the understanding of several problems in FTICR-MS. Mitchell’s first experiment was applied to the understanding of ion cloud coalescence. In this case of coalescence, two ion clouds with similar cyclotron frequencies could phase-lock, begin rotating together, and generate a single peak in the mass spectrum. Mitchell’s simulations confirmed a $B^2$ dependence for the minimum ion density required to cause coalescence. In 2007, Nikolaev et al. used PIC simulations to determine the minimum number of ions required for an ion cloud to stabilize and generate a long-term signal (condensation) [58]. They determined that condensation was improved quadratically with magnetic field strength and that the number of ions required for condensation was generally greater than the number required to produce a detectable image current. These experiments also showed that an electric field
gradient results in a gradual dephasing of an ion cloud and signal decay due to ions of the same \textit{m/z} ratio having different observed frequencies. Prior to this, collisional dampening was considered the primary mode of signal decay. Later, several FTICR-MS analyzer cells were developed with harmonized electric fields, some of which were first explored via PIC simulation [19, 20, 92]. In 2010, Leach et al. compared PIC simulations to experimentally observed frequency shifts between ions of the same \textit{m/z} [44]. As explained above, theory suggests that ions of the same \textit{m/z} should not induce a frequency shift in each other. Experimentally, a shift is present and different from the shift induced by traditional space charge. PIC simulation confirmed that the shifts were due to interactions between ions and their induced image charge. PIC has also been applied to the understanding of other Fourier transform mass spectrometry methods, namely the orbitrap [93]. These simulations looked at the performance of an orbitrap under non-ideal circumstances [84]. The research presented in this dissertation addresses some of the problems associated with the application of PIC to FTICR-MS mass analyzers and improves upon the technique.

One downside of PIC simulations is the way image charge is determined. Image current is determined on the boundaries of the PIC workspace, which works well when studying rectilinear analyzer cells, but fails in the case of cylindrical analyzer cells. \textbf{Chapter 3} describes a new method for determining image charge and the force due to image charge on surfaces of arbitrary geometry. This method, called the ‘charge colocation method’ is parallelizable and results in accurate accounting of image charge in a reasonable timeframe. Frequency shifts due to image charge are examined for a 3D quadrupolar trapping potential and a Tolmachev type analyzer cell.
With a method to determine image charge on arbitrary surfaces, we can examine a more radical cell design. **Chapter 4** applies PIC simulations to the Narrow Aperture Detection Electrodes (NADEL) cell [76]. This analyzer is not harmonized and it is expected to lose ion cloud coherence and signal rapidly. Instead of rapid decay of signal, excitation of the magnetron motion generates a stable signal that contains the unperturbed cyclotron frequency. The ability to measure this frequency offers advantages in increasing mass accuracy and calibration. This chapter explores how the unique ion cloud structures caused by the electric fields generates the unperturbed cyclotron frequency. Coalescence in this analyzer is compared to coalescence in a DHC.

A final method for increasing resolution in FTICR-MS is to measure the ion cloud’s motion multiple times per cyclotron orbit, which is accomplished by increasing the number of detection electrode pairs. The biggest issue with detection at multiples of the cyclotron frequency is the inclusion of unwanted subharmonic peaks. For example, if the cell is designed to detect the third harmonic, peaks also appear at the second harmonic and fundamental. **Chapter 5** outlines the factors that cause these unwanted signals and suggests methods to minimize their intensities. The effect of signal intensity as a function of detection harmonic is also explored.


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CHAPTER 2
EXPERIMENTAL METHODS

The Particle-in-Cell Method

Any simulation method used for studying ion motion inside a FTICR-MS mass analyzer must account for all forces acting on the ions. An ion in an ICR cell experiences the Lorentz force due to the magnetic field, applied electric fields (excitation and trapping), the electric fields from other ions (space charge), and the electric field induced in the metal detection plates (image charge). The magnetic field is constant throughout the experiment and the electric field only changes in predictable ways. Space charge and image charge forces however, must be calculated at every time-step. In theory, these forces could be calculated directly at every time-step via the Green function. This is known as the particle-particle method [1]. The particle-particle method determines the electric field due to every individual ion, then applies that electric field to every other ion present. This means that as the number of ions being simulated increases, the number of calculations needed increases quadratically. This requires an extremely long time to calculate the total force acting on each ion for a realistic number of ions.

The particle in cell (PIC) method differs from the particle-particle method in the way it handles interactions between charged particles [2-4]. PIC circumvents this exponential explosion by interpolating the charge from each ion to a position on a computational mesh grid as shown in Figure 2.1. The Poisson equation is then solved using the charge density at each node on the computational mesh. In this case, the number of calculations needed increases linearly with the number of ions present.
Figure 2.1. 2D example of charge distribution in the particle-in-cell method. An ion’s charge is spread among the nodes of a computational mesh grid. The amount of charge distributed to each node is determined by the ion’s proximity.

The Particle-in-Cell Algorithm

The PIC algorithm utilizes a series of consecutive time-steps, for which the ion positions and velocities are integrated. Calculations at each time-step can be broken down into the individual calculations as shown in Figure 2.2. Ions are given a starting position and starting velocity, then the charge is interpolated to the mesh grid by means of a 3D weighting algorithm. Next, fast Fourier transform (FFT) methods are used to solve the Poisson equation for the charge density at that step resulting in an electric field due to ions. For a standard cubic cell or rectilinear cell, the charge present on the workspace boundaries determines the image charge and the resulting point in the transient signal. Next, we can superimpose the electric field due to the ions to the applied electric fields, which are imported from SIMION models, and calculate the force of ions due to the electric field. This can be added to the force on ions due to the magnetic field in the force equation:
\[ m \frac{dv}{dt} = q [v \times B] + qE(r,t) \quad \text{Equation 2.1} \]

New ion positions are then solved via a Boris integrator, and the cycle starts again. In this model, accurate accounting of magnetic fields, electric fields, space charge and image charge are maintained for ions in an analyzer of rectilinear geometry. Image charge forces are not accurately accounted for cylindrical analyzer cells, and the addition of a charge colocation based method for accurately modelling image charge in cells of arbitrary geometry is the subject of Chapter 3. This separate calculation is added to the algorithm after solving the Poisson equation and the resulting electric field is added to the electric field calculations.

Figure 2.2. PIC workflow. Without a separate image charge calculation, the transient signal can be determined after charge interpolation by considering the charge distributed to node on the workspace boundaries, but this is only accurate for rectilinear analyzer cells.

Even with the PIC method, calculations can take a long time to complete and so the PIC code has been parallelized to run on massively parallel ad-hoc processors, Graphics Processing Units (GPUs). This saves time as the force on each ion can be calculated in parallel. Every calculation is performed in parallel except for solving the Poisson equation.
The particle-in-cell code was executed on z-cluster, a Linux cluster at the University of Georgia, on nodes equipped with Intel Xeon processors and NVIDIA K40m GPU cards. The PIC software is highly parallelized and uses the GPU cards to decrease calculation times. It also includes a charge colocation based method for determining image charge as described in Chapter 3. The simulations utilized a homogeneous magnetic field with a strength of 7, 10, or 12 Tesla. The analyzer cell geometry is defined by a Lua script and the electric fields are refined in SIMION. Ions are generated in a Gaussian or line distribution along an ellipsoid with the major axis parallel to the magnetic field. The initial particle velocity distribution is Maxwellian at 300K and the direction of the velocity vector is randomized. Ions are subjected to an excitation field then the ion image charge is detected for a period of time. A simulated time domain transient was collected for each experiment and a frequency domain spectrum was derived using FOM-AMOLF’s AWE software [5]. The ion cloud and the resulting image charge distribution was visualized with in-house software developed at FOM-AMOLF [6].
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CHAPTER 3

FAST IMAGE CHARGE CALCULATIONS FOR MULTIPARTICLE SIMULATIONS IN FT-ICR ANALYZER CELLS OF ARBITRARY GEOMETRY

ABSTRACT

As improvements in Fourier transform ion cyclotron resonance (FT-ICR) mass analyzers continue to provide higher resolving power and better mass accuracy, it becomes important to consider small perturbations to the observed frequency such as those resulting from the interaction between an ion and its image charge. Multi-particle simulations can help in understanding these forces. Previously, particle-in-cell simulations have used a basic implementation of the image charge force on the flat edges of the workspace. In the case of cylindrical cells, however, this does not provide an accurate representation of these forces. Until recently, the calculation of image charge on curved electrodes has been impractical due to the high computational cost, but this cost can be mitigated by parallelizing the calculations on general purpose Graphic Processing Units (GPUs). In this paper, a new parallelizable charge collocation based method for including high resolution image charge effects on surfaces of arbitrary geometry is presented. This method is then used to explore the effects of image charge interactions on observed cyclotron frequency in cylindrical ICR analyzer cells by simulating the trajectories of populations of Cs$^+$ ranging from 20,000 ions to 1,000,000 ions.
INTRODUCTION

Multi-particle simulations provide a useful approach for studying collective ion motion in an FTICR analyzer cell, and to accurately model the influence of subtle effects such as space-charge and ion-image charge interactions [1-5]. Simulations provide the ability to test the effects of parameters that are difficult to control experimentally such as the precise number and spatial distribution of ions in an analyzer cell [6]. The design of high-performance Fourier transform mass analyzers can be assisted by multiparticle simulations, which can predict the improvements in coherence of ion motion, mass resolving power, and mass accuracy resulting from novel cell designs [7]. Accurate simulation of ion dynamics requires an accounting of subtle effects such as the force introduced by the image charge upon ions moving in the trap. Until recently, modeling precise image charge behavior (i.e. with a sufficiently large number of surface charges) in cells of arbitrary geometry was impractical due to the significantly increased amount of computation time required by existing surface charge calculation methods [1]. However, recent progress in massively parallel coprocessors has made it possible to significantly speed-up such calculations.

To track each ion’s evolution in time, we need to integrate the force equation:

\[ m \frac{dv}{dt} = q [v \times B] + qE(r, t) \quad \text{Equation 3.1} \]

to find the ion’s velocity vector \( v \) where \( q \) is the charge on the ion, \( B \) is the magnetic field acting on the ion, \( E \) is the composition of electric fields acting on the ion, \( r \) is ion’s coordinate vector, \( P \) is the number of other ions, \( m \) is ion’s mass, and \( t \) is the time step. The largest force is due to the
magnetic field, and is given by \( q[v \times B] \). This force produces cyclotron motion, which in the absence of electric fields, has a frequency given by:

\[
\omega_c = \frac{qB}{m}
\]  

Equation 3.2

The second term, \( qE \) comprises the forces due to electric fields [8, 9].

\[
E = E_{\text{app}} + E_{\text{sc}} + E_{\text{ic}}
\]  

Equation 3.3

Here \( E_{\text{app}} \) is the applied electric field created by voltages that are applied to cell electrodes, \( E_{\text{sc}} \) is the electric field due to ion-ion interactions, also known as space-charge, \( E_{\text{ic}} \) is the electric field from the image charge induced on the analyzer cell plates. \( E_{\text{app}} \) is the strongest of the electric fields, while \( E_{\text{ic}} \) is the weakest.

\( E_{\text{app}} \) includes both trapping (quadrupolar) and excitation (dipolar) electric fields. Ideally, the ratio of \( E/r \) is constant for the trapping potential (\( r \) is radial displacement from the central axis of the analyzer cell). The radially repulsive force of the trapping potential leads to magnetron motion of the ion, and a reduction in the observed orbital frequency from the ideal value given by equation 2. For most commonly used analyzer cells, there is a spatial gradient in the trapping field, leading to a change in magnetron frequency across the analyzer cell, and thus, a loss of coherence as ions undergo axial motion [8]. However, the development of harmonized analyzer cells has improved this undesirable behavior [7, 10-13]; magnetron frequency is very close to a constant over the volume of such compensated analyzer cells. One of the advantages of harmonized cells is their ability to maintain cloud coherence at a higher radius of excitation.
where space charge effects are less prominent due to the decrease in ion density. However, an increase in excitation radius leads to an increase in the effects of image charge interactions [5]. This means it is necessary to find a compromise between these effects in order to optimize FTICR performance. As mass accuracy continues to improve due to advances in controlling the adverse effects of applied electric fields and space charge on ion motion, smaller effects like image charge can now play a significant role. It would be advantageous to have a better understanding of the magnitude of image charge effects and how they vary due to changes in various parameters.

Next in magnitude are the effects of space charge $E_{sc}$, specifically ion-ion interaction [14, 15]. This perturbation of ion motion can be treated in a global fashion and acts on all ions in a similar manner. Developments such as automated gain control [16] and external calibration functions [17-21] that account for space charge have thoroughly reduced their effects on mass accuracy to the point where other smaller perturbations can be considered. The implementation difficulty comes from the number of calculations, which grows with the number of ions. There are a number of frameworks circumventing this problem and the particle-in-cell (PIC) method, borrowed from the plasma physics community, offers a computationally tractable way to examine motion of realistic numbers of ions while maintaining an accurate account of space charge [22-24]. It avoids the need for calculating $N^2/2$ pairwise forces between $N$ different ions. Instead, the PIC method determines the charge density at each node of a computational mesh, then using this charge density to determine the forces acting on each ion. The number of such calculations scales with $N$ using the PIC approach, rather than $N^2$ for the particle-particle approach, greatly reducing the computational effort when modeling the behavior of large populations of ions.
Even smaller in magnitude than space-charge interactions are image-charge interactions with ions $E_{ie}$. Previously, attempts have been made to isolate the effects of ion-image charge interactions [5]. These experiments showed that populations of Cs$^+$ ions interacted with their image charge to cause a frequency shift that increases in magnitude with ion number and excitation radius. However, these attempts were based on a cubic analyzer cell and used only the basic implementation of image charge interactions provided by PIC calculations in which image charge is calculated on the walls of the orthorhombic PIC grid and included in the $qE(r,t)$ term. The PIC approach calculates the electric field of the trapped ions at each PIC node in the workspace. The electric field at the extents of the cubic workspace is equivalent to image charge, and aligns with the electrode surfaces in a cubic cell simulation, as shown in Figure 3.1 (left).

For a cylindrical cell simulation in a cubic workspace, the location of the image charge force on the flat edges of the workspace is a poor representation of the actual image charge which should accumulate on the cylindrical cell surfaces. To examine these effects in cells with newer...
cylindrical geometries, more accurate results require the calculation of the image charge on the inner surface of the cylindrical electrodes rather than on the edges of the PIC workspace.

Prior attempts to implement high-resolution image charge simulations experienced performance difficulties due to the need to perform linear algebra operations or even solve the Poisson equation. The capacitance matrix method, for example, has been used to calculate image charge on cylindrical cells [1], but it cannot be parallelized, and therefore is highly inefficient for simulations of transients of even nominal length. The challenge of making accurate calculations of the image charge created in an arbitrary shaped electrode can be solved by allocating a number of virtual charges on the electrode surface. Then the detected signal is the current of charges between the halves of the outer electrode:

\[ I(t) = \frac{dQ_{1,2}}{dt} \]  

Equation 3.4

where \( Q_{1,2} = Q_1 - Q_2 \) is the difference of total surface charges on detection electrodes “1” and “2”: \( Q_{1,2} = \sum_{i=1}^{N} \sigma_{1,2i} \). This approach, called charge collocation, has the advantage that it can be implemented as parallelizable computer code that can executed using graphical processing units for processing quickly and efficiently. This paper demonstrates this approach, validates by comparison with earlier, slower methods, and applies it to the examination of image charge effects on mass accuracy in a compensated analyzer cell.

**EXPERIMENTAL**

Multi-particle simulations were performed on Linux clusters at the University of Georgia and the Foundation for Fundamental Research on Matter-Institute for Atomic and Molecular
Physics (FOM-AMOLF). Data analysis was performed with FOM-AMOLF’s AWE and A. Kharchenko’s ParticleVis software. The parameters for the simulations are summarized in Table 1. The analyzer cell geometry is in accordance with a Tolmachev cell design with a diameter of 6 cm. Simulations utilized an idealized quadrupolar trapping potential or a trapping potential defined by a SIMION model of a Tolmachev cell. A monoisotopic population of Cs$^+$ ions (m/z = 139.905) was generated in a Gaussian distribution along an ellipsoid (major axis = 20 mm; minor axis = 5 mm) with the major axis parallel to the magnetic field. The initial particle velocity distribution is Maxwellian at 300K and the direction of the velocity vector is randomized. For excitation, an on-resonance radiofrequency burst is used at excite voltages between 40 and 320 V\textsubscript{p-p} in order to achieve excite radii between 10% and 80% of the cell radius. A simulated time domain transient was collected for each experiment and a frequency domain spectrum was derived using FOM-AMOLF’s AWE software [25]. The ion cloud and the resulting image charge distribution was visualized with in-house software developed at FOM-AMOLF [2].

Calculating the surface charge distribution

Let the surface charges having charge density $\rho(x,y,z)$, where $x,y,z$ are Cartesian coordinates, be located in some volume $V$. If $V$ is bounded, say with a conductor surface $S$, the Laplace equation $\nabla^2 \varphi = 0$ in such a volume will be

$$\frac{1}{4\pi\varepsilon\varepsilon_0} \int_V \frac{\rho}{r} dV = \varphi$$

Equation 3.5
where \( r \) is distance between the integration and observation points. In the case where the charge is located on some surface, for some points \( A \) and \( B \) on that surface the equation (5) can be reformulated as

\[
\frac{1}{4\pi\varepsilon\varepsilon_0} \int_S \frac{\sigma_A}{r_{AB}} dS_A = \varphi_B \quad \text{Equation 3.6}
\]

where \( S \) is the conductor surface, \( \sigma_A \) is the surface charge density at location \( A \), \( dS_A \) – element of surface at location \( A \), \( r_{AB} \) – distance between the points, and \( \varphi_B \) – potential at point \( B \).

If we allocate a grid of \( N \) discrete points on the surface \( S \), not necessarily regularly spaced, charge density of each element is constant (\( \sigma_i = \text{const} \)), then equation (6) will become

\[
\frac{1}{4\pi\varepsilon\varepsilon_0} \sum_{i=1}^{N} \int_{S_i} \frac{\sigma_i}{r_i} dS_i = \frac{1}{4\pi\varepsilon\varepsilon_0} \sum_{i=1}^{N} \sigma_i \int_{S_i} \frac{dS_i}{r_i} = \varphi_B \quad \text{Equation 3.7}
\]

Such a substitution of a surface integral with a sum of integrals of the surface’s elements allows one to find surface charge densities at discrete locations by solving the corresponding system of linear equations with \( N \) unknowns \( \sigma_i \) and \( N \) coefficients \( a_{ij} = \int_{S_i} \frac{dS_i}{r_{ij}} \):

\[
\begin{pmatrix}
    a_{11} & a_{12} & \cdots & a_{1N} \\
    a_{21} & \ddots & \vdots & \vdots \\
    \vdots & \ddots & \ddots & \vdots \\
    a_{n1} & a_{n2} & \cdots & a_{nn}
\end{pmatrix}
\begin{pmatrix}
    \sigma_1 \\
    \vdots \\
    \vdots \\
    \sigma_n
\end{pmatrix}
= 4\pi\varepsilon\varepsilon_0
\begin{pmatrix}
    \varphi_1 \\
    \vdots \\
    \vdots \\
    \varphi_n
\end{pmatrix}
\quad \text{Equation 3.8}
\]

Getting back to the mass spectrometry theme, remember that in an ion trap, surface charges are distributed in a certain way not only under the influence of potentials \( \varphi_i \) but mainly
influenced by the ions $q_1 ... q_P$, each at a distance $d_{ik}$, whose field can be approximated by the point charge potential $\varphi_Q = \frac{q_i}{4\pi\varepsilon\varepsilon_0 d_i}$. Accordingly, equations (7) and (8) should be reformulated as

$$\sum_{i=1}^N \sigma_i \int_{S_i} \frac{dS_i}{r_i} = \frac{1}{4\pi\varepsilon\varepsilon_0} \left( \varphi_B - \sum_{k=1}^P \frac{q_k}{d_{ik}} \right) \quad \text{Equation 3.9a}$$

and

$$\begin{pmatrix} a_{11} & a_{12} & \cdots & a_{1n} \\ a_{21} & \ddots & \vdots \\ \vdots & \ddots & \vdots \\ a_{n1} & a_{n2} & \cdots & a_{nn} \end{pmatrix} \begin{pmatrix} \sigma_1 \\ \vdots \\ \vdots \\ \sigma_n \end{pmatrix} = 4\pi\varepsilon\varepsilon_0 \begin{pmatrix} \varphi_1 - \sum_{k=1}^P \frac{q_k}{d_{1k}} \\ \vdots \\ \varphi_n - \sum_{k=1}^P \frac{q_k}{d_{nk}} \end{pmatrix} \quad \text{Equation 3.9b}$$

where $d_{ik}$ is a distance between the $k$-th ion and $i$-th surface charge location. The negative sign of the sums of ions’ potentials is explained by the opposite charges of the ions and surface charges that they induce. At $i \neq j$ coefficient $a_{ij}$ is finite, but it has a singularity at $i = j$, however, the expression is integrable: if we consider a disc of small radius $R$ around point $i$, then remembering that $dS = rdrd\alpha$, we can state that

$$\int_{S_i} \frac{dS_i}{r_{ij}} = \int_0^{2\pi} \int_0^R \frac{rdrd\alpha}{r_{ij}} = 2\pi R \quad \text{Equation 3.10}$$

which proves that $a_{ij}$ is finite at both $i \neq j$ and $i = j$. Figure 3.2 demonstrates how this is applied to the electrode surface of an FTICR mass analyzer.

A more detailed description of the PIC method and how it incorporates charge collocation can be found in the Supplemental Data.
Figure 3.2. Principle of surface charge density calculation in the presence of ions in the trap. The grid of surface charges are shown as colored balls, where the color represents charge density (blue is maximum negative charge density, red is maximum positive charge density, with intermediate values following the color scale of the rainbow.) Ions are represented by $q_n$ and $q_m$. The charge density at a specific node is determined from the charges at surrounding nodes and from ions trapped in the analyzer cell (see supplemental text).

Remark on the capacitance matrix approach

Matrix

$$A = \begin{pmatrix} a_{11} & a_{12} & \cdots & a_{1n} \\ a_{21} & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & \vdots \\ a_{n1} & a_{n2} & \cdots & a_{nn} \end{pmatrix}$$

Equation 3.11
in equation 9 can also be considered as the Maxwell capacitance matrix $C$ of a system of conductors having voltages $V$ and charges $Q$:

$$Q = CV$$

Equation 3.12

This suggests an alternative method of calculating elements of $A$: to calculate the $k$-th column one should set the potential of $k$-th conductor (that is, $k$-th element of $V$) to 1 leaving the other conductors’ potentials equal to 0 and the resulting vector of $Q$ will yield the $k$-th column of $C$. As a result we have a system of $N$ equations for $N$ unknowns which determines values of the surface charges induced on each electrode. It can be numerically solved via pseudo-inversion. This method has been used previously to study space charge in an orbitrap FTMS analyzer [1, 3], however, it is not parallelizable and thus requires a large amount of computational time.

**RESULTS AND DISCUSSION**

**Method validation and stability**

To determine the number of image charge points necessary for stability, simulations were performed with increasing density of surface charges and the observed frequency was monitored, as shown in Figure 3.3a. With very few surface charges, the frequency varies as much as 0.35 Hz with surface charge density. Once a sufficient number of surface charges are used, the frequency is stable. Figure 3.3a shows that the observed shifts will be reproducible if the number of surface charges is greater than about 4 per square cm of conductor surface.
Figure 3.3. Frequency shift as function of the surface charge grid size and as observed for different methods for calculating image charge. (a) Relative error in observed frequency for increasing number of surface charges in 5 cm cubic cell, determined by comparison of simulation results using the collocation method versus results using the PIC workspace grid. (b) Comparison of image charge induced frequency shifts in the cubic cell for the collocation method for calculating image charge versus using the implicit image charge on the surface of the PIC workspace. These give identical results, as expected for a cubic cell. When the image charge calculation is eliminated in the PIC simulation, the observed cyclotron frequency is constant for all excitation radii, as shown by the green line.

To make sure the charge collocation method returned accurate results, it was necessary to make a comparison with an established method. The simplest way of doing this was to compare directly to the previous particle in cell method for determining image charge shifts in a cubic cell. Surface charges were placed equidistant along the boundaries of the workspace for a 2 in cubic cell. This effectively mimics the previous PIC method of calculating image charge forces on the rectilinear boundaries of the workspace [24]. At first, this setup resulted in frequency shifts approximately twice that of the original PIC method. It became apparent then that we had to remove the boundary PIC points from the force equation in order to not have the image charge
force applied from both the PIC calculation and the charge collocation method. This removal of points becomes especially important for application of this method to cylindrical cells because without this extra step the image charge force on the ions would be the force from the edges of the workspace superimposed upon that of the cylindrical electrodes. Figure 3.3b shows the observed frequency shifts vs. increasing excitation radius for both the charge collocation method and the PIC method. The average difference between these two methods is 2.6 mHz or a relative error of 3.2 ppb. The simulations show a shift of $2.0 \times 10^{-6}$ Hz per ion in a 5 cm (2 inch) cubic cell at 7.0 T, due to the interaction of an ion with its image charge. Several groups have previously made analytical calculations of image charge force for a single ion, which we can use as a baseline for comparison [26, 27]. Marshall and coworkers calculated the force in a 2.5 cm cubic cell at 3.0 T to be $1.0 \times 10^{-5}$ Hz per ion for excitation to 50% of the cell radius. Correcting for the $1/B$ dependence, this shift becomes $4.6 \times 10^{-6}$ Hz per ion at 7.0 T. Tinkle and Barlow calculated the shift in a 4 cm cubic cell at 7.0 T to be $2.7 \times 10^{-6}$ Hz per ion. Given the differences in cell design and initial ion locations, our simulations are in good agreement with these analytically derived values. We can also consider a comparison to experimental results as additional evidence of this method’s validity. Even though we cannot accurately determine the number of ions in the analyzer cell during an experiment, we can check that the observed frequency shift corresponds to a reasonable number of ions. Wong et al. have measured a cyclotron frequency shift as a function of Cs$^+$ ion intensity, with a 50 fold difference in ion intensity between the highest and lowest ion numbers used in this experiment [28]. The frequency shift between the largest and smallest population of ions is 0.7 Hz, roughly corresponding to 350000 ions, using the PIC derived value for frequency shift per ion of
2.0 × 10^{-6} \text{ Hz}. This number of ions seems reasonable for a high intensity peak, and suggests agreement with the PIC calculated value for image-charge induced frequency shift.

**Implementation and performance**

![Figure 3.4](image)

Figure 3.4. Snapshots of 100K Cs ion cloud with the induced image charge distribution in the Tolmachev (left) and cubic (right) analyzer cells. The charge distribution on the cubic surface is shown without the front XY edge.

An incentive to use the charge collocation method, albeit its computational cost, is its intrinsic parallelism allowing an efficient implementation on a computation cluster of the multiple-instruction multiple-data (MIMD) type. Being performed on independent processing units, equation 9, apart from parallelism, require accessing a large number of adjacent memory locations (the arrays of ion charge and position) which motivated our choice of Graphics Processing Units (GPUs) hardware of the single-instruction multiple-data (SIMD) type, known
to excel in computational schemes with coalesced memory access. Error! Reference source not found.

3.4 presents graphical

Figure 3.5. Simulation time comparison between GPU and CPU calculations. (a) Performance versus number of surface charges, using a GPU for the image charge calculation. The metric for performance is the duration of one time step (calculating the new position of all ions, and the electric field and image charge distribution). (b) Same calculation as in (a), but using the CPUs of the Linux cluster to perform the image charge calculation. (c) Scalability of the overall simulation time as function of the number of surface charges.
examples of charge collocation method solutions performed on a NVidia Tesla K2. The images represent snapshots of the image charge and ion distribution for simulations of 100,000 singly charged ions (m/z 133) undergoing cyclotron motion in an open-ended cylindrical cell and a cubic cell. The optimized parallel structuring of the calculations greatly decreases the computation time for each integration step. This reduction in computation time becomes even more significant as the number of surface charges and the number of ions increases, as shown in Figure 3.5. A comparison of performance of the detection signal simulation on a GPU (Figure 3.5a) versus a conventional computer architecture (Figure 3.5b) shows a speedup of over two orders of magnitude. The speedup is independent of the number of surface charges or the number of ions in the simulation, as shown in Figure 3.5c.

**Analysis of Image Charge Effects in a Harmonized Cylindrical Cell**

![Ideal Field Image Charge Shifts](image)

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>Excitation radius (% cell radius)</th>
<th>Shift in ppb</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>808792.25</td>
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<tr>
<td>808792.10</td>
<td>80</td>
<td>-200</td>
</tr>
</tbody>
</table>

- 20000 ions
- 50000 ions
- 100000 ions
- 200000 ions
The principal utility of the collocation method for image charge calculations is its ability to be readily applied to analyzer cells of arbitrary geometry. We have applied this approach to investigate the performance of a compensated cylindrical cell based on the design of Tolmachev [12]. In order to examine only the effects of image charge, simulations were performed with a single mass-to-charge value of 132.905 corresponding to the Cs+ ion. By using ions of a single mass-to-charge, conventional ion-ion space charge shifts to cyclotron frequency are eliminated, and only image charge shifts will be observed [5]. Figure 3.6 shows the observed frequency of simulated populations of ions at different radii of excitation in an ideal 3D hyperbolic trapping field. The results show a frequency shift that increases as the ions go to higher radius by a factor of $1/d^2$ as would be expected for two point charges. Additionally, the frequency shift grows with increasing numbers of ions, due to their higher charge density creating a larger image potential on the electrode surface. For 100k ions of the same mass-to-charge, there is an $\sim 80$ ppb shift in frequency from detection at 10% of the cell radius and detection at 80% of the cell radius with most of this shift occurring at higher radii. This shift becomes $\sim 120$ ppb with 500k ions. This is problematic since one goal of many harmonized analyzer cells is to be able to utilize higher radius excitation to mitigate frequency shifts due to traditional space charge.

For the Tolmachev cell design, the results become more complex. Because there can only be a finite number of shimming electrodes (in this case 4) the resulting trapping field cannot be perfectly quadrupolar. There are small perturbations in the electric field that cause the observed...
frequency to deviate even without image charge forces taken into account. This is normally a
detriment to the Tolmachev design, since the anharmonicity of the cell leads to quicker ion cloud
destruction. In this case, however, these frequency shifts run counter to those caused by image
charge and compensate for the image charge forces to a small degree. Figure 3.7 shows that this
effect is most notable at ~ 100k ions as the anharmonic terms of the electric field and the force
from image charge nearly cancel each other out giving a very small (~ 50 ppb) change from
excitation of 50% to 80% of the cell radius. These small perturbations in the electric field are a
constant effect, and with higher numbers of ions can be overwhelmed to create a situation that
looks very similar to the ideal electric field radial dependence.

Figure 3.7. Absolute image charge frequency shifts in the trap field of Tolmachev design
compensated cell as a function of radius of gyration and number of trapped ions. The orbital
frequency from the simulation is shown on the left vertical axis, and a scale in ppb is displayed
on the right vertical axis.
Considerations for Mass Calibration and Cell Design

In the case of mass spectra in which the distribution of intensities is relatively uniform and ions are excited to the same radius, image charge effects will be negligibly small. There are, however, several cases where this is not possible. Certain MS/MS methods with low conversion efficiency, such as electron capture dissociation \cite{29} or electron detachment dissociation \cite{30}, result in a very intense precursor, but product ion peaks of relatively low intensity. In this case the frequency shift due to image charge will be higher for the precursor than for the products and as a result the precursor should not be used for internal or lock-mass calibration. For example, assuming a precursor consisting of 500,000 ions where the products are approximately 5 percent of the parent, the shift for the parent ion due to image charge would be 1.3 ppm and the shift for the products would be 60 ppb at 7 T. At higher magnetic fields this problem is alleviated somewhat; at 15 T the shift on the parent would be 0.5 ppm and the product would be 30 ppb. Additionally, image charge forces should be taken into account when calibrating spectra in which ions are excited to different radii as in the case of 2D FTICR/MS \cite{31} or to reduce the effects of conventional ion-ion space charge \cite{32}.

In terms of cell design, image charge creates the transient and so cannot be completely eliminated. We can however limit the effect it has on the observed frequency. One of the biggest contributors to image charge force is the ion charge density. The Tolmachev cell design only holds ions in the space inside the compensated area of the cell. The ideal electric field is compensated over the entire space and therefore there is more room for ions to spread out along the z-axis, decreasing ion charge density and, as a result, image charge force. This advantage can be applied to real cells that utilize the entirety of the cell to hold ions, such as the Boldin-Nikolaev \cite{7} and the externally shimmed ‘window’ cell \cite{33}.
CONCLUSIONS

Particle-in-cell ion trajectory calculations provide the means to gain insight into the fundamentals of ion behavior in FTICR-MS. An extended PIC algorithm for arbitrary electrode surfaces high-resolution image charge calculation has been implemented on CUDA-compliant graphical processors and is being run on a range of graphical cards: Nvidia Tesla C1070, C2070, and K20. The charge collocation method allows modeling real ICR cells’ performance in critical regimes of interaction with the image charge (e.g. high excitation radius, large ion population) in a reasonable time frame via the inherent parallelizability of the method.

ACKNOWLEDGEMENTS

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REFERENCES


CHAPTER 4

MULTIPARTICLE SIMULATIONS OF QUADRUPOLAR ION DETECTION IN AN ICR
CELL WITH FOUR NARROW APERTURE DETECTION ELECTRODES


ABSTRACT

Recent improvements in the already high performance of Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometers have been achieved through innovations in the design of the analyzer cell. The current paradigm in FT-ICR cell design is to approximate the ideal 3-dimensional quadratic trapping potential as closely as possible to maintain ion cloud spatial coherence and achieve long transients, either with shimming electrodes, or by dynamic harmonization. In sharp contrast, the FT-ICR analyzer cell with four narrow aperture detection electrodes (NADEL) introduces non-negligible anharmonic terms to the trapping potential. This analyzer cell is of interest as it has advantages for quadrupolar detection, by which one can measure a close estimate of the unperturbed cyclotron frequency, which by definition is independent of trapping potential and space charge shifts. The quadrupolar mode of ion detection in NADEL cells has been examined previously by SIMION simulations of ion clouds with up to 500 ions per simulation. Here, the behavior of the NADEL analyzer cell is examined through particle-in-cell (PIC) simulations, which allows us to examine the behavior of large populations (tens of thousands) of ions with space charge considerations, and to calculate the induced charge on the NADEL detection electrodes, and thus the transient signal. The PIC simulations confirm that this analyzer produces a unique, stable mode of cloud coherence. Dependencies of the ion cloud structure on cell design ion energy, and magnetron radius are examined. Coalescence effects in this mode of detection are compared to those found in a dynamically harmonized cell.
INTRODUCTION

FT-ICR mass spectrometry (FT-ICR MS) offers the highest mass accuracy and resolution of any mass spectrometer [1]. These features and others have made FT-ICR MS an important tool in many areas of study including proteomics and petroleomics [2-6]. Petroleum samples in particular require high mass accuracy, resolution, and dynamic range, due to the high peak density in their mass spectra. As ICR technology has improved, there has been increasing interest in designing new analyzer cells to obtain the highest resolution and the best mass accuracy.

Ions contained in a strong magnetic field will execute circular orbits, known as cyclotron motion, in a plane perpendicular to the field, with a frequency given by:

$$\omega_c = \frac{qB}{m} \quad (1)$$

where $q$ is the charge on the ion, $B$ is the magnetic field acting on the ion, and $m$ is the ion’s mass. To incorporate this principle in a mass spectrometer, the ions must be trapped along the magnetic field axis during the measurement of their cyclotron frequency, requiring the application of a static trapping field. In the quadratic trapping potential approximation, the trapping field perturbs the ion’s motion, adding another periodic mode, called drift or magnetron motion, with a frequency given by [7]:

$$\omega_\perp = \frac{E_r}{rB} \quad (2)$$

where $E_r$ is the radial component of the trapping electric field that repels ions away from the principal axis of the cell, and $r$ is the radial displacement from that central axis. The frequency of the signal that is measured in a conventional FT-ICR MS is approximately equal to the cyclotron frequency ($\omega_c$) minus the magnetron frequency, ($\omega_\perp$). This is known as the observed frequency or the reduced cyclotron frequency ($\omega_\perp$). For cells with an ideal quadratic trapping potential, for
which the ratio of electric field radial component to the radial displacement, \( \frac{E_r}{r} \), is a constant over the volume of the cell, the initial spatial distribution of ions (generally, an ellipsoid of revolution) is maintained during excitation and detection. This provides a transient with a long period of duration, from the differential charge induced on an opposing set of detection electrodes. For simple analyzer cells (either cubic or cylindrical), there is a spatial gradient in the trapping field, meaning \( \frac{E_r}{r} \) (and thus \( \omega_r \)) is not constant throughout the analyzer cell. Consequently, the ion packet loses spatial coherence as ions oscillate along the trapping axis, due to the inhomogeneous nature of the radial electric field as a function of displacement along the z-coordinate [1]. This leads to the formation of a comet structure which accelerates damping of the transient signal, as the resulting symmetric distribution of ions does not produce an induced charge signal at \( \omega_r \), with dipolar detection circuits [8].

Analyzer cells with hyperbolically-shaped electrodes produce a purely quadratic trapping potential, and have been employed by physicists who make high precision mass measurements of atomic species [9]. However, the trapping volume of such a cell is small, and is not useful for analytical applications. To improve the resolution and mass accuracy of FT-ICR, efforts to improve analyzer cell design have focused on shimming the electric field to make it more closely match the ideal quadratic trapping potential, through static or dynamic harmonization [9-12]. This reduces variation in the magnetron frequency, thus improving ion cloud coherence. A more coherent ion cloud can be measured for a longer period of time, increasing resolution.

In stark contrast to this design philosophy, a recent publication described an analyzer cell that deviates from the quadratic trapping potential. The Narrow Aperture Detection Electrodes (NADEL) cell [13], or NADEL, utilizes flat detection electrodes that extend in from the
cylindrical excitation electrodes, toward the center of the analyzer cell [14]. Figure 4.1 shows a variant of a NADEL cell with four flat detection electrodes.

Figure 4.1. SIMION model of the NADEL cell with four detection electrodes. The trapping electrodes are shown in red and the detection electrodes are shown in blue.

These electrodes create a significant perturbation to the quadratic trapping potential, Figure 4.2, and the electric field gradient, $\frac{E_y}{r}$, varies considerably over the volume of the cell. Using both dipolar and quadrupolar ion detection [15], NADEL cells were able to demonstrate long transients, and high resolution, as well as a capability to detect the unperturbed cyclotron frequency, $\omega_c$ [14]. The latter feature makes the mass calibration less dependent on trapping voltage and space charge, and thus improves the frequency measurement precision and, consequently, the mass accuracy.
Figure 4.2. Comparison of electric fields in SIMION models of a 3D quadratic trapping potential, NADEL cell and cubic cell. The 3D quadratic trapping potential causes no (a) angular or (b) axial variation in Er/r, and there are no perturbations to in the (c) potential contour lines. In fact, all data points are the same because Er/r is a constant for this cell. The NADEL cell, in contrast, has simple trapping electrodes and inward protruding detection electrodes that cause (d) axial and (e) angular variation in Er/r respectively. The (f) potential contour lines at the center of the analyzer for the NADEL cell show the perturbations caused by the protruding detection electrodes. A cubic cell produces (g, h) variations in Er/r and (i) perturbations to the contour lines that are very similar to those produced by the NADEL cell.
This is not the first demonstration of the generation of the unperturbed cyclotron frequency, or even observing it as the primary signal. This concept was introduced by Schweikhard et al. in 1989 when he showed theoretically and experimentally that by using quadrupolar detection, one could generate two signals corresponding to $\omega_{+} - \omega_{-}$ and $\omega_{+} + \omega_{-}$, the latter being equal to the unperturbed cyclotron frequency [16]. It was later shown that by using two pairs of electrodes, the signal for the unperturbed cyclotron frequency could be increased, while the $\omega_{+} - \omega_{-}$ signal was decreased [15]. If the magnetron radius is equal to the cyclotron radius, the $\omega_{+} - \omega_{-}$ signal would decrease to zero [15]. However, these experiments used an analyzer cell with hyperbolic-shaped electrodes and were performed only on low mass ions. Since that finding was published, this method has not been pursued in conventional ICR cells.

For the NADEL cell design with 2 pairs of detection electrodes, the unperturbed cyclotron frequency can be observed without loss of signal or resolution. This is interesting as the NADEL cell, unlike Schweikhard’s original Penning trap experiments, introduces significant anharmonic terms to the trapping field. By conventional understanding, one would expect the ion cloud to quickly lose coherence, leading to a swiftly decaying transient [8]. Instead, the signal was shown to be stable and produce the unperturbed cyclotron frequency due to a unique cloud structure [14, 17]. SIMION simulations of up to 500 ions in NADEL cells suggested that phase-coherent spatial dispersion of ions in a non-linear, azimuthally-dependent electric trapping fields is responsible for the observation of frequency spectra at the unperturbed cyclotron frequency [18]. Each ion in such a field is characterized by its own cyclotron frequency with a center of the ion orbit drifting about the off-axis electric center of the trapping field. As a result, most if not all ions in a cell will contribute to the intensity of the cyclotron frequency peak but will introduce a destructive interference for the reduced cyclotron frequency peak [14, 17]. To gain further
insights into the manner in which the NADEL cell is able to achieve its remarkable performance, one needs to consider the collective motion of the ions in more details, using multi-particle computer simulations with more features than offered by SIMION. Such simulations have shown to be a useful approach for examining the performance of FT-ICR analyzer cells, for example to accurately model the influence of subtle effects such as space-charge and ion-induced charge interactions [19-23]. Simulations provide the ability to test the effects of parameters that are difficult to control experimentally such as the precise number, initial energy, and spatial distribution of ions in an analyzer cell [24]. The particle-in-cell (PIC) method, borrowed from the plasma physics community, offers a computationally tractable way to examine motion of realistic numbers of ions while maintaining an accurate account of space charge [25-27]. Additionally, the PIC method has been extended to include image charge forces on surfaces of arbitrary geometry, which is crucial to understanding the signal generated on the narrow detection electrodes [28].

**EXPERIMENTAL**

Multi-particle simulations were performed on z-cluster, a Linux cluster at the University of Georgia, on nodes equipped with Intel Xeon processors and NVIDIA K40m GPU cards. The PIC software is highly parallelized and uses the GPU cards to decrease calculation times. It also includes a parallelizable charge colocation based method for determining image charge as described previously [28]. Simulations utilized a trapping potential defined by a SIMION model with the trapping plates set to 10 V. The simulations utilized a homogeneous magnetic field with a strength of 7 or 10 Tesla. The analyzer cell geometry is in accordance with a NADEL cell design with a diameter of 5.6 cm or a dynamically harmonized cell with a diameter of 6 cm. For most simulations, a monoisotopic population of 1000 ions with \( m/z = 524 \) was generated with an
ellipsoidal distribution (major axis = 2.5 mm; minor axis = 0.2 mm) with the major axis parallel to the magnetic field in the center of ICR cell and given an initial velocity (energy) distribution of 0.2-0.4 mm/μs in the z-axis. Coalescence simulations instead used a 23+ charge state of cytochrome c (22 most abundant masses in a theoretical distribution) with the same initial space and energy distribution and 50 V trapping potential. A broadband chirp excitation from $m/z$ 200 to $m/z$ 10,000 over 5 ms with $V_{p-p}$ of 25 V was used to excite ions to a higher cyclotron radius. The magnetron radius was then excited by applying DC potential of ± 5 V to opposing excite plates for a duration of 500 μs after cyclotron excitation. A simulated time domain transient was collected for each experiment by summing the induced signal on opposing electrodes and subtracting the signal from orthogonal electrodes. A frequency domain spectrum was derived using FOM-AMOLF’s AWE software [29]. Unless otherwise noted, experiments were performed with a quadrupolar detection scheme. The ion cloud and the resulting image charge distribution was visualized with in-house software developed at FOM-AMOLF [20].

**RESULTS AND DISCUSSION**

**NADEL cell with quadrupolar detection**

As shown by Schweikhard [15], the signal for the unperturbed cyclotron frequency is maximized when the center of an ion’s cyclotron orbit is offset from the center of the cell by a distance equal to the radius of its cyclotron orbit. This is consistent with experimental and computational (using SIMION) results with the NADEL cell [13, 14, 17, 18], and these conditions were examined by PIC simulations. Figure 4.3a shows a calculated transient from a PIC simulation of quadrupolar detection in the NADEL ICR cell, with initial conditions selected that make the cyclotron radius approximately equal to the magnetron radius. The first 0.1
seconds of the transient shows the expected cyclotron frequency (~293055.7 Hz) superimposed on the magnetron frequency (~25 Hz). During this time, the ion cloud retains its initial structural qualities: tightly packed ellipsoid with all ions moving in coherent motion (Figure 4.3c). This result is consistent with the experiments performed by Schweikhard [15, 16], generating a peak at the unperturbed cyclotron frequency ($\omega_c$) and two times the reduced cyclotron frequency ($2\omega_+$), the first due to combination frequencies ($\omega_+ + \omega_-$), the second due to measuring the coherent ion motion twice per cyclotron orbit.

Figure 4.3. (a) Simulated transient and (b) resulting frequency spectrum for quadrupolar detection in the NADEL cell. Visualization of the ion positions at (c) $t = 0.0$ s and (d) $t = 0.5$ s. The red circles describe two ions’ trajectories over the next 15 us; colored dots show ion positions over the next cyclotron orbit starting at blue and going to red.
After 0.1 seconds, however, the structure of the transient changes. Instead of the amplitude decay expected with dipolar detection, caused by comet formation, we see a stable signal which no longer oscillates at the frequency of the magnetron motion. By tracking the motion of an individual ion as shown in Figure 4.3d, we can see that ions continue to undergo cyclotron motion, but with a distribution of their magnetron phase, leading to the formation of a rotating slab structure, in line with the previously obtained SIMION results [14]. The results of PIC simulations reported here confirm slab and star-like ion cloud structure formation as observed with SIMION simulations. Increased ion number in PIC simulations make slab formation and observation even more compelling. During the first 0.2 seconds of the experiment, the ion cloud reorganizes to develop the slab distribution. Normally, the ions would spread along their magnetron orbit, forming a comet, then a cylinder of charge once the head is reincorporated into the tail. However, because the magnetron radius is not equal to zero, the dispersion of the ions along their magnetron orbit does not form a cylinder. Instead, the collective motion of ions at different points in their cyclotron orbit creates the slab-like structure rotating on its major axis at half of the unperturbed cyclotron frequency. Figure 4.4 shows how the slab position corresponds to points in the sinusoidal image current. Since quadrupolar detection produces two maxima in the induced signal per rotation, the all ions in the slab generate a signal at the unperturbed cyclotron frequency.
Figure 4.4. Simulated transient signal with corresponding ion positions showing detection of the slab-like clouds. The detection electrodes are shown as red (negative) and blue (positive) points and the transient at each time step is calculated by the image charges on the blue electrodes minus the image charge on the red electrodes. The red circle describes a single ion’s cyclotron orbit over this 4 us period. The slab rotates 180 degrees in the same amount of time it takes an ion to complete its cyclotron orbit, resulting in the slab rotating at half of the cyclotron frequency.

This slab distribution forms when the cyclotron radius is equal to the magnetron radius, which is also the ideal ratio for generating the unperturbed cyclotron frequency through combination frequencies [15]. In the case of the NADEL cell with quadrupolar detection, the signal switches between these two modes of observing the unperturbed cyclotron frequency.
Initially, ions are moving with coherent cyclotron motion at the reduced cyclotron frequency, generating a peak at $\omega_+ + \omega_-$ and $2\omega_+$. Within 0.2 seconds however, the slab ion distribution has formed, and generates an induced current signal at the unperturbed cyclotron frequency.

Interestingly, since the slab-like structure is formed when ions are spread over their magnetron orbit, the ions do not have spatially-synchronized cyclotron orbits and, as a result, this mode of detection does not produce significant signal at $2\omega_+$. Figure 4.3b shows the peak shapes and intensities in frequency space. Because of the non-linear trapping field, magnetron frequency appears as a broad distribution, which causes the reduced frequency, $\omega_+ = \omega_c - \omega_-$, to exhibit a similarly broad shape, as can be seen in the second harmonic peak, $2\omega_+$. In contrast, the signal at $\omega_c$ has no dependence on $\omega_-$, and appears as a sharp, well-defined peak.

Figure 4.5. (top) Transient for quadrupolar detection in the NADEL cell. (left) Frequency spectra for 0.0-0.1 s of above transient. (right) Frequency spectra for 0.4-0.5 s of above transient. Once the slab structure has formed, the intensity of the peak at $2\omega_+$ is reduced to ~1% of the base peak intensity.
Comparison of the signal intensities before and after the formation of the slab-like structure, Figure 4.5, shows that the intensity of the signal at $\omega_c$ is the same for the first 0.1 second and the last 0.1 second. The signal for $2\omega_+$, however, reduces 20-fold to only 1% of the base peak intensity. By processing the part of the transient acquired after this structure has formed, the unperturbed cyclotron frequency is the only signal of significant intensity in the spectrum, which confirms the reported earlier SIMION simulations and the experimental observations [14, 17].

Quadrupolar detection in DHC and Cubic cell analyzers

The detection of the unperturbed cyclotron frequency can be achieved with other cell geometries, but we expect those with ideal quadratic trapping potentials to maintain ion cloud spatial coherence, and therefore produce other peaks, e.g. at $n\omega_+$ and $n\omega_+ \pm k\omega_+$, in addition to the signal at $\omega_c$. This was examined with PIC simulations of both dynamically harmonized and cubic analyzer cells. Quadrupolar detection in a dynamically harmonized cell (DHC) resembles the experiments performed in a Penning trap by Schweikhard et al. [15, 16], as it has a nearly perfect 3D hyperbolic trapping field upon angular averaging [11]. Figures 4.6a and 4.6b show a simulated transient and the resulting frequency spectrum for quadrupolar detection in a DHC. To optimize quadrupolar detection for $\omega_c$ the cyclotron radius and magnetron radius are approximately equal. The frequency spectrum shows signals at $\omega_c$, $\omega_+$, and $2\omega_+$. The transient features are consistent for the entire simulation (corresponding to a transient duration of 0.5 s) and visualization of the ion cloud (Figures 4.6c and 4.6d) shows that it does not dephase during this time.
Figure 4.6. Simulated transient (a) and resulting frequency spectrum (b) for quadrupolar detection in a DHC. (b) Visualization of the ion positions for DHC at $t = 0.0$ s (c) and $t = 0.5$ s (d).

The first 0.1 s of the transient generates the same frequency spectrum as the 0.4 s-0.5 s section. This demonstrates that the signal at the unperturbed cyclotron frequency is due only to combination frequency detection, as no slab-like structure is generated. Since the ions maintain coherent cyclotron orbits, they continue to generate a signal at $2\omega_*$, increasing the complexity of the resultant spectrum. For a sample with many components, such as petroleum, this is undesirable. Although this analyzer cell does a nearly perfect job of replicating the ideal trapping field for dipolar detection, it is not ideal for use in detecting the unperturbed cyclotron frequency through quadrupolar detection since it continues to generate other frequencies.
Since the spatial dispersion of ions along their magnetron orbit is responsible for generating the unperturbed cyclotron frequency without also generating spurious frequencies, then it follows that any analyzer that deviates enough from an ideal trapping field should be able to replicate the results of the NADEL cell to some extent. A cubic analyzer cell is perhaps the simplest analyzer (although implementation of quadrupolar detection would be more complicated) and should work similarly to the NADEL cell in terms of detecting the unperturbed cyclotron frequency. Figures 4.7a and 4.7b show a simulated transient and the resultant frequency spectrum for quadrupolar detection in a cubic analyzer cell. Like the NADEL cell transient, the cubic cell transient is clearly divided into two parts; with the cyclotron signal superimposed on the magnetron signal early in the transient, followed by a stabilized signal that does not show magnetron oscillation. Visualization of the ion cloud (Figures 5g and 5h) shows that the cloud disperses along its magnetron orbit, leading to the rotating slab-structure. Analysis of the signal before and after the formation of the slab shows a drastic reduction in signal from $2\omega_c$ while $\omega_c$ remains the most intense peak.
Figure 4.7. Simulated transient (a) and resulting frequency spectrum (b) for quadrupolar detection in a cubic analyzer cell. (b) Visualization of the ion positions for cubic cell at t = 0.0 s (c) and t = 0.5 s (d).

**Effect of slab detection mode on coalescence**

Ion cloud coalescence is an undesirable phenomenon caused by space charge interactions, which are accurately modeled by the PIC method. It occurs when ion clouds that are close in frequency phase-lock, appearing as a single peak in the mass spectrum [24]. This occurs at high ion density and results in a peak at a frequency corresponding to the average observed frequency of the coalesced ion clouds. The ions in the slab distribution have a lower charge density than in the ellipsoidal cloud typical of dipolar detection. The average radial distance between ions in the slab structure is 5.6 mm, compared to an average radial distance of 0.2 mm in the initial ion cloud before slab formation begins. As a result, slab mode detection should be less sensitive to
ion cloud coalescence effects. To test this, we examined a simulated isotope distribution for cytochrome C (23+ charge state, \( m/z \sim 512 \)). By increasing the number of ions in the simulation from 50,000 to 400,000 at a constant excite radius, the onset of coalescence can be observed. Figure 4.8 compares the mass spectra and ion positions at \( t = 0.05 \) s for increasing ion number in both the NADEL cell and a DHC. For this experiment, the goal was to compare quadrupolar detection in the NADEL cell to dipolar detection in the DHC. Both simulations are run at 50 V trapping, with a cyclotron radius equal to 20% of the cell radius (30 mm). The ions in the NADEL cell undergo magnetron excitation between cyclotron excite and detection, while the ions in the DHC are centered around the principal axis.

Figure 4.8. Comparison of DHC and NADEL cell ion clouds and simulated mass spectra for cytochrome C 23+ charge state. (left) Mass spectra for DHC and NADEL cell with increasing numbers of charges present. (right) Ion positions 0.05 s after the start of detection. Colors correspond to individual \( m/z \) values as shown on the mass spectra. The DHC signal is observed at the reduced cyclotron frequency leading to higher \( m/z \) values if not calibrated.
As can be seen in Figure 4.8, the DHC and NADEL cell spectra worsen at approximately the same rate. The DHC shows partial coalescence with 200,000 charges present and full coalescence with 400,000 charges. Examination of the NADEL cell shows a similar result despite the lower charge density in the slab structure. This is because coalescence begins before the slab structure has formed, and prevents the slab structure from forming properly. Effectively, at high charge density, the ion clouds in a NADEL cell are not participating in the same detection mode. The cyclotron frequency is still generated for high intensity and high mass ions, but the lower intensity and lower mass ion clouds do not form the necessary cloud structures for this mode of detection. Space charge can be a problem for slab formation and steps should be taken to reduce its effects during detection. This suggests that one of the anticipated advantages of quadrupolar detection, increasing the trapping voltage to hold more ions in the cell must be tempered with space charge limitations in mind.

It is important to note that the DHC can be potentially run at 2-4-fold higher cyclotron radius which will raise the charge threshold required for coalescence. A comparable simulation with excite radius equal to 40 % of the cell radius shows no coalescence even with 400,000 charges. The maximum cyclotron radius will be limited in the NADEL cell due to the inward protruding detection electrodes. The distance between electrodes could be increased to alleviate this, but would require further study. Conversely, the DHC has a set aspect ratio of 2.6, but the NADEL cell used in these experiments had an aspect ratio of 1.5. Extending the NADEL cell would decrease the charge density without altering its other capabilities.
Effect of ion z-axis energy on quadrupolar detection in the NADEL cell

Figure 4.9. Increasing ion energy spread for 1000 ions in the NADEL cell where Vt = 50 V. As the initial energy increases, the ions can move farther along the z-axis, increasing the disparity between Er/r. This results in a wider array of magnetron frequencies, reducing the intensity of the peak at 2ω+.

If ions are quickly spread over the magnetron orbit, the signal at ωc will be strong, but the signal for ω+ and 2ω+ should be spread out over many frequencies resulting in minimal intensity. Ideally detection should not start until the slab structure has formed. One method to make the
slab structure form more quickly is to increase the ion z-axis energy and the spread of energies present, as suggested by the experimental and simulated data [14, 17]. Figure 4.9 demonstrates how increasing the ion energy spread results in quicker dephasing of the cloud as well as greater spread of $\omega_\perp$, resulting in a lower intensity of $2\omega_\perp$. Eventually however, the ions dephase so quickly that they do not present a coherent cloud during excitation of the magnetron radius. This leads to ions of the same mass to charge having different ratios of magnetron radius to cyclotron radius, causing the ions to form a misaligned slab structure that eventually becomes isotropic. Adding a delay prior to detection will allow the slab to form and stabilize and should result in the best possible spectra. The length of this delay will be dependent on the range of energies present within each ion cloud as well as the trapping voltage [14, 17].

**Effect of ratio of magnetron to cyclotron radius**

Unless the electric trapping field closely approximates a 3D hyperbolic electric field, the ion cloud will eventually lose coherence even in the absence of neutral collisions. If the magnetron radius is zero, loss of coherence will form a cylinder of charge when the head of the comet is reincorporated into the tail [8]. This charge distribution will be isotropic, and therefore undetectable. If, however, the magnetron radius is greater than zero but less than the cyclotron radius, loss of coherence instead forms an elliptic cylinder of charge. This cylinder will still be isotropic for the purposes of dipolar detection, but will generate a sinusoidal signal for quadrupolar detection at the ions’ unperturbed cyclotron frequency. When magnetron radius equals cyclotron radius, the result is a slab of charge that appears to rotate, which behaves in the same manner as the elliptic cylinder structure. Further increasing magnetron radius beyond the cyclotron radius creates a mismatch between the alignments of the head and tail of the comet,
leading to widely spread structures that require further study to determine their usefulness.

Figure 4.10 shows how magnetron radius affects the shape of the ion cloud after dephasing.

Figure 4.10. Ion cloud structure development as magnetron radius ($R_m$) approaches cyclotron radius ($R_c$). These ion clouds will produce no signal in dipolar detection after 0.15 s, but will still be detectable by quadrupolar detection, with $R_m = R_c$ producing the most intense signal.

Furthermore, the signal from the first three cloud structures will not deteriorate due to the electric fields. For $R_m > R_c$, the head and tail of the ion cloud do not meet up within the timeframe shown here, and the ions will continue to spread around the analyzer cell.
Advantages of quadrupolar detection in the NADEL cell

Since the ions spread along their magnetron orbit to form the slab-like structure, a stable signal is produced as continued loss of coherence does not affect the shape of the cloud. Beyond stability, the signal generated from the slab-like structure has a few unique properties making it useful for accurate mass measurements. As with the signal generated through combination frequencies, the slab-like structure signal produces a peak at the unperturbed cyclotron frequency. This may allow mass calibration to be done without including a term for the magnetron frequency. Also, $\omega_c$ does not depend on the trapping voltage as $\omega$ does, meaning trapping voltages could be raised to increase the number of ions present in the analyzer cell, although space charge can still cause limitations. Additionally, since the magnetron frequency is not a single peak, but a very broad distribution, the signal does not produce a peak at $2\omega_c$, resulting in a spectrum that is not more complex than its dipolar detection counterpart.

The NADEL cell is particularly suited for quadrupolar detection for several reasons. The trapping field already deviates from the conventional trapping field enough to allow swift dephasing into the slab structure. The detection electrodes are also well designed for use here. Because the detection electrodes are narrow, quadrupolar detection can be performed without needing to use the same plates for excite and detect. With the NADEL setup, there can easily be four plates for detect, two for excitation of cyclotron motion, and two for excitation of magnetron motion. Since the detection electrodes have lower capacitance compared to the conventional 90 degree electrodes and protrude into the analyzer cell, this setup can be utilized without loss in signal. Furthermore, the performance of the NADEL cell should be less sensitive to imperfections in its fabrication (machining tolerances, plate alignments, spacing), as ion behavior does not rely upon an adherence to the ideal quadratic trapping potential. In fact, a
design with rectangular NADELs instead of the curved ones leads to further deviation from the quadratic trapping potential [13], which could lead to faster slab formation without higher trapping potential.

CONCLUSIONS

The NADEL cell design is a radical departure from high-performance ICR cell designs that seek to emulate the ideal 3D quadratic electric potential. Due to its unique properties, the NADEL cell has renewed interest in the concept of quadrupolar detection for use in accurate mass measurements. Through particle-in-cell ion trajectory calculations we have gained additional insight into how this method of detection works in the NADEL cell. The obtained here results are in line with and extend those from the previously reported SIMION simulations for the same NADEL cell geometry but fewer number of charges (ions). We have confirmed here that quadrupolar detection can achieve stable and long-lived induced signals, despite the large non-quadratic terms in the trapping potential, and yet, it does not add complexity to the spectrum. This is achieved through the generation of a unique cloud structure that, once formed, does not undergo rapid decay. This results in long transients with highly accurate mass measurements. Although very high charge density can result in slab cloud destruction, careful experiment design will make this a useful tool in FT-ICR mass spectrometry.

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CHAPTER 5

PARTICLE-IN-CELL SIMULATIONS OF ION DETECTION AT MULTIPLES OF THE CYCLOTRON FREQUENCY

ABSTRACT

Detection at multiples of the cyclotron frequency offers the ability to decrease the analysis time of Fourier transform ion cyclotron resonance mass spectrometry while maintaining high resolving power by measuring the ion clouds multiple times per cyclotron orbit. However, there are inherent difficulties associated with this method, including generation of unwanted spectral peaks and loss of sensitivity. Multi-particle simulations can help in understanding how these problems arise and suggest methods to mitigate them. In this paper, particle-in-cell simulations are used to examine the effect of magnetron offset and excitation radius on the measured signals for $N\omega$ detection. Simulated transients of IgG at $1\omega$ and $10\omega$ detection are compared and beat patterns for $N\omega$ detection are examined.
INTRODUCTION

Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) offers the highest mass accuracy and resolution of any mass spectrometer [1, 2]. Proteomics, metabolomics, and petroleomics can benefit from the extremely high resolving power to determine elemental composition [3-8]. Petroleum samples have especially high peak density in their mass spectra, and require high resolving power to determine the compositions of closely spaced peaks [9, 10].

Normally, high resolution is achieved by measuring for long periods of time, but the resolution is limited by the amount of time an ion cloud can maintain coherence. Additionally, long acquisition times limit options for separations, since the separation sets the timescale. Currently, there are some methods for increasing resolution without increasing acquisition time. One method is to increase the magnetic field strength, however the cost involved with moving to higher magnetic fields can be prohibitive [1]. Another method is to use absorption mode transforms rather than magnitude mode, leading to a potential two-fold increase in resolving power [11-14]. This requires determining the phase of the signal, which is too computationally costly to allow for real time analysis [15]. Other data processing super-resolution methods suffer from a similar computational cost [16-18]. The method we will focus on in this paper is measuring the signal at whole-number multiples of the cyclotron frequency. This method can reduce the amount of time required to achieve a certain resolution [19].

In an FT-ICR MS experiment, the ion cloud rotates at the cyclotron frequency and an image current is generated on the detection electrodes. The output is then the difference in the signals generated on these opposing electrodes and shown in Figure 5.1 (1ω detection). For a single m/z ion cloud, the output produces a single sine wave per rotation, generating a signal at
the reduced cyclotron frequency (\( \omega \)). It is possible to design an FTICR-MS analyzer cell to primarily measure a harmonic or frequency multiple peak directly by adding more detection electrodes. If the detection electrodes were arranged as shown in Figure 5.1 for \( 2\omega \) detection ion motion would produce two sine waves per rotation, generating a signal at two times the reduced cyclotron frequency. Adding even more pairs of detection electrodes will increase the number of sine waves per rotation and further increase resolving power.

![Figure 5.1. Detection setup for normal detection (1\( \omega \)) and for detection at two times the cyclotron frequency (2\( \omega \)).](image)

This method was first described for FTICR-MS by Pan et al. in 1987 [19] and was briefly a subject of some interest [20-24]. The primary disadvantages of this type of analyzer cell were poor signal to noise at normal ion orbital radius and the presence of unwanted spectral peaks if magnetron motion could not be suppressed. These analyzers produce a signal at \( N\omega \), where \( N \) is a multiple of the fundamental cyclotron frequency, but can also produce peaks for \( 1\omega, 2\omega, \ldots, (N-1)\omega \). These undertones or subharmonics increase the complexity of the spectrum. Additionally, it was determined that an increase in resolving power primarily occurred when the
resolving power was limited by acquisition time. The limitations of FTICR-MS at the time suggested that this technique would not be useful. Since these early attempts, FTICR-MS technology has improved substantially, and this idea has recently made a resurgence, with its efficacy being demonstrated on peptides and proteins [25-27].

Measuring the harmonics offers several benefits when compared to normal dipolar detection. Obviously, there is the potential of increased resolving power if the transient decay is longer than the acquisition time. Perhaps more importantly, the same resolving power could be achieved over a much shorter timeframe. This makes the high resolving power of FTICR-MS more applicable to separation methods. A shorter transient also has the potential to reduce discrimination against low abundance ions through ion cloud destruction or coalescence. Despite these potential advantages, detection at frequency multiples has not been extensively applied. Further understanding of how ion motion generates unwanted frequencies in the spectrum can aid experiment design for this promising method of improving FTICR-MS.

Multi-particle simulations provide a useful approach for studying collective ion motion in an FTICR analyzer cell, and for accurately modeling the influence of subtle effects such as space-charge and ion-image charge interactions [28-33]. Simulations provide the ability to test the effects of parameters that are difficult to control experimentally such as the precise number and spatial distribution of ions in an analyzer cell [34]. The particle-in-cell (PIC) method, borrowed from the plasma physics community, offers a computationally tractable way to examine motion of realistic numbers of ions while maintaining an accurate account of space charge [35-37]. Additionally, the PIC method has been extended to include image charge forces on surfaces of arbitrary geometry, which is crucial to understanding the signal generated on multiple electrodes [38].
EXPERIMENTAL

Multi-particle simulations were performed on z-cluster, a Linux cluster at the University of Georgia, on nodes equipped with Intel Xeon processors and NVIDIA K40m GPU cards. The PIC software is highly parallelized and uses the GPU cards to decrease calculation times. It also includes a charge colocation based method for determining image charge as described previously [38].

The simulations utilized a homogeneous magnetic field with a strength of 12 Tesla. The analyzer cell geometry is in accordance with a SIMION model of a dynamically harmonized cell [39] with a diameter of 6 cm. For most simulations, a monoisotopic population of 1000 ions with $m/z = 1000$ was generated with an ellipsoidal distribution (major axis = 40 mm; minor axis = 1 mm) with the major axis parallel to the magnetic field in the center of the analyzer cell. These simulations use single frequency burst excitation over 0.225 ms with $V_{p-p}$ of 35-135 V. Antibody simulations instead used a 10+ charge state of IgG (55 most abundant masses in a theoretical distribution) with the same initial space and energy distribution and were excited via chirp excitation from $m/z$ 1476.75 to $m/z$ 14779.95 over 0.225 ms with $V_{p-p}$ of 80 V.

A simulated time domain transient was collected for each experiment by summing or subtracting the signal induced on electrodes per the detection scheme as shown in Figure 5.2. A frequency domain spectrum was derived using FOM-AMOLF’s AWE software [40]. The ion cloud and the resulting image charge distribution was visualized with in-house software developed at FOM-AMOLF [29].
RESULTS AND DISCUSSION

The effect of magnetron offset on undertone intensity

A major difficulty in the application of detection at $N\omega$ is the generation of peaks other than $N\omega$. These peaks occur primarily when the center of cyclotron motion is moved away from the center of the analyzer cell. This magnetron offset can be caused by several different mechanisms, including the sidekick method of trapping ions and some excitation methods. Figure 5.3 shows the how the frequency spectrum and time-domain signal for $3\omega$ detection changes with increasing magnetron offset. At approximately zero magnetron offset, the primary signal present is $3\omega$. Some signal is present for $2\omega$, but the signal at $1\omega$ is negligible. Increasing the offset causes the intensity of the undertones to increase as $x^{N-n}$ where $n$ is the frequency multiple of the undertone. For $3\omega$ detection, the signal for $2\omega$ increases linearly with offset and
the signal for $1\omega$ increases quadratically. For higher order detection schemes, the same offsets will cause an even greater increase in the undertone signal intensities. The time-domain signal shows how these undertone frequency components arise. The undertone frequencies increase the complexity of the spectrum and quickly become significant in intensity. Minimizing the magnetron offset should be a priority in experiment design for $N\omega$ detection, as this will suppress these unwanted peaks.

![Frequency spectra and time-domain transient signals for $3\omega$ detection as the ions’ starting positions are moved away from the center of the cell. As the magnetron offset increases, frequency components for $2\omega$ and $1\omega$ become more prevalent in the time-domain signal and the frequency spectrum.](image_url)

Figure 5.3. Frequency spectra and time-domain transient signals for $3\omega$ detection as the ions’ starting positions are moved away from the center of the cell. As the magnetron offset increases, frequency components for $2\omega$ and $1\omega$ become more prevalent in the time-domain signal and the frequency spectrum.
Simulation of IgG detection at the 10th harmonic

One of the potential advantages of $N\omega$ detection is being able to resolve high mass species in a shorter timeframe. Figure 5.4 compares detection of an IgG isotope packet at $1\omega$ detection and at $10\omega$ detection. With normal detection, resolution of isotopes requires ~12.5 seconds of transient. At this point, the resolving power for the most intense peak in the spectrum is approximately 90k. By detecting at $10\omega$, 130k resolving power can be achieved in 1.25s. Even greater resolving power, 1.3M, can be achieved if we measure at $10\omega$ for the full length of time.

Figure 5.4. Simulated transients for detection of the 10+ charge state of IgG. For $1\omega$ detection isotopic resolution requires ~12.5 seconds. With 10x detection, the same resolution can be acquired in 1/10th the time, or 10 times greater resolution can be achieved in the full time period. $10\omega$ detection contains abnormal beat patterns.
Although the resolution is much greater, it quickly becomes apparent that abnormal beat patterns exist in this last transient. Beats occur when ion clouds of different $m/z$ values briefly move in a way that generates coherent interference. The period of a beat is given by:

$$t = \frac{1}{f_1 - f_2}$$

Where $f_1$ and $f_2$ are the cyclotron frequencies of two ion clouds in the mass analyzer [41]. In this transient, there are more than 30 features that appear to be beats. Additionally, the intensity of peaks at undertones grows substantially in relative intensity to the peak of interest. By examining what is occurring in terms of ion motion during these different beats, we can show that a relationship exists between the additional beats and the intensity of specific peaks.

![Simulated Transient of an Antibody](image)

**Figure 5.5.** Correlation between the beats and the number of groups of ion clouds coming into coherent motion with each other. Beats occur at $1/(n\Delta f)$ where $n = 1, 2, 3, \ldots, N$. 
In the case of 55 masses equally spaced in frequency, there are many points during the transient for which the different ion clouds move in coherent motion for a brief period. The average difference between each isotope and its neighbors is 0.0846 Hz, leading to a beat period of ~11.82s. At $t = 0.00s$ and at $t = 11.82s$ all ion clouds are in coherent motion. In normal detection, this is the only time the coherent motion translates to coherent interference in the signal. For these ions and this magnetic field, there will be a beat at $t = 0.0$ seconds and $t = 11.82$ seconds and these beats are not dependent on the detection scheme.

Additionally, the beat period can be determined for every other ion cloud, every third ion cloud, up to every tenth ion cloud. Figure 5.5 demonstrates how the ion clouds separate into groups at the corresponding intervals. For $N\omega$ detection schemes, when the ion clouds arrange into a number of groups that are factors of $N$, a beat will be present in the signal. When detecting at the tenth harmonic and the ion clouds arrange into groups of one, two, five, and ten, the ion clouds align properly with the detection plates. These beats are on resonance with the detection scheme and improve the signal at $10\omega$. Alternatively, when the ion clouds arrange into a number of groups that are not factors of the detection scheme, the signal from each group should cancel out, generating no signal. This assumes the number of ions in each group is similar as will be the case in a Gaussian distribution. However, if there is any magnetron offset, a beat is still generated at those points due to the uneven image charge distribution. The larger the magnetron offset, the greater the intensity of the off-resonance beats. These off-resonance beats contain frequencies other than the desired frequency. For example, the beat that occurs when the ion clouds arrange into nine groups contains the frequencies at $9\omega$. Figure 5.6 compares transients for a small magnetron offset and a large magnetron offset and shows how the off-resonance beats
contribute to the signal intensity of undertones. Even a small magnetron offset can introduce large signal intensities for the undertone frequencies.

Figure 5.6. time-domain signal and frequency spectra for IgG detection at $10\omega$ with a small magnetron offset and a large magnetron offset. Increased magnetron offset causes undertones to increase in intensity. The frequency components of the undertones ($n\omega$) are contained in the beats that occur at $1/(n\Delta f)$. The beat at 1.18 s ($1/(10\Delta f)$) contains the frequencies for $10\omega$ while the beat at 1.98 s ($1/(6\Delta f)$) contains the frequencies for $6\omega$. 
Signal intensity vs detection order

Another major concern for detection at higher harmonics is loss of signal. Figure 5.7 shows the effect of increasing the excitation radius on signal intensity for several detection schemes. For normal (1\(\omega\)) detection, the signal intensity increases linearly with excitation radius as expected. For N\(\omega\) detection schemes, signal increases exponentially with excitation radius (\(\sim x^N\)). Unfortunately, even at very high excitation radius it does not reach the same intensity as 1\(\omega\) detection. This can be rationalized by considering how image charge is induced on multiple plates. For 1\(\omega\) detection, most of the image charge is on a single plate when the signal is at its maximum (and minimum). For 2\(\omega\) detection, the same ion cloud would also induce some image charge on the two plates with opposing signs, decreasing the maximum signal. This issue becomes worse as the detection scheme increases since the detection plates decrease in size and detection plates with opposing signs are closer together. As the excitation radius increases, the induced image charge is concentrated more on a single plate, leading to the exponential increase in signal intensity.

![Signal Intensity vs Excitation Radius](image-url)

Figure 5.7. Signal induced on the detection plates by an ion packet vs increasing excitation radius for different detection schemes. With higher detection schemes, the signal intensity decreases drastically.
Even without considering capacitance, the signal intensity will be higher for $1\omega$ detection than $N\omega$ detection schemes for analyzer cells of normal size. For applications that require extremely high sensitivity, $N\omega$ detection may not be useful due to this limitation. One method of mitigating this loss of signal would be to increase the diameter of the analyzer cell. A larger diameter cell would have larger detection plates and the plates with opposing signs would be farther apart. However, most analyzer cells already use as large a diameter as possible for the bore of the magnet, since space charge related problems are also reduced at higher excitation radius. For maximum signal at $N\omega$, it is important to excite ion clouds to very high radii.

CONCLUSIONS

Here we use PIC simulations to accurately simulate $N\omega$ detection and highlight the difficulties associated with it. $N\omega$ detection can increase the resolving power during a given timeframe by a factor of $N$ which would allow measurements to be performed quickly while maintaining the high resolving power of FTICR-MS. To obtain the best possible spectra for $N\omega$ detection, it is necessary to reduce magnetron offset and increase excitation radius as much as possible. Reducing magnetron offset is a difficult task. Quadrupolar excitation axialization (QEA) likely presents the best option for removing magnetron offset by converting any magnetron motion to cyclotron motion [42]. Care should also be taken during excitation to avoid moving ions off center.

Excitation to high ion orbital radius should be more straightforward as new analyzer cells have altered electric fields that harmonize their entire volume, allowing ions to orbit at high excitation radii without rapid dephasing of the ion cloud [39, 43]. These simulations do not consider signal loss due to the increased capacitance caused by increasing the number of
detection plates, but this will likely be a major concern for signal intensity as well. These two factors will limit the maximum value for $N$ that can produce useful data.

With careful experiment design, $N\omega$ detection provides an option to boost resolution that can be applied in combination with increased magnetic fields and computational methods. However, the difficulties associated with this method are substantial and will require unique procedures to resolve.

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A conceptual approach for FT-ICR cell harmonization utilizing external shim electrodes.
CHAPTER 6

CONCLUSIONS

The particle-in-cell method of multiparticle simulation has been extended to include accurate accounting of image charge for analyzer cells of arbitrary geometry. This charge colocation based method allows modeling image charge forces on the ions as well as way to accurately determine the time domain signal. The image charge force per ion was determined to be in line with the force determined through other methods. Though this force is small compared to other forces on the ions during detection, it can be significant for specific applications of FTICR-MS. Additionally, since image charge creates the detected signal, it cannot be eliminated. Instead the effects must be minimized or compensated by calibration. This can pose a problem for experiments with ion clouds of differing intensities. This method of image charge detection was then used to study quadrupolar detection in the NADEL cell and detection at multiples of the cyclotron frequency as these two modes of detection deviate substantially from the detection mechanism define by PIC alone.

The NADEL cell with four detection electrodes primarily generates a peak at the unperturbed cyclotron frequency instead of the reduced cyclotron frequency. PIC simulations confirm the mechanism by which it generates the unperturbed cyclotron frequency. The elliptic cylinder- and slab-type structures of the ion clouds differs from the cigar shaped ion clouds found in traditional dipolar detection. These structures are stable and maintain coherence despite imperfections in the electric fields. Due to their unique form of coherence, they do not increase the complexity of the spectrum. Furthermore, these simulations show that quadrupolar detection
can be performed with similar results in other analyzer cells if the trapping field deviates sufficiently from a 3D quadratic electric potential. The potential for improved mass accuracy and long-term signal stability is demonstrated through simulation.

Detection at multiples of the cyclotron frequency can increase the resolving power during a given timeframe. PIC simulations help to highlight the difficulties with using the method and suggest ways to mitigate the problems. Magnetron offset needs to be minimized and excitation radius needs to be maximized for even modest usefulness. Even under ideal circumstances, this method has limited sensitivity that only gets weaker with increasing frequency multiple.

Particle-in-cell ion trajectory calculations provide the means to gain insight into the fundamentals of ion behavior in FTICR-MS. As FTICR-MS analyzers change and improve, it is helpful to understand their effects on ion motion and detection. Experiment and analyzer cell design can be guided by the insight gained from these simulations.
APPENDIX A
SUPPLEMENTARY MATERIAL FOR CHAPTER 3

Multi-ion simulation and arbitrary electrode shape

Typically, an orbital cyclotron frequency shift of an ion represented by point charge $q$ at location $(x', y', z')$ bounded by a box with dimensions $a \times b \times c$ is found from an approximation

$$
\Delta \omega_z = \frac{q}{Brabc \varepsilon_0} \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} \frac{\sin^2 \frac{n \pi z'}{c}}{\sinh \frac{k_{mn} \pi}{c}} \int_0^{2\pi} d\phi' \left[ a \cos \phi' \sinh \frac{2k_{mn} \pi \rho'}{a} \cos \phi' \sin^2 \frac{m \pi x'}{a} + b \sin \phi' \sinh \frac{2k_{mn} \pi \rho'}{b} \sin \frac{m \pi y'}{a} \right]
$$

Equation A.1

which implies a uniform probability distribution of the ion’s location in the confinement geometry bounds. Moreover, such analytic models don’t address the multi-body nature of ion clouds and some important initial conditions like the ion cloud shape.

The purpose of multi-body simulation is incorporating the ion-ion and ion-image charge interactions between practical amounts of ions of different mass and charge state. Specifically, the particle in cell technique provides a spectacular treatment of the image charge according to certain geometric limitations.

The interior of the ion trap is arranged in the form of equidistant logical nodes forming a grid for a difference form of the Poisson equation which consumes the charge density interpolated on the nodes of this discrete grid from ions’ continuous locations and results in a discrete potential.
The external voltages e.g. trap and excite are applied in the form of boundary conditions. The electric fields at the particle locations are then calculated from the discrete potential at corresponding nearest grid nodes followed by motion integration.

If shape and orientation of conductors is aligned with the grid’s tetragonal geometry, their voltages are specified to the Poisson equation as Dirichlet boundary conditions and the electric field of the induced image charge is calculated trivially. Let \( \sigma \) – surface charge density, \( ds \) – element of the conductor surface \( F \). According to Gauss’ law the total surface charge induced within the area \( F \) is

\[
c = \int_F \sigma ds.
\]

Here the (local) charge density can be obtained from the normal component of the electric field

\[
E_n = \frac{\sigma}{\varepsilon_0},
\]

where \( \varepsilon_0 \) is the permittivity of the space, available as the electric field calculated at the wall of the computational grid. Although in case of an arbitrary shape of the conductor surface traversing the integration set \( F \) becomes computationally intractable.

**Eulerian ion dynamics and image charge interaction**

Based on the straightforward particle in cell scheme with tetragonal geometry of conducting surfaces (see table A.1, a) its modification is widely used allowing one consume arbitrary
configurations of electrodes in the form of pre-calculated arrays of electrostatic potential (table A.1, b).

**Table A.1.** Standard particle in cell algorithm and its extension to consume precalculated fields representing arbitrary electrode geometry.

<table>
<thead>
<tr>
<th>a) Standard PIC</th>
<th>b) Extended PIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Interpolate ion charge</td>
<td>1. Interpolate ion charge</td>
</tr>
<tr>
<td>( q_{1...Np} \rightarrow \rho_{N_1 \times N_2 \times N_3} )</td>
<td>( q_{1...Np} \rightarrow \rho_{N_1 \times N_2 \times N_3} )</td>
</tr>
<tr>
<td>2. Create boundary conditions</td>
<td>2. Solve Poisson equation</td>
</tr>
<tr>
<td></td>
<td>( \rho_{N_1 \times N_2 \times N_3} \rightarrow \varphi_{N_1 \times N_2 \times N_3} )</td>
</tr>
<tr>
<td>3. Solve Poisson equation</td>
<td>3. Calculate</td>
</tr>
<tr>
<td>( \rho_{N_1 \times N_2 \times N_3} \rightarrow \varphi_{N_1 \times N_2 \times N_3} )</td>
<td>( \varphi_{N_1 \times N_2 \times N_3} \rightarrow E^g_{N_1 \times N_2 \times N_3} )</td>
</tr>
<tr>
<td>4. Calculate</td>
<td>4. Map each ion’s position to custom field index and interpolate to the electric field at ions’ positions</td>
</tr>
<tr>
<td>( \varphi_{N_1 \times N_2 \times N_3} \rightarrow E^g_{N_1 \times N_2 \times N_3} )</td>
<td>( R_{1...Np} \rightarrow F_{T_1 \times T_2 \times T_3} \rightarrow E^F_{1...Np} )</td>
</tr>
<tr>
<td>5. Interpolate</td>
<td>5. Interpolate</td>
</tr>
<tr>
<td>( E^g_{N_1 \times N_2 \times N_3} \rightarrow E^p_{1...Np} )</td>
<td>( E^g_{N_1 \times N_2 \times N_3} \rightarrow E^p_{1...Np} )</td>
</tr>
<tr>
<td>6. Integrate motion</td>
<td>6. Add custom and Coulombical fields at ions’ positions</td>
</tr>
<tr>
<td>( (B, E^p_{1...Np}, R_{1...Np}) )</td>
<td>( E^p_{1...Np} \rightarrow E^p_{1...Np} + E^F_{1...Np} )</td>
</tr>
<tr>
<td>( \rightarrow (R_{1...Np}, V_{1...Np}) )</td>
<td></td>
</tr>
<tr>
<td>7. Integrate motion</td>
<td>7. Integrate motion</td>
</tr>
<tr>
<td>( (B, E^p_{1...Np}, R_{1...Np}) \rightarrow (R_{1...Np}, V_{1...Np}) )</td>
<td></td>
</tr>
</tbody>
</table>
Here: $N_p$ – number of ions, $q_{1...N_p}$ – an ion’s charge, $N_1 \times N_2 \times N_3$ – dimensions of the grid, $ho_{N_1 \times N_2 \times N_3}$, $\phi_{N_1 \times N_2 \times N_3}$, and $E^g_{N_1 \times N_2 \times N_3}$ – charge density, electrostatic potential, and electric field at the grid nodes, $E^p_{1...N_p}$ – electric field at ions’ positions, $B$ – magnetic field (assumed uniform everywhere within the geometry), $R_{1...N_p}$ - vector of ions’ positions, $V_{1...N_p}$ - vector of ions’ velocities, $T_1 \times T_2 \times T_3$ – dimensions of the precalculated electric field of a custom electrode geometry, $F_{T_1 \times T_2 \times T_3}$ – pre-calculated electrostatic potential, $E^F_{1...N_p}$ – precalculated electric field at ions’ positions.

The image charge available from the extended PIC remains limited in a sense that the charge is induced on the surface of the computational grid (Table 1, c and d). The detected signal produced in such a way is compromised in accuracy due to modulations of the projected detection surface and cannot serve industrial-level applications.
In order to calculate the non-trivial distribution on the custom electrode surface we consider all the conducting surfaces as the equivalent linear relation between charges \( c_i = \int_{F_i} \sigma ds \) of virtual disconnected elements \( F_i \) of the conducting surfaces and their voltages \( V \):

\[
\begin{align*}
    a_{11}c_1 + a_{12}c_2 + \cdots + a_{1n}c_n &= u_1 \\
    a_{21}c_1 + a_{22}c_2 + \cdots + a_{2n}c_n &= u_2 \\
    \vdots & \quad \text{Equation A.2} \\
    a_{n1}c_1 + a_{n2}c_2 + \cdots + a_{nn}c_n &= u_n
\end{align*}
\]

or in the matrix form

\[
\begin{pmatrix}
    a_{11} & \ldots & a_{1n} \\
    \vdots & \ddots & \vdots \\
    a_{n1} & \ldots & a_{nn}
\end{pmatrix}
\begin{pmatrix}
    c_1 \\
    \vdots \\
    c_n
\end{pmatrix}
= 
\begin{pmatrix}
    V_1 \\
    \vdots \\
    V_n
\end{pmatrix} \iff AC = U \quad \text{Equation A.3}
\]

This problem can be reformulated as

\[
A^{-1}U = BU = C \quad \text{Equation A.4}
\]

where elements \( b_{ii} \) and \( b_{ij} \) are capacitance and inductive coefficients, respectively. Under the assumption of the isotropic media between the virtual charges \( c_i \) they only depend on the mutual position of the charges which are thus linear functions of the corresponding potentials. Calculating its \( k \)-th column requires setting the potential of \( k \)-th conductor to 1 leaving the other conductors’ potentials equal to 0 and the resulting vector \( C \) will yield the \( k \)-th column of \( A \), etc. As a result we
will have a system of $N$ equations for $N$ unknowns which determines values of the surface charges induced on each electrode. It can then be solved numerically, and the corresponding process bears the informal name of capacitance matrix method (table A.2, a).

**Table A.2.** Extended particle in cell algorithm with image charge interaction calculated by the capacitance matrix and charge collocation methods.

<table>
<thead>
<tr>
<th>a) Extended PIC with capacitance matrix</th>
<th>b) Extended PIC with the charge collocation method</th>
</tr>
</thead>
<tbody>
<tr>
<td>0. Calculate the capacitance matrix $B$ once</td>
<td>0. Calculate matrix $A^{-1}$ once</td>
</tr>
<tr>
<td>For each time step $t$:</td>
<td>For each time step $t$:</td>
</tr>
<tr>
<td>1. Interpolate ion charge $q_{1...Np}$ → $\rho_{N_1 \times N_2 \times N_3}$</td>
<td>1. Interpolate ion charge $q_{1...Np}$ → $\rho_{N_1 \times N_2 \times N_3}$</td>
</tr>
<tr>
<td>2. Solve Poisson equation $\rho_{N_1 \times N_2 \times N_3}$ → $\varphi_{N_1 \times N_2 \times N_3}$</td>
<td>2. Solve Poisson equation $\rho_{N_1 \times N_2 \times N_3}$ → $\varphi_{N_1 \times N_2 \times N_3}$</td>
</tr>
<tr>
<td>3. Calculate $BV = C$ to obtain the virtual charges $V_{1...n}$ representing the conducting surfaces</td>
<td>3. For each virtual charge $i$ calculate the right hand side element $u_i = 4\pi \varepsilon_0 \sum_{k=1}^{Np} \frac{q_k}{d_{ik}}$ in parallel threads indexed by $i$.</td>
</tr>
<tr>
<td>4. Interpolate surface charge $V_{1...Np}$ → $\rho_{N_1 \times N_2 \times N_3}$</td>
<td>4. For each virtual charge $i$ calculate $A^{-1}U$ in parallel threads indexed by $i$, to obtain the virtual charges $C_{1...n}$ representing the conducting surfaces.</td>
</tr>
<tr>
<td>5. Solve Poisson equation again $\rho_{N_1 \times N_2 \times N_3}$ → $\varphi_{N_1 \times N_2 \times N_3}$</td>
<td>5. Calculate the electric field due to the image charge at ions’ positions $(C_{1...n}, R_{1...Np}) \rightarrow E_{1...Np}^{ic}$</td>
</tr>
</tbody>
</table>
6. Calculate
\[ \varphi_{N_1 \times N_2 \times N_3} \rightarrow E^g_{N_1 \times N_2 \times N_3} \]

7. Map each ion’s position to custom field index and interpolate to the electric field at ions’ positions
\[ R_{1...Np} \rightarrow F_{T_1 \times T_2 \times T_3} \rightarrow E^F_{1...Np} \]

8. Interpolate
\[ E^g_{N_1 \times N_2 \times N_3} \rightarrow E^p_{1...Np} \]

9. Add custom and Coulomb electric fields at ions’ positions
\[ E^p_{1...Np} \rightarrow E^p_{1...Np} + E^F_{1...Np} \]

10. Integrate motion
\[ (B, E^p_{1...Np}, R_{1...Np}) \rightarrow (R_{1...Np}, V_{1...Np}) \]

Here: \( n \) – number of virtual charges, \( d_{ik} \) – distance between virtual surface charge element \( i \) and ion \( k \).

While being at first glance computationally efficient in a sense that it requires the large matrix to be calculated once followed by relatively inexpensive matrix multiplication, this approach possesses a number of disadvantages. First, the spatial resolution of surface charge’s...
polarizing influence of the nontrivially shaped ion cloud in the form of potentials \( V_i \) is limited by the size of the computational grid of the Poisson equation solver (table A.2, a, step 2) which is usually chosen rather coarse to ensure practical computation performance. Second, the resulting surface charge approximation \( q_i \) whose elements’ absolute values are rather small is further blurred out by the second Poisson equation solution step (table A.2, a, step 5). Along with inevitable discretization of the virtual charge grid these disadvantages cause the method to fail to resolve the surface charge polarization in the fragments of critical gradual curvature change (e.g. cylindrical electrodes) and neighborhood of small details (e.g. isolation gaps between ICR cell electrodes).

An obvious improvement of the capacitance matrix method is incorporating positions \( d_{ik} \) of ions \( q_1 \ldots q_P \) inducing potentials

\[
  u_i = \sum_{k=1}^{N_P} \frac{q_k}{d_{ik}}
\]

at the locations of the virtual charges in the linear system (\( \mathbf{A} \)), see Figure A.1. On the other hand, due to the fact that those potentials are maintained by the system of virtual charges \( c_1 \ldots c_n \) and can in turn be expressed as distances between corresponding surface charge elements \( c_i \) and \( c_j \), the problem becomes

\[
\begin{pmatrix}
  a_{11} & a_{12} & \ldots & a_{1n} \\
  a_{21} & \ddots & & \vdots \\
  \vdots & & \ddots & \vdots \\
  a_{n1} & a_{n2} & \ldots & a_{nn}
\end{pmatrix}
\begin{pmatrix}
  c_1 \\
  \vdots \\
  \vdots \\
  c_n
\end{pmatrix}
= 4\pi\varepsilon_0
\begin{pmatrix}
  \sum_{k=1}^{N_P} \frac{q_k}{d_{1k}} \\
  \vdots \\
  \sum_{k=1}^{N_P} \frac{q_k}{d_{nk}}
\end{pmatrix}
\]

Equation A.6
where $a_{ij}$ and $d_{ik}$ are a distance between the i-th and j-th surface charge locations and between k-th ion and i-th surface charge locations, respectively – see A.1. At $i \neq j$ coefficient $a_{ij}$ is finite, but it has a singularity at $i = j$, however, the expression is integrable: if we consider a disc of small radius $R$ around point $i$, then remembering that $ds = rdrd\alpha$, we can state that

$$
\int_{F_i} \frac{ds_i}{r_{ij}} = \int_{0}^{2\pi} \int_{0}^{R} r\,dr\,d\alpha = 2\pi R
$$

which proves that $a_{ij}$ is finite at both $i \neq j$ and $i = j$. The corresponding simulation algorithm is presented in Table A.2, b.

Figure A.1. Surface charge density calculation in the presence of ions in the trap.
To keep the spatial accuracy of the polarization, the virtual charges $\sigma_i$ obtained this way can be included in the motion integration part of a simulation algorithm:

$$m \frac{dv}{dt} = \frac{1}{4\pi\varepsilon_0} \left[ \sum_{i=1}^{N_p} q_i \frac{(r - r_i)}{|r - r_i|^3} + \sum_{j=1}^{n} q_{cj} \frac{(r - r_j)}{|r - r_j|^3} \right] + q\left[E_{tr}(r, t) + E_{ex}(r, t)\right] + q[v \times B]$$

where $m$, $v$, $q$, and $r$ – ion mass, velocity, charge, and position, $E_{tr}(r, t)$ and $E_{ex}(r, t)$ are the trap and excite electric field at time $t$ and ion position $r$. Such a problem possesses multiple computational bottlenecks which luckily are avoidable due to the problem’s parallel nature which can be successfully solved on an array of graphical processors (Error! Reference source not found.).

**Effect on the performance of commercial ion traps**

For most commonly used analyzer cells, there is a spatial gradient in the trapping field, leading to a change in magnetron frequency across the analyzer cell, and thus, a loss of coherence as ions undergo axial motion. However, the development of harmonized analyzer cells [1-5] has improved this undesirable behavior; magnetron frequency is very close to a constant over the volume of such compensated analyzer cells.

This allows them to maintain cloud coherence at a higher radius of excitation where space charge effects are less prominent due to the decrease in ion density. However, an increase in excitation radius leads to an increase in the effects of image charge interactions [6]. This means it is necessary to find a compromise between these effects in order to optimize FTICR performance.
As mass accuracy continues to improve due to advances in controlling the adverse effects of applied electric fields and space charge on ion motion, smaller effects like image charge can now play a significant role. It would be advantageous to have a better understanding of the magnitude of image charge effects and how they vary due to changes in various parameters.

Previously, attempts have been made to isolate the effects of ion-image charge interactions [7]. These experiments showed that populations of Cs\(^+\) ions interacted with their image charge to cause a frequency shift that increases in magnitude with ion number and excitation radius. However, these attempts were based on a cubic analyzer cell and used only the basic implementation of image charge interactions provided by PIC calculations in which image charge is calculated on the walls of the orthorhombic PIC grid and included in the \(qE(r, t)\) term. To examine these effects in cells with newer cylindrical geometries, more accurate results require the calculation the image charge on the inner surface of the cylindrical electrodes.

**Example data**

![Example data image](image-url)
Figure A.2. An example of a transient and frequency spectrum produced via PIC simulation of 200000 ions at 7T excited to 50% of the cell radius.
References


