FUNDAMENTAL STUDIES OF THE QUADRUPOLE ION TRAP MASS SPECTROMETER: COMPOUND-DEPENDENT MASS SHIFTS AND SPACE CHARGE

By

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

2002
For my Father and Mother who have supported my every effort in life. I love you both.
ACKNOWLEDGMENTS

During my graduate career at the University of Florida, I have had a great deal of support from colleagues, friends and family. It has been a long road and I could not have made it this far without every one of them.

I would first like to thank my advisor, Dr. Richard Yost. I can truly say that Rick has touched my life. His thirst for knowledge and wonderful outlook on life has made me strive to become not only a better scientist but also a better person. He has shown confidence in my abilities and pushed me to accomplish things I never thought I could. I could not have asked for a better mentor.

During my first year at UF, I was fortunate enough to be introduced into the Yost group by Brody Guckenberger, Rick Troendle, Joseph McClellan, and Joseph “Mule” Muholland. I greatly appreciate their taking me under their wings early in my career. Everything I learned was based on the foundation that they laid for me. Rick Troendle is one of the most well-rounded people I have ever met. From auto mechanic to disc jockey, he has done it all. A conversation with Rick was always interesting. Joe McClellan, my roommate for two years and fellow Holy Crosser, always guided me through the tough times at UF. Joe Muholland was not the most popular TA for undergraduates but he was my best teacher. Even after Joe graduated he still continued to supply me with great advice. I look forward to spending some quality with him, Randy Pedder, and Sinatra at ASMS.
During the last two summers of my graduate career, I was fortunate enough to have an opportunity to work at Thermo Finnigan in Austin, Texas. The working experience I gained there was one of the most valuable aspects of my education. I worked with two of the most intelligent people I have ever met, Brody Guckenberger and Scott Quarmby. I was always amazed at Brody’s excitement about science. It was contagious. I wish him well in his new role as a father. Scott always made time in his busy schedule to talk with me. I learned a great deal from him and his jokes kept me on my toes. I was very lucky to work with them both. I would also like to acknowledge my other colleagues in Austin: Eric Johnson, Mark Okamura, Ed McCauley and Diana Baker. They all made me feel like one of the family. I couldn’t imagine having a better boss than Eric. He always looked after me.

In the four years I have spent in Florida, I have made some very close friends. Pat O’Donnell, my other roommate, was always up when I got home from a late night in the lab. I always valued our conversations. John “TJ” Banisaukas came to UF after his stand-up comic act didn’t work out. In spite of his bad jokes, TJ was an amazing friend to me. His sister, Heather “HB” Banisaukas, joined us for two years at UF. The years went by too quickly for me. She once told me we would all grow old together, and I plan on holding her to that. Andria Hobbs always seemed to be there when I really needed her. She is a very special person to me. I can only hope I can one day repay her for all her love and support. Olivia Bautista could always put a smile on my face. She has the greatest inner beauty of anyone I have ever met. Lastly I would like to thank Schwin. He kept me in shape while I was at UF. I always looked forward to our runs together.
I would like to thank the current members of the Yost group, Mike Belford, Todd Huml, and Leonard Rorrer, for their friendship. Each of them has taught me a great deal, from mass spectrometry to softball. I see nothing but great futures ahead for them all.

To my mother, Frances, my father, James, and my two sisters, Kerrie and Colleen, I look forward to making up for all the missed birthdays and family events. My life has been incomplete without them. I promise that if I attempt to obtain any further advanced degrees I will do it close to home. I would also like to acknowledge my Uncle Joe “UJ” Murphy who passed away during my second year at the University of Florida. He had become a close part of my family. My memories of him will never fade.

I would like to thank all my friends back home for their support: Billy “Greek” Chrisostomidis, Jarod Skowron, Jackie Kenyon, Trina Starr, John Paul “JP” Chalpin, Rick Fronaphel, Mike Brennan, Mark Healy, Eugene Hagan, Rebecca Hurley and Matt “Magoo” Hargus. My trips home to see you all always energized me. I thank them all for their support and words of encouragement over the past four-and-a-half years. I’ll see them all in Boston real soon. Go Cross!

In the last year of graduate school I was lucky enough to have met Erika Moxham. Within five short months she has become one of my closest friends and really helped me get through the tough times. I look forward to eventually taking her to see Neil Diamond in concert.

Lastly I would like to thank God. I have been through a great deal over the past four and half years. There were many times I contemplated quitting. But with His help I always pushed forward. I thank Him for keeping all my friends and relatives safe while I have been away.
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Abstract of Dissertation Presented to the Graduate School of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

FUNDAMENTAL STUDIES OF THE QUADRUPOLE ION TRAP MASS SPECTROMETER: COMPOUND-DEPENDENT MASS SHIFTS AND SPACE CHARGE

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May 2002

Chairman: Richard A. Yost
Major Department: Chemistry

The quadrupole ion trap, originally developed in the early 1950s by physicists Paul and Steinwedel as an ion storage device, has become one of the most powerful mass spectrometers available today. The modern quadrupole ion trap is most noted for its versatility, sensitivity and capability to provide multiple stages of mass spectrometry (MS^n). There are several issues, however, that have plagued the ion trap since the introduction of the first commercial instrument. The most severe of these are compound-dependent mass shifts and a limited dynamic range due to space charge effects.

Compound-dependent mass shifts may result from the resonant ejection of fragile ions. As these ions come into resonance with the ejection frequency, they gain kinetic energy, collide with buffer gas molecules, and dissociate. The resultant fragment ions, which are lower in m/z, will no longer be stable within the ion trap, and will be immediately ejected and detected before the intact ions. The fragment ions and the non-
dissociated precursor ion form one peak which has a significant amount of peak fronting and an overall broad peak shape.

The resonant ejection of fragile ions is not the only source of mass shifts. Overloading the ion trap can result in significant coulombic interactions, called space charge, leading to peak broadening and a shift to higher m/z. An ion of a particular m/z will experience a varying degree of space charge due to the number of ions of the same m/z value, the abundances and mass differences of neighboring ions, and the density of the charges in the trap controlled by the buffer gas pressure.

Space charge effects can be reduced by increasing the resonant ejection amplitude, increasing the drive frequency, or decreasing the trap pressure. At low buffer gas pressures, however, ions are allowed to venture near the endcap holes and experience a non-linear field. In a non-linear field an ion’s stability is no longer purely dependent on its m/z value as the field imperfections perturb the trajectories of ions inside the ion trap. As a result, ions of a specific m/z experience multiple opportunities to be ejected, resulting in a splitting of the resultant peak.
CHAPTER 1
INTRODUCTION

The quadrupole ion trap, originally developed in the early 1950s by physicists Paul and Steinwedel as an ion storage device, has become one of the most powerful mass spectrometers available today. The ion trap mass analyzers currently obtainable commercially are structurally very similar to the one described in Paul's early patent (Paul and Steinwedel, 1960). Since then, however, numerous technical advances have been made to convert this "ion cage" into a valuable bench-top mass spectrometer. The modern quadrupole ion trap is most noted for its versatility, sensitivity and superior MS^n capability. There are several issues, however, that have plagued the quadrupole ion trap since the introduction of the first commercial instrument. The most severe of these are compound-dependent mass shifts and a limited dynamic range due to space charge effects. The focus of the research presented here is to discover the root behind these issues and determine how they can be minimized or eliminated. In addition to the two areas presented above, fundamental research performed on peak splitting and ion injection in the quadrupole ion trap will also be reported.

To fully understand the basis of the presented research it is first important to understand the underlying principles of the quadrupole ion trap mass spectrometer. This introductory chapter will supply the reader with an understanding of the fundamental concepts of the quadrupole ion trap, which may be helpful for the informed ion trap user as well as a novice. This chapter, however, is not a complete review. For a more in-
depth understanding, other publications may be of help (March and Londry, 1995; Joscher and Yates, 1997; March, 1997 and 1998).

**History of the Quadrupole Ion Trap**

In the early 1950s, Wolfgang Paul and Helmut Steinwedel invented the quadrupole mass filter, arguably the most widely used mass analyzer in the world today. In the patent for the mass filter (Paul and Steinwedel, 1960) the two German physicists listed two other mass analyzers or “modified electrode arrangements.” The first consisted of an array of nine cylindrical rods; the second was what we consider today as the quadrupole ion trap (Figure 1-1).

![Figure 1-1 Depiction of the quadrupole ion trap in Paul's patent for the quadrupole mass filter. (Paul and Steinwedel, 1960)](image)

This novel design spent many years on the shelf before it was eventually transformed into a useful mass spectrometer. Physicists initially utilized the ion trap to investigate the properties of isolated ions. The method of detecting ions within the quadrupole ion trap was complex and evolved over several decades. In 1959, Fisher detected ions by resonance absorption (Fisher, 1959). Dawson and Whetten later devised
the idea of detecting ions by ejecting them from the trap to an electron multiplier (Dawson and Whetten, 1968). In 1972, Todd and co-workers published a series of papers in which they used the quadrupole ion trap as a novel source for a mass spectrometer (Lawson et al., 1973). This device, which was named the Quistor (quadrupole ion storage trap), was primarily used to study ion molecule reactions. Ions were created within the ion trap by passing an electron beam through holes in the ring electrode. Ions of a single m/z were then isolated by “mass selective stability”. In this mode RF (radio frequency) and DC voltages placed on the ring electrode are set to allow ions of a single m/z (mass-to-charge) to be trapped. After a variable storage time, ions were ejected into a quadrupole mass filter by using a DC (direct current) pulse on one of the endcap electrodes and detected by an electron multiplier. Although Todd proved this method for detection was useful in studying ion physics, it was not practical for many analytical purposes.

In the early 1980s, Stafford and co-workers saw the potential of the ion trap as a mass analyzer and took on the challenge of developing the novel instrument (Stafford et al., 1985). The technical advances made by Stafford and co-workers eventually pushed the ion trap into mainstream mass spectrometry. The first technical development was the creation of the “mass selective instability” mode of operation. In this mode ions of all m/z are trapped simultaneously and then ejected sequentially to a detector system. (Both the mass selective stability and instability modes will be further described later in this chapter.) The second development involved the addition of a light buffer gas in the trapping volume of the ion trap (Stafford et al., 1985). This greatly improved the mass
resolution and sensitivity of the instrument. With these innovations the commercialization of the Finnigan ITD (Ion Trap Detector) was realized in 1984.

The early ion trap instruments, the ITD and later the Finnigan ITMS (Ion Trap Mass Spectrometer), were all designed with internal ionization. Ions were generated within the ion trap by either electron ionization (EI) or low-pressure chemical ionization (CI). The ion trap proved to be very sensitive with internal ionization, but this limited the ionization methods that could be used. Modern ion trap instruments, such as the Thermo Finnigan GCQ, employ external ionization. With this innovation ion sources such as electrospray (McLuckey et al., 1995), MALDI (matrix assisted laser desorption ionization) (Brodbelt et al., 1995) and APCI (atmospheric pressure chemical ionization) (Hogenboom et al., 1998) have been coupled with the ion trap.

Today the quadrupole ion trap has become a useful tool in many areas of science. In its early inception the ion trap was coupled with GC (gas chromatography) and was capable of analyzing small, volatile molecules. That market has expanded to numerous areas as the ion trap has been linked with separation techniques such as LC (liquid chromatography) and CE (capillary electrophoresis) to study large biomolecules.

### The Quadrupole Ion Trap Mass Spectrometer

#### Ion Trap Geometry

The geometry of and the theory behind the quadrupole ion trap are very similar to those of the quadrupole mass filter. Instead of four hyperbolic rods that constrain an ion in two dimensions (x and y), the ion trap is composed of three electrodes that trap an ion
in all three dimensions (x, y and z). The quadrupole ion trap is constructed with three hyperbolic electrodes, one ring electrode positioned symmetrically between two virtually identical endcap electrodes. Figure 1-2 shows a cross section of the three electrodes.

The area within the ion trap is defined in terms of two coordinates, z and r. The electrode surfaces are all rotationally symmetric around the central or z-axis. This axial dimension of the trap, \( z_0 \), extends from the center of the trap to the closest point on either endcap electrode. Conversely, the r-axis or radial dimension, \( r_0 \), extends from the center of the device to the ring electrode and is simply the inscribed radius of the ring. The radial position of an ion within the ion trap can be derived from traditional Cartesian coordinates using the equation

\[
r = (x^2 + y^2)^{1/2}
\]  

(1-1)

To create an ion trap with a pure quadrupolar geometry, the physical dimensions of the ion trap have historically been controlled by equation 1-2 (March and Londry, 1995).

\[
r_0^2 = 2z_0^2
\]  

(1-2)

Knight, however has shown there is no real constraint on the r-z relationship as long as the Mathieu parameters are properly defined (Knight, 1983). Regardless of the ratio, the size of the ion trap is largely determined by the value of \( r_0 \). The majority of the commercial instruments today have an \( r_0 \) of either 10 or 7.07 mm.

For the ion trap to become a practical device structurally, two concessions have to be made. First, the electrodes have to be truncated. In theory, the electrodes for a pure quadrupolar device would extend out to infinity and meet the asymptotes (shown as dashed lines in Figure 1-2). The asymptotes arise from the hyperbolic geometries of the three electrodes. To limit the physical size of the trap and to provide electrical isolation
Figure 1-2 Cross section of the quadrupole ion trap. The three hyperbolic electrodes (one ring electrode positioned symmetrically between two endcap electrodes) creates the trapping volume. The area within the ion trap is defined in terms of two coordinates: $z$, the axial position and $r$, the radial position.
between the electrodes, the electrodes are shortened. Secondly, a perforation or hole has
to be placed in the center of each endcap electrode: one hole in the “entrance endcap” to
allow electrons and/or ions to enter the device, and another hole in the “exit endcap” to
allow ions to exit the device and be detected. Although these modifications may seem
minor, they are enough to distort the quadrupolar field that is generated inside the device.

To correct for the field distortions, the electrodes are typically assembled in such
a way that the $z_0$ has been stretched with no corresponding modification to the shape of
the electrodes which would be required in order to maintain pure quadrupolar geometry.
The value of $z_0$ on the Thermo Finnigan ITD and ITMS ion traps was actually increased
by 10.6% (Syka, 1995). This stretched geometry compensates for the higher order
multipole fields within the ion trap caused by the truncation of the electrodes and the
holes placed in the endcap electrodes.

**Quadrupolar Trapping Field**

A quadrupolar field is generated within the trapping volume by placing an RF
electric potential on the ring electrode while keeping the endcap electrodes at ground
potential. The RF potential is applied at a variable amplitude, $V$, and at a fixed angular
frequency, $\Omega$. Early ion trap instruments used a variable DC potential, $U$, on the ring
electrode to isolate ions within the trap (Todd, 1995). Modern commercial instruments,
however, now employ different methods for isolation, as will be discussed later in this
chapter. Placing an RF potential on the endcaps or even on all three electrodes can
produce the same quadrupolar field, but for simplicity the endcap electrodes are typically
kept at ground potential.
The RF potential applied to the ring creates a parabolic field inside of the trapping volume which varies quadratically from the center of the trap. The resultant field is most commonly depicted as a saddle (Jonscher and Yates, 1997). The trapping field is a dynamic field as its polarity constantly changes with the phase of the RF voltage. This active field is what collects and focuses ions toward the center of the device.

Figure 1-3 illustrates this saddle field and how an ion interacts with it. When the ring is at a positive potential, a positive ion situated close to the center of the ion trap is repelled from the ring and moves toward the endcap electrodes (Figure 1-3A). The RF potential, at frequencies in excess of 1 MHz, quickly changes polarity and the ion is drawn back towards the center of the ion trap. With a negative polarity, the ion now has a propensity to move towards the ring electrode (Figure 1-3B). With the polarity changing approximately every twice a microsecond, however, the ion remains focused in a space near the center of the ion trap.

The potential within the ion trap, \( \Phi(x,y,z) \), can be mathematically determined with the use of the following equation:

\[
\Phi(x,y,z) = -\frac{1}{2} E_0 \lambda (x^2 + y^2 - 2z^2) \tag{1-3}
\]

where \( E_0 \) is a position-independent component of the electric field and \( x, y \) and \( z \) are the Cartesian coordinates. Due to the rotational symmetry of the ion trap, this equation can also be written in cylindrical polar coordinates \( (r,z) \):

\[
\Phi(r,z) = -\frac{1}{2} E_0 \lambda (r^2 - 2z^2) \tag{1-4}
\]
Figure 1-3 The quadrupolar trapping potential within the ion trap. The potential on the ring electrode is represented by the sine waves on the left. (A) When the ring is at a positive potential, a positive ion situated close to the center of the ion trap is repelled from the ring and moves toward one of the endcap electrodes. (B) When the ring has a negative polarity, the ion has a propensity to move toward the ring electrode. With the polarity changing approximately twice a microsecond, the ion remains focused in a space near the center of the ion trap.
The electric field strength within the trapping volume varies linearly with the displacement from the center of the ion trap (The field strength is the derivative of the fields potential). The electric field \( E \) an ion experiences within the trap can be expressed as

\[
E = E_0(\lambda x + \sigma y + \gamma z)
\]  

(1-5)

where \( \lambda \), \( \sigma \) and \( \gamma \) are weighted constants for the \( x \), \( y \) and \( z \) coordinates. The equation is very similar to that for the force on a spring. In fact, an ion can be depicted as a ball attached to a spring at the center of the trap. As the ion ventures away from the center of the trap it will experience increasing field strengths focusing or pulling it back to the center like the tension on a spring. At the center of the trap, where \( x \), \( y \), and \( z = 0 \), an ion will experience no field at all, just like a relaxed spring, and the ion remains trapped.

**Mathieu Equation**

Once within the confines of the ion trap, an ion's motion will be defined by its \( m/z \) and the amplitude of the RF potential on the ring electrode. Ion motion can be described by the solution of a second-order linear differential equation described originally by Mathieu, called the Mathieu equation (Mathieu, 1868). From Mathieu’s investigation of simple harmonic oscillators, he was able to describe solutions in terms of regions of stability and instability. Mass spectrometrists have applied these solutions to describe the trajectories of ions within the quadrupolar devices and to define the limits of stability. The canonical or commonly accepted form of the Mathieu equation is shown below.

\[
\frac{\partial^2 u}{\partial \xi^2} + (a - 2q \cos 2\xi) u = 0
\]  

(1-6)
where $\xi$ is a dimensionless parameter equal to $\Omega t/2$ where $\Omega$ is frequency and $t$ is time.

The $u$ is the position of the ion in either the axial ($u=z$) or the radial ($u=r$) direction. The reduced parameters $a_z$ and $q_z$ are dimensionless parameters known as trapping parameters. They are represented by the equations below:

$$a_z = -2a_r = \frac{-16eU}{\Omega^2 (r_0^2 + 2z_0^2)}$$  \hspace{1cm} (1-7)

$$q_z = -2q_r = \frac{8eV}{\Omega^2 (r_0^2 + 2z_0^2)}$$  \hspace{1cm} (1-8)

where $e$ is the charge of an electron ($1.602 \times 10^{-19}$ C), $U$ is the DC voltage ($1 \text{ V}= \text{kg m}^2/\text{s}^2 \text{ C}^{-1}$), $V$ is the AC voltage volts (0 to peak), $m$ is the mass of the ion (in kg, kg mol$^{-1}$/6.022 x $10^{23}$ mol$^{-1}$), $\Omega$ is drive frequency ($2\pi f$ where $f$ is the drive frequency in s$^{-1}$) and $r_0$ and $z_0$ are the trap dimensions (m). $q_u$ is directly proportional to the RF amplitude on the ring and $a_u$ is proportional to the DC. Equations 1-7 and 1-8 are very important to quadrupole ion trap mass spectrometry and will be used frequently throughout this dissertation.

Mathieu Stability Diagram

Not all experimental conditions will produce an ion motion in the ion trap that is stable. For an ion to adopt a stable trajectory, it must be stable in both the axial and radial dimensions. Since the motion of an ion in a pure quadrupolar field is not coupled between the $r$ and $z$ directions, it is possible for an ion to be stable in one direction and not the other. The parameters $q_u$ and $a_u$ will determine whether an ion is stable. A graphical representation of these parameters, called the Mathieu stability diagram, can be seen in Figure 1-4. The stable solutions of the Mathieu equation in the $z$ direction are shown as regions that originate from the positive $y$-axis and the stable solutions for the $r$ direction originate from the negative $y$-axis. Ions can be stored within the ion trap
Figure 1-4 The Mathieu stability diagram is $a_z$ and $q_z$ space. The black regions designate where an ion is stable in the z dimension and the gray regions specify where an ion is stable in the r dimension. The major regions of simultaneous overlap are labeled A and B.
provided that their trajectories are simultaneously stable in both the $z$ and $r$ dimensions. The most commonly employed region of stability (where radial and axial stability overlap) is in the area closest to the origin (labeled A in Figure 1-4). An enlargement of this region can be seen in Figure 1-5. An ion with a given m/z can be trapped anywhere within that region. There are several other regions of stability, including the region labeled B in Figure 1-4. The stability diagram for negative ions is slightly different. It is the mirror image of that for positive ions and can be obtained by reflecting the stability diagram in Figure 1-4 about the $q_z$ axis.

The coordinates of the stability diagram are the Mathieu parameters $a_u$ and $q_u$ and the boundaries of the stability diagram correspond to the iso-beta lines $\beta_z$, $\beta_r = 0$ and $\beta_z$, $\beta_r = 1$. The $\beta_z = 1$ stability boundary intersects with the $q$ axis at $q_z = 0.908$. This boundary defines the range of masses that can be held within the ion trap. The position of the ions within the stability region can be moved by changing the amplitude of the applied RF or DC, which alters the ions, $q_z$ and $a_z$. For the research here no DC is applied to the ring electrode; therefore all ions fall on the $a_z = 0$ line (on the x axis).

The value $q_z$ is inversely proportional to m/z (equation 1-8); consequently, ions of higher m/z will have a lower $q_z$ value than lower m/z ions. In the Mathieu stability diagram ions will therefore arrange themselves from high to low m/z along the $a_z = 0$ line. The amplitude of the RF determines the lowest m/z that can be held within the ion trap. This amplitude is represented in terms of a LMCO (low-mass cut-off), which for simplicity is expressed in units of m/z. Ions with an m/z below the LMCO will not be trapped. For instance if the LMCO is m/z 100, than ions of m/z 100 will be seated at the
Figure 1-5 Stability diagram space for the region of simultaneously stability near the origin for the ion trap. The iso-\(\beta\) lines are shown in the diagram. The \(q_z\) axis intersects the \(\beta_z = 1\) boundary at \(q_z = 0.908\), which corresponds to the point of ejection in the "mass selective instability mode". The scan line for the "mass selective stability" mode intersects the lower apex of the stability diagram. (A similar mass selective stability line intersects the top apex.)
stability edge \( q_z = 0.908 \) and all masses below this m/z value will not be stable within the trap, due to their instability in the z-dimension. On the opposite side of the stability diagram, high m/z ions are packed down at low q values. The high-mass cut-off is not so easily defined. High masses can be lost due to a shallow potential well which exists at low \( q_z \) values or if they are slightly lifted off the \( a_z=0 \) line due to fields arising from space charge and become unstable.

The parameter \( q_z \) is very important in determining the position of an ion on the stability diagram during a scan event. Injection, ejection, isolation and excitation of ions are all typically related in terms of \( q_z \) for a specific m/z. Therefore it is useful to have an equation to determine the position of an ion in q space. By using Equation 1-9, the \( q_z \) position of any m/z can be determined by knowing the LMCO and the \( q_z \) of ejection.

\[
m_1 q_1 = m_2 q_2 \tag{1-9}
\]

This equation assumes that RF amplitude (V), geometry (r and z) and drive frequency (\( \Omega \)) are all fixed. Taking the example above, by knowing the LMCO is 100, m/z 100 is at \( q_z = 0.908 \) and m/z 600, for instance, would be at \( q_z = 0.151 \).

The position of an ion within the stability region can also be expressed in terms of \( \beta \). The iso-\( \beta \) lines are related both to a and q and stretch across the entire stability region.

For \( q < 0.4 \), \( \beta \) can be approximated by (March and Londry, 1995)

\[
\beta_s = (a + \frac{q^2}{2})^{1/2} \tag{1-10}
\]

However for \( q > 0.4 \) the relationship becomes non-linear and the method of successive approximations shown below must be used (March and Londry, 1995).
\[ \beta^2 = a + \frac{q^2}{(2+\beta)^2 - a} - \frac{q^2}{(4+\beta)^2 - a} + \frac{q^2}{(6+\beta)^2 - a} - \text{etc.} \]

\[ + \frac{q^2}{(\beta-2)^2 - a} - \frac{q^2}{(\beta-4)^2 - a} + \frac{q^2}{(\beta-6)^2 - a} - \text{etc.} \]  \hspace{1cm} (1-11)

**Pseudopotential Well Depth**

The ability of the trapping field to hold an ion varies with \( q_z \) and is measured in terms of potential well depth. The depth of this potential well determines the amount of kinetic energy an ion can acquire or maintain before it can overcome the field and be ejected from the ion trap. The pseudopotential well model was originally derived by Major and Dehmelt (cited in March and Hughes, 1989). For \( q_z < 0.4 \) the well depth is determined by

\[ D_a = \frac{mq_o^2\Omega^2u_o^2}{16e} \]  \hspace{1cm} (1-12)

Beyond a \( q_z \) of 0.4 this relationship no longer holds as the relationship between well depth and \( q_z \) becomes non linear. In most instruments \( r_0^2 \approx 2z_0^2 \) so the depth of the potential well the depth in the \( z \)-direction is considered twice that along the \( r \) axis. An important piece of information can be extracted from this equation. Ions, which are at a low \( q_z \), are in a shallow well, whereas ions situated at higher \( q_z \) values are held more tightly and require more energy to excite or eject them.
Ion Frequency

Ion motion within the ion trap is a complex phenomenon. A two-dimensional depiction of a three-dimensional ion trajectory closely resembles a Lissajous curve or a figure eight. Figure 1-6 shows a typical Lissajous trajectory followed by an aluminum microparticle suspended in an RF quadrupolar field. (Wuerker et al., 1959)

![Lissajous curve](image)

Figure 1-6 Aluminum microparticle suspended in a quadrupolar field

An ion within the ion trap oscillates at axial and radial frequencies called the secular frequencies of the ion ($\omega_x$ and $\omega_r$). This frequency is directly related to angular frequency ($\Omega$) which is applied to the ring electrode by

$$\omega_n = \beta_e \frac{\Omega}{2}$$  \hspace{1cm} (1-13)

The secular frequency of an ion is the frequency at which it travels a complete path within the device. An ion held at a specific $q_e$ (and therefore at a particular value of $\beta$) will have the same secular frequency no matter what the m/z may be. At the edge of the stability region where $\beta = 1$, the ion will have the secular frequency of half the drive frequency, $\Omega$. 
Ion motion is also composed of higher order frequencies, commonly referred to incorrectly as harmonics, which are derived by the following equation (March and Londry, 1995)

\[ \omega_n = (n \pm \frac{\beta_n}{2}) \Omega \]  

(1-14)

where \( n = 0, 1, 2, \ldots \) They appear as ripples (sometimes called "micromotion") in the Lissajous figure above. Figure 1-6 shows an FT (Fourier Transform) for several of the frequency components of an ion in the \( z \)-dimension. The ion motion was created by an ion simulation program SIMION v.7 (Idaho National Engineering Laboratory, Oak Ridge, TN) and a FT was performed by Excel (Microsoft Corp., Redmond, WA). The largest frequency component of ion motion, labeled A in Figure 1-6, is most commonly referred to as the secular frequency of the ion. Smaller higher order frequencies are labeled B through D.

Ions within the ion trap can be manipulated by creating a resonance condition between a supplementary AC potential, usually applied to the endcap electrodes, and this secular frequency of the ion. The ion will absorb energy from this supplementary field and its trajectory will increase towards the endcap electrodes (in the \( z \)-axis). This method had been employed to excite an ion in MS/MS and eject an ion for detection (Todd, 1995). Resonance excitation has also been performed with several other frequencies listed in Figure 1-6 but suffers from lower efficiency. An ion will possess many frequency components in the \( r \) dimension as well.
Figure 1-6 FT (Fourier Transform) of an ion motion created by SIMION v.7. The ion of interest is m/z 264 at a $q_z$ of 0.83 ($\beta_z = 0.742$). The drive frequency ($\Omega$) is 1.03 MHz, the same as the GCQ. The ion motion was sampled at a rate of 4 MHz.

Mass Spectrometer Events

To obtain a mass spectrum from an ion trap mass spectrometer, an analyte must be ionized and the ions directed into the trap, trapped, ejected and detected. Each process is unique and merits its own explanation.
Ionization

The instrumentation used in this study is capable of producing ions with either EI (electron ionization) or CI (chemical ionization). Most of the ions used in this fundamental study, however, were produced by EI. This section will therefore concentrate on that technique.

In EI, electrons are produced by hot filament and are directed towards a source region. Within the source they collide with analyte molecules and create ions by stripping the molecule of an electron (secondary electron). The ion created, called the molecular ion, will have a positive net charge. In positive EI, the interactions between an electron and an analyte molecule produce an ion with an efficiency of about 1 in 1000 to produce an ion (Chapman, 1994).

Positive ion formation: \[ \text{ABC} + e^- \rightarrow \text{ABC}^+ + 2e^- \]

The kinetic energy of the electrons entering the ion source is typically 70 eV for positive EI. The kinetic energy is defined by the potential difference between the filament and the source ground. The ionization potential of most organic molecules is on the order of 10 eV. This can leave a great deal of excess energy in the molecular ion. This surplus energy will typically cause dissociation of the molecular ion by one of the following processes (Rankin, 1971):

Fragmentation: \[ \text{ABC} + e^- \rightarrow A^+ + \text{BC} + 2e^- \]
\[ \text{ABC} + e^- \rightarrow \text{AB}^+ + \text{C} + 2e^- \]
\[ \text{ABC} + \text{e}^- \rightarrow \text{AC}^+ + \text{B} + 2\text{e}^- \]

**Rearrangement:**
\[ \text{ABC} + \text{e}^- \rightarrow \text{B}^+ + \text{AC} + 2\text{e}^- \]

EI can also produce ions with a negative charge through a process called resonance electron capture. This process can only occur, however, when the electron energy is below 2 eV. Normal filaments cannot efficiently emit such low energy electrons. Low kinetic energy electrons can be created, however, by inelastic collisions with a buffer gas in the source or can arise as secondary electrons from fragmentation of other molecules in the source. The capture of a low-energy electron will result in the production of an intact molecular anion, \( \text{M}^- \). The efficiency of this process can be improved with a high buffer gas pressure within the source. The buffer gas efficiently thermalizes low-energy electrons and collisionally stabilizes excited molecular ions.

Electron capture is often referred to as negative Cl due to its reliance on a buffer gas; true negative Cl, however, involves formation of reagent anions from appropriate reagent gases (e.g., \( \text{OH}^- \) formed from mixtures of \( \text{CH}_4 \) and \( \text{O}_2 \)) which react with sample molecules by proton abstraction to form [M-H]- ions.

**Resonance Capture:**
\[ \text{ABC} + \text{e}^- \rightarrow \text{ABC}^- \]

**Dissociative Resonance Capture:**
\[ \text{ABC} + \text{e}^- \rightarrow \text{AB}^- + \text{C} \]

**Ion Pair Formation:**
\[ \text{ABC} + \text{e}^- \rightarrow \text{A}^+ + \text{BC}^- + \text{e}^- \]
\[ \text{ABC} + \text{e}^- \rightarrow \text{AB}^+ + \text{C}^- + \text{e}^- \]
Dissociative resonance capture can occur for electron energies ranging from 2 to 10 eV, while ion pair formation occurs when the electron energy is greater than 10 eV.

**Ion Injection**

In early commercial ion trap instruments (e.g. the Thermo Finnigan ITD, ITMS, and ITS40), ions were formed directly inside the trap using either EI or low-pressure CI. Although internal ionization is a sensitive technique, it possesses several disadvantages. One such disadvantage is the likelihood of ion-molecule reactions, which lead to charge exchange and the formation of unwanted, adduct ions. This results from analyte neutrals and analyte ions occupying the same space within the ion trap.

To avoid these pitfalls, ions can be produced externally and then injected into the ion trap. Separating the ion source from the ion trap offers several advantages. It allows high-pressure ionization techniques, such as electrospray (ESI), glow discharge, negative chemical ionization and atmospheric pressure chemical ionization, to be coupled to the ion trap. Additionally, ion-molecule reactions within the ion trap are reduced, and the number and mass range of ions injected into the ion trap can be controlled. Controlling the number of ions within the ion trap is important because it reduces space charge effects, improving resolution, mass accuracy and sensitivity (Cox et al. 1995; Stafford et al. 1987).

Trapping externally generated ions is not a trivial task. Ion injection exhibits dependence on both the initial RF phase and the RF amplitude (LMCO) (Quarmby and Yost, 1999; He and Lubman, 1997; Wei et al., 1996). An ion which approaches the ion trap with a specific kinetic energy may not have enough energy to overcome the RF potential applied to the ring electrode and therefore will be turned around before it enters
the trap. As the RF potential changes polarity, that same ion may have too much energy and travel right through the trap without being captured. This RF dependence limits the ability of the ion trap to accept ions from an external source.

Ions which are accelerated from an external source must be relieved of excess kinetic energy to be trapped efficiently. A buffer gas is utilized to cool the analyte ions and confine them to the center of the ion trap. The reduction in momentum due to the collisions with the buffer gas helps remove excess ion kinetic energy and allow the ion to be trapped within the ion trap’s pseudopotential well. Unfortunately, these collisions may also add to an ion’s internal energy and cause fragmentation. Such fragmentation may be one source of discrepancy between spectra obtained from an ion trap and other mass analyzers, such as a quadrupole mass filter.

Collisional cooling with a buffer gas is an effective tool to trap ions, but it is limited to low pressures, typically 1 mtorr (March, 1997), by other requirements throughout the analytical scan. Increasing the buffer gas pressure may result in more efficient trapping but may potentially cause both increased fragmentation and decreased ion ejection efficiency. The buffer gas pressure can be varied during the analytical scan by the use of a pulse valve (Williams, 1997), but this has not been widely implemented.

In response to this, several other methods of improving trapping efficiency have been proposed. For pulsed ion sources such as matrix-assisted laser desorption ionization (MALDI) and laser desorption (LD), a dynamic trapping technique has been developed (Eiden et al., 1994; Doroshenko and Cotter, 1997). Other techniques used for pulsed sources involve adding either a DC pulse or a supplementary frequency to the endcaps upon injection to help damp the incoming ions (Wei et al., 1996; Moore and Guick,
Currently the only technique which has been demonstrated to be successful in trapping ions for continuous ion sources is collisional cooling with a buffer gas. Presently, all commercial instruments use helium as a buffer gas. Helium is attractive because it is inexpensive, non-reactive and can be used in conjunction with instruments such as a gas chromatograph (GC). Other buffer gases studied include air, argon, xenon and hydrogen (Lammert and Wells, 1996; Morand et al. 1992).

To control injection of ions into the trap, a gating lens pulses either positive or negative to either repel or attract ions into the trap. The time during which the gating lens allows ions into the trap is controlled to maximize the ion signal while minimizing space charge effects. Space charge occurs when there are too many ions within the ion trap, resulting in an overall poor performance of the mass analyzer.

**Ion Ejection**

In the ion trap’s initial development, detection was performed using “mass selective stability” scans. In this mode the ion trap was operated with both RF and DC so that ions of a single m/z were trapped. This usually was accomplished by employing the lower apex of the stability diagram (Figure 1-4). The isolated ions were then ejected from the ion trap by pulsing one endcap with a DC potential and detected with an electron multiplier. Although the ion trap operated in the mode proved to be a sensitive device, it did not pose any advantage over a simple quadrupole mass filter.

The ion trap became a practical mass spectrometer with the discovery of “mass selective instability” (Stafford et al., 1985). The mass selective instability mode uses no DC so the scan line lies on the $a_x = 0$ line. In this mode mass analysis is performed by raising the amplitude of the RF potential applied to the ring electrode. The ramping of
the RF amplitude causes q_z values associated with the ion to increase until they reach the LMCO at q_z = 0.908, at which point the ions adopt unstable trajectories in the axial direction (between the two endcap electrodes) but remain stable in the radial direction. Ions are subsequently ejected through the holes in the endcap electrodes and those ejected through the exit endcap are detected by an electron multiplier. Remember that ions with smaller m/z have larger q_z values; thus raising the RF will produce a mass spectrum from low m/z to high m/z. For a given set of conditions the maximum m/z is limited only by the maximum RF amplitude that can be generated by the RF system.

Even with a small number of ions in the trap, ejection of ions at the LMCO stability edge (β_z =1) results in poor peak shape and resolution (Stafford at al., 1985). Resolution and peak shape can be improved by adding a supplementary alternating current (AC) or resonant ejection amplitude across the endcap electrodes at the secular frequency of the ions just before ejection at the stability boundary (slightly below β_z =1, frequency slightly below half of the drive frequency, Ω) (Tucker et al., 1988). The supplementary AC causes ions to quickly move from the center of the trap so that they experience the main trapping field, whereupon they are accelerated in a tight packet towards the endcaps. The ions which are ejected through the exit endcap are then detected by an electron multiplier. This method of detection has been called resonant ejection or axial modulation (Stafford et al., 1985).

An additional advantage of axial modulation is that it can be carried out at any q_z value less than 0.908 (and thus any frequency less than half of Ω). Normally ejection occurs just below q_z values than 0.908. Lowering the q_z even further can extend the normal mass range of the ion trap. The frequency separation between adjacent ions
decreases at lower q values, however, and this leads to poorer resolution.

Several other means of ion ejection have been developed. Varian uses what is described as a “triple resonance” to eject ions. Instead of ejecting ions close to the edge of stability ($\beta_z = 1$), ions are ejected at a point of a non-linear hexapole trapping field resonance ($\beta_z = 2/3$) (Splendore et al. 1999), arising from imperfections in the quadrupolar field. At this point of ejection ion trajectories are reportedly less affected by collisions with the buffer gas and resolution is improved.

Several studies have shown that similar to ion injection, ion ejection may be phase dependent. (Londry and March, 1995) The ejection of positive ions is favorable when the supplementary field applied to the exit endcap and the fundamental RF potential placed on the ring electrode are in phase with one another. Simulations have shown that ejection occurs only when these two frequencies meet each other during their negative phase. A technique called phase locking has used this information to increase mass resolution. (Londry and March, 1995; Doroshenko and Cotter, 1996)

**Ion Isolation**

The focus up to this point has been concerned with the analysis of ions contained within the trap by ramping the RF potential and successively ejecting ions in order of increasing m/z. One very important feature not to be overlooked is an ion trap’s ability to selectively store (isolate) a specific m/z and eliminate the unwanted remaining ions. Ion isolation is essential for tandem mass spectrometry experiments (MS/MS) but is also an effective tool for improving the sensitivity of the ion trap in SIM methods (single ion monitoring).
An ion of interest can be isolated within an ion trap in one of three ways: through RF/DC isolation (McLuckey et al., 1991), forward and reverse scans (Ardanaz et al., 1991) or waveforms (Guan and Marshall, 1996). The first two methods were employed by early commercial mass spectrometers. In RF/DC isolation, the RF and DC potentials on the ring are altered to move a specific m/z ion near the stability apex permitting mass selective isolation. The apex most often used is the upper apex in Figure 1-4 where \( a_z = 0.150 \) and \( q_z = 0.781 \). In this case, ions of greater m/z would be unstable in the r dimension while ions of lower m/z would be unstable in the z dimension, leaving a single m/z stable in both regions.

An ion may also be isolated with the use of forward and reverse scans. This procedure employs two steps of resonant ejection. First a resonant ejection frequency is established just inside the stability boundary. Ions are scanned out just as in a normal mass scan, but stopping just before the ion of interest reaches the stability edge. This eliminates all ions with m/z lower than the ion of interest. To eliminate higher m/z ions, the resonant ejection frequency is now relocated to a lower q value behind the specified ion. The ion trap now performs a mass scan in the reverse direction towards the resonant ejection frequency, ejecting all of the higher m/z ions.

Modern ion trap instruments use tailored waveforms. Waveforms can be depicted as a summation of numerous sine waves with frequencies across the entire stability region. These wavebands of frequencies are applied to the endcap electrodes to excite and eject many ions simultaneously, leaving behind a single m/z or a small range of m/z values. A depiction of waveform isolation can be seen in Figure 1-7. The dark regions
of the stability diagram represent the areas where the waveform is applied. Ions within that region of higher and lower $q_z$ values are rapidly and efficiently ejected.

![Diagram of Mathieu stability diagram](image)

Figure 1-7 Waveform isolation of an ion depicted with the Mathieu stability diagram. The dark regions of the stability diagram represent the areas where the waveform is applied. Ions within that region are ejected leaving ions of a single or range of m/z values (within the white region) in the ion trap. The spheres represent ions of different m/z.

The $q_z$ at which isolation is performed (the white region in Figure 1-7) is chosen for a specific reason. Ions separate from each other in $q_z$ as well as in frequency as they are brought closer to the stability edge (Figure 1-8). For the purpose of using waveforms it is most advantageous to isolate ions where the frequency separation is highest. This allows the waveforms to effectively eliminate unwanted ions without perturbing the ion of interest. The Thermo Finnigan ion trap instruments isolate ions at a $q_z$ of 0.83.
Resolution and Mass Accuracy

In the early development of the ion trap, improvements in mass resolution were made with the addition of helium as a buffer gas (Stafford et al. 1984). Helium acts to collapse ion clouds to the center of the trap. This enables ions to be ejected in a tighter packet, thereby increasing resolution. In later studies, it was discovered that by slowing down the scan speed, resolution in excess of 5000 could be achieved (Williams and Cooks, 1992). The mass resolution of the ion trap is a function of the number of RF cycles that the ion spends interacting with the field, very similar to a quadrupole mass filter. Slowing down the scan allows the ions to experience more oscillations of the
resonant ejection frequency. With continued research the resolution on the quadrupole ion trap continues to improve; however, there is still a large gap between the ion trap and high-resolution mass analyzers (i.e. sector and Fourier-transform ion cyclotron resonance (FT-ICR) instruments) (Russell and Edmondson, 1997).
CHAPTER 2
INSTRUMENTATION

The research presented in this dissertation employed three separate Thermo Finnigan ion trap mass spectrometers, a research grade prototype GCQ, an ITMS, and a PolarisQ, as detailed below. The GCQ instrument is a prototype research instrument constructed at the University of Florida using GCQ electrodes and electronics. It is quite different than the commercial version of the GCQ. It consists of a large vacuum manifold that allows for easy instrument modifications for different scientific experiments. The ITMS was used in conjunction with a quadrupole mass filter from a TSQ45 to investigate the production of fragment ions during injection and resonant ejection. In contrast to the modified GCQ, the ITMS was designed for internal ionization. With numerous advances to ion trap instrumentation, the ITMS electronics and software have become outdated, but the instrument is still quite useful for studying ion trap fundamentals. Lastly the PolarisQ was used during my first summer internship with Thermo Finnigan to study space charge effects. The PolarisQ is the new generation GC/MS instrument based on the GCQ.

Research Grade GCQ

A majority of the work in my dissertation was performed on the modified GCQ. For this reason, I will supply a lengthy background of this instrument. A detailed account
of this instrument will provide not only insight into the experiments in my dissertation but also a suitable background for modern commercial ion trap instrumentation.

The modified GCQ is a differentially pumped instrument housed in a cast aluminum manifold. The manifold is separated into three distinct chambers by two adjustable baffle walls. Each chamber is evacuated with its own turbomolecular pump. The first chamber houses a GCQ ion source and ion lenses. The second chamber contains a bent octopole ion guide that transmits ions from the ion source to the GCQ ion trap. The third chamber houses the GCQ ion trap electrodes along with a conversion dynode and electron multiplier. Differential pumping allows the separation of the high-pressure source and the mass analyzer. This keeps neutral gasses such as the CI reagent gas and sample neutrals from reaching the ion trap. A glass cover covers the entire manifold.

Figure 2-1 Picture of the research-grade GCQ. The three separate chambers house, from left to right, the ion source (A), a bent octopole (B) and the mass analyzer with detection system (C). A heated transfer line (D) introduces both helium and analyte into the ion source.
Ion Source

The first chamber, far left in Figure 2-1, houses the ion source. The unmodified GCQ source is mounted to the baffle wall separating the first two chambers. The GCQ ion source is capable of both EI and CI. This is possible with the use of interchangeable ion volumes, the heart of the ion source. Structurally the ion volumes are similar with one difference: the EI ion volume has a large exit aperture while the CI volume has a small exit aperture to allow for high pressure CI (Figure 2-2).

![Figure 2-2 GCQ ion volumes. The ion volume on the left is designed for EI while the volume on the right with the enclosed end is made for CI.](image)

Both ion volumes have three holes in addition to the ion exit hole. The two 0.090” holes on either side of the ion volume are designed to receive GC effluent through the heated transfer line on one side and calibration gas and CI reagent gas on the other. The last hole, with the smallest aperture of 0.0015”, receives the electron beam from the filament.

In the GCQ ion source (Figure 2-3), a filament assembly lies directly above the ion volume. The filament assembly contains a filament, reflector, and electron lens. The filament is a rhenium wire that is electrically heated to produce electrons by thermionic emission. The hairpin filament, different than typical straight or coil designs, is made
with a sharp bend in it. The point created by this bend is capable of emitting electrons from a focused area into the ion volume. The reflector, situated behind the filament, repels electrons away from the filament towards the ion volume. The filament and the reflector are maintained at negative potential of 70 V relative to the ion volume. The electrons emitted by the filament are therefore accelerated into the ion volume which is held at ground potential. The kinetic energy of the electrons is equal to the difference in potential between the filament and the ion volume (-70 eV). The flow of electrons emitted by the filament is termed the filament emission current. The default value for the GCQ is 250 µA. Outside of the source block and filament assembly lie two

Figure 2-3 GCQ ion source. The filament assembly sits within the heated source block on top of the ion volume. The three ion lenses (not shown here) are mounted on the ends of the heater cartridges which extend through the ion source block, to the left in this drawing.
permanent magnets of opposite polarity (not shown in Figure 2-3). The magnets create a field which collimates the filament electrons into a beam and cause the beam to spiral through the ion volume. This increases the number of electrons which enter the ion volume and expands their path through the volume, maximizing the efficiency of the ionization process.

An electron lens, situated between the filament and the ion volume, helps focus electrons into the ion volume; it also helps prevent positive ions from traveling back into the filament assembly. Adsorption of positive ions to the filament can cause it to deteriorate. The voltage applied to this electron lens determines the flux of electrons that enter the ion volume. Therefore the electron lens can also be used to control ionization efficiency.

The ion volume and filament assembly are surrounded by a heated source block that can vary the source temperature from 40 to 225°C. The ion source block is heated for two reasons. One reason is to maintain the flow of sample molecules from the heated GC transfer line into the ion source and minimize condensation of sample molecules on the ion source block, lenses and ion volume. Condensation of sample molecules can reduce sensitivity and lead to band broadening of GC peaks and sample carry-over. The resulting deposits which form on these surfaces decrease ionization efficiency and ion transmission. The second reason is to assist in the rapid temperature equilibration of the ion source block and the ion volume after the filament is turned on. A variation in source temperature would affect ion ratios and ionization efficiency.

The source chamber is pumped by a Pfeiffer Balzers TPH 240H turbomolecular pump. The nominal pressure within the source chamber, monitored by a Granville
Phillips ion gauge, is approximately $3 \times 10^{-5}$ torr with helium being introduced into the ion source through the heated GC transfer line. This pressure will vary with the flow rate of helium from the GC.

**Ion Optics**

Three electrostatic lenses are positioned between the source and the entrance to the octopole to focus and gate ions from the ion volume to the ion trap. The lenses are made of stainless steel and are surrounded by an anodized aluminum spacer. The lens stack on this research instrument is slightly modified from the normal GCQ ion source. The first lens is a standard GCQ lens 1 (Figure 2-4). With a typical potential of $-20$V (for positive ions) it is used to extract ions from the ion volume. The second lens is a flat lens with an aperture slightly larger than that in lens 1. It is responsible for focusing the ions using a potential of $-130$V. As a general rule, large lens amplitudes increase ion velocity and focus ion beams, while small amplitudes tend to decelerate and diverge ion beams. A thin spacer is placed between the first two lenses to make the entire lens stack thicker than the heater cartridges, in which all three lenses are mounted. This keeps the heating elements from making contact with the baffle wall.

![Stainless Steel Lens and Anodized Spacer](image)

Figure 2-4 GCQ Lens 1 – Lens 1 is a small tube lens which extracts ions from the ion volume. The lens is made of stainless steel and is surrounded by an anodized spacer.
In contrast to the quadrupole mass filter, the quadrupole ion trap requires a pulse of ions from the source. To accomplish this, ions must be gated and allowed to enter the trap only during the injection portion of the analytical scan. The last lens in the GCQ lens stack is implemented as a gating lens. This flat lens controls the flow of ions into the octopole with two potentials: -130V (gate open) and +100V (gate closed). The +100 volt potential forces all ions to remain either in the ion volume or within the first two lenses. When the polarity of this lens is negative, ions are allowed to flow into the octopole which is seated just behind lens 3.

Octopole Ion Guide

The middle chamber in the vacuum manifold houses the transmission octopole. The octopole is 9 inches long and has a $r_o$ of 0.11". It has a $10^\circ$ bend in the center to keep photons and high-energy neutrals from the ion source from reaching the trap while still transmitting ions. These particles would be a source of noise if they were allowed to travel straight through the ion trap into the detector. The $10^\circ$ bend is consistent with the collision cells (Q2) in triple quadrupole instrument produced by Thermo Finnigan. A Thermo Finnigan TSQ 45 lens voltage power supply is used to set the amplitude of the octopole RF, utilizing a prototype RF amplifier also made by Thermo Finnigan. An RF amplitude of $200 - 500V_{op}$, at a frequency of 2.475MHz, transmits the entire m/z range that can be analyzed by the GCQ. Low amplitudes transmit low m/z ions efficiently, while high amplitudes more efficiently transmit high m/z ions. The octopole potential is offset from the GCQ source by a DC potential of +/- 30V, (positive potential for negative ions and a negative potential for positive ions) controlled by the TSQ lens supply.

The middle chamber where the octopole is housed is pumped by a Pfeiffer
Balzers TPH 170H turbomolecular pump. The pressure in this chamber is not typically monitored.

**Mass Analyzer and Detector**

The final chamber, far right in Figure 2-2, houses the GCQ mass analyzer and detector. The GCQ ion trap is composed of three stainless steel electrodes: a ring electrode sandwiched by two endcap electrodes (an entrance endcap and an exit endcap). The electrodes are separated by a set of silicon nitride spacers. The spacer rings position the electrodes at the proper separation and also serve as electrical insulators. Two non-conducting posts pass through the endcap electrodes and screw into the baffle wall. A spring washer and nut on the end of each post apply a force to the exit endcap electrode and hold the mass analyzer together (Figure 2-5). The $z_0$ and $r_0$ of the analyzer are 7.83 mm and 7.07 mm respectively. Ions produced in the GCQ ion source enter the mass analyzer through the entrance endcap electrode. The entrance endcap sits directly on the anodized baffle wall. Helium buffer gas also enters the mass analyzer through a nipple on the entrance electrode.

An RF voltage at a frequency of 1.03 MHz is applied to the ring electrode by a spring-loaded pin. The voltage has an amplitude range of 0 - 8.5 kV. At this frequency the mass limit of the instrument is m/z 1000. Lowering the drive frequency would increase the mass range of the instrument. The Thermo Finnigan LCQ, for instance, has a drive frequency of 760 kHz which corresponds to a mass range of 2000 m/z.

A DC offset of -13V (for positive ions) is applied to the ion trap electrodes (the ring and both endcap electrodes) with respect to the ion source. This is not to be confused with the DC placed on the ring to move off of the $a_z = 0$ line on the stability
diagram (Figure 1-5). The trap offset sets the ion’s kinetic energy as it enters the ion trap. The DC offset is limited to +/- 10V by the GCQ software but it can be extended to +/- 30V with the Custom Tune software.

![Diagram of GCQ mass analyzer with mounting bracket](image)

Figure 2-5 GCQ mass analyzer with mounting bracket. In the research-grade GCQ the ion trap is attached to the baffle wall instead of a mounting bracket.

During mass analysis, a resonant ejection amplitude is applied across the endcap electrodes at a frequency of 476.375 kHz, corresponding to a $q_z$ of 0.901643 (just inside the stability boundary).

An exit lens is located outside of the exit endcap electrode. This lens, usually held at ground potential, isolates the ion trap from the strong potential field emitted by the dynode, preventing this field from penetrating the field within the ion trap. It also serves to focus ions as they are ejected from the ion trap. A series of experiments were performed to characterize the effect of the potential on this lens during injection. A
pulsed positive potential during injection has shown to have an increased effect on trapping efficiency.

The detector for the modified GCQ is composed of a conversion dynode and a DeTech continuous-dynode electron multiplier. The dynode is typically set at $-15\text{kV}$ for positive ions. Both the dynode and the multiplier are off-axis from the ion trap. Ions ejected from the ion trap strike the dynode and emit secondary ions and electrons which are accelerated towards the multiplier (biased at $-1.5\text{kV}$). The charged particles which strike the surface of the electron multiplier cause secondary emission of electrons from the multiplier surface. The secondary electrons consequently cause a cascading emission of additional electrons that are drawn down into the more positive channel of the electron multiplier towards the grounded anode. This cascading of electrons creates a gain for the ion signal of typically $3\times10^5$. This gain can be modified with the voltage placed across the multiplier. The anode cup at the back end of the multiplier collects the focused electrons and passes the current to the electrometer. The electrometer circuit amplifies the current again, converts it to an analog voltage signal, and finally converts it to a digital signal. The digital signal is sent to a digital signal processor which processes it and sends the signal to the computer where it is recorded as a mass spectrum.

This analyzer chamber is pumped by a Pfeiffer Balzers TPH 190H turbomolecular pump. With 1 mtorr of helium present within the ion trap the pressure within this region is typically $3.0\times10^{-6}\text{torr}$.

The GCQ ion trap is controlled by a set of GCQ electronics and custom software (Custom Tune) supplied by Thermo Finnigan. Thermo Finnigan supplied both the instrument source code and a programmable Visual Basic interface. The custom software
allows experienced users to write and optimize scan functions that are normally outside of the constraints that have been set on the instrument. This allows parameters that are usually kept constant, such as the q2 of ejection, to be manipulated with a small amount of programming.

All data presented in this dissertation was acquired under calibrated conditions. The calibration was checked at the start of every day using the GCQ Tune software. If the calibration was not within tolerances, the instrument was recalibrated.

**GCQ Instrument Parameters**

**Ion Energies**

Ions are accelerated from the source towards the ion trap through a series of potential gradients created by the potentials applied to the three ion lenses, the octopole, and the trap. Singly charged ions of all m/z are accelerated through the same potentials and therefore will have similar kinetic energies as they enter the ion trap. The kinetic energy of an ion as it enters the ion trap is determined by the difference between the trap offset and the potential at which it is created. Ions which are generated within the grounded ion source are assumed to be formed at a ground potential; however, this is not always the case. The negative potential from lens 1, the extraction lens, extends into the source. Ions are therefore created at a slightly negative potential, depending upon their location in the ion source when formed. This occurs primarily in an EI ion volume due to its large exit aperture. CI ion volumes have a small aperture and the potential which leaks into the source is insignificant. For the GCQ using an EI ion volume the kinetic
energy of the ions entering the ion trap can be calculated by the following equation.

\[
KE = 0.13 \text{ (lens 1 potential)} - \text{trap offset} \tag{2-1}
\]

where the 0.13 represents the fraction of the lens 1 voltage which leaks into the source. This was determined by modeling the ion source with SIMION v.7. For example, an ion generated in the research-grade GCQ with a typical lens 1 potential of \(-20\) V and a trap offset of \(-13\) V will have a kinetic energy of 10.4 eV. With this knowledge the velocity and momentum of injecting ions can be derived through the following two equations.

\[
KE = \frac{1}{2}mv^2 \tag{2-2}
\]

\[
\text{Momentum} = mv \tag{2-3}
\]

where the KE is measured in eV (e is the charge of an electron and V is volts \((\text{kg m}^2\text{s}^{-2}\text{C}^{-1})\)), \(m\) is the mass of the ion (in kg), \(v\) is the velocity if an ion (in m/s) and momentum is in terms of kg m/s.

**Injection RF**

Ion injection efficiency has a large dependence on an ion’s mass, or more correctly its momentum. If an ion has too large a momentum, it has the potential to ignore the quadrupolar field and eject out the other side of the ion trap. For an ion to be efficiently trapped, it must be decelerated and allowed to undergo an oscillatory motion within the ion trap. The injection RF level is used to compensate for differences in ion momentum of injecting ions. Large RF amplitude on the ring electrode will increase the likelihood that ions with large momentum will decelerate and oscillate with the quadrupolar field (Quarmby and Yost, 1999).

As stated above, ions are accelerated from the source with the same kinetic energy. Through manipulation of equations 2-2 and 2-3 it can be seen that their
momentum, however, varies with the square root of ion mass.

\[
\frac{m_1v_1}{m_2v_2} = \sqrt{\frac{m_1}{m_2}}
\]  

(2-4)

Ions of greater mass will therefore need higher RF amplitudes to convert their forward momentum into oscillatory motion. If the injection RF is too large, however, the ion will absorb too much energy and will be ejected from the ion trap or fail to penetrate the trapping field and never enter the trap (Quarmby and Yost, 1999).

During injection, ions of all m/z values are allowed to enter the ion trap at the same time. It is therefore advantageous to find the optimal injection RF for a particular m/z range of interest or of a single ion of interest during the injection period. When looking at a large m/z range several levels of injection RF may be used during injection. This requires a calibration to be performed. The optimal injection RF level for each m/z is recorded as a function of maximum signal intensity during the initial increase of ion intensity, signified by the arrows in Figure 2-6. By plotting the optimal injection RF level versus the square root of m/z, a linear fit may be generated where

\[
\text{Optimal RF Level} = \text{slope} \sqrt{\text{m/z}} + b
\]

(2-5)

where b is the intercept. For the research grade GCQ with a -13V trap offset, the optimal RF level equals \(2.8 \sqrt{\text{m/z}} + 5\). As stated above the kinetic energy of the ions entering the trap, and therefore their momentum, will be determined by the trap offset. Therefore the optimal injection RF level will increase with increasing trap offsets. A difference in the helium buffer gas pressure will also have an effect; generally higher pressure requires a lower RF level.

An ideal calibration would show increasing m/z ions optimize at increasing RF
levels. Each m/z ion should have a small band of optimal RF levels. The nitrogen ion, m/z 28 in Figure 2-6 for example, optimizes at a LMCO between 10 and 25. When the injection RF amplitude reaches 28 the ion’s m/z falls below the LMCO and it is no longer trapped. Some ions, for instance m/z 131 in Figure 2-6, have an optimal RF level which seems to extend over a wide range. The m/z 131 ion from perfluorotributylamine, for instance, is not only injected into the trap as C₃F₅⁺ but it is also produced by the fragmentation of higher m/z ions entering the ion trap. Therefore, m/z 131 optimizes over a range for itself and its precursor ion. A similar trend can be seen when ion-molecule reactions or charge exchange occur within the ion trap. The injection RF

![Figure 2-6 Injection RF Calibration](image)

Figure 2-6 Injection RF Calibration - The optimal injection amplitudes are related in terms of a LMCO on the x-axis. The ions represented above are the positive ion of nitrogen (m/z 28) and several fragment ions of PFTBA, C₃F₅⁺ (m/z 131), C₅F₁₀N⁺ (m/z 264, and C₉F₂₀N⁺ (m/z 502).
curves as shown in Figure 2-6 generally are not smooth. The jaggedness in the injection RF curves may be due to non-linear resonances within the trapping field which decrease trapping efficiency (Dawson and Whetten, 1969).

The relationship between m/z and optimal RF amplitude during injection can also be related in terms of the pseudopotential well model derived by Major and Dehmelt.

\[ D_z = \frac{4zez_0^2V^2}{m(r_0^2 + 2z_0^2)^2\Omega^2} \]  

(2-6)

An ion which is injected into the ion trap will eventually be trapped and held within a pseudopotential well. For a given RF amplitude (V in equation 2-6), when the m/z of an ion is increased, the well depth (D_z) decreases proportionally and the ion is no longer efficiently trapped. Therefore a higher RF amplitude is needed to trap high m/z ions in the same potential well depth.

**Helium Pressure**

As stated above, ions generated from an external source enter the trap with a significant amount of kinetic energy. To relieve some of this energy and allow the ions to be trapped, a helium buffer gas is introduced into the trapping volume. Thermo Finnigan ion trap instruments introduce from 1 to 3 mtorr of helium into the trap. In the research grade GCQ instrument, 1 mtorr of helium is added through a 6-inch long, 0.0050-cm i.d. capillary restrictor with a head pressure of 5 psi.

To accurately determine the helium pressure within the ion trap both the flow of helium through the restrictor and the helium conductance out of the trap must be known. The flow of helium can be determined from the viscosity and linear velocity through the capillary (equations 2-6 and 2-7) (Thompson, 1994). The viscosity of helium, which is temperature-dependent, is given by
\[ n = 4.05 \times 10^{-7} T + 7.58 \times 10^{-5} \tag{2-7} \]

where \( n \) is the helium viscosity in dyne s/cm\(^2\) and \( T \) is temperature in Kelvin. The average linear velocity through a capillary into vacuum is given by

\[ V_{\text{avg}} = \frac{3(r)^2(P + 14.7)(68947)}{32n + l} \tag{2-8} \]

where \( r \) is the inner radius of the capillary (cm), \( P \) is the helium pressure at the inlet (psi), and \( l \) is the capillary length (cm). The helium flow in ml/min can now be determined by

\[ \text{Flow} = 60(r^2)V_{\text{avg}} \left( \frac{298}{T} \right) \left( \frac{2(P + 14.7)}{3(14.7)} \right) \tag{2-9} \]

Capillary inner diameters can differ from their stated value by the manufacturer. The capillary restrictor on the GCQ was calibrated by applying a high helium pressure to the inlet to obtaining a measurable flow by a flow meter (Figure 2-7). Knowing the temperature, length and head pressure on the capillary the actual diameter was determined.

![Figure 2-7 Apparatus to determine the actual i.d. of a capillary restrictor.](image)

Helium can escape from the GCQ ion trap through a series of holes in the endcap
electrodes. There are 0.060" diameter holes in the center of the electrodes which are used to transfer ions into and out of the trap. There is a second set of holes placed between the hyperbolic portion of the endcap electrode and ring spacers. The four holes of 0.095" in diameter are used for additional conductance. The conductance out of the each of these holes can be calculated by (O’Hanlon, 1989)

\[ C = \frac{avA}{4} \times 1000 \]  

(2-10)

where C is conductance (in L/s), \( a \) is the transmission probability, \( v \) is the average molecular velocity (in m/s), and \( A \) is area of the hole (in \( m^2 \)). The average molecular velocity of helium at 298 K is 1256 m/s. The transmission probabilities, found through a series of Monte Carlo simulations, depend on the structure, depth and diameter of the openings (O’Hanlon, 1989). For the ion entrance and exit holes the conductance is determined to be 0.81 L/s; the four conductance holes combine for 2.94 L/s. The total conductance out of the trap is the summation of both, 3.75 L/s.

The helium pressure within the ion trap can now be determined by the following equation

\[ \text{Pressure} = \left( \frac{\text{Flow}(ml/min)}{60000} \right) \left( \frac{760 \text{torr}}{3.75L/s} \right) \]  

(2-11)

with the pressure measured in torr. A head pressure of 5 psi should produce a helium flow of 0.3 ml/min through the capillary restrictor, resulting in a trap pressure of approximately 1 mtorr.

Some experiments required the trap pressure to be altered from its nominal setting. The pressure can be modified slightly by altering the head pressure on the capillary restrictor. For a large change in pressure the capillary restrictor may be
replaced with one of a different length or i.d.

Leak Checking

To maintain the proper daily performance all of the instruments described above were continually checked for leaks. The easiest way to check for a leak is to spray Dust-off around fittings and seals. The volatile compound can travel through leaks and be ionized by the ion source to indicate a leak. Dust-off usually comes in two compositions: difluoroethane with m/z 51 (CF\textsubscript{2}H) and 65 (C\textsubscript{2}F\textsubscript{2}H\textsubscript{3}) and tetrafluoroethane with m/z 69 (CF\textsubscript{3}) and 83 (C\textsubscript{2}F\textsubscript{3}H\textsubscript{2}).

Resonant Ejection Calibration

Ions can be resonantly ejected from the ion trap by placing a supplemental RF amplitude on the endcap electrode. This supplementary RF creates a dipolar field across the trapping volume, causing these ions whose secular frequencies are in resonance with the supplementary field to move away from the center such that they experience a greater amplitude of the quadrupolar field. The ions are accelerated by the quadrupolar field and can achieve kinetic energies of tens of electronvolts. The kinetic energy of the ions eventually exceeds the quadrupolar field potential well depth and the ion is ejected.

On the GCQ, resonant ejection is performed just before the stability edge at a q\textsubscript{x} of 0.901643. The supplementary RF amplitude, which can range from several hundred millivolts to tens of volts, has a significant effect on resolution. To obtain a constant resolution across the mass range the resonant ejection amplitude must be ramped with mass. This requires a calibration to be performed. The optimal resonant ejection amplitude for each m/z is determined by recording the peak width as a function of resonant ejection amplitude. A typical resonant ejection calibration can be seen in Figure
2-8 for several calibrant ions from perfluorotributylamine: CF$_3^+$ (m/z 69), C$_2$F$_4^+$ (m/z 100) and C$_3$F$_{10}$N$^+$ (m/z 264). The optimal amplitude lies between two extremes which both result in an increased peak width. When the amplitude is too high for a specific m/z, the tight ion cloud can actually scatter as they energetically collide with helium atoms within the trap before ejection, resulting in a larger ion cloud and increased peak widths. Helium collisions before ejection can also cause the ion to dissociate creating the same result. This effect will be discussed further in Chapter 3. When the resonant ejection amplitude is too small, there is not enough energy to divert the ions from the center of the ion trap. The ions do not experience the large quadrupolar field near the endcap electrodes and remain trapped. As the analytical scan continues the ions are eventually brought to the stability edge and are ejected there. These ions are often termed as “fence

![Graph showing peak widths at 10% for different m/z values and resonance ejection amplitudes.]

**Figure 2-8 Resonant Ejection Calibration** - The optimal amplitudes for m/z 69, m/z 100 and m/z 264 are 3.2, 3.7, 8.7 V$_{pp}$, respectively (signified by the arrows).
jumpers”. As stated in Chapter 1, ejection at the stability edge results in poor resolution and increased peak width. Between the two extremes lies the optimum amplitude that results in a minimum peak width. This optimum amplitude is then plotted as a function of m/z to complete the calibration process.

Ions can be ejected earlier or later than expected by raising or lowering the resonant ejection amplitude. For this reason a mass calibration is performed only after calibration of the resonant ejection amplitude is completed. This calibration must also be performed when parameters such as the helium pressure or the scan rate change.

**Mass Calibration**

As stated in Chapter 1, mass analysis in the quadrupole ion trap is performed by ramping the RF amplitude placed on the ring electrode. The RF ramp is composed of thousands of small DAC (digital to analog conversion) steps. The GCQ employs a 16-bit DAC, so a ramp from m/z 0 to 1000 (0 - 8.5 kV<sub>p</sub> RF) is composed of 16,384 discrete steps. When a particular m/z is ejected during this ramp it is linked with a specific DAC step. This association is used to calibrate the instrument. The mass calibration is defined in terms of a mass slope and intercept. These parameters are used to assign a mass to each DAC of acquired data by the following equation.

\[ \text{DAC} = (\text{mass slope}) \frac{m}{z} + (\text{mass intercept}) \]  \hspace{1cm} (2-12)

The GCQ ion trap is mass calibrated using perfluorotributylamine (PFTBA), C<sub>12</sub>F<sub>27</sub>N (MW=671). From this point on the calibration gas will be referred to its more common name PFTBA. PFTBA is used due to its variety of fragment ions stretching across a large mass range. The m/z ions in a typical EI spectrum of PFTBA are listed below.
<table>
<thead>
<tr>
<th>Exact Mass</th>
<th>Chemical Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>68.995</td>
<td>CF₃⁺</td>
</tr>
<tr>
<td>99.994</td>
<td>C₂F₄⁺</td>
</tr>
<tr>
<td>118.992</td>
<td>C₂F₅⁺</td>
</tr>
<tr>
<td>130.992</td>
<td>C₃F₅⁺</td>
</tr>
<tr>
<td>168.989</td>
<td>C₃F₇⁺</td>
</tr>
<tr>
<td>218.986</td>
<td>C₄F₉⁺</td>
</tr>
<tr>
<td>263.987</td>
<td>C₅F₁₀N⁺</td>
</tr>
<tr>
<td>413.978</td>
<td>C₈F₁₆N⁺</td>
</tr>
<tr>
<td>501.971</td>
<td>C₉F₂₀N⁺</td>
</tr>
<tr>
<td>613.965</td>
<td>C₁₂F₂₄N⁺</td>
</tr>
<tr>
<td>651.962</td>
<td>C₁₂F₂₆N⁺</td>
</tr>
</tbody>
</table>

Table 2-1 PBTBA calibrant ions with its exact mass.

Two of these ions, C₄F₉⁺ (m/z 219) and C₉F₂₀N⁺ (m/z 502), tend to exhibit a small mass shift due to ion fragility. Therefore, they are not typically used to calibrate the instrument.

**Scan Function**

To obtain a mass spectrum, an analyte must be ionized and the resultant ions injected into the trap, trapped, and then subsequently ejected. Each step is accompanied by various RF voltages applied to the ring and endcap electrodes, and to the gate lens and electron multiplier. The sequence of events described above can be represented graphically in the form of a scan function. A scan function is a visual representation of the series of programming events in the software which controls the ion trap operation. Figure 2-9 shows a typical scan function for a normal EI analytical scan for the GCQ.
The scan function provides information about the timing of different devices. The injection period, in this case, is made up of two steps each with its own injection RF level. The gate lens, which allows ions into the trap during injection with a negative potential, is held at a positive potential throughout the remainder of the scan. The resonant ejection amplitude is turned on during the mass analysis portion of the scan and is ramped with increasing mass. Lastly the multiplier is turned on only during the mass analysis ramp.

Each event is also associated with a particular time period which may vary from scan to scan (Table 2-2). The duration of the mass analysis portion of the scan, for instance, can fluctuate depending on the mass range and the scan rate. With a typical mass range of 600 amu (atomic mass units) and a normal scan rate of 180 μs/amu, the mass analysis will take 108 ms. This is typically the largest time portion of the scan. The ion time can also vary depending on the concentration of the analyte. The minimum ion time for the GCQ is 30 μs and the maximum is 25 ms.

Between the ion injection and mass analysis there are a few steps that warrant explanation. Subsequent to ion injection, a post-ion time or cool time is inserted allowing the ions to undergo enough helium collisions such that ion motion is slowed for efficient trapping. The ion of interest, positioned at a low $q_z$ during injection, is then moved or ramped to a $q_z$ of 0.9016 in preparation for ion ejection. During the multiplier warm up stage a voltage is placed on the electron multiplier and allowed to stabilize. Lastly the ion of interest, most commonly the first $m/z$ in a full scan, is moved to a $q_z$ value slightly lower than the resonant ejection $q_z$ defined by the backsteps.
Figure 2-9 A scan function for the quadrupole ion trap. The two major steps (injection and mass analysis) are shown here with associated potentials that accompany each step.

<table>
<thead>
<tr>
<th>Scan Event</th>
<th>Time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionization Time</td>
<td>25</td>
</tr>
<tr>
<td>Post-Ionization Time</td>
<td>3</td>
</tr>
<tr>
<td>Ramp Time</td>
<td>1</td>
</tr>
<tr>
<td>Multiplier Warm-Up Time</td>
<td>2</td>
</tr>
<tr>
<td>Backstep Time</td>
<td>1.08</td>
</tr>
<tr>
<td>Scan Time</td>
<td>108</td>
</tr>
<tr>
<td>(last mass - first mass) x 0.180 ms/amu</td>
<td>For m/z 50-650</td>
</tr>
<tr>
<td><strong>Total Time</strong></td>
<td><strong>140.08</strong></td>
</tr>
</tbody>
</table>

Table 2-2 Times associated with a typical scan event for the research-grade GCQ.
The mass calibrated DAC is assigned to a particular m/z as the ion is detected not ejected. There is a slight delay between the ejection of an ion and the detection due to the flight time of the ion and the processing time of the electrometer. Therefore if the scan began exactly at the mass calibrated DAC step, the ion of interest would not be properly ejected. To compensate for the necessary delay several backsteps, up to six, are subtracted to place the ion of interest at a suitable q_z for ejection.

A mass spectrum is obtained from running the scan function a number of times (usually 10) specified by the number of microscans. The data produced by the microscans are averaged to produce a single analytical scan.

**ITMS**

The ITMS was used in conjunction with a quadrupole mass filter from a TSQ45 to investigate the production of fragment ions during injection and resonant ejection. With numerous advances to ion trap instrumentation, the ITMS electronics and software have become outdated, but the instrument is still quite useful to study ion trap fundamentals. The information here will provide a brief insight into the ITMS instrument. Further information can be found in dissertations pre-dating mine in the Yost group.

The Finnigan ITMS was developed before the innovation of ion injection. This limits the instrument to internal ionization, either EI or low pressure CI. Internal ionization eliminates the need for ion transmission; therefore, the ITMS does not need either electrostatic lenses or an octopole as required for the modified GCQ. The design
of the ITMS trap electrodes is quite different than those of the GCQ. The entrance endcap is fitted with an EI filament and an electron lens. Instead of an ion gate the ITMS has an electron gate. The gate is a cylindrical electrode located inside the entrance endcap electrode. When electrons are not needed for ionization, the electron lens is maintained at -180 V potential. This negative potential prevents electrons emitted from the filament from entering the ion trap. When electrons are required, the potential on the electron gate is changed to +180 V. During that time electrons are accelerated into the ion trap. The acceleration is derived from several sources. First, is the potential between the filament and ground (12.5 V) and second is the electron gate at +180 V. The third source is dependent on the RF phase on the ring electrode (Johnson et al., 1995). During the positive phase of the RF voltage, electrons are attracted into the ion trap, whereas during the negative phase they are repelled from it. The net result of this complex set of potentials is that the electrons enter the ion trap with sufficient kinetic energy (50 to 80 eV) to achieve electron ionization.

The ITMS is an open trap designed to operate without ring spacers. The sample and carrier gas enter the ion trap in an open space between the ring electrode and the endcap electrodes. The helium buffer gas is allowed to flood the entire vacuum chamber while the analyte molecules are introduced into the trapping volume through a heated transfer line positioned next to the ion trap.

Other than the ionization procedure, the concept behind the ITMS is nearly identical to the GCQ. There are a few significant differences to discuss. The main frequency applied to the ring electrode is slightly higher at 1.1 MHz with amplitudes of 0-15 kV$_{pp}$. Resonant ejection is typically performed at a $q_z$ of 0.9066 with a frequency of
530 kHz. Unlike the modern GCQ, the resonant ejection amplitude is held constant across the entire mass range. The dynode, which is much smaller than that in the GCQ, is placed close to the entrance to the multiplier and is held at a potential of -1.5 kV (compared to -15 kV on the GCQ).

The ITMS ion trap is housed in a 12” diameter cylindrical stainless steel vacuum chamber. The trap is mounted on an optical rail-assembly, along with the dynode and multiplier housing. The chamber is kept at a constant temperature of 100°C by a pair of halogen bulbs placed on either side of the optical rail assembly.

**PolarisQ**

The PolarisQ is the newest generation of Thermo Finnigan ion traps that is coupled with a GC. The instrument design is fundamentally similar to the research grade GCQ with a few exceptions. First the PolarisQ is not differentially pumped. The ion source sits in front of the ion trap with the three electrostatic lenses inserted into the entrance endcap. (Figure 2-10) This increases ion transmission efficiency over the research-grade GCQ. The dynode is held at a potential of -10 kV instead of -15 kV on the GCQ. This was done to reduce noise. The ion source can be heated in excess of 300 °C. And finally, to compensate for highly concentrated samples, the minimum ion time on the PolarisQ was lowered from 30 μs to 5 μs.
Figure 2-10 Picture of the PolarisQ inside of a vacuum chamber. Ion source (A), the quadrupole ion trap (B) and the detection system(C). Analytes were introduced into the ion source through a heated transfer line (D).

Simulations

Computerized simulations of ion motion within the ion trap were critical to the success of the research reported in this dissertation. Simulations were performed using SIMION 3D Version 7 (Idaho National Engineering Laboratory, Idaho Falls, ID). SIMION is a PC-based ion optics simulation program capable of modeling instrument components with 3D electrostatic potential arrays. The field-induced forces are then used for ion trajectory calculations. A model of the GCQ electrodes was created using the program’s ion optics bench. User programming permits modeling dynamic devices such as the quadrupole ion trap. Subroutines have been written that control the variation of all parameters of the device and the starting ion conditions. These include the RF frequency, amplitude and its phase, an ion’s m/z and its initial position within the device.
CHAPTER 3
COMPOUND-DEPENDENT MASS SHIFTS

An ideal mass analyzer has the ability to record an ion's mass-to-charge ratio (m/z) regardless of physical or compound-dependent phenomena. In the quadrupole ion trap, however, it has been noted that properties other than an ion's mass and charge can affect its measured m/z. Space charge effects in the ion trap, for instance, can shift the apparent m/z of an ion to a higher mass and diminish mass resolution. Space charge (which will be discussed in detail in Chapter 5), however, is linked to the ion concentration within the trap and does not depend on an ion's structure. There are mass shifts that cannot be fully explained by space charge effects in which an observed m/z may be shifted depending on an ion's chemical structure. These mass shifts, most commonly referred to as compound-dependent or chemical mass shifts, have been a point of great debate since the early inception of the quadrupole ion trap.

Stafford and co-workers first discovered the presence of mass shifts in the early development of the Finnigan ion trap (Syka, 1995). It came to their attention while examining the mass spectrum of nitrobenzene. The molecular ion (m/z 123.11) was shifted to a lower m/z in excess of 0.5 amu. After much research, ion-molecule reactions, space charge effects and hardware problems were all systematically eliminated as sources of the shift. Numerous compounds were subsequently examined to determine if nitrobenzene was an isolated case, and several other mass shifts were discovered. The most extreme case found was the molecular ion of pyrene (m/z 202.25). It was shifted in the opposite direction, higher in m/z, by as much as 0.7 amu. The presence of this
compound-dependent mass shift became a major stumbling block in the development of the ion trap as a mass analyzer. After much research and debate, the problem was ultimately solved by altering the ion trap from its calculated ideal quadrupolar geometry to a “stretched geometry”. Specifically, each endcap was moved out by 10.7% (0.76 mm) resulting in a $z_o$ of 7.83 mm instead of the ideal 7.07 mm. This “stretched” geometry reduced these mass shifts and was used in the development and commercialization of Finnigan ion trap instruments. Note that this change in $z_o$ was made without a corresponding change in the hyperbolic shape of the electrodes, which would be necessary to maintain a pure quadrupolar field at the new $z_o$ value. It was believed that the mass shifts arose from structural imperfections with the ion trap. In the construction of a practical ion trap two alternations from the ideal geometry were necessary: the electrodes had to be truncated to control the size of the device and one or more holes had to be placed in the center of each endcap electrode to allow ions or electrons to enter and exit the device. These two modifications are enough to distort the quadrupolar field that is generated inside the device. Stretching the electrodes away from the center adds higher order fields within the trapping region of the ion trap that compensate for the imperfection in the quadrupolar field (Syka, 1995). Today all commercial ion trap instruments have been modified in similar ways to reduce compound-dependent mass shifts.

Despite the reduction of compound-dependent mass shifts with the novel ion trap geometry, mass shifts became the focus of considerable research. Traldi and co-workers published several papers reporting mass shifts for a series of ions examined with a Finnigan MAT ITMS (Bortolini et al., 1992; Traldi et al., 1993; Bortolini et al., 1994).
Traldi attempted to correlate the dipole moments or polarizability of several substituted benzene compounds, including trifluoromethylbenzene, with the amount that their \( M^+ \) (molecular) ions shifted in m/z. He suggested a small fraction of the RF power within the ion trap was used to align the induced or permanent dipole of an ion with the RF field. As a result, increased RF amplitude would be needed to eject the ion, allowing it to be ejected later than expected, leading to a mass shift. Londry and DeGnore, however, had little success in reproducing Traldi’s results, claiming the effect is too small to cause an observable mass shift (Londry and Morrison, 1995; DeGnore, 1997).

Cooks and co-workers have focused their attention on ion trap geometry to uncover the origin of compound-dependent mass shifts (Gill et al., 1998). They have shown that mass shifts observed for several ions, including the \( M^+ \) ion of n-butylbenzene, decrease linearly as the \( z_0 \) is increased from its theoretical value of 7.07 mm to a stretched configuration of 7.83 mm. In a recent publication, Cooks and co-workers have hypothesized that mass shifts are a result of an ion ejection delay originating from the field imperfection within the ion trap (Wells et al., 1999). They propose the delay can be shortened or eliminated by either increasing the \( z_0 \) dimension of the ion trap from the theoretical geometry or by ion collisions with the helium buffer gas, with the probability of such a collision depending on the size and nature of the ion.

The work presented in this dissertation indicates the compound-dependent mass shifts are directly related to how ions are ejected from the quadrupole ion trap. During the mass selective instability scan, a supplementary RF potential (resonant ejection amplitude), is placed across the endcap electrodes at a fixed frequency corresponding to a \( \beta_z \) value just inside of the LMCO (dotted line in Figure 3-1). The supplementary RF
forces ions which have secular frequencies equal to that of the supplementary RF waveform to quickly move from the center of the trap so they experience the main trapping field. Once displaced from the center of the trap, the ions quickly become unstable and are accelerated in a tight packet towards the endcap electrodes where they are eventually ejected. If an ion undergoes an energetic collision and dissociates during resonant ejection, however, the resultant fragment ions will be ejected even more rapidly. The fragment ions, which are lower in m/z, will typically fall beyond the stability boundary at $\beta_z = 1$ (Figure 3-1) and are no longer stable in the axial direction (recall that $q_z$ and $\beta_z$ are inversely proportional to m/z). Upon creation, these fragment ions will therefore be immediately ejected from the ion trap and will be detected before the intact ions can be resonantly ejected. The molecular ion of n-butylbenzene, for example, will fragment to form ions of m/z 91 and 92 under CID (collision induced dissociation) conditions. If the molecular ion of n-butylbenzene fragments during ejection, at a $q_z$ of 0.9016 for instance, the two fragment ions will be situated at a $q_z$ of approximately 1.33, well outside of the stability boundary. The ejection of the fragment ions and the non-dissociated precursor produce a peak which has a significant amount of peak asymmetry due to the early ejection of the fragment ions, and an overall broad peak shape. The peak will be shifted to a lower m/z with the degree of the mass shift directly related to an ion’s “fragility”. The more fragile an ion is under CID conditions, the greater the ion will shift in m/z. Other groups have offered similar hypotheses, but no conclusive studies have been presented (Londry and Morrison, 1995; Vachet et al., 1998).

This hypothesis has been validated by experiments on a hybrid ion trap/quadrupole mass filter instrument, which permitted mass analysis of the ions ejected
from the ion trap during resonant ejection (Murphy et al., 1999; Murphy and Yost, 2000). The data produced from this instrument conclusively show that dissociation of "fragile" ions produce mass shifts. A research-grade GCQ instrument and this hybrid instrument have been employed to explore in detail the experimental parameters that affect compound-dependent mass shifts.

Figure 3-1 Mathieu stability diagram depicting fragmentation of the M+ ion of n-butylbenzene during resonant ejection. The large sphere represents the molecular ion at the resonant ejection frequency and the smaller sphere represents the fragment ions m/z 91 and 92 created during resonant ejection. The fragment ions sit outside of the stability region and are immediately ejected, creating a shift in mass.
Instrumentation

Mass shift studies were performed on two custom mass spectrometers based on the Thermo Finnigan ITMS and the GCQ. A complete description of both instruments can be found in Chapter 2 of this dissertation. The ITMS was modified from its original configuration by the addition of a quadrupole mass filter between the ion trap and the detector. The mass filter was introduced to investigate the production of fragment ions during resonant ejection. The research grade GCQ instrument is a prototype research instrument constructed at the University of Florida using GCQ electronics and electrodes. This instrument, equipped with modern control and data processing software, was used successfully to quantify mass shifts.

ITMS (Hybrid Quadrupole Ion Trap / Quadrupole Mass Filter Instrument)

The ITMS instrument, with a large open vacuum chamber, proved to be ideal to study ion ejection. The ion trap and detector in the ITMS sit on an optical rail, which provides flexibility to make modifications to the instrument. A quadrupole mass filter originally from a Thermo Finnigan TSQ45 (triple stage quadrupole), was mounted between the exit endcap of the ITMS and the detector (Figure 3-2). In this configuration, ions ejected from the ion trap could be mass analyzed by the quadrupole mass filter before detection. Three electrostatic lenses, (a tube lens followed by two flat ion lenses), were positioned within the exit endcap to focus ions ejected from the ion trap into the mass filter. Typical voltages for these lenses were -100 V, -130 V and -100 V, respectively. The lens voltages were supplied by a Finnigan TSQ45 lens supply source. A single plate lens, held at ground potential, separated the exit of the quadrupole from the
conversion dynodes and multiplier mounted behind the mass filter.

The ITMS ion trap was replaced with a closed ITS40 ion trap with quartz spacers between the ring and endcaps. The helium buffer gas, which originally flooded the entire vacuum manifold in the ITMS open trap design, was leaked into the trap through PEEK tubing (0.05cm i.d.). This allowed the quadrupole mass filter situated directly behind the ion trap to operate at a lower pressure than the ion trap. The helium pressure in the vacuum manifold was monitored using a Bayard-Alpert ionization gauge mounted on the bottom of the manifold, and was typically $2.0 \times 10^{-5}$ torr (uncorrected). Individual samples were introduced into the ion trap through a Granville-Phillips (Boulder, CO) variable leak valve connected to a second piece of PEEK tubing. Both the helium and samples were

Figure 3-2 Picture of the ITMS hybrid instrument inside of a vacuum chamber: the ITS40 ion trap (A), and the quadrupole mass filter (C) with entrance lenses (B). The helium buffer gas and the analyte were introduced into the ion trap through PEEK tubing (D). Two halogen bulbs (E) were used to heat the vacuum chamber to 100°C.
fed into the ion trap through a gap between the exit endcap electrode and the quartz spacer. The vacuum chamber was kept at a constant temperature of 100°C by a pair of halogen bulbs placed on either side of the optical rail.

The ITMS was controlled by custom Ion Catcher software (ICMS) developed at the University of Florida (Yates, 1994). Samples were ionized by internal electron ionization (EI). The scan function on the ITMS included sequential periods of ionization (1-3 ms), isolation with forward and reverse scans, cooling of the ions, and an RF scan to eject and detect the ions via mass-selective instability with or without resonant ejection. The RF amplitude during ionization was selected according to the mass of interest and ranged from m/z 35 to 40. The scan rate of the instrument is normally fixed at 180 μs/amu and can only be altered through hardware modifications. A resonant ejection frequency was selected to eject the ions at a qz of either 0.9066 or 0.2267 (a frequency of 530 or 89 kHz, respectively) with a calibrated amplitude of 2.5Vpp. Ions were detected using a conversion dynode and electron multiplier system operated at −5 kV and 1.6 kV, respectively. Each spectrum obtained was the average of 60 to 100 scans.

The mass calibration on the ITMS was examined daily using several fragment ions of PFTBA (CF_{3}^{+} (m/z 69), C_{2}F_{4}^{+} (m/z 100), C_{3}F_{5}^{+} (m/z 131), C_{3}F_{10}N^{+} (m/z 264) and C_{8}F_{16}N^{+} (m/z 414)). A vial containing PFTBA was connected to the helium buffer gas line with a toggle valve. In this configuration PFTBA could be introduced into the ion trap with the helium buffer gas during calibration.

The quadrupole mass filter was originally a Q1 from a Finnigan TSQ45 (triple quadrupole mass spectrometer). Its rods are 6.3 mm in diameter and 13.5 cm long. A Finnigan QEM (Quadrupole Electronics Module) generated both the drive frequency of
2.27 MHz and the DC offset of -10 V for the quadrupole. Two Thermo Finnigan high voltage power supplies controlled the DC voltages for the mass filter. The quadrupole was operated in either RF-only or single ion monitoring (SIM) mode. In RF-only mode the quadrupole operates as a simple ion guide, allowing all positive ions above a LMCO to traverse through the mass filter. In this mode the mass spectrum obtained from the ITMS was observed to be identical to one obtained without the quadrupole mass filter. In SIM mode, only a select range (typically 1-3 amu wide) of m/z ions was allowed to pass through the quadrupole mass filter. The remainder of the ions ejected from the ion trap were not allowed to reach the detector.

The mass filter and the associated QEM were originally mass calibrated using PFTBA and a GCQ ion source inserted in the vacuum chamber in place of the ITS40 ion trap. The GCQ ion gate lens, which is normally pulsed, was kept at a constant negative potential to provide a steady source of calibrant ions for the mass filter. The mass spectra were viewed on an oscilloscope connected to the QEM. The QEM could then be calibrated with a series of potentiometers positioned inside the device.

Research Grade GCQ

The research-grade GCQ was used to successfully quantify mass shifts. Samples were introduced into the GCQ ion source either through a Varian 3400 GC connected directly to the ion source via a transfer line or through a Granville-Philips variable leak valve connected to the source. For most experiments, the leak valve was used to provide a constant supply of analyte vapor.

The scan rate, which is fixed on the ITMS without hardware modifications, can be easily altered on the modified GCQ. The data shown here, unless otherwise specified,
were obtained at a scan rate of 360 µs/amu, two times slower than the normal GCQ scan rate. This slower scan speed allowed for increased peak definition and resolution, with a sampling of over 36 points/amu. In contrast, data collection on the hybrid ITMS instrument provides only 6.3 points across a mass peak. This makes it impossible to measure small shifts precisely on the ITMS. Each spectrum obtained from the GCQ is the average of 50 analytical scans, each composed of 20 microscans.

The GCQ was calibrated using several fragment ions of PFTBA: \( \text{CF}_3^+ \) (m/z 69), \( \text{C}_2\text{F}_4^+ \) (m/z 100), \( \text{C}_3\text{F}_5^+ \) (m/z 131) and \( \text{C}_5\text{F}_{10}\text{N}^+ \) (m/z 264). This limited mass calibration, to m/z 264, allowed for a more precise calibration over a smaller mass range. The largest molecule studied was n-octylbenzene (m/z 190.33), which is well within this calibrated mass range. The m/z of an ion was determined from the peak apex, not the centroid value. Mass shifts are defined as the experimental centroid m/z minus the correct m/z. Therefore, an ion which is shifted to a lower m/z, as is observed for fragile ions, will be termed as a negative mass shift, while those shifted to higher m/z will be described as a positive mass shift. Note that this is different from the convention used by Cooks, (Gill et al., 1998), in which a shift to a lower m/z is termed as a positive mass shift.

To eliminate concerns about the effect of space charge, automatic gain control (AGC) was used. In the current version of software, AGC is controlled by an AGC factor that ranges from 5 to 50 and is directly related to the number of ions allowed to enter the ion trap. The default AGC target for EI is 50. Spectra here were taken at a factor of 5 to eliminate any contribution of space charge to the mass shifts. (More information about AGC will be provided in Chapter 5 of this dissertation)
Ions of interest were isolated using a SIM (single ion monitoring) scan function with an isolation width of 6 amu (the normal default is 1 amu). The ion of interest was then ejected by mass selective instability with the application of resonant ejection. The GCQ ramps the resonant ejection amplitude linearly with mass, allowing for efficient ejection of ions across a large mass range. In the SIM experiments presented here, however, the resonant ejection amplitude was kept at constant amplitude due to the small observable mass range.

**Analyte Compounds**

Several analyte compounds were chosen to produce both fragile and non-fragile ions. The fragile ion species which have previously shown to mass shift included the M+ ions of n-butylbenzene (MW 134.22), n-pentylbenzene (MW 148.25), n-hexylbenzene (MW 162.38), n-octylbenzene (MW 190.33), t-butylbenzene (MW 134.22), nitrobenzene (MW 123.11), and acetophenone (MW 120.15) (Figure 3-3A).

![Molecular structures of several compounds which produce fragile ions.](image)

Non-fragile ions included M+ ions of the naphthalene (MW 128.16), benzene (MW 78.11), and Xenon. Several fragment ions from the calibrant PFTBA, including C₃F₄⁺ (m/z 100) and C₃F₅⁺ (m/z 131) were also studied. (Figure 3-3B)
Figure 3-3B Molecular structures of several compounds which produce stable ions.

Instrumental Parameters

Several instrumental and experimental parameters, which would be expected to impact the degree of fragmentation upon ejection, were initially identified. They included: resonant ejection amplitude, helium buffer gas pressure, scan speed and the $q_z$ of ejection. Each of these parameters has been studied in-depth with both the modified GCQ instrument and the hybrid ITMS instrument. The molecular ion of n-butylbenzene was initially chosen as a model because it has been shown to exhibit a mass shift in the ion trap (Brittain et al., 1993).

Resonant Ejection Amplitude

Resolution in the quadrupole ion trap is optimized with the use of a resonant ejection amplitude that is calibrated with m/z, as discussed in Chapter 2. If the amplitude is too low for a particular m/z, resolution can degrade, as the minimal amplitude does not provide enough energy to properly displace ions from the center of the trap for efficient ejection. Subsequently, they may not be ejected until they reach the $\beta_z = 1$ stability boundary. If the amplitude is too high, resolution may again be degraded due to ion
scattering or fragmentation. High amplitudes increase the velocity to which ions are initially accelerated from the center of the ion trap. The kinetic energy imparted to the ion can lead to high-energy collisions, fragmentation and a resultant negative mass shift. To study the effect of resonant ejection amplitude, two ions of similar m/z were analyzed using two different resonant ejection amplitudes on the modified GCQ instrument: the stable C₃F₅⁺ (m/z 131) calibrant ion and the fragile molecular ion (M⁺) of n-butylbenzene (m/z 134). When the resonant ejection amplitude was increased from 1 Vpp to 7 Vpp the C₃F₅⁺ ion exhibits only slight peak broadening, a 50% increase in peak width at half height (Figure 3-4A). The seven-fold increase in amplitude has little effect on the peak shape or position. The same increase, however, had a dramatic effect on the molecular ion of n-butylbenzene (Figure 3-4B). The mass peak exhibits an enormous amount of peak fronting and the peak is spread across a four amu wide window. More importantly the peak top is shifted to lower m/z by 0.54 amu. Note that under the normal GCQ operating parameters (resonant ejection amplitude of approximately 2.0 Vpp), only a small mass shift is observed for the M⁺ ion of n-butylbenzene while looking at the spectrum in profile mode.

For proper mass calibration, the ions selected for calibration should behave in the same manner as analyte ions. At low resonant ejection amplitudes, this may be achieved for the ions in Figure 3-4. At higher resonant ejection amplitudes, however, the fragile molecular ion of n-butylbenzene does not behave the same way as the stable PFTBA calibrant ion (C₃F₅⁺). This difference in behavior will result in a mass shift and inaccurate mass assignment if the resonant ejection amplitude is set too high.
Figure 3-4 Profile mass spectrum obtained on the GCQ instrument with a resonant ejection amplitude of 1 $V_{pp}$ (the black trace) and 7 $V_{pp}$ (the gray trace) of (A) the $C_3F_5^+$ (m/z 131) calibrant ion and (B) the molecular ion (M$^+$) of n-butylbenzene (m/z 134). The peak top m/z values are shown.
In addition to n-butylbenzene, the molecular ions of several other n-alkylbenzenes were examined at resonant ejection amplitudes ranging from 1 V<sub>pp</sub> to 7 V<sub>pp</sub> increasing in half-volt increments (Figure 3-5). The instrument was mass calibrated at each amplitude with PFTBA. Note that the GCQ is calibrated using the peak top m/z, not the peak centroid value. As the resonant ejection amplitude was increased past the normal value of 2 V<sub>pp</sub>, the mass shifts for the n-alkyl benzene molecular ions became increasingly negative; at an amplitude of 7 V<sub>pp</sub>, the t-butylbenzene molecular ion is shifted negatively.

![Figure 3-5](image)

Figure 3-5 Mass shifts for fragile ions (n-alkylbenzene molecular ions) and non-fragile ions (\(^{134}\)Xe\(^+\), PFTBA calibrant ion, and aromatic molecular ions) recorded as a function of resonant ejection amplitude with a buffer gas pressure of 1 mtorr and scan speed of 3.6 \(\mu\)s/amu. Non-fragile ions are denoted with open symbols and the fragile ions are denoted with solid symbols. Mass shifts were determined by the measured centroid m/z minus the ions' actual mass. Data were taken with the modified GCQ; its normal operating resonant ejection amplitude is 1.5-2.5 V<sub>pp</sub>. The instrument was mass calibrated with PFTBA at each resonant ejection amplitude. *Error bars were all smaller than the symbol representing each point.*
by over 1.2 amu. All mass shifts were measured from the peak centroid, (rather than the peak top as in Figure 3-4).

From inspection of Figure 3-5, it would appear that the molecular ion of t-butylbenzene is the most fragile of these ions, resulting in the largest shift. To rationalize this, each ion must be looked at individually. The fragmentation of the $M^+$ ion of n-butylbenzene follows two pathways, a low-energy (1.0 eV) McLafferty rearrangement which results in a fragment ion of m/z 92 ($C_7H_8^+$), and a higher-energy pathway (1.7 eV) which produces a fragment at m/z 91 ($C_7H_7^+$) (Baer et al. 1988). These two distinct pathways, shown in Figure 3-6, have made the molecular ion of n-butylbenzene widely used an energetic thermometer for ions held in the ion trap (Johnson et al., 1995; McLuckey et al., 1991). Other n-alkylbenzene molecular ions fragments in the same manner. The $M^+$ ion of t-butylbenzene, however, has a third pathway for dissociation: it can lose a methyl group to form a stable tertiary carbocation m/z 119 ($C_9H_{11}^+$) (Figure 3-6B). This is an energetically favorable process and is very efficient in removing excess energy after a collision. This additional pathway classifies the $M^+$ ion of t-butylbenzene as the most fragile of the alkylbenzene ions.

Two non-substituted aromatic compounds, benzene and naphthalene, were examined in the same manner. The mass shifts recorded for the $M^+$ ions of these two stable species were minimal, as both behave very similar to the PFTBA calibrant ions. It could be argued that neither the calibrant ions nor the aromatic ions should fragment under resonant ejection, and therefore should not shift in mass. However, even such stable ions can undergo a degree of fragmentation if they are resonantly ejected with high
Figure 3-6 The most favored fragmentation pathways of n-butylbenzene (A) and t-butylbenzene (B). M/z 92 ion from n-butylbenzene forms via a rearrangement and loss of C$_3$H$_6$ with a low activation energy of 1.0 eV while the m/z 91 ion forms via direct cleavage of C$_3$H$_7$ associated with a high activation energy (1.7 eV). The most favorable fragmentation pathway for t-butylbenzene occurs with the loss of a methyl group creating a stable tertiary cation. The molecular ion can also undergo a McLafferty rearrangement to form m/z 92 but this is not a dominant fragment.

enough resonant ejection amplitudes (much as they show some fragmentation in their 70 eV EI spectra). Similarly, the PFTBA fragment ions which are used to calibrate the instrument can fragment under high-amplitude resonant ejection (just as they do under high collision-energy CID conditions). Thus, when they are compared to an atomic ion such as xenon that cannot fragment, they too will exhibit a slight shift. The small shift is apparent only under exaggerated conditions such as high resonant ejection amplitudes. If mass shifts are referenced to PFTBA calibrant ions, mass shifts in both directions will be observed. Fragile ions will exhibit a negative mass shift, whereas atomic ions and very stable ions, which fragment less than the PFTBA calibrant ions, will exhibit a positive
mass shift. If the mass spectrometer could be mass calibrated using only atomic ions such as neon, argon and xenon, only negative mass shifts would be seen.

Increasing the resonant ejection amplitude will not just result in a mass shift for fragile ions, but will also produce a very asymmetrical mass peak. The fragment ions formed during ejection of a fragile ion create the peak fronting; the more fragile the ion, the larger the peak front that occurs. In Figure 3-7 the peak asymmetries of several fragile and stable ions are plotted as a function of resonant ejection amplitude. Peak asymmetry was calculated as a width ratio (A/B) from the peak maximum to either side of the mass peak at 10% peak height (A is the peak maximum minus the peak front and B is the rear of peak minus the peak maximum.) (Foley and Dorsey, 1982). Therefore, a peak with an asymmetry value > 1 has a portion of its peak shifted towards lower mass.

At low resonant ejection amplitudes most of the ions studied have an asymmetry value close to one, indicating a symmetrical (Gaussian) peak (Figure 3-7). However, as the amplitude is increased the peak asymmetry of the fragile alkyl benzene molecular ions increase linearly to a value close to 2.5, showing a significant amount of the peak appearing to the front of the peak maximum. The non-fragile aromatic and calibrant ions show a low value of peak asymmetry even at high voltages, with the isotope of xenon never exceeding an asymmetry value of one. At amplitudes below the calibrated value of approximately 2.0 V_{pp} several ions (naphthalene, PFTBA m/z 131, and xenon) exhibit an asymmetry value less than one. At such the low amplitudes, the resonant ejection amplitude does not apply enough energy to efficiently eject the ions in a tight packet. Some ions therefore come out late, producing a peak tail and an asymmetry value less than one.
Figure 3-7 Peak asymmetry of fragile ions (solid symbols) and non-fragile ions (open symbols) as a function of resonant ejection amplitude. Peak asymmetry (A/B) was calculated as a ratio from the peak maximum to either side of the mass peak at 10% peak height (A = peak maximum – peak front and B = rear of peak – peak maximum). A peak with an asymmetry value > 1 has a portion of its peak shifted towards lower mass.

An increase in peak asymmetry for fragile ions is also accompanied by an increase in peak width. Under the normal operating conditions of the GCQ typical peak widths at 10% are less than half an amu. At high resonant ejection amplitudes, however, the peak width for fragile ions increases greatly (Figure 3-8); at a seven-volt amplitude, for example, the peak width of the n-butylbenzene M⁺ ions increased by a factor of four, whereas the peak widths of the stable ions never exceed one amu. The degree of peak broadening and peak asymmetry directly correlate with mass shifts (Figure 3-5). This increase in peak width may be most apparent during high-resolution (slow scan speed) experiments.
Figure 3-8 Peak width at 10% height of fragile ions (solid symbols) and non-fragile ions (open symbols) as a function of resonant ejection amplitude.

**Mass Analysis of Fragile Ions**

The data presented above clearly show that increasing the resonant ejection amplitude can result in large mass shifts for certain ions as well as increased peak width and peak asymmetry. To confirm that this behavior arises from dissociation of "fragile" ions, the ejected ions must be mass analyzed. This was accomplished by using the hybrid ITMS instrument described previously. The quadrupole, placed in the ITMS chamber, was employed to separate the fragment ions from the non-dissociated ions as ions of a single m/z were resonantly ejected from the ion trap.

N-butylbenzene was again used a model compound to examine ion fragility. The molecular ion at m/z 134 was isolated in the trap by a set of forward and reverse scans.
After a short cooling period, a mass-selective instability scan was performed with a calibrated resonance ejection amplitude of 2.5 \( V_{pp} \) at a \( q_z \) of 0.9066. Initially the quadrupole was used in RF only mode, passing all ions that were ejected from the ion trap. The resultant spectra (solid gray trace in Figure 3-9A) matched those obtained on the ITMS operated without the quadrupole mass filter. This showed that the presence of the quadrupole behind the ion trap had no effect on peak shapes or mass positions. Although the ITMS does not provide the high sampling rate of the GCQ, the mass shift and peak fronting exhibited by the \( M^+ \) ion of \( n \)-butylbenzene are still very noticeable. The mass peak extends over two amu and the centroid is shifted to lower m/z. Note that the ITMS places masses in bins, so m/z 134 actually appears at m/z 134.5 on the mass scale (in the center of a bin).

The quadrupole was then set to transmit only a 2-3 amu wide range of ions around the m/z 134 molecular ion of \( n \)-butylbenzene (solid black trace in Figure 3-9A). The intensity of the molecular ion was smaller in this mode than in the RF-only mode, as expected, since the ion transmission of the quadrupole was lower in a mass filter mode than in the RF-only mode. In contrast to the RF-only mode spectrum, however, the peak of the molecular ion was narrow and symmetrical and was located at the correct m/z. Under these conditions the molecular ion does not appear to have any characteristics that are associated with the resonant ejection of a fragile ion.

Finally, the quadrupole was set to pass only the fragment ions at m/z 91 and 92 as the ion trap ejected m/z 134. Any ions detected in this mode must arise from ion fragmentation during ion ejection from the trap. The fragment ions (dashed black trace in Figure 3-9A) were much less intense than m/z 134. The key observation, however, is that
the ejected fragment ions are ejected earlier (displaced to lower m/z) than the selected m/z 134 ions. The peak fronting which causes the mass shift for m/z 134 is composed of the fragment ions m/z 91 and 92. This confirms our hypothesis that mass shifts and peak fronting can arise by fragmentation of fragile ions. This effect was even more evident
Figure 3-9 Mass spectra of n-butylbenzene $M^+$ ion (MW 134) taken on the hybrid ITMS instrument at different levels of resonant ejection amplitude. The solid gray trace is the mass spectrum obtained with the quadrupole in RF-only mode (1/2 scale). The solid black trace is taken with the mass filter passing m/z 134-136 ($M^+$ ion of n-butylbenzene). The dashed black trace is taken with the mass filter passing m/z 91 and 92 (fragment ions). The $M^+$ ion was ejected with a resonant ejection amplitude of (A) 2.5 $V_{pp}$ (B) 6.0 $V_{pp}$ and (C) without resonant ejection (ejected at the stability edge). The instrument was mass calibrated with a resonant ejection amplitude of 1.0 $V_{pp}$ for Figure C. Data were taken at a chamber pressure of 2.0 x10^-5 torr. Each spectrum is the sum of 3 analytical scans of 20 microscans each.

when the resonant ejection amplitude was increased to 6$V_{pp}$ (Figure 3-9B). As discussed above, the increase in resonant ejection amplitude results in a larger mass shift; comparing Figures 3-9A and 3-9B makes it clear that the increased mass shift can be directly traced to the increase in fragment ions formed upon ejection. When the n-butylbenzene $M^+$ ion is ejected without resonance ejection (Figure 3-9C), little or no fragmentation is observed. The ejected ions depart the ion trap with low kinetic energy
and undergo less energetic collisions. The spectrum, however, suffers from very poor resolution as expected for a mass selective instability scan without resonant ejection.

Ions are ejected from the ion trap with a great deal of kinetic energy, proportional to the RF amplitude at the time of ejection. In a mass selective instability scan, m/z 134 ions will have an estimated 330 eV of kinetic energy upon ejection. At such high kinetic energies, these ions will travel at high velocities and will experience only approximately 14 cycles of 2.27 MHz RF field as they transverse the 13.5 cm long quadrupole mass filter. In a typical quadrupole mass filter, an ion of that m/z could see 38 cycles of RF for a 20 cm long quadrupole with a 10 V offset and a drive frequency of 1.1 MHz. The reduced number of RF cycles experienced by ions in the hybrid instrument reduces the mass resolution. Thus, it might be argued that some or all of the signal observed when the quadrupole mass filter is set to pass m/z 91-92 (dashed line in Figure 3-9) arises from high energy unfiltered m/z 134 ions. To eliminate this concern, the mass filter was set to pass ions just above or below m/z 91 and 92; no ion signal was observed. This confirms that the signal detected when the mass filter is set to m/z 91-92 does indeed correspond to fragment ions of that m/z. Note that this may still be a concern for the analysis of higher m/z ions, since they are resonantly ejected from the ion trap with even higher kinetic energy, estimated as 1.7-3.4 keV for a m/z 502 ion. Ion kinetic energy experiments will be described in detail later in this chapter.

Non-fragile ions of similar m/z were also investigated with the hybrid instrument. The C₃F₅⁺ ion of PFTBA (m/z 131) has been shown to be a relatively stable ion in previous experiments. Upon collision-induced dissociation (CID) within the ion trap, the C₃F₅⁺ ion will fragment to CF₃⁺ (m/z 69), although this requires much higher resonant
excitation amplitudes than the CID of the m/z 134 M⁺ ions of n-butylbenzene. The same procedure was followed as presented above. The ion trap was set to eject m/z 131 with the quadrupole operated in RF-only mode or as a mass filer set to pass the intact m/z 131 ion or its fragment ion at m/z 69. The spectrum (Figure 3-10A) reveals that a small fraction of the m/z 131 ions fragment to form m/z 69; this small amount of dissociation, which may ever occur after the ion has actually has left the ion trap, does not cause significant peak fronting. The molecular ion of naphthalene (m/z 128) behaves in a similar manner. As shown in Figure 3-10B, when the quadrupole is in RF-only mode, the peak shape of the molecular ion is very symmetrical. When the mass filter was set to allow only the molecular ion of naphthalene (m/z 128) to pass, there was no difference in peak shape. When the mass filter was set to pass a specific fragment ion, C₆H₆ (m/z 102) corresponding to the loss of C₂H₂, no ions were detected. This demonstrates that a stable ion such as the molecular ion of naphthalene does not fragment during resonant ejection and therefore does not produce peak fronting or a mass shift.

A number of ions produced from other compounds were observed in the same manner including the entire series of n-alkylbenzenes, benzene, and several compounds reported to shift by Traldi and co-workers (Bortolini et al., 1992), including 4-trifluoromethyl-benzonitrile. The compounds suggested by Traldi did not show an appreciable mass shift on the GCQ and only a minimal amount of fragment ions was detected during resonant ejection on the ITMS hybrid instrument.
Figure 3-10 Mass spectra of non-fragile ions taken on the hybrid ITMS instrument with a resonant ejection amplitude of 2.5 Vpp and a chamber pressure of $2.0 \times 10^{-5}$ torr. (A) Spectra of PFTBA calibrant ion $C_3F_5^+$ (m/z 131). The solid gray trace depicts the mass filter in RF-only mode (1/2 scale). The solid black trace is taken with the mass filter passing m/z 131-133. The dashed black trace is taken with the mass filter passing m/z 69-70 corresponding to the fragment ion $CF_3^+$ (m/z 69). (B) Spectra of the M$^+$ ion of naphthalene (m/z 128). The solid black trace is taken with the mass filter passing m/z 128-130. The dashed trace is taken with the mass filter passing m/z 102-103 corresponding to the loss of $C_2H_2$. 
**Buffer Gas Pressure**

During ion injection into the ion trap, a buffer gas (typically helium at 1 mtorr) is utilized to cool the analyte ions and confine them to the center of the ion trap. The reduction of momentum due to collisions with the buffer gas helps remove excess ion kinetic energy and allow the ion to be trapped within the ion trap's potential well. Increasing the buffer gas pressure above the typical 1 mtorr may result in more efficient trapping, but it may also cause increased fragmentation of fragile ions upon resonant ejection.

The mean free path for an ion, or the distance an ion may travel before it collides with a gas molecule, is determined by the following equation (Chapman, 1994)

\[
\lambda_i = \frac{\bar{v}_i}{z_i + z_j}
\]

where \(\lambda_i\) is the mean free path (in m), \(\bar{v}_i\) is the speed of the ion (m/s), and \(z\) is a collision rate (collisions/s) between ion and molecule \(i\) and \(j\). At a normal helium pressure of 1 mtorr, the mean free path within the trap for a m/z 134 ion (approx. 10 Å in diameter) is roughly 19 mm. An ion must therefore make a complete path between the two endcaps and more before it will typically undergo a single collision during resonant ejection. If the helium pressure is increased to 5 mtorr, however, the mean free path drops to 3.7 mm. Now an ion is likely to undergo at least four collisions as it travels between the two endcap electrodes during ejection. The greater number of collisions translates to a larger probability that an ion may fragment during ejection. Consequently, compound-dependent mass shifts should display a dependence on helium pressure.

To characterize the effect of buffer gas pressure, mass shifts for several fragile and non-fragile ions were measured as a function of helium pressure using the modified
GCQ instrument. The helium pressure was altered from 1 mtorr, its normal value 
pressure, to 3.4 mtorr by increasing the head pressure on the capillary restrictor. This 
upper limit is a reasonable pressure as the Finnigan LCQ operates with close to 3 mtorr of 
helium within the trap. Figure 3-11 shows that mass shifts increase with elevated helium 
pressure. The molecular ion of n-octylbenzene, for example, shifts negatively in excess 
of 0.32 amu at 3.4 mtorr of helium. Stable ions, such as xenon, exhibit an elevated 
positive shift at high pressures. The shift for a stable ion such as xenon is always related 
to the fragile nature of the calibrant ions. In profile mode, it is apparent that the mass 
shifts observed with

Figure 3-11 Mass shifts for fragile ions (solid symbols) and non-fragile ions (open 
symbols) recorded as a function of buffer gas pressure. Mass calibration and resonant 
ejection amplitude calibration was performed at each pressure setting with PFTBA. The 
buffer gas pressure was adjusted by varying the helium head pressure on the capillary 
restrictor as described in Chapter 2.
elevated buffer gas pressure are accompanied by peak fronting and increased peak width (data not shown).

To confirm that the increased mass shifts observed for fragile ions at higher buffer gas pressures arise from fragmentation, the ITMS hybrid instrument was again employed to study fragmentation of ions upon resonant ejection. The data shown previously in Figure 3-9A were taken at a normal indicated manifold pressure of $2.0 \times 10^{-5}$ torr. If the pressure is reduced to $4.4 \times 10^{-6}$ torr (Figure 3-12A) the signal for fragment ions produced upon resonant ejection is barely detectable and the peak fronting is minimized. If the helium pressure is raised above its normal value, however ($3.7 \times 10^{-5}$ torr and $4.4 \times 10^{-5}$ torr) the extent of fragmentation increases dramatically, along with the peak fronting and mass shift (Figure 3-12B,C).

(A)
Figure 3-12 Mass spectra of n-butylbenzene (m/z 134) taken on the hybrid ITMS instrument with a resonant ejection amplitude of 2.5 V<sub>pp</sub> and a chamber pressure of (A) 4.4x10<sup>-6</sup> torr (B) 3.7x10<sup>-5</sup> torr and (C) 4.4x10<sup>-5</sup> torr. The normal operating pressure for this instrument is 2.0x10<sup>-5</sup> torr. The instrument was calibrated at each pressure setting with PFTBA.
The intact molecular ions of n-butylbenzene form a very symmetric and narrow mass peak, while the fragment ions formed upon ejection create an increasingly intense and broad peak front with a width of several amu. Similar results were obtained for other fragile ions as the pressure of the buffer gas was varied.

Currently, except for the PolarisQ (which can be constructed with a helium flow module), the helium pressure is held constant for all commercial ion trap instruments. What might be a greater concern for normal ion trap users, as far as mass shifts are concerned, are air leaks into the vacuum chamber. An air leak can contaminate the helium buffer gas with nitrogen, oxygen and water vapor. These atmospheric gases may produce a larger mass shifts as their increased molecular weight will allow for greater center-of-mass collision energy. This can be seen with the following equation

\[ E_{CM} = \frac{m_2}{m_1 + m_2} E_{LAB} \]  

(3-3)

where \( m_1 \) is the mass of the ion, \( m_2 \) is the mass of the target gas, and \( E_{LAB} \) is the energy in the laboratory frame of reference. In the past, some heavy gasses have been purposefully pulsed into the ion trap to aid in the dissociation of stable ion species such as peptide ions (Vachet and Glish, 1996; Doroshenko and Cotter, 1996). Vacuum leaks are not the only source of helium contamination. If the ion source is positioned near the ion trap and is not differentially pumped, the CI reagent gas, such as methane, can also be a source of contamination. This is the primary advantage for constructing a differentially pumped instrument, such as the research grade GCQ.

**Scan Rate**

The GCQ is designed to obtain unit resolution; for most GC/MS applications this is acceptable. For some applications, however, a greater resolving power may be needed.
Determining the charge state of a multiply charged electrosprayed ion, for instance, requires greater than unit resolution. Slowing down the scan rate on a quadrupole ion trap can provide high-resolution mass analysis. The reduced scan rate provides additional time for ions to experience more cycles of the resonant ejection amplitude, allowing the ions to be ejected in a tighter packet, resulting in smaller peak widths and higher resolution (Kaiser et al., 1989; Schwartz et al., 1991). In the LCQ ZoomScan, for instance, a 20 times slower scan rate can produce narrow peaks on the order of 0.3 amu width at 10% height. Unfortunately, the reduced scan rate can degrade the resolution for fragile ions. The increased interaction time with the resonant ejection amplitude allows the ion to undergo more collisions, gain internal energy and readily fragment. Therefore, mass shifts due to ion fragility become a significant problem at low scan rates. The difference in peak widths between fragile and non-fragile ions becomes very significant at low scan rates.

Before different scan rates can be studied several instrumental parameters must be adjusted: the bandwidth and the sampling rate of the electrometer were set to the correct theoretical values for the GCQ using the following equations

\[
\text{Bandwidth (Hz)} = \frac{1}{\text{Scan Rate (sec/amu)}} \quad (3-4)
\]

\[
\text{Sampling Rate} = \text{Scan Rate (ms/amu)} \times 100 \quad (3-5)
\]

The bandwidth establishes a frequency limit, in Hz, of a low pass filter on the electrometer designed to eliminate high frequency noise. The mass peaks, which are ejected across a specific time scale or width, also have a frequency component. The objective is to position the filter at a frequency just above that of the ejecting ion. Equation 3-4 is based on the assumption that a peak will be one amu wide at the base.
With this assumption the frequency of an individual mass peak is the inverse of peak width, on a time scale. For slow scan rates this may not be the case as peak widths drop below 1 amu. The frequency of the mass peak is now much higher than expected and the bandwidth has to be adjusted manually for optimal resolution and signal intensity. Otherwise real data may be cut off. Sampling rate must also be adjusted for lower scan rates. Lower scan rates spread a mass peak out in the time domain, and an increased sampling rate is needed. The maximum number of data points that can be collected across a scan range is 16,500. (Note: advancing beyond this limit will crash the software.) Table 3-1 contains the optimal bandwidth and sampling values for several different scan rates.

<table>
<thead>
<tr>
<th>Scan Rate (ms/amu)</th>
<th>Sampling Rate</th>
<th>Bandwidth (Hz)</th>
<th>Res. Ej. Amp (Vpp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.09</td>
<td>9</td>
<td>11111</td>
<td>3.040</td>
</tr>
<tr>
<td>0.18</td>
<td>18</td>
<td>5556</td>
<td>2.149</td>
</tr>
<tr>
<td>0.36</td>
<td>36</td>
<td>2778</td>
<td>1.520</td>
</tr>
<tr>
<td>0.72</td>
<td>72</td>
<td>1389</td>
<td>1.075</td>
</tr>
<tr>
<td>1.08</td>
<td>108</td>
<td>926</td>
<td>0.877</td>
</tr>
<tr>
<td>1.44</td>
<td>144</td>
<td>694</td>
<td>0.760</td>
</tr>
<tr>
<td>1.8</td>
<td>180</td>
<td>556</td>
<td>0.680</td>
</tr>
<tr>
<td>2.16</td>
<td>216</td>
<td>463</td>
<td>0.620</td>
</tr>
<tr>
<td>2.52</td>
<td>252</td>
<td>397</td>
<td>0.574</td>
</tr>
<tr>
<td>2.88</td>
<td>288</td>
<td>347</td>
<td>0.537</td>
</tr>
<tr>
<td>3.24</td>
<td>324</td>
<td>309</td>
<td>0.507</td>
</tr>
<tr>
<td>3.6</td>
<td>360</td>
<td>278</td>
<td>0.481</td>
</tr>
</tbody>
</table>

Table 3-1 Optimal parameters for different scan rates on the modified GCQ.
In Figure 3-13, mass shift is displayed as a function of scan rate for several ionic species. The data were taken from the modified GCQ instrument. The resonant ejection amplitude was calibrated at the GCQ's normal scan rate (0.180 ms/amu) and was kept constant at the different scan rates. As the instrument scan rate was reduced, the mass shifts for the alkylbenzene molecular ions approach 1 amu. The $M^+$ ion of t-butylbenzene exhibits the largest mass shift (-1.5 amu) as the scan rate is reduced twenty-fold. The $Xe^+$ ion is again shifted slightly positive from the calibrant ions.

![Figure 3-13](image_url)

Figure 3-13 Mass shifts for fragile ions (solid symbols) and non-fragile ions (open symbols) recorded as a function of scan rate with a helium pressure of 1 mtorr. The resonant ejection amplitude was calibrated for each mass according to the normal operating scan rate on the GCQ (0.180 ms/amu).

The resonant ejection amplitude in Figure 3-13 was calibrated at the normal scan rate of 180 μs/amu. To get an accurate account of mass shifts with different scan rates, it
would be reasonable to calibrate the resonant ejection amplitude for each scan rate. In general the amplitude will decrease at low scan rates to obtain optimal resolution. The calibrated values can be seen in Table 3-1.

A second series of experiments was performed with the resonant ejection amplitude calibrated for each m/z at each different scan rate (Figure 3-14B). Optimizing the resonant ejection amplitude has little effect on the small mass shifts observed for most of the ions, but reduced the mass shifts seen for fragile ions by a factor of 3-4. The mass shift for the M+ ion of t-butylbenzene is lowered from -1.5 amu with an uncalibrated resonant ejection amplitude to -0.5 amu with optimized amplitude (Figure 3-14). Although the severity of the mass shift at slow scan rates is reduced by optimizing

![Figure 3-14 Mass shifts as a function of scan rate. The resonant ejection amplitude was calibrated for each mass and for each scan rate using PFTBA. The calibration optimized for efficient ejection and minimum peak width of the calibrant ion.](image)
resonant ejection amplitude, it is still much greater than at the normal scan rate. As stated above, increased peak width and asymmetry accompany mass shifts for fragile ions. This creates a problem when performing high-resolution experiments on such ions. If high mass accuracy is to be achieved by slow scans on quadrupole ion trap, dissociation of fragile ions upon ejection must be minimized.

**Lowering the q of Ejection**

Resonance ejection of ions is usually performed at a qz close to 0.9, just inside the edge of the stability region. In the case presented above, the molecular ion of n-butylbenzene dissociates during ejection and its fragment ions (m/z 91 and 92) fall at a qz value far outside of the stability region and are immediately ejected (Figure 3-1). If the molecular ion of n-butylbenzene is ejected at a lower qz, 0.55 for instance, any m/z 91 and 92 fragment ions formed will fall at a qz value below 0.9, within the stability region (Figure 3-15). Thus these ions will still be trapped and will not contribute to peak fronting or mass shifts. In actuality, the fragment ions will not be ejected from the ion trap until they reach the stability edge later in the analytical scan. Recall that, to calculate ion location with q, the following equation may be used:

\[ m_1 q_1 = m_2 q_2 \]

\[ (m/z 134)(0.55) = (m/z 91)(q_z) \]

\[ q_z = 0.81 \text{ for } m/z 91 \]

To test this idea, the qz of ejection was lowered on the modified GCQ from the normal 0.9016. This change can be performed with slight modifications to the C++ code which makes up the SIM scan matrix. With this modification, the molecular ion of n-butylbenzene was ejected at qz of 0.55 with resonant ejection amplitudes ranging from
Figure 3-15 Mathieu stability diagram depicting fragmentation of the $M^+$ ion of n-butylbenzene during resonant ejection at a $q_z$ of 0.55. The large sphere represents an ion at the resonant ejection frequency and the smaller spheres represent the fragment ions m/z 91 and 92 created during resonant ejection. The fragment ions created during resonant ejection sit at a $q_z$ of 0.81, well within the stability edge. These ions will not contribute to peak fronting or mass shifts. In actuality, the fragment ions will not be ejected from the ion trap until they reach the stability edge.

1.0 to 7.0 $V_{pp}$. The instrument was mass calibrated using PFTBA. Figure 3-16 shows the ejection of n-butylbenzene with 4.0 $V_{pp}$. The molecular ion does not appear to be shifted in mass or have any peak asymmetry. As expected however, the peak suffers from poor resolution due to the low $q_z$ of ejection. The fragment ions created during the ejection of the molecular ion subsequently are ejected at the stability edge without resonant ejection appear at m/z 142 - 145. The fragment ions also suffer from poor resolution as they are ejected at the stability edge. The relative intensity of the fragment ions seen in this range
Figure 3-16 The resonant ejection of the $M^+$ ion of n-butylbenzene (m/z 134) with 4.0 $V_{pp}$ resonant ejection amplitude. The molecular ion ejects at the expected m/z. The m/z 91 and 92 fragment ions created during resonant ejection are ejected at the stability edge and appear between m/z 142 and 145.

can be quantitated and is directly related to the resonant ejection amplitude used to eject the molecular ion (Figure 3-17). At an amplitude of 7.0 $V_{pp}$, the molecular ion comprises only 13% of the total ion current; the remaining molecular ions are fragmented to form m/z 91 and 92 and ejected at the stability edge.

The molecular ion of n-butylbenzene was reexamined at a $q_z$ of 0.4508, half of the GCQ's normal ejection $q_z$ value, to study mass shifts. Under these conditions, the masses appear at half their normal m/z value, which make the instrument easy to mass calibrate. The scan rate was lowered by a factor of two to achieve the same effective scan rate in ms/amu and to increase the resolution. As the resonant ejection amplitude is increased from 1$V_{pp}$ to 7 $V_{pp}$ no apparent mass shift is observed at this $q_z$ (Figure 3-18). Using the
Figure 3-17 The percentage of the total ion current divided into three ions: the M⁺ ion of n-butylbenzene ejected at qₑ of 0.55 and the two fragment ions C₇H₇⁺ (m/z 91) and C₇H₈⁺ (m/z 92) ejected at the stability edge, as a function of resonant ejection amplitude.

normal qₑ value of 0.9016, the n-butylbenzene M⁺ ion exhibited a mass shift of -0.65 with an amplitude of 7 Vpp (Figure 3-5). By lowering the qₑ, the fragment ions formed during ejection which usually lead to mass shifts and peak fronting are trapped. The fragile ions now behave in the same manner as the calibrant ions.

Lastly, the n-butylbenzene molecular ion was examined once more using the hybrid ITMS instrument. As in experiments performed on the modified GCQ, the qₑ for ejection was chosen to be half its normal value (0.4533), with a resonant ejection amplitude of 3.0 Vpp. The scan rate was again lowered by a factor of two. As shown in Figure 3-19A, with the quadrupole in RF-only mode the m/z 134 peak is symmetrical and at the correct m/z.
Figure 3-18 Mass shifts for the M+ ion of n-butylbenzene and PFTBA calibrant ions at a $q_z$ of 0.4508 (1/2 the normal value for the GCQ) with a buffer gas pressure of 1 mtorr and a scan speed of 360 μs/amu. Data were taken on the modified GCQ. The instrument was calibrated with PFTBA at each $q_z$.

With the quadrupole set to pass the m/z 91 and 92 fragment ions, only a very small intensity can be detected. The fragment ions now appear in the center of the peak, however, and do not contribute to peak fronting. This small amount of fragmentation may actually take place after the ion is ejected from the ion trap before reaching the quadrupole. At a $q_z$ of 0.2267 with a resonant ejection amplitude of 2.0 V_{pp}, (Figure 3-19B), no fragment ions are detected. The scan rate was lowered by a factor of four to compensate for the loss in resolution at low ejection $q_z$ values. Some of the m/z 134 ions may still fragment as they undergo resonant excitation, but the fragment ions are trapped and are not ejected early.
Although lowering the $q_z$ of ejection has been shown to eliminate mass shifts, it is not the proper solution to the problem. The underlying reason for lowering the $q_z$ of ejection is to "catch" the fragment ions created during resonant ejection. In the case of n-butylbenzene, ejection must take place below a $q_z$ of 0.62 to trap the fragment ions of m/z 91 and 92. For t-butylbenzene, however, the $q_z$ of ejection needed would be totally different. Its major fragment appears at m/z 119. One would only need to lower the $q_z$ to 0.80 to trap the fragment ion. The $q_z$ chosen will depend on the separation between the precursor ion and its fragments. Therefore, there is not a universal $q_z$ that would eliminate mass shifts. In addition, the fragment ions now appear at odd unidentifiable masses as they are ejected at the stability edge. This further complicates the mass spectrum.

**Waveform Isolation**

The data presented in this chapter thus far have shown that ion fragility can produce mass shifts and poor resolution in the quadrupole ion trap. Unfortunately, ion fragility also leads to poor ion isolation efficiency in MS/MS experiments. In modern ion trap instrumentation, ion isolation is performed with a notched broadband waveform. The waveform is composed of numerous sine waves with frequencies applied across the entire stability region with the exception of a specified notch. The ion of interest is centered within the notch at a $q_z$ of 0.83. All ions above and below the notch are resonantly excited and are immediately ejected. The default isolation width for the GCQ is 1 amu with an isolation time of 12 ms.

For a proper MS/MS scan function, the parent ion should be isolated with unit resolution. This requires a default isolation width of 1 amu. Fragile ions, however, have
Figure 3-19 Mass spectrum of n-butylbenzene taken on the hybrid ITMS instrument with and a resonant ejection amplitude of 3.0 $V_{pp}$ at a $q_z$ of 0.4533 (A) and 2.0 $V_{pp}$ at a $q_z$ of 0.2267 (B). The calibrated resonant ejection amplitude is decreased with the lower $q_z$ value.
shown poor isolation efficiency at an isolation width of 1 amu. Consequently the isolation width must be widened to properly isolate and store the ion before CID. Increasing the width however poses a problem. A large width may allow more than one precursor ion to remain within the ion trap before CID. This may create a complicated daughter ion spectrum as the fragments produced may come from more than one precursor ion.

Theoretically, an ion within the center of an isolation notch should not be affected by the applied waveform. Ions do, however, absorb a small amount energy from the nearby waveform, just as in resonant ejection. The absorbed energy will force an ion from the center of the trap where it may undergo dissociative collisions. The fragment ions generated will sit outside the waveform notch and will be immediately ejected by the waveform. The result will be a decrease in ion intensity during the isolation stage; this effect should worsen as the isolation width decreases.

Figure 3-20 shows the intensity of several ions as a function of isolation width in amu. The intensities of the M$^+$ ion of benzene and the PFTBA calibrant ion (C$_3$F$_5^+$) drop as the waveform closes in on the ion with less than 0.2 amu width. These stable ions may be resonantly excited by the nearby waveform, but they do not fragment and the ion intensity remains relatively constant. The M$^+$ ion of t-butylbenzene, however, reacts differently to the nearby waveform as the ion intensity drops nearly to zero at the default isolation width of 1 amu. The isolation width must be opened up to more than 1.4 amu to obtain sufficient ion intensity. This problem is not limited to the several n-alkylbenzene molecular ions studied in this dissertation and is common among fragile ions. (McClellan and Murphy, 2001).

The problem above can be worsened if an ion exhibits a mass shift in its full scan
Figure 3-20 Normalized ion intensity as a function of isolation width. Non-fragile ions are shown with open symbols and the fragile ion with a closed symbol. Experiments were performed with an MS/MS scan function with an excitation voltage of zero and an isolation time of 12ms.

spectrum. The incorrect m/z may be chosen for isolation, and as a result the ion will not be centered within the isolation notch. Remember that mass shifts occur due to the early ejection of fragment ions upon resonant ejection, and that the molecular ion itself does not shift in q2. If a fragile ion is placed closer to either side of the notch, it will have a greater chance to be fragmented upon resonant excitation.

The isolation waveform amplitude is calibrated as a function of both q2 and the isolated mass. High m/z ions at low q2 values require a significantly greater amount of energy to be promptly ejected from the trap than do low m/z ions at higher q2 values. For the GCQ, the calibrated amplitude of the notch surrounding m/z 134 is 26.7 Vpp. For a
stable ion this is sufficient amplitude to isolate with a 1 amu width with no loss in ion intensity. For a fragile ion, however, this amplitude is enough to produce fragmentation and the ion intensity and drops sharply as this waveform amplitude is further increased. Figure 3-21 shows the isolation width at which the ion intensity drops to 50 percent its maximum value as a function of the waveform amplitude directly around the isolation notch. Below $20\, V_{pp}$ the molecular ion of t-butylbenzene behaves like a stable ion, but above that value there is a sharp loss in intensity. (The calibrated value is displayed as a dashed vertical line.) Lowering the amplitude of the waveform or decreasing the isolation time (McClellan and Murphy, 2001) both decrease the likelihood of

![Graph](image)

Figure 3-21 The isolation width at which the ion intensity of the t-butylbenzene $M^+$ ion drops to 50 percent of its maximum value as a function of the waveform amplitude directly around the isolation notch. The isolation time was at the default of 12 ms. This calibrated value of 26.7 Vpp is displayed as a dashed vertical line. The helium pressure within the trap was 1 mtorr.
fragmentation, but also lower the efficiency with which surrounding ions are ejected.

Previous experiments have shown that dissociation of ions within the trap is dependent not only on the resonant ejection waveform amplitude but also on the buffer gas pressure. To determine the effect of helium buffer gas pressure on isolation efficiency, a second set of experiments was warranted. The helium pressure was altered from 1 mtorr, its normal operating pressure up to 8.5 mtorr (Figure 3-22). The isolation waveform amplitude was held constant at $26.7 \text{ V}_{pp}$. Over the 8.5 fold increase in pressure there is a slight decrease in isolation efficiency, as the isolation window must be widened at higher helium pressures to maintain the same ion intensity. The effect, however, is much less pronounced than the increasing isolation waveform amplitude.

![Figure 3-22](image)

Figure 3-22 The isolation width at which the ion intensity of the t-butylbenzene $M^+$ ion drops to 50 percent its maximum value as a function of helium buffer gas pressure. The waveform amplitude was $26.7 \text{ V}_{pp}$ with an isolation time of 12 ms. The normal operating pressure is 1 mtorr.
Ion Trap Geometry

The three hyperbolic electrodes are designed to create a linear electric field within the ion trap. The electric field within practical ion traps, as discussed previously, deviates from linearity because of constraints such as truncation of the electrodes and small perforations placed in the endcap electrodes. These imperfections superimpose a series of non-linear field terms on top of the quadrupolar field, most notably a negative octopolar field and a hexapolar field (Franzen, 1995).

These higher order fields do not generally affect an ion at the center of the ion trap; rather, the higher field terms become detrimental when the ion approaches an endcap electrode during resonant ejection, closer to the imperfection. Under ideal conditions the kinetic energy and frequency of an ion would increase as it moves towards a resonant ejection frequency in an analytical scan. The negative octopolar field, however, causes the ion secular frequency to “shift” to lower frequency, away from the resonant ejection frequency (Sevugarajan and Menon, 1999). This deters the ion from ejecting as it is essentially coming into and out of resonance with the resonant ejection amplitude due to the constant shift in frequency. The overall effect creates a delay in ion ejection (Wells et al., 1999).

This field imperfection can be overcome in one of two ways. An ion can be scanned in the reverse direction towards a resonant ejection amplitude at low $q_z$. The shift to lower frequency would move the ion into the resonant ejection amplitude, instead of away, facilitating ion ejection. Scanning backwards requires ejection at low $q_z$ values, however, which produces poor resolution.
The field imperfection can also be overcome by using an ion trap with a “stretched” geometry. A stretched trap is assembled in such a way that the $z_0$ has been stretched with no corresponding modification to the shape of the electrodes (Syka, 1995). This stretched geometry compensates for the higher order multipole fields within the ion trap by adding a positive octopolar term within the quadrupolar field. This positive term causes an ion to shift to higher frequency as it approaches the endcaps. Now as an ion will move into a resonant ejection frequency during an analytical scan, it will be ejected without a delay.

Several researchers have developed an analytical expression to relate the shift of secular frequency, $\Delta \omega$, to field aberrations: (Sevugarajan and Menon, 1999)

$$\Delta \omega = \omega_o \left[ \frac{(144f - 405h^2)}{48} \frac{z_o^2}{r_o^2} \right], \quad (3-2)$$

where $h$ and $f$ are the strength of the hexapole and octopole superposition, respectively. The ion secular frequency will depend on the sign of the octopole superposition, whereas it will be insensitive to the sign of the hexapole superposition. Hexapole superposition decreases secular frequency, but the effect is small compared to the octopole superposition.

Cooks and co-workers (Wells et al., 1999) have shown that mass shifts observed for several ions, including the n-butylbenzene $M^+$ ion, decrease linearly as the $z_o$ is elevated from its theoretical position of 7.07 mm to a stretched configuration of 7.83 mm. This study was reproduced using the modified GCQ described here in Chapter 2. A set of new electrode spacers were constructed to place the GCQ ion trap in an ideal geometry, with a $z_o$ of 7.07 mm. The spacers were made of delrin and were constructed
with the same dimensions as the GCQ spacers except for a new thickness of 0.5061 in. instead of the normal value is 0.5360 in. The change in spacer material and the altered spacing changed the capacitance of the ion trap, consequently changing the optimal drive frequency. The RF system on the GCQ had to be slightly modified to maintain the original 1.03 MHz drive frequency.

As expected, the resolution was degraded with the unstretched trap configuration. Peak widths were on the order of 1.5 amu at 10% height. The most alarming difference, however, was that the molecular ion of n-butylbenzene shifted in excess of 0.5 amu with a calibrated resonant ejection amplitude at normal buffer gas pressure.

To determine how trap geometry and field imperfections lead to mass shifts, several simulations were performed using Simon v.7 (Idaho National Engineering Laboratory, Idaho Falls, ID). (Chapter 6 will provide an in-depth coverage of simulations performed by SIMION) Simulations were performed for an m/z 134 ion in a stretched trap and an unstretched trap. In both cases the ion was ejected at the stability edge with no resonant ejection amplitude. Figure 3-23A shows the ejection profile of an ion in the axial direction in an ion trap with a normal "stretched" geometry ($r_0 = 7.83$ mm). The ion trajectory increases exponentially as it approaches the stability boundary where it is eventually ejected. A drastic difference occurs when the same ion is ejected from an unstretched trap. With the unstretched geometry the ion oscillation again increases but does not immediately eject. The ion remains within the ion trap and oscillates between the two endcaps at a high kinetic energy for a period of over 1.3 ms (Figure 3-23B).

The above simulations show that an ion ejected from an unstretched trap will behave differently than a stretched geometry. This does not, however, directly explain
Figure 3-23 Ion trajectories in the axial direction for m/z 134 with an ion trap with a stretched geometry, $r_0$ of 7.83 mm (A) an ion trap with an unstretched theoretical geometry, $r_0$ of 7.07 mm (B). The trajectories were created by SIMION v.7 with a computational quality of 10. The dotted lines indicate the position of the endcap electrodes.
the root of compound-dependent mass shifts seen with different trap geometries. If an unstretched geometry simply led to a delay in ion ejection, mass calibration could correct for the delay. Mass shifts occur as ions of various structures react differently to the negative octopolar field. This field allows an ion to remain in the trap for an increased time allowing for a greater number of energetic collisions, as in Figure 3-23. Furthermore, the ion is traveling with a great deal of kinetic energy. An ion of m/z 134, for example, will have as much as 200 eV of kinetic energy before ejection. Using equation 3-3 the center-of-mass collision energy for such a collision would be 7.0 eV. This is more than enough energy to fragment the molecular ion of n-butylbenzene with a single collision. Over this extended time scale, it would not be unreasonable to expect that the entire peak for the M+ ion of n-butylbenzene would consist primarily of fragment ions, causing the peak to shift in mass.

Predicting Ion Fragility

Ion fragility may be difficult to predict by just examining the chemical structure of an ion. Up to this point ion fragility has been shown with exaggerated resonant ejection amplitudes, helium buffer gas pressures and different trap geometries. Modern commercial instruments, however, make it difficult to change any of these parameters. Predictions of ion fragility can be made without instrument modification. Two ways discussed here are the inspection of an ion’s EI (electron ionization) mass spectrum or its MS/MS breakdown curve.
When a compound is ionized by EI, it is bombarded by high-energy electrons (70 eV). The ionization potential of organic molecules is typically on the order of 10 eV. This can leave a great deal of excess energy in the molecular ion from the interaction with the high energy electron. This surplus energy will typically cause dissociation of the molecular ion. The degree of fragmentation should be directly related to ion fragility.

Table 3-2 lists several fragile (in italics) and non-fragile ions with the percentage of ion current carried by the molecular ion in a 70 eV EI spectra from the NIST library. The percentage of the $M^+$ ion for t-butylbenzene is only 6.1 %, compared to 42% for a stable ion, the $M^+$ ion of naphthalene. The percentage of ion current carried by the intact $M^+$ ion can be related to the extent at which an ion shifts under adverse conditions. In Table 3-2 it is compared to the mass shift an ion exhibits with a 7 $V_{pp}$ resonant ejection amplitude. The extent of which an ion shifts in m/z clearly correlates to the ease with which it fragments during electron ionization. As a general rule, the molecular ions which carry less 20% of the ion current in the 70 eV spectrum will exhibit mass shifts.

<table>
<thead>
<tr>
<th>Molecular ion</th>
<th>% $M^+$ ion in EI Spectrum</th>
<th>Mass Shift at 7 $V_{pp}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>naphthalene</td>
<td>42.0</td>
<td>+0.01</td>
</tr>
<tr>
<td>benzene</td>
<td>38.8</td>
<td>+0.10</td>
</tr>
<tr>
<td>nitrobenzene</td>
<td>10.5</td>
<td>-0.47</td>
</tr>
<tr>
<td>n-pentylbenzene</td>
<td>9.3</td>
<td>-0.48</td>
</tr>
<tr>
<td>n-hexylbenzene</td>
<td>7.5</td>
<td>-0.62</td>
</tr>
<tr>
<td>n-butylbenzene</td>
<td>6.9</td>
<td>-0.63</td>
</tr>
<tr>
<td>t-butylbenzene</td>
<td>6.1</td>
<td>-1.24</td>
</tr>
</tbody>
</table>

Table 3-2 Several fragile (in italics) and non-fragile ions with the percentage of the ion current carried by the molecular ion in a 70 eV EI spectrum from the NIST library and the mass shift observed with a 7 $V_{pp}$ resonant ejection amplitude.
Ion fragility can also be predicted by examining an ion’s breakdown curve. A breakdown curve is created by performing MS/MS on an ion with successively increasing collision energies. As the ion dissociates its intensity drops and the intensity of its fragment ions increase. Breakdown curves are typically employed to determine the most efficient resonant excitation amplitude to optimally fragment an ion for MS/MS. Figure 3-35 shows several breakdown curves obtained on the ion trap for fragile and non-fragile ions. The curves show only the intensity of the molecular ion, with the fragment ion intensities omitted for clarity. MS/MS was performed on the modified GCQ with an excitation time of 5 ms at $q_z$ of 0.45. The isolation width (normally 1 amu) was increased to 5 amu to accommodate the fragile ions. The ion intensity of the two fragile ions drops

Figure 3-35 Breakdown curves for both fragile (solid symbols) and non-fragile ions (open symbols). The curves only show the intensity of the molecular ion. MS/MS was performed on the modified GCQ with an excitation time of 5 ms at $q_z$ of 0.45.
off at a lower resonant excitation amplitude than the stable ions. The voltage differs by more than a volt between the t-butylbenzene \( M^+ \) ion and \( C_3F_5^+ \) (m/z 131) from PFTBA.

**Ion Energy During Ejection**

When the quadrupole was used in the hybrid ITMS instrument to mass-analyze ions ejected from the ion trap it was important to estimate the kinetic energy of the ions as they were ejected from the ion trap. If the ion’s kinetic energy was too high, it would travel though the quadrupole with such a high velocity that it would not be efficiently mass analyzed. The kinetic energy of several ions was determined with a series of stopping potentials created by the lens stack between the ion trap and the quadrupole. The retarding potential was placed on the middle lens, while the two outer lenses were held at ground. Positive ions were decelerated in the region between the first and second lenses. Only ions with kinetic energies greater than the potential set by the middle lens were allowed into the quadrupole and eventually detected. The potential was supplied by a 0 – 5 kV DC Finnigan MAT power supply. Steps were 25 V up to 200 V and 50 V thereafter. Data were taken for several fragment ions of PFTBA. The ions were ejected from the ion trap at stability edge without resonant ejection.

The resulting ion signals for five different m/z ions was recorded. The stopping potential curve for m/z 69 is shown in Figure 3-34A. To calculate the kinetic energy distribution from this stopping potential curve, the first derivative was taken (Figure 3-34B). The average stopping potential is defined as the inflection point in the original stopping potential data and thus as the maximum value of the first derivative. From the
Figure 3-34 Stopping potential curve for m/z 69 (A) and its first derivative (B).
Stopping potentials, the average kinetic energy of several m/z ions exiting the ion trap was calculated (Table 3-3).

It was determined that the kinetic energy of the ions exiting the ion trap can be related to the potential well depth ($D_u$) where the ion kinetic energy increases linearly with mass and has a quadratic relationship with $q_z$.

\[
D_u = \frac{mq_0^3\Omega^2u_0^2}{16e}
\]  

(3-3)

Recall this equation applies only for $q_z$ values less than 0.4 and may not predict with much accuracy kinetic energies at the high $q_z$ values where ions are actually ejected. The average kinetic energy for each ion was plotted as a function of m/z, yielded the following relationship.

\[
KE \ (eV) = 3.7 \ (m/z) - 116.5
\]

(3-4)

As predicted by Equation 3-3, the kinetic energy decreases at the $q_z$ of ejection is lowered. As shown in Table 3-3, the m/z 131 ion has a kinetic energy of 325 eV when it is ejected at 0.908; it drops to 58 eV when ejected at a $q_z$ of 0.45 (with 1.5 $V_{pp}$ resonant ejection).

<table>
<thead>
<tr>
<th>m/z</th>
<th>$q_z$</th>
<th>Average KE</th>
<th>Max KE</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>0.908</td>
<td>163</td>
<td>450</td>
</tr>
<tr>
<td>131</td>
<td>0.908</td>
<td>325</td>
<td>700</td>
</tr>
<tr>
<td>264</td>
<td>0.908</td>
<td>863</td>
<td>1800</td>
</tr>
<tr>
<td>414</td>
<td>0.908</td>
<td>1475</td>
<td>2850</td>
</tr>
<tr>
<td>502</td>
<td>0.908</td>
<td>1700</td>
<td>3400</td>
</tr>
<tr>
<td>131</td>
<td>0.45</td>
<td>58</td>
<td>210</td>
</tr>
</tbody>
</table>

Table 3-3 Kinetic energies in eV for several PFTBA fragment ions ejected from the quadrupole ion trap.
Knowing the kinetic energy of an ion, its velocity (in m/s) can be determined with the following equation

\[ v = \sqrt{\frac{2KE}{m}} \]  \hspace{1cm} (1-12)

with \( KE \) in eV (Volts x \( 1.6 \times 10^{-19} \)) and mass \( m \) in kg. An ion of m/z 134 with 325 eV of kinetic energy will thus travel at a velocity of \( 2.2 \times 10^4 \) m/s. This ion will pass through a 13.4 cm long quadrupole in 6 \( \mu \)s and see only 14 cycles of RF at a drive frequency of 2.27 MHz. That is enough cycles to perform mass analysis with limited resolution.

**Conclusion**

Mass shifts can result from early ejection of fragment ions during resonant ejection of fragile ions. As these ions come into resonance with the ejection frequency, they gain kinetic energy, collide with buffer gas molecules, and can dissociate. The resultant fragment ions, which are lower in m/z, will no longer be stable within the ion trap as they will lie beyond the stability boundary at \( \beta_x = 1 \). The fragment ions are thus immediately ejected and detected before the intact ions are resonantly ejected. The fragment ions and the non-dissociated precursor ion form one peak which has a significant amount of peak fronting and an overall broad peak shape. The peak top may remain at the correct m/z in profile acquisition, but the peak centroid will be shifted to a lower m/z.

Several instrumental parameters may increase the mass shifts due to ion fragility. Increasing the resonant ejection amplitude increases the kinetic energy of an ejecting ion. This can cause a fragile ion to undergo energetic collisions and dissociate. Increasing the
helium buffer gas pressure within the ion trap will also increase the likelihood of an energetic collision. And lastly, lowering the scan rate allows the ion an increased amount of time to fragment before it is ejected. These mass shifts can be minimized or eliminated by minimizing the resonant ejection amplitude, maintaining the helium buffer gas at a modest pressure, or lowering the q of ejection so the fragment ions formed will be contained within the ion trap.

Mass shifts are not limited just to fragile ions. Any ion may undergo a degree of fragmentation as it is resonantly ejected. PFTBA ions used to mass-calibrate the ion trap, for example, are reasonably stable; nevertheless, when they are compared to an atomic ion such as xenon that cannot fragment they exhibit a slight mass shift. Since the ion trap is mass calibrated with PFTBA ions, mass shifts may be observed in both directions. Fragile ions will exhibit a negative mass shift, whereas atomic species or very stable ions which do not fragment will exhibit a positive mass shift.

The ejection characteristics of large molecular weight compounds limited this study to small molecules, the largest being n-octylbenzene (m/z 190.33). Ion fragility, however, is not limited to small molecules. Studies involving several fragment ions of PFTBA revealed C₄F₉⁺ (m/z 219) and C₉F₂₀N⁺ (m/z 502) also exhibit a small mass shift during resonant ejection.
CHAPTER 4
ION INJECTION

Early commercial ion trap instruments, designed to be incorporated with a GC (gas chromatograph), were restricted to the analysis of volatile, low molecular weight compounds. Ions were created directly inside the ion trap using either EI or low-pressure CI. The pressure limit inside the ion trap of approximately $10^{-3}$ torr prevented the use of high-pressure ionization techniques such as negative CI. Internal ionization proved to be a reasonably sensitive technique, but possessed several drawbacks. Sensitivity for certain types of samples such as highly polar compounds, for instance, was greatly reduced using internal ionization. This is believed to be due to the absorption of the sample on the large surface area of the metal electrodes (Stafford et al., 1985). The simultaneous presence of the neutral sample molecules and the charged ion fragments within the ion trap also caused undesired ion/molecule reactions (Guckenberger, 1999).

To avoid these pitfalls, modern commercial instruments produce ions externally and then transmit them into the ion trap. The use of an external EI ion source with a substantially reduced volume and surface area greatly reduces the problem of sample absorption. An external ion source also ensures that only the ions injected into the ion trap will be present in the trap, and that few neutral sample molecules make it from the external source into the ion trap. Undesired ion-molecule reactions within the ion trap can thereby be substantially reduced. External ionization also opens the ion trap to a variety of high-pressure ionization techniques, such as electrospray (ESI) (McLuckey et al., 1995), glow discharge (Song et al., 2001), negative CI (Faye et al., 2000) and
atmospheric pressure chemical ionization (APCI) (Hogenboom at al., 1998). Ion injection, however, is not an efficient process; typically only 5% of the ions formed in the ion source can be successfully trapped (Quarmby and Yost, 1999). As stated previously, ion injection exhibits a dependence on both the initial phase and amplitude defined by the low-mass cut-off, (LMCO) of the RF placed on the ring electrode, which limits the ability of the ion trap to accept ions from an external source (Quarmby and Yost, 1999; He and Lubman, 1997; Wei et al., 1996).

Ion injection can be depicted as a two-step process. First ions must be accelerated from an ion source through a hole in the endcap electrode into the RF trapping field within the ion trap. In the GCQ, ions are extracted from the ion source through a series of electrostatic lenses and are attracted into the trapping volume by a trap offset of typically 10V. This offset along with the RF field, however, imparts energy onto the ion. The second step in ion injection involves the removal of this kinetic energy. A buffer gas, usually helium, is used to decelerate the injecting ions. The reduction of momentum due to collisions with the buffer gas helps remove excess ion kinetic energy and allows the ion to be trapped in the pseudopotential well. Unfortunately, these collisions may also add to an ion's internal energy and lead to fragmentation. Such fragmentation may be one source of discrepancy between spectra obtained with an ion trap and other mass analyzers, such as a quadrupole mass filter. Dissociation may remove valuable spectral information by eliminating a molecular ion or fragment ion peak useful in structural determination. Additionally, it may disturb well-known ion ratios and add new unexpected ions to the mass spectrum.
A hybrid quadrupole mass filter/quadrupole ion trap instrument was constructed to examine fragmentation of ions upon injection. This hybrid instrument differed slightly from the instrument described in Chapter 3. The mass filter was placed in front of the ion trap instead of after and the ions produced in an external ion source mounted in front of the mass filter. In this arrangement, ions emitted from an ion source can be mass-selected by the quadrupole mass filter to allow a single m/z to enter the ion trap. The dissociation of injecting ions can then be monitored by the presence of fragment ions in the acquired mass spectrum. Several instrumental parameters were studied to understand what factors contribute to ion dissociation. This instrument also proved to be useful in investigating ion-molecule reactions which can occur within the ion trap.

The mass-selected injection of ions into an ion trap is a technique initially performed during the early stages of ion trap mass spectrometry by March and co-workers (March et al., 1984). In their experiments, ions were injected from a double focusing magnetic/electric sector instrument (EB) into the ion trap through a gap between the endcap and ring electrodes (where the spacers should be). The sector instrument transmits ions with high kinetic energy, so ions were injected into the ion trap with up to 4 keV of energy. The aim of the experiment was to study high-energy CID processes. The ion trap was used as a sophisticated collision cell with a collision gas admitted into the ion trap through a pulsed valve. The resultant fragment ions were stored momentarily and ultimately ejected into a quadrupole mass filter to be mass analyzed. Similar experiments were performed by Cooks and co-workers to study both collision-activated dissociation (CAD) and surface-induced dissociation (SID) (Schwartz et al., 1990; Morand et al., 1991). These initial studies demonstrated that ions could fragment within
the ion trap when injected at high energies. The study presented in this chapter will focus on ion injection from an EI ion source into the ion trap, with much lower kinetic energies.

**Instrumentation**

The hybrid tandem-in-space instrument was built within the ITMS vacuum chamber previously described in Chapter 3. Ions were created using a GCQ EI ion source mounted to an optical rail within the chamber. The filament circuit was controlled by a Finnigan quadrupole electronics module (QEM) with an emission current set below 150 μA and an electron energy of 70 eV. The electron lens, controlled by a Finnigan TSQ45 lens supply source, was set to +15 V. The GCQ ion source lens assembly remained unchanged, with two ion lenses, typically held at −15 V surrounding one gating lens. For simplicity, the ITMS electron lens was used to supply voltage to the gating lens which is responsible for emitting ions into the mass filter and the ion trap. Remember that the ITMS was originally designed to operate with internal ionization, with injection of electrons, not ions into the trapping volume. Thus, the polarity of the electron lens was positive during ionization; the voltage was inverted in this study so ions of a positive charge could be injected into the trap instead of electrons. In addition to this modification, a 5 MΩ variable resistor was inserted into the gating circuit to lower the voltage from its normal amplitude of +180 V / -180 V to a nominal -100 / +100V. The end of the tube lens was placed directly inside of the quadrupole mass filter to obtain efficient ion injection into the device and eliminating fringe field concerns. Samples
were introduced into the EI ion volume through a Granville-Phillips leak valve and a piece of PEEK tubing.

The quadrupole mass filter (A in Figure 4-1) was originally a Q1 from a Finnigan TSQ45 triple quadrupole mass filter. This specific quadrupole and associated electronics were detailed in Chapter 3. The quadrupole potentials were offset from the ion source by -9 V. The exit end of the quadrupole was coupled to the ion trap by the use of two plate lenses and a tube lens with typical voltages of -10 V, -10 V and -25 V respectively. The tube lens was placed 2 mm from the endcap electrode and guided the ions directly into the ion trap. To calibrate the quadrupole mass filter during the initial construction of the instrument, the ion trap was removed from the vacuum chamber and the multiplier was moved into its place. The quadrupole was then calibrated using several fragment ions of PFTBA.

The ITMS ion trap used in this study is the same as the one described in Chapter 3 with several modifications. The ITMS ion trap was originally designed for internal ionization, and thus contained an endcap electrode with a filament assembly embedded within it. To accommodate for ion injection, this endcap was replaced with a second exit endcap electrode (B in Figure 4-1). The ITMS trap now most closely resembles the GCQ ion trap, with identical endcap electrodes on both sides. The ITMS ion trap also had to be modified to accept a DC trap offset. In its original configuration an optional DC potential could only be supplied to the ring electrode to assist in ion isolation. This DC was supplied by a Finnigan Selective Mass Storage high voltage power supply and was controlled through the ICMS software (Yates, 1994). To create a uniform trap offset to attract ions into the ion trap from the grounded ion source, a DC potential was also placed
Figure 4-1 Photograph of the ITMS hybrid instrument inside the vacuum chamber: the GCQ ion source (not shown) the quadrupole mass filter (A) with associated lenses and the ITMS ion trap (B). The entrance endcap of the ITMS ion trap was replaced with an ITS40 exit endcap to allow for ion injection. Helium was introduced into the ion trap through a piece of PEEK tubing (C). Two halogen bulbs were used to heat the vacuum chamber to 100°C.

on the endcap electrodes though the balun circuit. The balun accepts a signal such as the resonant ejection amplitude and divides it between the two endcap electrodes. It had to be modified to accept a DC potential. The DC potential added to the endcap electrodes was then matched to the DC potential on the ring electrode. The ion trap offset optimized at -6 V compared to the ion source.

The scan function of the ITMS used in these studies included sequential stages of ionization (1-70 ms), a post-ionization time (2 ms) and an RF scan to eject and detect ions with resonant ejection. The RF amplitude (LMCO) during ionization ranged from m/z 35 to 40. The resonant ejection amplitude was set to 3.5 V_{pp} at a q_z of 0.906. Ions
were detected using a conversion dynode and electron multiplier operated at -4 kV and 1.6 kV, respectively. Each spectrum obtained was the average of 50 scans.

The helium buffer gas was leaked into the closed trap through a piece of PEEK tubing fed between the endcap electrode and the quartz spacer. The normal operating helium pressure was recorded as the chamber pressure indicated on a Bayard-Alpert ionization gauge and was typically 7.8x10^{-5} torr. This is different from previous experiments in Chapter 3 where the chamber pressure was typically 2.0x10^{-5}. The holes in the second exit endcap allows for a greater conductance of helium out of the trap; therefore the flow of helium into the trap had to be increased to maintain the same operating pressure within the ion trap. The entire chamber was kept a temperature of 100°C by four halogen bulbs.

Injection of Mass Filtered Ions

The initial studies performed on the hybrid instrument involved the analysis of perfluorotributylamine (PFTBA). The EI spectrum of this calibration compound contains numerous fragment ions varying in m/z, stability and reactivity. The C_{4}F_{9}^{+} (m/z 219) ion is particularly noteworthy, as its relative intensity varies with different mass analyzers. The m/z 219 ion is dominant in spectra obtained with a quadrupole mass filter (66% relative intensity) but has a very low intensity in spectra obtained with an ion trap (20% relative intensity). The hybrid instrument was used to provide an insight into why the ion intensity of m/z 219 is so much lower with the ion trap. The C_{4}F_{9}^{+} ion created in the GCQ source was mass-selected by the quadrupole and injected into the ion trap. The
resultant spectra contained numerous product ions of both higher and lower m/z (Figure 4-2). To verify that the quadrupole was properly passing the C₄F₉⁺ ion and filtering all others, it was readjusted to pass ions both slightly above and below m/z 219. No ion signal was detected, proving that these product ions derived from the injection of C₄F₉⁺ (m/z 219). Three out of the four product ions are common PFTBA fragment ions (m/z 69, 131 and 414). The last ion, m/z 197, is commonly seen in the ion trap spectrum of PFTBA but is absent from the quadrupole spectrum.

In previous studies, C₄F₉⁺ has been classified as a fragile ion as it has shown to fragment upon resonant ejection. It would seem reasonable then to assume that the ion would also fragment during ion injection as well. To confirm this, C₄F₉⁺ was

![Image: Mass spectrum showing m/z 69, 131, 219, 197, and 414.]

Figure 4-2 C₄F₉⁺ (m/z 219) from PFTBA was mass-selected by the quadrupole mass filter and injected into the ion trap. The resultant spectra contained numerous product ions of both higher and lower m/z. Conditions include a chamber pressure of 1.3x10⁻⁵ torr, a LMCO of 35 during injection, ion time of 10 ms and a cool time of 2 ms.
dissociated by MS/MS in the ion trap. The resulting fragment ions matched the two ions of lower mass (m/z 69 and 131) and appeared in the same ratio as those in Figure 4-2.

Fragmentation pathways:

\[
\begin{align*}
\text{C}_4\text{F}_9^+ (m/z \ 219) & \rightarrow \text{CF}_3^+ (m/z \ 69) + \text{C}_3\text{F}_6 \\
\text{C}_4\text{F}_9^+ (m/z \ 219) & \rightarrow \text{C}_3\text{F}_5^+ (m/z \ 131) + \text{CF}_4
\end{align*}
\]

MS/MS experiments also confirmed that the last two product ions (m/z 197, 414) are not produced from dissociation of C₄F₉⁺. They therefore must be a result of a secondary process, most likely ion-molecule reactions. Although external ionization reduces the presence of reactive neutrals in the ion trap, ion molecule reactions may continue to pose a problem. Water, for instance, is difficult to eliminate from the ion trap as it is present in the helium buffer gas at low levels and also continually outgases from the vacuum manifold and o-rings (Guckenberger, 1999). The extent to which water molecules and other reactive neutrals affect the mass spectrum is directly related to the amount of time the ions are held within the ion trap. To illustrate this point the post ion time or “cool time” was extended beyond its default value of 2 ms to allow for a greater reaction time. The cool time is normally used to allow injected ions time to focus toward the center of the ion trap. Figure 4-3 shows that the longer the C₄F₉⁺ ion is held within the ion trap, the more of it is converted to C₄F₇O⁺ (m/z 197) by an ion-molecule reaction with water.

\[
\text{C}_4\text{F}_9^+ (m/z \ 219) + \text{H}_2\text{O} \rightarrow \text{C}_4\text{F}_7\text{O}^+ (m/z \ 197) + 2\text{HF}
\]
The intensity of the product ion at m/z 414 also intensifies with increased reaction time. The C₈F₁₆N⁺ (m/z 414) ion is derived from an ion-molecule reaction with neutral PBTBA molecules:

\[ \text{C}_4\text{F}_9^+ (m/z \ 219) + (\text{C}_4\text{F}_9)_3\text{N} \rightarrow \text{C}_8\text{F}_{16}\text{N}^+ (m/z \ 414) + 2\text{C}_4\text{F}_{10} \]

Although PFTBA is leaked directly into the source, there is no wall separating the ion source from the mass analyzer; consequently neutral molecules are allowed to diffuse throughout the entire vacuum chamber and react in the trap. This further emphasizes the importance of differential pumping.

![Graph](image)

Figure 4-3 The relative ion intensity of C₄F₉⁺ (m/z 219), C₄F₇O⁺ (m/z 197) and C₈F₁₆N⁺ (m/z 414) with varying cool times. C₄F₉⁺ is converted to C₄F₇O⁺ and C₈F₁₆N⁺ by a series of ion-molecule reactions.
The remaining PFTBA fragment ions (listed in Table 2-1) were inspected in the same manner. It was revealed that CF$_3^+$ (m/z 69) vigorously reacts with neutral PFTBA molecules in the ion trap to form C$_4$F$_9^+$ (m/z 219), C$_8$F$_{16}N^+$ (m/z 414) and C$_{12}$F$_{24}N^+$ (m/z 614). The C$_9$F$_{20}N^+$ (m/z 502) ion, similar to C$_4$F$_9^+$, is known as a fragile ion and dissociates readily upon injection to form C$_5$F$_{16}N^+$ (m/z 264).

These initial experiments show that both fragmentation of ions upon injection and ion molecule reactions can alter ion intensities and the appearance of a mass spectrum. This can make compound identification difficult when matching ion trap spectra with common EI spectral libraries. In contrast to the quadrupole, the ion trap injects ions into a high-pressure region with an energetic field where ions can dissociate. In addition, ions can be held for a long period of time during which time they may react. Ion-molecule reactions have been decreased with external ionization, and can be further reduced with differential pumping. Fragmentation of injecting ions, however, still poses a problem.

The remaining portion of this chapter will focus on characterizing instrumental parameters which facilitate fragmentation in the hope of limiting its adverse effects.

**Instrumental Parameters**

Several instrumental and experimental parameters which would be expected to impact the dissociation of ions upon injection were initially identified. They included the RF amplitude during injection (Van Berkel et al., 1991; Schwartz and Cooks, 1988), helium buffer gas pressure, trap offset and the electrostatic lens potentials. Each of these parameters has been studied in-depth with the hybrid ITMS instrument.
RF Amplitude or $q_z$ during Injection

As described in Chapter 2, the optimal RF level during injection directly affects the momentum of the injecting ion. Ions with large momentum and m/z will require large RF amplitudes to be efficiently trapped. Modern commercial instruments calibrate the RF amplitude with mass during injection by choosing the lowest amplitude to obtain a constant ion signal for each m/z (Figure 2-1). An ion may still, however, be trapped at higher values. The hybrid quadrupole mass filter/ion trap hybrid instrument was used to take a closer look at ion injection across the entire $q_z$ axis. The CF$_3^+$ (m/z 69) fragment ion of PFTBA was initially chosen as an ideal ion because of its stability and resistance to fragmentation. CF$_3^+$ formed in the EI source was mass-selected by the quadrupole and injected into the ion trap. The LMCO (RF amplitude) during injection was incremented from 5 to 70 in 0.5 amu steps. The LMCO during injection can be related in terms of the $q_z$ of injection of m/z 69 by using the following equation.

$$q_z \text{ of injection} = \frac{\text{LMCO} \times 0.908}{69}$$  \hspace{1cm} (4-1)

There are restricted ranges of the stability region where an ion can be injected and trapped efficiently (Figure 4-4). At low $q_z$ values (below 0.12) no ion signal is typically detected as the ion sits within a shallow potential well. The RF field is not strong enough a low $q_z$ values to hold an ion for a significant period of time and an ion can easily pass out of the shallow potential well and will probably be neutralized by a collision with an electrode. The ion signal drops off again as the ion approaches a $q_z$ value of 0.908 at the edge of the stability region. Between these two limits the potential well is deeper and can effectively trap kinetically hot ions until they undergo sufficient collisional cooling and collapse to the center of the RF field. In this region, however, there are great variations
in injection efficiency for CF$_3$ across the large range of q$_z$ values. Several of these variations have been previously linked to non-linear resonances (Eades et al., 1993).

As explained in Chapter 3, several structural concessions were made in the production of the quadrupole ion trap. These concessions include the truncation of the electrodes, the perforations placed in the endcap electrodes and the “stretched” geometry of the commercial ion trap. Due to these physical changes, the ion trap deviates from an ideal quadrupolar device and an imperfect and distorted quadrupolar field is formed within the ion trap. Higher order fields are superimposed upon the main quadrupolar field and manifest themselves as non-linear resonances. The non-linear resonances can have a negative effect during ion injection by perturbing ion motion and lowering ion injection efficiency. When the secular frequency of an ion comes into resonance with a non-linear field, the ion absorbs energy and is displaced away from the center of the trap. Unfortunately, the further an ion moves from the center the more greatly it is affected by the non-linear resonance (Eades et al., 1993). The ion can subsequently either collide with one of the electrodes or eject from the trap. These resonances, where ion intensities drop dramatically, are called “black holes”. All of the major “black holes” can be matched to a frequency which corresponds to a particular non-linear multipole: dodecapole, decapole, octopole and hexapole (Table 4-1). Yost and co-workers have shown that non-linear resonances not only exist on the a$_z$ = 0 axis but also stretch across the entire stability diagram. These resonances, which extend in the a$_z$ direction, are termed as “black canyons” (Eades and Yost, 1992). Similar results have been shown by several other research groups (Guidugli et al., 1991; Morand et al., 1991).
The non-linear resonances do not eliminate all injected ions however. As an ion is excited and its trajectory increases, its secular frequency changes slightly so it is no longer in resonance with the non-linear term, allowing the ion to remain trapped. Ions may also be cooled and focused into the center of the ion trap through collisions with helium molecules. In the center of the trap the non-linear fields are very weak and an ion

![Graph showing relative intensity against qz of injection with peaks labeled A, B, C, D.]

Figure 4-4 Injection of CF$_3^+$ ions (m/z 69) into the ion trap analyzed as a function of qz during injection. The significant reductions in ion injection efficiency have been labeled with letters A through D and are directly related to several non-linear resonances.

<table>
<thead>
<tr>
<th></th>
<th>$q_z$</th>
<th>$\beta_z$</th>
<th>Frequency ($\omega$)</th>
<th>Non-linear Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.46</td>
<td>1/3</td>
<td>$\Omega/6$</td>
<td>Dodecapole</td>
</tr>
<tr>
<td>B</td>
<td>0.54</td>
<td>2/5</td>
<td>$\Omega/5$</td>
<td>Decapole</td>
</tr>
<tr>
<td>C</td>
<td>0.64</td>
<td>1/2</td>
<td>$\Omega/4$</td>
<td>Octopole</td>
</tr>
<tr>
<td>D</td>
<td>0.78</td>
<td>2/3</td>
<td>$\Omega/3$</td>
<td>Hexapole</td>
</tr>
</tbody>
</table>

Table 4-1 The “black holes” observed in Figure 4-4 can be directly linked to several non-linear resonances. Each can be linked to a specific multipole and frequency.
may not feel any affect.

The data from Figure 4-2 show that non-linear resonances can have a detrimental effect on ion injection efficiency. There is also evidence that it may aid it as well. A large increase in ion injection efficiency for CF$_3^+$, can be seen at q$_z$ values directly preceding the octopolar resonance at $\beta_z = 1/2$ line ($q_z = 0.64$). This same trend was seen for ions of different m/z, as long as they were stable enough to be injected at high q$_z$ values.

The CF$_3^+$ ion represented an ideal ion with a low molecular weight and great resistance to fragmentation. The molecular ion of n-butylbenzene was examined in the same manner to represent the opposite extreme of a fragile ion. The molecular ion of n-butylbenzene (m/z 134) was mass selected by the quadrupole mass filter with a 2 amu wide window and injected into the ion trap as the LMCO was varied from 10 to 70 amu which relates to a q$_z$ of n-butylbenzene of 0.067 to 0.47. The low-resolution quadrupole window of 2 amu was used to provide a greater ion flux into the ion trap. In contrast to the CF$_3^+$ ion, the trapping efficiency is poor and the molecular ion of n-butylbenzene ions is only detected over a very small range of q$_z$ values (0.16 to 0.3) and at low intensities (Figure 4-5).

Inspection of the mass spectra reveals that the majority of the molecular ion is dissociated upon injection to form the two characteristic fragment ions at m/z 91 and 92 (Figure 4-6). Due to the differences in ion fragility, ions with similar m/z may have very different injection efficiencies at the same q$_z$ of injection. The m/z 129 isotope of xenon, for example, has a consistent ion intensity over a q$_z$ range between 0.15 and 0.9. The
Figure 4-5 Injection of the molecular ion of n-butylbenzene (m/z 134) into the ion trap. The molecular ion intensity was recorded as a function of $q_z$ during injection.

The molecular ion of n-butylbenzene (m/z 134), however, cannot be detected at $q_z$ values above 0.3. Above this value all of the molecular ions entering the trap dissociate. The small $q_z$ range of acceptance hinders the study of non-linear resonances. Previous results have shown that these field imperfections can excite ions during injection, leading to poor injection efficiency. It could be predicted that non-linear resonances may also lead to further dissociation of fragile ions upon injection. In the case of n-butylbenzene, however, it is impossible to determine. The lowest non-linear resonance appears at a $q_z$ of approximately 0.46 (dodecapolar), at this value the molecular ion of n-butylbenzene is already completely dissociated.

The $q_z$ or LMCO during injection is directly proportional to the RF amplitude on the ring electrode. When the $q_z$ of injection is increased, the injecting ions are accelerated by the strong quadrupolar field and can obtain high kinetic energies (Basic et
Figure 4-6 The molecular ion of n-butylbenzene (m/z 134) was mass selected by the quadrupole mass filter and injected into the ion trap. Conditions include a chamber pressure of $1.3 \times 10^{-5}$ torr, a LMCO of 40 during injection (m/z 134 situated at a $q_z$ of 0.27), an ion time of 10 ms and a cool time of 2 ms.

Al., 1993). Energetic collisions with the helium buffer gas can then lead to ion dissociation. As a result, at high $q_z$ values very few fragile ions may survive. In the case of n-butylbenzene, fragment ions were detected over the entire $q_z$ range studied here (0.067 to 0.47) even when the molecular ion could no longer be detected (Figure 4-7).

Historically, n-butylbenzene has often been the molecule of choice for examination of energy deposition of various ionization and collisional techniques. The activation energies of two major fragmentation pathways (Figure 3-6) are well characterized. A direct cleavage leads to the formation of m/z 91 ($C_7H_{17}^+$) requiring 1.7 eV of energy (Plomley et al., 1996; Croye et al., 1999). A rearrangement process forms
Figure 4-7 Relative intensities of the molecular ion of n-butylbenzene (m/z 134) and its two fragment ions at m/z 91 and 92 with increasing q\textsubscript{z} of injection for the molecular ion of n-butylbenzene.

m/z 92 (C\textsubscript{7}H\textsubscript{8}+) requiring 1.0 eV of energy. By examining the ratios of these two fragment ions (m/z 91/92), an estimate of internal energy deposition can be obtained. A large 91/92 ratio, for instance, would represent high-energy deposition. This will prove useful in determining the instrumental parameters that most affect fragmentation upon injection. The ratio of the fragment ions at m/z 91 and 92 from the data in Figure 4-7 is displayed in Figure 4-8. The 91/92 ratios increased from zero at a q\textsubscript{z} of 0.17 to 3.4 at a q\textsubscript{z} of 0.47, with the most dramatic increase occurring between q\textsubscript{z} of 0.27 and 0.37.

Figure 4-8 confirms that the amplitude of the RF during injection indicates the amount of kinetic energy an ion has. Therefore it would seem logical that the amount of fragmentation of injected ions would be directly related to the q\textsubscript{z} of injection.
Figure 4-8 The ratio of m/z 91 / m/z 92 of n-butylbenzene as a function of increasing LMCO during injection. The LMCO during injection is displayed as the $q_z$ at which the molecular ion of n-butylbenzene is injected into the ion trap.

The molecular ion of t-butylbenzene was examined in the same manner. In the previous chapter the t-butylbenzene $M^+$ ion was shown to be more fragile than n-butylbenzene. As for n-butylbenzene, fragment ions of t-butylbenzene were detected over the entire $q_z$ range which was studied here (0.1 to 0.46), whereas the molecular ion could only be detected across a very small range of $q_z$ (0.1 to 0.22) (Figure 4-9). The molecular ion of t-butylbenzene, however, was completely dissociated at a $q_z$ of 0.25, while a very small amount of t-butylbenzene may be trapped over this higher range of $q_z$ but all of it is dissociated. Figure 4-9 shows that the intensities of the fragment ions increase even when no molecular ion is seen. Therefore the molecular ion must spend a small period of
Figure 4-9 Relative intensities of the molecular ion of t-butylbenzene (m/z 134) and its three fragment ions at m/z 119, 92 and 91 as a function of increasing \( q_z \) of injection for the molecular ion of t-butylbenzene.

time within the trap to experience the RF quadrupolar field and fragment.

Furthermore, the fragment ions may be trapped with greater efficiency than the molecular ion. For instance, if the molecular ion of t-butylbenzene is injected a \( q_z \) value of 0.20, its fragment ion of m/z 119 will sit at a \( q_z \) of 0.23, placed in a deeper potential well and trapped with greater efficiency.

The extent of fragmentation of ions upon injection is related to the nature of the ion. The molecular ion of t-butylbenzene behaves very similarly to n-butylbenzene. They are both fragile and readily dissociate. Other more stable ions may require a larger \( q_z \) of injection to notice a significant amount of fragmentation. To show this, several non-fragile ions of similar m/z were injected under the same conditions as the two fragile
ions. Figure 4-10 shows the percent fragmentation for the fragile (closed symbols) and non-fragile molecular ions (open symbols) as a function of $q_z$ of injection. The molecular ions of benzene and naphthalene require a $q_z$ of injection of 0.25 or greater to notice any fragmentation. Under these same conditions, the entire mass spectrum of injected t-butylbenzene $M^+$ ions is composed of fragment ions. This is an important observation. Ion-molecule reactions aside, it shows the mass spectrum of a fragile ion may deviate dramatically from a typical quadrupole spectrum while that of a non-fragile ion may not.

![Graph showing percent fragmentation of molecular ions](image)

Figure 4-10 Percent fragmentation of the molecular ions of several fragile ions (solid symbols) and several non-fragile ions (open symbols) during ion injection.

Ion injection efficiency is directly linked to the RF amplitude on the ring electrode. Modern commercial instruments divide the ion injection period into several steps, each with a specific RF level calibrated according to the desired mass range. The data
presented above show it is advantageous to apply the lowest RF amplitude possible
during this period to obtain a good signal. If the amplitude is too high it may lead to ion
fragmentation during injection and the loss of variable spectral information.

**Buffer Gas Pressure**

Ions generated from an external source are introduced into the ion trap with a
significant amount of kinetic energy. To remove some of this energy and allow the ions
to be trapped, a helium buffer gas in introduced into the trapping volume. The purpose of
a buffer gas within the ion trap is to decelerate and focus injecting ions into the center of
the ions trap. The studies presented above show that if the RF amplitude is high enough,
an ion may have enough kinetic energy during injection to dissociate upon an energetic
collision with a helium atom. To determine the role that helium pressure has on ion
fragmentation, the molecular ion of n-butylbenzene was again injected into the ion trap as
pressure was altered from its normal value of approximately 1.3x10^5 torr (Figure 4-11).

With no helium added to the trap, a small signal is still observed. This can be
attributed to collisions with background gasses (the background pressure is 2.9x10^-6 torr).
As soon as the helium is added to a pressure of 3.7x10^-6 torr, the signal intensity
increased dramatically with the largest increase, between 4.4x10^-6 and 8.2x10^-6 torr. The
increased pressure allows an injected ion to undergo multiple collisions needed to trap the
ion efficiently. The signal intensity improved up to a limit where the ion intensity levels
off at a chamber pressure of 2x10^-5 torr. The increase in ion intensity, however, is
accompanied by degradation in mass resolution and a shift to lower mass due to increased
fragmentation of ions upon ejection.
As the pressure increases it might be assumed that ions are undergoing a greater number of dissociative collisions upon injection. It was found, however, that the 10-fold increase in helium pressure actually yielded a greater abundance of the molecular ion of n-butylbenzene relative to its fragment ions (Figure 4-11), with a ratio of 91/92 nearly constant at 0.3 at pressures above $7.0 \times 10^{-6}$ torr (Figure 4-12). The 91/92 ratio was highest at lower pressures, with a ratio of 0.56 at $3.9 \times 10^{-6}$ torr. At low helium pressures the distance between collisions will be greater, and thus ions can be accelerated to

![Graph](image-url)

Figure 4-11 Ion intensity of the molecular ion of n-butylbenzene (m/z 134) and its fragment ions (m/z 91 and 92). The LMCO during injection was 30 amu (m/z 134 situated at a $q_e$ of 0.20). Ions were ejected with a resonant ejection amplitude of 3.5 V\textsubscript{pp}. The normal chamber pressure with helium buffer gas at its normal value was approximately $1.3 \times 10^3$ torr (uncorrected).
greater velocities. This will allow the ion more time to accumulate kinetic energy before colliding with a helium atom. At high helium pressures, in contrast, the greater collision frequency prevents the injected ion from accelerating appreciably between collisions, and accumulating enough energy to undergo a dissociative collision. Note that this trend may not apply with a higher molecular weight buffer gas, as the higher mass would result in a greater center-of-mass collision energy.

![Graph showing the ratio of m/z 91/92 of n-butylbenzene with increasing chamber pressure. The LMCO during injection was 35 (a q_z of 0.24 for m/z 134).](image)

**Figure 4-12** The ratio of m/z 91/92 of n-butylbenzene with increasing chamber pressure. The LMCO during injection was 35 (a q_z of 0.24 for m/z 134).

**Ion Energy (Trap Offset)**

When ions are injected from an external source they must be supplied with enough kinetic energy to overcome the potential barrier created by the quadrupolar field within the ion trap. Ions are originally created within the source at ground potential.
They are accelerated out of the source by the potentials placed on the ion lenses and the negative DC potential placed on the ion trap; this trap “offset” from the ion source provides the ion with the energy it needs to enter the ion trap. The hybrid instrument was used to determine if higher kinetic energy of an injecting ion could lead to increased fragmentation.

The molecular ion of benzene (m/z 78), the PFTBA fragment ion C\textsubscript{3}F\textsubscript{5}\textsuperscript{+} (m/z 131), and the molecular ion of n-butylbenzene (m/z 134) were chosen to represent both fragile and non-fragile ions. Each of the ions had a calibrated trap offset of -6.0 V, which relates to an injection kinetic energy of 4.0 eV, based on equation 2-1. The ion intensity for all of the ions quickly drops after the optimal offset. The drop in ion intensity is

![Graph showing the relative intensities of molecular ions and PFTBA calibrant ion with trap offsets.](image)

Figure 4-13 Relative intensities of the molecular ion of n-butylbenzene (m/z 134), benzene (m/z 78) and the PFTBA calibrant ion C\textsubscript{3}F\textsubscript{5}\textsuperscript{+} at m/z 131 with an increasing trap offset. The LMCO during injection was 35 (a q\textsubscript{z} of 0.24 for m/z 134).
related to poor trapping efficiency. Examining the individual mass spectra of n-butylbenzene at higher trap offsets, it can be seen that excessive ion injection energy does not increase the amount of fragmentation. At the optimal offset of −6.0 V the 91/92 ratio of n-butylbenzene is 0.32 and remains constant to a trap offset of −20 V.

The last instrumental parameter examined in this study was the ion lens potential. The potentials on these three lenses had a large influence on the injection efficiency but had little or no effect on the amount of fragmentation observed in the mass spectrum of n-butylbenzene. This would make sense as the ions kinetic energy as it enters the trap is primarily determined by the trap offset. It is the energy of the ions within the trap that matters, not the in energy en route to the trap.

**Conclusion**

Injection energy, RF amplitude during injection, and the helium buffer gas pressure are the three most significant parameters affecting ion injection efficiency. The RF amplitude during injection had the greatest effect on the fragmentation of ions upon injection. When the $q_z$ of injection is increased, the injecting ions are accelerated by the higher quadrupolar field and can obtain high kinetic energies. Energetic collisions with the helium buffer gas can then lead to ion dissociation. Fragmentation upon injection will most greatly affect fragile ions. At high injection $q_z$ values, very few fragile ions may survive. The increase in the ions internal energy as reflected in the 91/92 ratio for n-butylbenzene observed with increasing RF field during injection is far greater than the increases observed with changing helium buffer gas pressure or trap offset.
CHAPTER 5
SPACE CHARGE

The quadrupole ion trap is most noted for its ability to accommodate multiple stages of mass spectrometry while providing superior sensitivity and mass range. The utility of the ion trap continues to grow as recent technical advancements have led to the incorporation of various external ion sources. However, in spite of the many improvements, the ion trap mass analyzer is still limited by relatively poor mass accuracy. The presence of mass shifts has been observed since the early development of the ion trap (Syka, 1995). The previous chapter presented a systematic study linking compound-dependent mass shifts with resonant ejection and ion fragility. These factors, however, are not the only sources of mass shifts. Overloading the ion trap can produce significant coulombic interactions, commonly known as space charge, which lead to peak broadening and a shift to higher m/z (Cleven et al., 1994; Cox et al., 1995). Currently, commercial instruments avoid space charge effects by limiting the number of ions held within the ion trap. This limit restricts both the instrument’s dynamic range and level of precision, as the relative standard deviation is directly related to the number of ions within the trap.

\[
\%RSD \approx \frac{1}{\sqrt{\text{Number of Ions}}} \quad (5-1)
\]

Therefore, it would be advantageous to increase this space charge limit and thus allow a greater number of ions to be trapped without detrimental effects. The experiments presented in this chapter will focus on the characterization of space charge in the ion trap.
in order to reduce its effects. Emphasis will be placed on instrumental parameters such as drive frequency, scan rate, buffer gas make-up and pressure, as well as on the ion trap geometry.

McLuckey and co-workers theorized the ultimate storage capacity of the ion trap to be approximately $10^6$ ions (McLuckey et al. 1994). At this storage space charge limit, the ion density may become so large that the ion trap is essentially full. Additional ions injected into the quadrupolar field may not be successfully trapped or may displace previously trapped ions. Although this limit would provide a more than adequate number of ions for detection, it is rarely attained. Before the storage limit is reached, the ion trap arrives at the spectral space charge limit. With only a fraction of the $10^6$ ions in the trap, spectral quality is sacrificed. A mass shift can be observed even with a limited number of ions within the ion trap. Under severe space charge conditions, ion repulsive forces may become overwhelming as mass peaks become broad, and the peak height may be reduced to the point where the peaks disappear into the baseline.

Space charge effects are not limited to the quadrupole ion trap and are present in other types of mass spectrometers in particular in FT-ICR instruments, where an analogous but less pronounced degradation in performance occurs when large numbers of ions are present (Ledford et al., 1984; Uechi and Dunbar, 1992; Easterling, M. L. et al., 1999).

**Automatic Gain Control**

As with any instrument, the ion trap has a limited dynamic range. The ion trap is most accurate when it is filled with an optimal number of ions. If too few ions are present in the ion trap, sensitivity is low and peaks may be difficult to discern from noise.
If too many ions are present in the trap, space charge effects can significantly distort peak shape and degrade resolution. Either extreme can reduce reproducibility from one experiment to the next unless the ion population is held at a constant level. To this end, an ion injection method was developed by Thermo Finnigan called automatic gain control (AGC) to control the number of ions that accumulate in the ion trap. AGC is designed to keep the total number of ions in the ion trap at a steady level, retaining mass accuracy and resolution from scan to scan by optimizing the injection time for each scan (Yost et al., 1987; Stafford et al., 1987). The AGC scan function is comprised of a rapid automated scan (15 μs/amu) covering the entire mass range of the analyzer with a fixed injection time (0.2 ms) called a pre-scan. This pre-scan, which precedes each analytical scan, quantitatively assesses the ion production rate from the source and calculates the proper injection time needed to fill the ion trap to capacity, ensuring that the number of ions in the trap never reaches an adverse level of space charge. The proper injection time is determined to be inversely proportional to the total ion counts (TIC) from the pre-scan and can be calculated by the equation below.

\[
\text{Injection Time} = \left( \frac{\text{AGC Target}}{\text{Prescan TIC}} \right) \times \text{Prescan Injection Time} \quad (5-2)
\]

With AGC, sensitivity is maximized at low sample concentrations by using a long injection time (a maximum of 250 ms). Linear dynamic range is extended by lowering the injection time for high sample concentrations. For the PolarisQ, the minimum injection time is 5 μs, which is restricted by a fast switching gating circuit. If a highly concentrated sample requires an even lower injection time, space charge conditions may
occur. Figure 5-1 compares the response of the AGC scan function on the PolarisQ (solid line) with the ITMS ion trap, originally developed with a fixed injection time, (dashed line) as a function of sample concentration. With an AGC scan function, the ionization time will be set anywhere between the two extremes, maintaining the ion concentration below the spectral space charge limit; in this hypothetical case it is maintained below 100,000 ions. In contrast, with a fixed ionization time no concessions are made for highly concentrated, samples and the space charge limit can be easily reached.

Figure 5-1 With the AGC scan function (solid line), dilute samples will require a large injection time while concentrated samples will necessitate a minimum injection time. Even with AGC, samples which require less than a 5μs injection time may encounter space charge effects. This can be compared to the ITMS ion trap which was originally developed with a fixed injection time (dashed line). In this arrangement concentrated samples are easily space charged. This figure was reproduced from an ASMS abstract by Stafford el al., 1987. The x and y axes are in arbitrary units.
The actual number of ions injected into the ion trap during the analytical scan is controlled by the AGC target variable, which is simply the desired TIC for the analytical scan. Once this target is established, AGC will regulate the ion time to maintain this TIC. The default value for an EI analysis on the GCQ is 50, which is a scaled factor representing $50 \times 10^7$ counts on the electrometer. The gain of the electrometer on the PolarisQ is 2.25 times lower that of the GCQ and a target of 50 actually represents $22 \times 10^7$ counts. The target may be scaled differently, but it pertains to the same number of ions within the ion trap as the GCQ. The PolarisQ currently permits variation of the AGC target over a range of 0.001 to 2000.

The AGC scan function is a method used exclusively by Thermo Finnigan instrumentation, although other ion trap manufacturers implement similar methods. Varian ion trap instruments, for instance, use a pre-scan before each analytical scan, where the ionization parameters used in the pre-scan are not fixed, but are based on the previous analytical scan. This was designed to avoid space charge conditions during the pre-scan (Wells, 1995).

**Calculation of the Number of Ions in the Ion Trap**

The AGC target is directly proportional to the number of ions in the ion trap during an analytical scan. Equation 5-2 shows the calculated number of ions in the ion trap with an AGC target of 50 ($50 \times 10^7$ counts) and the default settings for the PolarisQ: a detector gain of $3.5 \times 10^5$, a sampling rate of 15 samples/amu, and a scan rate of 180 $\mu$s/amu. Remember that the target of 50 is actually scaled by a factor of 2.25 for the PolarisQ compared to the GCQ to allow for the new electrometer with a greater dynamic range.
\[
5.0 \times 10^8 \text{ counts} \times \frac{1}{2.25 \text{ ScaleFactor}} \times \frac{14.84 \times 10^{-6} \text{ eA}}{2.68 \times 10^8 \text{ counts}} \times \frac{1 \text{ ion}}{3.5 \times 10^7 \text{ e}} \times \frac{1 \text{ e}}{1.6021 \times 10^{-19} \text{ A} \cdot \text{s}}
\]

\[
\left( \frac{180 \times 10^{-6} \text{ s/amu}}{15 \text{ samples/amu}} \right) = 2580 \frac{\text{ ions}}{\text{ sample}} \text{ detected} \times 2 \approx 5000 \text{ ion in the trap}
\]  

(5-2)

The (eA/counts) term represents the response of the analog-to-digital converter. The ions detected can be multiplied by a factor of two based on the assumption that half of the ions are ejected through the exit endcap of the ion trap and half are ejected through the entrance endcap. This equation shows that approximately 5000 ions are analyzed in a typical analytical scan.

For AGC to properly control the number of ions in the ion trap, the detector must be properly calibrated. A detector gain of \(3 \times 10^5\) is necessary for the pre-scan to accurately adjust the injection time. If the detector gain is too low, the injection time will be too long, and there will be too many ions in the ion trap.

**Ion Intensity Determination**

AGC regulates the injection time to keep a constant number of ions within the ion trap. The TIC detected at the electrometer will therefore be constant even as compounds may elute (Figure 5-2A). Unlike other mass spectrometers, the true ion intensity cannot be determined purely by the electrometer signal. The ion intensity can be obtained only by scaling the constant detected TIC with the injection time (Figure 5-2B) by the following equation

\[
\text{True Signal Intensity} = \frac{I'}{\text{IonTime}} \times (\text{Norm Ion Time})
\]  

(5-3)
Figure 5-2 When AGC is used, the TIC at the electrometer is constant even though three compounds have eluted (A). The injection time, however, drops as each peak elutes (B). By scaling the detected intensity with the injection time, the true signal is obtained (C). Figure derived from Thermo Finnigan, GC/MS division.
where I' is the signal intensity at the electrometer, and norm ion time is a scaling factor used within the PolarisQ software to limit the amount of stored data. The true ion intensity is essentially the inverse of the ion time (Figure 5-2C). Just as highly concentrated samples may saturate a detector, the ion trap will experience space charge effects if the minimum ion time is reached.

**Instrumentation**

All experiments in this chapter were performed using a prototype Thermo Finnigan PolarisQ ion trap mass spectrometer, the newest generation of GC/MS ion traps. The PolarisQ ion trap instrument is housed in an extruded aluminum manifold pumped by a 250 L/s Edwards turbopump (Figure 2-10). The drive frequency for this instrument is 1.024 MHz. The helium pressure within the trap is approximately 1 mtorr with a chamber pressure of 1.2x10^-5 torr.

A few modifications were made to compensate for highly concentrated samples. The minimum ion time on the PolarisQ was lowered from 30 μs (on the GCQ) to 5 μs. In addition, the new generation ion source can be heated in excess of 300°C to keep the ion source clean even with the dirtiest of sample matrices. The ion source and mass analyzer are held together as one unit, and a significant amount of heat may be transferred to the ion trap. An adjustment in the source temperature may cause the trap to expand or contract slightly and alter its capacitance, resulting in a different resonant drive frequency. In the experiments described in this chapter, the source temperature was maintained at 250°C.
Analyte Compounds

Perfluorotributylamine (PFTBA) was primarily used as the analyte as it produces numerous fragment ions of varying m/z. Traditionally, a calibrant compound is introduced into the mass spectrometer through a needle valve. This method suffers from poor regulation due to variations in headspace pressure, lack of reproducibility when returning to a previous valve setting, unknown mass delivery and poor equilibration time. A novel calibration gas module containing several capillary restrictors that are continually pumped was designed for the PolarisQ. It overcomes these shortcomings and establishes a constant flow of 0.004 ml/min for the calibrant into the ion source through a heated transfer line.

Several other compounds were used to analyze space charge effects: hexachlorobenzene and decachlorodiphenyl (Figure 5-3), which provided complex isotopic patterns, and perfluorokerosene (PFK) which supplied analyte ions up to m/z 1017. They were introduced into the ion source through a Thermo Finnigan TRACE GC.

Figure 5-3 Molecular structures of hexachlorobenzene (MW=282) and decachlorodiphenyl (MW = 494).
Introduction - Space Charge Effects

A typical EI spectrum of the PFTBA calibrant compound with a default AGC target of 50 is shown in Figure 5-4A. With a calibrated resonant ejection amplitude, the mass resolution at this target is typically constant across the entire mass range. However, when the ion injection time is increased tenfold to an exaggerated target of 500, the low m/z ions (below m/z 219) are observed as broad peaks extending over several amu. (Figure 5-4B) As a result, their peak heights decrease, giving the illusion that peaks associated with higher m/z ions (m/z 264 and above) have become more intense. In addition to peak broadening, the peak positions of the low m/z ions are shifted towards higher m/z. Both broadening and mass shifts are manifestations of space charge perturbations brought by ion-ion interactions.

Tomographical studies have shown there is a direct correlation between peak width and the radial distribution of the ion cloud within the ion trap. Cooks and co-workers used spatially resolved laser photo-dissociation to show that, as the number of trapped ions increases, the size of the ion cloud expands and the enlarged spatial profile results in broad peak widths (Cleven et al., 1996).

A further increase to an AGC target of 5000 led to further changes in the PFTBA mass spectrum. Low m/z ions (m/z 69) still appear with very poor resolution; however, ions of m/z greater than m/z 219 either are not detected or are observed with very weak signal intensity (Figure 5-4C). At this point it appears the AGC target has moved past the spectral space charge limit and now exceeds the storage space charge limit. The ion trap is essentially full, and injected low m/z ions begin to be favored over higher m/z ions.
Figure 5-4 Full scan spectrum of PFTBA with an AGC target of 50 and an injection time of 0.36 ms (A), a target of 500 and an injection time of 3.5 ms (B), and a target of 5000 and an injection time of 35.3 ms (C). The resonant ejection amplitude was calibrated with an AGC target of 50.
Order of Ion Ejection

At the AGC target of 5000 (Figure 5-4C), the m/z 69 peak of PFTBA is quite broad, whereas the m/z 131 peak appears to obtain unit resolution. It is theorized that once ions of low m/z have been ejected, their contribution to space charge is diminished, and the mass selective ejection of ions of higher m/z becomes less affected. Therefore, under space charge conditions, the first ions ejected out of the trap will experience the greatest effect, and the remaining higher m/z ions (m/z 131) will be ejected with little appearance of space charge.

This effect is dramatic with a condensed isotopic pattern. The isotopic pattern for hexachlorobenzene (MW 282), for example, shows the effect of severe space charge when analyzed in the electron capture negative chemical ionization (NCI) mode at the AGC target of 20 (Figure 5-5). Although all of the most intense isotope peaks in this pattern can be discerned, the initial two $^{13}$C isotope peaks (m/z 283 and 285) are poorly resolved. It is not until the lower m/z ions exit the ion trap that the ions at the back end of

Figure 5-5 NCI spectra of hexachlorobenzene with an AGC target of 20.
the isotopic distribution become resolved. In addition to exhibiting poor resolution, the initial isotope peaks of this pattern also shift in m/z, with the isotope peaks appearing at irregular spacing. The exact mass for $^{12}\text{C}_6^{35}\text{Cl}_6$ is 281.81 amu; however, under space charge conditions, this ion appears at m/z 282.3. This positive mass shift for the lower m/z isotope peaks condenses the isotopic pattern. The spacing between the isotopic species is typically smaller initially than the spacing observed between the higher m/z isotopes. (Each of the most intense isotope peaks in Figure 5-5 should be spaced 2 amu apart.)

In Figure 5-5, hexachlorobenzene was analyzed using electron capture negative CI, a soft ionization technique that produces primarily molecular anions. Therefore the ion population is typically concentrated in a narrow range of m/z and the ions in close m/z proximity to each other can further contribute to space charge effects. To combat this problem, the default AGC target is usually lowered for negative CI from an EI default target of 50 to as low as 5. Unfortunately, at these low targets, the number of ions in the trap is lowered and ion intensity suffers.

Ejection order appears to be an important aspect of space charge, as ions of low m/z consistently leave under highly space charged conditions, and as the number of ions within the trap decreases, high masses are ejected with unit resolution. To investigate wether this trend is due only to the ejection order and is not linked to the m/z of the ion, the scan direction was reversed to allow ions of high m/z to be ejected first. The $q_e$ of ejection on the PolarisQ was lowered from its normal value of 0.9016 to 0.40 (Figure 5-6). The highest m/z of interest was placed at a $q_e$ just slightly higher than the new resonant ejection frequency and the analytical scan was performed in the reverse order,
from high m/z to low m/z (i.e., the RF amplitude on the ring electrode was ramped from higher to lower potential during the scan). The scan rate was lowered to 0.36 ms/amu to compensate for the loss of resolution resulting from a reverse scan at low q_z values. The resolution is typically lower for reverse scans. Due to the complexity of the reverse scan function, an AGC prescan, which normally mirrors the analytical scan, was not used. Instead, the number of ions within the ion trap was controlled by manually setting the ion injection time.

Figure 5-6 Mathieu stability diagram depicting a reverse scan. The resonant ejection frequency, which is typically held at a q_z of 0.9016, is lowered to a q_z of 0.40. Before the analytical scan the ions of interest are placed at a q_z greater than the new resonant ejection frequency. They are subsequently scanned in the reverse direction towards lower q_z values with ions of higher m/z ejected first. (The large sphere represents an ion of high m/z and the smaller spheres represents ions of lower m/z.)
Figure 5-7A shows the results of a reverse scan of PFTBA with a scan range of m/z 140 to 50 and an ion time of 0.5 ms. The mass spectrum appears as the mirror image of a normal forward scan spectrum. (The mass scale on the x-axis produced by the instrument is not corrected.) The $^{13}$C peak of m/z 131 ($C_3F_5^+$) now becomes the first ion to be ejected from the ion trap instead of m/z 69 ($CF_3^+$). Now, when the ion time is increased to 25 ms (Figure 5-7B), the higher m/z ion, in this case m/z 131, shows an increase in peak width and is the first to exhibit space charge instead of the lower m/z. This further substantiates that space charge effects are directly related to the order of ejection, not the m/z of an ion.

When the ion time is further increased to 50 ms, the intensity of m/z 131 drops dramatically (Figure 5-4C). The ion trap begins to experience the storage space charge limit as low m/z ions are again trapped preferentially to high m/z ions. In contrast to spectral space charge, however, the preferential ion storage within the trap does not appear to be linked to the scan direction of the mass spectrometer.

**Storage Space Charge**

The storage space charge of the ion trap appears to be linked to the m/z of the ions stored within the device. The initial loss of high m/z ions as the ion trap approaches the storage space charge limit indicates that the storage potential well for these ions is highly perturbed. Low m/z ions at high q_z values reside in a deep potential well and have a small spatial distribution near the center of the ion trap (Hemberger at al., 1993). In contrast, high m/z ions, held at low q_z, are placed in a much shallower well and have a larger ion cloud within the ion trap. Higher m/z ions can therefore be viewed as sitting outside lower m/z ions. As the density of the low m/z ions increases with large AGC
Figure 5 - 7 The mass spectrum of PFTBA implementing a reverse scan function with a scan range of m/z 140 to 50. The mass scale on x-axis is incorrect; the actual mass assignment has been labeled with each peak. Ion time of 0.5 ms (A) 25 ms (B) and 50 ms (C). An ion time for a default AGC target of 50 is typically on the order of 0.35 ms.
targets, the low m/z ions may push high m/z ions outward towards the ion trap electrodes and close to non-linear fields which greatly perturb ion motion. The trajectories of the high m/z ions, which are held by a shallow potential well, can quickly become unstable and the ion may be lost.

Figure 5-8 demonstrates this effect for several fragment ions of the calibrant compound PFTBA. Initially, ion intensities for each of the fragment ions increase linearly as the AGC target is raised from its nominal value of 50. As the AGC target approaches 800, however, the area of m/z 502 begins to level off and subsequently decrease as the areas of low m/z ions continue to increase. M/z 502 is eventually
followed by m/z 414 and then m/z 264; thus, the ion ratios for PFTBA constantly change as the injection of low m/z ions continues to displace higher m/z ions. Eventually there is a point where this ion exchange is restrained and the ion trap is almost entirely filled with m/z 69. At this point the TIC from the PFTBA fragment ions levels off (Figure 5-9) at a substantial AGC target of 15000. This AGC target is associated with approximately $1.5 \times 10^6$ ions (Equation 5-2). The presence of m/z 69 will eventually decrease as the ion trap begins to preferentially fill with background ions of lower m/z, such as N$_2$ (m/z 28) and CO$_2$ (m/z 44) which may sit just above the LMCO.

![Figure 5-9](image)

Figure 5-9 The TIC from PFTBA as a function of AGC target with a mass scan from 50 to 650 amu. Using AGC the TIC had to be acquired by setting norm ion time to 1 and multiplying the raw ion intensity obtained by the electrometer by the ion time. (Equation 5-3)

The fragmentation pattern of PFTBA includes eight intense ions spread across a mass range of approximately 550 amu. Typical sample matrices, however, often yield far
more complex mass spectra. Ionization of a matrix will often produce large numbers of ions with m/z’s below the ion of interest. As described earlier, low m/z ions are troublesome because they decrease the trapping efficiency of the higher m/z ions. This can be a problem for trace analysis in particularly dirty matrices. Matrix ions may displace the ion of interest and drop its concentration within the ion trap to an undetectable level. With a particularly complex sample matrix, this may occur even at modest AGC targets much lower than the exaggerated targets studied above.

**Frequency Shift**

Elevated peak widths and the loss of high m/z ions, two detrimental effects of space charge, are always accompanied by a shift in the apparent m/z of an ion. Unlike mass shifts produced by the dissociation of ions upon ejection, space charge generates a positive mass shift, a shift to higher m/z. A late ejection, under space charge conditions, would then indicate that a larger than expected RF amplitude was required to properly eject an ion. This could occur if the secular frequency of an ion was lowered by the excessive number of ions present within the trap. To this end, the secular frequency of an ion was studied with an increasing AGC target.

A scan function similar to that of a typical MS/MS scan was created to probe the frequency of an ion within the ion trap. In a typical MS/MS scan, an ion is placed at a low qz value, typically 0.3, and a waveform consisting of a single frequency, commonly referred to as the tickle frequency, is applied across the endcap electrodes to excite the ion at that qz. The ion absorbs kinetic energy from the waveform and either dissociates upon collision with a neutral gas, or if the energy is high enough it is ejected. This same principle was used to accurately determine the actual secular frequency of an ion.
Initially, with a default AGC target of 50, CF$_3^+$ (m/z 69) was placed at a $q_z$ of 0.83 which correlates with a secular frequency of approximately 377 kHz. Unlike a typical SIM or MS/MS scan function, the remaining fragment ions of PFTBA were allowed to remain within the ion trap at lower $q_z$ values. A tickle voltage was then applied at a frequency starting at 365 kHz with an amplitude of 4 V$_{pp}$ for a duration of 15 ms. The voltage at this high $q_z$ should be sufficient to eject all ions of a particular m/z if they are in resonance. The ions were then scanned out normally, and the intensity of the remaining ion current was recorded. This process was repeated as the supplementary frequency was increased to 385 kHz in steps of approximately 240 Hz. As the supplementary frequency approached the secular frequency of the ion, its intensity temporarily dropped but then returned as the supplementary frequency moved on (Figure 5-10). The actual frequency of the ion was taken as the lowest point of the curve in Figure 5-10, revealing that the actual frequency of the CF$_3^+$ ion was indeed close to 377 kHz. This entire process was repeated with AGC targets of 250 and 500. The results in Figure 5-10 show that the secular frequency of CF$_3^+$ shifted approximately 2 kHz with a target of 500. At this high target 4 V$_{pp}$ does not appear to be enough to properly eject the same proportion of ions as lower targets. The secular frequencies of m/z 264 and 414, sitting at lower $q_z$ values, were also probed with similar results.

In addition to shifting an ion's apparent mass, the shift in an ion's frequency at high targets may also decrease MS/MS efficiency. In MS/MS an ion is isolated with a notched waveform centered on the frequency of the ion of interest. If a small shift in frequency moves the ion away from the center of the isolation notch, it may absorb
energy from the nearby waveform and be ejected during isolation. This would subsequently decrease the number of ions available for fragmentation or analysis.

![Graph](image)

**Figure 5-10** The amount of CF$_3^+$ (m/z 69) remaining in the ion trap after a supplementary voltage of 4 V$_{pp}$ was applied at the specific frequency displayed on the x-axis. This experiment was performed with three separate AGC targets.

**High-Mass Cut-Off**

The LMCO of the instrument defines the lowest m/z ion that can be held within the ion trap for a specific RF amplitude. On the stability diagram (Figure 1-4) the ion corresponding to the LMCO is situated at a q$_{z}$ of 0.908, just within the stability region. The high-mass cut-off of the ion trap, however, is not so well defined. High m/z ions are condensed at q$_{z}$ values near zero on the opposite side of the stability diagram and do not have a distinct limit. In fact under normal conditions, the mass range of the instrument is
limited only by the maximum RF amplitude of the device available to eject the ion for detection (Equation 1-8). The loss of high m/z ions at high AGC targets, however, may indicate a modification in the instrument’s high-mass cut-off.

A scan function was developed to determine if the AGC target affects the high-mass cut-off of the ion trap. Following injection, an ion of interest was positioned at low $q_z$, initially 0.3, and held for a period of 15 ms. The ion was then scanned out in the normal manner and the intensity was recorded. The high-mass cut-off was probed by repeating this scan with successively lower $q_z$ values moving closer to the origin of the stability diagram. The results of the scan for C$_3$F$_5^+$ (m/z 131) are presented in Figure 5-11.

![Figure 5-11 Area of C$_3$F$_5^+$ (m/z 131) after the ion was held at a specific $q_z$ (shown on the x-axis) for 15 ms before ejection and detection.](image-url)
At the default AGC target of 50, the intensity of the C$_3$F$_5^+$ ion began to decrease at a $q_z$ of 0.08 until it reached zero at a $q_z$ of 0.04. The potential well at this low $q_z$ is very shallow. Ions are not stable for an extended period of time and can “leak” out of the ion trap. This experiment was then repeated at larger AGC targets. The minimum $q_z$ value increased with larger AGC targets. At an AGC target of 1000, C$_3$F$_5^+$ is no longer stable below a $q_z$ of 0.1. High m/z ions can no longer be stored at low $q_z$ values. A high AGC target essentially creates an artificial stability edge or a high-mass cut-off. This high-mass cut-off may be explained by a differential DC potential arising from the space charge, as described below.

**Differential DC**

Qualitatively, the frequency shift of an ion and the emergence of a high-mass cut-off under space charge conditions can be represented by a net DC potential placed on the ion trap (Fischer, 1959; Schuessler et al., 1969; Guan and Marshall, 1994) or as a shift in the stability diagram (Todd et al., 1980). The large ion cloud composed of positive ions may create a positive DC potential within the RF trapping field, lowering the mass-instability scan line below the $a_z = 0$ line in the Mathieu stability diagram (Figure 5-12); recall that a negative value of $a_z$ corresponds to a positive DC potential on the ring electrode). Subsequently, ions may be shifted to lower frequency. In Figure 5-12 the lowest m/z ion, represented by the smallest sphere, is at a $\beta_z$ of 0.7 on the $a_z = 0$ line. With the addition of a positive DC, the scan line is lowered and the ion is shifted closer to a $\beta_z$ of 0.6, resulting in a lower secular frequency. The lowered scan line also causes the low-mass cut-off to occur at a greater $q_z$ value. An ion would therefore require a larger RF amplitude for ejection, ensuring a delay in ejection or a positive mass shift.
The positive DC also creates a high-mass cut-off for ion trap. The highest m/z on the left side of the stability diagram, represented by the large sphere in Figure 5-12 is stored at a low qz where az = 0. However with the addition of a positive DC (negative az), potential the ion no longer resides within the boundaries of the stability diagram and is ejected. The stability edge is essentially pulled inward, creating a high-mass cut-off. As the number of ions within the trap increases, the operating scan line shifts further downward yielding greater space charge effects.

Figure 5-12 Mathieu stability diagram depicting the addition of a positive differential DC. The spheres represent ions with their size proportional to the ions’ m/z value. For negative ions, the opposite occurs as the stability diagram for negative ions is mirrored on the az = 0 axis.
Realistically, as soon as there is more than one ion within the ion trap, the field acting seen by one ion will be perturbed from that predicted theoretically because of the influence of the space charge arising from the other ions. As ions are ejected, this influence is diminished and the superimposed positive DC potential is effectively bled away. Theoretically, this effect could be neutralized by the addition of a supplementary negative DC potential on the ring electrode, which could be decreased during the scan as ions are ejected from the ion trap. Practically, this would prove to be a difficult and complex solution and still would not address the problem of increased peak width due to space charge. A more realistic approach would be to focus on reducing the detrimental effects of space charge by identifying the optimal instrumental parameters.

**Instrumental Parameters**

The remaining portion of this chapter consists of an in-depth study focused on understanding how each instrumental parameter of the ion trap can be controlled to diminish space charge effects.

**Single Ion Monitoring (SIM)**

As discussed above, revealed an ion of a select m/z will exhibit the effects of space charge in the presence of ions of different m/z within the ion trap. A SIM scan was used to determine if ions of a single m/z can space charge themselves. Several major fragment ions of PFTBA were isolated individually within the trap with a 5 amu wide SIM window. A large window was chosen to account for large peak widths as well as any frequency shift of the ion that might result from space charge at high AGC targets.
The degree of space charge was measured with two figures of merit: a positive mass shift and an increased peak width.

Figure 5-13 shows the mass shift for CF$_3^+$ (m/z 69) resulting from an increase in the AGC target from 25 to 1000. Each point on the graph consists of 10 μscans. Recall that a mass shift is determined by the measured centroid m/z minus the ions actual m/z. A mass shift for m/z 69 is immediately initiated as the target is increased, but appears to level off at higher AGC targets at a relatively modest mass shift of +0.27. This is well within the tolerances of the instrument. The extent of the mass shift in SIM appears to increase with m/z, as m/z 131 had a shift of 0.036 and m/z 264 had a shift of 0.055 at the same AGC target of 1000.

![Graph showing mass shift for CF$_3^+$ (m/z 69) in SIM scan with increasing AGC target.](image)

Figure 5-13 Mass shift for CF$_3^+$ (m/z 69) in a SIM scan with an increasing AGC target. The data were taken with two cool times of 3ms and 30ms. Mass shifts were determined by the measured centroid m/z minus the ions actual m/z. Each point consists of 10 μscans.
In contrast to the mass shift seen for m/z 69, the peak width initially decreases with an elevated AGC target, and reaches a minimum at a target of 150 (Figure 5-14). The decrease in peak width is linked with an increase in peak height as the overall area (scaled for ionization time) of the mass peak appears to be conserved. This trend is reversed as the AGC target is further increased and the mass peak begins to broaden. With a target of 1000, m/z 69 has a peak width (FWHM) of 0.34 amu. This is still a minimal change in peak width compared to a full scan spectrum, where the peak width for m/z 69 expands to 0.84 amu (FWHM) at the same target.

It appears that only minimal space charge effects are observed in a SIM scan due to the fact the entire ion population within the trap is composed of ions of a single m/z.

Figure 5-14 Peak width measured at full-width half-max (FWHM) for CF$_3^+$ (m/z 69) in a SIM scan with an increasing AGC target. The data were taken with cool times of 3ms and 30ms. Each point consists of 10 µscans.
During the scan, as ions of that particular m/z leave the trap, the potential for space charge may actually be eliminated as the rest of the peak is scanned out. An ion with the same m/z ejected during a full scan, however, would still be affected by ions of higher m/z present in the trap and would exhibit greater space charge effects.

Another distinct difference between a SIM scan and full scan is the overall scan time. A SIM scan requires several additional steps within the scan function to isolate the ion of interest before it can be ejected. The actual analytical scan, however, is very short due to the small range of ions that are ejected. A full scan with a large mass range could then have a much longer duty cycle (a 600 amu mass range would require 108 ms of scan time). The post ion time or cool time was altered in the above experiment to determine if space charge effects were related to the total scan time or the amount of time the ion spent in the ion trap. A larger interaction time may contribute to greater space charge effects. The normal cool time of 3 ms was increased to 30 ms, but no significant effects were observed (Figure 5-13 and 5-14). Space charge is a dynamic process, and may be initiated or relieved in a much smaller time scale than investigated here.

**Full Scan**

It is clear that space charge has the greatest effect in a full scan acquisition. In a full scan from m/z 50 to 650, CF$_3^+$ (m/z 69) had a mass shift in excess of 1.7 amu at an AGC target of 1000 (Figure 5-15). Higher m/z ions exhibited a smaller shift (Table 5-1). C$_5$F$_{10}$N$^+$ (m/z 264), for instance, has a gradual increase in mass shift with increasing target while CF$_3^+$ (m/z 69) has a large jump at a target of 300. The ions peak widths followed the same trend.
Figure 5-15 Mass shifts for CF$_3^+$ (m/z 69) and C$_5$F$_{10}$N$^+$ (m/z 264) in a full scan with an increasing AGC target. Each point consists of 10 μscans. The error bars correspond to +/-1 standard deviation.

<table>
<thead>
<tr>
<th>m/z</th>
<th>Mass Shift</th>
</tr>
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<tbody>
<tr>
<td>69</td>
<td>1.66</td>
</tr>
<tr>
<td>131</td>
<td>1.11</td>
</tr>
<tr>
<td>264</td>
<td>0.28</td>
</tr>
<tr>
<td>414</td>
<td>0.09</td>
</tr>
<tr>
<td>502</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 5-1 Mass shifts for several fragment ions of PFTBA in a full scan at an AGC target of 1000.
Resonant Ejection Amplitude

The introduction of the mass selective instability scan (Chapter 3) by Stafford and co-workers transformed the ion trap into a useful mass spectrometer (Stafford et al., 1985). However, even with a small number of ions in the trap, ejection of ions at the stability edge ($\beta_z = 1$) resulted in poor peak shape and resolution (Stafford et al., 1985). Resolution was improved by adding a resonant ejection amplitude at the frequency of the ions just before ejection at the stability boundary. In current commercial instruments the resonant ejection amplitude is calibrated with m/z and can provide unit mass resolution across the entire mass range.

The resonant ejection amplitude may also have to be calibrated according to the number of ions held in the trap. Figure 5-16A shows a section of a mass spectrum of PFTBA with an AGC target of 1000. The resonant ejection amplitude for this mass range of 3 V$_{pp}$ has been calibrated with a normal AGC target of 50. The resultant mass spectrum contains oddly shaped mass peaks, with the peaks at m/z 69 and 131 exhibiting a tail towards higher m/z with large widths and the peak at m/z 131 exhibiting peak splitting. Raising the resonant ejection amplitude by 20 V$_{pp}$ (Figure 5-16B) improves mass resolution and enables the ion trap to hold a larger number of ions without a great sacrifice in peak shape. An increased resonant ejection amplitude may therefore be more tolerant of space charge effects.

The loss of resolution at high AGC targets may be due to ion shielding, where ions on the outer surface of a large ion cloud may shield ions situated at the center of the trap from feeling the effects of the supplementary RF field. This may limit the number of ions that can be ejected during resonant ejection. The improvement in resolution at high
Figure 5-16 A section of a full scan mass spectrum of PFTBA with an AGC target of 1000 and a resonant ejection amplitude of approximately (A) $3 \, \text{V}_{\text{pp}}$ and (B) $23 \, \text{V}_{\text{pp}}$ for this mass range at a $q_e$ of 0.9016. Scan rate was 0.180 ms/amu, sampling rate 18 points/amu, and bandwidth was 5555 Hz.
resonant ejection amplitude may occur due to the stronger uniform electric field created in the axial dimension within the ion trap which reduces ion shielding and therefore space charge effects.

To examine this effect, the resonant ejection frequency was lowered from its normal operating $q_z$ value of 0.901643 to 0.85 (Figure 5-17). The broad mass peak which was associated with space charge in Figure 5-16A is now split into two peaks consisting of ions which are resonantly ejected at $q_z = 0.85$ and ions ejected at the stability edge at $q_z = 0.908$. Based on the explanation above, at large AGC targets, ions will be shielded from the resonant ejection amplitude and only a portion of the ions will be ejected at the resonant ejection frequency. The remaining ions will be held within the ion trap as it is scanned past the $q_z$ of 0.85 and will eventually be ejected when they reach the stability edge. These ions are often referred to as fence jumpers as the ion "jumps" past the resonant ejection frequency. Fence jumpers appear as a broad peak with a tail towards higher m/z and are situated at odd m/z values which can be derived from the equation below.

$$\frac{m/ z_{\text{fence}}}{} = \frac{m/ z_{\text{real}} (0.908)}{q_{\text{eject}}}$$  \hspace{1cm} (5-3)

With a resonant ejection $q_z$ of 0.85, for instance, ions of m/z 69 ejected at the stability edge would emerge at an apparent m/z of 73.7 (Figure 5-17). When the resonant ejection frequency is situated close to the stability edge, the two peaks are indistinguishable as they merge into one broad peak. The portion of ions ejected at the edge increases the overall peak width and forms a peak tail which creates the illusion the ion is shifting to higher mass. Fence jumpers are primarily responsible for the dramatic mass shift for m/z...
Figure 5-17 Mass spectrum of PFTBA acquired with a resonant ejection $q_z$ of 0.85 with an AGC target of 1000. A portion of the CF$_3^+$ (m/z 69) and C$_3$F$_5^+$ (m/z 131) ions are resonantly ejected at $q_z = 0.85$, but the rest are ejected at the stability edge and appear at odd m/z values following the resonantly ejected peak. The resonant ejection amplitude is calibrated for a target of 50.

Although fence jumpers were responsible for a majority of the mass shift and excessive peak width in Figure 5-16A, a small mass shift can still be seen for the resonantly ejected ions at high AGC targets. While maintaining a low $q_z$ of ejection of 0.85, Figure 5-18 shows that as the AGC target is increased, the resonantly ejected ions initially shift in mass (Figure 5-18A), followed by an increase in peak width (Figure 5-18B). CF$_3^+$ (m/z 69), the lowest m/z ion in this study, was the first to encounter the space charge effects. Above an AGC target of 225 the m/z shift and peak width of the resonantly ejected m/z 69 ions increase only slightly. This trend is eventually followed by m/z 131. This upper limit defines the ejection space charge limit of the ion trap. At a
Figure 5-18 Mass shift (A) and peak width at 15% peak height (B) for m/z 69 and 131 of PFTBA resonantly ejected at a q_z of 0.85 as a function of the AGC target. The error bars correspond to +/-1 standard deviation.
particular resonant ejection amplitude, only a certain number of ions can be resonantly ejected. After this limit, ion shielding becomes dominant and the number of ions which are resonantly ejected decreases and any additional ions which remain within the trap will eventually be ejected at the stability edge (Figure 5-19).

![Graph](image)

Figure 5-19 Peak areas of CF$_3^+$ ions ejected by resonant ejection as m/z 69 and at the stability edge as m/z 73.7. The resonant ejection amplitude was calibrated at an AGC target of 50. The error bars correspond to +/-1 standard deviation.

A second series of experiments was performed with an elevated resonant ejection amplitude calibration to compensate for the high AGC target. The linear calibration was optimized to resonantly eject ions at a $q_z$ of 0.85 and reduce space charge effects at low m/z. A faster scan rate of 0.090 ms/amu was chosen to accommodate the high resonant ejection amplitudes. Figure 5-20 shows the results of a full scan spectrum with an AGC target of 400 (8 times the normal target). The peak tops of m/z 69, 131 and 414 from
Figure 5-20 PFTBA calibrant ions from a full scan acquisition with an AGC target of 400 (8x the normal target), scan rate of 0.09 ms/amu and a resonant ejection slope and intercept of 0.02 and 10V, respectively.
PFTBA all appear at the correct m/z values. Unfortunately, the high resonant ejection amplitude, appropriate for space charged peaks at low m/z, may be excessive for an ion at high m/z. C₉F₂₀N⁺ (m/z 502), for example, is a fragile ion and will readily dissociate upon ejection at this amplitude to cause to peak fronting and a shift to lower m/z. The isotopic resolution also suffers at this high target, as m/z 131 and m/z 132 do not exhibit baseline resolution.

A proper resonant ejection calibration would have to compensate for space charge as ions are ejected from the trap. Figure 5-21 shows an ideal calibration for high AGC targets. The optimal amplitudes relate to the minimum peak width for each m/z. At an AGC target of 25, the resonant ejection calibration is linear; however, as the target increases above this value, the calibration becomes parabolic. The resonant ejection

![Figure 5-21](image)

Figure 5-21 The optimal resonant ejection amplitude calibrated for each m/z at different AGC targets selected according to minimum peak width. The qₑ of ejection was 0.85.
amplitude is initially high at low m/z and decreases as ions are ejected from the ion trap. It eventually returns to its normal linear calibration as the number of ion dips below the spectral space charge limit. This calibration is not universal, however, as it is based solely on the fragmentation pattern, ion ratios, and intensities of the EI spectrum of PFTBA. It would have to be altered to accommodate for different compounds as well as different ionization modes (EI versus CI, for instance). This would make a resonant ejection calibration optimized as a function of AGC target very difficult to implement on the ion trap.

q_z of Ejection

A portion of the excessive mass shift and peak width observed under space charge conditions can be attributed to boundary-ejected ions or fence jumpers. With this in mind, it may be advantageous to raise the q_z of ejection above the nominal 0.901643. This would merge the resonantly ejected ions and their boundary-ejected counterparts, forming a smaller peak and reducing a possible mass shift. Figure 5-22 demonstrates the opposite trend, however, as the peak width of C_3F_5 (m/z 131) saw its most dramatic increase with an increasing ACG target at a high q_z value. This can be directly linked to the calibrated resonant ejection amplitude for each q_z of ejection. At the normal q_z of ejection of 0.901643, m/z 131 optimizes with 3.1 V_{pp} of resonant ejection potential (Figure 5-23). With a higher q_z, closer to the stability edge, the pseudo-potential well becomes shallow and ions do not require a great deal of energy to be ejected. The instrument will therefore optimize at lower resonant ejection amplitudes (0.95 V_{pp} at a q_z of ejection of 0.907) making it susceptible to space charge effects. Lowering the q_z, in contrast, allows the instrument to optimize at higher resonant ejection amplitudes limiting
Figure 5-22 Peak width of C₃F₅ (m/z 131) in a full scan with an increasing AGC target with a qₑ of ejection of 0.88, 0.901643 (the default value) and 0.907. The resonant ejection amplitude was calibrated for each qₑ at 6.4, 3.1, 1.8 Vₚₚ, respectively. Each point consists of the average of 5 analytical scans each composed of 10 μscans.

space charge effects (Figure 5-23). High resonant ejection amplitudes, however, impart a greater amount of kinetic energy onto an ejecting ion, which may lead to fragmentation upon ejection, producing a shift to lower m/z. A proper qₑ must be chosen to create a balance between the two extremes.

Scan Rate

Slowing down the scan rate on a quadrupole ion trap can provide high-resolution mass analysis (Kaiser et al., 1989). The reduced scan rate provides additional time for ions to experience more cycles of the resonant ejection amplitude allowing the ions to be ejected in a tighter packet, resulting in smaller peak widths. Low scan rates optimize at minimal resonant ejection amplitudes, however, making a high resolution scan more
Figure 5-23 The optimal resonant ejection amplitude determined by minimum peak width for \( \text{C}_3\text{F}_5 \) (m/z 131) for different \( q_z \) values for ejection. The normal \( q_z \) of ejection is 0.9016. The two major dips are associated with non-linear resonances: an octopolar resonance at \( \beta_z = 1/2, \, q_z = 0.64 \) and a hexapolar resonance at \( \beta_z = 2/3, \, q_z = 0.77 \).

Initially two scan rates were chosen to investigate space charge effects, the normal scan rate of 0.180 ms/amu and a 2 times faster scan rate of 0.090 ms/amu. The optimal resonant ejection amplitudes for m/z 69 at these to scan rates are 2.7 \( V_{pp} \) and 4.5 \( V_{pp} \), respectively. As explained in chapter 3 the bandwidth, which is adjusted for each scan rate, acts as a filter and can artificially alter the peak width. To eliminate this concern the bandwidth was turned off in this experiment. At low targets the peak widths for m/z 69 at the different scan rates are very similar (Figure 5-24). Above an AGC target of 350, however, the peak width at the lower scan rate increases dramatically and eventually levels off at approximately 1 amu (FWHM), while the peak width at the faster
scan rate levels off at 0.6 amu (Figure 5-24). The mass shift for m/z 69 followed the same trend. Faster scan speeds can be viewed as more tolerant of space charge. Several other scan rates were explored, and the extent of space charge effects was directly related to the calibrated resonant ejection amplitude.

![Figure 5-24](image)

Figure 5-24 Peak widths (FWHM) for m/z 69 with scan rates of 0.180 ms/amu and 0.090 ms/amu. The optimal resonant ejection amplitude for the two scan rates was 2.7 V_{pp} and 4.5 V_{pp}, respectively. The error bars correspond to +/-1 standard deviation.

It may be argued the slower scan speed will allow a larger interaction time and contribute to greater space charge effects; however, as shown in previous studies, the amount of time the ions spend in the trap has no correlation with space charge effects.

**Dual Isolation Experiment**

Up until this point, space charge has been studied in either a full scan or a SIM acquisition. The most extreme space charge effects were observed at low m/z in a full
scan mass spectrum. In order to obtain a better understanding of how the m/z of ions affects space charge, a dual isolation scan function was created. This scan function is designed to isolate a pair of m/z ions at variable intensity ratios, with the aim of determining how different ion intensities and mass separation may affect space charge.

Figure 5-25 shows an example of a dual isolation scan function used to determine how an elevated number of ions at m/z 264 would affect an ion at m/z 69 within the trap. Initially ions of all m/z values are allowed to enter the ion trap during a normal ionization step. The low m/z ion of interest, m/z 69, is then placed at a $q_z$ of 0.83, the default $q_z$ of isolation. The first isolation step isolates the high m/z ion, m/z 264, within the trap by applying a waveform with a notch centered at its low $q_z$ value. With ions of m/z 264 still held within the ion trap, a second ion injection period is initiated. Afterward m/z 69 is

1. First Ion Injection – Ions of all masses fill the trap

2. Isolation #1 – Isolate one m/z ion (i.e. m/z 264)
   The low m/z ion is always isolated at $q_z = 0.83$

3. Second Ion Injection

4. Isolation #2 – Isolate a pair of m/z ions (i.e. m/z 69 and 264)

Figure 5-25 Dual isolation scan function.
again placed at a $q_z$ of 0.83 and a dual-notch isolation waveform is applied to isolate both the high and low m/z ions. This allows two ions with different m/z values to be trapped simultaneously at different ratios. The number of ions of low m/z (m/z 69) is typically held constant within the ion trap by fixing the ion injection time in the second ionization step. Conversely, changing the ion injection time before the first isolation step can vary the number of high m/z ions (m/z 264). Due to the complexity of this scan function AGC was not used.

A Fourier transform of the dual-notch isolation waveform can be seen in Figure 5-26. In this illustration, m/z 69 is isolated at a $q_z$ of 0.83 with an isolation width of 1 amu and m/z 131 is isolated at a $q_z$ of 0.44 with an isolation width of 10 amu. The isolation width had to be widened at low $q_z$ to match that of m/z 69 in the frequency domain. The waveform was sampled by a Tektronics digital oscilloscope (Beaverton, OR) and the FT was performed by Mathworks (The Mathworks Inc., Natick, MA). The main RF amplitude was turned off as the waveform was measured from the balun circuit to eliminate interference.

The relationship between the peak position for m/z 69 and the number of m/z 264 ions can be seen in Figure 5-27A. The intensity of CF$_3^+$ (m/z 69) was held at 5x10$^5$ counts with an injection time of 0.14 ms for the second ionization step, and the number of ions of m/z 264 was altered by varying the ionization time for the first injection step from 0.01 ms to 250 ms. Each point of the graph is the average of 3 μscans. The stable CF$_3^+$ ion exhibits a positive mass shift with increasing numbers of C$_5$F$_{10}$N$^+$ ions (m/z264), reaching a maximum of 0.2 amu before leveling off. At this point the intensity ratio of
Figure 5-26 A Fourier transform of the dual-isolation waveform. M/z 69 is isolated at a q<sub>z</sub> of 0.83 with an isolation width of 1 amu (the notch at high frequency) and m/z 131 is isolated at a q<sub>z</sub> of 0.44 with an isolation width 10 amu (the notch at low frequency).

m/z 264 to m/z 69 is approximately 80:1. The variation in the mass shift after this limit is due to a large deviation in the peak centroid calculated by the software. The peak width of the m/z 69 ion (at 15% height) stayed approximately constant at +0.4 amu up until the intensity ratio of m/z 264 to m/z 69 reached approximately 30:1. Beyond this point the peak width increased linearly with the area of m/z 264 (Figure 5-27B).

**Frequency Separation**

This same experiment was performed with numerous ion pairs with different m/z separations, using ions from PFTBA and a second calibrant, perfluorokerosene (PFK). PFK was introduced into the ion source by a 0.5 ml/min flow of helium gas flowing through a ¼” Swagelok tee (Swagelok, Cleveland, OH) to which a stainless steel cap
containing 50 µl of PFK was attached. The calibrant was carried through a 30 meter, 0.25 mm i.d. deactivated column and delivered a constant supply into the source. The two calibrants supplied numerous ion pairs with varying m/z separation and frequency separation. The rate at which each ion shifted or broadened was measured as the slope

\[
\text{Slope} = \frac{\text{Peak Width or Mass Shift}}{\text{Area of High m/z Ion}}
\]

of plots such as those seen in Figure 5-27. It was found that the closer a pair of ions are in m/z and therefore in secular frequency, the more pronounced the space charge effect (Figure 5-28). The mass shift and peak width appeared to escalate dramatically below a frequency separation of 150 kHz. Ions with similar frequency or m/z will occupy the same space within the ion trap (Cleven et al., 1996) leading to increased ion/ion interactions and greater space charge effects. Therefore ions that are bunched together within an isotopic pattern or an abundant matrix will experience a greater space charge effect than two ions distant in m/z.

**Drive Frequency**

Ions separate from each other in \( q_z \) as well as in frequency as they are brought close to the stability edge. For the purpose of resonant ejection, it is most advantageous to eject ions where the frequency separation is highest to obtain the best resolution. Unfortunately, a high \( q_z \) value for ejection is associated with a low resonant ejection amplitude and less tolerance to space charge (Figure 5-23). Another method of increasing the frequency separation between adjacent ions is to increase the drive frequency of the instrument.
Figure 5-27 Mass shift (A) and peak width (B) of m/z 69 with increasing numbers of ions of m/z 264. Each point consists of 3 μscans. The straight line represents the slope used to quantitate the amount of space charge.
Figure 5-28 Rate at which mass shift (A) and peak width (B) for a low m/z ion increase in the presence of the increasing area of higher m/z versus the frequency separation between the two ions. The error bars correspond to +/-1 standard deviation.
This is expressed by the following equation

\[
\Delta \omega = (\beta_1 - \beta_2) \frac{\Omega}{2}
\]  

(5-5)

where \( \Delta \omega \) is the frequency separation, \( \beta \) is correlated to the position of two ions within the stability diagram and \( \Omega \) is the drive frequency. Figure 5-29 shows the linear relationship linking the frequency separation between ions of m/z 69 and 131 and an increased drive frequency. Decreasing the drive frequency may separate ions spatially and diminish space charge effects.

![Graph showing linear relationship between drive frequency and frequency separation between ions of m/z 69 and 131](image)

Figure 5-29 The frequency separation between m/z 69 at a \( q_z \) of 0.9016 and m/z 131 with increasing drive frequency.

The RF system on the PolarisQ had to be modified to alter the drive frequency of the instrument therefore a short discussion detailing the RF system is warranted. The RF
system on an ion trap is very demanding as it needs to maintain extreme voltage accuracy, within a few ppm, while scanning and switching between various voltage levels with great agility. The overall design of the system, however, is relatively simple. Figure 5-30 shows a diagram of a typical RF system for an ion trap consisting of an RF generator, a DC power supply and an RF coil. The RF generator creates a low amplitude RF frequency that is fed into the primary of the RF coil. The coil acts as a transformer and amplifies the RF voltage to an amplitude which is practical for mass analysis. A DC potential is fed into the secondary and supplies the system with the voltage for the

![Diagram of the RF system for the quadrupole ion trap.](image)

Figure 5-30 Diagram of the RF system for the quadrupole ion trap.
Trap offset. The amplified voltage at the terminal end of the secondary is split between the ring electrode and a detector capacitor. The capacitor feeds a DC potential into a closed loop RF control system.

When the system is tuned properly, it will operate at a resonant frequency of the circuit. The resonant frequency can be adjusted by changing the inductance of the circuit or the capacitance by including a variable capacitor in the system. The addition of a capacitor makes tuning much simpler, but is ruled out in a high voltage system because of cost and size of the high voltage capacitor. It is therefore necessary to change the inductance of the circuit by altering the number of secondary turns of the RF coil. Increasing the drive frequency requires a decrease in the number of coil windings and an associated decrease in the matching capacitor (Figure 5-30). An RF coil was created with multiple taps on the secondary coil to provide a drive frequency range of 965 kHz – 1.33 MHz (Figure 5-31). A low pass filter limits the PolarisQ to a maximum drive frequency of 1.355 MHz.

To properly tune the RF system, a SWR (standing wave ratio) bridge method may be used, a method commonly employed by radio amateurs. It identifies the resonant frequency of the circuit as well as the impedance at that frequency. If the impedance is higher than the accepted value of 50 ohms, the circuit can be slightly adjusted by altering the matching capacitor. If the circuit is not properly tuned, the system will fail to obtain the ion trap full mass range. This method is described in detail elsewhere. (Stephenson, 1995) For the majority of experiments presented in this chapter, the RF system was tuned with a HP 8714C network frequency analyzer (Hewlett-Packard, Boise, ID).
Figure 5-31 RF coil with multiple taps on the secondary fashioned as loops. The coil has a frequency range of 965 kHz – 1.33 MHz.

Increasing the drive frequency does come with a price. Raising the drive frequency will reduce the mass range of the instrument as shown by the following equation:

$$m = \frac{8eV_{\text{max}}}{qz\Omega^2(r_0^2 + 2z_0^2)}$$  \hspace{1cm} (5-6)

where m is the highest possible mass. In fact, the desired mass range typically dictates the drive frequency of the instrument. The Thermo Finnigan LCQ, for example, with a
mass range of 2000 amu must operate at a low frequency of 760 kHz compared to 1.024 MHz for the PolarisQ, with its mass range of 1000 amu.

A dual isolation experiment was performed with an ion pair to determine if an increased drive frequency reduced space charge effects. CF$_3^+$ (m/z 69) and C$_3$F$_5^+$ (m/z 131) were chosen due to their large intensities in the EI mass spectrum of PFTBA. For the two drive frequencies of 965 kHz and 1146 kHz, the mass shift for m/z 69 increased at a similar rate with increasing amounts of m/z 131 (Figure 5-32). At a frequency of 1220 kHz, a greater amount of m/z 131 was required before a mass shift was initiated for m/z 69. This demonstrates that, as a pair ions is separated from one another in frequency,

![Figure 5-32 Mass shift of m/z 69 with increasing amounts of m/z 131 with three different drive frequencies. M/z 69 was held at 5x10^5 counts. Each point consists of 3 μscans. A waveform and mass and calibration for the instrument was performed with each drive frequency.](image-url)
a greater number of ions of the higher m/z is needed to observe the same space charge effects.

The dual isolation experiment dealt with a pair of ions that are 62 amu apart. The increased drive frequency could have a much more dramatic effect for ions which are directly adjacent to one another. Figure 5-33 shows a condensed isotopic pattern of decachlorobiphenyl. At a drive frequency of 965 kHz (Figure 5-33A) the isotope peaks are not baseline resolved as the more intense isotope peak show significant peak tailing and shift to higher m/z. However, at a drive frequency of 1.22 MHz the isotopic pattern is fully baseline resolved (Figure 5-33C). The currently accepted method for obtaining such resolution on the PolarisQ is to lower the AGC target, reducing the effect of space charge.

Buffer Gas

Helium buffer gas, present in the ion trap at a pressure of approximately 1 mtorr, stabilizes ion trajectories through collisional relaxation and confines their orbits close to the center of the ion trap. Once in the center of the trap, ions are more efficiently extracted for mass analysis (Hemberger et al., 1993) leading to an increase the mass resolution and sensitivity (Stafford et al., 1994). The helium buffer gas may also initiate unwanted space charge effects. Increasing the helium pressure will increase ion density by restricting ion excursions (Cleven et al., 1996), and may thus trigger a greater extent of ion/ion interactions.

Thermo Finnigan ion trap instruments introduce from 1 to 3 mtorr of helium into the trap. In the PolarisQ, 1 mtorr of helium is added through a 15.24 cm long, 0.0050-cm
Figure 5-33 A segment of a full scan mass spectrum of decachlorobiphenyl at drive frequencies of 965 kHz (A), 1.07MHz (B) and 1.22 MHz (C).
i.d. capillary restrictor with a head pressure of 5 psi. In order to obtain a broader range of helium pressures to study, the normal restrictor was replaced with two different helium restrictors, each with its own pressure range. A 7.29 cm long restrictor with a calibrated i.d. of 0.0223 mm was used for helium pressures below 0.4 mtorr, and a 34.06 cm long restrictor with a 0.0548 mm i.d. was used for helium pressures above 0.4 mtorr. The maximum pressure studied here was approximately 2.2 mtorr. Beyond this range resolution is greatly reduced due to ion scattering. The resonant ejection amplitude was calibrated for each buffer gas pressure. Higher helium pressures required a lower resonant ejection amplitude to maintain the same resolution.

The dual isolation experiment was used to determine how buffer gas pressure affects space charge. CF$_3^+$ (m/z 69) was again chosen to measure the space charge effects of increased peak width and mass shift. Chapter 3 illustrated that an increased helium pressure can cause a fragile ion to shift to lower m/z. CF$_3^+$ has a low probability of fragmenting in the ion trap, reducing the likelihood of a compound-dependent mass shift. Any observed shift should then be correlated directly to space charge. Figure 5-34A shows that, as the helium pressure within the trap was increased, CF$_3^+$ (m/z 69) progressively shifted to higher m/z in the presence of C$_3$F$_5^+$ (m/z 131). When the area of m/z 131 was adjusted to 20x10$^6$ counts (40 times more m/z 131 in the trap than m/z 69), only a small mass shift of 0.03 amu could be detected at pressure of 0.1067 mtorr. At a trap pressure of 1.684 mtorr, this shift expands to 0.12 amu (Figure 5-34A). The peak width of m/z 69 followed the same trend (Figure 5-34B). At a helium pressure of 2.2024 mtorr, the peak width starts at a much higher value, most likely due to ion scattering.
Figure 5-34 Mass shift (A) and peak width (B) for m/z 69 with increasing amounts of m/z 131 at different helium buffer gas pressures. M/z 69 was held at 5x10^5 counts. Each point consists of 5 μscans.
<table>
<thead>
<tr>
<th>Helium Press (mtorr)</th>
<th>Optimal Res. Ej. Amp. ($V_{pp}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1067</td>
<td>2.16</td>
</tr>
<tr>
<td>0.489</td>
<td>2.29</td>
</tr>
<tr>
<td>0.9969</td>
<td>2.31</td>
</tr>
<tr>
<td>1.684</td>
<td>2.83</td>
</tr>
<tr>
<td>2.2042</td>
<td>2.76</td>
</tr>
</tbody>
</table>

Table 5-2 Optimal resonant ejection amplitude for m/z 69 with helium buffer gas pressure.

Helium is an ideal buffer gas because of its low reactivity and low cost. Several research groups have attempted to use air as a buffer gas with the aim of making the ion trap a portable, field-friendly instrument (Cameron et al., 1993; Hendricker et al., 1998). Unfortunately a higher molecular weight buffer gas is often associated with a loss in sensitivity and resolution. A heavier buffer gas was introduced into the ion trap to determine its effects on space charge. Neon was chosen due to its low reactivity and low mass (if any of the neon were ionized in the source and injected in to the trap, it would fall below the LMCO and be immediately ejected in the same manner as helium ions). This would confirm that any adverse space charge effect would be due to its buffering capacity not due to an increased number of ions within the ion trap. The neon gas was introduced into the trap with a second capillary restrictor 5.08 cm long and 0.0223 mm. in i.d.

The dual isolation experiment was again used to determine neon’s effect on space charge. The neon and helium were added in proportions to total 1 mtorr, keeping the total buffer pressure constant. Figure 5-35 shows that, as the amount of neon increased in
Figure 5-35 Mass shift for m/z 69 with increasing amounts of m/z 131 with different compositions of buffer gas. M/z 69 was held at 5x10^5 counts. Each point consists of 5 μscans. The resonant ejection amplitude was calibrated with each trial and is displayed above.

The trap, m/z 69 showed an increase in mass shift, clearly illustrating neon had an adverse effect. The increased molecular weight of the gas may cause the ion cloud to further condense, increasing coulombic interactions. These results were duplicated with even heavier gasses such as CO₂ (data not shown). These results also provide an insight on how a small vacuum leak might affect space charge, as air may be unknowingly introduced into the buffer gas.

<table>
<thead>
<tr>
<th>He Press. (mtrr)</th>
<th>Ne Press (mtrr)</th>
<th>Res. Ej. Amp. (V&lt;sub&gt;pp&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>◆ 0.81</td>
<td>0.20</td>
<td>3.26</td>
</tr>
<tr>
<td>□ 0.60</td>
<td>0.41</td>
<td>2.90</td>
</tr>
<tr>
<td>▲ 0.49</td>
<td>0.50</td>
<td>2.54</td>
</tr>
</tbody>
</table>
Trap Geometry

The quadrupole ion trap was initially developed by Finnigan with a ring electrode radius of 1.0 cm. Modern Thermo Finnigan ion trap instruments (PolarisQ and LCQ) are constructed with a 0.707 cm radius ring with no adjustment in the shape or position of the endcap electrodes. Several ring electrode geometries were studied to determine if the change in ring size has any effect on space charge.

Altering the ring geometry will change the drive frequency of the instrument, as seen by the manipulation of the Mathieu equation below.

\[
\Omega = \sqrt{\frac{8eV_{\text{max}}}{q_m(r_0^2 + 2z_0^2)}}
\]

The RF system was adjusted in order to maintain a drive frequency of 1.028 MHz.

Figure 5-36 shows the results of a dual isolation study with three different ring electrodes with radii of 0.5 cm, 0.707 cm and 1.0 cm. The resonant ejection amplitude was calibrated with each ring electrode at an amplitude of 2.28, 2.69, 1.83 V_{pp}, respectively. The two smallest ring electrodes showed the most significant space charge effects (Figure 5-36). In contrast the largest radius ring permitted more m/z 131 ions to be stored before m/z 69 began to shift. This presumably reflects the larger internal volume of the 1.0 cm ring. Further studies of the effect of ring radius are warranted, however, since the extent of the field imperfections may differ significantly as the ring radius (but not the endcap geometry) is changed.
Figure 5-36 Mass shift for m/z 69 with increasing amounts of m/z 131 with different ring electrode radii (0.5, 0.707 and 1.0 cm). M/z 69 was held at 5x10^5 counts. Each point consists of 5 μscans.

**Conclusion**

Overloading the ion trap can produce significant coulombic interactions, called space charge, leading to peak broadening and a shift to higher m/z. The buildup of ion density within the ion trap can alter the electric field within the ion trap and shift the operating scan line on the stability diagram. This will shift the secular frequencies of an ion and result in a positive mass shift.

An ion of a particular m/z will experience a varying degree of space charge due to the number of ions of the same m/z value, the abundances and mass differences of
neighboring ions and the density of the charges in the trap controlled by the helium pressure. An in-depth study presented here demonstrated space charge effects can be reduced by increasing the resonant ejection amplitude, increasing the drive frequency, decreasing the trap pressure, lowering the $q_z$ of ejection, or altering the trap geometry.
CHAPTER 6
PEAK SPLITTING

The previous chapter showed that space charge effects are dependent not only on the number of ions held within the ion trap, but also their proximity to each other in frequency or m/z. This can limit the ion trap’s resolution in the analysis of dense isotopic patterns such as those created by PCB’s (polychlorinated biphenyl). The currently accepted way to obtain proper resolution is to lower the number of ions within the trap by decreasing the AGC target. This restricts both the instrument’s dynamic range and its level of precision. Several instrumental parameters could be modified as an alternative to lowering the AGC target. An increased resonant ejection amplitude or a lower helium buffer gas pressure can also reduce space charge effects (Chapter 5). With this in mind a PCB, decachlorobiphenyl, was analyzed in a low-pressure, high-amplitude scan. The resultant mass spectrum (Figure 6-1) still appears to be space charged, as the lower intensity isotope peaks are unresolved. However, the experimental parameters at which this mass spectrum was taken (helium pressure of 0.107 mtorr, 1/10 the normal value, and a resonant ejection amplitude of 3.9V_{pp}) individually reduce the effects of space charge. Upon closer examination, it was discovered the poor resolution is actually due to peak splitting, and not space charge. This splitting phenomenon complicates the mass spectrum, making interpretation difficult.

The C_{5}F_{10}N^{+} ion (m/z 264) from PFTBA was examined at the same pressure to observe this splitting phenomenon on a single mass peak with on a small 13C isotope
Figure 6-1 A segment of a full scan mass spectrum of decachlorobiphenyl with a helium buffer gas pressure of 0.107 mtorr, a resonant ejection amplitude of $3.9 \, V_{pp}$ and an AGC target of 50. The arrows indicate the correct m/z for each isotope peak.

peak (approximately 6% relative abundance) (Figure 6-2). The bandwidth on the electrometer was turned off in this analysis so the fine structure of the mass peak could be studied. As the resonant ejection amplitude was increased from its calibrated value of 1.6 $V_{pp}$, the mass peak broadened (Figure 6-3) and began to split. Initially, at an amplitude of 4.0 $V_{pp}$ (Figure 6-2A) only a single split appears between m/z 264 and its $^{13}$C peak at m/z 265. At an exaggerated amplitude of 9.0 $V_{pp}$ (Figure 6-2C) the number of splits elevates to four across a single mass unit. The peak splitting appears to originate from the high mass side. Examining m/z 264 over a range of resonant ejection amplitudes demonstrated that the number of splits across the peak is directly proportional to the increased amplitude and indirectly proportional to the separation between the splits (Figure 6-4). The same splitting pattern was seen for other ionic species, including the
Figure 6-2 Mass spectra of PFTBA showing the C₅F₁₀N⁺ ion (m/z 264) with a helium pressure 0.103 mtorr and a resonant ejection amplitude of (A) 4.0, (B) 7.0, (C) 9.0 V_{pp}. The calibrated resonant ejection amplitude at this pressure is 1.6 V_{pp}. The mass calibration is based on a resonant ejection amplitude of 1.6 V_{pp}. 
Figure 6-3 Peak width at 10 % height for C₅F₁₀N⁺ (m/z 264) with increasing resonant ejection amplitudes at a helium pressure of 0.103 mtorr and a qₑ of ejection of 0.9016.

Figure 6-4 Average separation between peak splits for C₅F₁₀N⁺ (m/z 264) with increasing resonant ejection amplitudes at a helium pressure of 0.103 mtorr and a qₑ of ejection of 0.9016.
$M^+$ ion of n-butylbenzene, a fragile ion.

The peak splitting can be eliminated by raising the helium pressure back to its default setting of 1 mtorr, which condenses the ion cloud towards the center of the trap. At a buffer gas pressure of 0.298 mtorr and a resonant ejection amplitude of 8 $V_{pp}$ (Figure 6-5A), peak splitting is clearly visible. At helium pressure of 0.71 mtorr (Figure 6-5B), the split appears only as a hump of right side of the peak. At 1.11 mtorr (Figure 6-5C) a normal peak shape is observed. Splitting dominates at low buffer gas pressures and high resonant ejection amplitudes. At the normal helium pressure of 1 mtorr, a high resonant ejection amplitude (above the calibrated value) will only produce a slight shoulder for stable ions (Figure 6-6). Ions which are fragile, however, will produce a peak front towards low m/z due to fragmentation upon ejection, although splitting is not observed.

Boundary Ejected Ions

Boundary-ejected ions or fence jumpers (see Chapter 5) can provide the illusion of peak splitting in the ion trap. At a high $q_z$ of ejection, resonantly ejected ions and their boundary-ejected counterparts can emerge adjacent to one another on the mass scale and appear to be a split peak. To determine if the splitting seen in Figure 6-3 is due to ions ejected at the stability edge, the $q_z$ of ejection was lowered to 0.75. At this $q_z$ the boundary-ejected ions would appear over 46 amu away from the resonantly ejected ions (Equation 1-9). Peak splitting was still observed although the split separation increases from 0.3 amu at a $q_z$ of 0.9016 to 1.0 amu at a $q_z$ of 0.75 (Figure 6-7). This split separation provides evidence that the peak splitting phenomenon is not linked to boundary-ejected ions.
Figure 6-5 Mass spectral peak for C₅F₁₀N⁺ (m/z 264) with a resonant ejection amplitude of 8 Vₚₚ and a helium pressure of (A) 0.298, (B) 0.71 and (C) 1.11 mtorr.
Figure 6-6 Mass spectrum of PFTBA showing the C$_3$F$_5^+$ ion (m/z 131) with a resonant ejection amplitude of 4.0 V$_{pp}$ and a helium pressure of 1.11 mtorr. The calibrated amplitude is approximately 2.0 V$_{pp}$.

Figure 6-7 Mass spectrum of PFTBA showing the C$_3$F$_{10}$N$^+$ ion (m/z 264) with a resonant ejection amplitude of 12 V$_{pp}$ at a $q_z$ of 0.75.
Phase-Dependent Ion Ejection

During a mass selective instability scan, ions are ejected from the ion trap at specific phases of the main RF and supplementary AC potentials (Kirkish, 1990). The interaction between the drive frequency and the resonant ejection frequency creates a beat pattern for ion motion, allowing ions to eject in discrete packets. This occurs when the main RF amplitude is at its maximum negative potential and the exit endcap electrode is also negative. Steven Kirkish derived a mathematical interpretation of this interaction (Kirkish, 1990). According to his calculations, with a drive frequency of 1.028 MHz and a resonant ejection $q_{e}$ of 0.908, (resonant ejection frequency = 510 kHz) an ion packet would be ejected approximately every 2 $\mu$sec. This ejection rate occurs at a much higher frequency than the splitting observed in Figure 6-2, however, demonstrating that the splitting observed here is not due to phase dependant ejection.

Simulation of Ion Ejection

An ion optics simulation program was employed to help elucidate the root source of peak splitting in the ion trap. SIMION v.7 (Idaho National Engineering Laboratory, Idaho Falls, ID) was used to model the GCQ/Polaris$Q$ ion trap. The actual electrode geometry was input into SIMION point by point on an 800 by 800 grid (Figure 6-8). The ion source, entrance lenses and a portion of the exit lens were also included. The electrostatic potential at each point within the device, was calculated by using an over-relaxation finite difference technique (iteration limit of $5 \times 10^{4}$, an over-relaxation factor of 90, a historical memory factor of 0.70 and a convergence objective of $5 \times 10^{-6}$). The
resultant potentials were then used to calculate the electric field gradient and the force on an ion. As the ion travels in small discrete steps within the device, its position and velocity are calculated using a fourth-order Runge-Kutta numerical integration. An extensive user program was written to incorporate RF potentials on the ring and endcap electrodes and to define the initial conditions for an ion. Focusing solely on ion ejection, ions were initially positioned within the trap, several grid units away from the center and flown separately. The initial RF phase on the ring electrode was varied between $-180^\circ$ and $+180^\circ$ in $0.5^\circ$ increments for each ion to generate a diverse population
of 720 ions. Ions were allowed to eject from the ion trap through either the exit endcap or the entrance endcap, doubling the number of usable ions. Once an ion exited the trap, its flight time was recorded and converted to m/z scale by the following equation

\[
\text{Recorded m/z} = \text{Start m/z} + \frac{\text{Ion Ejection Time (\mu s)}}{\text{Scan Rate}}
\]  

(6-1)

where the scan rate is in \(\mu\)amu. The total computing time for a single mass peak was typically three days.

A series of initial simulations was performed to determine the optimal resonant ejection amplitude for the simulated ion trap. An ion of m/z 264 was chosen to provide a comparison with experimental results. The ion trap was scanned from m/z 244 to 284. The resultant mass peaks for three resonant ejection amplitudes (1.0, 3.0 and 5.0 V\(_{pp}\)) can be seen in Figure 6-9. At 1.0 V\(_{pp}\) (Figure 6-9A) the resonant ejection amplitude is so low that the ions do not absorb enough energy to be properly ejected at a \(q_z\) of 0.9016. Subsequently, all of the ions are ejected at the stability edge, resulting in a mass peak which is ejected late (shifted to higher m/z) with poor resolution. An amplitude of 3.0 V\(_{pp}\) (Figure 6-9B) is enough to properly eject approximately 20% of the ion population resulting in a peak. Amplitude of 5.0 V\(_{pp}\) (Figure 6-9C) is sufficient to resonantly eject all of the ions, producing a mass peak with a 0.3 amu width at 15% height. This value of 5.0 V\(_{pp}\) was accepted as the calibrated amplitude for m/z 264.

Raising the resonant ejection amplitude above its calibrated value caused the simulated mass peak to split, as predicted by the experimental data. An amplitude of 8 V\(_{pp}\) produces a peak with a large width and multiple splits (Figure 6-10A). To obtain the same peak splitting pattern as observed experimentally (Figure 6-10B), a larger voltage had to be applied during the simulation. This may be due to minor differences in initial
Figure 6-9 Simulated mass peaks for m/z 264 with a mass scan was from m/z 244 to 284 and a resonant ejection amplitude of 1.0 (A), 3.0 (B), and 5.0 V_{pp} (C), respectively. A computational quality of 10 was used.
Figure 6-10 (A) Simulated mass peak for m/z 264 with a mass scan from m/z 244 to 284 and a resonant ejection amplitude of 8.0 V<sub>pp</sub>. (B) Experimental mass spectral peak of C₅F₁₀N⁺ (m/z 264) with a resonant ejection amplitude of 4.0 V<sub>pp</sub> and a helium pressure of 0.103 mtorr.
ion energies or other experimental conditions such as helium pressure. The user program can incorporate a collision model to simulate ion collisions with a buffer gas. The same splitting pattern was seen with or without collisions included, however. Thus, to simplify the simulation, collisions with a helium buffer gas were not considered.

Dropping the $q_z$ of ejection to 0.85 from its normal value of 0.9016 further increases the peak splitting (Figure 6-11A) for the simulated peak. This matched experimental results (Figure 6-11B).

Although simulated data closely matched experimental, a more in-depth study was pursued to help elucidate the cause of the splitting. Individual ion trajectories were examined to understand the differences between ions at various resonant ejection amplitudes. Figure 6-12 shows the trajectory (the last 300 $\mu$s before ejection) of a m/z 264 ion with three different resonant ejection amplitudes. For these simulations, a computational quality of 20 was used instead of a default of 10. This improved the accuracy of the numerical integration, but required a longer time to simulate. For a single ion trajectory, however, this did not pose a problem. The axial positions of the ions are plotted versus the scan time. The endcap electrodes are positioned at 7.83 mm and $-7.83$ mm on the z-axis. Any ion that exceeds that boundary was considered to be ejected from the trap.

Figure 6-12A shows the trajectory of m/z 264 with a calibrated resonant ejection amplitude of $5.0V_{pp}$. During the mass scan the ion comes into resonance with the resonant ejection frequency and absorbs energy. The ion’s axial excursions increase linearly (after a scan time of 3770 $\mu$s) as the ion achieves kinetic energies in excess of 500 eV (Figure 6-13A). The kinetic energy of the ion eventually exceeds the
Figure 6-11 (A) Simulated mass peak for m/z 264 with $q_z$ of ejection of 0.85 and a resonant ejection amplitude of 11.5 $V_{pp}$. (B) Experimental mass spectral peak of C$_3$F$_{10}$N$^+$ (m/z 264) with a helium pressure of 0.13 mtorr, $q_z$ of ejection of 0.85 mtorr and a resonant ejection amplitude of 9.5 $V_{pp}$. 
Figure 6-12 Ion trajectories for m/z 264 recorded in the z dimension as a function of scan time with a resonant ejection amplitude of (A) 5.0, (B) 8.0, and (C) 16.0 V_{pp}. The arrows indicate the first time the trajectory exceeds a $z_o$ of 7.00 mm.
Figure 6-13 The kinetic energy of m/z 264 recorded as a function of scan time with a resonant ejection amplitude of (A) 5.0, (B) 8.0, and (C) 16.0 V\textsubscript{pp}. 
quadrupolar field potential well depth and the ion is ejected.

When the resonant ejection amplitude is increased to 8.0 \( V_{pp} \) (Figure 6-12B), the ion trajectory exhibits a different behavior. Once again the ion’s axial position and kinetic energy increase as it moves towards the resonant ejection frequency. At 3800 \( \mu s \) into the scan the ion appears to have enough energy to be ejected but, instead its kinetic energy decreases and the ion settles back down toward the center of the trap. It appears that this particular ion missed an “opportunity” to eject from the trap. After a period of time the ion trajectory again increases in amplitude and the ion is ejected. At an even higher resonant ejection amplitude of 16.0 \( V_{pp} \) (Figure 6-12C) the ion trajectory increases and then is damped twice before the ion is eventually ejected.

Each time an ion’s trajectory approaches an endcap electrode, the ion is provided a window of opportunity or a chance to eject. At high resonant ejection amplitudes, a group of ions of a particular m/z may eject at multiple points in time, resulting in a splitting in the observed mass peak.

The simulation results presented here closely resemble ion trajectories modeled within a non-linear ion trap (Franzen et al., 1995). Non-linear fields complicate ion motion and can lead to detrimental effects such as undesirable ion losses and abnormal peak shapes (Dawson and Whetten, 1969). Thus, a brief description of non-linear fields is warranted to fully understand their effects within the quadrupole ion trap and to provide insight into the research presented here.
Non-linear Fields

In a pure quadrupole ion trap the RF field strength would increase linearly in both the r and z directions. The RF field acts to restrict ion motion and focus ions in the center of the ion trap. Non-linear ion traps include a field component which deviates from linearity. Such deviations have been described as field faults or superposition of higher order fields. These higher order fields do not significantly generally affect an ion at the center of the ion trap, but become detrimental when the ion approaches an endcap electrode during resonant ejection.

Under ideal conditions an ion’s kinetic energy would increase as it comes into resonance with the resonant ejection frequency in an analytical scan until it is eventually ejected. In a non-linear device the secular frequency of an ion becomes dependent on the amplitude of motion. As an ion comes into resonance, absorbs energy and increases its amplitude of motion, its frequency shifts out of resonance with the resonant ejection frequency and the amplitude of the oscillation decreases again (Sevugarajan and Menon, 1999). As the ion’s amplitude decreases its, frequency shifts back into resonance and the process begins again. The ion essentially comes into and out of resonance with the resonant ejection frequency due to the constant shift in frequency, creating a beating pattern (Franzen et al., 1995). The non-linear fields can perturb ion trajectories inside the ion trap and affect ion ejection.

The direction in which the frequency of an ion shifts depends upon the sign of the multipole superposition (Franzen et al., 1995). When the quadrupole ion trap contains a significant positive octopolar contribution, the pseudopotential forces within the trap
increase more than linearly. When the amplitude of an ion increases, the repelling force causes the ion to oscillate faster and the secular frequency shifts to higher values. This pushes an ion towards the stability edge and facilitates ejection. With a negative octopolar contribution, in contrast, the pseudopotential forces increase less than linearly and the secular frequency is lowered as an ion’s amplitude increases. This constantly draws the ion back into the stability region.

**Imperfections in the Quadrupolar Field**

The importance of field imperfections was first discovered during the commercialization of the first Thermo Finnigan ion trap instrument. The ion trap was assembled with a non-ideal or stretched geometry. A stretched trap is assembled in such a way that the $z_e$ has been increased with no corresponding modification to the shape of the electrodes (Syka, 1995). This stretched geometry allowed the mass-selective instability scan to obtain unit resolution (Stafford et al., 1992).

Realistically, it is impossible to create an ion trap with a pure quadrupolar field. Even with perfectly machined electrodes, the electric field within the ion trap will deviate from linearity because of constraints such as truncation of the electrodes and small holes placed in the endcap electrodes. A perforation or hole has to be placed in at least one of the electrodes to allow electrons and/or ions to enter and exit the device. Although this modification may seem minor, it is enough to distort the quadrupolar field that is generated inside the device. The holes produce a sub-linear electric field in the axial direction, $z$, on or close to the symmetry axis. An ion with a trajectory near the endcap will feel a sudden drop-off of the field close to the endcap holes. Figure 6-14 shows a simulated quadrupolar field within the GCQ trap with a voltage of 2.2 kV on the ring
electrode. The electric field appears to leak out of the ion trap through the holes and create a weakness in the quadrupolar field.

Figure 6-14 Depiction of a quadrupolar field within the GCQ ion trap created by SIMION with 2.2 kV on the ring electrode. Equipotential contours near the endcap electrodes indicate a weakness or a sub-linear dependence of the RF trapping field.

The quadrupolar field within the ion trap can also be disturbed by the addition of a supplementary dipolar AC used for resonant ejection. Ideally, the dipolar field is designed to accelerate ions from the center of the trap towards the endcaps for detection. The dipolar field created between the two endcaps, however, is not purely dipolar because it is created between two hyperbolic surfaces instead of two flat plates. Figure 6-
15 shows the field is actually bowed towards the center of the trap and is also greatly affected by the endcap hole. At high resonant ejection amplitudes the supplementary AC may actually accentuate the octopolar resonance created by the hole in the endcap electrode.

Figure 6-15 Electric field within the ion trap with a resonant ejection potential of 8V placed on the endcap and the ring electrode is held at a ground potential. The endcap is positioned at 7.83 mm on the x-axis.

Simulations have shown that when the ion takes up energy and increases its amplitude, its frequency shifts out of resonance and the amplitude of the oscillation decreases again, ending up in a beating pattern. The ions of a specific m/z are subsequently provided with multiple opportunities to eject, which creates a splitting in the resultant mass peak.
In a pure quadrupolar device an ion’s stability should only be dependent on its m/z value. Conversely, in a non-linear field, the behavior of ions within the trap is quite different. The ions experience the nonlinearity of the field throughout the trapping volume and the characteristics of ion motion, including stability of an ions trajectory, can depend significantly on the initial conditions of the ion (Franzen et al., 1995). Therefore, an ion’s initial energy or position will allow some ions to be ejected early and some late.

These effects can be limited with a high buffer gas pressure which restricts ion motion to the center of the ion trap away from the field imperfection near the endcap holes. When the ions are settled near the center of the ion trap, they do not see any nonlinear effects but see only the quadrupole trapping field.

Simulation with Meshed Endcap Holes

The holes placed in the endcap electrodes, although vital to the ion trap’s ability to inject and detect ions, create an imperfect field within the ion trap. The endcap holes may be reduced in size to lessen their detrimental effects, but the injection and ejection efficiencies would suffer. A wire mesh placed over the endcap holes might limit the nonlinear effects from the holes whole maintaining injection and ejection efficiency. A simulated field in Figure 6-16 shows that the meshed holes correct the non-linear field imperfection near the endcap.

A second round of simulations was performed with m/z 264 in a new ion trap model with meshed endcap holes. The same procedures were followed as described earlier. Even with a high resonant ejection amplitude of 8.0 V_pp, the simulated mass peak shows no trace of peak splitting (Figure 6-17). All of the ions behave similarly in this pure field, resulting in a small band of ejection times and a narrow peak width of 0.25
Figure 6-16 Depiction of a quadrupolar field within the GCQ ion trap with meshed encap holes created by SIMION. Equipotential contours near the endcap electrodes indicate a linear RF trapping field.

amu at 10% height. Previous simulation results with an unmodified endcap hole (Figure 6-10A) show a wide peak with multiple splits under the same conditions.

Figure 6-18 shows the ion kinetic energy of an m/z 264 ion ejected at the apex of the mass peak shown in Figure 6-16. During the mass scan the ion comes into resonance with the resonant ejection frequency and absorbs energy. The ion’s trajectory increases in the z axis until the ion’s kinetic energy exceeds the quadrupolar field potential well depth and the ion is ejected. With the new trap design, ions are no longer settled toward the center of the trap before ejection. The meshed design appears to eliminate the
detrimental nonlinear effects. The same results were seen with an endcap with no holes (not shown).

Figure 6-17 Simulated mass peak for m/z 264 with a mass scan from m/z 244 to 284 and a resonant ejection amplitude of 8.0 V_{pp} with an ion trap with meshed endcap holes.

Figure 6-18- Ion kinetic energy for m/z 264 recorded as a function of scan time with a resonant ejection amplitude of 8.0 V_{pp}. 

![Graph showing number of ejected ions vs. m/z](image)

![Graph showing ion kinetic energy vs. time](image)
Conclusion

During the initial commercialization of the ion trap, several concessions were made to convert the ion trap into a functional mass spectrometer. The most important of these are the endcap holes, which allow electrons or ions to travel into and out of the ion trap. Although this modification may seem minor, it is enough to distort the quadrupolar field that is generated inside the device (Syka, 1995). The imperfect quadrupolar field produced compound-dependent mass shifts and sacrificed the effectiveness of the ion trap. A stretched geometry was developed to compensate for the field imperfections and limit mass shifts.

Although the stretched ion trap geometry limits mass shifts within the ion trap, it does not eliminate the imperfect field adjacent to the endcap holes. The electric field appears to leak out of the ion trap through the holes and create a weakness in the quadrupolar field. At low buffer gas pressures ions are allowed to venture near the endcap holes and experience the non-linearity of the field. In a non-linear field an ion’s stability is no longer purely dependent on its m/z value, as the field imperfections can actually stabilize ions inside the ion trap. The ions of a specific m/z are subsequently provided with multiple opportunities to eject, which creates a splitting of the resultant mass peak. A wire mesh placed over the endcap holes may limit non-linear effects and also maintain proper ion injection and ejection efficiency.
CHAPTER 7
CONCLUSIONS AND FUTURE WORK

The quadrupole ion trap, originally developed in the early 1950s by physicists Paul and Steinwedel as an ion storage device, has become one of the most powerful mass spectrometers available today. The modern quadrupole ion trap is most noted for its versatility, sensitivity and capability to provide multiple stages of mass spectrometry (MS^n). There are several issues, however, that have plagued the ion trap since the introduction of the first commercial instrument. The most severe of these are compound-dependent mass shifts and a limited dynamic range due to space charge effects.

Compound-dependent mass shifts can result from early ejection of fragment ions during resonant ejection of fragile ions. As these ions come into resonance with the ejection frequency, they gain kinetic energy, collide with buffer gas molecules, and dissociate. The resultant fragment ions, which are lower in m/z, will no longer be stable within the ion trap as they will lie beyond the stability boundary at βz = 1. The fragment ions are thus immediately ejected and detected before the intact ions are resonantly ejected. The fragment ions and the non-dissociated precursor ion form one peak which has a significant amount of peak fronting and an overall broad peak shape. The peak top may remain at the correct m/z in profile acquisition, but the peak centroid will be shifted to a lower m/z.

This hypothesis has been validated by experiments on a hybrid ion trap / quadrupole mass filter instrument which permitted mass analysis of the ions ejected from
the ion trap during resonant ejection. The data produced from this instrument conclusively show that dissociation of "fragile" ions produce mass shifts.

Several instrumental parameters may increase the mass shifts due to ion fragility. Raising the resonant ejection amplitude increases the kinetic energy of an ejecting ion. This can cause a fragile ion to undergo energetic collisions and dissociate. Increasing the helium buffer gas pressure within the ion trap will also increase the likelihood of an energetic collision. And lastly, lowering the scan rate allows the ion an increased amount of time to fragment before it is ejected. These mass shifts can therefore be minimized or eliminated by minimizing the resonant ejection amplitude, maintaining the helium buffer gas at a modest pressure, or lowering the $q_e$ of ejection so the fragment ions formed will be contained within the ion trap.

Mass shifts are not limited just to fragile ions. Any ion may undergo a degree of fragmentation as it is resonantly ejected. PFTBA ions used to mass-calibrate the ion trap, for example, are reasonably stable; nevertheless, when they are compared to an atomic ion such as xenon that cannot fragment, they exhibit a slight mass shift. Since the ion trap is mass calibrated with PFTBA ions, mass shifts may be observed in both directions. Fragile ions will exhibit a negative mass shift, whereas atomic species or very stable ions which do not fragment will exhibit a positive mass shift.

The hybrid ion trap / quadrupole mass filter instrument used to study ion ejection was rearranged to examine fragmentation of ions upon injection. The quadrupole mass filter was placed in front of the ion trap instead of after and the ions were produced in an external ion source which was mounted in front of the mass filter. In this arrangement, ions emitted from an ion source can be mass-selected by the quadrupole mass filter to
ions of only a single m/z are allowed to enter the ion trap. Experiments performed with this hybrid instrument show that both fragmentation of ions upon injection and ion molecule reactions can alter ion intensities and the appearance of a mass spectrum. This can make compound identification difficult when matching ion trap spectra with common EI spectral libraries.

In contrast to the quadrupole, the ion trap injects ions into a high-pressure region with an energetic field. Research showed that the RF amplitude during injection has the greatest effect on the fragmentation of ions upon injection. When the qz of injection is increased, the injecting ions are accelerated by the strong quadrupolar field and can attain high kinetic energies. Energetic collisions with the helium buffer gas can then lead to ion dissociation.

The resonant ejection of fragile ions is not the only source of mass shifts in the quadrupole ion trap. Overloading the ion trap can produce significant coulombic interactions, called space charge, leading to peak broadening and a shift to higher m/z. The buildup of ion density within the ion trap can alter the electric field within the ion trap and lower the operating scan line within the stability diagram. This will shift the secular frequencies of an ion and result in a positive mass shift.

The most severe space charge effects appear at low m/z in a full scan acquisition. It was shown, once ions of low m/z have been ejected from the trap, their contribution to space charge is diminished and the mass selective ejection of ions higher m/z become less affected. Therefore, the first ions ejected out of the trap will experience the greatest space charge effect, while the remaining higher m/z ions are ejected with little appearance of space charge.
The loss of resolution at high ion densities may be due to ion shielding where ions on the exterior of a large ion cloud may shield ions situated at the center of the trap from feeling the effects of the supplementary RF field. This may limit the number of ions that can be ejected during resonant ejection. The improvement in resolution at high resonant ejection amplitude occurs due to a stronger uniform electric field created in the axial dimension within the ion trap which reduces ion shielding and therefore space charge effects.

A dual isolation scan function, designed to isolate a pair of m/z ions at variable intensity ratios, was developed to determine the instrumental parameters which most greatly effect space charge. It was determined an ion of a particular m/z will experience a varying degree of space charge due to the number of ions and mass differences of neighboring ions and the density of the charges in the trap controlled by the buffer gas pressure.

Space charge effects can be reduced by increasing the resonant ejection amplitude, increasing the drive frequency, or decreasing the trap pressure. At low buffer gas pressures, however, ions are allowed to venture near the endcap holes and experience a non-linear field. In a non-linear field an ion’s stability is no longer purely dependent on its m/z value as the field imperfections perturbs the trajectories of ions inside the ion trap. As a result, ions of a specific m/z experience multiple opportunities to be ejected, resulting in a splitting of the peak. A wire mesh placed over the endcap holes may limit non-linear effects and also maintain proper ion injection and ejection efficiency.
Future Work

Modern commercial ion trap instruments control the number of ions that accumulate in the ion trap by employing an ion injection method called automatic gain control (AGC). AGC is designed to keep the total number of ions in the ion trap at a steady level, retaining mass accuracy and resolution from scan to scan by optimizing the injection time for each scan. The AGC scan function is comprised of a rapid automated scan called a pre-scan covering the entire mass range of the analyzer. This pre-scan, which precedes each analytical scan quantitatively assesses the ion production rate from the source and calculates the proper injection time needed to fill the ion trap to capacity, ensuring that the number of ions in the trap never reaches an adverse level of space charge.

The actual number of ions injected into the ion trap during the analytical scan is controlled by the AGC target variable, which is usually associated with the ionization mode (EI or CI). However, it has been shown that different compounds can tolerate a diverse numbers of ions within the trap according to the fragmentation pattern, ion ratios, and intensities of their mass spectrum. An ion within a dense isotopic pattern may exhibit poor resolution compared to an isolated ion at the same target. The target can therefore be seen as compound specific.

With this in mind, the idea of a “smart” AGC scan was developed. The prescan may be used to identify typical indicators of space charge within a mass spectrum such as a dense isotopic pattern or a large sample matrix and adjust the target of the individual analytical scans accordingly. This would minimize space charge effects for any
compound or analysis. A computer may also be programmed to control the resonant
ejection amplitude or helium buffer gas pressure to reduce space charge. Although the
idea has not yet been implemented, the concept may prove to be beneficial to ion trap
mass spectrometry.
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BIOGRAPHICAL SKETCH

James Patrick Murphy III was born in Providence, Rhode Island, on November 19, 1973. He grew up in Smithfield, Rhode Island, with his two sisters, Kerrie and Colleen, his mother, Frances, and his father, James, and spent most of his childhood enjoying outdoor activities including soccer, cross-country and mountain biking.

James went to high school at Mount Saint Charles Academy in Woonsocket, Rhode Island. There he met one of the most influential teachers in his life, a biology teacher by the name of Mrs. Ferry. Mrs. Ferry was a very dynamic teacher who piqued James’ interest in science. She encouraged him to enter science fairs and excel in his classes. Her influence, which began during his career in high school, extended into college as James enrolled at the College of the Holy Cross, as a biology major. Mrs. Ferry tragically passed away during his second year at Holy Cross but her influence lived on.

Holy Cross is a small liberal arts college in Worcester, Massachusetts. A liberal arts education allowed James to study a myriad of subjects, including psychology, religion, and chemistry. When it came time to focus solely on his biology courses during his junior year, James found it difficult to part with his newly found interest in chemistry. Feeling this was something he had to explore, James decided to change his major to chemistry.

James soon found himself heavily involved in the chemistry department at Holy Cross. He joined the honors research program and studied analytical chemistry under Professor Jane VanDoren. His research, which focused on atmospheric chemistry,
allowed him to collaborate with several institutions including MIT, Denver University and Hanscom Air Force Base.

After working as an environmental chemist for a year, James enrolled at the University of Florida in 1997 to obtain his doctorate degree. He performed research in analytical chemistry under the direction of Dr. Richard Yost and advanced his areas of knowledge into programming and instrument development.

James' college career brought him to many places including Louisiana, California, Colorado, Texas, Illinois and Florida and opened up many opportunities, but he desired to be closer to his family and friends in the northeast. After graduating from UF, James returned home to continue his career in Boston, Massachusetts.
I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Doctor of Philosophy.

Richard A. Yost, Chair  
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Doctor of Philosophy.

John R. Eyler  
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Doctor of Philosophy.

Robert T. Kennedy  
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Doctor of Philosophy.

David H. Powell  
Scientist of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a thesis for the degree of Doctor of Philosophy.

John Toth  
Associate Research Scientist of Food Science and Human Nutrition
This thesis was submitted to the Graduate Faculty of the Department of Chemistry in the College of Liberal Arts and Sciences and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

May, 2002

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